SUPPORTING INFORMATION

Rapid Nickel-Catalyzed Suzuki– Miyaura Cross-Couplings of Aryl Carbamates and Sulfamates Utilizing Microwave Heating

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General Experimental Details: ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300/360 MHz instrument at 300/360 and at 75/90 MHz, respectively. Chemical shifts (δ) are expressed in ppm downfield from TMS as internal standard. The letters s, d, t, q and m are used to indicate singlet, doublet, triplet, quadruplet and multiplet. High-resolution mass spectra were obtained on a FT-ICR-MS instrument using atmospheric pressure chemical ionization (APCI) in positive mode. Analytical HPLC analysis was carried out on a C18 reversed-phase (RP) analytical column (119 × 3 mm, particle size 5 mm) or a reversed-phase column (150 × 4.6 mm, particle size 5 mm) at 25 °C using a mobile phase A (water/acetonitrile 90:10 (v/v) + 0.1 % TFA) and B (MeCN + 0.1 % TFA) at a flow rate of 1 mL/min. The following gradient was applied: linear increase from solution 30% B to 100 % B in 6 min, hold at 100% solution B for 2.2 min. GC–MS conditions were as follows: splitless injection, injection temperature 250 °C, HP-5 MS column (30m×0.25mm ID, 0.25 μm film); carrier gas helium 5.0, flow 1 mL/min, temperature gradient programmed from 60 to 300 °C at 20 °C/min after an initial time of 6min. The MS conditions were as follows: positive EI ionization, ionization energy 70 eV, ionization source temperature 280 °C, emission current 100 μA. Melting points were obtained on a standard melting point apparatus in open capillary tubes. The synthesized compounds were purified via flash chromatography on silica gel or an automated flash chromatography system using cartridges packed with KP-SIL, 60 Å (32-63 μm particle size). TLC analyses were performed on pre-coated (silica gel 60 HF254) plates.

Starting materials including aryl carbamates,[S1,S2] aryl sulfamates,[S1] and **5**,[S3] were synthesized according to known procedures; characterization data (^{1}H and ^{13}C NMR/MS) are in agreement with literature values. The purity of all synthesized starting materials and products was determined by HPLC-UV (215 nm) chromatography and ^{1}H NMR spectroscopy. All anhydrous solvents (stored over molecular sieves), and chemicals were obtained from standard commercial vendors and were used without any further purification except where stated otherwise. Importantly, K_3PO_4 from Acros (purity 97%, anhydrous), Cat.No. 387680250 was employed for successful cross-couplings. Extra dry toluene (99.85%, water <50 ppm, AcroSeal) was purchased from Acros (Cat.No. 364410010). $Ni(PCy_3)_2Cl_2$ were purchased from Strem Chemicals Inc.

Microwave Irradiation Experiments. Microwave irradiation experiments were performed using a Monowave 300 single-mode microwave reactor from Anton Paar GmbH (Graz,

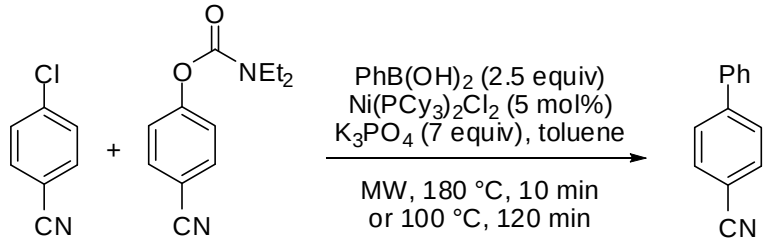
Austria).[S4] The instrument uses a maximum of 850 W magnetron output power and can be operated at 300 °C reaction temperature and 30 bar pressure. The reaction temperature is monitored by an external infrared sensor (IR) housed in the side-walls of the microwave cavity measuring the surface temperature of the reaction vessel, and/or by an internal fiber-optic (FO) temperature probe (ruby thermometer) protected by a borosilicate immersion well inserted directly to the reaction mixture. The magnetron output power can either be controlled by the FO probe (IR as slave) or by the IR sensor (FO as slave). Pressure sensing is achieved by a hydraulic sensor integrated in the swiveling cover of the instrument. The reusable Pyrex vials (10 mL and 30 mL) are sealed with PEEK snap caps and standard PTFE coated silicone septa. In case of FO temperature measurement punched seals to insert the immersing tube are employed. Seals and caps can be used for both Pyrex vial types and the 10 mL SiC vial as well. Precision of internal temperature measurement is provided by efficient stirring at a fixed rate of 600 rpm. Reaction cooling is performed by compressed air automatically after the heating period has elapsed. The required force of 6-8 bar is also used to pneumatically seal the vials tightly at the beginning to withstand 30 bar, and to ensure smooth release of potentially remaining pressure before opening the cover.

Microwave irradiation experiments on large scale were performed using a Masterwave Bench-Top Reactor from Anton Paar GmbH (Graz, Austria).[S5]

Figure S1. Masterwave BTR reactor (left) and 1 L PTFE vessel for up to 700 mL scale processes with stirring system (right).

Comparison Experiments Involving Aryl Chlorides and Aryl Carbamates in Ni-Catalyzed Suzuki–Miyaura Cross-Couplings

In order to evaluate the relative reactivity of aryl carbamates and aryl chlorides in these coupling processes a competition experiment was designed where equimolar amounts of both types of substrates were reacted with phenylboronic acid using the optimized coupling conditions (see Scheme below). At 180 °C full conversion was achieved within 10 min for aryl the chloride, while only 20% of the aryl carbamate had converted to biaryl product. Performing the same experiment at 100 °C, similar results were obtained after 2 h: 90% conversion for the aryl chloride, versus only 5% for the aryl carbamate. These results clearly demonstrate that aryl chlorides are far more reactive than the corresponding carbamates. Therefore, chloride substitution is not tolerated on either the aryl carbamate/sulfamate or the boronic acid coupling partner in these nickel-catalyzed Suzuki–Miyaura cross-coupling reactions involving phenol derived electrophiles.

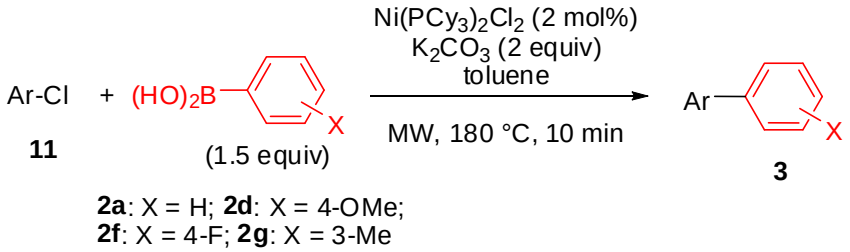


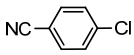
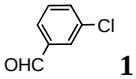
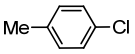
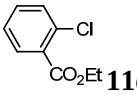
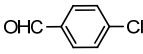
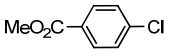
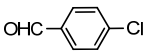
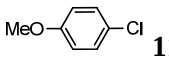
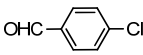
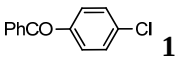
Optimization Experiments Using Aryl Chlorides in Ni-Catalyzed Suzuki–Miyaura Cross-Couplings

Having an optimized set of highly efficient cross-coupling conditions for aryl carbamates and sulfamates in hand, we decided to re-optimize the coupling parameters also for aryl chloride substrates. Although nickel-catalyzed Suzuki–Miyaura cross-coupling reactions involving aryl chlorides have been reported previously, high-speed microwave-assisted methods have –with very few exceptions–[S6] not been reported. Since aryl chlorides are significantly more reactive compared to aryl carbamates and sulfamates, it was possible to achieve high conversions with lower catalyst and base loadings for this type of substrate. Optimized conditions involved the use of 2 mol % of $Ni(PCy_3)_2Cl_2$ as catalyst, 2 equiv of K_2CO_3 base and 1.5 equiv of aryl boronic acid, keeping the other reaction parameters unchanged. Under these set of conditions a diverse range of aryl chlorides **11a-h** could be cross-coupled with

aryl boronic acids **2** providing the desired biaryl cross-coupling products **3** in high yields (Table S1). Para-, meta-, and ortho-substituted aryl chlorides all coupled with aryl boronic acids in excellent yields. Notably, the presence of aldehyde groups was well tolerated under the reaction conditions (entries 3-6). Functional group compatibility extended to alkyl esters (entries 7 and 8), ketones (entry 10), and nitriles (entries 1). Reactions of electron-rich aryl chlorides proved to be more difficult under these modified conditions (entry 9), however, by reinstating the original reaction conditions optimized for aryl carbamates and sulfamates also these substrates could be coupled in high yield within 10 min. Conversely, for reactive aryl chlorides (entries 3,5,6 and 10) the amount of nickel catalyst could be reduced to 1 mol% using only 1 equiv of K_2CO_3 base.

Table S1. Aryl Chlorides in Microwave-Assisted Suzuki–Miyaura cross-coupling reactions[a]

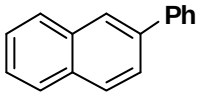


entry	11	$ArB(OH)_2$	3 (yield, %)	entry	11	$ArB(OH)_2$	3 (yield, %)
1	 **11a**	**2a**	**3i** (85)	6[b]	 **11d**	**2a**	**3r** (93)
2	 **11b**	**2d**	**3g** (84)	7	 **11e**	**2a**	**3s** (78)
3[b]	 **11c**	**2a**	**3o** (95)	8	 **11f**	**2f**	**3t** (85)
4	 **11c**	**2f**	**3p** (95)	9	 **11g**	**2a**	**3h** (45) [82][c]
5[b]	 **11c**	**2g**	**3q** (85)	10[b]	 **11h**	**2a**	**3u** (80)

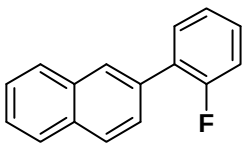
[a] Reaction conditions: sealed vessel single-mode microwave heating (Monowave 300) with internal fiber-optic temperature control and magnetic stirring; 0.3 mmol of **9**, 0.45 mmol of **2**, 0.006 mmol of $Ni(PCy_3)_2Cl_2$, 0.60 mmol of K_2CO_3 in 2 mL toluene; 180 °C for 10 min.
[b] Reaction performed with 1 mol% of $Ni(PCy_3)_2Cl_2$ catalyst and 1 equiv of base.
[c] 3 mol% of $Ni(PCy_3)_2Cl_2$ and 7 equiv of K_3PO_4.

General Procedure for the Cross-Coupling Reaction of Aryl Carbamate and/or Aryl Sulfamates with Aryl Boronic Acids (Table 2)

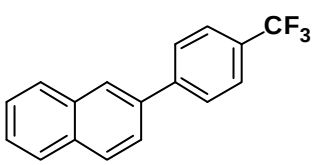
Aryl carbamate and/or aryl sulfamate (0.3 mmol), arylboronic acid (0.75 mmol, 2.5 equiv), potassium phosphate (2.1 mmol, 450 mg, 7 equiv) and bis(tricyclohexylphosphine)nickel(II) chloride (10.3 mg, 0.015 mmol, 5 mol%) were added to a 10 mL flame dried microwave vial containing a Teflon coated stir bar. After the vial was sealed dry toluene (2 mL) was transferred to the vial and the mixture was purged with Ar for 2 min. The vessel was subsequently placed in the microwave cavity and irradiated for 10 min at 180 °C (hold time). After cooling, ethyl acetate (10 mL) was added and the crude reaction mixture was subsequently washed with 25% aqueous ammonia (2 × 10 mL). The aqueous ammonium layer was reextracted again with ethyl acetate (2 × 10 mL). The combined organic phases were dried over $MgSO_4$ and the residue after evaporation purified by flash chromatography using a mixture of petroleum ether and ethyl acetate as eluent solvent. All compounds are literature known and NMR data are in agreement with published data.



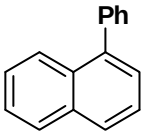
3a:[S2] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.48 (m, 1H), 7.53-7.60 (m, 4H), 7.78-7.83 (m, 3H), 7.91-7.99 (m, 3H), 8.11 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.2, 138.6, 133.7, 132.6, 128.9, 128.4, 128.2, 127.7, 127.5, 127.4, 126.3, 126.0, 125.8, 125.6.



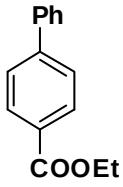
3b:[S7] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23-7.33 (m, 2H), 7.33-7.44 (m, 1H), 7.54-7.65 (m, 3H), 7.77 (dt, *J* = 8.4, 1.8, 1H), 7.92-7.99 (m, 3H), 8.10 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.0 (d, *J*CF = 246.3 Hz), 133.4, 133.3, 132.7, 131.1 (d, *J*CF = 3.4 Hz), 129.1 (d, *J*CF = 8.2 Hz), 128.3, 128.1 (d, *J*CF = 2.8 Hz), 128.0, 127.7, 127.1 (d, *J*CF = 2.9 Hz), 126.3, 124.5 (d, *J*CF = 3.7 Hz), 116.2 (d, *J*CF = 22.6 Hz).



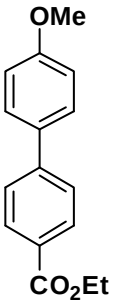
3c:[S7] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54-7.61 (m, 2H), 7.74-7.78 (m, 3H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.91-7.99 (m, 3H), 8.09 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 137.0, 133.6, 133.0, 129.8, 129.4 (q, *J*CF = 32.2 Hz), 128.8, 128.3, 127.7, 127.6, 126.5, 126.4, 126.3, 125.8 (q, *J*CF = 3.8 Hz), 125.2, 119.0.



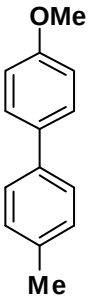
3d:[S2] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.62 (m, 9H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.96-8.00 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.8, 140.3, 133.8, 131.6, 130.1, 128.8, 128.3, 127.7, 127.3, 127.2, 126.9, 126.1, 125.8, 125.4.



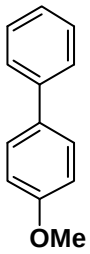
3e:[S8] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44 (t, *J* = 7.2 Hz, 3H), 4.43 (q, *J* = 7.2 Hz, 2H), 7.39-7.52 (m, 3H), 7.63-7.70 (m, 4H), 8.12-8.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 145.5, 140.0, 130.0, 129.2, 128.9, 128.1, 127.3, 127.0, 61.0, 14.4.



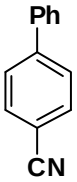
3f:[S8] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (t, *J* = 7.2 Hz, 3H), 3.87 (s, 3H), 4.43 (q, *J* = 7.2 Hz, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 7.57-7.64 (m, 4H), 8.11 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 159.8, 145.1, 132.4, 130.0, 128.3, 126.4, 114.3, 60.9, 55.3, 14.4.



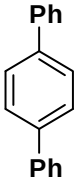
3g:[S9] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 3.89 (s, 3H), 7.03 (d, *J* = 9 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9, 138.0, 136.3, 133.7, 129.5, 128.0, 126.6, 114.2, 55.3, 21.1.



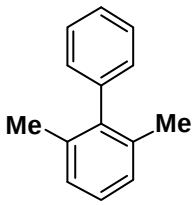
3h:[S10] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 3H), 7.02 (d, *J* = 8.7 Hz, 2H), 7.34 (tt, *J* = 7.5, 2.1 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.55-7.62 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1, 140.8, 133.8, 128.7, 128.1, 126.7, 126.7, 114.2, 55.3.



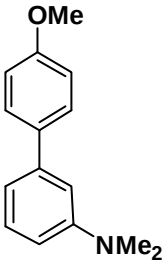
3i:[S10] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.53 (m, 3H), 7.59-7.63 (m, 2H), 7.68-7.76 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 139.1, 132.6, 129.1, 128.6, 127.7, 127.2, 118.9, 110.9.



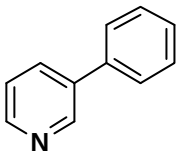
3j:[S11] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36-7.41 (m, 2H), 7.46-7.51 (m, 4H), 7.66-7.71 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.7, 140.1, 128.8, 127.5, 127.3, 127.0.



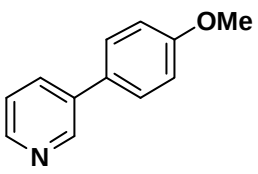
3k:[S1] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.06 (s, 6H), 3.89 (s, 3H), 6.74-6.78 (m, 1H), 6.95-7.03 (m, 3H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.9, 141.1, 136.0, 129.0, 128.4, 127.3, 127.0, 126.6, 20.8.



3l:[S9] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.06 (s, 6H), 3.89 (s, 3H), 6.74-6.78 (m, 1H), 6.95-7.03 (m, 3H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.0, 150.9, 141.8, 134.8, 129.4, 128.3, 115.6, 114.0, 111.3, 111.2, 55.3, 40.8.



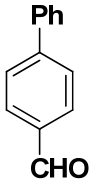
3m:[S2] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.52 (m, 4H), 7.57-7.61 (m, 2H), 7.89 (dt, *J* = 7.5, 1.8 Hz, 1H), 8.60 (dd, *J* = 4.8, 1.8 Hz, 1H), 8.87 (d, *J*= 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.4, 148.2, 137.8, 136.6, 134.4, 129.1, 128.1, 127.1, 123.5.



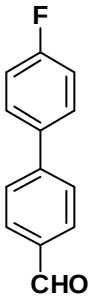
3n:[S2] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (s, 3H), 7.03 (d, *J* = 8.7 Hz, 2H), 7.32-7.37 (m, 1H), 7.53 (d, *J* = 9 Hz, 2H), 7.82-7.86 (m, 1H), 8.56 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.83 (d, *J*= 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 148.0, 147.8, 136.2, 133.8, 130.2, 128.2, 123.5, 114.5, 55.4.

General Procedure for the Cross-Coupling Reaction of Aryl Chlorides with Aryl Boronic Acids (Table S1)

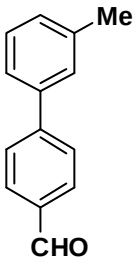
Aryl chloride (0.3 mmol), arylboronic acid (0.45 mmol), potassium carbonate (0.6 mmol, 84 mg, 2 equiv) and bis(tricyclohexylphosphine)nickel(II) chloride (4 mg, 0.006 mmol, 2 mol%) were added to a 10 mL flame dried microwave vial containing a Teflon coated stir bar. After the vial was closed dry toluene (2 mL) was transferred to the vial and the mixture was purged with Ar for 2 min. The vial was subsequently placed in the microwave cavity and irradiated for 10 min at 180 °C (hold time). After cooling, ethyl acetate (10 mL) was added and the crude reaction mixture was subsequently washed with 25% aqueous ammonia (2 × 10 mL). The aqueous ammonium layer was reextracted with ethyl acetate (2 × 10 mL). The combined organic phases were dried over $MgSO_4$ and the residue after evaporation purified by flash chromatography using a mixture of petroleum ether and ethyl acetate as eluent solvent.



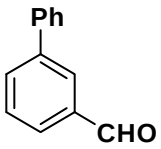
3o:[S10] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41-7.53 (m, 3H), 7.64-7.67 (m, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H), 10.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 147.2, 139.7, 135.2, 130.3, 129.0, 129.0, 128.5, 127.7, 127.3.



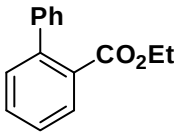
3p:[S6] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.15-7.21 (m, 2H), 7.54-7.64 (m, 2H), 7.72 (d, *J* = 7.5 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 10.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.8, 163.1 (d, *J*CF = 246.9 Hz), 146.1, 135.8 (d, *J*CF = 3.2 Hz), 135.1, 129.0 (d, *J*CF = 8.2 Hz), 127.5, 115.1 (d, *J*CF = 21.4 Hz).



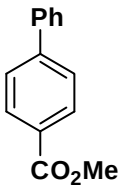
3q:[S12] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.46 (s, 3H), 7.24-7.27 (m, 1H), 7.36-7.47 (m, 3H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 10.07 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 147.3, 139.7, 138.7, 135.1, 130.2, 129.2, 128.9, 128.1, 127.7, 124.5, 21.5.



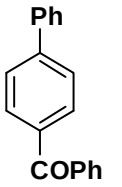
3r:[S13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.60 (m, 4H), 7.63-7.67 (m, 3H), 7.88 (dd, *J* = 7.5, 1.8 Hz, 2H), 8.12 (d, *J* = 1.8 Hz, 1H), 10.11 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.3, 142.1, 139.7, 136.9, 133.0, 129.5, 129.0, 128.6, 128.2, 128.0, 127.1.



3s:[S14] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (t, *J* = 7.2 Hz, 3H), 4.11 (q, *J* = 7.2 Hz, 2H), 7.33-7.46 (m, 7H), 7.54 (td, *J* = 7.5, 1.2 Hz, 1H), 7.86 (dd, *J* = 7.5, 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8, 142.4, 141.5, 131.3, 131.1, 130.6, 129.7, 128.4, 128.0, 127.1, 60.9, 13.6.



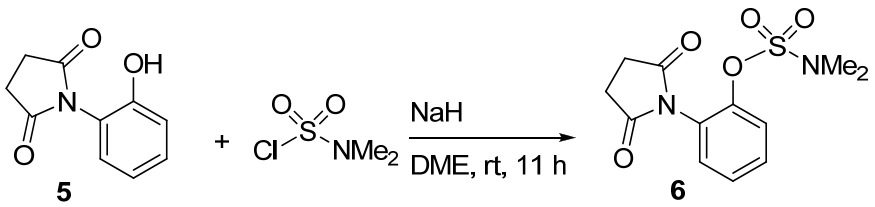
3t:[S10] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.96 (s, 3H), 7.39-7.51 (m, 3H), 7.63-7.70 (m, 4H), 8.13 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 145.6, 140.0, 130.1, 128.9, 128.9, 128.1, 127.2, 127.0, 52.1.



3u:[S15] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40-7.46 (m, 1H), 7.48-7.55 (m, 4H), 7.60-7.70 (m, 3H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.85-7.88 (m, 2H), 7.93 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.3, 145.2, 139.9, 137.7, 136.2, 132.4, 130.7, 130.0, 129.0, 128.3, 128.2, 127.3, 127.0.

Synthesis of 2-Phenylaniline 8 (Scheme 2)

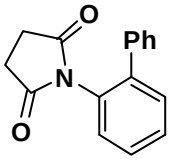
*1) Preparation of aryl sulfamate substrate **6***



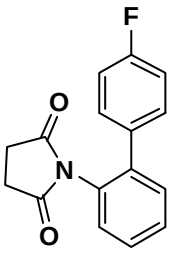
A round bottom flask was charged with NaH (0.2 g, 5 mmol, 1.2 equiv, 60% dispersion in oil), and cooled to 0 °C. Then a solution of substrate **5**[S3] (0.76 g, 4 mmol, 1 equiv) in DME (30 mL) was added dropwise to the NaH. The resulting solution was stirred for 20 min at 0 °C. A solution of dimethyl sulfamoyl chloride (1.2 equiv) in DME (6 mL) was then added dropwise to the reaction vessel. The reaction was warmed to rt, allowed to stir for 11 h, and then quenched with several drops of water. The solvent was removed under reduced pressure,

and the solid material was dissolved in EtOAc (50 mL) and H_20 (15 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with H_2O (15 mL). The combined aqueous layers were extracted with EtOAc (3×20 mL). The combined organic layers were then washed with brine (15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (1:3 ethyl acetate:petroleum ether) to yield 0.89 g of sulfamate **6** as a white solid powder, mp. 120-121 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.83 (s, 4H, 2 CH_2), 2.86 (s, 6H, 2 CH_3), 7.37 (dd, J = 7.5, 1.8 Hz, 1H), 7.43-7.50 (m, 2H), 7.53-7.59 (m, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ176.3, 145.7, 130.9, 130.6, 127.6, 125.9, 123.2, 38.7, 28.9. HRMS (APCI$^+$) m/z Calcd for $C_{12}H_{15}O_5N_2S$ $[M + H]^+$ 299.0696. Found 299.0696.

*2) Preparation of biaryl compounds **7a** and **7b** (see general procedure for aryl sulfamate coupling)*



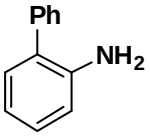
7a: mp. 132-133 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.46-2.82 (m, 4H, 2 CH_2), 7.21-7.27 (m, 3H), 7.31-7.41 (m, 3H), 7.46-7.56 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.4, 141.0, 138.5, 130.8, 129.9, 129.7, 128.6, 128.5, 128.3, 128.1, 127.7, 28.3. HRMS (APCI$^+$) m/z Calcd for $C_{16}H_{13}NO_2$ $[M + H]^+$ 252.1019. Found 252.1023.



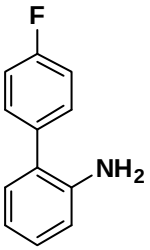
7b: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.48-2.84 (m, 4H, 2 CH_2), 7.03-7.10 (m, 2H), 7.19-7.25 (m, 3H), 7.42-7.53 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.3, 162.4 (d, JCF = 245.5 Hz), 140.081, 134.5 (d, JCF = 3.3 Hz), 130.877, 130.058, 129.9 (d, JCF = 8.0 Hz), 129.8, 128.8, 128.6, 115.3 (d, JCF = 21.3 Hz), 28.4. HRMS (APCI$^+$) m/z Calcd for $C_{16}H_{13}NFO_2$ $[M + H]^+$ 270.0925. Found 270.0924.

*3) General procedure for the synthesis **8a** and **8b** (**7**→**8**)*

A solution of succinimide **7** (0.6 mmol) in EtOH (3 mL) containing hydrazine monohydrate (133 μL, 2.74 mmol) was heated under microwave irradiation at 180 °C for 40 min. The solvent was removed under reduced pressure. The residue was triturated with Et_20 (3 × 10 mL), and the combined ethereal supernatants were concentrated under reduced pressure to give **8**.



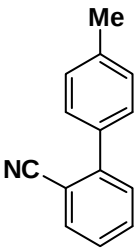
8a:[S16] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.67 (brs, 2H, NH_2), 6.63-6.74 (m, 2H), 7.01-7.07 (m, 2H), 7.30-7.36 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 139.5, 130.4, 129.1, 128.8, 128.5, 127.6, 127.1, 118.6, 115.6.



8b:[S17] ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.64 (brs, 2H, NH_2), 6.62-6.72 (m, 2H), 6.96-7.06 (m, 4H), 7.27-7.32 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.0 (d, *J*CF = 244.5 Hz), 143.6, 135.4 (d, *J*CF = 3.3 Hz), 130.7 (d, *J*CF = 7.8 Hz), 130.4, 128.6, 126.5, 118.6, 115.7 (d, *J*CF = 21.1 Hz), 115.6.

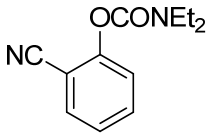
Preparation of the Sartan Precursor 2-(4-Tolyl)benzonitrile (10) (Scheme 3)

Ni-catalyzed crosss-coupling reactions were performed according to the general procedures for aryl carbamates, sulfamates and chlorides (see above).



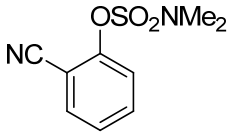
10:[S18] ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H, CH_3), 7.19 (d, *J* = 8.1 Hz, 1H), 7.27-7.40 (m, 4H), 7.51 (td, *J* = 7.8, 1.5 Hz, 1H), 7.63 (dd, *J* = 7.8, 0.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.5, 138.7, 135.3, 133.7, 132.8, 130.0, 129.4, 128.6, 127.3, 118.9, 111.1, 21.3.

Preparation of ***9b***[S1]



A round bottom flask was charged with NaH (200 mg, 5 mmol, 1.2 equiv, 60% dispersion in oil), and cooled to 0 ºC. Then a solution of 2-hydroxybenzonitrile (476 mg, 4 mmol, 1 equiv) in DME (20 mL) was added dropwise to the NaH. The resulting solution was warmed to rt for 10 min, and then cooled to 0 ºC. A solution of diethyl carbamoyl chloride (5 mmol, 1.2 equiv) was then added dropwise to the reaction mixture. The reaction was warmed to rt, allowed to stir for 24 h, and then quenched with several drops of water. The solvent was removed under reduced pressure, and the solid material was dissolved in Et_2O (50 mL) and H_2O (15 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with 1 M KOH (15 mL), then H_2O (15 mL). The combined aqueous layers were extracted with Et_2O (3×20 mL). The combined organic layers were then washed with brine (15 mL), dried over MgSO4, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (1:4 ethyl acetate:petroleum ether) to afford corresponding carbamate as a colorless oil in 78% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (t, *J* = 7.5 Hz, 3H, CH_3), 1.33 (t, *J* = 7.5 Hz, 3H, CH_3), 3.41 (q, *J* = 7.5 Hz, 2H, CH_2), 3.52 (q, *J* = 7.5 Hz, 2H, CH_2),7.28 (td, *J* = 7.8, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.4, 0.6, 1H), 7.57-7.66 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.3, 152.5, 133.8, 133.0, 125.3, 123.3, 115.6, 106.8, 42.6, 42.3, 14.1, 13.2. HRMS (APCI$^+$) m/z Calcd for $C_{12}H_{15}N_2O_2$ $[M + H]^+$ 219.1128. Found 219.1128.

Preparation of ***9c***[S1]



A round bottom flask was charged with NaH (200 mg, 5 mmol, 1.2 equiv, 60% dispersion in oil), and cooled to 0 ºC. Then a solution of 2-hydroxybenzonitrile (476 mg, 4 mmol, 1 equiv) in DME (20 mL) was added dropwise to the NaH. The resulting solution was warmed to rt for 10 min, and then cooled to 0 °C. A solution of dimethyl sulfamoyl chloride (1.2 equiv) in DME (6 mL) was then added dropwise to the reaction vessel. The reaction was warmed to rt,

allowed to stir for 11 h, and then quenched with several drops of water. The solvent was removed under reduced pressure, and the solid material was dissolved in Et_2O (50 mL) and H_20 (15 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with 1 M KOH (15 mL), then H_2O (15 mL). The combined aqueous layers were extracted with Et_2O (3×20 mL). The combined organic layers were then washed with brine (15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by flash chromatography (1:4 ethyl acetate:petroleum ether) to yield white solid sulfamate product in quantitative yield (Scheme 1). Mp: 70-71 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.12 (s, 6H),7.38 (td, J = 7.5, 1.5 Hz, 1H), 7.58-7.70 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.1, 134.4, 133.6, 126.7, 122.5, 114.9, 106.9, 38.9. HRMS ($APCI^+$) m/z Calcd for $C_9H_{11}N_2O_3S$ $[M + H]^+$ 227.0485. Found 227.0487.

General Procedure for Scale-Up Experiments

A) Monowave 300, 3 mmol scale

Aryl carbamate

Aryl carbamate **9b** (3 mmol, 654 mg), *p*-tolylboronic acid (**2e**) (7.5 mmol, 1020 mg, 2.5 equiv), potassium phosphate (21 mmol, 4.45 g, 7 equiv) and bis(tricyclohexylphosphine)nickel(II) chloride (103 mg, 0.15 mmol, 5 mol%) were added to a 30 mL flame dried microwave vial containing a Teflon coated stir bar. After the vial was sealed dry toluene (10 mL) was transferred to the vial and the mixture was purged with Ar for 2 min. The vial was subsequently placed in the microwave cavity and irradiated for 10 min at 180 °C (hold time). Similar work-up procedure as mentioned for small scale afforded 487 mg (84% yield) of pure product.

Aryl chloride

2-Chlorobenzonitrile (**9a**) (3 mmol, 411 mg), *p*-tolylboronic acid (**2e**) (4.5 mmol, 612 mg, 1.5 equiv), potassium carbonate (6 mmol, 828 mg, 2 equiv) and bis(tricyclohexylphosphine)nickel(II) chloride (41 mg, 0.06 mmol, 2 mol%) were added to a 30 mL flame dried microwave vial containing a Teflon coated stir bar. After the vial was closed dry toluene (10 mL) was transferred to the vial and the mixture was purged with Ar for

2 min. The vial was subsequently placed in the microwave cavity and irradiated for 10 min at 180 °C (hold time). Similar work-up procedure as mentioned for small scale afforded 526 mg (91% yield) of pure product.

