Design and application of intramolecular arylogous nitroaldol condensation to access 2-aryl-benzofuran, -indole derivatives and formal synthesis of Saprisartan

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Table of Contents:

Contents

1. General information

All the reactions were carried out in oven-dried round-bottom flasks/screw-cap vials. A thin layer chromatography (TLC) analysis was carried out after magnetic stirring to monitor the reactions. TLC was performed on Merck silica gel 60 F_{254}; UV lamp was used as visualizing agent, I_2 or $KMnO_4$ or ninhydrin were used as developing agents. In order to purify the products, we used 60–120/100–200/230–400 mesh silica as the chromatography stationary phase. EtOAc and hexane were then used as eluents, and rotary evaporators were used to concentrate under reduced pressure at 40–45 ºC. The yields were assigned to the isolated products. All reagents, substrates, catalysts, deuterated solvents, and solvents were obtained from commercial suppliers and used without additional purification. The ^{1}H-NMR spectra were obtained on 300/400/500 MHz instruments, ^{13}C{^{1}H}-NMR spectra on 75, 101 and 126 MHz instruments, and ^{19}F-NMR spectra on 376/471 MHz spectrometer. The residual solvent signals were used as references, and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). The following abbreviations were used to explain the multiplicity of the spectra: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet, brs = broad singlet. Peaks which appear at 0.86, 1.26 in ^{1}H-NMR and 29.7 in ^{13}C{^{1}H}-NMR correspond to the residual grease present in the solvent (H. E. Gottlieb, V. Kotlyar, A. Nudelman, NMR Chemical Shifts of Common Laboratory Solvents as Trace Impurities. *J. Org. Chem.* 1997, **62**, 7512–7515). High-resolution mass spectra (HRMS) were recorded on a Thermo scientific Exactive^{TM} Orbitrap mass spectrometer or Q STAR XL Hybrid MS/MS. Melting points (MPs) reported in this work are uncorrected.

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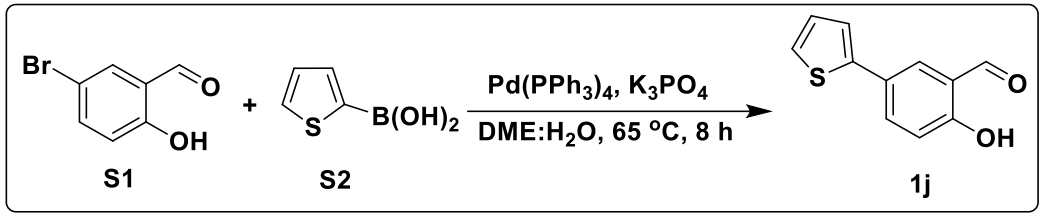
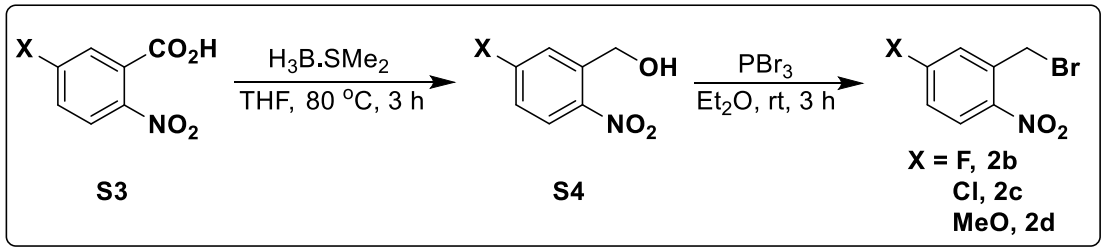
2. Synthesis of starting materials

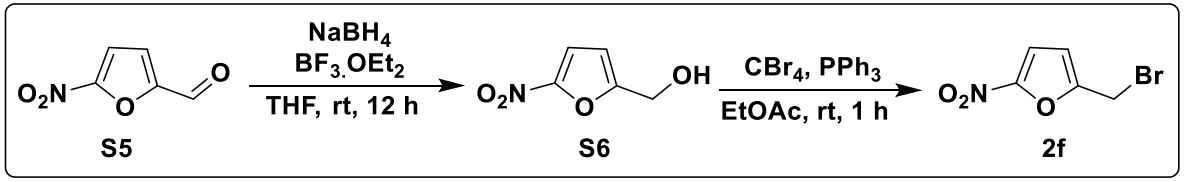
1.1 Synthesis of 2-hydroxy-5-(thiophen-2-yl)benzaldehyde **1j** was prepared by using reported method:[1]



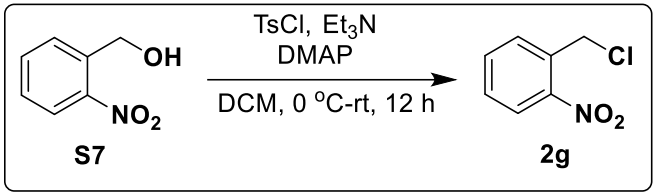
1.2 Synthesis of 5-substituted 2-(bromomethyl)-1-nitrobenzene **2b-2d** was prepared by using reported method:[2]



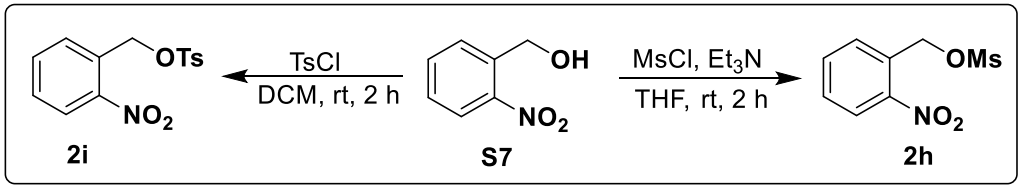
1.3 Synthesis of 2-(bromomethyl)-5-nitrofuran **2f** was prepared by using reported method:[3]



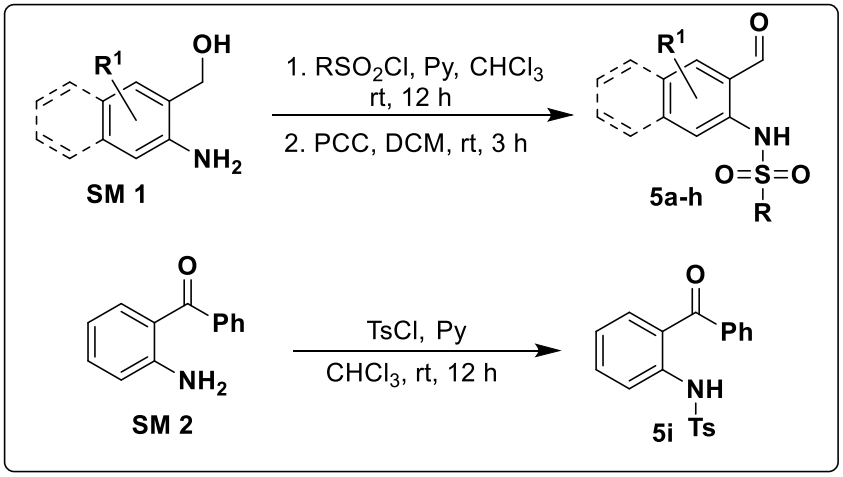
1.4 Syntheses of 1-(chloromethyl)-2-nitrobenzene was prepared by using reported method:[4]

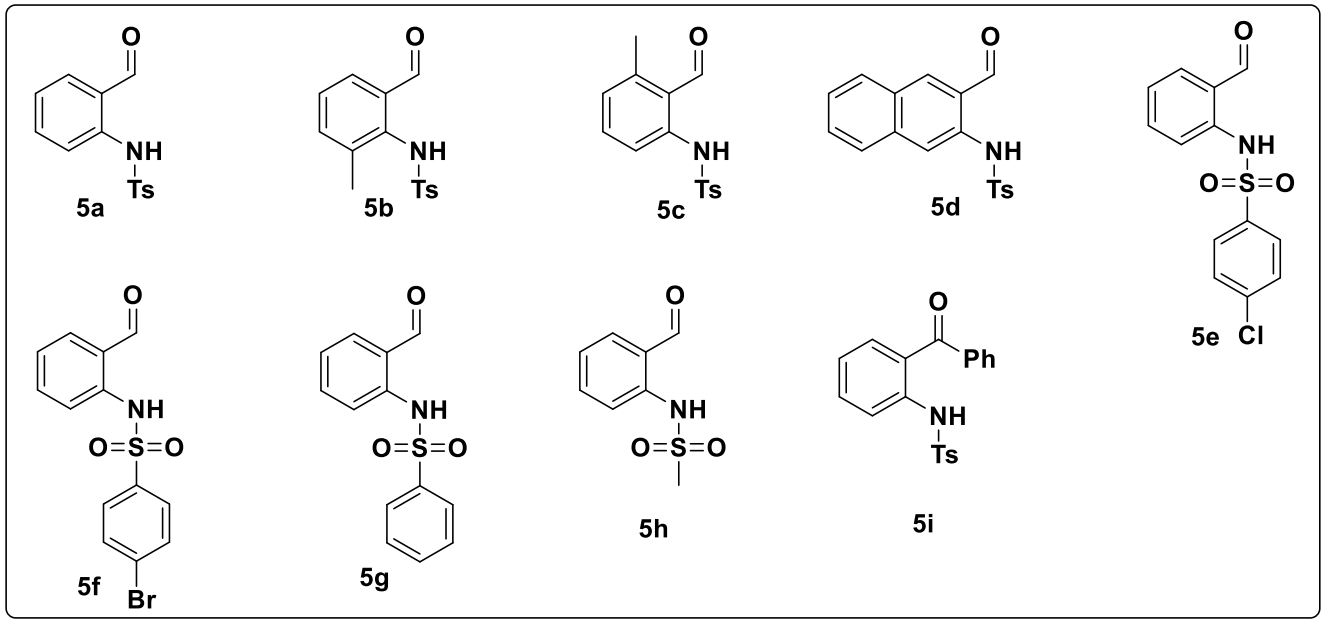


1.5 Syntheses of 2-nitrobenzyl methanesulfonate **2h** and 2-nitrobenzyl 4-methylbenzenesulfonate **2i** were prepared by using reported method:[5]

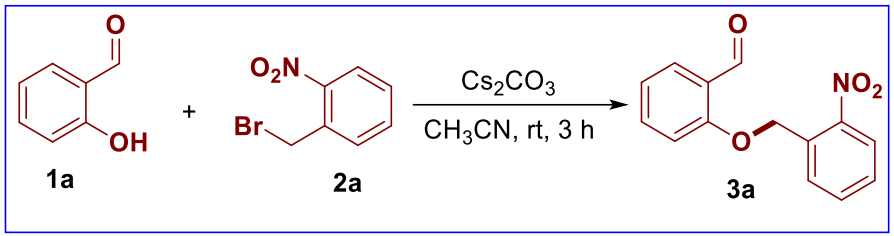


1.6 Synthesis of *ortho*-tosylaminobenzaldehyde derivatives **5a-5i** were prepared by using reported method:[6]



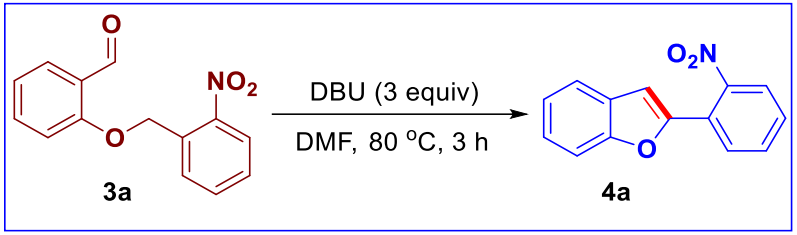

O
NH
Ts
5a
5b
5c
5d
O=S=O
5e
Cl
5f
Br
5g
5h
Ph
5i

3. Experimental procedure for the synthesis of 2-((2-nitrobenzyl)oxy)benzaldehyde 3a



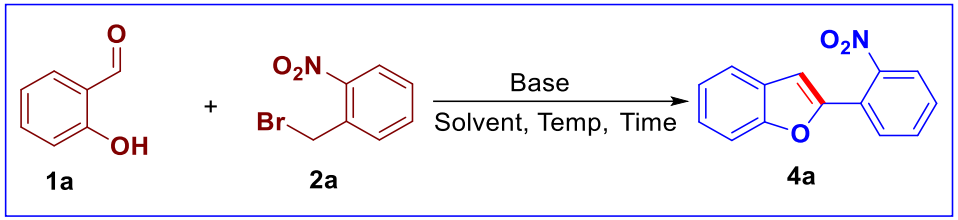
Salicylaldehyde **1a** (1 equiv, 1 mmol, 0.1 mL) and 2-nitrobenzyl bromide **2a** (1 equiv, 1 mmol, 216 mg) were taken in a 30 mL clean and dry screw cap vial. Then added acetonitrile (5 mL) followed by Cs_2CO_3 (2.5 equiv, 2.5 mmol, 812 mg). The reaction mixture was stirred at room temperature for 3 h. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with water (20 mL) and extracted using DCM (2 x 20 mL). The combined organic layer was washed with brine (10 mL) and the separated organic layer was dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under reduced pressure *in vacuo*. The crude residue was recrystallized from EtOH (20 mL) to afford the pure 2-((2-nitrobenzyl)oxy)benzaldehyde **3a** as a white solid in 75% yield.[7]

4. Experimental procedure for the synthesis of 2-(2-nitrophenyl)benzofuran 4a from 3a



2-((2-Nitrobenzyl)oxy)benzaldehyde **3a** (1 equiv, 1 mmol, 257 mg), was taken in a 30 mL clean and dry screw-cap vial in DMF (8 mL), and then DBU (3 equiv, 3 mmol, 0.44 mL) was added to the reaction mixture and it was stirred at 80 °C (temperature of the heating metal block) for 3 h. The reaction mixture was cooled to room temperature, diluted with ice cold water (50 mL), and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (10 mL) and the separated organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvent was removed *in vacuo* to afford a crude residue. The residue was purified by flash column chromatography (EtOAc/hexane, 2:98) on silica gel to obtain **4a** as a yellow solid in 55% yield.

5. General procedure for the optimization study for the sequential *O*-benzylation and intramolecular arylogous nitroaldol condensation

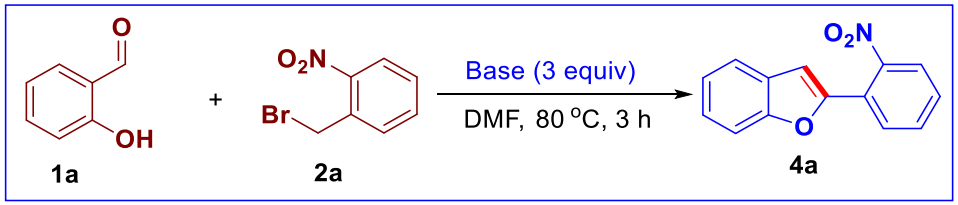


Salicylaldehyde **1a** (1 equiv, 0.5 mmol, 0.053 mL), and 2-nitrobenzyl bromide **2a** (1.2 equiv, 0.6 mmol, 129 mg) were taken a 15 mL clean and dry screw-cap vial in solvent (4 mL); base (3 equiv, 1.5 mmol) was added to the reaction mixture. Then reaction mixture was stirred at the temperature (temperature of the heating metal block) and time as mentioned in optimization Tables T1-T3. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL), and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (5 mL) and the separated organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 2:98) on 60-120 mesh silica gel to afford the 2-(2-nitrophenyl)benzofuran **4a** as a pure product.

Note: **please see tables T1-T3, for screening of various bases, solvents, leaving groups and reaction conditions**

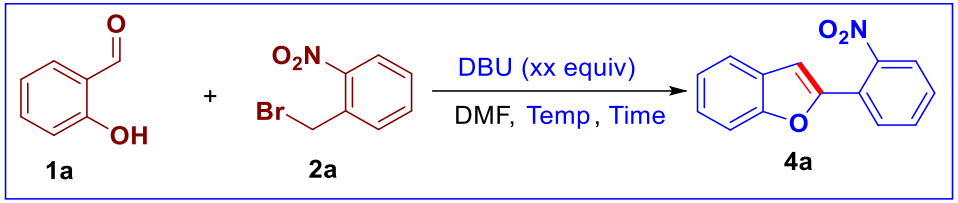
6. Optimization survey

Table T1: Screening of various bases



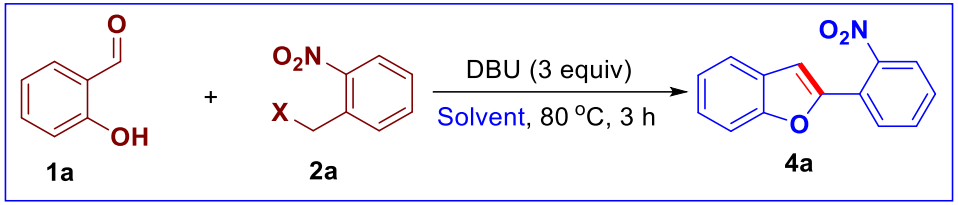
Entry	Base	% Yield of 4a
1	**1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)**	65
2	Et_3N	trace
3	1,4-Diazabicyclo[2.2.2]octane (DABCO)	21
4	1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD)	15
5	K_2CO_3	38
6	K_3PO_4	–
7	NaH	trace
8	Cs_2CO_3	46
9	KOH	–
10	KO^tBu	55

Table T2: Screening of molar equivalents of DBU and reaction conditions



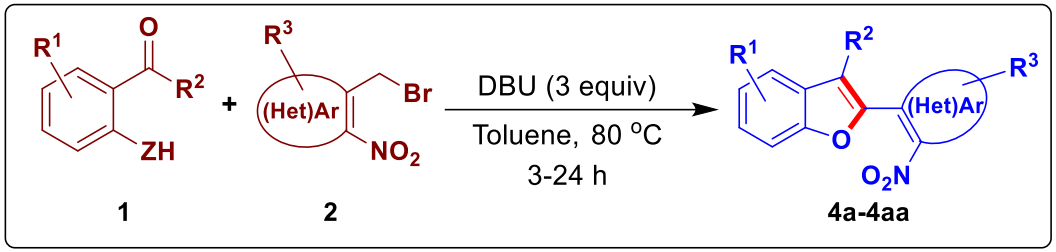
Entry	DBU (xx equiv)	Temp. (°C)	Time (h)	% Yield of 4a
1	1	80	3	trace
2	2	80	3	44
3	**3**	**80**	**3**	**65**
4	3	40	3	–
5	3	60	3	35
6	3	120	3	58
7	3	80	1	36
8	3	80	2	60
9	3	80	12	65
10	–	80	3	–

Table T3: Screening of various solvents and leaving group



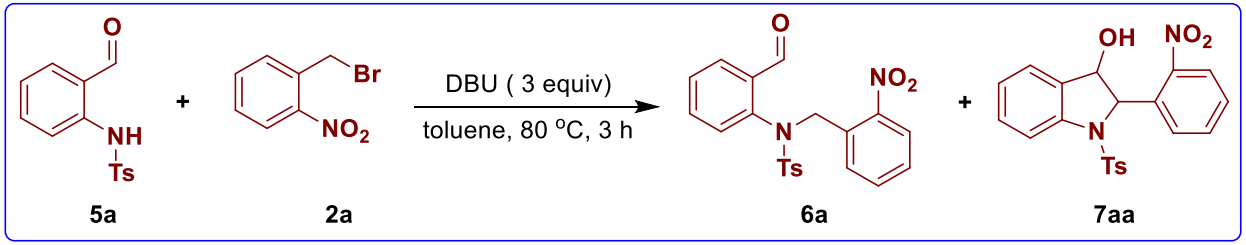
Entry	Solvents	X (Leaving group)	% Yield of 4a
1	DMF	Br	65
2	CH_3CN	Br	–
3	1,4-Dioxane	Br	–
4	Dimethyl sulfoxide (DMSO)	Br	45
5	1,2-Dimethoxyethane (DME)	Br	61
6	*t*-BuOH	Br	trace
7	1,2-Dichloroethane (DCE)	Br	trace
8	THF	Br	–
9	**Toluene**	**Br**	**85**
10	Toluene	Cl	53
11	Toluene	OMs	80
112	Toluene	OTs	76

7. General procedure for the synthesis of 2-(2-nitroaryl)benzofuran derivatives 4a-4aa



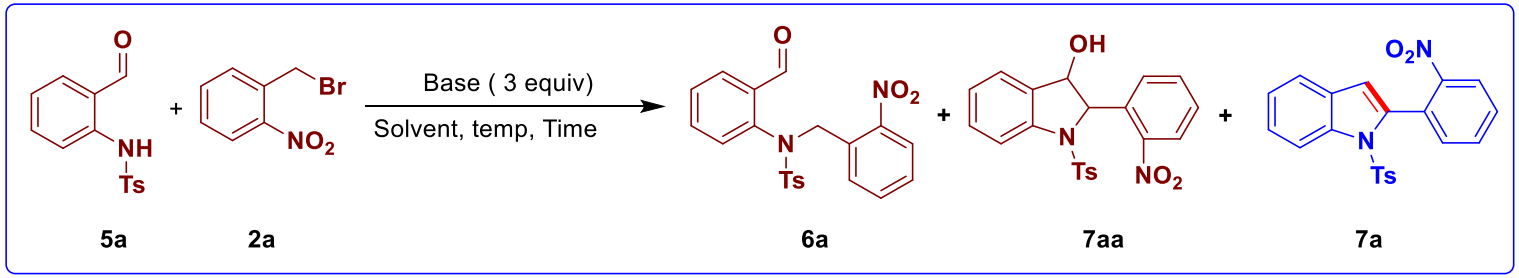
Substituted *ortho*-hydroxy arylaldehyde/ketone **1** (1 equiv, 0.5 mmol), and 2-nitrobenzyl bromide derivative **2** (1.2 equiv, 0.6 mmol) were taken in a 15 mL clean and dry screw-cap vial in toluene (4 mL); DBU (3 equiv, 1.5 mmol, 0.22 mL) was added to the reaction mixture. Then the reaction mixture was stirred at 80 ^{o}C (temperature of the metal block). After consumption of starting material (3 h to 24 h), the reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (5 mL), the separated organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford the desired compounds **4a-4aa** as pure product.

