Supporting Information

Recyclable Organocatalyst-promoted One-pot Michael/aza-Henry/lactamization Reactions for Fluorinated 2-Piperidinones Bearing Four Stereogenic Centers

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Contents

1. General Information

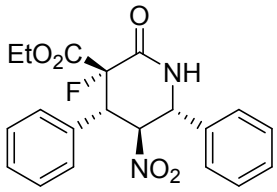
Chemicals and solvents were purchased from commercial suppliers and used as received. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz Varian NMR spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). LC-MS were performed on an Agilent 2100 system. A C_{18} column (5.0 μm, 6.0 x 50 mm) was used for the separation. The mobile phases were methanol and water both containing 0.05% trifluoro acetic acid. A linear gradient was used to increase from 25:75 v/v methanol/water to 100% methanol over 7.0 min at a flow rate of 0.7 mL/min. UV detections were conducted at 210 nm, 254 nm and 365 nm. Low resolution mass spectra were recorded in APCI (atmospheric pressure chemical ionization). The high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. Sorbent silica gel XHL TLC plates (130815) were used for the thin-layer chromatography (TLC). Flash chromatography separations were performed on YAMAZEN AI-580 flash column system with Agela silica gel columns (230-400μm mesh). The enantiomeric excesses of products were determined by chiral phase HPLC analysis on a SHIMADZU LC-20AD system with Agela Venusil Chiral OD-H, CA, CJ column and Regis (*R*,*R*)-Whelk-O1.

2. General Procedures for Asymmetric Synthesis of Fluorinated 2-Piperidinones

To a solution of fluorous catalysts **cat-1** (6 mg, 0.01 mmol) in toluene (0.5 mL) was added trans-*β*-Nitrostyrene **6** (0.1 mmol, 1.0 equiv). After being stirred at room temperature for 20 min, fluorinated 1,3-diester **5** (0.15 mmol, 1.5 equiv) was added. The reaction mixture was stirred for 24 h and then followed by the addition of ethanol (1 mL), benzaldehyde **3** (0.1 mmol, 1.0 equiv), NH_4OAc (0.12 mmol, 1.2 equiv) as well as 2 drops of piperidine. The reaction mixture was stirred for 24 h at 40 ^{o}C. The concentrated reaction mixture was loaded on to a fluorous SPE cartridge and eluted with 80:20 MeOH/H_2O, and then with MeOH. The MeOH fraction was concentrated to recover purified **cat-1**, and the concentrated MeOH/H_2O fraction was purified by YAMAZEN AI-580 flash column system (EtOAc/ CH_2Cl_2) with Agela silica gel columns.

3. Analytical data

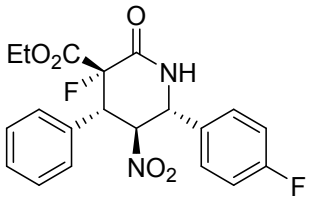
Ethyl -3-fluoro-5-nitro-2-oxo-4,6-diphenylpiperidine-3-carboxylate (4a):



4a

Following the general procedure, the title compound **4a** was obtained as a white solid (78% yield, 32 mg, 6:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 28.90 min, t_{major} = 16.90 min, 99% ee. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.28 (s, 1H), 7.47–7.28 (m, 8H), 7.26–7.11 (m, 2H), 5.53 (d, J = 3.7 Hz, 1H), 5.43 (t, J = 3.6 Hz, 1H), 4.57 (dd, J = 33.0, 3.4 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 14.3, 50.0, 50.2, 60.1, 62.7, 87.4, 91.2, 93.2, 128.1, 129.1, 129.4, 129.4, 129.4, 129.7, 129.9, 131.1, 136.4, 162.4, 162.6, 165.1; ^{19}F (282 MHz, DMSO-d_6): δ -162.9. MS (APCI) m/z: 387.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{19}FN_2O_5$[M+Na]$^+$ 409.1176; found 409.1170.

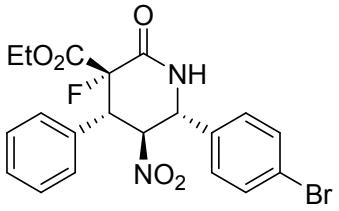
Ethyl 3-fluoro-6-(4-fluorophenyl)-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4b):



4b

Following the general procedure, the title compound **4b** was obtained as a white solid (85% yield, 34 mg, 8:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 80:20 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 11.66 min, t_{major} = 8.50 min, 98% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48–7.19 (m, 7H), 7.13 (d, J = 4.6 Hz, 2H), 6.10 (s, 1H), 5.35 (t, J = 9.1 Hz, 1H), 5.21 (d, J = 9.9 Hz, 1H), 4.39 (dd, J = 30.6, 12.3 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 50.2, 50.4, 59.9, 63.0, 87.7, 116.8, 117.0, 128.8, 128.9, 129.0, 129.2, 129.6, 216.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -110.2, -162.8. MS (APCI) m/z: 405.1 (M+1); HRMS (EI): calcd. for $C_{20}H_{18}F_2N_2O_5$ 404.1184; found 404.1183.

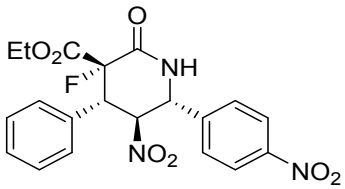
Ethyl 6-(4-bromophenyl)-3-fluoro-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4c):



4c

Following the general procedure, the title compound **4c** was obtained as a white solid (87% yield, 40 mg, 10:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 25.62 min, t_{major} = 19.97 min, 96% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59 (d, J = 11.1 Hz, 2H), 7.38–7.04 (m, 7H), 6.46 (s, 1H), 5.35 (t, J = 9.1 Hz, 1H), 5.17 (d, J = 9.9 Hz, 2H), 4.37 (dd, J = 30.7, 12.4 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 49.9, 50.4, 59.9, 63.0, 87.7, 124.8, 128.5, 129.0, 129.6, 132.9, 134.0, 162.6, 164.4, 178.4, 216.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -162.8. MS (APCI) m/z: 465.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{18}BrFN_2O_5[M+Na]^+$ 487.0281; found 487.0293.

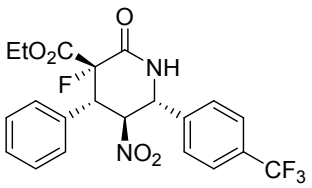
Ethyl 3-fluoro-5-nitro-6-(4-nitrophenyl)-2-oxo-4-phenylpiperidine-3-carboxylate (4d):



4d

Following the general procedure, the title compound **4d** was obtained as a white solid (83% yield, 35 mg, 10:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 97.22 min, t_{major} = 67.28 min, 96% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.45–7.04 (m, 5H), 6.76 (s, 1H), 5.45–5.15 (m, 2H), 4.59–4.26 (m, 1H), 4.18 (q, J = 7.2 Hz, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 216.0, 201.7, 141.9, 129.8, 129.1, 128.1, 125.0, 87.7, 63.2, 60.0, 50.3, 50.1, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -163.1. MS (APCI) m/z: 432.1 (M+1); HRMS (EI): calcd. for $C_{20}H_{18}FN_3O_7$ 431.1129; found 431.1125.

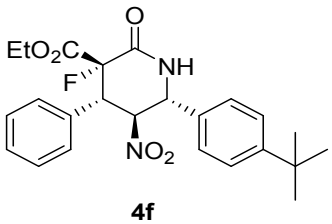
Ethyl3-fluoro-5-nitro-2-oxo-4-phenyl-6-(4-(trifluoromethyl)phenyl)piperidine-3-carboxylate (4e):



4e

Following the general procedure, the title compound **4e** was obtained as a white solid (85% yield, 38 mg, 15:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 26.56 min, t_{major} = 12.73 min, 97% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (d, J = 8.4 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.40–7.10 (m, 5H), 5.44–5.11 (m, 2H), 4.40 (dd, J = 30.7, 11.7 Hz, 1H), 4.18 (q, J = 7.2 Hz, 2H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 164.3, 163.1, 162.8, 129.7, 129.4, 129.1, 129.1, 129.1, 127.4, 126.7, 126.7, 88.1, 63.3, 60.3, 50.3, 50.1, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ -63.8, -163.3. MS (APCI) m/z 455.1 (M+1); HRMS (EI): calcd. for $C_{21}H_{18}F_4N_2O_5$ 454.1152; found 454.1147.

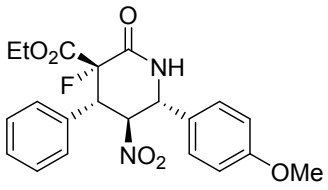
Ethyl 6-(4-(tert-butyl)phenyl)-3-fluoro-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4f):



4f

Following the general procedure, the title compound **4f** was obtained as a white solid (35% yield, 15 mg, 4:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 19.42 min, t_{major} = 13.77 min, 97% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J = 8.3 Hz, 2H), 7.34–7.06 (m, 7H), 6.91 (s, 1H), 5.80 (dd, J = 12.3, 6.2 Hz, 1H), 5.48–5.18 (m, 1H), 4.42 (dd, J = 30.9, 12.3 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.31 (s, 9H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 163.5, 153.1, 131.1, 130.3, 128.9, 128.6, 128.6, 127.0, 126.5, 126.2, 125.9, 83.7, 63.0, 57.0, 44.8, 44.5, 34.7, 31.2, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -63.8, -163.5. MS (APCI) m/z: 443.1 (M+1); HRMS (EI): calcd. for $C_{24}H_{27}FN_2O_5$ 442.1904; found 442.1903.

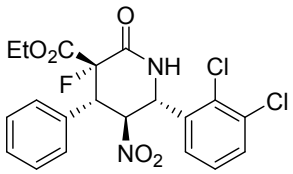
Ethyl 3-fluoro-6-(4-methoxyphenyl)-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4g):



4g

Following the general procedure, the title compound **4g** was obtained as a white solid (30% yield, 12 mg, 4:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 85:15 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 52.40 min, t_{major} = 25.26 min, 95% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37–7.21 (m, 7H), 6.95 (d, J = 8.7 Hz, 2H), 6.00 (s, 1H), 5.35 (t, J = 9.1 Hz, 1H), 5.16 (d, J = 10.1 Hz, 1H), 4.38 (dd, J = 30.7, 12.4 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.83 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.7, 129.5, 129.2, 129.0, 128.2, 118.7, 114.5, 63.2, 60.6, 55.1, 50.3, 13.8, 8.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -163.1. MS (APCI) m/z: 417.1 (M+1); HRMS (ESI): calcd. for $C_{21}H_{21}FN_2O_6$ $[M+H]^+$ 417.1462; found 417.1463.

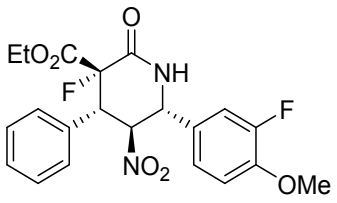
Ethyl 6-(2,3-dichlorophenyl)-3-fluoro-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4h):



4h

Following the general procedure, the title compound **4h** was obtained as a colorless oil (55% yield, 25 mg, 3.5:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CJ, 80:20 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 13.33 min, t_{major} = 11.44 min, 97% ee. ^{1}H NMR (300 MHz, CDCl3): δ 7.57 (dd, J = 7.8, 1.7 Hz, 1H), 7.49–7.15 (m, 7H), 6.30 (s, 1H), 5.84 (d, J = 10.0 Hz, 1H), 5.70–5.46 (m, 1H) , 4.42 (dd, J = 31.0, 12.4 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 216.2, 201.5, 132.5, 129.8, 129.3, 129.3, 129.2, 128.7, 86.0, 63.2, 57.6, 50.3, 50.1, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -164.1. MS (APCI) m/z: 455.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{17}C_{l2}FN_2O_5$ $[M+H]^+$ 455.0577; found 455.0573.

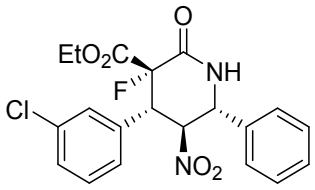
Ethyl 3-fluoro-6-(3-fluoro-4-methoxyphenyl)-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4i):



4i

Following the general procedure, the title compound **4i** was obtained as a white solid (62% yield, 27 mg, 2:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 95:5 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 25.02 min, t_{major} = 6.36 min, 93% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46–7.22 (m, 5H), 7.11 (dd, J = 10.7, 8.3 Hz, 1H), 7.02–6.74 (m, 2H), 5.45–5.22 (m, 1H), 5.17 (dd, J = 9.9, 2.7 Hz, 1H), 4.37 (dd, J = 30.8, 12.4 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 163.1, 155.2, 152.2, 129.6, 129.5, 129.1, 129.0, 128.6, 119.6, 119.5, 117.1, 116.9, 111.4, 87.7, 63.0, 60.4, 56.4, 50.4, 50.2, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -131.9, -132.7, -162.6, -164.7. MS (APCI) m/z: 435.1 (M+1); HRMS (ESI): calcd. for $C_{21}H_{20}F_2N_2O_6$ $[M+H]^+$ 435.1368; found 435.1363.

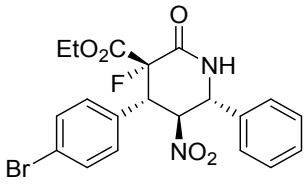
Ethyl 4-(3-chlorophenyl)-3-fluoro-5-nitro-2-oxo-6-phenylpiperidine-3-carboxylate (4j):



4j

Following the general procedure, the title compound **4j** was obtained as a white solid (65% yield, 27 mg, 3:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CA, 90:10 hexane/*i*-PrOH, 1.0 mL/min, λ = 254 nm): t_{minor} = 7.24 min, t_{major} = 10.32 min, 90% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.40 (m, 3H), 7.33 (dd, J = 6.7, 2.8 Hz, 2H), 7.29–7.23 (m, 2H), 7.23–7.16 (m, 1H), 7.14–7.06 (m, 1H), 6.55 (s, 1H), 5.79 (dd, J = 12.3, 6.2 Hz, 1H), 5.43 (d, 1H), 4.59–4.14 (m, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.9, 133.2, 130.5, 130.2, 123.0, 129.5, 129.4, 129.3, 128.9, 127.7, 127.2, 126.7, 126.7, 83.5, 63.3, 57.3, 44.5, 44.3, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -163.2. MS (APCI) m/z: 421.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{18}ClFN_2O_5$ $[M+H]^+$ 421.0967; found 421.0970.

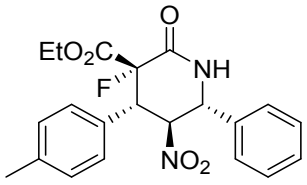
Ethyl 4-(4-bromophenyl)-3-fluoro-5-nitro-2-oxo-6-phenylpiperidine-3-carboxylate (4k):



4k

Following the general procedure, the title compound **4k** was obtained as a white solid (68% yield, 32 mg, 3.5:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 80:20 hexane/*i*-PrOH, 0.6 mL/min, λ = 254 nm): t_{minor} = 22.54 min, t_{major} = 13.57 min, 93% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 8.5, 5.5 Hz, 5H), 7.32 (dd, *J* = 6.7, 2.6 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.78 (s, 1H), 5.77 (dd, *J* = 12.4, 6.3 Hz, 1H), 5.41 (d, *J* = 6.5 Hz, 1H) , 4.54–4.08 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.3, 133.1, 132.6, 129.8, 129.6, 129.3, 129.2, 128.7, 124.8, 87.9, 63.2, 60.4, 50.6, 50.3, 14.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ -164.8. MS (APCI) m/z: 465.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{18}BrFN_2O_5$ $[M+H]^+$ 465.0461; found 465.0463.

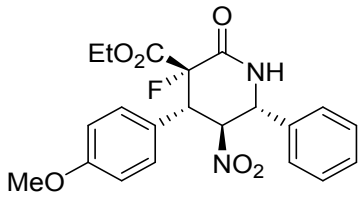
Ethyl 3-fluoro-5-nitro-2-oxo-6-phenyl-4-(p-tolyl)piperidine-3-carboxylate (4l):



4l

Following the general procedure, the title compound **4l** was obtained as a white solid (55% yield, 22 mg, 5:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 85:15 hexane/*i*-PrOH, 0.5 mL/min, λ = 254 nm): t_{minor} = 13.38 min, t_{major} = 10.54 min, 95% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46–7.41 (m, 2H), 7.35–7.28 (m, 2H), 7.07 (s, 5H), 5.78 (dd, *J* = 12.4, 6.2 Hz, 1H), 5.39 (d, *J* = 5.8 Hz, 1H), 4.56–4.11 (m, 3H) , 1.21 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.8, 133.5, 129.9, 129.7, 129.2, 128.4, 127.8, 127.2, 118.5, 83.8, 63.0, 57.2, 44.4, 44.1, 21.1, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -164.9. MS (APCI) m/z: 401.1 (M+1); HRMS (ESI): calcd. for $C_{21}H_{21}FN_2O_5$ $[M+H]^+$ 401.1513; found 401.1492.

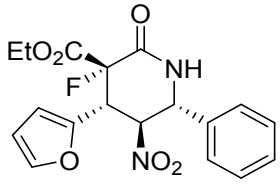
Ethyl 3-fluoro-4-(4-methoxyphenyl)-5-nitro-2-oxo-6-phenylpiperidine-3-carboxylate (4m):



4m

Following the general procedure, the title compound **4m** was obtained as a white solid (69% yield, 28 mg, 3:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1 mL/min, λ = 254 nm): t_{minor} = 45.22 min, t_{major} = 39.45 min, 91% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43 (dd, *J* = 6.5, 3.6 Hz, 2H), 7.39–7.29 (m, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.31 (s, 1H), 5.32 (dd, *J* = 12.2, 10.1 Hz, 1H), 5.18 (dd, *J* = 9.9, 2.7 Hz, 1H), 4.47–4.10 (m, 3H), 3.76 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 163.2, 162.9, 160.4, 135.4, 130.5, 129.8, 127.2, 127.0, 121.6, 114.6, 88.4, 63.1, 60.9, 55.4, 45.0, 49.7, 14.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ -163.3. MS (APCI) m/z: 417.1 (M+1); HRMS (ESI): calcd. for $C_{21}H_{21}FN_2O_6$ $[M+H]^+$ 417.1462; found 417.1462.

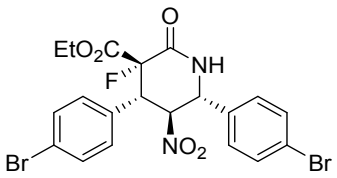
Ethyl 3-fluoro-4-(furan-2-yl)-5-nitro-2-oxo-6-phenylpiperidine-3-carboxylate (4n):



4n

Following the general procedure, the title compound **4n** was obtained as a white solid (62% yield, 23 mg, 3.5:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral CJ, 95:5 hexane/*i*-PrOH, 1 mL/min, λ = 254 nm): t_{minor} = 24.66 min, t_{major} = 22.90 min, 96% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (dd, *J* = 8.3, 4.9 Hz, 4H), 7.36–7.27 (m, 2H), 6.40 (s, 1H), 6.33–6.29 (m, 1H), 6.23 (d, *J* = 3.3 Hz, 1H), 5.76 (dd, *J* = 11.8, 6.1 Hz, 1H), 5.40 (d, *J* = 5.8 Hz, 1H), 4.65 (dd, *J* = 29.2, 11.9 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.6, 201.3, 144.0, 143.4, 134.8, 130.5, 129.7, 126.9, 110.8, 86.6, 73.2, 63.3, 60.4, 44.4, 41.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ -161.2, -170.0. MS (APCI) m/z: 377.1 (M+1); HRMS (ESI): calcd. for $C_{18}H_{17}FN_2O_6[M+Na]^+$ 399.0968; found 399.0978.

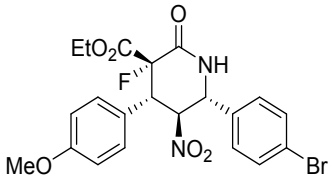
Ethyl 4,6-bis(4-bromophenyl)-3-fluoro-5-nitro-2-oxopiperidine-3-carboxylate (4o):



4o

Following the general procedure, the title compound **4o** was obtained as a white solid (67% yield, 36 mg, 4:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1 mL/min, λ = 254 nm): t_{minor} = 49.20 min, t_{major} =22.47 min, 99% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.29–7.01 (m, 5H), 5.32–5.21 (m, 1H), 5.16 (dd, J = 8.7, 3.8 Hz, 1H), 4.35 (dd, J = 30.4, 12.2 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.8, 164.6, 162.7, 133.9, 132.9, 132.5, 132.3, 132.2, 130.7, 130.2, 128.8, 128.4, 124.8, 124.0, 87.5, 63.2, 60.1, 49.8, 49.6, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -163.1, -164.7. MS (APCI) m/z: 545.1 (M+1); HRMS (ESI): calcd. for $C_{20}H_{17}Br_2FN_2O_5$[M+Na]$^+$ 564.9386; found 564.9384.

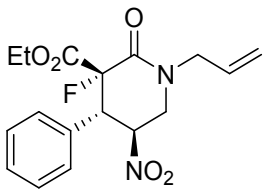
Ethyl 6-(4-bromophenyl)-3-fluoro-4-(4-methoxyphenyl)-5-nitro-2-oxopiperidine-3-carbo- xylate (4p):



4p

Following the general procedure, the title compound **4p** was obtained as colorless oil (65% yield, 28 mg, 3:1 dr). The enantiomeric excess was determined by HPLC analysis (Venusil Chiral OD-H, 90:10 hexane/*i*-PrOH, 1 mL/min, λ = 254 nm): t_{minor} = 30.16 min, t_{major} = 20.45 min, 98% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.35 (s, 1H) , 5.76 (dd, J = 12.4, 6.3 Hz, 1H), 5.38 (dd, J = 6.3, 3.1 Hz, 1H), 4.47–4.15 (m, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.2, 132.9, 132.6, 132.5, 130.3, 129.8, 129.6, 128.8, 128.5, 124.6, 121.2, 118.5, 114.4, 88.0, 63.0, 60.1, 55.2, 49.7, 49.5, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -165.3. MS (APCI) m/z: 495.1 (M+1); HRMS (ESI): calcd. for $C_{21}H_{20}BrFN_2O_6$ [M+H]$^+$ 495.0567; found 495.0565.

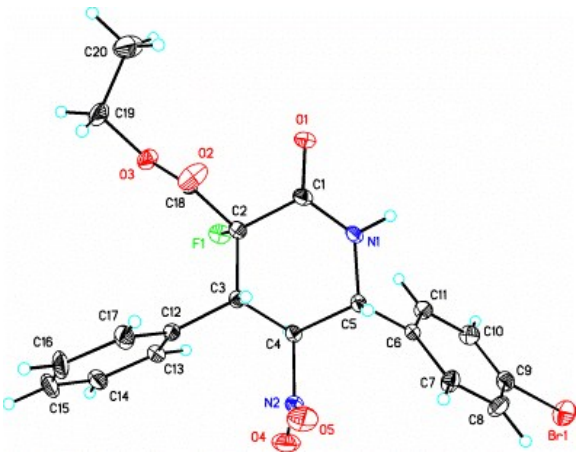
Ethyl 1-allyl-3-fluoro-5-nitro-2-oxo-4-phenylpiperidine-3-carboxylate (4q):

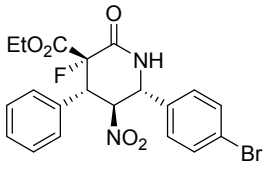


4q

Following the general procedure, the title compound **4q** was obtained as the colorless oil (57% yield, 20 mg, 5:1 dr). The enantiomeric excess was determined by HPLC analysis (Regis (*R*,*R*)-Whelk-O1, 80:20 hexane/*i*-PrOH, 1 mL/min, λ = 254 nm): t_{minor} = 12.34 min, t_{major} = 9.52 min, 92% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62–7.03 (m, 5H), 5.79 (ddd, J = 12.5, 10.4, 5.3 Hz, 1H), 5.45 (ddd, J = 11.4, 8.4, 6.2 Hz, 1H), 5.32 (dd, J = 21.1, 5.5 Hz, 2H), 4.43–4.11 (m, 3H), 4.10–3.82 (m, 4H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 131.2, 131.0, 130.4, 129.3, 129.2, 129.0, 128.1, 120.2, 81.3, 62.8, 49.6, 49.4, 48.4, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -158.9, -165.2. MS (APCI) m/z: 351.1 (M+1); HRMS (ESI): calcd. for $C_{17}H_{19}FN_2O_5[M+H]^+$ 351.1356; found 351.1354.

4. X-Ray Report of 4c



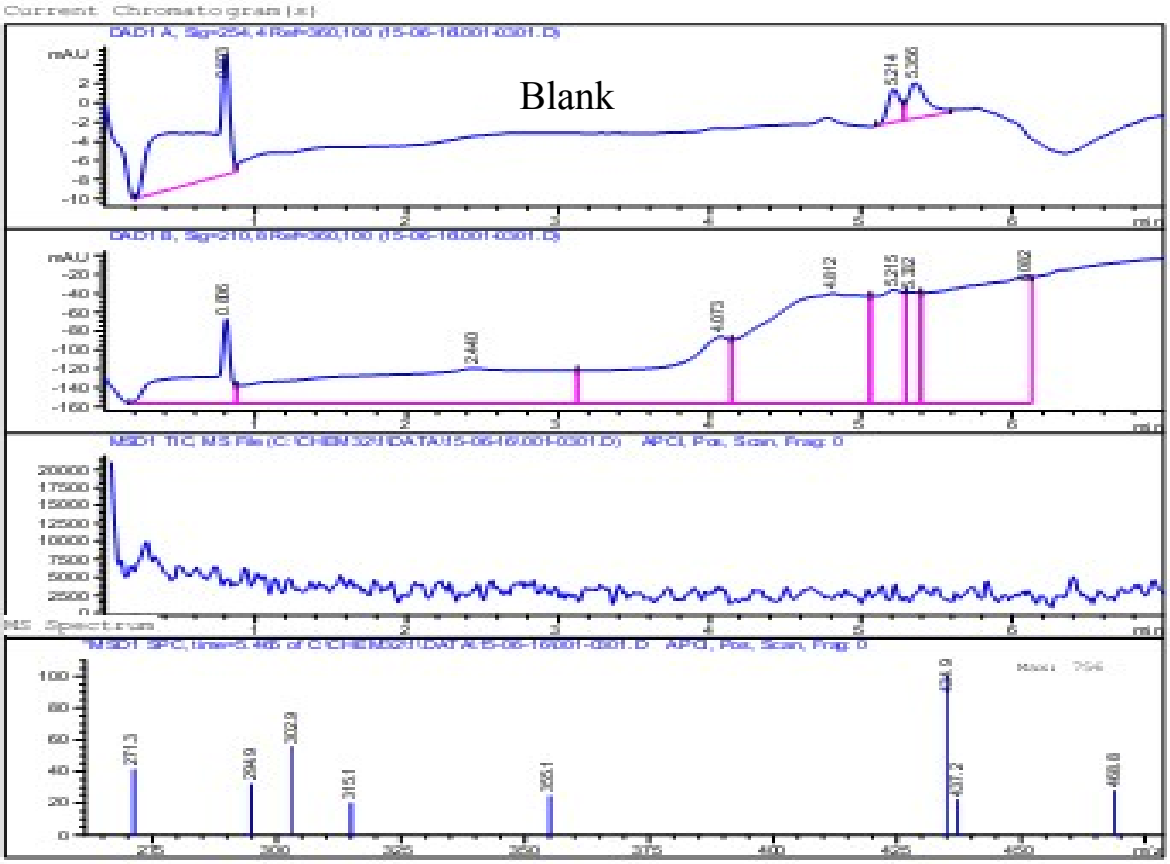


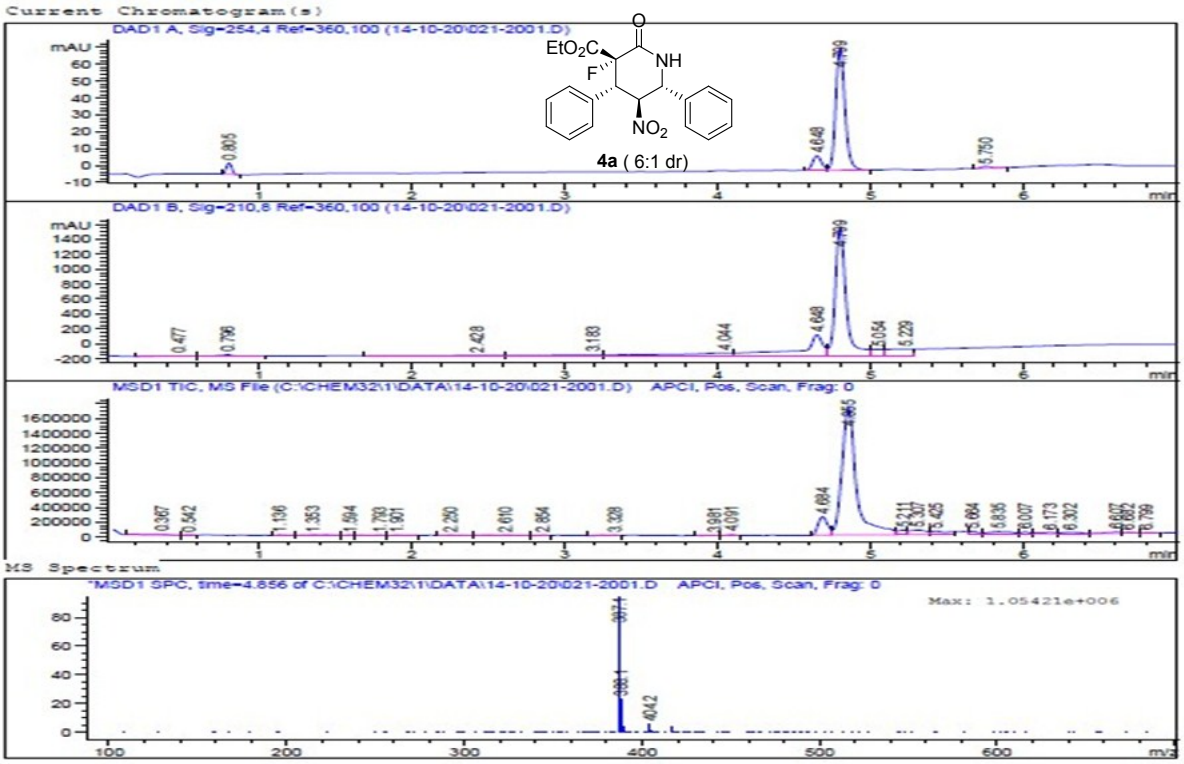
4c

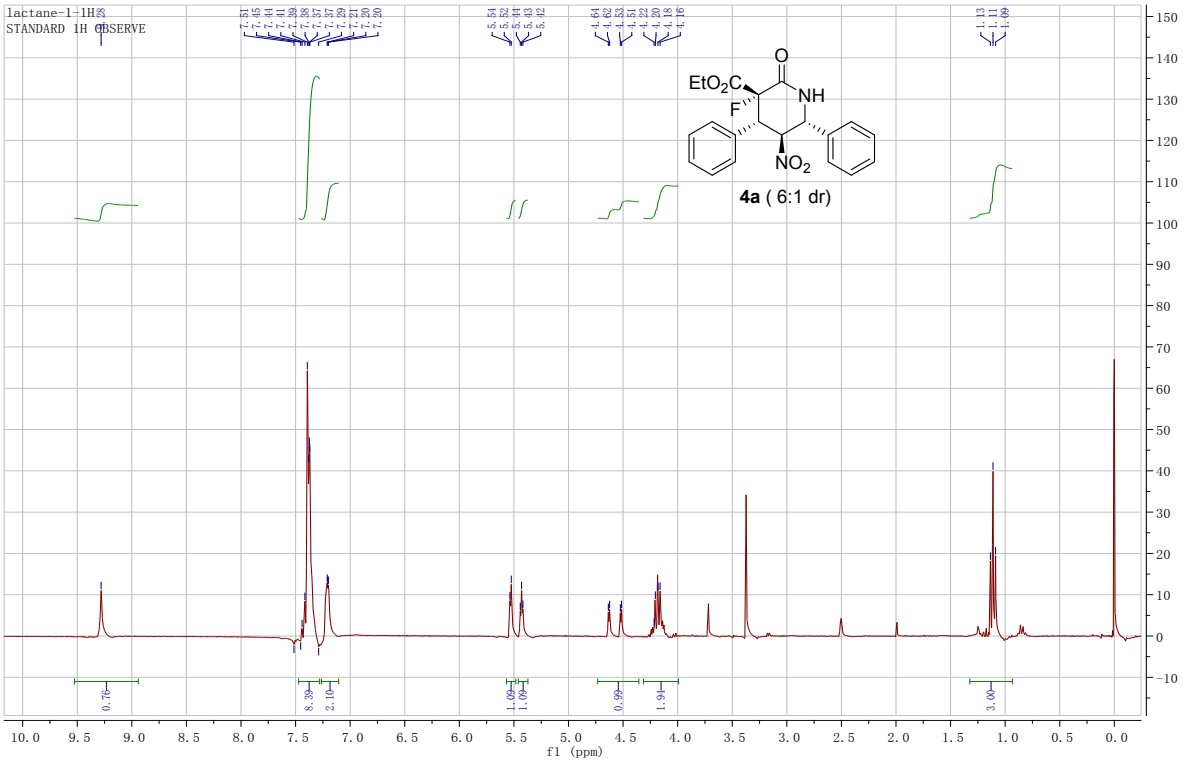
Bond precision	c-c=0.0097 Å Wavelength=1.54184	
Cell	a=22.744(3) b=7.5503(4) c=16.0634(18) α=90 β=131.075(18) γ=90	
Temperature	173K	
	Calculated	Reported
Volumn	2079.5(7)	2079.5(6)
Space group	C 2	C 1 2 1
Hall group	C 2y	C 2y
Moiety formula	C_{20} H_{18} Br F N_2 O_5	C_{20} H_{18} Br F N_2 O_5
Sum formula	C_{20} H_{18} Br F N_2 O_5	C_{20} H_{18} Br F N_2 O_5
Mr	465.26	465.27
Dx,g cm^{-3}	1.486	1.486
Z	4	4
Mu (mm^{-1})	3.073	3.073
F000	944.0	944.0
F000’	944.14	
h,k,lmax	27,9,19	27,9,19
Nref	4027[2174]	2972
Tmin,Tmax	0.541,0.782	0.398,1.000
Tmin’	0.232	
Data completeness= 1.37/0.74		Theta(max)= 71.104
R(reflections)= 0.0511(2872)		wR2(reflections)= 0.1329(2972)
S = 1.079 Npar= 264		

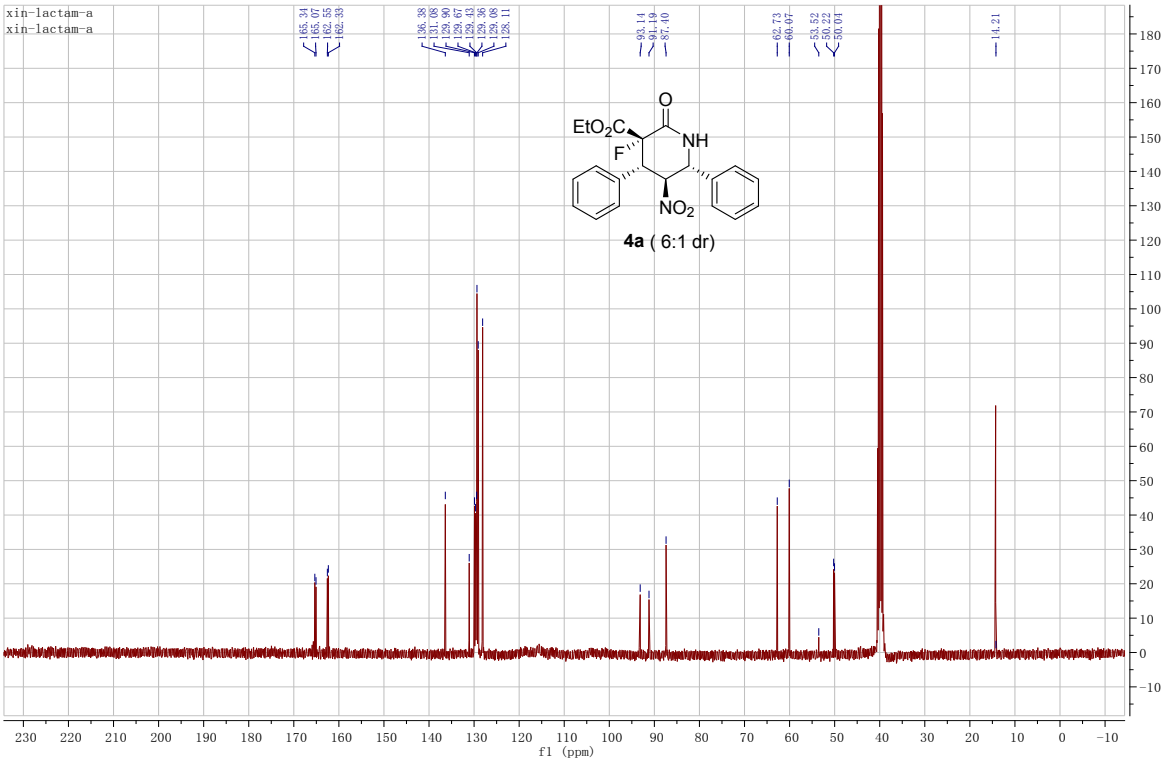
Crystallographic data (excluding structural factors) for compound **4c** also has been deposited at the Cambridge Crystallographic Data Centre under the deposition number CCDC 1043112.