B) Masterwave BTR, 0.375 mol scale

2-Chlorobenzonitrile (**9a**) (0.375 mol, 51.4 g), *p*-tolylboronic acid (**2e**) (0.562 mol, 76 g, 1.5 equiv), potassium carbonate (0.75 mol, 103.6 g, 2.0 equiv) and bis(tricyclohexylphosphine)nickel(II) chloride (0.0075 mol, 5.17 g, 2 mol%) were added to a 1000 mL PTFE Masterwave microwave vessel. After the addition of dry toluene (500 mL) the reactor was closed. Microwave heating at 180 °C was performed for 10 min (ramp time 2.5 min, cooling time 15 min). After cooling, the solvent was evaporated and ethyl acetate (500 mL) was added and the crude reaction mixture was subsequently washed with 25% aqueous ammonia (2 × 200 mL). The aqueous ammonium layer was reextracted with ethyl acetate (2 × 100 mL). The combined organic layers were then washed with brine (100 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford 76.25 g of crude product in 90% purity (HPLC-UV at 254 nm, ^{1}H NMR). These results are similar to what has been achieved in the smaller scale experiments. No further chromatographic work-up was performed.

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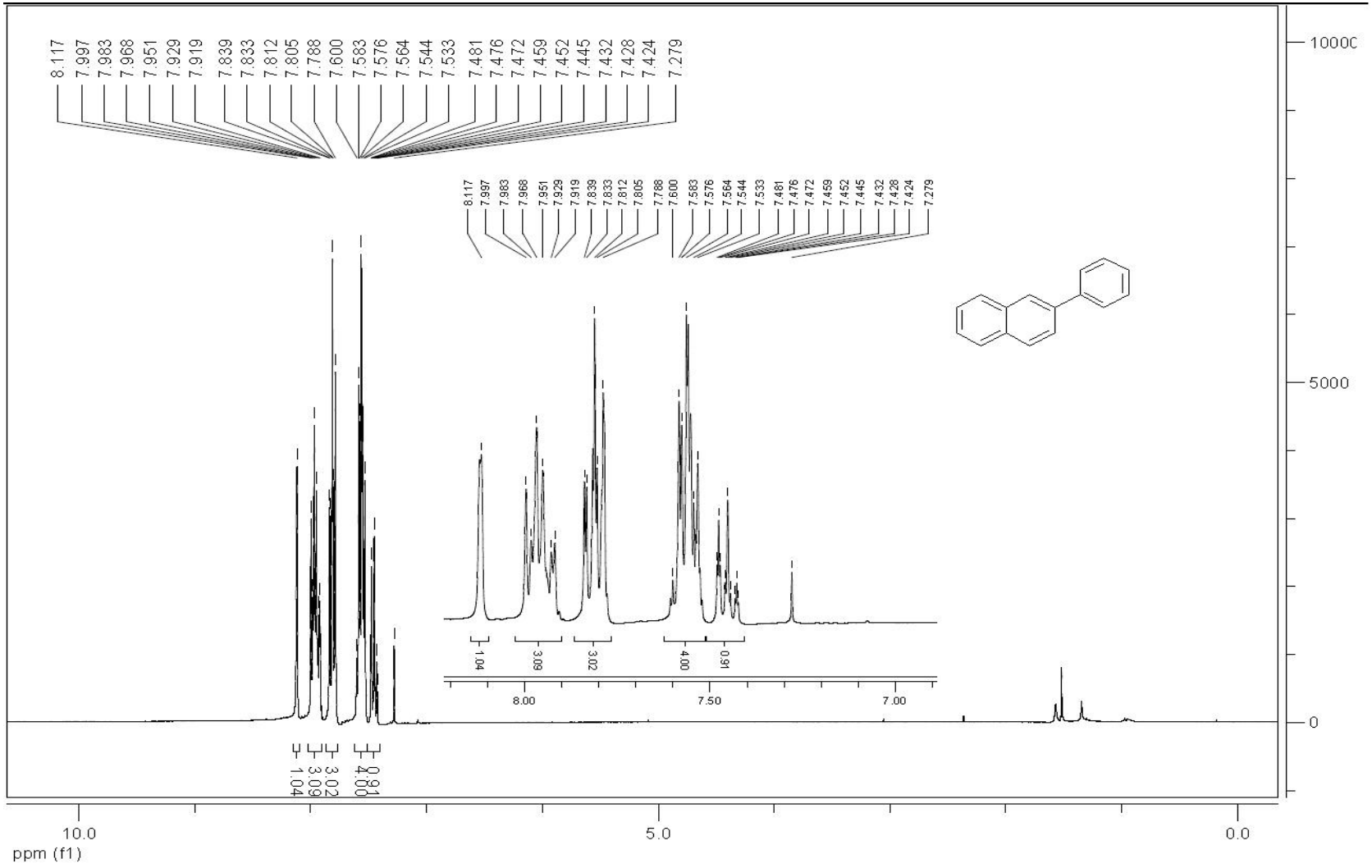
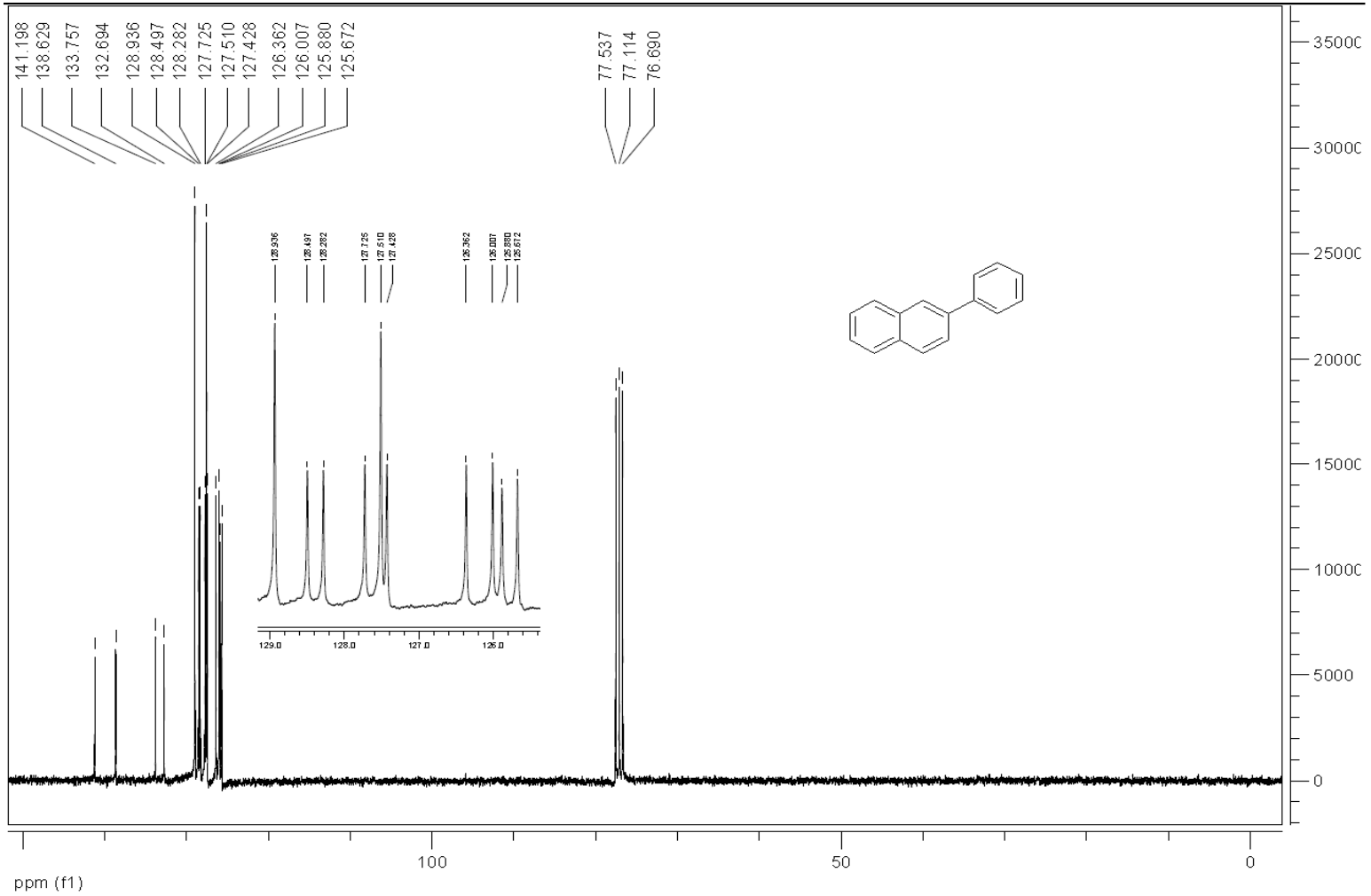
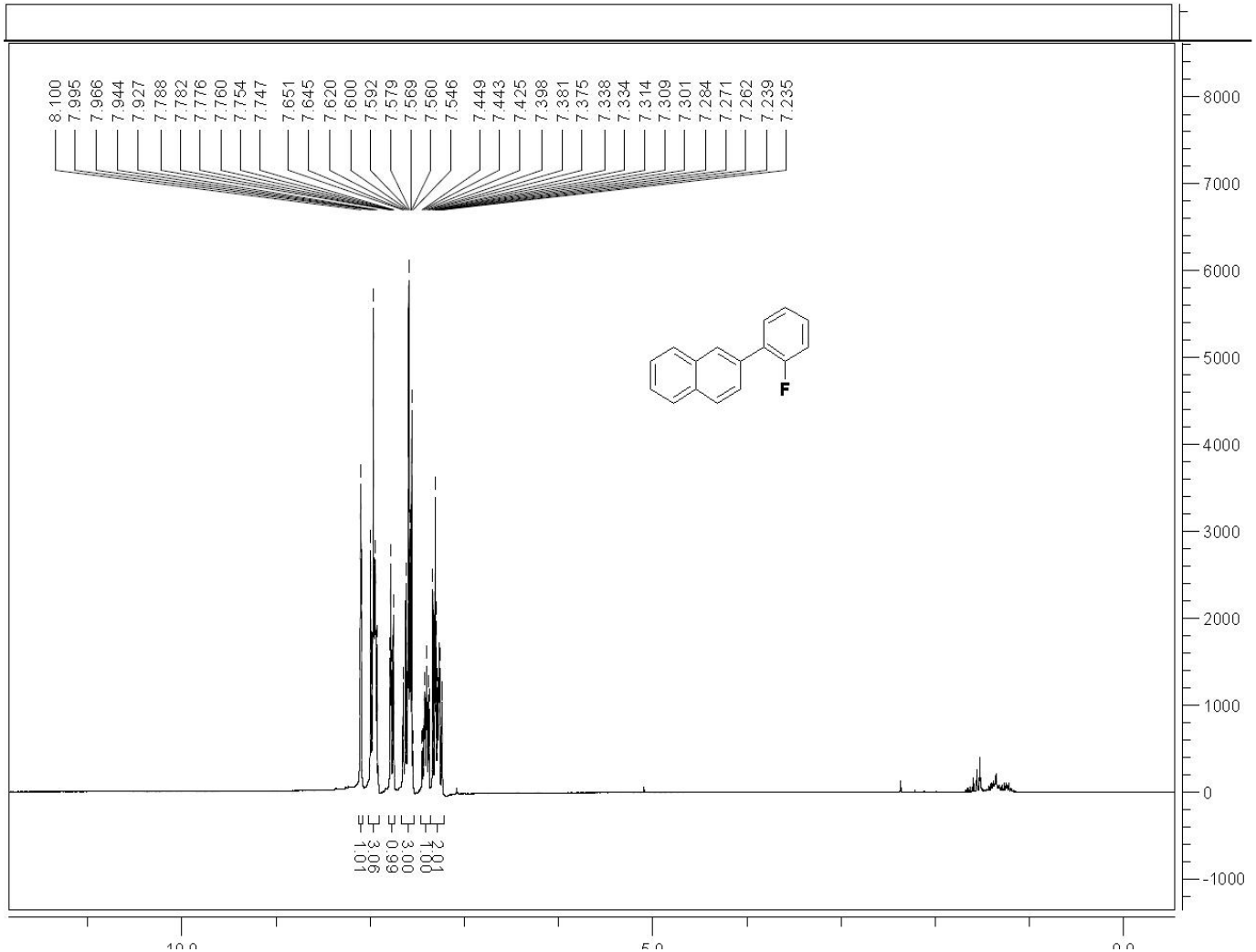


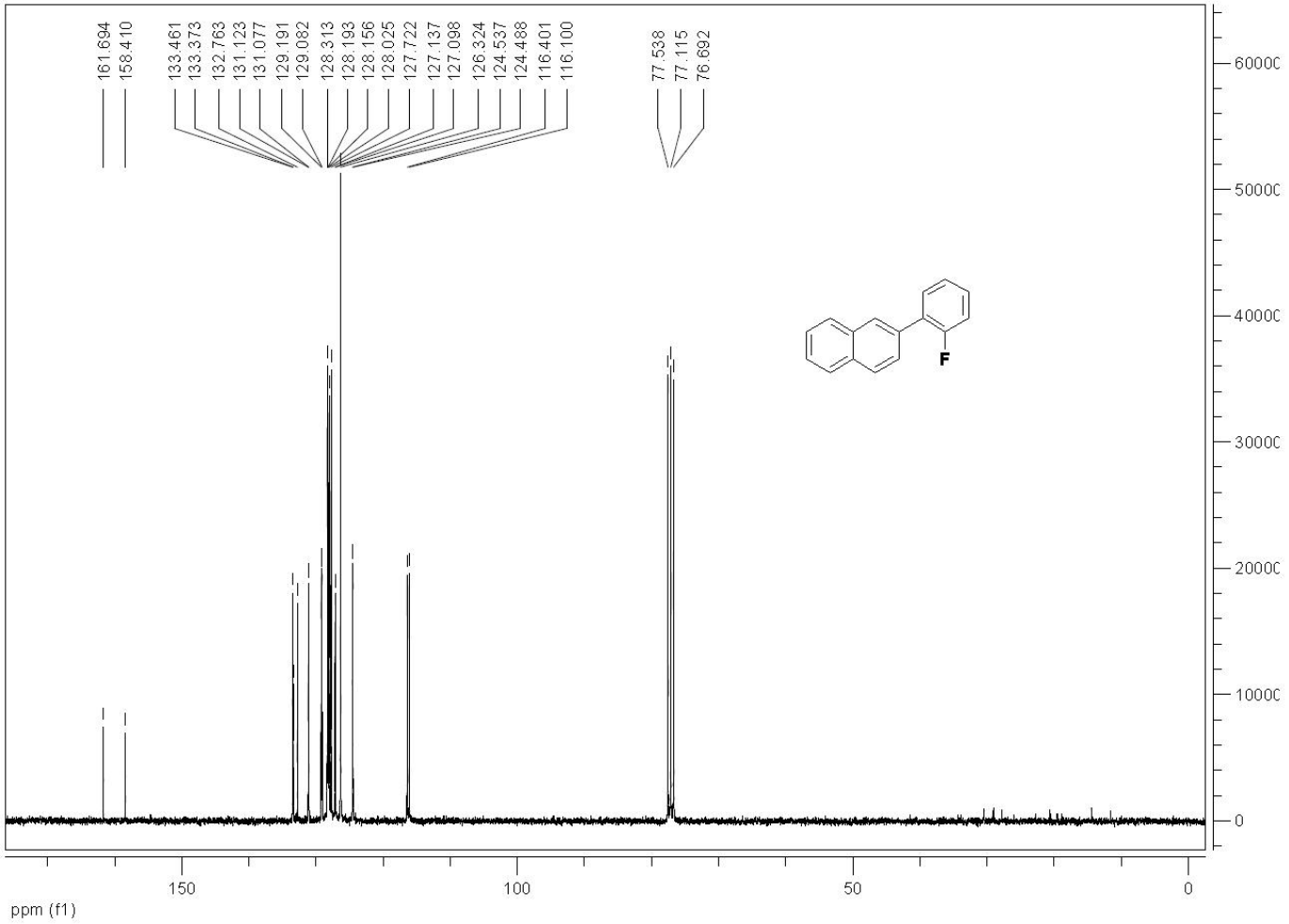
^{1}H NMR spectra of **3a** ($CDCl_3$, 300 MHz)



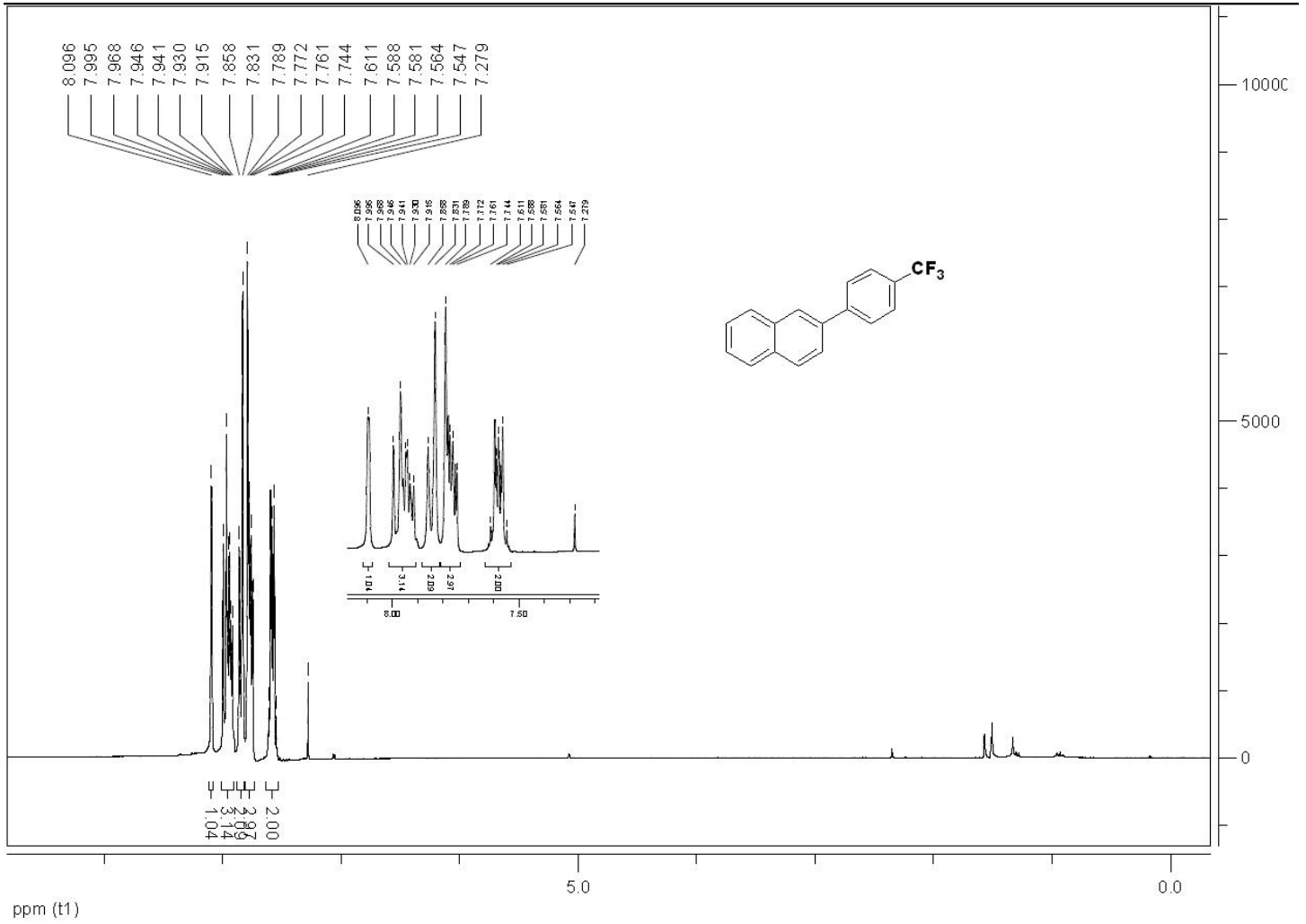
^{13}C NMR spectra of **3a** ($CDCl_3$, 75 MHz)



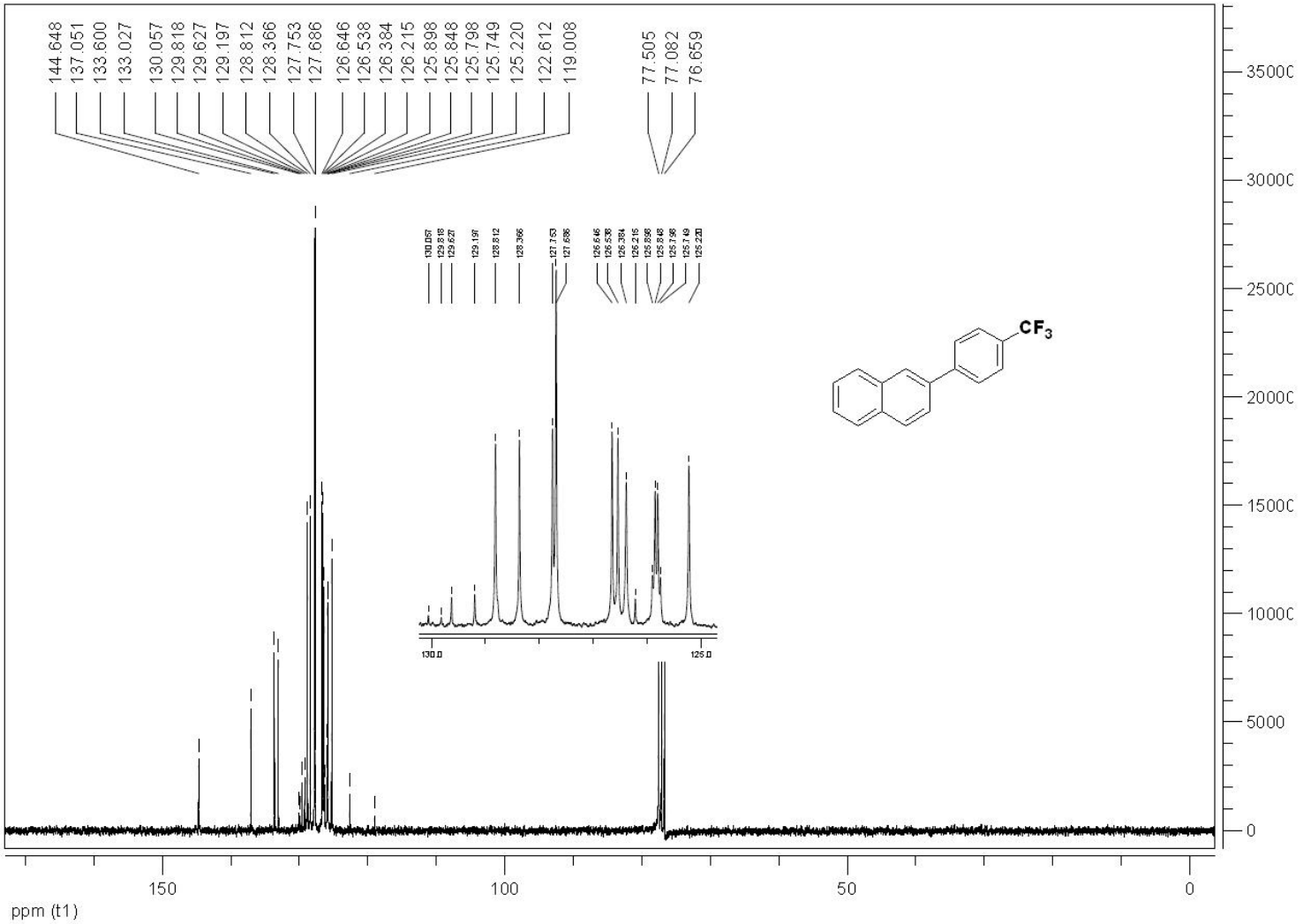
^{1}H NMR spectra of **3b** ($CDCl_3$, 300 MHz)



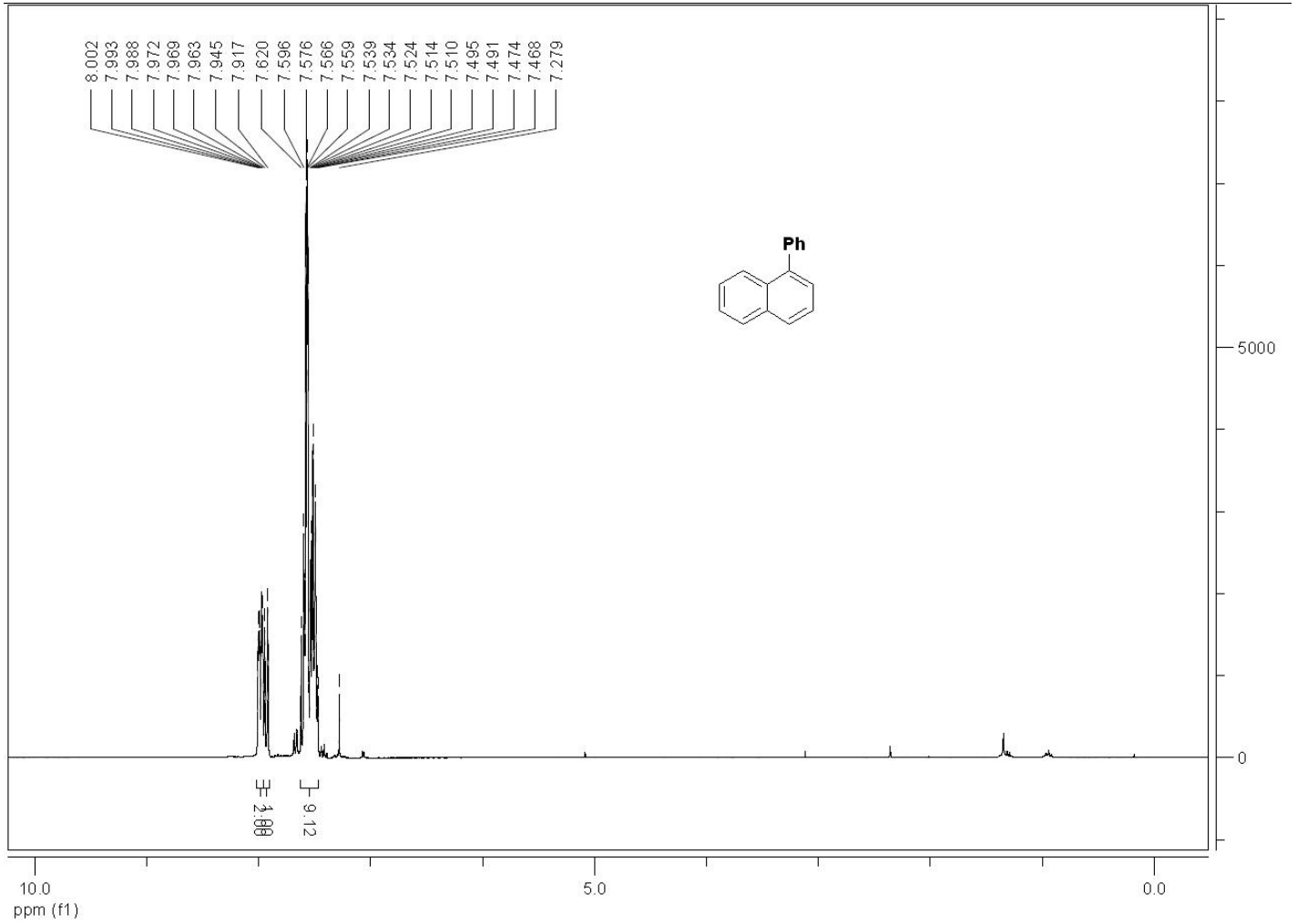
^{13}C NMR spectra of **3b** ($CDCl_3$, 75 MHz)



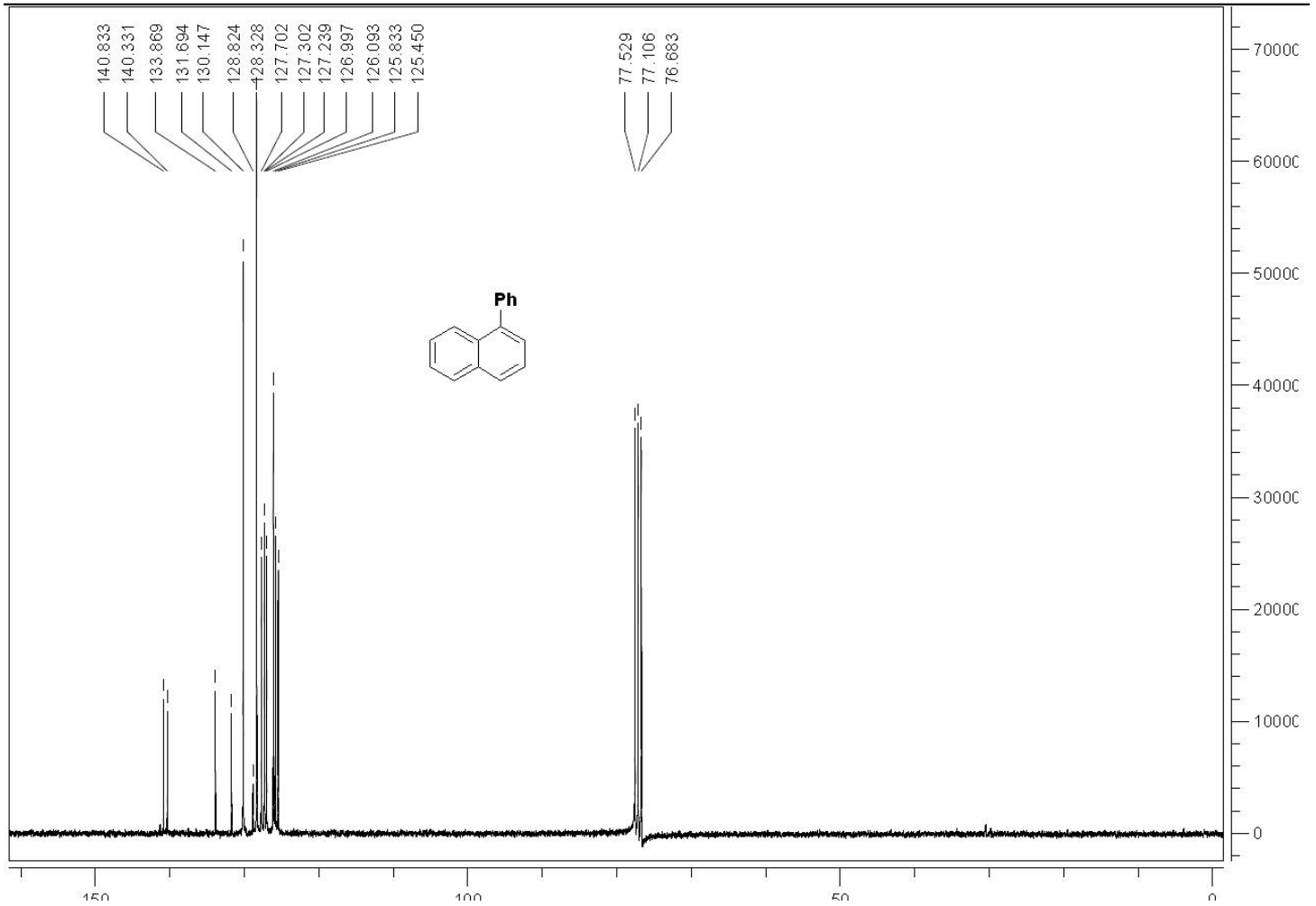
^{1}H NMR spectra of **3c** ($CDCl_3$, 300 MHz)



