Electronic Supplementary Material (ESI) for Chemical Science

Enantio- and Diastereoselective Addition of Cyclohexyl Meldrum's Acid to β- and α,β-Disubstituted Nitroalkenes via *N*-Sulfinyl Urea Catalysis

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Supporting Information

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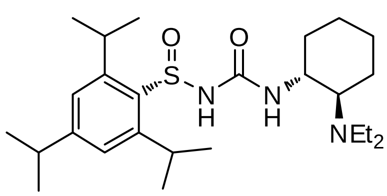
General Experimental. All reagents were obtained from commercial suppliers and used without further purification unless otherwise noted. Cyclopentyl methyl ether (CPME), tetrahydrofuran (THF), diethyl ether, methylene chloride (CH_2Cl_2) and dioxane were passed though columns of activated alumina under nitrogen pressure immediately prior to use. Cyclopentyl methyl ether was additionally distilled prior to passage through alumina to remove BHT stabilizer. All urea catalysts were dried under high vacuum over fresh P_2O_5 overnight prior to use. Dry potassium hydride was stored and weighed under inert atmosphere in the glove box. Diamine ***S*-1**[1] and triisopropylbenzenesulfinamide[2,3] were prepared according to literature procedures. Reactions were monitored by thin layer chomatography (TLC) and visualized with ultraviolet light and potassium permanganate stain. Flash column chromatography was carried out with Merck 60 230-240 mesh silica gel. NMR spectra were obtained on a Bruker AVB-400, Bruker AVB-500 or Varian 400 spectrometer, and unless otherwise noted, ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to either the residual solvent peak (^{1}H, ^{13}C) or TMS (^{1}H) as an internal standard. Enantiomeric excess was determined using an Agilent 1100 or 1200 series HPLC equipped with a Chiralcel IA column and a multiwavelength detector. IR spectra were recorded on a Nicolet 6700 FTIR spectrometer equipped with an attenuated total reflectance accessory as thin films on a KBr beamsplitter, and only partial data are listed. Melting points were determined on a Mel-Temp apparatus and are reported uncorrected. Specific rotations were determined using a Perkin-Elmer 341 polarimeter with a sodium lamp, and concentrations are reported in g/dL. Mass spectra (HRMS) analysis was performed by the Yale Protein Expression Database facility on a 9.4T Bruker Qe FT-ICR MS.

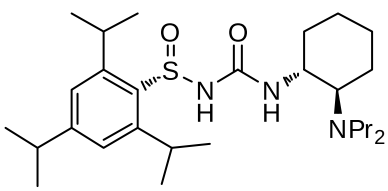
General Procedure for the Preparation of Sulfinyl Ureas (Procedure A).[4] To an oven-dried round-bottomed flask equipped with a magnetic stir bar and N_2 inlet was added potassium hydride (3 equiv) and sulfinamide (1.0 equiv). The reaction flask was cooled in an ice-water bath, and THF (0.6 M) was added. The suspension was stirred at 0 °C until bubbling ceased. The ice-water bath was removed, and the reaction mixture was allowed to warm to ambient temperature. 1,1'-Carbonyldiimidazole (1.0 equiv) was dissolved in 1,4-dioxane (1.0 M) and added to the reaction mixture, resulting in the formation of a white precipitate, and the reaction mixture was stirred for 1 h. A solution of diamine (1.2 equiv) in THF (1.0 M) was added, and the suspension was stirred at room temperature for 15-24 h. The reaction was quenched with a solution of acetic acid (3 equiv) in THF (1.0 M). The crude product was concentrated *in vacuo* and purified by chromatography or recrystallization.

General Procedure for the Preparation of Sulfinyl Ureas (Procedure B).[5] To a solution of sulfinyl urea **9** in acetonitrile (0.2 M) was added the appropriate aldehyde (5 equiv). After the reaction mixture was stirred for 15 min, $NaBH_3CN$ (2.1 equiv), and 15 min later, acetic acid (5 equiv) were added. The reaction mixture was stirred 3-12 h, then quenched by addition of 1 N $NaOH_{(aq)}$. The aqueous layer was extracted with ethyl acetate, and the organic layer was washed with 1 N NaOH. The crude product was concentrated *in vacuo* and purified by reverse phase chromatography.

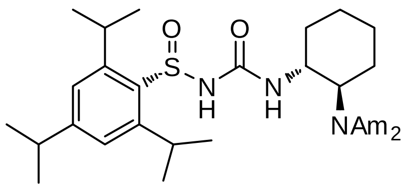


Urea 4. The general procedure (B) was followed using urea **7** (50 mg, 0.12 mmol), acetaldehyde (70 μL, 0.62 mmol), $NaBH_3CN$ (17 mg, 0.25 mmol), and acetic acid (35 μL, 0.62 mmol). Sulfinyl urea **4** was purified by reverse phase chromatography (1:1

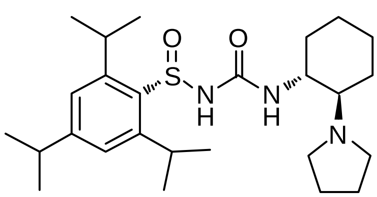
MeOH:H_2O to 100% MeOH), to yield 30 mg (53% yield) of a white solid, mp 170 °C. IR: 2965, 2931, 1735, 1666, 1628, 1535, 1385, 1265, 1088 cm^{-1}. ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.12 (s, 2H), 4.05 – 3.61 (br s, 2H), 3.61 – 3.36 (m, 1H), 2.96 – 2.68 (septet, J = 6.9 Hz, 1H,), 2.68 – 2.42 (m, 2H), 2.42 – 2.12 (m, 4H), 1.92 – 1.74 (m, 1H), 1.73 – 1.65 (m, 1H), 1.65 – 1.52 (m, 1H), 1.28 (d, J = 6.9 Hz, 6H), 1.18 (d, J = 6.9 Hz, 3H), 1.17 (d, J = 6.9 Hz, 3H), 1.15 (d, J = 6.9 Hz, 6H), 1.22-1.13 (m, 4H), 0.88 (t, J = 7.1 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.07, 152.83, 148.22, 136.62, 123.19, 77.20, 62.71, 52.08, 42.90, 34.33, 32.58, 28.47, 25.74, 24.54, 24.45, 23.99, 23.70, 23.68, 23.33, 14.66. HRMS (ESI) calcd for $C_{26}H_{45}O_2N_3S$ $[M+H]^+$ 464.33053; found 464.32943.



Urea 5. The general procedure (B) was followed using urea **7** (50 mg, 0.12 mmol), propionaldehyde (44 µL, 0.62 mmol), $NaBH_3CN$ (17 mg, 0.25 mmol), and acetic acid (35 µL, 0.62 mmol). Sulfinyl urea **5** was purified by reverse phase chromatography (1:1 MeOH:H_2O to 100% MeOH), to yield 33 mg (55% yield) of a white solid, mp 156-157 °C. IR: 3264, 2958, 2930, 2869, 1656, 1597, 1534, 1461, 1383, 1264, 1074, 877 cm^{-1}. ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.22 (s, 2H), 3.89 (br s, 2H), 3.54 (td, J = 10.8, 4.0 Hz, 1H), 2.94 (septet, J = 6.9 Hz, 1H), 2.53 – 2.22 (m, 5H), 1.97 – 1.86 (m, 1H), 1.86 – 1.77 (m, 1H), 1.71 (m, 1H), 1.38 (d, J = 6.8 Hz, 6H), 1.28 (d, J = 6.8 Hz, 3H), 1.27 (d, J = 6.8 Hz, 3H), 1.24 (d, J = 6.8 Hz, 6H), 1.49 – 1.12 (m, 7H), 0.96 – 0.93 (m, 2H), 0.83 (t, J = 7.4 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.11, 152.85, 148.15, 136.82, 123.16, 77.19, 73.93, 63.30, 52.14, 51.60, 34.34, 32.60, 28.46, 25.74, 24.54, 24.44, 24.00, 23.69, 23.14, 22.26, 11.84. HRMS (ESI) calcd for $C_{28}H_{49}O_2N_3S$ $[M+H]^+$ 492.36183; found 492.36060.

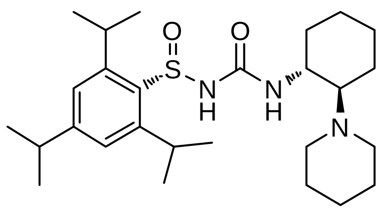


Urea 6. The general procedure (B) was followed using urea **7** (50 mg, 0.12 mmol), valeraldehyde (66 μL, 0.62 mmol), $NaBH_3CN$ (17 mg, 0.25 mmol), and acetic acid (35 μL, 0.62 mmol). Sulfinyl urea **6** was purified by reverse phase chromatography (1:1 MeOH:H_2O to 100% MeOH), to yield 48 mg (72% yield) of a white solid, mp 166-167 °C. IR: 2959, 2930, 2860, 1669, 1597, 1486, 1384, 1264, 1095 cm^{-1}. ^1H NMR (400 MHz, MeOH-d_4) δ 7.22 (s, 2H), 3.92 (br s, 2H), 3.55 (m, 1H), 2.99 – 2.89 (septet, *J* = 6.8 Hz, 1H), 2.60 – 2.21 (m, 6H), 1.89 (m, 1H), 1.84, (m, 1H), 1.72 (m, 1H), 1.38 (d, *J* = 6.8 Hz, 6H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.25 (d, *J* = 6.8 Hz, 6H), 1.47 – 1.12 (m, 16H), 0.87 (t, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.10, 152.77, 148.17, 136.95, 123.24, 63.15, 52.16, 49.54, 34.35, 32.49, 29.61, 28.80, 28.47, 25.75, 24.55, 24.42, 24.02, 23.71, 23.11, 22.58, 14.00. HRMS (ESI) calcd for $C_{32}H_{57}O_2N_3S$ $[M+H]^+$ 548.42443; found 548.42200.

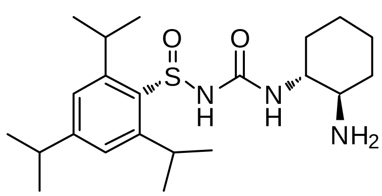


Urea 7. The general procedure (B) was followed using urea **7** (50 mg, 0.12 mmol), succinaldehyde$_{(aq)}$[6] (0.41 mL, 1.5 M), $NaBH_3CN$ (17 mg, 0.25 mmol), and acetic acid (35 μL, 0.62 mmol). Sulfinyl urea **7** was purified by reverse phase chromatography (1:1 MeOH:H_2O to 100% MeOH), to yield 27 mg (47% yield) of a white solid, mp 114-115 °C. IR: 2964, 2935, 2868, 1666, 1597, 1540, 1384, 1264, 1075, 906 cm^{-1}. ^1H NMR (400 MHz, MeOH-d_4) δ 7.23 (s, 2H), 3.94 (br s, 2H), 3.68 – 3.59 (m, 1H), 3.00 – 2.91 (septet, *J* = 6.8 Hz, 1H), 2.77 – 2.56 (m, 4H), 2.50 (m, 1H), 2.22 (m, 1H), 1.89-1.80 (m, 2H), 1.78-1.66 (m, 5H), 1.45-1.30 (m, 4H), 1.39 (d, *J* = 6.8 Hz, 6H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.51,

153.27, 148.77, 137.05, 123.65, 77.63, 62.41, 53.84, 47.59, 34.79, 32.70, 28.89, 25.32, 24.97, 24.72, 24.47, 24.15, 22.66. HRMS (ESI) calcd for $C_{26}H_{43}O_2N_3S$ $[M+H]^+$ 462.31488; found 462.31407.



Urea 8. The general procedure (A) was followed using (*S*)-triisopropylbenzenesulfinamide (4.0 g, 15 mmol), potassium hydride (1.8 g, 45 mmol), 1,1'-carbonyldiimidazole (2.4 g, 15 mmol), and (*R*,*R*)-diamine **S-1** (3.3 g, 18 mmol). Sulfinyl urea **8** was purified by trituration with methanol/water, then recrystallization from 0.4 L of warm methanol, to yield 4.1 g (59% yield) of a white solid, mp 169 °C. IR: 3325, 2959, 2929, 2855, 2799, 1655, 1597, 1535, 1384, 1206, 1076, 839 cm^{-1}. ^1H NMR (500 MHz, MeOH-d_4) δ 7.11 (s, 2H), 3.81 (br s, 2H), 3.48 – 3.40 (m, 1H), 2.83 (septet, *J* = 6.9 Hz, 1H), 2.53 (m, 2H), 2.27 – 2.10 (m, 4H), 1.79 (m, 1H), 1.69 (m, 1H), 1.59 (m, 1H), 1.43 – 0.98 (m, 10H), 1.27 (d, *J* = 6.8 Hz, 6H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.49, 152.94, 148.62, 136.73, 123.34, 67.99, 51.77, 50.51, 49.41, 34.55, 33.08, 28.70, 26.75, 25.80, 25.07, 24.79, 24.20, 23.96, 23.91, 23.30. HRMS (ESI) calcd for $C_{27}H_{45}O_2N_3S$ $[M+H]^+$ 476.33053; found 476.32973.

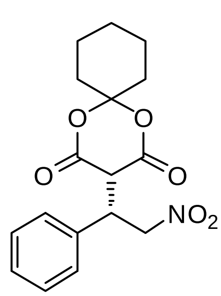


Urea 9. The general procedure (A) was followed using (*S*)-triisopropylbenzenesulfinamide (0.27 g, 1.0 mmol), potassium hydride (0.12 g, 3.0 mmol), 1,1'-carbonyldiimidazole (0.16 g, 1.0 mmol), and (1*R*,2*R*)-(-)-*trans*-1,2-cyclohexanediamine (0.34 g, 3.0 mmol). Sulfinyl urea **9** was purified by reverse phase chromatography (5:95 MeOH:H_2O to 100% MeOH), to yield 0.27 g (65% yield) of a white solid, mp 205 °C.

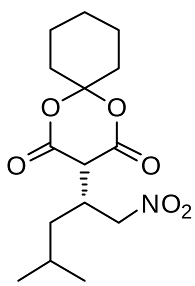
IR: 3301, 2960, 2928, 2864, 1664, 1597, 1543, 1384, 1057, 877 cm^{-1}. ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.22 (s, 2H), 3.95 (br s, 2H), 3.45 – 3.36 (m, 1H), 3.01 – 2.84 (septet, J = 6.8 Hz, 1H), 2.46 (m, 1H), 2.11 – 1.89 (m, 2H), 1.76-1.70 (m, 2H), 1.42 – 1.22 (m, 4H), 1.38 (d, J = 6.8 Hz, 6H), 1.28 (d, J = 6.8 Hz, 3H), 1.27 (d, J = 6.8 Hz, 3H), 1.25 (d, J = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, MeOH-d_4) δ 158.84, 154.63, 150.56, 137.47, 124.67, 57.83, 56.24, 36.08, 35.06, 33.90, 30.29, 26.58, 26.25, 25.56, 24.72. HRMS (ESI) calcd for $C_{22}H_{37}O_2N_3S$ $[M+H]^+$ 408.26793; found 408.26610.

Representative Procedure for Racemic Addition of Cyclohexyl Meldrum's Acid to *trans*-β-Nitrostyrene. To a solution of *trans*-β-nitrostyrene (15 mg, 0.10 mmol) in dichloromethane (1.0 mL) was added a few drops of triethylamine. Cyclohexyl Meldrum's acid (36 mg, 0.20 mmol) was added, and the reaction mixture was stirred for 18 h. The triethylamine was then removed by eluting the reaction mixture through a plug of silica gel with dichloromethane.

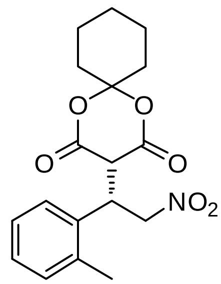
Representative Procedure for Enantio- and Diastereoselective Addition of Cyclohexyl Meldrum's Acid to *trans*-β-Nitrostyrenes. A mixture of *trans*-β-nitrostyrene (45 mg, 0.30 mmol) and sulfinyl urea catalyst *ent*-**8** (1.4 mg, 0.003 mmol) was dissolved in cyclopentyl methyl ether (1.0 mL). Cyclohexyl Meldrum's acid (83 mg, 0.45 mmol) was added. The reaction mixture was stirred at room temperature for 24 h, then eluted through a plug of silica with dichloromethane to remove the catalyst and then concentrated *in vacuo*. The crude product was purified by silica gel chromatography. Enantiomeric excess was determined by chiral HPLC analysis.



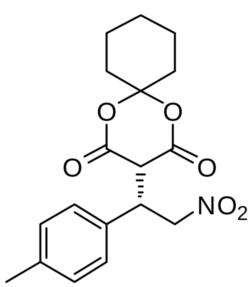
12a: (*R*)-3-(2-Nitro-1-phenylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 95 mg (95% yield) of a viscous colorless oil was isolated by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 98% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 12.2 min, t_R (major) = 13.5 min) $[\alpha]_D^{20}$ = -8.5 (*c* 1.0, $CHCl_3$): IR (neat): 2943, 1778, 1737, 1551, 1496, 1453, 1368, 1299, 1265, 1064, 986, 853 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 5H), 5.45 (dd, *J* = 14.0, 9.1 Hz, 1H), 5.04 (dd, *J* = 14.0, 6.5 Hz, 1H), 4.68 (ddd, *J* = 9.1, 6.5, 3.1 Hz, 1H), 4.05 (d, *J* = 3.1 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.74 – 1.66 (m, 2H), 1.60 (m, 2H), 1.54 – 1.40 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.53, 164.05, 135.19, 129.20, 128.92, 128.80, 106.71, 76.02, 48.89, 41.98, 36.82, 36.64, 23.81, 22.29, 21.70. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{19}NO_6$, 334.12851; found, 334.12830.



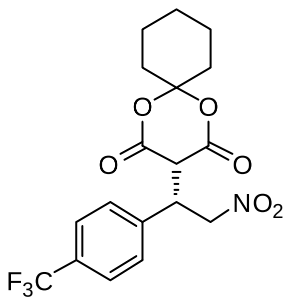
12b: (*R*)-3-(4-Methyl-1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 85 mg (90% yield) of a viscous colorless oil was isolated by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 94% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 7.6 min, t_R (major) = 7.2 min) $[\alpha]_D^{20}$ = -1.3 (*c* 1.0, $CHCl_3$): IR (neat): 2956, 2871, 1778, 1739, 1550, 1466, 1452, 1369, 1307, 1274, 1064, 981, 853 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 4.93 (dd, *J* = 13.3, 10.3 Hz, 1H), 4.46 (dd, *J* = 13.3, 4.2 Hz, 1H), 3.83 (d, *J* = 2.5 Hz, 1H), 3.33 – 3.19 (m, 1H), 1.91 (m, 4H), 1.76 – 1.68 (m, 2H), 1.67 – 1.60 (m, 2H), 1.57 – 1.42 (m, 4H), 1.17 – 1.10 (m, 1H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.19, 163.95, 106.34, 75.77, 47.32, 38.11, 36.61, 36.05, 34.45, 25.64, 23.98, 23.13, 22.59, 21.66, 21.42. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{23}NO_6$, 314.15981; found, 314.15973.



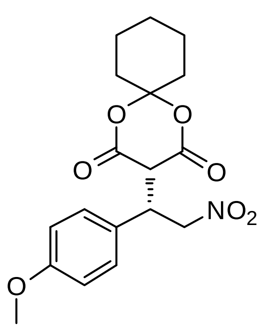
12c: (*R*)-3-(-2-Nitro-1-o-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 98 mg (94% yield) of a colorless oil was isolated by flash column chromatography using 70:30:1 hexanes:CPME:AcOH as eluent: 96% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 11.3 min, t_R (major) = 13.7 min) $[\alpha]_D^{20}$ = -88.9 (*c* 0.44, $CHCl_3$): IR (neat): 3023, 2944, 1775, 1738, 1552, 1493, 1452, 1368, 1304, 1272, 1065, 985, 853 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 1H), 7.20 – 7.13 (m, 3H), 5.28 (dd, *J* = 13.7, 9.0 Hz, 1H), 4.96 – 4.89 (ddd, *J* = 9.0, 6.6, 3.1 Hz, 1H), 4.83 (dd, *J* = 13.7, 6.6 Hz, 1H), 3.90 (d, *J* = 3.1 Hz, 1H), 2.43 (s, 3H), 1.93 – 1.85 (m, 2H), 1.71 – 1.57 (m, 6H), 1.43 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.16, 164.22, 137.05, 134.97, 131.66, 128.70, 127.24, 127.19, 106.94, 75.61, 48.66, 37.09, 37.06, 36.74, 24.10, 22.58, 21.98, 19.79. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{21}NO_6$, 348.14416; found, 348.14433.



12d: (*R*)-3-(2-Nitro-1-p-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 103 mg (99% yield) of a viscous colorless oil was isolated by flash column chromatography using 70:30:1 hexanes:CPME:AcOH as eluent: 98% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 12.0 min, t_R (major) = 13.9 min) $[\alpha]_D^{20}$ = -19.4 (*c* 0.77, $CHCl_3$): IR (neat): 2945, 1776, 1738, 1552, 1516, 1452, 1368, 1300, 1272, 1068, 988, 853 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.32 (dd, *J* = 13.9, 9.0 Hz, 1H), 4.92 (dd, *J* = 13.9, 6.6 Hz, 1H), 4.53 (ddd, *J* = 9.0, 6.6, 3.1 Hz, 1H), 3.94 (d, *J* = 3.1 Hz, 1H), 2.24 (s, 3H), 1.86 – 1.77 (m, 2H), 1.64 – 1.30 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.04, 164.58, 139.10, 132.55, 130.23, 129.21, 107.09, 76.65, 49.41, 42.11, 37.24, 37.05, 24.27, 22.73, 22.15, 21.45. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{21}NO_6$, 348.14416; found, 348.14317.

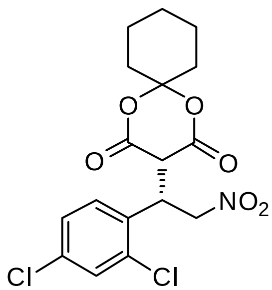


12e: (*R*)-3-(2-Nitro-1-(4-(trifluoromethyl)phenyl)ethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 99 mg (82% yield) of a viscous colorless oil was isolated by flash column chromatography using 50:50:1 hexanes:DCM:AcOH as eluent: 98% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 14.3 min, t_R (major) = 18.2 min) $[\alpha]_D^{20}$ = -13.0 (*c* 0.93, $CHCl_3$): IR (neat): 3024, 2949, 1779, 1740, 1622, 1555, 1453, 1369, 1324, 1275, 1069, 1001, 844 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.36 (d, *J* = 8.0 Hz, 2H), 7.20 – 7.13 (d, *J* = 8.0 Hz, 2H), 5.29 (dd, *J* = 13.7, 9.0 Hz, 1H), 5.00 (dd, *J* = 13.7, 6.6 Hz, 1H), 4.65 (ddd, *J* = 9.0, 6.6, 3.1 Hz, 1H), 4.03 (d, *J* = 3.1 Hz, 1H), 1.87 – 1.84 (m, 2H), 1.61 – 1.59 (m, 6H), 1.39-1.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.16, 163.59, 139.19, 130.94 (dd, *J* = 65.3, 32.5 Hz), 129.69, 126.00 (q, *J* = 3.7 Hz), 123.69 (q, *J* = 272.4 Hz), 106.91, 75.71, 48.84, 41.25, 36.59, 36.36, 23.78, 22.38, 21.60. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{18}F_3NO_6$, 402.11590; found, 402.11613.

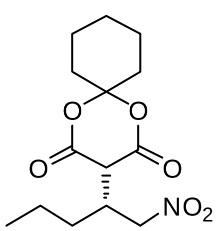


12f: (*R*)-3-(1-(4-Methoxyphenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 108 mg (99% yield) of a viscous colorless oil was isolated by flash column chromatography using 50:50:1 hexanes:DCM:AcOH as eluent: 96% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 16.7 min, t_R (major) = 18.7 min) $[\alpha]_D^{20}$ = -20.6 (*c* 0.73, $CHCl_3$): IR (neat): 2959, 1781, 1736, 1553, 1514, 1452, 1368, 1300, 1251, 1068, 986, 834 cm^{-1}. ^1H NMR (400 MHz,

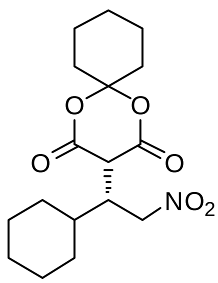
$CDCl_3$) δ 7.28 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 5.38 (dd, *J* = 13.9, 8.8 Hz, 1H), 5.02 (dd, *J* = 13.9, 6.8 Hz, 1H), 4.67 – 4.54 (ddd, *J* = 8.8, 6.8, 3.1 Hz, 1H), 4.03 (d, *J* = 3.1 Hz, 1H), 3.79 (s, 3H), 1.96 – 1.84 (m, 2H), 1.71 – 1.40 (m, 8H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.06, 164.63, 160.19, 130.61, 127.38, 114.87, 107.07, 76.84, 55.68, 49.49, 41.85, 37.23, 37.09, 24.26, 22.73, 22.15. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{21}NO_7$, 364.13908; found, 364.13880.



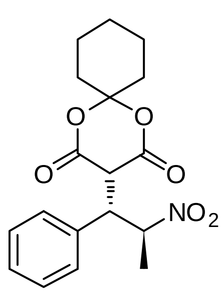
12g: (*R*)-3-(1-(2,4-Dichlorophenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 114 mg (95% yield) of a viscous colorless oil was isolated by flash column chromatography using 50:50:1 hexanes:DCM:AcOH as eluent: 96% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 12.6 min, t_R (major) = 15.5 min) $[\alpha]_D^{20}$ = -2.5 (*c* 0.73, $CHCl_3$): IR (neat): 2944, 1784, 1739, 1553, 1475, 1452, 1368, 1302, 1274, 1063, 974, 852 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.5 Hz, 1H), 7.44 (d, *J* = 2.2 Hz, 1H), 7.26 (dd, *J* = 8.5, 2.2 Hz, 1H), 5.12 – 5.05 (td, *J* = 7.4, 2.8 Hz, 1H), 5.00 (d, *J* = 7.4 Hz, 2H), 4.06 (d, *J* = 2.8 Hz, 1H), 1.95 (m, 4H), 1.80 – 1.71 (m, 2H), 1.66 (m, 2H), 1.53 – 1.43 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.90, 163.40, 135.39, 135.11, 132.94, 130.48, 130.37, 128.25, 107.32, 73.53, 48.35, 37.23, 36.79, 36.03, 24.37, 23.02, 22.15. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{17}Cl_2NO_6$, 402.05057; found, 402.05040.



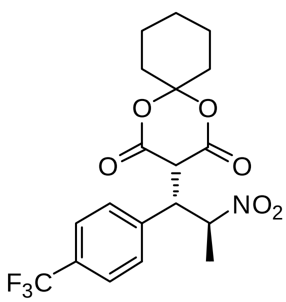
12h: (*R*)-3-(1-Nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 84 mg (94% yield) of a viscous colorless oil was isolated by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 94% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 11.4 min, t_R (major) = 13.5 min) $[\alpha]_D^{20}$ = +11.2 (*c* 0.50, $CHCl_3$): IR (neat): 2945, 2874, 1780, 1739, 1551, 1453, 1369, 1305, 1274, 1066, 976, 854 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.99 (dd, *J* = 13.4, 10.0 Hz, 1H), 4.58 (dd, *J* = 13.4, 4.5 Hz, 1H), 3.93 (d, *J* = 2.5 Hz, 1H), 3.30 (tddd, *J* = 12.2, 10.0, 4.5, 2.5 Hz, 1H), 2.09 – 1.93 (m, 4H), 1.80 (dt, *J* = 12.2, 6.3 Hz, 2H), 1.77 – 1.66 (m, 2H), 1.64 – 1.33 (m, 6H), 0.96 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.56, 106.79, 76.38, 47.60, 37.06, 36.70, 36.42, 31.83, 24.41, 23.01, 22.11, 20.98, 14.14. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{21}NO_6$, 300.14416; found, 300.14400.



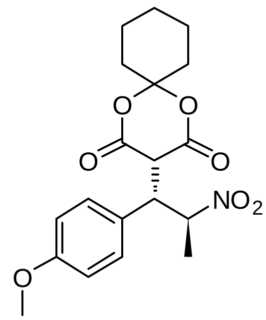
12i: (*R*)-3-(1-Cyclohexyl-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 74 mg (73% yield) of a viscous colorless oil was isolated by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 96% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 7.8 min, t_R (major) = 8.2 min) $[\alpha]_D^{20}$ = -0.6 (*c* 0.48, $CHCl_3$): IR (neat): 2928, 2855, 1780, 1740, 1552, 1451, 1369, 1305, 1265, 1067, 963, 853 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.92 (dd, *J* = 13.2, 10.2 Hz, 1H), 4.67 (dd, *J* = 13.2, 3.8 Hz, 1H), 3.85 (d, *J* = 2.1 Hz, 1H), 3.24 – 3.12 (m, 1H), 2.08 – 1.95 (m, 4H), 1.82 (m, 4H), 1.78 – 1.62 (m, 5H), 1.55 (m, 2H), 1.47 (m, 1H), 1.25 – 1.05 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.61, 106.35, 75.75, 45.37, 41.90, 37.74, 36.56, 36.15, 31.33, 30.87, 26.29, 26.04, 25.81, 23.99, 22.57, 21.68. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{17}H_{25}NO_6$, 340.17546; found, 340.17550.



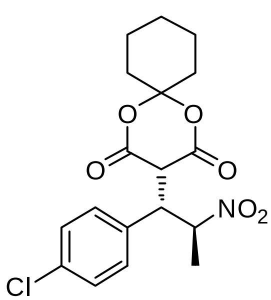
14a: 3-((1*R*,2*S*)-(2-Nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 94 mg (90% yield) of a single diastereomer, crude dr = 97:3, was isolated as a white solid, mp= 111 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 93% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 12.4 min, t_R (major) = 10.6 min) $[\alpha]_D^{20}$ = +22.1 (*c* 0.53, $CHCl_3$): IR (neat): 3021, 2946, 2870, 1776, 1741, 1549, 1497, 1452, 1368, 1297, 1274, 1070, 998, 853 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 5H), 5.90 (dq, *J* = 13.4, 6.7 Hz, 1H), 4.28 (dd, *J* = 11.6, 3.0 Hz, 1H), 3.81 (d, *J* = 3.1 Hz, 1H), 1.92 – 1.78 (m, 2H), 1.71 – 1.63 (m, 2H), 1.62 – 1.55 (m, 2H), 1.47-1.42 (m, 4H), 1.44 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 164.51, 164.19, 134.91, 129.74, 129.25, 128.75, 106.45, 83.31, 48.85, 48.53, 36.79, 36.69, 23.81, 22.25, 21.67, 19.31. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{21}NO_6$, 348.14416; found, 348.14377**.**



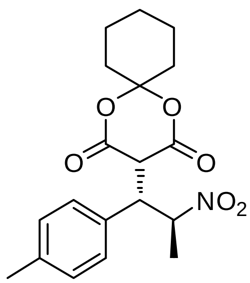
14b: 3-((1*R*,2*S*)-(2-Nitro-1-(4-trifluoromethylphenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 88 mg (71% yield) of a single diastereomer, crude dr = 95:5, was isolated as a white solid, mp 66-67 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 94% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 11.8 min, t_R (major) = 12.9 min) $[\alpha]_D^{20}$ = -4.0 (*c* 1.0, $CHCl_3$): IR (neat): 3024, 2947, 1777, 1742, 1621, 1552, 1453, 1369, 1325, 1276, 1069, 1001, 846 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.3 Hz, 2H), 5.93 (dq, *J* = 11.5, 6.7 Hz, 1H), 4.35 (dd, *J* = 11.5, 3.0 Hz, 1H), 3.85 (d, *J* = 3.0 Hz, 1H), 1.98 – 1.84 (m, 2H), 1.67 (m, 6H), 1.55 – 1.42 (m, 2H), 1.44 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 164.59, 164.13, 139.39, 131.42 (dd, *J* = 65.6, 32.9 Hz), 130.96, 126.52 (q, *J* = 3.5 Hz), 124.11 (q, *J* = 271.9 Hz), 107.07, 83.35, 48.77, 48.65, 37.00, 36.93, 24.24, 22.79, 22.02, 19.69. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{20}F_3NO_6$, 416.13155; found, 416.13137.



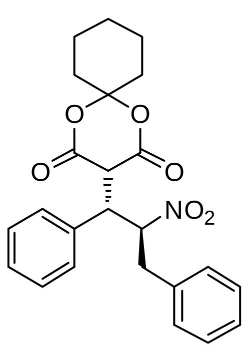
14c: 3-((1*R*,2*S*)-(1-(4-methoxyphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 103 mg (91% yield) of a single diastereomer, crude dr = 96:4, was isolated as a pale yellow solid, mp 124-125 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 92% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 19.9 min, t_R (major) = 14.1 min) $[\alpha]_D^{20}$ = -11.9 (*c* 1.0, $CHCl_3$): IR (neat): 2945, 1776, 1741, 1610, 1549, 1513, 1452, 1368, 1296, 1265, 1070, 998, 835 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.14 (dt, *J* = 8.5, 3.5 Hz, 2H), 6.87 – 6.74 (dt, *J* = 8.5, 3.5 Hz, 2H), 5.80 (dq, *J* = 11.7, 6.7 Hz, 1H), 4.16 (dd, *J* = 11.5, 3.1 Hz, 1H), 3.75 (s, 3H), 3.73 (d, *J* = 3.1 Hz, 1H), 1.86 – 1.73 (m, 2H), 1.60 (m, 2H), 1.54 (m, 2H), 1.46 (m, 2H), 1.43 – 1.36 (m, 2H), 1.36 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.58, 164.30, 159.69, 130.94, 126.53, 114.50, 106.38, 83.59, 55.23, 48.56, 48.19, 36.82, 36.65, 23.82, 22.27, 21.67, 19.32. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{23}NO_7$, 378.15473; found, 378.15460.



14d: 3-((1*R*,2*S*)-(1-(4-chlorophenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 87 mg (77% yield) of a single diastereomer, crude dr = 96:4, was isolated as a white solid, mp 123-124 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 91% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 0.8 mL/min, 210 nm, t_R (minor) = 18.4 min, t_R (major) = 16.3 min) $[\alpha]_D^{20}$ = -13.5 (*c* 2.0, $CHCl_3$): IR (neat): 2943, 2868, 1778, 1742, 1551, 1493, 1452, 1368, 1299, 1275, 1071 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 4H), 5.82 (dq, *J* = 11.6, 6.7 Hz, 1H), 4.20 (dd, *J* = 11.5, 3.1 Hz, 1H), 3.76 (d, *J* = 3.1 Hz, 1H), 1.88 – 1.78 (m, 2H), 1.62 (m, 6H), 1.39 (m, 2H), 1.38 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.28, 163.87, 134.81, 133.31, 131.34, 129.36, 106.50, 83.15, 48.37, 48.01, 36.65, 36.54, 23.82, 22.34, 21.61, 19.26. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{18}H_{20}ClNO_6$, 382.10519; found, 382.10497.

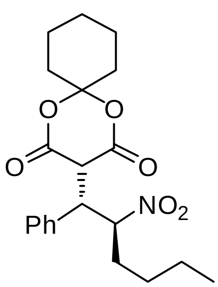


14e: 3-((1*R*,2*S*)-(1-(4-methylphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 98 mg (91% yield) of a single diastereomer, crude dr = 97:3, was isolated as a white solid, mp 142-143 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 92% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 0.8 mL/min, 210 nm, t_R (minor) = 14.7 min, t_R (major) = 13.0 min) $[\alpha]_D^{20}$ = -12.4 (*c* 2.0, $CHCl_3$): IR (neat): 2942, 2867, 1777, 1742, 1549, 1515, 1452, 1368, 1298, 1274, 1069 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 5.83 (dq, *J* = 11.6, 6.7 Hz, 1H), 4.18 (dd, *J* = 11.6, 3.1 Hz, 1H), 3.73 (d, *J* = 3.1 Hz, 1H), 2.29 (s, 3H), 1.85 – 1.77 (m, 2H), 1.61 (m, 2H), 1.55 (m, 2H), 1.46 – 1.37 (m, 4H), 1.38 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.55, 164.24, 138.60, 131.77, 129.86, 129.59, 106.36, 83.44, 48.56, 36.79, 36.68, 23.82, 22.25, 21.68, 20.98, 19.29. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{19}H_{23}NO_6$, 362.15981; found, 362.16030.

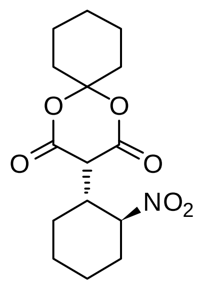


14f: 3-((1*R*,2*S*)-(3-Phenyl-2-nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 94 mg (74% yield) of a single diastereomer, crude dr = 98:2, was isolated as a white solid, mp 123-124 °C, by flash column chromatography using 80:19:1

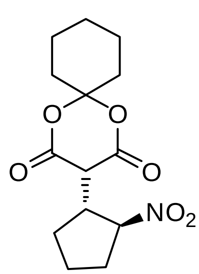
hexanes:EA:AcOH as eluent: 90% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 14.7 min, t_R (major) = 13.8 min) $[\alpha]_D^{20}$ = -18.3 (*c* 0.82, $CHCl_3$): IR (neat): 3026, 2943, 1778, 1743, 1552, 1495, 1455, 1368, 1299, 1267, 1072, 993, 859 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.31 (m, 5H), 7.26 (d, *J* = 3.0 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.07 – 6.92 (m, 2H), 6.02 (ddd, *J* = 11.8, 9.6, 4.1 Hz, 1H), 4.35 (dd, *J* = 11.8, 3.1 Hz, 1H), 3.66 (d, *J* = 3.1 Hz, 1H), 3.04 – 2.84 (m, 2H), 1.86 – 1.74 (m, 2H), 1.61 (m, 2H), 1.55 – 1.48 (m, 2H), 1.44 – 1.31 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.56, 135.45, 134.81, 130.42, 129.88, 129.43, 129.16, 129.09, 127.95, 106.95, 90.76, 77.22, 48.98, 48.49, 39.44, 37.21, 24.23, 22.67, 22.11. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{24}H_{25}NO_6$, 424.17546; found, 424.17557.



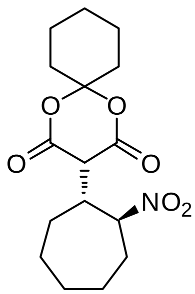
14g: 3-((1*R*,2*S*)-(2-Nitro-1-phenylhexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 82 mg (70% yield) of a single diastereomer, crude dr = 99:1, was isolated as a white solid, mp 95-96 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 83% ee (Chiralcel IA, 92 (1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm, t_R (minor) = 8.4 min, t_R (major) = 8.0 min) $[\alpha]_D^{20}$ = -12.2 (*c* 0.59, $CHCl_3$): IR (neat): 2959, 2873, 1777, 1745, 1550, 1496, 1453, 1368, 1299, 1264, 1077, 992, 853 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 5H), 5.82 (ddd, *J* = 11.7, 10.4, 3.0 Hz, 1H), 4.31 (dd, *J* = 11.7, 3.2 Hz, 1H), 3.67 (d, *J* = 3.2 Hz, 1H), 1.83 (m, 2H), 1.76 (m, 1H), 1.66 (m, 2H), 1.56 (m, 3H), 1.41 (m, 4H), 1.34 – 1.25 (m, 3H), 1.24 – 1.14 (m, 1H), 0.81 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.33, 164.21, 134.56, 129.76, 129.24, 128.77, 106.44, 88.76, 48.49, 48.15, 36.91, 36.70, 32.48, 27.41, 23.79, 22.21, 21.75, 21.66, 13.56. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{21}H_{27}NO_6$, 390.19111; found, 390.19107.