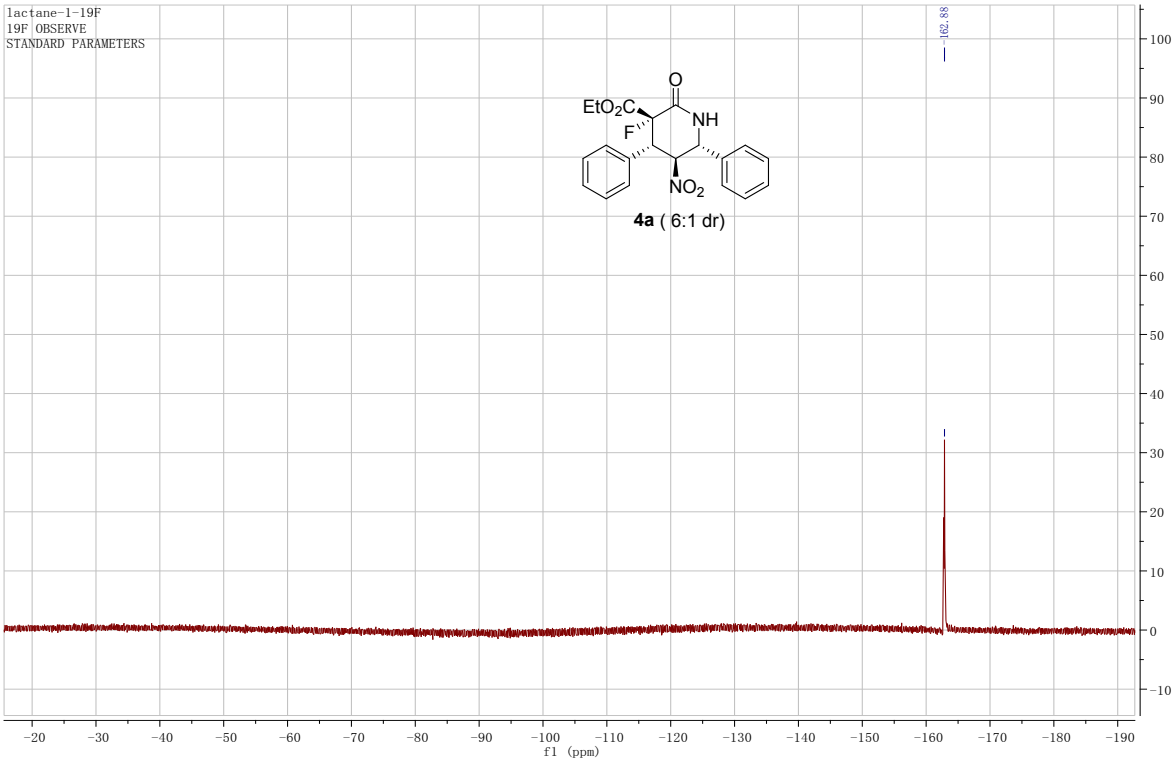
5. LC-MS, ^{1}H, ^{13}C, ^{19}F NMR of Products

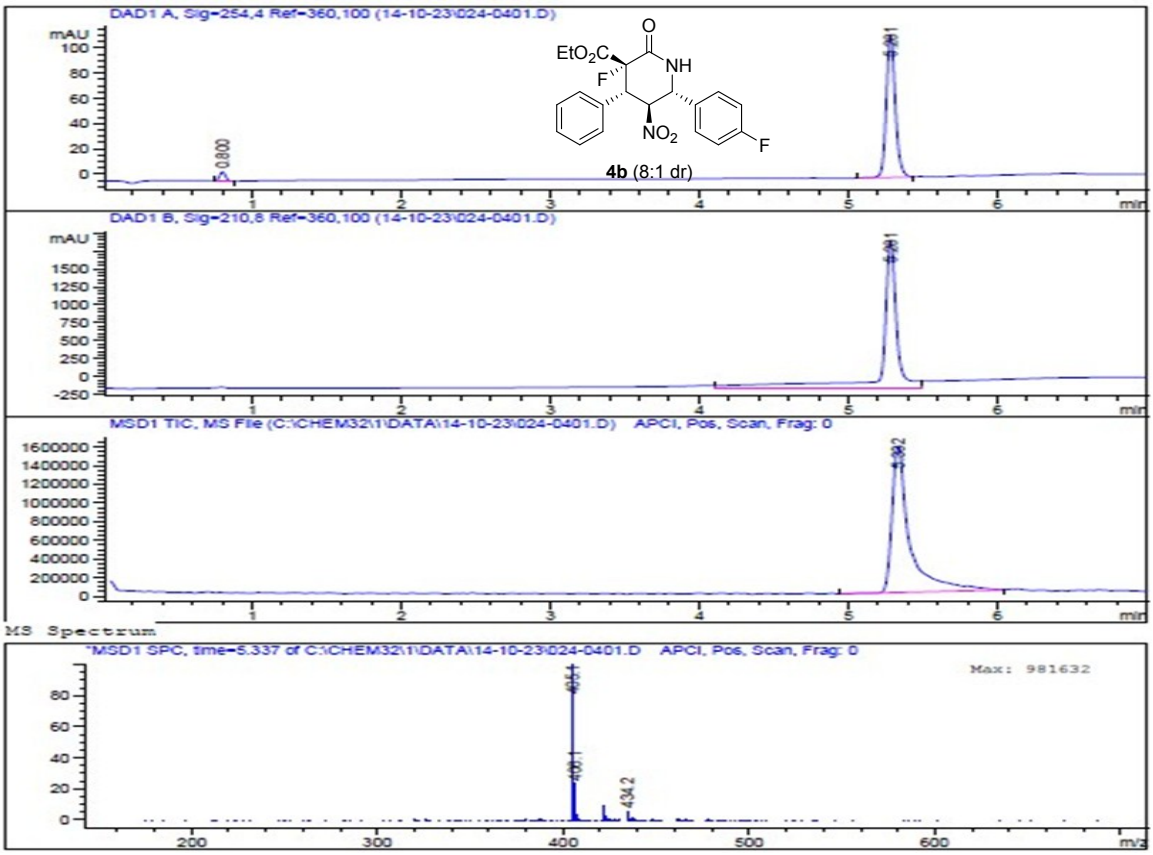

Current Chromatogram(s)
Blank
MS Spectrum


Current Chromatogram(s)
4a (6:1 dr)
MS Spectrum


lactane-1-1H
STANDARD 1H OBSERVE
EtO2C
F
O
NH
NO2
4a (6:1 dr)
f1 (ppm)


xin-lactam-a
xin-lactam-a
EtO2C
F
O
NH
NO2
4a (6:1 dr)
f1 (ppm)


lactane-1-19F
19F OBSERVE
STANDARD PARAMETERS
162.88
O
EtO2C
NH
F
NO2
4a (6:1 dr)
f1 (ppm)


DAD1 A, Sig=254,4 Ref=360,100 (14-10-23\024-0401.D)
mAU
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O
EtO2C
NH
F
NO2
F
4b (8:1 dr)
min
DAD1 B, Sig=210,8 Ref=360,100 (14-10-23\024-0401.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-10-23\024-0401.D) APCI, Pos, Scan, Frag: 0
min
MS Spectrum
*MSD1 SPC, time=5.337 of C:\CHEM32\1\DATA\14-10-23\024-0401.D APCI, Pos, Scan, Frag: 0
Max: 981632
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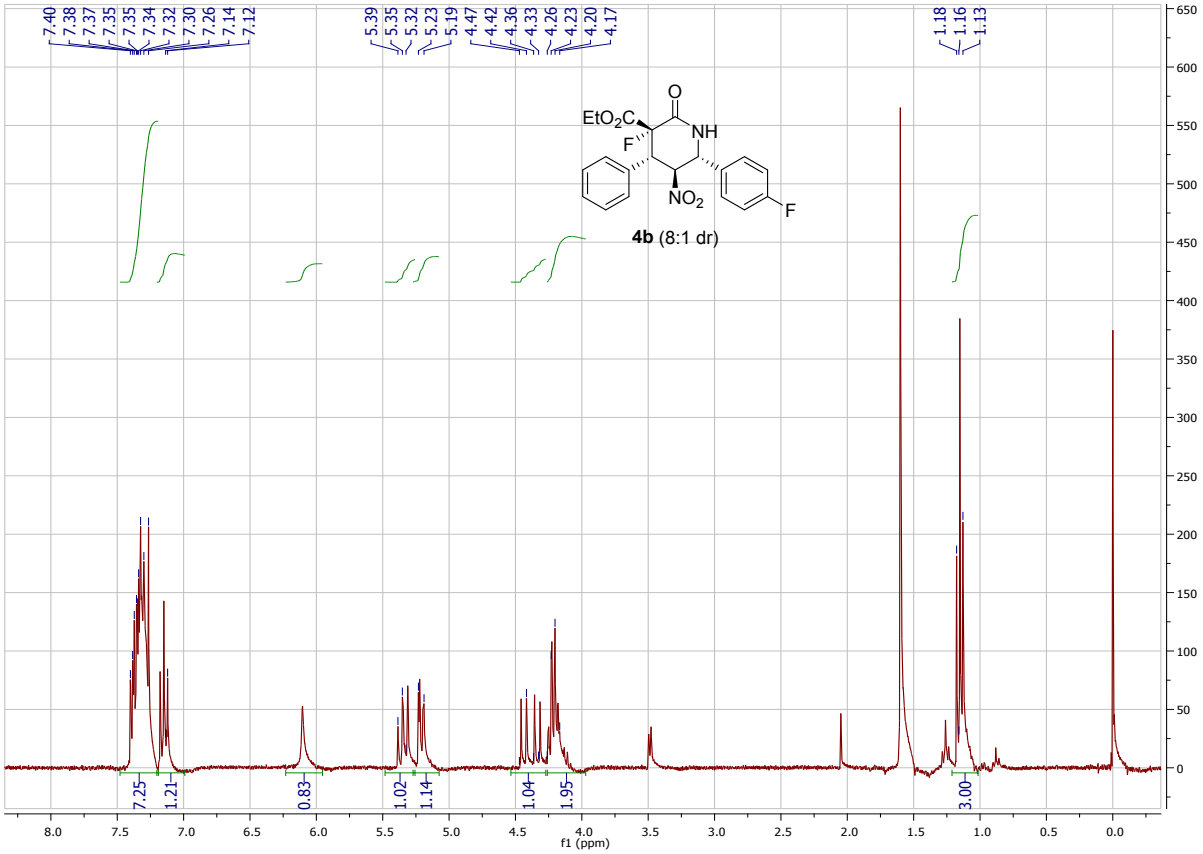
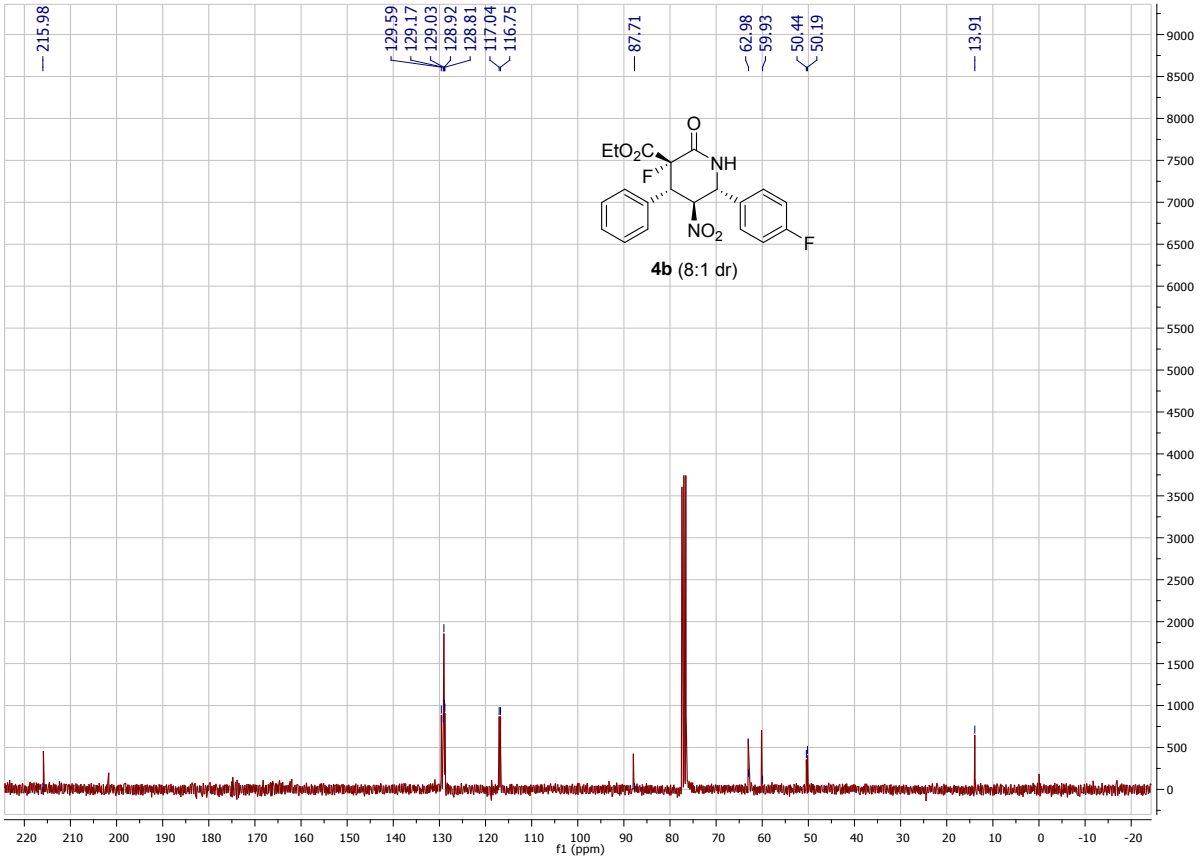
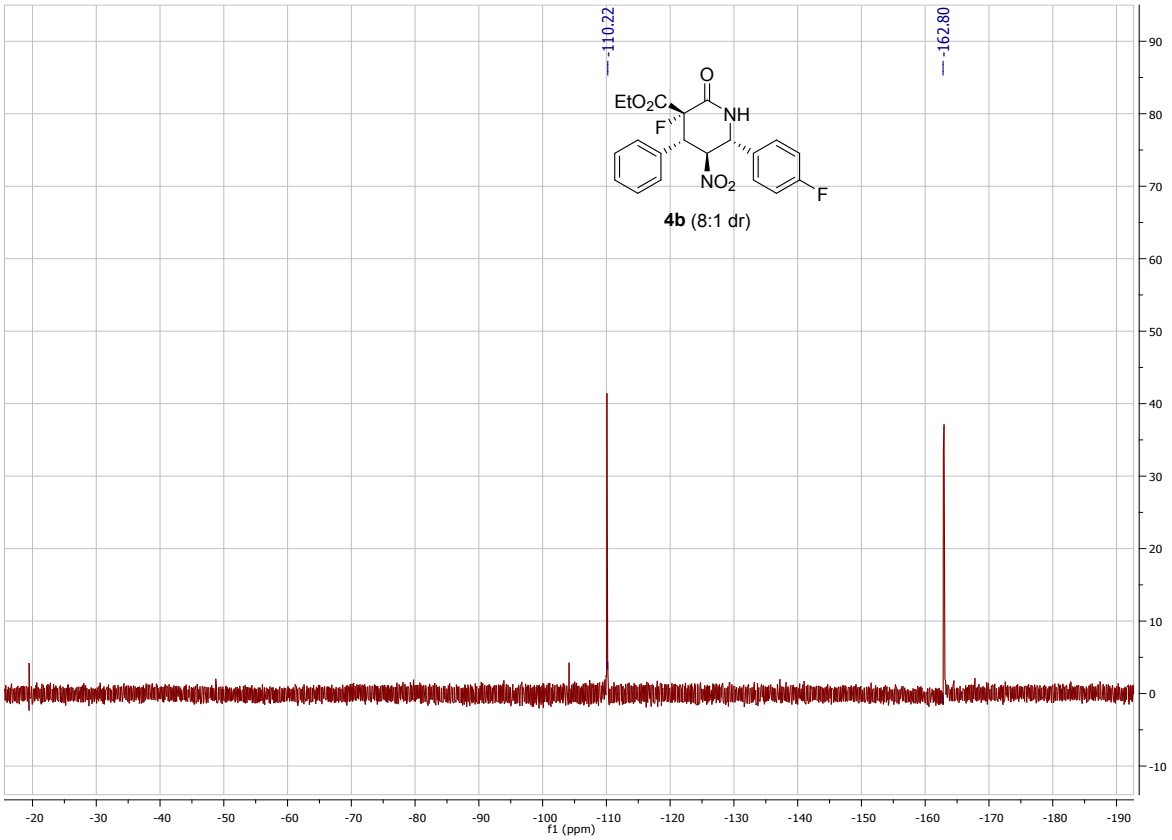
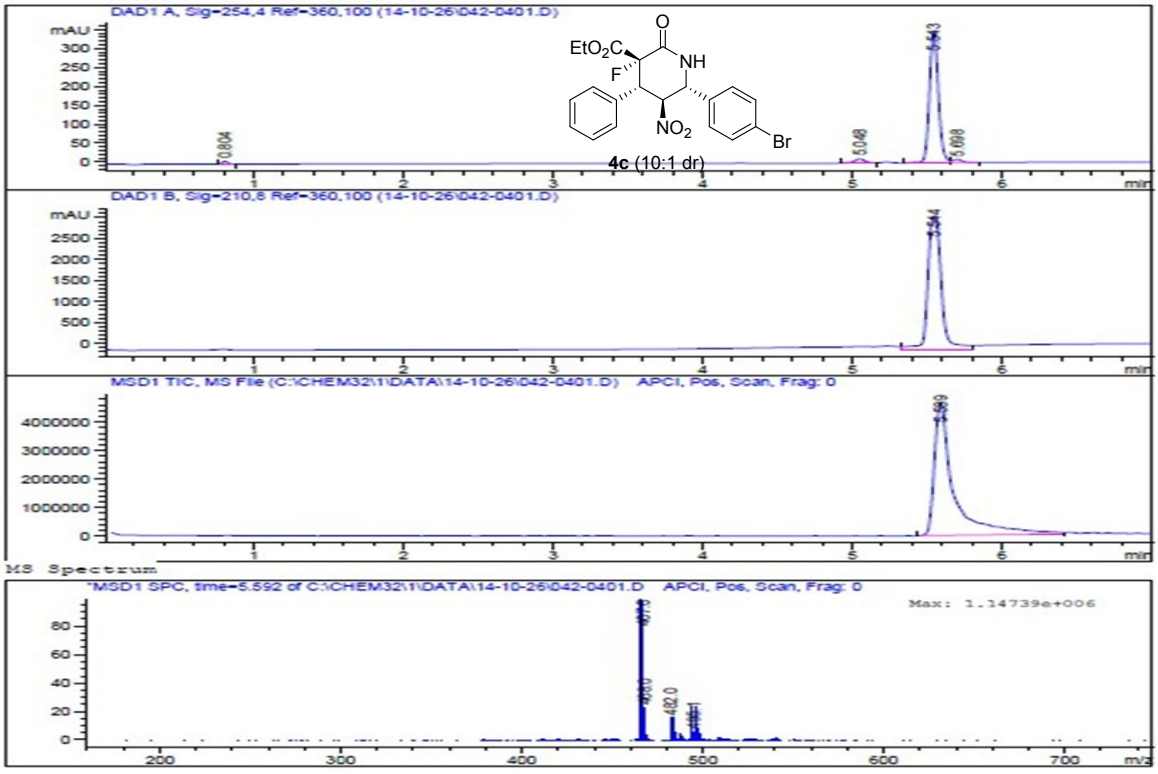
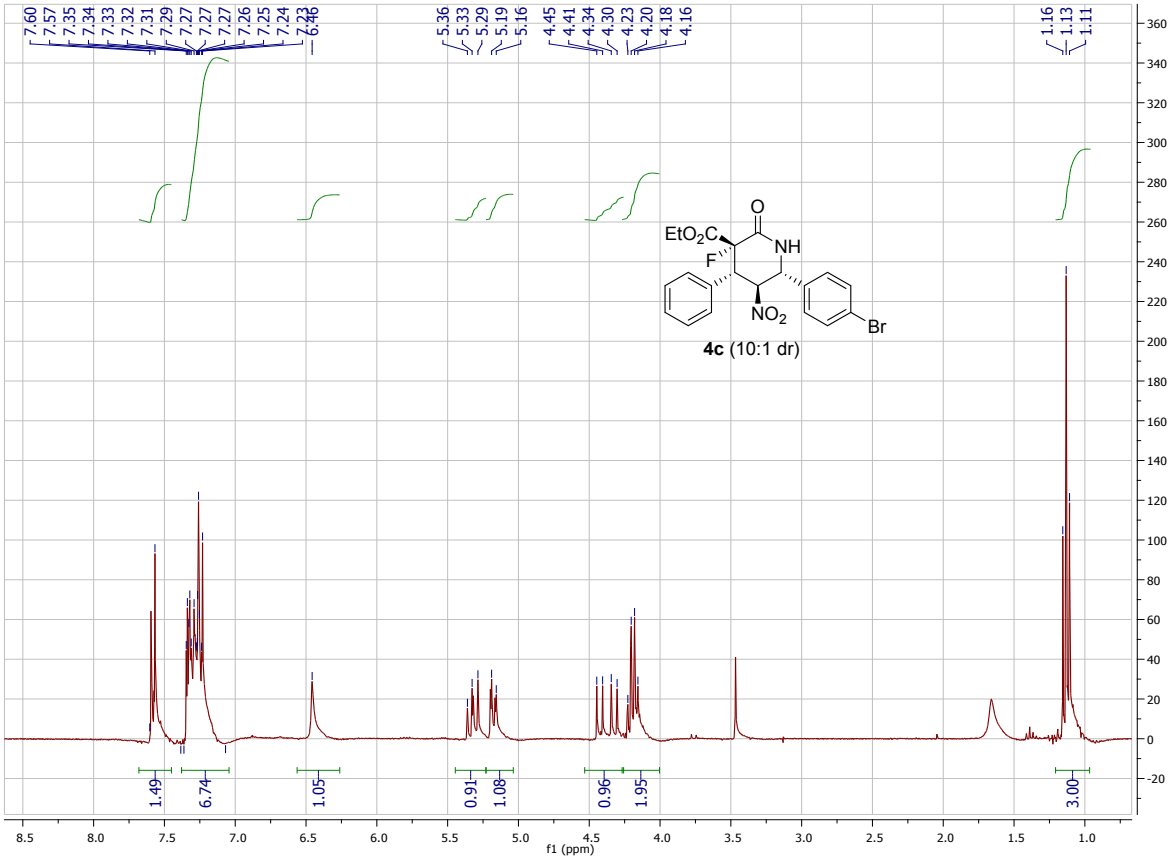
434.2
m/z

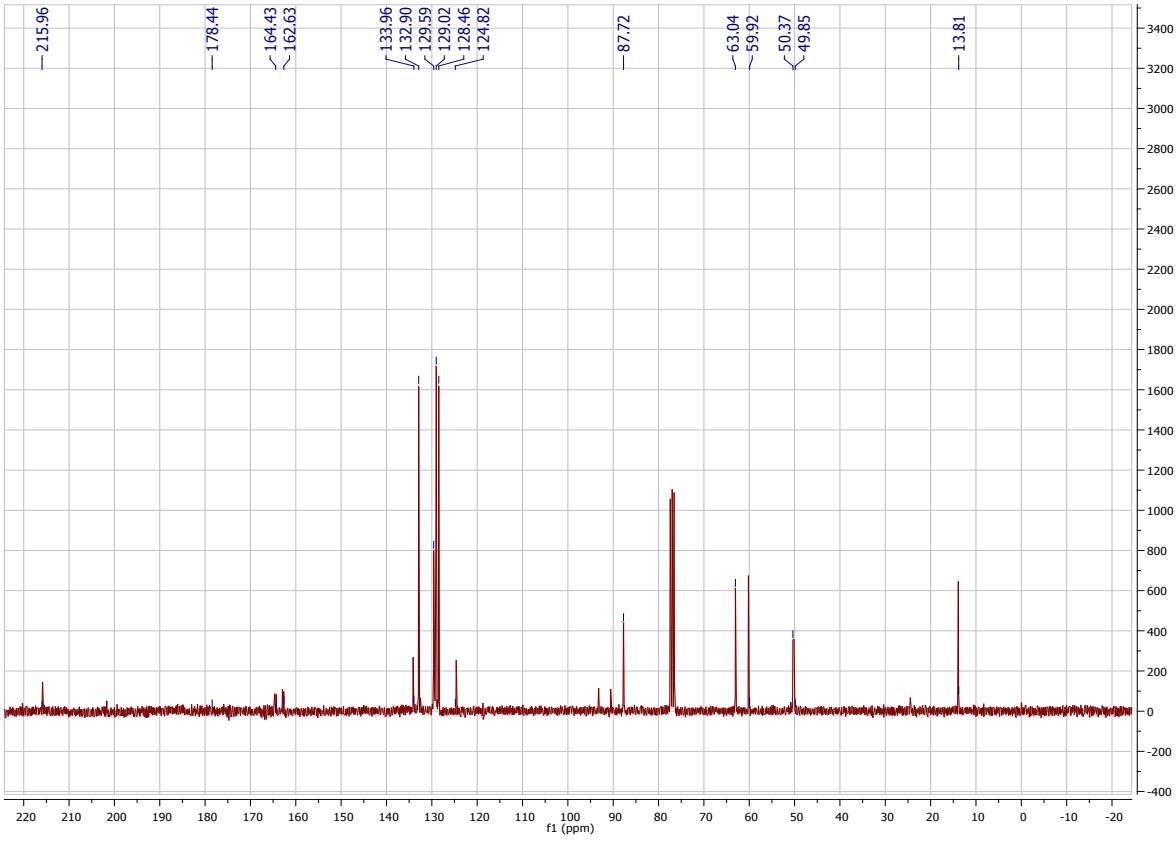

7.40
7.38
7.37
7.35
7.35
7.34
7.32
7.30
7.26
7.14
7.12
5.39
5.35
5.32
5.23
5.19
4.47
4.42
4.36
4.33
4.26
4.23
4.20
4.17
1.18
1.16
1.13
EtO2C
F
O
NH
NO2
F
4b (8:1 dr)
7.25
1.21
0.83
1.02
1.14
1.04
1.95
3.00
f1 (ppm)

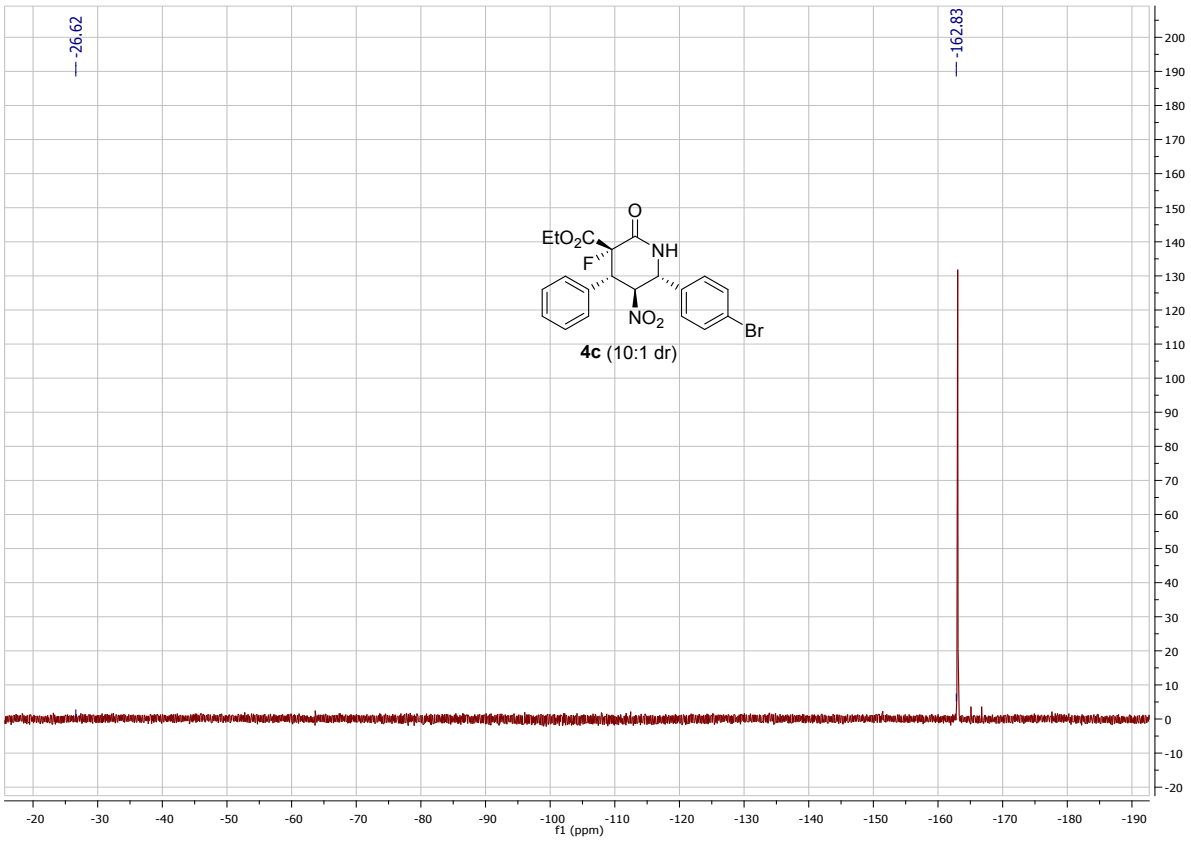

215.98
129.59
129.17
129.03
128.92
128.81
117.04
116.75
87.71
62.98
59.93
50.44
50.19
13.91
EtO2C
F
O
NH
NO2
F
4b (8:1 dr)
f1 (ppm)

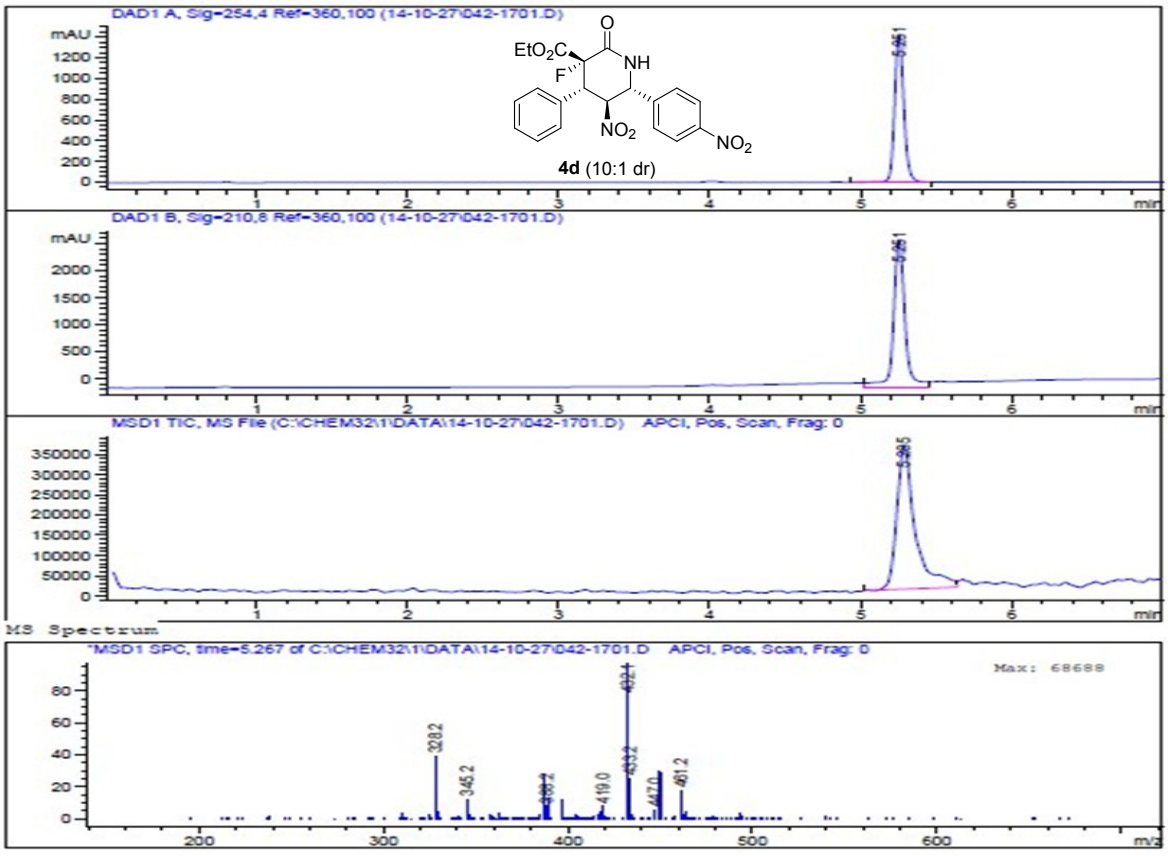

-110.22
-162.80
EtO2C
F
O
NH
NO2
F
4b (8:1 dr)
f1 (ppm)

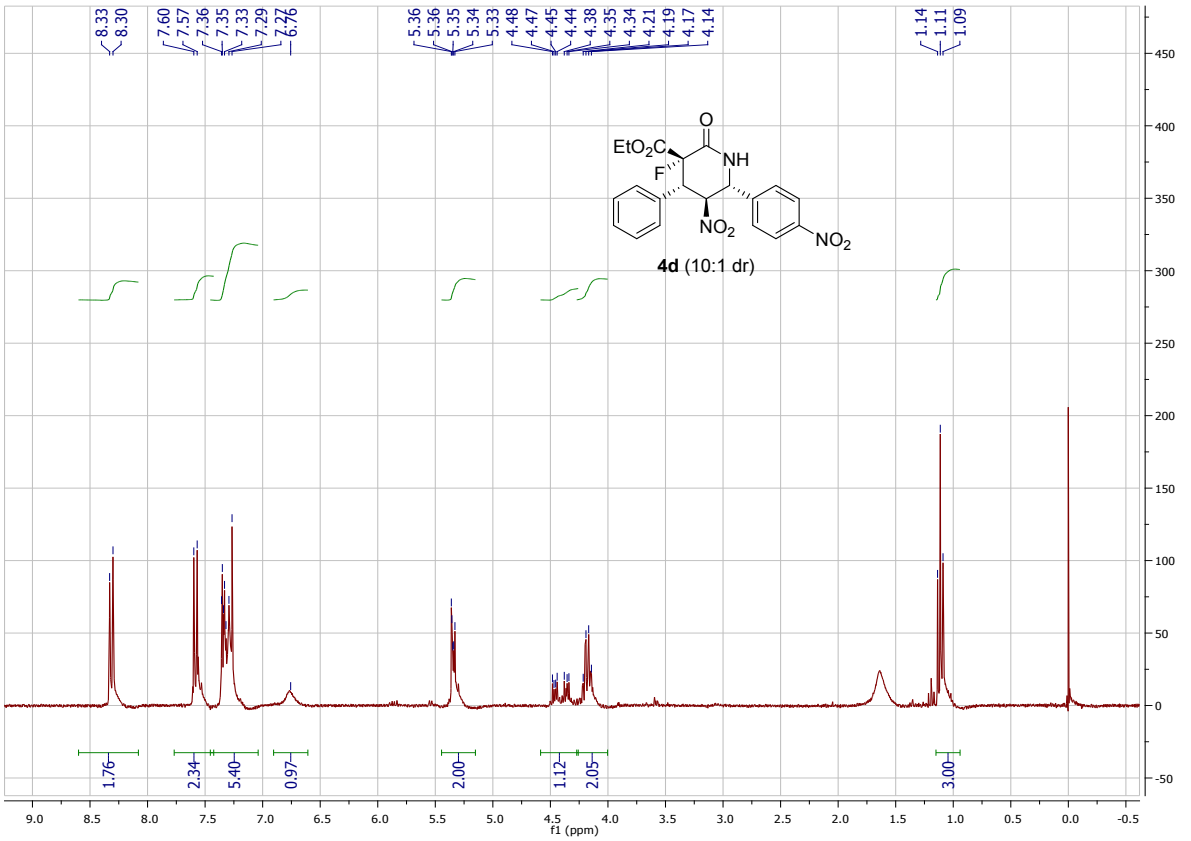

DAD1 A, Sig=254,4 Ref=360,100 (14-10-26\042-0401.D)
mAU
min
EtO2C
F
O
NH
NO2
Br
4c (10:1 dr)
DAD1 B, Sig=210,8 Ref=360,100 (14-10-26\042-0401.D)
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-10-26\042-0401.D) APCI, Pos, Scan, Frag: 0
MS Spectrum
*MSD1 SPC, time=5.592 of C:\CHEM32\1\DATA\14-10-26\042-0401.D APCI, Pos, Scan, Frag: 0
Max: 1.14739e+006
m/z


7.60
7.57
7.35
7.34
7.33
7.32
7.31
7.29
7.27
7.27
7.27
7.26
7.25
7.24
7.23
6.46
5.36
5.33
5.29
5.19
5.16
4.45
4.41
4.34
4.30
4.23
4.20
4.18
4.16
1.16
1.13
1.11
EtO2C
F
O
NH
NO2
Br
4c (10:1 dr)
1.49
6.74
1.05
0.91
1.08
0.96
1.95
3.00
f1 (ppm)


215.96
178.44
164.43
162.63
133.96
132.90
129.59
129.02
128.46
124.82
87.72
63.04
59.92
50.37
49.85
13.81
f1 (ppm)


-26.62
-162.83
O
EtO2C
NH
F
NO2
Br
4c (10:1 dr)
f1 (ppm)


DAD1 A, Sig=254,4 Ref=360,100 (14-10-27\042-1701.D)
mAU
min
DAD1 B, Sig=210,8 Ref=360,100 (14-10-27\042-1701.D)
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-10-27\042-1701.D) APCI, Pos, Scan, Frag: 0
O
EtO2C
NH
F
NO2
NO2
4d (10:1 dr)
MS Spectrum
*MSD1 SPC, time=5.267 of C:\CHEM32\1\DATA\14-10-27\042-1701.D APCI, Pos, Scan, Frag: 0
Max: 68688
328.2
345.2
419.0
433.2
461.2
m/z


8.33
8.30
7.60
7.57
7.36
7.35
7.33
7.29
7.27
6.76
5.36
5.36
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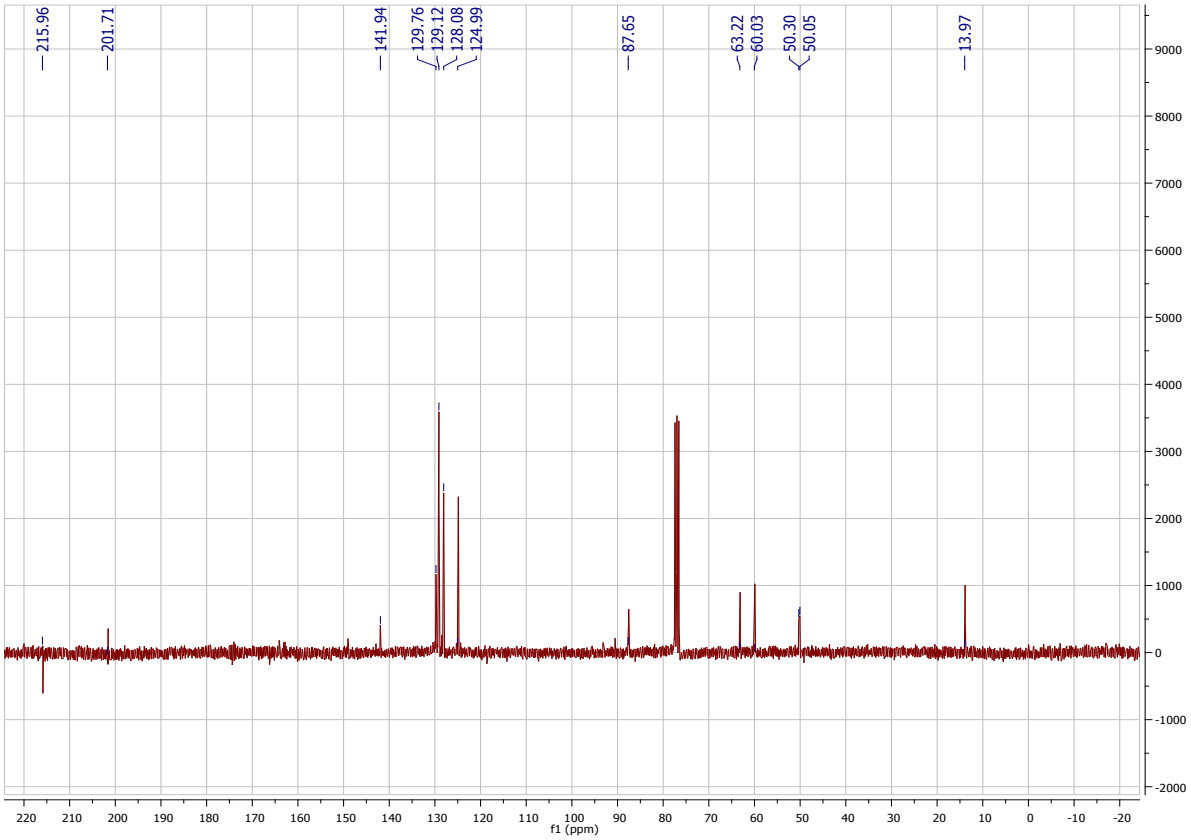
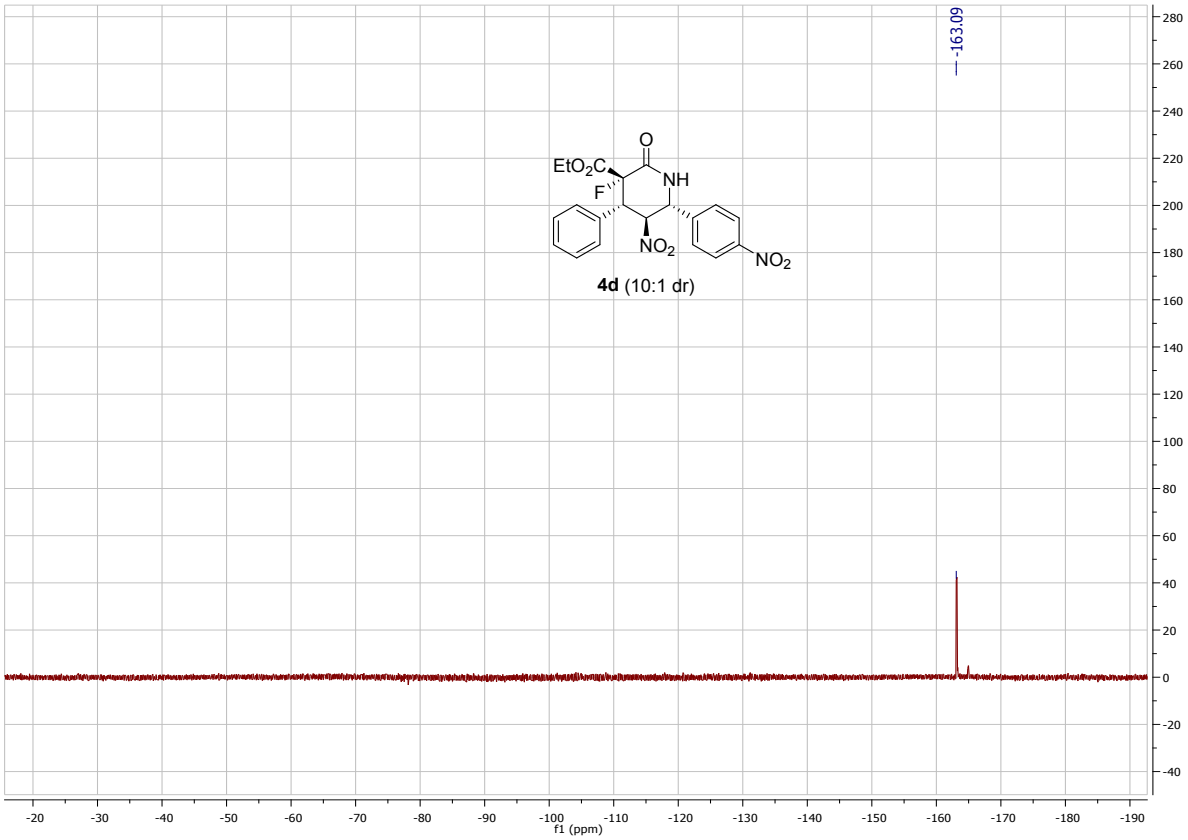
5.34
5.33
4.48
4.47
4.45
4.44
4.38
4.35
4.34
4.21
4.19
4.17
4.14
1.14
1.11
1.09
O
EtO2C
NH
F
NO2
NO2
4d (10:1 dr)
1.76
2.34
5.40
0.97
2.00
1.12
2.05
3.00
f1 (ppm)