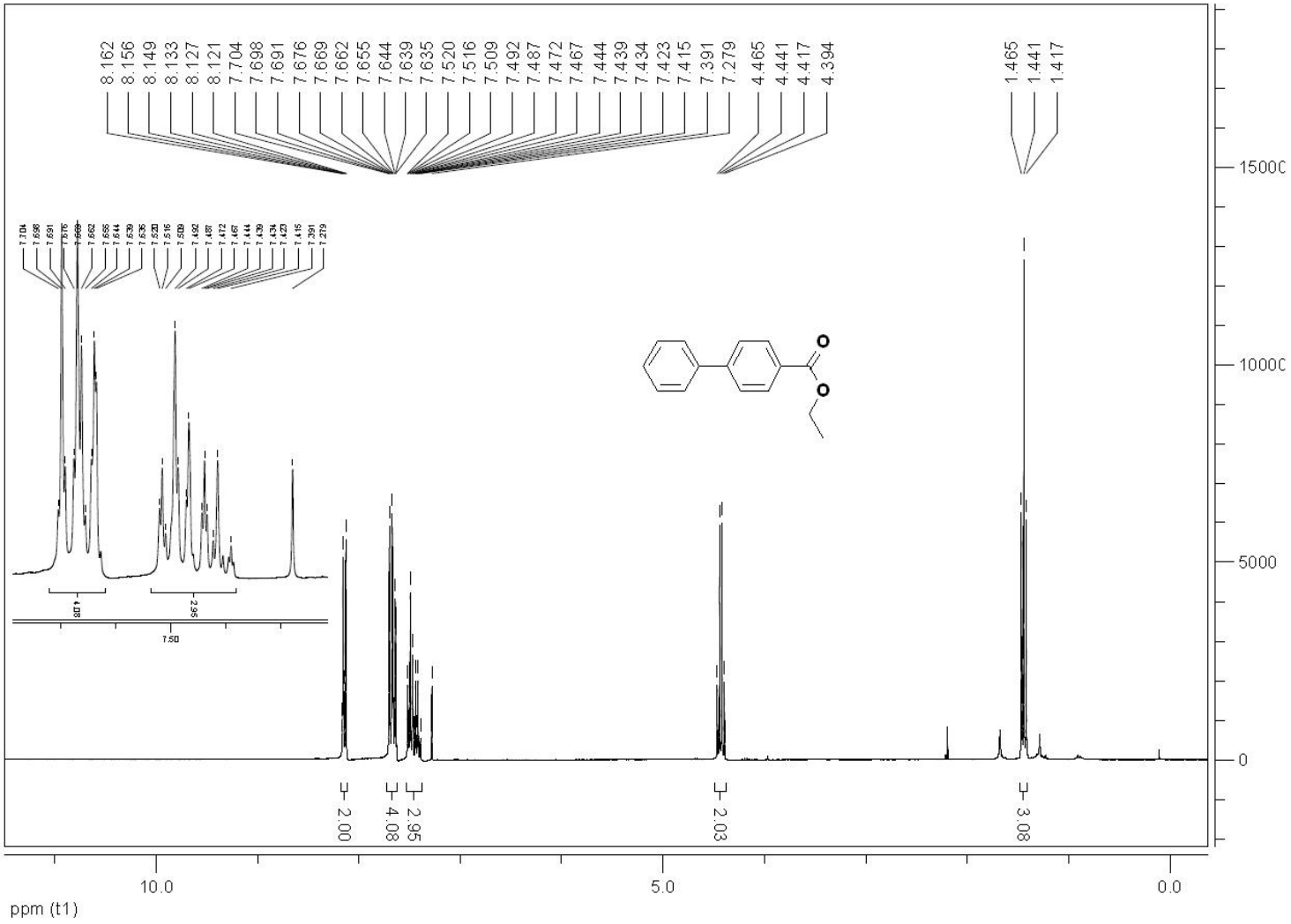
^{13}C NMR spectra of **3c** ($CDCl_3$, 75 MHz)



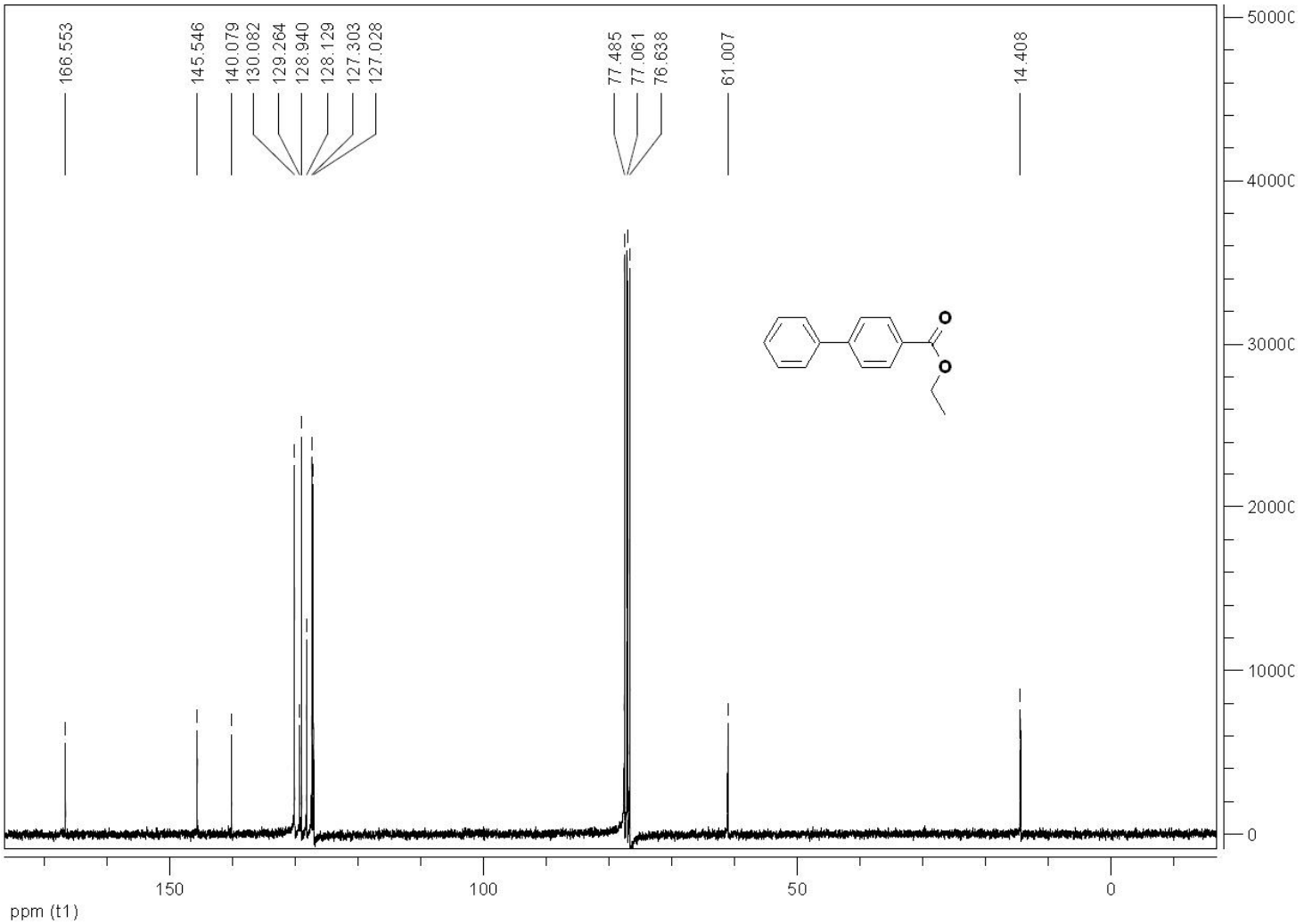
^{1}H NMR spectra of **3d** ($CDCl_3$, 300 MHz)



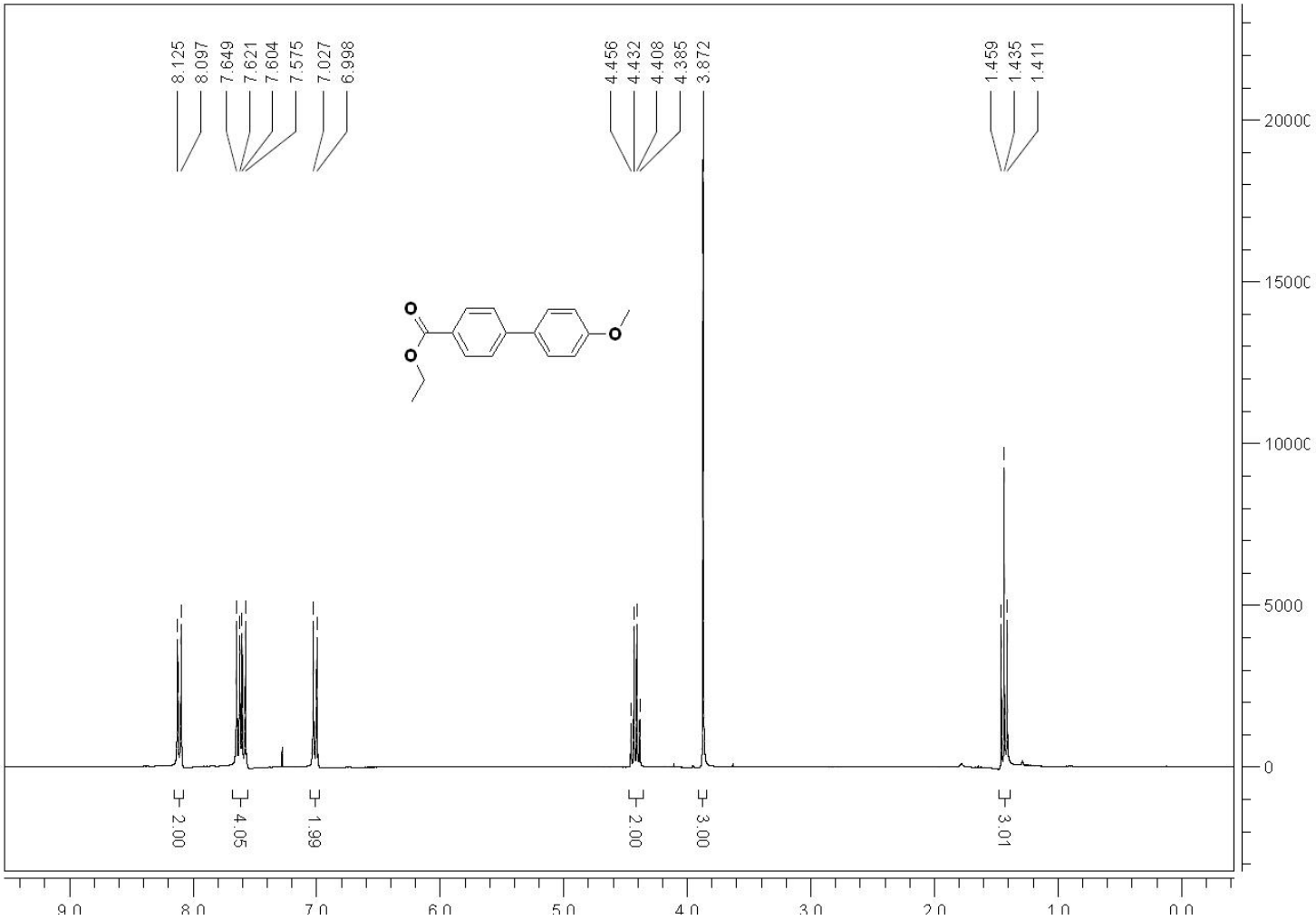
^{13}C NMR spectra of **3d** ($CDCl_3$, 75 MHz)



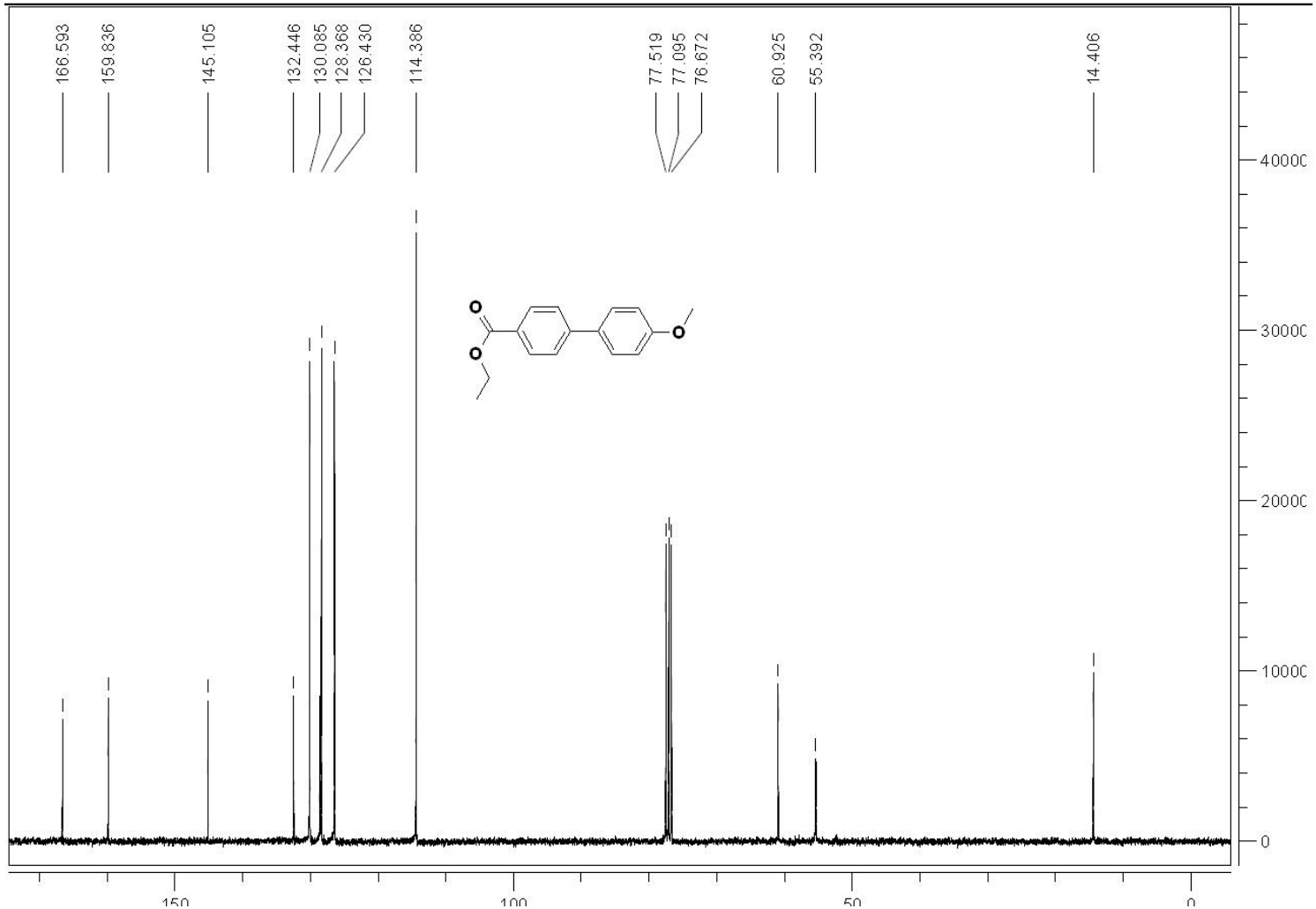
^{1}H NMR spectra of **3e** ($CDCl_3$, 300 MHz)



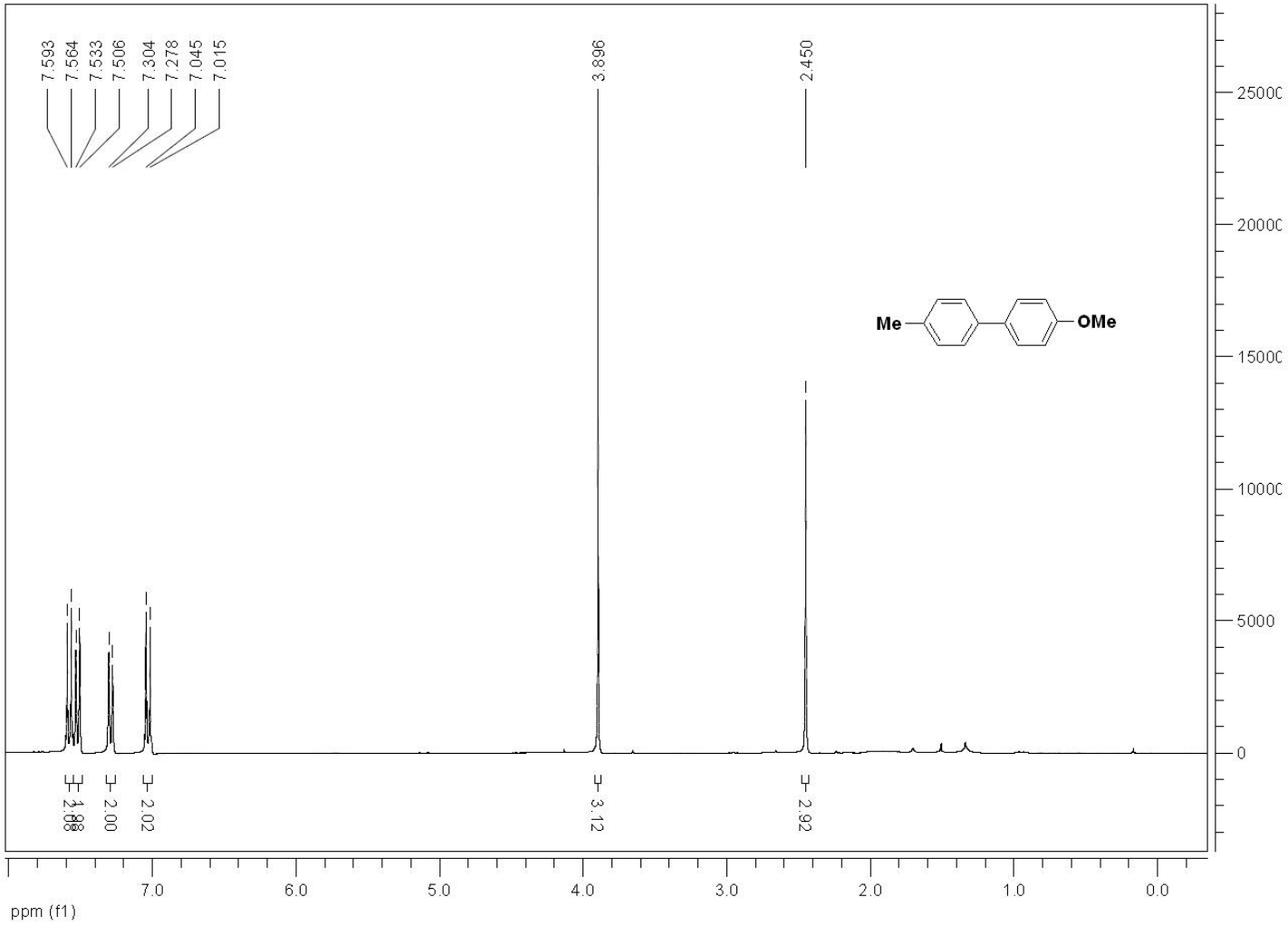
^{13}C NMR spectra of **3e** ($CDCl_3$, 75 MHz)



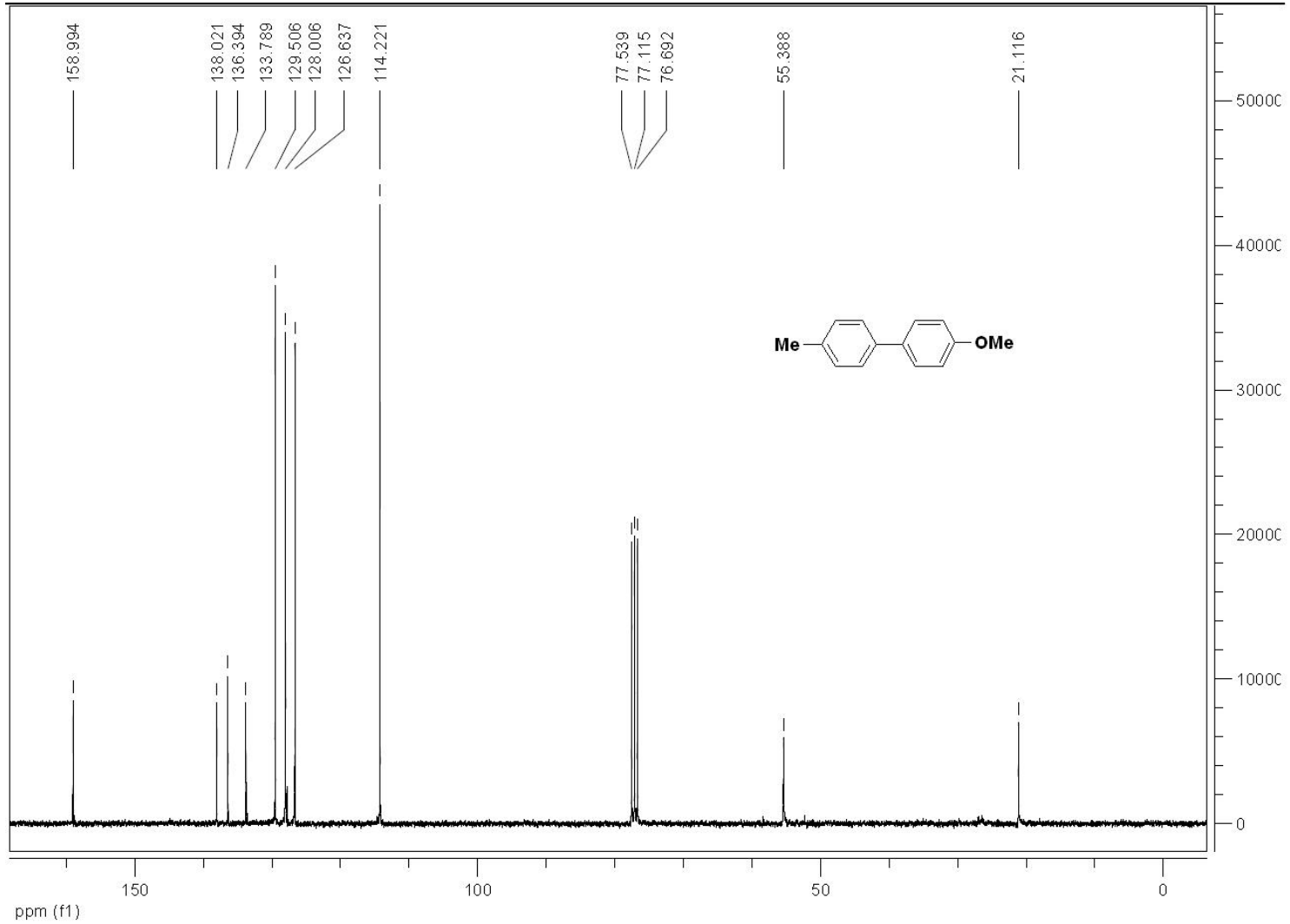
^{1}H NMR spectra of **3f** ($CDCl_3$, 300 MHz)



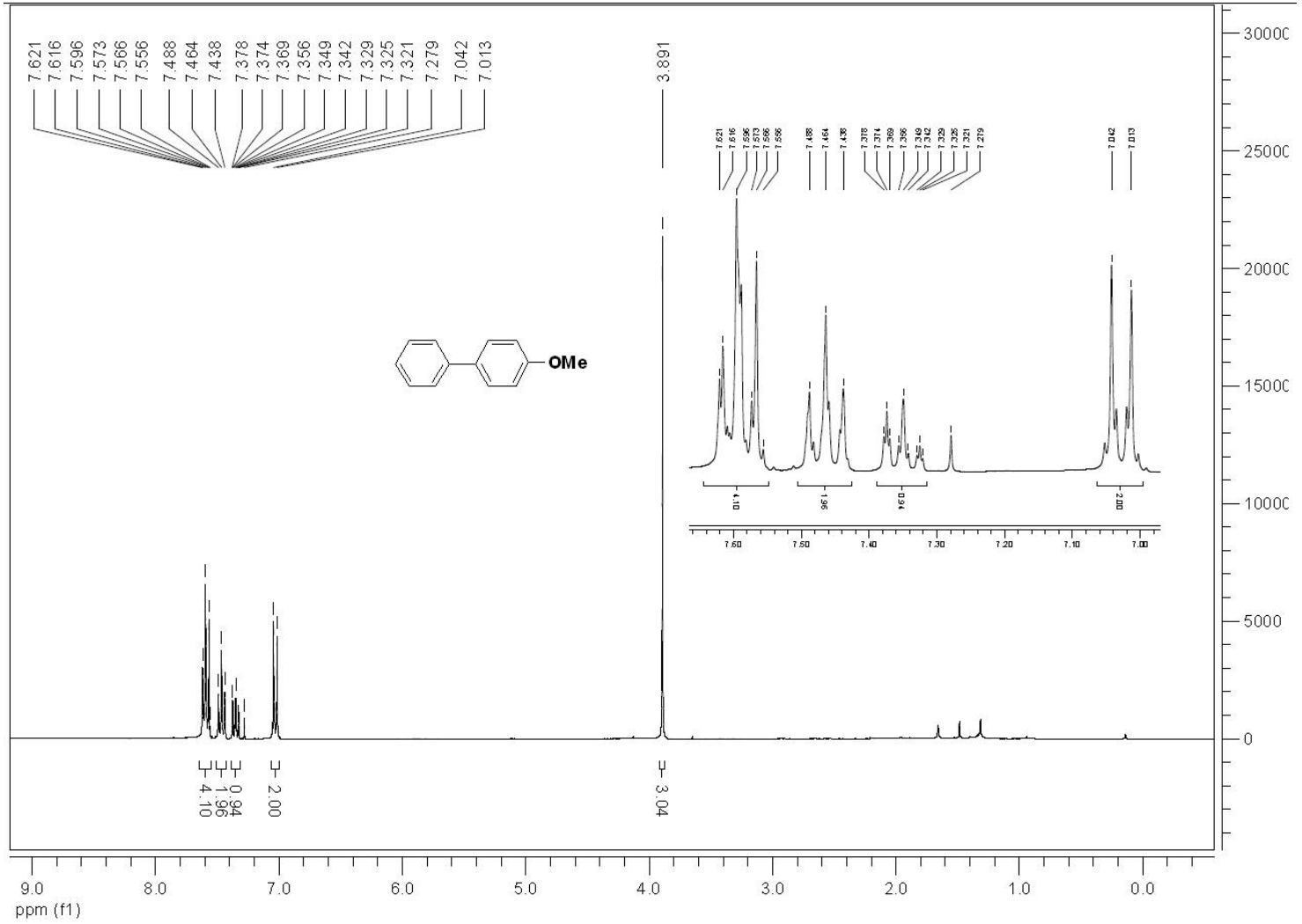
^{13}C NMR spectra of **3f** ($CDCl_3$, 75 MHz)



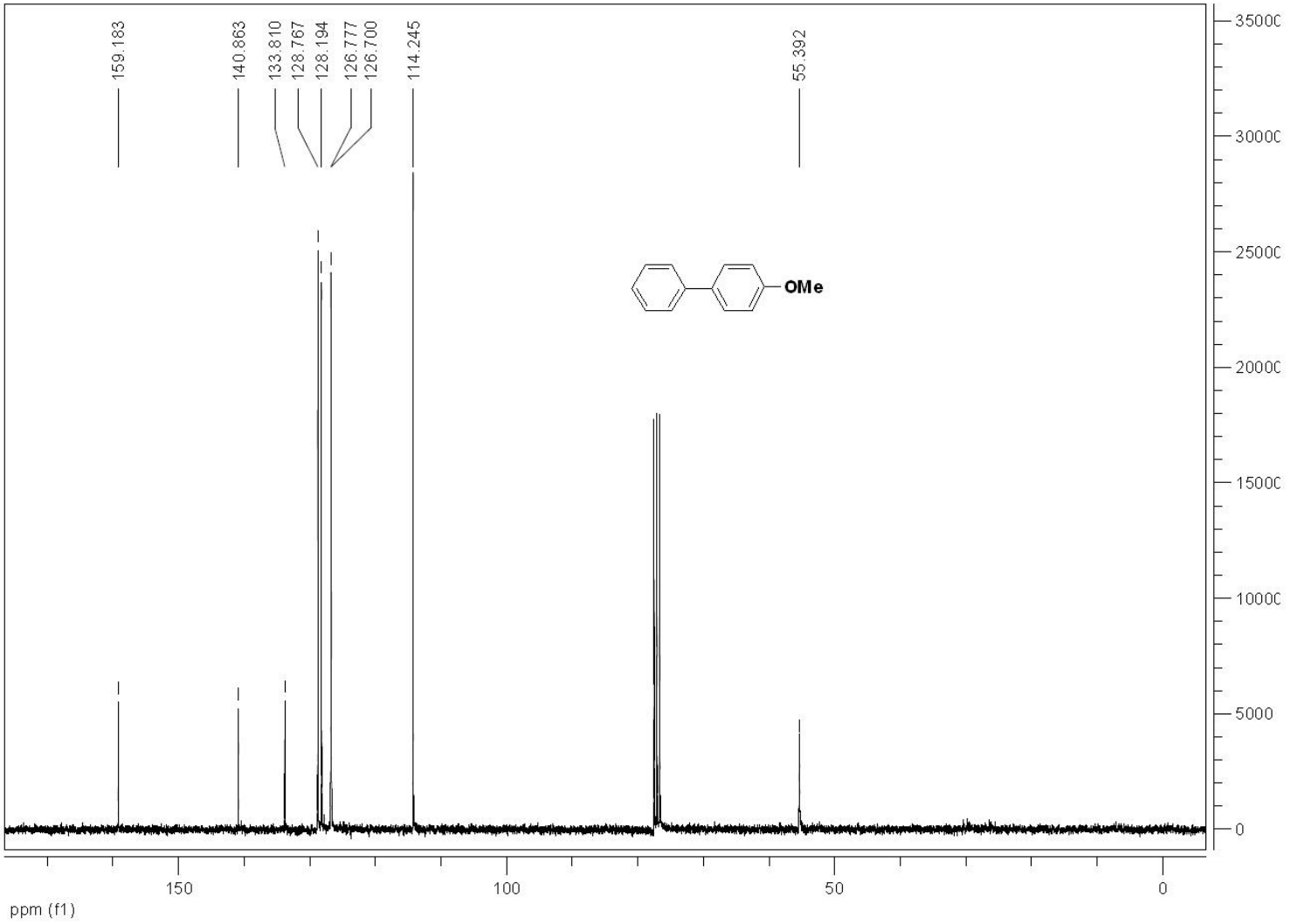
^{1}H NMR spectra of **3g** ($CDCl_3$, 300 MHz)



