Diverted Total Synthesis of Promysalin Analogs Demonstrates that an Iron-Binding Motif is Responsible for its Narrow-Spectrum Antibacterial Activity

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Supporting Information

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1. Synthesis

1.1 Instrumentation and General Notes

NMR spectra were recorded using the following spectrometers: Bruker Advance 500 (500/125 MHz) or Bruker Advance 400 (400/100 MHz). Chemical shifts are quoted in ppm relative to tetramethylsilane and with the indicated solvent as an internal reference. The following abbreviations are used to describe signal multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), dd (doublet of doublets), dt (doublet of triplets), etc. Accurate mass spectra were recorded on an Agilent 6520 Accurate-Mass Q-TOF LC/MS, infrared spectra were obtained using a Thermo Nicolet Nexus 670 FTIR spectrophotometer and specific rotation measurements were made with a 1 dm path length using a Perkin Elmer 341 Polarimeter.

Non-aqueous reactions were performed under an atmosphere of argon, in flame- dried glassware, with HPLC-grade solvents dried by passage through activated alumina. 2,6-lutidine, triethylamine, and diisopropylethylamine were freshly distilled from CaH_2 prior to use. Brine refers to a saturated aqueous solution of sodium chloride, sat. $NaHCO_3$ refers to a saturated aqueous solution of sodium bicarbonate, sat. NH_4Cl refers to a saturated aqueous solution of ammonium chloride, etc. 3 Å molecular sieves were activated in a round-bottom flask under vacuum heating at 120°C in an oil bath overnight. “Column chromatography”, unless otherwise indicated, refers to purification in a gradient of increasing EtOAc concentration in hexanes on a Biotage® flash chromatography purification system. Metathesis catalysts were obtained as generous gifts from Materia, Inc. All other chemicals were used as received from Oakwood, TCI America, Sigma-Aldrich, Alfa Aesar, or AK Scientific.

1.2 Experimental Procedures and Characterization Data

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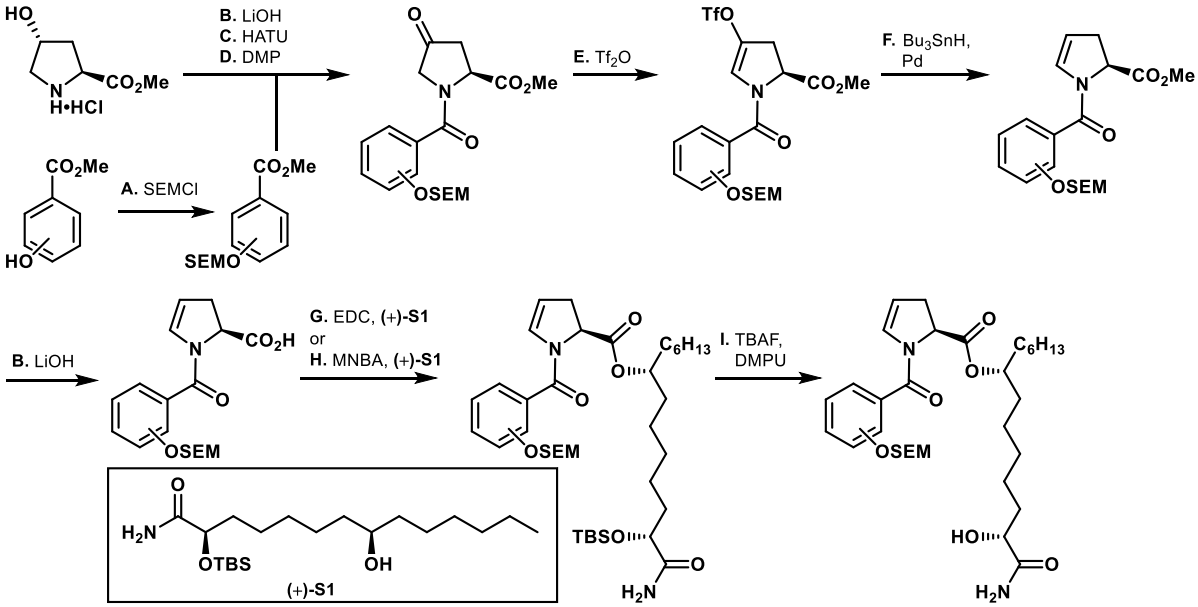


Scheme S1. General synthetic route for promysalin analogs.

General procedure A: SEM protection of methyl hydroxybenzoates.
To a methyl hydroxybenzoate (1 eq) dissolved in CH_2Cl_2 (2 M) was added SEMCl (2 eq) and then cooled to 0 °C. Diisopropylethylamine (4 eq) was added dropwise and the solution was allowed to warm to room temperature while stirring overnight. The following day, the mixture

was poured into water and extracted with Et_2O 3x. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography.

General procedure B: Hydrolysis of methyl esters.
Methyl ester (1.0 eq) was dissolved in 3:1:1 THF:MeOH:H_2O (1 M) and LiOH•H_2O (5 eq) was added as a solution in a minimal volume of water. The reaction was monitored by TLC and upon completion was carefully acidified by addition of 1M HCl or 5% AcOH (pH 5-6). The solution was extracted with CH_2Cl_2 3x, washed with brine, dried over $MgSO_4$, filtered, and concentrated.

General procedure C: HATU-mediated amide coupling of SEM-benzoic acids and hydroxyproline methyl ester.
Acid (1.0 eq) was dissolved in DMF (0.2 M) with HATU (1.2 eq) to which a solution of amine hydrochloride (1.2 eq) and diisopropylethylamine (1.5 eq) in an equal volume of DMF was added. Another portion of diisopropylethylamine (3 eq) was added and the reaction was allowed to stir overnight, then was poured into water and extracted with EtOAc 3x. The combined organic layers were washed with sat. NH_4Cl, sat. $NaHCO_3$, water 2x and brine 2x, then dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (0 → 50% EtOAc/CH_2Cl_2).

General procedure D: DMP oxidation.
An acylated trans-L-hydroxyproline derivative (1 eq) was dissolved in dry CH_2Cl_2 (0.05 M), and to the resulting solution was added $NaHCO_3$ (20 eq) and Dess-Martin periodinane (2 eq), and the reaction was allowed to stir overnight. The next day, the reaction was quenched with 2:1:1 H_2O:sat. $NaHCO_3$:sat. $Na_2S_2O_3$ and allowed to stir for an hour. The mixture was then extracted with CH_2Cl_2 3x and the combined organic layers were washed with sat. $Na_2S_2O_3$, sat. $NaHCO_3$, water, and brine, then dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography.

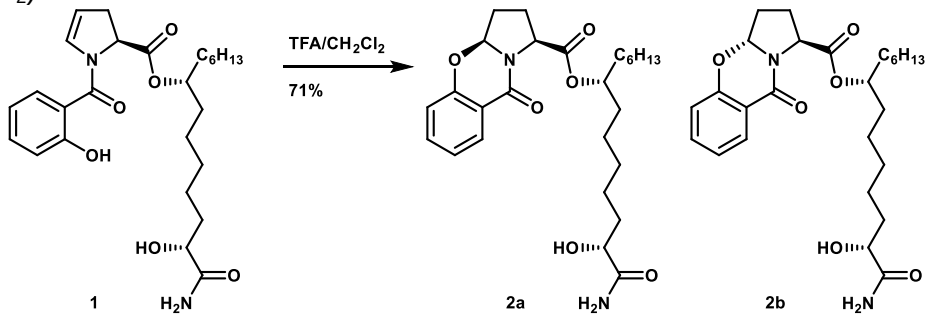
General procedure E: Synthesis of enol triflates from ketones.
Ketone (1 eq) was dissolved in CH_2Cl_2 (0.1 M) and cooled to -50 °C. 2,6-Lutidine (4 eq) was added, and trifluoromethanesulfonic anhydride (2 eq) was added dropwise. The reaction was allowed to warm to -35 °C. After 30 minutes the reaction was quenched with sat. $NaHCO_3$ and extracted with CH_2Cl_2 3x. The combined organic layers were washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, concentrated, and purified by column chromatography (0 → 5% EtOAc/hexanes held at 5% until 2,6-lutidine finished eluting, then 5 → 20% EtOAc/hexanes).

General procedure F: Reductive cleavage of enol triflates.
To a solution of enol triflate (1 eq) dissolved in THF (0.1 M) was added PPh_3 (0.3 eq), $Pd(OAc)_2$ (0.1 eq), and flame-dried LiCl (1.5 eq). Tributyltin hydride (1 eq) was then added dropwise. The reactions turned orange or brown upon completion, then were quenched with a solution of KF (1M) and extracted with Et_2O 3x. The combined organic layers were washed with 1M KF, water, and brine, dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography (0 → 30% EtOAc/hexanes, load in CH_2Cl_2).

General procedure G: EDC esterification.
An acid (1.4 eq) was dissolved in CH_2Cl_2 (0.2 M) was cooled to 0°C and EDC (2 eq) was added. A solution of alcohol **(+)-S1**[1] (1 eq) and DMAP (0.5 eq) were dissolved in an equal volume of dry CH_2Cl_2, added to the first solution, and allowed to stir overnight. The resulting mixture was poured into water and extracted with CH_2Cl_2 3x. The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated, and purified by column chromatography (0 → 30% Et_2O/CH_2Cl_2).

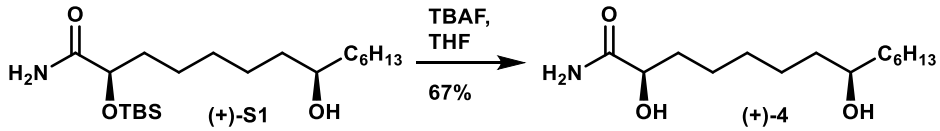
General procedure H: Shiina esterification.
To a solution of acid (1.4 eq) dissolved in CH_2Cl_2 (0.2 M) was added MNBA (2.6 eq) and Et_3N (3.3 eq), and the solution was stirred for 10 minutes. Then alcohol **(+)-S1**[1] (1 eq) and DMAP (0.1 eq) dissolved in an equal volume of CH_2Cl_2 as above was added, and the reaction was stirred overnight. The reaction was poured into sat. NH_4Cl, extracted with CH_2Cl_2 3x, washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (0 → 30% Et_2O/CH_2Cl_2).

General procedure I: Global deprotection.
The protected ester was dissolved in DMPU (.05 M, dried over 3Å molecular sieves). Tetrabutylammonium fluoride (20 eq, 1M solution in THF, dried over 3Å molecular sieves for 1 - 5 days) was added dropwise. The reaction was quenched with sat. NH_4Cl after 30 minutes. The mixture was extracted with Et_2O (3 – 5 times, TLC analysis of aqueous layer to confirm full extraction), and the combined organic layers were washed with aq. 1M NH_4Cl 5x followed by brine, dried over Na_2SO_4 , concentrated, and purified by column chromatography (0 → 5% $MeOH/CH_2Cl_2$).

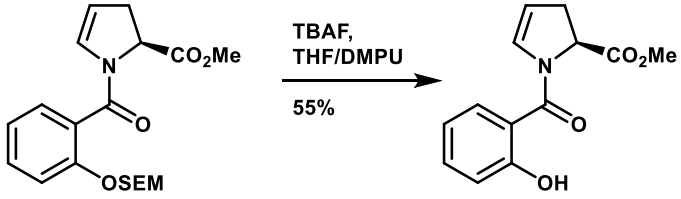


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (1S,3aS)-9-oxo-1,2,3,3a-tetrahydro-9H-benzo[e]pyrrolo[2,1-b][1,3]oxazine-1-carboxylate (2a), **(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (1S,3aR)-9-oxo-1,2,3,3a-tetrahydro-9H-benzo[e]pyrrolo[2,1-b][1,3]oxazine-1-carboxylate (2b).** To a solution of **1** (12 mg, 0.025 mmol) dissolved in CH_2Cl_2 (1 mL) was added trifluoroacetic acid (1 mL), and the reaction was stirred for 30 minutes at room temperature. The reaction was slowly quenched with sat. Na_2CO_3 solution until the pH was greater than 8, then extracted with CH_2Cl_2 3x, washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by preparative TLC (2% MeOH/EtOAc), yielding diastereomeric compounds **2a** and **2b** (configurations were not assigned). *Less polar isomer* (5.0 mg, 42% yield): **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 1H), 7.49 – 7.43 (m, 1H), 7.12 (td, J = 7.7, 0.9 Hz, 1H), 7.01 – 6.70 (m, 2H), 5.78 – 5.73 (m, 1H), 5.42 (s, 1H), 5.04 – 4.97 (m, 1H), 4.82 – 4.71 (m, 1H), 4.28 – 4.17 (m, 2H), 2.59 – 2.46 (m, 2H), 2.36 – 2.27 (m, 1H), 2.03 – 1.96 (m, 1H), 1.95 – 1.87 (m, 1H), 1.80 – 1.70 (m, 1H), 1.68 – 1.43 (m, 7H), 1.42 – 1.20 (m, 12H), 0.88 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl3) δ 177.48, 171.59, 171.49, 161.36, 157.42, 134.64, 128.18, 128.04, 123.12, 119.04, 116.94, 88.82, 75.73, 71.17, 58.31, 34.64, 33.98, 33.86, 31.87, 30.96, 29.84, 29.22, 27.73, 26.36, 25.56, 24.62, 24.28, 22.70, 14.21; **$[\alpha]^{25}_D$** +63.8 (c = 0.13 in $CHCl_3$) **IR** (film) 3326 (br, O-H), 2928, 2858, 2360, 1733 (C=O), 1660 (C=O), 1597, 1507, 1468, 1431, 1351, 1197, 1166, 1099, 1019, 959, 860, 822, 788, 758, 651, 608, 585; **HRMS** Accurate mass (ES^+): Found 475.2781 (-5.7 ppm), $C_{26}H_{39}N_2O_6$ ($M+H^+$) requires 475.2808; **R_f** (2% MeOH/EtOAc) = 0.37 *More polar isomer* (3.5 mg, 29% yield)*:* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 – 7.79 (m, 1H), 7.49 – 7.44 (m, 1H), 7.12 (td, J = 7.7, 1.0 Hz, 1H), 7.01 (dd, J = 8.2, 4.2 Hz, 1H), 6.94 – 6.73 (m, 1H), 5.58 (dt, J = 9.8, 4.9 Hz, 1H), 5.39 (s, 1H), 5.05 – 4.94 (m, 1H), 4.68 – 4.59 (m, 1H), 4.28 (d, J = 17.5 Hz, 1H), 4.17 – 4.09 (m, 1H), 2.53 – 2.47 (m, 1H), 2.44 – 2.25 (m, 2H), 2.19 (dd, J = 13.4, 7.8 Hz, 1H), 1.87 – 1.79 (m, 1H), 1.77 – 1.68 (m,

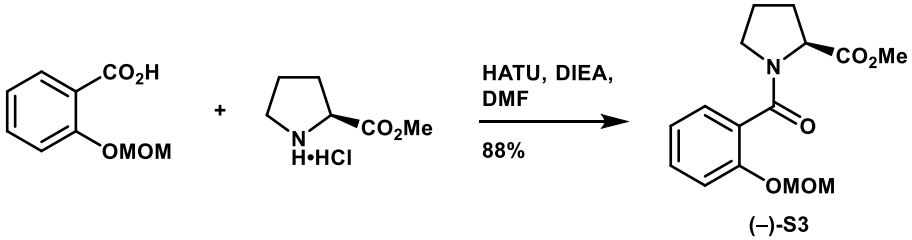
1H), 1.59 – 1.35 (m, 7H), 1.30 – 1.20 (m, 12H), 0.87 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl3) δ 177.36, 170.73, 161.68, 158.00, 134.67, 127.96, 123.01, 119.04, 117.12, 88.70, 75.62, 71.05, 57.27, 34.68, 33.93, 33.71, 31.85, 30.33, 29.84, 29.21, 27.61, 26.19, 25.57, 24.60, 24.05, 22.69, 14.22; **[α]$^{25}_{D}$** –28.1 (c = 0.11 in $CHCl_3$) **IR** (film) 3326 (br, O-H), 2927, 2856, 2360, 1734 (C=O), 1659 (C=O), 1613, 1578, 1469, 1432, 1351, 1225, 1196, 1079, 1024, 954, 907, 856, 785, 759, 732, 700, 652, 606, 584; **HRMS** Accurate mass (ES^+): Found 475.2783 (-5.3 ppm), $C_{26}H_{39}N_2O_6$ ($M+H^+$) requires 475.2808; **R_f** (2% MeOH/EtOAc) = 0.29.



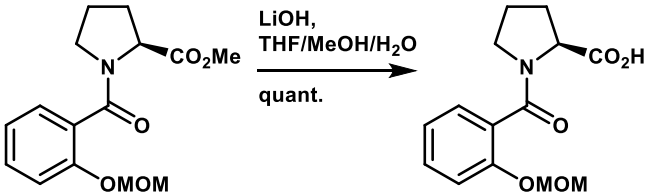
(2R,8R)-2,8-dihydroxytetradecanamide (+)-4. To a solution of silyl ether **(+)-S1**[1] (25 mg, 0.069 mmol) in THF (0.5 mL) was added TBAF (1M in THF, 0.34 mL, 0.34 mmol), and the reaction was stirred for 30 minutes, poured into sat. NH_4Cl, and extracted with Et_2O 3x. The combined organic layers were washed with 1M NH_4Cl 5x, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography (2:1 CH_2Cl_2:Et_2O) yielding the title compound as a white solid (12 mg, 67% yield). **^{1}H NMR** (500 MHz, MeOD) δ 3.98 (dd, J = 7.9, 3.9 Hz, 1H), 3.53 – 3.46 (m, 1H), 1.80 – 1.72 (m, 1H), 1.64 – 1.55 (m, 1H), 1.50 – 1.26 (m, 18H), 0.91 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, MeOD) δ 180.66, 72.68, 72.42, 38.47, 38.36, 35.64, 33.07, 30.63, 30.57, 26.80, 26.72, 26.13, 23.71, 14.43; **[α]$^{25}_{D}$** +14.8 (c = 0.59 in MeOH); **IR** (film) 3232 (br, O-H), 2953, 2922, 2852, 2545, 2410, 2361, 2342, 2159, 2027, 1978, 1734, 1622 (C=O), 1591, 1558, 1465, 1452, 1436, 1378, 1363, 1345, 1227, 1169, 1133, 1090, 1065, 1024, 957, 923, 906, 857, 803, 721, 668, 609; **HRMS** Accurate mass (ES^+): Found 282.2041 (-1.4 ppm), $C_{14}H_{29}NO_3Na$ ($M+Na^+$) requires 282.2045; **MP** 99.2 - 101.7 °C.



Methyl (2S)-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-5. Using modified procedure I (10 eq TBAF, 0.10 M DMPU), SEM-ether **S2**[1] (23 mg, 0.061 mmol) yielded the title compound as a clear oil (8.2 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.43 (dd, J = 7.8, 1.5 Hz, 1H), 7.41 – 7.35 (m, 1H), 7.01 (dd, J = 8.3, 0.8 Hz, 1H), 6.89 (td, J = 7.8, 1.1 Hz, 1H), 6.83 (s, 1H), 5.28 (dt, J = 4.4, 2.7 Hz, 1H), 5.04 (dd, J = 11.3, 5.2 Hz, 1H), 3.80 (s, 3H), 3.11 (ddt, J = 16.4, 11.3, 2.4 Hz, 1H), 2.73 (ddt, J = 17.1, 5.0, 2.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.45, 167.75, 159.36, 133.70, 130.99, 128.49, 118.98, 118.15, 110.85, 77.16, 59.29, 52.85, 33.49, 29.83. **[α]$^{25}_{D}$** –104.5 (c = 1.00 in $CHCl_3$); **IR** (film) 3119 (br, O-H), 2954, 2918, 2850, 2360, 2341, 2160, 2031, 1979, 1746 (C=O), 1616, 1590 (C=O), 1487, 1434, 1362, 1295, 1250, 1202, 1179, 1153, 1098, 1017, 984, 944, 855, 817, 757, 721, 667; **HRMS** Accurate mass (ES^+): Found 270.0751 (+3.3 ppm), $C_{13}H_{13}NO_4Na$ ($M+Na^+$) requires 270.0742.

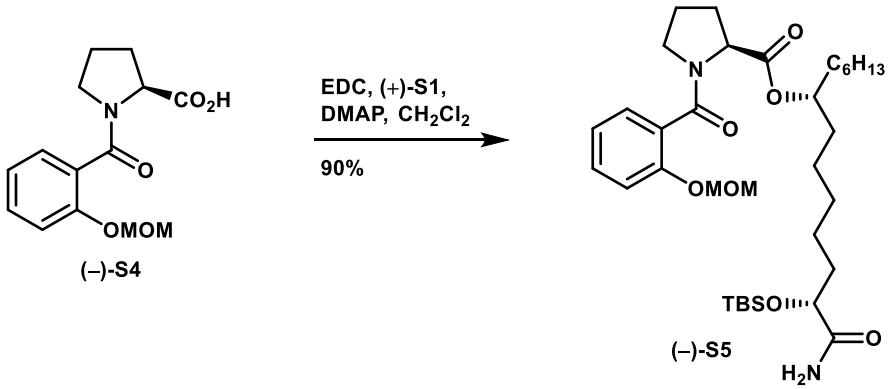


Methyl (2S)-1-[2-(methoxymethoxy)benzoyl]pyrrolidine-2-carboxylate (–)-S3. Using general procedure C, 2-methoxymethyloxybenzoic acid (248 mg, 1.364 mmol) and proline methyl ester hydrochloride (271 mg, 1.636 mmol) yielded the title compound as a clear oil (352 mg, 88% yield). **^{1}H NMR** (400 MHz, MeOD, mixture of rotamers/conformers) δ 7.43 – 7.34 (m, 1H), 7.28 (dd, J = 7.5, 1.7 Hz, 0.73H), 7.23 (d, J = 8.4 Hz, 0.71H), 7.20 (d, J = 8.3 Hz, 0.30H), 7.15 (d, J = 7.6 Hz, 0.26H), 7.09 (td, J = 7.5, 0.9 Hz, 0.74H), 7.04 (dd, J = 11.2, 3.8 Hz, 0.29H), 5.26 – 5.20 (m, 2H), 4.59 (dd, J = 8.7, 4.7 Hz, 0.72H), 4.30 (dd, J = 8.6, 2.8 Hz, 0.28H), 3.77 (s, 1.52H), 3.75 – 3.69 (m, 0.54H), 3.48 (s, 0.63H), 3.47 (s, 1.88H), 3.46 (s, 1.18H), 3.41 (dt, J = 17.4, 5.3 Hz, 1.40H), 3.35 (s, 1.28H), 2.44 – 2.25 (m, 1H), 2.09 – 1.86 (m, 3H); **^{13}C NMR** (100 MHz, MeOD) δ 173.83, 170.08, 169.82, 154.26, 131.97, 129.18, 128.65, 128.30, 127.93, 123.08, 122.81, 116.41, 116.07, 95.98, 61.55, 59.94, 56.67, 52.73, 49.54, 47.42, 31.87, 30.48, 25.55, 23.76; **[α]$^{25}_D$** –18.3 (c = 0.66 in $CHCl_3$) **IR** (film) 2054, 2359, 1741 (C=O), 1625 (C=O), 1601, 1489, 1455, 1418, 1362, 1281, 1234, 1198, 1152, 1107, 1078, 1041, 989, 922, 844, 747, 666; **HRMS** Accurate mass (ES^+): Found 316.1134 (-8.6 ppm), $C_{15}H_{19}NO_5Na$ ($M+Na^+$) requires 316.1161.



(–)-S3 (–)-S4

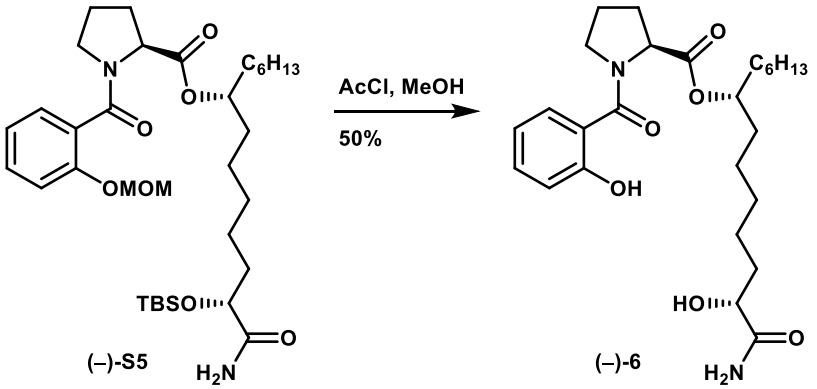
(2S)-1-[2-(methoxymethoxy)benzoyl]pyrrolidine-2-carboxylic acid (–)-S4. Using general procedure B, methyl ester (–)-**S3** (117 mg, 0.399 mmol) yielded the title compound as a clear oil (115 mg, quant. yield). **^{1}H NMR** (400 MHz, MeOD, mixture of rotamers/conformers) δ 7.91 (s, 0.55H), 7.43 – 7.34 (m, 1.06H), 7.31 (dd, J = 7.5, 1.6 Hz, 0.66H), 7.26 – 7.18 (m, 1.29H), 7.09 (td, J = 7.5, 0.9 Hz, 0.64H), 7.03 (t, J = 7.5 Hz, 0.31H), 5.26 – 5.19 (m, 2H), 4.57 (dd, J = 8.5, 4.5 Hz, 0.60H), 4.23 (d, J = 6.6 Hz, 0.31H), 3.80 – 3.67 (m, 0.66H), 3.47 (s, 3H), 3.45 – 3.35 (m, 1H), 2.44 – 2.22 (m, 1H), 2.14 – 1.84 (m, 3H); **^{13}C NMR** (100 MHz, MeOD) δ 175.57, 170.59, 170.23, 154.43, 132.01, 128.76, 128.55, 123.19, 122.97, 116.54, 116.05, 96.13, 96.01, 79.48, 56.66, 49.74, 47.41, 32.11, 30.81, 25.64, 23.78; **[α]$^{25}_D$** –71.4 (c = 1.28 in $CHCl_3$); **IR** (film) 2956, 2359, 1733 (C=O), 1592 (C=O), 1490, 1456, 1234, 1198, 1152, 1107, 1078, 1042, 979, 921, 845, 748, 665; **HRMS** Accurate mass (ES^+): Found 302.1012 (+2.6 ppm), $C_{14}H_{17}NO_5$ ($M+Na^+$) requires 302.1004.



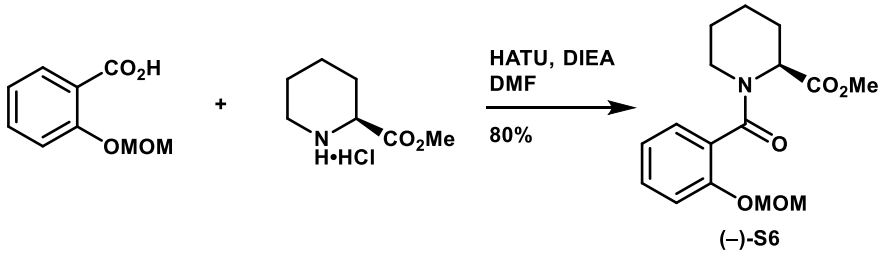
(–)-S4 (–)-S5

(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-[2-(methoxymethoxy)benzoyl]pyrrolidine-2-carboxylate (–)-S5. Using modified general procedure G (2 eq acid, 2 eq EDC, 1 eq alcohol, 0.1 eq DMAP), acid (–)-**S4** (43 mg, 0.154 mmol) yielded the title compound as a clear oil (43 mg, 90% yield). **^{1}H NMR** (500 MHz, $CDCl_3$,

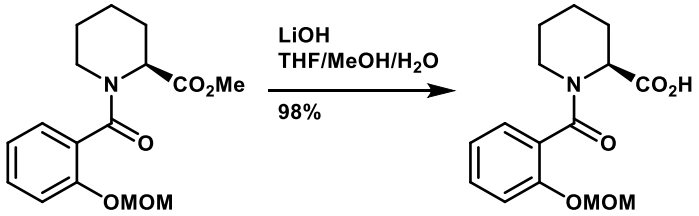
mixture of rotamers/conformers) δ 7.29 (tdd, J = 9.8, 8.2, 1.4 Hz, 1.36H), 7.25 – 7.20 (m, 0.86H), 7.14 (d, J = 8.2 Hz, 0.69H), 7.08 (d, J = 8.4 Hz, 0.41H), 7.03 (t, J = 7.4 Hz, 0.68H), 6.94 (t, J = 7.5 Hz, 0.39H), 6.53 (dd, J = 10.1, 4.3 Hz, 1H), 5.77 (s, 0.39H), 5.74 (s, 0.58H), 5.21 – 5.14 (m, 2H), 4.92 (dt, J = 12.2, 6.2 Hz, 0.62H), 4.69 – 4.60 (m, 1H), 4.27 – 4.21 (m, 0.34H), 4.12 (dt, J = 10.4, 5.0 Hz, 1H), 3.81 – 3.73 (m, 0.63H), 3.50 – 3.38 (m, 3.66H), 3.33 (dt, J = 10.6, 6.7 Hz, 1H), 2.34 – 2.17 (m, 1H), 2.06 – 1.79 (m, 4H), 1.79 – 1.47 (m, 5H), 1.42 – 1.16 (m, 18H), 0.94 – 0.88 (m, 9H), 0.85 (t, J = 6.8 Hz, 3H), 0.10 (d, J = 5.6 Hz, 1.78H), 0.06 (d, J = 6.1 Hz, 3.81H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.06, 172.01, 167.68, 153.19, 130.57, 128.16, 127.98, 122.31, 115.60, 95.22, 95.09, 75.56, 75.15, 73.54, 60.47, 58.90, 56.36, 48.31, 46.18, 35.23, 35.11, 34.10, 33.98, 33.77, 31.85, 31.78, 31.43, 29.92, 29.49, 29.29, 29.18, 25.85, 25.31, 25.11, 24.86, 24.10, 22.89, 22.69, 22.64, 18.12, 14.17, -4.73, -5.16; **$[\alpha]^{25}_D$** –21.4 (c = 0.95 in $CHCl_3$); **IR** (film) 3477 (N-H), 3307 (br O-H); 2927, 2856, 1738 (C=O), 1683 (C=O), 1626, 1601, 1558, 1489, 1456, 1417, 1338, 1281, 1235, 1194, 1153, 1079, 1042, 989, 922, 837, 755, 652; **HRMS** Accurate mass (ES^+): Found 635.4109 (+2.7 ppm), $C_{34}H_{59}N_2O_7Si$ ($M+H^+$) requires 635.4092.



(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-(2-hydroxybenzoyl)pyrrolidine-2-carboxylate (–)-6. To a solution of protected ester **(–)-S5** (43 mg, 0.068 mmol) in MeOH (1 mL) was added acetyl chloride (*ca.* 1 μL, 1 drop) at room temperature. After 1 hour, the reaction was quenched with sat. $NaHCO_3$ and extracted with CH_2Cl_2 3x. The combined organic layers were washed with water, dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography (0 → 10% MeOH/CH_2Cl_2), yielding the title compound as a clear oil (16 mg, 50% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.64 (s, 1H), 7.49 (d, J = 6.9 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 6.96 (t, J = 8.6 Hz, 1H), 6.86 (t, J = 7.3 Hz, 1H), 6.66 (s, 1H), 5.52 (s, 1H), 4.98 (s, 1H), 4.71 – 4.60 (m, 1H), 4.08 (s, J = 19.6 Hz, 1H), 3.93 – 3.83 (m, 1H), 3.83 – 3.73 (m, 1H), 3.66 (s, 1H), 2.40 – 2.28 (m, 1H), 2.15 – 2.05 (m, 1H), 2.05 – 1.90 (m, 2H), 1.87 – 1.76 (m, 3H), 1.68 – 1.48 (m, 5H), 1.48 – 1.33 (m, 6H), 1.33 – 1.16 (m, 11H), 0.86 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.22, 172.37, 170.30, 159.04, 133.20, 128.10, 118.83, 117.85, 117.73, 75.42, 71.48, 60.56, 50.78, 34.58, 34.39, 34.29, 31.84, 29.21, 28.52, 25.82, 25.49, 24.87, 24.65, 22.67, 14.19; **$[\alpha]^{25}_D$** –28.0 (c = 1.51 in $CHCl_3$); **IR** (film) 3189 (br O-H), 2928, 2857, 2360, 1736 (C=O), 1667 (C=O), 1583 (C=O), 1434, 1374, 1186, 1089, 1025, 877, 754, 651, 609, 563; **HRMS** Accurate mass (ES^+): Found 477.2935 (-6.3 ppm), $C_{26}H_{41}N_2O_6$ ($M+H^+$) requires 477.2965.

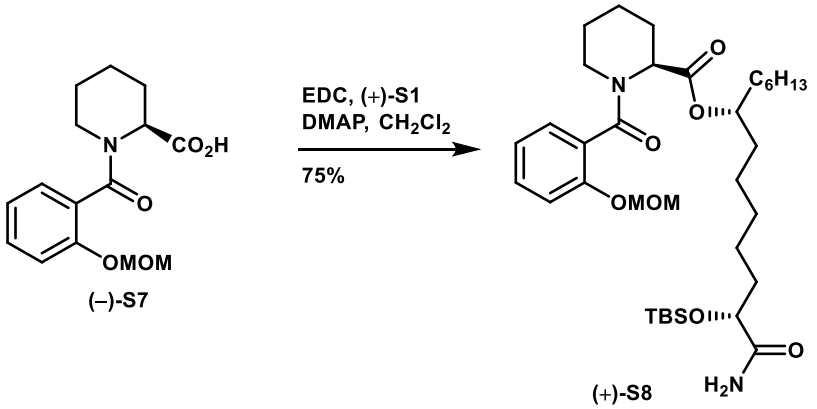


Methyl (2S)-1-[2-(methoxymethoxy)benzoyl]piperidine-2-carboxylate (–)-S6. Using general procedure C, 2-methoxymethyloxybenzoic acid (200 mg, 1.101 mmol) and methyl 2-piperidinecarboxylate hydrochloride (237 mg, 1.321 mmol) yielded the title compound as a clear oil (248 mg, 80% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.42 – 7.26 (m, 2.67H), 7.25 – 7.17 (m, 1.16H), 7.14 – 7.03 (m, 1.23H), 5.67 (s, 0.73H), 5.27 (dt, J = 11.7, 6.9 Hz, 2H), 5.15 (dd, J = 39.3, 6.6 Hz, 0.32H), 4.81 (d, J = 13.7 Hz, 0.31H), 4.43 (d, J = 5.1 Hz, 0.08H), 4.36 (d, J = 4.3 Hz, 0.22H), 3.85 (s, 2.22H), 3.76 (s, J = 4.4 Hz, 1.08H), 3.59 – 3.46 (m, 4.22H), 3.41 – 3.33 (m, 0.55H), 3.18 (td, J = 13.0, 2.4 Hz, 0.57H), 2.92 – 2.84 (m, 0.23H), 2.41 (t, J = 13.5 Hz, 0.75H), 2.28 (d, J = 12.8 Hz, 0.32H), 1.87 – 1.73 (m, 2.52H), 1.68 – 1.51 (m, 2.08H), 1.51 – 1.35 (m, 1.49H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.53, 171.34, 171.26, 168.93, 168.85, 168.72, 153.19, 152.82, 152.62, 130.27, 130.24, 127.98, 127.81, 127.42, 126.70, 126.65, 126.53, 122.28, 122.11, 122.05, 115.15, 114.77, 114.72, 94.85, 94.78, 94.70, 77.36, 60.27, 57.86, 56.17, 56.11, 52.28, 52.24, 52.07, 51.82, 51.60, 45.34, 44.53, 39.40, 39.05, 27.38, 26.87, 26.59, 25.49, 25.33, 24.64, 21.16, 21.10, 20.95, 14.12; **$[\alpha]^{25}_D$** –28.6 (c = 2.15 in $CHCl_3$); **IR** (film) 1076, 2945, 1737 (C=O), 1633 (C=O), 1599, 1488, 1452, 1422, 1339, 1286, 1232, 1199, 1143, 985, 921, 756, 645; **HRMS** Accurate mass (ES^+): Found 308.1502 (+1.3 ppm), $C_{16}H_{21}NO_5Na$ ($M+Na^+$) requires 308.1498.

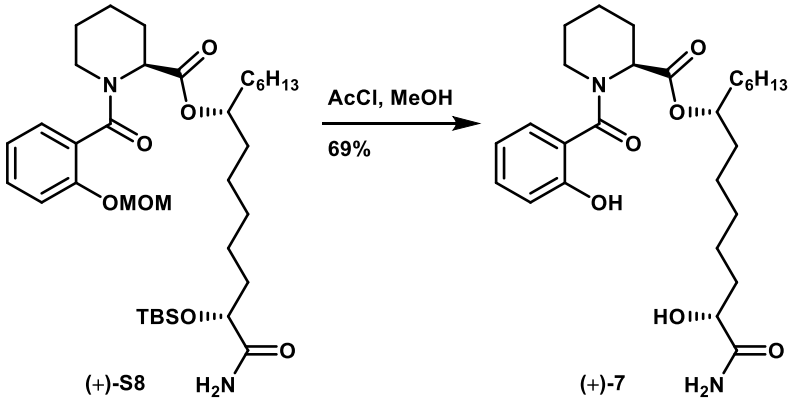


(–)-S6 (–)-S7

(2S)-1-[2-(methoxymethoxy)benzoyl]piperidine-2-carboxylic acid (–)-S7. Using general procedure B, methyl ester **(–)-S6** (215 mg, 0.700 mmol) yielded the title compound as a clear oil (200 mg, 98% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 9.53 (br s, 1H), 7.36 – 7.23 (m, 2.16H), 7.16 (dt, J = 18.2, 8.0 Hz, 1.56H), 7.04 (t, J = 7.3 Hz, 0.91H), 6.99 (t, J = 7.6 Hz, 0.37H), 5.64 – 5.56 (m, 0.75H), 5.18 (ddd, J = 14.8, 13.8, 7.3 Hz, 2H), 5.06 (dd, J = 40.1, 6.7 Hz, 0.40H), 4.72 (d, J = 10.5 Hz, 0.31H), 4.35 (d, J = 4.9 Hz, 0.09H), 4.27 (d, J = 4.0 Hz, 0.20H), 3.76 (t, J = 6.0 Hz, 0.60H), 3.49 – 3.40 (m, 3.74H), 3.32 – 3.22 (m, 0.61H), 3.12 (t, J = 12.0 Hz, 0.57H), 2.86 – 2.77 (m, 0.28H), 2.37 (d, J = 13.2 Hz, 0.77H), 2.19 (d, J = 13.3 Hz, 0.26H), 2.07 (d, J = 11.4 Hz, 0.12H), 1.89 – 1.82 (m, 0.62H), 1.82 – 1.63 (m, 2.67H), 1.56 (dd, J = 32.8, 13.9 Hz, 1.35H), 1.51 – 1.32 (m, 2.57H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.19, 174.99, 174.14, 169.79, 169.58, 169.27, 153.31, 152.97, 152.77, 130.68, 130.58, 128.22, 128.01, 127.59, 126.13, 122.40, 122.18, 115.15, 114.79, 94.92, 94.78, 67.95, 57.89, 56.29, 56.26, 52.02, 51.92, 45.59, 44.84, 39.64, 27.51, 26.73, 26.55, 25.61, 25.53, 25.36, 24.75, 21.17; **$[\alpha]^{25}_D$** –59.8 (c = 0.85 in $CHCl_3$); **IR** (film) 2941, 1731 (C=O), 1587 (C=O), 1442, 1286, 1233, 1199, 1151, 1077, 1041, 983, 921, 864, 755, 732, 700, 641; **HRMS** Accurate mass (ES^+): Found 316.1173 (+3.8 ppm), $C_{15}H_{19}NO_5Na$ ($M+Na^+$) requires 316.1161.

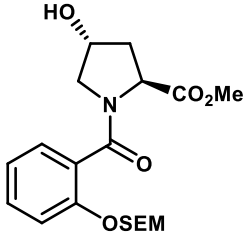


(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-[2-(methoxymethoxy)benzoyl]piperidine-2-carboxylate (+)-S8. Using modified general procedure G (1.5 eq acid, 1.7 eq EDC, 0.5 eq DMAP, 1.0 eq alcohol); acid **(–)-S7** (85 mg, 0.291 mmol) yielded the title compound as a clear oil (94 mg, 75% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.34 – 7.27 (m, 1.42H), 7.25 – 7.10 (m, 2.47H), 7.04 (t, J = 7.5 Hz, 0.82H), 6.96 (t, J = 6.9 Hz, 0.45H), 6.52 (s, 1.13H), 5.56 (s, 0.88H), 5.49 – 5.33 (m, 1.49H), 5.25 – 5.16 (m, 2.13H), 4.94 (s, 0.77H), 4.75 (d, J = 13.9 Hz, 0.71H), 4.16 – 4.07 (m, 1.93H), 3.48 (d, J = 3.8 Hz, 3H), 3.45 – 3.37 (m, 1.45H), 3.12 (t, J = 12.7 Hz, 0.59H), 2.90 – 2.80 (m, 0.48H), 2.39 – 2.29 (m, 0.81H), 2.23 – 2.15 (m, 0.51H), 1.82 – 1.68 (m, 4.11H), 1.60 – 1.45 (m, 9.21H), 1.45 – 1.11 (m, 17.89H), 0.93 (d, J = 6.7 Hz, 9.57H), 0.87 (t, J = 7.0 Hz, 4.95H), 0.11 – 0.06 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.93, 170.95, 170.77, 168.84, 153.37, 152.84, 130.34, 128.13, 127.04, 125.65, 122.31, 114.92, 94.96, 75.69, 73.53, 58.07, 56.43, 56.32, 52.06, 45.55, 35.20, 34.05, 31.83, 30.43, 29.55, 29.31, 25.86, 25.43, 25.32, 24.19, 22.70, 21.39, 18.14, 14.20, -4.71, -5.12; **$[\alpha]^{25}_D$** +13.9 (c = 2.42 in $CHCl_3$); **IR** (film) 3480, 2928, 2857, 1732 (C=O), 1687 (C=O), 1634 (C=O), 1600, 1489, 1455, 1424, 1286, 1251, 1233, 1198, 1153, 1096, 1078, 1042, 991, 922, 836, 778, 755, 730, 668, 645; **HRMS** Accurate mass (ES^+): Found 649.4264 (+2.3 ppm), $C_{35}H_{61}N_2O_7Si$ ($M+H^+$) requires 649.4249.



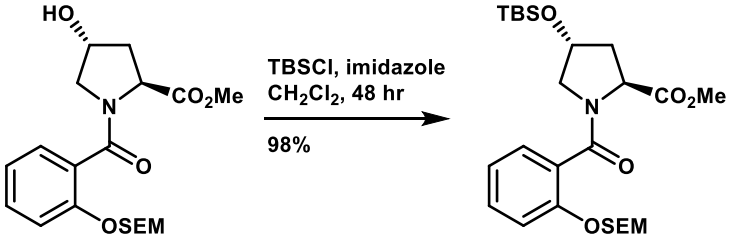
(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-(2-hydroxybenzoyl)piperidine-2-carboxylate (+)-7. To a solution of protected ester **(+)-S8** (25 mg, 0.038 mmol) dissolved in MeOH (1 mL) was added acetyl chloride (5 μL, 0.006 mmol) at 0°C. The reaction was stirred at this temperature for 45 minutes then warmed to room temperature and stirred for 2 hours. The reaction was quenched with sat. $NaHCO_3$, and extracted with CH_2Cl_2 3x. The combined organic layers were washed with brine, dried over MgSO4, filtered, concentrated, and purified by preparative TLC (100% EtOAc), yielding the title compound as a clear oil (12 mg, 69% yield). *Note: High temperature ^{1}H NMR was possible, but extended heating times caused decomposition*. **^{1}H NMR** (500 MHz, $CDCl_3$, 328K) δ 8.67 (br s, 0.39H), 8.54 (br s, 0.47H), 7.37 –

7.27 (m, 1H), 6.99 (d, J = 8.1 Hz, 1H), 6.87 (s, 1H), 5.21 (d, J = 34.3 Hz, 1H), 5.05 – 4.96 (m, 1H), 4.16 – 3.98 (m, 2H), 3.36 – 3.22 (m, 1H), 2.39 – 2.26 (m, 1H), 1.80 (d, J = 11.5 Hz, 3H), 1.60 (s, 10H), 1.30 (s, 15H), 0.90 (t, J = 6.6 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$, room temp) δ 171.55, 171.12, 157.86, 132.52, 132.41, 130.70, 128.11, 128.03, 119.41, 119.26, 118.08, 118.01, 60.41, 34.83, 34.56, 34.46, 34.23, 34.10, 31.88, 29.86, 29.29, 29.24, 29.03, 28.80, 26.95, 26.79, 25.58, 25.54, 25.36, 25.21, 25.14, 24.80, 22.66, 21.38, 21.24, 14.33, 14.03; **$[\alpha]^{25}_D$** +21.5 (c = 1.3 in $CHCl_3$); **IR** (film) 3291 (br O-H), 2928, 2857, 1731 (C=O), 1692 (C=O), 1624 (C=O), 1454, 1373, 1207, 1142, 1007, 935, 911, 847, 827, 753, 645, 602; **HRMS** Accurate mass (ES^+): Found 491.3097 (-4.9 ppm) $C_{27}H_{43}N_2O_6$ ($M+H^+$) requires 491.3121.



(–)-S9

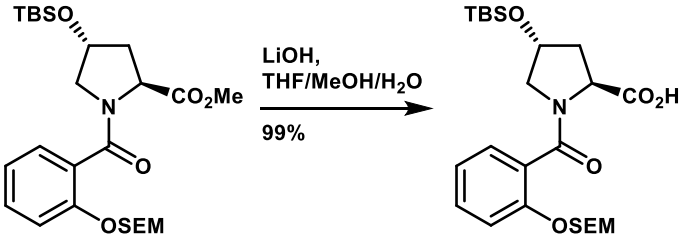
Methyl (2S,4R)-4-hydroxy-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)pyrrolidine-2-carboxylate (–)-S9. Prepared as previously described[1] with an additional purification by preparative TLC (2:1:1 EtOAc:CH_2Cl_2:Et_2O) yielded a pure sample of the title compound. **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.34 (ddt, J = 7.6, 3.2, 1.8 Hz, 1.50H), 7.32 – 7.29 (m, 0.25H), 7.20 (dd, J = 7.5, 1.7 Hz, 0.25H), 7.16 (d, J = 7.9 Hz, 1H), 7.05 (td, J = 7.5, 0.9 Hz, 0.75H), 6.99 (td, J = 7.5, 0.9 Hz, 0.25H), 5.24 (dt, J = 13.7, 5.1 Hz, 2H), 4.80 (t, J = 8.2 Hz, 0.75H), 4.56 (br s, 0.25H), 4.48 – 4.41 (m, 1H), 3.99 (d, J = 12.9 Hz, 0.25H), 3.82 – 3.72 (m, 4.50H), 3.62 (d, J = 8.4 Hz, 0.75H), 3.42 (s, 0.75H), 3.39 – 3.31 (m, 1H), 2.44 – 2.28 (m, 1H), 2.17 – 2.09 (m, 2H), 1.62 (br s, 1H), 0.95 (ddd, J = 8.3, 7.5, 4.2 Hz, 2H), 0.01 – -0.01 (m, 9H); **^{13}C NMR** (100 MHz, CDCl3) δ 172.74, 168.37, 153.34, 130.99, 130.93, 128.36, 127.03, 126.18, 122.23, 121.82, 115.72, 115.10, 93.87, 69.94, 68.81, 66.74, 60.52, 58.73, 57.31, 56.22, 54.71, 52.38, 52.14, 39.49, 38.17, 18.07, 14.25, -1.33; **$[\alpha]^{25}_D$** –62.5 (c = 2.14 in $CHCl_3$); **IR** (film) 3390 (br, O-H), 2951, 2944, 2360, 2160, 2028, 1979, 1747 (C=O), 1616 (C=O), 1601, 1491, 1455, 1432, 1359, 1248, 1229, 1248, 1201, 1175, 1148, 1084, 1042, 984, 916, 857, 834, 755; **HRMS** Accurate mass (ES^+): Found 418.1656 (-1.4 ppm), $C_{29}H_{29}NO_6SiNa$ ($M+Na^+$) requires 418.1662.



(–)-S9 **(–)-S10**

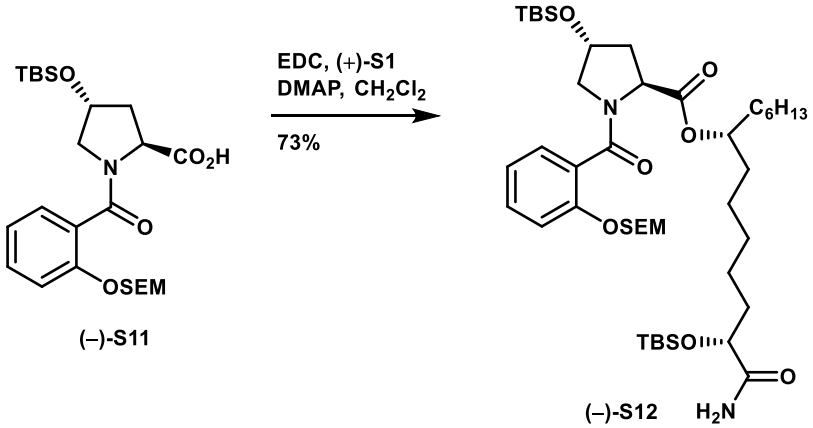
Methyl (2S,4R)-4-[(tert-butyldimethylsilyl)oxy]-1-(2-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)pyrrolidine-2-carboxylate (–)-S10. To a solution of compound **17** (64 mg, 0.162 mmol) in CH_2Cl_2 (1 mL) was added imidazole (22 mg, 0.324 mmol) followed by TBSCl (49 mg, 0.324 mmol), and the reaction was stirred for 24 hours, after which time TLC analysis indicated the reaction was incomplete. Another portion of imidazole (22 mg, 0.324 mmol) and TBSCl (49 mg, 0.324) were added, and the reaction was stirred at room temperature for an additional 24 hours, after which time TLC analysis indicated the consumption of starting material. The reaction was quenched with water and extracted with CH_2Cl_2 3x. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered,

concentrated and purified by column chromatography, yielding the title compound as a clear oil (80 mg, 98% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.36 – 7.27 (m, 1.36H), 7.20 – 7.17 (m, 1.31H), 7.03 (td, J = 7.5, 1.0 Hz, 0.68H), 6.98 (td, J = 7.5, 0.9 Hz, 0.33H), 5.25 – 5.19 (m, 2H), 4.75 (t, J = 7.8 Hz, 0.67H), 4.52 – 4.44 (m, 0.59H), 4.43 – 4.38 (m, 0.69H), 3.82 – 3.72 (m, 4.53H), 3.59 (dd, J = 10.9, 4.5 Hz, 0.68H), 3.37 (s, 0.89H), 3.18 (dd, J = 11.0, 1.7 Hz, 0.68H), 2.28 – 2.19 (m, 1H), 2.14 – 2.05 (m, 1H), 0.95 (td, J = 8.3, 2.5 Hz, 2H), 0.90 (s, J = 2.9 Hz, 2.84H), 0.82 (s, J = 2.9 Hz, 6H), 0.10 (s, J = 3.1 Hz, 0.85H), 0.09 (s, J = 3.0 Hz, 0.86H), 0.02 (s, J = 2.8 Hz, 1.79H), 0.00 – -0.01 (m, 8.25H), -0.04 (s, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.74, 168.16, 153.74, 130.77, 130.73, 128.24, 127.33, 122.04, 121.71, 115.89, 93.86, 93.47, 70.45, 69.40, 66.47, 57.47, 56.28, 54.78, 52.26, 51.98, 40.39, 38.58, 25.78, 25.65, 18.12, 18.02, 17.87, -1.32, -1.36, -4.81, -4.92; **$[\alpha]^{25}_D$** –65.9 (c = 0.72 in $CHCl_3$); **IR** (film) 2952, 2924, 2893, 2856, 1746 (C=O), 1644 (C=O), 1601 (C=O), 1489, 1455, 1412, 1359, 1317, 1249, 1227, 1197, 1175, 1144, 1086, 1023, 986, 920, 833, 775, 753, 693, 653; **HRMS** Accurate mass (ES^+): Found 532.2485 (-7.9 ppm), $C_{25}H_{43}NO_6Si_2Na$ ($M+Na^+$) requires 532.2527.



(–)-S10 (–)-S11

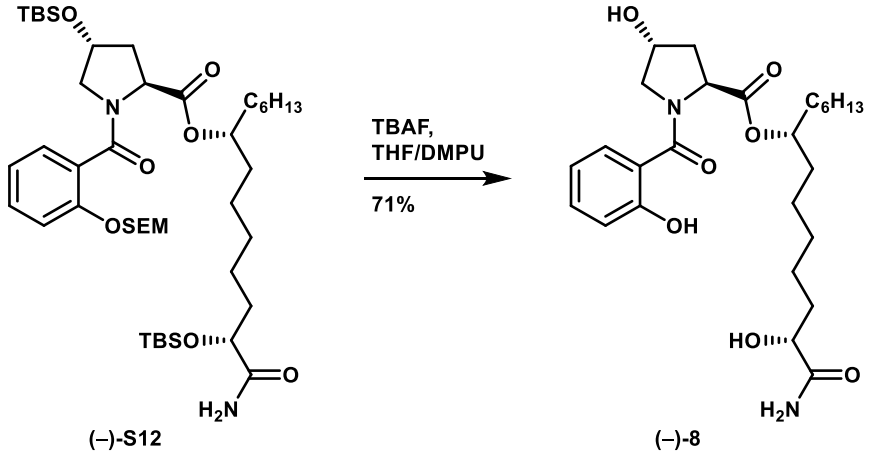
(2S,4R)-4-[(tert-butyldimethylsilyl)oxy]-1-(2-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)pyrrolidine-2-carboxylic acid (–)-S11. Using general procedure B, methyl ester (–)-**S10** (166 mg, 0.325 mmol) yielded the title compound as a clear oil (160 mg, 99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (br s, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.30 (d, J = 7.5 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.16 (d, J = 8.5 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 6.99 – 6.93 (m, 1H), 5.26 – 5.18 (m, 2H), 4.87 (t, J = 7.7 Hz, 1H), 4.36 (s, 1H), 3.49 (dd, J = 11.2, 4.1 Hz, 1H), 3.20 (t, J = 17.9 Hz, 1H), 2.53 – 2.44 (m, 1H), 2.25 – 2.12 (m, 1H), 0.98 – 0.87 (m, 3H), 0.82 (s, 9H), 0.03 (s, 3H), -0.01 (s, 9H), -0.06 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.72, 171.48, 153.73, 131.57, 128.02, 125.78, 122.12, 115.57, 93.64, 69.84, 66.80, 58.79, 57.12, 37.22, 25.72, 18.10, 17.95, -1.27, -4.73, -4.89; **$[\alpha]^{25}_D$** –86.6 (c = 1.75 in $CHCl_3$); **IR** (film) 2952, 2856, 2359, 2341, 1743 (C=O), 1595 (C=O), 1489, 1462, 1434, 1361, 1249, 1024, 988, 921, 754, 693, 667, 611; **HRMS** Accurate mass (ES^+): Found 518.2330 (-7.7 ppm), $C_{24}H_{41}NO_6Si_2Na$ ($M+Na^+$) requires 518.2370.



(–)-S11 (–)-S12

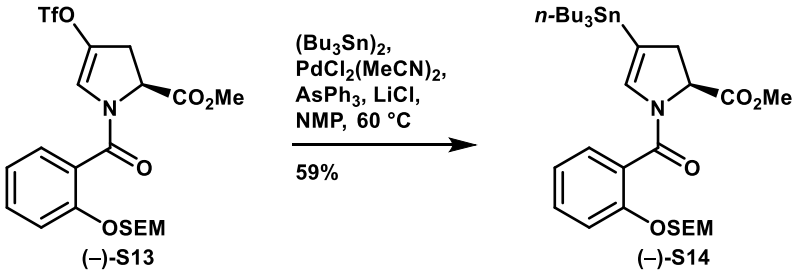
(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S,4R)-4-[(tert-butyldimethylsilyl)oxy]-1-(2-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)pyrrolidine-2-

carboxylate (–)-S12. Using modified general procedure G (1.5 eq acid, 2 eq EDC, 0.1 eq DMAP), acid **(–)-S11** (125 mg, 0.252 mmol) yielded the title compound as a clear oil (103 mg, 73% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.34 – 7.27 (m, 1.35H), 7.25 – 7.17 (m, 1.35H), 7.14 (d, J = 8.1 Hz, 0.33H), 7.02 (td, J = 7.5, 0.9 Hz, 0.65H), 6.93 (td, J = 7.5, 0.9 Hz, 0.32H), 6.60 – 6.48 (m, 1H), 5.73 (s, 0.40H), 5.68 (s, 0.60H), 5.24 – 5.19 (m, 2H), 4.97 – 4.90 (m, 0.63H), 4.72 (t, J = 7.6 Hz, 0.63H), 4.60 – 4.54 (m, 0.32H), 4.50 – 4.45 (m, 0.32H), 4.45 – 4.37 (m, 1H), 4.13 (dt, J = 13.1, 5.2 Hz, 1H), 3.87 – 3.69 (m, 2.72H), 3.57 (dd, J = 10.7, 4.3 Hz, 0.63H), 3.16 (dd, J = 10.9, 2.7 Hz, 0.63H), 2.24 (ddd, J = 12.8, 8.2, 4.7 Hz, 1H), 2.14 – 2.03 (m, 1H), 1.81 – 1.70 (m, 1H), 1.70 – 1.46 (m, 4H), 1.46 – 1.09 (m, 16H), 0.95 – 0.93 (m, 4H), 0.91 – 0.89 (m, 8.54H), 0.83 – 0.81 (m, 5.72H), 0.12 – 0.06 (m, 8.34H), 0.01 – -0.02 (m, 10.78H), -0.05 (s, 1.77H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.18, 171.97, 168.48, 168.01, 153.83, 130.67, 128.29, 127.45, 126.67, 122.04, 121.88, 115.88, 93.92, 93.43, 75.48, 75.11, 73.49, 70.42, 69.34, 66.48, 58.74, 57.83, 56.18, 54.35, 40.40, 38.72, 35.25, 35.12, 34.09, 33.74, 33.69, 31.82, 31.75, 29.55, 29.49, 29.24, 29.13, 25.82, 25.71, 25.31, 25.24, 25.10, 24.79, 24.08, 22.66, 22.61, 18.20, 18.08, 17.93, 14.15, -1.27, -4.76, -4.80, -4.90, -5.19; **$[\alpha]^{25}_{D}$** –20.8 (c = 0.86 in $CHCl_3$); **IR** (film) 3480 (N-H), 2927, 2856, 1739 (C=O), 1691 (C=O), 1644 (C=O), 1455, 1412, 1250, 1189, 1088, 991, 937, 897, 834, 754, 574; **HRMS** Accurate mass (ES^+): Found 873.5226 (-5.8 ppm), $C_{44}H_{82}N_2O_8Si_3Na$ ($M+Na^+$) requires 873.5277.

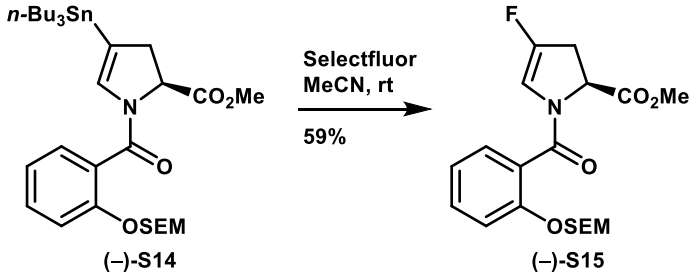


(–)-S12 (–)-8

(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S,4R)-4-hydroxy-1-(2-hydroxybenzoyl)pyrrolidine-2-carboxylate (–)-8. Using modified general procedure I (25 eq. TBAF, 0.040M DMPU), silyl ether **(–)-S12** (25 mg, 0.029 mmol) with column chromatography eluting in 0 → 5% MeOH/CH_2Cl_2 yielded the title compound as a clear oil (10 mg, 71% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.50 (br s, 1H), 7.41 (d, J = 7.2 Hz, 1H), 7.32 (t, J = 7.7 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 6.86 (t, J = 7.5 Hz, 1H), 6.74 (br s, 1H), 5.69 (br s, 1H), 4.97 (br s, 1H), 4.81 (t, J = 8.2 Hz, 1H), 4.53 (s, 1H), 4.05 (dd, J = 7.7, 3.4 Hz, 1H), 3.95 (d, J = 8.7 Hz, 1H), 3.82 – 3.61 (m, 2H), 3.15 (br s, 1H), 2.43 – 2.30 (m, 1H), 2.09 (ddd, J = 13.0, 8.7, 4.4 Hz, 1H), 1.85 – 1.72 (m, 1H), 1.65 – 1.32 (m, 9H), 1.30 – 1.12 (m, 10H), 0.86 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.57, 172.31, 170.88, 158.86, 133.28, 128.30, 118.98, 117.88, 75.73, 71.58, 70.44, 59.12, 58.36, 37.40, 34.48, 34.17, 34.04, 31.84, 29.23, 28.42, 25.46, 24.70, 24.50, 22.69, 14.21; **$[\alpha]^{25}_{D}$** –43.4 (c = 0.71 in $CHCl_3$); **IR** (film) 3303 (br O-H), 2928, 2857, 1732 (C=O), 1666 (C=O), 1586 (C=O), 1434, 1376, 1298, 1193, 1082, 1001, 958, 911, 878, 754, 728, 651, 609; **HRMS** Accurate mass (ES^+): Found 515.2691 (-8.2 ppm), $C_{26}H_{40}N_2O_7Na$ ($M+Na^+$) requires 515.2733; **R_f** (9:1 CH_2Cl_2:MeOH) = 0.34.

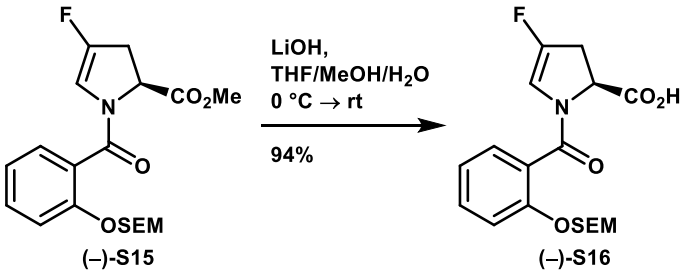


Methyl (S)-4-(tributylstannyl)-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S14. To a solution of triflate **(–)-S13**[1] (559 mg, 1.064 mmol) in NMP (6 mL) was added $PdCl_2(MeCN)_2$ (14 mg, 0.053 mmol), $AsPh_3$ (65 mg, 0.213 mmol), LiCl (135 mg, 3.191 mmol), and bis(tributyltin) (0.56 mL, 1.117 mmol). The solution was heated to 60 °C for 1 hour, after which time the reaction turned from orange to brown/black. The reaction was cooled to room temperature, quenched with 1M aq. KF, and extracted 2x with Et_2O. The combined organic layers were washed with 1M aq. KF, and brine 2x, then dried over $MgSO_4$, filtered, concentrated and purified by column chromatography, yielding the title compound as a yellow oil (416 mg, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.22 (dd, J = 8.8, 0.9 Hz, 1H), 7.09 – 7.03 (m, 1H), 5.97 (t, J = 2.1 Hz, 1H), 5.26 – 5.19 (m, 2H), 4.96 (dd, J = 11.4, 5.0 Hz, 1H), 3.84 – 3.72 (m, 5H), 3.15 (ddd, J = 16.8, 11.3, 2.3 Hz, 1H), 2.76 (ddd, J = 16.8, 5.0, 1.9 Hz, 1H), 1.52 – 1.38 (m, 6H), 1.33 – 1.20 (m, 8H), 0.98 – 0.82 (m, 18H), 0.00 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.83, 164.19, 154.01, 135.61, 131.09, 128.90, 126.25, 121.93, 118.43, 93.64, 66.39, 58.29, 52.28, 40.55, 29.08, 29.00, 27.24, 27.16, 17.92, 13.67, 13.63, 9.52 (J = 309 Hz, ^{13}C-^{117}Sn; J = 355 Hz, ^{13}C-^{119}Sn), -1.36; **$[\alpha]^{25}_D$** –41.5 (c = 1.63 in $CHCl_3$); **IR** (film) 2953, 2923, 2869, 2852, 1754 (C=O), 1651 (C=O), 1584, 1488, 1454, 1399, 1283, 1247, 1228, 1198, 1176, 1152, 1087, 1019, 989, 917, 856, 834, 753, 731, 692, 658, 599, 561; **HRMS** Accurate mass (ES^+): Found 668.2798 (+0.7 ppm), $C_{31}H_{54}NO_5SiSn$ ($M+H^+$) requires 668.2793.



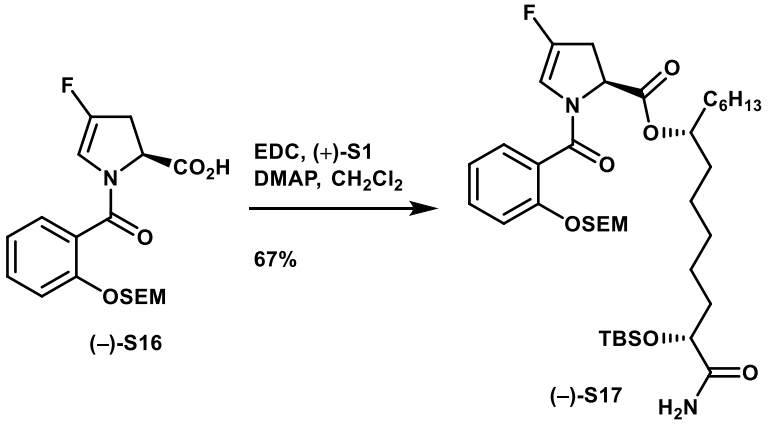
Methyl (S)-4-fluoro-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S15. To a solution of stannane **(–)-S14** (400 mg, 0.6001 mmol) in acetonitrile (5 mL) was added Selectfluor® (234 mg, 0.6601 mmol). After 5 minutes, solids crashed out and the solution was filtered into water. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 2x. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography, yielding the title compound as a clear oil (140 mg, 59%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.34 (m, 2H), 7.21 (t, J = 7.2 Hz, 1H), 7.05 (td, J = 7.5, 0.9 Hz, 1H), 6.06 (dd, J = 4.1, 2.2 Hz, 1H), 5.24 (q, J = 7.1 Hz, 2H), 5.05 (dd, J = 11.7, 4.7 Hz, 1H), 3.83 (s, 3H), 3.79 – 3.73 (m, 2H), 3.32 (dddd, J = 16.4, 11.8, 4.3, 2.3 Hz, 1H), 2.89 – 2.83 (m, 1H), 0.99 – 0.91 (m, 2H), -0.01 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.10, 165.21, 153.60, 151.05, 148.92, 131.45, 128.93, 124.94, 121.95, 115.07, 111.54 (d, J = 30 Hz ^{13}C-^{19}F), 93.20, 66.66, 56.30, 56.26, 52.70, 32.07, 31.91, 18.04, -1.47; **$[\alpha]^{25}_D$** –56.1 (c = 1.08 in $CHCl_3$; **IR** (film) 2953, 2924, 1749 (C=O), 1644 (C=O), 1600, 1488, 1456, 1417, 1356, 1229, 1306, 1247, 1231, 1201, 1179, 1144, 1086, 1028,

982, 934, 914, 857, 834, 754, 693, 658, 577; **HRMS** Accurate mass (ES^+): Found 418.1427 (-8.4 ppm), $C_{19}H_{26}FNO_5SiNa$ ($M+Na^+$) requires 418.1462.



(–)-S15 (–)-S16

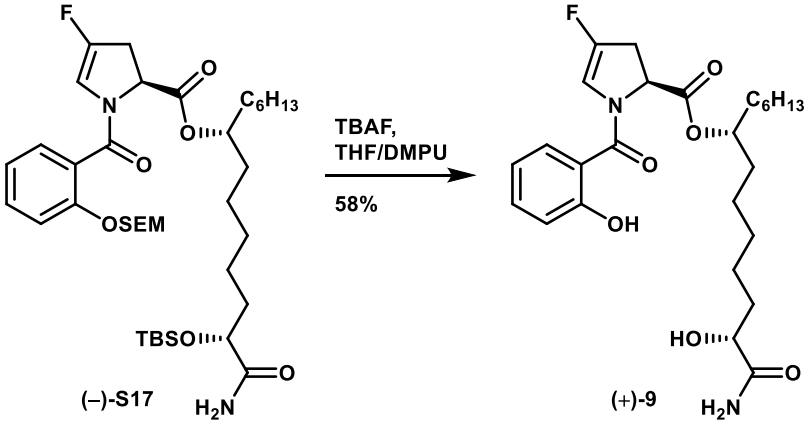
(S)-4-fluoro-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S16. To a solution of methyl ester **(–)-S15** (128 mg, 0.3236 mmol) in 3:1:1 THF:MeOH:H_2O (3 mL) was added LiOH•H_2O (14 mg) dissolved in water (0.5 mL) at 0 °C. The reaction was stirred for 15 minutes then warmed to room temperature and stirred for 2 hours. The reaction was acidified (pH ~ 5-6) with 5% aq. AcOH, and extracted with CH_2Cl_2 3x. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, concentrated and purified by column chromatography (0 → 5% MeOH/0.1% AcOH/CH_2Cl_2), yielding the title compound as a clear oil (116 mg, 94% yield). *Note:* While the acids in this study prepared by ester hydrolysis generally did not require chromatography, this one in particular required purification for acceptable yields in the next step. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 1H), 7.36 (dd, J = 7.5, 1.5 Hz, 1H), 7.24 (d, J = 8.5 Hz, 1H), 7.09 (td, J = 7.5, 0.7 Hz, 1H), 5.96 (d, J = 1.9 Hz, 1H), 5.28 – 5.20 (m, 3H), 3.76 – 3.70 (m, 2H), 3.62 – 3.54 (m, 1H), 3.27 – 3.14 (m, 1H), 0.97 – 0.91 (m, 2H), 0.00 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.19, 167.47, 153.70, 153.26, 150.58, 132.17, 129.05, 123.85, 122.08, 115.05, 110.80 (d, J = 31 Hz, ^{13}C-^{19}F), 93.26, 66.93, 57.71, 18.13, -1.39; **$[\alpha]^{25}_D$** –62.7 (c = 0.72 in $CHCl_3$); **IR** (film) 2954, 2923, 2853, 1742 (C=O), 1600 (C=O), 1458, 1425, 1354, 1315, 1248, 1231, 1144, 1086, 983, 916, 857, 834, 753, 693, 658 **HRMS** Accurate mass (ES^+): Found 404.1291 (-3.5 ppm), $C_{18}H_{24}FNO_5SiNa$ ($M+Na^+$) requires 404.1305; **R_f** (10% MeOH/0.1% AcOH/CH_2Cl_2) = 0.29.



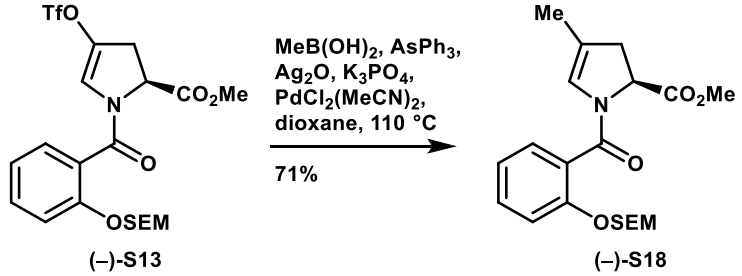
(–)-S16 (–)-S17

(7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl (S)-4-fluoro-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (S9). Using general procedure G, acid **(–)-S16** (39 mg, 0.102 mmol) yielded the title compound as a clear oil (36 mg, 67% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 2H), 7.20 (d, J = 8.2 Hz, 1H), 7.04 (t, J = 7.1 Hz, 1H), 6.57 – 6.48 (m, 1H), 6.05 (d, J = 1.8 Hz, 1H), 5.57 – 5.43 (m, 1H), 5.24 (q, J = 7.1 Hz, 2H), 5.08 – 4.91 (m, 2H), 4.13 (t, J = 5.1 Hz, 1H), 3.80 – 3.71 (m, 2H), 3.38 – 3.27 (m, 1H), 2.85 – 2.75 (m, 1H), 1.82 – 1.70 (m, 1H), 1.69 – 1.50 (m, 6H), 1.41 – 1.19 (m, 20H), 0.97 – 0.89 (m, 12H), 0.89 – 0.85 (m, 3H), 0.13 – 0.06 (m, 6H), -0.01 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.10, 169.48, 165.13, 153.75, 151.09, 148.97, 131.45, 129.02, 125.18, 122.02, 115.20, 111.72 (d, J = 31 Hz, ^{13}C-^{19}F), 93.33, 76.00, 73.52, 66.76, 56.71, 35.16,

35.06, 34.00, 33.95, 32.39, 32.23, 31.81, 29.80, 29.44, 29.27, 25.84, 25.31, 25.19, 25.00, 24.14, 24.07, 22.68, 18.17, 18.11, 14.16, -1.30, -1.35, -4.74, -5.16; **[α]$^{25}_{D}$** –12.5 (c = 1.18 in $CHCl_3$) **IR** (film) 3480, 2951, 2927, 2856, 2242, 1742 (C=O), 1688 (C=O), 1645 (C=O), 1601, 1488, 1456, 1419, 1353, 1249, 1189, 1142, 1088, 988, 916, 835, 778, 754, 730, 659, 577; **HRMS** Accurate mass (ES^+): Found 759.4182 (-4.0 ppm), $C_{38}H_{65}FN_2O_7Si_2Na$ ($M+Na^+$) requires 759.4212; **R_f** (2:1 CH_2Cl_2:Et_2O) = 0.60.

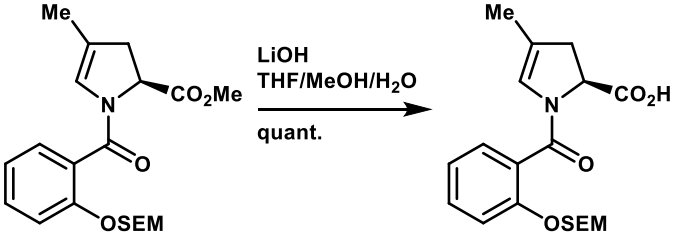


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-4-fluoro-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (+)-9. Using general procedure I, silyl ether **(–)-S17** (21 mg, 0.029 mmol) yielded the title compound as a clear oil (8.1 mg, 58% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.67 (br d, 1H), 7.41 – 7.33 (m, 2H), 7.02 – 6.96 (m, 1H), 6.91 (t, J = 7.6 Hz, 1H), 6.70 (d, J = 38.0 Hz, 1H), 6.55 (d, J = 28.6 Hz, 1H), 5.49 (d, J = 44.7 Hz, 1H), 5.07 – 4.92 (m, 2H), 4.09 (dd, J = 7.9, 3.5 Hz, 1H), 3.35 (t, J = 14.0 Hz, 1H), 3.03 (br s, 1H), 2.88 – 2.80 (m, 1H), 1.84 – 1.72 (m, 1H), 1.72 – 1.50 (m, 6H), 1.50 – 1.18 (m, 14H), 0.87 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.96, 176.73, 169.87, 169.56, 167.43, 159.01, 158.10, 152.93, 152.82, 150.67, 133.80, 133.63, 127.97, 119.49, 119.28, 118.22, 118.13, 117.08, 116.43, 112.12, 111.87, 76.58, 71.68, 71.48, 58.34, 57.83, 34.53, 34.45, 34.37, 34.14, 33.86, 31.82, 29.21, 28.81, 28.43, 25.52, 25.27, 24.95, 24.84, 24.61, 22.68, 14.19; **[α]$^{25}_{D}$** +12.0 (c = 0.45 in $CHCl_3$); **IR** (film) 3308 (br, O-H), 2929, 2858, 1734 (C=O), 1669 (C=O), 1653, 1623, 1594, 1521, 1457, 1436, 1354, 1337, 1300, 1192, 1142, 1097, 1037, 1004, 919, 859, 804, 755, 655; **HRMS** Accurate mass (ES^+): Found 493.2738 (+4.9 ppm), $C_{26}H_{38}FN_2O_6$ ($M+H^+$) requires 493.2714.



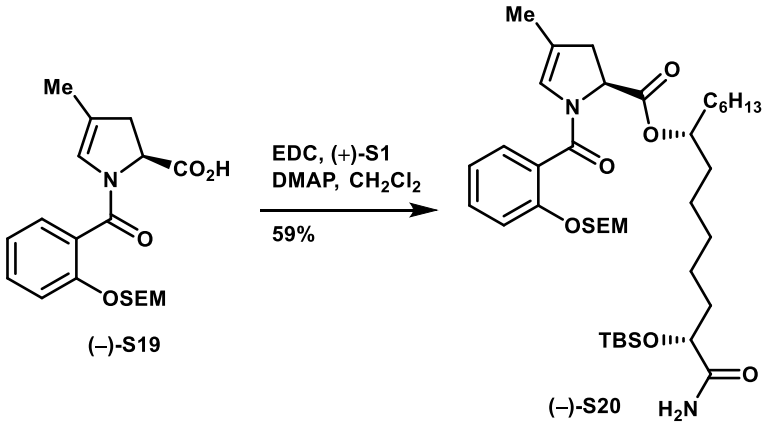
Methyl (S)-4-methyl-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S18. Triflate **(–)-S13**[1] (75 mg, 0.143 mmol) was dissolved in dioxane (1.5 mL), and triphenylarsine (18 mg, 0.057 mmol), methylboronic acid (30 mg, 0.501 mmol), silver oxide (133 mg, 0.572 mmol) and K_3PO_4 (182 mg, 0.858 mmol) were added, and the reaction flask was covered in foil. The flask was vacuumed and back-filled with argon 3x, then $PdCl_2(MeCN)_2$ (4 mg, 0.014 mmol) was added, and the reaction was heated to 110 °C. Upon heating, the reaction turned from green to dark red, and TLC analysis indicated the starting material was consumed. The reaction was filtered through Celite, concentrated, and purified by column chromatography, yielding the title compound as an orange oil (39 mg, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.39 – 7.28 (m, 2H), 7.20 (d, J = 8.1

Hz, 0.91H), 7.15 (d, J = 7.9 Hz, 0.15H), 7.04 (td, J = 7.5, 1.0 Hz, 0.92H), 6.99 (td, J = 7.5, 1.0 Hz, 0.14H), 5.88 (dd, J = 3.5, 1.7 Hz, 1H), 5.26 – 5.19 (m, 2H), 5.01 (dd, J = 11.6, 4.9 Hz, 1H), 3.80 (s, 3H), 3.78 – 3.71 (m, 2H), 3.06 – 2.96 (m, 1H), 2.61 – 2.53 (m, 1H), 1.64 (d, J = 1.4 Hz, 3H), 0.98 – 0.89 (m, 2H), 0.01 – -0.03 (m, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.70, 164.44, 153.83, 131.11, 128.90, 126.23, 125.30, 122.04, 119.42, 115.48, 93.48, 66.58, 58.32, 52.59, 38.23, 18.16, 13.54, -1.27; **$[\alpha]^{25}_D$** –18.5 (c = 0.43 in $CHCl_3$); **IR** (film) 2951, 2919, 2850, 2102, 1747 (C=O), 1670 (C=O), 1600, 1486, 1454, 1409, 1345, 1247, 1230, 1144, 1088, 1052, 976, 916, 857, 834, 755, 694, 664, 605; **HRMS** Accurate mass (ES^+): Found 414.1684 (-7.0 ppm), $C_{20}H_{29}NO_5SiNa$ ($M+Na^+$) requires 414.1713.



(–)-S18 (–)-S19

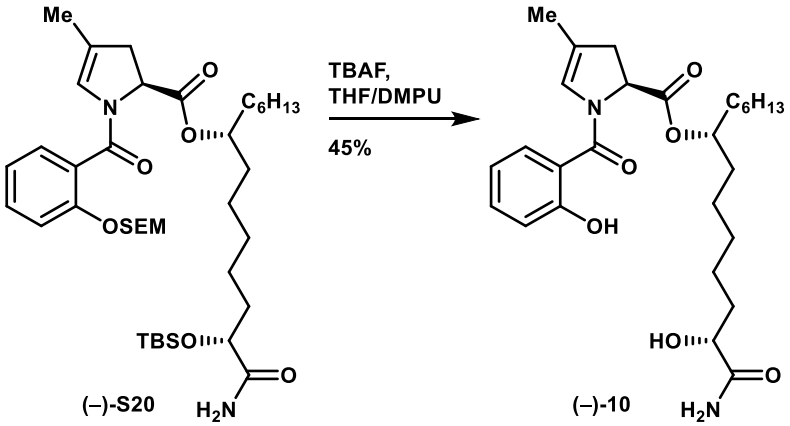
(S)-4-methyl-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S19. Using general procedure B, methyl ester **(–)-S18** (19 mg, 0.049 mmol) yielded the title compound as a clear oil (20 mg, quant. yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 6.5 Hz, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 5.78 (s, 1H), 5.22 (s, 2H), 5.20 – 5.11 (m, 1H), 3.75 – 3.69 (m, 2H), 3.22 (d, J = 16.4 Hz, 1H), 2.97 – 2.85 (m, 1H), 1.70 (s, 3H), 0.99 – 0.87 (m, 2H), -0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.97, 167.90, 153.86, 132.11, 124.43, 124.15, 123.55, 122.09, 115.25, 93.38, 66.87, 60.45, 36.19, 18.17, 13.61, -1.27; **$[\alpha]^{25}_D$** –80.6 (c = 0.70 in $CHCl_3$); **IR** (film) 2954, 2921, 2857, 1743, 1598, 1489, 1457, 1427, 1378, 1303, 1232, 1143, 1086, 1043, 983, 916, 856, 834, 754, 694, 658; **HRMS** Accurate mass (ES^+): Found 400.1573 (+4.2 ppm), $C_{19}H_{27}NO_5SiNa$ ($M+Na^+$) requires 400.1556.



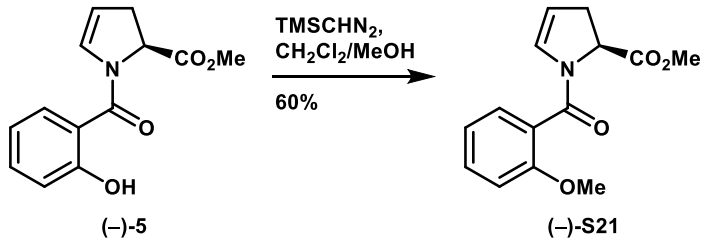
(–)-S19 (–)-S20

(7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl (S)-4-methyl-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S20). Using modified general procedure H (1.2 eq acid, 1.2 eq MNBA, 1.0 eq alcohol, 0.1 eq DMAP), acid **(–)-S19** (25 mg, 0.066 mmol) after purification by column chromatography eluting in 0 → 30% Et_2O/CH_2Cl_2, yielded the title compound as a yellow oil (24 mg, 59% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.19 (t, J = 9.5 Hz, 1H), 7.03 (td, J = 7.5, 0.9 Hz, 1H), 6.53 (t, J = 8.5 Hz, 1H), 5.87 (d, J = 1.6 Hz, 1H), 5.58 – 5.46 (m, 1H), 5.22 (dd, J = 17.5, 7.1 Hz, 2H), 5.03 – 4.91 (m, 2H), 4.16 – 4.09 (m, 1H), 3.79 – 3.70 (m, 2H), 3.08 – 2.96 (m, 1H), 2.51 (dd, J = 16.7, 4.8 Hz, 1H), 1.79 – 1.66 (m, 3H), 1.64 (s, 3H), 1.60 – 1.51 (m, 4H), 1.41 – 1.19 (m, 18H), 0.96 – 0.89 (m, 12H), 0.88 – 0.84 (m, 3H), 0.09 – 0.05 (m, 6H), 0.01 – -0.03 (m,

9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.96, 170.93, 164.26, 153.87, 131.01, 128.89, 126.36, 125.41, 121.99, 119.19, 115.47, 93.48, 75.41, 73.57, 66.56, 58.63, 38.46, 35.12, 34.08, 31.87, 29.52, 29.32, 25.88, 25.34, 25.05, 24.12, 22.73, 18.17, 14.22, 13.58, -1.26, -4.69, -5.13; **$[\alpha]^{25}_D$** – 18.3 (c = 0.69 in $CHCl_3$); **IR** (film) 2927, 2856, 2359, 2341, 1733 (C=O), 1683 (C=O), 1645 (C=O), 1601, 1506, 1488, 1456, 1419, 1377, 1248, 1188, 1141, 1086, 989, 834, 778, 754, 692, 667, 561; **HRMS** Accurate mass (ES^+): Found 733.4666 (+3.1 ppm), $C_{39}H_{69}N_2O_7Si_2$ ($M+H^+$) requires 733.4643.

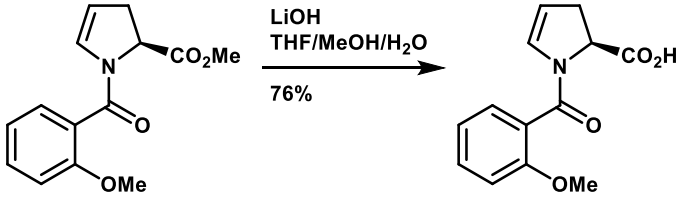


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(2-hydroxybenzoyl)-4-methyl-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-10. Using general procedure I, silyl ether **(–)-S20** (10.7 mg, 0.0146 mmol) yielded the title compound as a clear oil (3.2 mg, 45% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.44 – 7.32 (m, 2H), 7.01 – 6.96 (m, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.61 (s, 0.68H), 6.55 (s, 0.46H), 6.44 (s, 1H), 5.32 (s, 1H), 5.05 – 4.94 (m, 2H), 4.13 – 4.05 (m, 1H), 3.47 (s, 1H), 3.09 – 3.00 (m, 1H), 2.59 – 2.51 (m, 1H), 1.84 – 1.77 (m, 1H), 1.75 (s, J = 8.0 Hz, 3H), 1.68 – 1.49 (m, 12H), 1.48 – 1.36 (m, 4H), 1.36 – 1.22 (m, 12H), 0.87 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.97, 171.46, 166.42, 157.88, 133.25, 128.21, 125.19, 122.31, 119.35, 117.98, 117.92, 75.91, 71.33, 59.76, 56.13, 37.72, 34.59, 34.27, 34.20, 31.84, 29.85, 29.22, 28.26, 25.53, 24.81, 24.54, 22.69, 14.20, 13.70; **$[\alpha]^{25}_D$** –21.8 (c = 0.27 in $CHCl_3$); **IR** (film) 3306 (br O-H), 2921, 2855, 2493, 2361, 2159, 2031, 1978, 1734 (C=O), 1669 (C=O), 1591 (C=O), 1457, 1378, 1298, 1202, 1157, 1096, 1020, 867, 806, 756, 667; **HRMS** Accurate mass (ES^+): Found 489.2937 (-5.7 ppm), $C_{27}H_{41}N_2O_6$ ($M+H^+$) requires 489.2965.