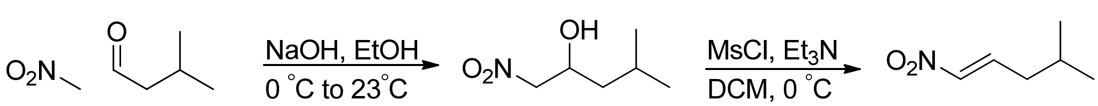
14h: 3-((1*R*,2*S*)-(2-Nitrocyclohexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 73 mg (78% yield) of a single diastereomer, crude dr = 87:13, was isolated as a white solid, mp 149 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 91% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 8.9 min, t_R (major) = 9.9 min) $[\alpha]_D^{20}$ = -15.4 (*c* 0.57, $CHCl_3$): IR (neat): 2946, 2867, 1778, 1743, 1547, 1453, 1369, 1295, 1265, 1056, 1000, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.22 (td, *J* = 11.6, 4.0 Hz, 1H), 3.59 (d, *J* = 2.5 Hz, 1H), 3.10 – 2.89 (tdd, *J* = 11.6, 4.0, 2.5 Hz, 1H), 2.47 – 2.29 (m, 1H), 1.99 – 1.83 (m, 6H), 1.83-1.74 (m, 4H), 1.72 – 1.65 (m, 2H), 1.64-1.56 (m, 1H), 1.53-1.46 (m, 2H), 1.44-1.33 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.14, 163.82, 106.20, 85.75, 47.02, 40.40, 36.61, 35.98, 32.04, 26.60, 24.78, 24.13, 23.96, 22.52, 21.67. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{15}H_{21}NO_6$, 312.14416; found, 312.14390.



14i: 3-((1*R*,2*S*)-(2-Nitrocyclopentyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 46 mg (52% yield) of a single diastereomer, crude dr = 90:10, was isolated as a white solid, mp 148 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 97% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 8.8 min, t_R (major) = 10.1 min) $[\alpha]_D^{20}$ = +21.3 (*c* 0.69, $CHCl_3$): IR (neat): 2946, 1782, 1742, 1644, 1546, 1452, 1369, 1307, 1265, 1064, 1001, 854 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.23 (td, *J* = 8.1, 5.3 Hz, 1H), 4.10 (d, *J* = 3.1 Hz, 1H), 3.27 (tdd, *J* = 8.1, 5.3, 3.1 Hz, 1H), 2.38 – 2.19 (m, 2H), 2.04 (m, 1H), 2.01 – 1.95 (m, 2H), 1.94 – 1.87 (m, 2H), 1.86 – 1.76 (m, 2H), 1.72 (m, 2H), 1.65 (m, 2H), 1.45 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.55, 164.51, 106.86, 88.06, 47.96, 44.06, 37.21, 36.05, 31.72, 28.50, 24.42, 24.35, 23.04, 22.15. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{14}H_{19}NO_6$, 298.12851; found, 298.12850.

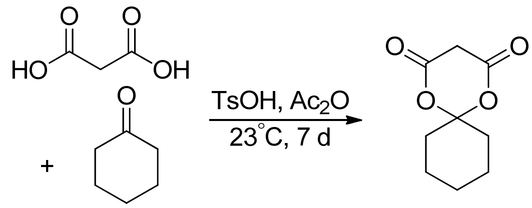


14j: 3-((1*R*,2*S*)-(2-Nitrocycloheptyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione: 90 mg (92% yield) of a single diastereomer, crude dr = >99:1, was isolated as a white solid, mp 122 °C, by flash column chromatography using 80:19:1 hexanes:EA:AcOH as eluent: 98% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 8.5 min, t_R (major) = 9.0 min) $[\alpha]_D^{20}$ = +20.0 (*c* 0.88, $CHCl_3$): IR (neat): 2939, 2860, 1781, 1743, 1545, 1453, 1369, 1303, 1265, 1067, 974, 859 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (td, *J* = 5.2, 4.8 Hz, 1H), 3.72 (d, *J* = 2.4 Hz, 1H), 3.30 (tdd, *J* = 11.2, 4.8, 2.4 Hz, 1H), 2.50 – 2.28 (m, 1H), 2.25 – 2.08 (m, 1H), 1.99 – 1.63 (m, 13H), 1.64 – 1.46 (m, 3H), 1.46 – 1.30 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.30, 164.01, 106.26, 88.72, 49.70, 41.80, 36.68, 35.77, 32.63, 29.09, 28.72, 28.34, 23.98, 22.56, 21.67. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{16}H_{23}NO_6$, 326.15981; found, 326.15983.



Large scale synthesis of *trans*-1-nitro-4-methyl-pent-1-ene. The following is a modified version of the procedure described by Bassas et al.[7] In a 3-L, 2 neck roundbottom flask with 5 cm oval stirbar and an internal temperature probe was added isovaleraldehyde (241 mL, 2.25 mol), nitromethane (124 mL, 2.30 mol) and ethanol (1 L). The flask was then submerged in an ice-water bath and stirred until the temperature was 8 °C at which point the flask was fitted with an additional funnel and a 10 M solution of NaOH (90 g, 2.25 mol) was added dropwise such that the internal temperature remained between 10-15 °C. After ~150 mL of the NaOH solution had been added, a white slurry formed. Eventually the flask required swirling by hand for the remaining addition. Once the addition is complete the flask is allowed to warm to room temperature (12 h). The reaction is then quenched by the addition of AcOH (129 mL, 2.26 mol) all at once. The contents of the flask are transferred to a 6-L separatory funnel and the product is extracted with 4 L of Et_2O. The Et_2O layer is washed with H_2O (4X ~500 mL) then washed with a saturated solution of $NaHCO_3$ (1 X 500 mL) and finally a brine solution (1 X 500 mL). The Et_2O layer is then dried over magnesium sulfate and concentrated. The concentrated product was then placed on a Kugelrohr distillation apparatus and gently rocked and warmed (35-45 °C) for 3 h. This was found to be necessary to remove trace ethanol. The crude nitro alcohol, 4-methyl-1-nitropentan-2-ol, was sufficiently pure for the next step (290.32 g, 87.8%).

In a 5-L, 4 neck round bottom flask equipped with a mechanical stirrer, nitrogen inlet, stopper and addition funnel was placed the nitroalcohol (292.32 g, 1.97 mol), DCM (1.97 L) and MsCl (167.3 mL, 2.17 mol), and the flask was placed in an ice bath and allowed to stir for 20 min. Then Et_3N (589 mL, 4.24 mol) was placed in the addition funnel and added over 1 h. The reaction becomes heterogeneous after ~2/3 of the amine has been added. The reaction was given an additional 30 minutes after all the Et_3N had been added. The reaction mixture is transferred to a 6-L separatory funnel and washed with H_2O (2 X 1 L) then 1 M HCl (1 X 0.3 L) and dried over MgSO4. The solvent is removed *in vacuo* and then the crude nitroalkene is purified by short path distillation (85 °C, 5 mmHg) affording *trans*-1-nitro-4-methyl-pent-1-ene (213.82 g, 84%).



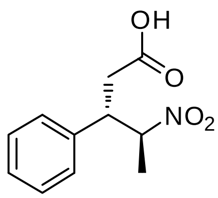
Large scale synthesis of cyclohexyl Meldrum's acid. In a procedure adapted from that of Velikorodov[8] a 3-L, 3 neck round bottom flask equipped with a 5 cm oval stir bar was fitted with rubber stoppers. Within the flask was placed malonic acid (500 g, 4.81 mol), TsOH*H_2O (15.5 g, 0.0818 mol), cyclohexanone (497 mL, 4.81 mol) and then Ac_2O (776 mL). The heterogeneous mixture was stirred until it became a homogenous black solution (~ 5 h), and then the stirring was discontinued. After 7 d, 2.38 L of H_2O was added, and the resulting mixture was stirred until the product precipitated. The flask was moved to an ice bath and allowed to cool. Then the product was filtered on a Buchner funnel and washed with hot hexanes. The product was dried on the filter and then recrystallized using 5 mL/g of hot 5:2 hexanes: EtOH (200 proof). The crystals were then filtered and washed with hot hexanes to remove any remaining color to afford pure cyclohexyl Meldrum's acid (445 g, 50%). This procedure has been performed on 20 mol scale with similar results.

Procedure for Large Scale Enantioselective Addition of Cyclohexyl Meldrum's Acid to *trans*-1-nitro-4-methyl-pent-1-ene. To a 3-neck, 3-L Morton type round bottom flask equipped with stir bar (1.5 inch, oval) was added *trans*-1-nitro-4-

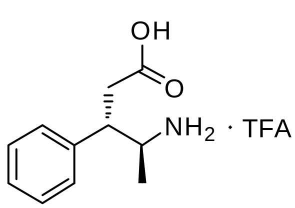
methyl-pent-1-ene (129 g, 1.00 mol), sulfinyl urea catalyst **8** (0.95 g, 2.00 mmol), cyclohexyl Meldrum's acid (368 g, 2.00 mol), and cyclopentyl methyl ether (0.83 L). The reaction flask was stoppered, and the heterogeneous reaction mixture was stirred at 35 °C (oil bath) for 48 h. The reaction mixture became homogeneous within ~1.5 h. The reaction progress was monitored by the disappearance of the nitroalkene by TLC (R_f = 0.8, 8:2 Hex:EA). Upon complete reaction conversion (48 h), the CPME was removed *in vacuo,* and the crude reaction mixture was diluted with 400 mL of toluene and then concentrated to remove trace CPME (dilution and concentration was repeated a 2nd time). The unpurified product was then used directly in the next step without further purification. A small sample of the product (< 5 mg) was taken aside for determination of enantiomeric excess: 92% ee (Chiralcel IA, 90 (1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm, t_R (minor) = 7.2 min, t_R (major) = 7.6 min). By ^{1}H NMR analysis, the reaction was determined to have proceeded to complete conversion.

Procedure for Large Scale One-Pot Hydrolysis and Decarboxylation of (*S*)-3-(4-methyl-1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione. The procedure for hydrolysis and decarboxylation was adapted from U.S. Patent WO2008117305 for industrial Lyrica production.[9] To the flask containing the crude (*S*)-3-(4-methyl-1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione (313 g, 1.00 mol) was added toluene (0.83 L) and *p*-toluenesulfonic acid monohydrate (86.0 g, 0.500 mol). It should be noted that 0.25 equiv of *p*-toluenesulfonic acid was used with respect to the sum of the adduct and excess cyclohexyl Meldrum's acid. Finally, H_2O (45 mL, 2.5 mol) was added and the flask was fitted with a condenser with an N_2 inlet at the top and with an internal temperature probe. The reaction mixture was heated in an oil bath such that the internal temperature was 90 ^{o}C for 24 h. An intermediate, which was presumably the diacid hydrolysis product, rapidly formed (<2 h) as determined by NMR analysis of an aliquot of the reaction mixture (vide infra). The reaction progress was monitored by taking an aliquot (5 μL) of the reaction mixture, blowing off the toluene, diluting the residue with $CDCl_3$, and monitoring by ^{1}H NMR for the disappearance of the diastereotopic α-CH_2 of the diacid intermediate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.71 (dd, *J* = 13.6, 5.7 Hz, 1H). Once the reaction was determined to be complete, the reaction mixture was allowed to cool to room temperature. Then the reaction flask was placed in an ice bath, and with rapid stirring a ~30% solution of Na_2CO_3 was slowly added until the pH was 8. Then the biphasic mixture was transferred to a 6 L separatory funnel. The aqueous layer was separated, and the organic layer was extracted a second time with 30% Na_2CO_3 solution. The combined aqueous layers were washed with toluene (250 mL) and then transferred to a x 4 L Erlenmeyer flask fitted with 1.5 inch oval stir bar. The flask was placed in an ice bath, toluene was added (0.5 L), and the resulting mixture was allowed to cool to 0 ^{o}C with stirring. Then, with stirring, 3 M HCl was added until the aqueous layer reached pH <2. The biphasic mixture was transferred back to the separatory funnel, and an additional 250 mL of toluene was added. The layers were separated, and the acidic layer was extracted a second time with toluene (250 mL). The combined organic layers were washed with brine (2 X 200 mL) and then dried over magnesium sulfate, filtered and concentrated to afford monoacid **15** (170 g, 0.90 mol), which was obtained as a viscous oil in 90% overall yield from *trans*-1-nitro-4-methyl-pent-1-ene. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 (dd, *J* = 12.4, 6.8 Hz, 1H), 4.46 (dd, *J* = 12.4, 5.8 Hz, 1H), 2.69 (dtd, *J* = 6.8, 6.4, 5.8 Hz, 1H), 2.52 (d, *J* = 6.4 Hz, 2H), 1.67 (septet, *J* = 6.8 Hz, 1H), 1.35 – 1.25

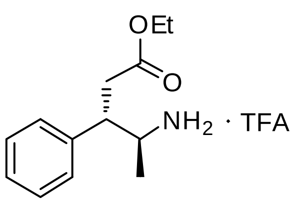
(m, 2H), 0.93 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.49, 78.90, 40.82, 36.16, 32.20, 25.44, 22.84, 22.63.



Intermediate 16: The procedure for hydrolysis and decarboxylation was adapted from U.S. Patent WO2008117305 for industrial Lyrica production.[9] To a vial containing adduct **14a** (104 mg, 0.3 mmol) was added toluene (0.25 mL), *p*-toluenesulfonic acid monohydrate (14 mg, 0.075 mmol), and water (6 μL). The reaction mixture was heated at 90 °C for 24 h and then was cooled to rt. The reaction mixture was diluted with toluene (1-2 mL) then washed with 2 x 1 mL of 5% $Na_2CO_{3(aq)}$. The combined aqueous layers were washed with 1 mL of toluene, and the toluene layers were discarded. The aqueous layer was acidified to pH 2 with 1 N $HCl_{(aq)}$, then extracted with 3 x 3 mL of toluene. The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford nitro monoacid **16** as a single diastereomer (62 mg, 93% yield). Intermediate **16** was obtained as an oil, $[\alpha]_D^{20}$ = +13.3 (*c* 1.0, $CHCl_3$): IR (neat): 3064, 3032, 2993, 2946, 1712, 1549, 1496, 1454, 1389, 1360, 1261, 1082 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 3H), 7.11 – 7.06 (m, 2H), 4.81 – 4.54 (dq, *J* = 6.8, 6.4 Hz, 1H), 3.65 – 3.45 (ddd, *J* = 10.0, 4.8, 6.8 Hz, 1H), 2.74 – 2.68 (dd, *J* = 16.4, 10.0 Hz, 1H), 2.64-2.58 (dd, *J* = 16.4, 4.8 Hz, 1H), 1.26 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.34, 134.14, 129.06, 128.12, 86.79, 45.87, 37.28, 17.65. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{11}H_{13}NO_4$, 246.07368; found, 246.07377**.**



Amino Acid 17: The procedure for reduction was adapted from a literature procedure by Grenning et al.[10] To a 10 mL vial with stir bar was added nitro acid **16** (50 mg, 0.224 mmol), zinc dust (283 mg, 4.35 mmol) then isopropanol (0.1 mL) and aqueous HCl (2.24 mL, 1 M). The reaction flask was placed in an oil bath and heated to 50 °C for 2 h. The reaction mixture was then filtered over a cotton plug to remove excess zinc metal, concentrated and then purified by reverse phase chromatography on a C18 column (5-100% methanol in water with 0.1% TFA) to provide the TFA salt of the amino acid as a single diastereomer (67 mg, 97%). Product **17** was obtained as an oil, $[\alpha]_D^{20}$ = +0.6 (*c* 0.85, MeOH): IR (neat): 2924, 2854, 1663, 1456, 1180, 1137, 799, 757, 701 cm^{-1}. ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.39 (m, 2H), 7.34 (m, 1H), 7.32 – 7.27 (m, 2H), 3.65 (dq, *J* = 7.0, 6.7 Hz, 1H), 3.38 – 3.36 (m, 1H), 2.92 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.80 (dd, *J* = 16.1, 9.1 Hz, 1H), 1.15 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, MeOH-d_4) δ 174.73, 139.58, 129.98, 129.71, 128.92, 52.04, 46.89, 38.02, 16.51. ^{19}F NMR (400 MHz, MeOH-d_4) δ -77.04. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{11}H_{15}NO_2$, 194.11756; found, 194.11717.



Amino Ethyl Ester 18: The procedure for reduction was adapted from a literature procedure by Kimmel et al.[4] To a 4-mL vial with a stir bar and plastic cap was added anhydrous tin(II) chloride (378 mg, 2.0 mmol) and nitro monoacid **16** (45 mg, 0.2 mmol). In a separate vial, dry ethanol (2 mL) and acetyl chloride (0.14 mL, 2.0 mmol) were premixed and let sit until heat of mixing subsided, and the mixture was then added to reaction vial all in one portion. The reaction vial was placed in a 95 °C oil bath and reaction mixture was stirred at reflux for 20 h and then was allowed to cool to room temperature. The solvent was evaporated *in vacuo* and the crude residue was purified by reverse phase chromatography on a C18 column (5-100% methanol in water with 0.1% TFA) to provide the TFA salt of the amino ethyl ester as a single diastereomer (41 mg, 61%).

Product **18** was obtained as an oil, $[\alpha]_D^{20}$ = +4.8 (*c* 1.0, MeOH): IR (neat): 2983, 1671, 1537, 1431, 1375, 1178, 1134, 1025, 907, 837, 721, 701 cm^{-1}. ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.46 – 7.23 (m, 5H), 4.00 (q, *J* = 7.1 Hz, 2H), 3.69 – 3.58 (m, 1H), 3.37 (m, 1H), 2.93 (dd, *J* = 15.7, 5.4 Hz, 1H), 2.82 (dd, *J* = 15.7, 9.8 Hz, 1H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, MeOH-d_4) δ 172.76, 139.31, 129.97, 129.72, 129.00, 61.76, 52.03, 47.13, 38.24, 16.60, 14.27. ^{19}F NMR (400 MHz, MeOH-d_4) δ -76.99. HRMS-ESI (m/z): $[M+H]^+$ calcd for $C_{13}H_{19}NO_2$, 222.14886; found, 222.14820**.**

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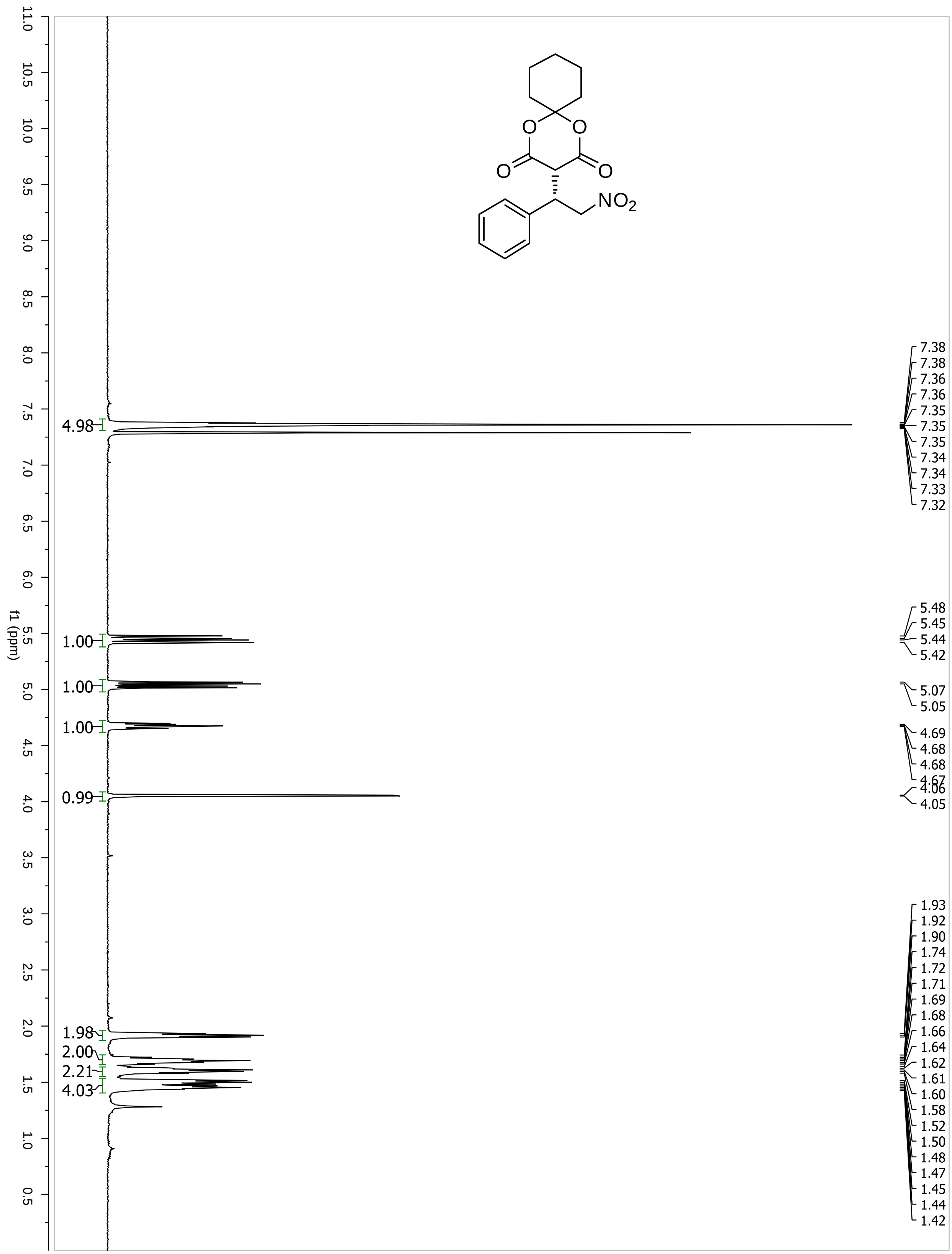
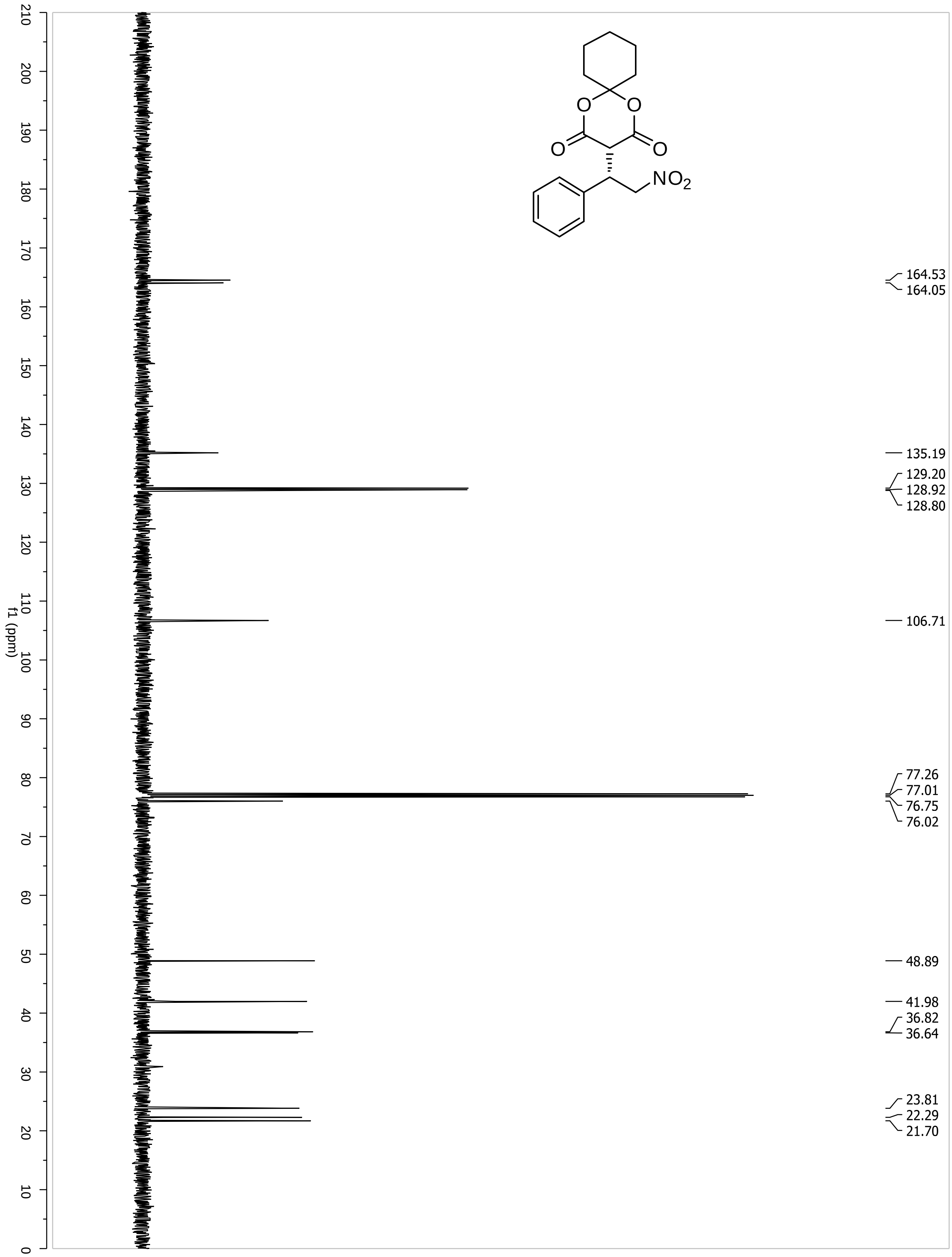
12a: (*R*)-3-(2-nitro-1-phenylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione

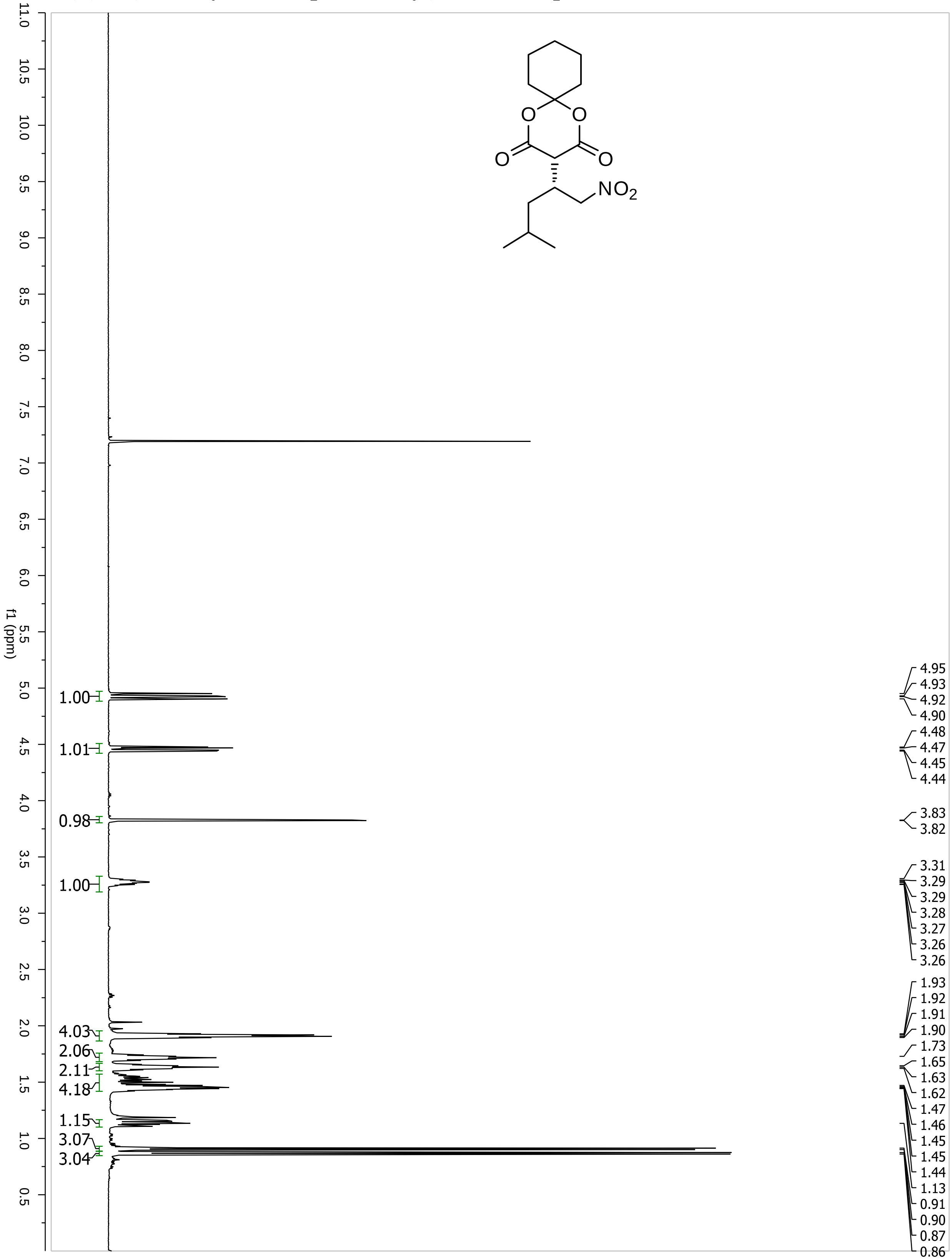
Electronic Supplementary Material (ESI) for Chemical Science



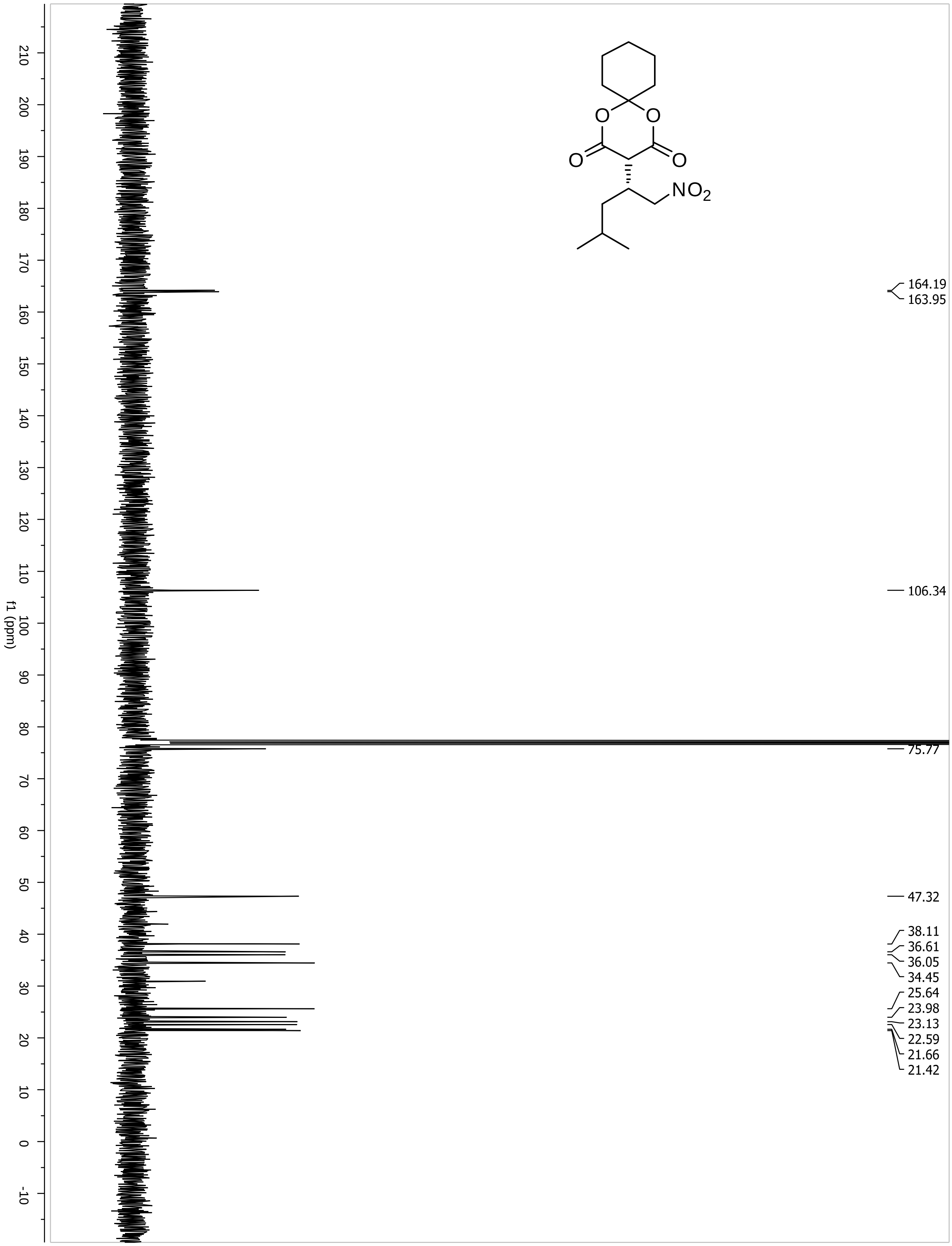
12a: (*R*)-3-(2-nitro-1-phenylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione


NO2
O
O
O
O
164.53
164.05
135.19
129.20
128.92
128.80
106.71
77.26
77.01
76.75
76.02
48.89
41.98
36.82
36.64
23.81
22.29
21.70
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

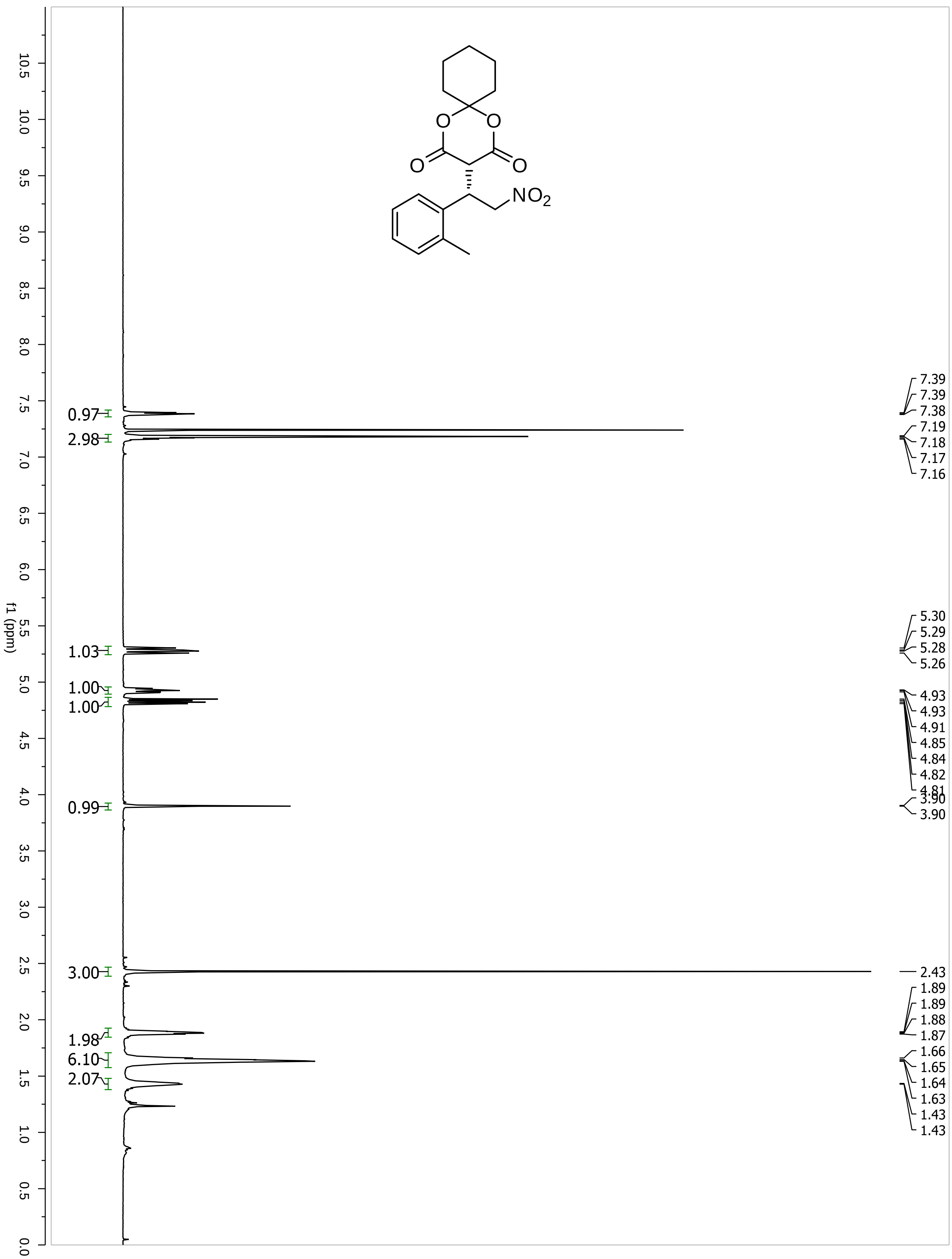
12b: (*R*)-3-(4-methyl-1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



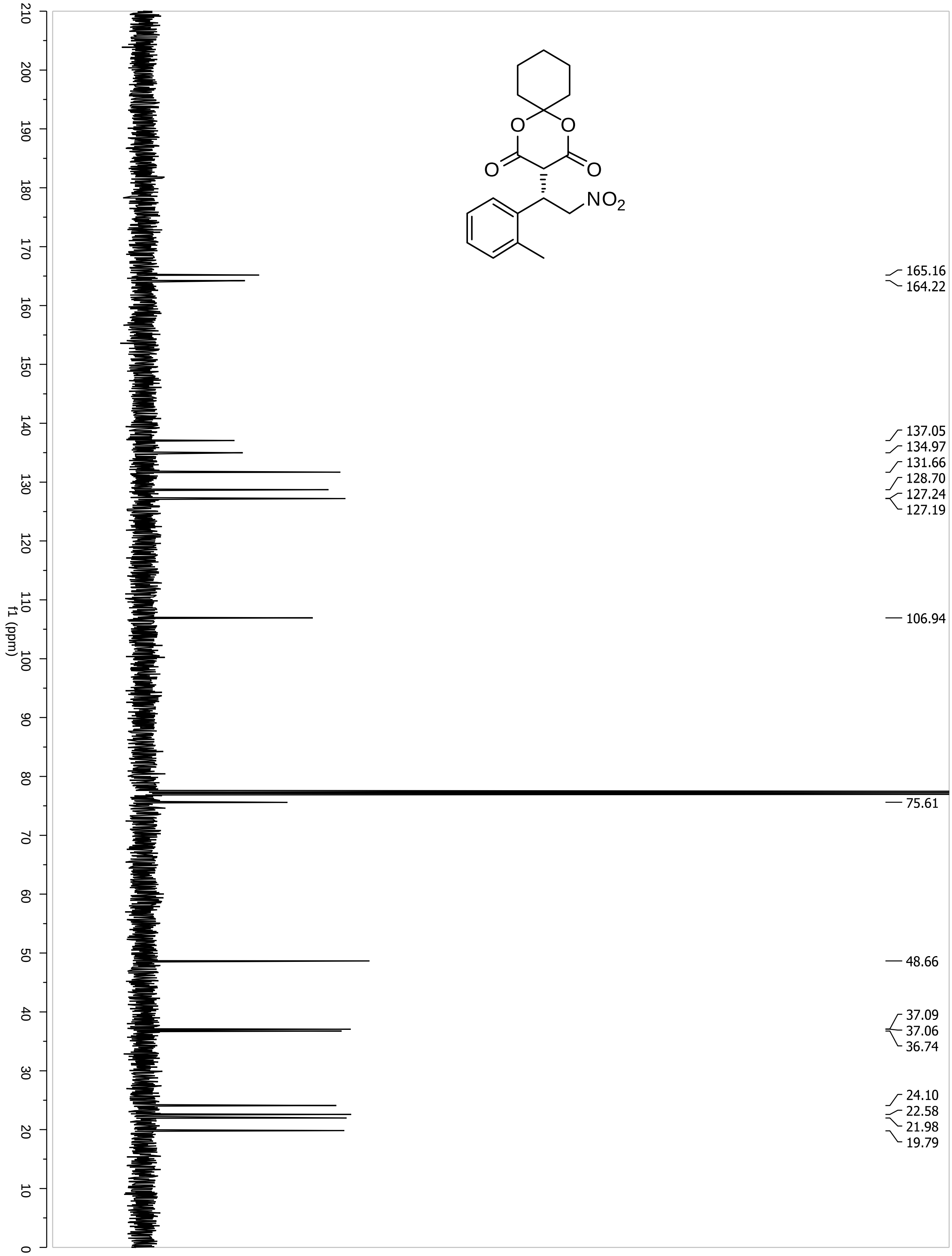
12b: (*R*)-3-(4-methyl-1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