215.96
201.71
141.94
129.76
129.12
128.08
124.99
87.65
63.22
60.03
50.30
50.05
13.97
f1 (ppm)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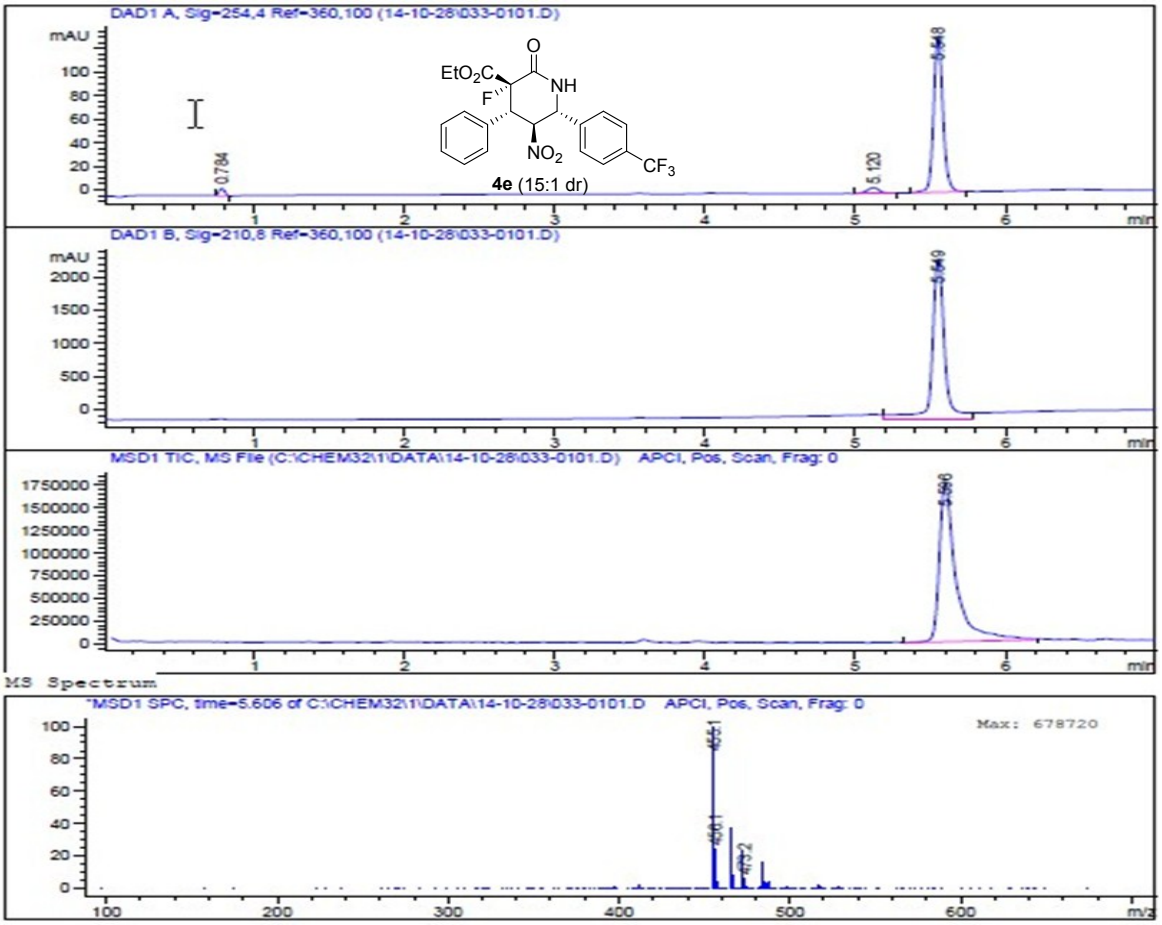
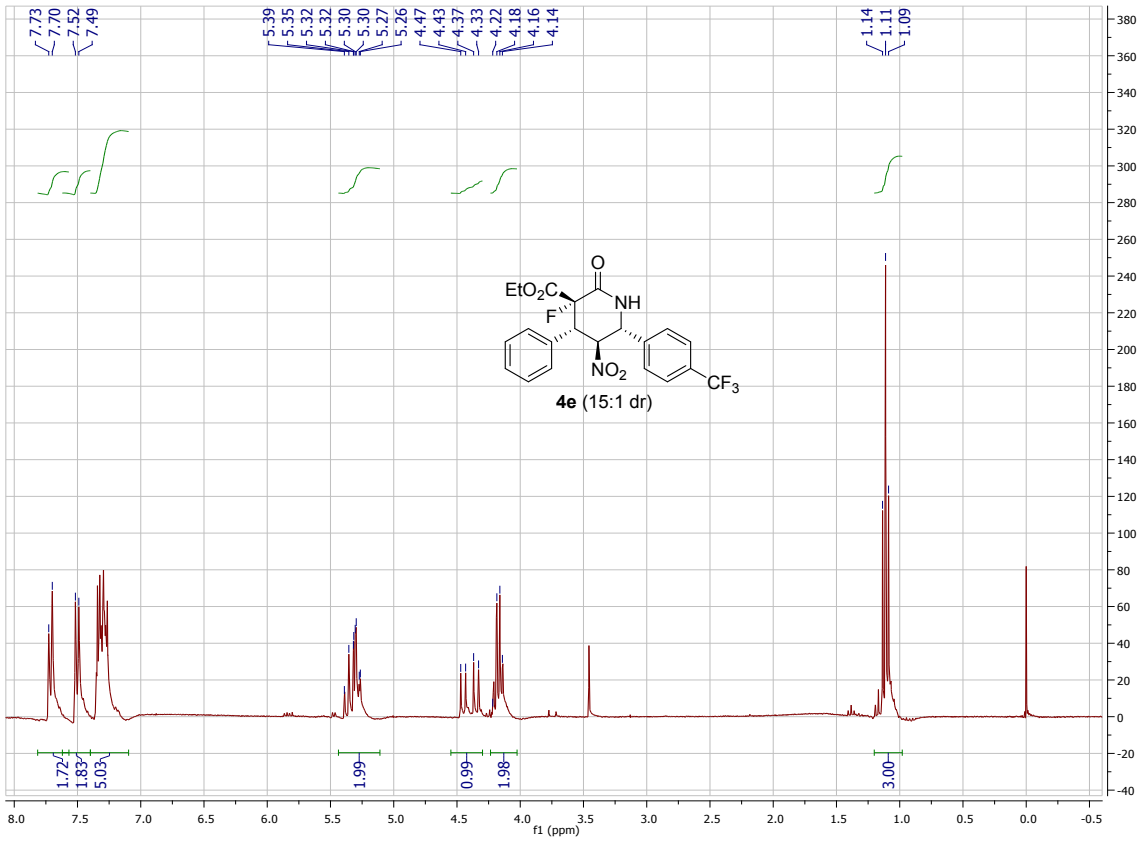
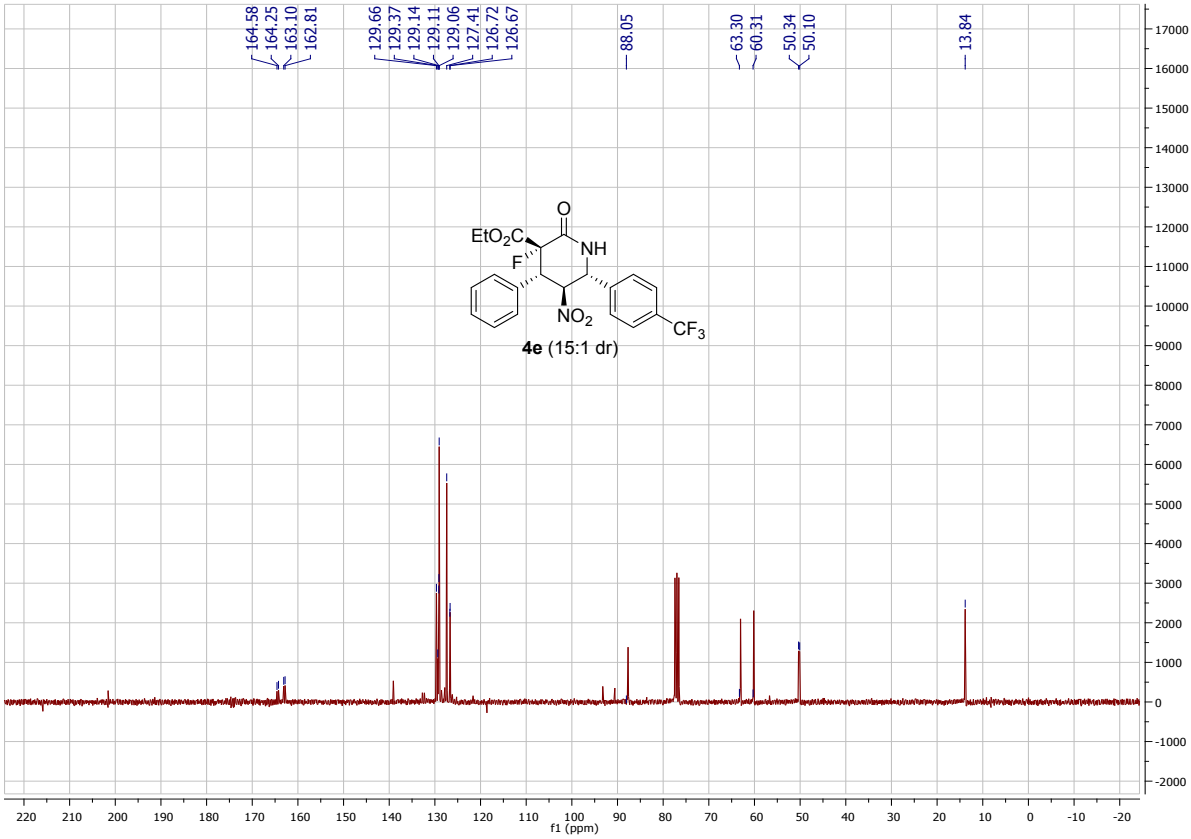
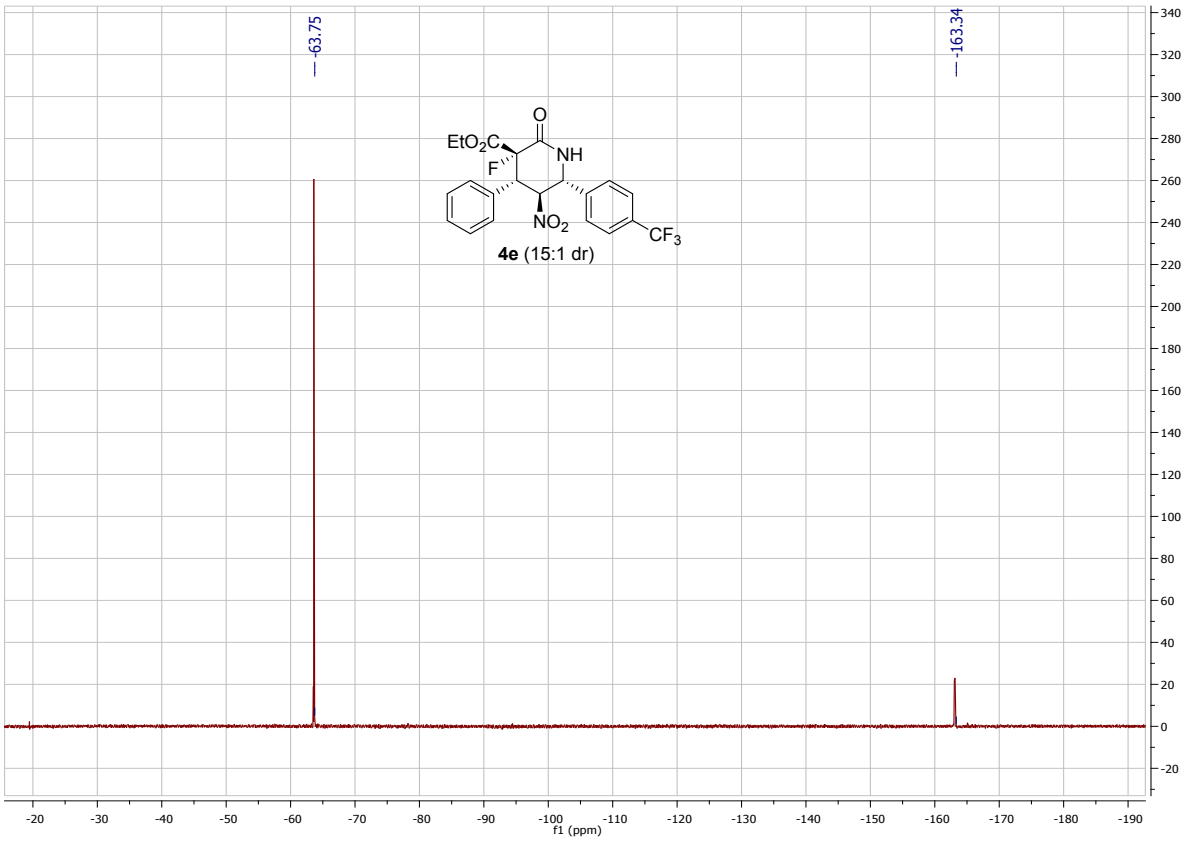
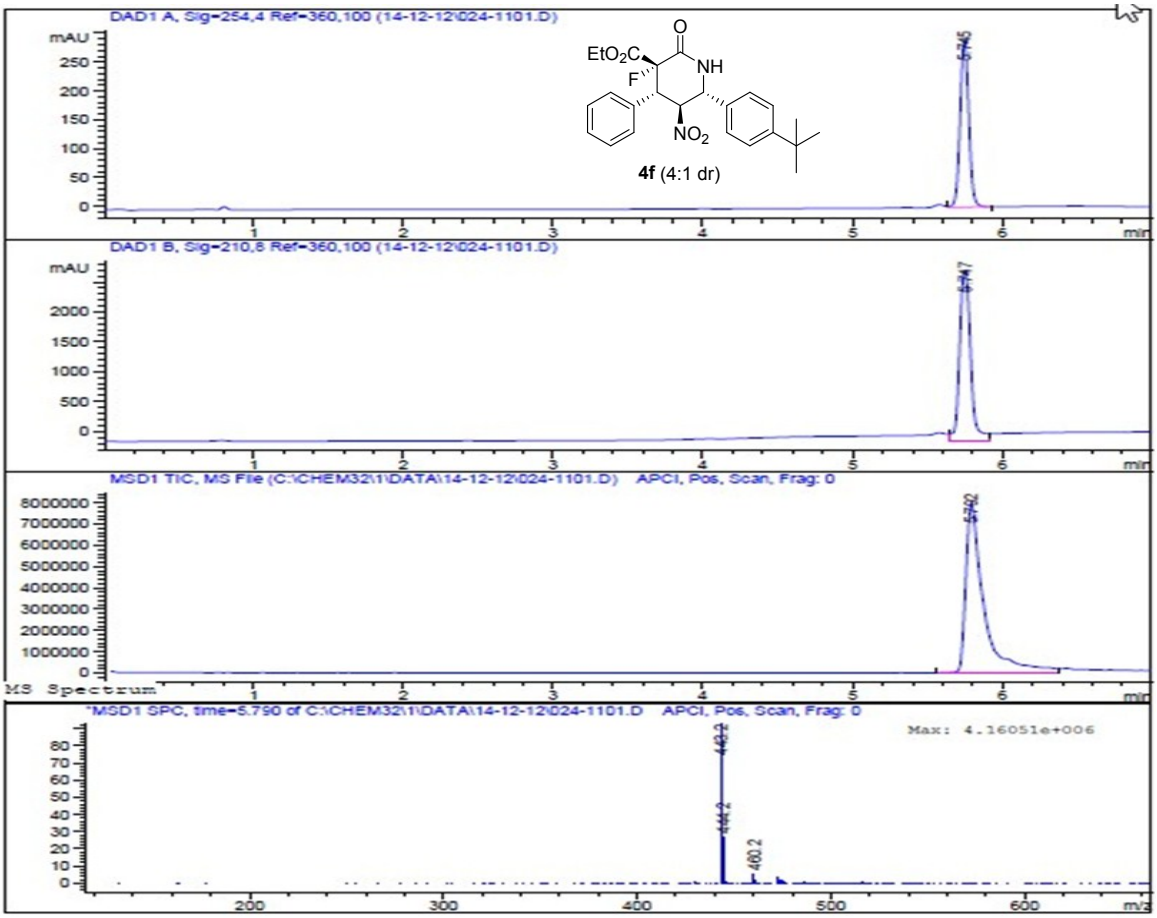
O
EtO2C
NH
F
NO2
NO2
4d (10:1 dr)
f1 (ppm)

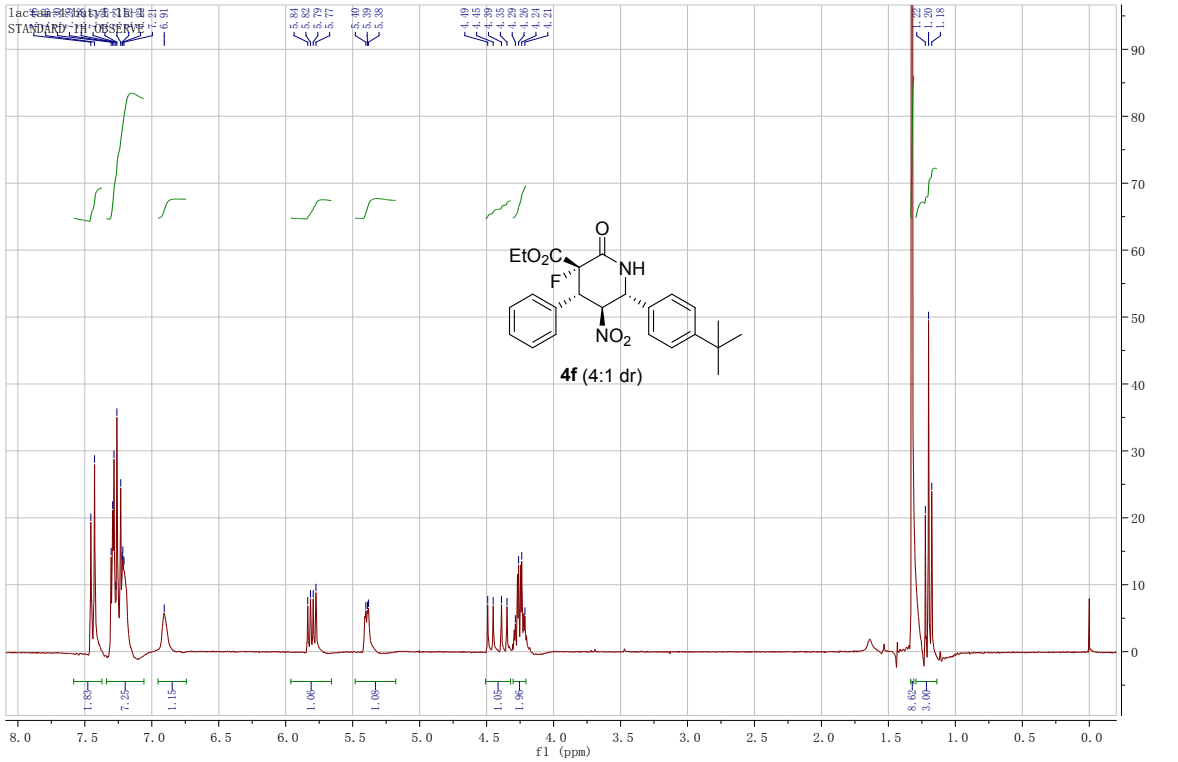

DAD1 A, Sig=254,4 Ref=360,100 (14-10-28\033-0101.D)
mAU
O
EtO2C
NH
F
NO2
CF3
4e (15:1 dr)
min
DAD1 B, Sig=210,8 Ref=360,100 (14-10-28\033-0101.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-10-28\033-0101.D) APCI, Pos, Scan, Frag: 0
min
MS Spectrum
*MSD1 SPC, time=5.606 of C:\CHEM32\1\DATA\14-10-28\033-0101.D APCI, Pos, Scan, Frag: 0
Max: 678720
m/z

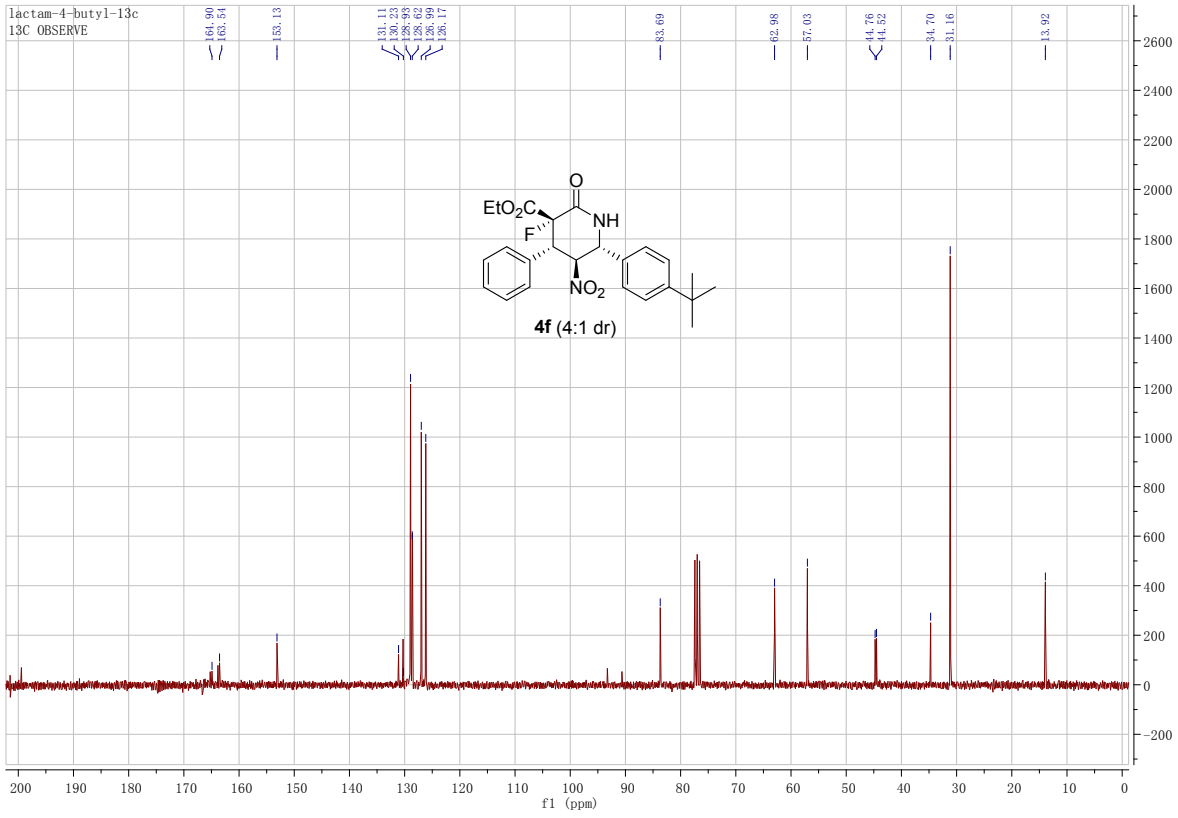

7.73
7.70
7.52
7.49
5.39
5.35
5.32
5.32
5.30
5.30
5.27
5.26
4.47
4.43
4.37
4.33
4.22
4.18
4.16
4.14
1.14
1.11
1.09
EtO2C
F
O
NH
NO2
CF3
4e (15:1 dr)
1.72
1.83
5.03
1.99
0.99
1.98
3.00
f1 (ppm)

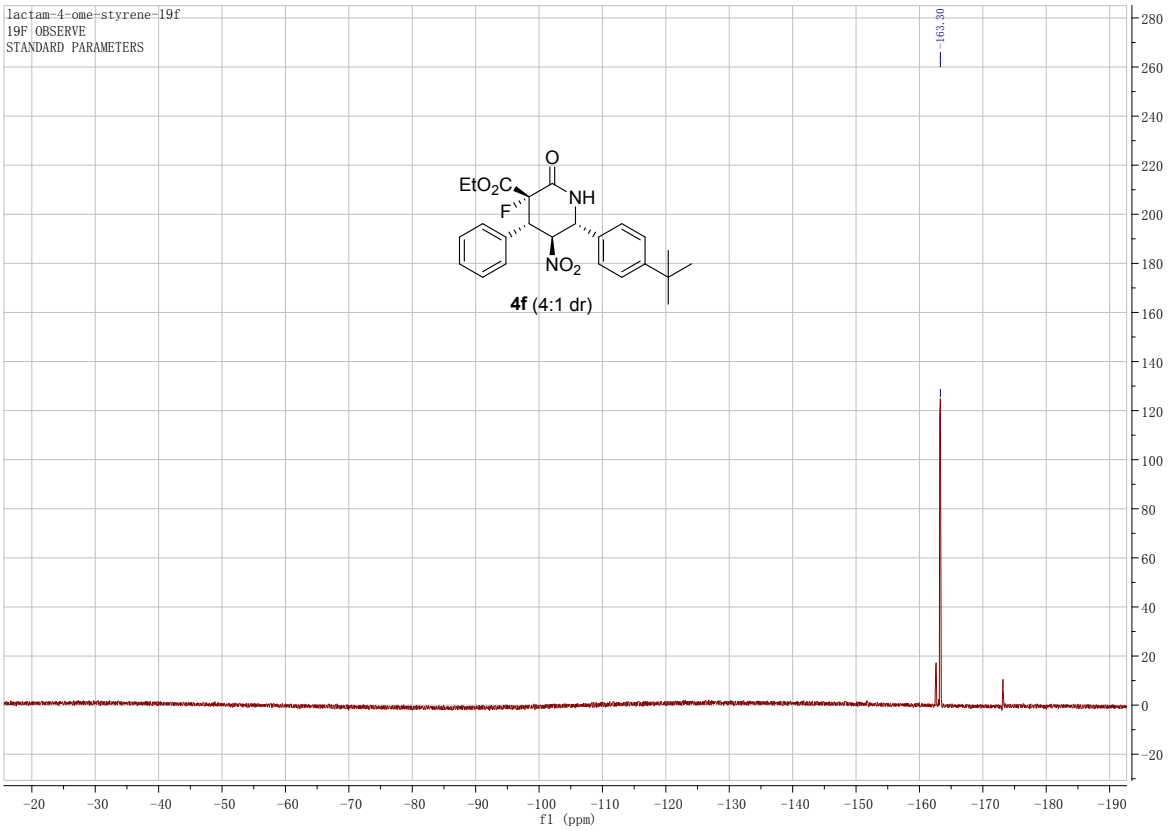

164.58
164.25
163.10
162.81
129.66
129.37
129.14
129.11
129.06
127.41
126.72
126.67
88.05
63.30
60.31
50.34
50.10
13.84
EtO2C
F
O
NH
NO2
CF3
4e (15:1 dr)
f1 (ppm)

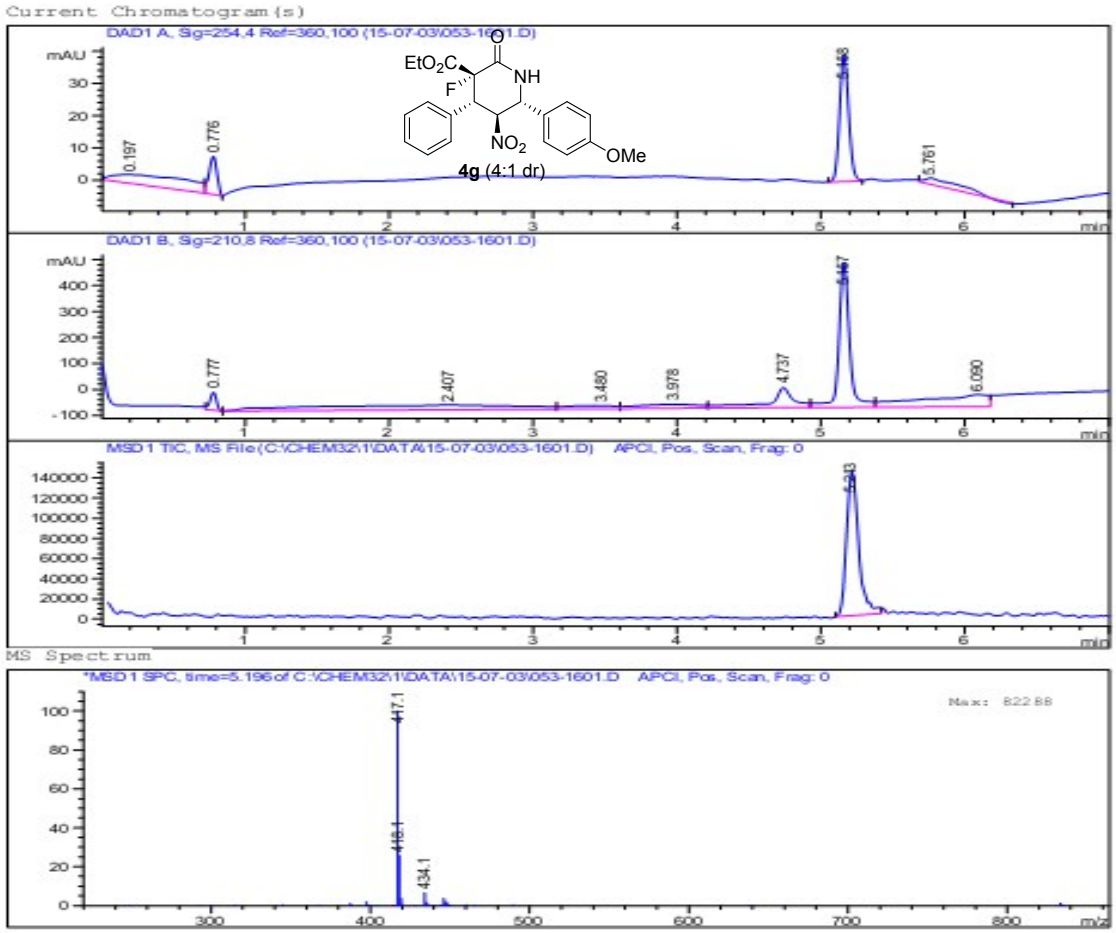

-63.75
-163.34
O
EtO2C
NH
F
NO2
CF3
4e (15:1 dr)
f1 (ppm)

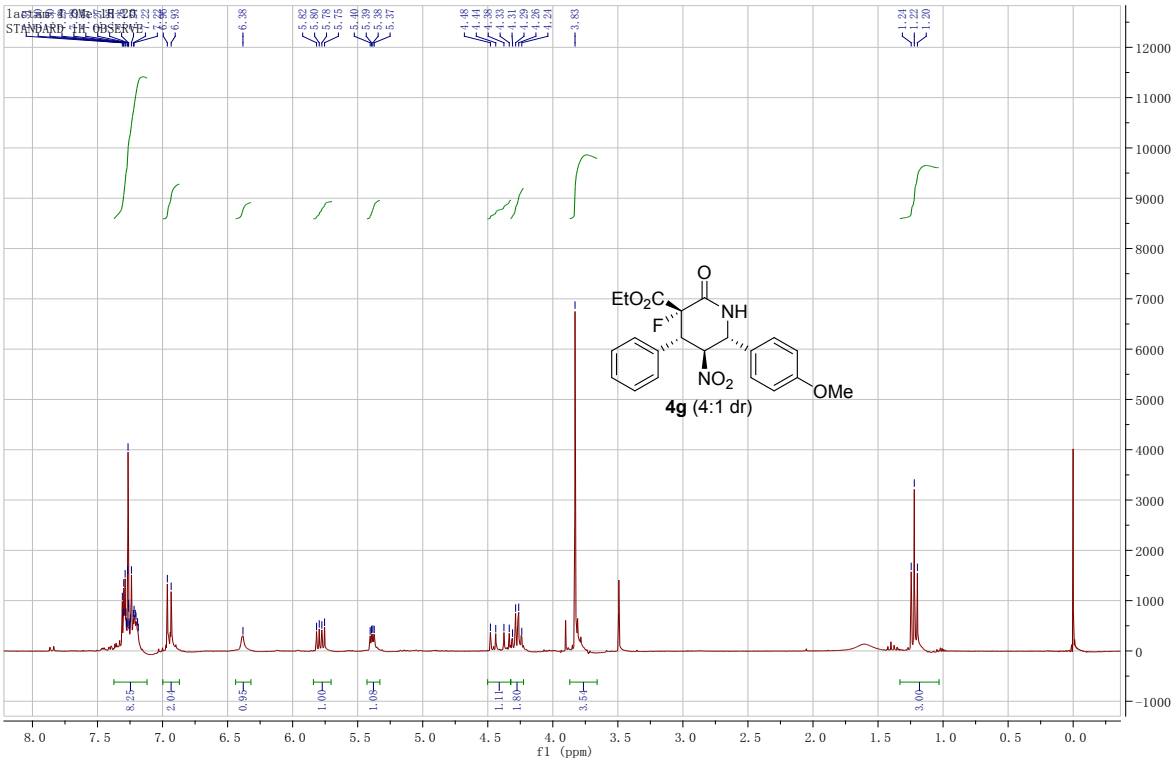

DAD1 A, Sig=254,4 Ref=360,100 (14-12-12\024-1101.D)
mAU
min
DAD1 B, Sig=210,8 Ref=360,100 (14-12-12\024-1101.D)
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-12-12\024-1101.D) APCI, Pos, Scan, Frag: 0
MS Spectrum
*MSD1 SPC, time=5.790 of C:\CHEM32\1\DATA\14-12-12\024-1101.D APCI, Pos, Scan, Frag: 0
Max: 4.16051e+006
460.2
m/z
O
EtO2C
NH
F
NO2
4f (4:1 dr)

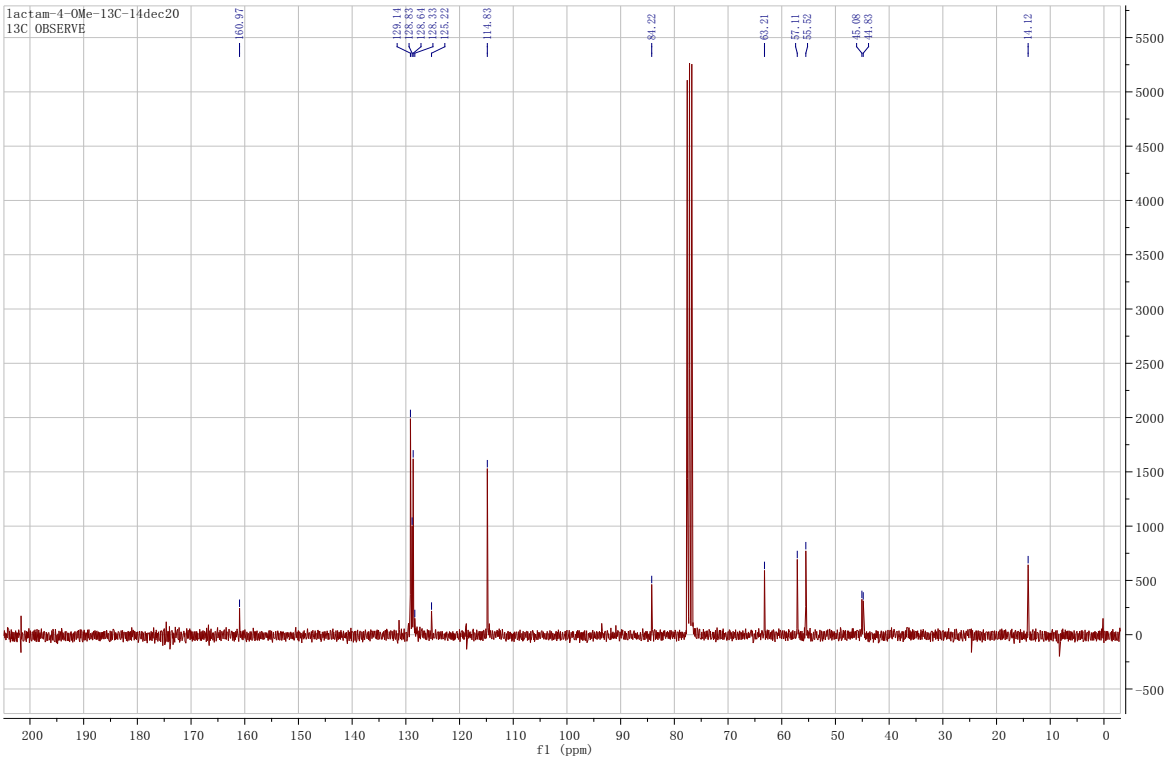

STANDARD-1H-OBSERVE
EtO2C
F
O
NH
NO2
4f (4:1 dr)
f1 (ppm)

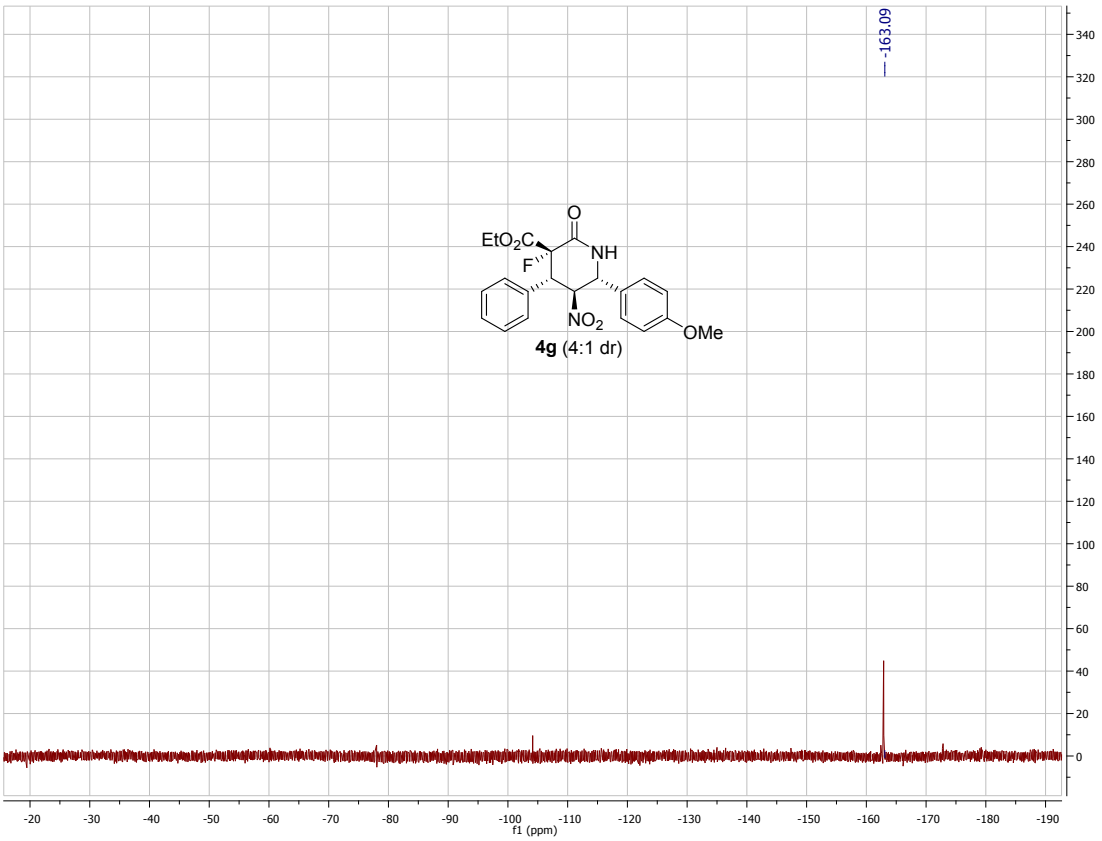

lactam-4-butyl-13c
13C OBSERVE
EtO2C
F
O
NH
NO2
4f (4:1 dr)
f1 (ppm)

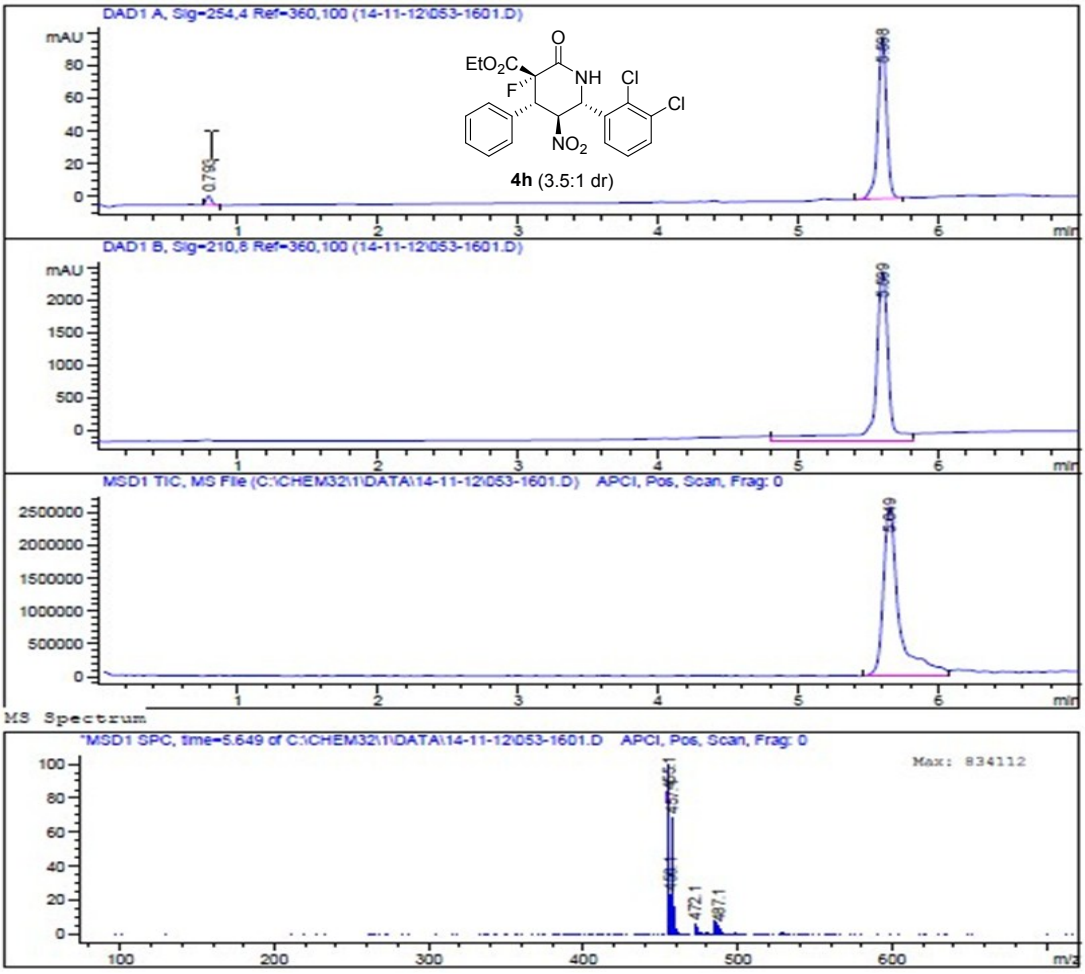

lactam-4-ome-styrene-19f
19F OBSERVE
STANDARD PARAMETERS
-163.30
O
EtO2C
NH
F
NO2
4f (4:1 dr)
f1 (ppm)