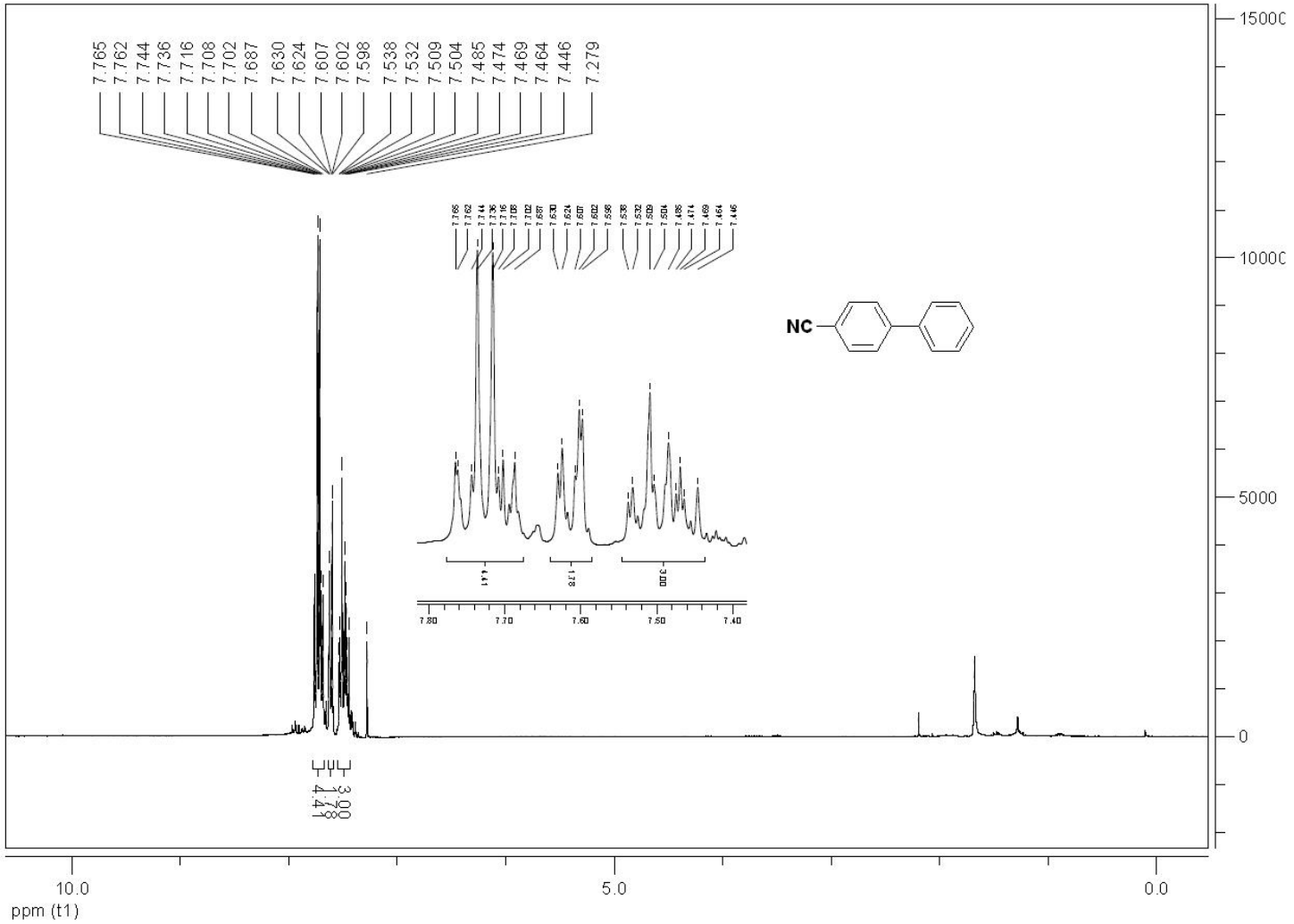
^{13}C NMR spectra of **3g** ($CDCl_3$, 75 MHz)



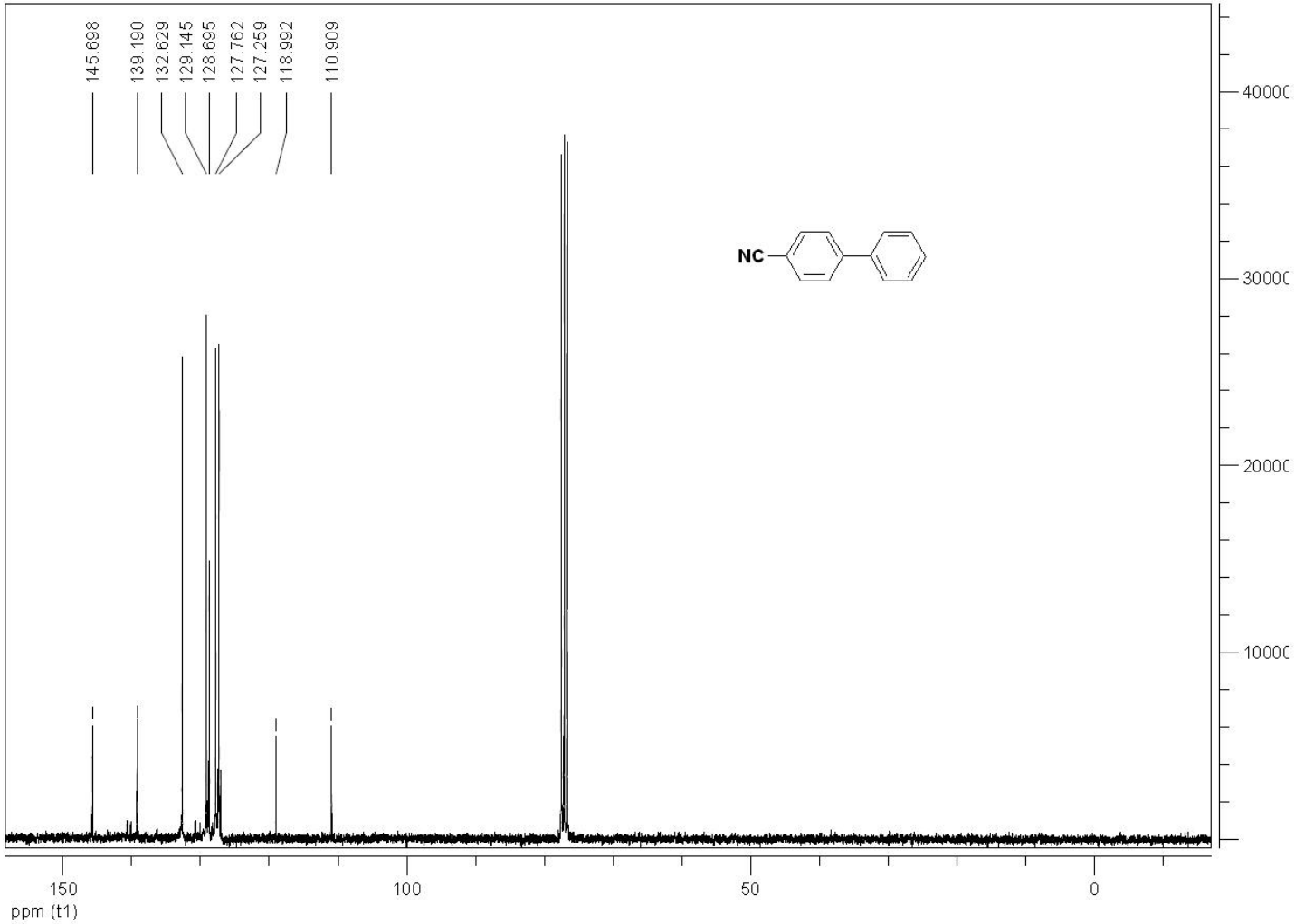
^{1}H spectra of **3h** ($CDCl_3$, 300 MHz)



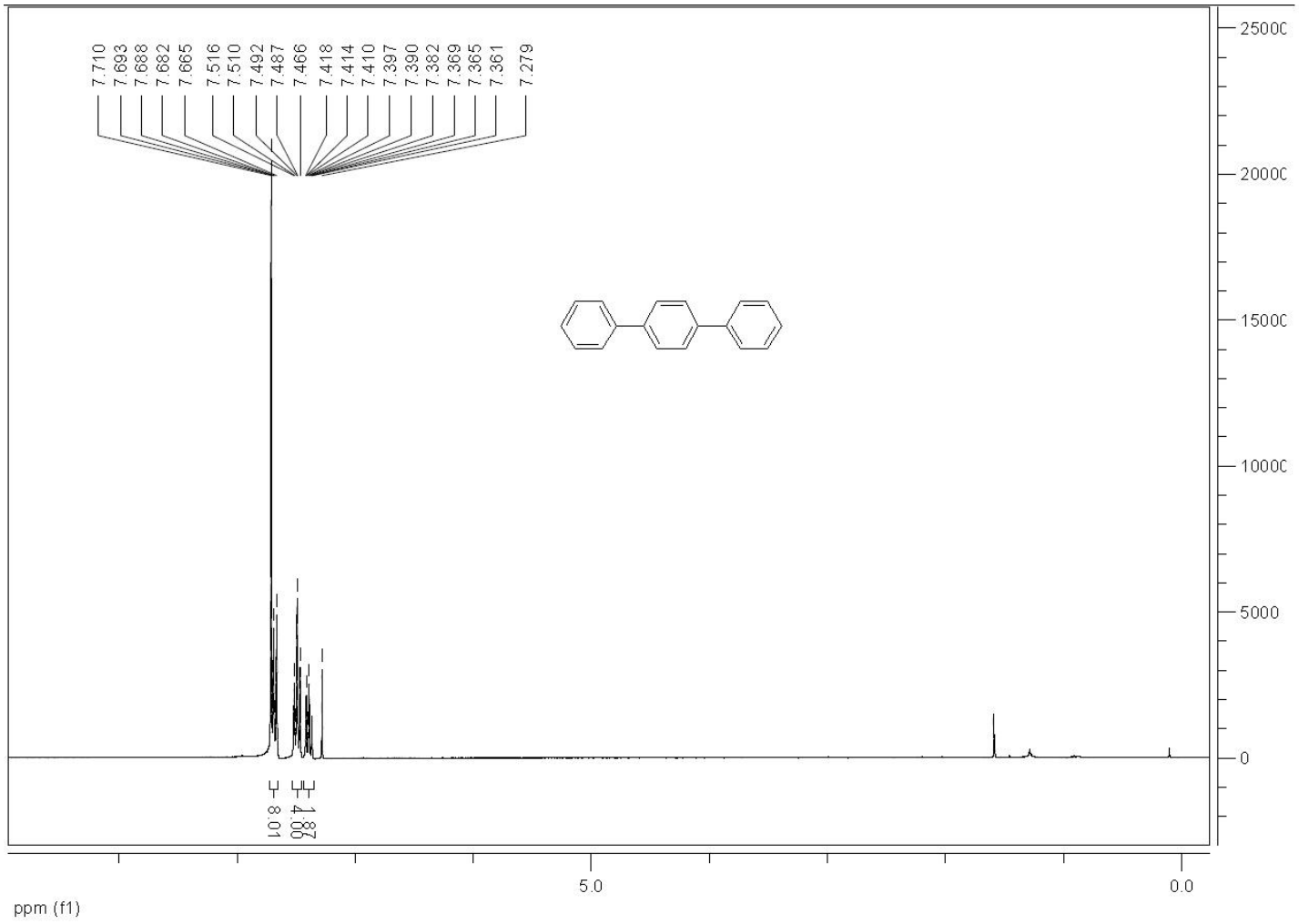
^{13}C NMR spectra of **3h** ($CDCl_3$, 75 MHz)



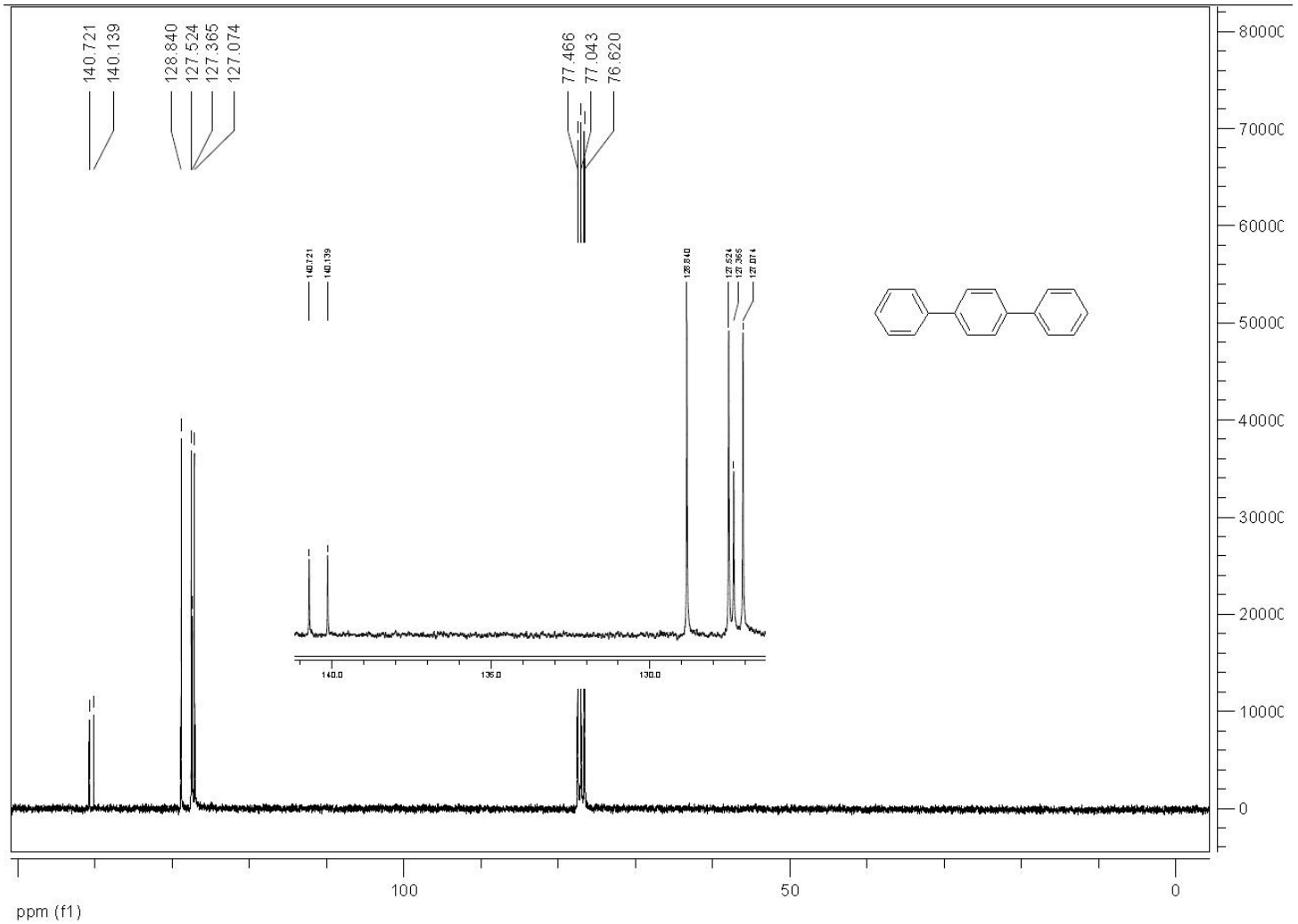
^{1}H NMR spectra of **3i** ($CDCl_3$, 300 MHz)



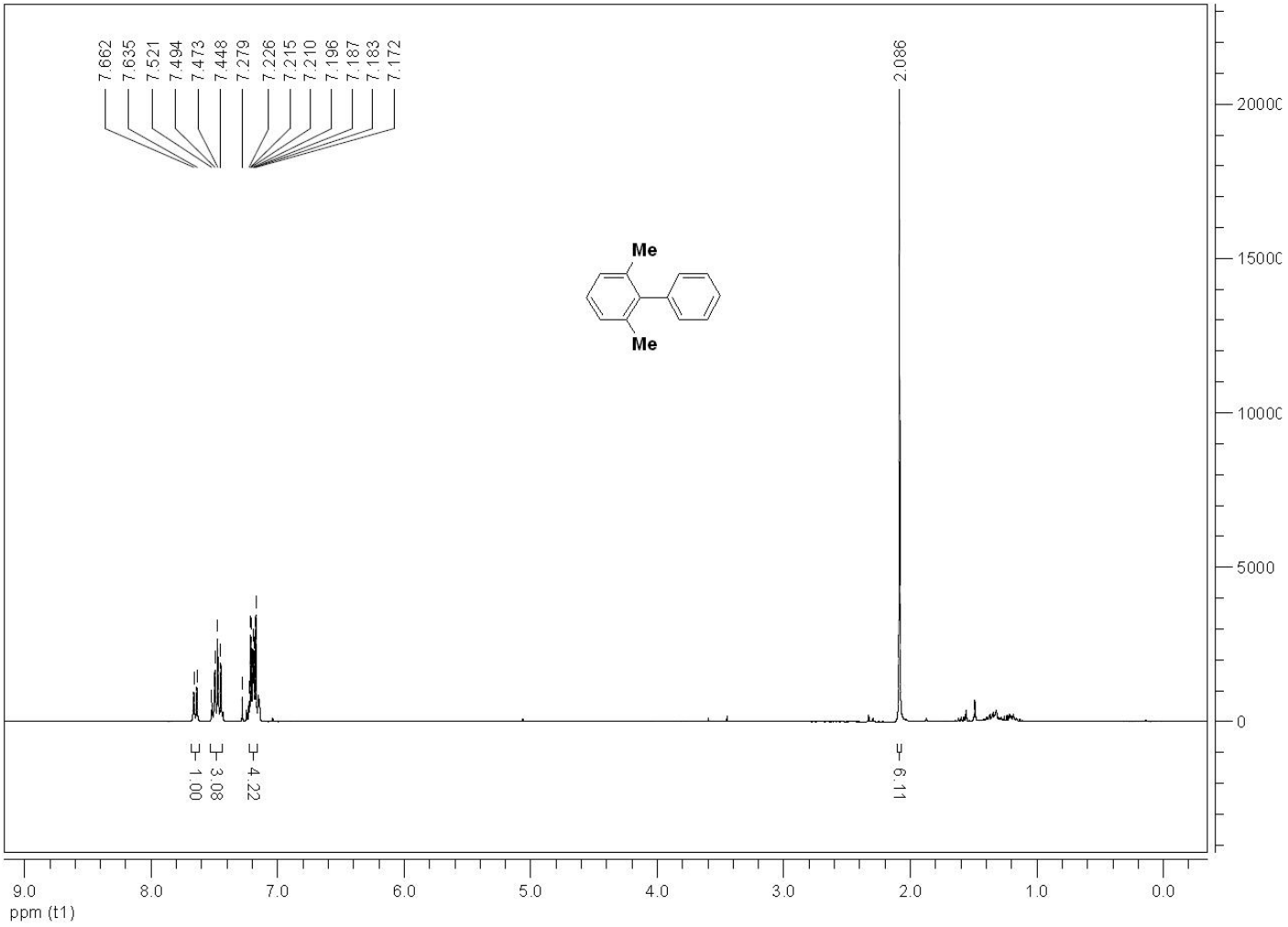
^{13}C NMR spectra of **3i** ($CDCl_3$, 75 MHz)



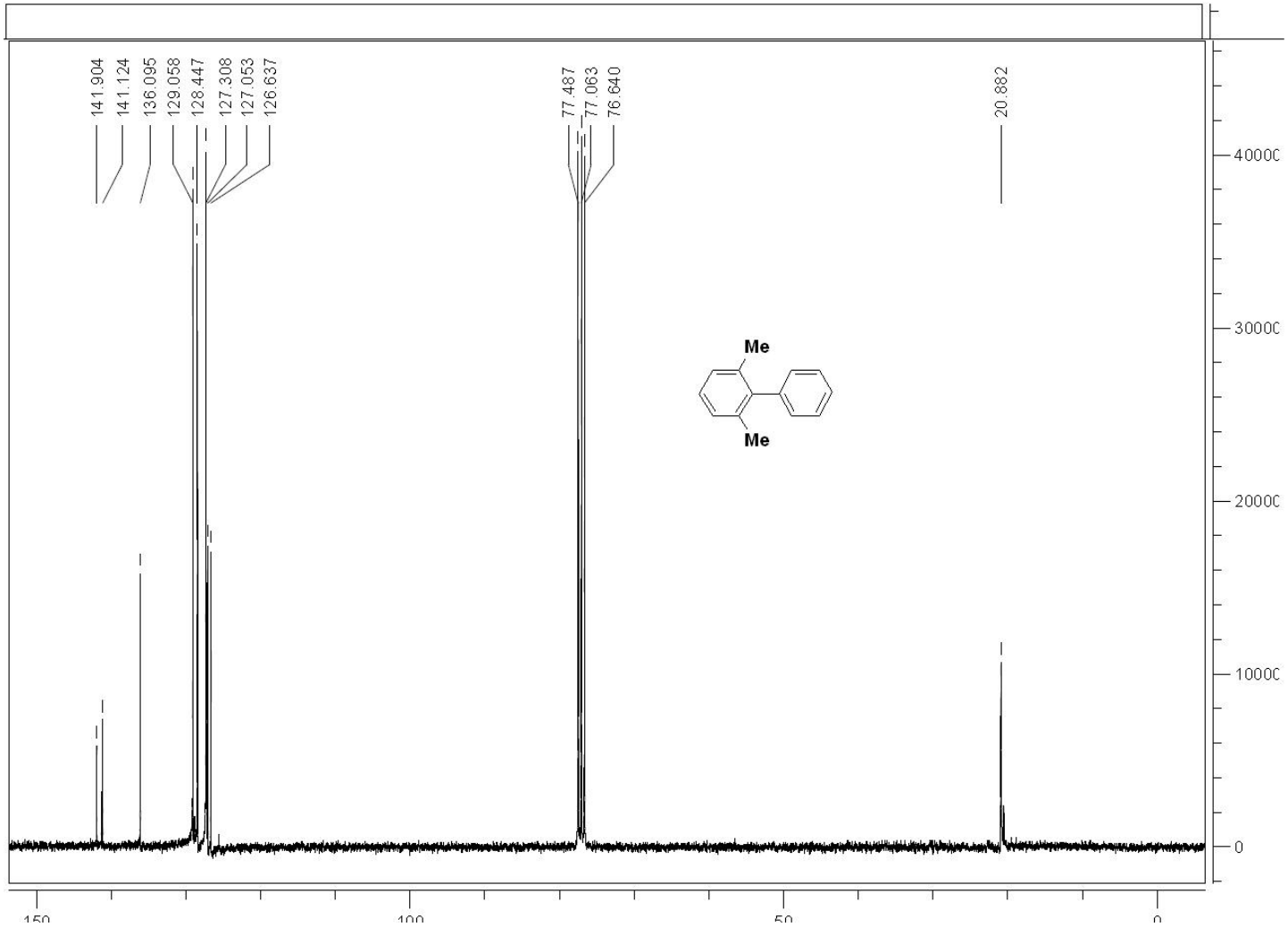
^{1}H NMR spectra of **3j** ($CDCl_3$, 300 MHz)



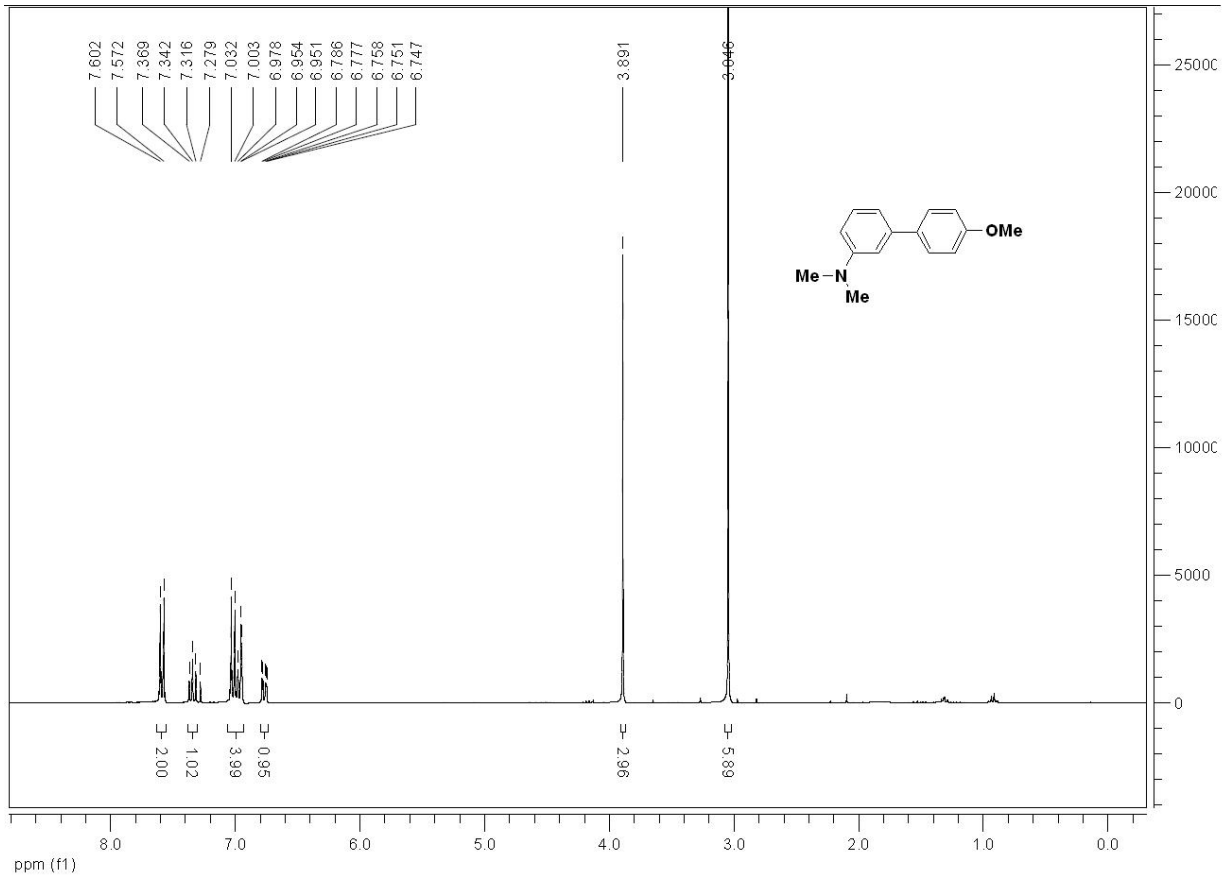
^{13}C NMR spectra of **3j** ($CDCl_3$, 75 MHz)



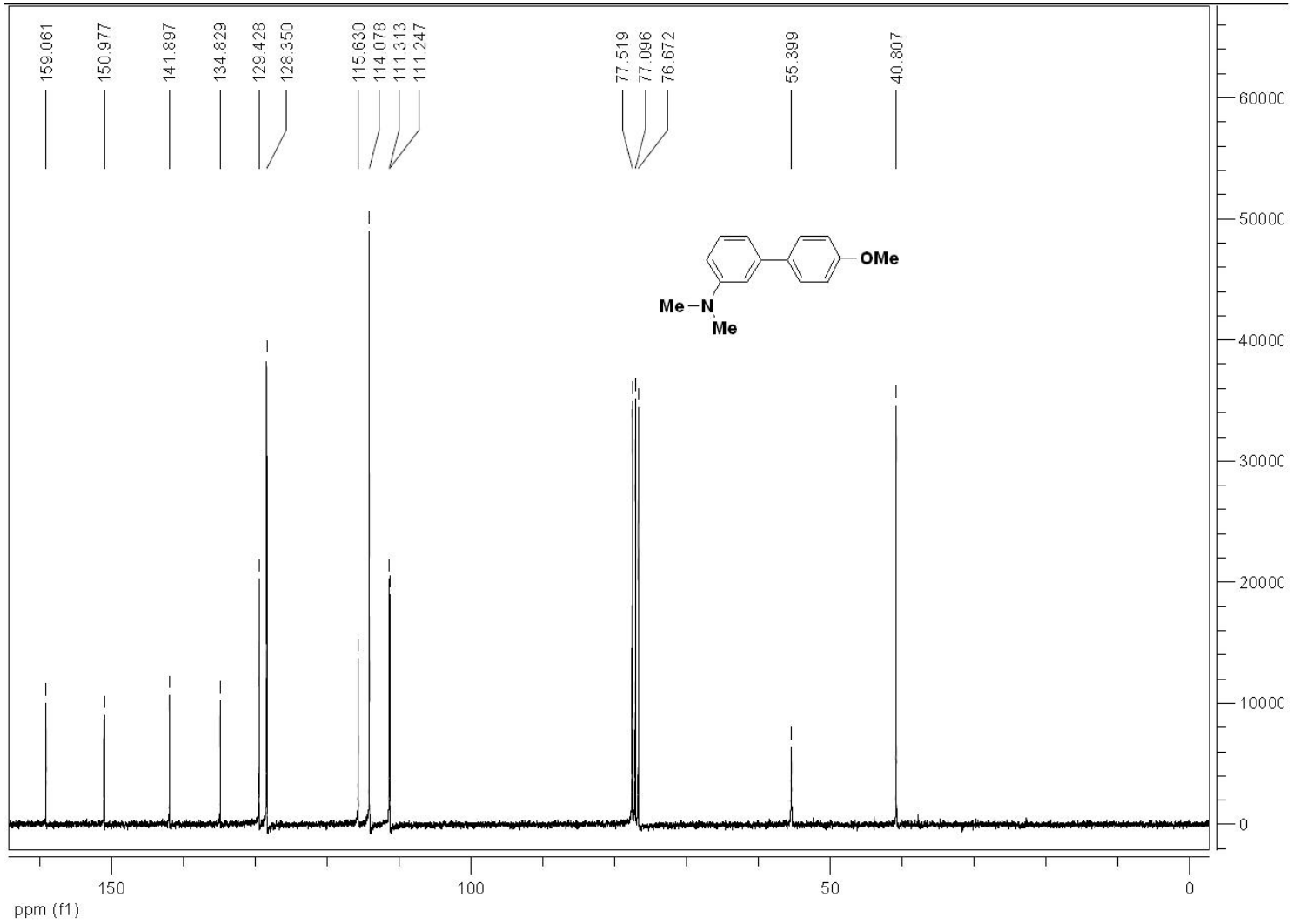
^{1}H NMR spectra of **3k** ($CDCl_3$, 300 MHz)



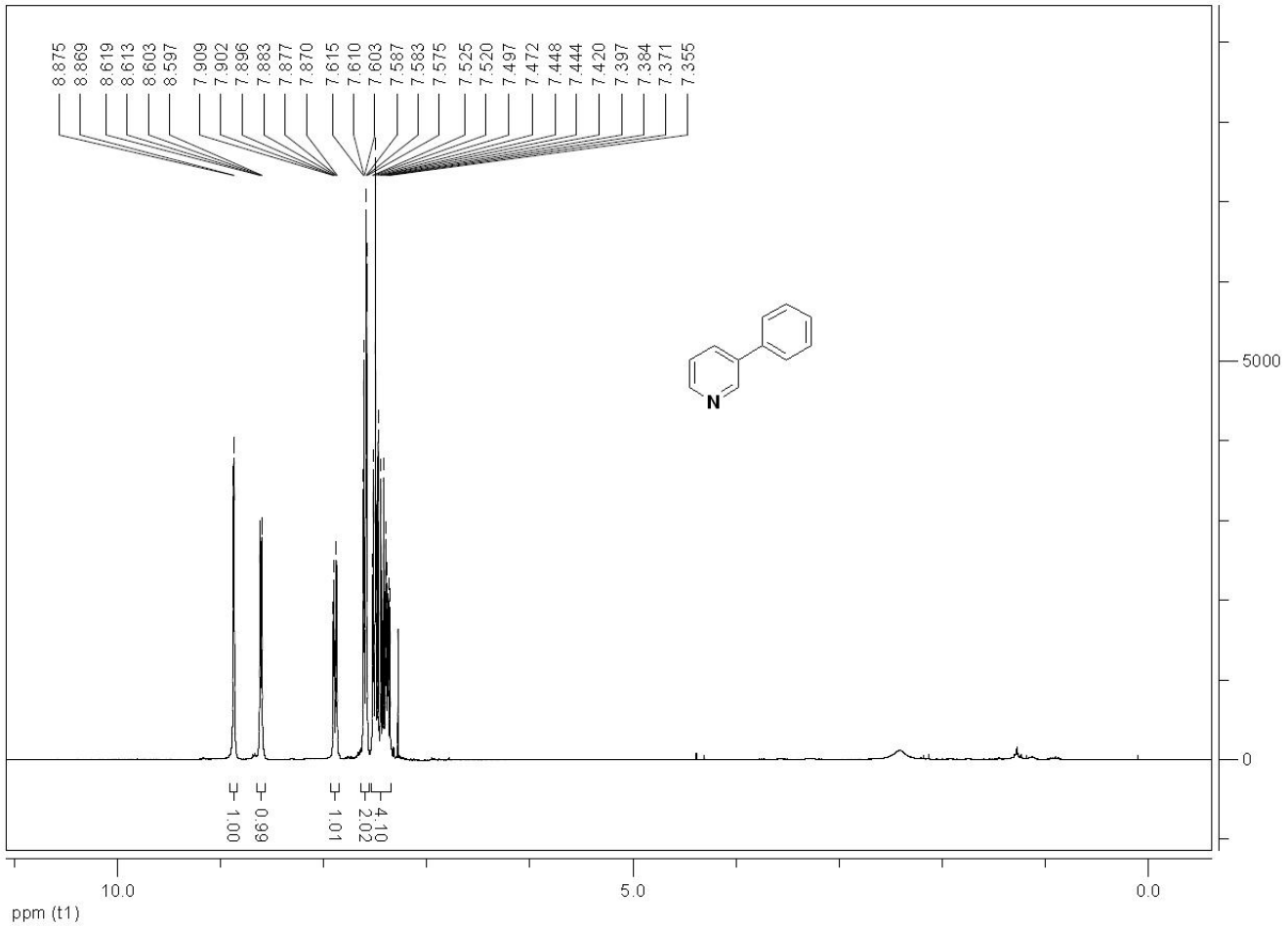
^{13}C NMR spectra of **3k** ($CDCl_3$, 75 MHz)



