Supporting Information

Electrochemical 5-*exo-dig* aza-cyclization of 2-alkynylbenzamides toward 3-hydroxyisoindolinone derivatives

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1. General Information

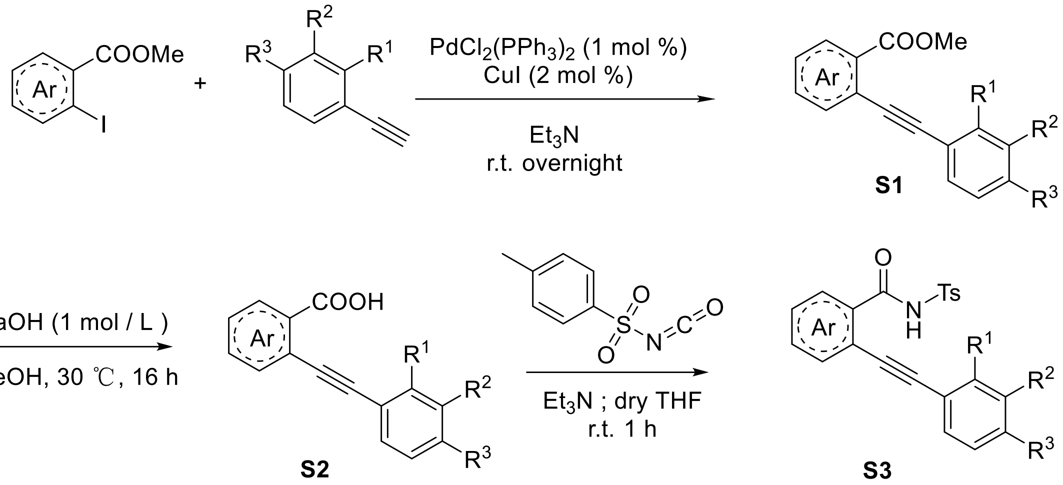
All reactions were performed under an atmosphere of argon using standard Schlenk techniques unless otherwise indicated. All commercial reagents were used without further purification unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) analysis. TLC plates were viewed under UV light and stained with potassium permanganate. Yields refer to products isolated after purification by column chromatography unless otherwise stated. Proton nuclear magnetic resonance (^{1}H NMR) spectra, carbon nuclear magnetic resonance (^{13}C NMR) spectra, and fluorine nuclear magnetic resonance (^{19}F NMR) were recorded on Bruker AV-400 (400 MHz), JEOL-500 (500 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances IR spectra were obtained from Thermo Scientific NICOLET 380 FT-IR (KCl card). HRMS were obtained on an Exactive Plus LC-MS (ESI) mass spectrometer with the use of a quadrupole analyzer. Cyclic voltammetry data were measured with a CHI 760E potentiostat (Chinstruments). All chemicals were purchased from *Innochem or Energy Chemical* and used as received.

Electrolysis experiments were performed using MESTEK DC power supply. Electrode clips (PT-1 or PT-3) and platinum plate (99.99%, 15*15*0.1 mm or 30*30*0.1 mm) were purchased from Gaoss Union. The carbon cloth (CeTech WOS1002) was cut into 15 x 15 x 0.1 mm pieces before use, and was clamped between electrode clips.

Figure S1. Electrolysis setups

2. General Procedures

Method A: General procedure for the preparation of substituted 2-(phenylethynyl)-N-tosylbenzamides [1]



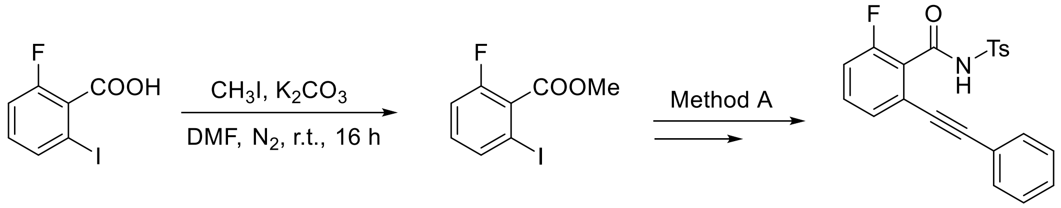
Ar = Ph, 5-MeC$_6$H$_3$; 5-FC$_6$H$_3$; 5-ClC$_6$H$_3$, thiophene; R^1 = F, Cl, Br; R^2 = Me, F, Cl, Br,
R^3 = ^{t}Bu, F, Cl, Br, CF$_3$,

Step 1: To a solution of the methyl 2-iodobenzoate (10.0 mmol, 1.0 equiv.) in Et$_3$N (30 mL), a terminal alkyne (12.0 mmol, 1.2 equiv.) and Pd(PPh$_3$)$_2$Cl$_2$ (0.1 mmol, 70 mg, 1 mol%) were added. After 5 min stirring at room temperature, CuI (0.2 mmol, 38 mg, 2 mol%) was added and the reaction mixture was stirred overnight. The reaction mixture was then filtered. The solvent was removed in *vacuo* and the crude residue was purified by flash chromatography on silica gel (300-400 mesh) to give **S1**.

Step 2: A 100 mL reaction flask was equipped with a magnetic stirring bar and charged with **S1** (5.0 mmol, 1.0 equiv.) in 30 mL MeOH. NaOH (1 N, 10 mL) was dropwise added to the solution through a dropping funnel. The reaction mixture was stirred at 30 °C for 16 h, then acidified by HCl (1 M). The resulting mixture was extracted by EtOAc (3 x 20 mL) and the combined organic layer was dried by Na$_2$SO$_4$, and then filtered. The solvent was removed in *vacuo* to afford **S2**, which was used without further purification.

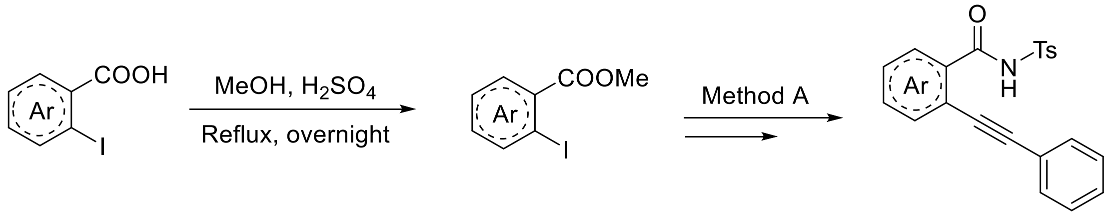
Step 3: The carboxylic acid **S2** (5.0 mmol, 1.0 equiv) was dissolved in dry THF (38.0 mL) under argon and tosyl isocyanate (6.0 mmol, 1.2 equiv.) was added to this solution. After stirring at r.t. for 10 min, Et$_3$N (6.0 mmol, 1.2 equiv.) was added dropwise to this flask, in which the formed CO$_2$ was released. After stirring for 1 h, the solution was diluted with an equal volume of EtOAc and washed with 1 M HCl and brine. After drying with Na$_2$SO$_4$, the organic phase was concentrated and the product **S3** was purified by recrystallization or flash chromatography.

Method B: General procedure for the preparation of substituted 2-(phenylethynyl)-N-tosylbenzamides[2]



6-Fluoro-2-iodobenzoic acid (2.66 g, 10.0 mmol, 1.0 equiv.) and K_2CO_3 (2.08 g, 15.0 mmol, 1.5 equiv.) were dissolved in DMF (100 ml) and stirred for 5 min. CH_3I (926 µl, 15.0 mmol, 1.5 equiv.) was then added and the mixture was stirred for 16 h at room temperature under N_2. The reaction was diluted with EtOAc and then the organic layer was washed with H_2O and brine, dried over Na_2SO_4, and evaporated under vacuum to give the desired compound, which was used in the next steps without further purification.

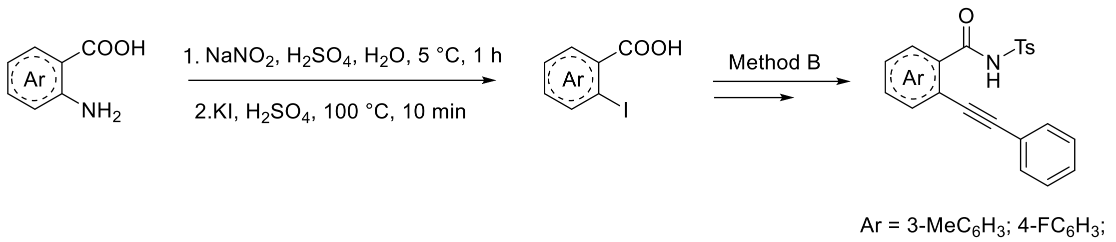
Method C: General procedure for the preparation of substituted 2-(phenylethynyl)-N-tosylbenzamides[3]



Ar = 4-ClC$_6$H$_3$; 5-OMeC$_6$H$_3$;

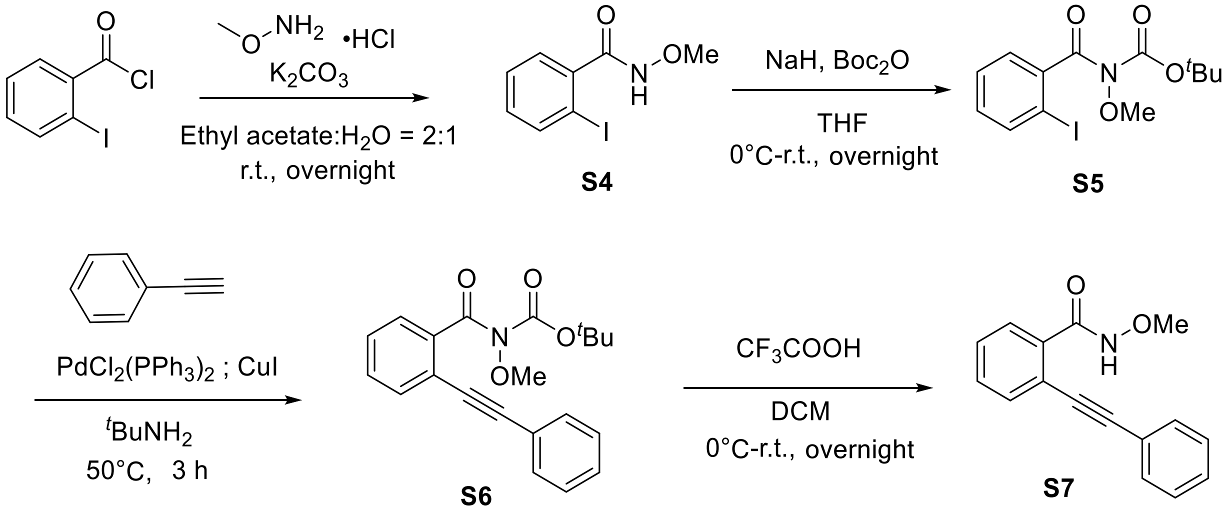
2-Iodobenzoic acid (10.0 mmol, 1.0 equiv.) was dissolved in MeOH (50 mL). Sulfuric acid (6.8 mL) was then slowly added and the mixture was stirred overnight and then heated at reflux. The reaction was cooled to room temperature, before diluting with diethyl ether. The organic layer was then washed with H_2O and brine, dried over Na_2SO_4, and evaporated under vacuum to give the desired compound, which was used in the next steps without further purification.

Method D: General procedure for the preparation of substituted 2-(phenylethynyl)-N-tosylbenzamides[4]



To a solution of anthranilic acid (10 mmol, 1.0 equiv) in water (1 M) was added concentrated sulfuric acid (25 mmol, 2.5 equiv.) at 5 °C and an aqueous solution of sodium nitrite (11 mmol, 1.1 equiv.) slowly. The resulting solution was stirred for 30 minutes before potassium iodide (15 mmol, 1.5 equiv.）in sulfuric acid (1 M) was added. The solution was then heated at 100 °C for 1 hour. The reaction was cooled to ambient temperature and the precipitate was filtered and washed with water. Further purification with column chromatography on silica gel or recrystallization provided 2-iodobenzoic acid.

Method E: Preparation of substituted N-methoxy-2-(phenylethynyl)benzamide[5]

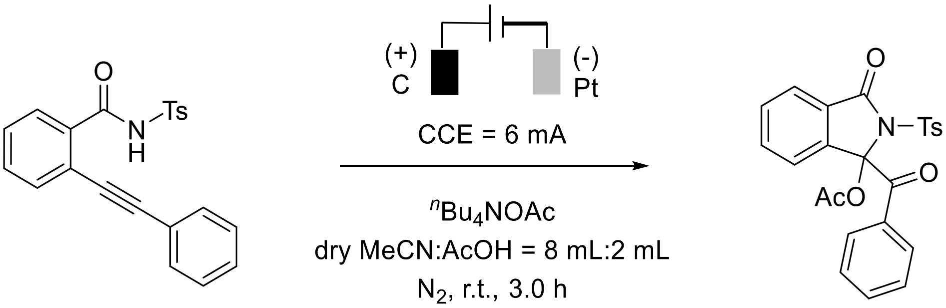


Step 1: To a solution of 2-iodobenzoyl chloride (4 g, 15.0 mmol, 1.0 equiv.) in EtOAc/H_2O (v/v = 2:1, 180 mL) were added potassium carbonate (4.14 g, 30 mmol, 2.0 equiv.) and methoxylamine hydrochloride (1.5 g, 18.0 mmol, 1.2 equiv.). The mixture was stirred at room temperature overnight and then extracted with EtOAc (3 × 40 mL), washed with water (50 mL) and brine (50 mL), and dried over Na_2SO_4. Evaporation gave a crude solid that was recrystallized from EtOAc afforded 2-iodo-N-methoxybenzamide **S4** (white solid, 4.46 g, 84% yield).

Step 2: Sodium hydride (640 mg, 16 mmol, 1.1 equiv.) was added into a solution of 2-iodo-N-methoxybenzamide **S4** (4.05 g, 14.6 mmol, 1.0 equiv.) in dry THF (100 mL) at 0 ℃. After that, Boc_2O (3.83 g, 17.5 mmol, 1.2 equiv) was added slowly at 0 ℃. The mixture was stirred at room temperature overnight and then quenched with saturated aqueous NH_4Cl solution (30 mL). The mixture was extracted with EtOAc (3 × 30 mL), washed with saturated aqueous bicarbonate solution (30 mL) and brine (30 mL), and dried over Na_2SO_4. Using flash column chromatography, a white solid tert-butyl methoxy(2-(phenylethynyl)benzoyl)carbamate **S5** was obtained (4.80 g, 87% yield).

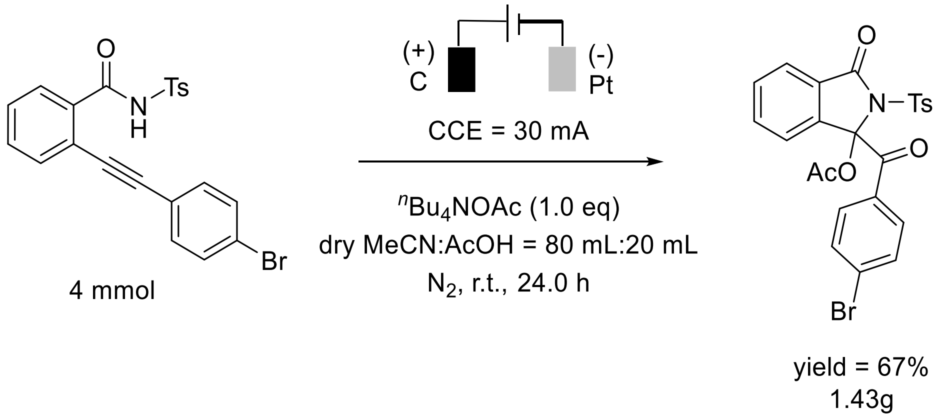
Step 3 and 4: To a solution of the above solid, *tert*-butyl methoxy(2-(phenylethynyl)benzoyl)carbamate **S5** (1.56 g, 4.4 mmol, 1.0 equiv.), in toluene (20 mL) were successively added $PdCl_2(PPh_3)_2$ (308.8 mg, 0.44 mmol, 10 mol%), CuI (41.9 mg, 0.22 mmol, 5 mol%), phenylacetylene (1.4 mL, 13.2 mmol, 3.0 equiv.), and *tert*-butylamine (0.93 mL, 8.8 mmol, 2.0 equiv.). The mixture was stirred at 50 ℃ in an oil bath for 3 h. Then the crude was filtrated by chromatography on silica gel (ether/ethyl acetate 50:1 to 20:1) to afford the crude product **S6**, to which trifluoroacetic acid (3 mL) in CH_2Cl_2 (5 mL) was added at 0 ℃. The crude mixture was purified by flash chromatography on silica gel to afford the pure product **S7** (0.905 g, 82%) as a white solid.

Method F: General procedure for the electrochemical cyclization reaction



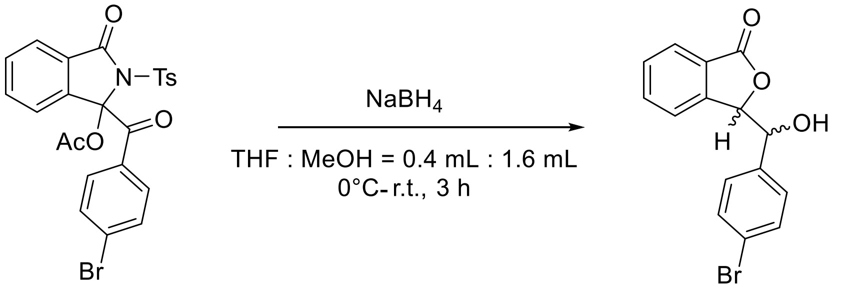
In an oven-dried undivided three-necked glassware (25 mL) equipped with a stirring bar, 2-(phenylethynyl)-N-tosylbenzamides (0.2 mmol, 1.0 equiv.) and $^n Bu_4NOAc$ (0.2 mmol, 1.0 equiv.) were added. The glassware was equipped with carbon cloth (15 mm × 15 mm × 0.1 mm) as the anode and platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode (Note: the electrodes need to be thoroughly dried before use). Under the protection of N_2, MeCN and CH_3CO_2H = 8:2 (10 mL) were injected into the glassware *via* syringes. The reaction mixture was stirred and electrolyzed at a constant current of 6 mA at an ambient temperature for 3.0 h. The reaction mixture was concentrated *in vacuo*, and the crude residue was subjected to flash column chromatography on silica gel to yield the desired product.

Method G: Scale-up synthesis



In an oven-dried undivided three-necked glassware (100 mL) equipped with a stirring bar, 2-((4-bromophenyl)ethynyl)-N-tosylbenzamide (1.82 g, 4 mmol, 1.0 equiv.) and ^{n}Bu$_4$NOAc (1.22 g, 4 mmol, 1.0 equiv.) were added. The glassware was equipped with carbon cloth (30 mm × 30 mm × 0.1 mm) as the anode and platinum plate (30 mm × 30 mm × 0.1 mm) as the cathode (Note: the electrodes needs to be thoroughly dried before use). Under the protection of N$_2$, MeCN and CH$_3$CO$_2$H = 80:20 (100 mL) were injected respectively into the glassware *via* syringes. The reaction mixture was stirred and electrolyzed at a constant current of 30 mA at an ambient temperature for 24.0 h. The reaction mixture was concentrated in vacuo, the crude residue was subjected to flash column chromatography on silica gel to give the desired product (67 % yield, 1.43 g).

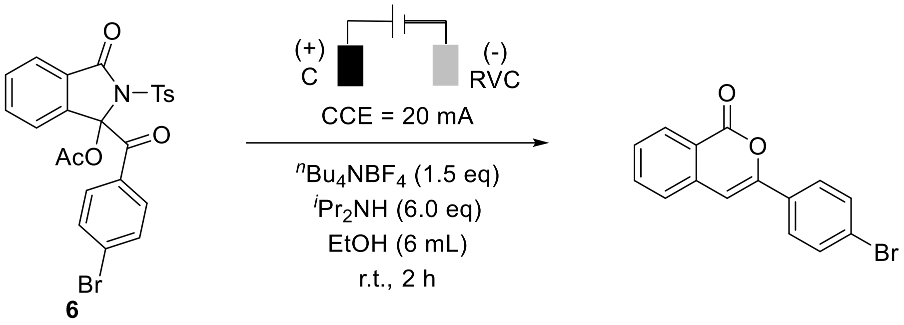
Method H: Preparation of 3-((4-bromophenyl)(hydroxy)methyl)isobenzofuran-1(3*H*)-one.[5]



6

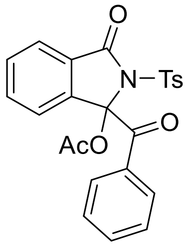
Compound **6** (52.8 mg, 0.1 mmol, 1.0 equiv.), THF and MeOH (2:8 v/v, 2 mL), and a stirring bar were added into a 10 mL bottom glassware. The reaction mixture was cooled to 0 ℃, and then NaBH$_4$ (9.1 mg, 0.24 mmol, 2.4 equiv.) was added. After stirring the reaction mixture at room temperature for 3 hours, an aqueous solution saturated NH_4Cl (50 mL) was added, and then diluted with H_2O (50 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2×50 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude product was purified using silica gel and a 1:5 v/v ethyl acetate: petroleum ether mixture as the eluent, and the product was obtained in a yield of 60% (dr = 1:1).

Method I: Preparation of 3-(4-bromophenyl)-1*H*-isochromen-1-one.[6]



In an undivided three-necked glassware (10 mL) equipped with a stirring bar, **6** (105.6 mg, 0.2 mmol, 1.0 equiv.), ^{n}Bu$_4$NBF$_4$ (98.8 mg, 0.3 mmol, 1.5 equiv.), ^{i}Pr$_2$NH (170 μL, 1.2 mmol, 6.0 equiv.) and EtOH (6 mL) were added. The glassware was equipped with carbon cloth (15 mm ×15 mm ×0.1 mm) as the anode and RVC (10 mm ×10 mm ×5 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current of 20 mA at an ambient temperature for 2.0 h. The reaction mixture was concentrated *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to afford the product in a yield of 29%.

3. Characterization of Products

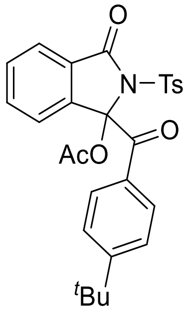


2: 1-benzoyl-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 61.1 mg (68% yield) of **2** as a white solid.

IR (neat, cm^{-1}): 3067 (w), 1750 (s), 1702 (m), 1596 (w), 1446 (w), 1367 (m), 1245 (s), 1170 (s), 1136 (s), 816 (w), 757 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.89 (d, *J* = 8.5 Hz, 2H), 7.87 (dd, *J* = 6.9, 1.9 Hz, 1H), 7.78 (d, *J* = 6.6 Hz, 2H), 7.61 – 7.53 (m, 3H), 7.44 – 7.37 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.40 (s, 3H), 2.09 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.3, 167.8, 165.4, 145.8, 140.9, 135.2, 134.9, 134.8, 133.3, 131.4, 130.2, 129.6, 129.4, 129.1, 128.7, 125.4, 122.9, 94.7, 21.9, 21.8.

HRMS (ESI) calculated for $C_{24}H_{19}NNaO_6S^+$ [M+Na$^+$]: 472.0825; found:472.0824.

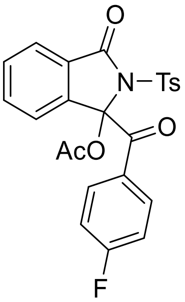


3: 1-(4-(tert-butyl)benzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 35.4 mg (35% yield) of **3** as a white solid.

IR (neat, cm^{-1}): 2963 (w), 1752 (s), 1696 (m), 1602 (m), 1466 (w), 1367 (m), 1247 (s), 1171 (s), 1138 (m), 839 (w), 766 (w); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.91 – 7.87 (m, 3H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.57 (m, 2H), 7.45 (dd, *J* = 6.5, 1.5 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 2.40 (s, 3H), 2.11 (s, 3H), 1.32 (s, 9H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.3, 167.9, 165.5, 157.3, 145.7, 141.2, 135.3, 134.7, 131.8, 131.3, 130.3, 129.8, 129.4, 129.2, 125.8, 125.4, 123.0, 94.8, 35.3, 31.1, 22.0, 21.8.

HRMS (ESI) calculated for $C_{28}H_{27}NNaO_6S^+$ [M+Na $^+$]: 528.1451; found:528.1449.

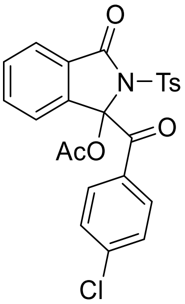


4: 1-(4-fluorobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 3.5 h, Q = 3.92 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 63.6 mg (68% yield) of **4** as a white solid.

IR (neat, cm^{-1}): 3071 (w), 1750 (s), 1699 (m), 1596 (s), 1467 (w), 1367 (m), 1243 (s), 1195 (s), 1161 (s), 1134 (s), 816 (m), 757 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.94 (d, J = 8.4 Hz, 2H), 7.90 – 7.87 (m, 1H), 7.87-7.84 (m, 2H), 7.63 – 7.53 (m, 2H), 7.40 (dd, J = 6.8, 2.2 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 7.09 (t, J = 8.6 Hz, 2H), 2.42 (s, 3H), 2.09 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 188.8, 167.7, 165.7 (d, J = 256.5 Hz), 165.3, 145.9, 140.9, 135.2, 134.9, 132.5 (d, J = 9.3 Hz), 131.5, 131.0（d, J = 3.0 Hz）, 130.2, 129.5, 129.1, 125.6, 122.8, 116.0 (d, J = 21.8 Hz), 94.7, 21.90, 21.86; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -103.8 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found:490.0726.

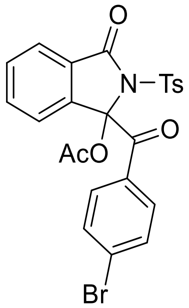


5: 1-(4-chlorobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 74.5 mg (77% yield) of **5** as a white solid.

IR (neat, cm^{-1}): 3068 (w), 1750 (s), 1702 (m), 1587 (m), 1466 (w), 1367 (m), 1245 (s), 1169 (s), 1136 (m), 818 (m), 762 (m), 729 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.88 (dd, *J* = 6.5, 2.1 Hz, 1H), 7.73 (d, *J* = 8.3 Hz, 2H), 7.62 – 7.55 (m, 2H), 7.41 – 7.37 (m, 3H), 7.30 (d, *J* = 8.1 Hz, 2H), 2.42 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.3, 167.7, 165.2, 145.9, 140.8, 139.9, 135.1, 134.9, 133.0, 131.5, 131.1, 130.2, 129.5, 129.1, 129.0, 125.6, 122.8, 94.5, 21.9, 21.8.

HRMS (ESI) calculated for $C_{24}H_{18}ClNNaO_6S^+$ [M+Na$^+$]: 506.0435; found:506.0436.

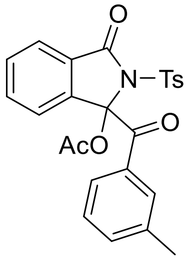


6: 1-(4-bromobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 78.2 mg (72% yield) of **6** as a white solid.

IR (neat, cm^{-1}): 3067 (w), 1750 (s), 1703 (m), 1583 (m), 1466 (w), 1367 (m), 1245 (s), 1169 (s), 1134 (s), 817 (m), 761 (m), 661 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.89 – 7.86 (m, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.62 – 7.56 (m, 2H), 7.56 – 7.52 (m, 2H), 7.39 (dd, *J* = 6.4, 1.2 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 2.07 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.6, 167.6, 165.2, 145.9, 140.7, 135.1, 134.9, 133.5, 132.0, 131.5, 131.1, 130.1, 129.5, 129.0, 128.6, 125.5, 122.7, 94.5, 21.8, 21.8.

HRMS (ESI) calculated for $C_{24}H_{18}BrNNaO_6S^+$ [M+Na$^+$]: 549.9930; found:549.9927.

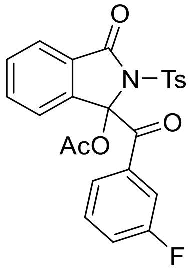


7: 1-(3-methylbenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 55.6 mg (60% yield) of **7** as a white solid.

IR (neat, cm^{-1}): 3062 (w), 1752 (s), 1701 (m), 1599 (m), 1466 (w), 1368 (m), 1249 (s), 1170 (s), 1134 (s), 815 (w), 754 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.95 – 7.82 (m, 3H), 7.65 (s, 1H), 7.57 (m, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.40 (dd, *J* = 21.0, 7.4 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 3H), 2.41 (s, 3H), 2.36 (s, 3H), 2.10 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.4, 167.8, 165.4, 145.7, 141.1, 138.6, 135.3, 134.8, 134.8, 134.1, 131.3, 130.5, 130.3, 129.4, 129.2, 128.5, 126.6, 125.4, 122.9, 94.8, 21.93, 21.85, 21.5.

HRMS (ESI) calculated for $C_{25}H_{21}NNaO_6S^+$ [M+Na$^+$]: 486.0981; found:486.0978.

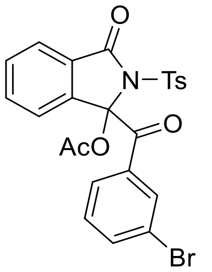


8: 1-(3-fluorobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 71.1 mg (76% yield) of **8** as a white solid.

IR (neat, cm^{-1}): 3073 (w), 1752 (s), 1708 (m), 1586 (m), 1467 (w), 1367 (m), 1247 (s), 1205 (s), 1170 (s), 1128 (s), 815 (m), 756 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.90 – 7.84 (m, 1H), 7.68 – 7.48 (m, 4H), 7.44 – 7.35 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.24 (m, 1H), 2.41 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.5, 167.6, 165.1, 162.4 (d, *J* = 248.2 Hz), 145.9, 140.7, 136.6 (d, *J* = 7.0 Hz), 135.1, 134.9, 131.5, 130.4 (d, *J* = 7.8 Hz), 130.1, 129.5, 128.9, 125.5, 125.2 (d, *J* = 3.0 Hz), 122.6, 120.4 (d, *J* = 21.1 Hz), 116.8 (d, *J* = 23.6 Hz), 94.6, 21.8, 21.8; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -110.9 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found: 490.0729.

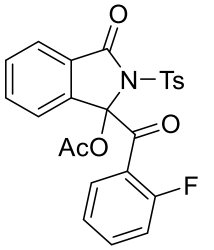


9: 1-(3-bromobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 82.4 mg (78% yield) of **9** as a white solid.

IR (neat, cm^{-1}): 3067 (w), 1751 (s), 1707 (m), 1597 (w), 1467 (w), 1367 (m), 1239 (s), 1169 (s), 1136 (s), 815 (m), 763 (m), 661 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.04 (t, *J* = 1.8 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.87 (dd, *J* = 6.6, 1.4 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.63 – 7.54 (m, 2H), 7.37 (d, *J* = 6.9 Hz, 1H), 7.33 – 7.26 (m, 3H), 2.42 (s, 3H), 2.09 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.7, 167.5, 165.1, 145.9, 140.7, 136.6, 136.1, 135.1, 134.9, 132.9, 131.5, 130.2, 130.1, 129.5, 129.0, 128.0, 125.6, 122.8, 122.5, 94.6, 21.9, 21.9.

HRMS (ESI) calculated for $C_{24}H_{18}BrNNaO_6S^+$ [M+Na$^+$]: 549.9930; found:549.9927.

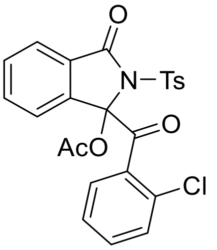


10: 1-(2-fluorobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 68.3 mg (73% yield) of **10** as a white solid.

IR (neat, cm^{-1}): 3069 (w), 1751 (s), 1714 (m), 1610 (m), 1467 (w), 1367 (m), 1246 (s), 1195 (s), 1169 (s), 1136 (s), 815 (w), 757 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.94 (d, *J* = 8.5 Hz, 2H), 7.87 – 7.81 (m, 1H), 7.76 (td, *J* = 7.7, 1.7 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.59 – 7.53 (m, 3H), 7.33 – 7.26 (m, 3H), 7.18 – 7.14 (m, 1H), 2.42 (s, 3H), 2.02 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 192.1, 167.6, 165.4, 159.7 (d, *J* = 253.2 Hz), 145.8, 140.9, 135.2, 134.7, 134.2 (d, *J* = 8.8 Hz), 131.9, 131.2, 130.5, 129.6, 129.0, 125.3, 125.0 (d, *J* = 14.3 Hz), 124.4 (d, *J* = 3.4 Hz), 122.3 (d, *J* = 7.3 Hz), 116.3 (d, *J* = 22.7 Hz), 94.1, 21.9, 21.7; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -109.2 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found:490.0728.

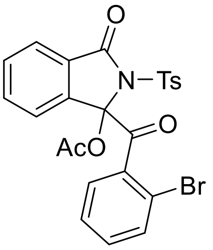


11: 1-(2-chlorobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 69.7 mg (72% yield) of **11** as a white solid.

IR (neat, cm^{-1}): 3070 (w), 1751 (s), 1723 (m), 1592 (w), 1467 (w), 1367 (m), 1246 (s), 1170 (s), 1140 (s), 815 (m), 769 (m), 740 (w); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.08 – 7.98 (m, 3H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.3 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.48 (td, *J* = 7.7, 1.7 Hz, 1H), 7.39 (td, *J* = 7.5, 1.4 Hz, 1H), 7.34 (t, *J* = 8.1 Hz, 3H), 2.43 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 191.4, 167.3, 165.3, 145.9, 140.5, 135.14, 135.06, 134.5, 132.5, 132.1, 131.3, 131.0, 130.7, 129.7, 129.5, 129.4, 126.1, 125.3, 122.4, 94.9, 21.9, 21.7.

HRMS (ESI) calculated for $C_{24}H_{18}ClNNaO_6S^+$ [M+Na$^+$]: 506.0435; found:506.0431.



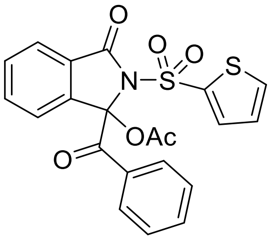
12: 1-(2-bromobenzoyl)-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 76.1 mg (72% yield) of **12** as a white solid.

IR (neat, cm^{-1}): 3066 (w), 1751 (s), 1722 (m), 1596 (w), 1466 (w), 1366 (m), 1245 (m), 1168 (s), 1141 (s), 815 (w), 769 (w), 658 (s); **^{1}H NMR (500 MHz, Chloroform-**

***d*)** δ 8.07 (dd, *J* = 7.7, 1.9 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.73 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.59 (td, *J* = 7.6, 1.3 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.45 (td, *J* = 7.6, 1.4 Hz, 1H), 7.40 (td, *J* = 7.7, 1.8 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 2.42 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 191.8, 167.3, 165.3, 145.9, 140.5, 136.9, 135.1, 134.5, 134.4, 132.7, 131.3, 131.0, 129.7, 129.5, 129.4, 126.6, 125.3, 122.7, 121.0, 94.8, 21.9, 21.8.

HRMS (ESI) calculated for $C_{24}H_{18}BrNNaO_6S^+$ [M+Na$^+$]: 549.9930; found:549.9931.

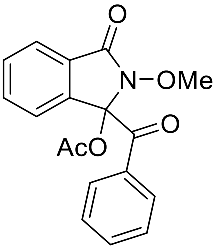


13: 1-benzoyl-3-oxo-2-(thiophen-2-ylsulfonyl)isoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 45.0 mg (51% yield) of **13** as a white solid.

IR (neat, cm^{-1}): 3102 (w), 3064 (w), 1750 (s), 1700 (m), 1596 (w), 1466 (w), 1368 (m), 1244 (s), 1170 (s), 1133 (s), 754 (m), 724 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.92 – 7.89 (m, 1H), 7.86 (dd, *J* = 3.9, 1.4 Hz, 1H), 7.81 – 7.77 (m, 2H), 7.69 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.63 – 7.53 (m, 3H), 7.46 – 7.36 (m, 3H), 7.07 (dd, *J* = 5.0, 3.9 Hz, 1H), 2.12 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.0, 167.8, 165.2, 140.9, 138.2, 136.1, 135.1, 134.9, 134.6, 133.4, 131.4, 130.0, 129.7, 128.7, 127.4, 125.5, 122.8, 94.9, 21.9.

HRMS (ESI) calculated for $C_{21}H_{15}NNaO_6S_2^+$ [M+Na$^+$]: 464.0233; found: 464.0243.



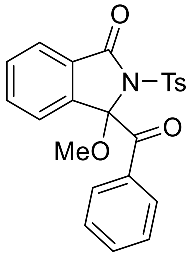
14: 1-benzoyl-2-methoxy-3-oxoisoindolin-1-yl acetate

Followed **Method F** (current = 5 mA, Q = 2.80 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 19.5 mg (30% yield) of **14** as a white solid.