8. Experimental procedure for the step-wise and sequential reactions of 5a and 2a



N-(2-Formylphenyl)-4-methylbenzenesulfonamide **5a** (1 equiv, 0.5 mmol, 138 mg) and 2-nitrobenzyl bromide **2a** (1.2 equiv, 0.6 mmol, 129 mg) were taken in a 15 mL clean and dry screw cap vial in toluene (4 mL), DBU (3 equiv, 1.5 mmol, 0.22 mL) was added to the reaction mixture. Then reaction mixture was stirred at the 80 °C (temperature of the heating metal block) for 3 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford *N*-(2-formylphenyl)-4-methyl-*N*-(2-nitrobenzyl)benzenesulfonamide **6a** and 2-(2-nitrophenyl)-1-tosylindolin-3-ol **7aa** in 20% and 15% yield, respectively.

8.1. General procedure for the optimization study

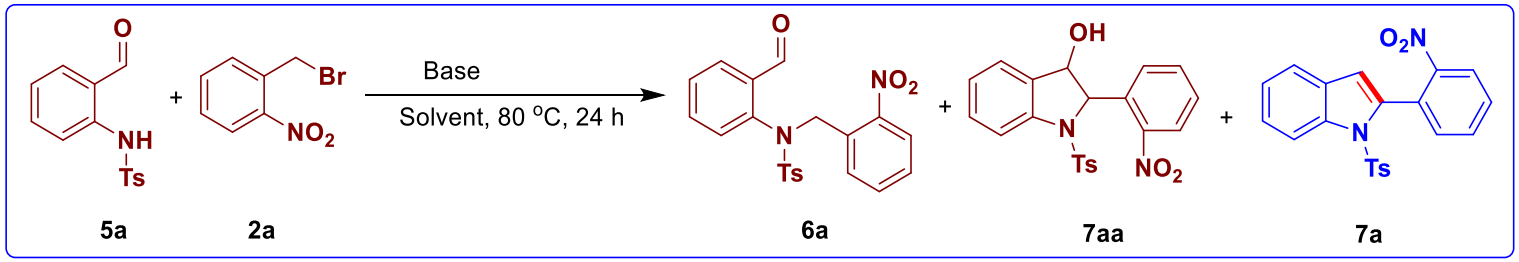


N-(2-Formylphenyl)-4-methylbenzenesulfonamide **5a** (1 equiv, 0.5 mmol, 138 mg) and 2-nitrobenzyl bromide **2a** (1.2 equiv, 0.6 mmol, 129 mg) were taken in 15 mL clean and dry screw cap vial in solvent (4 mL), base (3 equiv, 1.5 mmol) was added to the reaction mixture. Then reaction mixture was stirred at the temperature and time as mentioned in optimization Tables T1-T2. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL), and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 20:80) on 60-120 mesh silica gel to afford compounds **6a, 7aa** and **7a**.

Note: **please see tables T1-T2, for screening of various bases, solvents time and temperature.**

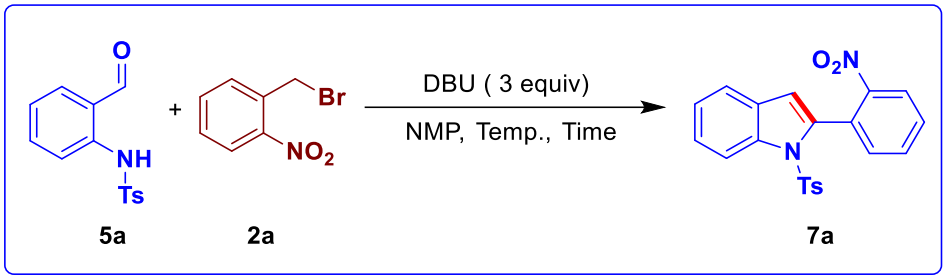
8.2. Optimization survey

Table T1: Screening of various bases and solvents



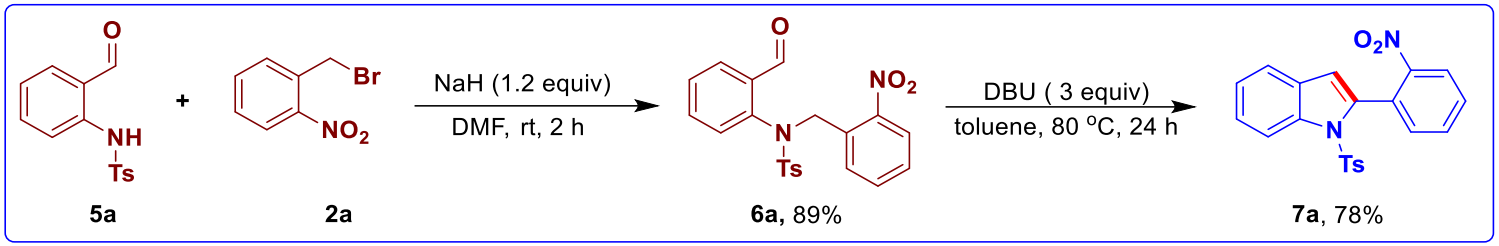
Entry	Base (equiv)	Solvent	% Yield of 6a	% Yield of 7aa	% Yield of 7a
1	DBU (3)	Toluene	–	25	37
2	DBU (2)	Toluene	–	65	–
3	DBU (1)	Toluene	68	–	–
4	NaH (3)	Toluene	64	20	trace
5	Cs_2CO_3 (3)	Toluene	40	18	–
6	K_2CO_3 (3)	Toluene	43	trace	-
7	**DBU (3)**	**NMP**	–	**trace**	**43**
8	DBU (3)	DMSO	–	18	17
9	DBU (3)	DMF	–	trace	24
10	DBU (3)	DMC	–	15	30

Table T2: Screening of reaction time and temperature



Entry	Temperature (ºC)	Time (h)	% Yield of 7a
1	**80**	**24**	**43**
2	80	36	40
3	120	24	36
4.	rt	48	–

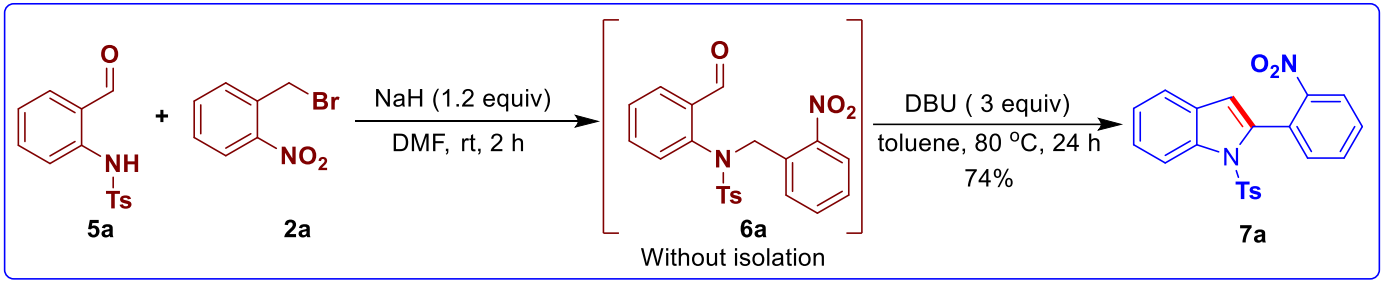
Step-wise reaction for the synthesis of 2-(2-nitrophenyl)-1-tosyl-1*H*-indole 7a:



To a solution of *N*-(2-formylphenyl)-4-methylbenzenesulfonamide **5a** (1 equiv, 0.5 mmol, 138 mg) in DMF (3 mL) kept at 0 °C temperature under N_2 atmosphere was added NaH (1.2 equiv, 0.6 mmol, 24 mg) slowly, and the resulting reaction mixture was stirred at 0 °C for 30 min. Then **2a** (1.2 equiv, 0.6 mmol, 129 mg) in DMF (1 mL) was added to the reaction mixture slowly, and the resulting reaction mixture was stirred at room temperature for 2 h. After this time, the reaction mixture was quenched with cold water (20 mL) and diluted with EtOAc (15 mL), extracted with EtOAc (2 x 15 mL). The combined organic phase was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. The crude was purified by column chromatography (EtOAc/Hex, 20:80) on silica gel to afford **6a** as a white solid in 89% yield.

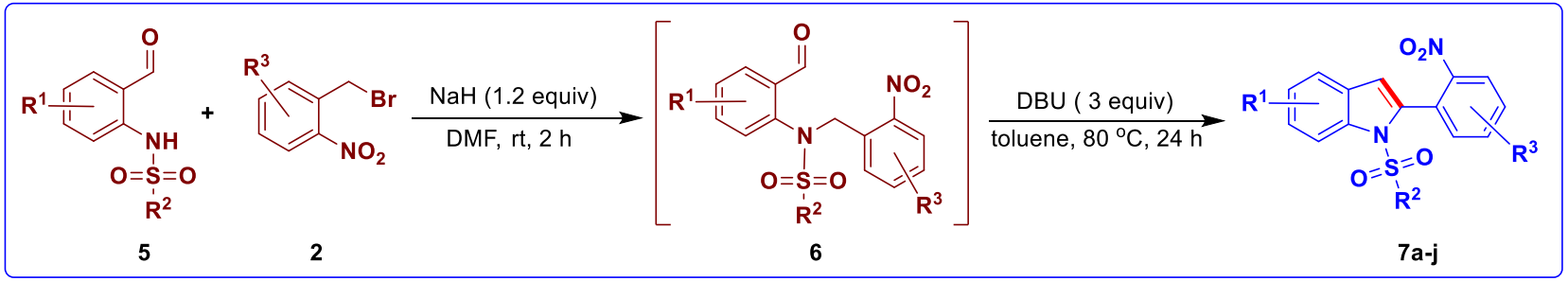
To a 15 mL clean and dry screw-cap vial, **6a** in toluene (4 mL), DBU (3 equiv, 1.5 mmol, 0.23 mL) was added. Then the reaction mixture was stirred at 80 °C (temperature of the heating metal block) for 24 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford 2-(2-nitrophenyl)-1-tosyl-1*H*-indole **7a** as a white solid in 78% yield.

Sequential reaction for the synthesis of 7a:



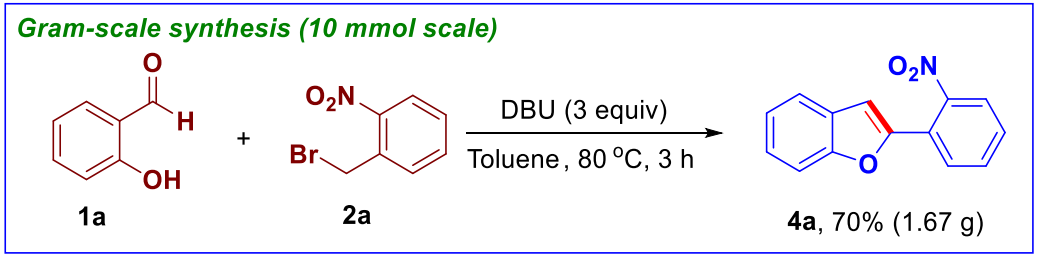
To a solution of **5a** (1 equiv, 0.5 mmol, 138 mg) in DMF (3 mL) kept at 0 °C temperature under N_2 atmosphere, was added NaH (1.2 equiv, 0.6 mmol, 24 mg) slowly, and the resulting reaction mixture was stirred at 0 °C for 30 min. After this time, **2a** (1.2 equiv, 0.6 mmol, 129 mg) in DMF (1 mL) was added to the reaction mixture slowly, and the resulting reaction mixture was stirred at room temperature for 2 h. Then, the reaction mixture was quenched with cold water (20 mL) and extracted with EtOAc (2 x 15 mL), and dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. Without further purification the crude **6a** used in the next step. This crude **6a** in toluene (4 mL) was transferred to a 15 mL clean and dry screw-cap vial; DBU (3 equiv, 1.5 mmol, 0.23 mL) was added. Then, the reaction mixture was stirred at 80 °C (temperature of the heating metal block) for 24 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford **7a** as a white solid in 74% yield.

9. General procedure for the synthesis of 2-(2-nitrophenyl)indole derivatives 7a-7j

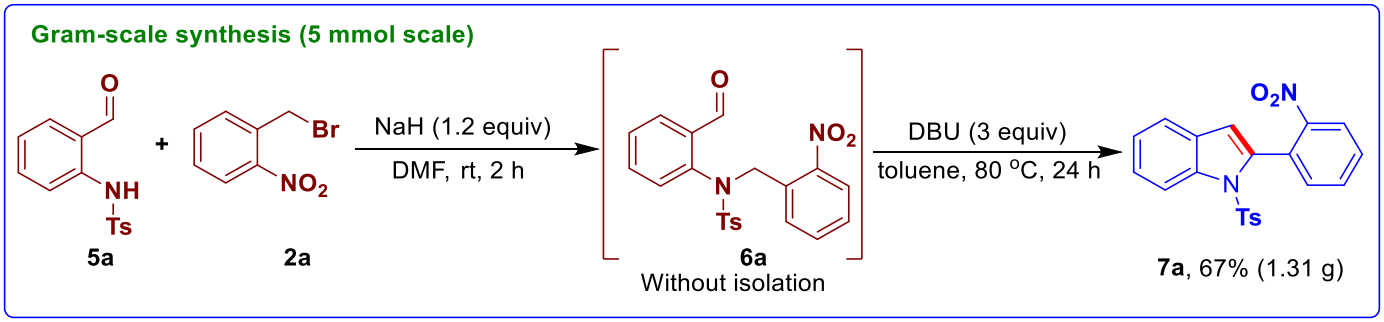


To a solution of *N*-(2-formylaryl)-sulfonamide derivative **5** (1 equiv, 0.5 mmol) in DMF (3 mL) kept at 0 °C temperature under N_2 atmosphere, was added NaH (1.2 equiv, 0.6 mmol, 24 mg) slowly, and the resulting reaction mixture was stirred at 0 °C for 30 min. After this time, **2** (1.2 equiv, 0.6 mmol) in DMF (1 mL) was added to the reaction mixture slowly, and the resulting reaction mixture was stirred at room temperature for 2 h. After this time, the reaction mixture was quenched with cold water (20 mL) and diluted with EtOAc (20 mL), extracted with EtOAc (2 x 15 mL), and dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. This crude compound **6** in toluene (4 mL) was transferred to a 15 mL clean and dry screw-cap vial; DBU (3 equiv, 1.5 mmol, 0.23 mL) was added to this solution. Then, the reaction mixture was stirred at 80 °C (temperature of the heating metal block) for 24 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to get desire compounds **7a-j**.

10. Gram-scale synthesis of 4a and 7a



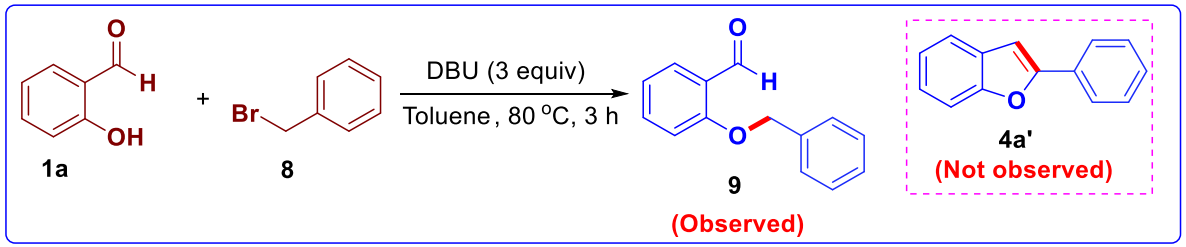
Salicylaldehyde **1a** (1 equiv, 10 mmol, 1 mL), and **2a** (1.2 equiv, 12 mmol, 2.59 g) were taken in a clean and dried round bottom flask in toluene (80 mL); DBU (3 equiv, 30 mmol, 4.4 mL) was added to the reaction mixture. Then the reaction mixture was stirred at 80 °C (oil bath) for 3 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (150 mL), and extracted with ethyl acetate (2 × 50 mL). The combined organic layer was washed with brine (30 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 2:98) on 60-120 mesh silica gel to afford **4a** as a yellow solid in 70% yield (1.67 g).



To a solution of **5a** (1 equiv, 5 mmol, 1.38 g) in DMF (30 mL) kept at 0 °C temperature under N_2 atmosphere was added NaH (1.2 equiv, 6 mmol, 239 mg) slowly, and the resulting reaction mixture was stirred at 0 °C for 30 min. After this time, **2a** (1.2 equiv, 6 mmol, 1.29 g) in DMF (10 mL) was added to the reaction mixture slowly, and the resulting reaction mixture was stirred at room temperature for 2 h. Then, the reaction mixture was

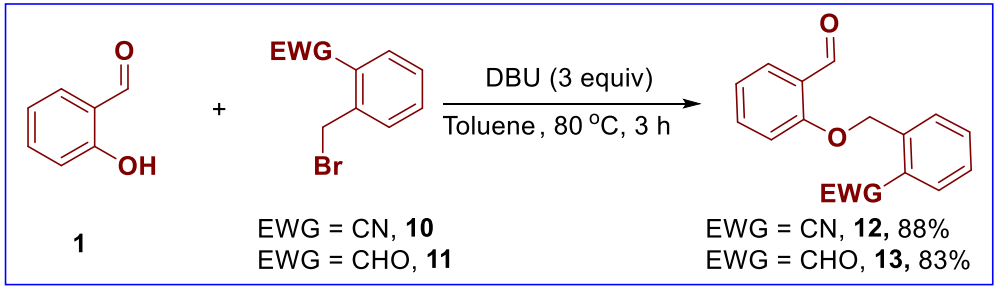
quenched with cold water (70 mL) and extracted with EtOAc (2 x 80 mL). The combined organic phase was washed with brine (25 mL) and dried over anhydrous Na_2SO_4, and the filtrate was concentrated under reduced pressure. This crude compound **6a** in toluene (40 mL) was transferred to a 100 mL round bottom flask; DBU (3 equiv, 15 mmol, 2.3 mL) was added to this solution. Then, the reaction mixture was stirred at 80 ^oC (oil bath) for 24 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (70 mL) and extracted with ethyl acetate (2 × 80 mL). The combined organic layer was washed with brine (30 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford **7a** as a white solid in 67% yield (1.31 g).