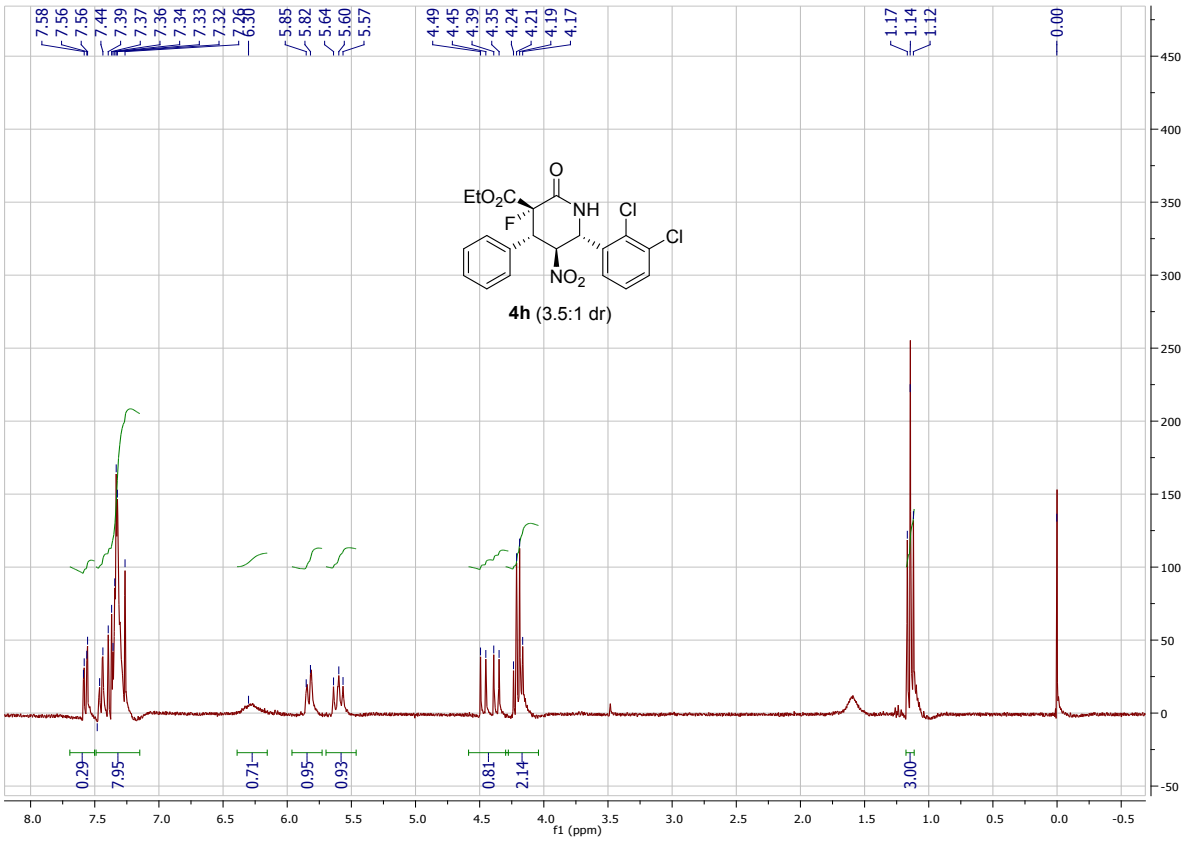

Current Chromatogram(s)
DAD1 A, Sig=254,4 Ref=360,100 (15-07-03\053-1601.D)
O
EtO2C
NH
F
NO2
OMe
4g (4:1 dr)
0.197
0.776
5.761
DAD1 B, Sig=210,8 Ref=360,100 (15-07-03\053-1601.D)
0.777
2.407
3.480
3.978
4.737
6.090
MSD1 TIC, MS File(C:\CHEM32\1\DATA\15-07-03\053-1601.D) APCI, Pos, Scan, Frag: 0
MS Spectrum
*MSD1 SPC, time=5.196 of C:\CHEM32\1\DATA\15-07-03\053-1601.D APCI, Pos, Scan, Frag: 0
417.1
418.1
434.1
min
m/z

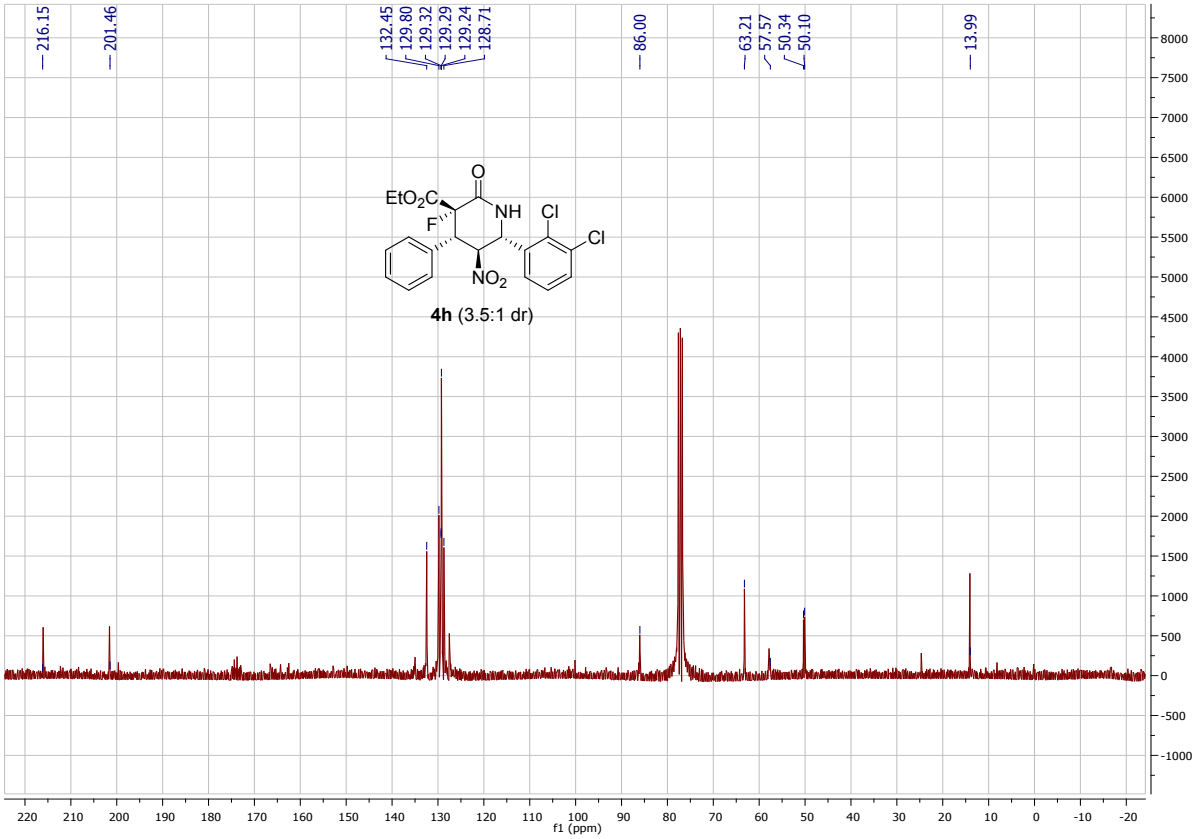

O
EtO2C
NH
F
NO2
OMe
4g (4:1 dr)
f1 (ppm)

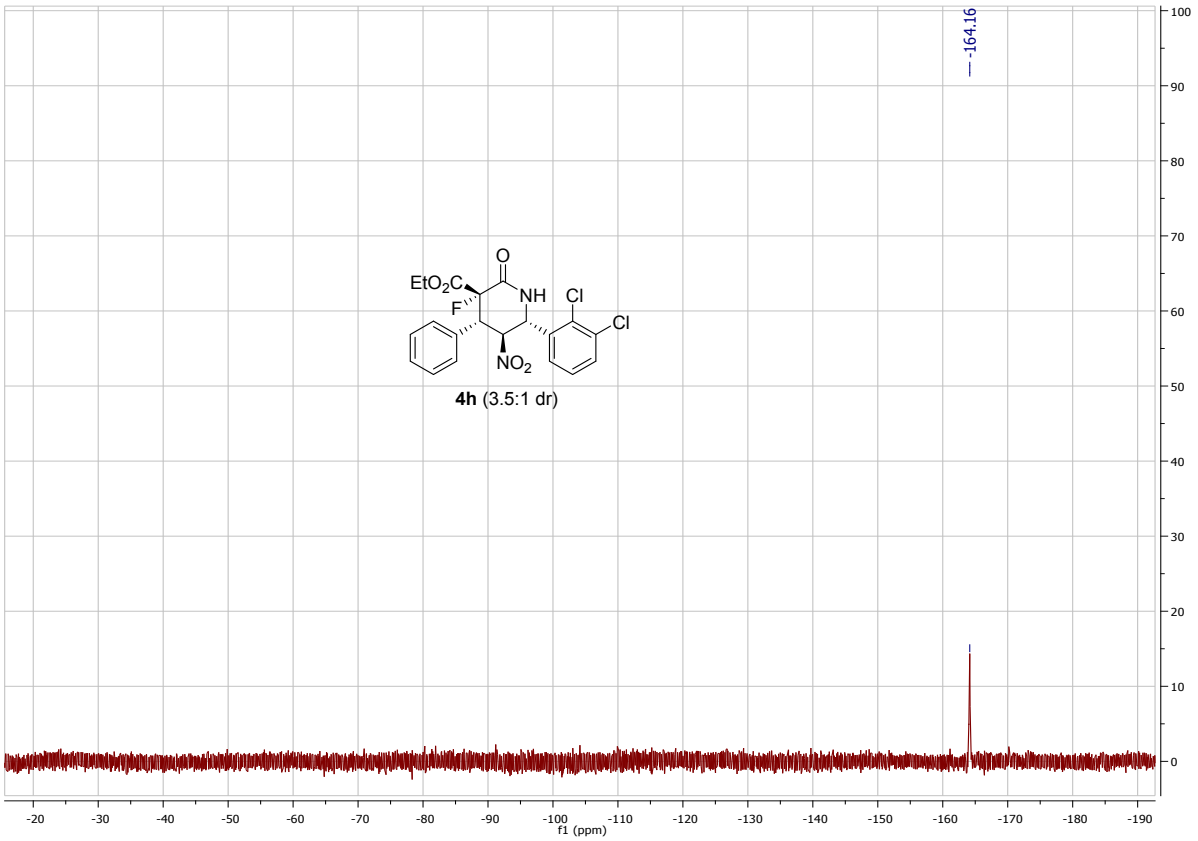

lactam-4-OMe-13C-14dec20
13C OBSERVE
f1 (ppm)


-163.09
O
EtO2C
NH
F
NO2
OMe
4g (4:1 dr)
f1 (ppm)

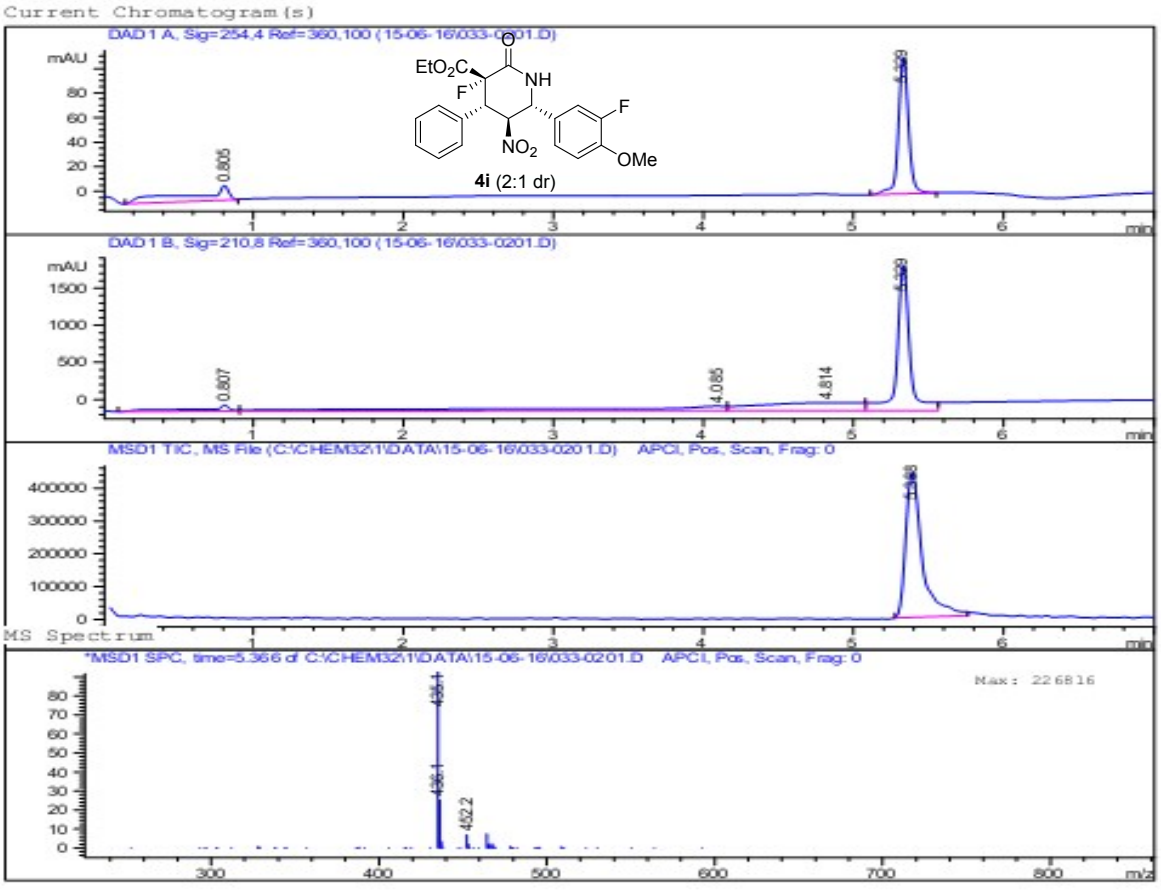

DAD1 A, Sig=254,4 Ref=360,100 (14-11-12\053-1601.D)
mAU
0.795
O
EtO2C
NH
Cl
Cl
F
NO2
4h (3.5:1 dr)
min
DAD1 B, Sig=210,8 Ref=360,100 (14-11-12\053-1601.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-11-12\053-1601.D) APCI, Pos, Scan, Frag: 0
min
MS Spectrum
MSD1 SPC, time=5.649 of C:\CHEM32\1\DATA\14-11-12\053-1601.D APCI, Pos, Scan, Frag: 0
Max: 834112
472.1
487.1
m/z


7.58
7.56
7.56
7.44
7.39
7.37
7.36
7.34
7.33
7.32
6.30
5.85
5.82
5.64
5.60
5.57
4.49
4.45
4.39
4.35
4.24
4.21
4.19
4.17
1.17
1.14
1.12
0.00
O
EtO2C
NH
Cl
F
Cl
NO2
4h (3.5:1 dr)
0.29
7.95
0.71
0.95
0.93
0.81
2.14
3.00
f1 (ppm)

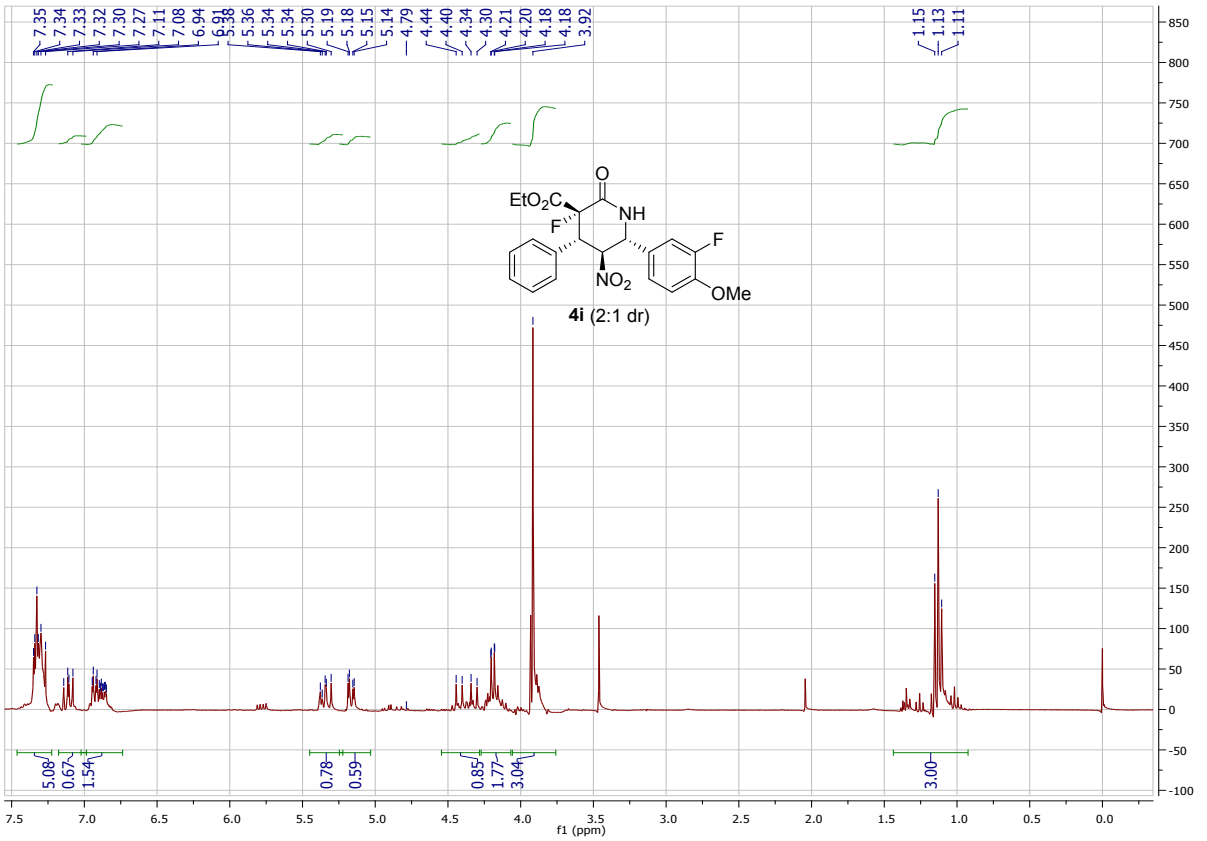

216.15
201.46
132.45
129.80
129.32
129.29
129.24
128.71
86.00
63.21
57.57
50.34
50.10
13.99
O
EtO2C
NH
Cl
F
Cl
NO2
4h (3.5:1 dr)
f1 (ppm)

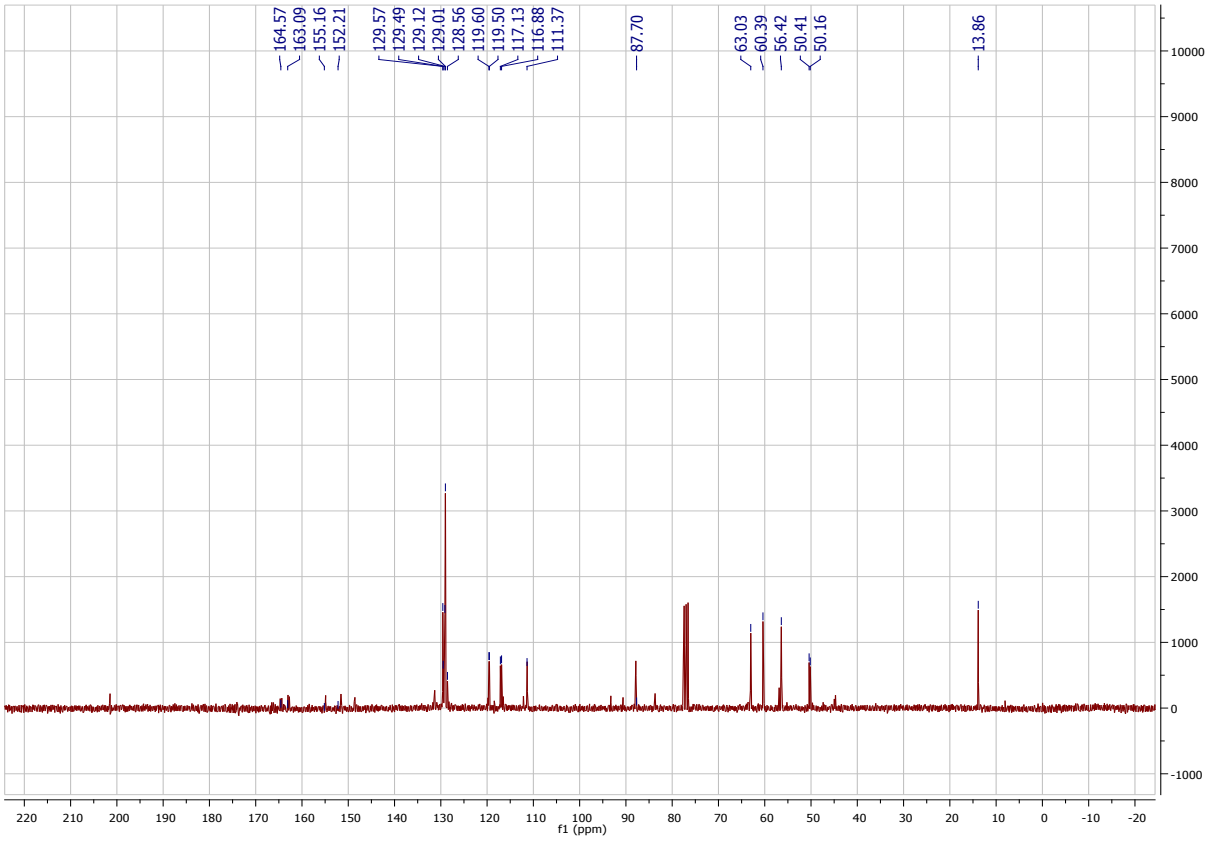


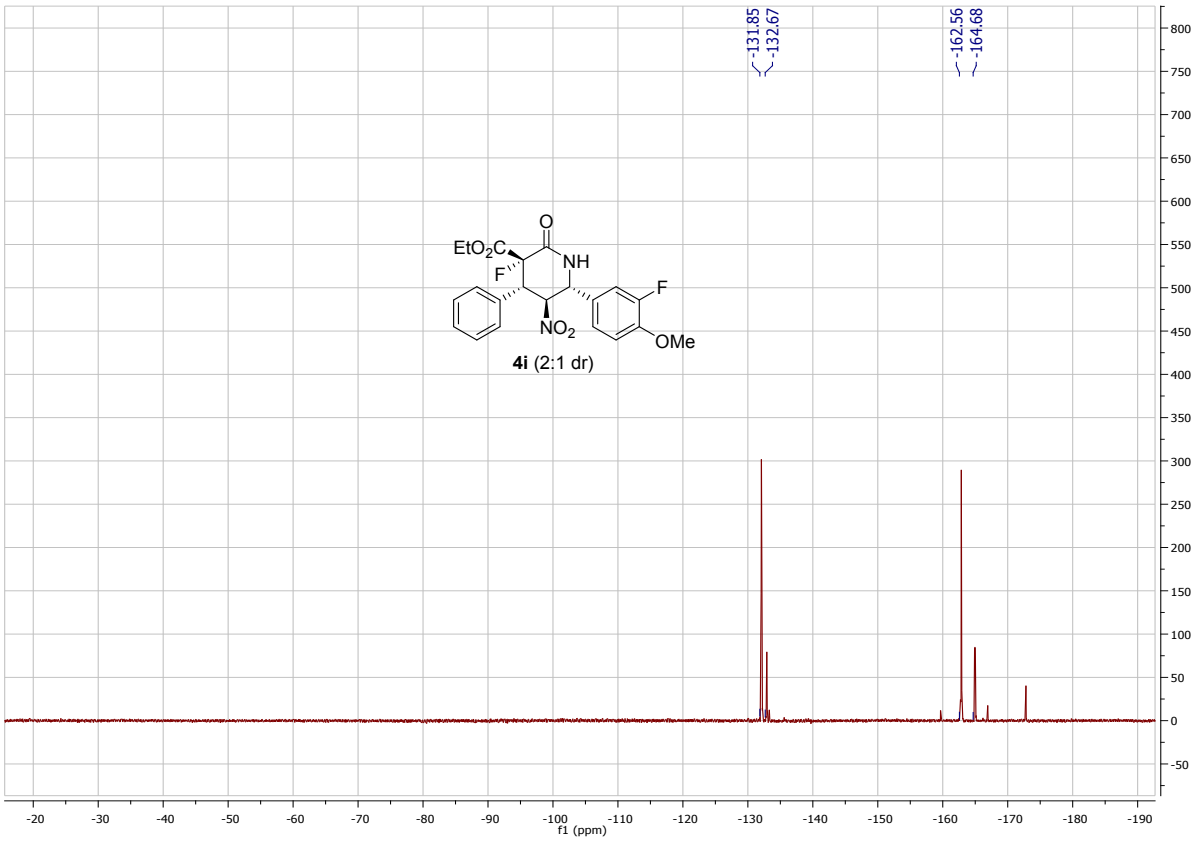
4h (3.5:1 dr)

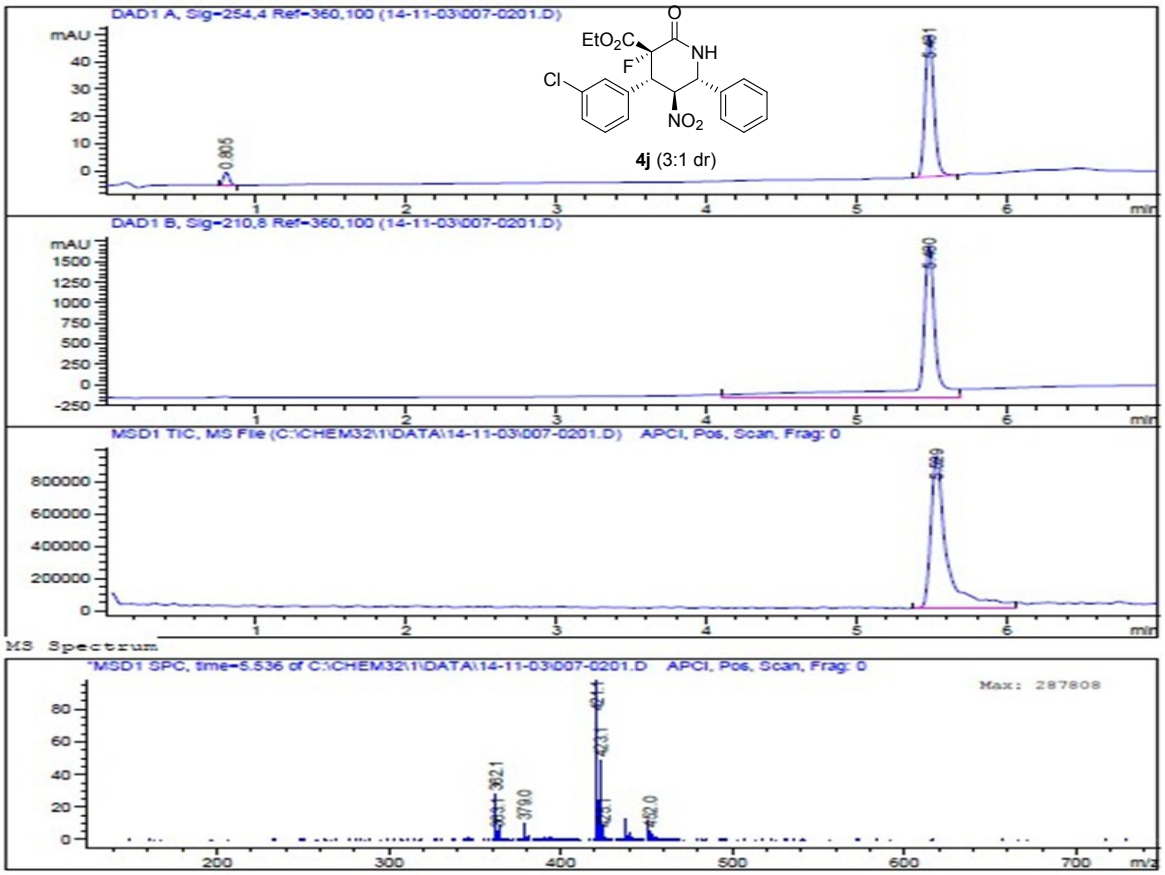


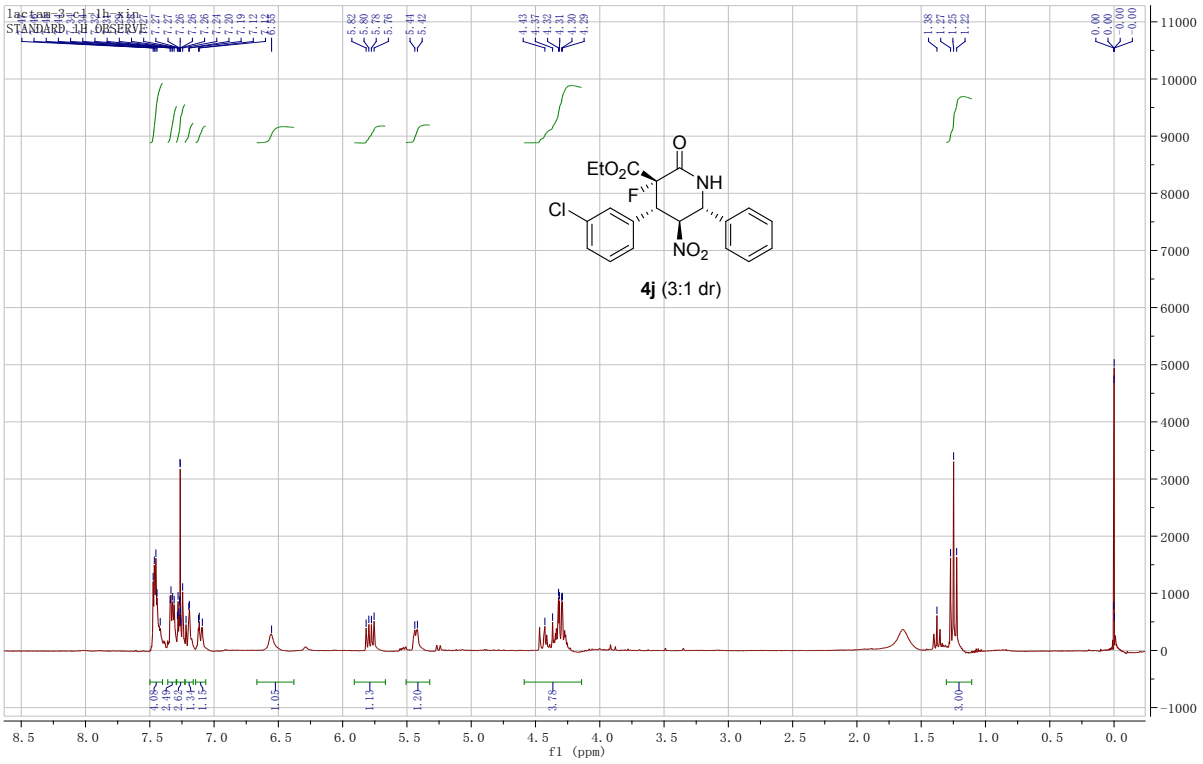
4i (2:1 dr)

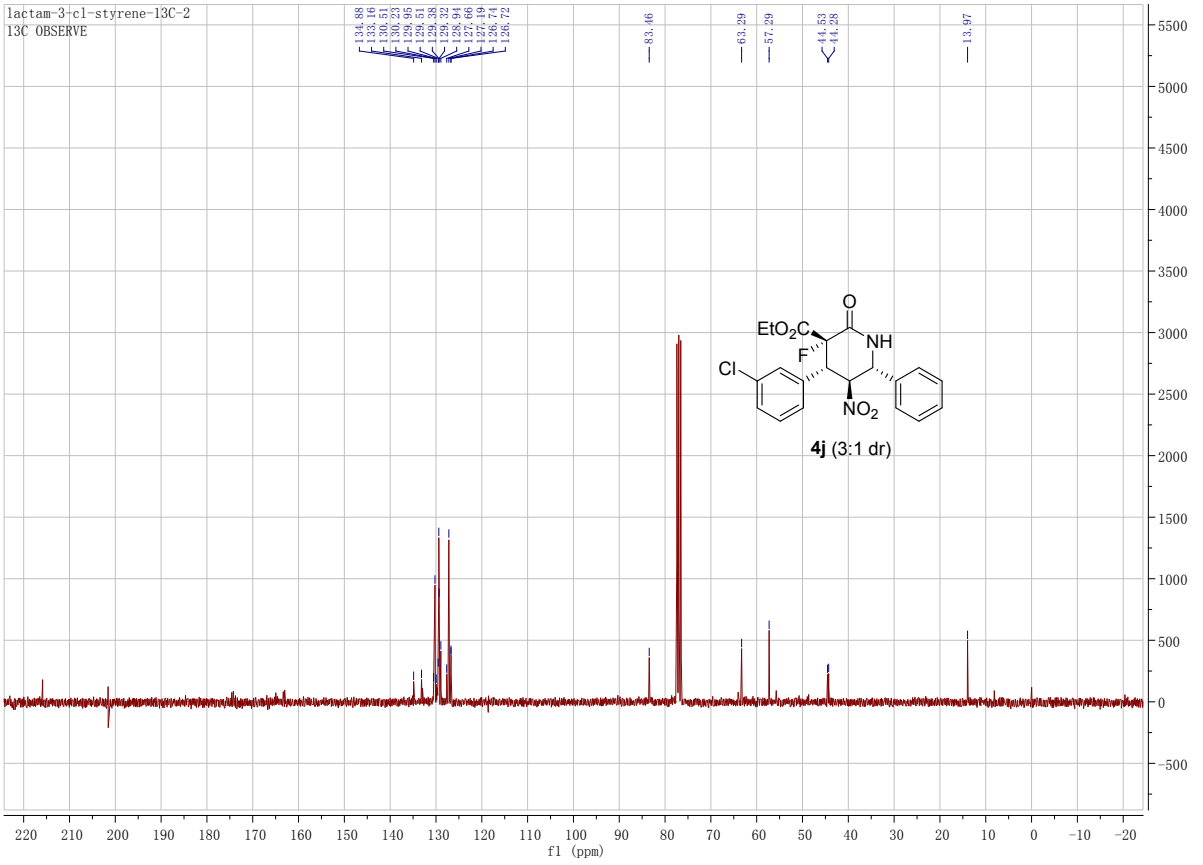

7.35
7.34
7.33
7.32
7.30
7.27
7.11
7.08
6.94
6.91
5.38
5.36
5.34
5.34
5.30
5.19
5.18
5.15
5.14
4.79
4.44
4.40
4.34
4.30
4.21
4.20
4.18
4.18
3.92
1.15
1.13
1.11
O
EtO2C
NH
F
F
NO2
OMe
4i (2:1 dr)
5.08
0.67
1.54
0.78
0.59
0.85
1.77
3.04
3.00
f1 (ppm)

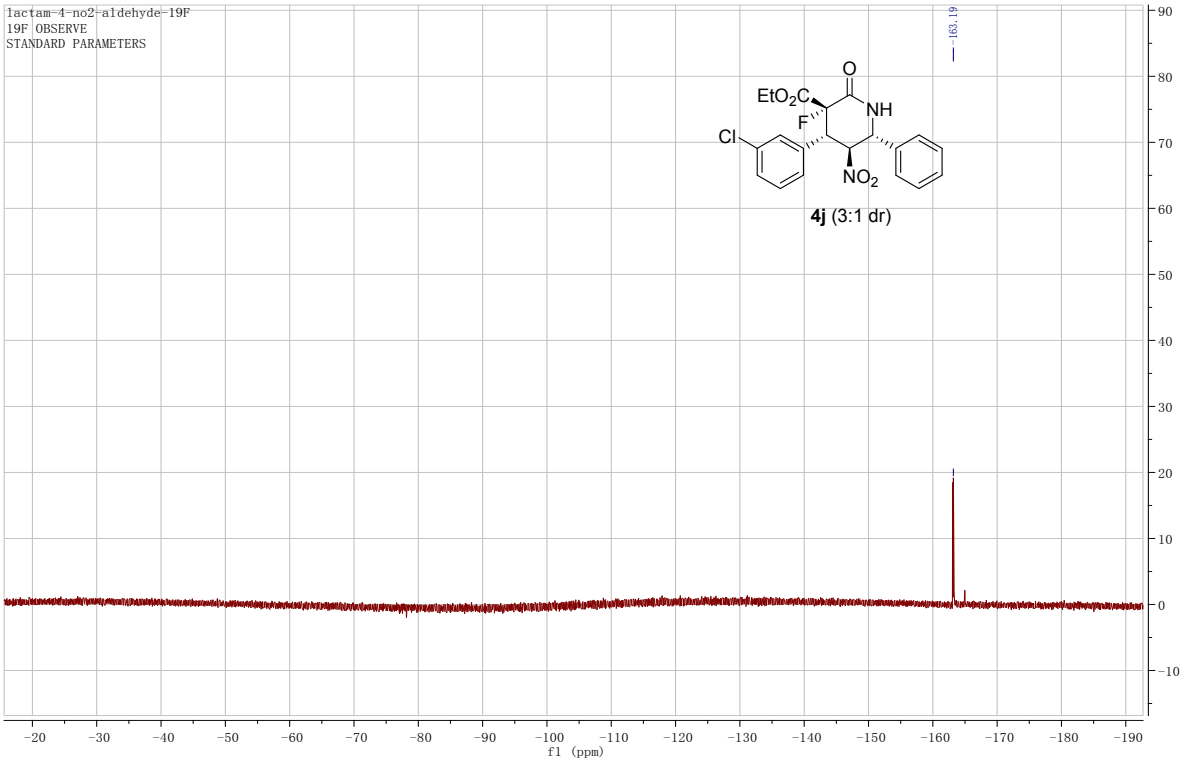

164.57
163.09
155.16
152.21
129.57
129.49
129.12
129.01
128.56
119.60
119.50
117.13
116.88
111.37
87.70
63.03
60.39
56.42
50.41
50.16
13.86
f1 (ppm)

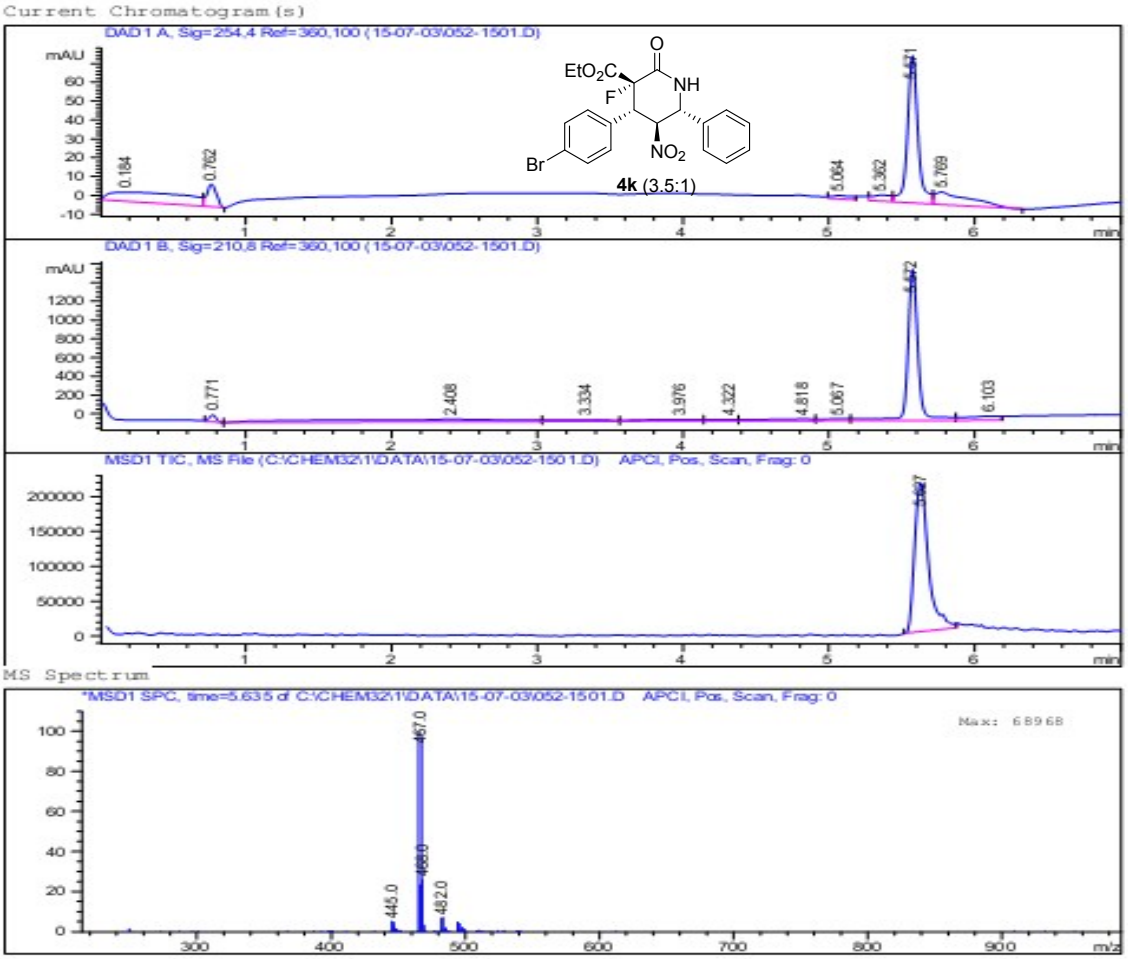

-131.85
-132.67
-162.56
-164.68
O
EtO2C
NH
F
F
NO2
OMe
4i (2:1 dr)
f1 (ppm)