IR (neat, cm^{-1}): 3068 (w), 1736 (s), 1694 (s), 1596 (w), 1467 (m), 1369 (m), 1239 (m), 1198 (s), 758 (m).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.92 – 7.88 (m, 1H), 7.71 – 7.68 (m, 2H), 7.68 – 7.65 (m, 1H), 7.61 – 7.54 (m, 2H), 7.52 – 7.48 (m, 1H), 7.37 – 7.33 (m, 2H), 3.89 (s, 3H), 2.17 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.7, 169.7, 165.9, 139.5, 134.8, 133.7, 133.4, 131.2, 128.94, 128.87, 128.7, 126.1, 124.5, 94.0, 65.5, 21.4.

HRMS (ESI) calculated for $C_{18}H_{15}NNaO_5^+$ [M+Na$^+$]: 348.0842; found:348.0841.

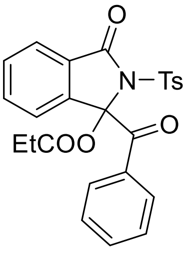


15: 3-benzoyl-3-methoxy-2-tosylisoindolin-1-one

Followed **Method F** (with MeCN : MeOH = 5 mL: 5 mL, Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 21.9 mg (26% yield) of **15** as a white solid.

IR (neat, cm^{-1}): 3062 (w), 1687 (s), 1597 (w), 1443 (w), 1359 (s), 1294 (s), 1170 (s), 1088 (m), 763 (m), 730 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.83 – 7.80 (m, 2H), 7.54 – 7.52 (m, 1H), 7.46 – 7.29 (m, 8H), 7.17 – 7.15 (m, 2H), 3.35 (s, 3H), 2.35 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 169.8, 144.9, 138.0, 135.6, 132.4, 131.9, 130.1, 129.6, 128.9, 128.5, 128.44, 128.40, 127.3, 122.6, 120.6, 93.8, 86.0, 34.3, 21.7.

HRMS (ESI) calculated for $C_{23}H_{19}NNaO_5S^+$ [M+Na$^+$]: 444.0876; found:444.0873.

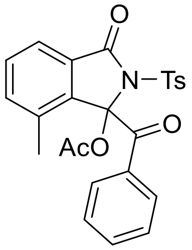


16: 1-benzoyl-3-oxo-2-tosylisoindolin-1-yl propionate

Followed **Method F** (with MeCN : propionic acid = 8 mL: 2 mL, Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 59.3 mg (64% yield) of **16** as a white solid.

IR (neat, cm^{-1}): 3064 (w), 1750 (s), 1702 (m), 1596 (m), 1466 (w), 1368 (m), 1245 (s), 1169 (s), 1141 (s), 815 (w), 756 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.88 – 7.85 (m, 1H), 7.80 (d, *J* = 7.8 Hz, 2H), 7.60 – 7.52 (m, 3H), 7.41 (t, *J* = 7.7 Hz, 3H), 7.27 (d, *J* = 8.3 Hz, 2H), 2.46 – 2.41 (m, 2H), 2.40 (s, 3H), 0.99 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.6, 171.4, 165.4, 145.7, 141.1, 135.2, 134.78, 134.83, 133.2, 131.3, 130.2, 129.6, 129.4, 129.0, 128.6, 125.4, 122.7, 94.7, 28.2, 21.8, 8.4.

HRMS (ESI) calculated for $C_{25}H_{21}NNaO_6S^+$ [M+Na$^+$]: 486.0981; found:486.0992.

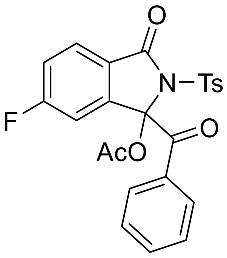


17: 1-benzoyl-7-methyl-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 38.9 mg (42% yield) of **17** as a white solid.

IR (neat, cm^{-1}): 3061 (w), 1751 (s), 1708 (m), 1596 (w), 1446 (w), 1367 (m), 1248 (m), 1174 (s), 1150 (s), 814 (w), 758 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 6.9 Hz, 2H), 7.53 – 7.49 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 2.38 (s, 3H), 2.20 (s, 3H), 2.06 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.0, 167.7, 165.7, 145.7, 138.4, 137.2, 135.4, 135.1, 134.0, 133.1, 131.4, 130.8, 129.5, 129.4, 128.7, 128.6, 123.0, 94.0, 21.8, 21.6, 17.5.

HRMS (ESI) calculated for $C_{25}H_{21}NNaO_6S^+$ [M+Na$^+$]: 486.0981; found:486.0992.

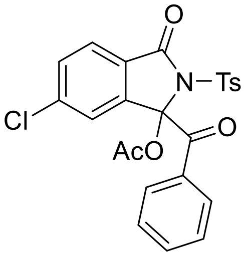


18: 1-benzoyl-6-fluoro-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 59.8 mg (64% yield) of **18** as a white solid.

IR (neat, cm^{-1}): 3071 (w), 1754 (s), 1702 (m), 1608 (m), 1446 (w), 1368 (m), 1270 (s), 1204 (s), 1174 (s), 1126 (s), 816 (m), 763 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.92 – 7.89 (m, 2H), 7.87 (dd, *J* = 8.4, 4.7 Hz, 1H), 7.83 (d, *J* = 7.1 Hz, 2H), 7.62 – 7.57 (m, 1H), 7.46 – 7.42 (m, 2H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.23 (td, *J* = 8.6, 2.2 Hz, 1H), 7.10 (dd, *J* = 7.5, 2.2 Hz, 1H), 2.41 (s, 3H), 2.12 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.9, 167.8, 166.5 (d, *J* = 257.9 Hz), 164.2, 145.9, 143.6 (d, *J* = 9.8 Hz), 135.1, 134.5, 133.5, 129.7, 129.5, 129.1, 128.8, 127.8 (d, *J* = 10.0 Hz), 126.2 (d, *J* = 2.4 Hz), 119.1 (d, *J* = 23.5 Hz), 110.8 (d, *J* = 25.5 Hz), 94.0, 21.8, 21.8; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -100.1 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found:490.0741.



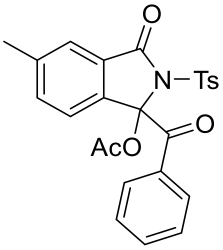
19: 1-benzoyl-6-chloro-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 68.7 mg (71% yield) of **19** as a white solid.

IR (neat, cm^{-1}): 3070 (w), 1753 (s), 1701 (m), 1596 (m), 1447 (w), 1368 (m), 1243 (s), 1171 (s), 1140 (s), 949 (w), 909 (m), 815 (w), 772 (w), 729 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.91 – 7.87 (m, 2H), 7.84 – 7.81 (m, 2H), 7.80 (d, *J* = 8.3 Hz, 1H), 7.63 – 7.58 (m, 1H), 7.53 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.38 (d, *J* =

1.7 Hz, 1H), 7.32 – 7.27 (m, 2H), 2.42 (s, 3H), 2.12 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.1, 167.8, 164.4, 146.0, 142.7, 141.3, 135.0, 134.6, 133.6, 131.9, 129.8, 129.5, 129.2, 128.8, 128.7, 126.6, 123.2, 94.0, 21.9, 21.9.

HRMS (ESI) calculated for $C_{24}H_{18}ClNNaO_6S^+$ [M+Na$^+$]: 506.0435; found:506.0436.

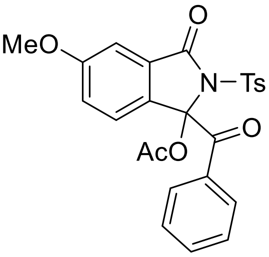


20: 1-benzoyl-5-methyl-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 64.0 mg (69% yield) of **20** as a white solid.

IR (neat, cm^{-1}): 3063 (w), 1752 (s), 1701 (m), 1596 (w), 1446 (w), 1366 (m), 1253 (s), 1164 (s), 1118 (m), 815 (m), 733 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.75 (d, *J* = 7.4 Hz, 2H), 7.67 (s, 1H), 7.58 – 7.51 (m, 1H), 7.39 (t, *J* = 7.7 Hz, 3H), 7.31 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 2H), 2.41 (s, 3H), 2.40 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.3, 167.9, 165.5, 145.7, 142.1, 138.1, 135.7, 135.3, 134.8, 133.2, 130.3, 129.6, 129.4, 129.0, 128.6, 125.7, 122.8, 94.6, 21.9, 21.8, 21.6.

HRMS (ESI) calculated for $C_{25}H_{21}NNaO_6S^+$ [M+Na$^+$]: 486.0981; found:486.0982.

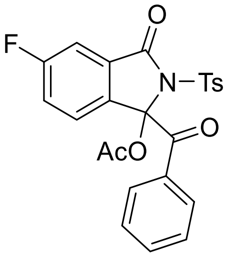


21: 1-benzoyl-5-methoxy-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (Q = 3.36 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 68.1 mg (71% yield) of **21** as a white solid.

IR (neat, cm^{-1}): 3070 (w), 1750 (s), 1702 (m), 1596 (m), 1447 (w), 1367 (m), 1257 (s), 1169 (s), 1126 (m), 816 (w), 763 (w); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 6.6 Hz, 2H), 7.56 – 7.51 (m, 1H), 7.41 – 7.36 (m, 2H), 7.35 – 7.32 (m, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 7.09 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.82 (s, 3H), 2.40 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.0, 168.0, 165.3, 162.2, 145.7, 135.2, 134.7, 133.2, 132.6, 131.9, 129.5, 129.4, 129.0, 128.7, 124.4, 122.1, 108.7, 94.6, 55.9, 21.9, 21.8.

HRMS (ESI) calculated for $C_{25}H_{21}NNaO_7S^+$ [M+Na$^+$]: 502.0931; found:502.0942.

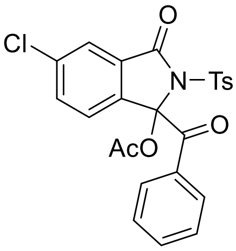


22: 1-benzoyl-5-fluoro-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 63.6 mg (68% yield) of **22** as a white solid.

IR (neat, cm^{-1}): 3071 (w), 1749 (s), 1702 (m), 1596 (m), 1444 (m), 1367 (m), 1252 (s), 1192 (s), 1167 (s), 1117 (m), 815 (m), 764 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.90 – 7.85 (m, 2H), 7.78 (d, *J* = 6.9 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.51 (dd, *J* = 7.0, 2.4 Hz, 1H), 7.44 – 7.36 (m, 3H), 7.29 – 7.26 (m, 2H), 7.25 – 7.22 (m, 1H), 2.40 (s, 3H), 2.09 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.0, 167.9, 164.3 (d, *J* = 253.9 Hz), 164.2 (d, *J* = 3.5 Hz), 146.0, 136.6 (d, *J* = 2.7 Hz), 135.0, 134.6, 133.5, 132.7 (d, *J* = 8.8 Hz), 129.7, 129.5, 129.2, 128.8, 125.0 (d, *J* = 8.6 Hz), 122.2 (d, *J* = 23.7 Hz), 112.5 (d, *J* = 24.4 Hz), 94.4, 21.9, 21.8; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -106.6 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found: 490.0731.

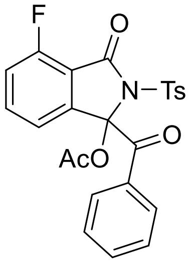


23: 1-benzoyl-5-chloro-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (current = 8 mA, reaction time = 2 h**,** Q = 2.98 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 39.7 mg (41% yield) of **23** as a white solid.

IR (neat, cm^{-1}): 3067 (w), 1751 (s), 1700 (w), 1596 (w), 1446 (w), 1367 (m), 1244 (s), 1169 (s), 1139 (m), 815 (m), 772 (w), 735 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.90 – 7.87 (m, 2H), 7.83 (d, *J* = 1.6 Hz, 1H), 7.80 (s, 1H), 7.79 – 7.78 (m, 1H), 7.63 – 7.55 (m, 1H), 7.53 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.11 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 189.9, 167.9, 164.1, 146.0, 139.2, 137.9, 135.0, 134.8, 134.6, 133.5, 132.0, 129.7, 129.5, 129.2, 128.8, 125.6, 124.2, 94.4, 21.9, 21.9.

HRMS (ESI) calculated for $C_{24}H_{18}ClNNaO_6S^+$ [M+Na$^+$]: 506.0435; found:506.0435.

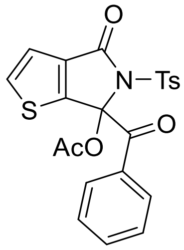


24: 1-benzoyl-4-fluoro-3-oxo-2-tosylisoindolin-1-yl acetate

Followed **Method F** (reaction time = 5 h, Q = 5.60 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 77.6 mg (83% yield) of **24** as a white solid.

IR (neat, cm^{-1}): 3066 (w), 1750 (s), 1698 (w), 1596 (m), 1482 (m), 1367 (s), 1236 (s), 1203 (s), 1175 (s), 1133 (m), 813 (m), 765 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 6.9 Hz, 2H), 7.65 – 7.57 (m, 1H), 7.57 – 7.53 (m, 1H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 2H), 7.22 – 7.14 (m, 2H), 2.41 (s, 3H), 2.12 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 190.3, 167.8, 162.0, 159.3 (d, *J* = 266.6 Hz), 146.0, 143.2, 137.0 (d, *J* = 8.0 Hz), 134.8, 134.7, 133.5, 129.8, 129.5, 129.3, 128.8, 119.1 (d, *J* = 19.1 Hz), 118.6 (d, *J* = 4.0 Hz), 117.4 (d, *J* = 13.3 Hz), 94.0, 21.9, 21.9; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -112.7 (m).

HRMS (ESI) calculated for $C_{24}H_{18}FNNaO_6S^+$ [M+Na$^+$]: 490.0731; found:490.0733.

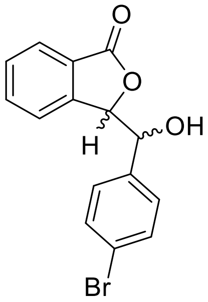


25: 6-benzoyl-4-oxo-5-tosyl-5,6-dihydro-4H-thieno[2,3-c]pyrrol-6-yl acetate

Followed **Method F** (current = 3 mA, Q = 1.68 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 28.2 mg (31% yield) of **25** as a white solid.

IR (neat, cm^{-1}): 3103 (w), 3068 (w), 1744 (s), 1704 (m), 1596 (w), 1431 (w), 1366 (m), 1283 (m), 1172 (s), 1134 (s), 814 (w), 756 (m); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.95 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 4.9 Hz, 1H), 7.67 (d, *J* = 6.7 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 4.9 Hz, 1H), 2.42 (s, 3H), 2.18 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 186.8, 168.0, 159.9, 152.0, 145.7, 138.7, 135.7, 134.5, 133.8, 133.6, 129.4, 129.2, 129.1, 128.9, 125.1, 93.5, 21.8, 21.5.

HRMS (ESI) calculated for $C_{22}H_{17}NNaO_6S_2^+$ [M+Na$^+$]: 478.0389; found: 478.0389.



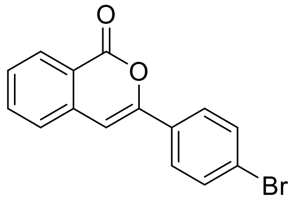
27: 3-((4-bromophenyl)(hydroxy)methyl)isobenzofuran-1(3*H*)-one

Followed **Method H**, the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1) to give 19.1 mg (60% yield, dr = 1:1) of **27** as a white solid.

IR (neat, cm^{-1}): 3404 (m), 3082 (w), 1749 (s), 1288 (m), 1070 (s), 726 (s), 692 (m).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.87 – 7.80 (m, 1H, diastereoisomer), 7.60 – 7.41 (m, 4H, diastereoisomer), 7.27 (d, *J* = 8.0 Hz, 2H, diastereoisomer 1), 7.21 (d, *J* = 8.4 Hz, 2H, diastereoisomer 2), 6.96 (d, *J* = 7.5 Hz, 1H, diastereoisomer 1), 6.88 (d, *J* = 7.5 Hz, 1H, diastereoisomer 2), 5.62 (d, *J* = 4.5 Hz, 1H, diastereoisomer 1), 5.59 (d, *J* = 6.5 Hz, 1H, diastereoisomer 2), 5.20 (t, *J* = 3.8 Hz, 1H, diastereoisomer 1), 4.85 (d, *J* = 6.5 Hz, 1H, diastereoisomer 2), 3.01 (s, 1H, diastereoisomer 1), 2.87 (d, *J* = 4.1 Hz, 1H, diastereoisomer 2); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 170.5, 170.0, 145.9, 145.7, 137.3, 136.6, 134.0, 133.8, 131.8, 129.8, 129.7, 129.4, 128.3, 127.0, 125.9, 125.8, 123.6, 123.5, 123.1, 122.5, 83.7, 83.5, 75.6, 73.4.

HRMS (ESI) calculated for $C_{15}H_{11}BrNaO_3^+$ [M+Na$^+$]: 340.9784; found:340.9791.



28: 3-((4-bromophenyl)(hydroxy)methyl)isobenzofuran-1(3*H*)-one

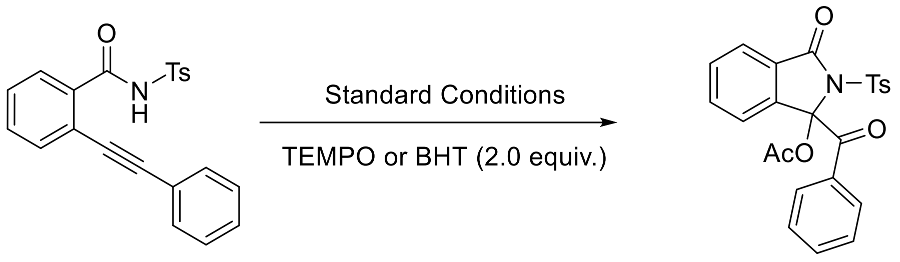
Followed **Method I** (Q = 7.46 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1) to give 17.5 mg (29% yield) of **28** as a white solid.

IR (neat, cm^{-1}): 3099 (w), 1725 (s), 1640 (w), 1239 (w), 1071 (m), 823 (m), 750 (w).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.30 – 8.17 (m, 1H), 7.72 – 7.66 (m, 3H), 7.57 – 7.53 (m, 2H), 7.50 – 7.44 (m, 2H), 6.90 (s, 1H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 161.9, 152.4, 137.1, 135.0, 132.0, 130.7, 129.6, 128.4, 126.6, 126.1, 124.3, 120.4, 102.1.

HRMS (ESI) calculated for $C_{15}H_9BrNaO_2^+$ [M+Na$^+$]: 322.9678; found:322.9674.

4. Radical Trapping Experiments

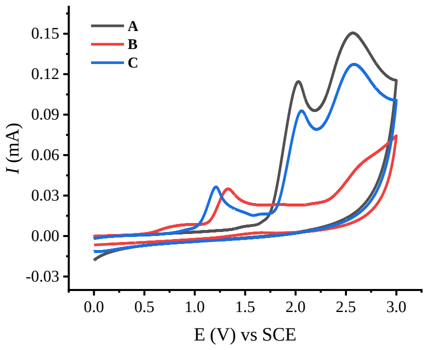


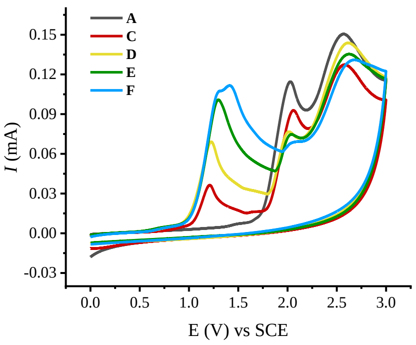
N.D.

In an oven-dried undivided three-necked glassware (25 mL) equipped with a stirring bar, 2-(phenylethynyl)-N-tosylbenzamides (0.2 mmol, 1.0 equiv.), ^{n}Bu$_4$NOAc (0.2 mmol, 1.0 equiv.) and either TEMPO or BHT (0.4 mmol, 2.0 equiv.) were added. The glassware was equipped with carbon cloth (15 mm × 15 mm × 0.1 mm) as the anode and platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode (Note: the electrodes need to be thoroughly dried before use). Under the protection of N_2, MeCN and CH_3CO_2H = 8:2 (10 mL) were injected into the glassware *via* syringes. The reaction mixture was stirred and electrolyzed at a constant current of 6 mA at an ambient temperature for 3.0 h. The reaction mixture was concentrated *in vacuo*. After flash column chromatography, no product was detected, and 80% and 76% of the starting material were recovered, respectively.

5. Cyclic Voltammetry Studies

General information: Cyclic voltammetry (CV) experiments were conducted in a 10 mL glass vial fitted with a glassy carbon working electrode (3 mm in diameter), a platinum wire auxiliary electrode, and an SCE reference electrode. The current was reported in A, while all potentials were reported in V. The scan rate was 0.1 V/s.

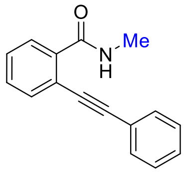




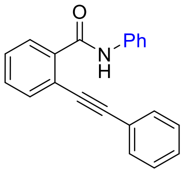
Cyclic voltammograms with ^{n}Bu$_4$NPF$_6$ (10 mM) as the electrolyte. **left:** (A) **1** (2 mM); (B) ^{n}Bu$_4$NOAc (2 mM); (C) **1** (2 mM) + ^{n}Bu$_4$NOAc (2 mM); **right**: (D) **1** (2 mM) + ^{n}Bu$_4$NOAc (4 mM); (E) **1** (2 mM) + ^{n}Bu$_4$NOAc (6 mM); (F) **1** (2 mM) + ^{n}Bu$_4$NOAc (8 mM).

6. Unsuccessful Substrates

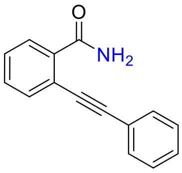
Unfortunately, the current protocol is not transferable to alkynylbenzamides bearing N-methyl, N-aryl, 2-(phenylethynyl)benzamide or an aliphatic alkyne moiety



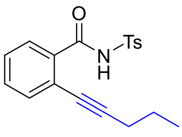
U1



U2

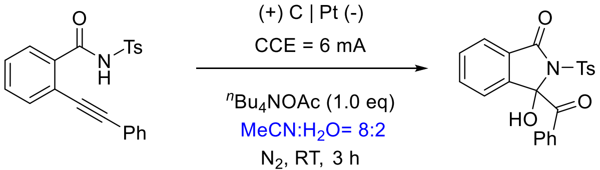


U3



U4

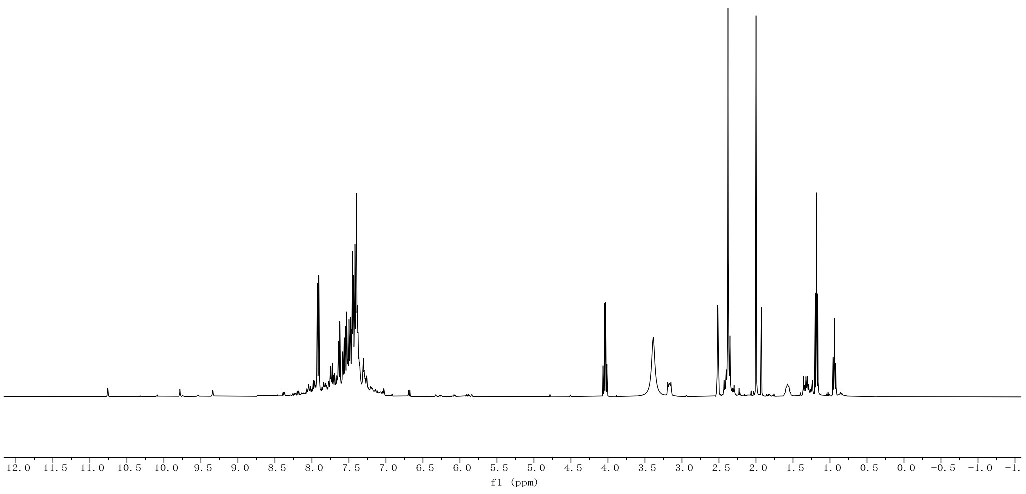
7. Attempt of Using Water as the Nucleophile



1

N.D.

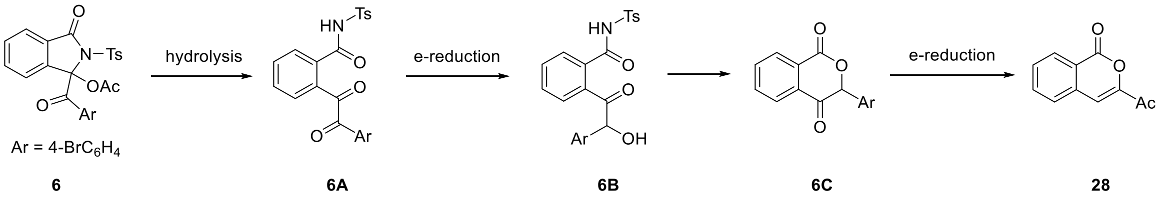
In an oven-dried undivided three-necked glassware (25 mL) equipped with a stirring bar, 2-(phenylethynyl)-N-tosylbenzamides (0.2 mmol, 1.0 equiv.) and ^{n}Bu$_4$NOAc (0.2 mmol, 1.0 equiv.) were added. The glassware was equipped with carbon cloth (15 mm × 15 mm × 0.1 mm) as the anode and platinum plate (15 mm × 15 mm × 0.1 mm) as the cathode. Under the protection of N_2, MeCN and H_2O = 8:2 (10 mL) were injected into the glassware *via* syringes. The reaction mixture was stirred and electrolyzed at a constant current of 6 mA at an ambient temperature for 3.0 h. The reaction was diluted with EtOAc and then the organic layer was washed with H_2O and brine, dried over Na_2SO_4. Following concentration in vacuo, the NMR spectroscopy (DMSO-d_6) of the crude residue showed no desired product but only the recovery of starting material.



^{1}H NMR of the crude reaction mixture (DMSO-d_6)

8. Proposed Mechanism for the Transformation from 6 to 28

Electrochemical reduction of the obtained isoindolinone (**6**) should be mechanistically distinct from the chemical reduction of $NaBH_4$. We reason a hydrolysis might take place before the selective electrochemical reduction of one of the three carbonyls of **6A** to form the corresponding hydroxyl counterpart (**6B**), which further undergoes cyclization to generate the precursor (**6C**) for the final electrochemical reduction to gove the observed isochromenone (**28**). While the electrochemical reduction of carbonyl groups is known,[7-8] the detailed mechanism of this transformation, however, needs further extensive investigations.



9. References

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5. Sultane, P.R., Ahumada, G., Janssen-Muller, D., and Bielawski, C.W. *Angew. Chem. Int. Ed*., 2019 ***58**,* 16320-16325.
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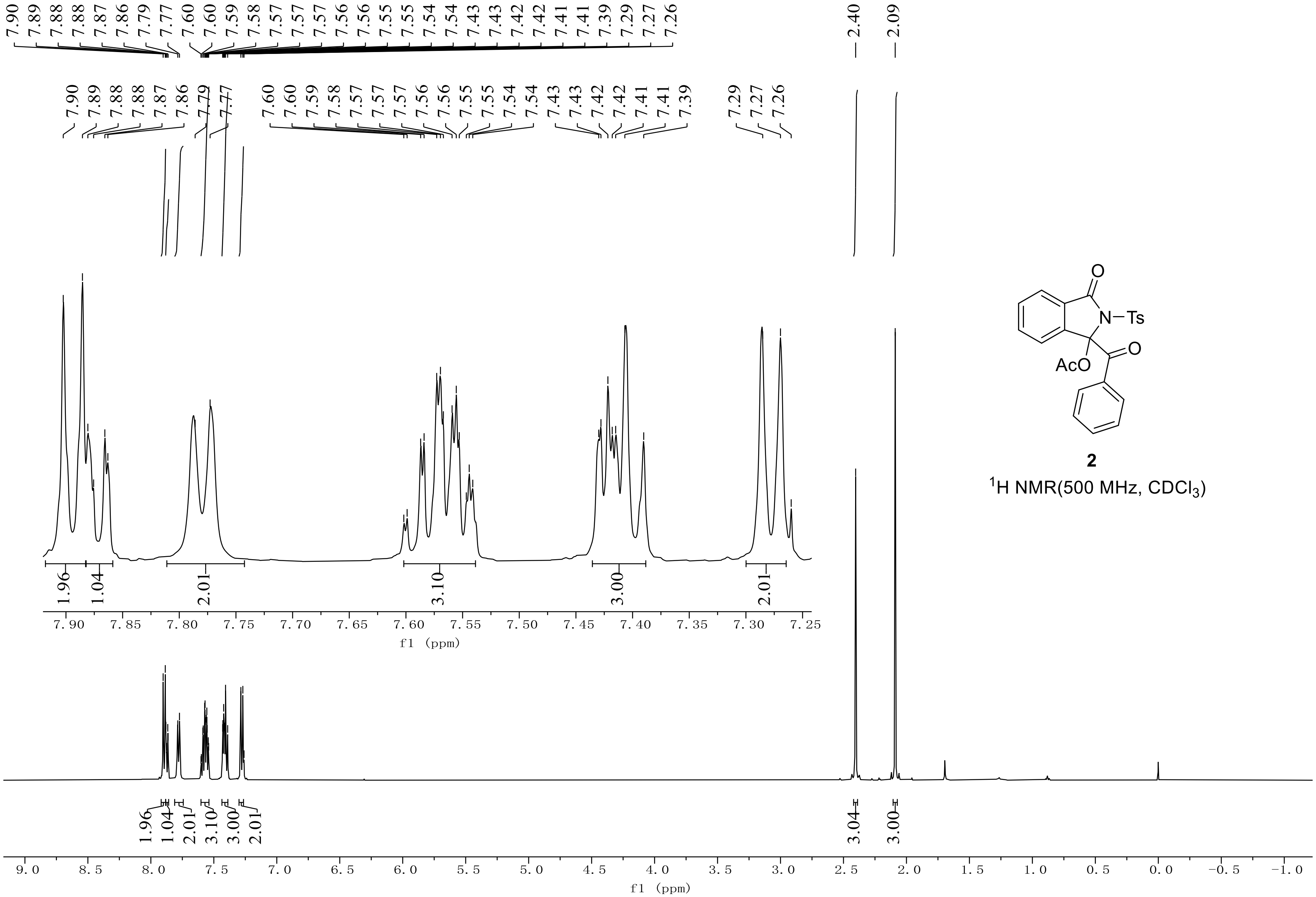
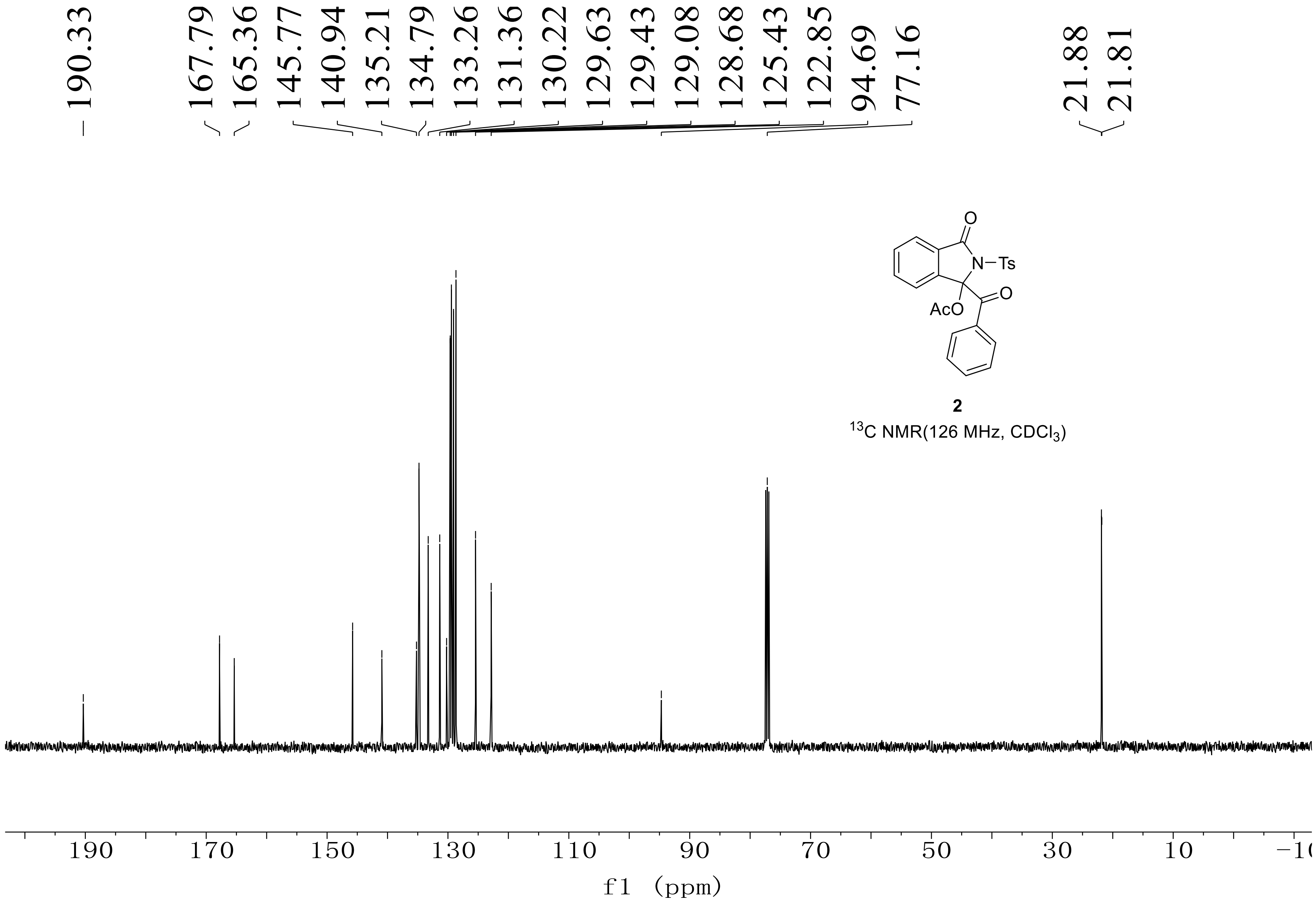
8. Y. Bai, L. Shi, L. Zheng, S. Ning, X. Che, Z. Zhang and J. Xiang, *Org. Lett*., 2021, **23**, 2298-2302.