11. Control experiments and mechanistic studies



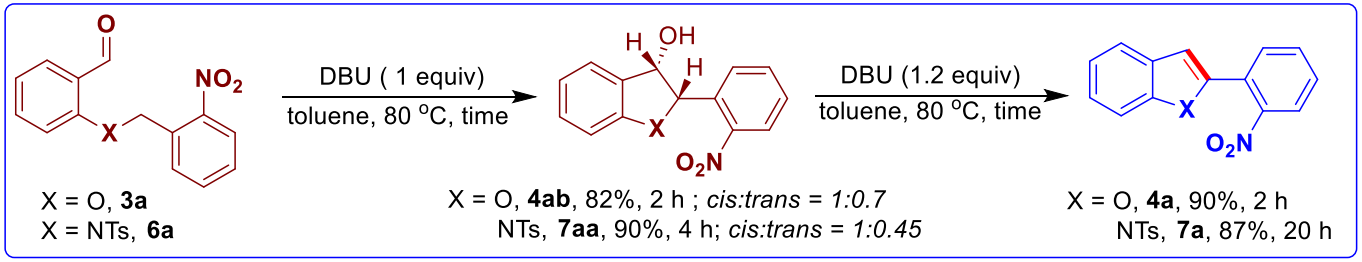
Salicylaldehyde **1a** (1 equiv, 1 mmol, 0.1 mL), and benzyl bromide **8** (1.2 equiv, 1.2 mmol, 0.142 mL) were taken in a 15 mL clean and dry screw-cap vial in toluene (8 mL); DBU (3 equiv, 3 mmol, 0.44 mL) was added to the reaction mixture. Then reaction mixture was stirred at 80 °C for (temperature of the heating metal block) 3 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (30 mL), and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 5:95) on 60-120 mesh silica gel to afford **9** as a colourless thick liquid in 80% yield.

Different EWG on coupling partner 10 and 11:



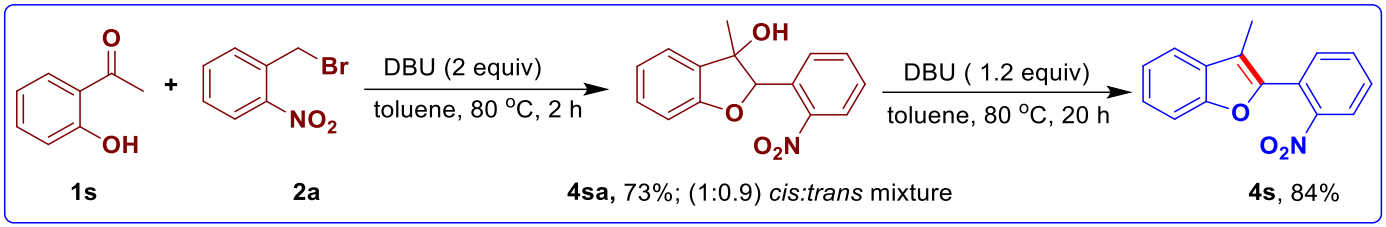
Salicylaldehyde **1a** (1 equiv, 0.5 mmol, 61 mg), and activated benzyl bromide derivative **10**/**11** (1.2 equiv, 0.6 mmol) were taken in a 15 mL clean and dry screw cap vial in toluene (4 mL); DBU (3 equiv, 1.5 mmol, 0.22 mL) was added to the reaction mixture. Then, the reaction mixture was stirred at 80 °C (temperature of the heating metal block). After the starting material consumption, within 3 h later, this reaction continued for another

24 h (monitored by TLC). The reaction mixture was cooled to room temperature, diluted with water (20 mL) and extracted with ethyl acetate (2 × 20 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane) on 60-120 mesh silica gel to afford the desired compounds **12** and **13** in 88% and 83% yield, respectively.



To a solution of the compound **3a/6a** (1 equiv, 0.5 mmol) in toluene (4 mL), DBU (1 equiv, 0.5 mmol, 0.08 mL) was added. Then, the reaction mixture was stirred at 80 °C (temperature of the heating metal block) for completion of starting material. After this time, the reaction mixture was quenched with water (20 mL) and diluted with EtOAc (15 mL), extracted with EtOAc (2 x 15 mL), The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified by column chromatography (EtOAc/Hex, 20:80) on silica gel to afford the 2-aryl-3-hydroxy dihydrobenzofuran **4ab/** dihydroindole **7aa** in 82% and 90% yield, respectively.

To a solution of **4ab/7aa** (1 equiv, 0.25 mmol) in toluene (3 mL), DBU (1.2 equiv, 0.3 mmol, 0.05 mL) was added. Then, the reaction mixture was stirred at 80 °C (temperature of the heating metal block) for completion of starting material. After this time, the reaction mixture was quenched with water (20 mL) and diluted with EtOAc (15 mL), The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified by column chromatography (EtOAc/Hex, 20:80) on silica gel to afford **4a**/**7a** in 90% and 87% yield, respectively.

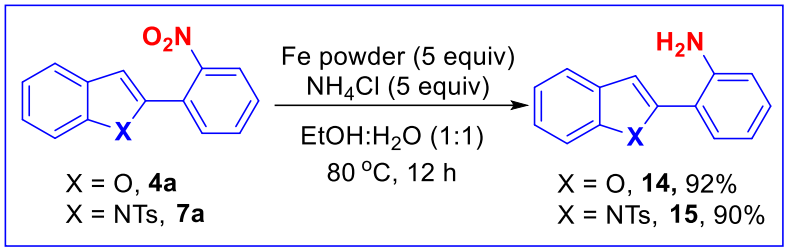


2-Hydroxyacetophenone **1s** (1 equiv, 0.5 mmol, 0.06 mL), and 2-nitrobenzyl bromide **2a** (1.2 equiv, 0.6 mmol, 129 mg) were taken in a 15 mL clean and dry screw-cap vial in toluene (4 mL); DBU (3 equiv, 1.5 mmol, 0.22 mL) was added to the reaction mixture. Then reaction mixture was stirred at the 80 °C (temperature of the heating metal block) for 2 h. After this time, the reaction mixture was cooled to room temperature, diluted with water (20 mL), and extracted with ethyl acetate (2 × 15 mL). The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 10:90) on 60-120 mesh silica gel to afford 3-methyl-2-(2-nitrophenyl)-2,3-dihydrobenzofuran-3-ol **4sa** as a yellow liquid in 73% yield.

To a solution of 3-methyl-2-(2-nitrophenyl)-2,3-dihydrobenzofuran-3-ol **4sa** (1 equiv, 0.25 mmol, 68 mg) were taken a 15 mL clean and dry screw-cap vial in toluene (3 mL); DBU (1.2 equiv, 0.3 mmol, 0.05 mL) was added to the reaction mixture. Then reaction mixture was stirred at the 80 °C (temperature of the heating metal block) for 20 h. After this time, the reaction mixture was quenched with water (10 mL) and diluted with EtOAc (15 mL). The combined organic layer was washed with brine (10 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified by column chromatography (EtOAc/Hex, 20:80) on silica gel to afford the 3-methyl-2-(2-nitrophenyl)benzofuran **4s** as a yellow solid in 84% yield.

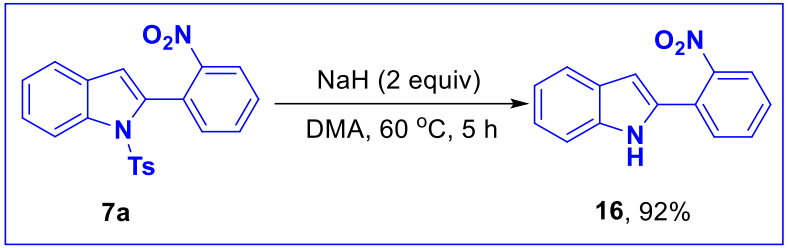
12. Post-synthetic transformations

a) Experimental procedure for nitro group reduction of benzofuran 4a and indole 7a:



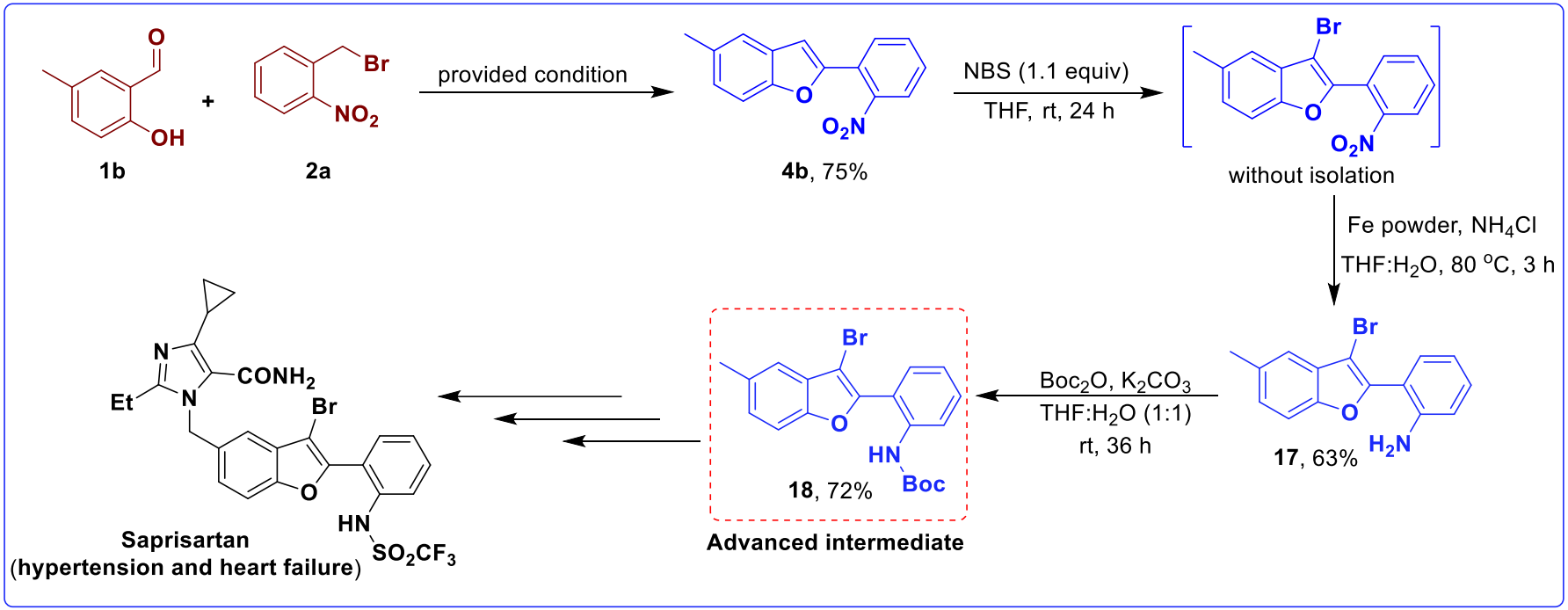
2-(2-Nitrophenyl)benzofuran **4a**/2-(2-nitrophenyl)-1-tosyl-1*H*-indole **7a** (1 equiv, 0.25 mmol) was dissolved in EtOH:H_2O (1:1, 4 mL) and then were added Fe powder (5 equiv, 1.25 mmol, 69 mg), NH_4Cl (5 equiv, 1.25 mmol, 67 mg) to this reaction mixture and resulting reaction mixture was stirred at 80 °C (oil bath) for 3 h. After this time, the reaction mixture was filtered through the Celite® bed and washed with MeOH. Thus, obtained filtrate was concentrated under reduced pressure to afford a crude reaction mixture. It was further diluted with water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain crude **14** or **15** in 92% and 90% yield, respectively.

b) Experimental procedure for detosylation reaction of indole 7a:



To a suspension of NaH (60% dispersion in mineral oil) (2 equiv, 0.5 mmol, 20 mg) in dry DMA (2 mL) under N_2 was added dropwise a solution of **7a** (1 equiv, 0.25 mmol, 93 mg) in dry DMA (1 mL) by syringe. Then, the mixture was heated at 60 °C (oil bath) for 5 h. A saturated aq. solution of NH_4Cl (5 mL) was added to quench the reaction and the reaction mixture was extracted with EtOAc (2 x 15 mL). The organic layer was washed with cold water (3 x 10 mL), and the organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 15:85) on 60-120 mesh silica gel to afford **16** as a white solid in a 92% yield.

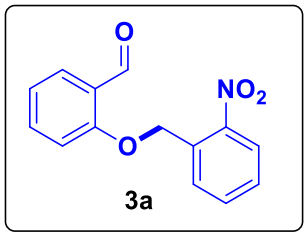
13. Experimental procedure for formal synthesis of saprisartan



Benzofuran **4b** (1 equiv, 0.6 mmol, 152 mg) and *N*-bromosuccinimide (1.1 equiv, 0.66 mmol, 118 mg) were taken in a clean dried double neck round bottom flask in THF (4 mL). Then reaction mixture was stirred at room temperature for 24 h (monitored by TLC 3-4 times eluted 2% EtOAc in Hexane). After this time, the reaction mixture was quenched with saturated $NaHCO_3$ (3 mL) and diluted with EtOAc (10 mL). The reaction mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was taken to the next step without further purification. The crude was dissolved in EtOH: H_2O (1:1, 4 mL) and then were added Fe powder (5 equiv, 3 mmol, 168 mg), NH_4Cl (5 equiv, 3 mmol, 162 mg) to this solution and resulting reaction mixture was stirred at 80 °C (oil bath) for 12 h. After this time, the reaction mixture was filtered through a Celite® bed and washed with MeOH. Thus, obtained filtrate was concentrated under reduced pressure to afford a crude residue.

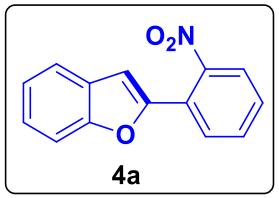
It was further diluted with water (10 mL) and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was washed with brine (5 mL), the organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 2:98) on 230-400 mesh neutral silica gel to afford **17** in 63% yield (2 steps). To a solution of **17** (1 equiv, 0.13 mmol, 40 mg) in 1:1 mixture of THF/H_2O (3 mL) were added K_2CO_3 (2 equiv, 0.26 mmol, 35 mg) and Boc_2O (1.5 equiv, 0.195, 43 mg) consecutively at 0 ^oC. After 30 min, the solution was stirred for 36 h at room temperature. Then, the reaction mixture was quenched with water (5 mL) and diluted with ethyl acetate (2 x 5 mL), extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude residue. The crude was purified using column chromatography (EtOAc/Hexane, 1:99) on 230-400 mesh silica gel to afford **18**, an advanced intermediate of saprisartan, in 72% yield.

14. Spectroscopic data



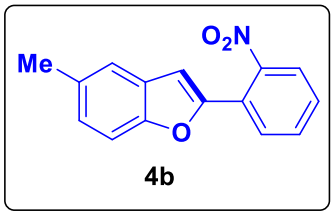
3a

2-((2-Nitrobenzyl)oxy)benzaldehyde (**3a**). White solid, 193 mg (0.750 mmol), 75% yield, R_f = 0.77; **MP** 120-122 °C; **IR** ($CHCl_3$) 3066, 2924, 1724, 1612, 1529, 1257 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 10.60 (s, 1H), 8.22 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.96 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.76-7.73 (m, 1H), 7.61-7.52 (m, 2H), 7.15-7.05 (m, 2H), 5.63 (s, 2H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 189.5, 160.2, 146.9, 136.2, 134.5, 133.1, 129.6, 128.9, 128.5, 125.3, 121.7, 113.1, 67.5; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{11}O_4NNa$ $[M+Na]^+$ 280.0580, found 280.0569. The spectroscopic data were in good agreement with the reported data.[7]



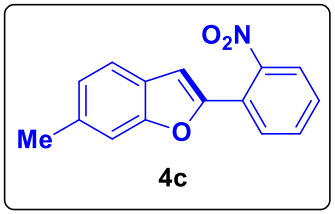
4a

2-(2-Nitrophenyl)benzofuran (**4a**). Yellow solid, 102 mg (0.425 mmol), 85% yield, R_f = 0.75 (EtOAc/Hex, 2:98); **MP** 55-57 °C; **IR** ($CHCl_3$) 3066, 1564, 1522, 1349, 1167 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.86 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.77 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.67-7.60 (m, 2H), 7.54-7.47 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.26 (t, *J* = 7.2 Hz, 1H), 7.01 (s, 1H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 155.3, 150.6, 148.3, 132.2, 130.1, 129.5, 128.6, 125.5, 124.3, 124.2, 123.4, 121.6, 111.6, 106.2; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{10}O_3N$ $[M+H]^+$ 240.0655, found 240.0650. The spectroscopic data were in good agreement with the reported data.[8]



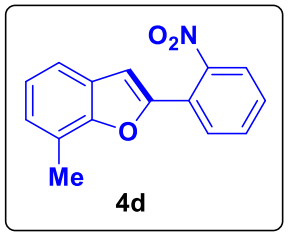
4b

5-Methyl-2-(2-nitrophenyl)benzofuran (**4b**). Light yellow solid, 95 mg (0.375 mmol), 75% yield, R_f = 0.78 (EtOAc/Hex, 2:98); **MP** 62-64 ºC; **IR** ($CHCl_3$) 3020, 2868, 1566, 1528, 1358, 1198 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.87-7.82 (m, 1H), 7.75 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.64-7.60 (m, 1H), 7.51-7.45 (m, 1H), 7.38-7.36 (m, 2H), 7.13 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.93 (s, 1H), 2.44 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 153.8, 150.6, 148.3, 132.9, 132.1, 130.0, 129.3, 128.7, 126.8, 124.4, 124.1, 121.4, 111.1, 106.0, 21.5; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_3N$ $[M+H]^+$ 254.0812, found 254.0806.



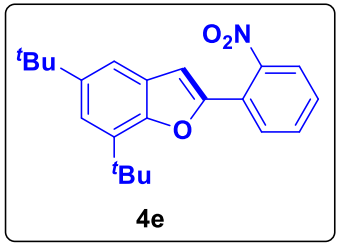
4c

6-Methyl-2-(2-nitrophenyl)benzofuran (**4c**). Light yellow solid, 89 mg (0.351 mmol), 70% yield, R_f = 0.76 (EtOAc/Hex, 2:98); **MP** 58-60 ºC; **IR** ($CHCl_3$) 3020, 2867, 1566, 1529, 1358, 1199 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.72 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.62-7.56 (m, 1H), 7.49-7.42 (m, 2H), 7.29 (s, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 2.46 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 155.8, 149.9, 148.2, 135.9, 132.1, 129.8, 129.1, 126.1, 124.9, 124.4, 124.1, 121.1, 111.7, 106.1, 21.9; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_3N$ $[M+H]^+$ 254.0812, found 254.0807. The spectroscopic data were in good agreement with the reported data.[9]



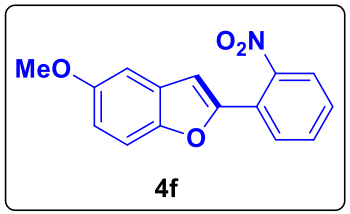
4d

7-Methyl-2-(2-nitrophenyl)benzofuran (**4d**). Light yellow solid, 81 mg (0.320 mmol), 64% yield, R_f = 0.69 (EtOAc/Hex, 2:98); **MP** 73-75 °C; **IR** ($CHCl_3$) 3021, 2868, 1565, 1526, 1356, 1198 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.86 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.64 (dd, *J* = 11.0, 4.3 Hz, 1H), 7.52-7.42 (m, 2H), 7.19-7.10 (m, 2H), 7.01 (s, 1H), 2.51 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 154.5, 150.2, 148.4, 132.0, 129.9, 129.3, 128.0, 126.3, 124.4, 124.1, 123.5, 121.9, 119.1, 106.3, 15.0; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_3N$ $[M+H]^+$ 254.0812, found 254.0807.