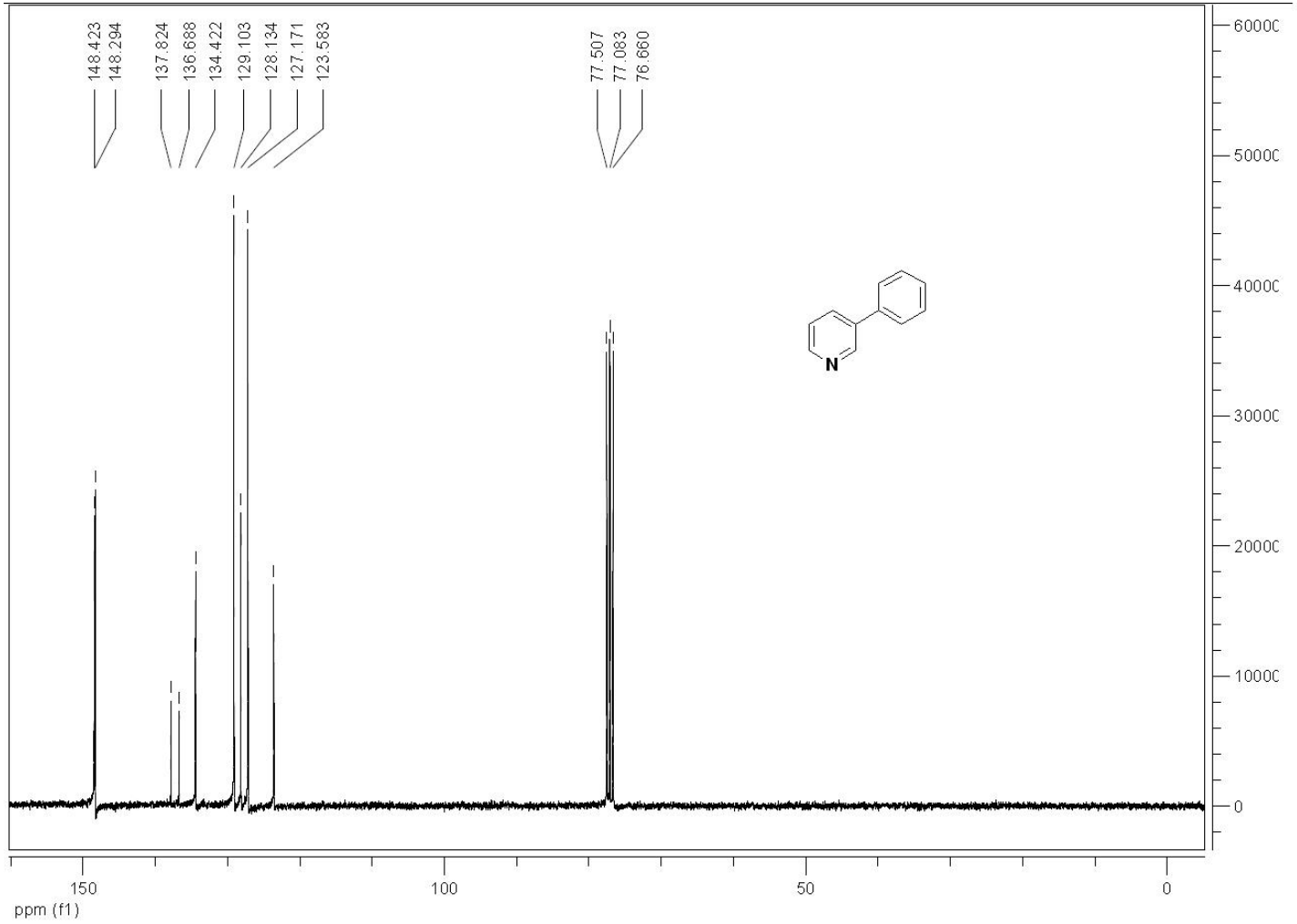
^{1}H NMR spectra of **3l** ($CDCl_3$, 300 MHz)



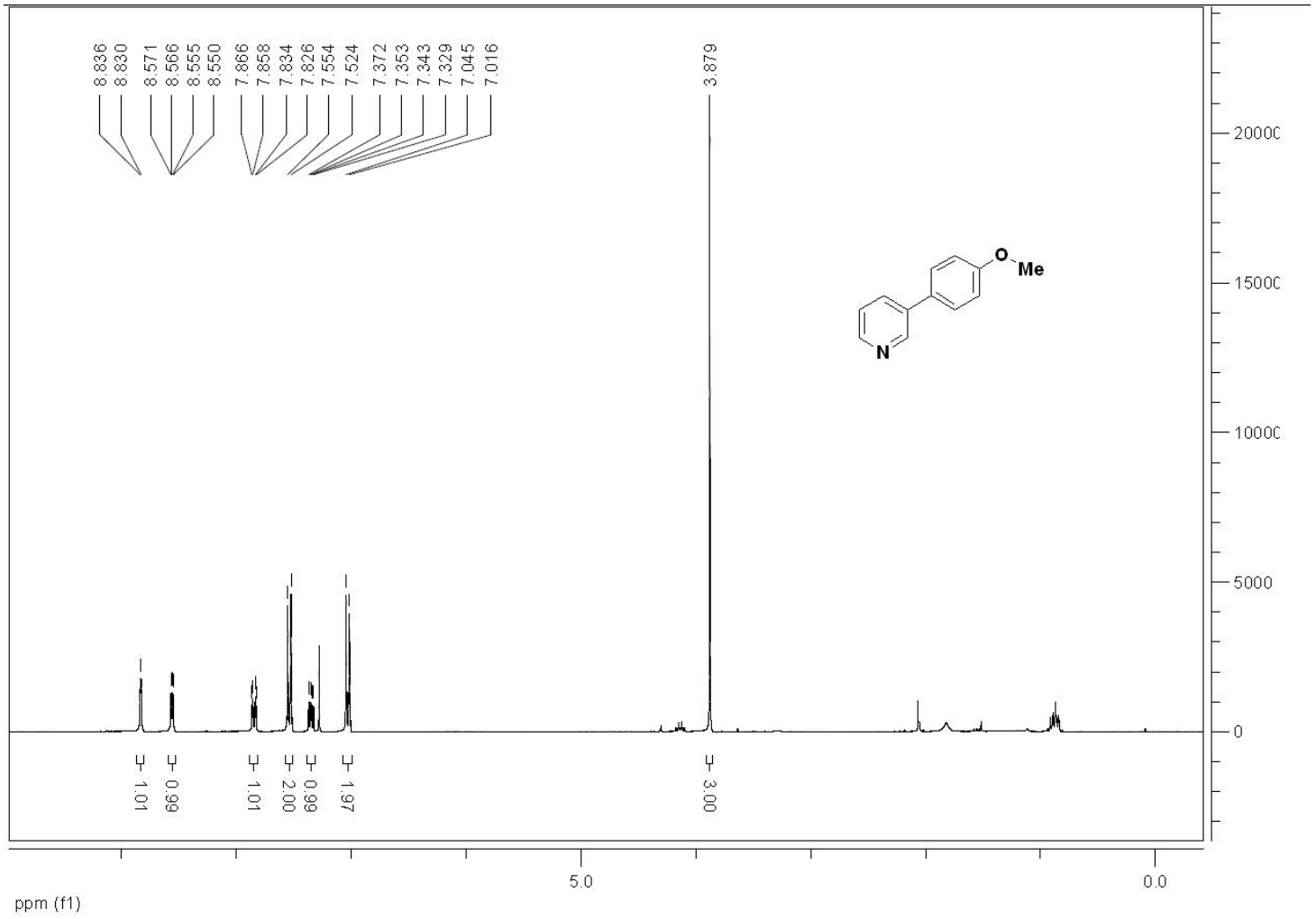
^{13}C NMR spectra of **3l** ($CDCl_3$, 75 MHz)



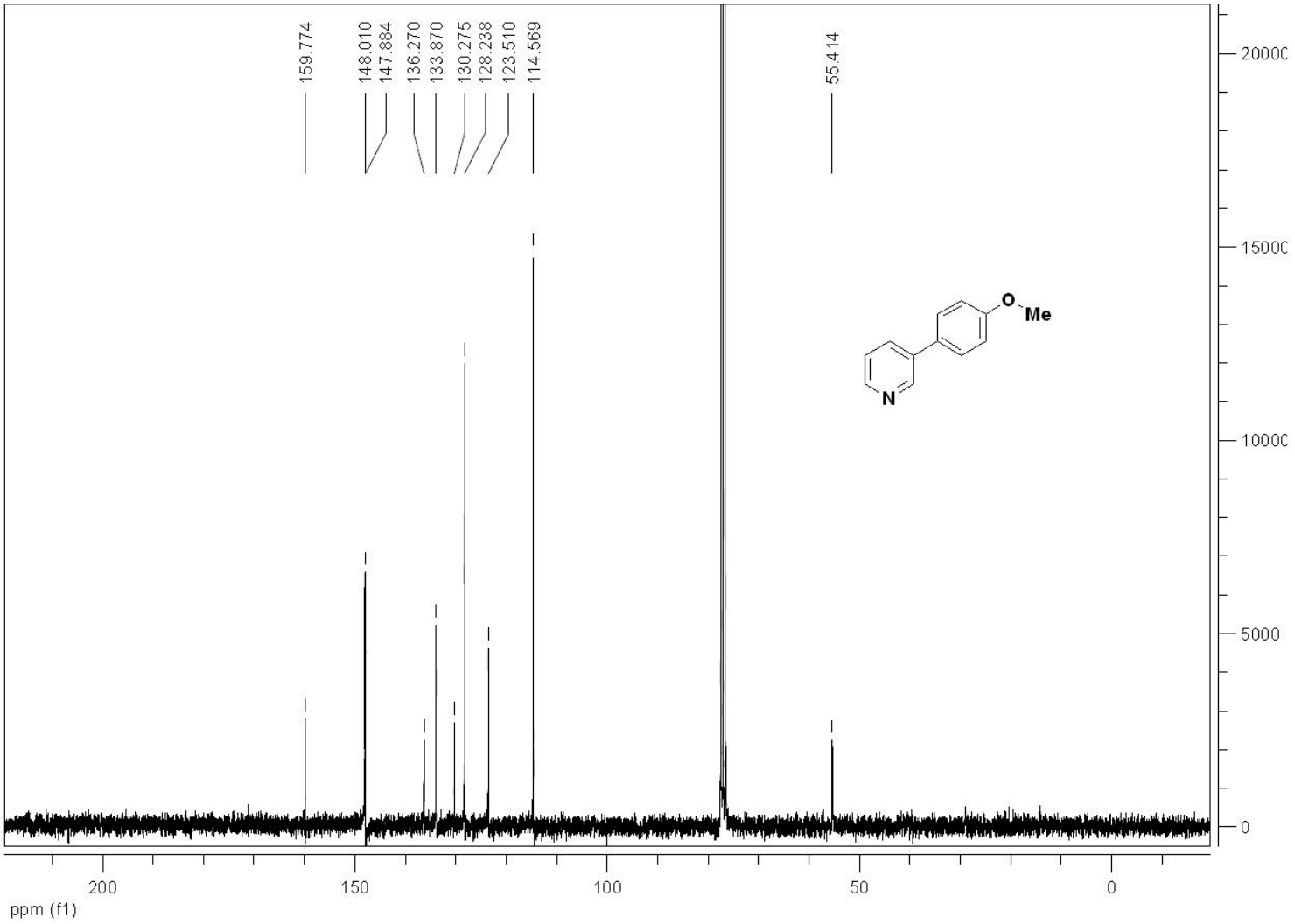
^{1}H NMR spectra of **3m** ($CDCl_3$, 300 MHz)



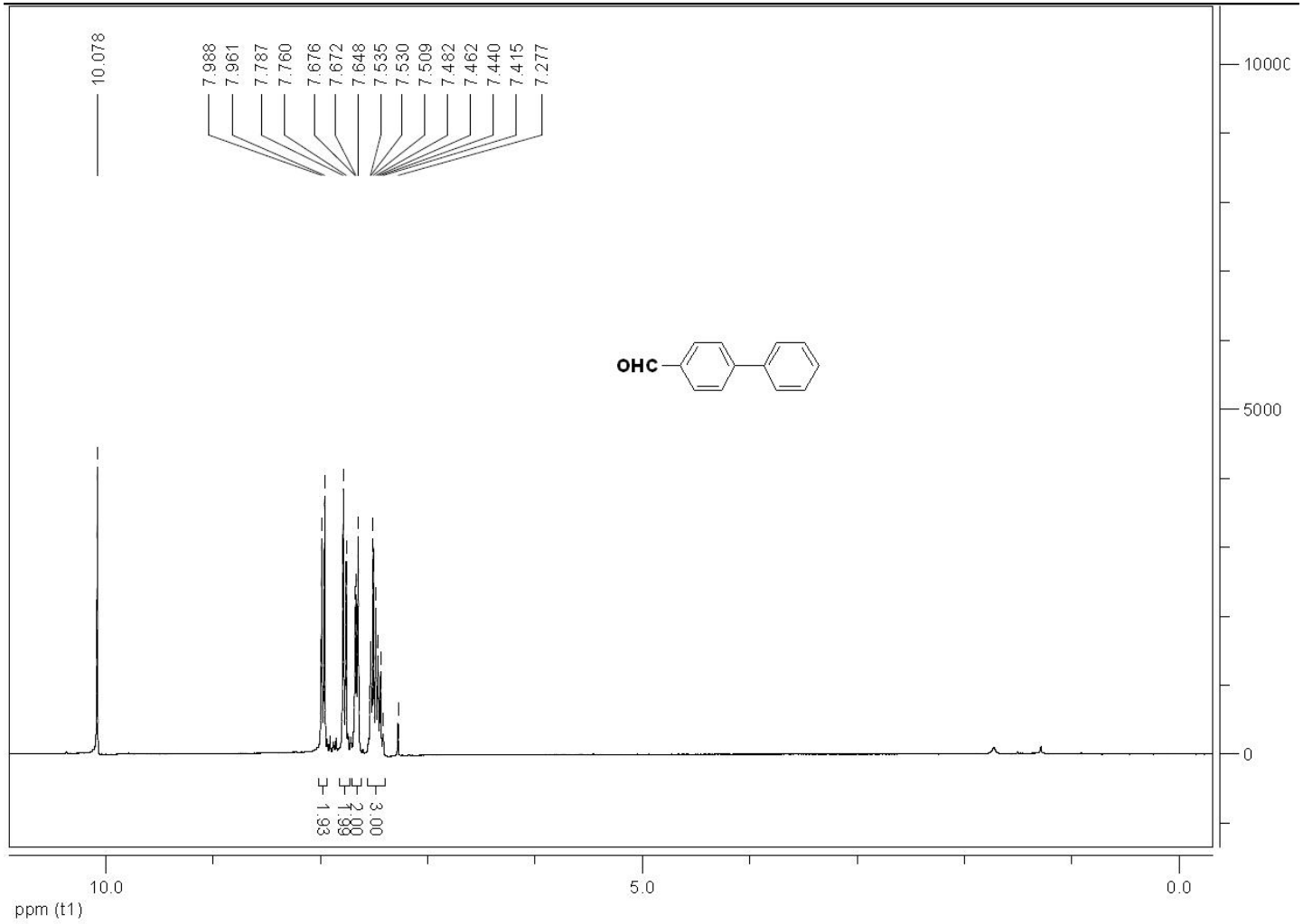
^{13}C NMR spectra of **3m** ($CDCl_3$, 75 MHz)



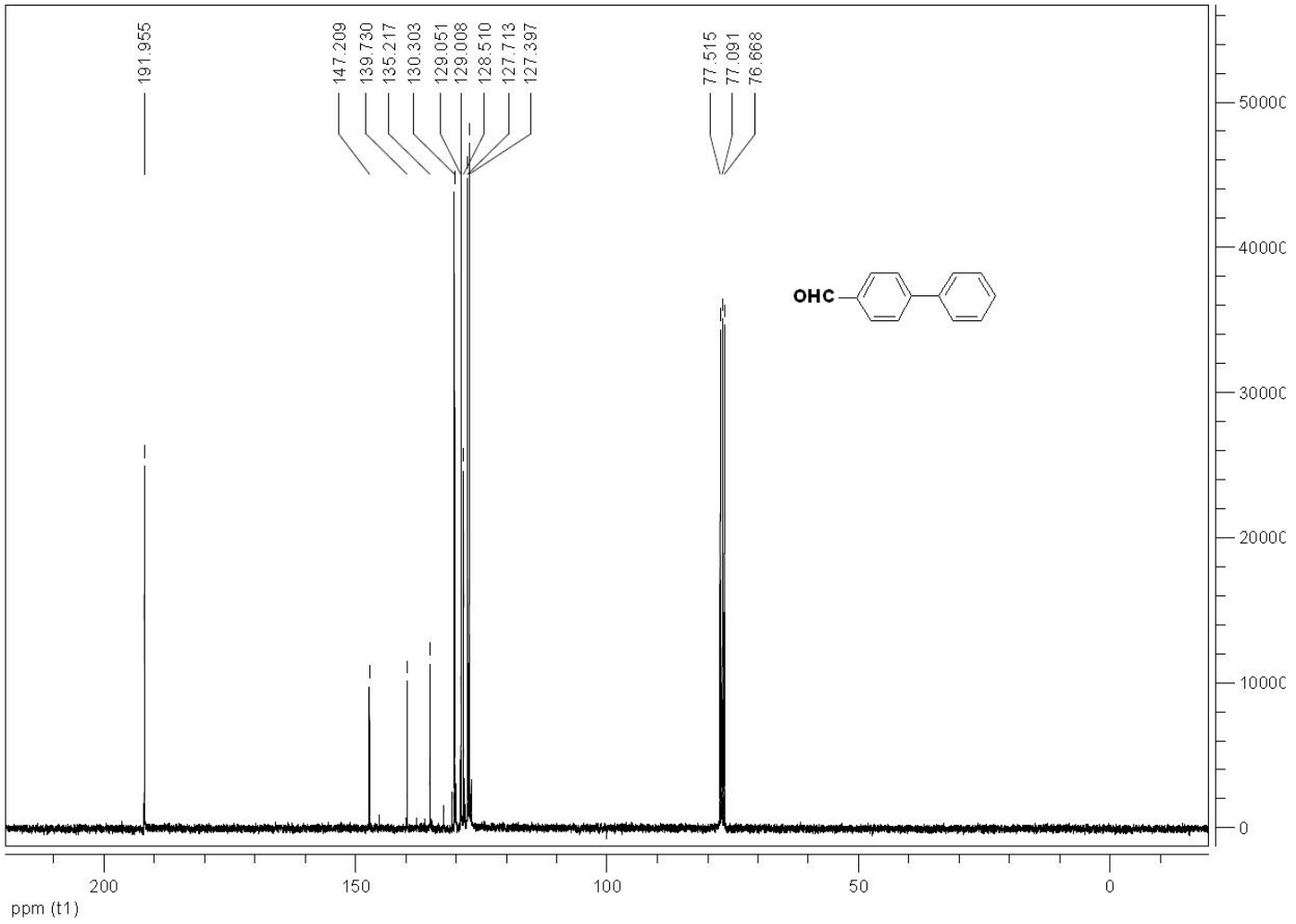
^{1}H NMR spectra of **3n** ($CDCl_3$, 300 MHz)



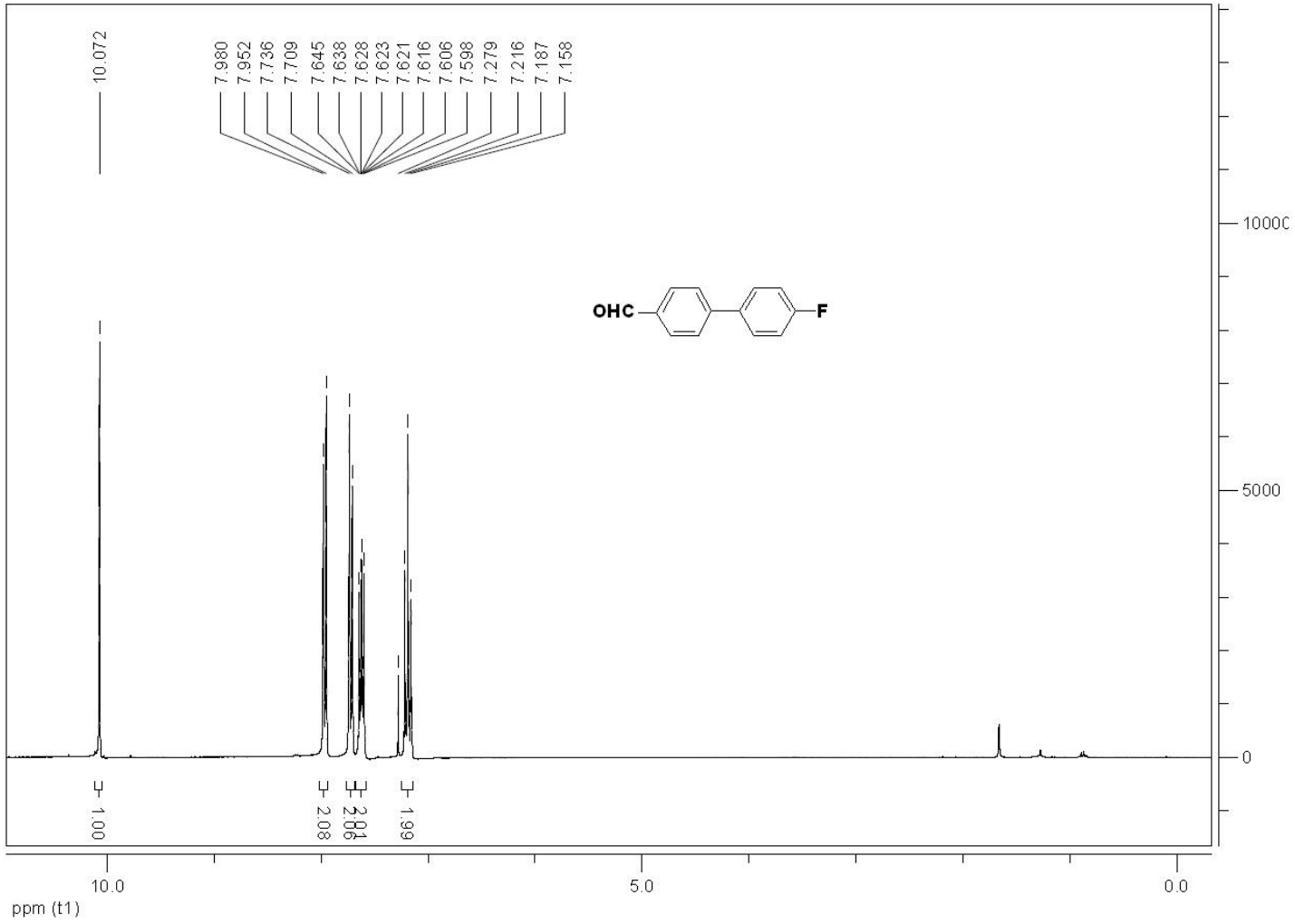
^{13}C NMR spectra of **3n** ($CDCl_3$, 75 MHz)



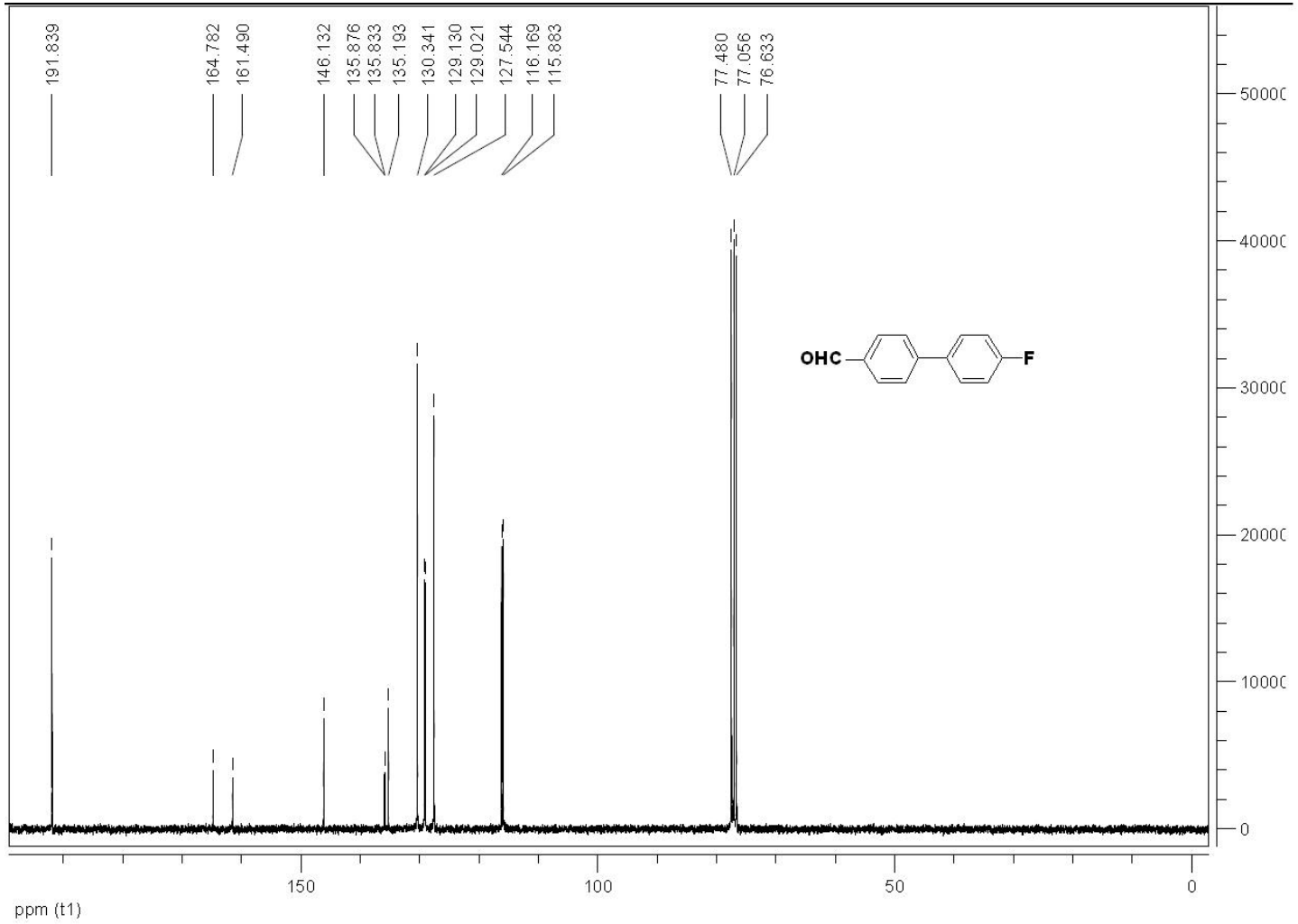
^{1}H NMR spectra of **3o** ($CDCl_3$, 300 MHz)



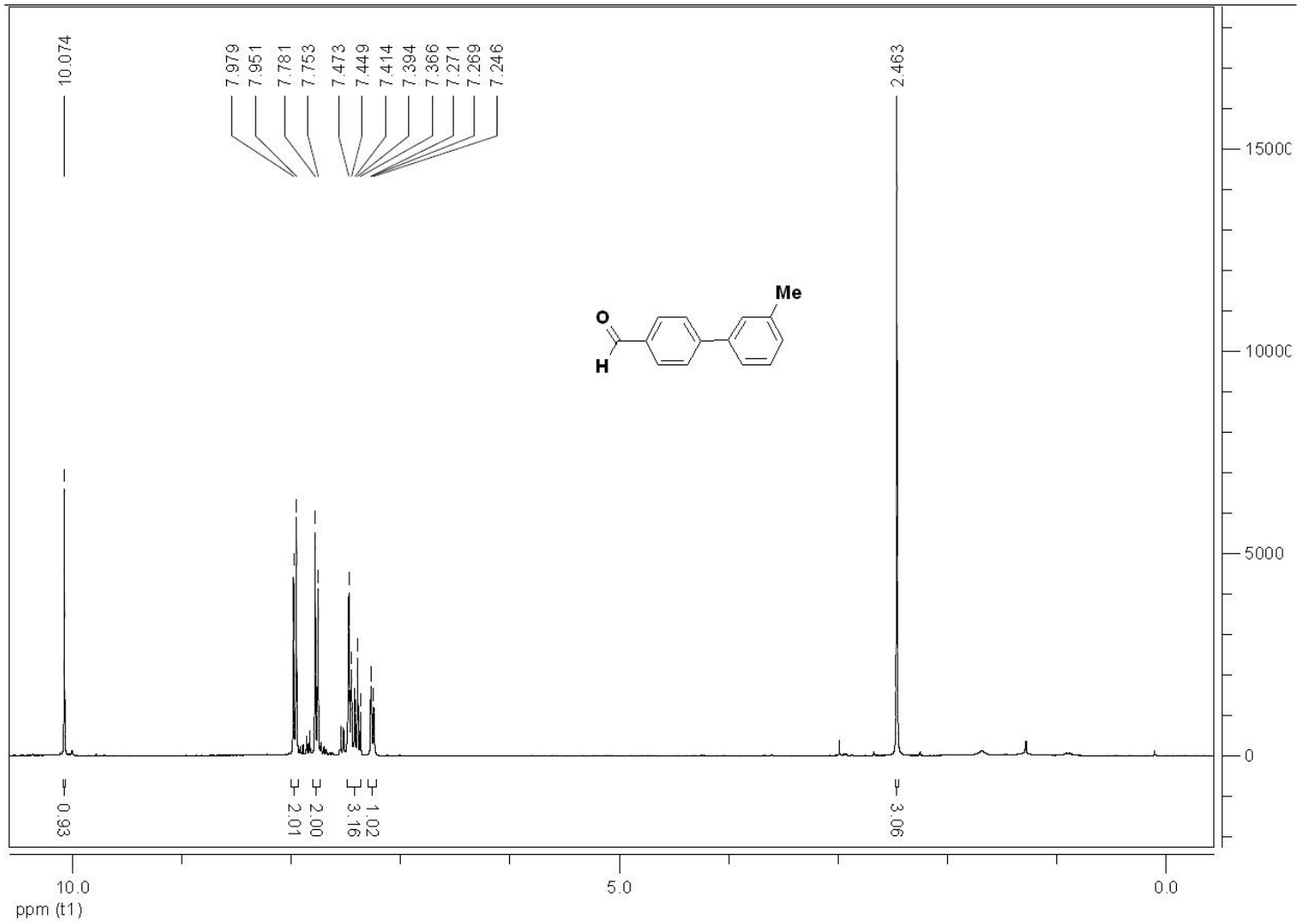
^{13}C NMR spectra of **3o** ($CDCl_3$, 75 MHz)