10. Spectral Data (^{1}H, ^{13}C, ^{19}F)



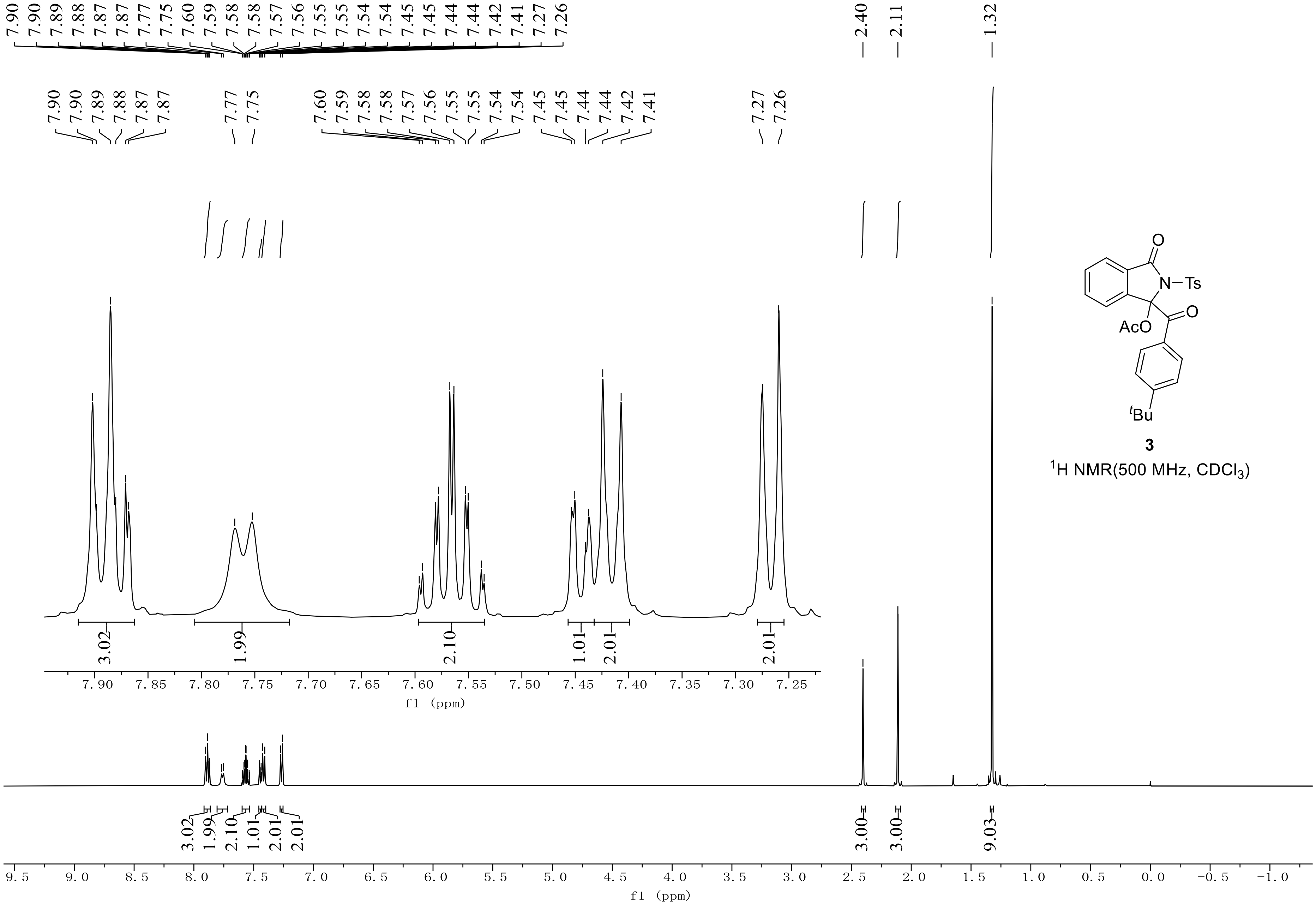
2

^{1}H NMR(500 MHz, CDCl$_3$)



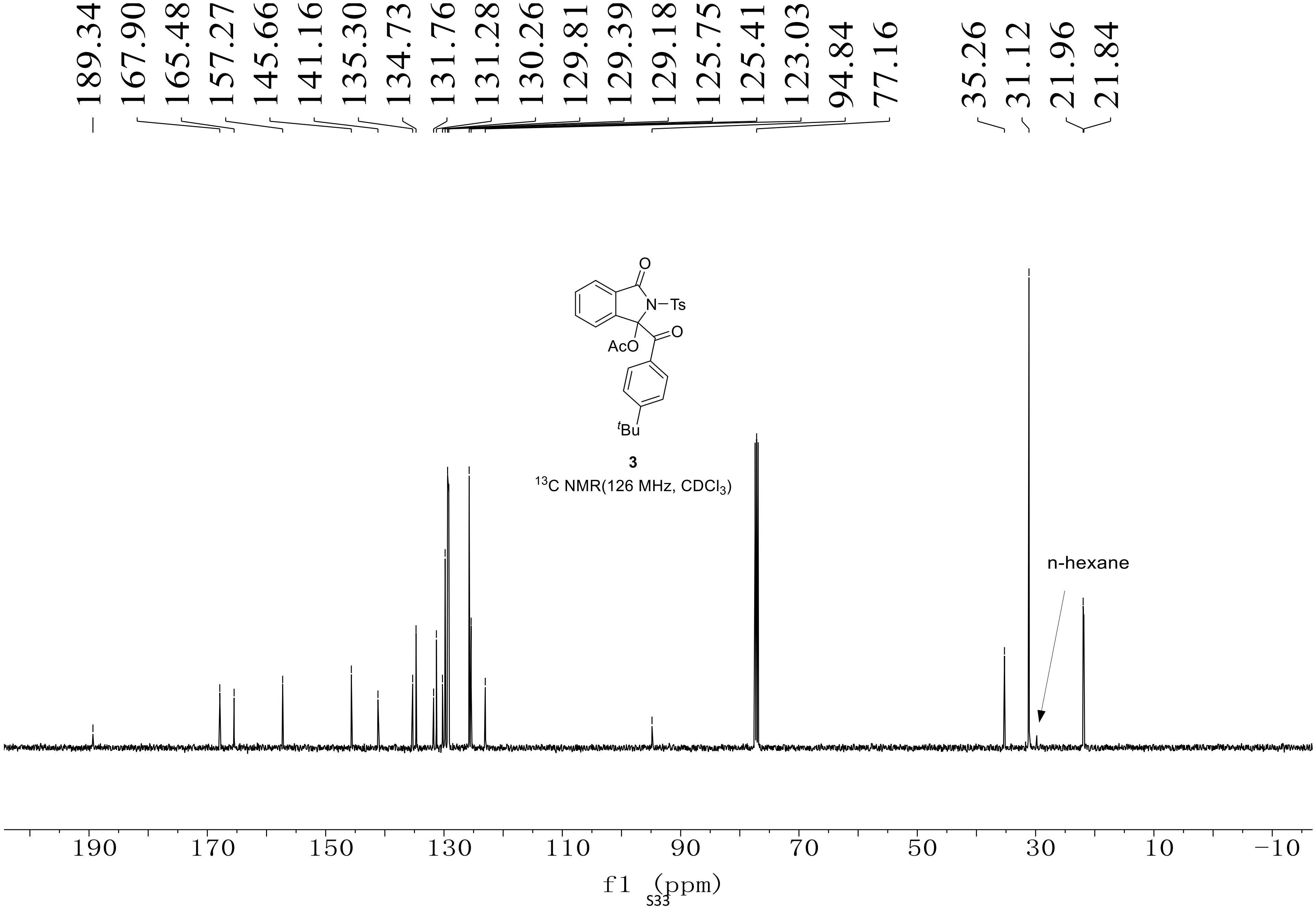
2

^{13}C NMR(126 MHz, $CDCl_3$)



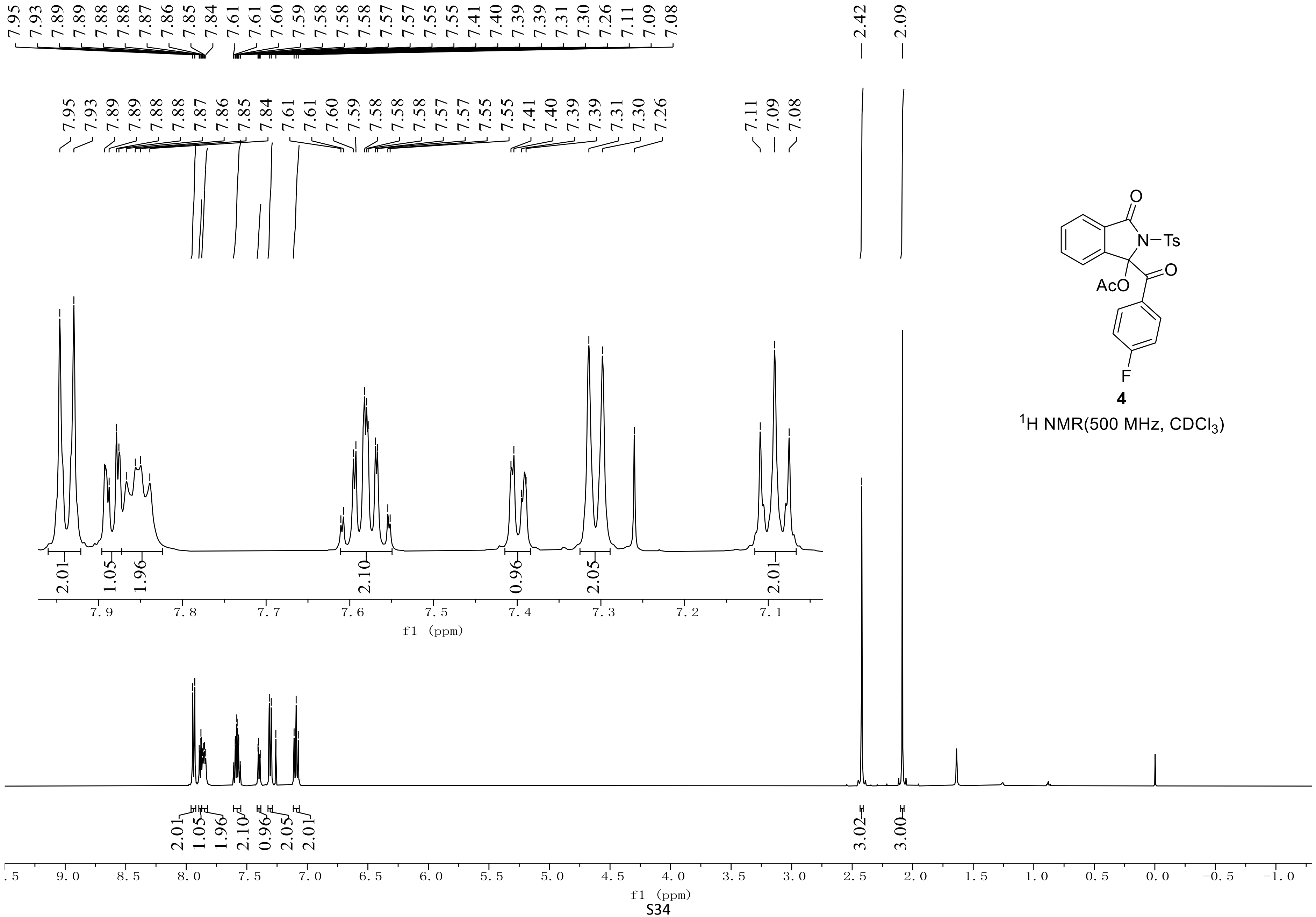
3

^{1}H NMR(500 MHz, $CDCl_3$)



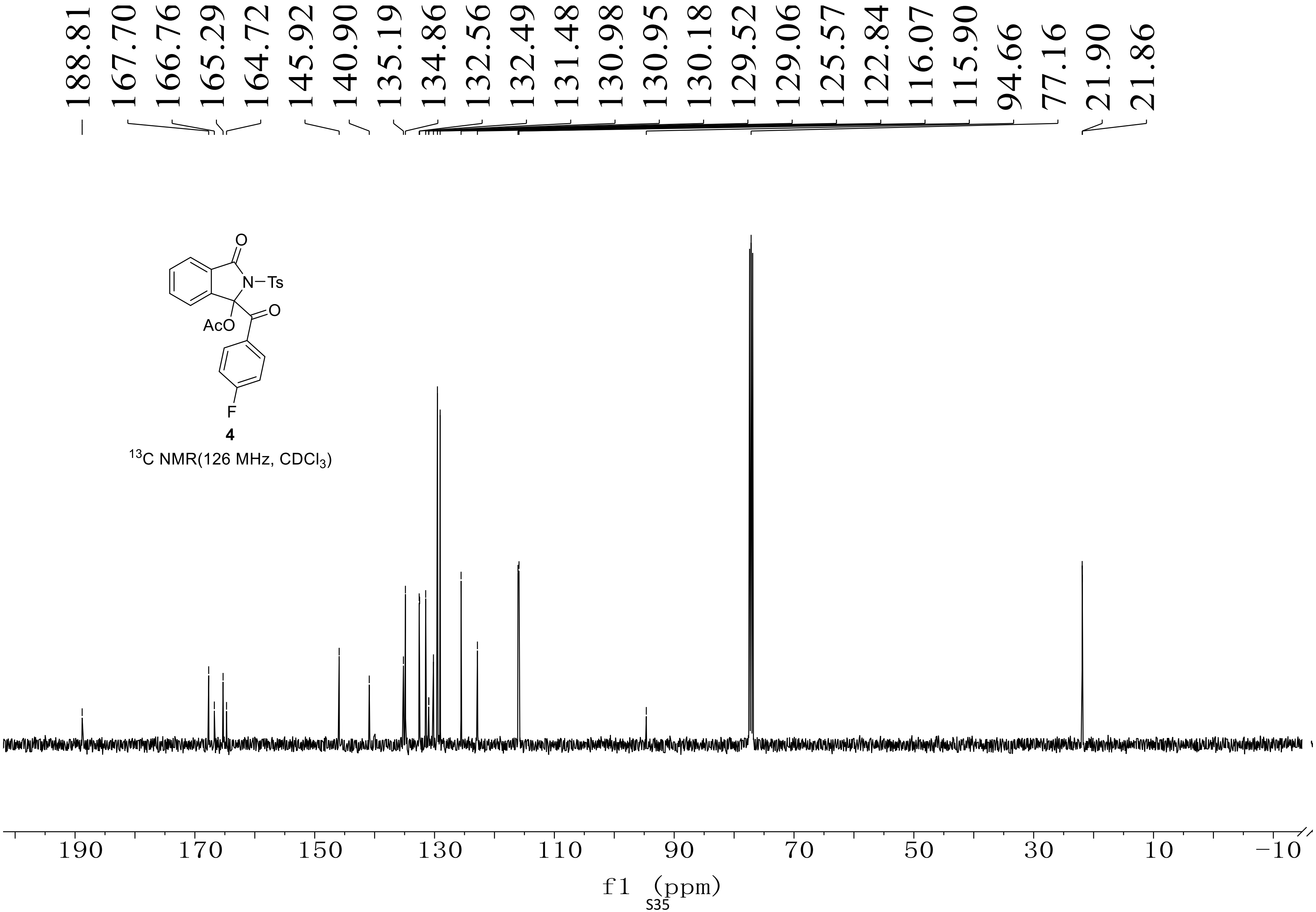
3

^{13}C NMR(126 MHz, CDCl$_3$)



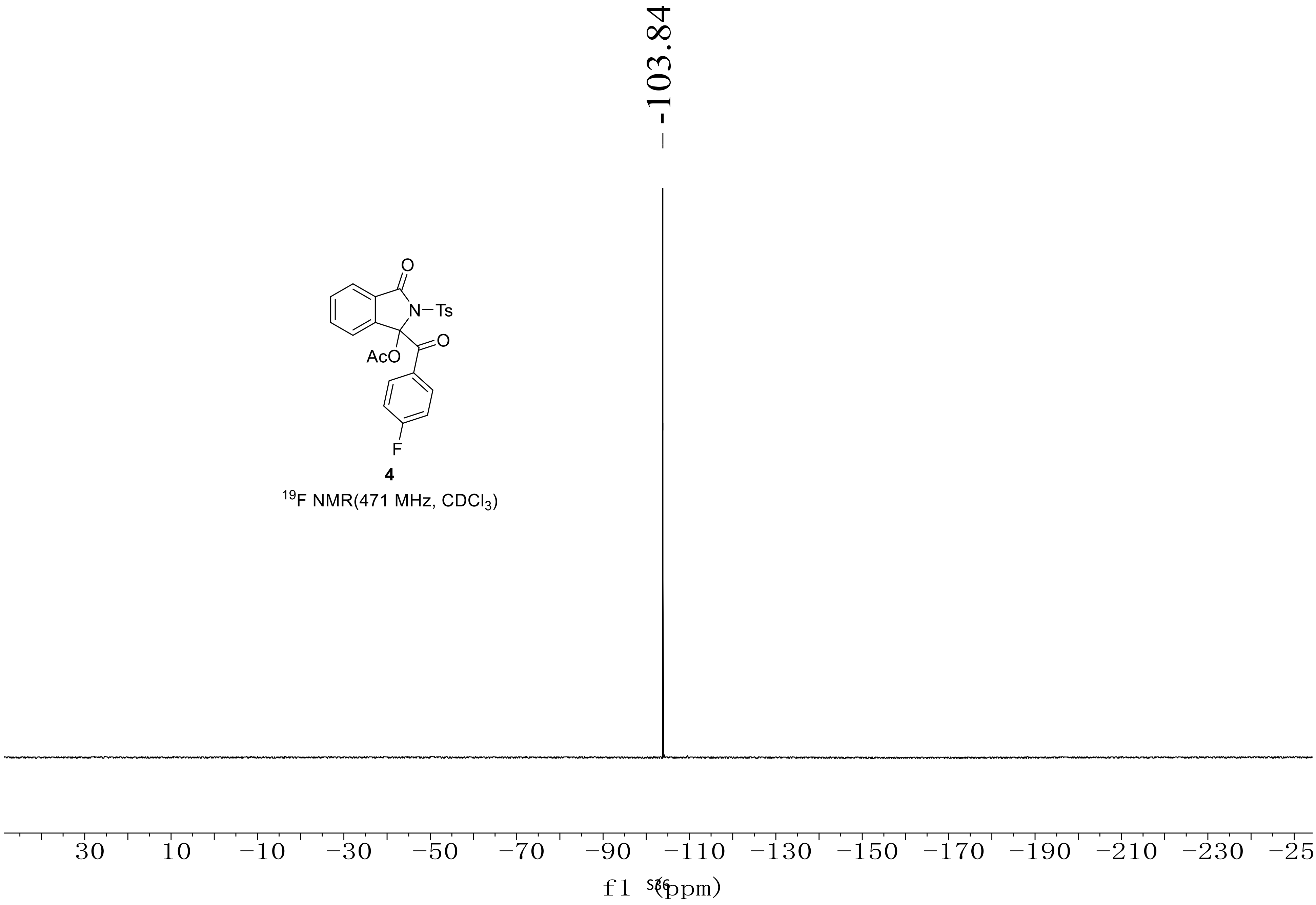
4

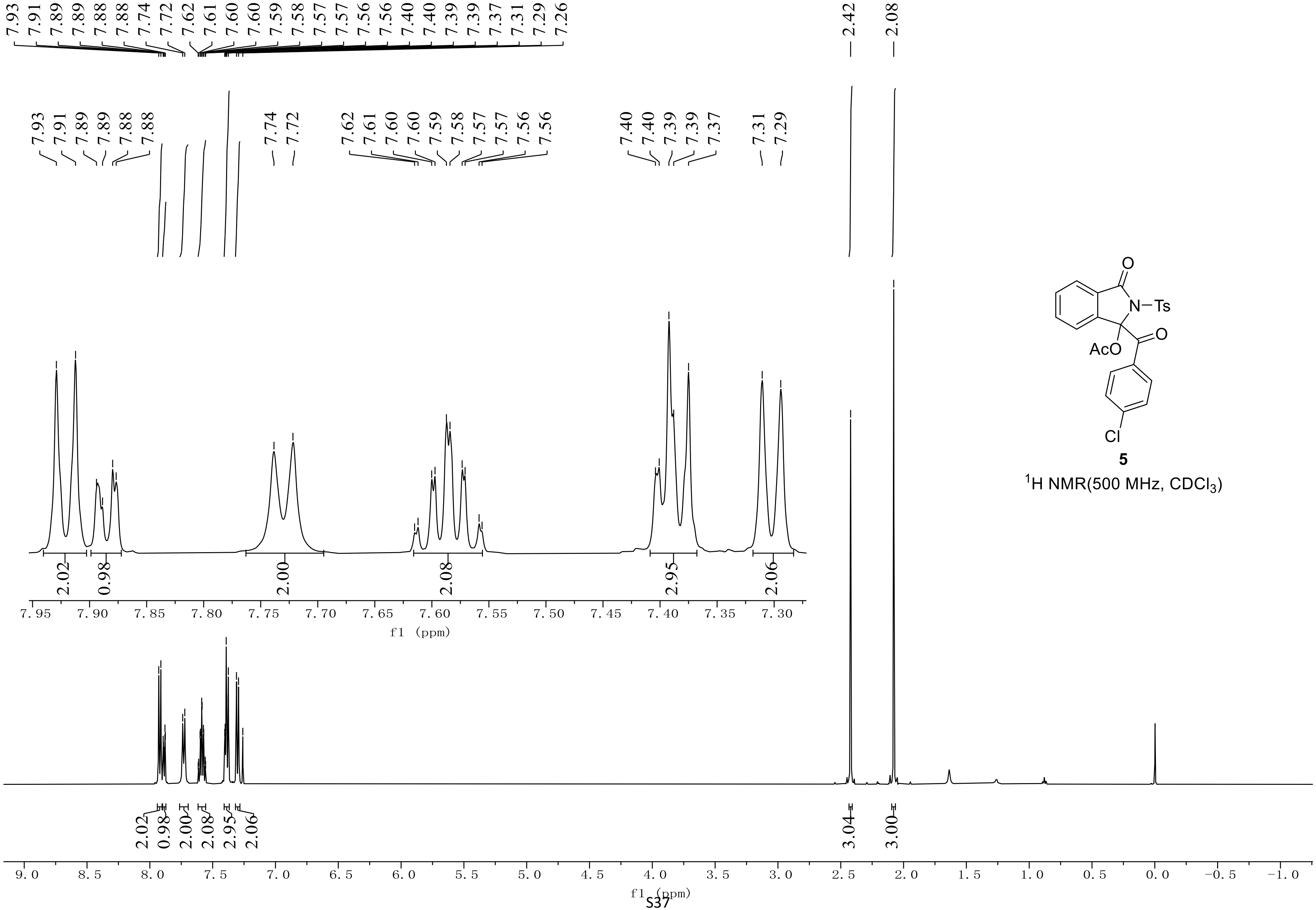
^1H NMR(500 MHz, $CDCl_3$)



4

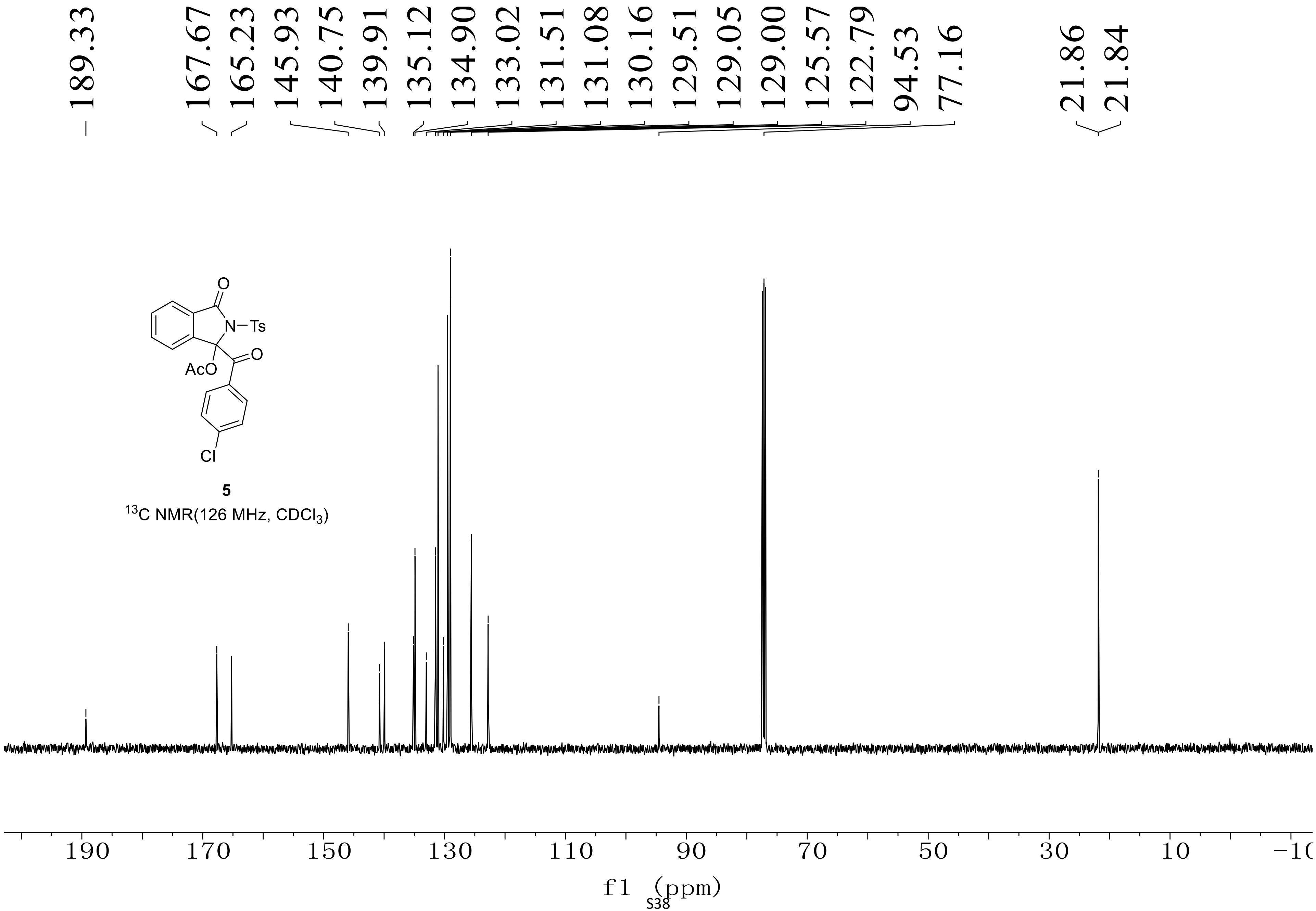
^{13}C NMR(126 MHz, CDCl$_3$)


-103.84
O
N−Ts
O
AcO
F
4
^{19}F NMR(471 MHz, CDCl$_3$)
30
10
−10
−30
−50
−70
−90
−110
−130
−150
−170
−190
−210
−230
−25
f1 (ppm)



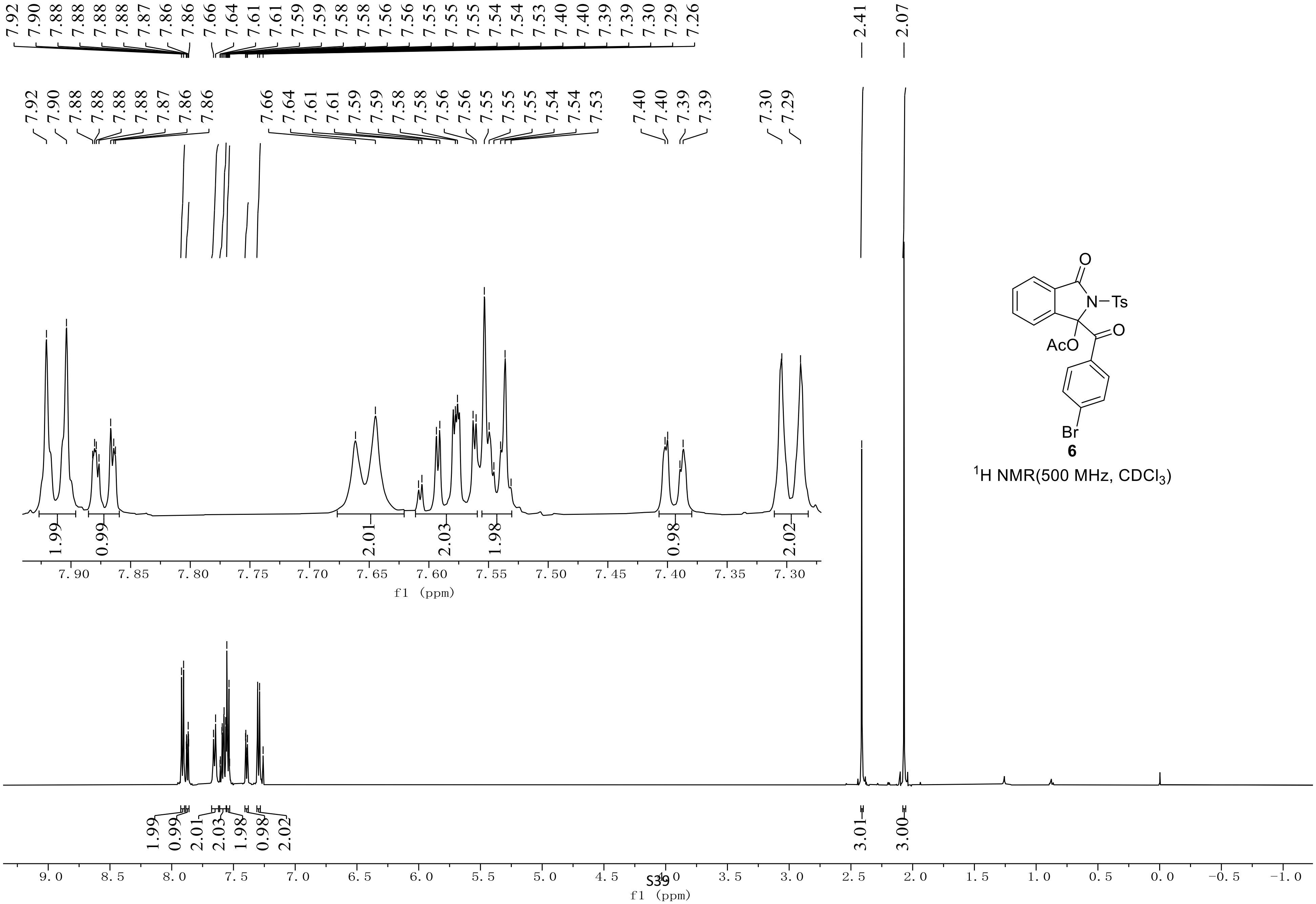
5

^{1}H NMR(500 MHz, CDCl$_3$)



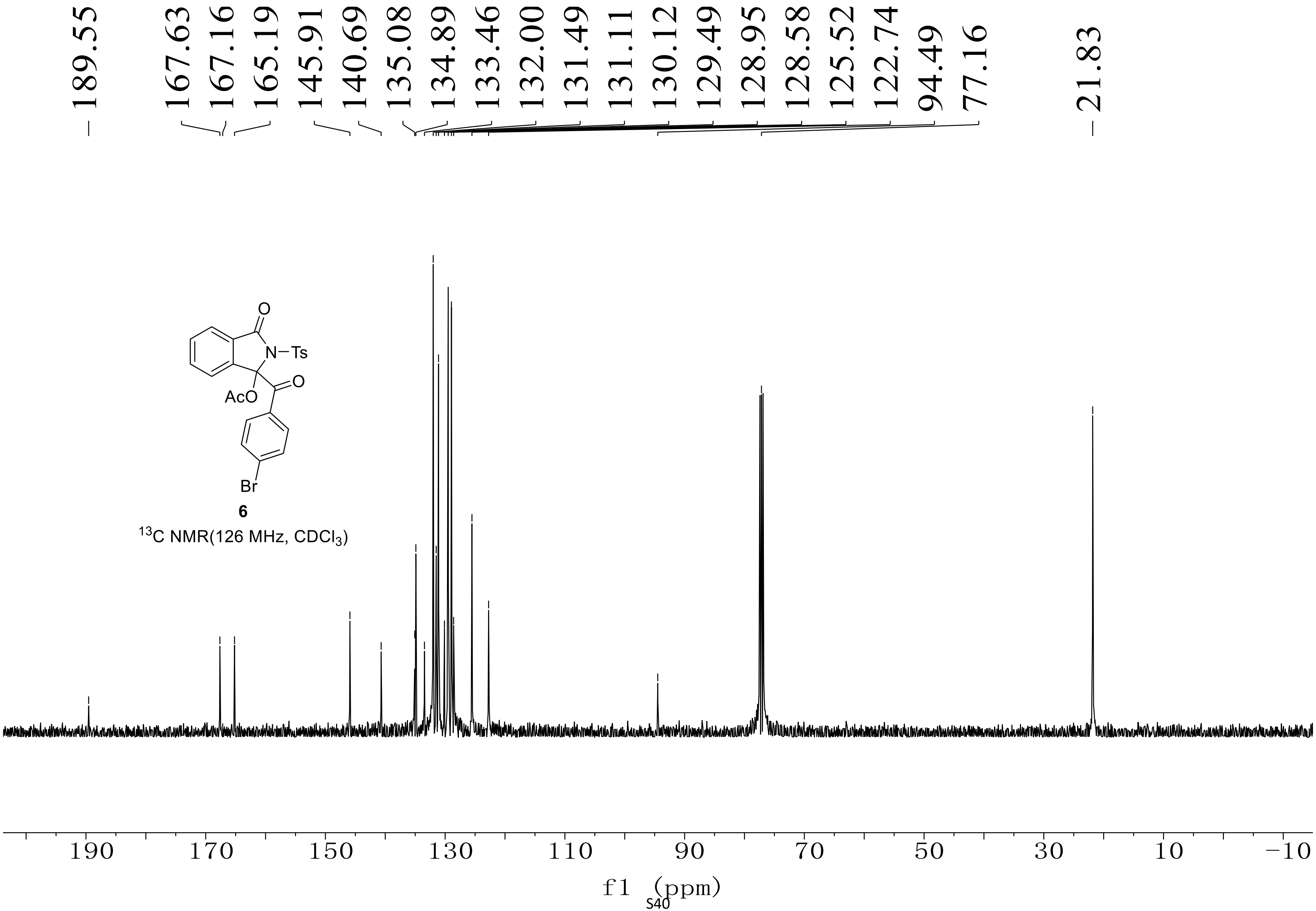
5

^{13}C NMR(126 MHz, $CDCl_3$)



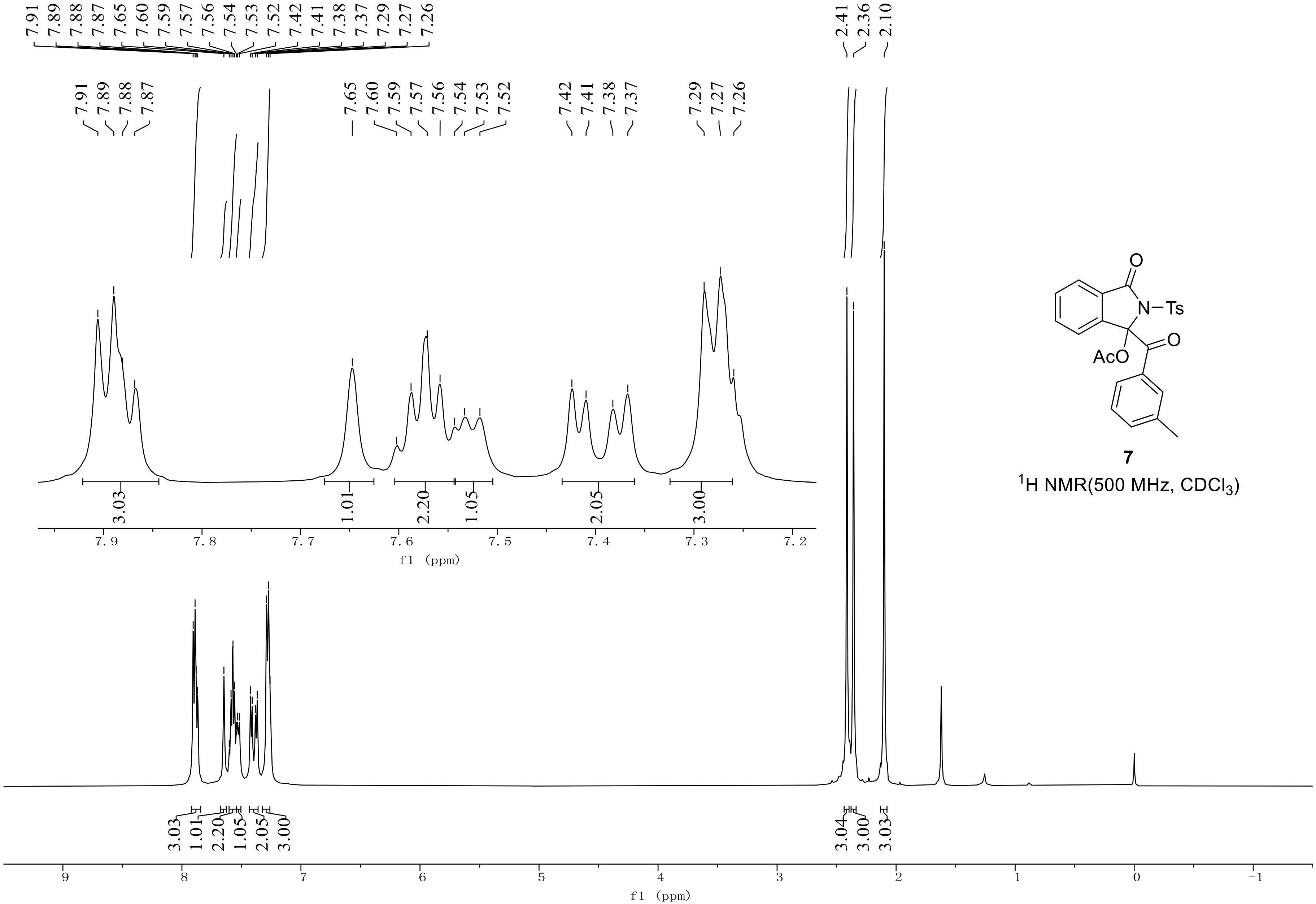
6

^{1}H NMR(500 MHz, CDCl$_3$)



