

Supporting Information

Palladium-Catalyzed Stereoretentive Olefination of Unactivated C(sp³)-H Bonds with Vinyl Iodides at Room Temperature: Synthesis of β -Vinyl α -Amino Acids

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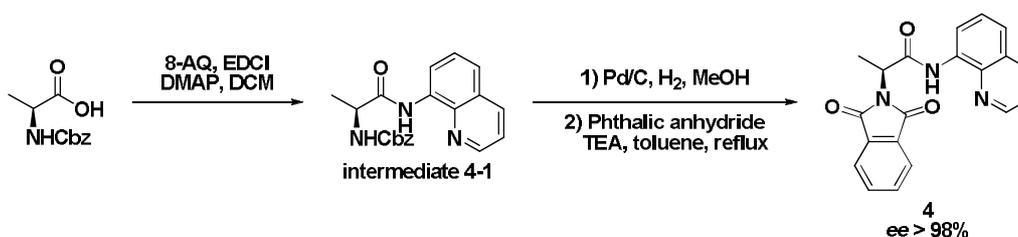
1. Reagents: All commercial materials were used as received unless otherwise noted. The toluene for reaction was obtained from a JC Meyer solvent dispensing system and used without further purification. Flash chromatography was performed using 230-400 mesh SiliaFlash 60® silica gel (Silicycle Inc.). Pd(OAc)₂ (98%, Aldrich), silver trifluoroacetate (98%, Alfa Aesar), silver acetate (98%, Alfa Aesar), 1,1,2,2-tetrachloroethane (98.5%, Acros), potassium bicarbonate (99.7%-100.5%, Alfa Aesar), trifluoroacetic acid (99.5+%, Alfa Aesar) and dioxane (99+%, Alfa Aesar) were used in the Pd-catalyzed reactions. 8-aminoquinoline (AQ) (98%, Aldrich) were purchased from Aldrich and used without further purification.

2. Instruments: NMR spectra were recorded on Bruker AV-360 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet, q = quartet. High resolution ESI mass experiments were operated on a Waters LCT Premier instrument.

3. Preparation of compound 4 and vinyl iodides for C-H olefination

Vinyl iodides **5**^[1], **13**^[1], **21**^[2], **25**^[3], **29**^[4], **33**^[5], and **35**^[6] were prepared as reported in the references. Alanine substrate **4** and vinyl iodides **9**, **11**, **15**, **17**, **19**, **23**, **27**, **31** were prepared as follows.

3.1 Preparation of alanine substrate 4



To an ice-water cooled solution in dichloromethane (60 mL) of *N*-Cbz alanine (2.23 g, 10 mmol, 1 equiv), 8-aminoquinoline (1.15 g, 8 mmol, 0.8 equiv) and DMAP (244 mg, 2 mmol, 0.2 equiv) was added EDCI (2.33 g, 15 mmol, 1.5 equiv) portionwise. After addition, the ice-water bath was removed and the reaction was stirred at room temperature for 4 hours. After completion, the reaction was diluted with dichloromethane (100 mL), washed with 0.1 M aqueous solution of sodium hydroxide and brine. The organic layer was dried over sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (hexanes : ethyl acetate =

4:1), giving 2.7 g of intermediate **4-1** as a yellowish syrup in a 96% yield (yield based on 8-aminoquinoline). ¹H NMR (CDCl₃, 360 MHz, ppm): δ 1.60-1.62 (d, *J* = 6.8 Hz, 1H), 4.65 (s, 1H), 5.20 (s, 2H), 5.75 (s, 1H), 7.29-7.54 (m, 8H), 8.15-8.18 (m, 1H), 8.76-8.78 (m, 2H), 10.27 (s, 1H); ¹³C NMR (CDCl₃, 90 MHz, ppm) δ 19.21, 51.83, 67.05, 116.65, 121.72, 122.00, 127.27, 127.91, 128.09, 128.18, 128.56, 133.96, 136.31, 138.50, 148.41, 155.94, 170.84.

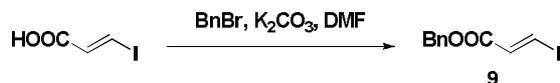
The intermediate **4-1** (2.0 g, 5.7 mmol, 1 equiv) and Pd/C (200 mg, 10% on carbon) in methanol (50 mL) was hydrogenated under H₂ atmosphere for 4 hours. After filtration to remove the Pd/C, the solution was concentrated *in vacuo* to remove the methanol. The residue was re-suspended in toluene (100 mL) with phthalic anhydride (931 mg, 6.3 mmol, 1.1 equiv) and triethylamine (1.2 mL, 8.6 mmol, 1.5 equiv). The reaction mixture was heated under reflux with Dean-Stark trap overnight. After concentration *in vacuo*, the residue was purified by flash silica gel chromatography (dichloromethane : ethyl acetate = 20:1), giving 1.4 g of alanine substrate **4** as a white crystal in a 71% yield over two steps.

3.2 Preparation of (*E*)-3-iodoacrylic acid



A mixture of propiolic acid (10 g, 143 mmol, 1 equiv) and aqueous hydroiodic acid (40 mL of a 47% w/w aqueous solution, 228 mmol, 1.6 equiv) was heated in a sealed flask at 95 °C for 20 hours. The resulting mixtures were cooled to room temperature to afford a suspension of the acid in excess aqueous hydroiodic acid. Filtration under vacuum gave 19.0 g of white needle in a yield of 67%.

3.3 Preparation of vinyl iodide **9**



To a solution of (*E*)-3-iodoacrylic acid (1.98 g, 10 mmol, 1 equiv) and potassium carbonate (2.07 g, 15 mmol, 1.5 equiv) in DMF (20 mL) was added benzyl bromide (1.18 mL, 10 mmol, 1 equiv). The reaction was diluted with diethyl ether (50 mL) after stirred at room temperature for 1 hour. The organic layer was washed thoroughly with water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 15:1), giving 2.5 g of product as a yellowish liquid in a 87% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 5.18 (s, 2H), 6.90-6.95 (d, *J* = 15.1 Hz, 1H), 7.37 (s, 5H), 7.91-7.96 (d, *J* = 15.1 Hz, 1H); ¹³C NMR (CDCl₃, 90 MHz, ppm)

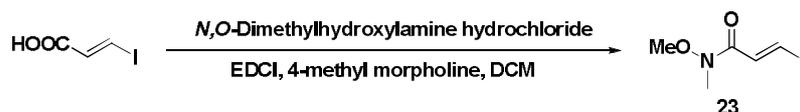
δ 66.83, 100.29, 128.45, 128.56, 128.73, 135.48, 136.27, 164.02.

3.4 Preparation of vinyl iodide 11



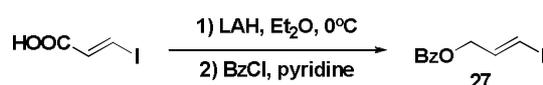
To a solution of (*E*)-3-iodoacrylic acid (1.98 g, 10 mmol, 1 equiv) and imidazol (1.00 g, 15 mmol, 1.5 equiv) in DMF (20 mL) was added TIPSCl (2.14 mL, 10 mmol, 1 equiv). The reaction was diluted with diethyl ether (100 mL) after stirred at room temperature for 1 hours. The solution was washed thoroughly with water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 30:1), giving 2.1 g of product as a colorless liquid in a 60% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 1.06-1.08 (m, 21H), 6.85-6.89 (d, *J* = 14.8 Hz, 1H), 7.81-7.85 (d, *J* = 14.8 Hz, 1H); ¹³C NMR (CDCl₃, 90 MHz, ppm) δ 17.85, 22.79, 100.07, 138.34, 163.65.

3.5 Preparation of vinyl iodide 23



To an ice-water cooled solution of (*E*)-3-iodoacrylic acid (1.98 g, 10 mmol, 1 equiv), *N,O*-dimethylhydroxylamine hydrochloride (1.07 g, 11 mmol, 1.1 equiv), 4-methyl morpholine (1.21 mL, 11 mmol, 1.1 equiv) in DCM (20 mL) was added EDCI (2.1 g, 11 mmol, 1.1 equiv) in small portions. The reaction was stirred at 0 °C for 2 hours. After completion, the solution was washed thoroughly with diluted hydrochloric acid and water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (hexanes : ethyl acetate = 2:1), giving 2.1 g of product as a yellowish syrup in a 88% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 3.13 (s, 3H), 3.63 (s, 3H), 7.32-7.36 (d, *J* = 14.8 Hz, 1H), 7.70-7.74 (d, *J* = 14.8 Hz, 1H); ¹³C NMR (CDCl₃, 90 MHz, ppm) δ 32.17, 61.98, 97.69, 133.93, 164.37; HRMS: calculated for C₅H₉INO₂ [M+H⁺]: 241.9672; found: 241.9673.

3.6 Preparation of vinyl iodide 27

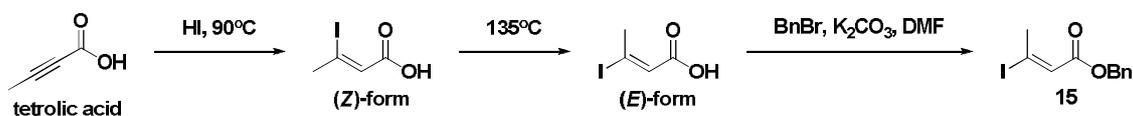


To an ice-water cooled solution of (*E*)-3-iodoacrylic acid (1.98 g, 10 mmol, 1 equiv) in diethyl ether (20 mL) was slowly added lithium aluminum hydride (570 mg, 15 mmol, 1.5 equiv).

The reaction was stirred at 0 °C for 2 hours. After completion, the reaction was quenched by **carefully** adding diluted hydrochloric acid. The organic layer was separated, and washed thoroughly with diluted hydrochloric acid and brine. The organic layer was dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was used for next step without further purification.

To an ice-water cooled solution of the residue above in pyridine (20 mL) was added benzoyl chloride (1.39 mL, 12 mmol, 1.2 equiv). The reaction was stirred overnight while warming up to room temperature. After completion, the reaction was diluted with diethyl ether, washed with diluted hydrochloric acid and brine and dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 5:1), giving 1.7 g of product as a colorless liquid in a 59% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 4.73-4.74 (d, *J* = 5.8 Hz, 1H), 6.56-6.60 (d, *J* = 14.8 Hz, 1H), 6.72-6.80 (m, 1H), 7.43-7.47 (m, 2H), 7.56-7.60 (m, 1H), 8.03-8.05 (d, *J* = 7.6 Hz, 2H); ¹³C NMR (CDCl₃, 90 MHz, ppm) δ 66.23, 81.21, 100.08, 128.58, 129.80, 133.38, 139.74, 166.08.

3.7 Preparation of vinyl iodide 15

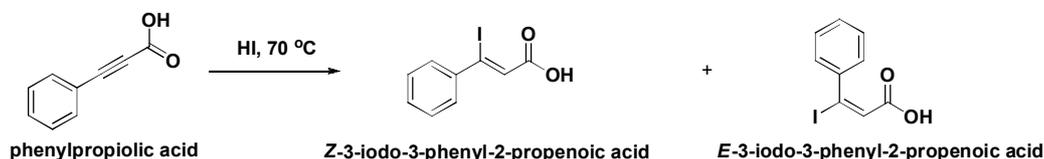


Tetrolic acid (3.10 g, 36.5 mmol, 1 equiv) was combined with hydroiodic acid (8.52 mL of a 47% w/w aqueous solution, 48.1 mmol, 1.3 equiv), and the resulting solution was heated to 90 °C and stirred for 4 hours. Cold water (75 mL) was added and the product was isolated by filtration and washed with cold water then dried under vacuum to give *Z*-3-iodo-2-butenoic acid as pale yellow needles (6.0 g, 77%). The (*Z*)-acid was heated to 135 °C in a sealed tube for 24 hours to provide a mixture of *Z*-3-iodo-2-butenoic acid and *E*-3-iodo-2-butenoic acid at a ratio of approximate 1:4. The mixture was used for next step without further purification.

To a solution of the mixture (2.12 g, 10 mmol, 1 equiv) and potassium carbonate (2.07 g, 15 mmol, 1.5 equiv) in DMF (20 mL) was added benzyl bromide (1.18 mL, 10 mmol, 1 equiv). The reaction was diluted with diethyl ether (100 mL) after stirred at room temperature for one hour. The solution was washed thoroughly with water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 30:1), giving 1.5 g of product as a yellowish liquid in a 50% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 3.01 (s, 3H), 5.15 (s, 2H), 6.70 (s, 1H), 7.37 (s, 5H);

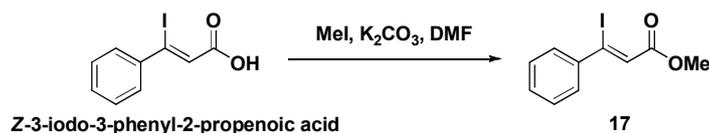
^{13}C NMR (CDCl_3 , 90 MHz, ppm) δ 31.16, 66.25, 121.32, 128.34, 128.41, 128.67, 131.14, 135.68, 163.88.

3.8 Preparation of *Z/E*-3-iodo-3-phenyl-2-propenoic acid



A 47% (W/W) solution of hydroiodic acid (4 mL, 22.6 mmol, 1.3 equiv) was added dropwise to phenylpropionic acid (2.5 g, 17.1 mmol, 1 equiv). The reaction mixture was stirred at 70 °C overnight. During the reaction, a yellow solid was formed. A 5% aqueous solution of sodium thiofulfate (8 mL) was then added. The phases were separated and the aqueous phase was extracted with diethyl ether (50 mL). The combined organic phases were washed with brine, dried with anhydrous sodium sulfate, filtered and concentrated under reduced pressure. Under this condition, a mixture of *Z*-3-iodo-3-phenyl-2-propenoic acid and *E*-3-iodo-3-phenyl-2-propenoic acid (3.46 g, 75%) was obtained in a ratio of *E*:*Z* = 1:4. To separate the two isomers, the product was recrystallized from diethyl ether and hexanes. The *E*-isomer crystallized first, leaving the *Z*-isomer in solution. Repeated recrystallization gave *Z*-3-iodo-3-phenyl-2-propenoic acid (920 mg, 20%) as a yellow crystal, and *E*-3-iodo-3-phenyl-2-propenoic acid (450 mg, 10%) as a white crystal.

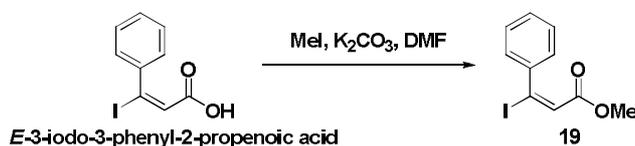
3.9 Preparation of vinyl iodide 17



To a solution of *Z*-3-iodo-3-phenyl-2-propenoic acid (920 mg, 3.36 mmol, 1 equiv) and potassium carbonate (695 mg, 5.04 mmol, 1.5 equiv) in DMF (10 mL) was added methyl iodide (0.27 mL, 4.37 mmol, 1.3 equiv). The reaction was diluted with diethyl ether (30 mL) after stirred at room temperature for one hour. The solution was washed thoroughly with water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 30:1), giving 890 mg of product as a yellowish liquid in a 92% yield. ^1H NMR (CDCl_3 , 360 MHz, ppm): δ 3.81 (s, 3H), 6.64 (s, 1H), 7.35-7.36 (d, J = 2.5 Hz, 3H), 7.51-7.52 (d, J = 3.6 Hz, 2H); ^{13}C NMR (CDCl_3 , 90 MHz, ppm) δ 51.96, 116.88, 126.52, 128.54, 128.87, 130.18, 143.35, 165.18; HRMS:

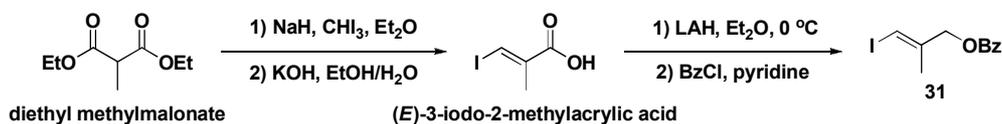
calculated for C₁₀H₁₀IO₂ [M+H⁺]: 288.9720; found: 288.9718.

3.10 Preparation of vinyl iodide 19



To a solution of *Z*-3-iodo-3-phenyl-2-propenoic acid (450 mg, 1.64 mmol, 1 equiv) and potassium carbonate (339 mg, 2.46 mmol, 1.5 equiv) in DMF (5 mL) was added methyl iodide (0.13 mL, 2.13 mmol, 1.3 equiv). The reaction was diluted with diethyl ether (30 mL) after stirred at room temperature for one hour. The solution was washed thoroughly with water, and then dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 30:1), giving 420 mg of product as a white crystal in a 89% yield. ¹H NMR (CDCl₃, 360 MHz, ppm): δ 3.56 (s, 3H), 6.86 (s, 1H), 7.32 (s, 5H); ¹³C NMR (CDCl₃, 90 MHz, ppm) δ 51.72, 118.53, 127.60, 128.04, 129.35, 131.86, 142.29, 164.04; HRMS: calculated for C₁₀H₁₀IO₂ [M+H⁺]: 288.9720; found: 288.9718.

3.11 Preparation of vinyl iodide 31



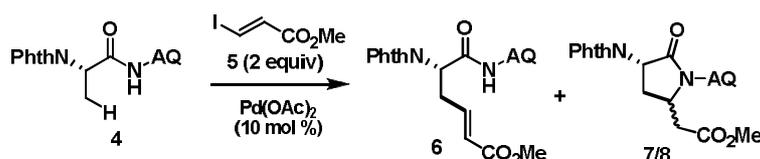
To a suspension of sodium hydride (60% in mineral oil, 550 mg, 13.8 mmol, 1.2 equiv) in diethyl ether (20 mL) was added diethyl methylmalonate (2.00 g, 11.5 mmol, 1 equiv) over 1 hour and the reaction mixture was heated under reflux for 2.5 hours. After being cooled to room temperature, iodoform (4.52 g, 11.5 mmol, 1 equiv) was added. The reaction mixture was again heated under reflux for 15 hours and then cooled to 0 °C. Hydrochloric acid (10%, 6 mL) was slowly added and stirred for 20 minutes. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was dissolved in hexanes and the precipitate filtered off. The filtrate was concentrated *in vacuo* and the residue dissolved in a mixture of ethanol (15 mL) and water (5 mL). To this solution was added potassium hydroxide (1.61 g, 28.7 mmol, 2.5 equiv) and the reaction mixture was heated under reflux for 16 hours. The reaction

mixture was then concentrated *in vacuo* and the residue treated with saturated aqueous K_2CO_3 solution (15 mL). The aqueous solution was washed with methylene chloride and the combined organic layers were discarded. It was then carefully acidified with hydrochloric acid (8 M, 10 mL) and extracted with methylene chloride. The combined organic layers were dried over sodium sulfate and concentrated *in vacuo*. The crude product was used for next step without further purification.

To an ice-water cooled solution of the crude product obtained above in diethyl ether (20 mL) was slowly added lithium aluminum hydride (570 mg, 15 mmol, 1.3 equiv). The reaction was stirred at 0 °C for 2 hours. After completion, the reaction was quenched by adding diluted hydrochloric acid. The organic layer was separated, and washed thoroughly with diluted hydrochloric acid and brine. The organic layer was dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue was used for next step without further purification.

To an ice-water cooled solution of the residue above in pyridine (20 mL) was added benzoyl chloride (1.39 mL, 12 mmol, 1.04 equiv). The reaction was stirred overnight while warming up to room temperature. After completion, the reaction was diluted with diethyl ether, washed with diluted hydrochloric acid and brine and dried with anhydrous sodium sulfate. The residue after concentration *in vacuo* was purified by flash silica gel chromatography (30-60 °C petroleum ether : diethyl ether = 5:1), giving 1.1 g of product as a colorless liquid in a 32% yield.

4. General procedure for screening conditions in Table 1

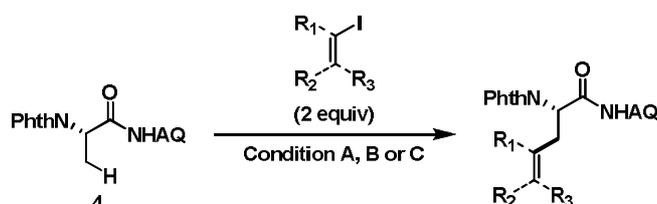


Reactions in **Table 1** were performed in 4 mL capped vials according to the conditions listed in **Table 1** at a 0.2 mmol scale with the concentration of 0.2 M. After completion, the reactions were diluted with dichloromethane (10 mL), then filtrated through a pad of Celite. After concentration *in vacuo*, the crude residue was dissolved in 1000 μ L of deuterated chloroform for 1H -NMR analysis. Dibromomethane (34.8 mg, 0.2 mmol, 1 equiv, set the integration of this peak around 4.9-5.0 ppm as 2.00) was added as internal standard for determining the yield. Yields of compound **6** and **7/8** were determined as follows:

$$\text{yield}_{\text{compound 6}} = \text{integration of doublet } (\delta 5.99-6.04) \times 100\%$$

$$\text{yield}_{\text{compound 7/8}} = \text{integration of multiplet } (\delta 2.99-3.07) \times 100\%$$

5. General procedure for AQ-directed Pd-catalyzed C-H olefination

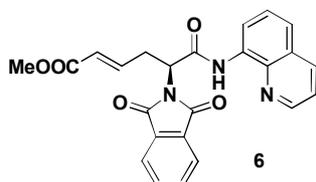


Olefination reactions under condition A: Alanine substrate **4** (69 mg, 0.2 mmol, 1 equiv), vinyl iodide (2 equiv), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 0.1 equiv), silver acetate (50 mg, 0.6 mmol, 3 equiv) and trifluoroacetic acid (15 μ L, 0.4 mmol, 2 equiv) were suspended into dioxane (1 mL). The resulting solution was stirred at room temperature. **Open to air! Protection with argon or nitrogen was not necessary.** After 24 hours, 1 M aq. NaOH solution (2 mL) and dichloromethane (5 mL) were added. Organic layer was separated, and the aqueous layer was re-extracted with dichloromethane (5 mL) twice. Combined organic layer was concentrated *in vacuo*, and the resulting residue was purified by flash silica gel chromatography.

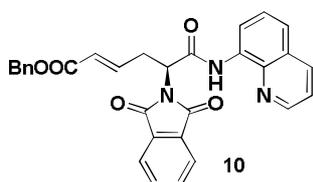
Olefination reactions under condition B: Alanine substrate **4** (69 mg, 0.2 mmol, 1 equiv), vinyl iodide (2 equiv), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 0.1 equiv) and silver trifluoroacetate (110.5 mg, 0.5 mmol, 2.5 equiv) were suspended into 1,1,2,2-tetrachloroethane (TCE) (1 mL) and water (1 mL). The resulting solution was stirred **vigorously** (important) at room temperature. **Open to air! Protection with argon or nitrogen was not necessary.** After 24 hours, 1 M aq. NaOH solution (2 mL) and dichloromethane (5 mL) were added. Organic layer was separated, and the aqueous layer was re-extracted with dichloromethane (5 mL) twice. Combined organic layer was concentrated *in vacuo*, and the resulting residue was purified by flash silica gel chromatography.

Olefination reactions under condition C: Alanine substrate **4** (69 mg, 0.2 mmol, 1 equiv), vinyl iodide (2 equiv), Pd(OAc)₂ (4.5 mg, 0.02 mmol, 0.1 equiv) and silver trifluoroacetate (110.5 mg, 0.5 mmol, 2.5 equiv) were suspended into 1,1,2,2-tetrachloroethane (TCE) (1 mL) and water (1 mL). The resulting solution was stirred **vigorously** (important) at 65 °C. **Open to air! Protection with argon or nitrogen was not necessary.** After 24 hours, 1 M aq. NaOH

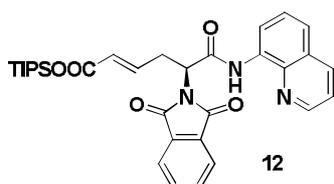
solution (2 mL) and dichloromethane (5 mL) were added. Organic layer was separated, and the aqueous layer was re-extracted with dichloromethane (5 mL) twice. Combined organic layer was concentrated *in vacuo*, and the resulting residue was purified by flash silica gel chromatography.



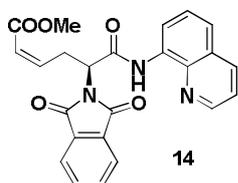
Flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave **65** mg of product as a white foam in 76% yield under **Condition A**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 3.32-3.49 (m, 2H), 3.66 (s, 3H), 5.26-5.30 (dd, $J = 5.8, 9.7$ Hz, 1H), 5.99-6.04 (d, $J = 15.8$ Hz, 1H), 6.93- 7.01 (m, 1H), 7.36-7.38 (dd, $J = 4.0, 8.3$ Hz, 1H), 7.47-7.48 (m, 2H), 7.73-7.76 (m, 2H), 7.87-7.89 (m, 2H), 8.08-8.10 (dd, $J = 1.1, 8.3$ Hz, 1H), 8.56-8.58 (dd, $J = 1.4, 4.0$ Hz, 1H), 8.65-8.67 (m, 1H), 10.25 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 31.77, 51.66, 53.65, 116.78, 121.75, 122.22, 123.86, 124.80, 127.28, 127.86, 131.64, 133.67, 134.52, 136.35, 138.41, 143.27, 148.41, 165.72, 166.29, 167.84; **HRMS**: calculated for $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}_5$ [$\text{M}+\text{H}^+$]: 430.1397; found: 430.1397.



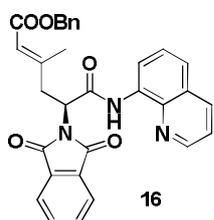
Flash silica gel chromatography (hexanes : ethyl acetate = 4:1) gave **86** mg of product as a white foam in 85% yield under **Condition A**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 3.31-3.44 (m, 2H), 5.07 (s, 3H), 5.22-5.27 (dd, $J = 6.1, 9.0$ Hz, 1H), 6.95-7.03 (m, 1H), 7.20-7.31 (m, 6H), 7.42-7.45 (m, 2H), 7.67-7.69 (m, 2H), 7.81-7.83 (m, 2H), 8.02-8.04 (d, $J = 8.3$ Hz, 1H), 8.49-8.50 (d, $J = 4.0$ Hz, 1H), 8.61-8.64 (m, 1H), 10.2 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 31.84, 53.60, 66.23, 116.74, 121.72, 122.19, 123.81, 124.90, 127.24, 127.82, 128.16, 128.23, 128.57, 131.62, 133.66, 134.47, 135.86, 136.29, 138.37, 143.64, 148.39, 165.59, 165.68, 167.81; **HRMS**: calculated for $\text{C}_{30}\text{H}_{24}\text{N}_3\text{O}_5$ [$\text{M}+\text{H}^+$]: 506.1710; found: 506.1704.



Flash silica gel chromatography (hexanes : ethyl acetate = **10:1**) gave **77** mg of product as a white foam in **68%** yield under **Condition A**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 0.94-0.97 (m, 18H), 1.15-1.25 (m, 3H), 3.29-3.36 (m, 1H), 3.39-3.48 (m, 1H), 5.27-5.31 (dd, *J* = 5.8, 10.8 Hz, 1H), 5.94-5.98 (d, *J* = 15.5 Hz, 1H), 6.85-6.94 (m, 1H), 7.32-7.36 (dd, *J* = 4.3, 8.3 Hz, 1H), 7.45-7.47 (m, 2H), 7.70-7.73 (m, 2H), 7.83-7.86 (m, 2H), 8.06-8.08 (dd, *J* = 1.4, 8.3 Hz, 1H), 8.56-8.58 (dd, *J* = 1.8, 4.3 Hz, 1H), 8.66-8.68 (m, 1H), 10.28 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 11.88, 17.71, 31.56, 53.57, 116.71, 121.69, 122.17, 123.74, 126.95, 127.22, 127.81, 131.52, 133.64, 134.45, 136.29, 138.37, 143.33, 148.41, 165.24, 165.70, 167.70; **HRMS**: calculated for C₃₂H₃₈N₃O₅Si [M+H⁺]: 572.2575; found: 572.2563.

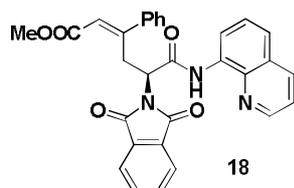


Flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave **9** mg of product as a white foam in **10%** yield under **Condition A**; 44 mg of product in **51%** yield under **Condition C**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 3.70 (s, 3H), 3.75-3.79 (m, 2H), 5.30-5.34 (dd, *J* = 6.8, 8.6 Hz, 1H), 5.91-5.94 (d, *J* = 11.5 Hz, 1H), 6.32-6.39 (m, 1H), 7.37-7.40 (dd, *J* = 4.3, 8.3 Hz, 1H), 7.49-7.50 (m, 2H), 7.74-7.75 (m, 2H), 7.87-7.89 (m, 2H), 8.10-8.13 (d, *J* = 8.3 Hz, 1H), 8.64-8.65 (m, 1H), 8.69-8.71 (m, 1H), 10.32 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 28.83, 51.49, 54.44, 116.84, 121.74, 122.12, 123.09, 123.77, 127.35, 127.92, 131.86, 133.93, 134.41, 136.35, 138.56, 143.82, 148.43, 166.14, 166.37, 167.98; **HRMS**: calculated for C₂₄H₂₀N₃O₅ [M+H⁺]: 430.1397; found: 430.1397.

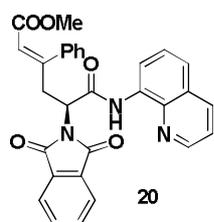


Flash silica gel chromatography (hexanes : ethyl acetate = **10:1**) gave **63** mg of product as a white foam in **61%** yield under **Condition A**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 2.29 (s, 3H), 3.21-3.26 (dd, *J* = 5.0, 14.0 Hz, 1H), 3.33-3.40 (dd, *J* = 10.8, 14.0 Hz, 1H), 5.01 (s, 2H), 5.38-5.42 (dd, *J* = 5.0, 10.8 Hz, 1H), 5.81 (s, 1H), 7.18-7.33 (m, 6H), 7.45-7.46 (m, 2H), 7.68-7.71 (m,

2H), 7.83-7.85 (m, 2H), 8.04-8.07 (dd, $J = 1.4, 8.3$ Hz, 1H), 8.50-8.52 (dd, $J = 1.4, 4.0$ Hz, 1H), 8.64-8.67 (m, 1H), 10.28 (s, 1H); ^{13}C NMR (CDCl₃, 90 MHz, ppm) δ 18.28, 39.82, 52.60, 65.54, 116.71, 119.18, 121.70, 122.18, 123.79, 127.24, 127.82, 128.00, 128.06, 128.50, 131.58, 133.65, 134.43, 136.09, 136.29, 138.38, 148.39, 154.84, 165.73, 165.94, 167.81; **HRMS**: calculated for C₃₁H₂₆N₃O₅ [M+H⁺]: 520.1867; found: 520.1862.

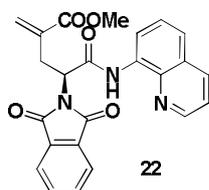


Flash silica gel chromatography (hexanes : ethyl acetate = **10:1**) gave **45** mg of product as a white foam in **45%** yield under **Condition A**. ^1H NMR (CDCl₃, 360 MHz, ppm): δ 3.76 (s, 3H), 3.96-4.03 (dd, $J = 11.5, 13.0$ Hz, 1H), 4.40-4.44 (dd, $J = 2.9, 13.0$ Hz, 1H), 5.37-5.41 (dd, $J = 3.2, 11.5$ Hz, 1H), 6.13 (s, 1H), 6.97-7.01 (m, 1H), 7.05-7.09 (m, 1H), 7.26-7.28 (m, 2H), 7.36-7.40 (q, $J = 4.3$ Hz, 1H), 7.48-7.52 (m, 2H), 7.59-7.66 (m, 4H), 8.10-8.12 (dd, $J = 1.4, 8.3$ Hz, 1H), 8.66-8.67 (dd, $J = 1.4, 4.0$ Hz, 1H), 8.72-8.75 (dd, $J = 2.9, 6.1$ Hz, 1H), 10.45 (s, 1H); ^{13}C NMR (CDCl₃, 90 MHz, ppm) δ 30.55, 51.63, 54.44, 116.92, 119.96, 121.64, 121.94, 123.21, 126.99, 127.38, 127.92, 128.48, 128.96, 131.60, 133.85, 134.22, 136.29, 138.71, 140.25, 148.34, 156.69, 166.12, 166.74, 167.64; **HRMS**: calculated for C₃₀H₂₄N₃O₅ [M+H⁺]: 506.1710; found: 506.1705.

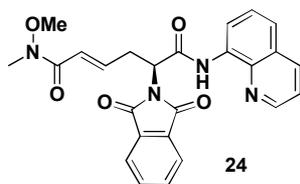


Flash silica gel chromatography (hexanes : ethyl acetate = **5:1**) gave **91** mg of product as a white foam in **90%** yield under **Condition A**. ^1H NMR (CDCl₃, 360 MHz, ppm): δ 3.52 (s, 3H), 3.62-3.67 (dd, $J = 4.3, 14.4$ Hz, 1H), 3.78-3.85 (dd, $J = 10.8, 14.0$ Hz, 1H), 5.11-5.15 (dd, $J = 4.7, 10.8$ Hz, 1H), 6.10 (s, 1H), 7.24-7.39 (m, 6H), 7.49-7.50 (m, 2H), 7.75-7.77 (m, 2H), 7.85-7.87 (m, 2H), 8.09-8.12 (d, $J = 8.3$ Hz, 1H), 8.56-8.57 (dd, $J = 1.1, 4.0$ Hz, 1H), 8.66-8.68 (m, 1H), 10.25 (s, 1H); ^{13}C NMR (CDCl₃, 90 MHz, ppm) δ 38.83, 51.21, 53.20, 116.65, 120.32, 121.69, 122.14, 123.66, 127.24, 127.67, 127.80, 128.15, 128.41, 131.57, 133.63, 134.36, 136.29, 137.50, 138.37, 148.35, 154.53, 165.77, 165.93, 167.70; **HRMS**: calculated for C₃₀H₂₄N₃O₅ [M+H⁺]:

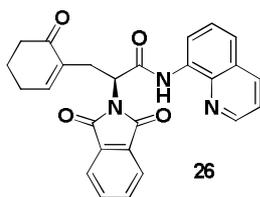
506.1710; found: 506.1705.



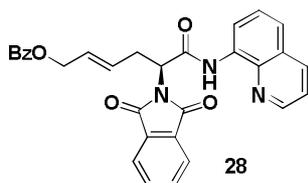
Flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave **58** mg of product as a white foam in **68%** yield under **Condition B**; **77** mg of product in **90%** yield under **Condition C**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 3.42-3.55 (m, 2H), 3.80 (m, 3H), 5.47-5.51 (dd, *J* = 5.0, 10.4 Hz, 1H), 5.65 (s, 1H), 6.19 (s, 1H), 7.35-7.38 (dd, *J* = 4.3, 8.3 Hz, 1H), 7.47-7.48 (m, 2H), 7.71-7.73 (m, 2H), 7.84-7.86 (m, 2H), 8.08-8.10 (d, *J* = 8.3 Hz, 1H), 8.61-8.62 (d, *J* = 2.5 Hz, 1H), 8.68-8.70 (m, 1H), 10.29 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 32.15, 52.30, 53.57, 116.70, 121.70, 122.04, 123.69, 127.27, 127.85, 129.45, 131.68, 133.83, 134.35, 135.95, 136.31, 138.43, 148.38, 166.22, 166.60, 167.92; **HRMS**: calculated for C₂₄H₂₀N₃O₅ [M+H⁺]: 430.1397; found: 430.1389.



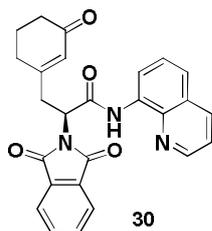
Flash silica gel chromatography (hexanes : ethyl acetate = ???) gave **69** mg of product as a yellowish solid in **75%** yield under **Condition A**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 3.16 (s, 3H), 3.34-3.41 (m, 1H), 3.50-3.59 (m, 4H), 5.29-5.34 (dd, *J* = 5.4, 10.4 Hz, 1H), 6.57-6.62 (d, *J* = 15.5 Hz, 1H), 6.91-7.00 (m, 1H), 7.37-7.41 (dd, *J* = 4.3, 8.3 Hz, 1H), 7.49-7.51 (m, 2H), 7.74-7.77 (m, 2H), 7.87-7.90 (m, 2H), 8.11-8.13 (dd, *J* = 1.8, 8.3 Hz, 1H), 8.61-8.62 (dd, *J* = 1.4, 4.3 Hz, 1H), 8.67-8.70 (m, 1H), 10.30 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 31.72, 53.97, 61.76, 116.84, 121.79, 122.22, 122.66, 123.83, 127.37, 127.93, 131.79, 133.79, 134.50, 136.41, 138.52, 141.20, 148.48, 165.99, 167.92; **HRMS**: calculated for C₂₅H₂₃N₄O₅ [M+H⁺]: 459.1663; found: 459.1658.



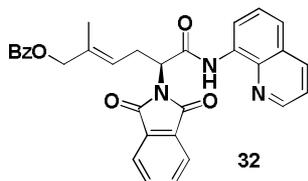
Flash silica gel chromatography (hexanes : ethyl acetate = **2:1**) gave **31** mg of product as a white solid (sensitive to light!) in **35%** yield under **Condition A**; **40** mg of product in **45%** yield under **Condition C**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 1.81-2.00 (m, 1H), 2.06-2.11 (m, 1H), 2.14-2.18 (m, 1H), 2.29-2.39 (m, 3H), 3.04-3.10 (dd, *J* = 10.8, 13.3 Hz, 1H), 3.43-3.48 (dd, *J* = 4.0, 13.3 Hz, 1H), 5.32-5.36 (dd, *J* = 4.7, 10.8 Hz, 1H), 6.87-6.89 (t, *J* = 3.6, 4.0 Hz, 1H), 7.55-7.69 (m, 3H), 7.95 (s, 4H), 8.36-8.38 (dd, *J* = 1.1, 8.3 Hz, 1H), 8.68-8.72 (m, 2H), 10.31 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 22.73, 25.85, 29.76, 29.85, 37.87, 53.57, 116.50, 122.09, 122.16, 123.34, 127.04, 128.12, 131.74, 134.14, 134.72, 135.19, 136.63, 148.78, 148.90, 166.42, 167.63, 197.83; **HRMS**: calculated for C₂₆H₂₂N₃O₄ [M+H⁺]: 440.1605; found: 440.1600.



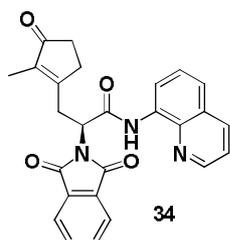
Flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave **76** mg of product as a white solid in **76%** yield under **Condition A**; **88** mg of product in **87%** yield under **Condition C**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 3.21-3.35 (m, 2H), 4.62-4.69 (m, 2H), 5.22-5.26 (dd, *J* = 6.1, 9.4 Hz, 1H), 5.83-5.97 (m, 2H), 7.32-7.36 (m, 3H), 7.45-7.50 (m, 3H), 7.63-7.65 (m, 2H), 7.80-7.83 (m, 4H), 8.05-8.08 (dd, *J* = 1.4, 8.3 Hz, 1H), 8.59-8.61 (dd, *J* = 1.4, 4.3 Hz, 1H), 8.69-8.71 (m, 1H), 10.30 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 32.00, 54.25, 64.74, 116.69, 121.64, 122.05, 123.55, 127.19, 127.78, 128.24, 128.82, 129.94, 129.94, 130.30, 131.55, 132.86, 133.75, 134.21, 136.24, 138.35, 148.32, 166.00, 166.18, 167.92; **HRMS**: calculated for C₃₀H₂₄N₃O₅ [M+H⁺]: 506.1710; found: 506.1704.



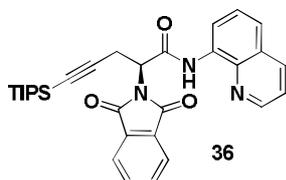
Flash silica gel chromatography (hexanes : ethyl acetate = **2:1**) gave **77** mg of product as a white solid in **88%** yield under **Condition A**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 1.92-2.05 (m, 2H), 2.29-2.42 (m, 3H), 2.53-2.58 (m, 1H), 3.29-3.44 (m, 2H), 5.35-5.40 (dd, $J = 5.0, 10.4$ Hz, 1H), 5.89 (s, 1H), 7.36-7.40 (dd, $J = 4.3, 8.3$ Hz, 1H), 7.51-7.52 (m, 2H), 7.76-7.78 (m, 2H), 7.88-7.90 (m, 2H), 8.11-8.13 (dd, $J = 1.4, 8.3$ Hz, 1H), 8.55-8.56 (m, 1H), 8.67-8.70 (m, 1H), 10.30 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 22.73, 29.08, 37.33, 37.37, 52.49, 116.87, 121.83, 122.35, 124.02, 127.39, 127.96, 128.80, 131.53, 133.67, 134.74, 136.45, 138.51, 148.50, 160.91, 165.77, 167.81, 199.40; **HRMS**: calculated for $\text{C}_{26}\text{H}_{22}\text{N}_3\text{O}_4$ [$\text{M}+\text{H}^+$]: 440.1605; found: 440.1600.



Flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave **54** mg of product as a white foam in **52%** yield under **Condition A**; **53** mg of product in **51%** yield under **Condition C**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 1.75 (s, 3H), 3.27-3.31 (m, 2H), 4.66 (s, 2H), 5.20-5.24 (dd, $J = 7.2, 9.0$ Hz, 1H), 5.64-5.68 (t, $J = 7.2, 6.8$ Hz, 1H), 7.35-7.40 (m, 3H), 7.48-7.53 (m, 3H), 7.70-7.72 (m, 2H), 7.84-7.90 (m, 4H), 8.09-8.11 (dd, $J = 1.4, 8.3$ Hz, 1H), 8.63-8.65 (dd, $J = 1.4, 4.0$ Hz, 1H), 8.71-8.74 (m, 1H), 10.30 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 14.42, 27.93, 54.45, 69.78, 116.82, 121.72, 122.09, 123.43, 123.67, 127.34, 127.91, 128.38, 129.60, 130.13, 131.78, 132.98, 133.93, 134.32, 135.19, 136.34, 138.51, 148.40, 166.23, 166.52, 168.03; **HRMS**: calculated for $\text{C}_{31}\text{H}_{26}\text{N}_3\text{O}_5$ [$\text{M}+\text{H}^+$]: 520.1867; found: 520.1861.



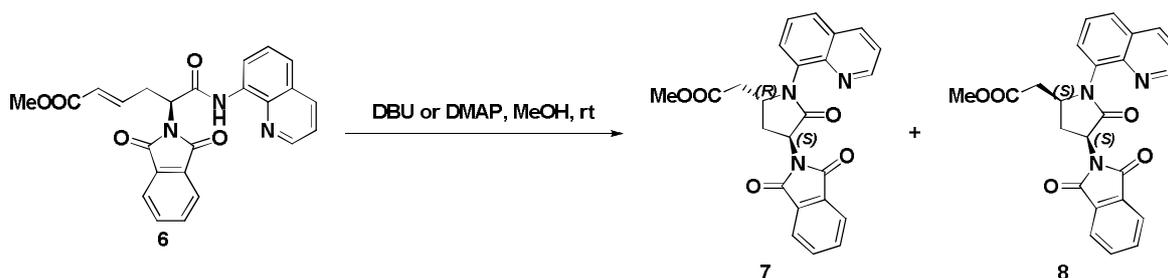
Flash silica gel chromatography (hexanes : ethyl acetate = 2:1) gave **26** mg of product as a white solid in **30%** yield under **Condition A**; **29** mg of product in **33%** yield under **Condition C**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 1.58 (s, 3H), 2.34-2.35 (m, 2H), 2.52-2.57 (d, $J = 18.0$ Hz, 1H), 2.70-2.75 (d, $J = 18.4$ Hz, 1H), 3.41-3.46 (dd, $J = 5.4, 14.0$ Hz, 1H), 3.67-3.74 (dd, $J = 10.4, 14.0$ Hz, 1H), 5.41-5.45 (dd, $J = 5.8, 10.4$ Hz, 1H), 7.31-7.35 (q, $J = 4.3$ Hz, 1H), 7.46-7.47 (d, 2H), 7.71-7.73 (m, 2H), 7.83-7.85 (m, 2H), 8.06-8.08 (d, $J = 7.9$ Hz, 1H), 8.50-8.52 (d, $J = 4.0$ Hz, 1H), 8.65-8.68 (m, 1H), 10.23 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 8.19, 28.90, 30.77, 34.19, 52.26, 116.70, 121.73, 122.24, 123.82, 127.21, 127.79, 131.38, 133.52, 134.63, 136.32, 138.30, 139.84, 148.39, 165.68, 166.91, 167.67, 209.78; **HRMS**: calculated for $\text{C}_{26}\text{H}_{22}\text{N}_3\text{O}_4$ [$\text{M}+\text{H}^+$]: 440.1605; found: 440.1599.



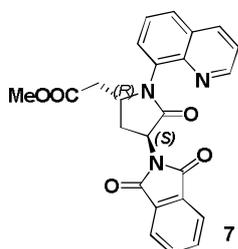
Flash silica gel chromatography (hexanes : ethyl acetate = 5:1) gave **65** mg of product as a white foam in **62%** yield under **Condition B**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 0.87 (s, 21H), 3.31-3.37 (dd, $J = 5.0, 17.3$ Hz, 1H), 3.65-3.73 (dd, $J = 11.5, 16.9$ Hz, 1H), 5.37-5.42 (dd, $J = 5.0, 11.5$ Hz, 1H), 7.39-7.42 (q, $J = 4.0$ Hz, 1H), 7.53-7.54 (m, 2H), 7.80-7.81 (m, 2H), 7.94-7.96 (m, 2H), 8.13-8.16 (d, $J = 7.9$ Hz, 1H), 8.63-8.64 (m, 1H), 8.72-8.74 (m, 1H), 10.35 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 11.02, 18.35, 20.56, 53.61, 83.95, 102.82, 116.75, 121.66, 122.14, 123.71, 127.25, 127.83, 131.91, 133.64, 134.31, 136.26, 138.46, 148.41, 165.59, 167.62; **HRMS**: calculated for $\text{C}_{31}\text{H}_{36}\text{N}_3\text{O}_3\text{Si}$ [$\text{M}+\text{H}^+$]: 526.2520; found: 526.2515.

6. Intramolecular cyclization reactions

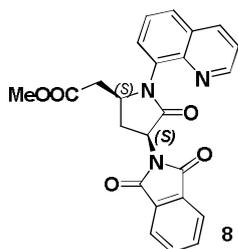
6.1 Intramolecular cyclization of substrate 6



To a suspension of substrate **6** (42.9 mg, 0.1 mmol, 1 equiv) in methanol (5 mL) was added DMAP (14.6 mg, 0.12 mmol, 1.2 equiv, **Condition 2a**) or DBU (18.2 mg, 0.12 mmol, 1.2 equiv, **Condition 2b**). After the starting material disappeared on TLC plate (approximate 4 hours under **Condition 2a** or approximate 20 minutes under **Condition 2b**), the reaction was diluted with ethyl acetate (20 mL) and washed thoroughly with diluted hydrochloric acid and water. The organic layer was dried with anhydrous sodium sulfate. Proton NMR of the crude products showed ratios of compound **7** : compound **8** as 13:1 (when DBU was used as base) or approximate 20:1 (when DMAP was used as base). To distinguish the two diastereomers: The spot of compound **7** run higher than that of compound **8** on TLC plate using hexanes and ethyl acetate (1:3) as eluent.

