Catalytic Enantioselective Asssembly of Complex Molecules Containing Embedded Quaternary Stereogenic Centers from Simple Anisidine Derivatives

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General Information

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded using a Bruker AM 400 (400 MHz) or an Avance 500 (500 MHz) spectrometer. Carbon nuclear magnetic resonance (^{13}C NMR) were recorded using a Bruker AM 400 (100 MHz) or an Avance 500 (125 MHz) spectrometer. All spectra were recorded at ambient temperature (298 K). Chemical shifts (δ) are quoted in ppm relative to residual solvent and coupling constants (*J*) are quoted in hertz (Hz). Multiplicity is reported with the following abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, septet=sp, m=multiplet, b=broad, app=apparent.

Infrared (IR) spectra were recorded on a Perkin Elmer Spectrum One-FT-IR spectrometer as thin films deposited in dichloromethane. HRMS were measured either at the University of Cambridge on a Micromass Q-TOF spectrometer using electrospray ionisation (ESI) or at the EPSRC Mass Spectrometry Service at the University of Swansea. Optical rotations were measured in $CHCl_3$ on a Perkin Elmer 343 Polarimeter; $[\alpha]_D$ values are reported in 10^{-1} degrees cm^2 g^{-1} at 589 nm. Chiral HPLC analysis was performed n HP Agilent 1100 apparatus. Melting points (m.p.) were recorded using a Reichert hot stage apparatus and are reported uncorrected.

Analytical thin layer chromatography (TLC) was performed using pre-coated Merck glass backed silica gel plates (Silicagel 60 F254). Flash column chromatography was undertaken on Merck Kieselgel 60 (230-400 mesh) under a positive pressure of nitrogen unless otherwise stated.

All solvents used were dried and distilled using standard methods. Dichloromethane was distilled from calcium hydride and 1,2-dichloroethane was purchased in anhydrous form. All reagents were purchased at the highest commercial quality. All reactions were monitored by TLC or from ^{1}H NMR spectra taken from reaction samples, with conversions confirmed by use of an NMR standard. Reactions were carried out under an atmosphere of nitrogen unless otherwise stated.

1: General procedure for amine coupling with 3-substituted-prop-2-ynoic acid

3-substituted-prop-2-ynoic acid (1eq), EDCI (1.2eq) and HOBT (0.1eq) were added to a solution of (*N*-4,4-diethoxyalkyl)-4-methoxyaniline (1eq) in CH_2Cl_2 (0.26 M) at room temperature. The resulting solution was stirred at room temperature until completion, quenched with $NaHCO_{3(aq.)}$ and extracted twice with CH_2Cl_2. The combined organic layers were washed with water and brine, dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel to afford the desired compounds.

2: General procedure for acetal removal

2N HCl (1.2 mL/mmol) was added dropwise to a solution of acetal (1 eq) in THF (6 mL/mmol) at room temperature, and the resulting solution was stirred until completion. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with diethyl ether. The organic layer was dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel.

3: General procedure for ECED transformation

ICl (2 eq) in CH_2Cl_2 (1 M) was added to a solution of the aldehyde **1** (1 eq) (**method A**) or the corresponding diethoxyacetal (1 eq) (**method B)** in CH_2Cl_2 (0.1 mM) at -78 ºC over a period of 15 minutes. The resulting solution was stirred for 10-30 minutes and quenched with saturated aqueous $Na_2S_2O_3$ solution. It was allowed to warm up to room temperature and extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, concentrated in vacuo to afford the corresponding iodo-cyclohexadienone that was subjected directly to enantioselective desymmetrizing cyclization without further purification.

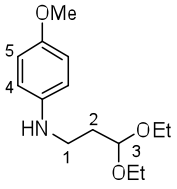
Catalyst (**3b**) (0.2 eq) and benzoic acid (0.2 eq) were added to the solution of aldehyde **1** (1 eq) in CH_2Cl_2 (0.3 M) at 0 or -20 ºC. The resulting mixture was stirred for 1.5 h to 48 h, quenched by water and extracted with CH_2Cl_2 (2 x 7 mL). The combined organic layers were dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel.

The ee of the reaction was determined by HPLC analysis of the corresponding Wittig olefination product (**7**), formed using the procedure outlined below (4).

4: General procedure for Wittig reaction

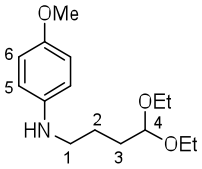
(tert-Butoxycarbonylmethylene)triphenylphosphorane (1.5 eq) or (Carbethoxy-methylene)triphenylphosphorane (1.5 eq) was added to a solution of the corresponding aldehyde at -78 ºC. The solution was stirred for 12 h, slowly warming to room temperature. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (2x), the combined organic layers were dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel.

N-(3,3-diethoxypropyl)-4-methoxyaniline (14)



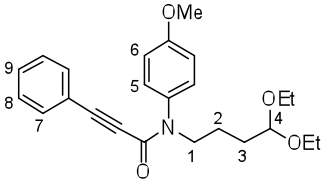
DMSO (5 mL) was added to a mixture of 4-iodoanisole (0.5 g, 2.14 mmol), CuI (0.0406 g, 0.21 mmol), L-proline (0.0493 g, 0.43 mmol) and K_2CO_3 (powdered) (0.59 g, 4.27 mmol) in a round bottom flask, and it was flushed with N_2 (3 times), followed by addition of 3,3-diethoxypropan-1-amine (0.52 mL, 3.21 mmol). The reaction mixture was degassed and stirred under N_2 atmosphere at 80ºC for 26h, diluted with water and extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel (Pet-ether:Et_2O; 0 – 15%) to afford the product as a yellow oil (**14**) (0.45 g, 83% yield); Rf 0.52 (Pet.-Ether:Diethyl ether, 1:1); λ_{max} (film) / cm^{-1} 3389, 1511, 1233, 1121, 1039, 977, 817; ^{1}H NMR (400 MHz, CD_3Cl_3) δ_H 6.78 (2H, d, J = 9.1 Hz, H^4), 6.60 (2H, d, J = 8.8 Hz, H^5), 4.63 (1H, t, J = 5.3 Hz, H^3), 3.73 (3H, s, OC$\underline{H_3}$), 3.69-3.53 (2H, m, OC$\underline{H_2}$CH$_3$), 3.50-3.42 (2H, m, OC$\underline{H_2}$CH$_3$), 3.18 (2H, t, J = 6.4 Hz, H^1), 1.95-1.82 (2H, m, H^2), 1.23 (6H, t, J = 6.8 Hz, OCH$_2$C$\underline{H_3}$); ^{13}C NMR (100 MHz, CD_3Cl_3) δ_C 152.6, 142.9, 115.3, 114.7, 102.6, 61.9, 56.2, 41.6, 33.6, 15.8; HRMS (ES^+) mass calc'd. For $C_{14}H_{23}NO_3$ 253.1678; found [$(M+H)^+$] 254.1759.

(*N*-4,4-diethoxyalkyl)-4-methoxyaniline (15)



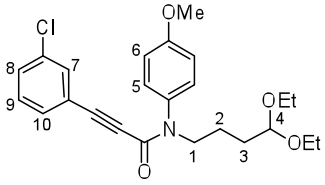
DMSO (40 mL) was added to a mixture of 4-iodoanisole (5 g, 21.36 mmol), CuI (0.405 g, 2.1 mmol), L-proline (0.493 g, 4.3 mmol) and K_2CO_3 (powdered) (5.9 g, 42.7 mmol) in a round bottom flask, and it was flushed with N_2 (3 times), followed by addition of 4,4-diethoxybutan-1-amine (5.16 g, 32.04 mmol). The reaction mixture was degassed and stirred under N_2 atmosphere at 80ºC for 26h, diluted with water and extracted with diethyl ether (3 x 25mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2:Et_2O; 0 – 15%) to afford the product as a yellow oil (**15**) (4.83 g, 85% yield); Rf 0.52 (Pet.-Ether:Diethyl ether, 1:1); λ_{max} (film) / cm^{-1} 3389, 2874, 1511, 1233, 1121, 1037, 816; ^1H NMR (400 MHz, C_6D_6) δ_H 6.90 (2H, d, J = 8.9 Hz, H^5), 6.50 (2H, d, J = 8.9 Hz, H^6), 4.47 (1H, t, J = 5.6 Hz, H^4), 3.58 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.45 (3H, s, OC$\underline{H_3}$), 3.40 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 2.92 (2H, t, J = 7.0 Hz, H^1), 1.75-1.68 (2H, m, H^2), 1.63-1.54 (2H, m, H^3), 1.19 (6H, t, J = 7.0 Hz, OCH$_2$C$\underline{H_3}$); ^{13}C NMR (100 MHz, C_6D_6) δ_C 152.8, 143.3, 115.4, 114.3, 103.0, 61.0, 55.5, 44.9, 31.7, 25.5, 15.8; HRMS (ES^+) mass calc'd. For $C_{15}H_{25}NO_3$ 267.1834; found [$(M+H)^+$] 268.1916.

_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)-3-phenylpropiolamide (16)



General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (2.0 g, 7.48 mmol) and 3-phenylprop-2-ynoic acid (1.09 g, 7.51 mmol), EDCI (1.72 g, 8.92 mmol), HOBT (101 mg, 0.75 mmol) and CH_2Cl_2 (30 mL), 16 h, chromatography on silica gel (CH_2Cl_2:Et_2O, 0-5 %) to afford compound **16** as a yellow oil (2.95 g, 95% yield); Rf 0.40 (Pet-Ether:Diethyl ether, 1:1); λ_{max} (film) / cm^{-1} 2973, 2214, 1631, 1510, 1392, 1293, 1247, 1058, 835, 757, 689; ^1H NMR (400 MHz, C_6D_6) δ_H 7.12-7.07 (2H, m, Ph), 7.03 (2H, d, J = 8.9 Hz, H^5), 6.92-6.88 (1H, m, H^9), 6.86-6.80 (2H, m, Ph), 6.71 (2H, d, J = 8.9 Hz, H^6), 4.49-4.43 (1H, m, H^4), 3.86-3.83 (2H, m, H^1), 3.54 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.37 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.32 (3H, s, OC$\underline{H_3}$), 1.79-1.67 (4H, m, H^2, H^3), 1.12 (6H, t, J = 7.0 Hz, OCH$_2$C$\underline{H_3}$); ^{13}C NMR (100 MHz, C_6D_6) δ_C 159.4, 154.1, 135.1, 132.5, 130.1, 129.7, 121.3, 114,4, 102.7, 90.4, 84.3, 61.0, 55.0, 48.4, 31.2, 23.4, 15.6; HRMS (ES^+) mass calc'd. For $C_{24}H_{29}NO_4$ 395.2097; found [$(M+Na)^+$] 418.2002.

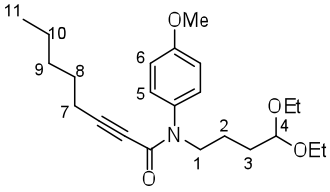
3-(3-chlorophenyl)-_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)propiolamide (17)



General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (500 mg, 1.87 mmol) and 3-chlorophenyl-propiolic acid (370.2 mg, 2.05 mmol), EDCI (553.5 mg, 2.80 mmol), HOBT (25.2 mg, 0.18 mmol) and CH_2Cl_2 (5 mL), 16 h, chromatography on silica gel (pet-ether:EtOAc, 7:3) to afford compound **17** as a yellow oil (781 mg, 97% yield); Rf 0.45 (pet.-ether/EtOAc, 6:4); λ_{max} (film) / cm^{-1} 1679, 1586, 1562, 1472, 1399, 1298, 1269, 1214, 1080, 1032, 971, 934, 901, 783, 735, 719, 679; ^1H NMR (500 MHz, C_6D_6) δ_H 7.00-6.86 (3H, m, H^5, H^7), 6.81-6.71 (2H, m, H^8, H^9), 6.63 (2H, d, J = 8.9, H^6), 6.44 (1H, t, J = 7.9 Hz, H^{10}), 4.44 (1H, t, J = 4.9, H^4), 3.79 (2H, t, J = 6.8, H^1), 3.5 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.33 (2H, qd, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.25 (3H, s, OC$\underline{H_3}$), 1.87-1.56 (4H, m, H^2, H^3),

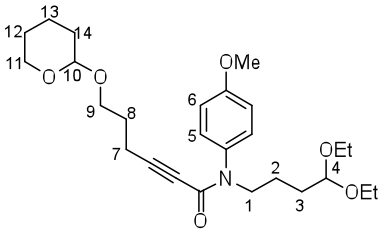
1.09 (6H, t, J = 7.0 Hz, $OCH_2C\underline{H_3}$); ^{13}C NMR (125 MHz, C_6D_6) δ_C 159.5, 153.8, 134.9, 134.3, 133.4, 130.3, 130.1, 129.8, 129.7, 123.0, 114.4, 102.7, 88.7, 85.1, 61.1, 55.0, 48.4, 31.2, 23.4, 15.6; HRMS (ES^+) mass calc'd. For $C_{24}H_{28}ClNO_4$ 429.1707; found $[(2M+NH_4)^+]$ 876.3756.

_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)oct-2-ynamide (18)



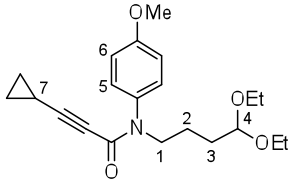
General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (300 mg, 1.12 mmol) and 2-octynoic acid (188 mg, 1.34 mmol), EDCI (257 mg, 1.34 mmol), HOBT (15 mg, 0.11 mmol) and CH_2Cl_2 (10 mL), 14 h, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) to afford compound **18** as a colourless oil (432 mg, 99% yield); Rf 0.52 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 2971, 2229, 1633, 1510, 1393, 1291, 1246, 1058, 834, 733; ^1H NMR (500 MHz, C_6D_6) δ_H 6.95 (2H, d, J = 7.2 Hz, H^5), 6,65 (2H, d, J = 7.2 Hz, H^6), 4.43 (1H, t, J = 6.4 Hz, H^4), 3.83-3.75 (2H, m, H^1), 3.50-3.38 (2H, m, $OC\underline{H_2}CH_3$), 3.37-3.21 (2H, m, $OC\underline{H_2}CH_3$), 3.25 (3H, s, $OC\underline{H_3}$), 1.81-1.62 (6H, m, H^2, H^3, H^7), 1.10 (6H, t, J = 5.6 Hz, $OCH_2C\underline{H_3}$), 1.09-0.82 (4H, m, H^8, H^9), 0.86-0.67 (2H, m, H^{10}), 0.74 (3H, t, J = 5.6 Hz, H^{11}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 159.2, 154.3, 135.6, 130.1, 114.4, 102.7, 92.8, 76.6, 61.0, 54.8, 48.4, 31.2, 30.8, 27.6, 23.4, 22.3, 18.7, 15.6, 13.9; HRMS (ES^+) mass calc'd. For $C_{23}H_{35}NO_4$ 389.2566; found $[(M+Na)^+]$ 412.2476.

_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)-6-(tetrahydro-2_H_-pyran-2-yloxy)hex-2-ynamide (19)



General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (400 mg, 1.5 mmol) and 6-(tetrahydro-2*H*-pyran-2-yloxy)hex-2-ynoic acid (382 mg, 1.8 mmol), EDCI (345 mg, 1.8 mmol), HOBT (20 mg, 0.15 mmol) and CH_2Cl_2 (12 mL), 15 h, chromatography on silica gel (CH_2Cl_2:acetone, 9:1) to afford compound **19** as a yellow oil (450 mg, 87% yield). Rf 0.40 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 2938, 1634, 151, 1247, 1032, 835, 733; ^1H NMR (500 MHz, C_6D_6) δ_H 6.94 (2H, d, J = 8.9 Hz, H^5), 6.71 (2H, d, J = 8.9 Hz, H^6), 4.48 (1H, t, J = 8.9 Hz, H^{10}), 4.45 (1H, t, J = 3.3 Hz, H^4), 3.82-3.69 (2H, m, H^1), 3.75-3.66 (1H, m, H^{11a}), 3.60-3.49 (3H, m, $OC\underline{H_2}CH_3$, H^{14a}), 3.44-3.33 (3H, m, $OC\underline{H_2}CH_3$, H^{14b}), 3.32 (3H, s, $OC\underline{H_3}$), 3.08-3.01 (1H, m, H^{11b}), 2.05-1.93 (2H, m, H^9), 1.78-1.65 (4H, m, H^2, H^3), 1.59-1.53 (2H, m, H^7), 1.44-1.22 (6H, m, H^8, H^{12}, H^{13}), 1.14 (6H, t, J = 7.05 Hz, $OCH_2C\underline{H_3}$);^{13}C NMR (125 MHz, C_6D_6) δ_C 159.3, 154.2, 135.5, 130.0, 114.4, 102.7, 98.4, 92.3, 76.7, 65.3, 61.4, 60.9, 54.9, 48.3, 31.2, 30.8, 28.3, 25.7, 23.4, 19.4, 15.7, 15.6; HRMS (ES^+) mass calc'd. For $C_{26}H_{39}NO_6$ 461.2777; found $[(M+H)^+]$ 462.2834.

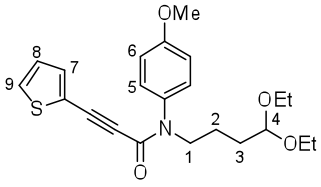
3-cyclopropyl-_N_-(4,4-diethylbutyl)-_N_-(4-methoxyphenyl)propiolamide (20)



General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (1.0 g, 4.50 mmol) and cyclopropylpropiolic acid (545 mg, 4.95 mmol), EDCI (2.44 g, 12.3 mmol), HOBT (91.2 mg, 0.68 mmol) and CH_2Cl_2 (20 mL), 20 h, chromatography on silica gel (pet-ether:EtOAc,

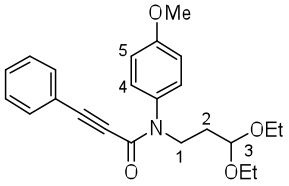
7:3) to afford compound **20** as a yellow oil (1.39 g, 86% yield); Rf 0.48 (Pet-Ether:EtOAc, 6:4); λ_{max} (film) / cm^{-1} 2973, 2343, 2226, 1630, 1511, 1443, 1395, 1292, 1248, 1170, 1125, 1059, 1032, 888, 836, 732**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 6.90 (2H, d, J = 8.8 Hz, H^5), 6.67 (2H, d, J = 8.8 Hz, H^6), 4.26-4.21 (1H, m, H^4), 3.58 (3H, s, OCH_3), 3.48-3.39 (2H, m, H^1), 3.37 (2H, dq, J = 9.2 Hz, J = 7.0 Hz, CH_2CH_3), 3.21 (2H, dq, J = 9.2 Hz, J = 7.0 Hz, OCH_2CH_3), 1.45-1.32 (4H, m, H^2, H^3), 0.92 (6H, t, J = 7.0 Hz, CH_2CH_3), 0.88-0.82 (1H, m, H^7), 0.48-0.32 (2H, m, CH_2, cycloprop.), 0.25-0.16 (2H, m, CH_2, cycloprop.); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 159.7, 155.2, 135.3, 130.3, 114.9, 103.2, 98.3, 70.9, 61.9, 56.1, 48.5, 31.4, 23.4, 15.9, 9.6, 9.5, 0.0; HRMS (ES^+) mass calc'd. For $C_{21}H_{29}NO_4$ 359.2097; found [$(M+H)^+$] 360.2170.

_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)-3-(thiophen-2-yl)propiolamide (21)



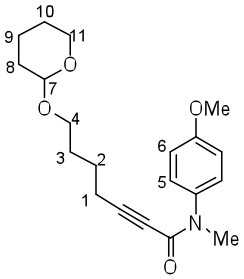
General procedure **1**, *N*-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (500 mg, 1.87 mmol) and 3-(thiophen-2-yl)propiolic acid (345.6 mg, 2.27 mmol), EDCI (435.84 mg, 2.27 mmol), HOBT (24.3 mg, 0.18 mmol) and CH_2Cl_2 (5 mL), 17 h, chromatography on silica gel (CH_2Cl_2:Et_2O, 0-5 %) to afford compound **21** as a yellow oil (714 mg, 97% yield); Rf 0.45 (Pet.-Ether:AcOEt, 6:4); λ_{max} (film) / cm^{-1} 2972, 2875, 2357, 1633, 1511, 1389, 1294, 1249, 1127, 915, 789; ^{1}H NMR (500 MHz, C_6D_6) δ_H 7.00 (2H, d, J = 8.9 Hz, H^5), 6.92 (1H, dd, J = 2.9 Hz, J = 1.0 Hz, H^9), 6.68 (2H, d, J = 8.9 Hz, H^6), 6.62 (1H, dd, J = 5.0 Hz, J = 1.0 Hz, H^7), 6.49 (1H, dd, J = 5.0 Hz, J = 2.9 Hz H^8), 4.46 (1H, t, J = 4.7 Hz, H^4), 3.85 (2H, t, J = 6.5 Hz, H^1), 3.55 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OCH_2CH_3), 3.38 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OCH_2CH_3), 3.28 (3H, s, OCH_3), 1.81-1.69 (4H, m, H^2, H^3), 1.14 (6H, t, J = 7.0 Hz, , OCH_2CH_3); ^{13}C NMR (125 MHz, C_6D_6) δ_C 159.4, 154.2, 135.1, 131.8, 130.1, 125.6, 120.5, 114,4, 102.7, 85.9, 84.4, 61.0, 54.9, 48.4, 31.2, 23.4, 15.6; HRMS (ES^+) mass cal'd. For $C_{22}H_{27}NO_4S$ 401.1661; found [$(M+H)^+$] 402.1732.

_N_-(3,3-diethoxypropyl)-_N_-(4-methoxyphenyl)-3-phenylpropiolamide (22)



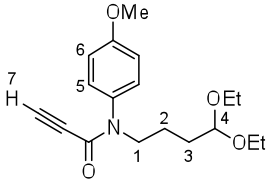
General procedure **1**, *N*-(3,3-diethoxypropyl)-4-methoxyaniline **14** (0.1 g, 0.39 mmol) and 3-phenylprop-2-ynoic acid (0.058 g, 0.39 mmol), EDCI (90.4 mg, 0.47 mmol), HOBT (5.26 mg, 0.039 mmol) and CH_2Cl_2 (5 mL), 15 h, chromatography on silica gel (CH_2Cl_2:acetone, 0-5 %) to afford compound **22** as a yellow oil (0.15 g, 99% yield); Rf 0.45 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 2974, 2215, 1632, 1510, 1247, 1054, 835, 757; ^{1}H NMR (400 MHz, C_6D_6) δ_H 7.06 (2H, d, J = 8.9.Hz, H^4), 7.00 (2H, d, J = 8.9 Hz, H^5), 6.81-6.75 (5H, m, Ph), 4.58 (1H, t, J = 4.6 Hz, H^3), 3.99-3.83 (2H, m, H^1), 3.57-3.46 (2H, m, OCH_2CH_3), 3.38-3.29 (2H, m, OCH_2CH_3), 3.22 (3H, s, OCH_3), 2.02-1.97 (2H, m, H^2), 1.12 (6H, t, J = 6.9 Hz, OCH_2CH_3); ^{13}C NMR (100 MHz, C_6D_6) δ_C 159.4, 154.1, 135.3, 132.6, 130.2, 129.6, 121.4, 114.4, 101.5, 90.3, 84.3, 61.3, 54.9, 45.3, 32.4, 15.6; HRMS (ES^+) mass calc'd. For $C_{23}H_{27}NO_4$ 381.1940; found [$(M+H)^+$] 382.1994.

_N_-(4-methoxyphenyl)-_N_-methyl-7-(tetrahydro-2_H_-pyran-2-yloxy)hept-2-ynamide (23)



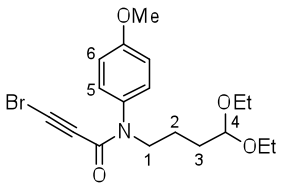
General procedure **1**, 4-Methoxy-_N_-methylaniline (330 mg, 2.40 mmol) and 7-(tetrahydro-2_H_-pyran-2-yloxy)hept-2-ynoic acid (700 mg, 3.09 mmol), EDCI (552 mg, 2.98 mmol), HOBT (33 mg, 0.24 mmol) and CH_2Cl_2 (15 mL), 17 h, chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **23** as a yellow oil (500 mg, 60% yield). Rf 0.42 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 2940, 2224, 1634, 1510, 1368, 1246, 1031, 836, 733; ^1H NMR (400 MHz, C_6D_6) δ_H 7.16 (2H, d, J = 8.9 Hz, H^5), 6.88 (2H, d, J = 8.9 Hz, H^6), 4.51 (1H, t, J = 3.6 Hz, H^7), 3.83-3.77 (4H, m, OC$\underline{H_3}$, H^{11a}), 3.62-3.54 (1H, m, H^{11b}), 3.50-3.44 (1H, m, H^{4a}), 3.27-3.20 (4H, m, NC$\underline{H_3}$, H^{4b}), 2.13 (2H, t, J = 6.7 Hz, H^1), 1.87-1.63 (2H, m, H^8), 1.61-1.46 (4H, m, H^{10}, H^9), 1.61-1.36 (4H, m, H^3, H^2); ^{13}C NMR (100 MHz, C_6D_6) δ_C 159.3, 154.3, 137.2, 129.1, 114.5, 98.7, 92.6, 76.8, 66.8, 61.8, 55.1, 36.3, 31.2, 28.9, 26.1, 25.0, 19.8, 18.7; HRMS (ES+) mass calc'd. For $C_{20}H_{27}NO_4$ 345.1940; found $[(M+Na)^+]$ 368.1822.

_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)propiolamide (24)



General procedure **1**, _N_-(4,4-diethoxybutyl)-4-methoxyaniline (**15**) (1.00 g, 3.74 mmol) and propiolic acid (288.18 mg, 4.11 mmol), EDCI (860.23 mg, 4.48 mmol), HOBT (50.50 mg, 0.374 mmol) and CH_2Cl_2 (50 mL), 15 h, chromatography on silica gel (CH_2Cl_2:Et_2O, 0-5 %) to afford compound **24** as a yellow oil (1.19 g, 79% yield); Rf 0.52 (Pet-Ether:Diethyl ether, 1:1); λ_{max} (film) / cm^{-1} 2974, 2104, 1634, 1510, 1395, 1247, 1031, 835, 736; ^1H NMR (400 MHz, C_6D_6) δ_H 6.90 (2H, d, J = 8.9 Hz, H^5), 6.65 (2H, d, J = 8.9 Hz, H^6), 4.43 (1H, t, J = 4.9 Hz, H^4), 3.73 (2H, t, J = 6.9 Hz, H^1), 3.52 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.35 (2H, dq, J = 9.3 Hz, J = 7.0 Hz, OC$\underline{H_2}$CH$_3$), 3.25 (3H, s, OC$\underline{H_3}$), 2.21 (1H, s, H^7), 1.70-1.65 (4H, m, H^2, H^3), 1.12 (6H, t, J = 7.0 Hz, OCH$_2$C$\underline{H_3}$); ^{13}C NMR (100 MHz, C_6D_6) δ_C 159.3, 152.8, 134.3, 129.7, 114,2, 102.7, 78.7, 77.3, 60.8, 54.6, 48.3, 30.8, 22.9, 15.3; HRMS (ES^+) mass calc'd. For $C_{18}H_{25}NO_4$ 319.1784; found $[(M+Na)^+]$ 342.1676.

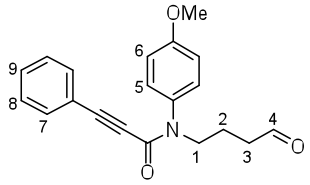
3-bromo-_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)propiolamide (9)



_N_-(4,4-diethoxybutyl)-_N_-(4-methoxyphenyl)propiolamide (**24**) (400 mg, 1.25 mmol) was placed in a flask and dissolved in dry acetone (30 mL). Silver nitrate was added (106.16 mg, 0.62 mmol) to the solution at room temperature. After 5 min the solution was cooled to 0 ºC and NBS (232.51 mg, 1.31 mmol) was added portion-wise over 30 min. The mixture was stirred until completion. The solids were filtered off on a pad of celite that was washed several times with acetone. After removal of the acetone under reduced pressure the residue was purified by column chromatography on silica gel (CH_2Cl_2:Et_2O, 0-10 %) to afford compound **9** as a colourless oil (420.7 mg, 86% yield); Rf 0.42 (Pet.-Ether:AcOEt, 6:4); λ_{max} (film) / cm^{-1} 2974, 2104, 1717, 1636, 1511, 1396, 1292, 1127, 1033, 836, 728; ^1H NMR (500 MHz, C_6D_6) δ_H 6.80 (2H, d, J = 8.9 Hz, H^5), 6.57 (2H, d, J = 8.9 Hz, H^6), 4.39 (1H, t, J = 5.2 Hz, H^4), 3.67 (2H, t, J

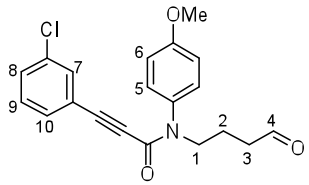
= 6.9 Hz, H^1), 3.48 (2H, dq, *J* = 9.3 Hz, *J* = 7.0 Hz, OC*H*$_2$CH$_3$), 3.31 (2H, dq, *J* = 9.3 Hz, *J* = 7.0 Hz, OC*H*$_2$CH$_3$), 3.16 (3H, s, OC*H*$_3$), 1.68-1.58 (4H, m, H^2, H^3), 1.12 (6H, t, *J* = 7.0 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, C_6D_6) δ_C 159.4, 152.6, 134.3, 129.8, 114,2, 102.4, 75.7, 61.8, 55.1, 54.8, 48.5, 31.1, 23.1, 15.6; HRMS (ES$^+$) mass calc'd. For $C_{18}H_{24}BrNO_4$ 397.0889; found [(M+NH$_4$)$^+$] 415.1230.

_N_-(4-methoxyphenyl)-_N_-(4-oxobutyl)-3-phenylpropiolamide (1a)



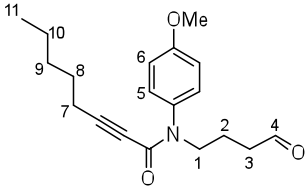
General procedure **2**, *N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)-3-phenylpropiolamide (16) (1 g, 2.53 mmol), 4 h, chromatography on silica gel (CH$_2$Cl$_2$:Et$_2$O, 0-10%) to afford compound **1a** as a colourless oil (817 mg, 99% yield); Rf 0.40 (CH$_2$Cl$_2$:acetone, 96:4) λ_{max} (film) / cm^{-1} 2936, 2214, 1721, 1629, 1509, 1391, 1247, 1028, 835, 757, 689; ^{1}H NMR (400 MHz, C_6D_6) δ_H 9.33 (1H, s, H^4), 7.16-7.12 (2H, m, Ph), 6.97 (2H, d, *J* = 8.9 Hz, H^5), 6.92-6.77 (3H, m, Ph), 6.72 (2H, d, *J* = 8.9 Hz, H^6), 3.67 (2H, t, *J* = 7.3 Hz, H^1), 3.29 (3H, s, OC*H*$_3$), 1.94 (2H, t, *J* = 7.3 Hz, H^3), 1.64 (2H, dt, *J* = 7.3 Hz, *J* = 7.3 Hz, H^2); ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.9, 159.7, 154.5, 135.2, 132,7, 130,2, 129.9, 128.6, 121.4, 114.6, 90.8, 84.3, 55.2, 48.0, 41.1, 20.7; HRMS (ES$^+$) mass calc'd. For $C_{20}H_{19}NO_3$ 321.1365; found [(M+H)$^+$] 322.1449.

3-(3-chlorophenyl)-_N_-(4-methoxyphenyl)-_N_-(4-oxobutyl)propiolamide (1b)



General procedure **2**, 3-(3-chlorophenyl)-*N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)propiolamide (**17**) (790 mg, 1.84 mmol), 15 h, chromatography on silica gel (pet.-ether/EtOAc, 7:3) to afford compound **1b** as yellow oil (568 mg, 87%). Rf 0.29 (pet.-ether/EtOAc, 6:4); λ_{max} (film) / cm^{-1} 2974, 2930, 2219, 1634, 1591, 1562, 1474, 1442, 1392, 1295, 1248, 1169, 1124, 1058, 1032, 996, 956, 882, 835, 786, 729, 694, 680; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 9.70 (1H, s, H^4), 7.21-7.25 (1H, m, H^8), 7.19 (1H, s, H^7), 7.16 (2H, d, *J* = 9.0 Hz, H^5), 7.11 (1H, dd, *J* = 8.3 Hz, *J* = 8.0 Hz, H^9), 7.09-6.92 (1H, m, H^{10}), 6.90 (2H, d, *J* = 9.0 Hz, H^6), 3.79 (3H, s, OC*H*$_3$), 3.72-3.76 (2H, m, H^1), 2.47 (2H, dt, *J* = 7.3 Hz, *J* = 1.0 Hz, H^3), 1.86-1.80 (2H, m, H^2); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 201.5, 159.9, 154.8, 134.6, 134.5, 132.6, 130.8, 130.6, 130.0, 128.5, 122.6, 114.9, 90.0, 83.8, 56.0, 48.2, 41.4, 20.5; HRMS (ES$^+$) mass calc'd. For $C_{20}H_{18}ClNO_3$ 355.0975; found [(M+H)$^+$] 356.1047.

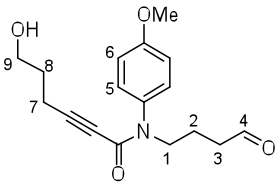
_N_-(4-methoxyphenyl)-_N_-(4-oxobutyl)oct-2-ynamide (1c)



General procedure **2**, *N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)oct-2-ynamide (**18**) (300 mg, 0.77 mmol), 16 h, chromatography by (CH$_2$Cl$_2$:acetone, 95:5) to afford compound **1c** as a colourless oil (0.240 g, 99% yield). Rf 0.55 (CH$_2$Cl$_2$:acetone, 95:5); λ_{max} (film) / cm^{-1} 2932, 2230, 1721, 1629, 1510, 1393, 1292, 1245, 1031, 834, 733; ^{1}H NMR (500 MHz, C_6D_6) δ_H 9.24 (1H, s, CHO), 6.89 (2H, d, *J* = 6.8 Hz, H^5), 6.65 (2H, d, *J* = 6.8 Hz, H^6), 3.57 (2H, t, *J* = 5.6 Hz, H^1), 3.25 (3H, s, OC*H*$_3$), 1.85 (2H, t, *J* = 5.6 Hz, H^3), 1.77-1.62 (2H, m, H^2), 1.60-1.56 (2H, m, H^7), 1.10-0.87 (4H, m, H^9, H^8), 0.88-0.72 (2H, m, H^{10}), 0.75 (2H, t, *J* = 5.6 Hz, H^{11}); ^{13}C NMR (125 MHz, C_6D_6) δ_C

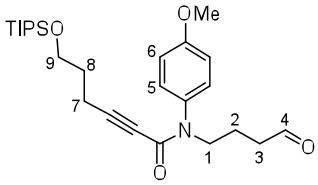
199.6, 159.1, 154.1, 135.1, 129.7, 114.2, 92.9, 76.2, 54.6, 47.6, 40.7, 30.5, 27.3, 22.1, 20.2, 18.5, 13.7; HRMS (ES^+) mass calc'd. For $C_{19}H_{25}NO_3$ 315.1834; found 316.1904.