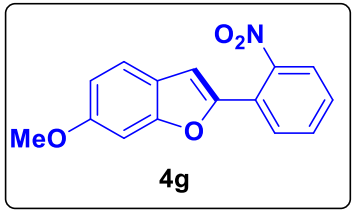
4e

5,7-Di-*tert*-butyl-2-(2-nitrophenyl)benzofuran (**4e**). Yellow solid, 102 mg (0.290 mmol), 58% yield, R_f = 0.8 (EtOAc/Hex, 2:98); **MP** 85-87 °C; **IR** ($CHCl_3$) 3037, 2957, 2869, 1568, 1532, 1362, 1162 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 7.8, 1.3 Hz, 1H) 7.74 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.64-7.60 (m, 1H), 7.51-7.45 (m, 2H), 7.30 (d, *J* = 1.9 Hz, 1H), 7.01 (s, 1H), 1.49 (s, 9H), 1.38 (s, 9H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 152.0, 150.0, 148.4, 146.3, 134.4, 132.0, 129.8, 128.9, 128.6, 124.7, 124.1, 120.4, 115.6, 106.3, 35.0, 34.6, 32.0, 30.1; **HRMS** (ESI, *m/z*): calcd for $C_{22}H_{26}O_3N$ $[M+H]^+$ 352.1907, found 352.1899.



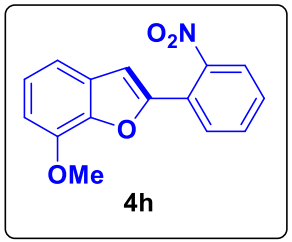
4f

5-Methoxy-2-(2-nitrophenyl)benzofuran (**4f**)**.** Yellow solid, 93 mg (0.345 mmol), 69% yield, R_f = 0.60 (EtOAc/Hex, 5:95); **MP** 101-103 °C; **IR** ($CHCl_3$) 3019, 2852, 1566, 1528, 1358, 1198, 1127 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 7.85 (d, *J* = 7.1 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.50 (dd, *J* = 11.3, 4.2 Hz, 1H), 7.39 (d, *J* = 9.0 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.98-6.91 (m, 2H), 3.85 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 156.4, 151.2, 150.4, 148.3, 132.1, 130.0, 129.4, 129.1, 124.4, 124.2, 114.6, 112.1, 106.3, 103.6, 56.1; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_4N$ $[M+H]^+$ 270.0761, found 270.0772.



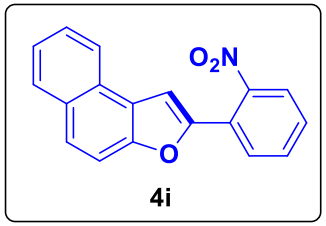
4g

6-Methoxy-2-(2-nitrophenyl)benzofuran (**4g**). Yellow solid, 97 mg (0.360 mmol), 72% yield, R_f = 0.59 (EtOAc/Hex, 5:95); **MP** 110-112 °C; **IR** ($CHCl_3$) 3033, 2854, 1562, 1524, 1348, 1165, 1120 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 7.86-7.81 (m, 1H), 7.72-7.62 (m, 3H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.03 (d, *J* = 1.5 Hz, 1H), 6.96 (s, 1H), 3.86 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 159.0, 156.5, 149.6, 148.0, 132.1, 131.0, 129.6, 128.9, 124.4, 124.2, 121.9, 112.8, 106.2, 95.8, 55.9; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_4N$ $[M+H]^+$ 270.0761, found 270.0757.



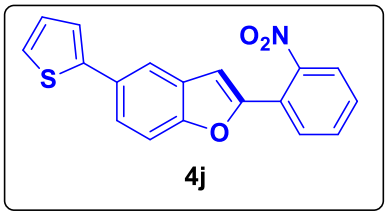
4h

7-Methoxy-2-(2-nitrophenyl)benzofuran (**4h**). Yellow solid, 89 mg (0.330 mmol), 66% yield, R_f = 0.60 (EtOAc/Hex, 5:95); **MP** 107-109 ºC; **IR** ($CHCl_3$) 3020, 2852, 1566, 1526, 1357, 1198, 1128 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.91 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.52 (dd, *J* = 11.2, 4.3 Hz, 1H), 7.24-7.15 (m, 2H), 6.99 (s, 1H), 6.85 (dd, *J* = 7.3, 1.3 Hz, 1H), 4.02 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 150.5, 148.4, 145.6, 144.8, 132.2, 130.4, 130.3, 129.5, 124.3, 124.1, 113.9, 108.1, 106.6, 56.5; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_4N$ $[M+H]^+$ 270.0761, found 270.0760 The spectroscopic data were in good agreement with the reported data.[10]



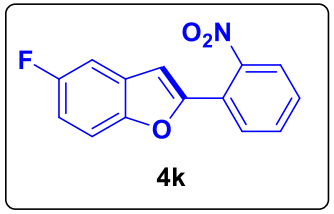
4i

2-(2-Nitrophenyl)naphtho[2,1-b]furan (**4i**). Yellow solid, 116 mg (0.400 mmol), 80% yield, R_f = 0.71 (EtOAc/Hex, 2:98); **MP** 87-89 ºC; **IR** ($CHCl_3$) 3079, 1566, 1530, 1359, 1198 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.736-7.73 (m, 2H), 7.64-7.56 (m, 3H), 7.51-7.42 (m, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 153.2, 149.8, 148.1, 132.2, 130.6, 129.8, 129.1, 129.0, 127.8, 126.8, 126.6, 125.0, 124.3, 124.2, 124.1, 123.5, 112.4, 105.3; **HRMS** (ESI, *m/z*): calcd for $C_{18}H_{12}O_3N$ $[M+H]^+$ 290.0812, found 290.0806.



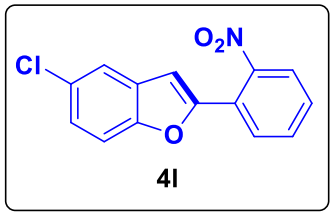
4j

2-(2-Nitrophenyl)-5-(thiophen-2-yl)benzofuran (**4j**). Yellow solid, 113 mg (0.351 mmol), 71% yield, R_f = 0.3 (EtOAc/Hex, 10:90); **MP** 158-160 °C; **IR** ($CHCl_3$) 3103, 2973, 1527, 1459, 1357 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.87 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.82 – 7.77 (m, 2H), 7.67 – 7.63 (m, 1H), 7.58 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.45 – 7.41 (m, 3H), 7.03 (d, *J* = 0.8 Hz, 1H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 154.8, 151.3, 148.4, 142.5, 132.2, 131.8, 130.1, 129.6, 129.1, 126.8, 126.4, 124.6, 124.2, 120.1, 119.3, 111.8, 106.3; **HRMS** (ESI, *m/z*): calcd for $C_{18}H_{12}O_3NS$ $[M+H]^+$ 322.0538, found 322.0525.



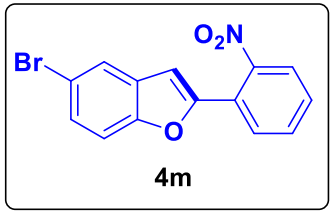
4k

5-Fluoro-2-(2-nitrophenyl)benzofuran (**4k**). Yellow solid, 89 mg (0.345 mmol), 69% yield, R_f = 0.74 (EtOAc/Hex, 2:98); **MP** 96-98 °C; **IR** ($CHCl_3$) 3106, 1699, 1527, 1354, 1187, 746 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.84 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 8.9, 4.0 Hz, 1H), 7.27 (d, *J* = 2.2 Hz, 1H), 7.07-7.03 (m, 1H), 6.97 (s, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 160.5, 158.6, 152.5, 151.6, 148.4, 132.3, 130.2, 129.8, 129.4 (d, J_{C-F} = 12.6 Hz), 124.3, 124.1, 113.4, 113.2, 112.3 (d, J_{C-F} = 10.1 Hz), 107.1, 106.9, 106.2 (d, J_{C-F} = 3.8 Hz); **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9O_3NF$ $[M+H]^+$ 258.0561, found 258.0559.



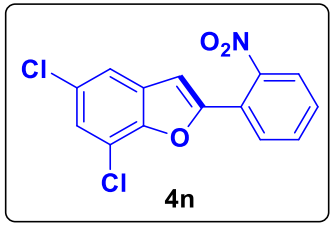
4l

5-Chloro-2-(2-nitrophenyl)benzofuran (**4l**). Light yellow solid, 106 mg (0.390 mmol), 78% yield, R_f = 0.74 (EtOAc/Hex, 2:98); **MP** 88-90 °C; **IR** ($CHCl_3$) 3080, 1586, 1529, 1355, 1163, 774 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.85-7.81 (m, 2H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.59-7.53 (m, 2H), 7.42 (d, *J* = 8.7 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 6.95 (s, 1H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 153.7, 152.2, 148.4, 132.4, 130.3, 130.0, 129.9, 129.0, 125.7, 124.3, 124.0, 121.1, 112.6, 105.6; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9O_3N^{35}Cl$ $[M+H]^+$ 274.0265, found 274.0266.



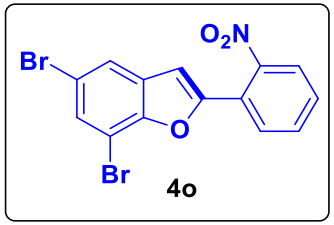
4m

5-Bromo-2-(2-nitrophenyl)benzofuran (**4m**). Light yellow solid, 115 mg (0.360 mmol), 72% yield, R_f = 0.75 (EtOAc/Hex, 2:98); **MP** 107-109 °C; **IR** ($CHCl_3$) 3079, 1608, 1529, 1356, 1162, 748 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.82 (t, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 1.4 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.44-7.36 (m, 2H), 6.95 (s, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 154.1, 152.1, 148.4, 132.4, 130.5, 130.3, 130.0, 128.4, 124.4, 124.2, 124.0, 116.5, 113.1, 105.5; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9{}^{79}BrO_3N$ $[M+H]^+$ 317.9761, found 317.9756.

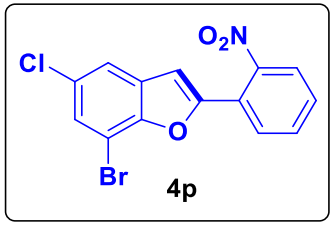


4n

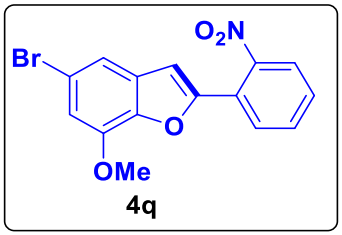
5,7-Dichloro-2-(2-nitrophenyl)benzofuran (**4n**). Yellow solid, 113 mg (0.370 mmol), 74% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 110-112 ºC; **IR** ($CHCl_3$) 3065, 1661, 1568, 1277, 1170, 702 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.91-7.83 (m, 2H), 7.73-7.67 (m, 2H), 7.63 (d, *J* = 1.7 Hz, 1H), 7.60-7.56 (m, 1H), 7.00 (s, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 152.8, 149.7, 148.5, 132.5, 130.8, 130.5, 130.4, 129.3, 125.6, 124.4, 123.4, 119.8, 117.7, 106.2; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_6O_3N^{35}Cl_2$ $[M-H]^+$ 305.9719, found 305.9731.



5,7-Dibromo-2-(2-nitrophenyl)benzofuran (**4o**). Yellow solid, 152 mg (0.385 mmol), 77% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 101-103 ºC; **IR** ($CHCl_3$) 3018, 1637, 1532, 1359, 1216, 748 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.91-7.84 (m, 2H), 7.72-7.68 (m, 1H), 7.62-7.56 (m, 1H), 7.50 (d, *J* = 1.9 Hz, 1H), 7.35 (d, *J* = 1.9 Hz, 1H), 6.97 (s, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 152.6, 151.5, 149.8, 148.5, 132.5, 130.4, 129.3, 125.6, 124.4, 123.4, 119.8, 117.7, 116.6, 106.1; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_6O_3N^{79}Br_2$ $[M-H]^+$ 393.8709, found 393.8716.

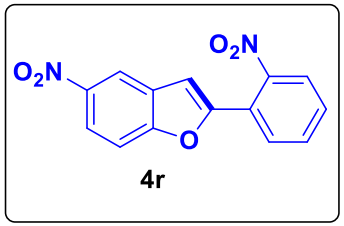


7-Bromo-5-chloro-2-(2-nitrophenyl)benzofuran (**4p**). Yellow solid, 139 mg (0.395 mmol), 79% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 112-114 ºC; **IR** ($CHCl_3$) 2955, 1602, 1534, 1274, 1122, 742 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.91-7.81 (m, 2H), 7.68 (dd, *J* = 9.8, 5.3 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.54-7.47 (m, 2H), 6.99 (d, *J* = 2.7 Hz, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 152.7, 151.1, 148.4, 132.4, 130.38, 130.36, 129.5, 128.2, 124.4, 123.4, 120.4, 106.3, 104.6; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_8O_3N^{79}Br^{35}Cl$ $[M+H]^+$ 351.9371, found 351.9369.



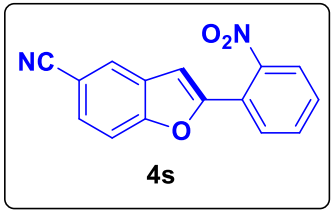
4q

5-Bromo-7-methoxy-2-(2-nitrophenyl)benzofuran (**4q**). Brown solid, 122 mg (0.355 mmol), 71% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 104-106 °C; **IR** ($CHCl_3$) 3026, 2925, 1610, 1520, 1046, 741 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.87-7.79 (m, 2H), 7.67-7.62 (m, 1H), 7.53 (dd, *J* = 5, 8.0 Hz, 1H), 7.34 (d, *J* = 9.8 Hz, 1H), 6.92 (dd, *J* = 15, 6.4 Hz, 2H), 3.98 (s, 3H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 151.6, 148.3, 145.8, 143.6, 132.3, 131.5, 130.4, 129.9, 124.3, 123.9, 116.5, 116.4, 111.5, 105.8, 56.7; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_9O_4N^{79}Br$ $[M-H]^+$ 345.9710, found 345.9720.

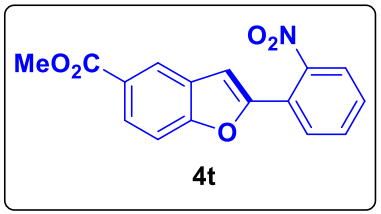


4r

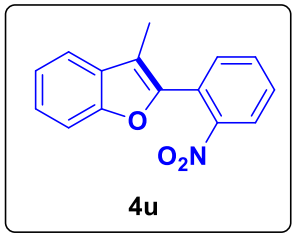
5-Nitro-2-(2-nitrophenyl)benzofuran (**4r**). Yellow solid, 71 mg (0.250 mmol), 50% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 88-90 °C; **IR** ($CHCl_3$) 3105, 1534, 1655, 1522, 1343 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.57 (d, *J* = 2.3 Hz, 1H), 8.28 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.91-7.85 (m, 2H), 7.75-7.70 (m, 1H), 7.66-7.57 (m, 2H), 7.14 (d, *J* = 0.7 Hz, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 157.9, 154.3, 148.4, 144.7, 132.7, 130.7, 129.0, 124.7, 123.5, 121.2, 118.2, 112.0, 106.6; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9O_5N_2$ $[M+H]^+$ 285.0506, found 285.0504.



2-(2-Nitrophenyl)benzofuran-5-carbonitrile (**4s**). Light yellow solid, 79 mg (0.30 mmol), 60% yield, R_f = 0.0.5 (EtOAc/Hex, 20:80); **MP** 150-152 °C; **IR** ($CHCl_3$) 2924, 2856, 2229, 1531, 1357 cm^{-1}; **^{1}H-NMR** (300 MHz, $CDCl_3$) δ = 7.99 – 7.96 (m, 1H), 7.89 – 7.83 (m, 2H), 7.74 – 7.68 (m, 1H), 7.65 – 7.56 (m, 3H), 7.05 (s, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 156.8, 153.4, 148.4, 132.6, 130.6, 129.2, 128.9, 126.6, 124.6, 123.5, 119.3, 112.8, 107.5, 105.7; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_9O_3N_2$ $[M+H]^+$ 265.0613, found 265.0594.

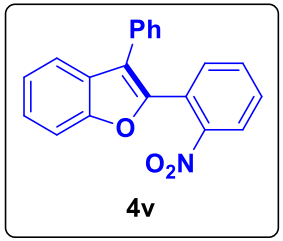


Methyl 2-(2-nitrophenyl)benzofuran-5-carboxylate (**4t**). Light yellow solid, 88 mg (0.295 mmol), 59% yield, R_f = 0.78 (EtOAc/Hex, 2:98); **MP** 163-165 °C; **IR** ($CHCl_3$) 2921, 2852, 1718, 1532, 1356 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.36 (d, *J* = 1.3 Hz, 1H), 8.06 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.87 – 7.82 (m, 2H), 7.70 – 7.66 (m, 1H), 7.59 – 7.50 (m, 2H), 7.07 (d, *J* = 0.7 Hz, 1H), 3.95 (s, 3H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 167.2, 157.8, 152.2, 148.4, 132.4, 130.4, 130.0, 128.6, 127.1, 125.9, 124.4, 124.1, 124.0, 111.5, 106.5, 52.4; **HRMS** (ESI, *m/z*): calcd for $C_{16}H_{12}O_5N$ $[M+H]^+$ 298.0715, found 298.0701.