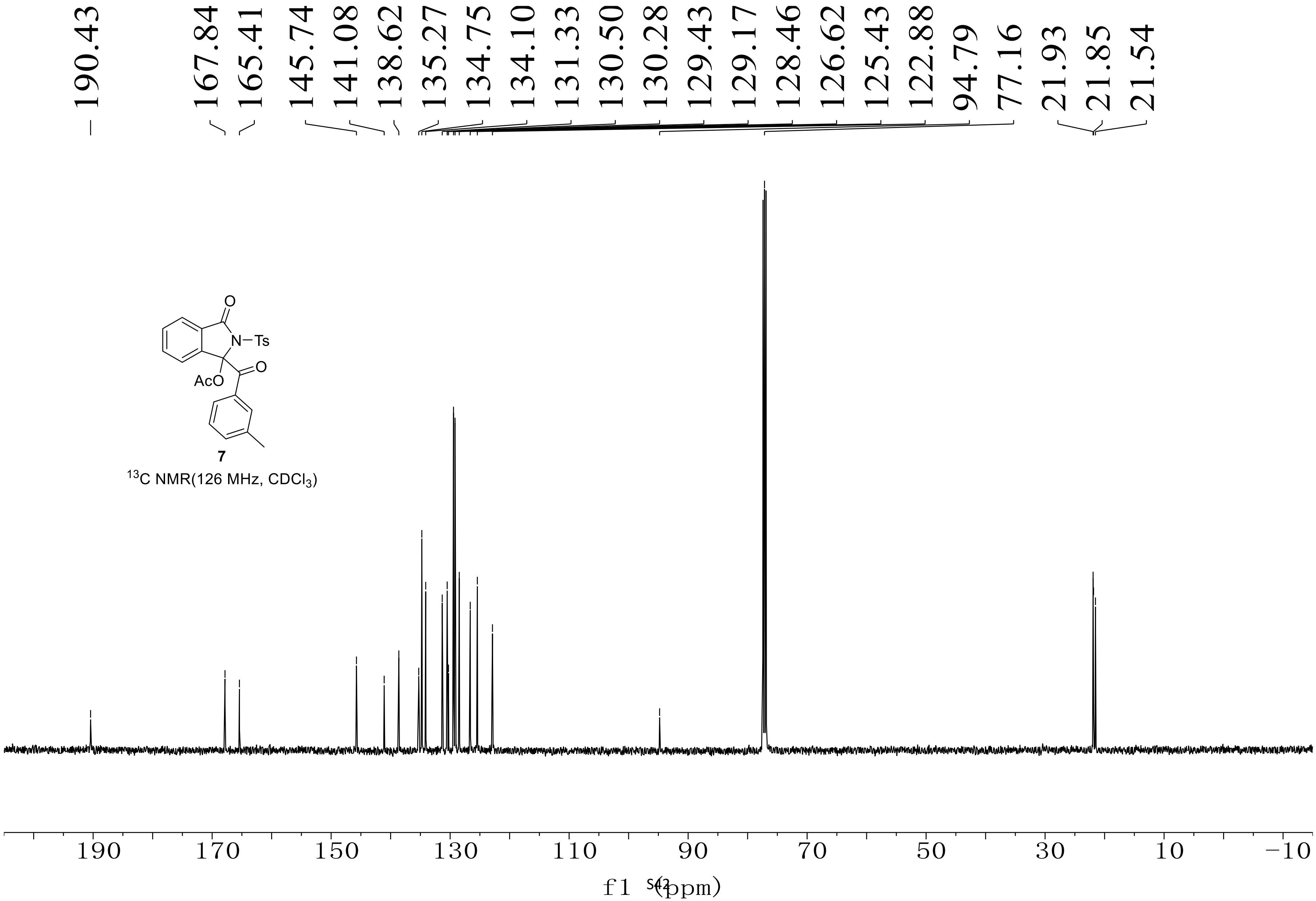
6

^{13}C NMR(126 MHz, CDCl$_3$)



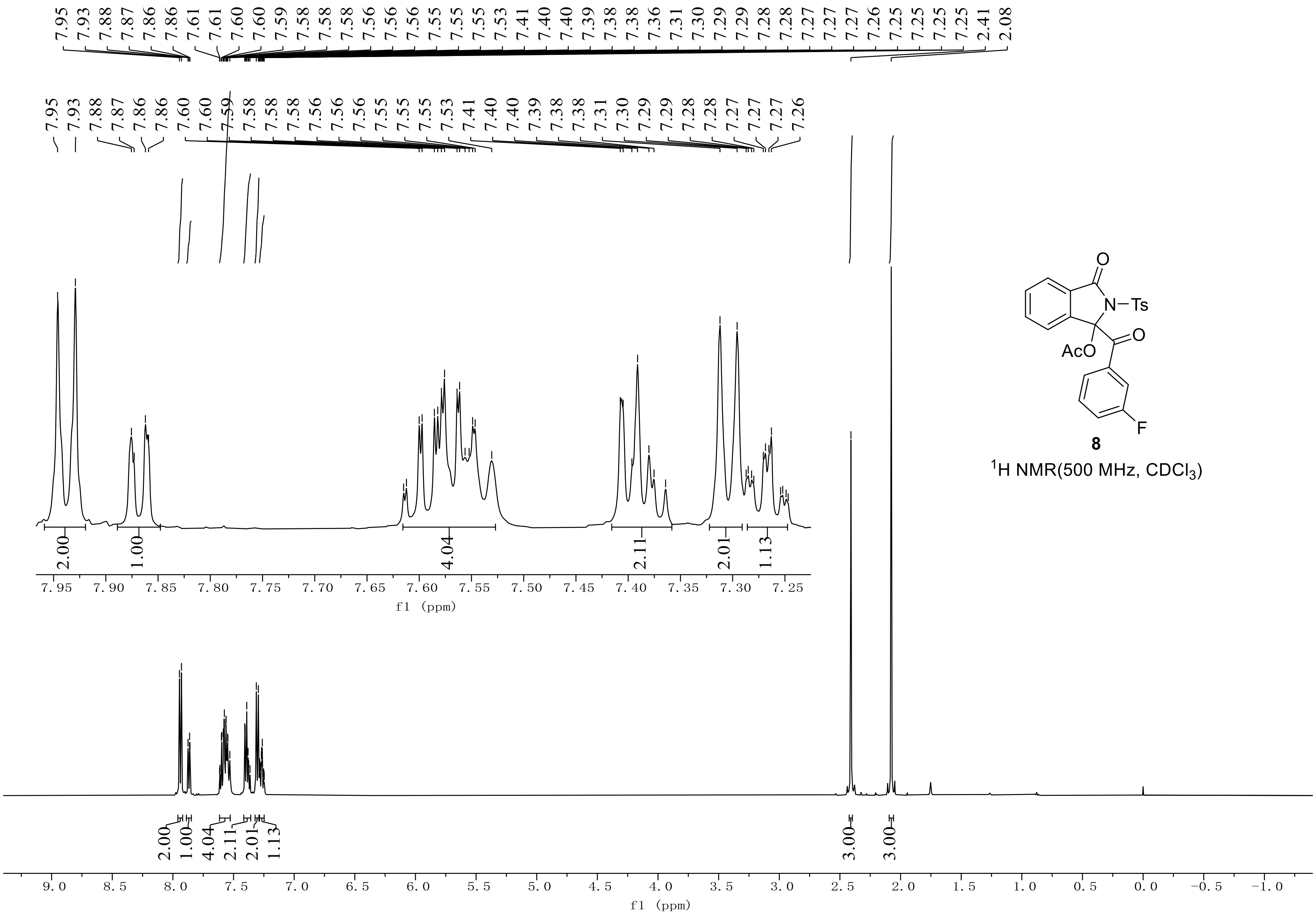
7

^{1}H NMR(500 MHz, CDCl$_3$)



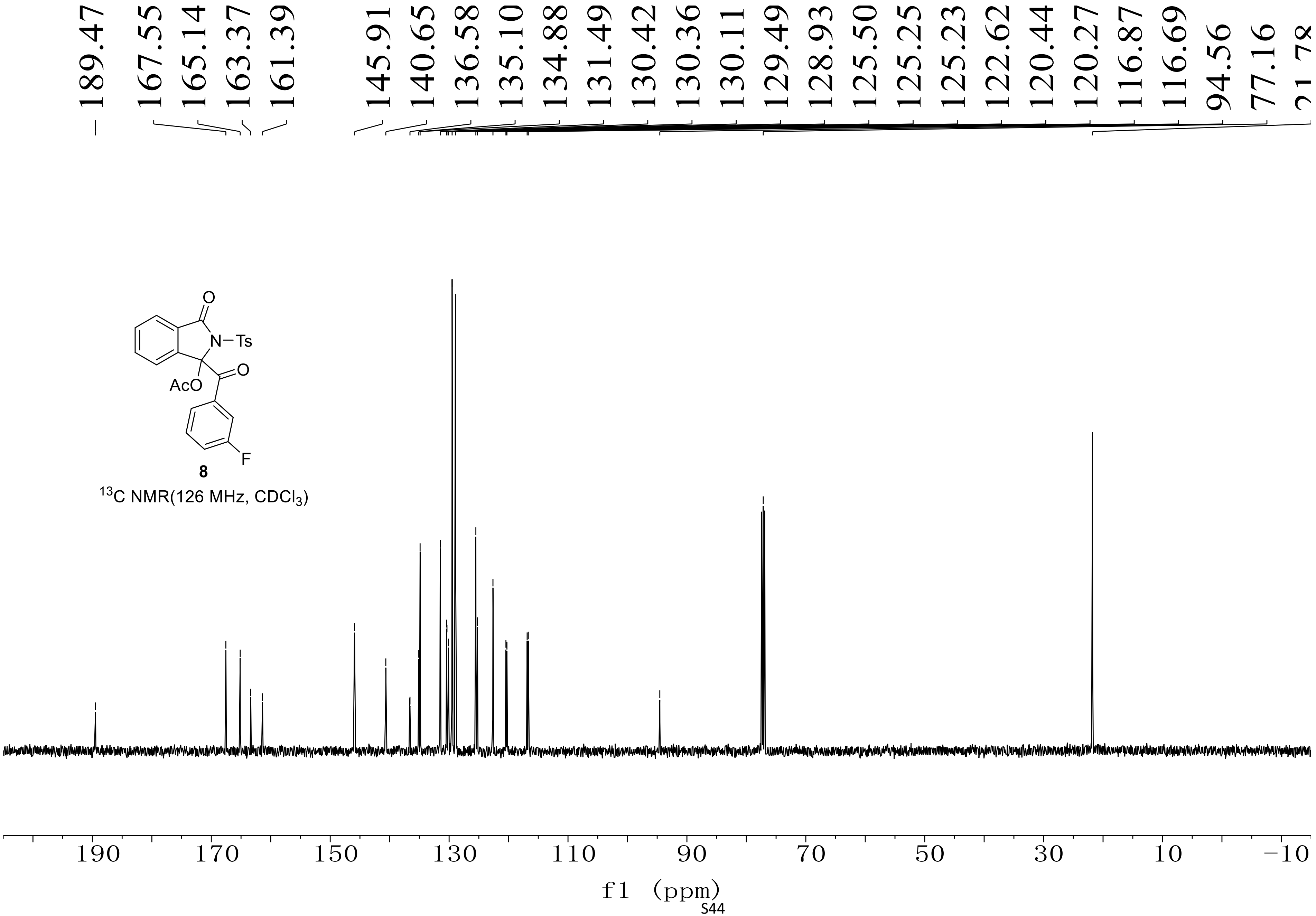
7

^{13}C NMR(126 MHz, $CDCl_3$)



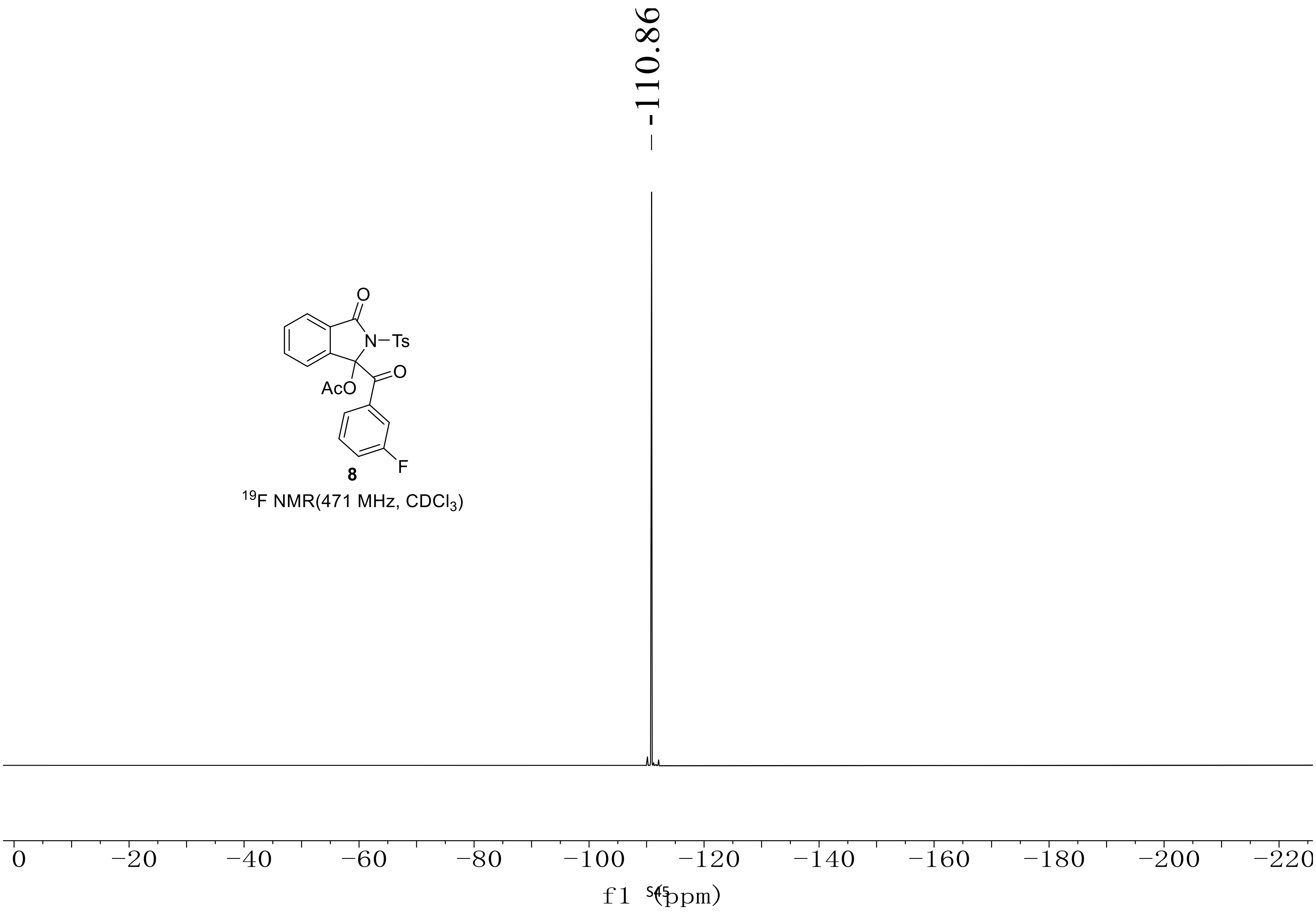
8

^{1}H NMR(500 MHz, CDCl$_3$)



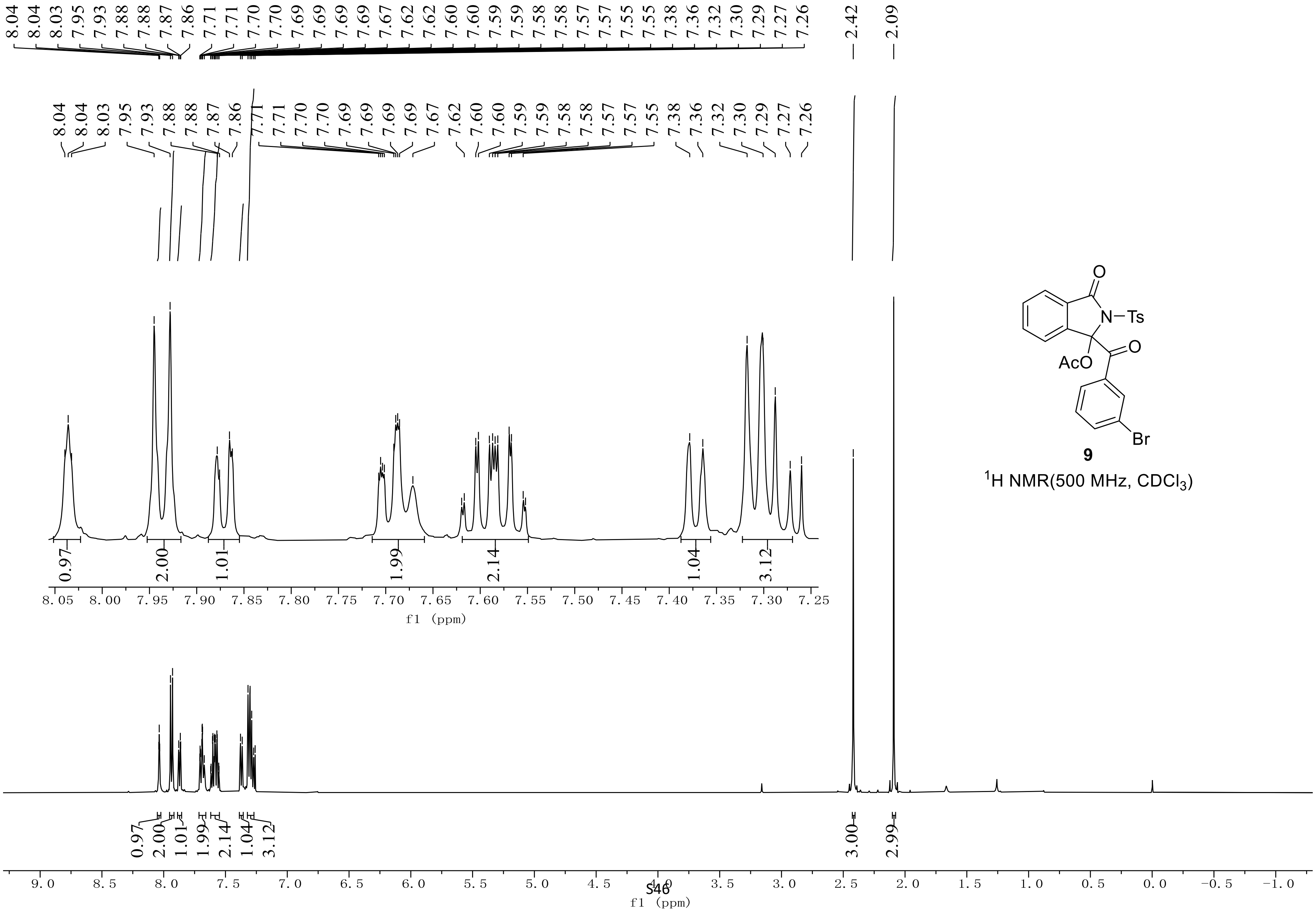
8

^{13}C NMR(126 MHz, $CDCl_3$)



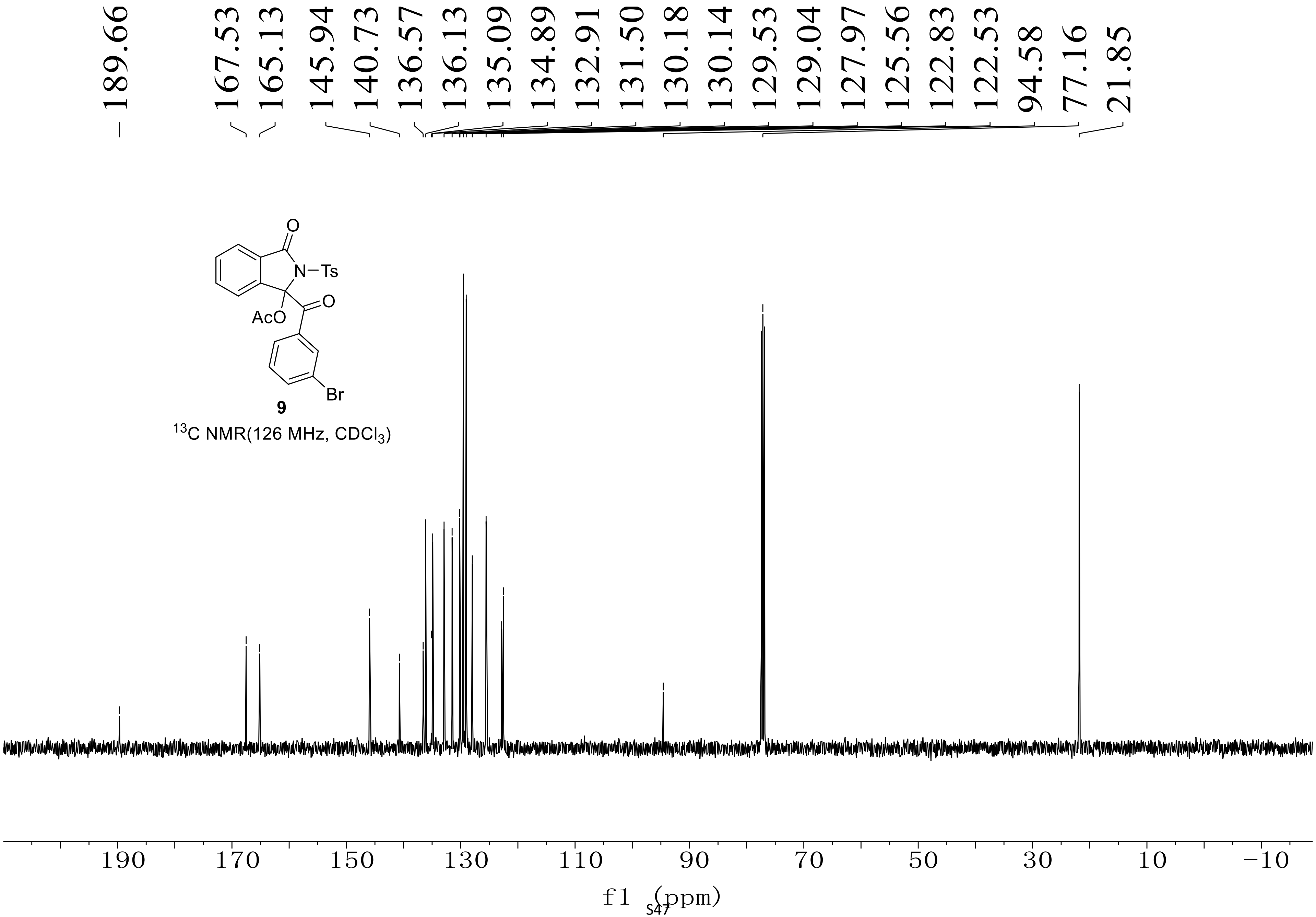
8

^{19}F NMR(471 MHz, CDCl$_3$)



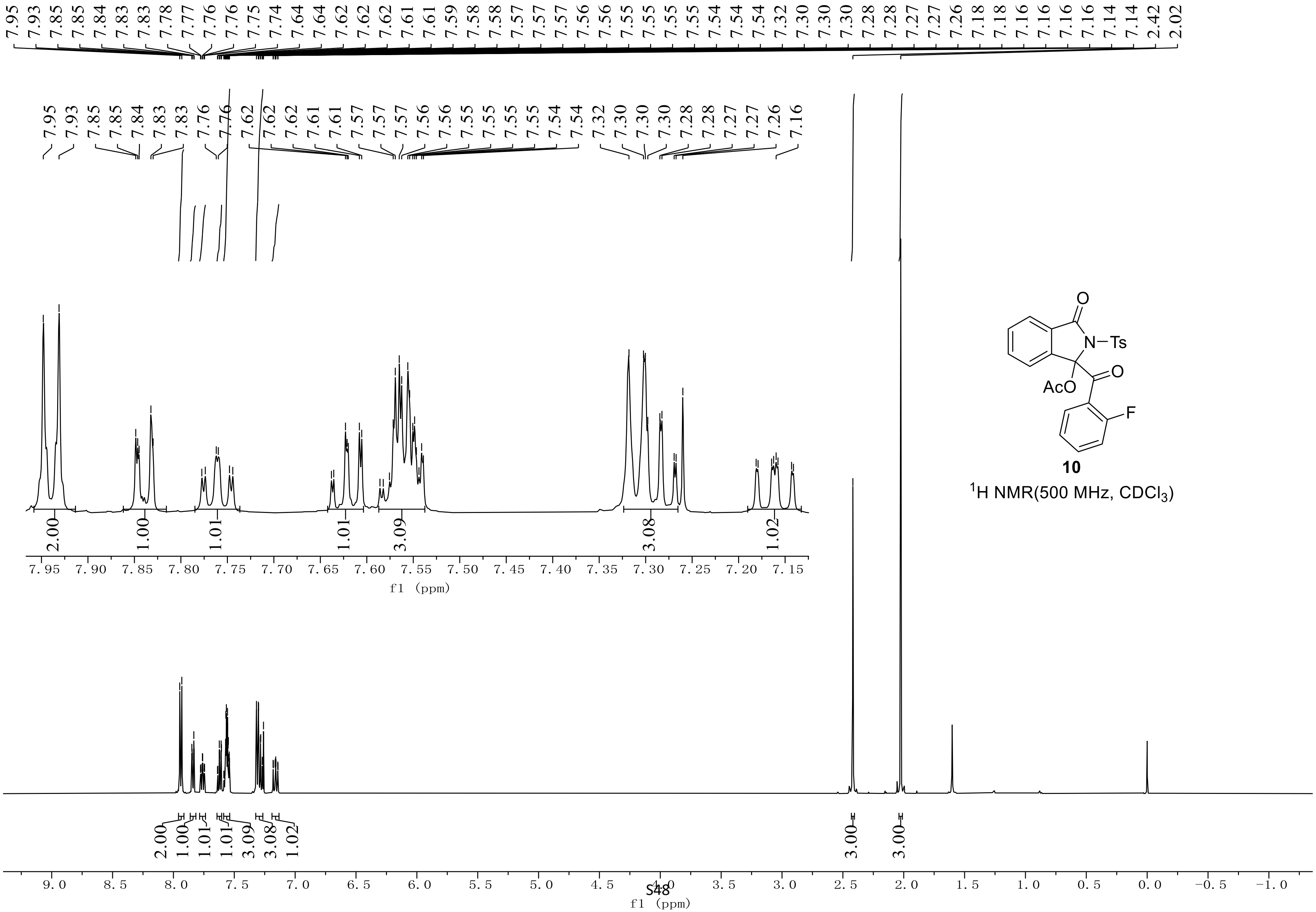
9

^{1}H NMR(500 MHz, CDCl$_3$)



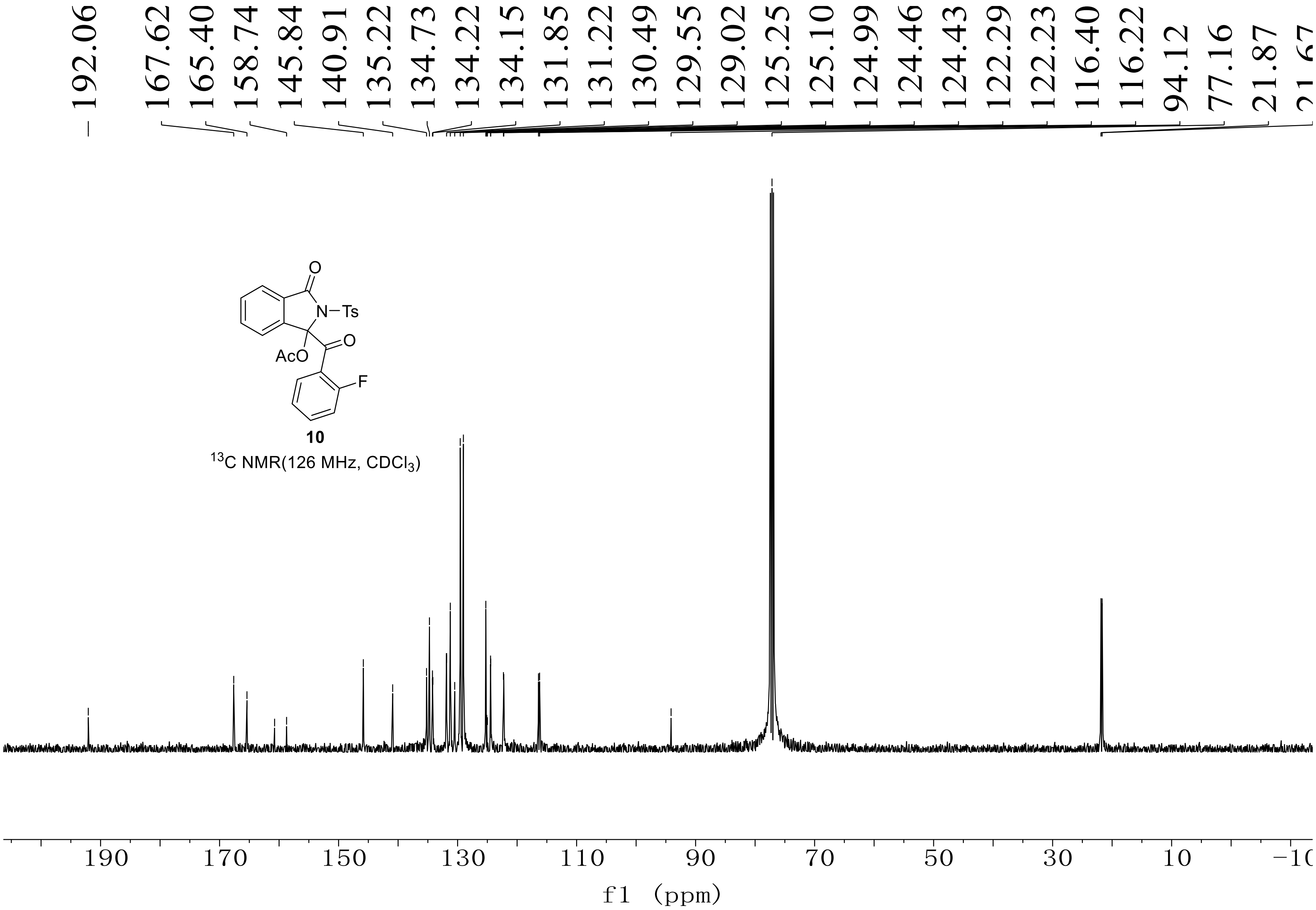
9

^{13}C NMR(126 MHz, CDCl$_3$)



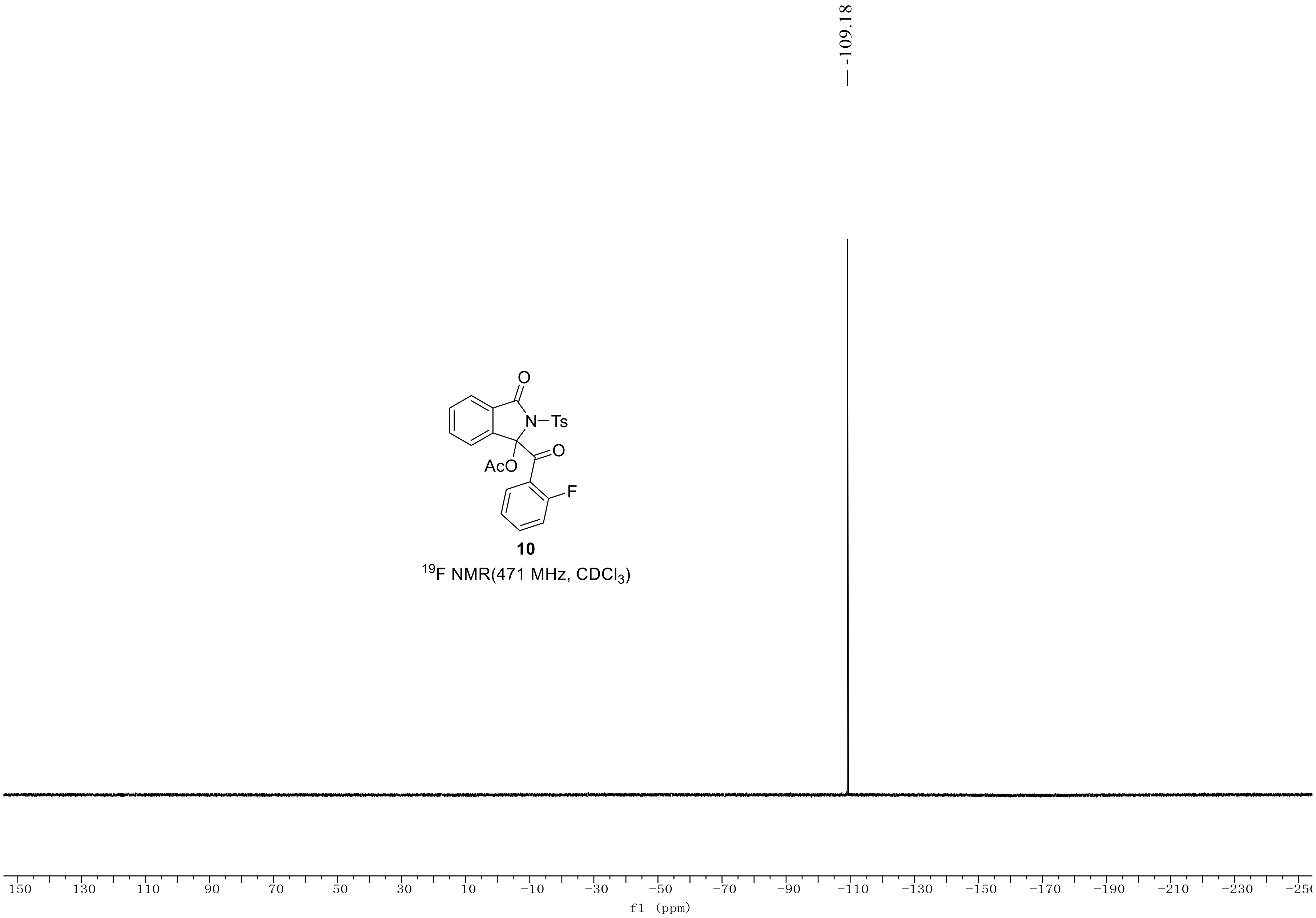
10

^{1}H NMR(500 MHz, $CDCl_3$)



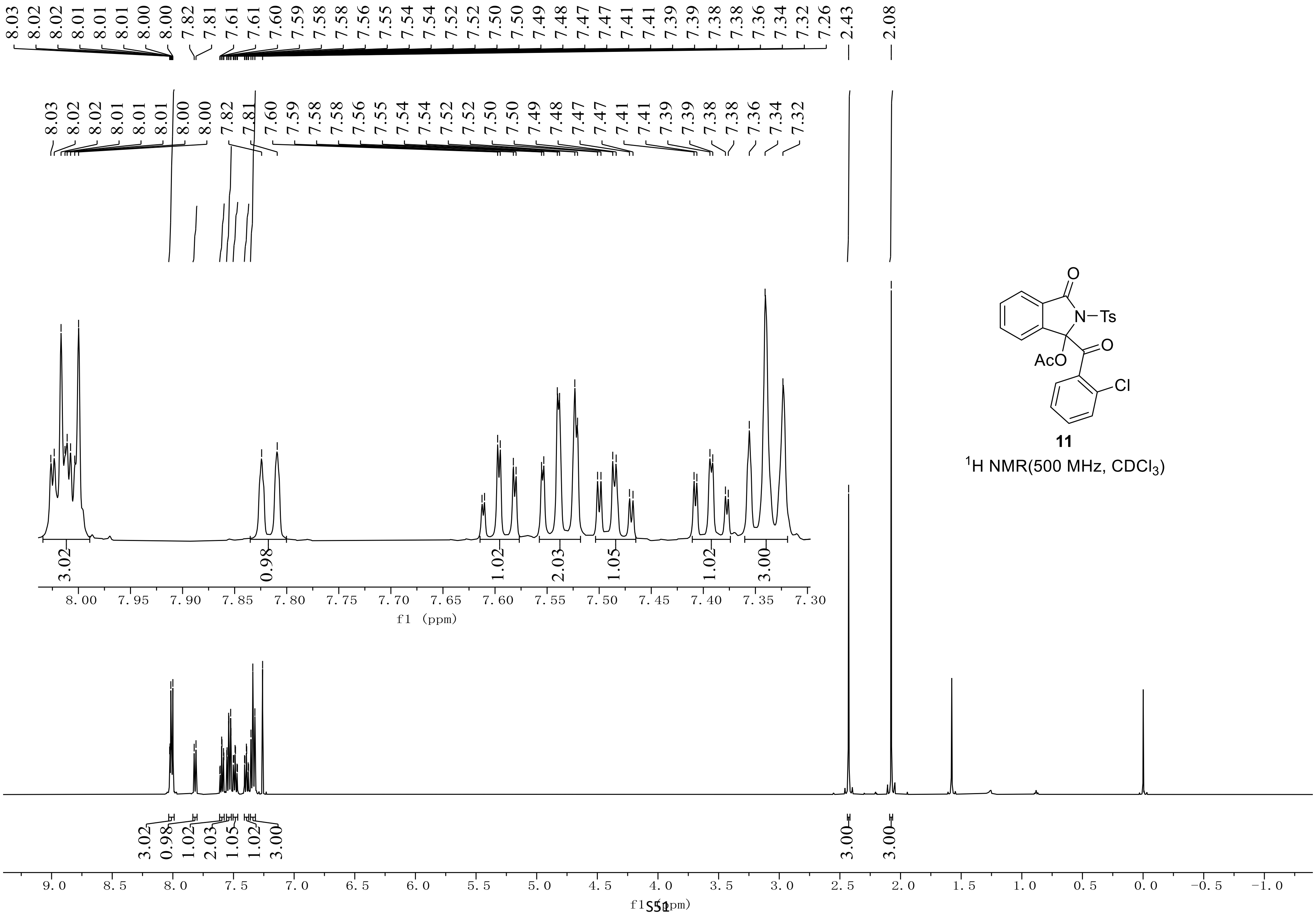
10

^{13}C NMR(126 MHz, CDCl$_3$)