6-hydroxy-*N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)hex-2-ynamide (25)



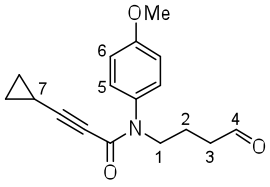
General procedure **2**, *N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)-6-(tetrahydro-2*H*-pyran-2yloxy)-hex-2-ynamide (**19**) (400 g, 0.87 mmol), 36 h, chromatography by (CH_2Cl_2:acetone, 6:4) to afford compound **25** as a colourless oil (0.210 g, 80% yield). Rf 0.33 (CH_2Cl_2:acetone, 6:4); λ_{max} (film) / cm^{-1} 3413, 2938, 2231, 1720, 1619, 1511, 1403, 1248, 1034, 837, 736; ^1H NMR (500 MHz, C_6D_6) δ_H 9.32 (1H, s, CHO), 6.93 (2H, d, J = 8.9 Hz, H^5), 6.72 (2H, d, J = 8.9 Hz, H^6), 3.59 (2H, t, J = 7.1 Hz, H^1), 3.33 (3H, s, OC$\underline{H_3}$), 3.17 (2H, t, J = 6.1 Hz, H^9), 3.09 (1H, s, O$\underline{H}$), 1.98-1.76 (4H, m, H^3, H^7), 1.65 (2H, dt, J = 7.1 Hz, J = 7.1 Hz, H^2), 1.22 (2H, tt, J = 6.8 Hz, H^8); ^{13}C NMR (125 MHz, C_6D_6) δ_C 200.0, 159.5, 154.6, 135.1, 129.9, 114.5, 93.4, 76.3, 60.6, 55.0, 47.8, 40.9, 30.7, 20.4, 15.2; HRMS (ES^+) mass calc'd. For $C_{17}H_{21}NO_4$ 303.1471; found [$(M+H)^+$] 304.1541.

***N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)-6-(triisopropylsilyloxy)hex-2-ynamide (1d)**



Triethylamine (171 µL, 1.23 mmol) and DMAP (6 mg, 0.049 mmol) were added to a solution of 6-hydroxy-*N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)hex-2-ynamide (**25**) (150 mg, 0.49 mmol) in CH_2Cl_2 (6 mL), followed by TIPSCl solution (126 µL, 0.59 mmol). The resulting mixture was stirred at room temperature for 48 h and quenched by aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **1d** as a colourless oil (170 mg, 75% yield). Rf 0.6 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 3390, 2962, 2256, 1633, 1394, 1249, 994, 733; ^1H NMR (500 MHz, C_6D_6) δ_H 9.29 (1H, s, CHO), 6.95 (2H, d, J = 8.9 Hz, H^5), 6.70 (2H, d, J = 8.9 Hz, H^6), 3.59 (2H, t, J = 7.1 Hz, H^1), 3.38 (2H, t, J = 5.8 Hz, H^9), 3.30 (3H, S, OC$\underline{H_3}$), 2.03 (2H, t, J = 7.1 Hz, H^3), 1.89 (2H, t, J = 5.8 Hz, H^7), 1.59 (2H, dt, J = 7.1 Hz, J = 7.1 Hz, H^2), 1.32 (2H, dt, J = 5.8 Hz, J = 5.8 Hz, H^8), 1.09-0.95 (21H, m, TIPS); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.8, 159.3, 154.3, 135.3, 129.9, 114.4, 92.9, 76.4, 61.6, 54.9, 47.8, 40.9, 31.4, 20.5, 18.2, 15.3, 12.2; HRMS (ES^+) mass calc'd. For $C_{26}H_{41}NO_4Si$ 459.2805; found [$(M+H)^+$] 460.2864.

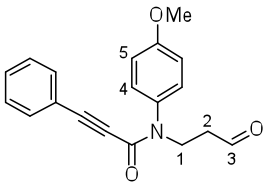
3-cyclopropyl-*N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)propiolamide (1e)



General procedure **2**, 3-cyclopropyl-*N*-(4,4-diethylbutyl)-*N*-(4-methoxyphenyl)propiolamide (**20**) (1 g, 2.78 mmol), 5 h, chromatography on silica gel (petrol ether/EtOAc, 7:3) to afford compound **1e** as yellow oil (732 mg, 92%). Rf 0.18 (pet.-ether/EtOAc, 7:3); λ_{max} (film) / cm^{-1} 2938, 2838, 2222, 1720, 1626, 1510, 1442, 1395, 1292, 1247, 1180, 1107, 1059, 1030, 938, 890, 836, 814, 732; ^1H NMR (500 MHz, C_6D_6) δ_H 9.26 (1H, s, H^4), 6.85 (2H, d, J = 8.9 Hz, H^5), 6.63 (2H, d, J = 8.9 Hz, H^6), 3.55 (2H, t, J = 7.2 Hz, H^1), 3.24 (3H, s, OC$\underline{H_3}$), 1.86

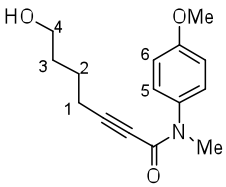
(2H, t, J = 7.2 Hz, H^3), 1.67 (2 H, tt, J = 7.2 Hz, J = 7.2 Hz, H^2), 0.68-0.64 (1H, m, H^7), 0.29-0.23 (2H, m, C$\underline{H_2}$, cycloprop.), 0.16-0.10 (2H, m, C$\underline{H_2}$, cycloprop.); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.8, 159.3, 154.3, 135.3, 129.9, 114.3, 96.8, 71.5, 54.9, 47.7, 40.9, 20.5, 8.8, 0.00; HRMS (ES$^+$) mass calc'd. For $C_{17}H_{19}NO_3$ 285.1365; found [(M+H)$^+$] 286.1432.

_N_-(4-methoxyphenyl)-N-(3-oxopropyl)-3-phenylpropiolamide (1g)



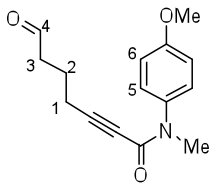
General procedure **2**, *N*-(3,3-diethoxypropyl)-*N*-(4-methoxyphenyl)-3-phenylpropiolamide (**22**) (0.35 g, 092 mmol), 4 h, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) to afford compound **1g** as a colourless oil (0.28 g, 91% yield); Rf 0.40 (CH_2Cl_2:acetone, 96:4) λ_{max} (film) / cm^{-1} 2962, 2214, 1720, 1627, 1509, 1392, 1293, 1246, 1027, 835, 757; ^{1}H NMR (400 MHz, C_6D_6) δ_H 9.33 (1H, s, H^3), 7.03 (2H, d, J = 8.8 Hz, H^4), 6.88 (2H, d, J = 8.8 Hz, H^5), 6.81-6.62 (5H, m, Ph), 3.88 (2H, t, J = 7.0 Hz, H^1), 3.22 (3H, s, OC$\underline{H_3}$), 2.17 (2H, m, H^2); ^{13}C NMR (100 MHz, C_6D_6) δ_C 198.9, 159.6, 154.2, 134.7, 132.6, 130.1, 129.8, 121.1, 114.5, 90.8, 83.8, 54.9, 42.9, 42.3; HRMS (ES$^+$) mass calc'd. For $C_{19}H_{17}NO_3$ 307.1208; found [(M+H)$^+$] 308.1287.

7-hydroxy-_N_-(4-methoxyphenyl)-_N_-methylhept-2-ynamide (26)



*p*TsOH (12 mg, 0.063 mmol) was added to a solution of *N*-(4-methoxyphenyl)-*N*-methyl-7-(tetrahydro-2*H*-pyran-2-yloxy)hept-2-ynamide (**23**) (400 mg, 1.16 mmol) in MeOH (8 mL) at room temperature. The resulting mixture was stirred for 6 h, quenched with aqueous $NaHCO_3$solution and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2:acetone, 75:25) to afford compound **26** as a colourless oil (290 mg, 96% yield). Rf 0.45 (CH_2Cl_2:acetone, 75:25); λ_{max} (film) / cm^{-1} 3413, 2937, 2226, 1619, 1510, 1375, 1246, 1169, 1030, 836, 733; ^{1}H NMR (400 MHz, C_6D_6) δ_H 6.90 (2H, d, J = 8.9 Hz, H^5), 6.75 (2H, d, J = 8.9 Hz, H^6), 3.34 (3H, s, OC$\underline{H_3}$), 3.31 (2H, t, J = 5.2 Hz, H^4), 3.13 (3H, s, NC$\underline{H_3}$), 1.81 (2H, t, J = 6.4 Hz, H^1), 1.25-1.12 (4H, m, H^2, H^3); ^{13}C NMR (100 MHz, C_6D_6) δ_C 159.3, 154.5, 137.1, 129.1, 114.5, 93.2, 76.7, 62.0, 55.1, 36.3, 31.9, 24.4, 18.7; HRMS (ES$^+$) mass calc'd. For $C_{15}H_{19}NO_3$ 261.1365; found [(M+H)$^+$] 262.1436.

_N_-(4-methoxyphenyl)-_N_-methyl-7-oxohept-2-ynamide (5)

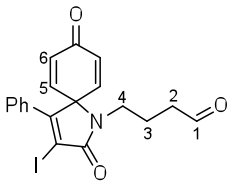


Dess Martin Peridinone (DMP) (424 mg, 1.15 mmol) was added to a solution of 7-hydroxy-*N*-(4-methoxyphenyl)-*N*-methylhept-2 ynamide (**26**) (255 mg, 0.98 mmol) in CH_2Cl_2 (12 ml) at 0 ºC. The reaction mixture was allowed warm up to room temperature over a period of 1 h and quenched with aqueous $NaHCO_3$ solution. It was extracted with CH_2Cl_2 (3 x 15 ml), dried over $MgSO_4$, concentrated in vacuo and purified by flash chromatography on silica gel (CH_2Cl_2:acetone, 9:1) to afford compound **5** as a colourless oil (250 mg, 99% yield). Rf 0.63 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 2940, 2225, 1720, 1629, 1509, 1368, 1245, 1155, 1029, 836, 733; ^{1}H NMR (400 MHz, C_6D_6) δ_H 9.17 (1H, s, CHO), 6.85

(2H, d, J = 8.8 Hz, H^5), 6.66 (2H, d, J = 8.8 Hz, H^6), 3.34 (3H, s, OC$\underline{H_3}$), 3.12 (3H, s, NC$\underline{H_3}$), 1.67 (2H, t, J = 6.7 Hz, H^3), 1.58 (2H, t, J = 7.6 Hz, H^1), 1.10 (2H, tt, J = 7.6 Hz, J = 6.7 Hz, H^2); ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.9, 159.3, 154.0, 137.0, 129.1, 114.5, 91.4, 77.3, 55.1, 42.2, 36.3, 20.3, 18.0; HRMS (ES^+) mass calc'd. For $C_{15}H_{17}NO_3$ 259.1208; found [$(M+H)^+$] 260.1280.

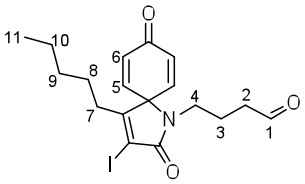
Even though the ECED process does not require the isolation of the iodo-cyclohexadienone, we have included the full data for their characterization. This data was obtained from a separate experiment.

4-(3-iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (2a)



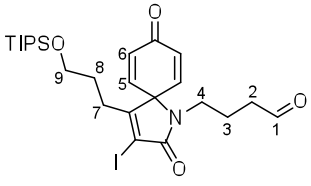
Method A: *N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)-3-phenylprop-2-ynamide (**1a**) (100 mg, 0.311 mmol), CH_2Cl_2 (7 mL), ICl (622 µL), 30 min, chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **2a** as a colourless oil (100 mg, 75% yield); Rf 0.42 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 3050, 1666, 1694, 1389, 1060, 873, 723; ^{1}H NMR (400 MHz, C_6D_6) δ_H 9.33 (1H, s, CHO), 7.15-7.00 (5H, m, $\underline{Ph}$), 6.02 (2H, d, J = 10.1 Hz, H^5), 5.53 (2H, d, J = 10.1 Hz, H^6), 3.00 (2H, t, J = 7.10 Hz, H^4), 1.87 (2H, t, J = 7.1 Hz, H^2), 1.59 (2H, dt, J = 7.10 Hz, J = 7.10 Hz, H^3); ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.9, 183.3, 167.7, 158.6, 144.1, 133.1, 132.9, 130.2, 128.9, 128.3, 128.2, 127.9, 99.5, 70.9, 41.6, 41.4, 22.8; HRMS (ES^+) mass calc'd. For $C_{19}H_{16}INO_3$ 433.0175; found [$(M+H)^+$] 434.0265.

4-(3-iodo-2,8-dioxo-4-pentyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (2c)



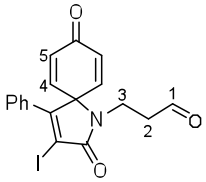
Method A: *N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)oct-2-ynamide (**1c**) (100 mg, 0.32 mmol), CH_2Cl_2 (10 mL), ICl (640 µL), 30 min, chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **2c** as a colourless oil (110 mg, 80% yield). Rf 0.40 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 2929, 1664, 1388, 1059, 858, 732; ^{1}H NMR (500 MHz, C_6D_6) δ_H 9.25 (1H, s, CHO), 6.07 (2H, d, J = 8.0 Hz, H^5), 5.35 (2H, d, J = 8.4 Hz, H^6), 2.89 (2H, t, J = 5.6 Hz, H^4), 1.89-1.77 (4H, m, H^2, H^3), 1.52-1.47 (2H, m, H^{10}), 1.28-1.21 (2H, m, H^7), 1.17-1.11 (2H, m, H^8), 1.07-1.01 (2H, m, H^9), 0.82 (3H, t, J = 5.6 Hz, H^{11}) ;^{13}C NMR (125 MHz, C_6D_6) δ_C 199.7, 183.3, 167.5, 159.7, 144.5, 132.6, 97.2, 70.6, 41.2, 40.9, 31.8, 29.2, 27.9, 22.5, 22.3, 13.9; HRMS (ES^+) mass calc'd. For $C_{18}H_{22}IN0_3$ 427.0644; found [$(M+H)^+$] 428.0722.

4-(3-iodo-2,8-dioxo-4-(3-((triisopropylsilyl)oxy)propyl)-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (2d)



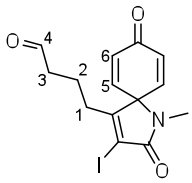
Method A: *N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)-6 (triisopropylsilyloxy)-hex-2-ynamide (**1d**) (40 mg, 0.087 mmol), CH_2Cl_2 (2 mL), ICl (170 µL), chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **2d** as a colourless oil (39 mg, 78% yield). Rf 0.45 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1}, ^{1}H NMR (400 MHz, C_6D_6) δ_H (NA),^{13}C NMR (100 MHz, C_6D_6) δ_C (NA) ; HRMS (ES^+) mass calc'd. For $C_{25}H_{38}INO_4Si$ 571.1615; found [$(M+H)^+$] 572.1686.

4-(3-iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (2g)



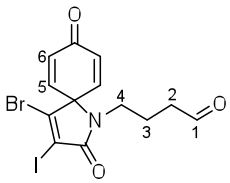
Method A: *N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)-3-phenylprop-2-ynamide (**1g**) (20 mg, 0.065 mmol), CH_2Cl_2 (3 mL), ICl (65 µL), 30 min, chromatography on silica gel (CH_2Cl_2:acetone, 95:5) to afford compound **2g** as a colourless oil (0.025 g, 95% yield); Rf 0.40 (CH_2Cl_2:acetone, 95:5); λ_{max} (film) / cm^{-1} 2971, 1693, 1389, 1059, 876, 724; ^1H NMR (400 MHz, CD_3Cl_3) δ_H 9.70 (1H, s, H^1), 7.15-7.39-7.24 (5H, m, Ph), 6.50 (2H, d, J = 10.1 Hz, H^4), 6.39 (2H, d, J = 10.1 Hz, H^5), 3.62 (2H, t, J = 7.0 Hz, H^3), 2.79 (2H, t, J = 7.1 Hz, H^2), ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.3, 182.1, 165.3, 155.2, 140.1, 132.3, 130.1, 128.2, 128.1, 127.3, 127.0, 125.9, 98.1, 70.3, 43.6, 40.4; HRMS (ES^+) mass calc'd. For $C_{18}H_{14}INO_3$ 419.0018; found [$(M+H)^+$] 420.0097.

4-(3-iodo-1-methyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-4-yl)butanal (27)



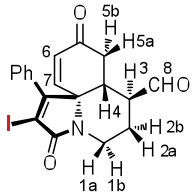
Method A: *N*-(4-methoxyphenyl)-*N*-methyl-7-oxohept-2-ynamide (**5**) (50 mg, 0.193 mmol), CH_2Cl_2 (3 mL), ICl (390 µL), chromatography on silica gel (CH_2Cl_2:acetone, 9:1) to afford compound **27** as a colourless oil (0.065 g, 91% yield). Rf 0.42 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 2956, 2300, 1690, 1367, 1265, 1063, 1005, 856, 733; ^1H NMR (500 MHz, C_6D_6) δ_H 9.19 (1H, s, CHO), 6.06 (2H, d, J = 10.1 Hz, H^5), 5.06 (2H, d, J = 10.1 Hz, H^6), 2.40 (3H, s, NCH_3), 1.70-1.62 (2H, m, H^3), 1.59 (2H, t, J = 7.2 Hz, H^1), 1.39-1.34 (2H, m, H^2); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.1, 183.0, 166.6, 158.6, 144.0, 133.0, 98.2, 69.9, 42.9, 28.3, 26.3, 20.6; HRMS (ES^+) mass calc'd. For $C_{14}H_{14}INO_3$ 371.0018; found [$(M+H)^+$] 372.0087.

4-(4-bromo-3-iodo-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (28)



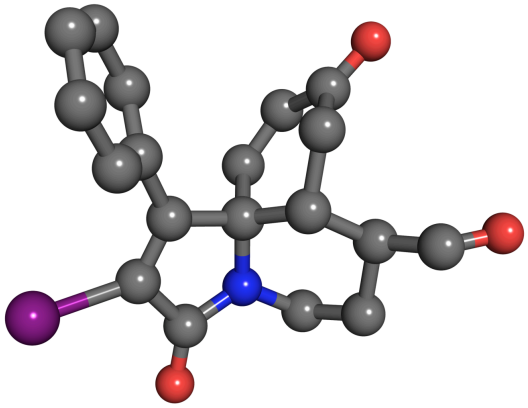
Method B: 3-bromo-*N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl) propiolamide (**9**) (150 mg, 0.376 mmol), CH_2Cl_2 (20 mL), ICl (753 µL), 30 min, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) to afford compound **28** colourless oil (160 mg, 97% yield); Rf 0.30 (CH_2Cl_2:MeOH, 95:5); λ_{max} (film) / cm^{-1} 2944, 2726, 1707, 1510, 1669, 1632, 1388, 1141, 1061, 870, 745; ^1H NMR (500 MHz, C_6D_6) δ_H 9.19 (1H, CHO), 6.08 (2H, d, J = 10.1 Hz, H^5), 5.08 (2H, d, J = 10.1 Hz, H^6), 2.89 (2H, t, J = 7.0 Hz, H^4), 1.98 (2H, t, J = 7.0 Hz, H^2) 1.53 (2H, dt, J = 7.0 Hz, J = 7.0 Hz, H^3); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.5, 182.9, 177.3, 164.2, 142.6, 133.6, 124.3, 69.0, 41.60, 30.7, 24.7; HRMS (ES^+) mass calc'd. For $C_{13}H_{11}BrINO_3$ 434.8967; found [$(M+H)^+$] 435.9037.

2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4a)

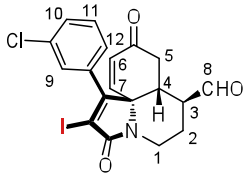


Method B: *N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)-3-phenylpropiolamide (**1a**) (500 mg, 1.55 mmol), CH_2Cl_2 (30 mL), ICl (3.1 mL) form 4-(3-Iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal **2a**; then catalyst (75.13 mg, 0.23 mmol),

benzoic acid (28.08 mg, 0.20 mmol), 48 h at 0 °C, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) gives compound **4a** as a white solid (452 mg, 90% yield); Rf 0.55 (CH_2Cl_2:MeOH, 95:5); MP: 232-234 ºC; λ_{max} (film) / cm^{-1} 3056, 2920, 2729, 1624, 1679, 1399, 1298, 1031, 733; ^1H NMR (500 MHz, C_6D_6) δ_H 8.80 (1H, d, *J* = 1.6 Hz, CHO), 6.99-6.94 (3H, m, Ph), 6.86-6.83 (2H, m, Ph), 5.85 (1H, d, *J* = 10.1 Hz, H^7), 5.12 (1H, dd, *J* = 10.1 Hz, *J* = 1.8 Hz, H^6), 4.19 (1H, ddd, *J* = 13.2 Hz, *J* = 4.8 Hz, *J* = 1.9 Hz, H^{1b}), 2.13 (1H, app. dt, *J* = 13.2 Hz, *J* = 2.9 Hz, H^{1a}), 2.08-2.00 (2H, m, H^{5a},H^4), 1.75 (1H, ddt, *J* = 12.9 Hz, *J* = 3.7 Hz, *J* = 1.5 Hz, H^3), 1.65 (1H, dd, *J* = 17.3 Hz, *J* = 13.2 Hz, H^{5b}), 0.95 (1H, app. dq, *J* = 13.1 Hz, *J* = 3.1 Hz, H^{2b}), 0.60 (1H, app. dq, *J* = 12.3 Hz, *J* = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.7, 194.6, 165.1, 163.0, 144.6, 135.3, 134.4, 130.2, 129.6, 128.9, 100.6, 69.1, 49.7, 39.5, 38.9, 37.5, 25.9; HRMS (ES^+) mass calc'd. For $C_{19}H_{16}INO_3$ 433.0175; found [$(M+H)^+$] 434.0273. $[\alpha]_D^{25}$ = + 168.00° (C = 0.67 mg/ml), $CHCl_3$ for 92% ee. HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 mL/min, retention time: major 22.78 min, minor enantiomer 25.67 min. CCDC number: pending. CIF file included.



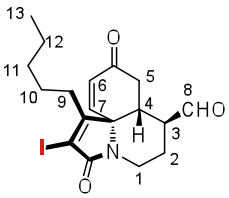
1-(3-chlorophenyl)-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4b)



Method B: 3-(3-chlorophenyl)-*N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)propiolamide (**17**) (100 mg, 0.23 mmol), CH_2Cl_2 (15 mL), ICl (465 µL) form 4-(3-Iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal; then catalyst (15 mg, 0.046 mmol), benzoic acid (5.61 mg, 0.046 mmol), CH_2Cl_2 (40 mL), 48 h at 0°C, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) gives aldehyde **4b** as a white solid (85 mg, 80%). MP: 188-190 ºC. Rf 0.12 (pet.-ether/EtOAc 6:4); λ_{max} (film) / cm^{-1} 2921, 1682, 1586, 1562, 1472, 1451, 1400, 1299, 1270, 1214, 1080, 1032, 934, 901, 782, 735, 719, 678; ^1H NMR (400 MHz, C_6D_6) δ_H 8.90 (1H, d, *J* = 1.6 Hz, CHO), 7.17 (1H, t, *J* = 1.6 Hz, H^9), 7.10 (1H, ddd, *J* = 8.0 Hz, *J* = 2.3 Hz, *J* = 1.2 Hz , H^{10}), 6.82 (1H, dd, *J* = 7.9 Hz, *J* = 7.8 Hz, H^{11}), 6.76 (1H, dt, *J* = 7.8 Hz, *J* = 1.2 Hz, H^{12}), 5.95 (1H, d, *J* = 10.0 Hz, H^7), 5.16 (1H, dd, *J* = 10.0 Hz, *J* = 2.0 Hz, H^6), 4.32 (1H, ddd, *J* = 13.4 Hz, *J* = 4.7 Hz, *J* = 1.9 Hz, H^{1b}), 2.24 (1H, app. dt, 13.1 Hz, *J* = 3.1 Hz, H^{1a}), 2.20 (1H, app. d, *J* = 17.5 Hz, H^{5a}), 2.14-2.08 (1H, m, H^4), 1.87 (1H, ddt, *J* = 12.2 Hz, *J* = 3.8 Hz, *J* = 1.9 Hz, H^3), 1.78 (1H, dd, *J* = 17.5 Hz, *J* = 5.3 Hz, H^{5b}), 1.09 (1H, app. dq, *J* = 13.1 Hz, *J* = 3.1 Hz, H^{2b}), 0.76 (1H, app. dq, *J* = 12.9 Hz, *J* = 4.7 Hz, H^{2a}); ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.6, 194.0, 164.3, 160.7, 144.2, 136.7, 135.2, 134.1, 130.0, 130.7, 128.3, 126.3, 77.9, 68.8,

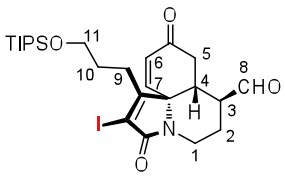
49.2, 39.0, 38.5, 37.1, 25.6; HRMS (ES^+) mass calc'd. For $C_{19}H_{15}ClINO_3$ 466.9785; found $[(M+H)^+]$ 467.9776. $[\alpha]_D^{25}$ = - 113.20° (C = 1.27 mg/ml), $CHCl_3$ for 92% ee.

2-iodo-3,9-dioxo-1-pentyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4c)



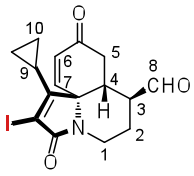
Method A: 4-(3-Iodo-2,8-dioxo-4-pentyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (**2c**) (10 mg, 0.023 mmol), catalyst (1.49 mg, 0.0046 mmol), benzoic acid (0.561 mg, 0.046 mmol), 12 h at -20 ºC, chromatography on silica gel (CH_2Cl_2:acetone, 9:1) gives ketone **4c** as a colourless oil (9 mg, 90% yield). Rf 0.48 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 2928, 1676, 1399, 1031, 746; ^1H NMR (500 MHz, C_6D_6) δ_H 8.7 (1H, d, *J* = 1.7 Hz, CHO), 5.82 (1H, d, *J* = 10.2 Hz, H^7), 4.92 (1H, dd, *J* = 10.2 Hz, *J* = 2.0 Hz, H^6), 4.11 (1H, ddd, *J* = 13.3 Hz, *J* = 4.7 Hz, *J* = 1.9 Hz, H^{1b}), 2.46-2.41 (2H, m, H^{1a}, H^{5a}), 2.08-2.00 (2H, m, H^9), 1.88-1.80 (1H, m, H^4), 1.70 (1H, ddt, *J* = 11.6 Hz, *J* = 3.8 Hz, *J* = 1.7 Hz, H^3), 1.48-1.41 (1H, m, H^{5b}), 1.25-1.12 (6H, m, H^{10}, H^{12}, H^{11}), 0.92-0.79 (4H, m, H^{2b}, H^{13}), 0.45 (1H, app. dq, *J* = 12.9 Hz, *J* = 4.4 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.0, 193.9, 164.4, 163.0, 146.2, 132.7, 98.7, 67.7, 49.7, 39.2, 38.3, 36.6, 32.0, 30.9, 27.8, 25.3, 22.2, 14.0; HRMS (ES^+) mass calc'd. For $C_{18}H_{22}INO_3$ 427.0644; found $[(M+H)^+]$ 428.0708; $[\alpha]_D^{25}$ = + 130.00º (C = 1 mg/mL), $CHCl_3$ for 90% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 mL/min, retention time: major enantiomer 11.28 min, minor enantiomer 12.93 min.

2-iodo-3,9-dioxo-1-(3-((triisopropylsilyl)oxy)propyl)-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4d)



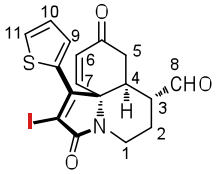
Method A: 4-(3-iodo-2,8-dioxo-4-(3-(triisopropylsilyloxy)propyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal (**2d**) (10 mg, 0.017 mmol), catalyst (1.5 mg, 0.034 mmol) and benzoic acid (0.6 mg, 0.034 mmol), 24 h at -20 ºC, chromatography on silica gel (CH_2Cl_2:acetone, 9:1) gives aldehyde **4d** as a colourless oil (8 mg, 80% yield). Rf 0.40 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 2941, 1688, 1399, 1103, 882, 747; ^1H NMR (500 MHz, C_6D_6) δ_H 8.76 (1H, d, *J* = 1.7 Hz, CHO), 5.89 (1H, d, *J* = 10.2 Hz, H^7), 4.97 (1H, dd, *J* = 10.2 Hz, *J* = 2.0 Hz, H^6), 4.14 (1H, ddd, *J* = 13.3 Hz, *J* = 4.7 Hz, *J* = 1.9 Hz, H^{1b}), 3.55 (1H, dt, *J* = 9.9 Hz, *J* = 4.8 Hz, H^{11a}), 3.45 (1H, ddd, *J* = 9.9 Hz, *J* = 8.5.1 Hz, *J* = 4.9 Hz, H^{11b}), 2.91 (1H, dd, *J* = 17.8 Hz, *J* = 5.4 Hz, H^{5b}), 2.53 (1H, dt, *J* = 13.2 Hz, *J* = 2.9 Hz, H^{5a}), 2.61-2.49 (1H, m, H^{9a}), 2.47-2.38 (1H, m, H^{9b}), 2.04 (1H, app. dt, *J* = 13.6 Hz, *J* = 3.0 Hz, H^{1a}), 2.0-1.92 (1H, m, H^4), 1.86-1.75 (1H, m, H^{10a}), 1.78-1.70 (1H, m, H^3), 1.49 (1H, ddt, *J* = 12.8 Hz, *J* = 8.5 Hz, *J* = 4.2 Hz, H^{10b}), 1.10-0.87 (21H, m, TIPS), 1.20 (1H, app. dq, *J* = 13.0 Hz, *J* = 2.9 Hz, H^{2b}), 1.20 (1H, app. dq, *J* = 13.0 Hz, *J* = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 199.0, 194.0, 164.4, 162.8, 145.8, 132.9, 99.0, 67.9, 62.8, 49.7, 39.4, 38.3, 36.6, 31.1, 27.8, 25.4, 18.2, 12.2; HRMS (ES^+) mass calc'd. For $C_{25}H_{38}INO_4Si$ 571.1615; found $[(M+H)^+]$ 572.1697; $[\alpha]_D^{25}$ = - 45.45º (C = 0.66 mg/mL), $CHCl_3$ for 89% ee; HPLC:DAICEL AD-H Chiralpak, 9:1 Hexane/isopropanol, flow 1 mL/min, retention time: major enantiomer 22.66 min, minor enantiomer 27.29 min.

1-cyclopropyl-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4e)



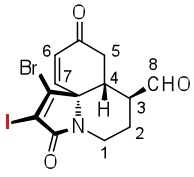
Method A: 3-cyclopropyl-*N*-(4-methoxyphenyl)-*N*-(4-oxobutyl)propiolamide (**1e**) (100 mg, 0.35 mmol), CH_2Cl_2 (15 mL), ICl (700 µL) form 4-(3-Iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal; then catalyst (22.7 mg, 0.07 mmol), benzoic acid (8.54 mg, 0.07 mmol), 48 h at 0°C, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) gives aldehyde **4e** as a white solid (108.8 mg, 78% yield); MP: 168-170 ºC; Rf 0.46 (CH_2Cl_2:MeOH, 95:5); λ_{max} (film) / cm^{-1} 2924, 2726, 1720, 1674, 1599, 1404, 1299, 1211, 1028, 955, 867, 732, 698; ^1H NMR (400 MHz, C_6D_6) δ_H 8.75 (1H, d, J = 1.6 Hz, CHO), 5.81 (1H, d, J = 10.2 Hz, H^7), 4.96 (1H, dd, J = 10.2 Hz, J = 1.9 Hz, H^6), 4.08 (1H, ddd, J = 13.4 Hz, J = 4.7 Hz, J = 1.9 Hz, H^{1b}), 2.82 (1H, dd, J = 17.8 Hz, J = 5.2 Hz, H^{5b}), 2.41 (1H, dt, J = 17.8 Hz, J = 0.9 Hz, H^{5a}), 2.00 (1H, app. dt, J = 13.4 Hz, J = 1.9 Hz, H^{1a}), 1.90-1.80 (1H, m, H^4), 1.78-1.72 (1H, ddt, J = 13.7 Hz, J = 3.6 Hz, J = 1.6 Hz, H^3) 1.32-1.26 (1H, m, H^9), 0.91 (1H, app. dq, J = 12.9 Hz, J = 3.0 Hz, H^{2b}), 0.79-0.57 (2H, m, Cycloprop, H^{10}), 0.53 (1H, app. dq, J = 12.9 Hz, J = 4.8 Hz, H^{2a}), 0.40-0.27 (2H, m, Cycloprop, H^{10}); ^{13}C NMR (100 MHz, C_6D_6) δ_C 199.4, 194.7, 164.9, 160.9, 146.6, 132.9, 92.9, 68.7, 49.9, 39.2, 38.9, 36.8, 25.3, 12.2, 8.6, 7.4; HRMS (ES^+) mass cal'd. For $C_{16}H_{16}INO_3$ 397.0175; found [$(M+H)^+$] 398.0247. $[\alpha]_D^{25}$ = - 69.70° (C = 1.15 mg/ml), $CHCl_3$ for 96% ee.

2-iodo-3,9-dioxo-1-(thiophen-2-yl)-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (4f)



Method B: *N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)-3-(thiophen-2-yl)propiolamide (**21**) (100 mg, 0.25 mmol), CH_2Cl_2 (10 mL), ICl (500 µL) form 4-(3-iodo-2,8-dioxo-4-(thiophen-2-yl)-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal; then catalyst (16.27 mg, 0.05 mmol), benzoic acid (6.10 mg, 0.05 mmol), 48 h at -20°C, chromatography on silica gel (CH_2Cl_2:acetone, 0-10%) gives aldehyde **4f** as a white solid (92.7 mg, 84% yield); MP: 215-217 ºC; Rf 0.46 (CH_2Cl_2:MeOH, 95:5); λ_{max} (film) / cm^{-1} 2971, 2908, 1720, 1683, 1400, 1298, 1067, 748; ^1H NMR (500 MHz, C_6D_6) δ_H 8.73 (1H, d, J = 1.6 Hz, CHO), 6.79 (1H, dd, J = 2.9 Hz, J = 1.2 Hz, H^{11}), 6.72 (1H, dd, J = 4.9 Hz, J = 2.9 Hz, H^{10}), 6.67 (1H, dd, J = 4.9 Hz, J = 1.2 Hz, H^9), 5.86 (1H, d, J = 10.1 Hz, H^7), 5.09 (1H, dd, J = 10.1 Hz, J = 2.0 Hz, H^6), 4.18 (1H, ddd, J = 13.1 Hz, J = 4.8 Hz, J = 1.9 Hz, H^{1b}), 2.12-2.06 (2H, m, H^{1a}, H^{5a}), 1.95-1.85 (1H, m, H^4), 1.75-1.68 (2H, m, H^3, H^{5b}), 0.90 (1H, app. dq, J = 13.4 Hz, J = 3.1 Hz, H^{2b}), 0.56 (1H, app. dq, J = 13.1 Hz, J = 4.8 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 198.9, 193.9, 164.3, 157.0, 144.0, 134.1, 133.9, 127.1, 126.6, 125.1, 99.1, 68.1, 49.2, 39.3, 38.1, 36.8, 25.3; HRMS (ES^+) mass cal'd. For $C_{17}H_{14}INO_3S$ 438.9739; found [$(M+H)^+$] 439.9811. $[\alpha]_D^{25}$ = + 72.40° (C = 1.32 mg/ml), $CHCl_3$ for 95% ee.