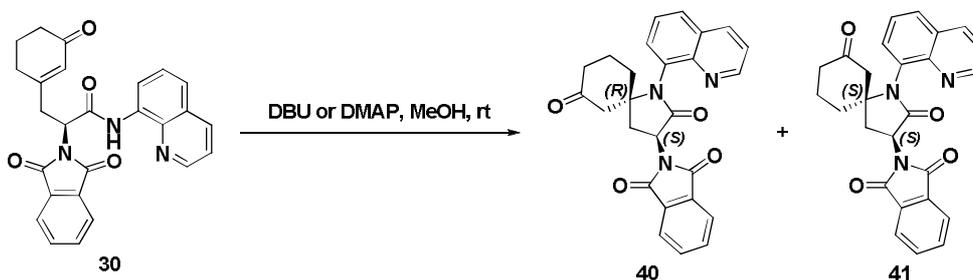


Flash silica gel chromatography (hexanes : ethyl acetate = 1:2) gave **32** mg of product as a white foam in **75%** yield under **Condition 2a**. **Failed to get the single crystal. Stereochemistry was assumed according to the same reaction with substrate 30.** ^1H NMR (CDCl_3 , 360 MHz, ppm): δ 2.28-2.36 (m, 1H), 2.49-2.62 (m, 2H), 2.99-3.07 (m, 1H), 3.39 (s, 3H), 5.18-5.22 (m, 1H), 5.36-5.42 (t, $J = 9.7, 10.1$ Hz, 1H), 7.36-7.39 (dd, $J = 3.2, 7.2$ Hz, 1H), 7.52-7.57 (t, $J = 7.9, 7.6$ Hz, 1H), 7.67-7.68 (m, 2H), 7.79-7.80 (m, 4H), 8.11-8.14 (d, $J = 8.3$ Hz, 1H), 8.86-8.87 (d, $J = 1.8$ Hz, 1H); ^{13}C NMR (CDCl_3 , 90 MHz, ppm) δ 31.10, 39.56, 49.86, 51.53, 54.07, 121.70, 123.40, 126.24, 128.51, 129.25, 131.02, 131.85, 133.50, 134.21, 136.31, 144.01, 150.43, 167.54, 170.27, 170.59; **HRMS**: calculated for $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}_5$ [$\text{M}+\text{H}^+$]: 430.1397; found: 430.1394.



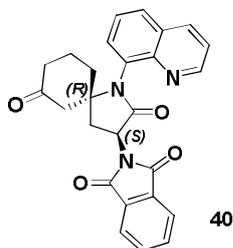
Flash silica gel chromatography (hexanes : ethyl acetate = 1:2) gave 2 mg of product as a colorless gum in less than **5%** yield under **Condition 2a**. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 2.50-2.71 (m, 3H), 2.98-3.06 (m, 1H), 3.50 (s, 3H), 5.11-5.13 (m, 1H), 5.38-5.43 (t, $J = 9.4, 9.0$ Hz, 1H), 7.43-7.46 (dd, $J = 3.6, 7.2$ Hz, 1H), 7.58-7.62 (t, $J = 7.6, 7.6$ Hz, 1H), 7.72-7.73 (m, 2H), 7.80-7.85 (m, 4H), 8.17-8.19 (d, $J = 8.3$ Hz, 1H), 8.97 (s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 30.33, 38.39, 49.43, 51.79, 56.45, 121.84, 123.62, 126.55, 128.66, 129.43, 129.47, 132.14, 134.28, 134.46, 136.35, 144.66, 150.82, 167.69, 170.00, 171.15; **HRMS**: calculated for $\text{C}_{24}\text{H}_{20}\text{N}_3\text{O}_5$ [$\text{M}+\text{H}^+$]: 430.1397; found: 430.1394.

6.2 Intramolecular cyclization of substrate **30**

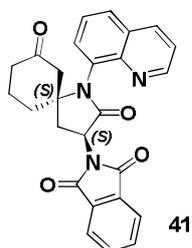


To a suspension of substrate **30** (43.9 mg, 0.1 mmol, 1 equiv) in methanol (5 mL) was added DMAP (14.6 mg, 0.12 mmol, 1.2 equiv, **Condition 2a**) or DBU (18.2 mg, 0.12 mmol, 1.2 equiv, **Condition 2b**). After the starting material disappeared on TLC plate (approximate 4 hours under **Condition 2a** or approximate 20 minutes under **Condition 2b**), the reaction was diluted with ethyl acetate (20 mL) and washed thoroughly with diluted hydrochloric acid and water. The organic layer was dried with anhydrous sodium sulfate. Proton NMR of the crude products showed ratios of compound **40** : compound **41** as 2.3:1 (when DBU was used as base) or approximate 1:5.5 (when DMAP was used as base). To distinguish the two diastereomers: the spot of compound **40** run higher than that of compound **41** on TLC plate using hexanes and ethyl acetate (1:3) as eluent. Single crystals of Compound **40** and Compound **41** could be obtained by volatilizing acetone slowly from acetone-hexanes solution of the corresponding compound. The

stereochemistry of both Compound **40** and Compound **41** were confirmed by X-ray.



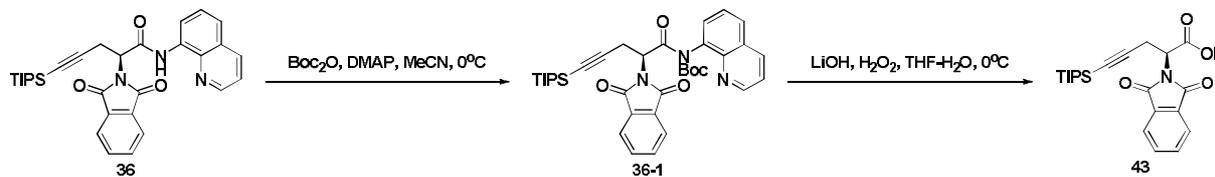
Flash silica gel chromatography (hexanes : ethyl acetate = 1:2) gave 26 mg of product as a white crystal in **60%** yield under **Condition 2b**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 1.60-1.72 (m, 1H), 1.96-2.05 (m, 3H), 2.27-2.30 (m, 2H), 2.36-2.40 (d, *J* = 14.0 Hz, 1H), 2.51-2.54 (m, 2H), 3.04-3.08 (d, *J* = 14.0 Hz, 1H), 5.45-5.50 (t, *J* = 9.7, 10.1 Hz, 1H), 7.36-7.39 (m, 1H), 7.58-7.62 (t, *J* = 7.6, 7.6 Hz, 1H), 7.68-7.70 (m, 2H), 7.76-7.88 (m, 4H), 8.13-8.15 (d, *J* = 8.3 Hz, 1H), 8.87-8.88 (d, *J* = 2.2 Hz, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 19.72, 35.27, 37.33, 40.14, 48.59, 51.76, 65.14, 121.87, 123.52, 126.12, 129.55, 129.57, 131.95, 132.29, 133.23, 134.29, 136.19, 145.16, 150.99, 167.60, 170.09, 209.21; **HRMS**: calculated for C₂₆H₂₂N₃O₄ [M+H⁺]: 440.1605; found: 440.1601. For X-ray data, please see section **9.1**.



Flash silica gel chromatography (hexanes : ethyl acetate = 1:2) gave 29 mg of product as a white crystal in **66%** yield under **Condition 2a**. **¹H NMR** (CDCl₃, 360 MHz, ppm): δ 1.54-1.74 (m, 2H), 1.90-2.24 (m, 3H), 2.42-2.46 (m, 2H), 2.65-2.78 (m, 2H), 2.91-2.95 (m, 1H), 5.41-5.46 (t, *J* = 9.7, 9.7 Hz, 1H), 7.38-7.40 (m, 1H), 7.56-7.60 (m, 1H), 7.65-7.69 (m, 3H), 7.81-7.87 (m, 3H), 8.13-8.15 (d, *J* = 7.9 Hz, 1H), 8.89 (s, 1H); **¹³C NMR** (CDCl₃, 90 MHz, ppm) δ 21.15, 33.83, 34.61, 40.13, 48.64, 54.40, 66.19, 121.81, 123.50, 126.17, 129.55, 129.61, 131.88, 132.01, 133.22, 134.27, 136.25, 145.47, 150.87, 167.52, 169.65, 208.34; **HRMS**: calculated for C₂₆H₂₂N₃O₄ [M+H⁺]: 440.1605; found: 440.1601. For X-ray data, please see section **9.2**.

7. Removal of AQ auxiliary

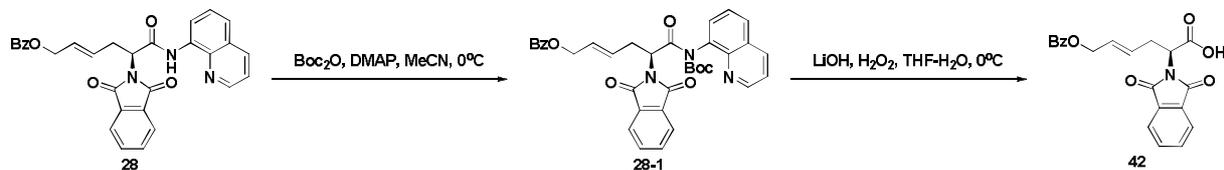
7.1 Removal of AQ auxiliary in Compound 36



Step 1: To a solution of compound **36** (105 mg, 0.2 mmol, 1 equiv) in dry acetonitrile (3 mL) was added 4-(dimethylamino)pyridine (32 mg, 0.26 mmol, 1.3 equiv) and Boc anhydride (57 mg, 0.26 mmol, 1.3 equiv). The mixture was stirred at room temperature for 24 hours then concentrated under reduced pressure. Purification of the crude mixture by flash silica gel chromatography (hexanes : ethyl acetate = 5:1) gave 112 mg of compound **36-1** as a white foam in 90% yield. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 0.84-0.85 (m, 21H), 1.17 (s, 9H), 3.21-3.27 (dd, $J = 4.3, 17.3$ Hz, 1H), 3.57-3.65 (dd, $J = 11.5, 16.9$ Hz, 1H), 6.13-6.17 (dd, $J = 4.0, 11.5$ Hz, 1H), 7.30-7.33 (dd, $J = 3.6, 7.9$ Hz, 1H), 7.52-7.61 (m, 1H), 7.67-7.68 (m, 3H), 7.76-7.81 (m, 3H), 8.08-8.10 (d, $J = 8.3$ Hz, 1H), 8.76-8.77 (d, $J = 3.2$ Hz, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 11.09, 18.42, 21.41, 27.46, 53.73, 83.49, 83.62, 103.34, 121.61, 123.31, 126.33, 128.36, 128.86, 131.96, 133.97, 135.97, 136.35, 144.02, 150.43, 152.29, 167.15, 171.48; **HRMS**: calculated for $\text{C}_{36}\text{H}_{44}\text{N}_3\text{O}_5\text{Si}$ [$\text{M}+\text{H}^+$]: 626.3045; found: 626.3033.

Step 2: A solution of compound **36-1** (120 mg, 0.19 mmol, 1 equiv) in THF and water (2.1 mL : 0.7 mL) was cooled to 0°C then 30% hydrogen peroxide (192 μL , 1.69 mmol, 8.8 equiv) and lithium hydroxide monohydrate (8.9 mg, 0.21 mmol, 1.1 equiv) were added and stirred at 0°C for 2.5 hours. The reaction was quenched at 0°C with 1.5 M aqueous sodium thiosulfate (1.4 mL) and the solvent was concentrated under reduced pressure. The residue was washed with dichloromethane (10 mL) twice then the aqueous phase was acidified to pH 2 with 10% aqueous hydrochloric acid and extracted with ethyl acetate (10 mL) twice. The organic extracts were dried with sodium sulfate and concentrated under reduced pressure and purified on flash silica gel chromatography (dichloromethane : methanol = 10:1), giving 55 mg product as a yellowish syrup in 72% yield. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 0.82 (s, 21H), 3.02-3.06 (d, $J = 15.5$ Hz, 1H), 3.30-3.38 (t, $J = 12.2, 16.6$ Hz, 1H), 5.08 (br s, 1H), 7.72-7.73 (d, $J = 2.9$ Hz, 2H), 7.84 (s, 2H), 9.00 (br s, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 11.07, 18.41, 20.68, 83.87, 102.47, 123.70, 131.88, 134.32, 167.31; **HRMS**: calculated for $\text{C}_{22}\text{H}_{30}\text{NO}_4\text{Si}$ [$\text{M}+\text{H}^+$]: 400.1939; found: 400.1934.

7.2 Removal of AQ auxiliary in Compound 28



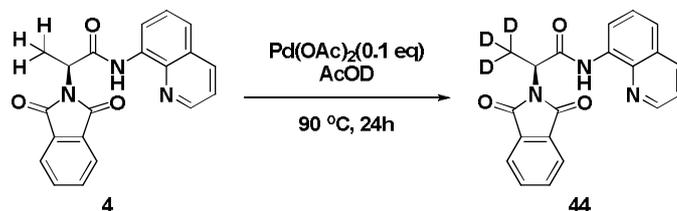
Step 1: To a solution of compound **28** (150 mg, 0.30 mmol, 1 equiv) in dry acetonitrile (5 mL) was added 4-(dimethylamino)pyridine (54 mg, 0.45 mmol, 1.5 equiv) and Boc anhydride (97 mg, 0.45 mmol, 1.5 equiv). The mixture was stirred at room temperature for 24 hours then concentrated under reduced pressure. Purification of the crude mixture by flash silica gel chromatography (hexanes : ethyl acetate = 3:1) gave 180 mg of compound **28-1** as a white foam in quantitative yield. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 1.07 (s, 9H), 3.10-3.20 (m, 2H), 4.62-4.64 (m, 2H), 5.72-5.80 (m, 1H), 5.92-6.00 (m, 1H), 6.10-6.14 (m, 1H), 7.30-7.36 (m, 3H), 7.47-7.54 (m, 2H), 7.60-7.62 (m, 2H), 7.66-7.68 (d, $J = 7.2$ Hz, 1H), 7.75-7.77 (m, 3H), 7.83-7.86 (m, 2H), 8.08-8.11 (dd, $J = 1.4, 8.3$ Hz, 1H), 8.78-8.79 (dd, $J = 1.4, 4.0$ Hz, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 27.30, 32.76, 54.51, 64.97, 83.13, 121.52, 123.28, 126.26, 127.84, 128.17, 128.23, 128.73, 129.52, 130.08, 131.41, 131.62, 132.80, 133.97, 135.93, 136.41, 144.02, 150.32, 152.47, 166.09, 167.51, 172.12; **HRMS**: calculated for $\text{C}_{35}\text{H}_{32}\text{N}_3\text{O}_7$ $[\text{M}+\text{H}^+]$: 606.2235; found: 606.2225.

Step 2: A solution of compound **28-1** (100 mg, 0.165 mmol, 1 equiv) in THF and water (3 mL : 1 mL) was cooled to 0°C then 30% hydrogen peroxide (165 μL , 1.45 mmol, 8.8 equiv) and lithium hydroxide monohydrate (7.6 mg, 0.18 mmol, 1.1 equiv) were added and stirred at 0°C for 2.5 hours. The reaction was quenched at 0°C with 1.5 M aqueous sodium thiosulfate (1.2 mL) and the solvent was concentrated under reduced pressure. The residue was washed with dichloromethane (10 mL) twice then the aqueous phase was acidified to pH 2 with 10% aqueous hydrochloric acid and extracted with ethyl acetate (10 mL) twice. The organic extracts were dried with sodium sulfate and concentrated under reduced pressure and purified on flash silica gel chromatography (dichloromethane : methanol = 10:1), giving 45 mg product as a colorless syrup in 73% yield. $^1\text{H NMR}$ (CDCl_3 , 360 MHz, ppm): δ 3.03 (s, 2H), 4.56-4.67 (m, 2H), 5.00 (br s, 1H), 5.72-5.76 (m, 1H), 5.88-5.92 (m, 1H), 7.41-7.46 (t, $J = 7.6, 7.6$ Hz, 1H), 7.57-7.61 (t, $J = 7.2, 7.2$ Hz, 1H), 7.76-7.83 (m, 6H); $^{13}\text{C NMR}$ (CDCl_3 , 90 MHz, ppm) δ 32.50, 65.33, 124.01, 128.74, 129.29, 130.02, 131.02, 132.03, 132.50, 133.75, 135.34, 166.15, 168.14; **HRMS**:

calculated for $C_{21}H_{17}NNaO_6$ $[M+H^+]$: 402.0948; found: 402.0943.

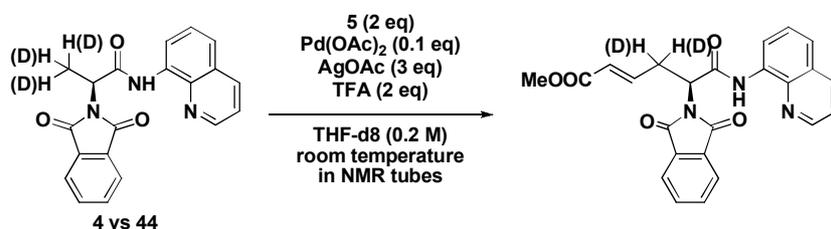
8. Kinetic isotope effect

8.1 Preparation of deuterated alanine 44



The solution of alanine substrate **4** (1.38 g, 4 mmol, 1 equiv) and $Pd(OAc)_2$ (90 mg, 0.4 mmol, 0.1 equiv) in deuterated acetic acid (10 mL) was heated at 90 °C for 24 hours. After completion the reaction was filtrated and concentrated. This procedure was repeated twice, and the product was purified on flash silica gel chromatography (ethyl acetate : dichloromethane=1:99), giving 1.0 g of deuterated alanine substrate **44** in 72% yield. 1H NMR ($CDCl_3$, 360 MHz, ppm): δ 5.25 (s, 1H), 7.38-7.42 (m, 1H), 7.49-7.53 (m, 2H), 7.73-7.75 (m, 2H), 7.88-7.90 (m, 2H), 8.11-8.14 (d, $J = 8.3$ Hz, 1H), 8.67-8.72 (m, 2H), 10.31 (s, 1H); HRMS: calculated for $C_{20}H_{13}D_3N_3O_3$ $[M+H^+]$: 349.1380; found: 349.1380.

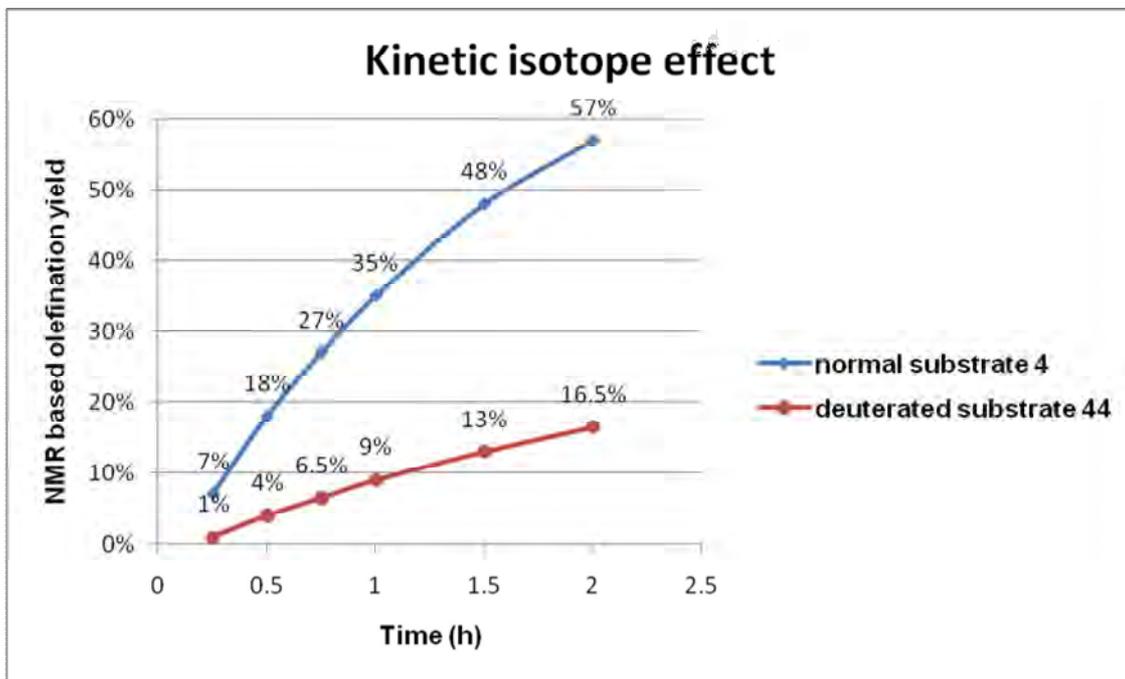
8.2 Method of collecting data and yield determination



Normal substrate **4** (34.5 mg, 0.1 mmol, 1 equiv) or deuterated substrate **44** (34.8 mg, 0.1 mmol, 1 equiv), vinyl iodide **5** (42.4 mg, 0.2 mmol, 2 equiv), $Pd(OAc)_2$ (2.24 mg, 0.01 mmol, 0.1 equiv), silver acetate (50 mg, 0.3 mmol, 3 equiv), trifluoroacetic acid (15 μ L, 0.2 mmol, 2 equiv) and dibromomethane (17.4 mg, 0.1 mmol, 1 equiv) were suspended into deuterated tetrahydrofuran (0.5 mL) in NMR tubes. The resulting reaction mixtures were shaken **vigorously** at room temperature. Data was collected at 15, 30, 45, 60, 90 and 120 minutes directly from 1H -NMR on Bruker AV-360 NMR instrument. Average data of three repeating experiments were used. $k_{H/D}$ was estimated based on the ratio of olefination yield. Olefination yields were determined as follows:

1) In the $^1\text{H-NMR}$ spectrum, set the integration of the singlet around δ 5.15 as 2.0, which is the peak of internal standard dibromomethane

2) yield = (integration of doublet around δ 6.00 ppm) \times 100%



9. X-ray single-crystal analysis data

9.1 Crystal data and structure refinement for compound 40

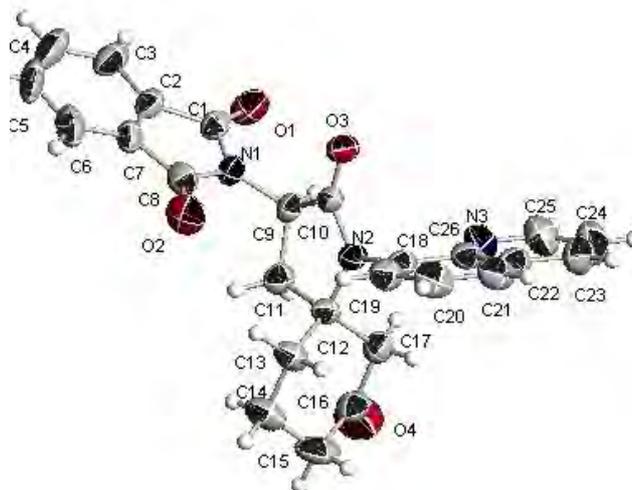


Figure 1. ORTEP view of **compound 40**

Empirical formula

C₂₉ H₂₇ N₃ O₅

Formula weight

497.54

Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal size	0.21 x 0.16 x 0.12 mm	
Crystal habit	colorless block	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.472(3) Å	$\alpha = 96.111(6)^\circ$
	b = 10.696(3) Å	$\beta = 90.184(6)^\circ$
	c = 14.252(4) Å	$\gamma = 94.806(6)^\circ$
Volume	1279.5(6) Å ³	
Z	2	
Density (calculated)	1.291 g/cm ³	
Absorption coefficient	0.089 mm ⁻¹	
F(000)	524	
Diffractometer	CCD area detector	
Radiation source	fine-focus sealed tube, MoK α	
Generator power	1600 watts (50 kV, 32mA)	
Detector distance	5.8 cm	
Data collection method	phi and omega scans	
Theta range for data collection	1.92 to 28.54°	
Index ranges	-11 ≤ h ≤ 11, -14 ≤ k ≤ 14, -18 ≤ l ≤ 16	

9.2 Crystal data and structure refinement for compound 41

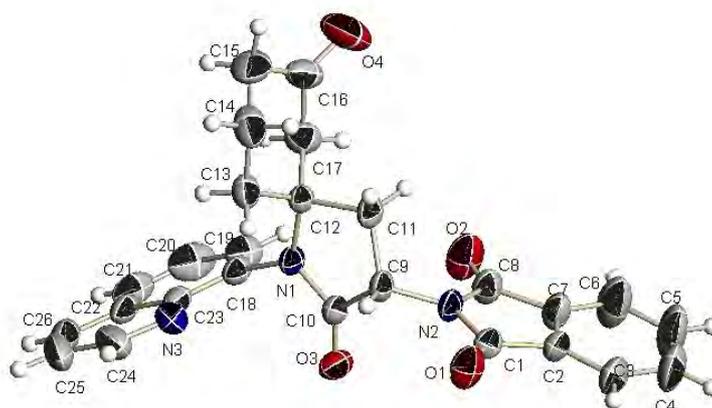


Figure 2. ORTEP view of **compound 41**

Empirical formula

C₂₆ H₂₁ N₃ O₄

Formula weight	439.46	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal size	0.28 x 0.19 x 0.10 mm	
Crystal habit	colorless block	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 15.440(5) Å	$\alpha = 90^\circ$
	b = 21.826(7) Å	$\beta = 110.809(6)^\circ$
	c = 13.714(4) Å	$\gamma = 90^\circ$
Volume	4320(2) Å ³	
Z	8	
Density (calculated)	1.351 g/cm ³	
Absorption coefficient	0.093 mm ⁻¹	
F(000)	1840	
Diffractionmeter	CCD area detector	
Radiation source	fine-focus sealed tube, MoK α	
Generator power	1600 watts (50 kV, 32mA)	
Detector distance	5.8 cm	
Data collection method	phi and omega scans	
Theta range for data collection	1.69 to 28.27°	
Index ranges	$-20 \leq h \leq 20, -28 \leq k \leq 29, -17 \leq l \leq 18$	

10. References

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- ⁶ P. B. González, J. Z. Chandanshive, M. Fochi, B. F. Bonini, A. Mazzanti, L. Bernardi, E. Locatelli, L. Caruana, C. Monasterolo, M. C. Franchini, *Eur. J. Org. Chem.*, **2013**, 8108

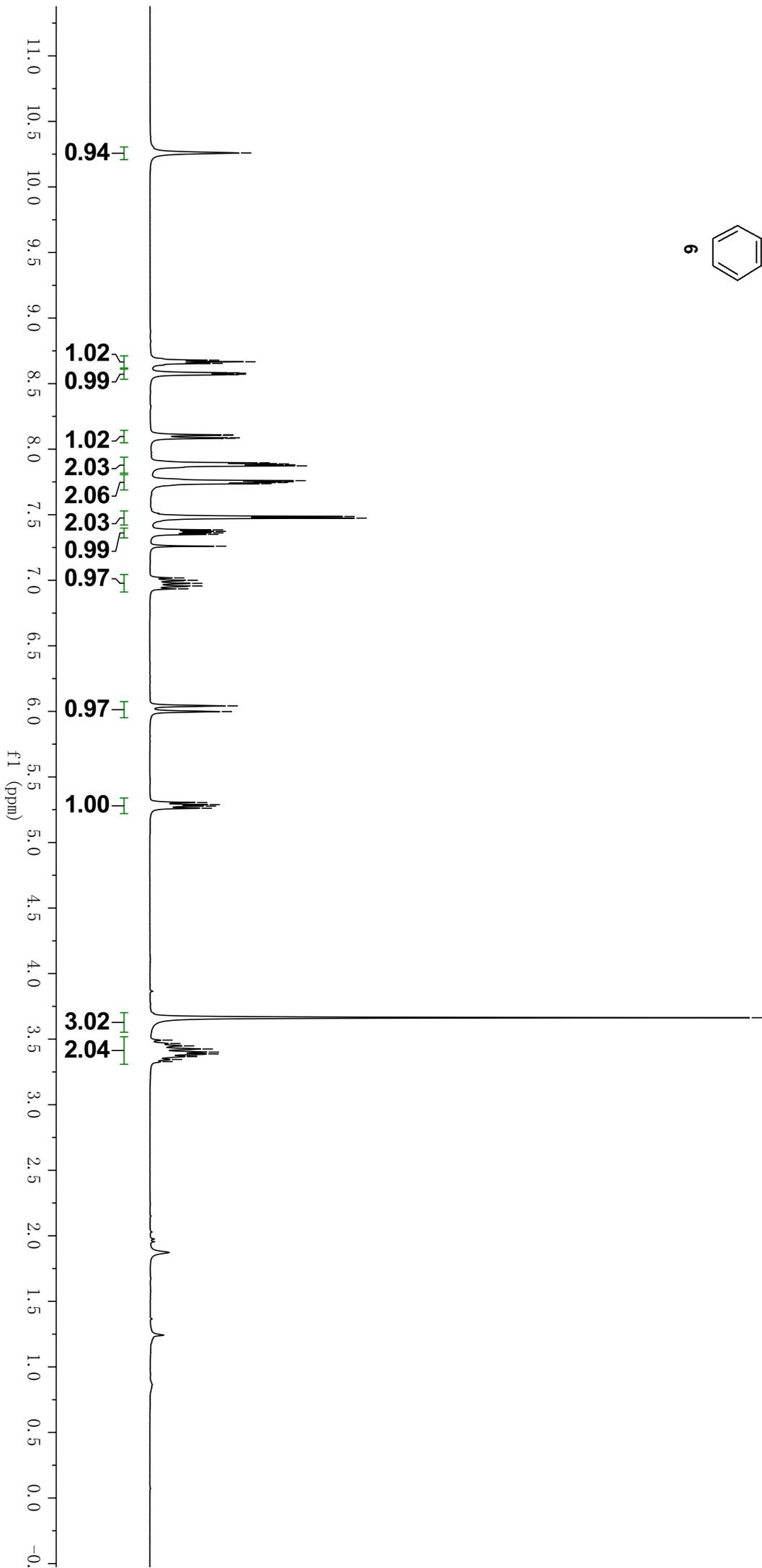
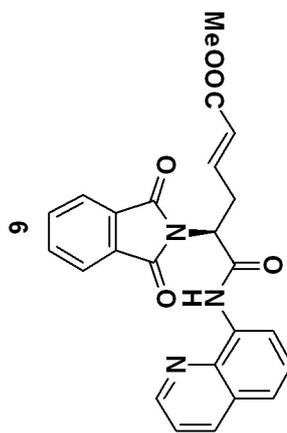
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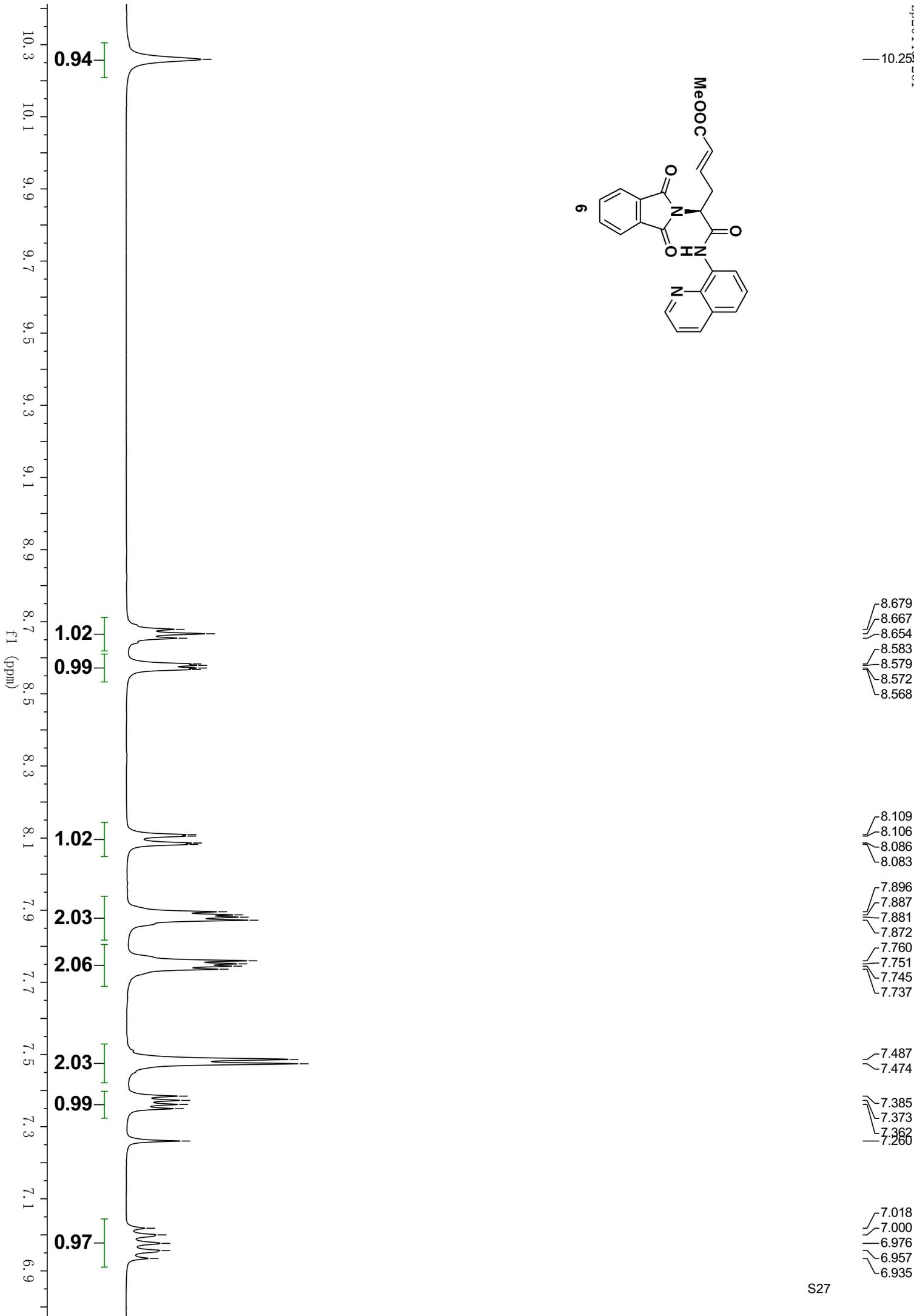
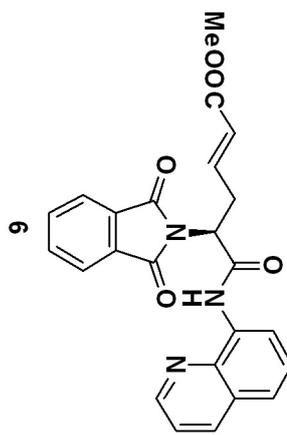
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5.288
5.277
5.261

3.663
3.493
3.467
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3.425
3.401
3.387
3.370
3.367
3.345
3.329



10.25



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127.284

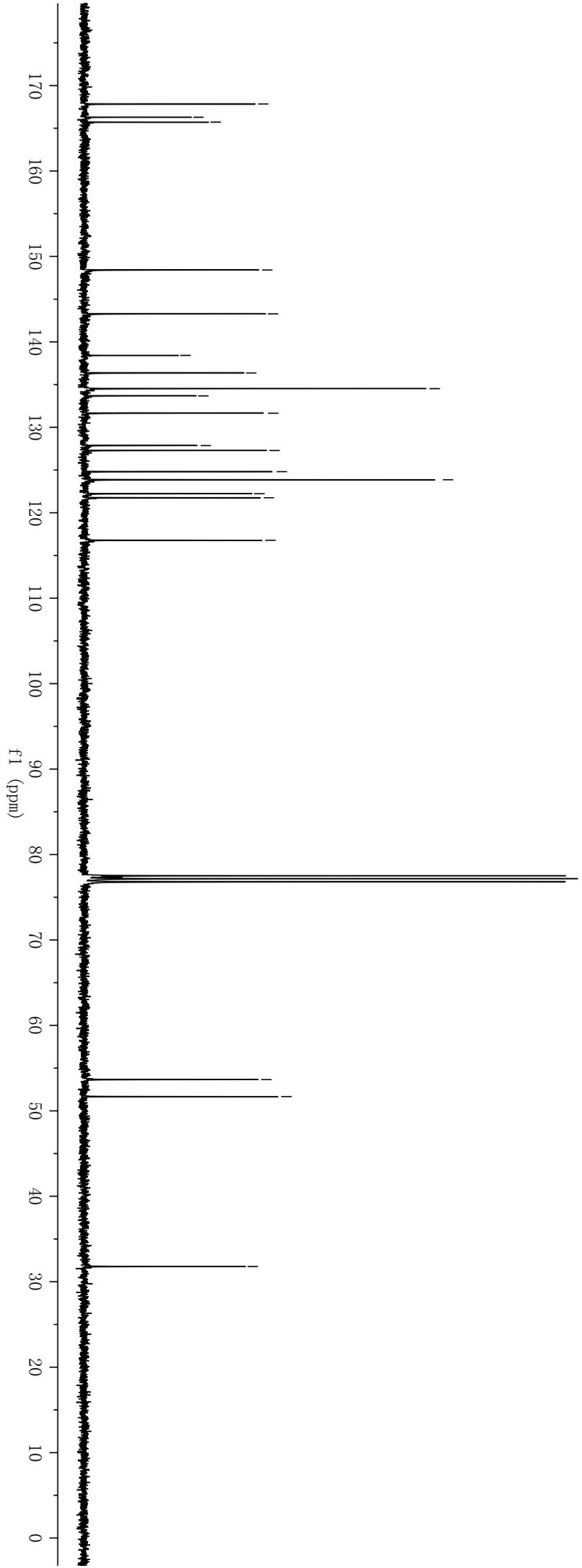
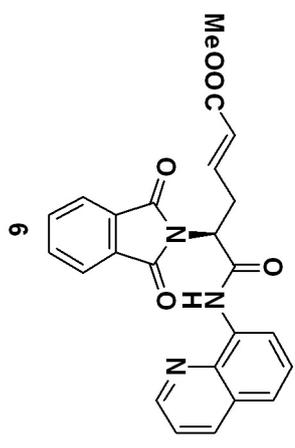
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53.659

51.669

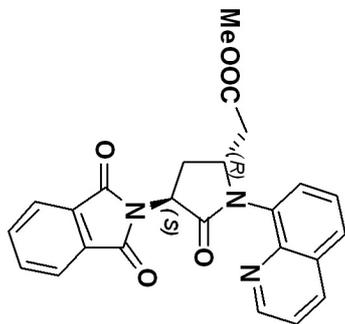
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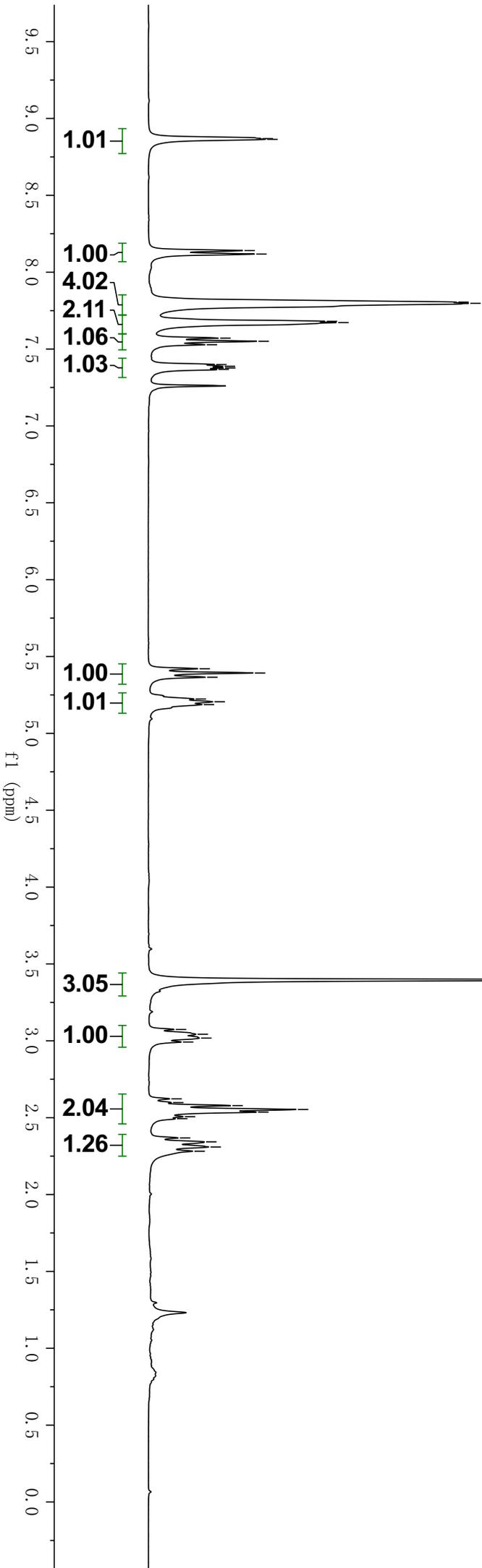
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5.420
5.392
5.365
5.223
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5.187

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2.992
2.623
2.598
2.579
2.553
2.536
2.506
2.494
2.368
2.343
2.309
2.282



7:preferred cyclized p product
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



170.592
170.271
167.540

150.439

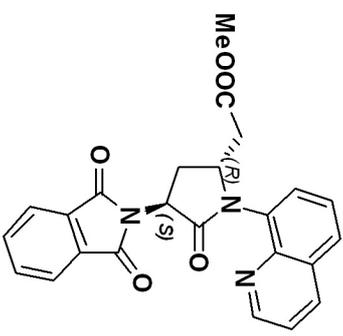
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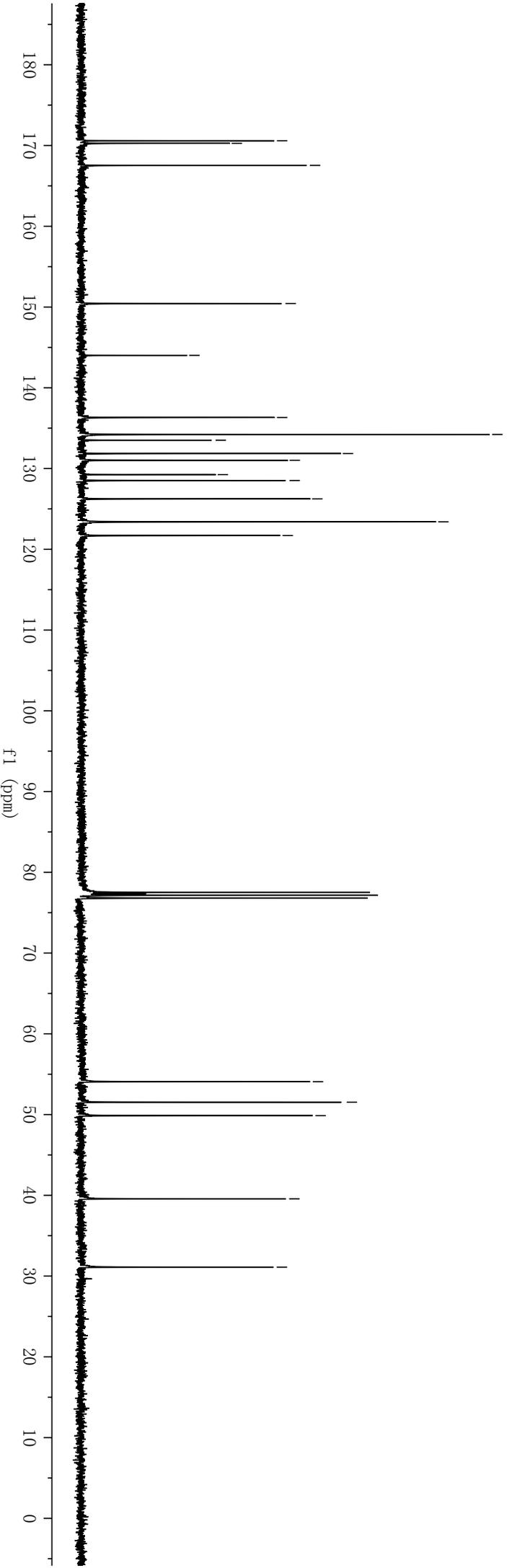
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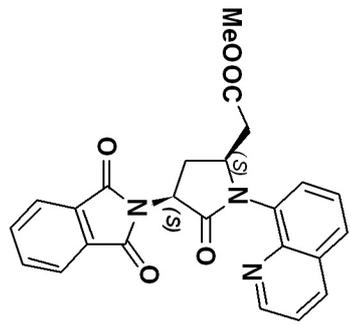
7:preferred cyclized p product
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



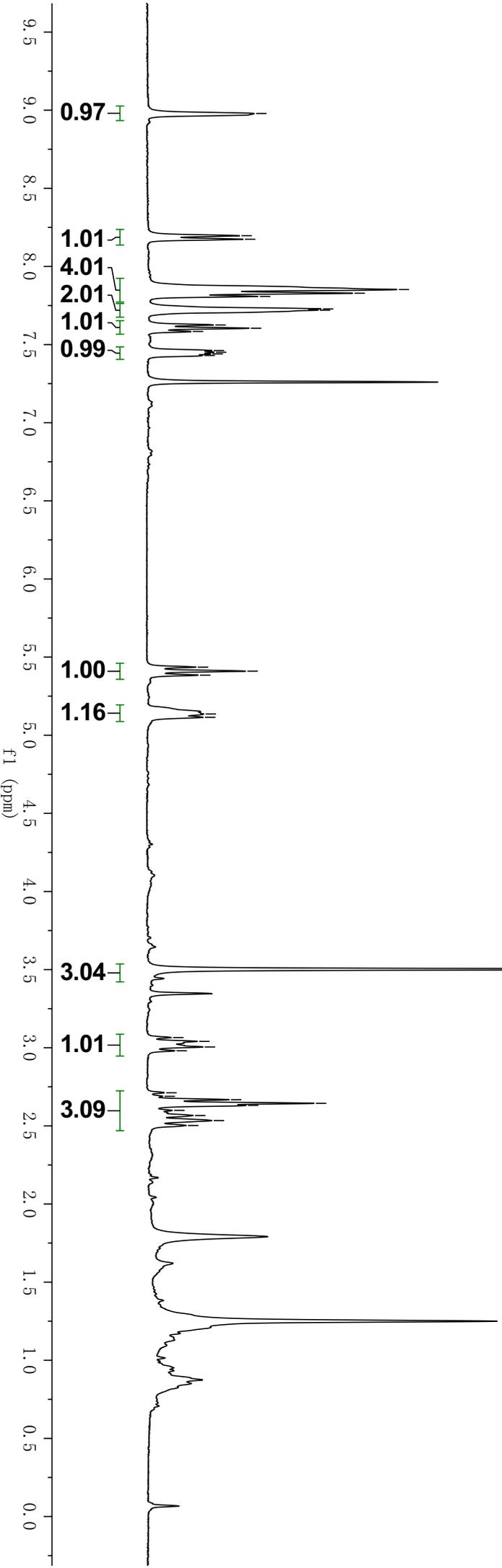
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- 8.197
- 8.174
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- 7.605
- 7.584
- 7.462
- 7.451
- 7.441
- 7.431