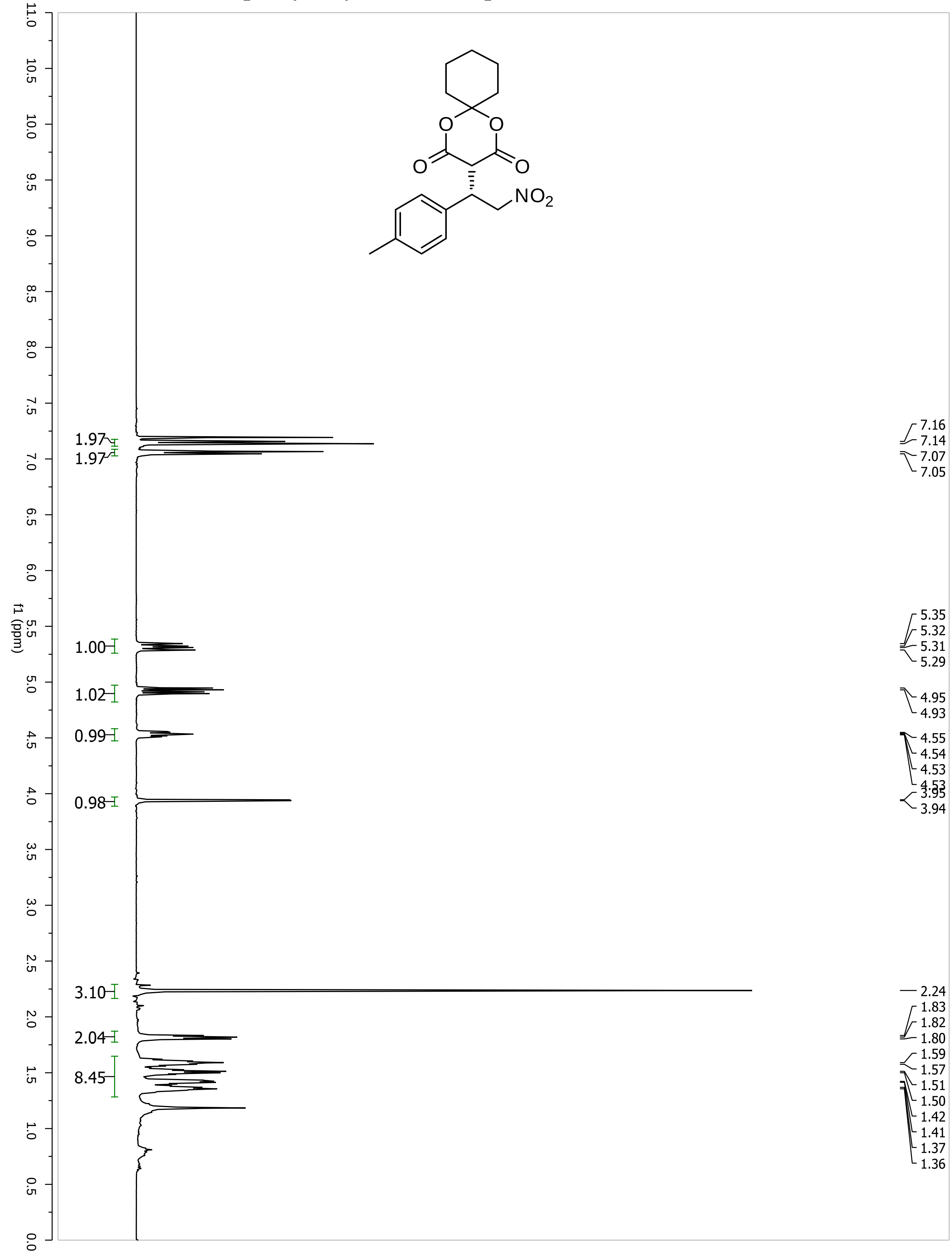
12c: **(*R*)-3-(2-nitro-1-o-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione**



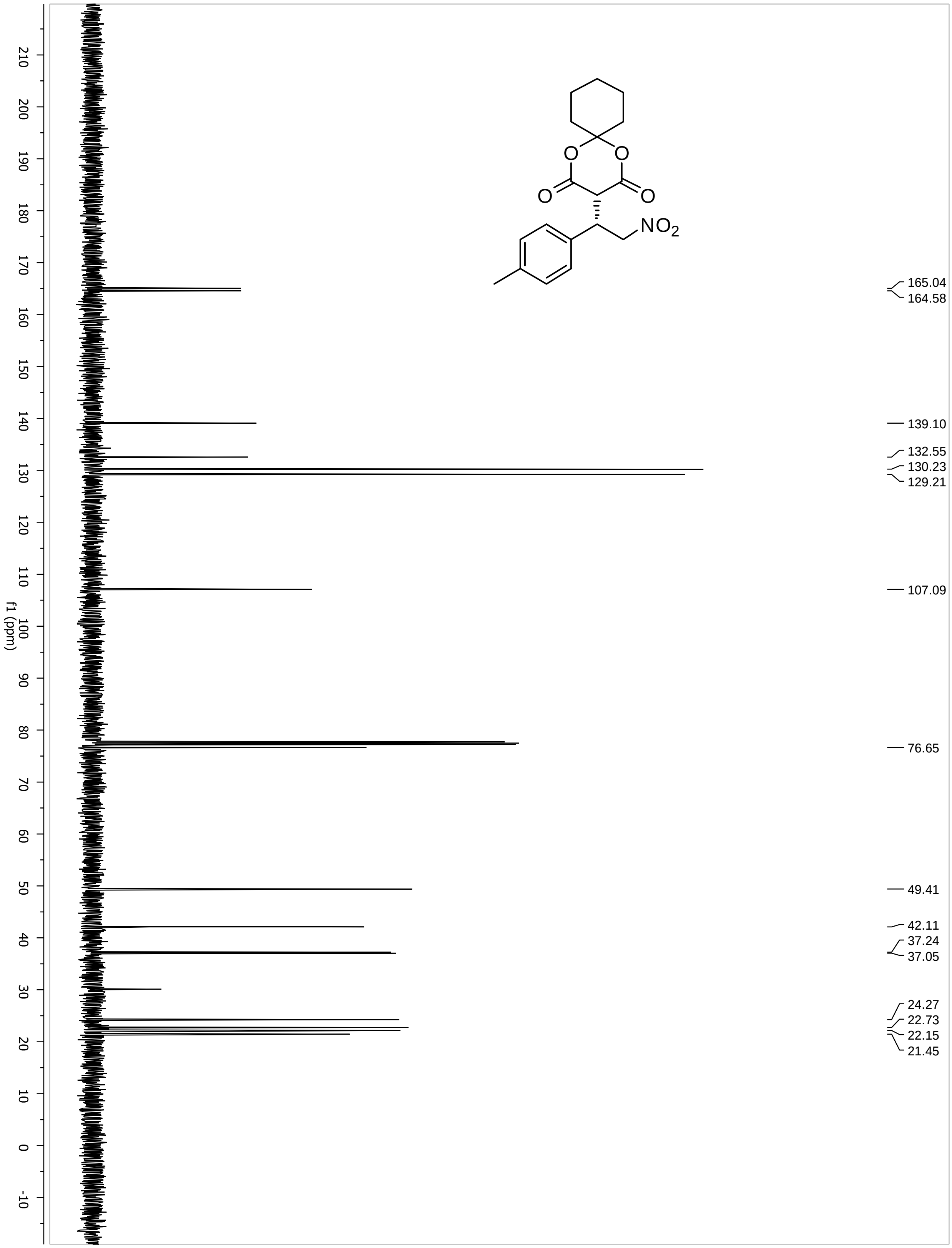
12c: (*R*)-3-(2-nitro-1-o-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



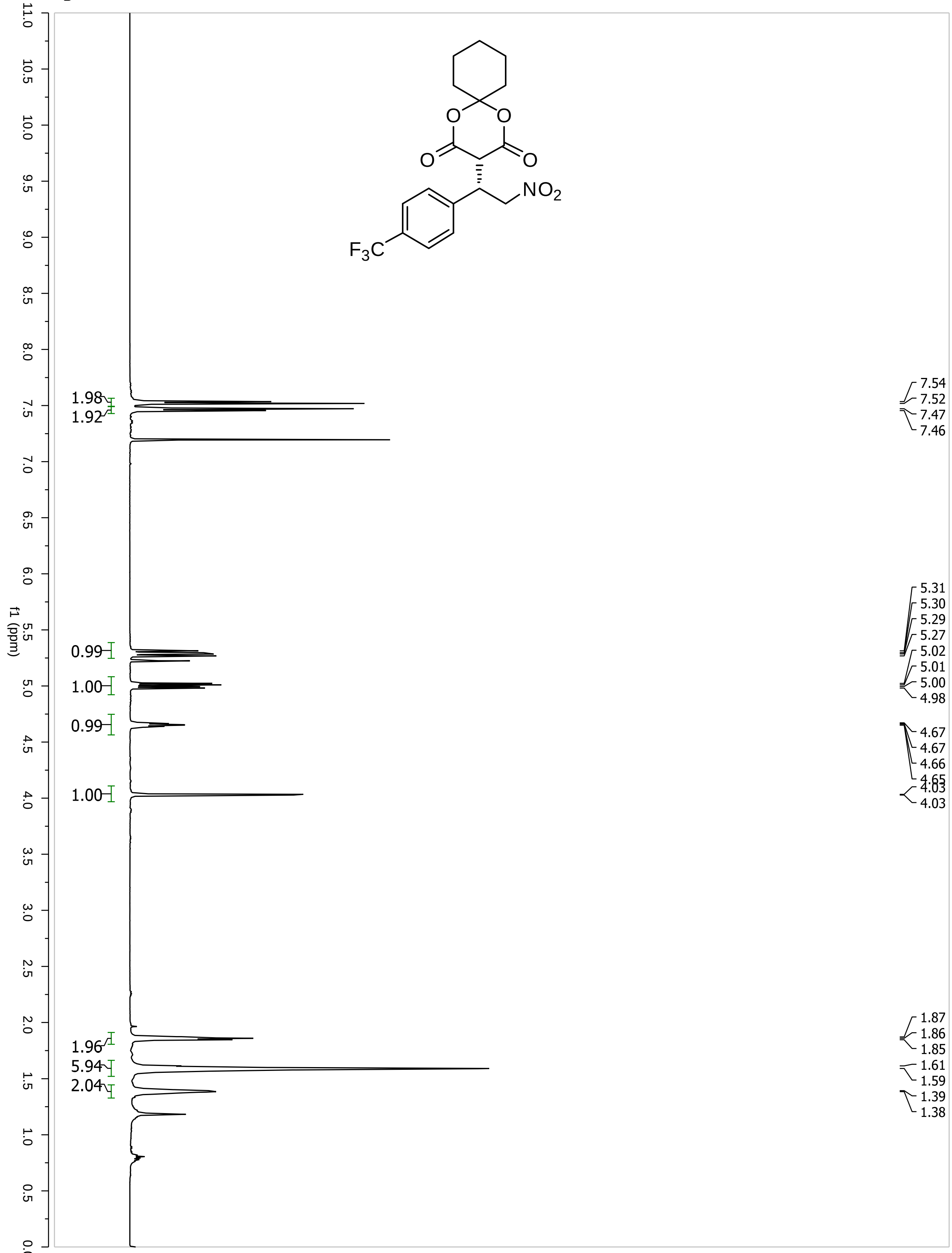
12d: **(*R*)-3-(2-nitro-1-p-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione**



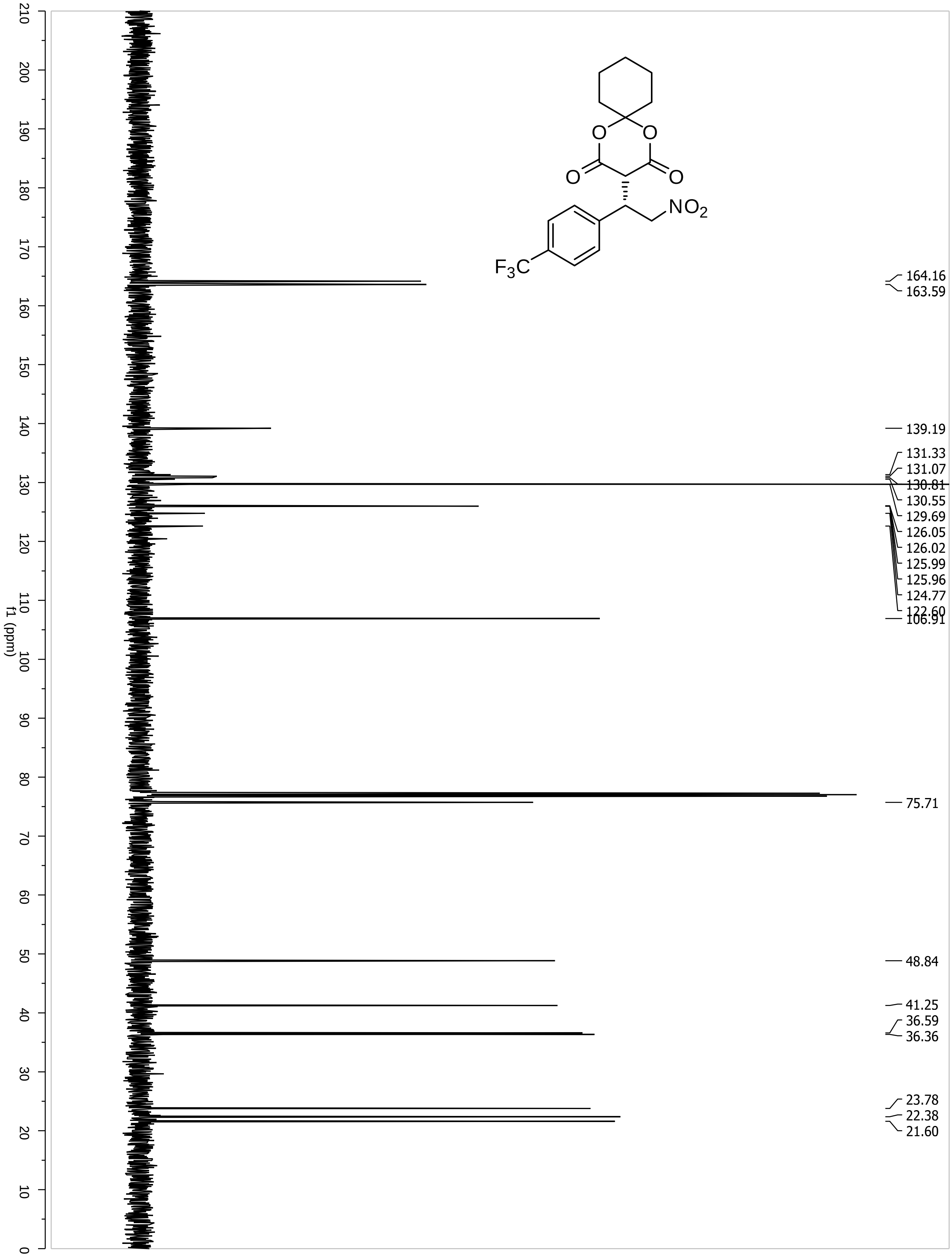
12d: (*R*)-3-(2-nitro-1-p-tolylethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



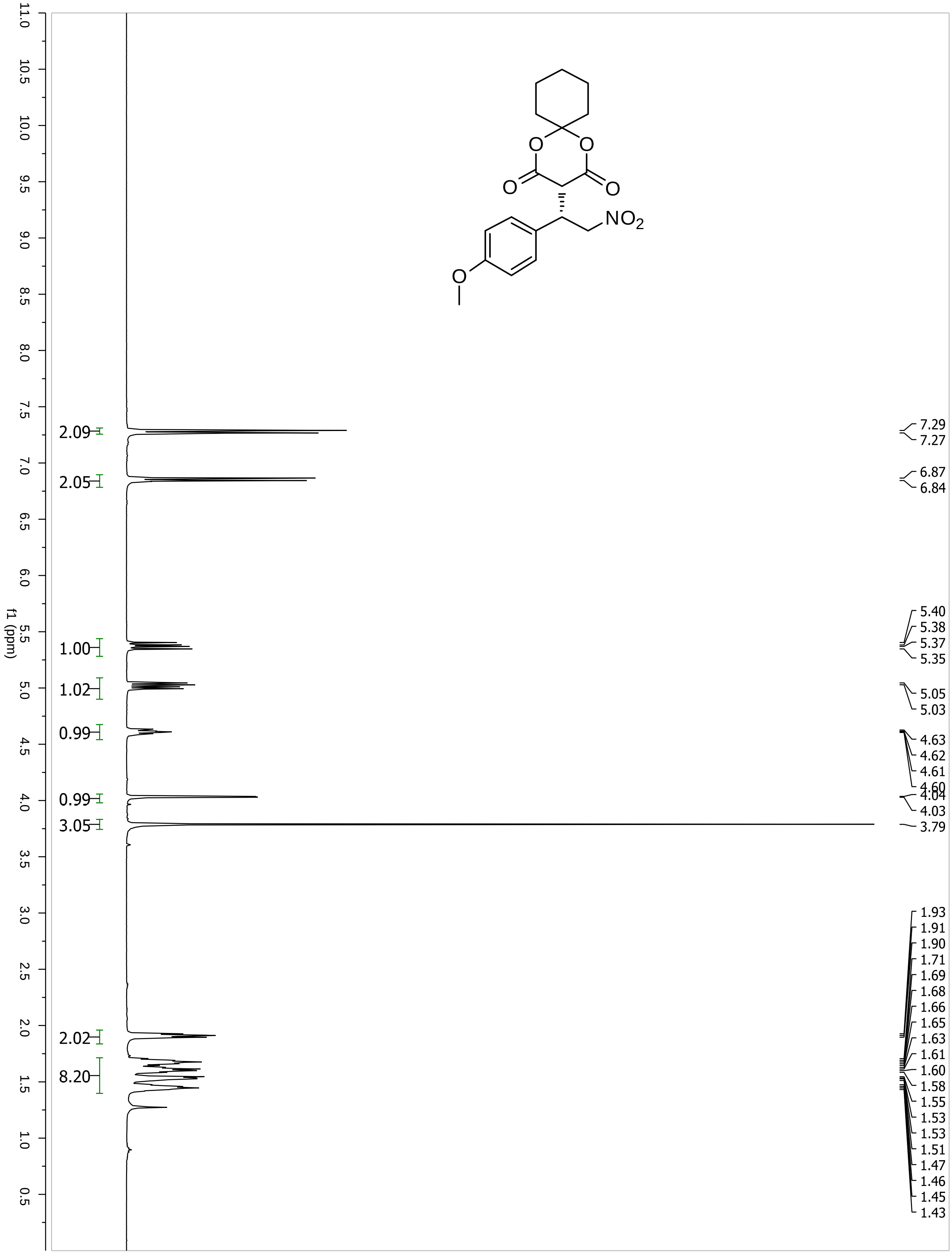
12e: (*R*)-3-(2-nitro-1-(4-(trifluoromethyl)phenyl)ethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



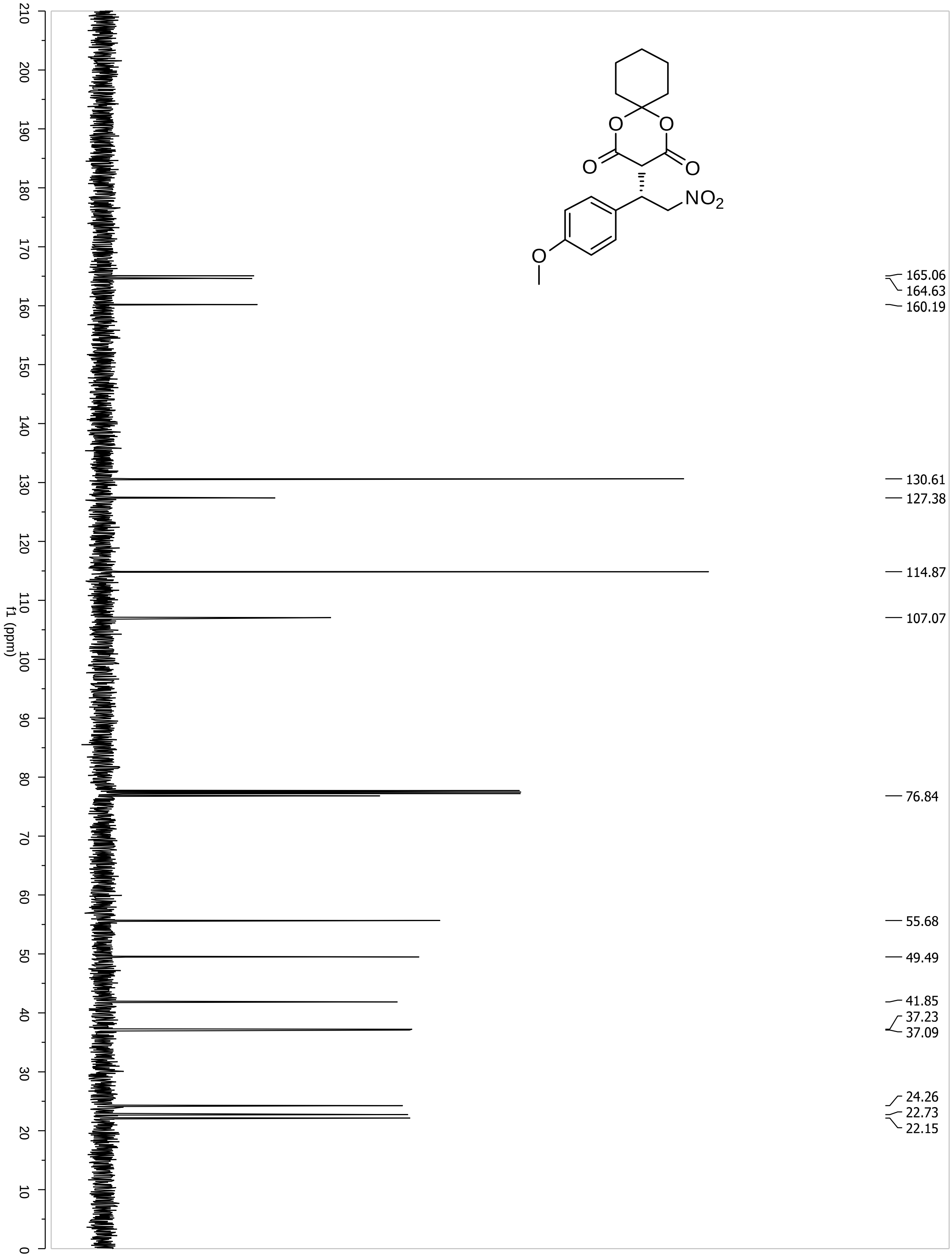
12e: (*R*)-3-(2-nitro-1-(4-(trifluoromethyl)phenyl)ethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



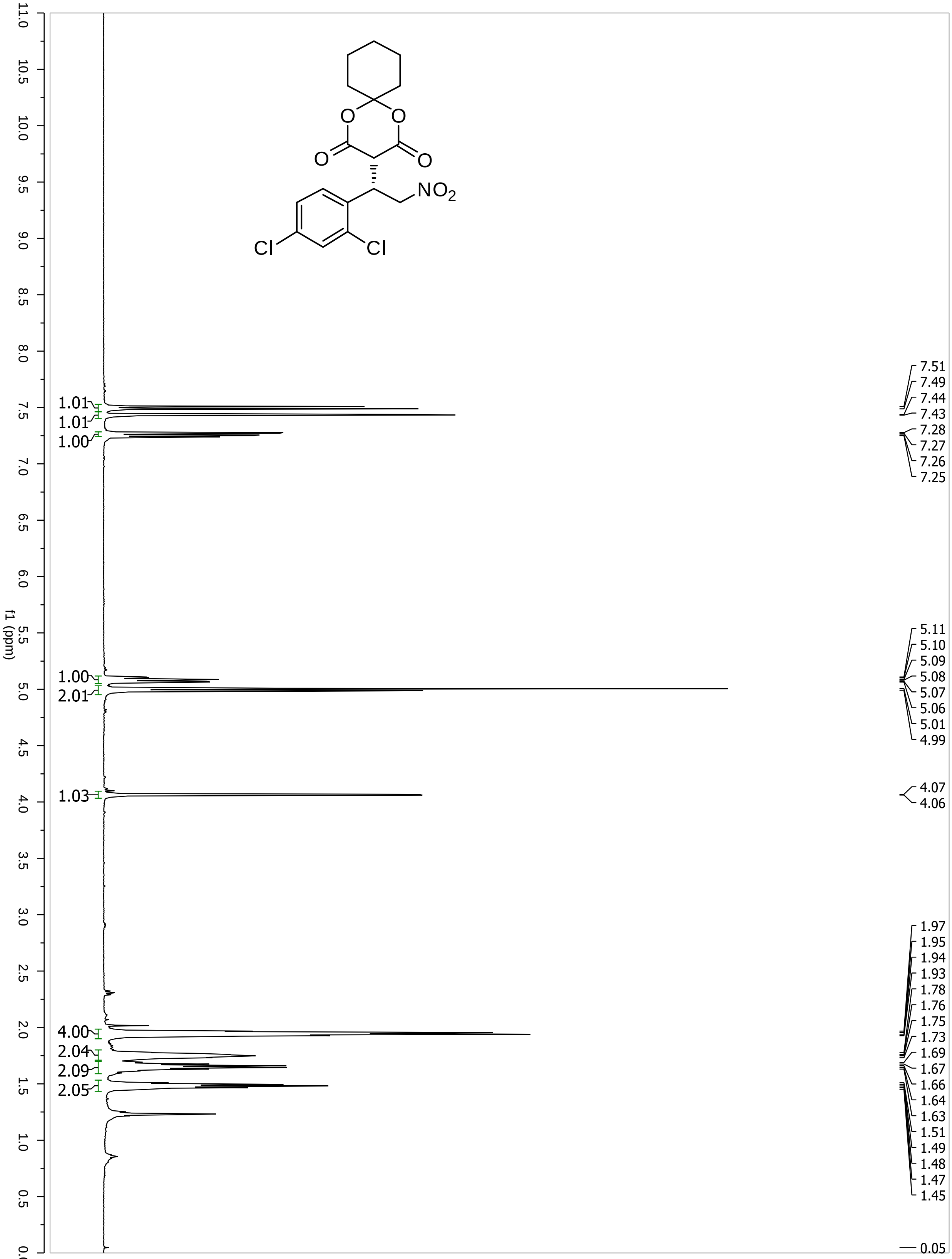
12f: (*R*)-3-(1-(4-methoxyphenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



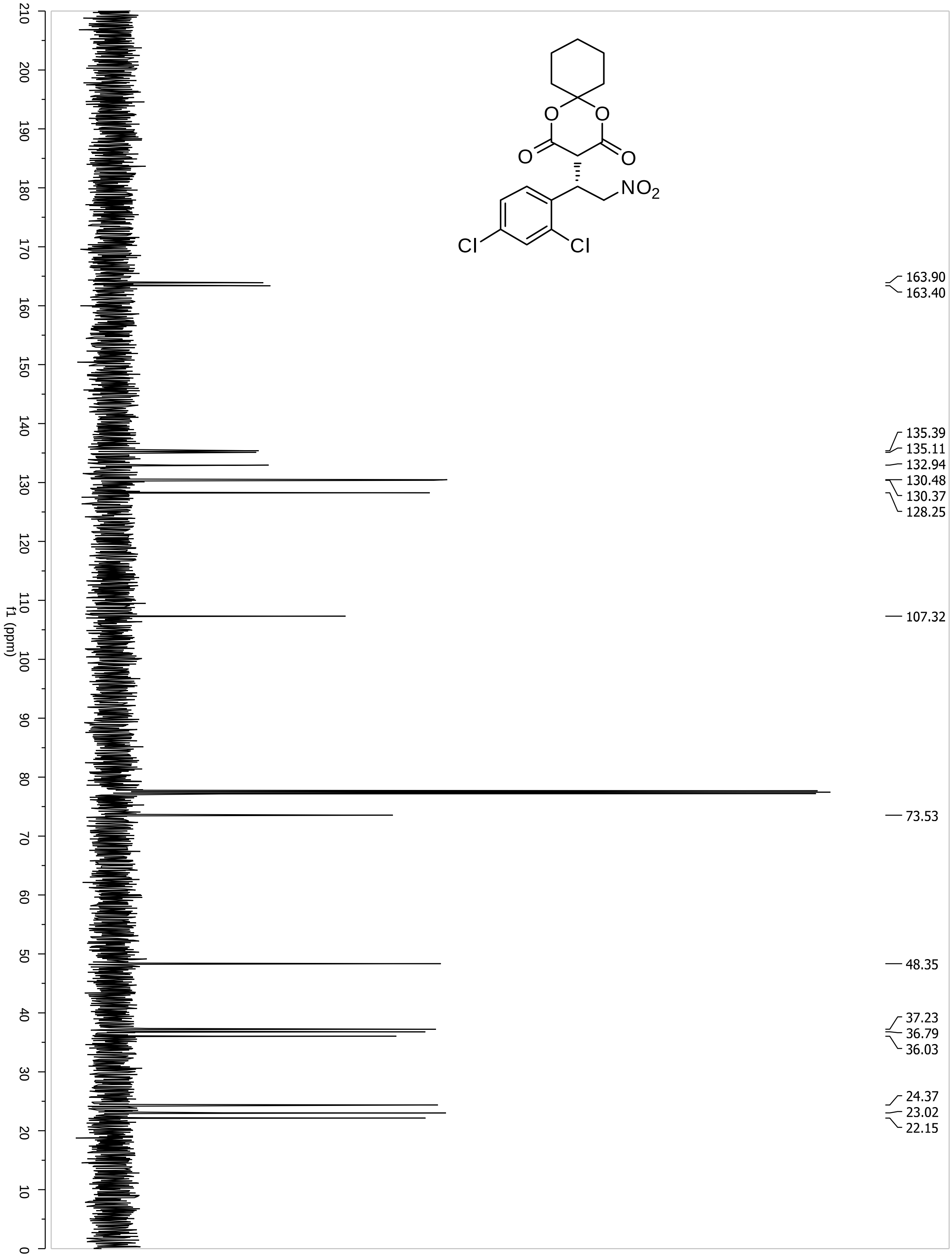
12f: (*R*)-3-(1-(4-methoxyphenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



12g: (*R*)-3-(1-(2,4-dichlorophenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



12g: (*R*)-3-(1-(2,4-dichlorophenyl)-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



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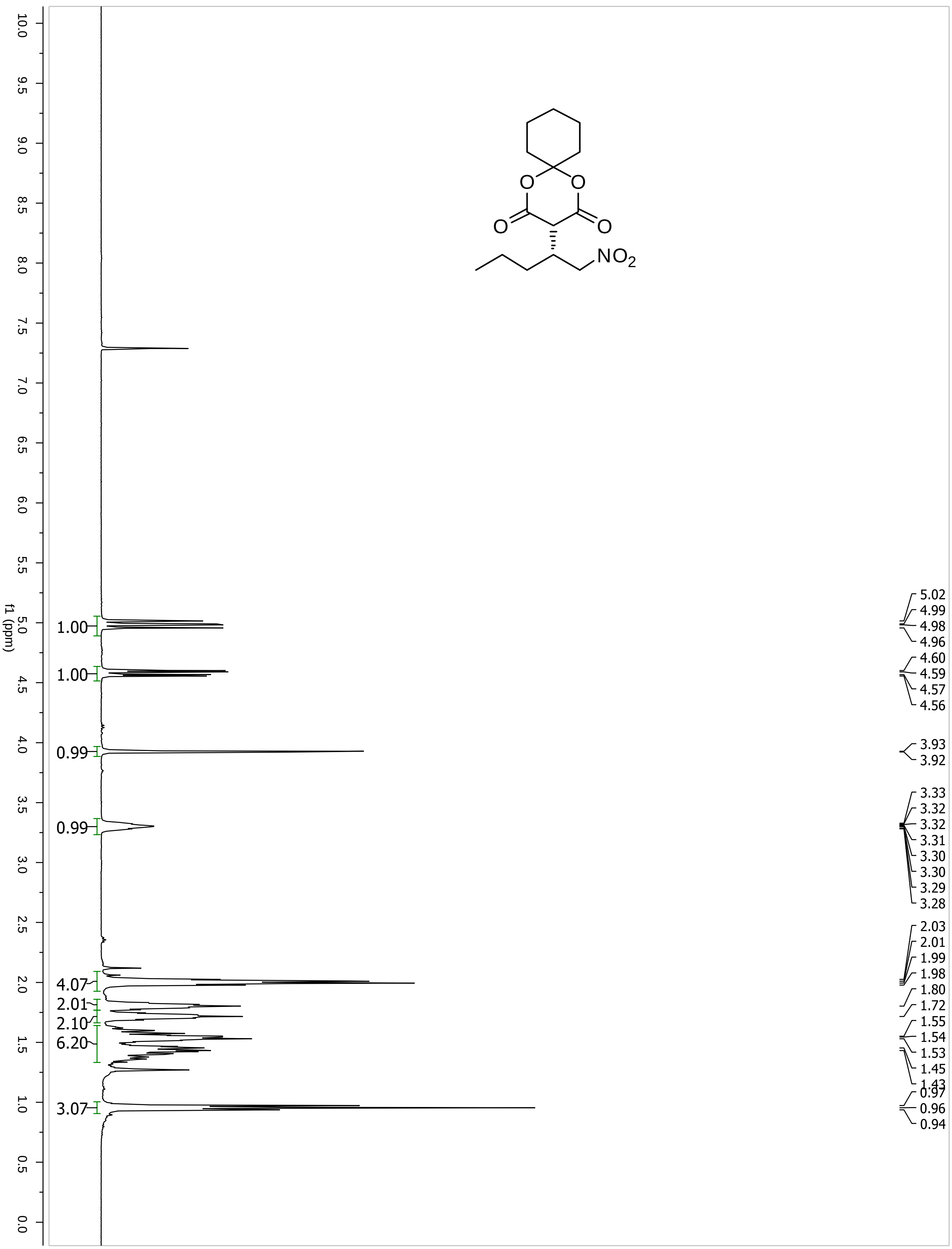
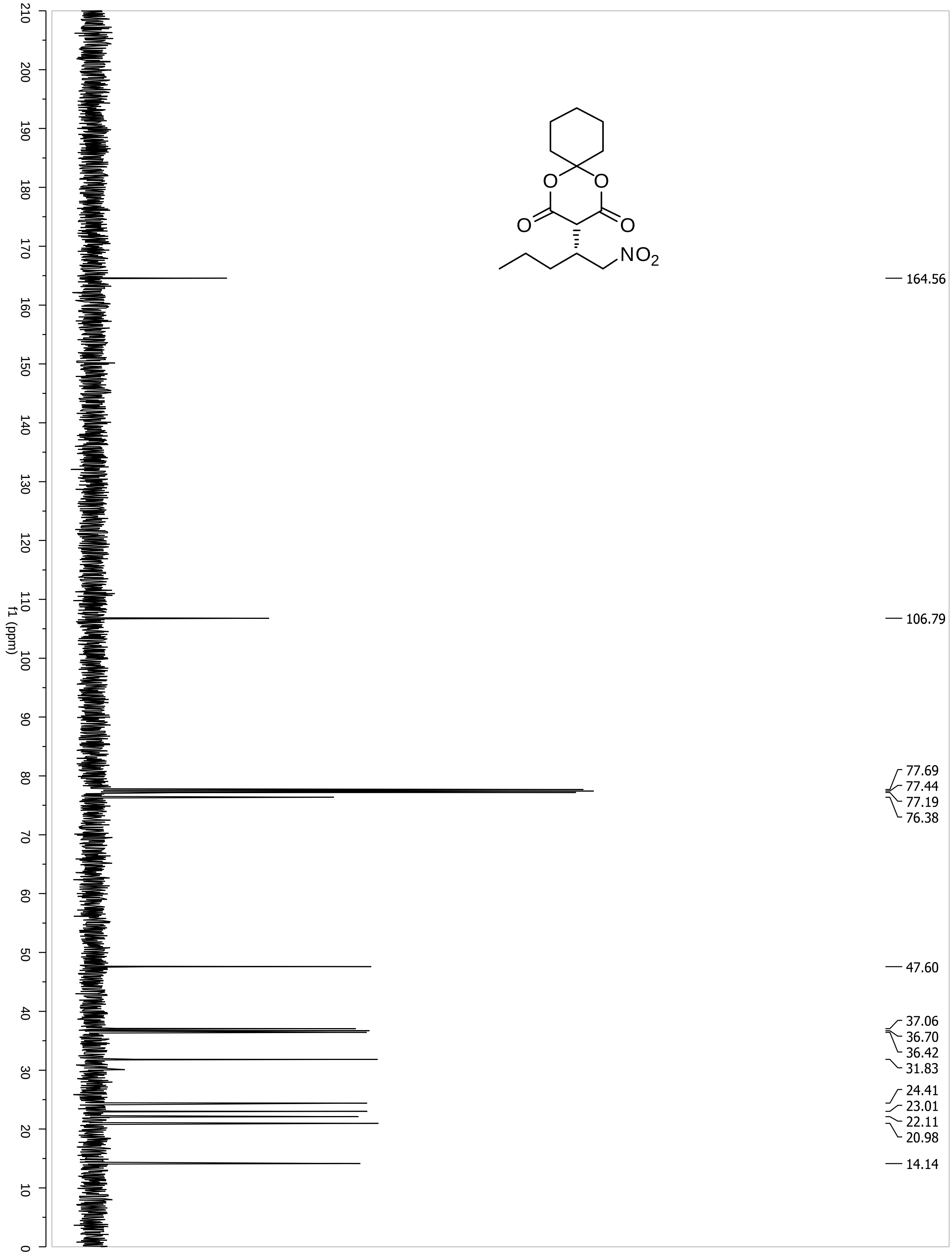
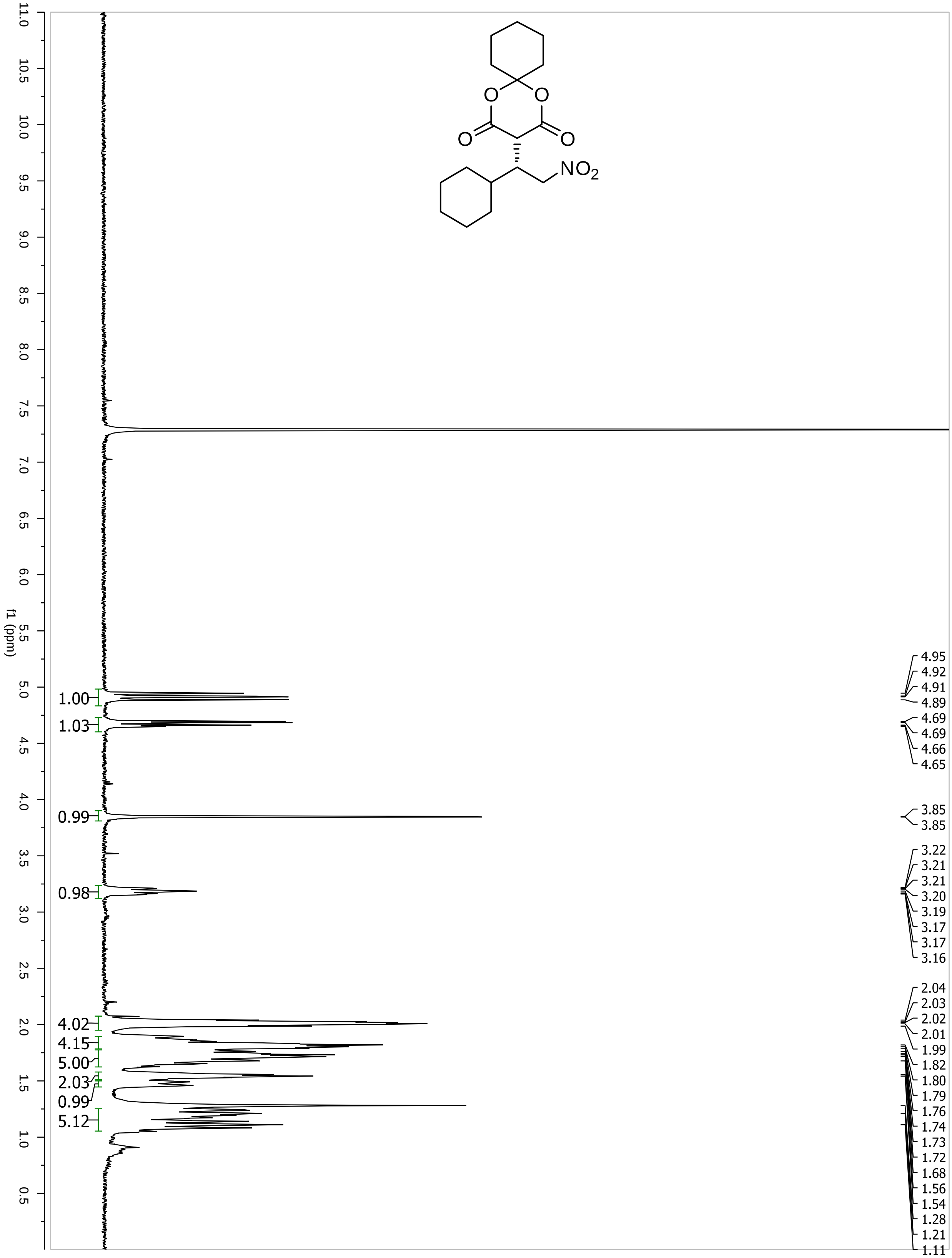
12h: (*R*)-3-(1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