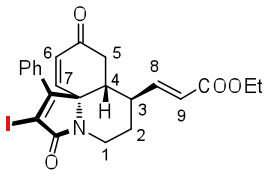
1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (10)



Method B: 3-bromo-*N*-(4,4-diethoxybutyl)-*N*-(4-methoxyphenyl)-propiolamide (**9**) (150 mg, 0.376 mmol), CH_2Cl_2 (20 mL), ICl (753

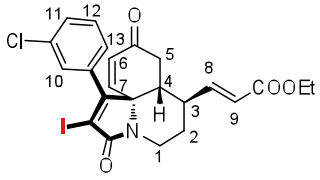
μL) form 4-(4-bromo-3-iodo-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)butanal; then catalyst (24.48 mg, 0.075 mmol), benzoic acid (9.18 mg, 0.075 mmol), 48 h at 0 °C, chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) gives compound **10** as a white solid (124.3 mg, 76% yield); Rf 0.44 (CH_2Cl_2:MeOH, 95:5); MP: 226-228 ºC; λ_{max} (film) / cm^{-1} 2925, 2124, 1724, 1679, 1572, 1398, 1299, 1040, 741; ^1H NMR (500 MHz, C_6D_6) δ_H 8.69 (1H, s, CHO), 5.85 (1H, d, J = 10.5 Hz, H^7), 4.80 (1H, dd, J = 10.5 Hz, J = 2.0 Hz, H^6), 4.04 (1H, ddd, J = 13.3 Hz, J = 4.7 Hz, J = 1.9 Hz, H^{1b}), 3.03 (1H, dd, J = 18.1 Hz, J = 5.4 Hz, H^{5b}), 2.31 (1H, dt, J = 18.1 Hz, J = 1.5 Hz, H^{5a}), 1.90 (1H, app. dt, J = 13.3 Hz, J = 3.2 Hz, H^{1a}), 1.64 (1H, ddt, J = 12.4 Hz, J = 5.6 Hz, J = 1.9 Hz, H^3), 1.60-1.53 (1H, m, H^4), 0.79 (1H, app. dq, J = 13.3 Hz, J = 3.1 Hz, H^{2b}), 0.43 (1H, app. dq, J = 13.3 Hz, J = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 198.7, 193.6, 163.3, 146.9, 143.6, 133.8, 103.6, 68.5, 49.3, 38.9, 38.5, 37.0, 25.0; HRMS (ES^+) mass calc'd. For $C_{13}H_{11}BrINO_3$ 434.8967; found $[(M+H)^+]$ 435.9041. $[\alpha]_D^{25}$ = - 128.40º (C = 1.65 mg/ml), $CHCl_3$ for 90% ee.

Ethyl 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (7b)



General procedure **5**, (carbethoxymethylene)triphenylphosphine (358.8 mg, 1.03 mmol) was added to the solution of 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (**4a**) (300 mg, 0.69 mmol) in CH_2Cl_2 (30 mL) at -78 ºC. The reaction mixture was stirred for 12h, slowly warming to room temperature. The reaction was quenched with water and extracted with CH_2Cl_2 (2 x 15 mL), the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Chromatography on silica gel (CH_2Cl_2:acetone, 0-2%) to afford compound **7b** as a white solid (289 mg, 83% yield). Rf 0.54 (CH_2Cl_2:MeOH, 95:5); MP: 234-236 ºC. λ_{max} (film) / cm^{-1} 2979, 2874, 1685, 1654, 1395, 1297, 1187, 1139, 1046, 986, 940, 884, 749, 749, 703; ^1H NMR δ_H (500 MHz, C_6D_6) δ_H 7.05-6.93 (3H, m, Ph), 6.92-6.87 (2H, m, Ph), 6.31 (1H, dd, J = 15.6, J = 10.1 Hz, H^8), 5.81 (1H, d, J = 10.1 Hz, H^7), 5.64 (1H, d, J = 15.6 Hz, H^9), 5.10 (1H, dd, J = 10.1 Hz, J = 1.9 Hz, H^6), 4.17 (1H, ddd, J = 13.2 Hz, J = 5.1 Hz, J = 2.0 Hz, H^{1b}), 4.08-3.88 (2H, m, CH_2CH_3), 2.16 (1H, app. dt, J = 13.2 Hz, J = 3.1 Hz, H^{1a}), 1.93 (1H, dt, J = 17.1 Hz, J = 1.8 Hz, H^{5a}), 1.75 (1H, ddt, J = 17.1 Hz, J = 11.5 Hz, J = 3.1 Hz, H^3), 1.47 (1H, dd, J = 17.1 Hz, J = 5.1 Hz, H^{5b}), 1.36-1.23 (1H, m, H^4), 0.94 (3H, t, J = 7.1 Hz, CH_2CH_3), 0.87 (2H, app. dq, J = 12.9 Hz, J = 2.1 Hz, H^{2b}), 0.72 (1H, app. dq, J = 12.9 Hz, J = 5.1 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 193.7, 165.2, 164.1, 161.8, 147.9, 143.8, 134.8, 133.5, 129.3, 128.7, 127.9, 124.2, 100.4, 68.8, 60.1, 43.0, 40.5, 37.7, 36.9, 30.5, 13.9; HRMS (ES^+) mass calc'd. For $C_{23}H_{22}INO_4$ 503.0594; found $[M+1]^+$ 504.0675. $[\alpha]_D^{25}$ = + 38.40º (C = 1.65 mg/ml), $CHCl_3$ for 92% ee.

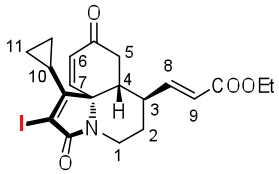
Ethyl 3-(1-(3-chlorophenyl)-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[1,2-*j*]quinolin-7-yl)acrylate (29)



General procedure **5**, 1-(3-chlorophenyl)-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[1,2-*j*]quinoline-7-carbaldehyde (**4b**) (40 mg, 0.085 mmol) in dry CH_2Cl_2 (12 mL), (carbethoxymethylene)triphenylphosphorane (44.50 mg, 0.127 mmol) was added at –78 °C,

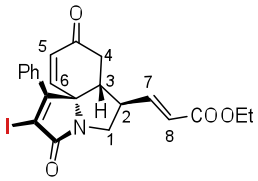
chromatography on silica gel (pet.-ether/EtOAc, 6:4) afforded **29** as a white solid. (28 mg, 61% yield). Rf 0.33 (pet.-ether/EtOAc, 6:4); MP: 182-184 ºC; λ_{max} (film) / cm^{-1} 2922, 1683, 1586, 1563, 1471, 1396, 1323, 1297, 1270, 1233, 1182, 1141, 1097, 1032, 988, 947, 864, 782, 751, 719; ^{1}H NMR (500 MHz, C_6D_6) δ_H 7.11 (1H, s, H^{10}), 6.98 (1H, ddd, J = 7.8 Hz, J = 2.1 Hz, J = 1.4 Hz, H^{11}), 6.78-6.61 (2H, m, H^{12}, H^{13}), 6.38 (1H, dd, J = 15.6 Hz, J = 9.4 Hz, H^8), 5.80 (1H, d, J = 10.1 Hz, H^7), 5.68 (1H, d, J = 15.6 Hz, H^9), 5.05 (1H, dd, J = 10.1 Hz, J = 2.1 Hz, H^6), 4.18 (1H, ddd, J = 13.4 Hz, J = 4.6 Hz, J = 1.8 Hz, H^{1b}), 4.07-3.94 (2H, m, $C\underline{H_2}CH_3$), 2.16 (1H, dt, J = 13.1 Hz, J = 3.1 Hz, H^{1a}), 1.94 (1H, app. d, J = 17.2 Hz, H^{5a}), 1.75 (1H, ddt, J = 15.4 Hz, J = 11.7 Hz, J = 3.9 Hz, H^3), 1.46 (1H, dd, J = 17.3 Hz, J = 5.1 Hz, H^{5b}), 1.27-1.21 (1H, m, H^4), 0.99 (3H, t, J = 7.1 Hz, $CH_2C\underline{H_3}$) 0.89 (1H, app. dq, J = 13.4 Hz, J = 1.9 Hz, H^{2b}), 0.78 (1H, app. dq, J = 11.7 Hz, J = 5.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 193.6, 165.4, 164.0, 160.2, 147.8, 143.7, 136.7, 135.0, 133.9, 130.3, 129.7, 125.9, 124.5, 101.6, 69.0, 60.4, 53.3, 43.1, 40.7, 37.9, 37.2, 30.7, 14.2; HRMS (ES^+) mass calc'd. For $C_{23}H_{21}ClINO_4$ 537.0204; found [$(M+H)^+$] 538.0276; $[\alpha]_D^{25}$ = + 102.65º (C = 0.82 mg/ml), $CHCl_3$ for 92% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 ml/min, retention time: major enantiomer 11.75 min, minor enantiomer 15.84 min.

(*E*)-ethyl 3-(1-cyclopropyl-2-iodo-3,9-dioxo-5,6,7,7a,8,9,-hexahydro-3*H*-pyrrolo[1,2-*j*]quinolin-7-yl)acrylate (30)



General procedure **5**, 1-cyclopropyl-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[1,2-*j*]quinoline-7-carbaldehyde (**4e**) (1.00 eq.) in dry CH_2Cl_2 (15 mL), (Carbethoxy-methylene)triphenylphosphorane (176 mg, 0.504 mmol) was added at –78 °C, 14 h, chromatography on silica (pet.-ether/EtOAc, 6:4) to afford **30** as a white solid (92.6 mg, 59% over 3 steps). Rf 0.32 (pet.-ether/EtOAc, 6:4); Mp: 222-226 ºC; λ_{max} (film) / cm^{-1} 2981, 1676, 1600, 1450, 1403, 1369, 1323, 1299, 1269, 1254, 1233, 1183, 1146, 1054, 1029, 1005, 974, 929, 877, 825, 773, 750, 733; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 6.54 (1H, dd, J =16.5 Hz, J = 9.5 Hz, H^8), 6.35 (1H, d, J = 10.0 Hz, H^7), 6.24 (1H, dd, J = 10.0 Hz, J = 2.0 Hz, H^6), 5.85 (1H, d, J = 16.5 Hz, H^9), 4.38 (1H, dd, J = 13.5 Hz, J = 4.6 Hz, H^{1b}), 4.17-4.08 (2H, m, $C\underline{H_2}CH_3$), 3.24 (1H, dd, J =17.8 Hz, J = 5.5 Hz, H^{5b}), 2.89 (1H, app. dt, J = 13.3 Hz, J = 2.9 Hz, H^{1a}), 2.64 (1H, app. d, J = 17.7 Hz, H^{5a}), 2.44 (1H, ddt, J = 15.3 Hz, J = 11.8 Hz, J = 3.8 Hz, H^3), 2.09-2.01 (1H, m, H^4), 1.70-1.62 (2H, m, H^{2b}, cycloprop.), 1.47-1.32 (2H, m, H^{2a}, cycloprop.), 1.26 (3H, t, J = 7.0 Hz, $CH_2C\underline{H_3}$), 1.14-1.05 (2H, m, cycloprop.), 0.96-0.89 (1H, m, cycloprop.); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 196.3, 166.1, 166.0, 161.7, 147.9, 147.4, 133.7, 125.1, 91.9, 70.3, 60.9, 44.1, 42.4, 38.9, 38.0, 31.5, 14.5, 12.6, 9.3, 8.1; HRMS (ES^+) mass calc'd. For $C_{20}H_{22}INO_4$ 467.0594; found [$(M+H)^+$] 468.0669. $[\alpha]_D^{25}$ = + 27.77º (C = 1.77 mg/ml), $CHCl_3$ for 96% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 ml/min, retention time: major enantiomer 14.46 min, minor enantiomer 18.57 min.

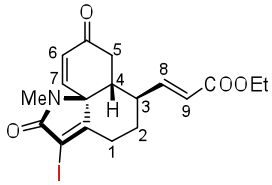
Ethyl 3-(2-iodo-3,8-dioxo-1-phenyl-3,5,6,6a,7,8-hexahydropyrrolo[2,1-i]indol-6-yl)acrylate (31)



Method A: Catalyst (**3b**) (0.0024 g, 0.007 mmol) and benzoic acid (0.007 mmol) was added to the solution of 3-

(3-iodo-2,8-dioxo-4-phenyl-1-azaspiro[4.5]deca-3,6,9-trien-1-yl)propanal (**2g**) (0.015 g, 0.036 mmol) in CH_2Cl_2 at -20 ºC. The resulting mixture was stirred for 1.5 h at -20 ºC, quenched by water and extracted with CH_2Cl_2 (2 x 7 ml). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and dissolved in CH_2Cl_2 (1.5 ml). After cooling to -78 ºC, (carbethoxymethylene)-triphenylphosphine (0.018 g, 0.052 mmol) was added. The reaction mixture was stirred for 12 h, slowly warming to room temperature. The reaction was quenched with water and extracted with CH_2Cl_2 (2 x 7 ml), the combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure. Chromatography on silica gel (CH_2Cl_2:acetone, 95:5) afforded compound **31** as a colourless oil (0. 0.017g, 97% yield). Rf 0.40 (CH2Cl2:acetone, 95:5); λ_{max} (film) / cm^{-1} 3675, 2972, 1709, 1262, 1066, 762; ^1H NMR δ_H (500 MHz, C_6D_6) δ_H 6.99-6.93 (3H, m, Ph), 6.91-6.85 (2H, m, Ph), 6.41 (1H, dd, J = 15.5, J = 9.1 Hz, H^7), 5.69 (1H, d, J = 10.1 Hz, H^6), 5.52 (1H, dd, J = 10.1 Hz, J = 2.0 Hz, H^5), 5.46 (1H, d, J = 15.5 Hz, H^8), 4.05-3.96 (2H, m, CH_2CH_3), 4.17 (1H, dd, J = 11.6 Hz, J = 8.8 Hz, J = 2.0 Hz, H^{1b}), 2.16 (1H, dd, J = 11.6 Hz, J = 8.8 Hz, H^{1a}), 2.43 (1H, ddt, J = 17.8 Hz, J = 8.8 Hz, J = 2.0 Hz, H^2), 1.87 (1H, dt, J = 17.6 Hz, J = 1.7 Hz, H^{4a}), 1.47 (1H, dd, J = 17.6 Hz, J = 5.5 Hz, H^{4b}), 1.46-1.31 (1H, m, H^3), 0.99 (3H, t, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR (125 MHz, C_6D_6) δ_C193.1, 170.3, 165.1, 164.4, 144.8, 144.5, 133.7, 131.7, 129.6, 124.3, 98.5, 75.9, 60.4, 50.3, 47.4, 45.5, 35.3, 14.2; HRMS (ES^+) mass calc'd. For $C_{22}H_{20}INO_4$ 489.0437; found $[M+1]^+$ 490.0485. $[\alpha]_D^{25}$ = - 9.0º (C = 1.33mg/ml), $CHCl_3$ for 25% ee; HPLC:DAICEL AD Chiralpak, 9:1 Hexane/isopropanol, flow 1 ml/min, retention time: major enantiomer 32.55 min, minor enantiomer 47.68 min.

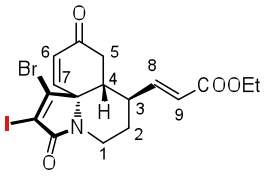
Ethyl 3-(3-iodo-1-methyl-2,8-dioxo-1,2,4,5,6,6a,7,8-octahydrobenzo[*h*]indol-6-yl)acrylate (32)



Method A: 4-(3-iodo-1-methyl-2,8-dioxo-1-azaspiro[4.5]deca-3,6,9-trien-1 yl)butanal (**27**) (20 mg, 0.058 mmol), catalyst **3b** (4 mg, 0.012 mmol) and benzoic acid (1.4g, 0.012 mmol) in CH_2Cl_2 at 0 ºC. The resulting mixture was stirred for 12 h at 0 ºC, quenched with water and extracted with CH_2Cl_2 (2 x 7 ml). The combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure and taken up in CH_2Cl_2 (2ml). After cooling to -78 ºC, (carbethoxymethylene)triphenylphosphine (30 mg, 0.086 mmol) was added. The solution was stirred for 4 h, slowly warming to room temperature. The reaction was quenched with water and extracted with CH_2Cl_2 (2 x 10 ml), the combined organic layers were dried over $MgSO_4$, concentrated under reduced pressure. Chromatography on silica gel (CH_2Cl_2:acetone, 9:1) afforded compound **32** as a white solid (20 mg, 79% yield). MP: 216-218 ºC; Rf 0.60 (CH_2Cl_2:acetone, 9:1); λ_{max} (film) / cm^{-1} 3674, 2923, 2300, 1681, 1367, 1231, 1021, 875, 757; ^1H NMR (500 MHz, C_6D_6) δH 6.38 (1H, dd, J = 15.6 Hz, J = 10.0 Hz, H^8), 5.83 (1H, d, J = 10.2 Hz, H^7), 5.71 (1H, d, J = 15.6 Hz, H^9), 4.69 (1H, dd, J = 10.2 Hz, J = 2.0 Hz, H^6), 4.20-3.92 (2H, m, CH_2CH_3), 2.50 (3H, s, NCH_3), 2.37 (1H, ddd, J = 13.4 Hz, J = 3.9 Hz, J = 2.7 Hz, H^{1b}), 2.21 (1H, dt, J = 17.7 Hz, J = 1.1 Hz, H^{5a}), 2.04 (1H, dd, J = 17.7 Hz, J = 5.2 Hz, H^{5b}), 1.59 (1H, ddt, J = 15.6 Hz, J = 11.8 Hz, J = 4.0 Hz, H^3), 1.40 (1H, app. dt, J = 13.6 Hz, J = 4.7 Hz, H^{1a}), 1.14-1.09 (1H, m, H^4), 1.02 (3H, t, J = 7.1 Hz, CH_2CH_3), 0.77-0.69 (1H, app. dq, J = 13.2 Hz, J = 1.8 Hz, H^{2b}), 0.64 (1H, app. dq, J = 13.3 Hz, J = 3.9 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 194.4, 166.5, 165.5, 164.0, 148.3, 141.3, 133.0, 124.4, 91.8, 66.8, 60.4, 45.4, 42.9, 38.4, 31.9, 28.3, 27.7, 14.2. HRMS (ES^+)

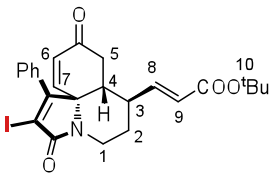
mass calc'd. For $C_{18}H_{20}INO_4$ 441.0437 found [$(M+H)^+$] 442.0501; $[\alpha]_D^{25}$ = - 15.00º (C = 4 mg/ml), $CHCl_3$ for 94% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 ml/min, retention time: major enantiomer 21.43 min, minor enantiomer 25.55 min.

Ethyl 3-(1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (11)



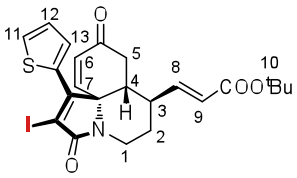
General procedure **5**, (carbethoxymethylene)triphenylphosphine (240.38 mg, 0.69 mmol) was added to a solution of 1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (**10**) (200 mg, 0.46 mmol) in CH_2Cl_2 (15 mL), at -78 ºC, 16 h, chromatography on silica gel (CH_2Cl_2:acetone, 9:1) to afford compound **11** as a white solid (205 mg, 90% yield). Rf 0.54 (CH_2Cl_2:MeOH, 95:5); MP: 218-220 ºC; λ_{max} (film) / cm^{-1} 2979, 2292, 1704, 1684, 1394, 1272, 1186, 1146, 1051, 851, 742; ^1H NMR (500 MHz, C_6D_6) δ_H 6.30 (1H, ddd, *J* = 15.6, *J* = 10.0 Hz, *J* = 3.9 Hz, H^8), 5.87 (1H, d, *J* = 10.0 Hz, H^7), 5.68 (1H, dd, *J* = 15.6 Hz, *J* = 2.5 Hz, H^9), 4.88 (1H, dd, *J* = 10.0 Hz, *J* = 2.5 Hz, H^6), 4.11-4.00 (3H, m, H^{1a}, $C\underline{H_2}CH_3$), 2.86 (1H, dd, *J* = 17.7 Hz, *J* = 7.1 Hz, H^{5b}), 2.25 (1H, app. d, *J* = 17.7 Hz, H^{5a}), 1.99 (1H, app. dt, *J* = 13.2 Hz, *J* = 3.0 Hz, H^{1a}), 1.66 (1H, ddt, *J* = 15.6 Hz, *J* = 11.8 Hz, *J* = 4.7 Hz, H^3), 1.01 (3H, t, *J* = 7.1 Hz, $CH_2C\underline{H_3}$), 0.82-0.73 (2H, m, H^{2b}, H^4), 0.62 (1H, app. dq, *J* = 13.2 Hz, *J* = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 193.9, 165.4, 163.4, 147.9, 147.1, 143.6, 133.8, 124.5, 103.8, 69.2, 60.4, 42.8, 41.0, 38.2, 37.4, 30.6, 14.2; HRMS (ES^+) mass calc'd. For $C_{17}H_{17}BrINO_4$ 504.9386; found [$(M+NH_4)^+$] 522.9712. $[\alpha]_D^{25}$ = + 83.4º (C = 1.95 mg/ml), $CHCl_3$ for 90% ee.

***tert*-butyl 3-(2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-*j*]quinolin-7-yl)acrylate (33)**



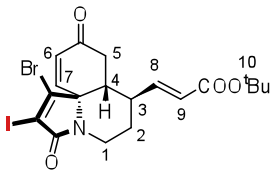
General procedure **5**, (tert-Butoxycarbonylmethylene)triphenylphosphorane (130 mg, 0.34 mmol) was added to a solution of 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (**4a**) (100 mg, 0.23 mmol) in CH_2Cl_2 (10 mL), at -78 ºC, 12 h, slowly warming to room temperature. Chromatography on silica gel (CH_2Cl_2:acetone, 1-2%) to afford compound **33** as a white solid (98 mg, 80% yield). Rf 0.59 (CH_2Cl_2:MeOH, 95:5); MP: 224-226 ºC; λ_{max} (film) / cm^{-1} 3053, 2927, 2923, 1679, 1393, 1326, 1153, 1136, 984, 847, 733, 701; ^1H NMR (500 MHz, C_6D_6) δ_H 7.13-6.98 (3H, m, Ph), 6.95-6.91 (2H, m, Ph), 6.41 (1H, dd, *J* = 15.5, *J* = 10.0, H^8), 5.87 (1H, d, *J* = 10.0 Hz, H^7), 5.71 (1H, d, *J* = 15.5 Hz, H^9), 5.14 (1H, dd, *J* = 10.0 Hz, *J* = 1.9 Hz, H^6), 4.23 (1H, ddd, *J* = 14.2 Hz, *J* = 4.6 Hz, *J* = 1.7 Hz, H^{1b}), 2.21 (1H, app. dt, *J* = 13.1 Hz, *J* = 2.9 Hz, H^{1a}), 2.02 (1H, app. d, *J* = 16.8 Hz, H^{5a}), 1.83 (1H, ddt, *J* = 15.2 Hz, *J* = 11.9 Hz, *J* = 3.9 Hz, H^3), 1.51 (1H, dd, *J* = 16.8 Hz, *J* = 5.0 Hz, H^{5b}), 1.44 (9H, s, H^{10}), 1.42-36 (1H, m, H^4), 0.95 (1H, app. dq, *J* = 12.6 Hz, *J* = 1.9 Hz, H^{2b}), 0.80 (1H, app. dq, *J* = 12.6 Hz, *J* = 5.0 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 193.7, 164.6, 164.0, 161.7, 146.9, 143.8, 134.8, 133.5, 129.3, 128.7, 128.0, 125.7, 100.4, 79.9, 68.8, 42.9, 40.3, 37.7, 36.9, 30.6, 27.8; HRMS (ES^+) mass calc'd. For $C_{25}H_{26}INO_4$ 531.0907; found [$(M+NH_4)^+$] 549.1238. $[\alpha]_D^{25}$ = + 46.1º (C = 4.1 x10^{-3} g/mL), $CHCl_3$ for 92% ee;

***tert*-butyl (2*E*)-3-(2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-*j*]quinolin-7-yl)acrylate (34)**



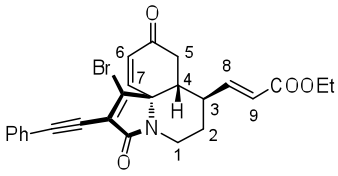
General procedure **5**, (tert-Butoxycarbonylmethylene) triphenylphosphorane (59.52 mg, 0.170 mmol) was added to a solution of 2-iodo-3,9-dioxo-1-(thiophen-2-yl)-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (**4f**) (50 mg, 0.114 mmol) in CH_2Cl_2 (5 mL), at -78 ºC, 13 h, chromatography on silica gel (CH_2Cl_2:acetone, 0-2%) to afford compound **34** as a white solid (42 mg, 69% yield). Rf 0.61 (CH_2Cl_2:MeOH, 95:5); MP: 220-222 ºC; λ_{max} (film) / cm^{-1} 2978, 1701, 1393, 1298, 1153, 989, 846, 749; ^1H NMR (500 MHz, C_6D_6) δ_H 6.90-6.86 (1H, m, H^{11}), 6.74-6.71 (2H, m, H^{12}, H^{13}),6.34 (1H, dd, J = 2.5 Hz, J = 1.7 Hz, H^8),5.85 (1H, d, J = 10.1, H^7), 5.68 (1H, d, J = 15.5, H^9), 5.1 (1H, dd, J = 13.1 Hz, J = 2.0 Hz, H^6), 4.20 (1H, ddd, J = 13.1 Hz, J = 4.5 Hz, J = 2.0 Hz, H^{1b}), 2.15 (1H, app. dt, J = 13.1 Hz, J = 2.0 Hz, H^{1a}), 2.00 (1H, dt, J = 17.2 Hz, J = 0.9 Hz, H^{5a}), 1.78 (1H, ddt, J = 15.5 Hz, J = 12.6 Hz, J = 4.5 Hz, H^3), 1.48 (1H, dd, J = 17.2 Hz, J = 4.5 Hz, H^{5b}), 1.42 (9H, s, H^{10}), 1.22-1.13 (1H, m, H^4), 0.90 (1H, app. dq, J = 13.2 Hz, J = 2.0 Hz, H^{2b}), 0.75 (1H, app. dq, J = 12.6 Hz, J = 5.0 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 194.1, 164.4, 164.3, 157.4, 147.2, 144,0, 134.4, 133.4, 126.9, 126.9, 125.7, 125.0, 100.3, 80.2, 68.7, 43.5, 40.6, 37.6, 37.2, 30.7, 28.0; HRMS (ES^+) mass calc'd. For $C_{23}H_{24}INO_4S$ 537.0471; found $[(M+H)^+]$ 538.0543. $[\alpha]_D^{25}$ = - 59.5º (C = 2.2 x 10^{-3} g/mL), $CHCl_3$ for 95% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 mL/min, retention time: major 15.39 min, minor enantiomer 12.15 min.

***tert*-butyl 3-(1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-*j*]quinolin-7-yl)acrylate (35)**



General procedure **5**, (tert-Butoxycarbonylmethylene) triphenylphosphorane (64.7 mg, 0.17 mmol) was added to a solution of 1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde **10** (50 mg in CH_2Cl_2 (7 mL), at -78 ºC, 15 h, chromatography on silica gel (CH_2Cl_2:acetone, 0-2%) to afford compound **35** as a white solid (47.5 mg, 77% yield). Rf 0.57 (CH_2Cl_2:MeOH, 95:5); MP: 222-224; λ_{max} (film) / cm^{-1} 3330, 2973, 2883, 1698, 1409, 1380, 1327, 1161, 1087, 1046, 880,739; ^1H NMR (500 MHz, C_6D_6) δ_H 6.26 (1H, dd, J = 15.5, J = 10.1 Hz, H^8), 5.81 (1H, d, J = 10.1 Hz, H^7), 5.64 (1H, d, J = 15.5 Hz, H^9), 4.83 (1H, dd, J = 10.1 Hz, J = 2.0 Hz, H^6), 4.02 (1H, ddd, J = 13.2 Hz, J = 4.6 Hz, J = 1.8 Hz, H^{1b}), 2.80 (1H, dd, J = 17.7 Hz, J = 5.6 Hz, H^{5b}), 2.23 (1H, app. d, J = 17.7 Hz, H^{5a}), 1.94 (1H, app. dt, J = 13.2 Hz, J = 3.4 Hz, H^{1a}), 1.64 (1H, ddt, J = 15.5 Hz, J = 11.4 Hz, J = 3.4 Hz, H^3), 1.39 (9H, s, H^{10}), 0.79-0.69 (2H, m, H^{2b}, H^4), 0.60 (1H, app. dq, J = 11.4 Hz, J = 3.4 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 193.9, 164.9, 163.4, 161.4, 147.1, 143.7, 133.7, 126.8, 103.9, 80.3, 69.2, 42.8, 40.9, 38.3, 37.4, 30.7, 28.1; For $C_{19}H_{21}BrINO_4$ 532.9699; found $[(M+NH_4)^+]$ 551.0033. $[\alpha]_D^{25}$ = + 75.7º (C = 2.8 x10^{-3} g/mL), $CHCl_3$ for 90% ee; HPLC:DAICEL AD Chiralpak, 8:2 Hexane/isopropanol, flow 1 mL/min, retention time: major 12.74 min, minor enantiomer 15.95 min.

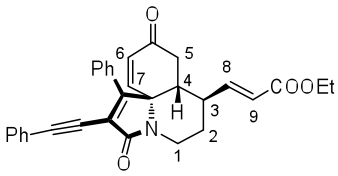
Ethyl 3-(1-bromo-3,9-dioxo-2-(phenylethynyl)-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (12)



Et_3N/Benzene (5:1) (9.2 ml) was added to a mixture of compound **10** (130 mg, 0.25 mmol), CuI (5 mg, 0.026 mmol) and $PdCl_2(PPh_3)_2$ (18.2 mg, 0.026 mmol), followed by the addition of ethynylbenzene (31.6 mg, 0.31 mmol). The reaction was stirred at room temperature for 24h. After the reaction was completed, it was filtrated over a pad of celite, extracted with CH_2Cl_2 and organic layer dried over $MgSO_4$. The solvent was evaporated under reduced pressure and chromatography on silica gel (CH_2Cl_2:acetone, 0-4%) gave compound **12** as a white solid (105 mg, 85% yield). Rf 0.70 (CH_2Cl_2:MeOH, 95:5) MP:198-200 ºC. λ_{max} (film) / cm^{-1} 2348, 1695, 1490, 1400, 1296, 1188, 1071, 996, 759; ^1H NMR (500 MHz, C_6D_6) δ_H 7.57-7.54 (2H, m, Ph), 7.03-6.90 (3H, m, Ph), 6.37 (1H, dd, J = 15.6, J = 10.1 Hz, H^8), 5.94 (1H, d, J = 10.1 Hz, H^7), 5.72 (1H, d, J = 15.6 Hz, H^9), 5.04 (1H, dd, J = 10.1 Hz, J = 2.0 Hz, H^6), 4.17 (1H, ddd, J = 13.2 Hz, J = 4.5 Hz, J = 1.6 Hz, H^{1b}), 4.13-4.00 (2H, m, CH_2CH_3), 3.00 (1H, dd, J = 17.1 Hz, J = 5.6 Hz, H^{5b}), 2.33 (1H, app. d, J = 17.8 Hz, H^{5a}), 2.08 (1H, app. dt, J = 13.2 Hz, J = 3.0 Hz, H^{1b}), 1.74 (1H, ddt, J = 15.2 Hz, J = 12.6 Hz, J = 4.0 Hz, H^3), 1.03 (3H, t, J = 7.1 Hz, CH_2CH_3), 0.98-0.93 (1H, m, H^4), 0.85 (2H, app. dq, J = 13.5 Hz, J = 2.1 Hz, H^{2a}), 0.71 (1H, app. dq, J = 12.6 Hz, J = 5.1 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 194.0, 165.4, 162.6, 148.1, 144.0, 142.1, 134.0, 132.4, 129.6, 128.7, 126,0, 124.5, 122.2, 101.7, 80.6, 65.9, 60.4, 43.2, 41.3, 38.2, 36.8, 30.6, 14.2; HRMS (ES^+) mass calc'd. For $C_{25}H_{22}BrINO_4$ 479.0732; found $[(M+NH_4)^+]$ 497.1068. $[\alpha]_D^{25}$ = + 131.1º (C = 0.85 mg/ml), $CHCl_3$ for 90% ee.

See, Camerel, F.; Ulrich, G.; Retailleau, P.; Ziessel, R., Ethynyl-boron subphthalocyanines displaying efficient cascade energy transfer and large Stokes shifts. *Angew Chem Int Ed Engl*, **2008,** 47, (46), 8876-80.

***tert*-butyl 3-(1-bromo-2-iodo-3,9-dioxo-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-*j*]quinolin-7-yl)acrylate (13)**

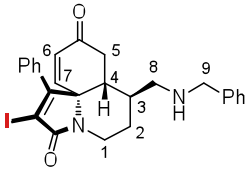


In air, $Pd(OAc)_2$ (0.77 mg, 0.004 mmol, 10%), PPh_3 (2.09 mg, 0.008 mmol, 20%), phenyl boronic acid (7.67mg, 0.063 mmol), compound **12** (20 mg, 0.042 mmol) and K_2CO_3 (11.6 mg, 0.084 mmol) were placed in a vial equipped with a stir bar. The vial was sealed with a septum screw-cap, and then it was evacuated and filled with argon (three cycles). Benzene/H_2O (5/1, 2.4 mL) was added, and the resulting heterogeneous reaction mixture was stirred vigorously for 15 hours at 60 ºC. The reaction mixture was then poured into Et_2O (30 mL), filtered through a short pad of celite, concentrated under reduced pressure, and purified by flash chromatography on silica gel (CH_2Cl_2:acetone, 0-5%) to afford compound **13** as a white solid (18.6 mg, 93%). Rf 0.66 (CH_2Cl_2:MeOH, 95:5); Mp: 174-176 ºC; λ_{max} (film) / cm^{-1} 2979, 2903, 1705, 1685, 1572, 1406, 1299, 1239, 759; ^1H NMR (500 MHz, C_6D_6) δ_H 7.37 (2H, dd, J = 8.0 Hz, J = 1.5 Hz, Ph), 7.31 (2H, dd, J = 7.4 Hz, J = 2.0 Hz, Ph), 7.15-6.99 (6H, m, Ph), 6.42 (1H, dd, J = 15.6 Hz, J = 9.5 Hz, H^8), 5.99 (1H, d, J = 10.1 Hz, H^7), 5.71 (1H, d, J = 15.6 Hz, H^9), 5.40 (1H, dd, J = 10.1 Hz, J = 2.0 Hz, H^6), 4.32 (1H, ddd, J = 13.2 Hz, J = 4.5 Hz, J = 1.6 Hz, H^{1b}), 4.13-4.00 (2H, m, CH_2CH_3), 2.22 (1H, app.

dt, J = 13.1 Hz, J = 3.1 Hz, H^{1a}), 2.02 (1H, dt, J = 17.8 Hz, J = 0.9 Hz, H^{5a}), 1.87 (1H, ddt, J = 17.2 Hz, J = 11.7 Hz, J = 3.9 Hz, H^{3}), 1.69 (1H, dd, J = 17.2 Hz, J = 5.0 Hz, H^{5b}), 1.47-1.23 (2H, m, H^{2b}, H^{4}), 1.00 (3H, t, J = 7.1 Hz, $CH_2C\underline{H_3}$), 0.87 (1H, app. dq, J = 12.7 Hz, J = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 194.2, 165.4, 164.6, 159.4, 148.1, 144.7, 134.1, 134,0, 132.4, 129.7, 129.0, 128.7, 128.5, 124.4, 122.7, 122.0, 98.7, 81.8, 65.9, 60.3, 43.9, 40.9, 38.0, 36.6, 30.7, 14.1; HRMS (ES^+) mass calc'd. For $C_{31}H_{27}NO_4$ 477.1940; found [$(M+H)^+$] 478.2012. $[\alpha]_D^{25}$ = + 46.6° (C = 0.6 mg/ml), $CHCl_3$ for 90% ee.