- 5.435
- 5.410
- 5.384
- 5.136
- 5.115

- 3.501
- 3.065
- 3.041
- 3.005
- 2.981
- 2.712
- 2.689
- 2.667
- 2.644
- 2.631
- 2.599
- 2.566
- 2.534
- 2.502



8: unpreferred cyclized product
polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



171.151
170.002
167.692

150.823

144.667

136.355

134.463

134.287

132.140

129.474

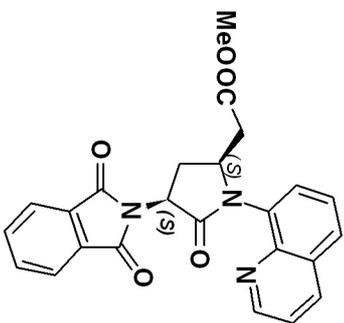
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128.662

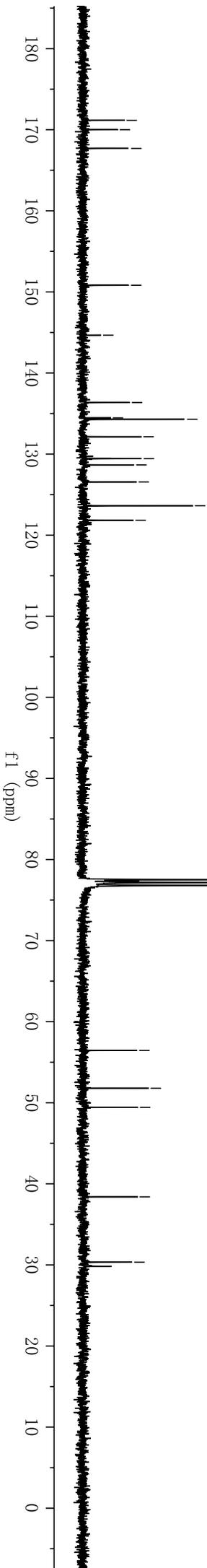
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123.628

121.841



8: unpreferred cyclized product
polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



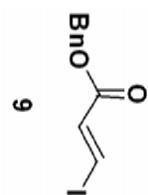
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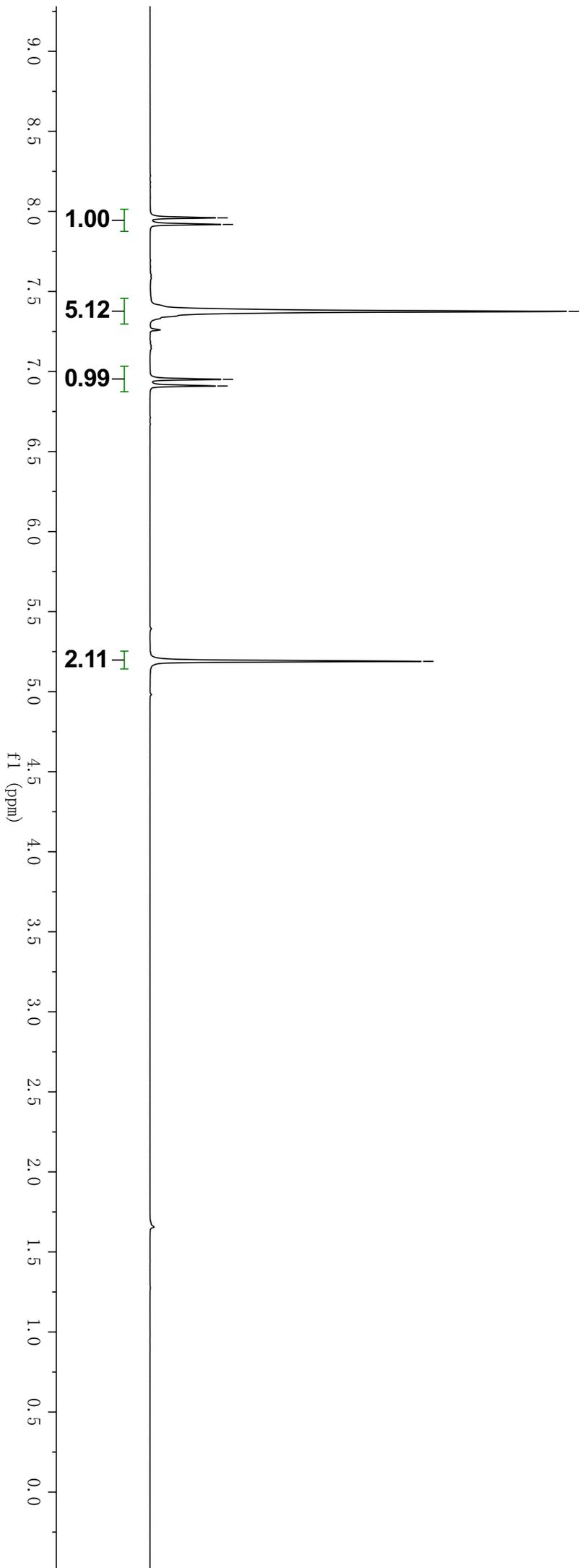


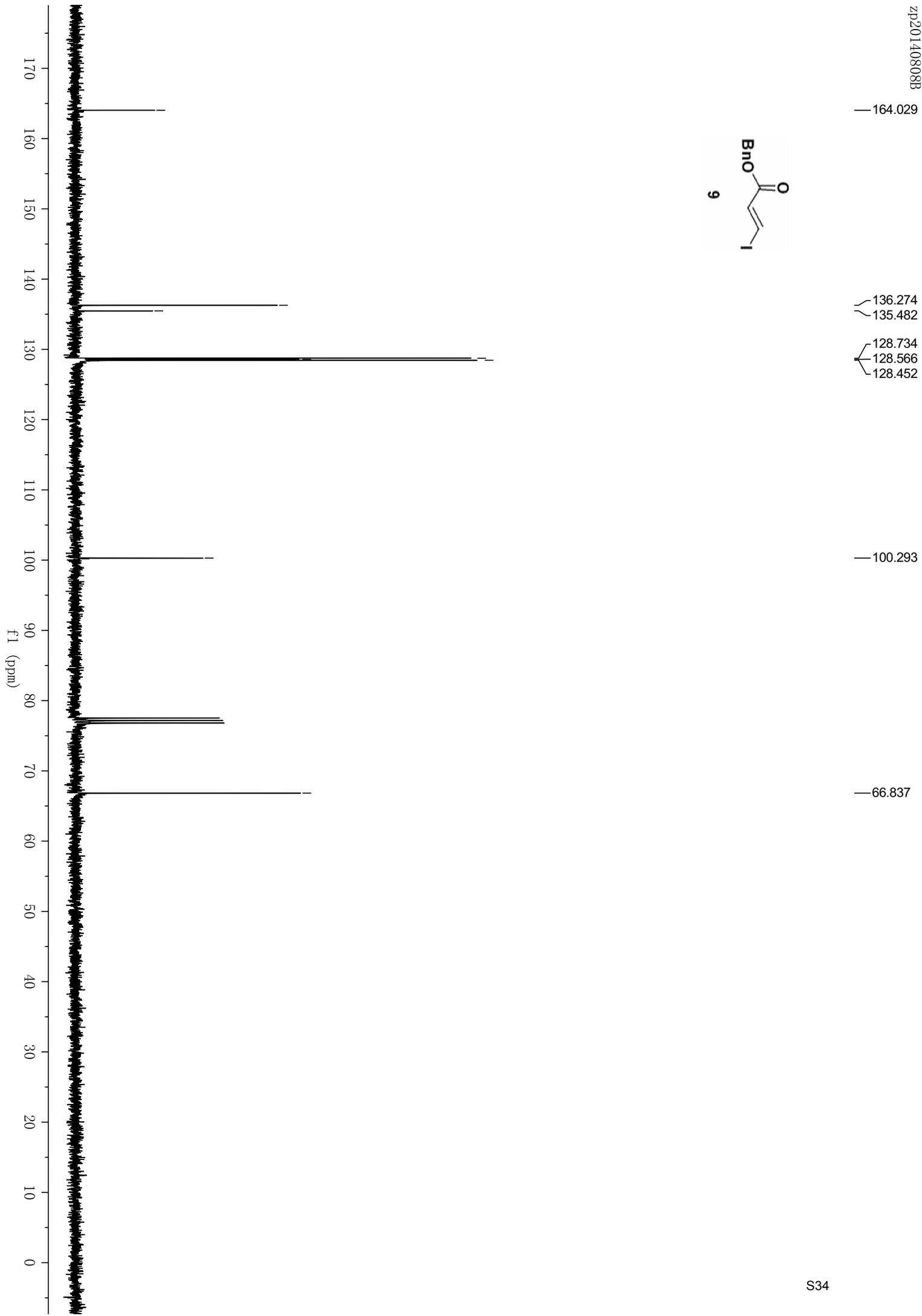
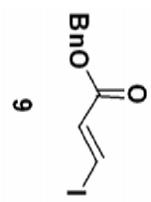
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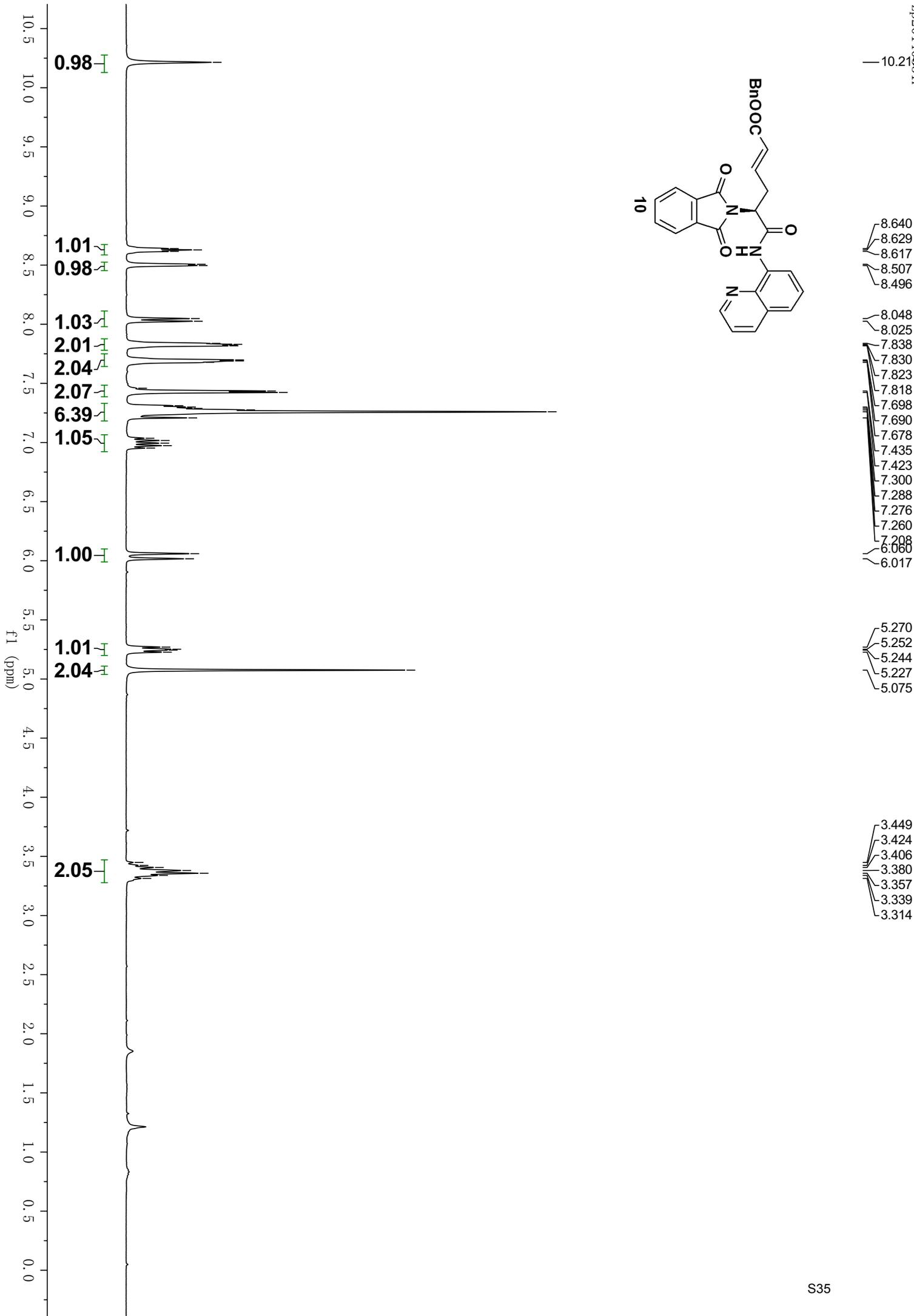
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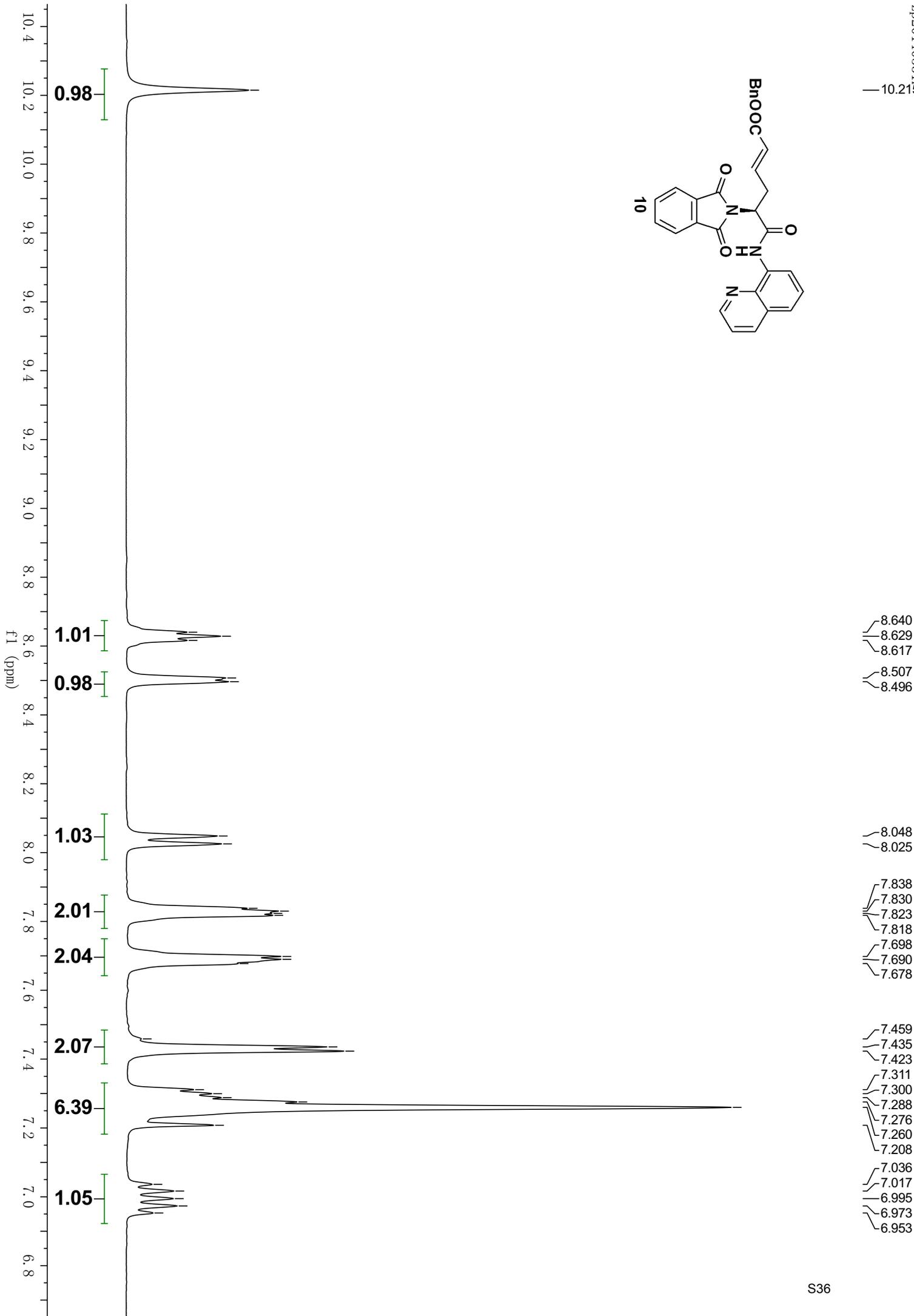
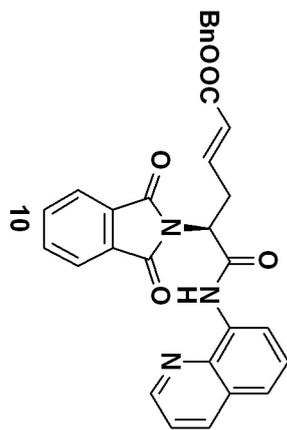
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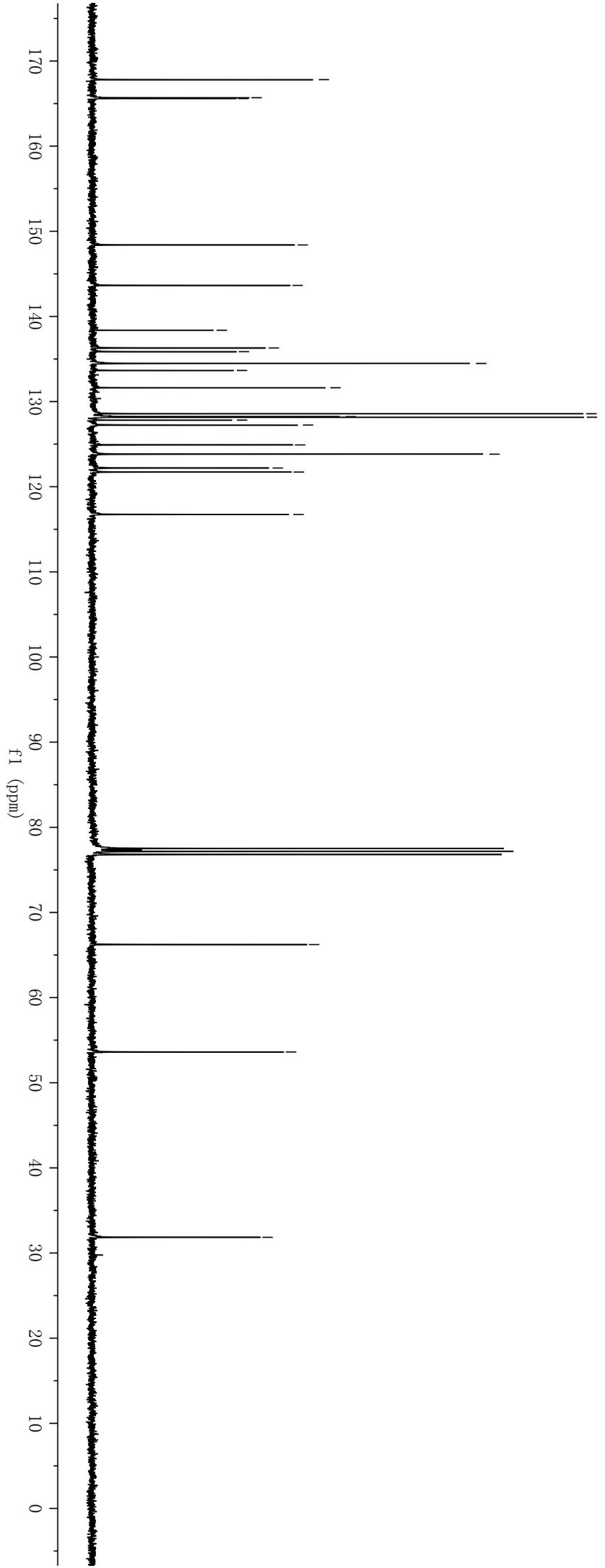
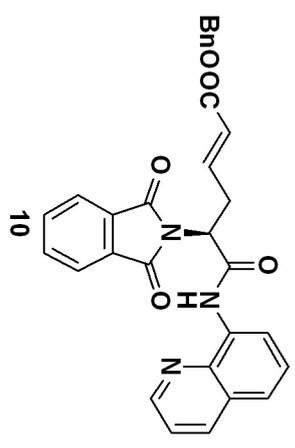


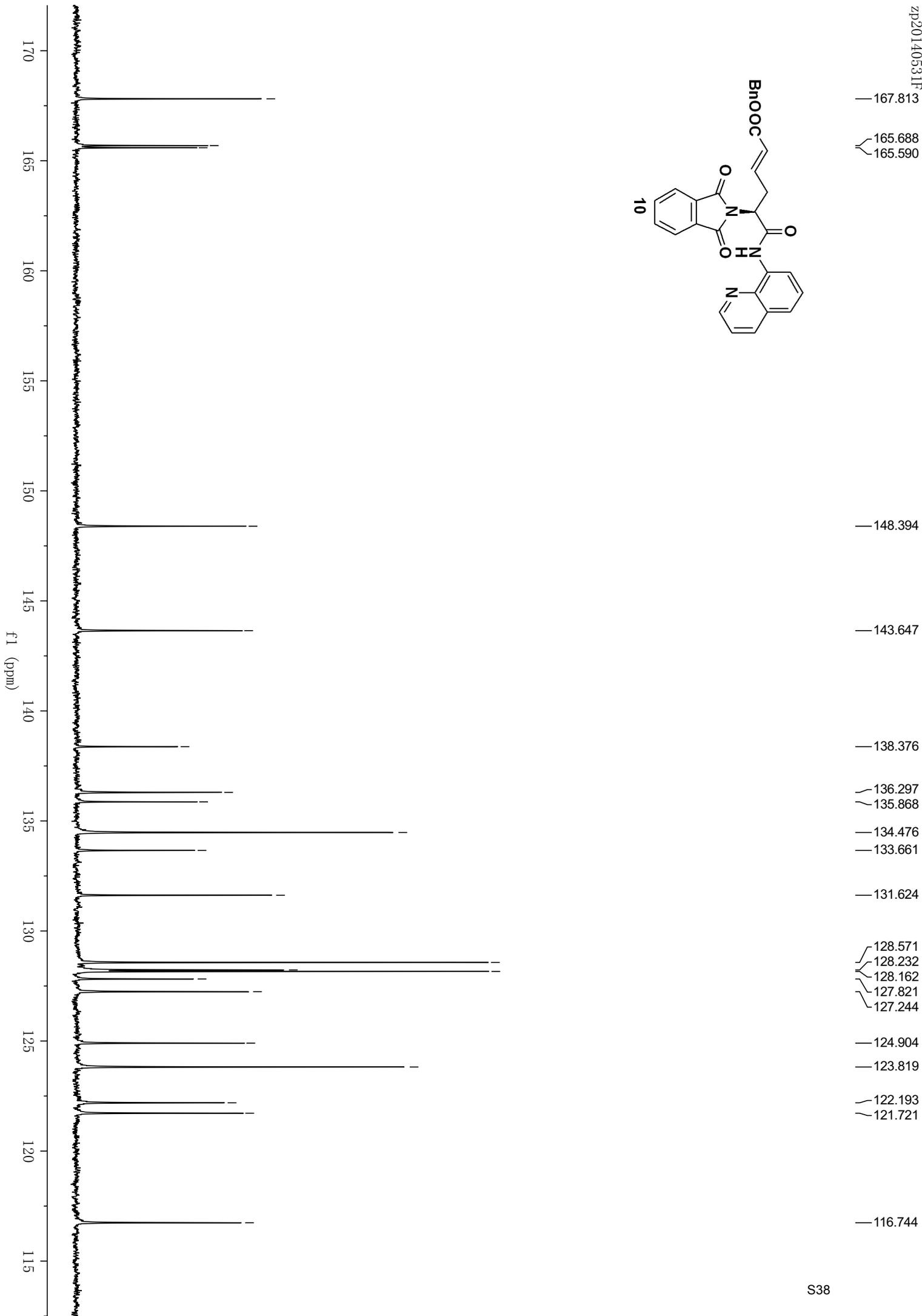
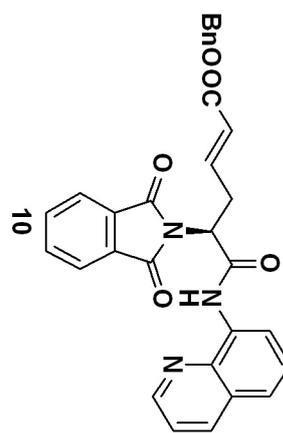


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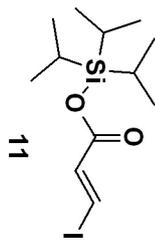
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- 165.590
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- 128.162
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- 66.231
- 53.608
- 31.844



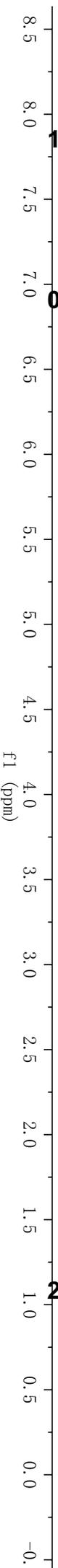


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7.810

6.897
6.856



1.081
1.060

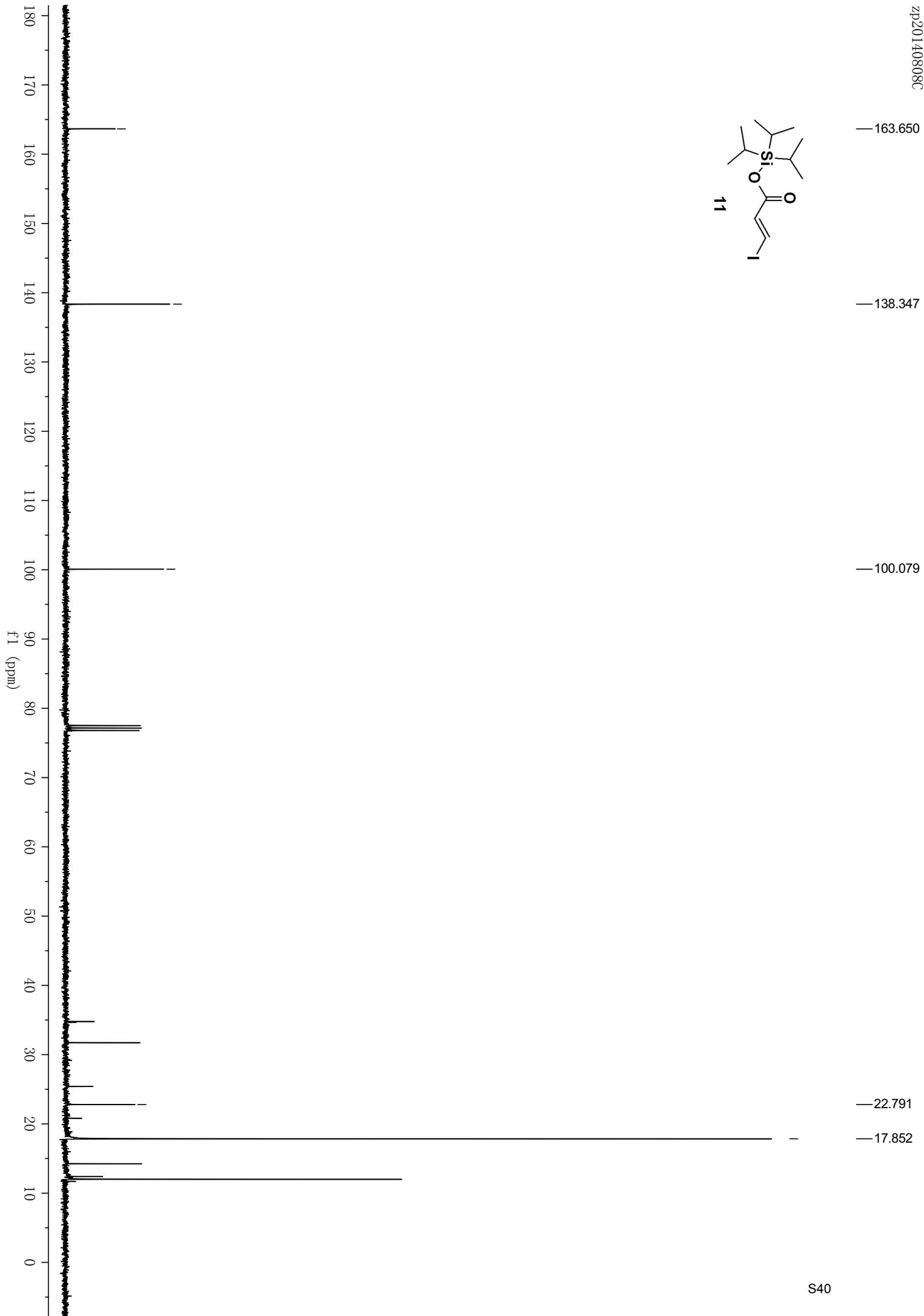
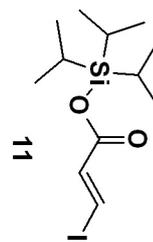


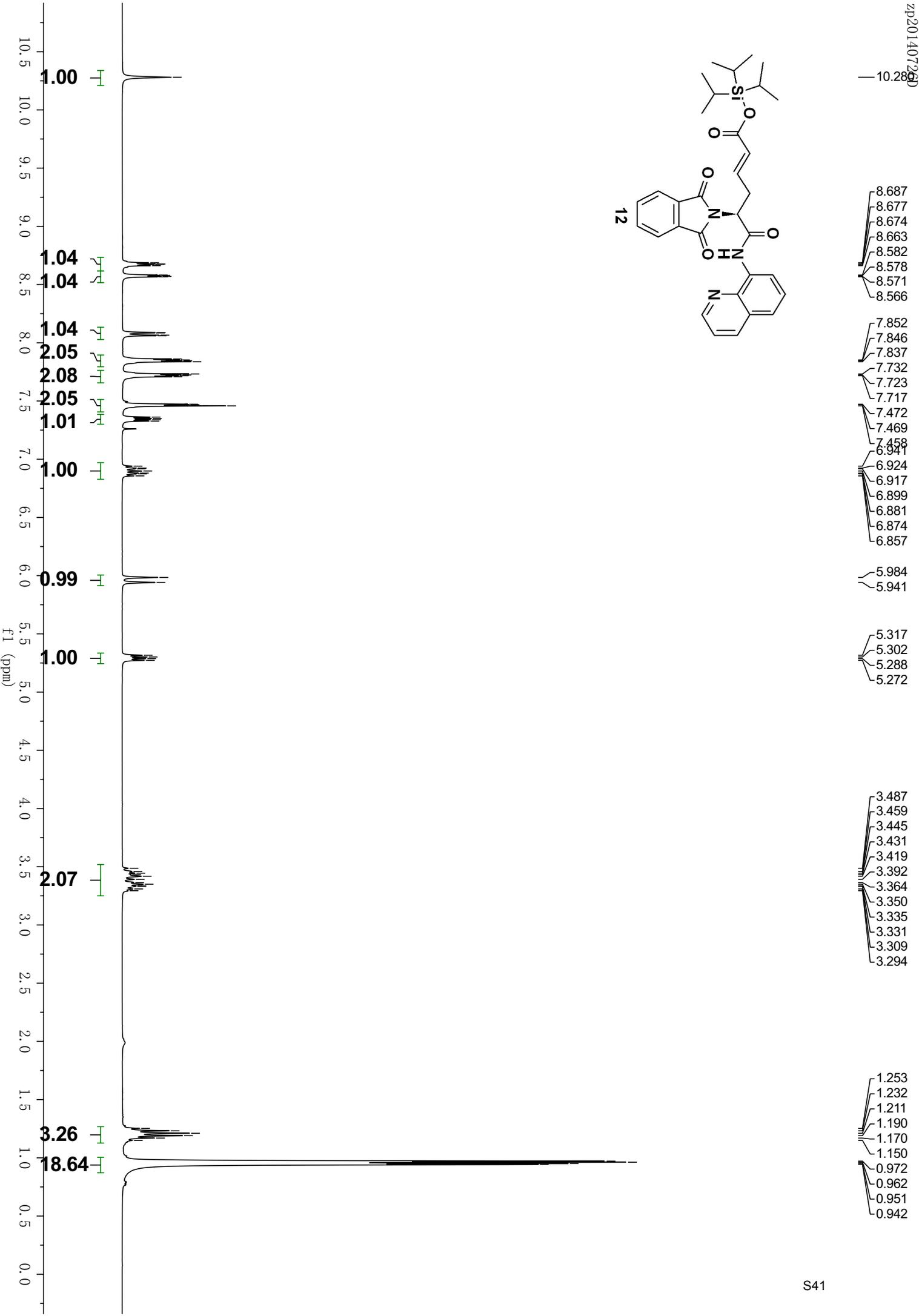
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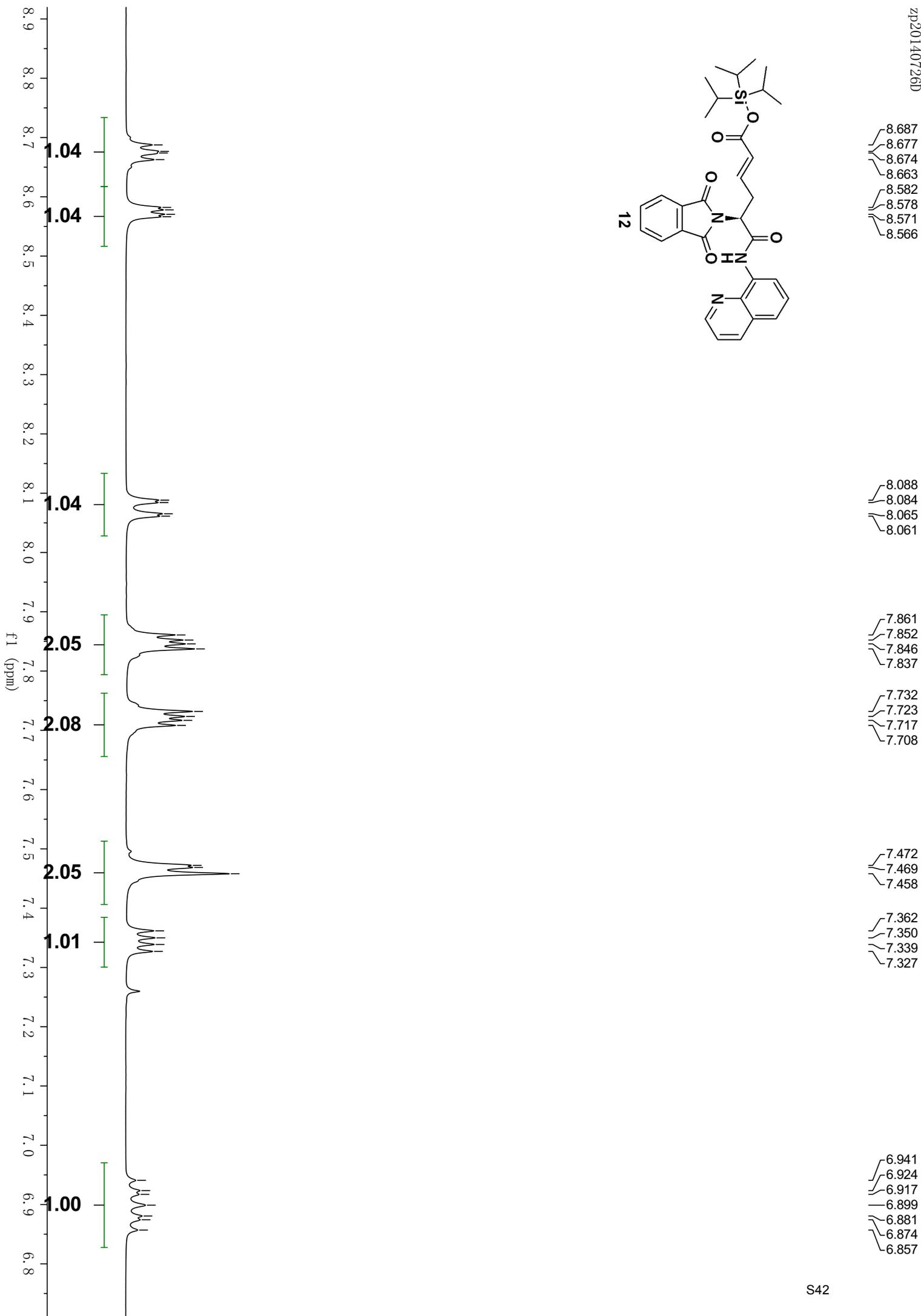
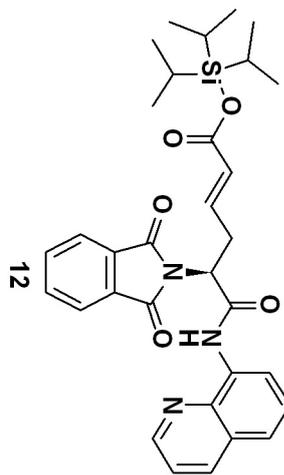
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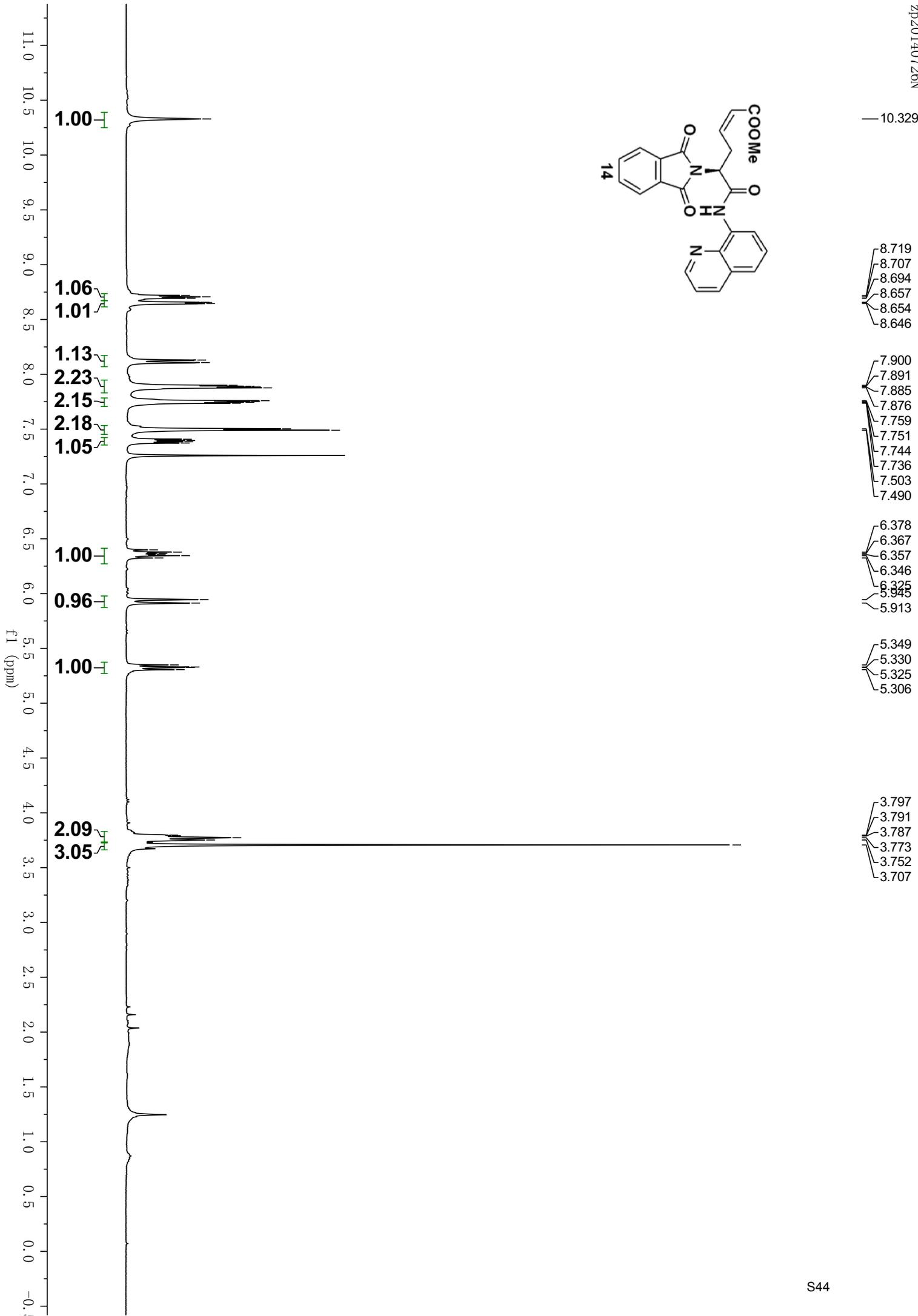
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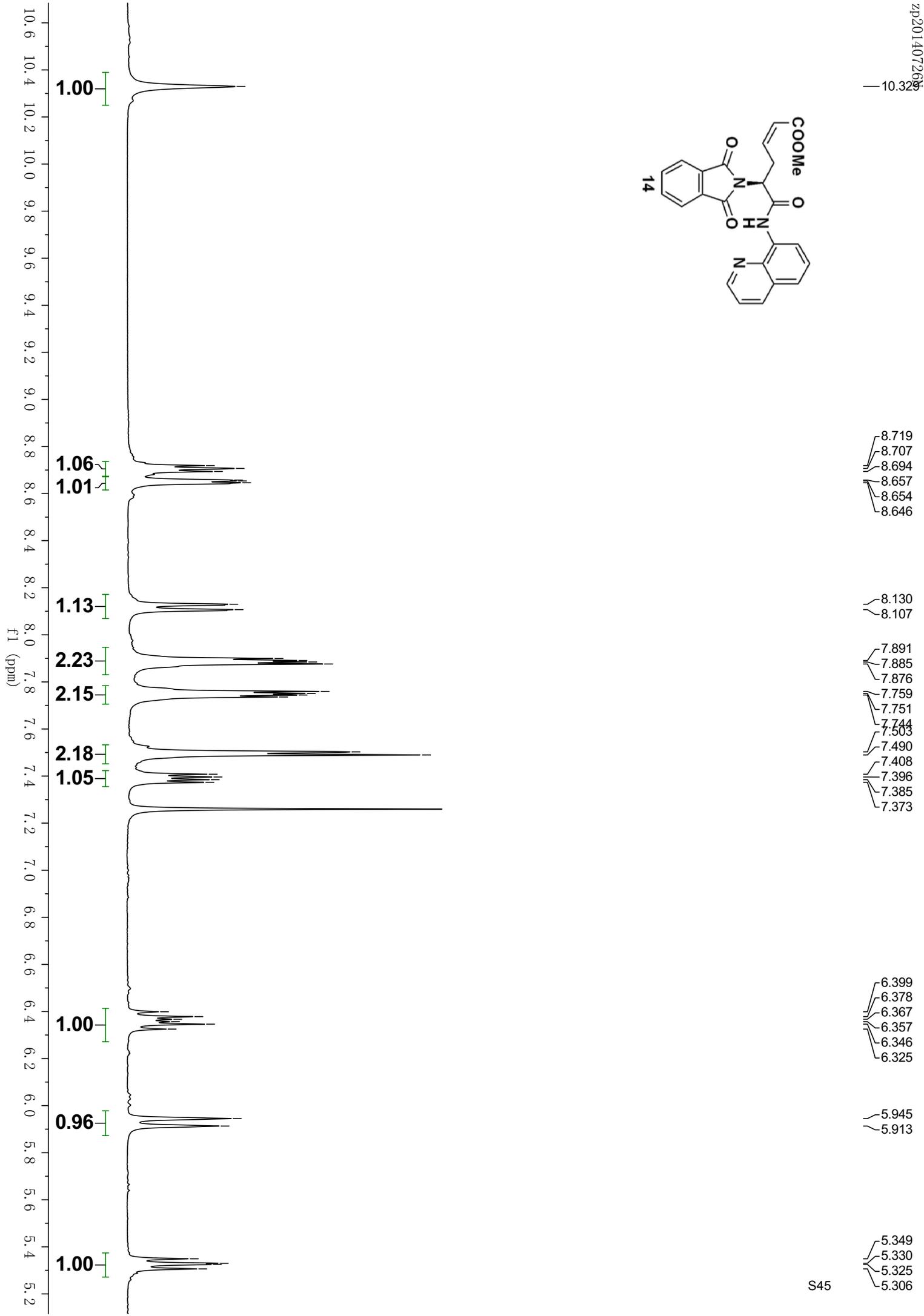
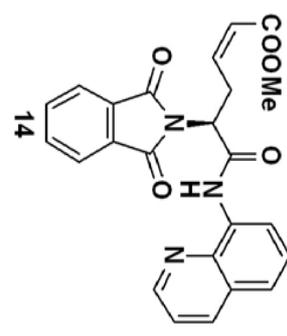
Hexanes