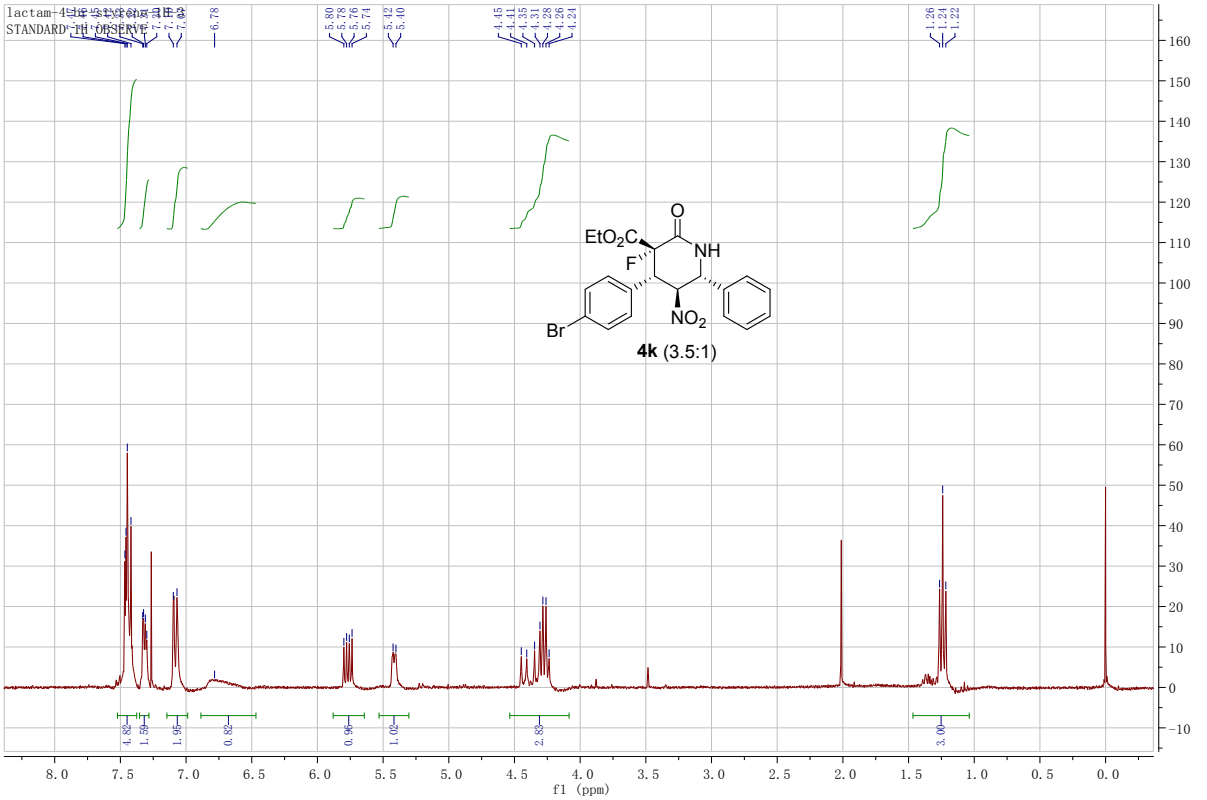

DAD1 A, Sig=254,4 Ref=360,100 (14-11-03\007-0201.D)
mAU
0.805
5.491
DAD1 B, Sig=210,8 Ref=360,100 (14-11-03\007-0201.D)
5.490
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-11-03\007-0201.D) APCI, Pos, Scan, Frag: 0
5.529
min
O
EtO2C
NH
F
Cl
NO2
4j (3:1 dr)
MS Spectrum
*MSD1 SPC, time=5.536 of C:\CHEM32\1\DATA\14-11-03\007-0201.D APCI, Pos, Scan, Frag: 0
Max: 287808
362.1
379.0
421.1
423.1
452.0
m/z

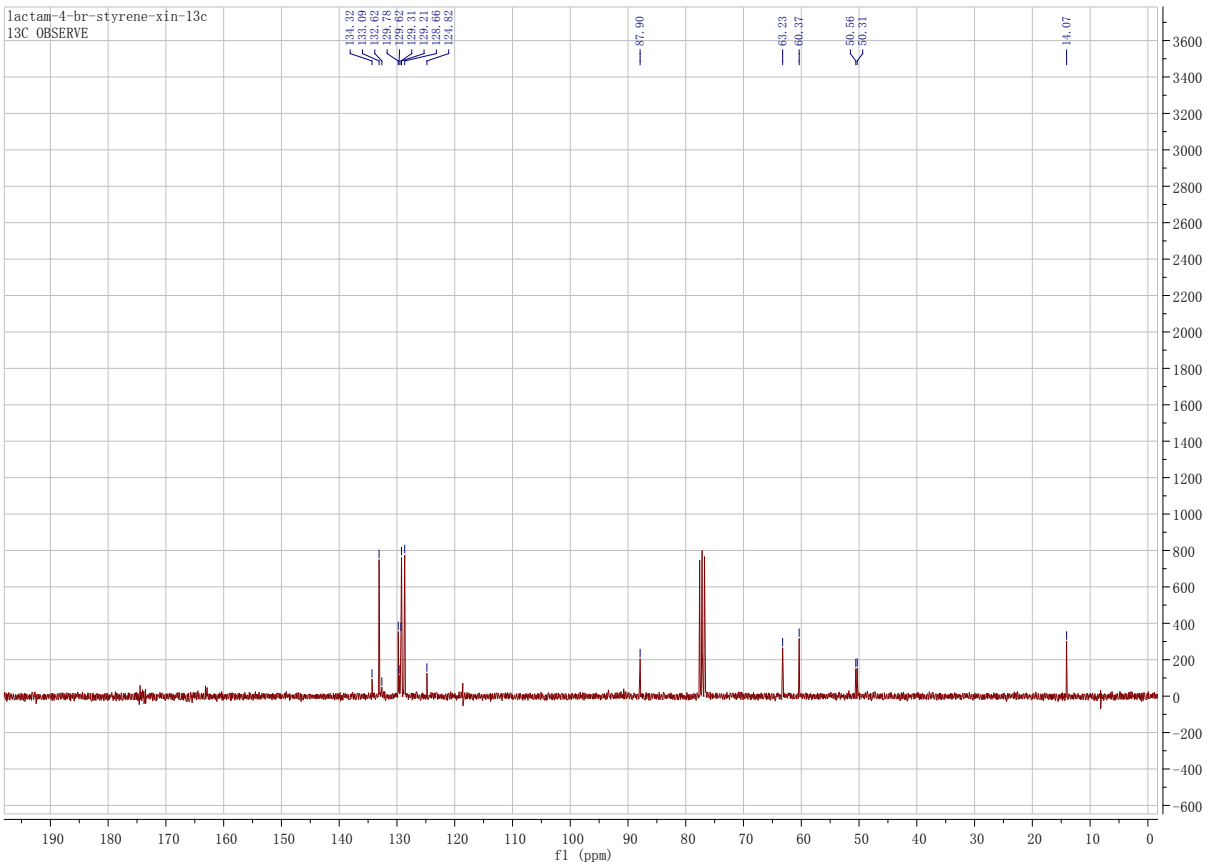

lactam-3-cl-1h-xin
STANDARD_1H.OBSERVE
EtO2C
F
O
NH
Cl
NO2
4j (3:1 dr)
f1 (ppm)

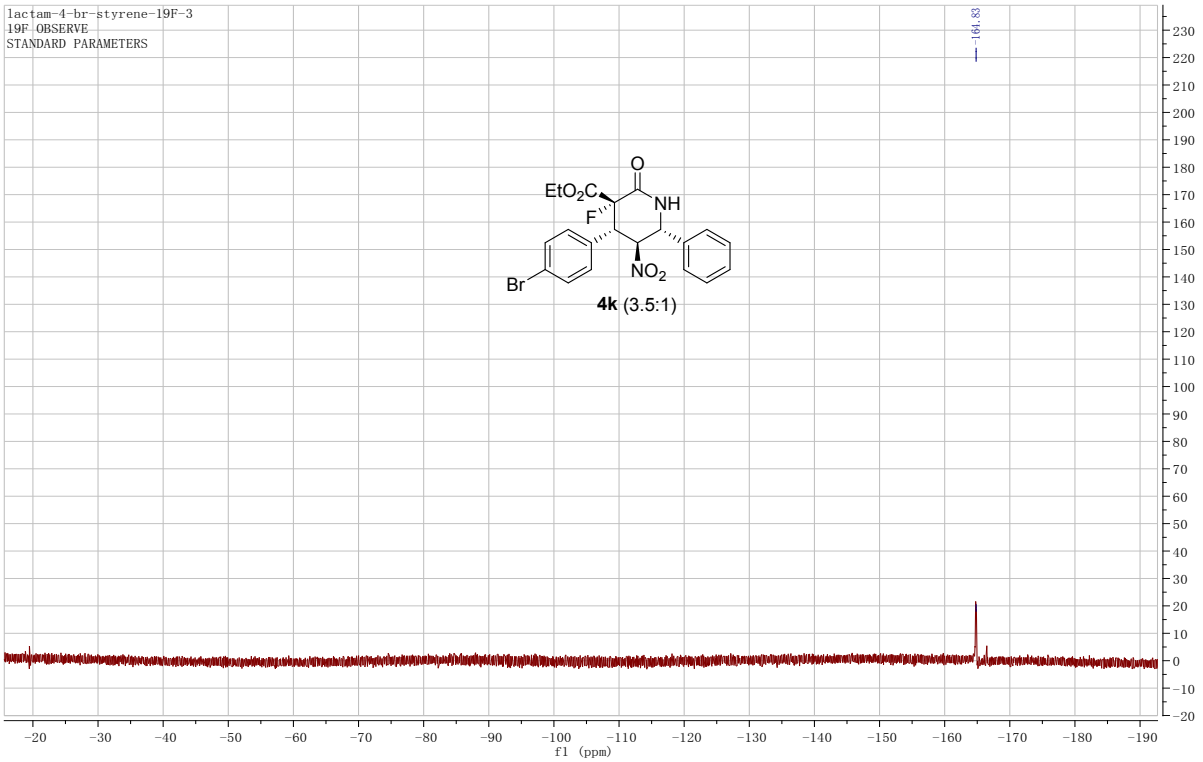

lactam-3-cl-styrene-13C-2
13C OBSERVE
EtO2C
F
O
NH
Cl
NO2
4j (3:1 dr)
f1 (ppm)

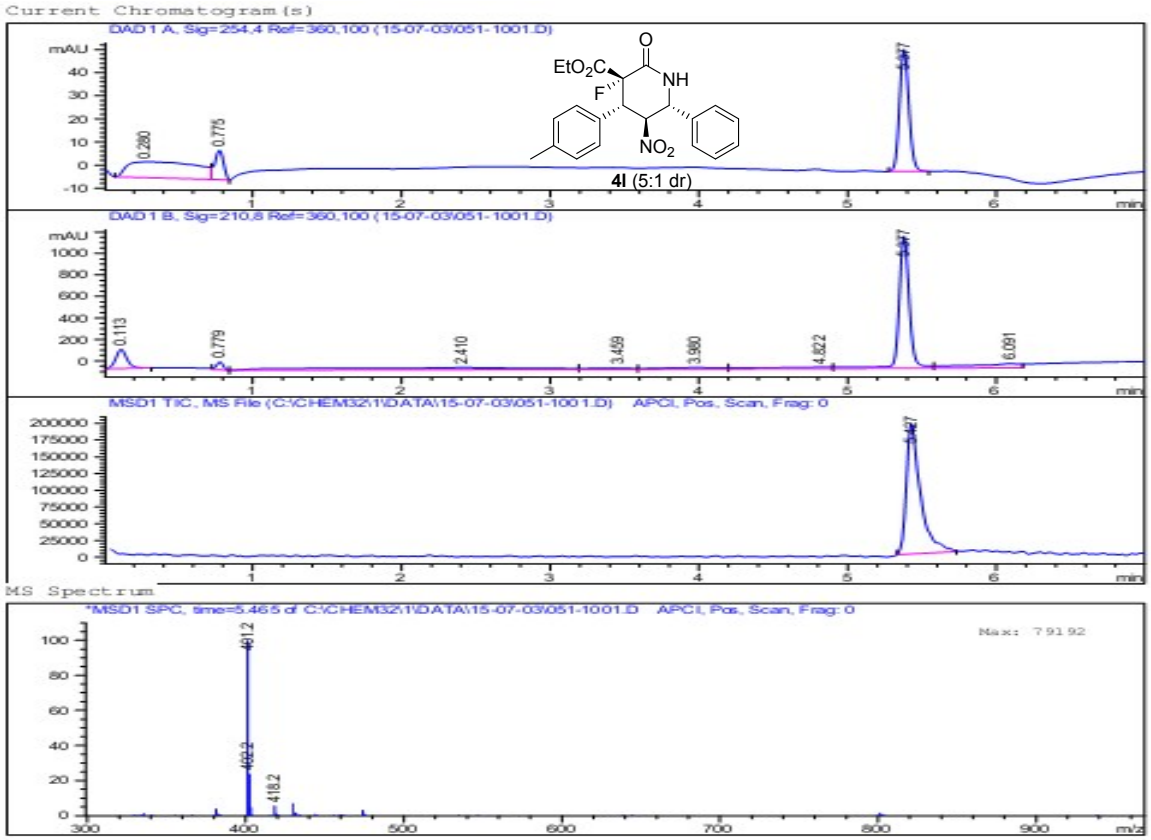

lactam-4-no2-aldehyde-19F
19F OBSERVE
STANDARD PARAMETERS
-163.19
EtO2C
O
NH
F
Cl
NO2
4j (3:1 dr)
f1 (ppm)

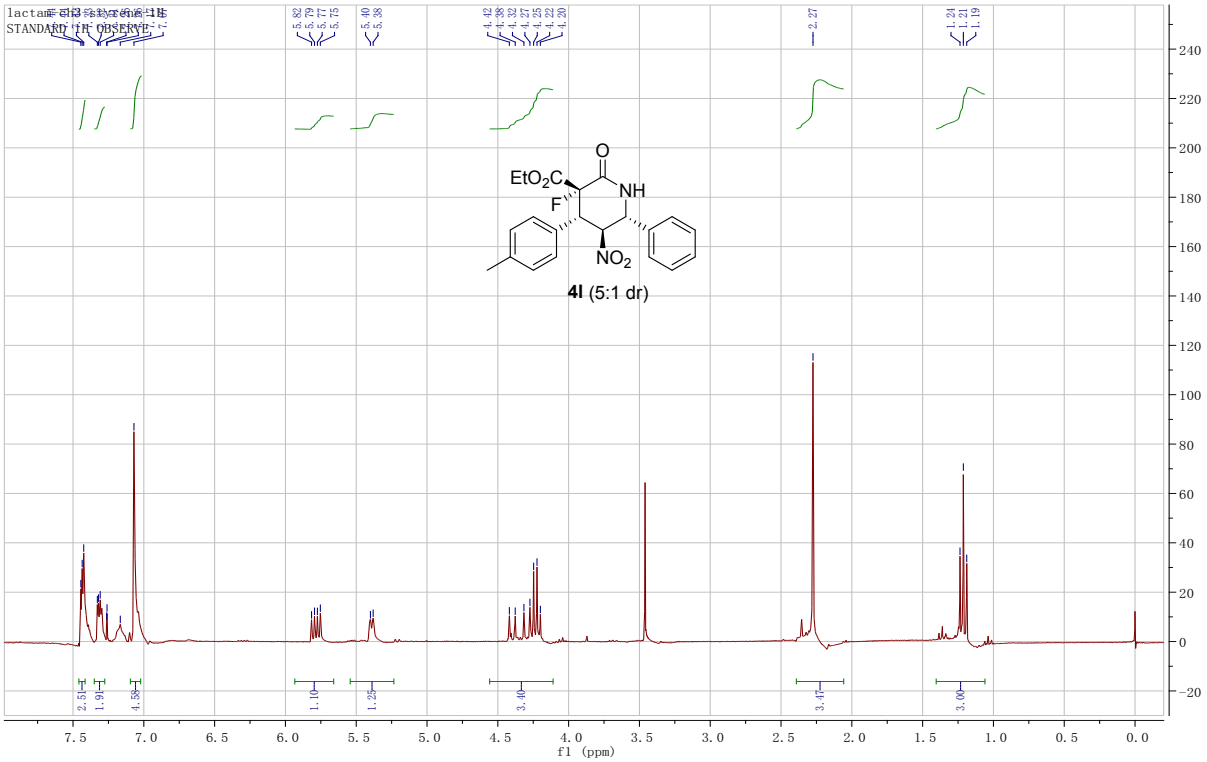

Current Chromatogram(s)
DAD1 A, Sig=254,4 Ref=360,100 (15-07-03\052-1501.D)
mAU
EtO2C
O
NH
F
Br
NO2
4k (3.5:1)
0.184
0.762
5.064
5.362
5.631
5.769
min
DAD1 B, Sig=210,8 Ref=360,100 (15-07-03\052-1501.D)
mAU
0.771
2.408
3.334
3.976
4.322
4.818
5.067
5.632
6.103
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\15-07-03\052-1501.D) APCI, Pos, Scan, Frag: 0
5.637
min
MS Spectrum
*MSD1 SPC, time=5.635 of C:\CHEM32\1\DATA\15-07-03\052-1501.D APCI, Pos, Scan, Frag: 0
Max: 68968
467.0
468.0
445.0
452.0
m/z

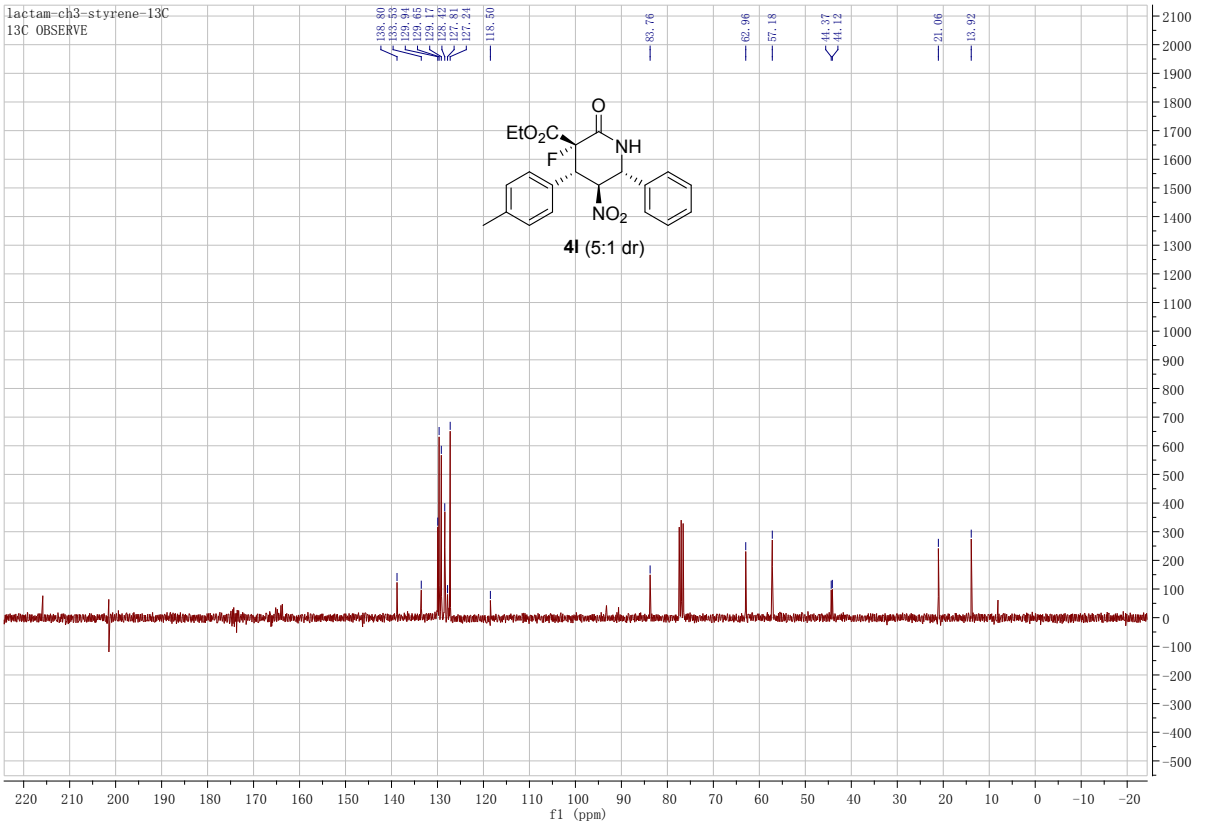

lactam-4-br-styrene-xin-1H
STANDARD-1H-OBSERVE
6.78
5.80
5.78
5.76
5.74
5.42
5.40
4.45
4.41
4.35
4.31
4.28
4.26
4.24
1.26
1.24
1.22
EtO2C
F
O
NH
NO2
Br
4k (3.5:1)
4.82
1.59
1.95
0.82
0.96
1.02
2.83
3.00
f1 (ppm)

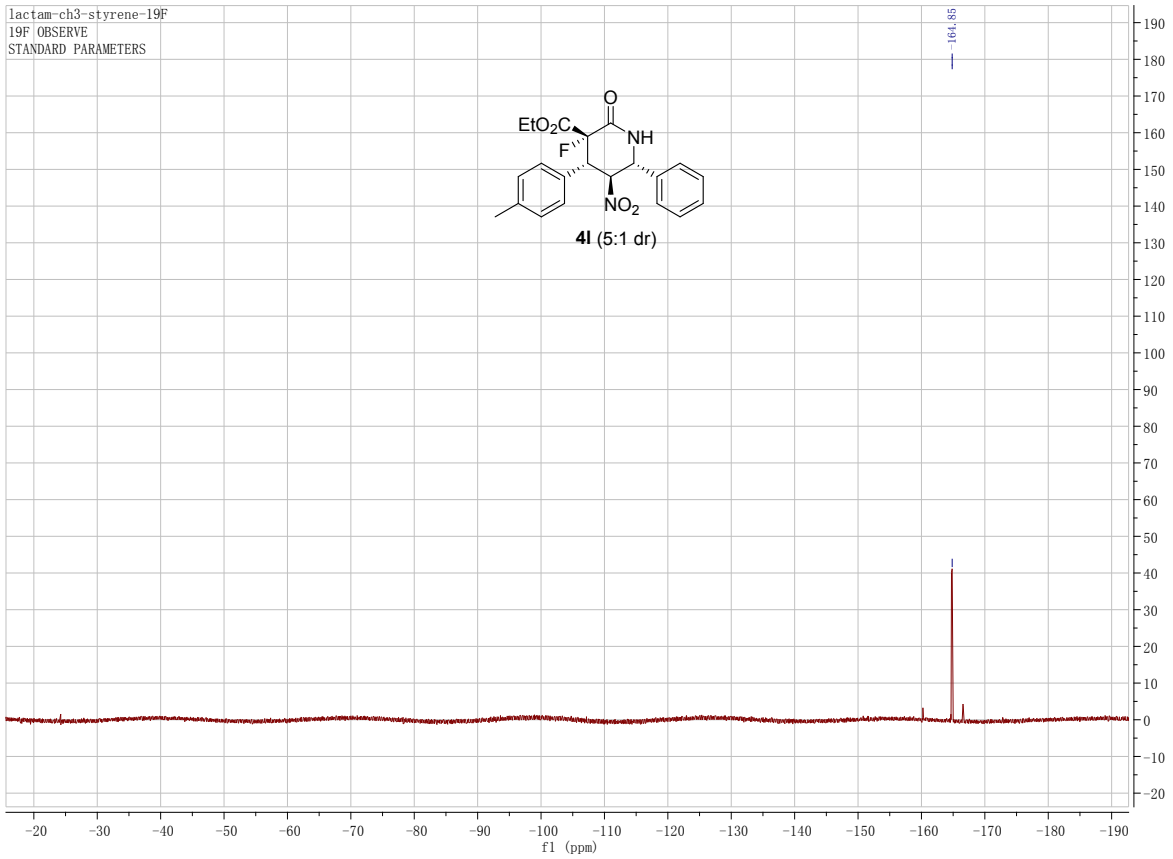

lactam-4-br-styrene-xin-13c
13C OBSERVE
134.32
133.09
132.62
129.73
129.62
129.31
129.21
128.66
124.82
87.90
63.23
60.37
50.56
50.31
14.07
f1 (ppm)

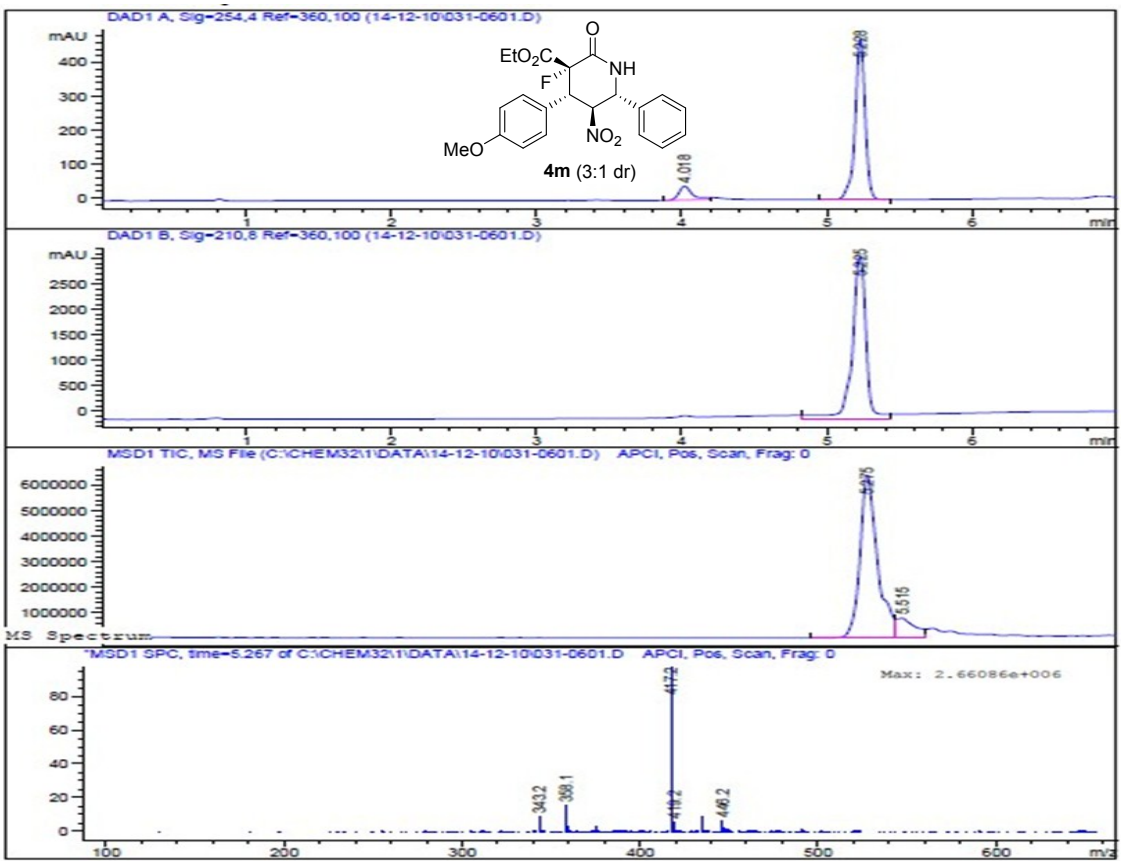

lactam-4-br-styrene-19F-3
19F OBSERVE
STANDARD PARAMETERS
-161.83
EtO2C
O
NH
F
NO2
Br
4k (3.5:1)
f1 (ppm)

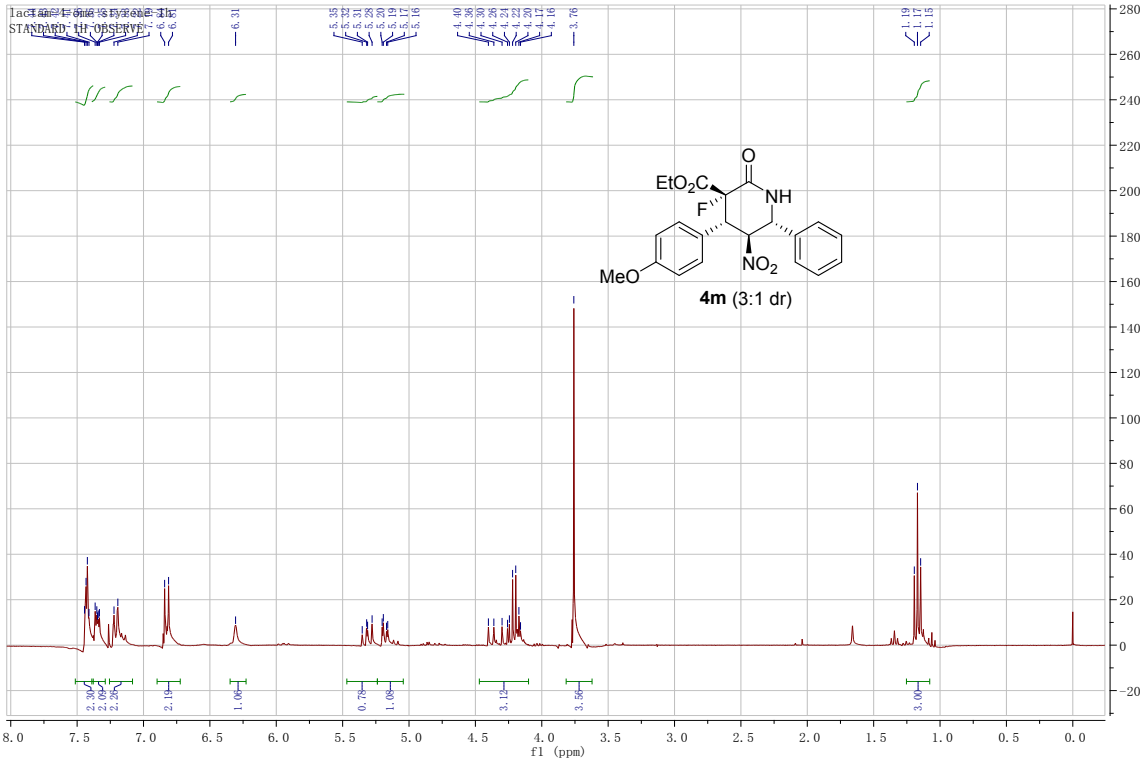

Current Chromatogram(s)
DAD1 A, Sig=254,4 Ref=360,100 (15-07-03\051-1001.D)
DAD1 B, Sig=210,8 Ref=360,100 (15-07-03\051-1001.D)
MSD1 TIC, MS File (C:\CHEM32\1\DATA\15-07-03\051-1001.D) APCI, Pos, Scan, Frag: 0
EtO2C
O
NH
F
NO2
4l (5:1 dr)
MS Spectrum
*MSD1 SPC, time=5.465 of C:\CHEM32\1\DATA\15-07-03\051-1001.D APCI, Pos, Scan, Frag: 0
Max: 79192
461.2
462.2
418.2
m/z

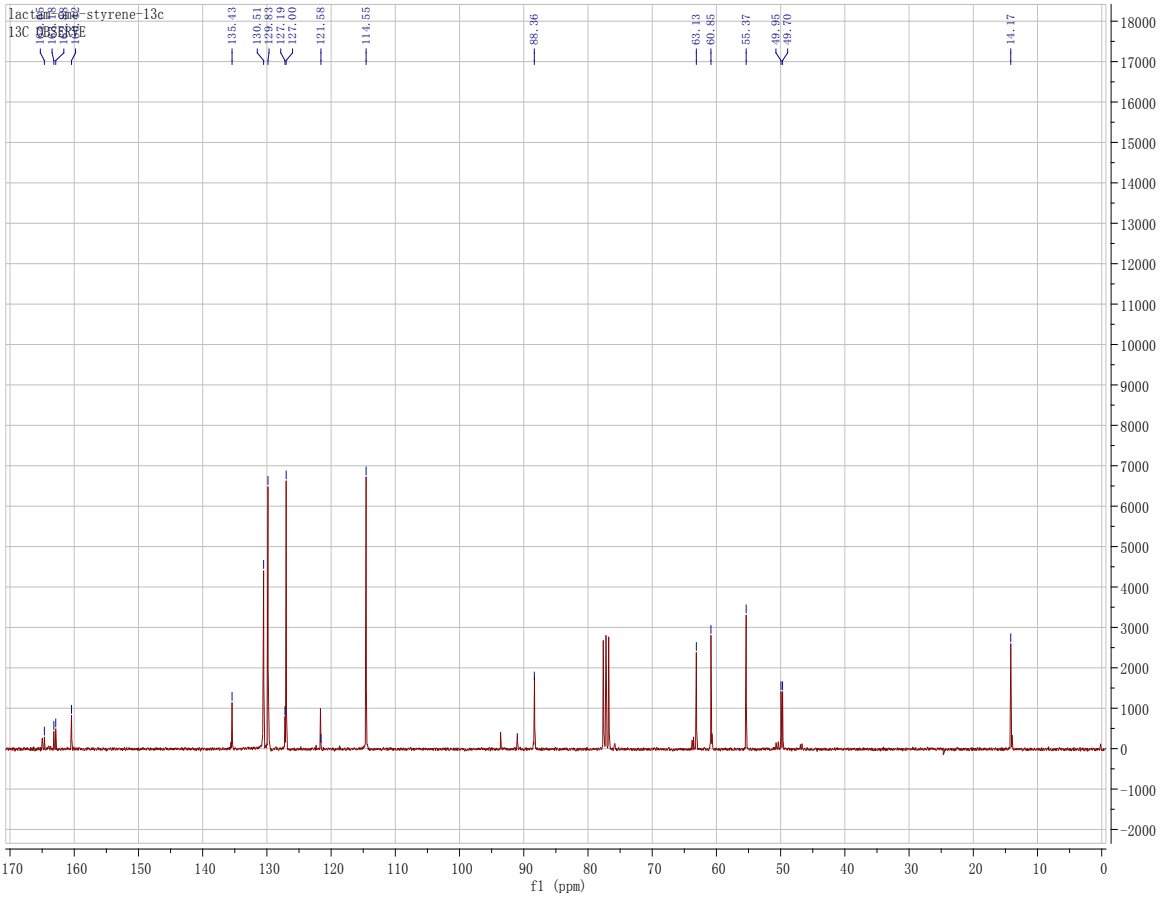

STANDARD 1H OBSERVE
EtO2C
F
O
NH
NO2
4l (5:1 dr)
f1 (ppm)

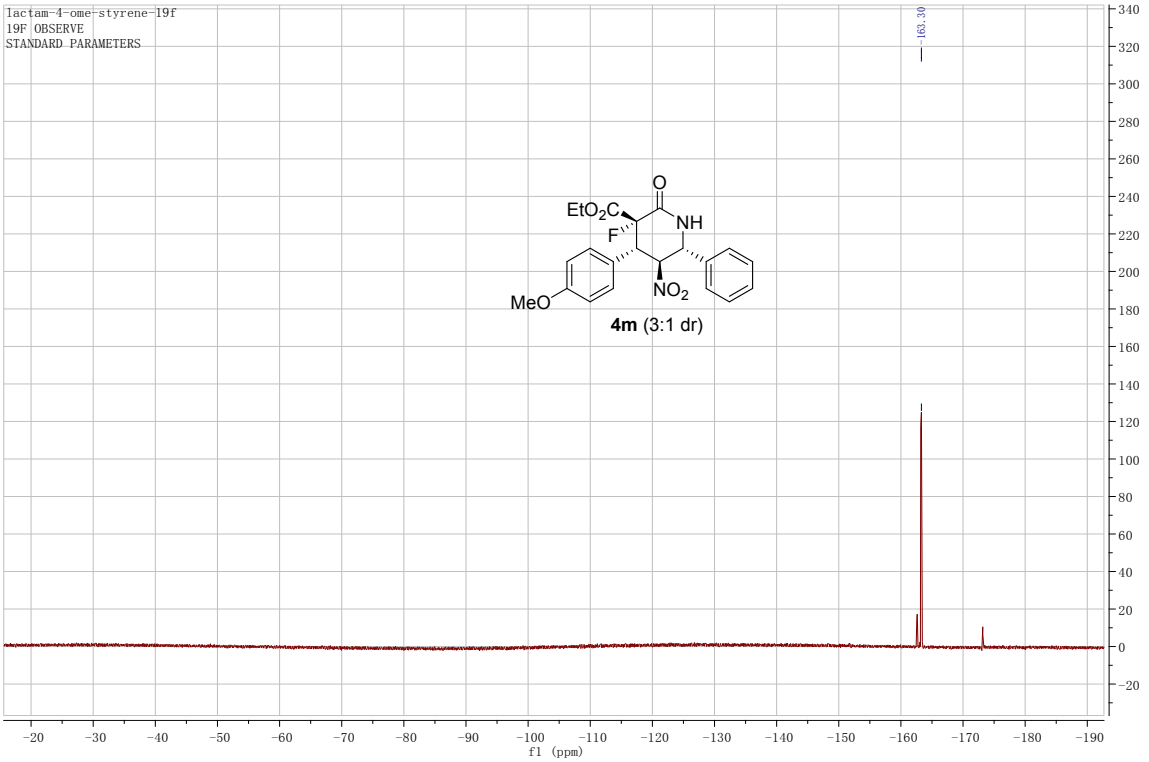

13C OBSERVE
EtO2C
F
O
NH
NO2
4l (5:1 dr)
f1 (ppm)

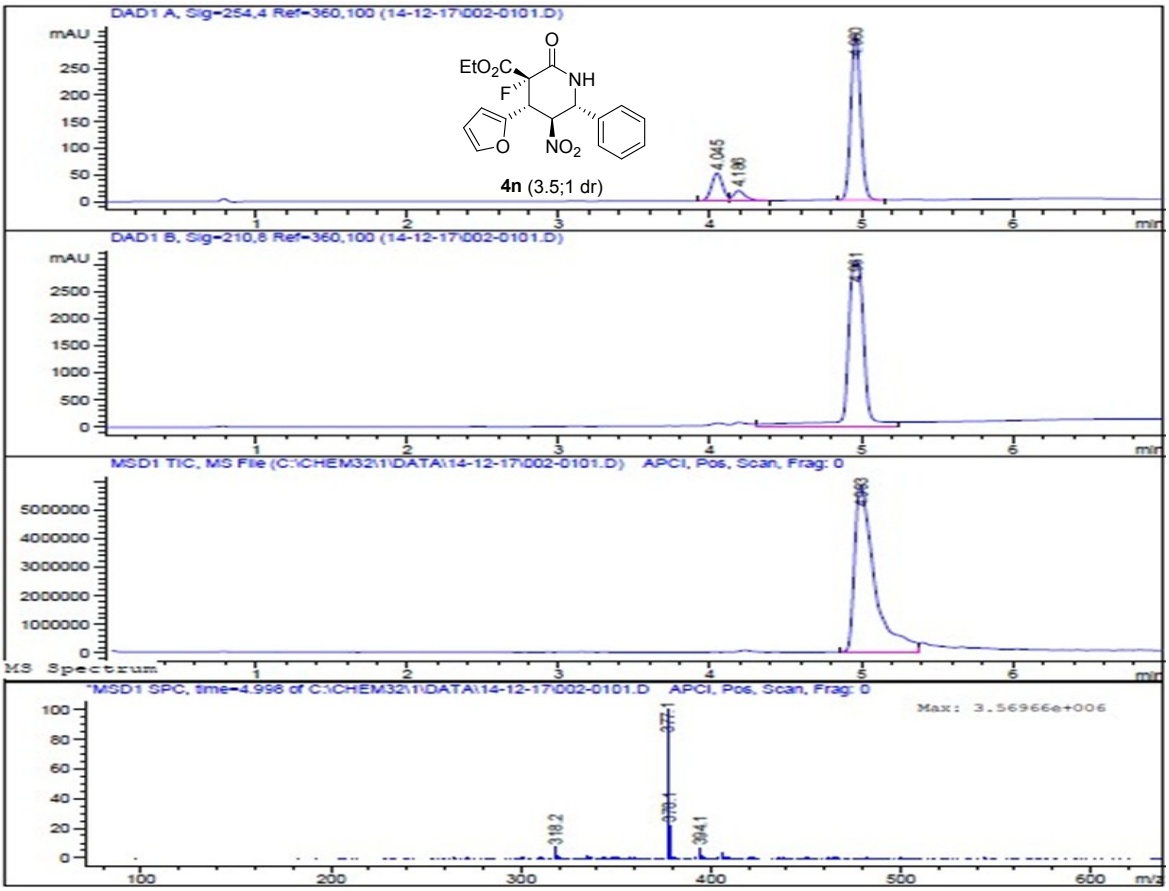

lactam-ch3-styrene-19F
19F OBSERVE
STANDARD PARAMETERS
-164.85
EtO2C
F
O
NH
NO2
4l (5:1 dr)
f1 (ppm)

