Paired Electrolysis Enabled Annulation for the Quinolyl-modification of Bioactive Molecules

Shiqi You,[a] Mengyao Ruan, [a] Cuifen Lu,[a] Li Liu,[a] Guichun Yang,[a] Shengchun Wang, [b] Hesham Alhumade,[c] Aiwen Lei* [b] and Meng Gao* [a]

Supporting Information

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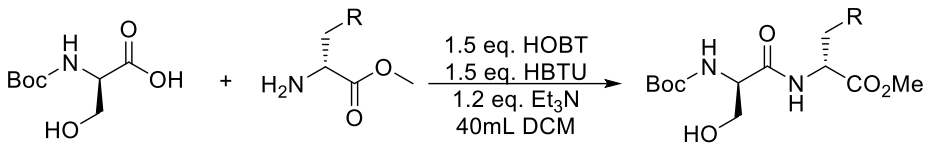
1. General Information

Unless otherwise stated, analytical grade solvents and commercially available reagents were used without further purification. All solvents were analytical reagent or better and were degassed prior to use. The instrument for electrolysis was dual display potentiostat (DJS-292B) (made in China). The anode electrode is carbon rod electrodes (Φ 6mm) and the cathode electrode is platinum plate electrodes (15 mm×15 mm×0.3 mm). Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (boiling point is between 60-90℃). Gradient flash chromatography was conducted eluting with a continuous gradient from petroleum to the indicated solvent, and they are listed as volume/volume ratios. High resolution mass spectra (HRMS) for polypeptides were measured with an Agilent 6224 instrument and accurate masses were reported for the molecular ion + Hydrogen (M+H) or molecular ion + Sodium (M+Na). The ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker Advance III (400 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. For ^{1}H NMR, chemical shifts (δ) were given in ppm relatives to internal standard (TMS at 0 ppm, $CDCl_3$ at 7.26 ppm, MeOH-d_4 at 3.31 ppm). For ^{13}C-NMR, chemical shifts (δ) were reported in ppm using solvent as internal standard ($CDCl_3$ at 77.00 ppm, MeOH-d_4 at 49.00 ppm). GC-MS spectra were recorded on a Varian GC-MS 3900-2100T and Shimadzu GCMS-QP2010SE.

2. Synthesis of Starting Materials

2.1 Synthesis of starting materials dipeptides[1][2]

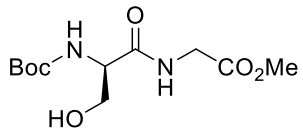


A
2.0 mmol

B
2.0 mmol

Dipeptides **3aa-3ag**

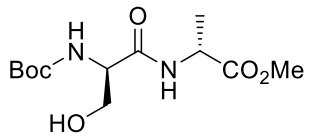
To a solution of Boc-L-serine **A** (410 mg, 2.0 mmol, 1.0 equiv.) in 40 mL CH_2Cl_2 was added HOBT (1-hydroxybenzotriazole) (3.0 mmol), HBTU (O-benzotriazole-*N*, *N*, *N'*, *N'*-tetramethyluronium-hexafluorophosphate) (3.0 mmol) and triethylamine (2.4 mmol). The mixture was stirred for 30 min at room temperature, and then, peptide **B** (2.0 mmol) was added to the solution. The reaction was stirred overnight. After regular workup, the reaction mixture washed by saturated $NaHCO_3$ solution (40 mL x 3), 2M hydrochloric acid solution (40 mL x 3) and H_2O (40 mL x 3). The organic layers were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by flash chromatography (DCM/MeOH) to afford corresponding dipeptides **3aa-3ag**.



3aa

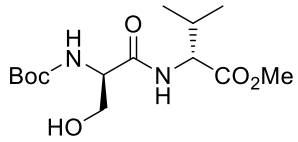
Dipeptide **3aa Boc-Ser-Gly-Ome**, white solid. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.94 (s, 1H), 6.63 (s, 1H), 4.76 (s, 1H), 4.48 (dt, J = 11.0, 7.0 Hz, 1H), 3.99 – 3.87 (m, 2H), 3.68 (s, 3H), 3.72

– 3.56 (m, 2H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.09, 170.46, 156.35, 79.55, 62.00, 55.00, 52.34, 41.60, 28.27.



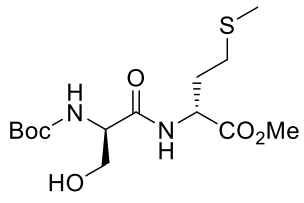
3ab

Dipeptide **3ab Boc-Ser-Ala-Ome**, colorless oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.75 (s, 1H), 6.66 (d, J = 11.0 Hz, 1H), 4.71 (s, 1H), 4.52 (dt, J = 11.0, 7.0 Hz, 1H), 4.32 (dq, J = 9.7, 6.8 Hz, 1H), 3.70 (s, 3H), 3.71 – 3.63 (m, 1H), 3.61 (dt, J = 12.3, 6.7 Hz, 2H), 1.40 (s, 9H), 1.33 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 173.13, 171.17, 156.35, 79.55, 62.02, 54.55, 52.61, 48.27, 28.27, 17.76.



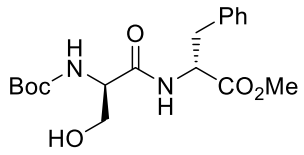
3ac

Dipeptide **3ac Boc-Ser-Val-Ome**, colorless oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.63 (d, J = 11.7 Hz, 1H), 6.65 (d, J = 11.0 Hz, 1H), 4.67 (s, 1H), 4.52 (dt, J = 11.0, 7.1 Hz, 1H), 4.08 (dd, J = 11.8, 7.0 Hz, 1H), 3.66 (s, 3H), 3.71 – 3.63 (m, 1H), 3.59 (dt, J = 12.5, 6.9 Hz, 1H), 2.14 (h, J = 6.8 Hz, 1H), 1.39 (s, 9H), 1.01 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 173.42, 171.40, 156.33, 79.55, 62.06, 57.90, 54.59, 52.40, 30.38, 28.28, 19.05.



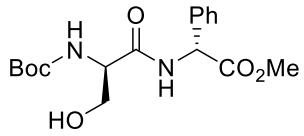
3ad

Dipeptide **3ad Boc-Ser-Met-Ome**, yellow oil. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.63 (d, J = 11.0 Hz, 1H), 6.67 (d, J = 11.0 Hz, 1H), 4.78 (s, 1H), 4.52 (dt, J = 11.0, 7.0 Hz, 1H), 4.26 (dt, J = 11.0, 7.0 Hz, 1H), 3.71(s, 3H) , 3.68 – 3.58 (m, 2H), 2.61 (td, J = 7.1, 1.4 Hz, 2H), 2.07 (s, 3H), 2.12 – 1.93 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 173.06, 171.23, 156.30, 79.55, 62.05, 54.47, 52.47, 51.60, 31.22, 30.82, 28.29, 14.82.



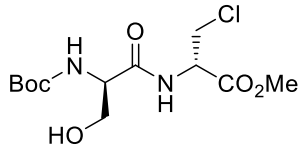
3ae

Dipeptide **3ae Boc-Ser-Phe-Ome,** white solid, ^{1}H NMR (400 MHz, Chloroform-d) δ 7.65 (d, J = 11.4 Hz, 1H), δ 7.23(d, J = 7.4 Hz, 2H), 7.04 (d, J=6.3 Hz, 3H)., 6.65 (d, J = 11.0 Hz, 1H), 4.77 (s, 1H), 4.58 – 4.48 (m, 2H), 3.68 (s, 3H), 3.67 – 3.56 (m, 2H), 3.03 – 2.92 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.56, 156.33, 136.71, 129.17, 128.60, 127.16, 79.34, 62.09, 54.49, 53.66, 52.35, 37.79, 28.30.



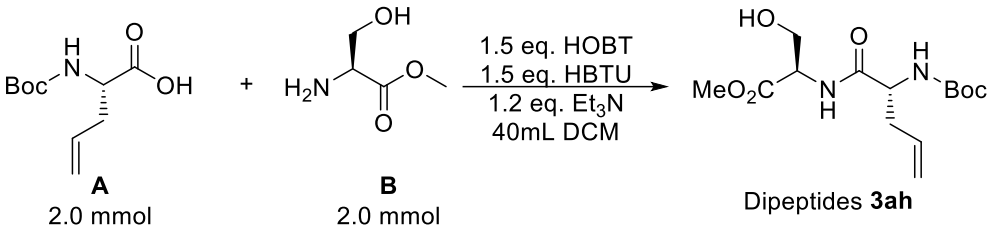
3af

Dipeptide **3af Methyl(*R*)-2-((*R*)-2-((tert-butoxycarbonyl)amino)-3-hydroxypropanamido)-2-phenylacetate,** colorless oil, ^{1}H NMR (400 MHz, Chloroform-d) δ 7.64 (d, J = 10.8 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.39 – 7.28 (m, 3H), 6.67 (d, J = 11.0 Hz, 1H), 5.51 (d, J = 8.9 Hz, 0H), 4.72 (s, 1H), 4.57 (dt, J = 11.0, 7.1 Hz, 1H), 3.74 (s, 3H), 3.72 – 3.63 (m, 1H), 3.65 – 3.56 (m, 1H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.45, 170.84, 156.32, 136.83, 128.91, 128.49, 128.02, 79.44, 62.11, 55.43, 54.80, 52.92, 28.30.

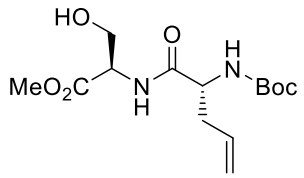


3ag

Dipeptide **3ag Methyl(*S*)-2-((*R*)-2-((*tert*-butoxycarbonyl)amino)-3-hydroxypropanamido)-3-chloropropanoate,** colorless oil, ^{1}H NMR (400 MHz, Chloroform-d) δ 7.68 (d, J = 10.6 Hz, 1H), 6.65 (d, J = 11.0 Hz, 1H), 4.74 (s, 1H), 4.55 – 4.92 (m, 2H), 3.86 (dd, J = 12.5, 7.0 Hz, 1H), 3.76 (dd, J = 12.4, 7.1 Hz, 1H), 3.70 (s, 2H), 3.69 – 3.56 (m, 2H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.78, 171.07, 156.31, 79.55, 62.08, 54.71, 54.08, 52.43, 45.98, 28.27.



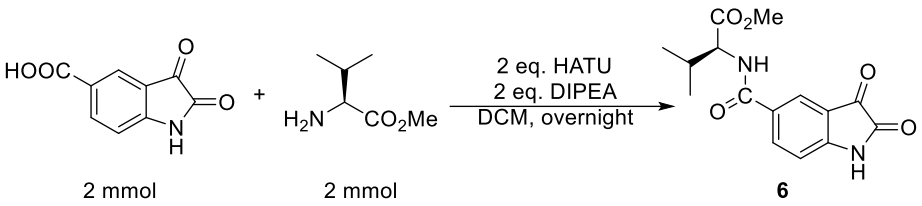
In a round bottomed flask, equipped with a stir bar, peptide **A** (2.0 mmol), HOBT (1-hydroxybenzotriazole) (3.0 mmol), HBTU (O-benzotriazole-*N*, *N*, *N'*, *N'*-tetramethyluronium-hexafluorophosphate) (3.0 mmol), dichloromethane (40 mL) and triethylamine (2.4 mmol) were combined and added. The mixture was stirred for 30 min at room temperature, and then, peptide **B** (2.0 mmol) was added to the solution. The reaction was stirred overnight. After regular workup, the reaction mixture washed by saturated $NaHCO_3$ solution (40 mL x 3), 2M hydrochloric acid solution (40 mL x 3) and H_2O (40 mL x 3). The organic layers were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by flash chromatography (DCM/ MeOH) to afford corresponding dipeptides **3ah**.



3ah

Dipeptide **3ah Methyl ((*R*)-2-((*tert*-butoxycarbonyl)amino)pent-4-enoyl)-D-serinate,** colorless oil, ^{1}H NMR (500 MHz, Chloroform-d) δ 7.36 (d, J = 12.1 Hz, 1H), 6.35 (d, J = 10.4 Hz, 1H), 5.80 – 5.71 (m, 1H), δ 5.10 (dd, J = 13.3, 4.7 Hz, 1H), 4.33 – 4.21 (m, 3H), 4.19 (t, J = 6.7 Hz, 1H), 3.84 – 3.74 (m, 3H), 3.69 (s, 3H), 2.52 – 2.39 (m, 3H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 172.15, 155.42, 133.00, 118.57, 79.55, 64.87, 54.59, 53.61, 52.64, 35.89, 28.32.

2.2 Synthesis of Methyl (2,3-dioxoindoline-5-carbonyl)-L-valinate (6)[3]



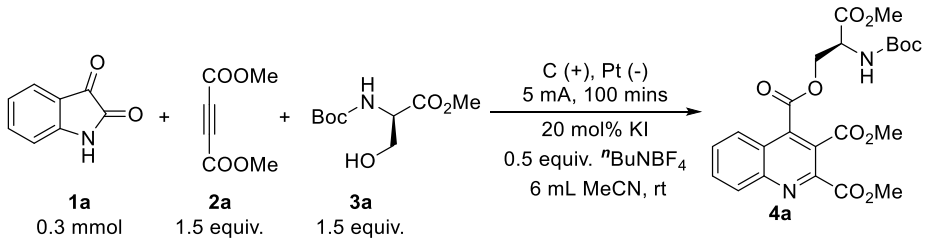
L-Valine Methyl Ester Hydrochloride (2.0 mmol), HATU (3.0 mmol) and DIPEA (3.0 mmol) were dissolved in DCM (20 mL) and the solution was stirred at 0 °C under an argon atmosphere for 10min. Then, 2,3-Dioxoindoline-5-carboxylic Acid (2.0 mmol) in DCM (10 mL) was added dropwise, and the reaction mixture was stirred overnight at 0 °C to room temperature. The solvent was removed by reduced pressure, and the crude product was purified by silica gel chromatography with CH_2Cl_2/MeOH to get the product **5**, a yellow solid. Yield was 95%. ^{1}H NMR (400 MHz, Methanol-d4) δ 8.09 – 8.02 (m, 1H), 7.92 – 7.79 (m, 1H), 6.97 (dd, J = 21.8, 8.2 Hz, 1H), 4.49 – 4.45 (m, 1H), 3.75 (s, 3H), 2.28 – 2.21 (m, 1H), 1.02 (dd, J = 11.5, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, Methanol-d4) δ 183.37, 172.46, 167.37, 160.07, 153.03, 128.82, 123.90, 123.40, 117.69, 111.91, 58.88, 51.27, 30.34, 18.30, 17.88.

3. General Procedure

3.1. Reaction optimization

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, isatin (0.3 mmol), dimethyl but-2-ynedioate (0.45 mmol), serine residue (0.45 mmol), $^{n}Bu_4NBF_4$ (0.15 mmol) and KI (0.06 mmol) were combined and added. Then, solvent (6 mL) were injected into the tubes via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current under room temperature. When the reaction was finished, the solvent was removed by reduced pressure and the crude product was purified by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate= 5:1). A summary of optimization results is presented in **Table S1** below.

Table S1. Investigation of the reaction conditions



Entry	Variation from Standard Conditions[a]	Yield (%)
1	none	85
2	Without KI	N.D.
3	CH_2Cl_2 as the solvent	Trace
4	5mL CH_3CN, 1 mL H_2O was used	35
5	Carbon as cathode	70
6	$^nBu_4NPF_6$ instead of $^nBu_4NBF_4$	74
7	$^nBu_4ClO_4$ instead of $^nBu_4NBF_4$	63
8	KI as electrolyte	89
9	I_2 instead of KI	N.D.
10	0.1 equiv. KI was added	67
11	10 mA, 90 mins	76
12	without electric current	N.R.

[a]Reaction conditions: Undivided cell, carbon rod anode, Pt cathode, **1a** (0.3 mmol), **2a** (1.5 equiv.), **3a** (1.5 equiv.), $^nBu_4NBF_4$ (0.5 equiv.), KI (0.2 equiv.), 6 mL MeCN, air, rt, 5 mA, 100 mins. Yields of isolated products are shown. N.D. = Not Detected. N.R. = No Reaction.

3.2 General procedure for cyclic voltammetry (CV)

Cyclic voltammetry was performed in a three-electrode cell connected to a schlenk line at room temperature. The working electrode was a steady glassy carbon disk electrode, the counter electrode was a platinum wire. The reference was an Ag/AgCl electrode submerged in saturated aqueous KCl solution and separated from a reaction by a salt bridge. The cyclic voltammetry (CV) experiments on 0.015 M **$^nBu_4NBF_4$** with 0.003 M substrate and 20 mol% **KI** with 0.003 M substrate were performed, respectively. The scan rate is 0.1 V/s. The positive scan range was from 0 V to 2.0 V and 0 V to -2.0 V.

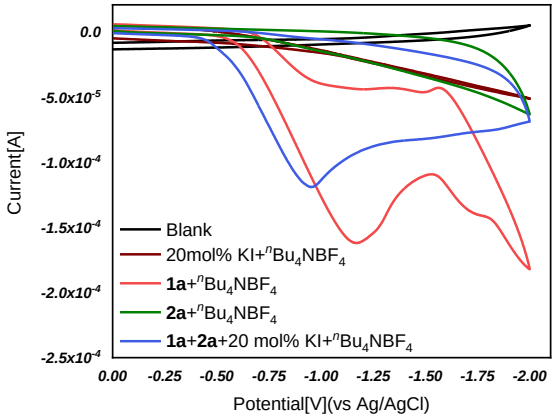


Figure S1. As shown in this graphic, the cyclic voltammograms showed irreversible reduction waves for isatin (**1a**).

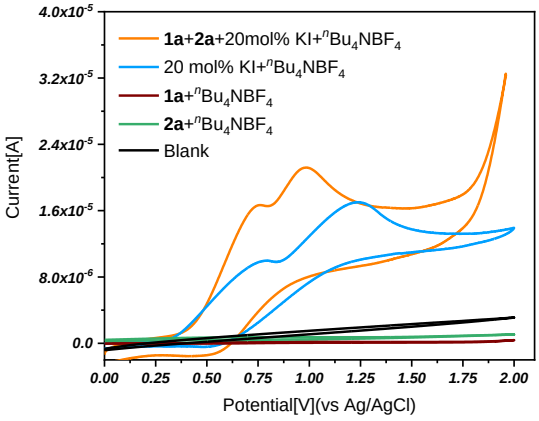


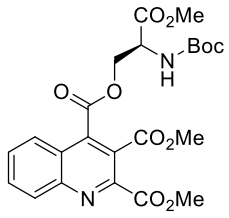
Figure S2. These results illustrated that two oxidation peak of **KI** was observed at 0.82 V and 1.22 V while the oxidation peaks of **^{n}Bu$_4$BF$_4$** and substrate were not observed.

3.3 Bioactive molecules scope and characterization

General procedure for bioconjugated product (4a): In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, isatin (0.3 mmol), dimethyl but-2-ynedioate (0.45 mmol), serine residue (0.45 mmol), ^{n}Bu$_4$NBF$_4$ (0.15 mmol) and KI (0.06 mmol) were combined and added. Then, CH_3CN (6 mL) were injected into the tubes via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate

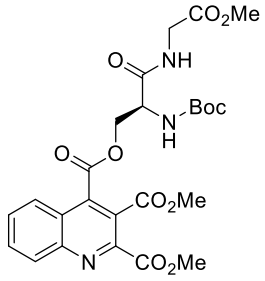
(15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at a constant current of 5 mA under room temperature for 100 mins. After completion of the reaction, as indicated by TLC and LC-MS, the pure product (yield: 85%, 124.95 mg) was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate= 5:1).

Detailed descriptions for products:



4a

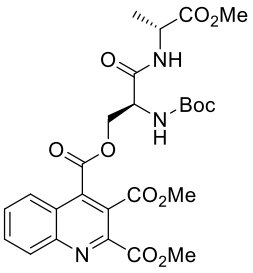
(*S*)-4-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)2,3-dimethyl quinoline-2,3,4-tricarboxylate (4a): light yellow solid (Yield: 85 %, 124.95 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.24 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H), 7.87 (t, J = 7.7 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 5.56 (d, J = 8.4 Hz, 1H), 4.80 (d, J = 3.3 Hz, 2H), 4.68 (s, 1H), 4.02 (s, 3H), 3.95 (s, 3H), 3.74 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.39, 169.83, 165.85, 165.75, 164.98, 155.30, 147.97, 147.60, 139.85, 132.41, 130.50, 130.23, 125.51, 123.62, 80.46, 66.25, 53.50, 52.91, 52.84, 52.54, 28.25. HRMS (ESI) cald. for $(M+H)^+$ $C_{23}H_{27}N_2O_{10}$: 491.1587 found,491.1589.



4aa

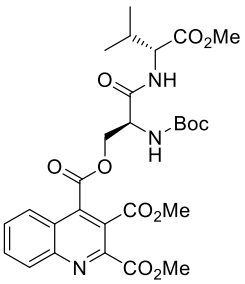
(*S*)-4-(2-((tert-butoxycarbonyl)amino)-3-((2-methoxy-2-oxoethyl)amino)-3-oxopropyl)2,3-dimethyl quinoline-2,3,4-tricarboxylate (4aa): light yellow oil (Yield: 53 %, 86.97 mg) , 1H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.89 (t, J =

7.1 Hz, 1H), 7.74 (t, J = 7.7 Hz, 1H), 7.11 (s, 1H), 5.67 (dd, J = 47.0, 7.7 Hz, 2H), 4.96 – 4.74 (m, 2H), 4.03 (s, 3H), 3.97 (s, 3H), 3.62 (s, 2H), 2.77 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.94, 169.38, 168.99, 165.73, 165.09, 155.70, 147.90, 147.65, 139.86, 132.49, 130.54, 130.38, 125.62, 123.64, 122.35, 80.63, 65.79, 53.71, 53.54, 52.97, 52.30, 38.61, 28.28. HRMS (ESI) cald. for (M+H)+ $C_{25}H_{30}N_3O_{11}$:548.1836 found,548.1839.



4ab

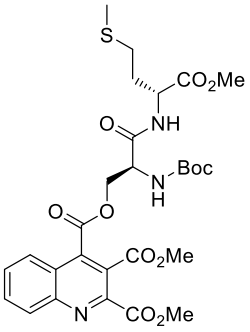
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-1-methoxy-1-oxopropan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ab): light yellow solid (Yield: 61 %, 102.48 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 4.1 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.88 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.73 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 5.61 (s, 1H), 4.90 (dd, J = 11.0, 4.5 Hz, 1H), 4.65 (dd, J = 11.0, 5.1 Hz, 1H), 4.58 (s, 1H), 4.54 – 4.48 (m, 1H), 4.04 (s, 3H), 3.98 (s, 3H), 3.60 (s, 3H), 1.45 (s, 9H), 1.29 (d, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.66, 167.44, 165.35, 164.13, 154.41, 146.77, 146.61, 139.08, 131.43, 129.46, 129.29, 124.76, 122.62, 121.43, 79.94, 64.73, 52.64, 52.51, 51.38, 47.28, 27.23, 17.13. HRMS (ESI) cald. for (M+H)+ $C_{26}H_{32}N_3O_{11}$:5618.1992 found,561.1988.



4ac

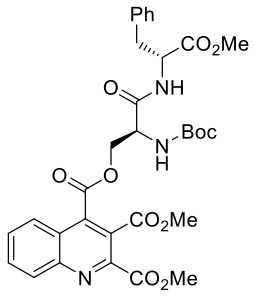
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-1-methoxy-3-methyl-1-oxobutan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ac): white solid (Yield:

58 %, 102.46 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.89 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.74 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 5.68 (s, 1H), 4.92 (dd, J = 11.0, 4.6 Hz, 1H), 4.70 (dd, J = 11.0, 4.9 Hz, 1H), 4.58 (s, 1H), 4.45 (dd, J = 8.8, 5.0 Hz, 1H), 4.05 (s, 3H), 4.00 (s, 3H), 3.58 (s, 3H), 2.02 (dt, J = 13.3, 6.6 Hz, 1H), 1.47 (s, 9H), 0.70 (d, J = 6.5 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.64, 168.87, 166.43, 165.72, 165.18, 155.49, 147.80, 147.62, 140.32, 132.49, 130.47, 130.30, 125.78, 123.58, 122.30, 80.86, 65.69, 64.89, 57.30, 53.67, 53.52, 52.05, 31.14, 28.26, 18.65, 17.40. HRMS (ESI) cald. for (M+H)+ $C_{28}H_{36}N_3O_{11}$:590.2305,found,590.2300.



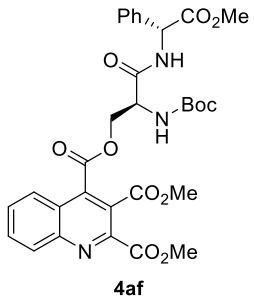
4ad

4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-1-methoxy-4-(methylthio)-1-oxobutan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ad): yellow solid (Yield: 62 %, 115.46 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.29 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.91 (t, J = 7.7 Hz, 1H), 7.77 (t, J = 7.7 Hz, 1H), 7.15 (d, J = 7.9 Hz, 1H), 5.70 (s, 1H), 4.93 (dd, J = 11.0, 4.4 Hz, 1H), 4.72 (dd, J = 11.0, 4.9 Hz, 1H), 4.66 (dt, J = 7.7, 3.8 Hz, 1H), 4.61 (d, J = 8.6 Hz, 1H), 4.06 (s, 3H), 4.02 (s, 3H), 3.62 (s, 3H), 2.29 (d, J = 6.5 Hz, 2H), 2.10 – 2.02 (m, 1H), 1.92 – 1.87 (m, 1H), 1.84 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.63, 168.78, 166.59, 165.67, 165.16, 155.42, 147.66, 140.09, 132.49, 130.53, 130.39, 128.78, 127.46, 125.70, 123.61, 80.87, 65.76, 53.72, 53.54, 52.45, 51.67, 31.38, 29.69, 29.58, 28.27, 15.16. HRMS (ESI) cald. for (M+Na)+ $C_{28}H_{35}N_3NaO_{11}S$:644.1885,found, 644.1910.



4ae

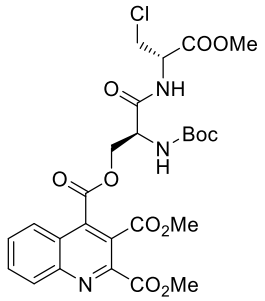
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ae): white solid (Yield: 53 %, 101.26 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.3 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.89 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.74 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.13 (s, 1H), 7.00 (d, J = 7.4 Hz, 2H), 6.95 – 6.84 (m, 3H), 5.58 (s, 1H), 4.88 (dd, J = 11.0, 4.2 Hz, 1H), 4.81 – 4.76 (m, 1H), 4.67 (dd, J = 11.0, 4.9 Hz, 1H), 4.56 (s, 1H), 4.05 (s, 3H), 3.97 (s, 3H), 3.59 (s, 3H), 3.00 (t, J = 6.3 Hz, 2H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.20, 168.57, 166.25, 165.75, 165.19, 155.39, 147.91, 147.66, 140.24, 135.47, 132.51, 130.50, 130.32, 129.02, 128.33, 126.98, 125.77, 123.64, 122.28, 80.81, 65.67, 60.41, 53.64, 53.53, 53.44, 52.27, 37.69, 28.24. HRMS (ESI) cald. for (M+H)+ $C_{32}H_{36}N_3O_{11}$:638.2305,found, 638.2310.



4af

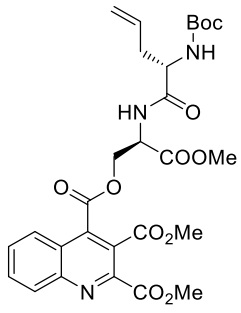
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-2-methoxy-2-oxo-1-phenylethyl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4f): light yellow oil (Yield: 50 %, 93.45 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.2 Hz, 1H), 7.96 – 7.86 (m, 2H), 7.68 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.33 (s, 1H), 7.16 (d, J = 7.1 Hz, 2H), 7.07 (t, J = 7.3 Hz, 1H), 7.00 (t, J = 7.3 Hz, 2H), 5.72 (s, 1H), 5.48 (d, J = 7.2 Hz, 1H), 4.89 (dd, J = 11.0, 4.2 Hz, 1H), 4.70 (dd, J = 11.0, 4.7 Hz, 1H), 4.62 (s, 1H), 4.06 (s, 3H), 3.96 (s, 3H), 3.61 (s, 3H), 1.46 (s, 9H). ^{13}C

NMR (101 MHz, Chloroform-d) δ 170.59, 168.35, 166.44, 165.75, 155.47, 147.65, 135.92, 132.51, 130.41, 130.33, 128.61, 128.36, 126.91, 125.78, 123.60, 80.91, 65.85, 56.49, 53.68, 53.54, 53.41, 52.80, 28.25. HRMS (ESI) cald. for (M+H)+ $C_{31}H_{34}N_3O_{11}$:624.2149,found, 624.2140.



4ag

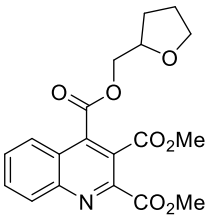
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*S*)-3-chloro-1-methoxy-1-oxopropan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ag): yellow oil (Yield: 61 %, 110.64 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.88 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.73 (ddd, J = 8.2, 7.0, 1.1 Hz, 1H), 7.31 (d, J = 7.7 Hz, 1H), 5.68 (s, 1H), 4.92 (dq, J = 6.6, 3.8, 3.0 Hz, 2H), 4.77 – 4.59 (m, 2H), 4.04 (s, 4H), 3.99 (s, 3H), 3.88 – 3.78 (m, 2H), 3.66 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 168.99, 168.69, 166.17, 165.79, 165.21, 155.44, 148.04, 147.64, 140.29, 132.48, 130.48, 130.24, 125.72, 123.61, 122.14, 80.98, 65.48, 53.67, 53.50, 53.20, 52.97, 44.59, 28.24. HRMS (ESI) cald. for (M+H)+ $C_{26}H_{31}ClN_3O_{11}$:596.1642,found, 596.1662.



4ah

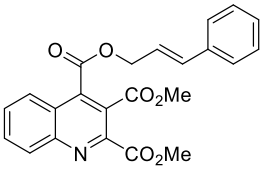
4-((*R*)-2-((*S*)-2-((tert-butoxycarbonyl)amino)pent-4-enamido)-3-methoxy-3-oxopropyl)2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ah): yellow oil (Yield: 62 %, 109.15 mg), ^{1}H NMR

(400 MHz, Chloroform-d) δ 8.24 (d, J = 8.4 Hz, 1H), 7.94 – 7.83 (m, 2H), 7.72 (td, J = 7.6, 7.1, 1.1 Hz, 1H), 7.25 (d, J = 4.5 Hz, 1H), 5.78 – 5.66 (m, 1H), 5.22 (s, 1H), 5.12 – 5.01 (m, 3H), 4.97 (s, 1H), 4.69 (dd, J = 11.2, 2.8 Hz, 1H), 4.29 (s, 1H), 4.02 (s, 3H), 3.98 (s, 3H), 3.73 (s, 3H), 2.58 (dt, J = 12.6, 6.0 Hz, 1H), 2.47 (dt, J = 14.3, 7.1 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 171.72, 169.15, 166.13, 165.80, 165.01, 155.38, 148.13, 147.63, 140.35, 132.93, 132.53, 130.53, 130.28, 125.49, 123.53, 121.88, 118.95, 80.00, 65.49, 53.89, 53.81, 53.51, 53.00, 51.74, 36.90, 28.22. HRMS (ESI) cald. for (M+H)+ $C_{28}H_{34}N_3O_{11}$:588.2149,found, 588.2158.



4aj

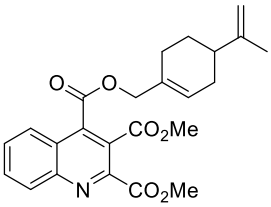
2,3-dimethyl 4-((tetrahydrofuran-2-yl)methyl) quinoline-2,3,4-tricarboxylate (4aj): light yellow liquid (Yield: 80 %, 89.30 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.23 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.3 Hz, 1H), 7.84 (ddd, J = 8.3, 6.8, 1.1 Hz, 1H), 7.70 (ddd, J = 8.1, 6.7, 0.9 Hz, 1H), 4.52 (dd, J = 11.4, 3.5 Hz, 1H), 4.35 (dd, J = 11.4, 6.6 Hz, 1H), 4.22 (qd, J = 6.9, 3.6 Hz, 1H), 4.01 (s, 3H), 3.93 (s, 3H), 3.85 (q, J = 7.5, 6.8 Hz, 1H), 3.76 (q, J = 7.7, 7.2 Hz, 1H), 2.03 (dt, J = 12.3, 6.3 Hz, 1H), 1.87 (p, J = 6.5, 5.6 Hz, 2H), 1.66 (dq, J = 12.2, 7.3 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.89, 165.75, 165.45, 147.78, 147.58, 140.18, 132.22, 130.46, 130.16, 125.80, 123.83, 123.02, 75.96, 68.47, 68.39, 53.49, 53.35, 27.95, 25.70. HRMS (ESI) cald. for (M+H)+ $C_{19}H_{20}NO_7$:374.1195,found, 374.1193.



4ak

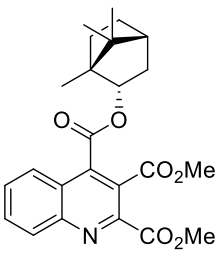
4-cinnamyl 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ak): yellow liquid (Yield: 72 %,

89.30 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.1 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.87 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.73 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 7.42 (d, J = 7.1 Hz, 2H), 7.33 (t, J = 7.3 Hz, 2H), 7.28 (d, J = 7.1 Hz, 1H), 6.79 (d, J = 15.9 Hz, 1H), 6.41 (dt, J = 15.9, 6.6 Hz, 1H), 5.12 (d, J = 7.7 Hz, 2H), 4.04 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 166.02, 165.68, 165.21, 147.61, 139.79, 135.82, 135.72, 132.22, 130.61, 130.27, 128.76, 128.48, 126.75, 125.65, 123.87, 123.40, 121.63, 67.29, 53.58, 53.35. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{20}NO_6$:406.1246,found, 406.1243.



4al

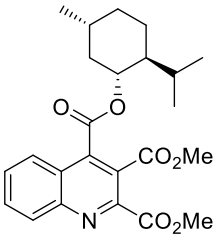
2,3-dimethyl 4-((4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl) quinoline-2,3,4-tricarboxylate (4al): yellow liquid (Yield: 72 %, 101.32 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.73 (t, J = 7.7 Hz, 1H), 5.90 (s, 1H), 4.83 (d, J = 5.6 Hz, 2H), 4.70 (d, J = 10.1 Hz, 2H), 4.04 (s, 3H), 3.94 (s, 3H), 2.23 – 2.10 (m, 9H), 2.03 – 1.94 (m, 1H), 1.85 (d, J = 16.5 Hz, 1H), 1.71 (s, 3H), 1.48 (ddd, J = 20.1, 12.7, 8.6 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.94, 165.73, 165.38, 149.26, 147.76, 147.63, 140.20, 132.14, 131.65, 130.58, 130.11, 127.88, 125.67, 123.90, 123.13, 108.96, 70.95, 53.50, 53.26, 40.62, 30.51, 27.23, 26.50, 20.76. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{26}NO_6$: 424.1755,found, 424.1760.



4am

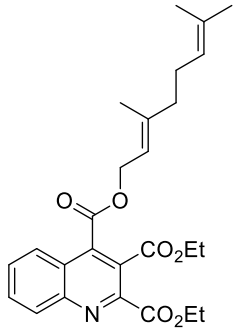
2,3-dimethyl 4-((1*R*,2*S*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) quinoline-2,3,4-

tricarboxylate (4am): yellow solid (Yield: 40%, 50.72 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.87 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.72 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.06 (t, J = 5.8 Hz, 1H), 4.04 (s, 3H), 3.93 (s, 3H), 2.03 (d, J = 5.8 Hz, 2H), 1.84 – 1.69 (m, 2H), 1.63 (td, J = 12.1, 11.6, 3.8 Hz, 1H), 1.26 (d, J = 13.1 Hz, 2H), 0.93 (s, 3H), 0.83 (d, J = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.91, 165.66, 165.26, 148.13, 147.59, 141.15, 132.14, 130.58, 129.96, 125.47, 123.83, 122.31, 84.40, 53.48, 53.20, 48.95, 47.07, 45.13, 38.59, 33.85, 27.01, 20.01, 19.78, 11.76. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{28}NO_6$:426.1872,found, 426.1877.



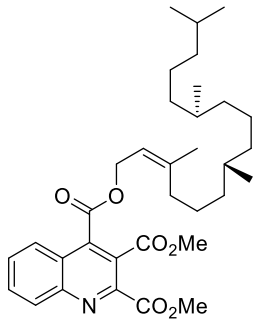
4an

4-((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4an): yellow solid (Yield: 42%, 53.82 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.1 Hz, 1H), 8.02 (d, J = 9.1 Hz, 1H), 7.88 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.74 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.11 (td, J = 10.9, 4.4 Hz, 1H), 4.05 (s, 3H), 3.95 (s, 3H), 2.37 (d, J = 11.7 Hz, 1H), 1.96 (td, J = 7.0, 2.6 Hz, 1H), 1.74 (d, J = 12.5 Hz, 2H), 1.68 – 1.56 (m, 2H), 1.47 (t, J = 11.6 Hz, 1H), 1.21 – 1.11 (m, 2H), 1.00 (d, J = 6.5 Hz, 3H), 0.88 (t, J = 7.4 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.84, 165.20, 147.73, 147.58, 140.73, 132.02, 130.66, 130.01, 125.47, 123.92, 122.84, 77.63, 53.49, 53.17, 46.87, 40.54, 34.08, 31.56, 25.80, 23.03, 22.09, 20.80, 15.96. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{30}NO_6$:428.2028,found, 428.2022.



4ao

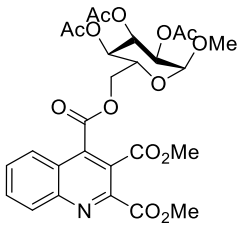
(*E*)-4-(3,7-dimethylocta-2,6-dien-1-yl) 2,3-diethyl quinoline-2,3,4-tricarboxylate (4ao): yellow liquid (Yield: 70 %, 95.02 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.86 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.71 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.49 (t, J = 7.2 Hz, 1H), 5.12 – 5.06 (m, 1H), 4.98 (d, J = 7.2 Hz, 2H), 4.50 (q, J = 7.1 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 2.10 (p, J = 8.5, 7.5 Hz, 4H), 1.79 (s, 3H), 1.66 (s, 3H), 1.59 (s, 3H), 1.41 (dt, J = 22.3, 7.2 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.66, 165.55, 165.30, 148.69, 147.63, 144.15, 140.57, 132.04, 132.01, 130.50, 129.79, 125.62, 123.81, 123.54, 122.63, 117.13, 63.46, 62.64, 62.45, 39.61, 26.29, 25.68, 17.70, 16.65, 14.13, 13.95. HRMS (ESI) cald. for (M+H)+ $C_{26}H_{32}NO_6$:454.2185,found, 454.2194.



4ap

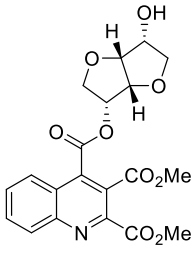
2,3-dimethyl 4-((7*S*,11*R*,*Z*)-3,7,11,15-tetramethylhexadec-2-en-1-yl) quinoline-2,3,4-tricarboxylate (4ap): yellow liquid (Yield: 65 %, 115.92 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.87 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.72 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 5.48 (t, J = 7.3 Hz, 1H), 4.98 (d, J = 7.3 Hz, 2H), 4.04 (s, 3H), 3.93 (s, 3H), 2.05 (t, J = 7.1 Hz, 2H), 1.78 (s, 3H), 1.52 – 1.35 (m, 4H), 1.32 – 1.19 (m, 8H), 1.18 –

0.97 (m, 7H), 0.85 – 0.81 (m, 12H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 165.90, 165.72, 165.45, 147.74, 147.61, 144.79, 140.30, 132.08, 130.55, 130.02, 125.71, 123.94, 123.10, 116.88, 63.57, 53.47, 53.15, 39.97, 39.36, 37.42, 37.34, 37.28, 36.68, 32.78, 32.69, 27.97, 25.09, 24.79, 24.46, 22.72, 22.63, 19.74, 19.69, 16.54. HRMS (ESI) cald. for (M+H)+ $C_{34}H_{50}NO_6$:568.3633,found, 568.3645.



4aq

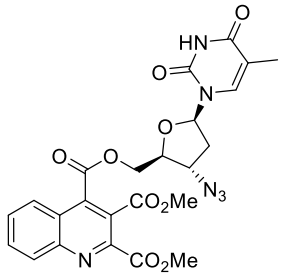
2,3-dimethyl 4-(((2*S*,3*S*,4*S*,5*S*,6*R*)-3,4,5-triacetoxy-6-methoxytetrahydro-2H-pyran-2-yl)methyl) quinoline-2,3,4-tricarboxylate (4aq): yellow oil (Yield: 53%, 93.82 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.5 Hz, 1H), 8.11 (d, J = 9.2 Hz, 1H), 7.89 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.76 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.52 – 5.47 (m, 1H), 5.04 – 4.99 (m, 1H), 4.95 (d, J = 3.5 Hz, 1H), 4.86 – 4.82 (m, 2H), 4.52 (d, J = 4.2 Hz, 2H), 4.13 – 4.09 (m, 1H), 4.03 (s, 3H), 3.95 (s, 3H), 3.34 (s, 3H), 2.04 (d, J = 4.4 Hz, 6H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 170.17, 170.06, 169.68, 165.74, 165.71, 165.19, 147.83, 147.66, 139.72, 132.33, 130.55, 130.22, 125.79, 123.77, 123.06, 96.68, 70.73, 69.85, 69.03, 66.94, 64.59, 55.71, 53.51, 53.36, 20.70, 20.66. HRMS (ESI) cald. for (M+H)+ $C_{27}H_{30}NO_{14}$:592.1622,found, 592.1618.



4ar

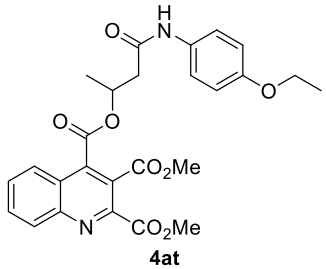
4-((3*R*,3a*R*,6*R*,6a*R*)-6-hydroxyhexahydrofuro[3,2-b]furan-3-yl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ar): yellow solid (Yield: 67%, 53.82 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.24 (t, J = 8.3 Hz, 2H), 7.87 (ddd, J = 8.6, 6.9, 1.5 Hz, 1H), 7.73 (ddd, J = 8.2,

6.9, 1.3 Hz, 1H), 5.49 (q, J = 5.9 Hz, 1H), 4.91 (t, J = 5.3 Hz, 1H), 4.52 (t, J = 5.2 Hz, 1H), 4.29 (s, 1H), 4.18 (dd, J = 9.9, 6.1 Hz, 1H), 4.03 (s, 3H), 4.00 – 3.94 (m, 2H), 3.93 (s, 3H), 3.85 (d, J = 5.8 Hz, 1H), 3.46 (dd, J = 9.1, 7.4 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.81, 164.88, 147.79, 147.64, 139.90, 132.42, 130.38, 130.22, 126.07, 123.81, 122.63, 95.16, 81.77, 80.46, 76.23, 73.61, 72.18, 70.78, 53.51, 53.30. HRMS (ESI) cald. for (M+H)+ $C_{20}H_{20}NO_9$: 418.1093,found, 418.1095.



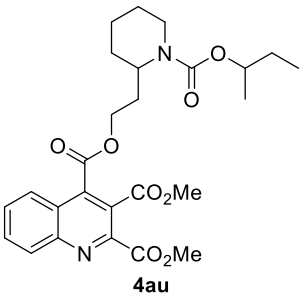
4as

4-(((2*S*,3*S*,5*R*)-3-azido-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4as): yellow solid (Yield: 48%, 77.47 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 9.18 (s, 1H), 8.30 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.91 (t, J = 7.7 Hz, 1H), 7.75 (t, J = 7.2 Hz, 1H), 7.01 (s, 1H), 6.21 – 6.11 (m, 1H), 4.84 (dd, J = 12.3, 3.7 Hz, 1H), 4.69 (dd, J = 12.3, 3.1 Hz, 1H), 4.39 (q, J = 6.4 Hz, 1H), 4.11 (dt, J = 6.4, 3.4 Hz, 1H), 4.05 (s, 3H), 3.94 (s, 3H), 2.49 – 2.33 (m, 2H), 1.35 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.04, 165.59, 165.30, 163.52, 150.19, 147.89, 147.66, 139.89, 135.20, 132.65, 130.79, 130.56, 125.23, 123.47, 122.70, 111.50, 84.89, 81.22, 64.57, 59.50, 53.59, 37.35, 29.69, 11.78. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{23}N_6O_9$:539.1482,found, 539.1485.



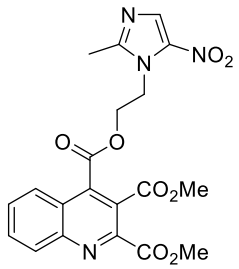
4at

4-(4-((4-ethoxyphenyl)amino)-4-oxobutan-2-yl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4at): light yellow solid (Yield: 48%, 111.07 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.21 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.88 (s, 1H), 7.79 (t, J = 7.7 Hz, 1H), 7.49 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 9.0 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 5.88 – 5.75 (m, 1H), 4.04 (s, 3H), 3.97 (t, J = 7.0 Hz, 2H), 3.93 (s, 3H), 2.79 – 2.63 (m, 2H), 1.53 (d, J = 6.4 Hz, 3H), 1.37 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 167.21, 166.48, 165.77, 164.88, 155.73, 147.59, 147.52, 140.73, 132.33, 130.89, 130.36, 130.25, 125.73, 123.62, 122.41, 121.55, 114.64, 71.37, 63.68, 53.46, 43.55, 19.56, 14.38. HRMS (ESI) cald. for (M+H)+ $C_{26}H_{27}N_2O_8$:495.1723,found, 495.1728.



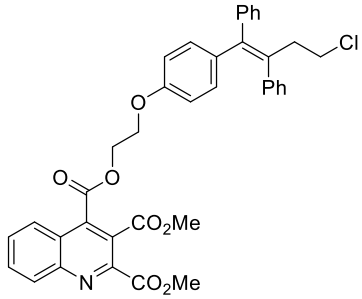
4au

4-(2-(1-(sec-butoxycarbonyl)piperidin-2-yl)ethyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4au): yellow oil (Yield: 67%, 100.32 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.29 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 7.6 Hz, 1H), 7.90 (t, J = 8.4 Hz, 1H), 7.77 (t, J = 8.3 Hz, 1H), 4.72 (q, J = 6.2 Hz, 1H), 4.46 (s, 2H), 4.06 (s, 3H), 3.96 (s, 3H), 2.86 (t, J = 12.6 Hz, 1H), 2.26 (ddd, J = 13.7, 9.8, 6.8 Hz, 1H), 1.92 (dt, J = 13.8, 6.5 Hz, 1H), 1.64 (q, J = 12.4 Hz, 8H), 1.48 – 1.40 (m, 2H), 1.16 (d, J = 6.1 Hz, 2H), 0.88 – 0.82 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.94, 165.75, 165.48, 155.56, 147.74, 147.62, 140.35, 132.22, 130.55, 130.19, 125.84, 123.84, 123.04, 73.15, 73.08, 64.52, 53.52, 53.22, 47.76, 39.00, 32.15, 31.92, 29.37, 29.00, 19.73, 9.66. HRMS (ESI) cald. for (M+H)+ $C_{26}H_{33}N_2O_8$:501.2192,found, 501.2188.



4av

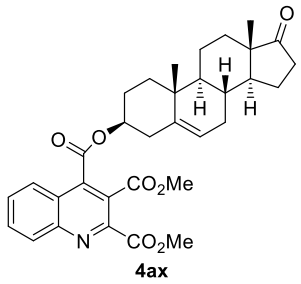
2,3-dimethyl 4-(2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethyl) quinoline-2,3,4-tricarboxylate (4av): yellow solid (Yield: 60%,79.47 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.5 Hz, 1H), 7.97 (s, 1H), 7.89 (dd, J = 8.5, 4.2 Hz, 1H), 7.71 (d, J = 3.7 Hz, 2H), 4.81 (t, J = 5.3 Hz, 2H), 4.70 (t, J = 5.3 Hz, 2H), 4.03 (s, 3H), 3.88 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.68, 165.68, 165.04, 151.23, 147.99, 147.64, 139.55, 133.24, 132.99, 132.59, 130.67, 130.47, 125.11, 123.35, 122.57, 64.69, 53.56, 53.43, 44.76, 14.28. HRMS (ESI) cald. for (M+H)+ $C_{20}H_{19}N_4O_8$: 443.1158,found, 443.1161.



4aw

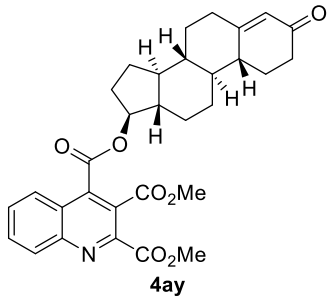
(*Z*)-4-(2-(4-(4-chloro-1,2-diphenylbut-1-en-1-yl)phenoxy)ethyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4aw): white solid (Yield: 73%,142.02 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.29 – 8.22 (m, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.83 (t, J = 7.3 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.29 (d, J = 7.3 Hz, 3H), 7.15 (q, J = 6.9 Hz, 5H), 6.82 (d, J = 8.7 Hz, 2H), 6.60 (d, J = 8.7 Hz, 2H), 4.83 – 4.70 (m, 2H), 4.23 – 4.15 (m, 2H), 4.03 (s, 3H), 3.85 (s, 3H), 3.41 (t, J = 7.3 Hz, 2H), 2.92 (t, J = 7.4 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.83, 165.75, 165.41, 156.43, 147.85, 147.61, 142.77, 141.63, 140.92, 140.01, 135.63, 135.56, 132.26, 131.87, 130.50, 130.21, 129.58, 129.41, 128.42, 128.26, 127.06, 126.67, 125.77, 123.78,

123.04, 113.56, 65.17, 64.71, 53.53, 53.38, 42.86, 38.54. HRMS (ESI) cald. for (M+H)+ $C_{38}H_{33}ClNO_7$:650.1940,found, 650.1948.



4ax

4-((3*S*,8*R*,9*S*,10*R*,13*S*,14*S*)-10,13-dimethyl-17-oxo-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)2,3-dimethylquinoline-2,3,4-tricarboxylate (4ax): yellow solid (Yield: 52%, 87.37 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 8.2 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.86 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.72 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.48 (d, J = 5.2 Hz, 1H), 5.03 (tt, J = 11.4, 4.8 Hz, 1H), 4.02 (s, 3H), 3.94 (s, 3H), 2.56 (ddd, J = 13.1, 5.1, 2.1 Hz, 1H), 2.48 – 2.40 (m, 2H), 2.17 – 2.05 (m, 3H), 1.97 – 1.89 (m, 3H), 1.82 (t, J = 9.3 Hz, 2H), 1.70 – 1.60 (m, 4H), 1.56 – 1.41 (m, 3H), 1.33 – 1.24 (m, 2H), 1.03 (s, 3H), 0.86 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 220.91, 165.85, 164.80, 147.76, 147.58, 140.53, 139.29, 132.12, 130.57, 130.08, 125.53, 123.81, 122.64, 120.81, 76.63, 53.46, 53.15, 51.67, 50.12, 47.50, 37.84, 36.87, 36.75, 35.82, 31.44, 31.39, 30.78, 30.76, 27.58, 21.86, 20.33, 19.30, 13.54. HRMS (ESI) cald. for (M+H)+ $C_{33}H_{38}NO_7$:560.2604,found, 560.26048.



4ay

2,3-dimethyl 4-((8*R*,9*S*,10*R*,13*S*,14*S*,17*S*)-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl) quinoline-2,3,4-tricarboxylate (4ay):

yellow solid (Yield: 54%, 85.37 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.2 Hz, 1H), 8.00 (d, J = 7.8 Hz, 1H), 7.89 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.74 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 5.74 (s, 1H), 5.04 – 4.96 (m, 1H), 4.05 (s, 3H), 3.94 (s, 3H), 2.50 – 2.25 (m, 5H), 2.07 – 1.92 (m, 2H), 1.91 – 1.56 (m, 8H), 1.50 – 1.24 (m, 4H), 1.15 – 0.95 (m, 2H). 13C NMR (101 MHz, Chloroform-d) δ 199.41, 170.69, 165.81, 165.79, 147.93, 147.61, 140.77, 132.12, 130.65, 130.05, 125.50, 124.05, 123.83, 122.72, 85.35, 53.68, 53.52, 53.26, 50.15, 42.79, 38.61, 36.65, 35.73, 35.39, 33.94, 31.45, 29.71, 27.31, 23.58, 20.56. HRMS (ESI) cald. for (M+H)+ $C_{31}H_{34}NO_7$:532.2291,found, 532.2286.

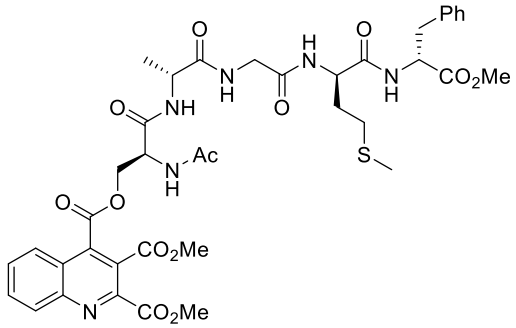
3.4 Gram-Scale Experiments

General procedure for Gram-Scale Experiments: In an oven-dried undivided three-necked bottle (50 mL) equipped with a stir bar, isatin (3 mmol), dimethyl but-2-ynedioate (4.5 mmol), serine residue (4.5 mmol), $^{n}Bu_4NBF_4$ (1.5 mmol) and KI (0.9 mmol) were combined and added. Then, CH_3CN (20 mL) were injected into the tubes via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 5 mA under room temperature overnight. The solvent was removed under vacuum. The crude product was purified by flash column chromatography on silica gel to afford pure product.

3.5 Polypeptide scope and characterization：

The procedure for the bioconjugated product (4ai): In an oven-dried undivided three-necked bottle (15 mL) equipped with a stir bar, polypeptides (5 mg), isatin (10 mg), but-2-ynedioate(12 μL) , $^{n}Bu_4NBF_4$ (5 mg), KI (2 mg) and CH_3CN (0.75 mL) were combined and added. The bottle was equipped carbon paper (10 mm×10 mm×0.1 mm) as the anode and platinum plate (10 mm×10

mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at constant current of 5 mA under room temperature for 30 min. After completion of the reaction, the solution was analyzed by TOF-LC/MS spectroscopy. The reaction was analyzed by reverse phase HPLC using a gradient of 70% to 60% buffer B over 20 minutes on an Agilent Zorbax SB-Aq 5μm column of 250 mm length. HPLC analysis used buffers A (water) and B (acetonitrile + 0.1% TFA). Conversion reported as a % conversion as determined.



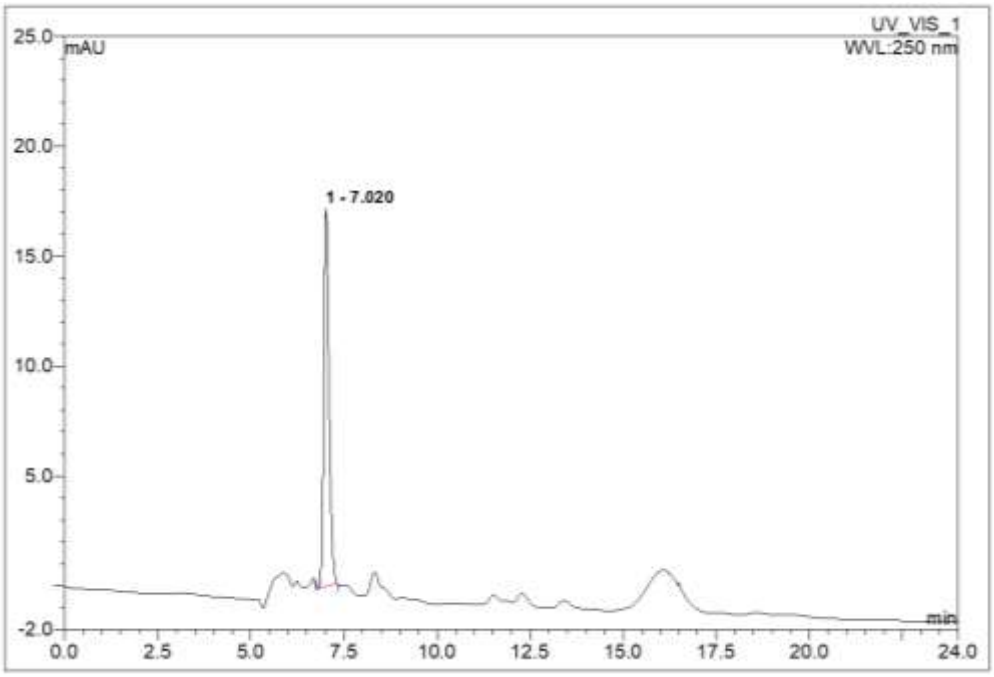
bioconjugated product 4ai : Ac-S(Quinoline)AGMF-Ome

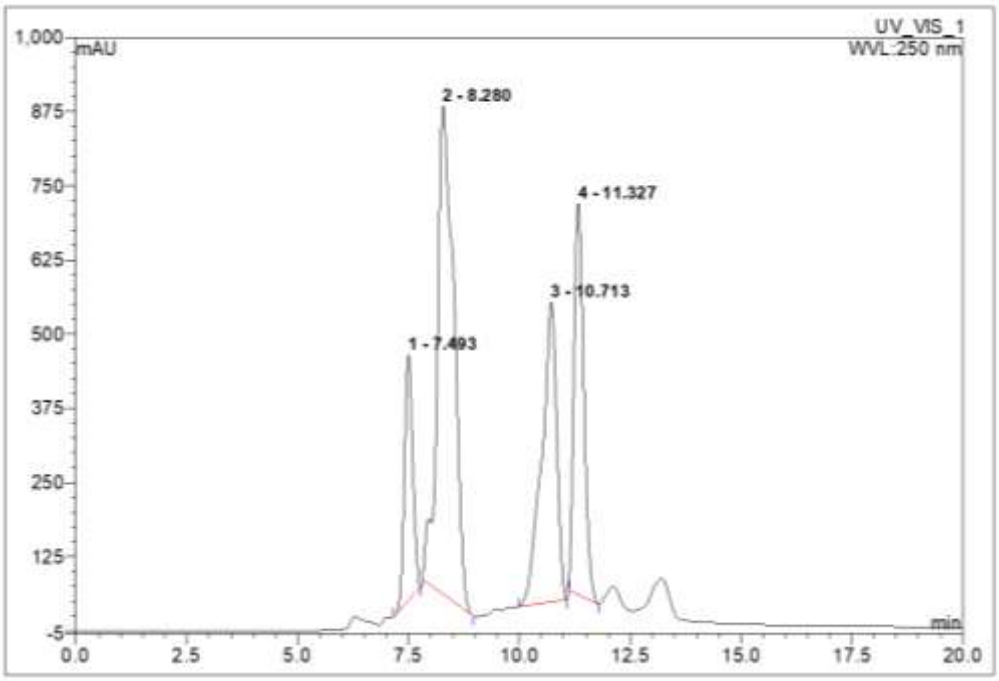
HPLC: >99% conversion.

After the reaction finished, there are four peaks that elute at 60% buffer B (acetonitrile + 0.1% TFA) with retention times of 7.493 min , 8.280 min, 10.713 min and 11.327 min. Polypeptide **3ai** is a peak that elutes at 60% buffer B (acetonitrile + 0.1% TFA) with a retention time of 7.020 min.

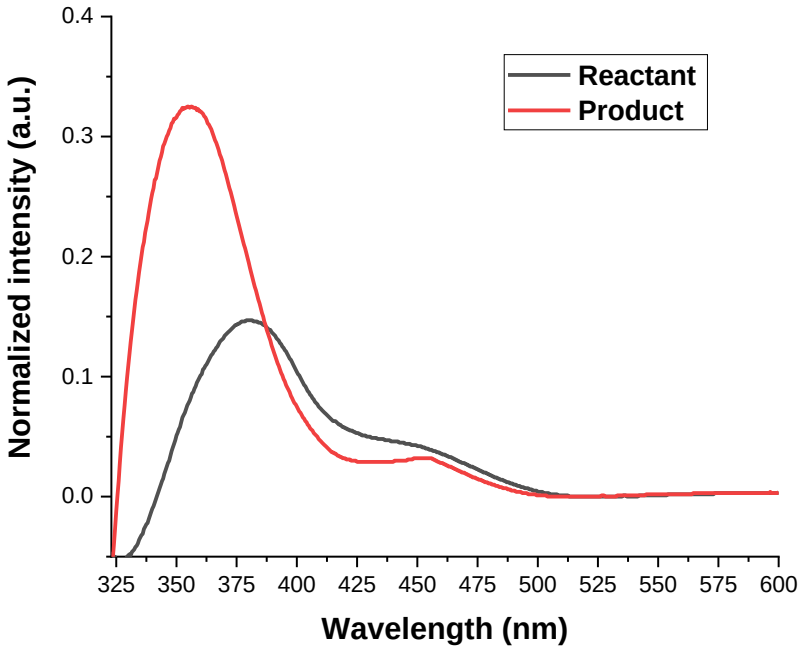
HRMS (ESI-TOF) calcd for $C_{39}H_{47}N_6O_{13}S$, [M+H]+, 839.2922, found 839.2928. calcd for $C_{39}H_{46}N_6NaO_{13}S$, [M+Na]+, 861.2741, found 861.2736.

HPLC Spectra:





Normalized UV-VIS Spectra of Reactants and Products:



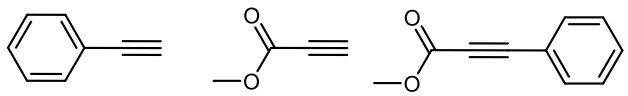
3.6 Isatins, alkynes and selected small-molecule alcohols scope and characterization.

General procedure for quinoline-substituted product: In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, isatin (0.3 mmol), dimethyl but-2-ynedioate (0.45 mmol), alcohol (0.45 mmol), $^{n}Bu_4NBF_4$ (0.15 mmol) and KI (0.03 mmol) were combined and added. Then, CH_3CN (6 mL) were injected into the tubes via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at a constant current of 5 mA under room temperature for 100 min. After completion of the reaction, as indicated by TLC and GC-MS, the pure product was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate).

We tested various other alkynes, including phenylacetylene, methyl 3-phenylpropiolate and methyl propiolate, no reaction occurred under standard conditions and led to full recovery of the starting material. We have also tested the substrates the containing amine group. Unfortunately,

the reaction was messy and no product could be obtained.

Some inert alkynes:

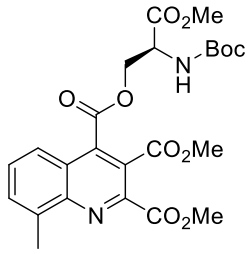


n.r. n.r. n.r.

Substrates containing NH group:

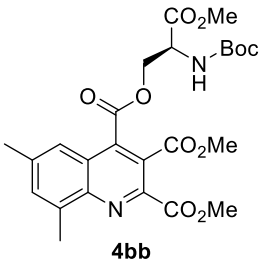
mess mess

Detailed descriptions for products:



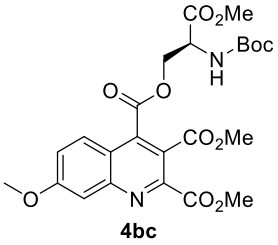
4ba

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 8-methylquinoline-2,3,4-tricarboxylate (4ba): yellow oil (Yield: 74%, 110.67 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 7.73 (dd, J = 17.0, 7.7 Hz, 2H), 7.62 – 7.56 (m, 1H), 5.55 (d, J = 8.4 Hz, 1H), 4.81 (t, J = 3.9 Hz, 2H), 4.69 (s, 1H), 4.01 (s, 3H), 3.96 (s, 3H), 3.74 (s, 3H), 2.81 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.86, 166.36, 165.81, 165.47, 155.29, 147.32, 146.88, 140.46, 138.99, 132.50, 129.81, 123.57, 123.27, 121.05, 80.41, 66.16, 53.43, 53.21, 52.89, 28.28, 17.96. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{29}N_2O_{10}$:505.1777,found, 505.1766.



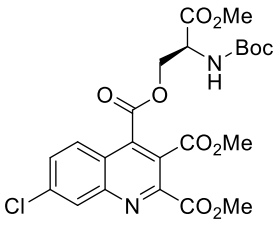
4bb

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 6,8-dimethylquinoline-2,3,4-tricarboxyla (4bb): yellow solid (Yield: 65%, 100.67 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 7.53 (d, J = 15.7 Hz, 2H), 5.56 (d, J = 8.4 Hz, 1H), 4.81 (d, J = 3.4 Hz, 2H), 4.69 (s, 1H), 4.01 (s, 3H), 3.96 (s, 3H), 3.75 (s, 3H), 2.77 (s, 3H), 2.52 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.90, 166.43, 166.07, 165.63, 155.33, 146.21, 145.63, 140.43, 139.46, 138.46, 134.91, 123.72, 122.01, 121.29, 80.41, 66.12, 53.39, 53.16, 52.90, 52.87, 28.29, 22.04, 17.84. HRMS (ESI) cald. for (M+H)+ $C_{25}H_{31}N_2O_{10}$:519.1973,found, 519.1984.