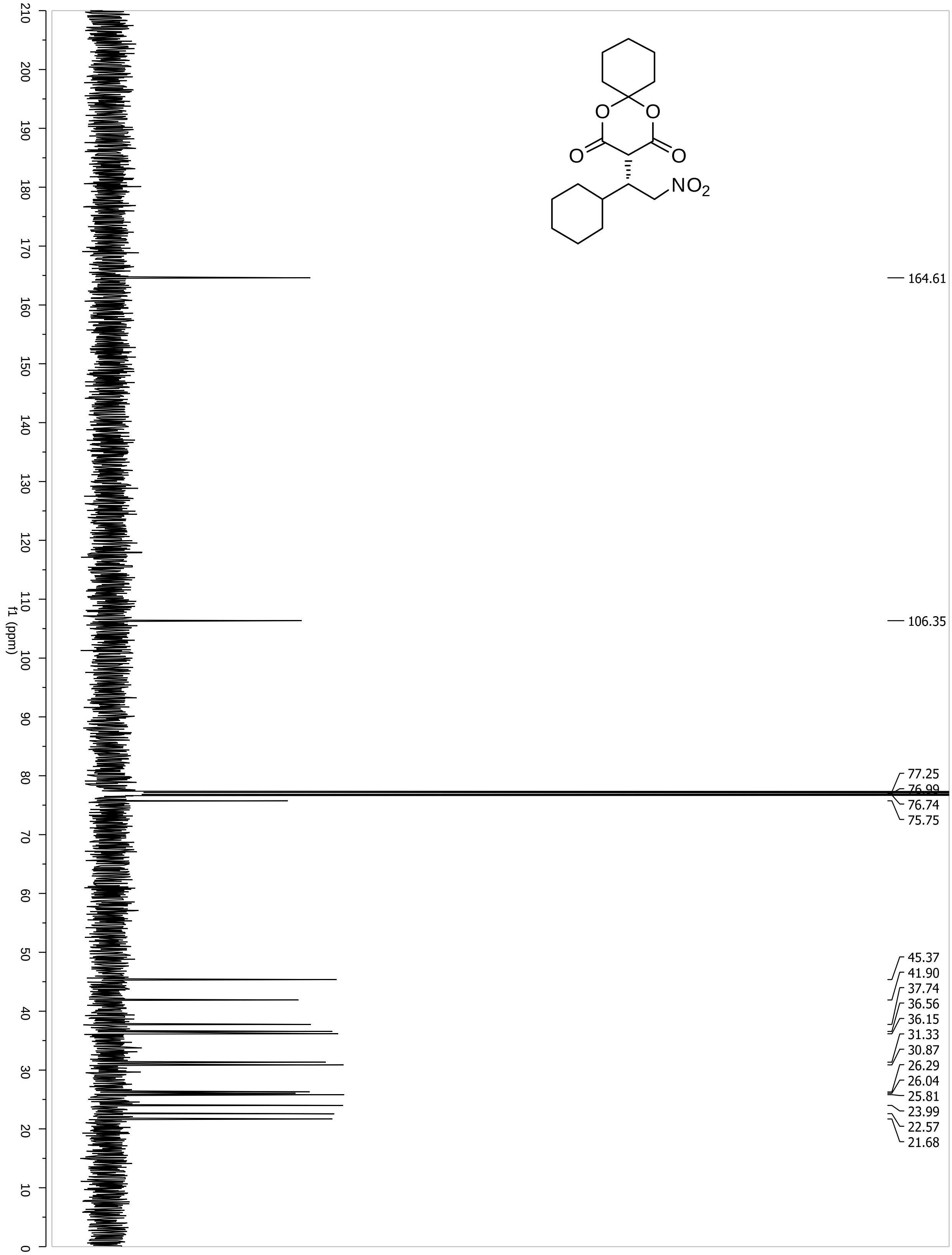
12h: (*R*)-3-(1-nitropentan-2-yl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



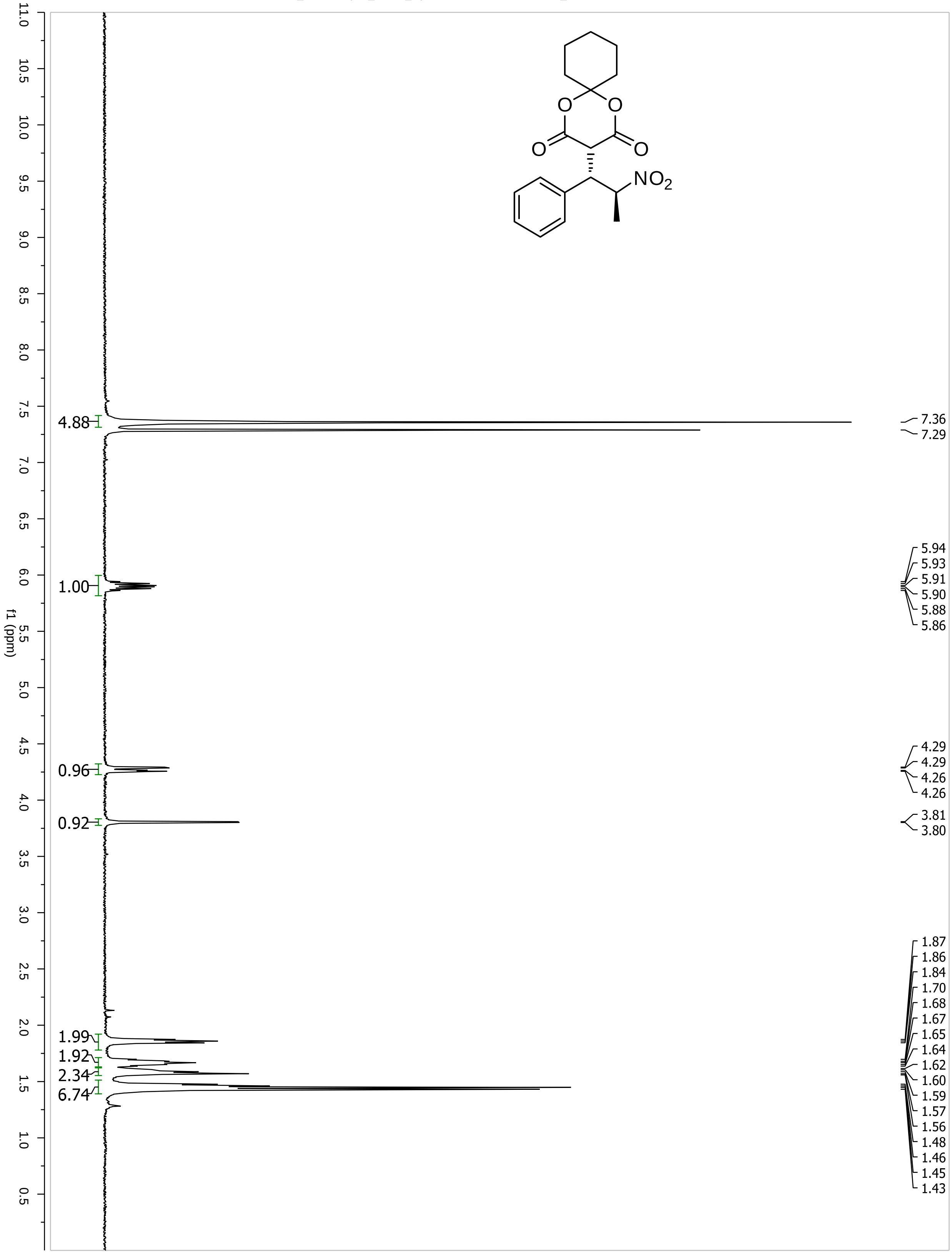
12i: (*R*)-3-(1-cyclohexyl-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



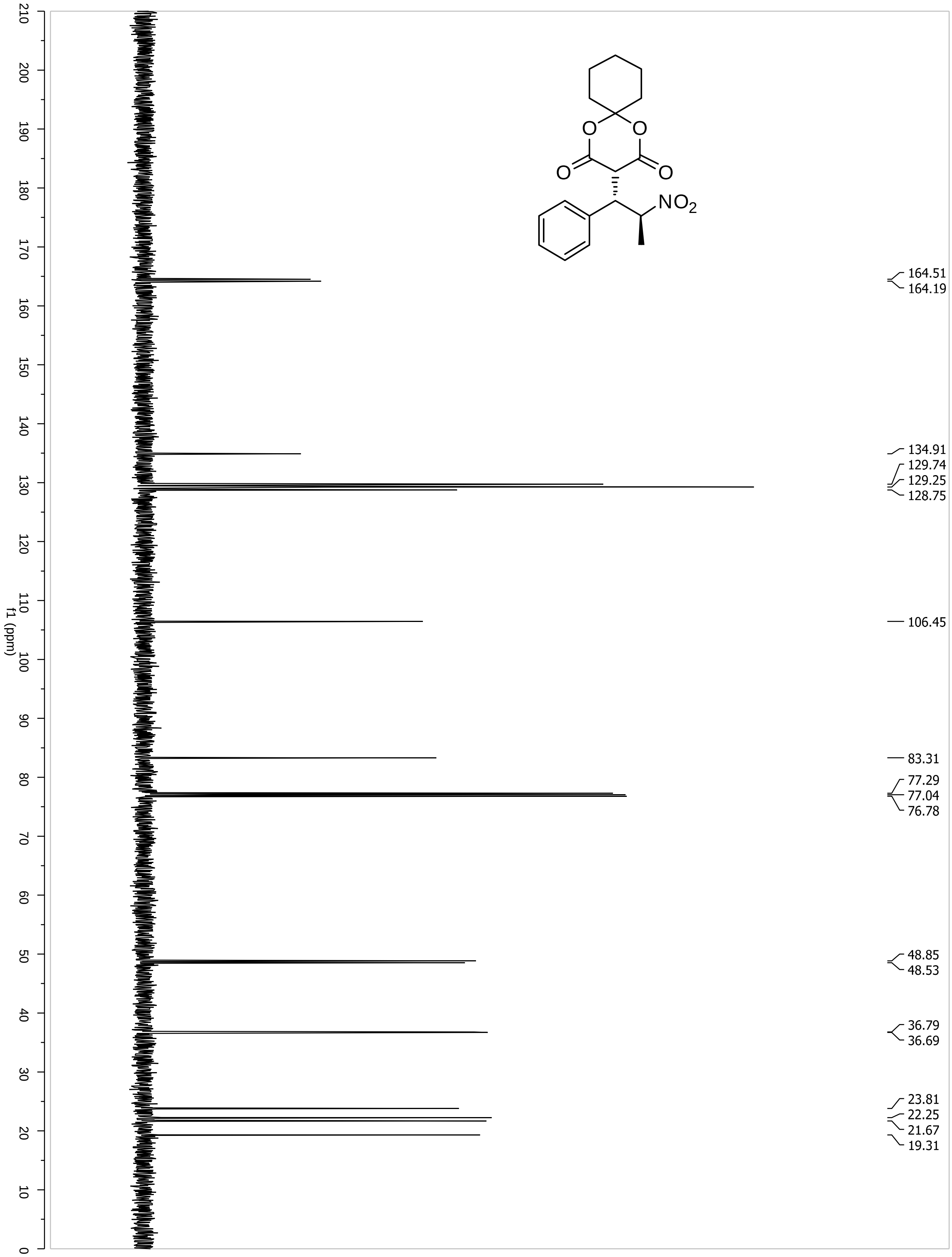
12i: **(*R*)-3-(1-cyclohexyl-2-nitroethyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione**



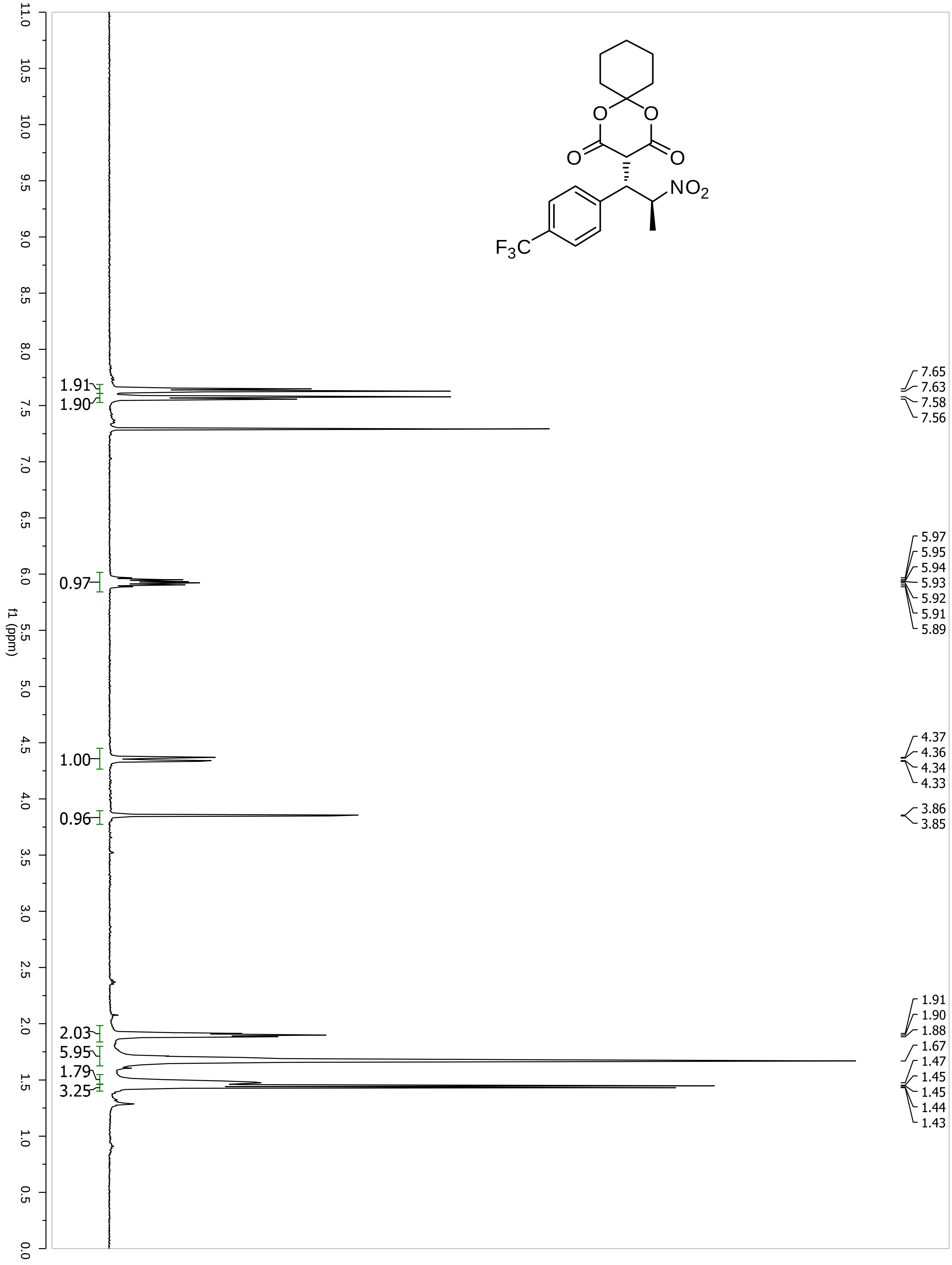
14a: 3-((1*R*,2*S*)- (2-nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



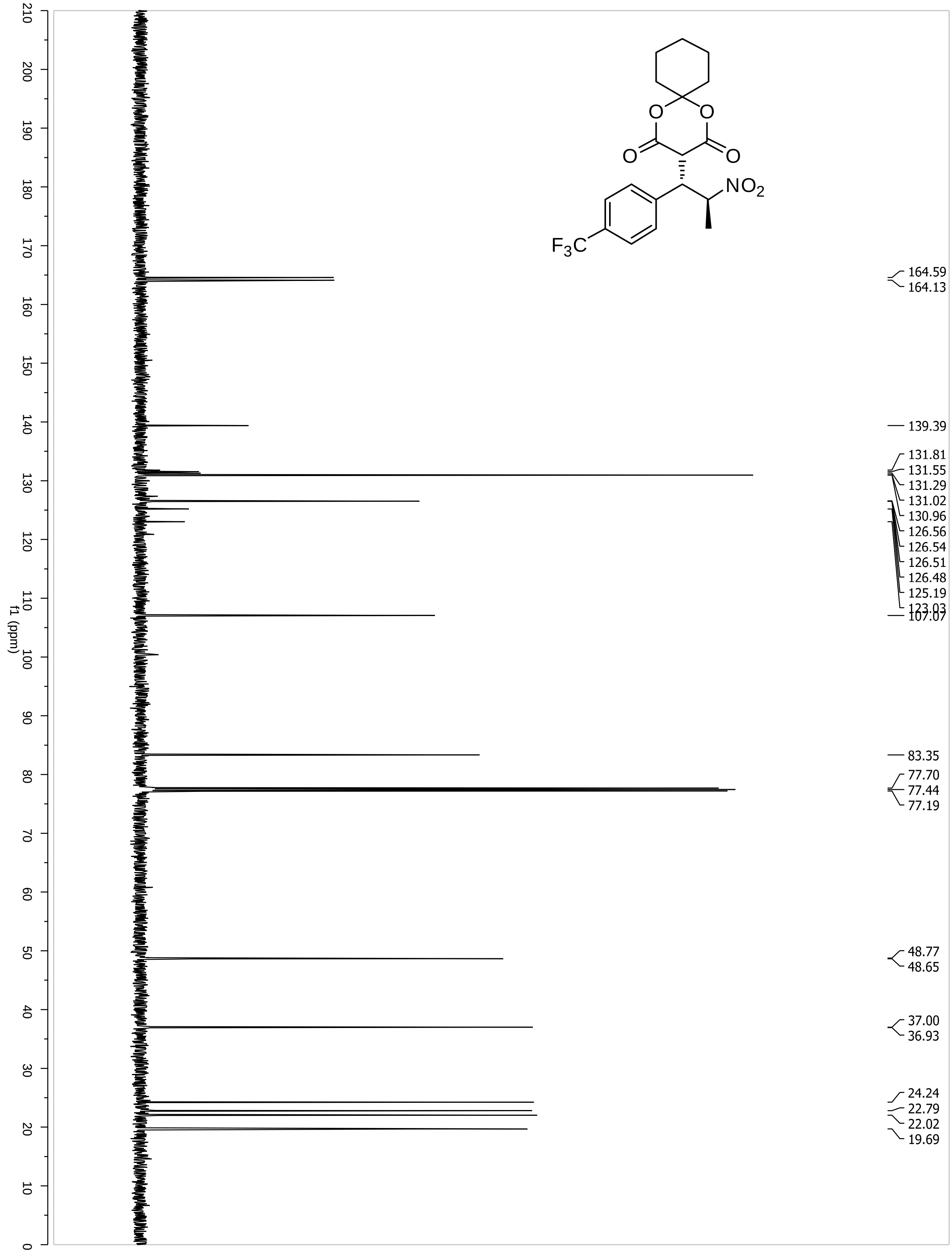
14a: 3-((1*R*,2*S*)- (2-nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



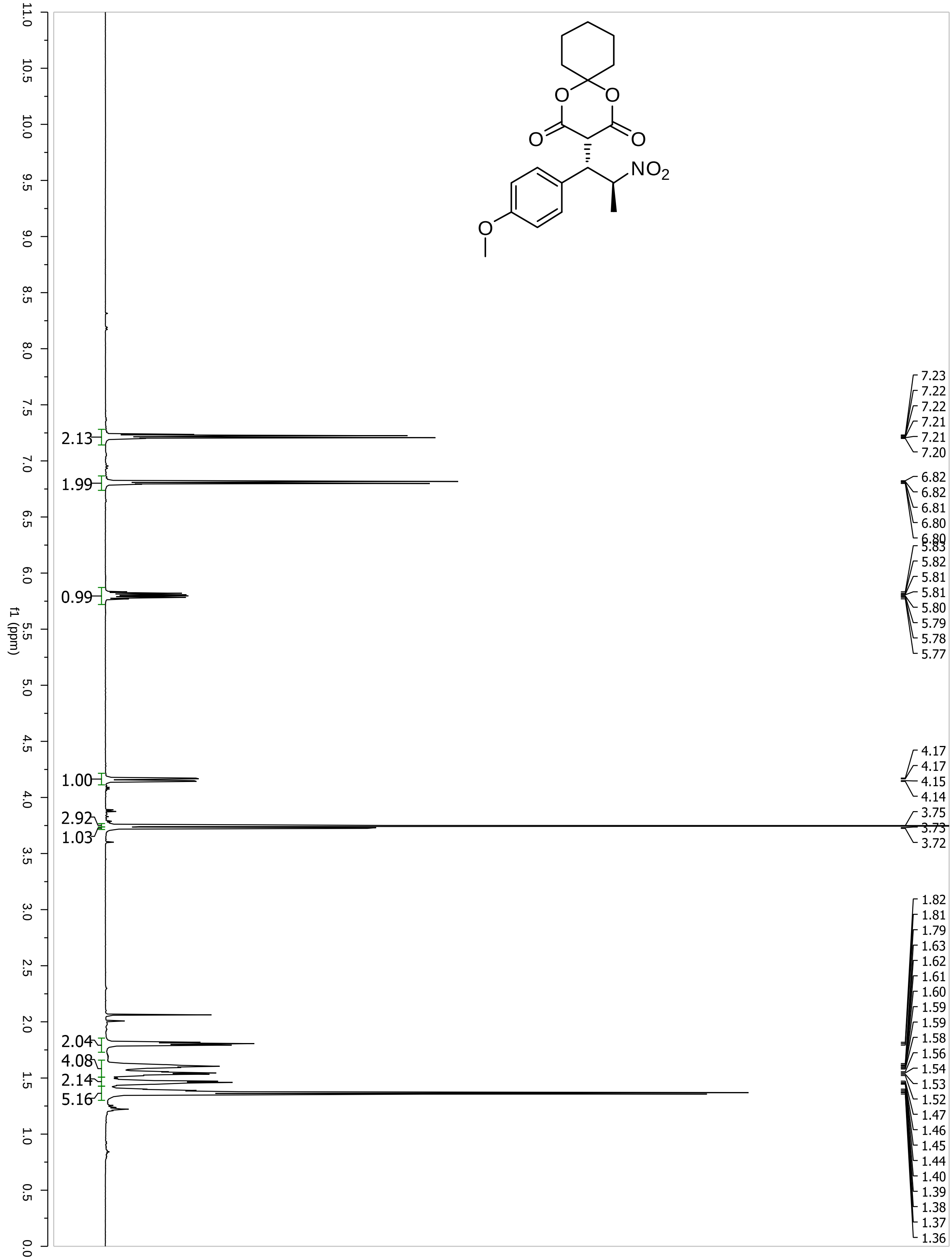
14b: 3-((1*R*,2*S*)- (2-nitro-1-(4-(trifluoromethyl)phenyl)propyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



14b: 3-((1*R*,2*S*)- (2-nitro-1-(4-(trifluoromethyl)phenyl)propyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



14c: 3-((1*R*,2*S*)- (1-(4-methoxyphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



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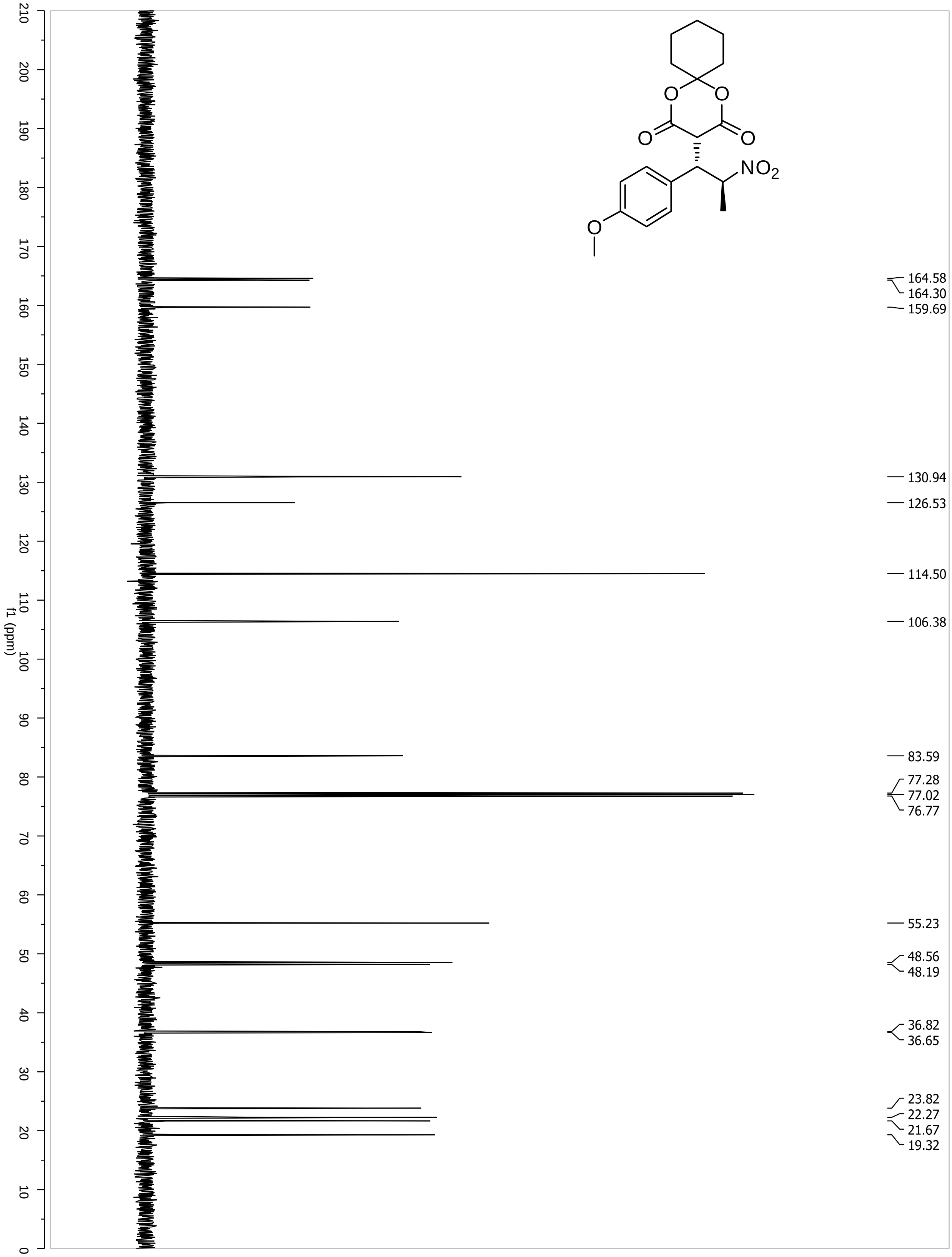
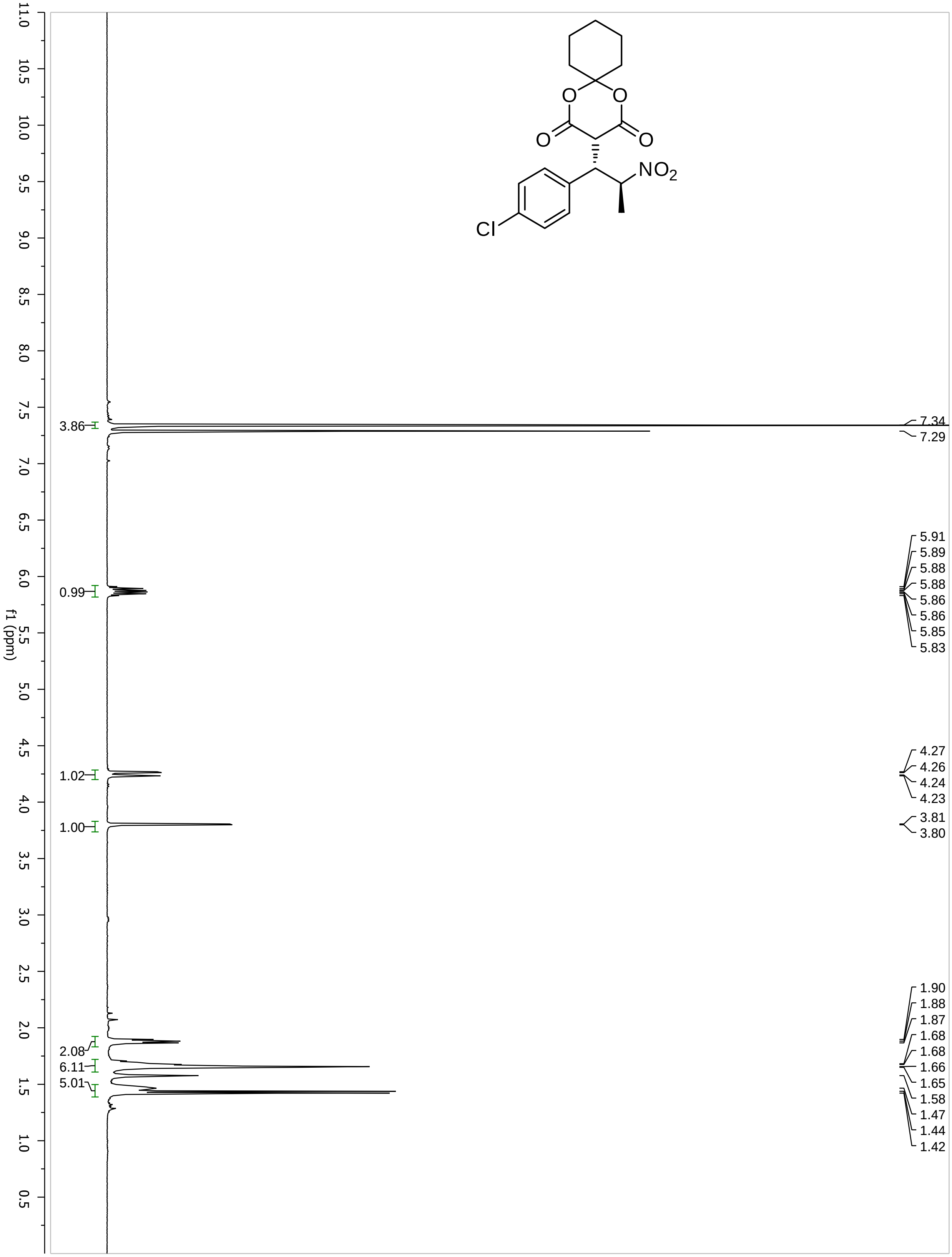
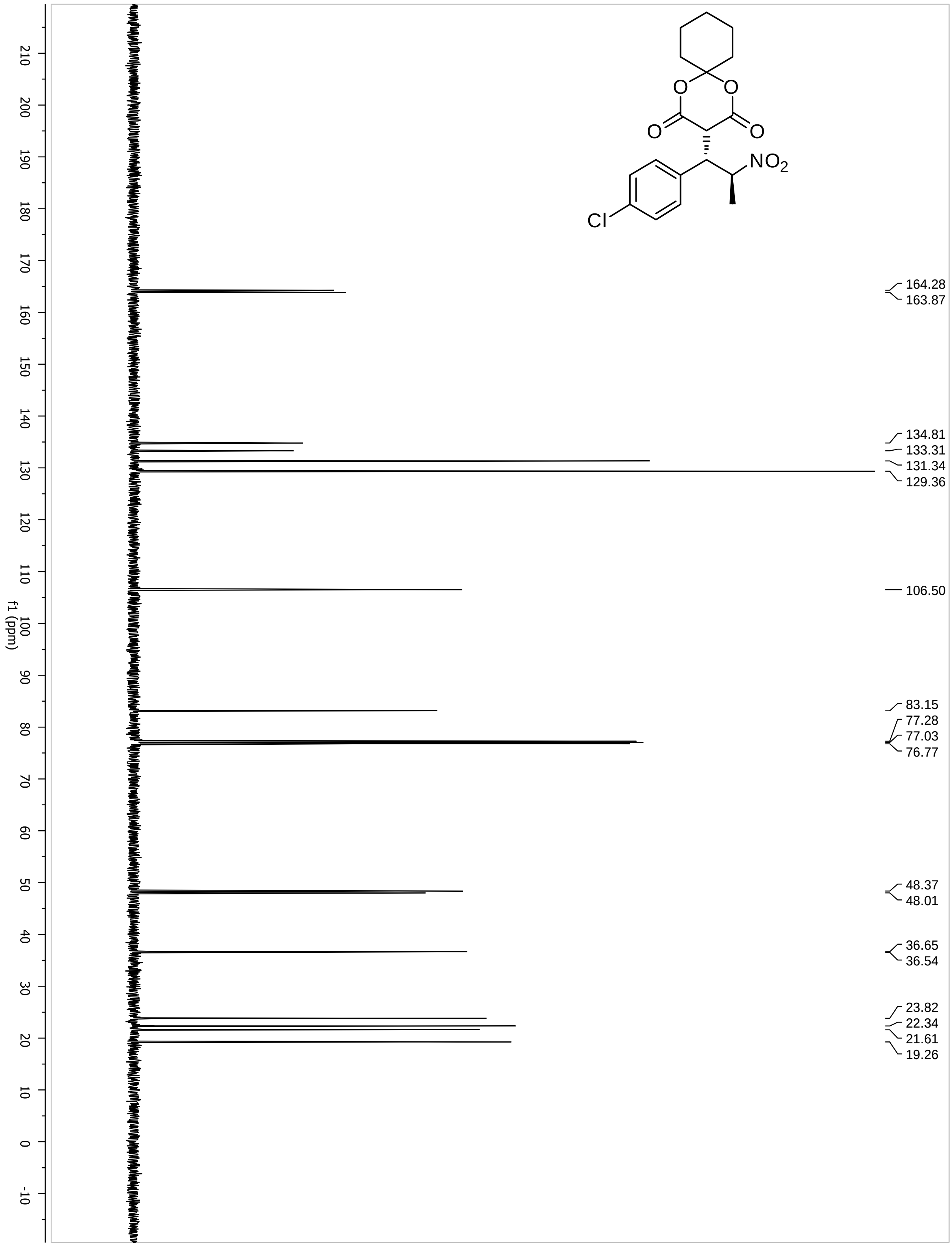
14c: 3-((1*R*,2*S*)- (1-(4-methoxyphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



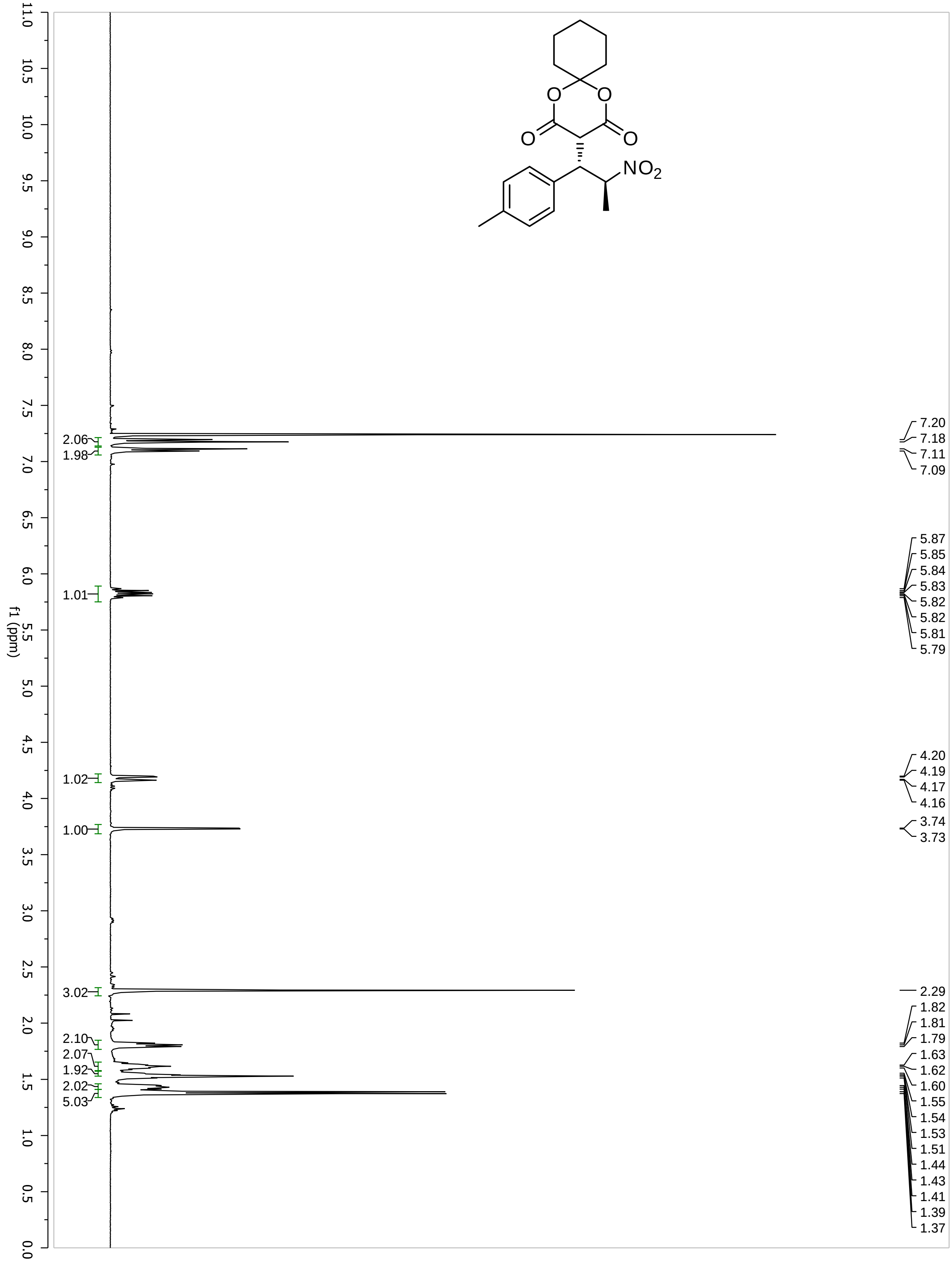
14d: 3-((1*R*,2*S*)- (1-(4-chlorophenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



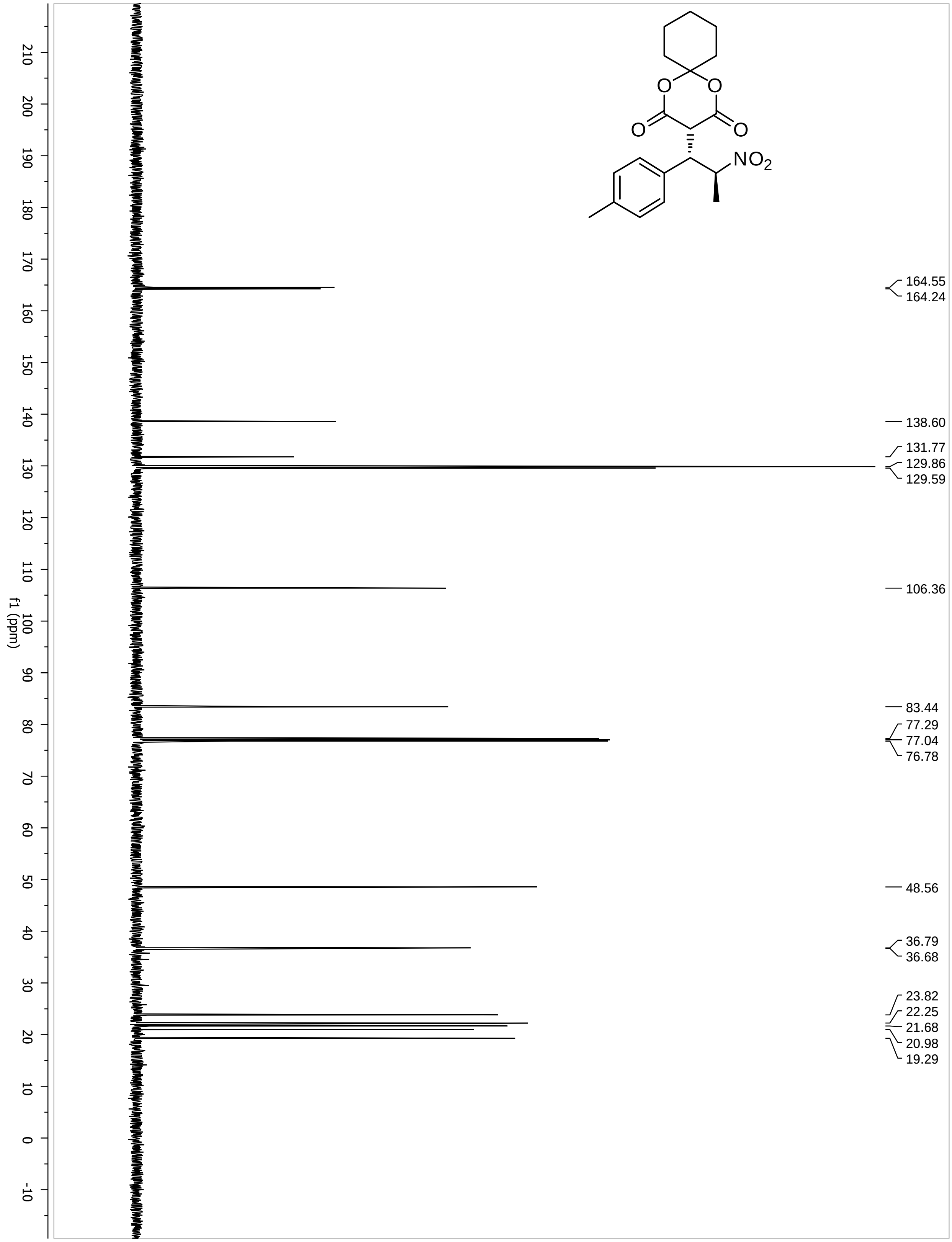
14d: 3-((1*R*,2*S*)- (1-(4-chlorophenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