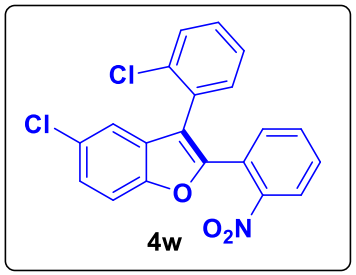
4u

3-Methyl-2-(2-nitrophenyl)benzofuran (**4u**). Yellow solid, 86 mg (0.34 mmol), 68%, R_f = 0.5 (EtOAc/Hexane, 10:90); **MP** 122-124 ^oC ; **IR** ($CHCl_3$) 3066, 2926, 1529, 1451, 1354 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.96 (d, *J* = 8.1 Hz, 1H), 7.70-7.62 (m, 2H), 7.58-7.51 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 1H), 7.34-7.30 (m, 1H), 7.29-7.24 (m, 1H), 2.31 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 154.6, 149.0, 146.7, 132.6, 131.9, 130.0, 129.6, 125.4, 125.2, 124.9, 122.8, 119.9, 114.4, 111.4, 8.8; **HRMS** (ESI, m/z): calcd for $C_{15}H_{12}NO_3$ $[M+H]^+$ 254.0812, found 254.0808. The spectroscopic data were in good agreement with the reported data.[10]

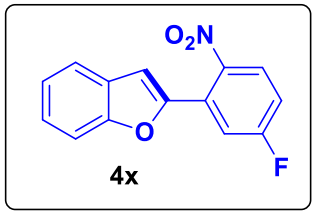


4v

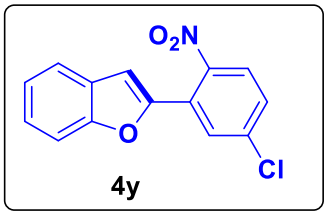
2-(2-Nitrophenyl)-3-phenylbenzofuran (**4v**). Yellow solid, 115 mg (0.365 mmol), 73%, R_f = 0.4 (EtOAc/Hexane, 10:90); **MP** 130-132 ^oC ; **IR** ($CHCl_3$) 3064, 1530, 1449, 1354 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.99-7.94 (m, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.55-7.50 (m, 3H), 7.46-7.44 (m, 4H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.39-7.36 (m, 2H), 7.34-7.29 (m, 1H); **^{13}C{^{1}H}NMR** (126 MHz, $CDCl_3$) δ = 155.0, 149.3, 146.9, 132.64, 132.62, 131.6, 129.8, 129.4, 129.1, 128.5, 127.9, 125.6, 125.5, 124.9, 123.4, 120.6, 120.1, 111.7; **HRMS** (ESI, m/z): calcd for $C_{20}H_{14}O_3N$ $[M+H]^+$ 316.0968, found 316.0963.



5-Chloro-3-(2-chlorophenyl)-2-(2-nitrophenyl)benzofuran (**4w**). Yellow solid, 92 mg (0.24 mmol), 48% yield, R_f = 0.6 (EtOAc/Hex, 20:90); **MP** 174-176 °C; **IR** ($CHCl_3$) 3072, 2922, 1531, 1444, 1352 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.97 – 7.93 (m, 1H), 7.53 – 7.49 (m, 3H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.38 – 7.33 (m, 3H), 7.32 – 7.27 (m, 2H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ 153.1, 149.7, 148.9, 134.4, 132.8, 132.5, 132.0, 130.34, 130.26, 130.12, 130.07, 130.0, 129.1, 127.4, 125.8, 124.9, 124.8, 120.7, 117.7, 112.8; **HRMS** (ESI, *m/z*): calcd for $C_{20}H_{12}{}^{35}Cl_2O_3N$ $[M+H]^+$ 384.0194, found 384.0173.

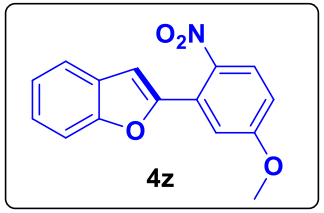


2-(5-Fluoro-2-nitrophenyl)benzofuran (**4x**). Yellow solid, 81 mg (0.315 mmol), 63% yield, R_f = 0.4 (EtOAc/Hex, 10:90); **MP 1**63-165 °C; **IR** ($CHCl_3$) 3080, 2923, 1529, 1354, 1225 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 7.83 (dd, *J* = 8.9, 4.9 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.57 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.51 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.30 – 7.26 (m, 1H), 7.19 – 7.15 (m, 1H), 7.06 (d, *J* = 0.8 Hz, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 164.9, 162.9, 155.3, 149.2, 144.4, 128.4, 126.9 (d, *J* = 9.7 Hz), 126.0, 123.6, 121.9, 116.8 (d, *J* = 25.2 Hz), 116.2 (d, *J* = 23.9 Hz), 111.6, 107.3; **^{19}F-NMR** (376 MHz, $CDCl_3$) δ = -104.9.; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9O_3NF$ $[M+H]^+$ 258.0566, found 258.0556.



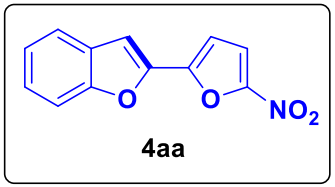
4y

2-(5-Chloro-2-nitrophenyl)benzofuran (**4y**). Orange solid, 89 mg (0.326 mmol), 65% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **MP** 118-120 ºC; **IR** ($CHCl_3$) 3065, 1599, 1521, 1256, 741 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.87 (d, *J* = 2.2 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.52-7.45 (m, 2H), 7.38-7.34 (m, 1H), 7.30-7.27 (m, 1H), 7.06 (d, *J* = 0.8 Hz, 1H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 155.4, 149.1, 146.4, 138.5, 129.8, 129.2, 128.4, 126.04, 126.00, 125.7, 123.6, 121.9, 111.7, 107.3; **MS** (ESI, *m/z*): **HRMS** (ESI, *m/z*): calcd for $C_{14}H_9O_3N^{35}Cl$ $[M+H]^+$ 274.0265, found 274.0258.



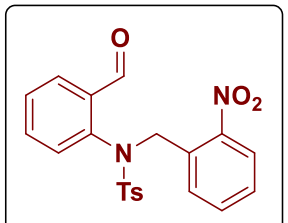
4z

2-(5-Methoxy-2-nitrophenyl)benzofuran (**4z**). Yellow solid, 78 mg (0.29 mmol), 58% yield, R_f = 0.5 (EtOAc/Hex, 10:90); **MP** 135-137 ºC; **IR** ($CHCl_3$) 2923, 2853, 1518, 1342,1240 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.90 (d, *J* = 9.0 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.29 – 7.23 (m, 2H), 7.00 (s, 1H), 6.96 (dd, *J* = 9.0, 2.8 Hz, 1H), 3.93 (s, 3H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 162.5, 155.3, 151.1, 141.7, 128.6, 127.3, 127.1, 125.4, 123.4, 121.6, 115.6, 114.3, 111.6, 106.4, 56.2; **HRMS** (ESI, *m/z*): calcd for $C_{15}H_{12}O_4N$ $[M+H]^+$ 270.0766, found 270.0755.



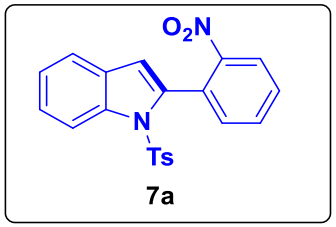
4aa

2-(5-Nitrofuran-2-yl)benzofuran (**4aa**). Yellow solid, 76 mg (0.33 mmol), 66% yield, R_f = 0.6 (EtOAc/Hex, 10:90); **MP** 127-129 ºC; **IR** ($CHCl_3$) 3140, 3140, 3073, 1518, 1470, 1353, 1242 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 7.7 Hz, 1H), 7.49 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.40 (d, *J* = 3.8 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.29 – 7.21 (m, 2H), 6.90 (d, *J* = 3.8 Hz, 1H); **^{13}C{^{1}H}-NMR** (75 MHz, $CDCl_3$) δ = 155.6, 148.4, 145.0, 128.0, 126.6, 124.1, 122.2, 113.9, 111.7, 109.7, 106.6; **HRMS** (ESI, *m/z*): calcd for $C_{12}H_8O_4N$ $[M+H]^+$ 230.0453, found 230.0441.



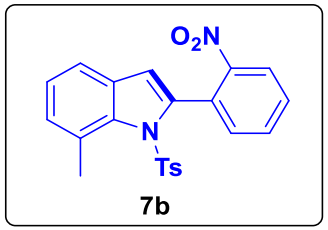
6a

***N*-(2-Formylphenyl)-4-methyl-*N*-(2-nitrobenzyl)benzenesulfonamide** (**6a**). White solid, 182 mg (0.445 mmol), 89%, R_f = 0.4 (EtOAc/Hexane, 20:80); **MP** 167-169 ºC ; **IR** ($CHCl_3$) 3068, 2921, 1722, 1616, 1448, 1257 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 10.17 (s, 1H), 7.89 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.78 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.68-7.64 (m, 1H), 7.51-7.48 (m, 2H), 7.46-7.43 (m, 1H), 7.42-7.38 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.78 (dd, *J* = 7.8, 1.2 Hz, 1H), 5.32 (s, 1H), 5.02 (s, 1H), 2.47 (s, 3H); **^{13}C{^{1}H}NMR** (75 MHz, $CDCl_3$) δ = 189.4, 149.0, 144.9, 141.3, 135.6, 134.5, 133.8, 133.6, 131.8, 130.8, 130.0, 129.3, 129.0, 128.9, 128.2, 127.9, 124.8, 51.3, 21.8; **HRMS** (ESI, m/z): calcd for $C_{21}H_{19}O_5N_2S$ $[M+H]^+$ 411.1009, found 411.1004.



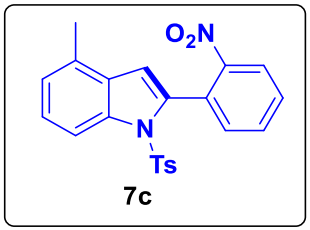
7a

2-(2-Nitrophenyl)-1-tosyl-1*H*-indole (**7a**). White solid, 145 mg (0.37 mmol), 74%, R_f = 0.4 (EtOAc/Hexane, 20:80); **MP** 170-172 ^oC; **IR** ($CHCl_3$) 3063, 1528, 1446, 1359, 1174 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.22 (d, *J* = 8.4 Hz, 1H), 8.19-8.14 (m, 1H), 7.67-7.58 (m, 2H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.40-7.32 (m, 4H), 7.27 (dd, *J* = 11.7, 4.4 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.60 (s, 1H), 2.29 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3, 145.1, 137.4, 136.4, 135.4, 133.4, 132.4, 130.1,129.8, 129.6, 127.6, 126.8, 125.4, 124.6, 124.1, 121.2, 115.4, 112.8, 21.6; **HRMS** (ESI, m/z): calcd for $C_{21}H_{17}O_4N_2S$ $[M+H]^+$ 393.0897, found 393.0904.



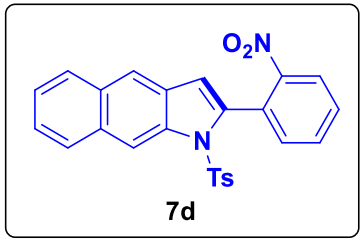
7b

7-Methyl-2-(2-nitrophenyl)-1-tosyl-1*H*-indole (**7b**). Light yellow solid, 152 mg (0.375 mmol), 75%, R_f = 0.5 (EtOAc/Hexane, 20:80); **MP** 183-185 ^oC ; **IR** ($CHCl_3$) 3041, 2924, 1528, 1450, 1360, 1175 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.97 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.62-7.58 (m, 1H), 7.55-(m, 1H), 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.27-7.18 (m, 3H), 7.04-6.97 (m, 4H), 6.67 (s, 1H), 2.78 (s, 3H), 2.29 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.2, 144.7, 140.2, 139.8, 133.8, 133.3, 132.13, 132.08, 129.9, 129.8, 129.5, 129.1, 127.8, 126.8, 125.6, 124.4, 119.2, 118.4, 22.0, 21.7; **HRMS** (ESI, m/z): calcd for $C_{22}H_{19}N_2O_4S$ $[M+H]^+$ 407.1060, found 407.1052.



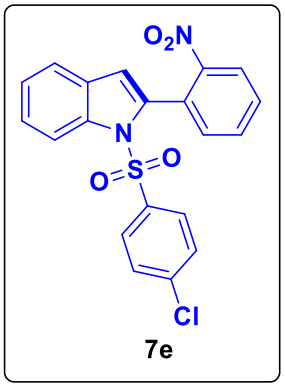
7c

4-Methyl-2-(2-nitrophenyl)-1-tosyl-1*H*-indole (**7c**). Light yellow solid, 164 mg (0.405 mmol), 81%, R_f = 0.5 (EtOAc/Hexane, 20:80); **MP** 191-193 °C ; **IR** ($CHCl_3$) 3032, 2824, 1529, 1446, 1359, 1179, 1099 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.15 (dd, *J* = 7.5, 1.8 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.66-7.56 (m, 2H), 7.36 (dd, *J* = 10.3, 5.3 Hz, 3H), 7.25-7.20 (m, 1H), 7.05 (t, *J* = 8.3 Hz, 3H), 6.61 (s, 1H), 2.42 (s, 3H), 2.27 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3, 145.0, 137.1, 135.7, 135.6, 133.6, 132.3, 130.8, 130.0, 129.7, 127.9, 126.9, 125.5, 124.6, 124.5, 112.9, 111.3, 21.7, 18.5; **HRMS** (ESI, m/z): calcd for $C_{22}H_{19}O_4N_2S$ $[M+H]^+$ 407.1060, found 407.1052.



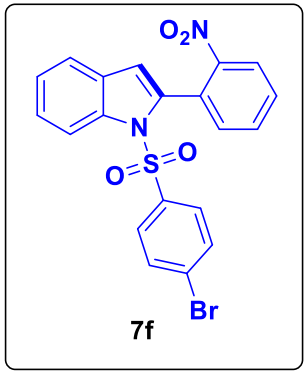
7d

2-(2-Nitrophenyl)-1-tosyl-1*H*-benzo[f]indole (**7d**). Yellow solid, 139 mg (0.315 mmol), 63%, R_f = 0.6 (EtOAc/Hexane, 30:70); **MP** 163-165 °C ; **IR** ($CHCl_3$) 3059, 1529, 1439, 1360, 1173 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.70 (s, 1H), 8.21 (dd, *J* = 7.6, 1.7 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.97 (s, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.71-7.62 (m, 2H), 7.53-7.46 (m, 2H), 7.45-7.41 (m, 1H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.04 (d, *J* = 8.2 Hz, 2H), 6.75 (s, 1H), 2.26 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3 , 145.1, 139.5, 136.8, 135.0, 133.2, 132.5, 131.9, 131.0, 130.3, 129.6, 128.7, 128.0, 127.6, 126.9, 125.5, 125.2, 124.7, 119.3, 113.5, 113.0, 21.7; **HRMS** (ESI, m/z): calcd for $C_{25}H_{19}O_4N_2S$ $[M+H]^+$ 443.1060, found 443.1049.



7e

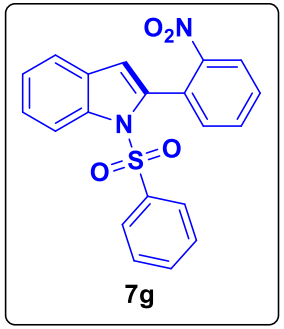
1-((4-Chlorophenyl)sulfonyl)-2-(2-nitrophenyl)-1*H*-indole (7e): Light yellow Solid, 157 mg (0.38 mmol), 76%, R_f = 0.3 (EtOAc/Hexane, 20:80); **MP** 181-183 ^oC ; **IR** ($CHCl_3$) 3049, 1528, 1448, 1365, 1178 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.18 (dd, *J* = 10.5, 5.3 Hz, 2H), 7.69-7.61 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.40 (t, *J* = 9.1 Hz, 4H), 7.30 (dd, *J* = 13.5, 8.1 Hz, 3H), 6.64 (s, 1H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3, 140.6, 137.3, 136.6, 136.2, 133.5, 132.4, 130.3, 129.9, 129.4, 128.3, 127.4, 125.7, 124.7, 124.5, 121.5, 115.4, 113.4; **HRMS** (ESI, m/z): calcd for $C_{20}H_{14}O_4N_2{}^{35}ClS$ $[M+H]^+$ 413.0357, found 413.0346.



7f

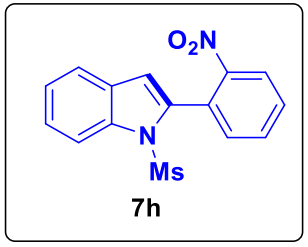
1-((4-Bromophenyl)sulfonyl)-2-(2-nitrophenyl)-1*H*-indole (**7f**). Yellow solid, 184 mg (0.405 mmol), 81%, R_f = 0.4 (EtOAc/Hexane, 20:80); **MP** 175-177 ^oC ; **IR** ($CHCl_3$) 3087, 1527, 1447, 1364, 1176 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.22-8.16 (m, 2H), 7.69-7.61 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.41-7.37 (m, 2H), 7.32 (dd, *J* = 13.4, 7.9 Hz, 3H), 6.64 (s, 1H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3,

137.2, 137.1, 136.2, 133.5, 132.43, 132.40, 130.3, 129.9, 129.3, 128.3, 127.3, 125.7, 124.7, 124.5, 121.5, 115.4, 113.5; **HRMS** (ESI, m/z): calcd for $C_{20}H_{14}O_4N_2{}^{79}BrS$ $[M+H]^+$ 456.9852, found 456.9840.



7g

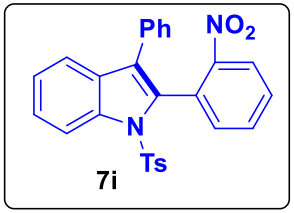
2-(2-Nitrophenyl)-1-(phenylsulfonyl)-1*H*-indole (**7g**). White solid, 161 mg (0.425 mmol), 85%, R_f = 0.4 (EtOAc/Hexane, 20:80); **MP** 177-179 ^oC ; **IR** ($CHCl_3$) 3056, 1529, 1450, 1363, 1179, 1086 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.24 (d, *J* = 8.4 Hz, 1H), 8.19 (dd, *J* = 6.0, 3.4 Hz, 1H), 7.67-7.61 (m, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 3H), 7.43-7.33 (m, 3H), 7.31 (d, *J* = 7.7 Hz, 2H), 6.62 (s, 1H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.3, 138.4, 137.4, 136.3, 134.0, 133.6, 132.4, 130.2, 129.8, 129.1, 127.5, 126.9, 125.5, 124.7, 124.2, 121.3, 115.5, 112.9; **HRMS** (ESI, m/z): calcd for $C_{20}H_{15}O_4N_2S$ $[M+H]^+$ 379.0747, found 379.0739. The spectroscopic data were in good agreement with the reported data.[11]



7h

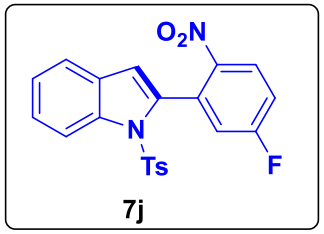
1-(Methylsulfonyl)-2-(2-nitrophenyl)-1*H*-indole (**7h**). Yellow solid, 109 mg (0.345 mmol), 69%, R_f = 0.6 (EtOAc/Hexane, 30:70); **MP** 155-157 ^oC ; **IR** ($CHCl_3$) 3051, 2925, 1526, 1446, 1355, 1168 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.10 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.70-7.66 (m, 1H), 7.64-7.57 (m, 3H), 7.47-7.40 (m, 1H), 7.36 (dd, *J* = 11.0, 4.0 Hz, 1H), 6.60 (s, 1H), 3.14 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz,

$CDCl_3$) δ = 148.8, 136.6, 135.9, 134.1, 132.6, 130.1, 129.6, 127.9, 125.5, 124.3, 124.2, 121.5, 114.2, 111.1, 40.2; **HRMS** (ESI, m/z): calcd for $C_{15}H_{13}O_4N_2S$ $[M+H]^+$ 317.0591, found 317.0584.



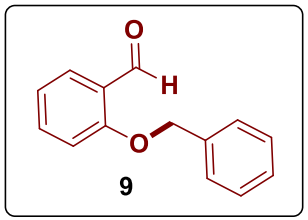
7i

2-(2-Nitrophenyl)-3-phenyl-1-tosyl-1*H*-indole (**7i**). Yellow solid, 180 mg (0.385 mmol), 77% yield, R_f = 0.4 (EtOAc/Hex, 10:90); **MP** 186-188 ºC; **IR** ($CHCl_3$) 3064, 2923, 1528, 1445, 1351 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.4 Hz, 1H), 8.15 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.57 – 7.52 (m, 2H), 7.47 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.41 – 7.38 (m, 2H), 7.33 – 7.29 (m, 1H), 7.23 – 7.20 (m, 3H), 7.14 – 7.10 (m, 5H), 2.33 (s, 3H); **^{13}C{^{1}H}-NMR** (101 MHz, $CDCl_3$) δ = 150.1, 145.1, 136.8, 135.8, 134.9, 132.3, 132.1, 131.9, 130.1, 130.0, 129.7, 128.6, 127.5, 127.1, 127.0, 125.7, 124.6, 124.5, 124.1, 120.4, 115.4, 21.7; **HRMS** (ESI, *m/z*): calcd for $C_{27}H_{21}O_4N_2S$ $[M+H]^+$ 469.1222, found 469.1199.