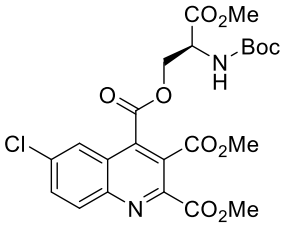
4bc

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 7-methoxyquinoline-2,3,4-tricarboxylate (4bc): light yellow solid (Yield: 76%, 118.17 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 7.83 (d, J = 9.3 Hz, 1H), 7.53 (d, J = 2.5 Hz, 1H), 7.34 (dd, J = 9.3, 2.6 Hz, 1H), 5.55 (d, J = 8.3 Hz, 1H), 4.79 (t, J = 3.3 Hz, 2H), 4.68 (s, 1H), 4.02 (s, 3H), 3.94 (s, 6H), 3.75 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.86, 166.05, 165.89, 165.25, 162.94, 155.28, 150.01, 148.81, 139.84, 126.59, 123.78, 119.70, 118.88, 108.07, 80.43, 66.21, 55.95, 53.45, 53.38, 52.91, 52.86, 28.28. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{29}N_2O_{11}$:521.1727,found, 521.1731.



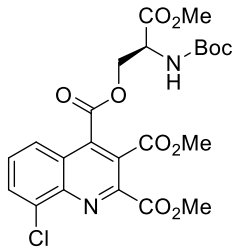
4bd

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 7-chloroquinoline-2,3,4-tricarboxylate (4bd): yellow solid (Yield: 75%, 117.57 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.24 (s, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 5.52 (d, J = 7.8 Hz, 1H), 4.81 (d, J = 3.0 2H), 4.69 (s, 1H), 4.03 (s, 3H), 3.96 (s, 3H), 3.76 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.79, 165.53, 165.45, 164.60, 155.23, 149.17, 147.98, 139.79, 138.81, 131.25, 129.39, 126.89, 122.62, 122.13, 80.52, 66.44, 53.59, 52.97, 52.82, 28.27. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}ClN_2O_{10}$: 525.1198,found, 525.1201.



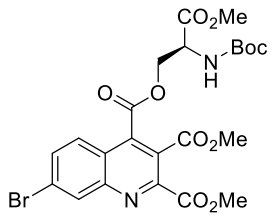
4be

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 6-chloroquinoline-2,3,4-tricarboxylate (4be): yellow oil (Yield: 71%, 110.15 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.19 (d, J = 9.0 Hz, 1H), 8.00 (s, 1H), 7.81 (d, J = 11.3 Hz, 1H), 5.56 – 5.48 (m, 1H), 4.81 (d, J = 3.2 Hz, 2H), 4.70 (s, 1H), 4.03 (s, 3H), 3.97 (s, 3H), 3.78 (s, 3H), 1.43 (s, 9H). 13C NMR (101 MHz, Chloroform-d) δ 169.76, 165.71, 165.32, 164.40, 155.24, 147.78, 145.98, 138.36, 136.77, 133.39, 132.05, 124.45, 124.42, 124.04, 80.51, 66.56, 53.63, 53.61, 53.02, 52.79, 28.26. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}ClN_2O_{10}$:525.1198,found, 525.1194.



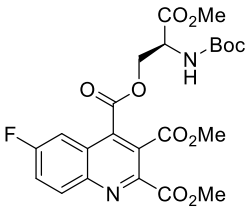
4bf

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 8-chloroquinoline-2,3,4-tricarboxylate (4bf): light yellow solid (Yield: 67%, 103.74 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.00 (d, J = 7.5 Hz, 1H), 7.91 (d, J = 9.4 Hz, 1H), 7.66 (t, J = 8.3, 1H), 5.50 (d, J = 8.2 Hz, 1H), 4.88 – 4.76 (m, 2H), 4.70 (s, 1H), 4.05 (s, 3H), 3.98 (s, 3H), 3.76 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.78, 165.51, 165.46, 164.74, 155.24, 148.63, 144.06, 140.50, 135.17, 132.43, 129.96, 125.11, 124.52, 123.10, 80.53, 66.46, 53.65, 53.55, 52.97, 52.84, 28.29. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}ClN_2O_{10}$:525.1198,found, 525.1196.



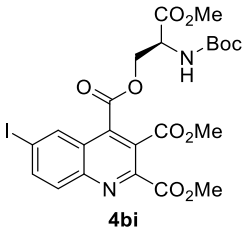
4bg

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 7-bromoquinoline-2,3,4-tricarboxylate (4bg): yellow solid (Yield: 67%, 118.95 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.38 (s, 1H), 7.82 (d, J = 9.0 Hz, 1H), 7.74 (d, J = 9.0 Hz, 1H), 5.55 (d, J = 8.2 Hz, 1H), 4.77 (t, J = 3.9 Hz, 2H), 4.66 (s, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 3.72 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.77, 165.50, 165.35, 164.49, 155.22, 149.01, 147.97, 139.80, 133.69, 132.67, 127.10, 126.80, 122.73, 122.33, 80.42, 66.40, 53.58, 53.55, 52.93, 52.79, 28.24. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}BrN_2O_{10}$: 569.0771,found, 569.0776.



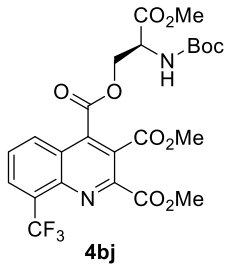
4bh

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 6-fluoroquinoline-2,3,4-tricarboxylate (4bh): yellow oil (Yield: 72%, 118.95 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.25 (dd, J = 9.2, 5.3 Hz, 1H), 7.68 – 7.61 (m, 2H), 5.52 (d, J = 8.2 Hz, 1H), 4.83 – 4.74 (m, 2H), 4.68 (s, 1H), 4.01 (s, 3H), 3.96 (s, 3H), 3.76 (s, 3H), 1.41 (s, 9H). ^{19}F NMR (376 MHz, Chloroform-d) δ -105.46. ^{13}C NMR (101 MHz, Chloroform-d) δ 169.76, 165.88, 165.31, 164.48, 162.65 (d, J = 254.6 Hz), 155.22, 146.83 (d, J = 2.8 Hz), 144.74, 138.40 (d, J = 6.2 Hz), 133.37 (d, J = 9.5 Hz), 124.98 (d, J = 10.9 Hz), 124.26, 122.85 (d, J = 26.1 Hz), 109.40 (d, J = 24.5 Hz), 80.49, 66.44, 53.58, 53.56, 52.95, 52.78, 28.22. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{25}FN_2O_{10}$:508.1493,found, 508.1487.



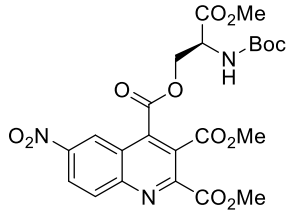
4bi

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 6-iodoquinoline-2,3,4-tricarboxylate (4bi): light yellow oil (Yield: 75%, 138.56 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.39 (d, J = 1.7 Hz, 1H), 8.12 (d, J = 10.8 Hz, 1H), 7.95 (d, J = 8.9 Hz, 1H), 5.53 (d, J = 7.3 Hz, 1H), 4.81 (d, J = 3.2 Hz, 2H), 4.70 (s, 1H), 4.03 (s, 3H), 3.97 (s, 3H), 3.79 (s, 3H), 1.43 (s, 9H). 13C NMR (101 MHz, Chloroform-d) δ 169.76, 165.64, 165.38, 164.41, 155.26, 148.06, 146.51, 141.28, 138.11, 134.33, 131.78, 125.07, 123.69, 97.34, 80.53, 66.59, 53.64, 53.61, 53.09, 52.79, 28.30. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}IN_2O_{10}$:617.0632,found, 617.0635.



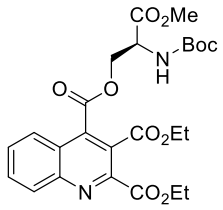
4bj

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 8-(trifluoromethyl)quinoline-2,3,4-tricarboxylate (4bj): white solid (Yield: 66%, 110.45 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.21 (dd, J = 18.8, 7.8 Hz, 2H), 7.79 (t, J = 7.9 Hz, 1H), 5.51 (d, J = 8.2 Hz, 1H), 4.83 (td, J = 11.5, 3.4 Hz, 2H), 4.70 (s, 1H), 4.03 (s, 3H), 3.98 (s, 3H), 3.76 (s, 3H), 1.43 (s, 9H). ^{19}F NMR (376 MHz, Chloroform-d) δ -60.17. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.77, 165.56, 165.28, 164.60, 155.24, 149.09, 144.19, 140.15, 130.65 (q, J = 5.3 Hz), 129.86, 128.96 (q, J = 124.0 Hz), 128.70, 124.05, 123.17 (q, J = 274.0 Hz), 122.75, 80.53, 66.48, 53.68, 53.48, 52.96, 52.84, 28.27. HRMS (ESI) cald. for (M+H)+ $C_{24}H_{26}F_3N_2O_{10}$:559.1540,found, 559.1538.



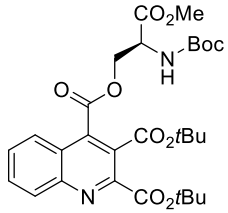
4bk

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-dimethyl 6-nitroquinoline-2,3,4-tricarboxylate (4bk): yellow solid (Yield: 71%, 112.57 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 9.00 (d, J = 2.3 Hz, 1H), 8.64 (dd, J = 9.3, 2.4 Hz, 1H), 8.43 (d, J = 9.3 Hz, 1H), 5.54 (d, J = 7.8 Hz, 1H), 4.88 (t, J = 2.9 Hz, 2H), 4.73 (s, 1H), 4.07 (s, 3H), 4.01 (s, 3H), 3.80 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.69, 165.08, 164.93, 163.82, 155.23, 151.03, 149.25, 147.77, 141.09, 132.54, 125.60, 124.82, 123.10, 122.49, 80.64, 66.97, 53.85, 53.10, 52.81, 51.76, 28.25. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}N_3O_{12}$:536.1516,found, 536.1518.



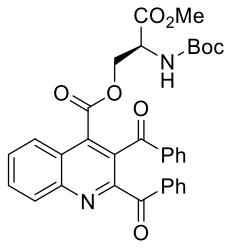
4bl

(*S*)-4-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-diethyl quinoline-2,3,4-tricarboxylate (4bl): light yellow oil (Yield: 81%, 125.57 mg) , ^{1}H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 8.5 Hz, 1H), 7.97 – 7.84 (m, 2H), 7.72 (t, J = 7.6 Hz, 1H), 5.55 (d, J = 8.1 Hz, 1H), 4.82 (d, J = 3.2 Hz, 2H), 4.69 (s, 1H), 4.46 (dq, J = 28.1, 7.1 Hz, 4H), 3.75 (s, 3H), 1.43 (t, J = 5.5 Hz, 12H), 1.38 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 193.54, 169.60, 164.79, 164.54, 155.24, 147.51, 147.18, 144.74, 138.02, 134.60, 131.70, 131.55, 130.94, 130.50, 129.51, 129.30, 125.38, 124.23, 80.34, 66.12, 62.77, 52.81, 52.60, 28.32, 21.81, 13.73. HRMS (ESI) cald. for (M+H)+ $C_{25}H_{31}N_2O_{10}$:519.1979,found, 519.1978.



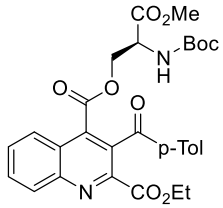
4bm

(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2,3-di-tert-butyl quinoline-2,3,4-tricarboxylate (4bm): light yellow solid (Yield: 60%, 103.24 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.23 (d, J = 8.4 Hz, 1H), 7.87 – 7.77 (m, 2H), 7.67 (t, J = 7.6 Hz, 1H), 5.49 (d, J = 8.1 Hz, 1H), 4.84 (qd, J = 11.2, 3.3 Hz, 2H), 4.72 (s, 1H), 3.74 (s, 3H), 1.66 (s, 9H), 1.58 (s, 9H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.85, 165.69, 165.13, 164.20, 155.20, 150.59, 147.41, 139.73, 131.74, 130.53, 129.37, 125.19, 123.27, 122.83, 84.05, 83.65, 80.48, 65.92, 53.45, 52.96, 28.30, 28.09, 27.95. HRMS (ESI) cald. for (M+H)+ $C_{29}H_{39}N_2O_{10}$:575.2605,found, 575.2603.



4bn

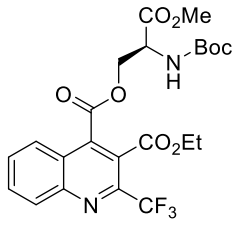
(*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl 2,3-dibenzoylquinoline-4-carboxylate (4bn): white solid ((Yield: 65%, 113.47 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.06 (d, J = 7.1 Hz, 2H), 7.93 – 7.89 (m, 1H), 7.80 (t, J = 7.9 Hz, 3H), 7.61 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.40 (t, J = 7.7 Hz, 2H), 5.21 (d, J = 8.3 Hz, 1H), 4.58 – 4.43 (m, 2H), 4.22 (d, J = 11.7 Hz, 1H), 3.67 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 194.55, 192.72, 169.65, 164.71, 155.18, 154.51, 146.71, 137.80, 136.95, 135.25, 133.75, 133.69, 132.25, 131.74, 131.21, 130.75, 130.39, 129.29, 128.70, 128.30, 125.51, 123.56, 80.41, 66.08, 52.86, 52.54, 28.33. HRMS (ESI) cald. for (M+H)+ $C_{33}H_{31}N_2O_8$:583.2080,found, 583.2084.



4bo, 71%

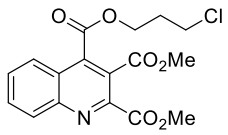
(*S*)-4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 2-ethyl 3-(4-methylbenzoyl)quinoline-2,4-dicarboxylate (4bo): light yellow oil (Yield: 71%, 120.12 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.36 (d, J = 8.5 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.90 (t, J = 7.2 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.65 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 5.26 (d, J = 8.1 Hz, 1H), 4.59 – 4.48 (m, 2H), 4.36 (dd, J = 10.7, 2.5 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.66 (s, 3H), 2.40 (s, 3H), 1.45 (s, 9H), 1.16 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 193.54, 169.60, 164.79, 164.54, 155.24, 147.51, 147.18, 144.74, 138.02, 134.60, 131.70, 131.55, 130.94, 130.50, 129.51, 129.30, 125.38, 124.23, 80.34, 66.12, 62.77, 52.81, 52.60, 28.32, 21.81,

13.73. HRMS (ESI) cald. for (M+H)+ $C_{30}H_{33}N_2O_9$: 565.2186,found, 565.2184.



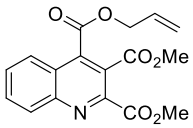
4bp, 80%

(S)-4-(2-((tert-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 3-ethyl 2-(trifluoromethyl)quinoline-3,4-dicarboxylate: light yellow oil (Yield: 80%, 123.12 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.24 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.90 (t, J = 7.7 Hz, 1H), 7.76 (t, J = 7.7 Hz, 1H), 5.54 (d, J = 8.2 Hz, 1H), 4.81 (d, J = 3.3 Hz, 2H), 4.71 (s, 1H), 4.46 (t, J = 7.1 Hz, 2H), 3.76 (s, 3H), 1.43 (s, 9H), 1.40 (t, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.76, 165.01, 164.69, 155.23, 146.86, 143.92 (q, J = 35.3 Hz), 140.00, 132.44, 130.67, 130.50, 125.38, 123.84, 122.56, 119.48, 80.44, 67.89, 63.18, 52.92, 52.83, 28.22, 13.75. HRMS (ESI) cald. for (M+H)+ $C_{23}H_{26}F_3N_2O_8$:515.1641,found, 515.1648.



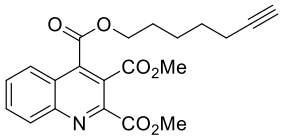
4ca

4-(3-chloropropyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4ca): light yellow oil (Yield: 70%, 76.62 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 7.89 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.74 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 4.64 (t, J = 6.0 Hz, 2H), 4.04 (s, 3H), 3.96 (s, 3H), 3.66 (t, J = 6.2 Hz, 2H), 2.24 (p, J = 6.1 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.90, 165.75, 165.37, 147.83, 147.60, 140.16, 132.33, 130.61, 130.25, 125.54, 123.74, 122.83, 63.26, 53.59, 53.43, 40.91, 31.18. HRMS (ESI) cald. for (M+H)+ $C_{17}H_{17}ClNO_6$:366.0744,found, 366.0739.



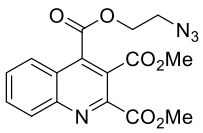
4cb

4-allyl 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4cb): yellow oil (Yield: 67%, 66.12 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 9.0 Hz, 1H), 7.88 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.74 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 6.05 (ddt, J = 17.2, 10.4, 6.0 Hz, 1H), 5.46 (dq, J = 17.2, 1.4 Hz, 1H), 5.36 (dq, J = 10.4, 1.1 Hz, 1H), 4.95 (dt, J = 6.0, 1.3 Hz, 2H), 4.05 (s, 3H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.95, 165.68, 165.10, 147.69, 147.63, 139.82, 132.16, 130.93, 130.61, 130.18, 125.61, 123.87, 123.32, 119.98, 67.30, 53.51, 53.25. HRMS (ESI) cald. for (M+H)+ $C_{17}H_{16}NO_6$:330.0978,found, 330.0979.



4cc

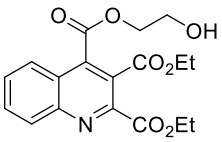
4-(hept-6-yn-1-yl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4cc): yellow liquid (Yield: 56%, 64.23 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (dd, J = 8.3, 3.4 Hz, 1H), 8.05 (dd, J = 8.5, 4.2 Hz, 1H), 7.88 (td, J = 8.4, 7.6, 4.1 Hz, 1H), 7.73 (td, J = 7.0, 3.5 Hz, 1H), 4.47 (d, J = 4.1 Hz, 2H), 4.04 (s, 3H), 3.95 (s, 3H), 2.23 (t, J = 3.9, 2H), 1.97 – 1.90 (m, 1H), 1.84 – 1.72 (m, 2H), 1.57 (s, 4H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.90, 165.75, 165.53, 147.80, 147.61, 140.38, 132.18, 130.58, 130.11, 125.64, 123.84, 122.98, 84.03, 68.63, 66.70, 53.52, 53.26, 27.97, 27.95, 25.01, 18.27. HRMS (ESI) cald. for (M+H)+ $C_{21}H_{22}NO_6$:384.1447,found, 384.1445.



4cd

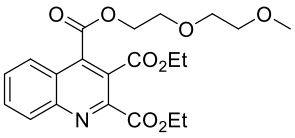
4-(2-azidoethyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4cd): yellow solid (Yield: 60 %, 64.23 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.23 (d, J = 8.5 Hz, 1H), 8.00 (d, J = 8.4 Hz,

1H), 7.85 (ddd, J = 8.4, 7.0, 1.2 Hz, 1H), 7.70 (ddd, J = 8.2, 6.9, 1.1 Hz, 1H), 4.57 (t, J = 5.2 Hz, 2H), 4.01 (s, 3H), 3.94 (s, 3H), 3.64 (t, J = 5.1, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.78, 165.67, 165.27, 148.06, 147.61, 140.01, 132.38, 130.51, 130.24, 125.49, 123.59, 122.56, 64.67, 53.48, 53.35, 49.44. HRMS (ESI) cald. for (M+H)+ $C_{16}H_{15}N_4O_6$:359.0986,found, 359.0987.



4ce

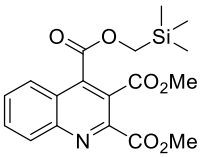
2,3-diethyl 4-(2-hydroxyethyl) quinoline-2,3,4-tricarboxylate (4ae): yellow oil (Yield: 60%, 64.05 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.33 – 8.24 (m, 1H), 8.06 (d, J = 9.1 Hz, 1H), 7.89 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.74 (ddd, J = 8.3, 7.0, 1.2 Hz, 1H), 4.61 (t, J = 4.5 Hz, 2H), 4.51 (q, J = 7.2 Hz, 2H), 4.43 (q, J = 7.2 Hz, 2H), 3.98 (d, J = 3.6Hz, 2H), 2.66 (s, 1H), 1.45 (t, J = 7.2 Hz, 3H), 1.39 (t, J = 7.2 Hz, 3H). 13C NMR (101 MHz, Chloroform-d) δ 165.99, 165.61, 165.46, 148.47, 147.55, 140.48, 132.27, 130.38, 130.05, 125.60, 123.59, 122.31, 68.23, 62.92, 62.73, 60.54, 14.12, 13.88. HRMS (ESI) cald. for (M+H)+ $C_{18}H_{20}NO_7$:362.1240,found, 362.1236.



4cf

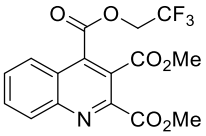
4-(2-(2-methoxyethoxy)ethyl) 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4cf) : yellow oil (Yield: 56%, 65.42 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.86 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.71 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 4.65 – 4.61 (m, 2H), 4.50 (q, J = 7.1 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H), 3.86 – 3.82 (m, 2H), 3.68 – 3.65 (m, 2H), 3.56 – 3.52 (m, 2H), 3.35 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.69, 165.58, 165.25, 148.75, 147.64, 140.51, 132.10, 130.43, 129.86, 125.87, 123.75, 122.55, 71.92, 70.57, 68.68, 65.48, 62.65, 62.55, 59.06, 14.12, 13.94.

HRMS (ESI) cald. for (M+H)+ $C_{21}H_{26}NO_8$:420.1658,found, 420.1660.



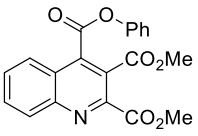
4cg

2,3-dimethyl 4-((trimethylsilyl)methyl) quinoline-2,3,4-tricarboxylate (4cg): yellow solid (Yield: 55%, 61.74 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 7.9 Hz, 1H), 7.87 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.72 (ddd, J = 8.3, 7.0, 1.1 Hz, 1H), 4.15 (s, 2H), 4.04 (s, 3H), 3.94 (s, 3H), 0.12 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 166.50, 165.95, 165.85, 147.89, 147.65, 140.82, 132.15, 130.62, 130.06, 125.72, 123.99, 123.12, 60.36, 53.54, 53.35, -3.02. HRMS (ESI) cald. for (M+H)+ $C_{18}H_{22}NO_6Si$: 376.1216,found, 376.1213.



4ch

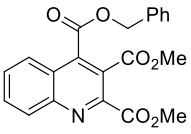
2,3-dimethyl 4-(2,2,2-trifluoroethyl) quinoline-2,3,4-tricarboxylate (4ch): yellow solid (Yield: 60%, 66.89 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 9.0 Hz, 1H), 7.90 (ddd, J = 8.4, 7.0, 1.3 Hz, 1H), 7.75 (ddd, J = 8.3, 7.0, 1.1 Hz, 1H), 4.81 (q, J = 8.3 Hz, 2H), 4.04 (s, 3H), 3.94 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-d) δ -73.20. ^{13}C NMR (101 MHz, Chloroform-d) δ 165.66, 165.51, 164.00, 148.04, 147.67, 138.50, 132.52, 130.68, 130.52, 125.14, 123.48, 122.91, 122.62 (q, J = 277.1 Hz), 61.92 (q, J = 37.3 Hz), 53.54, 53.44. HRMS (ESI) cald. for (M+H)+ $C_{16}H_{13}F_3NO_6$:372.0689,found, 372.0690.



4ci

2,3-dimethyl 4-phenyl quinoline-2,3,4-tricarboxylate (4ci): yellow liquid (Yield: 42%, 46.01mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.33 (d, J = 8.5 Hz, 1H), 8.21 (d, J = 8.5 Hz, 1H),

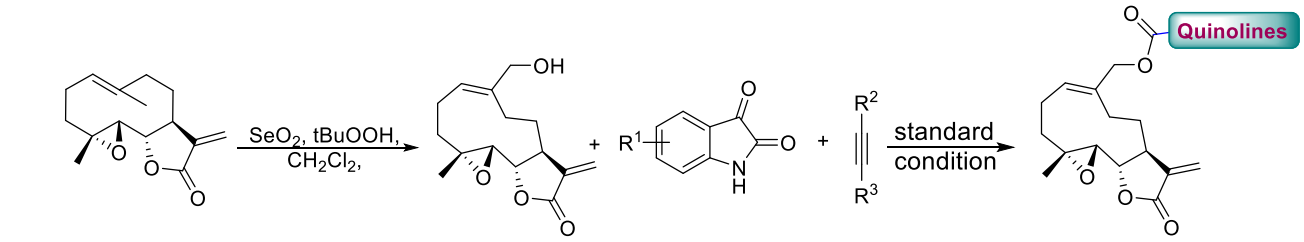
7.94 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.80 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.49 (dd, J = 8.7, 7.1 Hz, 2H), 7.38 – 7.31 (m, 3H), 4.08 (s, 3H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.81, 165.75, 150.38, 147.99, 147.74, 132.40, 130.73, 130.42, 129.83, 126.75, 125.47, 123.82, 123.02, 121.21, 53.56, 53.50. HRMS (ESI) cald. for (M+H)+ $C_{20}H_{16}NO_6$:366.0978,found, 366.0980.



4cj

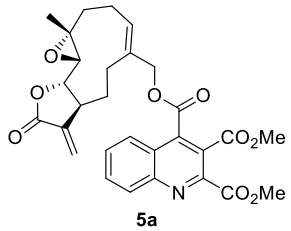
4-benzyl 2,3-dimethyl quinoline-2,3,4-tricarboxylate (4cj): yellow oil (Yield : 67%, 74.73mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.5 Hz, 1H), 8.04 – 8.00 (m, 1H), 7.87 (ddd, J = 8.4, 6.9, 1.3 Hz, 1H), 7.70 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.46 (dd, J = 7.9, 1.6 Hz, 2H), 7.42 – 7.35 (m, 3H), 5.49 (s, 2H), 4.03 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.84, 165.71, 165.26, 147.74, 147.60, 139.83, 134.48, 132.21, 130.58, 130.19, 128.93, 128.90, 128.78, 125.60, 123.86, 123.17, 68.51, 53.56, 53.08. HRMS (ESI) cald. for (M+H)+ $C_{21}H_{18}NO_6$: 380.1134,found, 380.1132.

3.7 PTL derivatives.



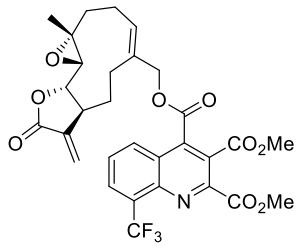
Synthesis of PTL derivatives: In a round bottomed flask, equipped with a stir bar, Parthenolide (PTL) (2.0 mmol), SeO_2 (0.4 mmol), t-BuOOH (70% in water, 3 mmol) dissolved in DCM (20 mL). The mixture was stirred for 36 h at room temperature. The resulting crude product was

purified by flash chromatography (dichloromethane : ethyl ether, containing 0.5% of NEt_3) to afford MMB as a white solid[4]. Then, in an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, isatins (0.3 mmol), MMB (0.45 mmol), alkyne (0.45 mmol), $^nBu_4NBF_4$ (0.15 mmol) and KI (0.03 mmol) were combined and added. Then, CH_3CN (6 mL) were injected into the tubes via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at a constant current of 5 mA under room temperature for 100 min. After completion of the reaction, as indicated by TLC and LC-MS, the pure product was obtained by flash column chromatography on silica gel (eluent: dichloromethane : ethyl ether).



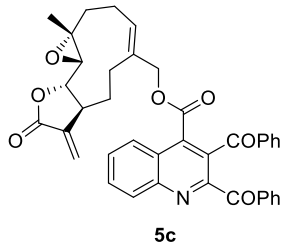
5a

PTL derivative (PTL-OMe**) 5a :** light yellow oil (Yield: 50%, 73.83 mg), ^1H NMR (400 MHz, Chloroform-d) δ 8.29 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.90 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.75 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 6.13 (d, J = 3.5 Hz, 1H), 5.85 (t, J = 8.2 Hz, 1H), 5.49 (d, J = 3.2 Hz, 1H), 5.06 (d, J = 12.1 Hz, 1H), 4.84 (d, J = 12.2 Hz, 1H), 4.05 (s, 3H), 3.92 (s, 3H), 3.84 (t, J = 9.3 Hz, 1H), 2.89 – 2.78 (m, 2H), 2.53 – 2.41 (m, 2H), 2.40 – 2.29 (m, 2H), 2.27 – 2.14 (m, 2H), 1.73 – 1.61 (m, 1H), 1.54 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 169.24, 166.01, 165.68, 165.37, 147.71, 147.61, 140.15, 138.43, 134.24, 132.47, 132.41, 130.73, 130.33, 125.34, 123.68, 122.93, 120.39, 80.93, 69.26, 63.36, 59.94, 53.60, 53.32, 42.71, 36.54, 25.50, 24.24, 23.93, 17.99. HRMS (ESI) cald. for (M+H)+ $C_{29}H_{30}NO_9$:536.1921,found, 536.1923.



5b

PTL derivative (PTL-CF_3**) 5b :** light yellow oil (Yield: 42%, 75.98 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.21 (dd, J = 15.9, 7.9 Hz, 2H), 7.80 (t, J = 7.9 Hz, 1H), 6.14 (d, J = 3.5 Hz, 1H), 5.84 (t, J = 8.2 Hz, 1H), 5.52 (d, J = 3.1 Hz, 1H), 5.05 (d, J = 12.1 Hz, 1H), 4.85 (d, J = 12.2 Hz, 1H), 4.03 (s, 3H), 3.92 (s, 3H), 3.84 (t, J = 9.3 Hz, 1H), 2.88 – 2.77 (m, 2H), 2.56 – 2.42 (m, 2H), 2.41 – 2.29 (m, 2H), 2.19 (ddd, J = 29.8, 9.7, 6.1 Hz, 2H), 1.72 – 1.63 (m, 1H), 1.53 (s, 3H). ^{19}F NMR (376 MHz, Chloroform-d) δ -60.12. ^{13}C NMR (101 MHz, Chloroform-d) δ 169.23, 165.48, 165.38, 164.91, 148.85, 144.13, 140.47, 138.51, 134.10, 132.61, 130.66 (q, J = 5.3 Hz), 129.68, 129.15 (q, J = 30.8 Hz), 128.81, 124.08, 123.19 (q, J = 274.0 Hz), 123.16, 120.35, 80.94, 69.37, 63.32, 59.93, 53.51, 53.44, 42.69, 36.51, 25.37, 24.09, 23.92, 17.94. HRMS (ESI) cald. for (M+H)+ $C_{30}H_{29}F_3NO_9$:604.1794,found, 604.1793.



5c

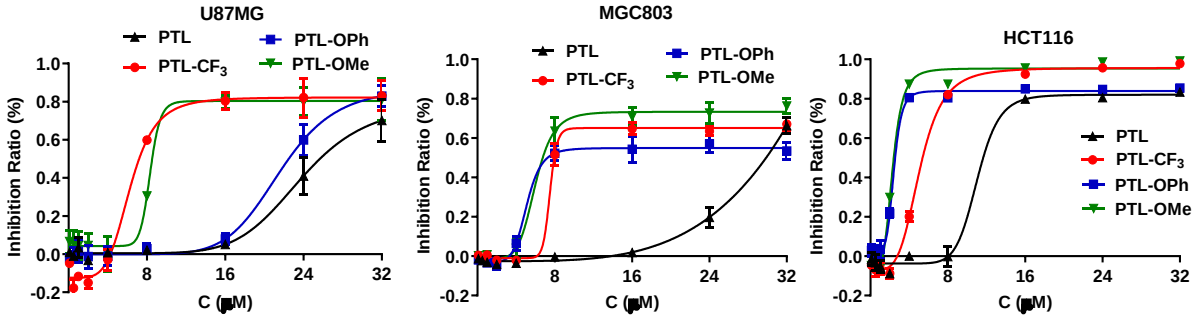
PTL derivative (PTL-OPh**) 5c :** light yellow oil (Yield: 40%, 73.36 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 8.9 Hz, 2H), 8.03 (d, J = 7.3 Hz, 2H), 7.91 (t, J = 8.0 Hz, 1H), 7.79 (dd, J = 22.1, 7.7 Hz, 3H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (dt, J = 22.0, 7.6 Hz, 3H), 7.36 (d, J = 7.7 Hz, 2H), 6.07 (d, J = 3.4 Hz, 1H), 5.55 (t, J = 7.8 Hz, 1H), 5.38 (d, J = 3.1 Hz, 1H), 4.56 (d, J = 12.3 Hz, 1H), 4.47 (d, J = 12.3 Hz, 1H), 3.74 (t, J = 9.3 Hz, 1H), 2.71 – 2.54 (m, 2H), 2.26 (td, J = 13.5, 4.4 Hz, 1H), 2.20 – 2.00 (m, 5H), 1.46 (s, 3H), 1.44 – 1.32 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 194.31, 192.75, 169.26, 164.99, 154.36, 146.74, 138.45, 138.14, 137.17, 135.27,

133.76, 133.63, 133.59, 132.29, 132.25, 131.79, 131.14, 130.85, 130.47, 129.10, 128.74, 128.33, 125.37, 123.68, 120.22, 80.86, 68.97, 63.24, 59.86, 42.51, 36.47, 25.44, 24.18, 23.83, 17.92. HRMS (ESI) cald. for (M+H)+ $C_{39}H_{40}NO_9$:628.2335,found, 628.2330.

In vitro antitumor activity of PTL derivatives in human cancer cell lines: The in vitro antiproliferative activity of was evaluated in three human cancer cell lines using the CCK-8 (Cell Counting Kit-8) assay, including U87MG (glioblastoma), MGC803 (gastric carcinoma), HCT116 (colorectal carcinoma). Parthenolide (PTL) was used as the experiment control.

IC_{50} (μM)	**PTL**	**5a** (PTL-Ome)	**5b** (PTL-OPh)	**5c** (PTL-CF_3)
MGC803	> 50	5.985 ± 0.744	5.105 ± 0.578	7.498 ± 0.661
HCT116	11.050 ± 0.857	2.288 ± 1.022	2.420 ± 0.814	5.118 ± 1.026
U87MG	23.760 ± 0.783	8.323 ± 0.761	21.620 ± 0.872	6.295 ± 0.946

It could be seen in the graph that all synthesized compounds showed moderate to significant potency toward three cancer cell lines.

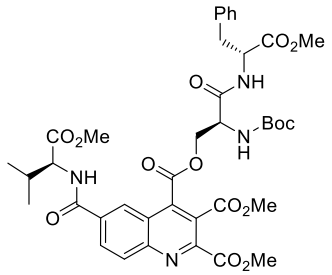


3.8 Chemoselective transformations of quinoline-substituted bioactive molecule.

Synthesis of Product 7:

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, compounds **6** (0.3 mmol), dimethyl but-2-ynedioate (0.45 mmol), peptides (0.45 mmol), $^{n}Bu_4NBF_4$ (0.15 mmol) and KI (0.03 mmol) were combined and added. Then, CH_3CN (6 mL) were injected into the tubes

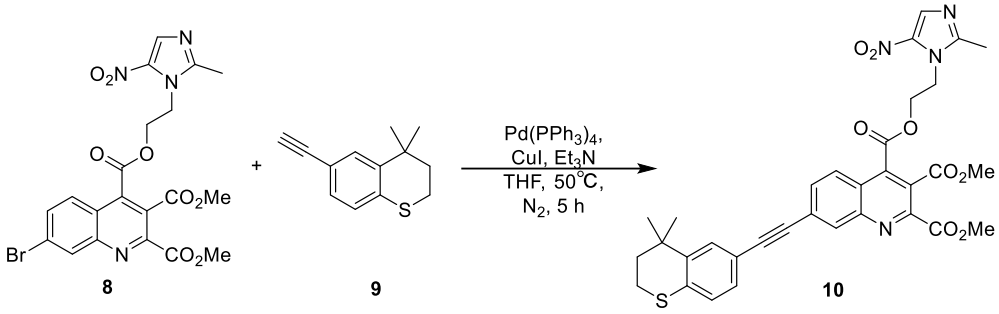
via syringes. The bottle was equipped with carbon rod (ϕ 6 mm, about 10 mm immersion depth in solution) as the anode and platinum plate (15 mm×15 mm×0.3 mm) as the cathode. The reaction mixture was stirred and electrolysis at a constant current of 5 mA under room temperature for 100 min. After completion of the reaction, as indicated by TLC and LC-MS, the pure product was obtained by flash column chromatography on silica gel (eluent: CH_2Cl_2/MeOH).



7

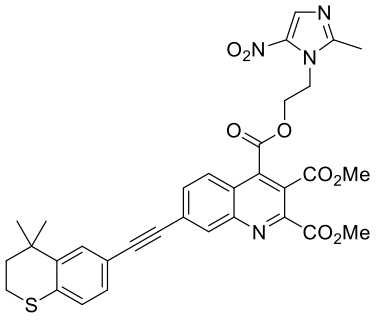
4-((*S*)-2-((tert-butoxycarbonyl)amino)-3-(((*R*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino)-3-oxopropyl) 2,3-dimethyl 6-(((*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl)carbamoyl)quinoline-2,3,4-tricarboxylate (7): light yellow oil (Yield: 48%, 114.13 mg), ^{1}H NMR (400 MHz, Methanol-d4) δ 8.57 (s, 1H), 8.36 (dd, J = 8.8, 1.9 Hz, 1H), 8.28 (d, J = 8.8 Hz, 1H), 7.15 – 7.07 (m, 5H), 4.76 (ddd, J = 17.5, 9.3, 5.0 Hz, 2H), 4.63 – 4.50 (m, 3H), 4.02 (s, 3H), 3.96 (s, 3H), 3.75 (s, 3H), 3.51 (s, 3H), 3.08 (dd, J = 13.9, 5.5 Hz, 1H), 2.95 (dd, J = 13.9, 8.2 Hz, 1H), 2.29 (dq, J = 14.1, 7.0 Hz, 1H), 1.32 (s, 9H), 1.06 (dd, J = 10.2, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, Methanol-d4) δ 172.20, 171.44, 169.56, 167.55, 165.56, 165.34, 164.51, 156.08, 149.78, 148.50, 141.20, 136.37, 130.98, 129.92, 128.79, 128.03, 126.44, 122.75, 122.71, 79.78, 65.85, 59.30, 53.56, 52.86, 52.58, 51.28, 51.22, 36.80, 31.68, 30.28, 29.38, 29.35, 29.08, 22.34, 18.33, 18.03, 13.05. HRMS (ESI) cald. for (M+H)+ $C_{39}H_{47}N_4O_{14}$:795.3089,found, 795.3093.

Synthesis of Product 10:



8 9 10

In a round bottomed three-necked flask, equipped with a stir bar, compounds **8** (1 equiv. , 260 mg), 6-Ethynyl-4,4-dimethylthiochroman **9** (2.5equiv. 254 mg), CuI (10 mol%, 10 mg), and $Pd(PPh_3)_4$ (10mol%, 115 mg) were dissolved in anhydrous THF (5 mL) under N_2 atmosphere. Then, Et_3N (5 mL) were injected into the solution via syringes. The reaction mixture was stirred at 50 ℃ for 5 h. When the reaction was finished, the solvent was removed by reduced pressure and the crude product **10** (Yield: 82%, 255 mg) was purified by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate=1:1).



10

2,3-dimethyl 4-(2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethyl) 7-((4,4-dimethylthiochroman-6-yl)ethynyl)quinoline-2,3,4-tricarboxylate (10): yellow oil (Yield: 82%, 255 mg), ^{1}H NMR (400 MHz, Chloroform-d) δ 8.32 (d, J = 1.2 Hz, 1H), 7.96 (s, 1H), 7.73 (dd, J = 8.7, 1.6 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.55 (d, J = 1.7 Hz, 1H), 7.20 (dd, J = 8.1, 1.8 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 4.79 (t, J = 5.3 Hz, 2H), 4.68 (t, J = 5.3 Hz, 2H), 4.01 (s, 3H), 3.86 (s, 3H), 3.06 – 2.98 (m, 2H), 2.32 (s, 3H), 1.96 – 1.89 (m, 2H), 1.33 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-d) δ 165.60, 165.48, 164.86, 151.23, 148.85, 147.55, 142.25, 139.32, 138.38, 134.62, 133.25, 132.88, 132.73, 129.97, 129.19, 128.34, 126.66, 125.07, 122.60, 122.28, 117.35, 95.35, 95.22, 87.42,

64.79, 53.52, 53.44, 44.73, 37.05, 32.98, 29.93, 23.24, 14.31. HRMS (ESI) cald. for (M+H)+ $C_{33}H_{31}N_4O_8S$:643.1863,found, 643.1860.

4. References

[1] R. A. Serwa, J.-M. Swiecicki, D. Homann, C. P. R. Hackenberger, Phosphoramidate-peptide synthesis by solution- and solid-phase Staudinger-phosphite reactions. *J. Pept. Sci.* **2010**, *16*, 563–567.

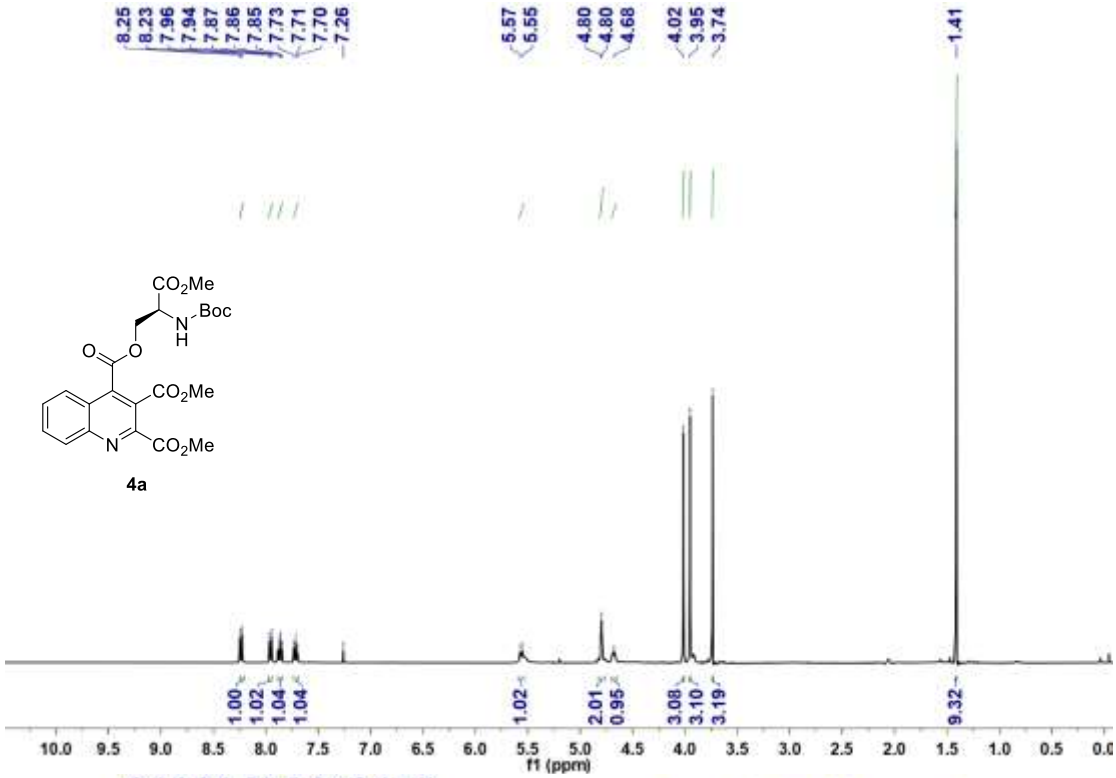
[2] Alam J, Keller T H, Loh T P. Functionalization of peptides and proteins by Mukaiyama aldol reaction. *J. Am. Chem. Soc.* **2010**, *132*, 9546-9548.

[3] Gu, K., Liu, Y., Guo, Z., Lian, C., Yan, C., Shi, P., … & Zhu, W. H. In situ ratiometric quantitative tracing of intracellular leucine aminopeptidase activity via an activatable near-infrared fluorescent probe. *ACS Appl. Mater. Inter.* **2016**, *8*, 26622-26629.

[4] Bravo, F., McDonald, F. E., Neiwert, W. A., & Hardcastle, K. I. Alkene Substituents for Selective Activation of *Endo*-Regioselective Polyepoxide Oxacyclizations. *Org. Lett.* **2004**, *6*, 4487-4489.