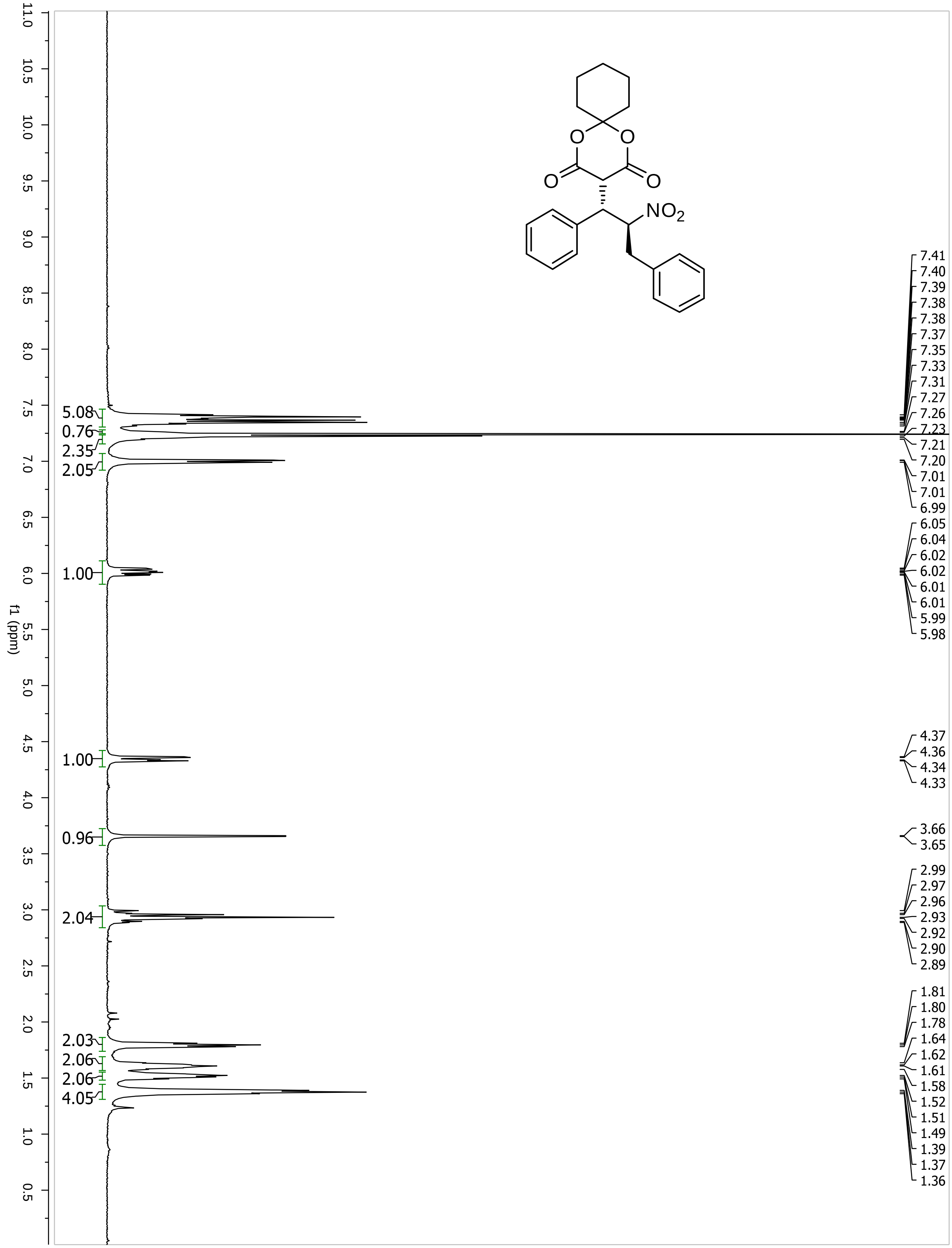
14e: 3-((1*R*,2*S*)- (1-(4-methylphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



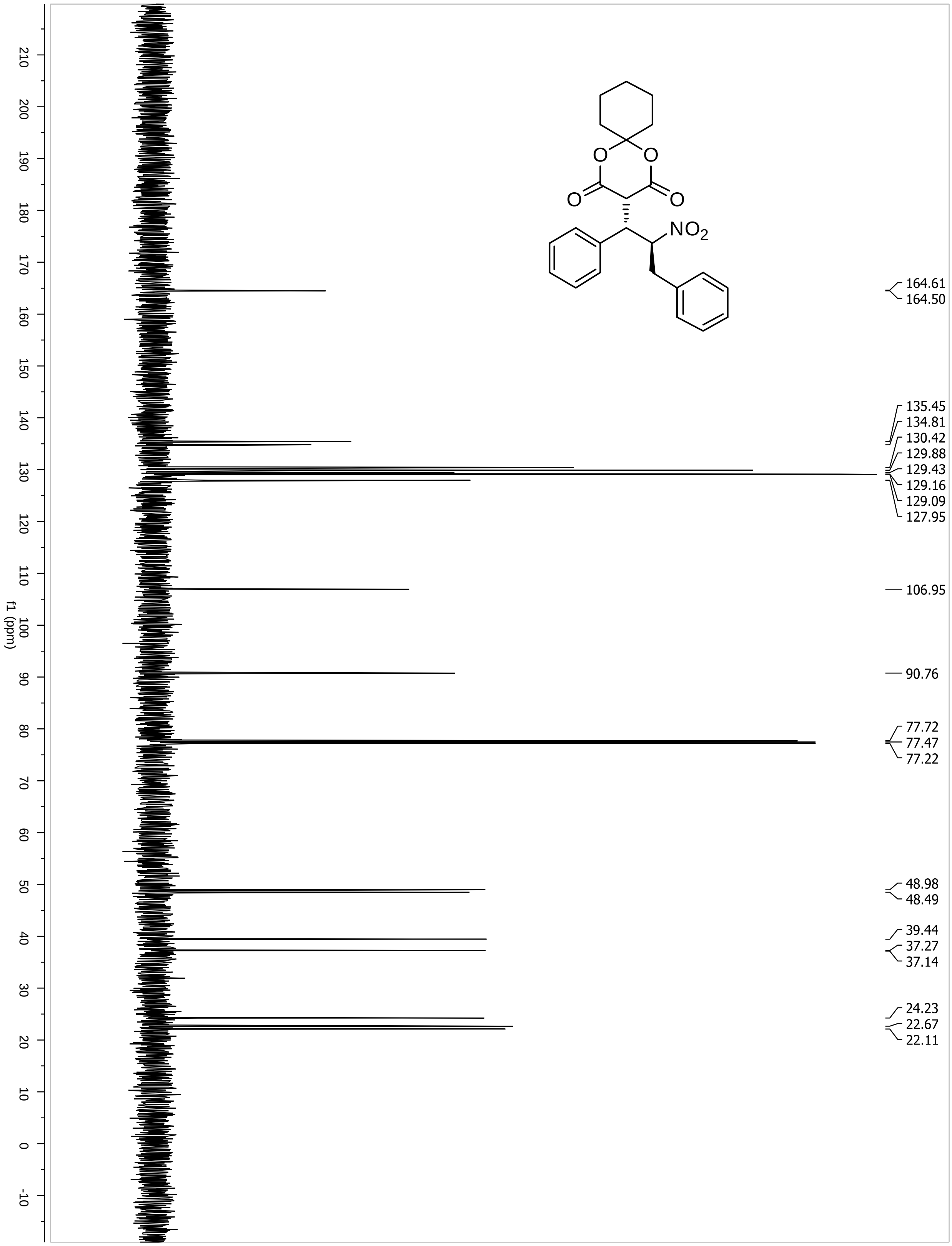
14e: 3-((1*R*,2*S*)- (1-(4-methylphenyl)-2-nitropropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



14f: 3-((1*R*,2*S*)-(3-phenyl-2-nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



14f: 3-((1*R*,2*S*)-(3-phenyl-2-nitro-1-phenylpropyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



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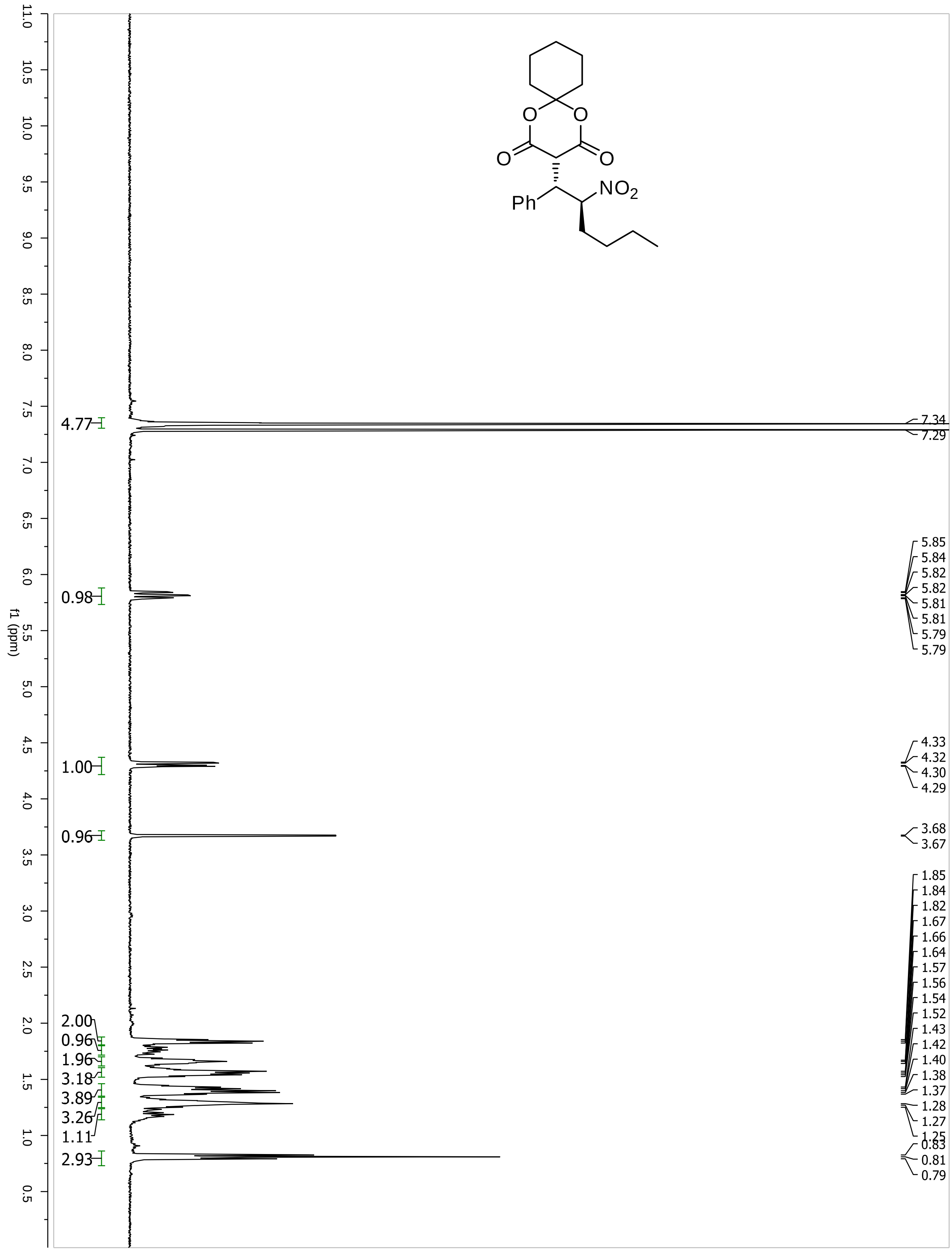
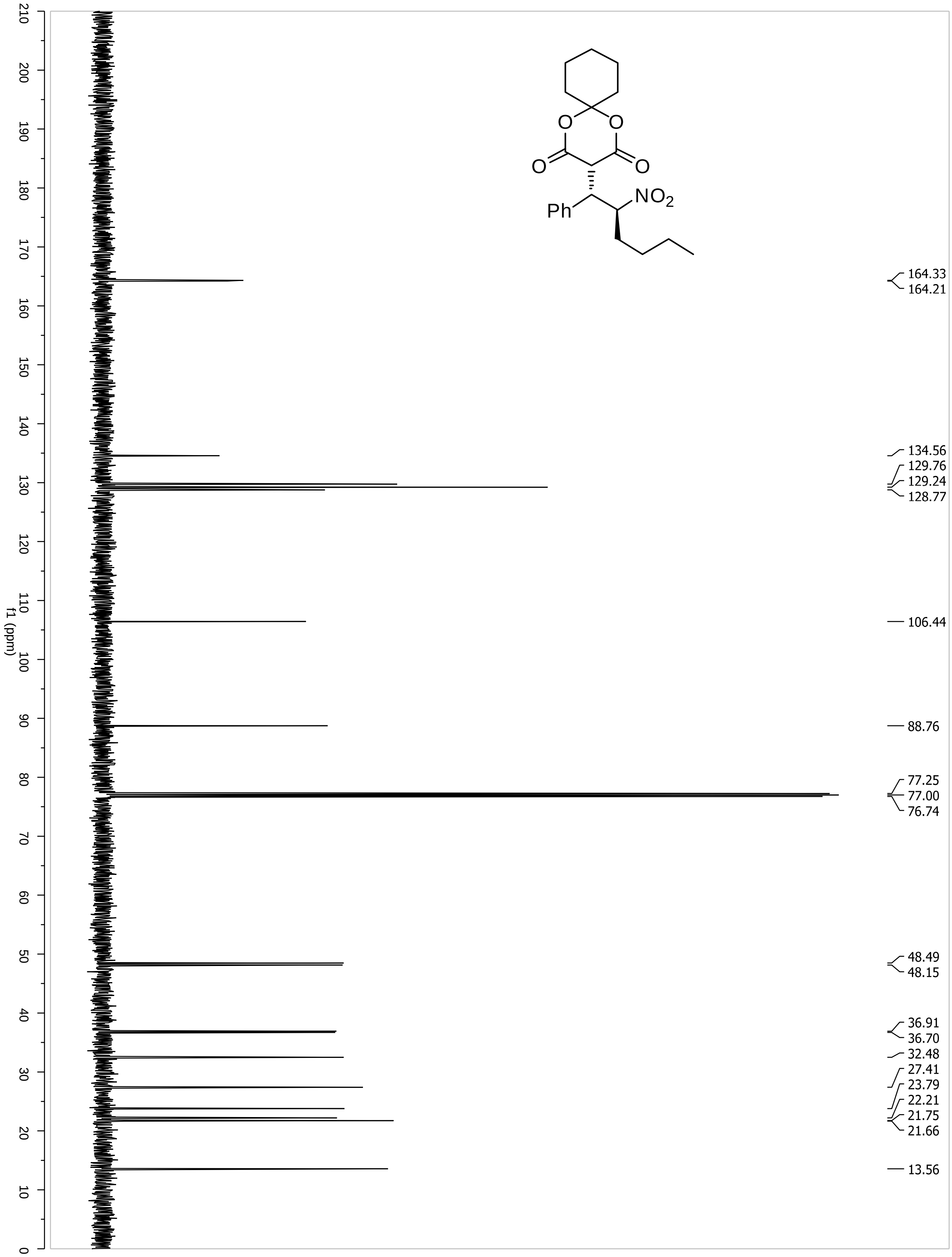
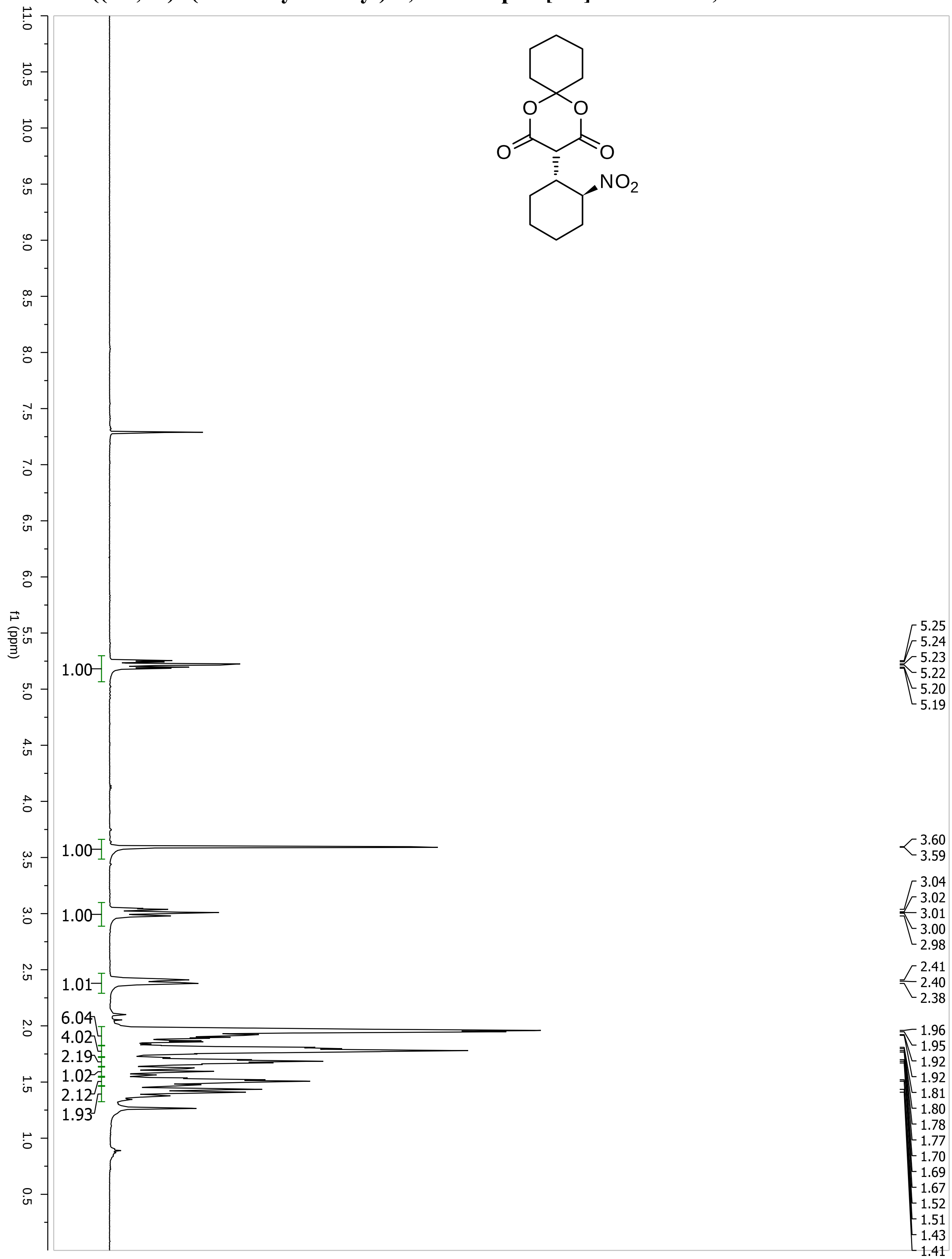
14g: 3-((1*R*,2*S*)- (2-nitro-1-phenylhexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



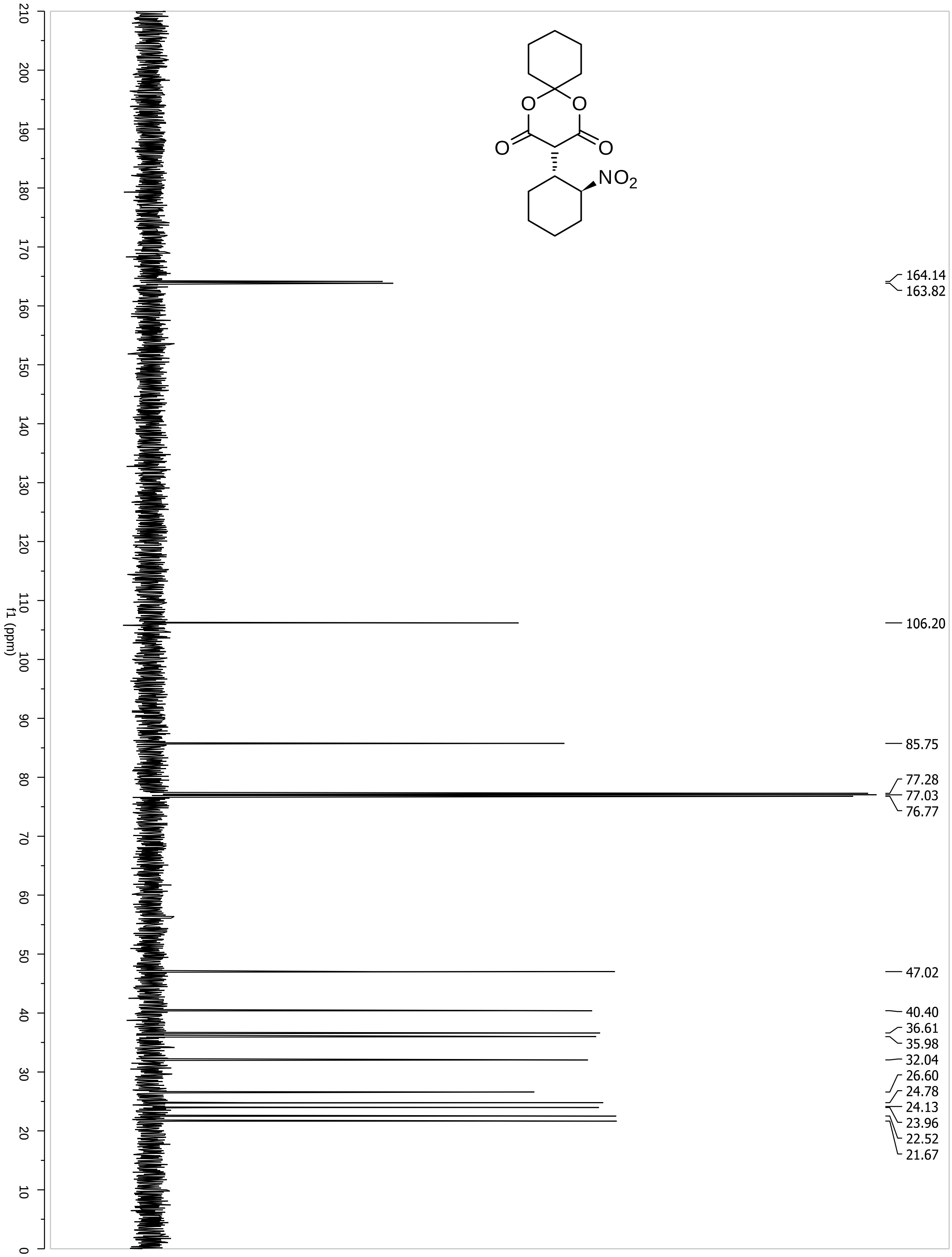
14g: **3-((1*R*,2*S*)- (2-nitro-1-phenylhexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione**



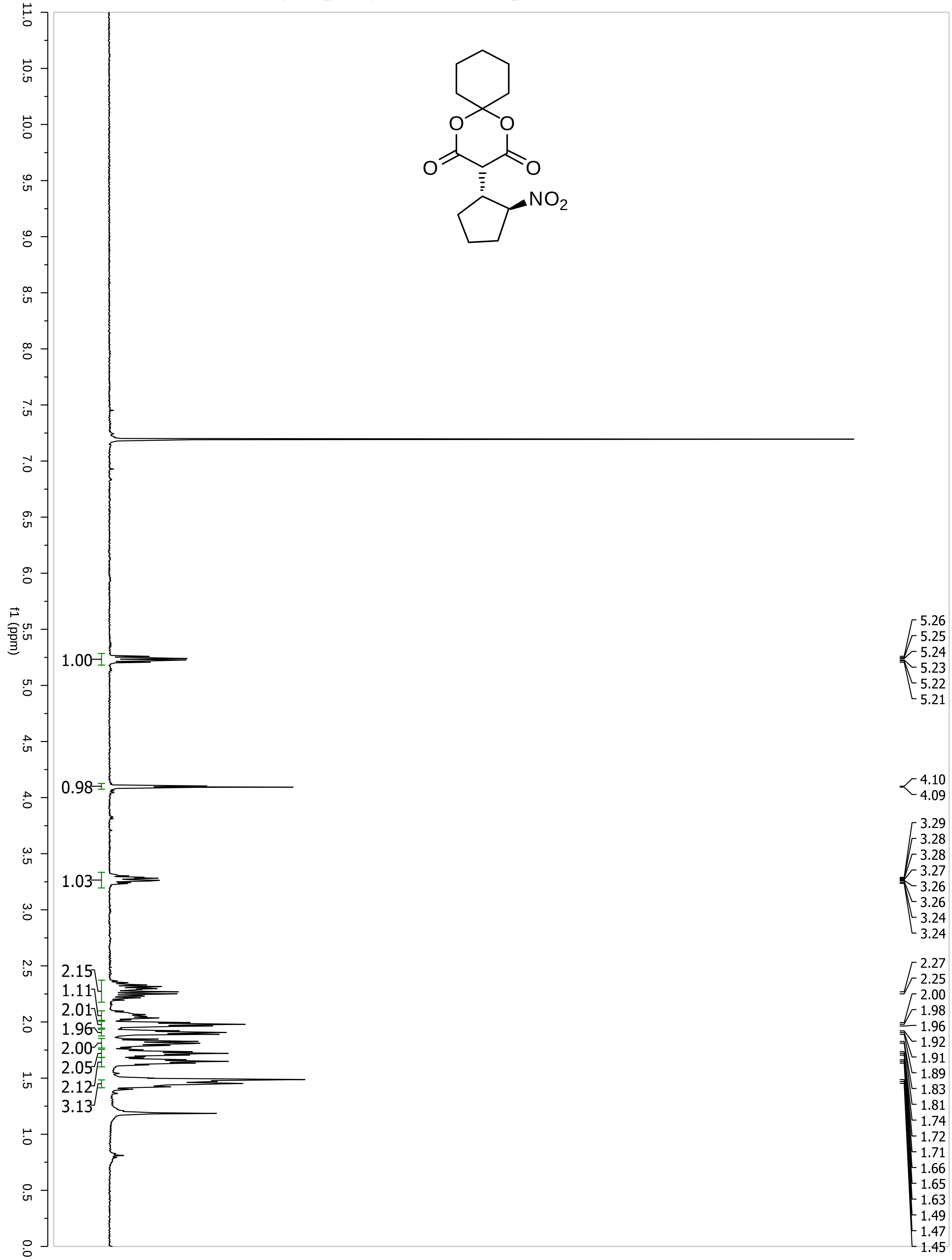
14h: 3-((1*R*,2*S*)- (2-nitrocyclohexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



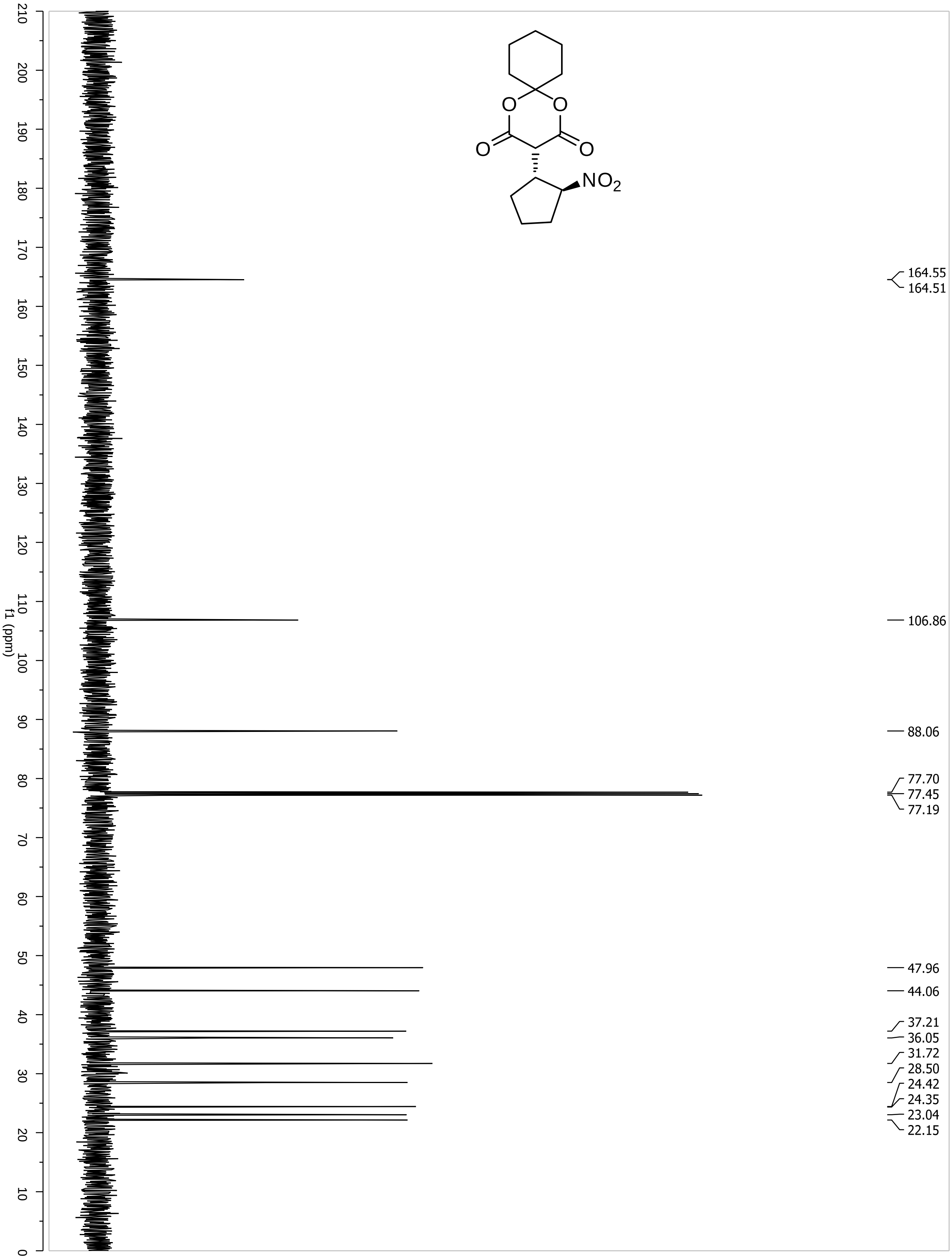
14h: 3-((1*R*,2*S*)- (2-nitrocyclohexyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



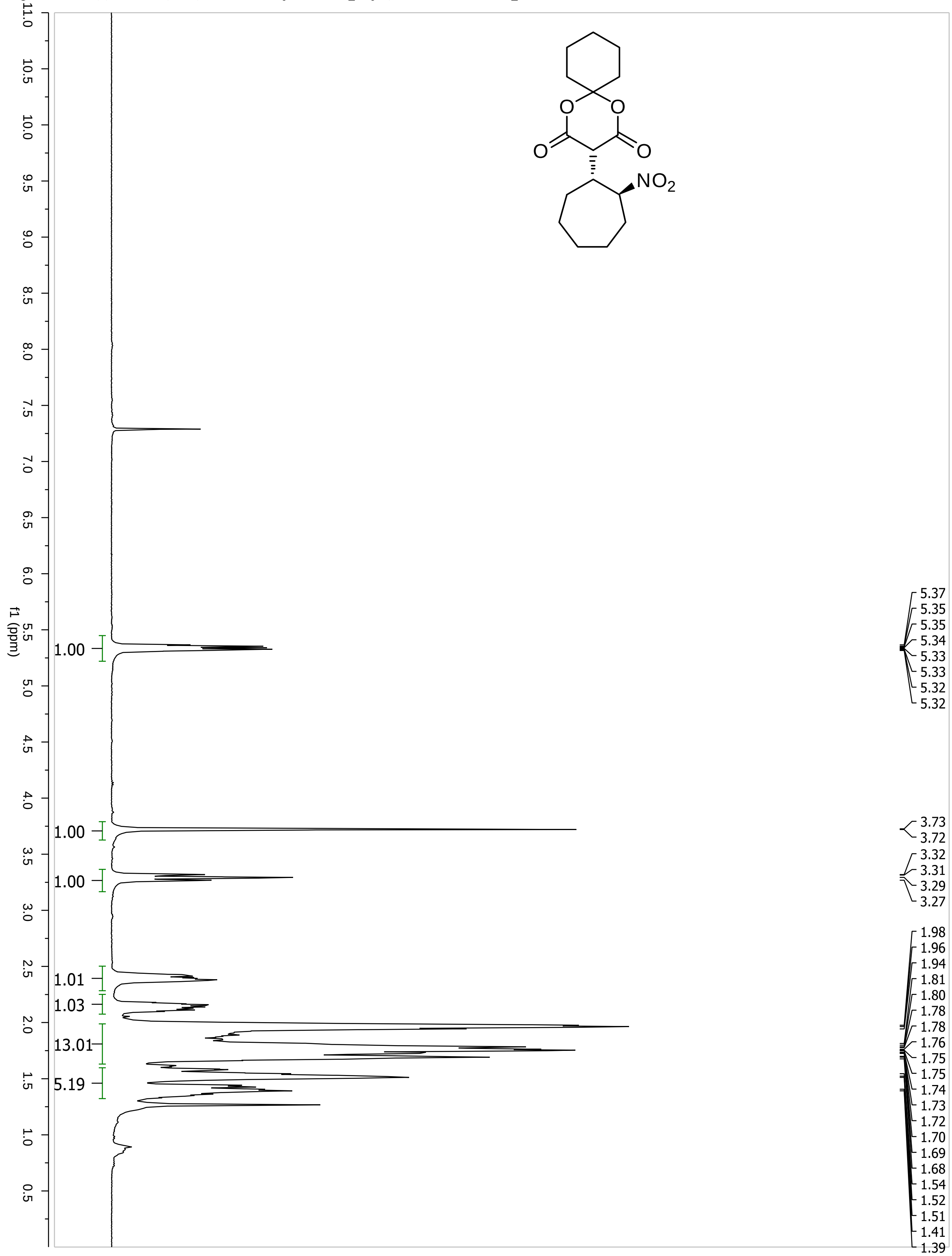
14i: 3-((1*R*,2*S*)- (2-nitrocyclopentyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



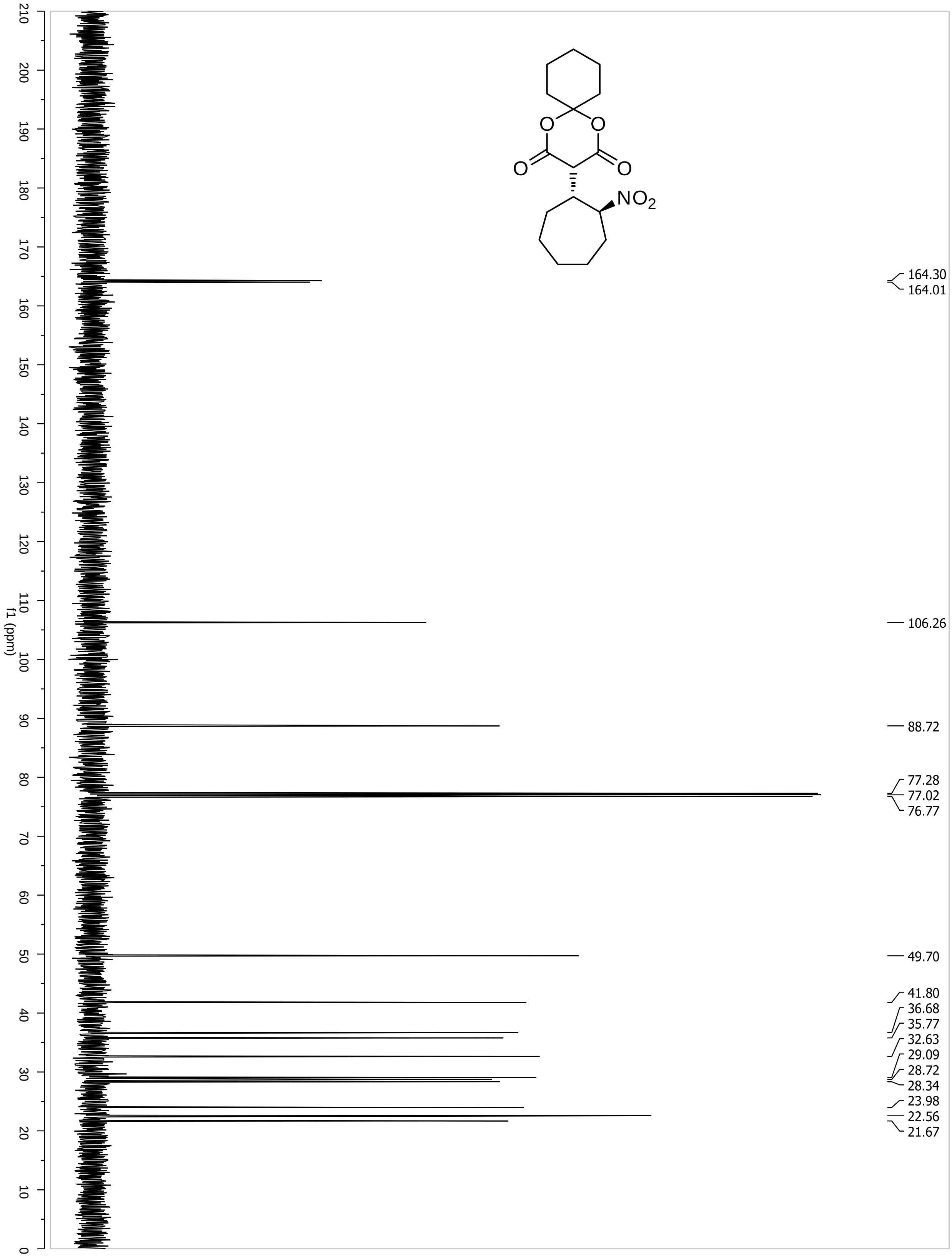
14i: **3-((1*R*,2*S*)- (2-nitrocyclopentyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione**