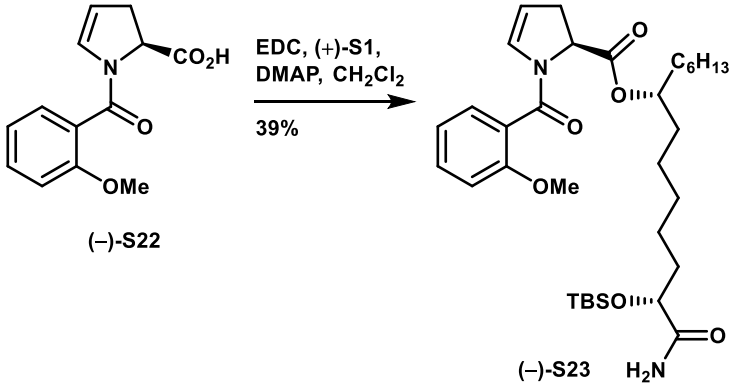
Methyl (2S)-1-(2-methoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S21. To a solution of phenol **(–)-5** (45 mg, 0.182 mmol) in 3:1 CH_2Cl_2:MeOH (2 mL) was added $TMSCHN_2$ (0.46 mL, 2M in hexanes, 0.920 mmol), and the reaction went from a clear to yellow color, with effervescence. After 2 hours, TLC analysis indicated remaining starting material, and more MeOH (0.5 mL) was added, after another 30 minutes the starting material was consumed. The reaction was concentrated and purified by column chromatography, yielding the title compound as a yellow oil (28 mg, 60% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 2H), 7.00 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 6.17 – 6.13 (m, 1H), 5.07 – 5.00 (m, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 3.16 – 3.07 (m, 1H), 2.75 – 2.67 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.61, 165.22, 155.94, 131.42, 130.91, 129.11, 124.94, 120.92, 111.44, 108.60, 57.88, 55.90, 52.59,

34.17; **[α]$^{25}_{D}$** –85.9 (c = 1.27 in $CHCl_3$); **IR** (film) 2951, 2923, 2851, 2160, 2032, 1979, 1746 (C=O), 1643 (C=O), 1618, 1600, 1491, 1461, 1436, 1406, 1363, 1280, 1249, 1201, 1179, 1103, 1046, 1016, 843, 754, 654; **HRMS** Accurate mass (ES^+): Found 284.0875 (-8.4 ppm), $C_{14}H_{15}NO_4Na$ ($M+Na^+$) requires 284.0899.



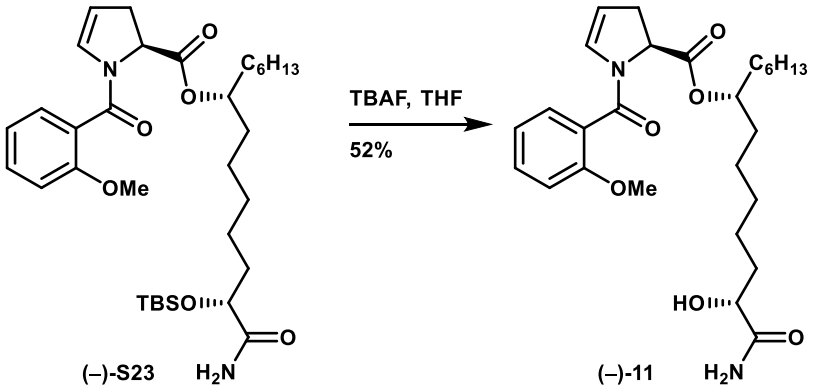
(–)-S21 (–)-S22

(2S)-1-(2-methoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S22. Using general procedure B, methyl ester **(–)-S21** (27 mg, 0.103 mmol) yielded the title compound as a yellow oil (19 mg, 76% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.46 – 7.41 (m, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.03 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.06 (dt, J = 4.3, 2.2 Hz, 1H), 5.23 (dd, J = 4.3, 2.4 Hz, 1H), 5.13 (dd, J = 11.0, 4.2 Hz, 1H), 3.84 (s, 3H), 3.19 (d, J = 17.1 Hz, 1H), 3.09 – 3.00 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 172.39, 167.64, 155.96, 132.16, 129.76, 129.23, 123.82, 121.07, 111.58, 111.51, 59.25, 55.89, 32.89, 29.82; **[α]$^{25}_{D}$** –82.1 (c = 1.80 in $CHCl_3$); **IR** (film) 3444 (br, CO_2-H), 2930, 1738 (C=O), 1598 (C=O), 1492, 1464, 1437, 1412, 1356, 1282, 1249, 1185, 1163, 1104, 1047, 1018, 941, 848, 754, 723, 652; **HRMS** Accurate mass (ES^+): Found 270.0721 (-7.8 ppm), $C_{13}H_{13}NO_4Na$ ($M+Na^+$) requires 270.0742.

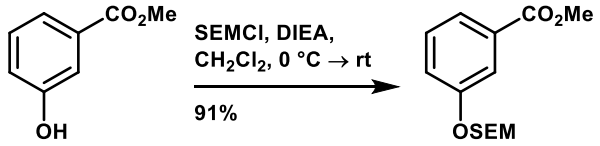


(–)-S22 (–)-S23

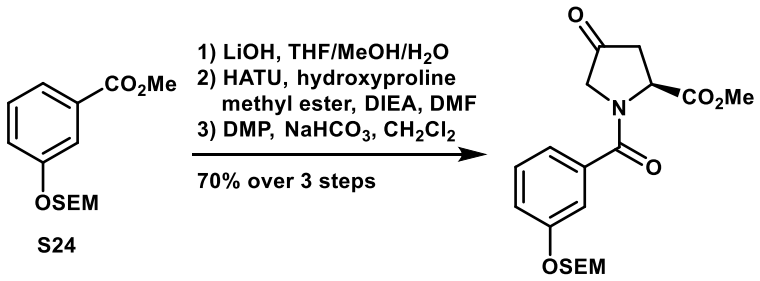
(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-(2-methoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S23. Using modified general procedure G (1.2 eq acid, 1.5 eq EDC, 1.0 eq alcohol, 0.1 eq DMAP), acid **(–)-S22** (18 mg, 0.073 mmol), after purification by column chromatography eluting with 0 → 2% MeOH/CH_2Cl_2, yielded the title compound as a clear oil (14 mg, 39% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 2H), 7.17 (d, J = 7.2 Hz, 1H), 6.99 (s, 1H), 6.93 (d, J = 8.2 Hz, 1H), 6.54 (s, 1H), 6.14 (dd, J = 4.1, 1.9 Hz, 1H), 5.71 – 5.59 (m, 1H), 5.05 – 4.95 (m, 2H), 4.17 – 4.06 (m, 2H), 3.83 (s, 3H), 3.12 (ddd, J = 14.1, 11.6, 2.0 Hz, 1H), 2.91 – 2.85 (m, 1H), 2.66 (ddd, J = 17.1, 4.3, 2.1 Hz, 1H), 1.76 – 1.54 (m, 6H), 1.39 – 1.19 (m, 20H), 0.91 (s, 9H), 0.89 – 0.83 (m, 3H), 0.08 (d, J = 6.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.11, 170.92, 165.02, 155.98, 131.32, 131.01, 129.17, 129.11, 127.43, 125.11, 120.89, 111.42, 108.46, 75.50, 73.55, 69.78, 58.23, 55.86, 53.93, 41.65, 35.11, 34.39, 34.08, 34.02, 31.85, 29.83, 29.51, 29.33, 25.87, 25.31, 25.05, 24.11, 22.72, 18.15, 14.21, -4.70, -5.13; **[α]$^{25}_{D}$** –27.2 (c = 1.11 in $CHCl_3$); **IR** (film) 3481, 2927, 2856, 1745, 1683, 1646, 1619, 1601, 1491, 1463, 1437, 1406, 1360, 1280, 1251, 1194, 1101, 1048, 1019, 939, 837, 778, 754, 701, 655; **HRMS** Accurate mass (ES^+): Found 603.3802 (-4.5 ppm), $C_{33}H_{55}N_2O_6Si$ ($M+H^+$) requires 603.3829; **R_f** (2:1 CH_2Cl_2:Et_2O) = 0.60.



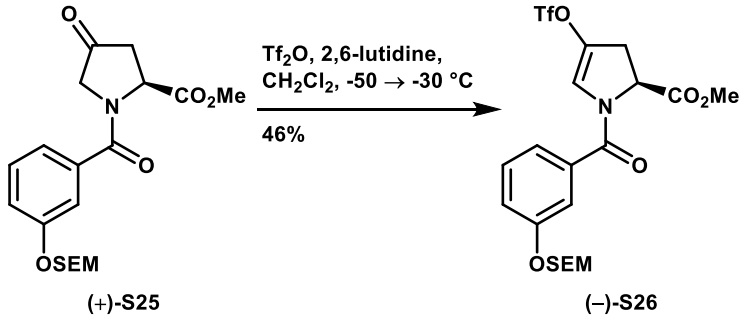
(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-(2-methoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-11. To a solution of protected ester **(–)-S23** (11 mg, 0.018 mmol) dissolved in THF (0.5 mL) was added TBAF (0.18 mL, 1M in THF, 0.180 mmol). After 5 minutes the reaction was poured into 1M aq. NH_4Cl and extracted with Et_2O 3x. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, concentrated and purified by preparative TLC (2% MeOH/EtOAc), yielding the title compound as a clear oil (4.6 mg, 52% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 1H), 7.33 (d, J = 7.3 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.97 – 6.91 (m, 2H), 6.19 – 6.12 (m, 1H), 5.15 – 5.02 (m, 3H), 4.95 (dd, J = 11.6, 4.8 Hz, 1H), 4.43 (s, 1H), 4.06 (d, J = 4.4 Hz, 1H), 3.83 (s, 3H), 3.18 – 3.09 (m, 1H), 2.68 (ddd, J = 14.7, 4.5, 2.2 Hz, 1H), 1.87 – 1.77 (m, 1H), 1.69 – 1.35 (m, 17H), 1.35 – 1.16 (m, 21H), 0.88 (t, J = 6.8 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.75, 170.61, 165.90, 155.96, 131.80, 130.74, 128.96, 124.24, 120.99, 111.52, 109.73, 74.99, 70.35, 58.07, 55.92, 34.99, 34.27, 33.52, 31.86, 29.85, 29.26, 27.29, 25.65, 24.65, 24.22, 22.71, 14.22; **$[\alpha]^{25}_D$** –8.9 (c = 0.45 in $CHCl_3$); **IR** (film) 2920, 2850, 1740 (C=O), 1668 (C=O), 1618 (C=O), 1492, 1463, 1439, 1412, 1377, 1280, 1253, 1196, 1102, 1047, 1021, 847, 803, 755, 720; **HRMS** Accurate mass (ES^+): Found 489.2941 (-4.9 ppm), $C_{27}H_{41}N_2O_6$ ($M+H^+$) requires 489.2965; **R_f** (2% MeOH/EtOAc) = 0.45.



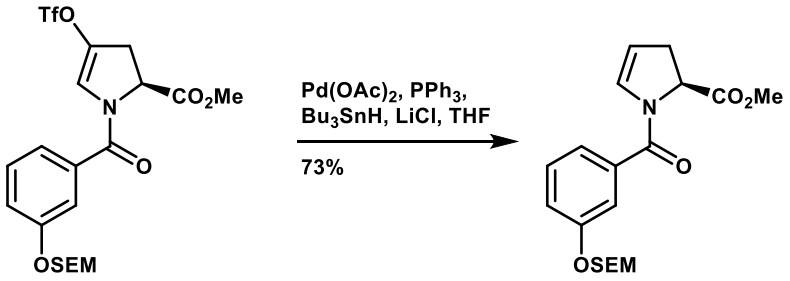
Methyl 3-((2-(trimethylsilyl)ethoxy)methoxy)benzoate S24. Using general procedure A, methyl 3-hydroxybenzoate (250 mg, 1.640 mmol) yielded the title compound as a clear oil (421 mg, 91% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.34 (dd, J = 11.9, 4.2 Hz, 1H), 7.23 (ddd, J = 8.2, 2.6, 1.1 Hz, 1H), 5.26 (s, 2H), 3.91 (s, J = 2.9 Hz, 3H), 3.80 – 3.73 (m, 2H), 0.98 – 0.93 (m, 2H), -0.01 (s, J = 3.3 Hz, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.58, 157.34, 131.42, 129.27, 122.79, 120.89, 116.93, 92.73, 77.16, 66.22, 51.93, 17.91, -1.51; **IR** (film) 2952, 2897, 1723 (C=O), 1586, 1488, 1447, 1380, 1274, 1248, 1211, 1153, 1106, 1083, 1009, 994, 918, 857, 833, 783, 755, 683; **HRMS** Accurate mass (ES^+): Found 305.1195 (+3.3 ppm), $C_{14}H_{22}O_4SiNa$ ($M+Na^+$) requires 305.1185.



Methyl (S)-4-oxo-1-(3-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)pyrrolidine-2-carboxylate (+)-S25. Using general procedure B, methyl ester **S24** (264 mg, 0.934 mmol) yielded the corresponding acid, which was used directly in the next step. Using general procedure C, the acid yielded the corresponding acylhydroxyproline methyl ester compound, whose purity made it unsuitable for characterization. Using general procedure D, the alcohol intermediate yielded the title compound as a yellow oil (254 mg, 70% over 3 steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 1H), 7.19 – 7.11 (m, 3H), 5.37 – 5.27 (m, 1H), 5.24 (s, 2H), 3.85 – 3.70 (m, 5H), 2.97 (dd, J = 18.8, 10.6 Hz, 1H), 2.70 (d, J = 20.3 Hz, 1H), 0.98 – 0.91 (m, 2H), -0.00 (s, J = 3.4 Hz, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 207.21, 171.60, 170.18, 157.50, 136.18, 129.90, 120.19, 118.61, 114.92, 92.81, 66.44, 55.37, 52.90, 40.02, 18.04, -1.39; **$[\alpha]^{25}_{D}$** +25.3 (c = 0.91 in $CHCl_3$); **IR** (film) 2950, 2395, 2342, 1757 (C=O), 1635 (C=O), 1575 (C=O), 1445, 1393, 1296, 1264, 1250, 1228, 1186, 1151, 1122, 1078, 1030, 1008, 990, 950, 862, 833, 817, 774, 753, 694, 600, 562; **HRMS** Accurate mass (ES^+): Found 394.1700 (+3.6 ppm), $C_{19}H_{28}NO_6Si$ ($M+H^+$) requires 394.1686.

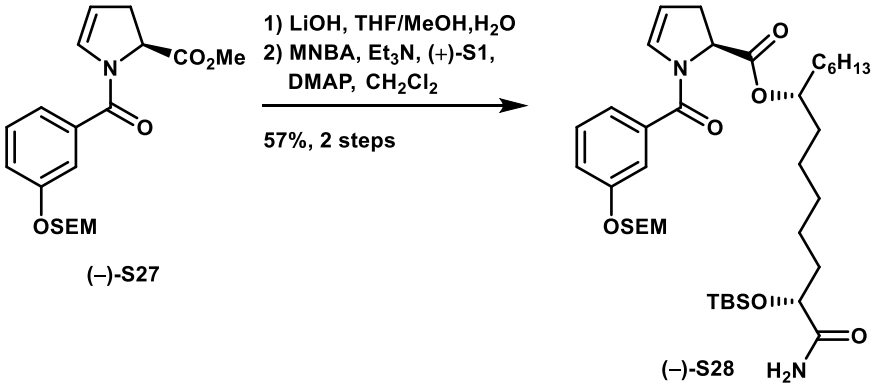


Methyl (S)-4-(((trifluoromethyl)sulfonyl)oxy)-1-(3-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S26. Using general procedure E, ketone **(+)-S25** (150 mg, 0.388 mmol) yielded the title compound as an orange oil (95 mg, 46% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 (t, J = 7.9 Hz, 1H), 7.18 (dt, J = 24.8, 8.2 Hz, 3H), 6.81 (s, 1H), 5.24 (s, 2H), 5.08 (d, J = 6.5 Hz, 1H), 3.83 (s, 3H), 3.78 – 3.72 (m, 2H), 3.46 – 3.36 (m, 1H), 2.97 (ddd, J = 16.4, 4.8, 1.5 Hz, 1H), 0.99 – 0.92 (m, 2H), 0.00 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.70, 167.12, 159.69, 157.65, 144.29, 137.47, 134.65, 134.45, 130.04, 124.14, 123.29, 123.07, 120.90, 119.79, 119.45, 117.23, 115.61, 92.84, 66.56, 58.33, 57.60, 53.02, 33.18, 24.36, 18.09, -1.42; **$[\alpha]^{25}_{D}$** –56.4 (c = 0.45 in $CHCl_3$); **IR** (film) 2954, 2359, 2341, 1749 (C=O), 1652 (C=O), 1581 (C=O), 1488, 1427, 1398, 1207, 1137, 1086, 1005, 990, 917, 857, 832, 744, 693, 667, 605; **HRMS** Accurate mass (ES^+): Found 548.1028 (+5.5 ppm), $C_{20}H_{26}NO_8SSiNa$ ($M+Na^+$) requires 548.0998.



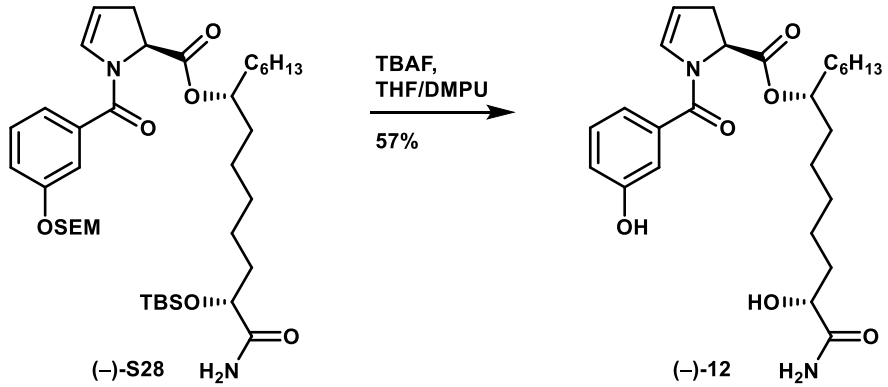
(–)-S26 (–)-S27

Methyl (S)-1-(3-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S27. Using general procedure F, triflate **(–)-S26** (90 mg, 0.171 mmol) yielded the title compound as a yellow oil (47 mg, 73% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (t, J = 7.9 Hz, 1H), 7.23 (s, 1H), 7.18 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 6.58 – 6.52 (m, 1H), 5.23 (s, 2H), 5.11 (d, J = 5.1 Hz, 1H), 5.01 (dd, J = 11.6, 5.0 Hz, 1H), 3.80 (s, 3H), 3.77 – 3.72 (m, 2H), 3.15 – 3.06 (m, 1H), 2.76 – 2.67 (m, 1H), 0.98 – 0.93 (m, 2H), 0.00 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.56, 166.75, 157.46, 136.25, 130.97, 129.71, 121.15, 118.65, 115.86, 109.05, 92.95, 66.49, 58.51, 52.64, 33.87, 18.14, -1.31; **$[\alpha]^{25}_D$** –44.0 (c = 0.31 in $CHCl_3$); **IR** (film) 2953, 2359, 2341, 1749 (C=O), 1646, 1617, 1488, 1446, 1398, 1362, 1317, 1086, 1005, 989, 858, 834, 694, 668; **HRMS** Accurate mass (ES^+): Found 378.1706 (-8.2 ppm), $C_{19}H_{28}NO_5Si$ ($M+H^+$) requires 378.1737.

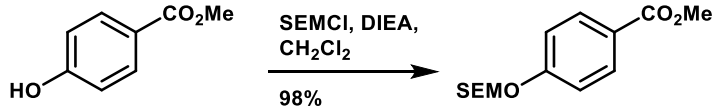


(–)-S27 (–)-S28

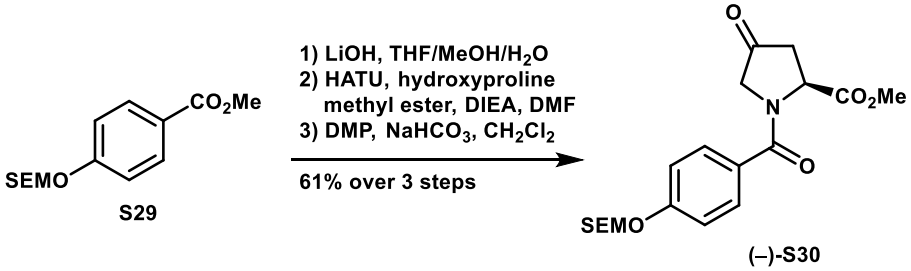
(7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl (S)-1-(3-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S28. Using general procedure B, methyl ester **(–)-S27** (26 mg, 0.069 mmol) yielded the acid intermediate as a yellow oil. This compound was not of sufficient purity for characterization. Next, using modified general procedure H (1.2 eq acid and MNBA), acid intermdiate (25 mg, 0.069 mmol) yielded the title compound as a yellow oil (24 mg, 57% yield, 2 steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 (q, J = 7.8 Hz, 1H), 7.20 (s, J = 11.1 Hz, 1H), 7.15 (dd, J = 15.5, 7.9 Hz, 2H), 6.52 (s, 2H), 5.54 – 5.44 (m, 1H), 5.23 (s, 2H), 5.08 (d, J = 1.9 Hz, 1H), 5.01 – 4.90 (m, 2H), 4.17 – 4.08 (m, 1H), 3.80 – 3.67 (m, 2H), 3.15 – 3.06 (m, 1H), 2.67 (d, J = 16.9 Hz, 1H), 1.81 – 1.70 (m, 1H), 1.69 – 1.47 (m, 7H), 1.26 (dd, J = 14.1, 6.9 Hz, 17H), 0.97 – 0.89 (m, 12H), 0.85 (t, J = 6.9 Hz, 3H), 0.10 – 0.06 (m, 6H), -0.01 (s, J = 3.2 Hz, 9H); **13C NMR** (100 MHz, $CDCl_3$) δ 176.94, 170.86, 166.62, 157.49, 136.52, 131.08, 129.70, 121.13, 118.46, 115.85, 108.87, 92.97, 75.62, 73.60, 66.51, 58.80, 35.13, 34.05, 31.85, 29.85, 29.51, 29.32, 25.89, 25.31, 25.08, 24.11, 22.72, 18.17, 14.22, -1.28, -4.68, -5.12; **$[\alpha]^{25}_D$** –16.1 (c = 1.18 in $CHCl_3$); **IR (**film) 3480, 2927, 2867, 1739 (C=O), 1689 (C=O), 1651 (C=O), 1618, 1579, 1488, 1446, 1397, 1248, 1192, 1088, 1029, 1005, 991, 938, 857, 834, 778, 745, 694, 668; **HRMS** Accurate mass (ES^+): Found 719.4445 (-5.8 ppm), $C_{38}H_{67}N_2O_7Si_2$ ($M+H^+$) requires 719.4487.



(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(3-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-12. Using general procedure I, silyl ether **(–)-S28** (24 mg, 0.033 mmol) yielded the title compound as a clear oil (9 mg, 57% yield) after purification by column chromatography (50 → 100% EtOAc/hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, J = 7.8 Hz, 1H), 7.05 – 6.87 (m, 5H), 6.57 (s, 1H), 5.91 (s, 1H), 5.16 (s, 1H), 5.09 – 5.01 (m, 1H), 4.93 (dd, J = 11.4, 5.1 Hz, 1H), 4.12 – 4.02 (m, 1H), 3.18 – 3.07 (m, 1H), 2.67 (d, J = 17.3 Hz, 1H), 1.87 – 1.76 (m, 1H), 1.61 – 1.23 (m, 27H) 0.88 (t, J = 5.6 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.78, 171.03, 167.83, 167.38, 157.46, 157.32, 135.46, 130.94, 129.78, 118.82, 115.06, 110.10, 75.42, 71.04, 58.70, 34.90, 34.43, 33.97, 33.75, 31.85, 29.84, 29.24, 27.91, 25.63, 24.83, 24.60, 22.70, 14.21; **$[\alpha]^{25}_D$** +14.4 (c = 0.90 in $CHCl_3$); **IR** (film) 3195 (br, O-H), 2925, 2856, 1732 (C=O), 1662 (C=O), 1579, 1416, 1273, 1196, 998, 880, 746; **HRMS** Accurate mass (ES^+): Found 475.2838 (+6.3 ppm), $C_{26}H_{39}N_2O_6$ ($M+H^+$) requires 475.2808.

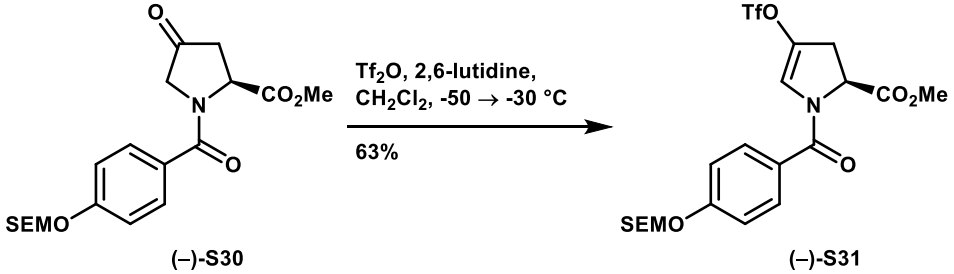


Methyl 4-((2-(trimethylsilyl)ethoxy)methoxy)benzoate S29. Using general procedure A, methyl 4-hydroxybenzoate (250 mg, 1.640 mmol) yielded the title compound as a clear oil (454 mg, 98% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dd, J = 8.9, 1.9 Hz, 2H), 7.05 (dd, J = 8.8, 1.9 Hz, 2H), 5.27 (s, J = 1.8 Hz, 2H), 3.89 (s, 3H), 3.78 – 3.73 (m, 2H), 0.95 (s, 2H), -0.01 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.96, 161.32, 131.63, 123.55, 115.75, 92.71, 66.73, 52.02, 18.17, -1.28, -1.31; **IR** (film) 2952, 2896, 1717 (C=O), 1605, 1580, 1510, 1435, 1381, 1315, 1276, 1234, 1191, 1168, 1090, 1013, 986, 938, 917, 851, 834, 770, 696, 668, 610; **HRMS** Accurate mass (ES^+): Found 283.1373 (+2.5 ppm), $C_{14}H_{23}O_4Si$ ($M+H^+$) requires 283.1366.



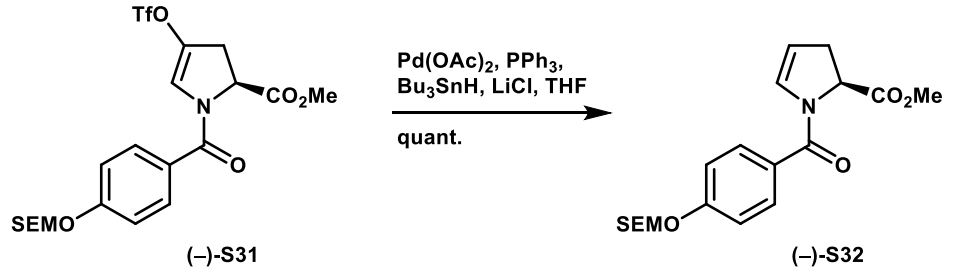
Methyl (2S)-4-oxo-1-(4-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)pyrrolidine-2-carboxylate (–)-S30. Using general procedure B, methyl ester **S29** (445 mg, 1.577 mmol) yielded the corresponding acid, which was used directly in the next step. Using general procedure C, the acid yielded the corresponding acylhydroxyproline methyl ester compound, whose purity made it unsuitable for characterization. Using general procedure D, the alcohol intermediate yielded the title compound as a yellow oil (394 mg, 61% over 3 steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (br s, J = 12.1 Hz, 2H), 7.12 – 7.06 (m, 2H), 5.25 (s, 2H), 3.83 – 3.72

(m, 5H), 2.96 (dd, J = 18.8, 10.5 Hz, 1H), 2.69 (dd, J = 18.8, 2.2 Hz, 1H), 1.03 – 0.91 (m, 2H), -0.00 (s, J = 3.3 Hz, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 207.52, 207.36, 171.78, 171.05, 170.65, 159.54, 129.46, 129.22, 127.41, 125.35, 116.02, 115.53, 92.59, 66.57, 65.02, 52.91, 18.00, -1.42; **[α]$^{25}_D$** –24.2 (c = 1.39 in $CHCl_3$); **IR** (film) 2953, 1764 (C=O), 1745 (C=O), 1606 (C=O), 1513, 1404, 1230, 1168, 1090, 1025, 986, 918, 834, 764, 692, 612; **HRMS** Accurate mass (ES^+): Found 394.1698 (+3.0 ppm), $C_{19}H_{28}NO_6Si$ ($M+H^+$) requires 394.1686.



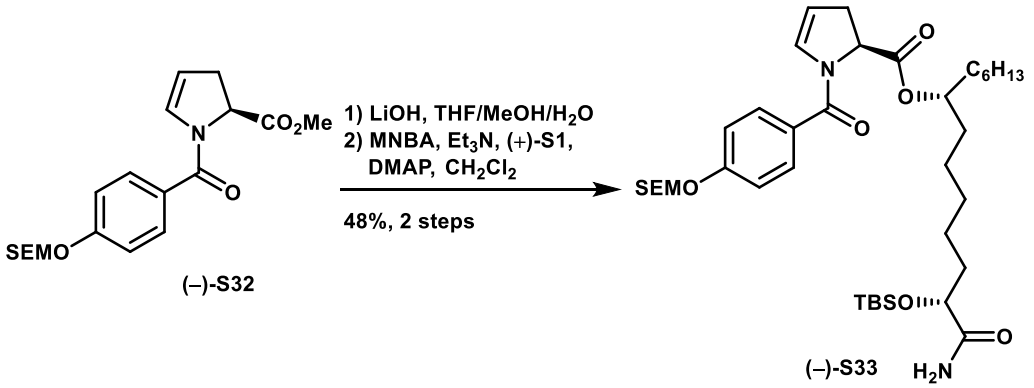
(–)-S30 (–)-S31

Methyl (2S)-4-(trifluoromethanesulfonyloxy)-1-(4-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S31. Using general procedure E, ketone **(–)-S30** (100 mg, 0.254 mmol) yielded the title compound as a yellow oil (85 mg, 63% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.87 (s, 1H), 5.27 (s, 2H), 5.08 (dd, J = 11.6, 5.1 Hz, 1H), 3.82 (s, 3H), 3.80 – 3.72 (m, 2H), 3.44 – 3.35 (m, 1H), 2.97 (ddd, J = 16.4, 5.1, 1.6 Hz, 1H), 1.00 – 0.91 (m, 2H), 0.00 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.86, 167.25, 160.10, 134.28, 129.89, 126.40, 123.58, 119.82, 117.26, 116.24, 92.72, 66.71, 57.83, 53.01, 33.25, 29.79, 18.12, -1.36; **[α]$^{25}_D$** –18.5 (c = 0.20 in 2:1 $CHCl_3$/MeOH); **IR** (film) 2954, 2899, 1750 (C=O), 1644, 1606, 1512, 1424, 1398, 1306, 1280, 1208, 1170, 1136, 1091, 1027, 987, 935, 910, 833, 759, 694, 644, 607; **HRMS** Accurate mass (ES^+): Found 526.1148 (-5.9 ppm), $C_{20}H_{27}F_3NO_8SSi$ ($M+H^+$) requires 526.1179.

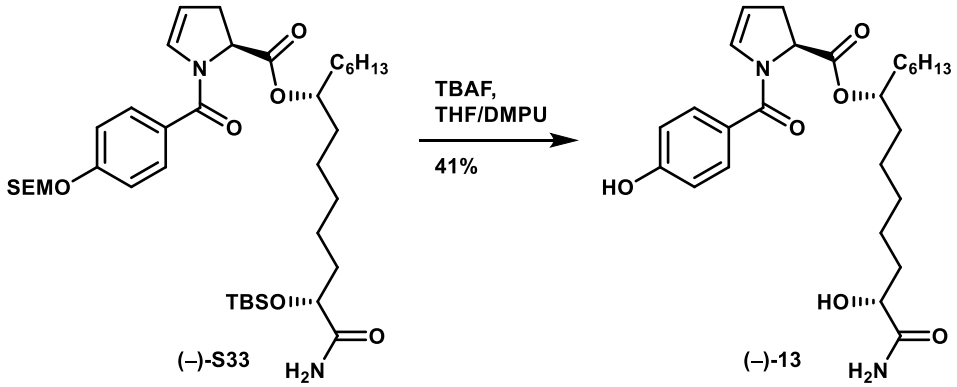


(–)-S31 (–)-S32

Methyl (2S)-1-(4-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S32. Using general procedure F, triflate **(–)-S31** (62 mg, 0.117 mmol) yielded the title compound as a yellow oil (47 mg, quant. yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.5 Hz, 2H), 7.08 – 7.03 (m, 2H), 6.60 (s, 1H), 5.25 (s, 2H), 5.11 (s, 1H), 5.04 – 4.95 (m, 1H), 3.84 – 3.71 (m, 5H), 3.17 – 3.03 (m, 1H), 2.77 – 2.66 (m, 1H), 0.97 – 0.90 (m, 2H), -0.01 (s, J = 3.3 Hz, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.72, 166.83, 159.49, 131.22, 129.91, 128.10, 115.94, 108.69, 92.76, 66.60, 58.70, 52.59, 33.82, 18.16, -1.31; **[α]$^{25}_D$** –60.2 (c = 1.22 in MeOH); **IR** (film) 2952, 2924, 2872, 1749 (C=O), 1644 (C=O), 1606, 1574, 1511, 1396, 1362, 1291, 1231, 1201, 1170, 1089, 1023, 985, 917, 834, 759, 694, 582; **HRMS** Accurate mass (ES^+): Found 378.1710 (-7.1 ppm), $C_{19}H_{28}NO_5Si$ ($M+H^+$) requires 378.1737; **R_f** (3:1 hexanes:EtOAc) = 0.20.

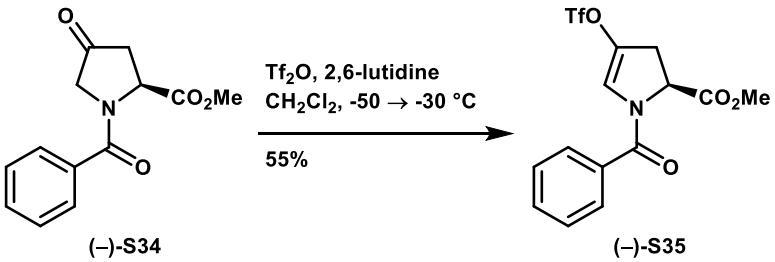


(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-(4-{[2-(trimethylsilyl)ethoxy]methoxy}benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S33. Using general procedure B, methyl ester **(–)-S32** (22 mg, 0.055 mmol) was converted to the corresponding acid, which was not of sufficient purity for characterization. Next, using modified general procedure H (1.2 eq acid, 1.2 eq MNBA), the acid intermediate yielded the title compound as a yellow oil (19 mg, 48% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6 Hz, 2H), 6.60 – 6.51 (m, 2H), 5.45 (m, 2H), 5.25 (s, 2H), 5.09 (s, 1H), 5.01 – 4.89 (m, 2H), 4.88 – 4.81 (m, 1H), 4.15 – 4.12 (m, 2H), 3.78 – 3.72 (m, 2H), 3.14 – 3.06 (m, 1H), 2.71 – 2.64 (m, 1H), 1.80 – 1.70 (m, 1H), 1.69 – 1.65 (m, 1H), 1.61 – 1.47 (m, 7H), 1.40 – 1.17 (m, 27H), 0.91 (s, 9H), 0.86 (t, J = 8.0 Hz, 3H), 0.08 (d, J = 6.0 Hz, 6H), -0.00 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.97, 171.07, 166.70, 159.41, 131.32, 129.85, 128.40, 115.93, 108.50, 92.80, 75.56, 74.45, 73.60, 66.61, 58.98, 35.20, 35.15, 34.26, 34.18, 34.02, 31.84, 29.56, 29.51, 29.32, 25.88, 25.40, 25.33, 25.28, 25.07, 24.18, 24.12, 22.71, 21.42, 18.18, 14.20, -1.30, -4.69, -5.12; **$[\alpha]^{25}_{D}$** –16.8 (c = 0.95 in $CHCl_3$); **IR** (film) 2926, 2856, 1733 (C=O), 1688 (C=O), 1645 (C=O), 1607, 1510, 1463, 1396, 1248, 1195, 1169, 1089, 991, 939, 760, 713, 580; **HRMS** Accurate mass (ES^+): Found 719.4447 (-5.6 ppm), $C_{38}H_{67}N_2O_7Si_2$ ($M+H^+$) requires 719.4487.



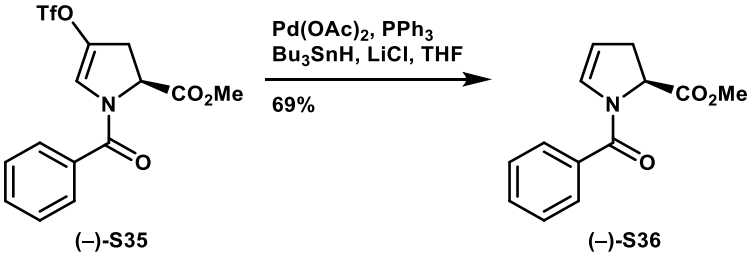
(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-(4-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-13. Using general procedure I, silyl ether **(–)-S33** (18.9 mg, 0.026 mmol) yielded the title compound as a clear oil (5.3 mg, 41% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.38 (d, J = 7.9 Hz, 2H), 6.94 (s, 1H), 6.79 (d, J = 8.1 Hz, 2H), 6.53 (d, J = 45.0 Hz, 1H), 5.63 (s, 1H), 5.17 (s, 1H), 4.96 (s, 2H), 4.03 (s, 2H), 3.18 – 3.09 (m, 1H), 2.69 (d, J = 16.8 Hz, 1H), 1.77 – 1.12 (m, 37H), 0.87 (t, J = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.12, 168.20, 159.37, 131.12, 129.98, 115.68, 109.85, 74.51, 70.77, 60.57, 58.82, 34.80, 34.27, 34.21, 34.06, 31.85, 29.85, 29.32, 29.25, 28.97, 27.62, 25.60, 25.45, 25.23, 24.78, 24.32, 22.70, 21.47, 14.34, 14.21; **$[\alpha]^{25}_{D}$** +17.9 (c = 0.24 in $CHCl_3$); **IR** (film) 3300 (br O-H), 2956, 2923, 2853, 2361, 2341, 2159, 2028, 1976, 1733, 1669, 1653, 1609, 1558, 1516, 1507, 1467, 1436,

1378, 1260, 1198, 1165, 1093, 1021, 948, 847, 798, 761, 721, 667; **HRMS** Accurate mass (ES^+): Found 475.2804 (-0.8 ppm), $C_{26}H_{39}N_2O_6$ ($M+H^+$) requires 475.2808.



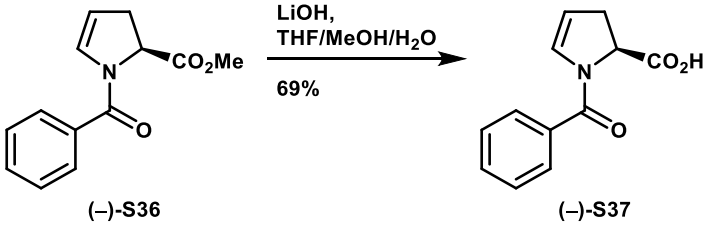
(–)-S34 (–)-S35

Methyl (2S)-1-benzoyl-4-(trifluoromethanesulfonyloxy)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S35. Using general procedure E, ketone **(–)-S34**[2] (50 mg, 0.202 mmol) yielded the title compound as an orange oil (44 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 – 7.43 (m, 5H), 6.79 (s, 1H), 5.16 – 5.05 (m, 1H), 3.83 (s, 3H), 3.45 – 3.37 (m, 1H), 2.98 (ddd, J = 16.5, 4.9, 1.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.78, 167.56, 134.52, 133.50, 131.67, 128.95, 127.93, 123.31, 120.14, 116.95, 77.16, 57.65, 53.12, 33.26; **$[\alpha]^{25}_D$** –47.6 (c = 1.49 in $CHCl_3$); **IR** (film) 2957, 2921, 2851, 2361, 2160, 2031, 1979, 1749 (C=O), 1648 (C=O), 1578, 1495, 1448, 1426, 1404, 1306, 1208, 1135, 1029, 937, 909, 843, 752, 721, 702, 669; **HRMS** Accurate mass (ES^+): Found 402.0244 (+2.2 ppm), $C_{14}H_{12}F_3NO_6SNa$ ($M+Na^+$) requires 402.0235.



(–)-S35 (–)-S36

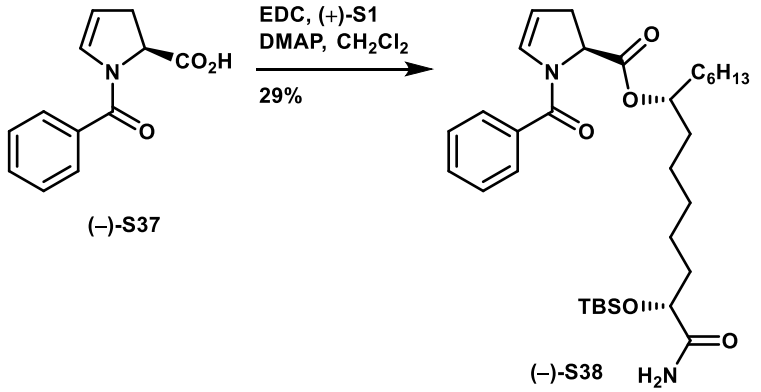
Methyl (2S)-1-benzoyl-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S36. Using general procedure F, triflate **(–)-S35** (100 mg, 0.252 mmol) yielded the title compound as a yellow oil (40 mg, 69% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, J = 7.3 Hz, 2H), 7.50 – 7.37 (m, 3H), 6.53 (s, 1H), 5.12 (s, 1H), 5.02 (dd, J = 11.5, 5.0 Hz, 1H), 3.81 (s, 3H), 3.15 – 3.07 (m, 1H), 2.72 (d, J = 16.9 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.6, 167.2, 135.1, 131.0, 130.9, 128.6, 128.0, 109.1, 58.5, 52.7, 33.9; **$[\alpha]^{25}_D$** –110.8 (c = 1.00 in $CHCl_3$); **IR** (film) 2953, 2923, 2160, 2029, 1979, 1747 (C=O), 1641, 1615, 1576, 1496, 1447, 1403, 1362, 1290, 1201, 1179, 1106, 1016, 936, 841, 790, 724, 700, 662; **HRMS** Accurate mass (ES^+): Found 254.0813 (+7.9 ppm), $C_{13}H_{13}NO_3Na$ ($M+Na^+$) requires 254.0793.



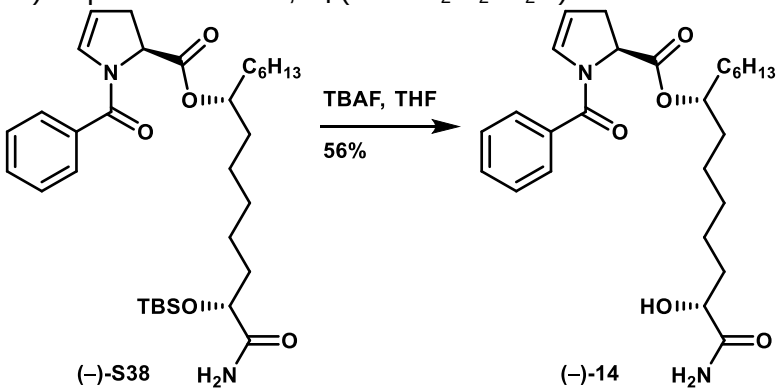
(–)-S36 (–)-S37

(2S)-1-benzoyl-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S37. Using general procedure B, methyl ester **(–)-S36** (37 mg, 0.160 mmol) yielded the title compound as a yellow oil (24 mg, 69% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 – 7.43 (m, 5H), 6.47 (s, 1H), 5.30 (s, 1H), 5.12 (d, J = 7.5 Hz, 1H), 3.19 (d, J = 17.1 Hz, 1H), 3.10 – 3.02 (m, 1H); **13C NMR** (100 MHz, $CDCl_3$) δ 173.24, 168.67, 131.41, 130.06, 128.71, 128.56, 128.23, 111.50, 59.52, 32.97, 29.83; **$[\alpha]^{25}_D$** –

85.3 (c = 1.20 in $CHCl_3$); **IR** (film) 3061 (br, CO_2-H), 2953, 2924, 2918, 1716 (C=O), 1596 (C=O), 1573, 1497, 1448, 1408, 1352, 1315, 1289, 1195, 1106, 1017, 941, 846, 787, 753, 719, 700, 660; **HRMS** Accurate mass (ES^+): Found 218.0825 (+3.2 ppm), $C_{12}H_{12}NO_3$ ($M+H^+$) requires 218.0818.

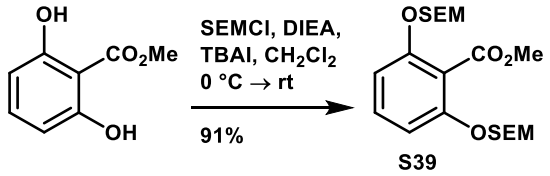


(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-benzoyl-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S38. Using modified general procedure G (1.2 eq acid, 1.5 eq EDC, 1.0 eq alcohol, 0.5 eq DMAP), acid **(–)-S37** (24 mg, 0.111 mmol) after purification by preparative TLC (2:1 CH_2Cl_2:Et_2O), yielded the title compound as a clear oil (15 mg, 29% yield). **^{1}H NMR** (500 MHz, CDCl3) δ 7.57 (d, J = 7.5 Hz, 2H), 7.45 (dt, J = 14.5, 7.1 Hz, 3H), 6.53 (s, 2H), 5.58 (s, 1H), 5.02 (dd, J = 11.5, 4.7 Hz, 1H), 4.98 – 4.94 (m, 1H), 3.18 – 3.08 (m, 1H), 2.70 (d, J = 17.1 Hz, 1H), 1.85 – 1.16 (m, 10H), 0.92 (s, 9H), 0.87 (t, J = 6.6 Hz, 3H), 0.10 (s, 3H), 0.09 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.0, 170.9, 167.0, 135.3, 131.1, 130.7, 128.6, 127.9, 108.9, 75.6, 73.6, 58.8, 35.1, 34.0, 31.8, 29.8, 29.5, 29.3, 25.9, 25.3, 25.1, 24.1, 22.7, 18.2, 14.2, -4.7, -5.1; **$[\alpha]^{25}_D$** –38.6 (c = 1.43 in $CHCl_3$); **IR** (film) 3480, 2927, 2856, 1738 (C=O), 1688 (C=O), 1645 (C=O), 1618, 1577, 1463, 1495, 1402, 1360, 1253, 1195, 1100, 1004, 940, 836, 779, 723, 699, 666; **HRMS** Accurate mass (ES^+): Found 573.3695 (-5.1 ppm), $C_{32}H_{53}N_2O_5Si$ ($M+H^+$) requires 573.3724; **R_f** (2:1 CH_2Cl_2:Et_2O) = 0.70.



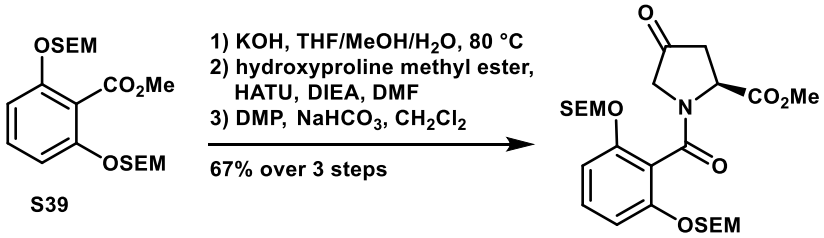
(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-benzoyl-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-14. To a solution of silyl ether **(–)-S38** (14 mg, 0.025 mmol) dissolved in THF (0.5 mL) was added TBAF (0.25 mL, 1M in THF, 0.250 mmol) at room temperature. After 5 minutes, the reaction was quenched with 1M aq. NH_4Cl and extracted with Et_2O 3x. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, concentrated, and purified by preparative TLC (2% MeOH/EtOAc), yielding the title compound as a clear oil (6.4 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 – 7.36 (m, 5H), 6.95 (s, 0.16H), 6.91 (s, 0.45H), 6.83 (s, 0.67H), 6.52 – 6.47 (m, 1H), 5.47 (s, 0.37H), 5.27 (s, 1H), 5.16 (d, J = 4.0 Hz, 1H), 5.08 – 5.02 (m, 1H), 5.02 – 4.94 (m, 1H), 4.35 (s, 0.55H), 4.14 – 3.99 (m, 1H), 3.18 – 3.08 (m, 1H), 2.76 – 2.66 (m, 1H), 1.87 – 1.79 (m, 1H), 1.77 – 1.48 (m, 11H), 1.48 – 1.16 (m, 22H),

0.87 (t, J = 6.8 Hz, 3H); **^{13}C NMR** (125 MHz, CDCl3) δ 177.59, 170.92, 170.62, 167.88, 167.49, 134.93, 134.69, 131.09, 130.80, 128.81, 128.76, 127.78, 127.69, 110.01, 109.84, 75.54, 75.24, 70.64, 59.14, 58.60, 34.84, 34.53, 34.39, 34.15, 34.02, 33.78, 33.61, 31.85, 29.84, 29.25, 27.73, 27.49, 25.60, 25.31, 24.68, 24.50, 24.24, 24.00, 22.70, 14.20; **$[\alpha]^{25}_D$** –5.3 (c = 0.62 in $CHCl_3$); **IR** (film) 3325 (br, O-H), 2925, 2856, 2360, 1733 (C=O), 1668 (C=O), 1615 (C=O), 1576, 1496, 1448, 1406, 1197, 1153, 1082, 1017, 1001, 944, 844, 788, 724, 699, 660; **HRMS** Accurate mass (ES^+): Found 481.2650 (-5.8 ppm), $C_{26}H_{38}N_2O_5Na$ ($M+Na^+$) requires 481.2678; **R_f** (2% MeOH/EtOAc) = 0.50.



S39

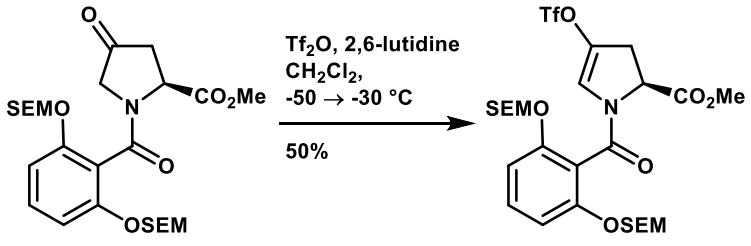
Methyl 2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoate S39. Using modified general procedure A (double equivalents of SEMCl and DIEA, and 0.1 eq tetrabutylammonium iodide), 2,6-dihydroxy methyl benzoate (563 mg, 3.348 mmol) yielded the title compound as a yellow oil (1.308g, 91% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 (t, J = 8.4 Hz, 1H), 6.82 (d, J = 8.4 Hz, 2H), 5.21 (s, 4H), 3.90 (s, J = 2.6 Hz, 3H), 3.76 – 3.71 (m, 4H), 0.96 – 0.92 (m, 4H), 0.01 – -0.02 (m, 18H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.89, 155.07, 130.98, 115.47, 108.36, 93.22, 66.55, 52.41, 18.12, -1.30; **IR** (film) 2951, 2897, 2359, 2341, 1738 (C=O), 1599, 1469, 1272, 1245, 1145, 1111, 1038, 936, 917, 895, 856, 831, 757, 692, 667, 609**; HRMS** Accurate mass (ES^+): Found 451.1915 (-7.3 ppm), $C_{20}H_{36}O_6Si_2Na$ ($M+Na^+$) requires 451.1948; **R_f** (7:1 hexanes:EtOAc) = 0.34.



S39 **(–)-S40**

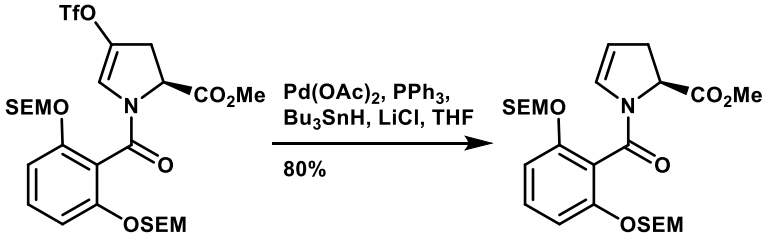
Methyl (S)-1-(2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-4-oxopyrrolidine-2-carboxylate (–)-S40. Methyl ester **S39** (1.283g, 2.993 mmol) was dissolved in 9:1:1 MeOH:THF:H_2O (11 mL), and KOH (1.914g, 34.117 mmol) was added as a solid. The reaction was heated to reflux (80 °C) overnight. The following day, the reaction was cooled to room temperature, acidified (pH 5-6) with 5% aq. AcOH, and extracted with CH_2Cl_2 3x. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The crude acid was unstable and used directly in the next step. Using general procedure C, the acid yielded the corresponding acylhydroxyproline methyl ester compound, whose purity made it unsuitable for characterization. Using general procedure D, the alcohol intermediate yielded the title compound as a yellow oil (1.075g, 67% over 3 steps). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 7.29 – 7.24 (m, 1H), 6.86 (tt, J = 7.4, 4.3 Hz, 2H), 5.32 – 5.15 (m, 4.56H), 5.11 (t, J = 5.8 Hz, 0.35H), 4.64 – 4.59 (m, 0.33H), 4.43 (d, J = 19.7 Hz, 0.34H), 4.07 – 4.03 (m, 0.18H), 4.03 – 3.99 (m, 0.16), 3.93 – 3.90 (m, 0.30), 3.90 – 3.86 (m, 0.41H), 3.82 – 3.66 (m, 6.48H), 3.63 – 3.59 (m, 0.83H), 3.03 – 2.93 (m, 0.73H), 2.90 – 2.82 (m, 0.38H), 2.72 – 2.62 (m, 0.73H), 2.57 (d, J = 18.1 Hz, 0.35H), 0.98 – 0.88 (m, 4H), 0.05 – -0.06 (m, 18H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 207.70, 170.94, 165.99, 154.92, 154.16, 131.50, 131.17, 116.27, 109.11, 108.75, 108.54, 108.23, 93.81, 93.63, 93.47, 93.31, 66.84, 66.73, 66.68, 57.33, 54.73, 52.69, 52.55, 51.82, 41.95, 40.69, 18.10, 14.31, -1.27, -1.30, -1.31; **$[\alpha]^{25}_D$** –1.8 (c = 1.41 in $CHCl_3$); **IR** (film) 2952, 2896, 1765 (C=O), 1747 (C=O), 1658 (C=O), 1596, 1467, 1404, 1245,

1177, 1142, 1094, 1035, 918, 893, 856, 832, 790, 751, 693, 664; **HRMS** Accurate mass (ES^+): Found 562.2232 (-6.4 ppm), $C_{25}H_{41}NO_8Si_2Na$ ($M+Na^+$) requires 562.2268; $\mathbf{R_f}$ (3:1 hexanes:EtOAc) = 0.25.



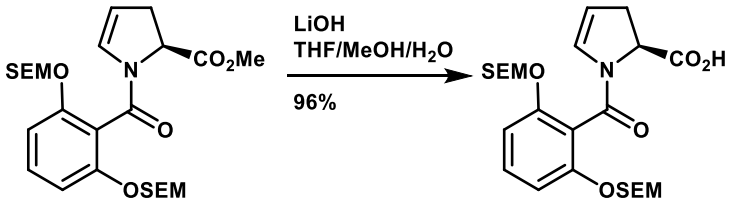
(–)-S40 (–)-S41

Methyl (S)-1-(2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-4-(((trifluoromethyl)sulfonyl)oxy)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S41. Using general procedure E, ketone **(–)-S40** (238 mg, 0.440 mmol) yielded the title compound as an orange oil (149 mg, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 1H), 6.87 (t, J = 8.2 Hz, 2H), 6.35 (s, 1H), 5.28 – 5.16 (m, 4H), 5.10 (dd, J = 11.8, 5.0 Hz, 1H), 3.82 (s, 3H), 3.74 (dt, J = 21.8, 8.0 Hz, 4H), 3.45 – 3.34 (m, 1H), 2.95 (dd, J = 16.5, 4.9 Hz, 1H), 0.93 (dd, J = 16.0, 7.7 Hz, 4H), -0.01 (s, J = 7.4 Hz, 18H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.52, 163.25, 155.19, 133.94, 131.84, 123.14, 114.23, 108.67, 108.37, 93.48, 93.16, 66.69, 66.64, 56.77, 52.81, 33.66, 18.04, -1.34, -1.38; **$[\alpha]^{25}_D$** –41.3 (c = 1.04 in $CHCl_3$); **IR** (film) 3269, 2954, 2899, 1747 (C=O), 1605 (C=O), 1425, 1363, 1311, 1208, 1136, 1028, 912, 833, 755, 693, 605; **HRMS** Accurate mass (ES^+): Found 694.1727 (-4.9 ppm), $C_{26}H_{40}F_3NO_{10}SSi_2Na$ ($M+Na^+$) requires 694.1761; $\mathbf{R_f}$ (3:1 hexanes:EtOAc) = 0.48.

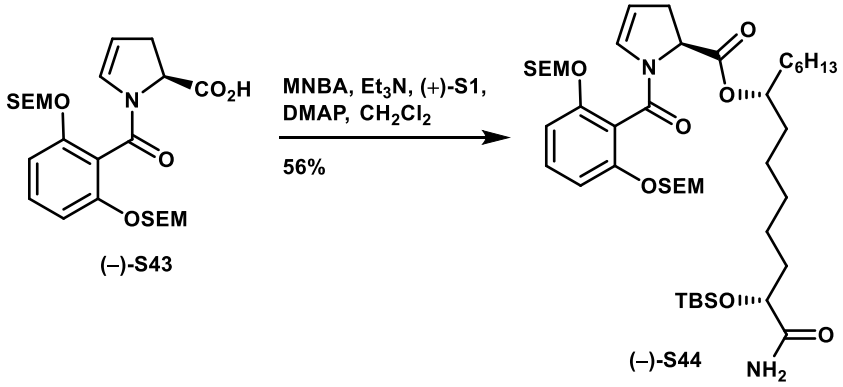


(–)-S41 (–)-S42

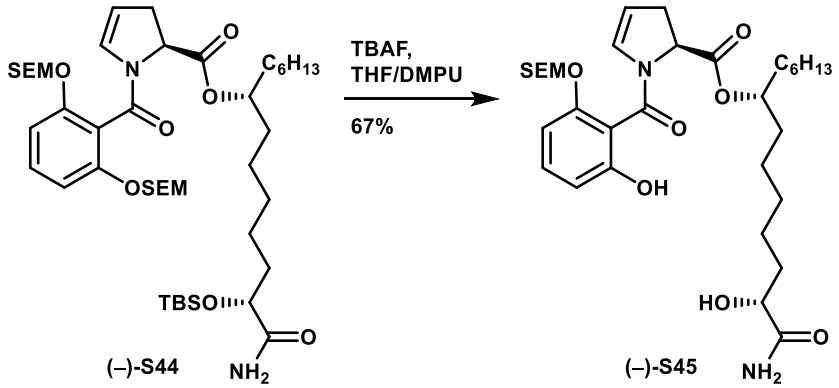
Methyl (S)-1-(2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S42. Using general procedure F, triflate **(–)-S41** (130 mg, 0.194 mmol) yielded the title compound as a yellow oil (82 mg, 80% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 1H), 6.83 (dt, J = 12.5, 6.2 Hz, 2H), 6.11 (dt, J = 4.4, 2.2 Hz, 1H), 5.29 (d, J = 7.1 Hz, 1H), 5.24 – 5.13 (m, 3H), 5.01 (ddd, J = 8.3, 6.9, 3.8 Hz, 2H), 3.86 – 3.64 (m, 7H), 3.12 (ddt, J = 16.7, 11.6, 2.3 Hz, 1H), 2.74 – 2.68 (m, 1H), 0.99 – 0.87 (m, 4H), 0.02 – -0.06 (m, 18H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.27, 162.64, 154.96, 154.81, 130.92, 130.58, 115.96, 108.57, 108.29, 108.10, 93.02, 92.96, 66.43, 57.50, 52.35, 34.42, 18.05, -1.36; **$[\alpha]^{25}_D$** –55.9 (c = 1.49 in $CHCl_3$); **IR** (film) 2952, 2921, 2899, 1744 (C=O), 1656 (C=O), 1620, 1596, 1468, 1404, 1245, 1199, 1178, 1151, 1094, 1038, 917, 895, 857, 832, 741, 694, 608; **HRMS** Accurate mass (ES^+): Found 546.2288 (-5.7 ppm), $C_{25}H_{41}NO_7Si_2Na$ ($M+Na^+$) requires 546.2319.



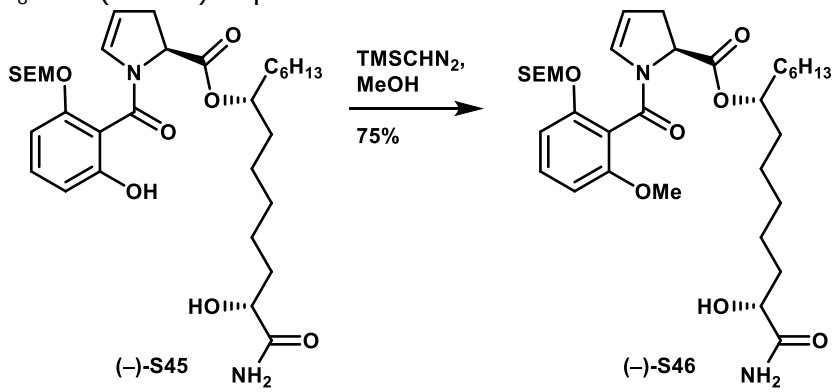
(S)-1-(2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S43. Using general procedure B, methyl ester **(–)-S42** (73 mg, 0.139 mmol) yielded the title compound as a yellow oil (68 mg, 96% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (t, J = 8.4 Hz, 1H), 6.85 (dd, J = 8.5, 0.8 Hz, 2H), 6.02 (dt, J = 4.4, 2.2 Hz, 1H), 5.28 – 5.16 (m, 6H), 3.74 – 3.67 (m, 4H), 3.48 – 3.40 (m, 1H), 2.98 (ddt, J = 17.4, 11.0, 2.5 Hz, 1H), 0.95 – 0.89 (m, 4H), -0.01 (d, J = 1.7 Hz, 18H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.36, 166.43, 154.97, 154.62, 131.84, 129.07, 114.45, 112.17, 108.27, 107.97, 93.08, 92.94, 77.36, 66.75, 66.67, 59.24, 32.64, 30.43, 29.81, 18.10, -1.30, -1.33; **$[\alpha]^{25}_{D}$** –66.4 (c = 1.38 in $CHCl_3$); **IR** (film) 2952, 2924, 2896, 1748 (C=O), 1652 (C=O), 1619, 1595, 1468, 1405, 1245, 1183, 1150, 1093, 1039, 832, 738, 693, 664; **HRMS** Accurate mass (ES^+): Found 532.2130 (-6.2 ppm), $C_{24}H_{39}NO_7Si_2Na$ ($M+Na^+$) requires 532.2163.



(7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl (S)-1-(2,6-bis((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S44. Using general procedure H, acid **(–)-S43** (81 mg, 0.158 mmol) yielded the title compound as a yellow oil (55 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 1H), 6.92 – 6.75 (m, 2H), 6.57 – 6.48 (m, 1H), 6.10 (dt, J = 4.2, 2.0 Hz, 1H), 5.46 – 5.35 (m, 1H), 5.30 – 5.12 (m, 5H), 4.98 (dt, J = 8.7, 5.3 Hz, 2H), 4.13 (t, J = 5.1 Hz, 1H), 3.83 – 3.64 (m, 4H), 3.17 – 3.07 (m, 1H), 2.70 – 2.62 (m, 1H), 1.81 – 1.70 (m, 1H), 1.70 – 1.62 (m, 1H), 1.43 – 1.17 (m, 16H), 0.98 – 0.89 (m, 12H), 0.87 (t, J = 6.3 Hz, 3H), 0.14 – 0.04 (m, 6H), 0.03 – -0.06 (m, 18H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.02, 170.41, 162.48, 155.04, 154.97, 130.87, 130.79, 116.20, 108.76, 108.22, 108.10, 93.11, 93.03, 75.01, 73.54, 66.43, 57.85, 35.10, 34.67, 34.07, 34.02, 31.85, 29.48, 29.30, 25.85, 25.28, 25.06, 24.11, 22.68, 18.16, 18.10, 14.17, -1.30, -4.73, -5.15; **$[\alpha]^{25}_{D}$** –25.4 (c = 1.27 in $CHCl_3$); **IR** (film) 2927, 2857, 1749 (C=O), 1689 (C=O), 1657 (C=O), 1621, 1596, 1467, 1404, 1247, 1188, 1151, 1095, 1040, 937, 896, 833, 778, 751, 694, 665, 580, 554; **HRMS** Accurate mass (ES^+): Found 865.5290 (+4.6 ppm), $C_{44}H_{81}N_2O_9Si_3$ ($M+H^+$) requires 865.5250; **R_f** (4:1 CH_2Cl_2:Et_2O) = 0.67.

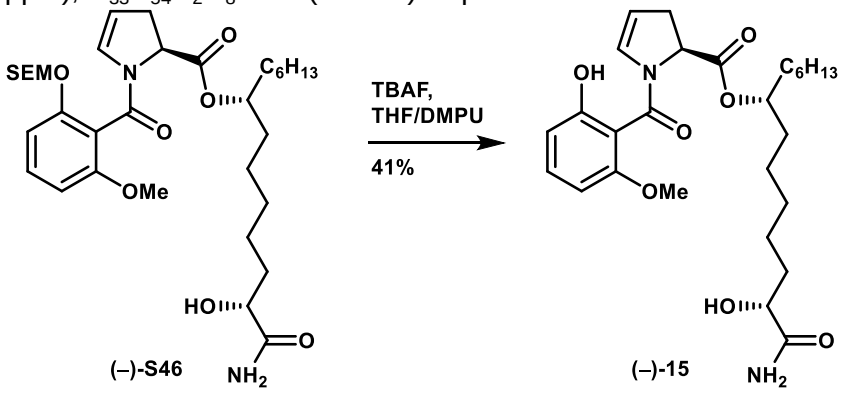


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(2-hydroxy-6-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S45. Using general procedure I, compound **(–)-S44** (37 mg, 0.043 mmol) yielded the title compound, after purification by preparative TLC (4% MeOH/EtOAc), as a yellow oil (18 mg, 67% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 – 7.89 (m, 1H), 7.22 (t, J = 8.3 Hz, 1H), 6.81 (s, 1H), 6.71 (t, J = 7.2 Hz, 1H), 6.62 (d, J = 8.3 Hz, 1H), 6.31 – 6.25 (m, 1H), 5.33 – 5.02 (m, 6H), 4.14 – 3.99 (m, 2H), 3.77 – 3.68 (m, 2H), 3.23 – 3.10 (m, 1H), 2.70 (d, J = 17.5 Hz, 1H), 1.86 – 1.74 (m, 1H), 1.73 – 1.15 (m, 22H), 0.99 – 0.81 (m, 5H), -0.01 (d, J = 2.9 Hz, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.79, 172.11, 164.33, 155.46, 154.76, 132.20, 130.96, 130.57, 111.63, 110.73, 110.27, 106.20, 93.42, 76.45, 70.80, 66.78, 58.28, 34.75, 34.29, 34.13, 33.84, 31.81, 29.17, 27.77, 25.59, 24.78, 24.40, 22.66, 18.13, 14.18, -1.29; **[α]$^{25}_D$** –1.7 (c = 0.93 in $CHCl_3$); **IR** (film) 3338 (br, O-H), 2927, 2858, 1748 (C=O), 1661, 1616, 1601, 1466, 1432, 1378, 1292, 1247, 1193, 1153, 1102, 1038, 941, 835, 792, 721; **HRMS** Accurate mass (ES^+): Found 643.3417 (+4.0 ppm), $C_{32}H_{52}N_2O_8SiNa$ ($M+Na^+$) requires 643.3391.

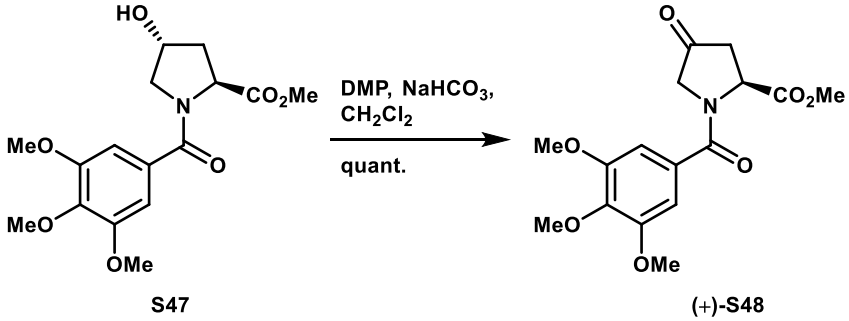


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(2-methoxy-6-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S46. To a solution of compound **(–)-S45** (19 mg, 0.031 mmol) in MeOH (1 mL) was added $TMSCHN_2$ (0.070 mL, 2M in hexanes, 0.140 mmol). The reaction was stirred overnight at room temperature, over which time the reaction turned from yellow to clear. The reaction was concentrated and purified by preparative TLC (5% MeOH/EtOAc), yielding the title compound as a yellow oil (15 mg, 75% yield). **^{1}H NMR** (500 MHz, $CDCl_3$, mixture of rotamers/conformers) δ 8.00 (dd, J = 8.3, 1.3 Hz, 1H), 7.61 – 7.56 (m, 0.39H), 7.45 (t, J = 7.8 Hz, 1H), 7.28 (td, J = 8.0, 1.9 Hz, 1H), 6.97 (d, J = 26.7 Hz, 1H), 6.78 (dd, J = 8.2, 6.7 Hz, 1H), 6.58 (dd, J = 8.3, 2.7 Hz, 1H), 6.43 (s, 0.37H), 6.10 (ddq, J = 12.7, 6.4, 2.2 Hz, 1H), 5.32 – 5.03 (m, 5H), 4.98 – 4.88 (m, 2H), 4.26 (dd, J = 7.0, 3.2 Hz, 0.38H), 4.16 – 4.11 (m, 0.42H), 4.06 (d, J = 6.6 Hz, 0.62H), 3.84 – 3.80 (m, 1.84H), 3.80 – 3.76 (m, 2.25H), 3.75 – 3.66 (m, 1.59H), 3.18 – 3.08 (m, 1H), 2.74 – 2.63 (m, 1H), 1.89 – 1.68 (m, 2H), 1.68 – 1.37 (m, 12H), 1.36 – 1.14 (m, 24H), 0.98 – 0.77 (m, 9H), -0.02 (d, J = 5.9 Hz, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.21, 178.09, 170.41, 170.07,

165.15, 163.64, 157.65, 157.10, 155.01, 154.80, 133.70, 131.56, 131.47, 130.53, 129.95, 128.63, 113.96, 113.59, 109.58, 107.87, 107.12, 104.95, 104.55, 101.07, 93.07, 92.78, 82.51, 79.60, 77.16, 74.43, 74.34, 70.81, 70.12, 69.95, 66.72, 66.65, 63.15, 57.71, 56.30, 56.06, 35.11, 34.57, 34.35, 33.50, 32.06, 31.87, 29.84, 29.50, 29.29, 27.22, 27.04, 26.15, 25.66, 24.80, 24.63, 24.23, 24.15, 22.83, 22.71, 18.15, 18.10, 14.22, -1.28; **[α]$^{25}_{D}$** –19.8 (c = 1.72 in $CHCl_3$); **IR** (film) 3329 (br, O-H), 2924, 2854, 1721, 1658, 1619, 1595, 1472, 1409, 1379, 1291, 1247, 1190, 1107, 1073, 1002, 951, 898, 858, 835, 789, 716; 668, 604; **HRMS** Accurate mass (ES^+): Found 657.3570 (+3.5 ppm), $C_{33}H_{54}N_2O_8SiNa$ ($M+Na^+$) requires 657.3547.

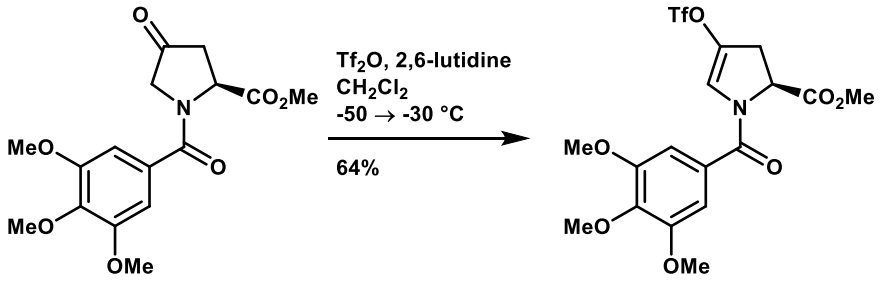


(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(2-hydroxy-6-methoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-15. Using modified general procedure I (10 eq TBAF, 0.1M DMPU), silyl ether **(–)-S46** (17 mg, 0.027 mmol) after purification by column chromatography (0 → 3% MeOH/CH_2Cl_2), yielded the title compound as a clear oil (5.6 mg, 41% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.28 – 7.23 (m, 1H), 6.83 (s, 1H), 6.60 (dd, J = 8.3, 4.8 Hz, 1H), 6.47 (t, J = 8.7 Hz, 1H), 6.25 (dt, J = 4.4, 2.2 Hz, 1H), 5.19 (dt, J = 4.6, 2.4 Hz, 1H), 5.14 – 5.04 (m, 2H), 4.60 (d, J = 5.9 Hz, 1H), 4.08 – 4.00 (m, 1H), 3.83 – 3.79 (m, 3H), 3.21 – 3.12 (m, 1H), 2.69 (d, J = 18.6 Hz, 1H), 1.84 – 1.74 (m, 1H), 1.71 – 1.19 (m, 22H), 0.88 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.47, 176.57, 172.39, 172.24, 164.48, 164.39, 157.00, 155.68, 132.38, 130.55, 110.52, 110.44, 110.14, 110.10, 102.72, 102.63, 76.66, 76.46, 70.77, 70.70, 64.51, 58.37, 58.33, 56.07, 56.02, 34.79, 34.35, 34.21, 34.07, 33.81, 33.58, 31.83, 29.84, 29.18, 27.72, 27.53, 25.63, 24.75, 24.69, 24.33, 24.14, 22.68, 14.20; **[α]$^{25}_{D}$** –10.5 (c = 0.56 in $CHCl_3$); **IR** (film) 3307 (br, O-H), 2926, 2856, 1733 (C=O), 1653, 1592, 1470, 1435, 1250, 1194, 1088, 1016, 947, 847, 791, 720, 601; **HRMS** Accurate mass (ES^+): Found 527.2751 (+3.4 ppm), $C_{27}H_{40}N_2O_7Na$ ($M+Na^+$) requires 527.2733.



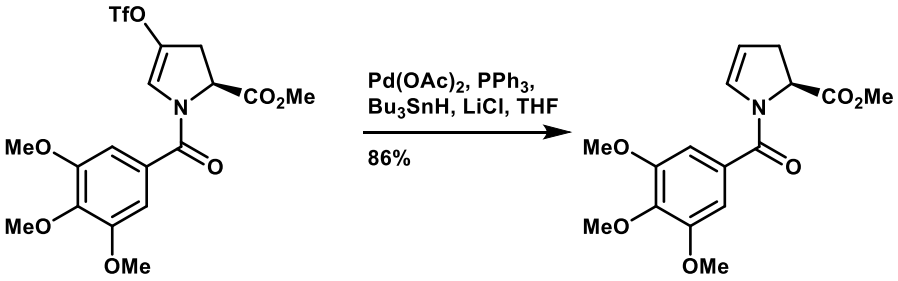
Methyl (2S)-4-oxo-1-(3,4,5-trimethoxybenzoyl)pyrrolidine-2-carboxylate (+)-S48. Using general procedure D, alcohol **S47**[3] (1.340g, 3.950 mmol) yielded the title compound as a white foam (1.33g, quant. yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.66 (s, 2H), 5.19 (br s, 1H), 3.97 (br s, 1H), 3.83 – 3.67 (m, 12H), 2.91 (dd, J = 18.8, 10.5 Hz, 1H), 2.59 (d, J = 18.6 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl3) δ 207.11, 171.59, 170.16, 153.24, 139.94, 129.95, 104.43, 77.36, 60.80, 56.19, 52.80; **[α]$^{25}_{D}$** +4.4 (c = 0.45 in 2:1 $CHCl_3$/MeOH); **IR** (film) 3451, 2953, 2360, 1728 (C=O),

1633 (C=O), 1580, 1506, 1448, 1414, 1324, 1238, 1179, 1119, 998, 922, 879, 840, 763, 723, 691, 603; **HRMS** Accurate mass (ES^+): Found 360.1072 (+3.6 ppm), $C_{16}H_{19}NO_7Na$ ($M+Na^+$) requires 360.1059.



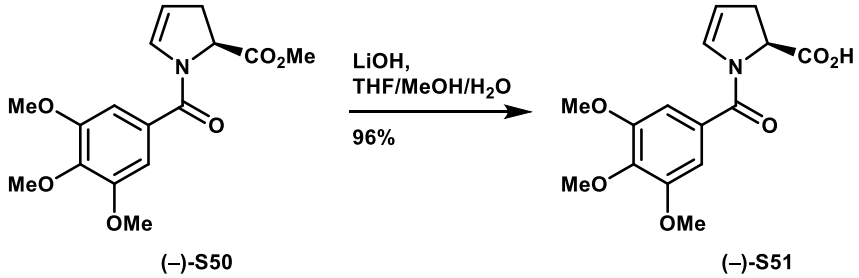
(+)-S48 (+)-S49

Methyl (2S)-4-(trifluoromethanesulfonyloxy)-1-(3,4,5-trimethoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (+)-S49. Using general procedure E, ketone **(+)-S48** (145 mg, 0.431 mmol) yielded the title compound as an orange oil (129 mg, 64% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.75 (s, 2H), 5.10 – 5.00 (m, 1H), 3.88 – 3.78 (m, 12H), 3.40 (dd, J = 15.2, 13.1 Hz, 1H), 3.00 – 2.90 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.72, 167.22, 153.49, 140.84, 134.51, 128.35, 123.32, 105.35, 61.03, 56.37, 53.10; **$[\alpha]^{25}_D$** +7.3 (c = 0.26 in $CHCl_3$); **IR** (film) 2953, 2359, 1745 (C=O), 1636 (C=O), 1582, 1413, 1326, 1234, 1120, 999, 924, 819, 760, 725, 637, 605; **HRMS** Accurate mass (ES^+): Found 470.0756 (+4.9 ppm), $C_{17}H_{19}F_3NO_9S$ ($M+H^+$) requires 470.0733.



(+)-S49 (–)-S50

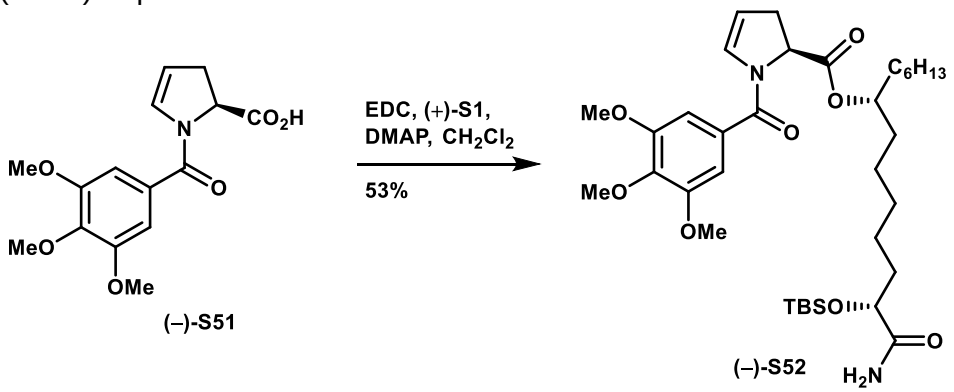
Methyl (2S)-1-(3,4,5-trimethoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S50. Using general procedure F, triflate **(+)-S49** (110 mg, 0.234 mmol) yielded the title compound as a yellow oil (61 mg, 86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.78 (s, 2H), 6.60 (s, 1H), 5.13 (s, 1H), 4.98 (dd, J = 11.2, 4.6 Hz, 1H), 3.91 – 3.76 (m, 12H), 3.16 – 3.07 (m, 1H), 2.71 (ddd, J = 17.0, 4.7, 2.3 Hz, 1H); **$[\alpha]^{25}_D$** –48.3 (c = 0.40 in $CHCl_3$); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.56, 166.79, 153.30, 140.20, 131.00, 130.21, 109.13, 105.39, 61.02, 58.61, 56.43, 52.65, 33.81; **IR** (film) 2997, 2950, 2832, 1751 (C=O), 1642 (C=O), 1619, 1582, 1506, 1462, 1404, 1361, 1315, 1235, 1196, 1177, 1143, 1119, 1000, 964, 895, 850, 810, 754, 734, 675, 570; **HRMS** Accurate mass (ES^+): Found 344.1087(-6.7 ppm), $C_{16}H_{19}NO_6Na$ ($M+Na^+$) requires 344.1110.



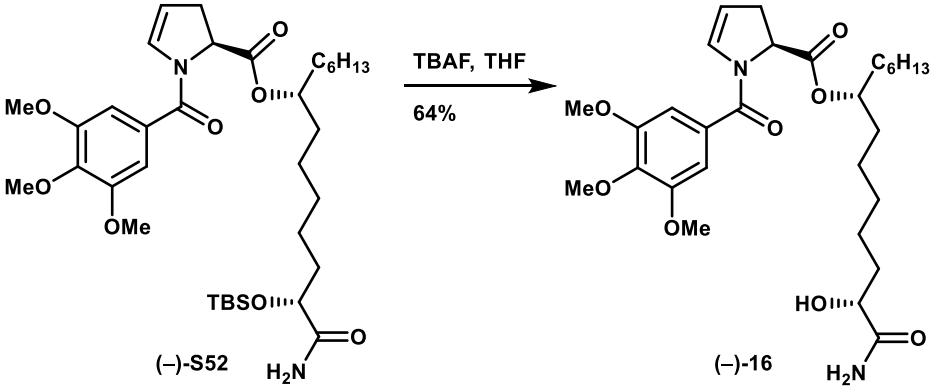
(–)-S50 (–)-S51

(2S)-1-(3,4,5-trimethoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S51. Using general procedure B, methyl ester **(–)-S50** (55 mg, 0.180 mmol) yielded the title compound as a

yellow oil (50 mg, 96% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.83 – 6.76 (m, 2H), 6.55 (s, 1H), 5.28 (d, J = 11.1 Hz, 1H), 5.06 (d, J = 6.1 Hz, 1H), 3.92 – 3.83 (m, 12H), 3.14 – 3.00 (m, 2H); **^{13}C NMR (**100 MHz, $CDCl_3$) δ 173.49, 167.90, 153.29, 140.45, 132.30, 132.20, 130.28, 129.39, 128.76, 128.64, 110.99, 105.54, 68.02, 61.02, 59.25, 56.42; **$[\alpha]^{25}_D$** –104.3 (c = 0.29 in $CHCl_3$); **IR** (film) 3269, 2954, 2899, 1747 (C=O), 1631 (C=O), 1605, 1467, 1425, 1363, 1311, 1208, 1136, 1028, 912, 833, 755, 693, 665, 605; **HRMS** Accurate mass (ES^+): Found 308.1148 (+4.5 ppm), $C_{15}H_{18}NO_6$ ($M+H^+$) requires 308.1134.

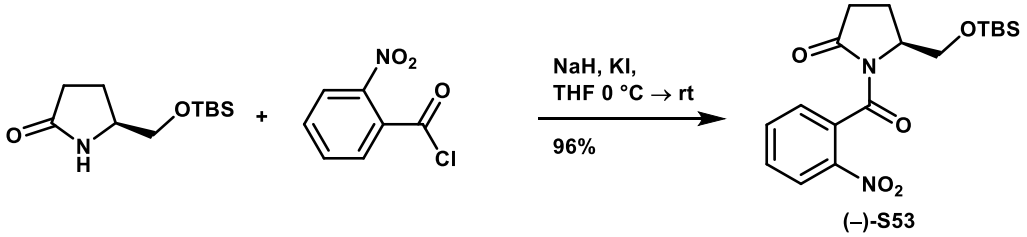


(1R,7R)-1-[(tert-butyldimethylsilyl)oxy]-1-carbamoyltridecan-7-yl (2S)-1-(3,4,5-trimethoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S52. Using general procedure G, acid **(–)-S51** (26 mg, 0.085 mmol) yielded the title compound as a yellow oil (21 mg, 53% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.78 (s, 2H), 6.58 (s, 1H), 6.53 (d, J = 4.1 Hz, 1H), 5.47 (d, J = 4.1 Hz, 1H), 5.12 (s, 1H), 5.01 – 4.91 (m, 2H), 4.13 (t, J = 5.1 Hz, 1H), 3.87 (s, 9H), 3.16 – 3.06 (m, 1H), 2.68 (d, J = 16.5 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.68 – 1.46 (m, 10H), 1.39 – 1.16 (m, 20H), 0.91 (s, J = 6.5 Hz, 9H), 0.86 (t, J = 7.0 Hz, 3H), 0.08 (d, J = 5.8 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.02, 170.84, 166.66, 153.28, 140.01, 131.08, 130.50, 129.10, 108.95, 105.25, 75.67, 73.52, 61.03, 58.84, 56.39, 35.10, 34.01, 31.83, 29.49, 29.31, 25.85, 25.30, 25.03, 24.06, 22.69, 18.13, 14.18, -4.72, -5.15; **$[\alpha]^{25}_D$** –34.7 (c = 0.86 in $CHCl_3$); **IR** (film) 3480, 2927, 2856, 1738 (C=O), 1687 (C=O), 1645 (C=O), 1616, 1582, 1506, 1456, 1414, 1358, 1236, 1192, 1126, 1004, 951, 836, 810, 778, 720, 671; **HRMS** Accurate mass (ES^+): Found 663.4066 (+3.8 ppm), $C_{35}H_{59}N_2O_8Si$ ($M+H^+$) requires 663.4041.

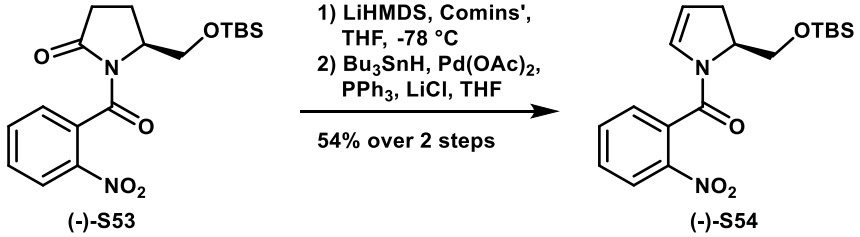


(1R,7R)-1-carbamoyl-1-hydroxytridecan-7-yl (2S)-1-(3,4,5-trimethoxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-16. To a solution of silyl ether **(–)-S52** (12.5 mg, 0.0189 mmol) dissolved in THF (0.5 mL) was added TBAF (0.094 mL, 1M in THF, 0.094 mmol). After 20 minutes, the reaction was diluted with Et_2O, and washed with sat. NH_4Cl 4x, dried over Na_2SO_4, filtered, concentrated, and purified by preparative TLC (100% EtOAc), yielding the title compound as a clear oil (6.7 mg, 64% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.96 – 6.66 (t, J = 14.9 Hz, 2H), 6.57 (s, 1H), 5.20 (dd, J = 64.4, 27.8 Hz, 2H), 5.11 – 4.96 (m, 1H), 4.96 – 4.85 (m,

1H), 4.28 (d, J = 25.3 Hz, 1H), 4.05 (d, J = 39.2 Hz, 1H), 3.87 (s, J = 6.2 Hz, 9H), 3.13 (s, 1H), 2.69 (d, J = 16.0 Hz, 1H), 1.82 (s, 1H), 1.75 – 1.40 (m, 12H), 1.35 – 1.16 (m, 10H), 0.87 (s, J = 6.3 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.45, 170.66, 167.47, 153.39, 140.28, 130.92, 129.85, 110.16, 109.95, 105.18, 75.30, 70.81, 61.09, 58.71, 56.48, 34.77, 34.04, 33.98, 33.81, 31.85, 29.25, 27.53, 25.59, 24.67, 24.28, 22.69, 14.20; **$[\alpha]^{25}_D$** –32.4 (c = 0.67 in $CHCl_3$); **IR** (film) 3337 (br O-H), 2927, 2856, 1733 (C=O), 1668 (C=O), 1614 (C=O), 1581, 1506, 1414, 1318, 1236,1194, 1124, 1002, 951, 853, 810, 756, 722, 674**;** **HRMS** Accurate mass (ES^+): Found 549.3152 (-4.4 ppm), $C_{29}H_{45}N_2O_8$ ($M+H^+$) requires 283.1366.