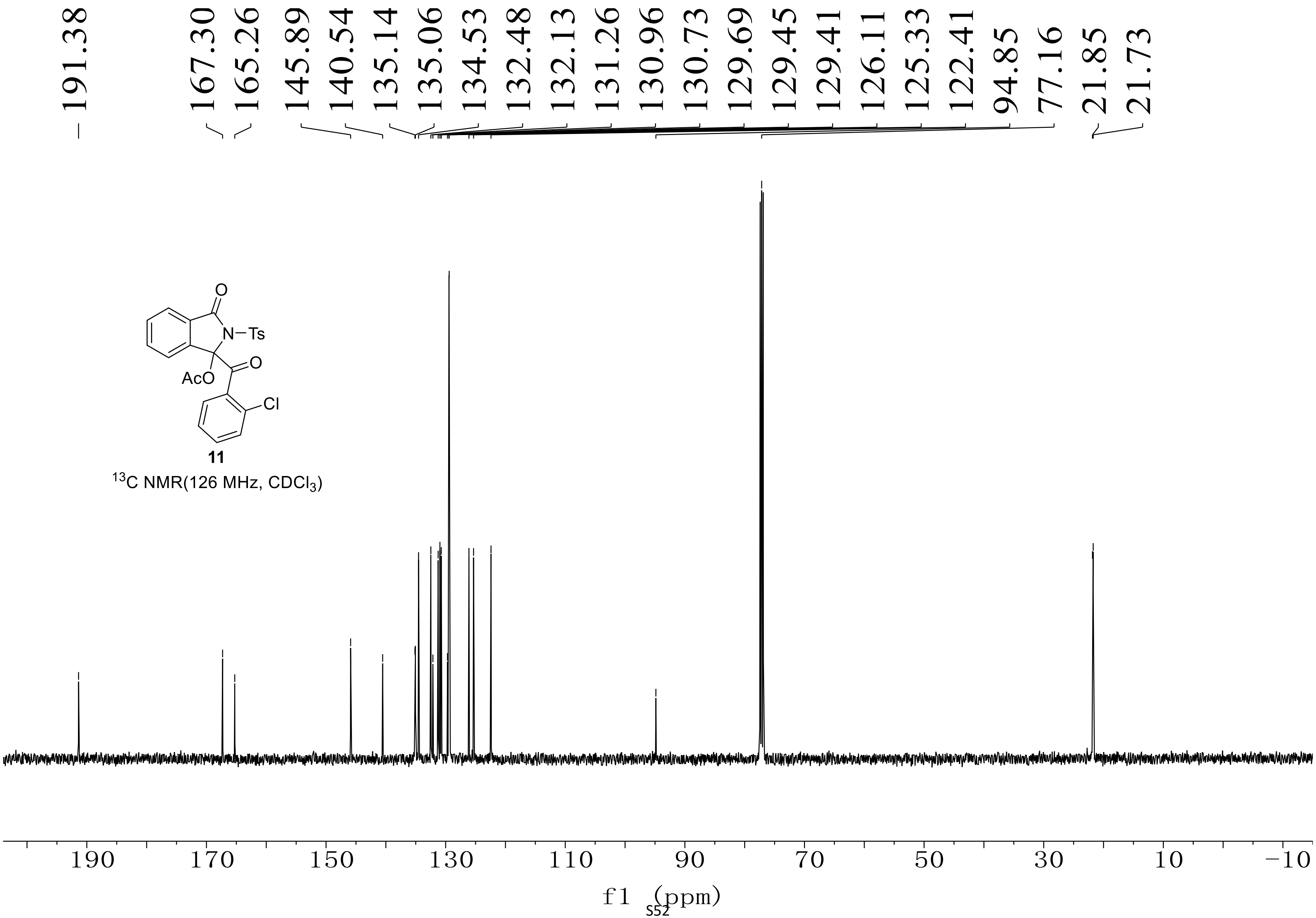
10

^{19}F NMR(471 MHz, CDCl$_3$)



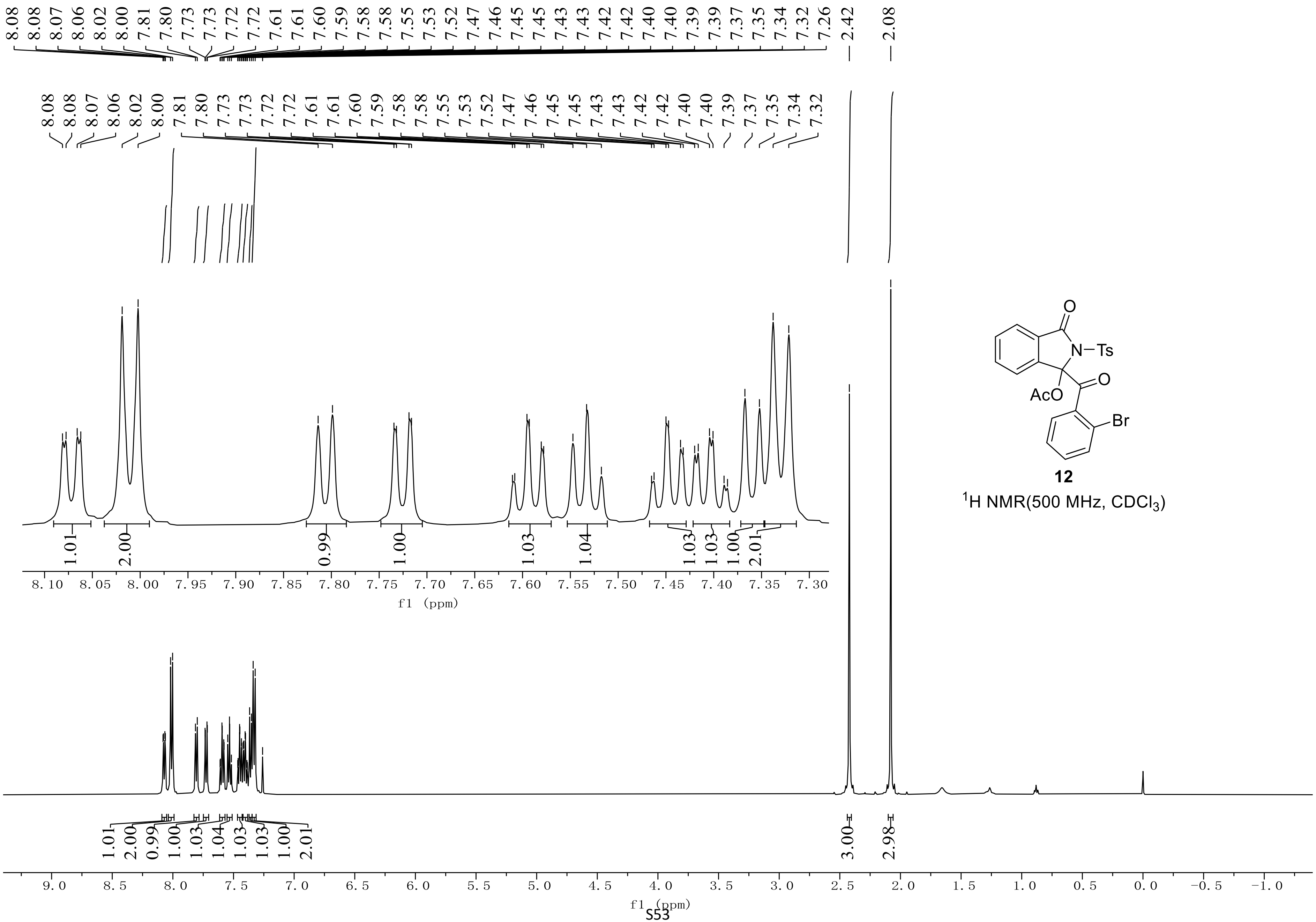
11

^{1}H NMR(500 MHz, CDCl$_3$)



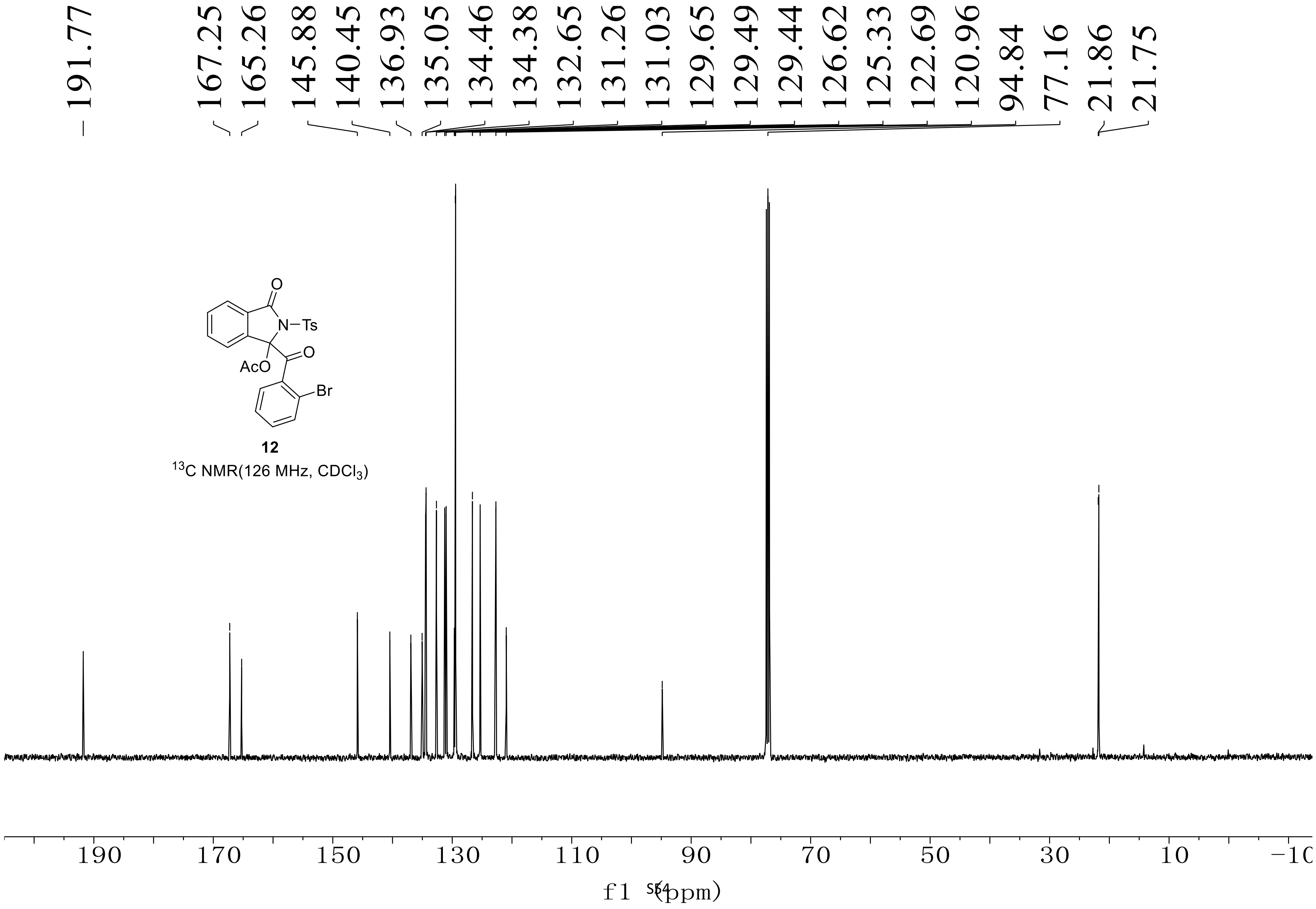
11

^{13}C NMR(126 MHz, $CDCl_3$)



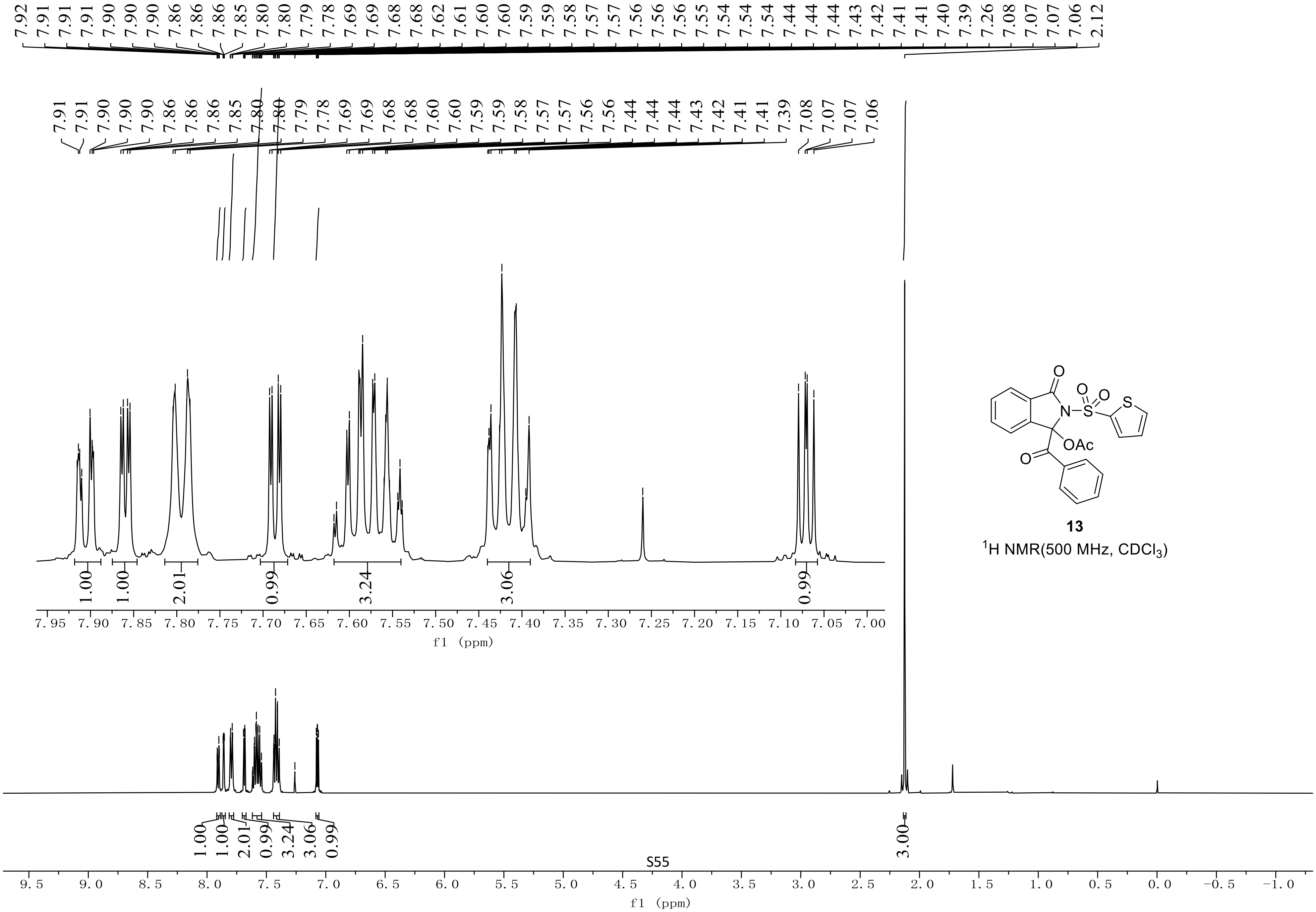
12

^{1}H NMR(500 MHz, CDCl$_3$)



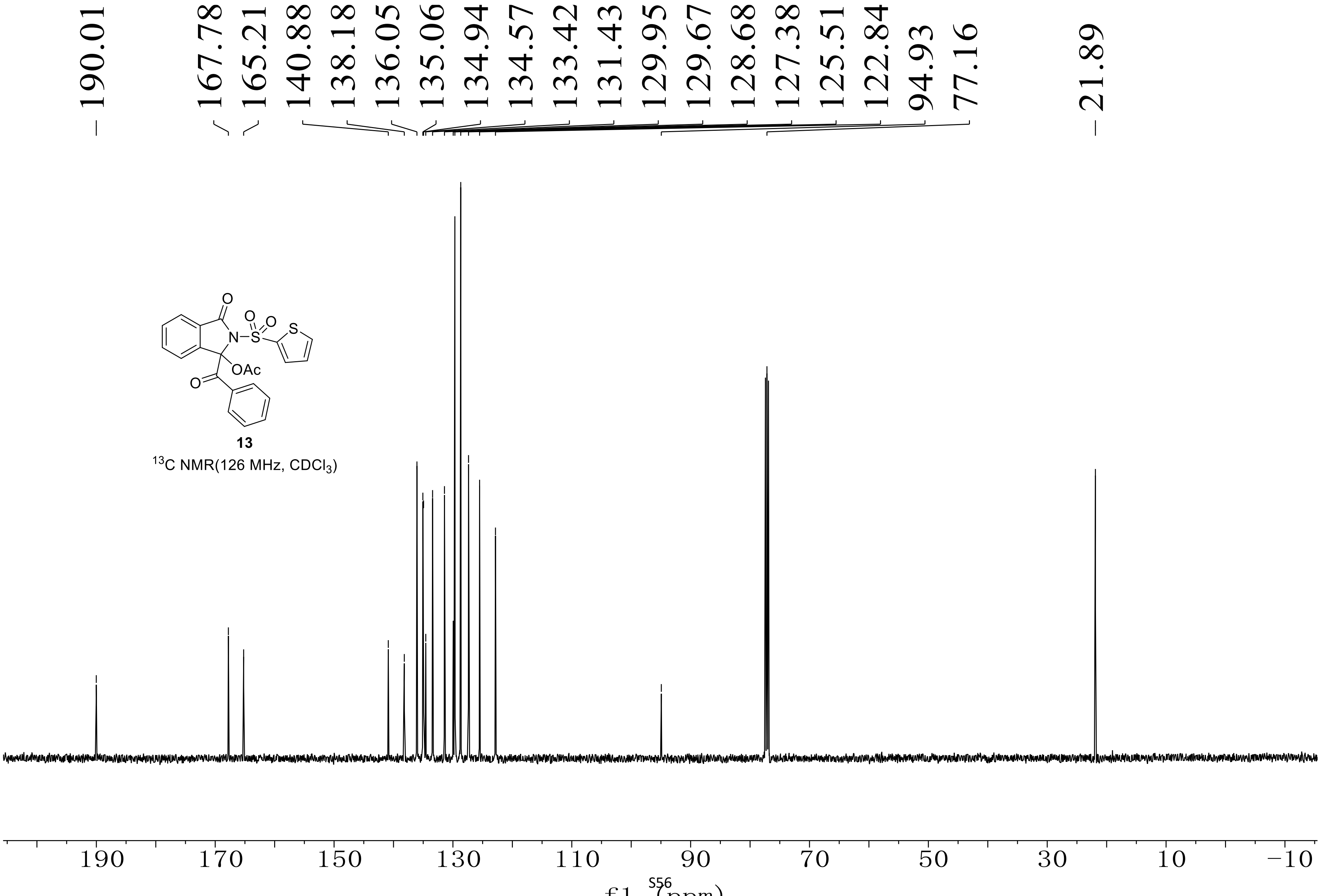
12

^{13}C NMR(126 MHz, $CDCl_3$)



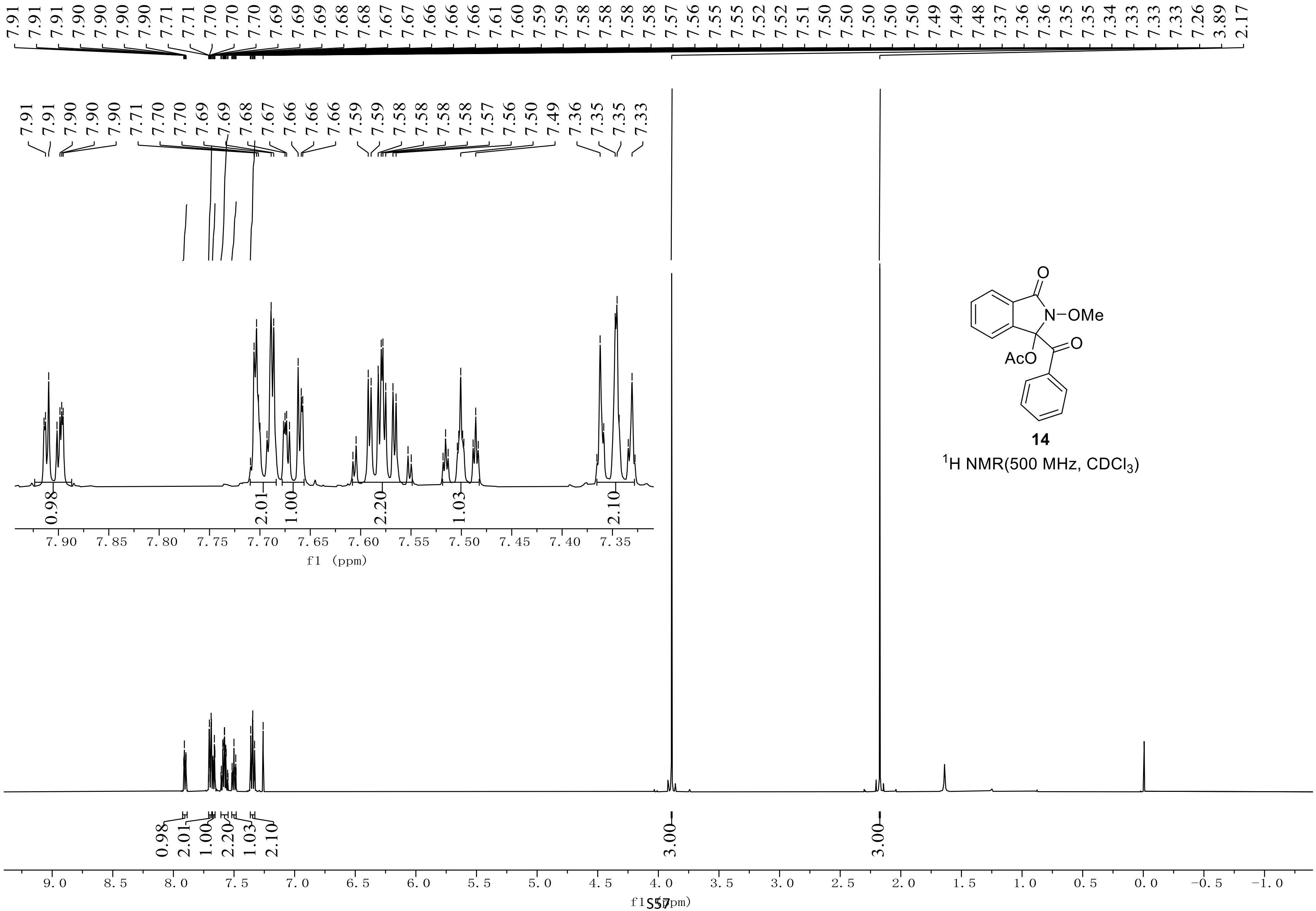
13

^{1}H NMR(500 MHz, CDCl$_3$)



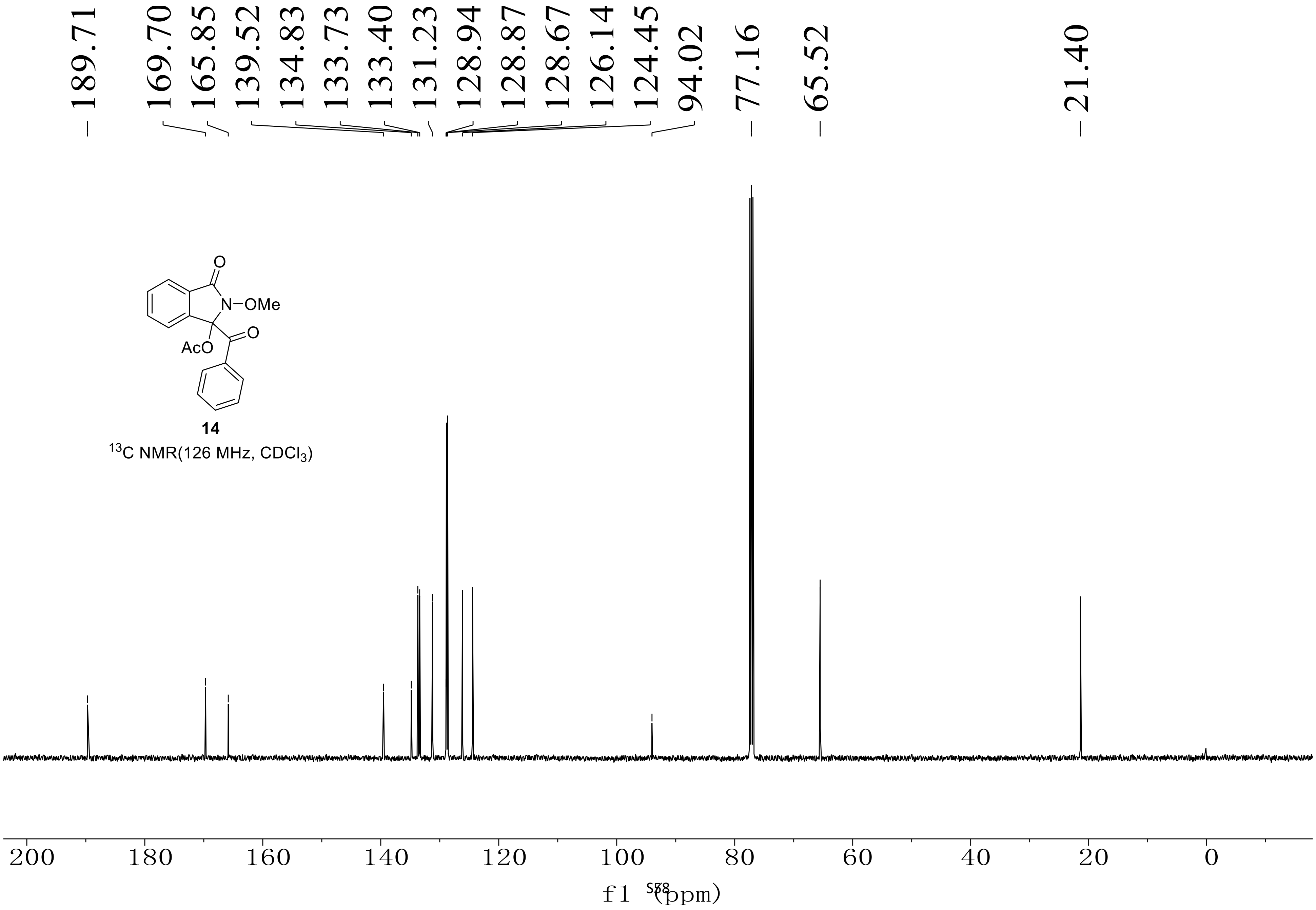
13

^{13}C NMR(126 MHz, CDCl$_3$)



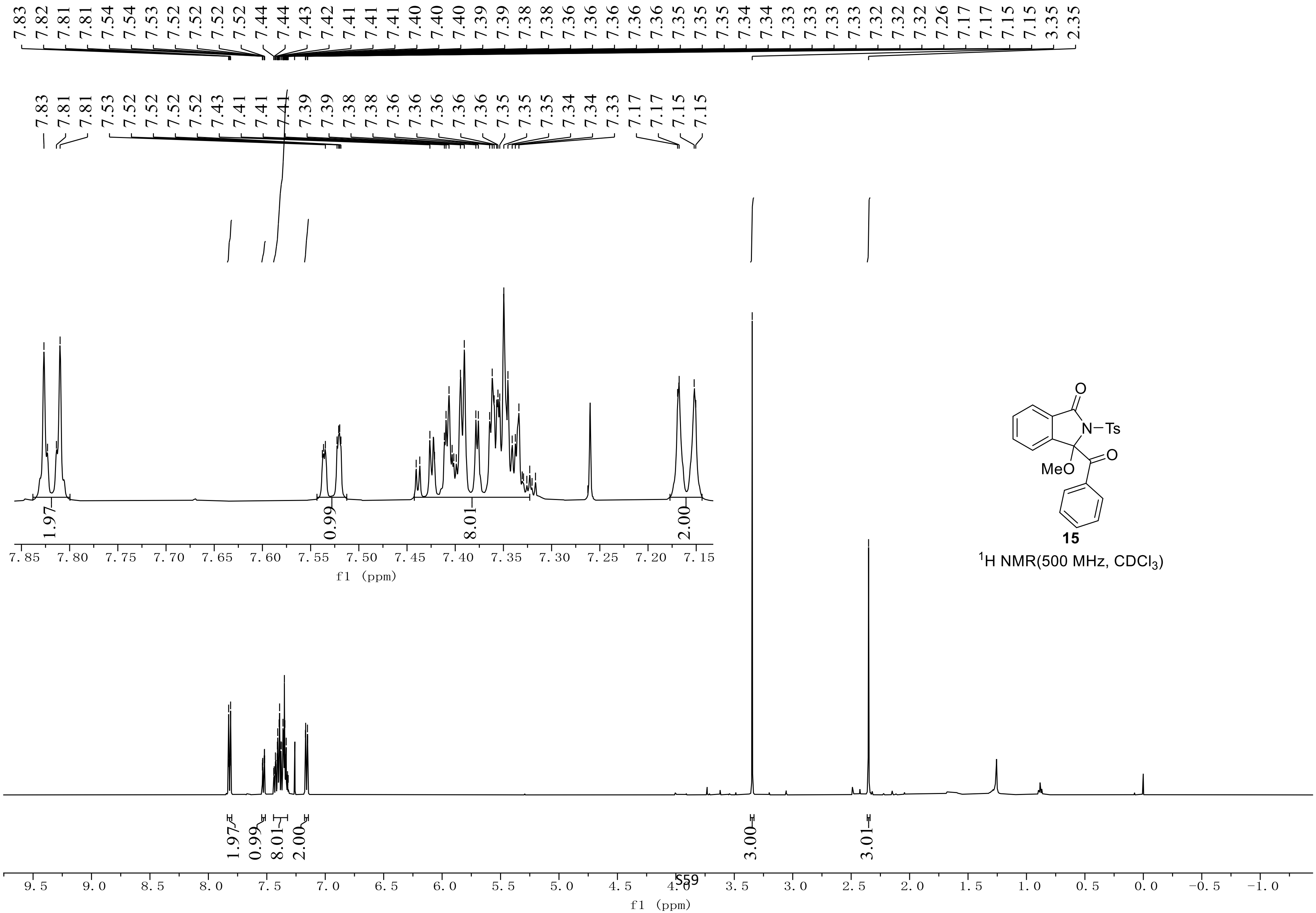
14

^{1}H NMR(500 MHz, $CDCl_3$)



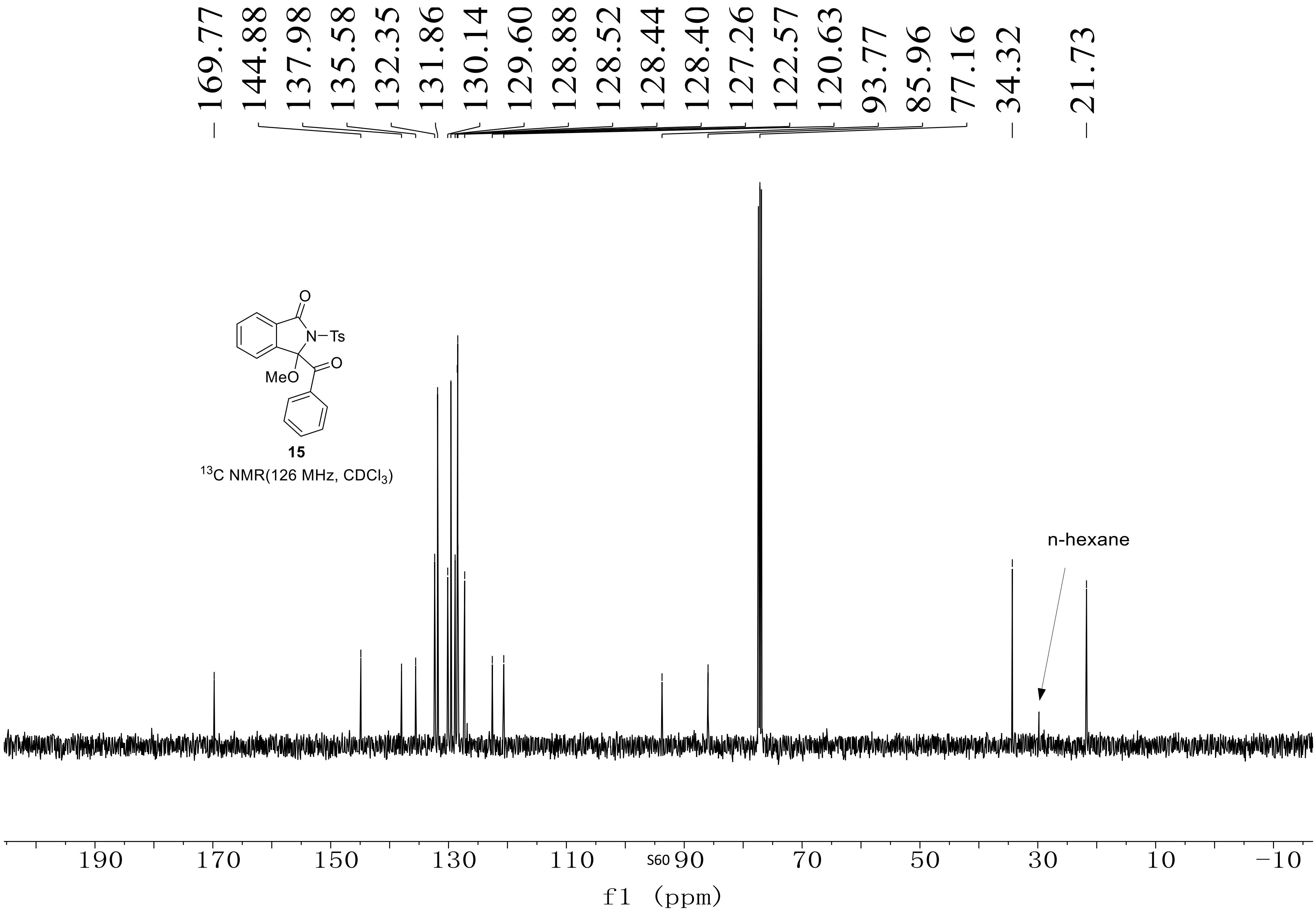
14

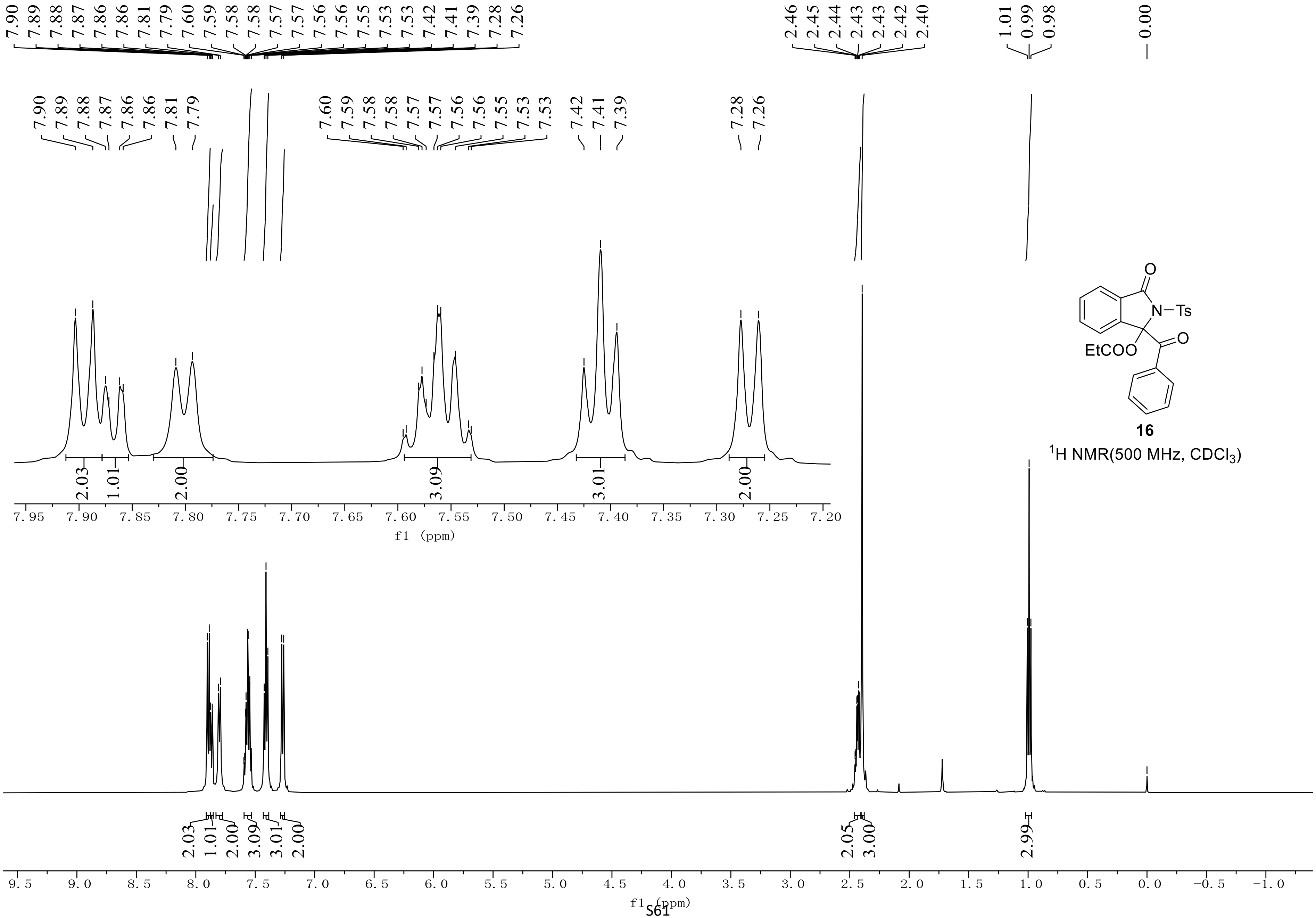
^{13}C NMR(126 MHz, CDCl$_3$)