5. Spectra

5.1. NMR Spectra of Products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4.80
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3.74
1.41
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Boc
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H
O
O
CO2Me
N
CO2Me
4a
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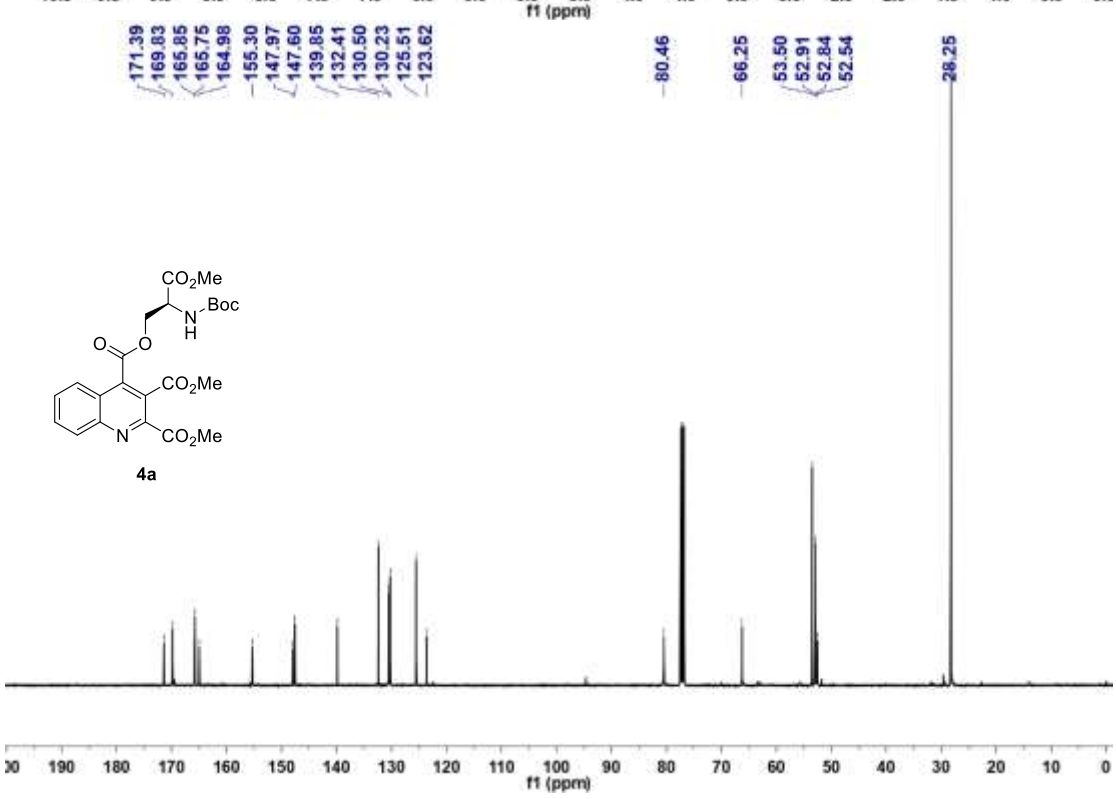
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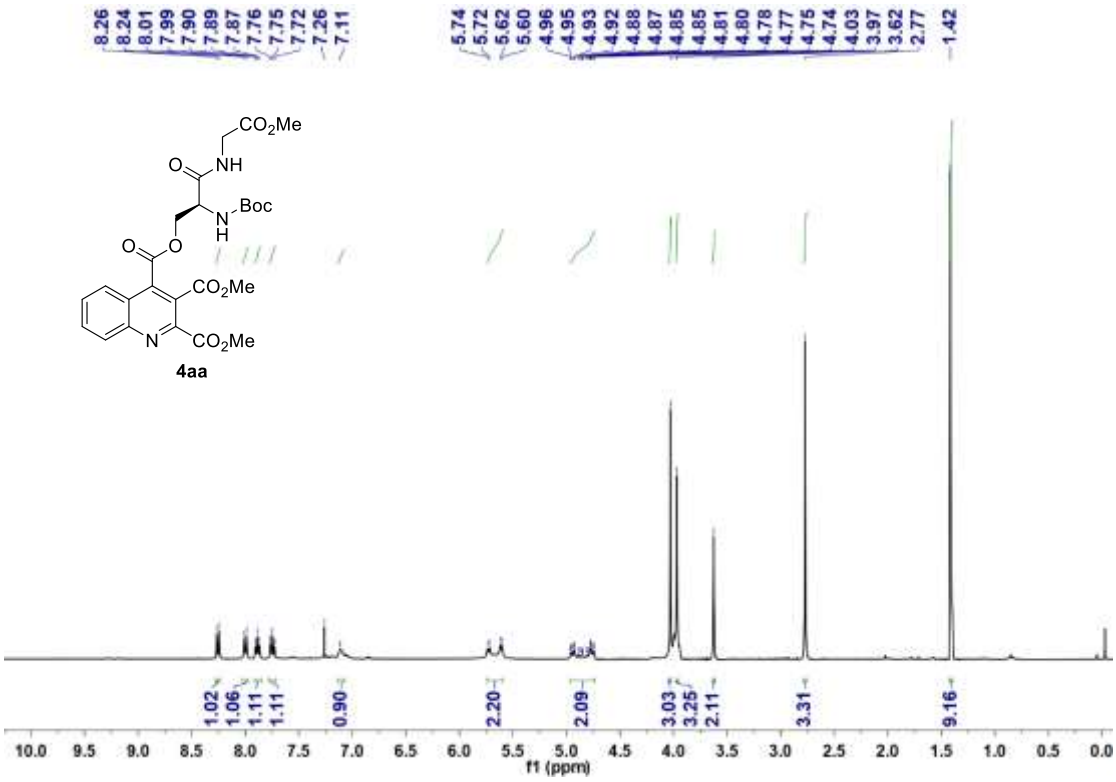
f1 (ppm)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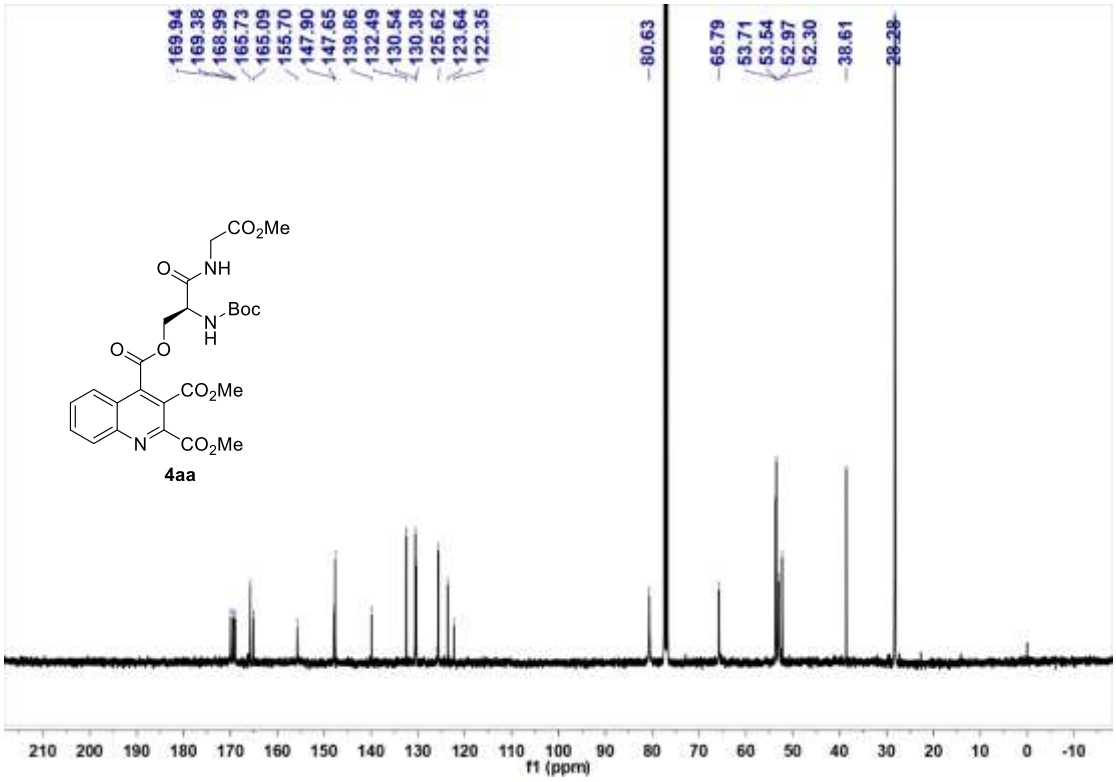
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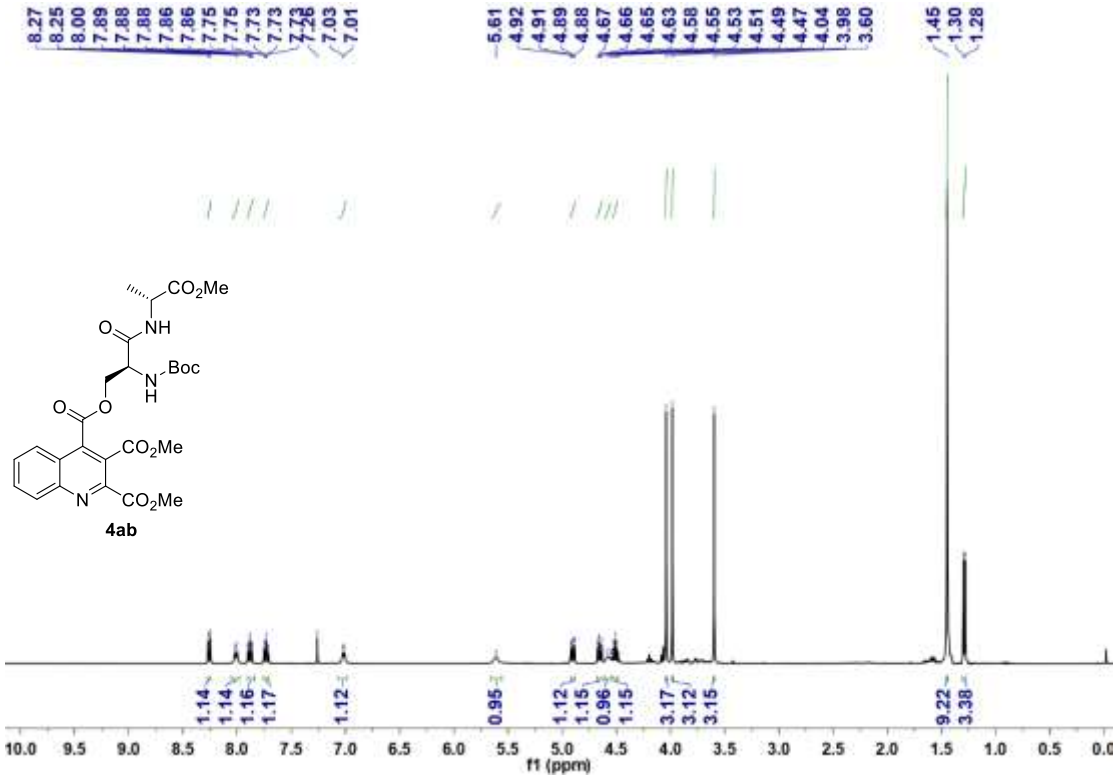
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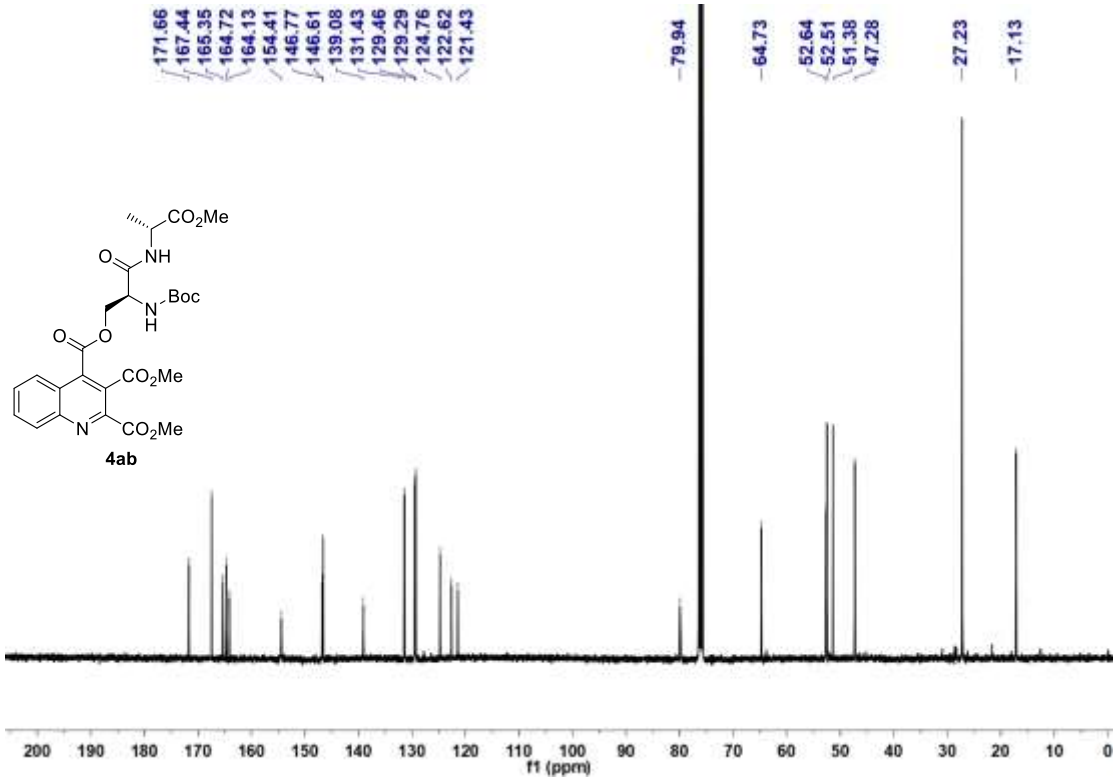
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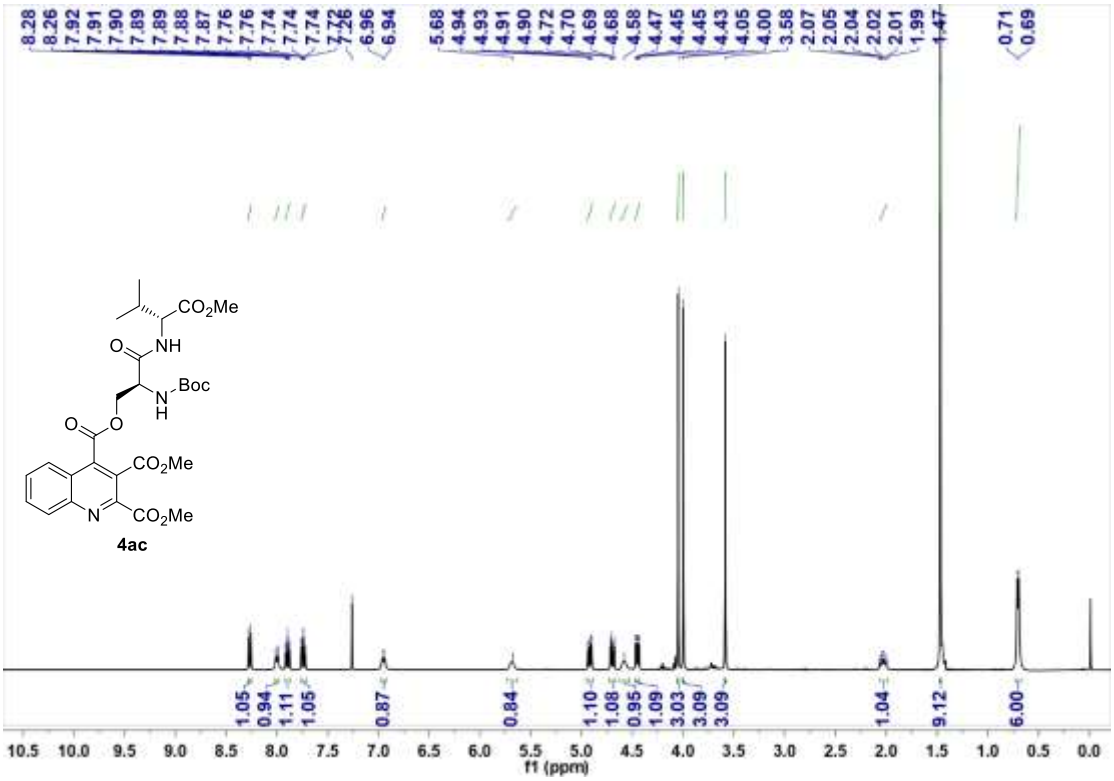
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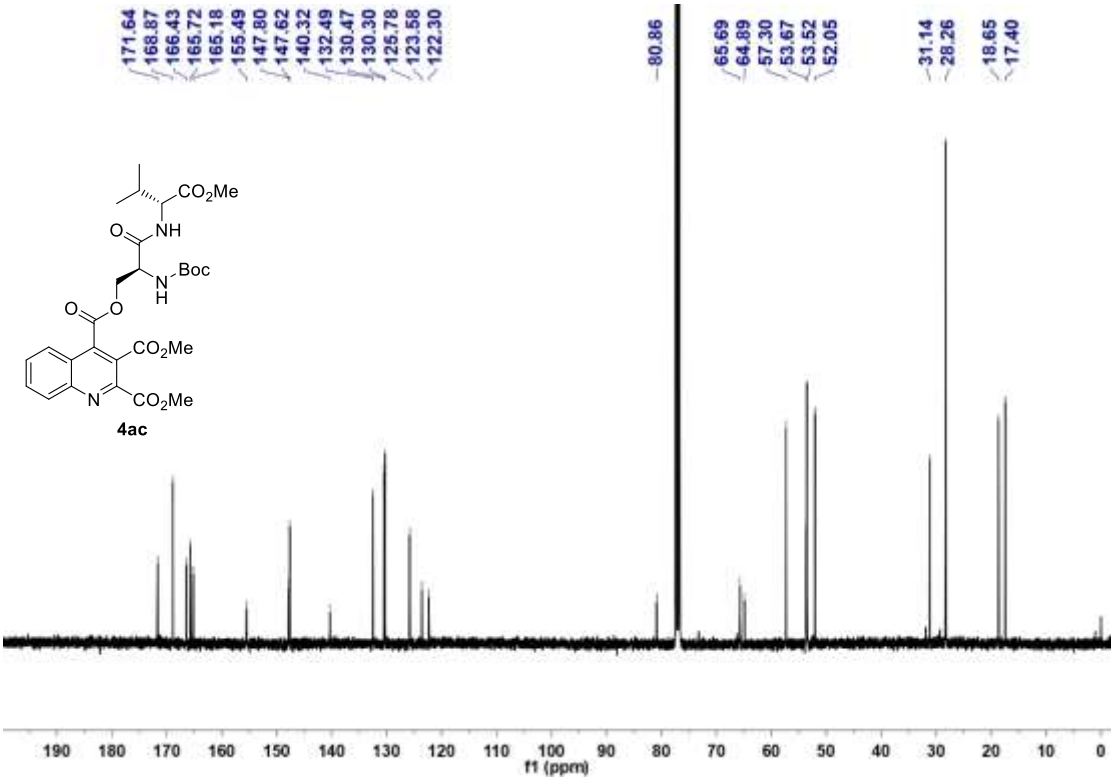
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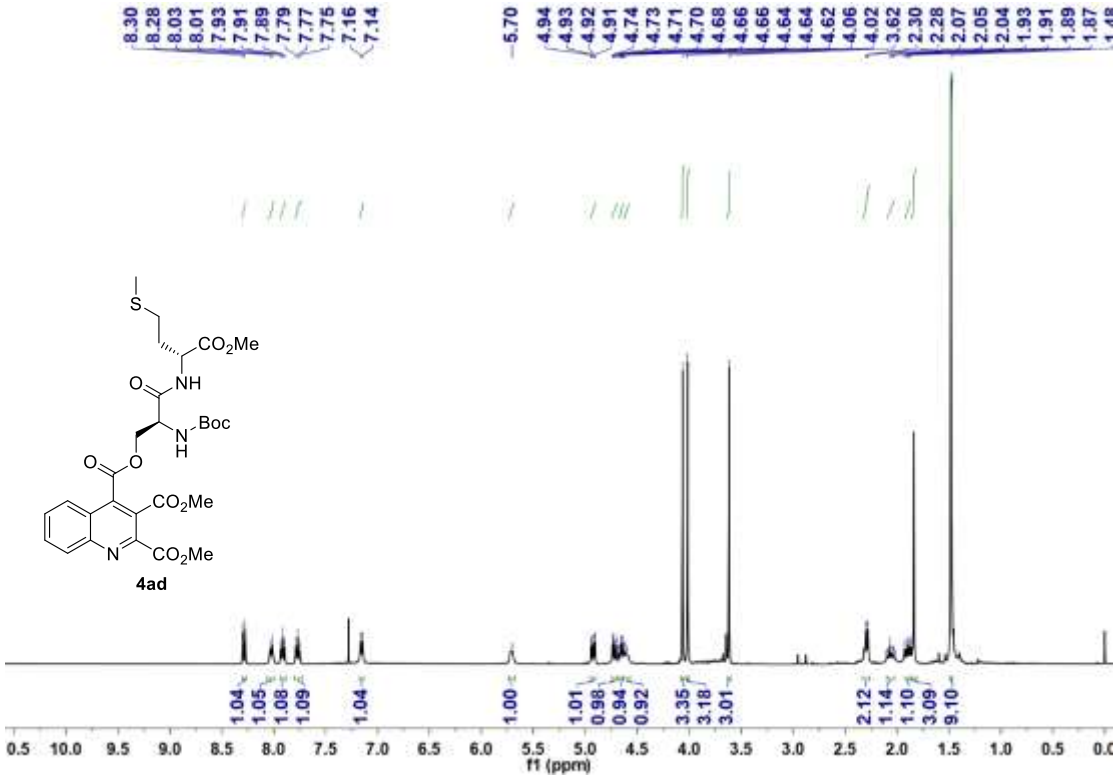
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1.08
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1.01
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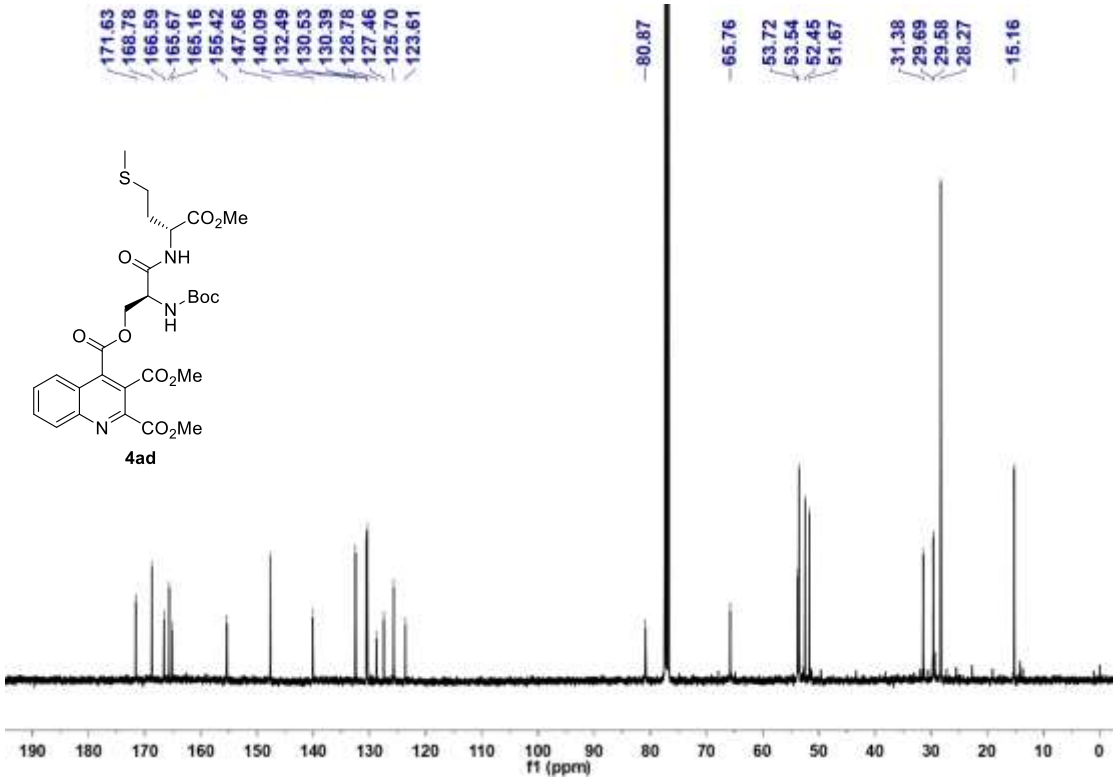
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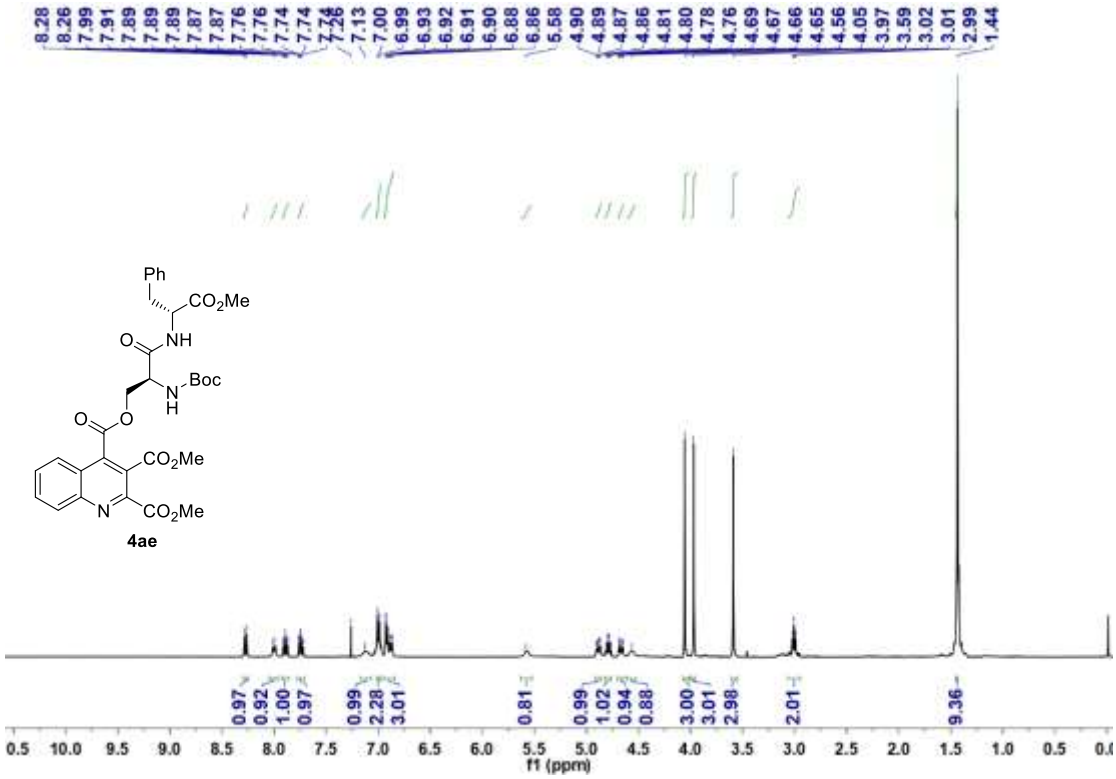
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Boc
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CO2Me
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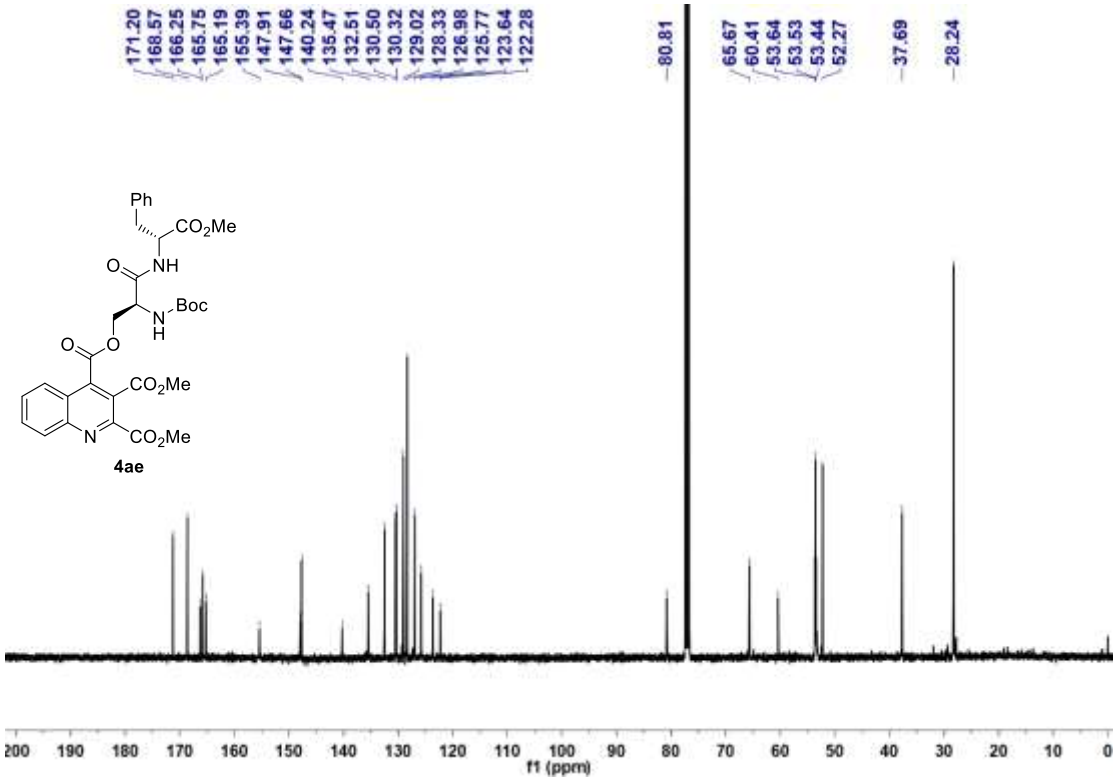
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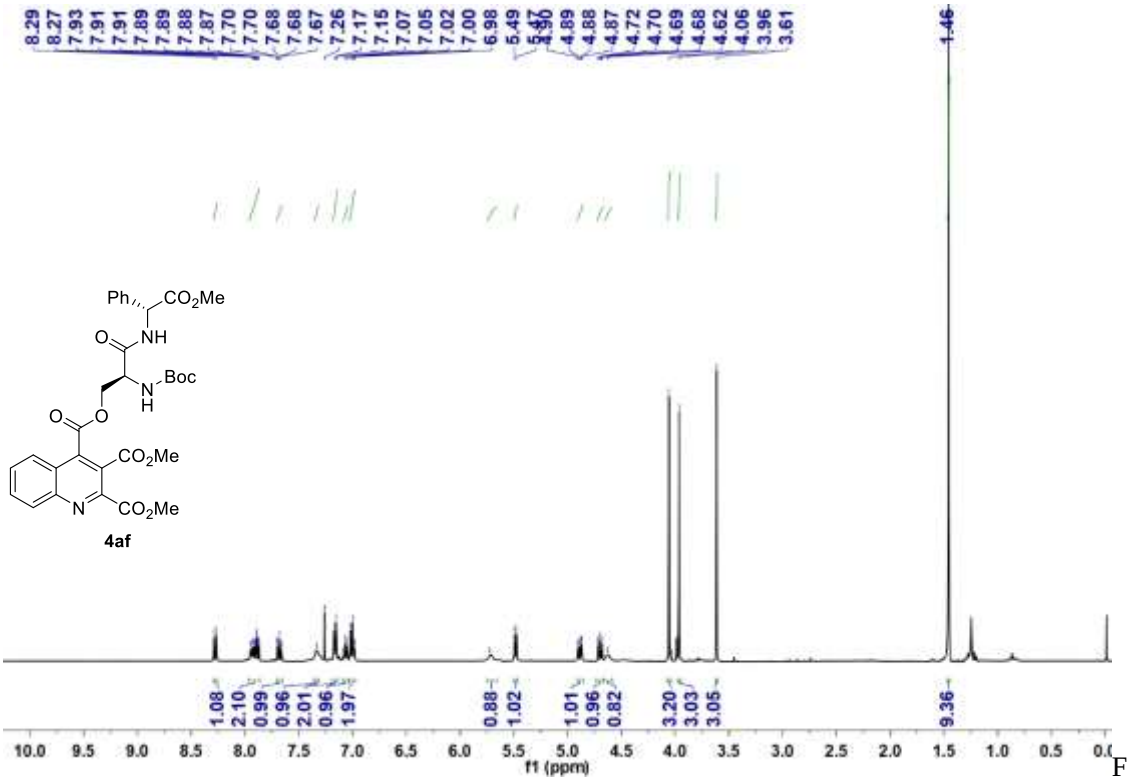
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Ph CO2Me NH O Boc N H O O CO2Me CO2Me N
4af
1.08 2.10 0.99 0.96 2.01 0.96 1.97 0.88 1.02 1.01 0.96 0.82 3.20 3.03 3.05 9.36
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
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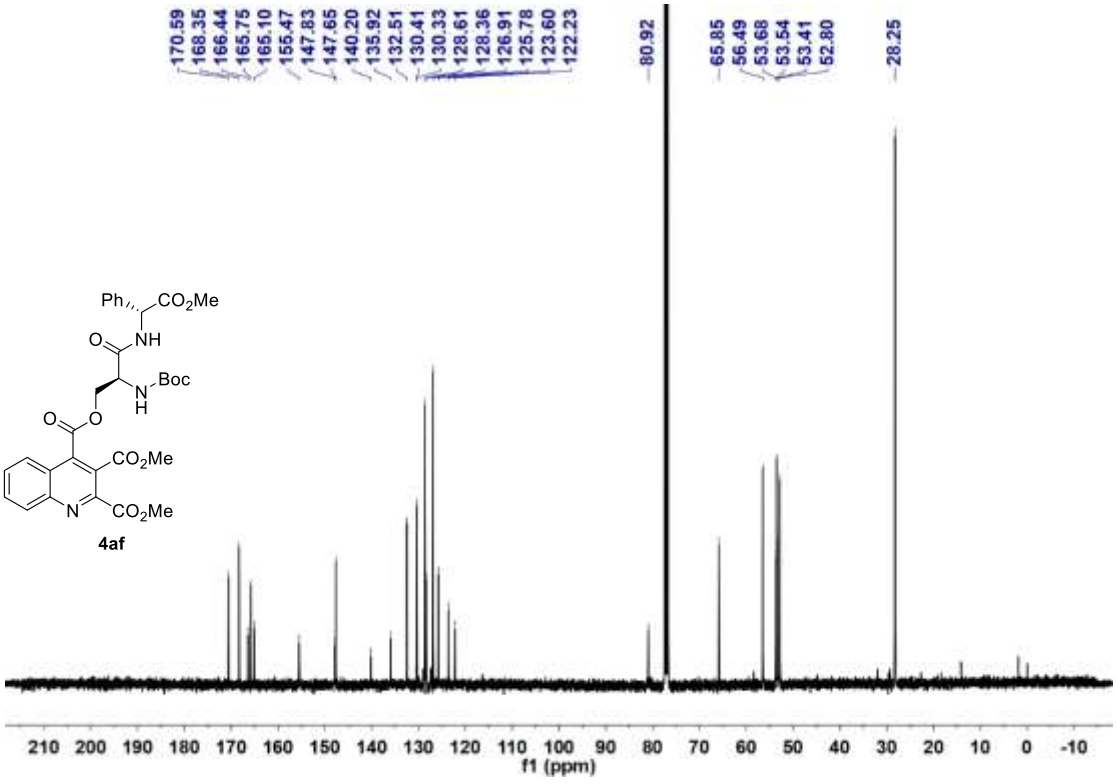
F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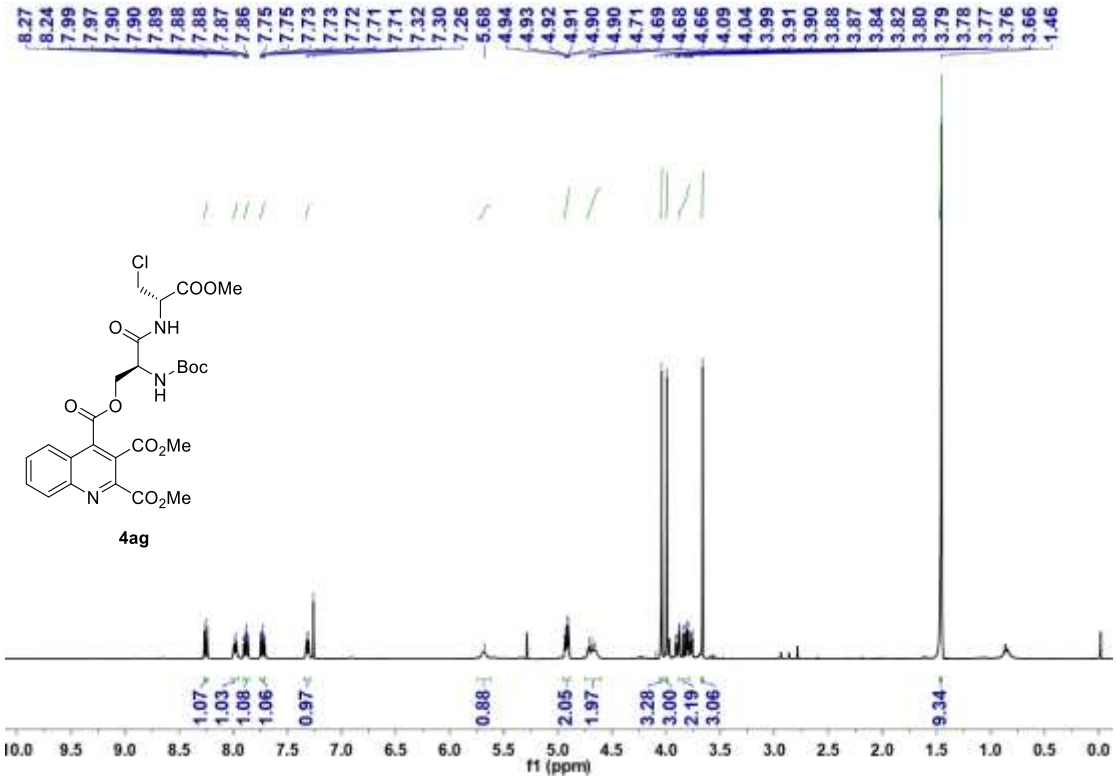
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Boc
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O
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CO2Me
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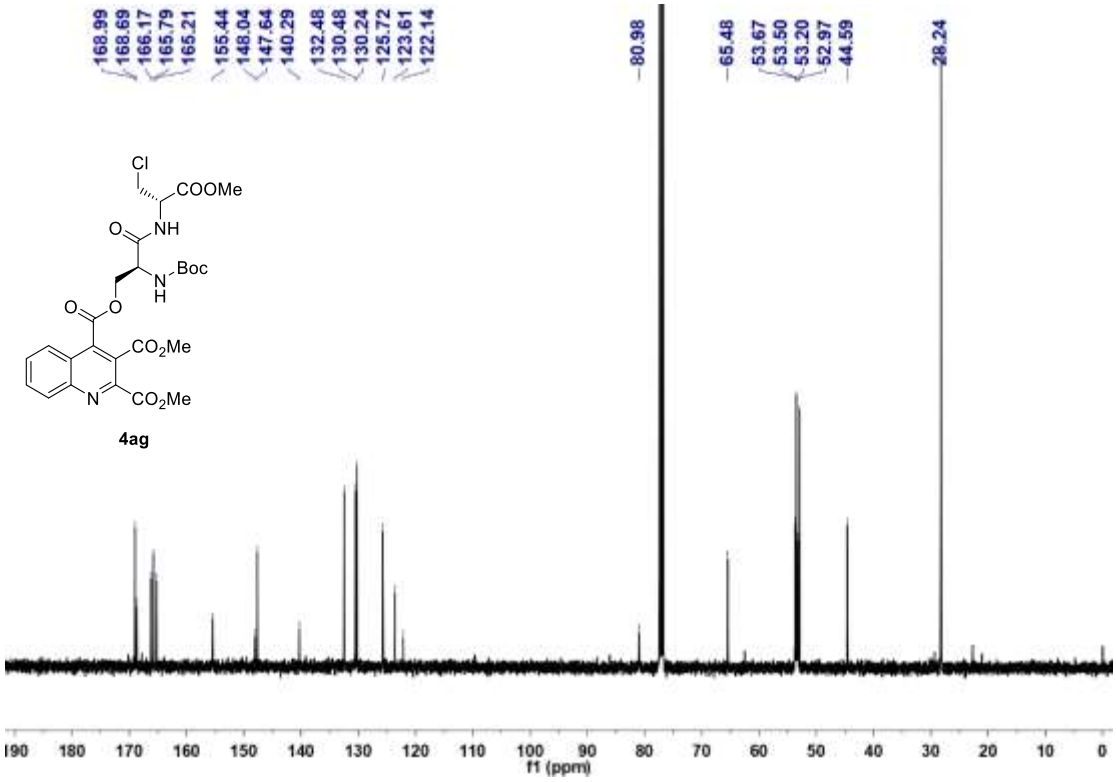
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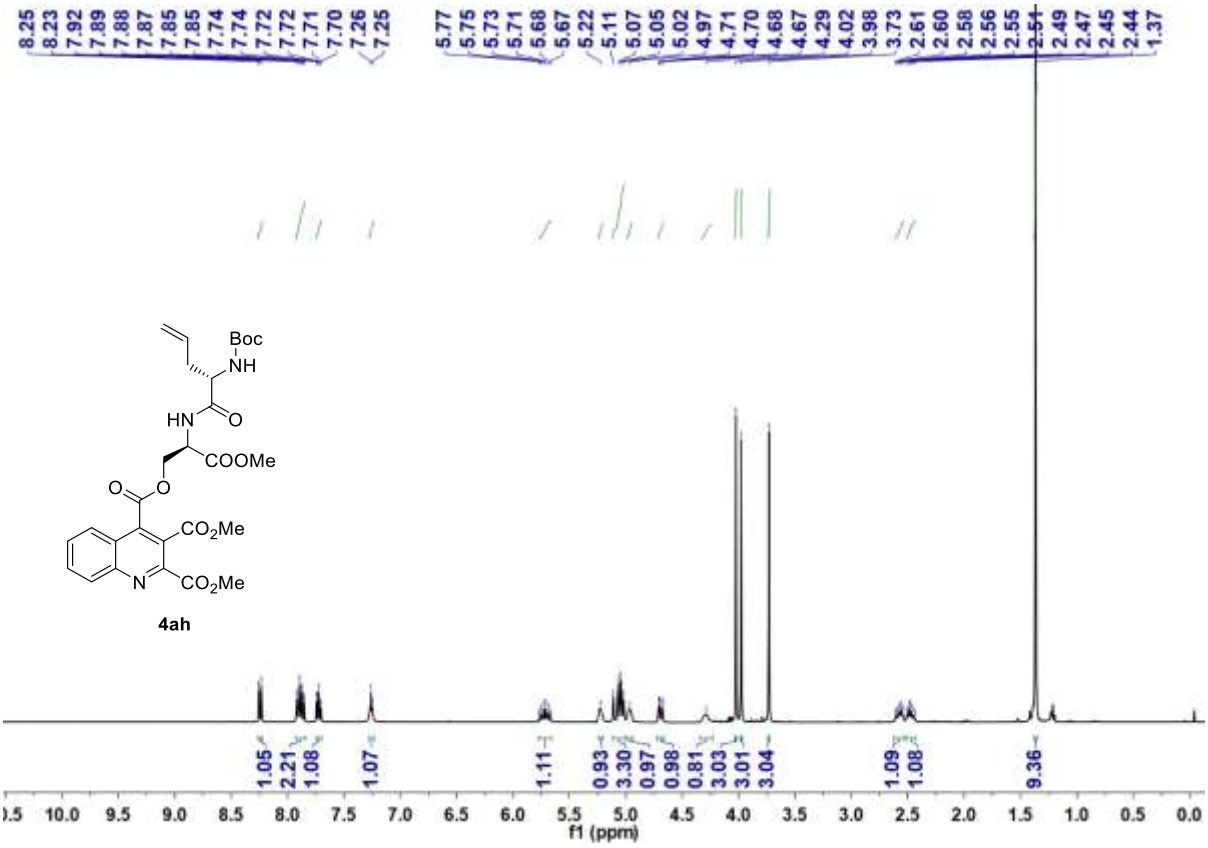
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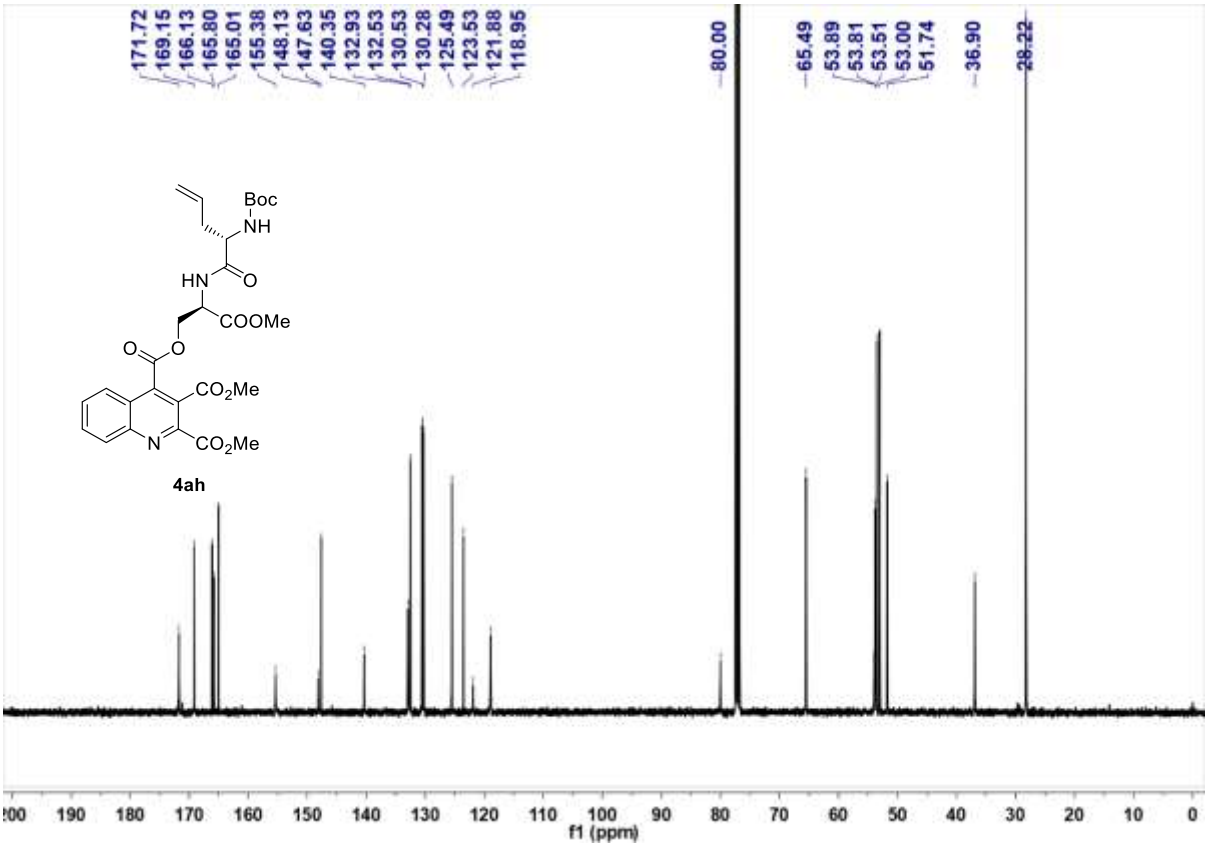
f1 (ppm)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Boc
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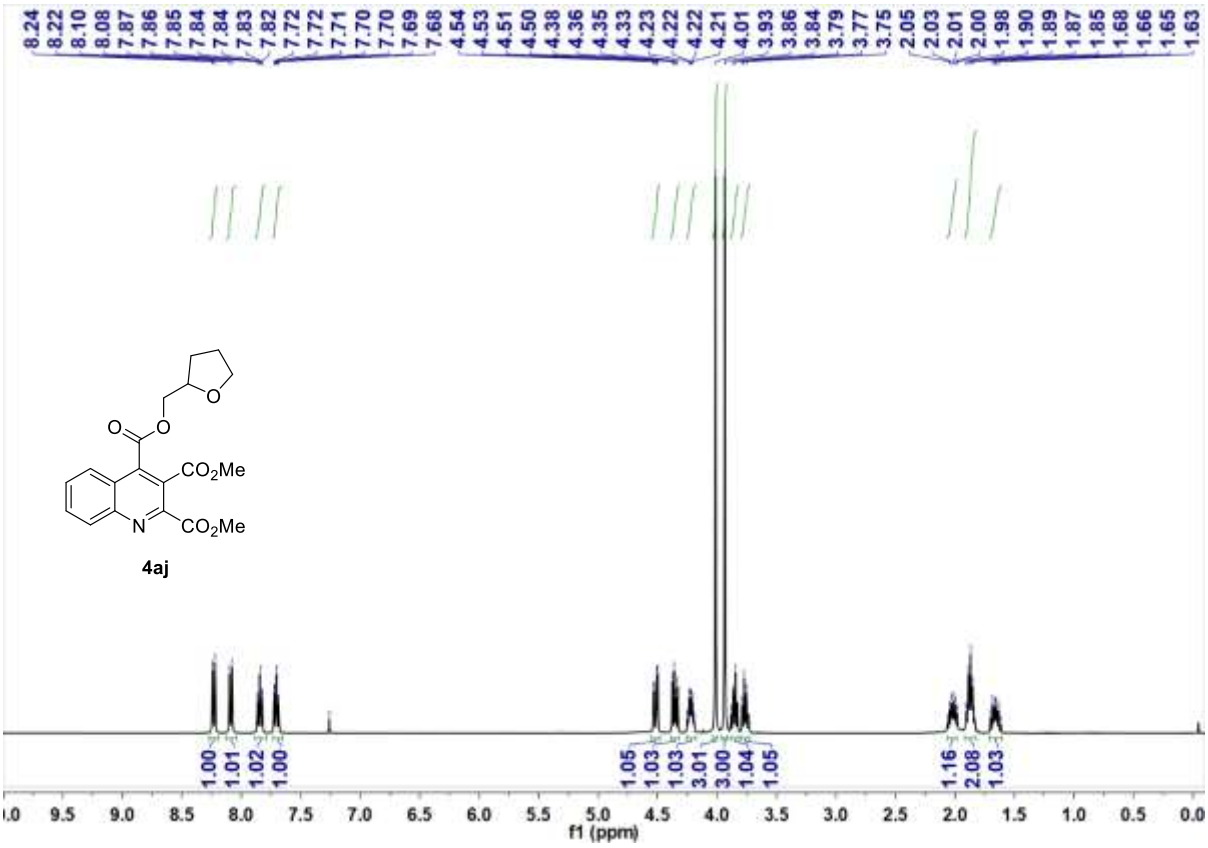
CO2Me
N
CO2Me
4ah
f1 (ppm)


8.24 8.22 8.10 8.08 7.87 7.86 7.85 7.84 7.84 7.83 7.82 7.72 7.72 7.71 7.70 7.70 7.69 7.68 4.54 4.53 4.51 4.50 4.38 4.36 4.35 4.33 4.23 4.22 4.22 4.21 4.01 3.93 3.86 3.84 3.79 3.77 3.75 2.05 2.03 2.01 2.00 1.98 1.90 1.89 1.87 1.85 1.68 1.66 1.65 1.63
O
O
O
CO2Me
N
CO2Me
4aj
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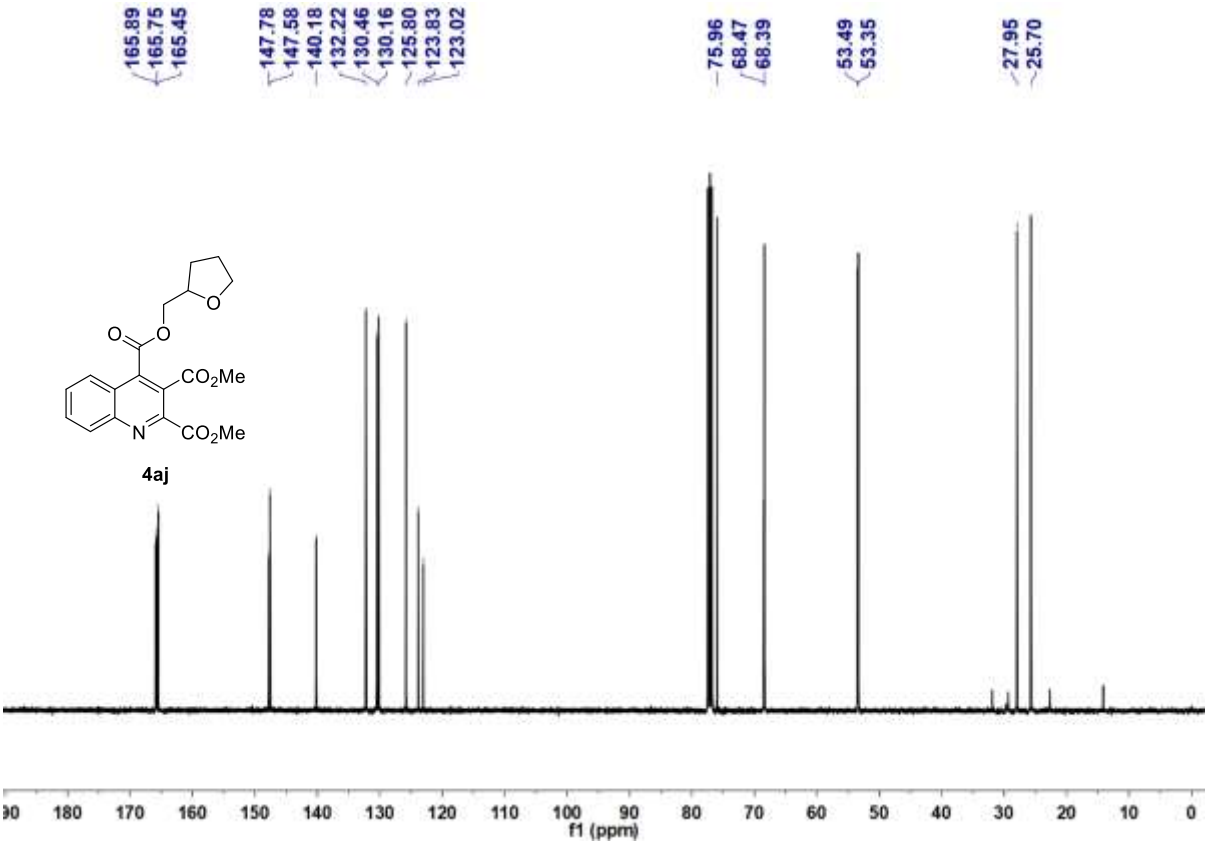
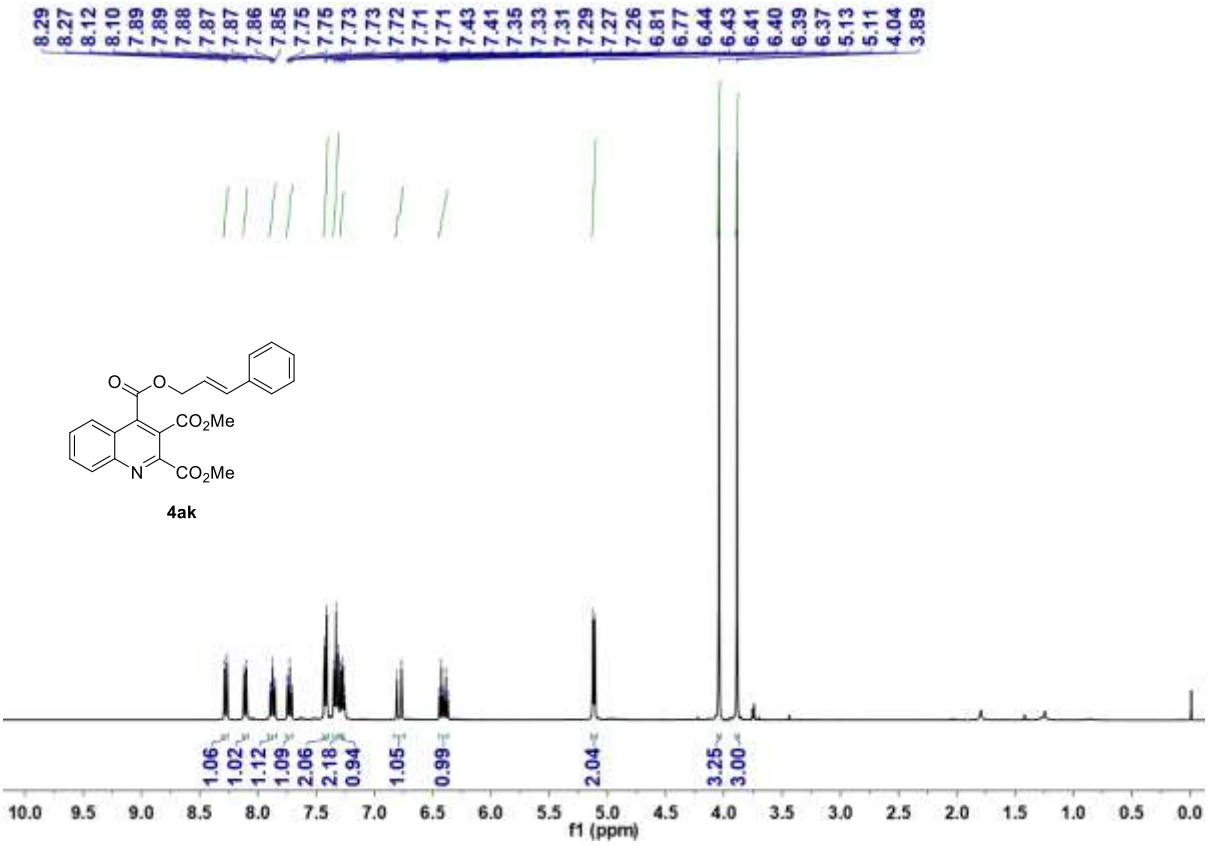
f1 (ppm)


165.89 165.75 165.45 147.78 147.58 140.18 132.22 130.46 130.16 125.80 123.83 123.02 75.96 68.47 68.39 53.49 53.35 27.95 25.70
O
O
O
CO2Me
N
CO2Me
4aj
f1 (ppm)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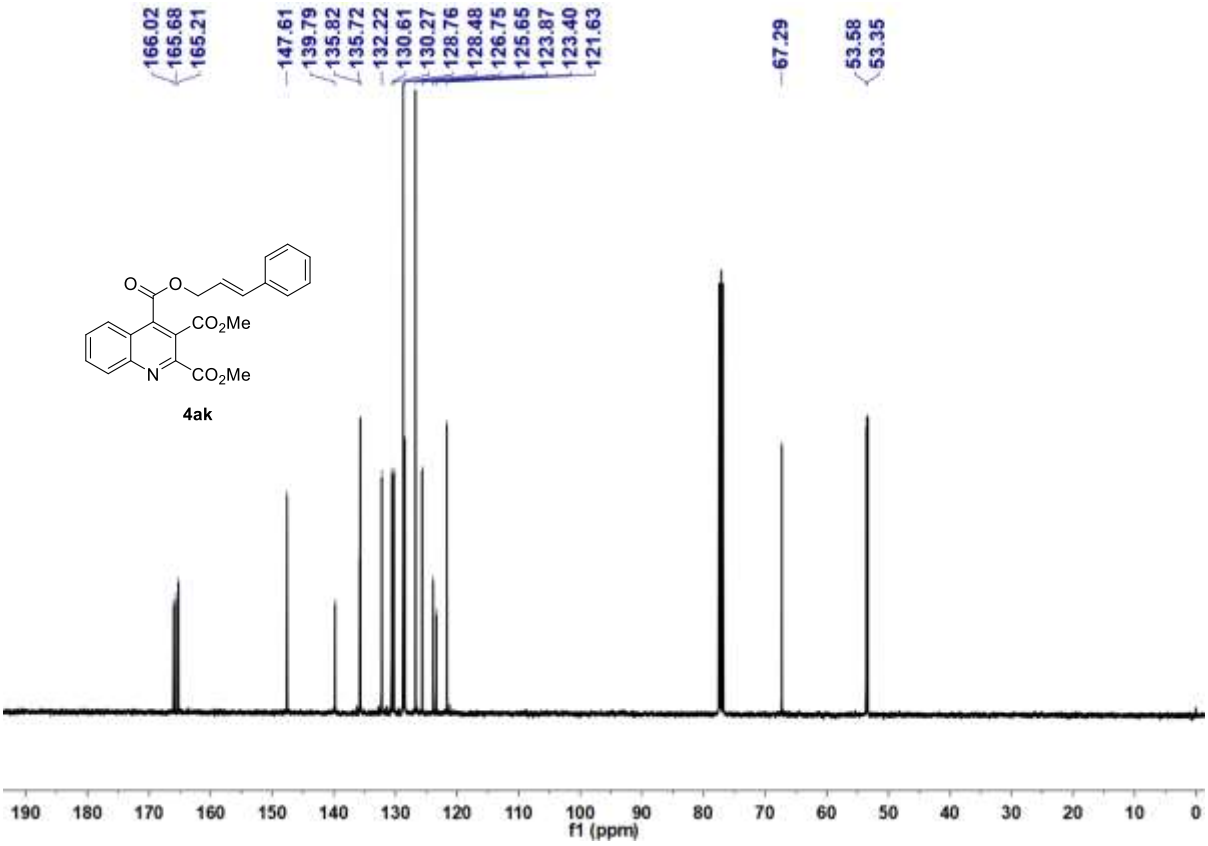
7.88
7.87
7.87
7.86
7.85
7.75
7.75
7.73
7.73
7.72
7.71
7.71
7.43
7.41
7.35
7.33
7.31
7.29
7.27
7.26
6.81
6.77
6.44
6.43
6.41
6.40
6.39
6.37
5.13
5.11
4.04
3.89
O
O
CO2Me
N
CO2Me
4ak
1.06
1.02
1.12
1.09
2.06
2.18
0.94
1.05
0.99
2.04
3.25
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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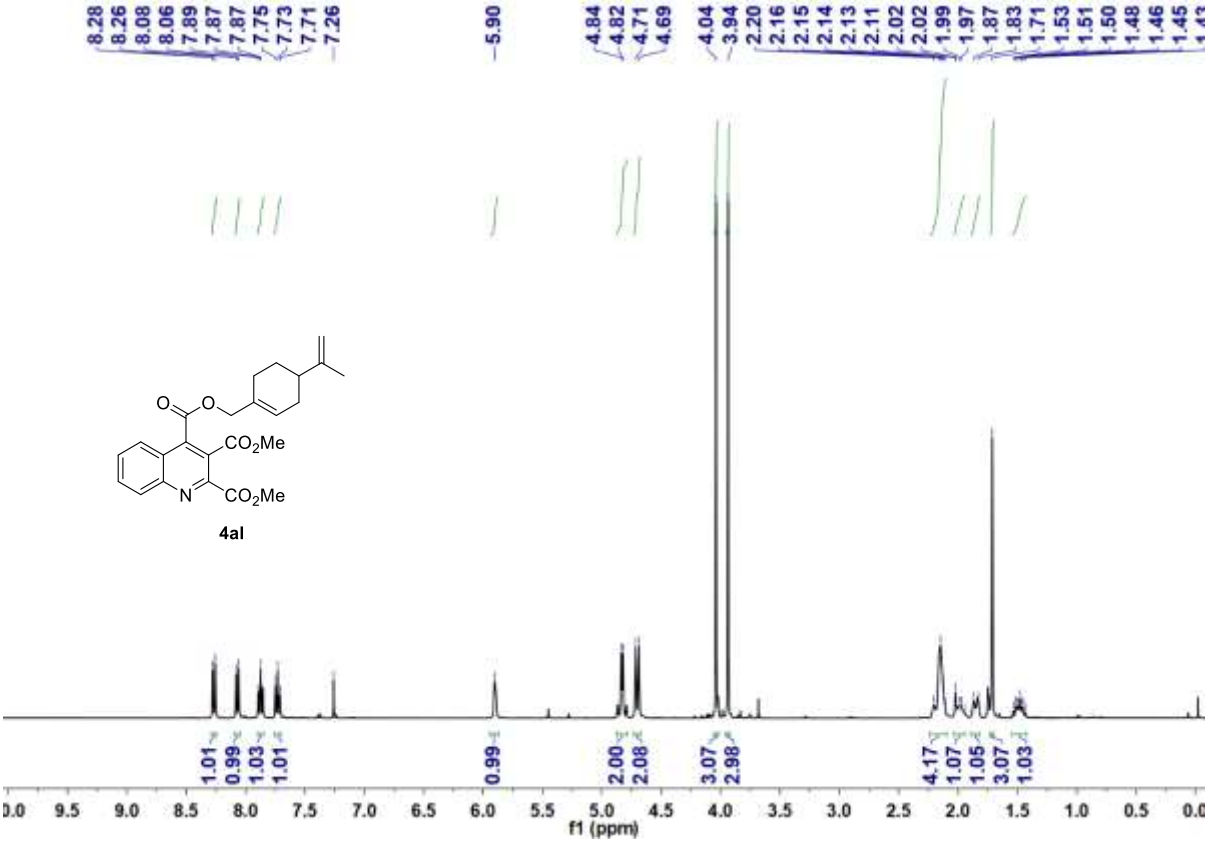
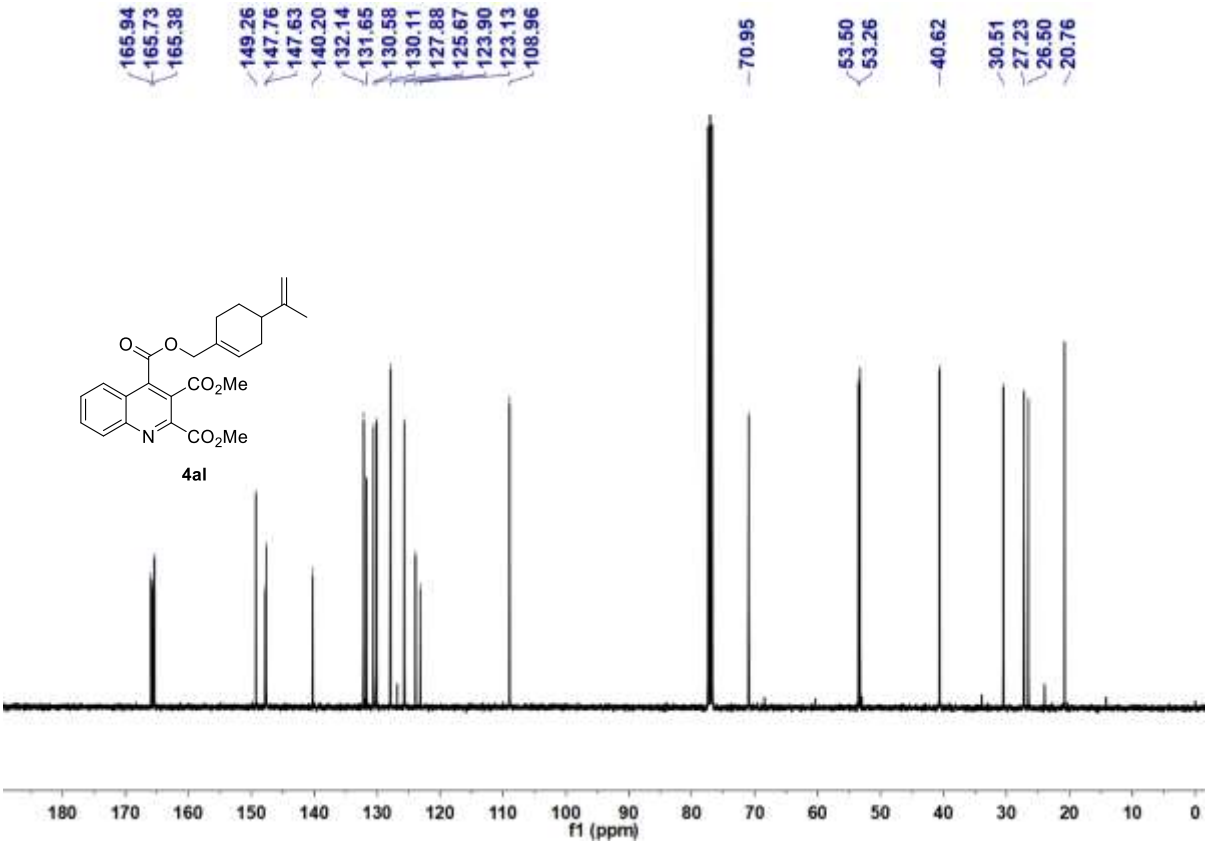
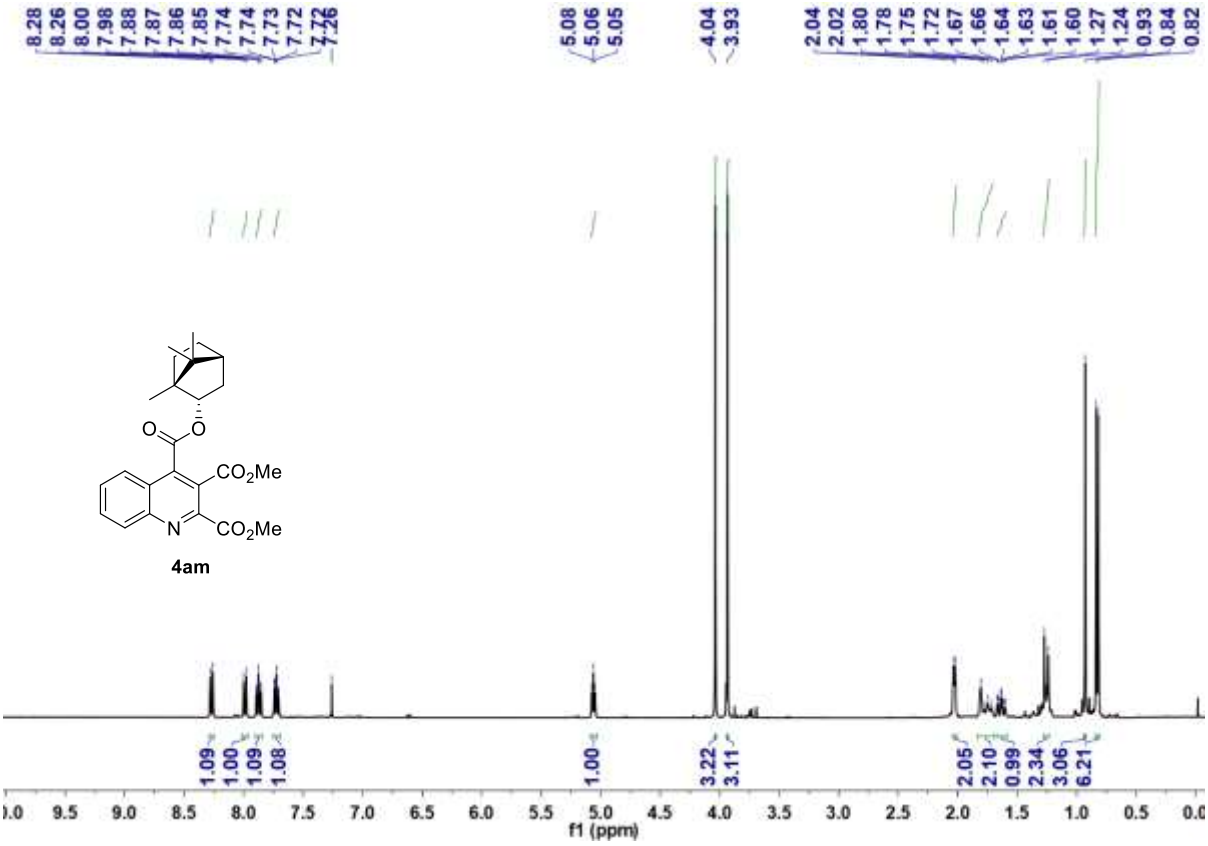
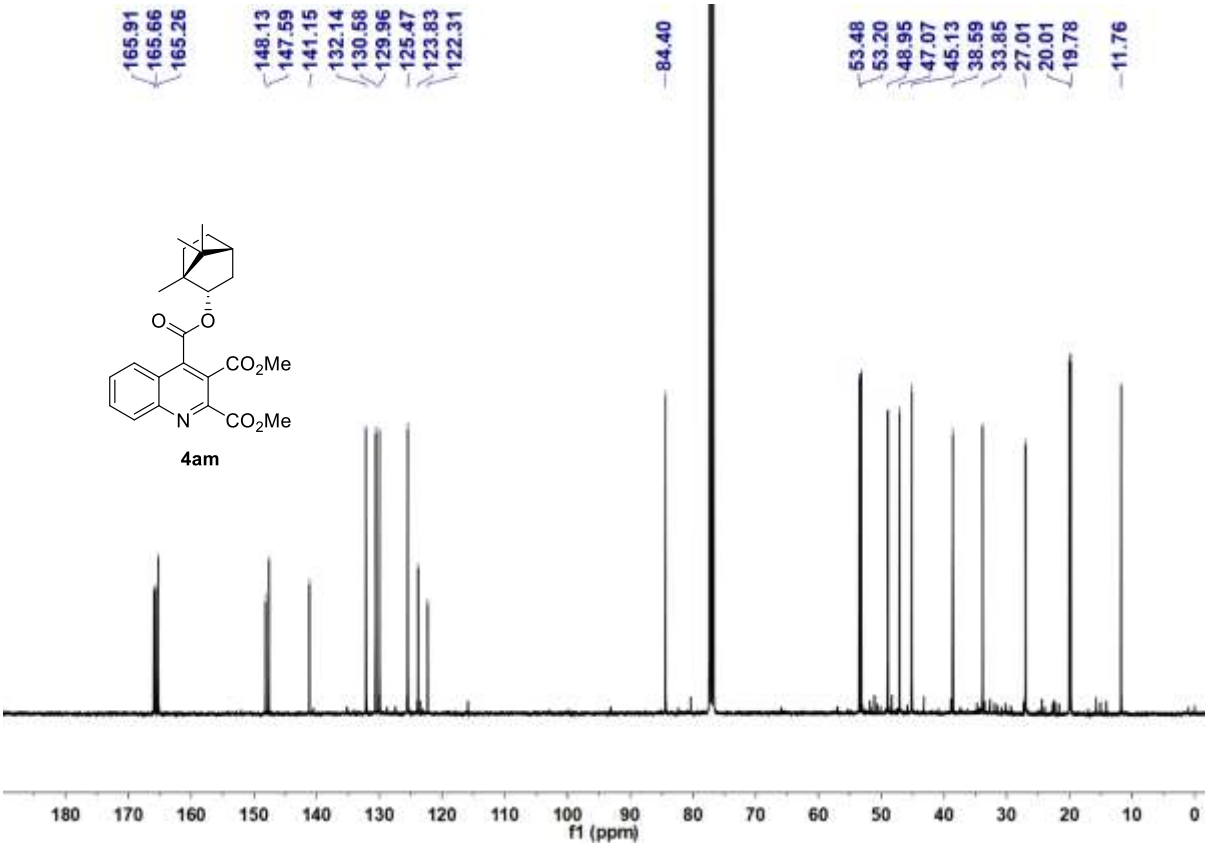
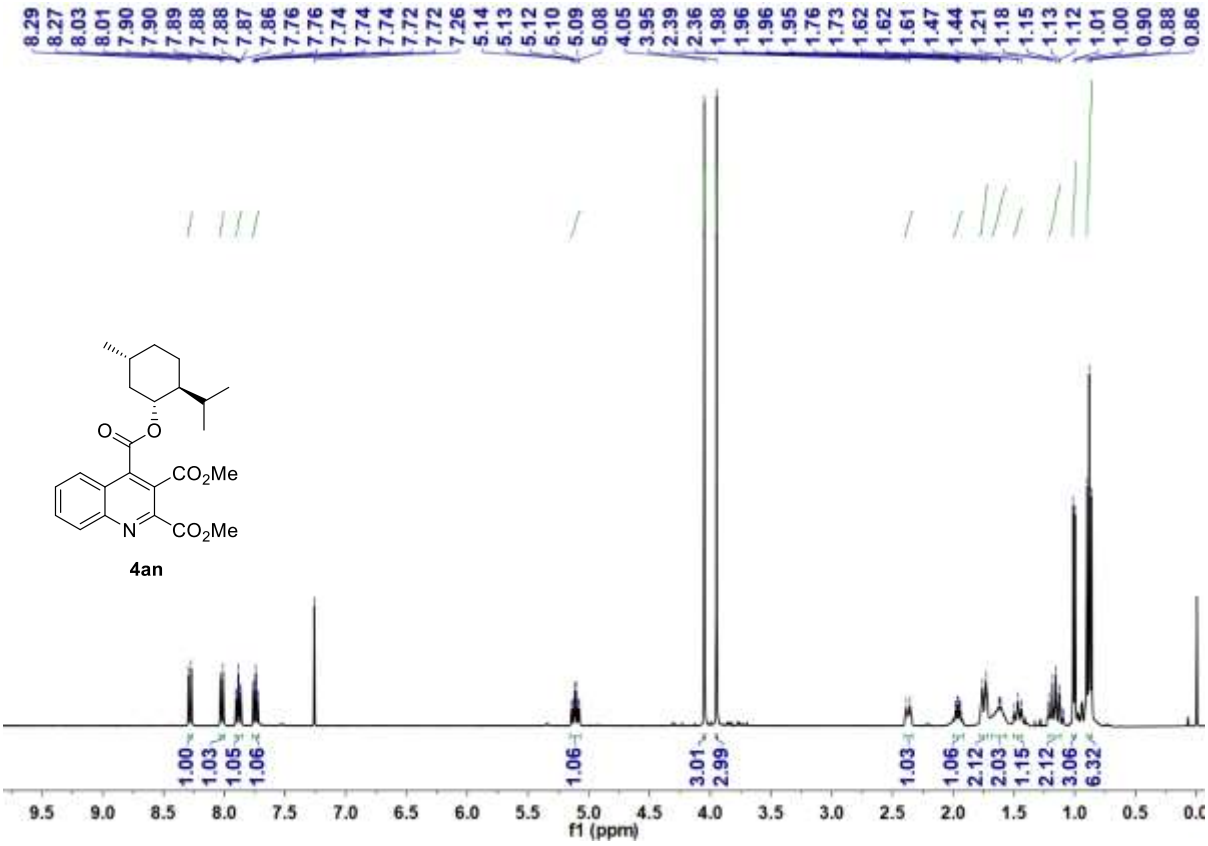
139.79
135.82
135.72
132.22
130.61
130.27
128.76
128.48
126.75
125.65
123.87
123.40
121.63
67.29
53.58
53.35
O
O
CO2Me
N
CO2Me
4ak
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

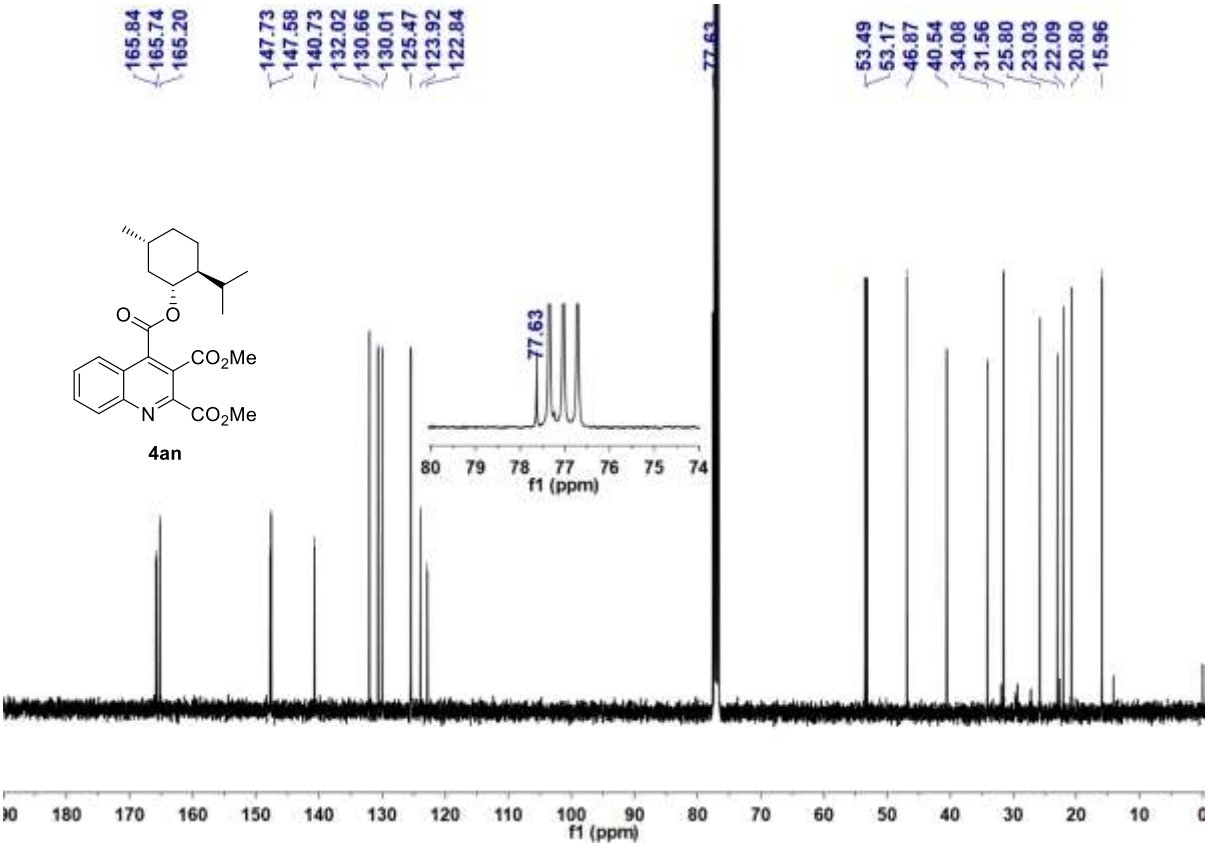

8.28
8.26
8.08
8.06
7.89
7.87
7.87
7.75
7.73
7.71
7.26
5.90
4.84
4.82
4.71
4.69
4.04
3.94
2.20
2.16
2.15
2.14
2.13
2.11
2.02
2.02
1.99
1.97
1.87
1.83
1.71
1.53
1.51
1.50
1.48
1.46
1.45
O
O
CO2Me
N
CO2Me
4al
1.01
0.99
1.03
1.01
0.99
2.00
2.08
3.07
2.98
4.17
1.07
1.05
3.07
1.03
f1 (ppm)

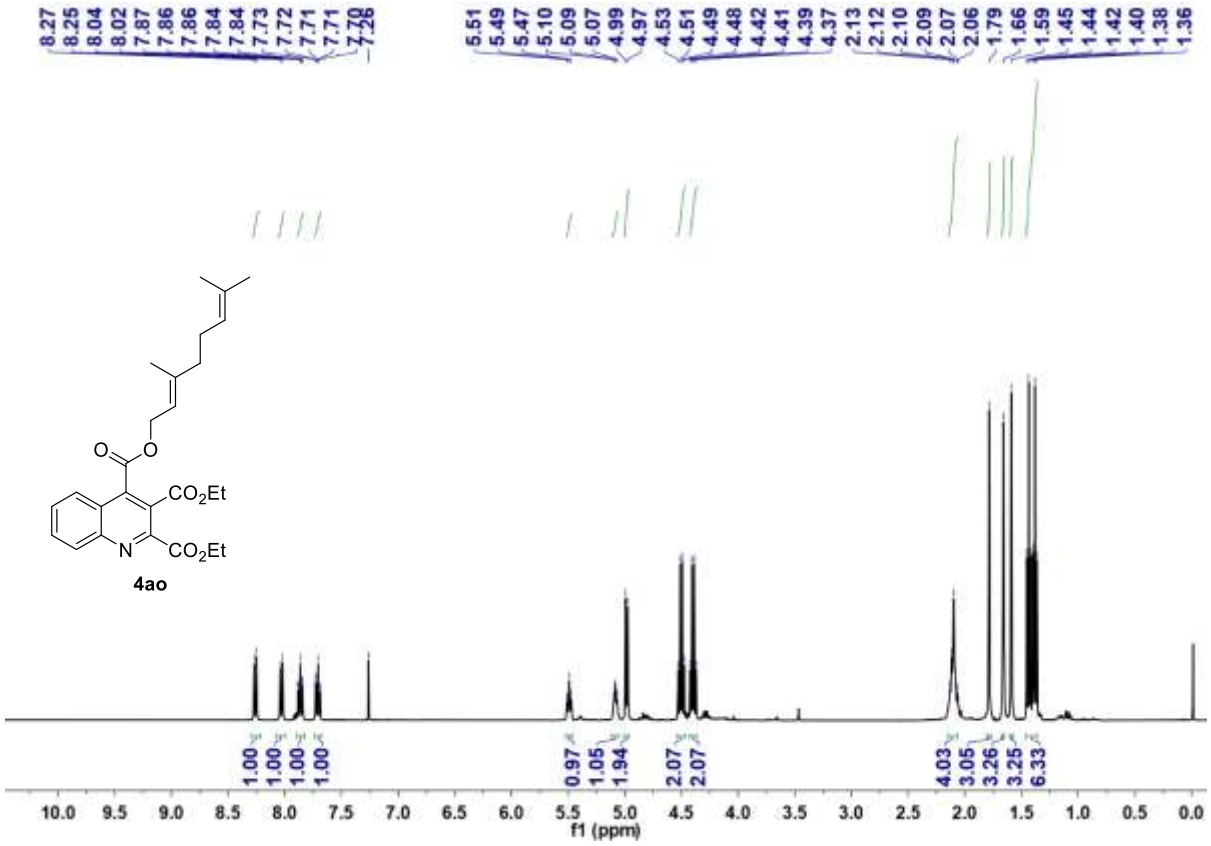

165.94
165.73
165.38
149.26
147.76
147.63
140.20
132.14
131.65
130.58
130.11
127.88
125.67
123.90
123.13
108.96
70.95
53.50
53.26
40.62
30.51
27.23
26.50
20.76
O
O
CO2Me
N
CO2Me
4al
f1 (ppm)