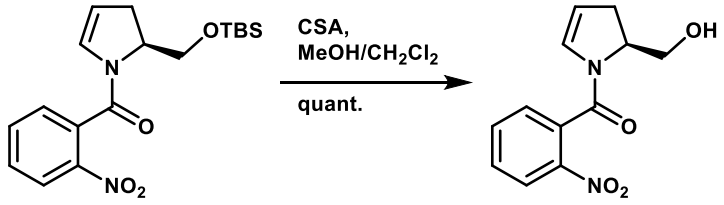


(S)-5-(((tert-butyldimethylsilyl)oxy)methyl)-1-(2-nitrobenzoyl)pyrrolidin-2-one (–)-S53. To a suspension of NaH (60% in mineral oil, 74 mg, 1.852 mmol) and KI (307 mg, 1.852 mmol) in THF (4 mL) at 0°C was added a solution of (S)-5-(((tert-butyldimethylsilyl)oxy)methyl)pyrrolidin-2-one[4] (386 mg, 1.683 mmol) dropwise in THF (2 mL). The solution was allowed to warm to room temperature and stir for 90 minutes. Then 2-nitrobenzoyl chloride (0.27 mL, 2.020 mmol) was added as a solution in THF (2 mL). After 10 minutes, the reaction was quenched with sat. NH_4Cl (10 mL) and extracted 3x with EtOAc. The combined organic layers were washed 2x with sat. Na_2CO_3, water, and brine, dried over $MgSO_4$, filtered, concentrated, and filtered through a plug of silica gel, which was washed with 3:1 hexanes:EtOAc. The filtrate was concentrated then triturated with MeOH, yielding the title compound as a white solid (609 mg, 96% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.23 (dd, J = 8.3, 0.9 Hz, 1H), 7.71 (td, J = 7.5, 1.2 Hz, 1H), 7.58 (ddd, J = 8.3, 7.5, 1.4 Hz, 1H), 7.32 (dt, J = 6.7, 3.4 Hz, 1H), 4.69 – 4.62 (m, 1H), 4.14 (dd, J = 10.4, 3.7 Hz, 1H), 3.85 (d, J = 10.6 Hz, 1H), 2.75 (dt, J = 17.8, 10.3 Hz, 1H), 2.36 (ddd, J = 17.8, 9.8, 2.0 Hz, 1H), 2.21 (ddd, J = 34.5, 22.6, 11.4 Hz, 2H), 0.90 (s, 9H), 0.11 (s, 3H), 0.11 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.70, 166.50, 145.21, 134.37, 133.47, 129.94, 127.72, 124.17, 63.52, 58.18, 32.27, 25.94, 21.33, 18.29, -5.39, -5.50; **$[\alpha]^{25}_D$** –76.1 (c = 0.77 in $CHCl_3$); **IR** (film) 2925, 2891, 2853, 1743 (C=O), 1668 (C=O), 1533, 1471, 1353, 1319, 1264, 1226, 1193, 1104, 1087, 1028, 1005, 986, 967, 872, 837, 776, 744, 703, 640, 560;; **HRMS** Accurate mass (ES^+): Found 401.1536 (+6.7 ppm), $C_{18}H_{26}N_2O_5SiNa$ ($M+Na^+$) requires 401.1509; **MP** 121.5 – 124.0°C.



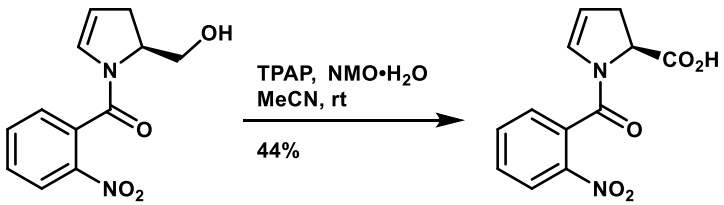
(S)-(2-(((tert-butyldimethylsilyl)oxy)methyl)-2,3-dihydro-1H-pyrrol-1-yl)(2-nitrophenyl)methanone (-)-S54. LiHMDS (1M in THF, 2.83 mL, 2.83 mmol) was diluted with THF (12 mL) and cooled to -78°C. A solution of compound **(–)-S53** (713 mg, 1.884 mmol) was added dropwise as a solution in THF (6 mL), and the reaction turned a deep purple color. After 1 hour, Comins' reagent (1.849g, 4.710 mmol) was added dropwise as a solution in THF (5 mL), and the reaction was stirred for 2 hours at -78°C, quenched with sat. NH_4Cl, warmed to room temperature, and extracted 3x with EtOAc. The combined organic layers were washed with sat $NaHCO_3$ and brine, then purified by column chromatography [triflate R_f (4:1 hexanes:EtOAc) =

0.49], which yielded the triflate intermediate as a yellow oil, which was highly unstable (decomposed overnight in a freezer). The triflate was immediately taken up in THF (15 mL) and to the resulting solution was added LiCl (240 mg, 5.651 mmol), $Pd(OAc)_2$ (42 mg, 0.188 mmol), PPh_3 (148 mg, 0.565 mmol), and Bu_3SnH (0.40 mL, 1.484 mmol) dropwise; during addition of the stannane the solution turned from a yellow suspension to a clear orange/brown solution. After 10 minutes, the reaction was quenched with aqueous 1M KF and extracted 3x with EtOAc. The combined organic layers were washed with aqueous 1M KF, water, and brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography, yielding the title compound as a yellow solid (366 mg, 54% over two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.20 (dd, J = 8.3, 1.0 Hz, 1H), 7.72 (td, J = 7.5, 1.2 Hz, 1H), 7.63 – 7.57 (m, 1H), 7.45 (dd, J = 7.6, 1.4 Hz, 1H), 5.87 – 5.83 (m, 1H), 5.15 – 5.10 (m, 1H), 4.70 (qd, J = 7.1, 3.7 Hz, 1H), 4.09 – 3.95 (m, 1H), 3.90 – 3.80 (m, 1H), 2.86 (ddt, J = 12.3, 9.9, 2.6 Hz, 1H), 2.73 (ddd, J = 17.0, 5.0, 3.3 Hz, 1H), 0.91 (s, J = 2.8 Hz, 9H), 0.11 (s, 3H), 0.10 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.35, 145.47, 134.47, 132.51, 130.27, 128.78, 128.71, 124.75, 112.36, 58.64, 32.34, 25.86, 18.23, -5.31, -5.32; **$[\alpha]^{25}_D$** –144.6 (c = 0.81 in $CHCl_3$); **IR** (film) 2952, 2929, 2856, 1633 (C=O), 1615, 1571, 1528, 1480, 1471, 1422, 1388, 1345, 1286, 1248, 1205, 1179, 1104, 1077, 1060, 1006, 969,941, 832, 775, 763, 740, 723, 701, 687, 666, 642, 607; **HRMS** Accurate mass (ES^+): Found 363.1754 (+3.9 ppm), $C_{18}H_{27}N_2O_4Si$ ($M+H^+$) requires 363.1740. **MP** 90.1 – 94.7°C.



(–)-S54 (–)-S55

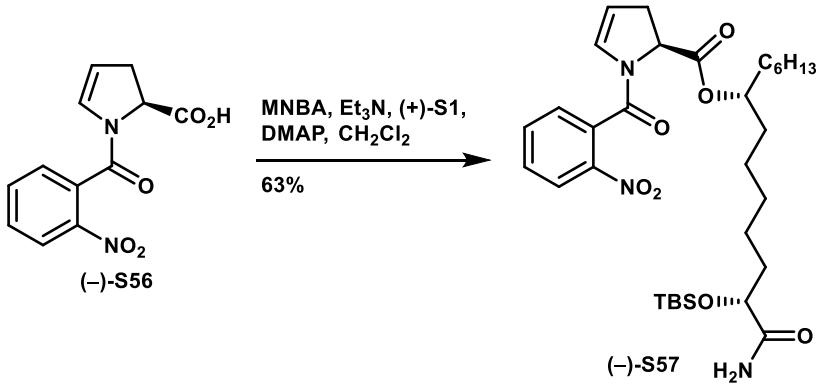
(S)-(2-(hydroxymethyl)-2,3-dihydro-1H-pyrrol-1-yl)(2-nitrophenyl)methanone (–)-S55. To a solution of compound **(–)-S54** (285 mg, 0.786 mmol) in 1:1 MeOH:CH_2Cl_2 (8 mL) was added CSA (183 mg, 0.7862 mmol). The reaction was stirred for 1 hour at rt then quenched with sat. $NaHCO_3$ and extracted 3x with CH_2Cl_2. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography, yielding the title compound as a yellow oil (209 mg, quant. yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (dd, J = 8.3, 0.9 Hz, 1H), 7.77 (td, J = 7.5, 1.1 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.52 – 7.49 (m, 1H), 5.88 (dt, J = 4.4, 2.2 Hz, 1H), 5.18 (dt, J = 4.4, 2.7 Hz, 1H), 4.78 (td, J = 10.0, 4.9 Hz, 1H), 3.92 (d, J = 4.5 Hz, 2H), 3.01 (ddt, J = 17.1, 10.5, 2.5 Hz, 1H), 2.44 (d, J = 16.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.39, 145.33, 134.82, 132.02, 130.72, 128.81, 128.69, 124.98, 113.00, 66.05, 61.30, 33.25; **$[\alpha]^{25}_D$** –105.2 (c = 1.23 in $CHCl_3$); **IR** (film) 3392 (br O-H), 2928, 2359, 2341, 1610 (C=O), 1574, 1526, 1482, 1418, 1343, 1240, 1046, 967, 789, 761, 687, 668, 643; **HRMS** Accurate mass (ES^+): Found 271.0715 (+7.4 ppm), $C_{12}H_{12}N_2O_4Na$ ($M+Na^+$) requires 271.0695.



(–)-S55 (–)-S56

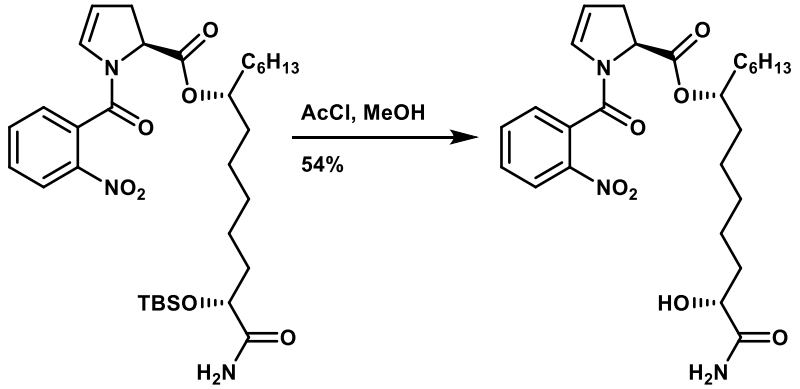
(S)-1-(2-nitrobenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylic acid (–)-S56. To a solution of compound **(–)-S55** (52 mg, 0.210 mmol) in MeCN (2 mL) was added NMO•H2O (294 mg, 2.096 mmol), and the solution was stirred until complete dissolution. Then TPAP (7 mg, 0.021 mmol) was added, and the reaction was stirred for 1 hour, quenched with IPA, concentrated, and

filtered over a plug of silica gel, which was washed with 1% AcOH/MeCN. The filtrate was concentrated and purified by column chromatography, eluting with 0 → 3% MeOH/0.1% AcOH/ CH_2Cl_2, yielding the title compound as a brown residue (24 mg, 44% yield). **1H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.1 Hz, 1H), 7.73 (t, J = 7.0 Hz, 1H), 7.64 – 7.55 (m, 2H), 5.92 (s, 1H), 5.17 (s, 1H), 5.02 (s, 1H), 3.17 – 3.01 (m, 1H), 2.97 – 2.85 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 174.39, 164.60, 145.33, 134.98, 131.34, 130.80, 129.52, 128.51, 124.76, 112.48, 99.77, 59.21, 53.58, 33.98; **$[\alpha]^{25}_D$** –127.8 (c = 0.94 in $CHCl_3$); **IR** (film) 3446, 3098, 2921, 2851, 1733 (C=O), 1615 (C=O), 1526, 1485, 1417, 1344, 1200, 1119, 1080, 1018, 941, 860, 840, 790, 762, 737, 704, 642; **HRMS** Accurate mass (ES^+): Found 263.683 (+5.7 ppm), $C_{12}H_{11}N_2O_5$ ($M+H^+$) requires 263.0668.



(–)-S56 (–)-S57

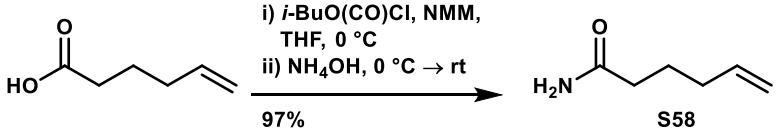
(7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl (S)-1-(2-nitrobenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (xx). Using general procedure H, acid **(–)-S56** (19 mg, 0.073 mmol), after purification by preparative TLC (2:1 CH_2Cl_2: Et_2O) yielded the title compound as a clear oil (24 mg, 63% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.2 Hz, 1H), 7.74 (td, J = 7.5, 1.0 Hz, 1H), 7.64 – 7.55 (m, 2H), 6.52 (d, J = 3.9 Hz, 1H), 6.01 (dt, J = 4.2, 2.1 Hz, 1H), 5.49 (s, 1H), 5.14 – 5.11 (m, 1H), 5.07 (dd, J = 11.7, 5.0 Hz, 1H), 5.02 – 4.95 (m, 1H), 4.14 – 4.09 (m, 1H), 3.23 – 3.15 (m, 1H), 2.72 (ddd, J = 19.5, 4.8, 2.4 Hz, 1H), 1.74 (dd, J = 14.9, 9.5 Hz, 1H), 1.69 – 1.51 (m, 6H), 1.37 – 1.21 (m, 16H), 0.90 (s, J = 3.0 Hz, 9H), 0.87 (t, J = 6.8 Hz, 3H), 0.12 – 0.04 (m, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.07, 170.65, 163.28, 145.61, 134.56, 131.99, 130.59, 129.38, 129.26, 124.80, 110.35, 75.99, 73.59, 58.19, 35.15, 34.45, 34.14, 34.09, 31.86, 29.48, 29.29, 25.87, 25.41, 25.08, 24.11, 22.71, 18.14, 14.20, -4.70, -5.14; **$[\alpha]^{25}_D$** –71.1 (c = 1.21 in $CHCl_3$); **IR** (film) 3480, 2927, 2856, 1739 (C=O), 1658 (C=O), 1622 (C=O), 1574, 1531, 1463, 1413, 1347, 1252, 1198, 1098, 1005, 940, 836, 779, 739, 705, 669, 642, 582; **HRMS** Accurate mass (ES^+): Found 618.3548 (-4.4 ppm), $C_{32}H_{52}N_3O_7Si$ ($M+H^+$) requires 618.3575.



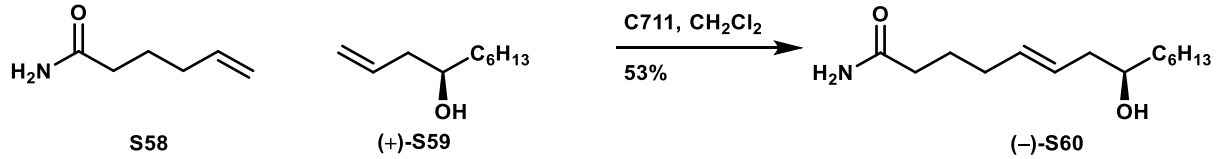
(–)-S57 (–)-17

(7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl (S)-1-(2-nitrobenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-17. To a solution of silyl ether **(–)-S57** (13 mg, 0.021 mmol)

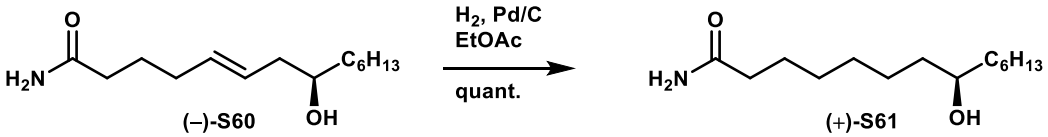
dissolved in MeOH (0.5 mL) was added acetyl chloride (ca. 1 μL, 1 drop). After 10 minutes, the reaction was diluted with EtOAc and quenched with sat. $NaHCO_3$, then extracted with EtOAc 3x. The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered, concentrated, and purified by preparative TLC (10% MeOH/CH_2Cl_2), yielding the title compound as a yellow oil (7.0 mg, 54% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.21 (dd, J = 8.3, 0.9 Hz, 1H), 7.76 (tt, J = 4.0, 2.0 Hz, 1H), 7.67 – 7.60 (m, 2H), 6.64 (s, 1H), 6.03 (dt, J = 4.4, 2.2 Hz, 1H), 5.26 – 5.21 (m, 1H), 5.20 – 5.17 (m, 1H), 5.11 – 5.02 (m, 2H), 4.04 – 3.99 (m, 1H), 3.90 (t, J = 7.0 Hz, 1H), 3.21 (ddt, J = 16.8, 11.7, 2.4 Hz, 1H), 2.76 – 2.69 (m, 1H), 1.85 – 1.76 (m, 1H), 1.68 – 1.36 (m, 16H), 1.36 – 1.20 (m, 14H), 0.88 (t, J = 7.0 Hz, 3H); **$[\alpha]^{25}_D$** –64.6 (c = 0.22 in $CHCl_3$); **IR** (film) 3350 (br, O-H), 2926, 2856, 1733 (C=O), 1652 (C=O), 1621, 1530, 1483, 1417, 1346. 1197, 1079, 840, 791, 763, 740, 705; **HRMS** Accurate mass (ES^+): Found 526.2540 (+2.1 ppm), $C_{26}H_{37}N_3O_7Na$ ($M+Na^+$) requires 526.2529.



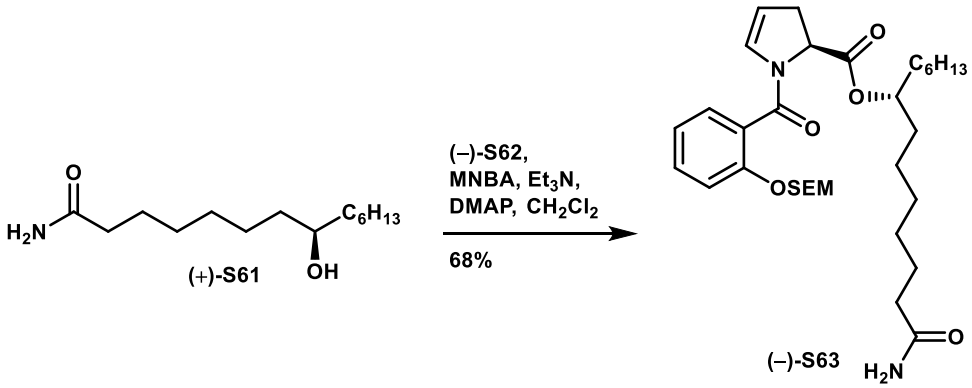
Hex-5-enamide S58. To a solution of 5-hexenoic acid (0.44 mL, 3.701 mmol) dissolved in THF (5 mL) was added N-methylmorpholine (0.45 mL, 4.071 mmol) and the solution was cooled to 0 °C. Isobutyl chloroformate (0.53 mL, 4.071 mmol) was added dropwise and the reaction was stirred at 0 °C for 30 minutes, then ammonium hydroxide (28% NH_3 in H_2O, 0.64 mL) was added and the reaction was allowed to warm to room temperature and stir overnight. The reaction was quenched with sat. NH_4Cl and extracted with EtOAc 3x. The combined organic layers were washed with 1M HCl and brine, dried over $MgSO_4$, filtered and concentrated, yielding the title compound as a white solid (407 mg, 97% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.79 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.34 (br s, 2H), 5.10 – 4.95 (m, 2H), 2.28 – 2.21 (m, 1H), 2.12 (dd, J = 14.2, 7.1 Hz, 2H), 1.82 – 1.70 (m, 1H); **^{13}C NMR** (101 MHz, CDCl3) δ 175.73, 137.90, 115.51, 35.16, 33.16, 24.57; **IR** (film) 3361 (br N-H), 3184 (br N-H), 2944, 2359, 2342, 1633 (C=O), 1415, 1229, 1135, 1077, 991, 908, 775, 667; **HRMS** Accurate mass (ES^+): Found 114.0917 (-1.8 ppm), $C_6H_{12}NO$ ($M+H^+$) requires 114.0919; **MP** 70.0 – 75.1°C.



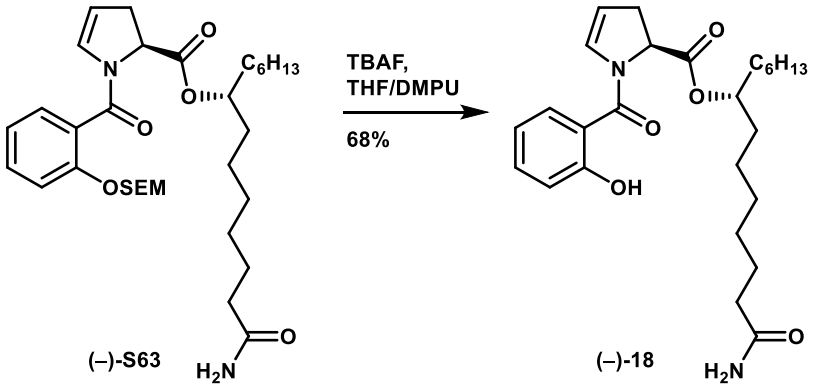
(R,E)-8-hydroxytetradec-5-enamide (–)-S60. To a solution of **S58** (41 mg, 0.362 mmol) and alcohol **(+)-S59**[5] (283 mg, 1.812 mmol) in CH_2Cl_2 (1 mL) was added catalyst C711 (13 mg, 0.018 mmol, CAS #635679-24-2). The reaction was stirred for overnight at room temperature, concentrated and purified by column chromatography (0 → 5% MeOH/CH_2Cl_2) yielding the title compound as a tan solid (46 mg, 53% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.52 – 5.44 (m, 2H), 5.30 (br s, 1H), 3.59 (br s, 1H), 2.23 (dd, J = 13.6, 6.1 Hz, 2H), 2.08 (dt, J = 14.3, 6.8 Hz, 2H), 1.74 (dt, J = 14.3, 7.2 Hz, 2H), 1.66 – 1.54 (m, 3H), 1.50 – 1.38 (m, 3H), 1.29 (t, J = 15.3 Hz, 7H), 0.93 – 0.84 (m, 10H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.13, 132.67, 127.69, 71.13, 40.68, 37.00, 35.02, 31.95, 31.90, 29.41, 25.83, 25.76, 24.93, 22.67, 14.15; **$[\alpha]^{25}_D$** –1.8 (c = 1.69 in $CHCl_3$); **IR** (film) 3361, 3183,2954, 2921, 2850, 2359, 1650 (C=O), 1416, 1349, 1268, 1202, 1126, 1068, 1040, 1008, 966, 940, 863, 647, 598, 559; **HRMS** Accurate mass (ES^+): Found 264.1950 (+3.8 ppm), $C_{14}H_{27}NO_2Na$ ($M+Na^+$) requires 264.1940; **MP** 54.6 - 56.8°C; **R_f** (5% MeOH/CH_2Cl_2) = 0.23.



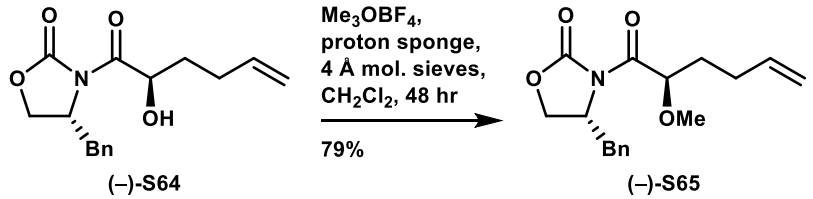
(R)-8-hydroxytetradecanamide (+)-S61. To a solution of alkene **(–)-S60** (89 mg, 0.168 mmol) dissolved in EtOAc (5 mL) was added 10% Pd/C (50 mg), then the reaction flask was vacuum and backfilled with H_2 5x and stirred under a H_2 balloon overnight. The reaction was filtered over Celite and concentrated, yielding the title compound as a white solid (91 mg, quant. yield). **^{1}H NMR (**400 MHz, $CDCl_3$) δ 5.24 (br d, 2H), 3.58 (br s, 1H), 2.38 (td, J = 7.4, 4.2 Hz, 1H), 2.27 – 2.16 (m, 2H), 1.69 – 1.60 (m, 2H), 1.48 – 1.21 (m, 18H), 0.90 – 0.85 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.89, 72.02, 37.65, 37.46, 35.99, 35.87, 31.96, 29.49, 29.45, 29.27, 25.75, 25.56, 22.74, 14.22; **$[\alpha]^{25}_D$** +7.0 (c = 1.34 in $CHCl_3$); **IR** (film) 3207 (br O-H), 2922, 2849, 1651 (C=O), 1614, 1467, 1413, 1129, 1066, 1012, 913, 850, 793, 720, 655; **HRMS** Accurate mass (ES^+): Found 266.2102 (+2.3 ppm), $C_{14}H_{29}NO_2Na$ ($M+Na^+$) requires 266.2096; **MP** 95.4 - 98.7 °C.



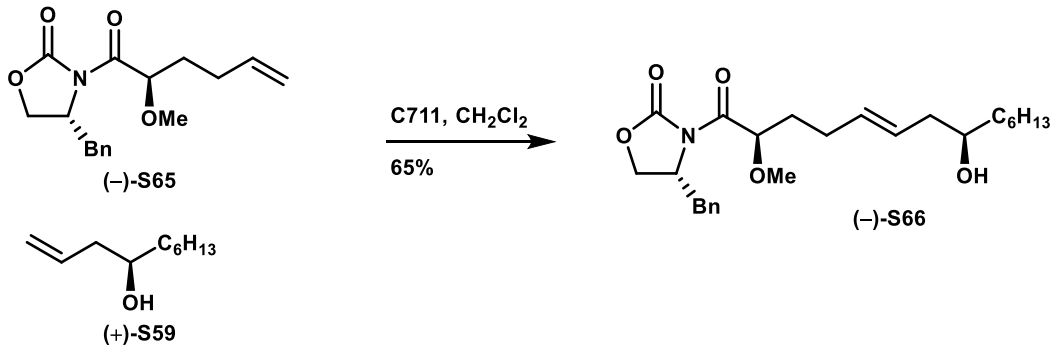
(R)-14-amino-14-oxotetradecan-7-yl (S)-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S63. Using modified general procedure H (1.2 eq acid, 1.2 eq MNBA), acid **(–)-S62**[1] (18 mg, 0.050 mmol) and alcohol **(+)-S61** (9.7 mg, 0.040 mmol) yielded the title compound as a yellow oil (16 mg, 68% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 2H), 7.19 (t, J = 8.0 Hz, 1H), 7.04 (td, J = 7.5, 0.8 Hz, 1H), 6.31 (s, 1H), 6.19 – 6.12 (m, 1H), 5.22 (ddd, J = 16.3, 7.1, 2.9 Hz, 2H), 5.11 (s, 1H), 5.04 (td, J = 5.4, 2.9 Hz, 1H), 5.03 – 4.93 (m, 2H), 3.79 – 3.69 (m, 2H), 3.19 – 3.10 (m, 1H), 2.72 – 2.64 (m, 1H), 2.23 – 2.11 (m, 1H), 1.66 – 1.52 (m, 6H), 1.45 – 1.16 (m, 16H), 0.97 – 0.90 (m, 2H), 0.90 – 0.83 (m, 3H), 0.03 – -0.05 (m, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.73, 165.29, 153.74, 131.43, 130.96, 128.89, 125.67, 122.05, 115.33, 108.77, 93.34, 75.35, 66.70, 58.08, 35.99, 34.60, 34.37, 31.85, 29.27, 28.83, 28.55, 25.48, 25.09, 24.70, 22.70, 18.15, 14.19, -1.28; **$[\alpha]^{25}_D$** –27.2 (c = 0.79 in $CHCl_3$); **IR** (film) 2925, 2856, 1738 (C=O), 1645 (C=O), 1618 (C=O), 1600, 1487, 1455, 1406, 1355, 1277, 1229, 1193, 1150, 1085, 1043, 987, 938, 917, 857, 834, 754, 696, 655; **HRMS** Accurate mass (ES^+): Found 611.3533 (+6.7 ppm), $C_{32}H_{52}N_2O_6SiNa$ ($M+Na^+$) requires 611.3492.



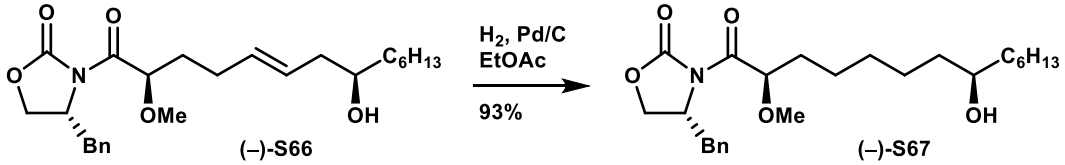
(R)-14-amino-14-oxotetradecan-7-yl (S)-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-18. Using modified general procedure I (10 eq TBAF, 0.1M DMPU), SEM ether **(–)-S63** (7.5 mg, 0.013 mmol) yielded the title compound as a clear oil (4.1 mg, 68% yield) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.83 (d, J = 46.9 Hz, 1H), 7.44 – 7.34 (m, 2H), 6.99 (dd, J = 7.4, 3.5 Hz, 1H), 6.89 (t, J = 7.8 Hz, 1H), 6.79 (s, 1H), 5.60 (br d, 1H), 5.29 (d, J = 10.2 Hz, 2H), 5.05 – 4.90 (m, 2H), 3.17 – 3.08 (m, 1H), 2.70 (d, J = 18.0 Hz, 1H), 2.23 – 2.16 (m, 2H), 1.66 – 1.48 (m, 8H), 1.39 – 1.16 (m, 15H), 0.86 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.77, 171.03, 167.50, 159.30, 158.93, 133.56, 131.00, 128.41, 119.11, 118.06, 110.79, 75.99, 74.40, 59.54, 36.00, 35.90, 34.33, 34.19, 31.82, 29.25, 29.08, 29.02, 28.91, 25.41, 25.24, 24.90, 22.69, 14.20; **[α]$^{25}_{D}$** –20.8 (c = 0.24 in $CHCl_3$); **IR** (film) 3190 (br O-H), 2926, 2856, 1733 (C=O), 1660 (C=O), 1593, 1456, 1414, 1294, 1252, 1194, 1152, 1098, 1016, 945, 912, 859, 816, 755, 723, 654, 617, 567; **HRMS** Accurate mass (ES^+): Found 481.2700 (+4.6 ppm), $C_{26}H_{38}N_2O_5Na$ ($M+Na^+$) requires 481.2678.



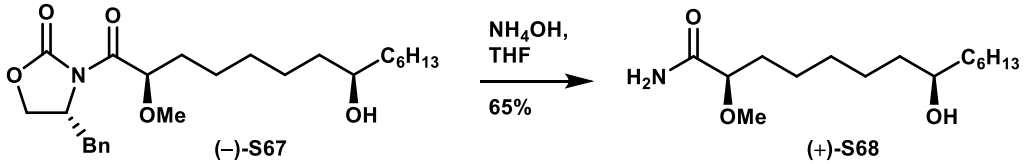
(R)-4-benzyl-3-((R)-2-methoxyhex-5-enoyl)oxazolidin-2-one (–)-S65. 4 Å molecular sieves were flame-dried in a round-bottom flask, and alcohol **(–)-S64**[1] (121 mg, 0.418 mmol) was added to the flask as a solution in CH_2Cl_2 (2 mL) followed by trimethyloxonium tetrafluoroborate (493 mg, 3.333 mmol) and 1,8-Bis(dimethylamino)naphthalene (714 mg, 3.333 mmol). The reaction was stirred at room temperature for 48 hours, then quenched with isopropanol and filtered. The solution was diluted with Et_2O and washed with 1M HCl, sat. $NaHCO_3$, and brine, dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography (4:1 hexanes:EtOAc) yielding the title compound as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 3H), 7.25 – 7.20 (m, 2H), 5.82 (ddt, J = 16.9, 10.1, 6.7 Hz, 1H), 5.09 – 4.97 (m, 2H), 4.91 (dd, J = 8.3, 3.5 Hz, 1H), 4.68 (ddt, J = 10.1, 6.7, 3.3 Hz, 1H), 4.28 – 4.21 (m, 2H), 3.42 (s, 3H), 3.36 (dd, J = 13.3, 3.1 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.26 (dt, J = 14.0, 6.9 Hz, 2H), 1.88 – 1.68 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.15, 153.22, 137.59, 135.13, 129.54, 129.11, 127.57, 115.42, 79.27, 66.87, 58.17, 55.61, 37.93, 32.13, 29.67; **[α]$^{25}_{D}$** –6.0 (c = 0.63 in $CHCl_3$); **IR** (film) 2923, 2854, 1723 (C=O), 1583, 1452, 1376, 1313, 1271, 1109, 1070, 1028, 967, 817, 743, 710; **HRMS** Accurate mass (ES^+): Found 326.1381 (+4.0 ppm), $C_{17}H_{21}NO_4Na$ ($M+Na^+$) requires 326.1368.



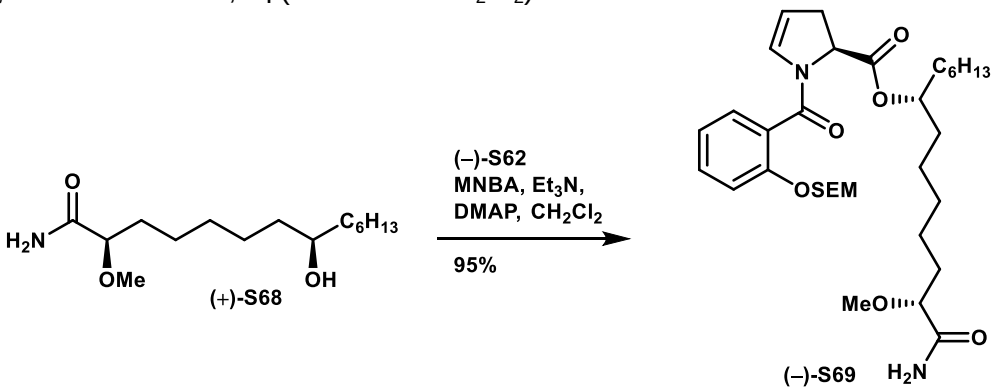
(R)-4-benzyl-3-((2R,8R,E)-8-hydroxy-2-methoxytetradec-5-enoyl)oxazolidin-2-one (–)-S66. Catalyst C711 (13 mg, 0.017 mmol - CAS #635679-24-2) was added to a solution of alcohol **(+)-S59** (258 mg, 1.651 mmol) and methyl ether **(–)-S65** (100 mg, 0.330 mmol) dissolved in CH_2Cl_2 (2 mL) and stirred at room temperature overnight. The reaction was concentrated and purified by column chromatography (4:1 hexanes:EtOAc), yielding the title compound as a yellow oil (95 mg, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 3H), 7.23 (d, J = 6.9 Hz, 2H), 5.52 (dt, J = 13.2, 8.3 Hz, 3H), 4.91 (dd, J = 8.1, 3.6 Hz, 1H), 4.73 – 4.65 (m, 1H), 4.27 – 4.20 (m, 2H), 3.60 (br s, 2H), 3.41 (s, J = 3.4 Hz, 3H), 3.39 – 3.33 (m, 1H), 2.87 – 2.78 (m, 1H), 2.32 – 2.20 (m, 3H), 2.14 – 2.07 (m, 1H), 1.85 – 1.70 (m, 2H), 1.64 – 1.56 (m, 2H), 1.51 – 1.39 (m, 6H), 1.34 – 1.24 (m, 14H), 0.88 (t, J = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.25, 153.23, 135.11, 132.69, 130.09, 129.53, 129.11, 127.56, 79.13, 70.95, 70.84, 66.91, 58.18, 55.61, 40.85, 40.72, 37.94, 37.03, 36.86, 32.68, 31.93, 29.44, 28.51, 25.80, 25.76, 22.72, 14.19; **[α]$^{25}_D$** –17.5 (c = 0.83 in $CHCl_3$); **IR** (film) 3500 (br, O-H), 2925, 2854, 1778 (C=O), 1705 (C=O), 1455, 1387, 1349, 1290, 1252, 1211, 1113, 1073, 1049, 971, 814, 761, 732, 700; **HRMS** Accurate mass (ES^+): Found 454.2585 (+3.5 ppm), $C_{25}H_{37}NO_5Na$ ($M+Na^+$) requires 454.2569.



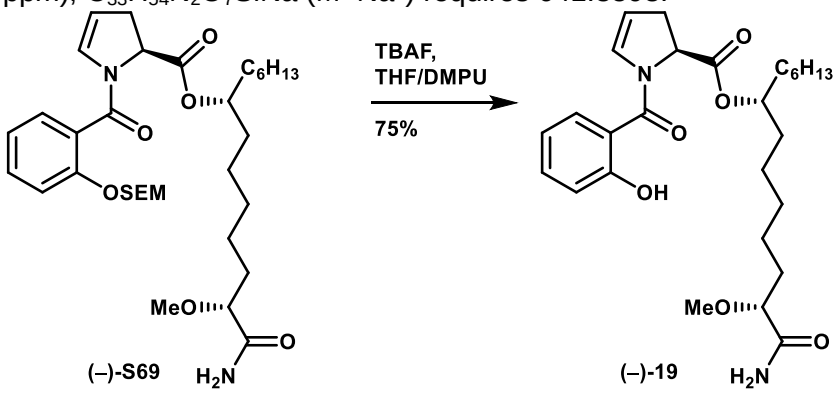
(R)-4-benzyl-3-((2R,8R)-8-hydroxy-2-methoxytetradecanoyl)oxazolidin-2-one (–)-S67. To a solution of alkene **(–)-S66** (95 mg, 0.220 mmol) dissolved in EtOAc (10 mL) in a round-bottom flask was added 10% Pd/C (50 mg), and the flask was vacuum and backfilled with H_2 5x then stirred under a balloon of H_2 overnight. The reaction was filtered over Celite and concentrated, yielding the title compound as a clear oil (89 mg, 93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 3H), 7.24 – 7.20 (m, 2H), 4.90 (dd, J = 7.9, 3.5 Hz, 1H), 4.72 – 4.66 (m, 1H), 4.28 – 4.22 (m, 2H), 3.59 (br s, 2H), 3.41 (s, 3H), 3.34 (dd, J = 7.3, 4.2 Hz, 1H), 2.83 (dd, J = 13.4, 9.5 Hz, 1H), 2.39 (dt, J = 10.8, 7.4 Hz, 1H), 1.70 – 1.59 (m, 2H), 1.50 – 1.37 (m, 10H), 1.32 – 1.23 (m, 12H), 0.88 – 0.85 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.14, 153.17, 135.05, 129.43, 128.97, 127.42, 79.81, 71.80, 71.69, 66.76, 58.04, 55.46, 37.80, 37.52, 37.47, 37.35, 37.31, 32.79, 31.85, 29.39, 29.24, 25.62, 25.39, 22.62, 14.10; **[α]$^{25}_D$** –12.0 (c = 0.93 in $CHCl_3$); **IR** (film) 2924, 2855, 1781 (C=O), 1705, 1456, 1387, 1349, 1211, 1107, 1019, 814, 754, 700, 667; **HRMS** Accurate mass (ES^+): Found 434.2911 (+1.2 ppm), $C_{25}H_{40}NO_5$ ($M+H^+$) requires 434.2906.



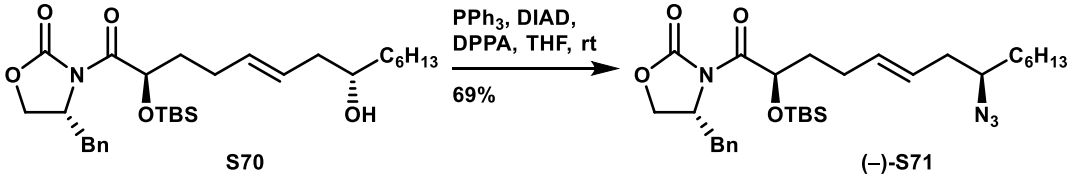
(2R,8R)-8-hydroxy-2-methoxytetradecanamide (+)-S68. To a solution of oxazolidinone **(–)-S67** (88 mg, 0.203 mmol) in THF (3 mL) was added ammonium hydroxide (28% NH_3 in H_2O, 2 mL), and the reaction was tightly sealed and stirred for 48 hours. The reaction was diluted with MeOH and concentrated, and this process was repeated 2x. Purification by column chromatography (0 → 8% MeOH/CH_2Cl_2) yielded the title compound as a white solid (36 mg, 65% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.46 (br s, 1H), 5.57 (br s, 1H), 3.62 (dd, J = 6.9, 4.4 Hz, 1H), 3.57 (br s, 1H), 3.41 (s, 3H), 1.82 – 1.74 (m, 1H), 1.73 – 1.63 (m, 2H), 1.47 – 1.35 (m, 9H), 1.35 – 1.22 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.75, 99.78, 82.49, 72.06, 58.47, 37.62, 37.47, 32.44, 31.99, 29.58, 29.51, 25.76, 25.59, 24.85, 22.76, 14.24; **$[\alpha]^{25}_D$** +21.0 (c = 0.67 in $CHCl_3$); **IR** (film) 3366 (br, N-H), 3189 (br, N-H), 2916, 2852, 1636 (C=O), 1532, 1462, 1431, 1340, 1221, 1207, 1133, 1112, 1067, 1050, 1001, 926, 859, 806, 726, 682, 617; **HRMS** Accurate mass (ES^+): Found 274.2385 (+1.1 ppm), $C_{15}H_{32}NO_3$ ($M+H^+$) requires 274.2382; **MP** 106 – 110°C, **R_f** (8% MeOH/CH_2Cl_2) = 0.36.



(7R,13R)-14-amino-13-methoxy-14-oxotetradecan-7-yl (S)-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S69. Using general procedure H, alcohol **(+)-S68** (9 mg, 0.033 mmol) and acid **(–)-S62**[1] (17 mg, 0.047 mmol) yielded the title compound as a yellow oil (19 mg, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 2H), 7.21 – 7.16 (m, 1H), 7.03 (td, J = 7.5, 0.8 Hz, 1H), 6.52 (br s, 1H), 6.20 – 6.11 (m, 1H), 5.60 (br s, 1H), 5.25 – 5.18 (m, 1H), 5.04 – 5.00 (m, 1H), 5.01 – 4.93 (m, 2H), 3.74 (dd, J = 16.0, 7.6 Hz, 2H), 3.60 (dd, J = 6.8, 4.5 Hz, 1H), 3.37 (s, 3H), 3.12 (ddd, J = 14.2, 10.4, 5.8 Hz, 1H), 2.70 – 2.62 (m, 1H), 1.77 – 1.64 (m, 2H), 1.62 – 1.48 (m, 4H), 1.41 – 1.17 (m, 17H), 0.93 (dd, J = 10.6, 6.2 Hz, 2H), 0.85 (t, J = 5.8 Hz, 3H), -0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.79, 170.79, 165.03, 153.82, 131.26, 131.02, 129.01, 125.91, 121.98, 115.24, 108.45, 99.74, 93.34, 82.37, 75.46, 66.63, 58.33, 58.16, 34.40, 34.18, 34.09, 32.33, 31.85, 29.30, 25.35, 25.01, 24.68, 22.71, 18.15, 14.20, -1.28; **$[\alpha]^{25}_D$** –10.0 (c = 0.24 in $CHCl_3$); **IR** (film) 2927, 2858, 1733 (C=O), 1652 (C=O), 1619, 1601, 1488, 1456, 1278, 1407, 1248, 1230, 1194, 1153, 1087, 988, 836, 754, 697, 656, 609; **HRMS** Accurate mass (ES^+): Found 641.3621 (+3.6 ppm), $C_{33}H_{54}N_2O_7SiNa$ ($M+Na^+$) requires 641.3598.

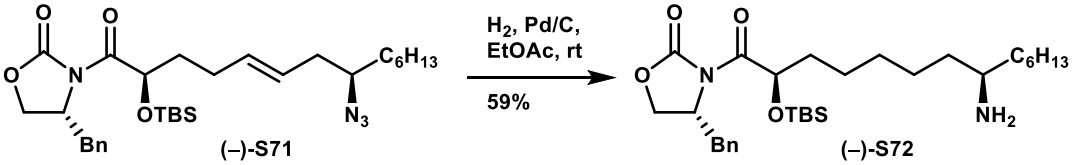


(7R,13R)-14-amino-13-methoxy-14-oxotetradecan-7-yl (S)-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-19. Using modified general procedure I (10 eq TBAF, 0.1M DMPU), SEM-ether **(–)-S69** (13.7 mg, 0.022 mmol) yielded the title compound as a clear oil (8.1 mg, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.42 (dd, J = 7.8, 1.4 Hz, 1H), 7.39 – 7.34 (m, 1H), 6.99 (dd, J = 8.3, 0.9 Hz, 1H), 6.93 – 6.86 (m, 1H), 6.81 (br s, 1H), 6.47 (br s, 1H), 5.40 (br s, 1H), 5.27 (d, J = 4.2 Hz, 1H), 5.06 – 4.91 (m, 2H), 3.61 (dd, J = 6.7, 4.5 Hz, 1H), 3.38 (s, 3H), 3.18 – 3.07 (m, 1H), 2.70 (d, J = 17.0 Hz, 1H), 1.79 – 1.62 (m, 2H), 1.61 – 1.46 (m, 5H), 1.43 – 1.17 (m, 15H), 0.85 (t, J = 6.9 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 175.68, 170.88, 167.53, 159.28, 133.54, 131.05, 128.48, 118.96, 118.09, 117.03, 110.68, 82.44, 75.98, 59.61, 58.39, 34.16, 34.09, 33.66, 32.34, 31.82, 29.27, 25.35, 25.05, 24.71, 22.69, 14.21; **$[\alpha]^{25}_D$** –21.3 (c = 0.39 in $CHCl_3$); **IR** (film) 3386 (N-H), 3348 (N-H), 3144 (br, O-H), 2927, 2858, 1719 (C=O), 1688 (C=O), 1672, 1619, 1567, 1487, 1445, 1431, 1355, 1303, 1281, 1252, 1230, 1191, 1147, 1120, 1095, 1070, 1039, 1020, 1003, 992, 954, 943, 905, 857, 822, 796, 759, 730, 699, 667, 643; **HRMS** Accurate mass (ES^+): Found 489.2979 (+2.9 ppm), $C_{27}H_{41}N_2O_6$ ($M+H^+$) requires 308.1498.



S70 (–)-S71

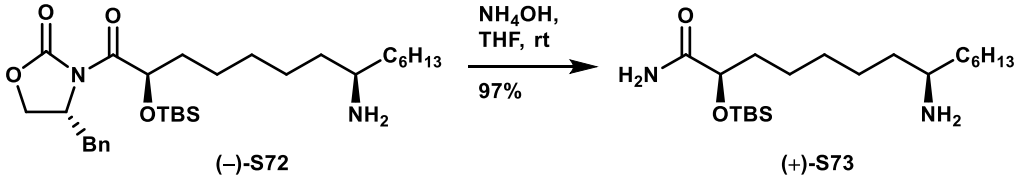
(R)-3-((2R,8R,E)-8-azido-2-((tert-butyldimethylsilyl)oxy)tetradec-5-enoyl)-4-benzyloxazolidin-2-one (–)-S71. To a solution of compound **S70**[1] (153 mg, 0.288 mmol) in THF (2 mL) was added PPh_3 (302 mg, 1.153 mmol), diisopropyl azodicarboxylate (DIAD) (0.23 mL, 1.153 mmol), and diphenylphosphoryl azide (DPPA) (0.25 mL, 1.153 mmol). After 30 minutes, the reaction was concentrated and purified by prep TLC (neat CH_2Cl_2), yielding the title compound as a yellow oil (111 mg, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 3H), 7.15 – 7.11 (m, 2H), 5.48 – 5.29 (m, 2H), 5.27 (dd, J = 8.2, 3.4 Hz, 1H), 4.55 – 4.47 (m, 1H), 4.12 – 4.04 (m, 2H), 3.30 (dd, J = 13.3, 3.0 Hz, 1H), 2.58 (dd, J = 13.2, 10.2 Hz, 1H), 2.19 – 2.01 (m, 2H), 1.72 – 1.52 (m, 2H), 1.42 – 1.26 (m, 3H), 1.26 – 1.10 (m, 8H), 0.86 – 0.82 (m, 9H), 0.77 (t, J = 6.7 Hz, 3H), 0.02 – -0.03 (m, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.33, 153.18, 135.34, 132.97, 129.56, 129.11, 127.51, 126.26, 71.01, 66.62, 62.84, 55.71, 37.79, 35.00, 33.98, 31.82, 29.17, 28.68, 26.15, 25.93, 22.69, 18.44, 14.18, 1.13, -4.49, -4.95; **$[\alpha]^{25}_D$** –5.0 (c = 0.42 in $CHCl_3$); **IR** (film) 2927, 2856, 2097, 1780 (C=O), 1712 (C=O), 1455, 1386, 1347, 1249, 1209, 1194, 1106, 1012, 969, 835, 777, 749, 700, 663, 593; **HRMS** Accurate mass (ES^+): Found 579.3367 (+4.1 ppm), $C_{30}H_{48}N_4O_4SiNa$ ($M+Na^+$) requires 579.3343.



(–)-S71 (–)-S72

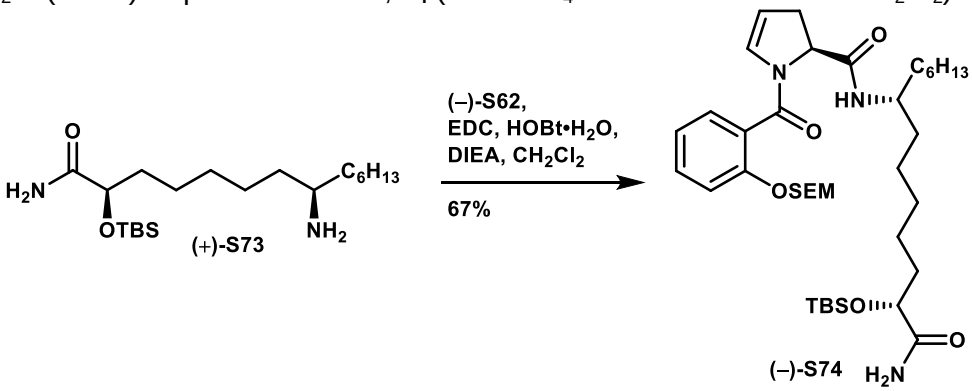
(R)-3-((2R,8R)-8-amino-2-((tert-butyldimethylsilyl)oxy)tetradecanoyl)-4-benzyloxazolidin-2-one (–)-S72. To a solution of compound **(–)-S71** (111 mg, 0.199 mmol) in EtOAc (10 mL) was added Pd/C (10% by wt., 100 mg), and stirred for 16 hours under a balloon of H_2. The reaction was filtered through Celite and purified by column chromatography, eluting in 50% → 0% hexanes/CH_2Cl_2 then 0 → 20% MeOH/CH_2Cl_2, yielding the title compound as a clear oil (63 mg, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 3H), 7.25 – 7.22 (m, 2H), 5.40 – 5.34 (m, 1H), 4.70 – 4.59 (m, 1H), 4.32 – 4.24 (m, 1H), 4.15 (dd, J = 9.0, 2.2 Hz, 1H), 3.42 – 3.35 (m, 1H), 3.15 – 3.07 (m, 1H), 2.70 (dd, J = 13.3, 10.1 Hz, 1H), 1.74 – 1.57 (m, 10H), 1.52 – 1.19 (m, 20H), 0.93 (s, 9H), 0.86 (t, J = 6.1 Hz, 3H), 0.10 (s, 3H), 0.08 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.56, 153.26, 135.40, 129.58, 129.12, 127.51, 71.45, 66.64, 55.72, 37.83, 35.33,

31.98, 29.58, 29.48, 26.15, 26.04, 25.95, 25.63, 22.77, 18.48, 14.22, -4.50, -4.95; **[α]$^{25}_{D}$** –9.3 (c = 0.45 in $CHCl_3$); **IR** (film) 2927, 2856, 1779 (C=O), 1711 (C=O), 1605, 1519, 1455, 1387, 1348, 1248, 1210, 1145, 1109, 1051, 1007, 977, 939, 835, 776, 762, 700, 663, 593; **HRMS** Accurate mass (ES^+): Found 533.3745 (-5.6 ppm), $C_{30}H_{53}N_2O_4Si$ ($M+H^+$) requires 533.3775; **R_f** (9:1 CH_2Cl_2:MeOH) = 0.18, stains brown in ninhydrin).



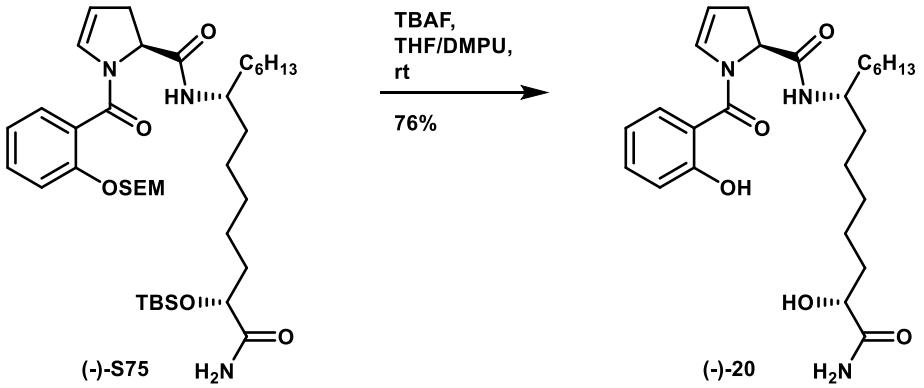
(–)-S72 (+)-S73

(2R,8R)-8-amino-2-((tert-butyldimethylsilyl)oxy)tetradecanamide (+)-S73. Compound **(–)-S72** (44 mg, 0.083 mmol) was dissolved in THF (3 mL) and 28% ammonium hydroxide (2 mL), sealed tightly and stirred at rt for 48 hours. MeOH was added and the reaction was concentrated, and this process was repeated two more times. The resulting mixture was purified by column chromatography, eluting in 0 → 15% MeOH/0.1% NH_4OH/CH_2Cl_2, yielding the title compound as a clear oil (29 mg, 97% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.64 – 6.50 (m, 2H), 4.15 – 4.09 (m, 1H), 3.12 (dt, J = 14.7, 7.4 Hz, 2H), 1.79 (ddd, J = 15.1, 10.2, 4.9 Hz, 1H), 1.75 – 1.57 (m, 6H), 1.45 – 1.23 (m, 22H), 0.91 (s, 9H), 0.86 (t, J = 6.6 Hz, 3H), 0.09 (s, 3H), 0.08 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.56, 73.20, 52.12, 34.60, 33.25, 32.94, 31.71, 29.78, 29.20, 29.04, 25.84, 25.40, 24.94, 23.51, 22.68, 18.11, 14.16, -4.73, -5.16; **[α]$^{25}_{D}$** +5.8 (c = 1.47 in $CHCl_3$); **IR** (film) 3477, 2925, 2854, 1672 (C=O), 1557, 1462, 1388, 1361, 1337, 1252, 1101, 1005, 938, 836, 778, 721, 668, 588; **HRMS** Accurate mass (ES^+): Found 373.3264 (+3.8 ppm), $C_{20}H_{45}N_2O_2Si$ ($M+H^+$) requires 373.3250; **R_f** (0.1% NH_4OH/10% MeOH/90% CH_2Cl_2) = 0.18.

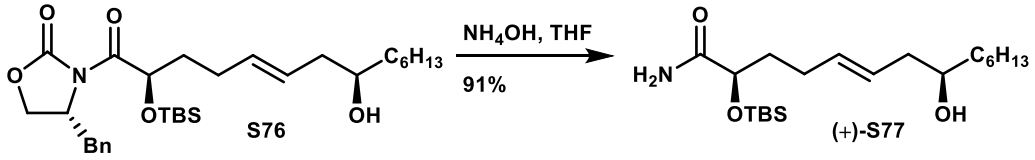


(S)-N-((7R,13R)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradecan-7-yl)-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxamide (–)-S74. To a solution of acid **(–)-S62**[1] (19 mg, 0.053 mmol) dissolved in CH_2Cl_2 (1 mL), was added EDC (9 mg, 0.056 mmol), HOBt•H_2O (9 mg, 0.056 mmol), DIEA (0.02 mL, 0.113 mmol), and amine **(+)-S73** (14 mg, 0.038 mmol) dissolved in CH_2Cl_2 (1 mL). The reaction was stirred overnight, then poured into water, extracted 3x with CH_2Cl_2, washed with water and brine, dried over $MgSO_4$ and purified by column chromatography, eluting in 0 → 20% Et_2O/CH_2Cl_2, yielding the title compound as a yellow oil (18 mg, 67% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 1H), 7.25 (d, J = 8.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.98 (s, 1H), 6.52 (d, J = 4.3 Hz, 1H), 6.11 – 6.02 (m, 1H), 5.52 (s, 1H), 5.23 (t, J = 7.2 Hz, 2H), 5.19 – 5.14 (m, 1H), 5.09 (dd, J = 15.0, 5.4 Hz, 1H), 4.18 – 4.08 (m, 1H), 3.93 (s, 1H), 3.77 – 3.69 (m, 2H), 3.18 – 2.89 (m, 2H), 1.80 – 1.45 (m, 6H), 1.40 – 1.17 (m, 22H), 0.96 – 0.89 (m, 12H), 0.88 – 0.81 (m, 3H), 0.08 (s, 3H), 0.08 (s, 3H), -0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.95, 169.89, 153.58, 131.57, 129.66, 128.59, 125.53, 122.27, 114.83, 111.81, 93.28, 73.55, 66.95, 59.47, 56.12, 49.30, 35.34, 35.07, 31.87, 29.84, 29.58, 29.36, 25.87, 24.17, 22.74, 18.22, 18.15, 14.21, 1.16, -1.25, -4.69, -5.12; **[α]$^{25}_{D}$** –46.4 (c = 0.74 in $CHCl_3$); **IR** (film) 3480, 3295, 2926, 2855, 1662, 1618, 1551, 1487,

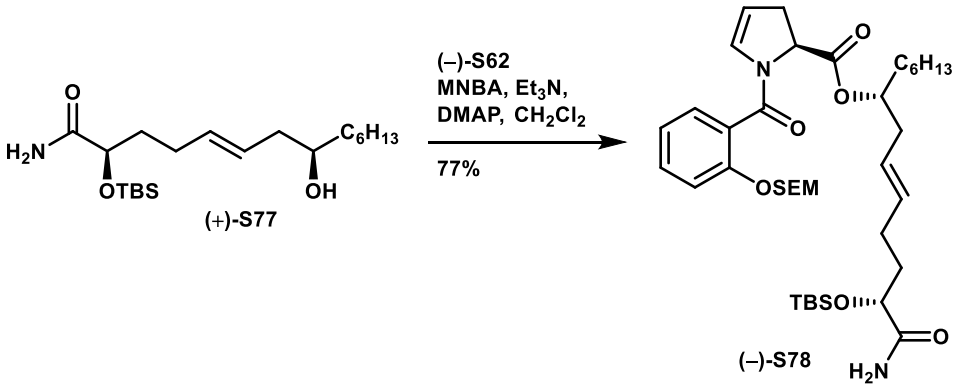
1455, 1404, 1249, 1228, 1087, 985, 938, 778, 754, 730, 667, 506; **HRMS** Accurate mass (ES^+): Found 740.4447 (-2.6 ppm), $C_{38}H_{67}N_3O_6Si_2Na$ ($M+Na^+$) requires 740.4466; $\mathbf{R_f}$ (1:1 Et_2O:CH_2Cl_2) = 0.51.



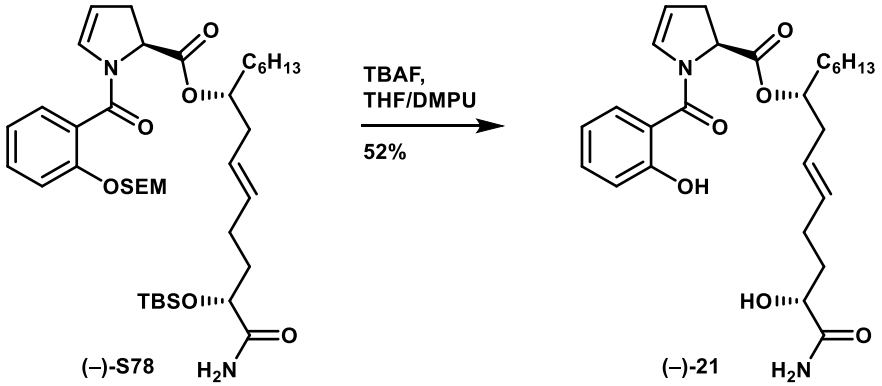
(S)-N-((7R,13R)-14-amino-13-hydroxy-14-oxotetradecan-7-yl)-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxamide (–)-20. Using general procedure I, silyl ether **(–)-S75** (15 mg, 0.021 mmol) yielded the title compound as translucent oil (7.6 mg, 76% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.33 (t, J = 7.2 Hz, 2H), 6.97 (d, J = 8.2 Hz, 1H), 6.89 (t, J = 7.3 Hz, 1H), 6.82 (s, 1H), 6.61 (s, 1H), 6.45 (s, 1H), 5.74 (s, 1H), 5.26 (s, 1H), 5.08 – 4.99 (m, 1H), 4.14 (s, 1H), 4.03 (s, 1H), 3.92 (s, 1H), 3.07 – 2.96 (m, 1H), 2.90 (d, J = 15.2 Hz, 1H), 1.81 (d, J = 69.1 Hz, 2H), 1.64 – 1.11 (m, 22H), 0.86 (t, J = 6.5 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.87, 170.68, 167.49, 156.12, 132.93, 130.44, 128.40, 119.71, 117.58, 112.13, 71.27, 60.12, 49.71, 35.65, 34.89, 33.89, 31.89, 29.32, 28.13, 26.13, 25.18, 24.29, 22.73, 14.22; $\mathbf{[\alpha]^{25}_D}$ –57.5 (c = 0.76 in $CHCl_3$); **IR** (film) 3287 (br, O-H), 2927, 2856, 1653 (C=O), 1616 (C=O), 1558, 1540, 1507, 1489, 1457, 1398, 1295, 1235, 1155, 1096, 1016, 944, 855, 817, 754, 723, 653, 620, 566; **HRMS** Accurate mass (ES^+): Found 496.2817 (+6.0 ppm), $C_{26}H_{39}N_3O_5Na$ ($M+Na^+$) requires 496.2787; $\mathbf{R_f}$ (5% MeOH/ 95% CH_2Cl_2) = 0.23.



(2R,8R,E)-2-((tert-butyldimethylsilyl)oxy)-8-hydroxytetradec-5-enamide (+)-S77. To a solution of oxazolidinone **S76**[1] (50 mg, 0.094 mmol) dissolved in THF (3 mL) was added ammonium hydroxide (28% in H_2O, 2 mL). The reaction was tightly sealed and stirred for 24 hours. Another portion of ammonium hydroxide (1 mL) was added after this time, and the reaction was stirred for another 24 hours. The reaction was diluted with MeOH and concentrated. This process was repeated another 2x, and the crude product was purified by column chromatography (0 → 30% Et_2O/CH_2Cl_2 → 5% MeOH/30% Et_2O/65% CH_2Cl_2), yielding the title compound as a yellow oil (32 mg, 91% yield). **^{1}H NMR (**400 MHz, $CDCl_3$) δ 6.63 – 6.46 (m, 1H), 5.60 – 5.40 (m, 3H), 4.21 – 4.12 (m, 1H), 3.55 (d, J = 16.1 Hz, 1H), 2.28 – 1.99 (m, 4H), 1.95 – 1.80 (m, 1H), 1.80 – 1.71 (m, 3H), 1.47 – 1.39 (m, 2H), 1.33 – 1.23 (m, 6H), 0.93 (s, J = 2.9 Hz, 9H), 0.88 (t, J = 6.7 Hz, 3H), 0.13 – 0.07 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.15, 133.16, 126.95, 72.95, 71.03, 56.05, 40.79, 36.87, 34.91, 31.92, 29.44, 27.36, 25.82, 22.70, 18.09, 14.18, -4.73, -5.15; $\mathbf{[\alpha]^{25}_D}$ +9.3 (c = 1.64 in $CHCl_3$); **IR** (film) 3479, 2954, 2927, 2855, 1682 (C=O), 1556, 1463, 1388, 1361, 1253, 1101, 1005, 967, 912, 836, 778, 722, 669, 578; **HRMS** Accurate mass (ES^+): Found 394.2757 (+1.0 ppm), $C_{20}H_{41}NO_3SiNa$ ($M+Na^+$) requires 394.2753; $\mathbf{R_f}$ (2:1 CH_2Cl_2:Et_2O) = 0.25.



(7R,13R,E)-14-amino-13-((tert-butyldimethylsilyl)oxy)-14-oxotetradec-9-en-7-yl (S)-1-(2-((2-(trimethylsilyl)ethoxy)methoxy)benzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-S78. Using general procedure H, acid **(–)-S62** (22 mg, 0.060 mmol) and alcohol **(+)-S77** (16 mg, 0.043 mmol) yielded the title compound as a yellow oil (24 mg, 77% yield). **^{1}H NMR** (500 MHz, CDCl3) δ 7.38 – 7.31 (m, 2H), 7.20 (d, J = 8.2 Hz, 1H), 7.03 (td, J = 7.5, 0.8 Hz, 1H), 7.00 – 6.92 (m, 1H), 6.53 (d, J = 4.2 Hz, 1H), 6.15 (dd, J = 4.2, 2.1 Hz, 1H), 5.70 (s, 1H), 5.44 (dtd, J = 22.1, 15.3, 6.6 Hz, 2H), 5.27 – 5.19 (m, 2H), 5.06 – 4.90 (m, 3H), 4.19 – 4.09 (m, 1H), 3.79 – 3.69 (m, 2H), 3.16 – 3.06 (m, 1H), 2.70 – 2.63 (m, 1H), 2.33 – 2.26 (m, 2H), 2.14 – 2.02 (m, 3H), 1.89 – 1.78 (m, 2H), 1.77 – 1.68 (m, 2H), 1.61 – 1.51 (m, 3H), 1.35 – 1.17 (m, 12H), 0.96 – 0.89 (m, 9H), 0.86 (t, J = 6.9 Hz, 3H), 0.11 – 0.06 (m, 6H), -0.02 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 176.80, 170.68, 164.99, 153.84, 132.90, 131.25, 131.00, 128.99, 125.92, 125.52, 121.97, 115.21, 108.43, 93.33, 74.91, 73.13, 66.63, 58.24, 37.36, 34.89, 34.39, 33.45, 31.84, 30.43, 29.82, 29.26, 27.44, 25.86, 25.28, 22.70, 18.15, 14.19, -1.28, -4.70, -5.12; **$[\alpha]^{25}_{D}$** –19.8 (c = 1.20 in $CHCl_3$); **IR** (film) 3479, 2952, 2926, 2856, 1736 (C=O), 1689, 1650, 1619, 1600, 1488, 1455, 1406, 1359, 1249, 1230, 1191, 1151, 1087, 1043, 988, 917, 778, 754; **HRMS** Accurate mass (ES^+): Found 717.4299 (-4.3 ppm), $C_{38}H_{65}N_2O_7Si_2$ ($M+H^+$) requires 717.4330; **R_f** (2:1 CH_2Cl_2:Et_2O) = 0.76.



(7R,13R,E)-14-amino-13-hydroxy-14-oxotetradec-9-en-7-yl (S)-1-(2-hydroxybenzoyl)-2,3-dihydro-1H-pyrrole-2-carboxylate (–)-21. Using general procedure I, silyl ether **(–)-S78** (24 mg, 0.034 mmol) yielded the title compound as a clear oil (8.3 mg, 52% yield). **^{1}H NMR** (500 MHz, CDCl3) δ 9.06 (s, 1H), 7.42 – 7.34 (m, 2H), 7.03 – 6.95 (m, 1H), 6.95 – 6.87 (m, 1H), 6.62 (d, J = 17.8 Hz, 2H), 5.52 (s, 2H), 5.35 – 5.29 (m, 1H), 5.29 – 5.23 (m, 1H), 5.03 (dd, J = 11.5, 4.6 Hz, 2H), 4.08 – 4.00 (m, 1H), 3.90 (s, 1H), 3.20 – 3.08 (m, 1H), 2.70 (d, J = 17.2 Hz, 1H), 2.34 – 2.11 (m, 2H), 1.96 – 1.87 (m, 1H), 1.72 – 1.49 (m, 5H), 1.34 – 1.18 (m, 10H), 0.87 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.53, 171.32, 167.40, 157.36, 133.41, 132.37, 130.76, 128.36, 126.87, 119.55, 118.26, 118.03, 111.07, 70.14, 59.13, 37.82, 34.65, 33.75, 33.34, 31.79, 29.16, 27.87, 25.45, 22.66, 14.20; **$[\alpha]^{25}_{D}$** –40.3 (c = 0.83 in $CHCl_3$); **IR** (film) 3200 (br, O-H), 2926, 2855, 1733 (C=O), 1662 (C=O), 1592, 1487, 1430,1194, 1152, 1097, 1017,

969, 860, 755; **HRMS** Accurate mass (ES^+): Found 473.2689 (+7.8 ppm), $C_{26}H_{37}N_2O_6$ ($M+H^+$) requires 473.2652.

1.3 References

1) Steele, A. D.; Knouse, K. W.; Keohane, C. E.; Wuest, W. M. *J. Am. Chem. Soc.* **2015**, *137* (23), 7314.
2) Prepared as previously described: Yoshifuji, S.; Kaname, M. *Chem. Pharm. Bull.* **1995**, *43* (8), 1302; with general procedure D in place of Swern oxidation.
3) Li, X.; Li, Y.; Xu, W. *Bioorg. & Med. Chem.* **2006**, *14* (5), 1287.
4) Torssell, S., Wanngren, E., Somfai, P. *J. Org. Chem.* **2007**, *72* (11), 4246.
5) Hanawa, H.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125* (7), 1708.

2. Biology

2.1 Bacterial Strains and Culture Conditions

P. aeruginosa PA01, and PA14 were gifts from Prof. George O'Toole (Dartmouth Medical School). Bacterial cultures were grown from freezer stocks overnight (16-24 hr) with shaking at 37°C in Tryptic Soy Broth (TSB) media (10 mL). Growth curves were obtained for PA01 and PA14 to determine the OD of each strain in exponential growth; OD readings at 595 nm were taken every 10 minutes for 6 hours in a plate reader at 37°C with shaking and repeated six times (Figure S1).

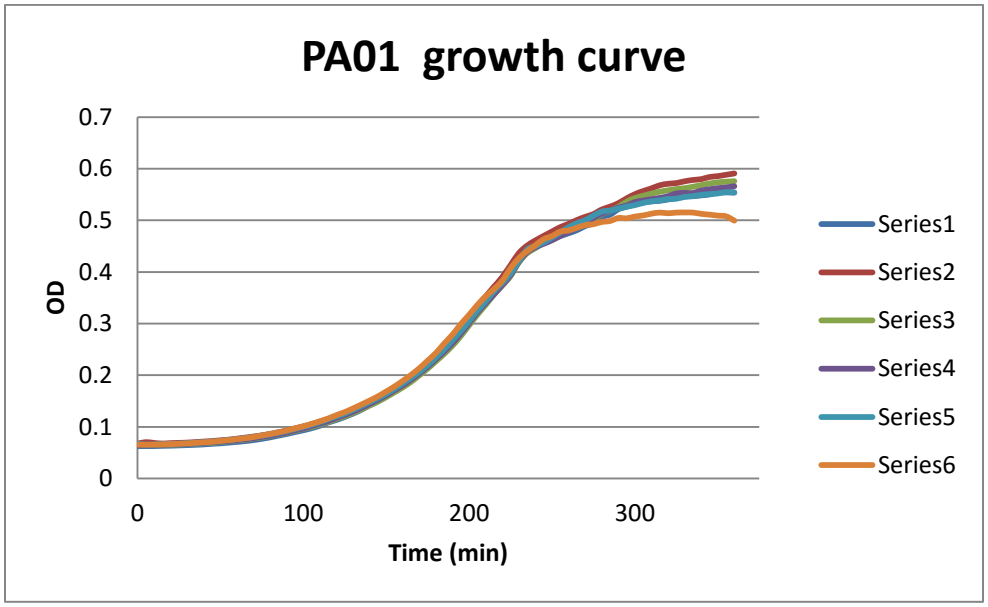


Figure S1. PA01 growth curve: OD_{595} readings over a period of 6 hours.

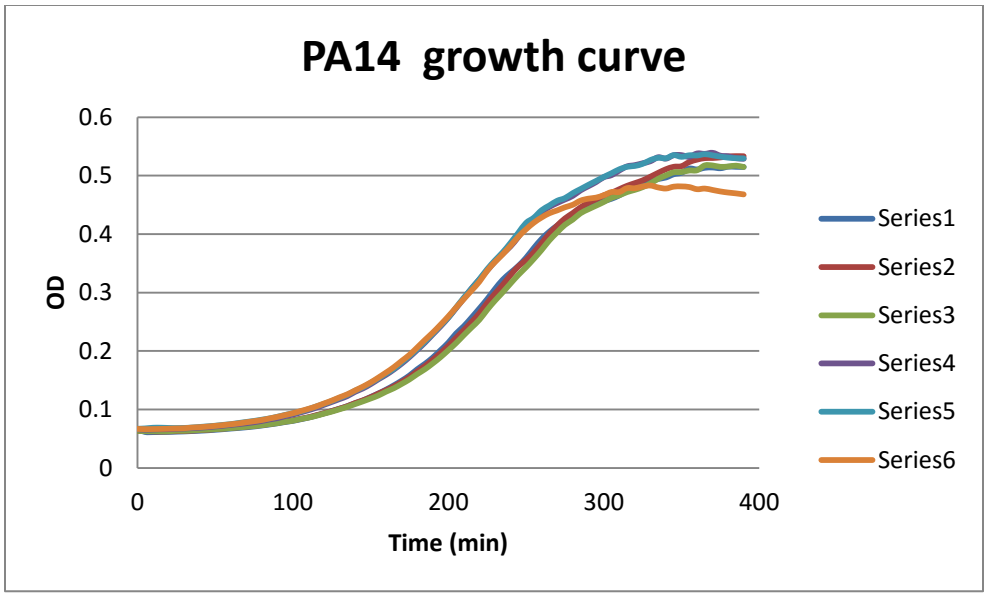


Figure S2. PA14 growth curve: OD_{595} readings over a period of 6 hours.

2.2 IC_{50} Assay

Compounds were serially diluted in sterile DI water from a stock solution (1 mM in 10% DMSO/90% H_2O) to yield twenty-four test concentrations. Overnight cultures were diluted 1:100 in 5 mL fresh media and grown with shaking at 37 °C to an OD of 0.32 (see growth curves). Bacteria were diluted to a concentration of 0.004 using the following equation:

(x µL O/N)(OD reading) = (0.004)(volume needed)

and 100 µL was inoculated into each well of a flat-bottom 96-well plate (Corning 3370) containing 100 µL of compound solution. Plates were incubated statically at 37°C for 24 hours, upon which time the OD at 595 nm was measured using a plate reader. IC_{50} values were calculated by fitting the OD readings vs. concentration with a 4 parameter logistic model. Controls were prepared by serially diluting a 10% DMSO/90% H_2O the same as the compound stock solution. Compounds were tested in triplicate from separate O/N cultures and results averaged.

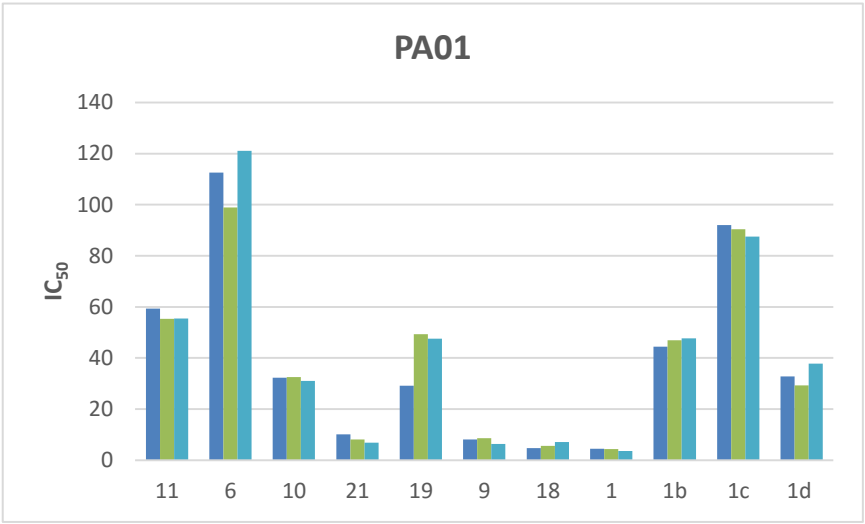


Figure S3. Compiled IC_{50} values for active analogs against PA01.

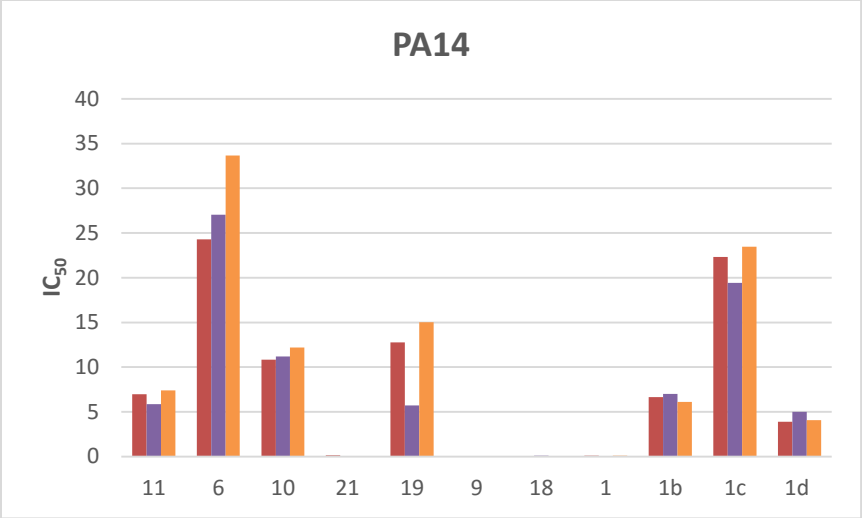


Figure S4. Compiled IC_{50} values for active analogs against PA14.

	PA01					PA14				
	TRIAL 1 (μM)	TRIAL 2 (μM)	TRIAL 3 (μM)	AVERAGE (μM)	ST. DEV (μM)	TRIAL 1 (μM)	TRIAL 2 (μM)	TRIAL 3 (μM)	AVERAGE (μM)	ST. DEV (μM)
11	59.28	55.37	55.49	56.71	2.22	6.98	5.86	7.39	6.74	0.791
6	112.60	98.88	121.10	110.86	11.21	24.28	27.05	33.66	28.33	4.82
10	32.26	32.53	31.07	31.95	0.78	10.83	11.18	12.18	11.40	0.70
21	10.13	8.07	6.81	8.34	1.67	0.12	0.05	0.03	0.067	0.044
19	29.15	49.29	47.56	38.34	11.69	12.78	5.72	15.03	11.18	4.86
9	8.11	8.57	6.41	7.70	1.14	0.04	0.01	0.01	0.019	0.019
18	4.78	5.64	7.12	5.85	1.18	0.02	0.09	0.00	0.035	0.048
1 (R,R)	4.44	4.37	3.54	4.12	0.50	0.10	0.02	0.08	0.067	0.042
1b (R,S)	44.44	46.88	47.67	46.33	1.68	6.64	7.02	6.10	6.59	0.46
1c (S,S)	92.05	90.36	87.58	90.00	2.26	22.31	19.44	23.45	21.73	2.07
1d (S,R)	32.72	29.25	37.85	33.27	4.33	3.88	5.01	4.08	4.32	0.60

Table S1. Values of all IC_{50} trials of active analogs against PA01 and PA14.

2.3 CAS Assay

CAS agar was prepared as described previously (Cordero, O. X.; Ventouras, L.; DeLong, E. F.; Polz, M. F., *PNAS*, **2012**, *109*, 49, 29059). 10 μL of solution at given concentration were dosed onto plates and imaged after 24 hours. Stock solutions were made in 10% DMSO/H_2O.

CAS Liquid Assay: To 100 μL of CAS-Fe-HDTMA dye was added 100 μL of water (control), 100 μL of 1 mM promysalin, or 100 μL 1mM EDTA with 2 μL shuttle solution (0.2 M 5-sulfosalicylic acid in water). Optical density measurements were taken at 630 nm.

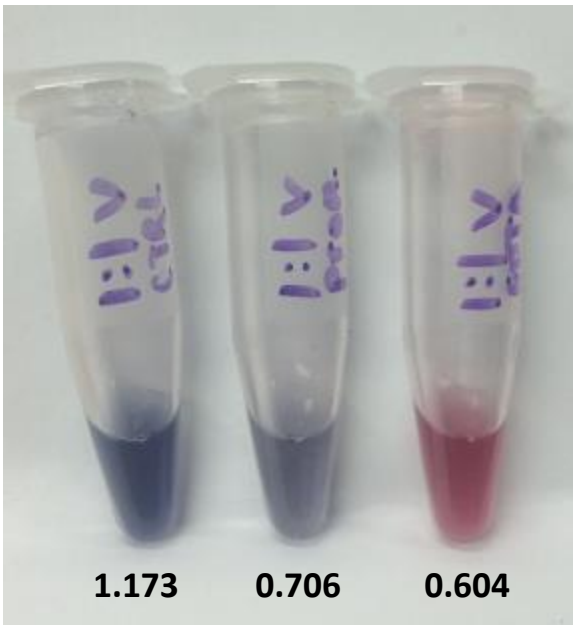
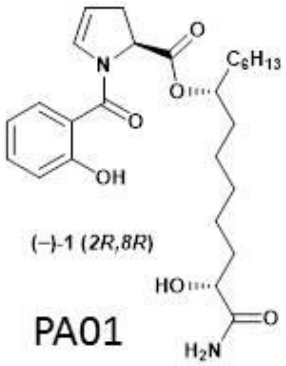
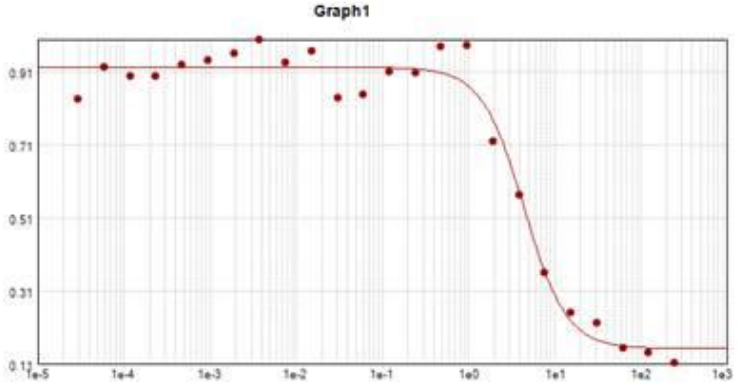


Figure S5. (L to R) Control, promysalin, and EDTA. Numbers below to tubes indicate the OD_{630} of the solution above.