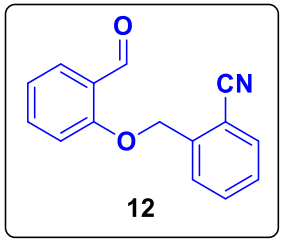
7j

2-(5-Fluoro-2-nitrophenyl)-1-tosyl-1*H*-indole (**7j**). Yellow solid, 144 mg (0.35 mmol), 70% yield, R_f = 0.4 (EtOAc/Hex, 10:90); **MP** 145-147 ºC; **IR** ($CHCl_3$) 3077, 2924, 1531, 1370, 1350 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.26 – 8.20 (m, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.34 – 7.27 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.04 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.63 (d, *J* = 0.7 Hz, 1H), 2.32 (s, 3H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 164.9, 162.9, 145.4 (d, *J* = 17.7 Hz), 137.4, 135.3, 135.1, 130.8 (d, *J* = 9.9 Hz), 129.8, 129.6, 127.4, 126.8, 125.8, 124.2, 121.4, 120.5, 120.3, 116.9, 116.7, 115.5, 113.1, 21.7; **^{19}F-NMR** (376 MHz, $CDCl_3$) δ = -104.6; **HRMS** (ESI, *m/z*): calcd for $C_{21}H_{16}FN_2O_4S$ $[M+H]^+$ 411.0815, found 411.0798.



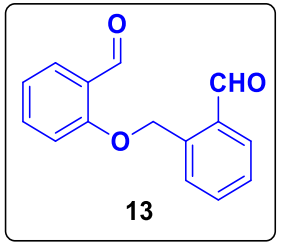
9

2-(Benzyloxy)benzaldehyde (**9**). Colorless thick liquid, 170 mg (0.80 mmol), 80% yield, R_f = 0.77 (EtOAc/Hex, 2:98); **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 10.60 (s, 1H), 7.89 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.49 – 7.34 (m, 5H), 7.08 – 7.01 (m, 2H), 5.17 (s, 2H).; **MS** (ESI, *m/z*): $[M+H]^+$ 213. The spectroscopic data were in good agreement with the reported data.[12]



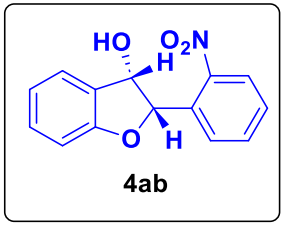
12

2-((2-Formylphenoxy)methyl)benzonitrile (**12**). Light pink solid, 100 mg (0.415 mmol), 83%, R_f = 0.4 (EtOAc/Hexane, 5:95); **MP** 112-124 ^oC ; **IR** ($CHCl_3$) 3070, 2882, 2225, 1682, 1247 cm^{-1}; **^{1}H-NMR** (400 MHz, DMSO d_6) δ = 10.41 (s, 1H), 7.93 (d, *J* = 7.5 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.80 – 7.66 (m, 3H), 7.59 (dd, *J* = 10.9, 4.1 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 5.45 (s, 2H); **^{13}C{^{1}H}NMR** (101 MHz, DMSO d_6) δ = 189.0, 160.2, 139.5, 136.4, 133.6, 129.7, 129.3, 127.9, 124.7, 121.5, 117.3, 114.1, 111.2, 68.3; **HRMS** (ESI, m/z): calcd for $C_{15}H_{12}O_2N$ $[M+H]^+$ 238.0868, found 238.0869. The spectroscopic data were in good agreement with the reported data.[13]



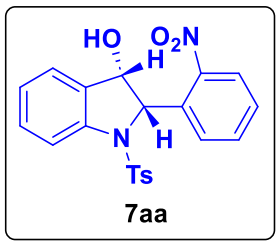
13

2-((2-Formylbenzyl)oxy)benzaldehyde (**13**). White solid, 104 mg (0.44 mmol), 88%, R_f = 0.5 (EtOAc/Hexane, 5:95); **MP** 118-120 °C; **IR** ($CHCl_3$) 2921, 2857, 1691, 1594, 1194 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 10.62 (s, 1H), 10.17 (s, 1H), 7.96 – 7.83 (m, 3H), 7.71 – 7.67 (m, 1H), 7.62 – 7.52 (m, 2H), 7.14 – 7.04 (m, 2H), 5.66 (s, 2H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 193.6, 189.7, 160.8, 138.6, 136.2, 135.1, 134.4, 132.9, 129.1, 128.3, 127.3, 125.2, 121.3, 113.3, 68.2; **HRMS** (ESI, m/z): calcd for $C_{15}H_{12}O_3Na$ $[M+Na]^+$ 263.0684, found 263.0662. The spectroscopic data were in good agreement with the reported data.[14]



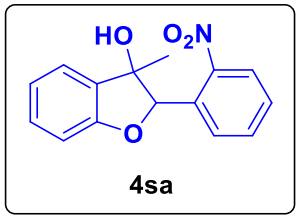
4ab

2-(2-Nitrophenyl)-2,3-dihydrobenzofuran-3-ol (4ab): (*cis*:*trans* = 1:0.7), Colorless thick liquid, 105 mg (0.41 mmol), 82%, R_f = 0.6 (EtOAc/Hexane, 30:70); **IR** ($CHCl_3$) 3471, 3396, 3059, 2922, 1521, 1466, 1344 cm^{-1}; **^{1}H-NMR** (300 MHz, DMSO-d_6) δ = 8.17-8.14 (m, 1H), 8.08* (dd, *J* = 8.1, 1.3 Hz, 0.7H), 7.83-7.75 (m, 2H), 7.71-7.68* (m, 0.7H), 7.66-7.55 (m, 1H + 0.7H), 7.42-7.37 (m, 2H), 7.34-7.27 (m, 2H), 7.03-6.95 (m, 2H + 1.4H), 6.21 (d, *J* = 6.6 Hz, 1H), 6.07* (br, 0.7H), 6.07 (br, 0.7H), 5.92* (d, *J* = 3.1 Hz, 0.7H), 5.55 (d, *J* = 6.0 Hz, 1H), 5.48 (d, *J* = 6.1 Hz, 1H), 5.09* (br, 0.7H); **^{13}C{^{1}H}NMR** (101 MHz, DMSO-d_6) δ = 159.5, 158.5, 147.4, 134.2, 133.8, 133.6, 132.8, 130.2, 130.0, 129.3, 129.1, 128.9, 128.6, 127.5, 126.3, 126.2, 124.9, 124.4, 121.4, 121.1, 109.9, 109.8, 87.5, 84.6, 79.2, 78.0, 71.4; **HRMS** (ESI, m/z): calcd for $C_{14}H_{11}NO_4Na$ $[M+Na]^+$ 280.0586, found 280.0576.



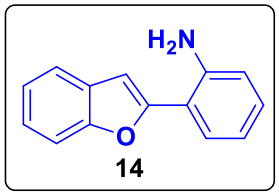
7aa

2-(2-Nitrophenyl)-1-tosylindolin-3-ol (7aa): (*cis*:*trans* = 1:0.5), White solid, 185 mg (0.45 mmol), 90%, R_f = 0.4 (EtOAc/Hexane, 20:80); **IR** ($CHCl_3$) 3518, 3032, 2924, 1525, 1469, 1349, 1165 cm^{-1}; **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 8.11 (d, *J* = 8.1 Hz, 1H), 8.05* (d, *J* = 8.1 Hz, 0.5H), 7.75-7.62 (m, 3H + 1.5H), 7.59-7.54 (m, 4H), 7.42-7.34 (m, 5H), 7.29* (d, *J* = 7.4 Hz, 0.5H), 7.19-7.10 (m, 2.5H), 6.08 (t, *J* = 8.0 Hz, 1H + 0.5H), 5.80 (d, *J* = 6.7 Hz, 1H), 5.53* (br, 0.5H), 5.25 (t, *J* = 7.6 Hz, 1H), 4.86* (br, 0.5H), 2.35 (s, 3H + 1.5H); **^{13}C{^{1}H}NMR** (126 MHz, DMSO-d_6) δ = 148.2, 147.6, 144.9, 144.5, 141.3, 140.2, 134.9, 134.1, 134.0, 133.5, 133.4, 133.1, 132.5, 132.2, 130.1, 130.0, 129.9, 129.7, 129.1, 128.5, 128.1, 127.3, 127.0, 126.6, 126.0, 125.3, 124.9, 124.5, 124.4, 115.7, 114.2, 77.1, 71.3, 69.8, 65.4, 21.0; **DEPT-135 NMR** δ = 134.4, 133.9, 130.6, 130.43, 130.37, 130.2, 129.6, 129.0, 128.5, 127.8, 127.5, 127.1, 126.5, 125.8, 125.3, 125.0, 124.9, 116.2, 114.7, 77.6, 71.7, 70.3, 65.9, 21.5; **HRMS** (ESI, m/z): calcd for $C_{21}H_{17}O_4N_2S$ $[M\text{-}OH]^+$ 393.0904, found 393.0895.



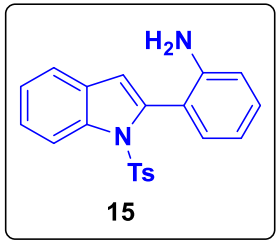
4sa

3-Methyl-2-(2-nitrophenyl)-2,3-dihydrobenzofuran-3-ol (4sa): (*csi:trans* mixture dr = 1:0.9), Yellow liquid, 99 mg (0.365 mmol), 73%, R_f = 0.4 (EtOAc/Hexane, 10:90); **IR** ($CHCl_3$) 3492, 3414, 2926, 1604, 1530, 1474, 1354 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.08* (dd, *J* = 8.5, 1.2 Hz, 0.9H), 8.01 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.63-7.57 (m, 3H), 7.50-7.44 (m, 3H), 7.37-7.28 (m, 4H), 7.06-6.94 (m, 4H), 6.23* (s, 0.9H), 6.12 (s, 1H), 1.86 (s, 3H), 1.27* (s, 2.7H); **^{13}C{^{1}H}NMR** (126 MHz, $CDCl_3$) δ = 159.1, 158.3, 148.6, 148.1, 134.8, 134.1, 133.5, 132.7, 131.7, 130.9, 130.8, 130.5, 129.02, 129.00, 128.7, 128.0, 124.9, 124.8, 124.4, 124.1, 122.2, 122.0, 110.31, 110.26, 90.9, 89.0, 82.6, 81.0, 29.2, 25.1; **HRMS** (ESI, m/z): calcd for $C_{15}H_{12}O_3$ $[M\text{-}OH]^+$ 254.0812, found 254.0806.



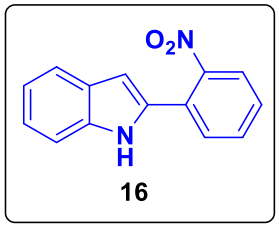
14

2-(Benzofuran-2-yl)aniline (**14**). Yellow solid, 48 mg (0.23 mmol), 92% yield, R_f = 0.6 (EtOAc/Hex, 20:80); **MP** 68-70 ºC; **IR** ($CHCl_3$) 3405, 3035, 2924, 1724, 1615, 1579, 1458 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 7.64-7.58 (m, 2H), 7.53-7.51 (m, 1H), 7.28-7.22 (m, 3H), 6.94 (d, *J* = 0.9 Hz, 1H), 6.94-6.77 (m, 2H), 4.49 (br, 2H); **^{13}C{^{1}H}-NMR** (126 MHz, $CDCl_3$) δ = 155.8, 154.4, 144.3, 130.0, 129.0, 128.7, 124.1, 123.1, 120.8, 118.7, 117.0, 115.6, 111.1, 103.1; **MS** (ESI, *m/z*): $[M+H]^+$ 210; **HRMS** (ESI, *m/z*): calcd for $C_{14}H_{12}ON$ $[M+H]^+$ 210.0913, found 210.0912. The spectroscopic data were in good agreement with the reported data.[15]



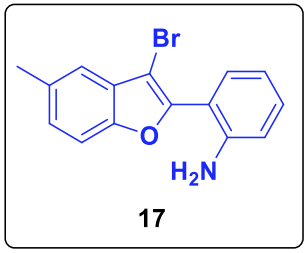
15

2-(1-Tosyl-1*H*-indol-2-yl)aniline (15): Yellow solid, 81 mg (0.225 mmol), 90%, R_f = 0.6 (EtOAc/Hexane, 30:70); **MP** 182-184 ºC ; **IR** ($CHCl_3$) 3473, 3385, 3060, 2924, 1615, 1449, 1369 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8.3 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.36 (dd, *J* = 12.6, 4.8 Hz, 3H), 7.32-7.20 (m, 2H), 7.08 (d, *J* = 8.1 Hz, 2H), 6.94 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.81-6.72 (m, 2H), 6.55 (s, 1H), 3.91 (brs, 2H), 2.31 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 146.6, 144.9, 138.6, 137.9, 135.1, 131.7, 130.6, 130.5, 129.5, 127.2, 124.9, 124.2, 120.9, 118.2, 117.6, 116.2, 115.6, 113.5, 21.7; **HRMS** (ESI, m/z): calcd for $C_{21}H_{19}O_2N_2S$ $[M+H]^+$ 363.1162, found 363.1156.



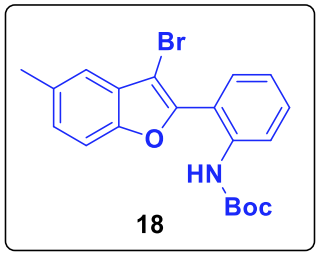
16

2-(2-Nitrophenyl)-1*H*-indole (**16**). White solid, 109 mg (0.46 mmol), 92%, R_f = 0.6 (EtOAc/Hexane, 30:70); **MP** 160-162 ºC ; **IR** ($CHCl_3$) 3406, 3068, 2926, 1527, 1354, 1296 cm^{-1}; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ = 8.48 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.70 – 7.58 (m, 3H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.21 (m, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.72 (s, 1H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 149.0, 137.1, 132.5, 131.8, 128.8, 128.4, 127.0, 124.3, 123.3, 121.1, 120.6, 111.4, 104.5; **HRMS** (ESI, m/z): calcd for $C_{14}H_{11}O_2N_2$ $[M+H]^+$ 239.0815, found 239.0812. The spectroscopic data were in good agreement with the reported data.[16]



17

2-(3-Bromo-5-methylbenzofuran-2-yl)aniline (**17**). Light yellow thick liquid, 125 mg (0.378 mmol), 63%, R_f = 0.4 (EtOAc/Hexane, 2:98); **IR** ($CHCl_3$) 3433, 3054, 2922, 2856, 1447, 1235 cm^{-1}; **^{1}H-NMR** (400 MHz, DMSO-d_6) δ = 7.53 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.33 (d, *J* = 0.7 Hz, 1H), 7.26 – 7.15 (m, 2H), 6.81 (dd, *J* = 8.2, 0.8 Hz, 1H), 6.69 – 6.61 (m, 1H), 5.42 (s, 2H), 2.46 (s, 3H); **^{13}C{^{1}H}NMR** (101 MHz, DMSO d_6) δ = 151.9, 151.4, 147.2, 132.9, 130.9, 130.6, 128.2, 126.5, 118.7, 115.7, 115.5, 111.5, 111.4, 94.1, 20.9; **HRMS** (ESI, m/z): calcd for $C_{15}H_{13}NOBr$ $[M+H]^+$ 302.0181, found 302.0155.