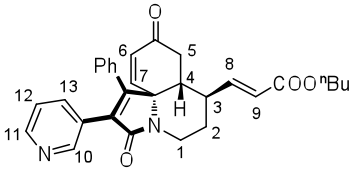
See, Lunazzi, L.; Mancinelli, M.; Mazzanti, A., Arylbiphenylene Atropisomers: Structure, Conformation, Stereodynamics, and Absolute Configuration. *The Journal of Organic Chemistry* **2008,** 73, (6), 2198-2205.

7-((benzylamino)methyl)-2-iodo-1-phenyl-6,7,7a,8-tetrahydro-3*H*-pyrrolo[2,1-j]quinoline-3,9(5H)-dione (7a)



Benzylamine (12.4 mg, 0.116 mmol) was added to the solution of 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinoline-7-carbaldehyde (**4a**) (50 mg, 0.116 mmol) in 1,2-dichloroethane (5 mL) and it was stirred for 1h. The reaction mixture was then treated with sodium triacetoxyborohydride (31.9 mg, 0.150 mmol) at 0ºC. The mixture was stirred at rt under N_2 atmosphere for 16 h. The reaction mixture was quenched by adding aqueous saturated $NaHCO_3$ solution, and the product was extracted with CH_2Cl_2 (3 x 10 mL). The organic layer was dried over $MgSO_4$, and the solvent was concentrated under reduced pressure. Flash chromatography on silica gel (CH_2Cl_2:acetone, 0-10%) afforded compound **7a** as a white solid (53 mg, 87% yield). Rf 0.24 (CH_2Cl_2:MeOH, 95:5); MP: 154-156 ºC. λ_{max} (film) / cm^{-1} 3060, 2921, 2342, 1682, 1452, 1400, 1210, 1028, 932, 805, 744, 702; ^{1}H NMR (500 MHz, CH_2Cl_2) δ_H 7.59-7.35 (3H, m, Ph), 7.33-7.19 (7H, m, Ph), 6.38 (1H, dd, J = 10.1, J = 2.0 Hz, H^6), 6.27 (1H, d, J = 10.1 Hz, H^7), 4.39 (1H, ddd, J = 13.4 Hz, J = 4.5 Hz, J = 2.0 Hz, H^{1b}), 3.75 (2H, d, J = 13.3 Hz, H^{9a}), 3.65 (2H, d, J = 13.3 Hz, H^{9b}), 2.92 (1H, app. dt, J = 13.2 Hz, J = 2.9 Hz, H^{1a}), 2.70 (1H, dd, J = 12.5 Hz, J = 3.1 Hz, H^{8b}), 2.47 (1H, dd, J = 12.4 Hz, J = 6.5 Hz, H^{8a}), 2.30-2.21 (2H, m, H^4, H^{5a}), 1.88 (1H, app. dq, J = 13.3 Hz, J = 2.2 Hz, H^{2b}), 1.78-1.71 (2H, m, H^3, H^{5b}), 1.35 (1H, app. dq, J = 12.8 Hz, J = 4.2 Hz, H^{2a}); ^{13}C NMR (125 MHz, CH_2Cl_2) δ_C 196.1, 164.8, 162.7, 145.0, 135.0, 133.9, 129.7, 129.1, 128.5, 128.4, 127.9, 127.2, 99.6, 70.20, 63.5, 50.9, 43.1, 41.7, 38.5, 37.5, 36.7, 30.0; HRMS (ES^+) mass calc'd. For $C_{26}H_{25}IN_2O_2$ 524.0961; found [$(M+H)^+$] 525.1027. $[\alpha]_D^{25}$ = + 86.32° (C = 1.42 mg/ml), $CHCl_3$ for 92% ee.

Butyl 3,9-dioxo-1-phenyl-2-(pyridin-3-yl)-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (8a)

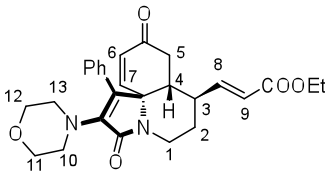


An-oven dried tube was charged with $Pd_2(dba)_3$ (3.6 mg, 0.004 mmol), X-Fos (0.016 mmol), 3-pyridine boronic acid (7.3 mg, 0.06 mmol), ethyl 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (**7b**) (20 mg, 0.04 mmol) and powdered anhydrous K_3PO_4 (16.9 mg, 0.08 mmol). The tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was

carried out three times). *n*-butanol (1 mL) was added via syringe, through the septum. The septum was then replaced with a Teflon screwcap and the vial tube was sealed. The reaction mixture was heated to 100 ºC overnight. After completion the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a short pad of celite (eluting with DCM) and the eluent was concentrated under reduced pressure. The crude material obtained was purified *via* flash chromatography on silica gel (CH_2Cl_2:acetone, 5-30%) to afford compound **8a** as a white solid (14 mg, 77% yield) (^{t}Butyl esther isolated). Rf 0.15 (CH_2Cl_2:MeOH, 95:5); MP: 170-172 ºC. λ_{max} (film) / cm^{-1} 2958, 2871, 2343, 2144, 1682, 1407, 1300, 1233, 1185, 1066, 943, 818, 760, 699; ^{1}H NMR δ_H (500 MHz, CD_2Cl_2) δ_H 8.49 (1H, d, J = 1.5 Hz, H^{10}), 8.42 (1H, dd, J = 4.8 Hz, J = 1.5 Hz, H^{13}), 7.81 (1H, dd, J = 8.1 Hz, J = 1.5 Hz, H^{11}), 7.44-7.33 (3H, m, Ph), 7.23 (1H, dd, J =8.1 Hz, J = 4.8 Hz, H^{12}), 7.21-7.15 (2H, m, Ph), 6.54-6.49 (2H, m, H^7, H^8), 6.36 (1H, d, J = 10.1 Hz, H^9), 5.81 (1H, dd, J = 15.6 Hz, J = 0.5 Hz, H^6), 4.49 (1H, ddd, J = 13.5 Hz, J = 4.7 Hz, J = 1.9 Hz, H^{1b}), 4.07 (2H, t, J = 7.1 Hz, J = 0.99 Hz, $OCH_2CH_2CH_2CH_3$), 2.97 (1H, app. dt, J = 13.1 Hz, J = 2.9 Hz, H^{1a}), 2.48 (1H, ddd, J = 21.2 Hz, J = 11.8 Hz, J = 3.8 Hz, H^3), 2.24-2.06 (2H, m, H^{5b}, H^4), 1.76 (1H, app. dq, J = 13.5 Hz, J = 2.6 Hz, H^{2b}), 1.72 (1H, dd, J = 17.7 Hz, J = 5.6 Hz, H^{5a}), 1.60 (2H, dt, J = 14.4 Hz, J = 7.4 Hz, $OCH_2CH_2CH_2CH_3$), 1.52 (1H, app. dq, J = 13.5 Hz, J = 5.7 Hz, H^{2a}), 1.40-1.32 (2H, m, $OCH_2CH_2CH_2CH_3$), 0.91 (3H, t, J = 7.4 Hz, $OCH_2CH_2CH_2CH_3$); ^{13}C NMR (125 MHz, CD_2Cl_2) δ_C 195.9, 166.9, 166.2, 155.9, 149.9, 148.8, 148.2, 145.9, 137.9, 134.8, 133.7, 131.9, 130.0, 129.8, 129.0, 127.7, 124.9, 123.6, 66.6, 64.9, 44.0, 42.0, 38.5, 37.4, 31.8, 31.2, 19.7, 14.0; HRMS (ES^+) mass calc'd. For $C_{30}H_{30}N_2O_4$ 482.2206; found [$(M+H)^+$] 483.2267. $[\alpha]_D^{25}$ = + 29.3º (C = 0.45 mg/ml), $CHCl_3$ for 92% ee.

See, Billingsley, K.; Buchwald, S. L., Highly efficient monophosphine-based catalyst for the palladium-catalyzed suzuki-miyaura reaction of heteroaryl halides and heteroaryl boronic acids and esters. *J Am Chem Soc* **2007,** 129, (11), 3358-66.

Ethyl 2-morpholino-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (8b)

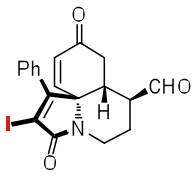


An-oven dried tube was charged with $Pd_2(dba)_3$ (3.6 mg, 0.004 mmol), BINAP (7.4 mg, 0.012 mmol), ethyl 2-iodo-3,9-dioxo-1-phenyl-5,6,7,7a,8,9-hexahydro-3*H*-pyrrolo[2,1-j]quinolin-7-yl)acrylate (**7b**) (20 mg, 0.04 mmol) and powdered anhydrous $CsCO_3$ (65.2 mg, 0.2 mmol). The tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out three times). Toluene (1 mL) was added via syringe through the septum and morpholine (5.2 mg, 0.06 mmol) in the same manner. The septum was then replaced with a Teflon screwcap and the vial tube was sealed. The reaction mixture was heated to 120 ºC overnight. When the reaction was completed, the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a short pad of celite (eluting with DCM) and the eluent was concentrated under reduced pressure. The crude material obtained was purified via flash chromatography on silica gel (CH_2Cl_2:acetone, 5-15%) to afford compound **8b** as a white solid (16 mg, 86% yield). Rf 0.57 (CH_2Cl_2:MeOH, 95:5); MP: 178-180 ºC. λ_{max} (film) / cm^{-1} 2926, 2343, 2144, 1681, 1629, 1382, 1269, 1163, 1114, 762, 701; ^{1}H NMR δ_H (500 MHz, C_6D_6) δ_H

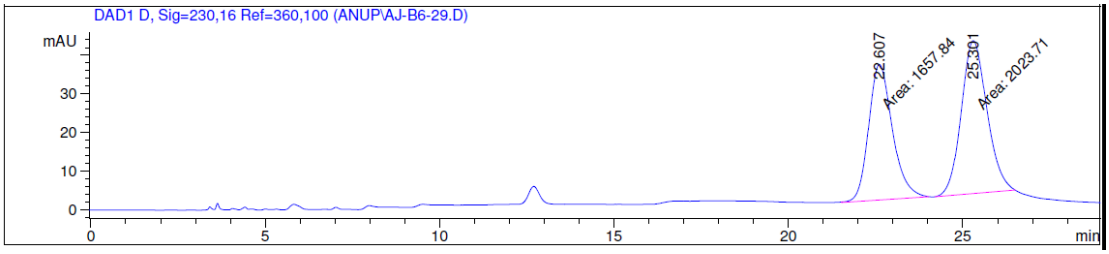
7.03-6.91 (5H, m, Ph), 6.48 (1H, dd, J = 15.6, J = 9.4 Hz, H^{8}), 5.93 (1H, d, J = 10.1 Hz, H^{7}), 5.72 (1H, d, J = 15.6 Hz, H^{9}), 5.36 (1H, dd, J = 10.1 Hz, J = 1.9 Hz, H^{6}), 4.29 (1H, ddd, J = 13.4 Hz, J = 4.6 Hz, J = 1.6 Hz, H^{1b}), 4.08-3.88 (2H, m, CH_2CH_3), 3.62-3.53 (2H, m, H^{10a}, H^{13a}), 3.52-3.44 (4H, m, H^{11}, H^{12}), 2.85-2.78 (2H, m, H^{10b}, H^{13b}), 2.23 (1H, ddd, J = 13.1 Hz, J = 5.3 Hz, J = 2.9 Hz, H^{1b}), 2.06 (1H, app. d, J = 17.1 Hz, H^{5a}), 1.94-1.85 (1H, m, H^{3}), 1.60-1.47 (2H, m, H^{5b}), 1.36-1.29 (1H, m, H^{4}), 0.97 (3H, t, J = 7.1 Hz, CH_2CH_3), 0.94-0.89 (1H, m, H^{2b}), 0.83 (1H, app. dq, J = 12.9 Hz, J = 4.7 Hz, H^{2a}); ^{13}C NMR (125 MHz, C_6D_6) δ_C 194.6, 165.5, 164.4, 148.8, 147.0, 139.6, 135.2, 132.6, 130.6, 130.5, 128.5, 127.3, 124.3, 67.0, 63.0, 60.3, 49.7, 44.0, 41.7, 38.0, 36.3, 31.0, 14.2; HRMS (ES^+) mass calc'd. For $C_{27}H_{30}N_2O_5$ 462.2155; found $[(M+H)^+]$ 463.2219. $[\alpha]_D^{25}$ = + 76.1^o (C = 0.9 mg/ml), $CHCl_3$ for 92% ee.

See, Meyers, C.; Maes, B. U.; Loones, K. T.; Bal, G.; Lemiere, G. L.; Dommisse, R. A., Study of a new rate increasing "base effect" in the palladium-catalyzed amination of aryl iodides. *J Org Chem* **2004,** 69, (18), 6010-7.

HPLC data

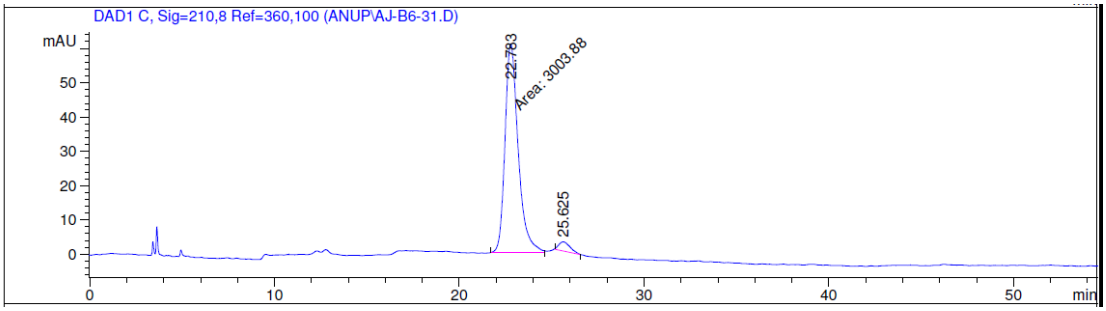


4a



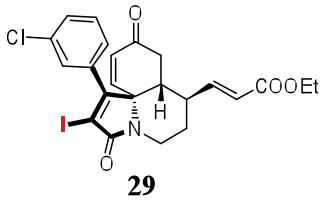
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.607	MM	0.7890	1657.84106	35.01900	45.0311
2	25.301	MM	0.8541	2023.70618	39.48777	54.9689
Totals :				3681.54724	74.50677	

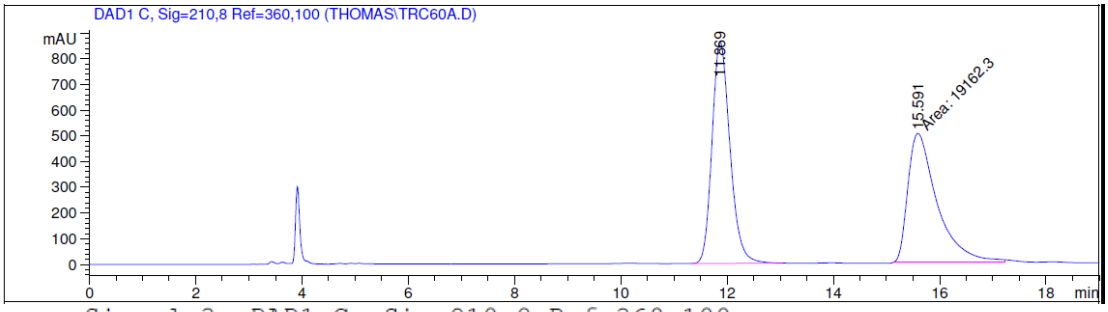


Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.783	MM	0.8266	1815.32031	36.60227	96.1851
2	25.670	MM	0.7156	71.99899	1.67691	3.8149
Totals :				1887.31930	38.27918	

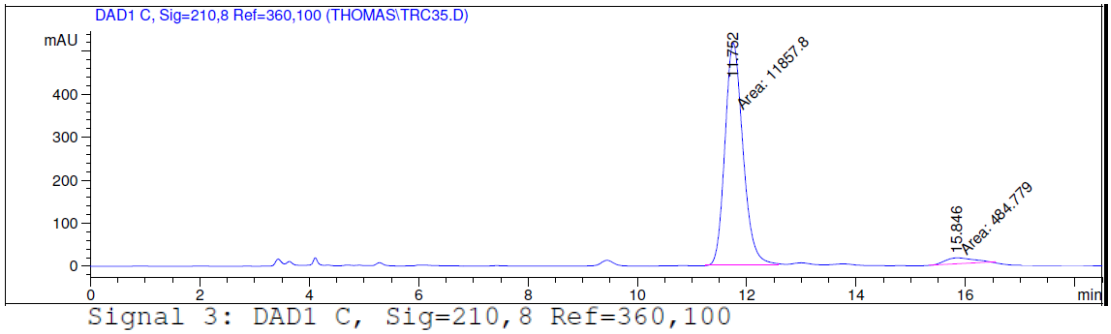


29



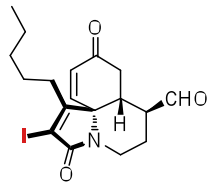
Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.869	BB	0.3629	2.03060e4	861.82404	51.4489
2	15.591	MM	0.6371	1.91623e4	501.29669	48.5511
Totals :				3.94683e4	1363.12073	

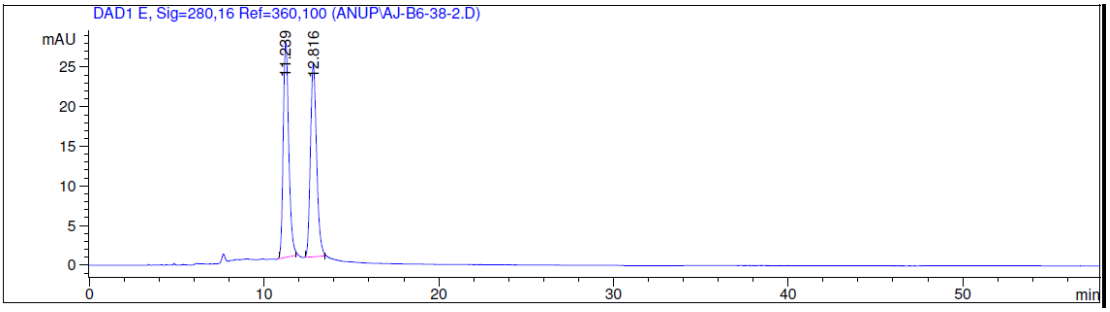


Signal 3: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.752	MM	0.3824	1.18578e4	516.76367	96.0723
2	15.846	MM	0.5872	484.77917	13.75989	3.9277
Totals :				1.23426e4	530.52356	

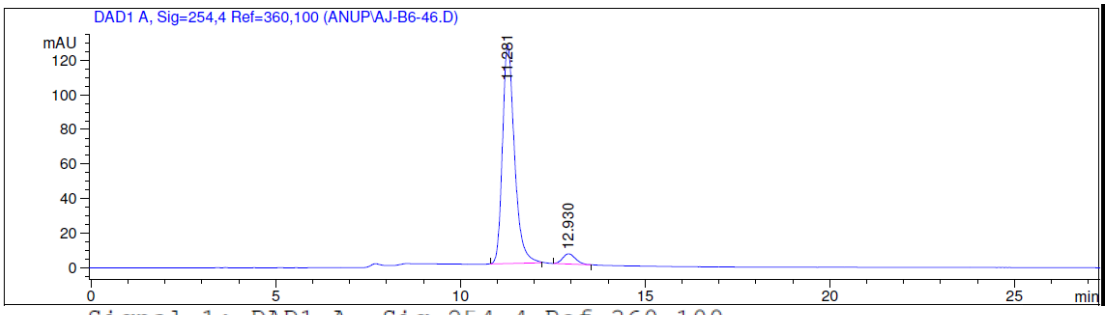


4c



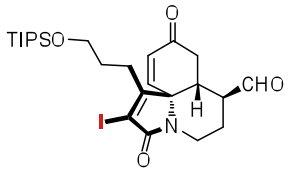
Signal 5: DAD1 E, Sig=280,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.239	BB	0.3324	593.33521	27.20999	49.9663
2	12.816	BB	0.3725	594.13586	24.36515	50.0337
Totals :				1187.47107	51.57515	

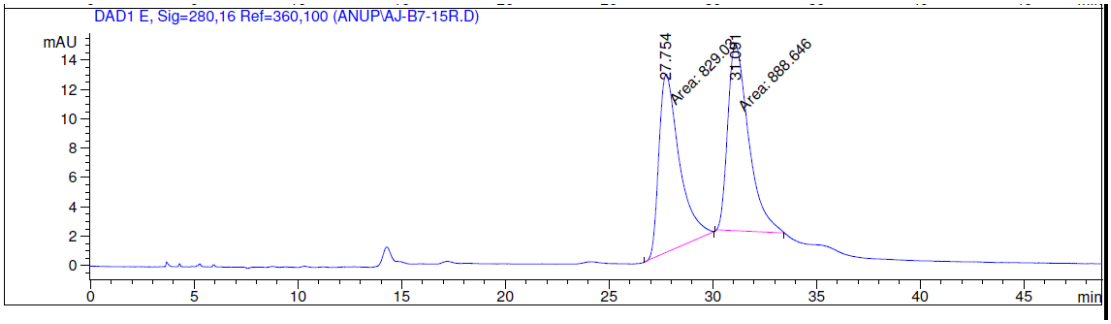


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.281	BB	0.3438	2856.18945	126.33053	95.2119
2	12.930	BB	0.3706	143.63457	5.92921	4.7881
Totals :				2999.82402	132.25974	

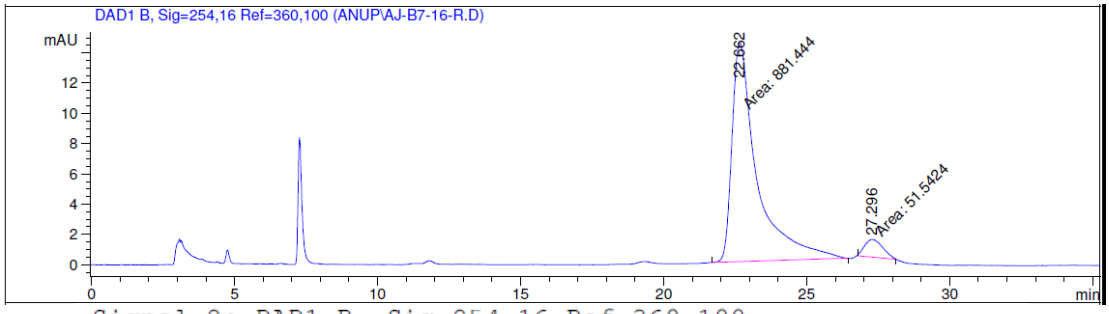


4d



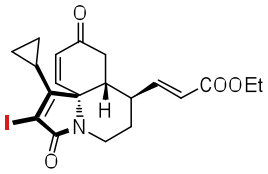
Signal 5: DAD1 E, Sig=280,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.754	MM	1.1383	829.03027	12.13868	48.2647
2	31.091	MM	1.1683	888.64557	12.67732	51.7353
Totals :				1717.67584	24.81599	

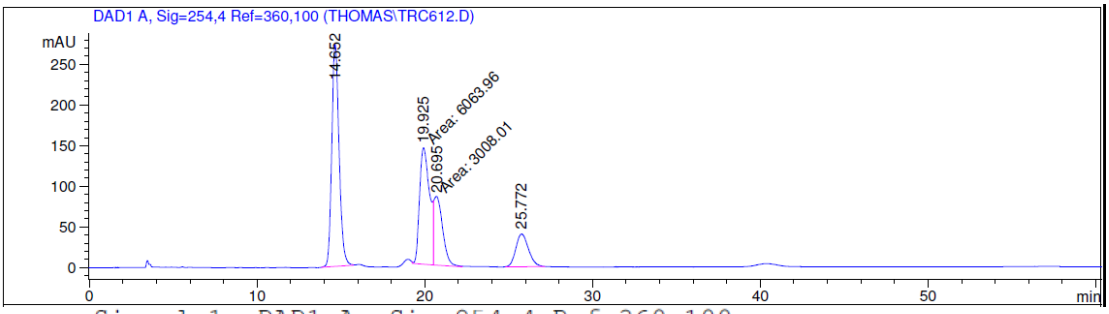


Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.662	MM	1.0173	881.44360	14.44128	94.4755
2	27.296	MM	0.7384	51.54240	1.16334	5.5245
Totals :				932.98600	15.60462	

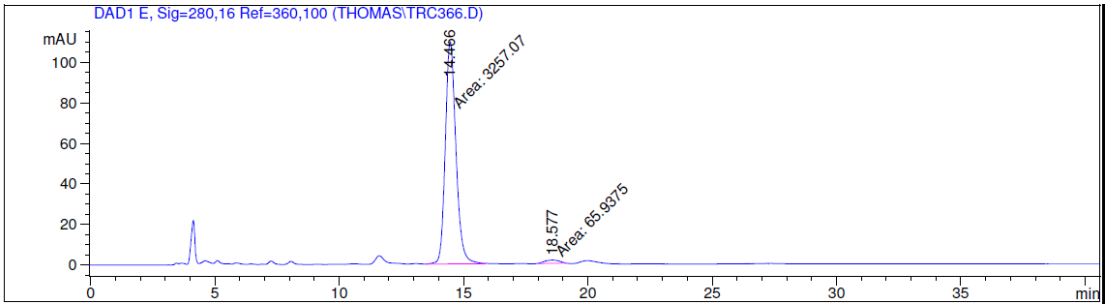


30



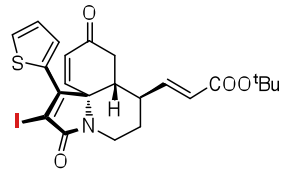
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.652	BB	0.4666	8252.71484	273.03915	42.4531
2	19.925	MF	0.7061	6063.95752	143.12820	31.1938
3	20.695	FM	0.5941	3008.01440	84.38504	15.4736
4	25.772	BB	0.8015	2114.92407	40.35032	10.8795
Totals :				1.94396e4	540.90272	

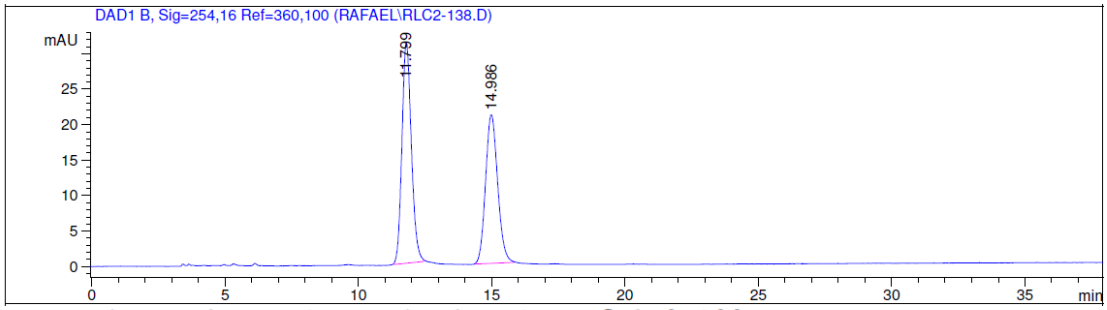


Signal 5: DAD1 E, Sig=280,16 Ref=360,10C

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.466	MM	0.4951	3257.06665	109.63950	98.0157
2	18.577	MM	0.6648	65.93747	1.65314	1.9843
Totals :				3323.00412	111.29264	

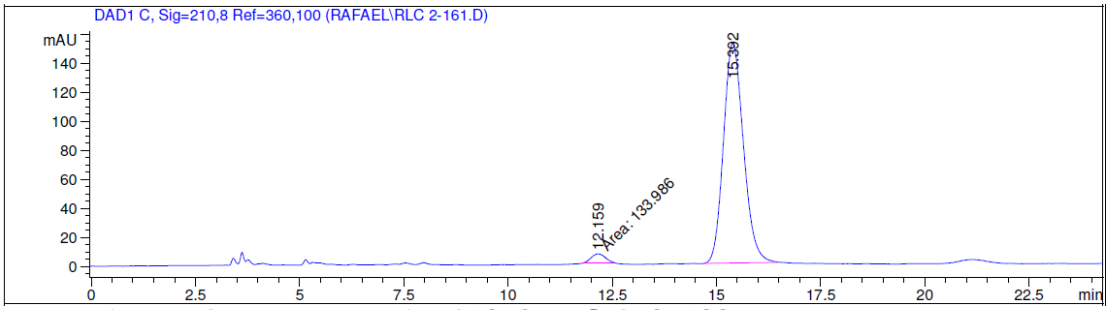


34



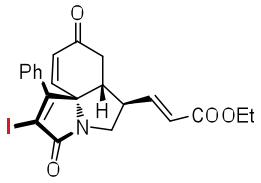
Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.799	BB	0.3791	763.44293	31.02274	53.6420
2	14.986	BB	0.4875	659.77454	20.94677	46.3580
Totals :				1423.21747	51.96951	

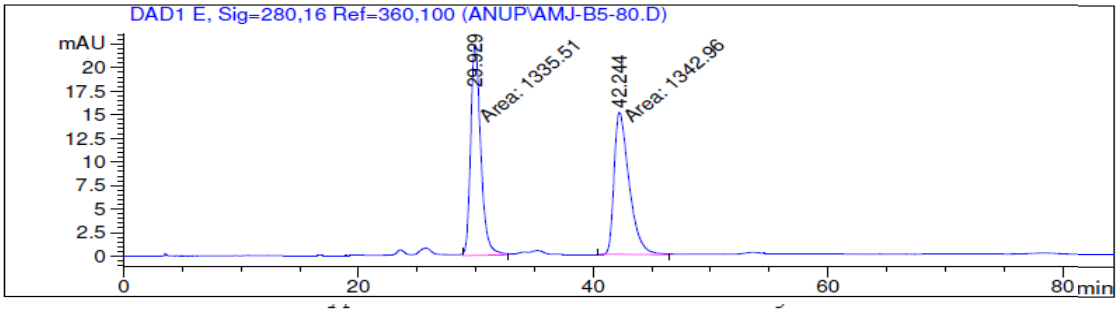


Signal 3: DAD1 C, Sig=210,8 Ref=360,100

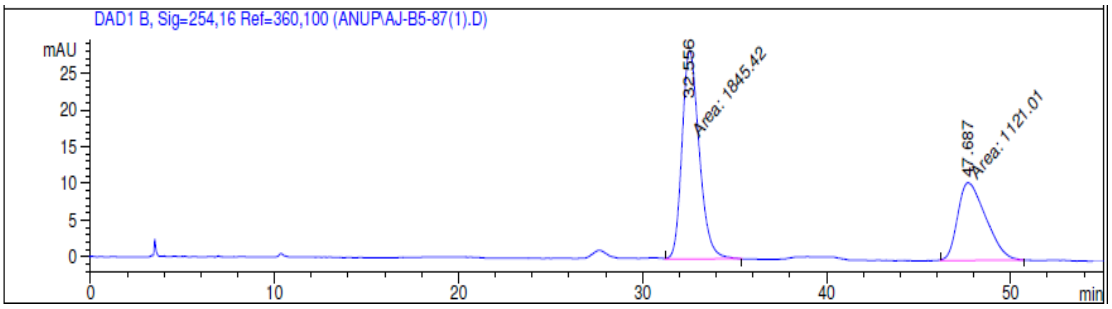
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.159	MM	0.3709	133.98601	6.02144	2.5824
2	15.392	BB	0.5171	5054.41797	151.56317	97.4176
Totals :				5188.40398	157.58461	



31

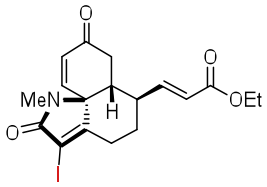


#	[min]		[min]	[mAU*s]	[mAU]	%
1	29.929	MM	0.9938	1335.51001	22.39656	49.8609
2	42.244	MM	1.4865	1342.95947	15.05691	50.1391
Totals :				2678.46948	37.45348	

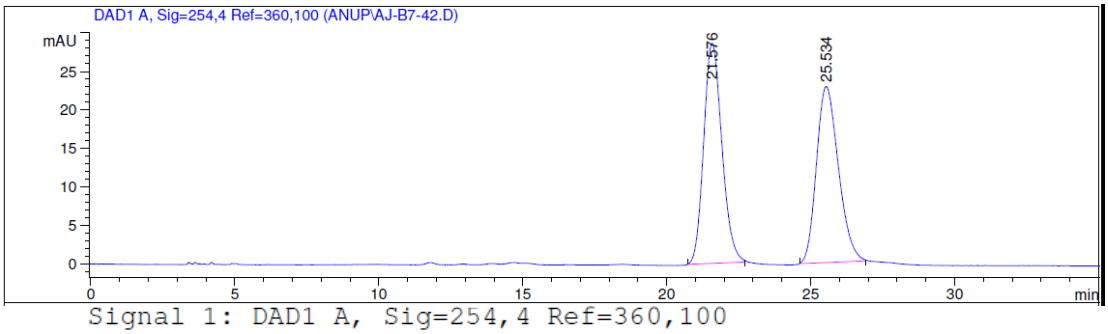


Signal 2: DAD1 B, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.556	MM	1.0835	1845.41748	28.38797	62.2100
2	47.687	MM	1.7687	1121.01392	10.56342	37.7900
Totals :				2966.43140	38.95139	

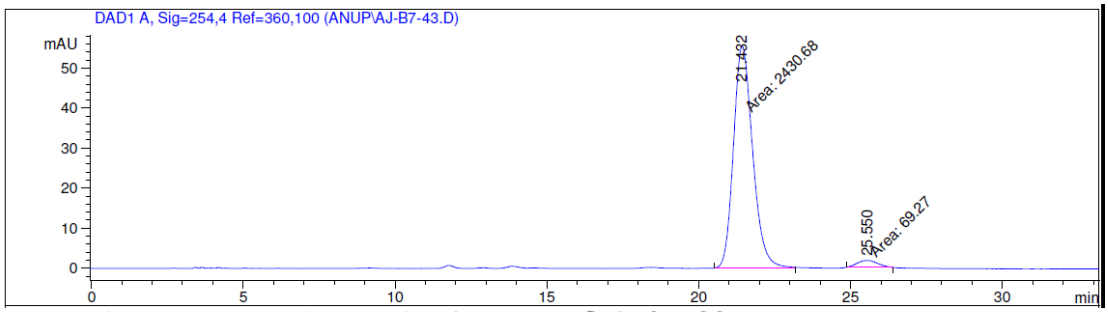


32



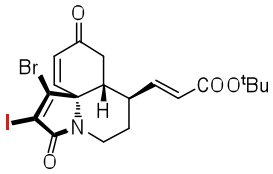
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.576	BB	0.6675	1252.11560	28.55925	50.8397
2	25.534	BB	0.7902	1210.75330	22.85095	49.1603
Totals :				2462.86890	51.41020	



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.432	MM	0.7318	2430.67700	55.36012	97.2291
2	25.550	MM	0.7127	69.27002	1.61996	2.7709
Totals :				2499.94702	56.98008	