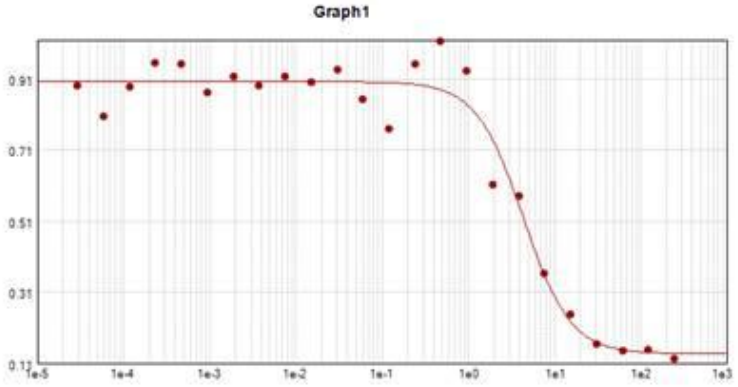
3. Appendix: IC_{50} & Spectral Data





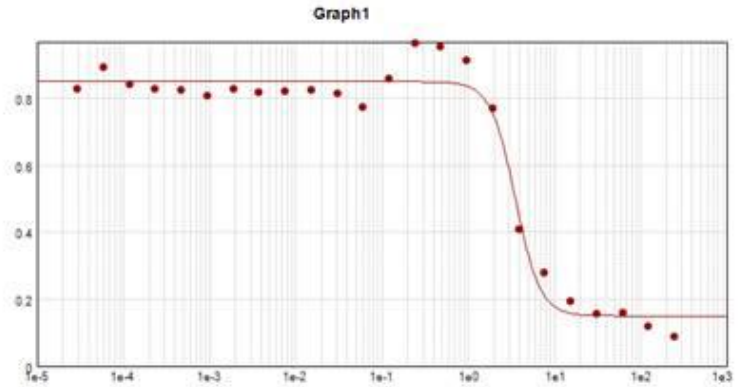
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.976 EC50 = 4.437	A	0.923
	B	1.769
	C	4.437
	D	0.151



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

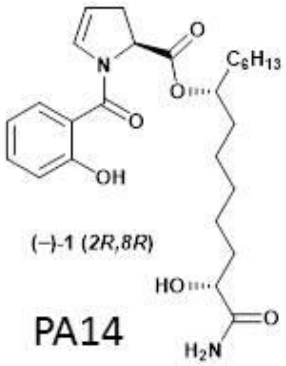
	Parameter	Estimated Value
Plot1 R^2 = 0.963 EC50 = 4.370	A	0.902
	B	1.592
	C	4.370
	D	0.136

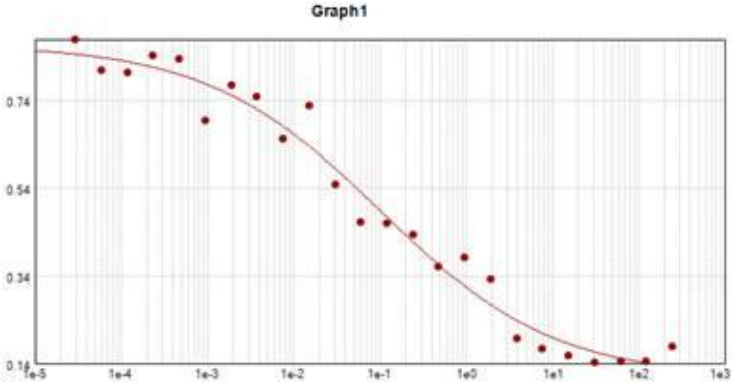


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.973 EC50 = 3.544	A	0.851
	B	3.040
	C	3.544
	D	0.150

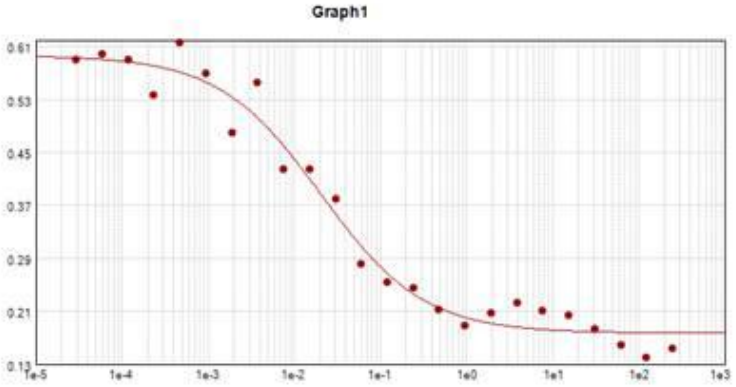
3. Appendix: IC_{50} & Spectral Data





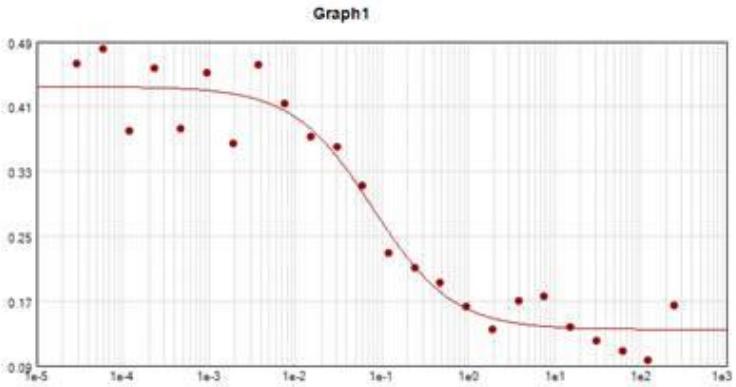
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.975 EC50 = 0.103	A	0.868
	B	0.430
	C	0.103
	D	0.106



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

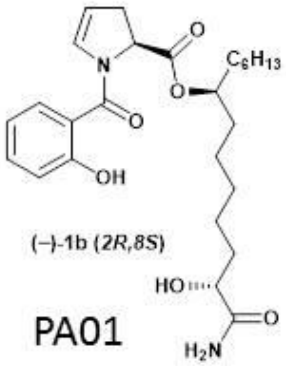
	Parameter	Estimated Value
Plot1 R^2 = 0.974 EC50 = 0.021	A	0.596
	B	0.730
	C	0.021
	D	0.177

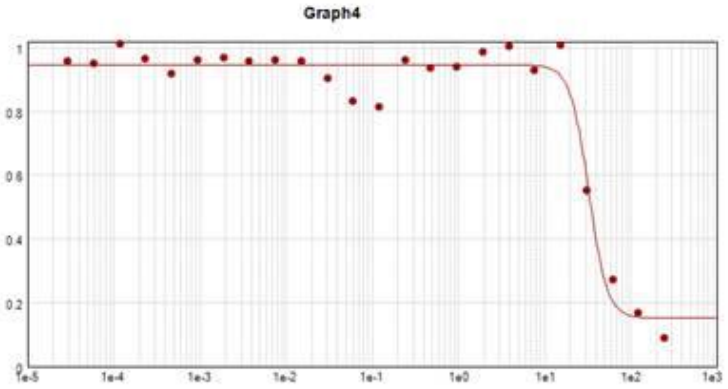


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.948 EC50 = 0.079	A	0.435
	B	0.940
	C	0.079
	D	0.135

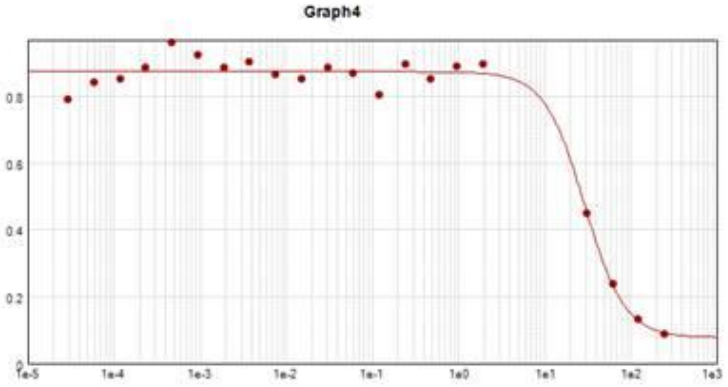
3. Appendix: IC_{50} & Spectral Data





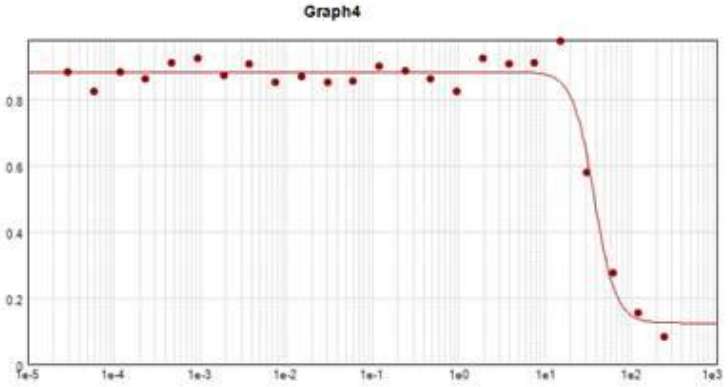
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.962 EC50 = 32.72	A	0.947
	B	4.089
	C	32.72
	D	0.151



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

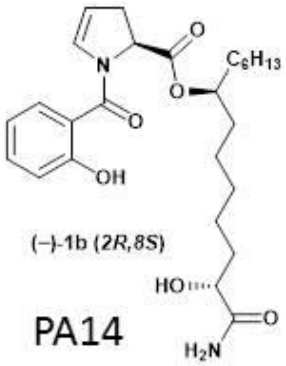
	Parameter	Estimated Value
Plot1 R^2 = 0.981 EC50 = 29.25	A	0.875
	B	1.869
	C	29.25
	D	0.077

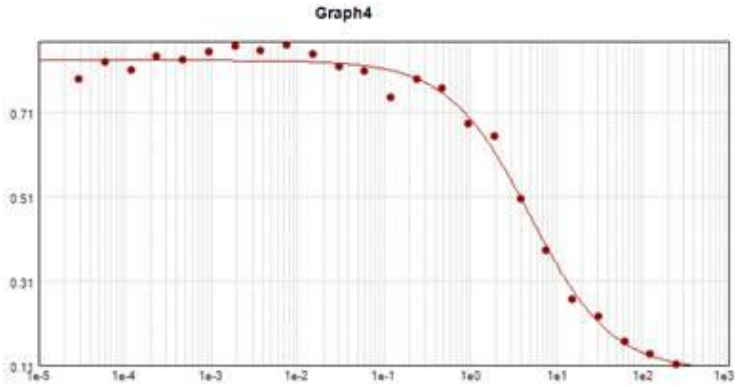


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.972 EC50 = 37.85	A	0.883
	B	3.505
	C	37.85
	D	0.124

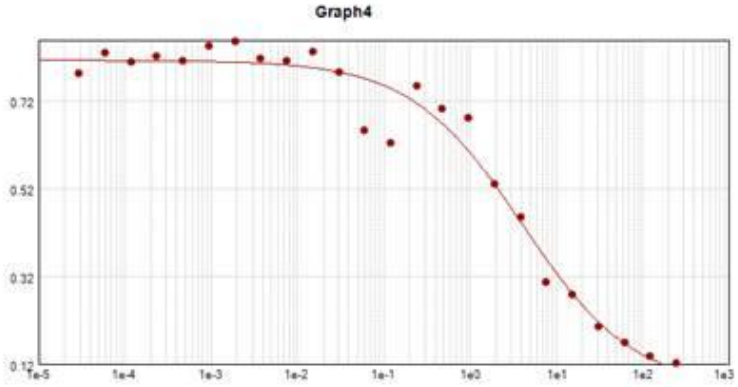
3. Appendix: IC_{50} & Spectral Data





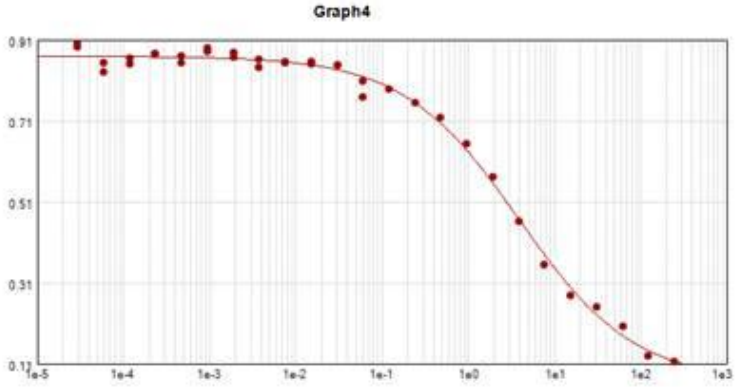
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.992 EC50 = 5.010	A	0.834
	B	0.918
	C	5.010
	D	0.096



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

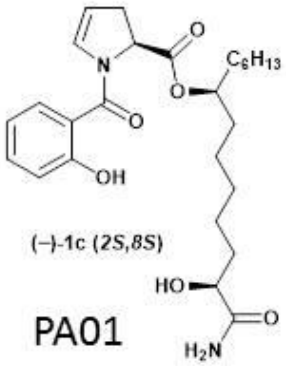
	Parameter	Estimated Value
Plot1 R^2 = 0.970 EC50 = 4.082	A	0.814
	B	0.673
	C	4.082
	D	0.064

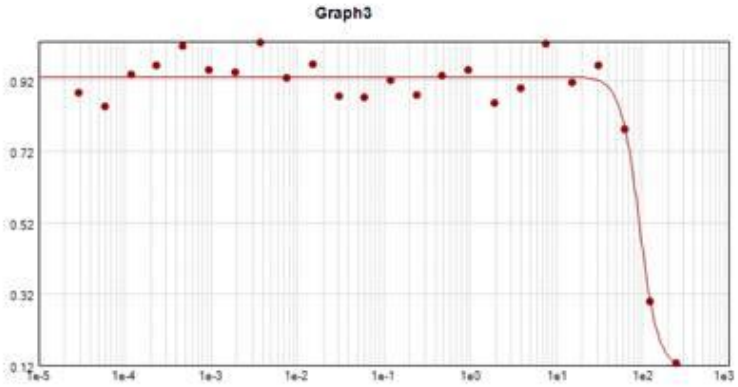


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.995 EC50 = 3.877	A	0.869
	B	0.649
	C	3.877
	D	0.065

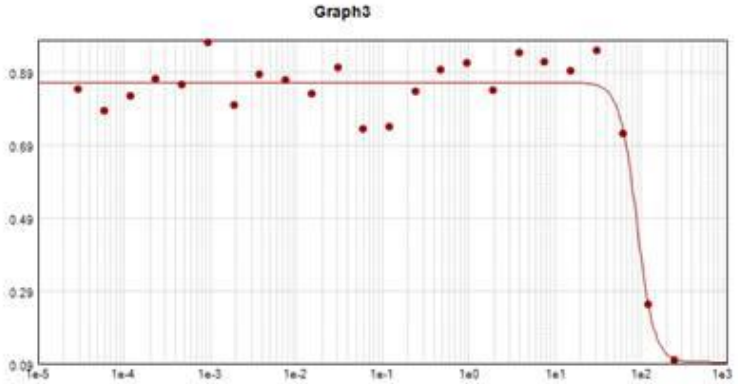
3. Appendix: IC_{50} & Spectral Data





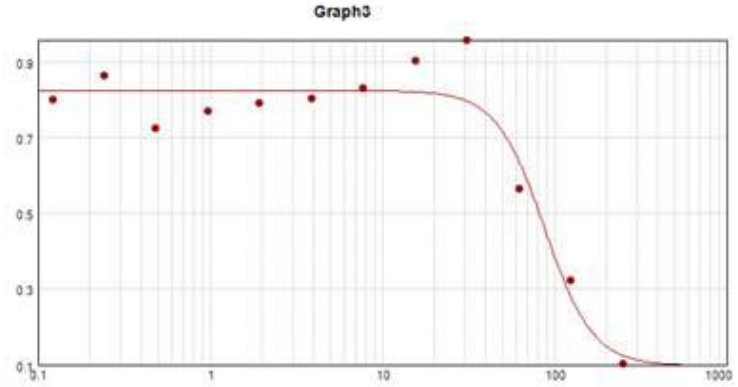
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.946 EC50 = 92.05	A	0.930
	B	4.046
	C	92.05
	D	0.111



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

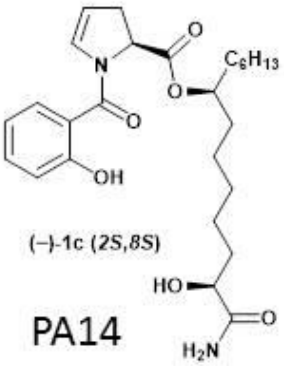
	Parameter	Estimated Value
Plot1 R^2 = 0.913 EC50 = 90.36	A	0.863
	B	4.355
	C	90.36
	D	0.093

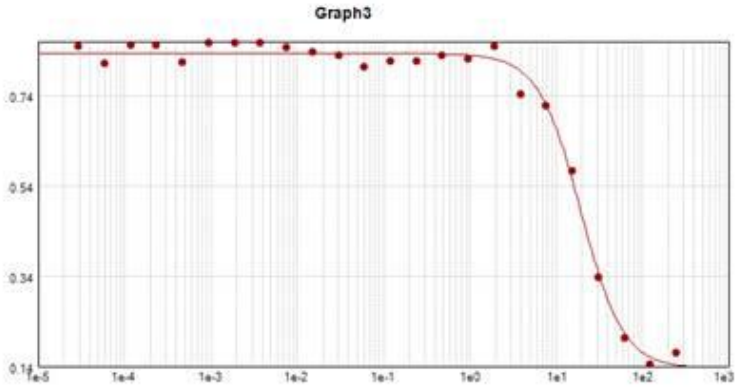


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.919 EC50 = 87.58	A	0.826
	B	3.109
	C	87.58
	D	0.097

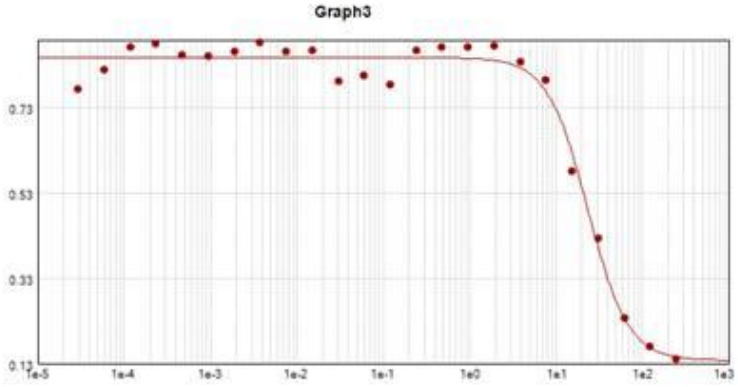
3. Appendix: IC_{50} & Spectral Data





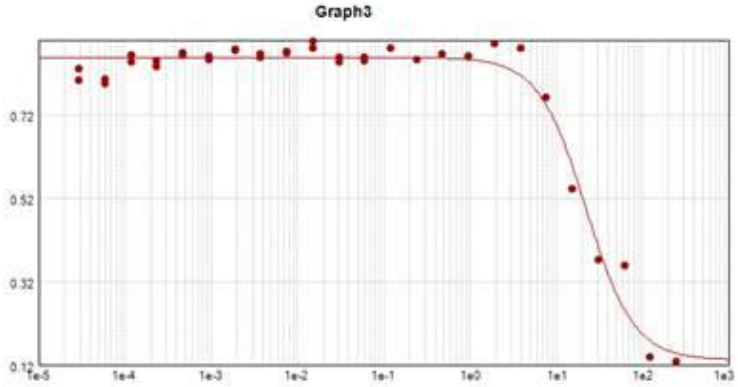
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.992	A	0.833
EC50 = 19.44	B	1.777
	C	19.44
	D	0.135



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

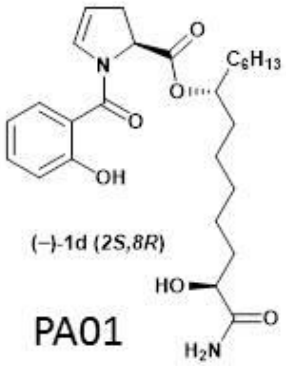
	Parameter	Estimated Value
Plot1 R^2 = 0.981	A	0.849
EC50 = 23.45	B	1.865
	C	23.45
	D	0.137

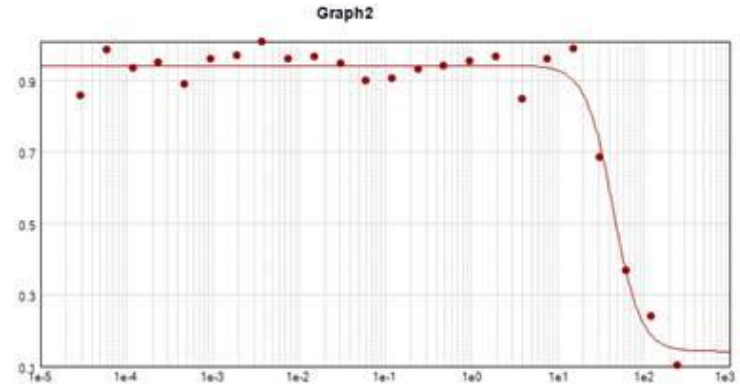


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.973	A	0.858
EC50 = 22.31	B	1.575
	C	22.31
	D	0.132

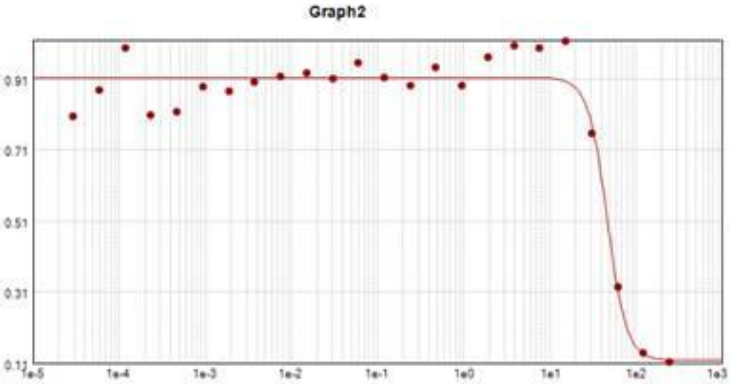
3. Appendix: IC_{50} & Spectral Data





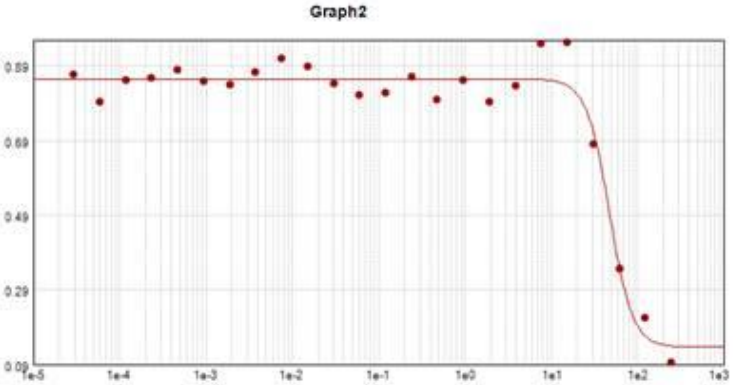
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.967	A	0.943
EC50 = 44.44	B	2.739
	C	44.44
	D	0.141



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

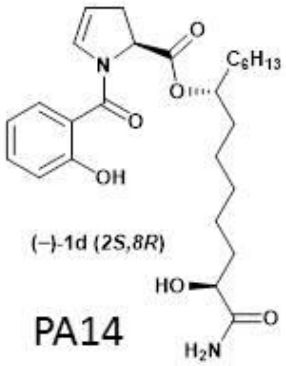
	Parameter	Estimated Value
Plot1 R^2 = 0.947	A	0.914
EC50 = 46.88	B	3.886
	C	46.88
	D	0.117

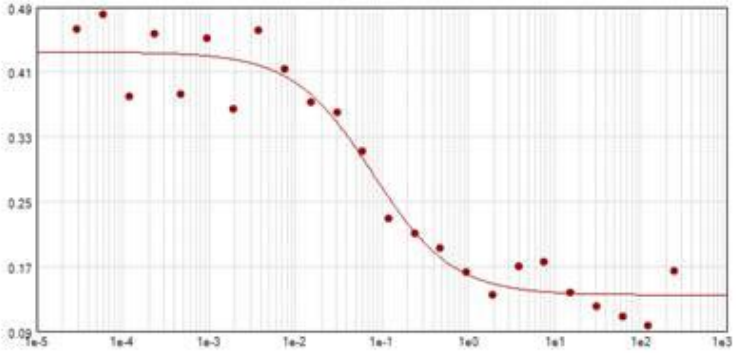


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.958	A	0.855
EC50 = 47.67	B	3.266
	C	47.67
	D	0.136

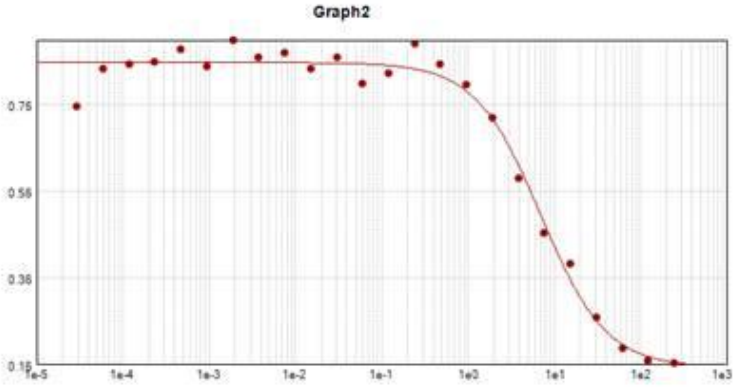
3. Appendix: IC_{50} & Spectral Data





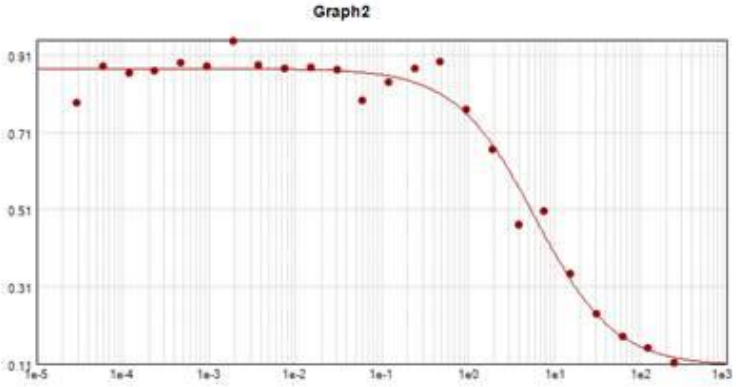
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.948 EC50 = 0.079	A	0.435
	B	0.940
	C	0.079
	D	0.135



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

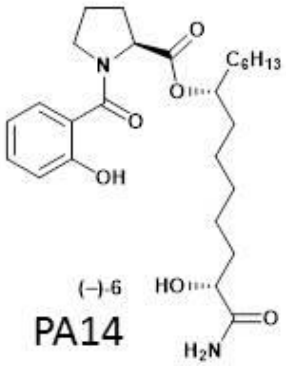
	Parameter	Estimated Value
Plot1 R^2 = 0.984 EC50 = 7.017	A	0.858
	B	1.147
	C	7.017
	D	0.152

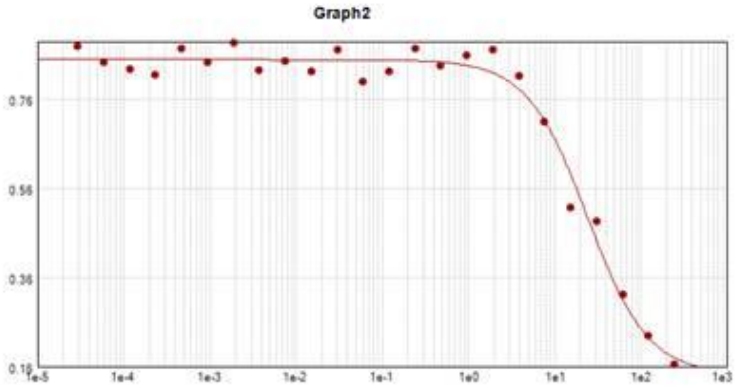


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.977 EC50 = 6.013	A	0.875
	B	0.943
	C	6.013
	D	0.104

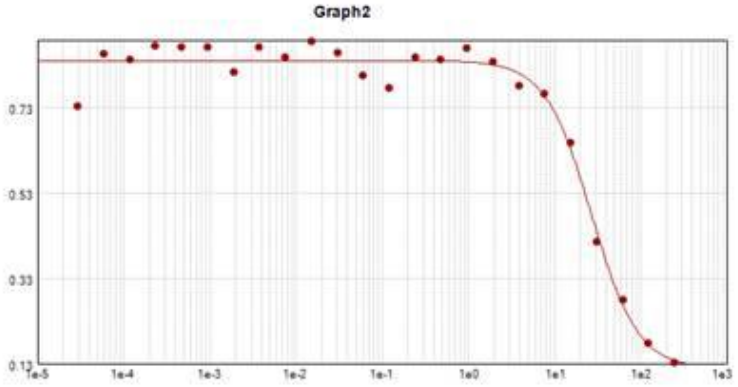
3. Appendix: IC_{50} & Spectral Data





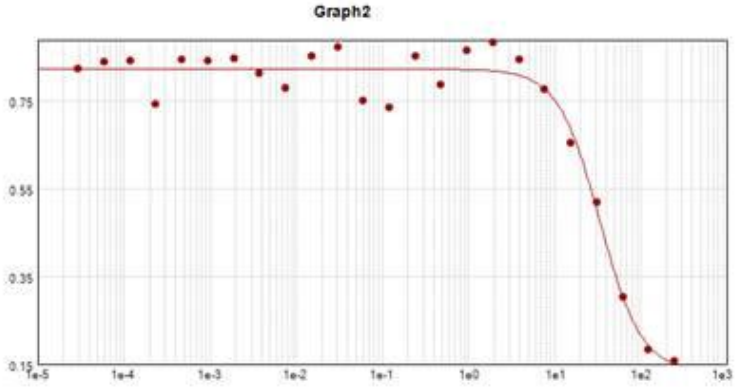
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.980 EC50 = 24.28	A	0.849
	B	1.238
	C	24.28
	D	0.142



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

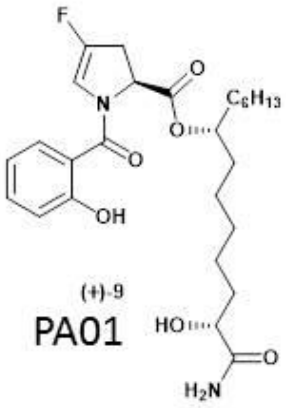
	Parameter	Estimated Value
Plot1 R^2 = 0.977 EC50 = 27.05	A	0.842
	B	1.620
	C	27.05
	D	0.118



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.965 EC50 = 33.66	A	0.823
	B	1.798
	C	33.66
	D	0.132

3. Appendix: IC_{50} & Spectral Data



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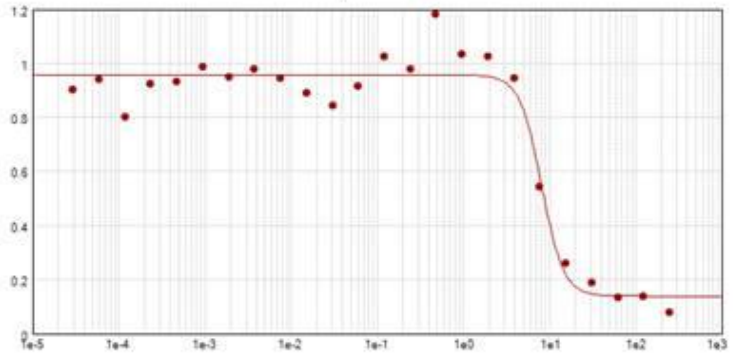
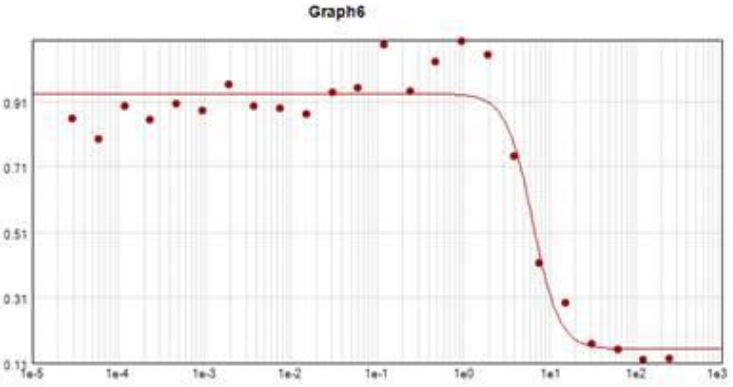


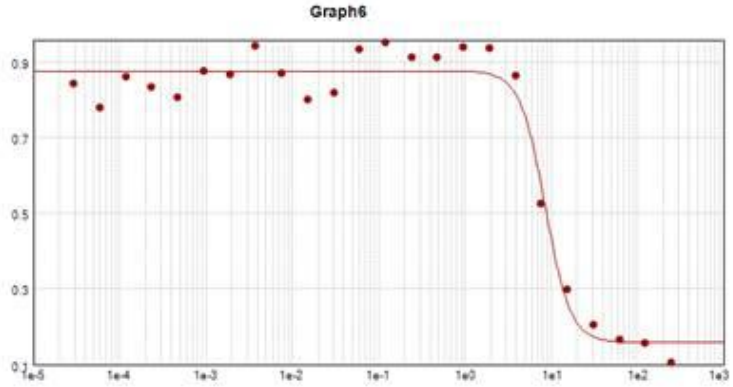
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.952 EC50 = 8.114	A	0.957
	B	3.429
	C	8.114
	D	0.139



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

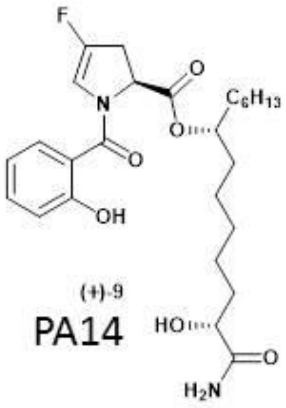
	Parameter	Estimated Value
Plot1 R^2 = 0.945 EC50 = 6.410	A	0.935
	B	2.825
	C	6.410
	D	0.152

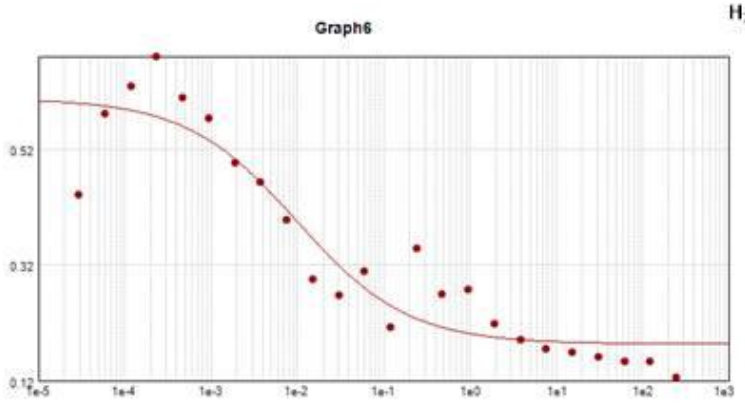


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.969 EC50 = 8.567	A	0.878
	B	2.987
	C	8.567
	D	0.159

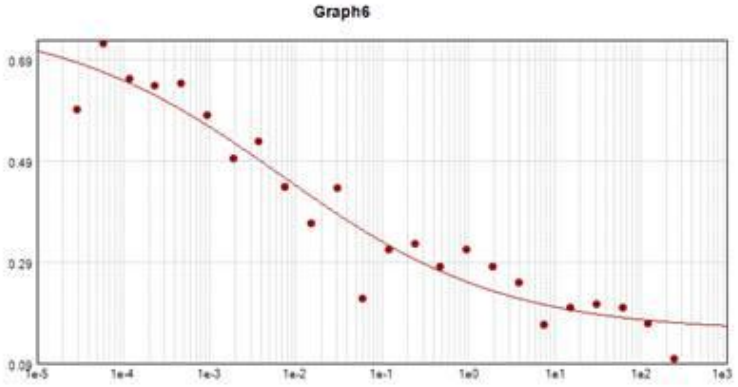
3. Appendix: IC_{50} & Spectral Data





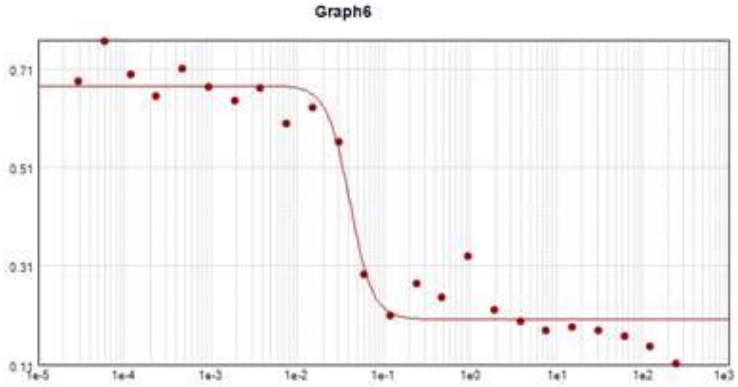
Curve Fit : 4-Parameter $y = D + \frac{A-D}{1+\left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.884 EC50 = 0.010	A	0.607
	B	0.676
	C	0.010
	D	0.183



Curve Fit : 4-Parameter $y = D + \frac{A-D}{1+\left(\frac{x}{C}\right)^B}$

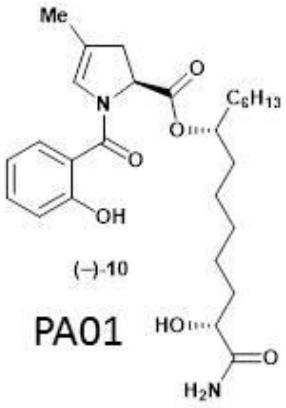
	Parameter	Estimated Value
Plot1 R^2 = 0.927 EC50 = 0.007	A	0.770
	B	0.337
	C	0.007
	D	0.153

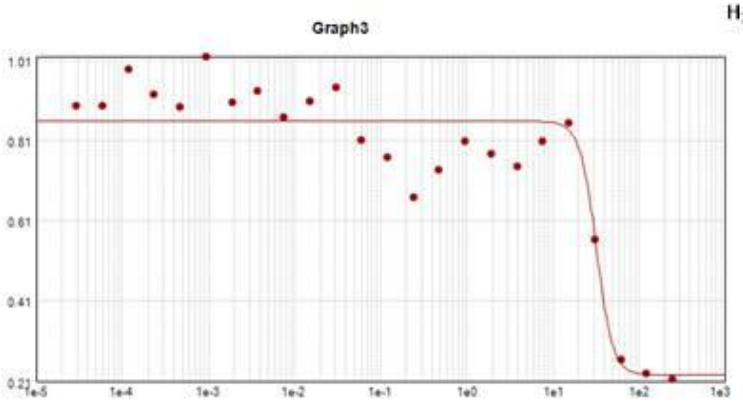


Curve Fit : 4-Parameter $y = D + \frac{A-D}{1+\left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.957 EC50 = 0.041	A	0.677
	B	3.269
	C	0.041
	D	0.202

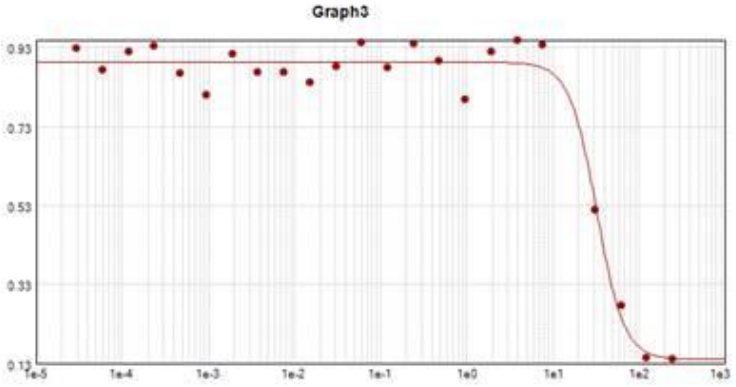
3. Appendix: IC_{50} & Spectral Data





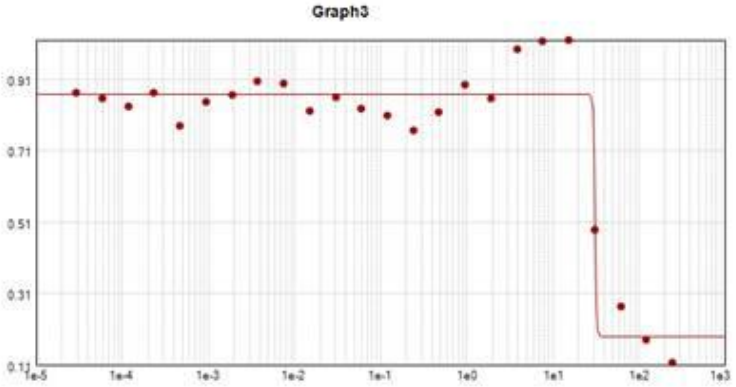
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.872 EC50 = 32.26	A	0.858
	B	4.585
	C	32.26
	D	0.226



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

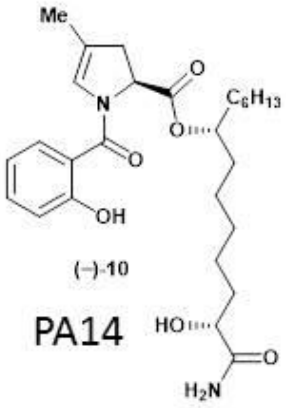
	Parameter	Estimated Value
Plot1 R^2 = 0.973 EC50 = 32.53	A	0.893
	B	2.744
	C	32.53
	D	0.139

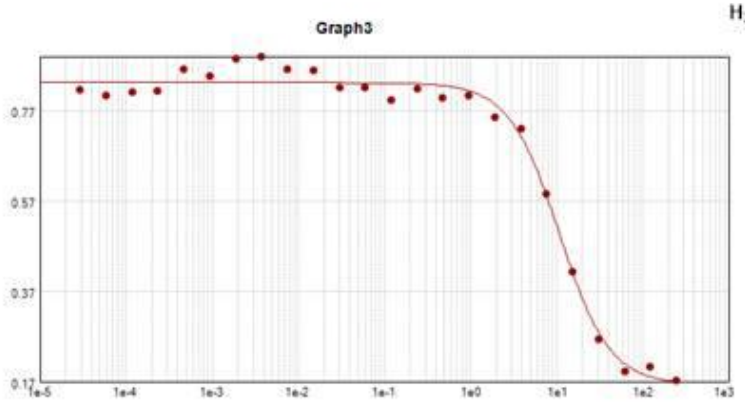


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.923 EC50 = 31.07	A	0.869
	B	42.63
	C	31.07
	D	0.189

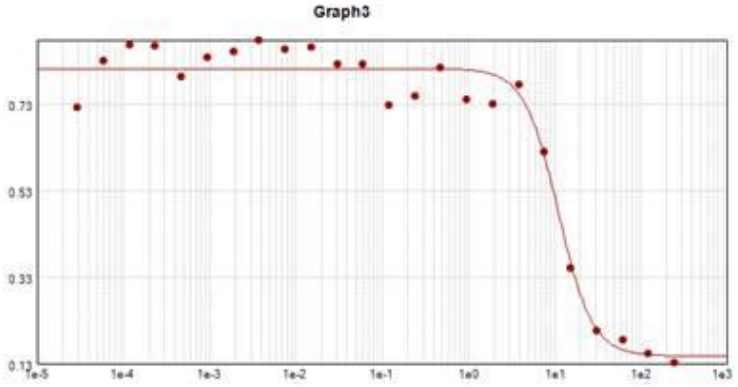
3. Appendix: IC_{50} & Spectral Data





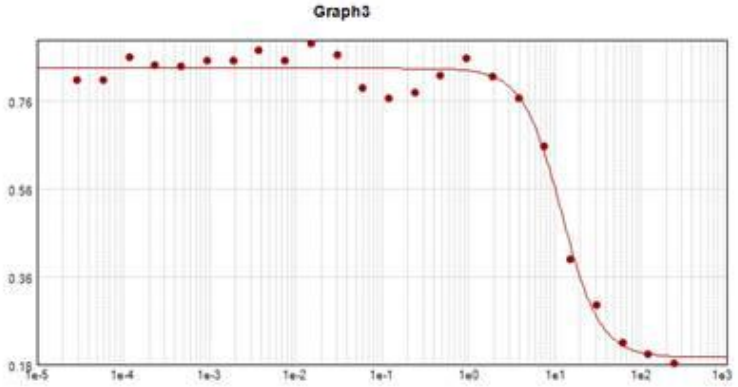
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.989 EC50 = 10.83	A	0.832
	B	1.493
	C	10.83
	D	0.163



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

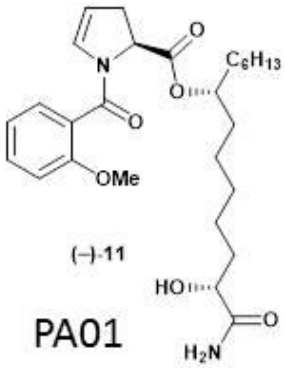
	Parameter	Estimated Value
Plot1 R^2 = 0.969 EC50 = 11.18	A	0.814
	B	2.213
	C	11.18
	D	0.147

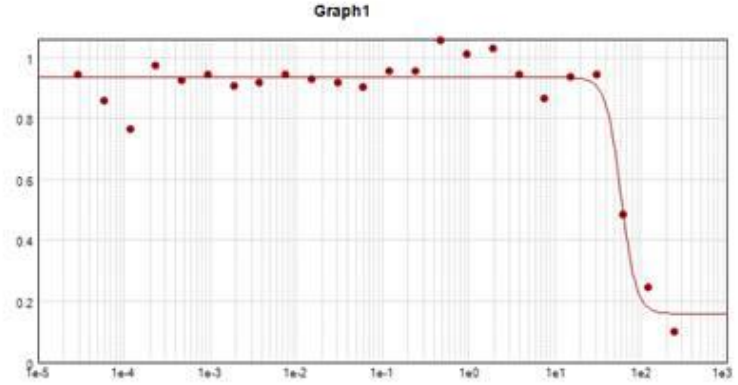


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.984 EC50 = 12.18	A	0.835
	B	1.936
	C	12.18
	D	0.176

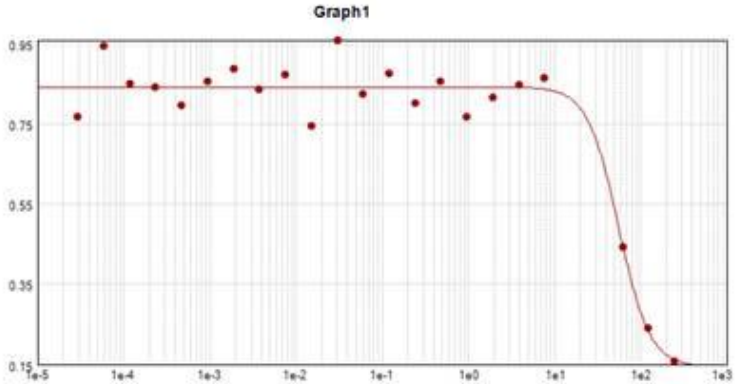
3. Appendix: IC_{50} & Spectral Data





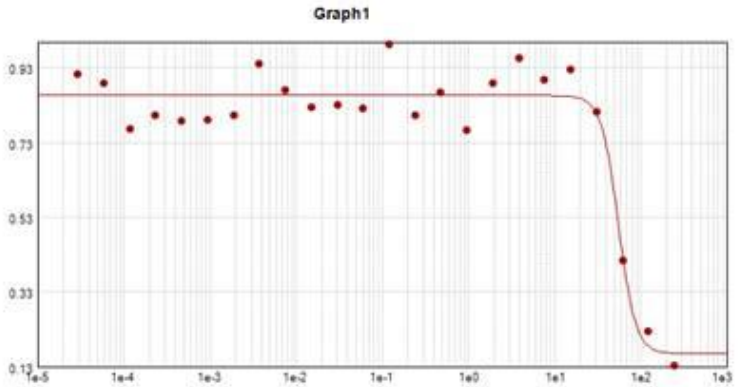
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.934 EC50 = 59.28	A	0.934
	B	4.979
	C	59.28
	D	0.159



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

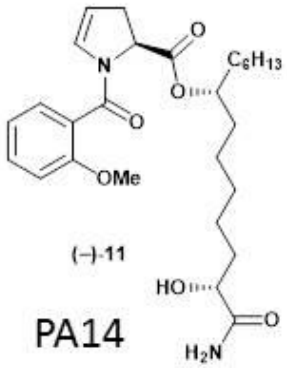
	Parameter	Estimated Value
Plot1 R^2 = 0.941 EC50 = 55.73	A	0.843
	B	2.421
	C	55.73
	D	0.144

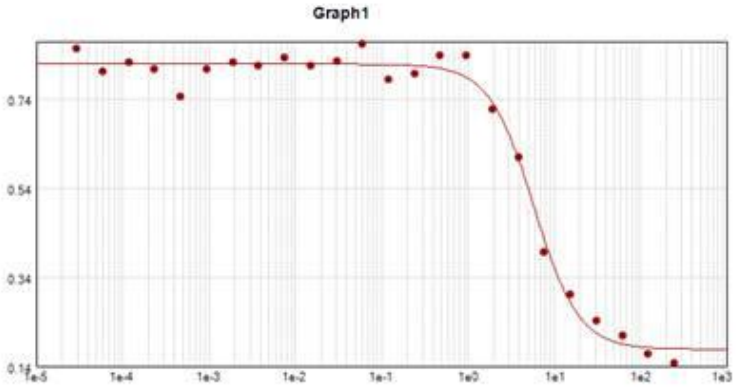


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.916 EC50 = 55.49	A	0.856
	B	4.403
	C	55.49
	D	0.165

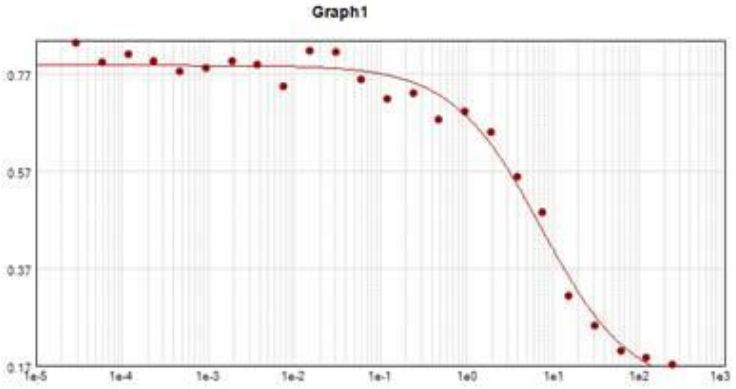
3. Appendix: IC_{50} & Spectral Data





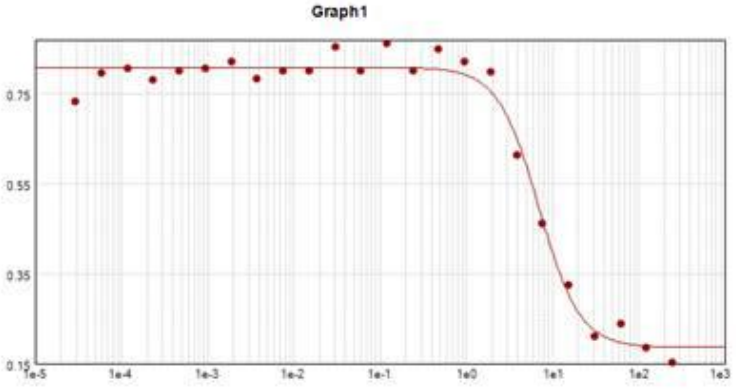
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.988 EC50 = 5.860	A	0.819
	B	1.680
	C	5.860
	D	0.178



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

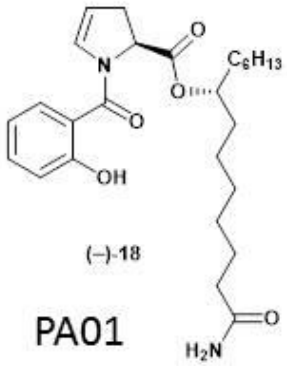
	Parameter	Estimated Value
Plot1 R^2 = 0.985 EC50 = 7.388	A	0.788
	B	0.845
	C	7.388
	D	0.119

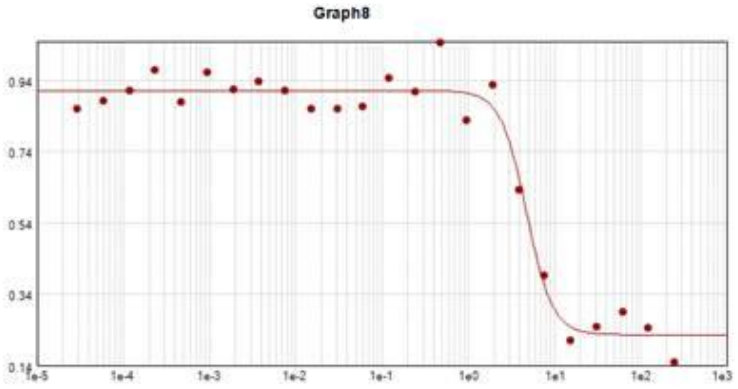


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.984 EC50 = 6.978	A	0.809
	B	1.833
	C	6.978
	D	0.186

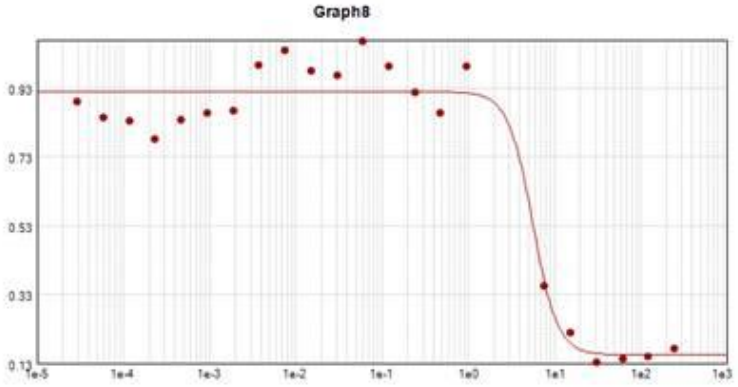
3. Appendix: IC_{50} & Spectral Data





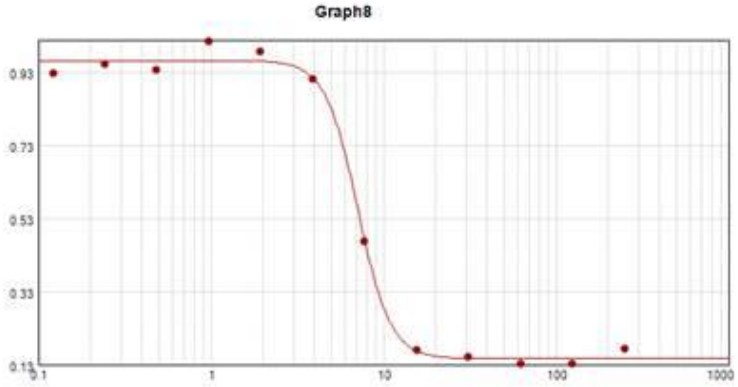
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.968 EC50 = 4.783	A	0.911
	B	2.885
	C	4.783
	D	0.226



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

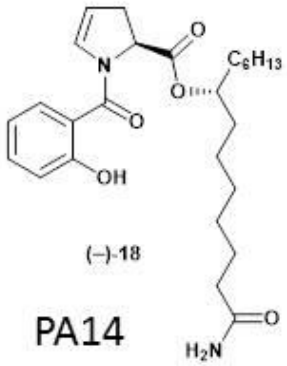
	Parameter	Estimated Value
Plot1 R^2 = 0.954 EC50 = 5.639	A	0.919
	B	3.052
	C	5.639
	D	0.154

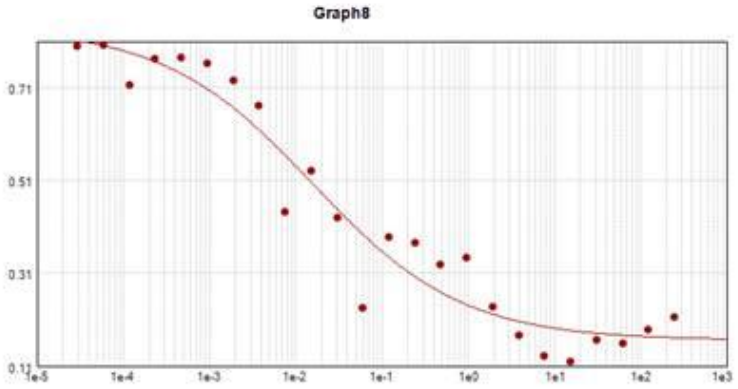


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.996 EC50 = 7.117	A	0.963
	B	4.608
	C	7.117
	D	0.146

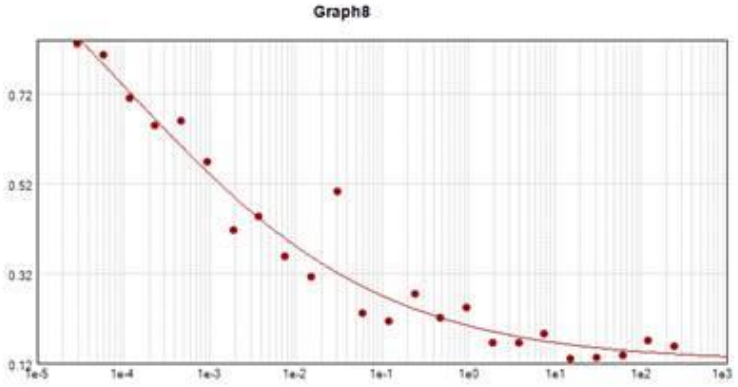
3. Appendix: IC_{50} & Spectral Data





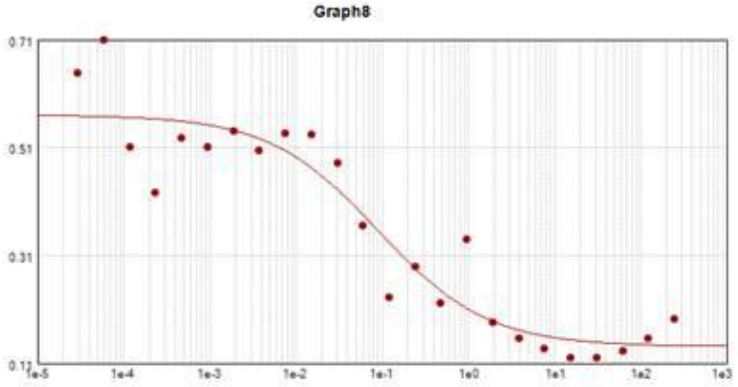
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.938 EC50 = 0.016	A	0.839
	B	0.500
	C	0.016
	D	0.166



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

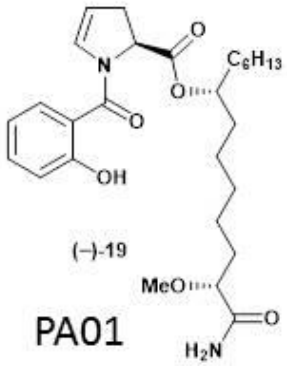
	Parameter	Estimated Value
Plot1 R^2 = 0.951 EC50 = 1.03e-4	A	1.350
	B	0.289
	C	1.03e-4
	D	0.123



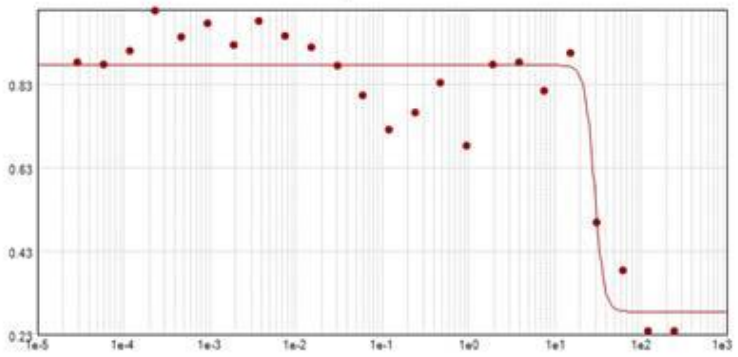
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.887 EC50 = 0.090	A	0.570
	B	0.685
	C	0.090
	D	0.141

3. Appendix: IC_{50} & Spectral Data

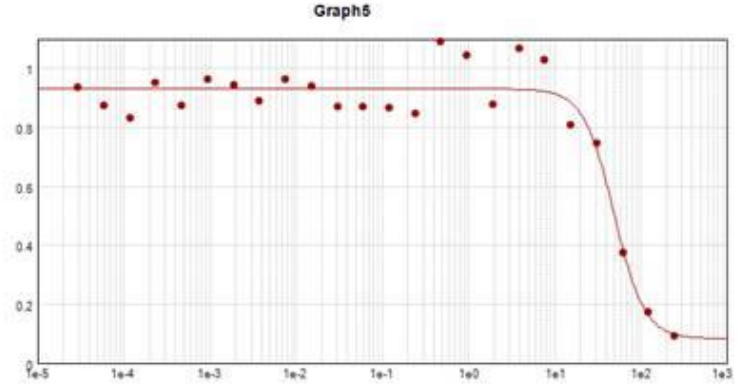


PA01



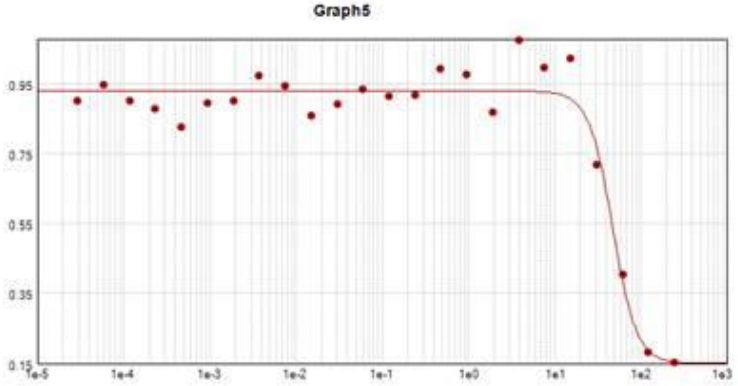
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.866 EC50 = 29.15	A	0.876
	B	7.872
	C	29.15
	D	0.284



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

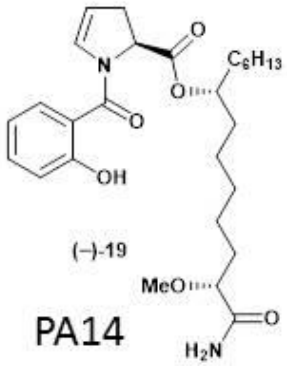
	Parameter	Estimated Value
Plot1 R^2 = 0.922 EC50 = 49.29	A	0.931
	B	2.476
	C	49.29
	D	0.083

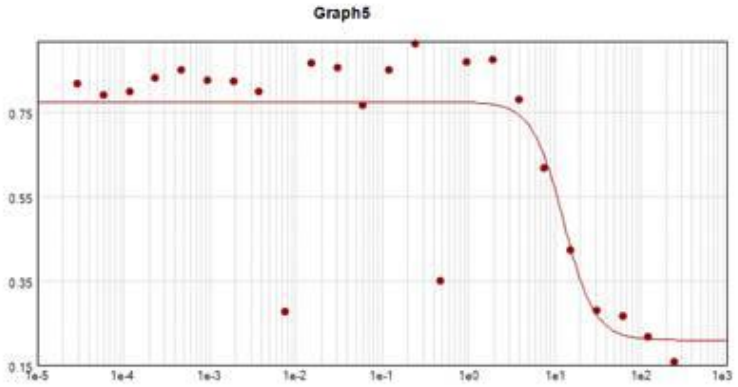


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.942 EC50 = 47.56	A	0.931
	B	3.146
	C	47.56
	D	0.151

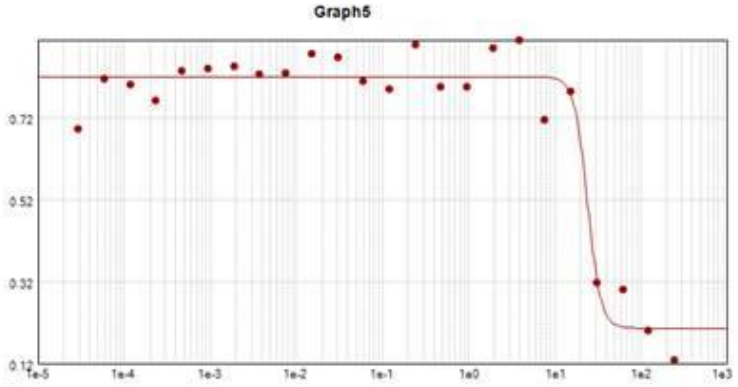
3. Appendix: IC_{50} & Spectral Data





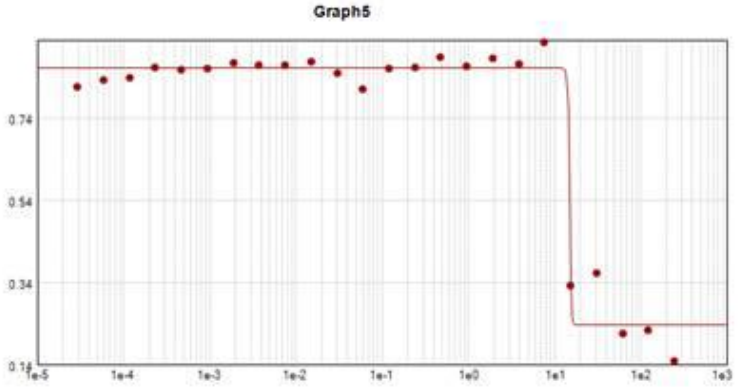
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.669 EC50 = 12.78	A	0.776
	B	2.395
	C	12.78
	D	0.209



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

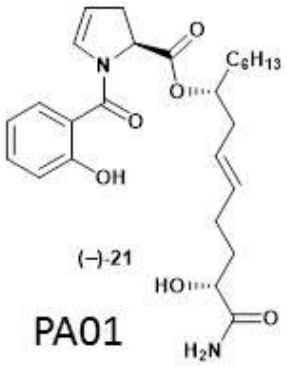
	Parameter	Estimated Value
Plot1 R^2 = 0.939 EC50 = 24.21	A	0.820
	B	5.682
	C	24.21
	D	0.206

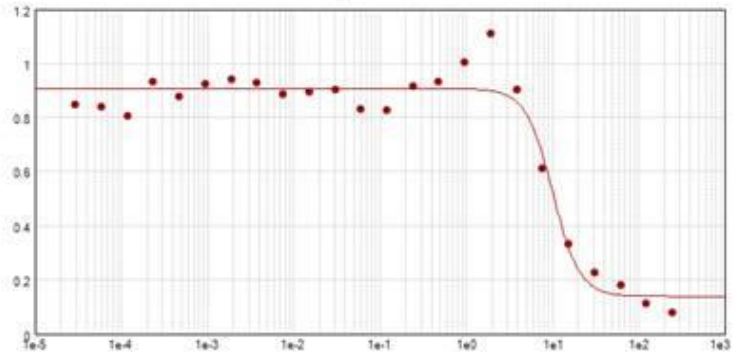


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.976 EC50 = 15.03	A	0.861
	B	44.45
	C	15.03
	D	0.236

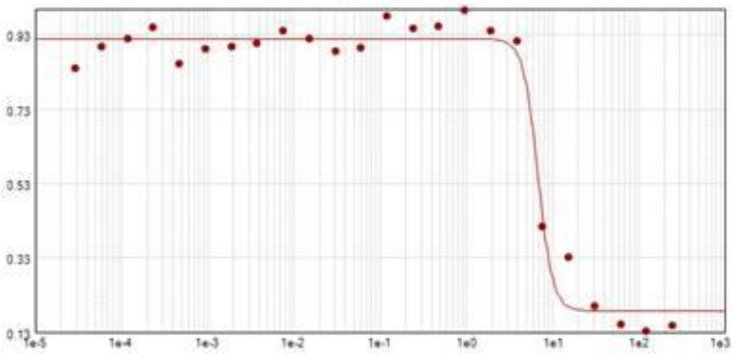
3. Appendix: IC_{50} & Spectral Data





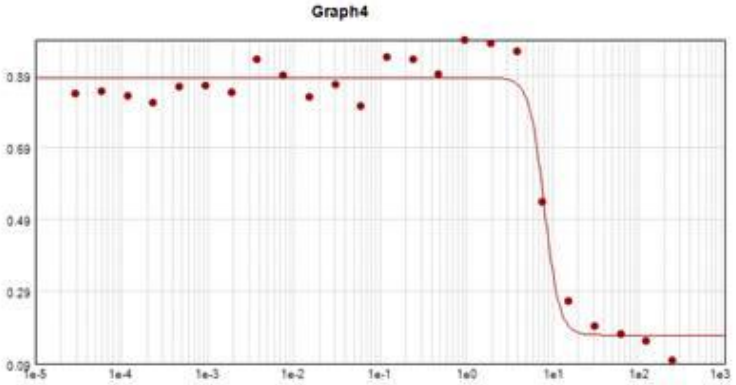
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.953 EC50 = 10.13	A	0.907
	B	2.789
	C	10.13
	D	0.139



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

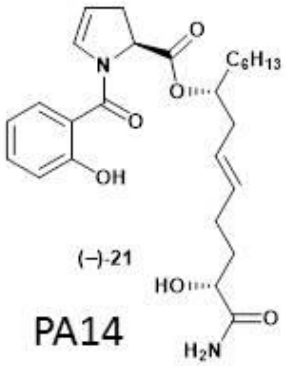
	Parameter	Estimated Value
Plot1 R^2 = 0.976 EC50 = 6.814	A	0.920
	B	5.080
	C	6.814
	D	0.187

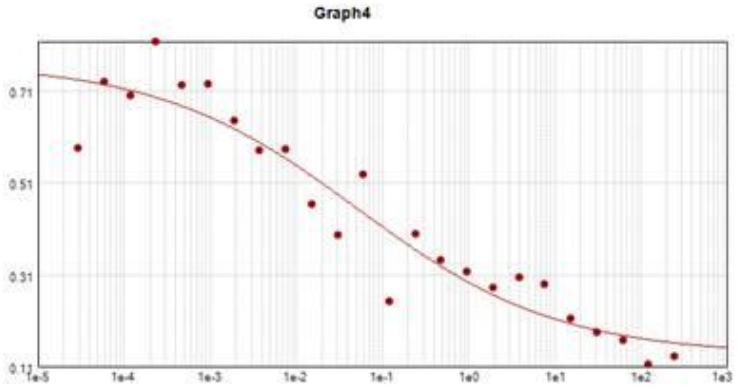


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.966 EC50 = 8.071	A	0.885
	B	5.052
	C	8.071
	D	0.169

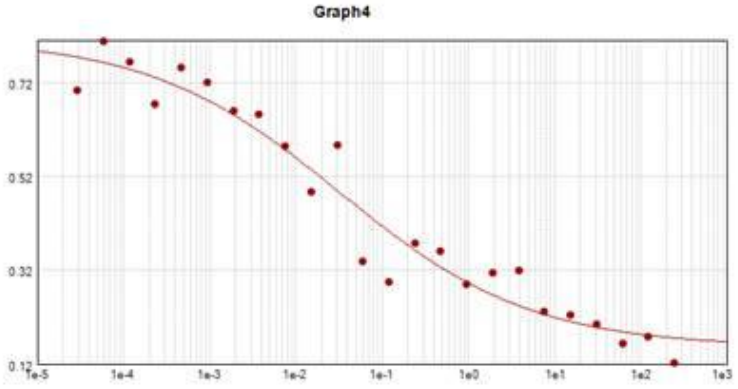
3. Appendix: IC_{50} & Spectral Data





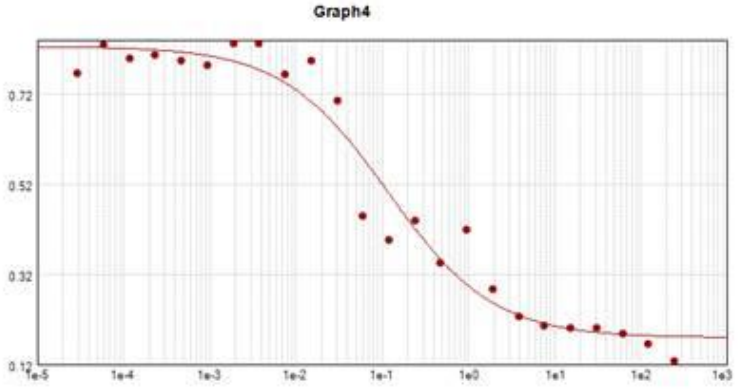
Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

	Parameter	Estimated Value
Plot1 R^2 = 0.907 EC50 = 0.052	A	0.773
	B	0.373
	C	0.052
	D	0.135



Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

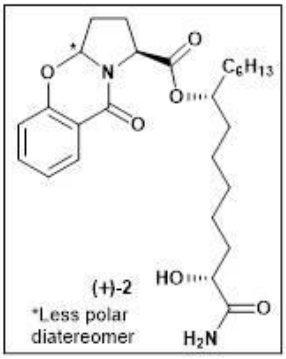
	Parameter	Estimated Value
Plot1 R^2 = 0.945 EC50 = 0.033	A	0.813
	B	0.391
	C	0.033
	D	0.156

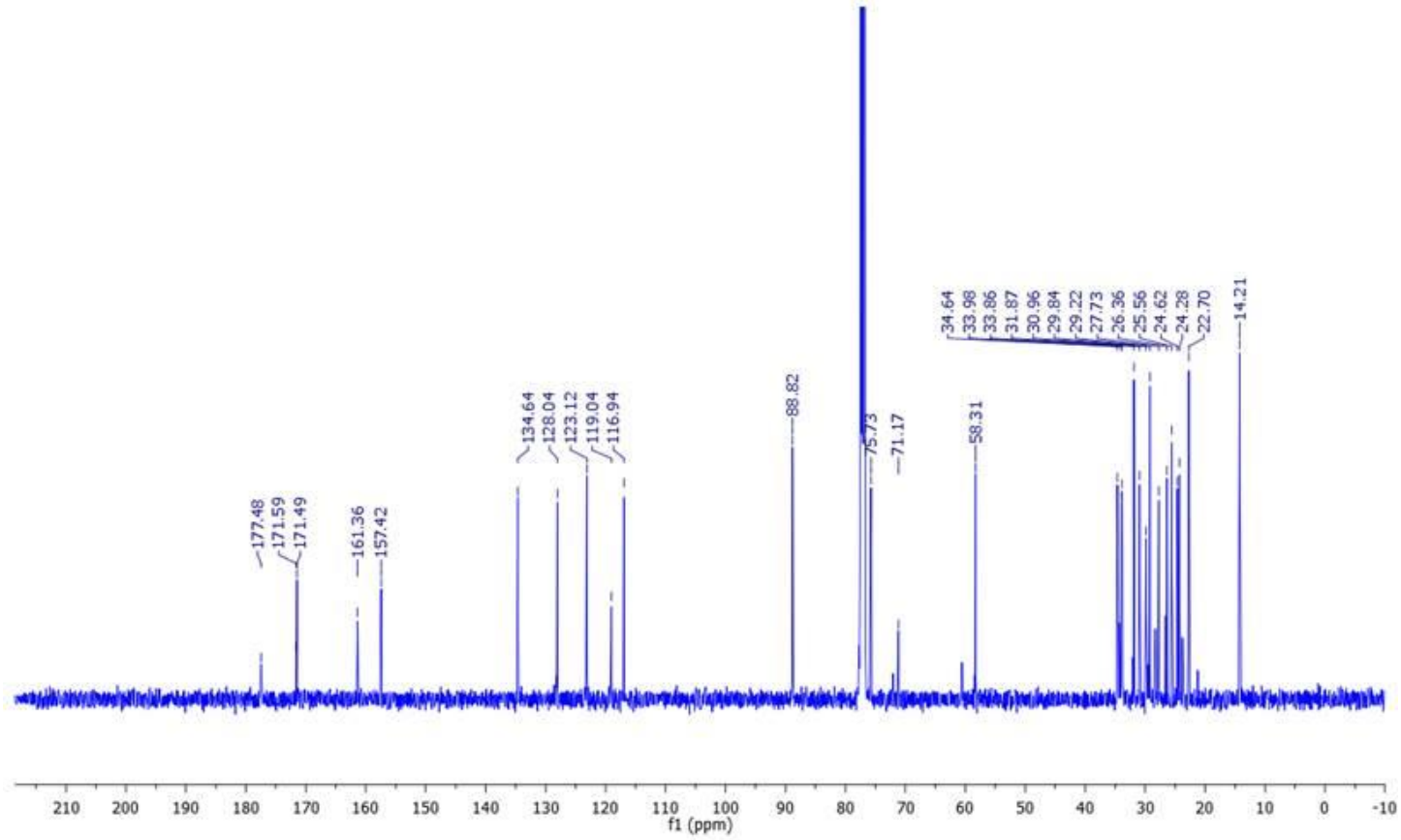


Curve Fit : 4-Parameter $y = D + \frac{A - D}{1 + \left(\frac{x}{C}\right)^B}$

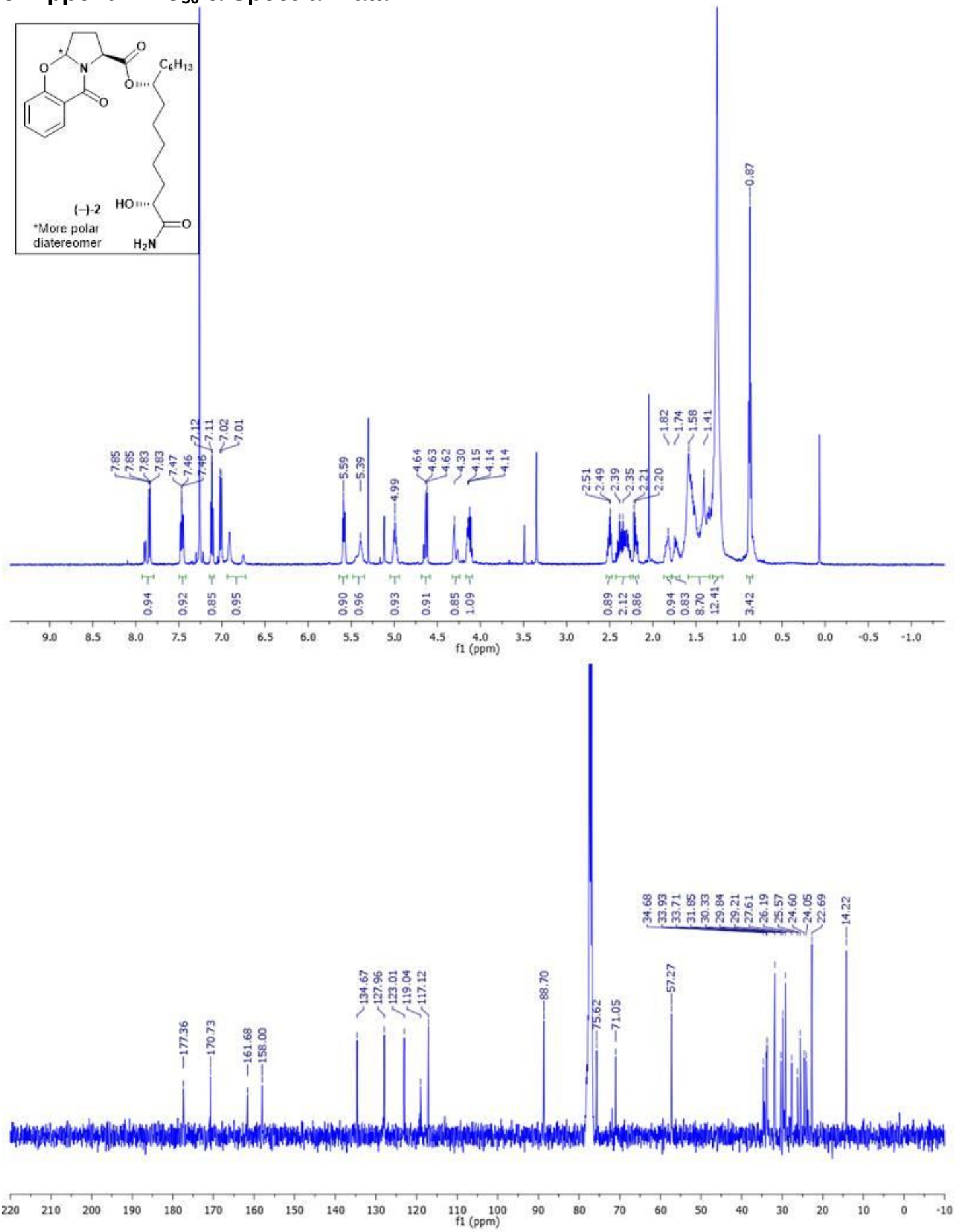
	Parameter	Estimated Value
Plot1 R^2 = 0.961 EC50 = 0.118	A	0.825
	B	0.712
	C	0.118
	D	0.179

3. Appendix: IC_{50} & Spectral Data

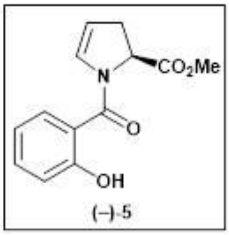




3. Appendix: IC_{50} & Spectral Data



3. Appendix: IC_{50} & Spectral Data



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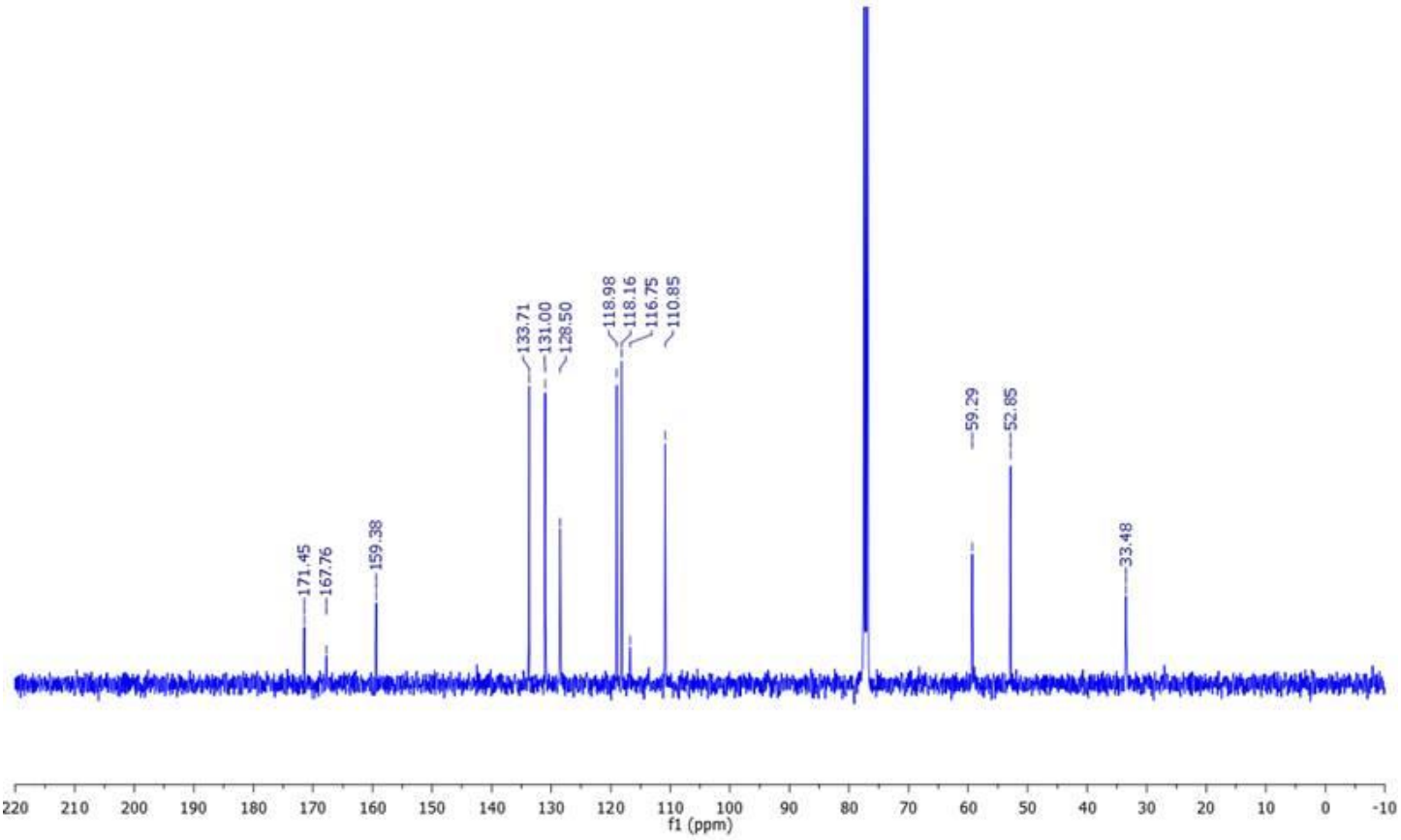
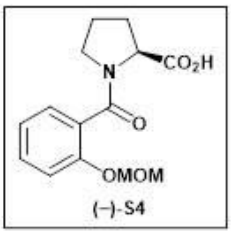
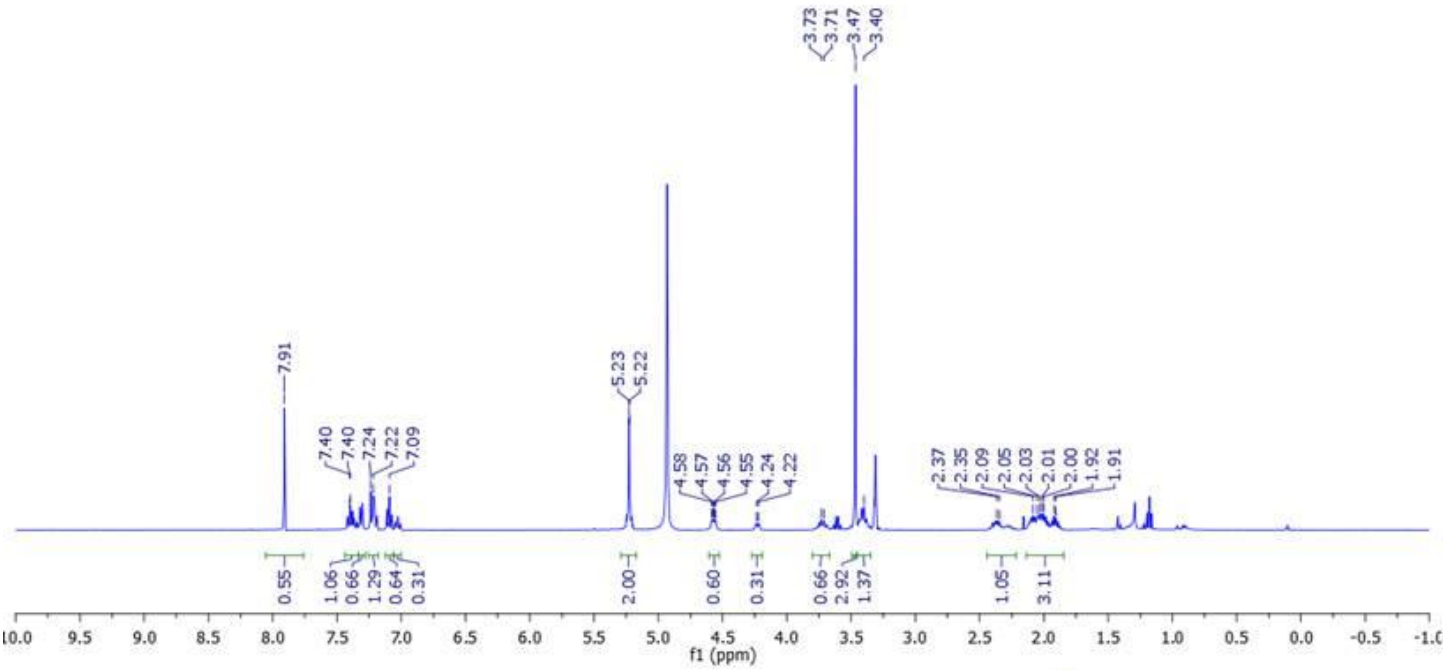
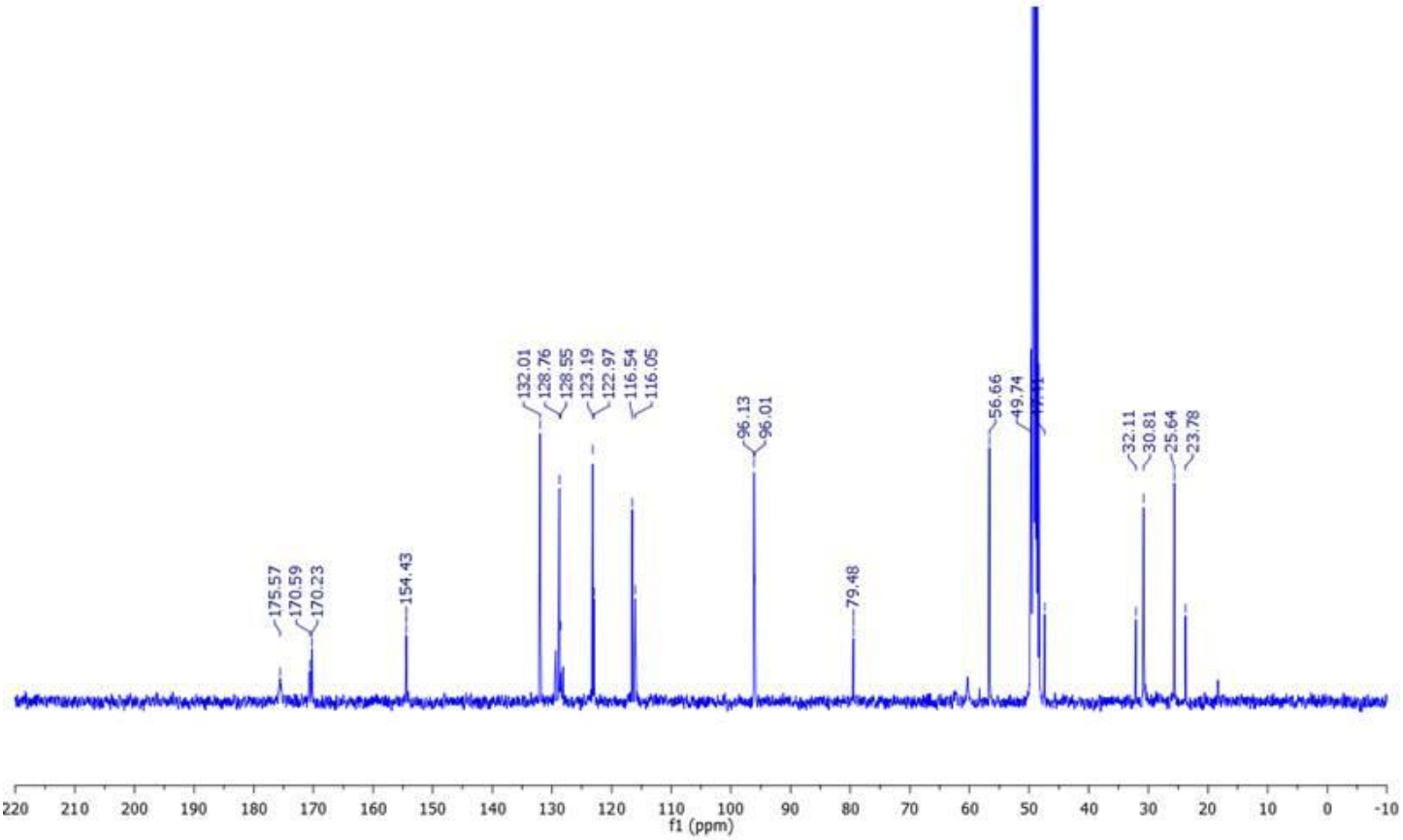