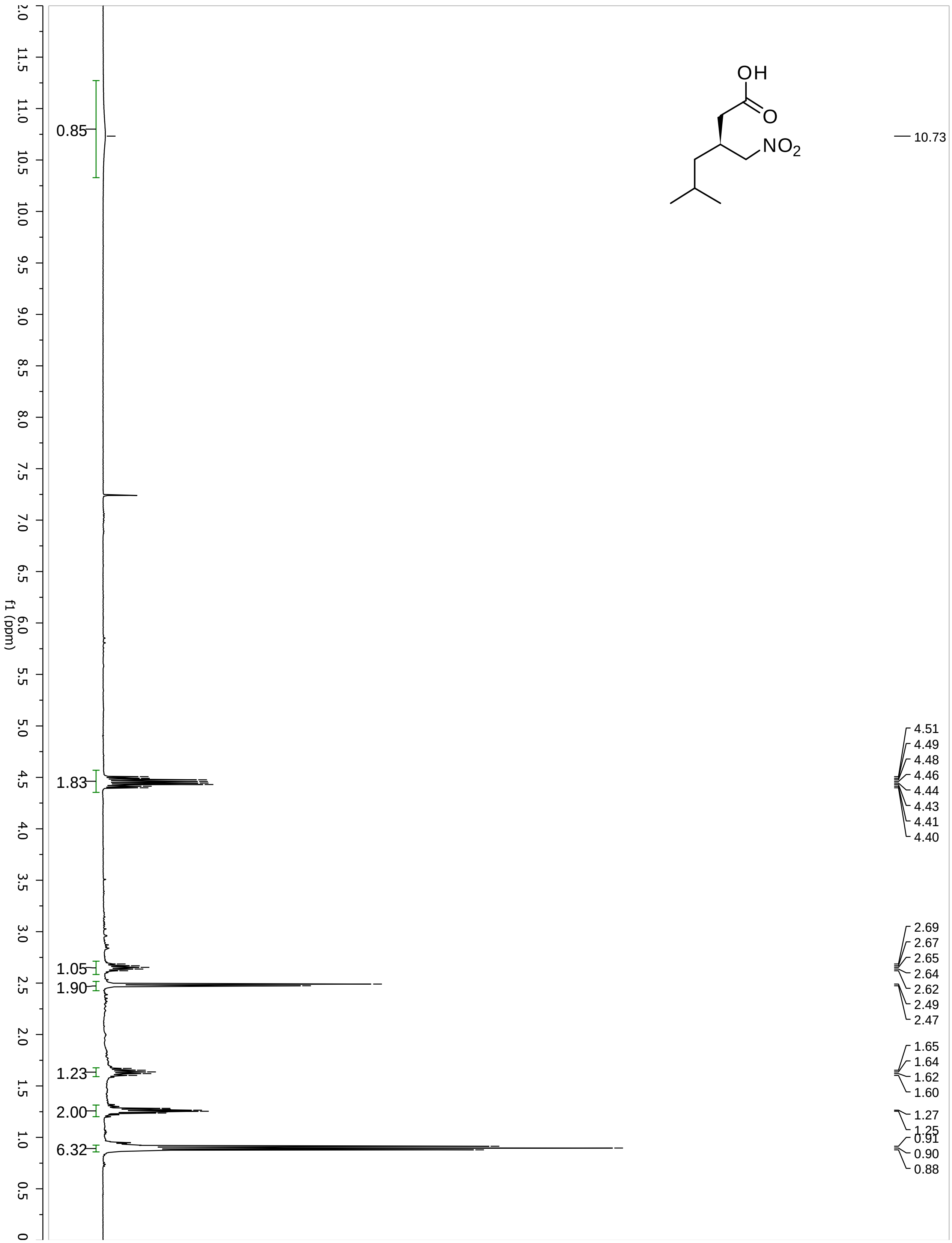
14j: 3-((1*R*,2*S*)- (2-nitrocycloheptyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



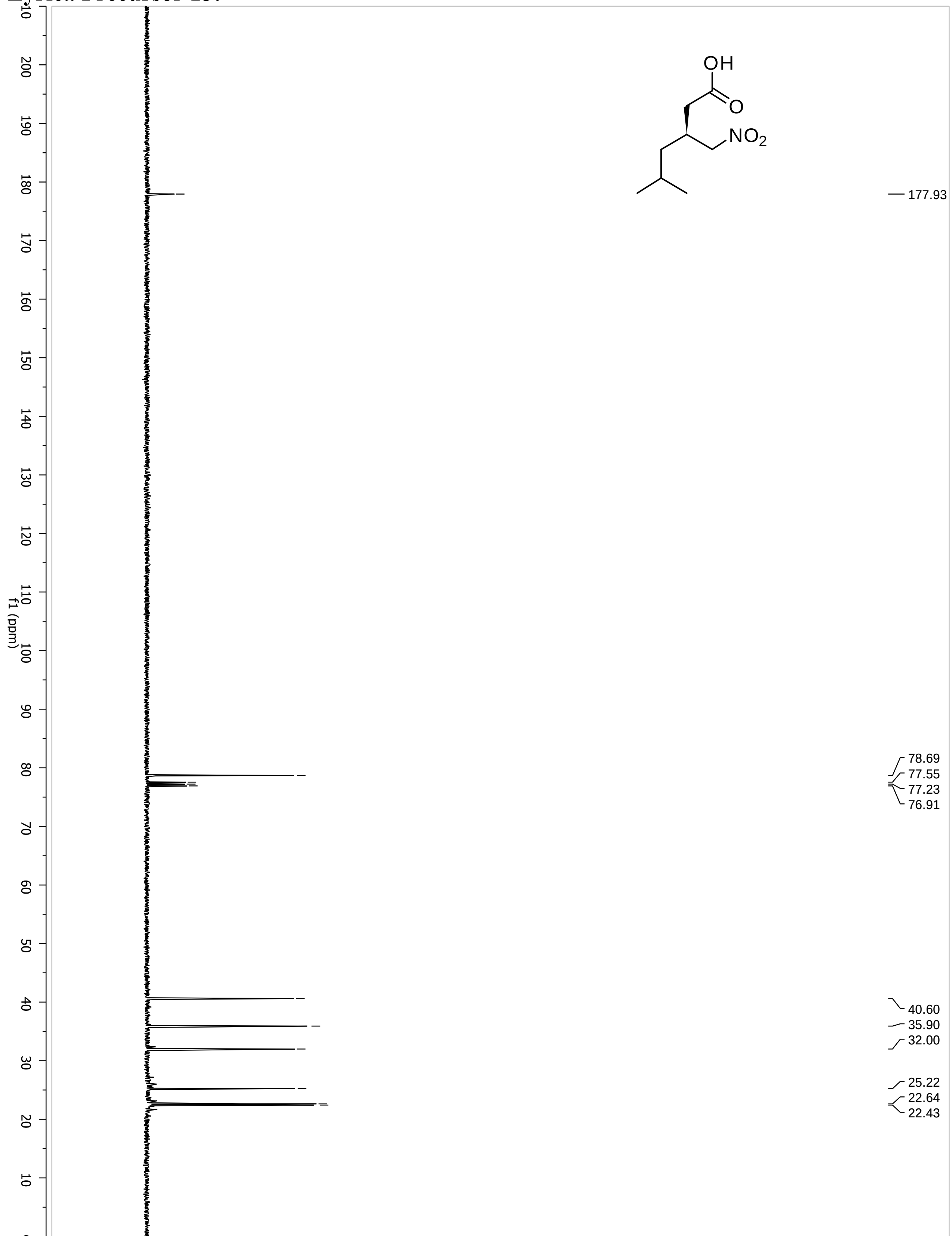
14j: 3-((1*R*,2*S*)- (2-nitrocycloheptyl)-1,5-dioxaspiro[5.5]undecane-2,4-dione



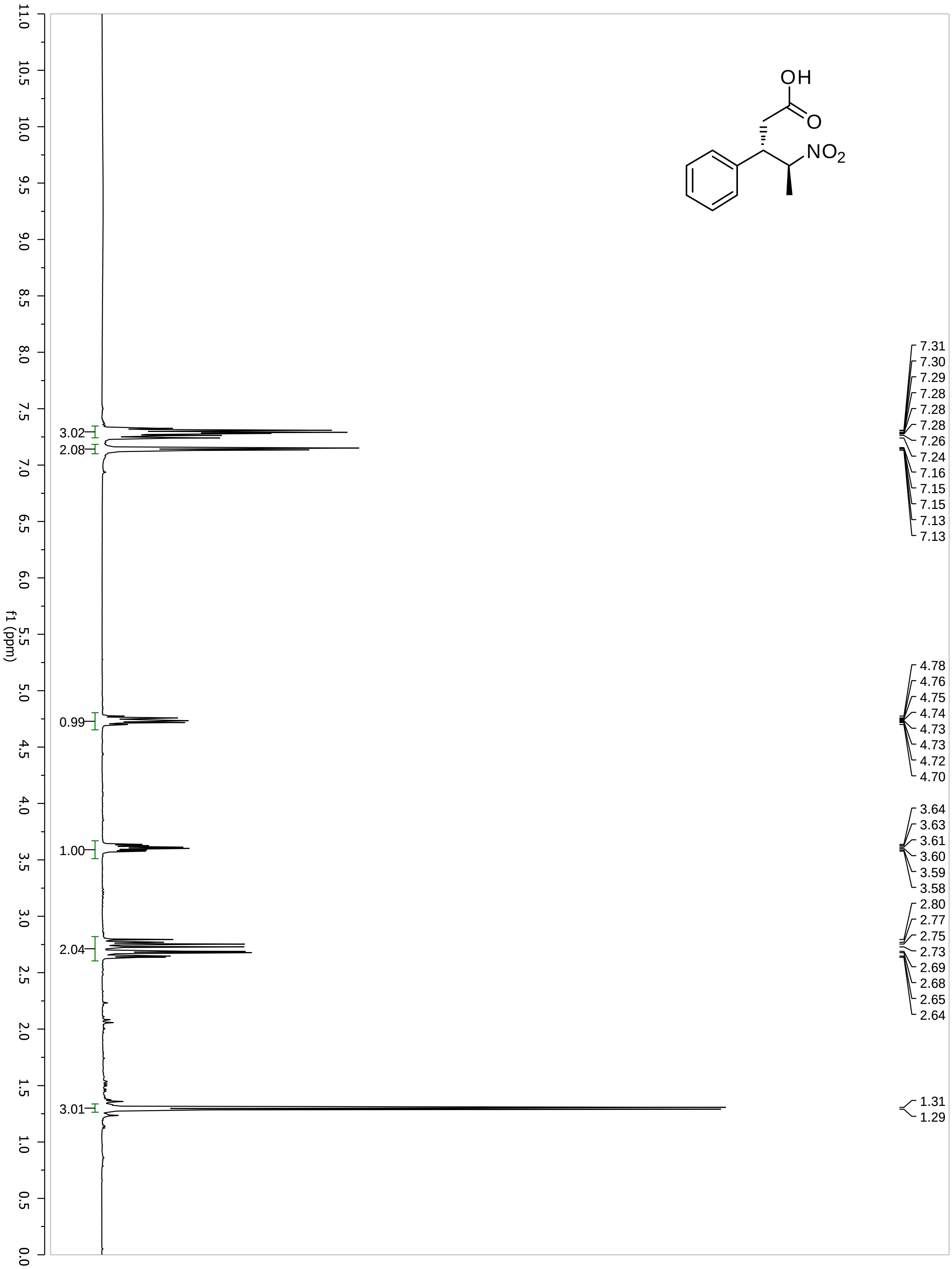
Lyrica Precursor 15:



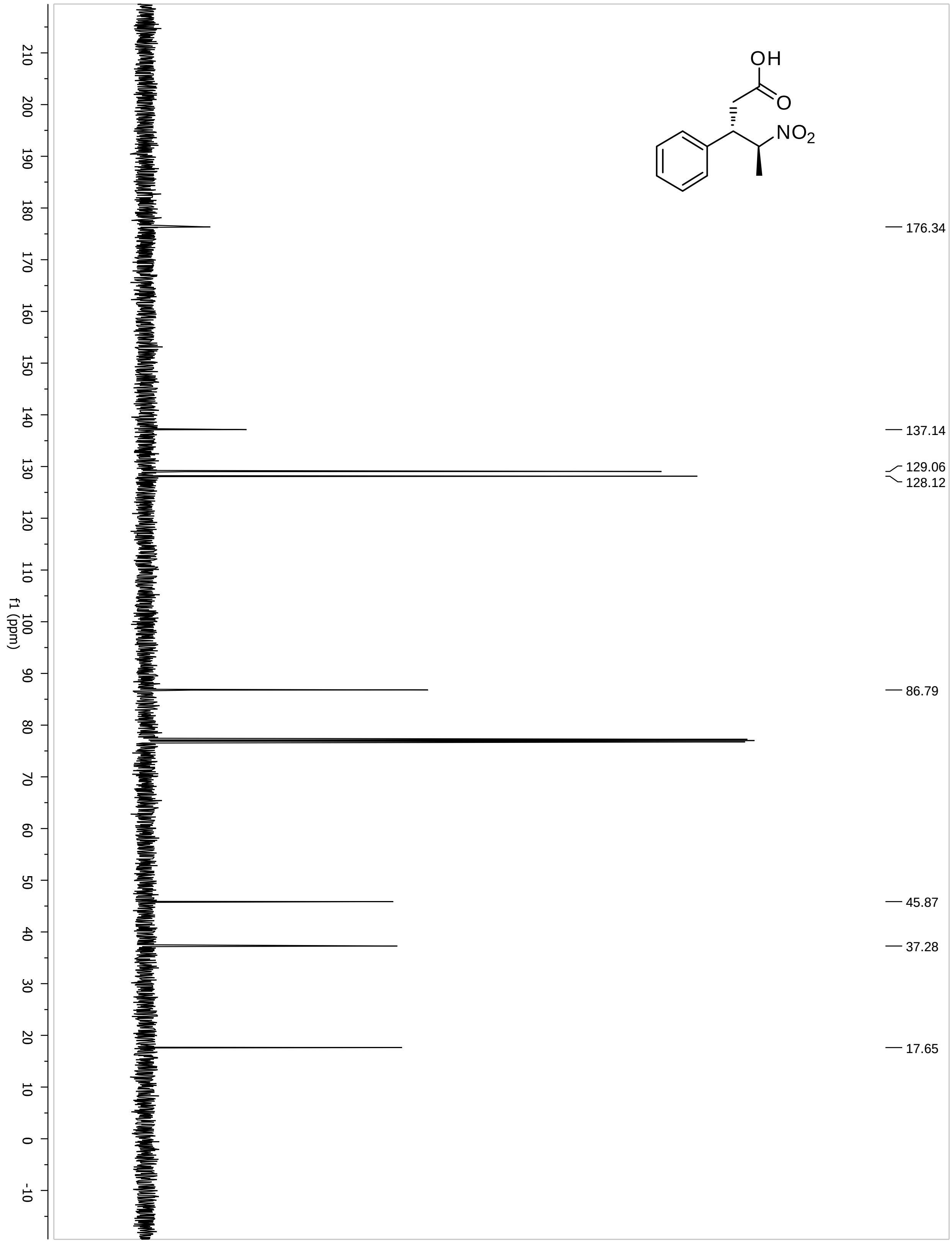
Lyrica Precursor 15:



Intermediate 16:



Intermediate 16:



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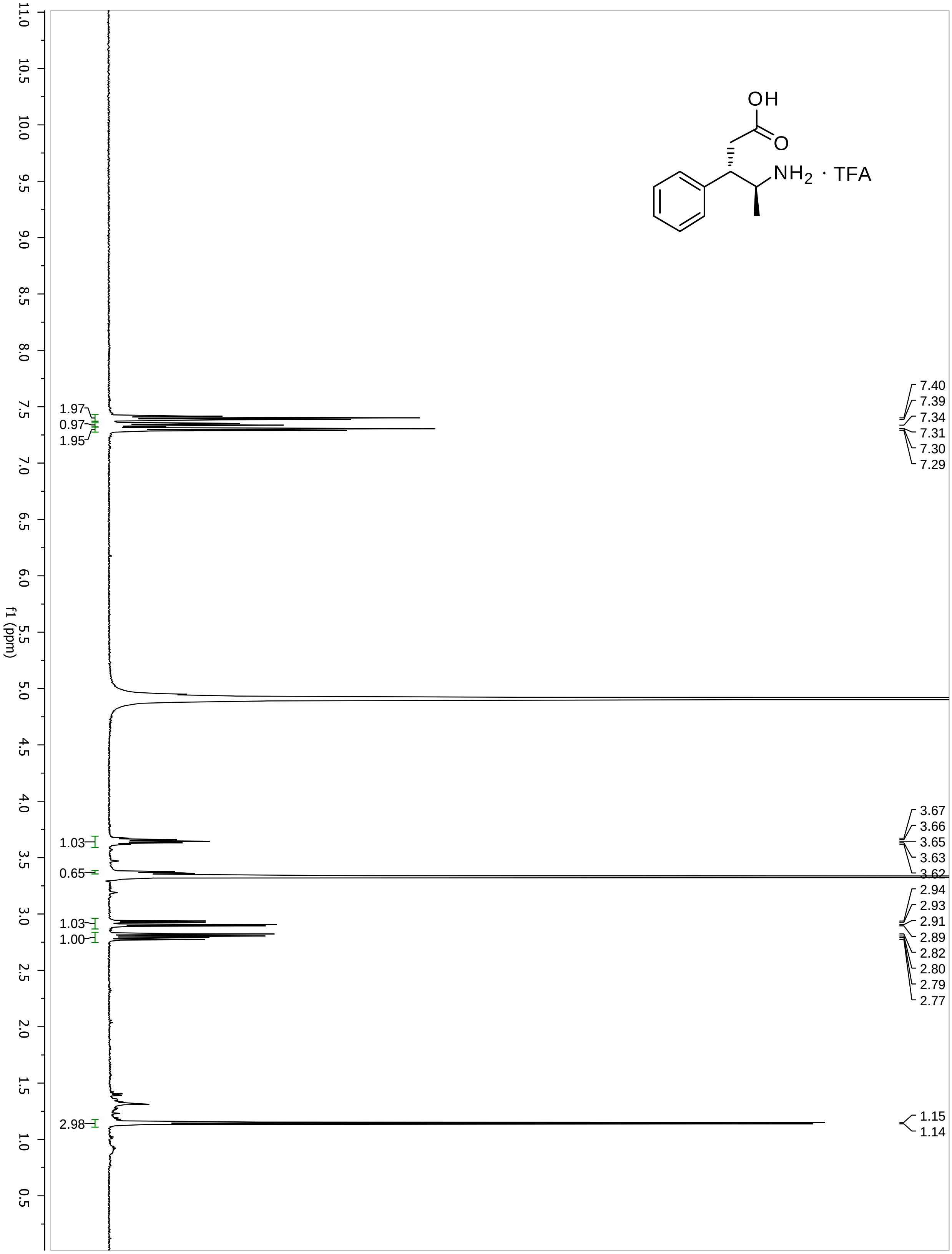
Product 17:



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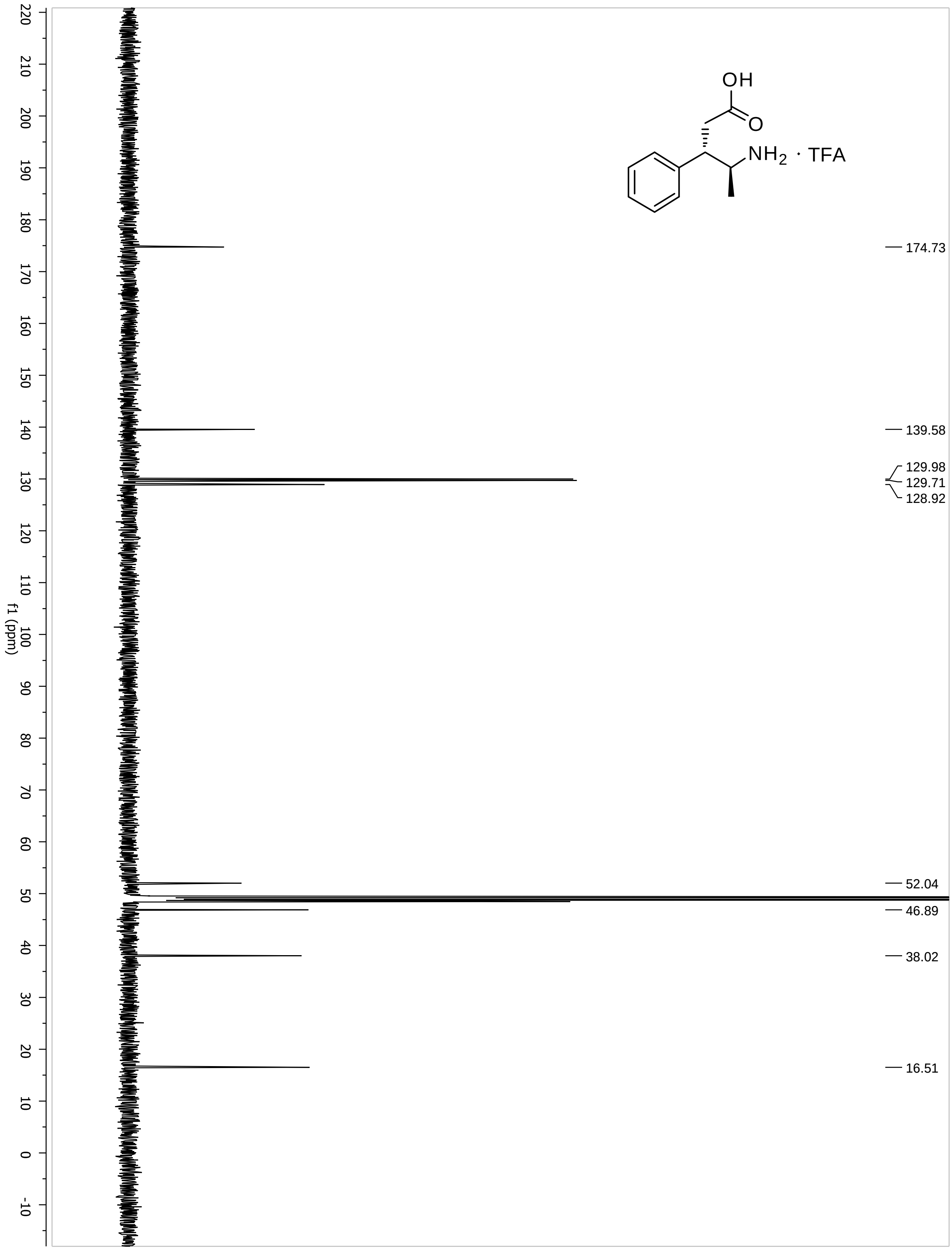
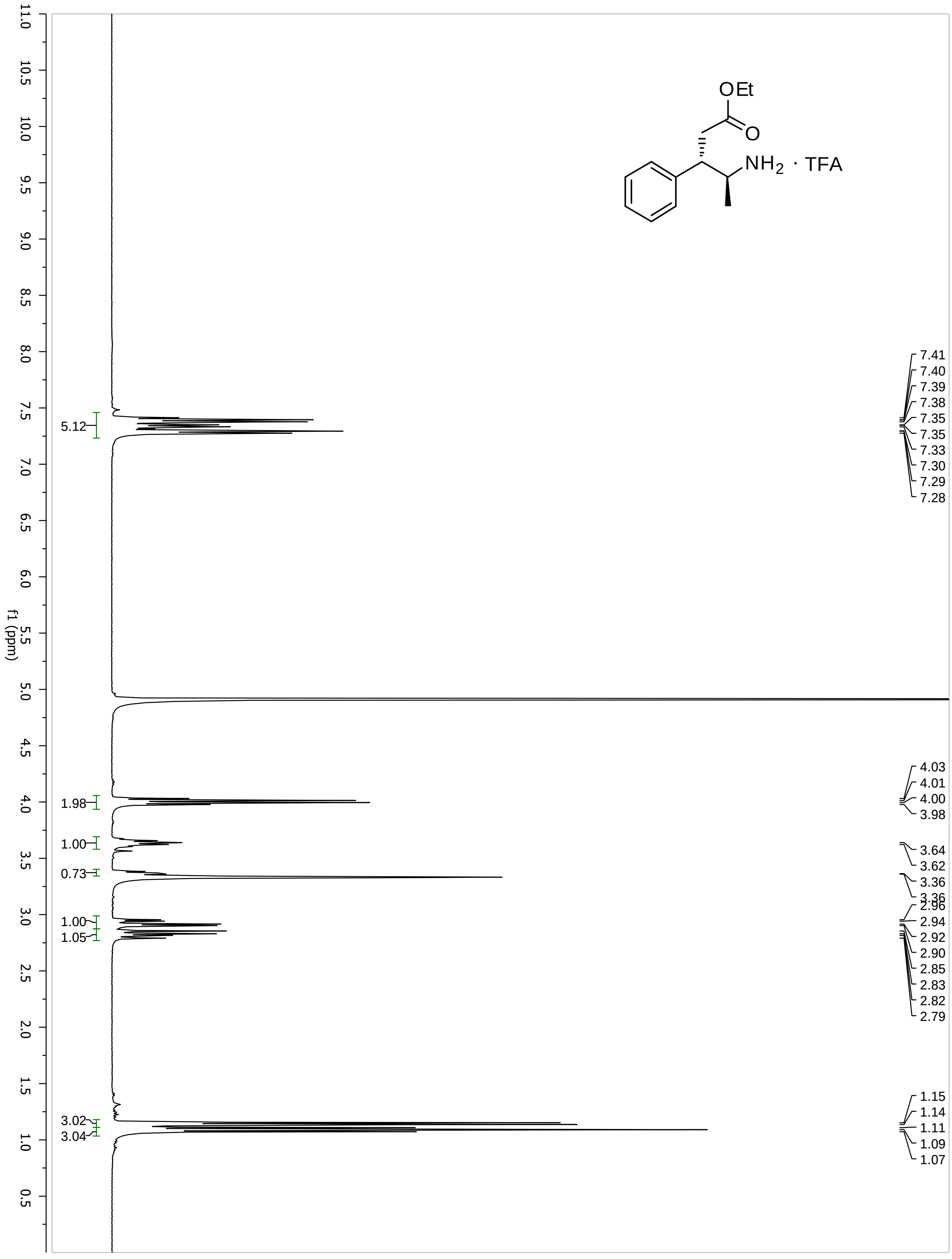

OH
O
NH2 · TFA
174.73
139.58
129.98
129.71
128.92
52.04
46.89
38.02
16.51
f1 (ppm)

Product 18:


OEt
O
NH2 · TFA
7.41
7.40
7.39
7.38
7.35
7.35
7.33
7.30
7.29
7.28
4.03
4.01
4.00
3.98
3.64
3.62
3.36
3.36
2.96
2.94
2.92
2.90
2.85
2.83
2.82
2.79
1.15
1.14
1.11
1.09
1.07
5.12
1.98
1.00
0.73
1.00
1.05
3.02
3.04
f1 (ppm)
11.0
10.5
10.0
9.5
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

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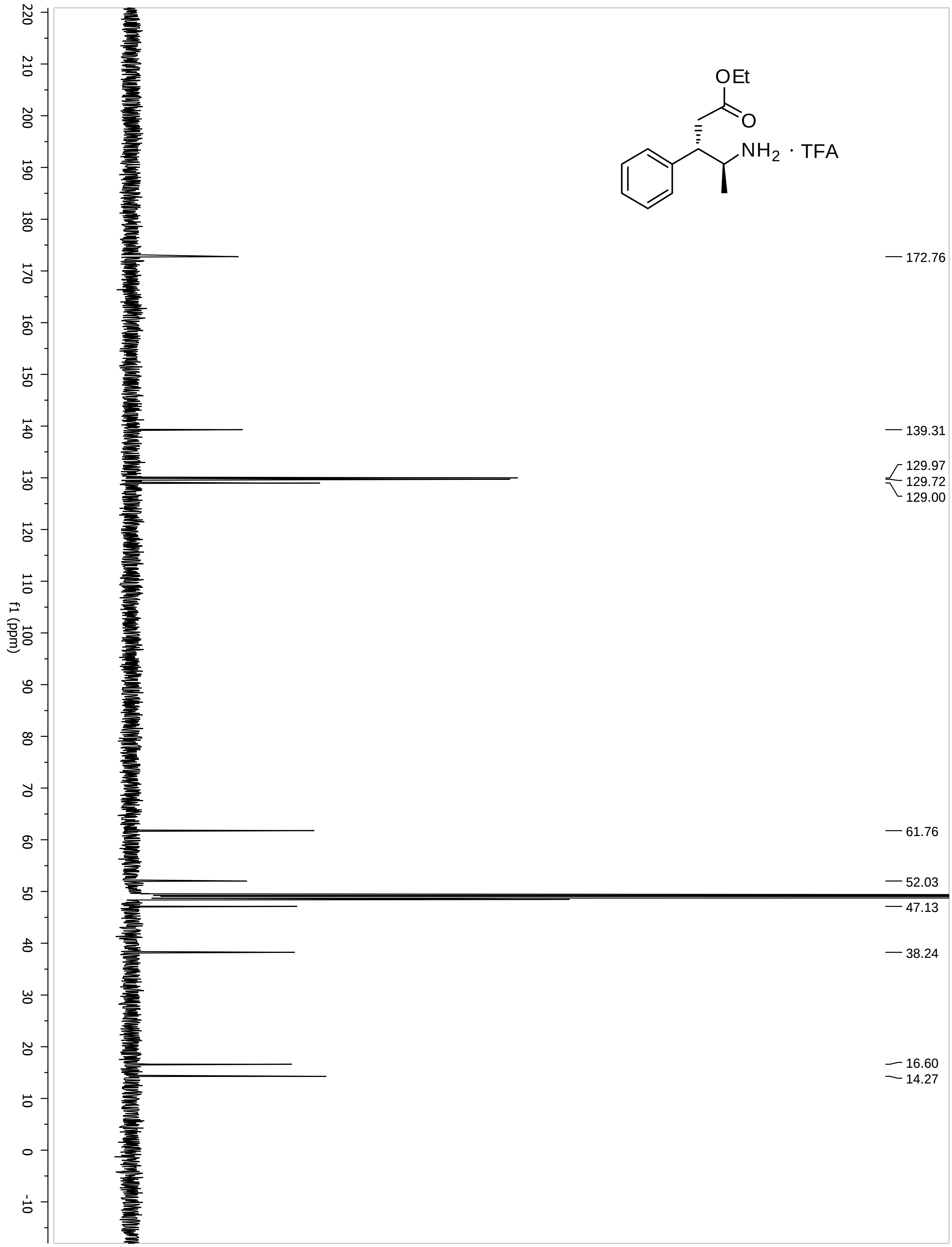
OEt
O
NH2 · TFA
172.76
139.31
129.97
129.72
129.00
61.76
52.03
47.13
38.24
16.60
14.27
f1 (ppm)
220
210
200
190
180
170
160
150
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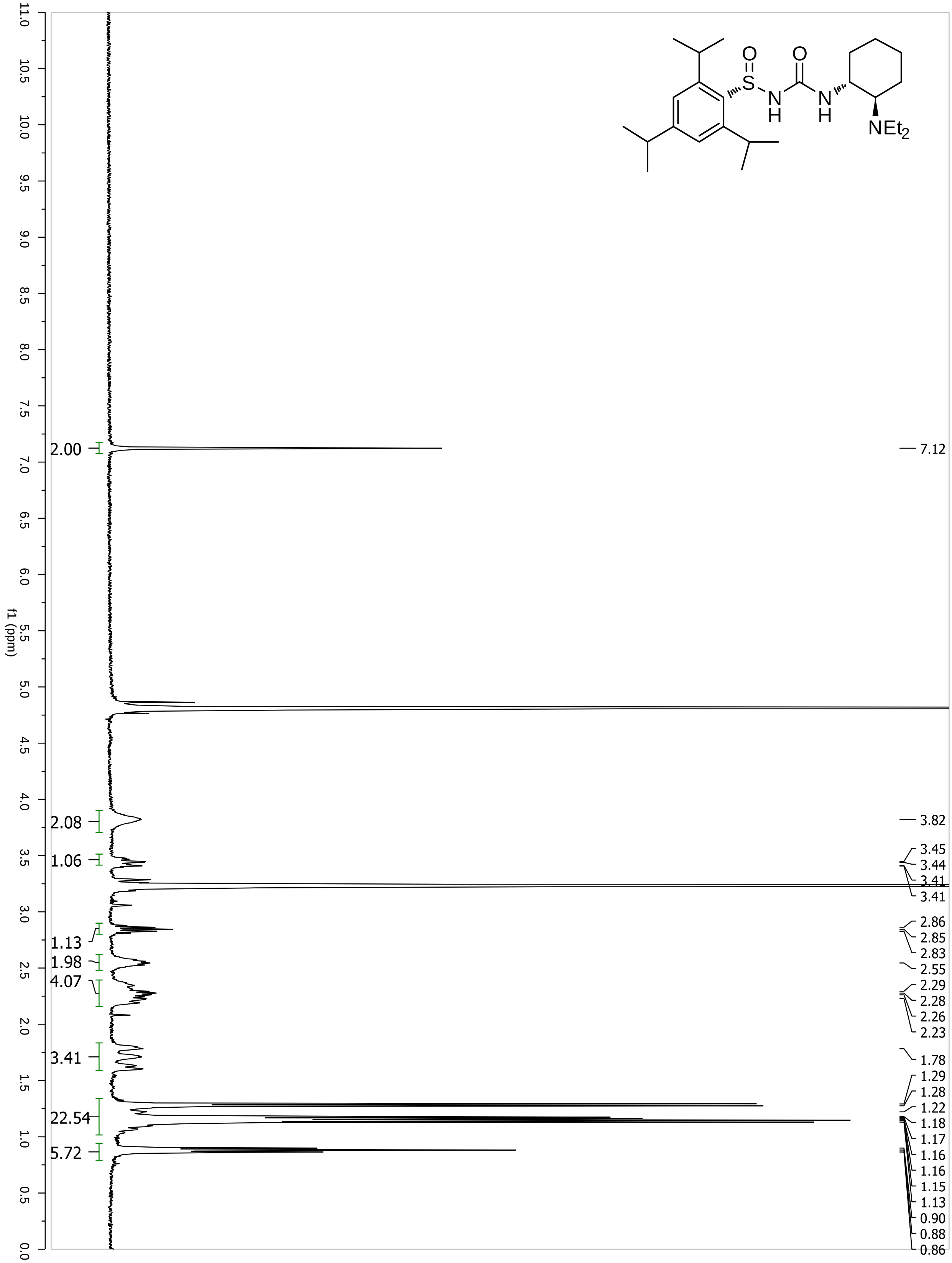
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

sulfinyl urea 4



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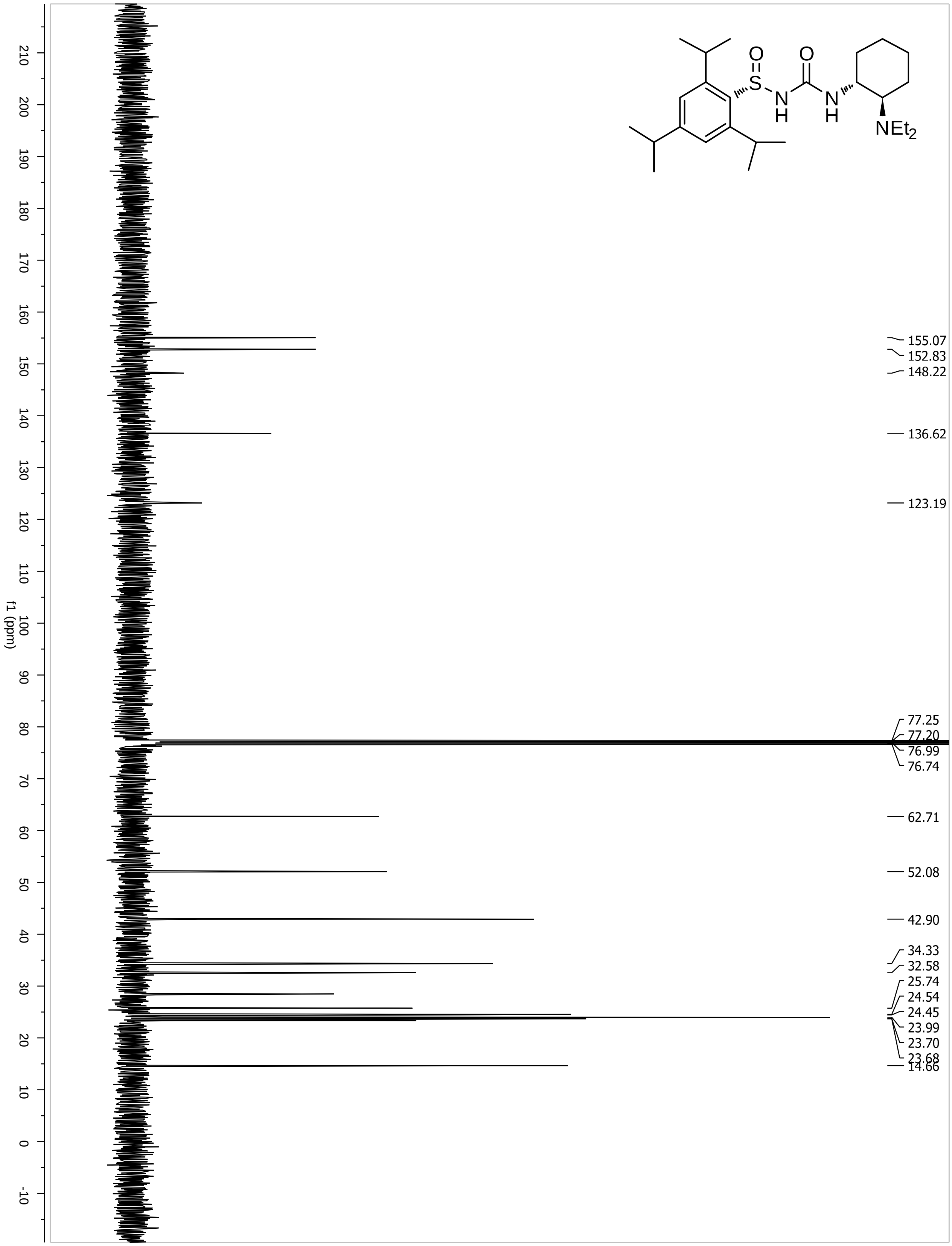
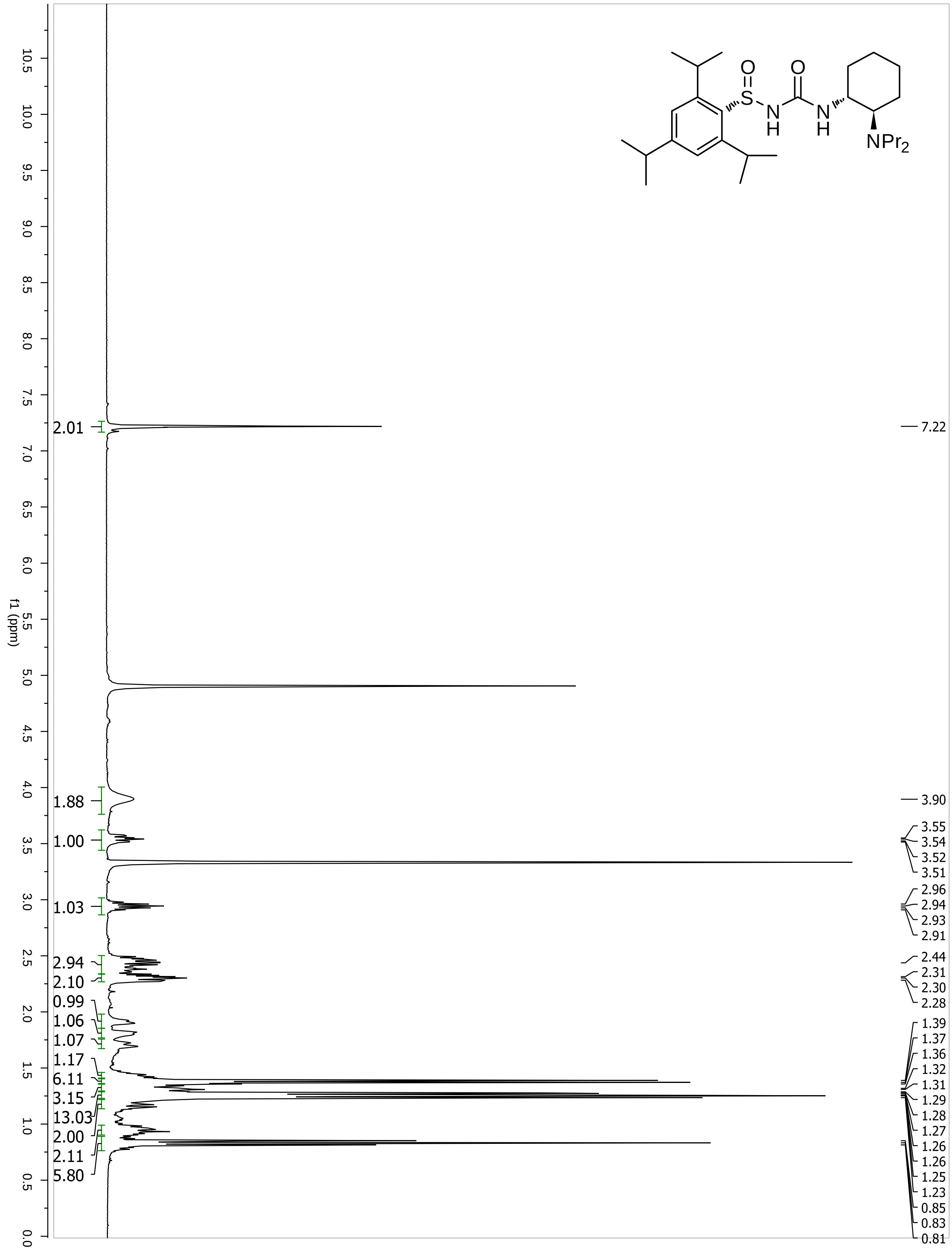


sulfinyl urea 5



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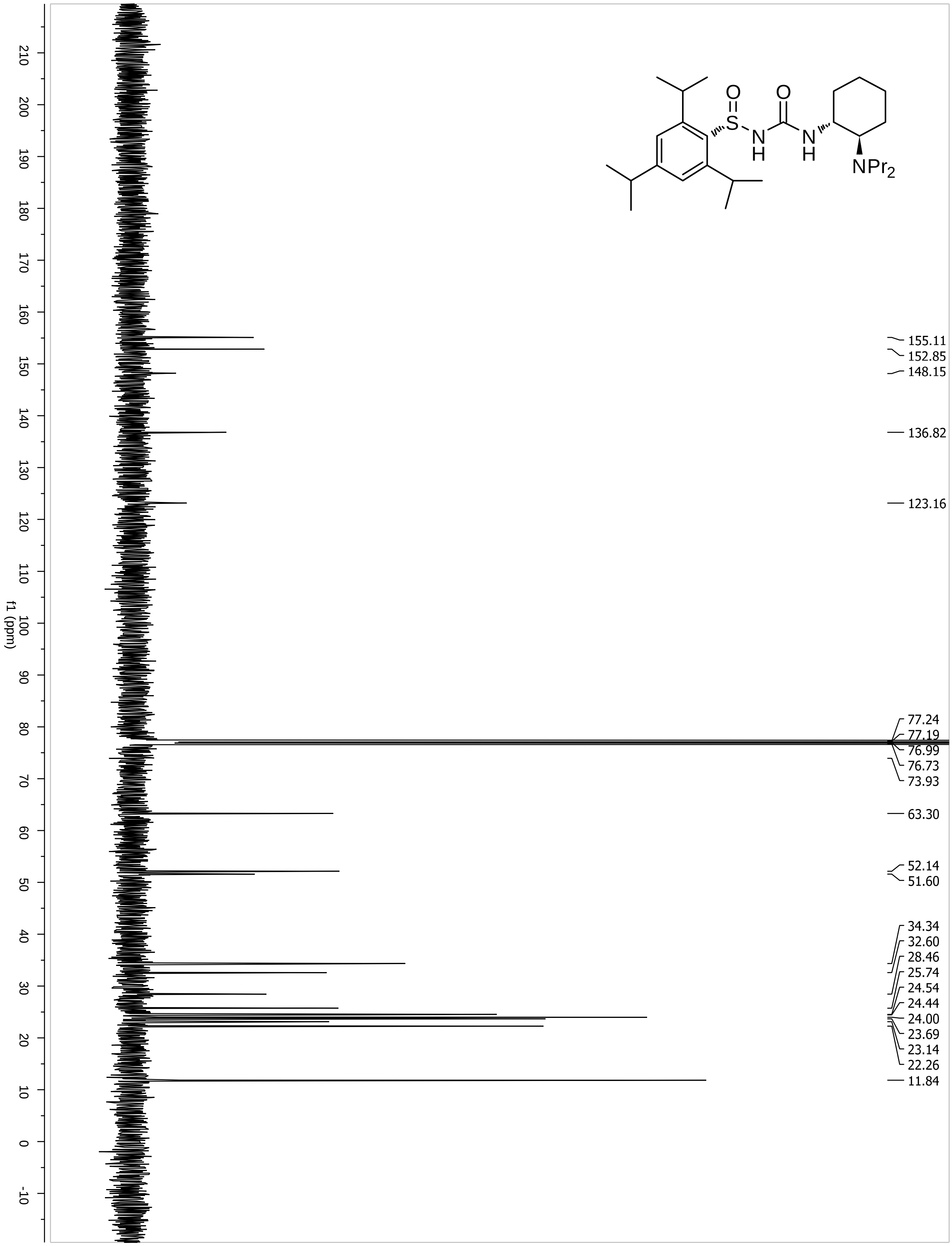
sulfinyl urea 5