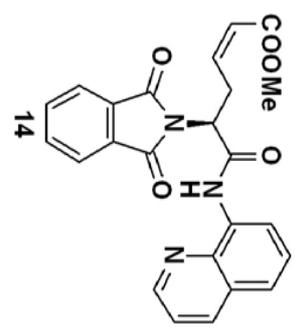




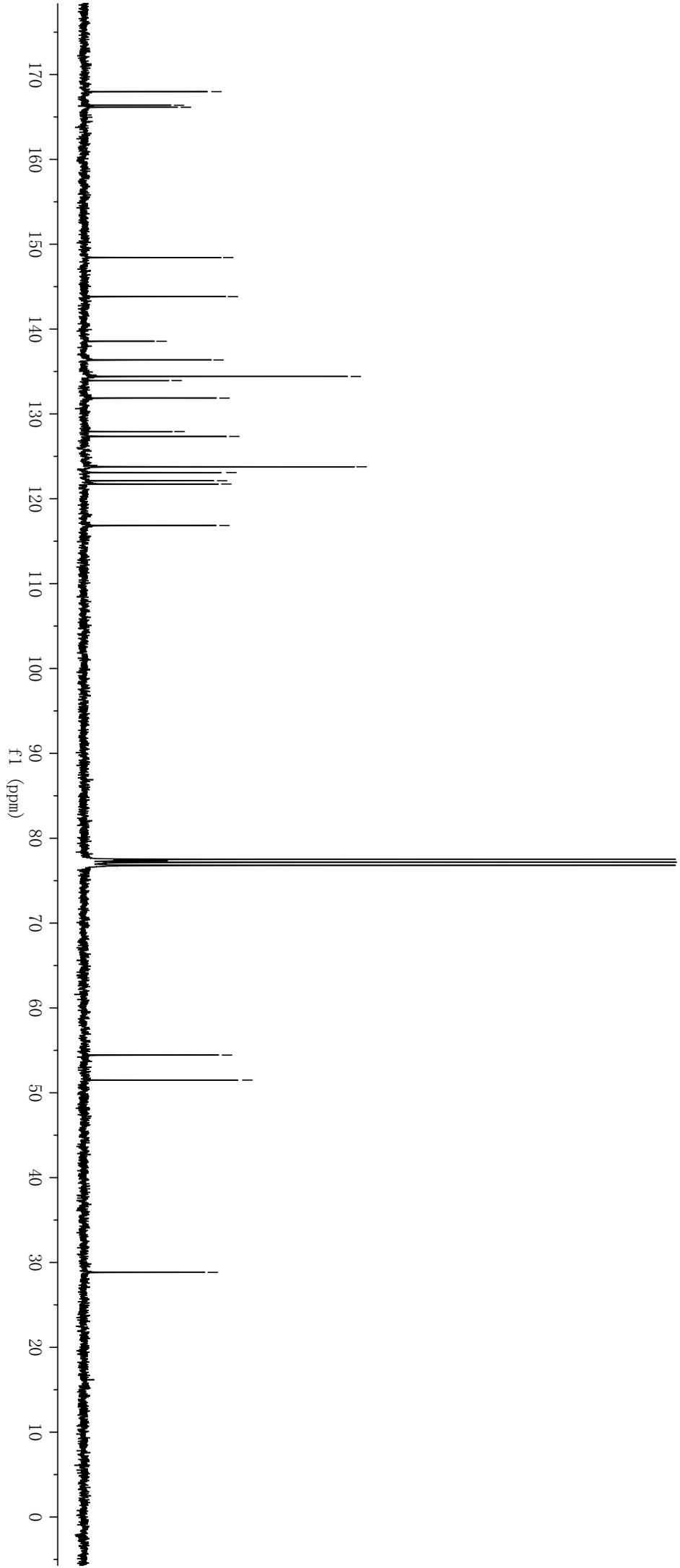




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166.147

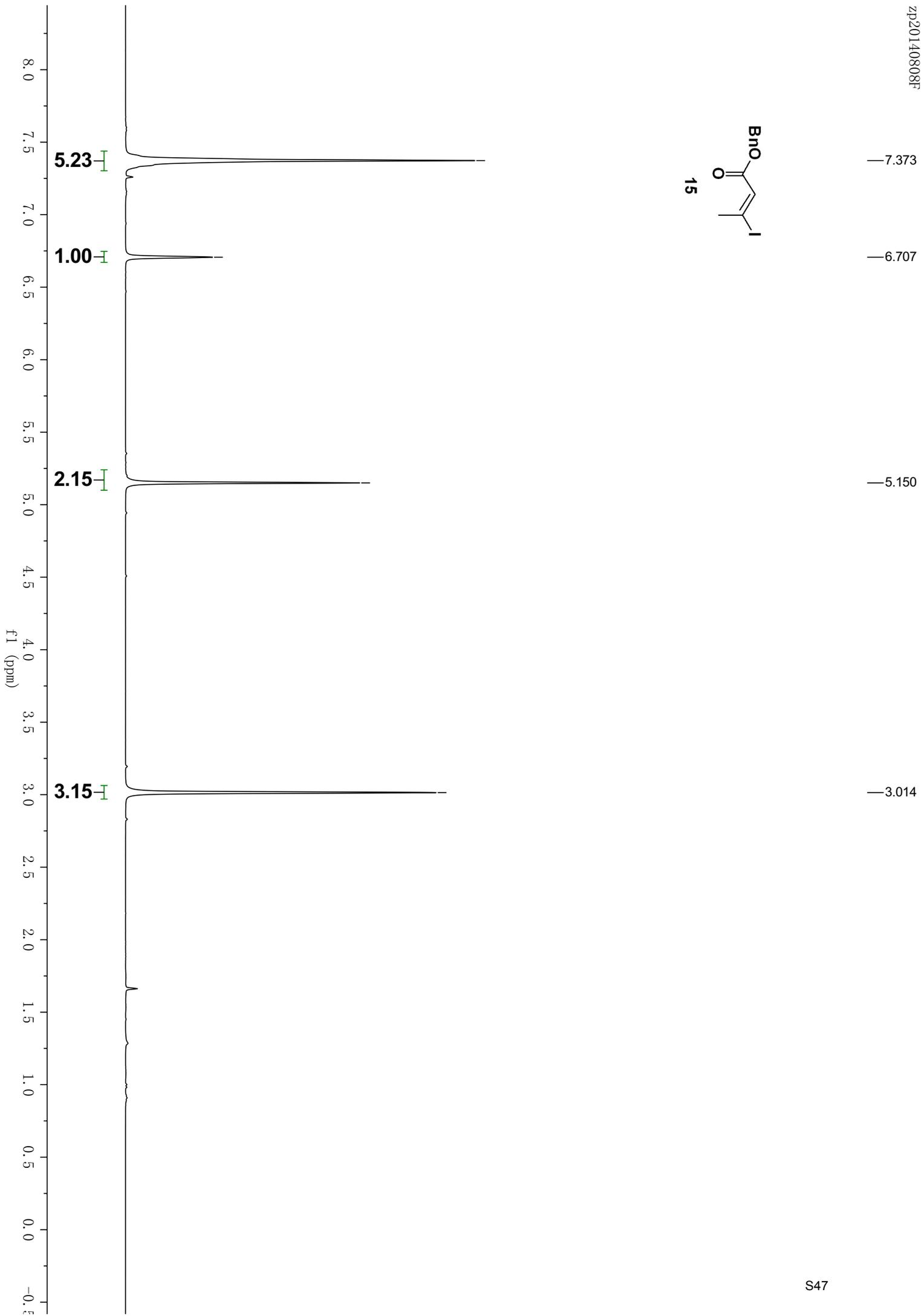
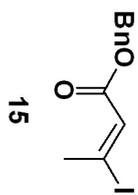


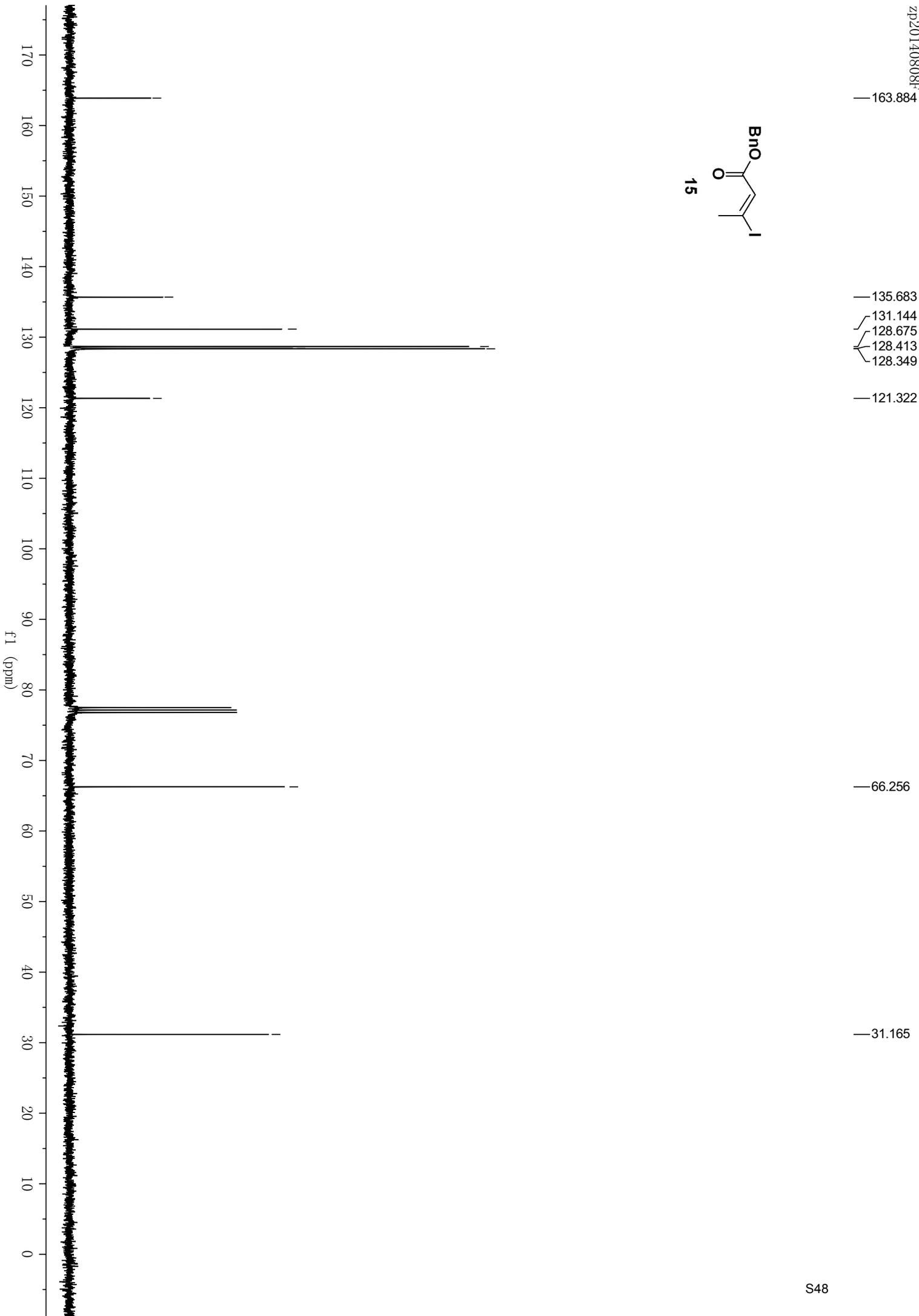
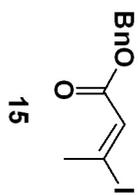
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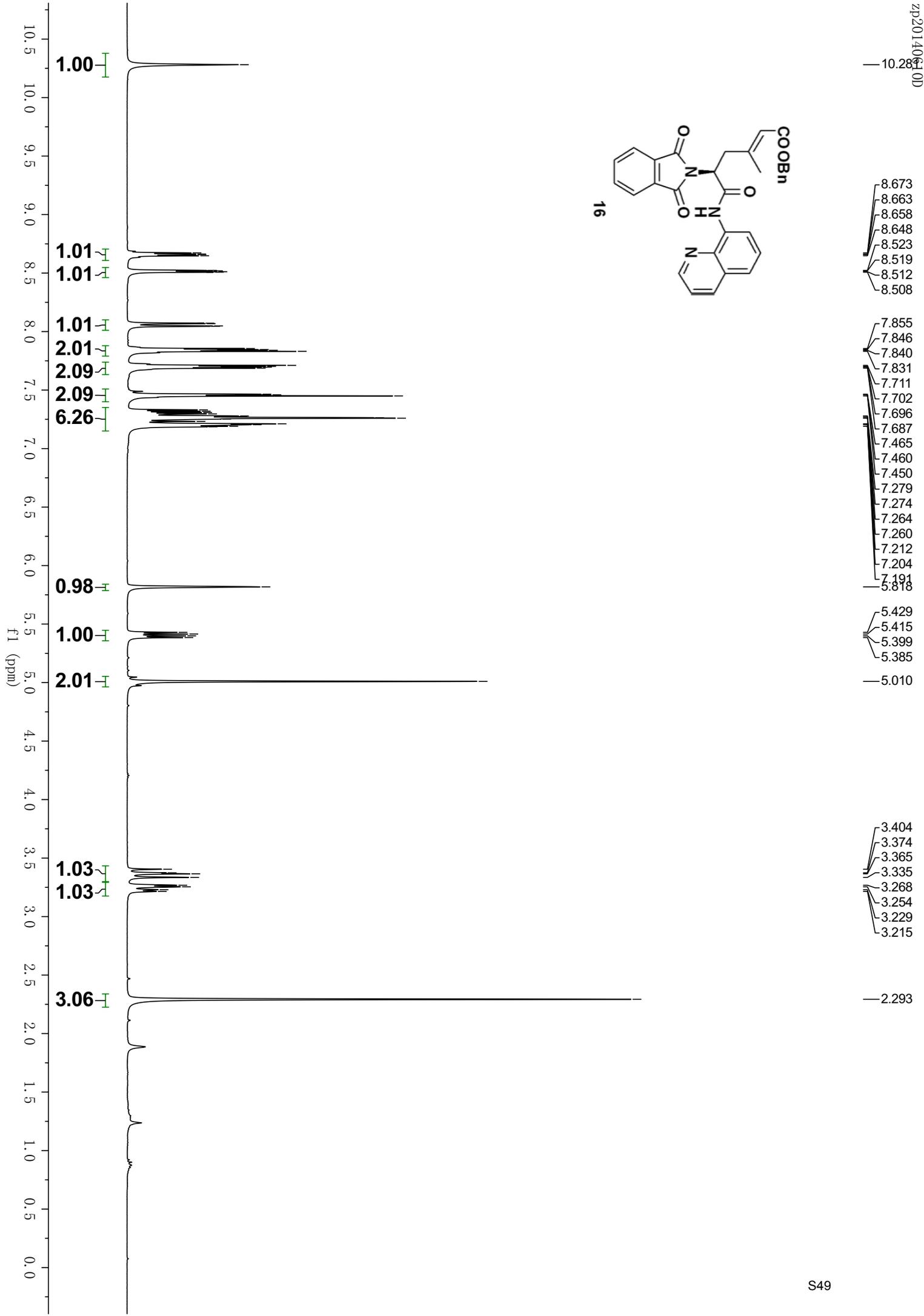


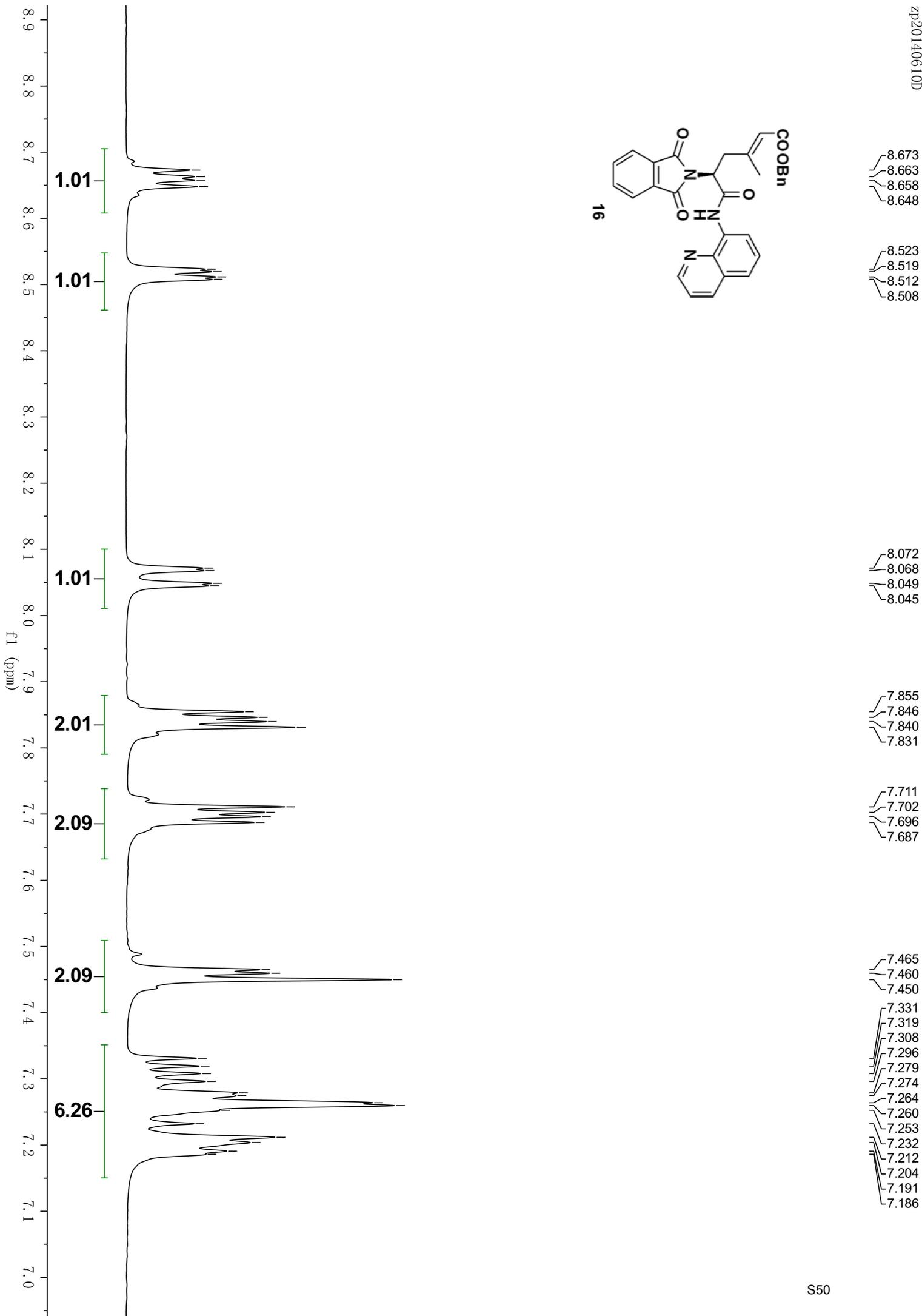
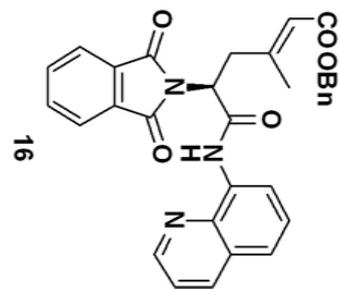
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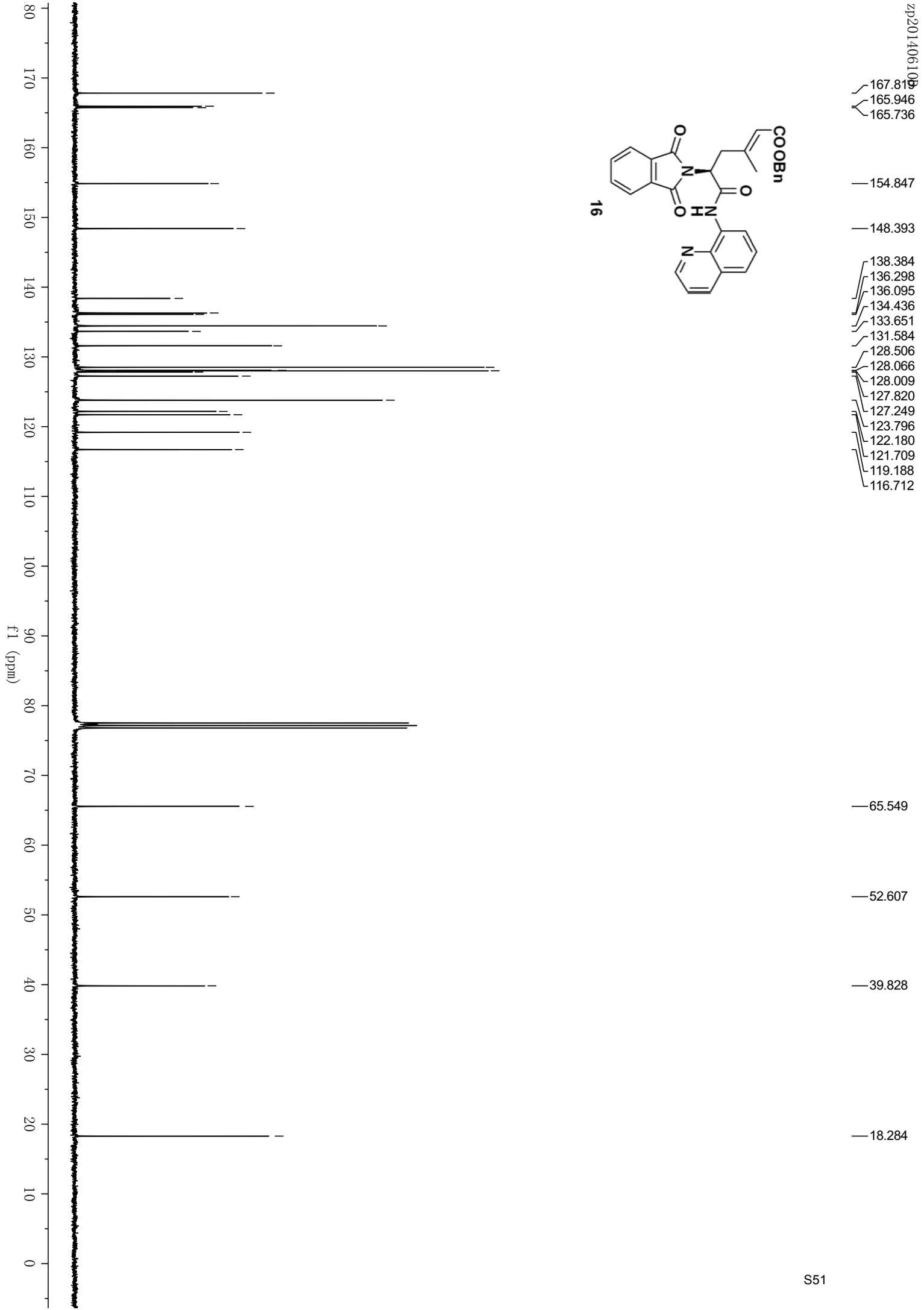
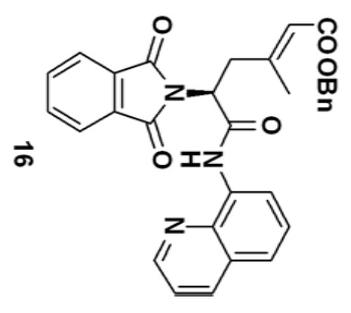
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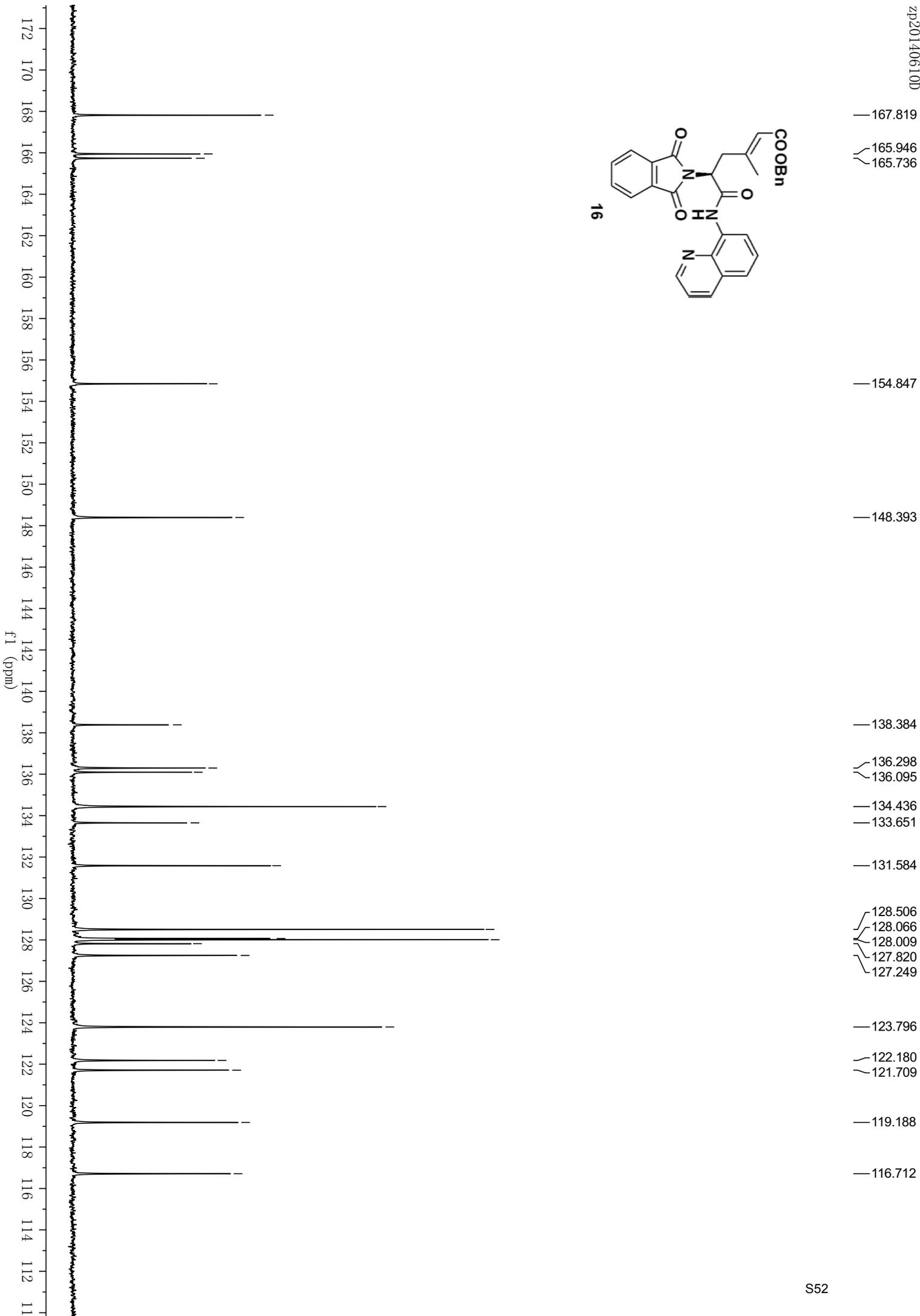
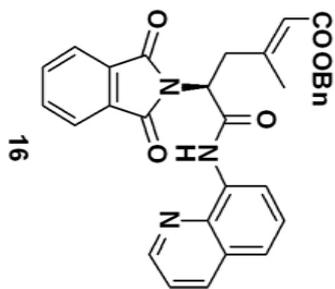


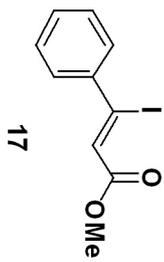








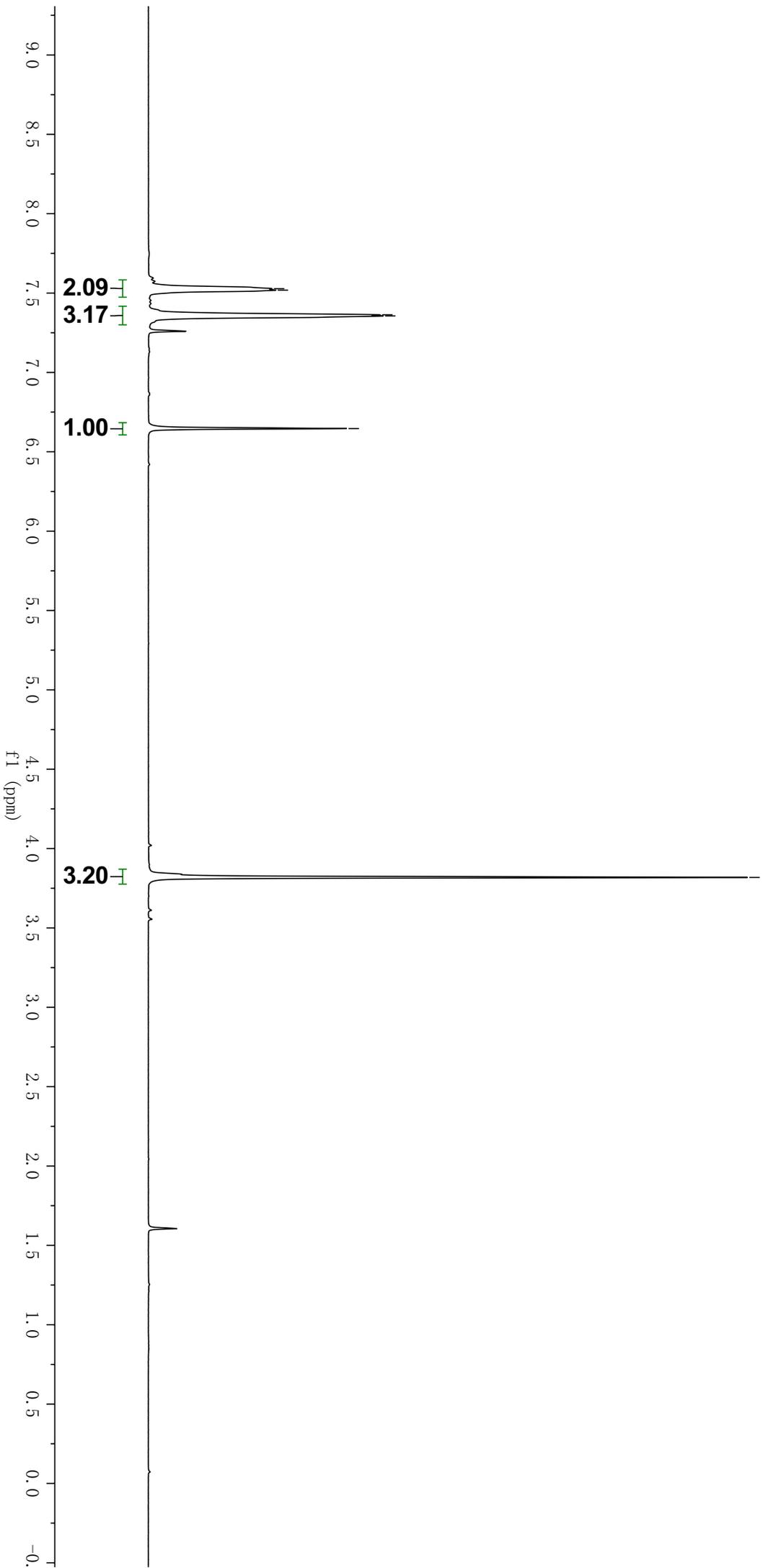


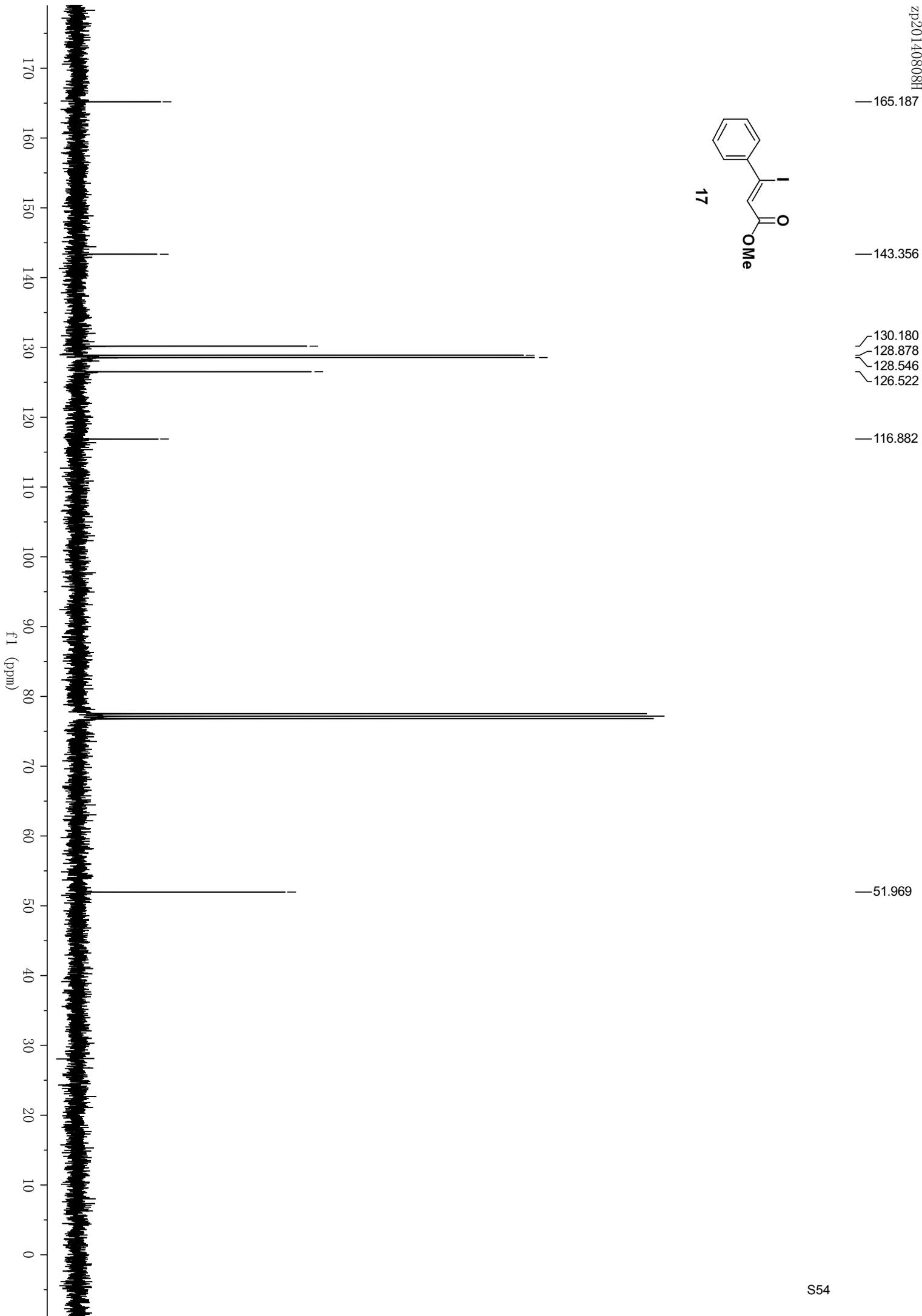
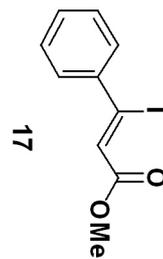


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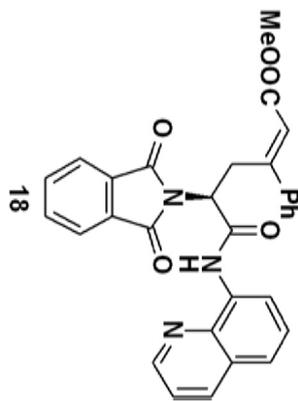
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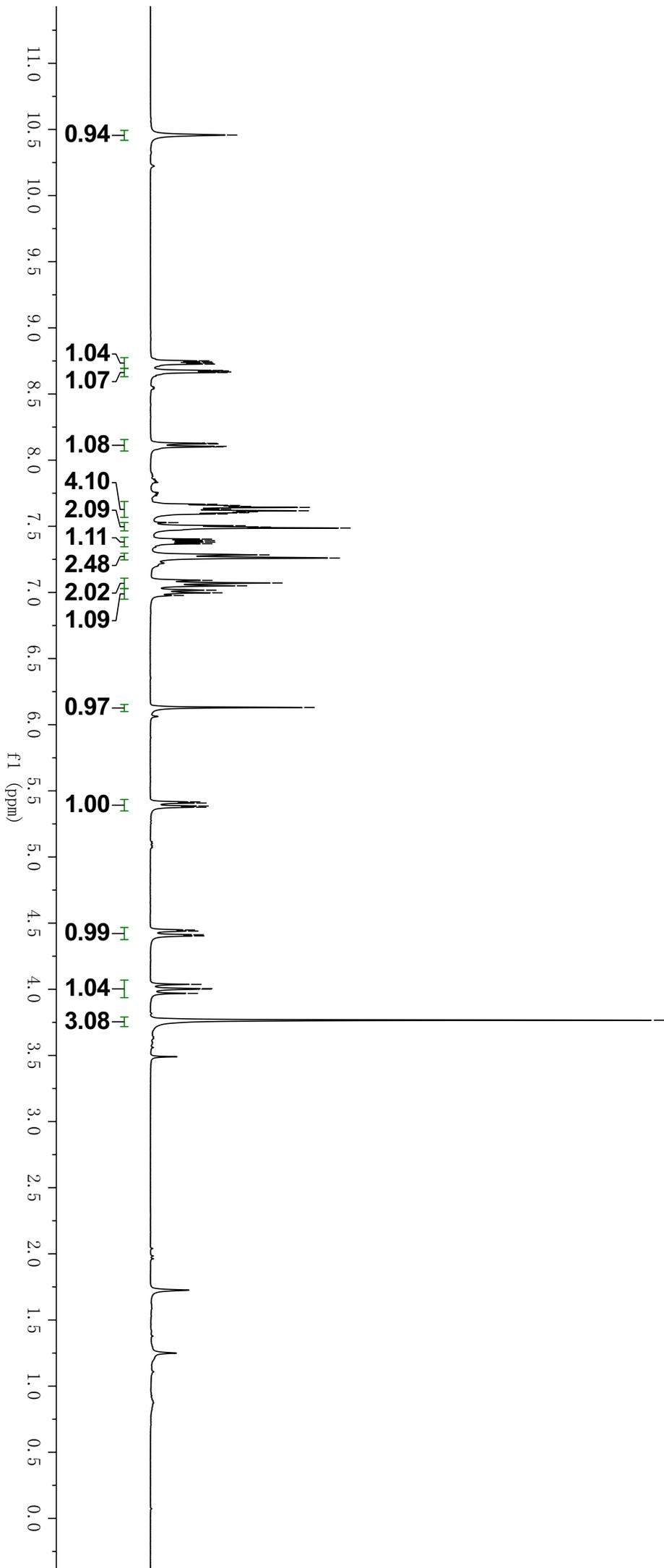
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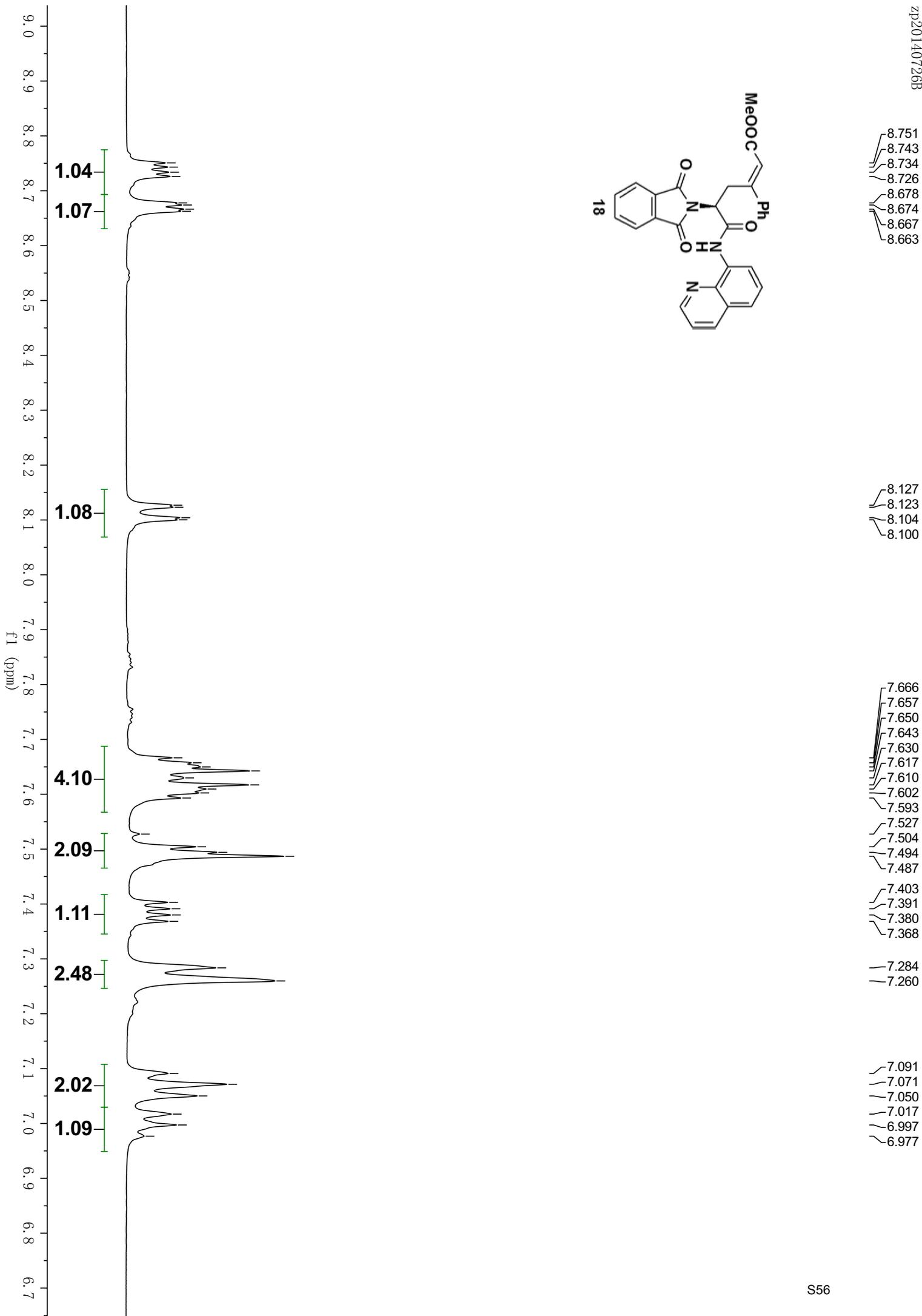
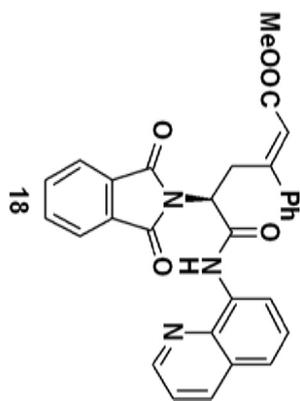
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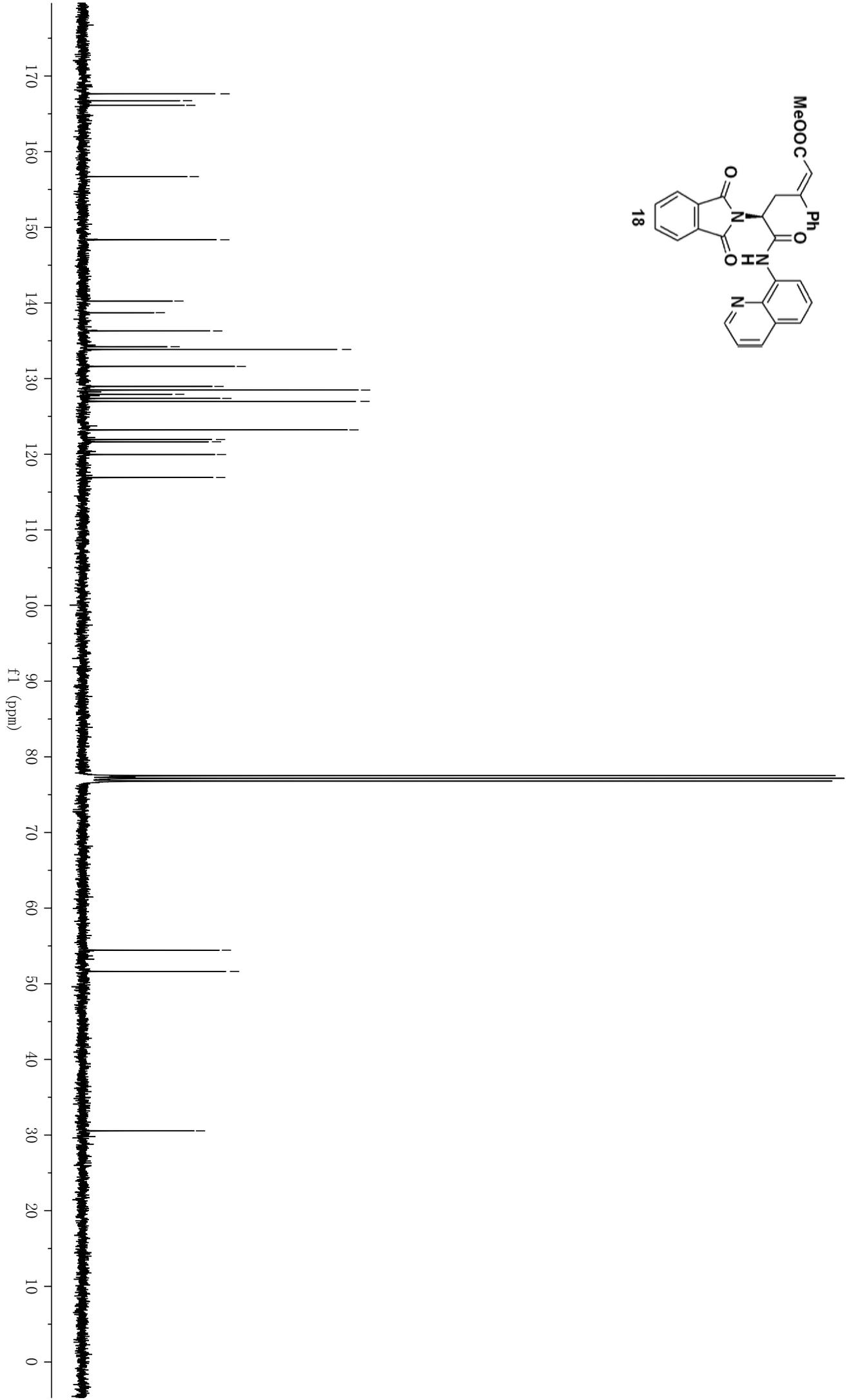
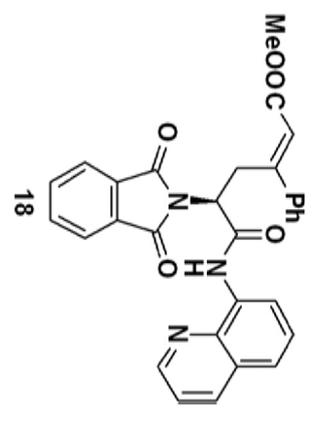
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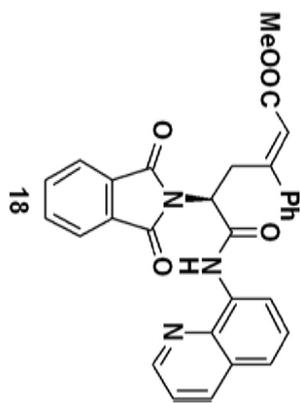
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- 54.444
- 51.634
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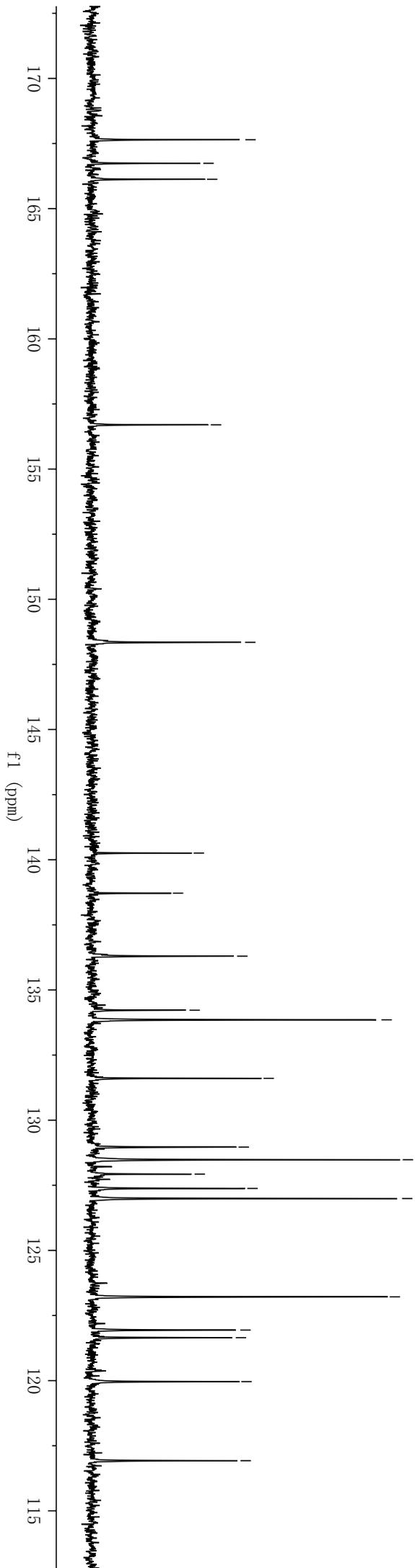
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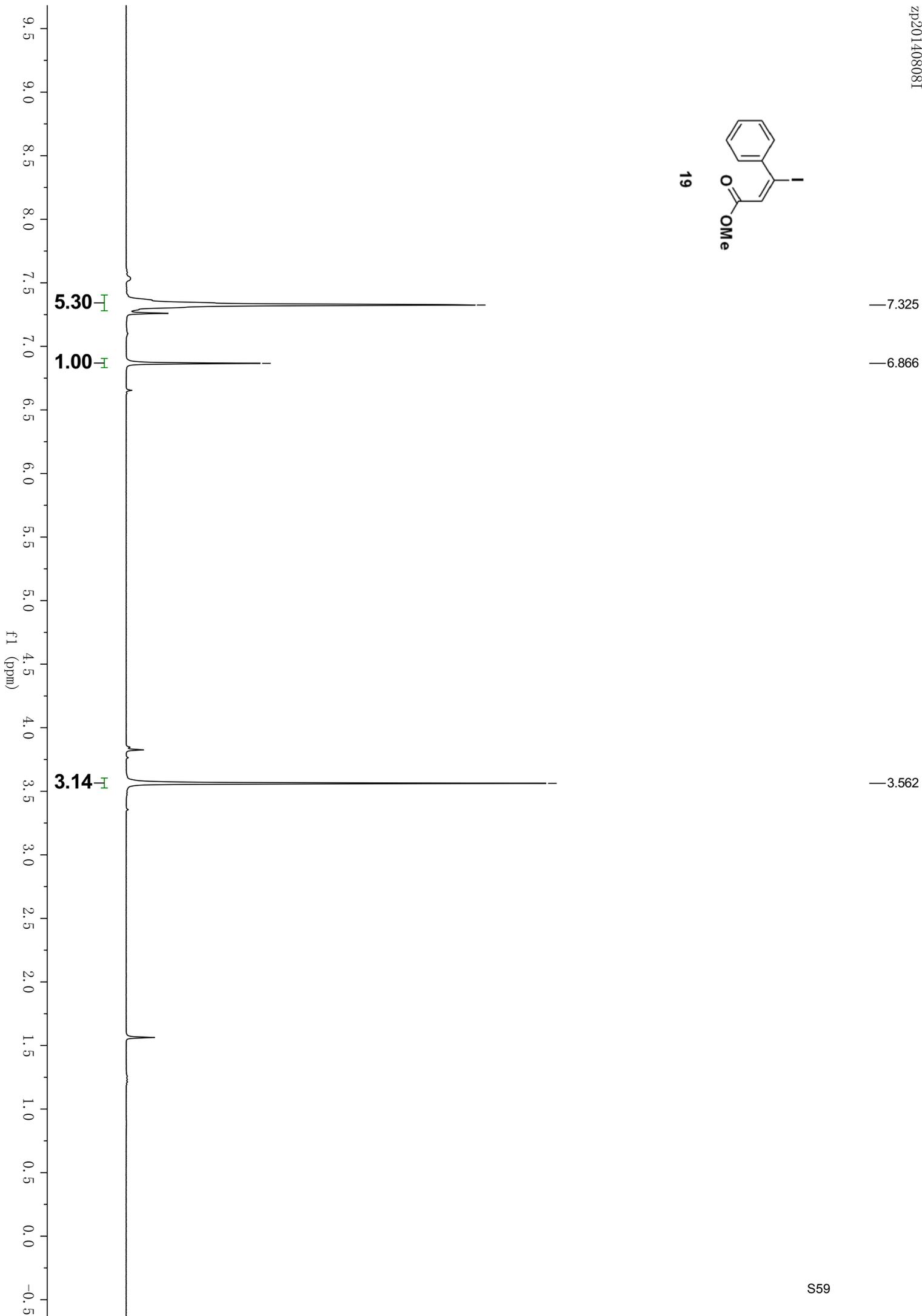
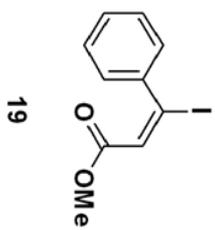
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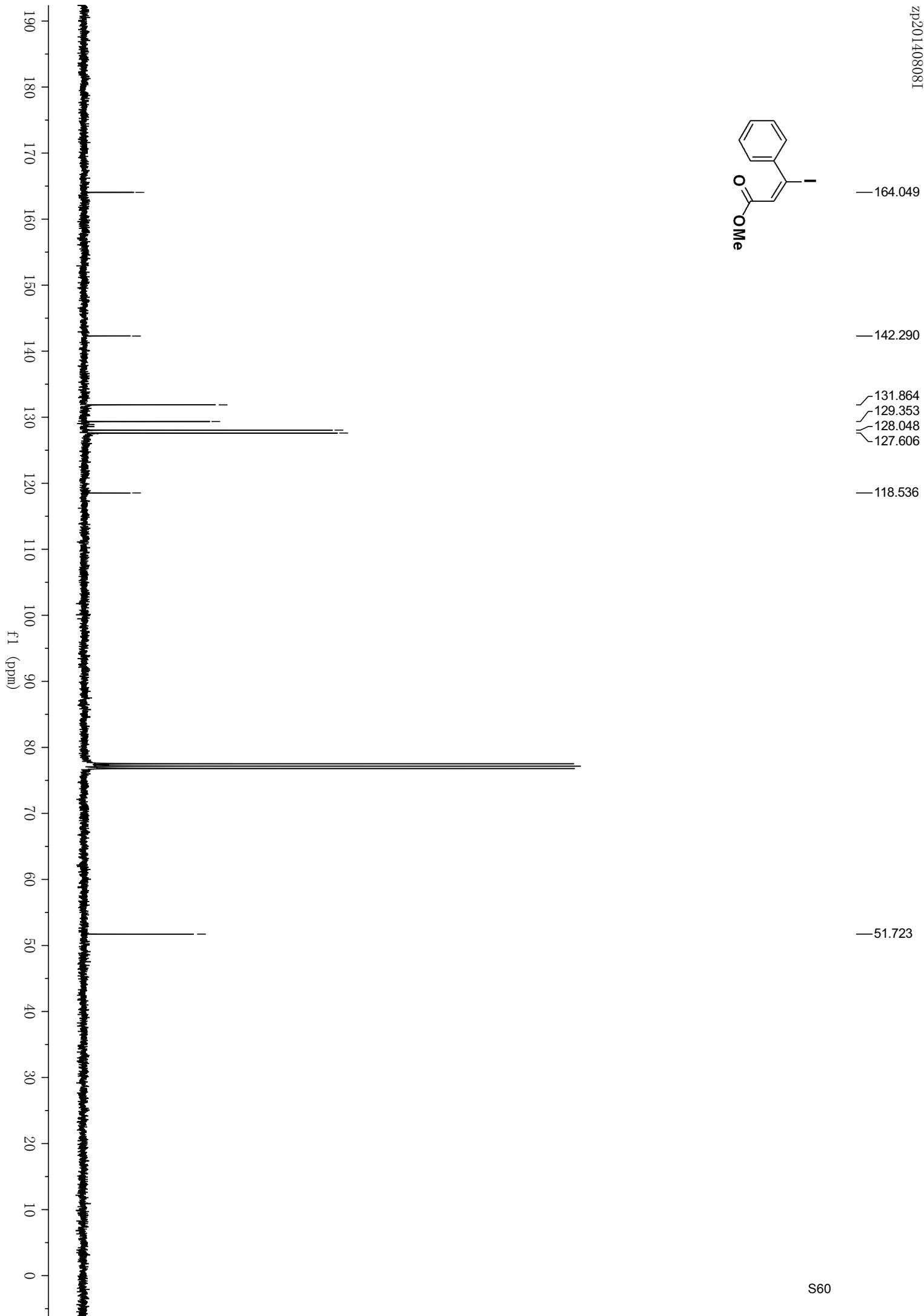
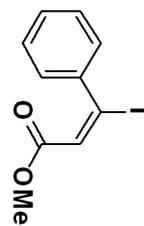
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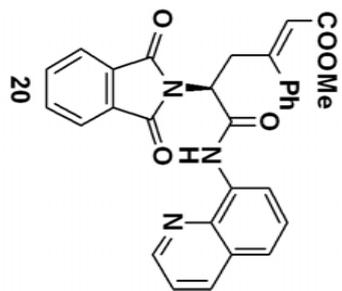
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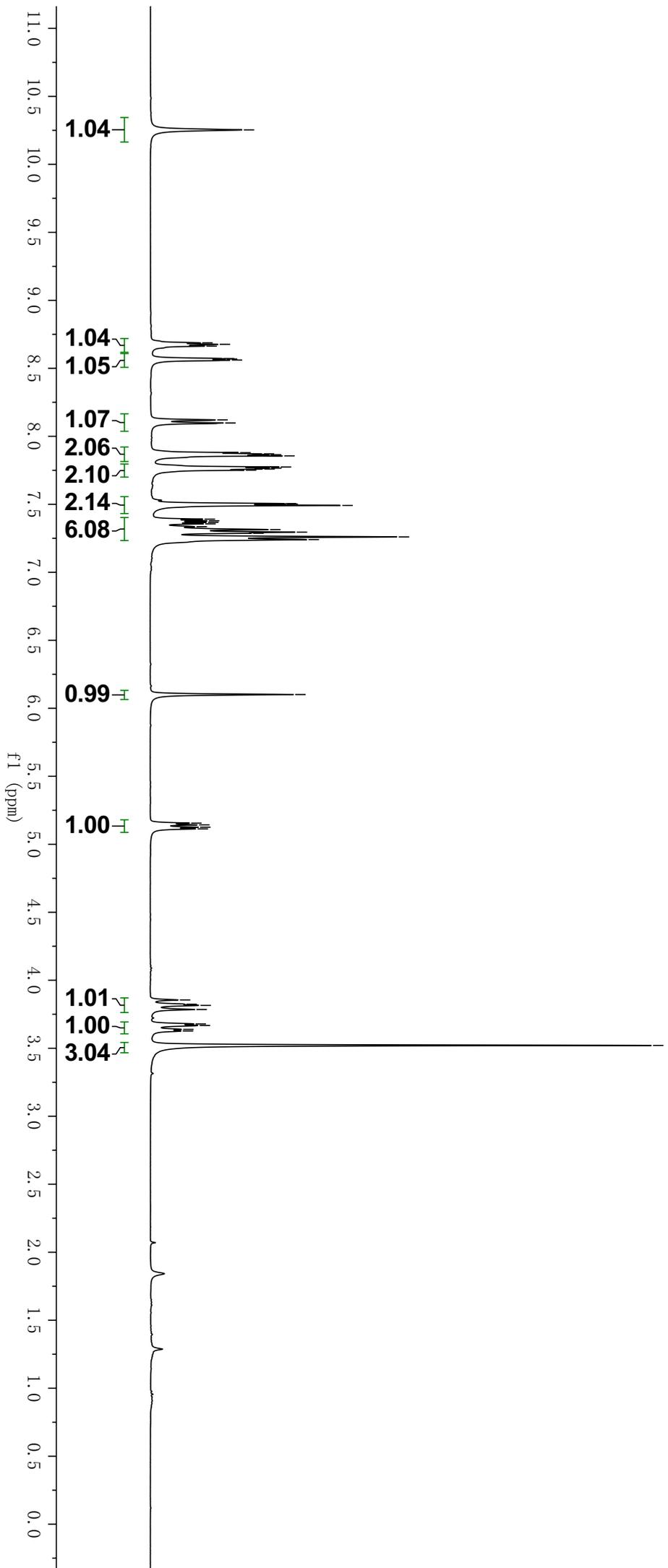