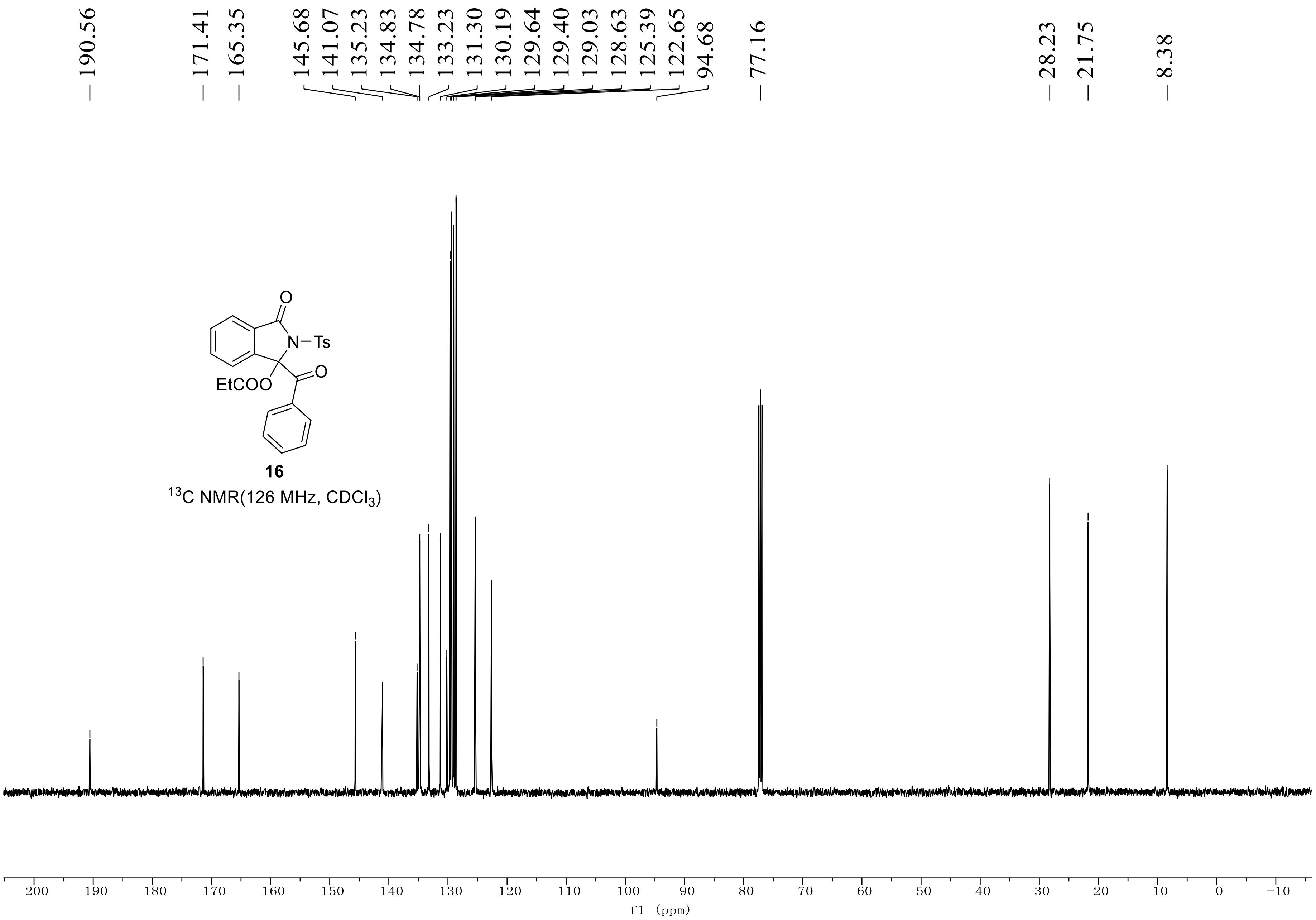


15

^{1}H NMR(500 MHz, CDCl$_3$)

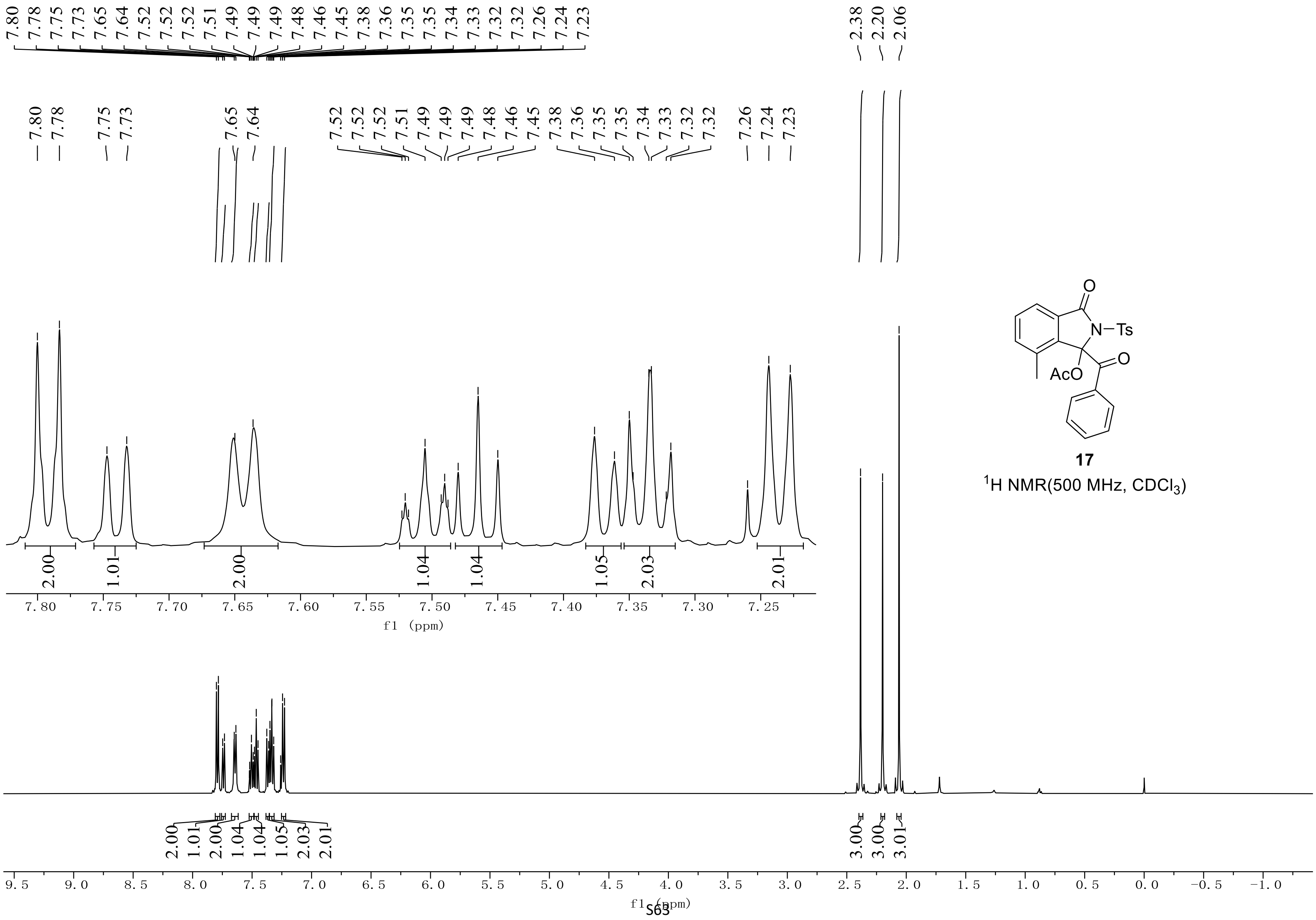

169.77
144.88
137.98
135.58
132.35
131.86
130.14
129.60
128.88
128.52
128.44
128.40
127.26
122.57
120.63
93.77
85.96
77.16
34.32
21.73
O
N−Ts
O
MeO
15
^{13}C NMR(126 MHz, CDCl$_3$)
n-hexane
190
170
150
130
110
90
70
50
30
10
−10
f1 (ppm)


7.90 7.89 7.88 7.87 7.86 7.86 7.81 7.79 7.60 7.59 7.58 7.58 7.57 7.57 7.56 7.56 7.55 7.53 7.53 7.42 7.41 7.39 7.28 7.26
2.46 2.45 2.44 2.43 2.43 2.42 2.40
1.01 0.99 0.98
0.00
2.03
1.01
2.00
3.09
3.01
2.00
7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20
f1 (ppm)
O
N−Ts
O
EtCOO
16
^{1}H NMR(500 MHz, CDCl$_3$)
2.03 1.01 2.00 3.09 3.01 2.00
2.05 3.00
2.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)



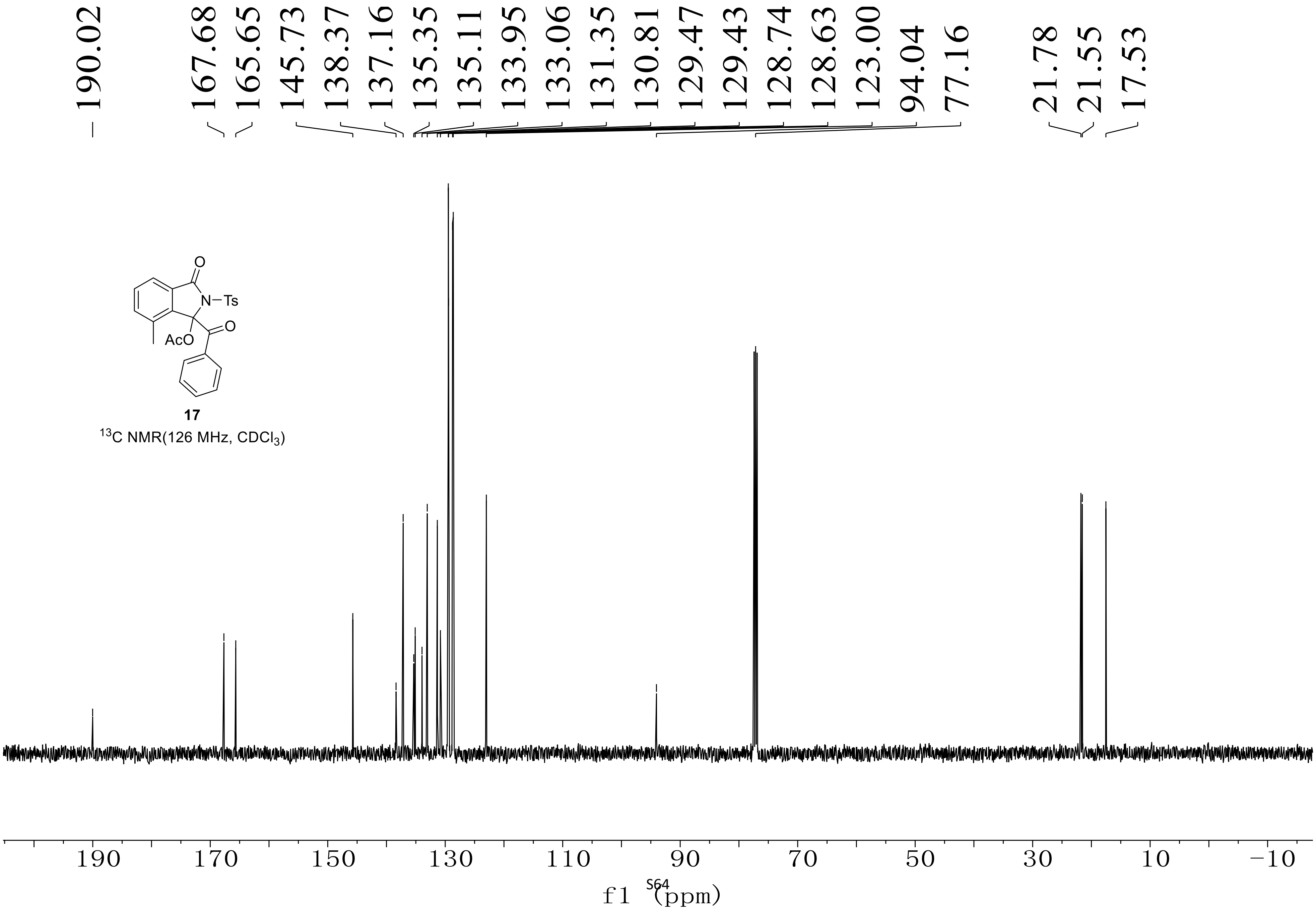
16

^{13}C NMR(126 MHz, CDCl$_3$)



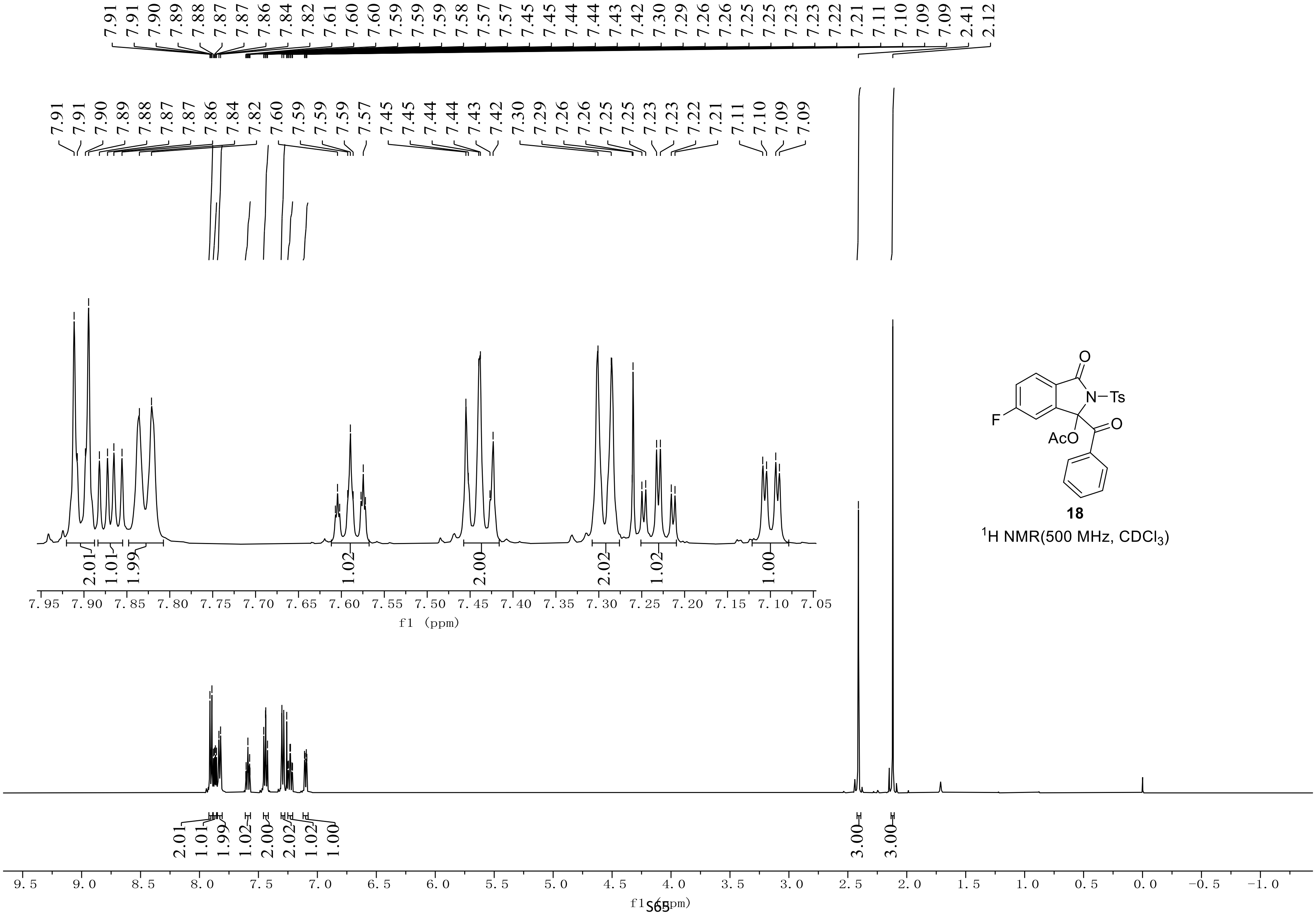
17

^{1}H NMR(500 MHz, CDCl$_3$)



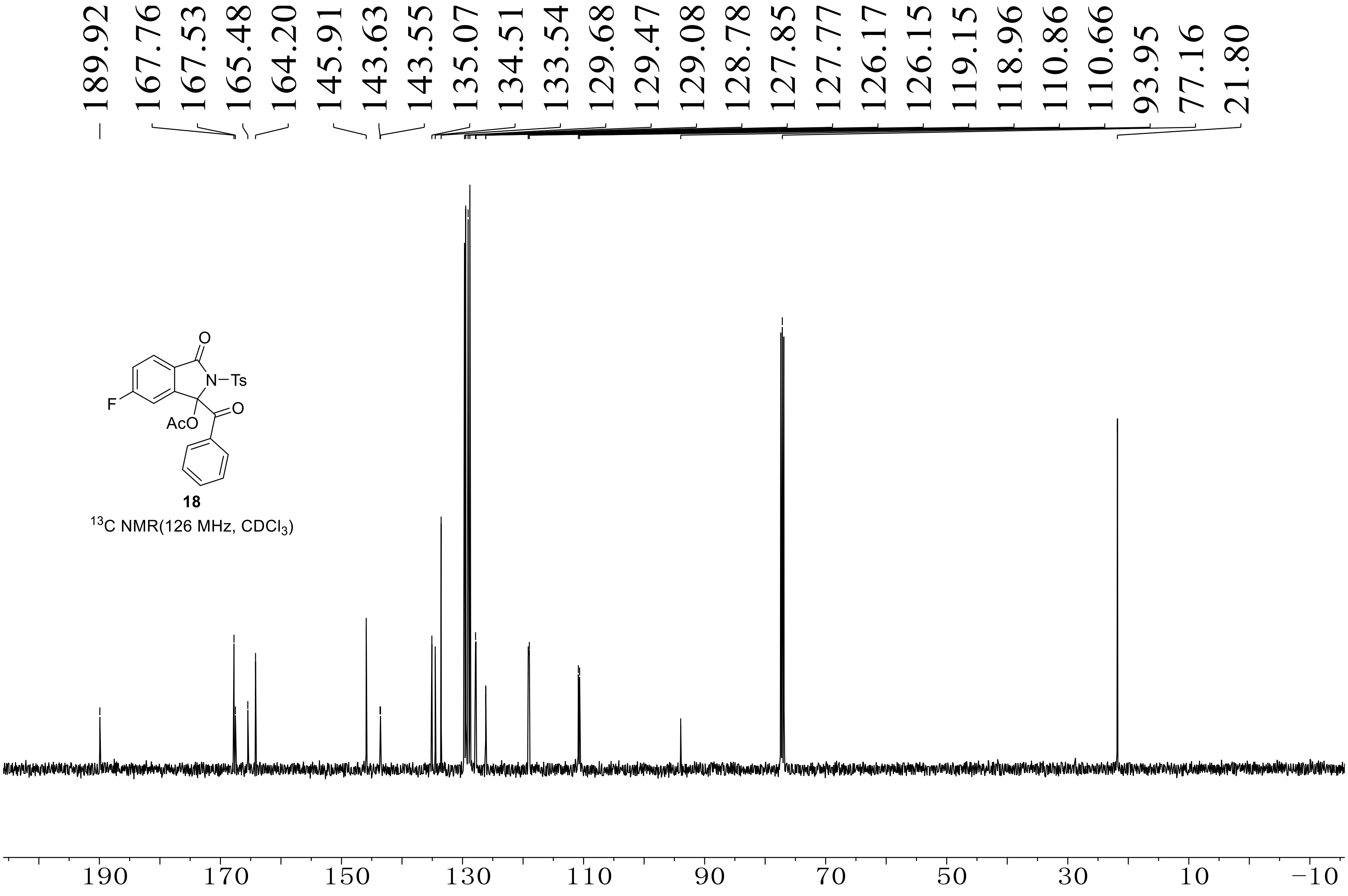
17

^{13}C NMR(126 MHz, CDCl$_3$)



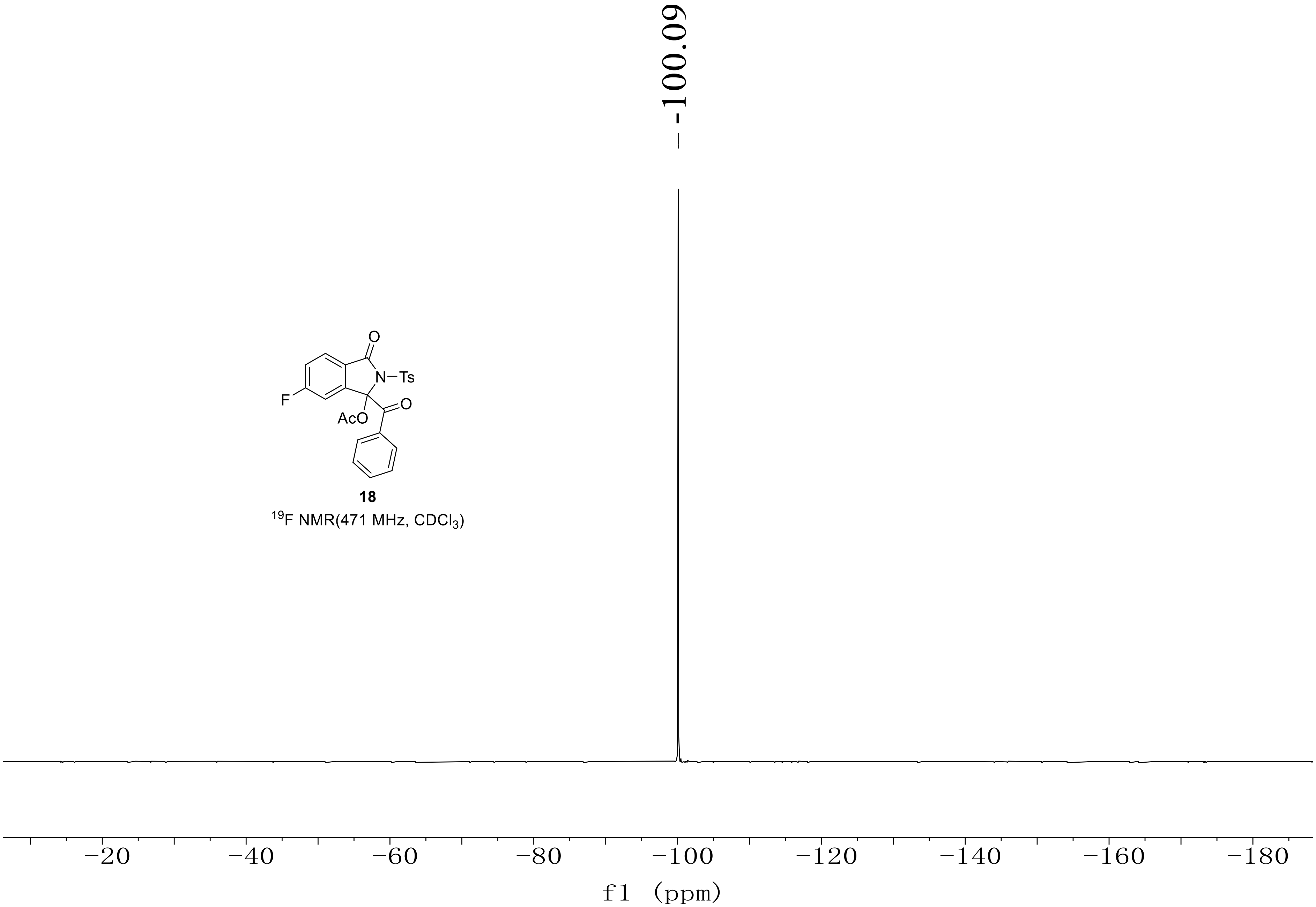
18

^{1}H NMR(500 MHz, $CDCl_3$)



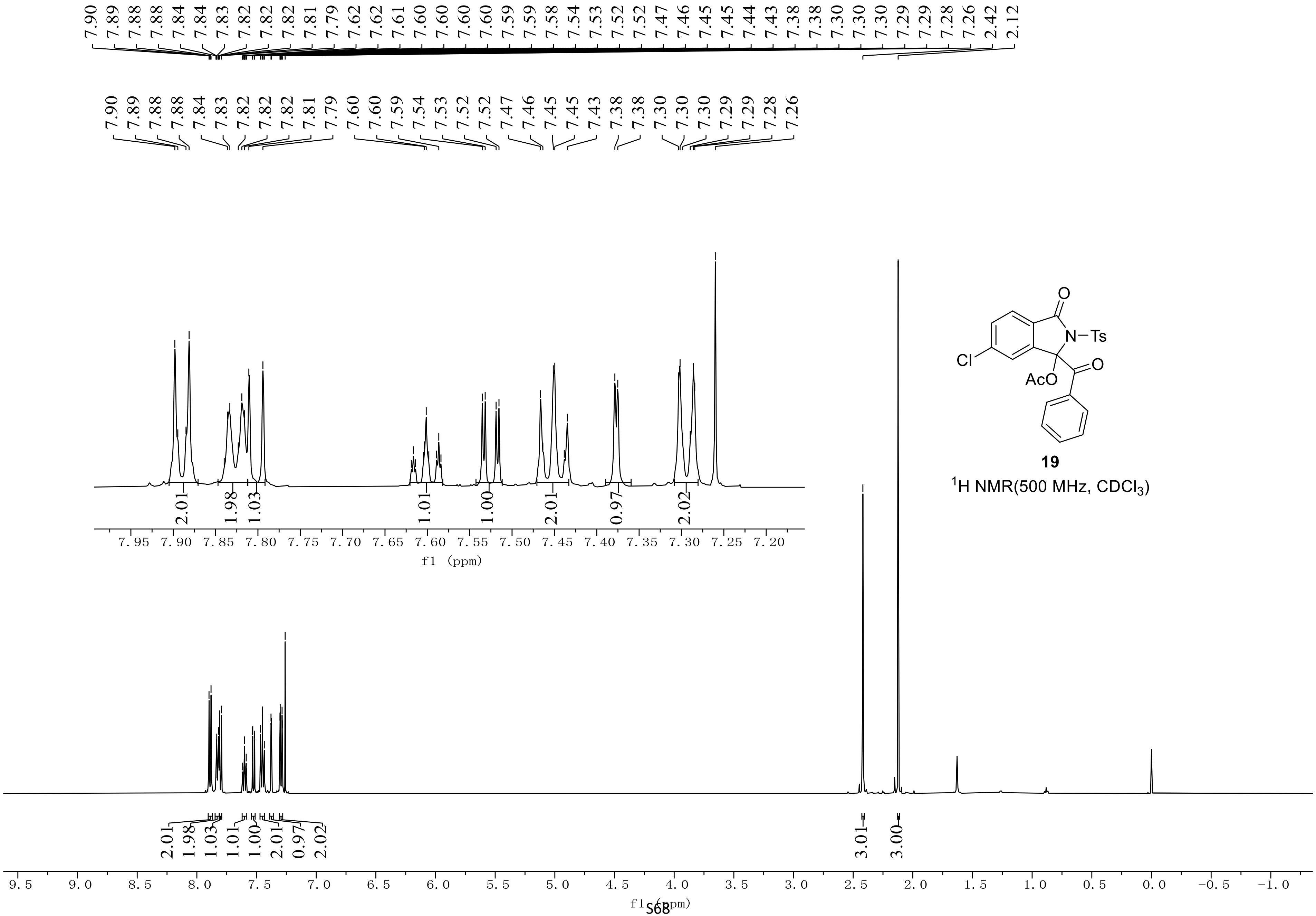
18

^{13}C NMR(126 MHz, CDCl$_3$)



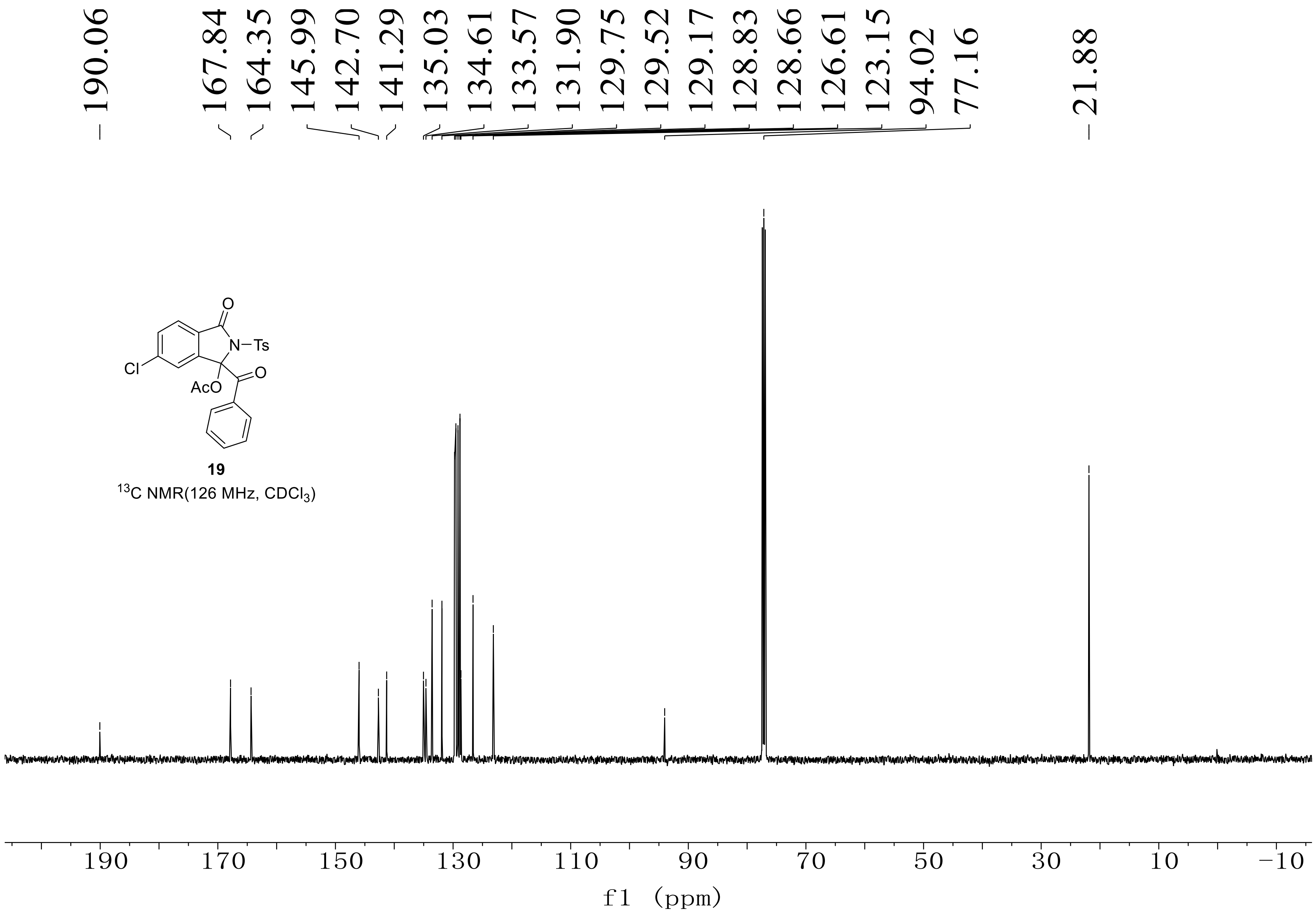
18

^{19}F NMR(471 MHz, CDCl$_3$)



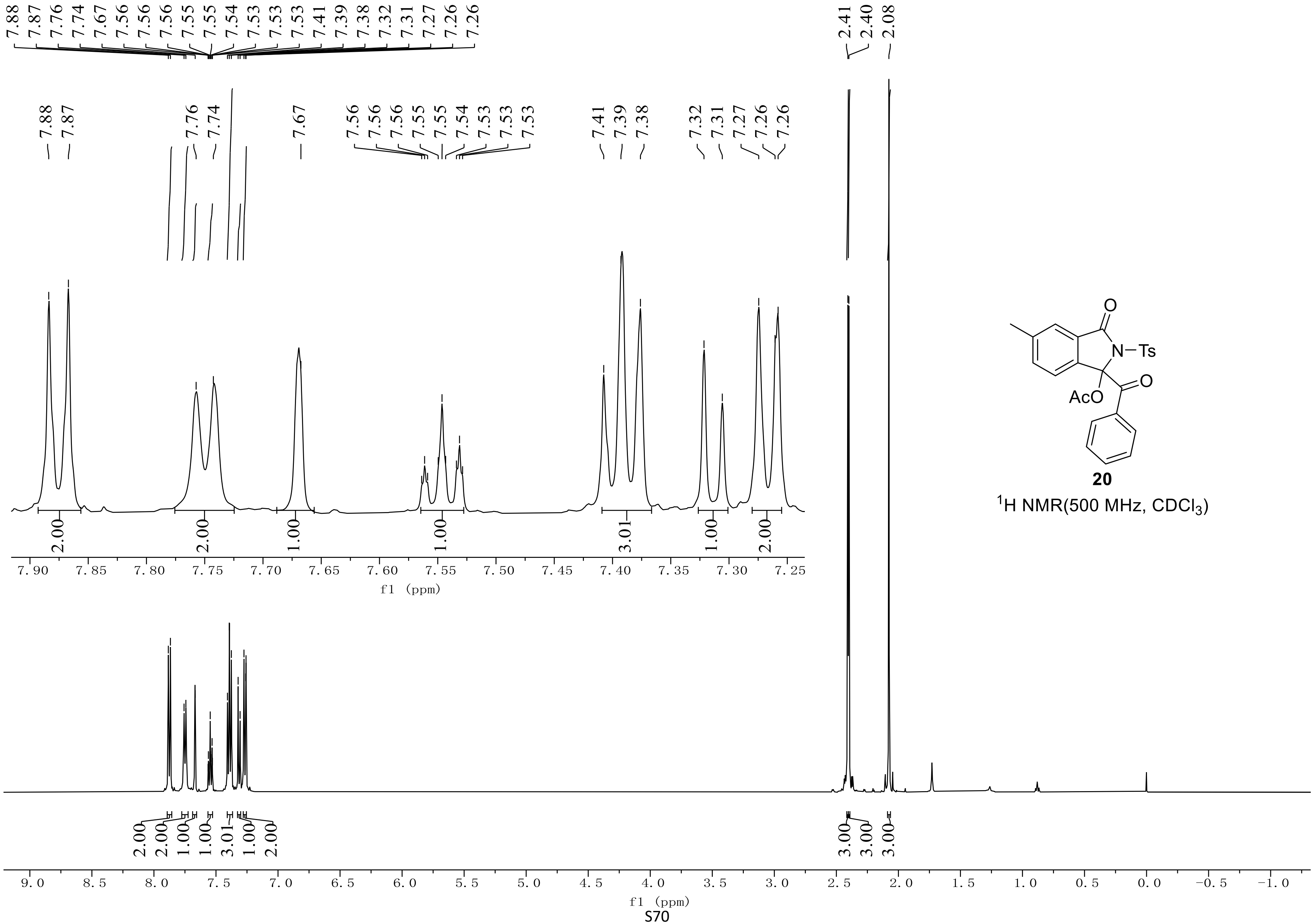
19

^{1}H NMR(500 MHz, CDCl$_3$)