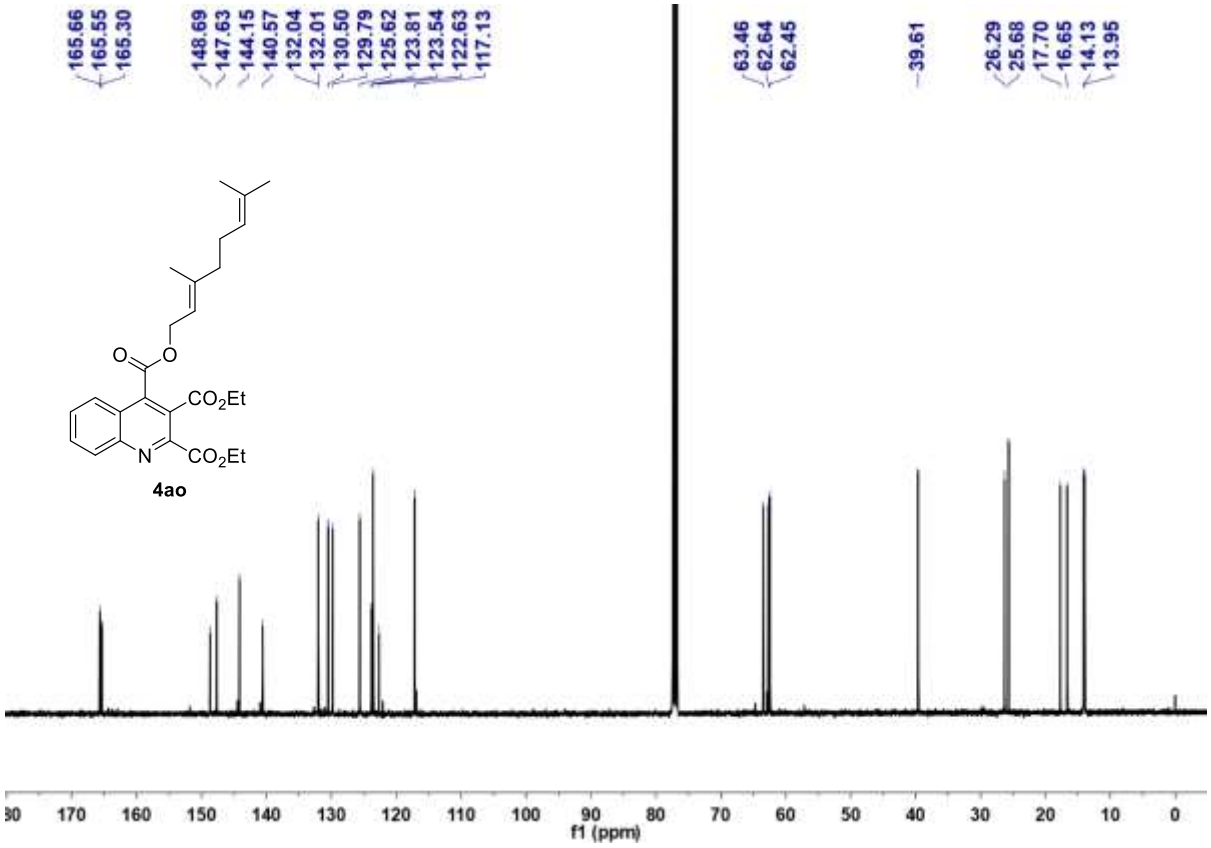

8.28
8.26
8.00
7.98
7.88
7.87
7.86
7.85
7.74
7.74
7.73
7.72
7.72
7.26
5.08
5.06
5.05
4.04
3.93
2.04
2.02
1.80
1.78
1.75
1.72
1.67
1.66
1.64
1.63
1.61
1.60
1.27
1.24
0.93
0.84
0.82
O
O
CO2Me
N
CO2Me
4am
1.09
1.00
1.09
1.08
1.00
3.22
3.11
2.05
2.10
0.99
2.34
3.06
6.21
f1 (ppm)

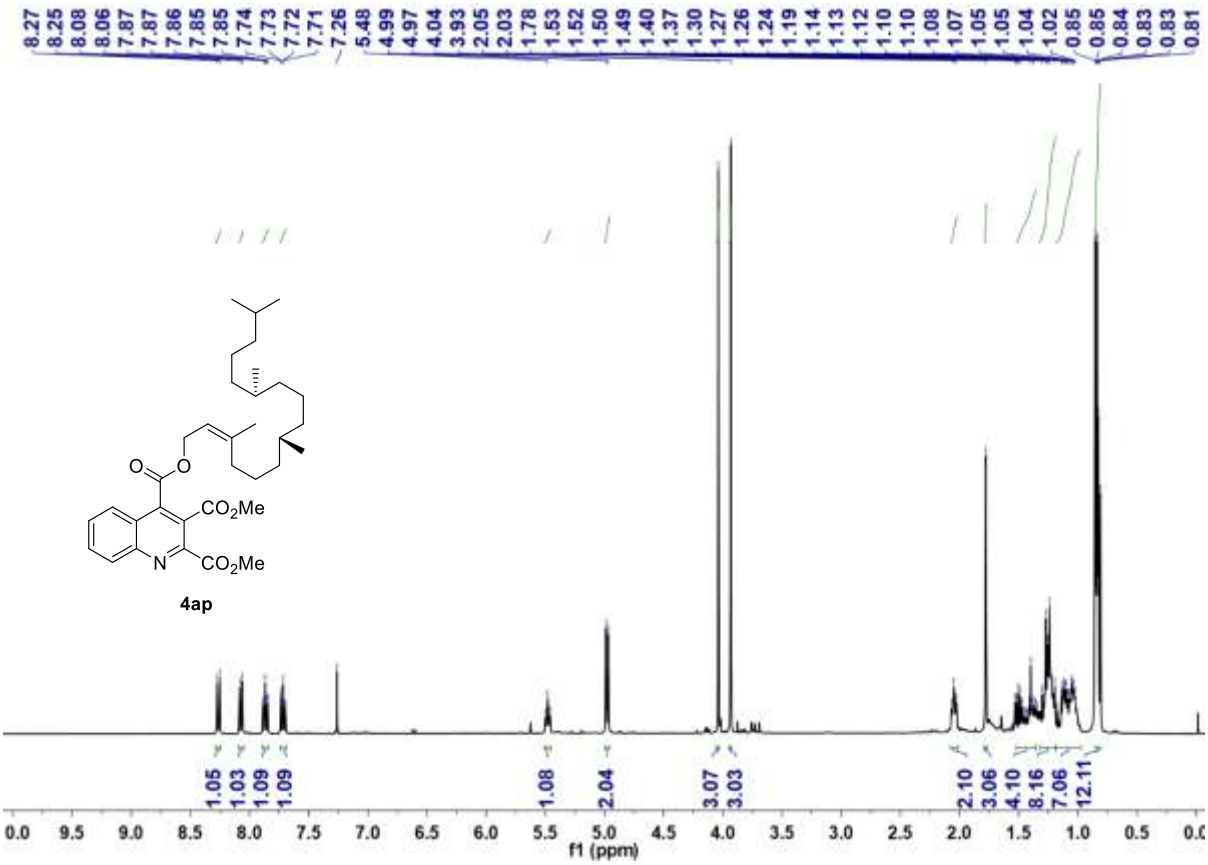

165.91
165.66
165.26
148.13
147.59
141.15
132.14
130.58
129.96
125.47
123.83
122.31
84.40
53.48
53.20
48.95
47.07
45.13
38.59
33.85
27.01
20.01
19.78
11.76
O
O
CO2Me
N
CO2Me
4am
f1 (ppm)

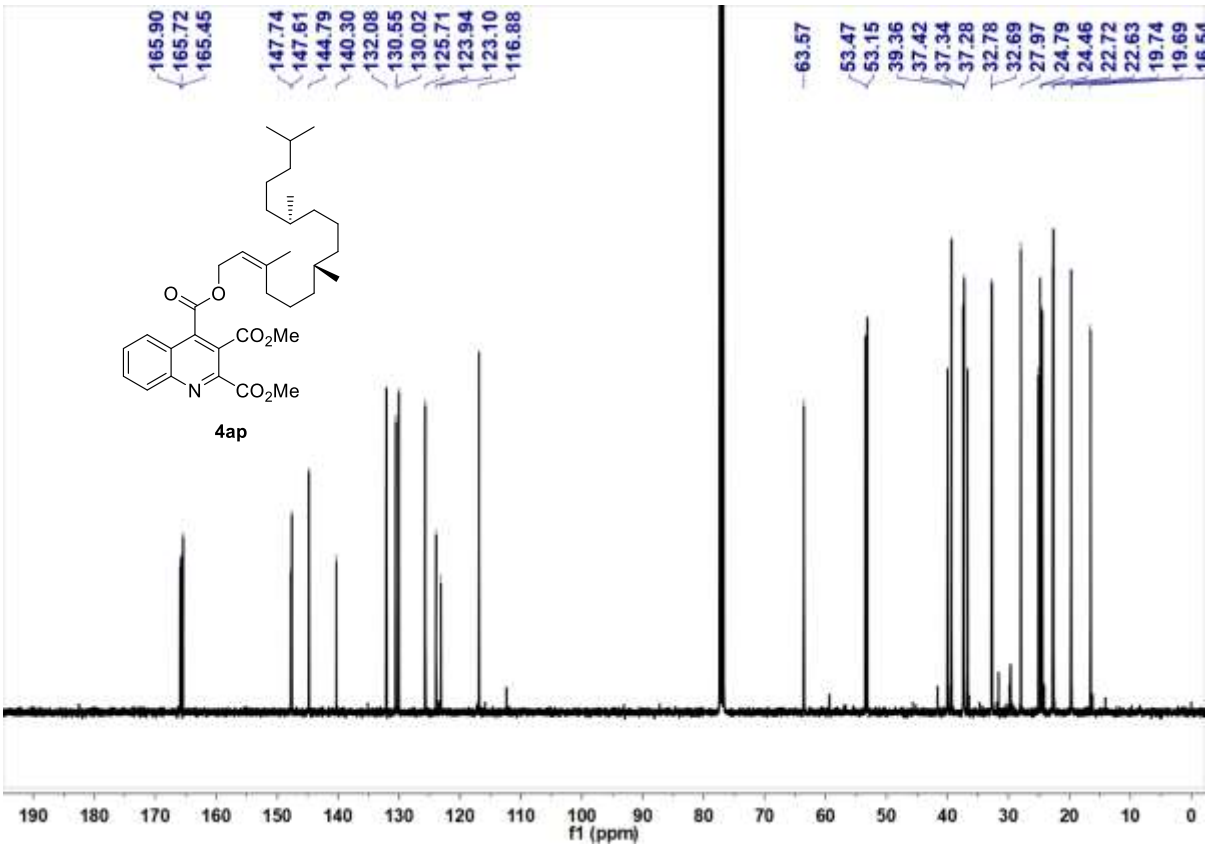

8.29 8.27 8.03 8.01 7.90 7.90 7.89 7.88 7.88 7.87 7.86 7.76 7.76 7.74 7.74 7.74 7.72 7.72 7.26 5.14 5.13 5.12 5.10 5.09 5.08 4.05 3.95 2.39 2.36 1.98 1.96 1.96 1.95 1.76 1.73 1.62 1.62 1.61 1.47 1.44 1.21 1.18 1.15 1.13 1.12 1.01 1.00 0.90 0.88 0.86
CO2Me
CO2Me
4an
1.00 1.03 1.05 1.06 1.06 3.01 2.99 1.03 1.06 2.12 2.03 1.15 2.12 3.06 6.32
f1 (ppm)

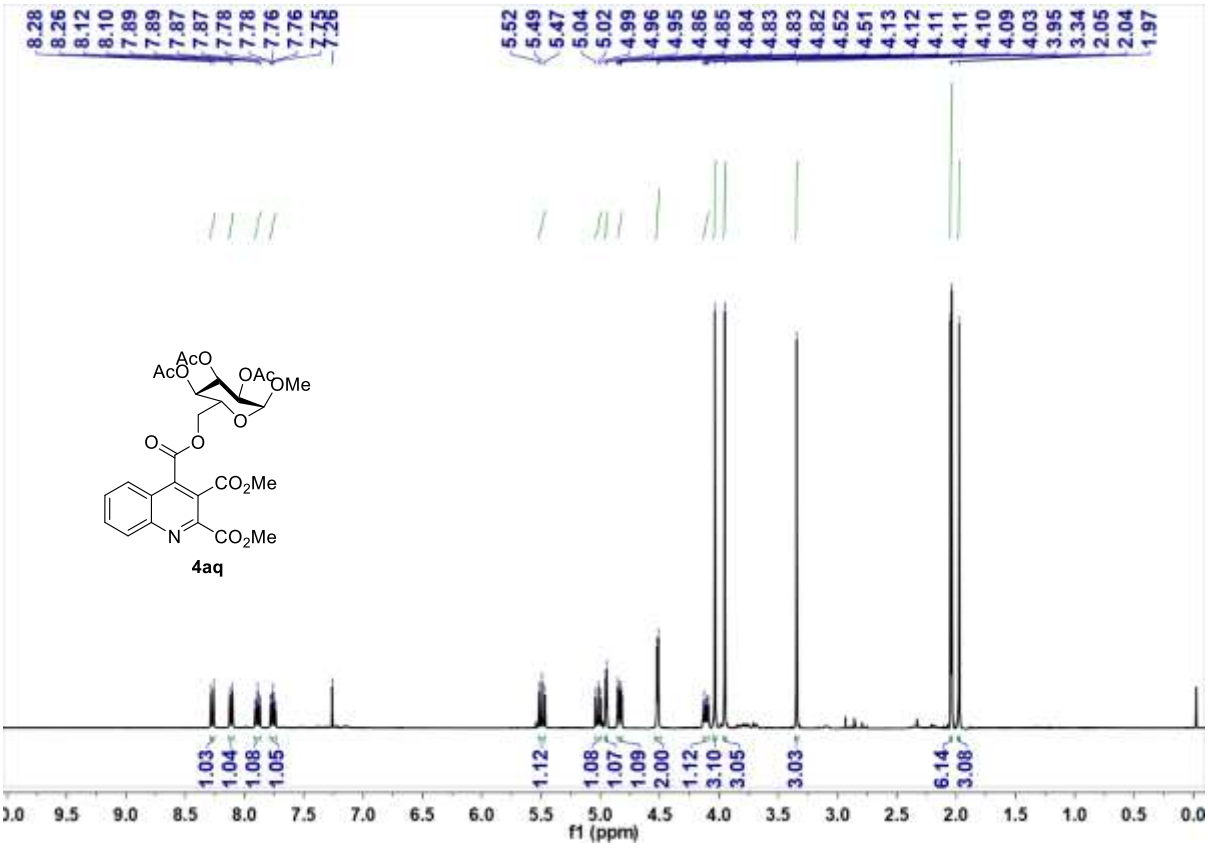

165.84 165.74 165.20 147.73 147.58 140.73 132.02 130.66 130.01 125.47 123.92 122.84 77.63 53.49 53.17 46.87 40.54 34.08 31.56 25.80 23.03 22.09 20.80 15.96
CO2Me
CO2Me
4an
77.63
f1 (ppm)
f1 (ppm)

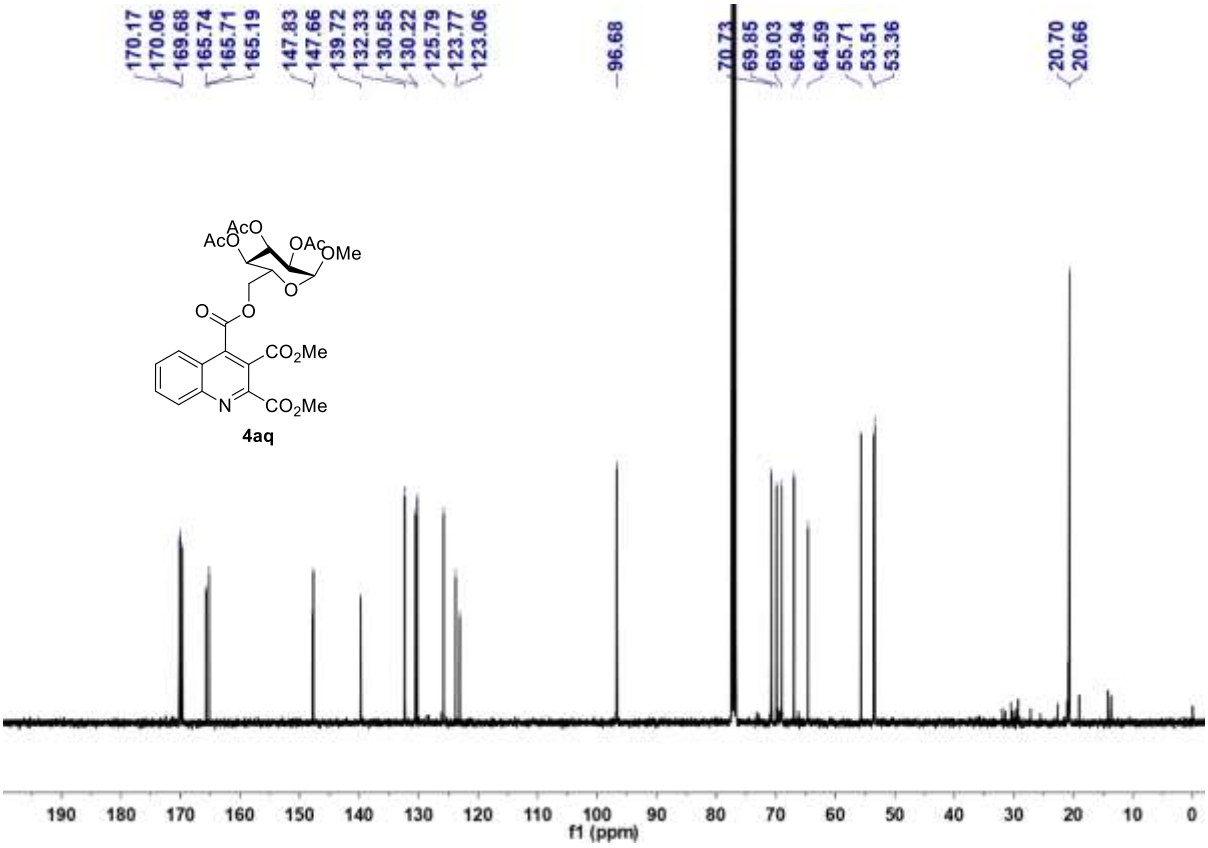

8.27
8.25
8.04
8.02
7.87
7.86
7.86
7.84
7.84
7.73
7.72
7.71
7.71
5.51
5.49
5.47
5.10
5.09
5.07
4.99
4.97
4.53
4.51
4.49
4.48
4.42
4.41
4.39
4.37
2.13
2.12
2.10
2.09
2.07
2.06
1.79
1.66
1.59
1.45
1.44
1.42
1.40
1.38
1.36
O
O
CO2Et
N
CO2Et
4ao
1.00
1.00
1.00
1.00
0.97
1.05
1.94
2.07
2.07
4.03
3.05
3.26
3.25
6.33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

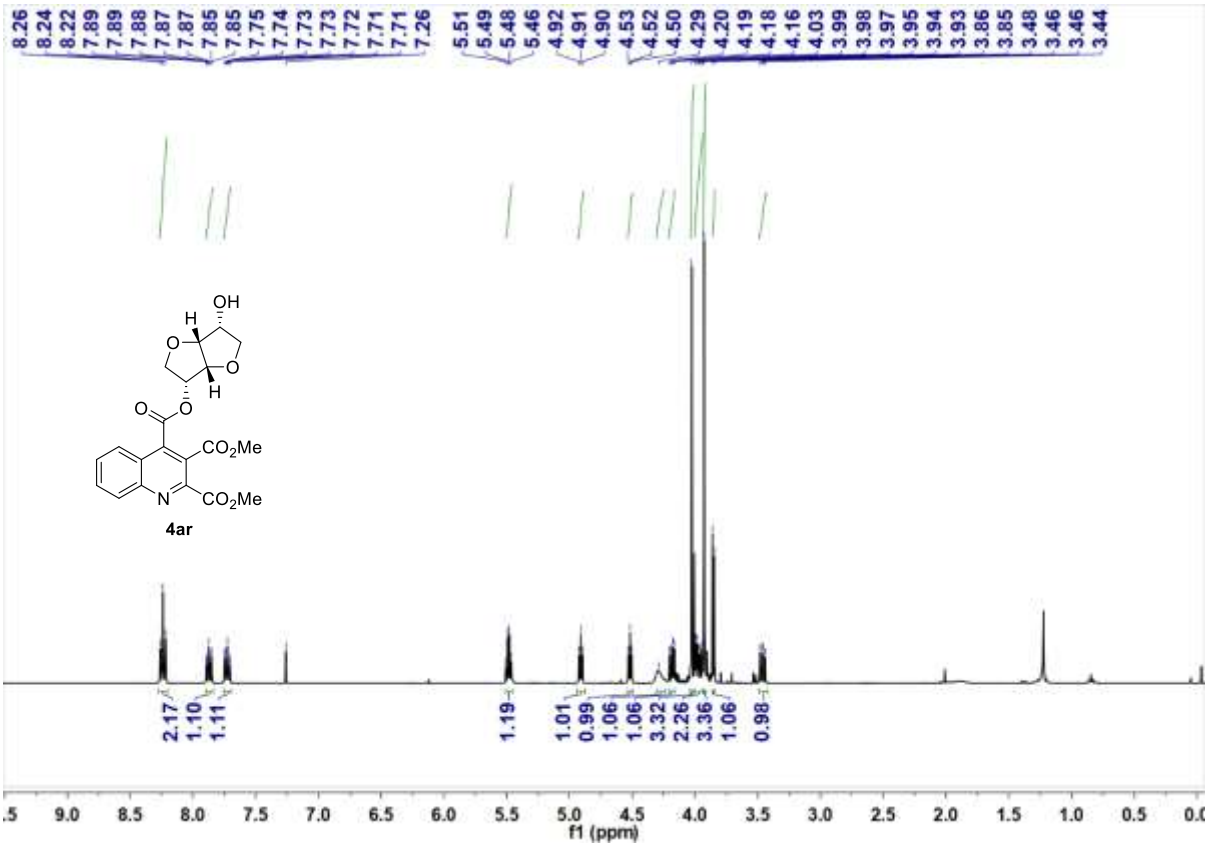

165.66
165.55
165.30
148.69
147.63
144.15
140.57
132.04
132.01
130.50
129.79
125.62
123.81
123.54
122.63
117.13
63.46
62.64
62.45
39.61
26.29
25.68
17.70
16.65
14.13
13.95
O
O
CO2Et
N
CO2Et
4ao
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

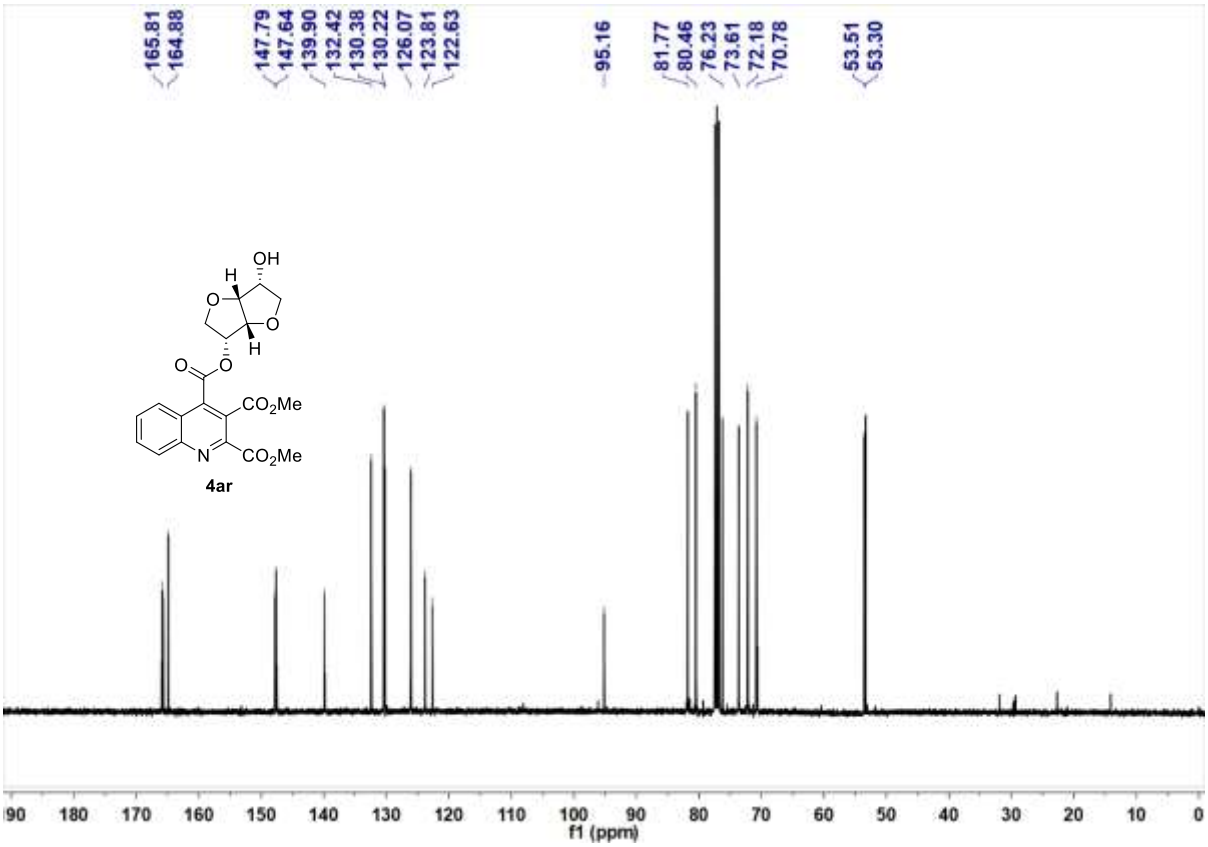

8.27 8.25 8.08 8.06 7.87 7.87 7.86 7.85 7.85 7.74 7.73 7.72 7.71 7.26 5.48 4.99 4.97 4.04 3.93 2.05 2.03 1.78 1.53 1.52 1.50 1.49 1.40 1.37 1.30 1.27 1.26 1.24 1.19 1.14 1.13 1.12 1.10 1.10 1.08 1.07 1.05 1.05 1.04 1.02 0.85 0.85 0.84 0.83 0.83 0.81
O
O
CO2Me
N
CO2Me
4ap
1.05 1.03 1.09 1.09 1.08 2.04 3.07 3.03 2.10 3.06 4.10 8.16 7.06 12.11
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

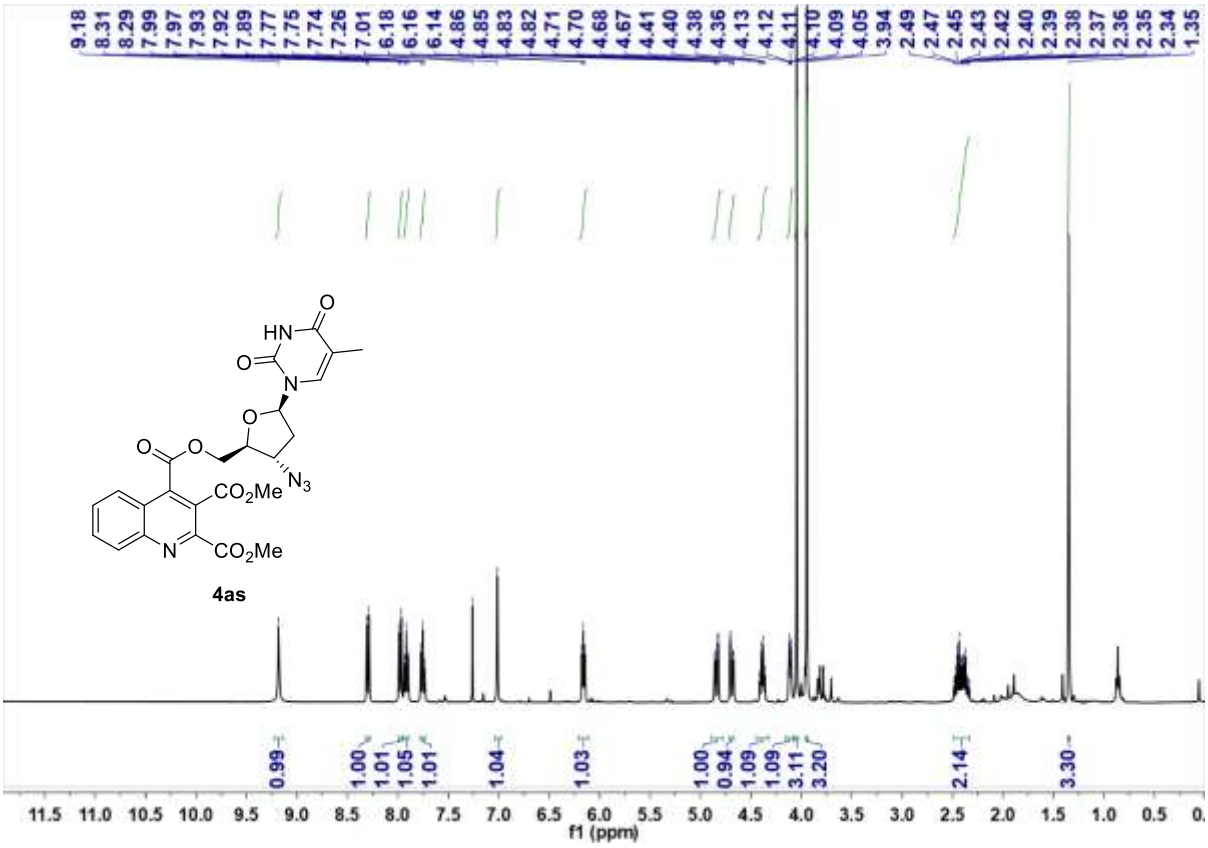

165.90 165.72 165.45 147.74 147.61 144.79 140.30 132.08 130.55 130.02 125.71 123.94 123.10 116.88 63.57 53.47 53.15 39.36 37.42 37.34 37.28 32.78 32.69 27.97 24.79 24.46 22.72 22.63 19.74 19.69
O
O
CO2Me
N
CO2Me
4ap
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.28 8.26 8.12 8.10 7.89 7.89 7.87 7.87 7.78 7.78 7.76 7.76 7.75 7.75
5.52 5.49 5.47 5.04 5.02 4.99 4.96 4.95 4.86 4.85 4.84 4.83 4.83 4.82 4.52 4.51 4.13 4.12 4.11 4.11 4.10 4.09 4.03 3.95 3.34 2.05 2.04 1.97
AcO
AcO
OAc
OMe
O
O
O
CO2Me
N
CO2Me
4aq
1.03 1.04 1.08 1.05 1.12 1.08 1.07 1.09 2.00 1.12 3.10 3.05 3.03 6.14 3.08
f1 (ppm)


170.17 170.06 169.68 165.74 165.71 165.19 147.83 147.66 139.72 132.33 130.55 130.22 125.79 123.77 123.06
96.68
70.73 69.85 69.03 66.94 64.59 55.71 53.51 53.36
20.70 20.66
AcO
AcO
OAc
OMe
O
O
O
CO2Me
N
CO2Me
4aq
f1 (ppm)


8.26 8.24 8.22 7.89 7.89 7.88 7.87 7.87 7.85 7.85 7.75 7.74 7.73 7.73 7.72 7.71 7.71 7.26
5.51 5.49 5.48 5.46 4.92 4.91 4.90 4.53 4.52 4.50 4.29 4.20 4.19 4.18 4.16 4.03 3.99 3.98 3.97 3.95 3.94 3.93 3.86 3.85 3.48 3.46 3.46 3.44
OH
H
O
O
H
O
O
CO2Me
N
CO2Me
4ar
2.17 1.10 1.11 1.19 1.01 0.99 1.06 1.06 3.32 2.26 3.36 1.06 0.98
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


165.81 164.88 147.79 147.64 139.90 132.42 130.38 130.22 126.07 123.81 122.63 95.16 81.77 80.46 76.23 73.61 72.18 70.78 53.51 53.30
OH
H
O
O
H
O
O
CO2Me
N
CO2Me
4ar
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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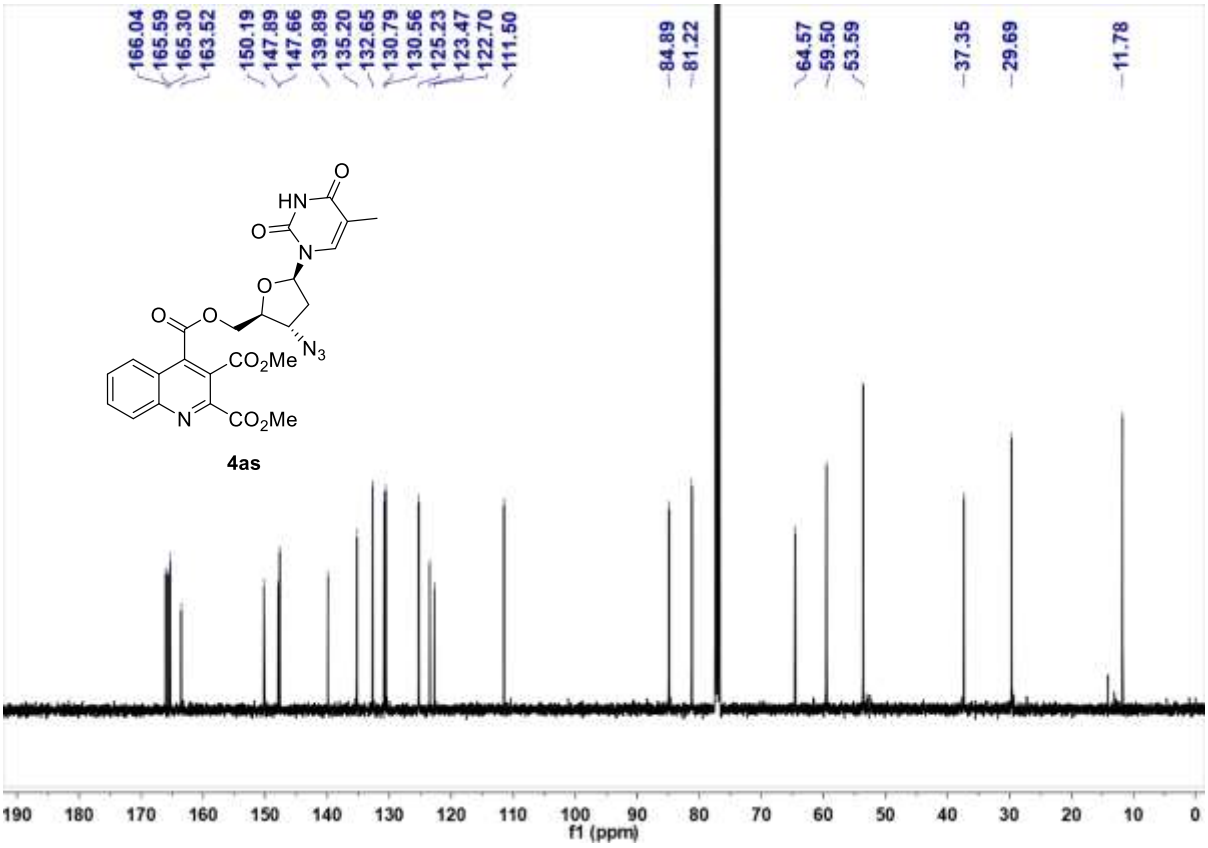
7.97
7.93
7.92
7.89
7.77
7.75
7.74
7.26
7.01
6.18
6.16
6.14
4.86
4.85
4.83
4.82
4.71
4.70
4.68
4.67
4.41
4.40
4.38
4.36
4.13
4.12
4.11
4.10
4.09
4.05
3.94
2.49
2.47
2.45
2.43
2.42
2.40
2.39
2.38
2.37
2.36
2.35
2.34
1.35
HN
O
O
N
O
O
O
CO2Me
N3
N
CO2Me
4as
0.99
1.00
1.01
1.05
1.01
1.04
1.03
1.00
0.94
1.09
1.09
3.11
3.20
2.14
3.30
f1 (ppm)


166.04
165.59
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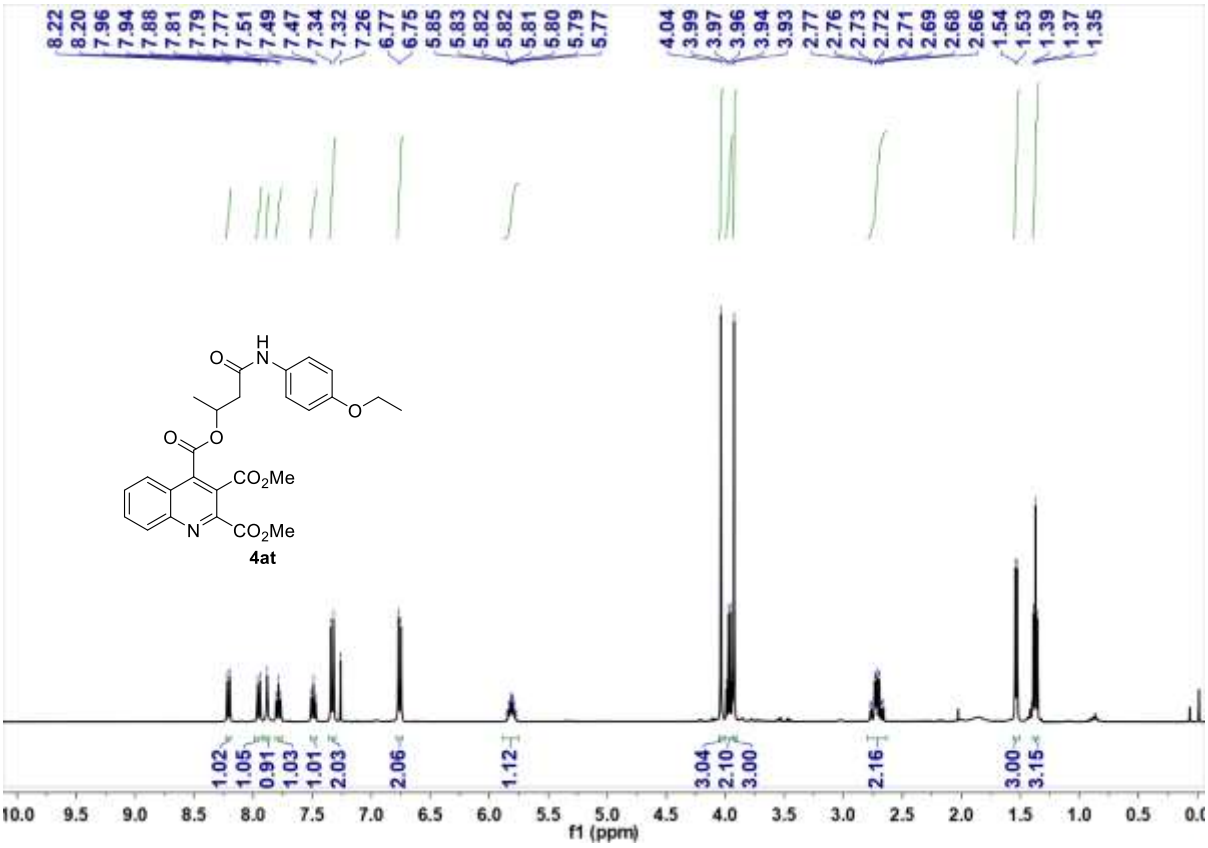
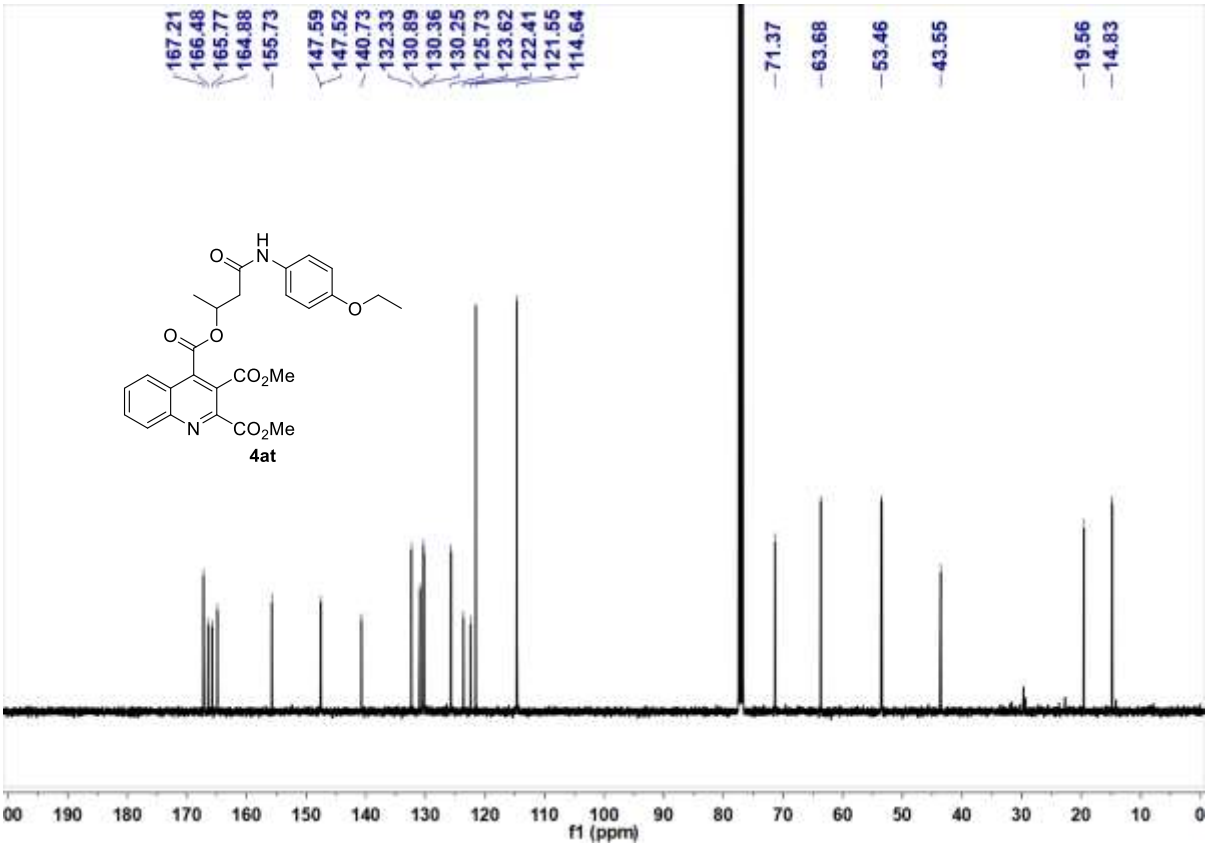
163.52
150.19
147.89
147.66
139.89
135.20
132.65
130.79
130.56
125.23
123.47
122.70
111.50
84.89
81.22
64.57
59.50
53.59
37.35
29.69
11.78
HN
O
O
N
O
O
O
CO2Me
N3
N
CO2Me
4as
f1 (ppm)


8.22
8.20
7.96
7.94
7.88
7.81
7.79
7.77
7.51
7.49
7.47
7.34
7.32
7.26
6.77
6.75
5.85
5.83
5.82
5.82
5.81
5.80
5.79
5.77
4.04
3.99
3.97
3.96
3.94
3.93
2.77
2.76
2.73
2.72
2.71
2.69
2.68
2.66
1.54
1.53
1.39
1.37
1.35
4at
1.02
1.05
0.91
1.03
1.01
2.03
2.06
1.12
3.04
2.10
3.00
2.16
3.00
3.15
f1 (ppm)


167.21
166.48
165.77
164.88
155.73
147.59
147.52
140.73
132.33
130.89
130.36
130.25
125.73
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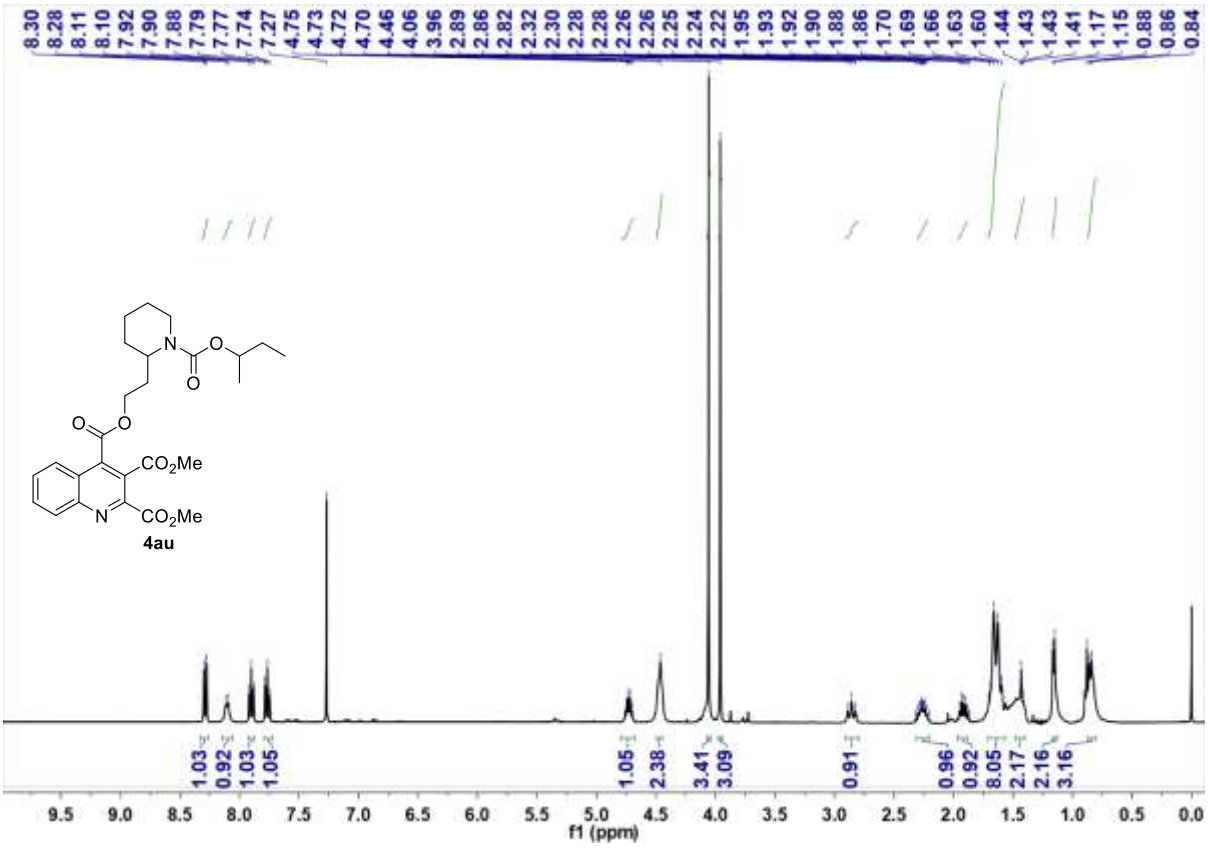
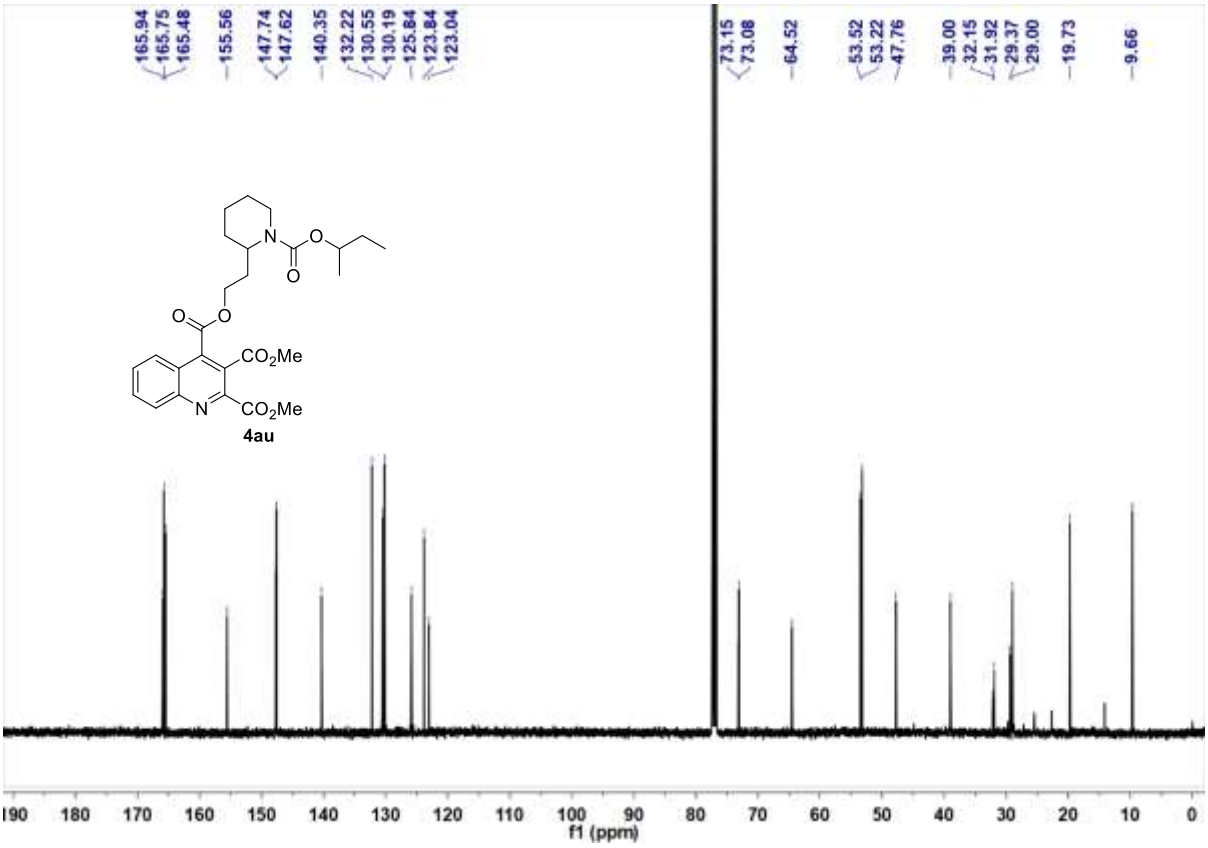
43.55
19.56
14.83
4at
f1 (ppm)


8.30
8.28
8.11
8.10
7.92
7.90
7.88
7.79
7.77
7.74
7.27
4.75
4.73
4.72
4.70
4.46
4.06
3.96
2.89
2.86
2.82
2.32
2.30
2.28
2.28
2.26
2.26
2.25
2.24
2.22
1.95
1.93
1.92
1.90
1.88
1.86
1.70
1.69
1.66
1.63
1.60
1.44
1.43
1.43
1.41
1.17
1.15
0.88
0.86
0.84
1.03
0.92
1.03
1.05
1.05
2.38
3.41
3.09
0.91
0.96
0.92
8.05
2.17
2.16
3.16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
CO2Me
CO2Me
4au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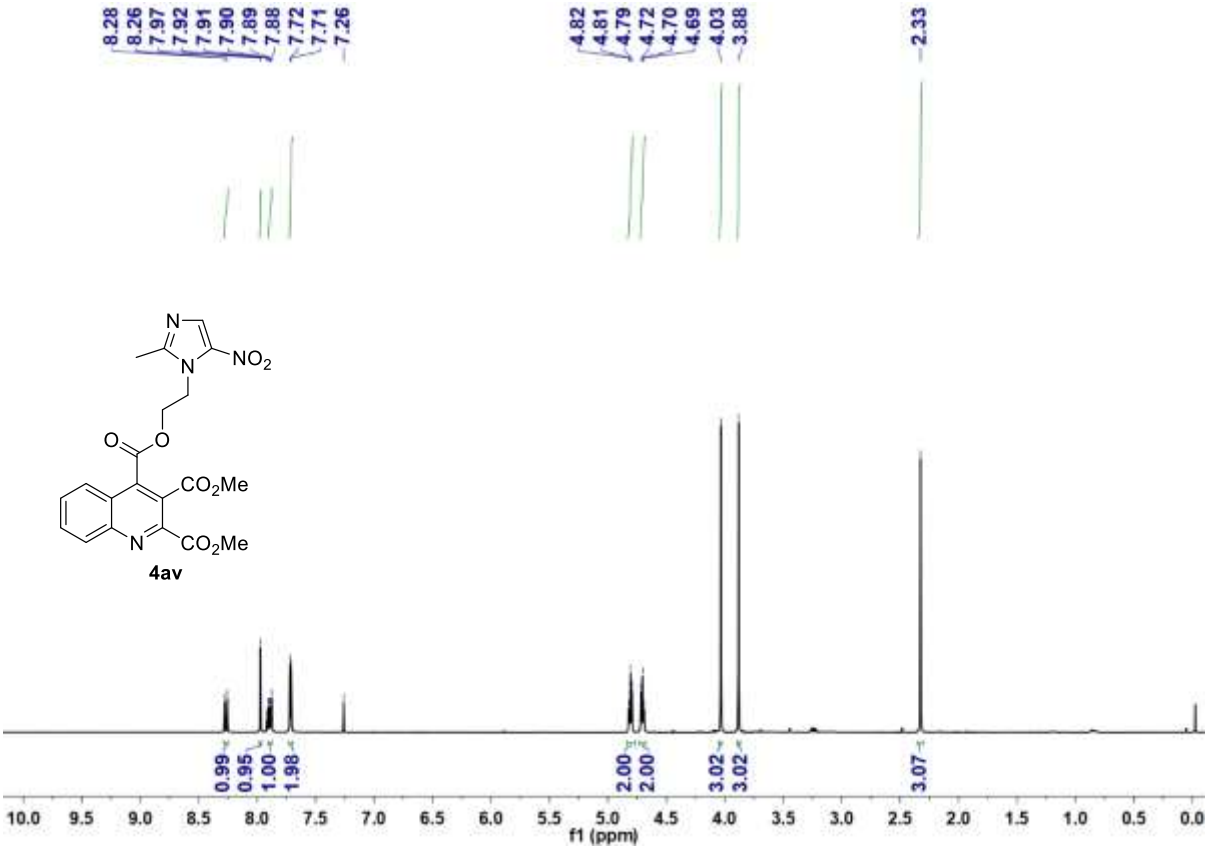
132.22
130.55
130.19
125.84
123.84
123.04
73.15
73.08
64.52
53.52
53.22
47.76
39.00
32.15
31.92
29.37
29.00
19.73
9.66
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CO2Me
CO2Me
4au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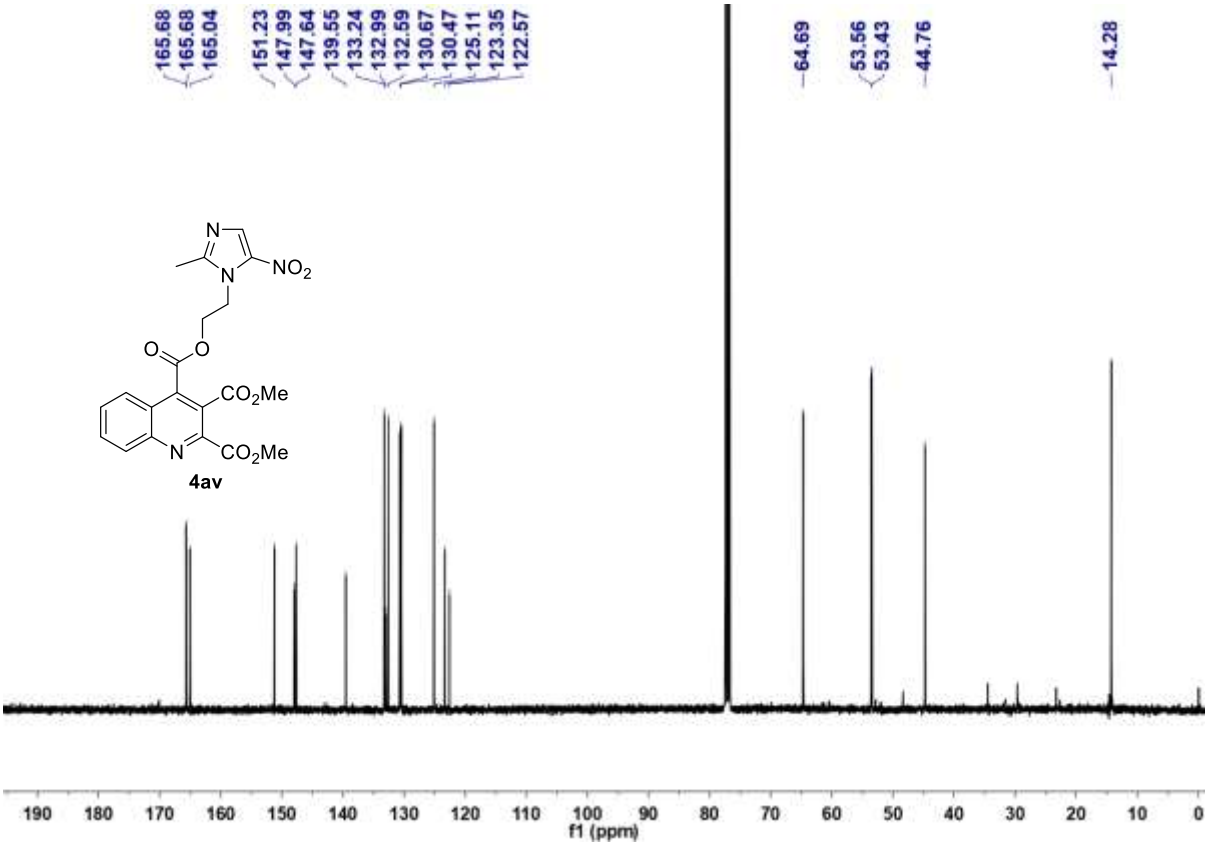
7.89
7.88
7.72
7.71
7.26
4.82
4.81
4.79
4.72
4.70
4.69
4.03
3.88
2.33
N
N
NO2
O
O
CO2Me
N
CO2Me
4av
0.99
0.95
1.00
1.98
2.00
2.00
3.02
3.02
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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133.24
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132.59
130.67
130.47
125.11
123.35
122.57
64.69
53.56
53.43
44.76
14.28
N
N
NO2
O
O
CO2Me
N
CO2Me
4av
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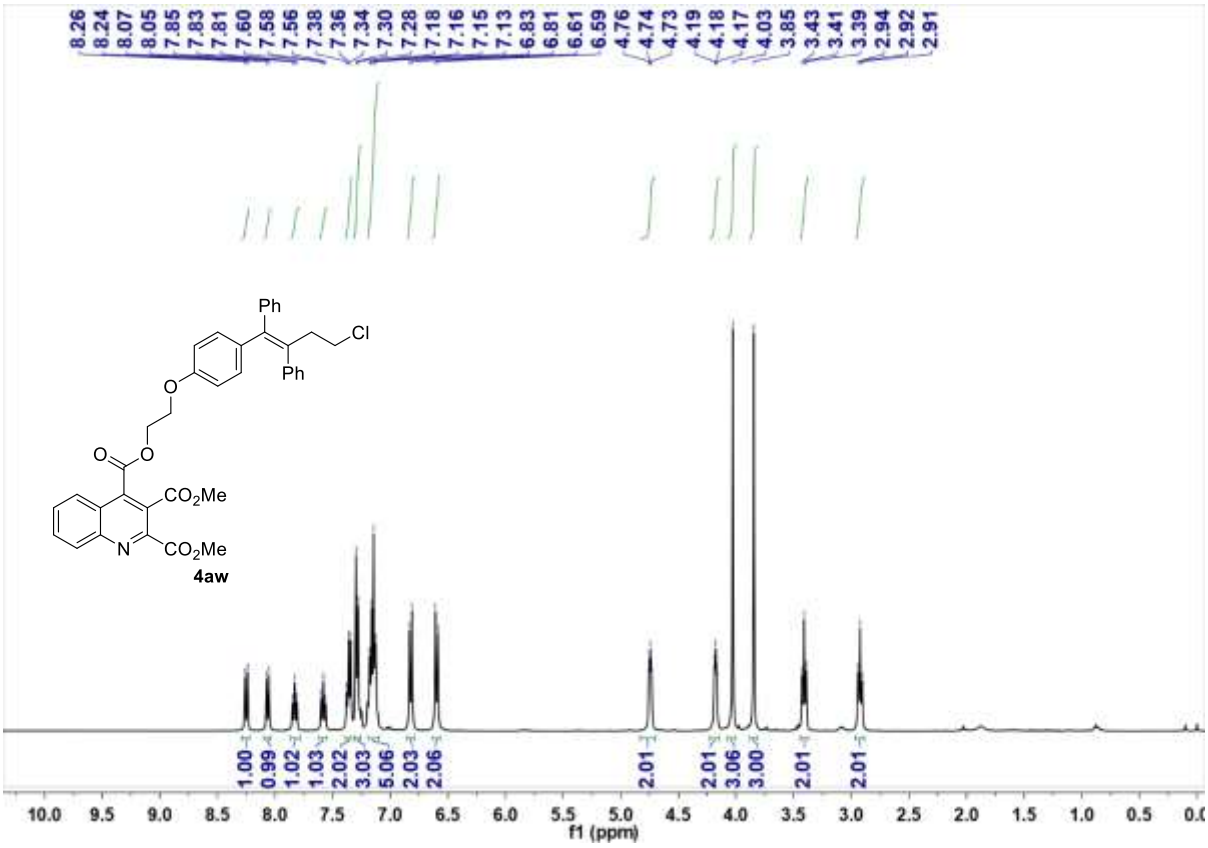
f1 (ppm)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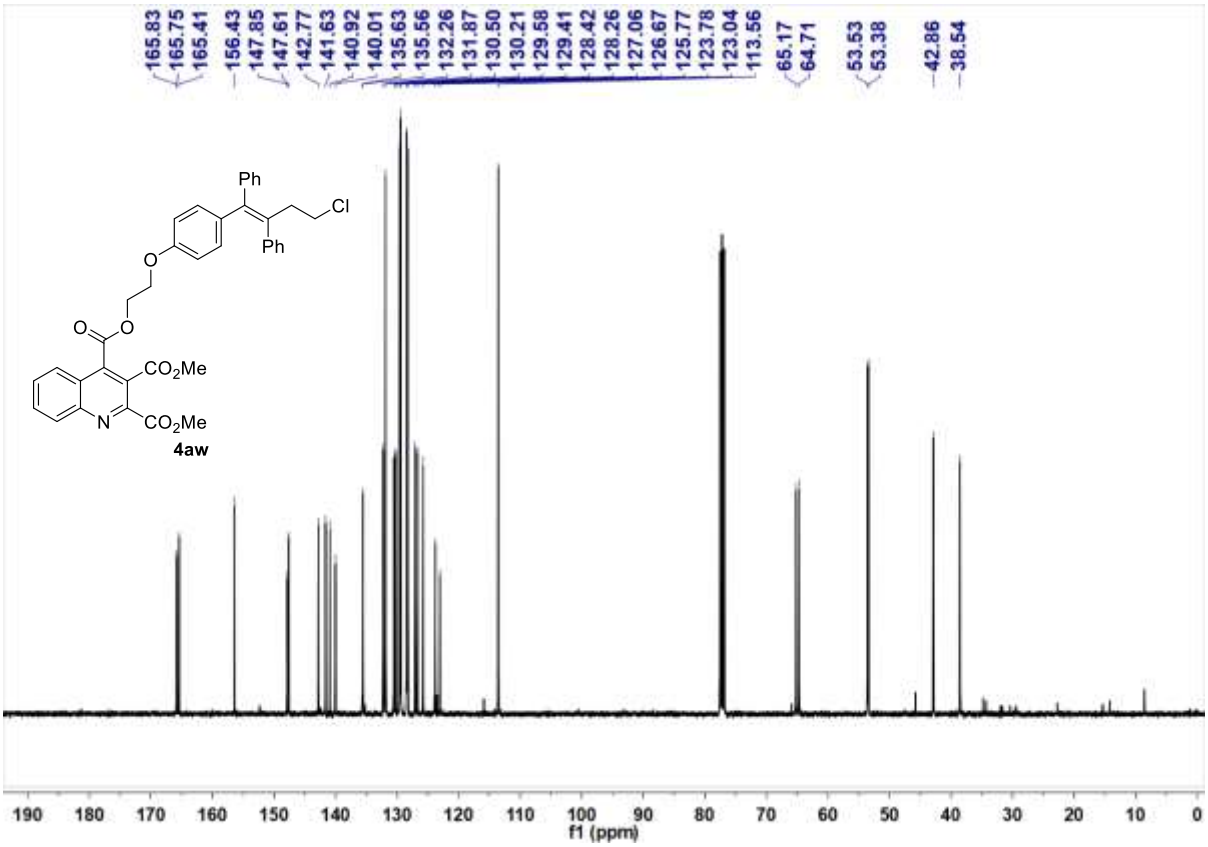
7.60
7.58
7.56
7.38
7.36
7.34
7.30
7.28
7.18
7.16
7.15
7.13
6.83
6.81
6.61
6.59
4.76
4.74
4.73
4.19
4.18
4.17
4.03
3.85
3.43
3.41
3.39
2.94
2.92
2.91
Ph
Cl
Ph
O
O
O
CO2Me
N
CO2Me
4aw
1.00
0.99
1.02
1.03
2.02
3.03
5.06
2.03
2.06
2.01
2.01
3.06
3.00
2.01
2.01
f1 (ppm)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165.75
165.41
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135.63
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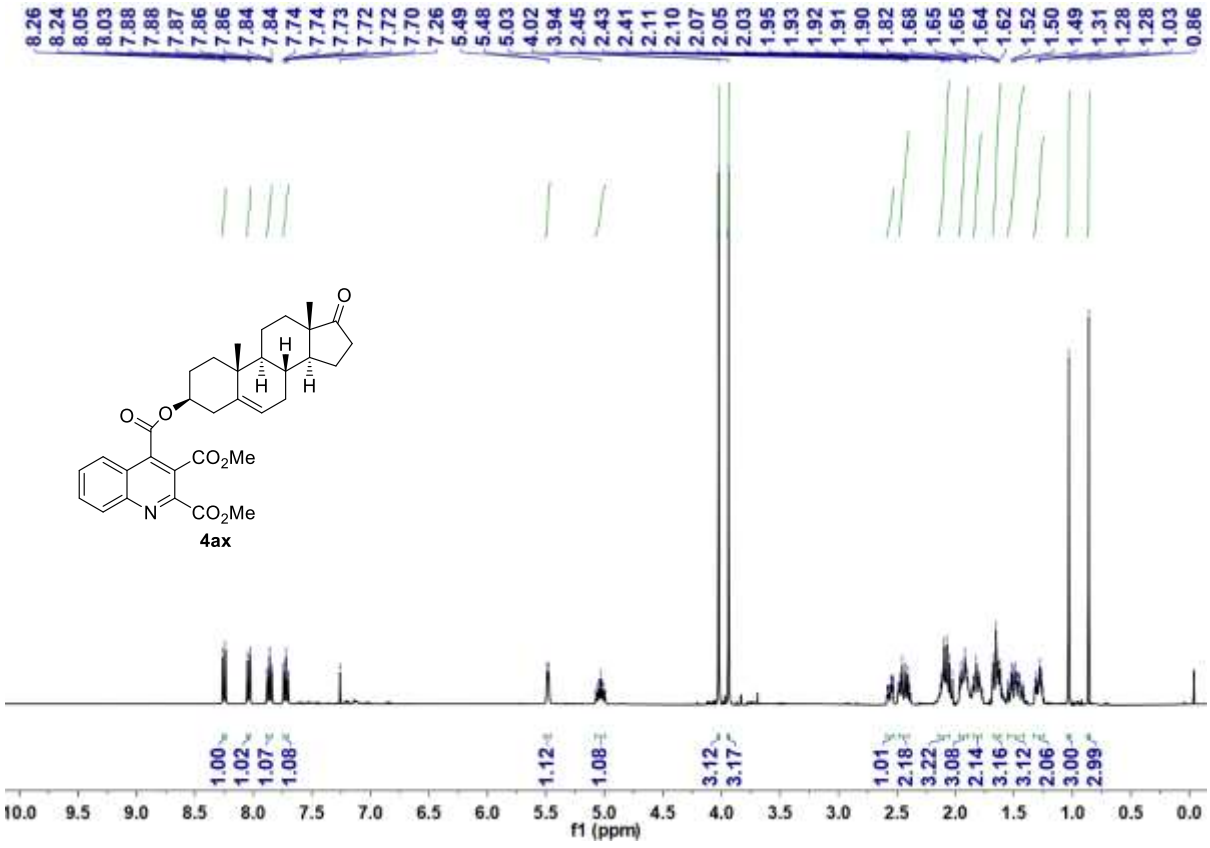
132.26
131.87
130.50
130.21
129.58
129.41
128.42
128.26
127.06
126.67
125.77
123.78
123.04
113.56
65.17
64.71
53.53
53.38
42.86
38.54
Ph
Cl
Ph
O
O
O
CO2Me
N
CO2Me
4aw
f1 (ppm)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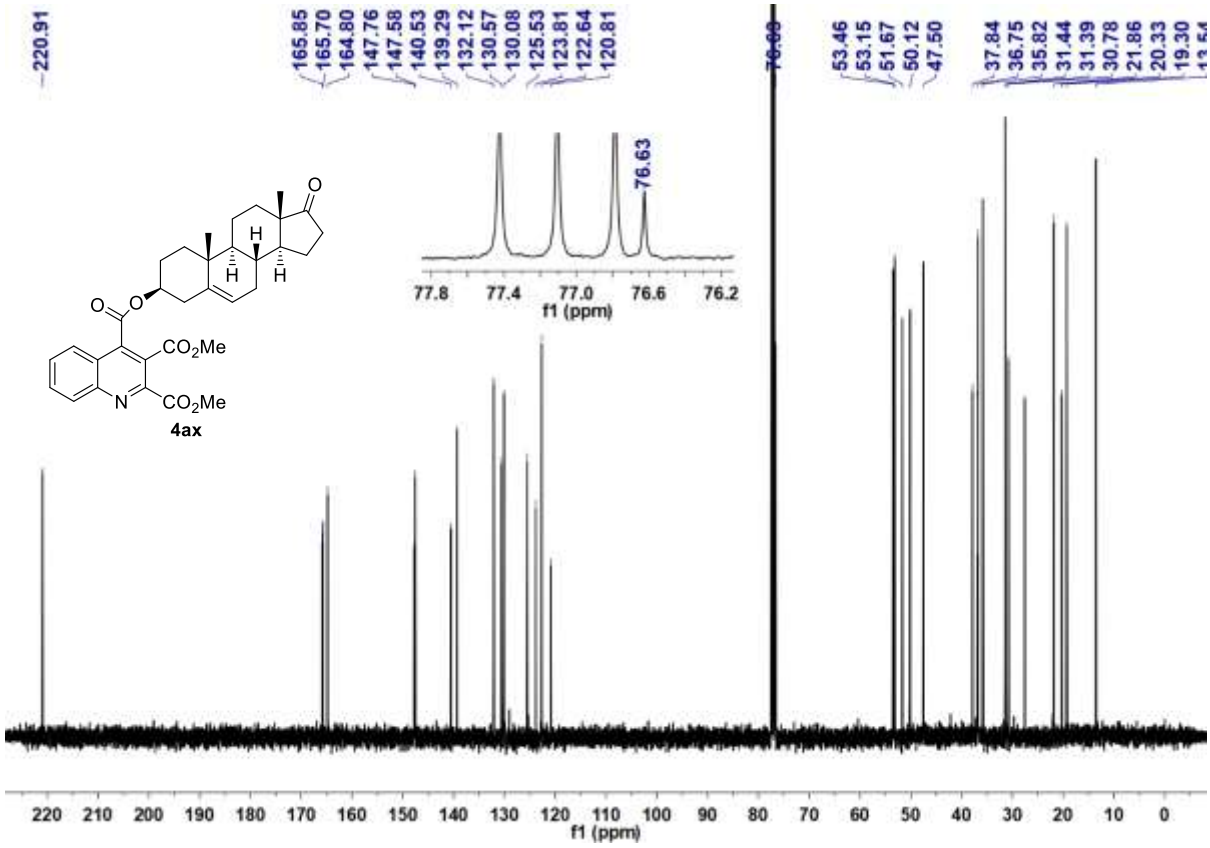
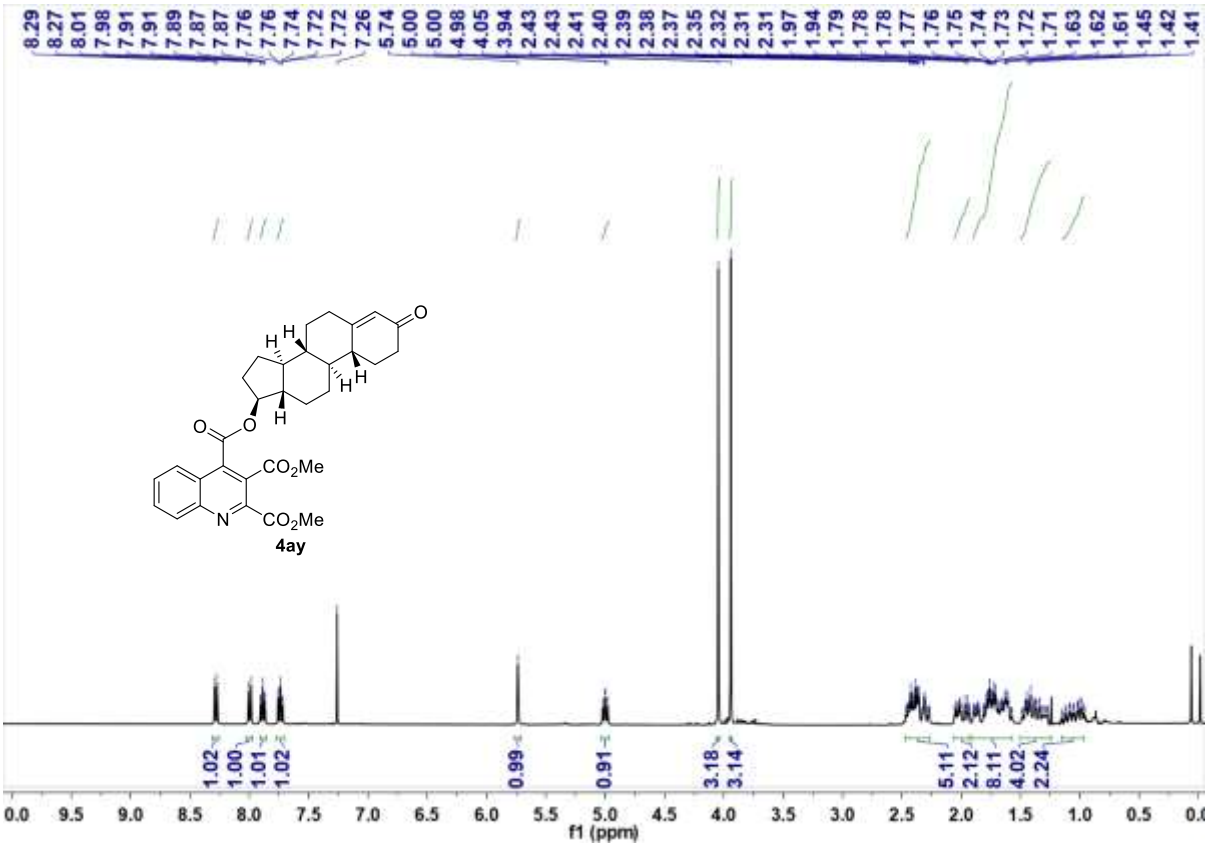
1.00 1.02 1.07 1.08 1.12 1.08 3.12 3.17 1.01 2.18 3.22 3.08 2.14 3.16 3.12 2.06 3.00 2.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
CO2Me
CO2Me
4ax