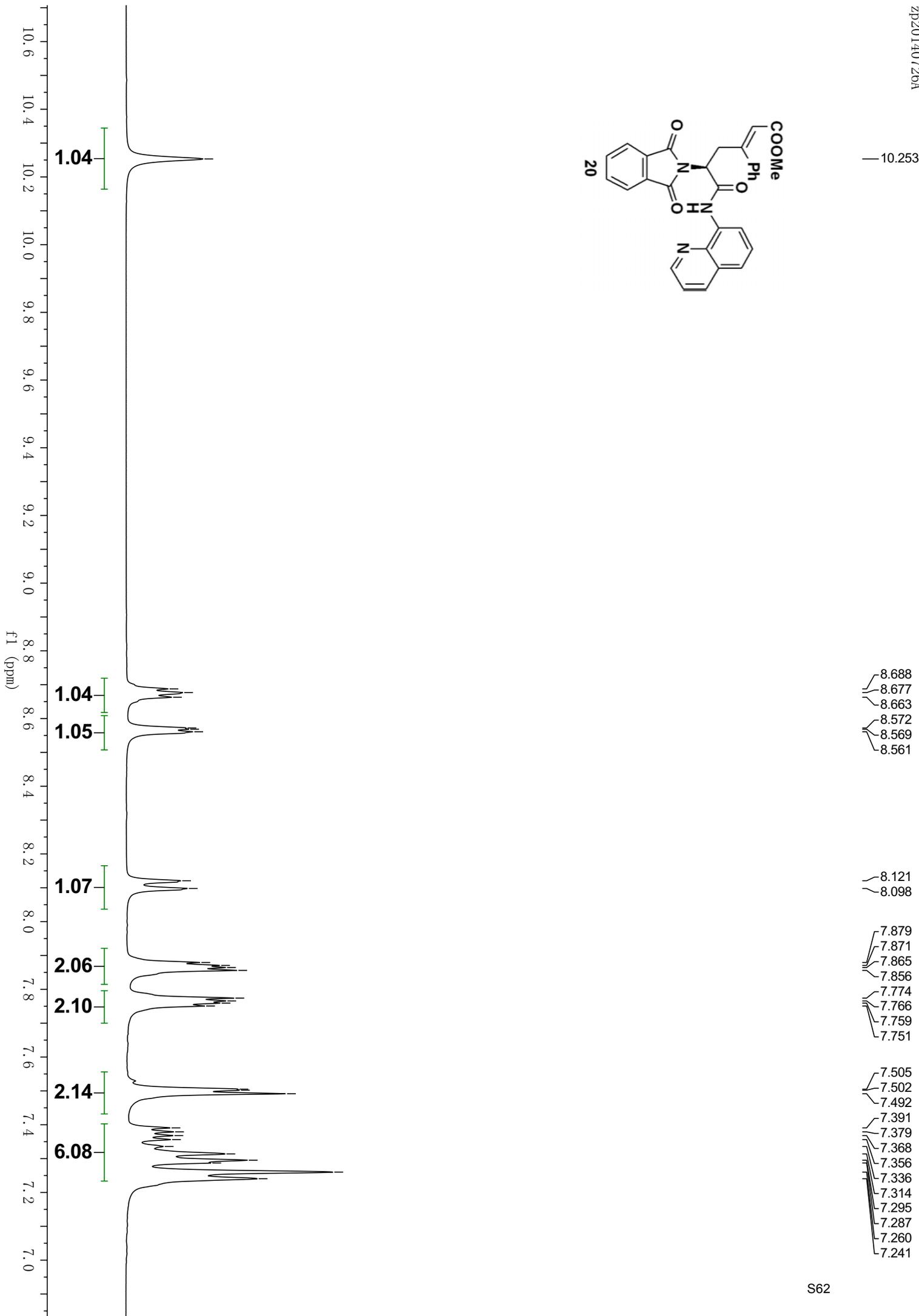
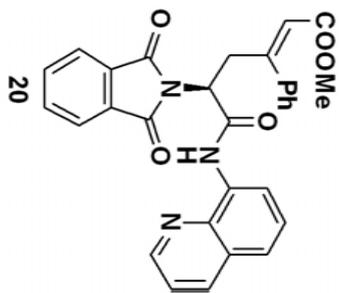
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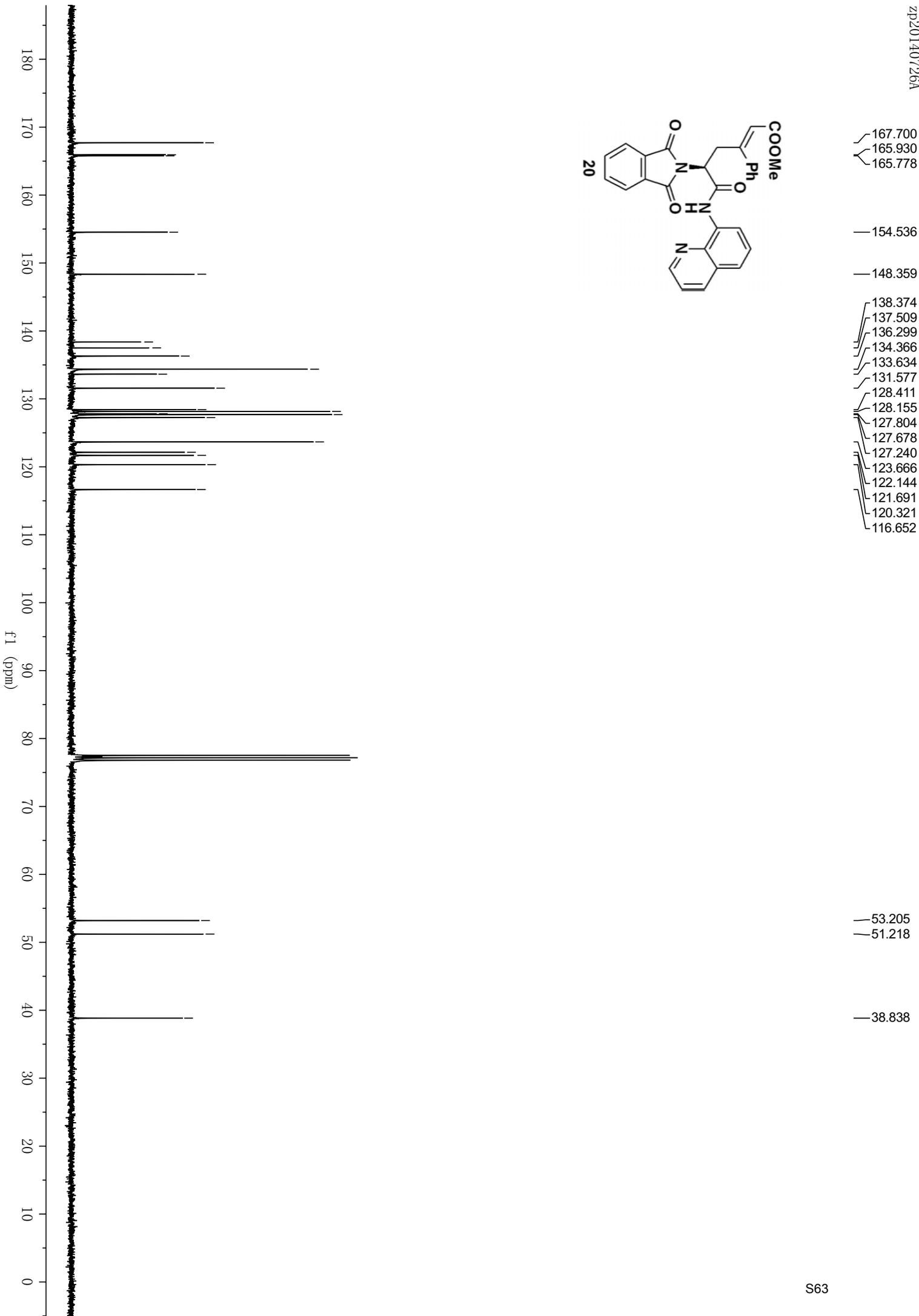
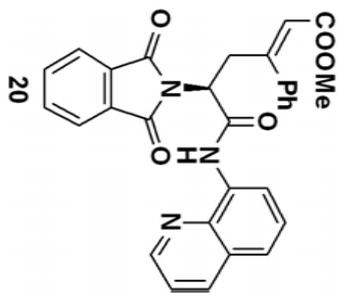
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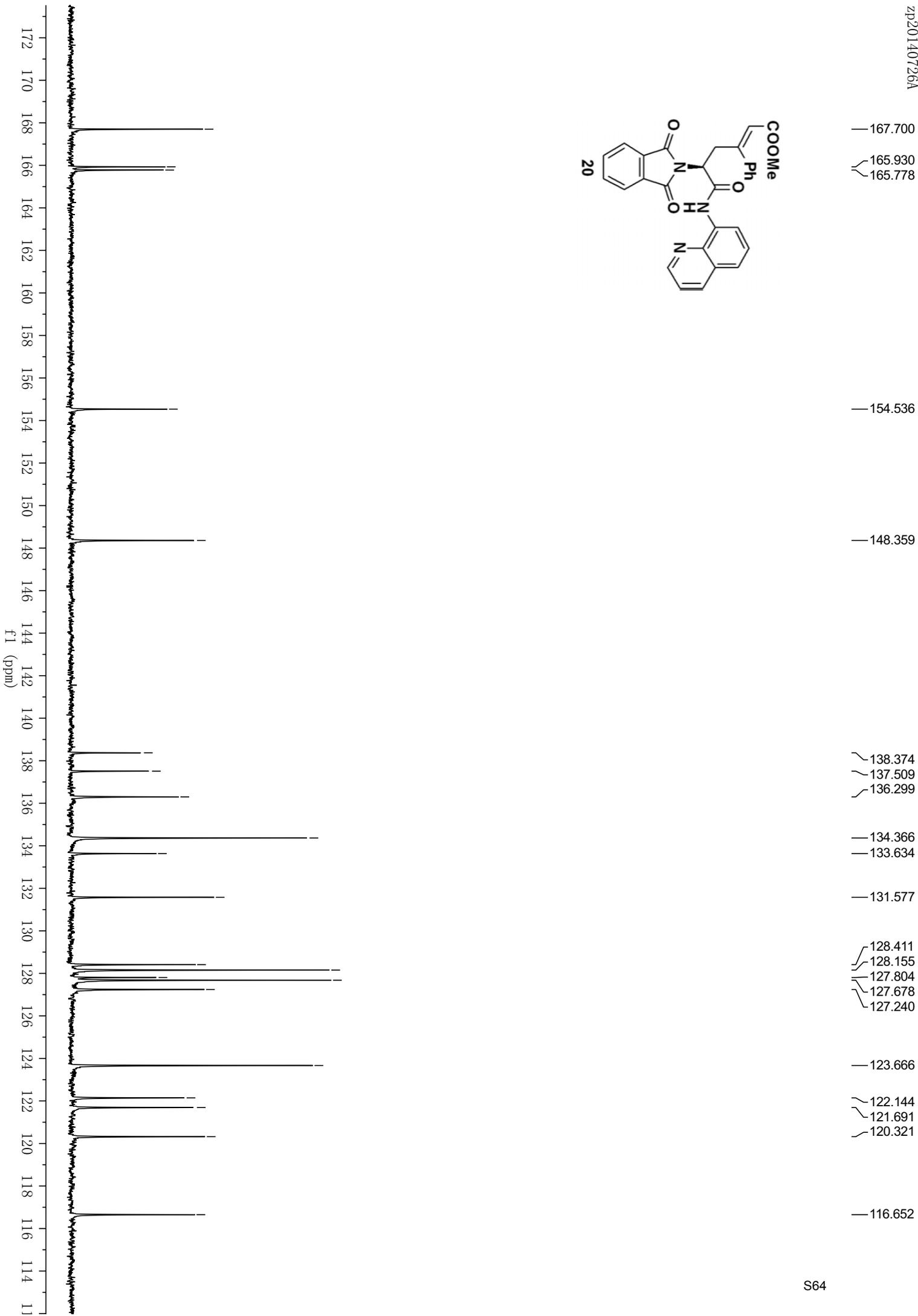
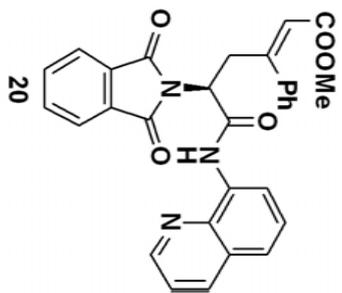
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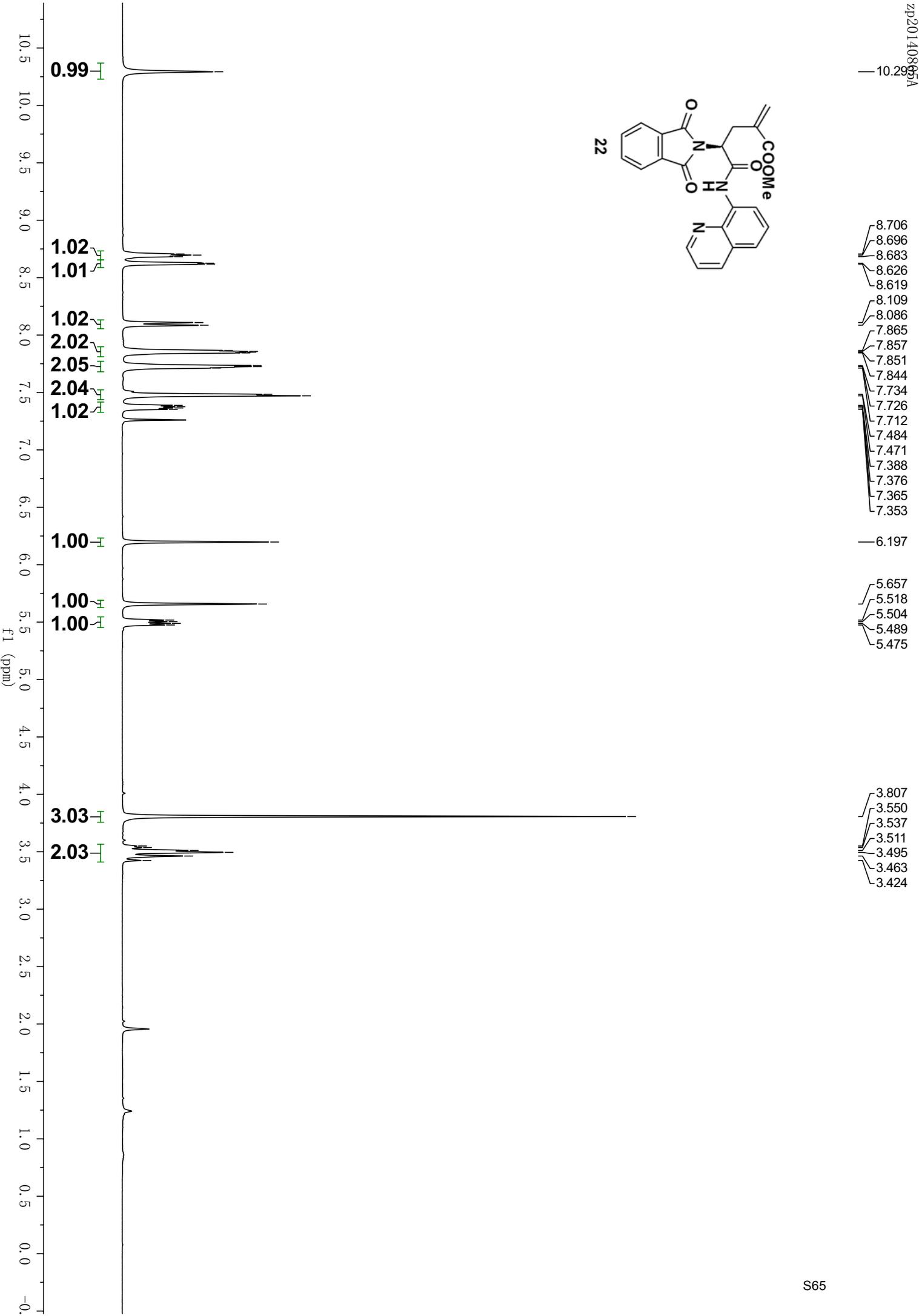
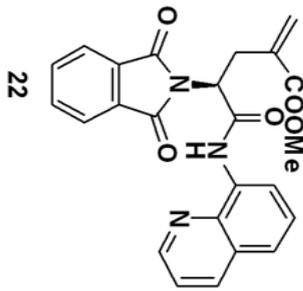




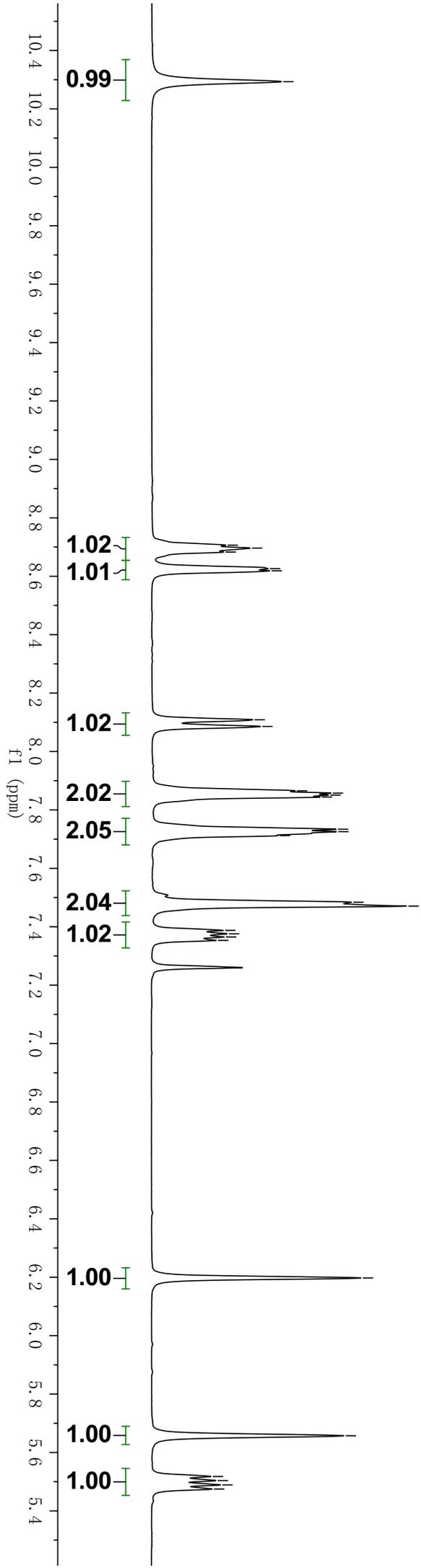
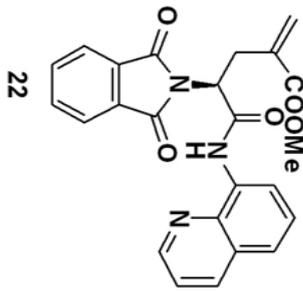




10.296A



10.296



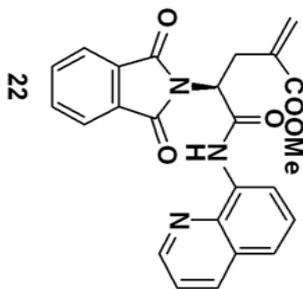
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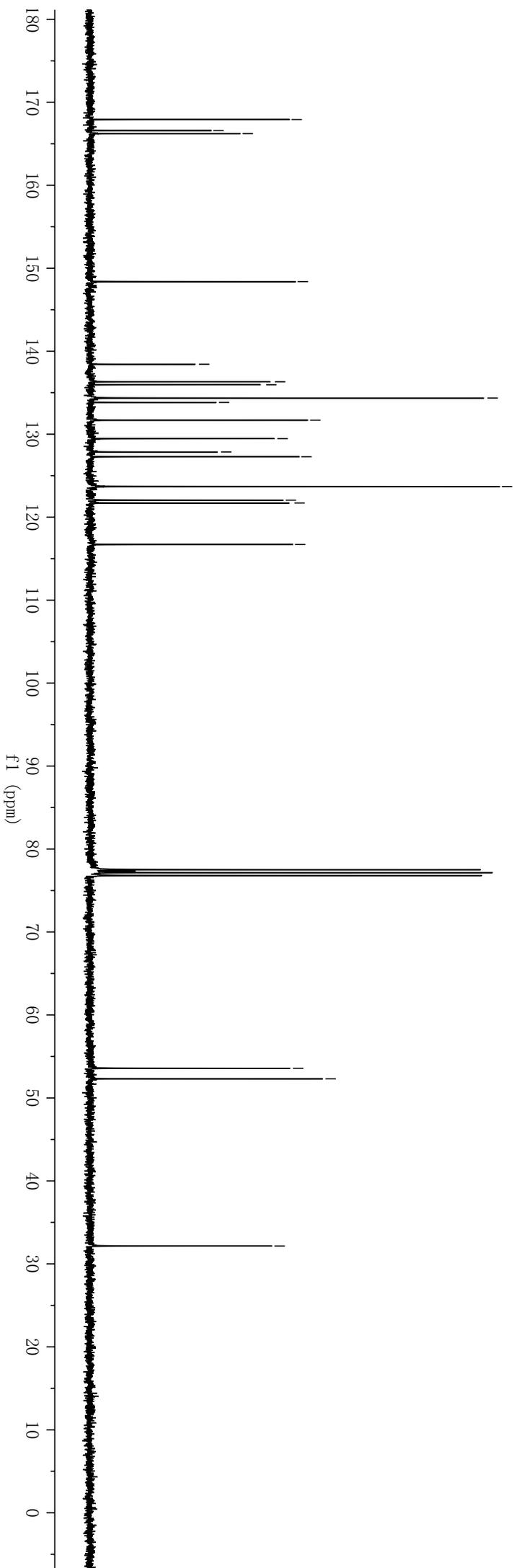
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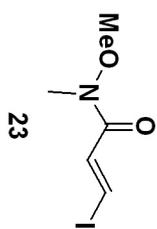


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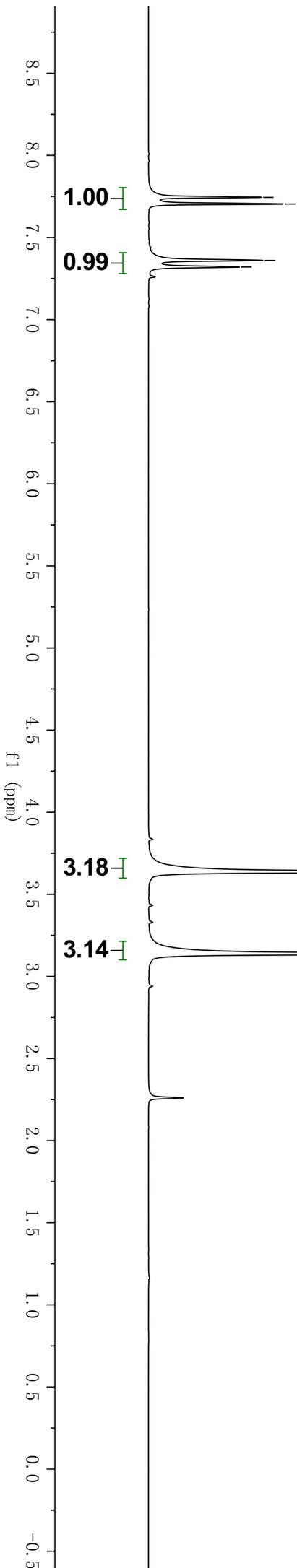
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7.704

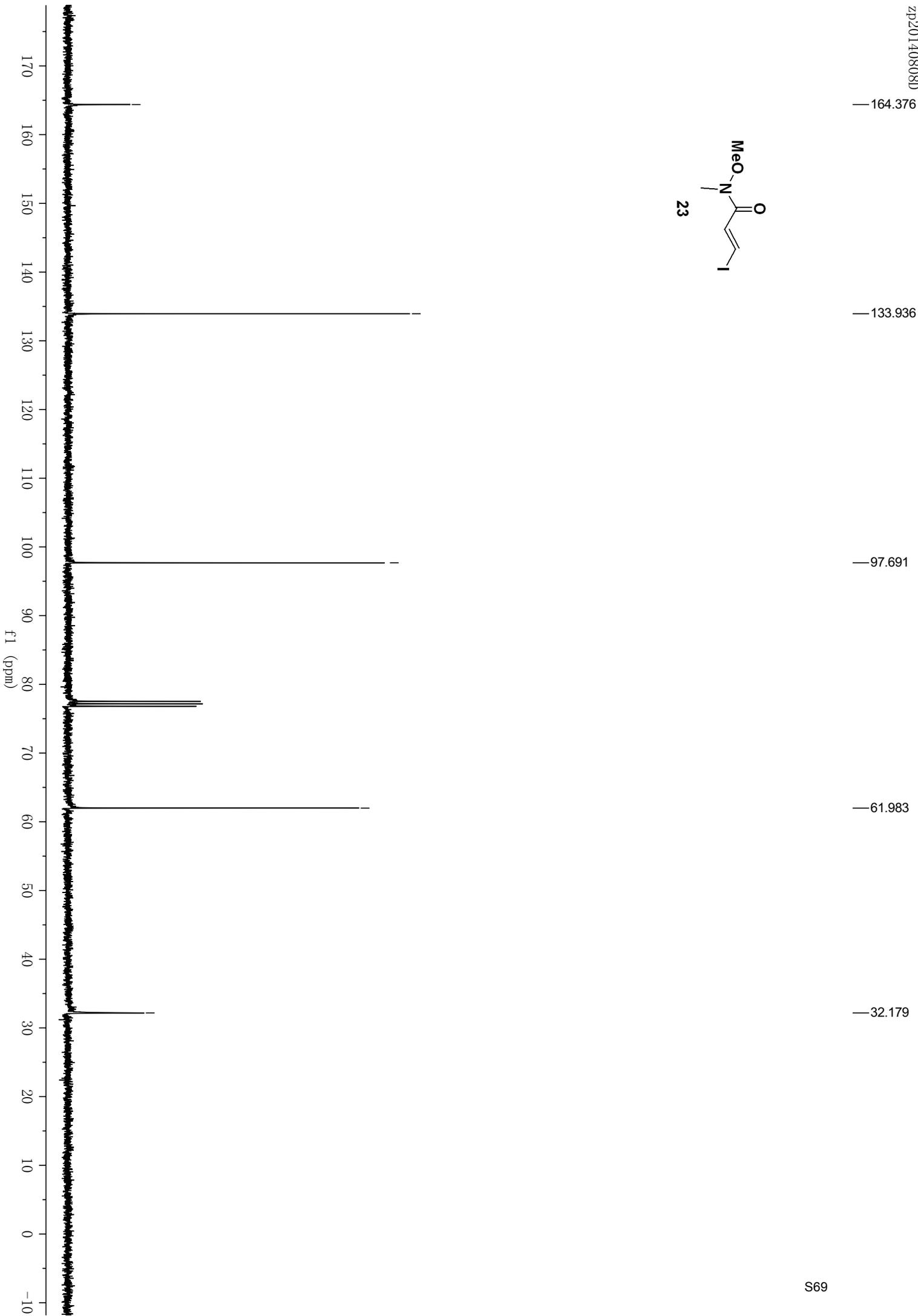
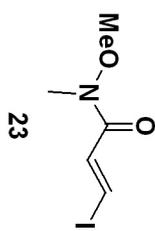
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7.320



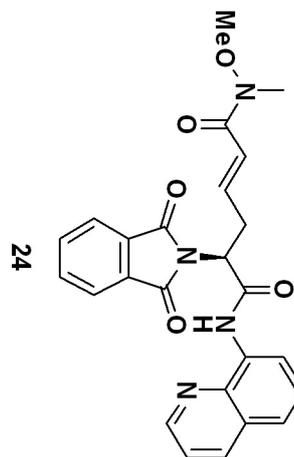
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3.137





10.308



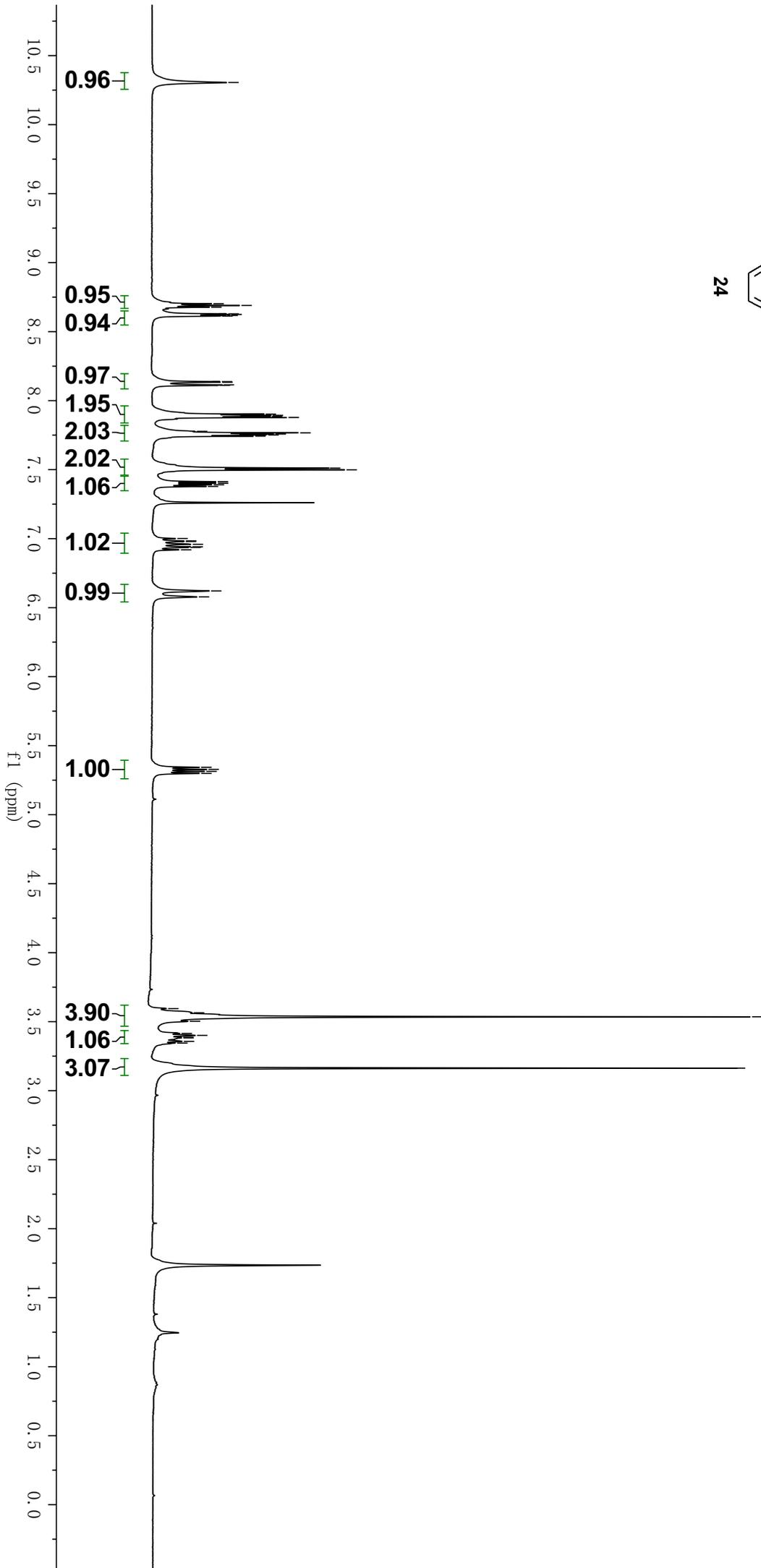
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8.613

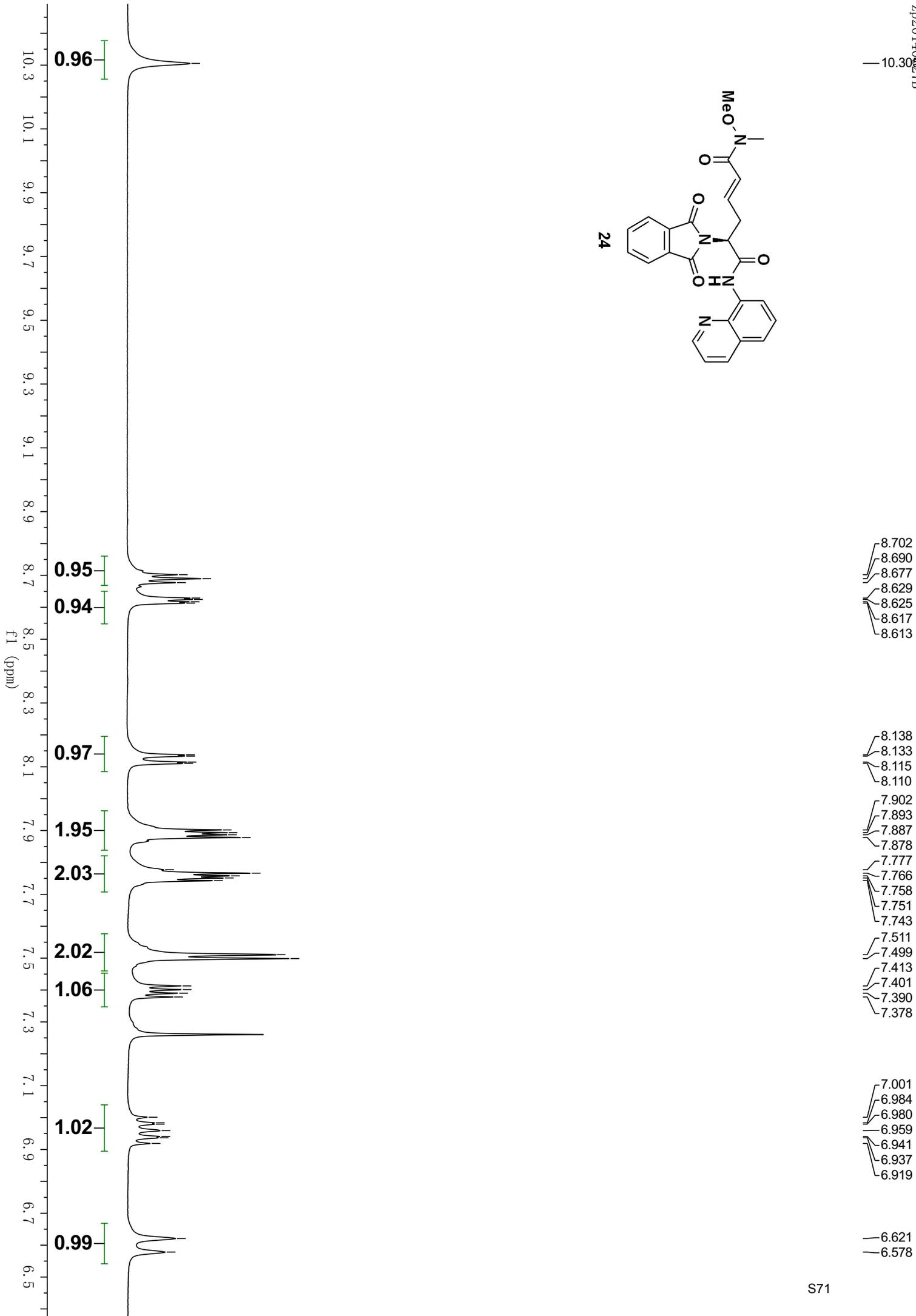
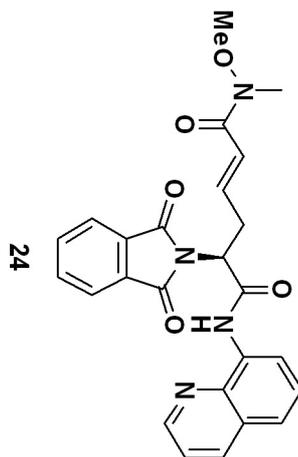
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7.751
7.499