3. Appendix: IC_{50} & Spectral Data

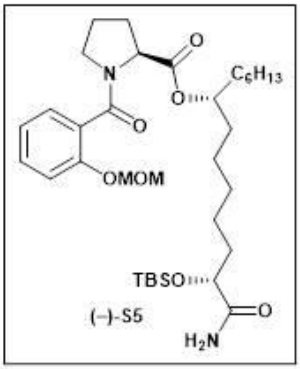


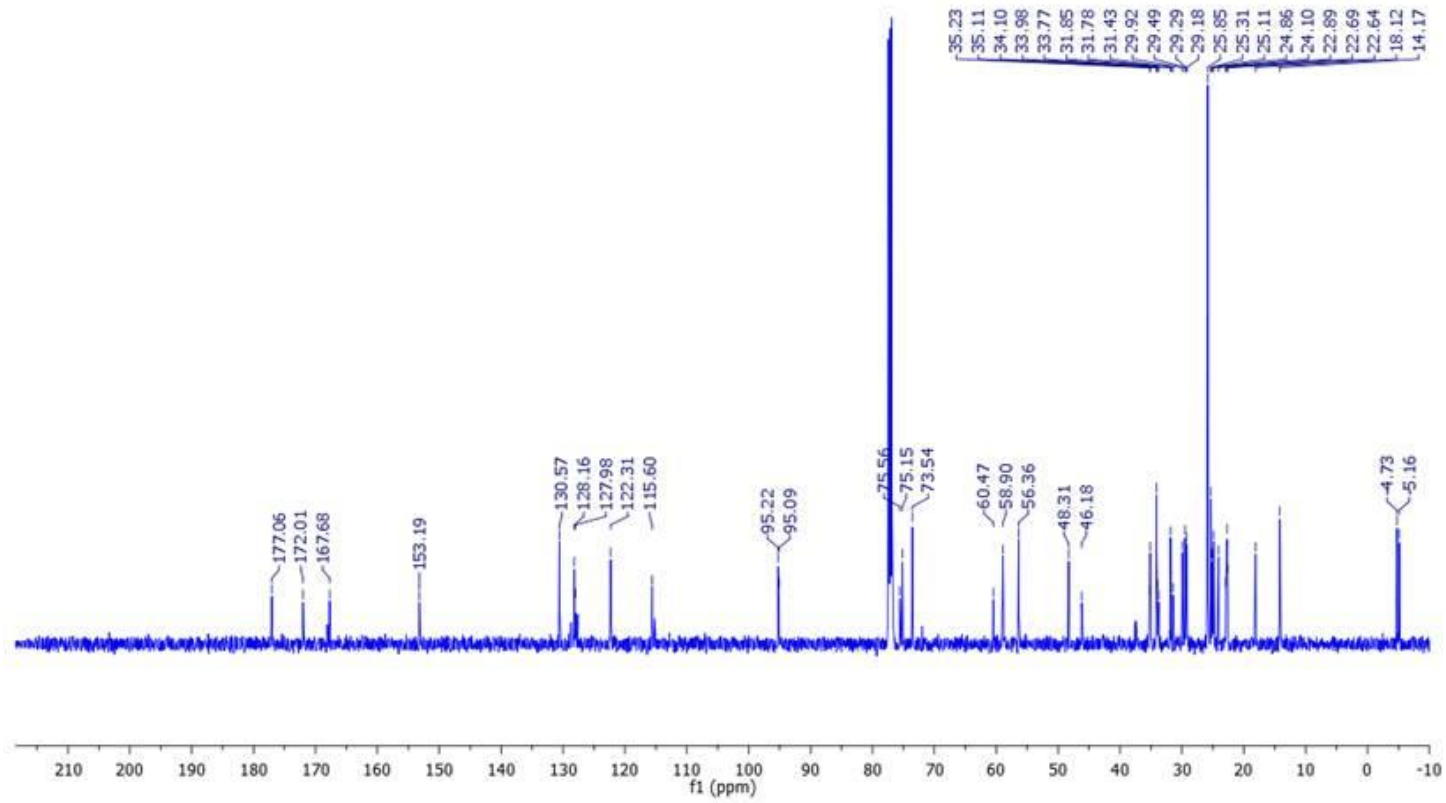
(−)-S4



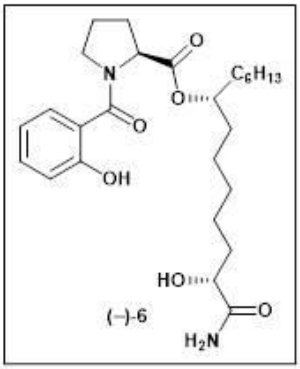


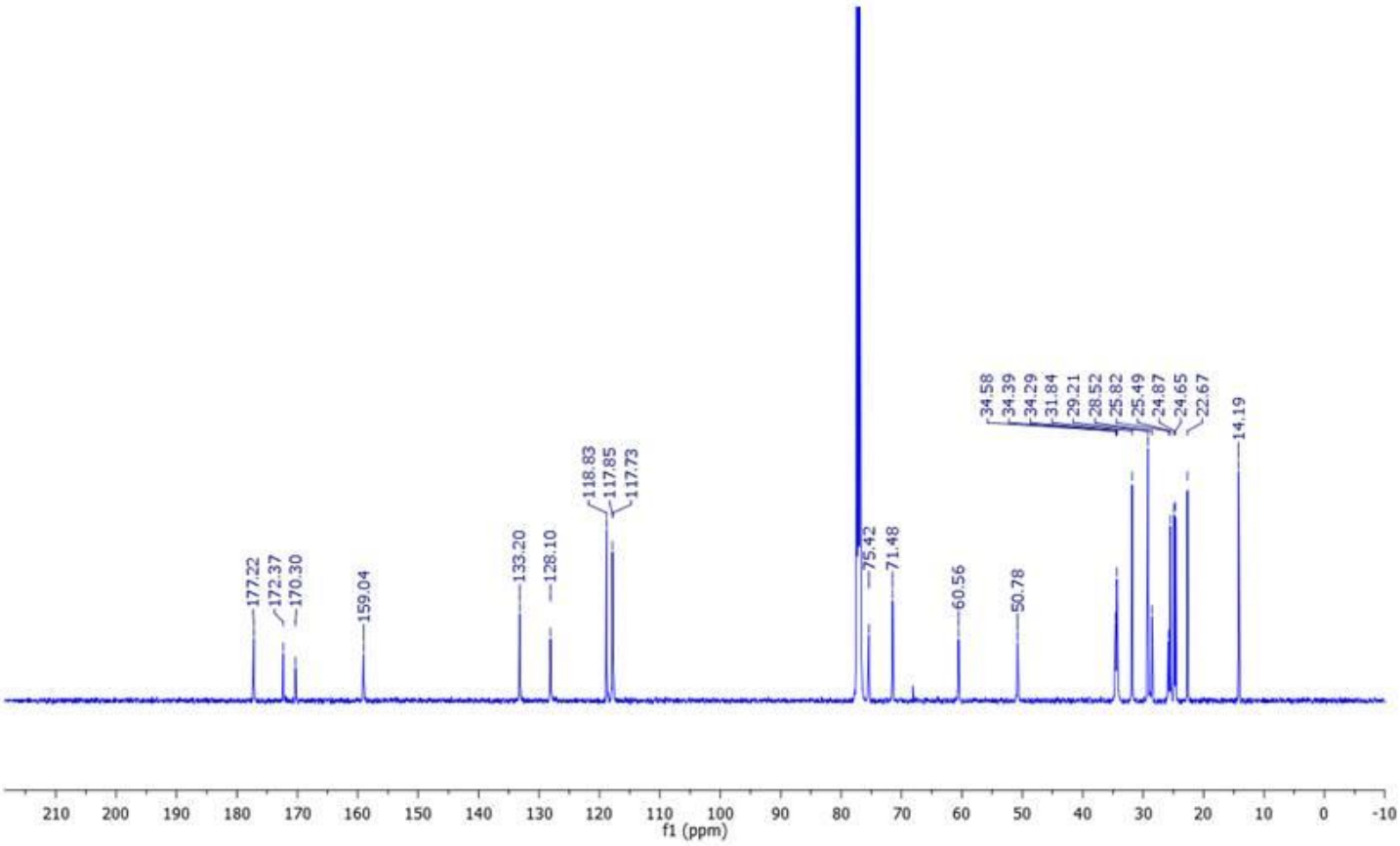
3. Appendix: IC_{50} & Spectral Data



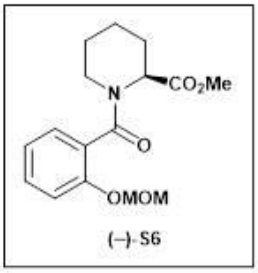


3. Appendix: IC_{50} & Spectral Data

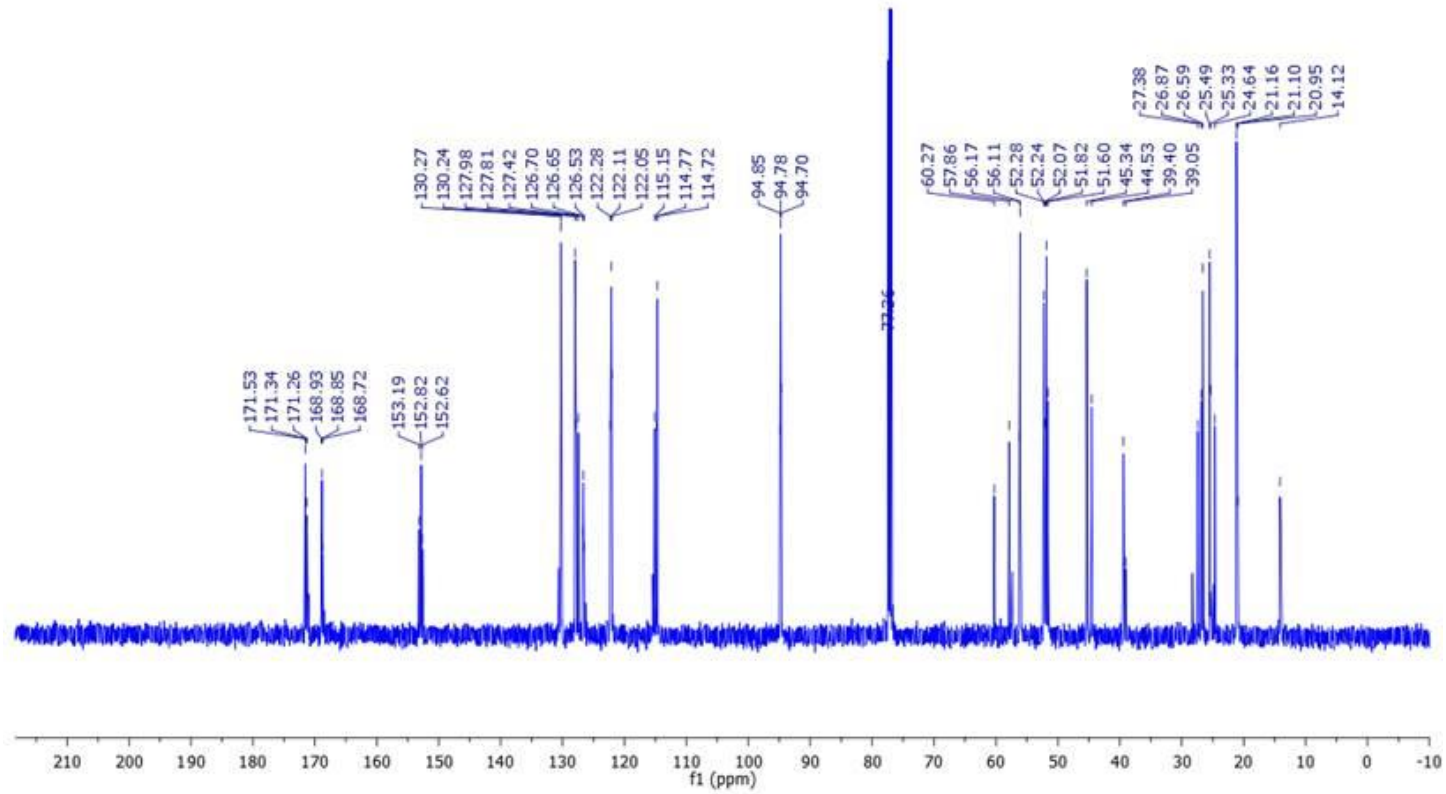




3. Appendix: IC_{50} & Spectral Data



(–)-S6



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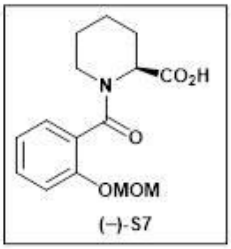

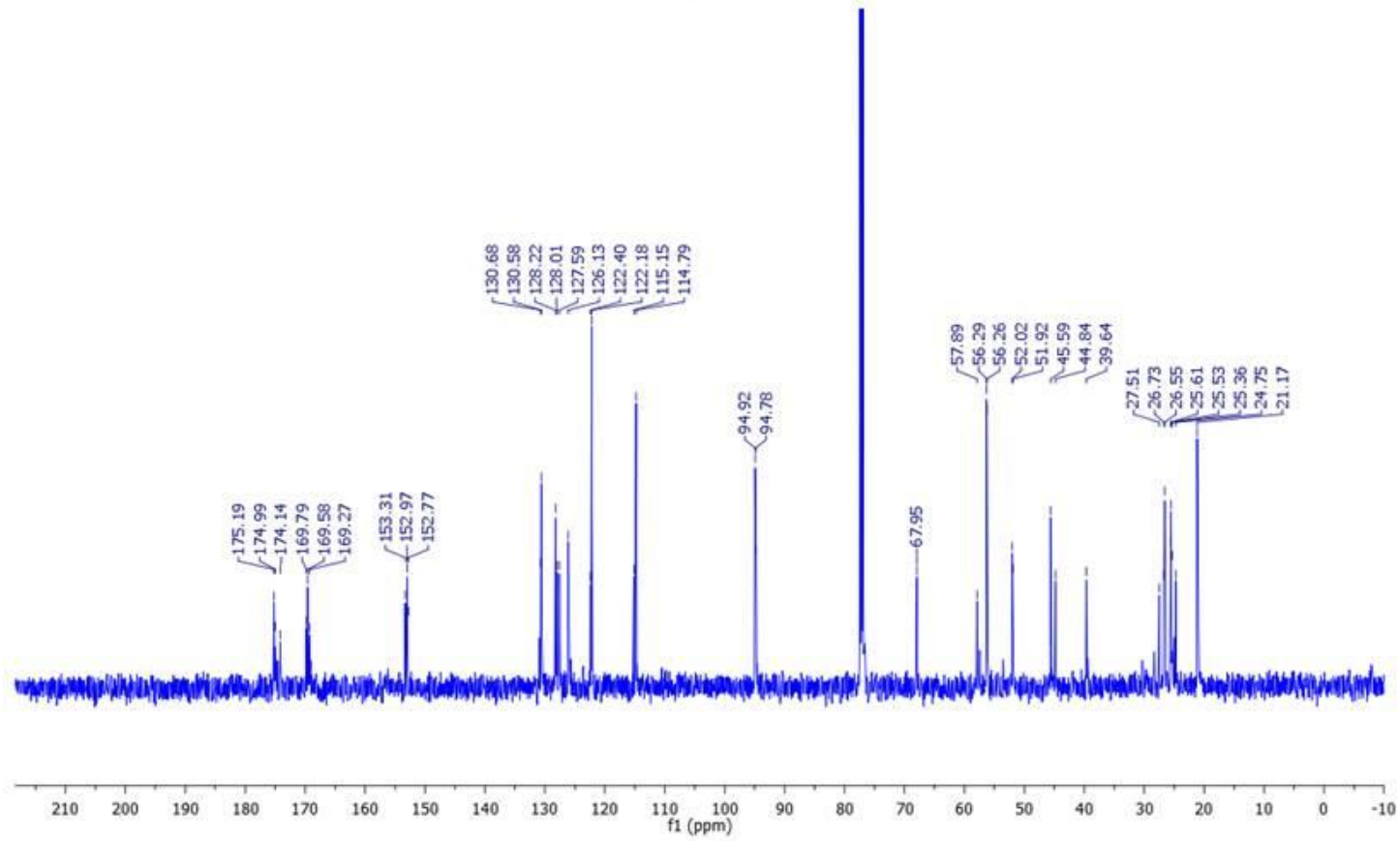

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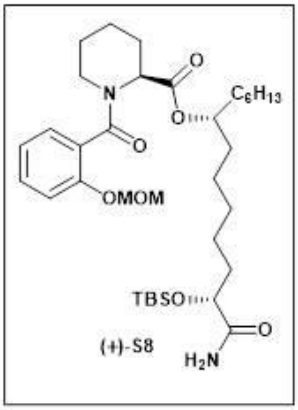

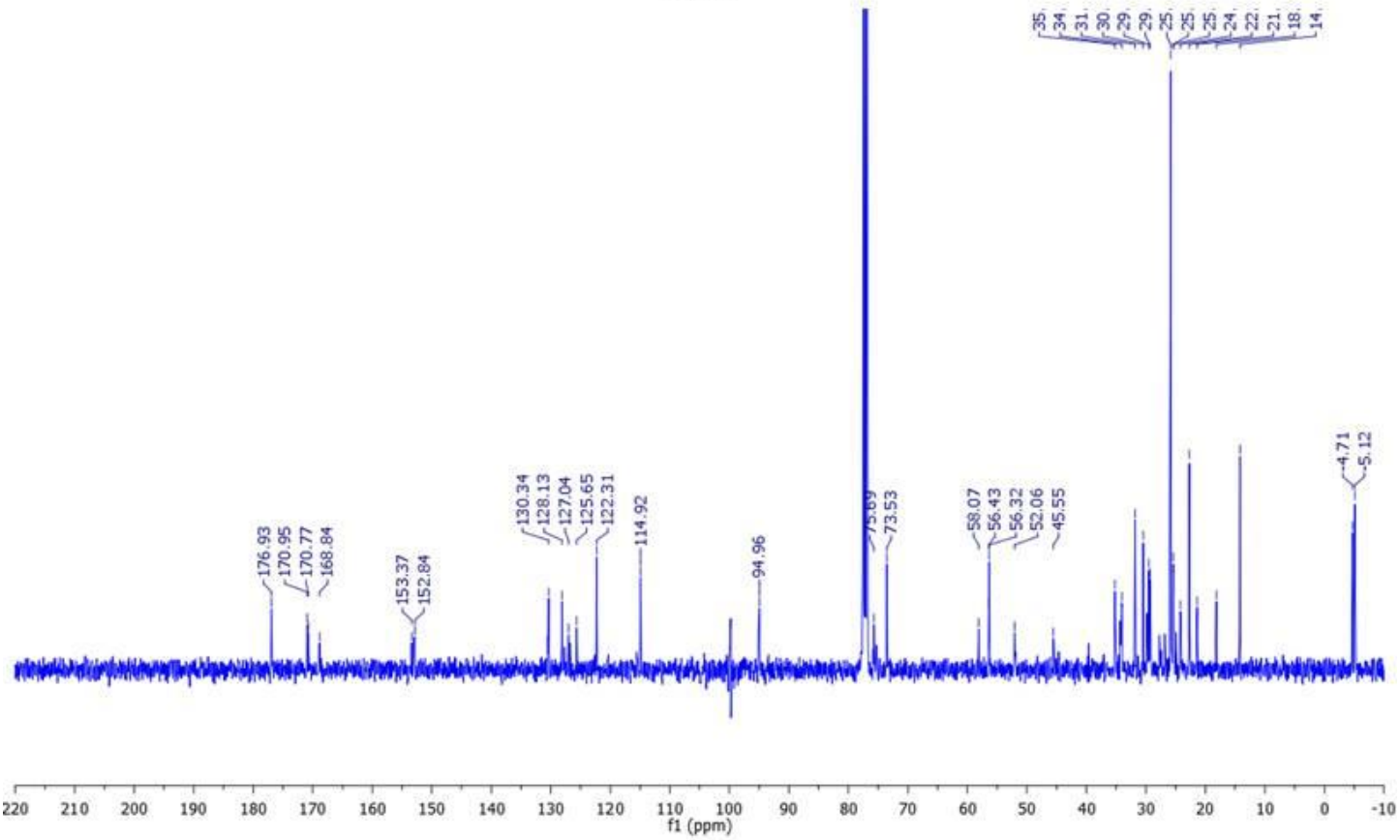

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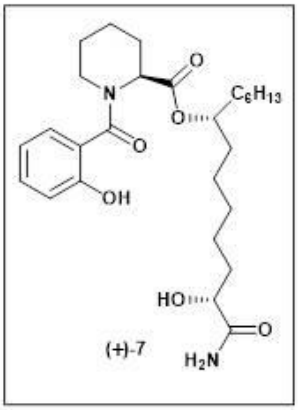

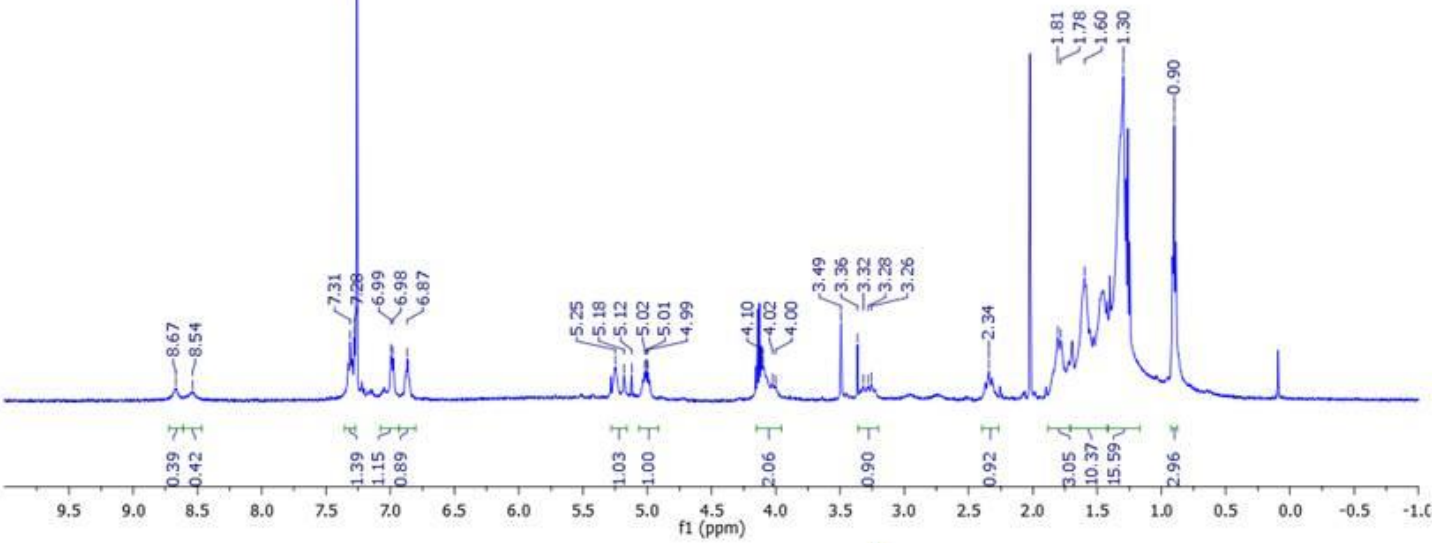

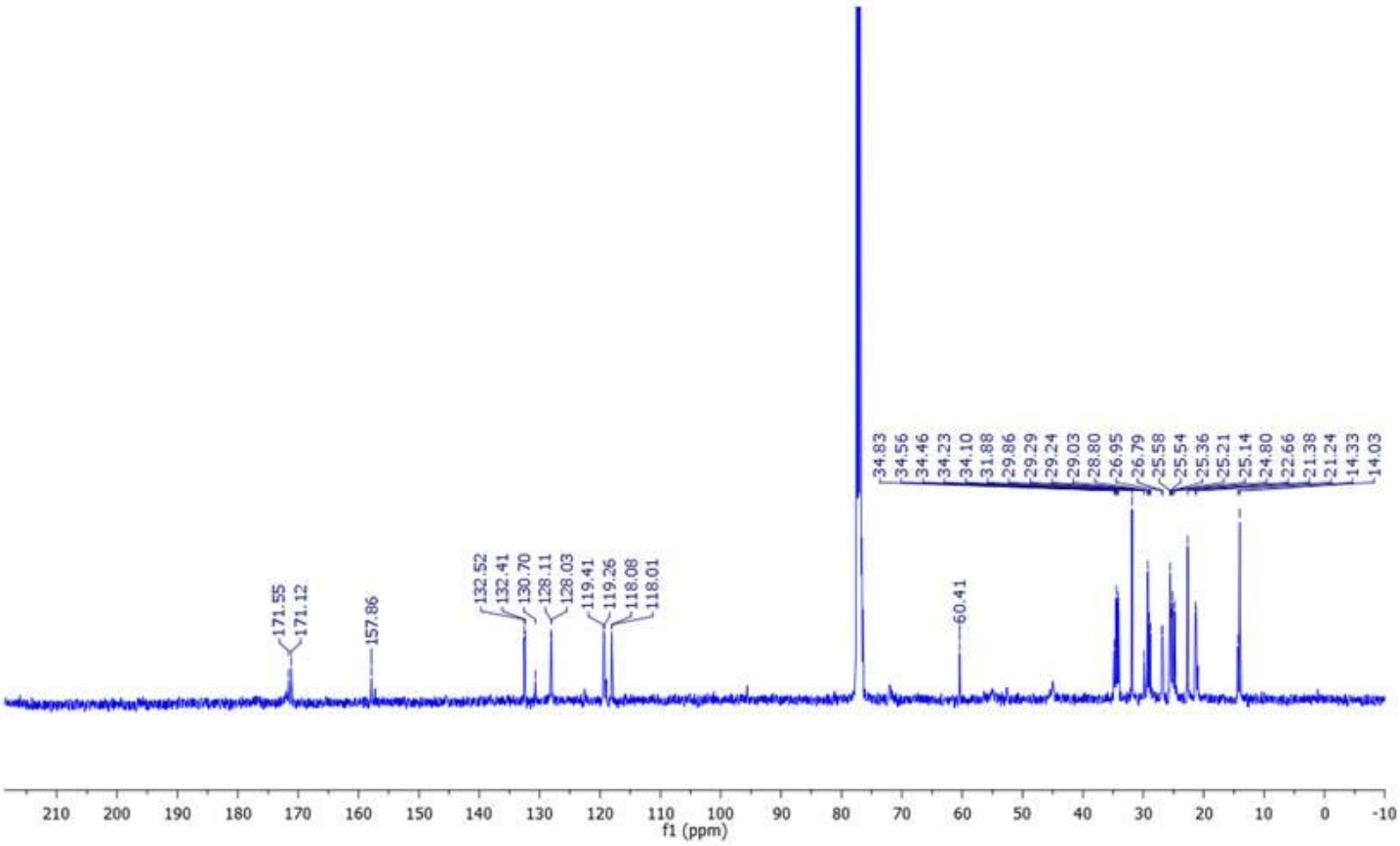

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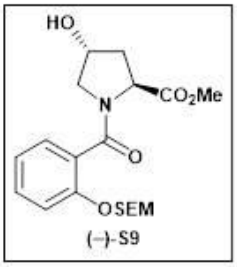

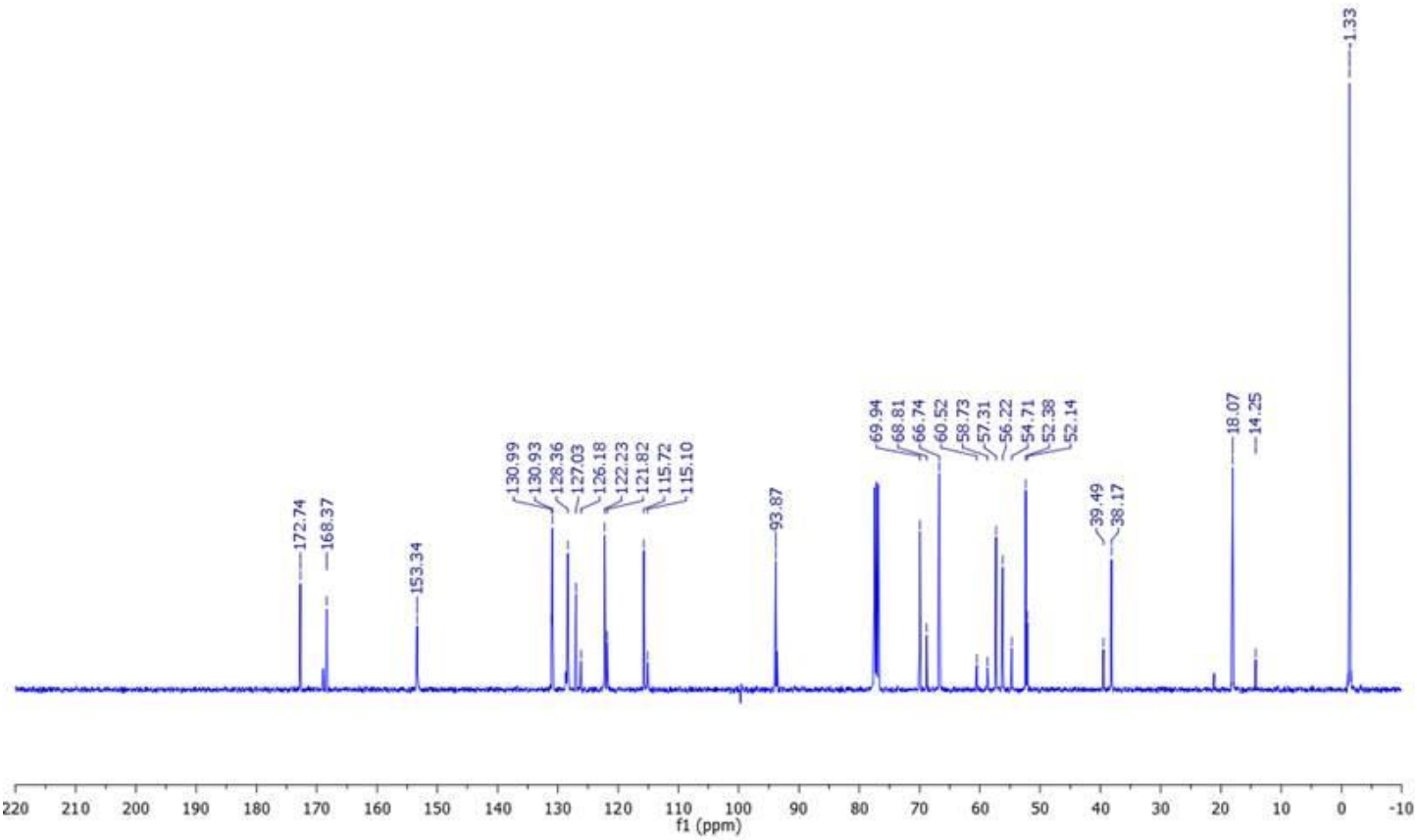

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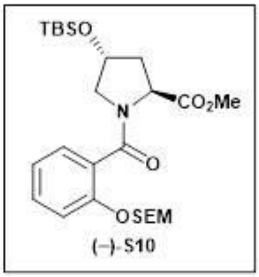

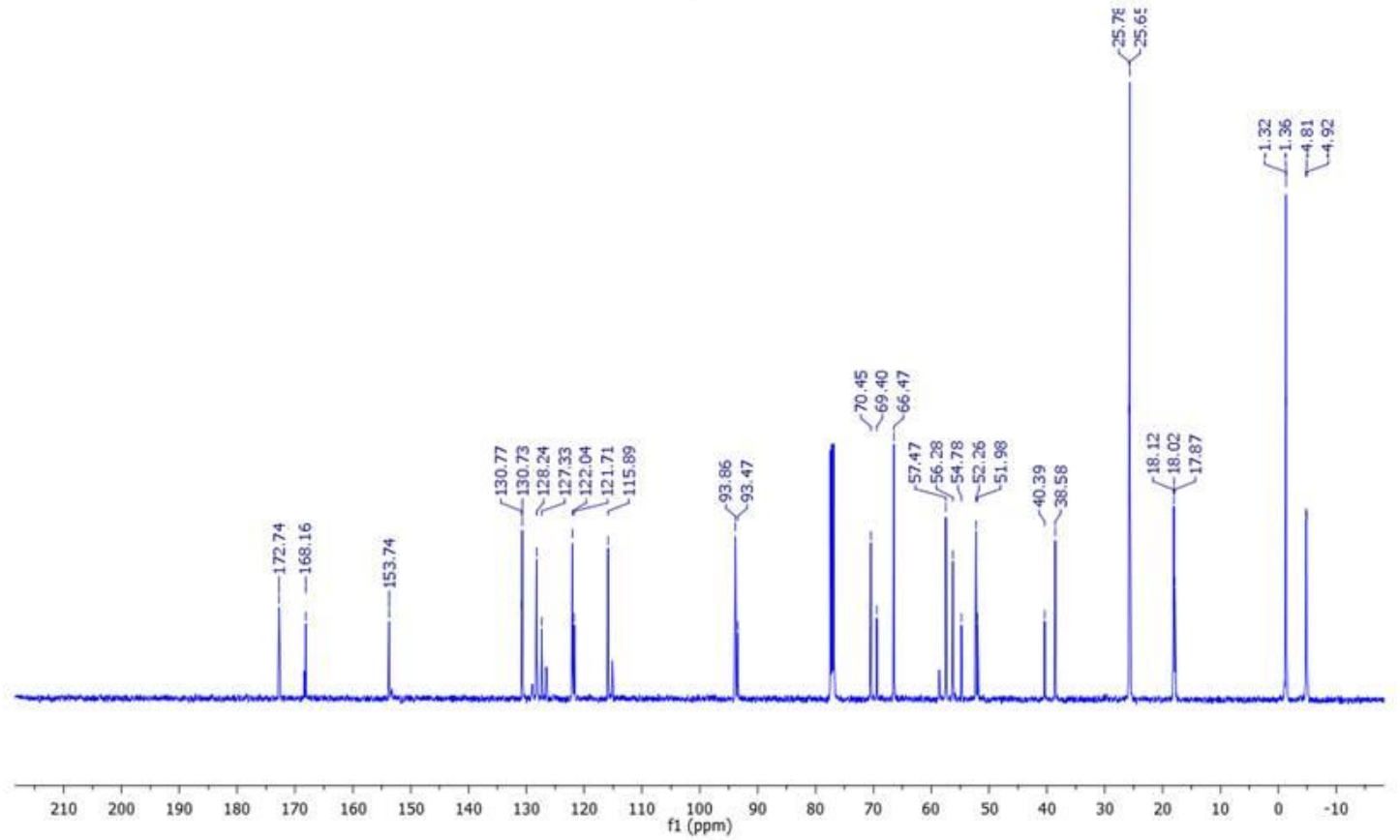

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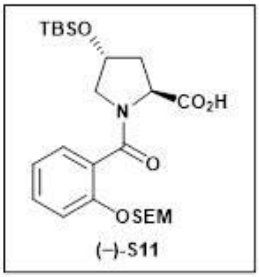

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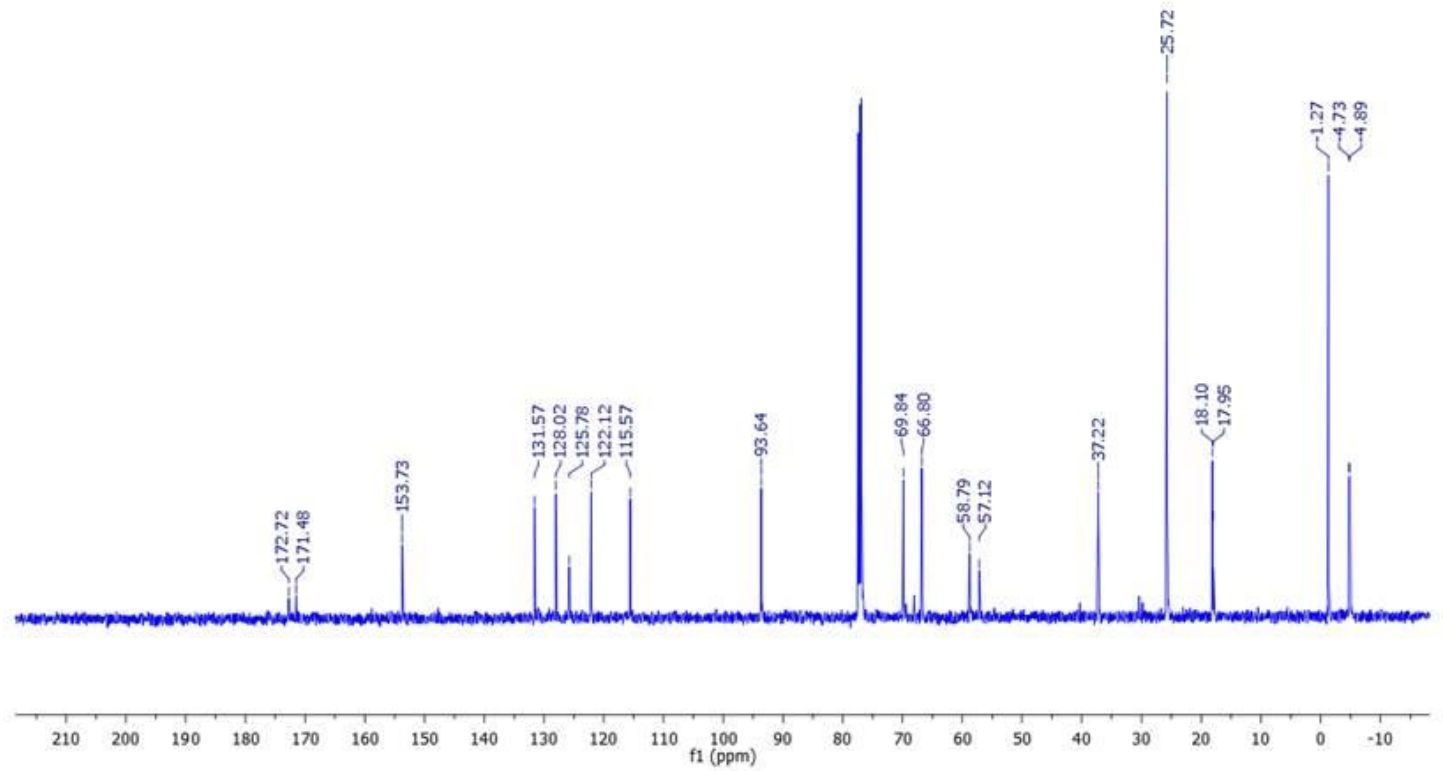

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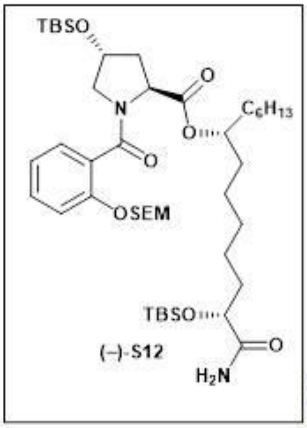

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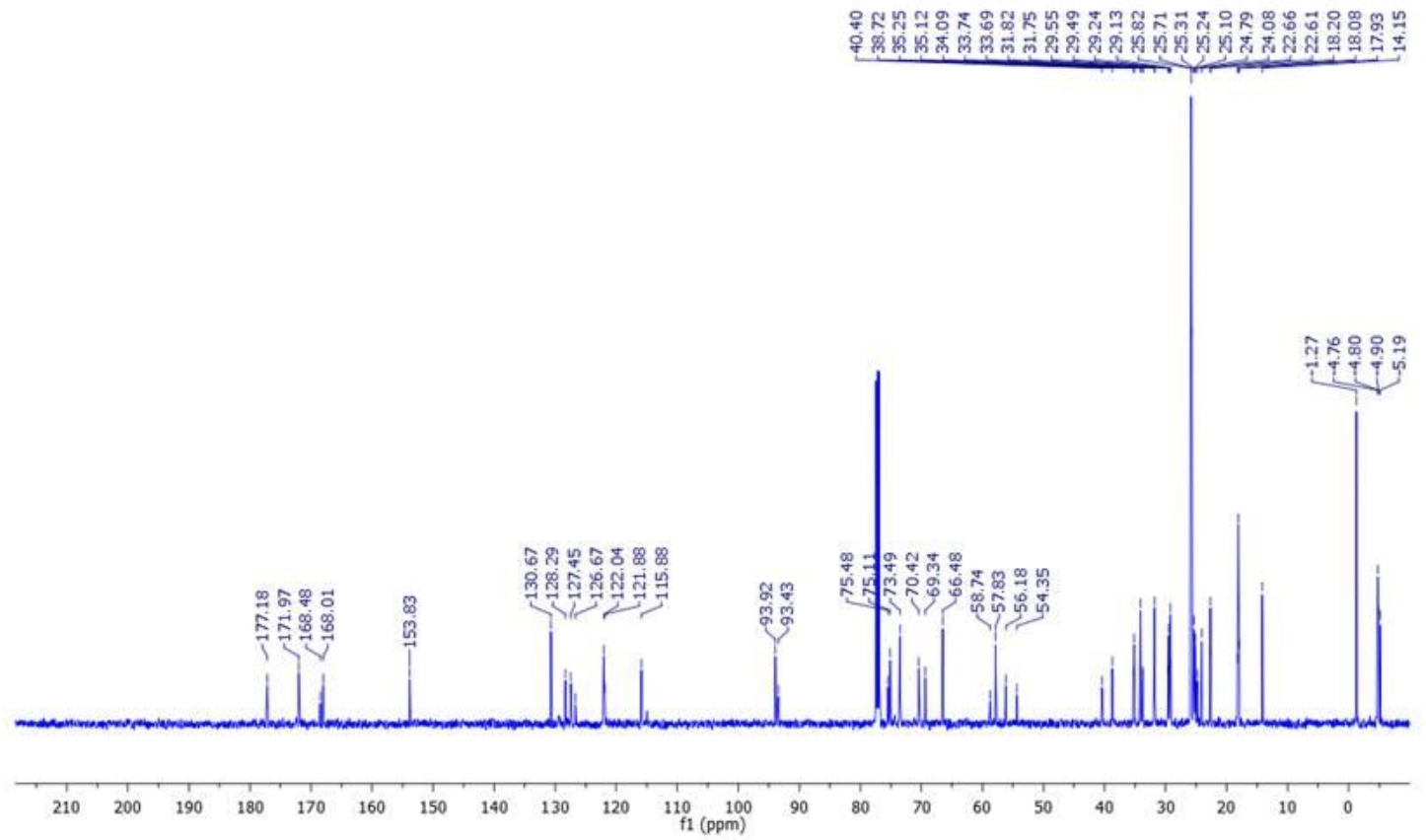

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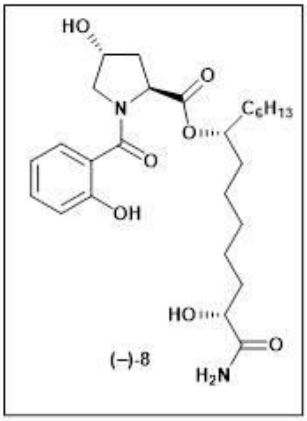

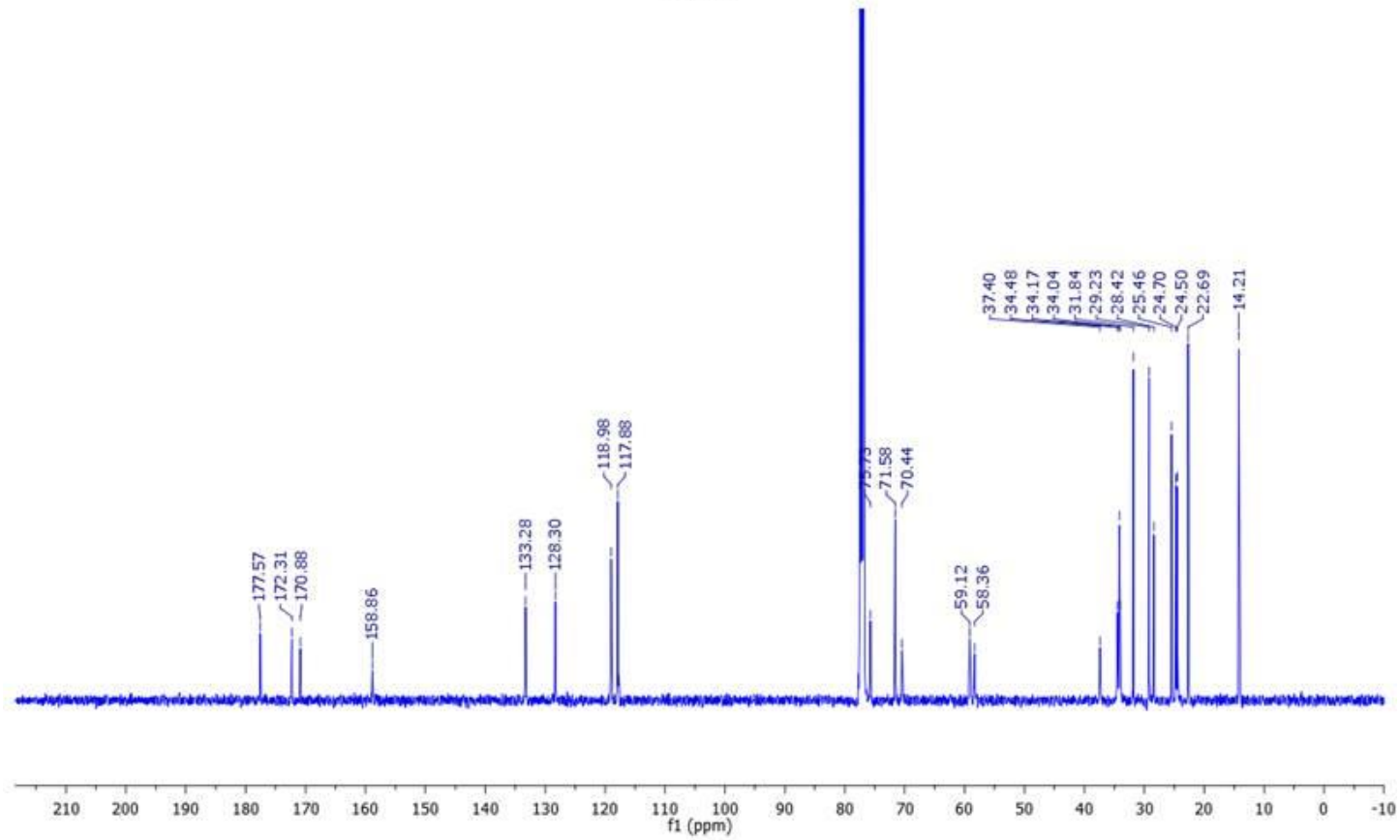

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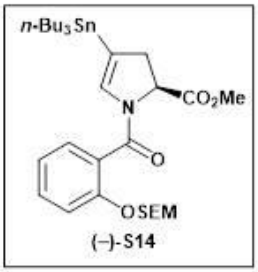
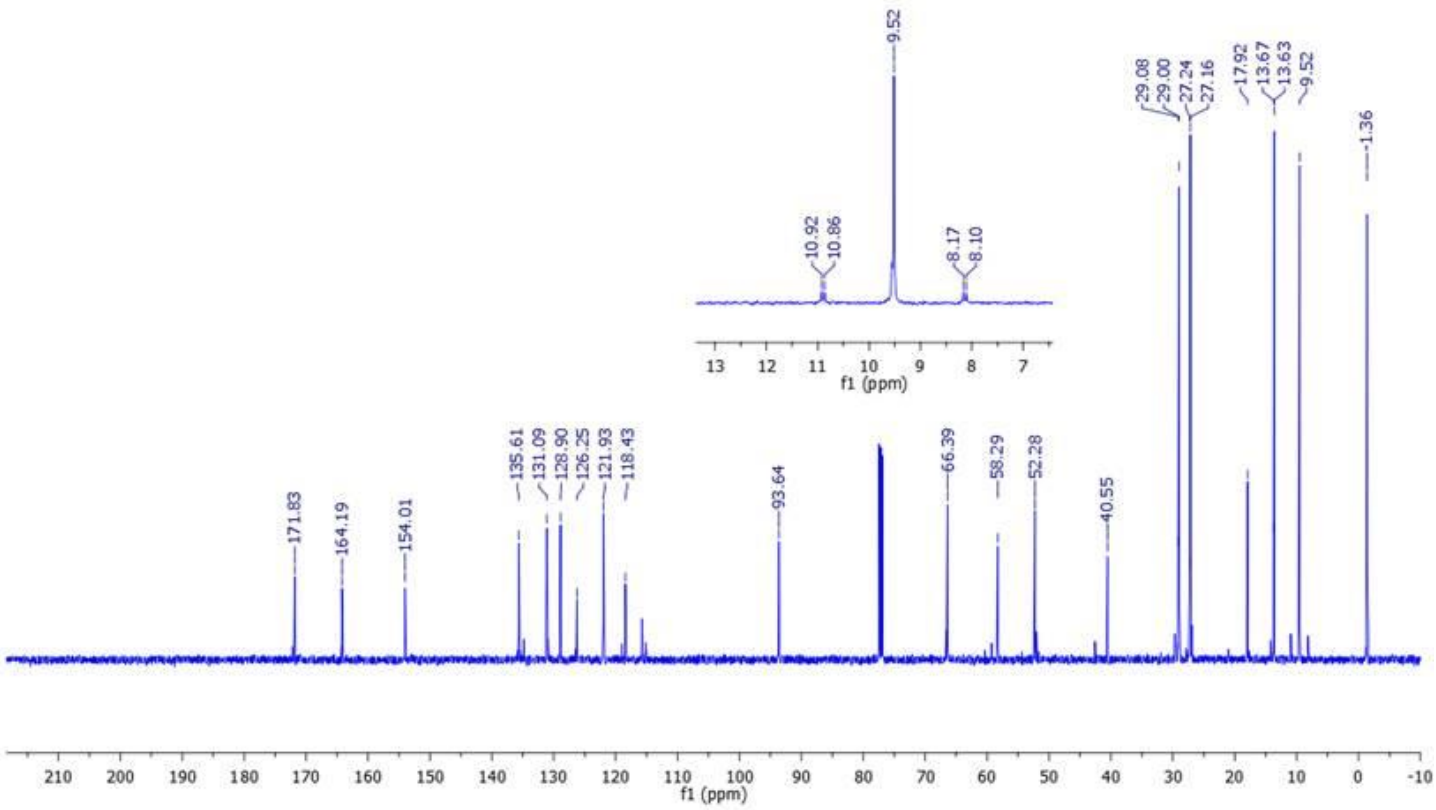


(–)-S14



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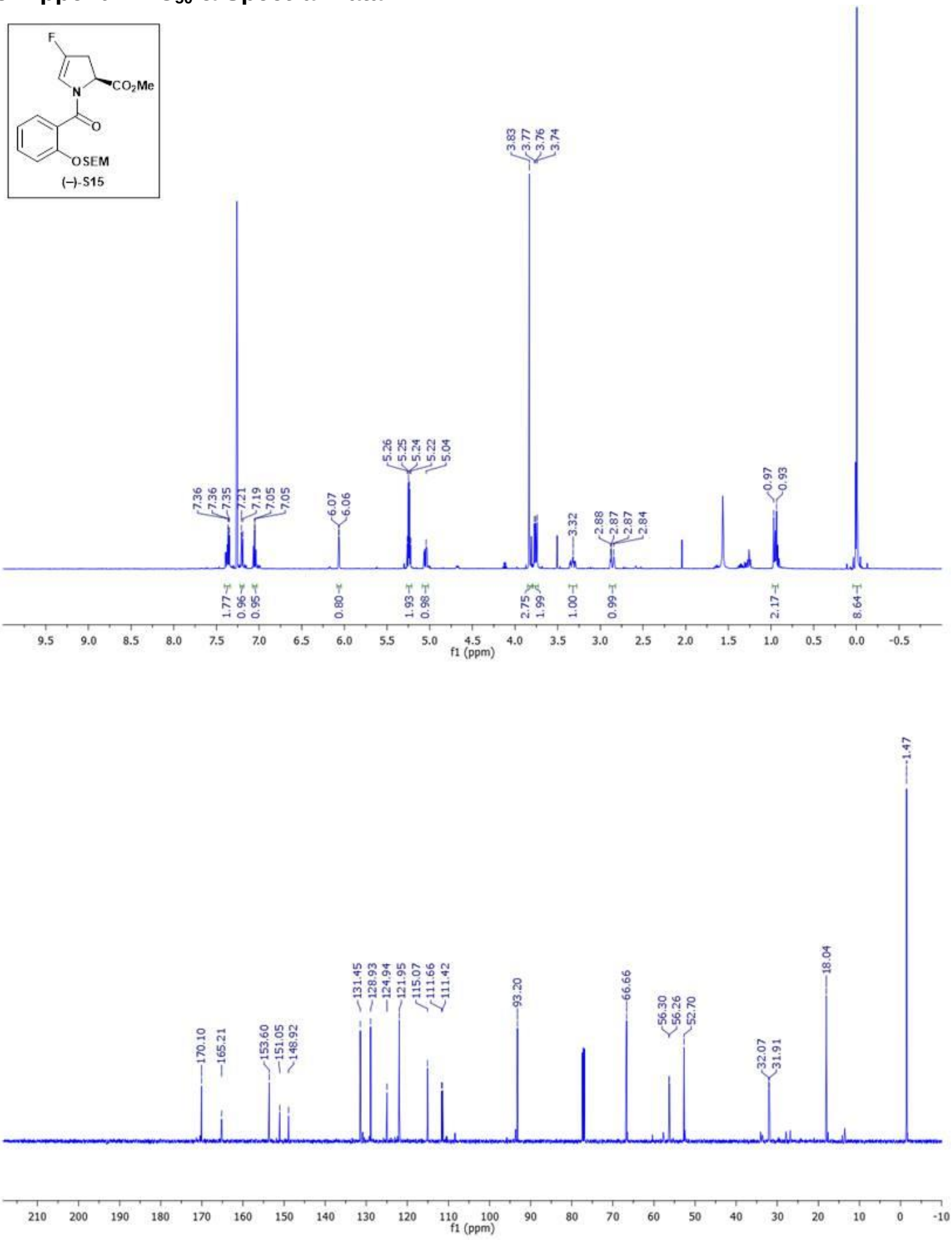

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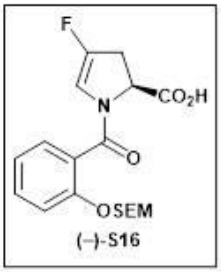

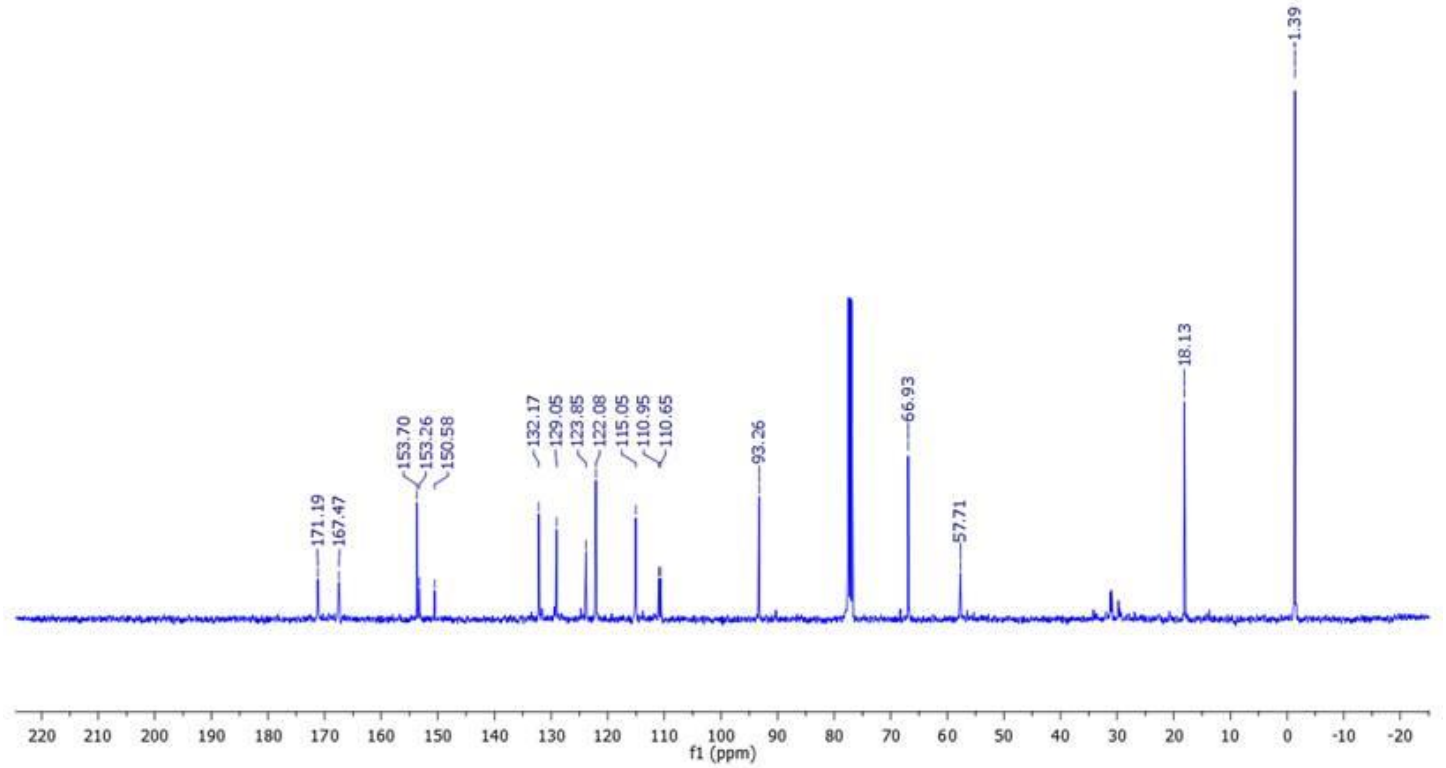

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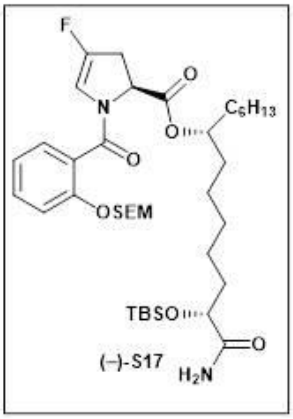

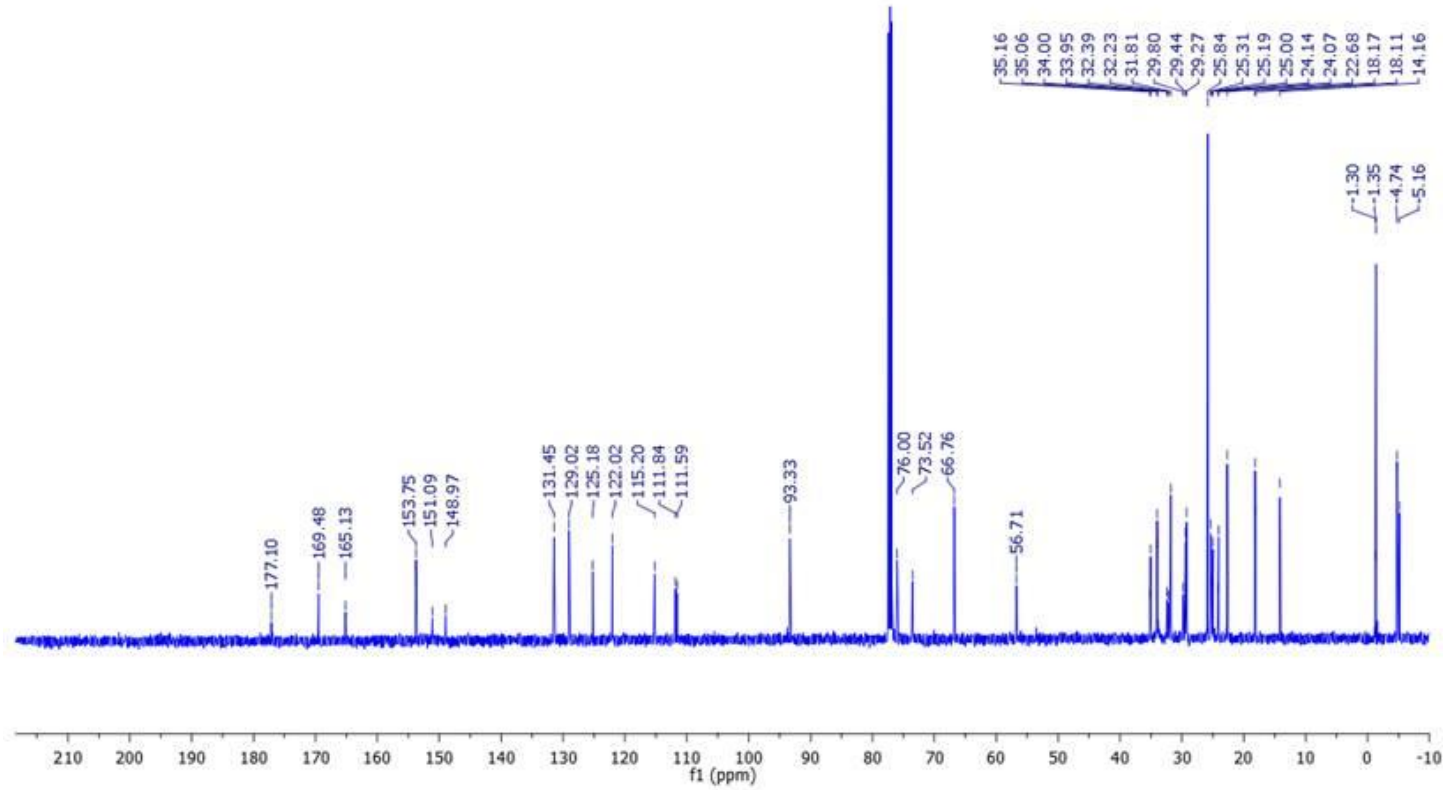

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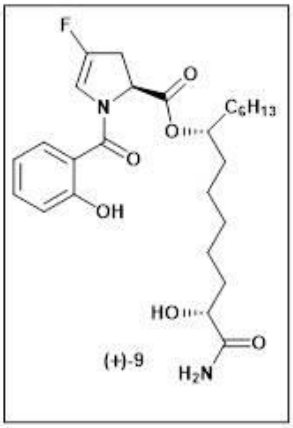

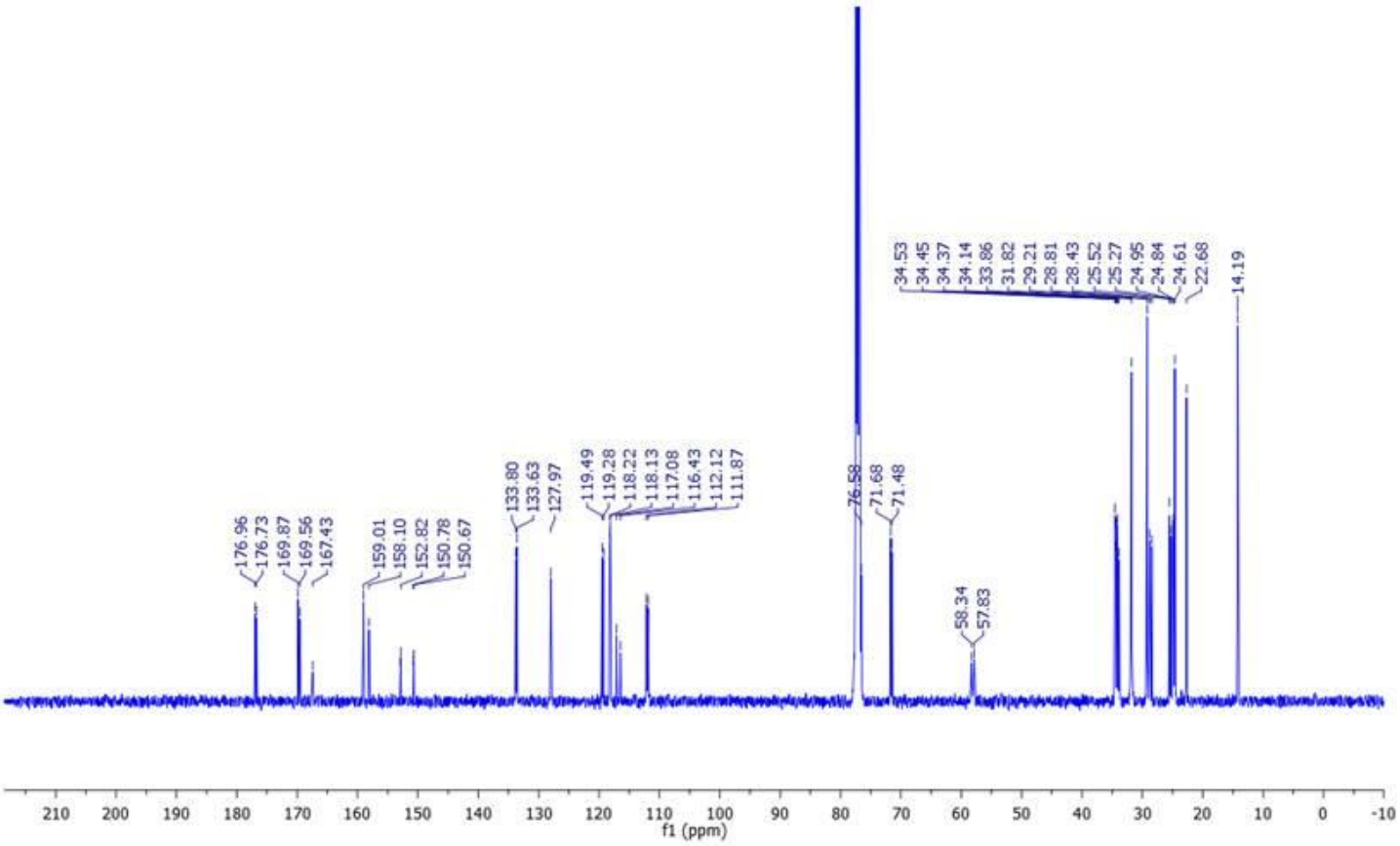

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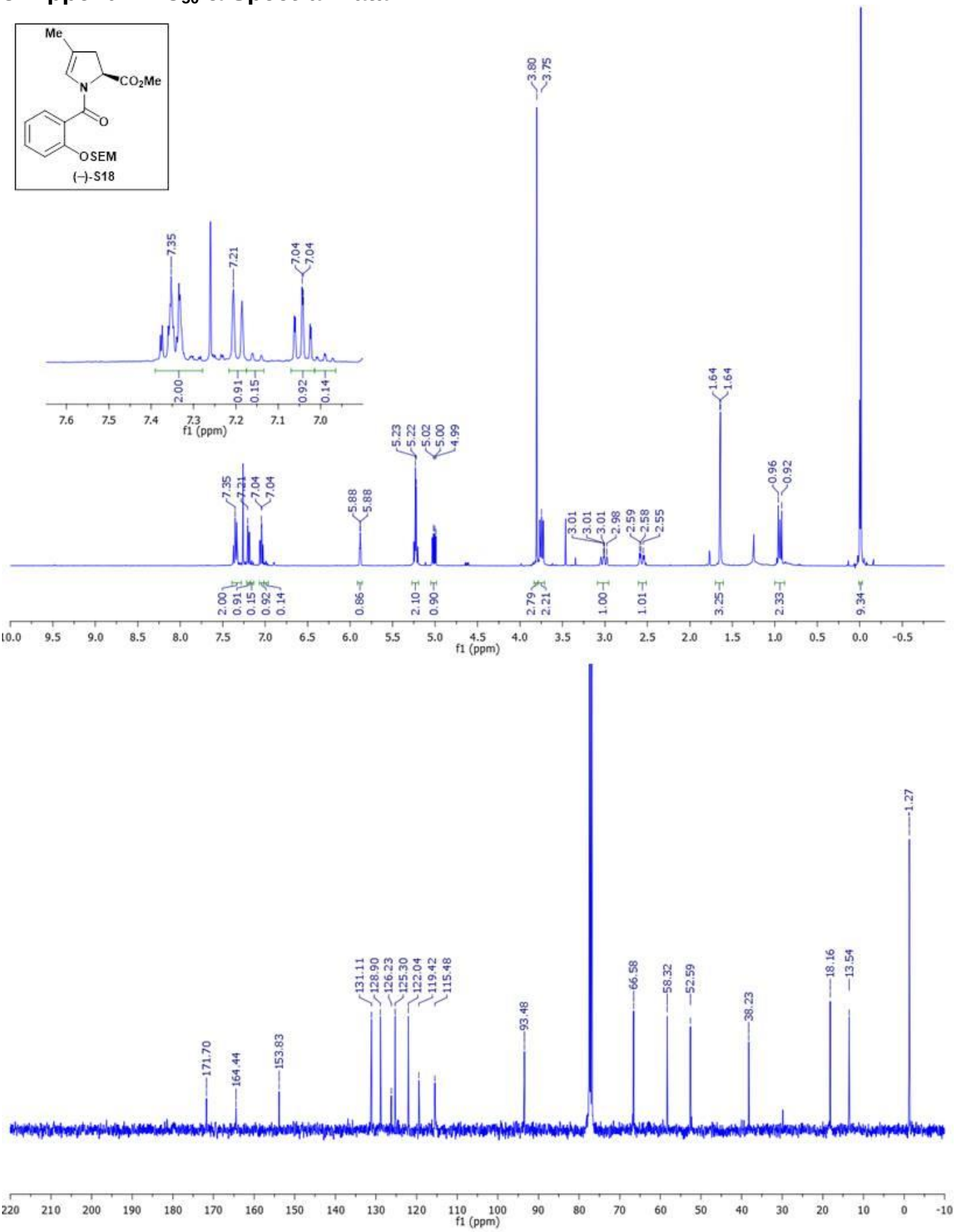

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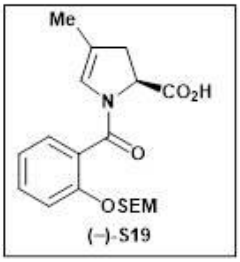
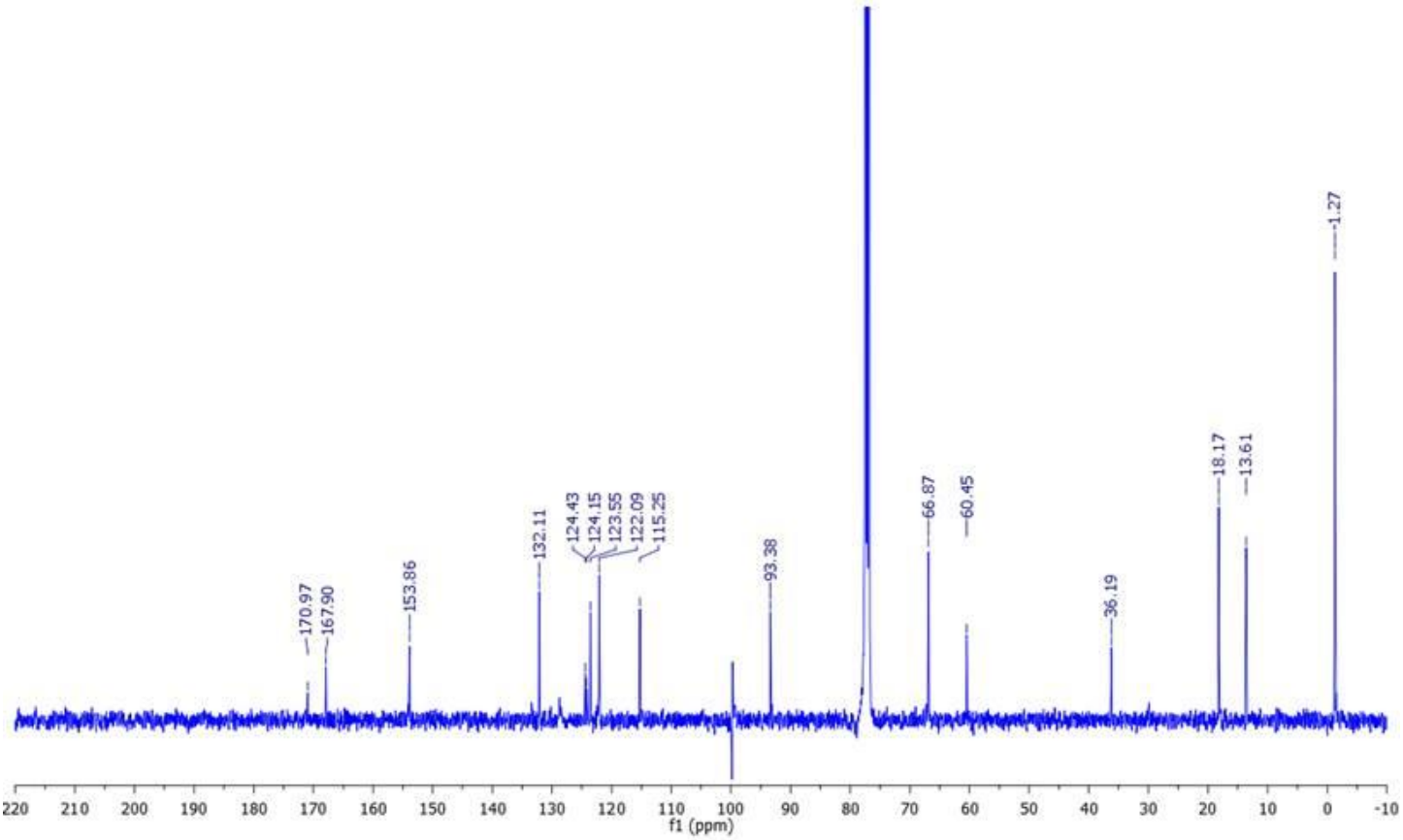


(−)-S19



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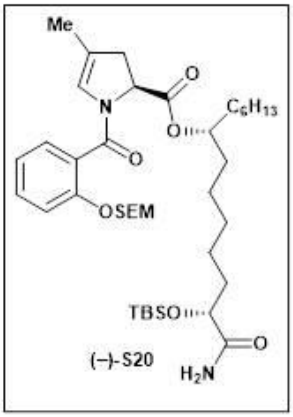

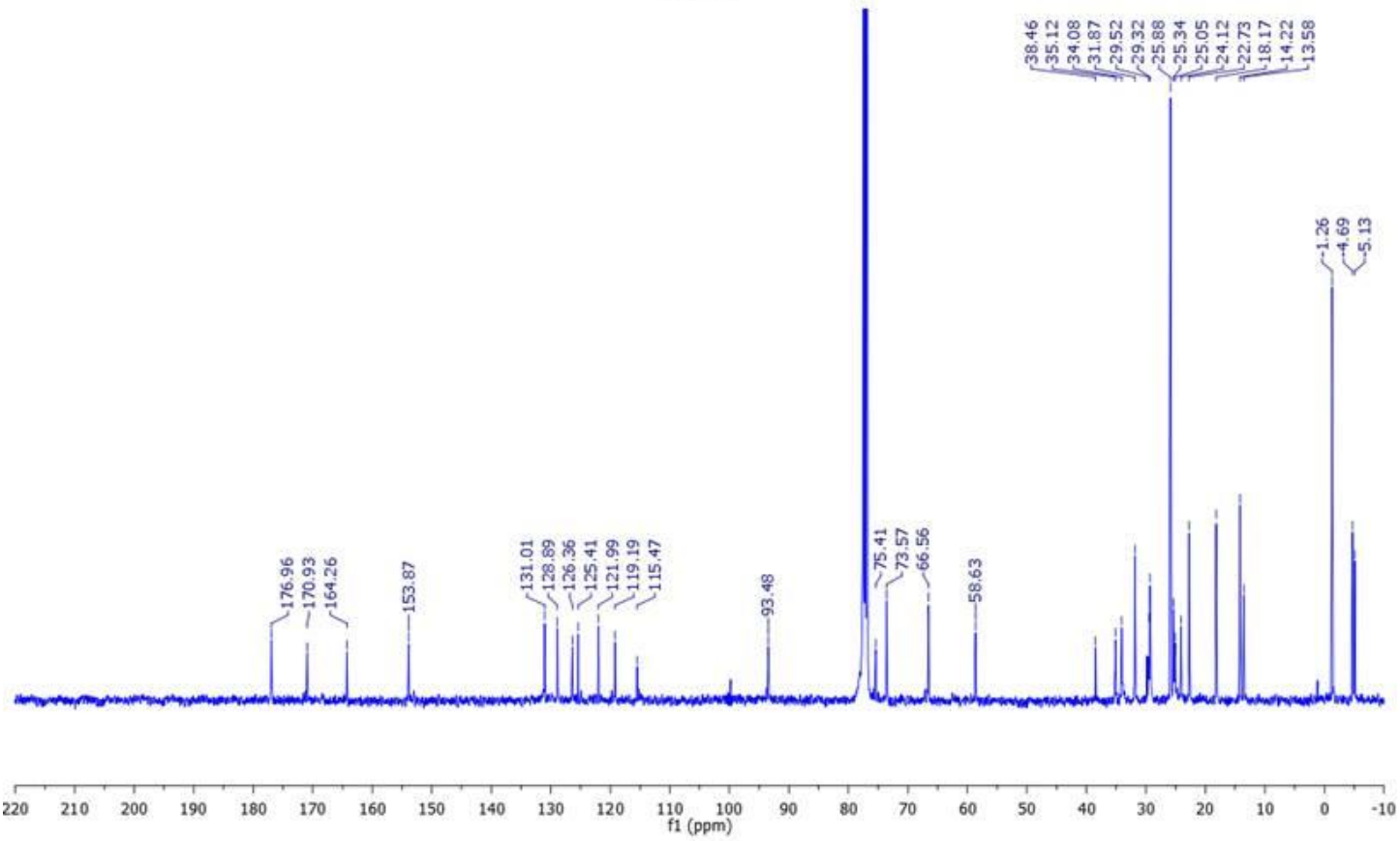

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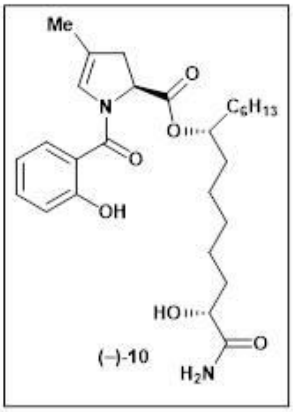

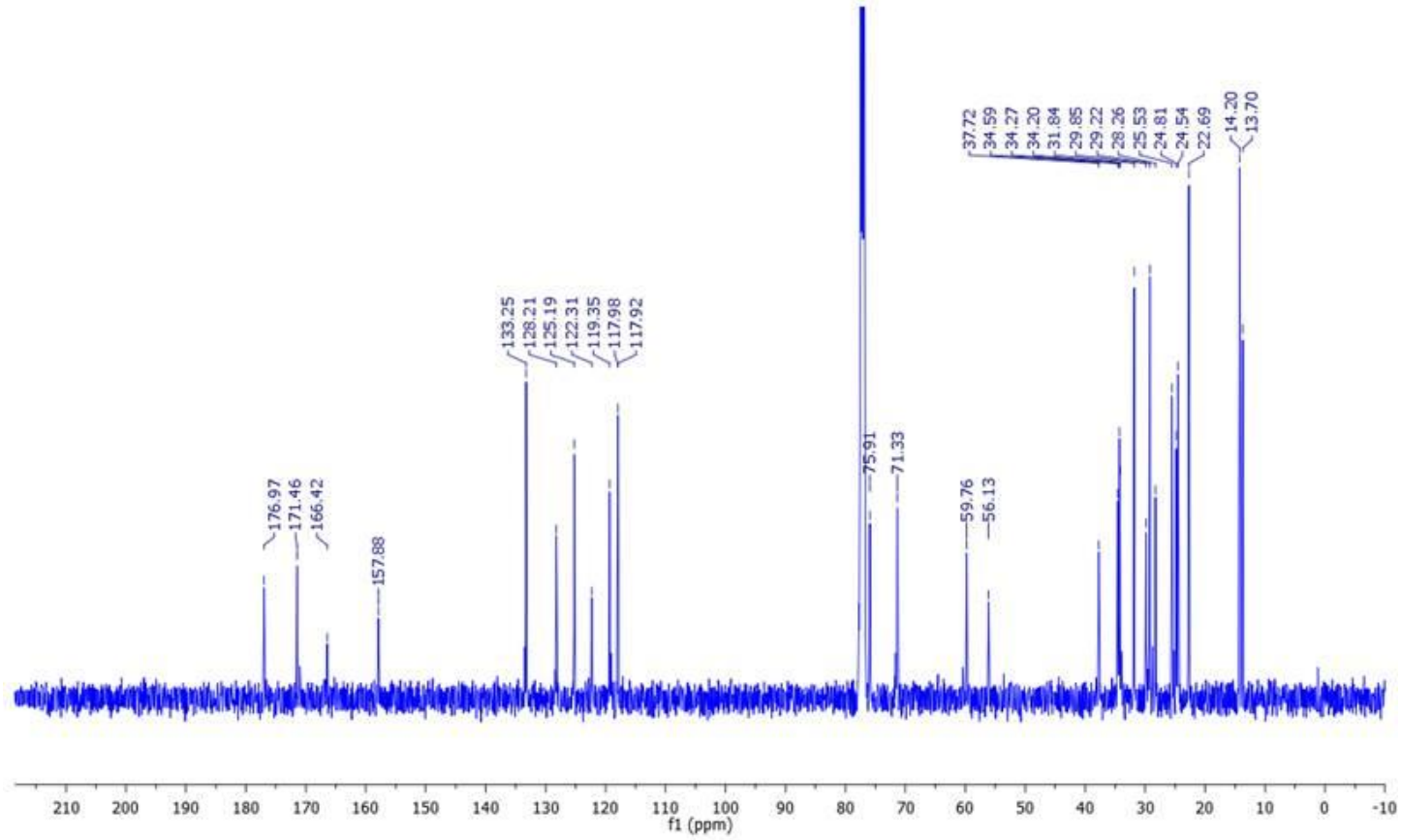

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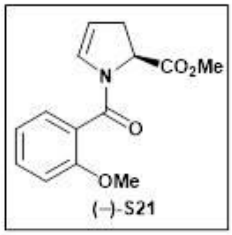

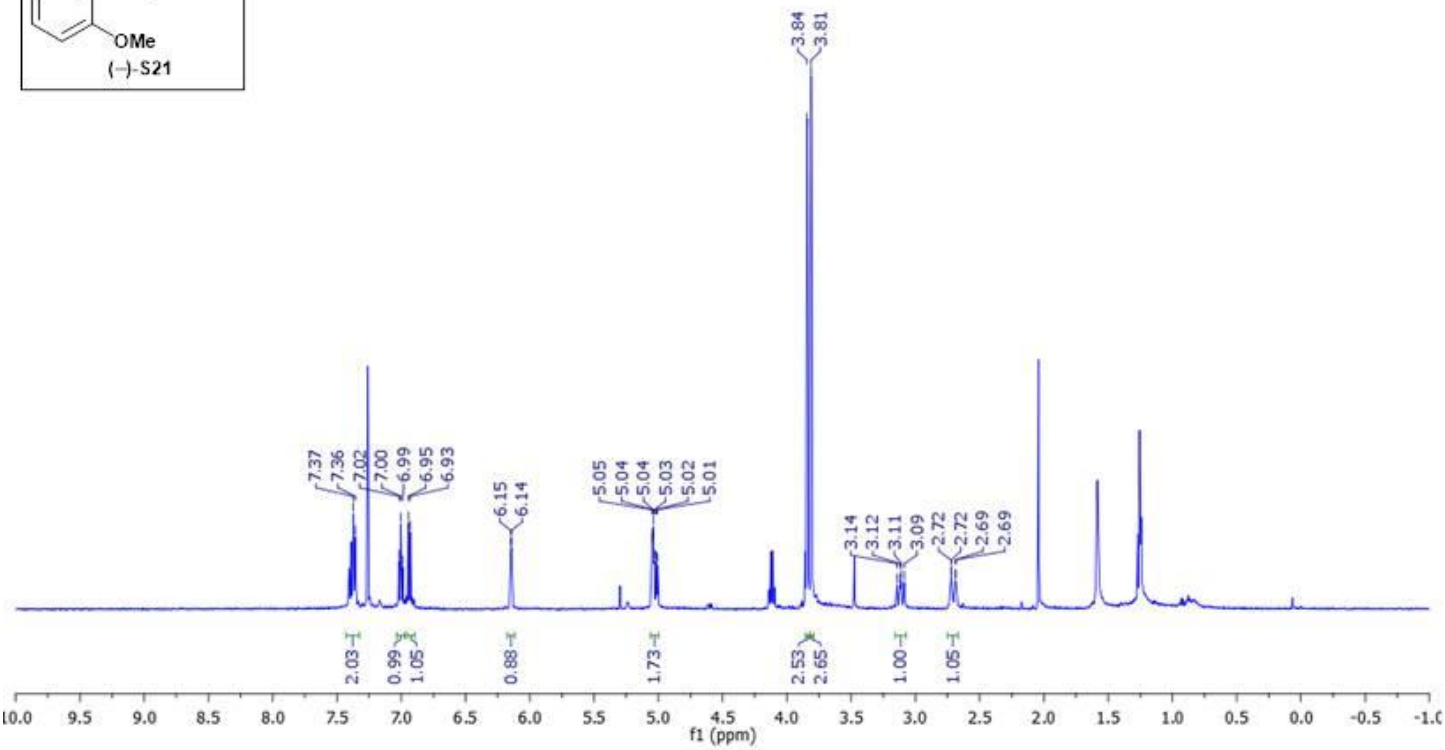

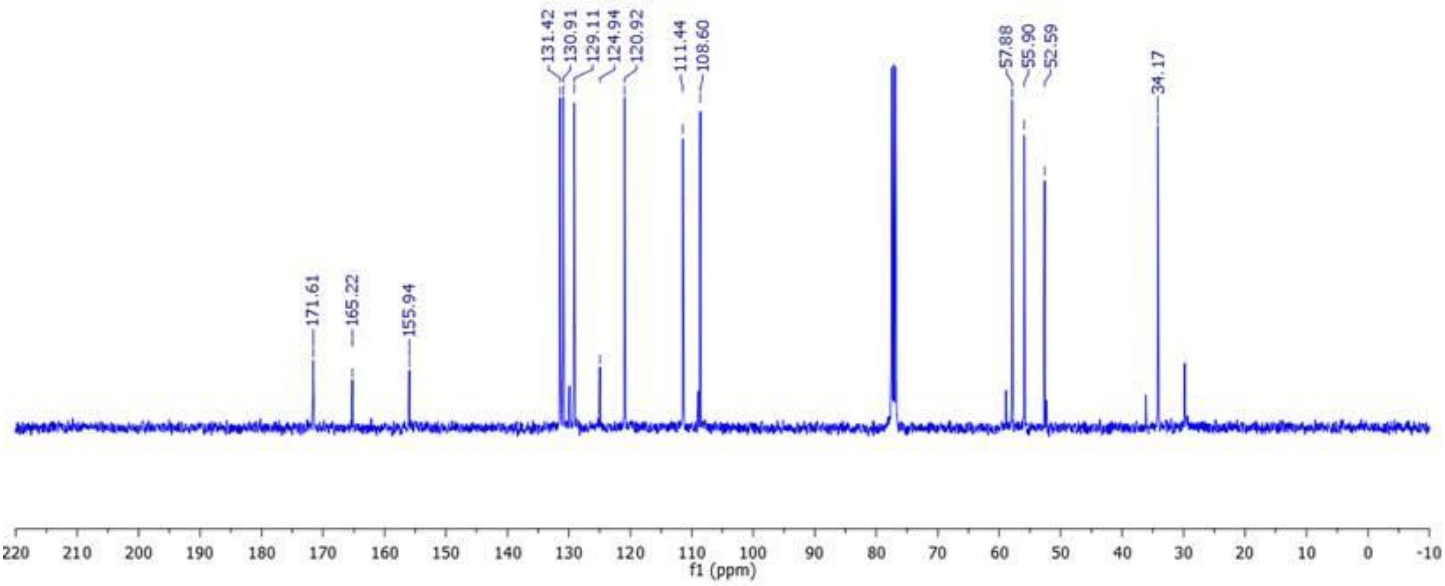

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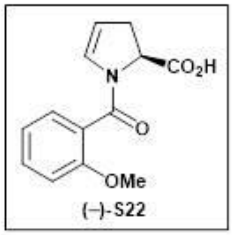