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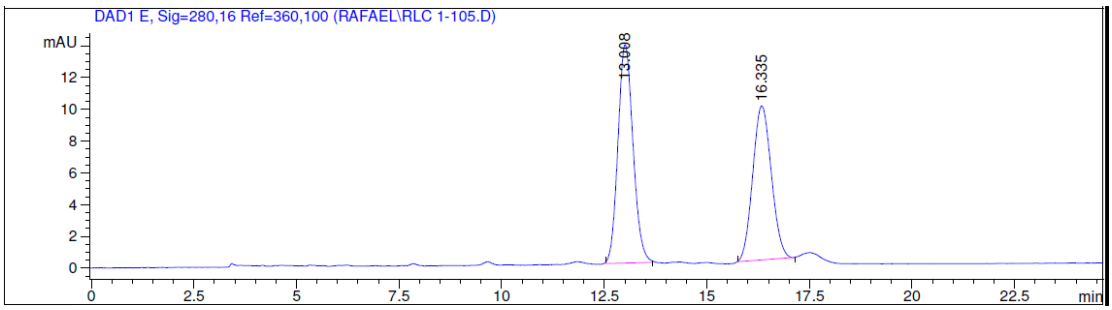
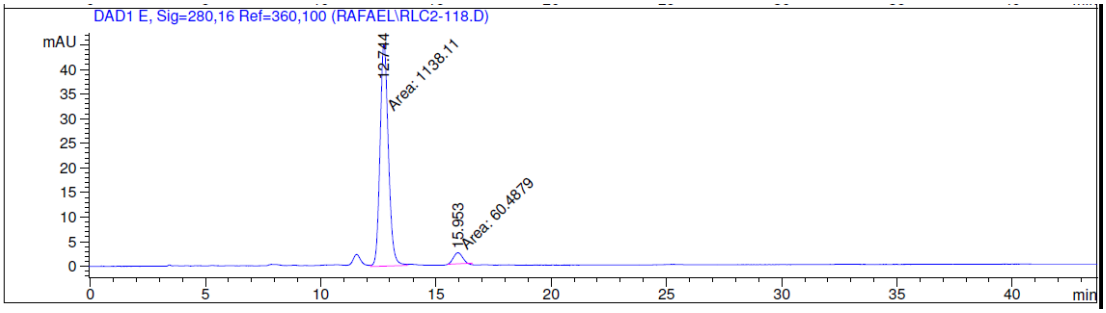


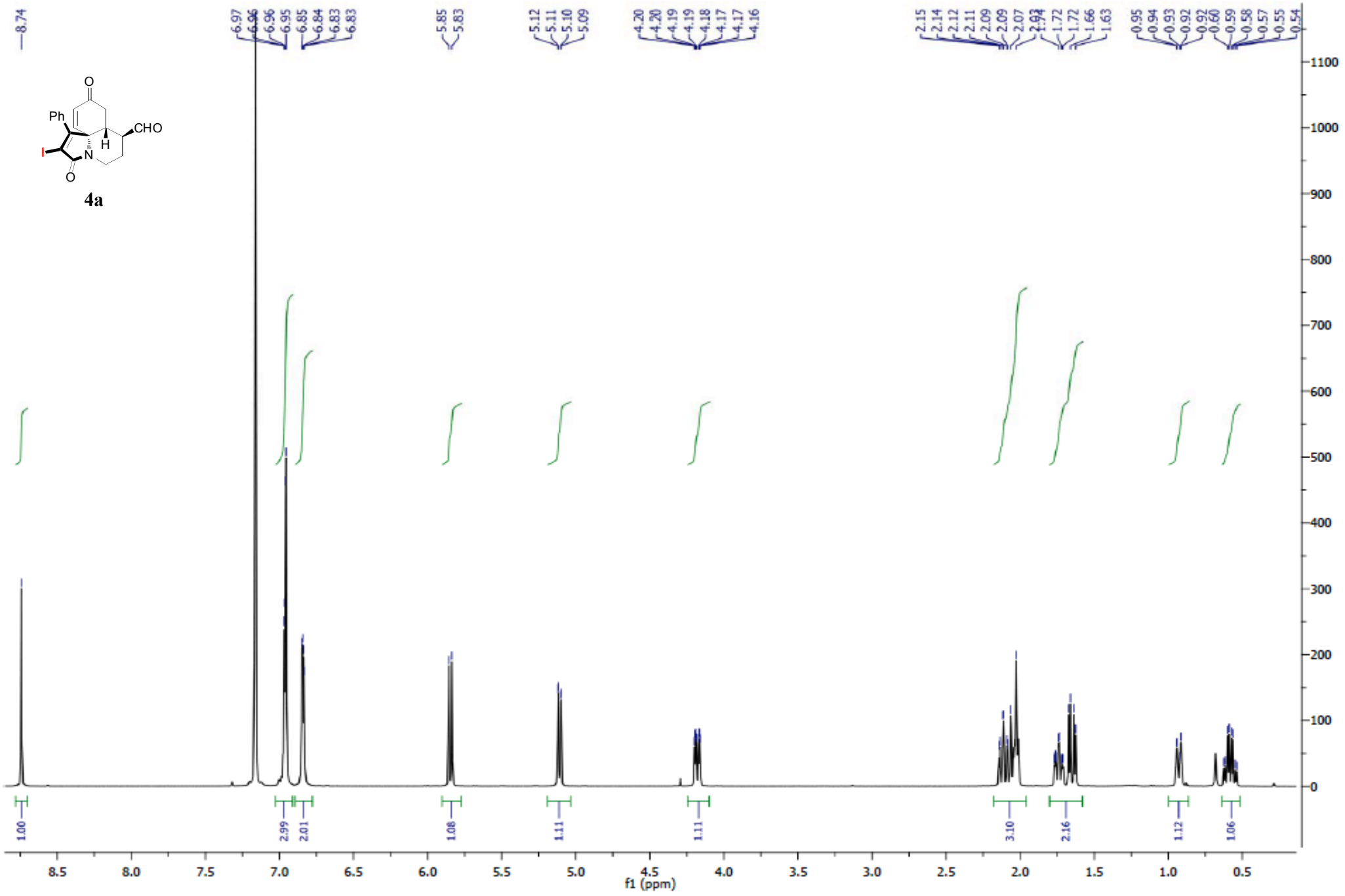
Signal 4: DAD1 D, Sig=230,16 Ref=360,100

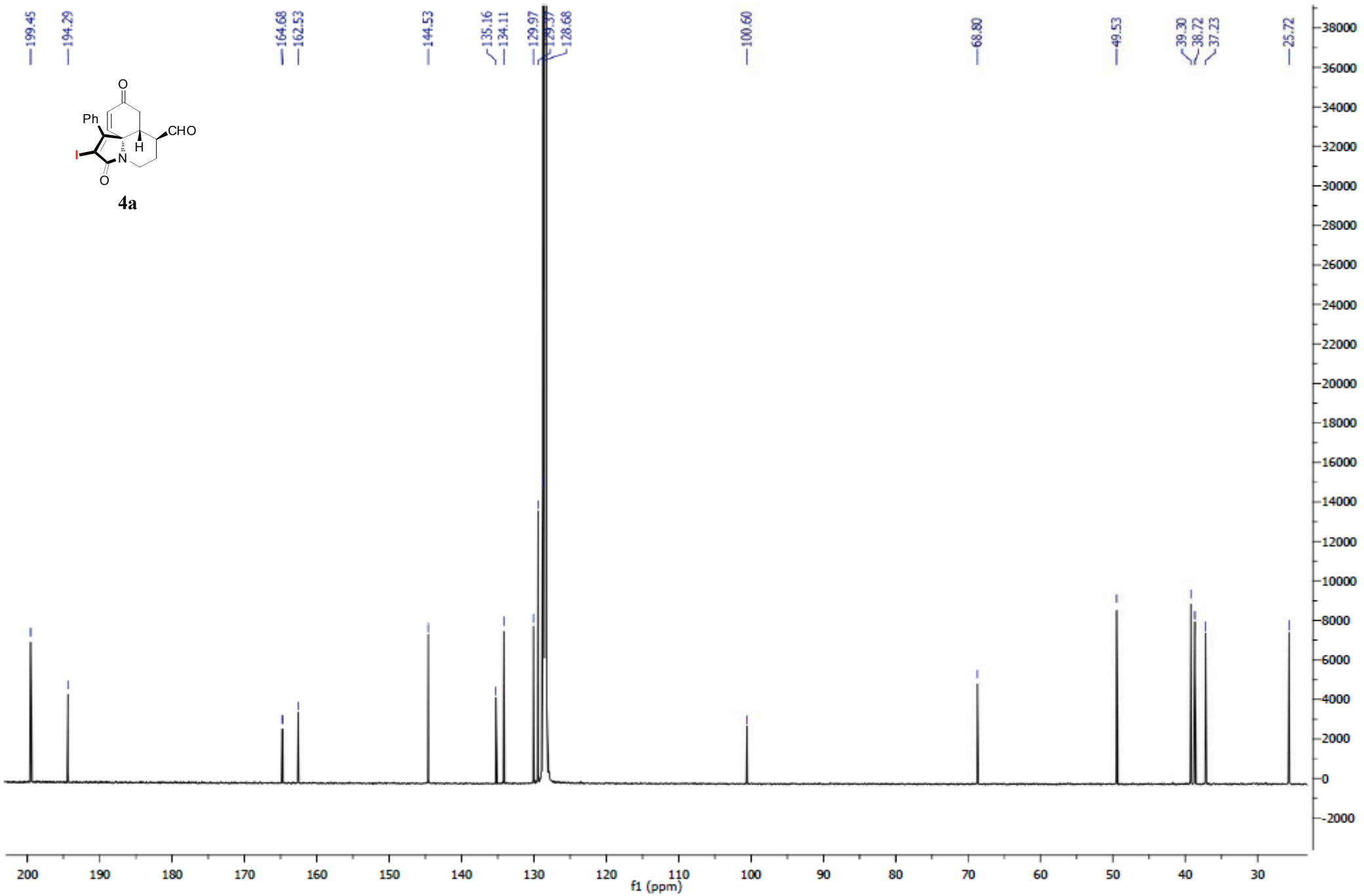
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.007	BB	0.3952	1730.73657	67.49666	51.7714
2	16.336	BB	0.5123	1612.29944	48.69204	48.2286
Totals :				3343.03601	116.18870	



Signal 5: DAD1 E, Sig=280,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.744	MM	0.4210	1138.10669	45.05976	94.9534
2	15.953	MM	0.4515	60.48792	2.23300	5.0466
Totals :				1198.59461	47.29277	





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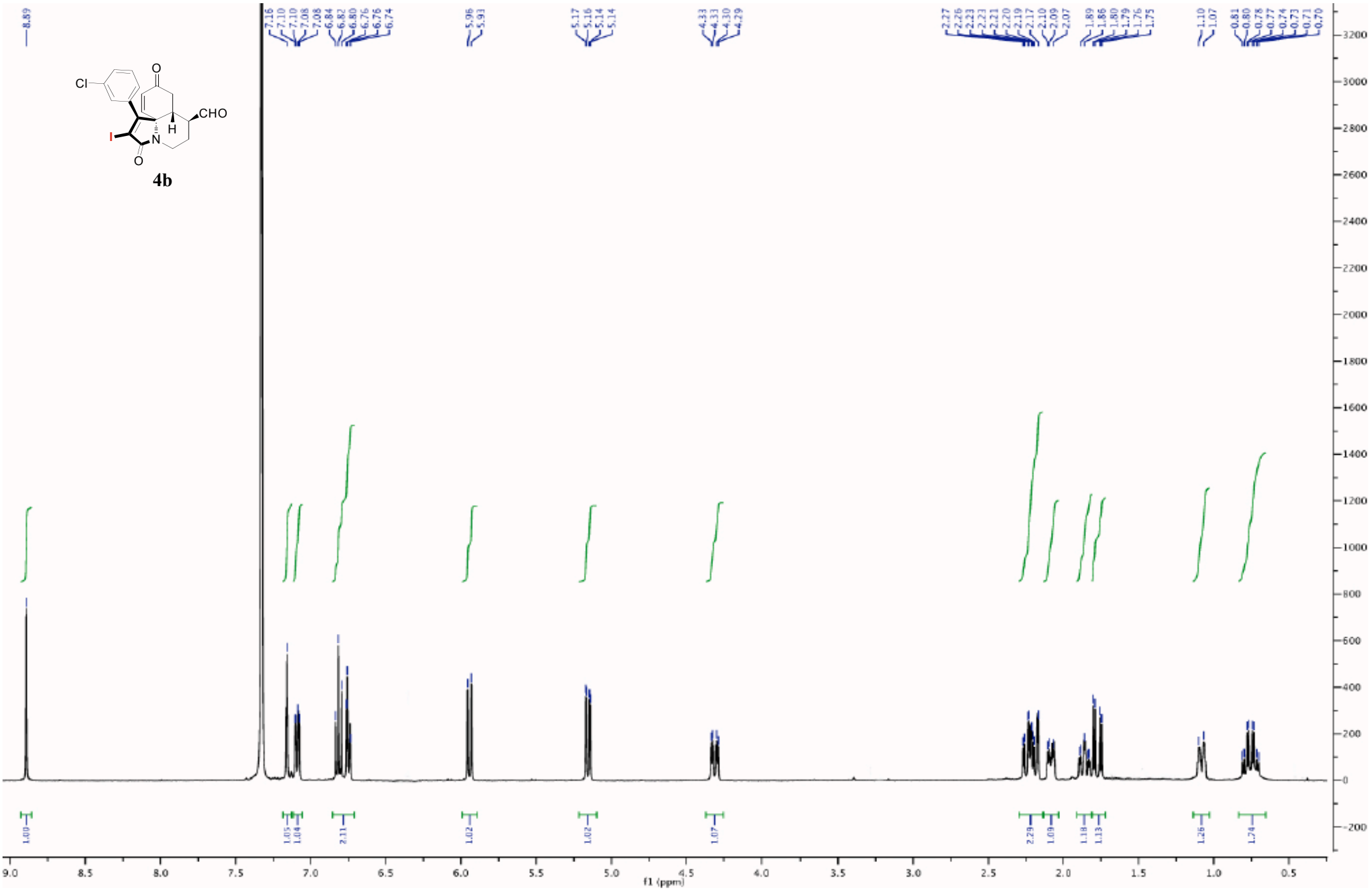