220.91 165.85 165.70 164.80 147.76 147.58 140.53 139.29 132.12 130.57 130.08 125.53 123.81 122.64 120.81 76.63 53.46 53.15 51.67 50.12 47.50 37.84 36.75 35.82 31.44 31.39 30.78 21.86 20.33 19.30
76.63
77.8 77.4 77.0 76.6 76.2
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CO2Me
CO2Me
4ax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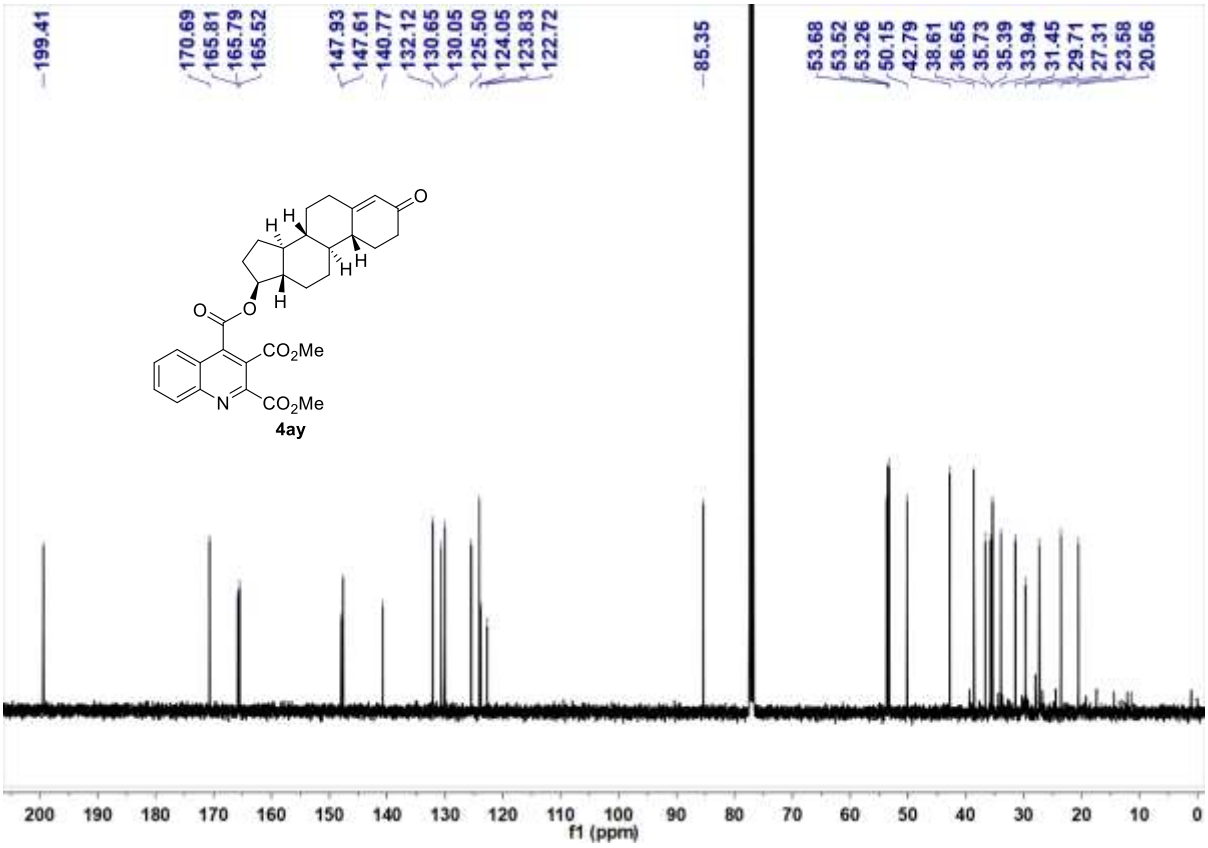
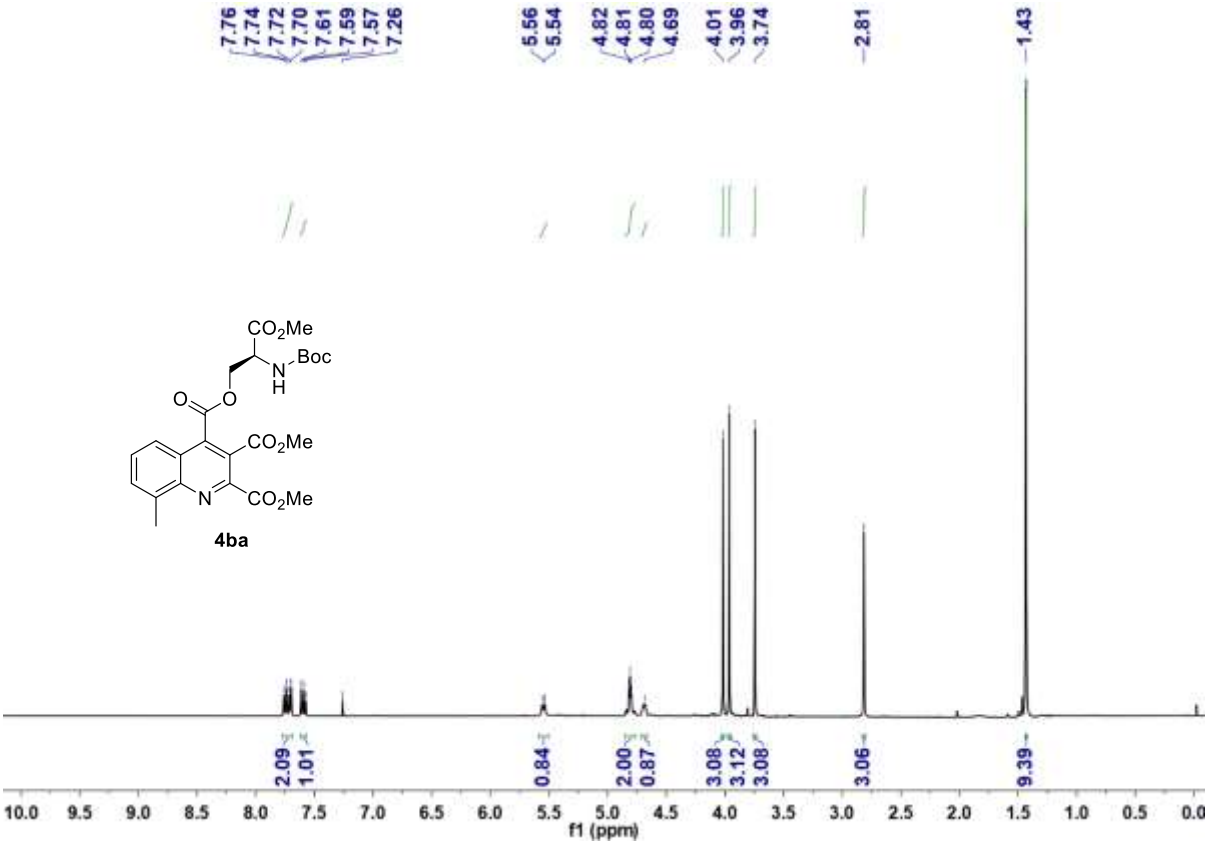
1.02 1.00 1.01 1.02 0.99 0.91 3.18 3.14 5.11 2.12 8.11 4.02 2.24
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
CO2Me
CO2Me
4ay


199.41 170.69 165.81 165.79 165.52 147.93 147.61 140.77 132.12 130.65 130.05 125.50 124.05 123.83 122.72 85.35 53.68 53.52 53.26 50.15 42.79 38.61 36.65 35.73 35.39 33.94 31.45 29.71 27.31 23.58 20.56
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
CO2Me
CO2Me
4ay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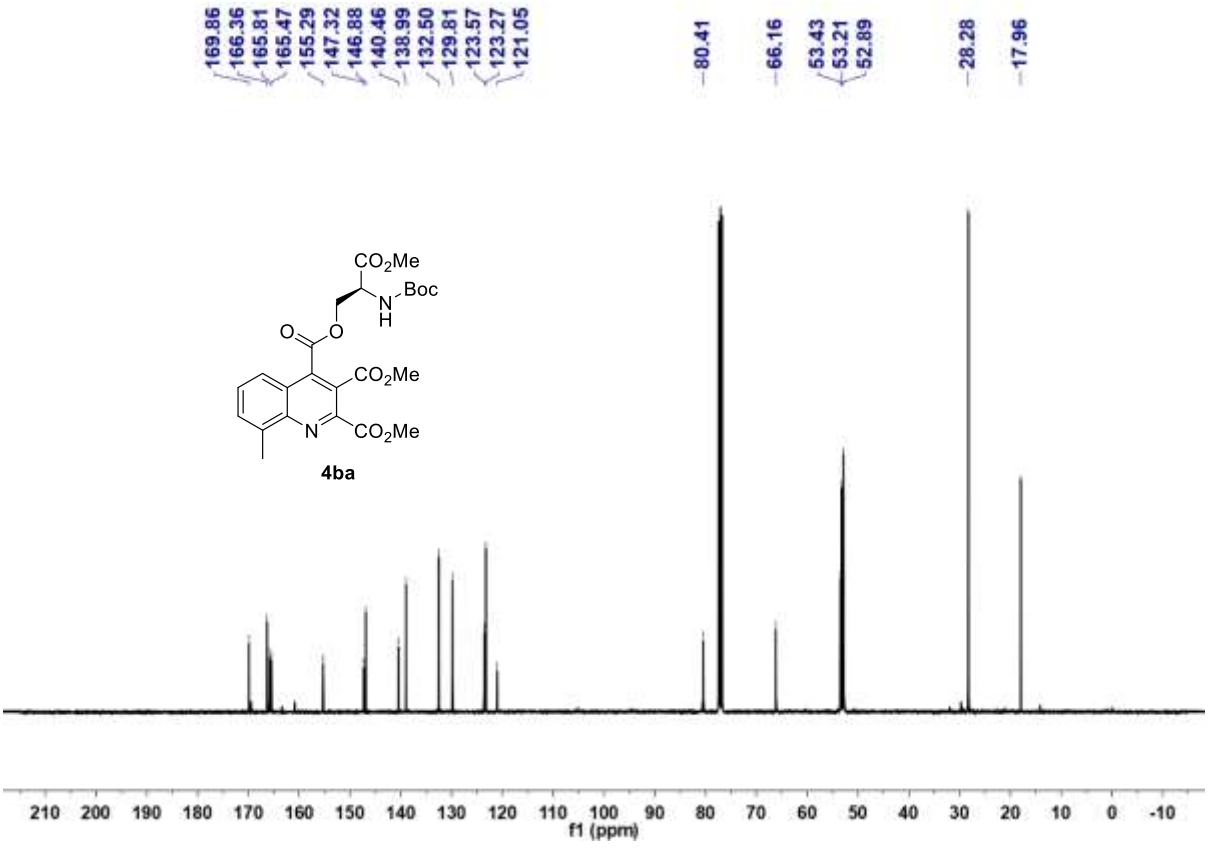
7.74
7.72
7.70
7.61
7.59
7.57
7.26
5.56
5.54
4.82
4.81
4.80
4.69
4.01
3.96
3.74
2.81
1.43
CO2Me
Boc
N
H
O
O
CO2Me
N
CO2Me
4ba
2.09
1.01
0.84
2.00
0.87
3.08
3.12
3.08
3.06
9.39
f1 (ppm)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146.88
140.46
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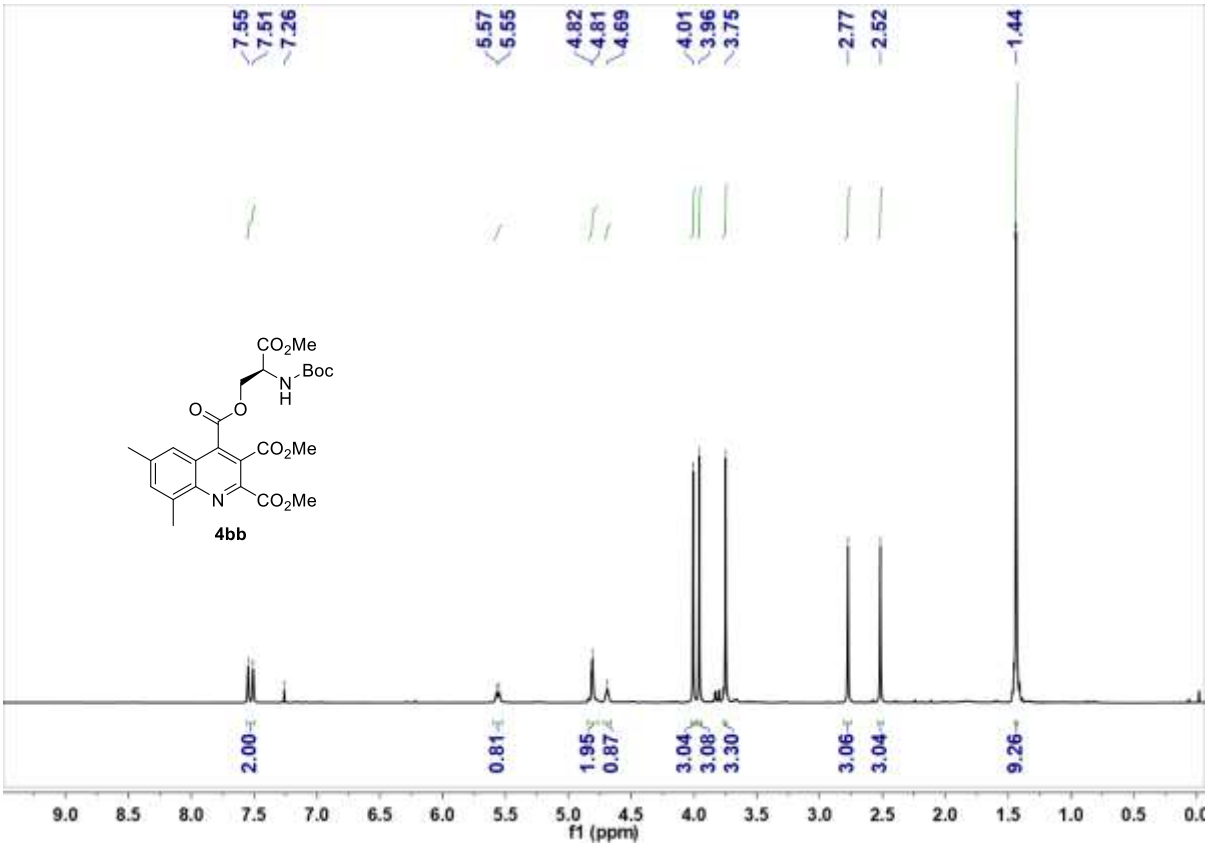
132.50
129.81
123.57
123.27
121.05
80.41
66.16
53.43
53.21
52.89
28.28
17.96
CO2Me
Boc
N
H
O
O
CO2Me
N
CO2Me
4ba
f1 (ppm)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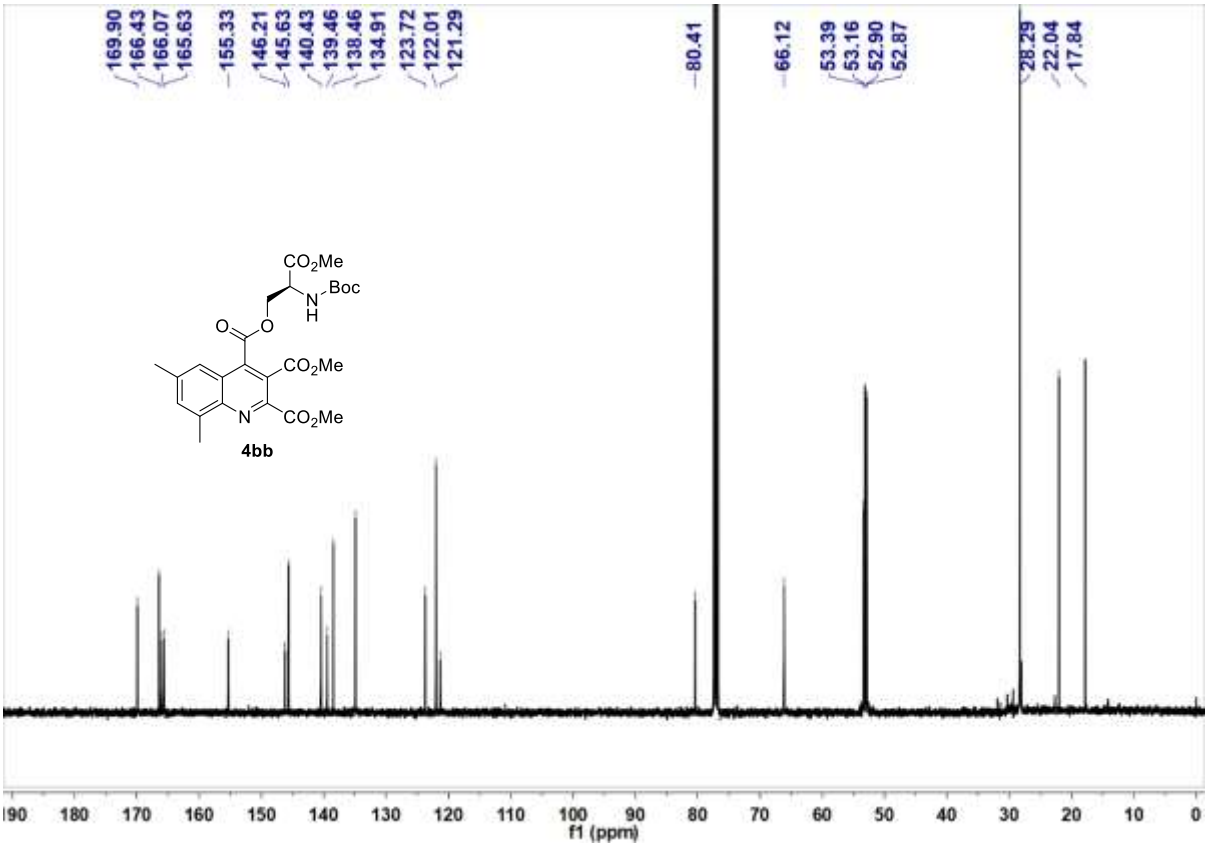
7.51
7.26
5.57
5.55
4.82
4.81
4.69
4.01
3.96
3.75
2.77
2.52
1.44
CO2Me
Boc
N
H
O
O
CO2Me
N
CO2Me
4bb
2.00
0.81
1.95
0.87
3.04
3.08
3.30
3.06
3.04
9.26
f1 (ppm)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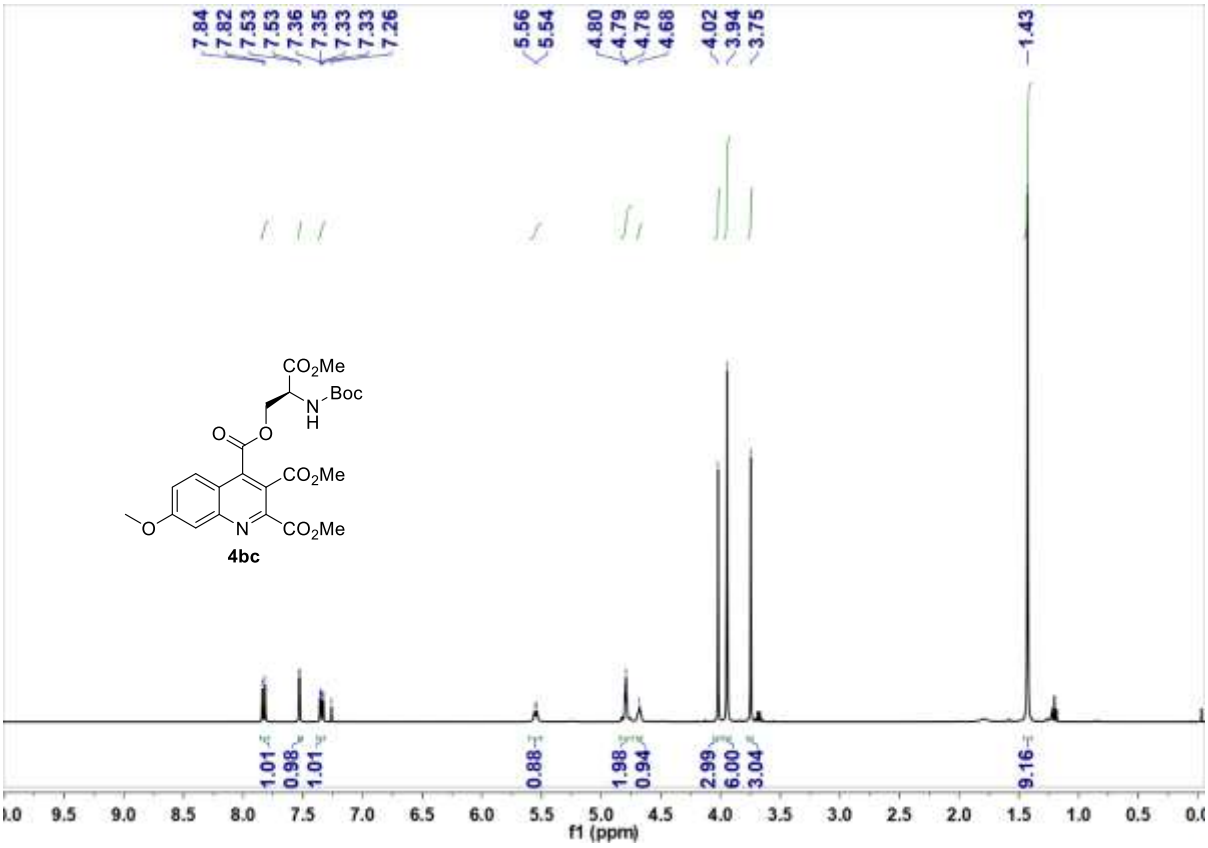
145.63
140.43
139.46
138.46
134.91
123.72
122.01
121.29
80.41
66.12
53.39
53.16
52.90
52.87
28.29
22.04
17.84
CO2Me
Boc
N
H
O
O
CO2Me
N
CO2Me
4bb
f1 (ppm)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7.33
7.26
5.56
5.54
4.80
4.79
4.78
4.68
4.02
3.94
3.75
1.43
CO2Me
Boc
N
H
O
O
CO2Me
O
N
CO2Me
4bc
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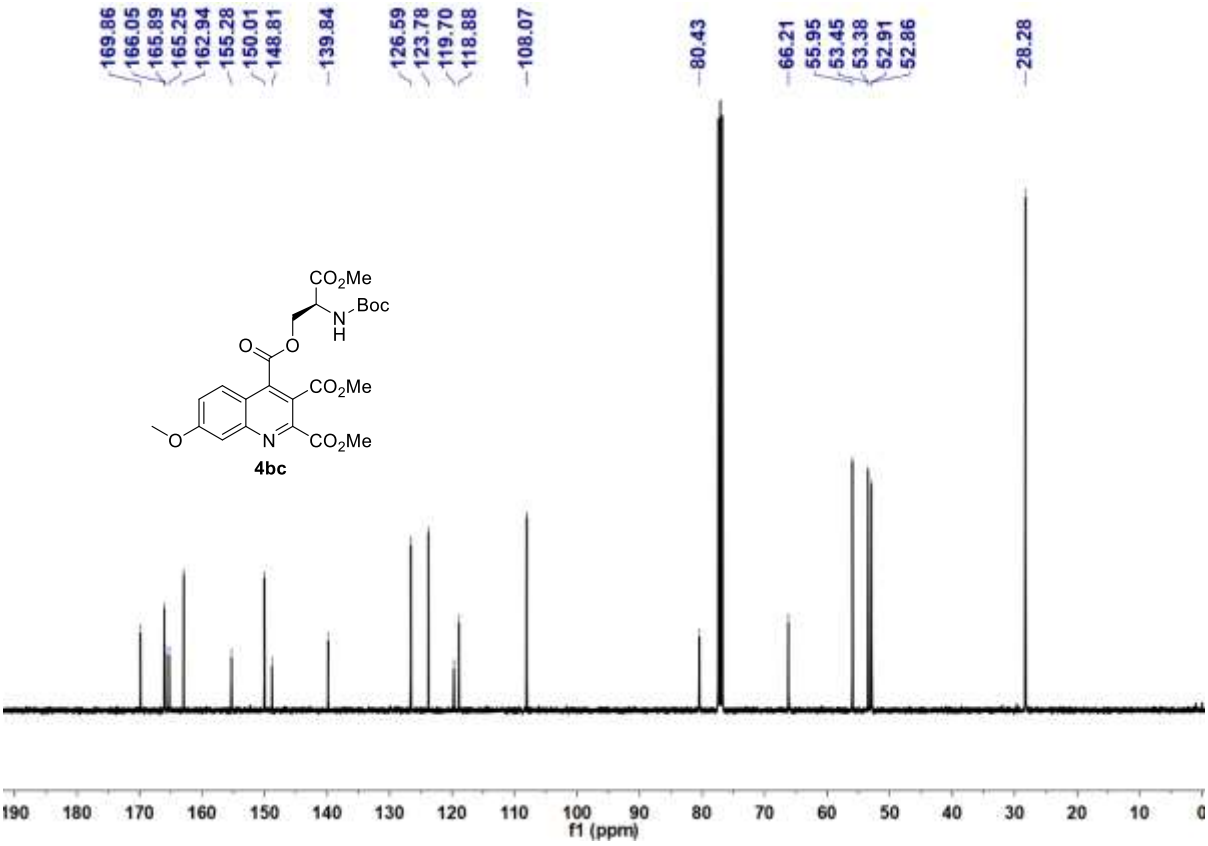
0.98
1.01
0.88
1.98
0.94
2.99
6.00
3.04
9.16
f1 (ppm)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150.01
148.81
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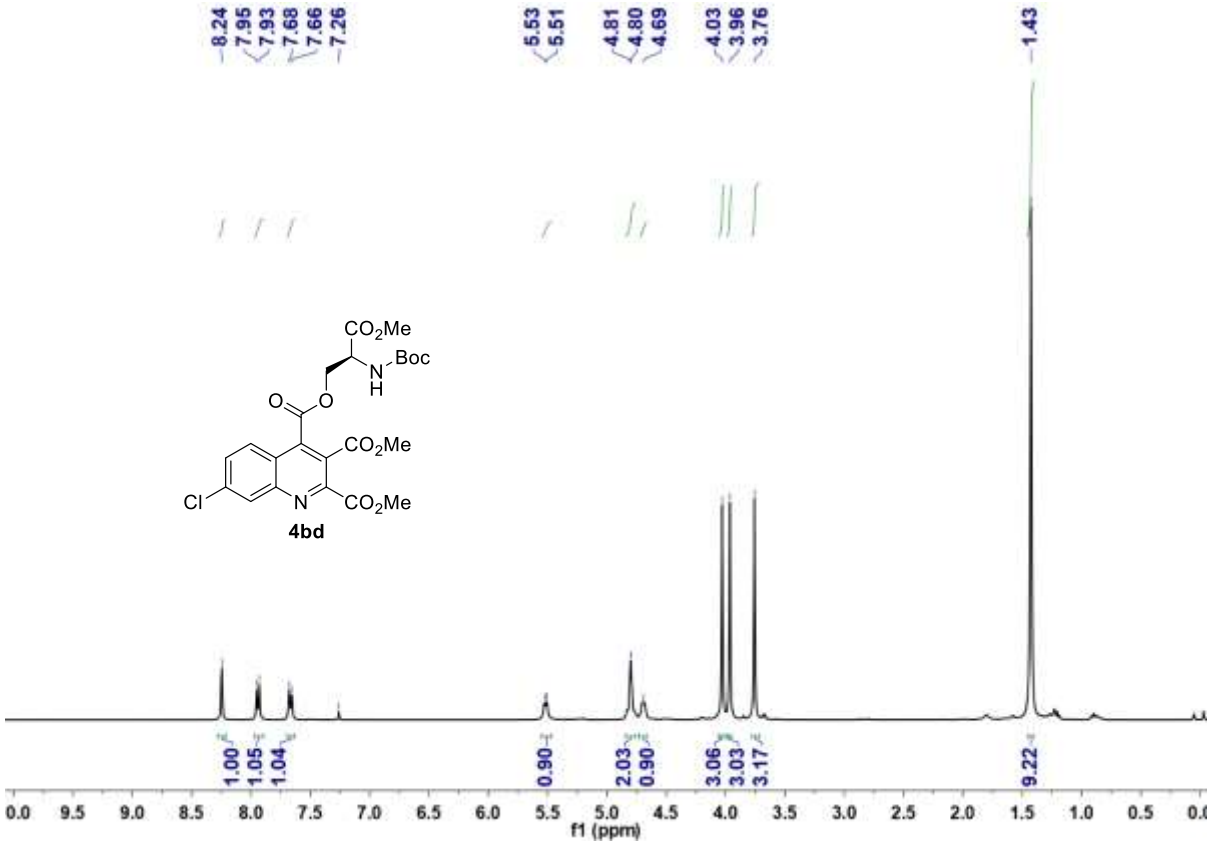
126.59
123.78
119.70
118.88
108.07
80.43
66.21
55.95
53.45
53.38
52.91
52.86
28.28
CO2Me
Boc
N
H
O
O
CO2Me
O
N
CO2Me
4bc
f1 (ppm)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7.26
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5.51
4.81
4.80
4.69
4.03
3.96
3.76
1.43
CO2Me
Boc
N
H
O
O
CO2Me
Cl
N
CO2Me
4bd
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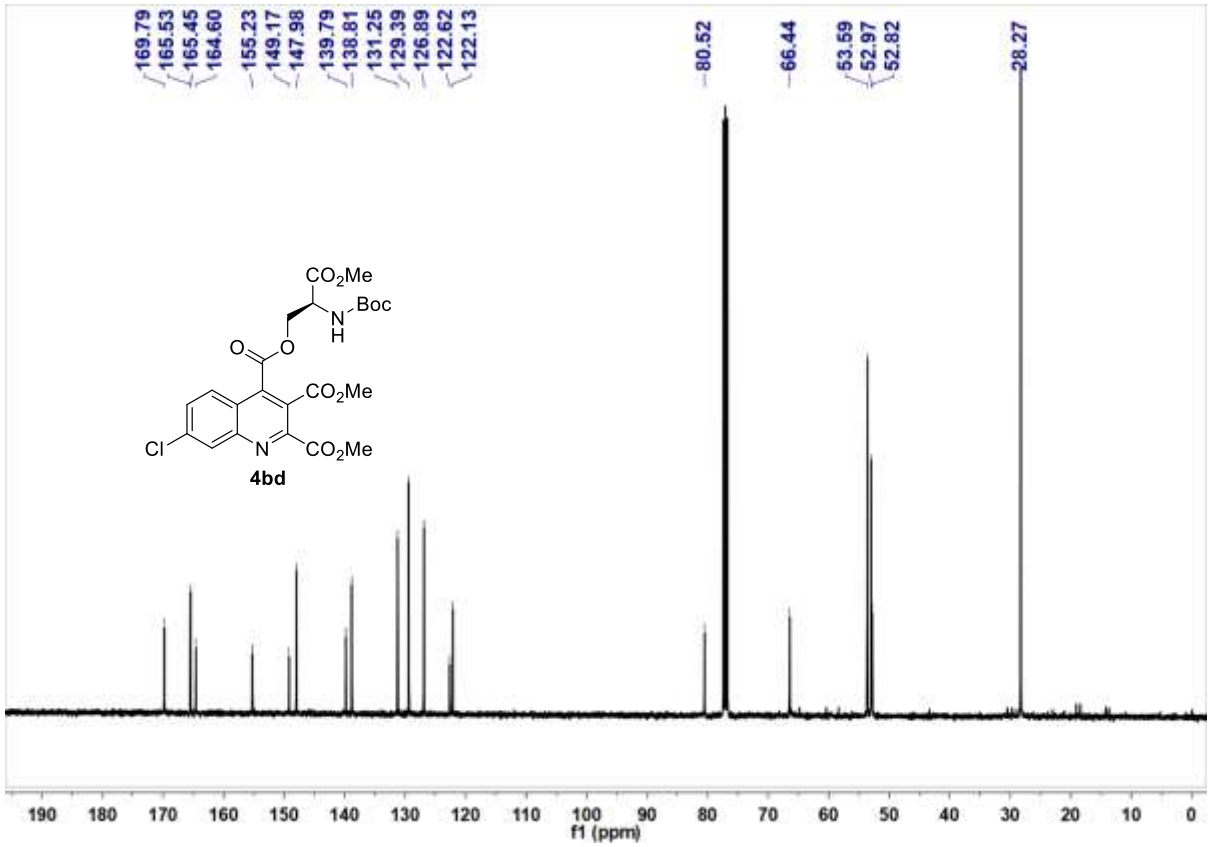
1.05
1.04
0.90
2.03
0.90
3.06
3.03
3.17
9.22
f1 (ppm)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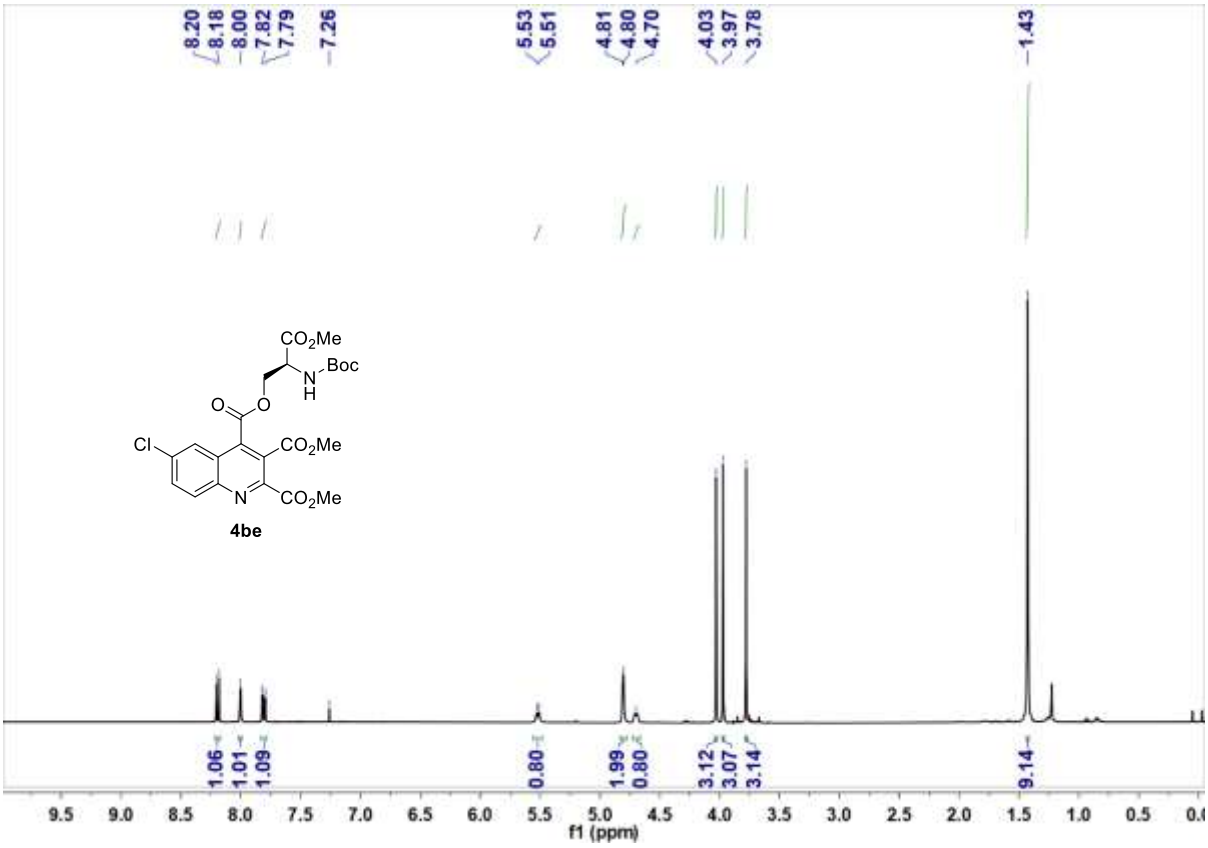
139.79
138.81
131.25
129.39
126.89
122.62
122.13
80.52
66.44
53.59
52.97
52.82
28.27
CO2Me
Boc
N
H
O
O
CO2Me
Cl
N
CO2Me
4bd
f1 (ppm)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7.26
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5.51
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4.80
4.70
4.03
3.97
3.78
1.43
CO2Me
Boc
N
H
O
O
Cl
CO2Me
N
CO2Me
4be
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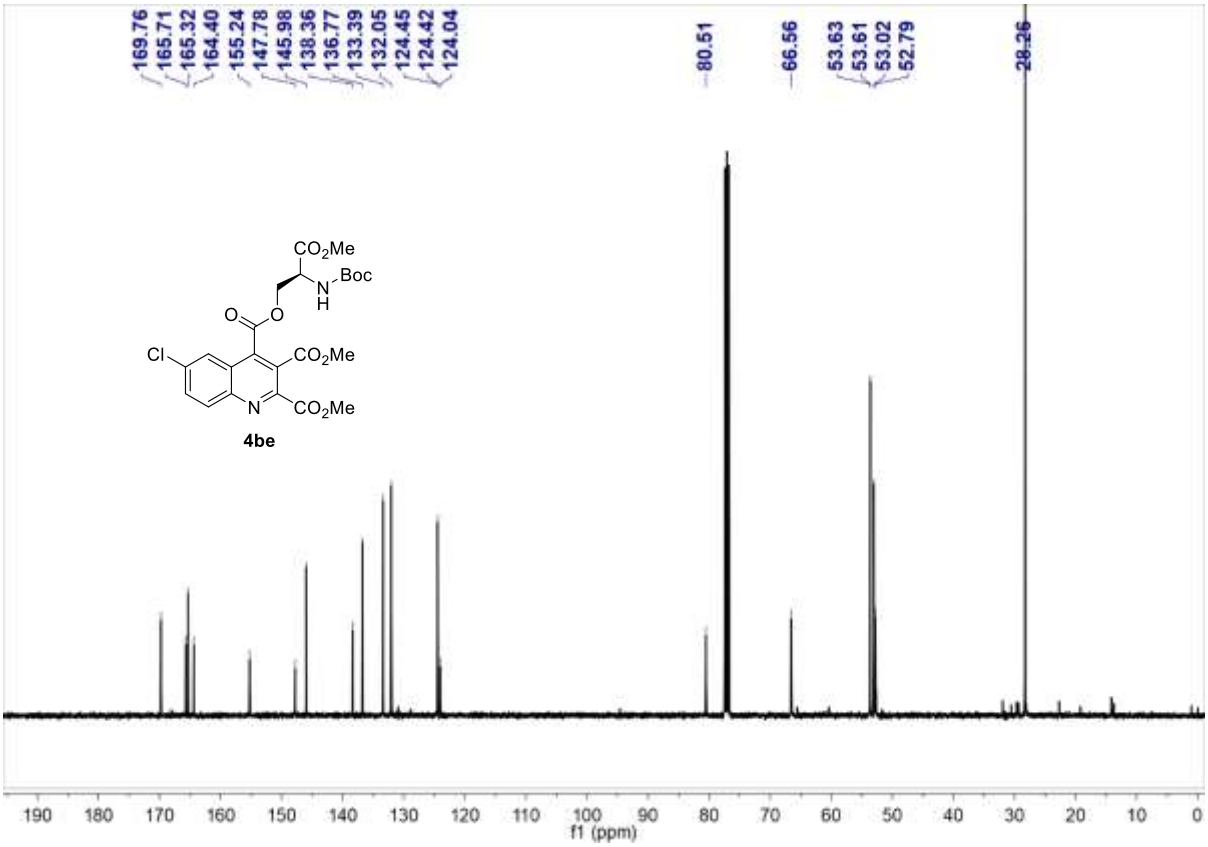
1.01
1.09
0.80
1.99
0.80
3.12
3.07
3.14
9.14
f1 (ppm)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124.42
124.04
80.51
66.56
53.63
53.61
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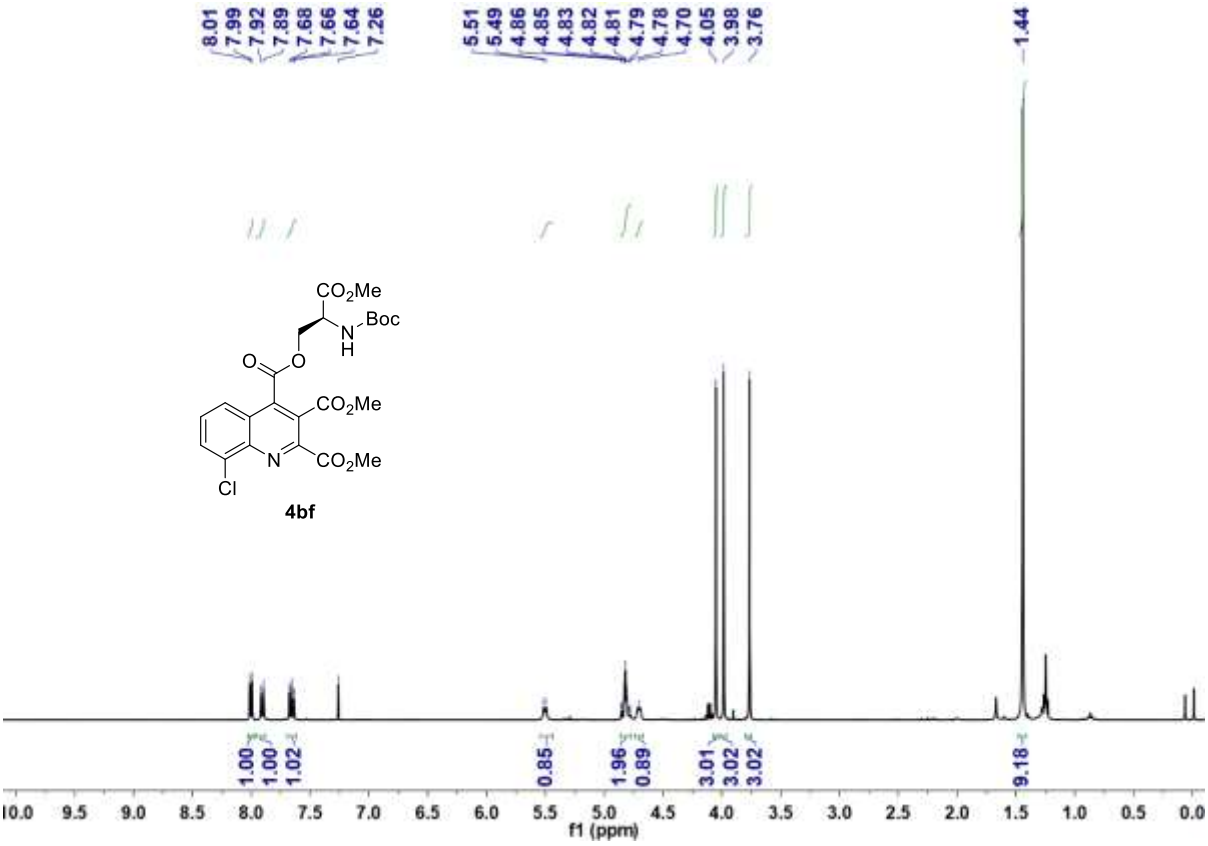
28.26
CO2Me
Boc
N
H
O
O
Cl
CO2Me
N
CO2Me
4be
f1 (ppm)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7.26
5.51
5.49
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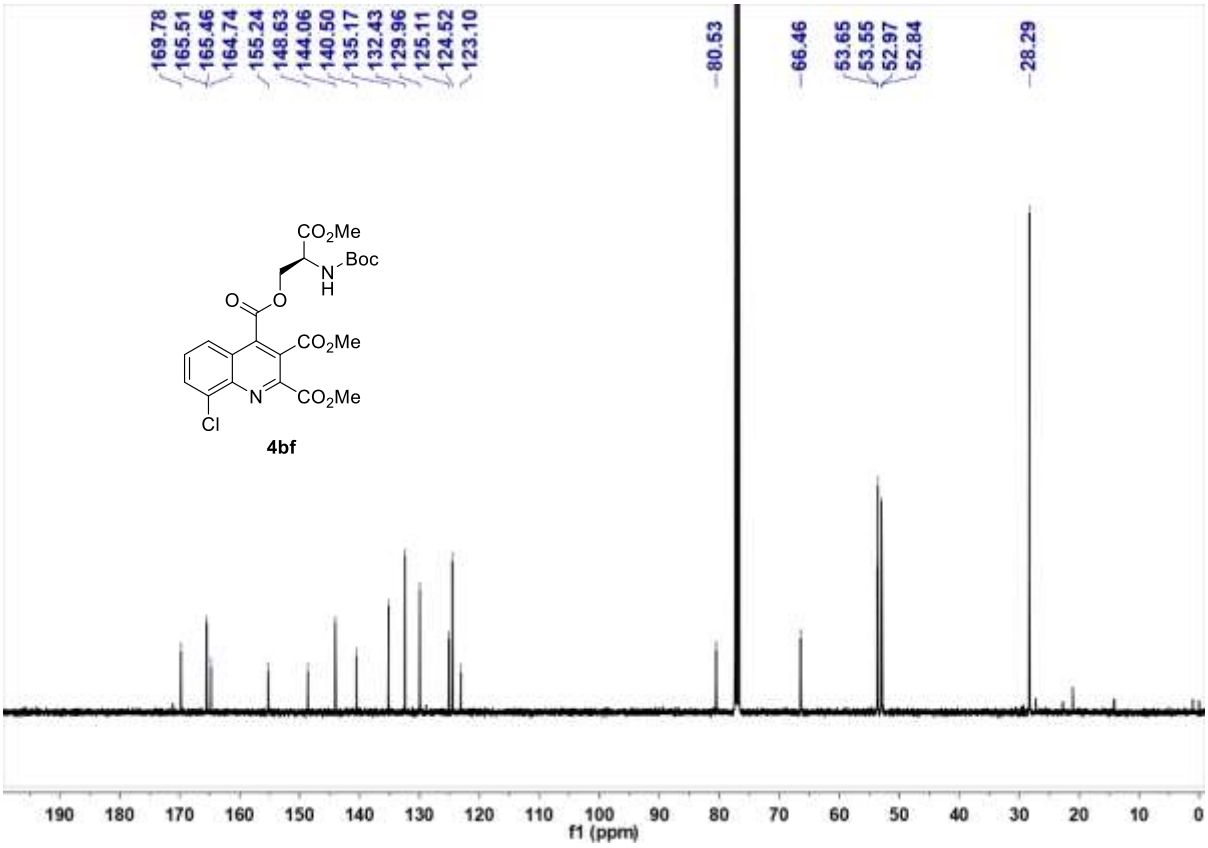
4.85
4.83
4.82
4.81
4.79
4.78
4.70
4.05
3.98
3.76
1.44
CO2Me
Boc
N
H
O
O
CO2Me
CO2Me
N
Cl
4bf
1.00
1.00
1.02
0.85
1.96
0.89
3.01
3.02
3.02
9.18
f1 (ppm)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132.43
129.96
125.11
124.52
123.10
80.53
66.46
53.65
53.55
52.97
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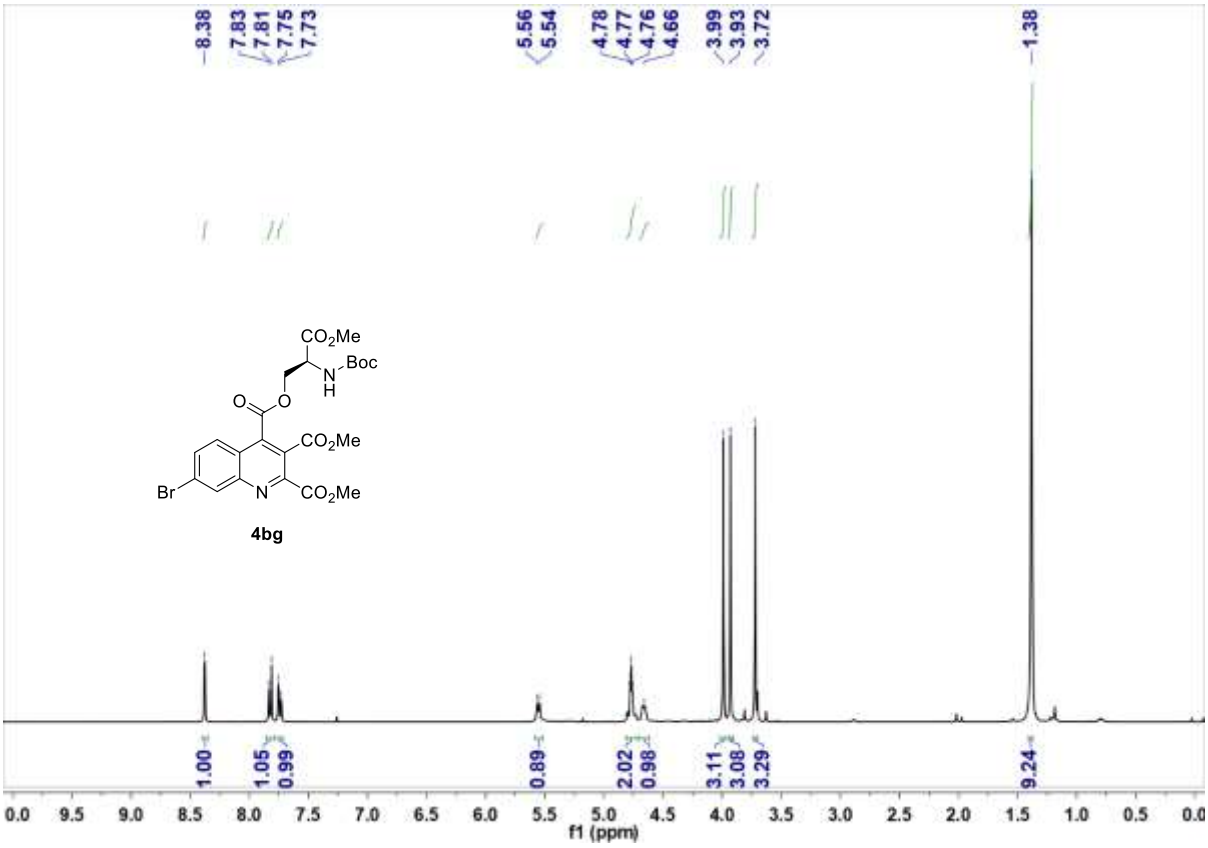
CO2Me
Boc
N
H
O
O
CO2Me
CO2Me
N
Cl
4bf
f1 (ppm)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4.77
4.76
4.66
3.99
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3.72
1.38
CO2Me
Boc
N
H
O
O
CO2Me
Br
N
CO2Me
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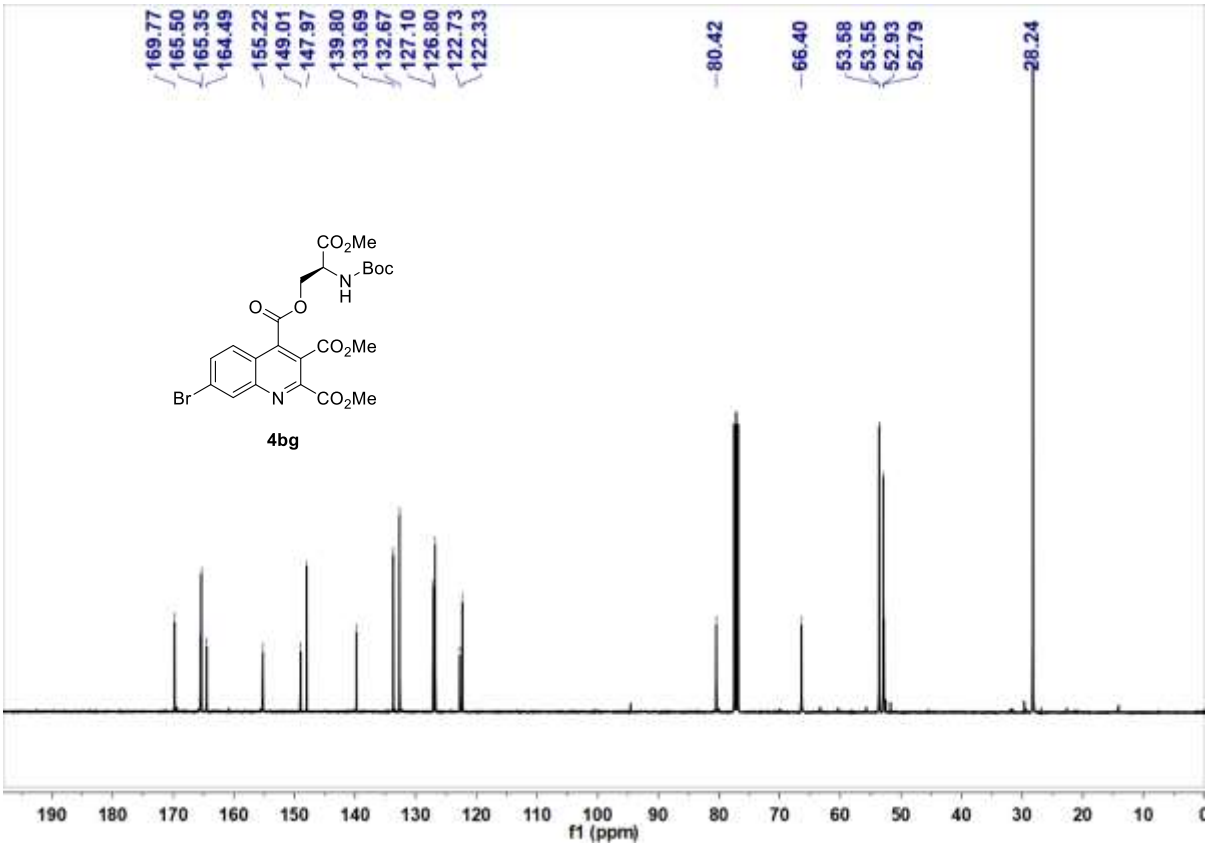
0.89
2.02
0.98
3.11
3.08
3.29
9.24
f1 (ppm)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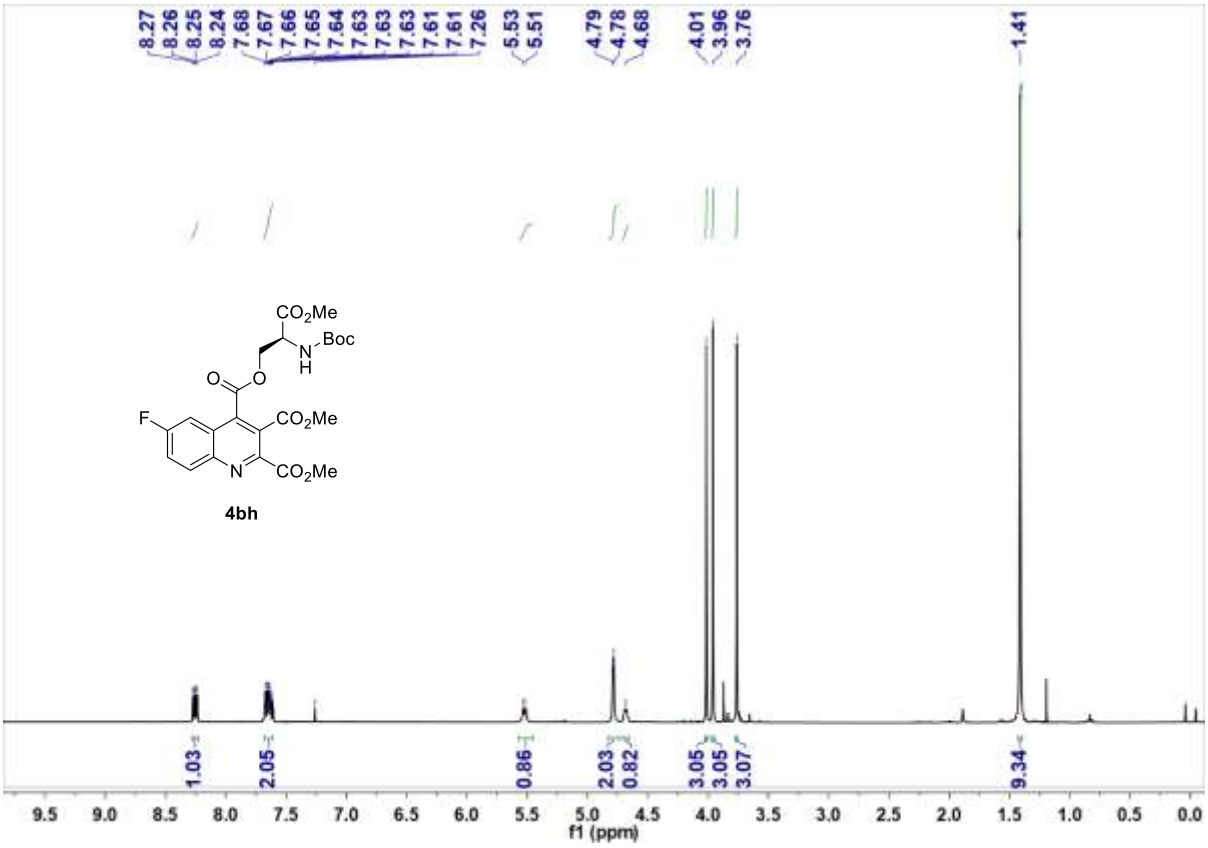
132.67
127.10
126.80
122.73
122.33
80.42
66.40
53.58
53.55
52.93
52.79
28.24
CO2Me
Boc
N
H
O
O
CO2Me
Br
N
CO2Me
4bg
f1 (ppm)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8.26
8.25
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7.68
7.67
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7.65
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7.63
7.63
7.63
7.61
7.61
7.26
5.53
5.51
4.79
4.78
4.68
4.01
3.96
3.76
1.41
CO2Me
Boc
N
H
O
O
F
CO2Me
N
CO2Me
4bh
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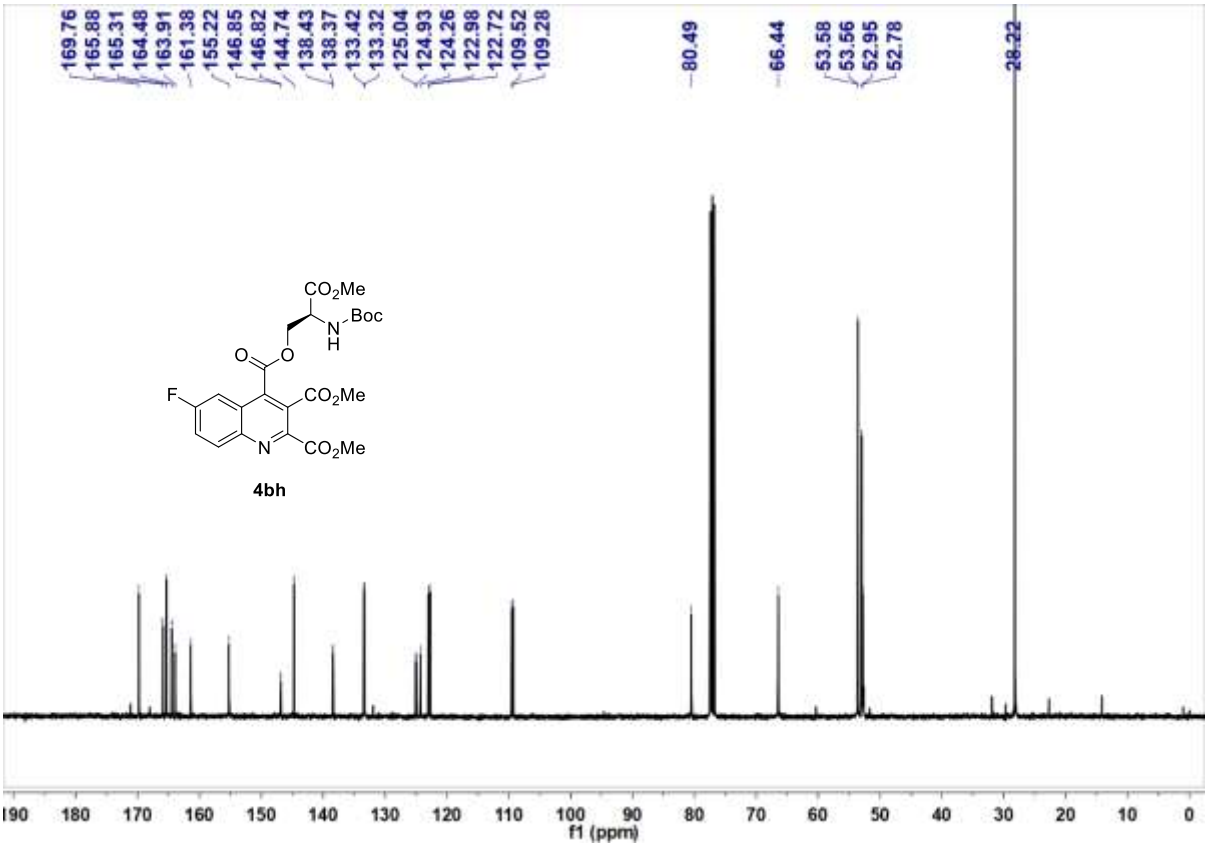
2.05
0.86
2.03
0.82
3.05
3.05
3.07
9.34
f1 (ppm)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161.38
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146.85
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144.74
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138.37
133.42
133.32
125.04
124.93
124.26
122.98
122.72
109.52
109.28
80.49
66.44
53.58
53.56
52.95
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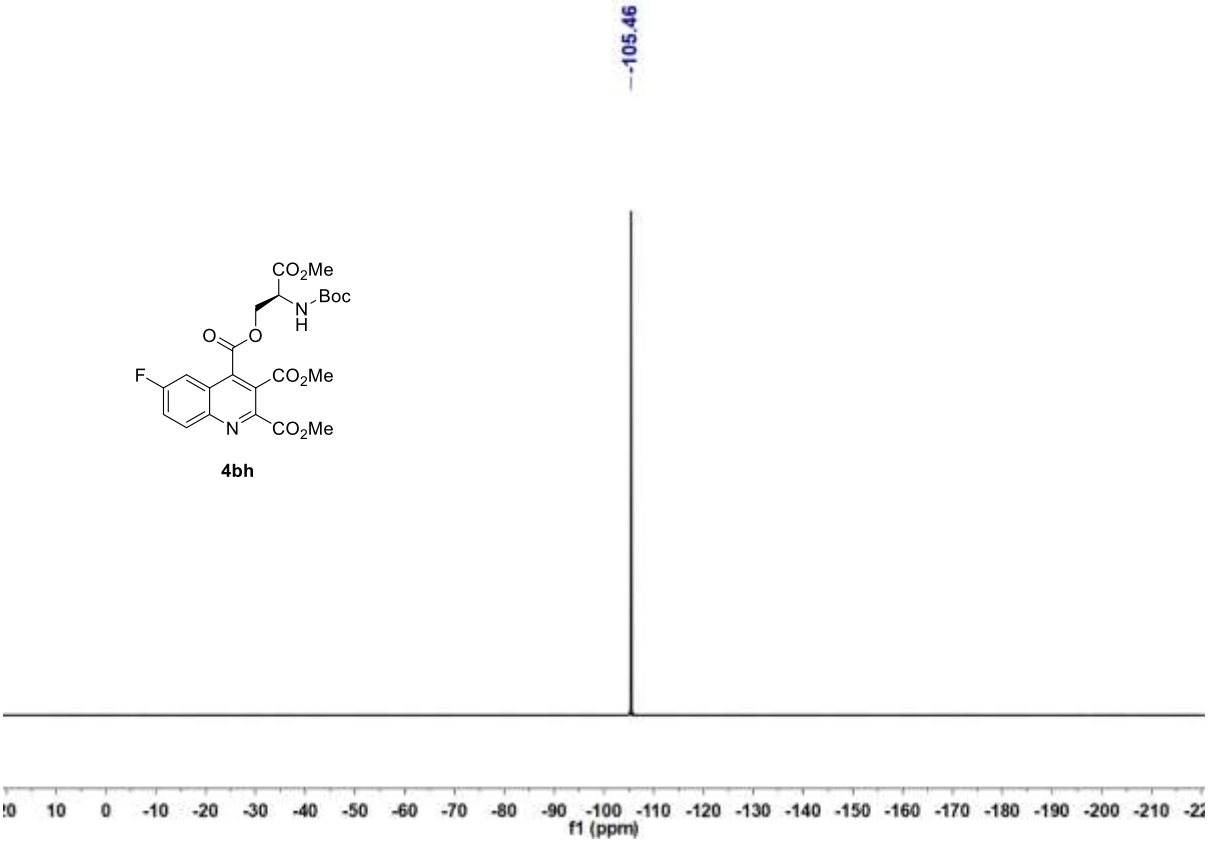
O
F
CO2Me
N
CO2Me
4bh
f1 (ppm)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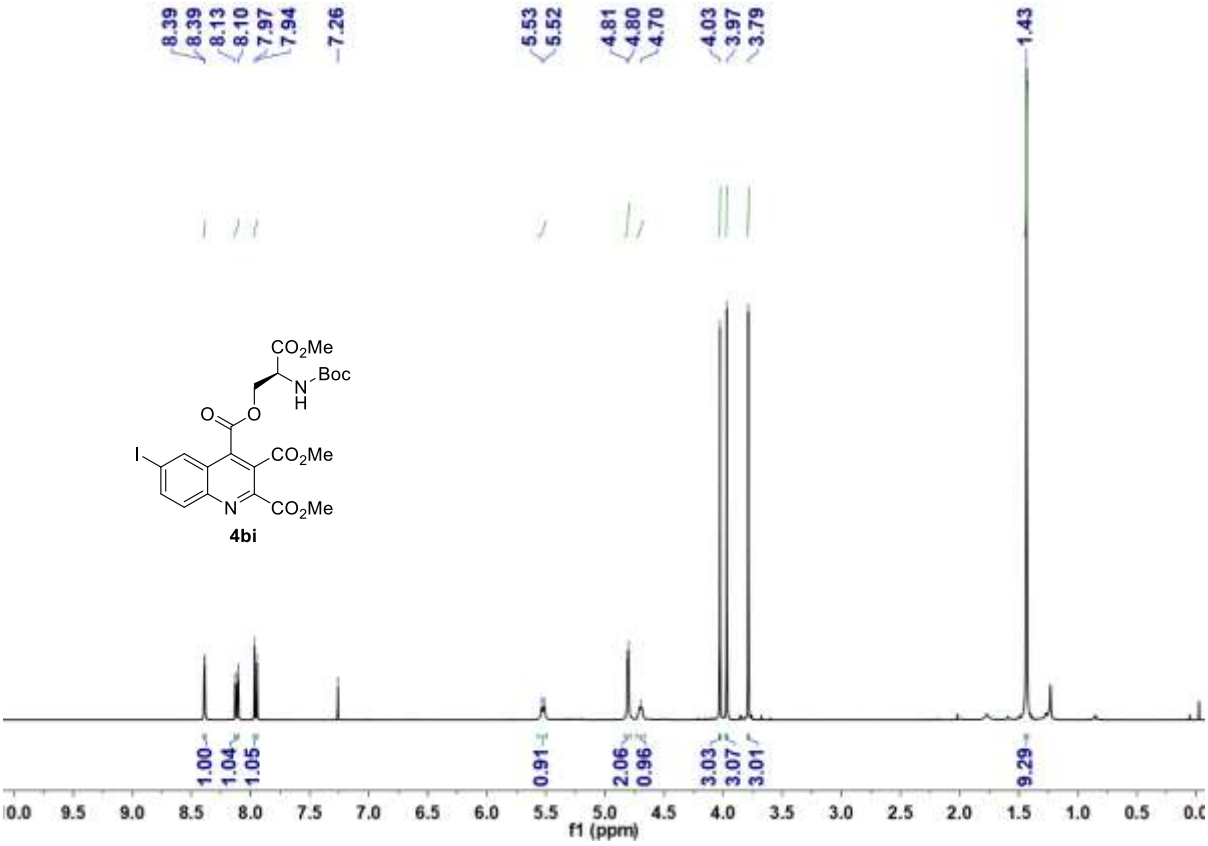
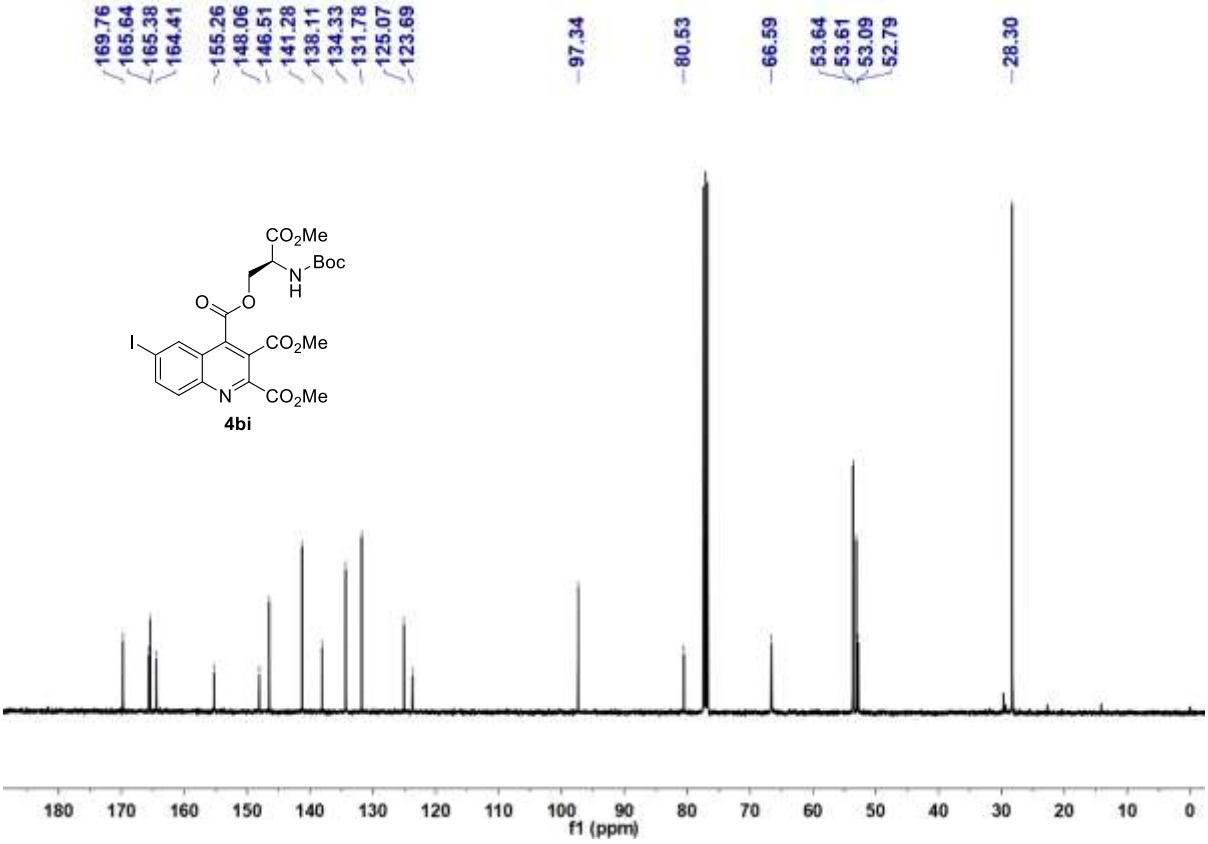
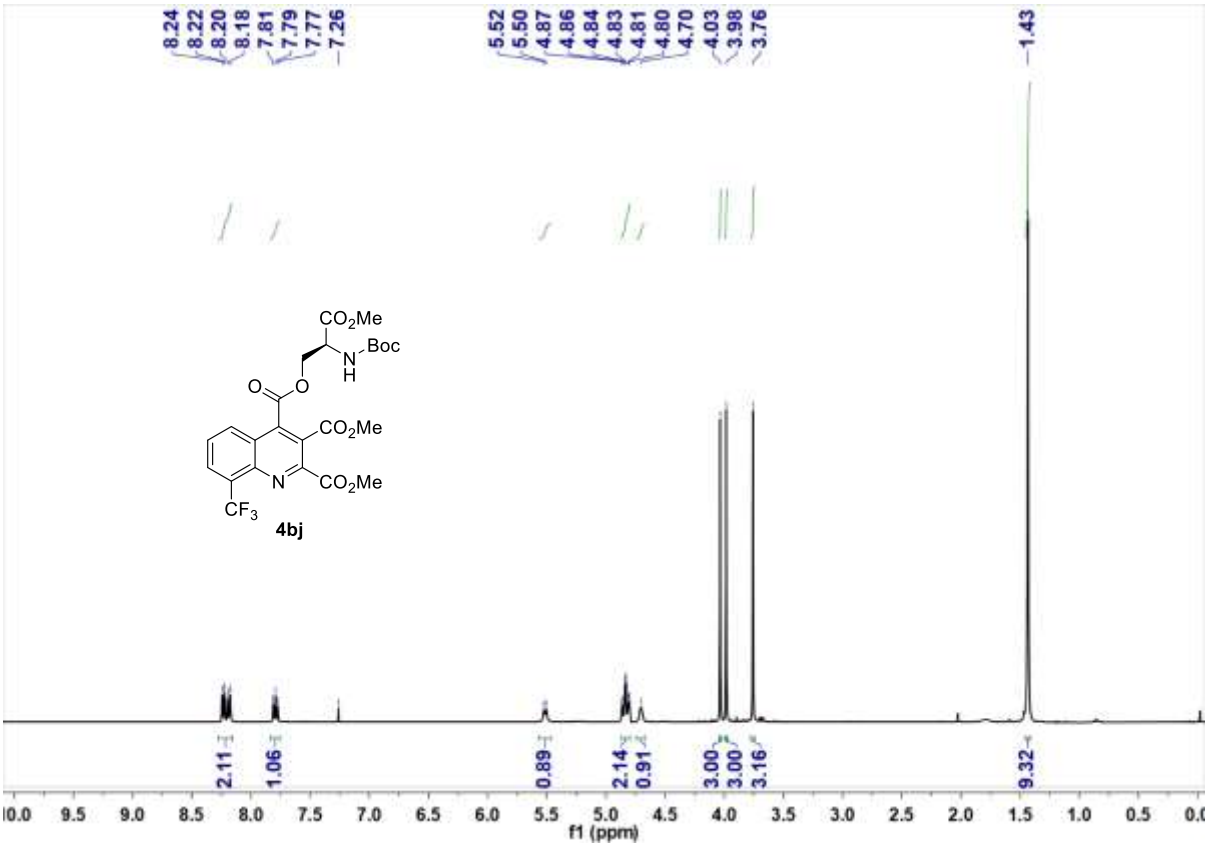
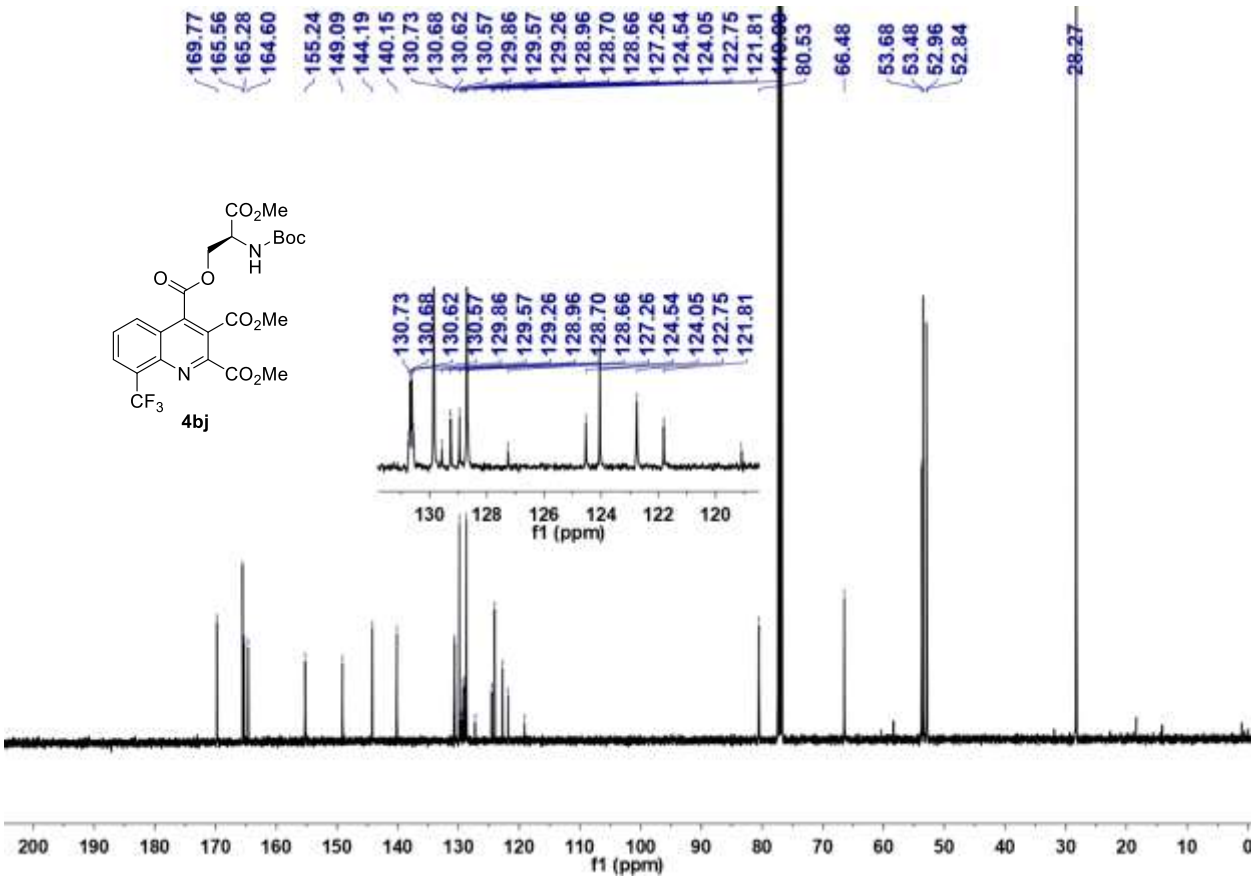
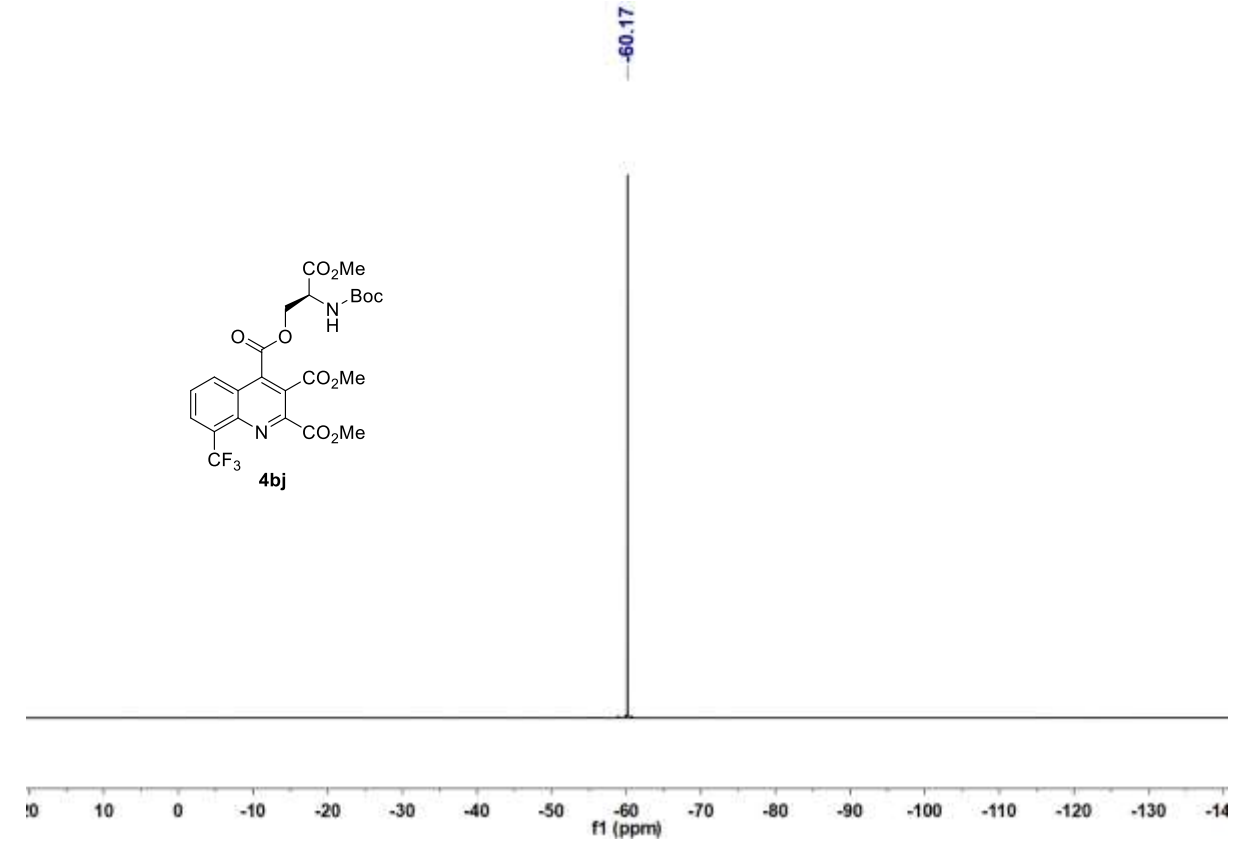
CO2Me
Boc
N
H
O
O
F
CO2Me
N
CO2Me
4bh
f1 (ppm)