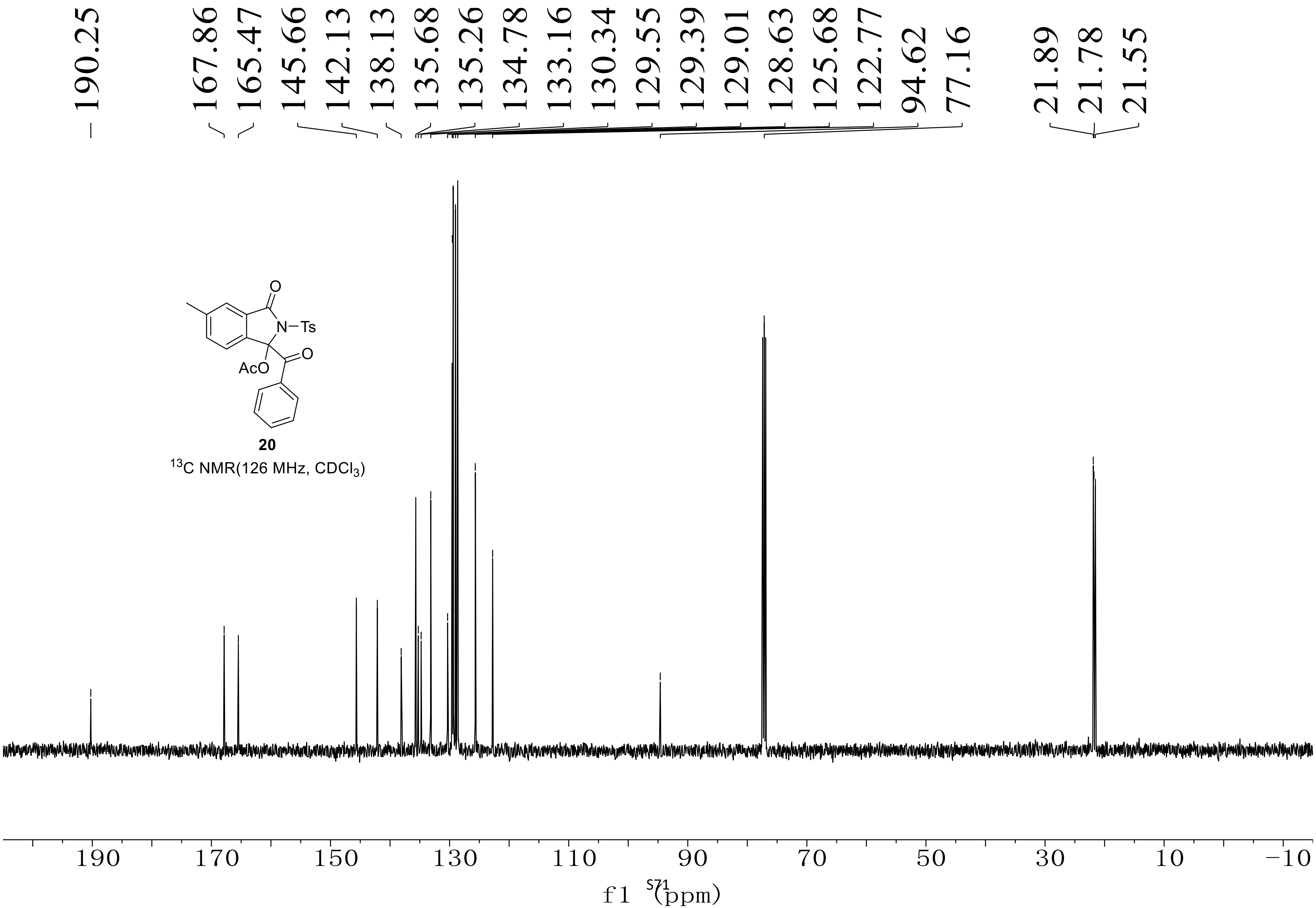
19

^{13}C NMR(126 MHz, CDCl$_3$)



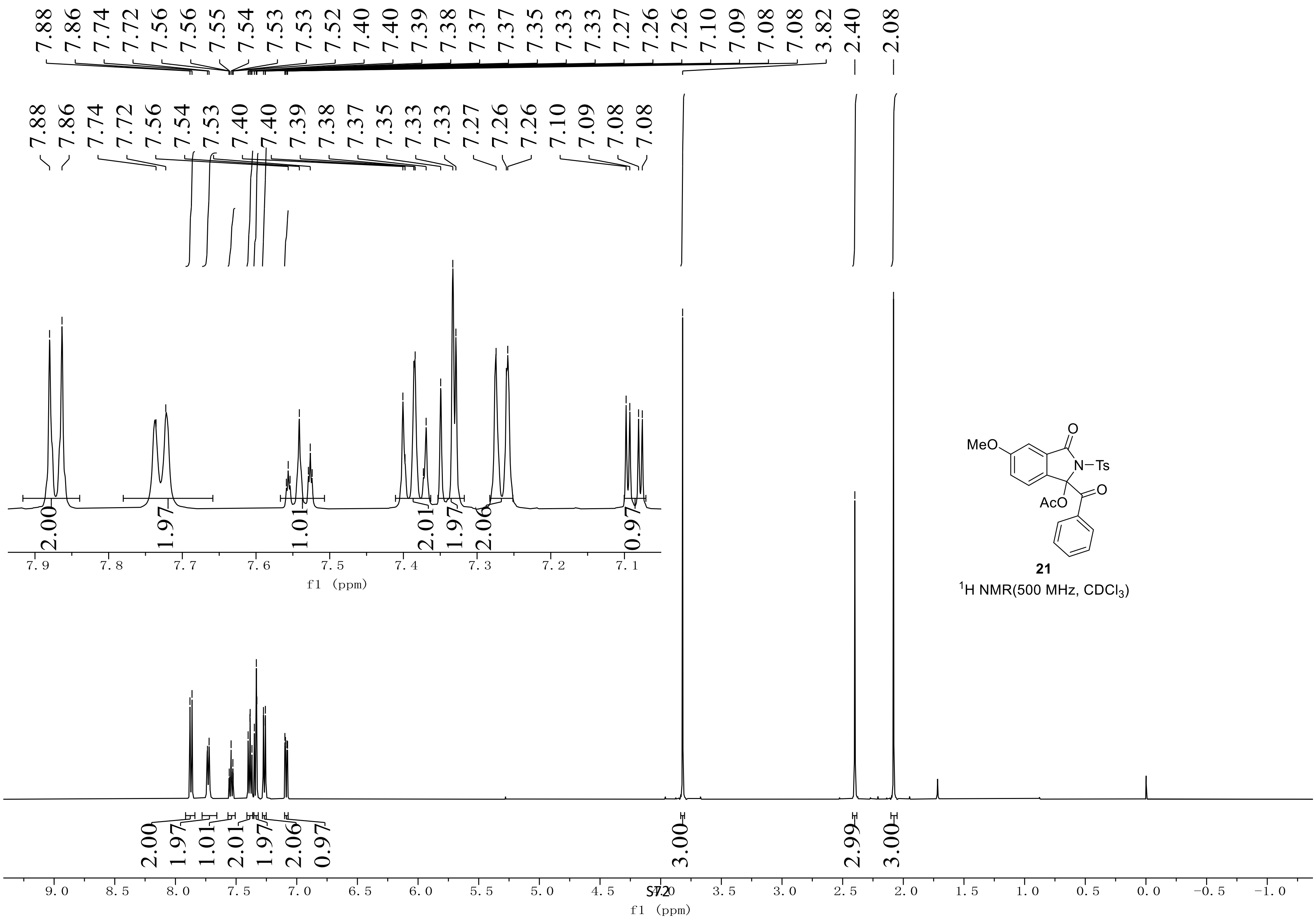
20

^{1}H NMR(500 MHz, $CDCl_3$)



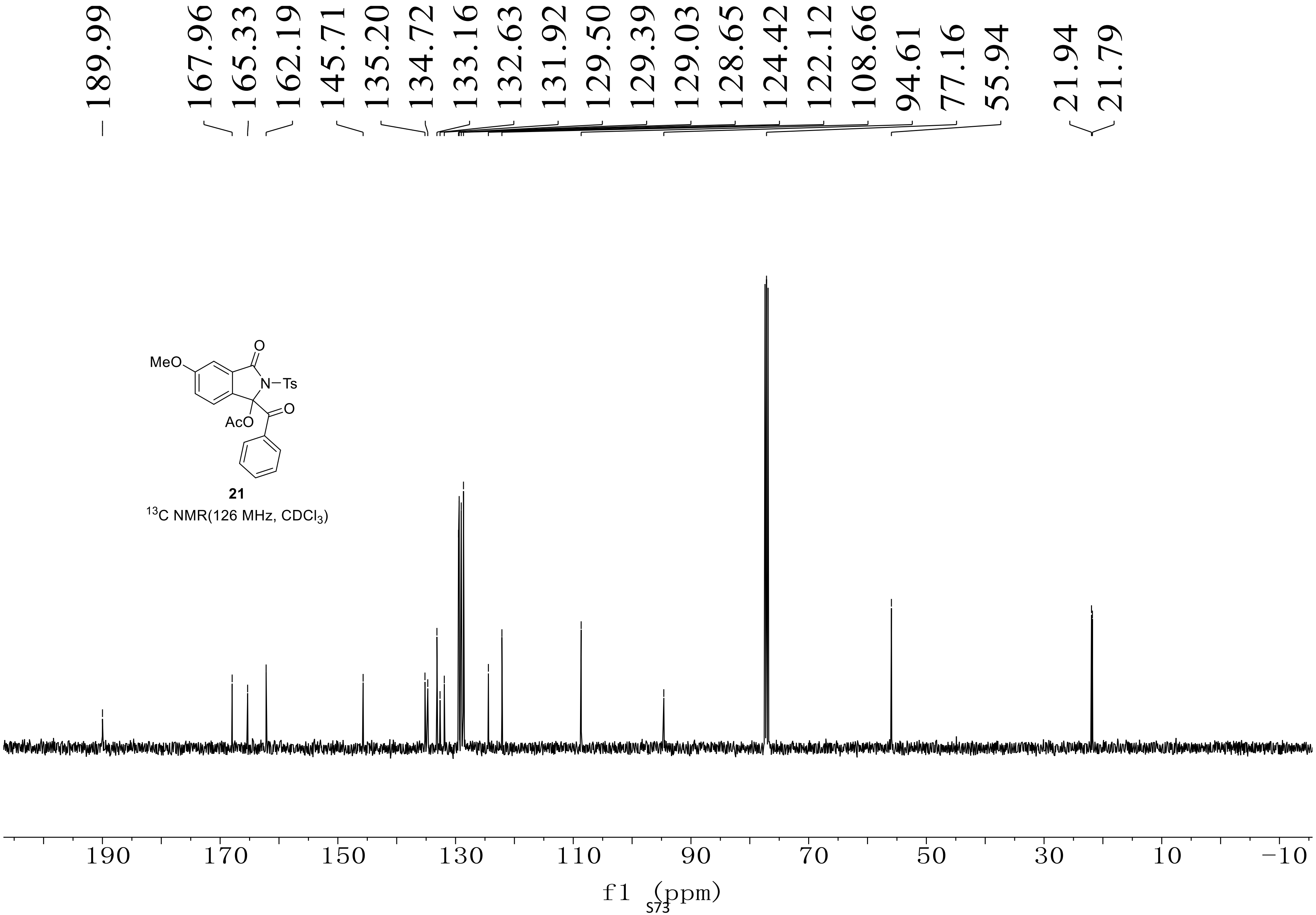
20

^{13}C NMR(126 MHz, CDCl$_3$)



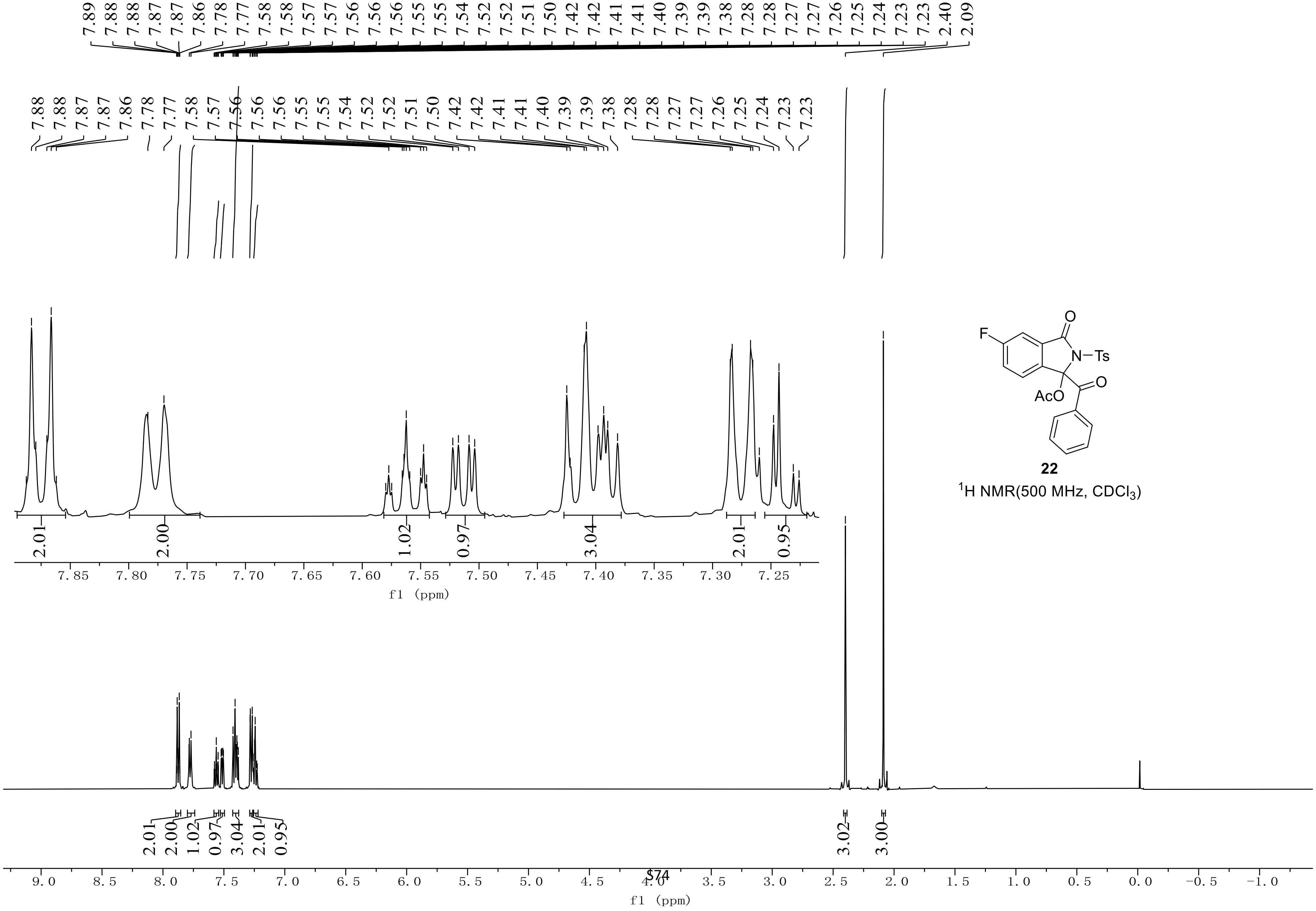
21

^{1}H NMR(500 MHz, CDCl$_3$)



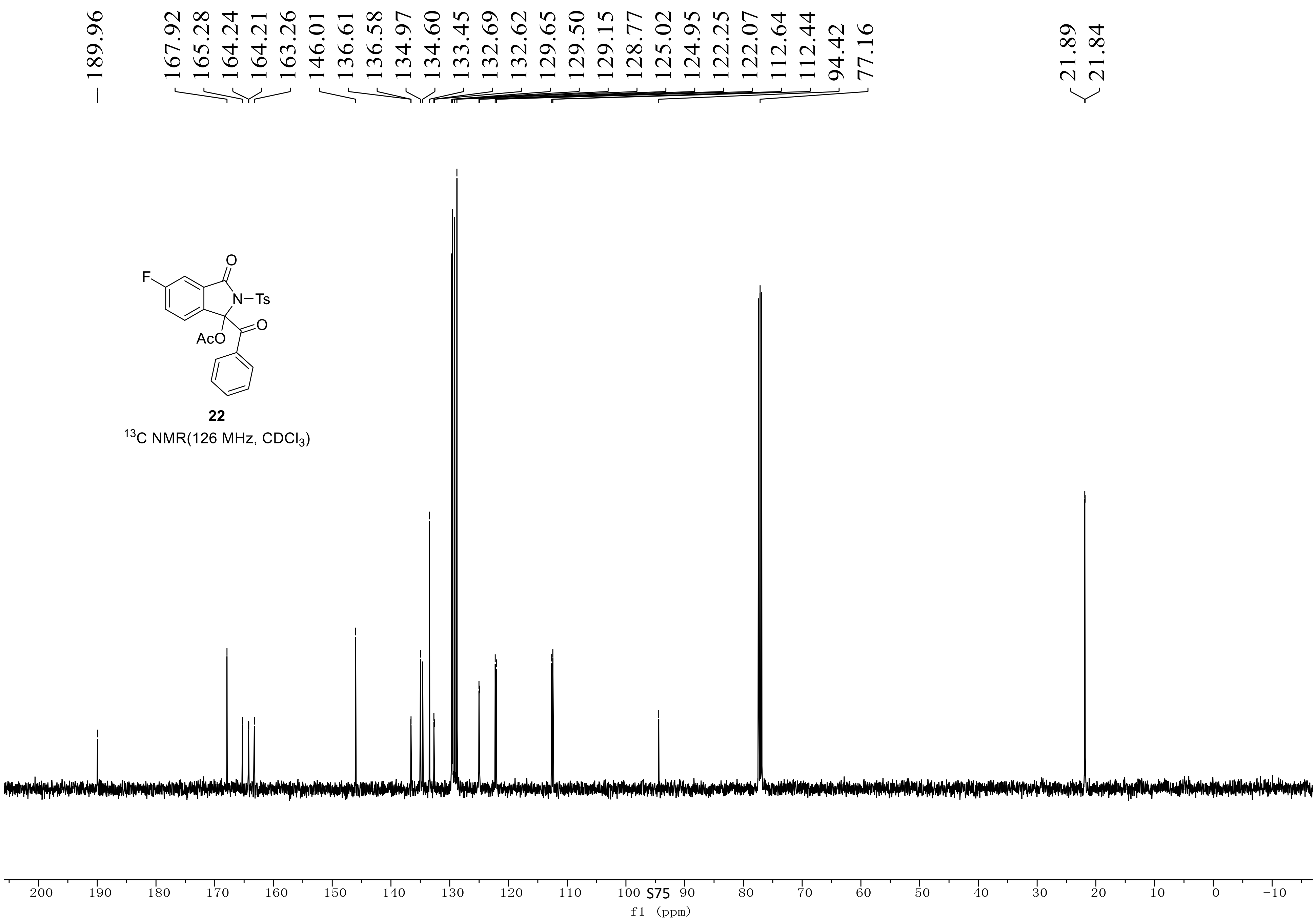
21

^{13}C NMR(126 MHz, $CDCl_3$)



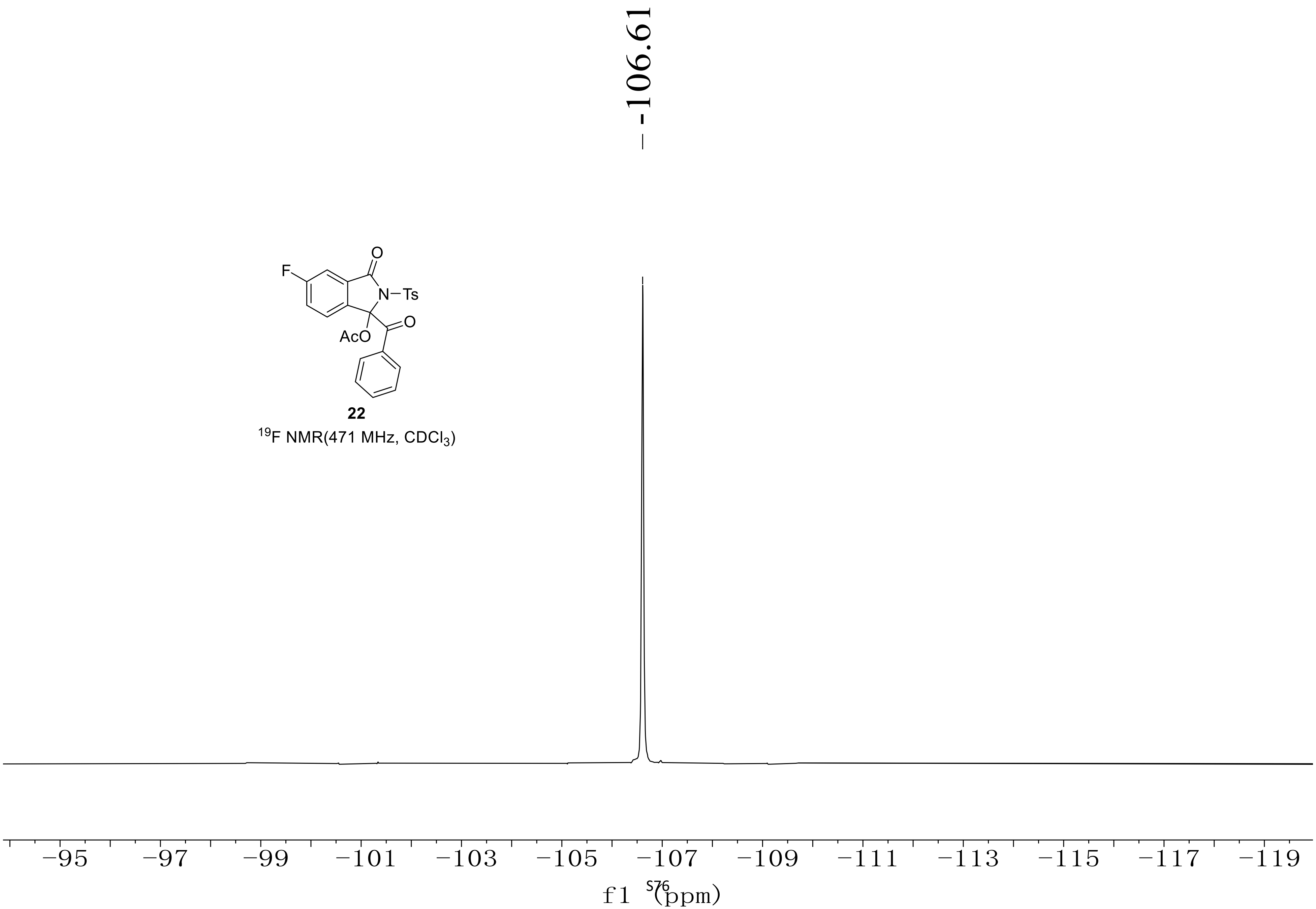
22

^{1}H NMR(500 MHz, CDCl$_3$)



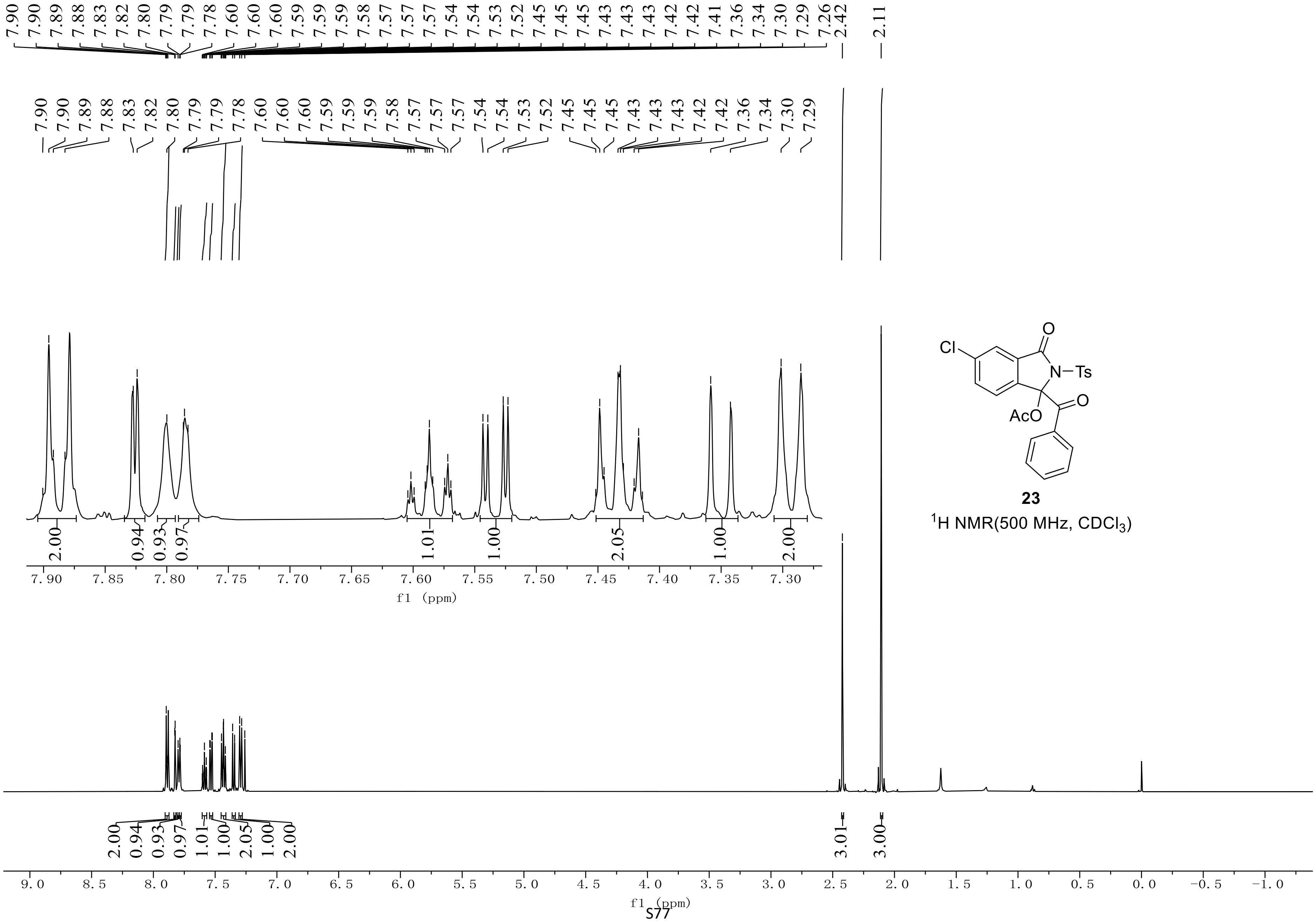
22

^{13}C NMR(126 MHz, CDCl$_3$)



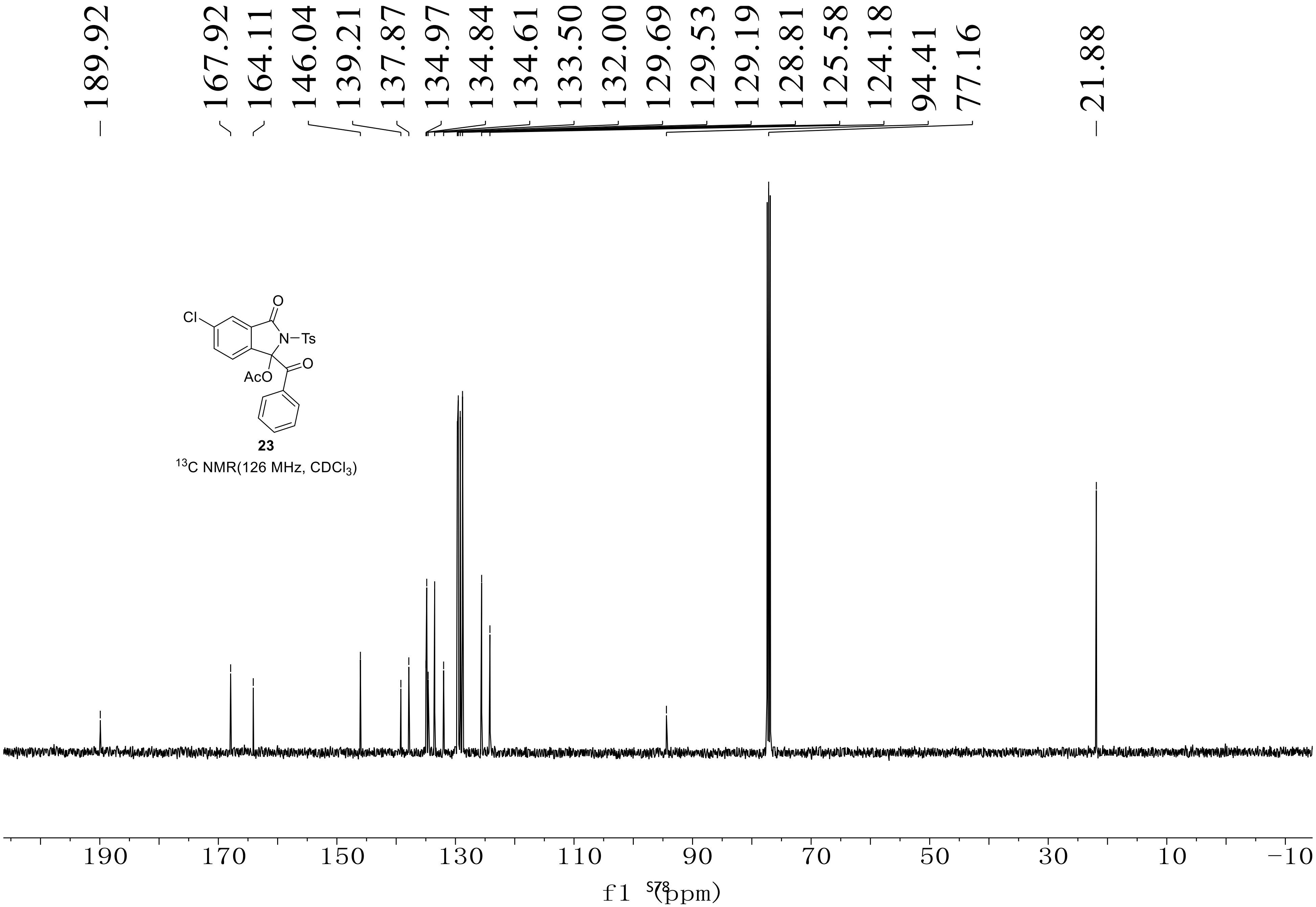
22

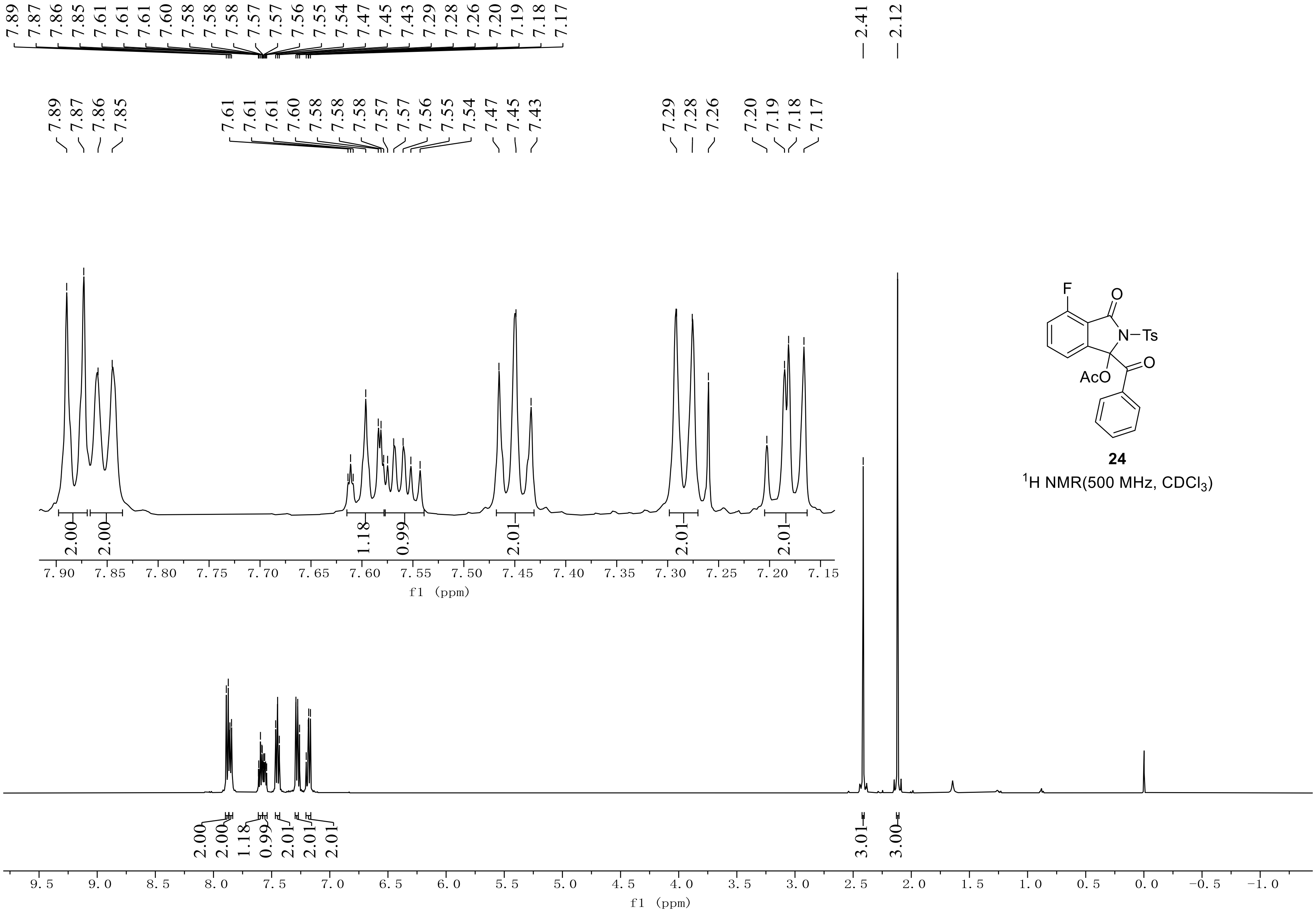
^{19}F NMR(471 MHz, CDCl$_3$)



23

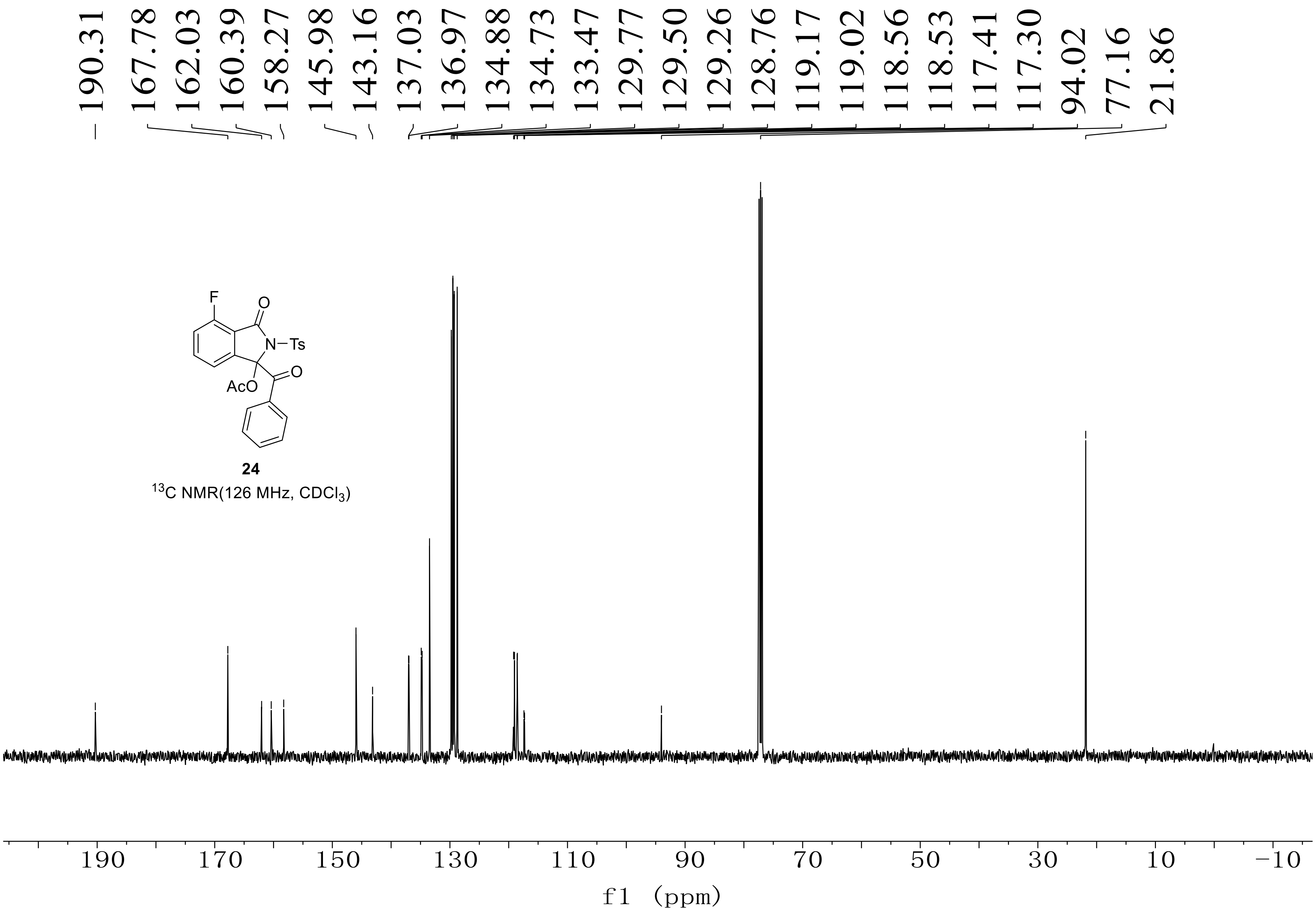
^{1}H NMR(500 MHz, CDCl$_3$)