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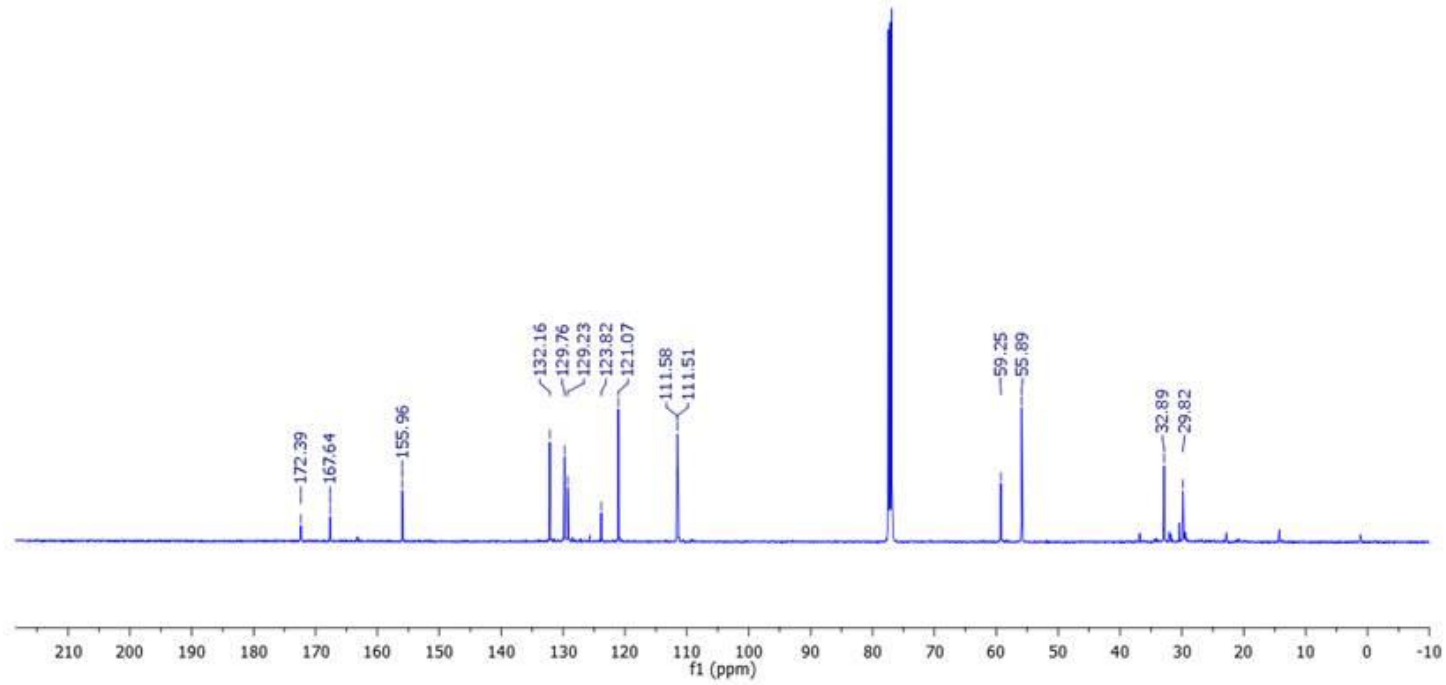

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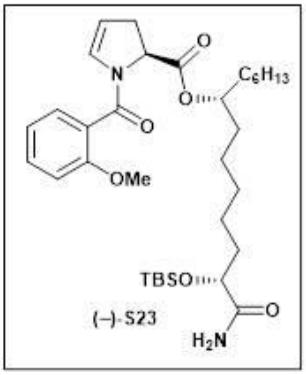

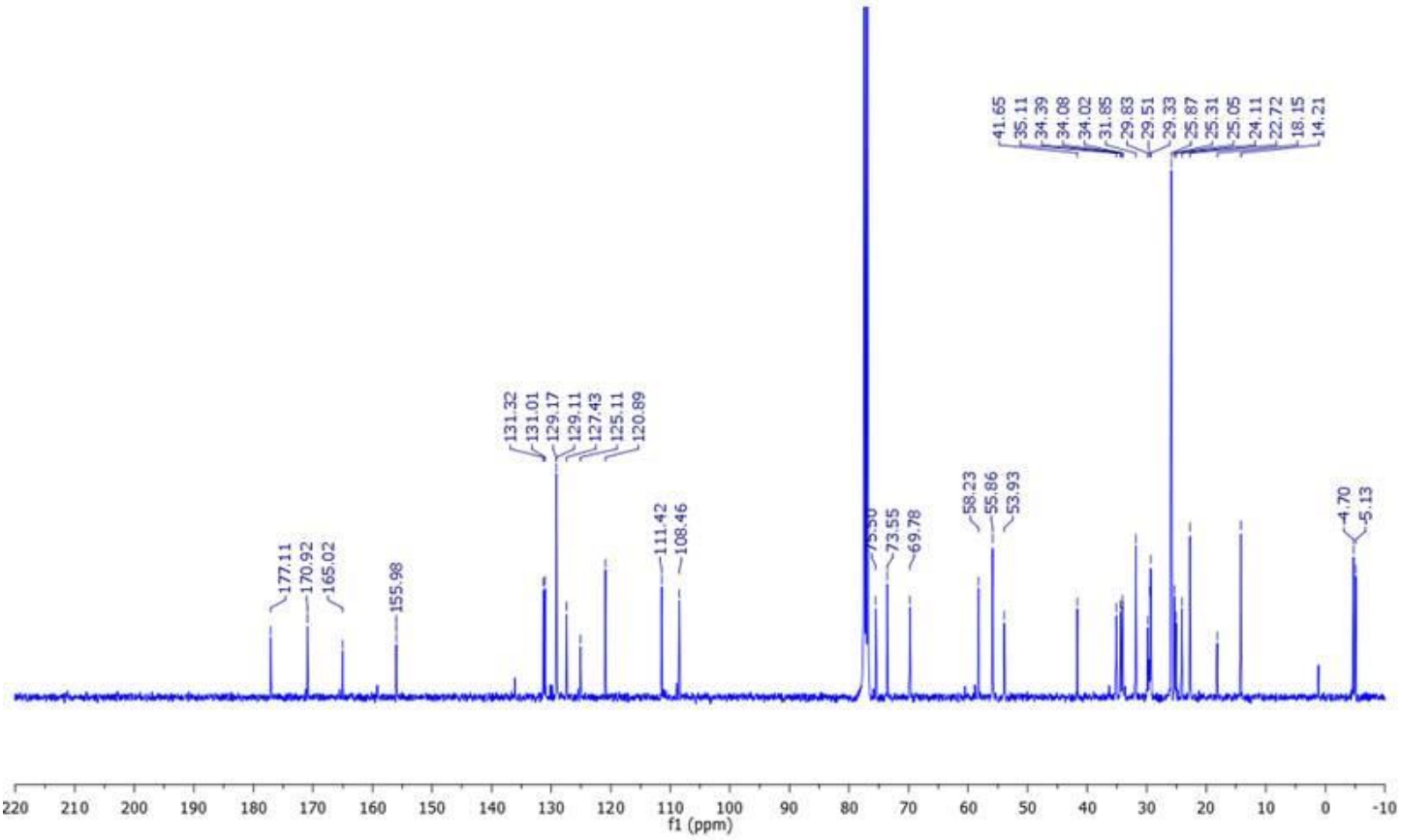

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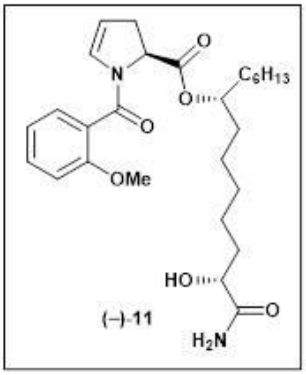

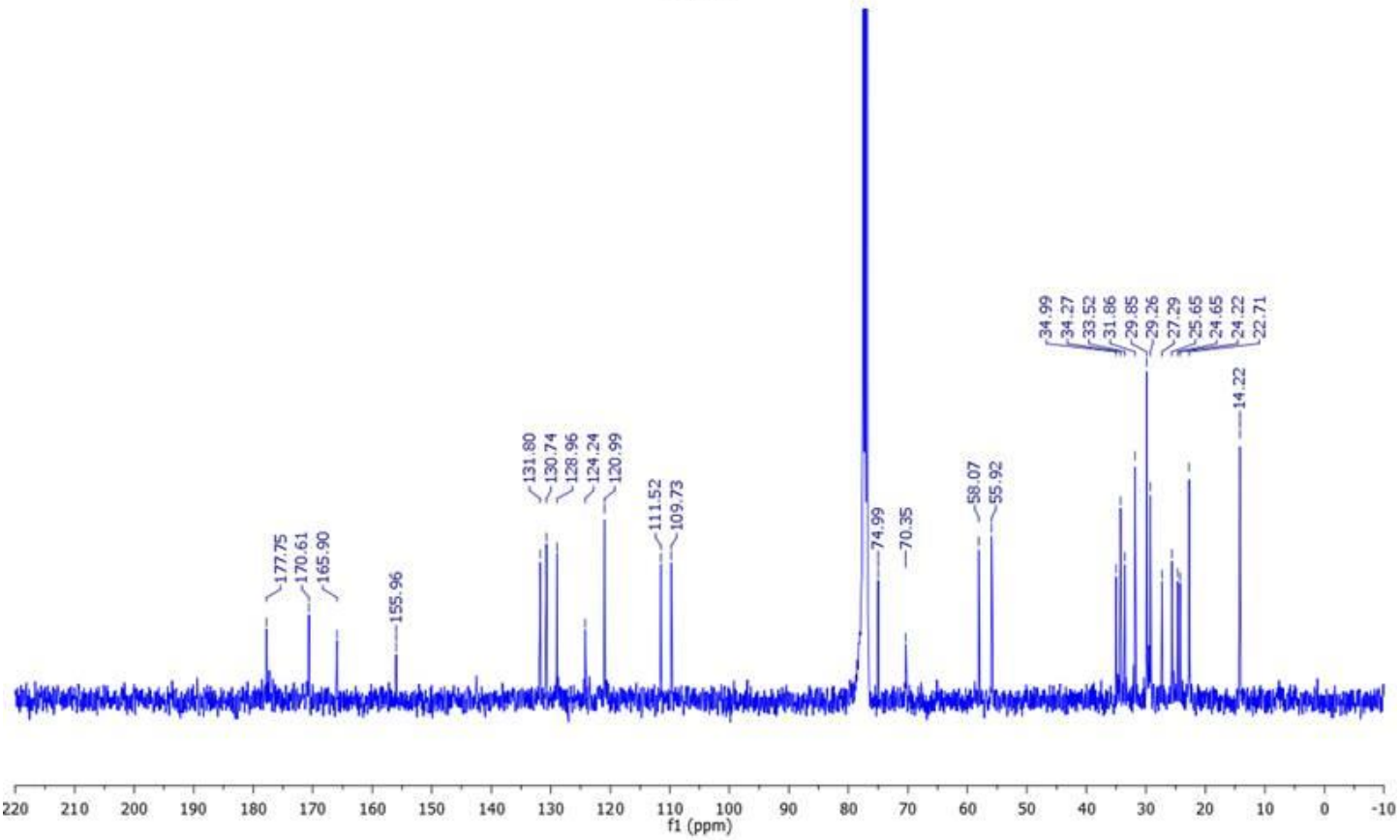

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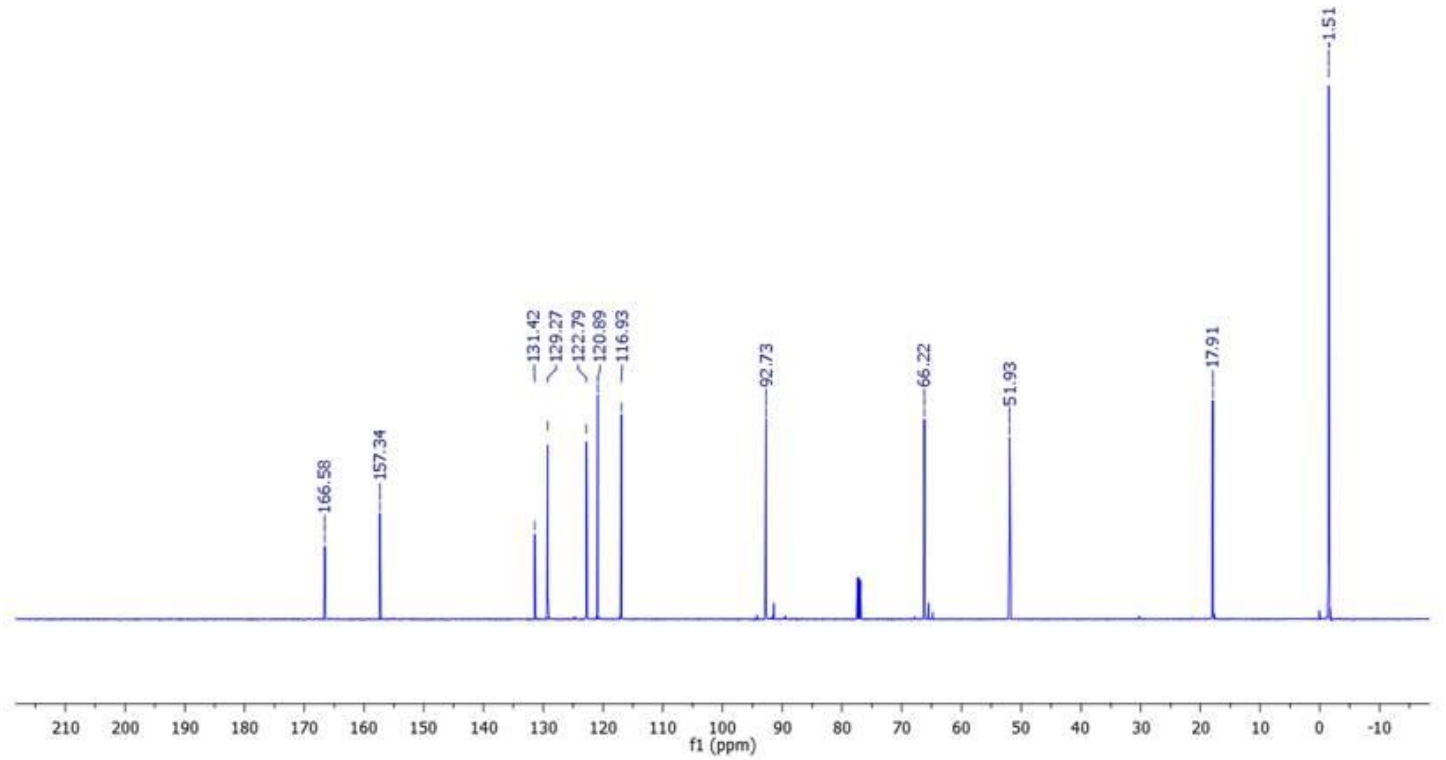

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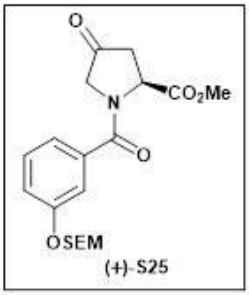
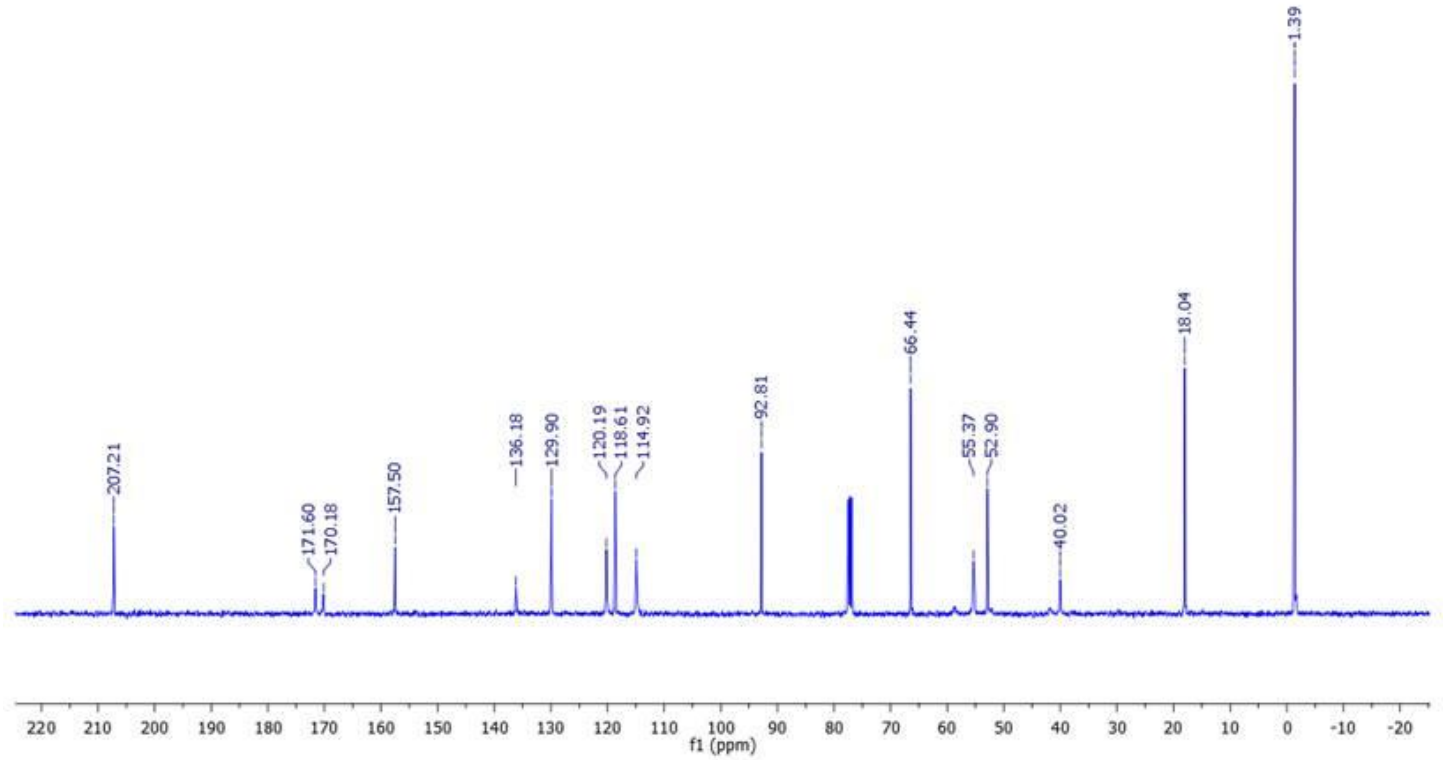


(+)-S25



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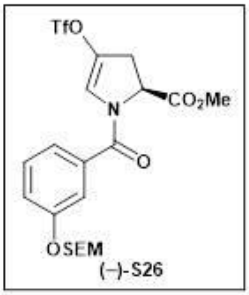

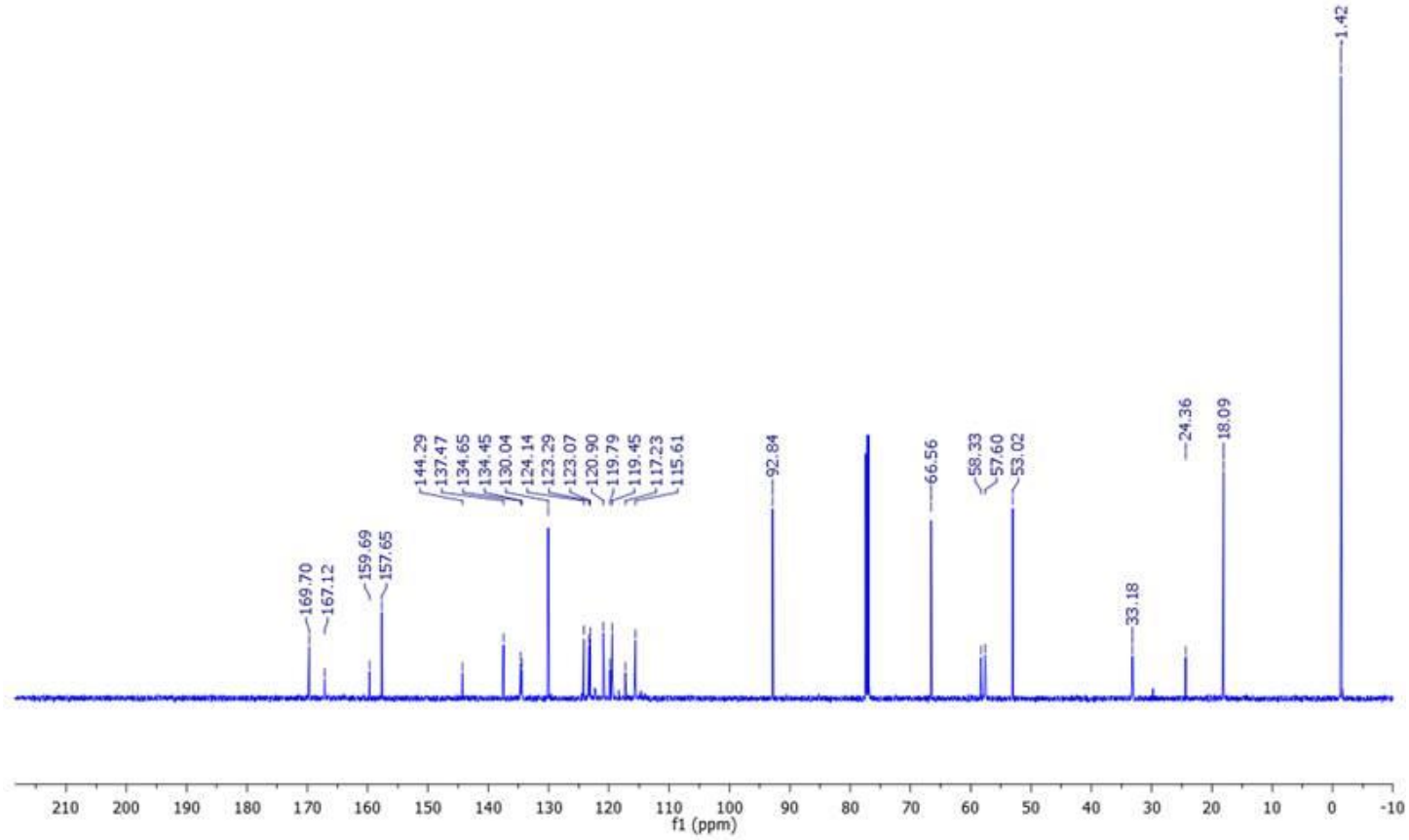

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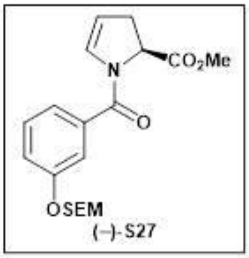

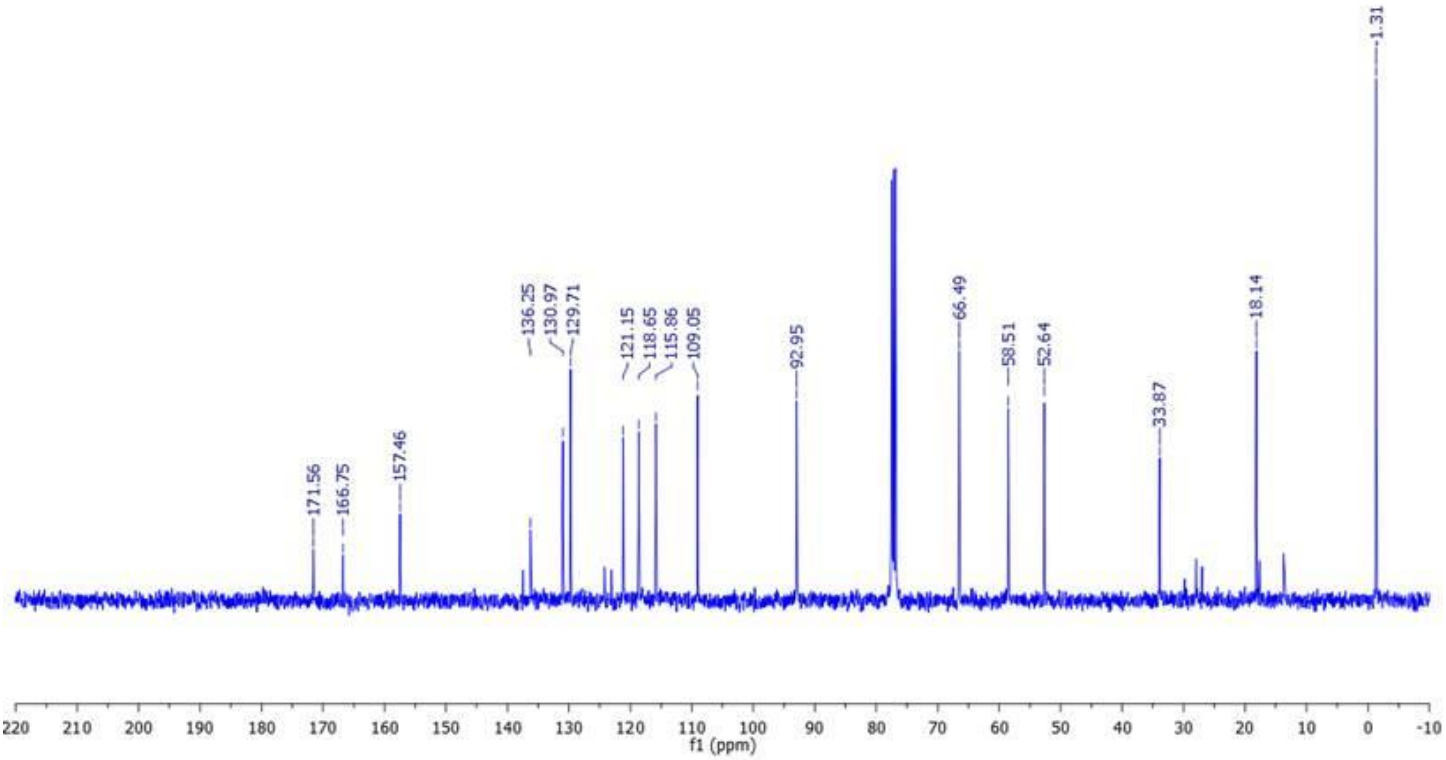

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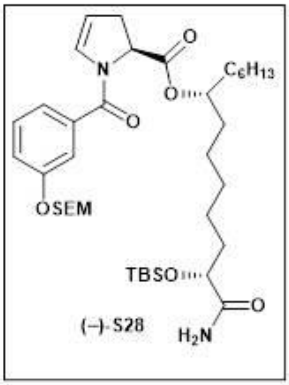

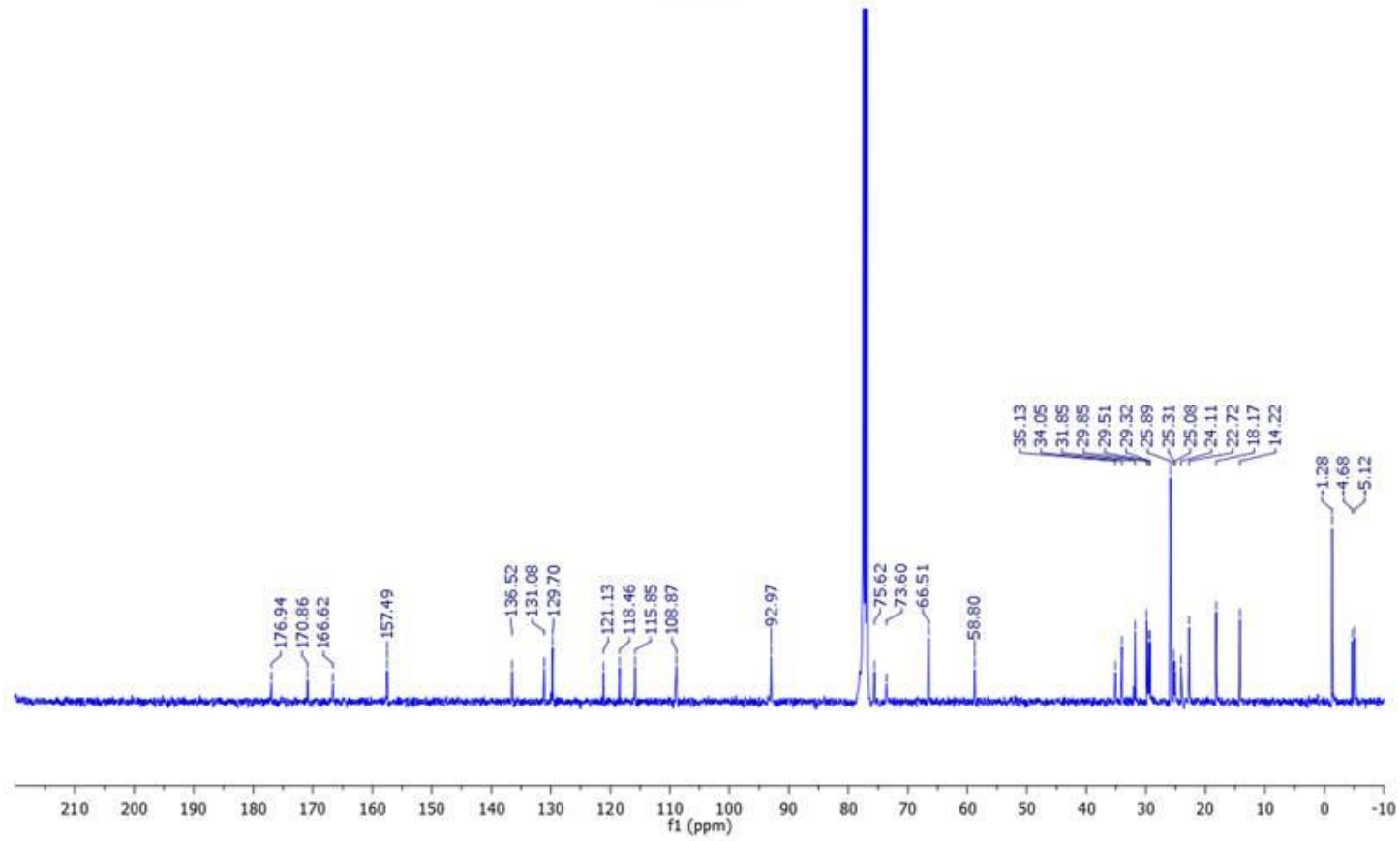

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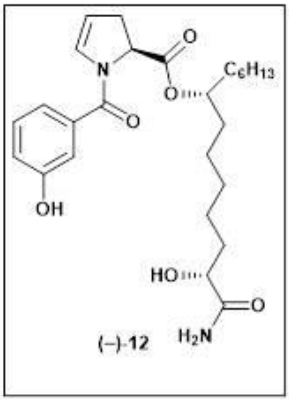

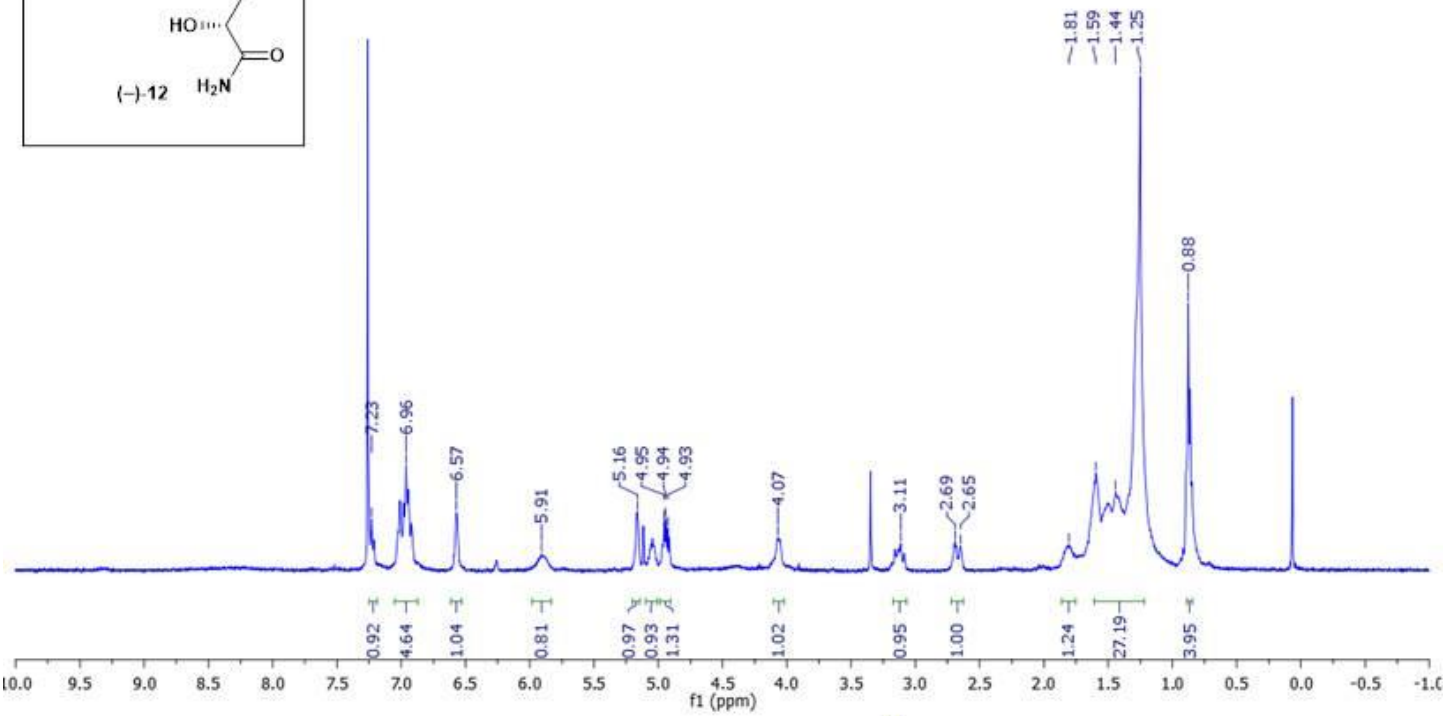

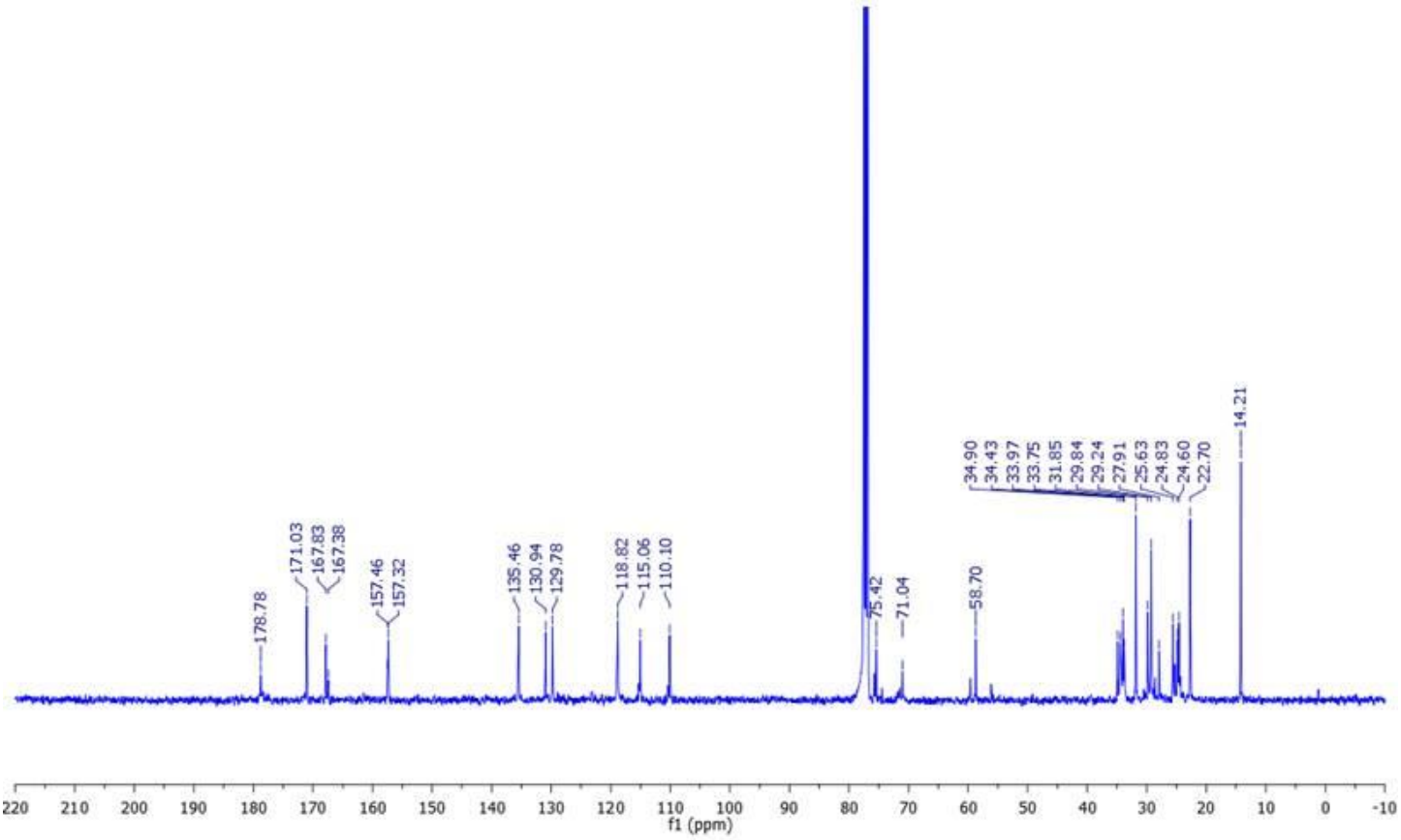

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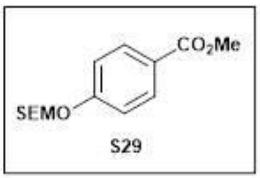
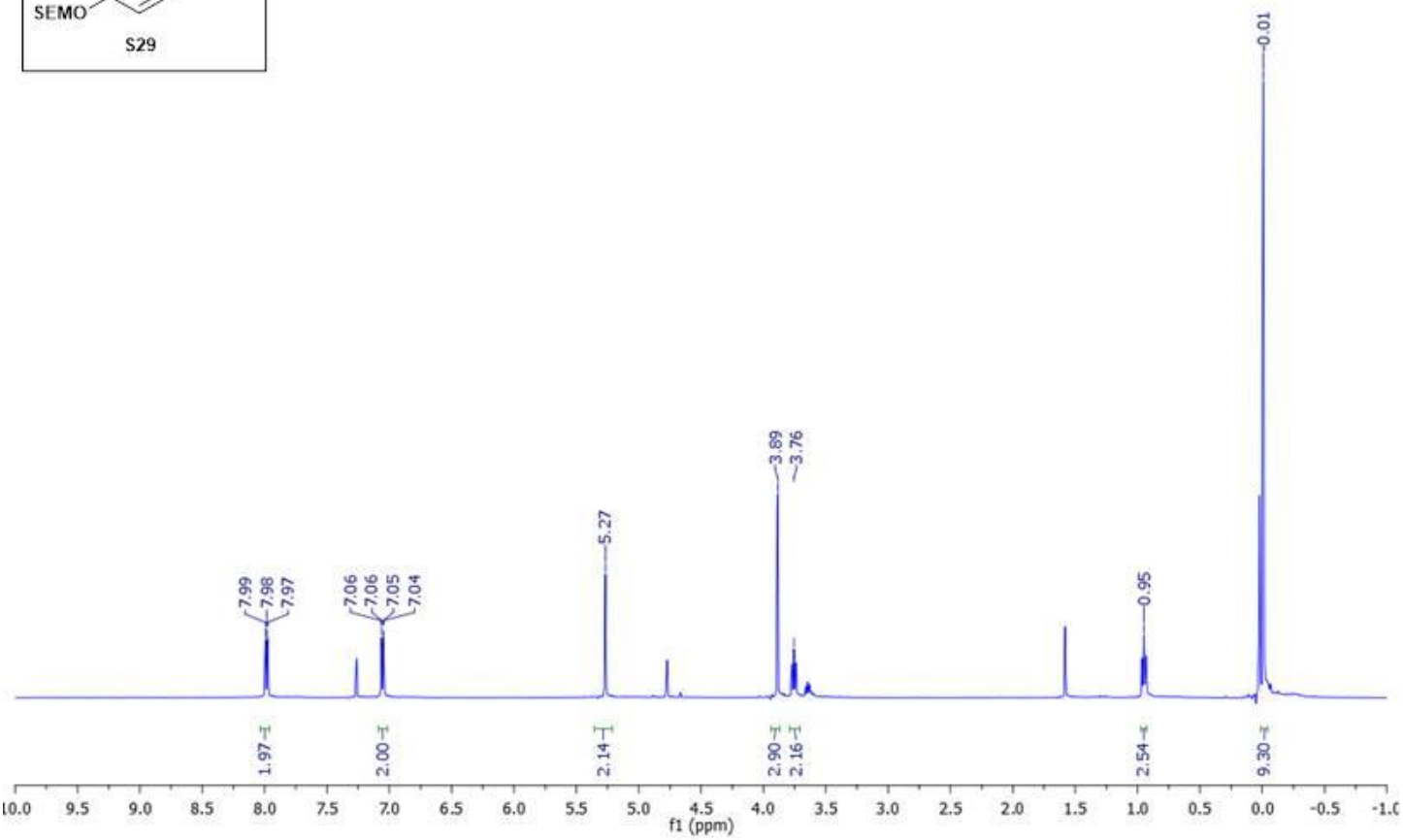
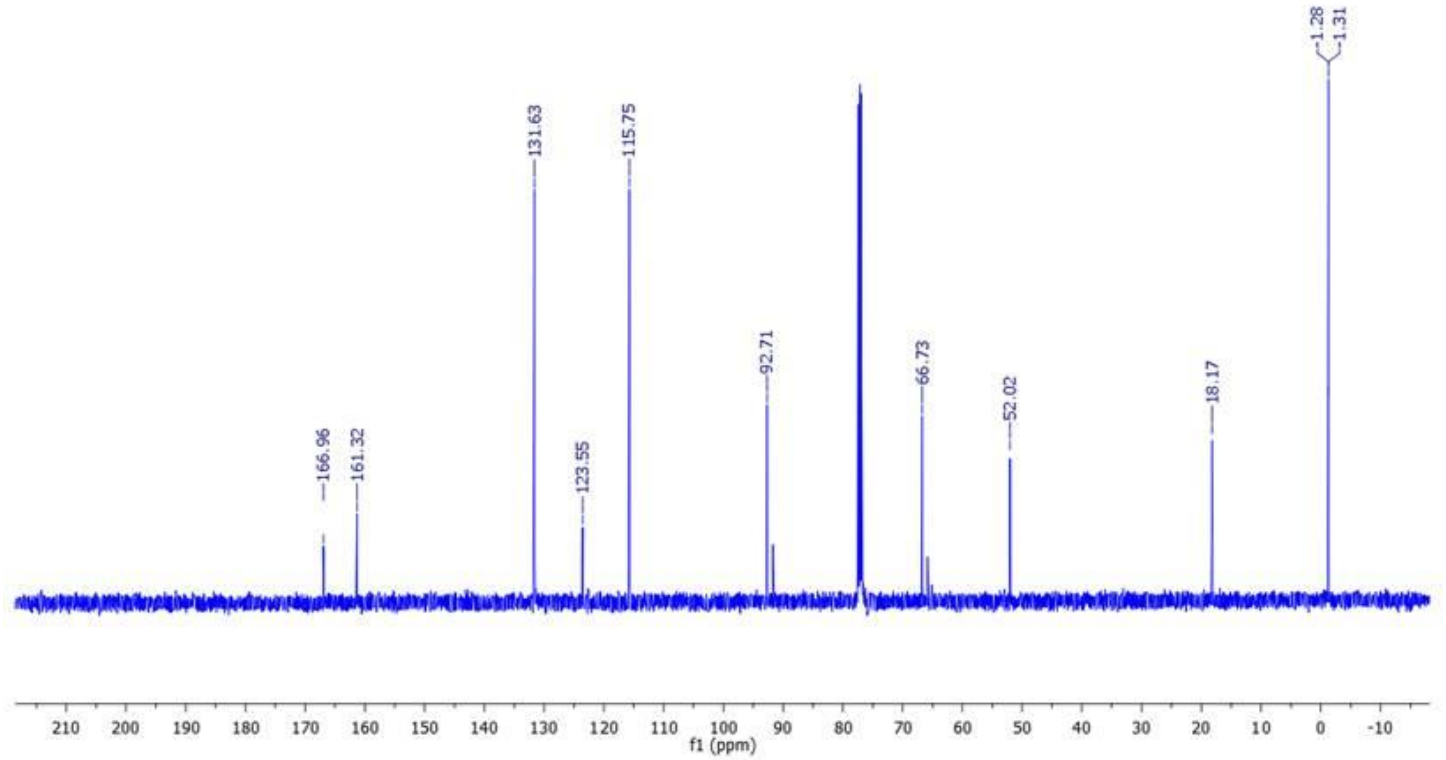
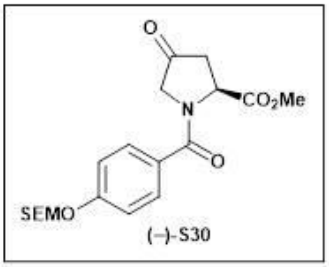


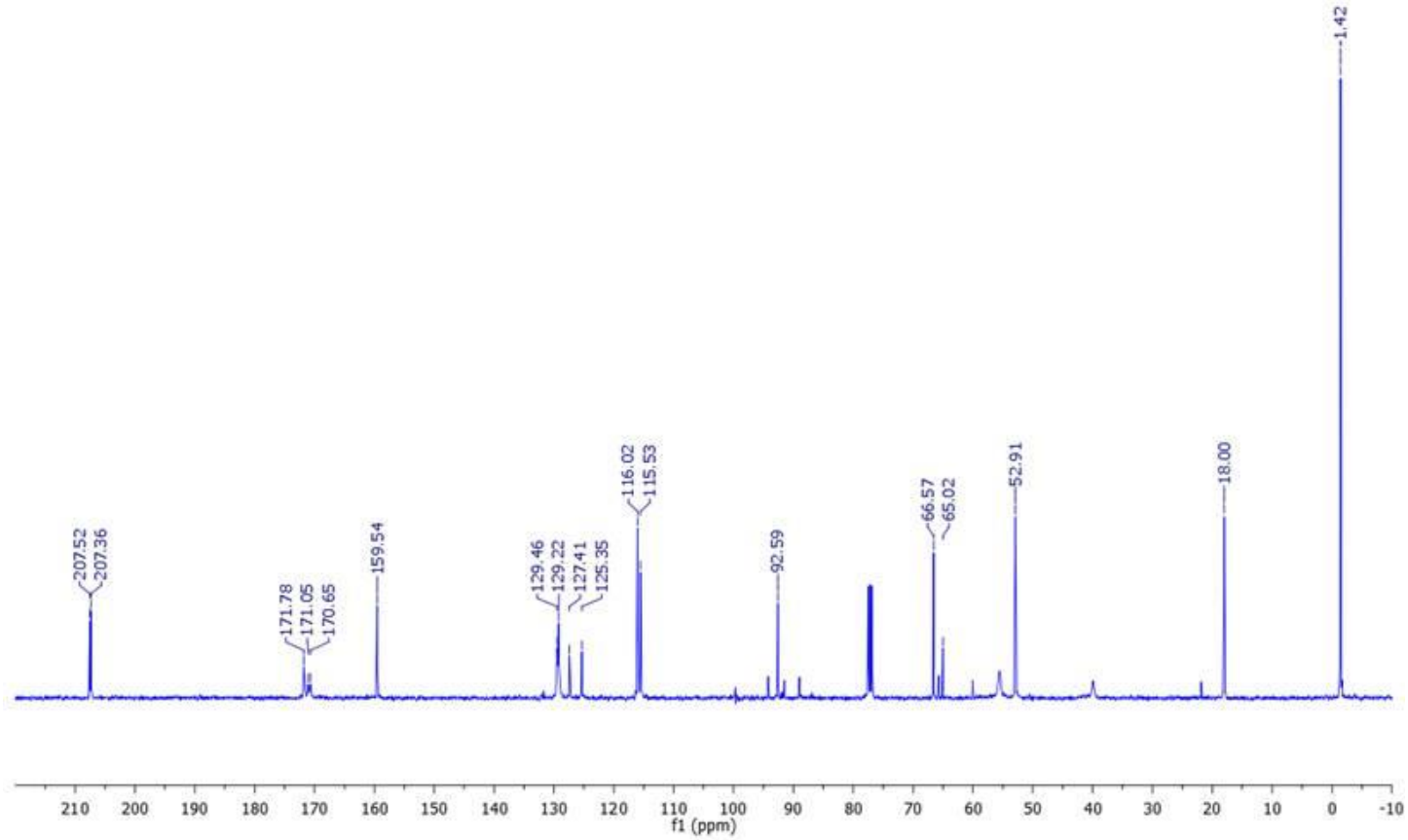
S29





3. Appendix: IC_{50} & Spectral Data





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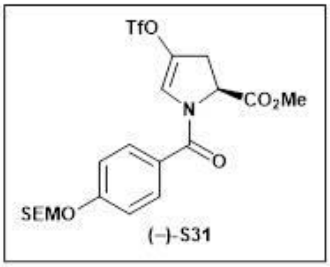

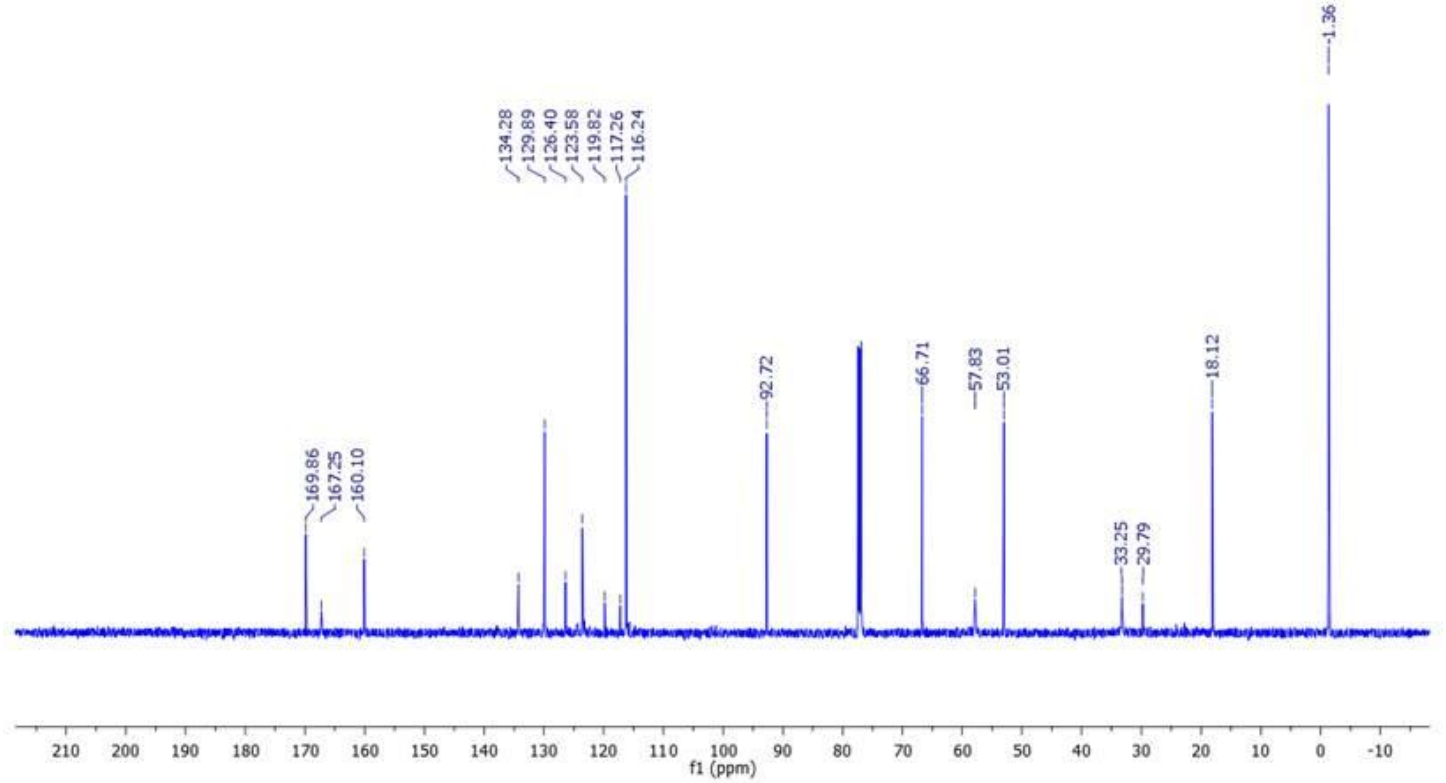

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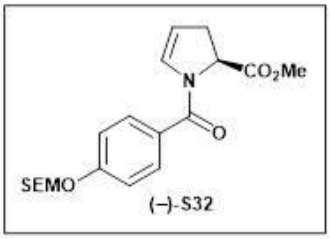

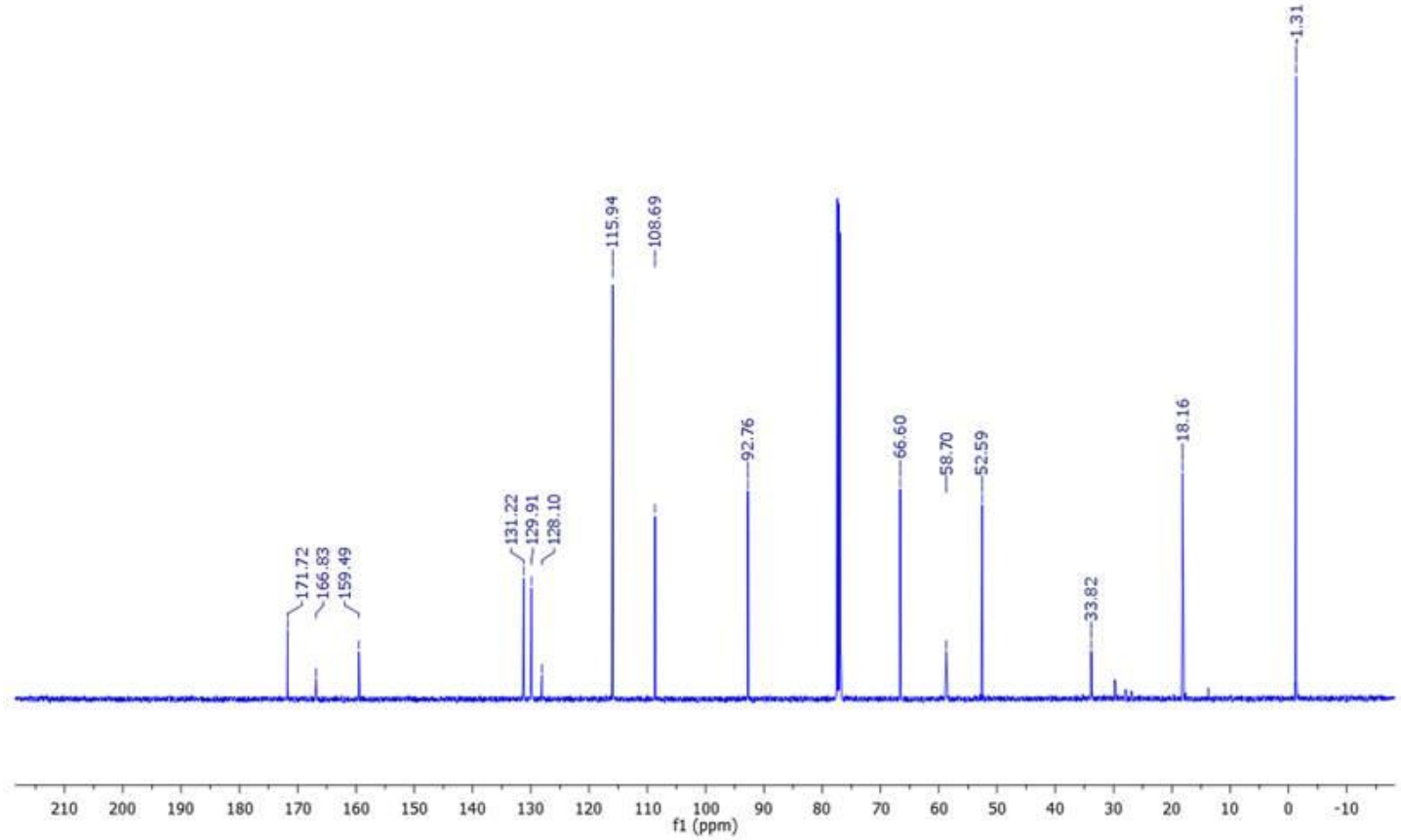

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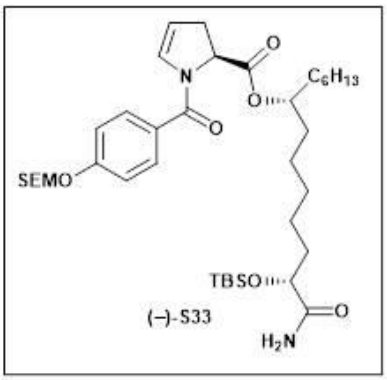

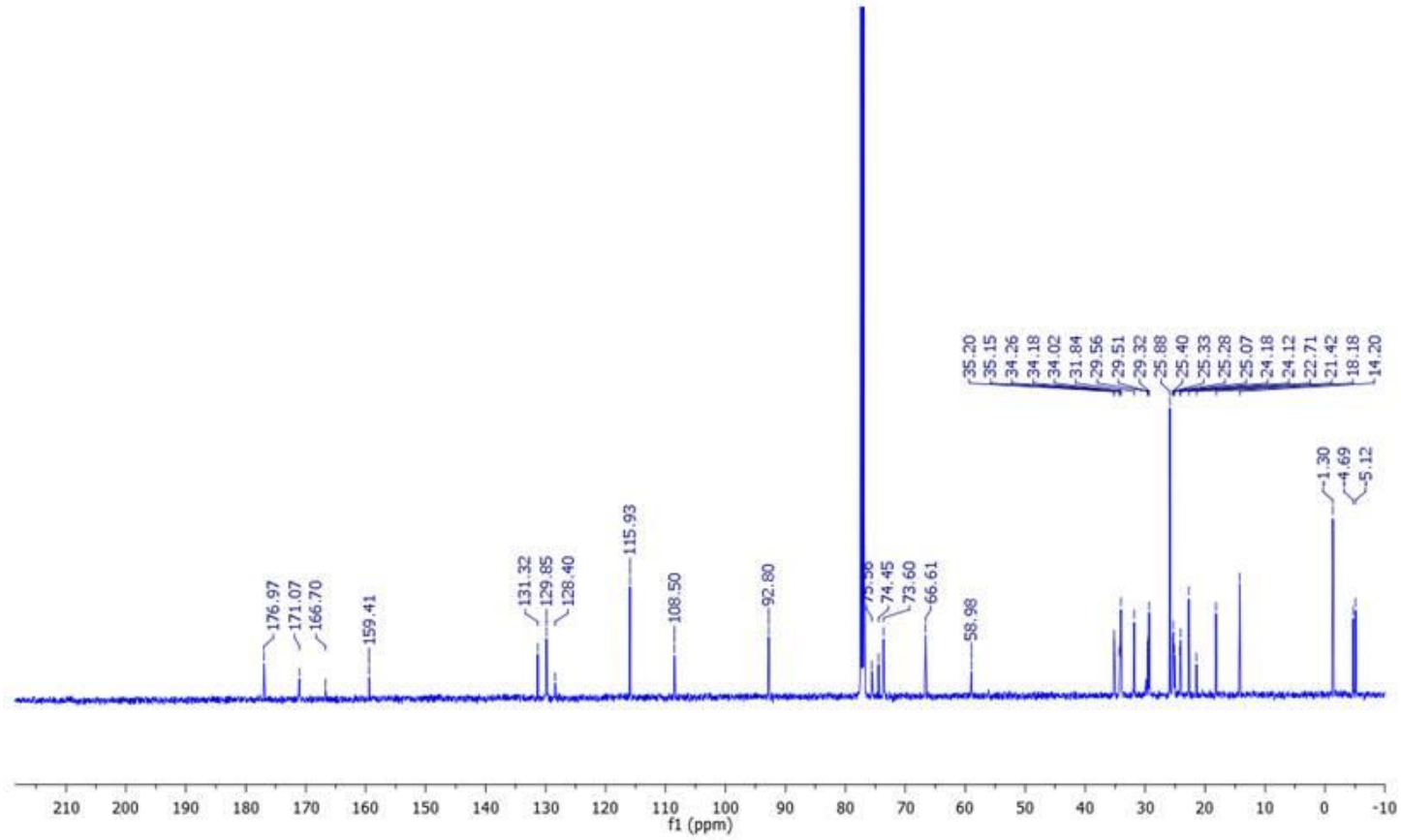

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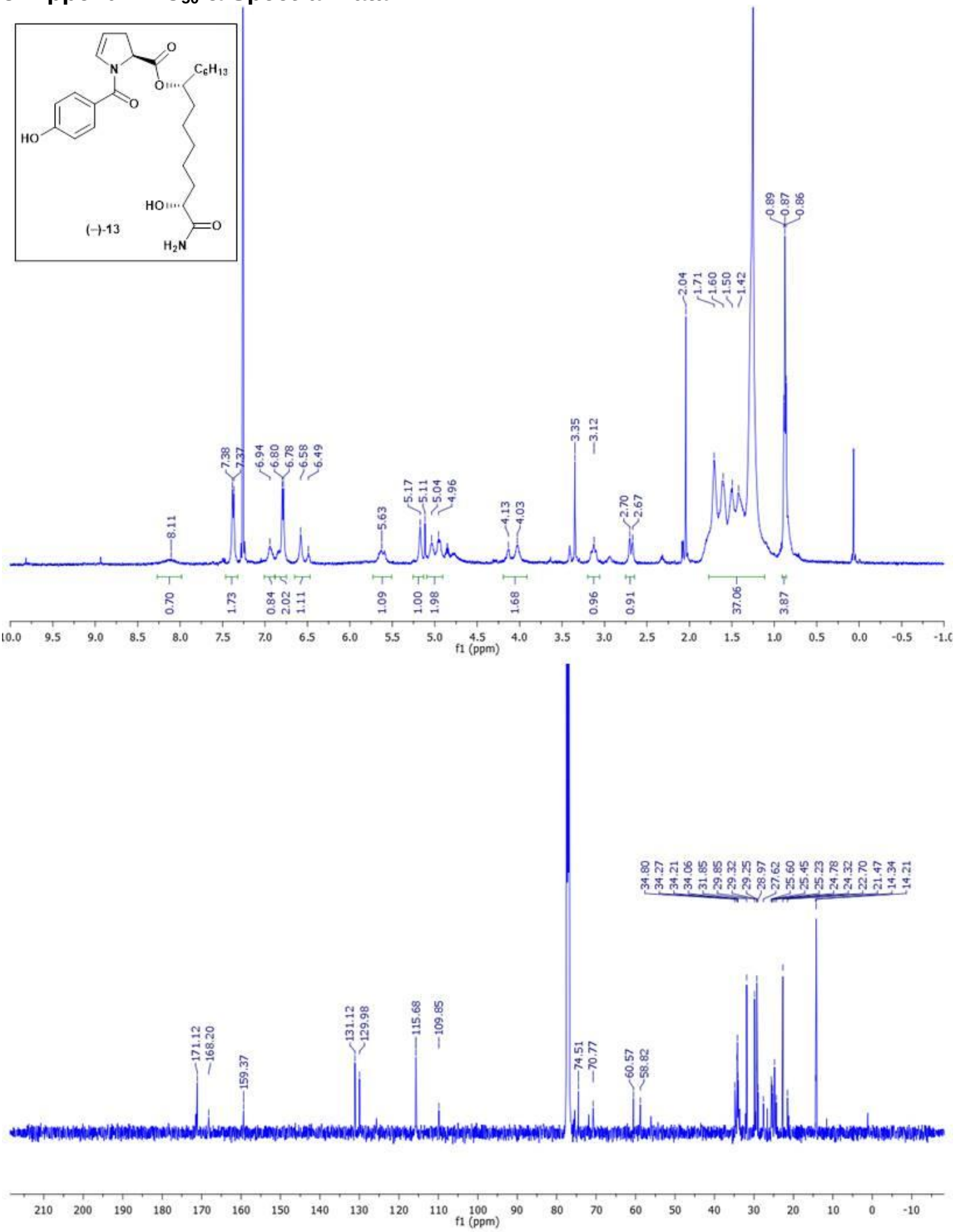

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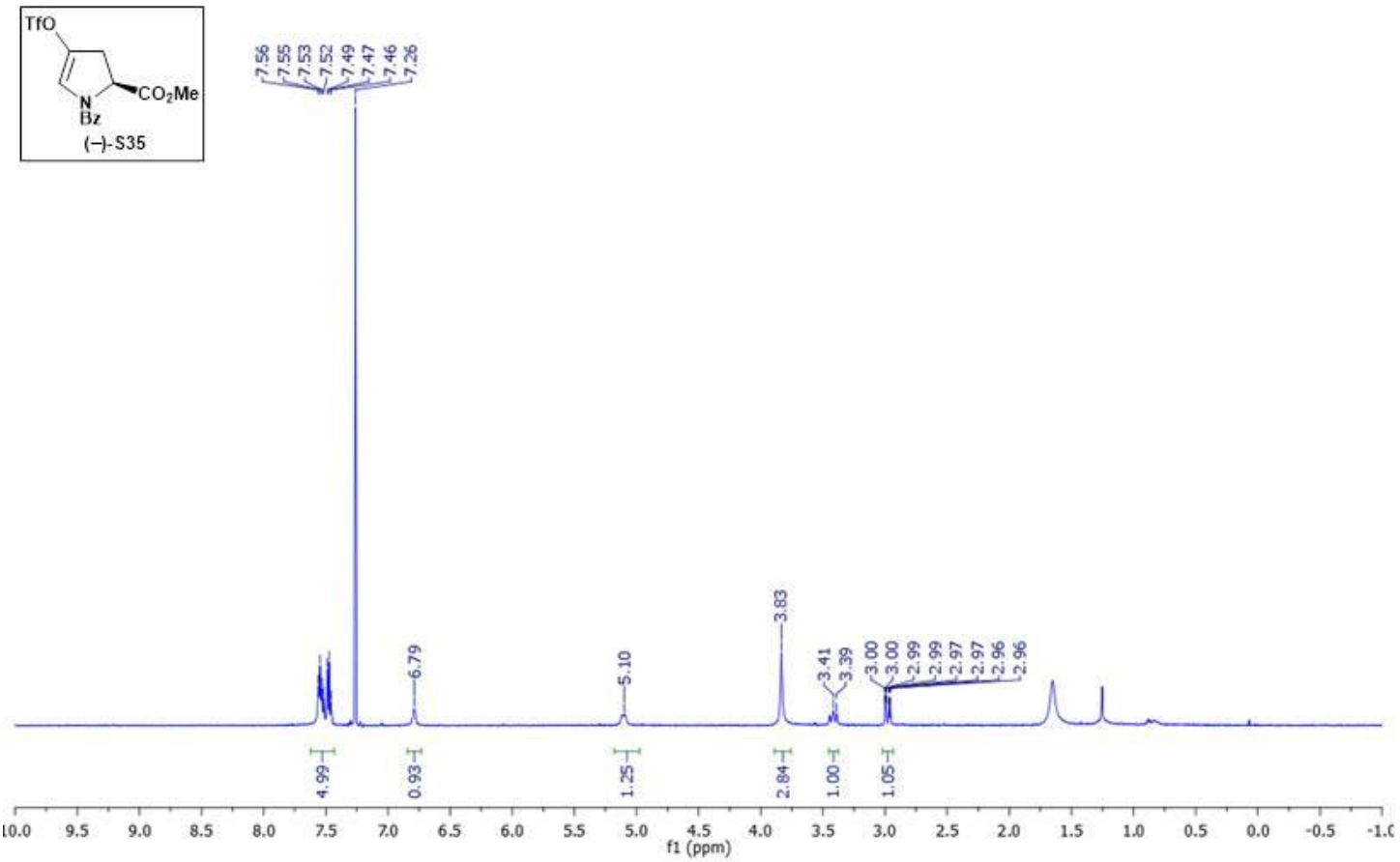

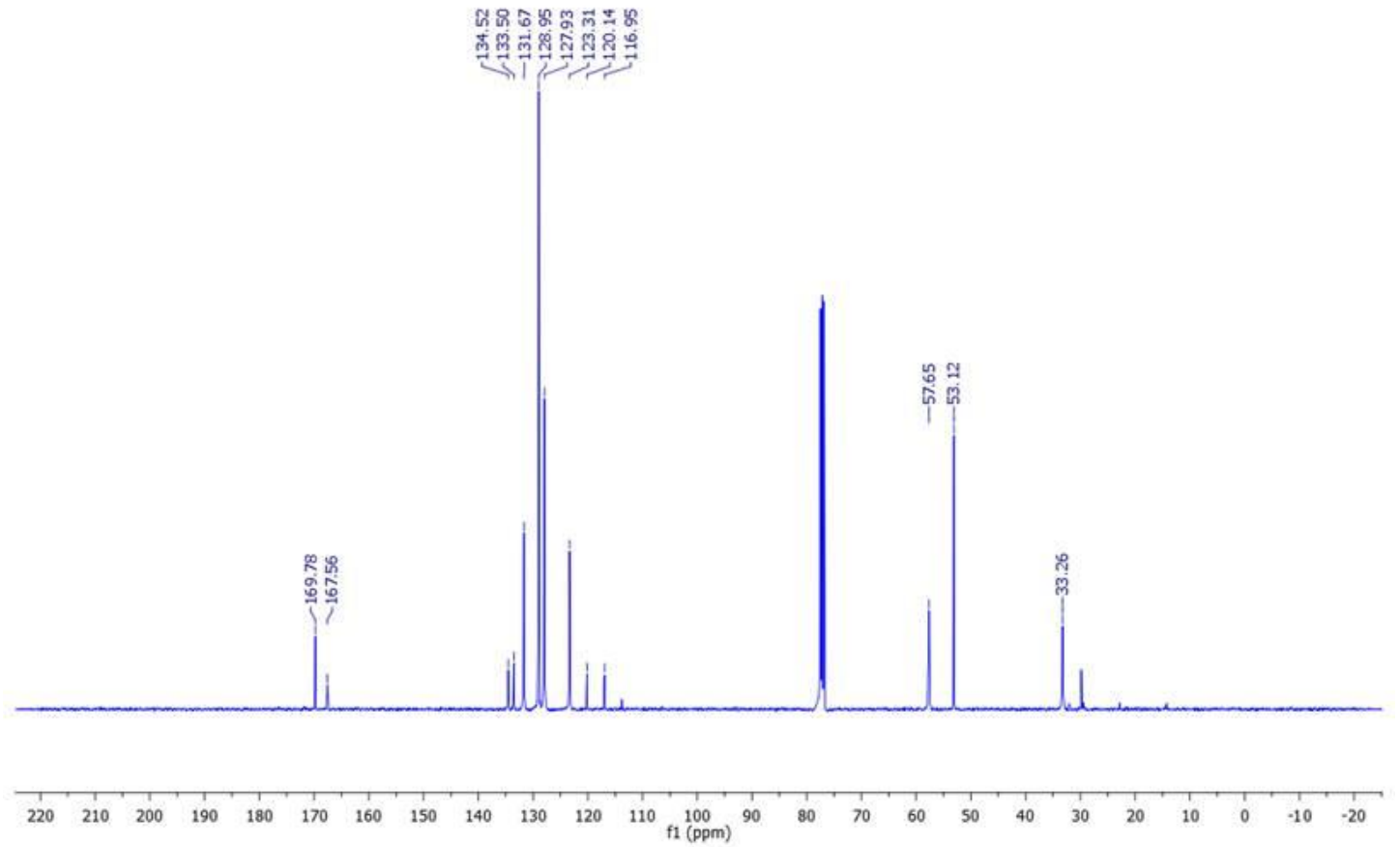

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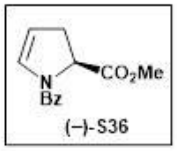

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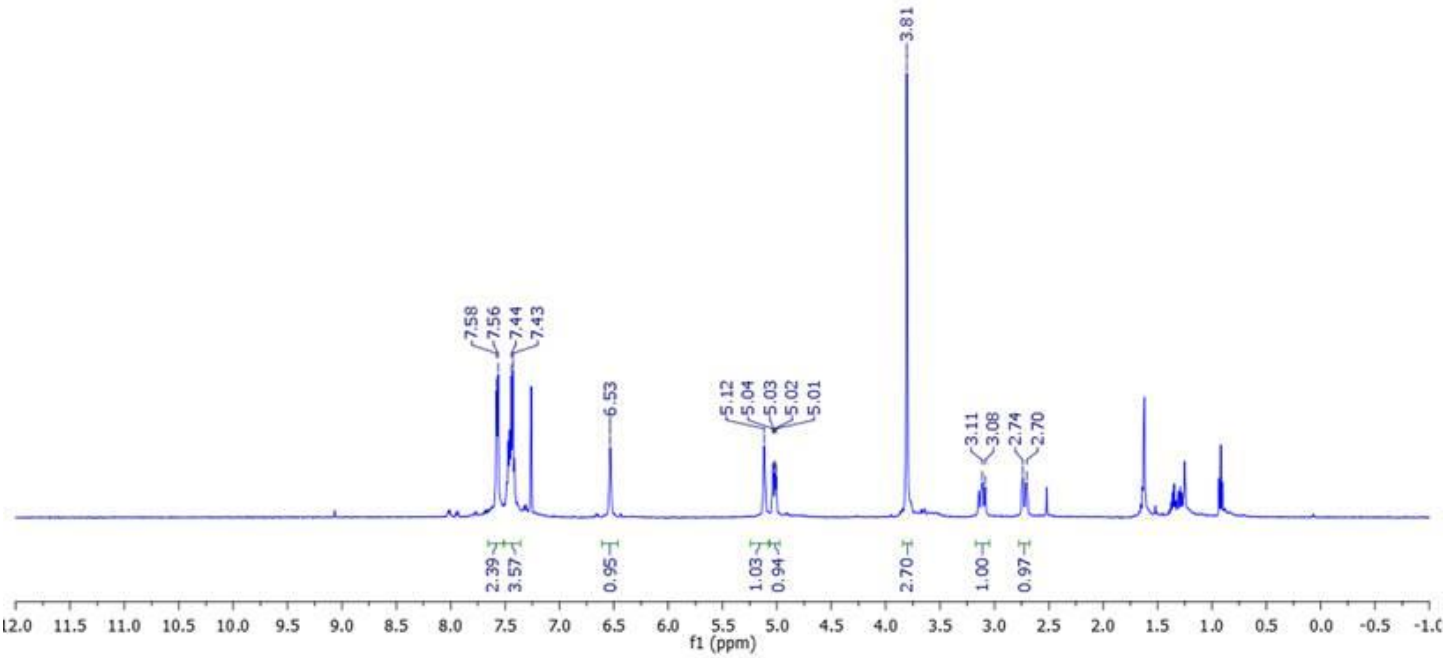

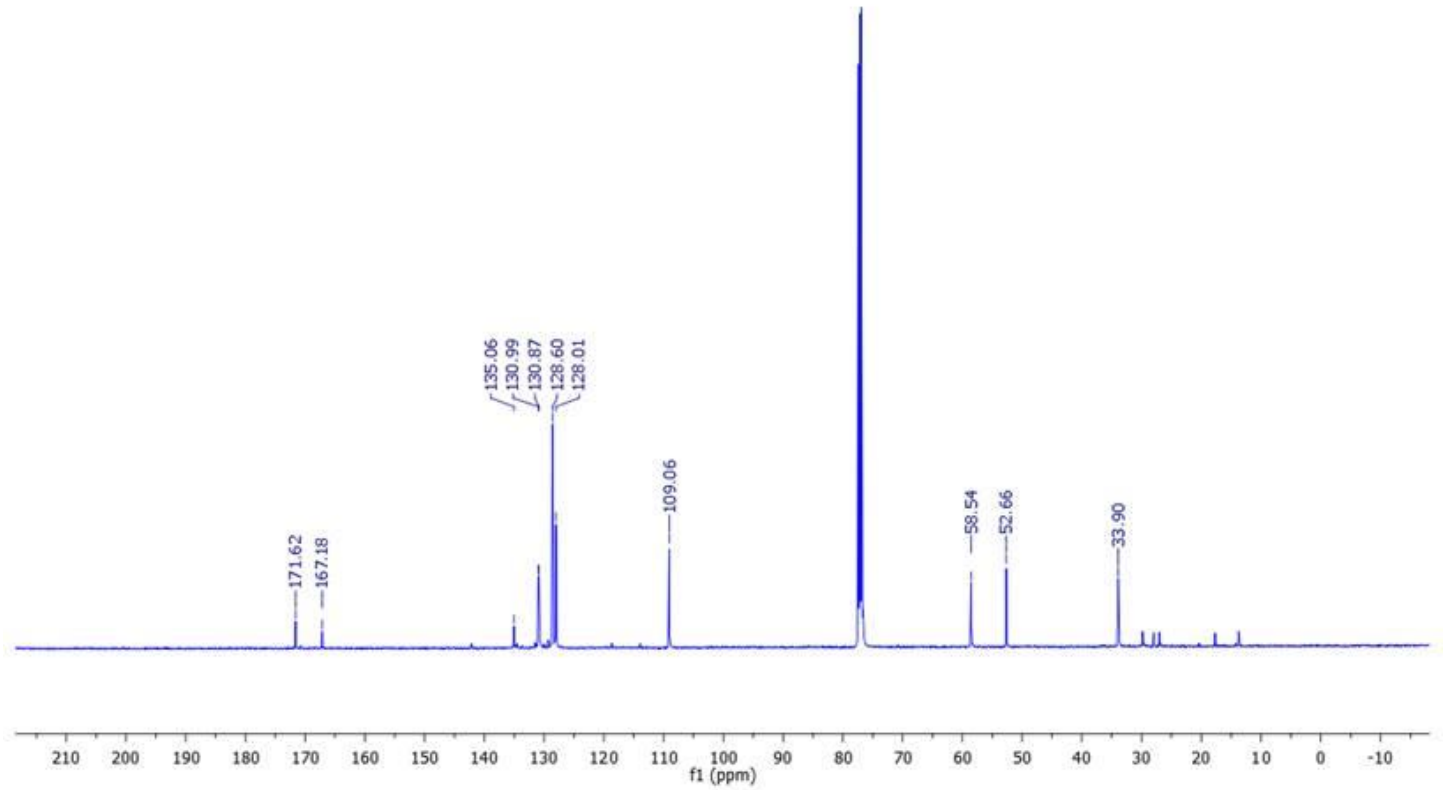

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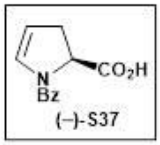

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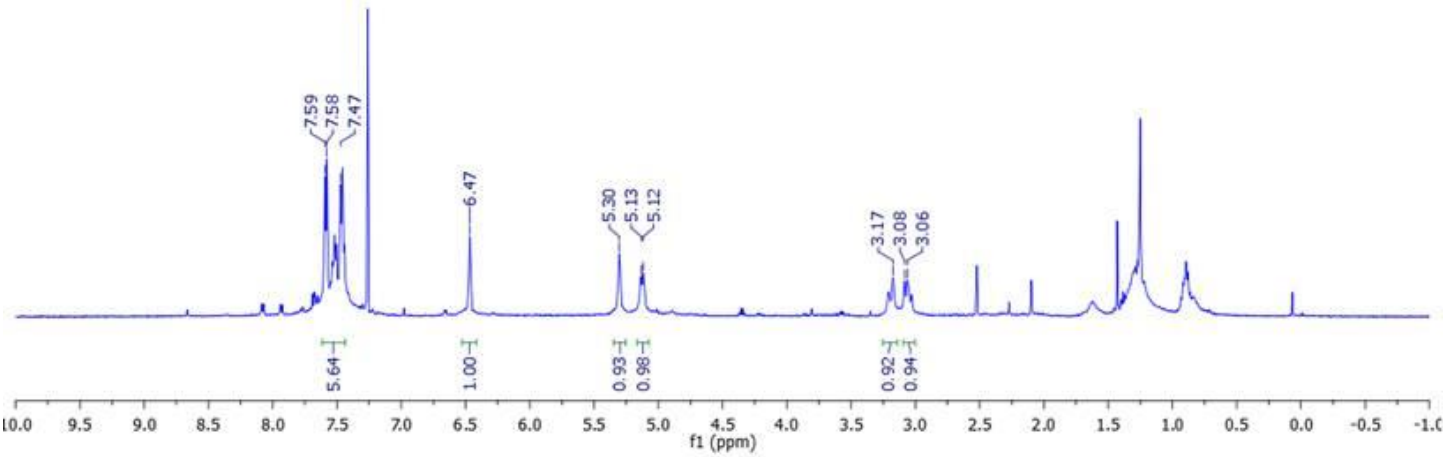

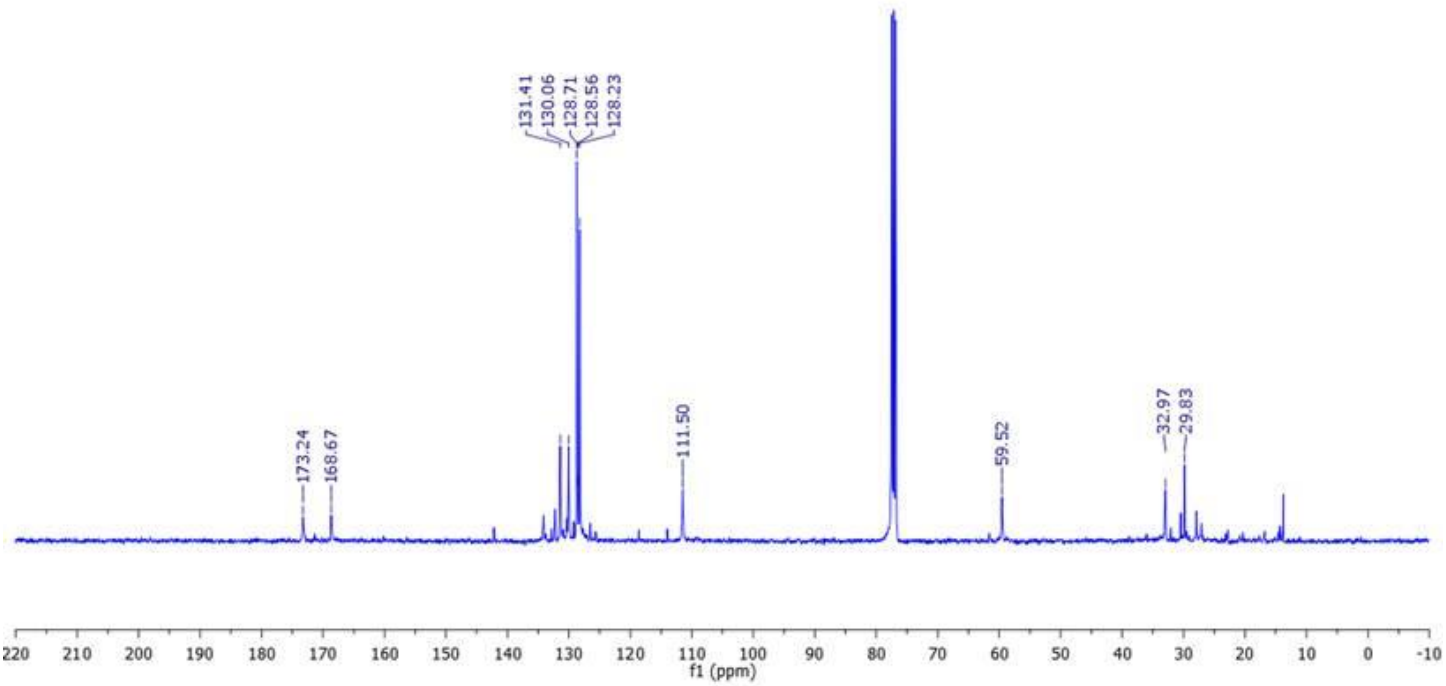

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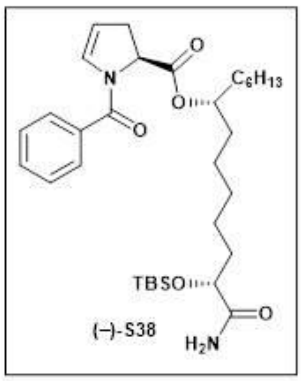

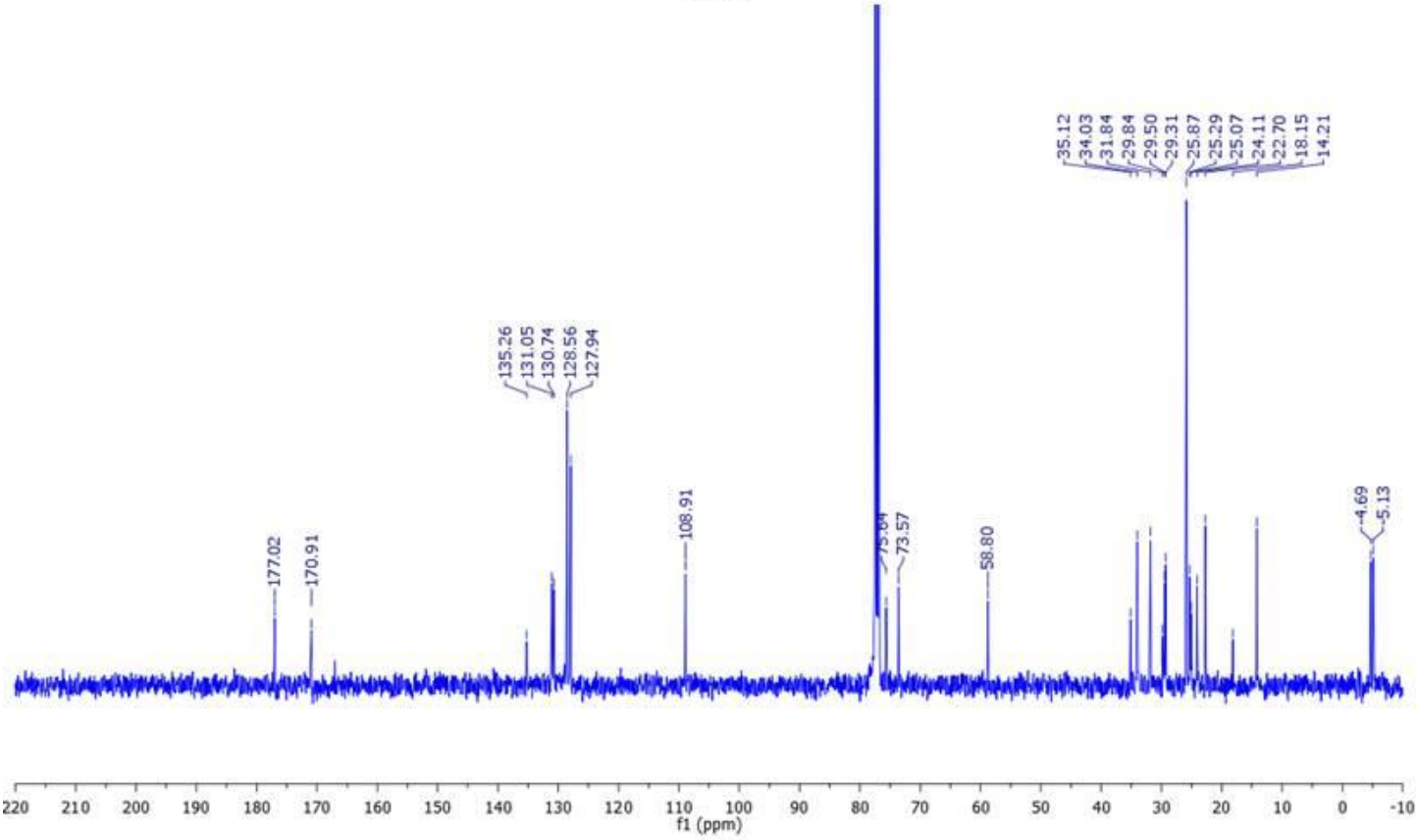

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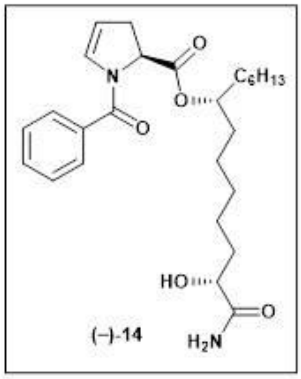