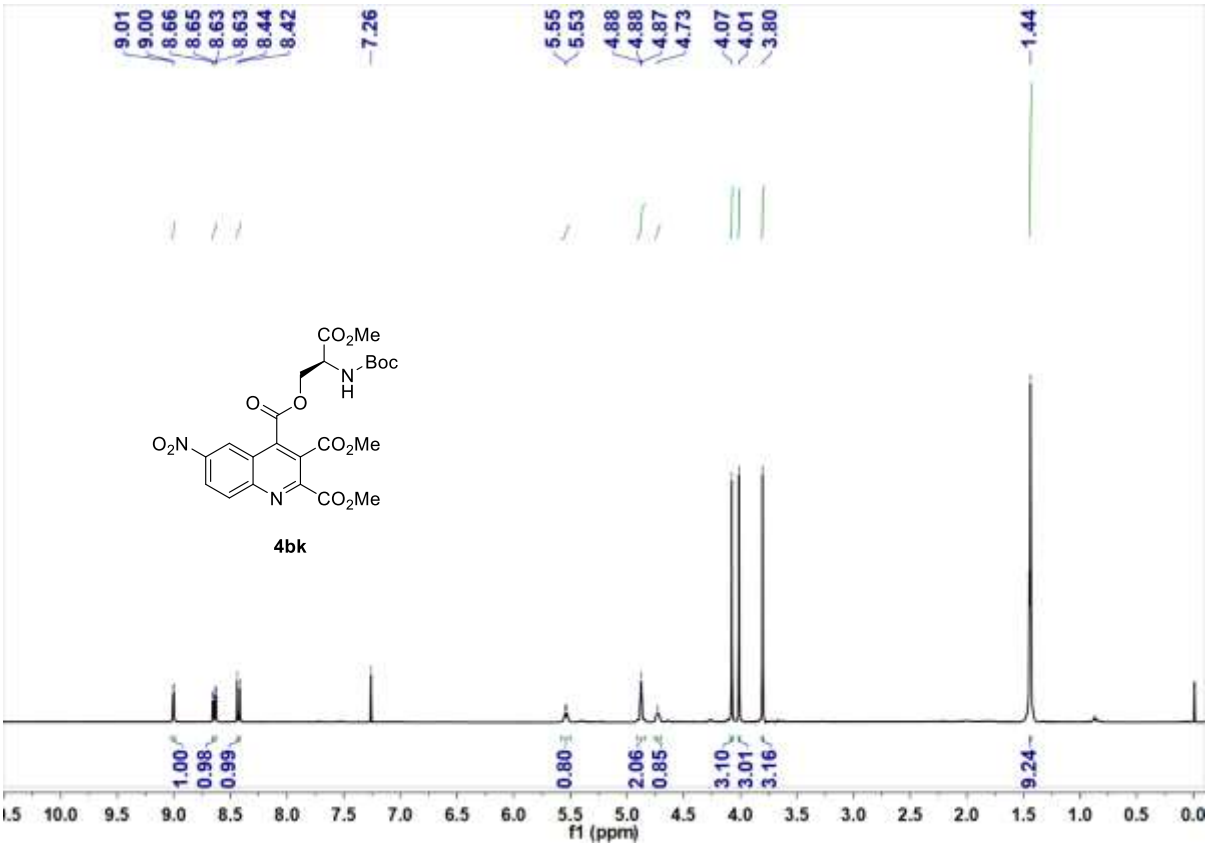

8.39
8.39
8.13
8.10
7.97
7.94
7.26
5.53
5.52
4.81
4.80
4.70
4.03
3.97
3.79
1.43
CO2Me
Boc
N
H
O
O
I
CO2Me
N
CO2Me
4bi
1.00
1.04
1.05
0.91
2.06
0.96
3.03
3.07
3.01
9.29
f1 (ppm)


169.76
165.64
165.38
164.41
155.26
148.06
146.51
141.28
138.11
134.33
131.78
125.07
123.69
97.34
80.53
66.59
53.64
53.61
53.09
52.79
28.30
CO2Me
Boc
N
H
O
O
CO2Me
I
CO2Me
N
CO2Me
4bi
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

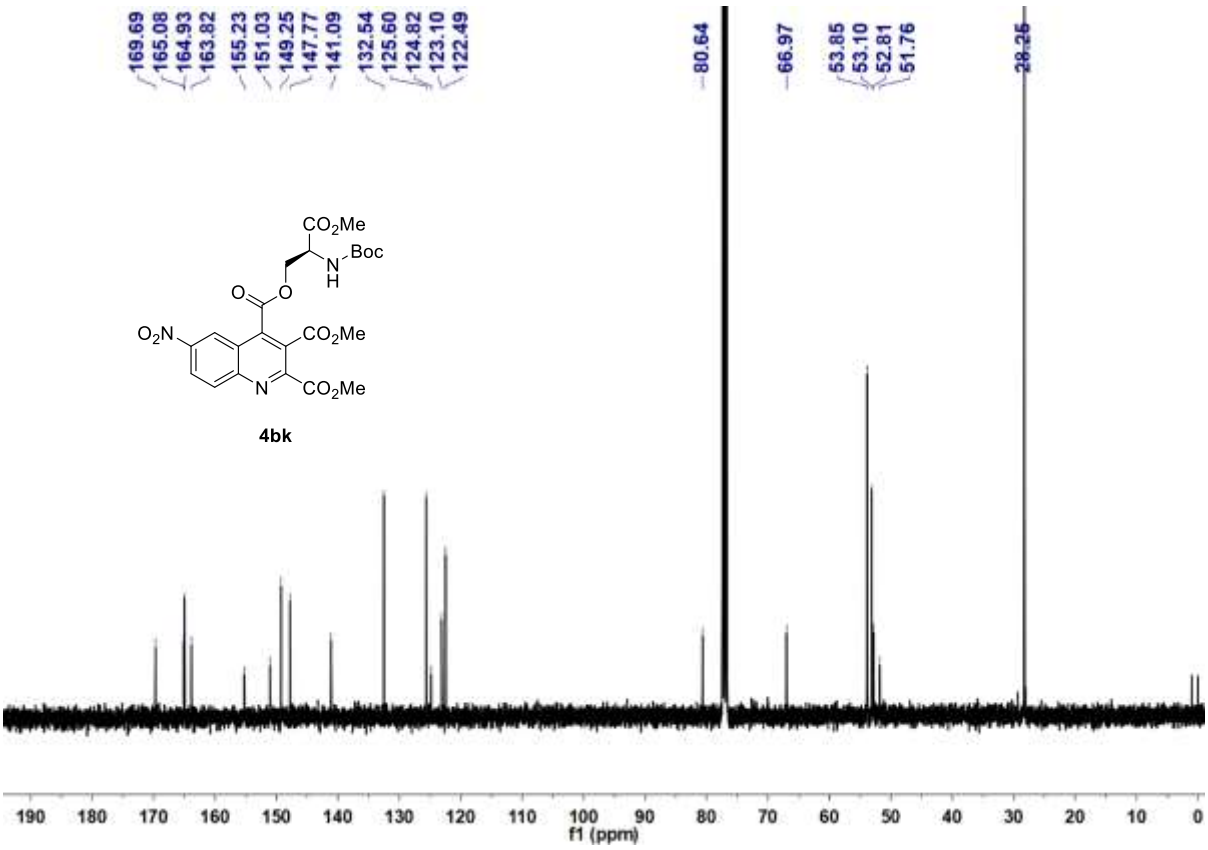

8.24
8.22
8.20
8.18
7.81
7.79
7.77
7.26
5.52
5.50
4.87
4.86
4.84
4.83
4.81
4.80
4.70
4.03
3.98
3.76
1.43
CO2Me
Boc
N
H
O
O
CO2Me
CO2Me
N
CO2Me
CF3
4bj
2.11
1.06
0.89
2.14
0.91
3.00
3.00
3.16
9.32
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


169.77
165.56
165.28
164.60
155.24
149.09
144.19
140.15
130.73
130.68
130.62
130.57
129.86
129.57
129.26
128.96
128.70
128.66
127.26
124.54
124.05
122.75
121.81
110.00
80.53
66.48
53.68
53.48
52.96
52.84
28.27
CO2Me
Boc
N
H
O
O
CO2Me
CO2Me
N
CF3
4bj
f1 (ppm)

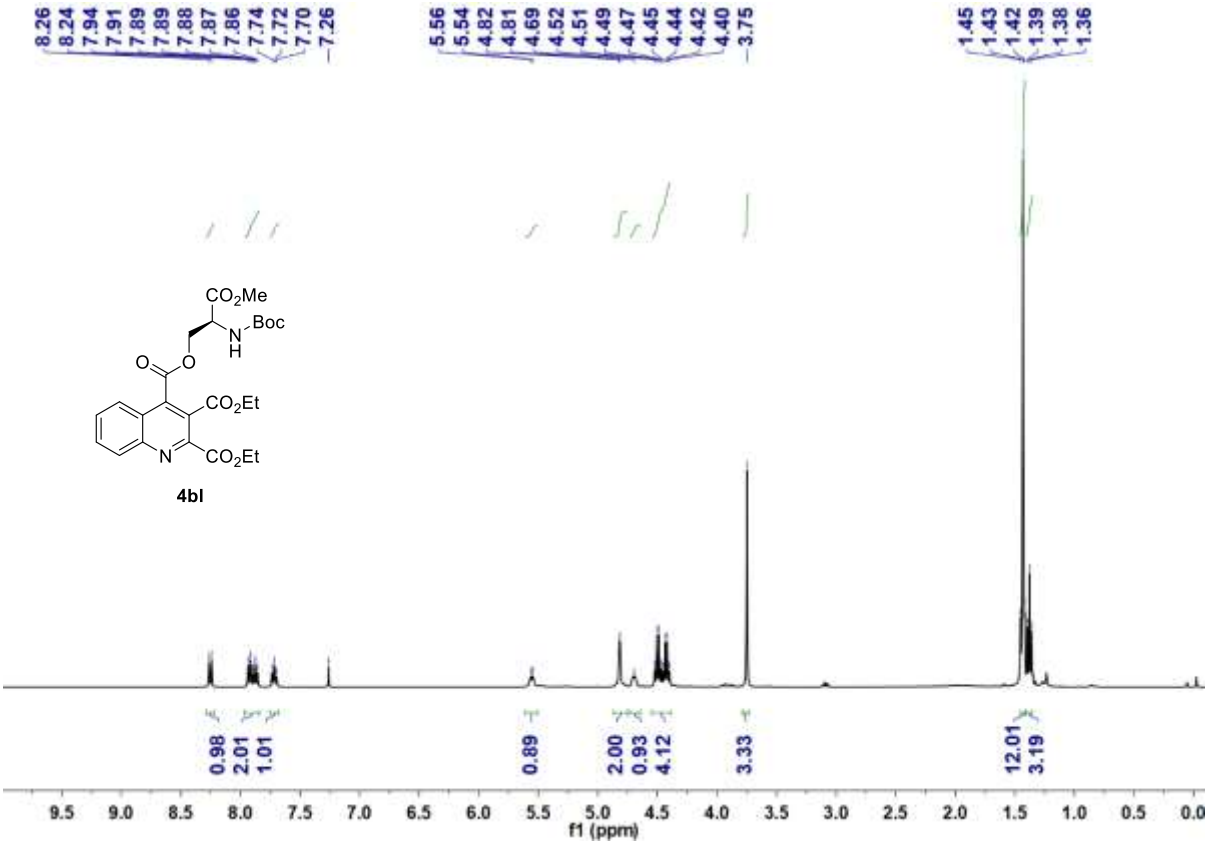

-60.17
CO2Me
Boc
N
H
O
O
CO2Me
CO2Me
N
CF3
4bj
f1 (ppm)


9.01
9.00
8.66
8.65
8.63
8.63
8.44
8.42
7.26
5.55
5.53
4.88
4.88
4.87
4.73
4.07
4.01
3.80
1.44
CO2Me
Boc
N
H
O
O
O2N
CO2Me
CO2Me
N
CO2Me
1.00
0.98
0.99
0.80
2.06
0.85
3.10
3.01
3.16
9.24
f1 (ppm)

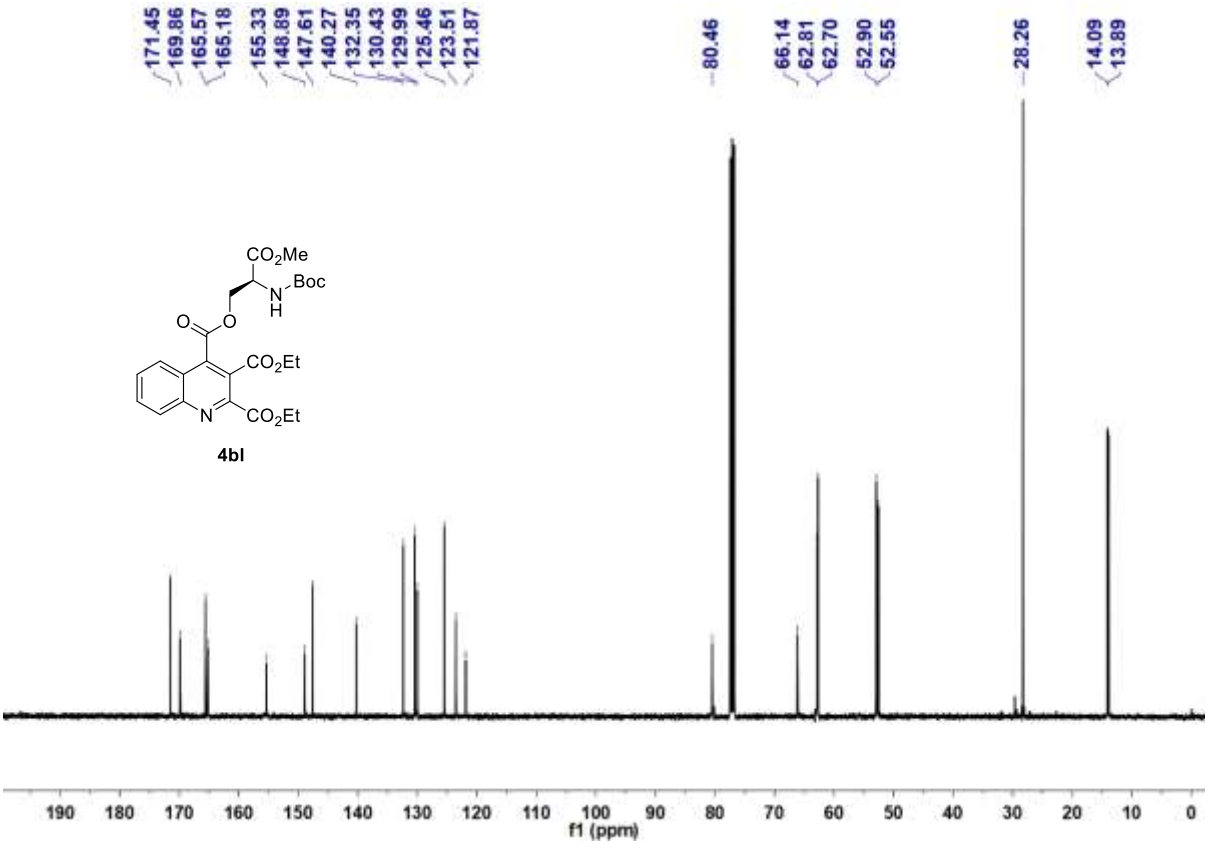
4bk


169.69
165.08
164.93
163.82
155.23
151.03
149.25
147.77
141.09
132.54
125.60
124.82
123.10
122.49
80.64
66.97
53.85
53.10
52.81
51.76
28.25
CO2Me
Boc
N
H
O
O
O2N
CO2Me
CO2Me
N
CO2Me
f1 (ppm)

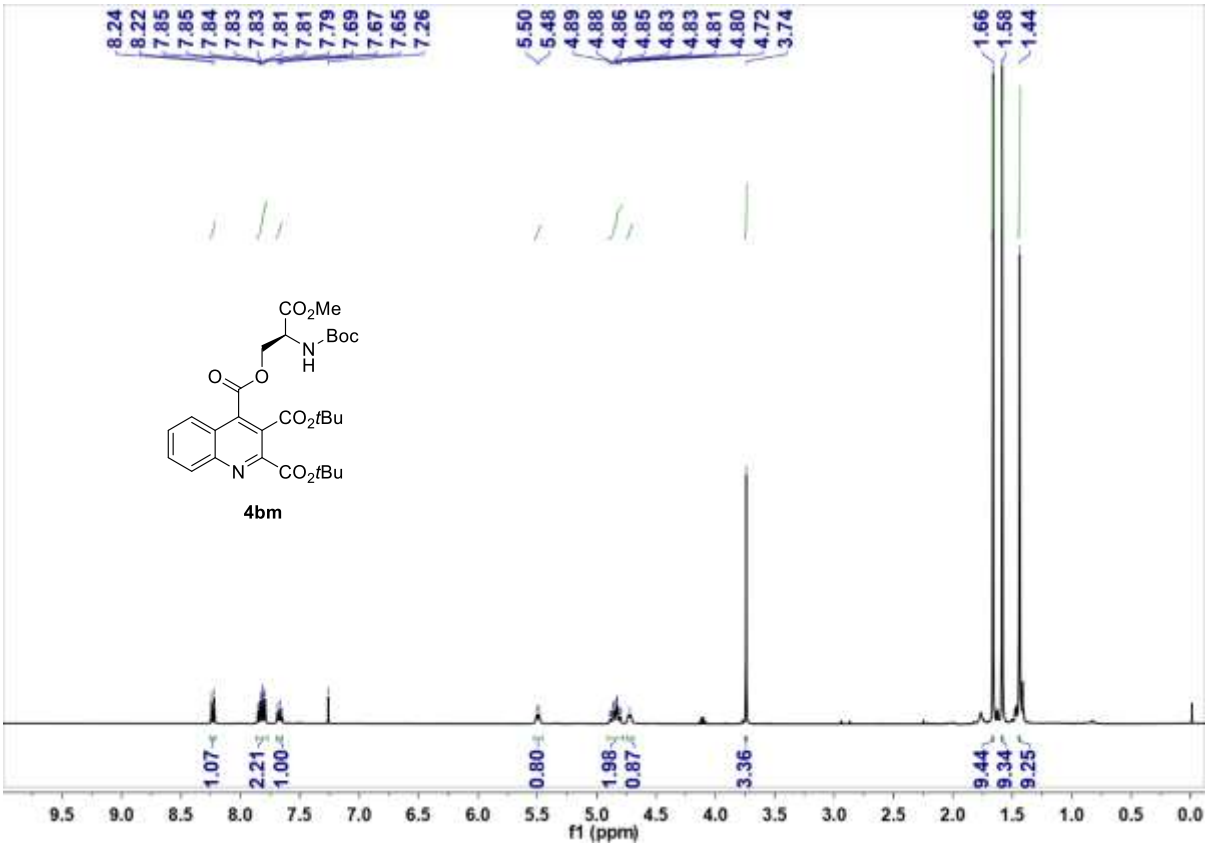
4bk

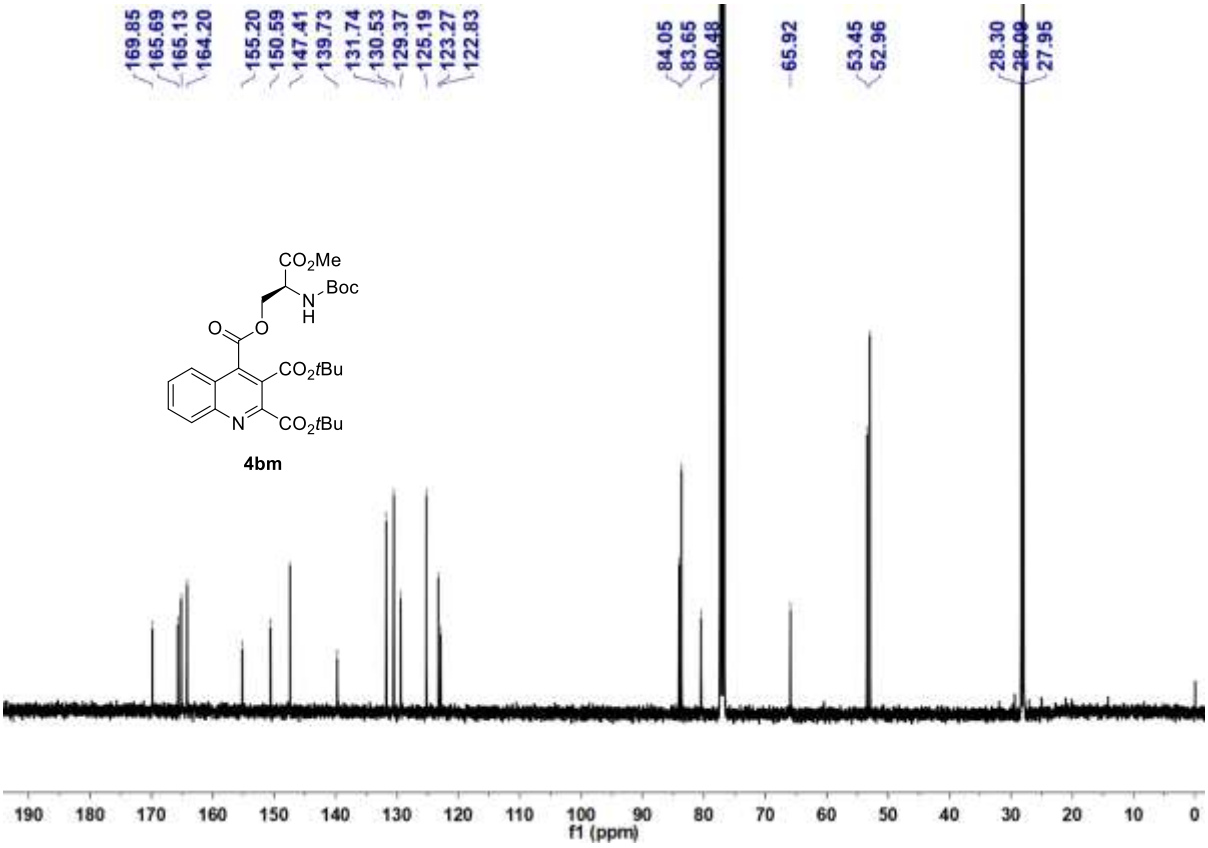

8.26
8.24
7.94
7.91
7.89
7.89
7.88
7.87
7.86
7.74
7.72
7.70
7.26
5.56
5.54
4.82
4.81
4.69
4.52
4.51
4.49
4.47
4.45
4.44
4.42
4.40
3.75
1.45
1.43
1.42
1.39
1.38
1.36
CO2Me
Boc
N
H
O
O
CO2Et
N
CO2Et
0.98
2.01
1.01
0.89
2.00
0.93
4.12
3.33
12.01
3.19
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

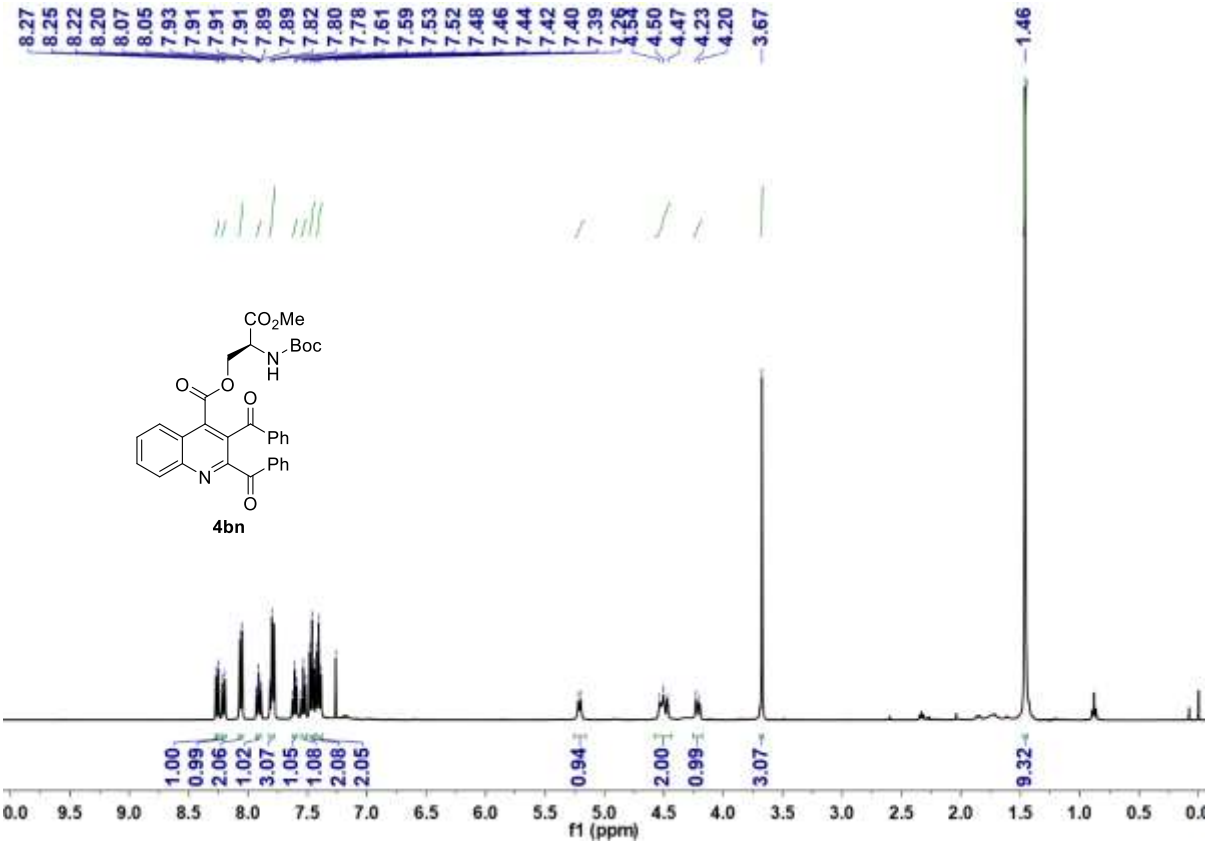
4bl

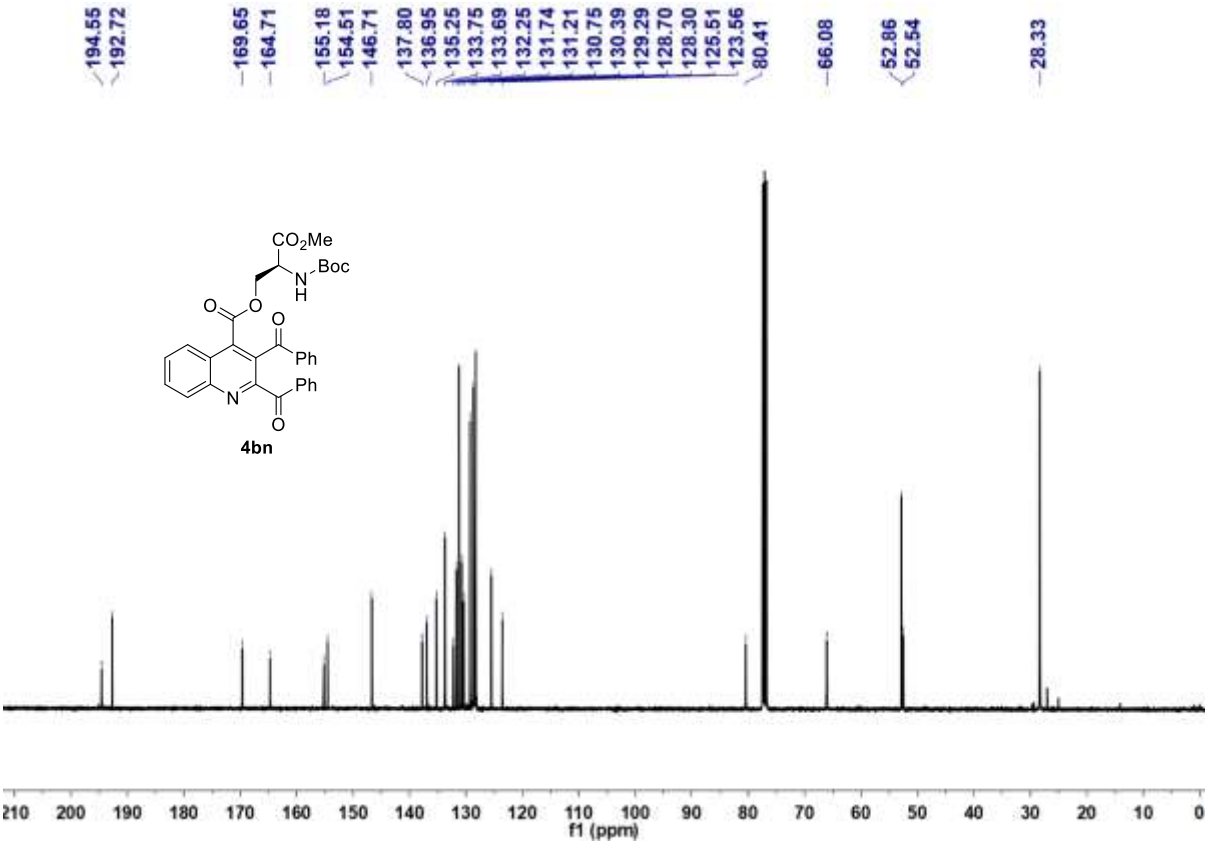

171.45
169.86
165.57
165.18
155.33
148.89
147.61
140.27
132.35
130.43
129.99
125.46
123.51
121.87
80.46
66.14
62.81
62.70
52.90
52.55
28.26
14.09
13.89
CO2Me
Boc
N
H
O
O
CO2Et
N
CO2Et
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

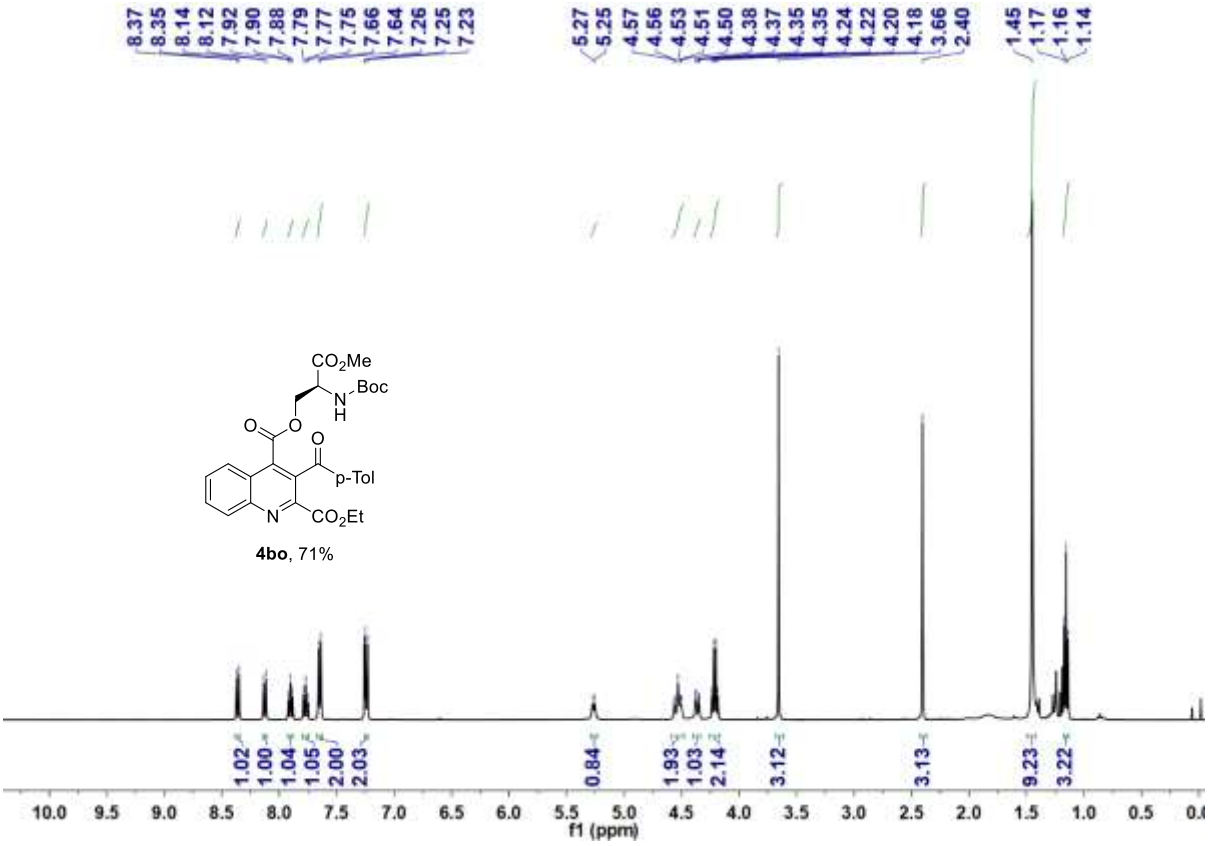
4bl

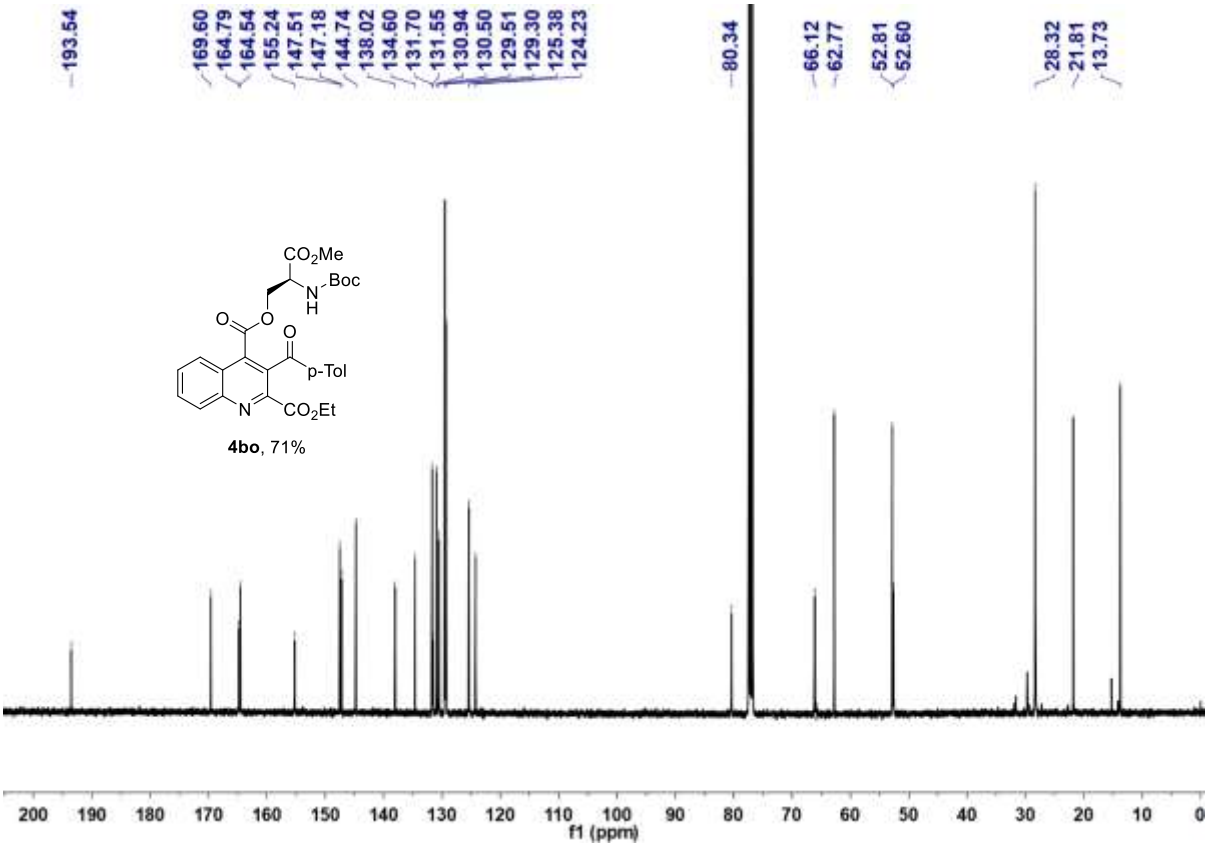

8.24
8.22
7.85
7.85
7.84
7.83
7.83
7.81
7.81
7.79
7.69
7.67
7.65
7.26
5.50
5.48
4.89
4.88
4.86
4.85
4.83
4.83
4.81
4.80
4.72
3.74
1.66
1.58
1.44
CO2Me
Boc
N
H
O
O
CO2tBu
CO2tBu
N
4bm
1.07
2.21
1.00
0.80
1.98
0.87
3.36
9.44
9.34
9.25
f1 (ppm)

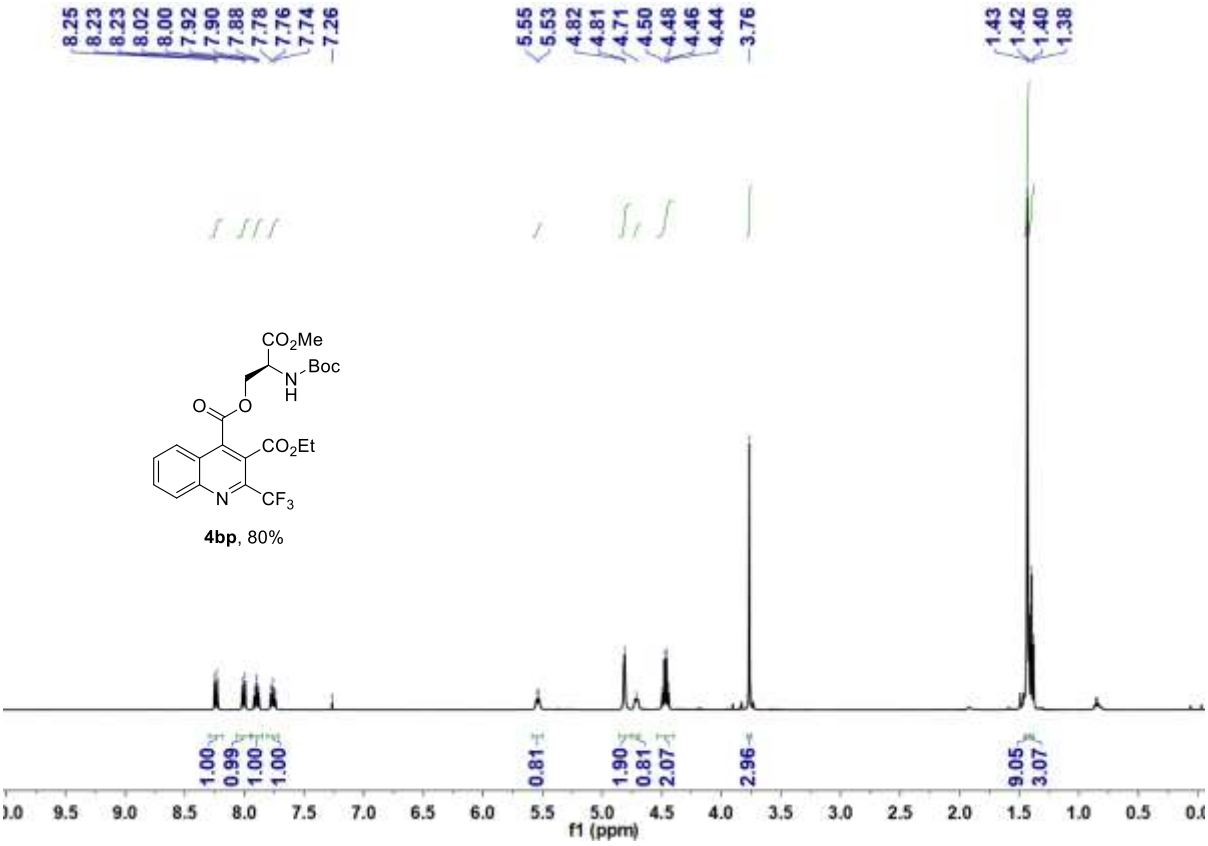

169.85
165.69
165.13
164.20
155.20
150.59
147.41
139.73
131.74
130.53
129.37
125.19
123.27
122.83
84.05
83.65
80.48
65.92
53.45
52.96
28.30
28.09
27.95
CO2Me
Boc
N
H
O
O
CO2tBu
CO2tBu
N
4bm
f1 (ppm)