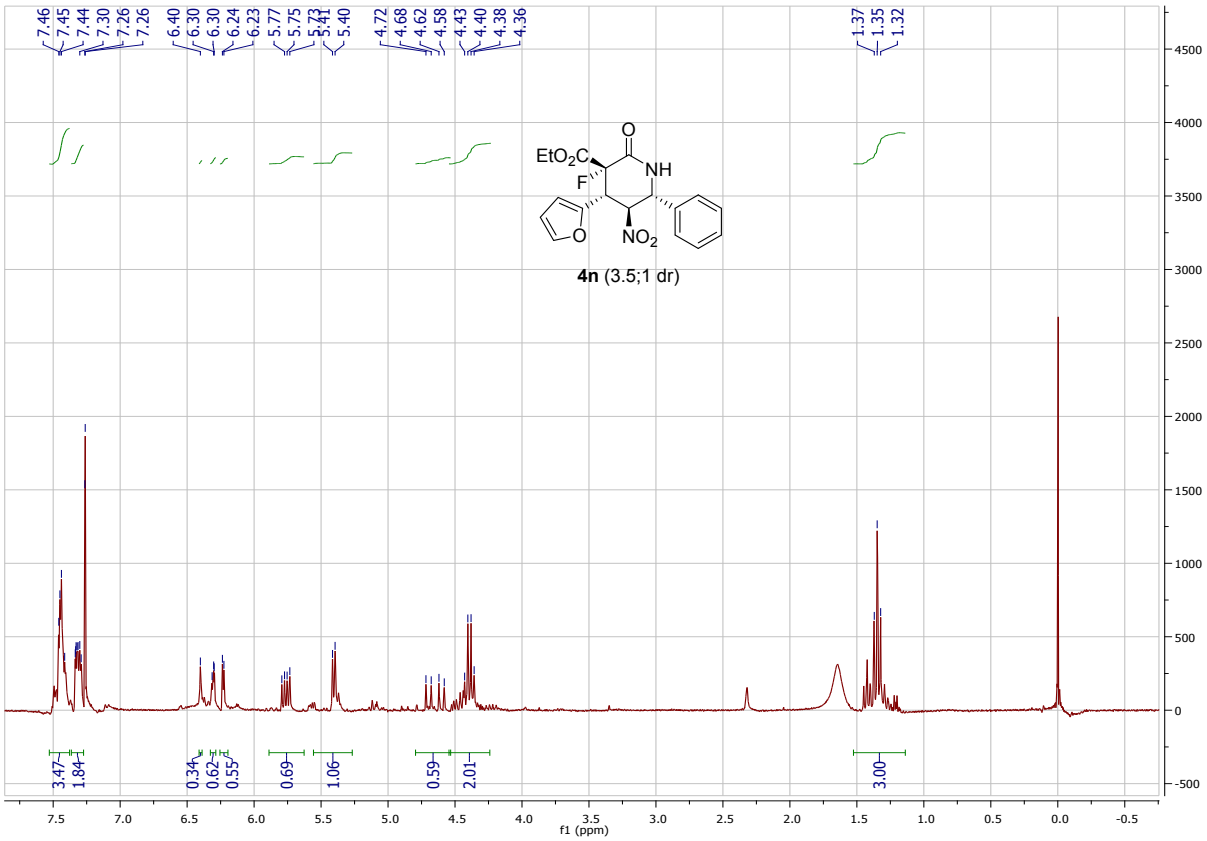

DAD1 A, Sig=254,4 Ref=360,100 (14-12-10\031-0601.D)
mAU
4.018
min
DAD1 B, Sig=210,8 Ref=360,100 (14-12-10\031-0601.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-12-10\031-0601.D) APCI, Pos, Scan, Frag: 0
5.515
MS Spectrum
MSD1 SPC, time=5.267 of C:\CHEM32\1\DATA\14-12-10\031-0601.D APCI, Pos, Scan, Frag: 0
Max: 2.66086e+006
343.2
359.1
417.2
461.2
m/z
EtO2C
F
O
NH
NO2
MeO
4m (3:1 dr)

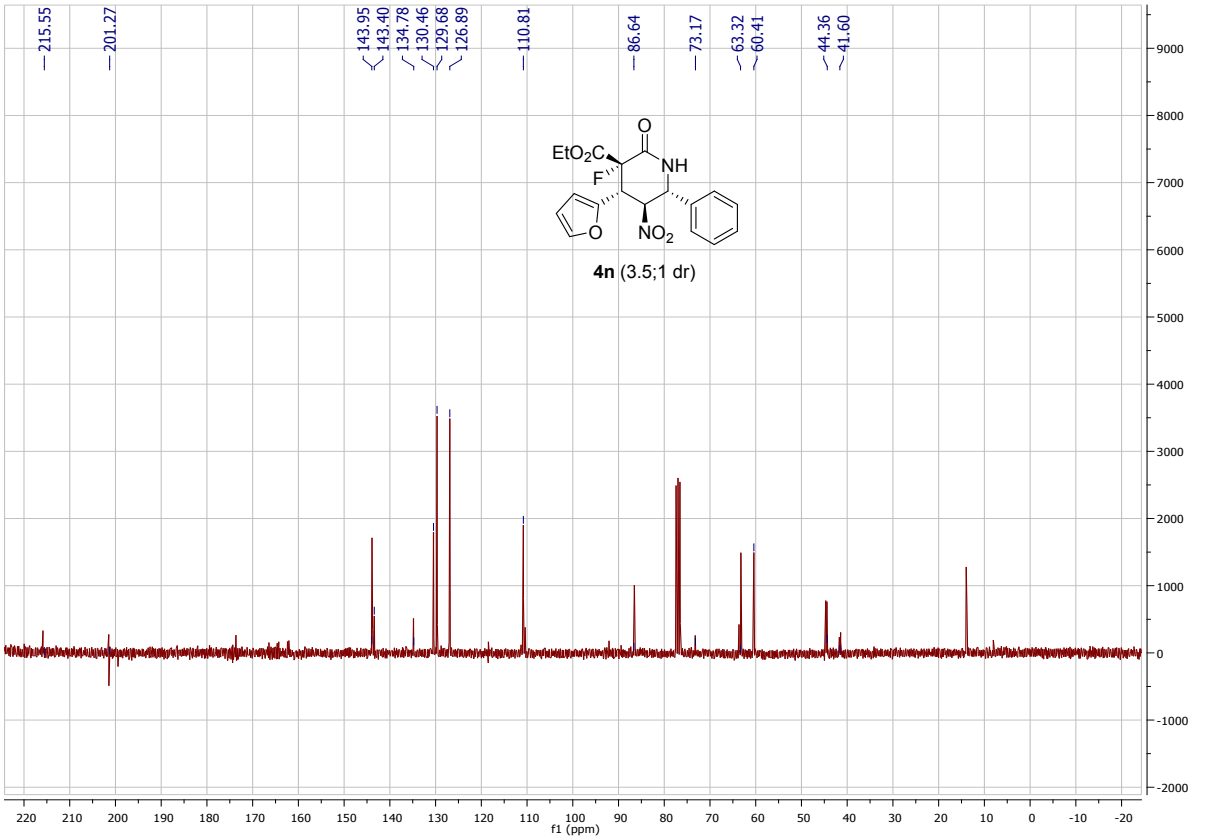

STANDARD 1H OBSERVE
6.31
5.35
5.32
5.31
5.28
5.20
5.19
5.17
5.16
4.40
4.36
4.30
4.26
4.24
4.22
4.20
4.17
4.16
3.76
1.19
1.17
1.15
O
EtO2C
NH
F
NO2
MeO
4m (3:1 dr)
2.30
2.09
2.26
2.19
1.06
0.78
1.08
3.12
3.56
3.00
f1 (ppm)

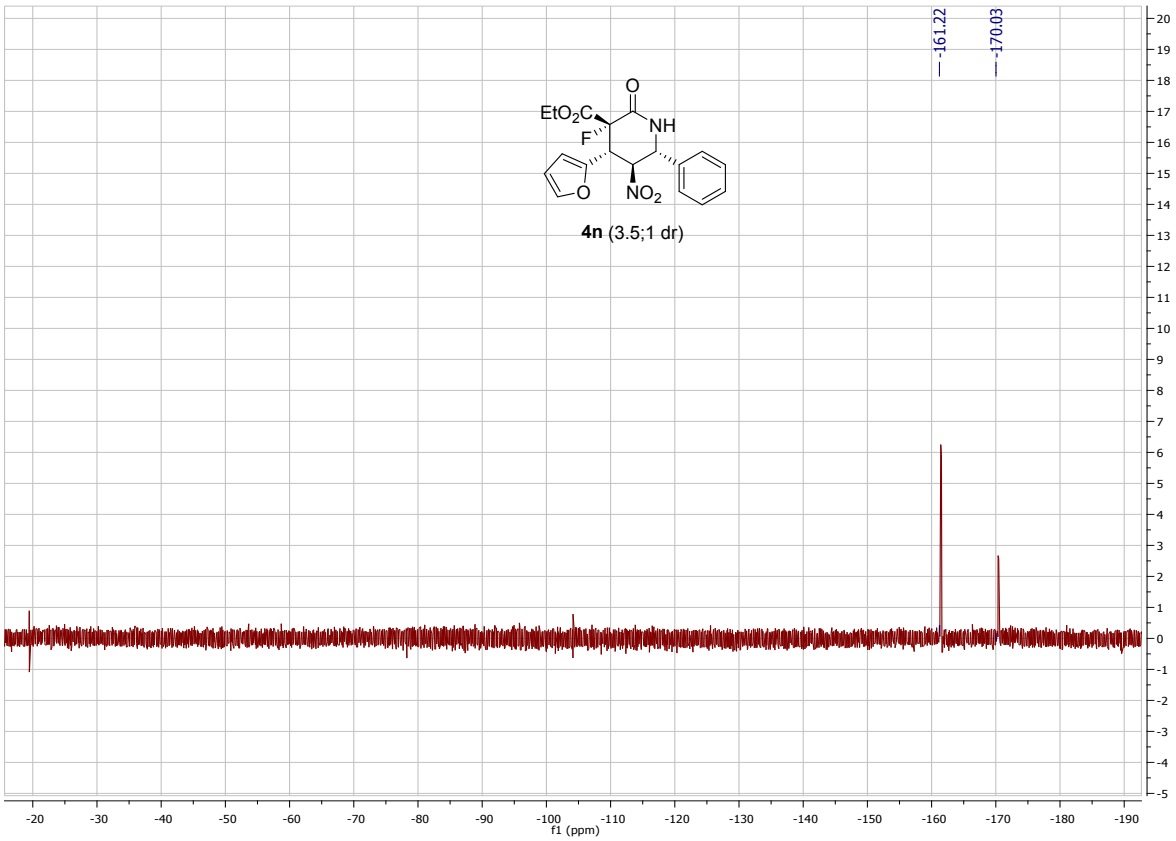

13C OBSERVE
135.43
130.51
129.83
127.19
127.00
121.58
114.55
88.36
63.13
60.85
55.37
49.95
49.70
14.17
f1 (ppm)


lactam-4-ome-styrene-19f
19F OBSERVE
STANDARD PARAMETERS
-163.30
EtO2C
F
O
NH
NO2
MeO
4m (3:1 dr)
f1 (ppm)

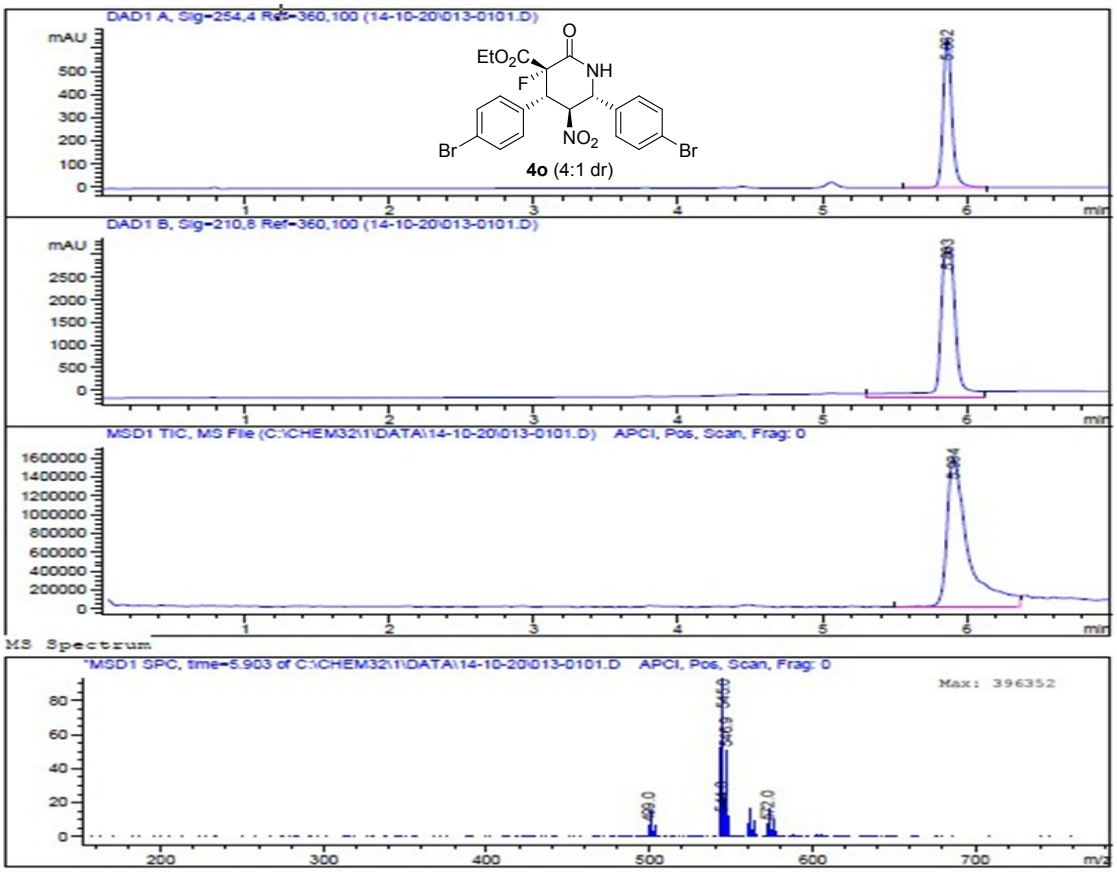

DAD1 A, Sig=254,4 Ref=360,100 (14-12-17\002-0101.D)
mAU
4.045
4.188
min
DAD1 B, Sig=210,8 Ref=360,100 (14-12-17\002-0101.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-12-17\002-0101.D) APCI, Pos, Scan, Frag: 0
MS Spectrum
min
*MSD1 SPC, time=4.998 of C:\CHEM32\1\DATA\14-12-17\002-0101.D APCI, Pos, Scan, Frag: 0
Max: 3.56966e+006
377.1
318.2
394.1
m/z
EtO2C
F
O
NH
NO2
O
4n (3.5;1 dr)


7.46
7.45
7.44
7.30
7.26
7.26
6.40
6.30
6.30
6.24
6.23
5.77
5.75
5.73
5.41
5.40
4.72
4.68
4.62
4.58
4.43
4.40
4.38
4.36
1.37
1.35
1.32
EtO2C
F
O
NH
O
NO2
4n (3.5;1 dr)
3.47
1.84
0.34
0.62
0.55
0.69
1.06
0.59
2.01
3.00
f1 (ppm)

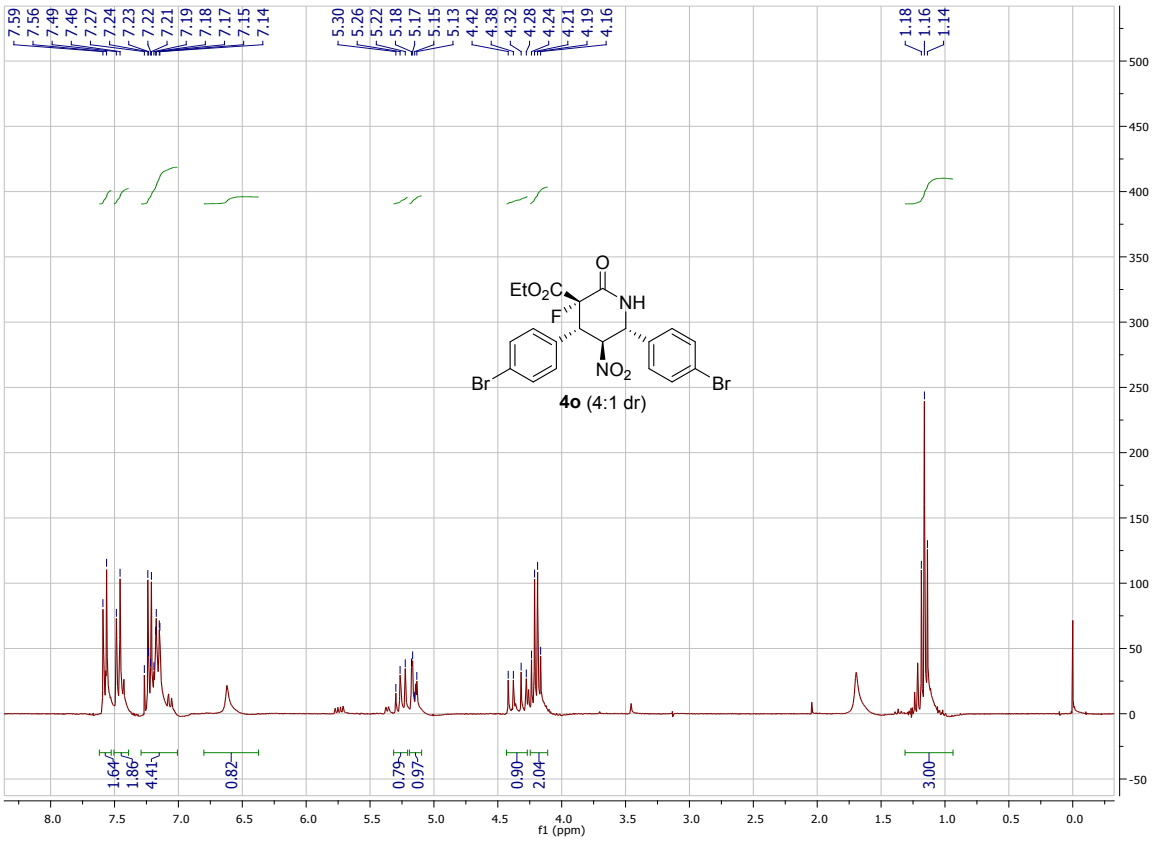

215.55
201.27
143.95
143.40
134.78
130.46
129.68
126.89
110.81
86.64
73.17
63.32
60.41
44.36
41.60
EtO2C
F
O
NH
O
NO2
4n (3.5;1 dr)
f1 (ppm)

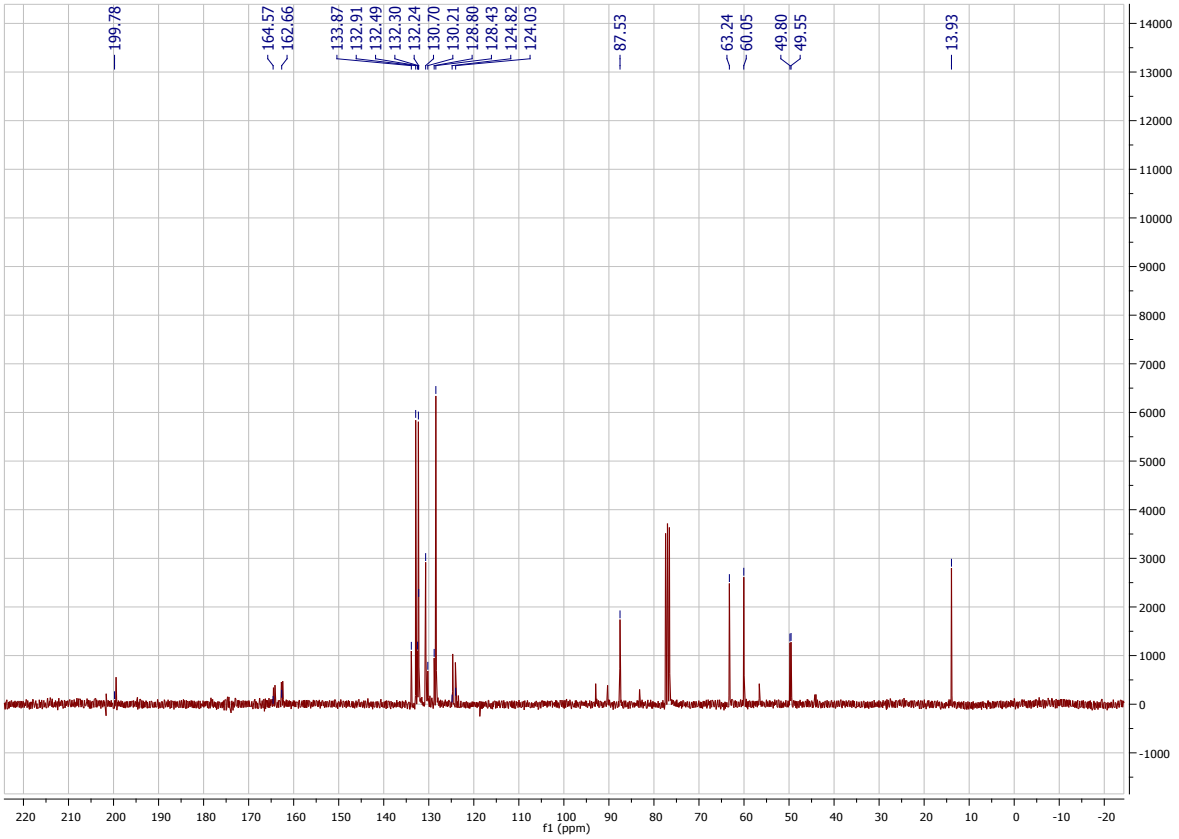


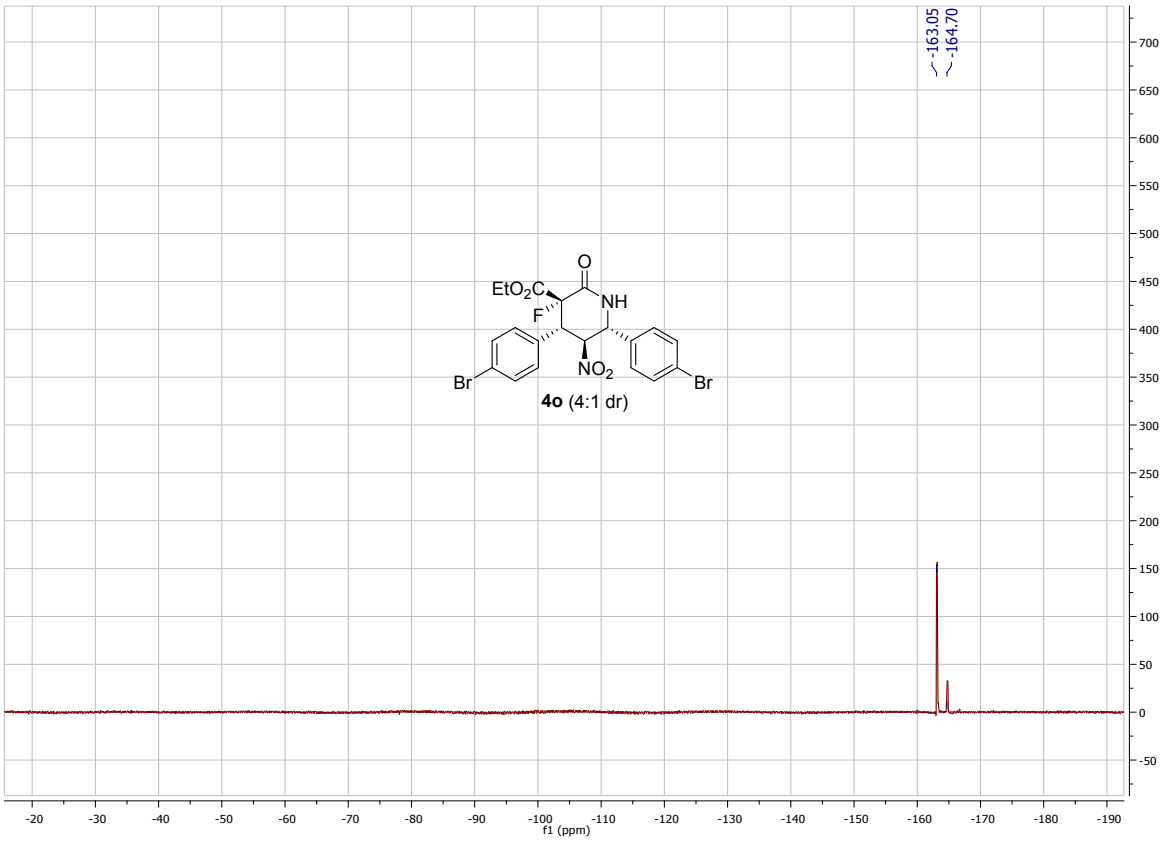
4n (3.5;1 dr)



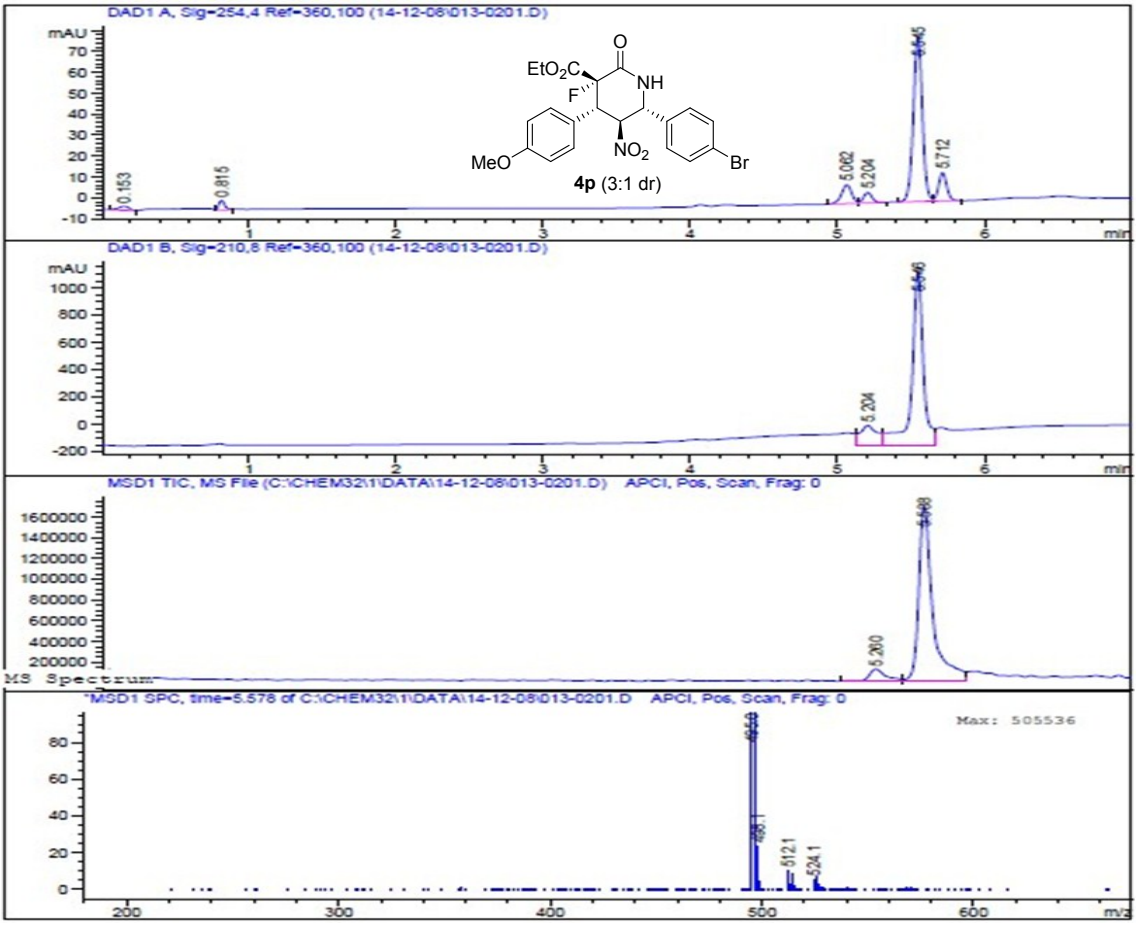
4o (4:1 dr)


7.59 7.56 7.49 7.46 7.27 7.24 7.23 7.22 7.21 7.19 7.18 7.17 7.15 7.14
5.30 5.26 5.22 5.18 5.17 5.15 5.13
4.42 4.38 4.32 4.28 4.24 4.21 4.19 4.16
1.18 1.16 1.14
EtO2C
O
NH
F
NO2
Br
Br
4o (4:1 dr)
1.64 1.86 4.41 0.82 0.79 0.97 0.90 2.04 3.00
f1 (ppm)

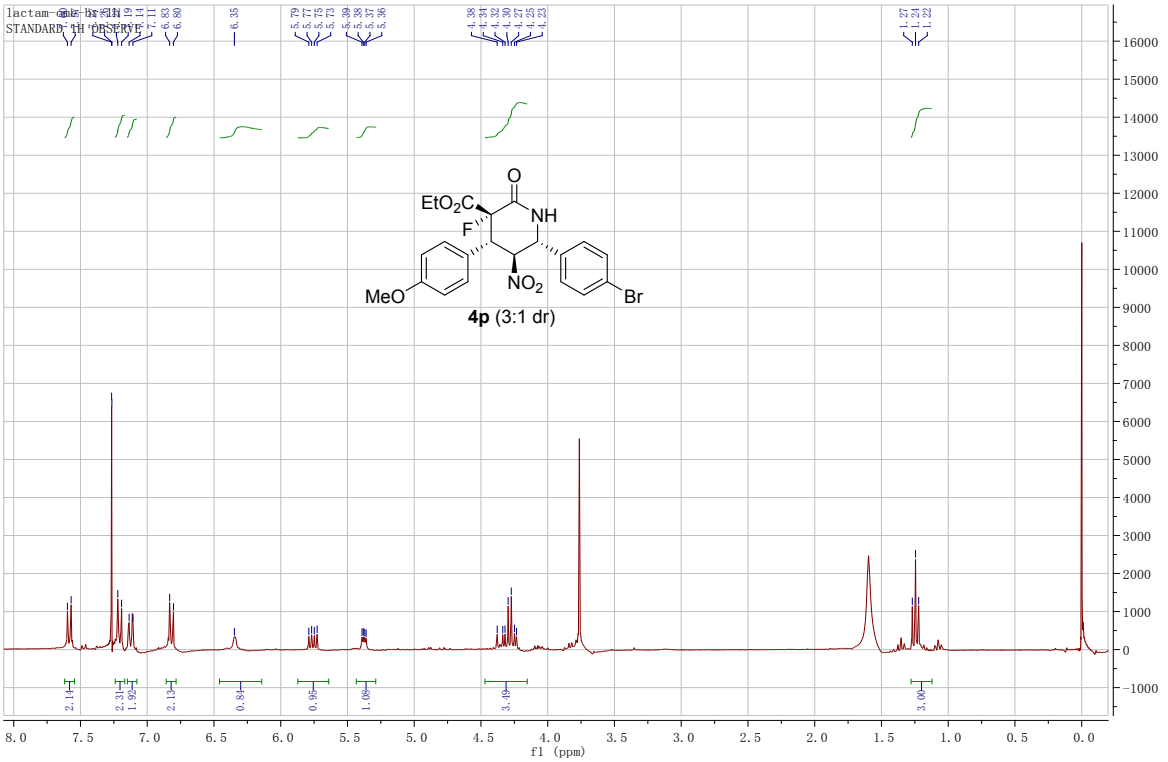

199.78
164.57 162.66
133.87 132.91 132.49 132.30 132.24 130.70 130.21 128.80 128.43 124.82 124.03
87.53
63.24 60.05
49.80 49.55
13.93
f1 (ppm)

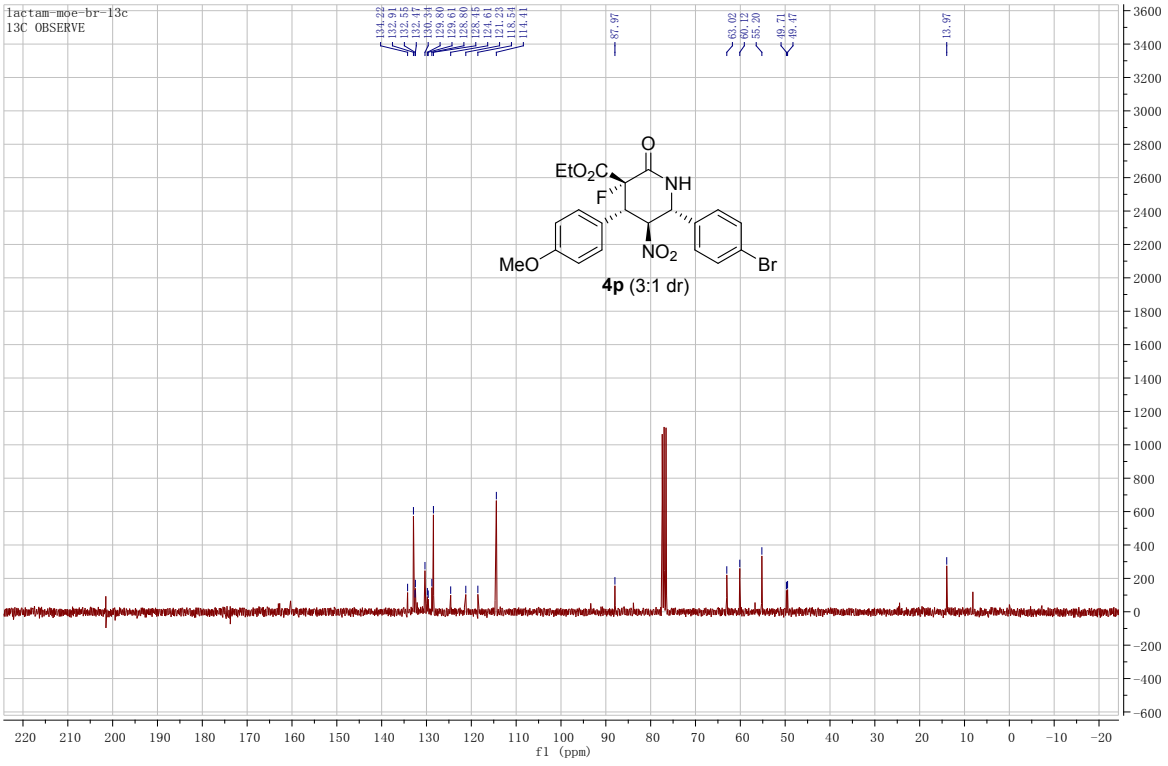


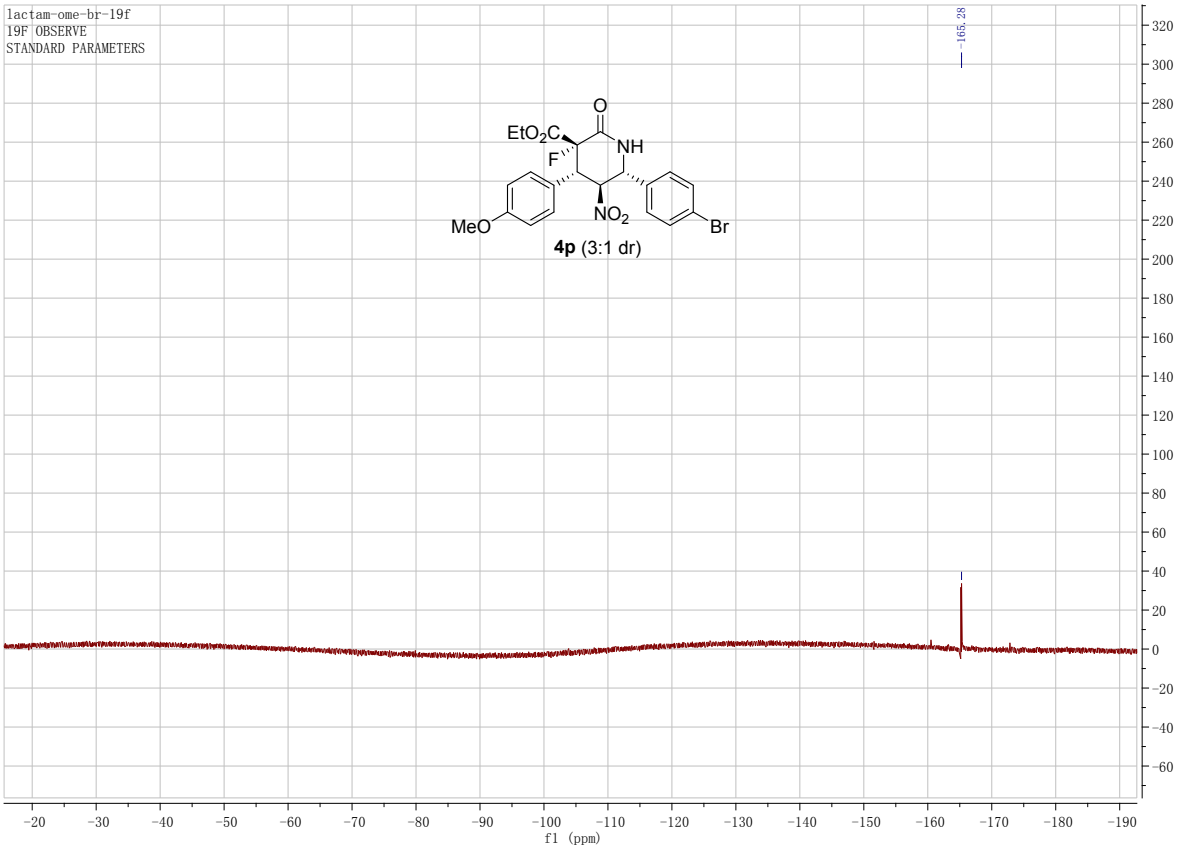
4o (4:1 dr)

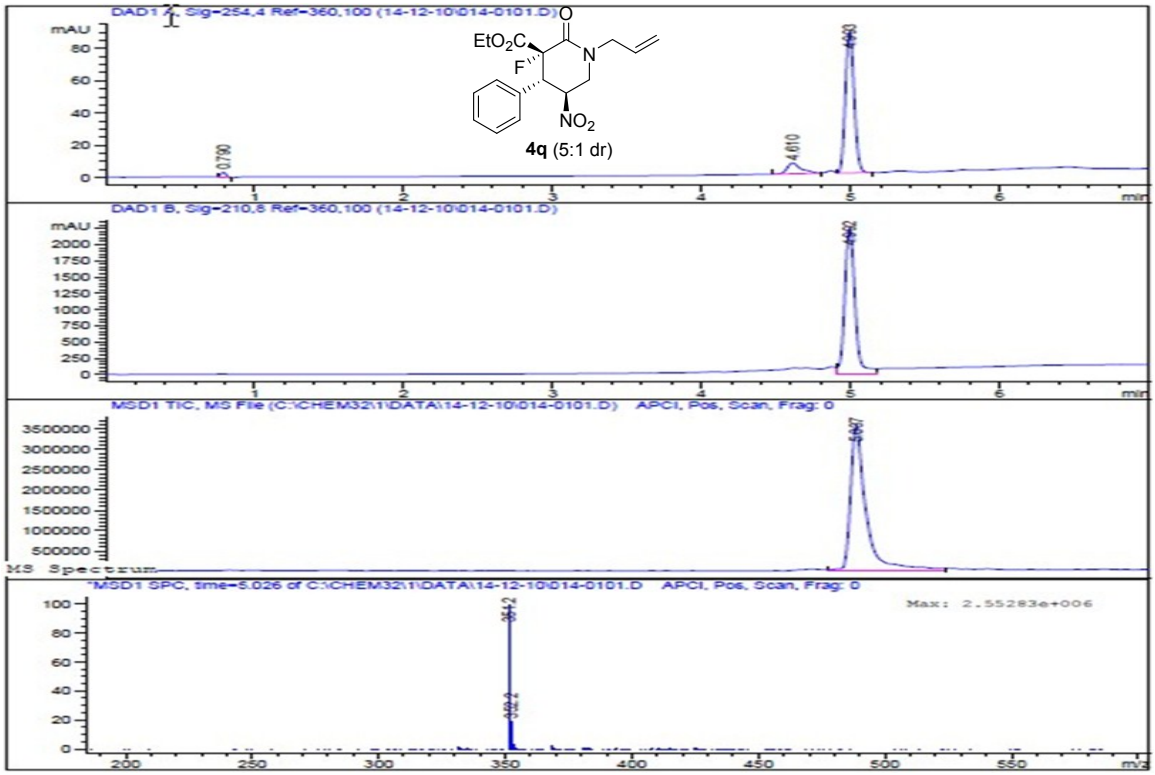


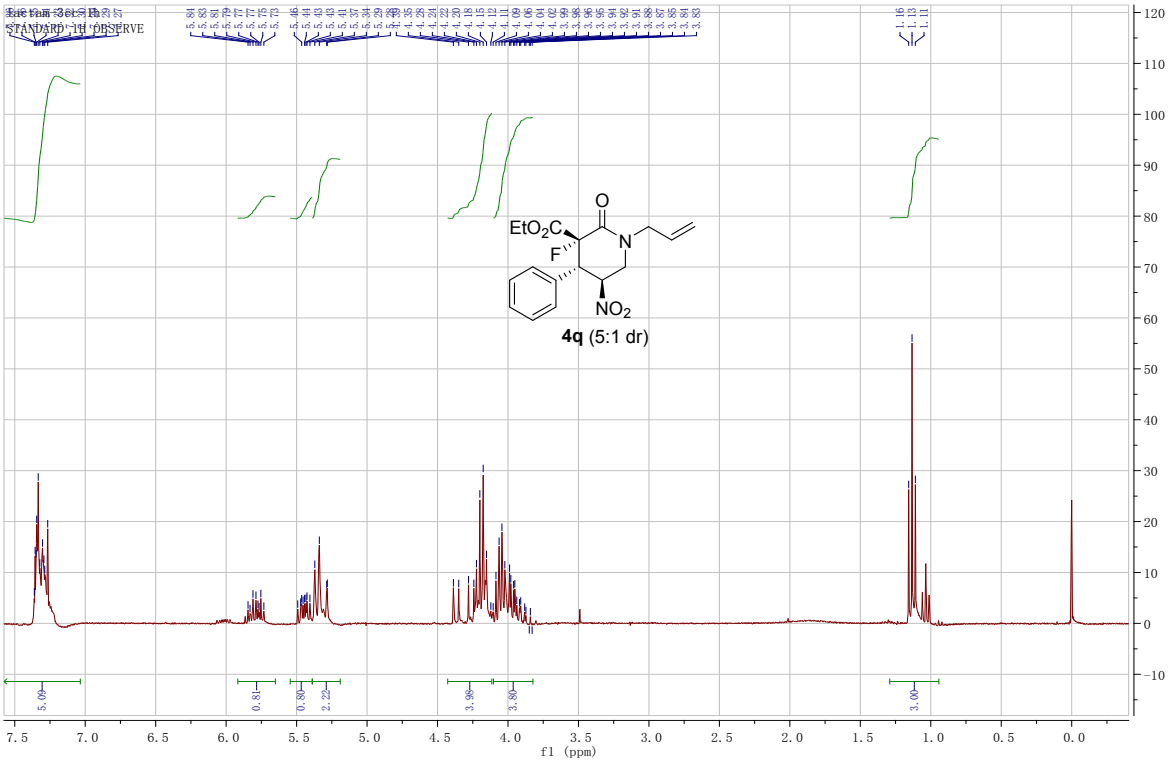
4p (3:1 dr)