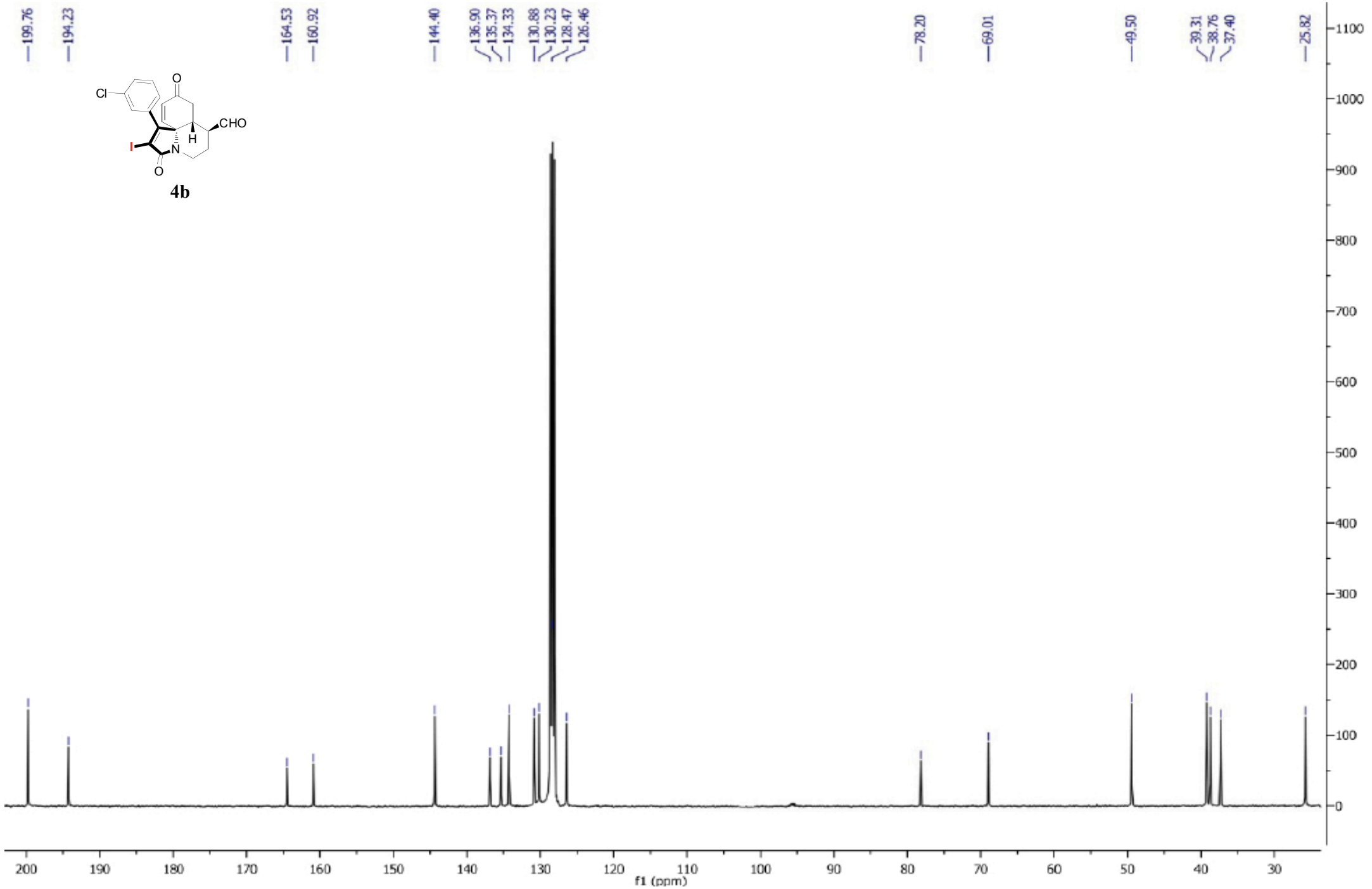

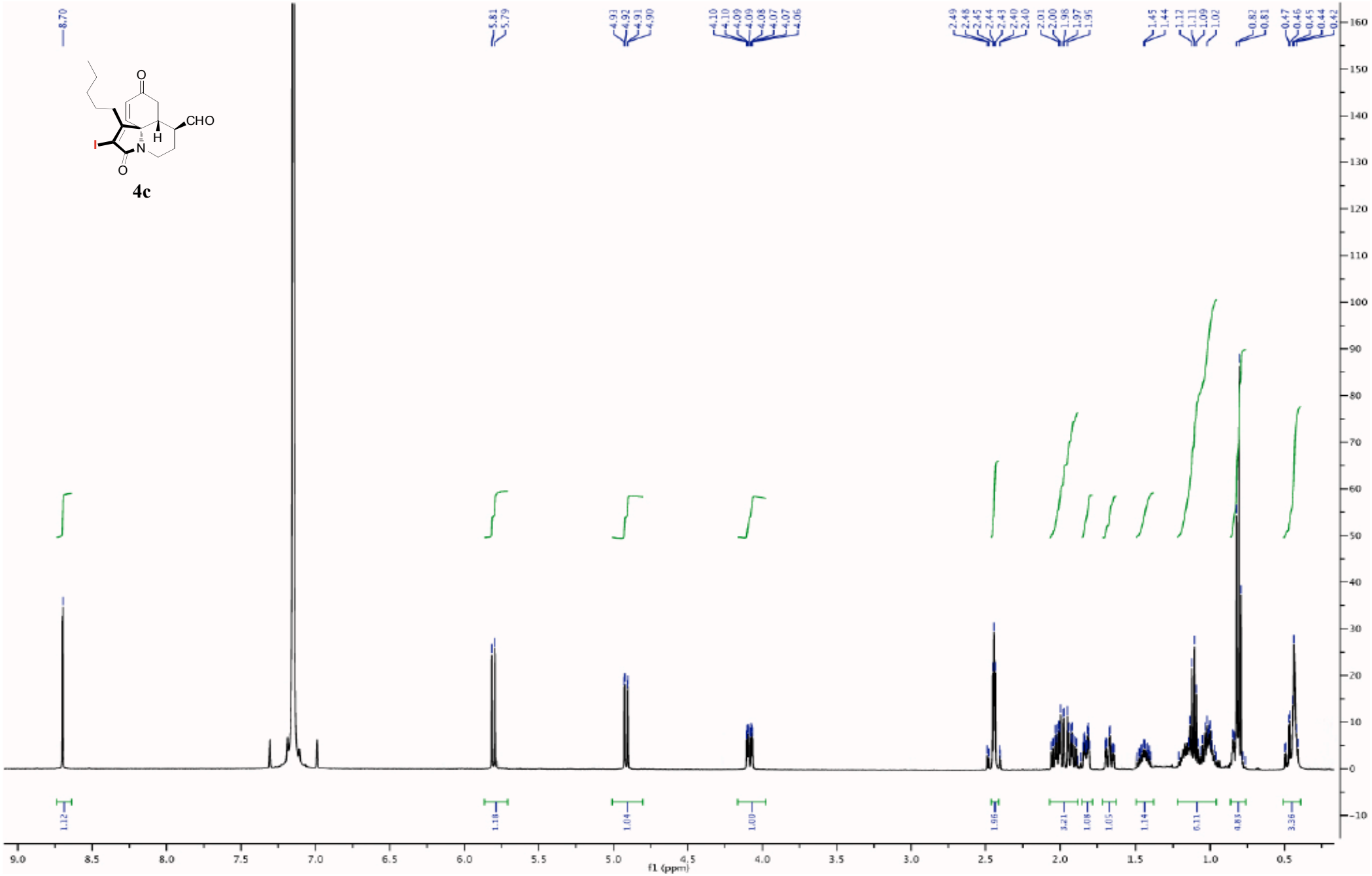

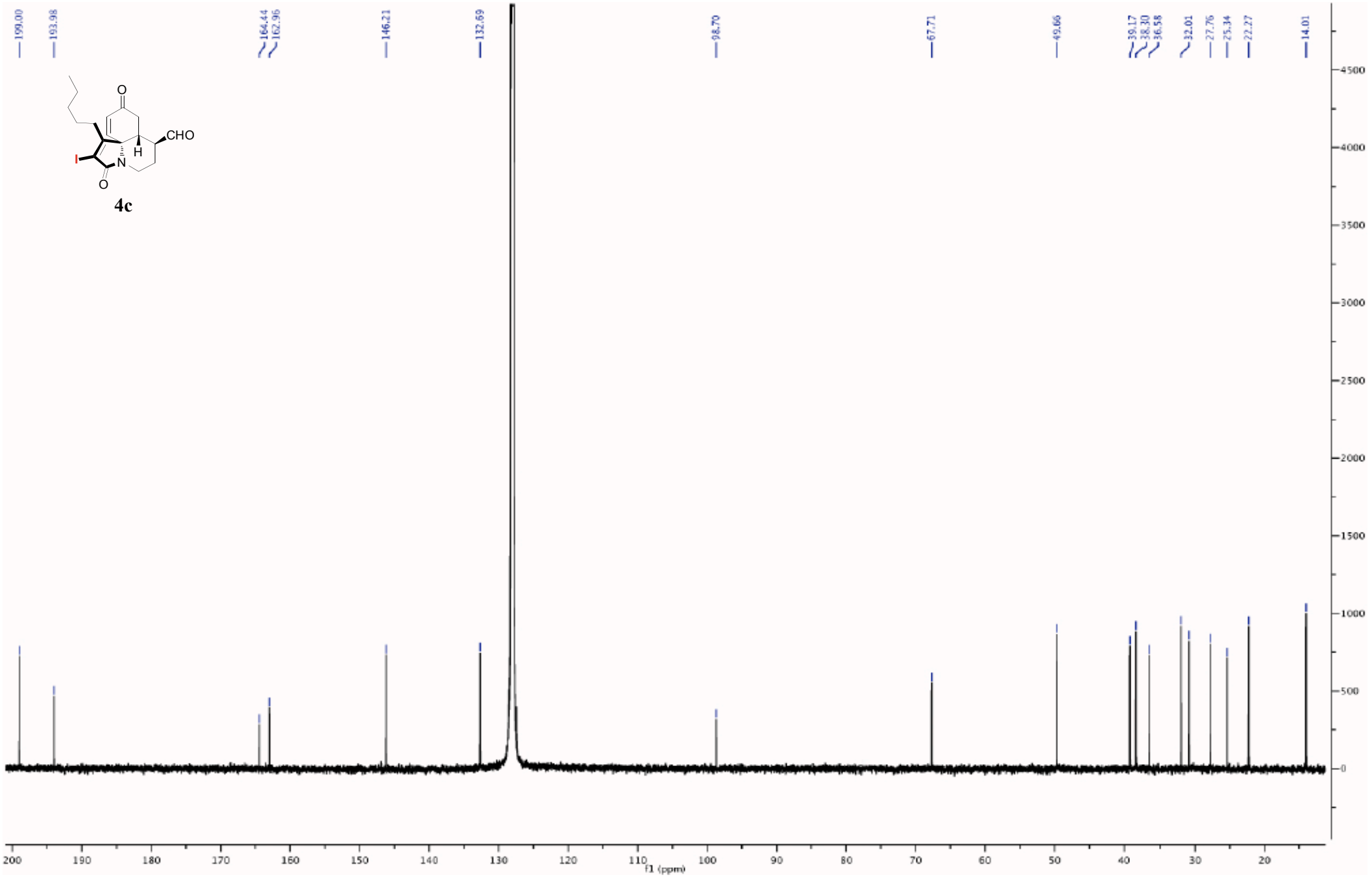

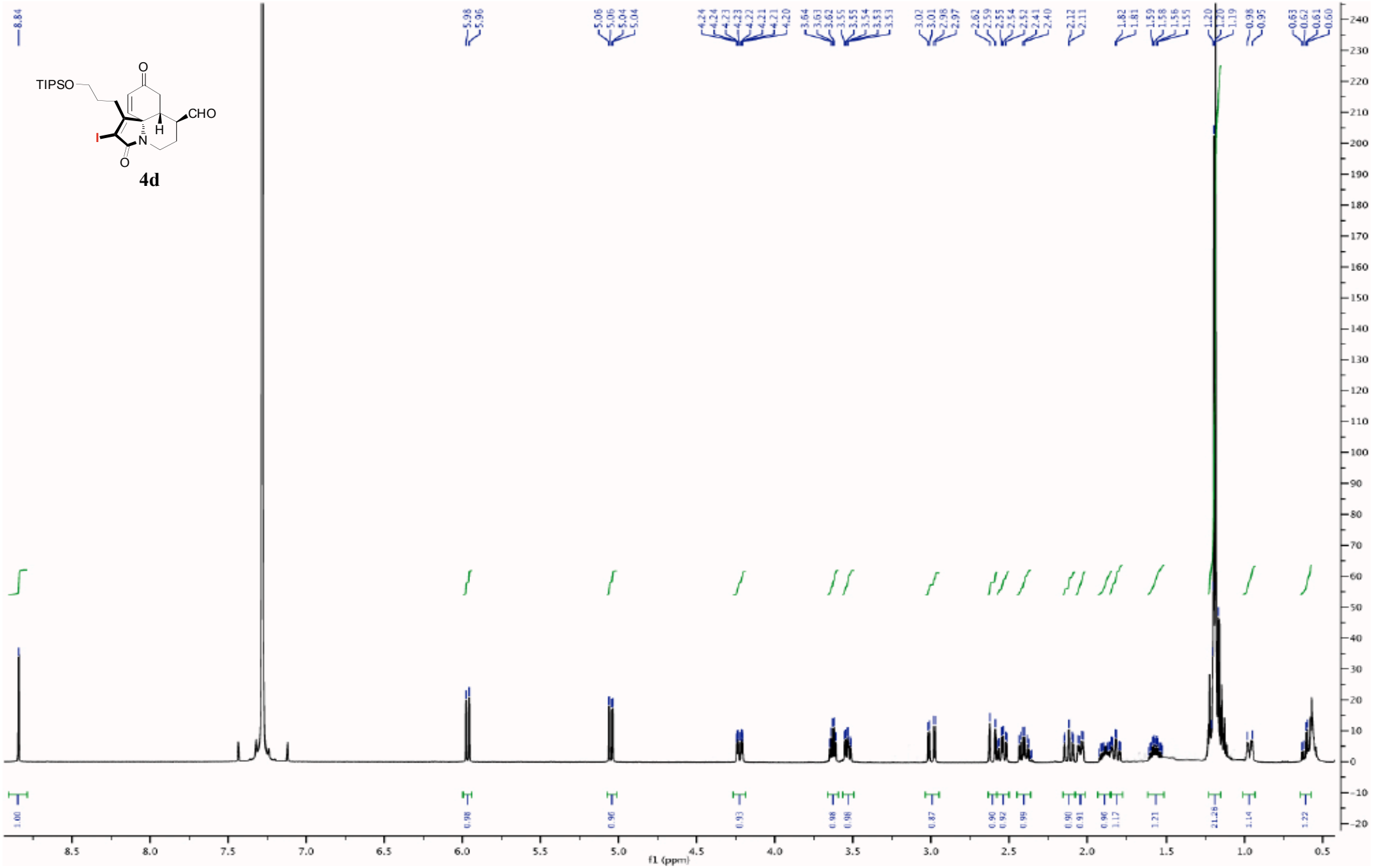

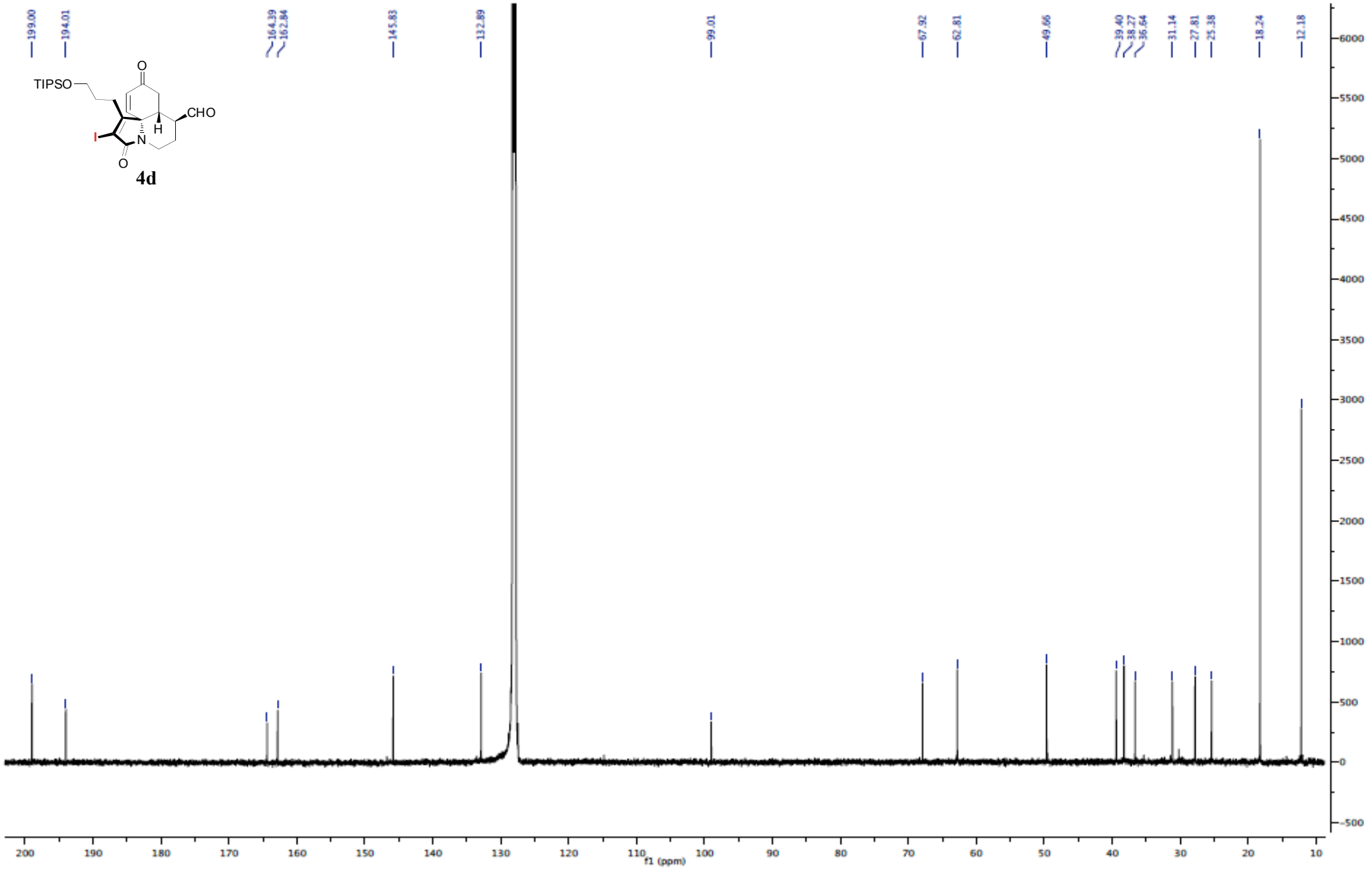

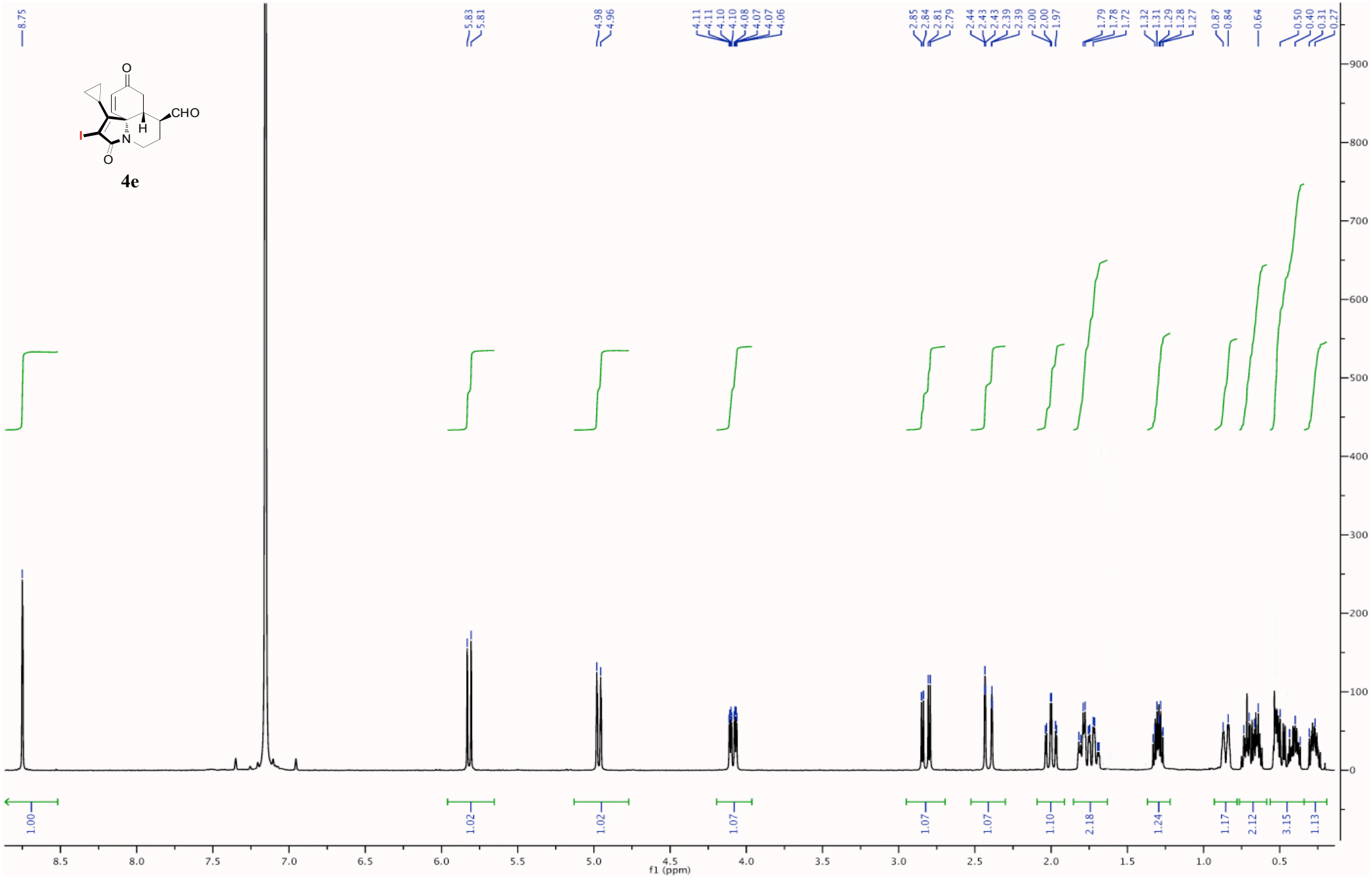

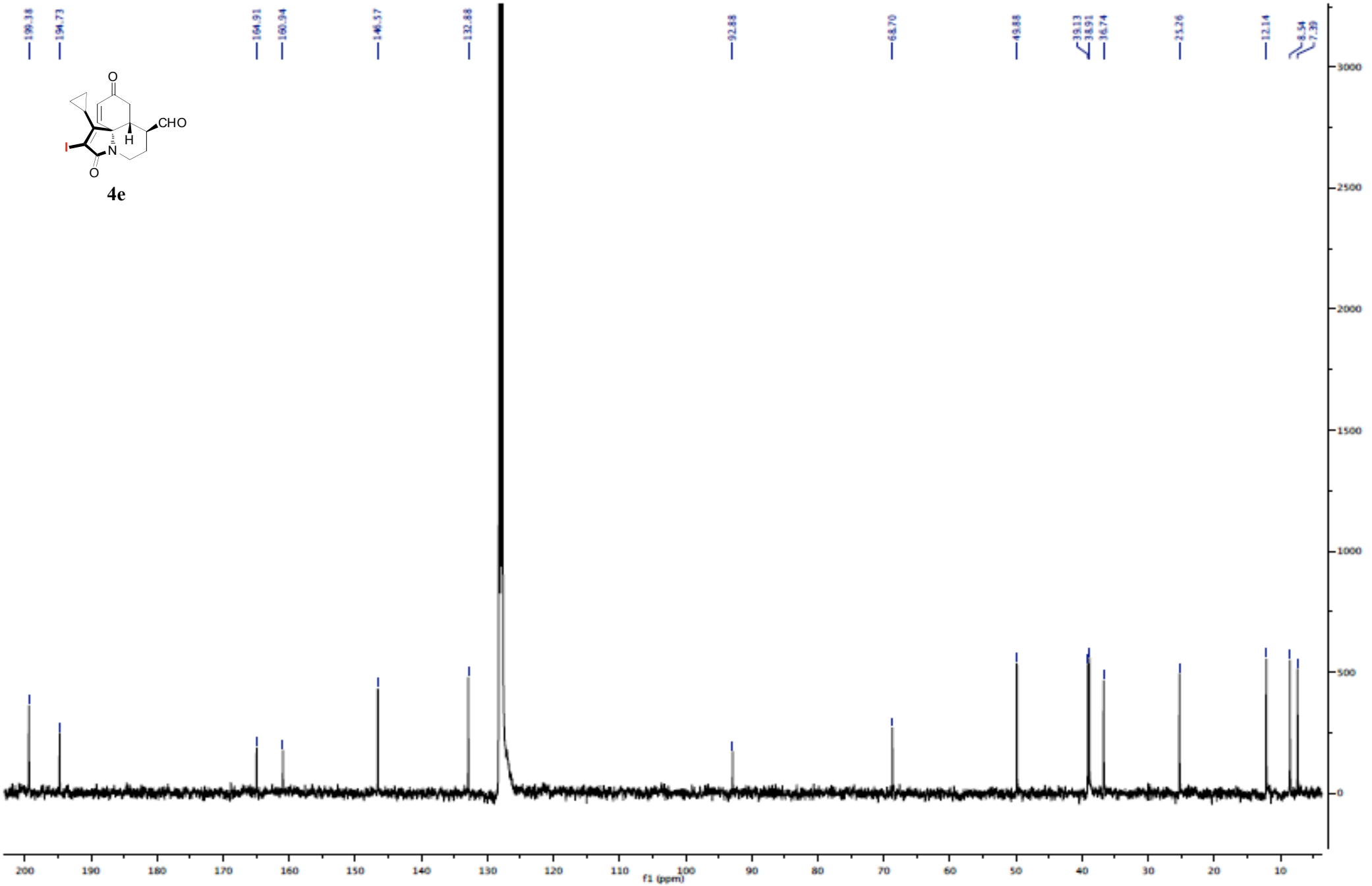

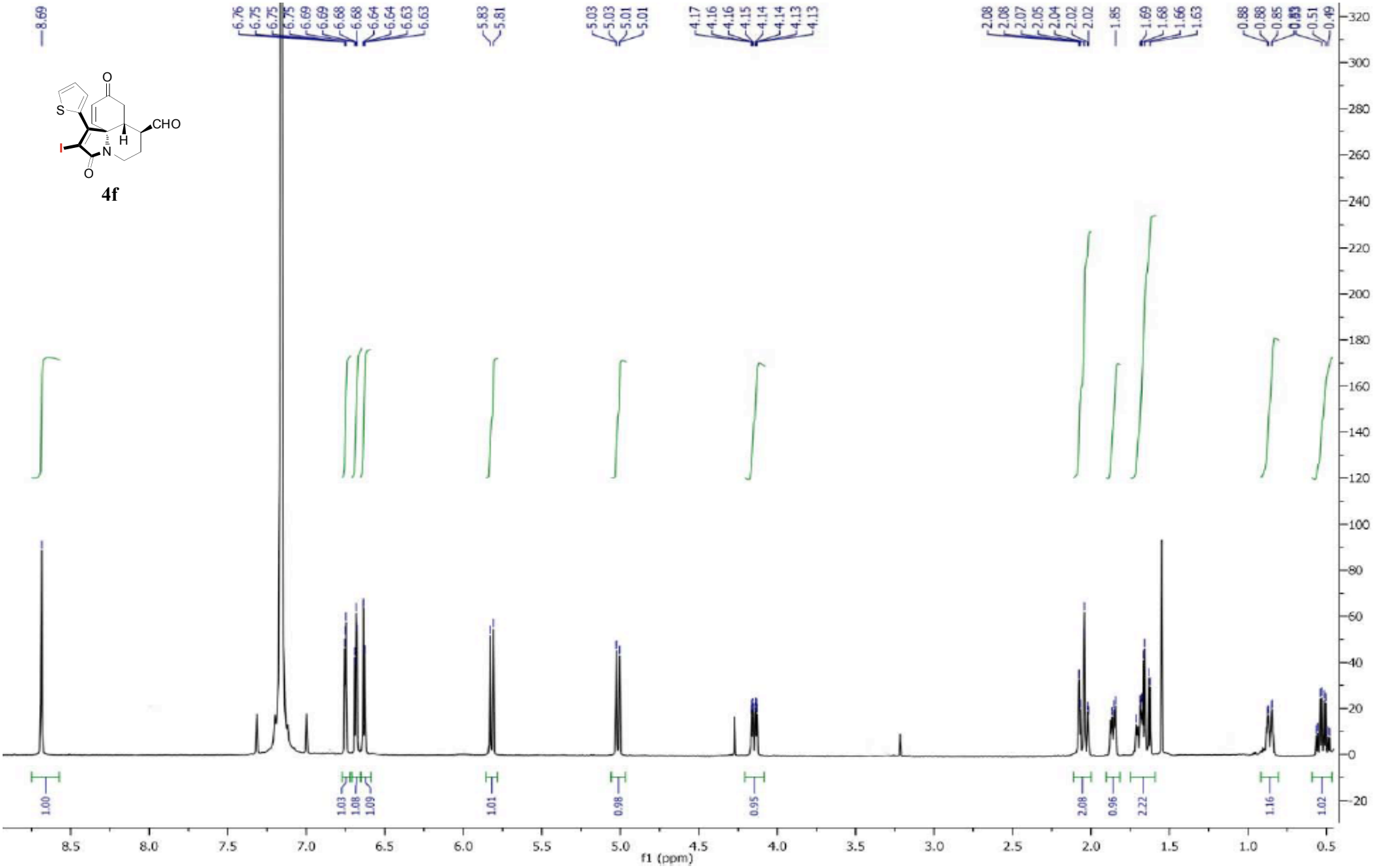

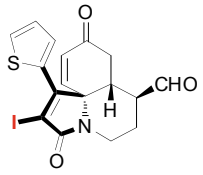

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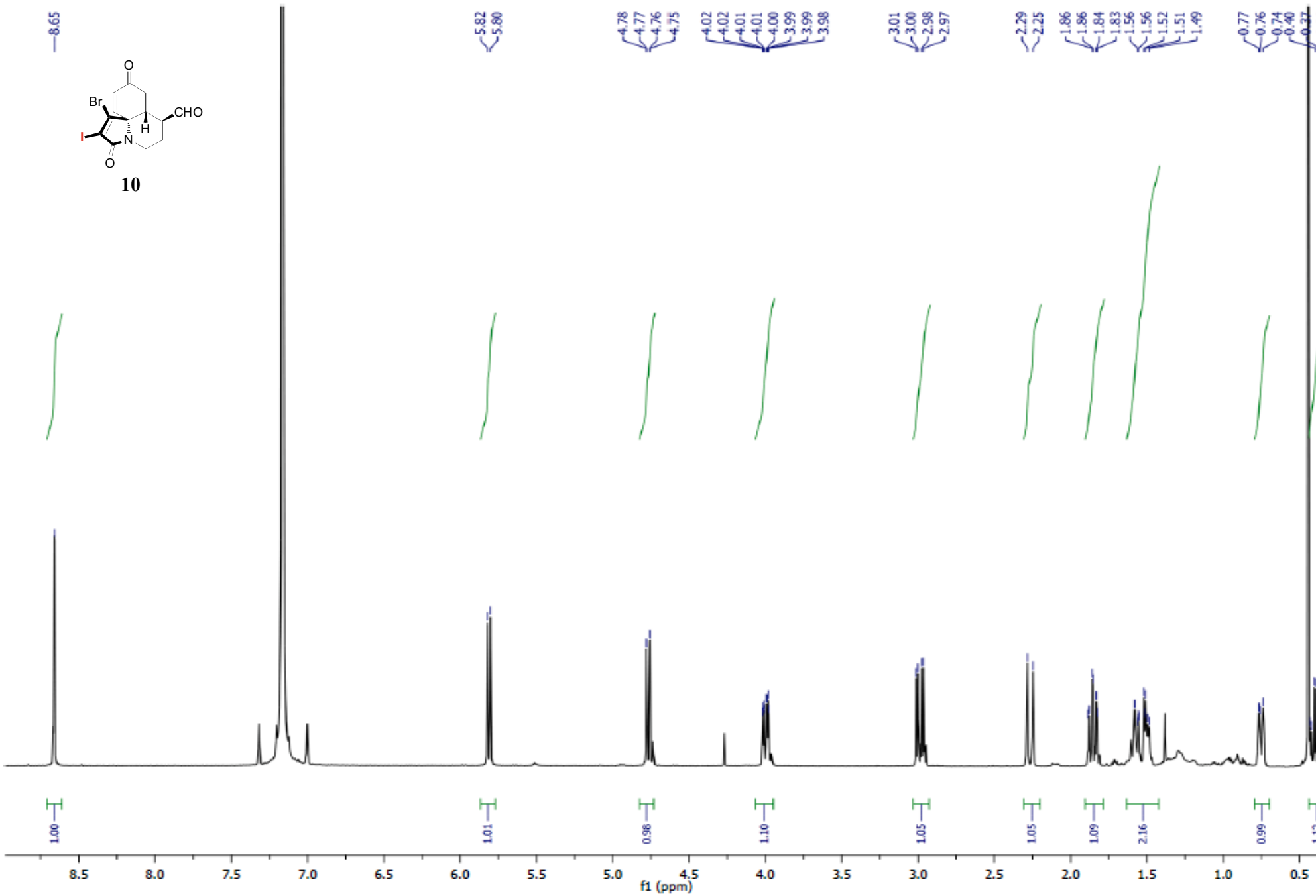
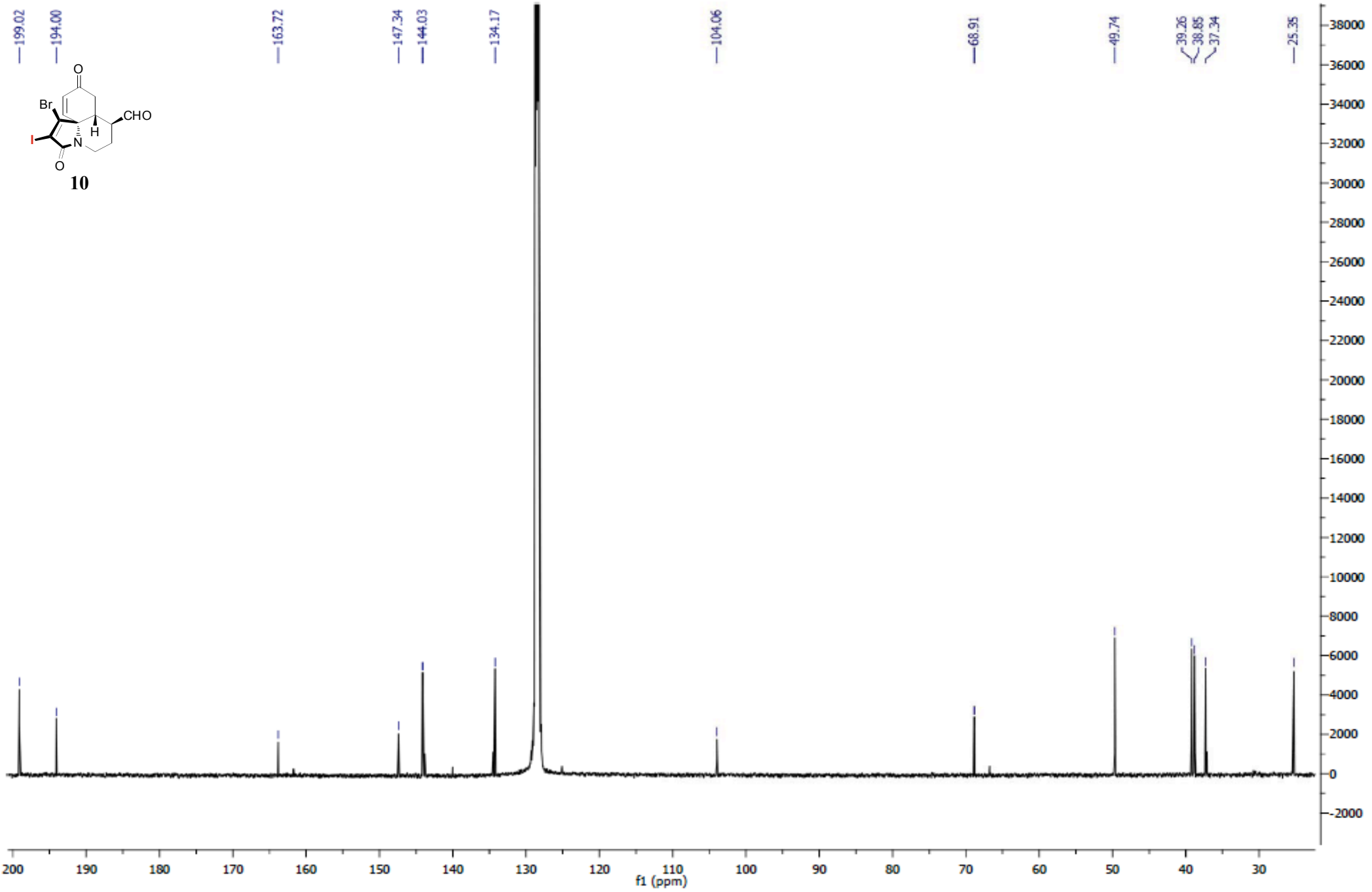
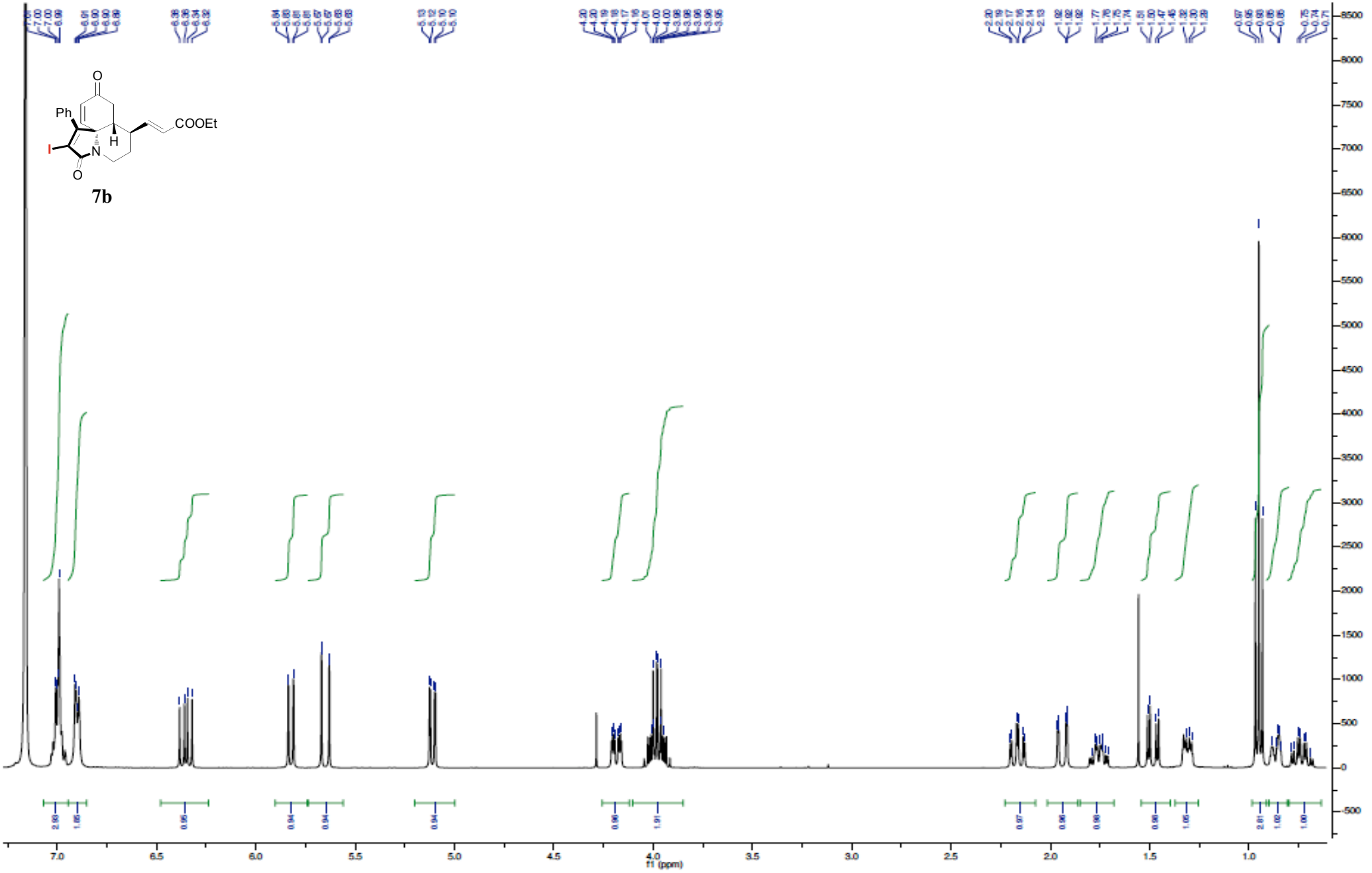
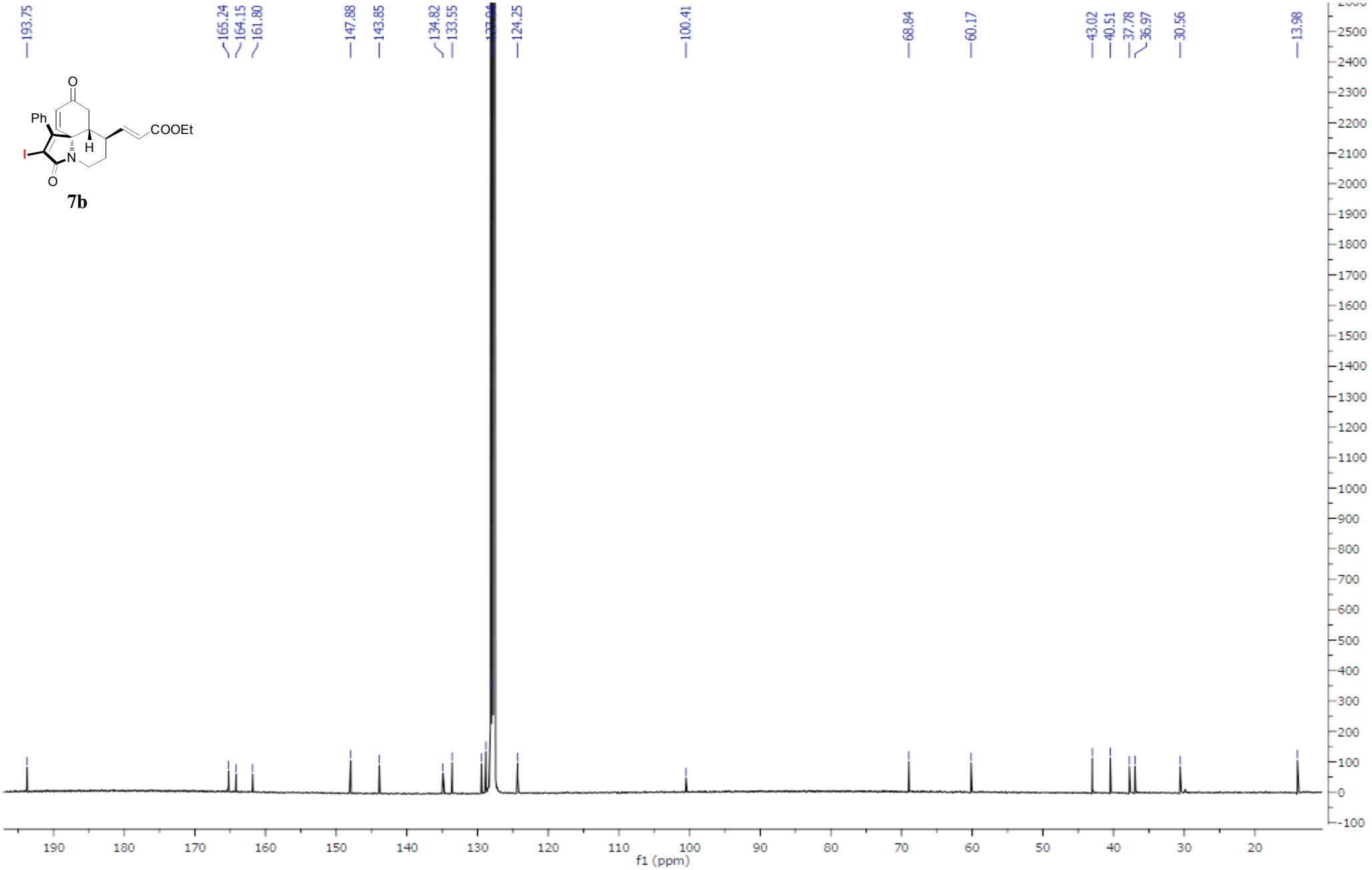


10







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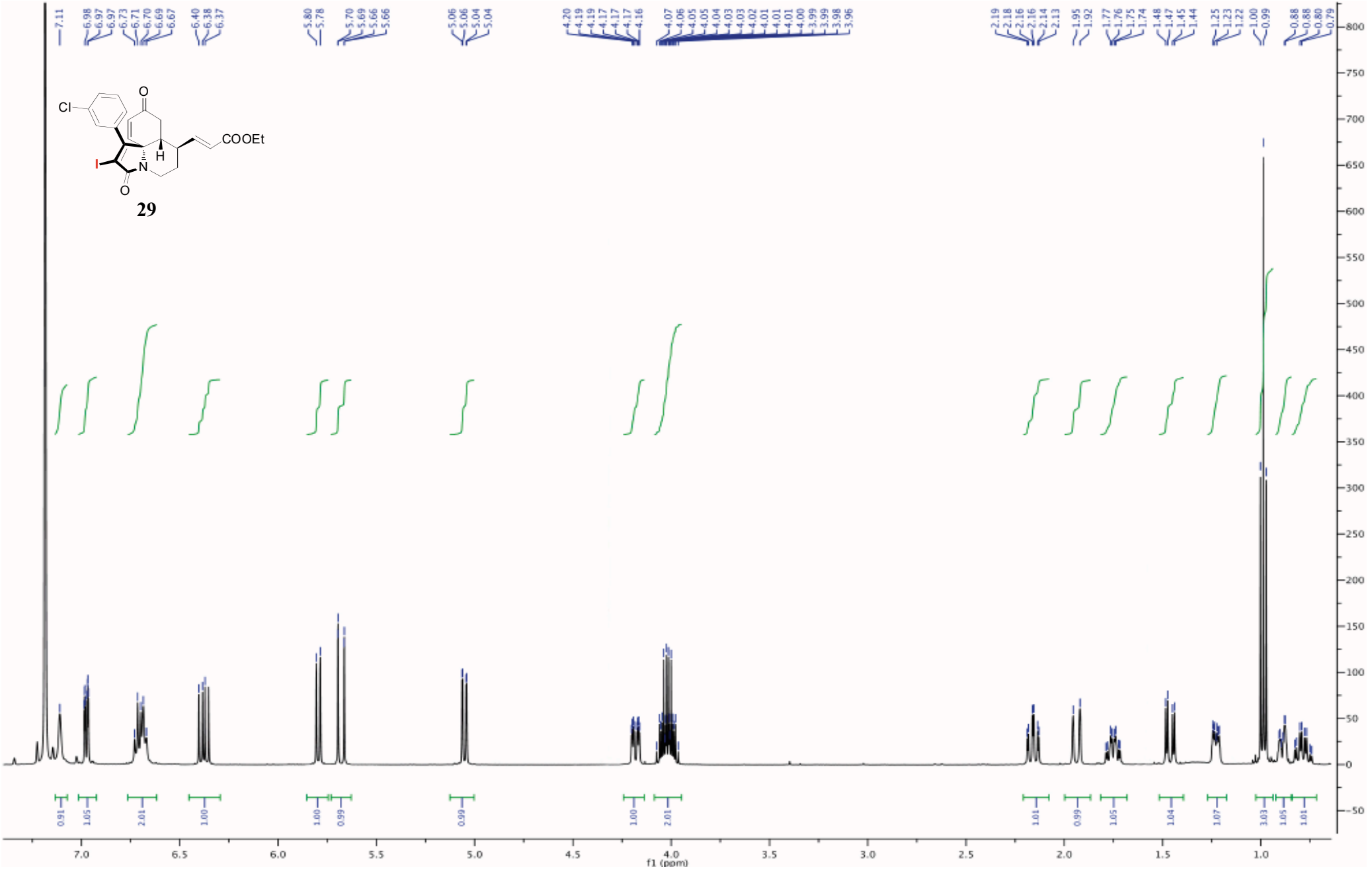