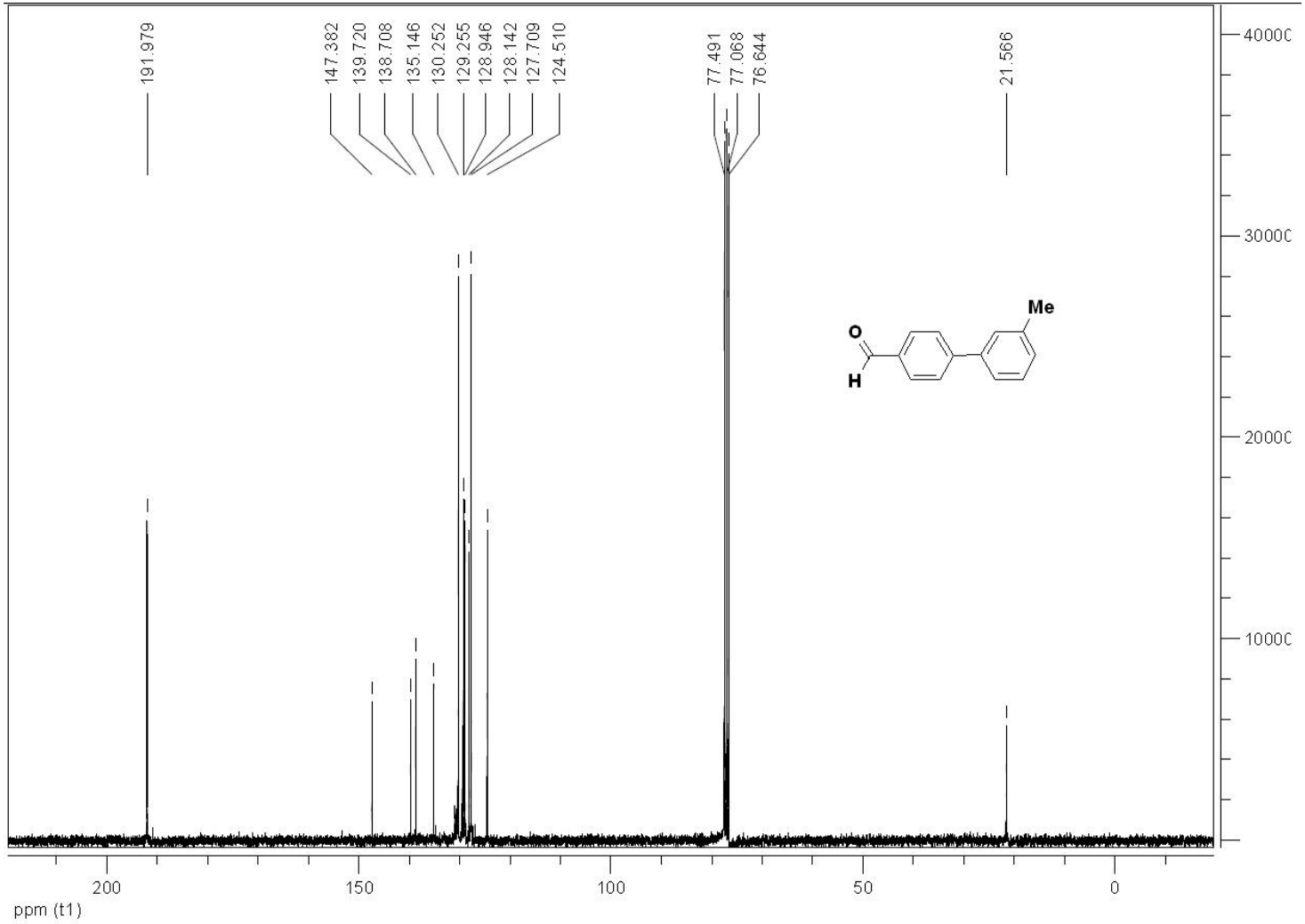
^{1}H NMR spectra of **3p** ($CDCl_3$, 300 MHz)



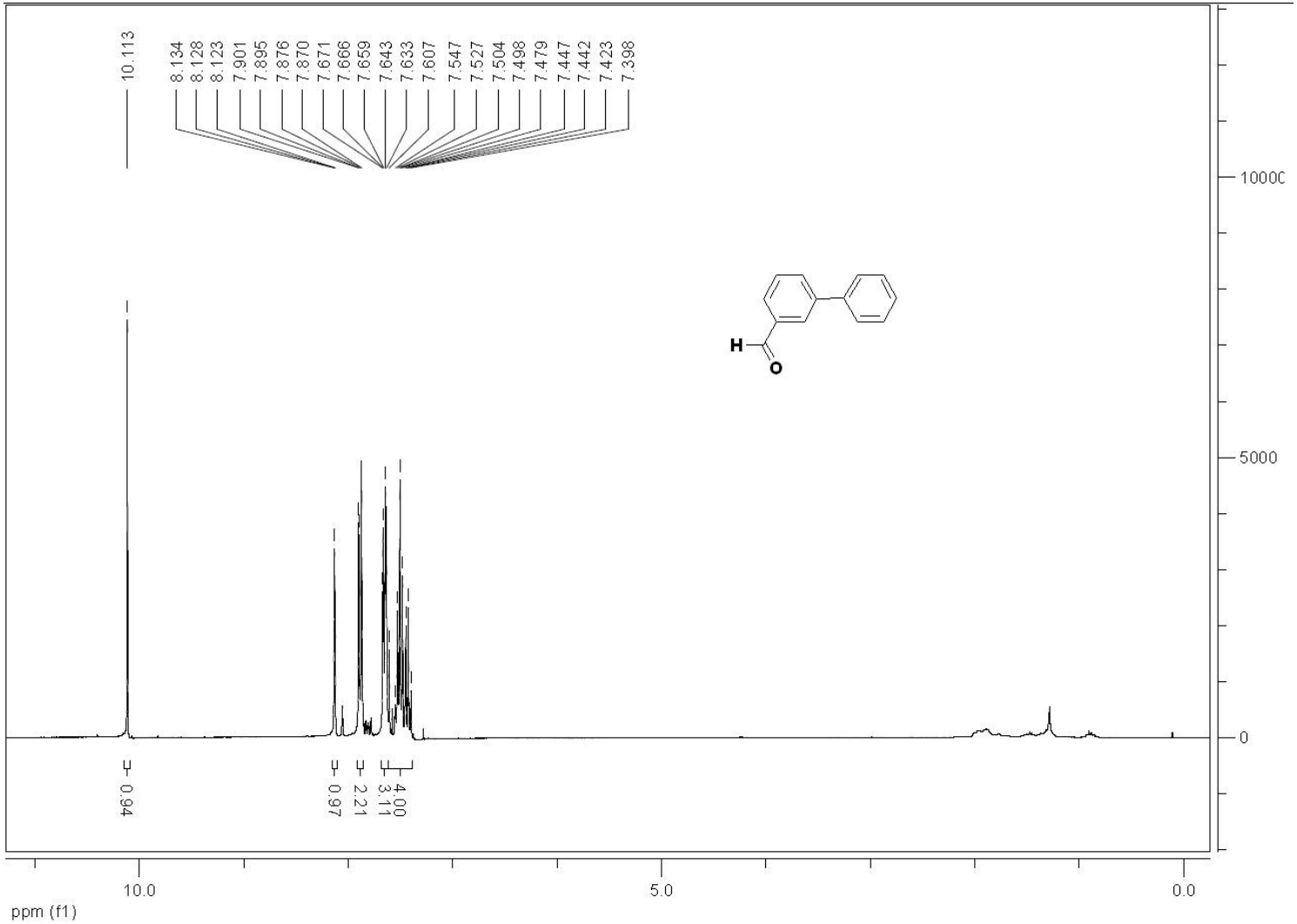
^{13}C NMR spectra of **3p** ($CDCl_3$, 75 MHz)



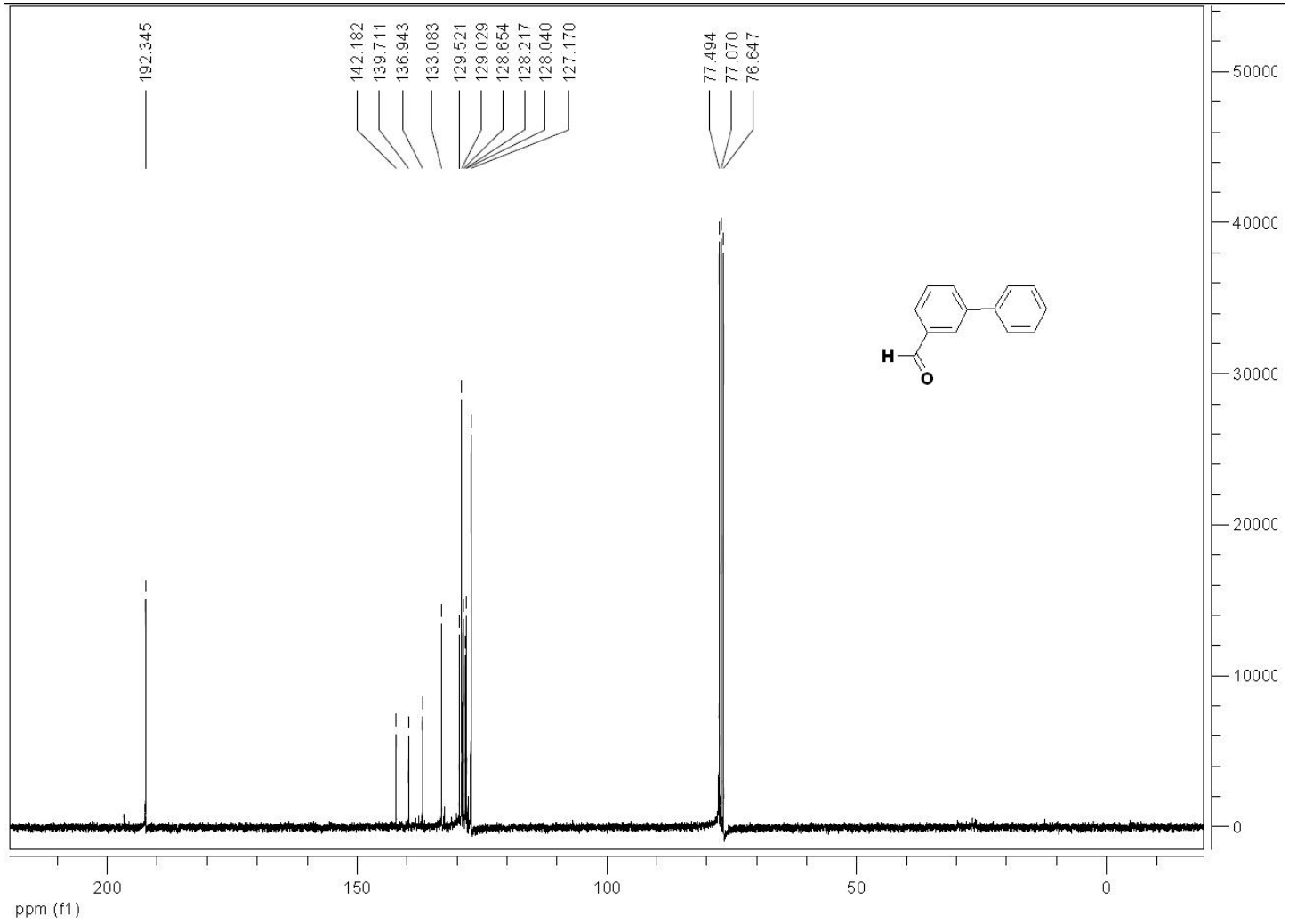
^{1}H NMR spectra of **3q** ($CDCl_3$, 300 MHz)



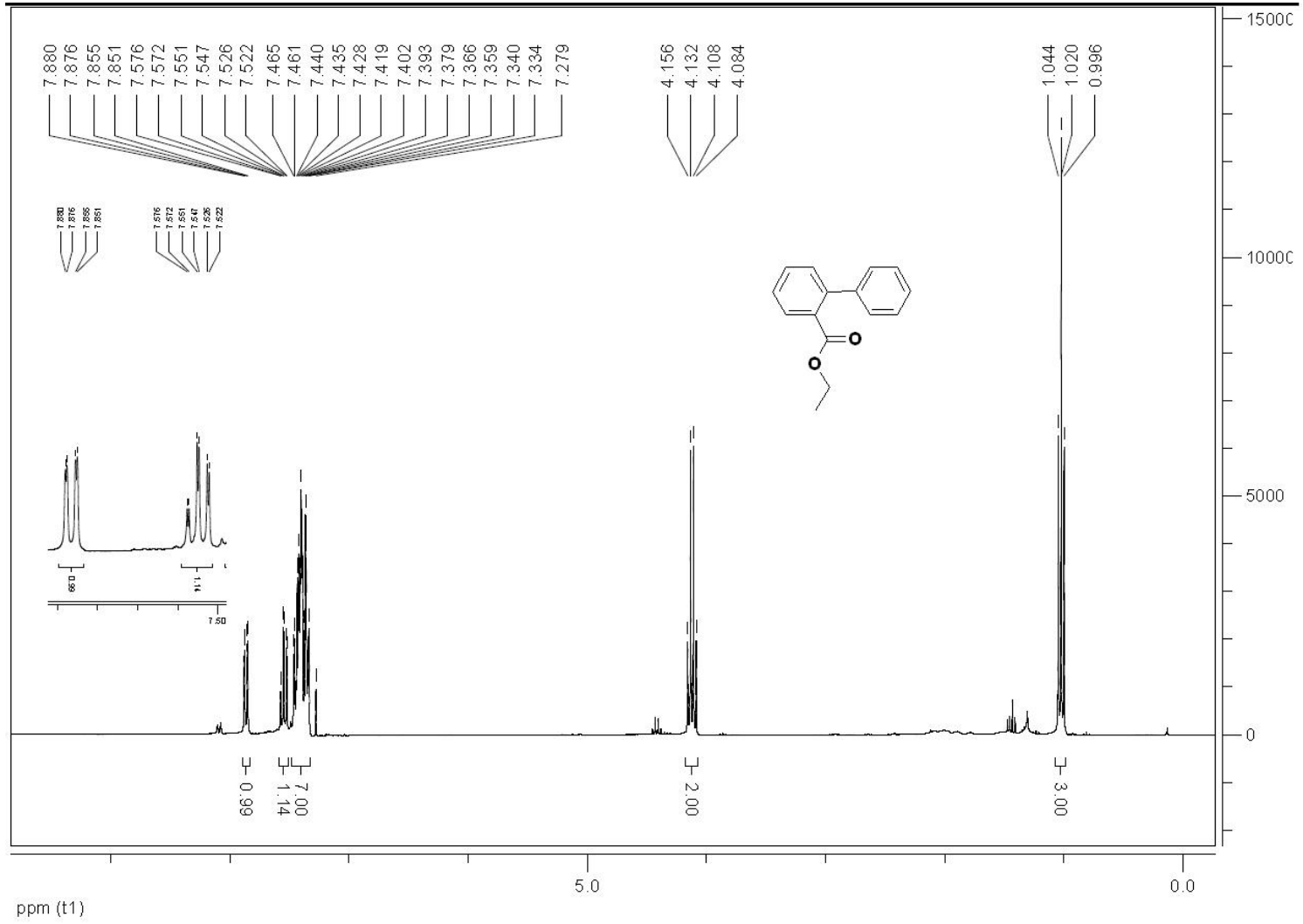
^{13}C NMR spectra of **3q** ($CDCl_3$, 75 MHz)



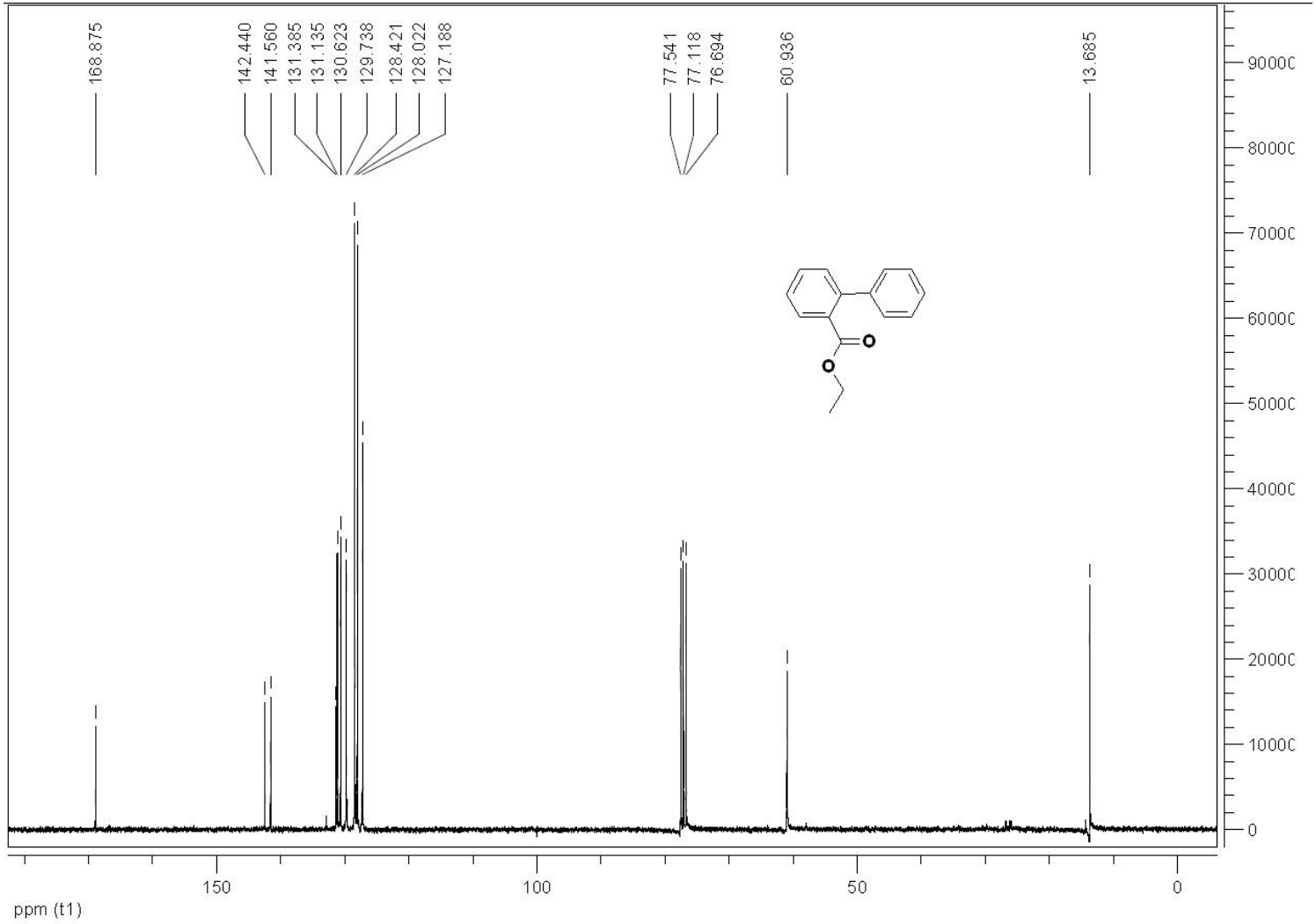
^{1}H NMR spectra of **3r** ($CDCl_3$, 300 MHz)



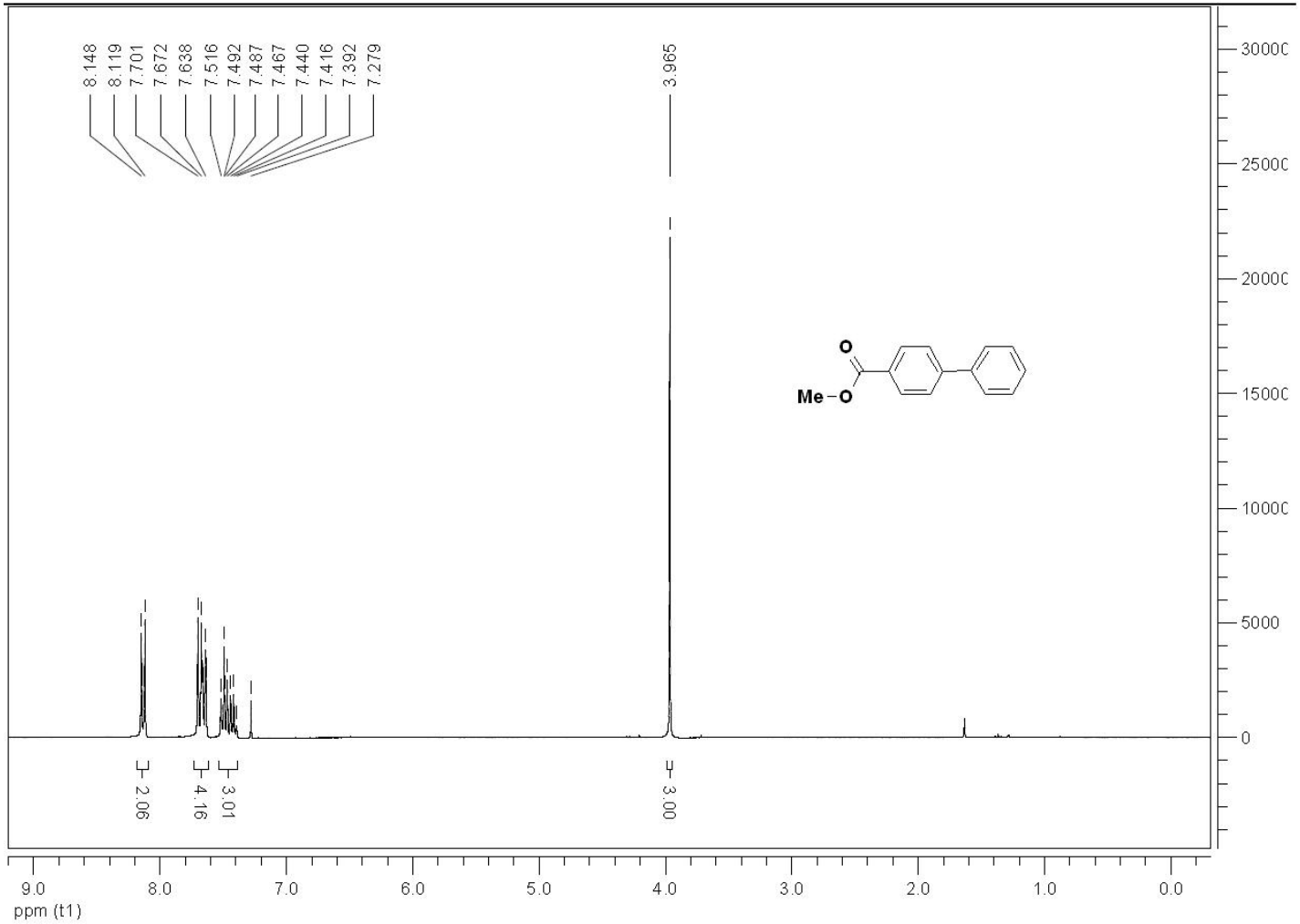
^{13}C NMR spectra of **3r** ($CDCl_3$, 75 MHz)



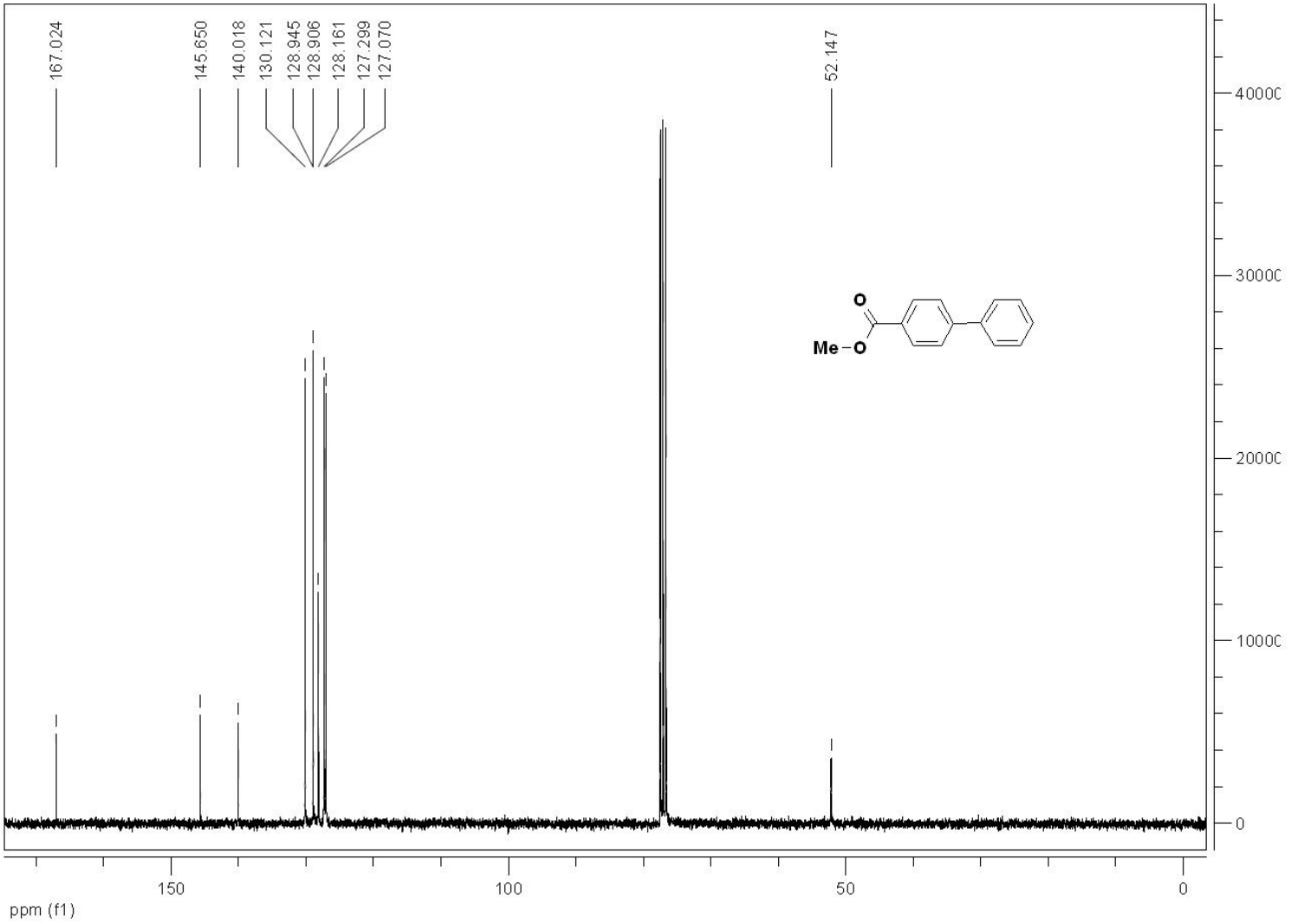
^{1}H NMR spectra of **3s** ($CDCl_3$, 300 MHz)



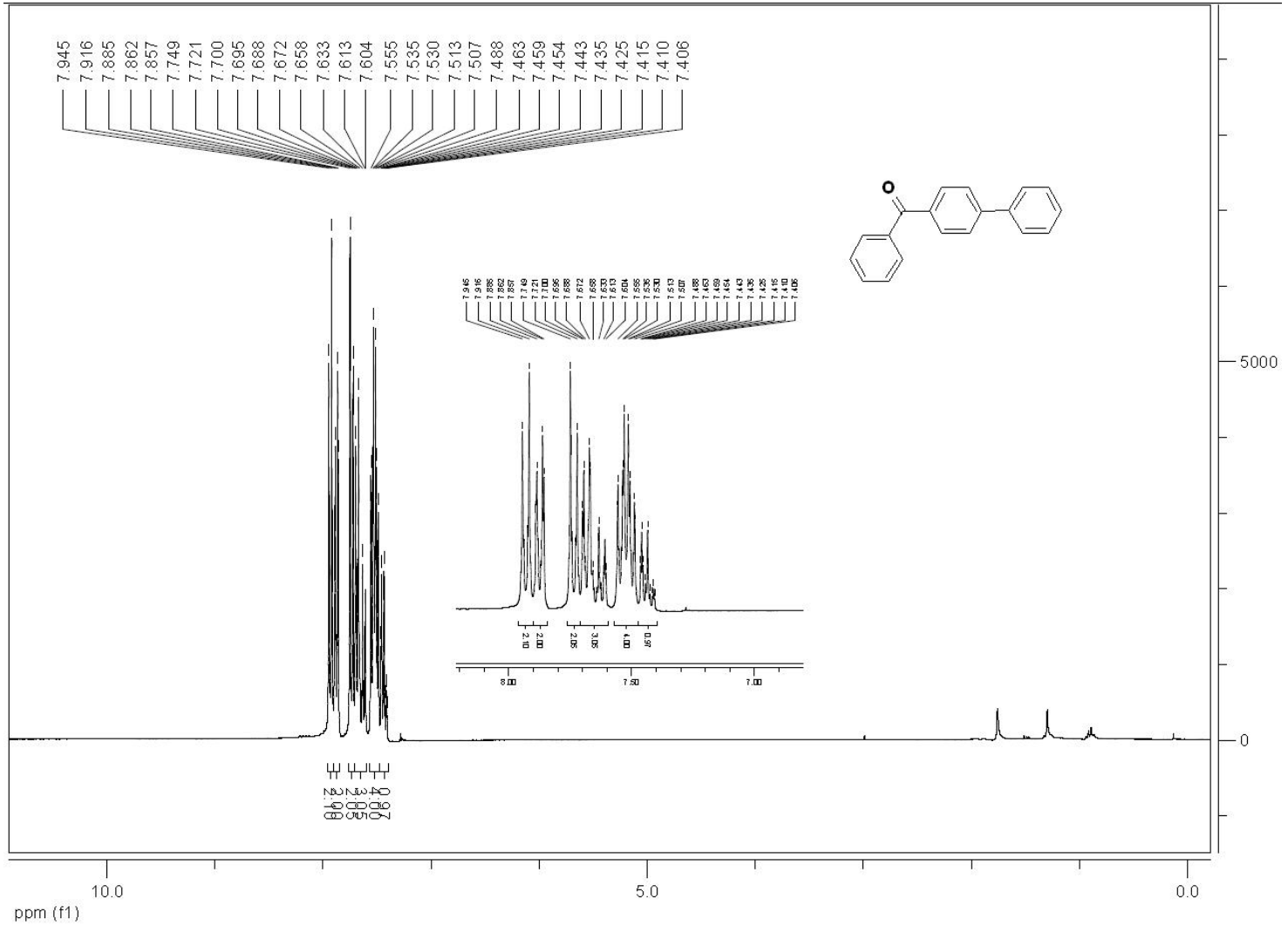
^{13}C NMR spectra of **3s** ($CDCl_3$, 75 MHz)