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6.937
6.621
6.578

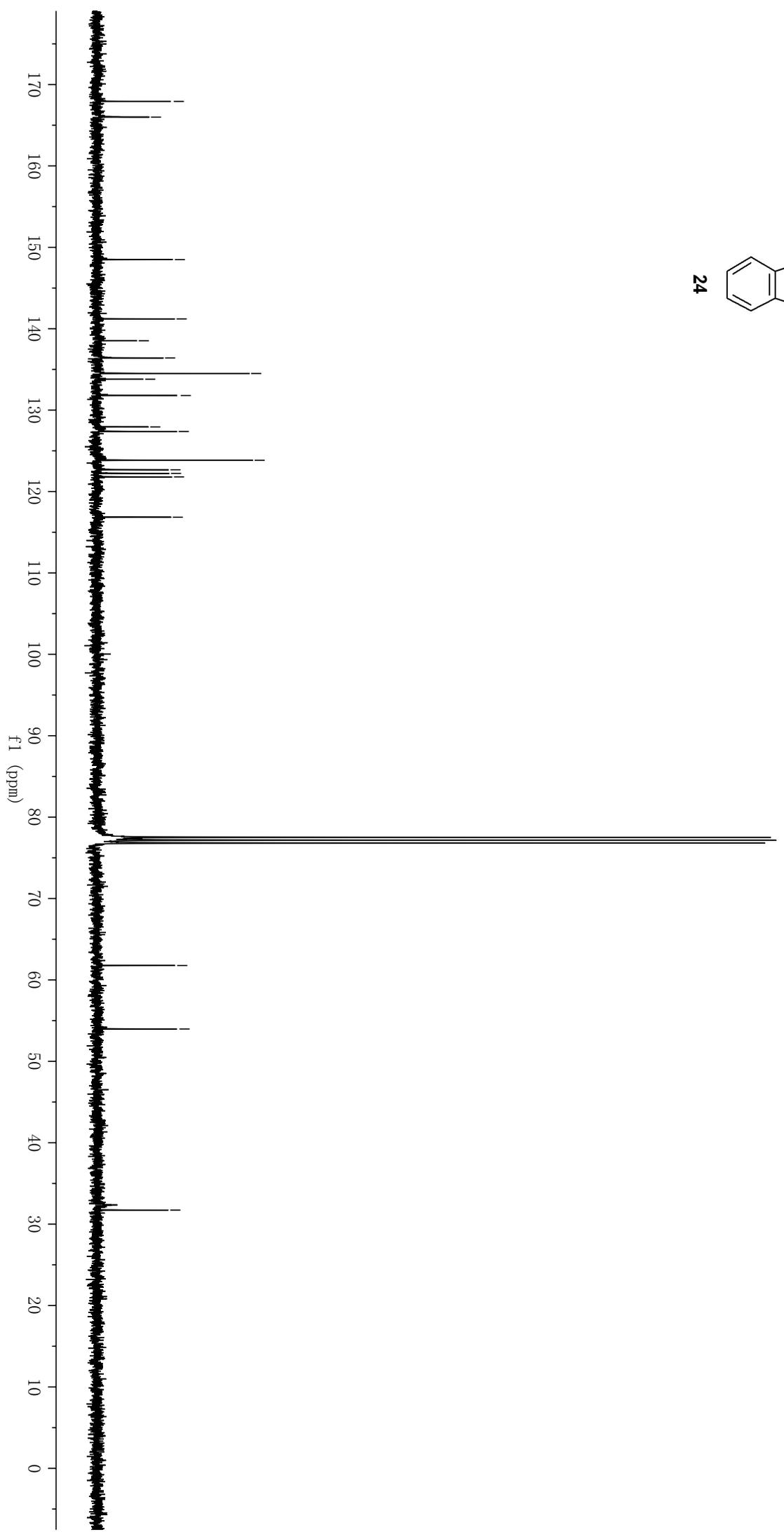
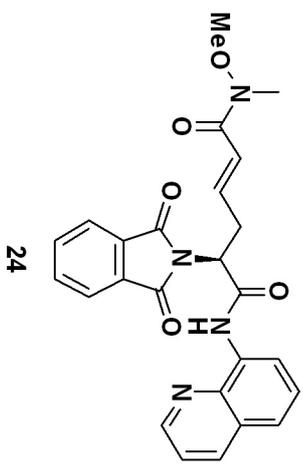
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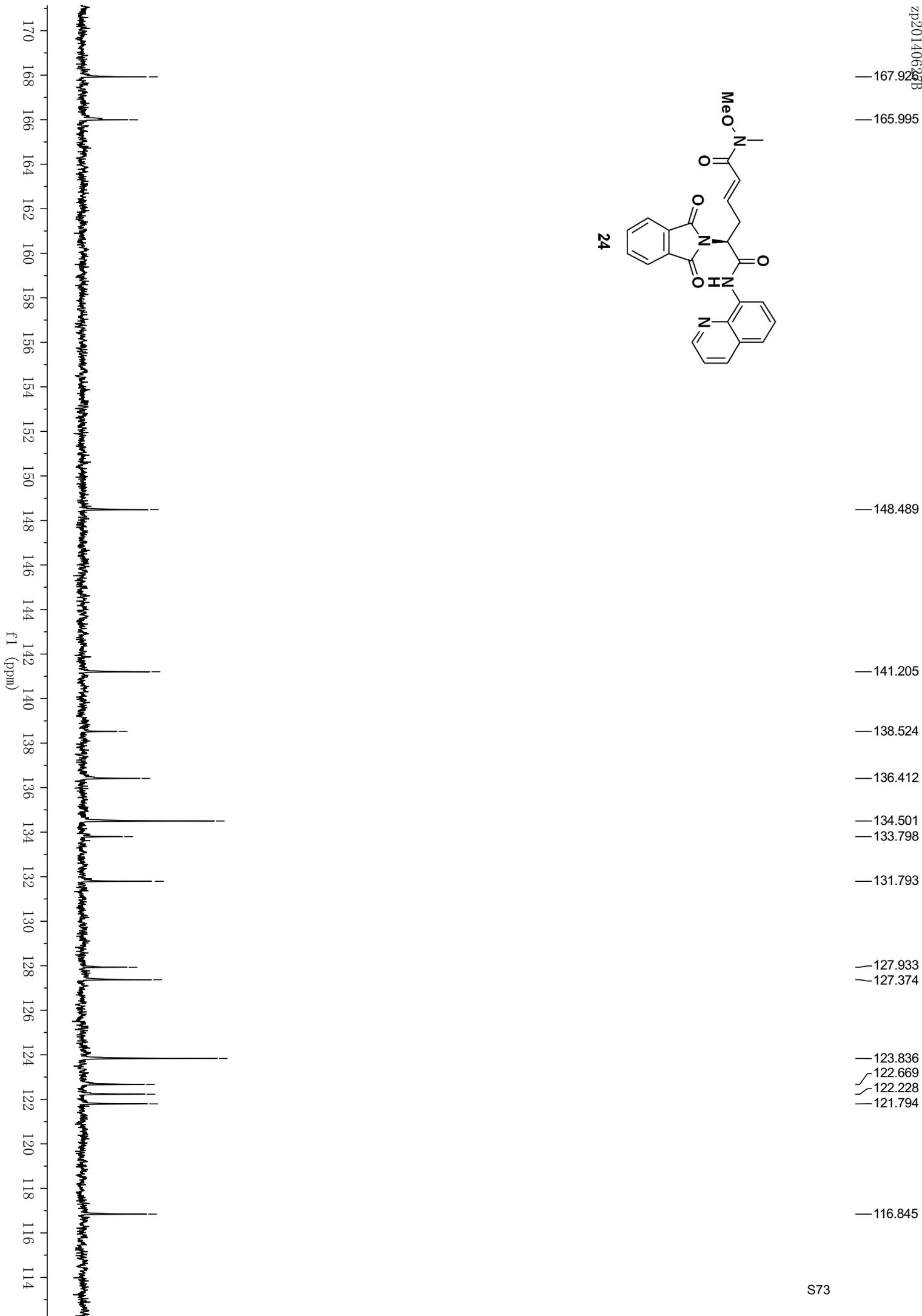
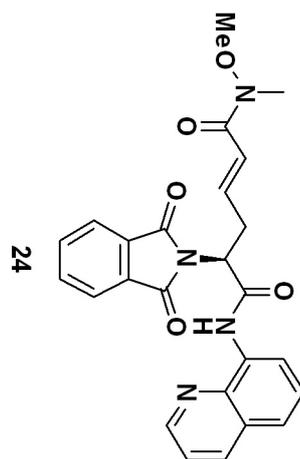
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3.535
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3.387
3.382
3.357
3.345
3.163

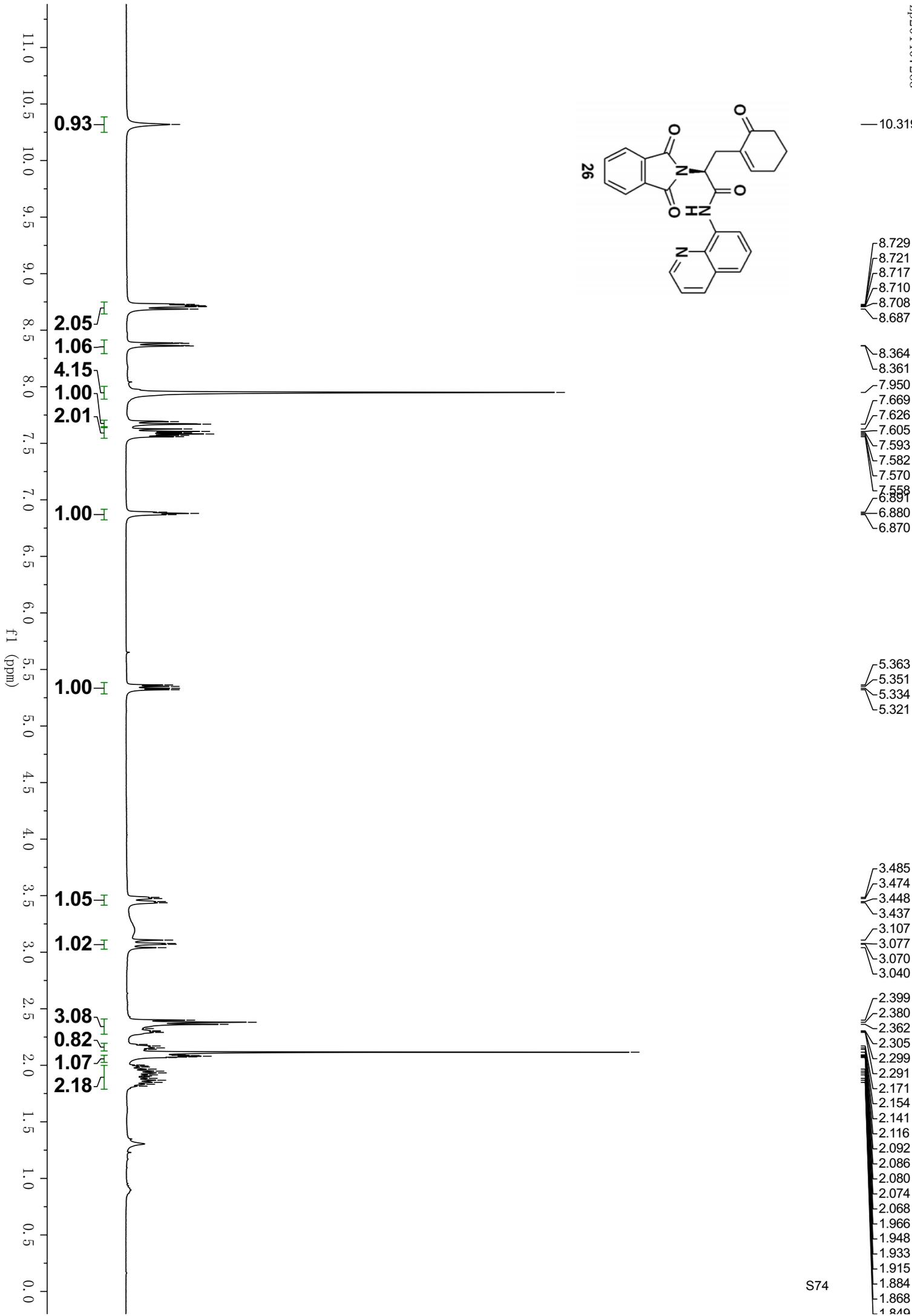




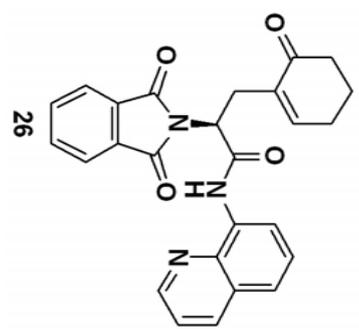
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- 165.995
- 148.489
- 141.205
- 138.524
- 136.412
- 134.501
- 133.798
- 131.793
- 127.933
- 127.374
- 123.836
- 122.669
- 122.228
- 121.794
- 116.845
- 61.764
- 53.971
- 31.722



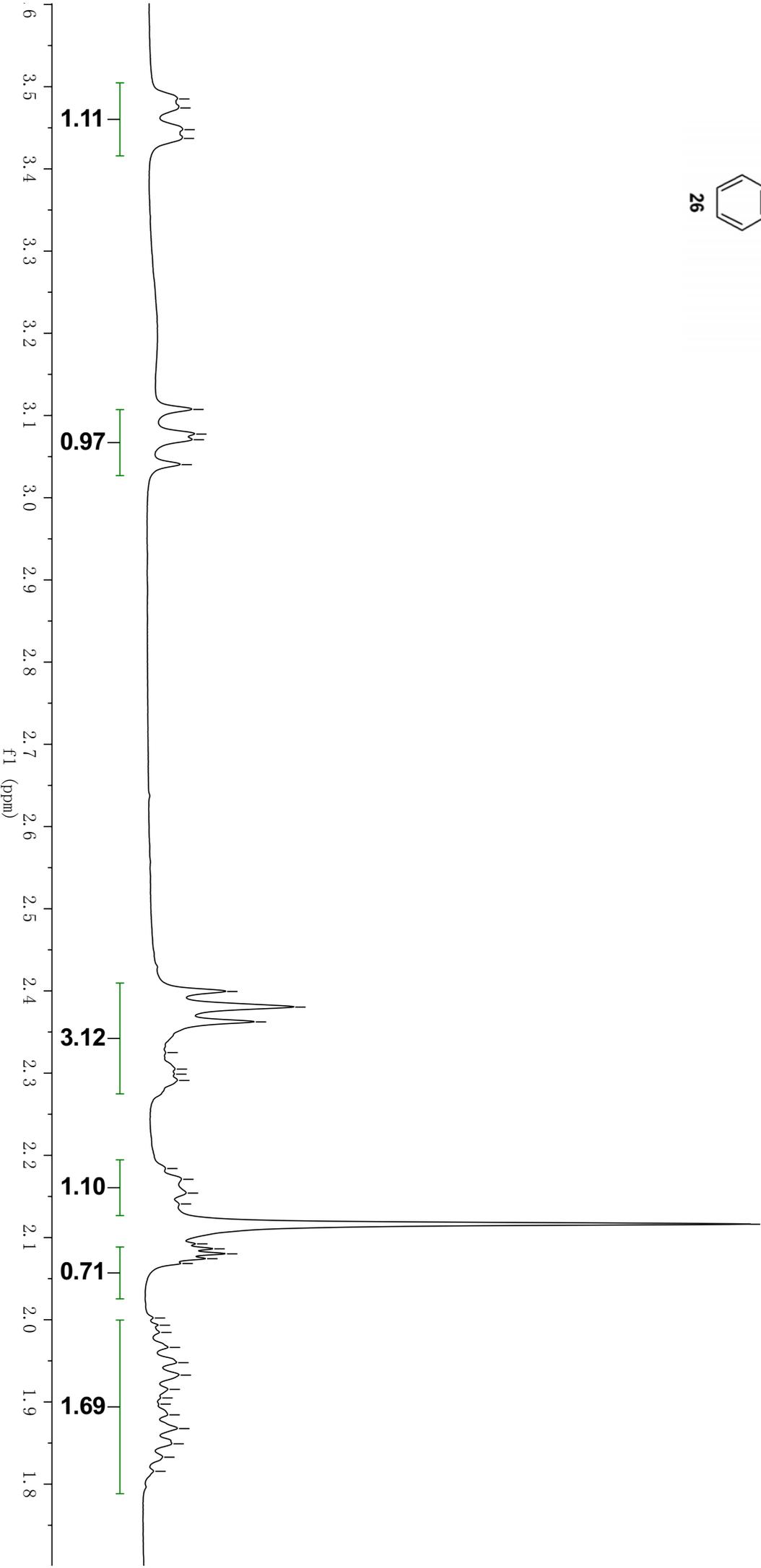




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3.474
3.448
3.437



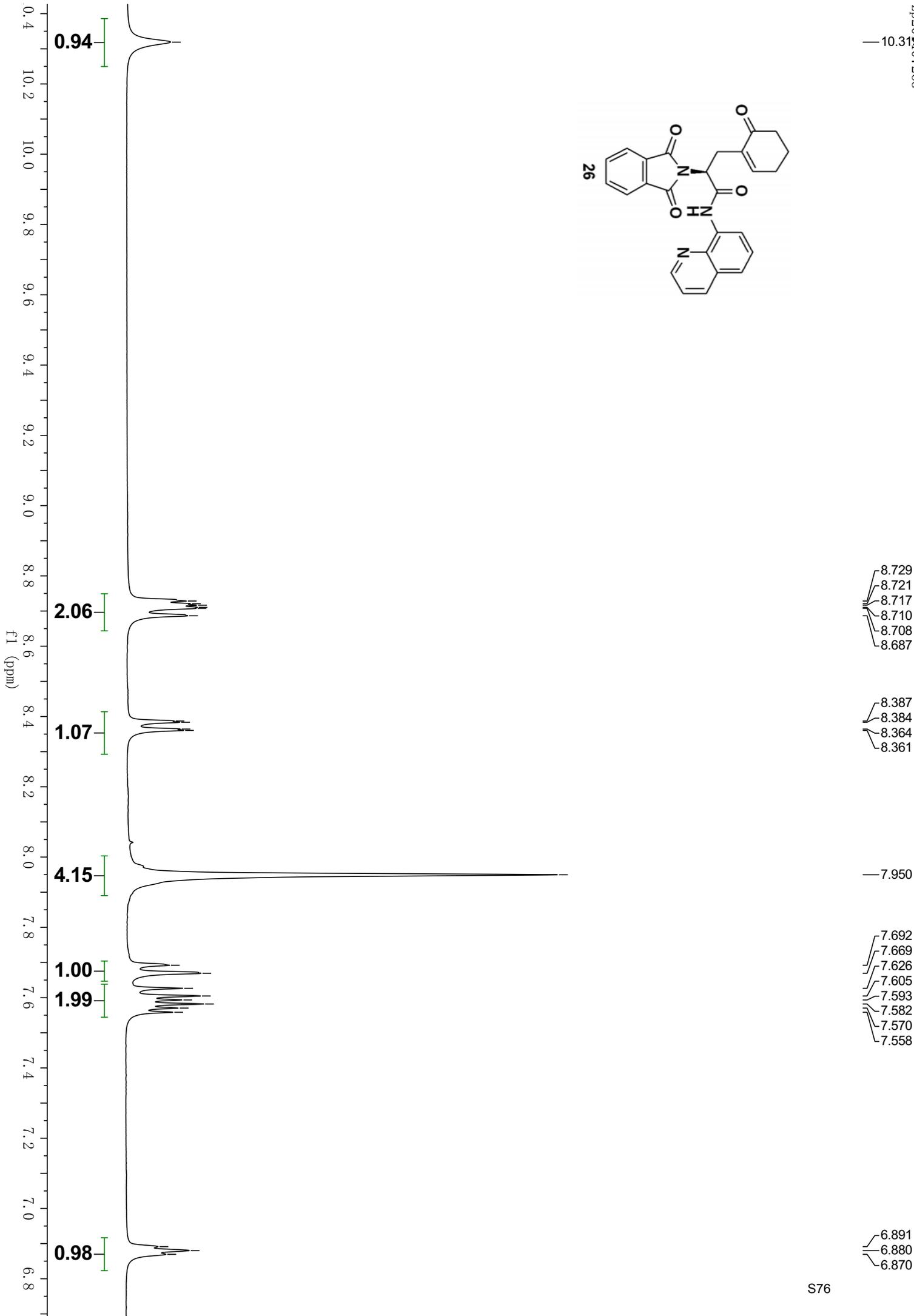
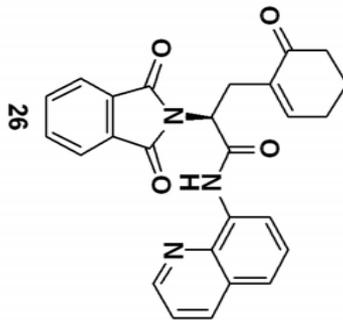
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3.070
3.040

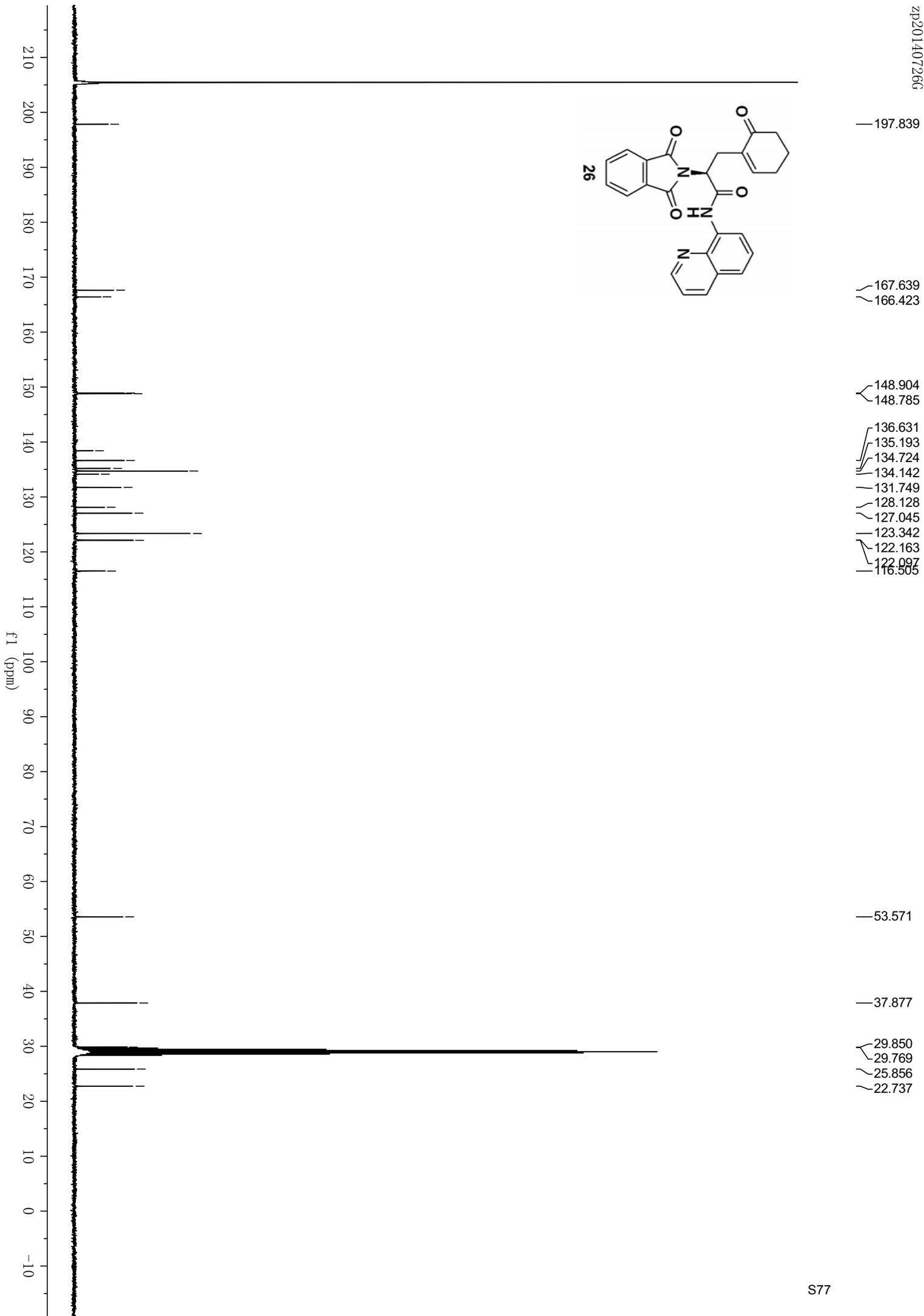


2.399
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2.362
2.325
2.305
2.299
2.291

2.184
2.171
2.154
2.141
2.116
2.092
2.086
2.080
2.074
2.068

2.002
1.993
1.985
1.966
1.948
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1.884
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1.849
1.833
1.816





8.059
8.038

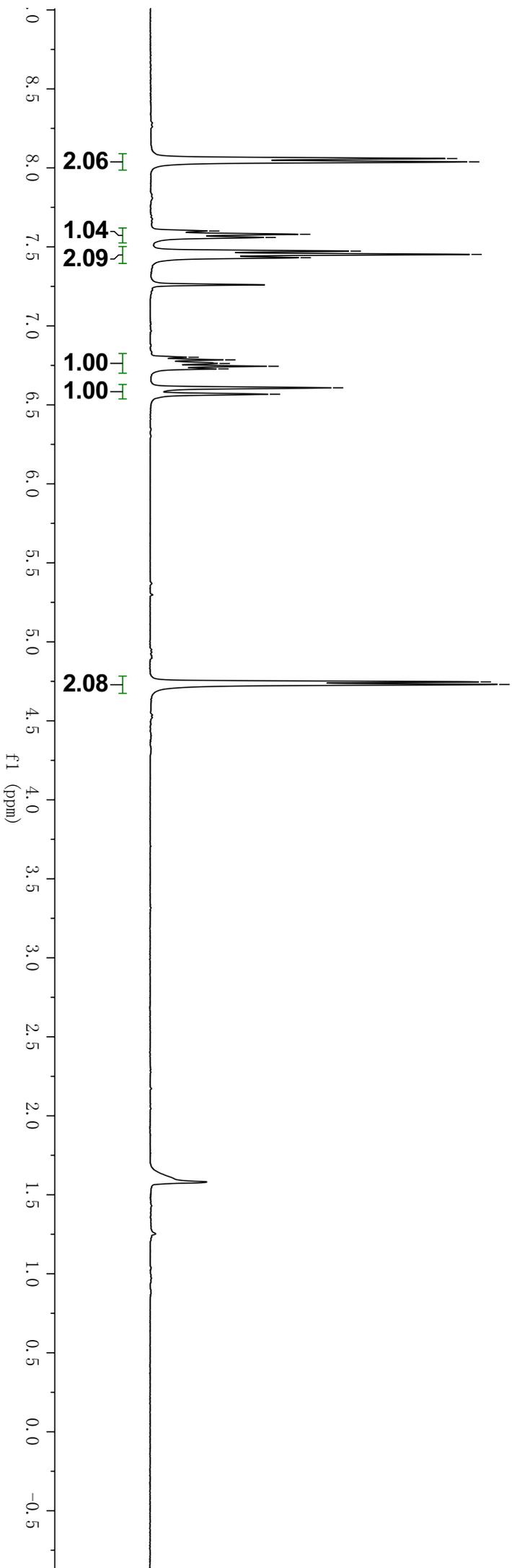
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7.431

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6.608
6.567

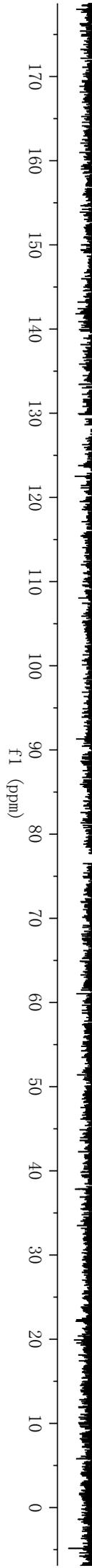
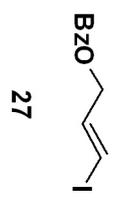
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4.730



27

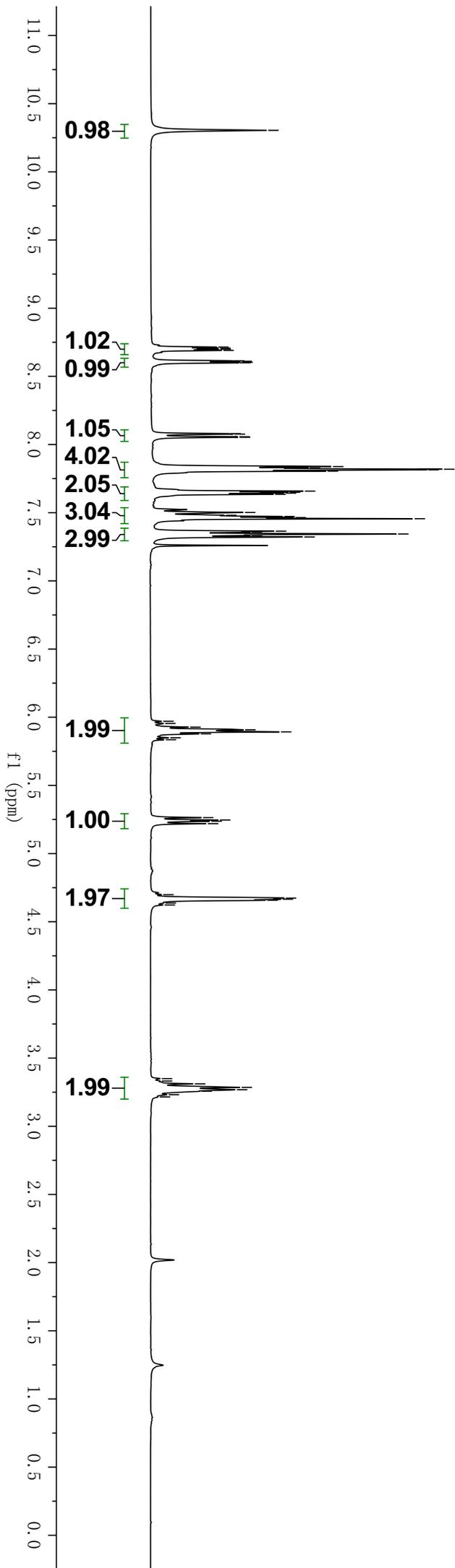
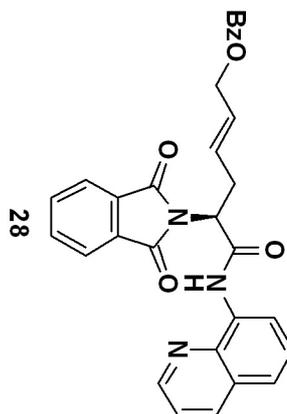


166.087
139.747
133.383
129.808
128.587



100.083
81.213
66.236

10.304



8.715
8.707
8.699
8.690
8.614
8.611
8.603
8.599

7.838
7.828
7.819
7.815
7.805
7.805
7.658
7.650
7.643
7.473
7.464
7.456
7.344
7.322
5.970
5.955
5.927
5.908
5.893
5.878
5.849
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5.246
5.237
5.220
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4.673
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4.658
4.637
4.623

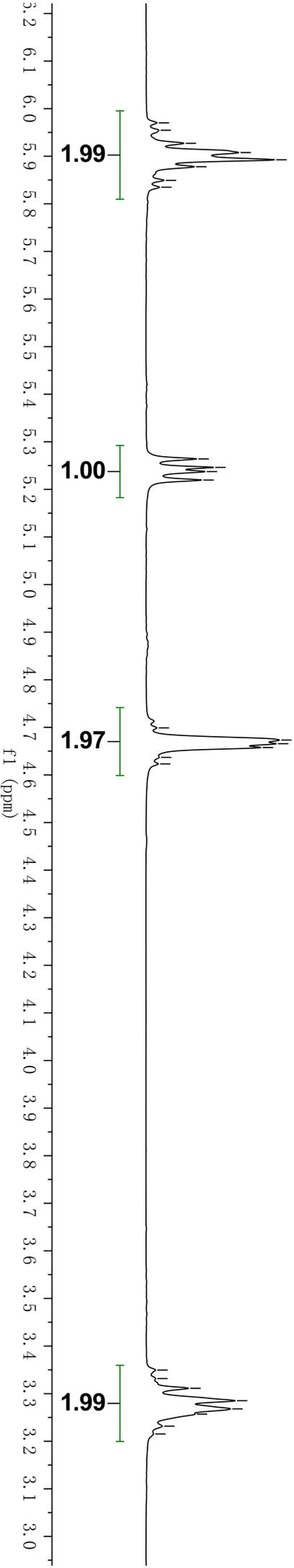
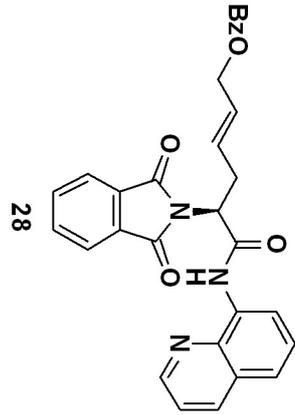
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3.332
3.311
3.285
3.268
3.257
3.232
3.215

5.976
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5.927
5.908
5.893
5.878
5.849
5.835

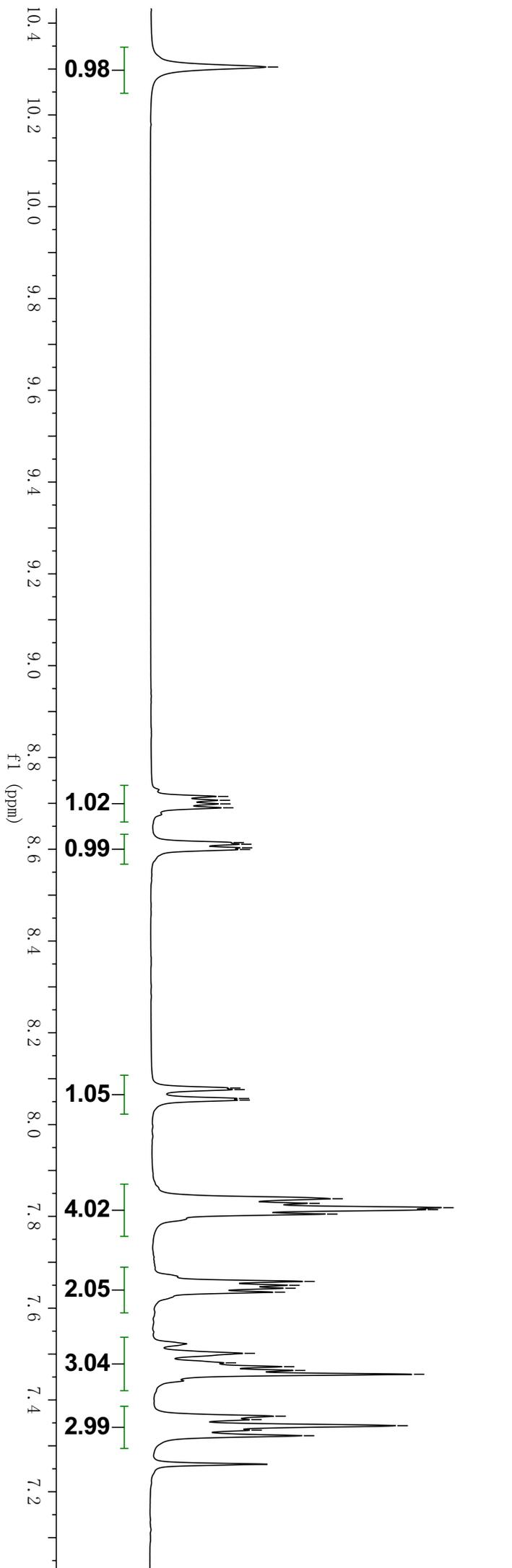
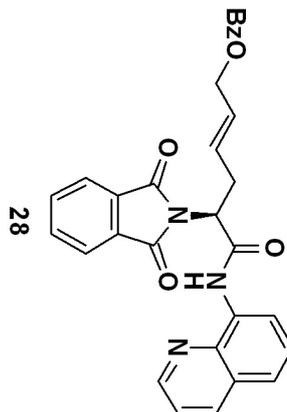
5.264
5.246
5.237
5.220

4.699
4.673
4.666
4.658
4.637
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3.350
3.332
3.311
3.285
3.268
3.257
3.232
3.215



10.309



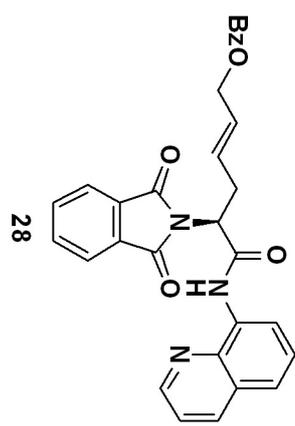
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8.707
8.699
8.690
8.614
8.611
8.603
8.599

8.080
8.076
8.057
8.053

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7.815
7.805
7.658
7.650
7.643
7.635

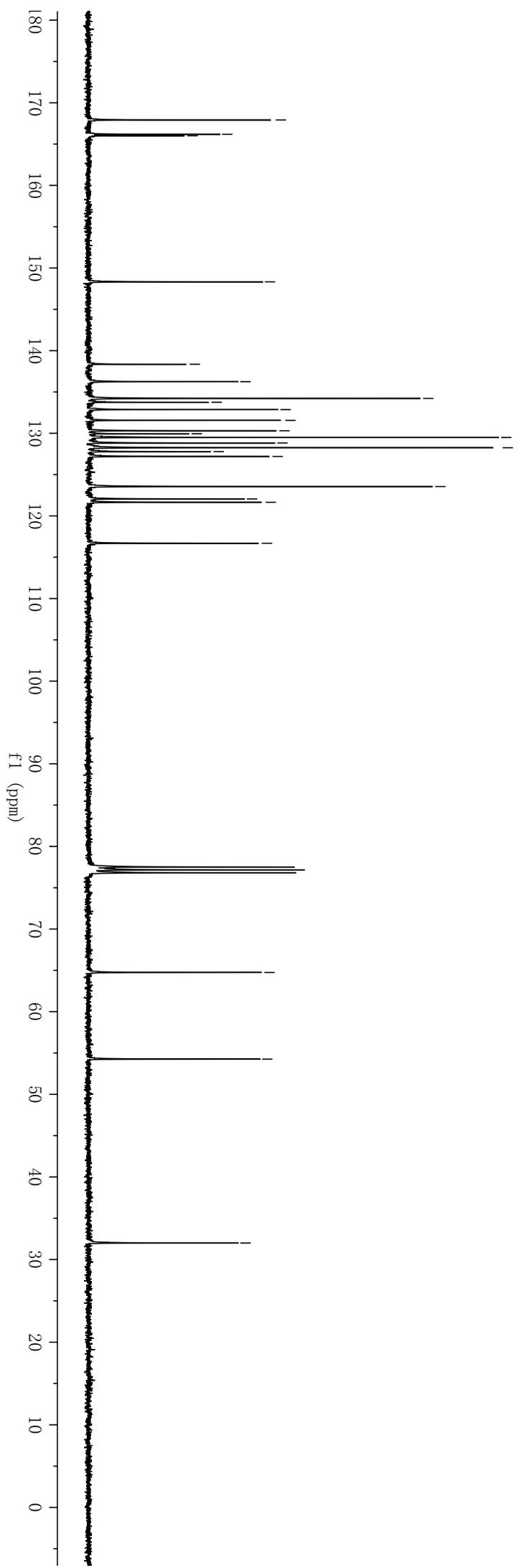
7.502
7.473
7.464
7.456
7.365
7.357
7.344
7.334
7.322

167.928
166.186
166.009



148.329

136.242
134.217
132.864
131.558
130.307
129.491
128.827
128.246
127.785
127.195
123.553
122.054
121.648
116.692

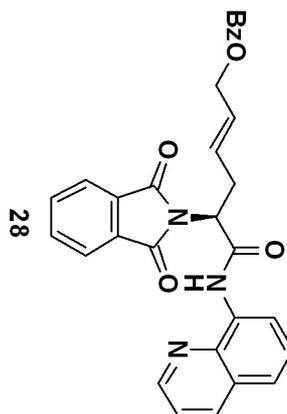


64.740

54.256

32.000

— 167.920
 ~ 166.186
 ~ 166.009



— 148.329

— 138.359

— 136.242

~ 134.217

~ 133.752

~ 132.864

~ 131.558

~ 130.307

~ 129.942

~ 129.491

~ 128.827

~ 128.246

~ 127.785

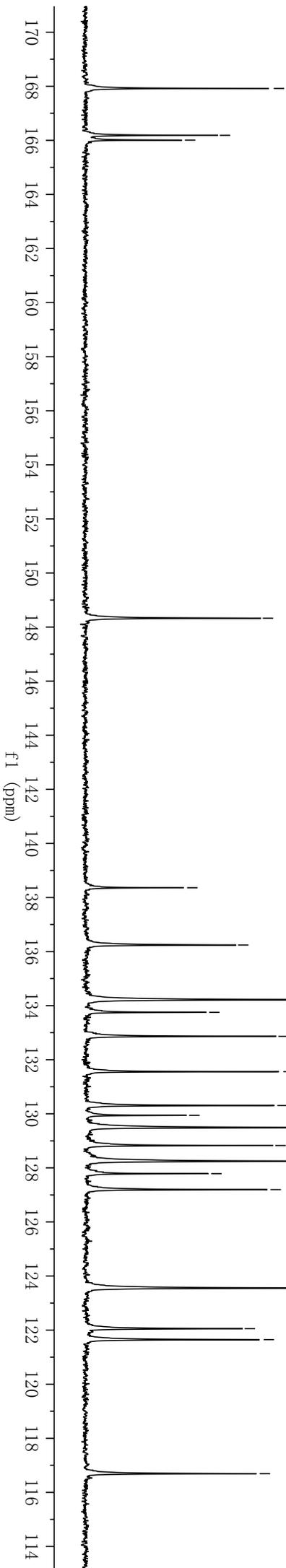
~ 127.195

— 123.553

~ 122.054

~ 121.648

— 116.692

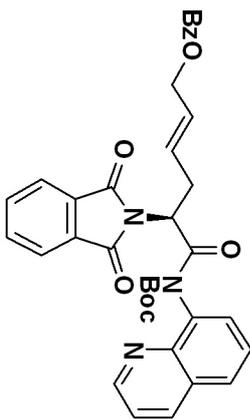


- 8.796
- 8.792
- 8.785
- 8.781
- 7.863
- 7.843
- 7.839
- 7.779
- 7.771
- 7.764
- 7.756
- 7.624
- 7.615
- 7.608
- 7.600
- 7.367
- 7.344
- 7.331
- 7.323
- 6.143
- 6.129
- 6.118
- 6.105
- 6.002
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- 5.920
- 5.803
- 5.786
- 5.768
- 5.743
- 5.726

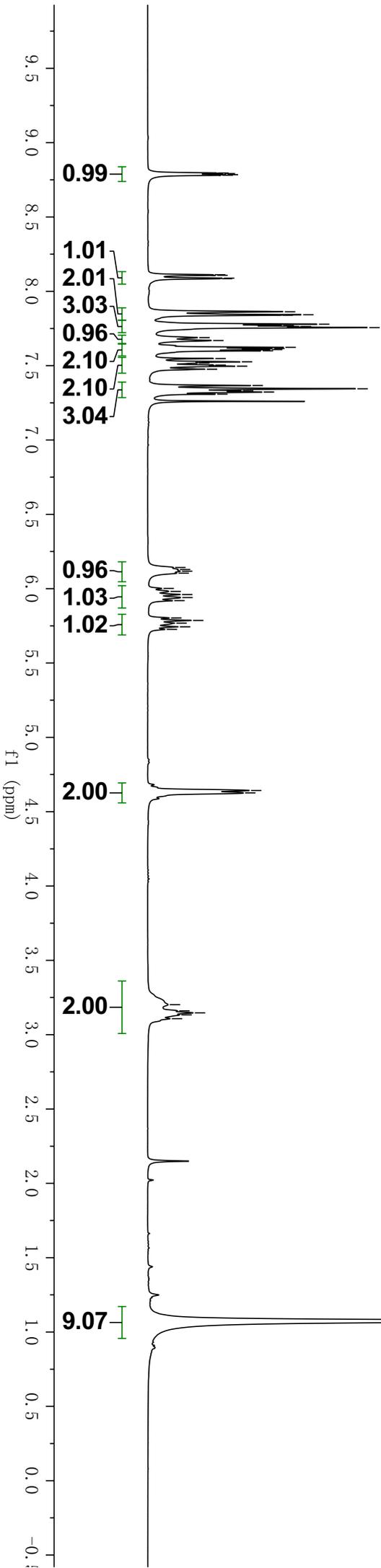
- 4.642
- 4.626

- 3.202
- 3.160
- 3.147
- 3.133
- 3.108

- 1.075



Boc intermediate for Compound 28

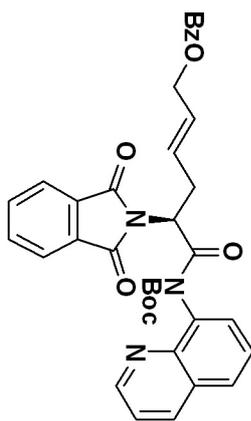


- 6.143
- 6.129
- 6.118
- 6.105
- 6.002
- 5.982
- 5.960
- 5.940
- 5.920
- 5.803
- 5.786
- 5.768
- 5.743
- 5.726

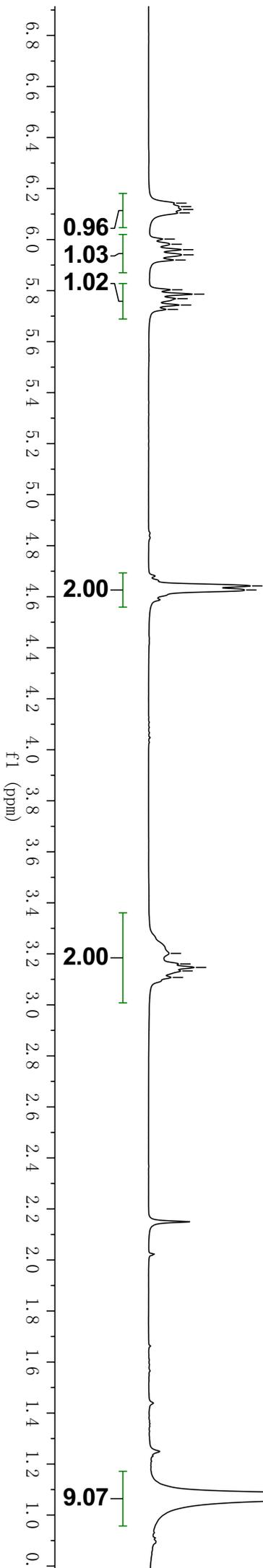
- 4.642
- 4.626

- 3.202
- 3.160
- 3.147
- 3.133
- 3.108

- 1.075



Boc intermediate for Compound 28
28-1



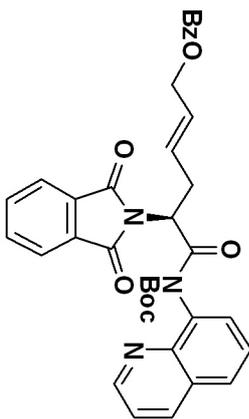
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8.785
8.781