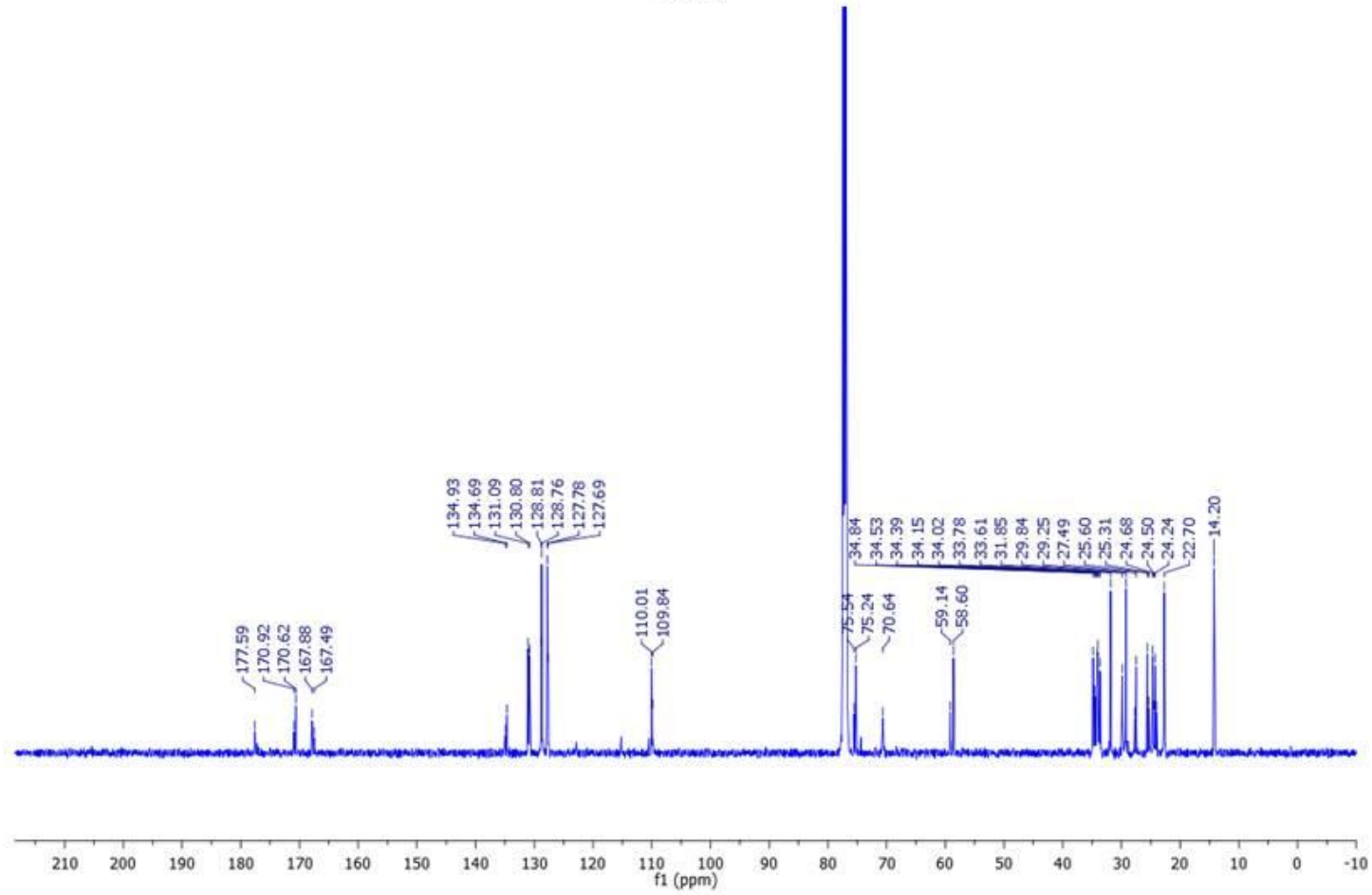

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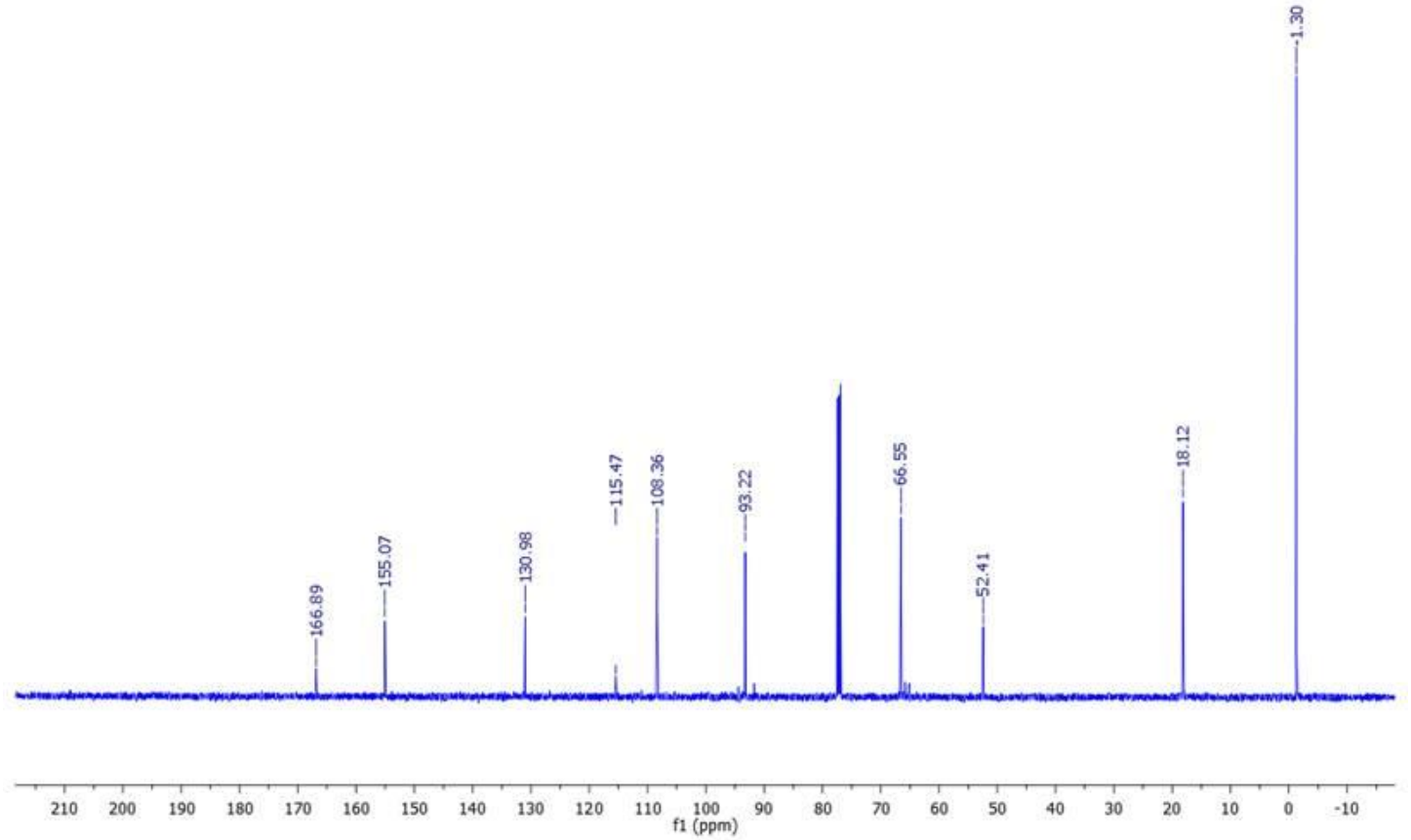

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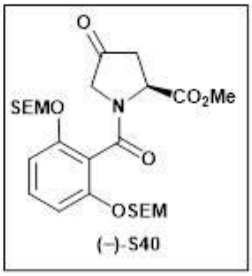
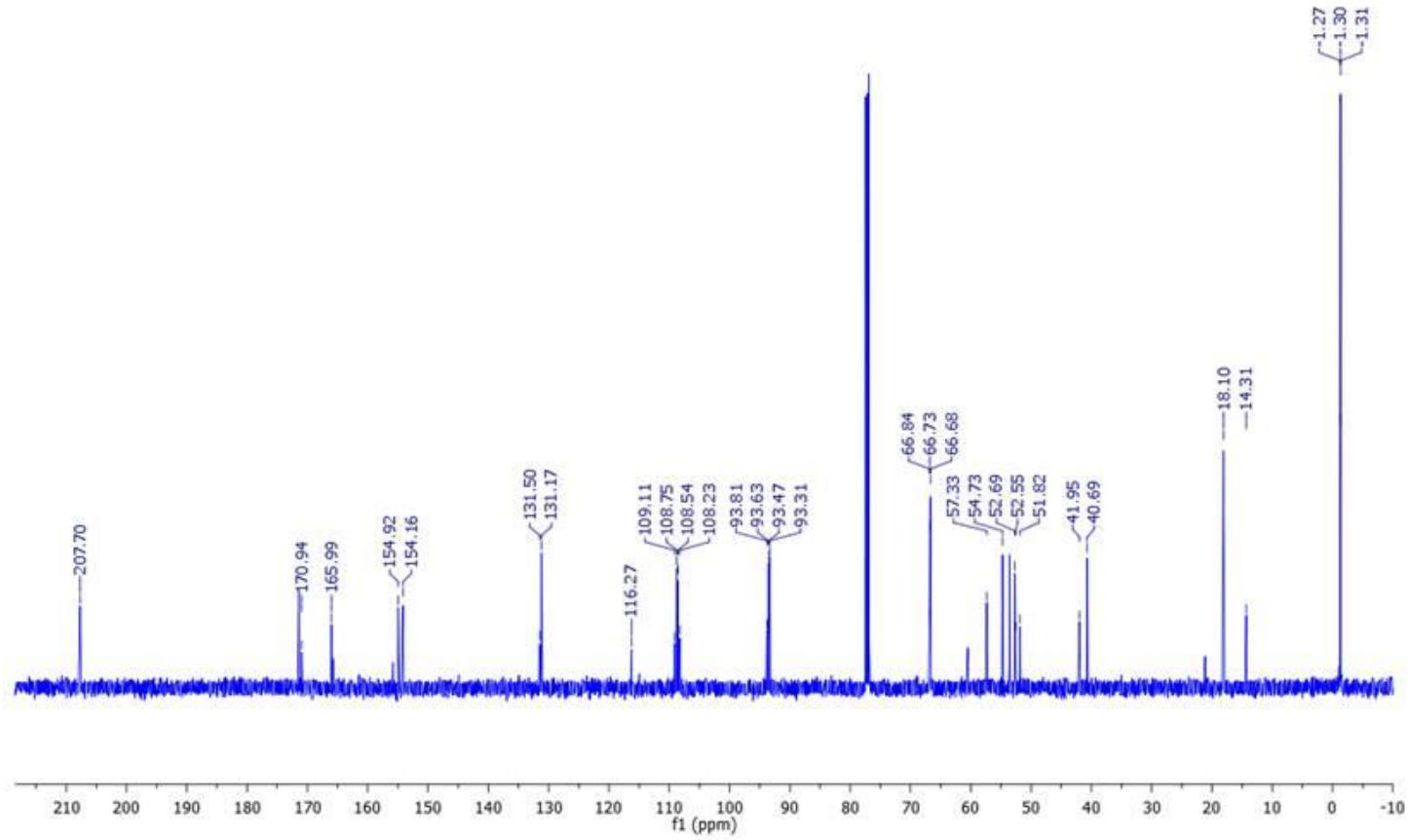


(−)-S40



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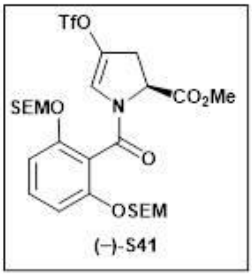

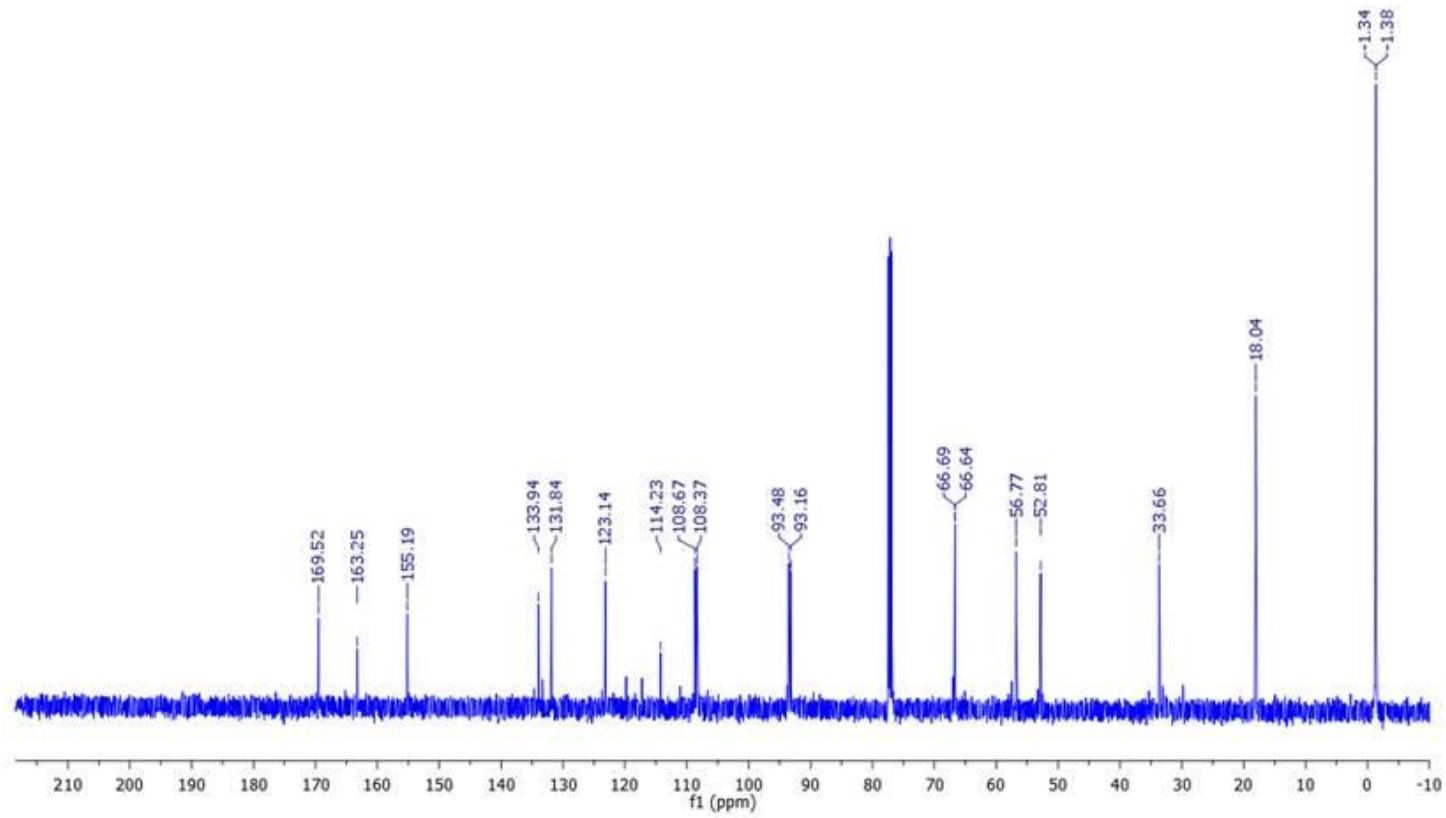

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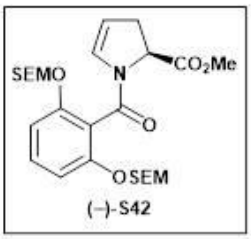

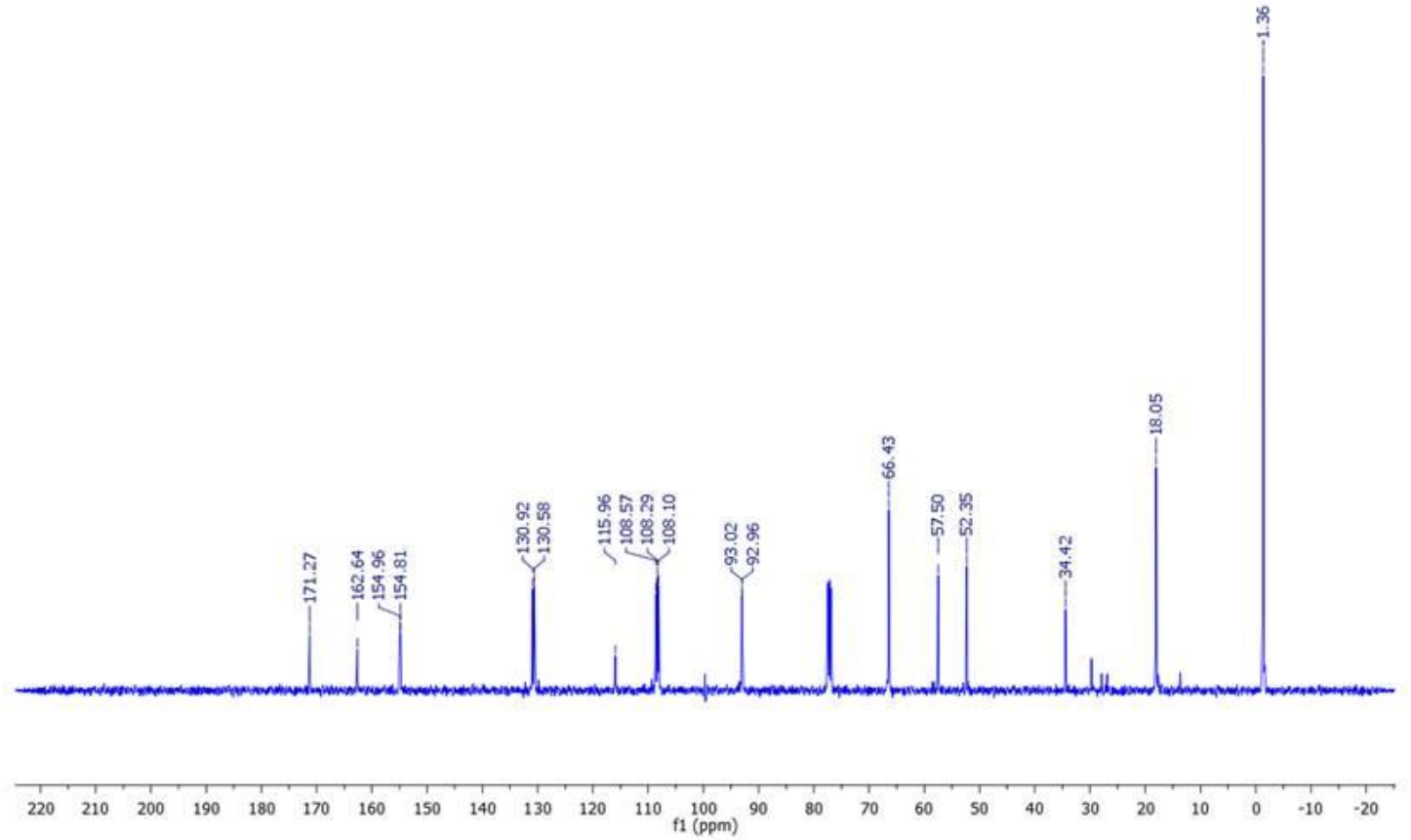

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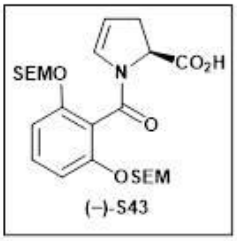

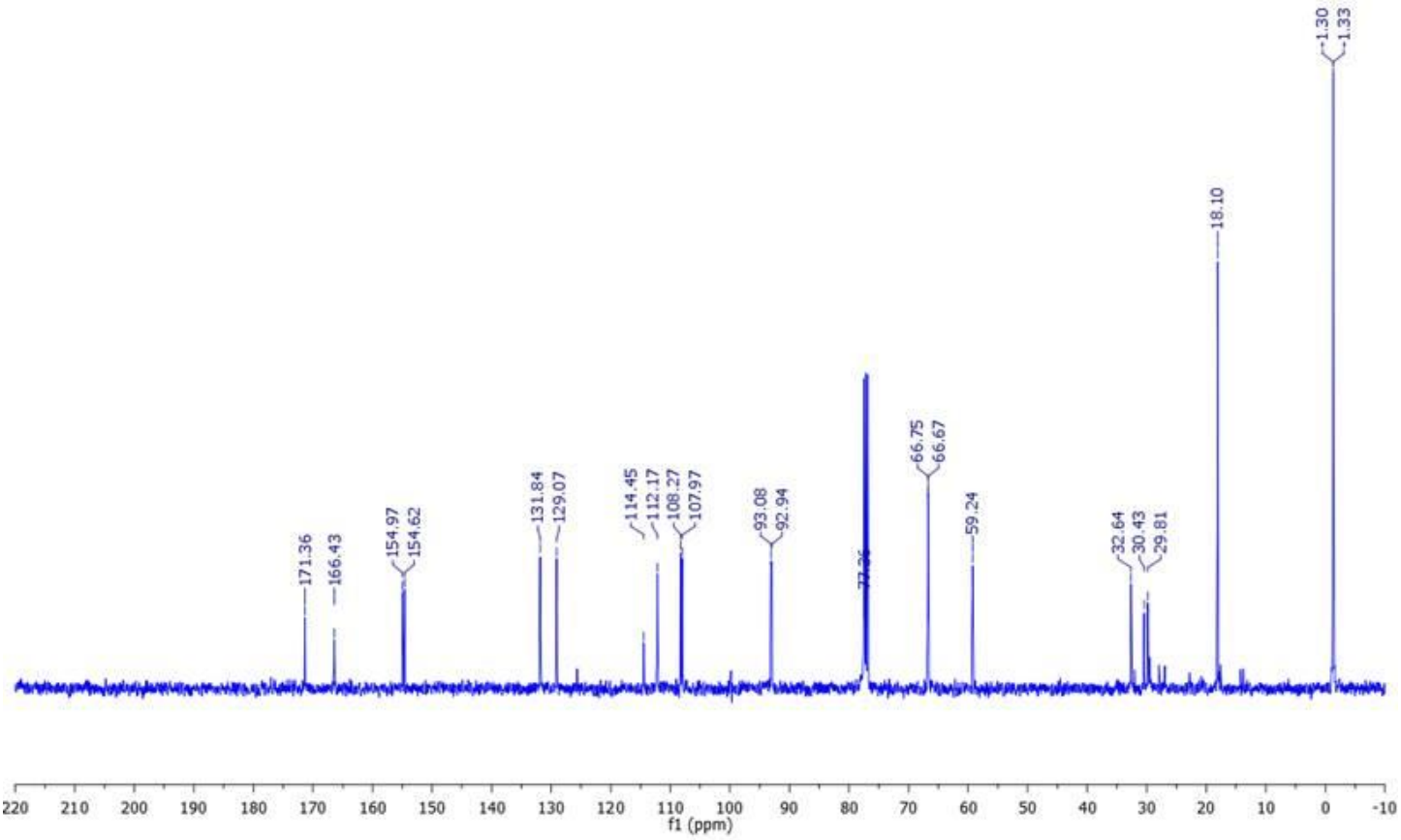

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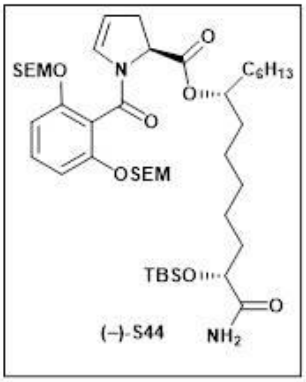

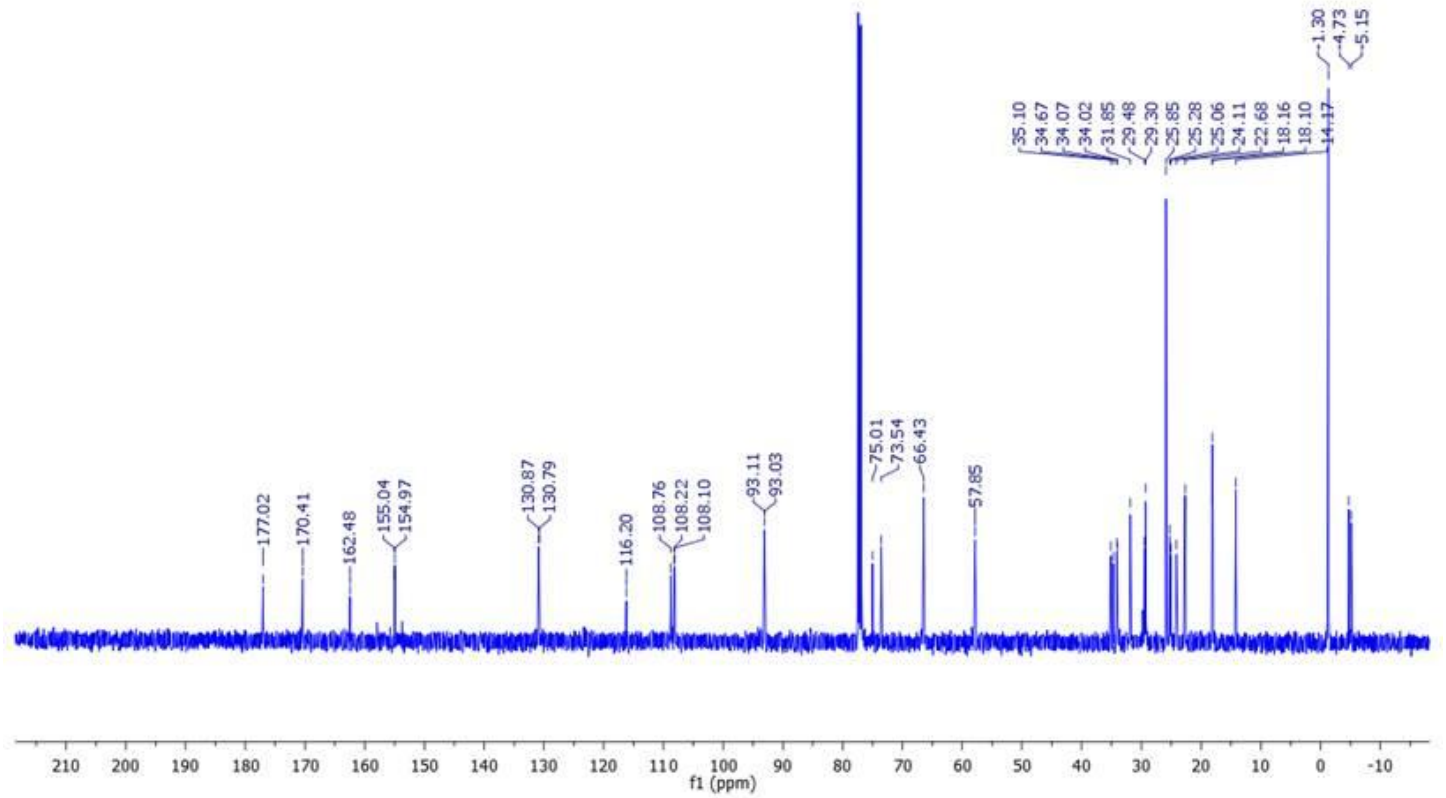

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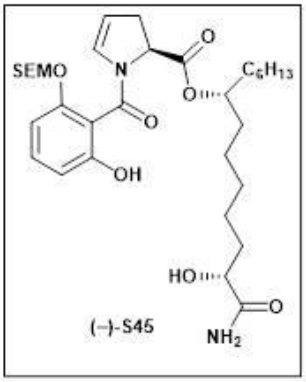

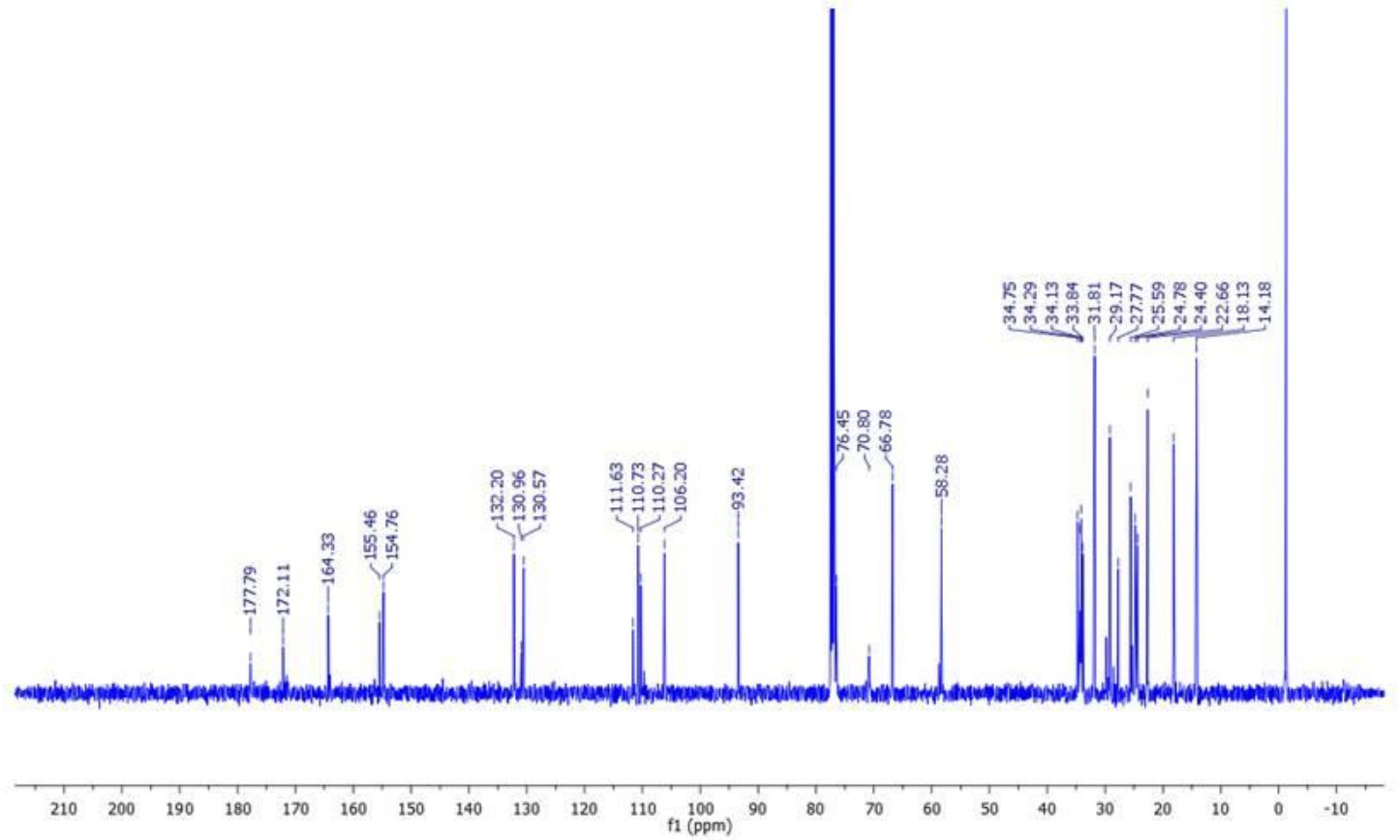

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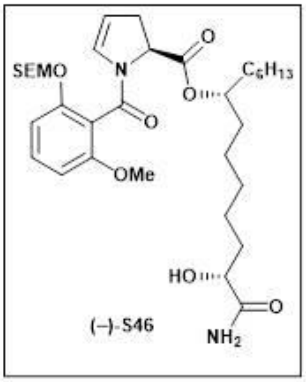

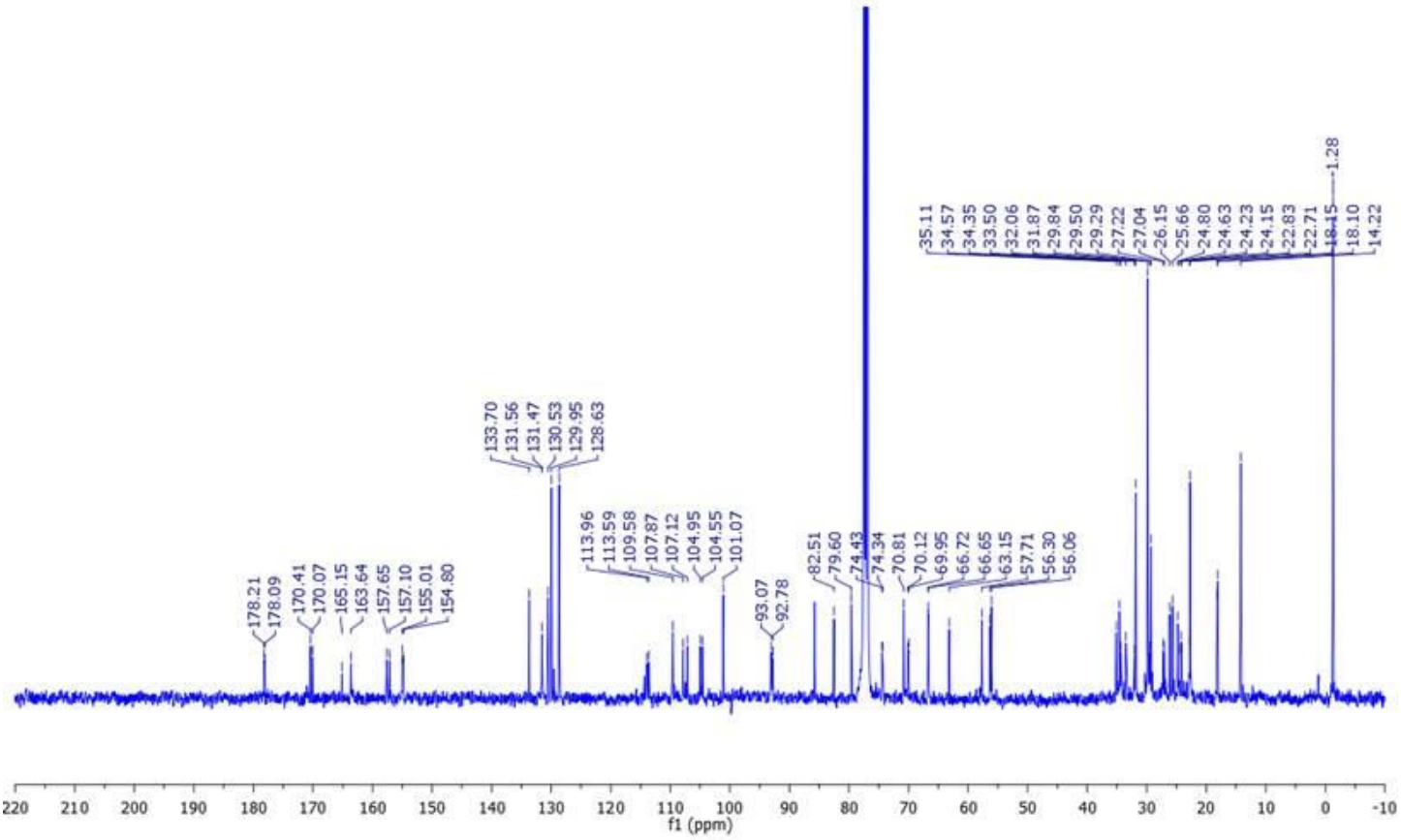

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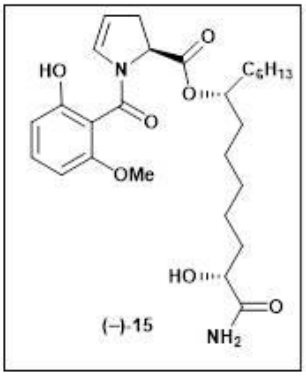

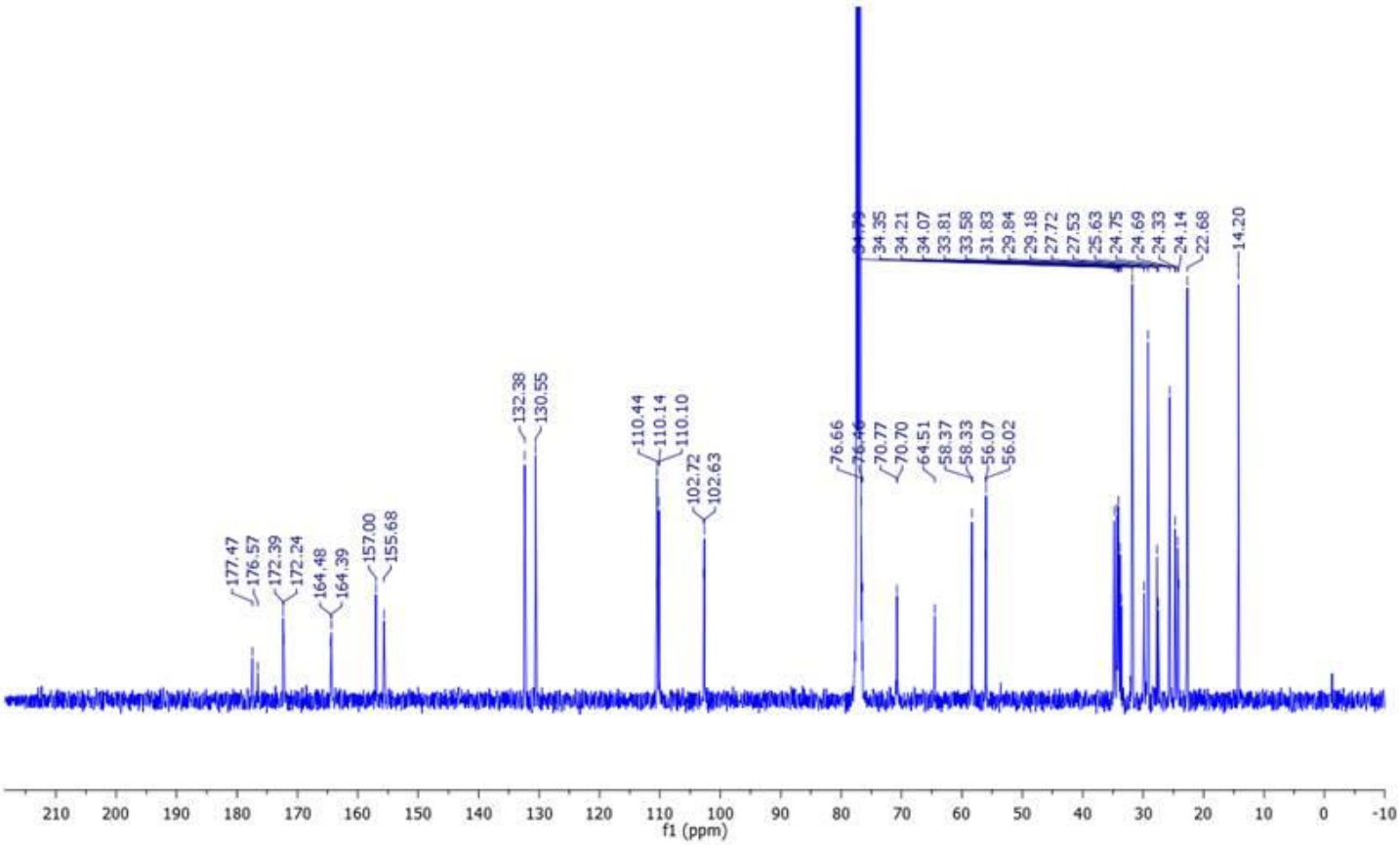

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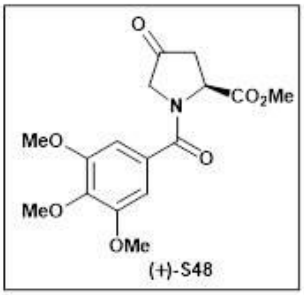

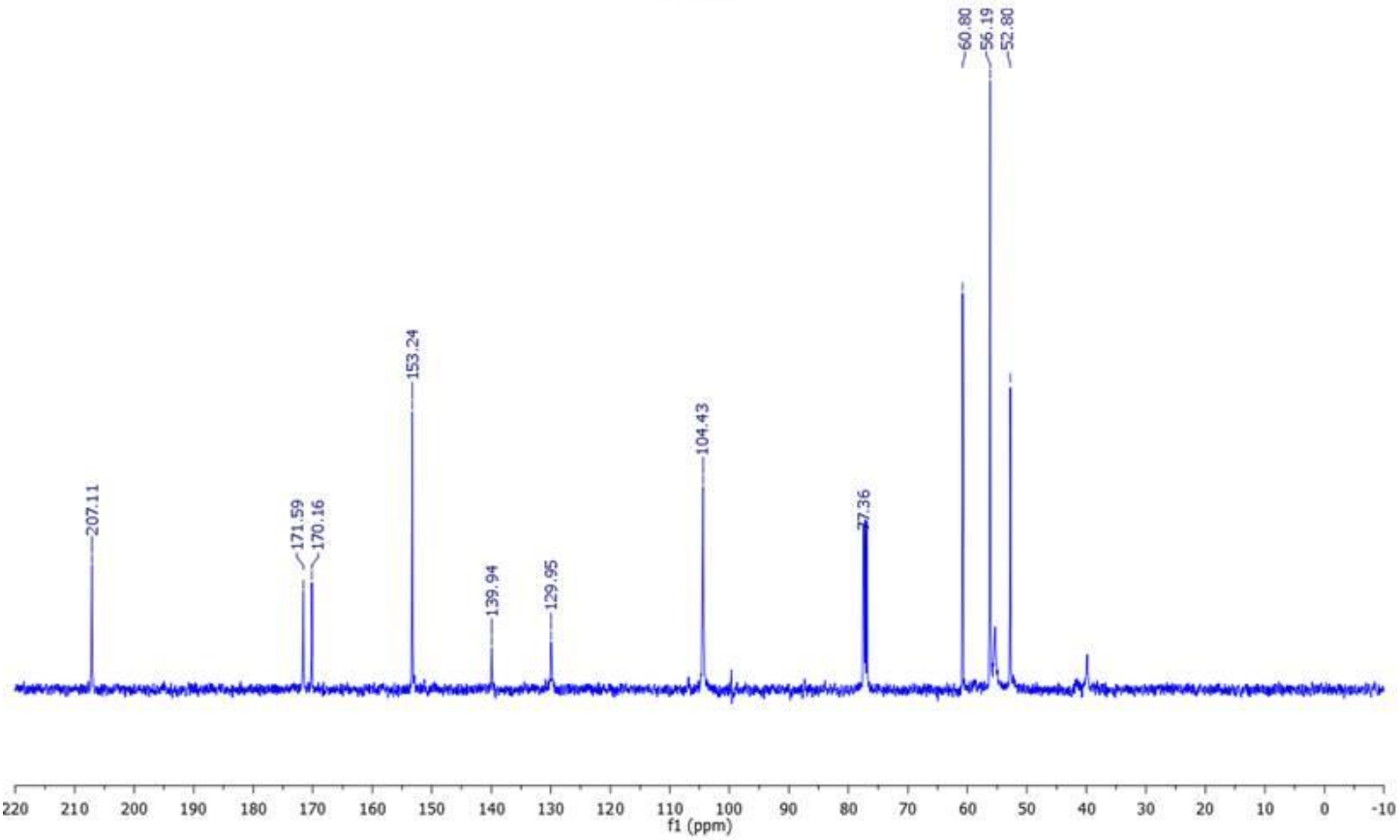

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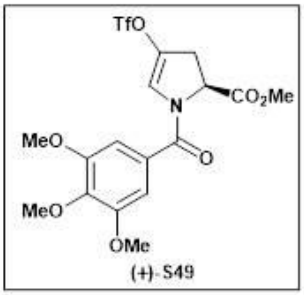

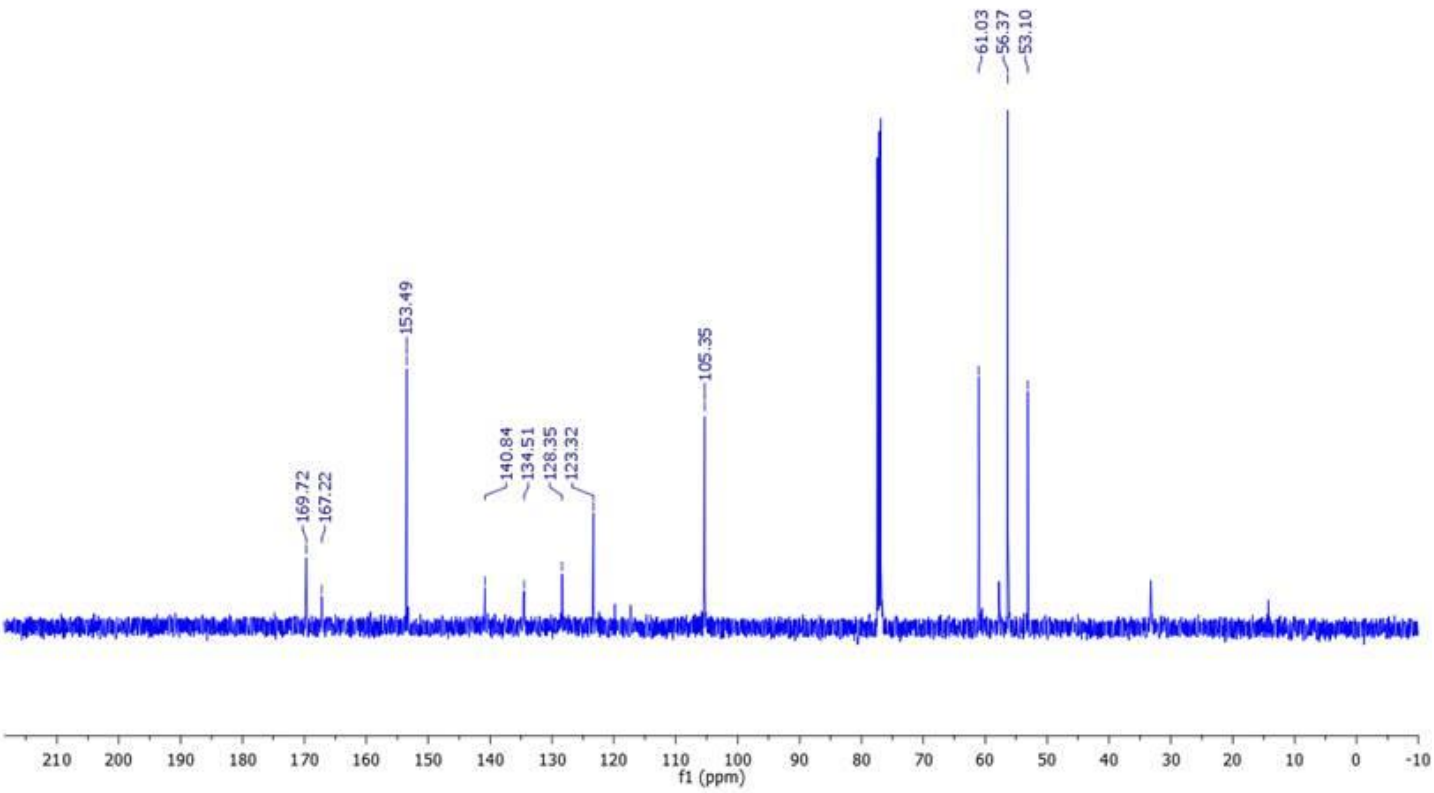

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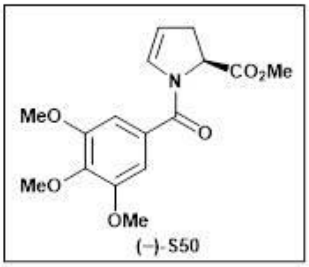

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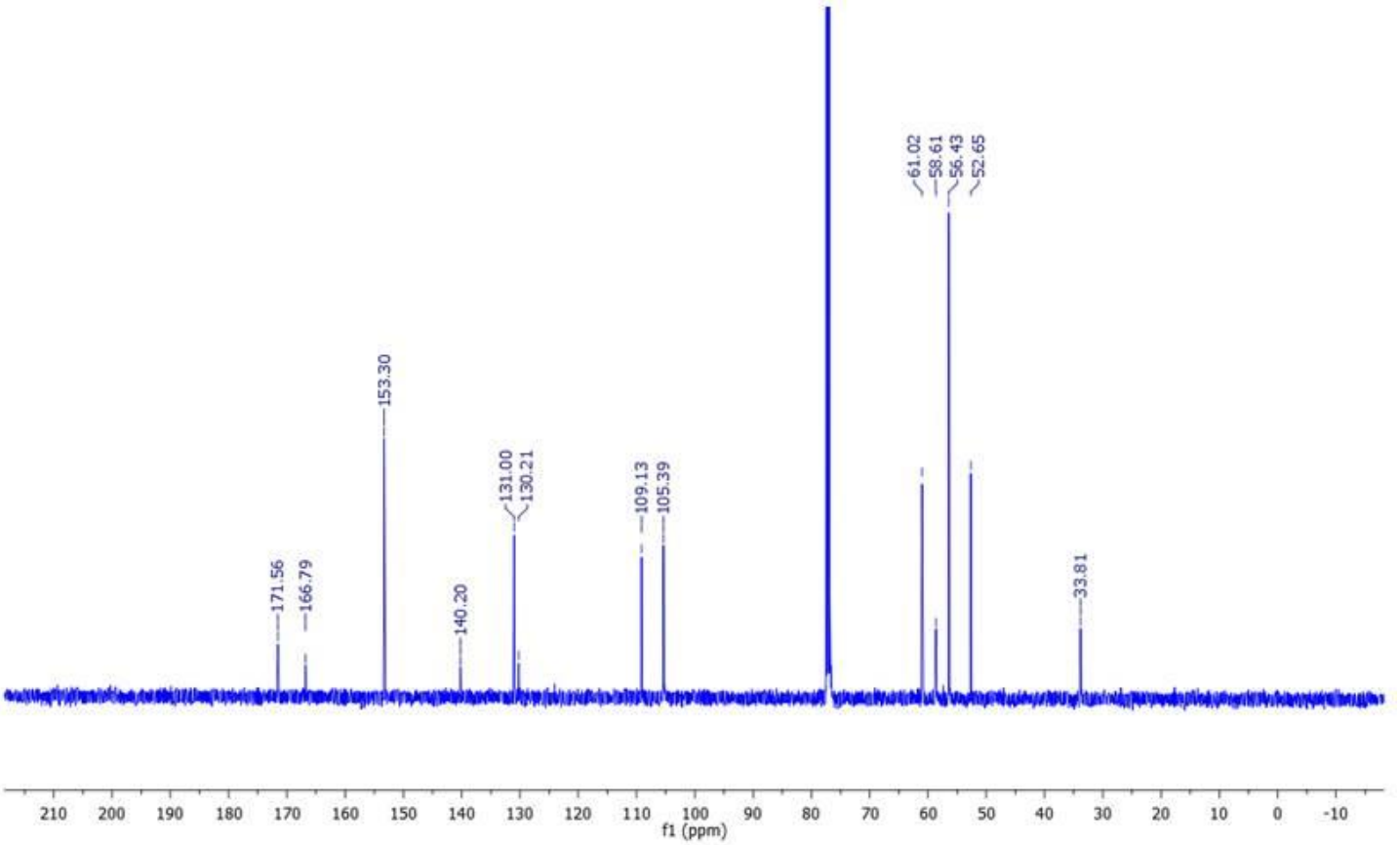

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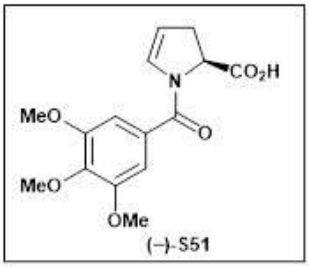

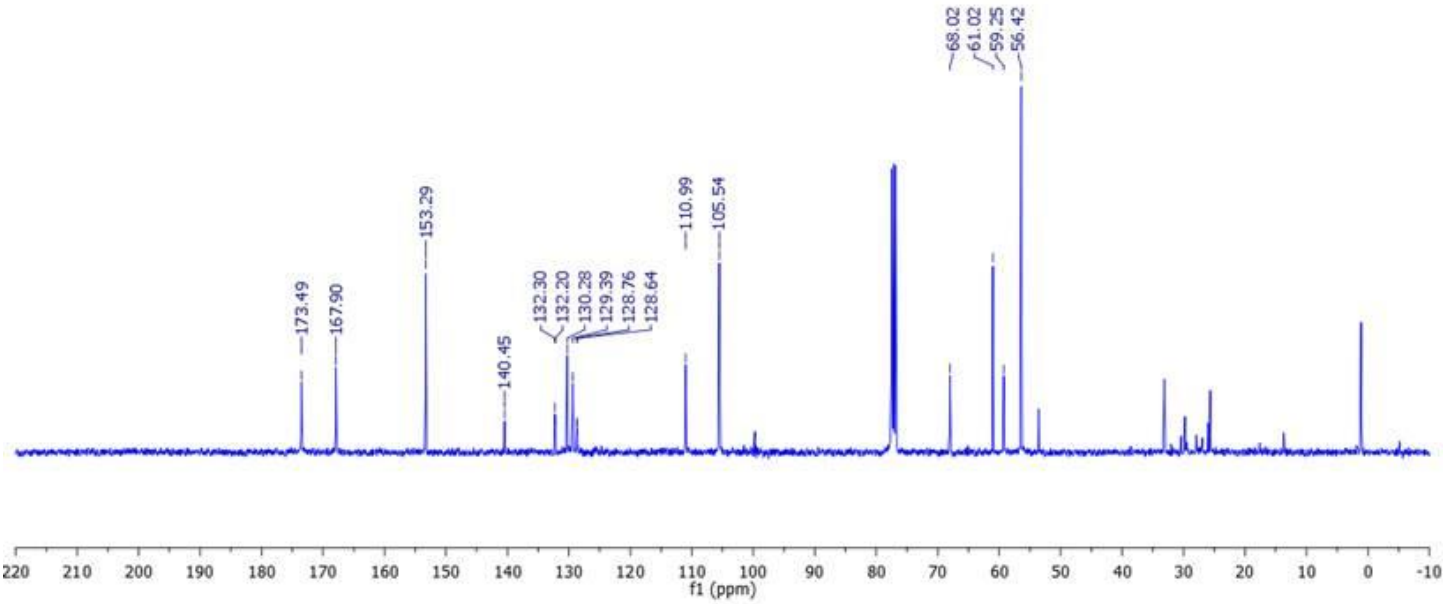

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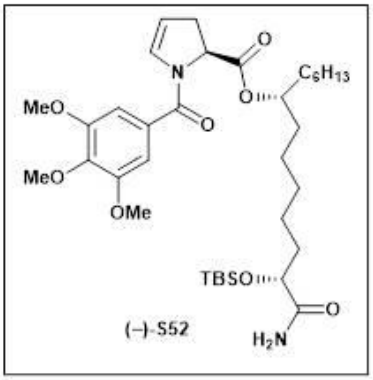

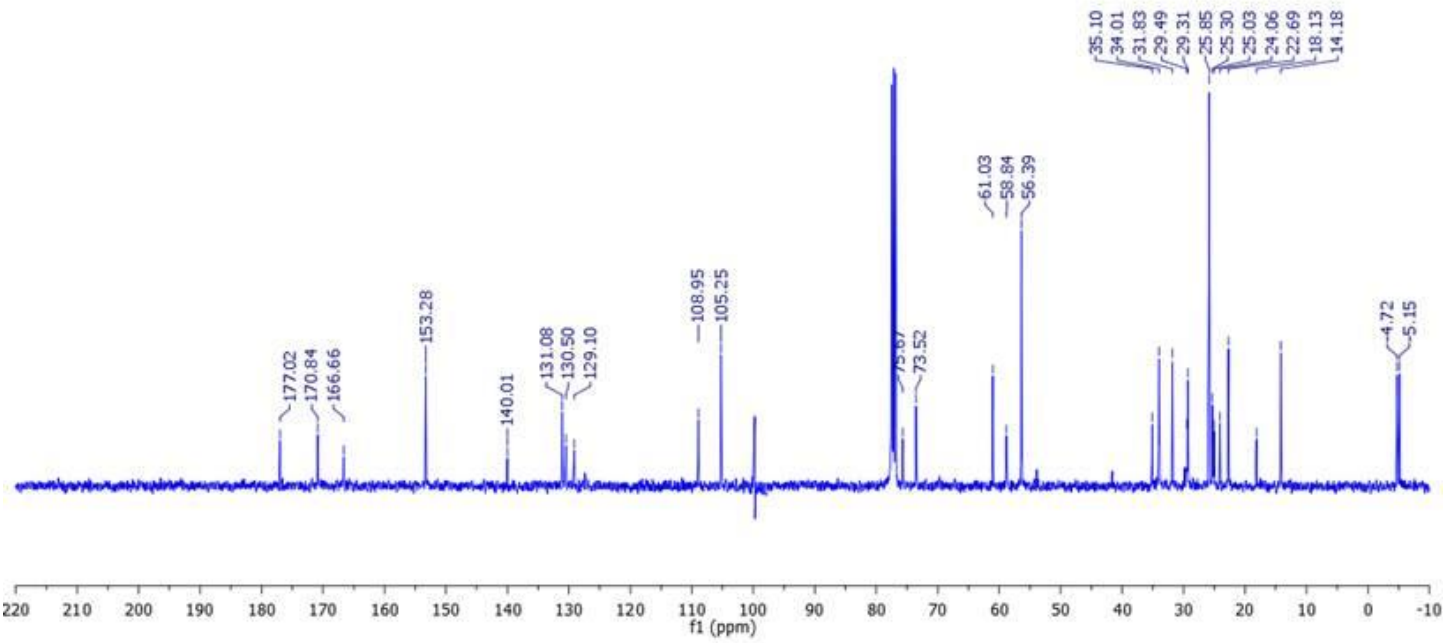

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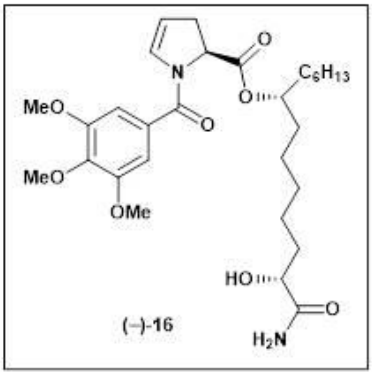

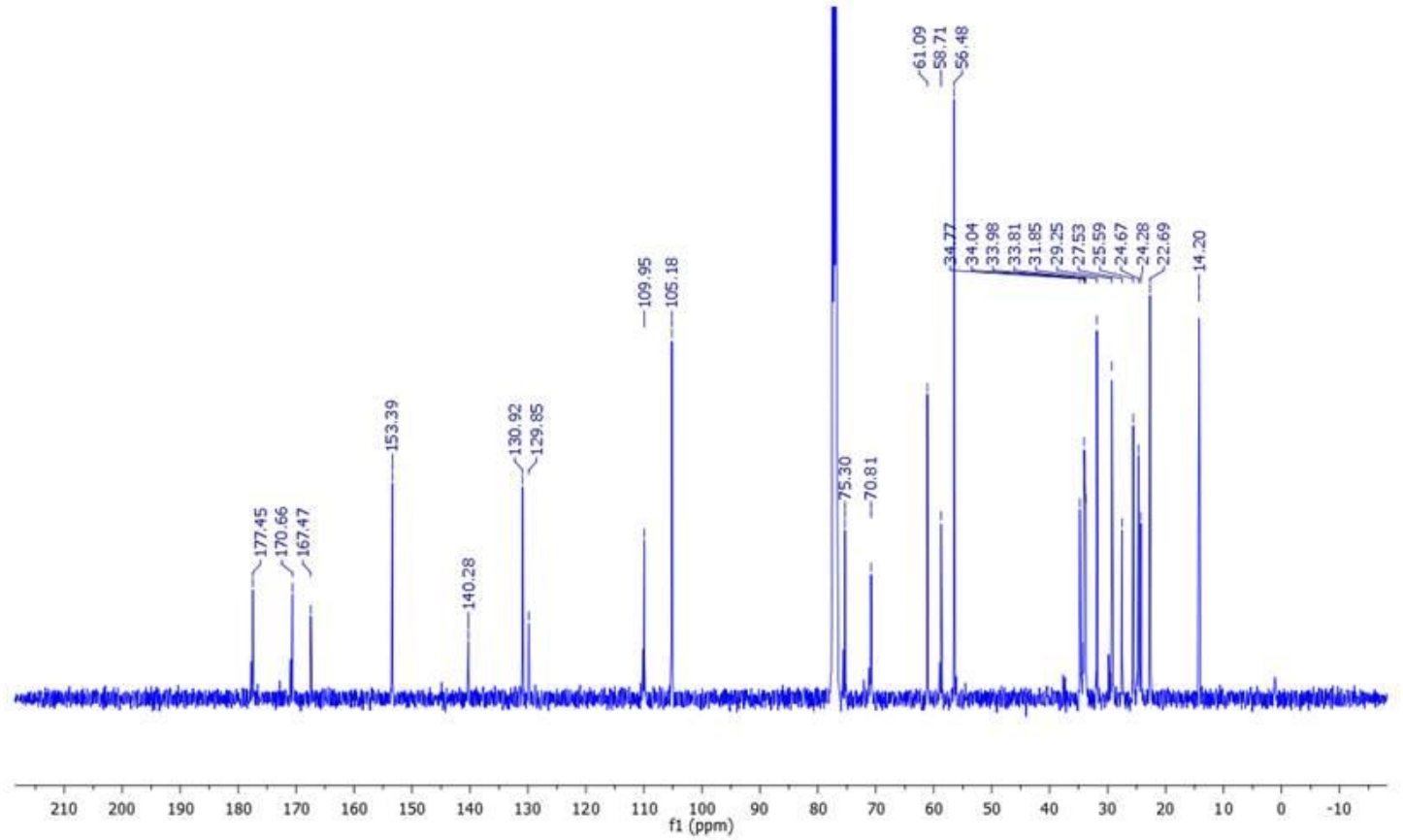

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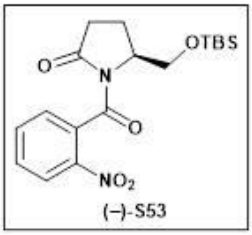
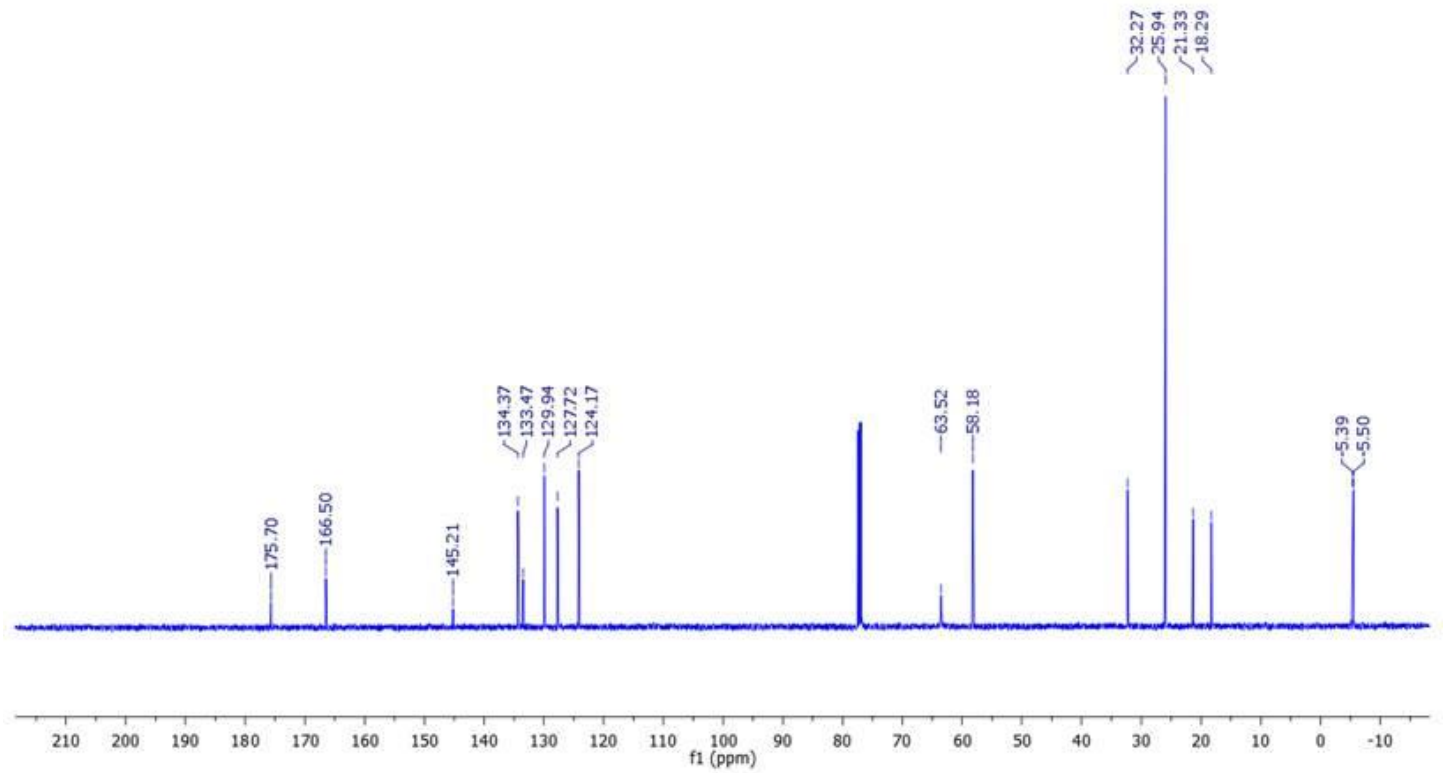


(–)-S53



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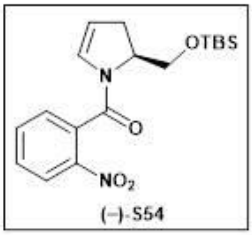
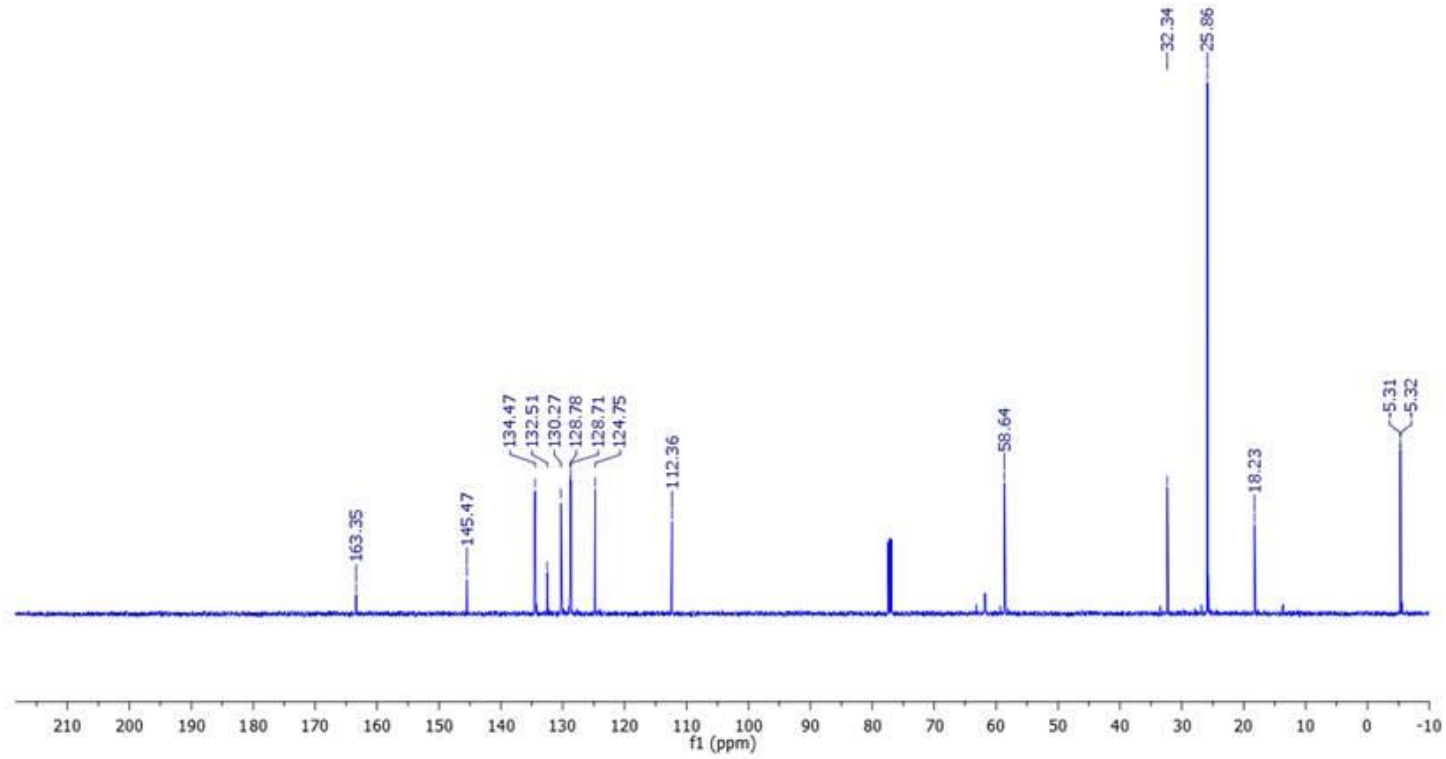


(−)-S54



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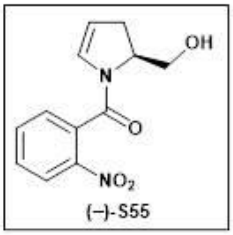

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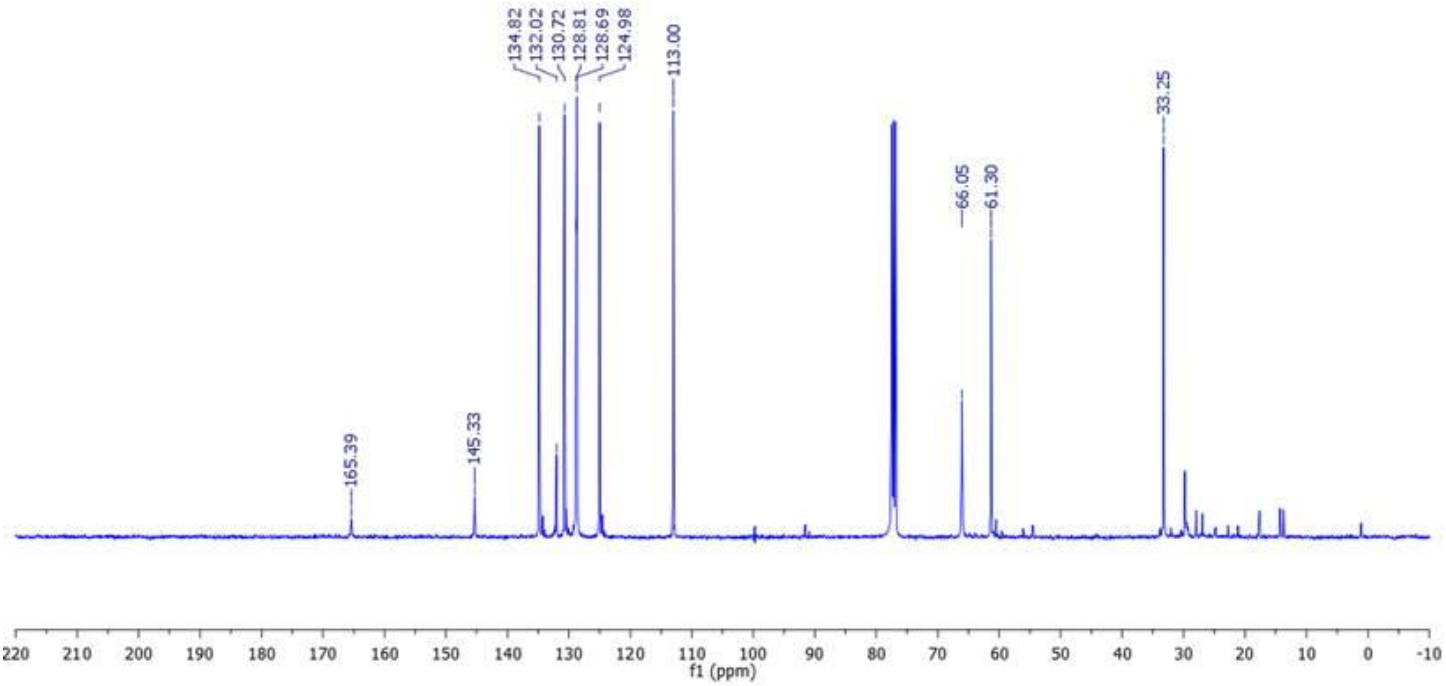

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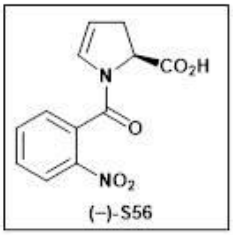
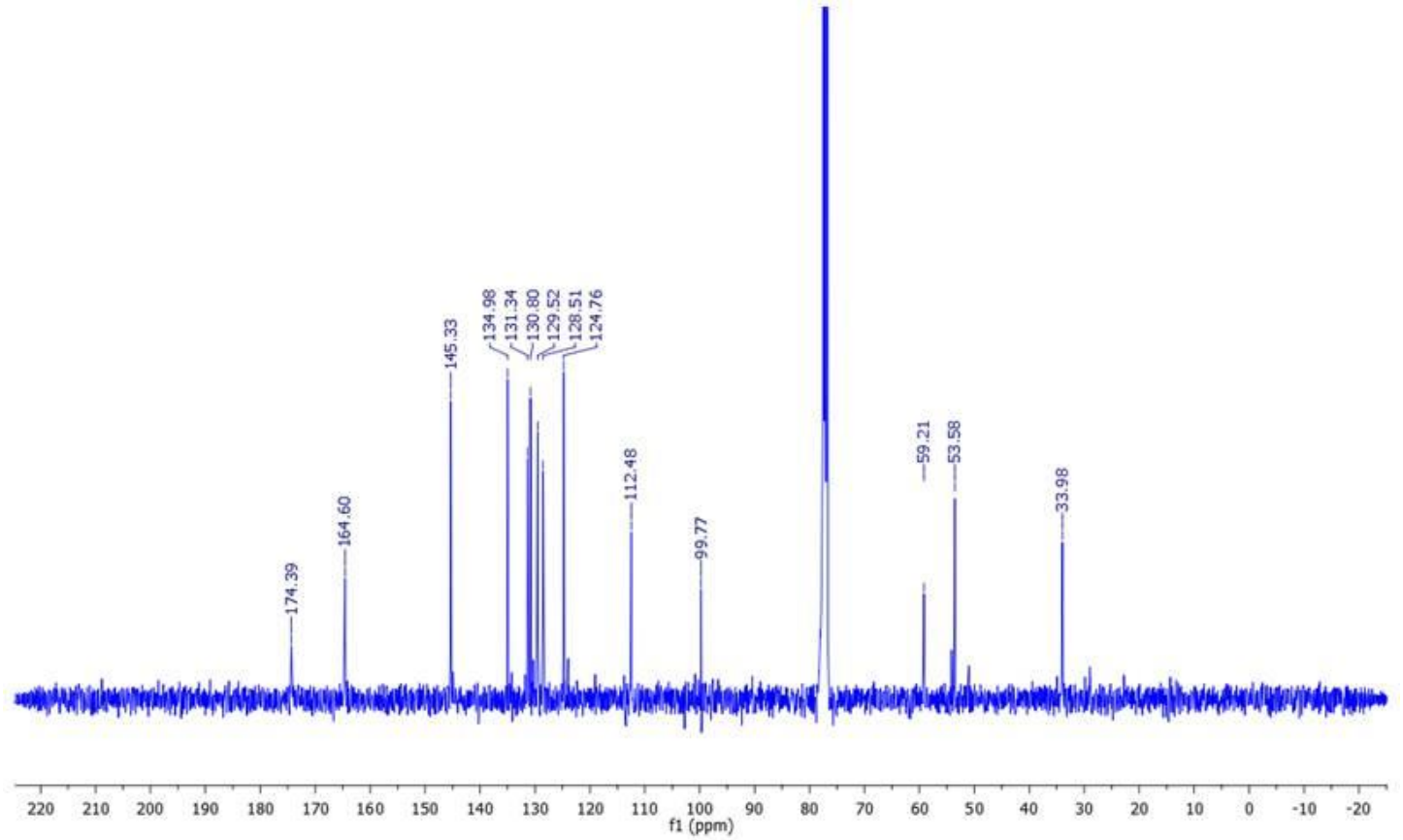
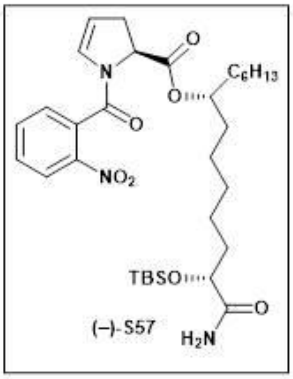
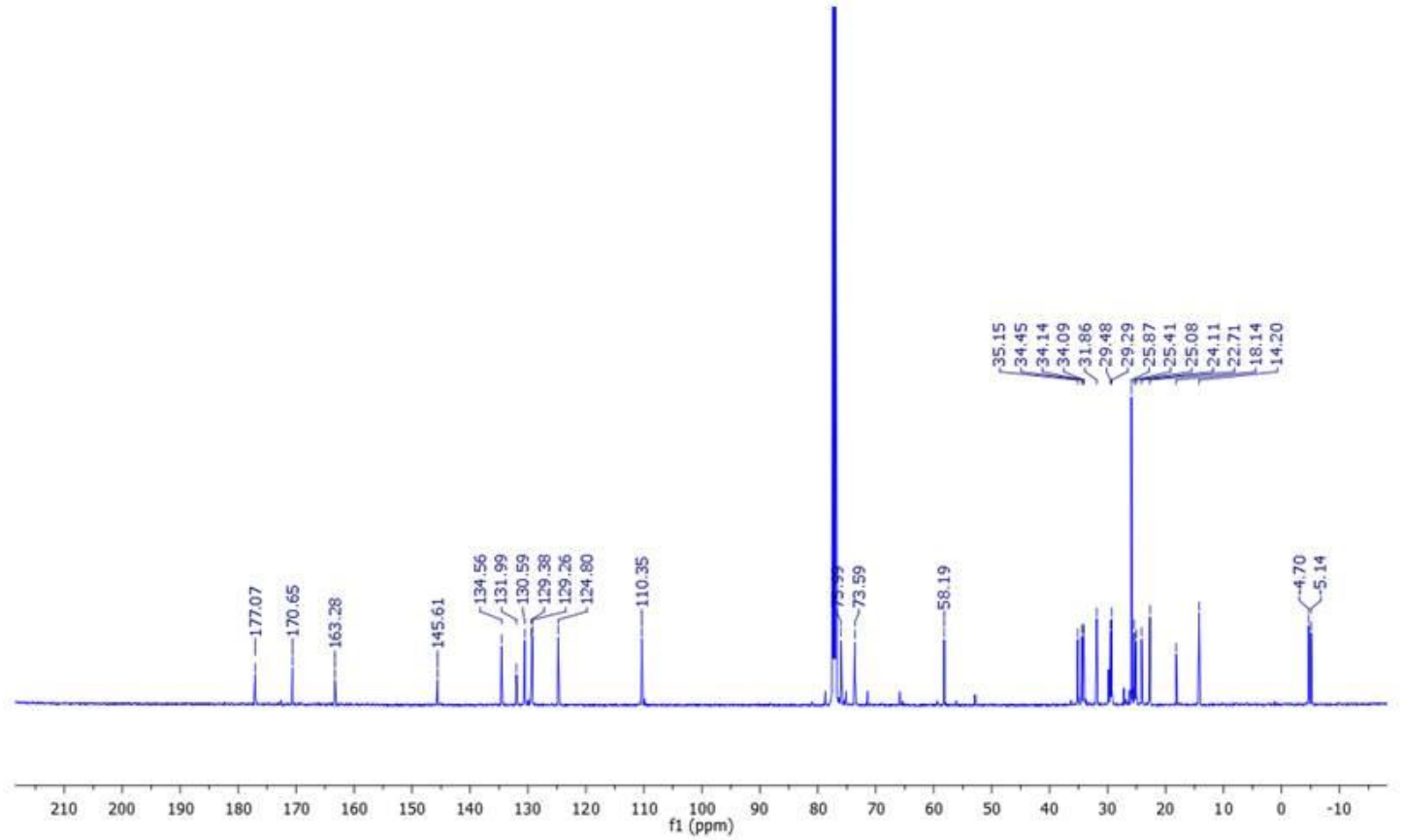