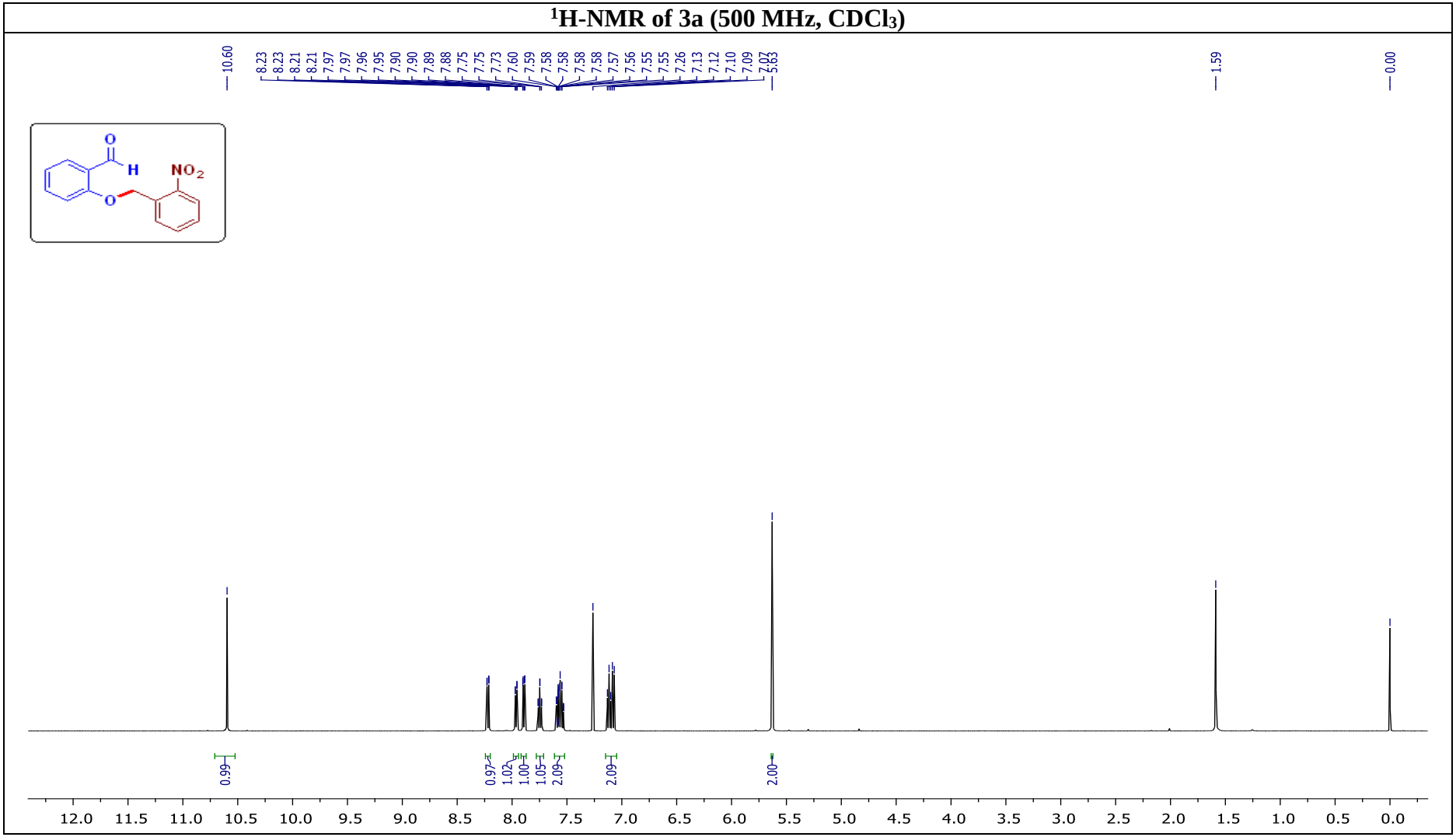


18

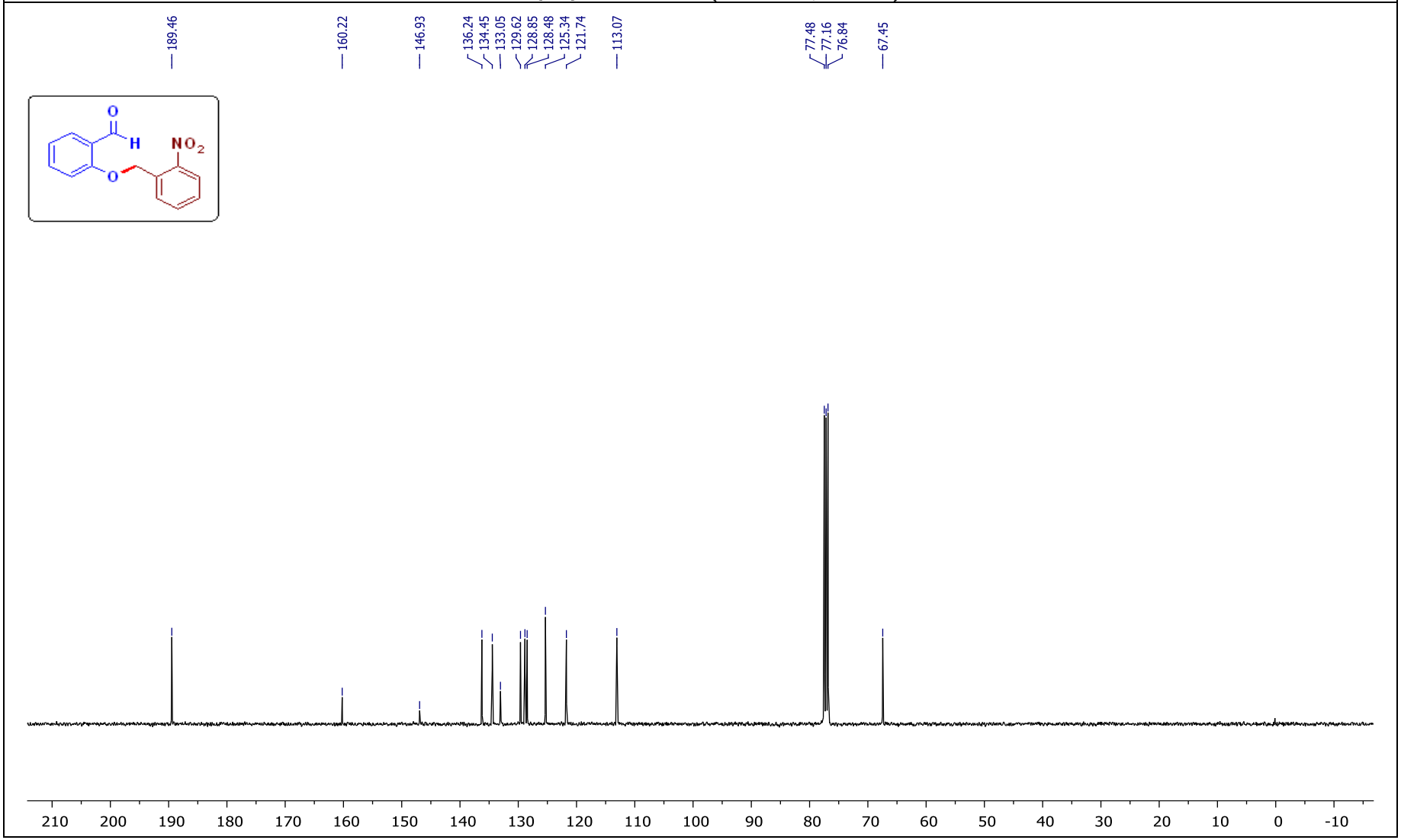
***tert*-Butyl (2-(3-bromo-5-methylbenzofuran-2-yl)phenyl)carbamate** (**18**). Colorless thick liquid, 38 mg (0.09 mmol), 72%, R_f = 0.4 (EtOAc/Hexane, 1:99); **IR** ($CHCl_3$) 3434, 2922, 2854, 1732, 1950, 1159 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ = 8.19 (d, *J* = 8.3 Hz, 1H), 7.65 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.47 – 7.39 (m, 3H), 7.25 – 7.20 (m, 2H), 7.17 – 7.13 (m, 1H), 2.51 (s, 3H), 1.49 (s, 9H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ = 152.9, 152.3, 150.1, 137.1, 133.8, 130.9, 128.8, 127.3, 122.8, 120.7, 120.0, 118.2, 111.3, 96.9, 80.9, 28.4, 21.5; **HRMS** (ESI, m/z): calcd for $C_{20}H_{20}O_3NNaBr$ $[M+Na]^+$ 424.0524, found 424.0494. The spectroscopic data were in good agreement with the reported data.[17]

15. Copies of spectra (^{1}H-NMR and ^{13}C{^{1}H}-NMR)

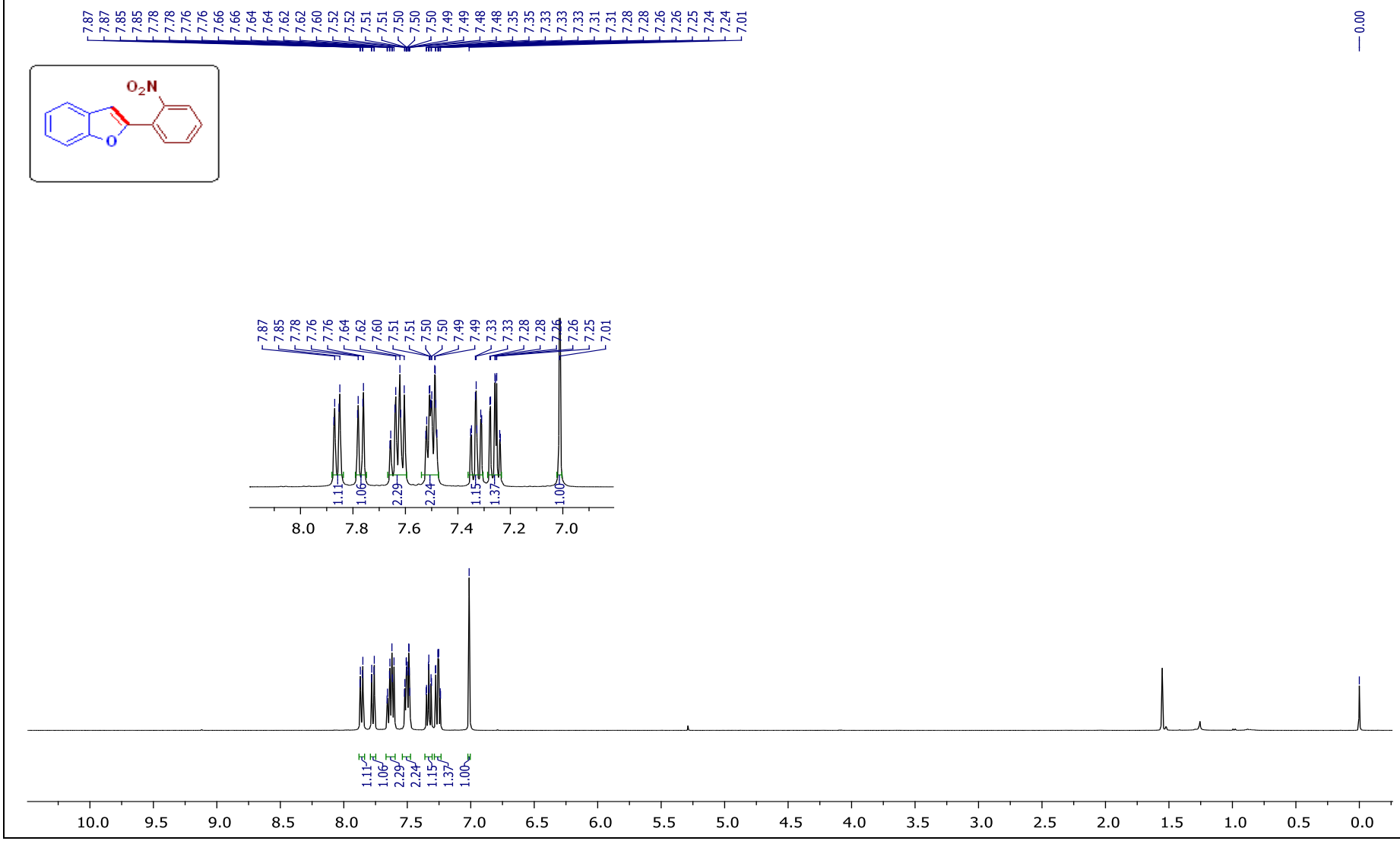
^{1}H-NMR of 3a (500 MHz, $CDCl_3$)



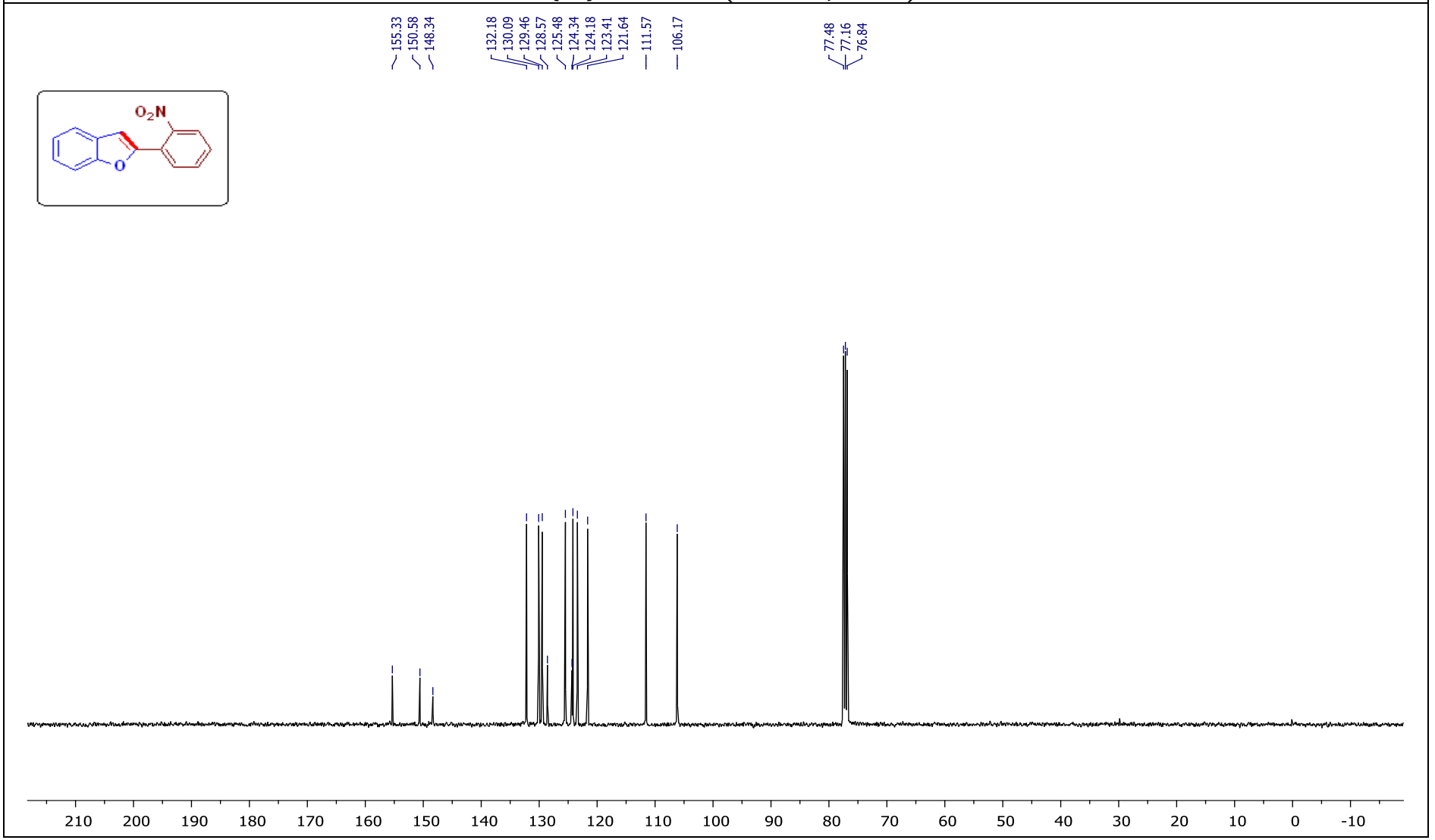
$^{13}C\{^{1}H\}$-NMR of 3a (126 MHz, $CDCl_3$)



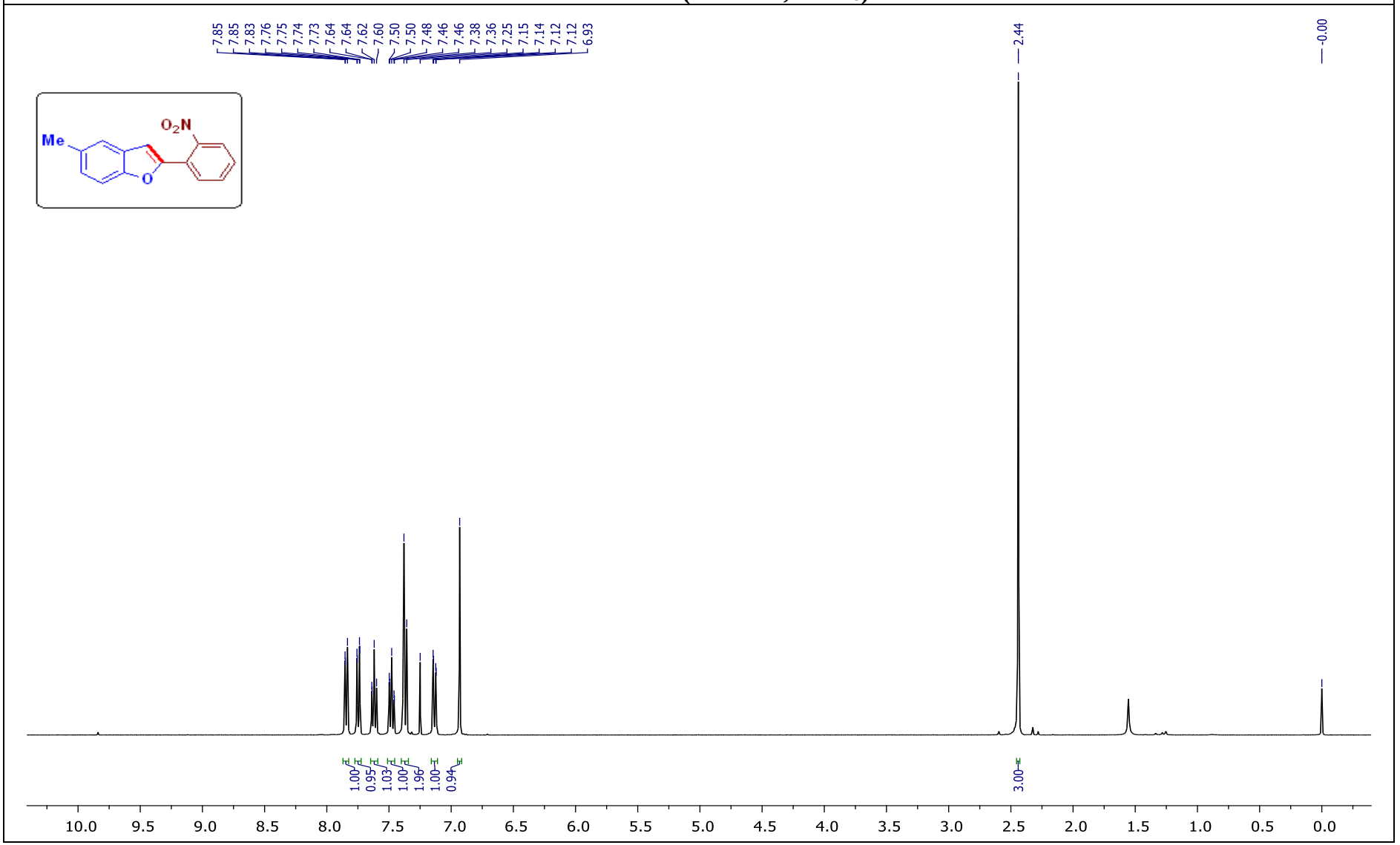
^{1}H-NMR of 4a (400 MHz, $CDCl_3$)



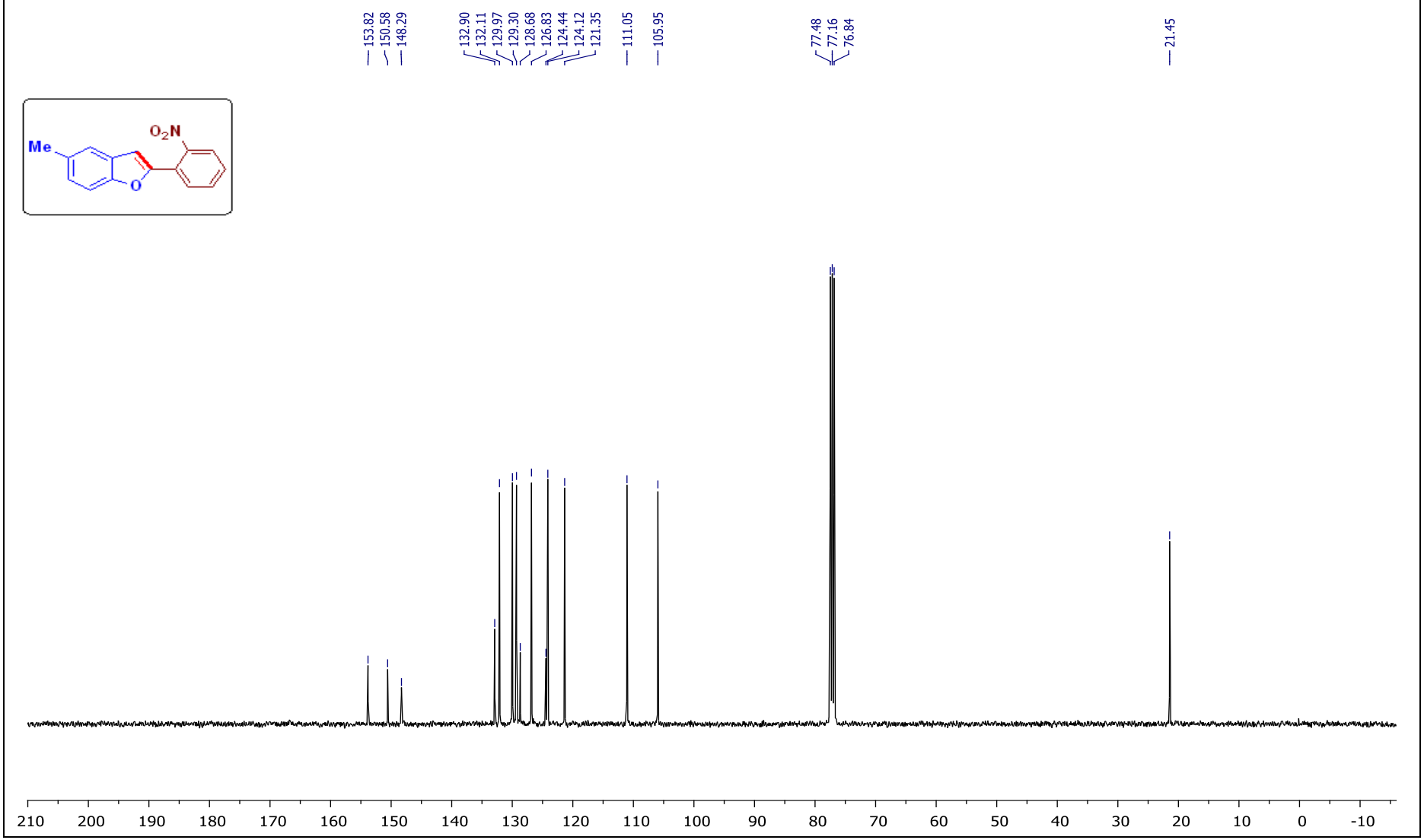
$^{13}C\{^{1}H\}$-NMR of 4a (101 MHz, $CDCl_3$)