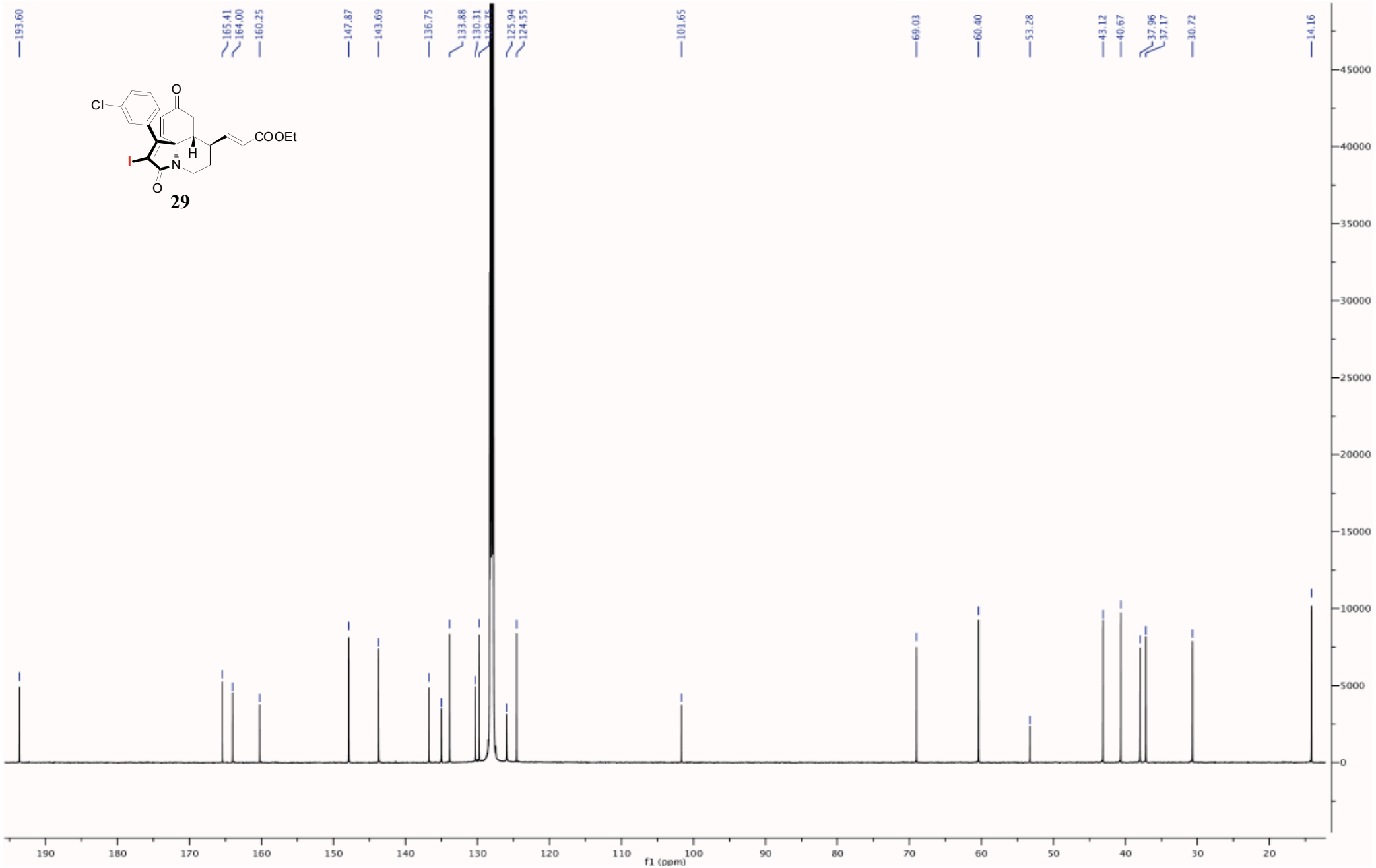

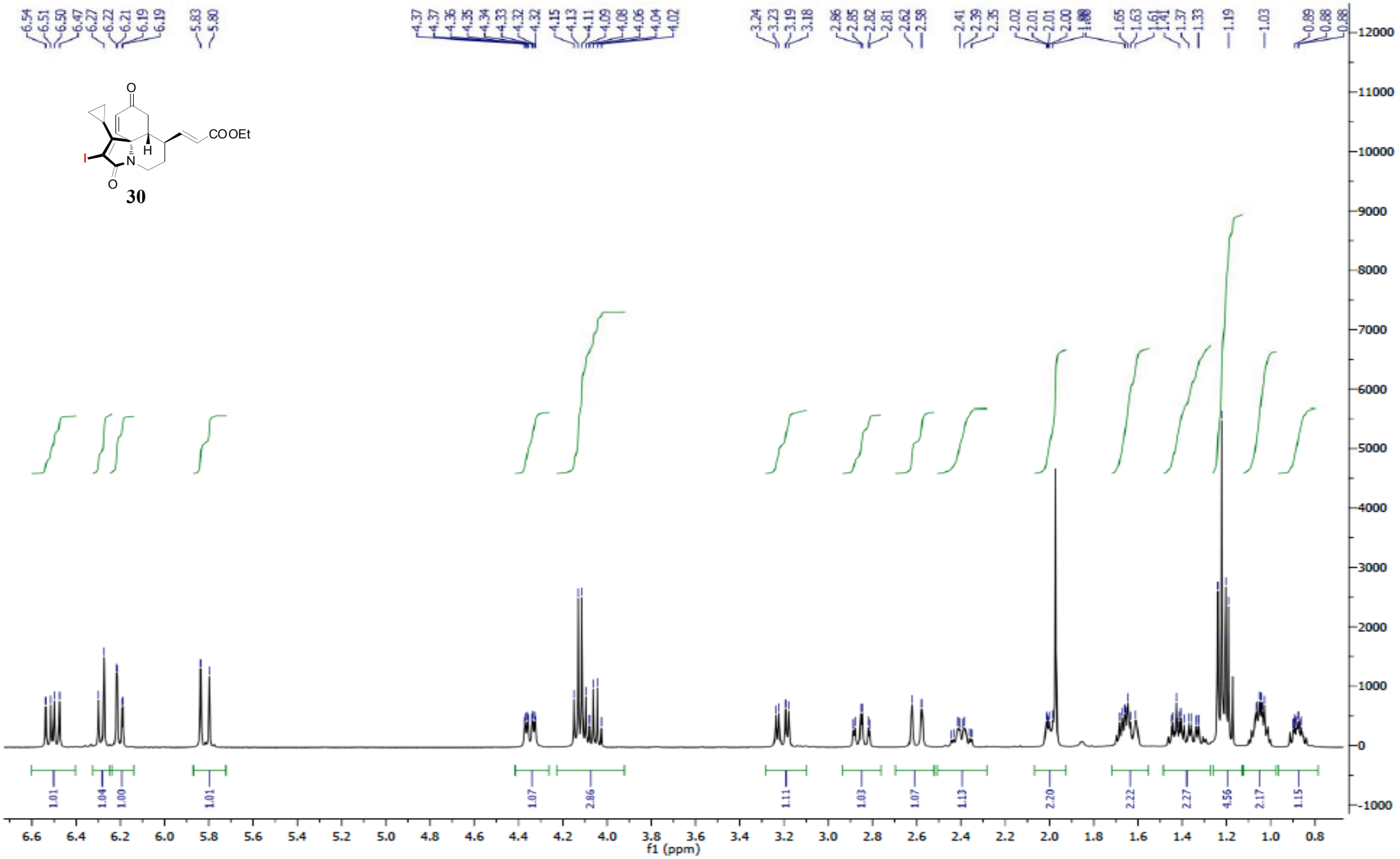

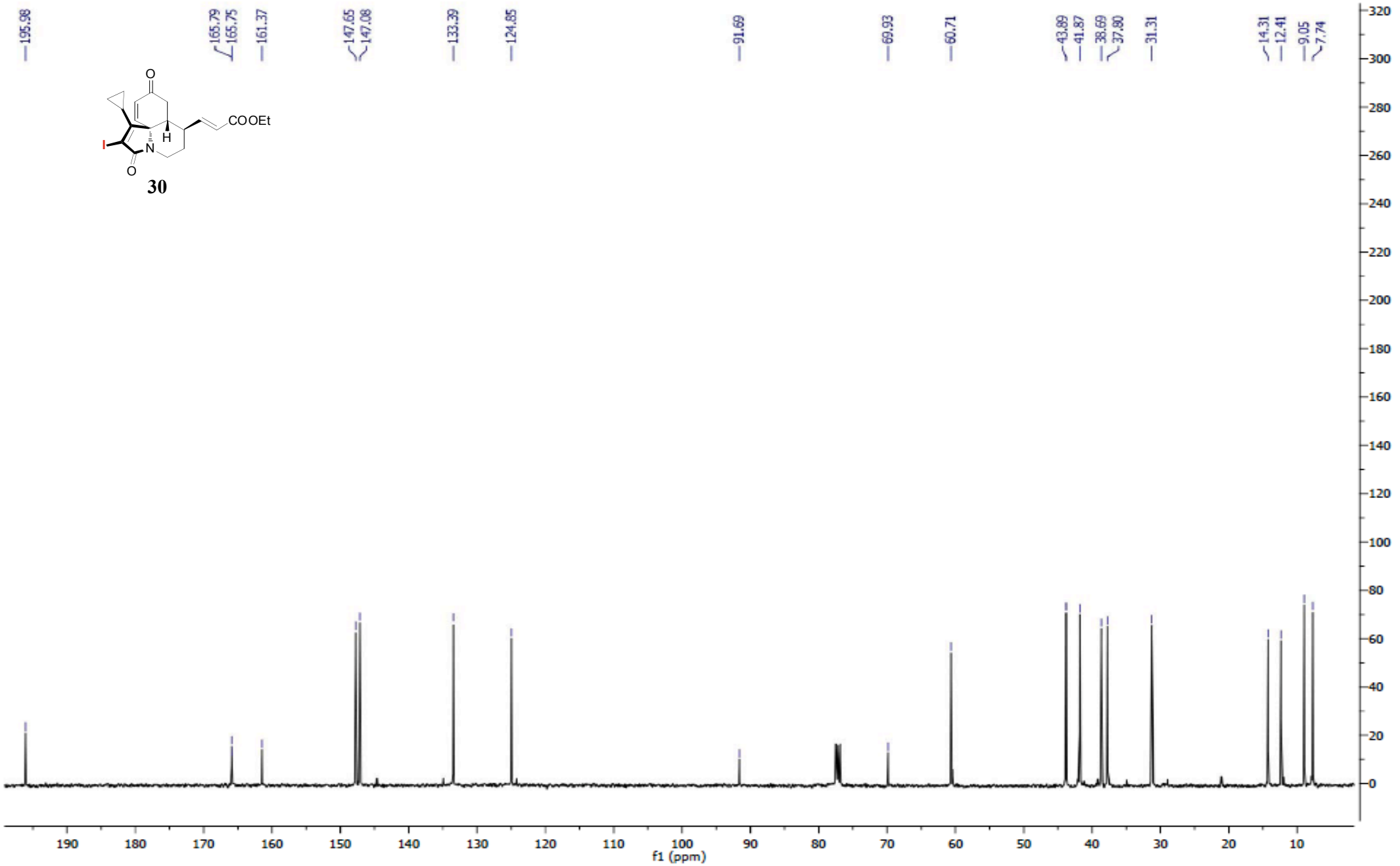

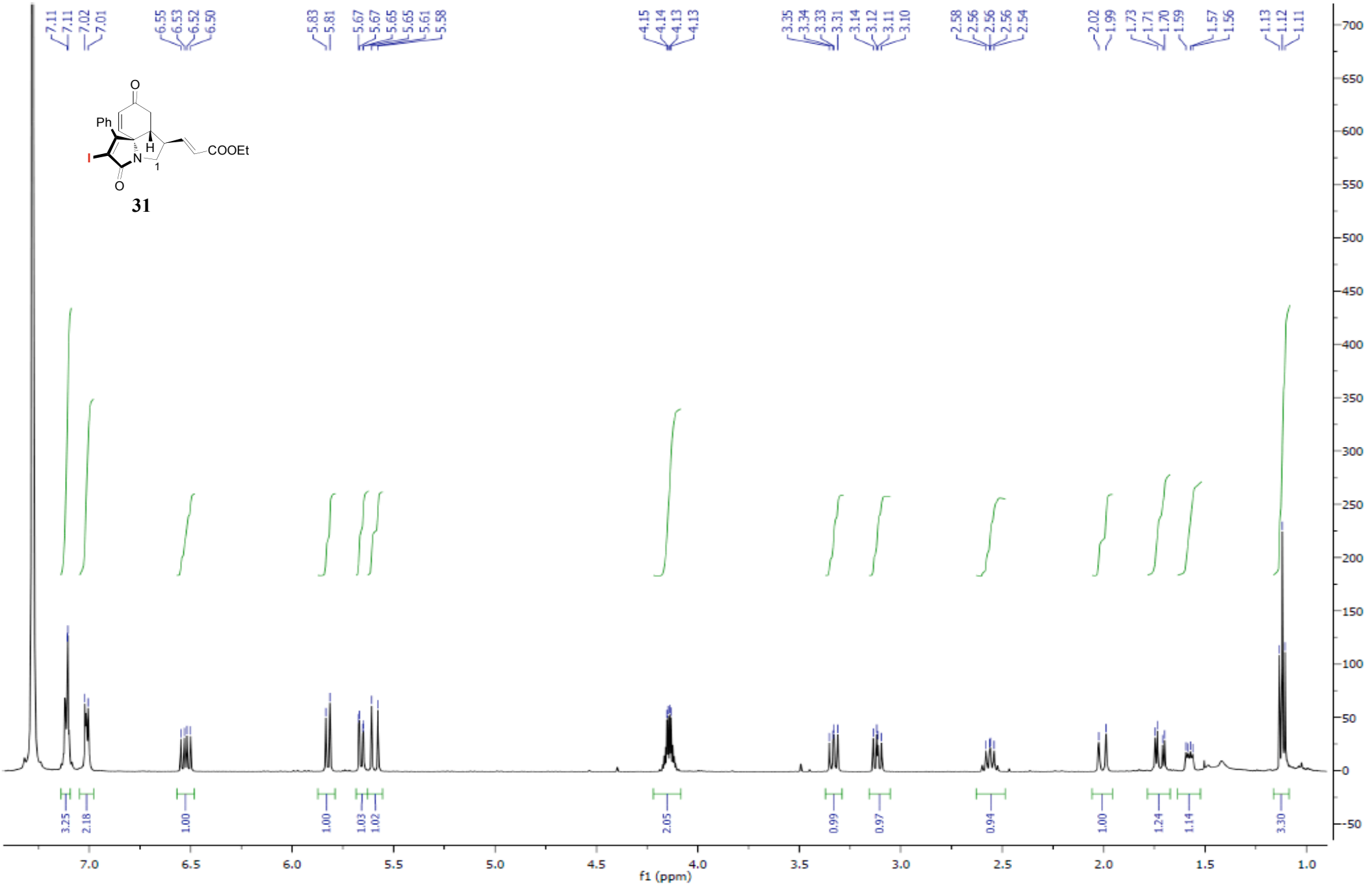

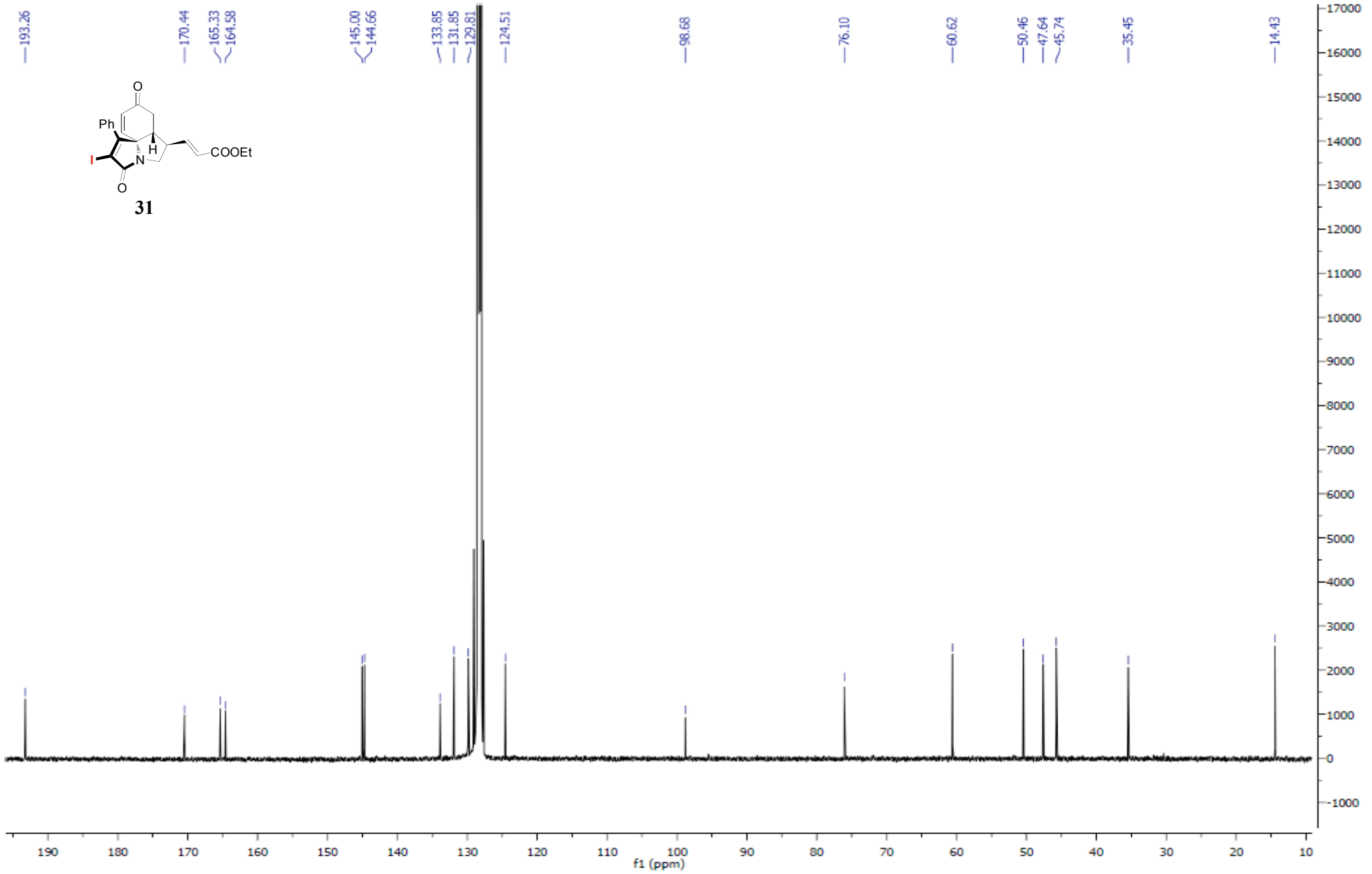

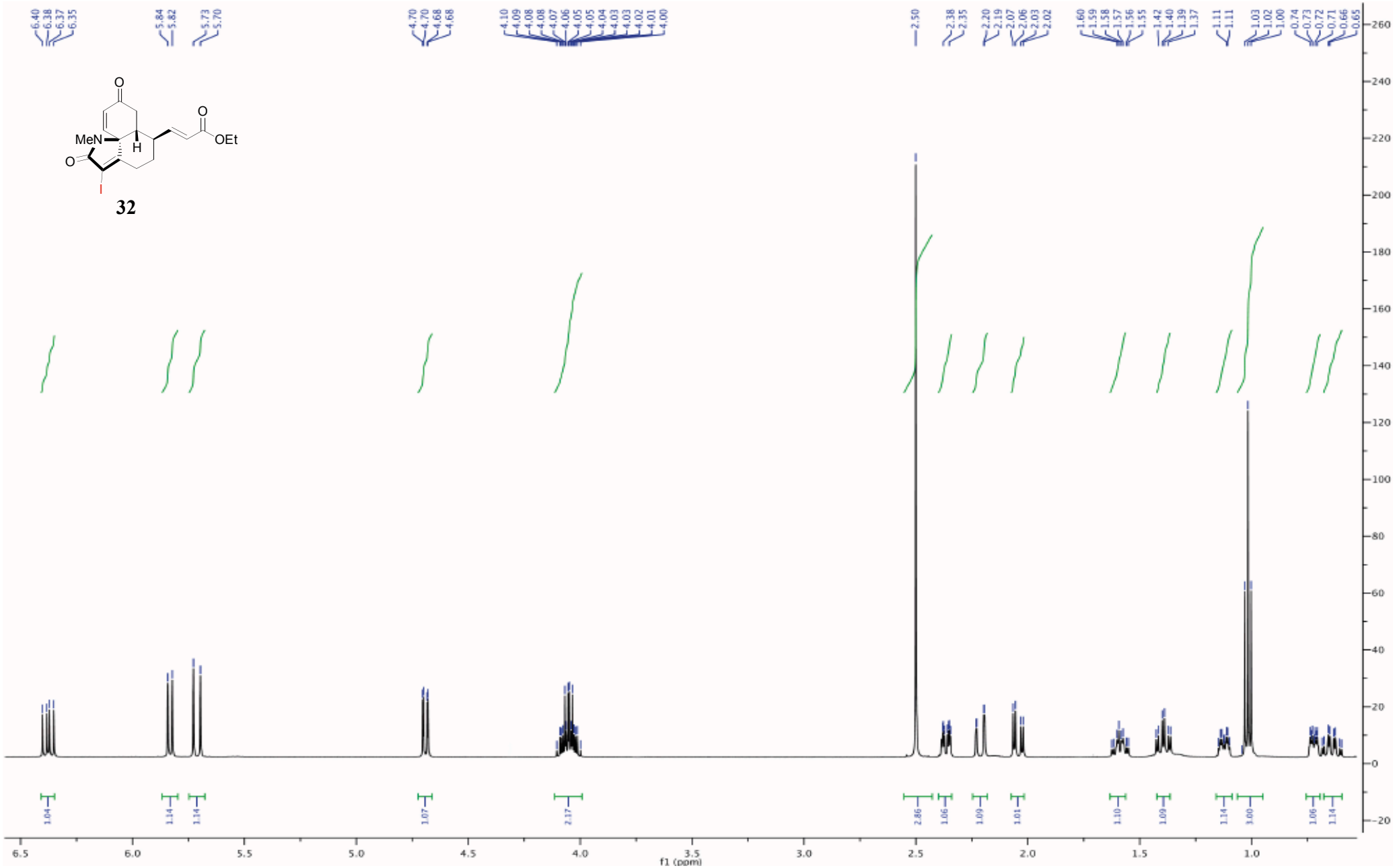

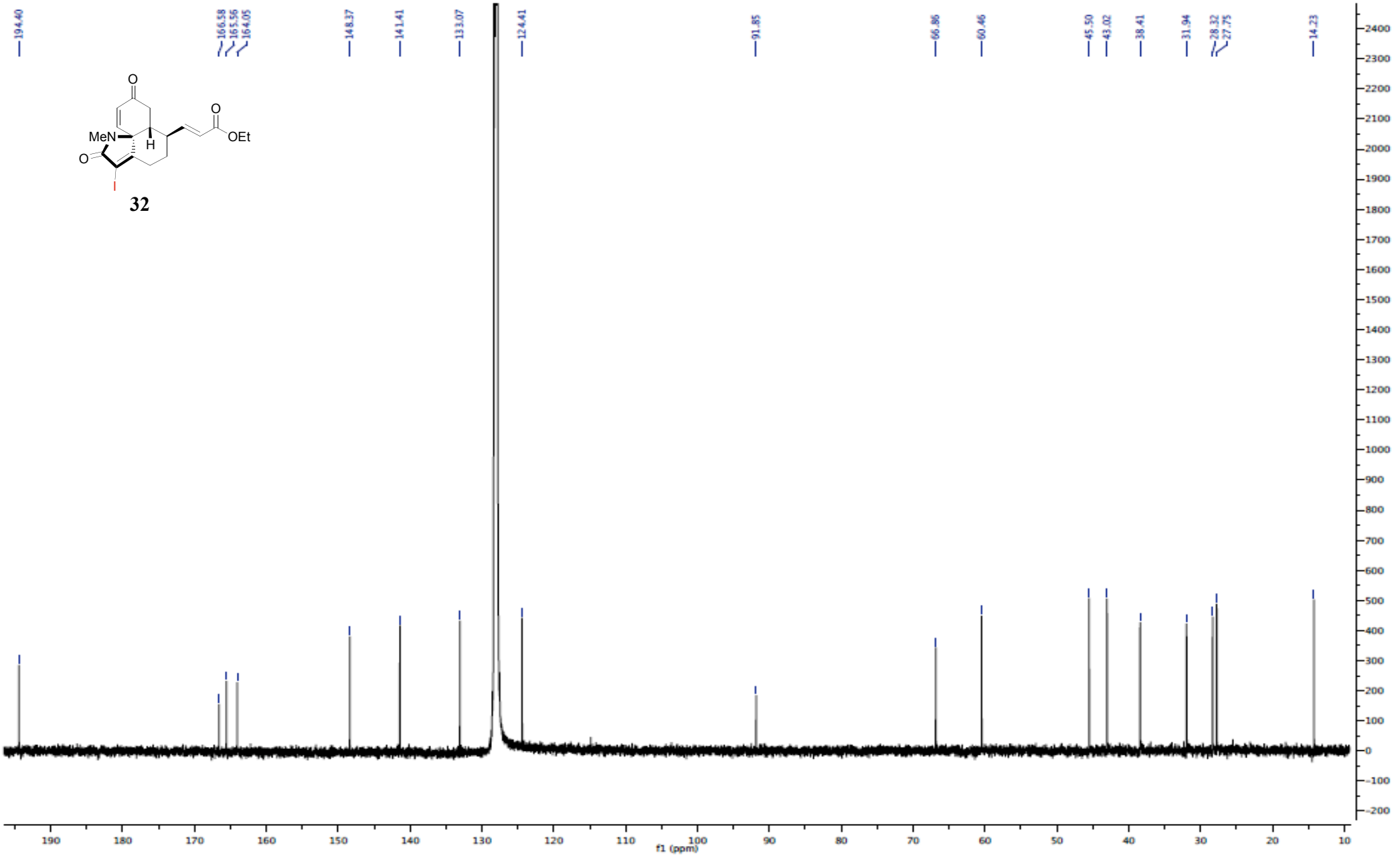

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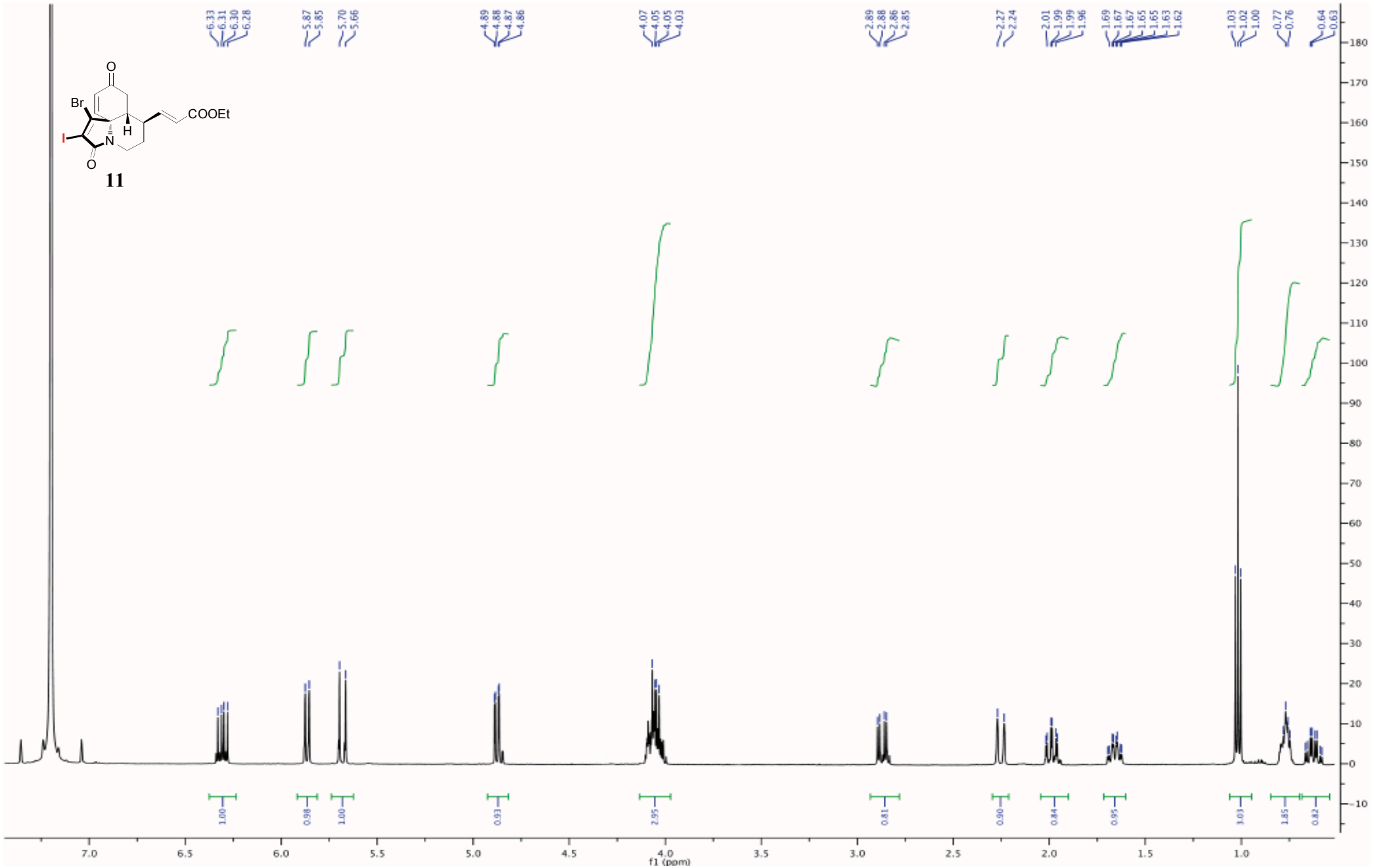