(–)-S56

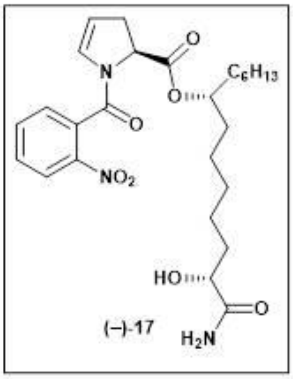


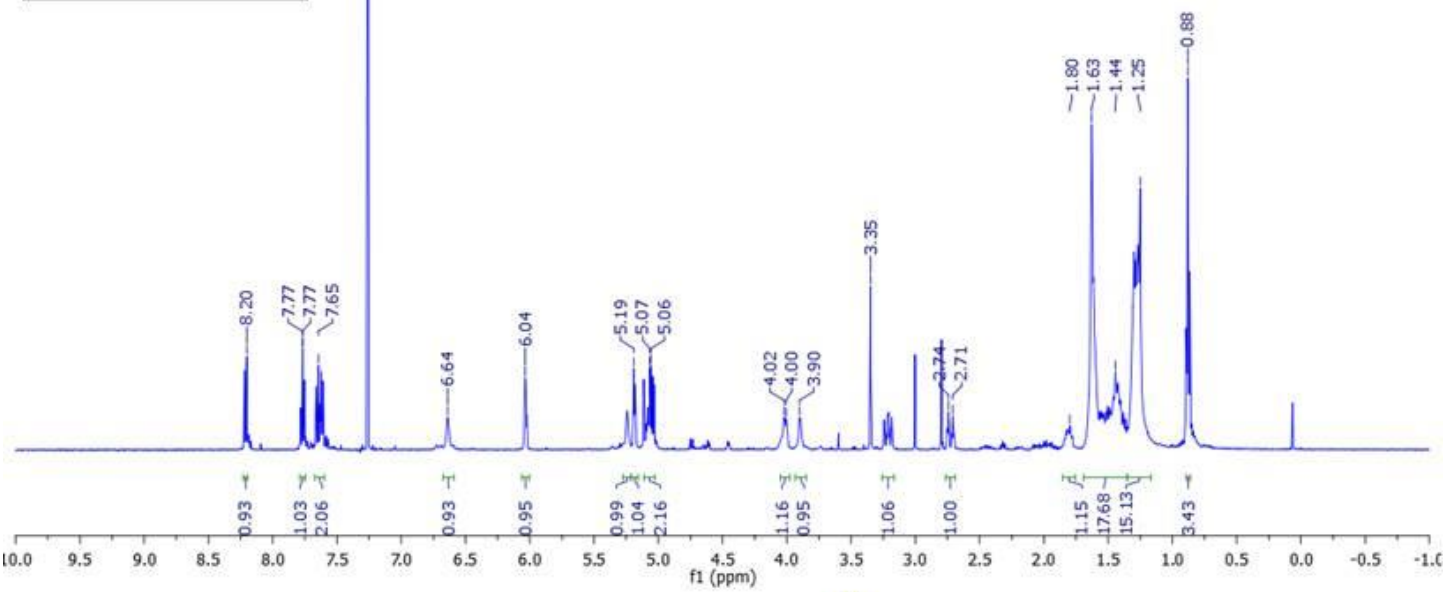
3. Appendix: IC_{50} & Spectral Data

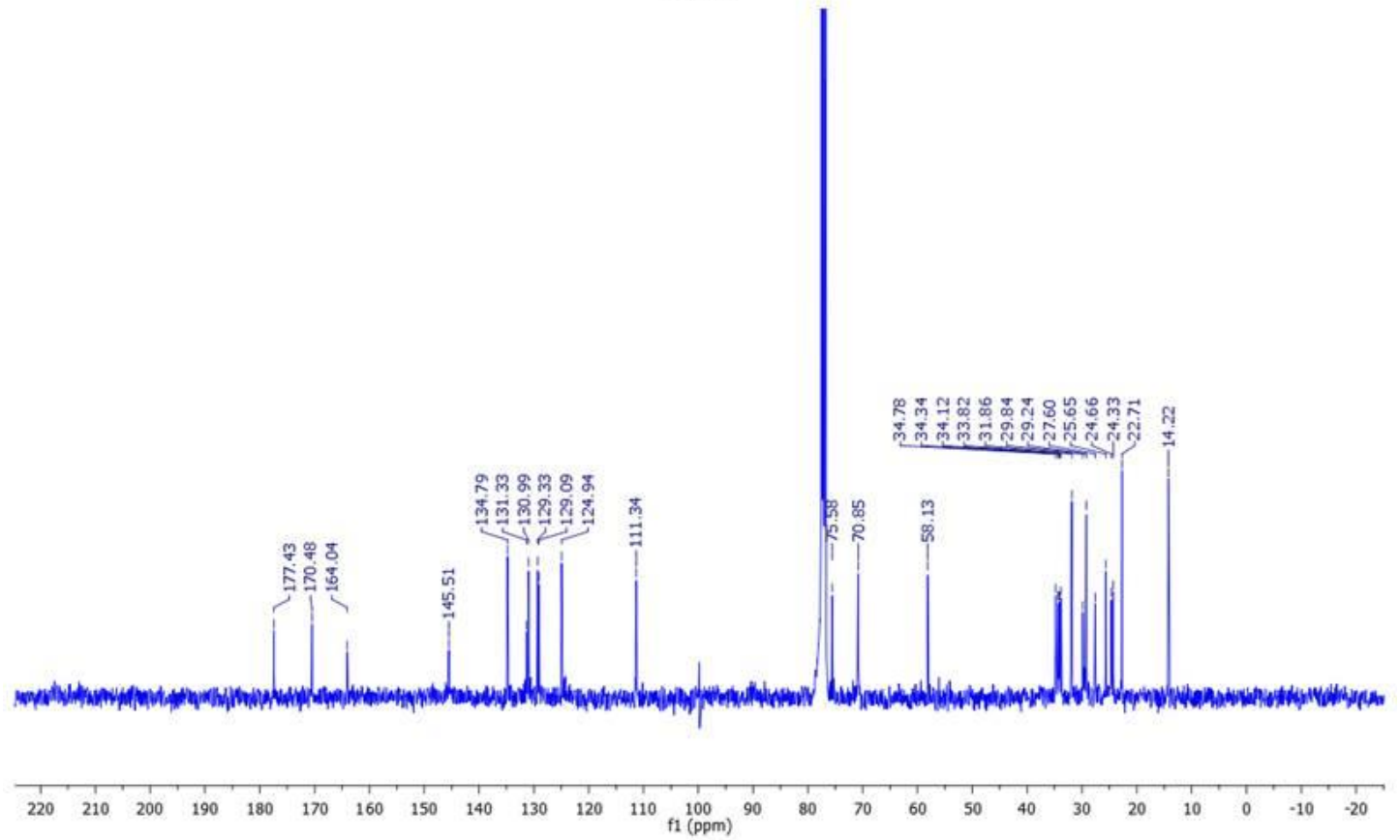




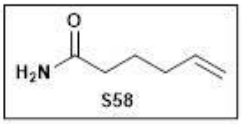
3. Appendix: IC_{50} & Spectral Data



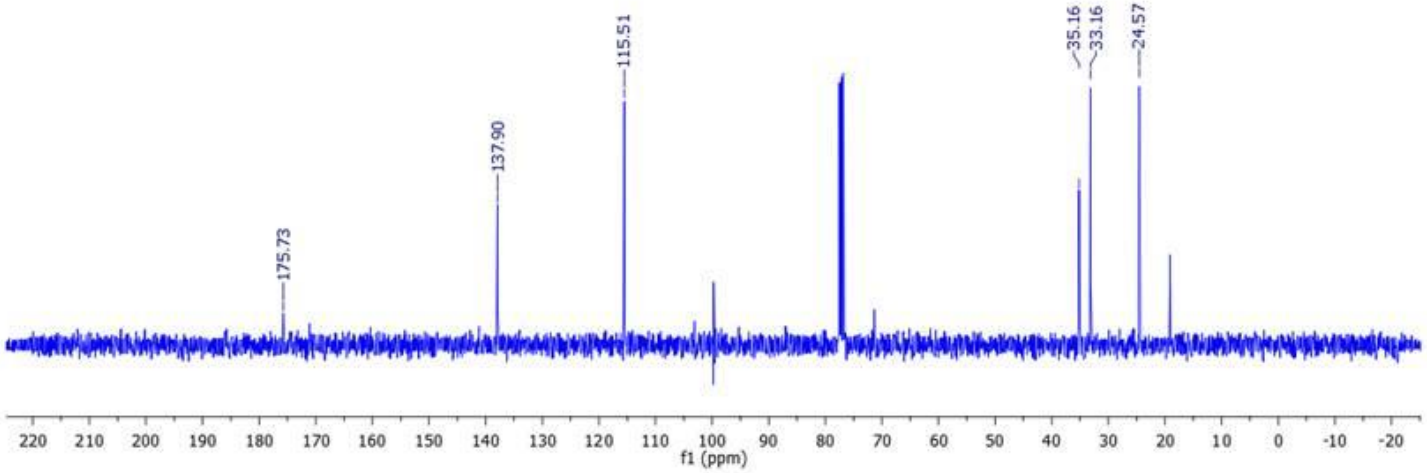




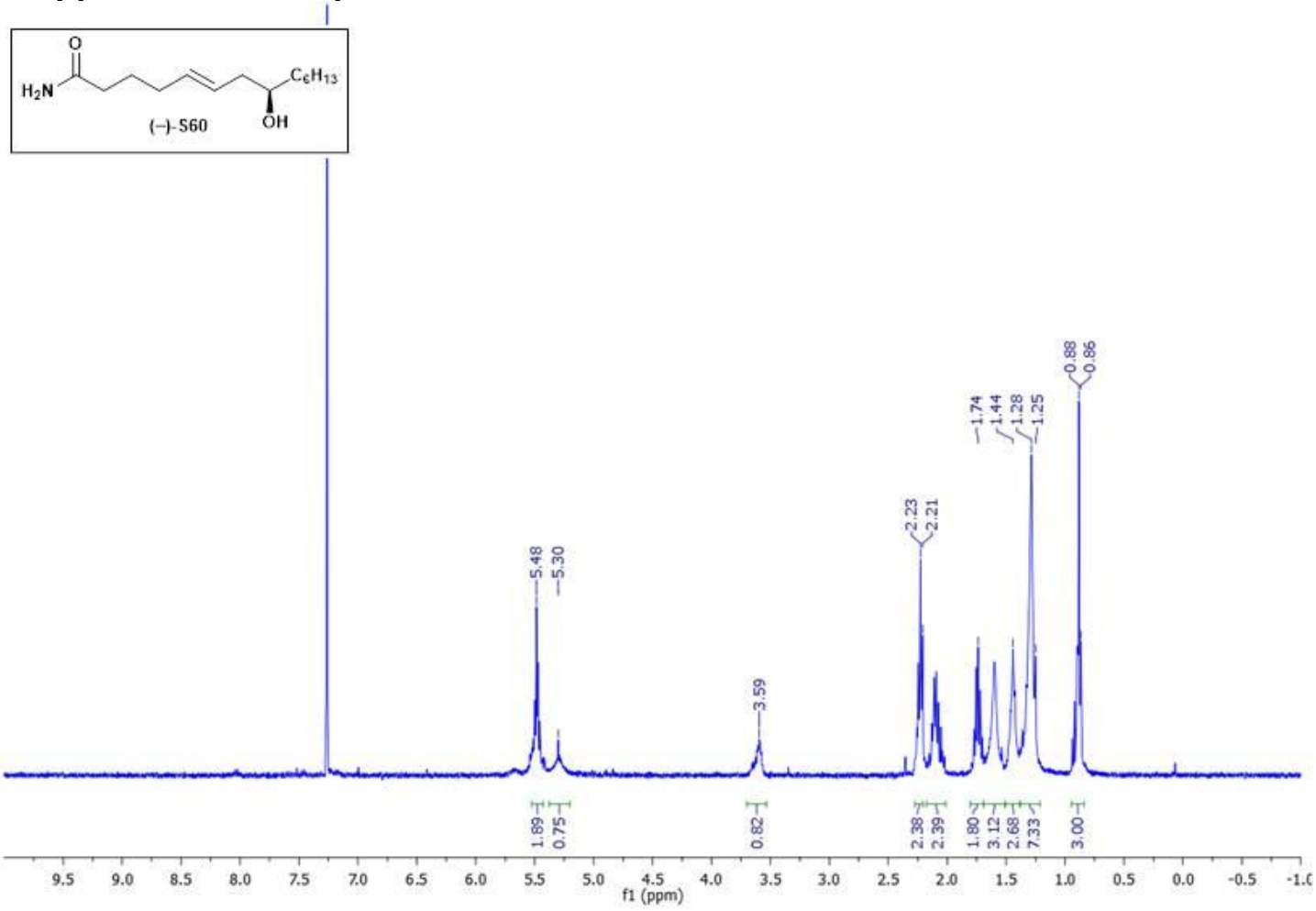
3. Appendix: IC_{50} & Spectral Data

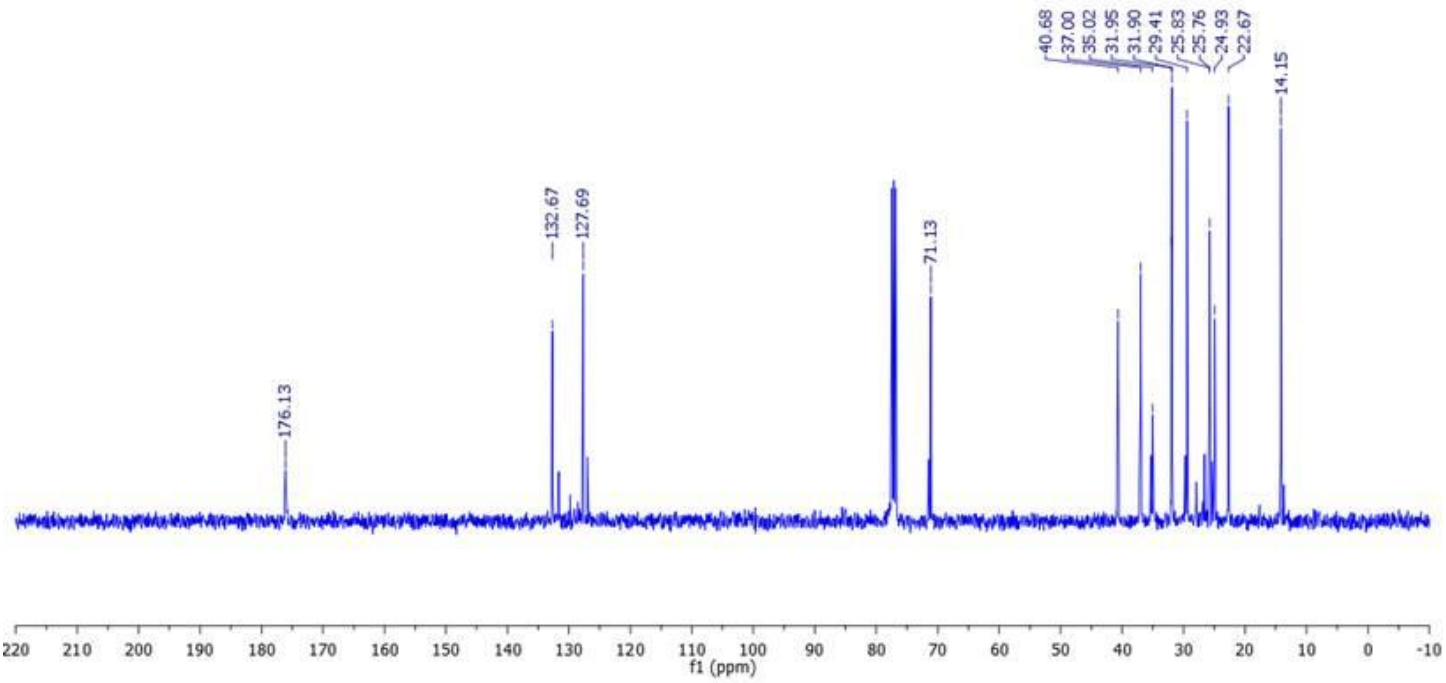


S58



3. Appendix: IC_{50} & Spectral Data





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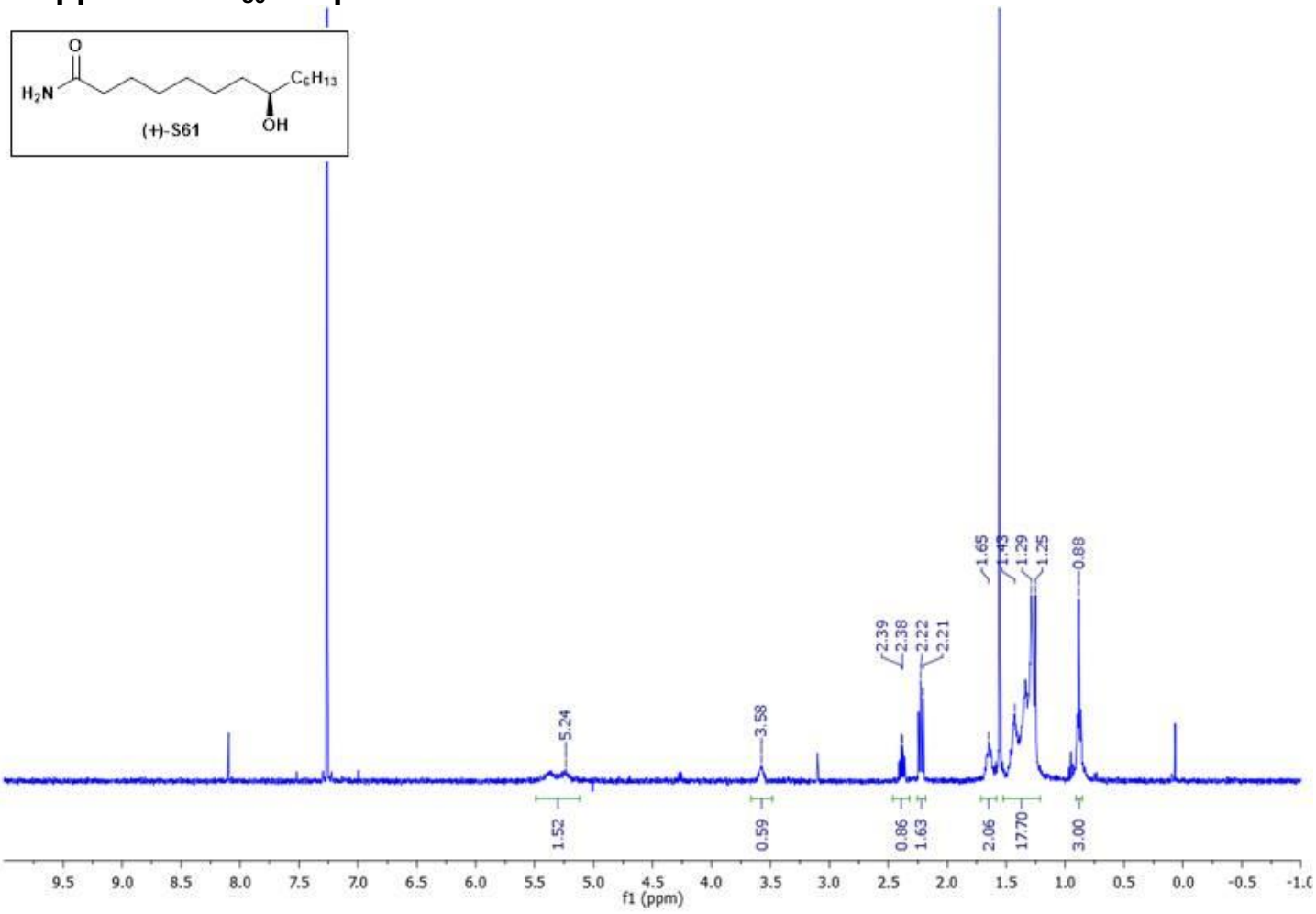

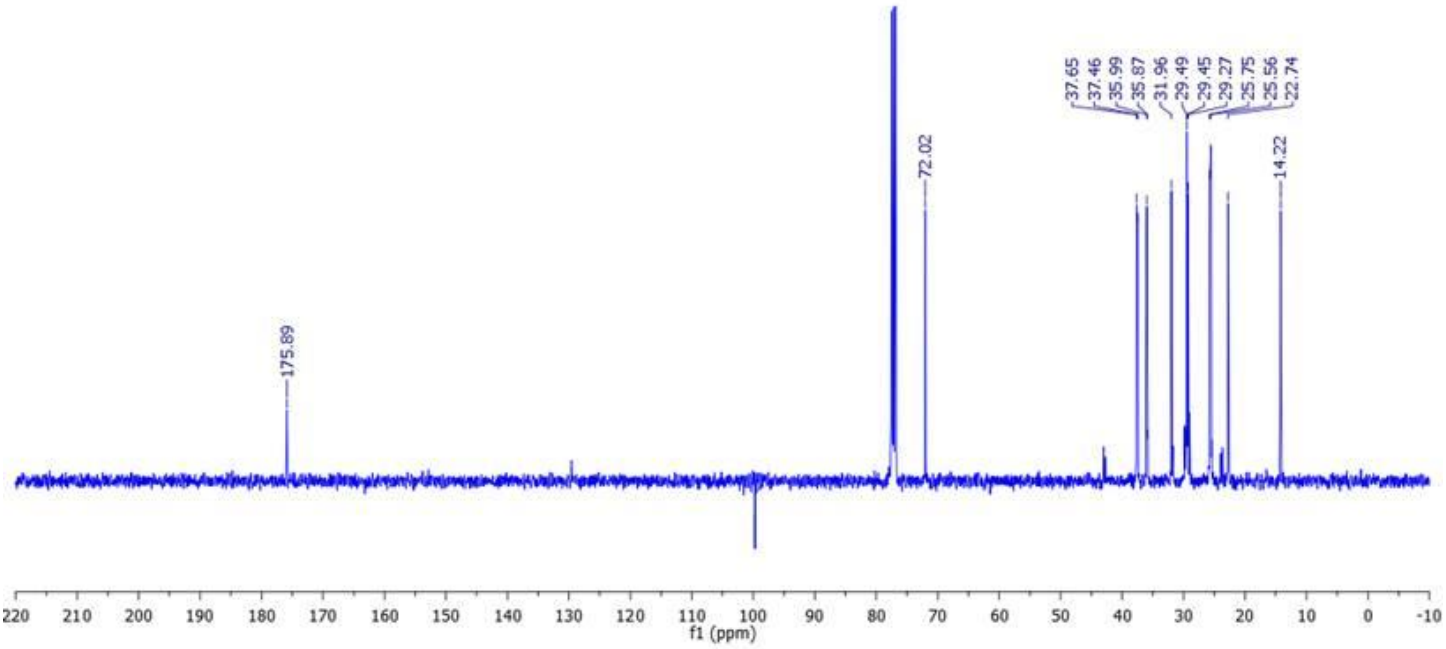

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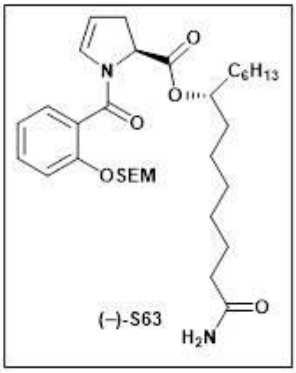

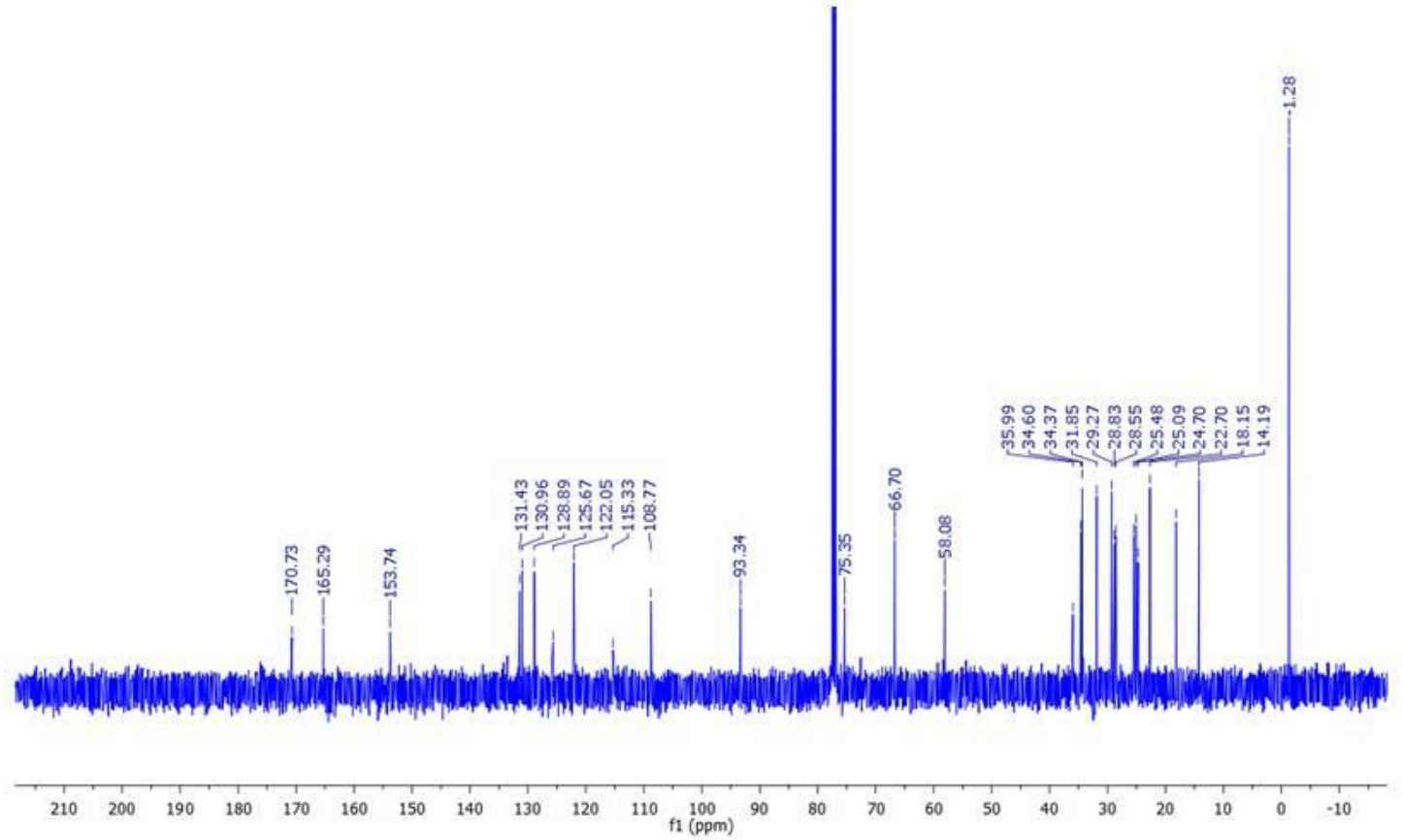

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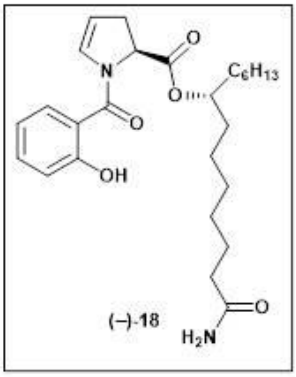
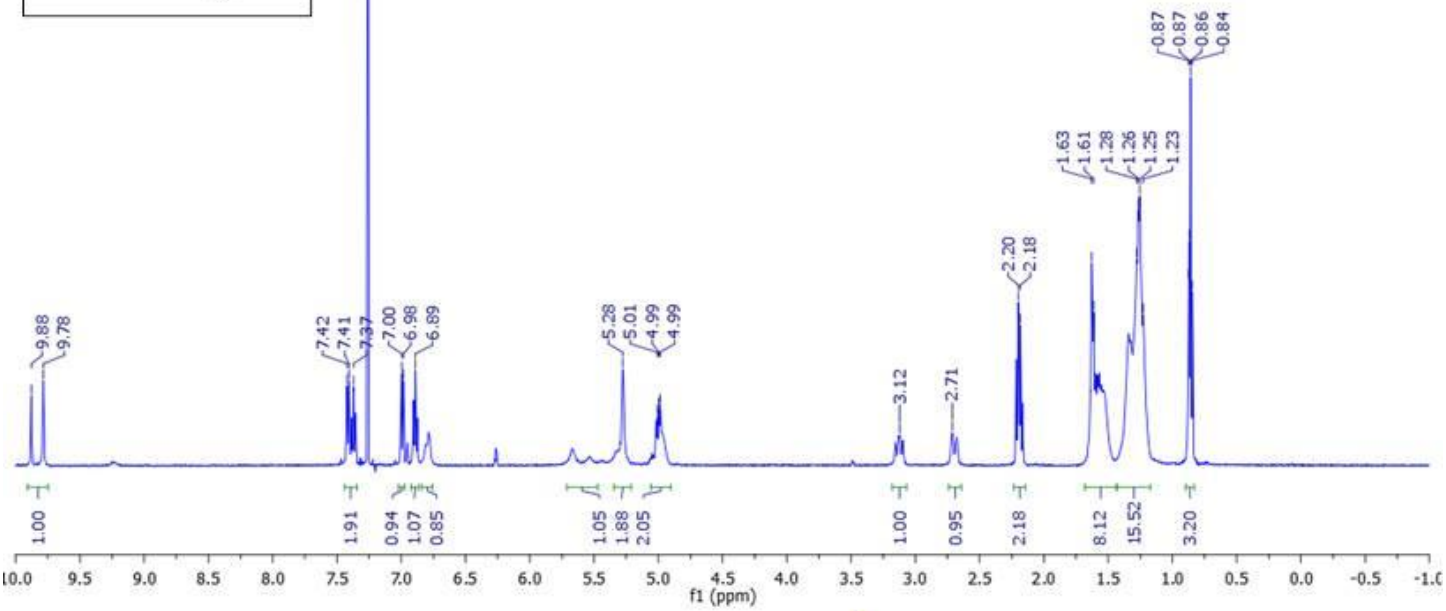
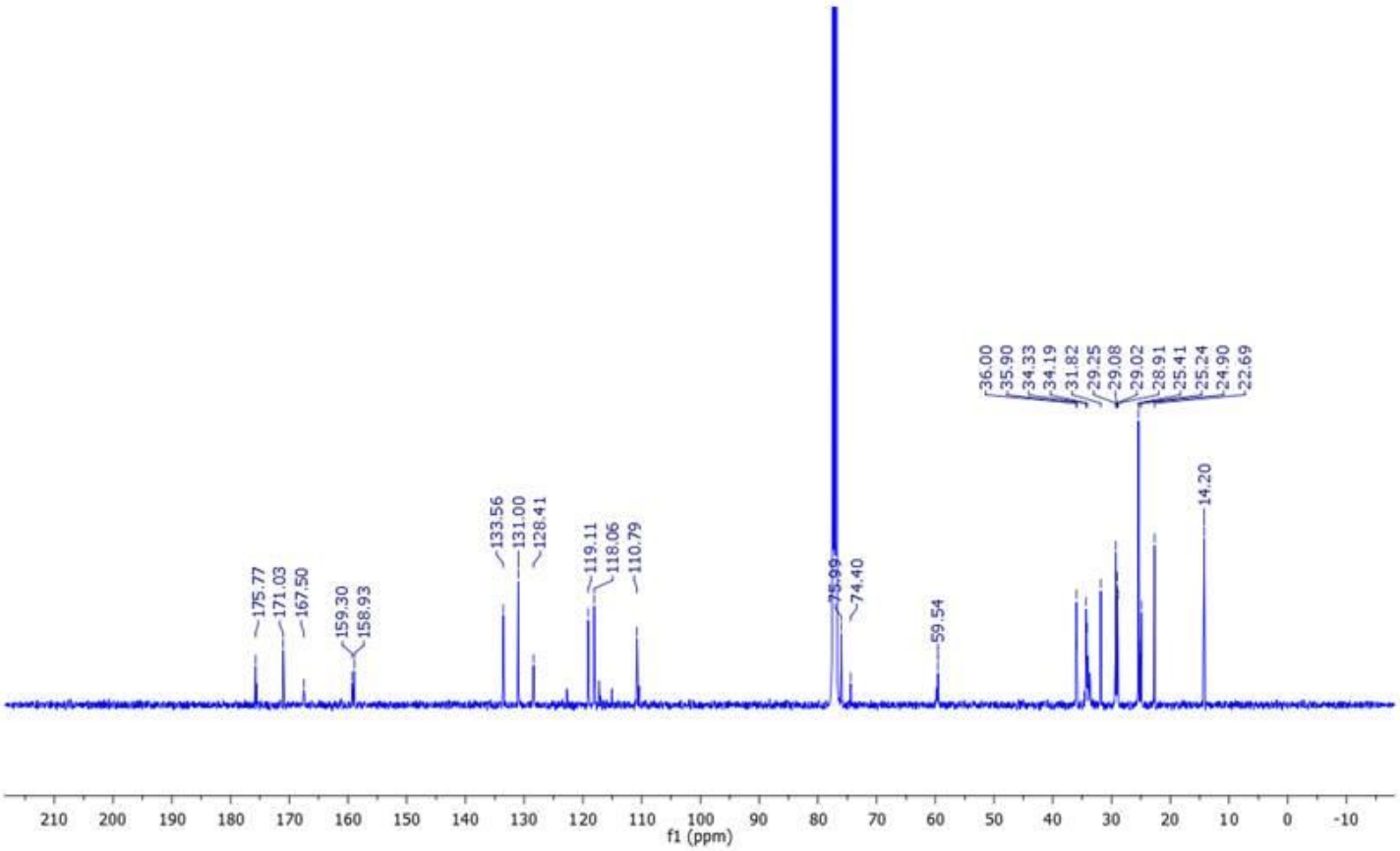
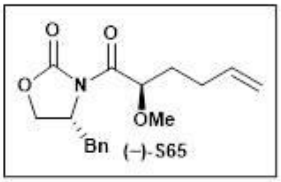
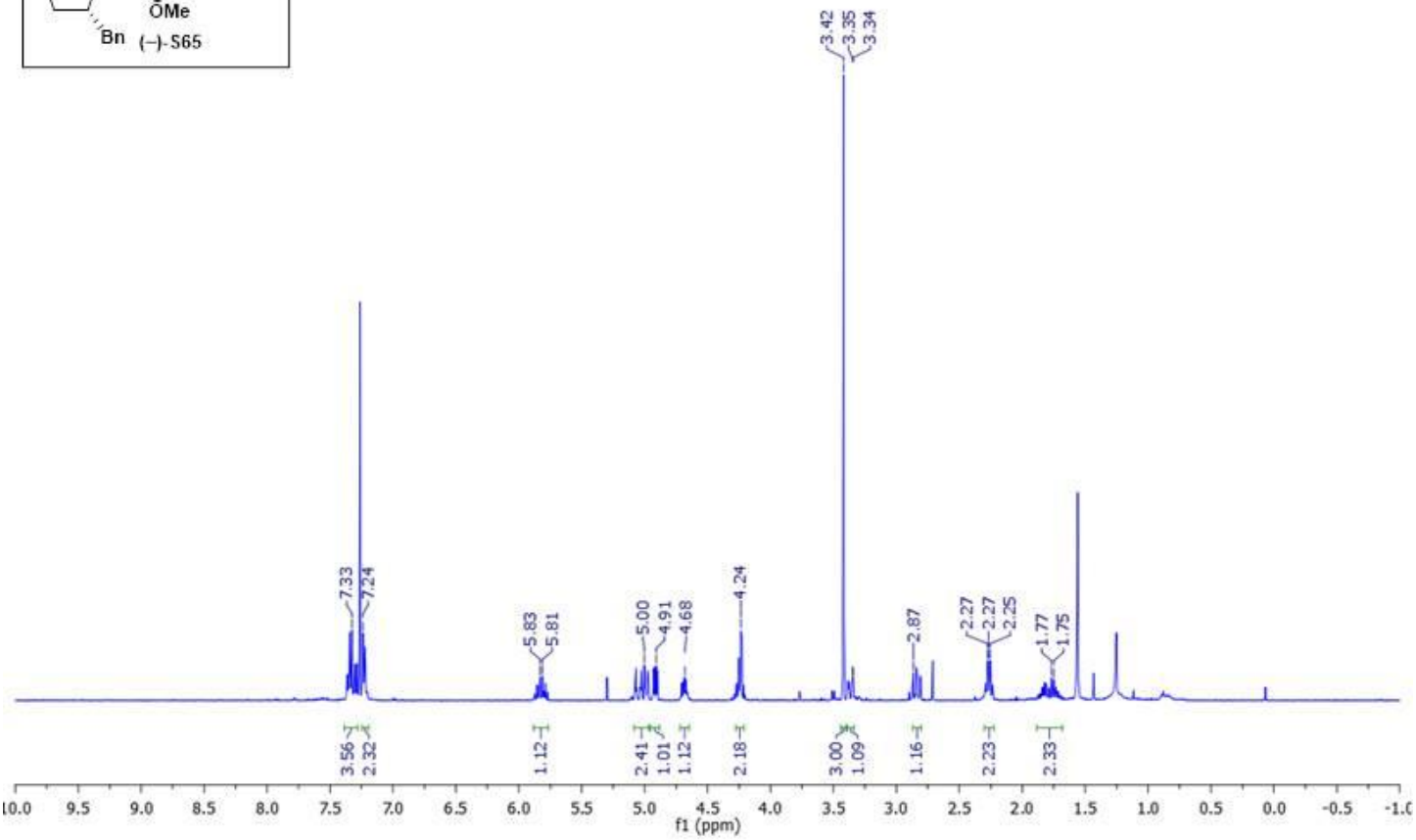


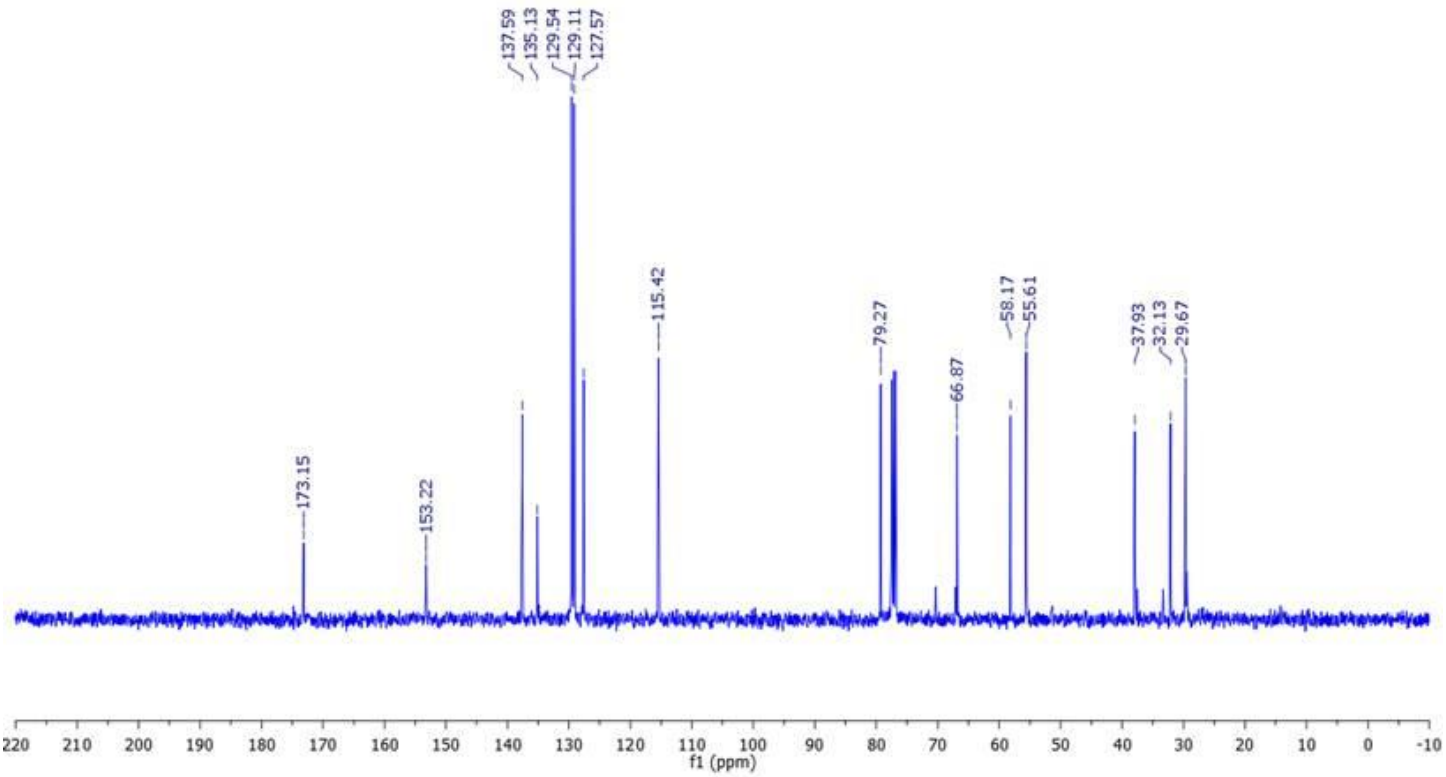




3. Appendix: IC_{50} & Spectral Data







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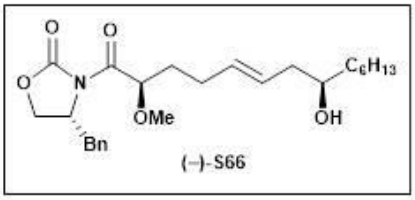
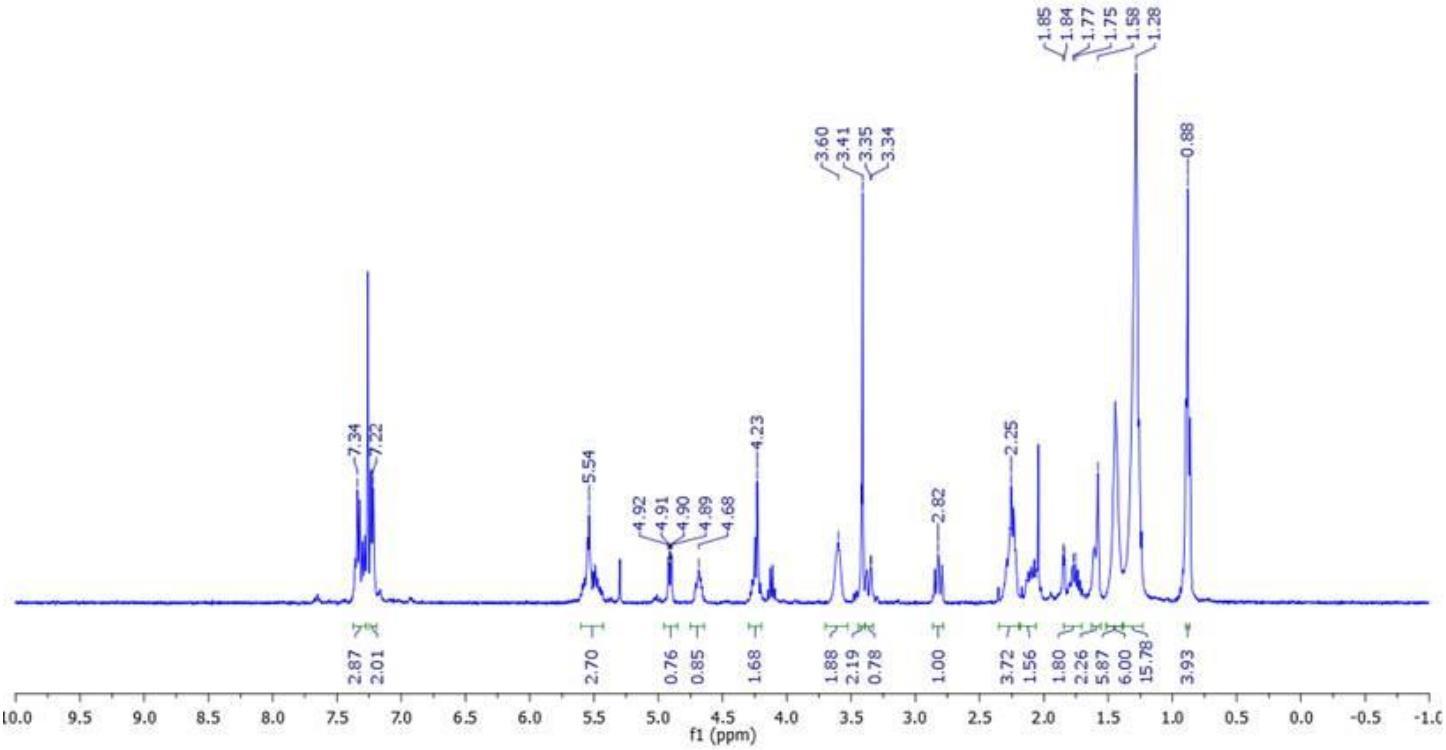
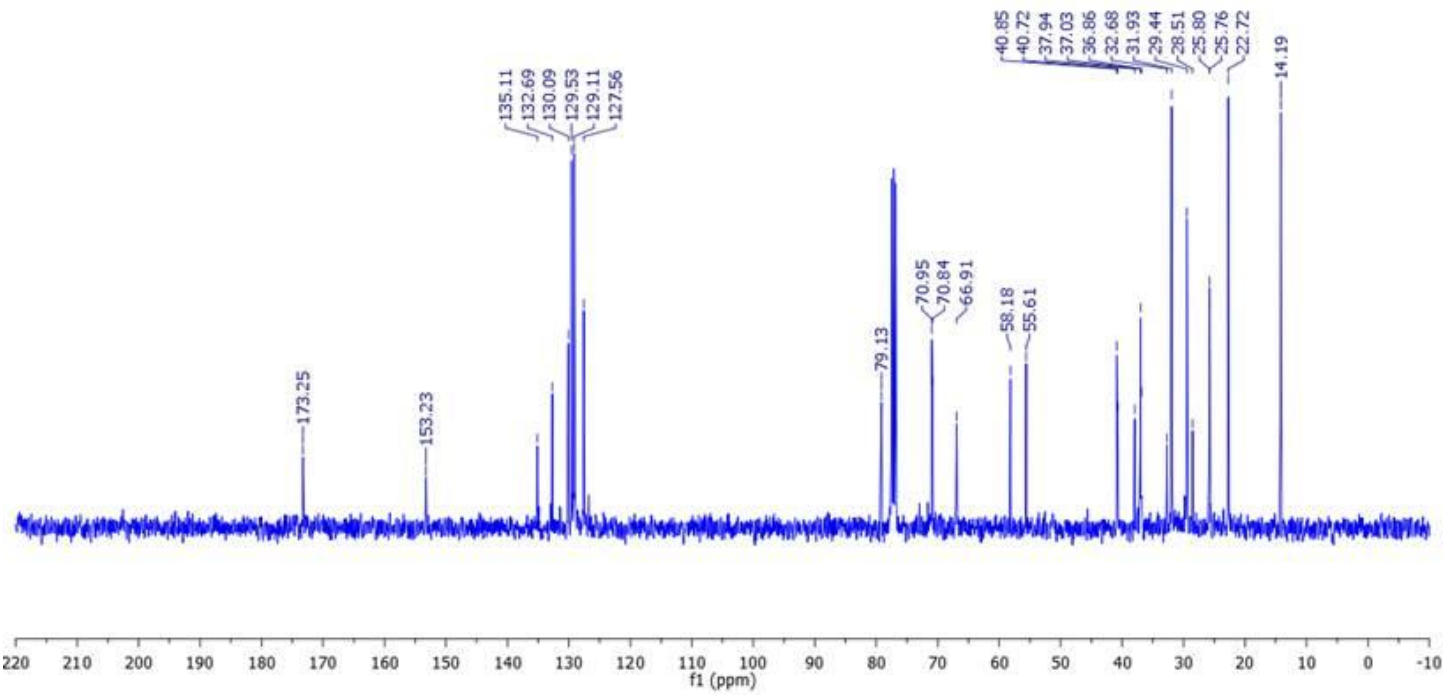


(−)-S66





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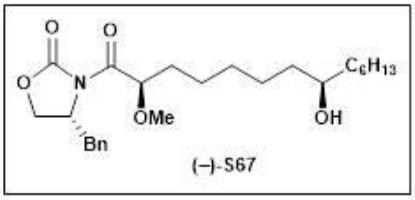
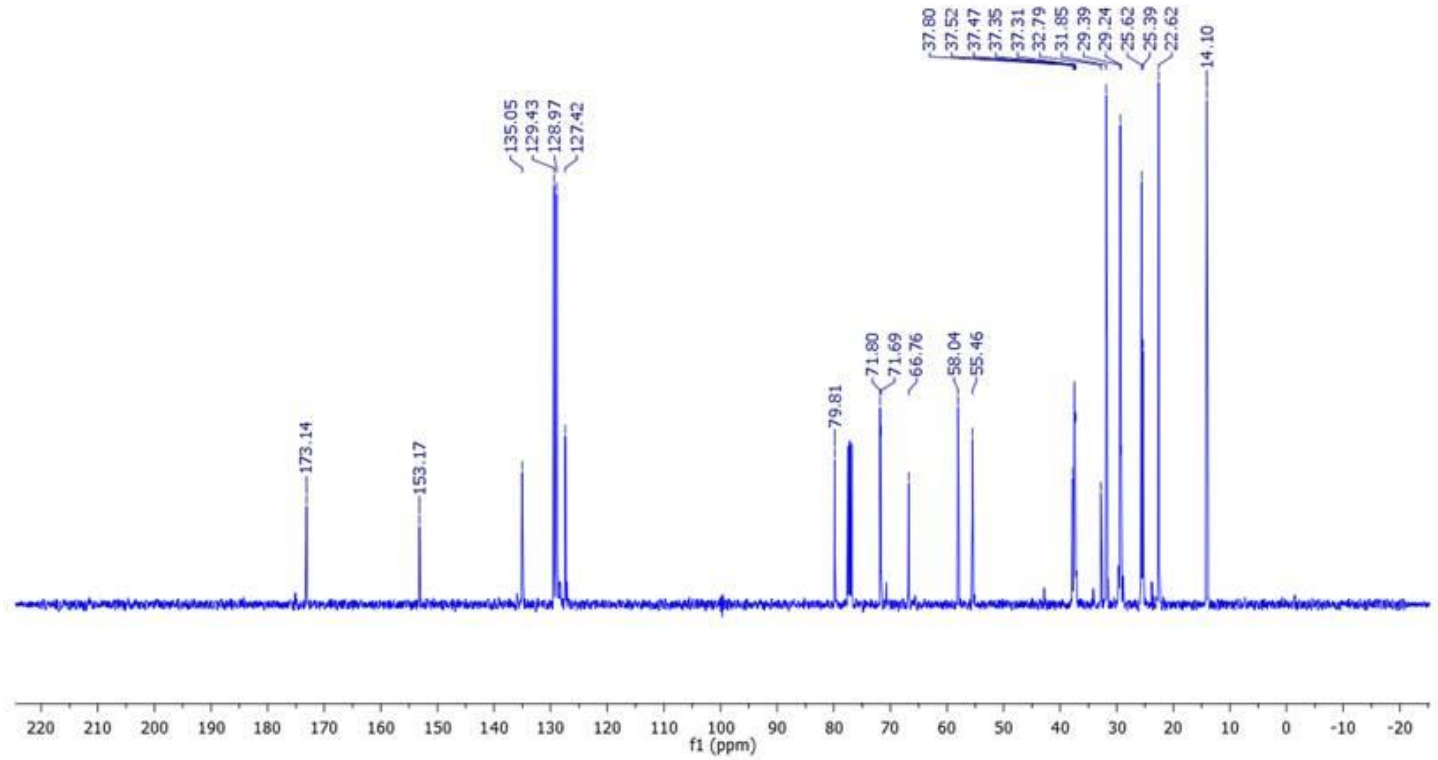


(–)-S67



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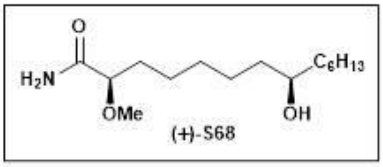
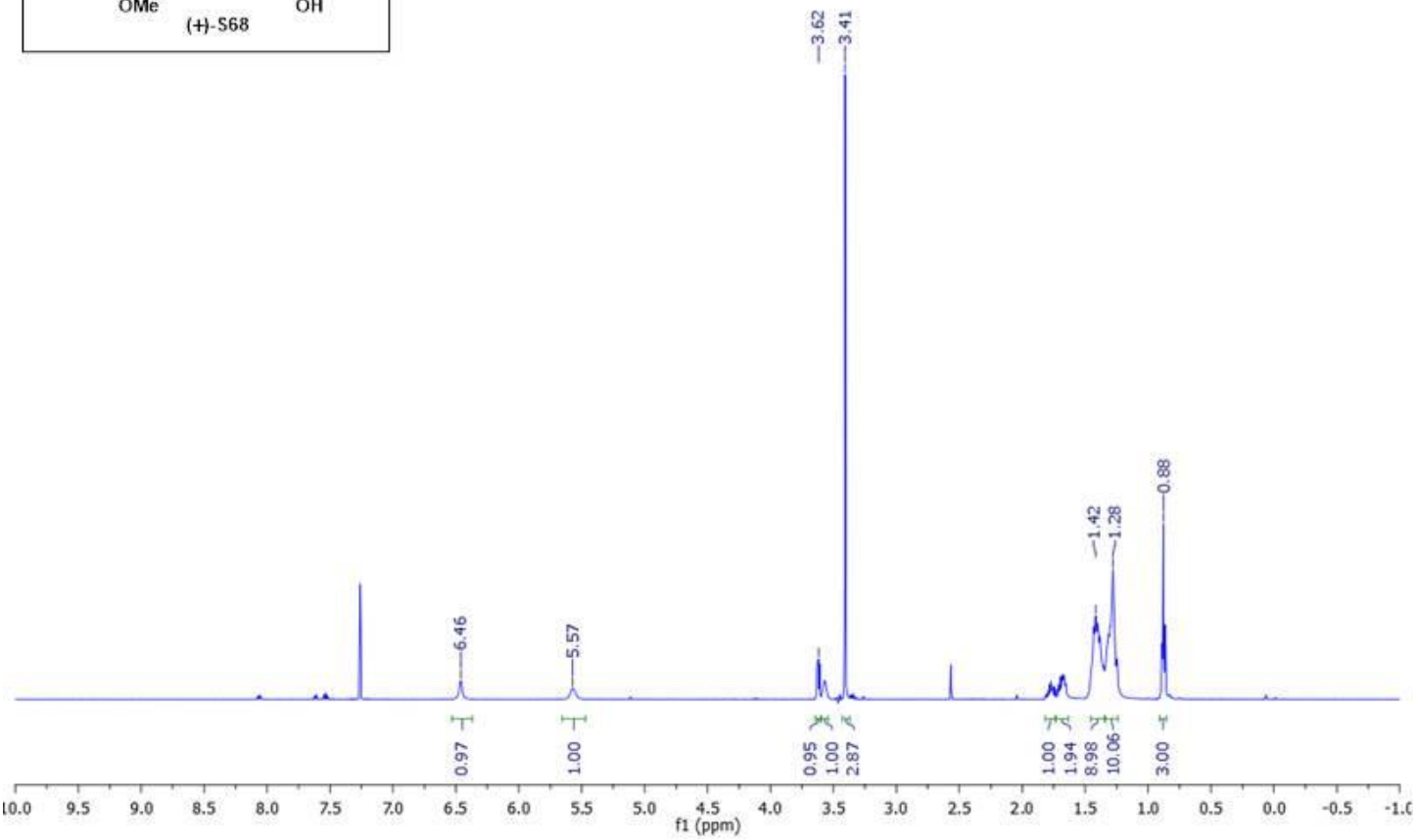
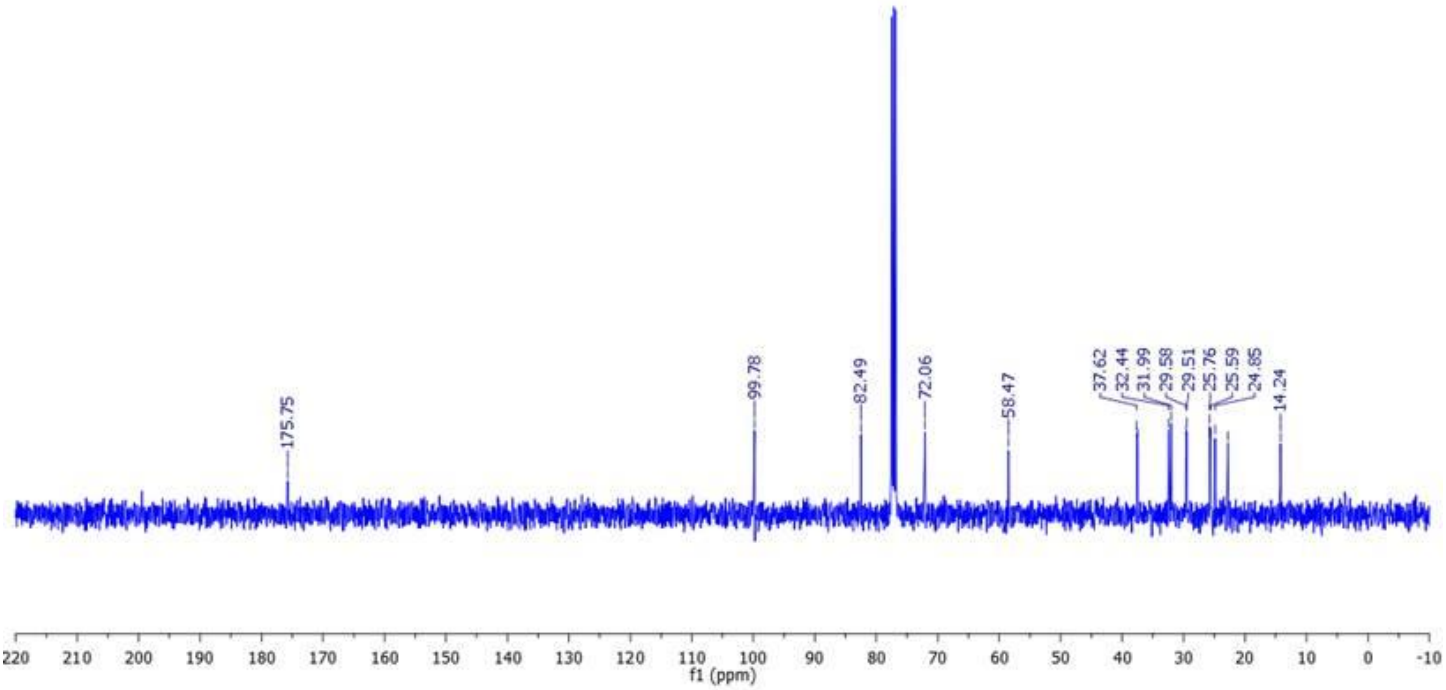


(+)-S68





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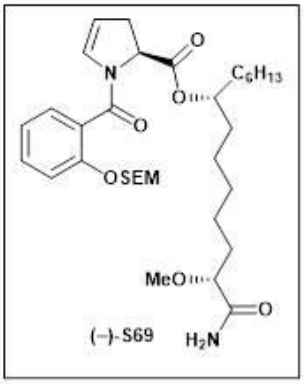

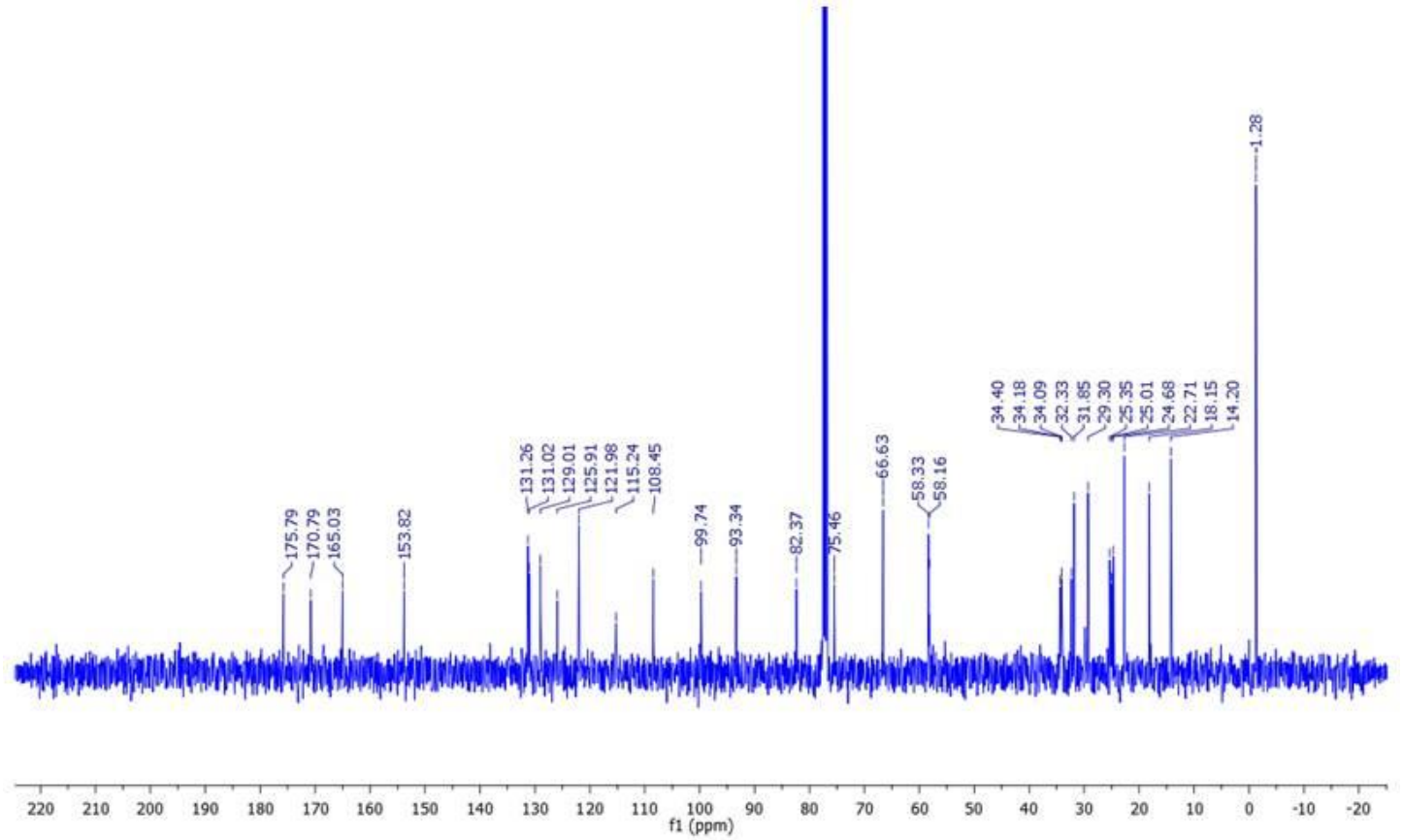

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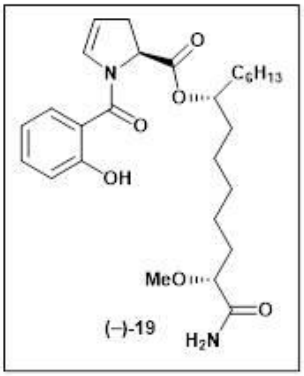
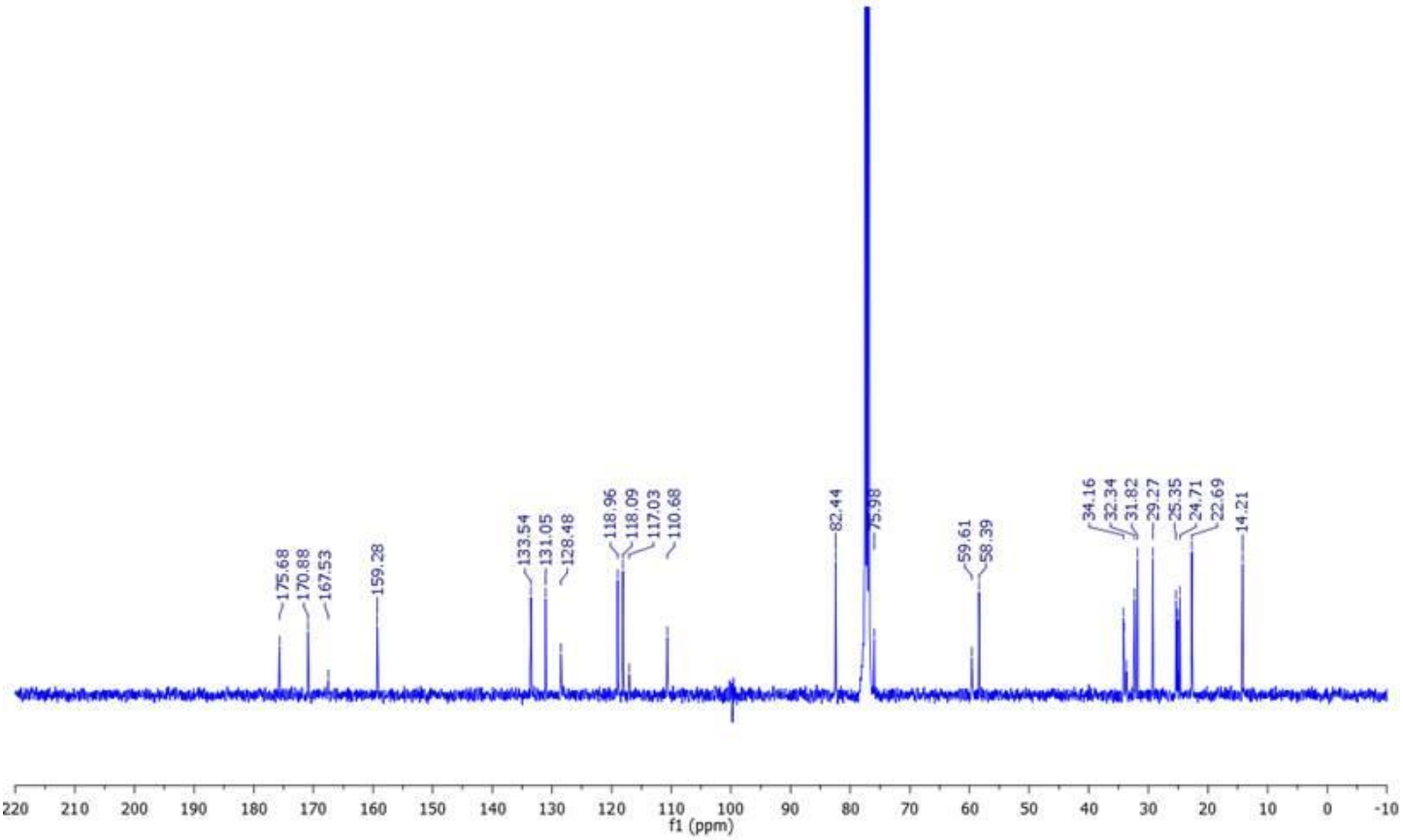


(−)-19



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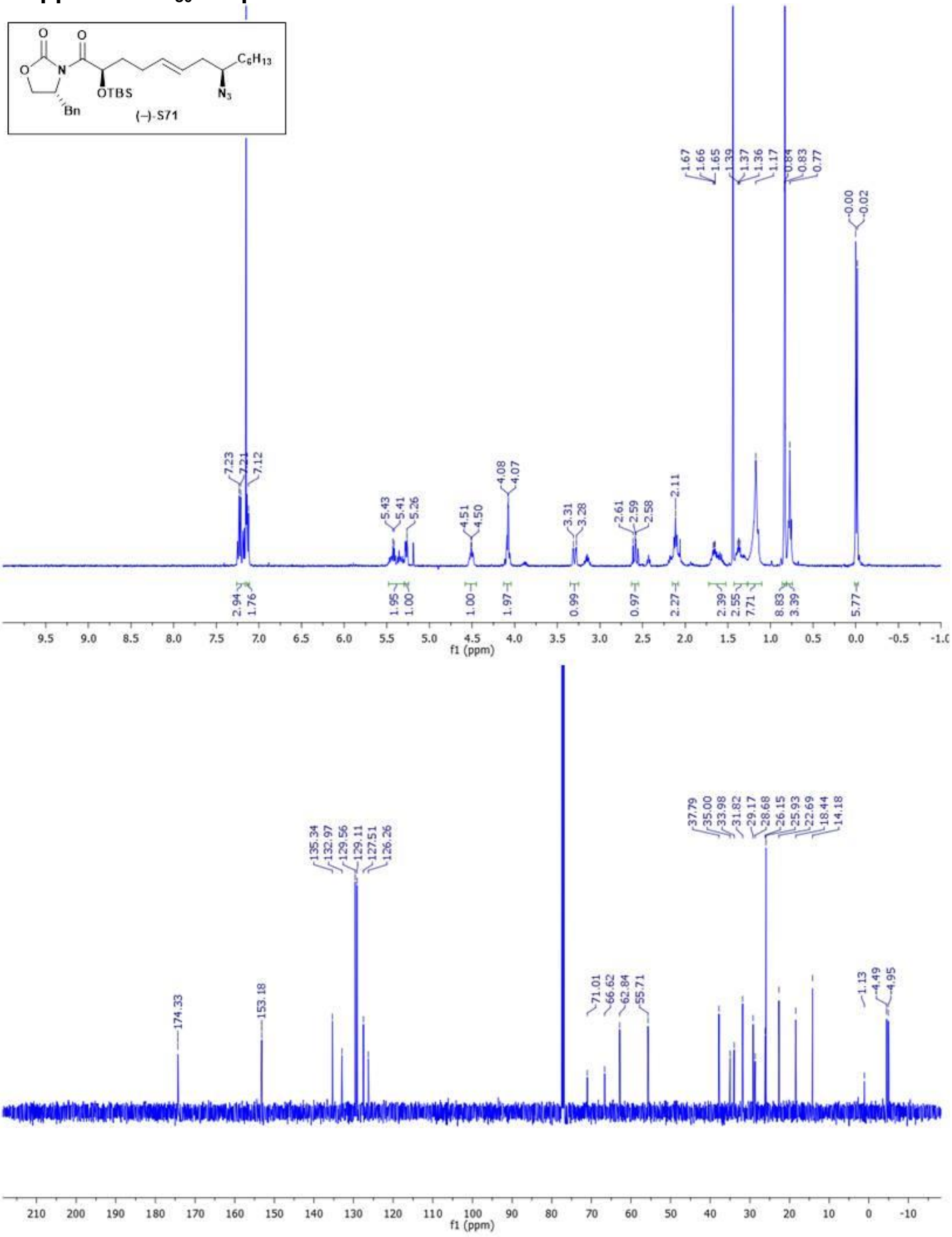

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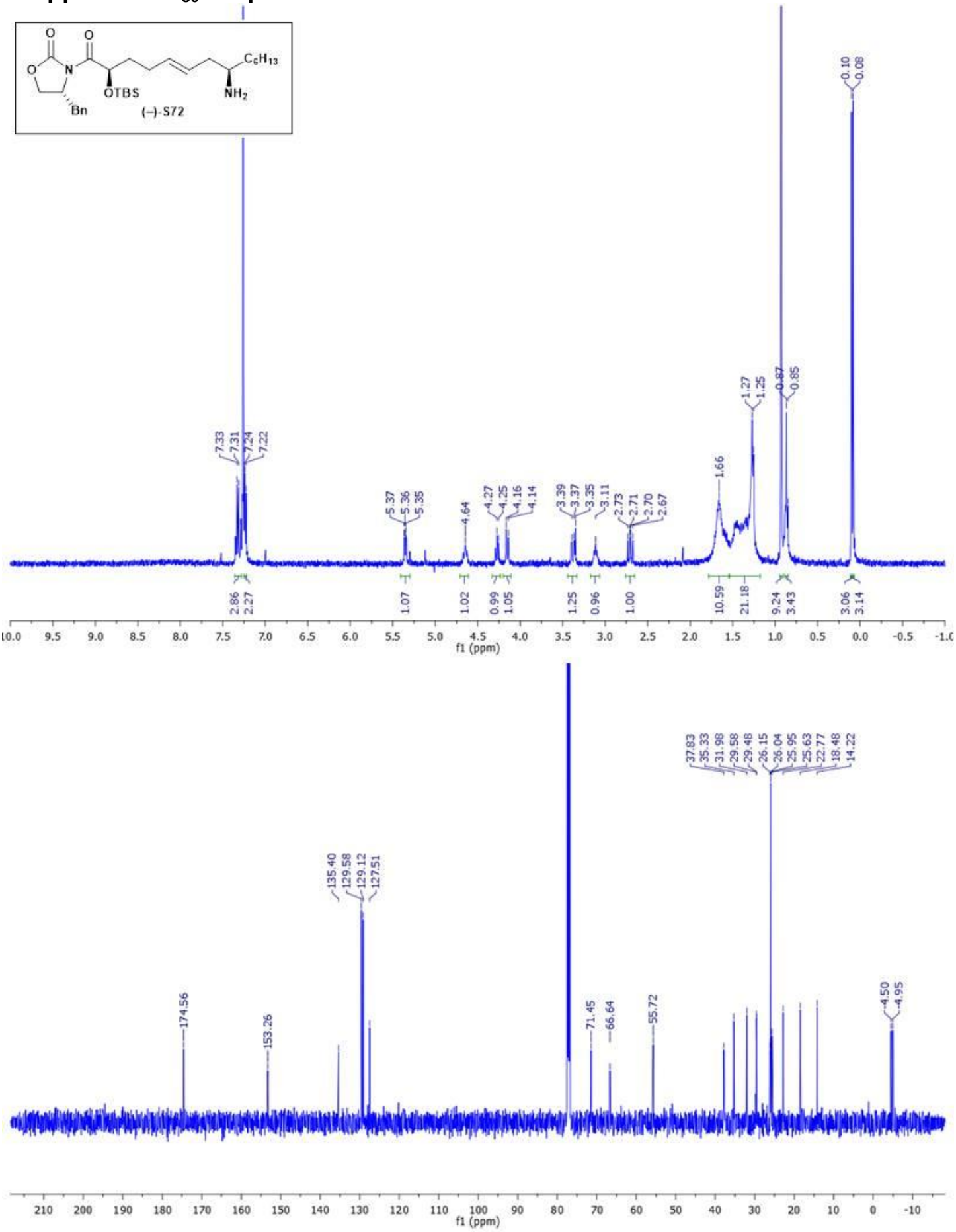

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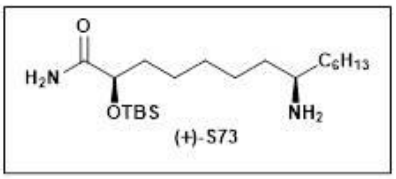

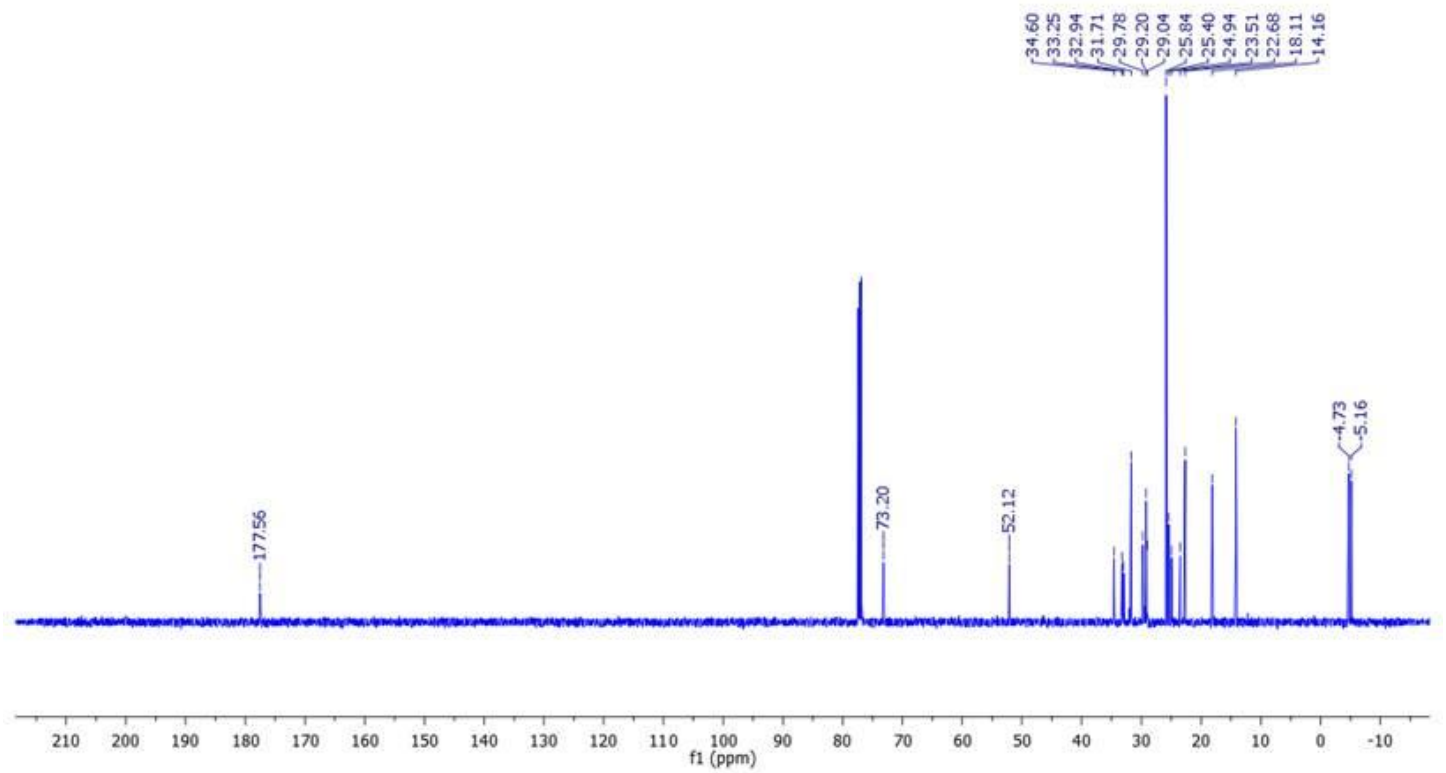

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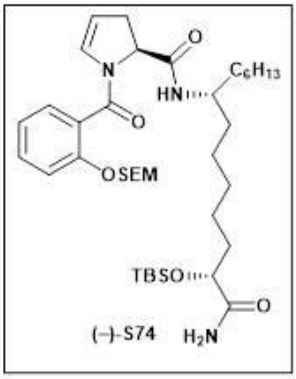

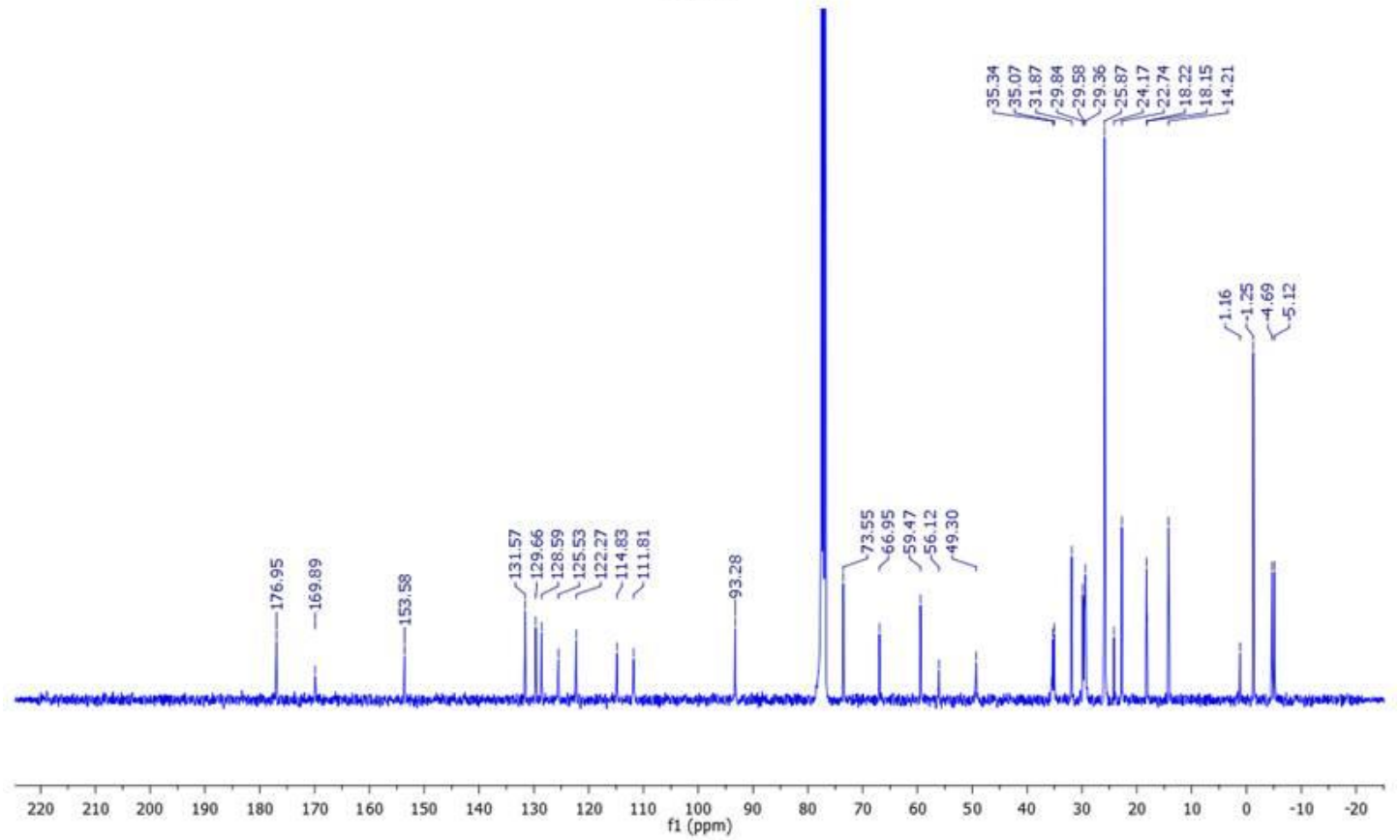

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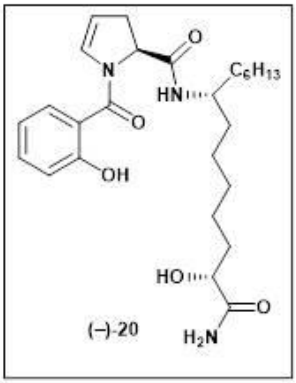

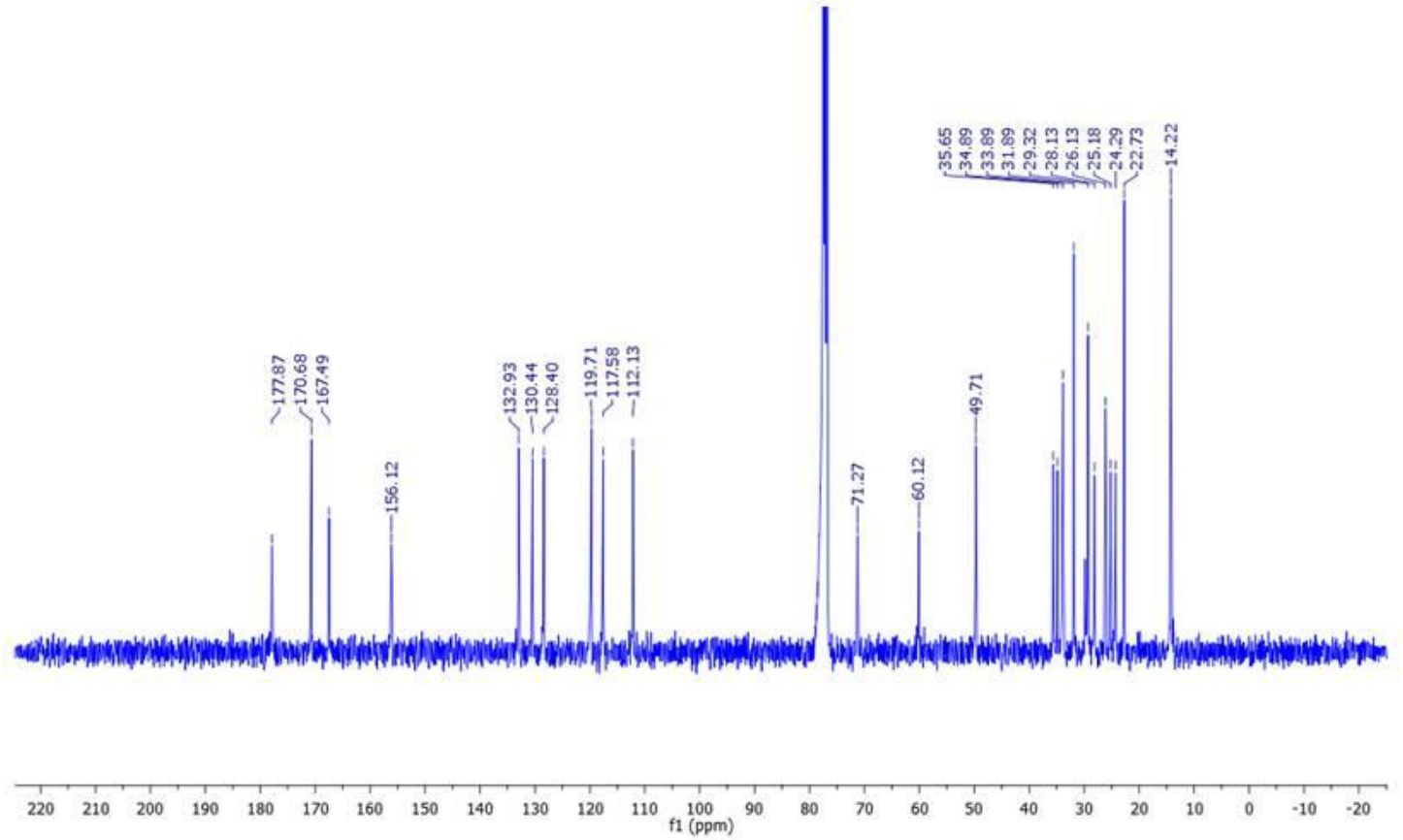

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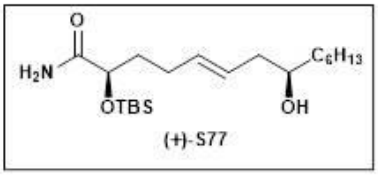
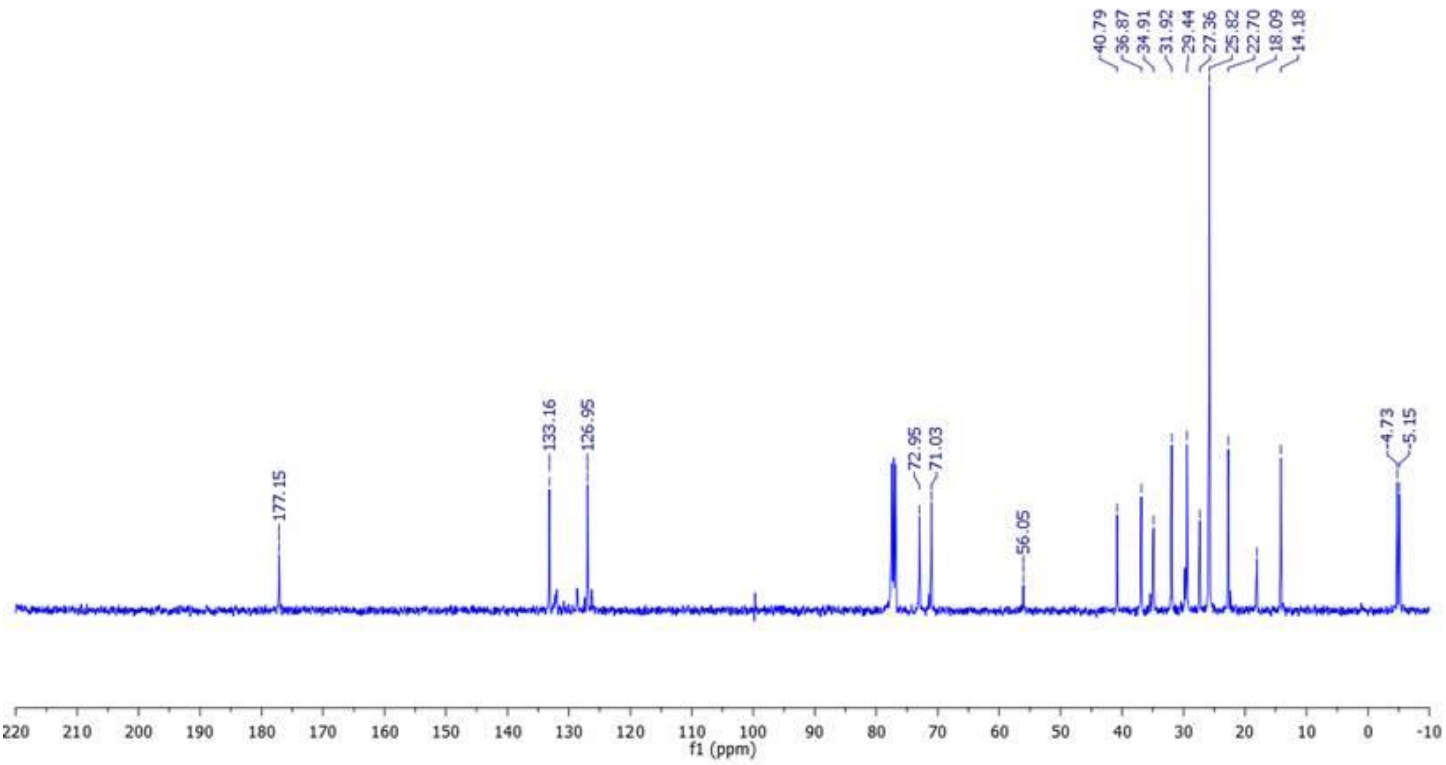


(+)-S77



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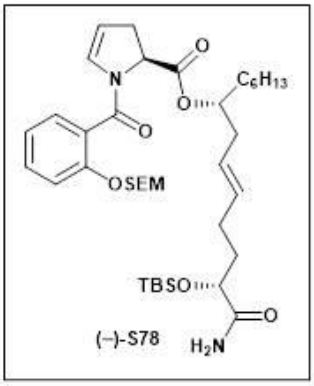

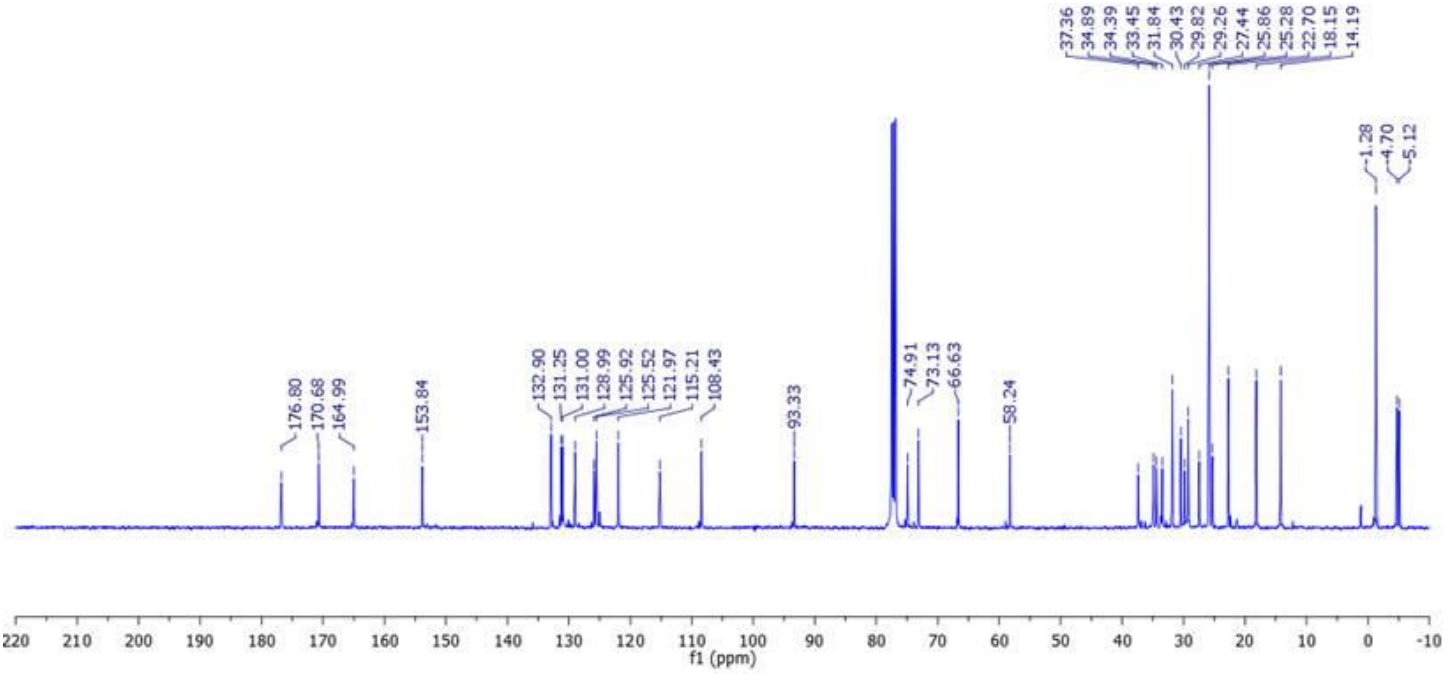

3. Appendix: IC_{50} & Spectral Data