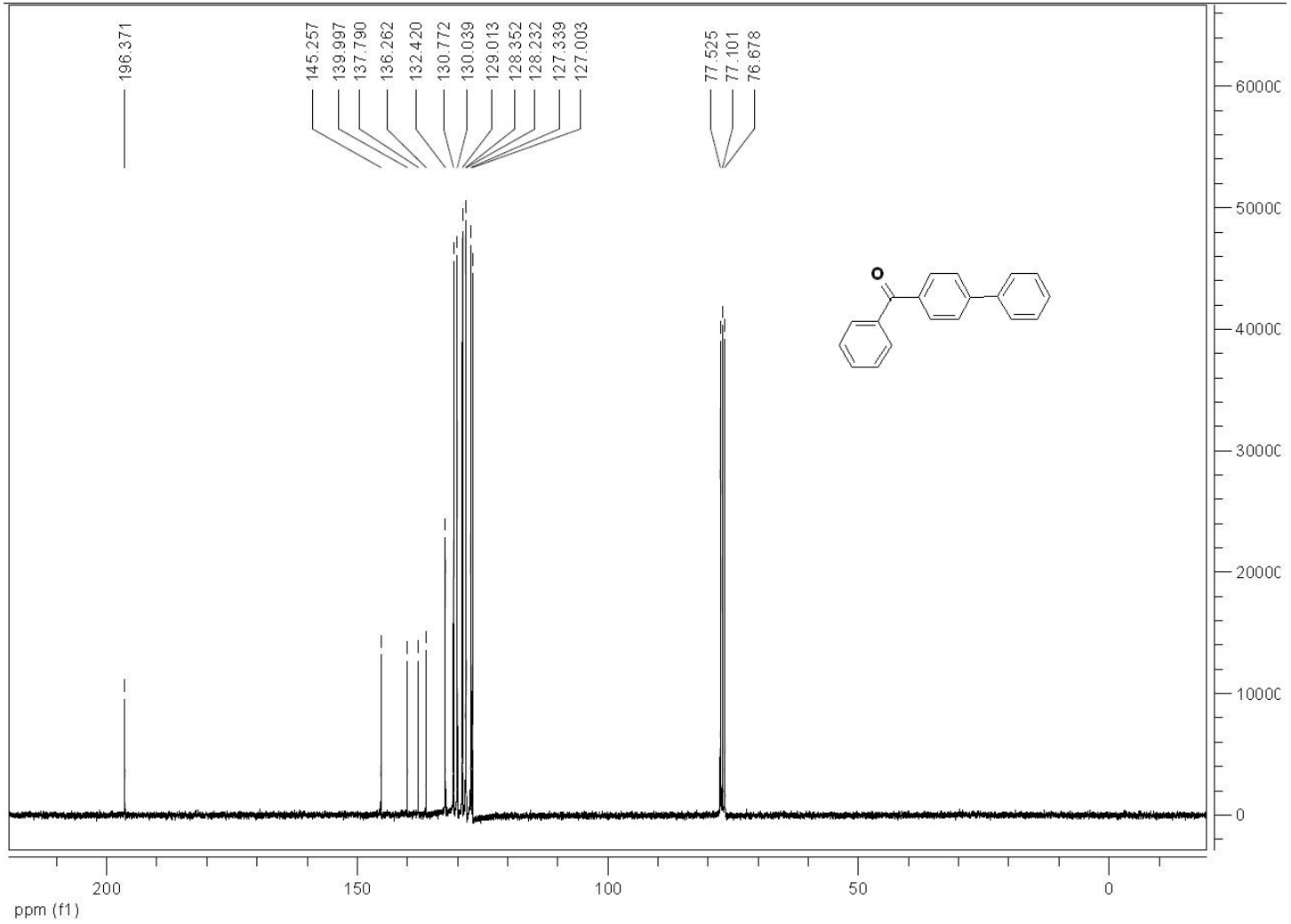
^{1}H NMR spectra of **3t** ($CDCl_3$, 300 MHz)



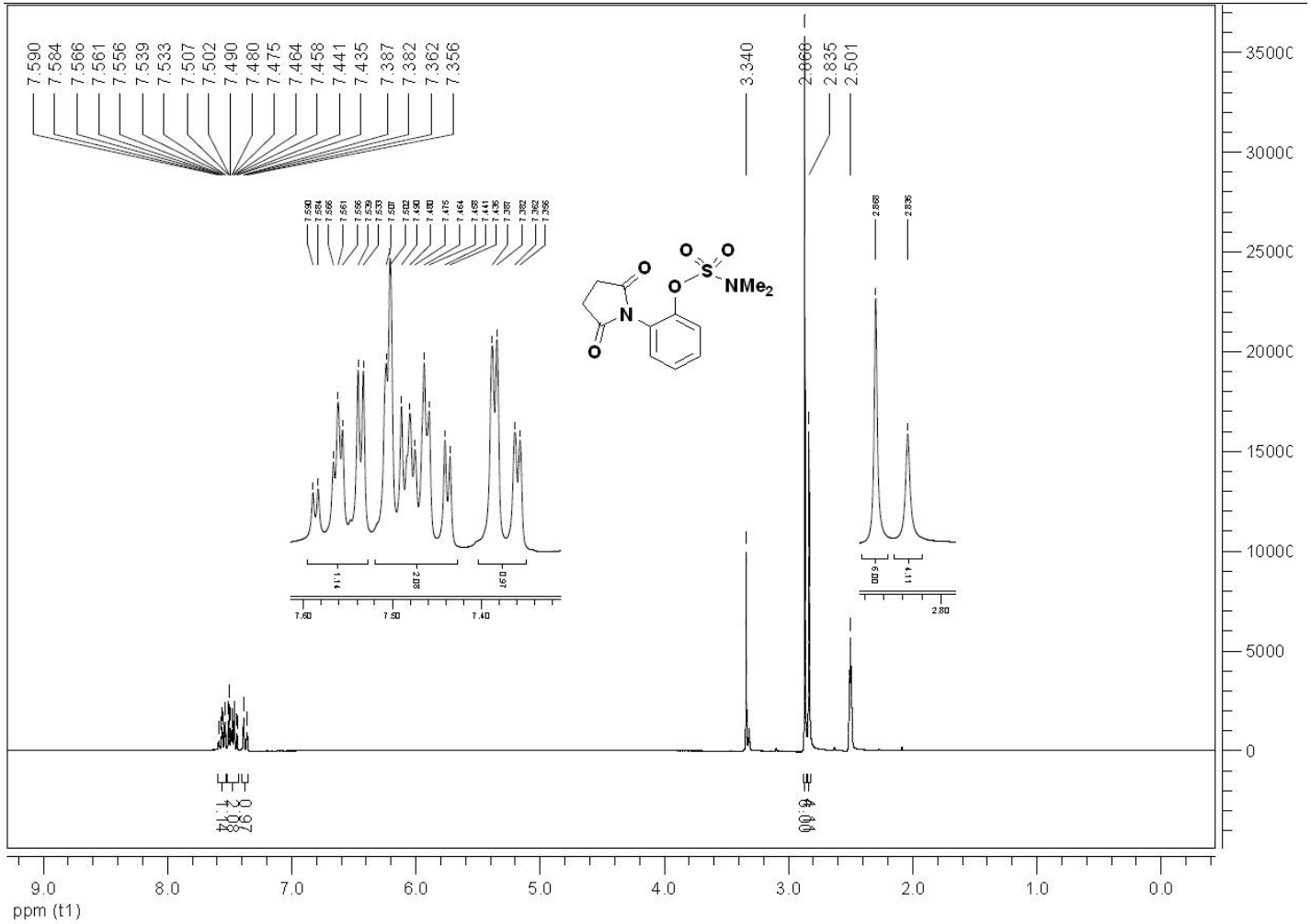
^{13}C NMR spectra of **3t** ($CDCl_3$, 75 MHz)



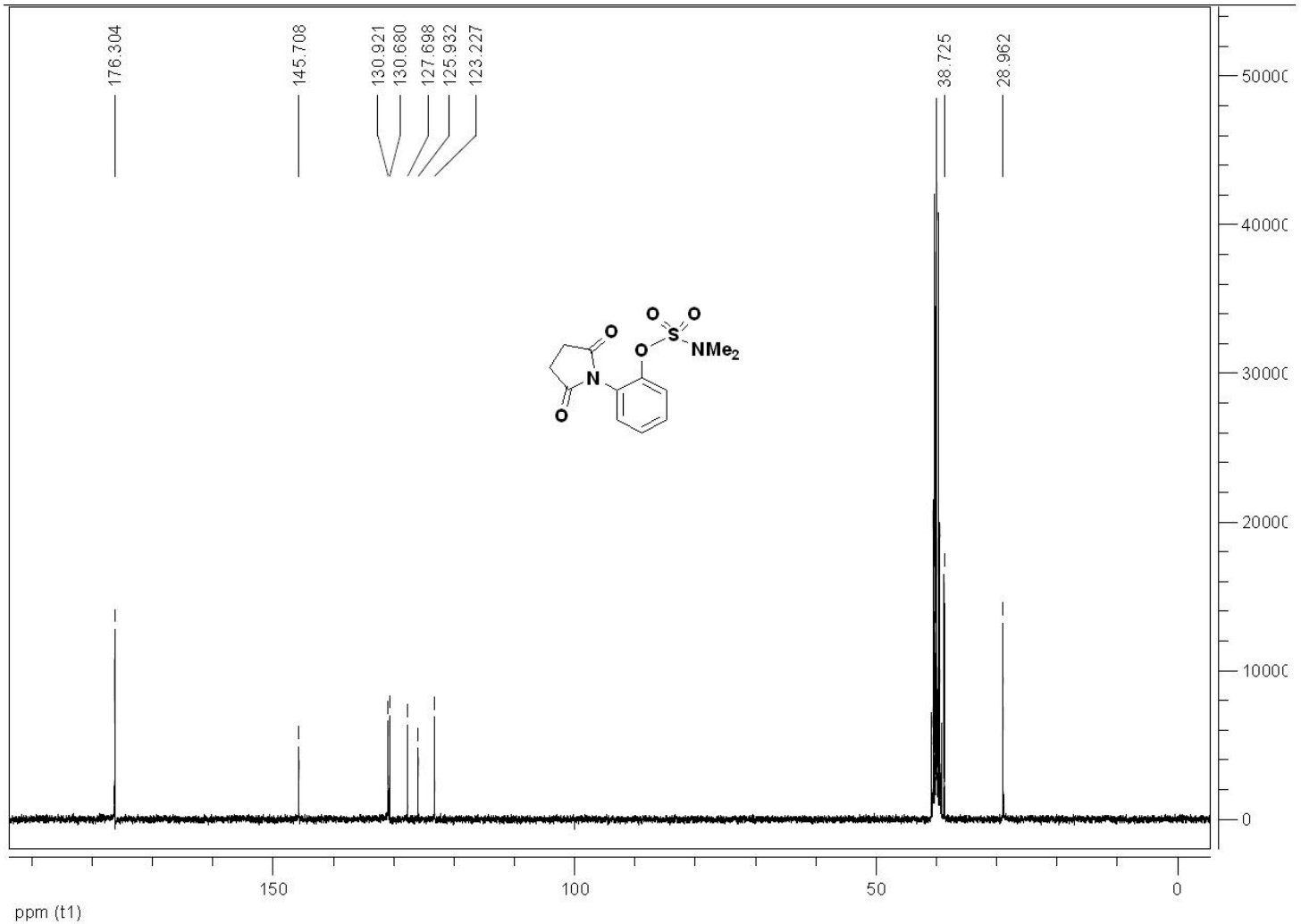
^{1}H NMR spectra of **3u** ($CDCl_3$, 300 MHz)



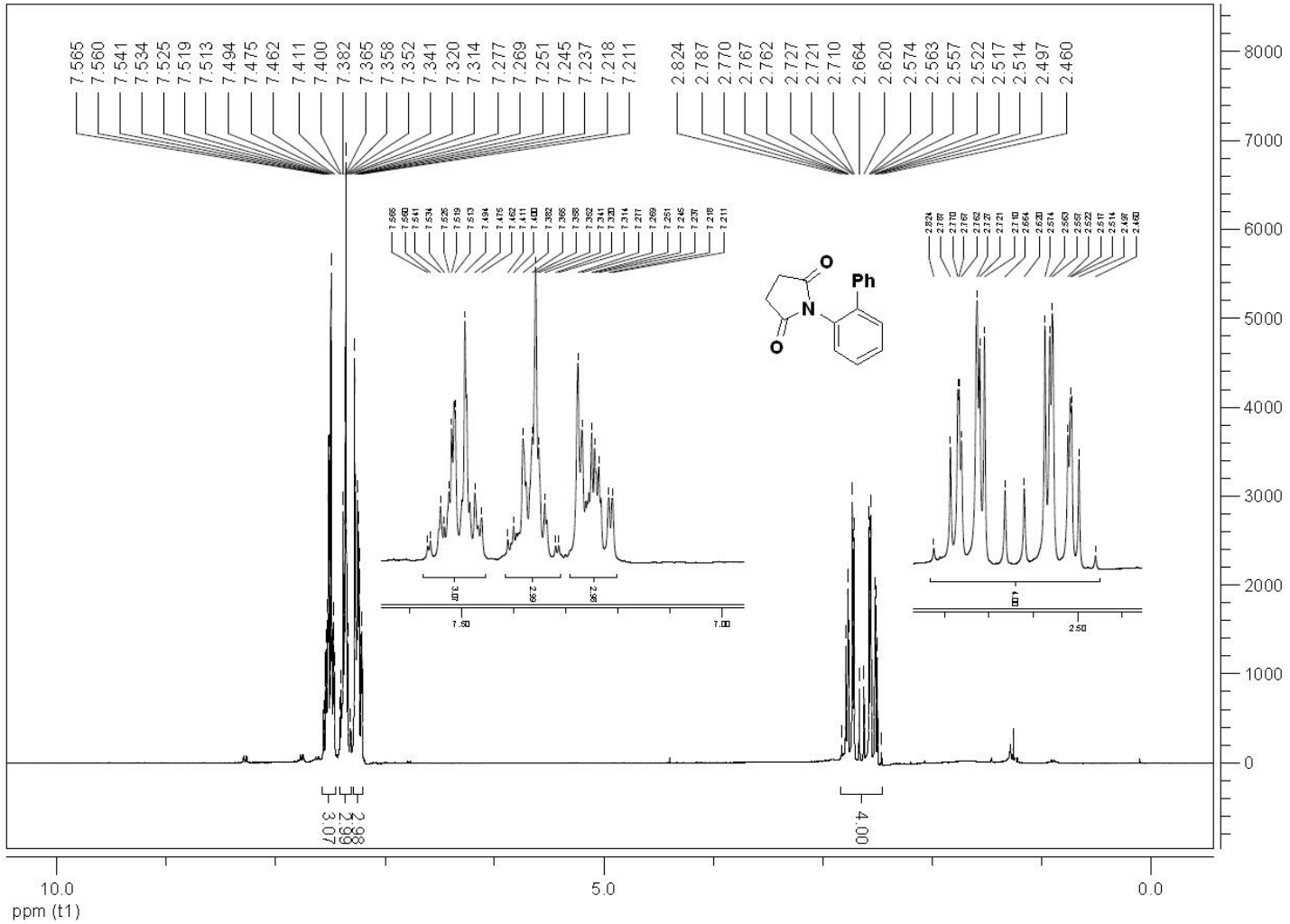
^{13}C NMR spectra of **3u** ($CDCl_3$, 75 MHz)



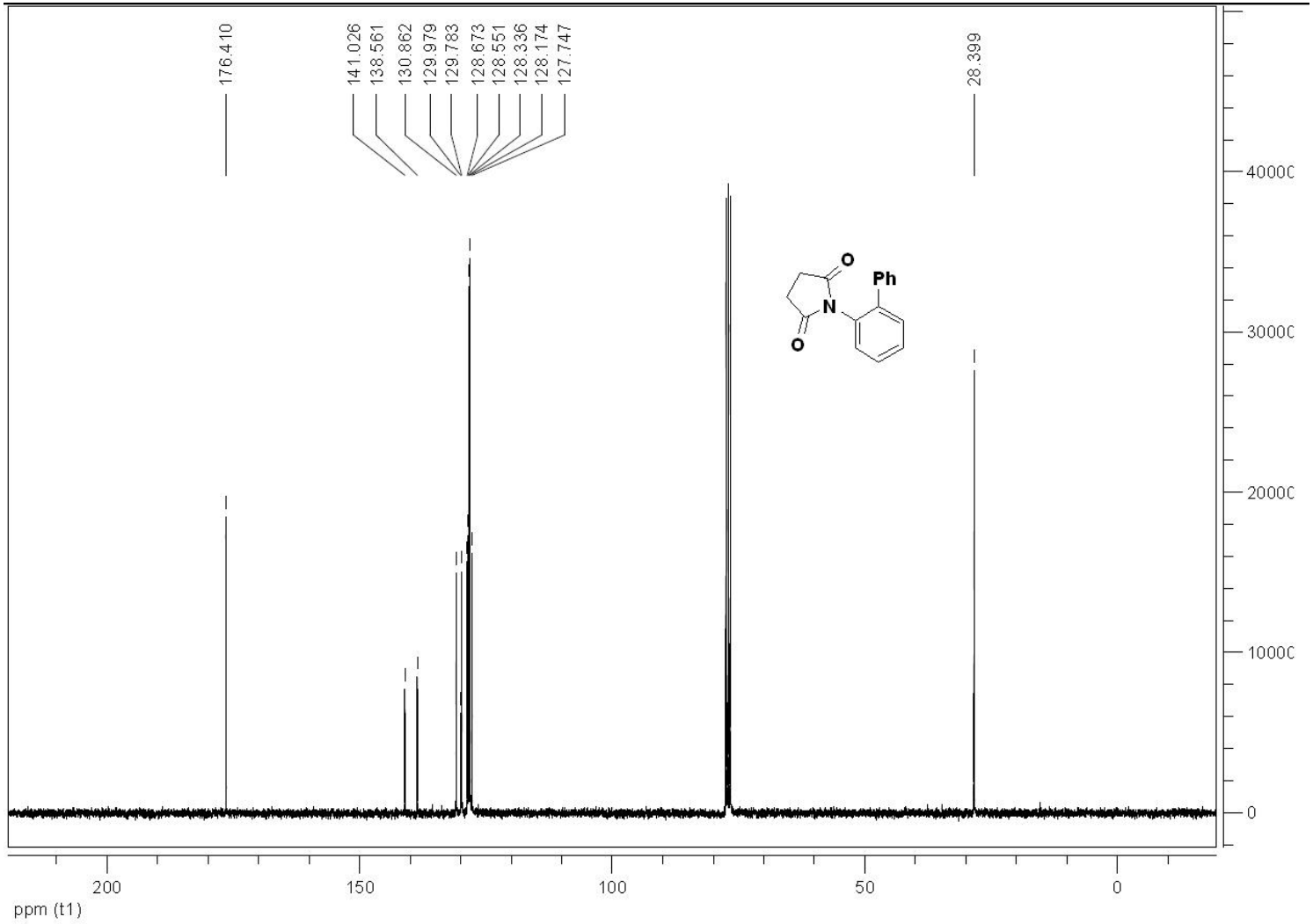
^{1}H NMR spectra of **6** (DMSO-d_6, 300 MHz)



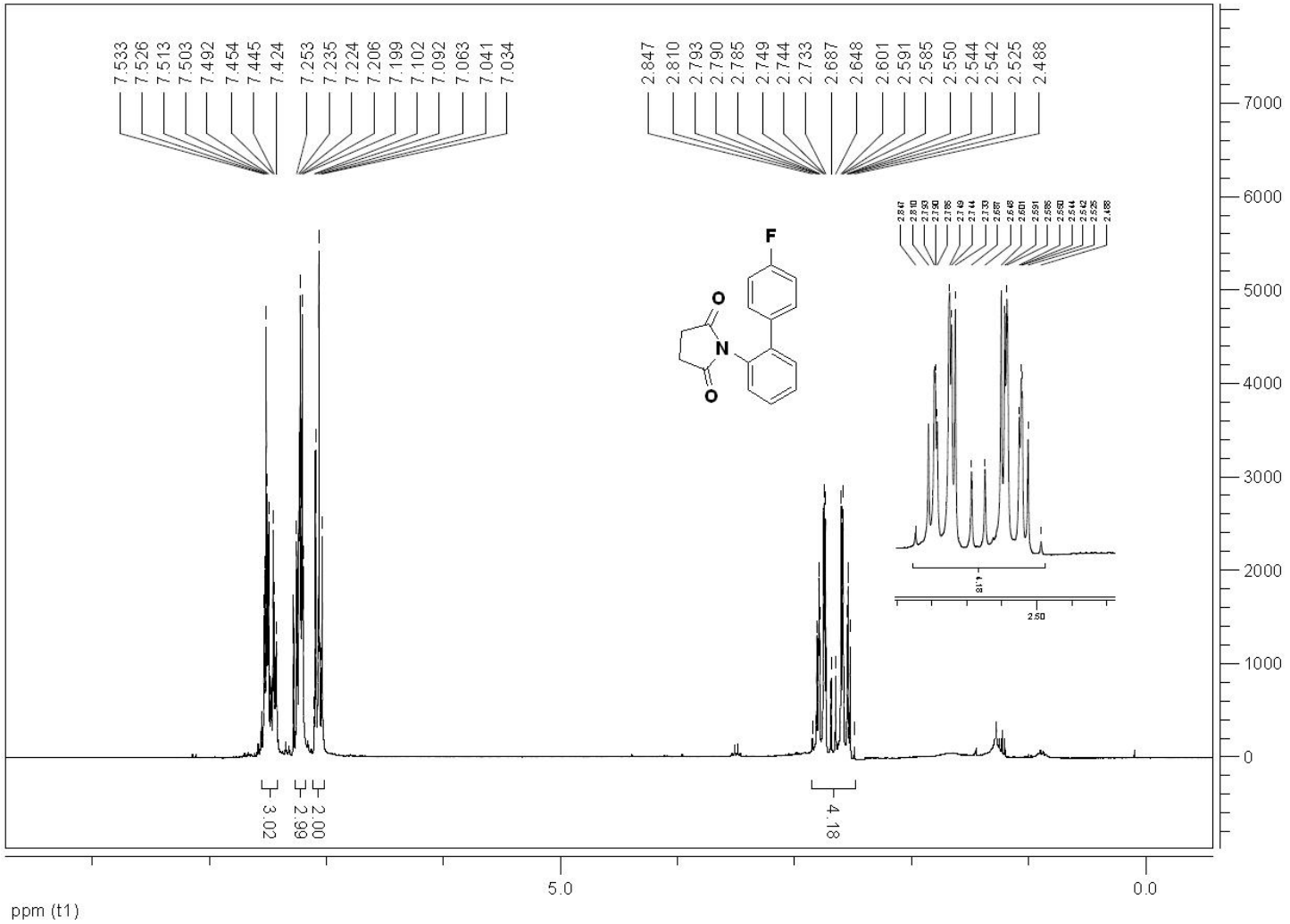
^{13}C NMR spectra of **6** (DMSO-d_6, 75 MHz)



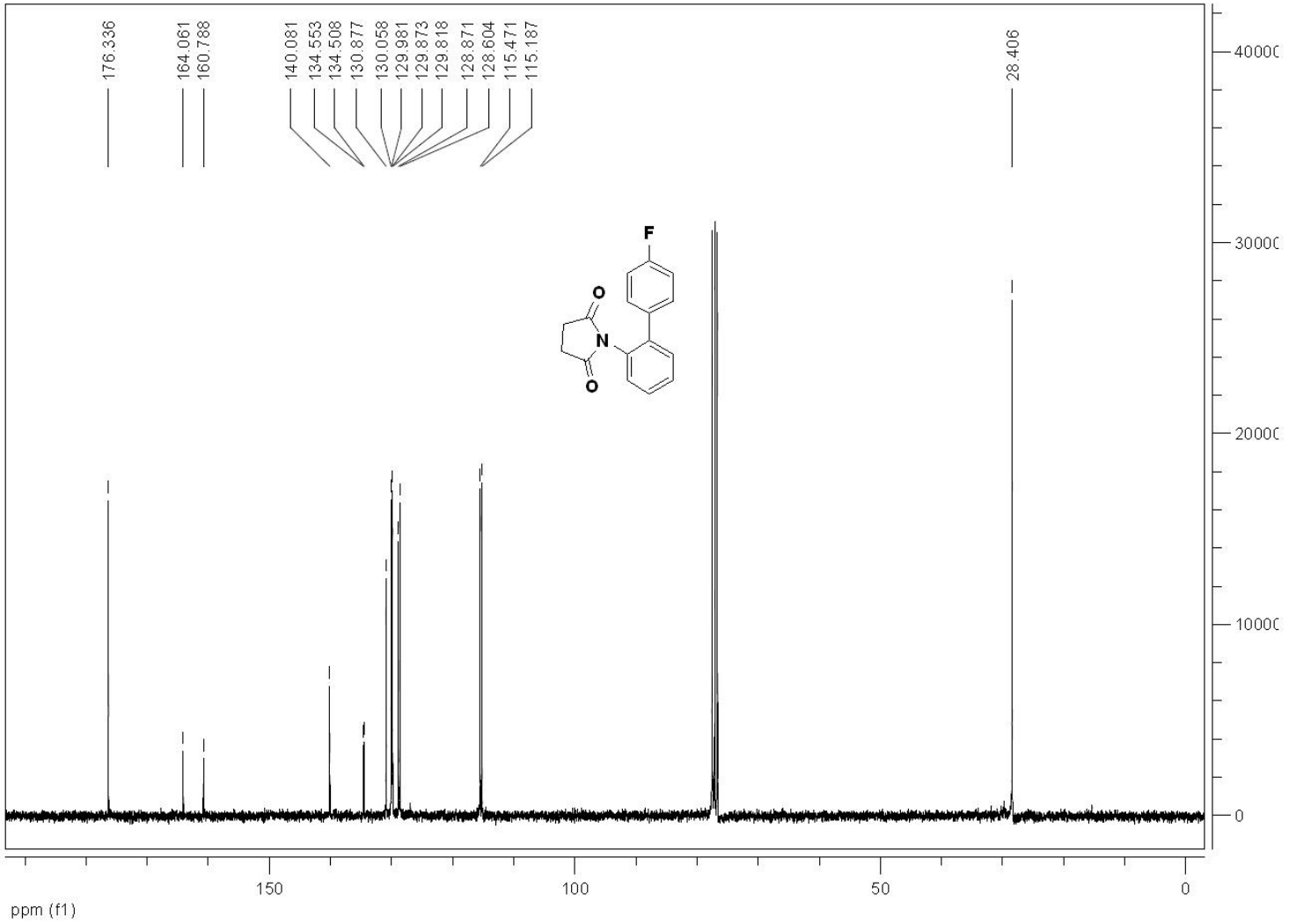
^{1}H NMR spectra of **7a** ($CDCl_3$, 300 MHz)



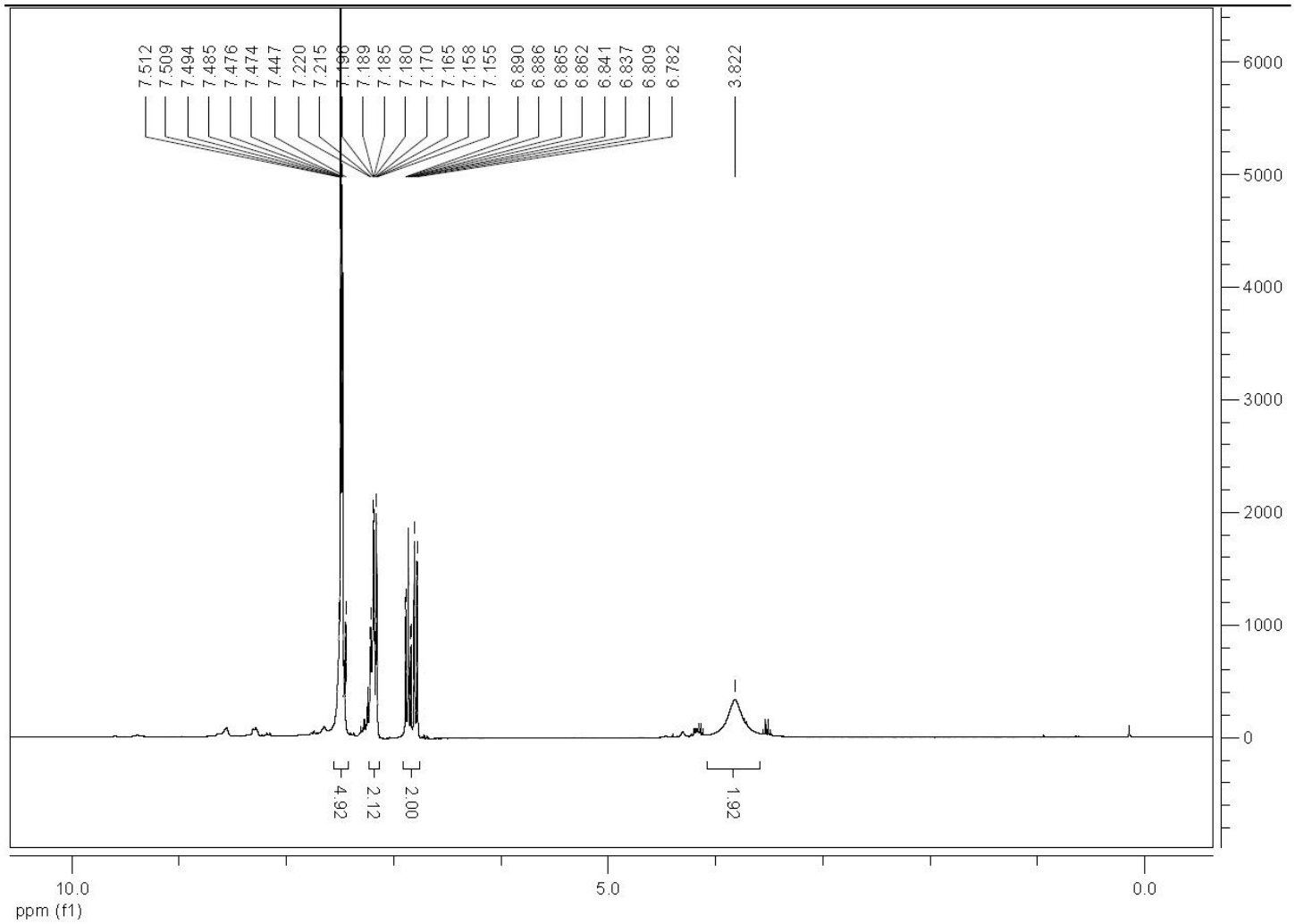
^{13}C NMR spectra of **7a** ($CDCl_3$, 75 MHz)



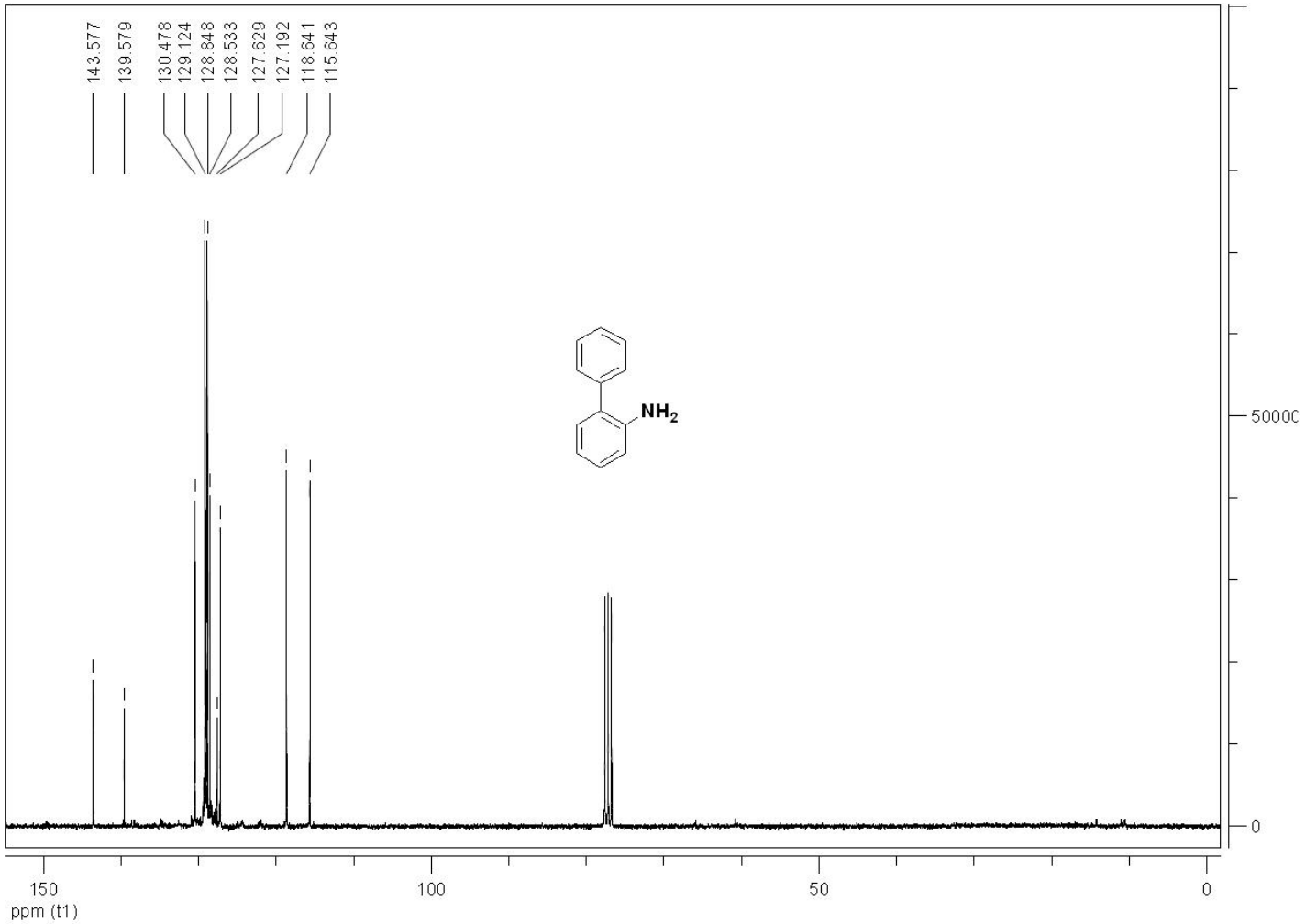
^{1}H NMR spectra of **7b** ($CDCl_3$, 300 MHz)