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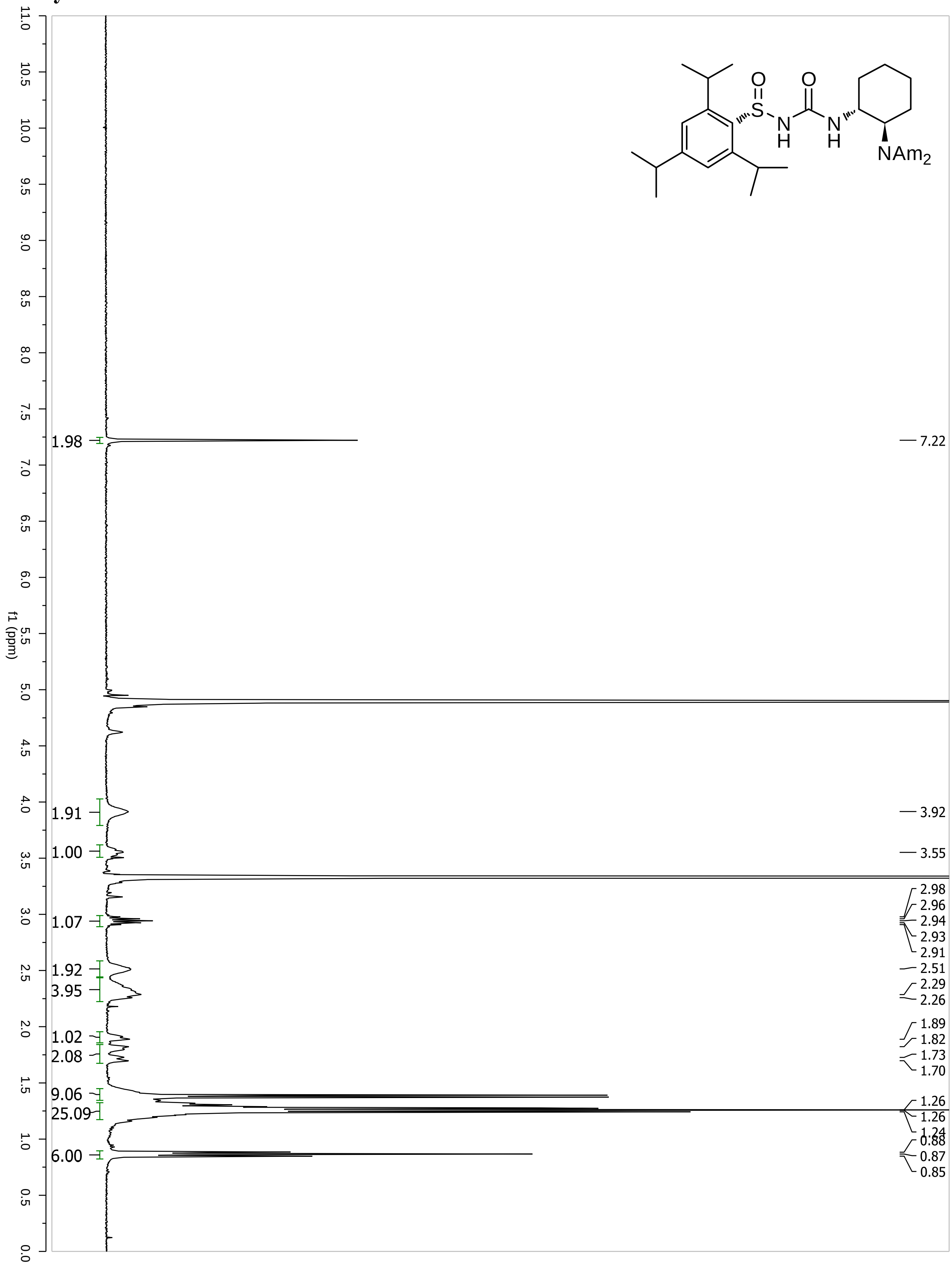
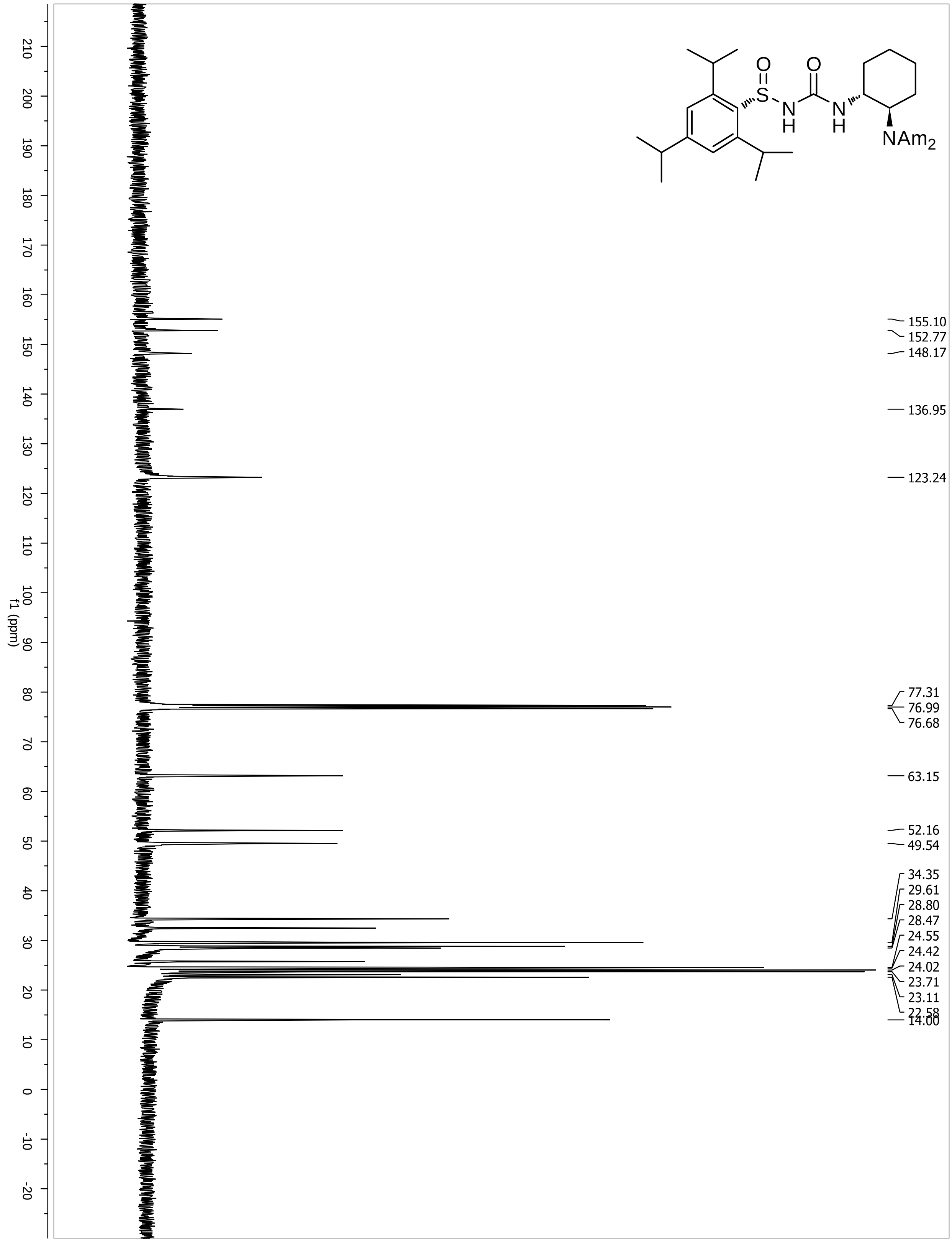
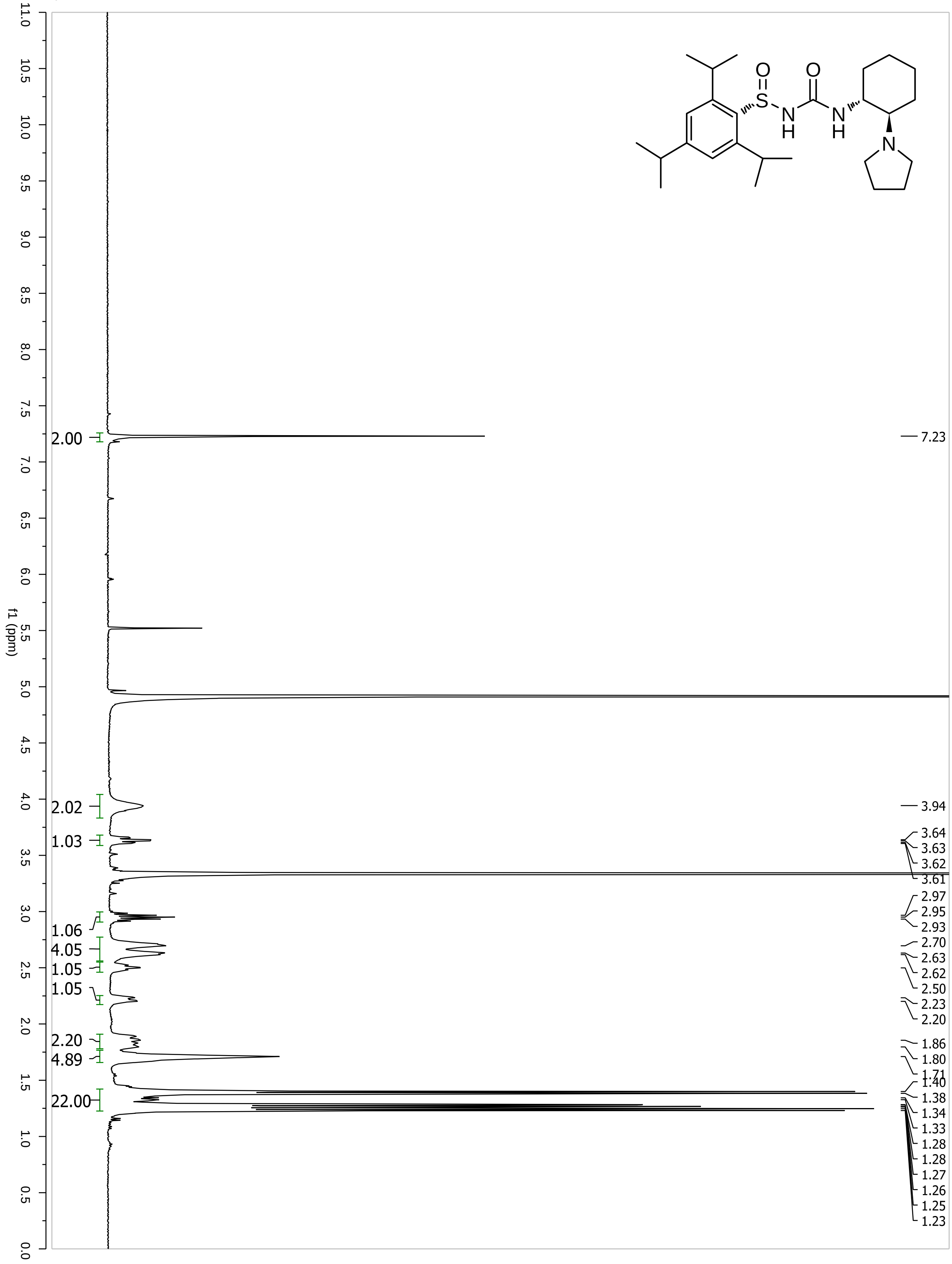


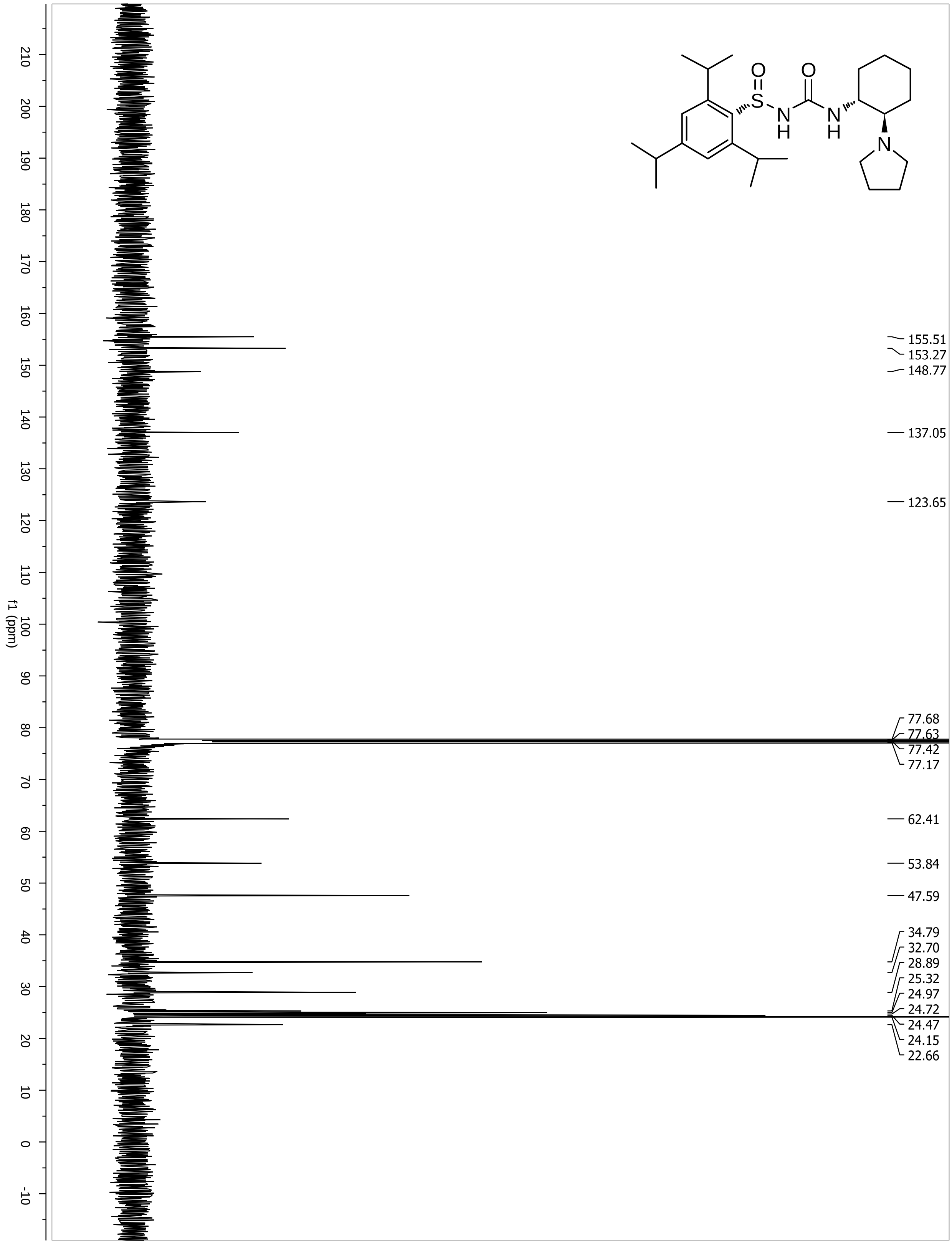
sulfinyl urea 6



sulfinyl urea 7



sulfinyl urea 7



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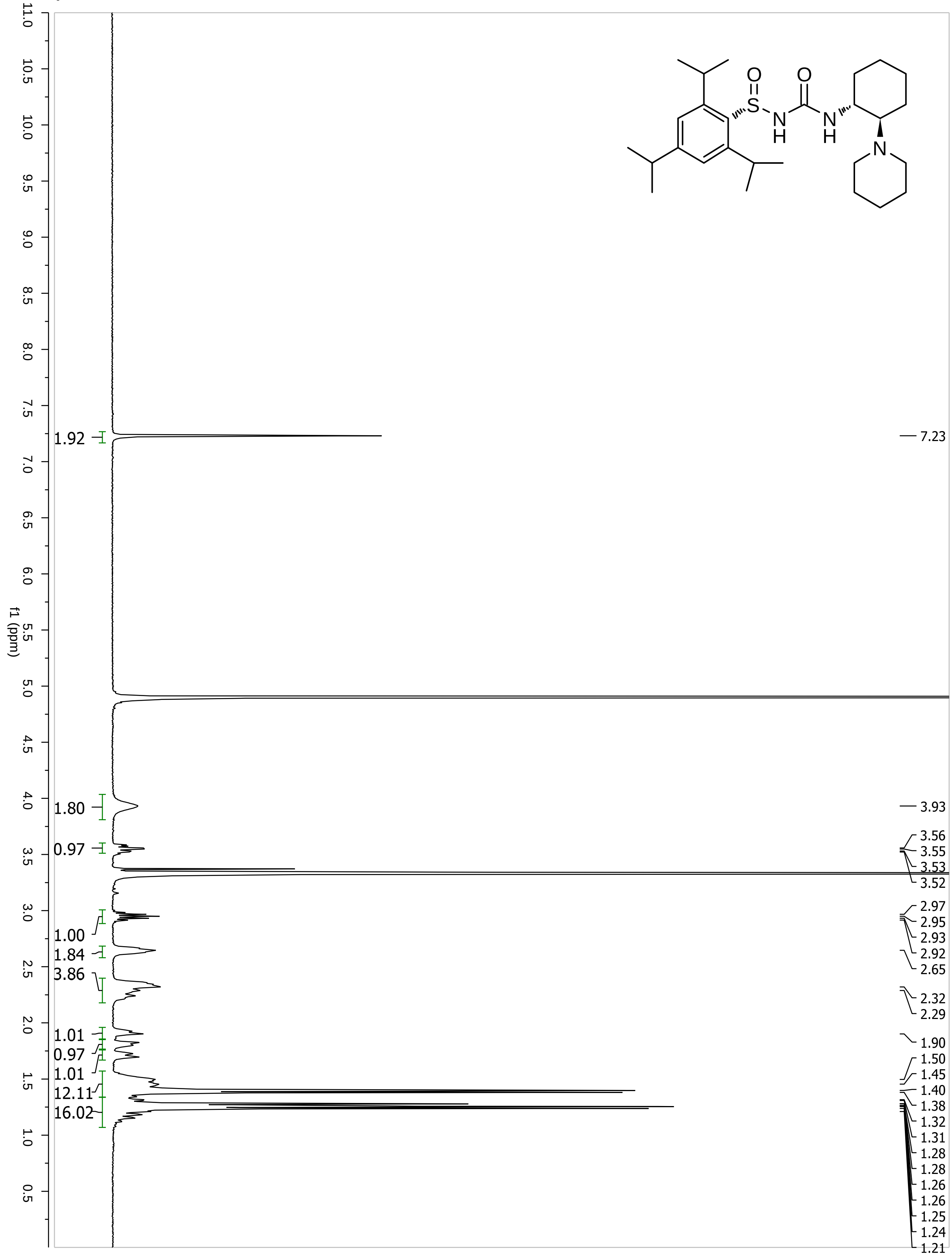
sulfinyl urea 8



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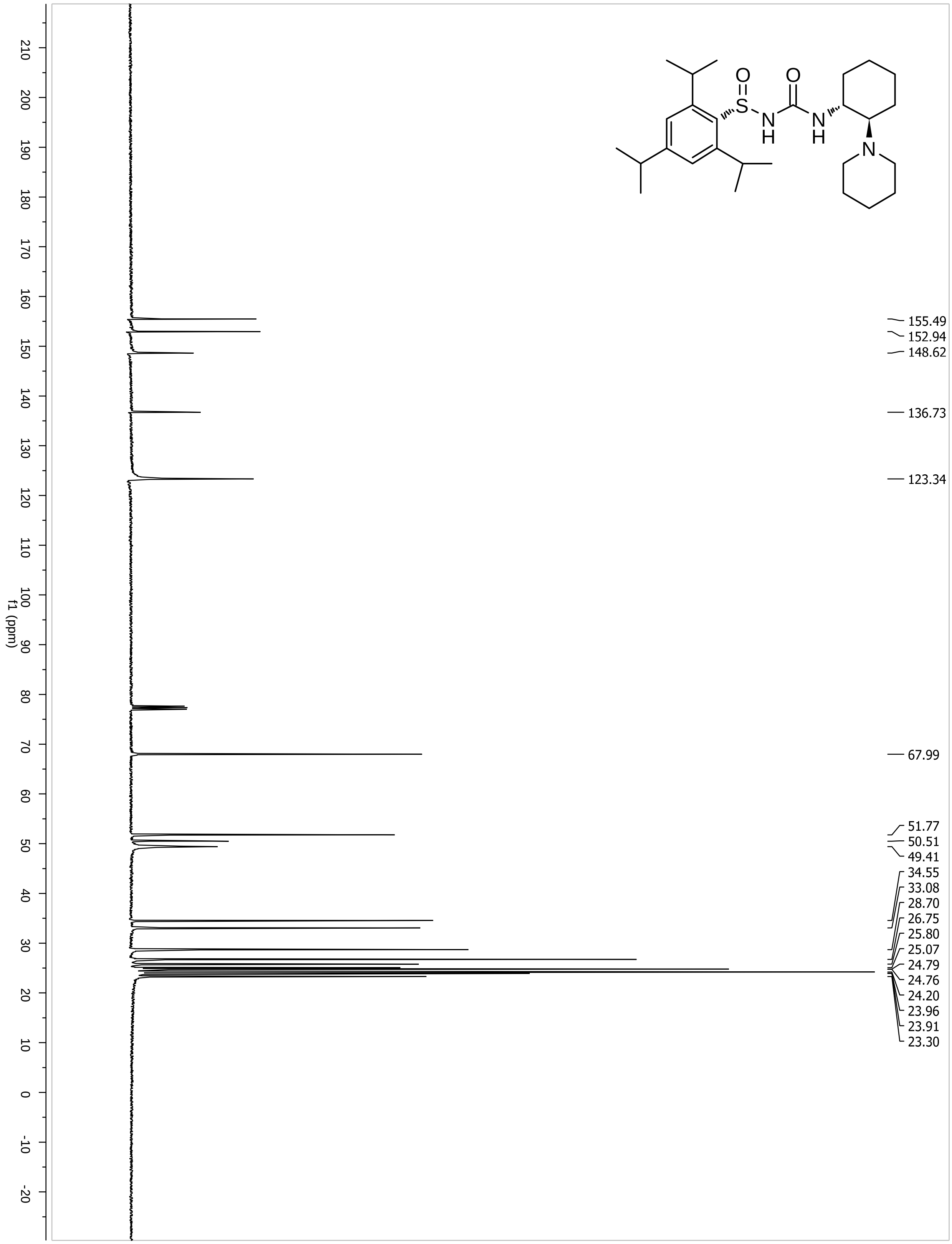
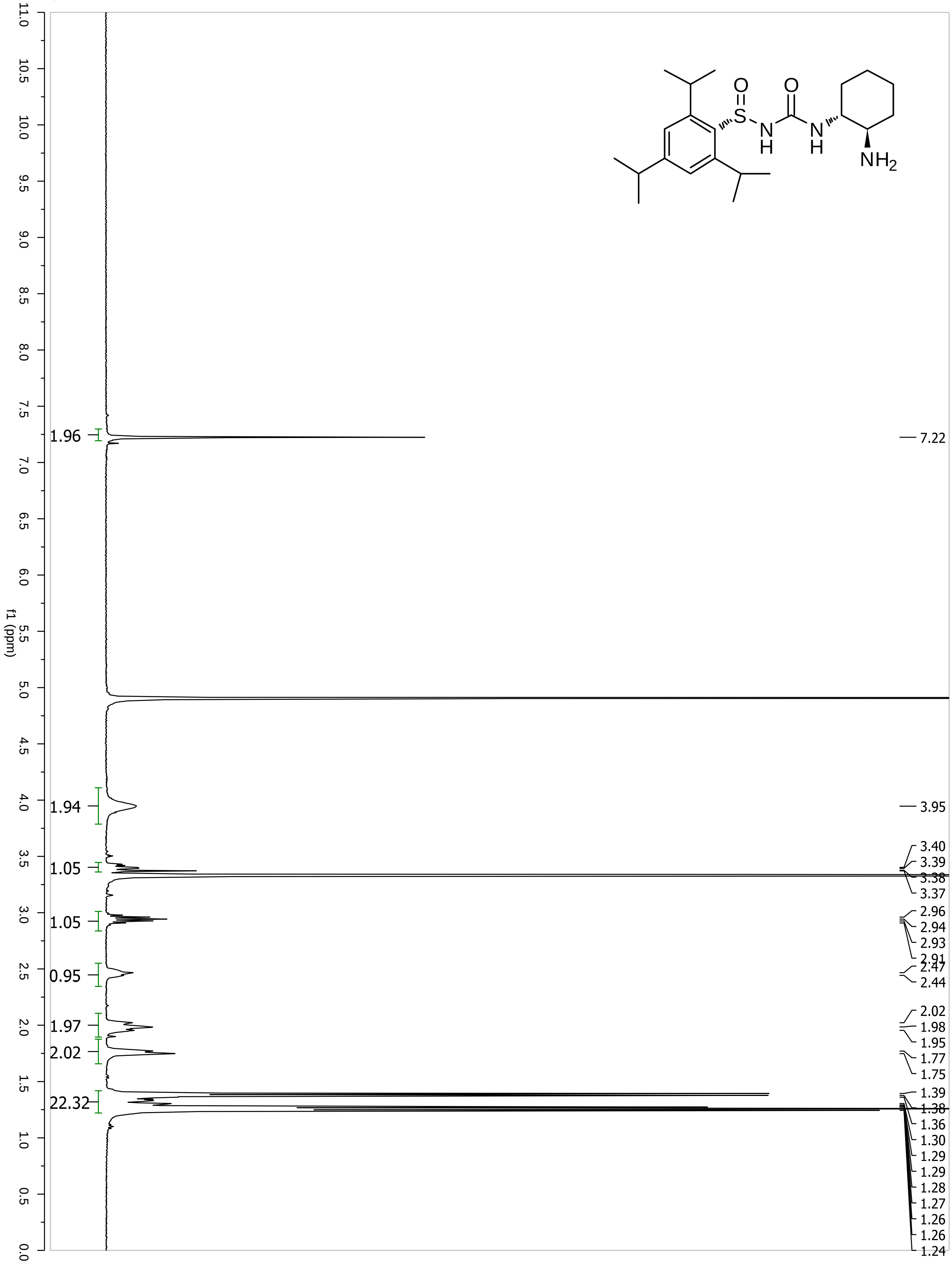
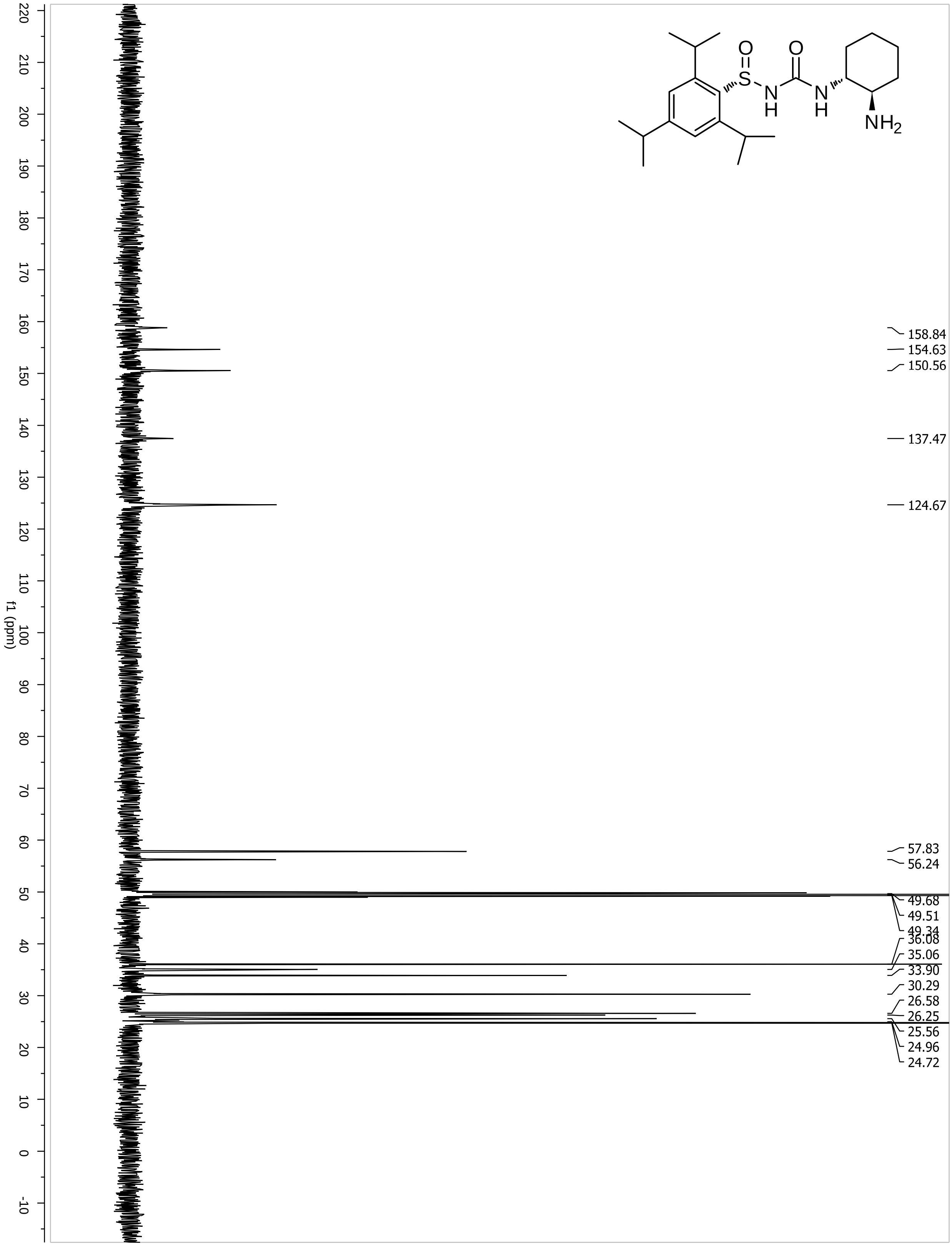
sulfinyl urea 8



sulfinyl urea 9

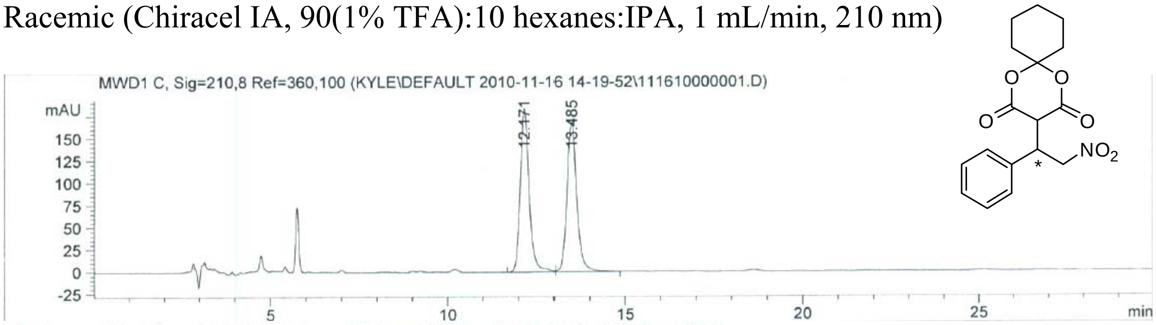


sulfinyl urea 9



Product 12a.

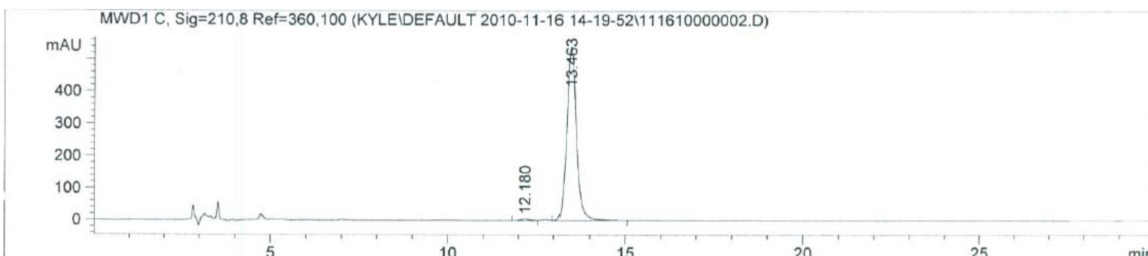
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.171	BV	0.2676	3249.64233	184.36560	49.9267
2	13.485	VB	0.2911	3259.18848	168.95094	50.0733

Enantiomerically enriched (98% ee)

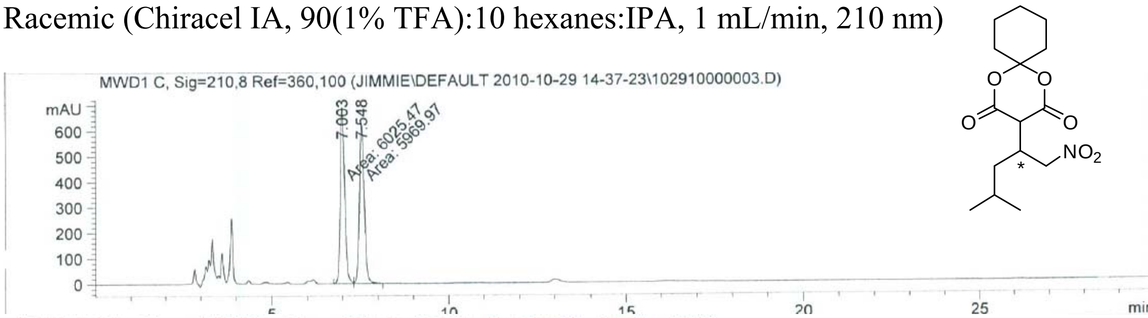


Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.180	BV	0.2718	106.10869	5.95597	1.0279
2	13.463	VB	0.2861	1.02169e4	541.54675	98.9721

Product 12b.

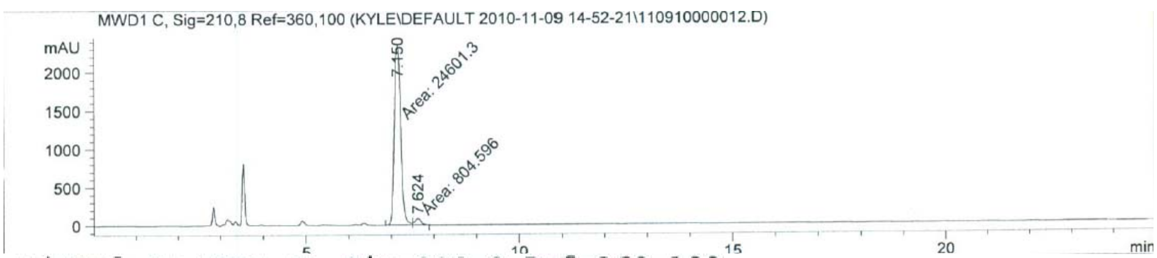
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.003	MF	0.1457	6025.46875	689.20428	50.2313
2	7.548	FM	0.1579	5969.97217	629.99774	49.7687

Enantiomerically enriched (94% ee)

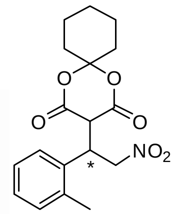


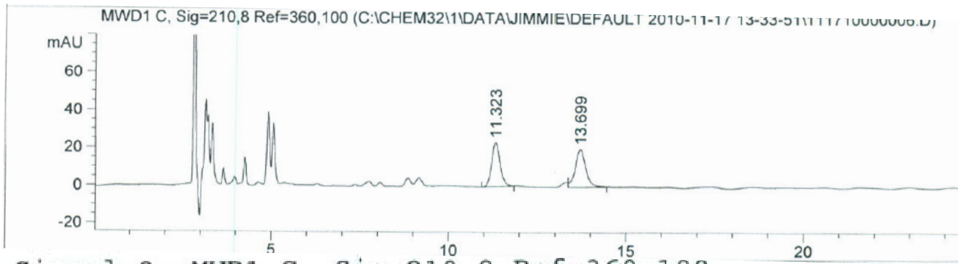
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.150	MM	0.1753	2.46013e4	2338.92871	96.8330
2	7.624	MM	0.1604	804.59576	83.61231	3.1670

Product 12c.

Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)

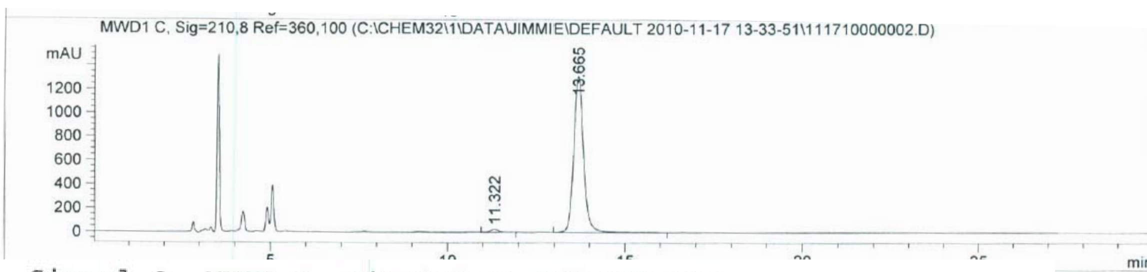




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.323	BB	0.2513	383.11395	23.36245	48.4374
2	13.699	VB	0.3081	407.83191	19.98423	51.5626

Enantiomerically enriched (96% ee)

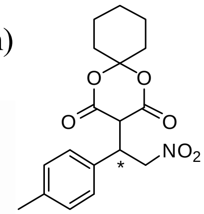


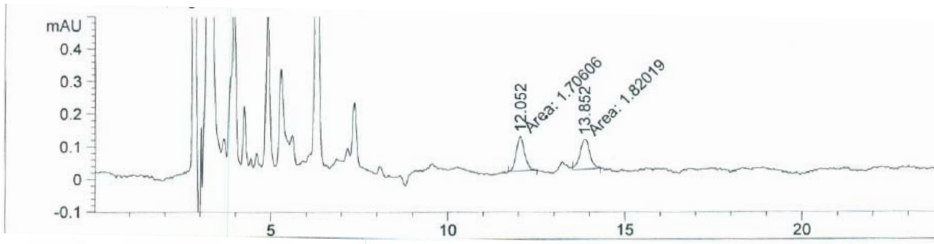
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.322	VB	0.2593	428.82278	25.09845	1.6539
2	13.665	VB	0.2965	2.54998e4	1313.40662	98.3461

Product 12d.

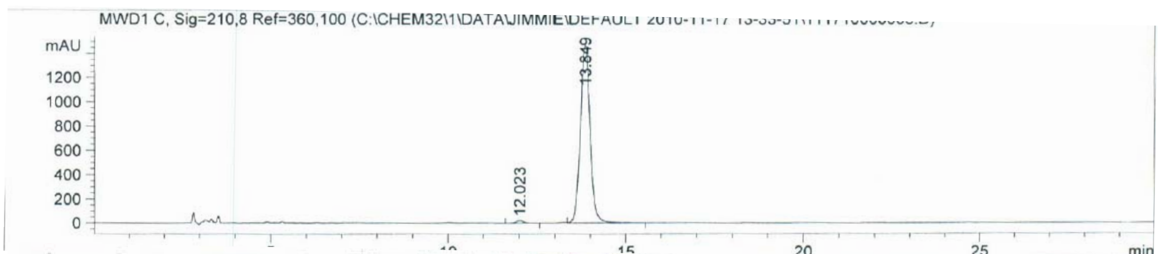
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.052	MM	0.2706	1.70606	1.05070e-1	48.3818
2	13.852	MM	0.3297	1.82019	9.20134e-2	51.6182

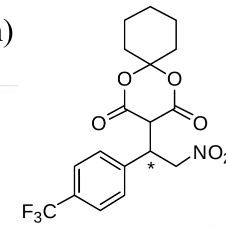
Enantiomerically enriched (98% ee)



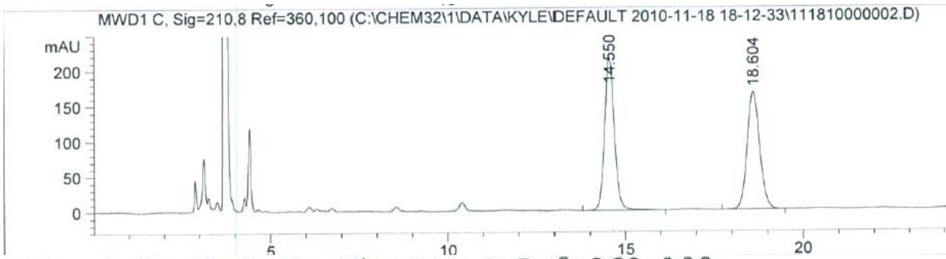
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.023	VB	0.2556	346.48251	20.88085	1.2140
2	13.849	VB	0.2962	2.81935e4	1467.31274	98.7860

Product 12e.



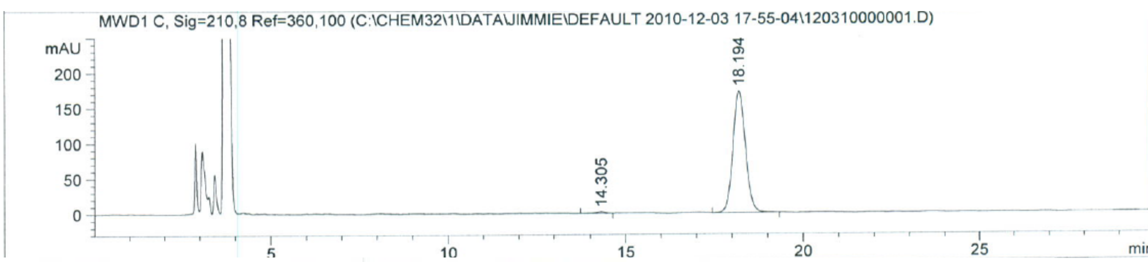
Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.550	VB	0.2964	4225.37012	217.72339	50.5719
2	18.604	VB	0.3800	4129.80078	167.31418	49.4281

Enantiomerically enriched (98% ee)

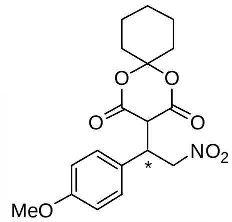


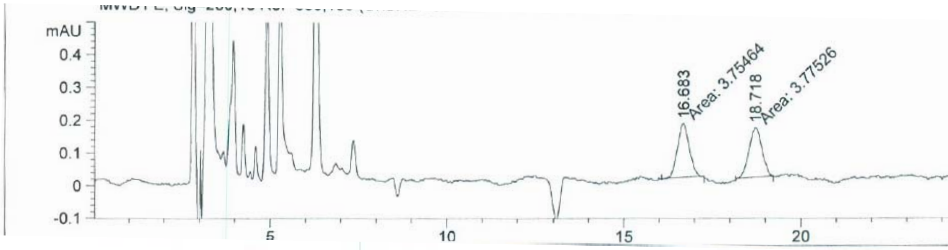
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.305	BV	0.3032	46.49001	2.26733	1.0839
2	18.194	VB	0.3765	4242.54541	172.76634	98.9161

Product 12f.

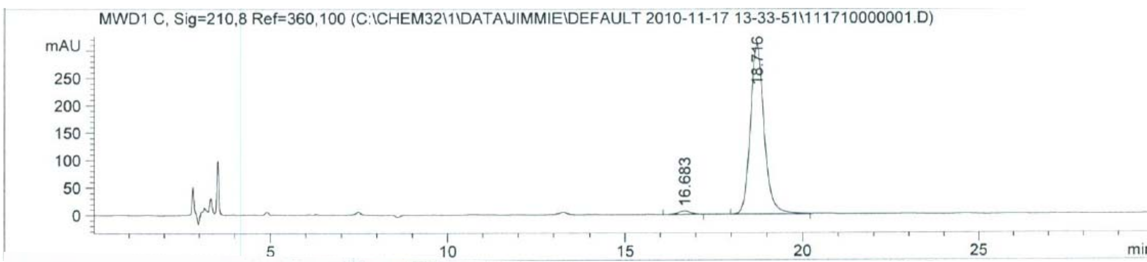
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.683	MM	0.3800	3.75464	1.64691e-1	49.8631
2	18.718	MM	0.4163	3.77526	1.51146e-1	50.1369

Enantiomerically enriched (96% ee)

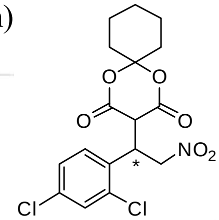


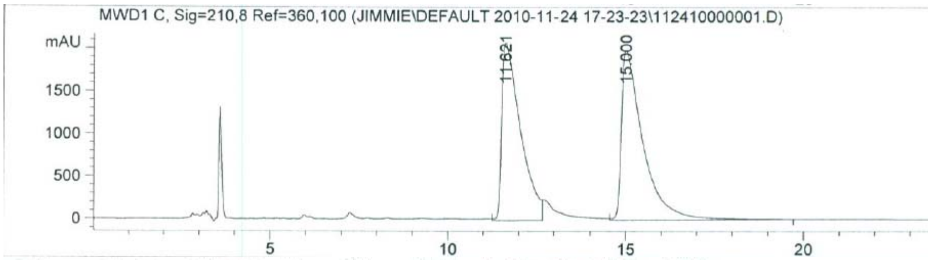
Signal 3: MWD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.684	BB	0.3573	108.54615	4.66804	1.7311
2	18.716	BB	0.4107	6161.97021	228.44705	98.2689

Product 12g.

Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)

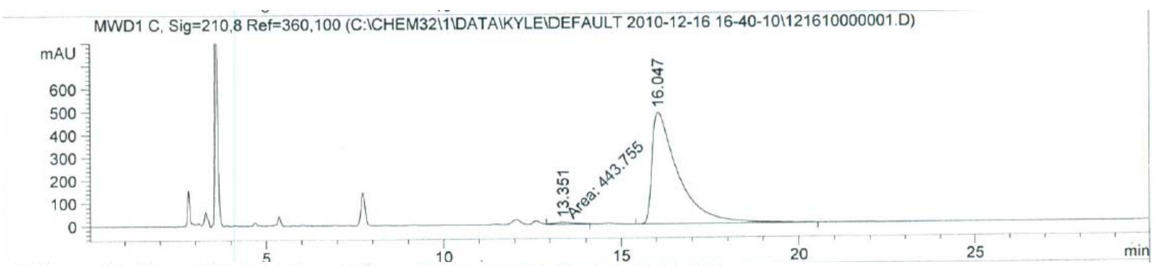




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.621	VV	0.5449	7.64165e4	2078.62891	47.7471
2	15.000	VB	0.6094	8.36279e4	1985.56482	52.2529

Enantiomerically enriched (96% ee)

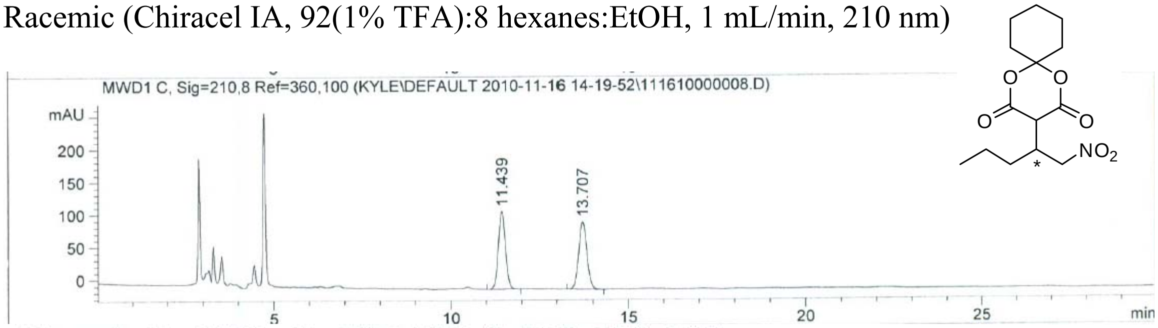


Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.351	MM	0.7691	443.75479	9.61618	1.7431
2	16.047	VB	0.7198	2.50143e4	489.78738	98.2569

Product 12h.

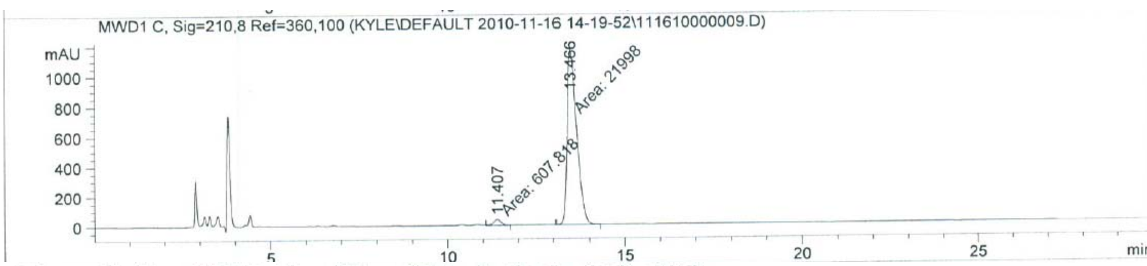
Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.439	VB	0.2158	1660.03430	119.66300	49.9239
2	13.707	BB	0.2478	1665.09375	103.41457	50.0761

Enantiomerically enriched (94% ee)

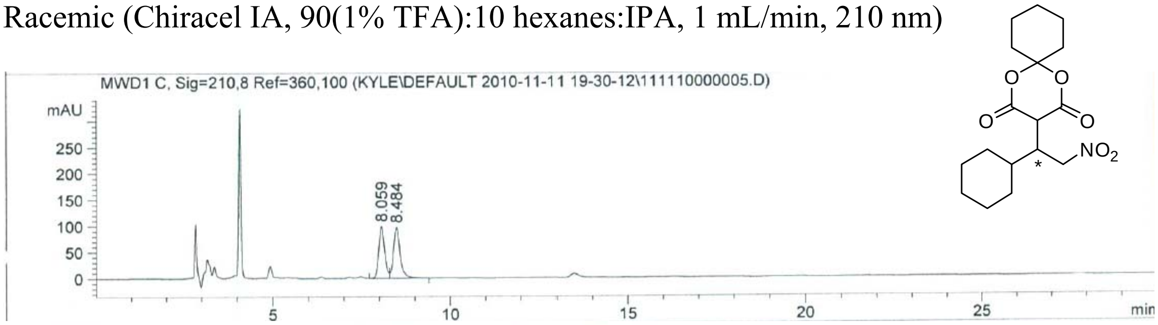


Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.407	MM	0.2464	607.81775	41.10920	2.6888
2	13.466	MM	0.3135	2.19980e4	1169.53650	97.3112

Product 12i.

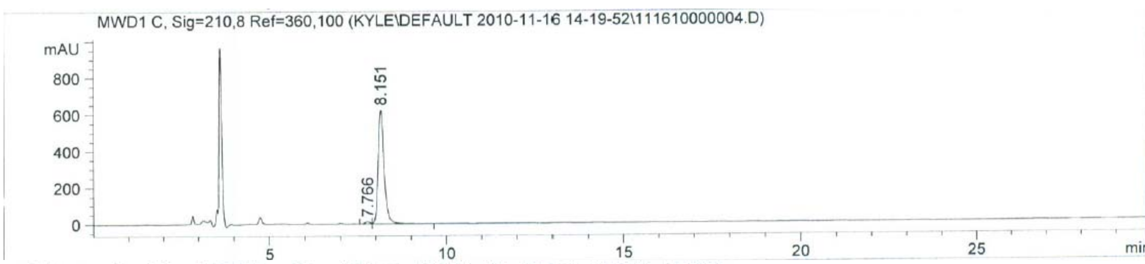
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.059	VV	0.1773	1155.21533	99.59238	47.6443
2	8.484	VB	0.1960	1269.44897	97.40547	52.3557

Enantiomerically enriched (96% ee)

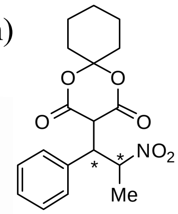


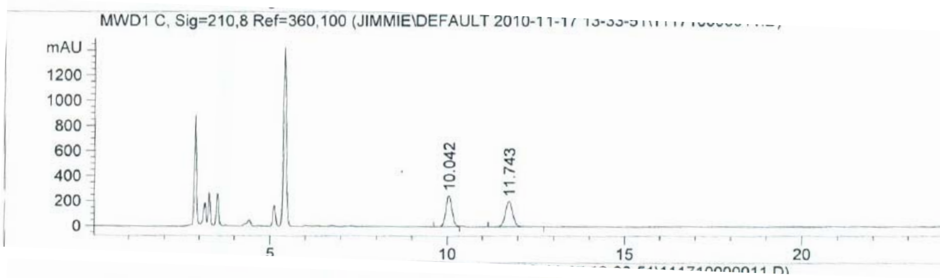
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.766	VV	0.1654	135.95309	12.65262	1.8147
2	8.151	VB	0.1780	7355.77637	621.73523	98.1853

Product 14a.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)

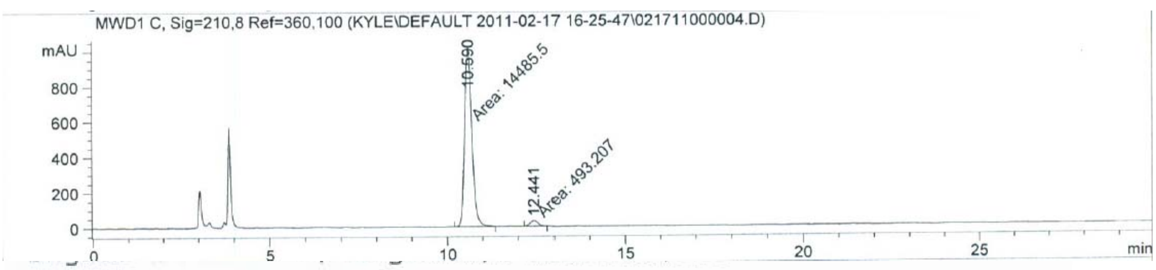




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.042	VV	0.1861	3024.98975	248.41452	50.1504
2	11.743	VB	0.2270	3006.84351	202.74911	49.8496

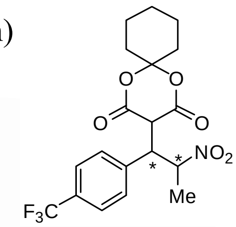
Enantiomerically enriched (93% ee)



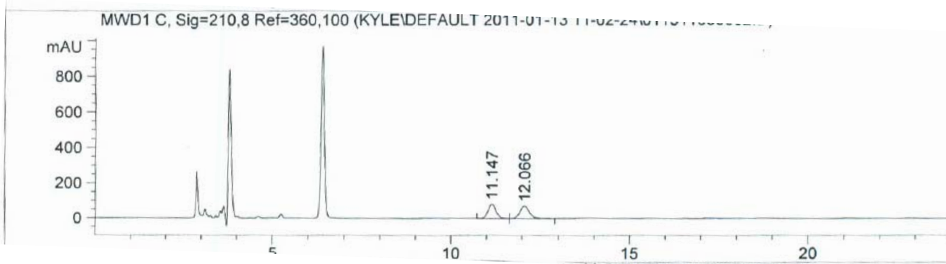
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.590	MM	0.2374	1.44855e4	1017.06580	96.7073
2	12.441	MM	0.2614	493.20709	31.44804	3.2927

Electronic Supplementary Material (ESI) for Chemical Science

Product 14b.



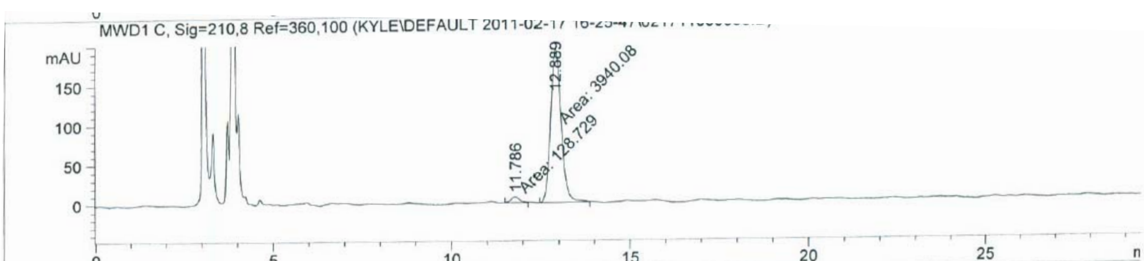
Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.147	VV	0.2434	1312.27698	82.59743	49.6280
2	12.066	VB	0.2850	1331.95068	71.61419	50.3720

Enantiomerically enriched (94% ee)

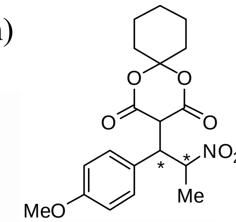


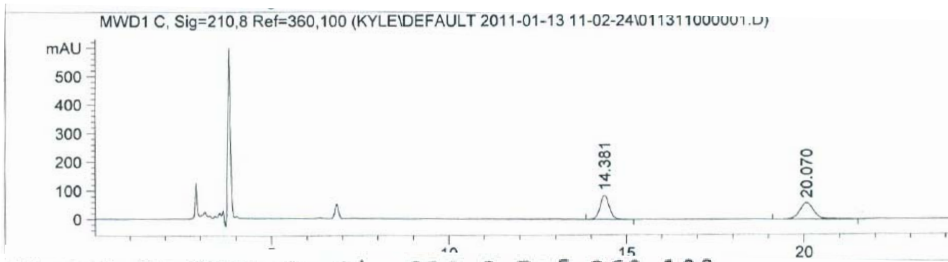
Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.786	MM	0.2987	128.72871	7.18237	3.1638
2	12.889	MM	0.3442	3940.08423	190.77631	96.8362

Product 14c.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)

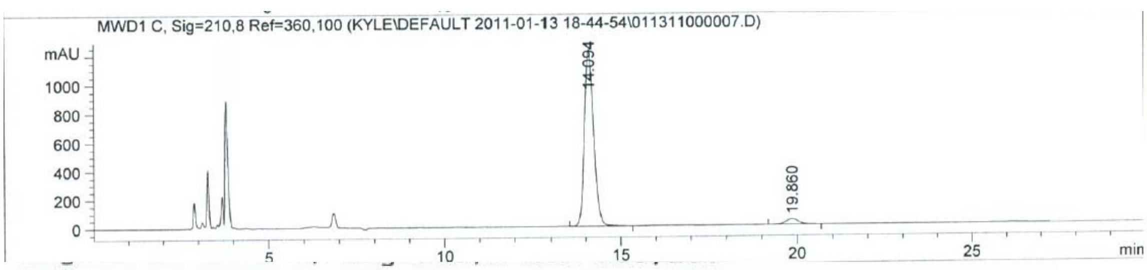




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.381	BB	0.2811	1555.71436	85.17610	49.0931
2	20.070	VB	0.4207	1613.19116	58.31782	50.9069

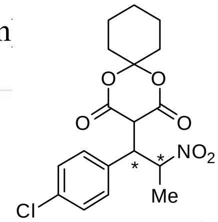
Enantiomerically enriched (92% ee)

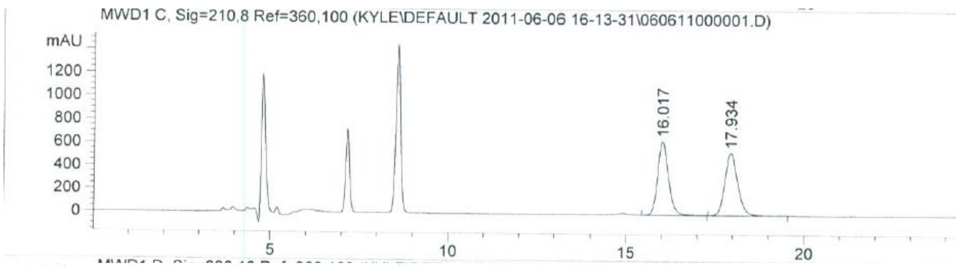


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.094	VB	0.2810	2.25246e4	1233.74744	95.9480
2	19.860	BB	0.3869	951.25140	37.88362	4.0520

Product 14d.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 0.8 mL/min, 210 nm)

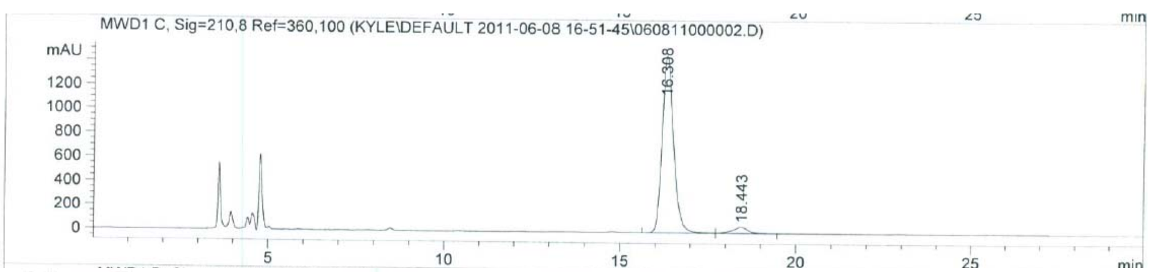




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.017	VB	0.3228	1.35458e4	640.33673	49.9698
2	17.934	BB	0.3835	1.35621e4	542.87994	50.0302

Enantiomerically enriched (91% ee)

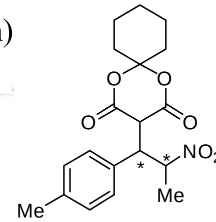


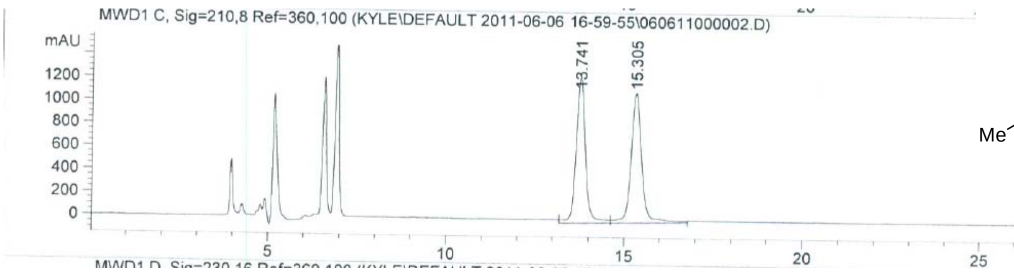
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.308	VV	0.3434	3.32120e4	1470.83679	95.5132
2	18.443	VB	0.4498	1560.17578	50.59335	4.4868

Product 14e.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 0.8 mL/min, 210 nm)

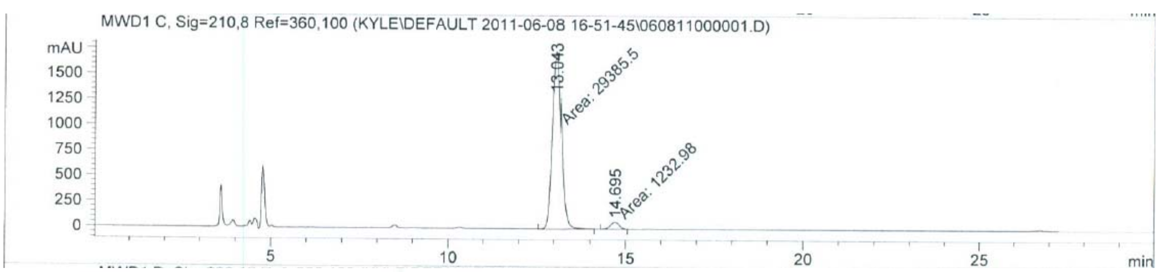




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.741	BV	0.2752	2.32784e4	1274.03772	49.5223
2	15.305	VB	0.3167	2.37274e4	1122.00000	50.4777

Enantiomerically enriched (92% ee)

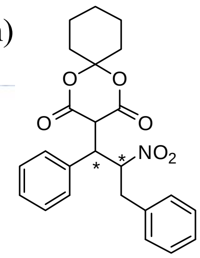


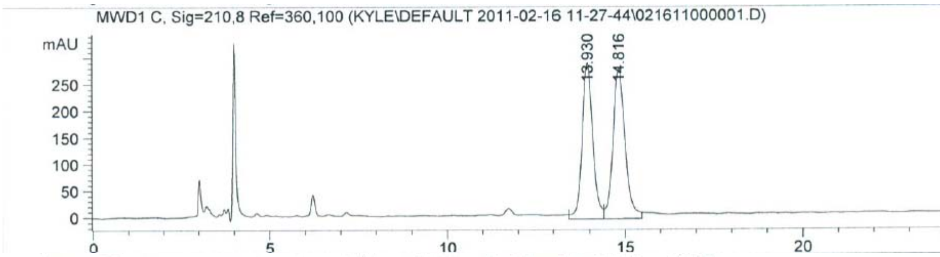
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.043	MM	0.2811	2.93855e4	1742.01489	95.9731
2	14.695	MM	0.2939	1232.97864	69.92357	4.0269

Product 14f.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)

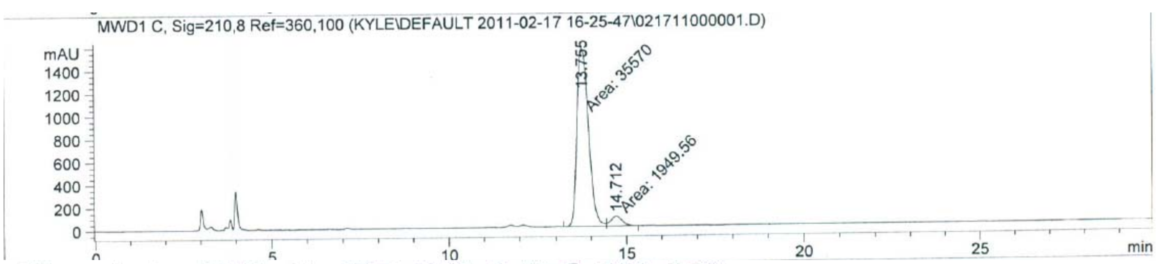




Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.930	VV	0.3203	6160.19043	294.23013	47.8921
2	14.816	VV	0.3530	6702.44678	282.30951	52.1079

Enantiomerically enriched (90% ee)

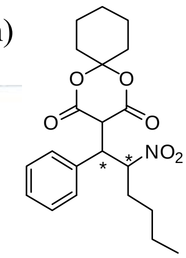


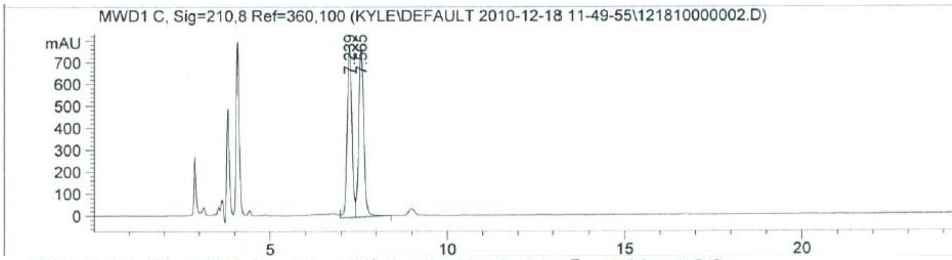
Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.755	MM	0.3800	3.55700e4	1559.89685	94.8039
2	14.712	MM	0.3749	1949.55615	86.67139	5.1961

Product 14g.

Racemic (Chiracel IA, 92(1% TFA):8 hexanes:EtOH, 1 mL/min, 210 nm)

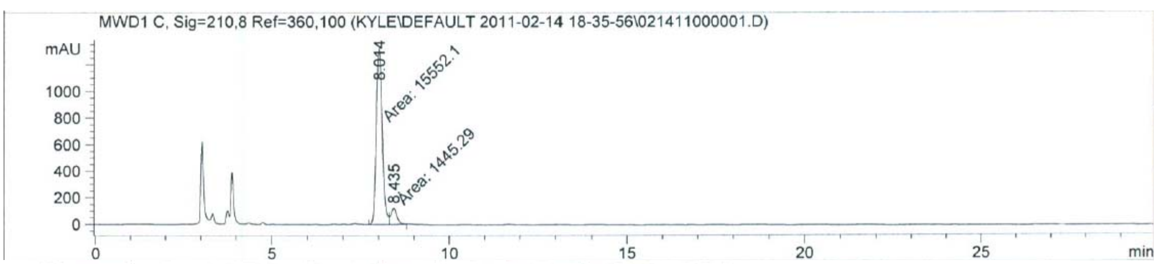




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.239	VV	0.1403	7094.31934	778.26367	48.2328
2	7.565	VB	0.1508	7614.17822	773.90112	51.7672

Enantiomerically enriched (83% ee)

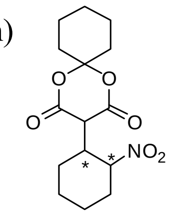


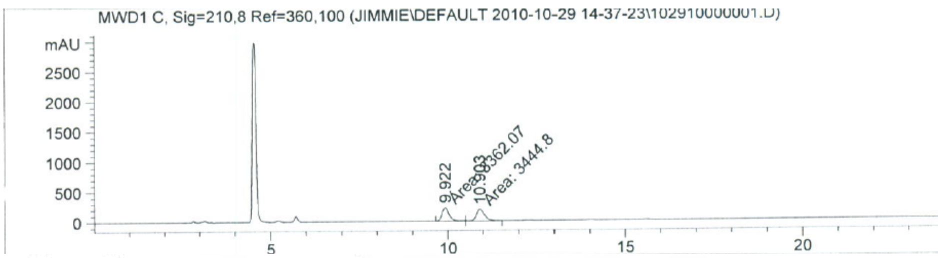
Signal 3: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.014	MM	0.1958	1.55521e4	1323.97107	91.4970
2	8.435	MM	0.1961	1445.28528	122.84429	8.5030

Product 14h.

Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)

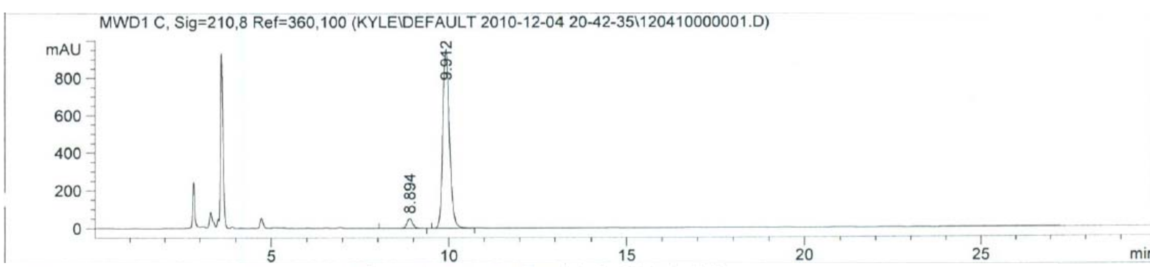




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.922	MF	0.2420	3362.06812	231.56804	49.3923
2	10.903	FM	0.2835	3444.80469	202.51933	50.6077

Enantiomerically enriched (91% ee)

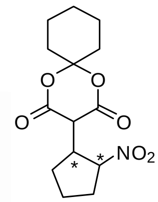


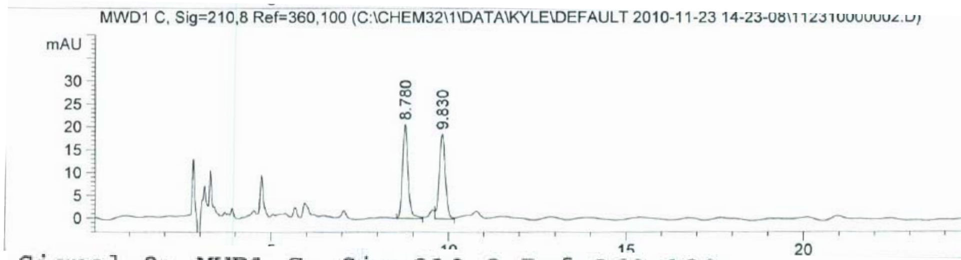
Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.894	VB	0.1741	584.49542	51.62966	4.4749
2	9.912	BB	0.2000	1.24771e4	957.41907	95.5251

Product 14i.

Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)

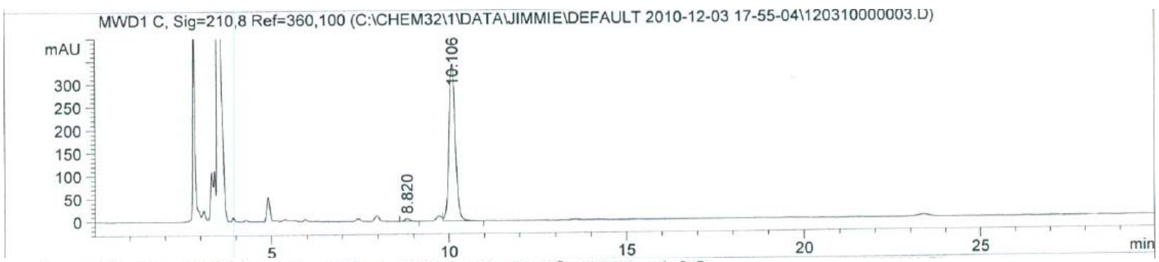




Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.780	BB	0.1655	224.47943	20.54615	50.3349
2	9.830	VB	0.1835	221.49229	18.52153	49.6651

Enantiomerically enriched (97% ee)

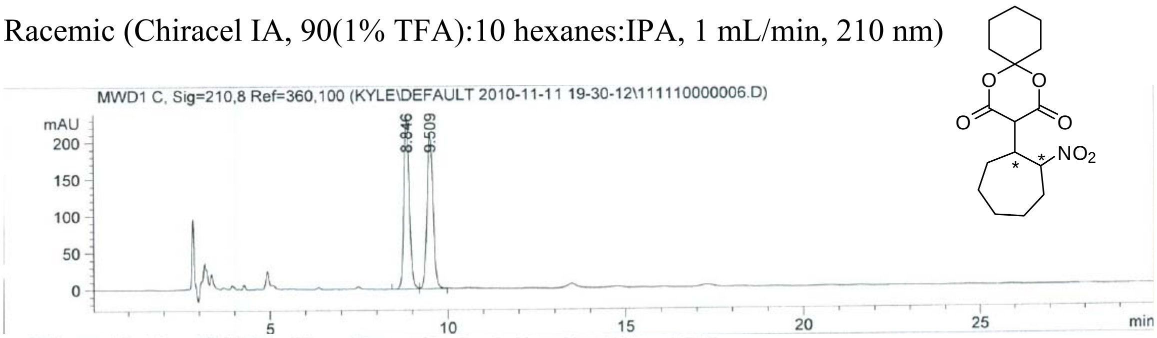


Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.820	BB	0.1649	62.75285	5.85931	1.4546
2	10.106	VB	0.1925	4251.27051	343.24030	98.5454

Product 14j.

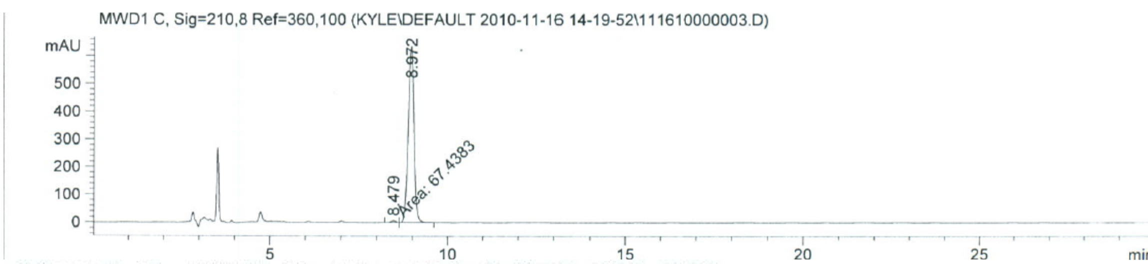
Racemic (Chiracel IA, 90(1% TFA):10 hexanes:IPA, 1 mL/min, 210 nm)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.846	BV	0.1652	2444.88623	227.88142	49.5233
2	9.509	VB	0.1819	2491.95557	210.75783	50.4767

Enantiomerically enriched (98% ee)



Signal 2: MWD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.479	MM	0.1606	67.43831	6.99987	0.9293
2	8.972	VB	0.1761	7189.48926	635.02319	99.0707