8.112
8.108
8.089
8.085

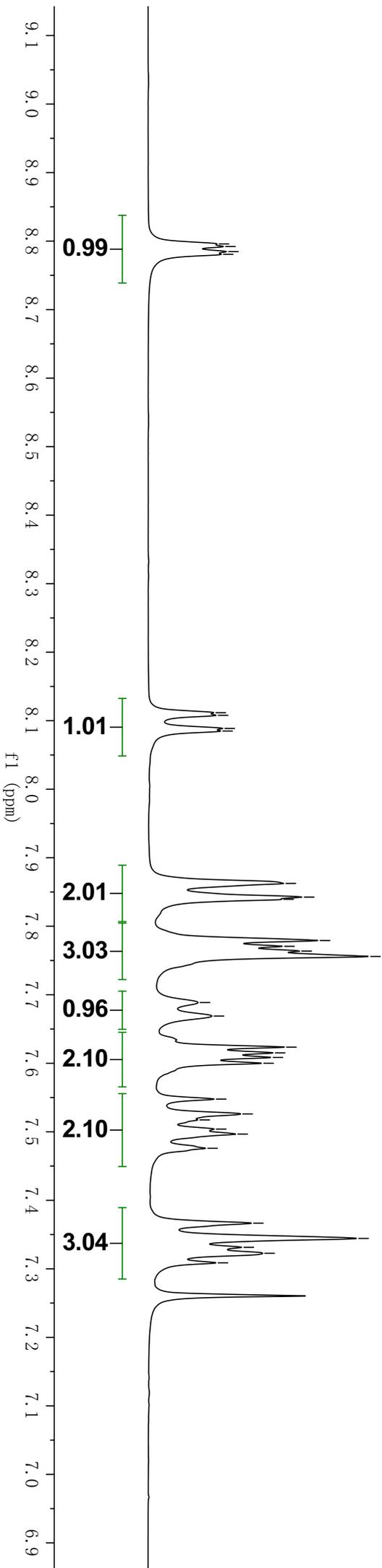
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7.839

7.779
7.764
7.756
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7.669
7.624
7.615
7.608
7.600
7.548
7.526
7.517
7.504
7.497
7.476

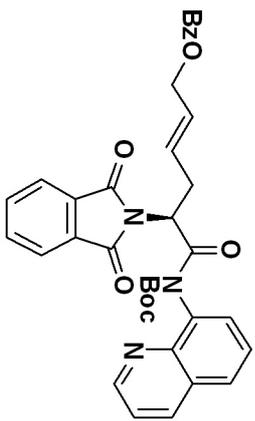
7.367
7.344
7.331
7.323
7.309



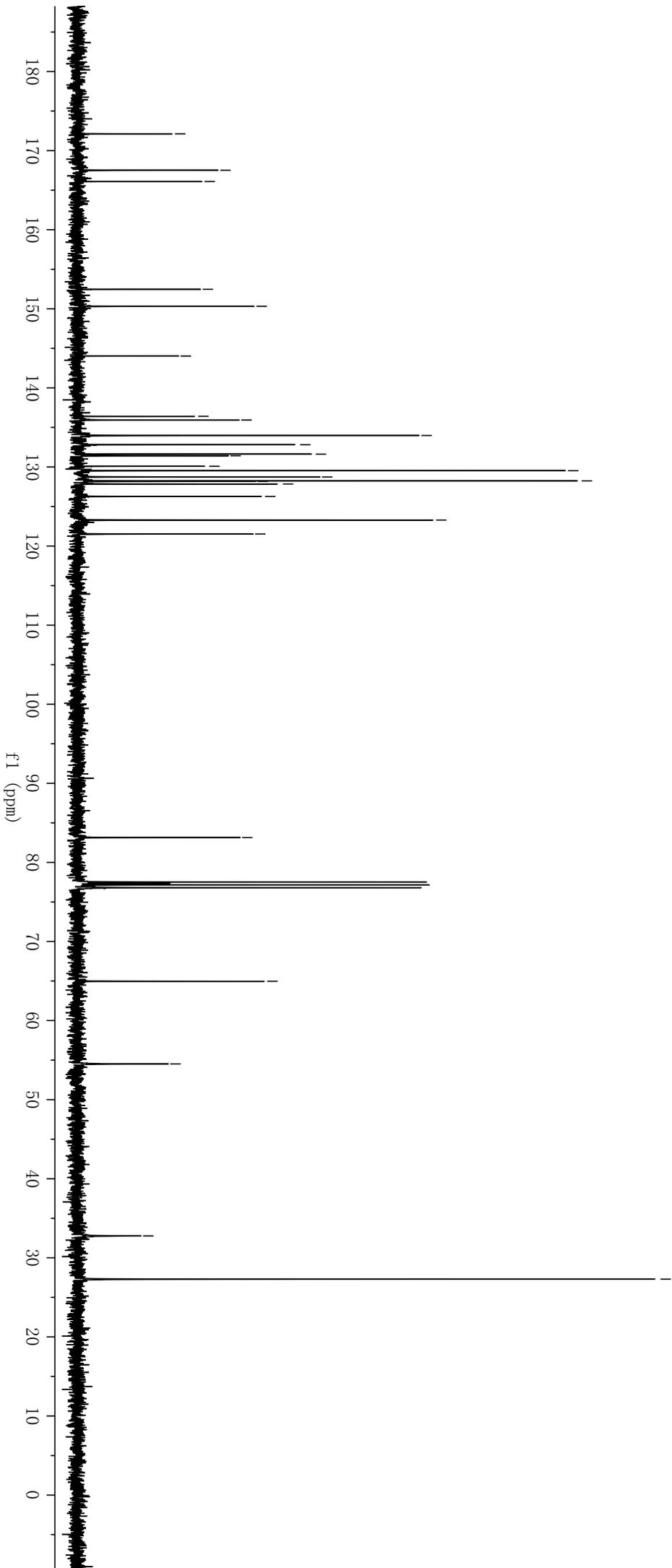
28-1
Boc intermediate for Compound 28



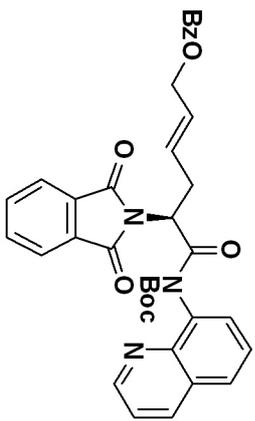
- 172.127
- 167.516
- 166.097
- 152.470
- 150.321
- 144.023
- 136.410
- 135.937
- 133.978
- 132.809
- 131.620
- 131.415
- 130.088
- 129.525
- 128.733
- 128.238
- 128.172
- 127.846
- 126.269
- 123.288
- 121.527



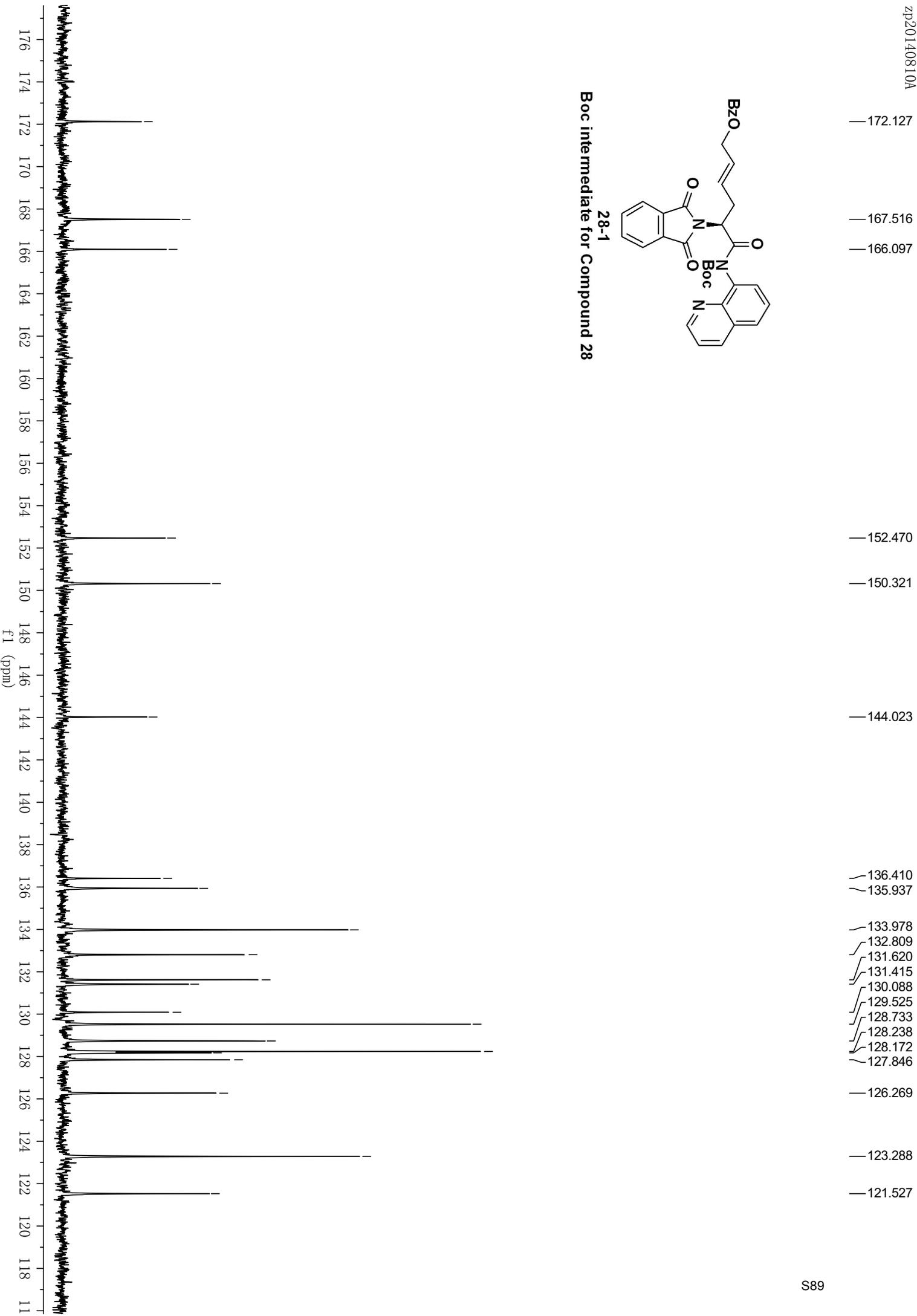
Boc intermediate for Compound 28-1

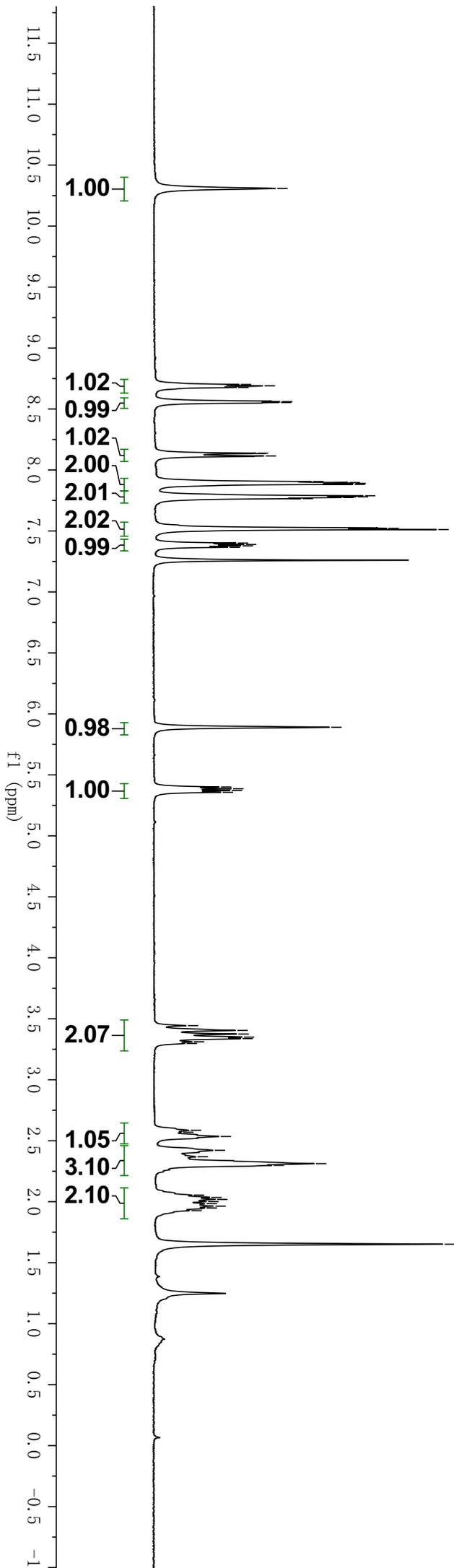
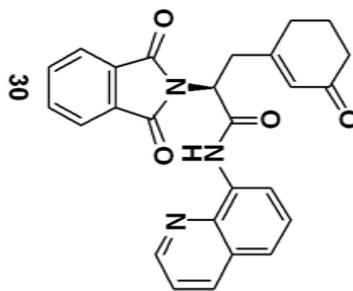


- 83.136
- 64.970
- 54.516
- 32.766
- 27.301



Boc intermediate for Compound 28
28-1





- 10.309
- 8.701
- 8.691
- 8.677
- 8.561
- 8.553
- 8.138
- 8.134
- 8.115
- 7.905
- 7.897
- 7.890
- 7.882
- 7.789
- 7.780
- 7.774
- 7.765
- 7.522
- 7.512
- 7.401
- 7.389
- 7.378
- 5.890
- 5.401
- 5.386
- 5.371
- 5.357
- 3.444
- 3.404
- 3.375
- 3.350
- 3.337
- 3.311
- 3.297
- 2.586
- 2.570
- 2.535
- 2.422
- 2.369
- 2.312
- 2.298
- 2.054
- 2.034
- 2.019
- 2.001
- 1.984
- 1.963
- 1.949
- 1.927
- 1.651

5.890

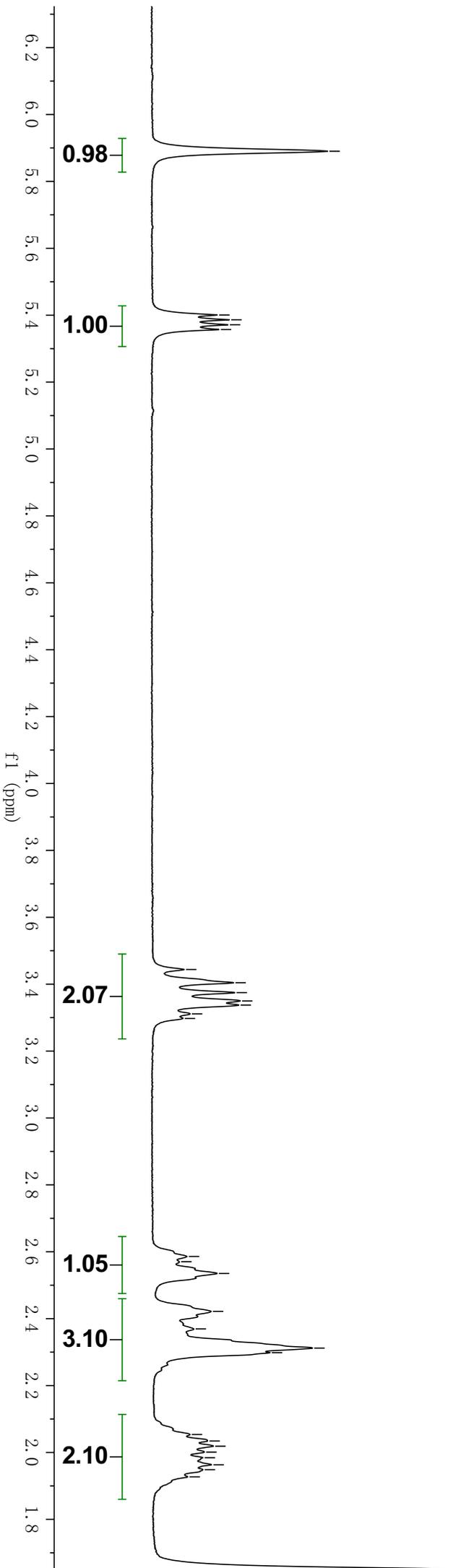
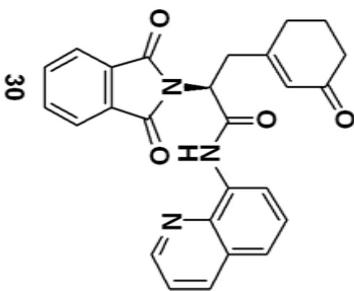
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3.404
3.375
3.350
3.337
3.311
3.297

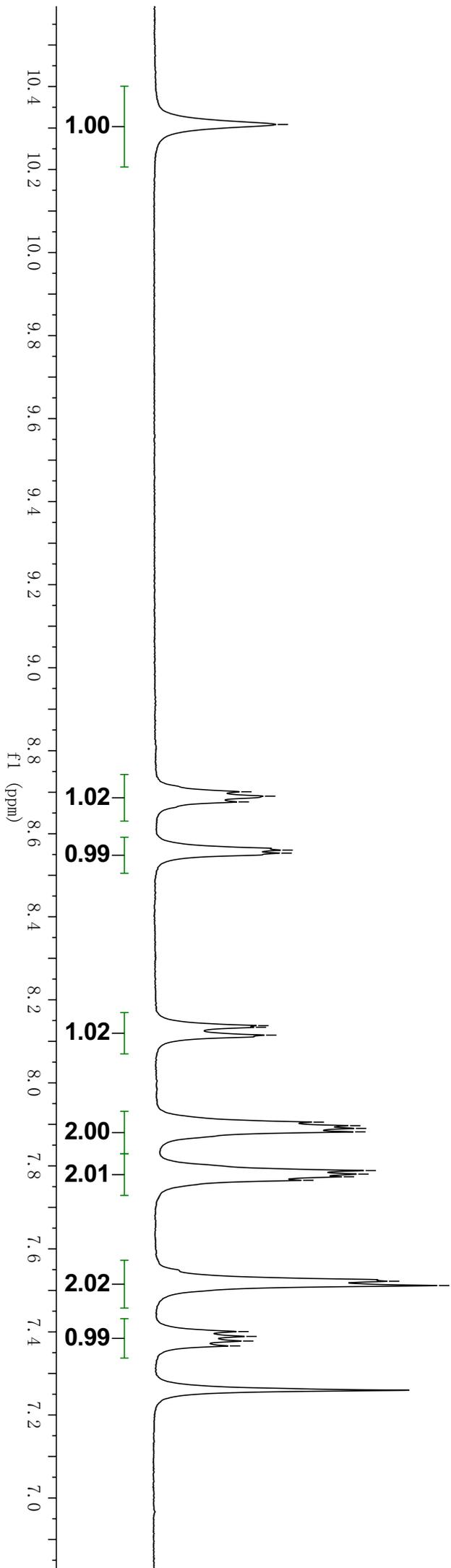
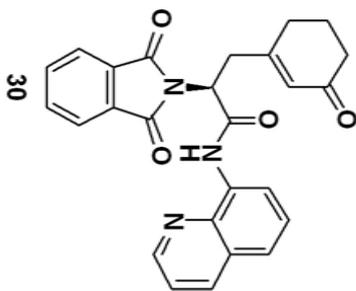
2.586
2.570
2.535
2.422
2.369
2.312
2.298

2.054
2.034
2.019
2.001
1.984
1.963
1.949
1.927

1.651



— 10.309

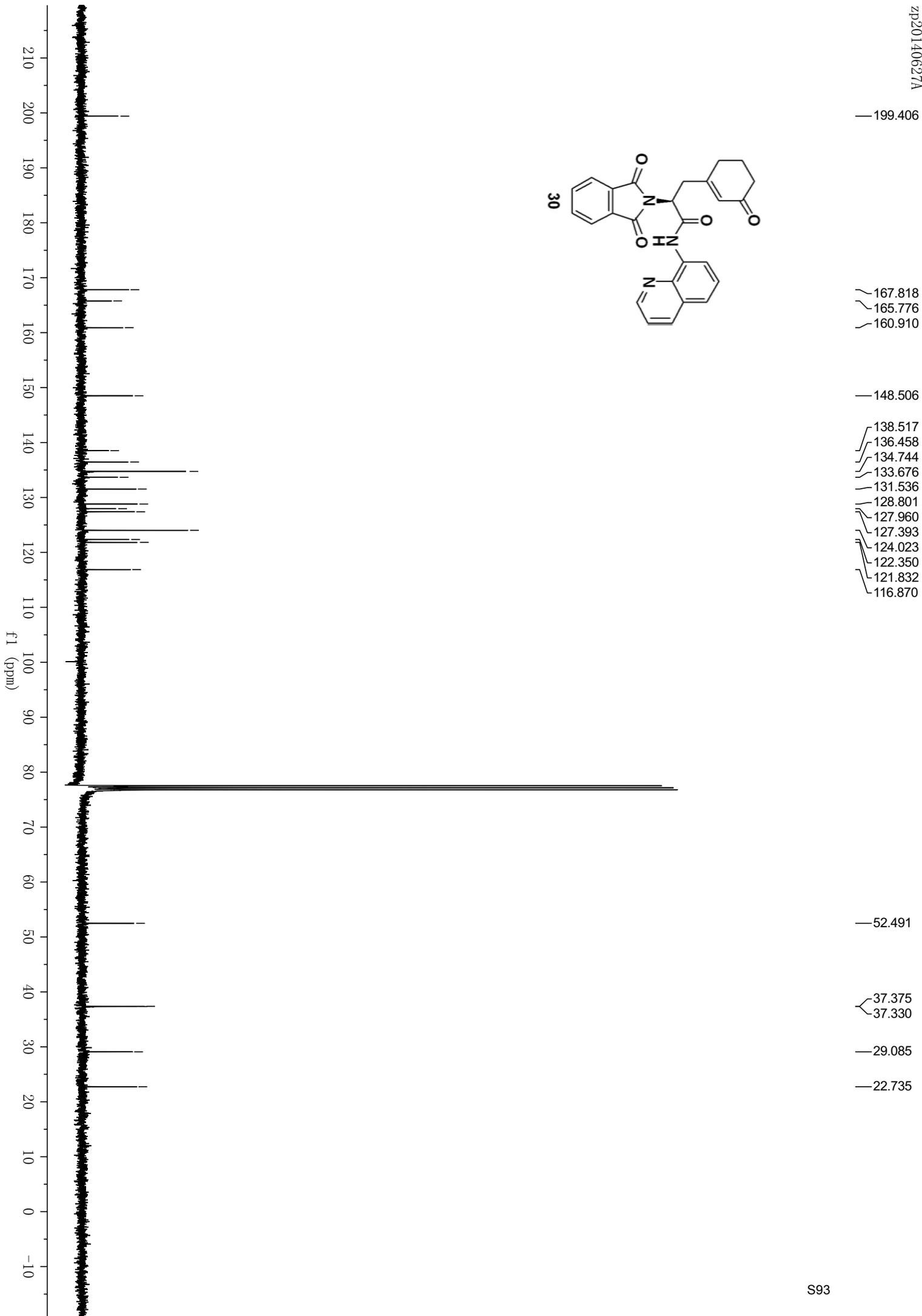
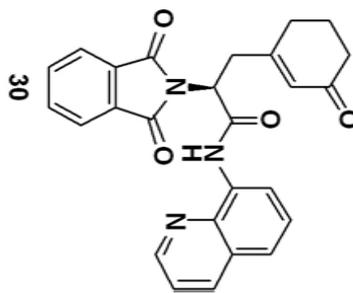


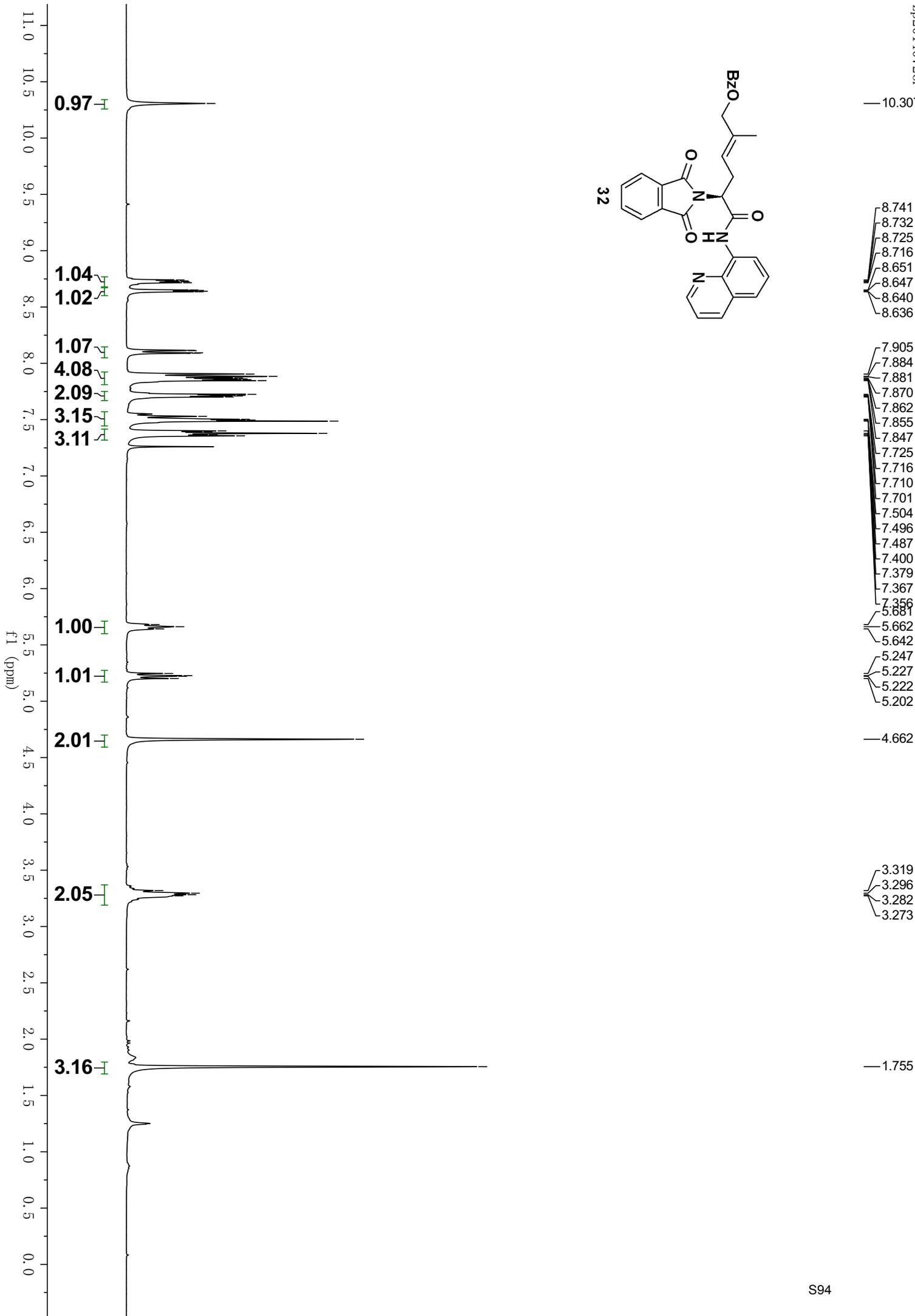
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8.561
8.553

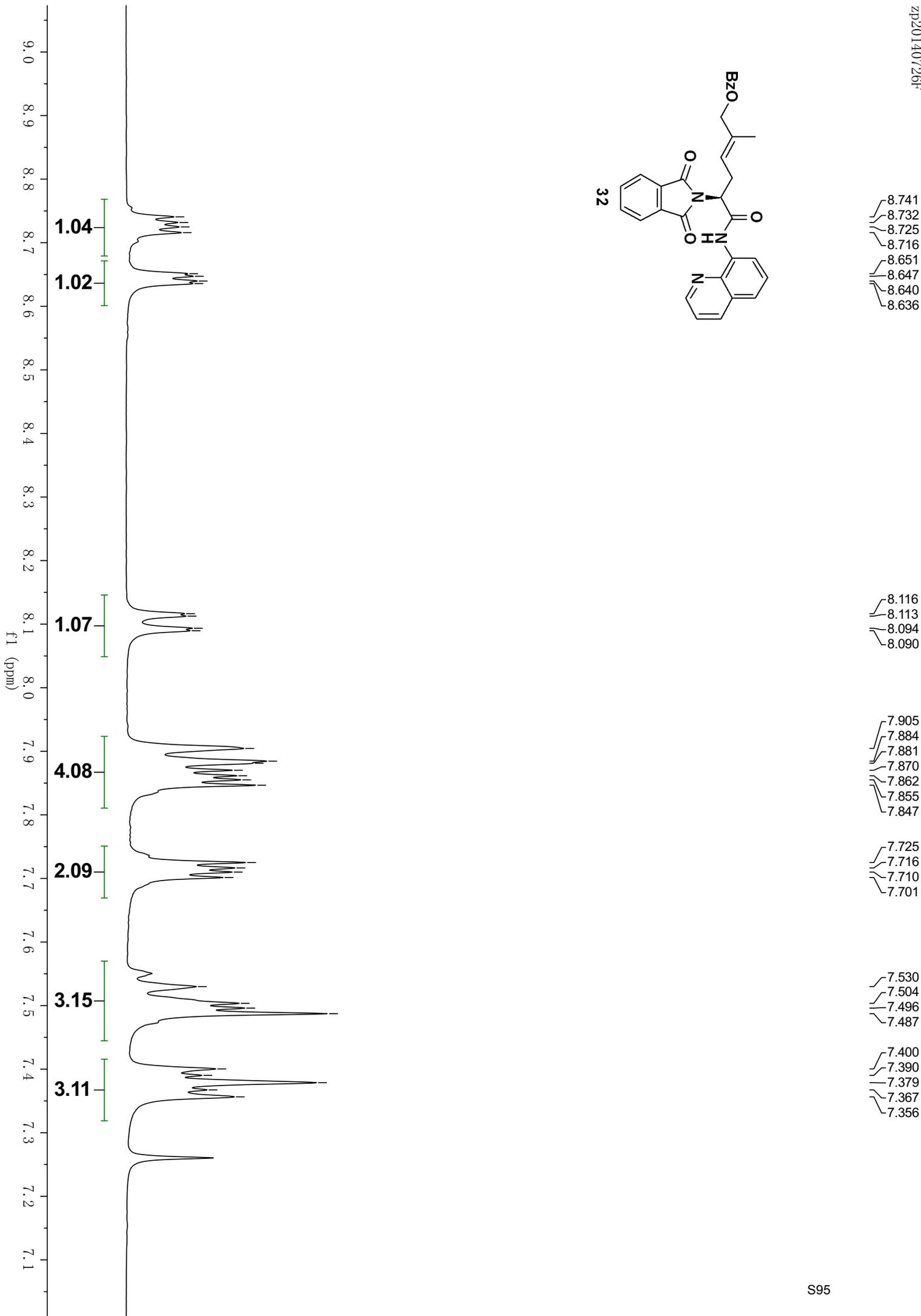
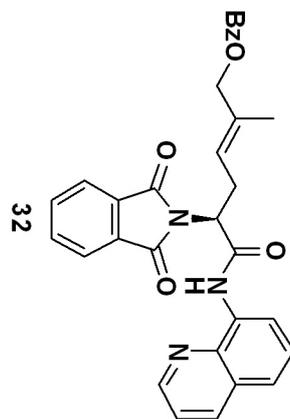
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8.134
8.115

7.905
7.897
7.890
7.882
7.789
7.780
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7.765

7.522
7.512
7.401
7.389
7.378
7.366







168.033
166.526
166.235

148.406

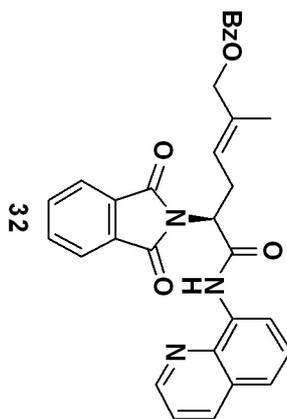
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121.727
116.826

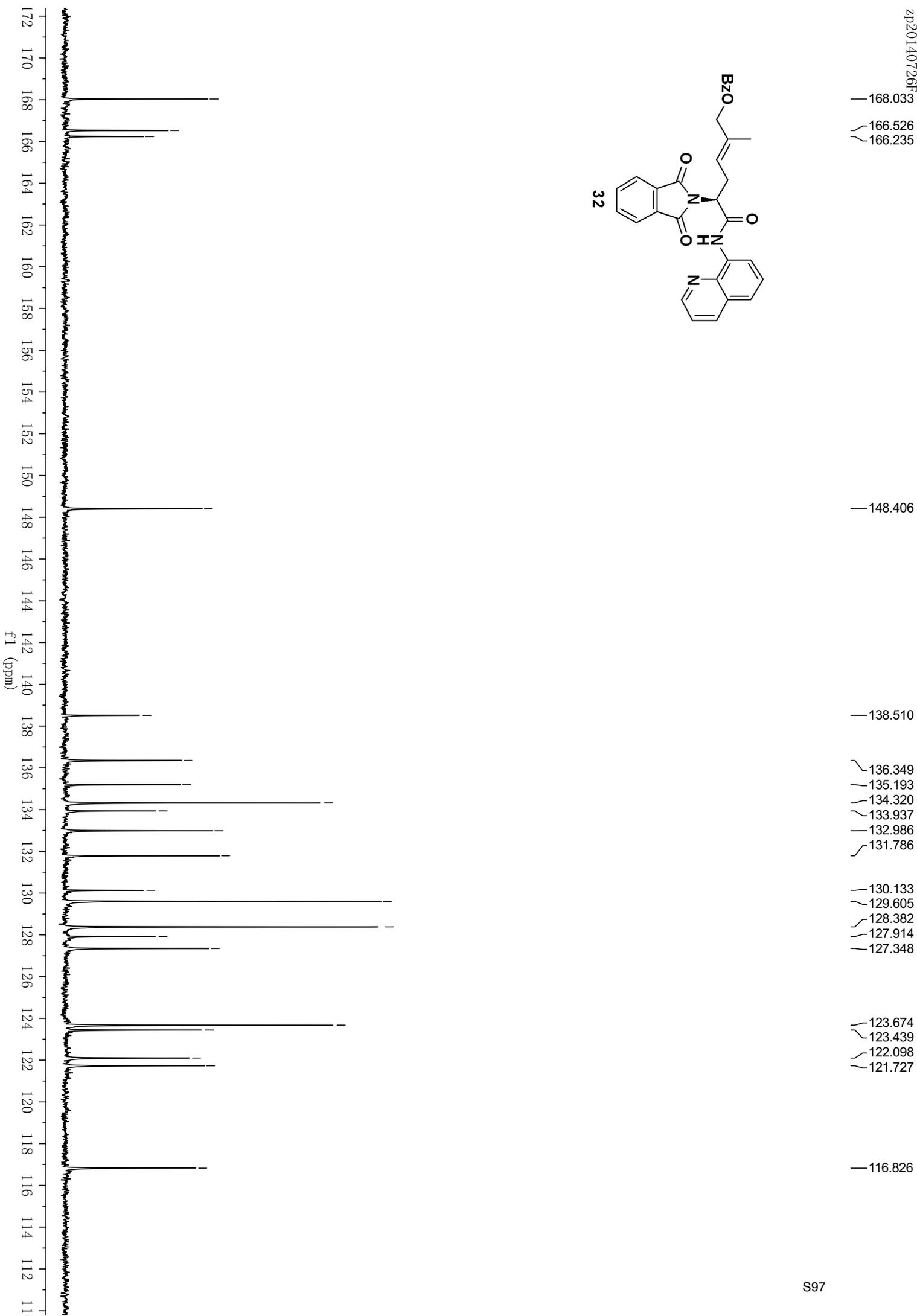
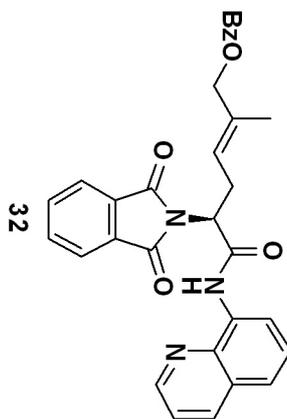
69.784

54.450

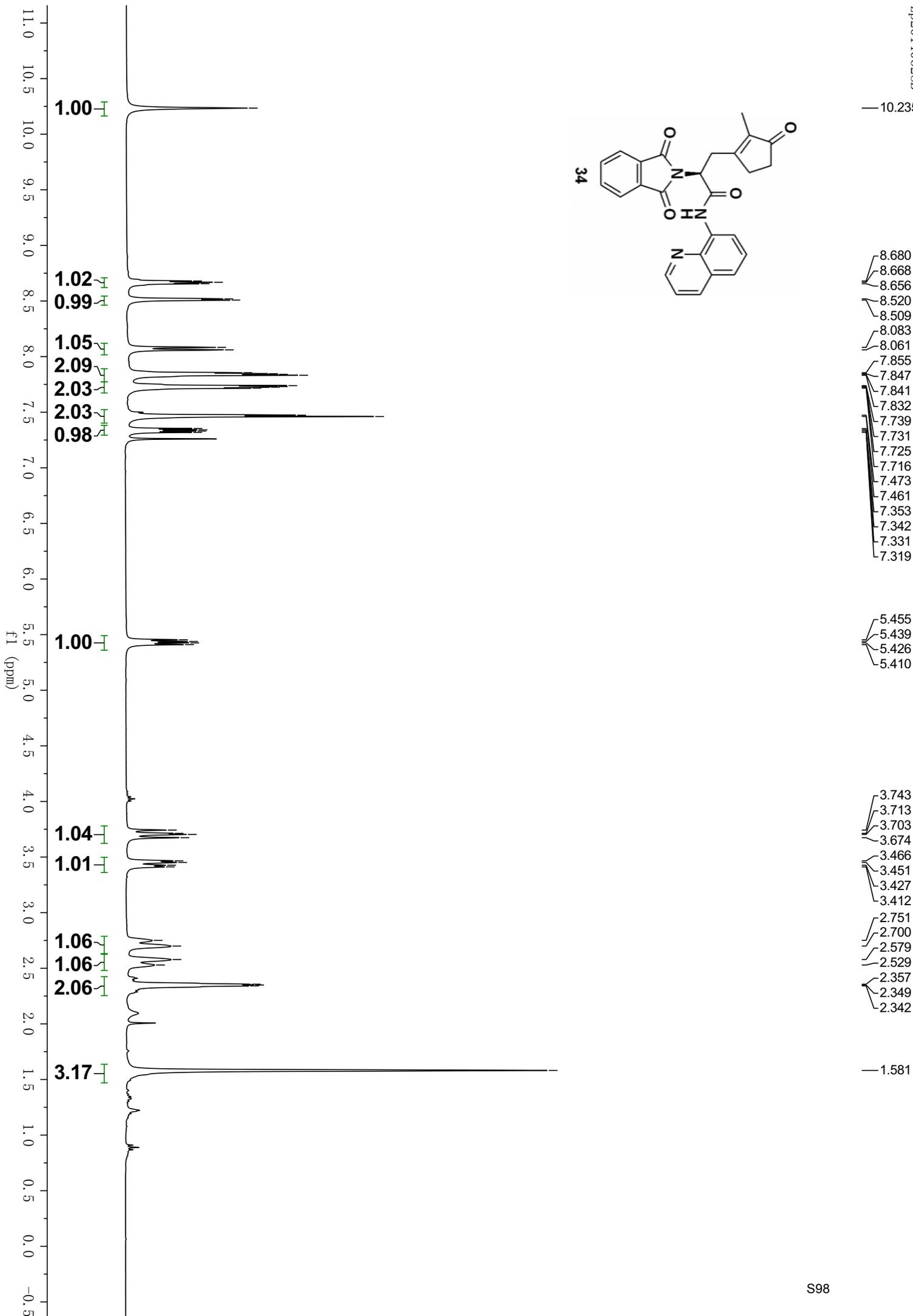
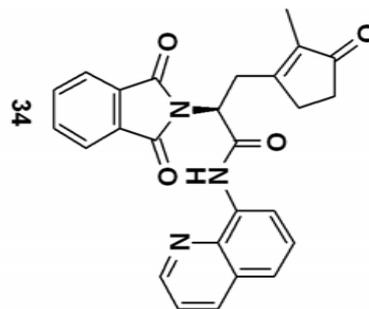
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14.422

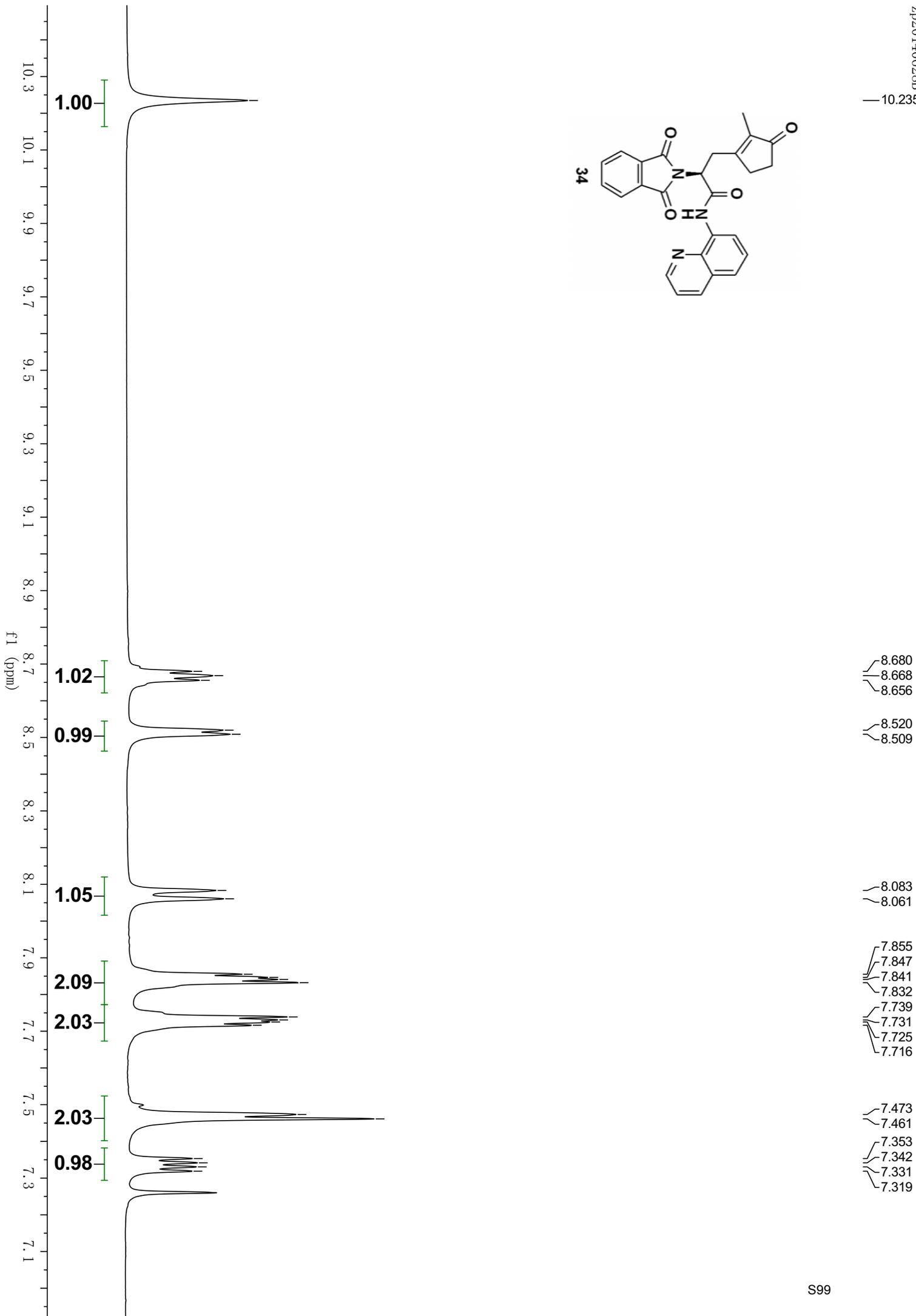
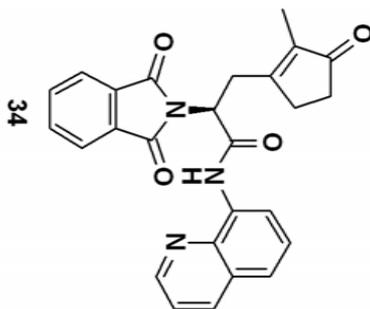