8.27
8.25
8.22
8.20
8.07
8.05
7.93
7.91
7.91
7.91
7.89
7.89
7.82
7.80
7.78
7.61
7.59
7.53
7.52
7.48
7.46
7.44
7.42
7.40
7.39
4.50
4.47
4.23
4.20
3.67
1.46
1.00
0.99
2.06
1.02
3.07
1.05
1.08
2.08
2.05
0.94
2.00
0.99
3.07
9.32
f1 (ppm)
CO2Me
Boc
N
H
O
Ph
Ph
N
4bn

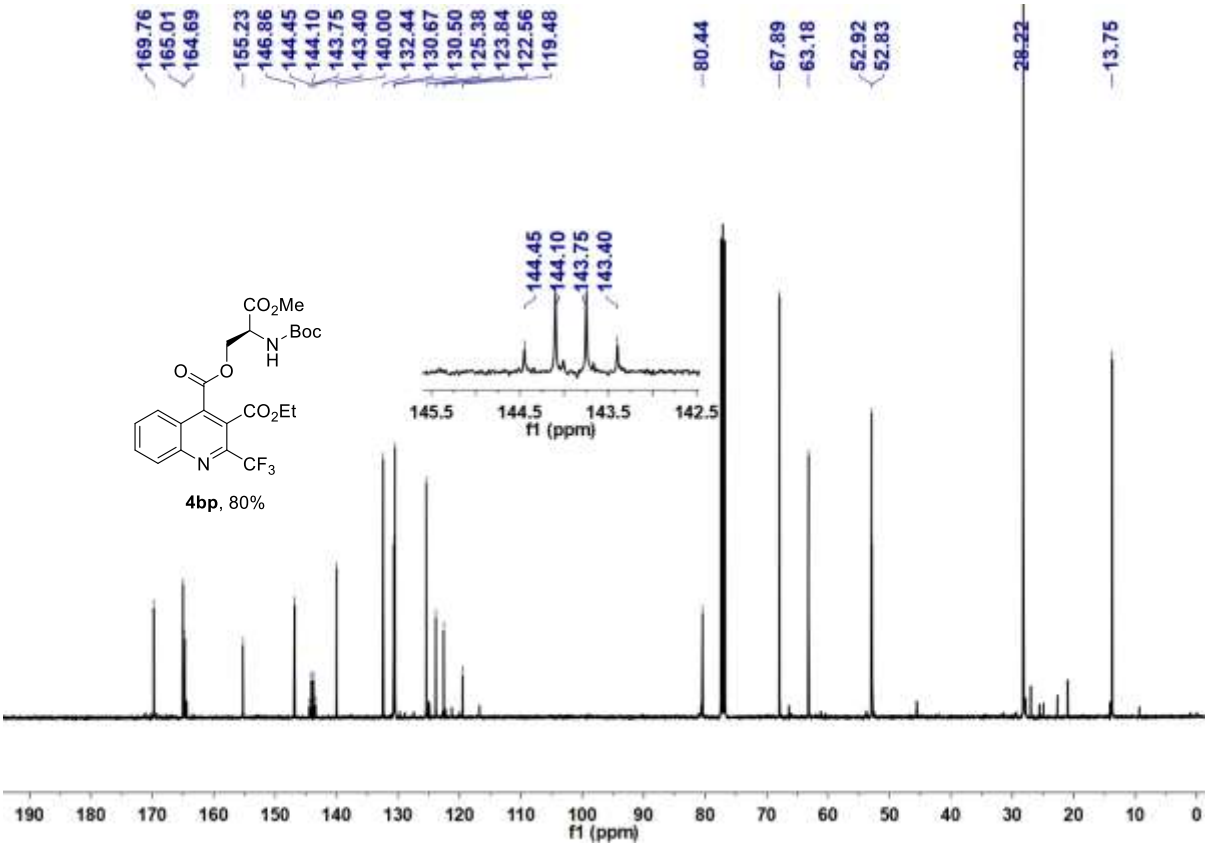

194.55
192.72
169.65
164.71
155.18
154.51
146.71
137.80
136.95
135.25
133.75
133.69
132.25
131.74
131.21
130.75
130.39
129.29
128.70
128.30
125.51
123.56
80.41
66.08
52.86
52.54
28.33
f1 (ppm)
CO2Me
Boc
N
H
O
Ph
Ph
N
4bn


8.37
8.35
8.14
8.12
7.92
7.90
7.88
7.79
7.77
7.75
7.66
7.64
7.26
7.25
7.23
5.27
5.25
4.57
4.56
4.53
4.51
4.50
4.38
4.37
4.35
4.35
4.24
4.22
4.20
4.18
3.66
2.40
1.45
1.17
1.16
1.14
CO2Me
Boc
N
H
O
O
O
p-Tol
N
CO2Et
4bo, 71%
1.02
1.00
1.04
1.05
2.00
2.03
0.84
1.93
1.03
2.14
3.12
3.13
9.23
3.22
f1 (ppm)

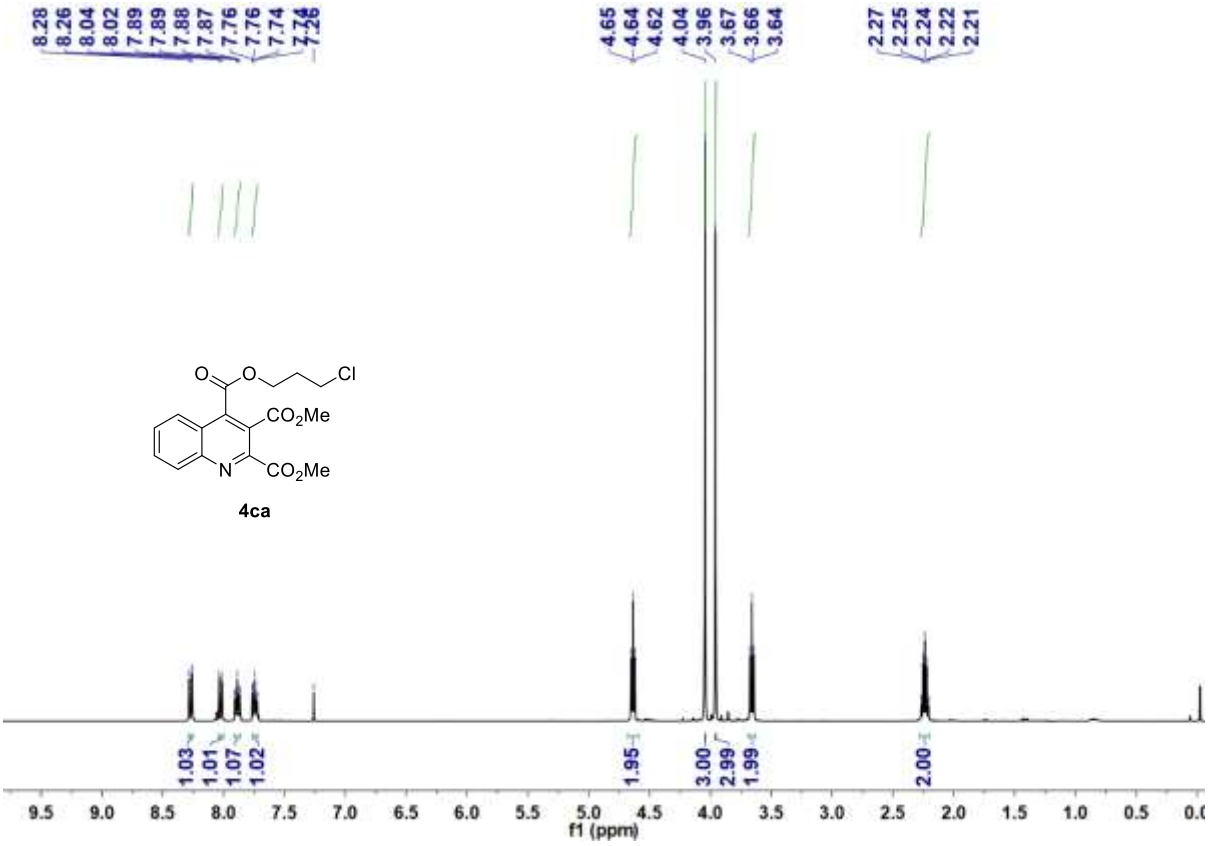

193.54
169.60
164.79
164.54
155.24
147.51
147.18
144.74
138.02
134.60
131.70
131.55
130.94
130.50
129.51
129.30
125.38
124.23
80.34
66.12
62.77
52.81
52.60
28.32
21.81
13.73
CO2Me
Boc
N
H
O
O
O
p-Tol
N
CO2Et
4bo, 71%
f1 (ppm)


8.25
8.23
8.23
8.02
8.00
7.92
7.90
7.88
7.78
7.76
7.74
7.26
5.55
5.53
4.82
4.81
4.71
4.50
4.48
4.46
4.44
3.76
1.43
1.42
1.40
1.38
CO2Me
Boc
N
H
O
O
CO2Et
N
CF3
1.00
0.99
1.00
1.00
0.81
1.90
0.81
2.07
2.96
9.05
3.07
f1 (ppm)

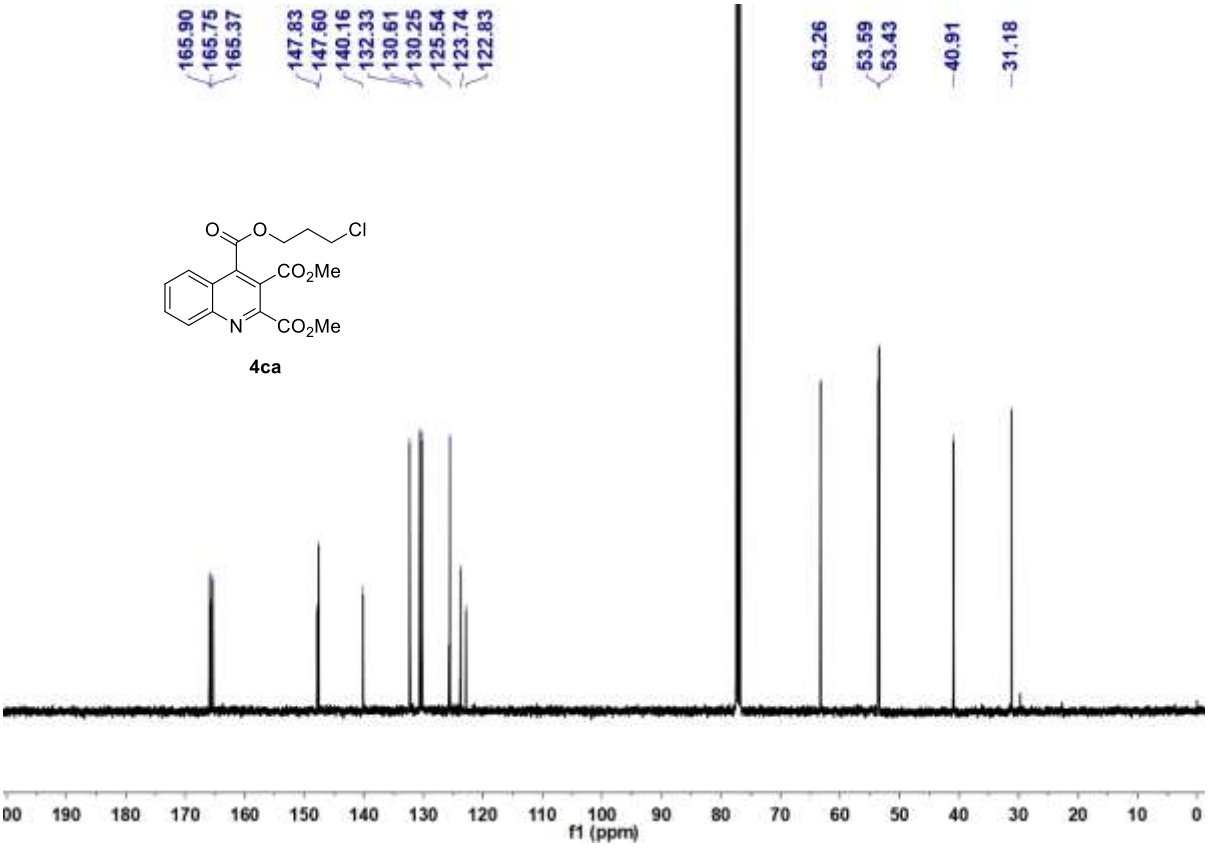
4bp, 80%


169.76
165.01
164.69
155.23
146.86
144.45
144.10
143.75
143.40
140.00
132.44
130.67
130.50
125.38
123.84
122.56
119.48
80.44
67.89
63.18
52.92
52.83
28.22
13.75
144.45
144.10
143.75
143.40
145.5
144.5
143.5
142.5
f1 (ppm)
CO2Me
Boc
N
H
O
O
CO2Et
N
CF3
f1 (ppm)

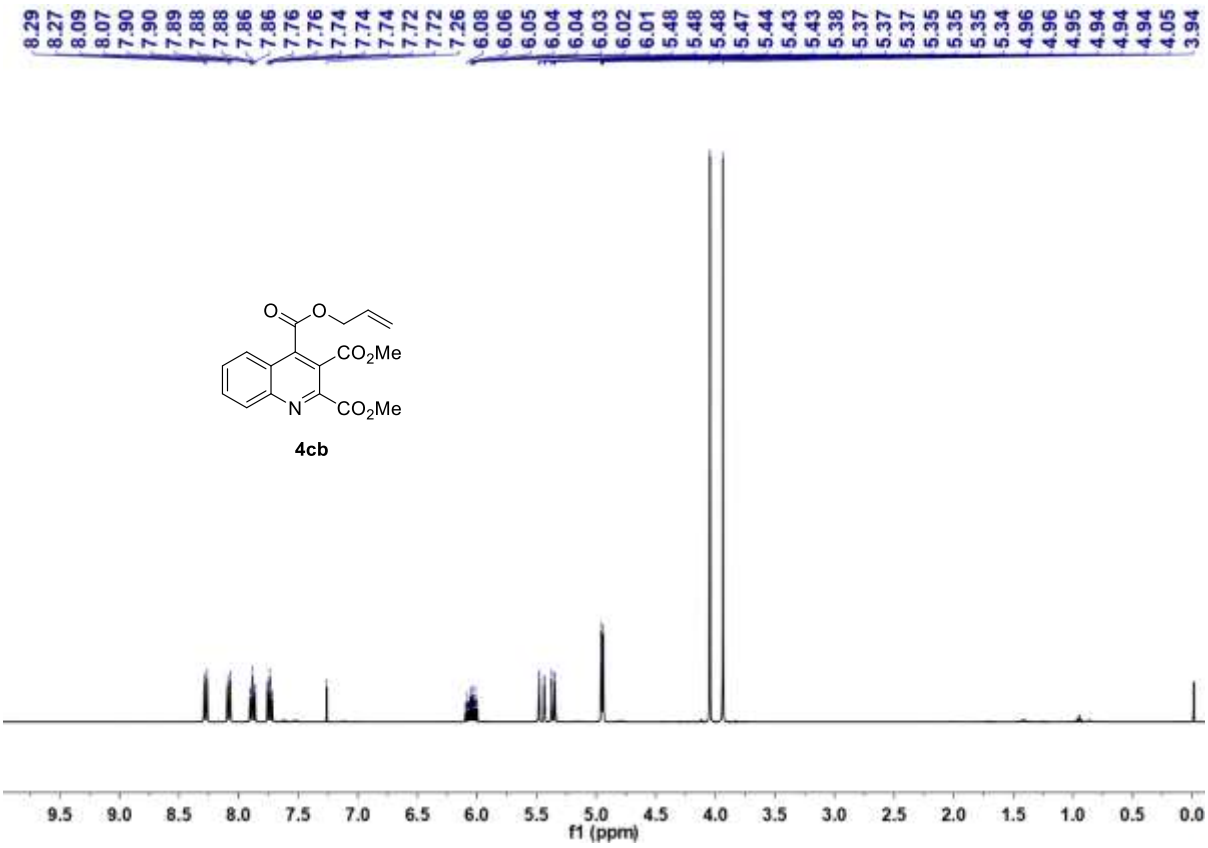
4bp, 80%

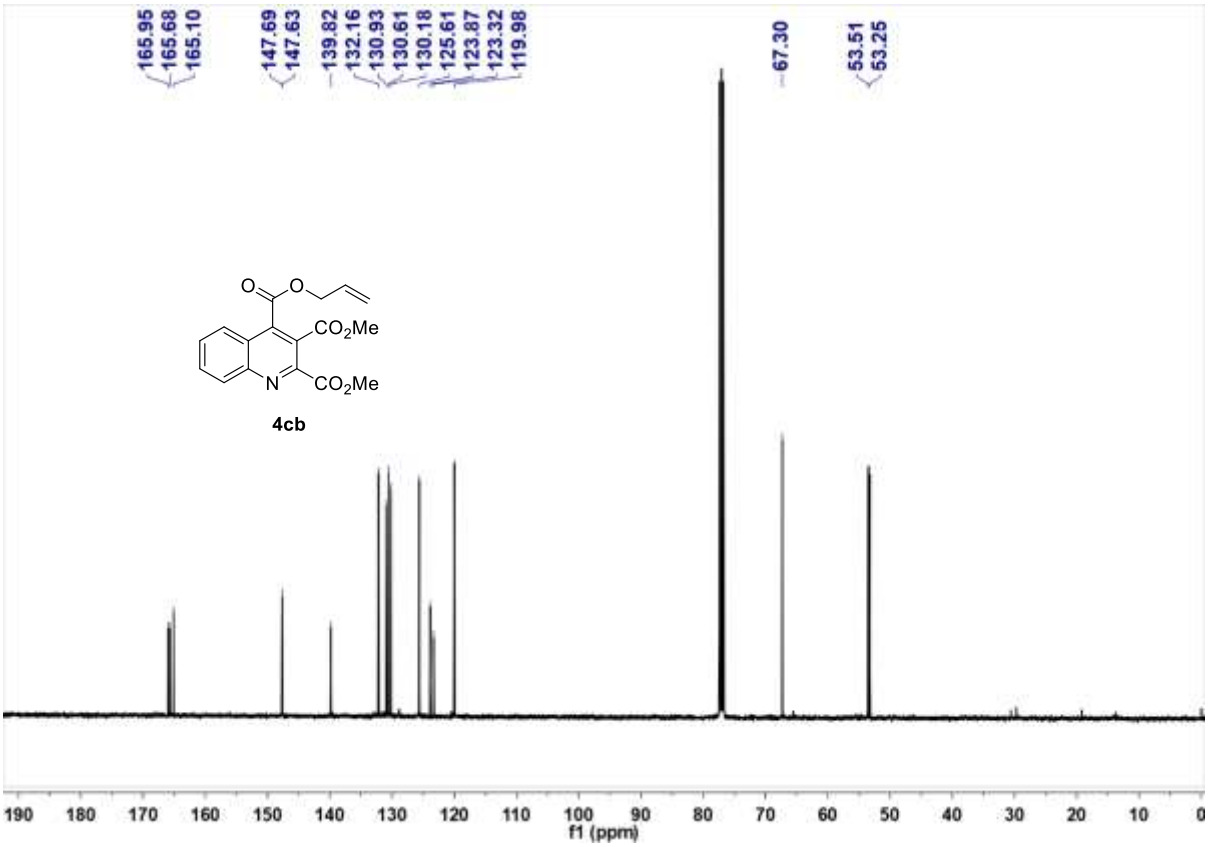

8.28
8.26
8.04
8.02
7.89
7.89
7.88
7.87
7.76
7.76
7.74
4.65
4.64
4.62
4.04
3.96
3.67
3.66
3.64
2.27
2.25
2.24
2.22
2.21
O
O
Cl
CO2Me
N
CO2Me
1.03
1.01
1.07
1.02
1.95
3.00
2.99
1.99
2.00
f1 (ppm)

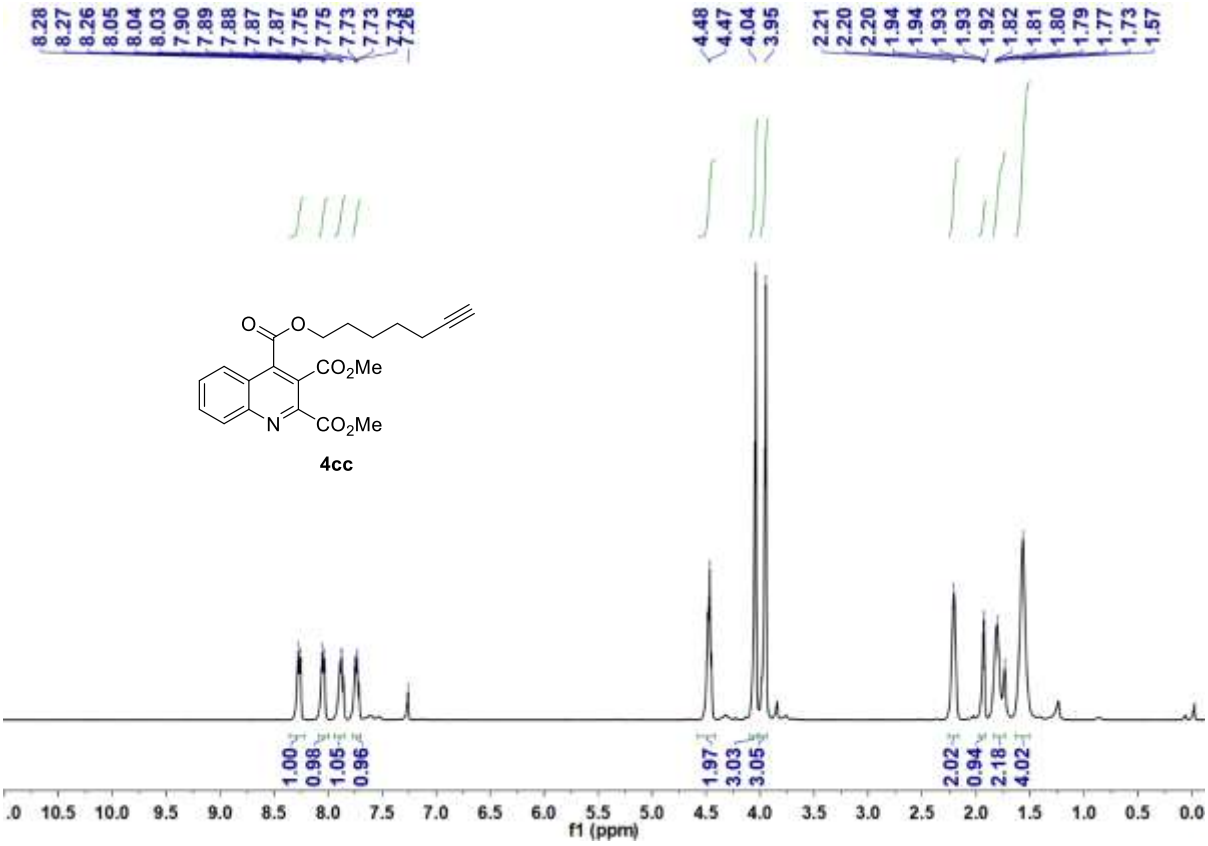
4ca

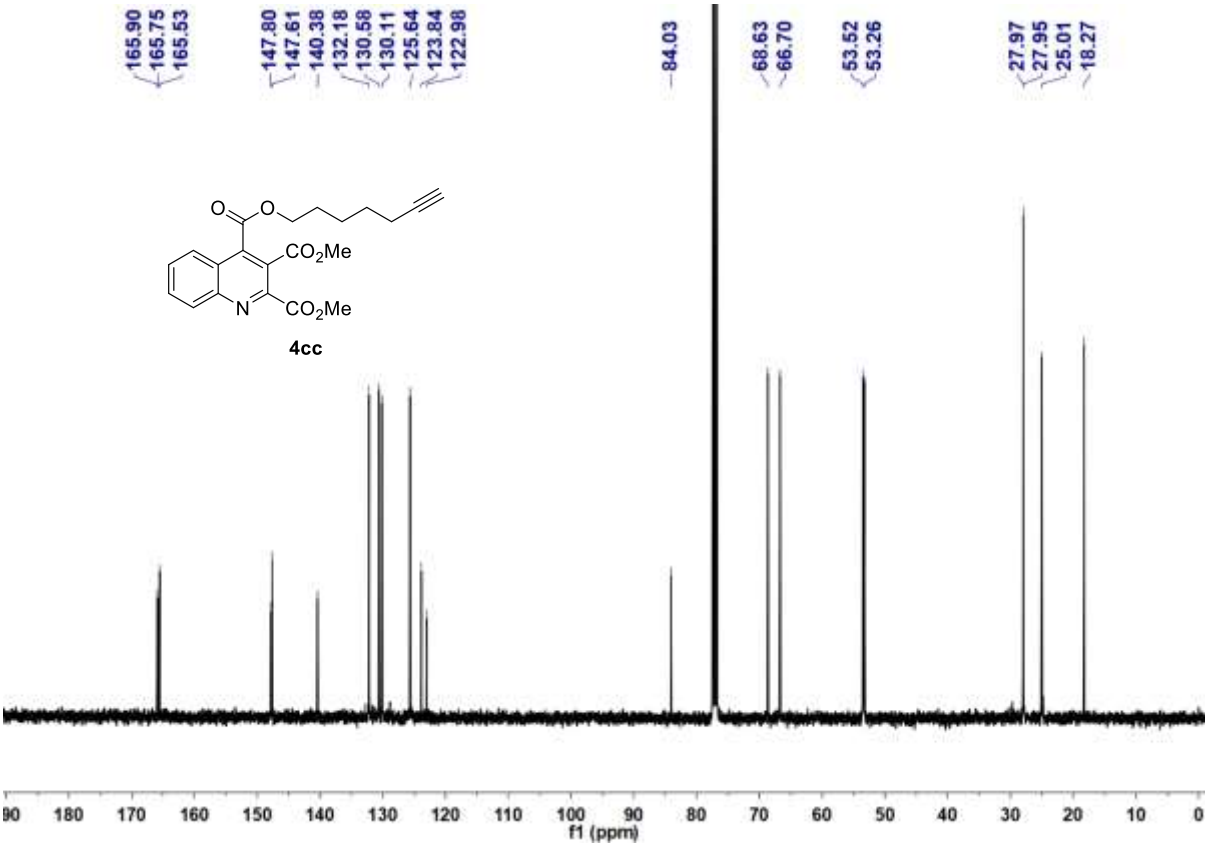

165.90
165.75
165.37
147.83
147.60
140.16
132.33
130.61
130.25
125.54
123.74
122.83
63.26
53.59
53.43
40.91
31.18
O
O
Cl
CO2Me
N
CO2Me
f1 (ppm)

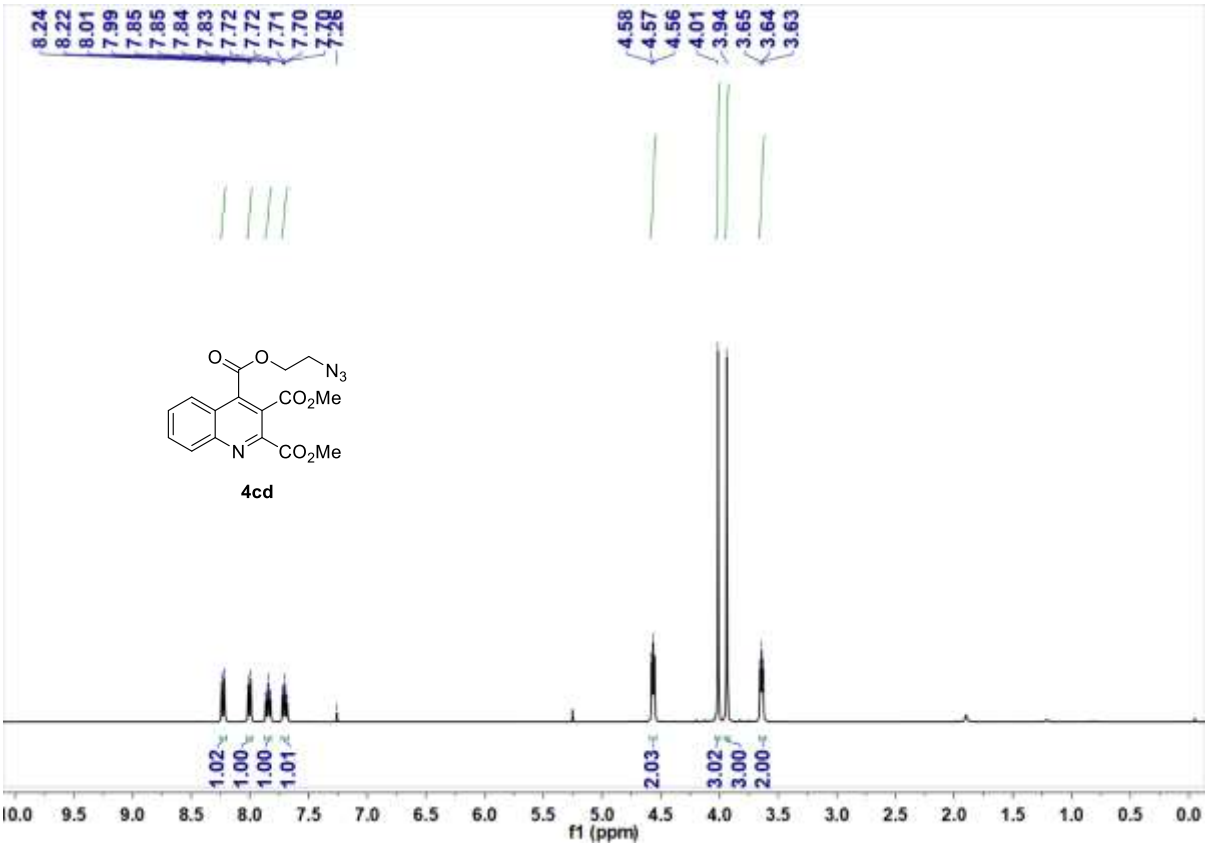
4ca


8.29
8.27
8.09
8.07
7.90
7.90
7.89
7.88
7.88
7.86
7.86
7.76
7.76
7.74
7.74
7.74
7.72
7.72
7.26
6.08
6.06
6.05
6.04
6.04
6.03
6.02
6.01
5.48
5.48
5.48
5.47
5.44
5.43
5.43
5.38
5.37
5.37
5.37
5.35
5.35
5.35
5.34
4.96
4.96
4.95
4.94
4.94
4.94
4.94
4.05
3.94
O
O
CO2Me
CO2Me
N
4cb
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

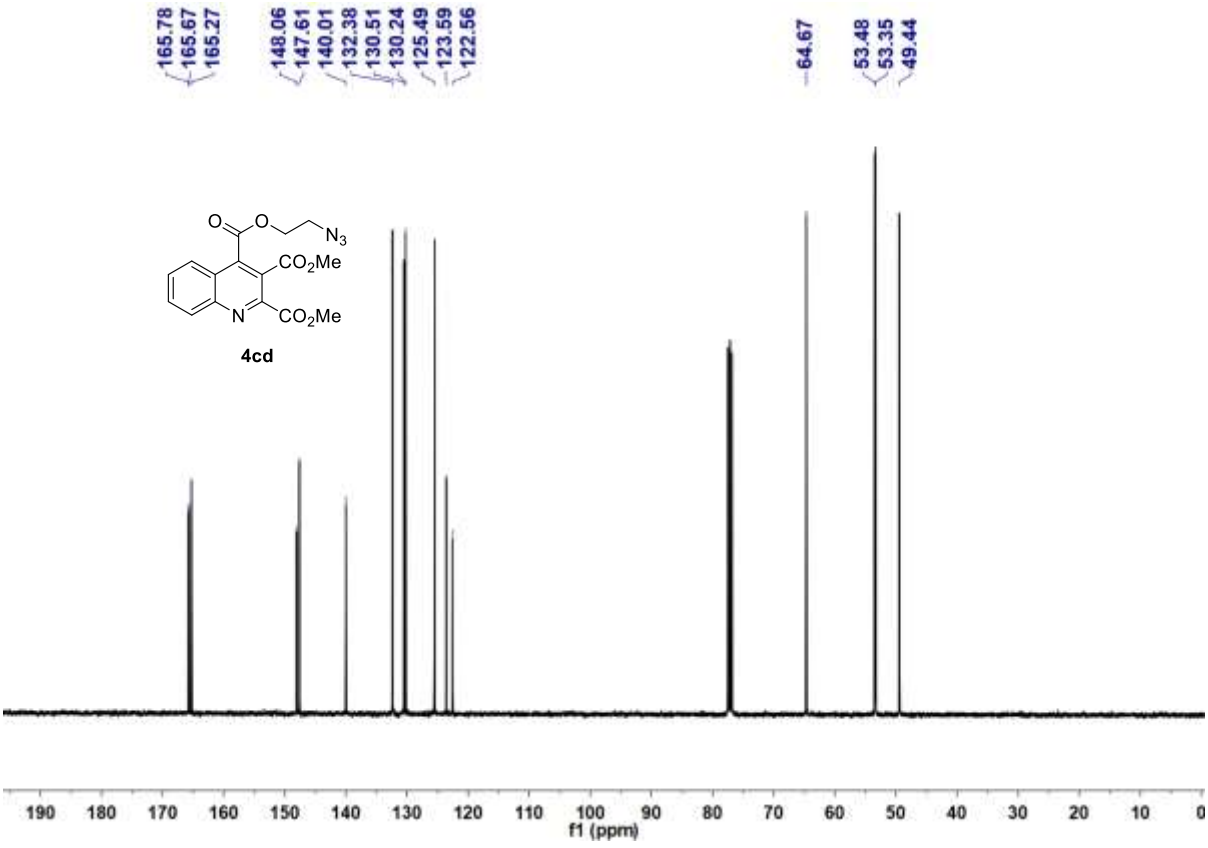

165.95
165.68
165.10
147.69
147.63
139.82
132.16
130.93
130.61
130.18
125.61
123.87
123.32
119.98
67.30
53.51
53.25
O
O
CO2Me
CO2Me
N
4cb
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.28
8.27
8.26
8.05
8.04
8.03
7.90
7.89
7.88
7.87
7.87
7.87
7.75
7.75
7.73
7.73
7.73
7.26
4.48
4.47
4.04
3.95
2.21
2.20
2.20
1.94
1.94
1.93
1.93
1.92
1.82
1.81
1.80
1.79
1.77
1.73
1.57
O
O
CO2Me
N
CO2Me
4cc
1.00
0.98
1.05
0.96
1.97
3.03
3.05
2.02
0.94
2.18
4.02
f1 (ppm)

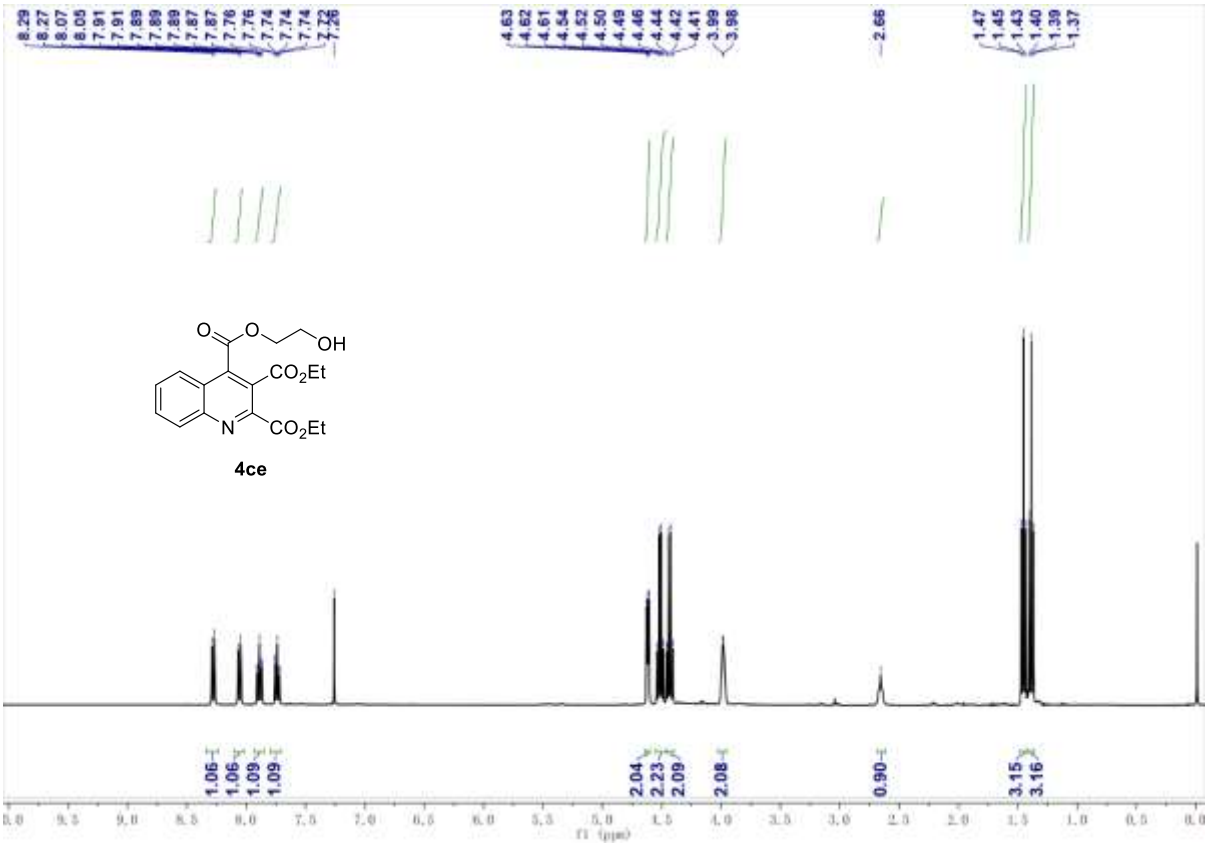

165.90
165.75
165.53
147.80
147.61
140.38
132.18
130.58
130.11
125.64
123.84
122.98
84.03
68.63
66.70
53.52
53.26
27.97
27.95
25.01
18.27
O
O
CO2Me
N
CO2Me
4cc
f1 (ppm)

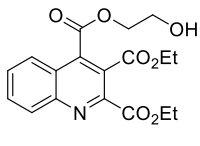

8.24
8.22
8.01
7.99
7.85
7.85
7.84
7.83
7.72
7.72
7.71
7.70
4.58
4.57
4.56
4.01
3.94
3.65
3.64
3.63
O
O
N3
CO2Me
N
CO2Me
1.02
1.00
1.00
1.01
2.03
3.02
3.00
2.00
f1 (ppm)

4cd


165.78
165.67
165.27
148.06
147.61
140.01
132.38
130.51
130.24
125.49
123.59
122.56
64.67
53.48
53.35
49.44
O
O
N3
CO2Me
N
CO2Me
f1 (ppm)

4cd


8.29
8.27
8.07
8.05
7.91
7.91
7.89
7.89
7.89
7.87
7.87
7.76
7.76
7.74
7.74
7.74
7.72
7.26
4.63
4.62
4.61
4.54
4.52
4.50
4.49
4.46
4.44
4.42
4.41
3.99
3.98
2.66
1.47
1.45
1.43
1.40
1.39
1.37
1.06
1.06
1.09
1.09
2.04
2.23
2.09
2.08
0.90
3.15
3.16
f1 (ppm)

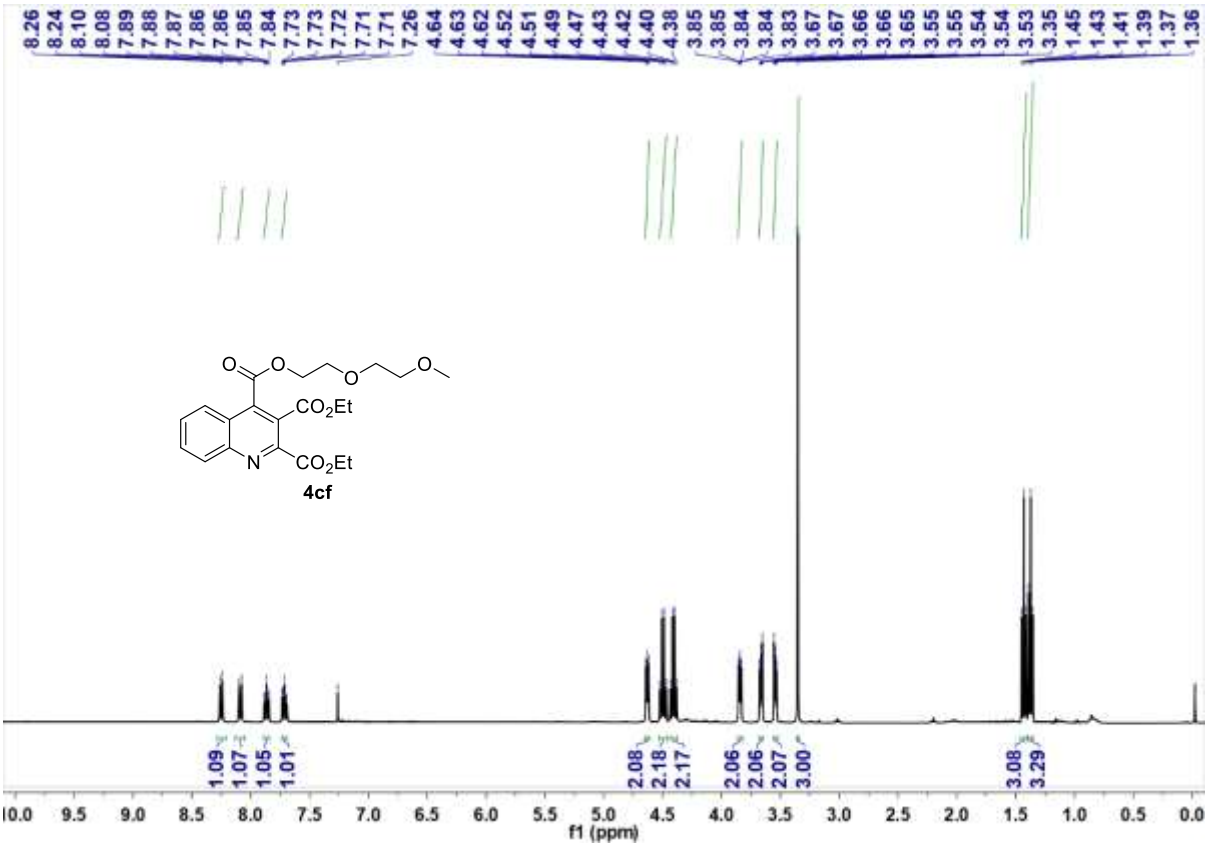

O
O
OH
CO2Et
N
CO2Et

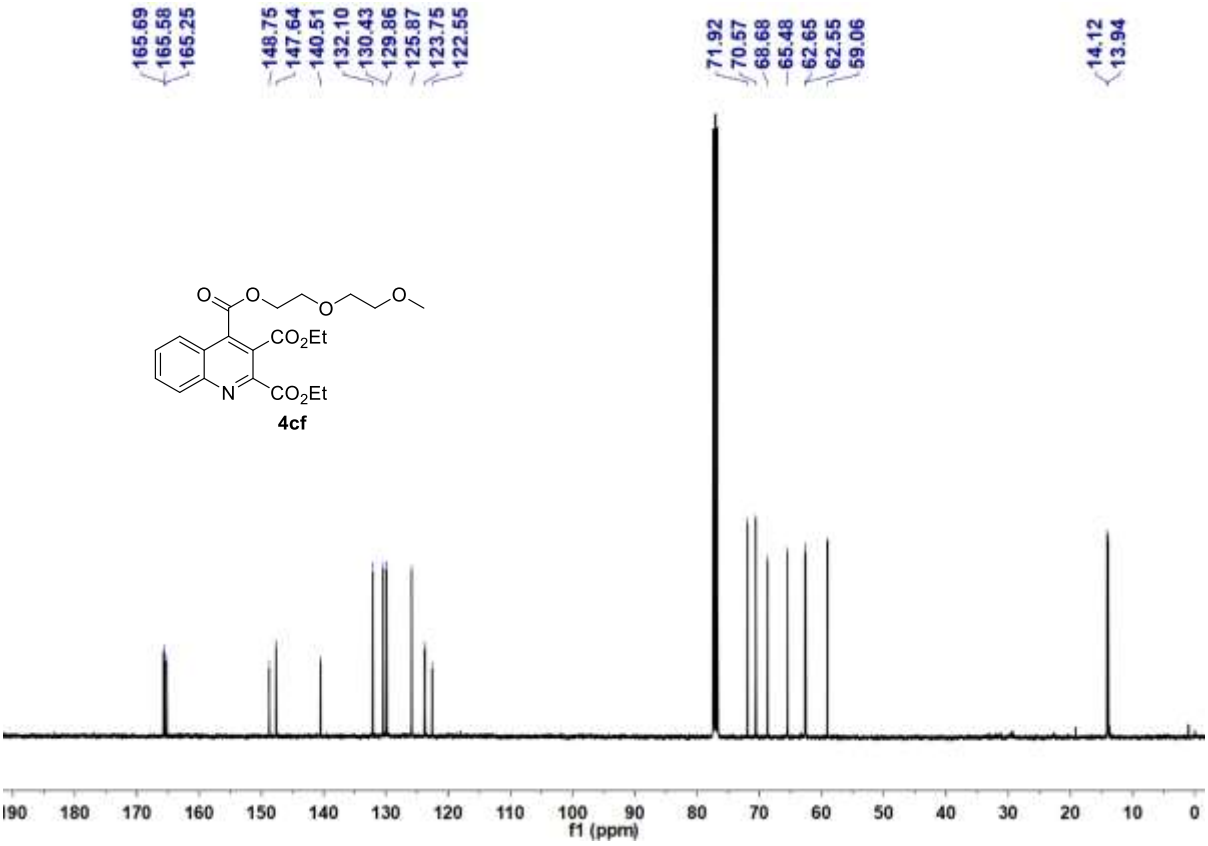
4ce

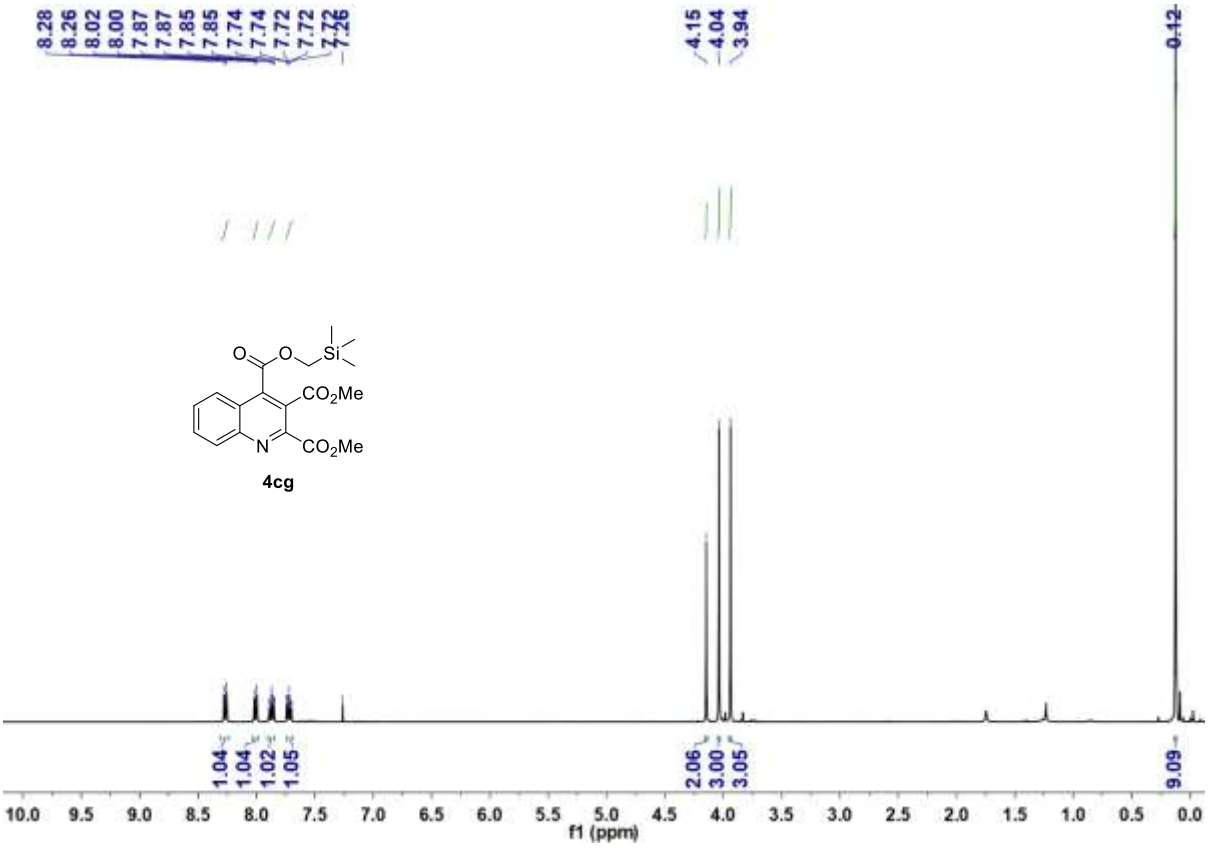
165.99
165.61
165.46
148.47
147.55
140.48
132.27
130.38
130.05
125.60
123.59
122.31
68.23
62.92
62.73
60.54
14.12
13.88
f1 (ppm)

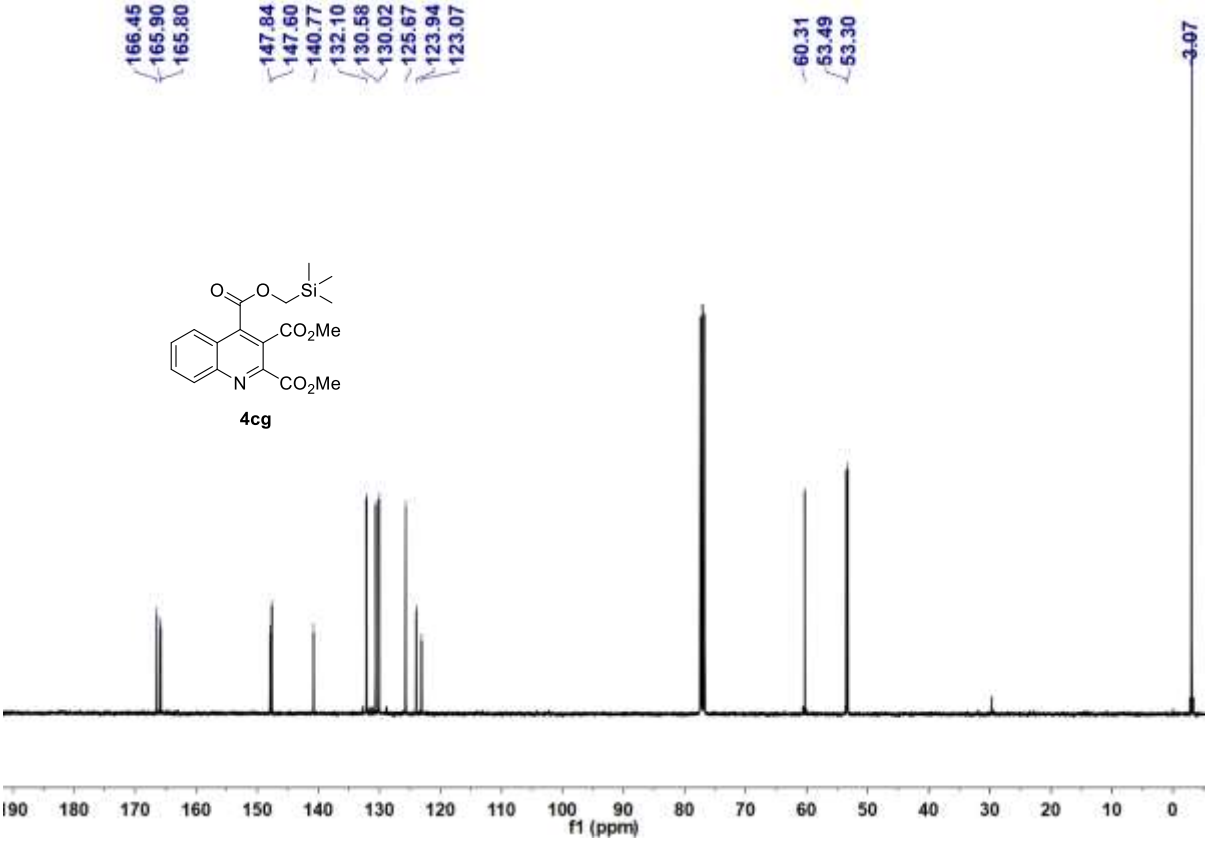
O
O
OH
CO2Et
N
CO2Et

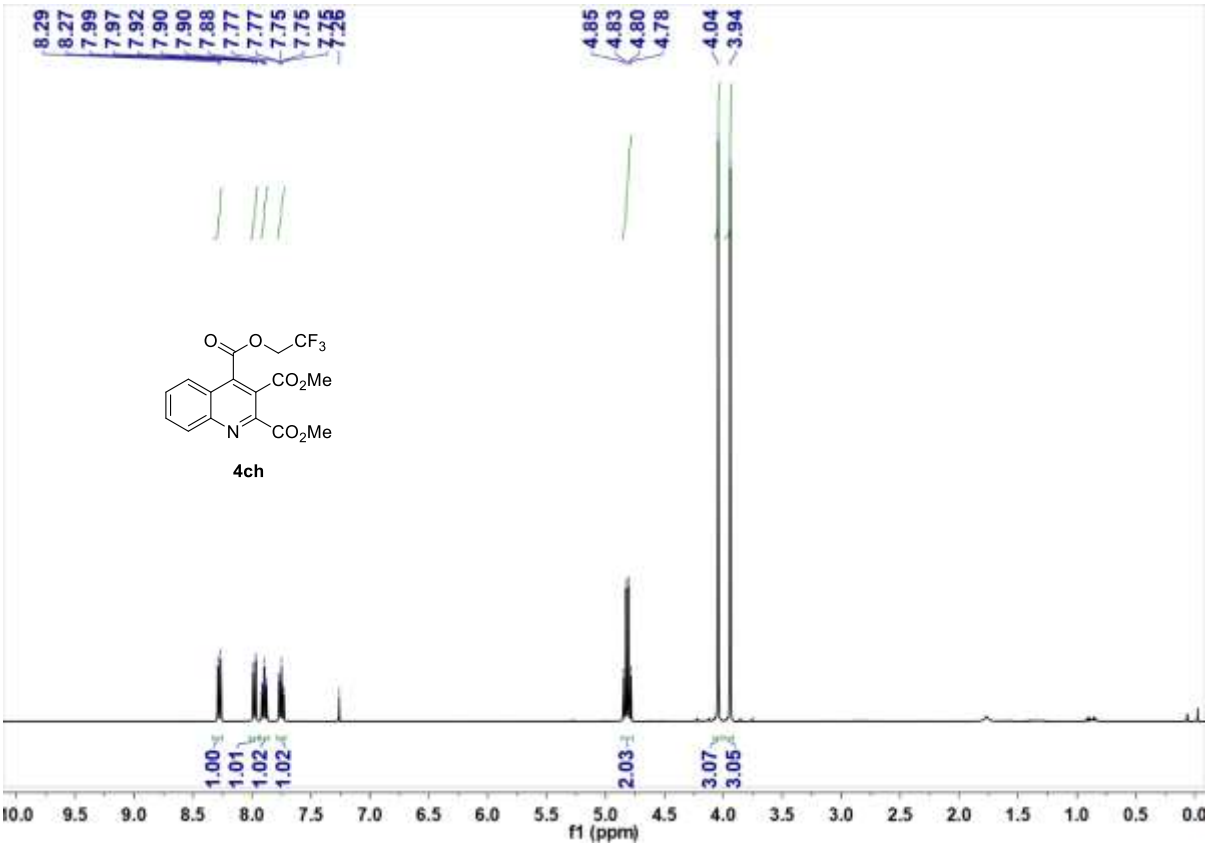
4ce

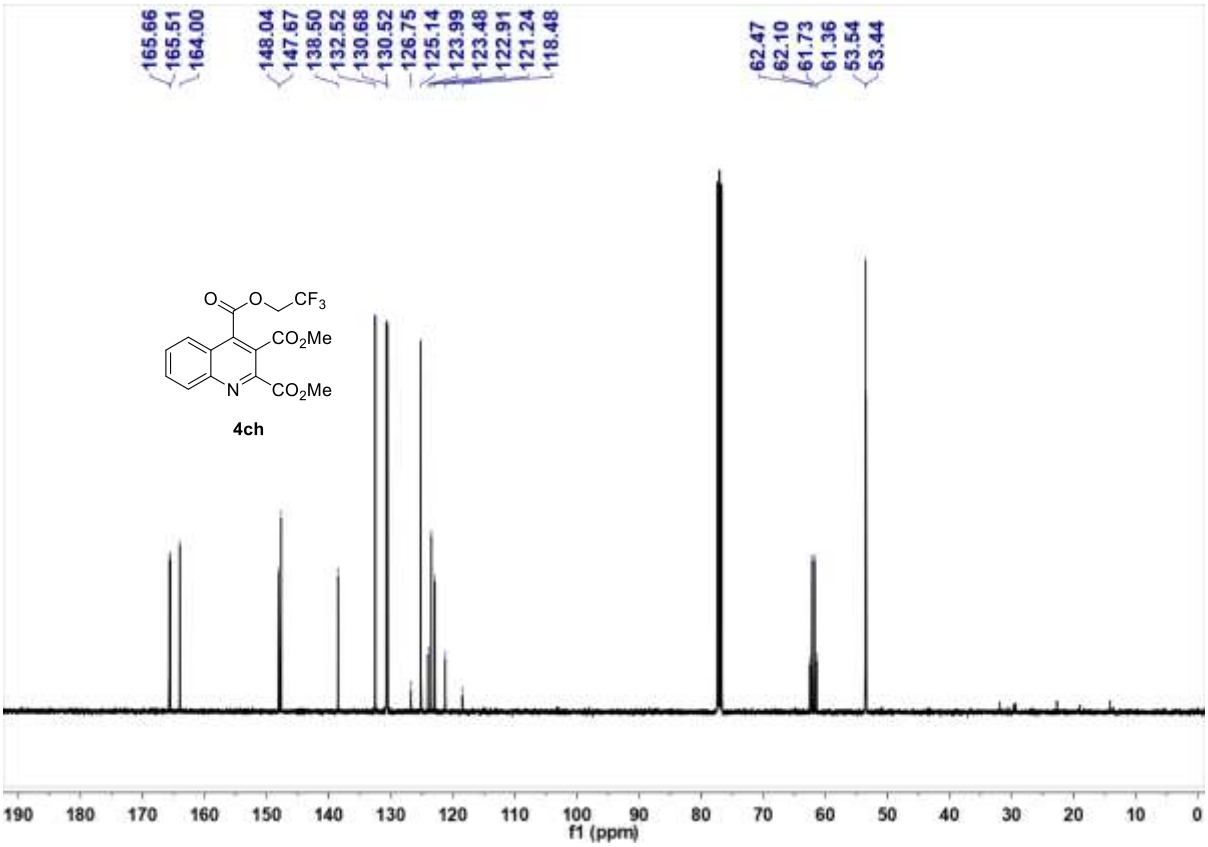

8.26 8.24 8.10 8.08 7.89 7.88 7.87 7.86 7.86 7.85 7.84 7.73 7.73 7.72 7.71 7.71 7.26 4.64 4.63 4.62 4.52 4.51 4.49 4.47 4.43 4.42 4.40 4.38 3.85 3.85 3.84 3.84 3.83 3.67 3.67 3.66 3.66 3.65 3.55 3.55 3.54 3.54 3.53 3.35 1.45 1.43 1.41 1.39 1.37 1.36
1.09 1.07 1.05 1.01 2.08 2.18 2.17 2.06 2.06 2.07 3.00 3.08 3.29
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
O O O O O
CO2Et
N
CO2Et
4cf

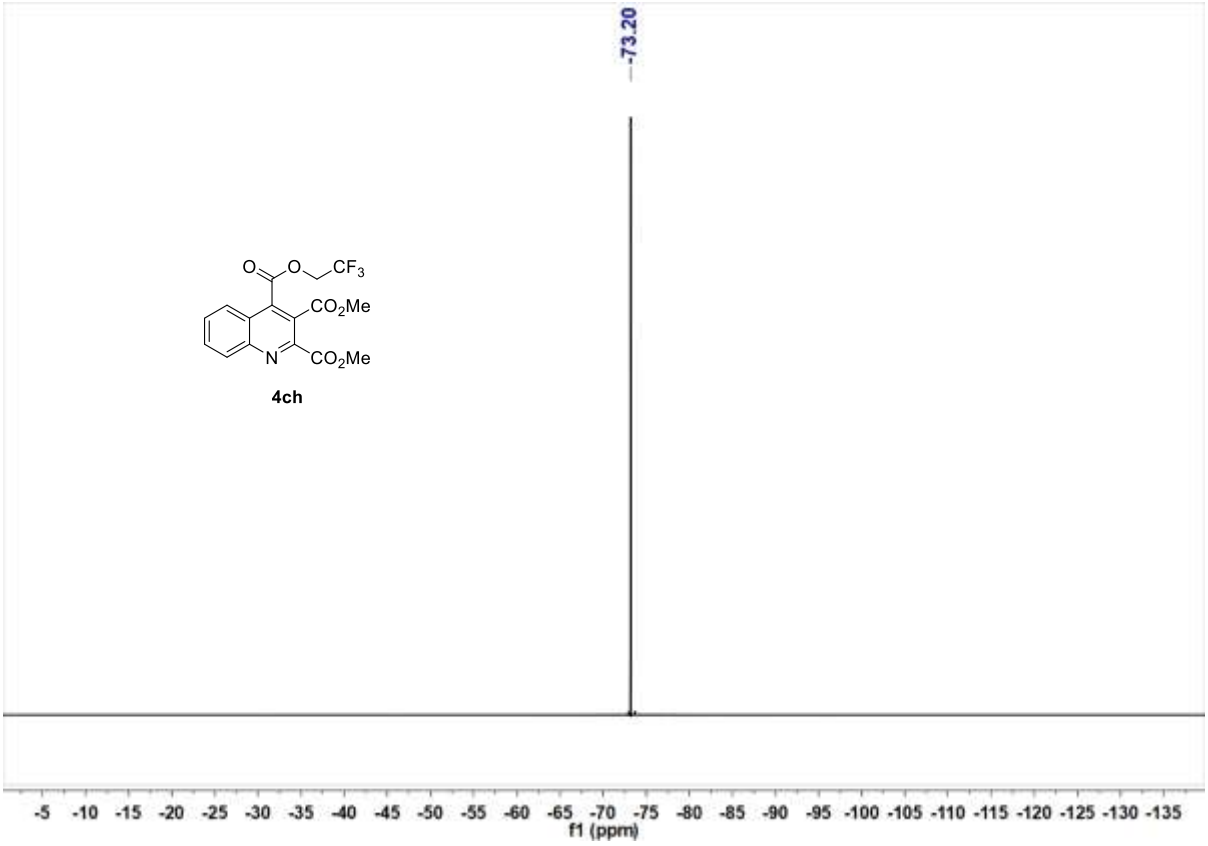

165.69 165.58 165.25 148.75 147.64 140.51 132.10 130.43 129.86 125.87 123.75 122.55 71.92 70.57 68.68 65.48 62.65 62.55 59.06 14.12 13.94
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
O O O O O
CO2Et
N
CO2Et
4cf