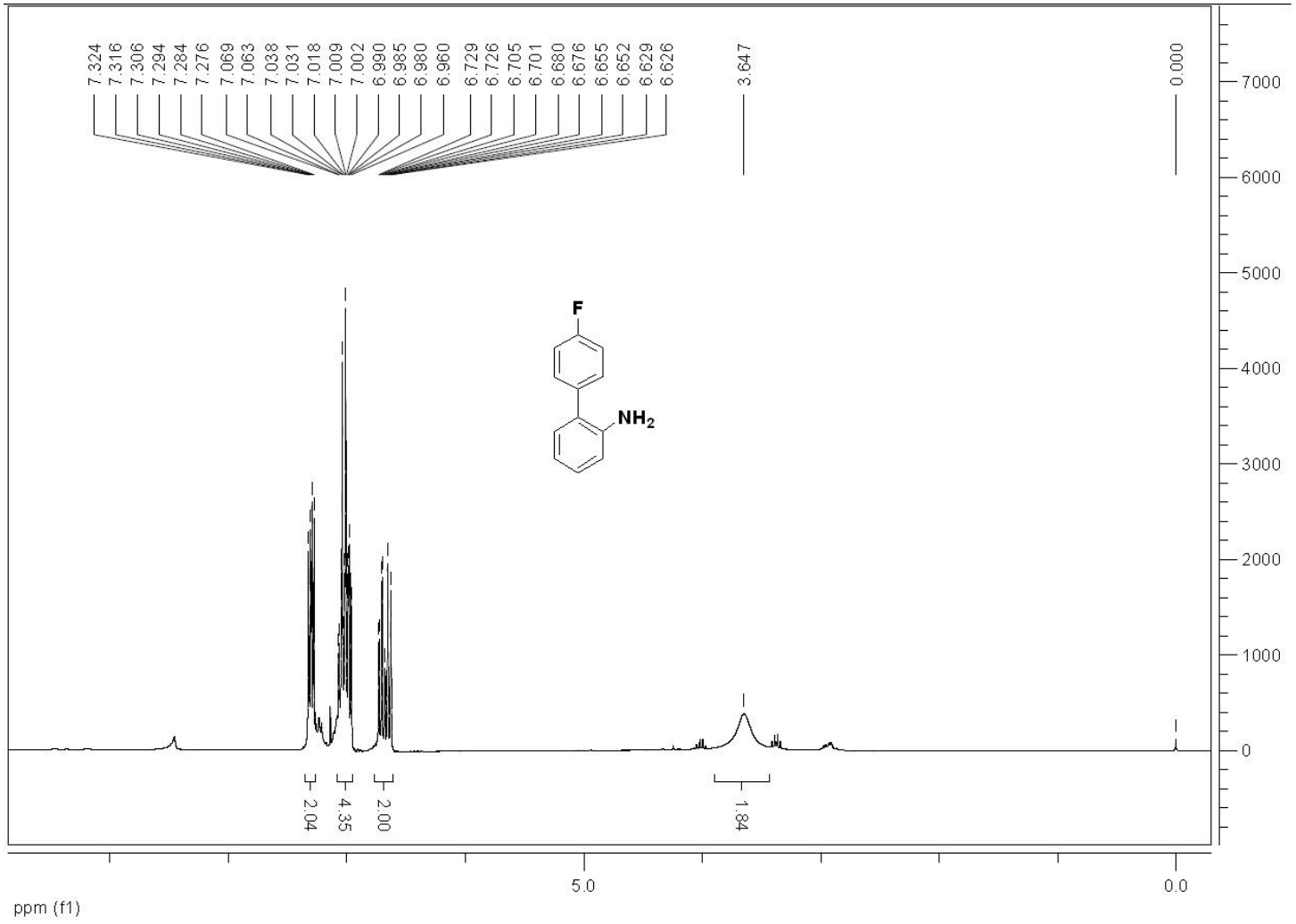
^{13}C NMR spectra of **7b** ($CDCl_3$, 75 MHz)



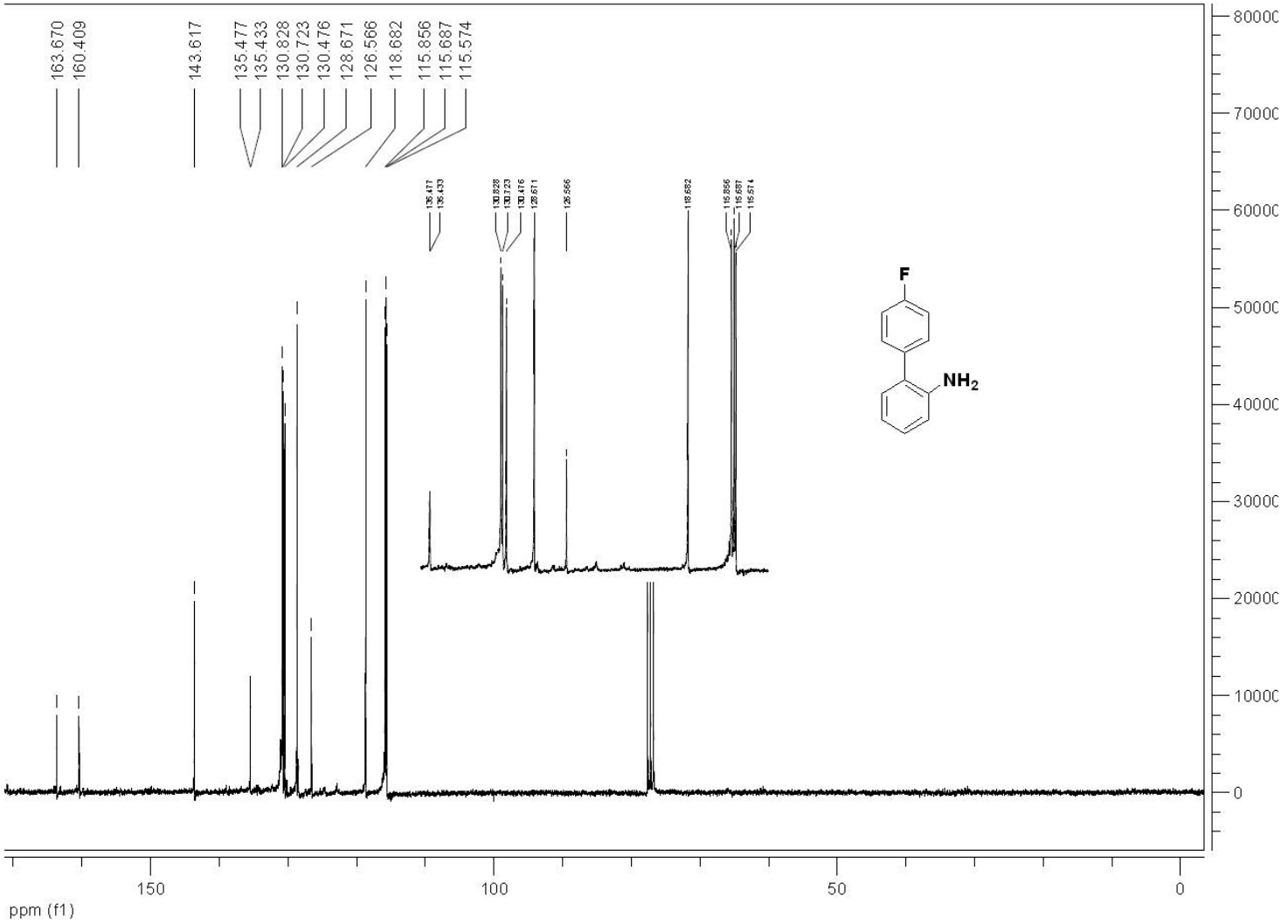
^{1}H NMR spectra of **8a** ($CDCl_3$, 300 MHz)



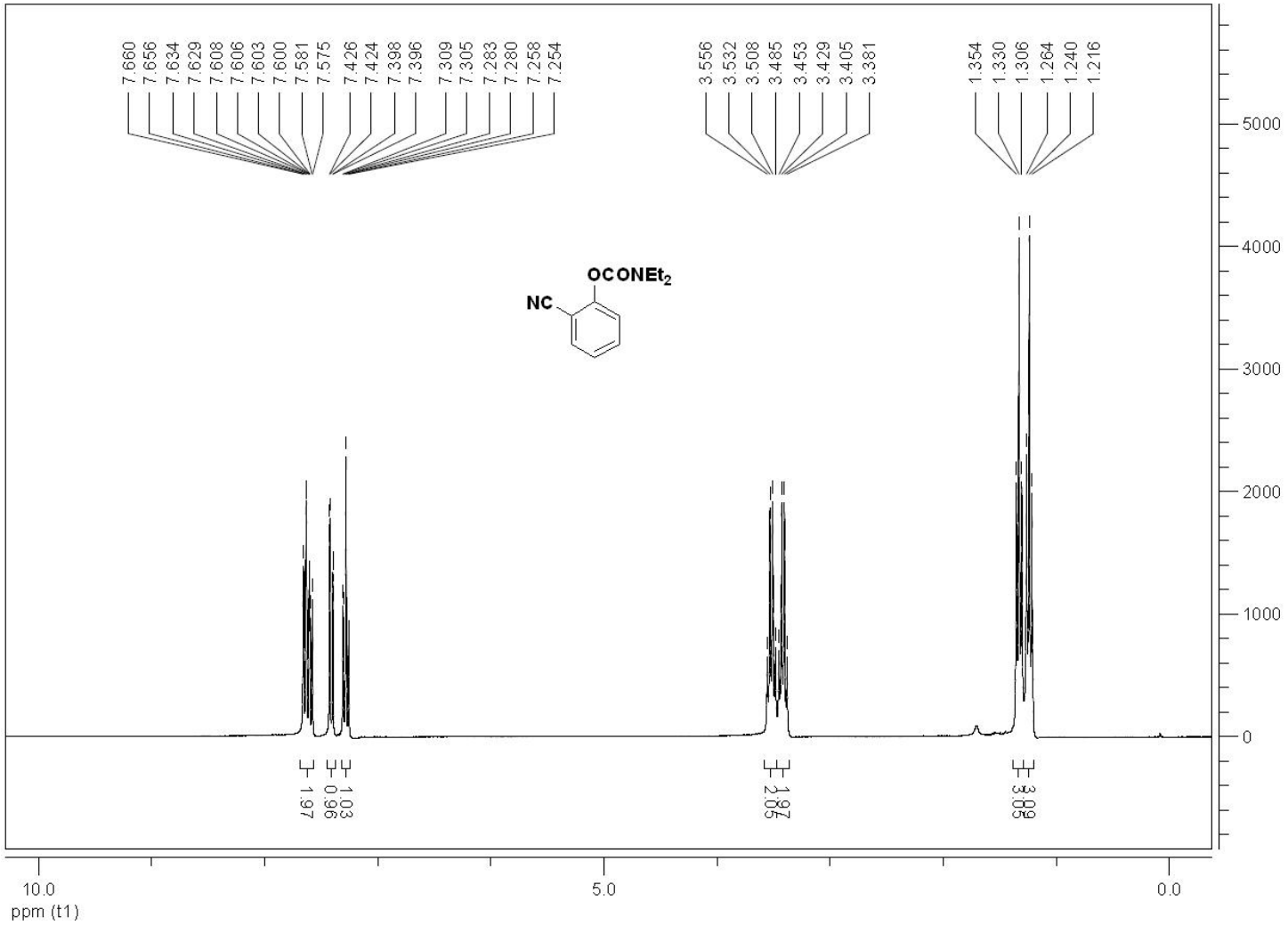
^{13}C NMR spectra of **8a** ($CDCl_3$, 75 MHz)



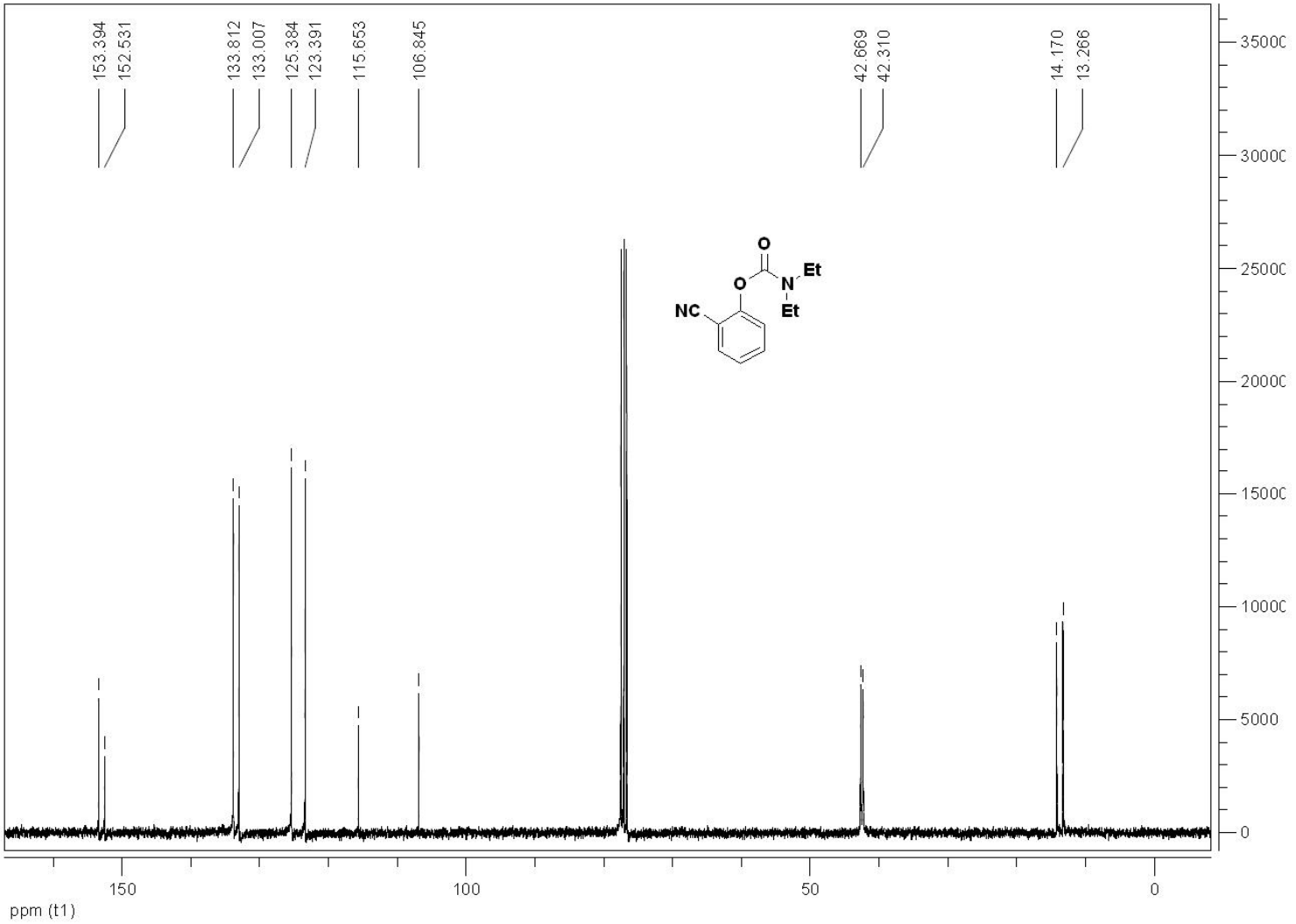
^{1}H NMR spectra of **8b** ($CDCl_3$, 300 MHz)



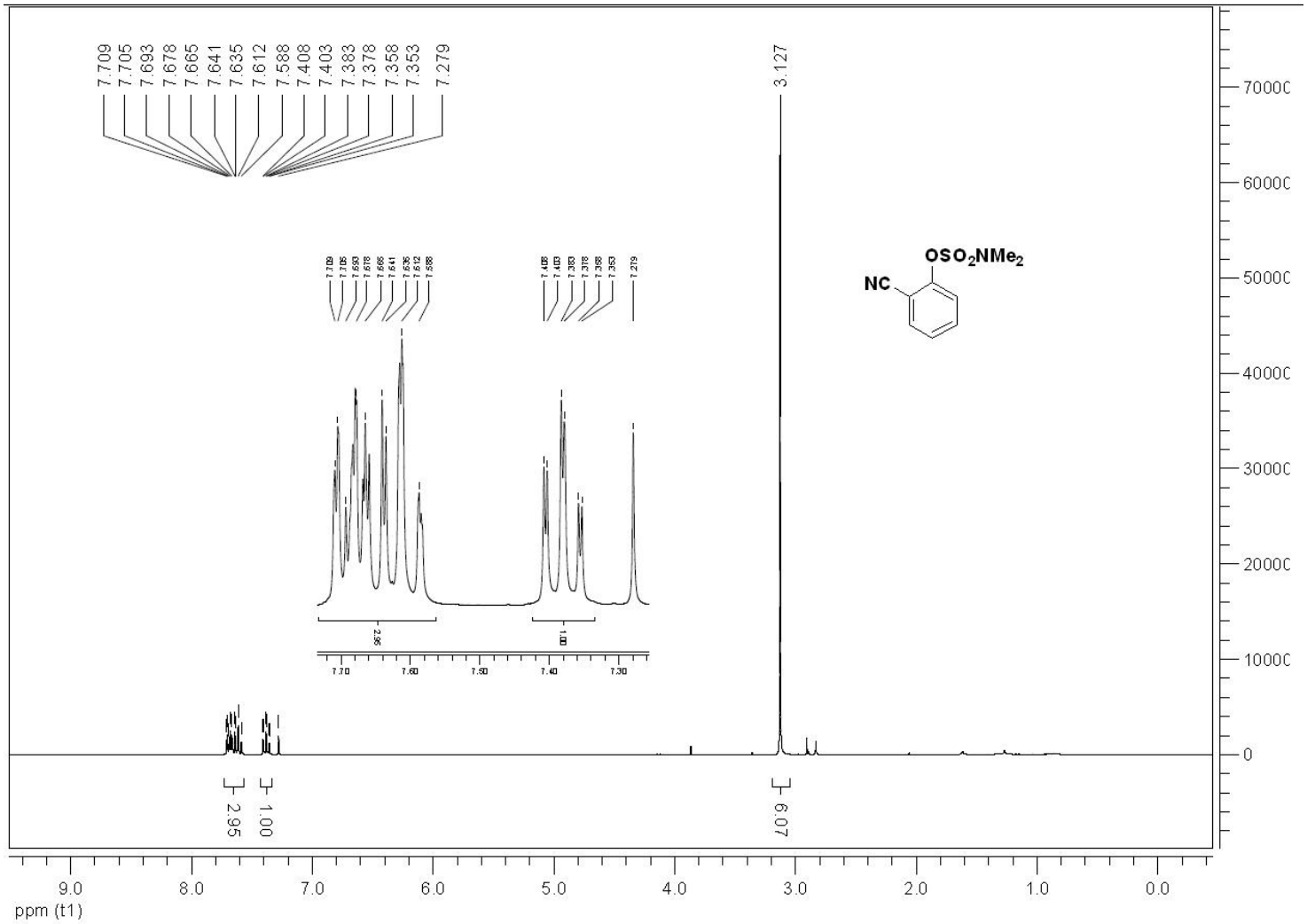
^{13}C NMR spectra of **8b** ($CDCl_3$, 75 MHz)



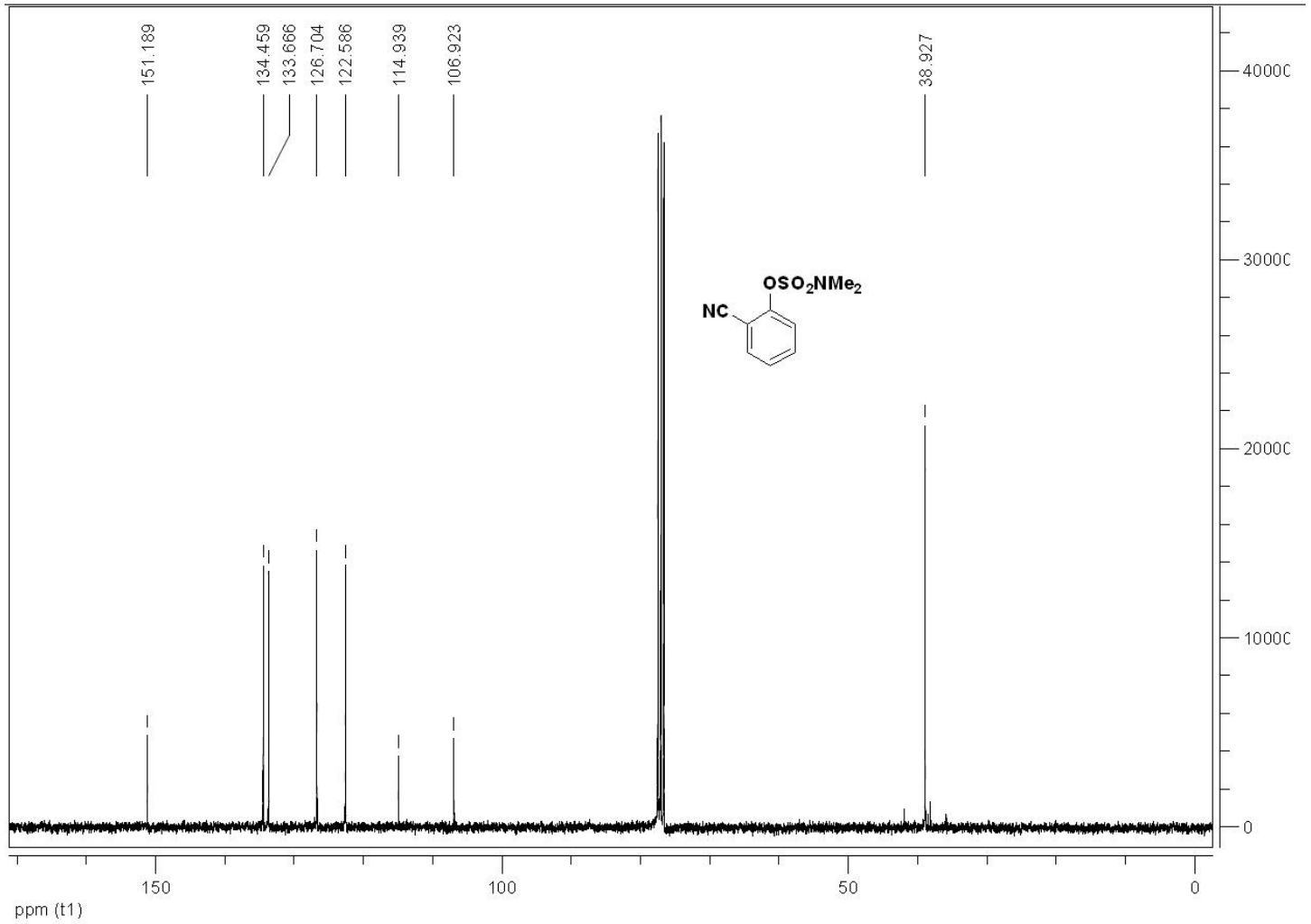
^{1}H NMR spectra of **9b** ($CDCl_3$, 300 MHz)



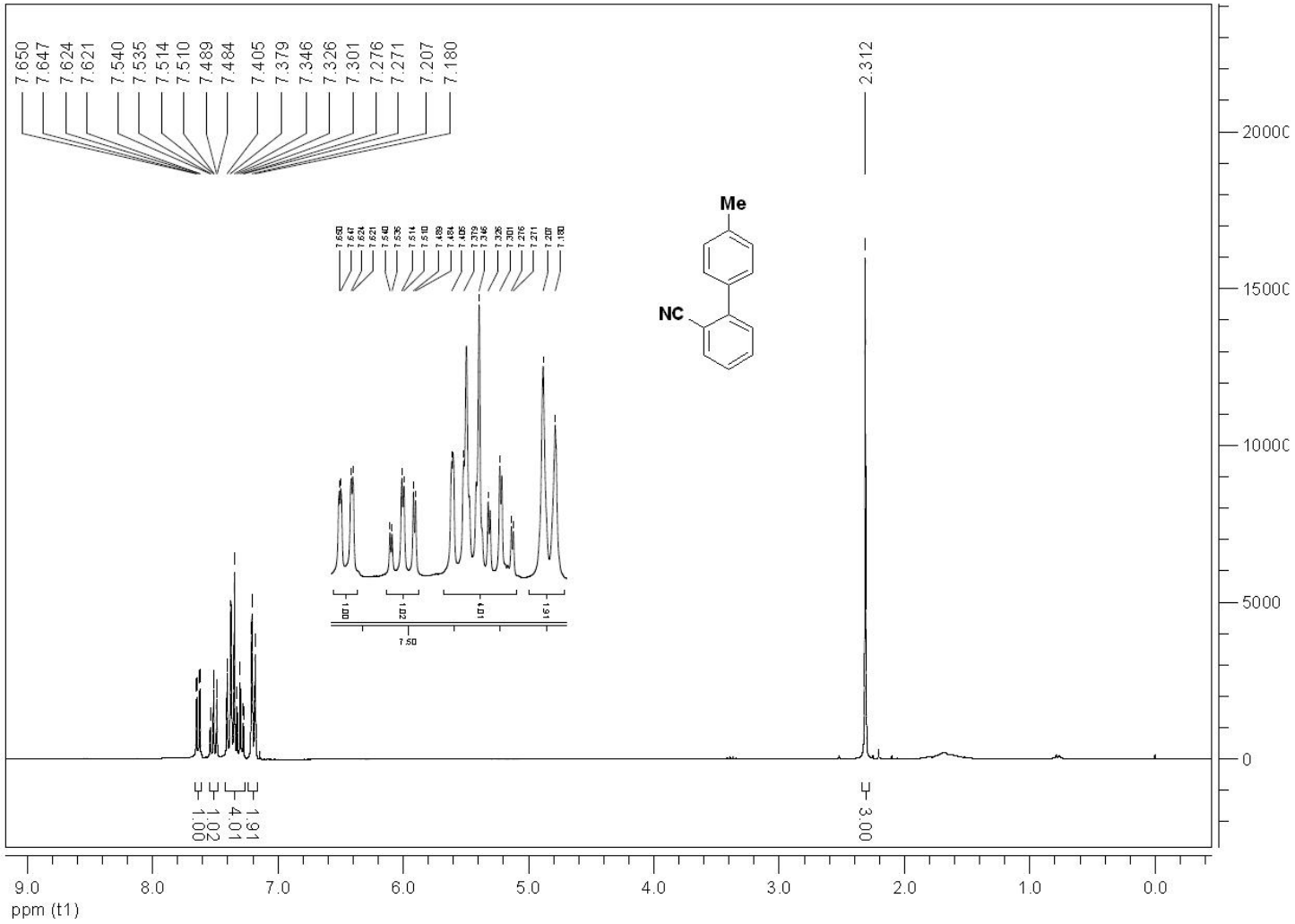
^{13}C NMR spectra of **9b** ($CDCl_3$, 75 MHz)



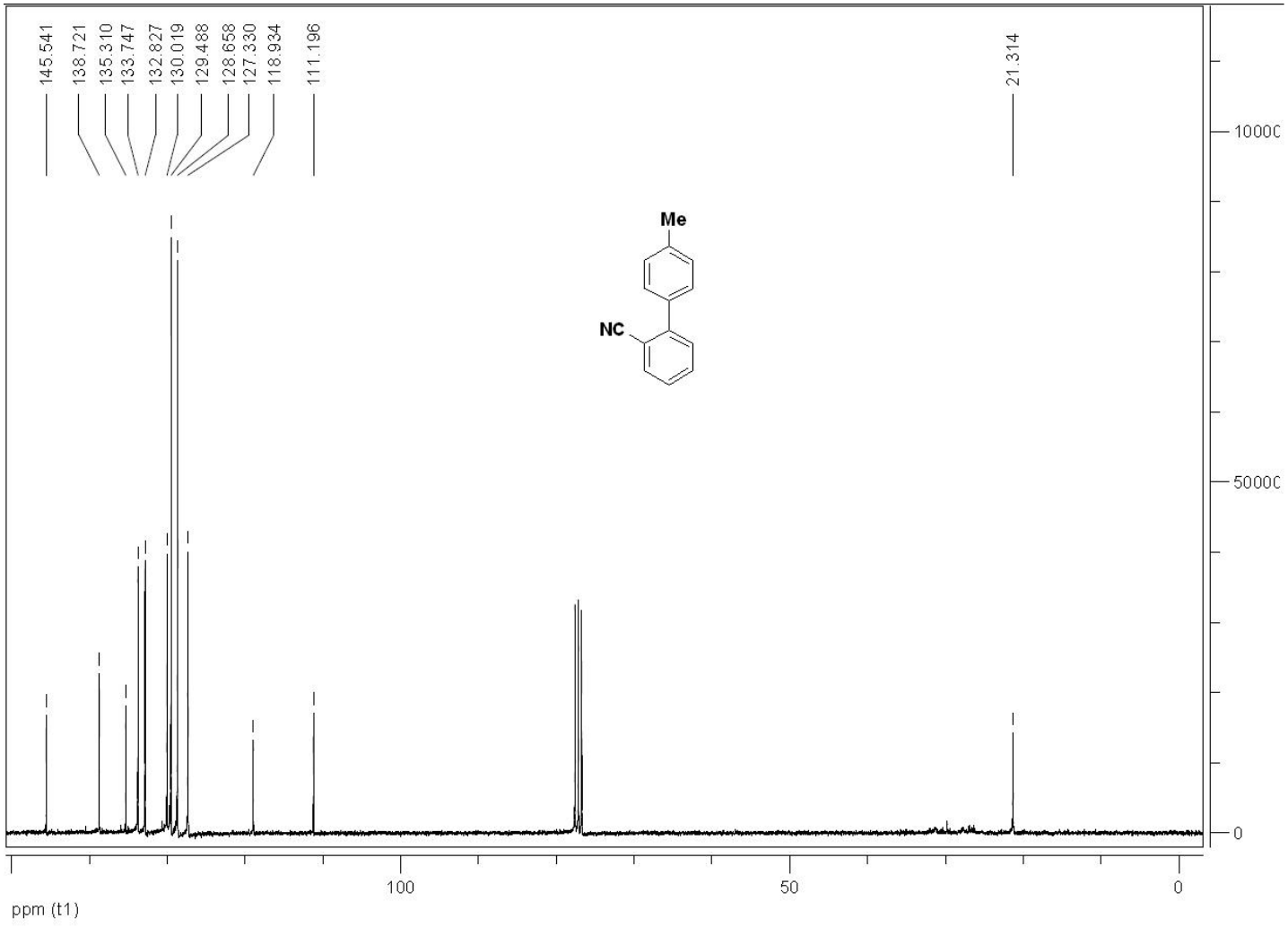
^{1}H NMR spectra of **9c** ($CDCl_3$, 300 MHz)



^{13}C NMR spectra of **9c** ($CDCl_3$, 75 MHz)



^{1}H NMR spectra of **10** ($CDCl_3$, 300 MHz)



^{1}H and ^{13}C NMR spectra of **10** ($CDCl_3$, 75 MHz)