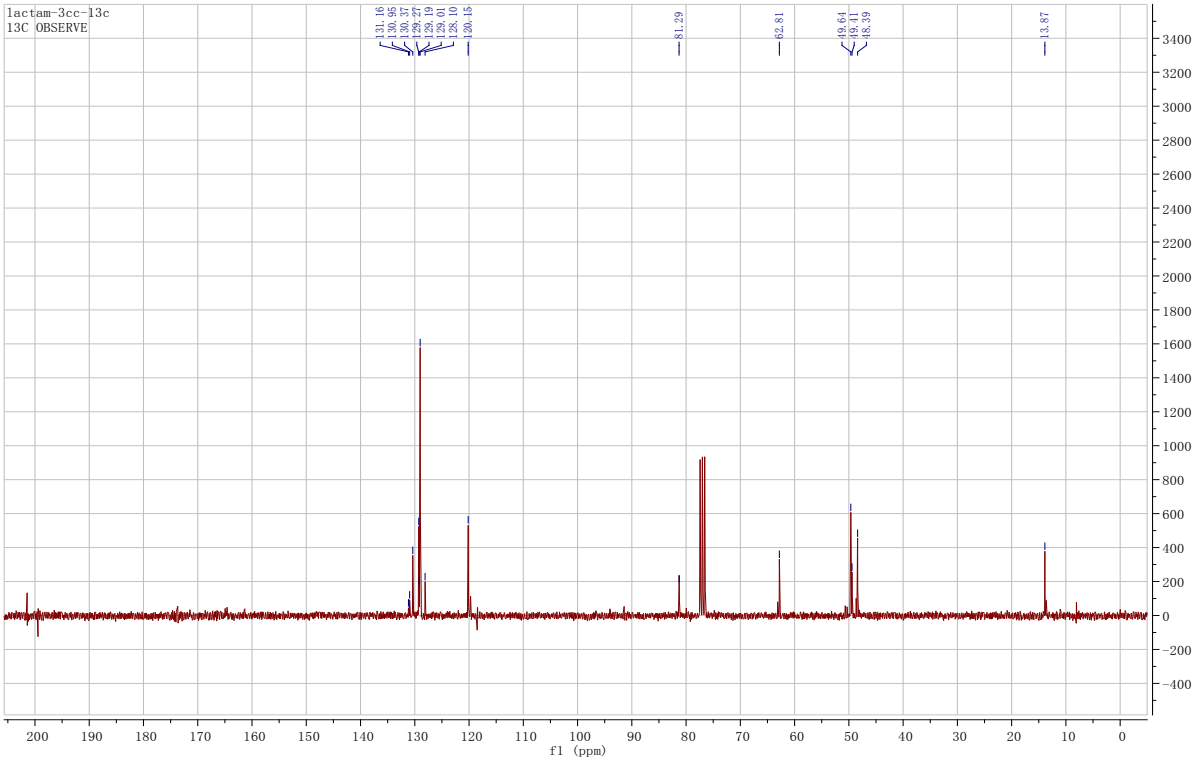

STANDARD 1H OBSERVE
EtO2C
F
NH
O
NO2
MeO
Br
4p (3:1 dr)
f1 (ppm)

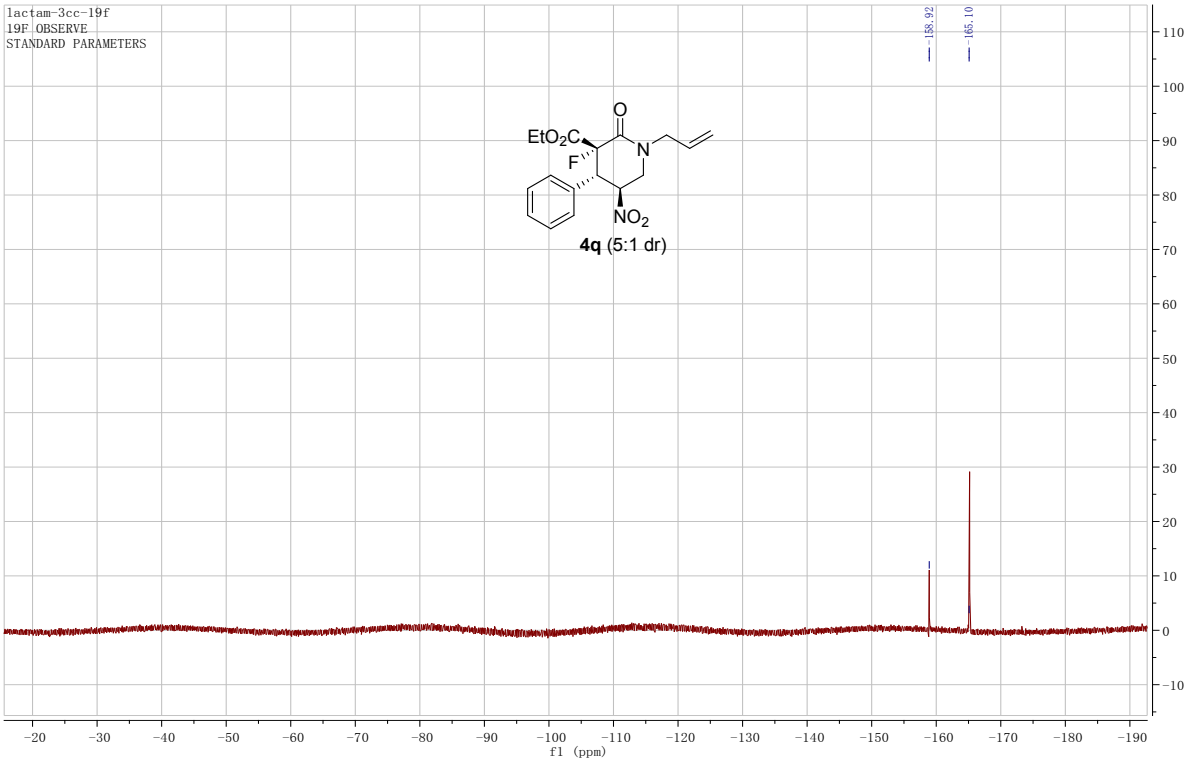

13C OBSERVE
EtO2C
F
NH
O
NO2
MeO
Br
4p (3:1 dr)
f1 (ppm)


lactam-ome-br-19f
19F OBSERVE
STANDARD PARAMETERS
-165.28
EtO2C
F
O
NH
NO2
MeO
Br
4p (3:1 dr)
f1 (ppm)

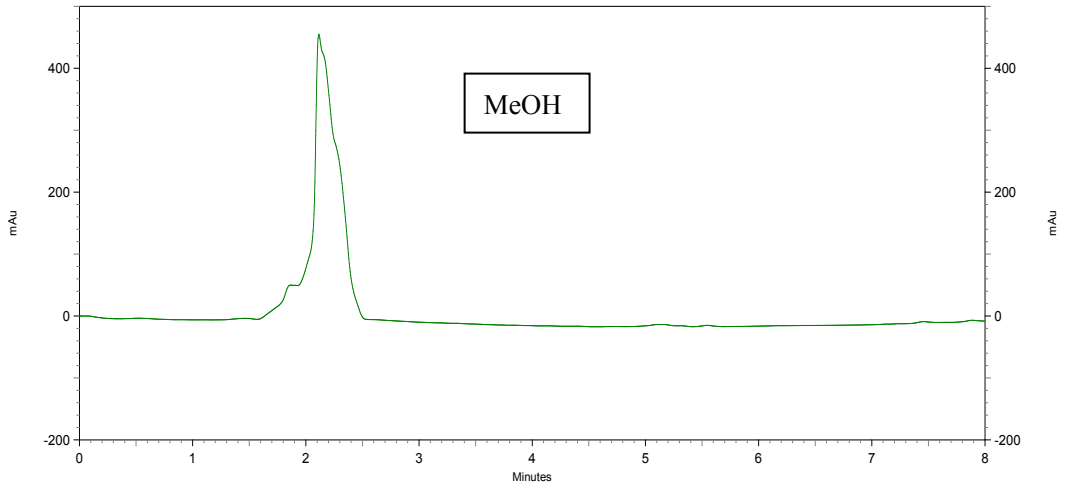

DAD1 A, Sig=254,4 Ref=360,100 (14-12-10\014-0101.D)
mAU
4.610
min
DAD1 B, Sig=210,8 Ref=360,100 (14-12-10\014-0101.D)
mAU
min
MSD1 TIC, MS File (C:\CHEM32\1\DATA\14-12-10\014-0101.D) APCI, Pos, Scan, Frag: 0
MS Spectrum
*MSD1 SPC, time=5.026 of C:\CHEM32\1\DATA\14-12-10\014-0101.D APCI, Pos, Scan, Frag: 0
Max: 2.55283e+006
EtO2C
F
O
N
NO2
4q (5:1 dr)

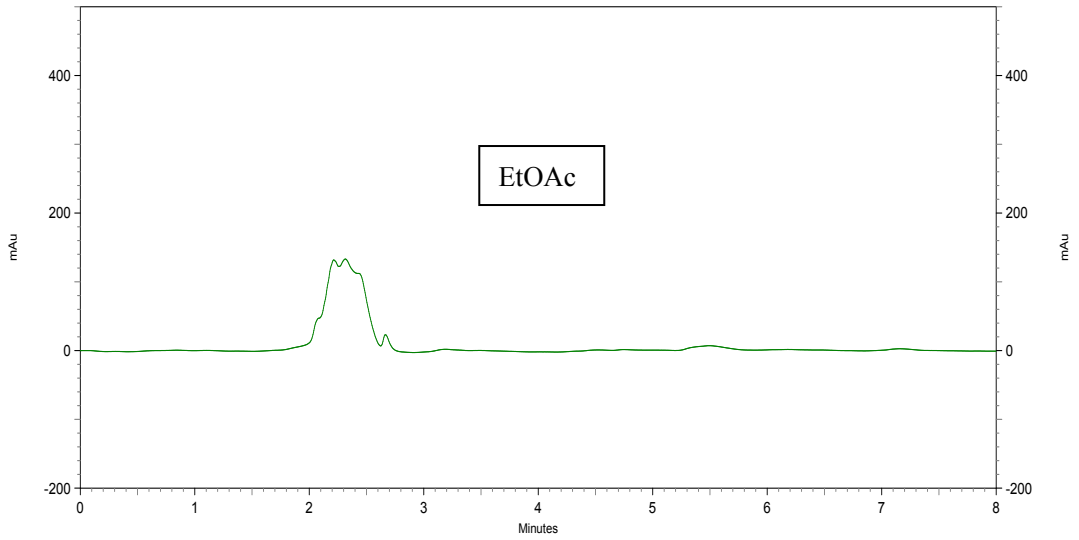

STANDARD 1H OBSERVE
EtO2C
F
O
N
NO2
4q (5:1 dr)
f1 (ppm)

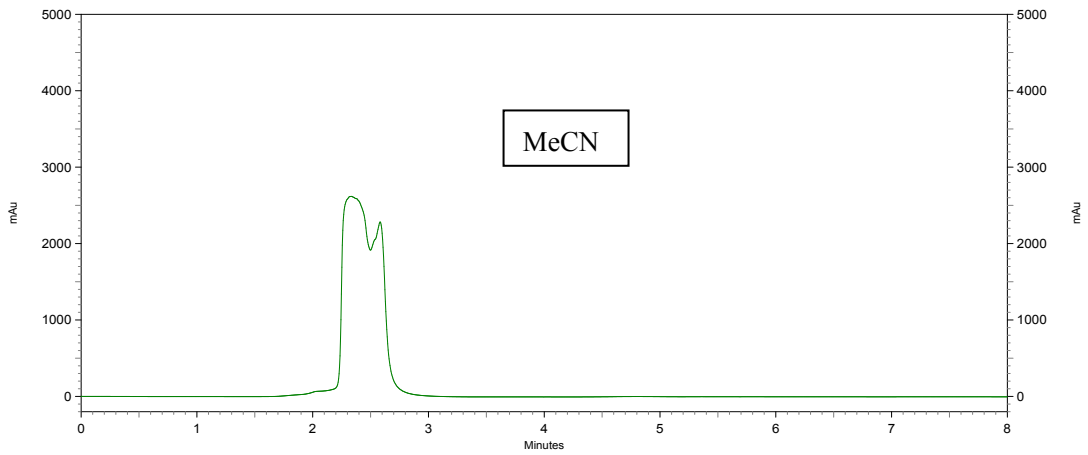

1actam-3cc-13c
13C OBSERVE
f1 (ppm)

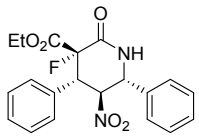

lactam-3cc-19f
19F OBSERVE
STANDARD PARAMETERS
-158.92
-165.10
O
EtO2C
F
N
NO2
4q (5:1 dr)
f1 (ppm)

6. Chiral LC of Products

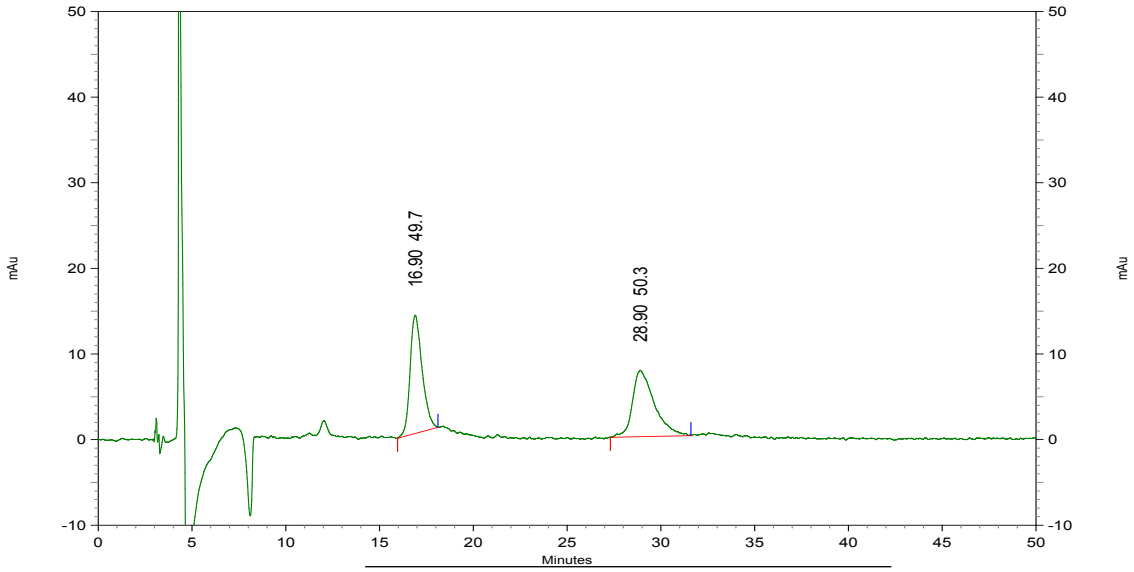




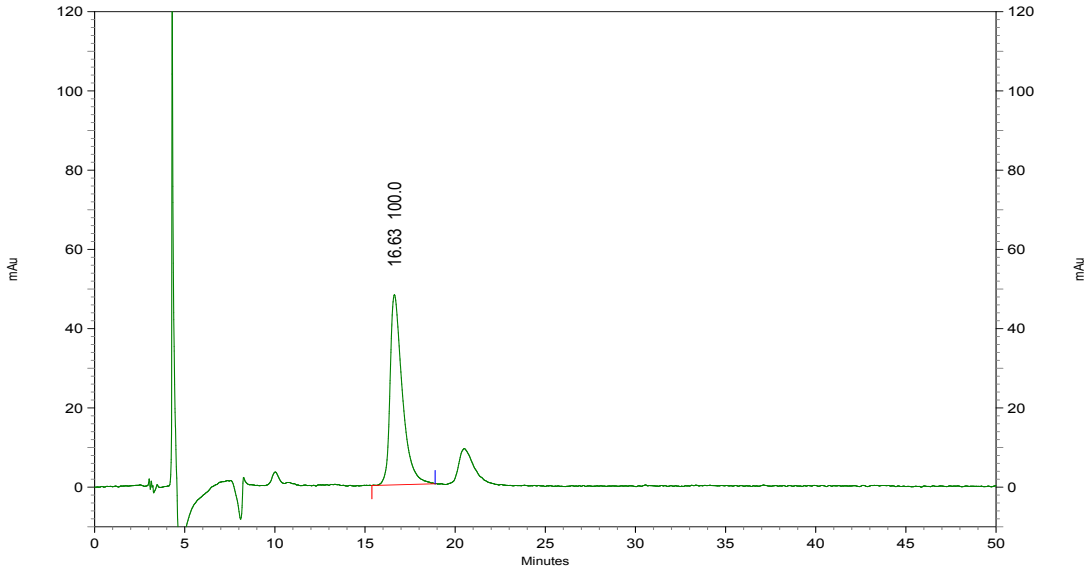




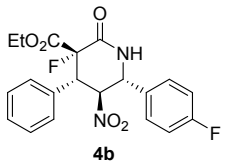
4a



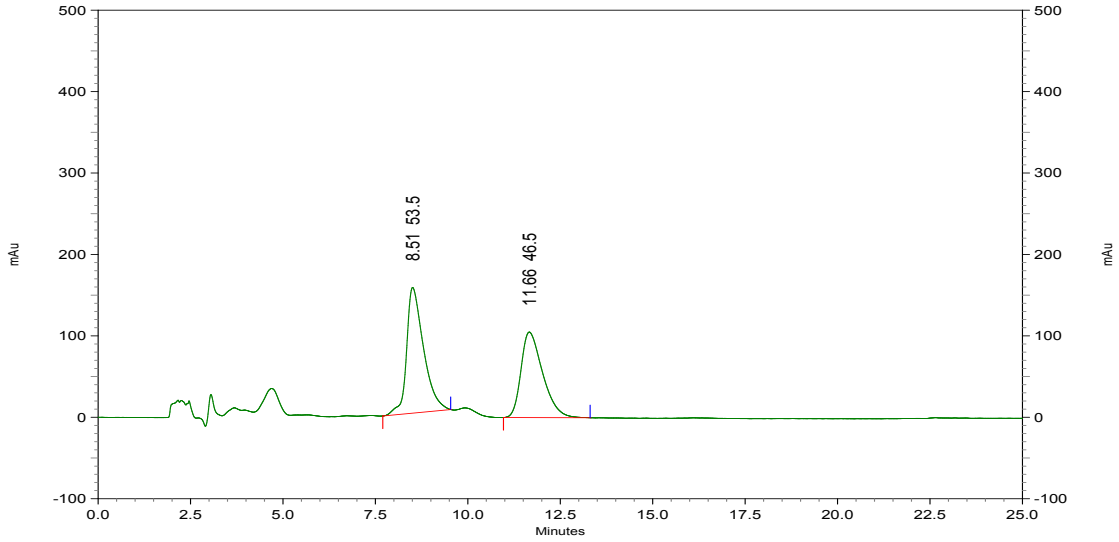
Time	Area %	Height %
16.900	49.66	64.05
28.900	50.34	35.95



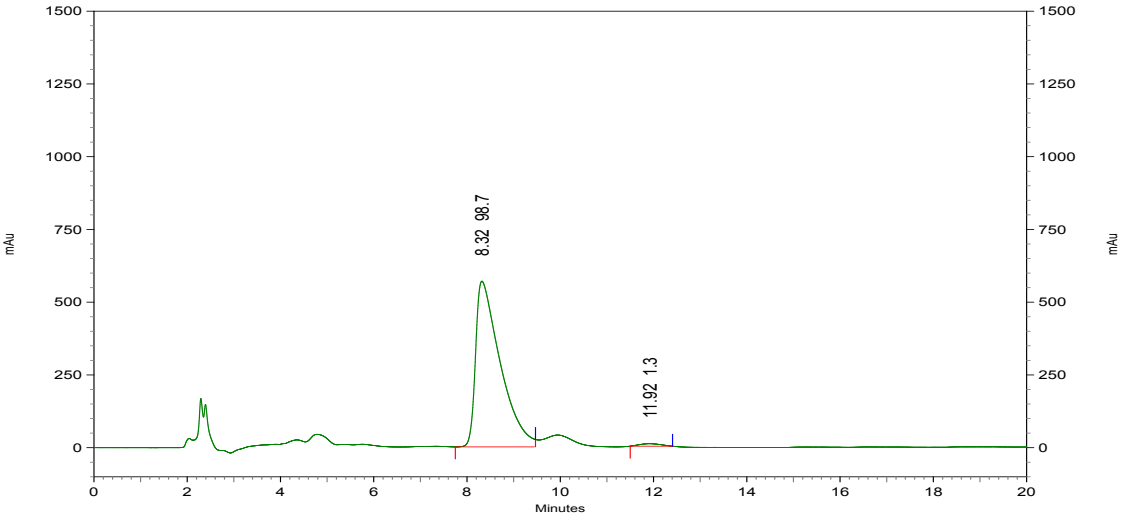
Time	Area %	Height %
16.628	100.00	100.00



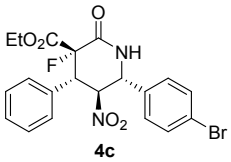
4b



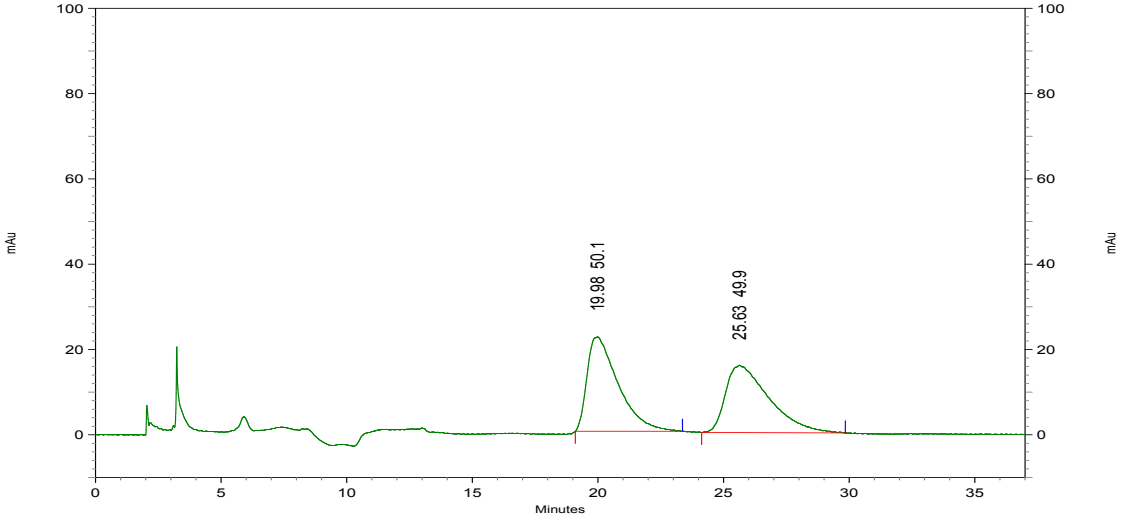
Time	Area %	Height %
8.508	53.52	59.51
11.664	46.48	40.49



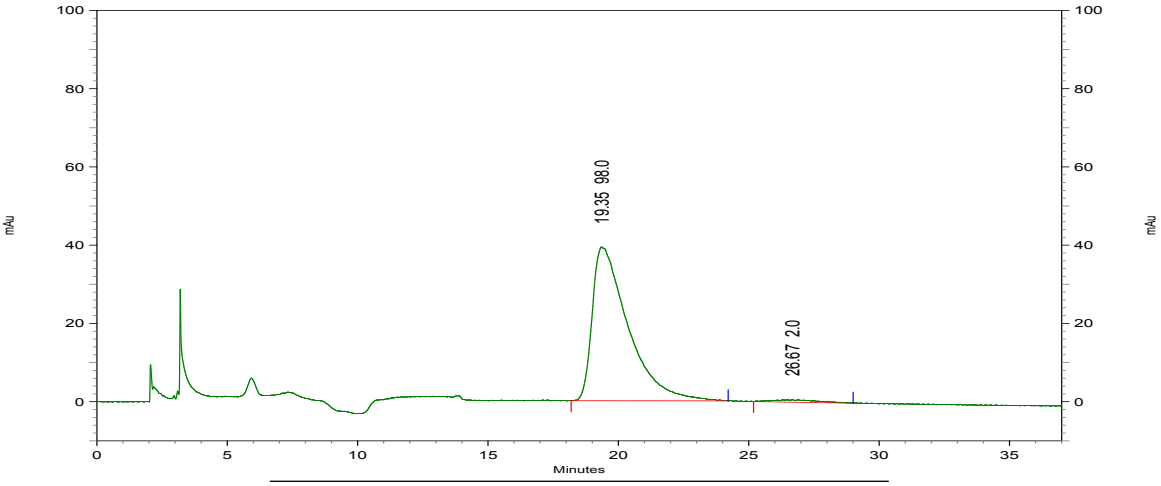
Time	Area %	Height %
8.320	98.70	98.52
11.920	1.30	1.48



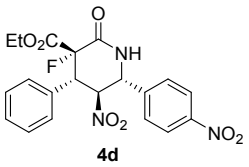
4c



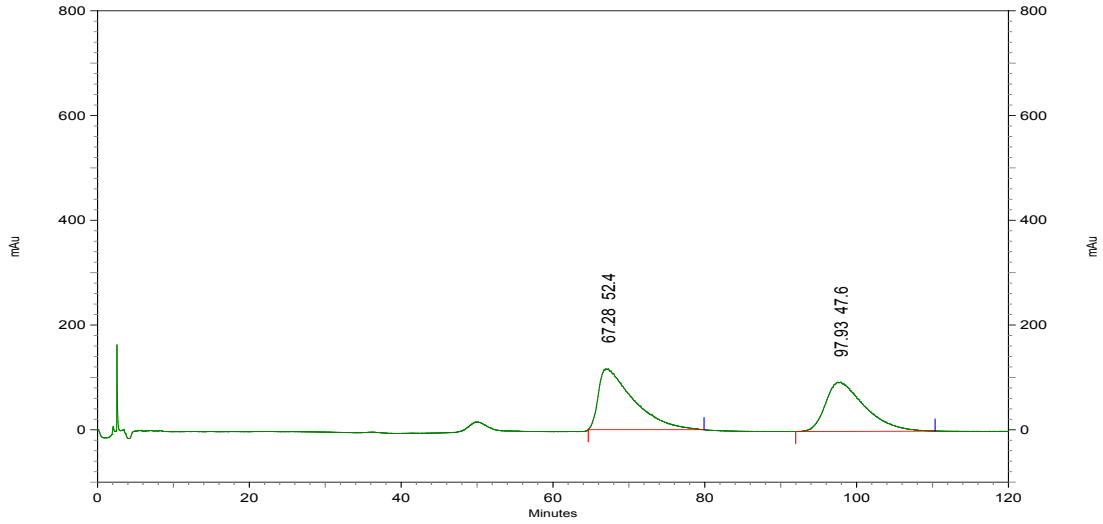
Time	Area %	Height %
19.976	50.11	58.36
25.628	49.89	41.64



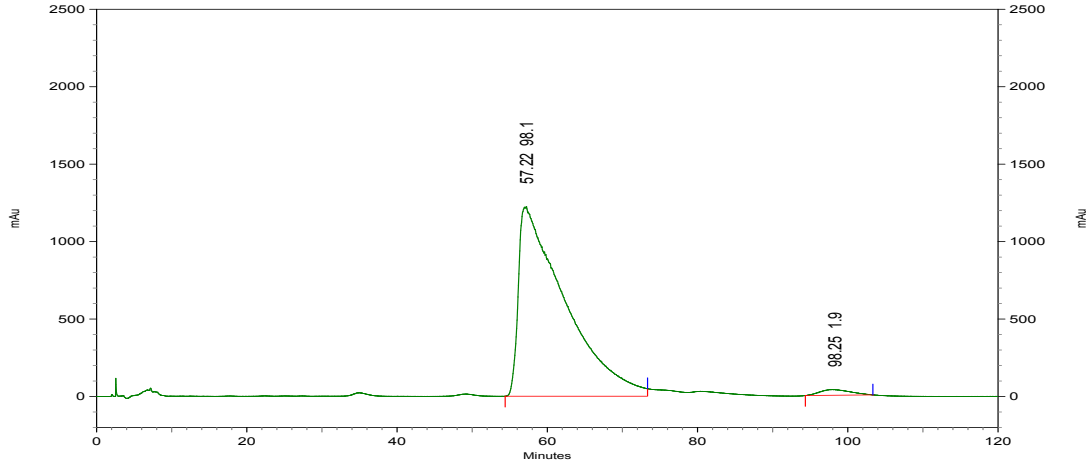
Time	Area %	Height %
19.352	98.02	98.42
26.672	1.98	1.58



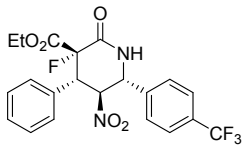
4d



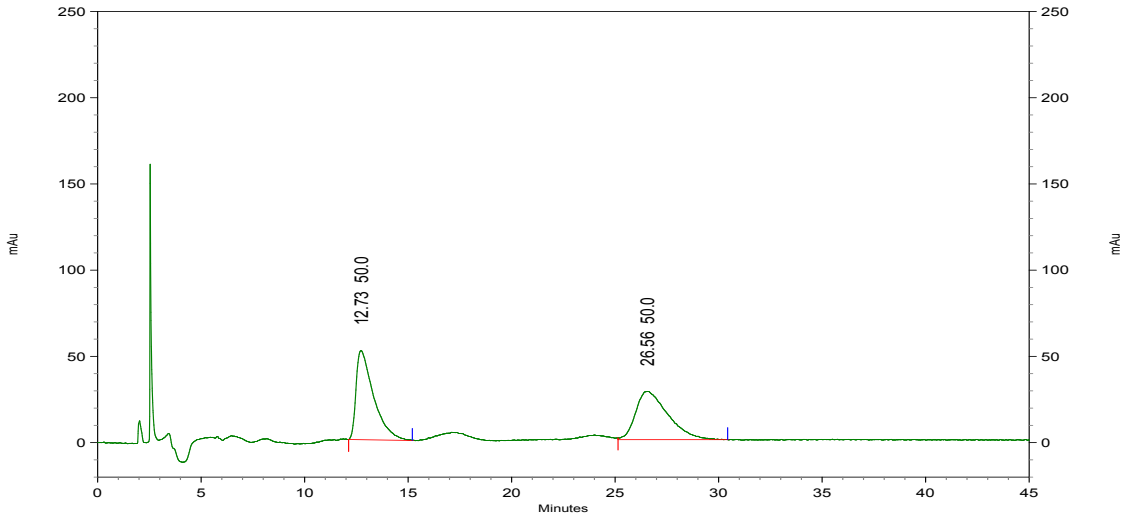
Time	Area %	Height %
67.280	52.40	55.30
97.932	47.60	44.70



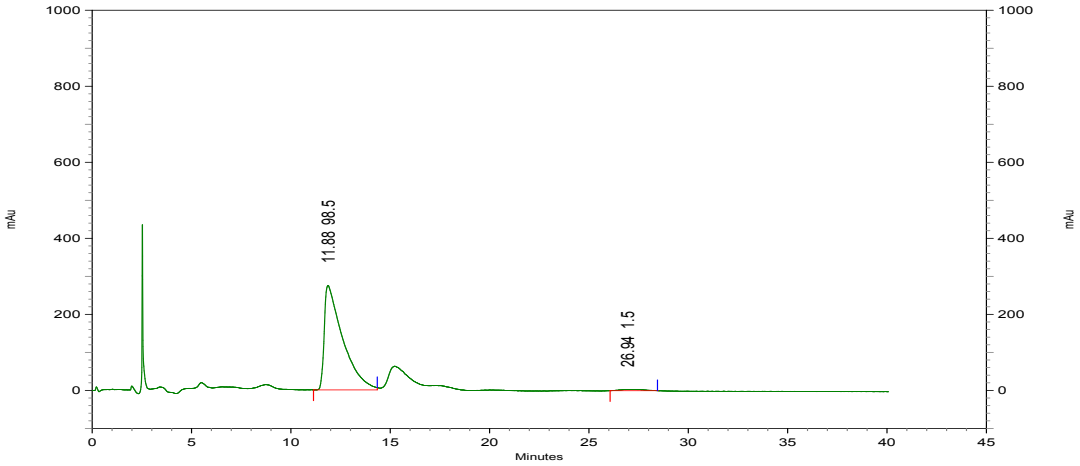
Time	Area %	Height %
57.224	98.08	97.09
98.252	1.92	2.91



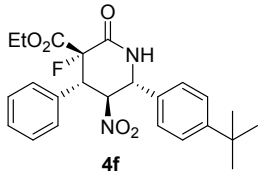
4e



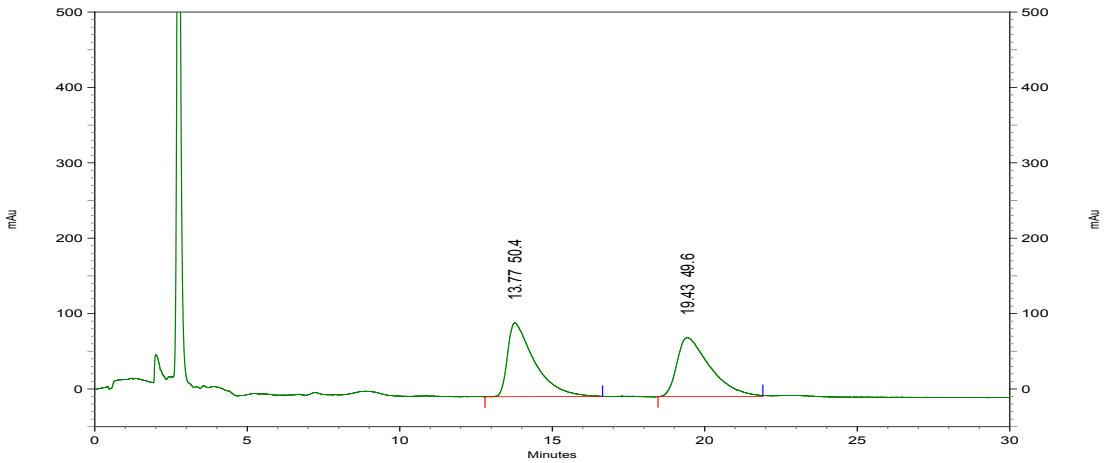
Time	Area %	Height %
12.732	49.78	56.39
26.567	50.22	43.61



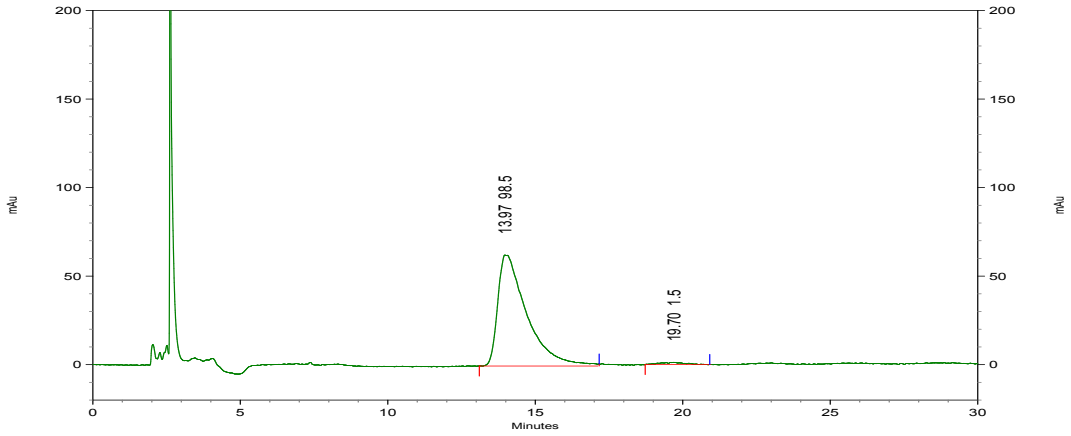
Time	Area %	Height %
11.876	98.54	98.79
26.936	1.46	1.21



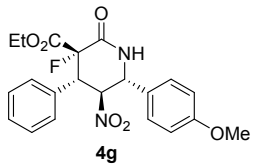
4f



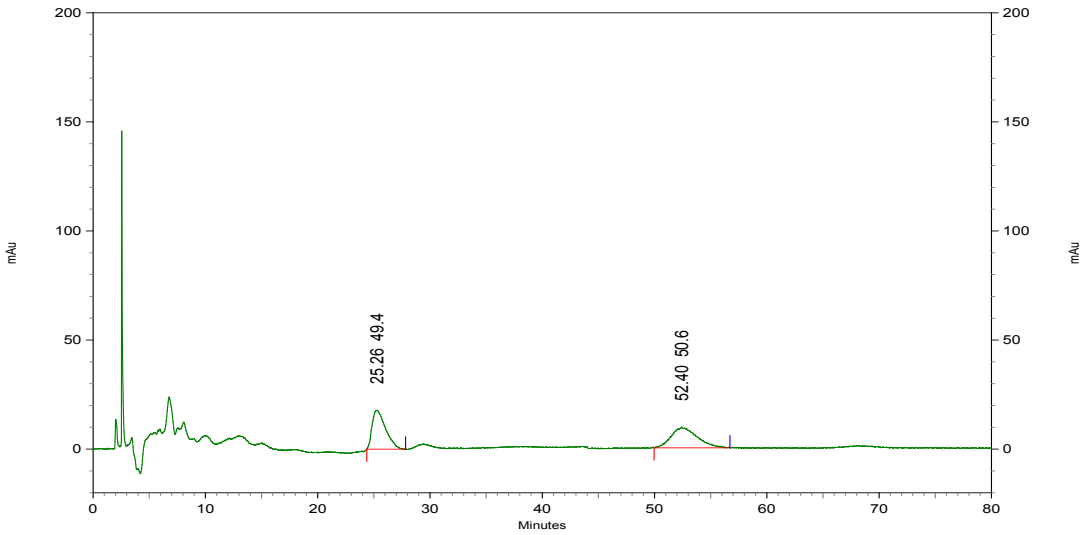
Time	Area %	Height %
13.772	50.35	55.59
19.428	49.65	44.41



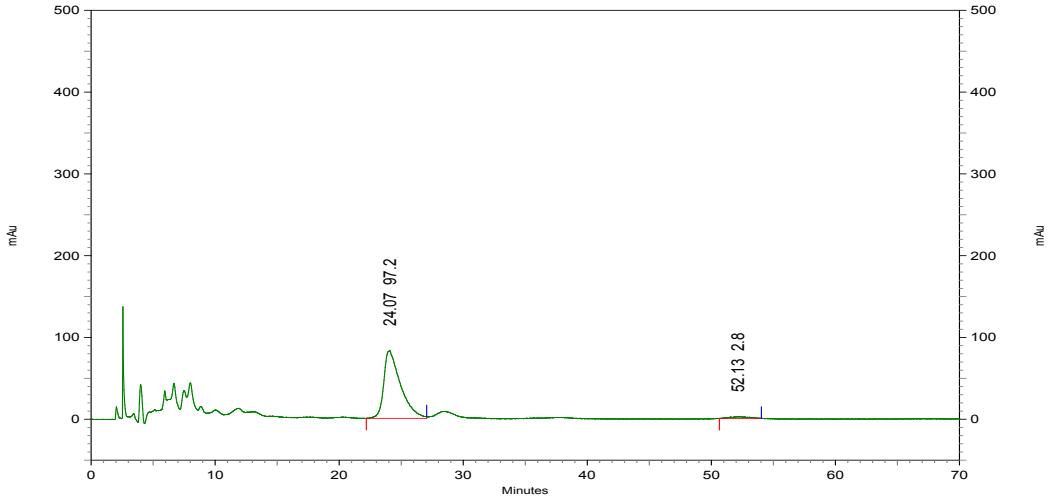
Time	Area %	Height %
13.968	98.51	98.12
19.700	1.49	1.88