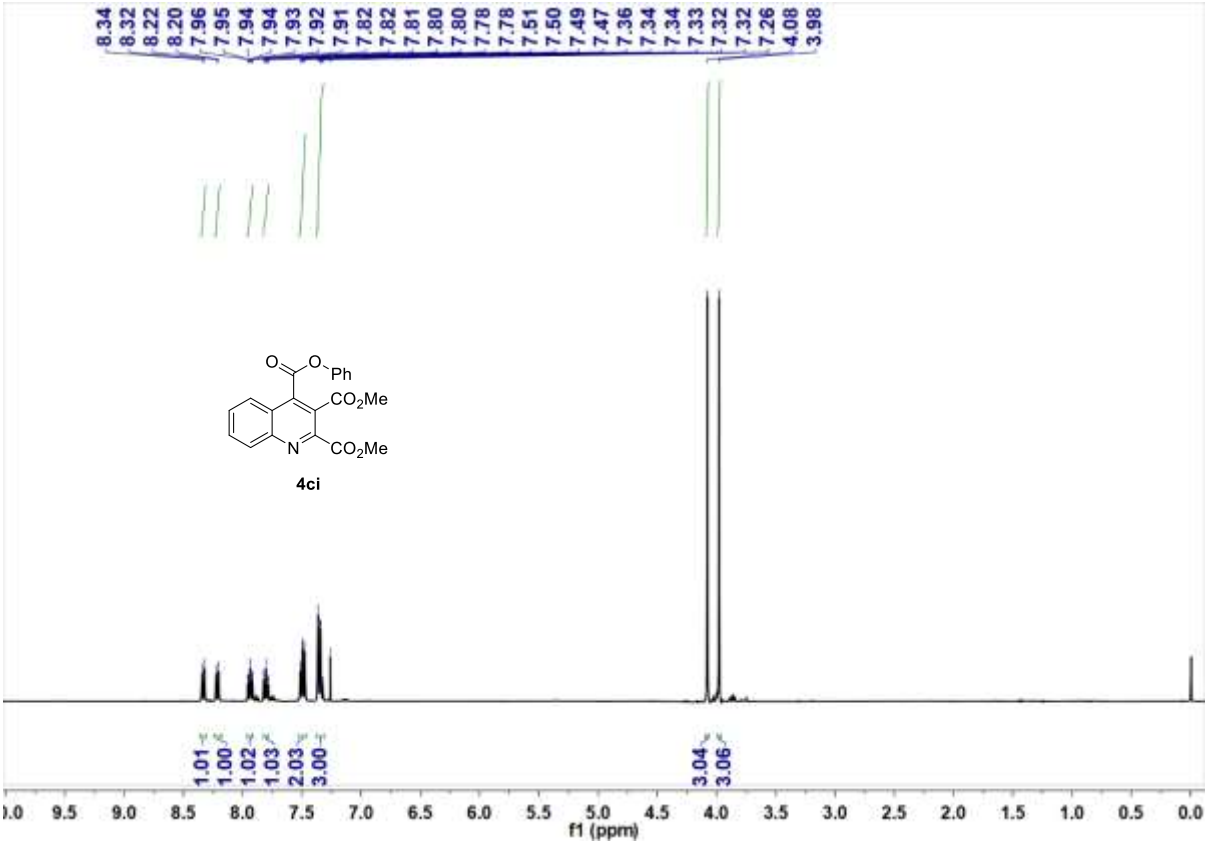

8.28
8.26
8.02
8.00
7.87
7.87
7.85
7.85
7.74
7.74
7.72
7.72
4.15
4.04
3.94
0.12
O
O
Si
CO2Me
N
CO2Me
4cg
1.04
1.04
1.02
1.05
2.06
3.00
3.05
9.09
f1 (ppm)

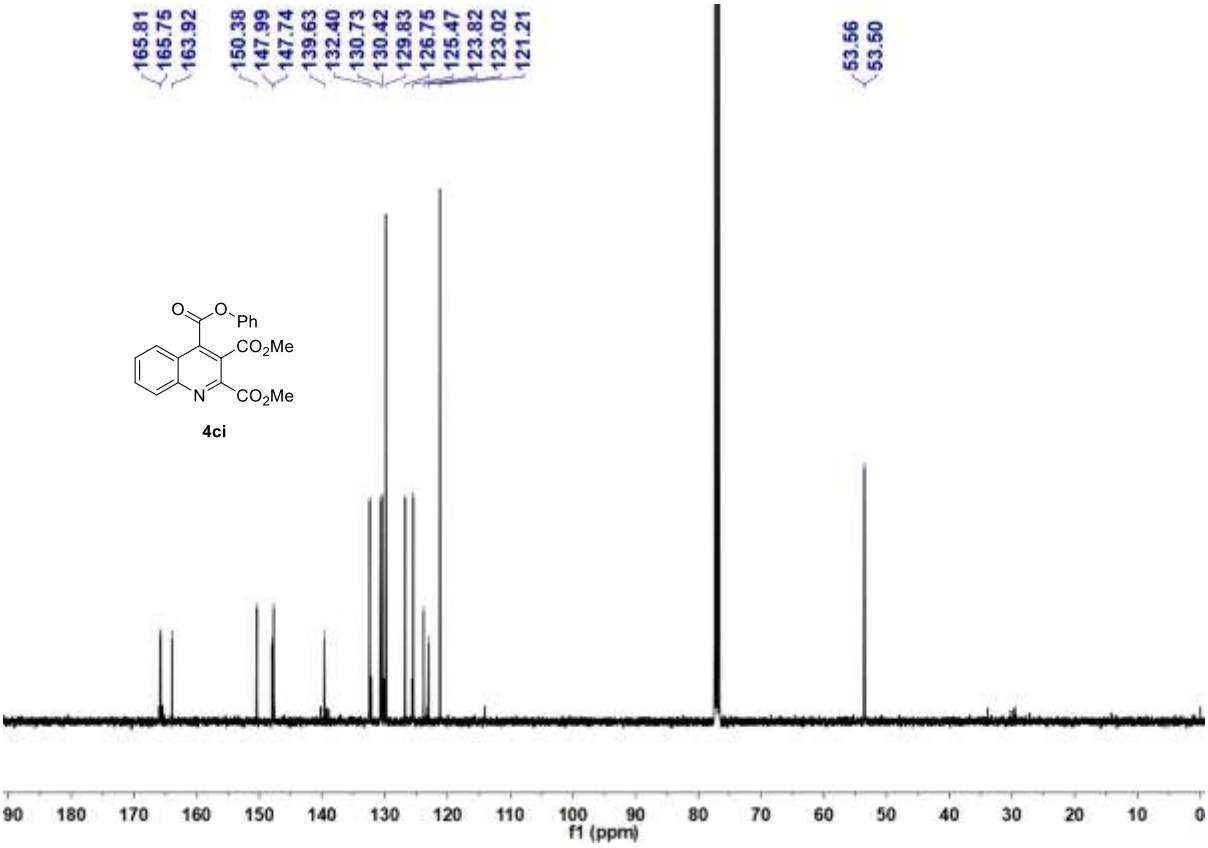

166.45
165.90
165.80
147.84
147.60
140.77
132.10
130.58
130.02
125.67
123.94
123.07
60.31
53.49
53.30
3.07
O
O
Si
CO2Me
N
CO2Me
4cg
f1 (ppm)

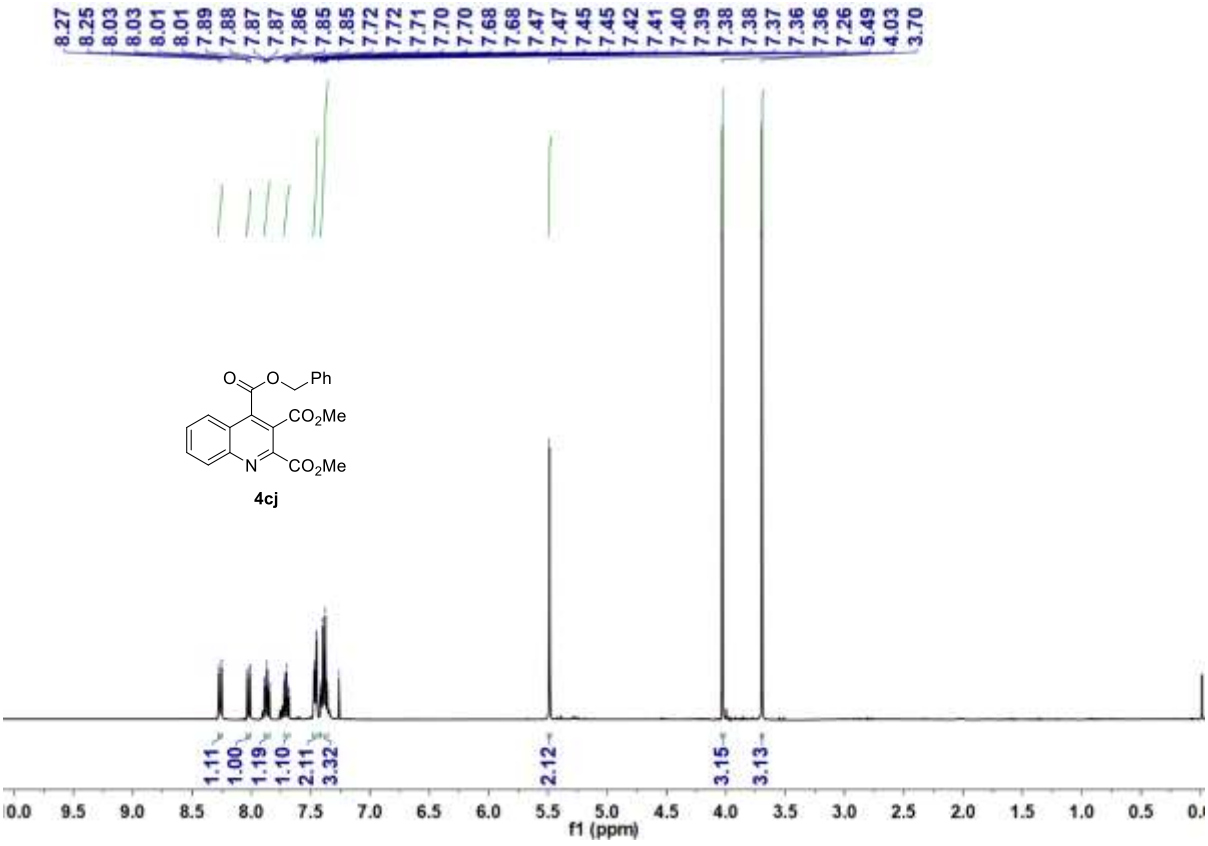

8.29
8.27
7.99
7.97
7.92
7.90
7.90
7.88
7.77
7.77
7.75
7.75
4.85
4.83
4.80
4.78
4.04
3.94
O
O
CF3
CO2Me
N
CO2Me
4ch
1.00
1.01
1.02
1.02
2.03
3.07
3.05
f1 (ppm)

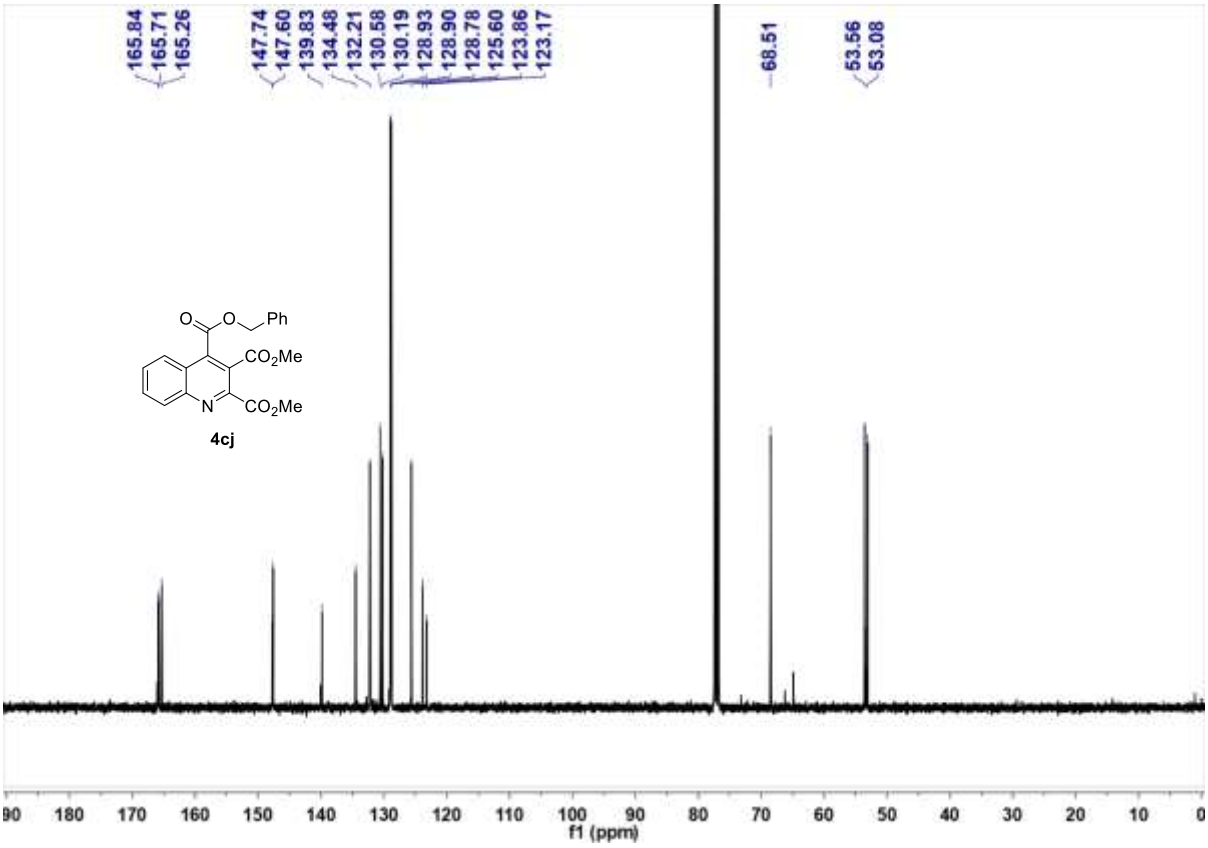

165.66
165.51
164.00
148.04
147.67
138.50
132.52
130.68
130.52
126.75
125.14
123.99
123.48
122.91
121.24
118.48
62.47
62.10
61.73
61.36
53.54
53.44
O
O
CF3
CO2Me
N
CO2Me
4ch
f1 (ppm)

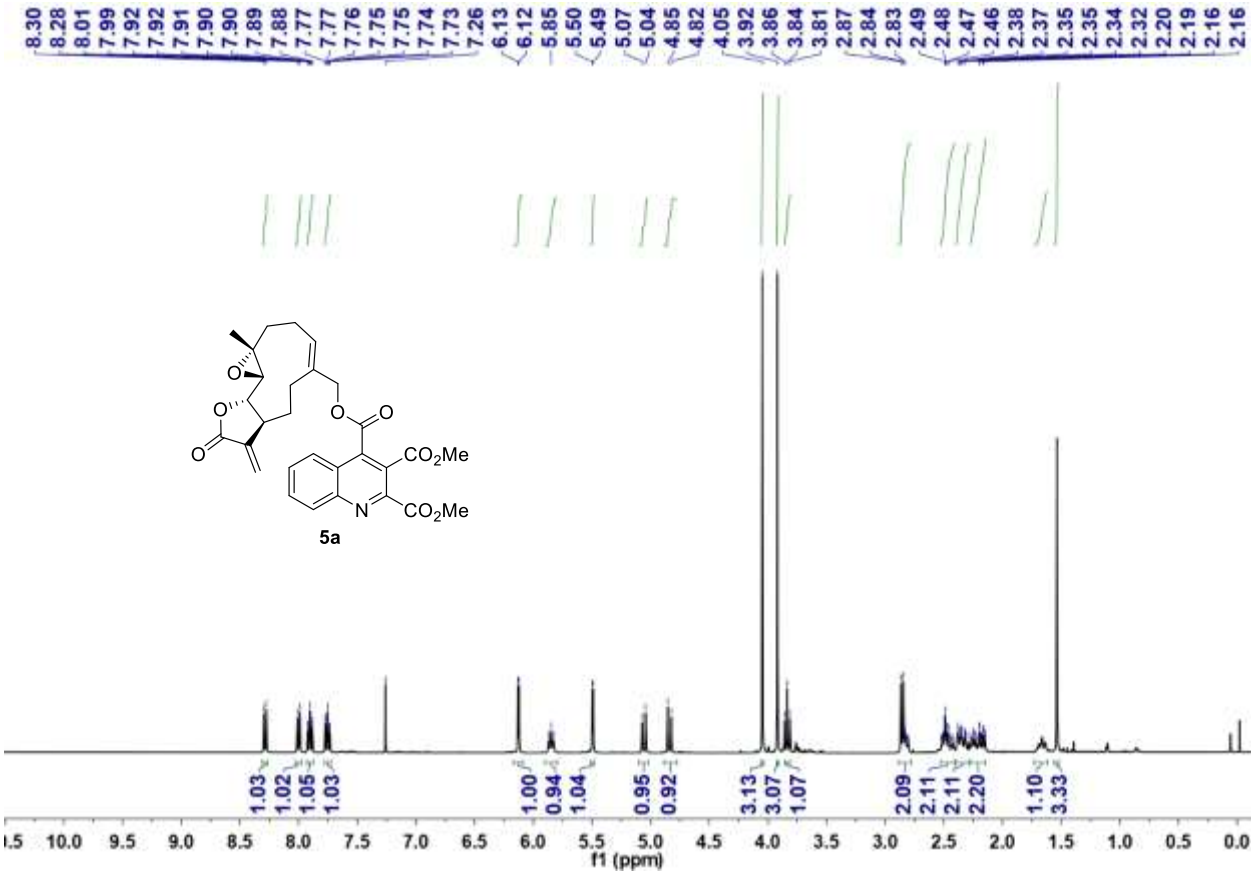

-73.20
O
O
CF3
CO2Me
N
CO2Me
4ch
-5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135
f1 (ppm)

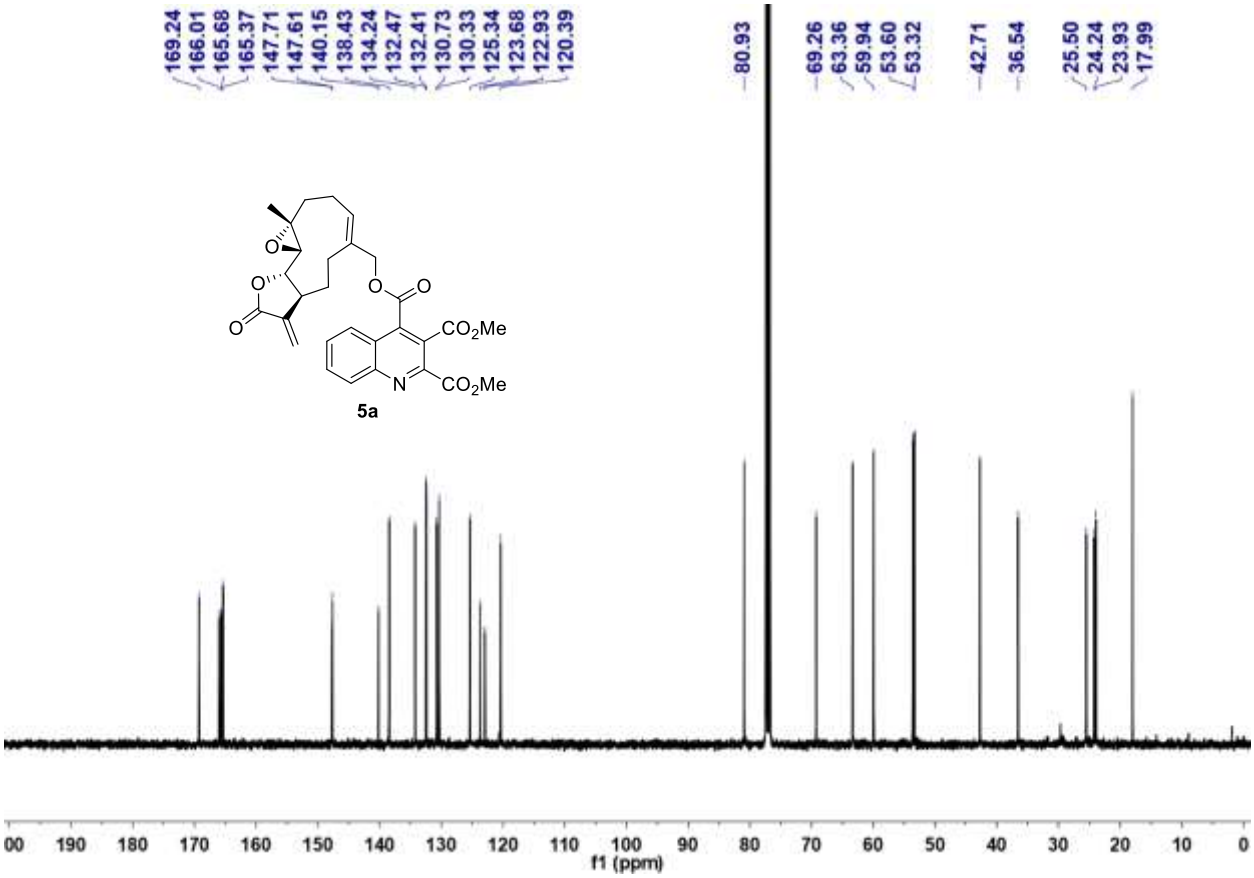

8.34 8.32 8.22 8.20 7.96 7.95 7.94 7.94 7.93 7.92 7.91 7.82 7.82 7.81 7.80 7.80 7.78 7.78 7.51 7.50 7.49 7.47 7.36 7.34 7.34 7.33 7.32 7.32 7.26 4.08 3.98
O
O
Ph
CO2Me
N
CO2Me
4ci
1.01 1.00 1.02 1.03 2.03 3.00 3.04 3.06
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

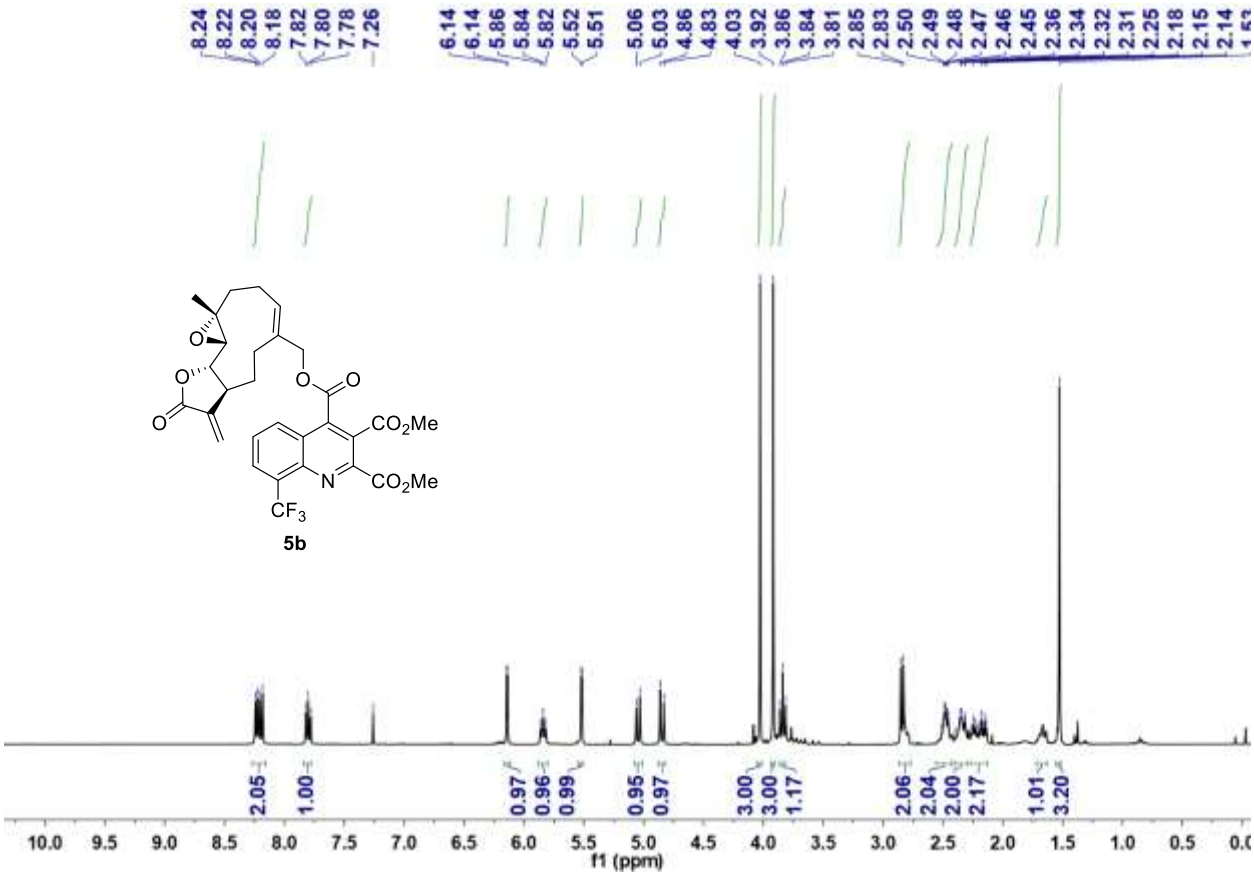

165.81
165.75
163.92
150.38
147.99
147.74
139.63
132.40
130.73
130.42
129.83
126.75
125.47
123.82
123.02
121.21
53.56
53.50
O
O
Ph
CO2Me
N
CO2Me
4ci
f1 (ppm)

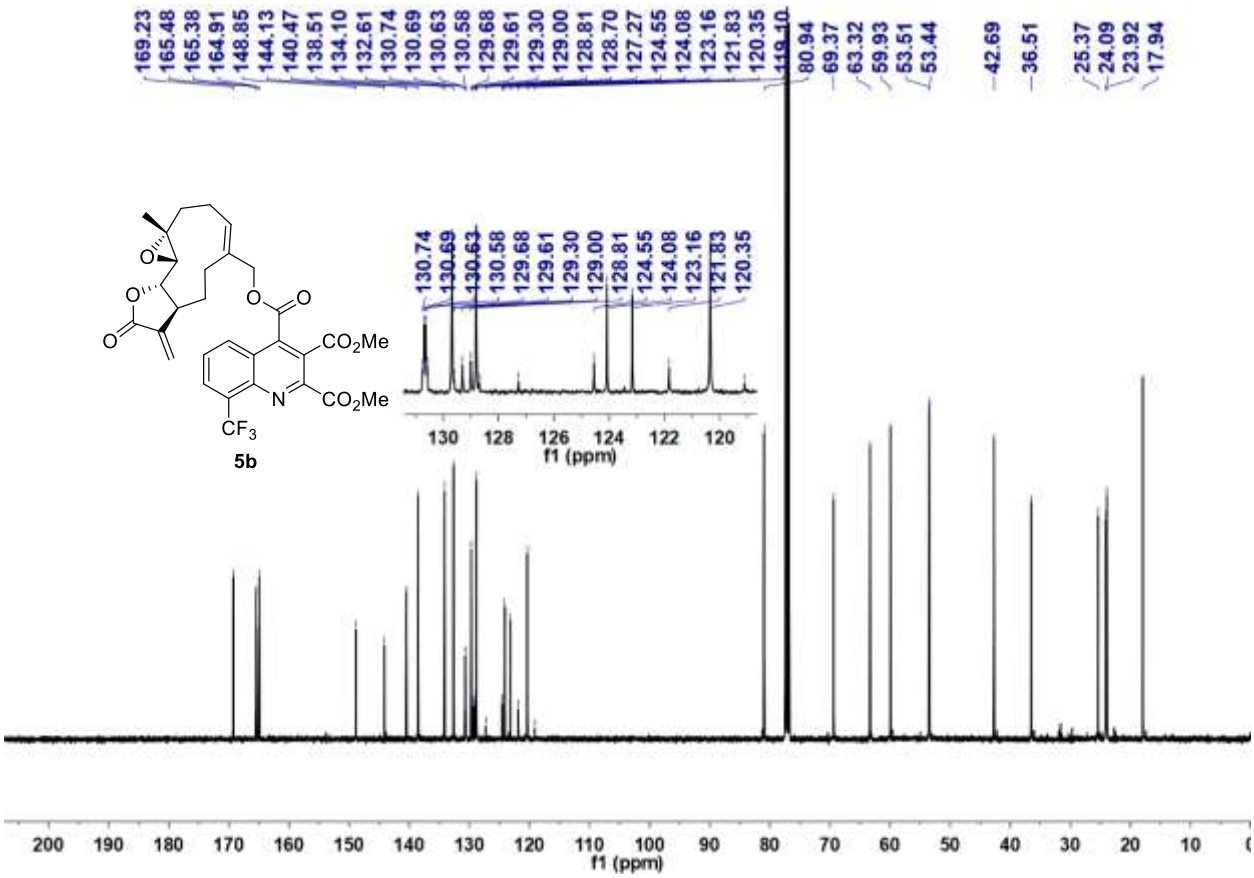

8.27
8.25
8.03
8.03
8.01
8.01
7.89
7.88
7.87
7.87
7.86
7.85
7.85
7.72
7.72
7.71
7.70
7.70
7.68
7.68
7.47
7.47
7.45
7.45
7.42
7.41
7.40
7.39
7.38
7.38
7.37
7.36
7.36
7.26
5.49
4.03
3.70
O
O
Ph
CO2Me
N
CO2Me
4cj
1.11
1.00
1.19
1.10
2.11
3.32
2.12
3.15
3.13
f1 (ppm)

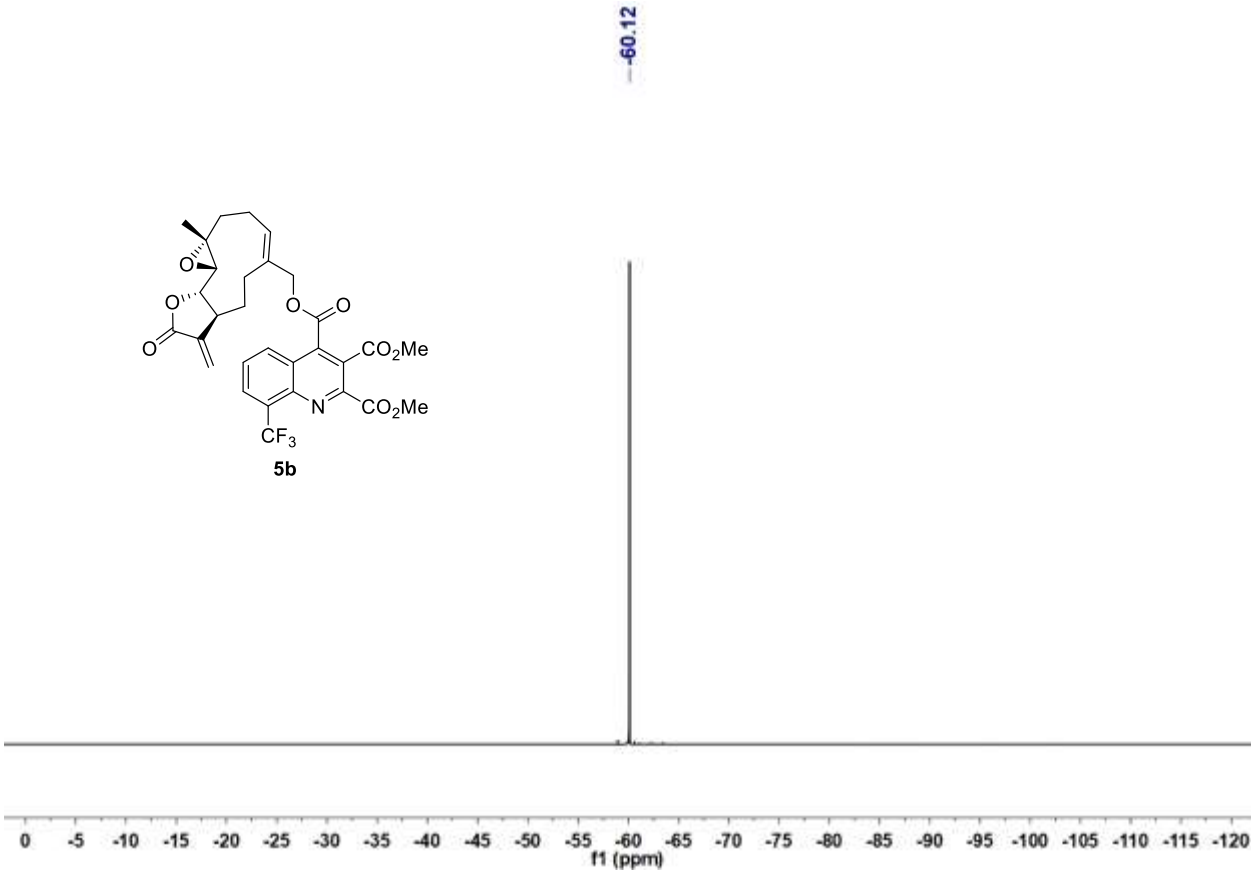

165.84
165.71
165.26
147.74
147.60
139.83
134.48
132.21
130.58
130.19
128.93
128.90
128.78
125.60
123.86
123.17
68.51
53.56
53.08
O
O
Ph
CO2Me
N
CO2Me
4cj
f1 (ppm)

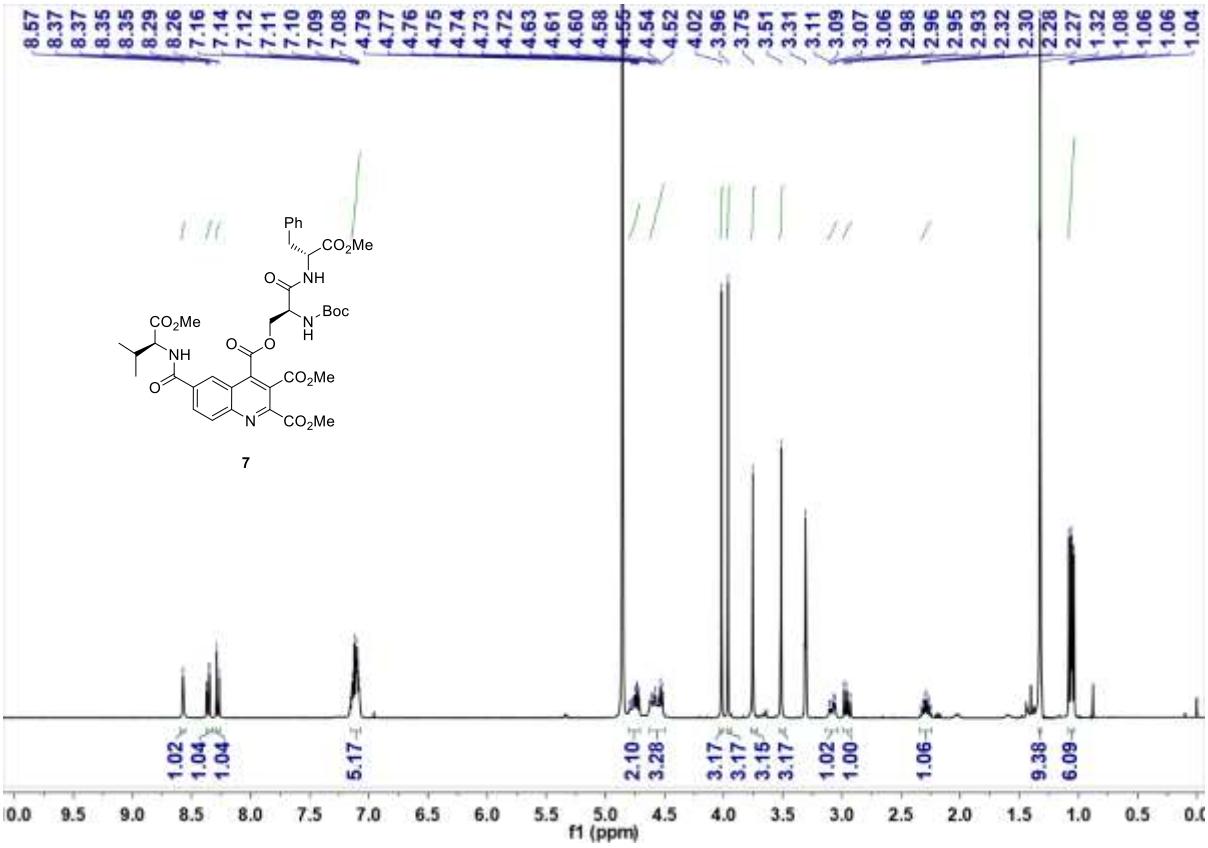

8.30
8.28
8.01
7.99
7.92
7.92
7.91
7.90
7.90
7.89
7.88
7.77
7.77
7.76
7.75
7.75
7.74
7.73
7.26
6.13
6.12
5.85
5.50
5.49
5.07
5.04
4.85
4.82
4.05
3.92
3.86
3.84
3.81
2.87
2.84
2.83
2.49
2.48
2.47
2.46
2.38
2.37
2.35
2.35
2.34
2.32
2.20
2.19
2.16
2.16
O
O
O
O
O
CO2Me
N
CO2Me
5a
1.03
1.02
1.05
1.03
1.00
0.94
1.04
0.95
0.92
3.13
3.07
1.07
2.09
2.11
2.11
2.20
1.10
3.33
f1 (ppm)

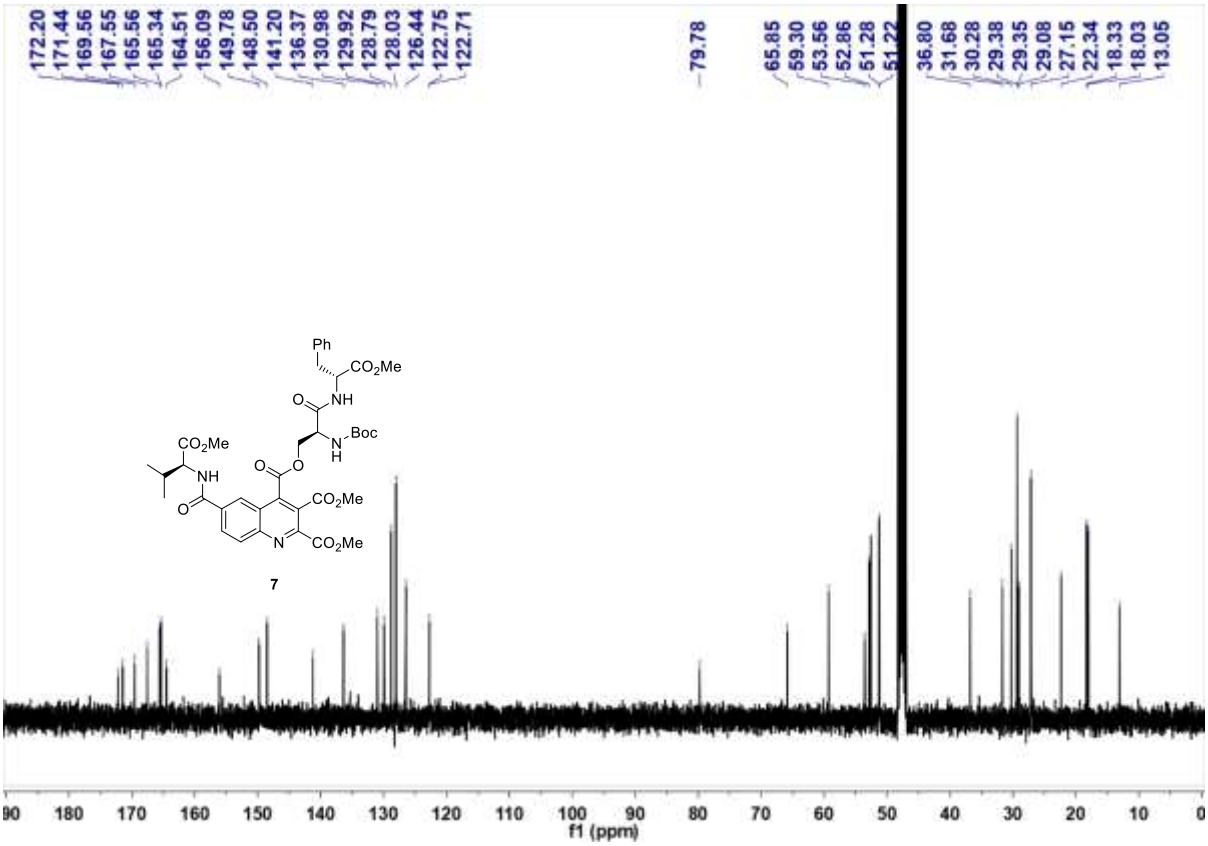

169.24
166.01
165.68
165.37
147.71
147.61
140.15
138.43
134.24
132.47
132.41
130.73
130.33
125.34
123.68
122.93
120.39
80.93
69.26
63.36
59.94
53.60
53.32
42.71
36.54
25.50
24.24
23.93
17.99
CO2Me
CO2Me
5a
f1 (ppm)

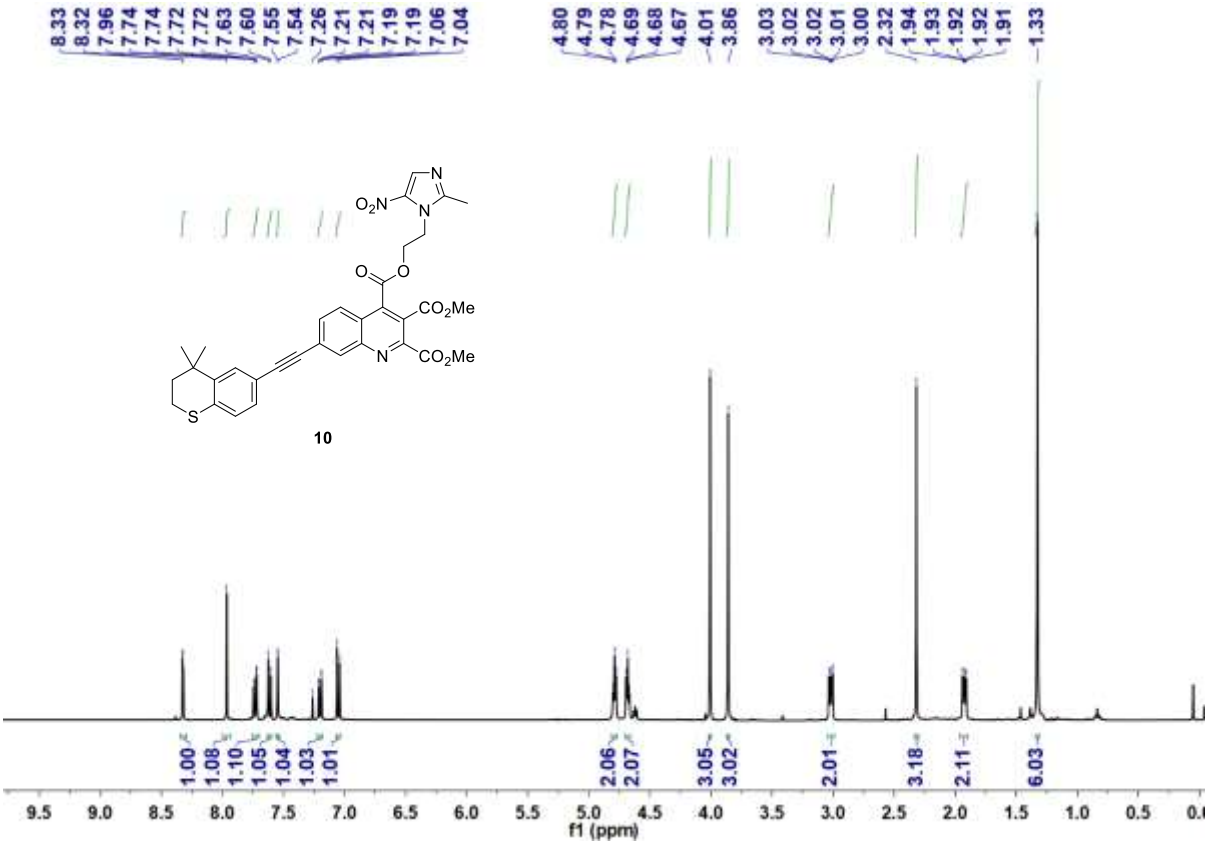

8.24
8.22
8.20
8.18
7.82
7.80
7.78
7.26
6.14
6.14
5.86
5.84
5.82
5.52
5.51
5.06
5.03
4.86
4.83
4.03
3.92
3.86
3.84
3.81
2.85
2.83
2.50
2.49
2.48
2.47
2.46
2.45
2.36
2.34
2.32
2.31
2.25
2.18
2.15
2.14
CO2Me
CO2Me
CF3
5b
2.05
1.00
0.97
0.96
0.99
0.95
0.97
3.00
3.00
1.17
2.06
2.04
2.00
2.17
1.01
3.20
f1 (ppm)


169.23
165.48
165.38
164.91
148.85
144.13
140.47
138.51
134.10
132.61
130.74
130.69
130.63
130.58
129.68
129.61
129.30
129.00
128.81
128.70
127.27
124.55
124.08
123.16
121.83
120.35
119.10
80.94
69.37
63.32
59.93
53.51
53.44
42.69
36.51
25.37
24.09
23.92
17.94
CO2Me
CO2Me
CF3
5b
f1 (ppm)

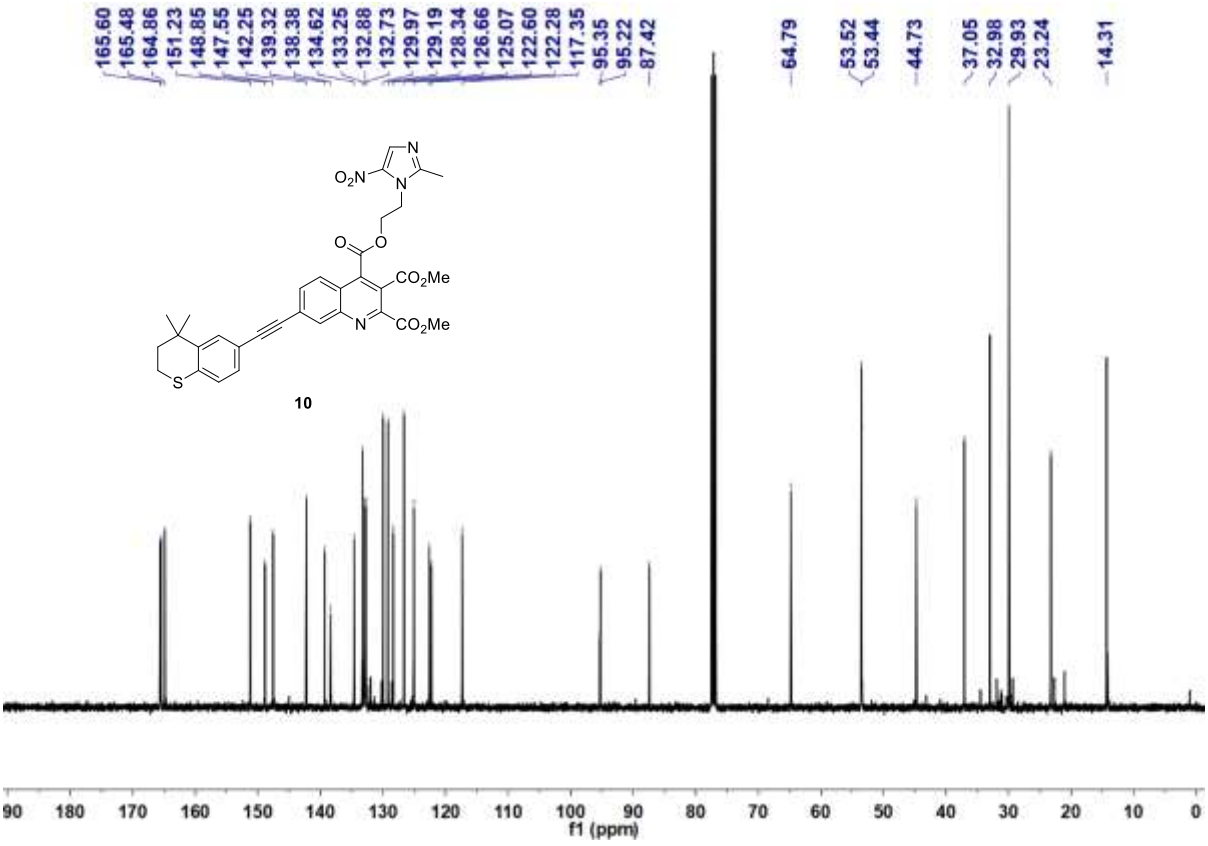

-60.12
CO2Me
CO2Me
CF3
5b
f1 (ppm)


8.57 8.37 8.37 8.35 8.35 8.29 8.26 7.16 7.14 7.12 7.11 7.10 7.09 7.08 4.79 4.77 4.76 4.75 4.74 4.73 4.72 4.63 4.61 4.60 4.58 4.55 4.54 4.52 4.02 3.96 3.75 3.51 3.31 3.11 3.09 3.07 3.06 2.98 2.96 2.95 2.93 2.32 2.30 2.28 2.27 1.32 1.08 1.06 1.06 1.04
1.02 1.04 1.04 5.17 2.10 3.28 3.17 3.17 3.15 3.17 1.02 1.00 1.06 9.38 6.09
f1 (ppm)
7

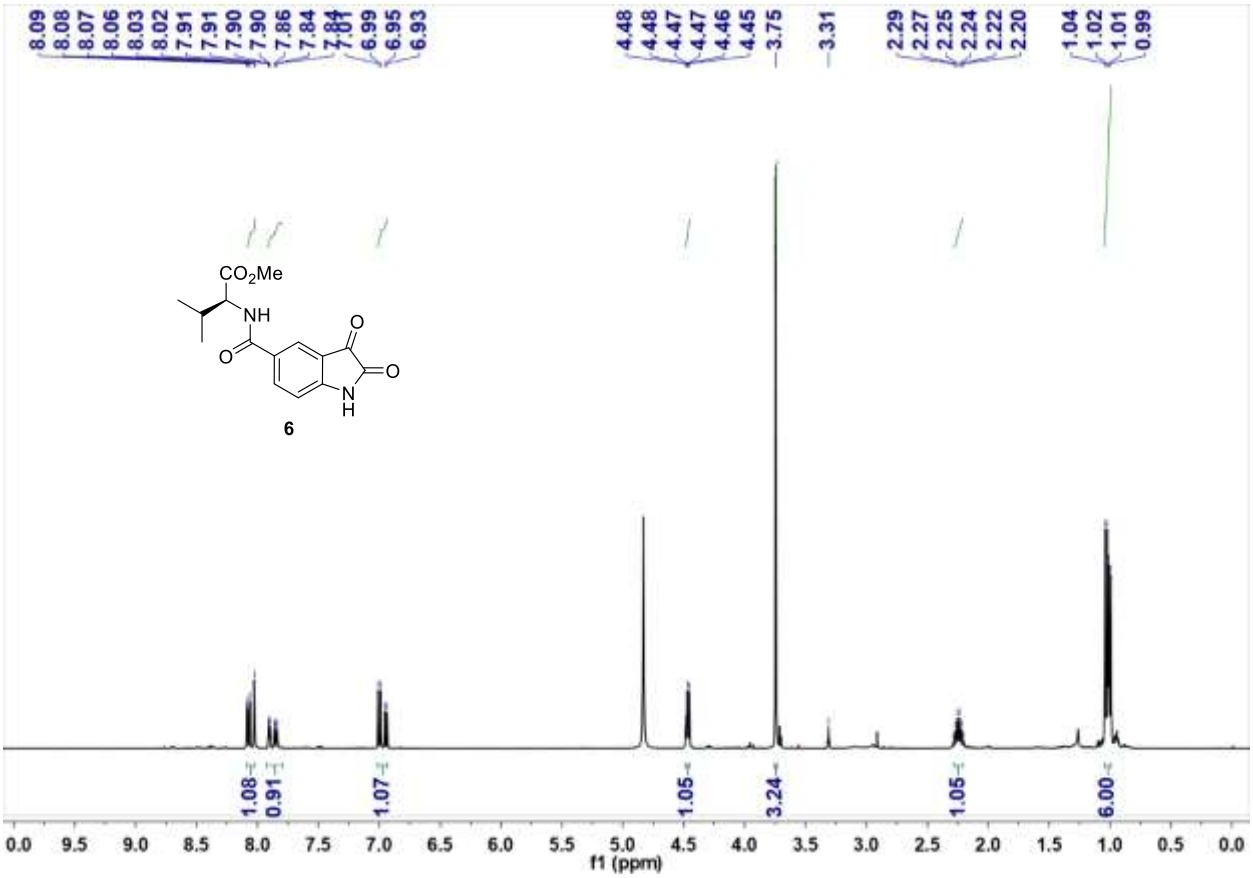

172.20 171.44 169.56 167.55 165.56 165.34 164.51 156.09 149.78 148.50 141.20 136.37 130.98 129.92 128.79 128.03 126.44 122.75 122.71 79.78 65.85 59.30 53.56 52.86 51.28 51.22 36.80 31.68 30.28 29.38 29.35 29.08 27.15 22.34 18.33 18.03 13.05
f1 (ppm)
7

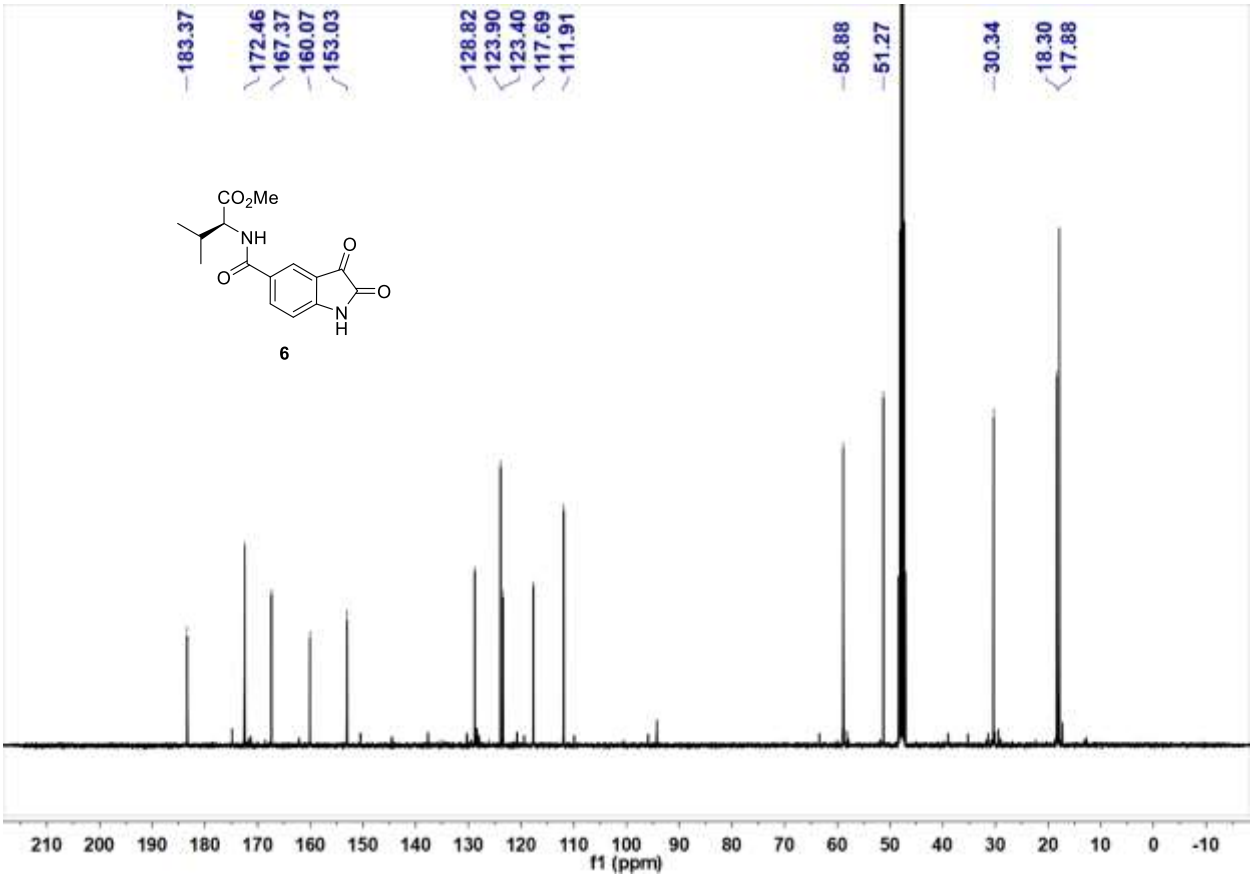

8.33
8.32
7.96
7.74
7.74
7.72
7.72
7.63
7.60
7.55
7.54
7.26
7.21
7.21
7.19
7.19
7.06
7.04
4.80
4.79
4.78
4.69
4.68
4.67
4.01
3.86
3.03
3.02
3.02
3.01
3.00
2.32
1.94
1.93
1.92
1.92
1.91
1.33
1.00
1.08
1.10
1.05
1.04
1.03
1.01
2.06
2.07
3.05
3.02
2.01
3.18
2.11
6.03
f1 (ppm)

10

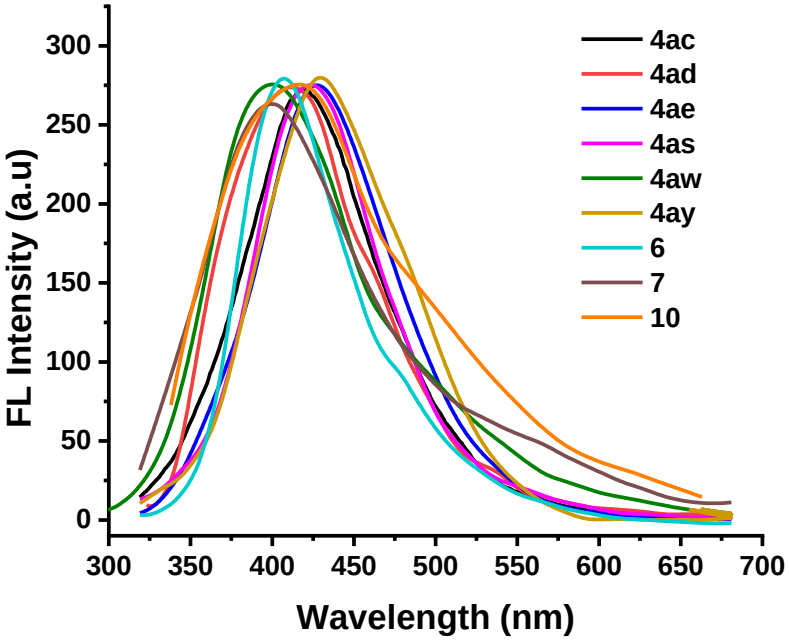

165.60
165.48
164.86
151.23
148.85
147.55
142.25
139.32
138.38
134.62
133.25
132.88
132.73
129.97
129.19
128.34
126.66
125.07
122.60
122.28
117.35
95.35
95.22
87.42
64.79
53.52
53.44
44.73
37.05
32.98
29.93
23.24
14.31
f1 (ppm)

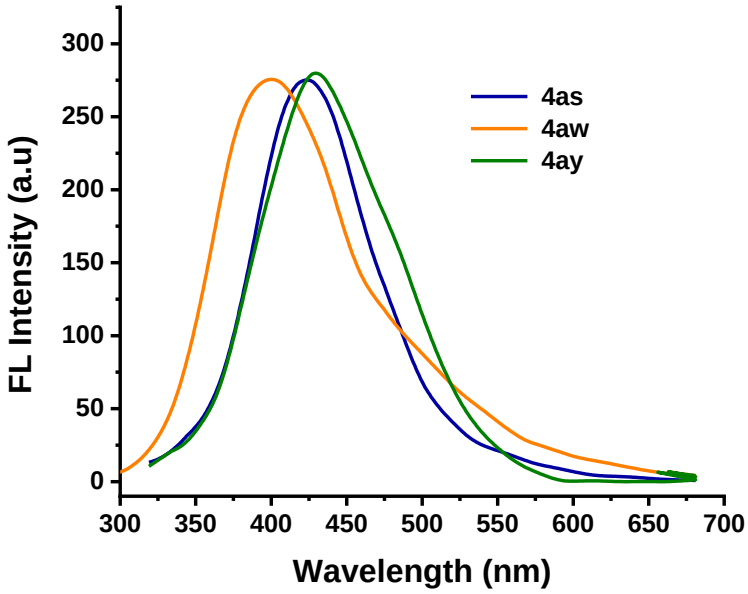
10


8.09
8.08
8.07
8.06
8.03
8.02
7.91
7.91
7.90
7.90
7.86
7.84
7.84
7.81
6.99
6.95
6.93
4.48
4.48
4.47
4.47
4.46
4.45
3.75
3.31
2.29
2.27
2.25
2.24
2.22
2.20
1.04
1.02
1.01
0.99
CO2Me
NH
O
O
O
O
N
H
6
1.08
0.91
1.07
1.05
3.24
1.05
6.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

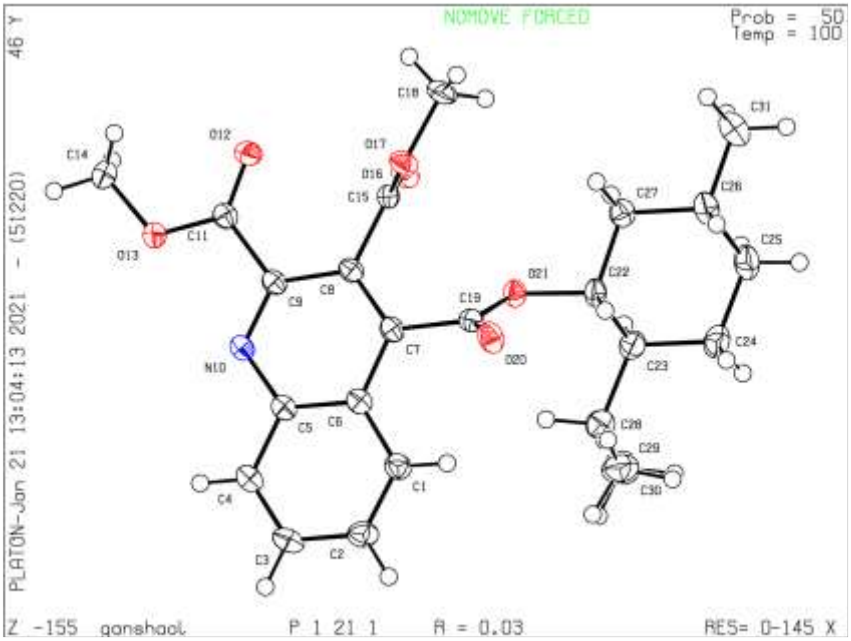

183.37
172.46
167.37
160.07
153.03
128.82
123.90
123.40
117.69
111.91
58.88
51.27
30.34
18.30
17.88
CO2Me
NH
O
O
O
O
N
H
6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

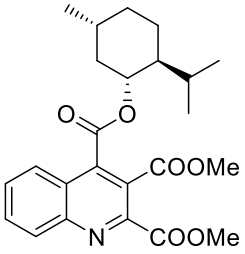
5.2 Fluorescence Measurement of selected Products





6. X-ray single-crystal data





4an : CCDC-2079883

CCDC-2079883	
Formula	$C_{24}H_{29}NO_6$
Formula weight	427.48
Temperature / K	100
Crystal system	Monoclinic
space group	*P 1 21 1*
a / Å	8.42220(10)
b / Å	8.60860(10)
c / Å	15.5730(2)
a / °	90
β / °	93.6740(10)
γ/ °	90
V / Å3	1126.77(2)
Z	2
Dx (g/cm^3)	1.260
μ / mm^{-1}	0.741

F (000)	456.0
Reflections collected	21426
Independent reflections	4277
*R*int	0.0351
GOF	1.040
Final R indices ($I > 2\sigma(I)$)	0.0278,0.0717
R indices (all data)	0.0284,0.0723

Datablock:

Bond precision: C-C = 0.0023 A Wavelength=1.54184

Cell: a=8.4222(1) b=8.6086(1) c=15.5730(2)
alpha=90 beta=93.674(1) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	1126.77(2)	1126.77(2)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C24 H29 N O6	C24 H29 N O6
Sum formula	C24 H29 N O6	C24 H29 N O6
Mr	427.48	427.48
Dx,g cm-3	1.260	1.260
Z	2	2
Mu (mm-1)	0.741	0.741
F000	456.0	456.0
F000'	457.46	
h,k,lmax	10,10,19	10,10,19
Nref	4573[2447]	4277
Tmin,Tmax	0.837,0.929	0.890,1.000
Tmin'	0.801	

Correction method= # Reported T Limits: Tmin=0.890 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.75/0.94 Theta(max)= 73.984

R(reflections)= 0.0278(4190) wR2(reflections)= 0.0723(4277)

S = 1.040 Npar= 285

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

PLAT791_ALERT_4_G Model has Chirality at C22 (Sohnke SpGr) R Verify
PLAT791_ALERT_4_G Model has Chirality at C23 (Sohnke SpGr) S Verify
PLAT791_ALERT_4_G Model has Chirality at C26 (Sohnke SpGr) R Verify
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L= 0.600 97 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density. 2 Info
PLAT992_ALERT_5_G Repd & Actual _reflns_number_gt Values Differ by 2 Check

0 ALERT level A = Most likely a serious problem - resolve or explain
0 ALERT level B = A potentially serious problem, consider carefully
0 ALERT level C = Check. Ensure it is not caused by an omission or oversight
6 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
1 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
4 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check