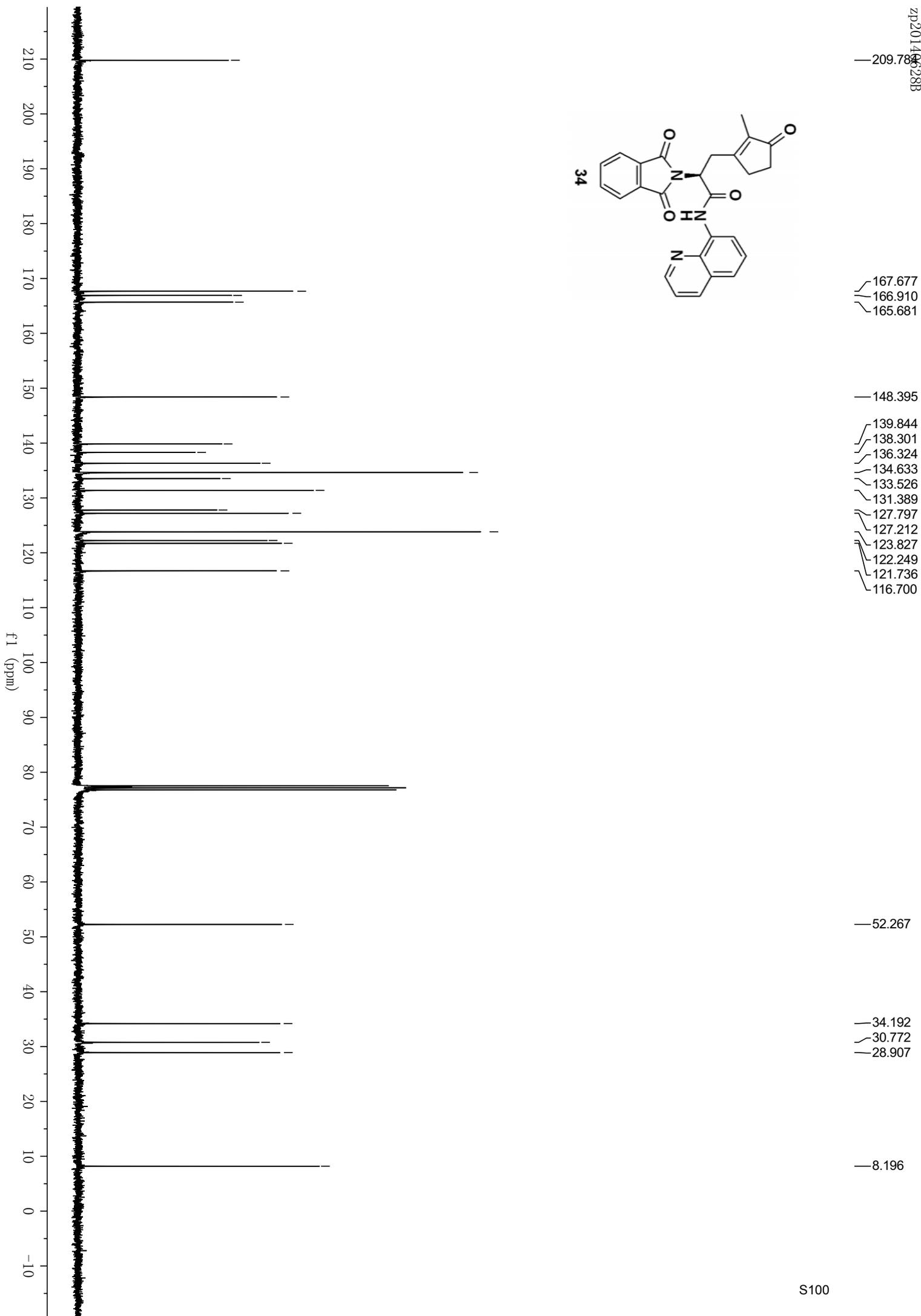


— 10.235

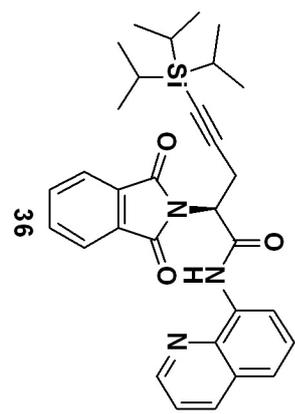


— 10.235





— 10.354

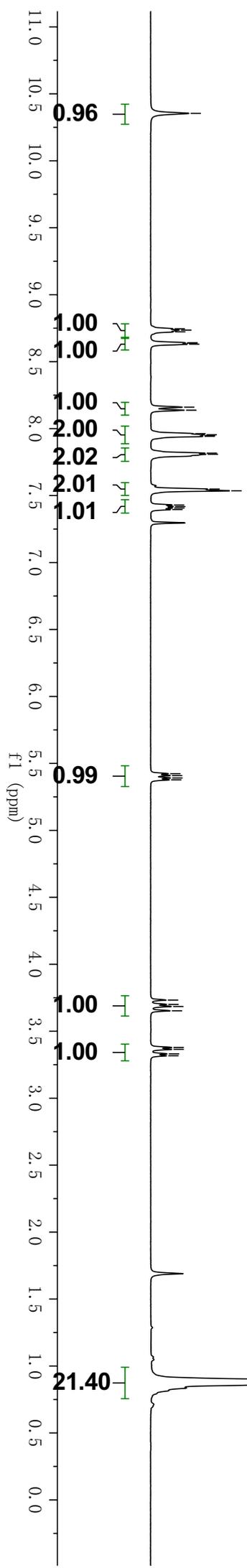


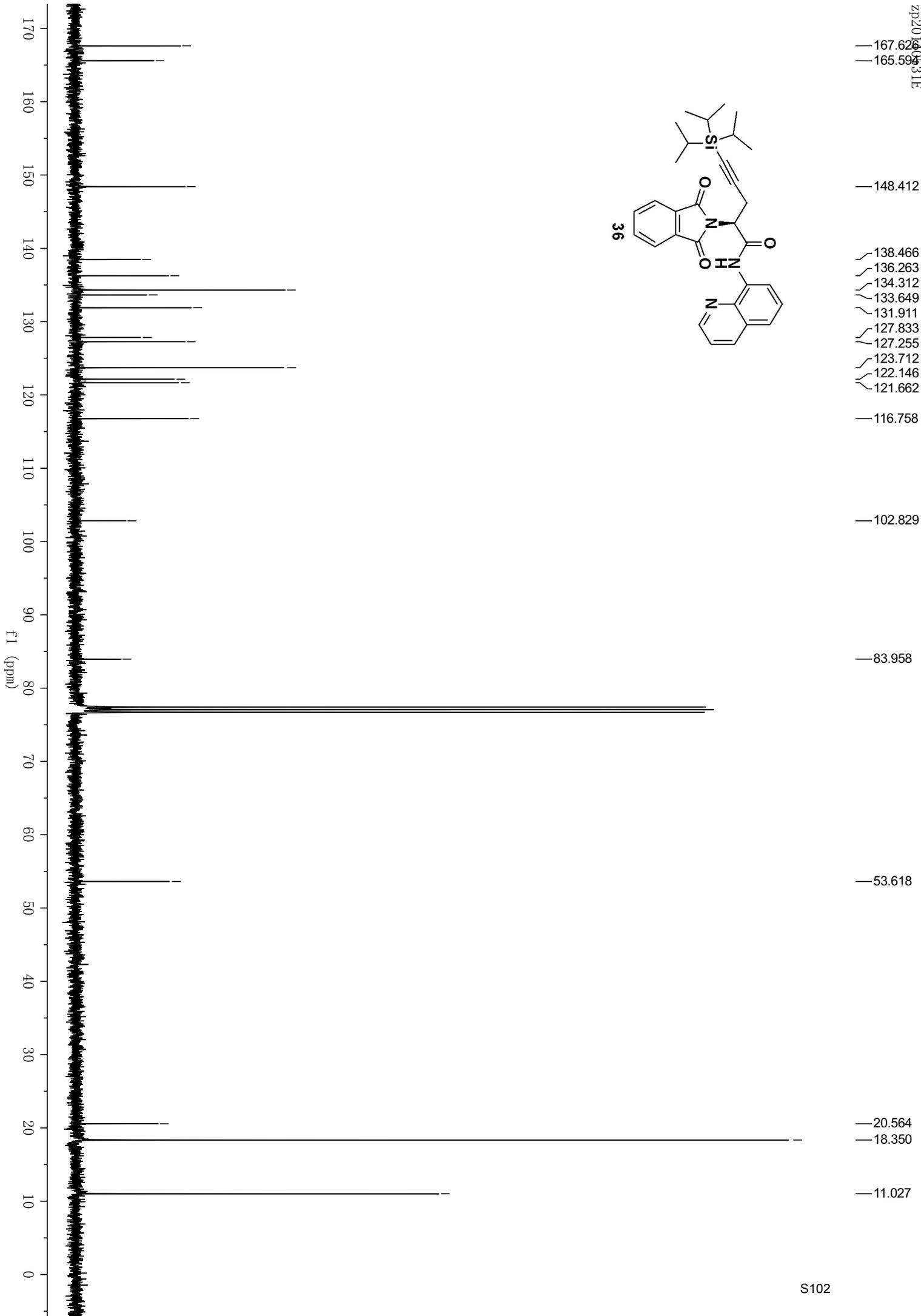
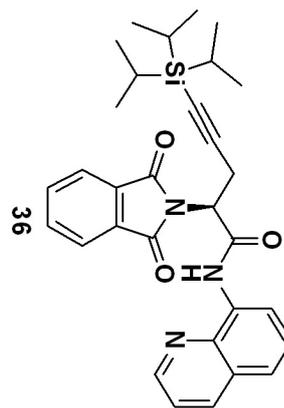
- 8.746
- 8.736
- 8.723
- 8.642
- 8.638
- 8.631
- 8.160
- 8.138
- 7.962
- 7.954
- 7.948
- 7.942
- 7.817
- 7.808
- 7.549
- 7.536
- 7.429
- 7.418
- 7.407
- 7.396

- 5.423
- 5.409
- 5.391
- 5.377

- 3.732
- 3.700
- 3.685
- 3.653
- 3.379
- 3.365
- 3.331
- 3.317

— 0.879





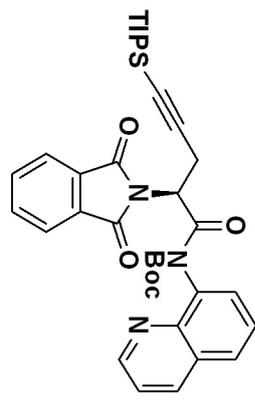
8.769
8.760

8.109
8.086

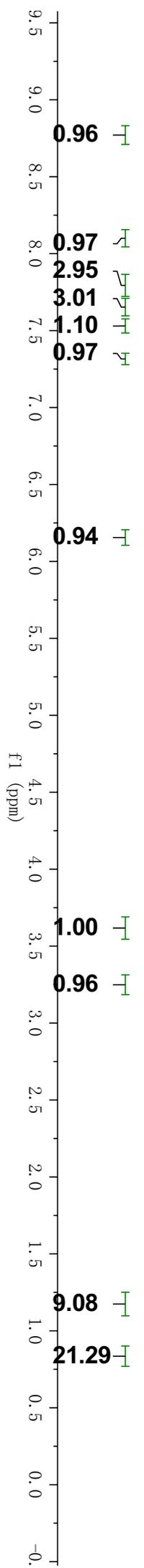
7.811
7.802
7.790
7.767
7.683
7.674
7.638
7.618
7.546
7.525
7.333
7.322
7.310
6.774
6.163
6.142
6.131

3.658
3.625
3.610
3.578
3.275
3.263
3.227
3.215

1.177
0.853
0.845



Boc intermediate for Compound 36
36-1



8.769
8.760

8.109
8.086

7.811
7.802
7.790

7.767
7.683
7.674

7.618
7.525
7.333

7.322
7.310
7.300

6.174
6.163
6.142

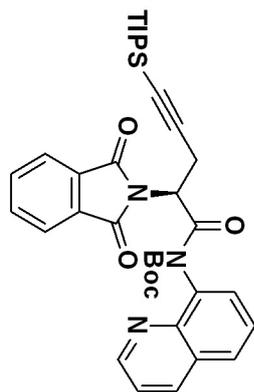
6.131

3.658
3.625
3.610

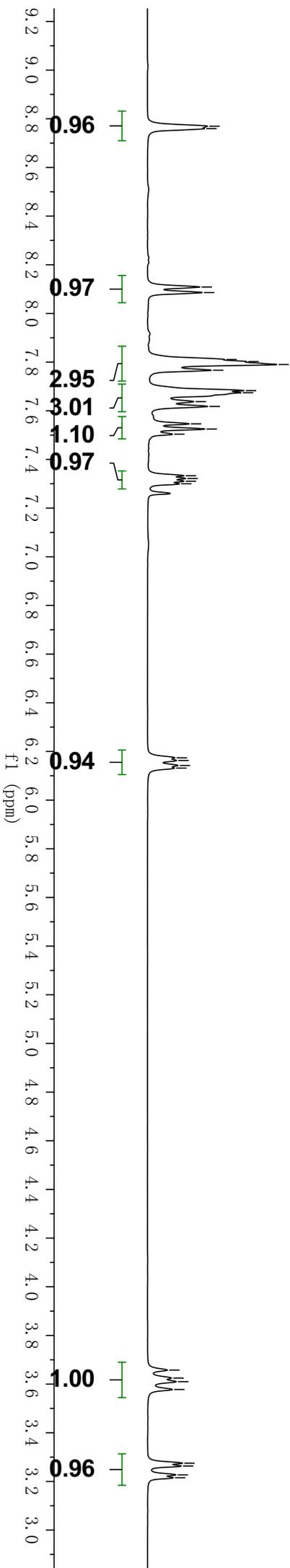
3.578

3.275
3.263
3.227

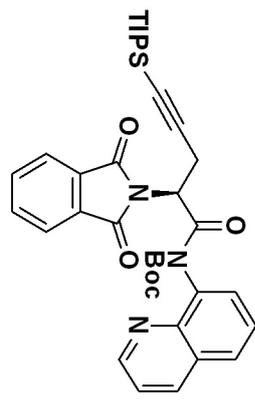
3.215



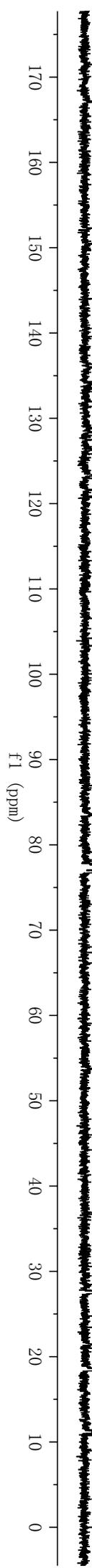
36-1
Boc intermediate for Compound 36



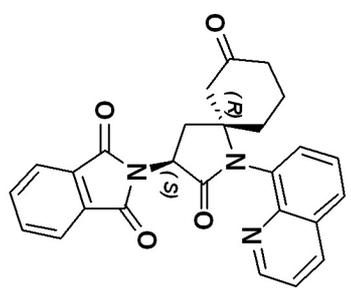
- 171.484
- 167.158
- 152.294
- 150.434
- 144.023
- 136.351
- 135.978
- 133.975
- 131.962
- 128.869
- 128.361
- 126.332
- 123.319
- 121.617
- 103.345
- 83.627
- 83.496
- 53.738
- 27.464
- 21.411
- 18.423
- 11.095



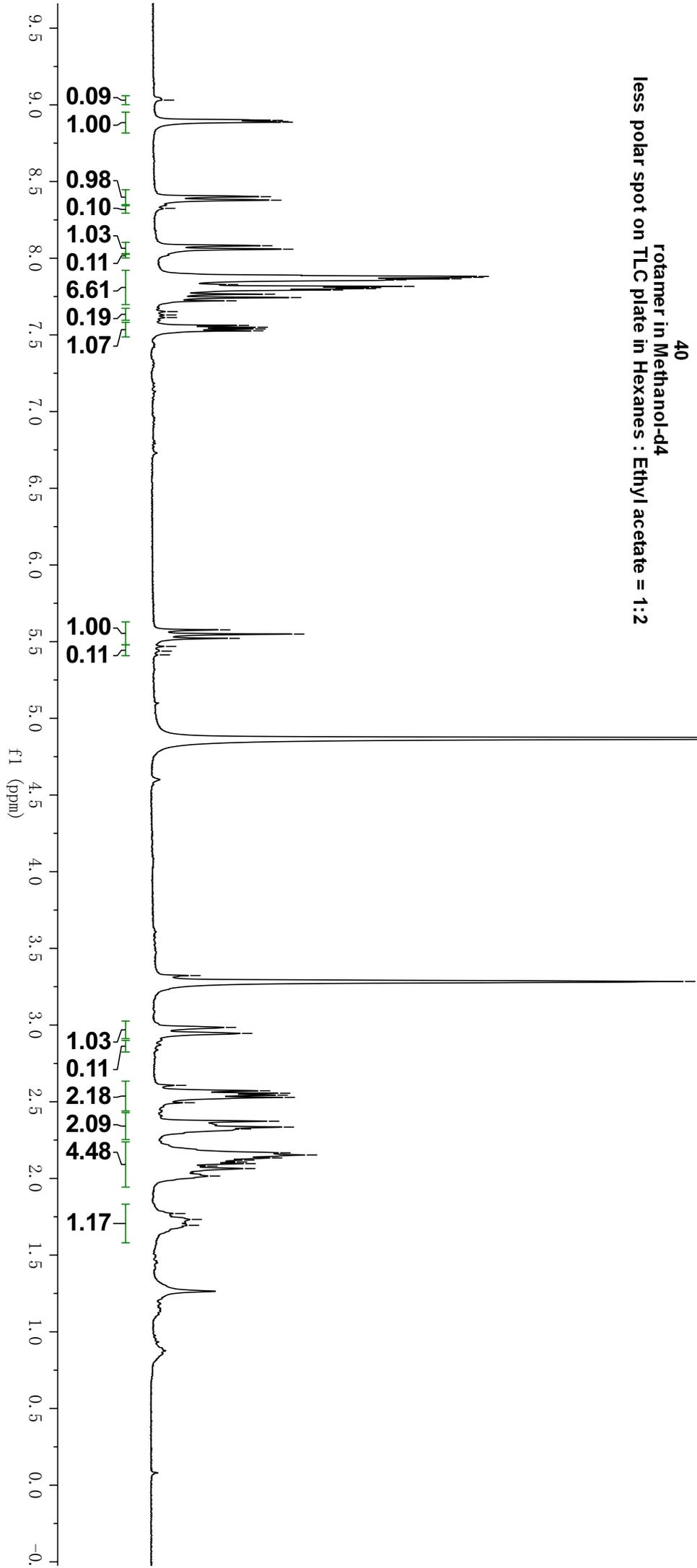
Boc intermediate for Compound 36
36-1



- 9.034
- 8.899
- 8.891
- 8.887
- 8.401
- 8.378
- 8.325
- 8.081
- 8.059
- 7.881
- 7.875
- 7.866
- 7.859
- 7.828
- 7.817
- 7.808
- 7.802
- 7.793
- 7.766
- 7.744
- 7.722
- 7.652
- 7.613
- 7.562
- 7.550
- 7.539
- 7.527
- 5.877
- 5.549
- 5.521
- 5.469
- 5.438
- 5.414

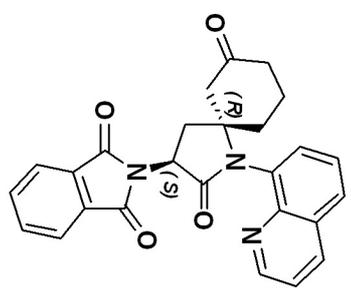


rotamer in Methanol-d4
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2

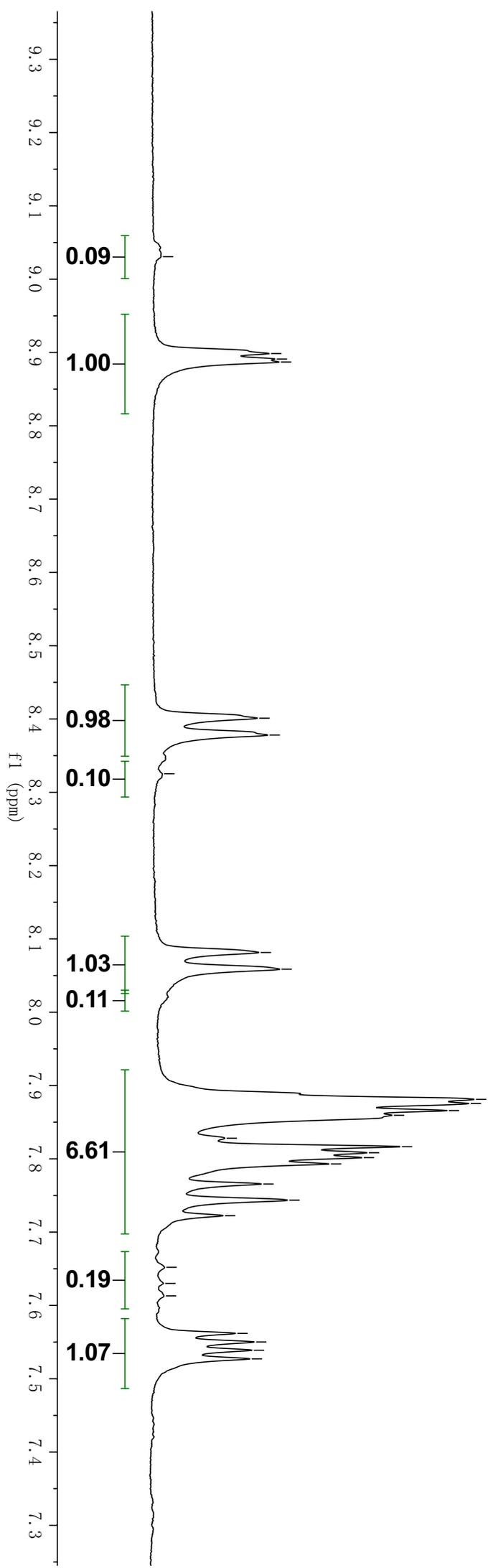


- 3.323
- 3.284
- 2.985
- 2.946
- 2.556
- 2.543
- 2.529
- 2.373
- 2.335
- 2.167
- 2.153
- 2.134
- 1.771
- 1.733
- 1.694

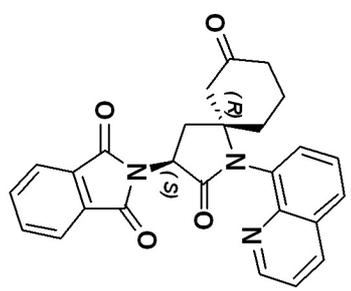
- 9.031
- 8.899
- 8.891
- 8.887
- 8.401
- 8.378
- 8.325
- 8.081
- 8.059
- 7.881
- 7.875
- 7.866
- 7.859
- 7.828
- 7.817
- 7.808
- 7.802
- 7.793
- 7.766
- 7.744
- 7.722
- 7.652
- 7.630
- 7.613
- 7.562
- 7.550
- 7.539
- 7.527



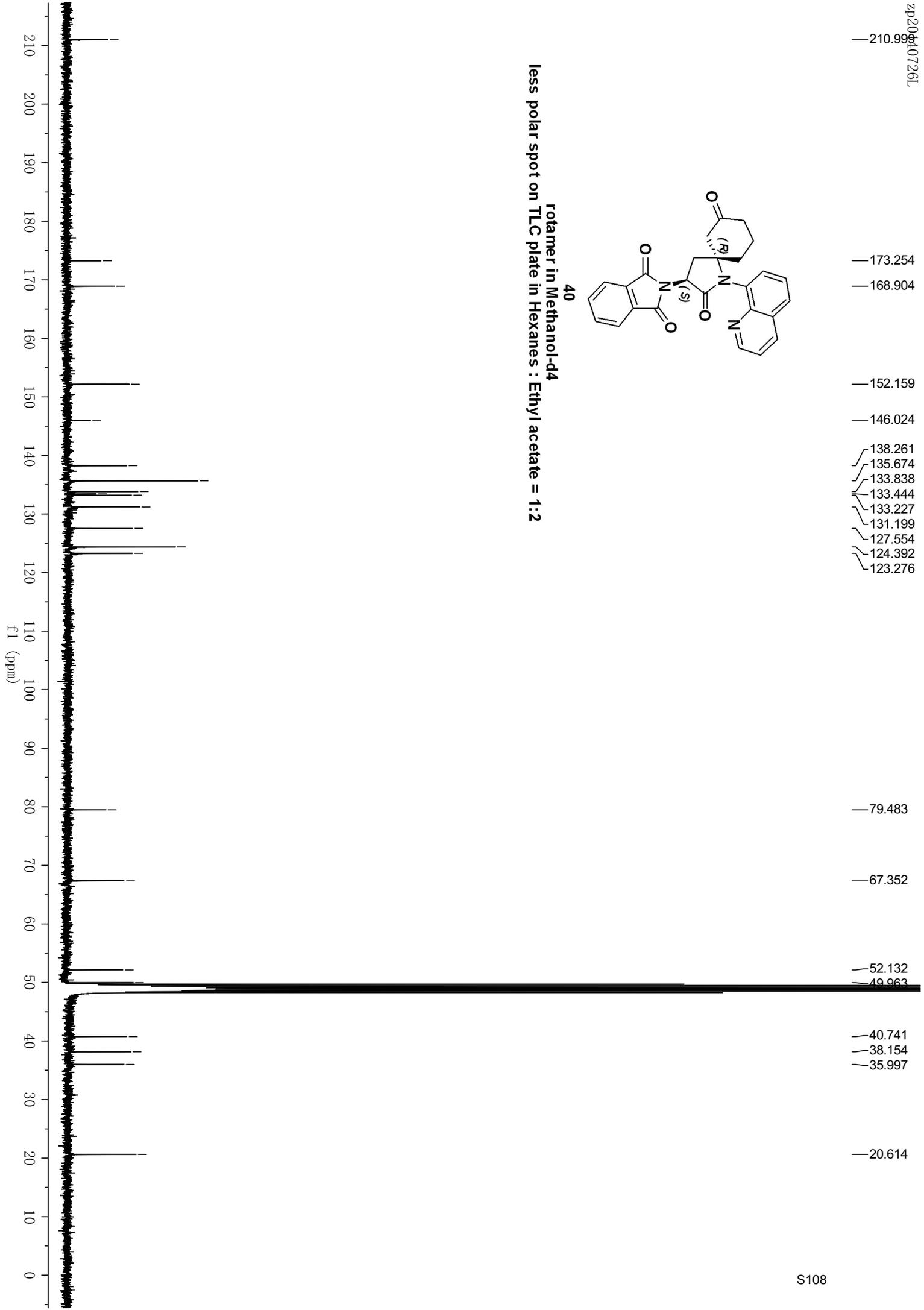
rotamer in Methanol-d4
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



- 210.99
- 173.254
- 168.904
- 152.159
- 146.024
- 138.261
- 135.674
- 133.838
- 133.444
- 133.227
- 131.199
- 127.554
- 124.392
- 123.276



rotamer in Methanol-d4
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



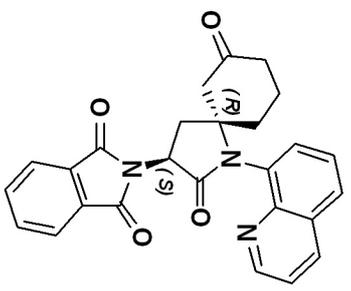
9.110
8.876
8.870

8.154
8.131
7.888
7.865
7.825
7.782
7.762
7.705
7.698
7.684
7.628
7.607
7.586
7.452
7.433
7.399
7.387
7.376
7.365

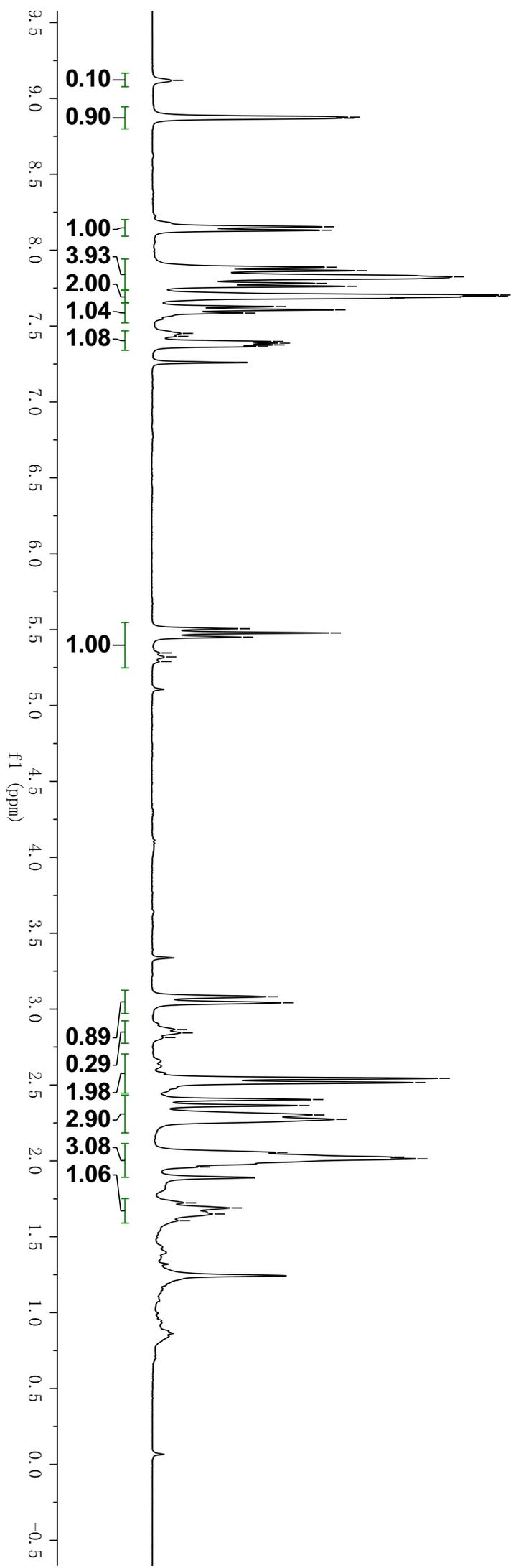
5.506
5.478
5.451
5.346
5.320
5.291

3.081
3.042
2.865
2.843
2.812

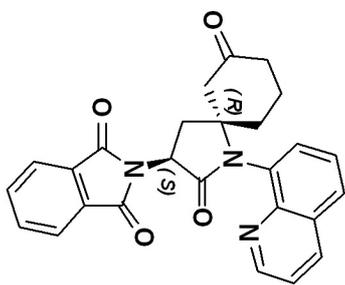
2.544
2.516
2.404
2.303
2.273
2.025
2.014
1.724
1.690
1.650
1.607



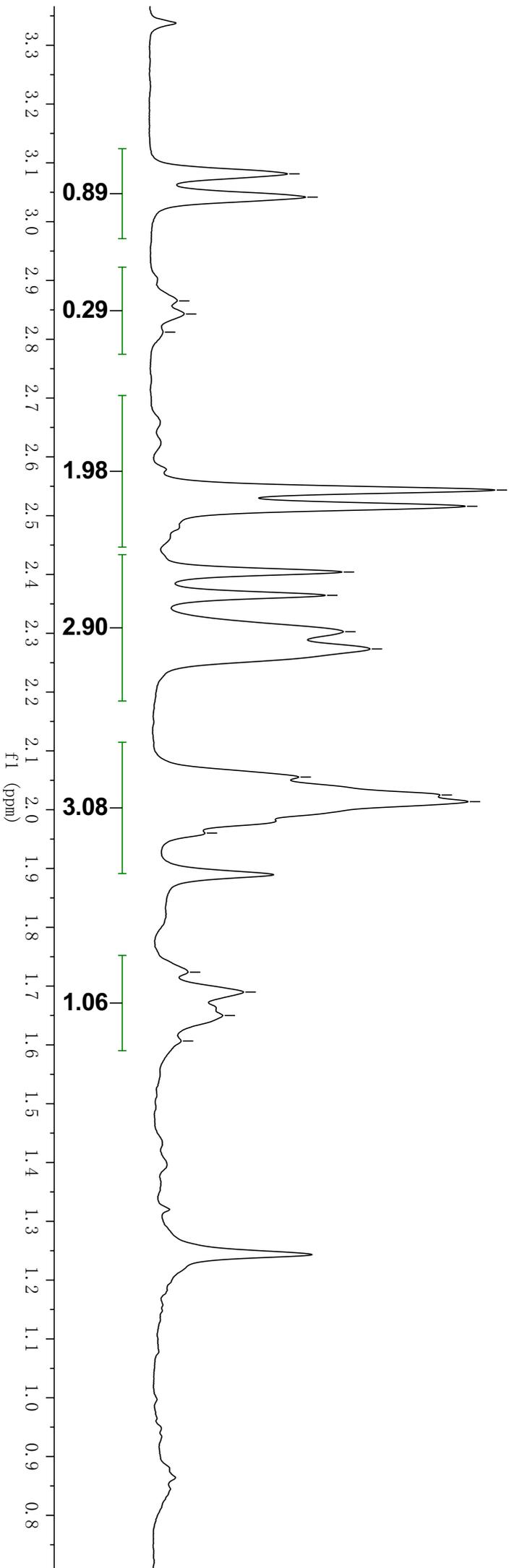
rotamer in CDCl₃
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



- 3.081
- 3.042
- 2.865
- 2.843
- 2.812
- 2.544
- 2.516
- 2.404
- 2.365
- 2.303
- 2.273
- 2.055
- 2.025
- 2.014
- 1.960
- 1.724
- 1.690
- 1.650
- 1.607



rotamer in CDCl₃
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



9.119

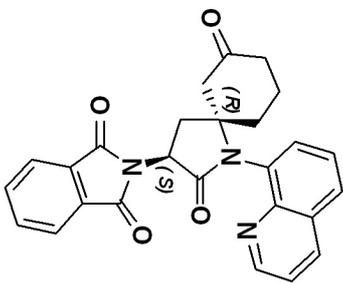
8.876
8.870

8.154
8.131

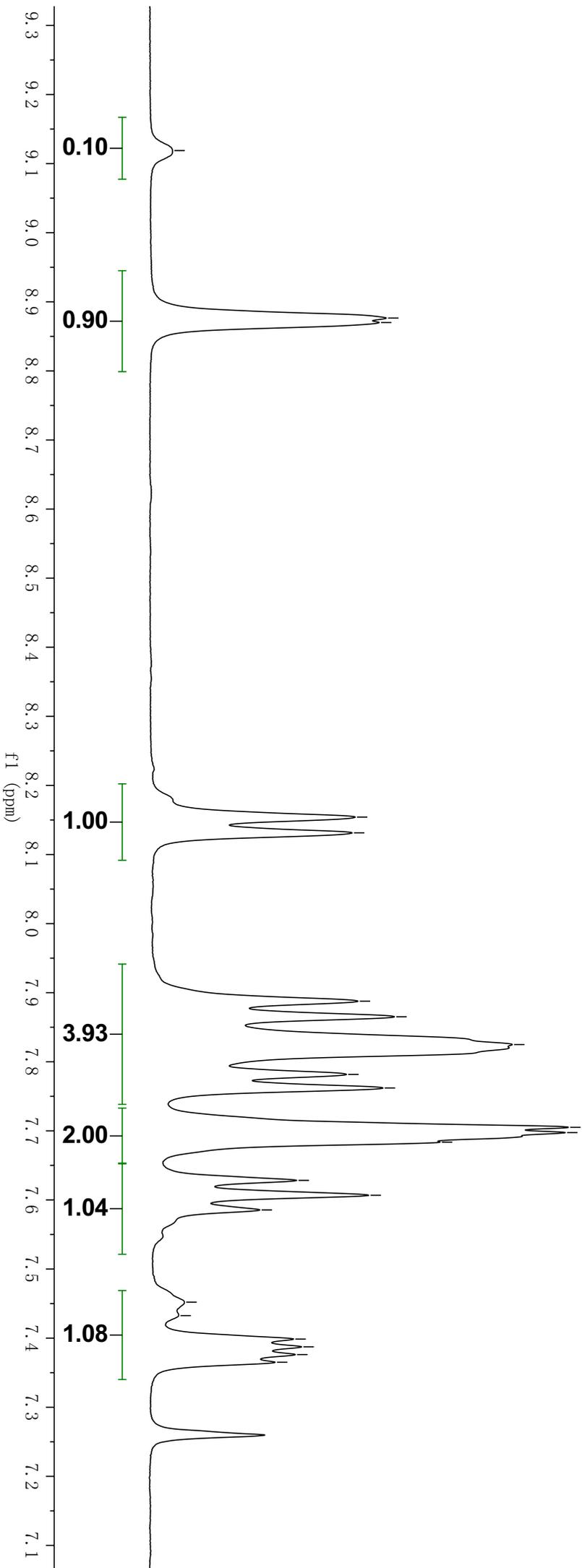
7.888
7.865
7.825
7.782
7.762

7.705
7.698
7.684
7.628
7.607
7.586

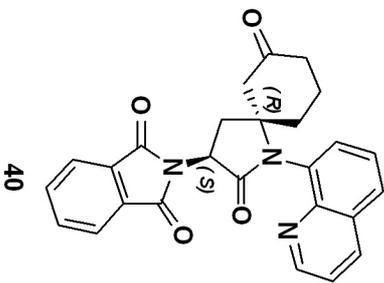
7.452
7.433
7.399
7.387
7.376
7.365



rotamer in $CDCl_3$
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2

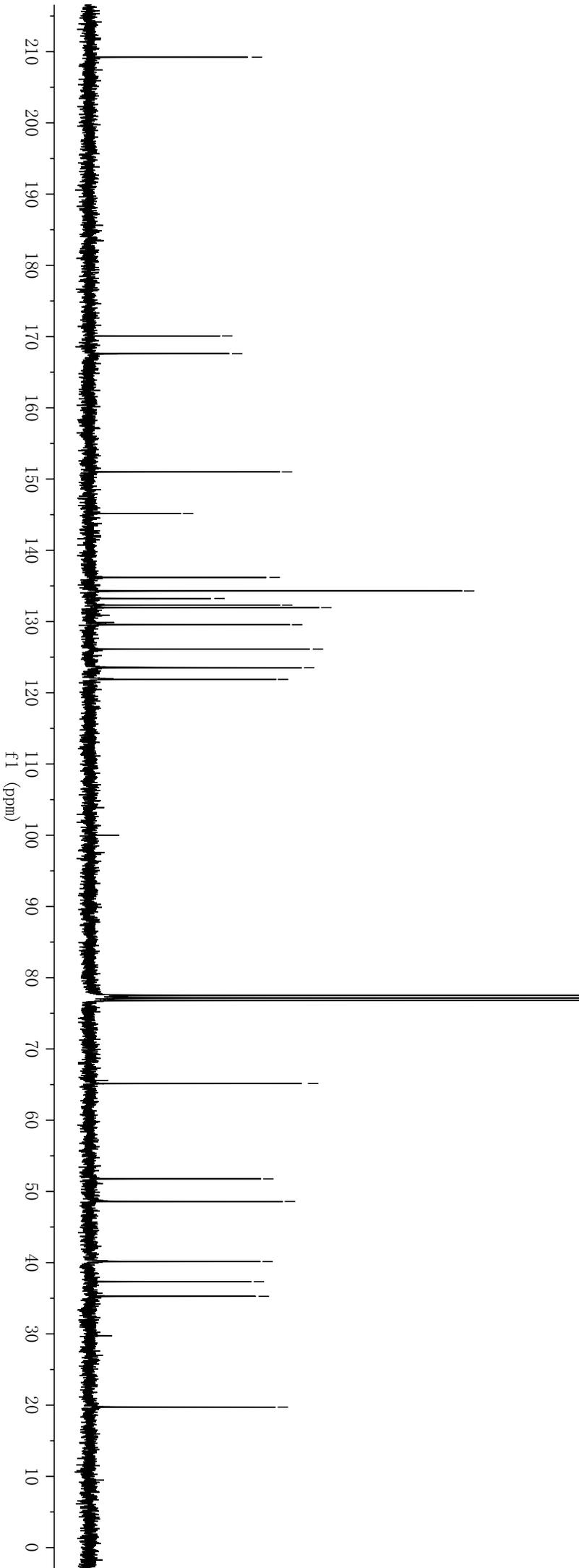


- 209.214
- 170.092
- 167.607
- 150.999
- 145.162
- 136.196
- 134.294
- 133.238
- 132.299
- 131.952
- 129.579
- 129.552
- 126.129
- 123.523
- 121.875
- 65.144
- 51.761
- 48.591
- 40.147
- 37.330
- 35.277
- 19.725

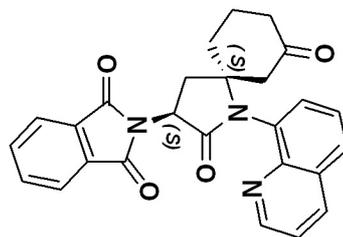


40

rotamer in CDCl₃
less polar spot on TLC plate in Hexanes : Ethyl acetate = 1:2



- 9.083
- 8.898
- 8.155
- 8.133
- 7.876
- 7.853
- 7.814
- 7.694
- 7.686
- 7.679
- 7.656
- 7.602
- 7.581
- 7.561
- 7.406
- 7.396
- 7.386

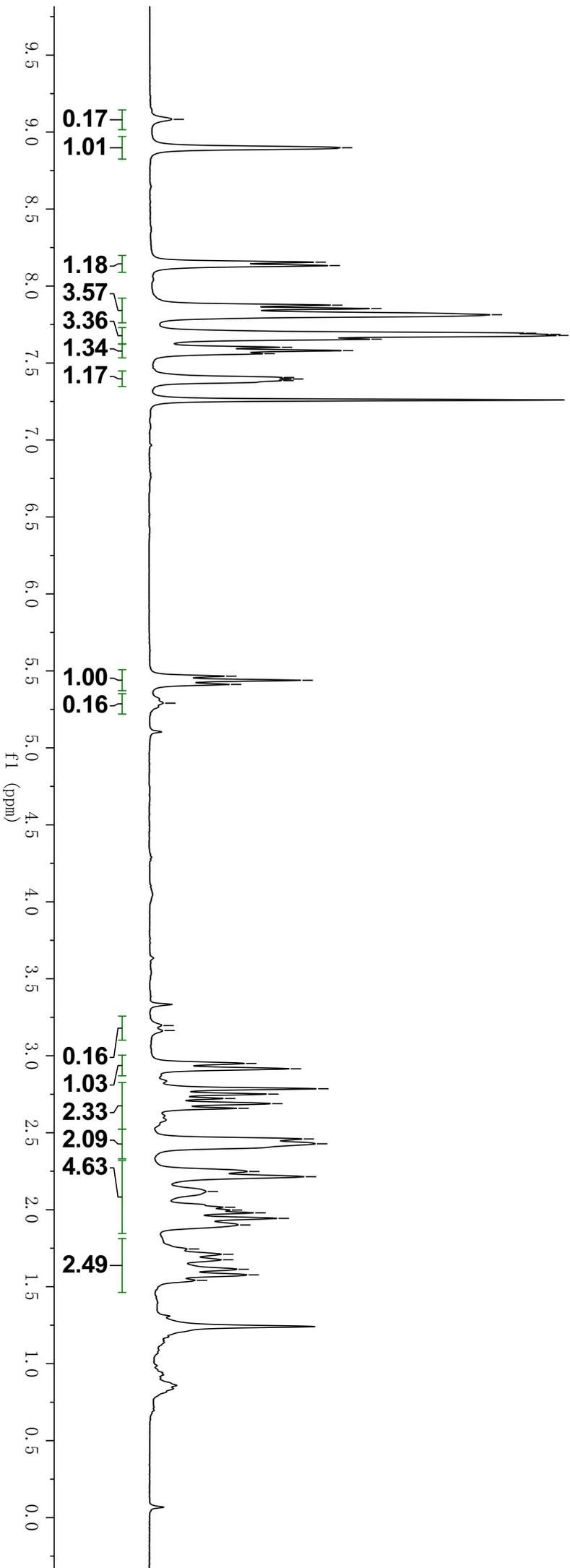


41

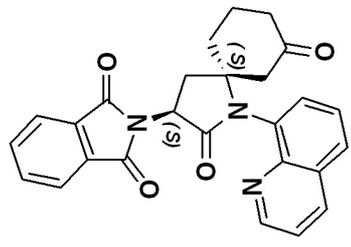
rotamer in CDCl₃
polar spot on TLC plate in Hexanes : Ethyl acetate = 1 : 2

- 5.466
- 5.439
- 5.412
- 5.290

- 3.196
- 3.164
- 2.950
- 2.915
- 2.786
- 2.751
- 2.723
- 2.689
- 2.659
- 2.460
- 2.428
- 2.249
- 2.215
- 2.118
- 2.016
- 1.998
- 1.980
- 1.944
- 1.901
- 1.745
- 1.711
- 1.675
- 1.613
- 1.577
- 1.541

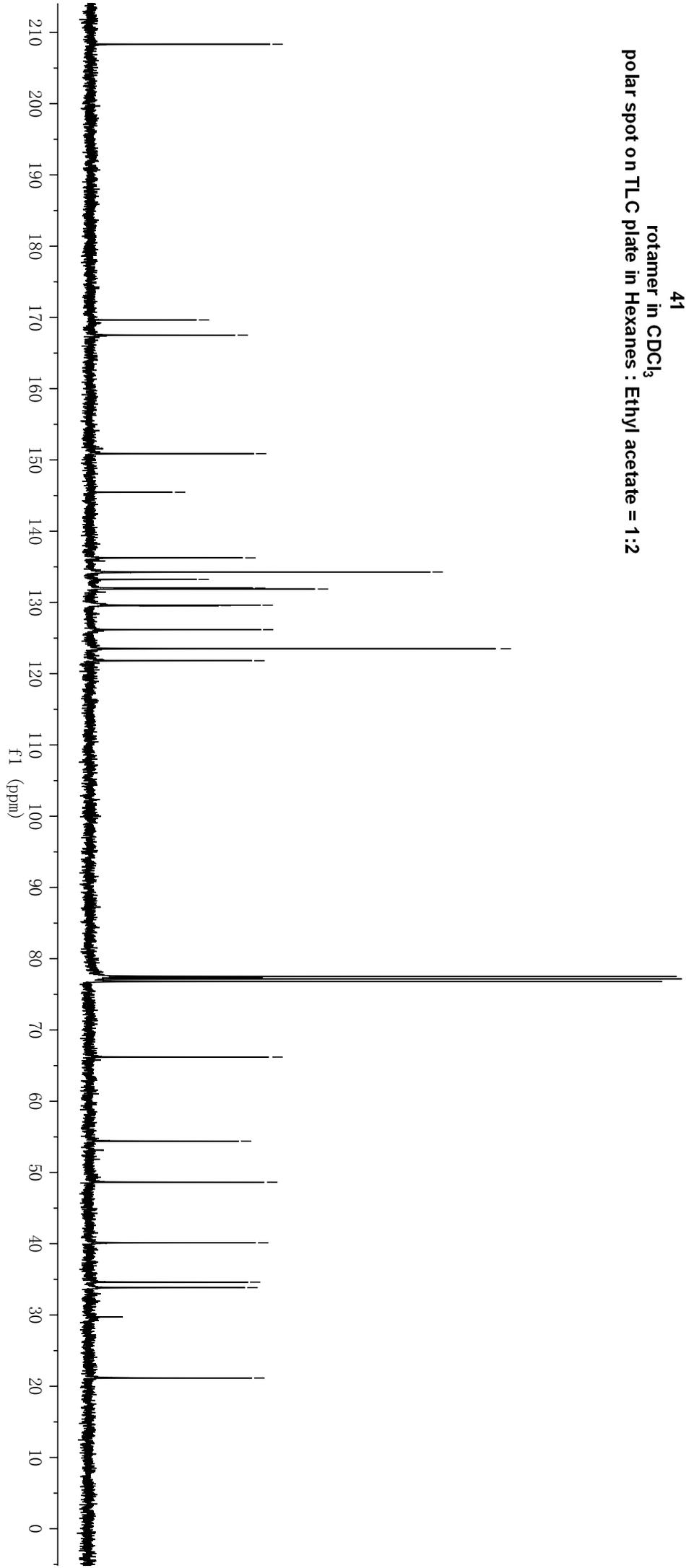


- 208.34
- 169.654
- 167.520
- 150.875
- 145.471
- 136.255
- 134.272
- 133.226
- 132.014
- 131.888
- 129.615
- 129.553
- 126.179
- 123.507
- 121.815



41

rotamer in CDCl₃
polar spot on TLC plate in Hexanes : Ethyl acetate = 1 : 2



- 66.198
- 54.402
- 48.640
- 40.131
- 34.611
- 33.835
- 21.154

7.832
7.788
7.767
7.617
7.597
7.577
7.460
7.439
7.418

5.923
5.900
5.881
5.766
5.748
5.724

5.006
4.675
4.659
4.639
4.622
4.602
4.568

3.035