189.92
167.92
164.11
146.04
139.21
137.87
134.97
134.84
134.61
133.50
132.00
129.69
129.53
129.19
128.81
125.58
124.18
94.41
77.16
21.88
Cl
O
N−Ts
O
AcO
23
^{13}C NMR(126 MHz, CDCl$_3$)
190
170
150
130
110
90
70
50
30
10
−10
f1 (ppm)



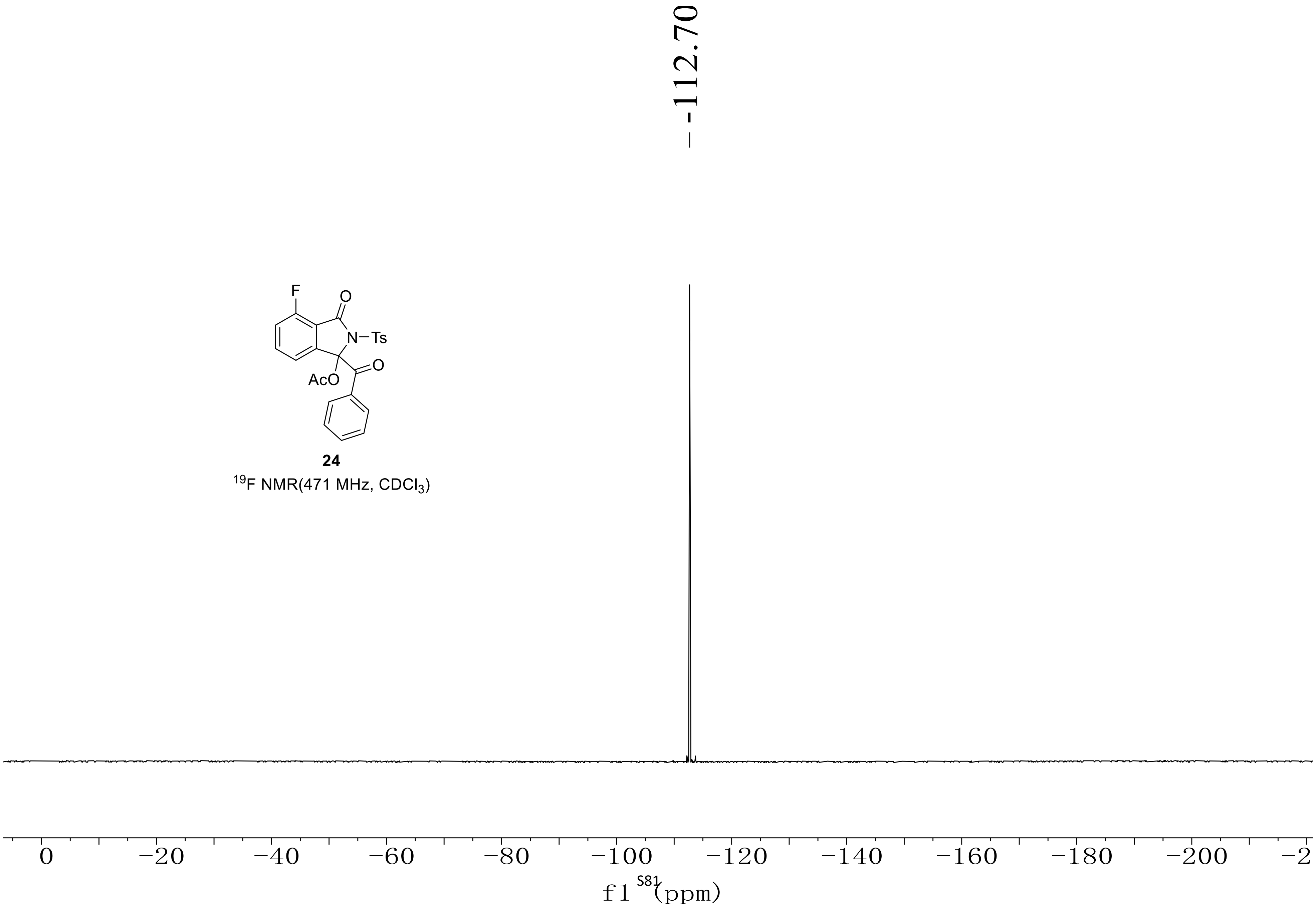
24

^{1}H NMR(500 MHz, CDCl$_3$)



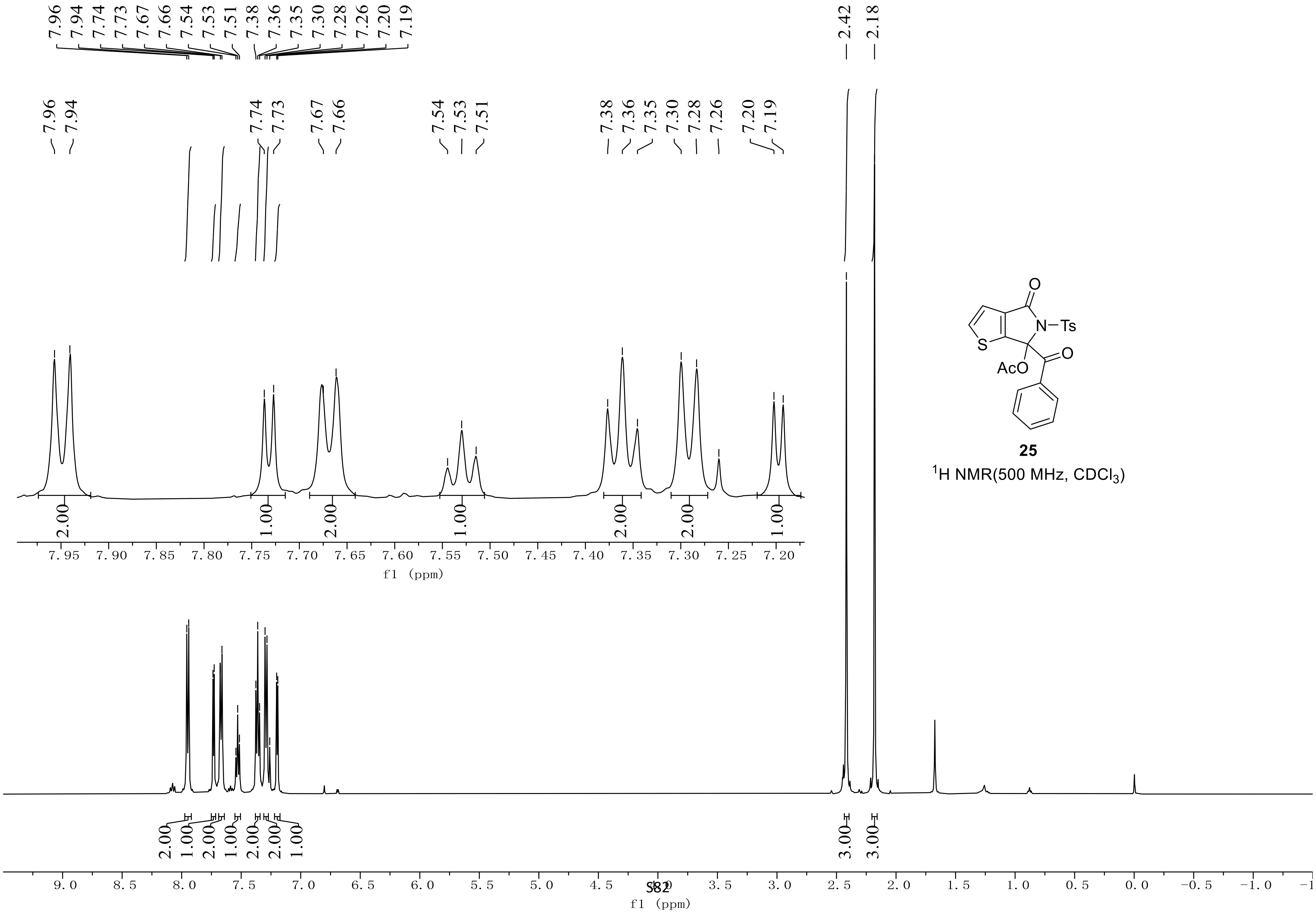
24

^{13}C NMR(126 MHz, $CDCl_3$)



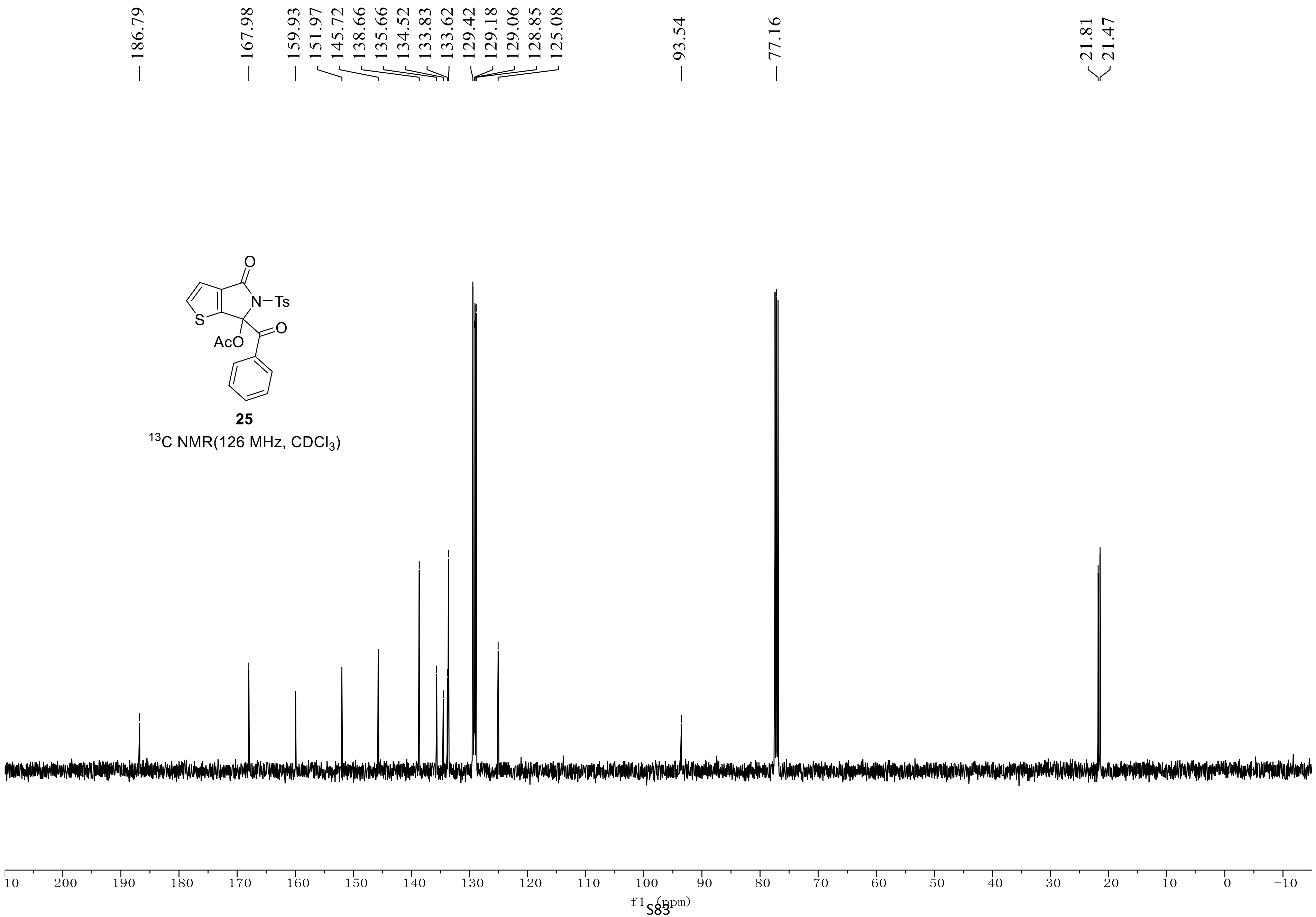
24

^{19}F NMR(471 MHz, $CDCl_3$)



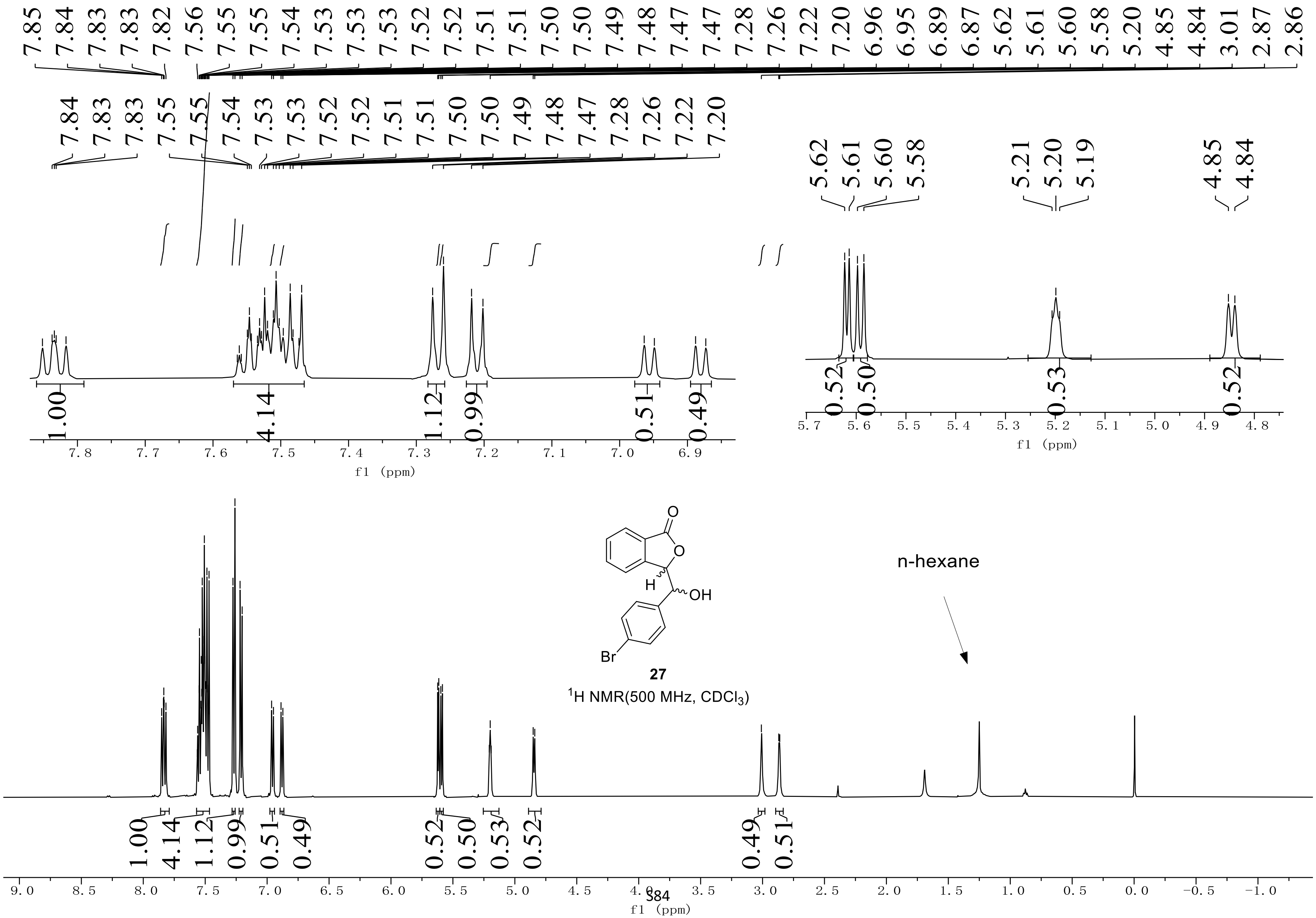
25

^{1}H NMR(500 MHz, $CDCl_3$)



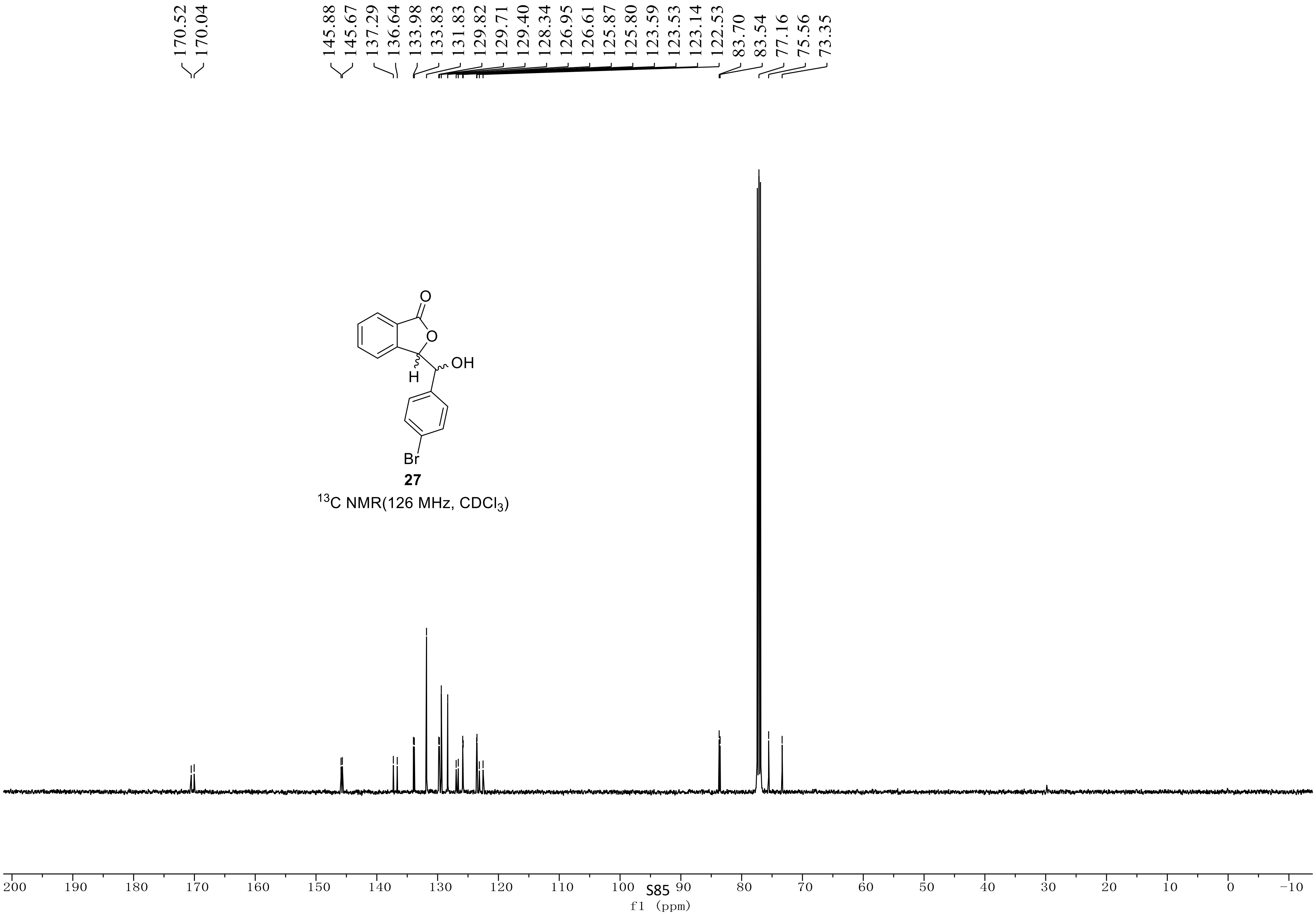
25

^{13}C NMR(126 MHz, CDCl$_3$)



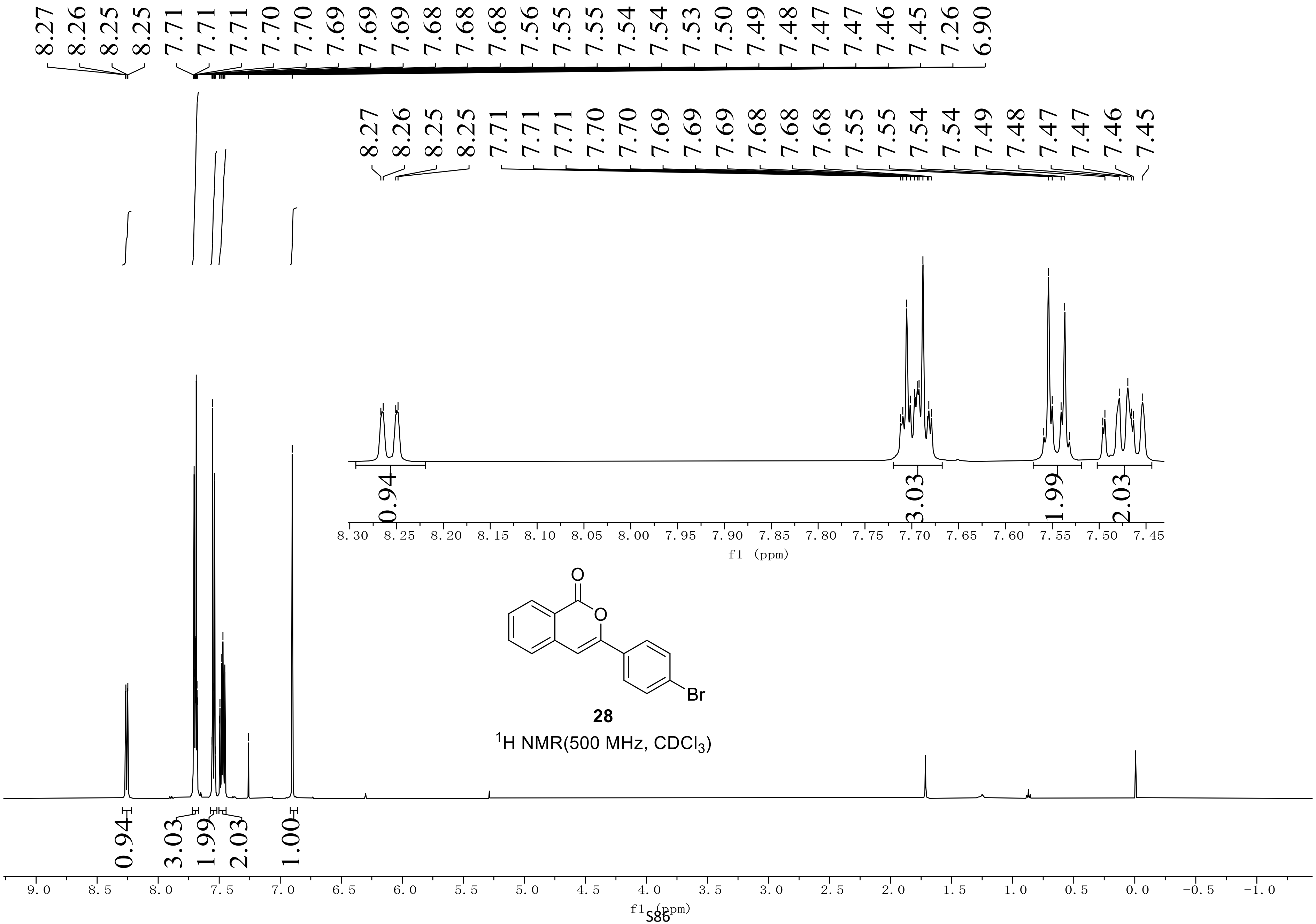
27

^{1}H NMR(500 MHz, $CDCl_3$)



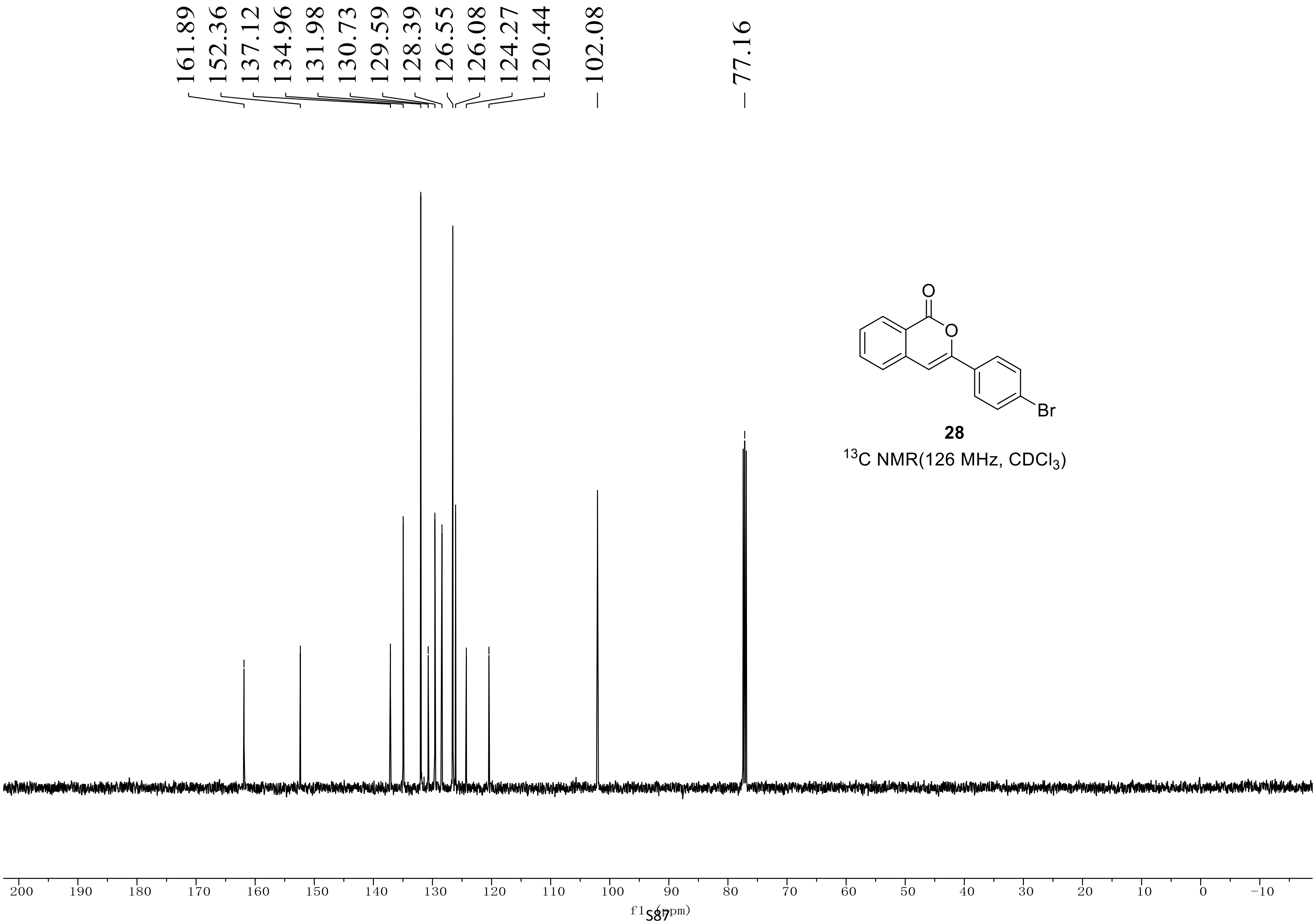
27

^{13}C NMR(126 MHz, $CDCl_3$)



28

^{1}H NMR(500 MHz, CDCl$_3$)



28

^{13}C NMR(126 MHz, CDCl$_3$)

11. X-ray Crystallographic Data

11.1 The structure of **2** was determined by the X-ray diffraction. Recrystallized from dichloromethane and petroleum ether. Further information can be found in the CIF file (Deposition number: CCDC 2115491)

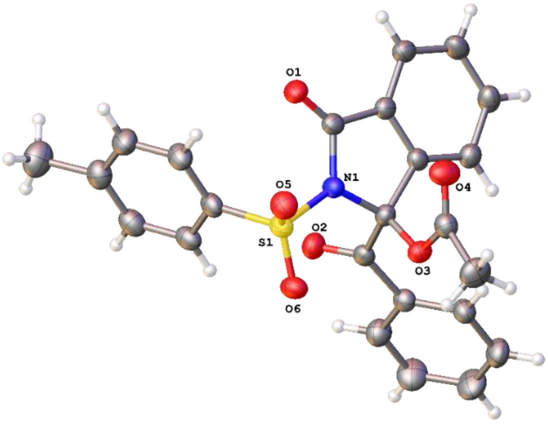


Figure S2. X-ray structure of 2

```
Bond precision:  C-C = 0.0029 A          Wavelength=0.71073

Cell:            a=13.649(3)     b=14.265(3)        c=11.970(2)
                 alpha=90        beta=112.46(3)     gamma=90
Temperature:     296 K

                Calculated                  Reported
Volume          2153.8(9)                   2153.9(9)
Space group     P 21/n                      P 1 21/n 1
Hall group      -P 2yn                      -P 2yn
Moiety formula  C24 H19 N O6 S              C24 H19 N O6 S
Sum formula     C24 H19 N O6 S              C24 H19 N O6 S
Mr              449.46                      449.46
Dx,g cm-3       1.386                       1.386
Z               4                           4
Mu (mm-1)       0.192                       0.192
F000            936.0                       936.0
F000'           936.98
h,k,lmax        18,19,16                    18,19,16
Nref            5891                        5762
Tmin,Tmax       0.977,0.981                 0.714,0.746
Tmin'           0.977

Correction method= # Reported T Limits: Tmin=0.714 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.978           Theta(max)= 29.293

R(reflections)= 0.0492( 3334)      wR2(reflections)= 0.1075( 5762)

S = 1.028                  Npar= 291
```

11.2 The structure of **27** was determined by the X-ray diffraction. Recrystallized from dichloromethane and petroleum ether. Further information can be found in the CIF file (Deposition number: CCDC 2115493)

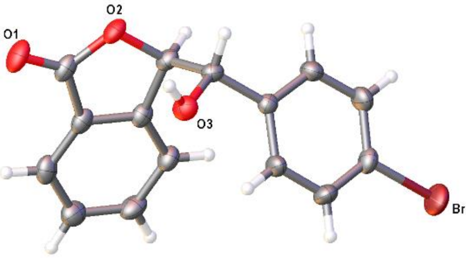
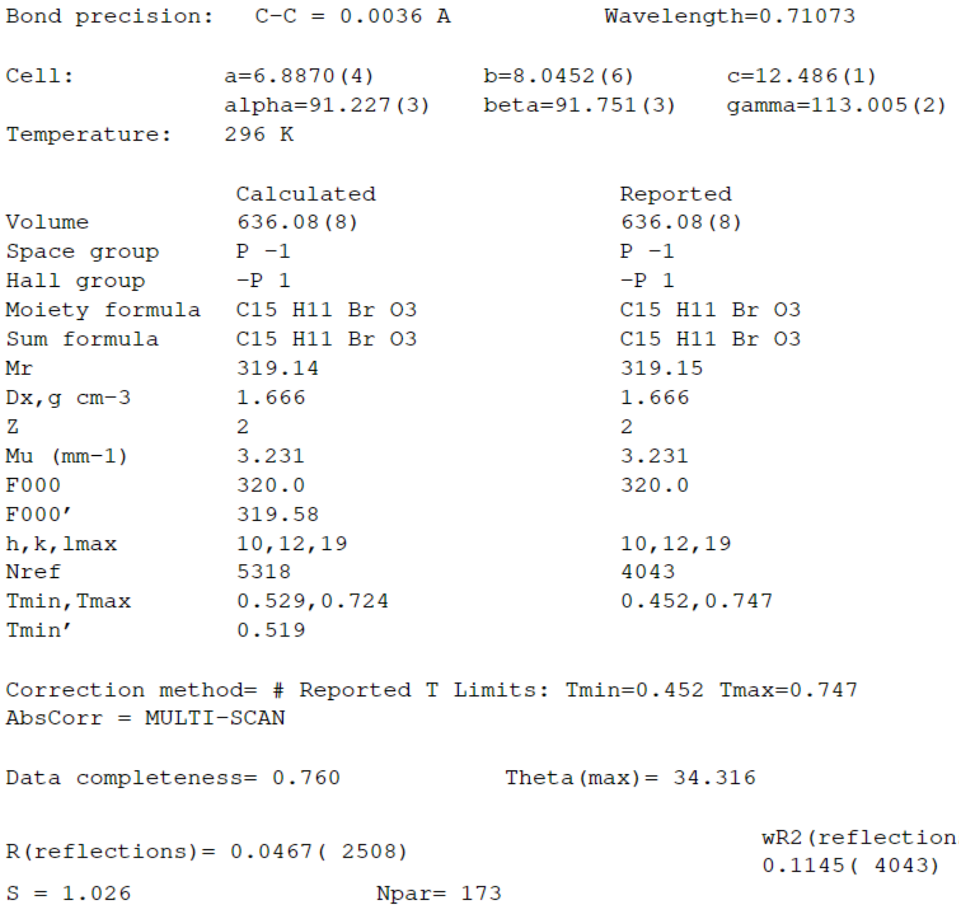


Figure S3. X-ray structure of 27



```
Bond precision:    C-C = 0.0036 A          Wavelength=0.71073

Cell:              a=6.8870(4)       b=8.0452(6)       c=12.486(1)
                   alpha=91.227(3)   beta=91.751(3)    gamma=113.005(2)
Temperature:       296 K

                    Calculated                  Reported
Volume              636.08(8)                   636.08(8)
Space group         P -1                        P -1
Hall group          -P 1                        -P 1
Moiety formula      C15 H11 Br O3               C15 H11 Br O3
Sum formula         C15 H11 Br O3               C15 H11 Br O3
Mr                  319.14                      319.15
Dx,g cm-3           1.666                       1.666
Z                   2                           2
Mu (mm-1)           3.231                       3.231
F000                320.0                       320.0
F000'               319.58
h,k,lmax            10,12,19                    10,12,19
Nref                5318                        4043
Tmin,Tmax           0.529,0.724                 0.452,0.747
Tmin'               0.519

Correction method= # Reported T Limits: Tmin=0.452 Tmax=0.747
AbsCorr = MULTI-SCAN

Data completeness= 0.760            Theta(max)= 34.316

                                                  wR2(reflections)=
R(reflections)= 0.0467( 2508)                     0.1145( 4043)

S = 1.026                  Npar= 173
```

11.3 The structure of **28** was determined by the X-ray diffraction. Recrystallized from dichloromethane and petroleum ether. Further information can be found in the CIF file (Deposition number: CCDC 2115495)

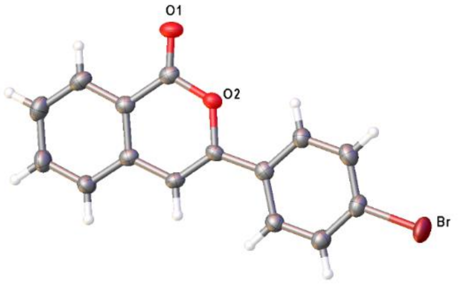


Figure S4. X-ray structure of 28

```
Bond precision:   C-C = 0.0060 A          Wavelength=0.71073

Cell:             a=7.106(10)        b=7.215(11)      c=13.194(19)
                  alpha=104.92(6)    beta=94.22(7)    gamma=111.29(6)
Temperature:      296 K

                  Calculated                    Reported
Volume            598.5(16)                     598.4(16)
Space group       P -1                          P -1
Hall group        -P 1                          -P 1
Moiety formula    C15 H9 Br O2                  C15 H9 Br O2
Sum formula       C15 H9 Br O2                  C15 H9 Br O2
Mr                301.12                        301.13
Dx,g cm-3         1.671                         1.671
Z                 2                             2
Mu (mm-1)         3.423                         3.423
F000              300.0                         300.0
F000'             299.56
h,k,lmax          8,8,15                        8,8,15
Nref              2140                          2123
Tmin,Tmax         0.670,0.710                   0.486,0.745
Tmin'             0.499

Correction method= # Reported T Limits: Tmin=0.486 Tmax=0.745
AbsCorr = MULTI-SCAN

Data completeness= 0.992           Theta(max)= 25.109

                                                      wR2(reflections)=
R(reflections)= 0.0423( 1749)                         0.1036( 2123)
S = 1.082                  Npar= 163
```