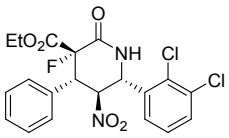
4g



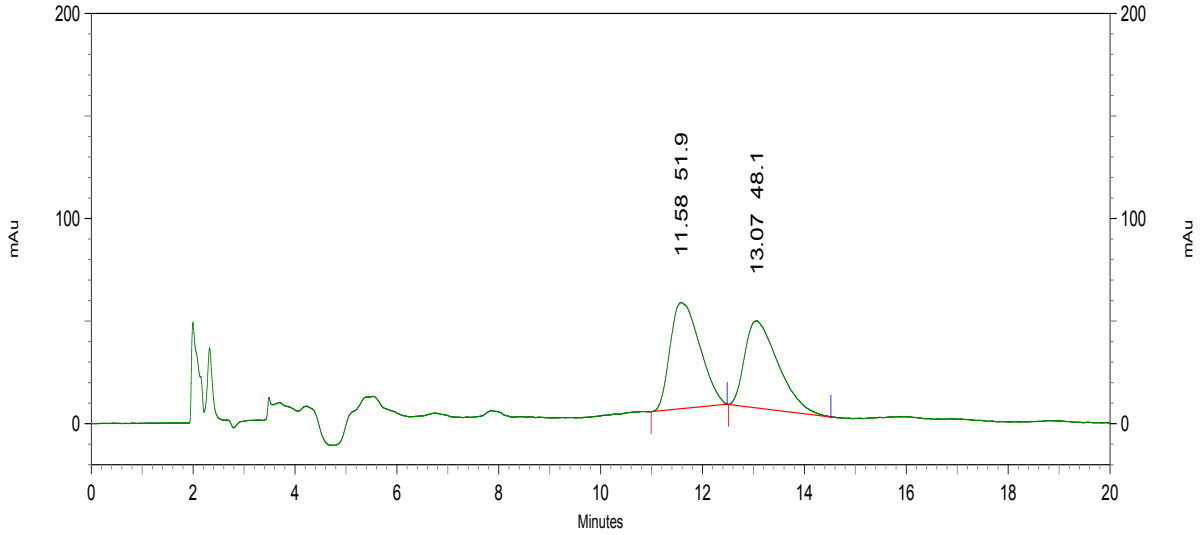
Time	Area %	Height %
25.264	49.41	65.21
52.404	50.59	34.79



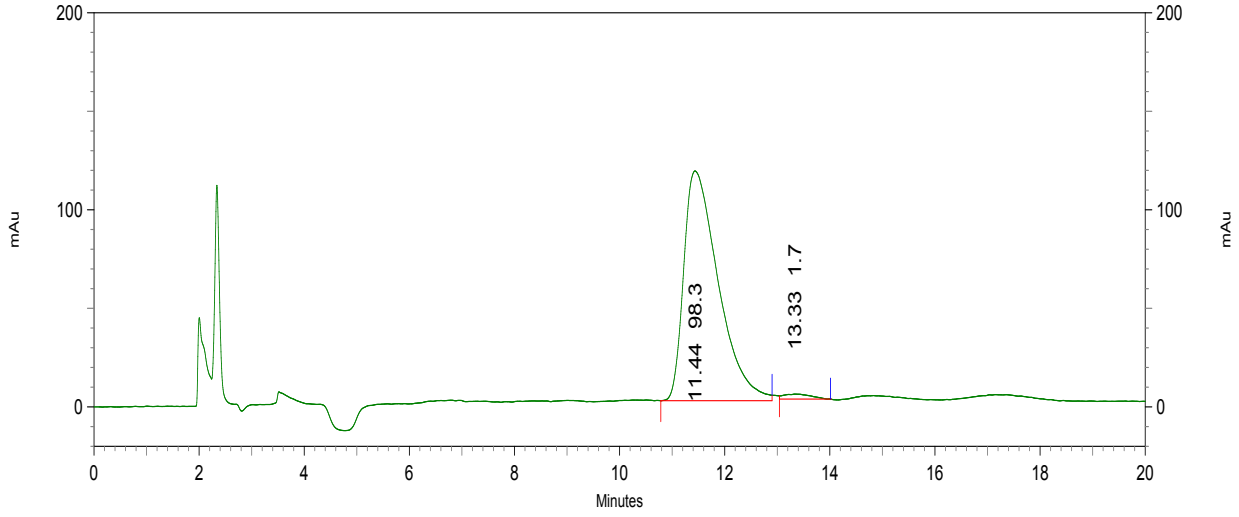
Time	Area %	Height %
24.072	97.19	97.53
52.132	2.81	2.47



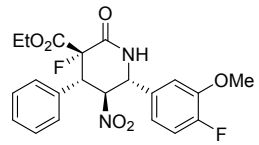
4h



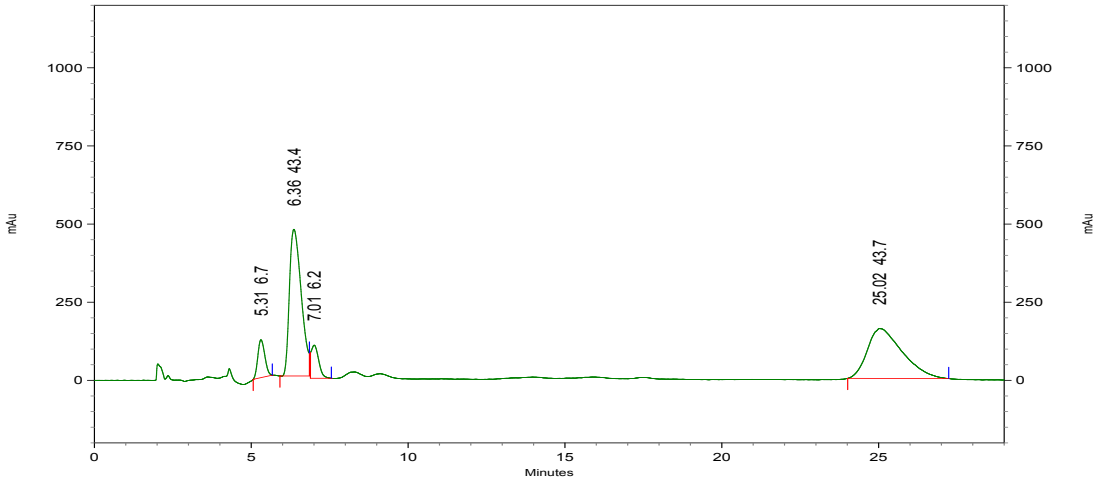
Retention Time	Area %	Height %
11.580	51.90	54.95
13.068	48.10	45.05



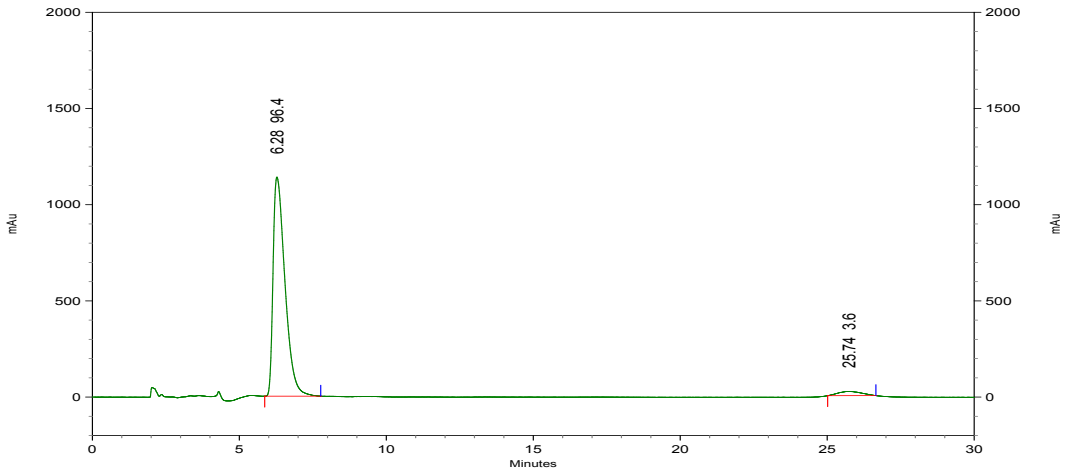
Retention Time	Area %	Height %
11.436	98.31	97.88
13.332	1.69	2.12



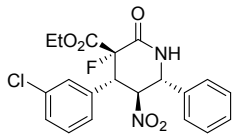
4i



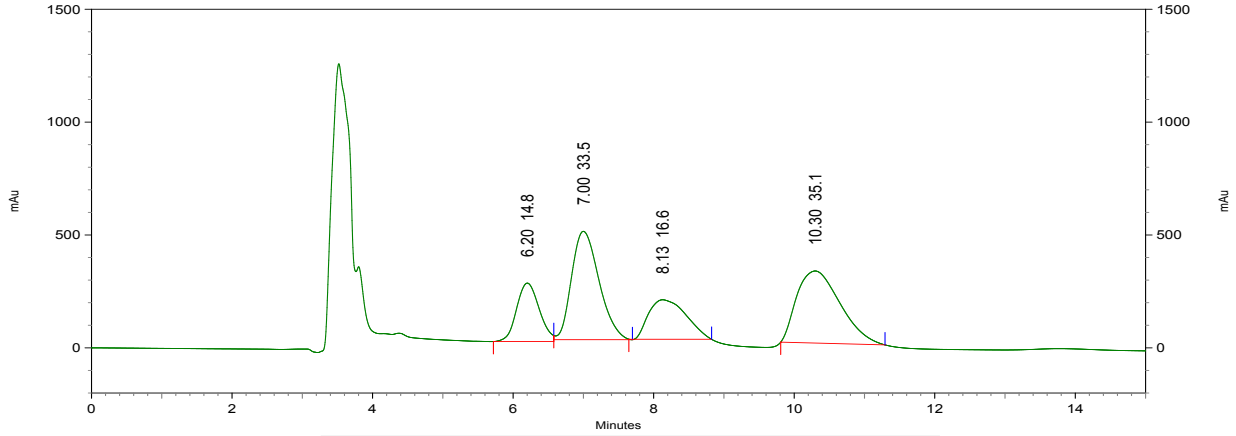
Time	Area %	Height %
5.308	6.66	14.14
6.360	43.43	54.86
7.008	6.18	12.38
25.020	43.74	18.62



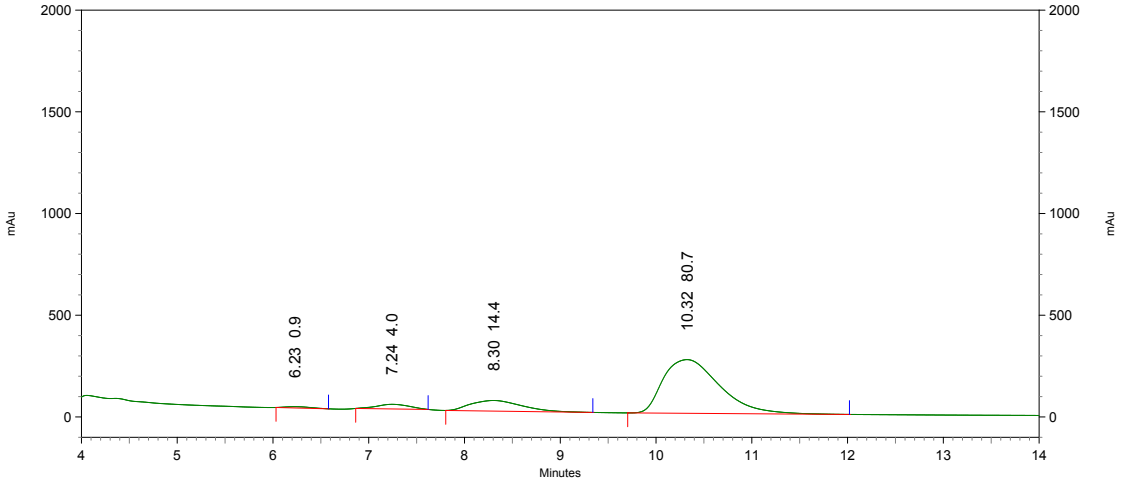
Time	Area %	Height %
6.280	96.38	98.14
25.744	3.62	1.86



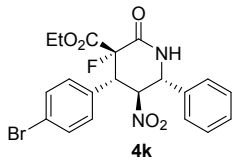
4j



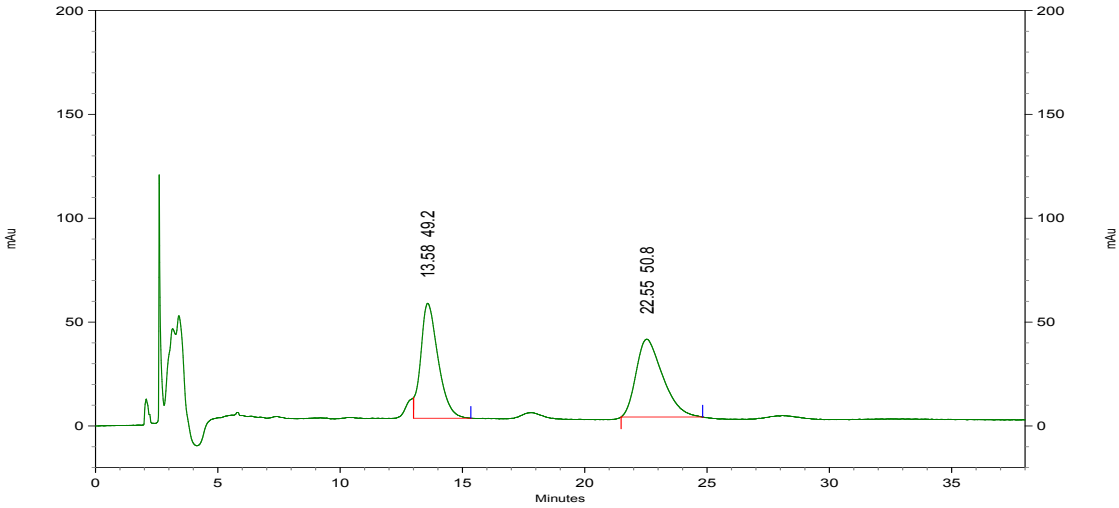
Retention Time	Area %	Height %
6.200	14.78	20.99
7.000	33.50	38.93
8.128	16.64	14.19
10.300	35.09	25.89



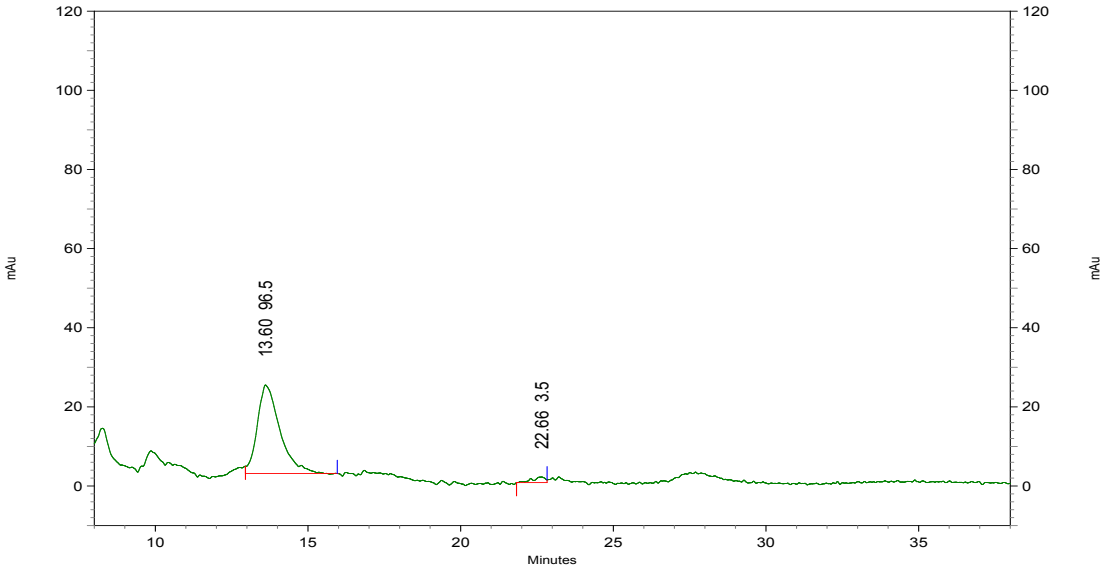
Retention Time	Area %	Height %
6.228	0.86	1.80
7.240	4.02	6.56
8.304	14.39	15.11
10.324	80.74	76.52



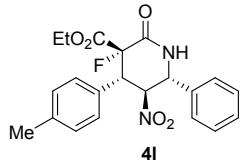
4k



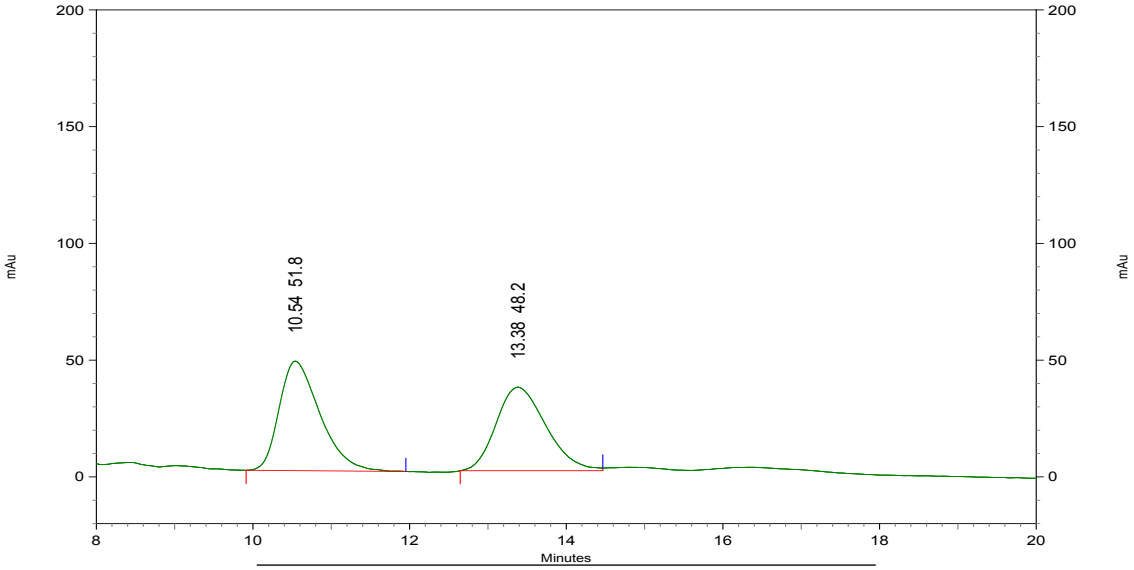
Time	Area %	Height %
13.576	49.18	59.64
22.548	50.82	40.36



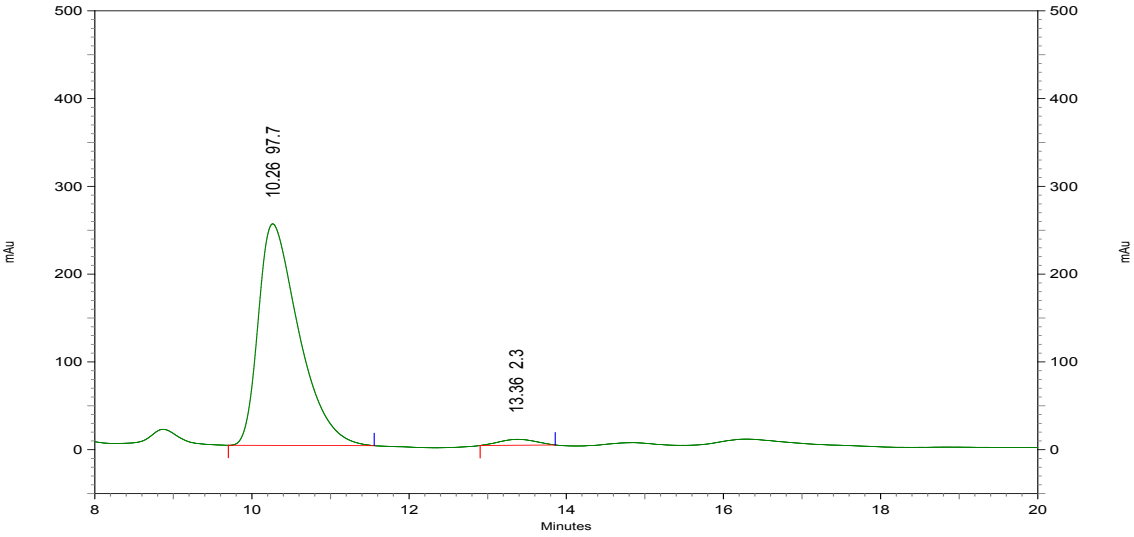
Time	Area %	Height %
13.604	96.55	94.04
22.656	3.45	5.96



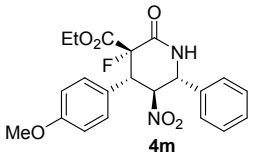
4l



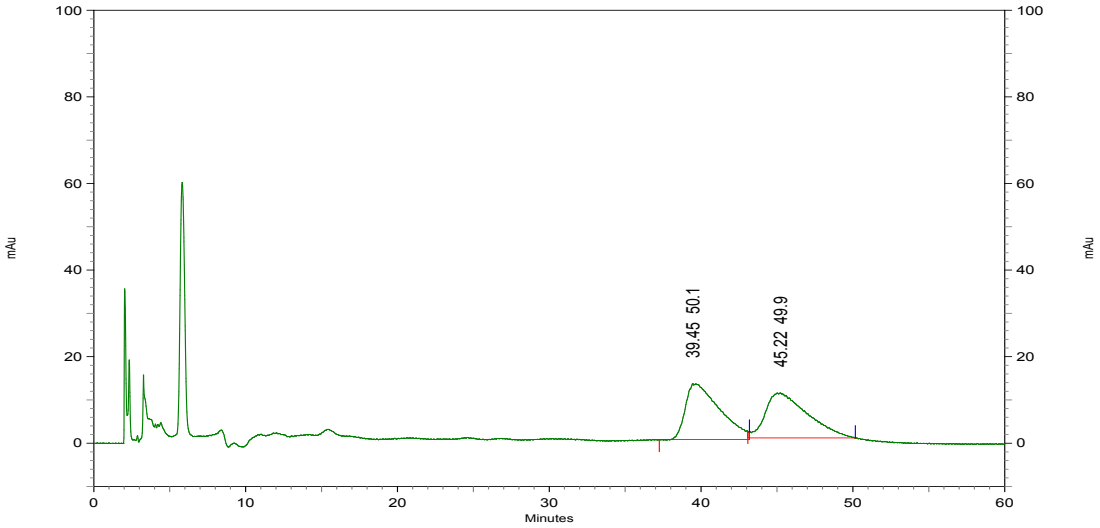
Time	Area %	Height %
10.540	51.76	56.70
13.380	48.24	43.30



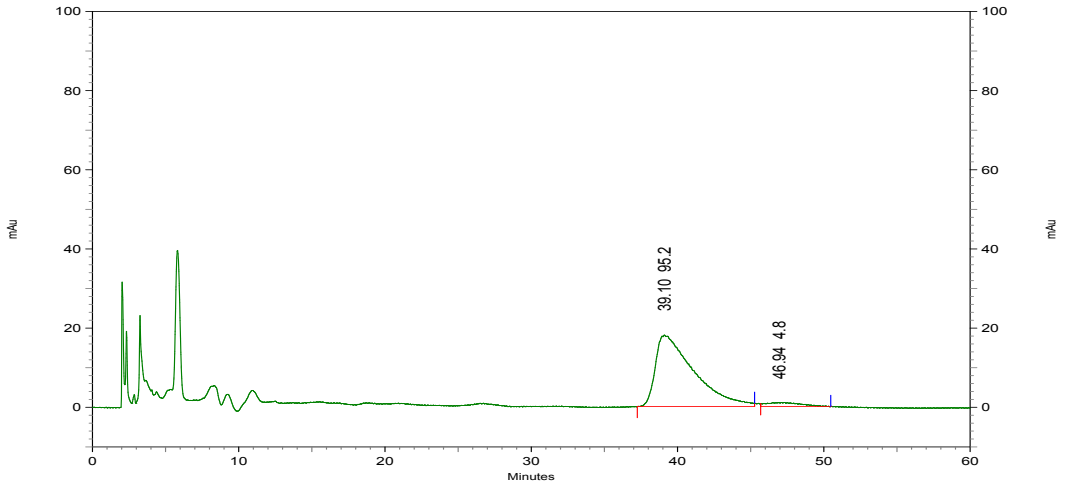
Time	Area %	Height %
10.264	97.68	97.42
13.364	2.32	2.58



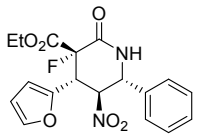
4m



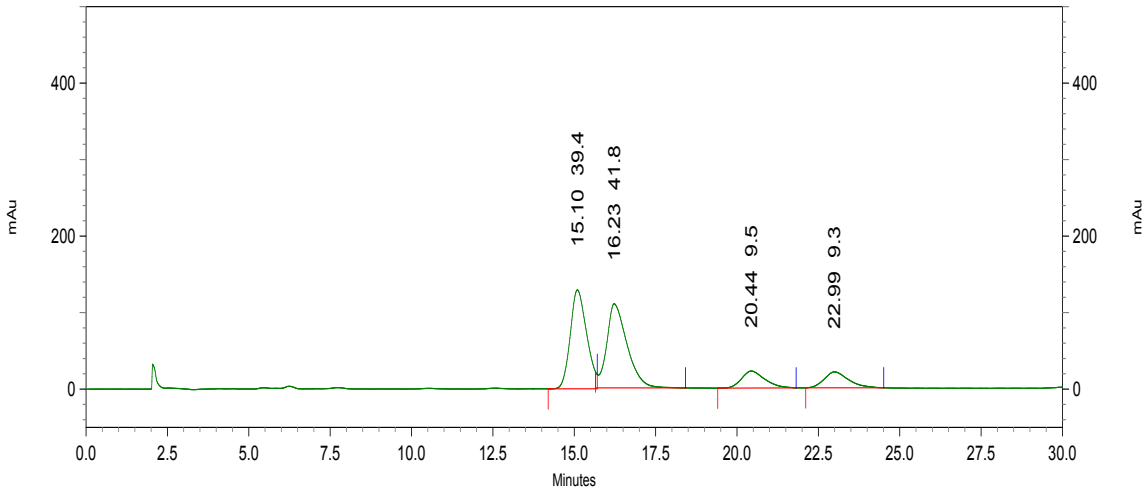
Time	Area %	Height %
39.452	50.13	55.45
45.224	49.87	44.55



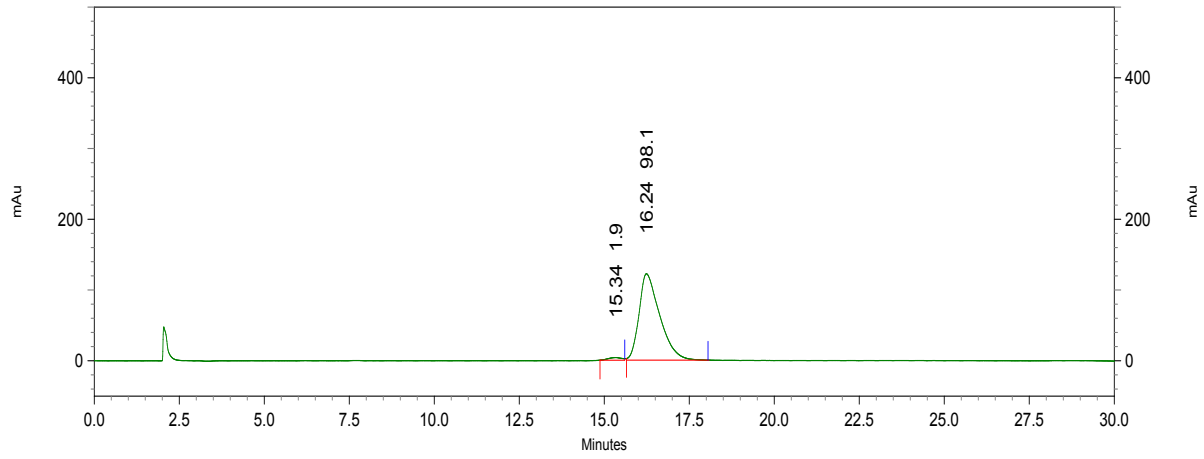
Time	Area %	Height %
39.096	95.20	94.57
46.940	4.80	5.43



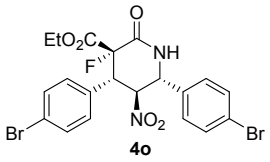
4n



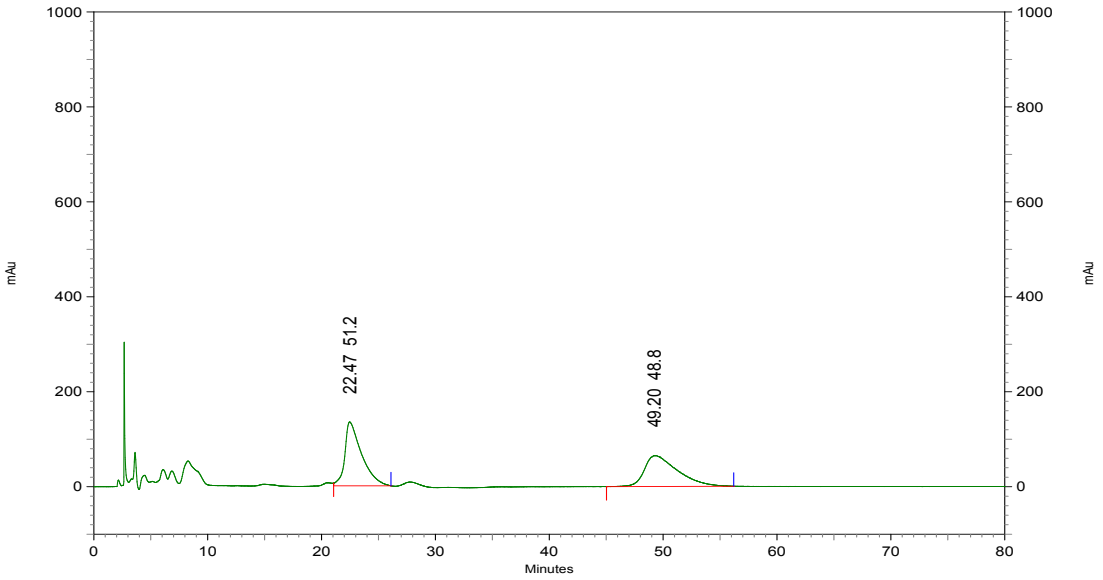
Retention Time	Area %	Height %
15.096	39.39	45.80
16.228	41.84	38.98
20.436	9.48	7.86
22.988	9.29	7.36



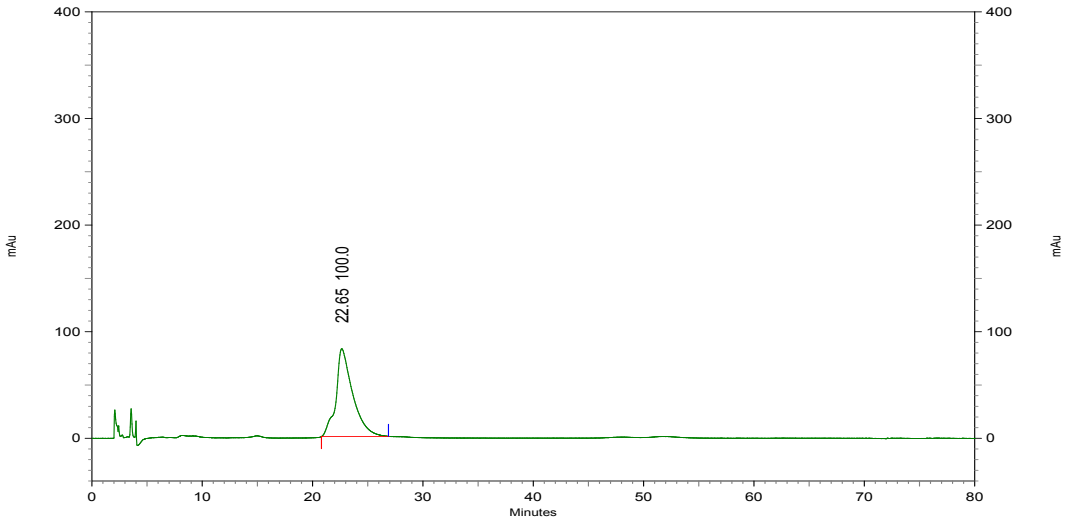
Retention Time	Area %	Height %
15.340	1.92	2.96
16.240	98.08	97.04



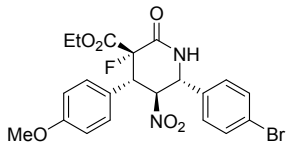
4o



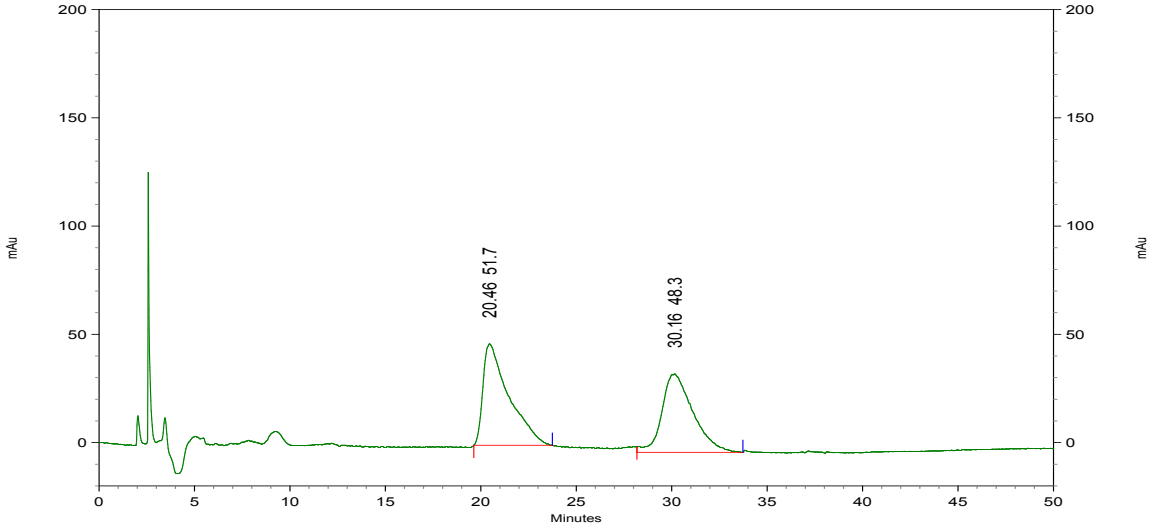
Time	Area %	Height %
22.472	51.23	67.47
49.200	48.77	32.53



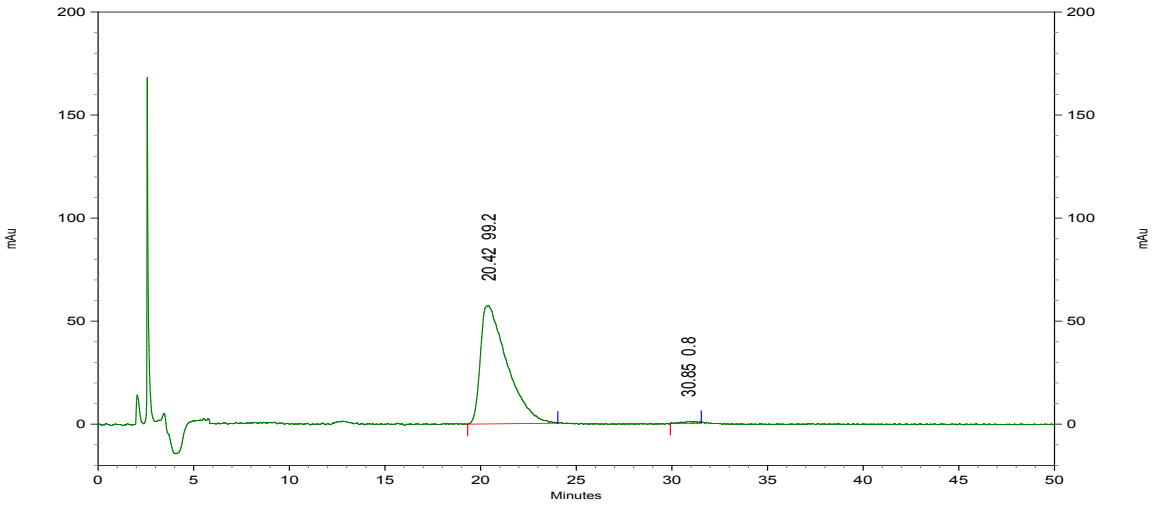
Time	Area %	Height %
22.648	100.00	100.00



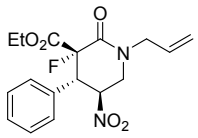
4p



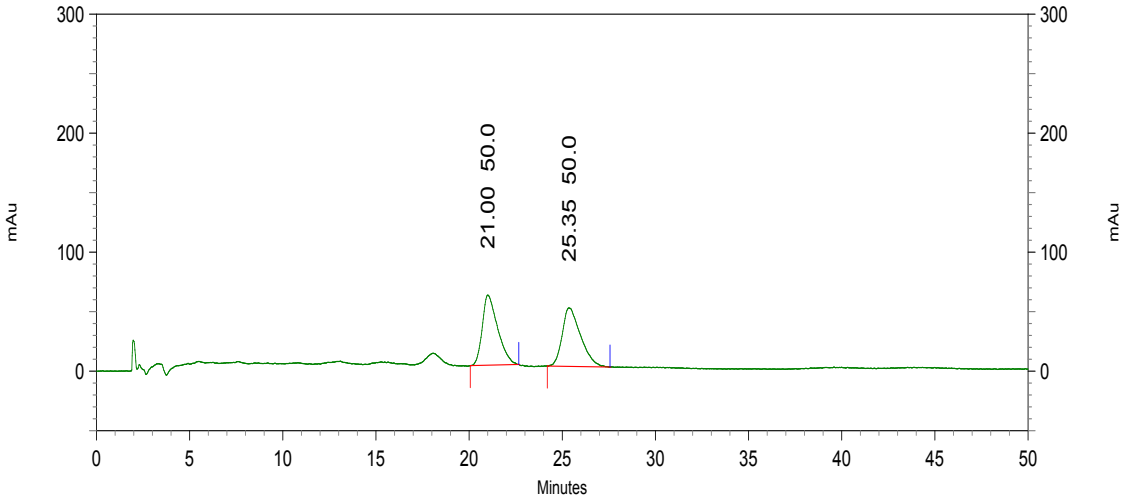
Time	Area %	Height %
20.456	51.66	56.39
30.160	48.34	43.61



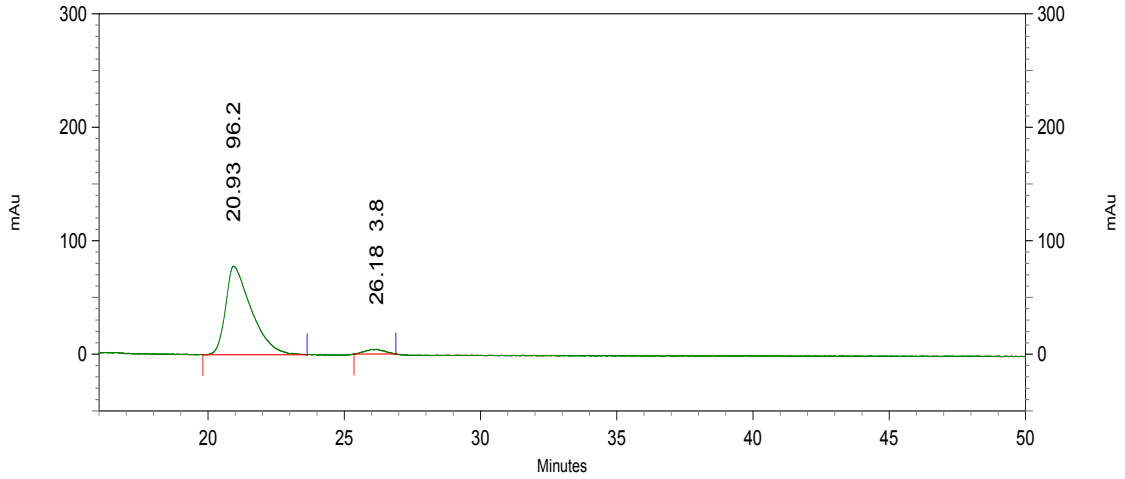
Time	Area %	Height %
20.420	99.17	98.51
30.852	0.83	1.49



4q



Time	Area %	Height %
21.003	50.00	55.40
25.352	50.00	44.60



Time	Area %	Height %
20.928	96.23	94.94
26.180	3.77	5.06