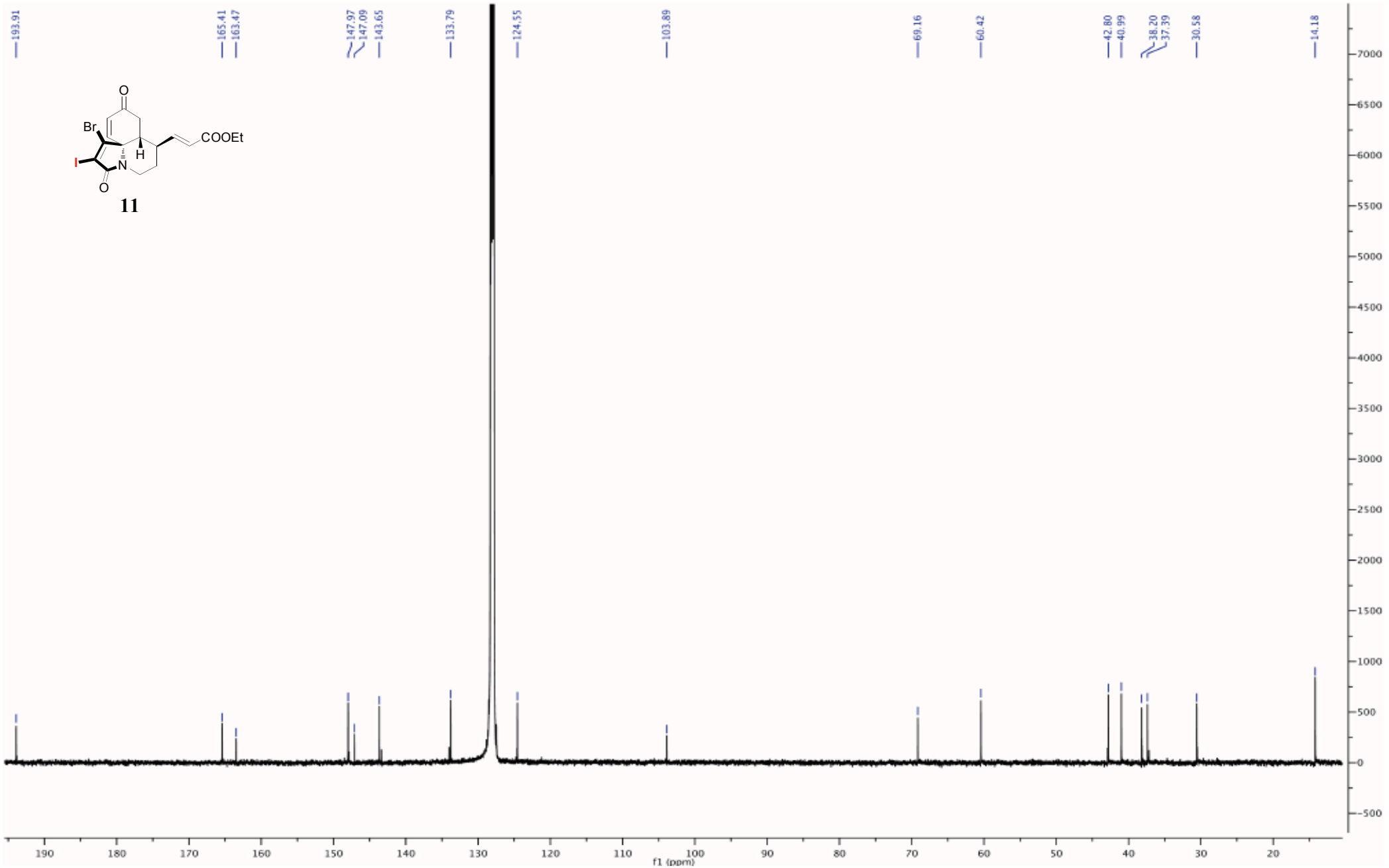

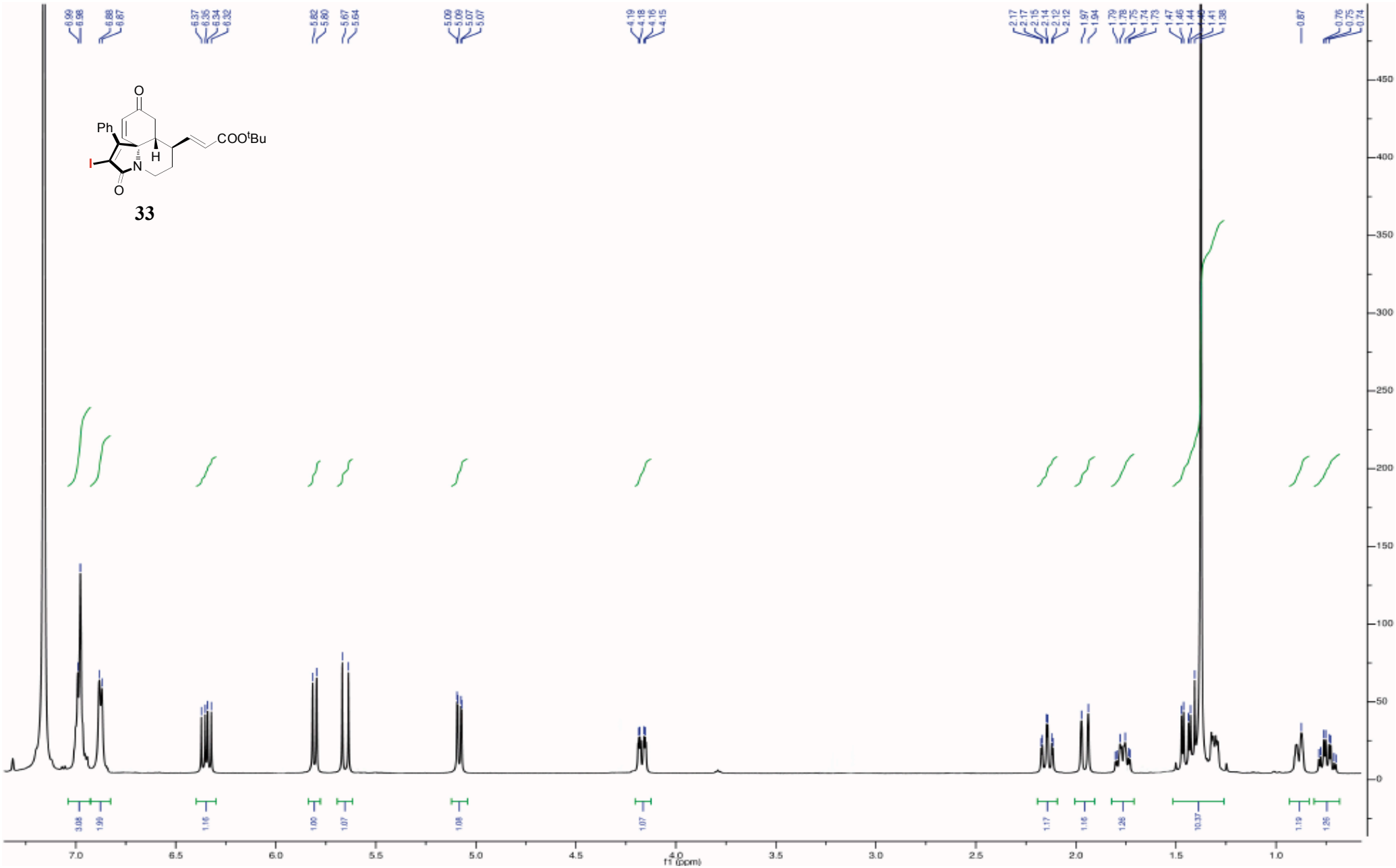

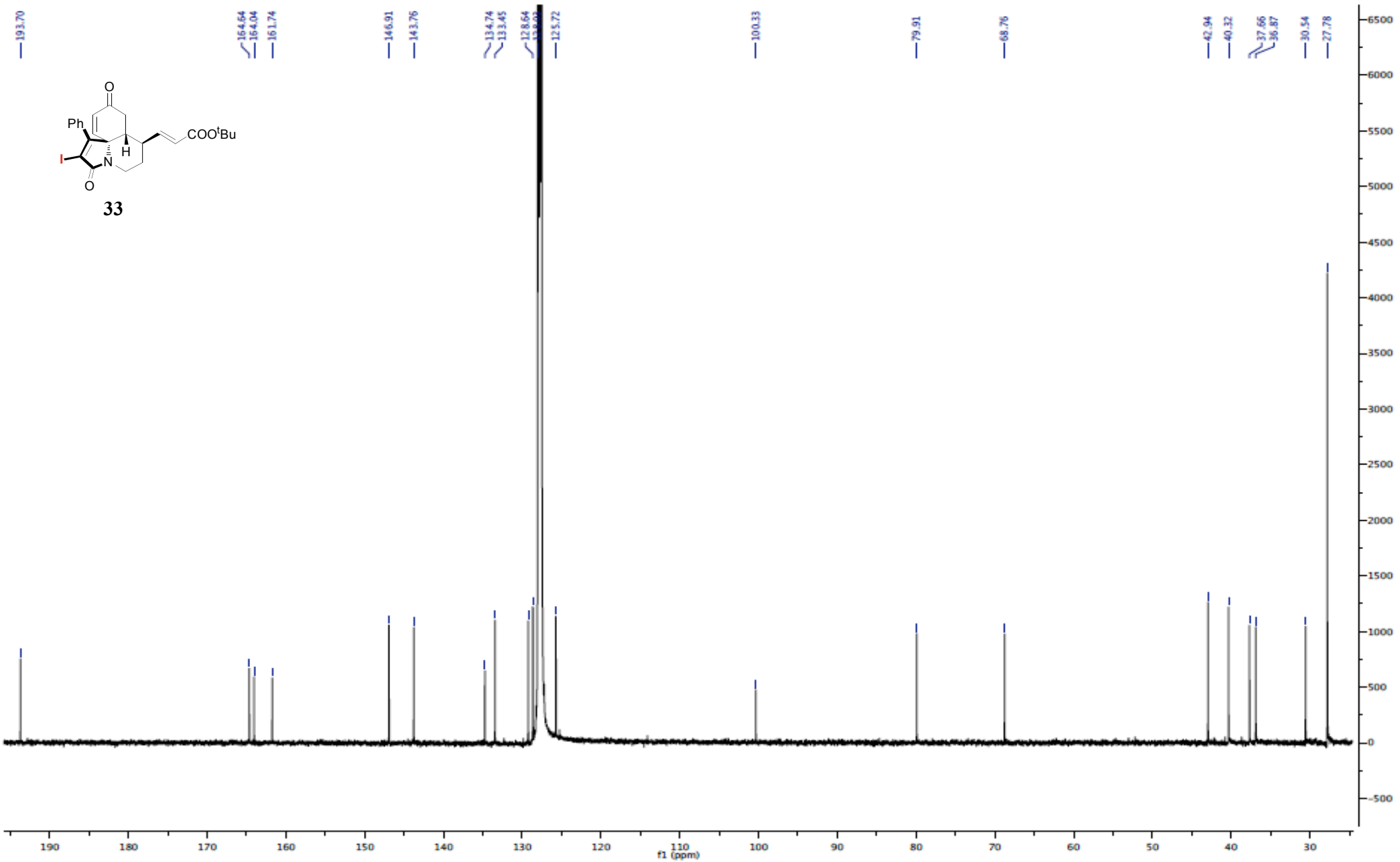

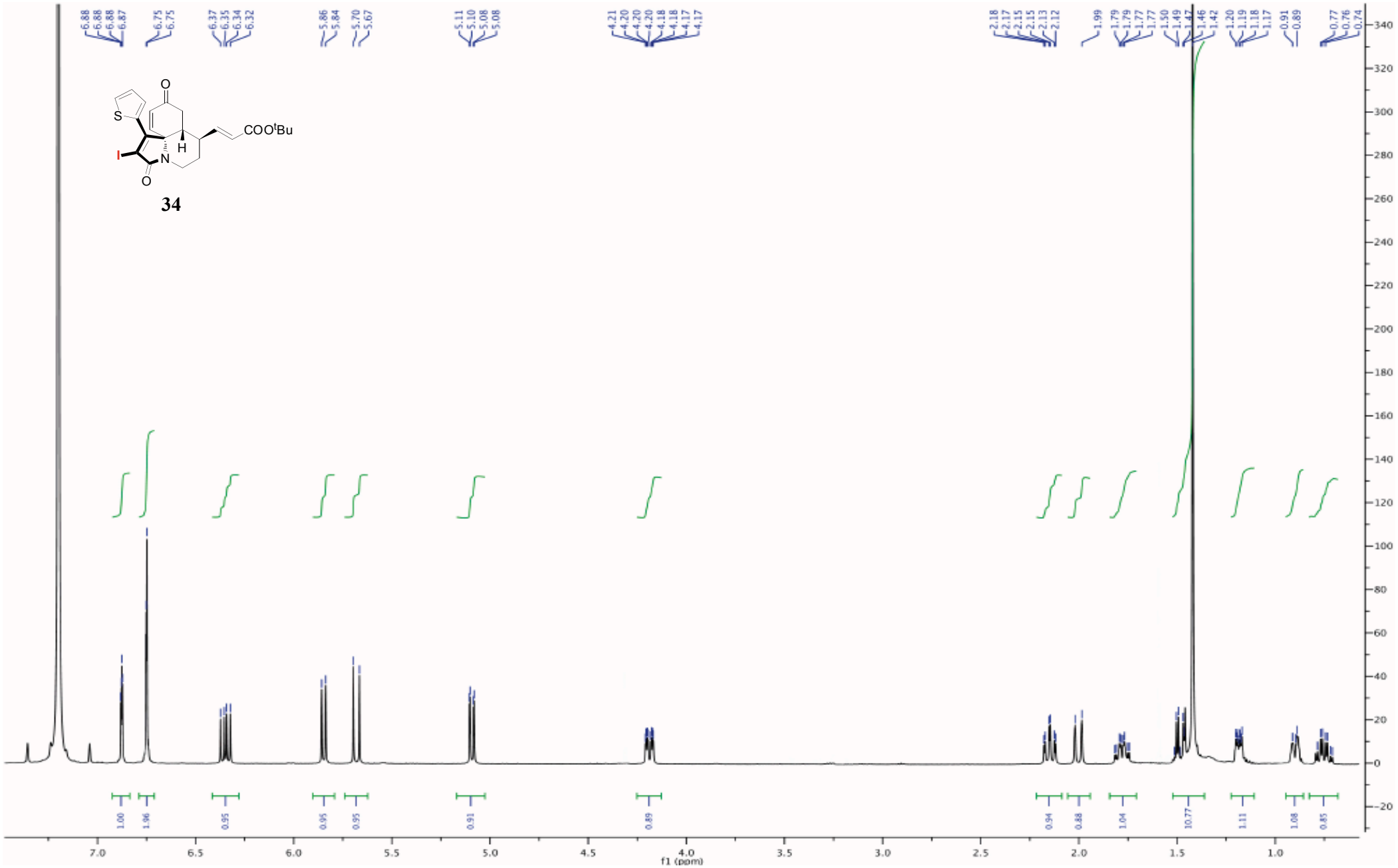

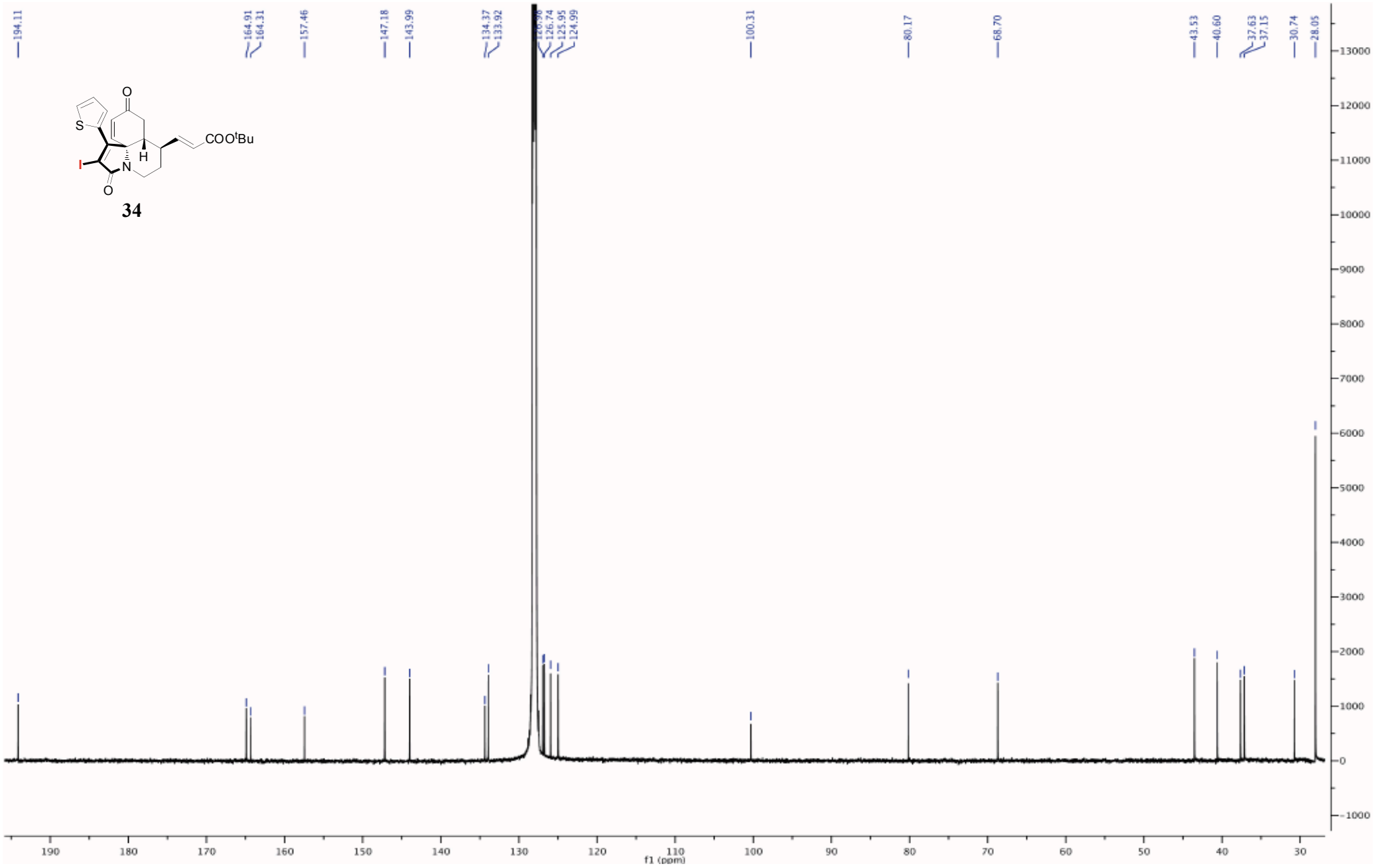

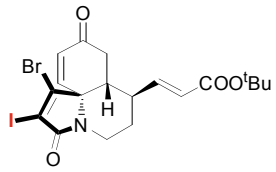

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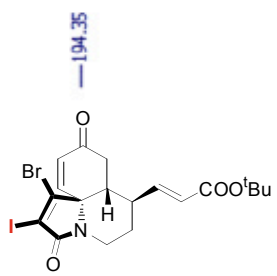

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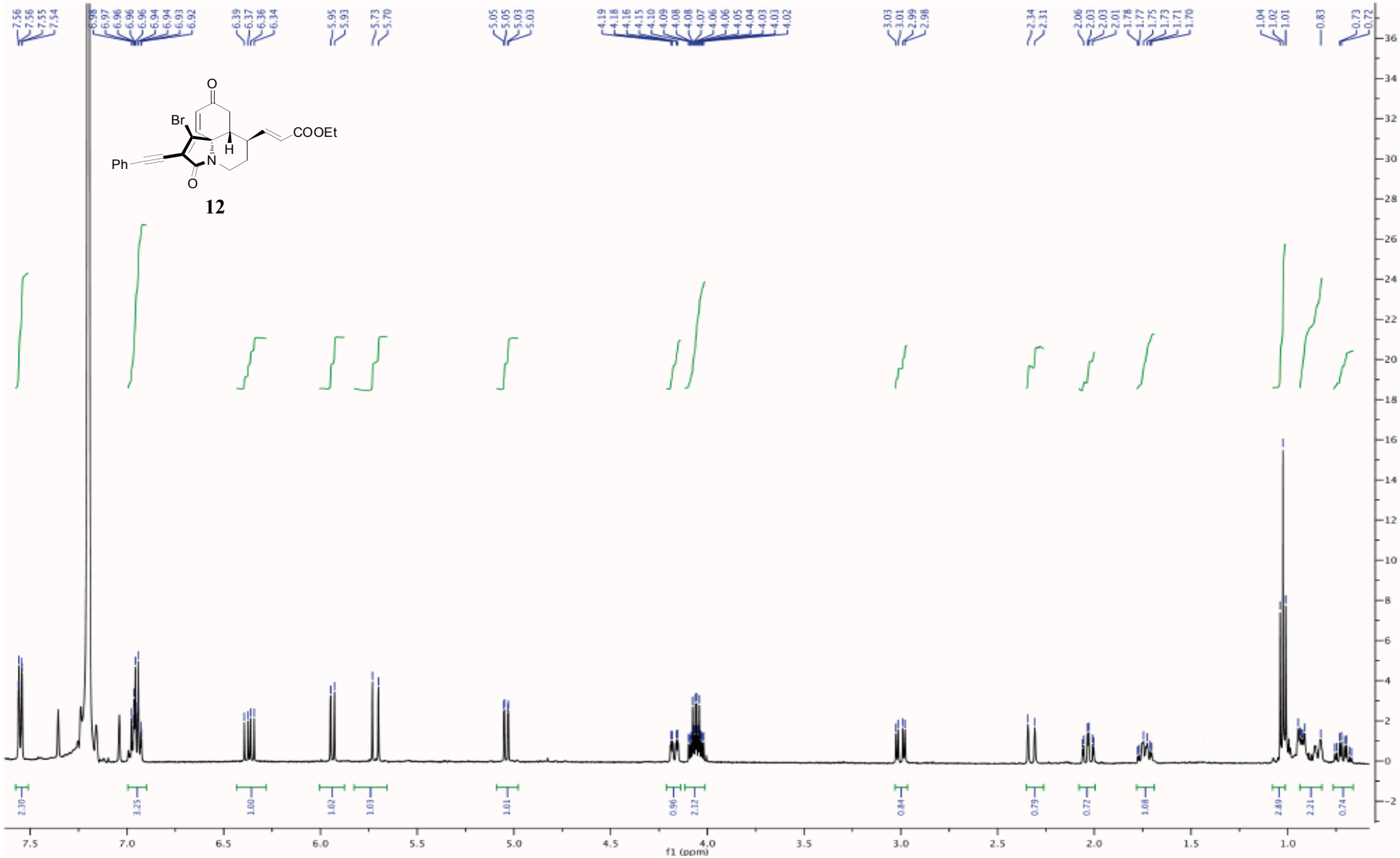

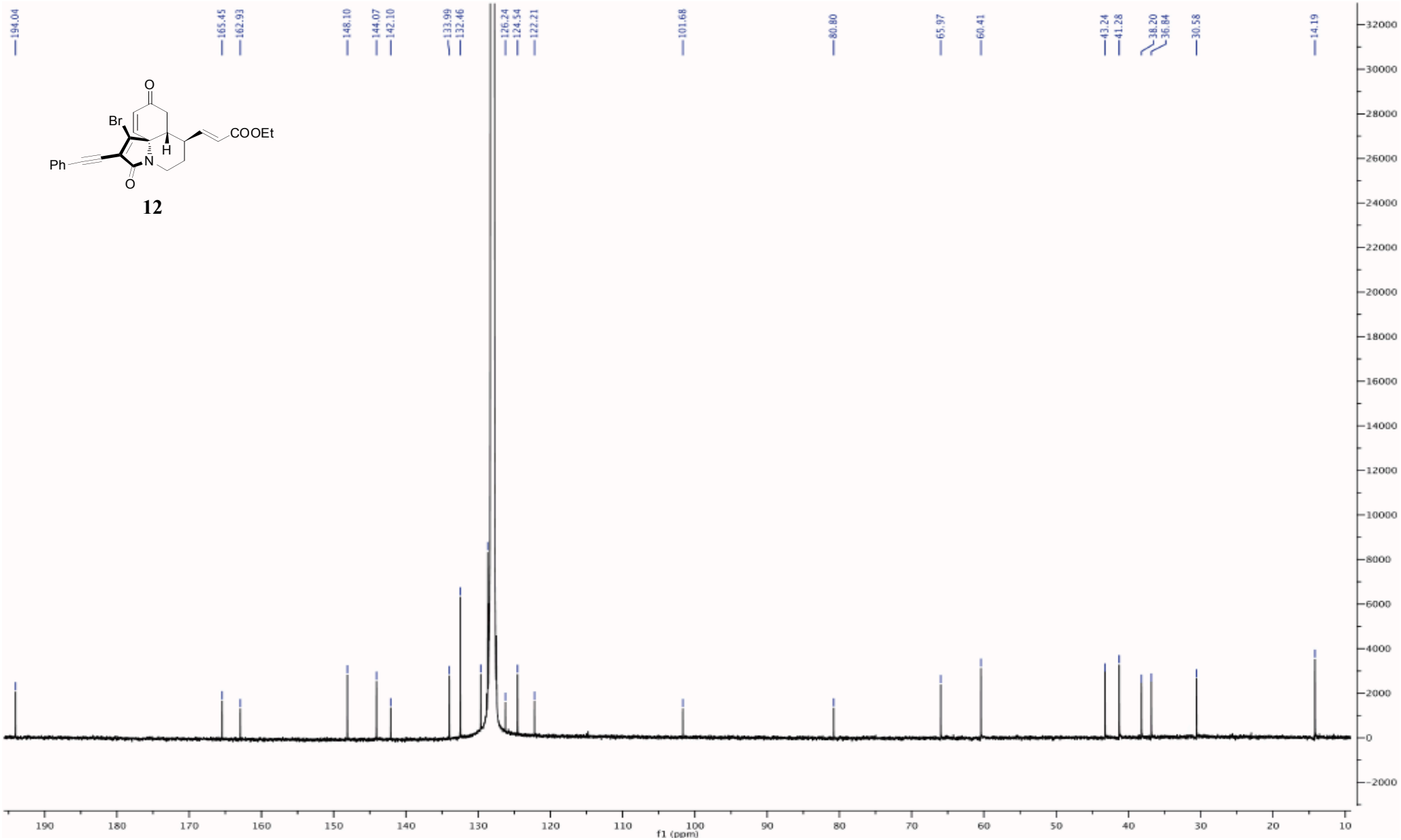

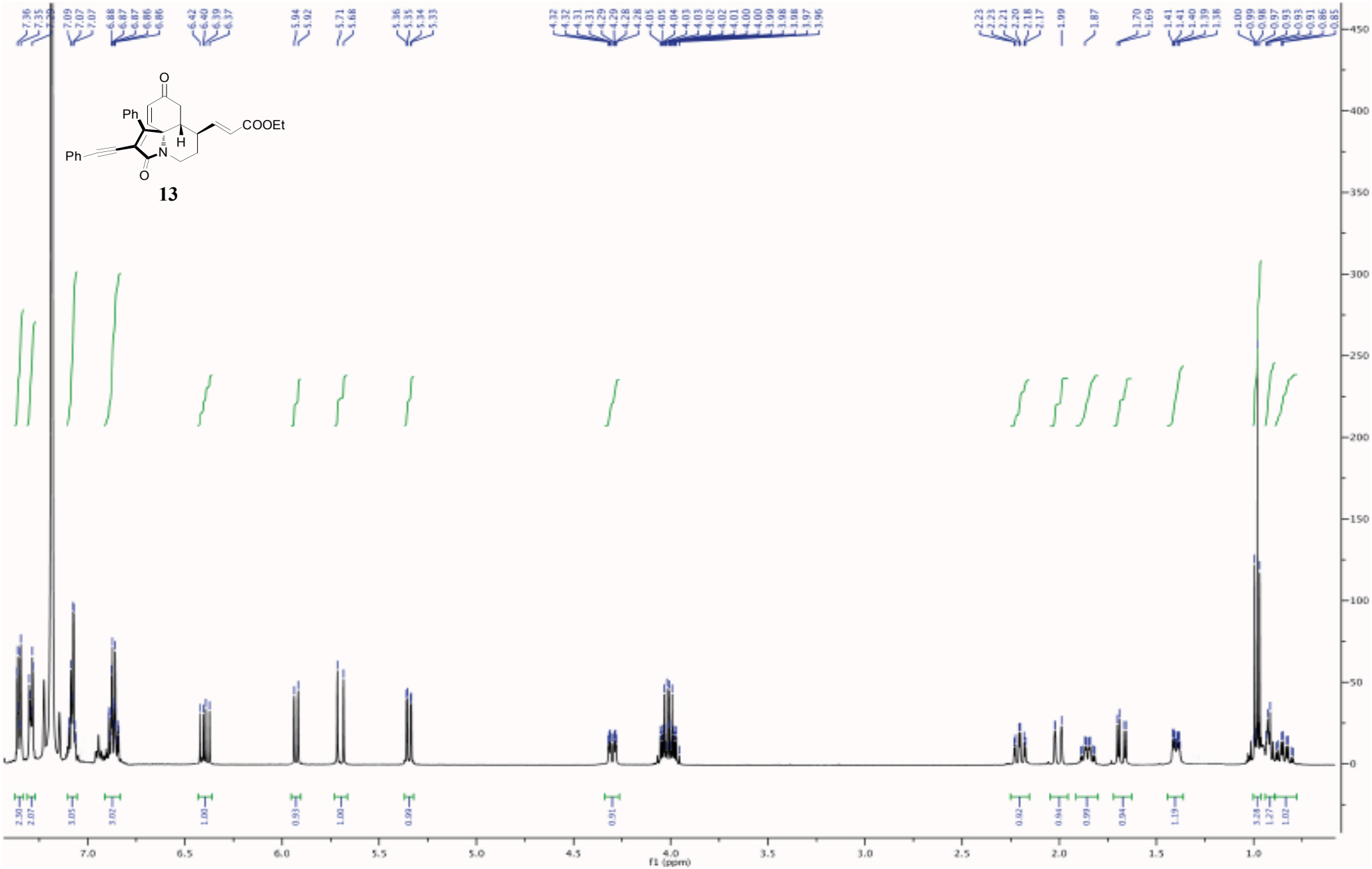

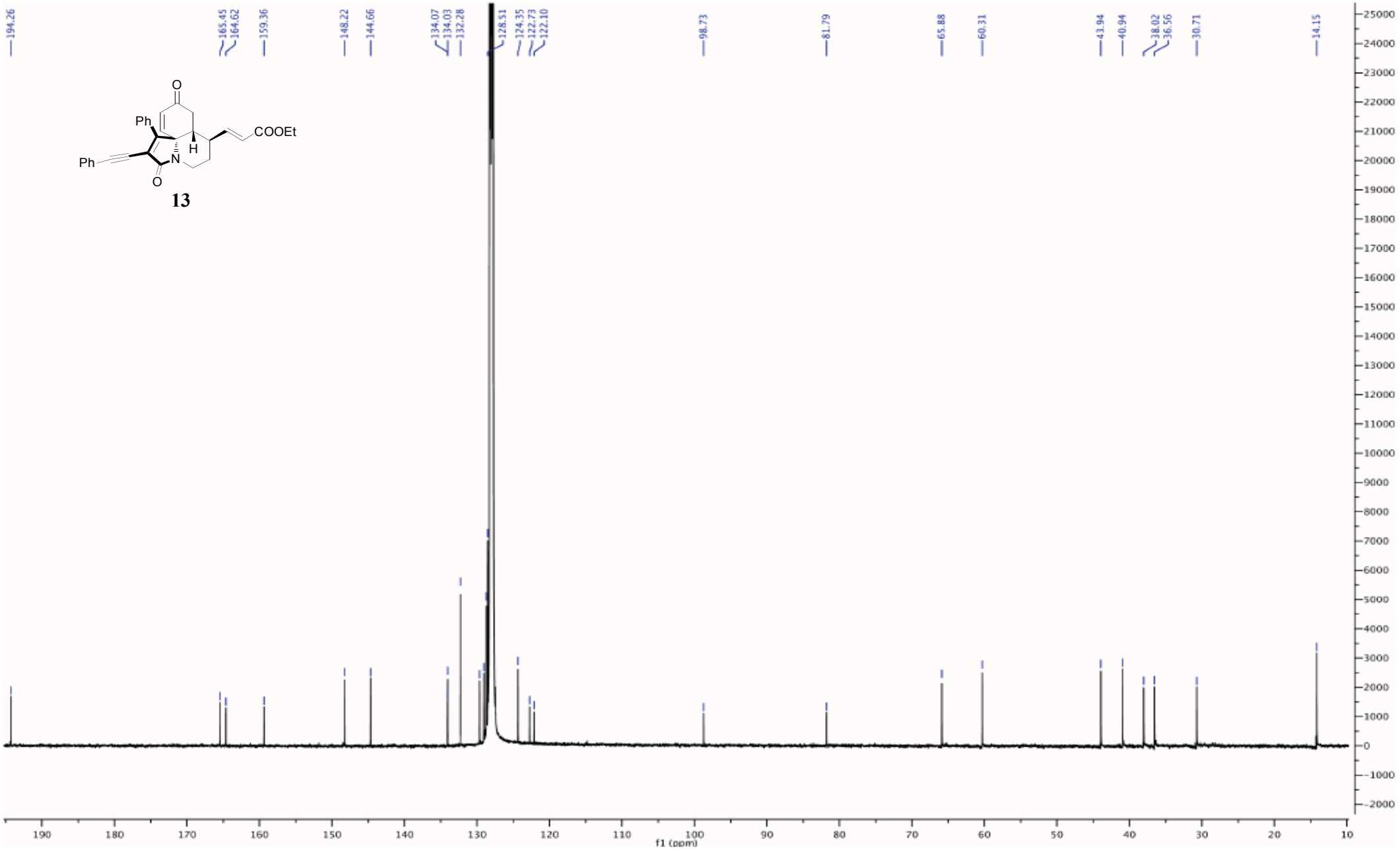

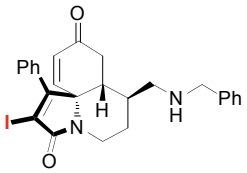

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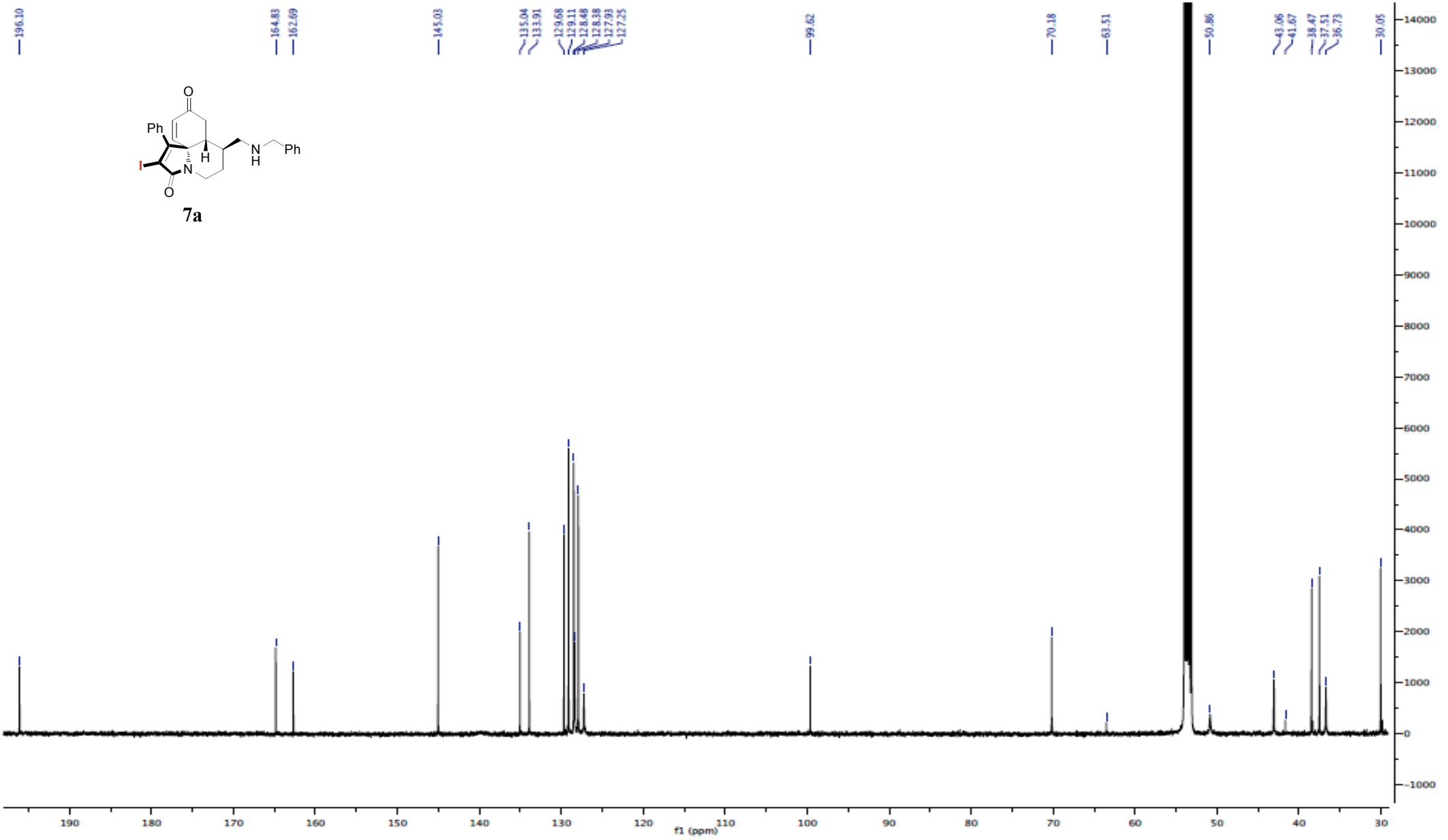

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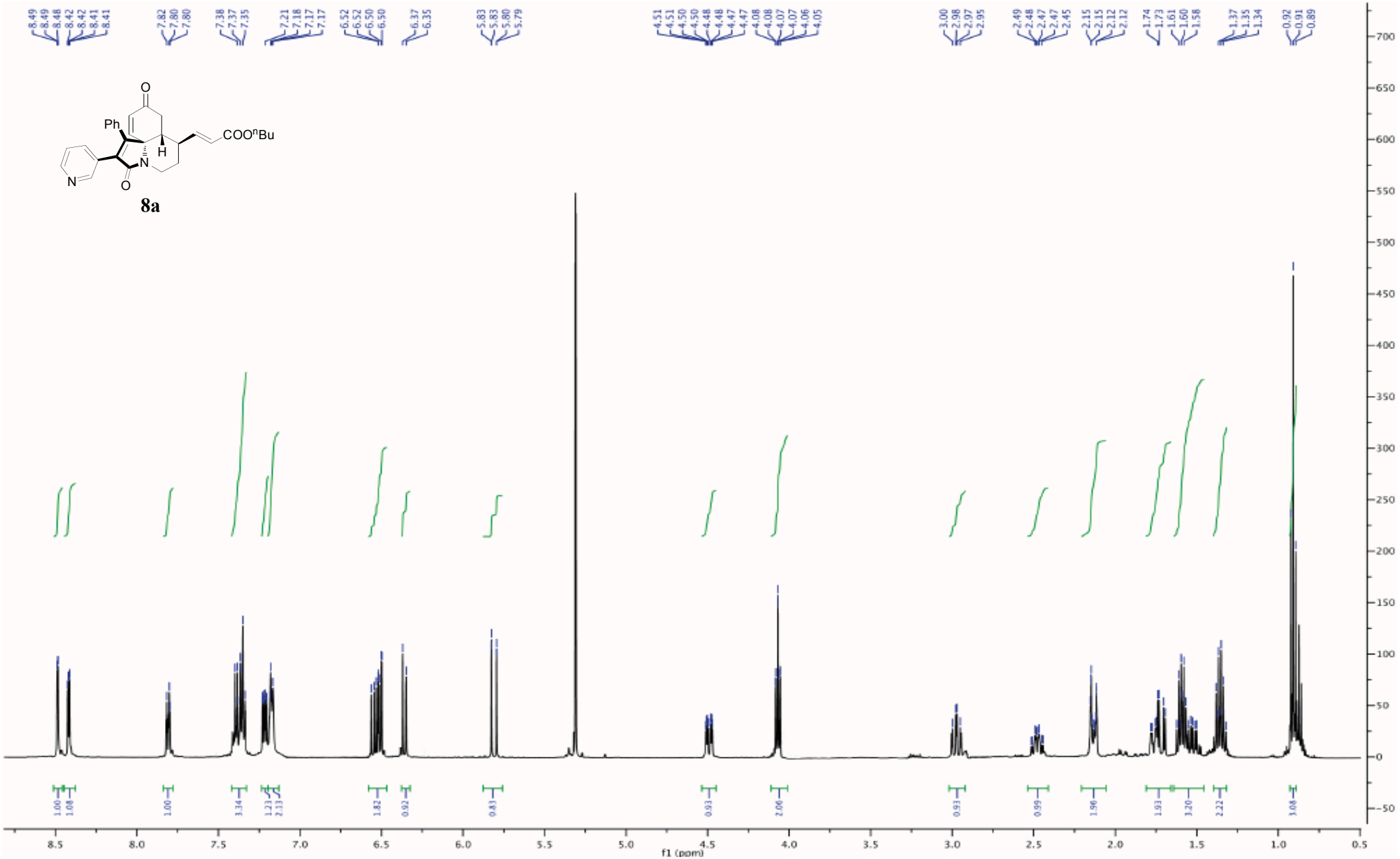

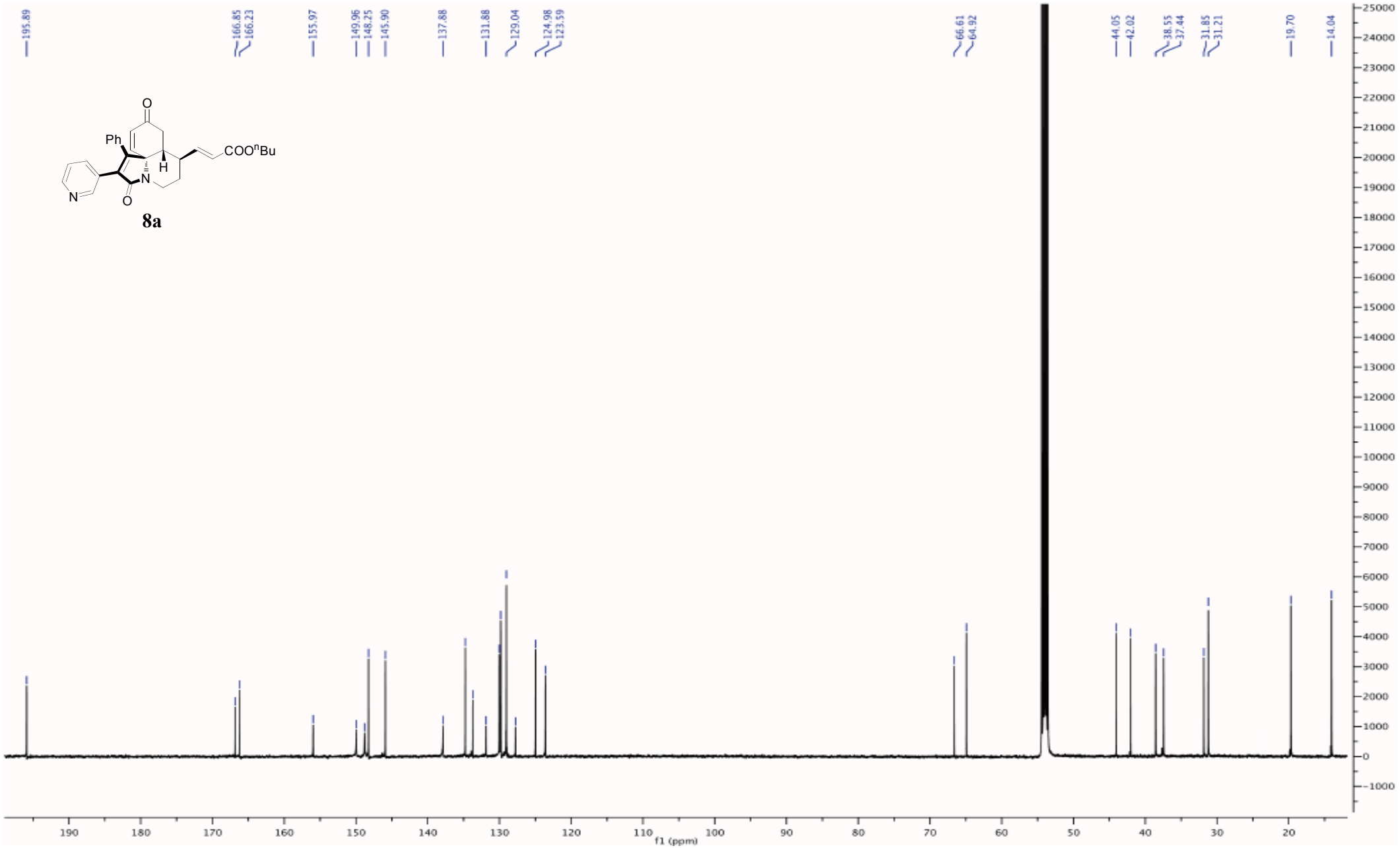

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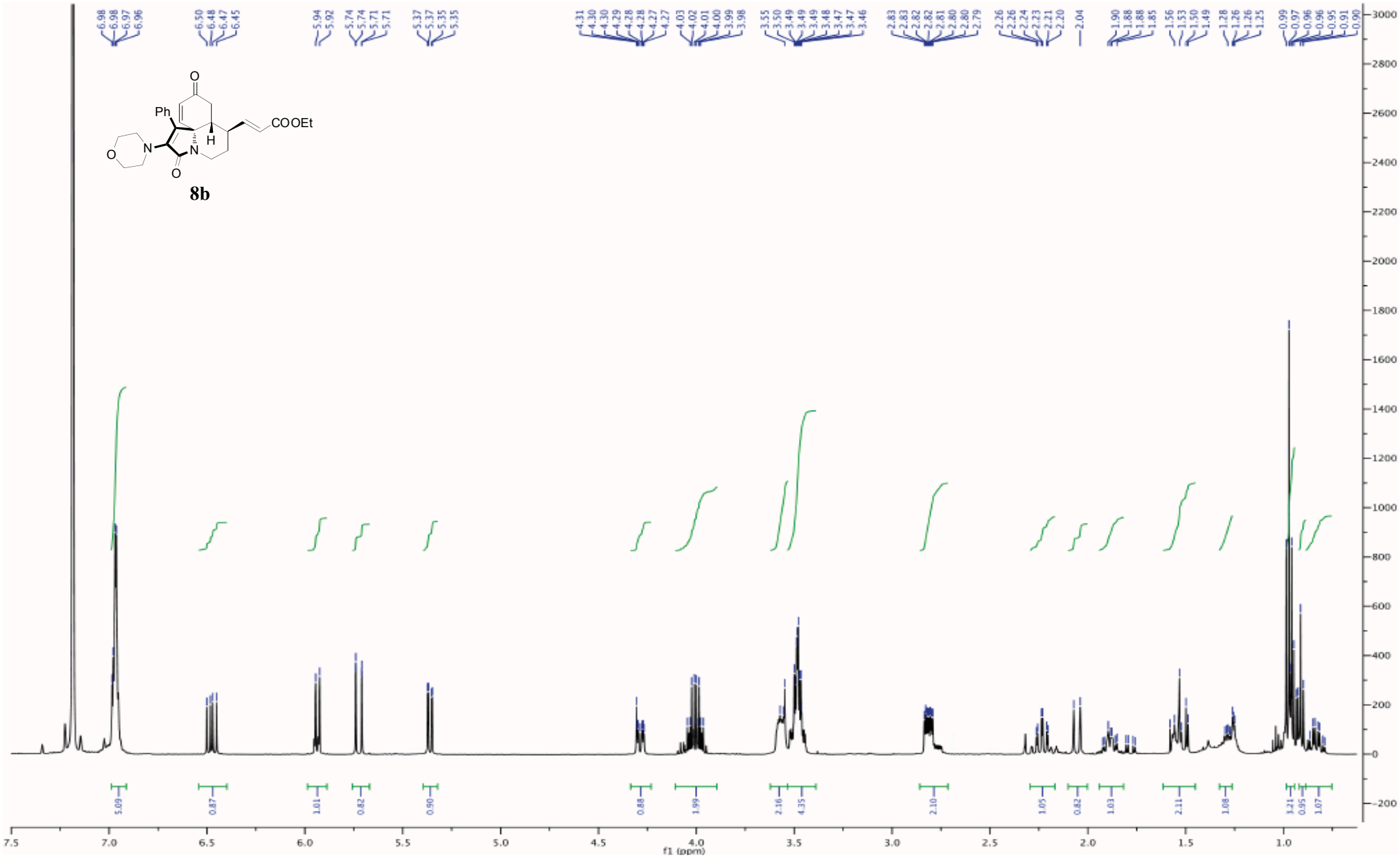

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