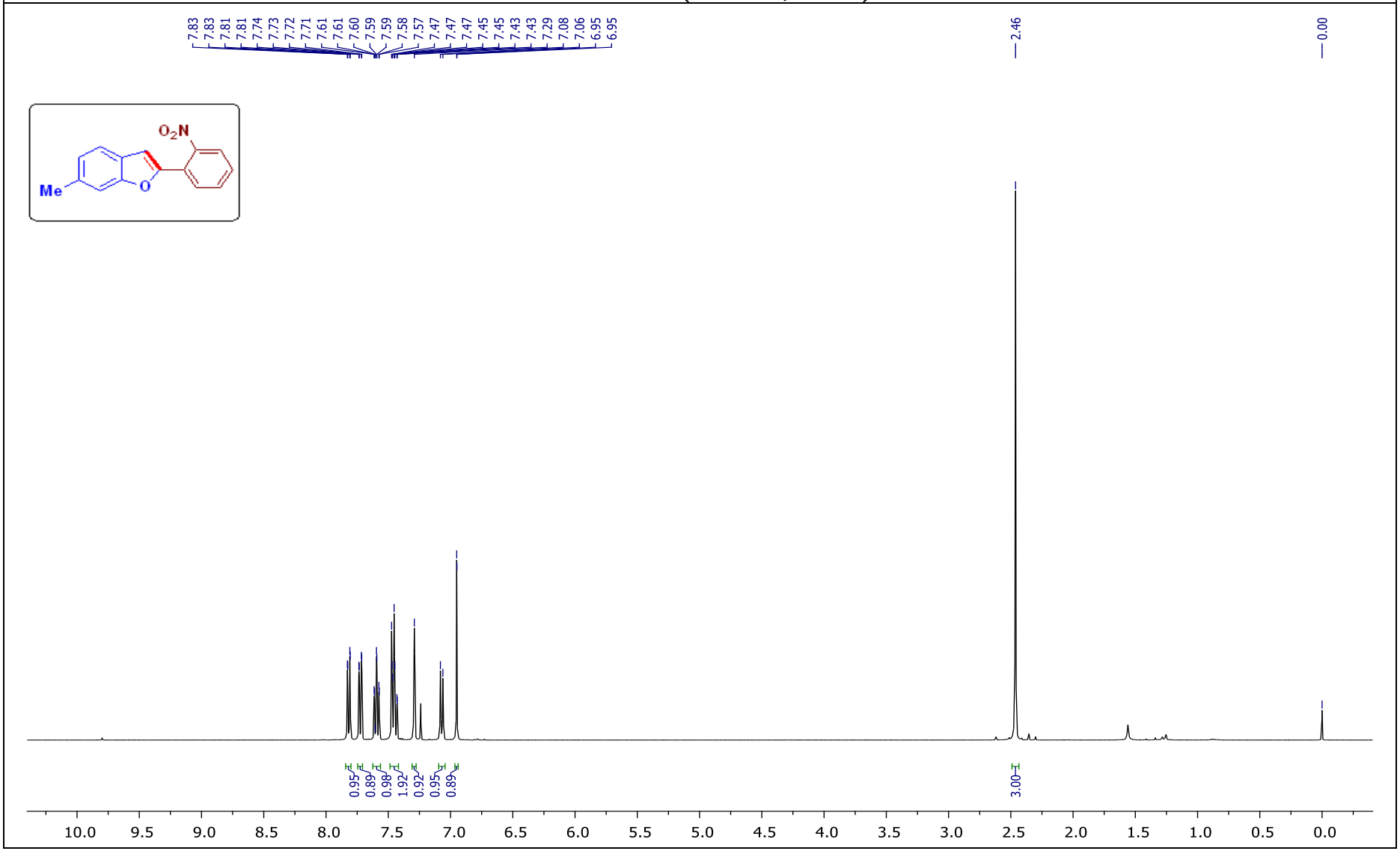
^{1}H-NMR of 4b (400 MHz, $CDCl_3$)



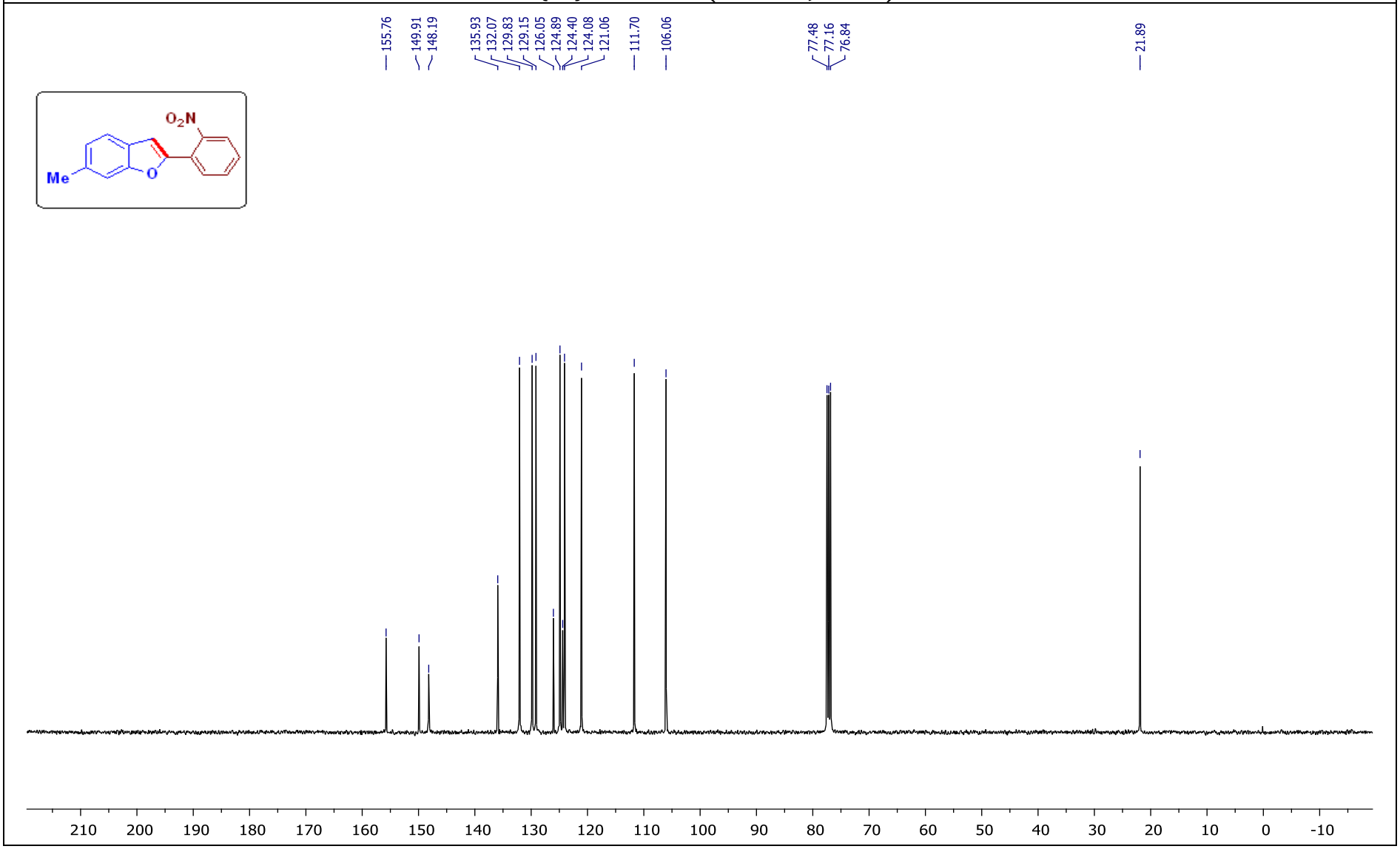
$^{13}C\{^{1}H\}$-NMR of 4b (101 MHz, $CDCl_3$)



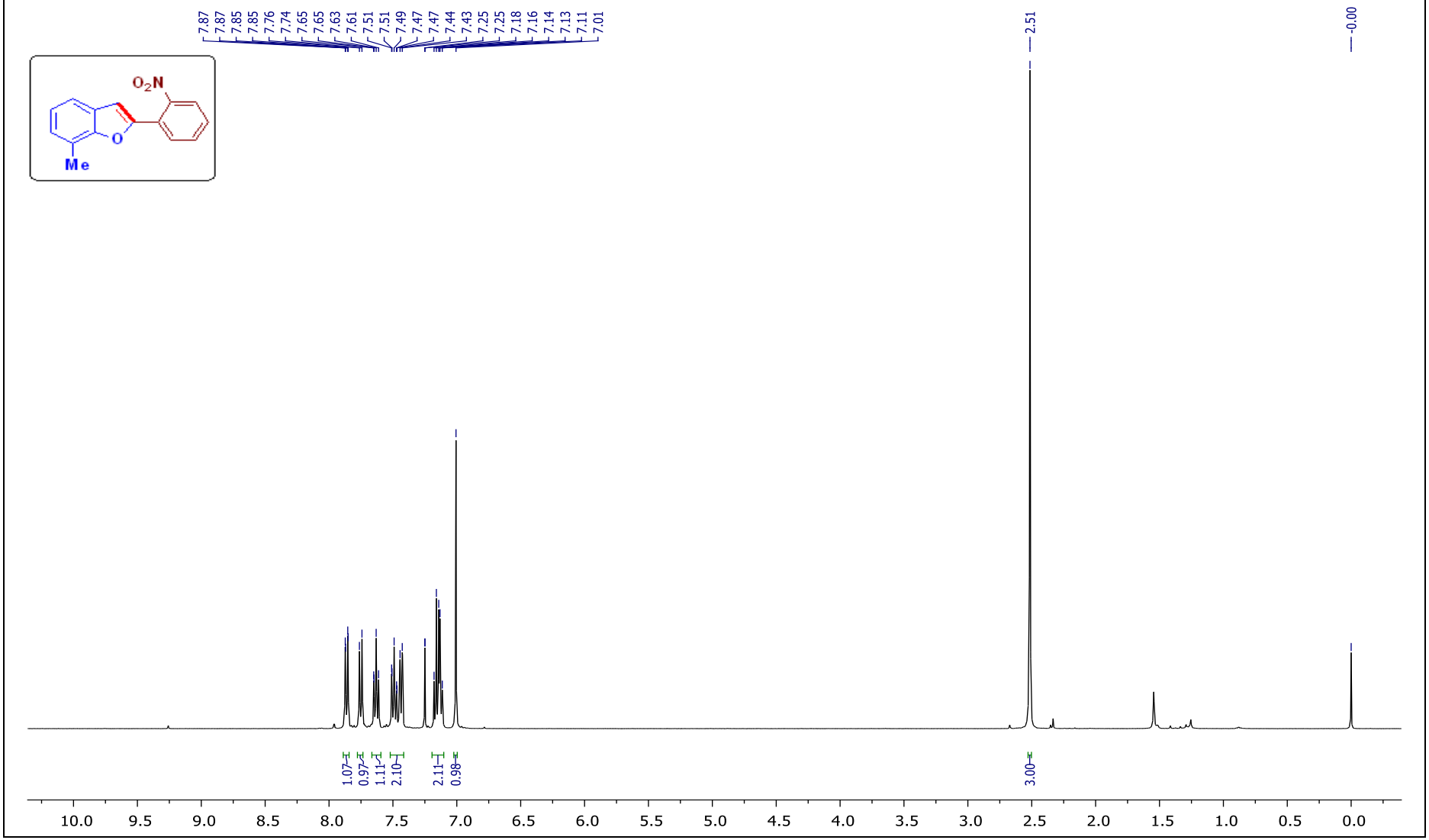
^{1}H-NMR of 4c (400 MHz, $CDCl_3$)



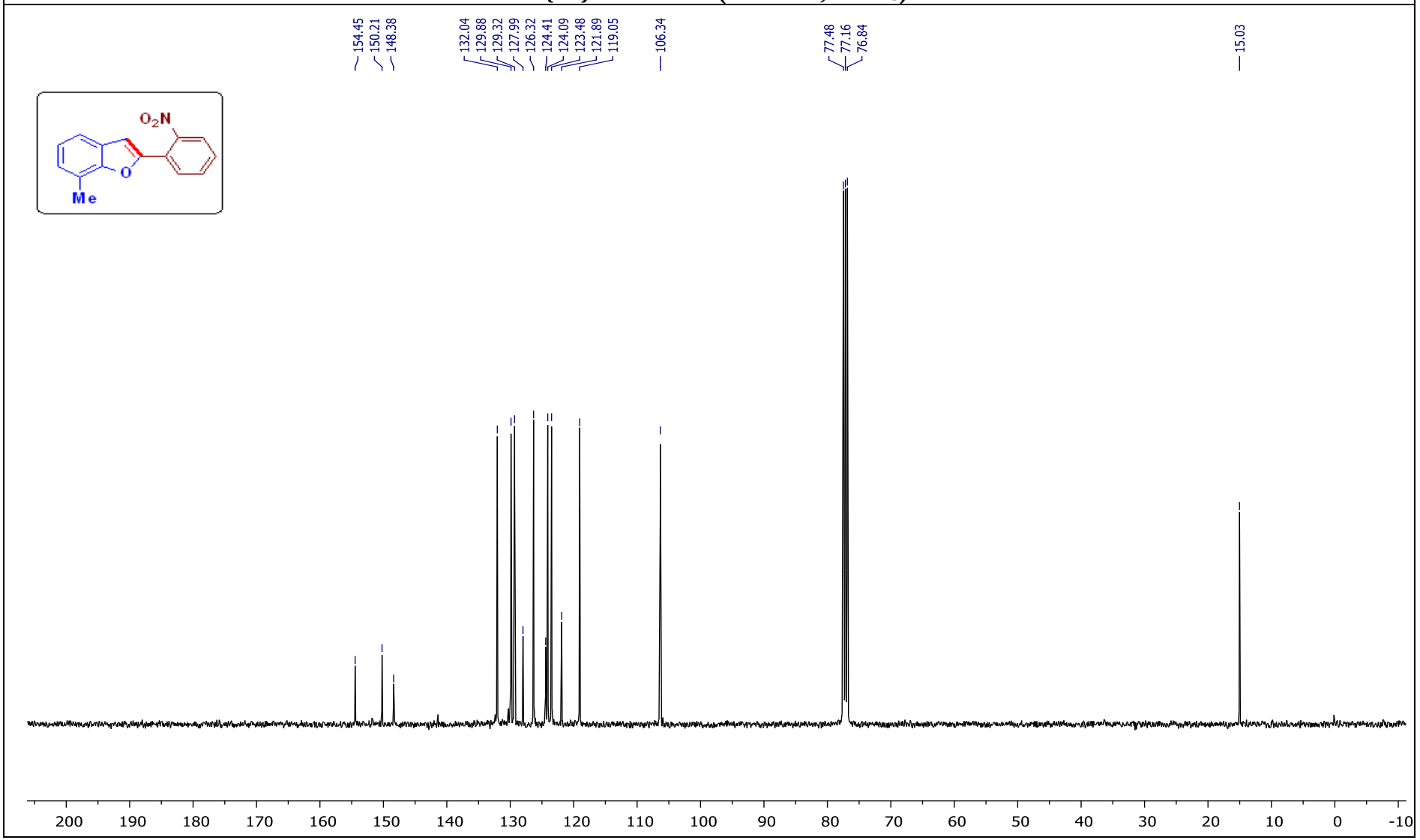
$^{13}C\{^{1}H\}$-NMR of 4c (101 MHz, $CDCl_3$)



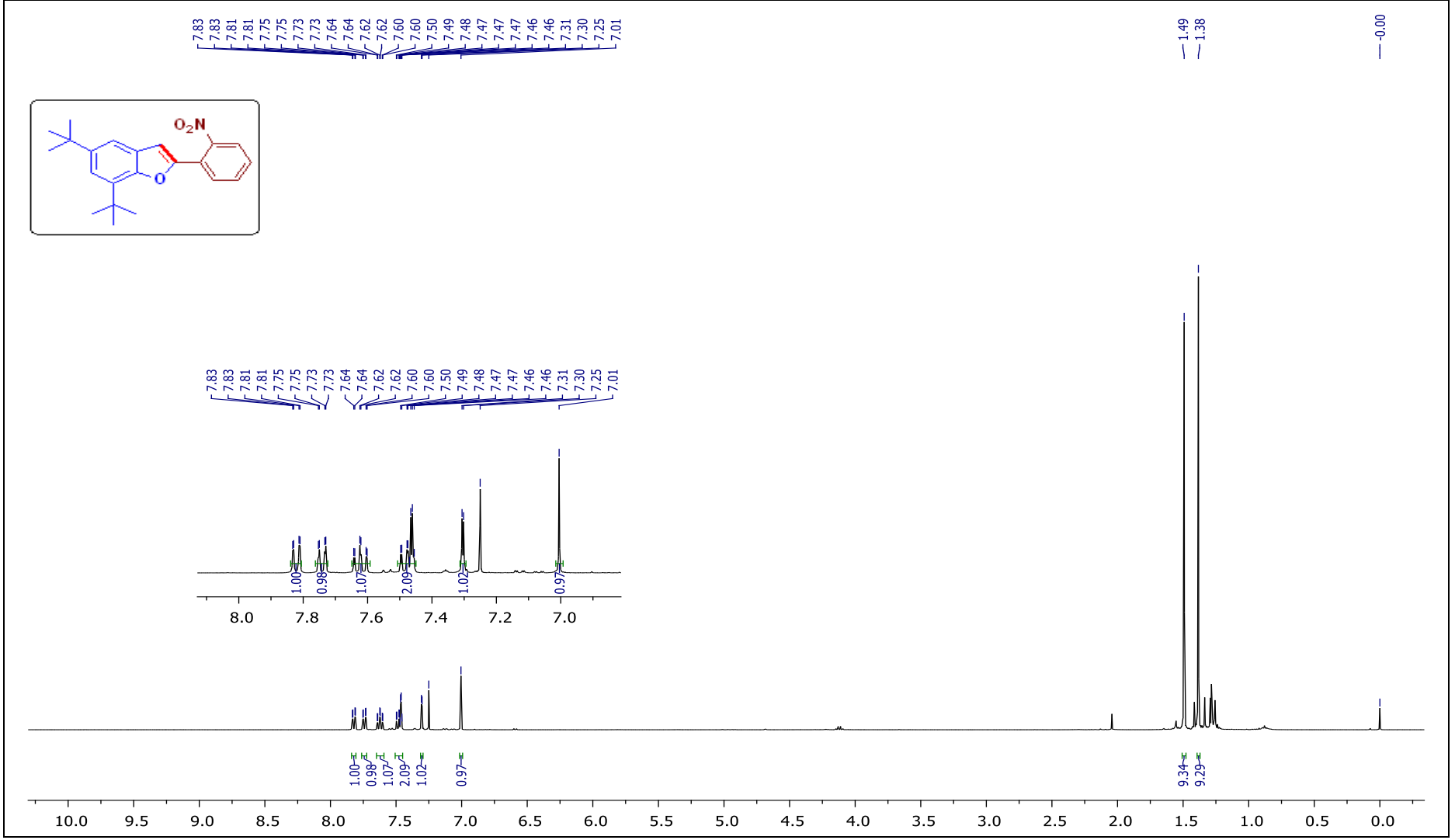
^{1}H-NMR of 4d (400 MHz, $CDCl_3$)



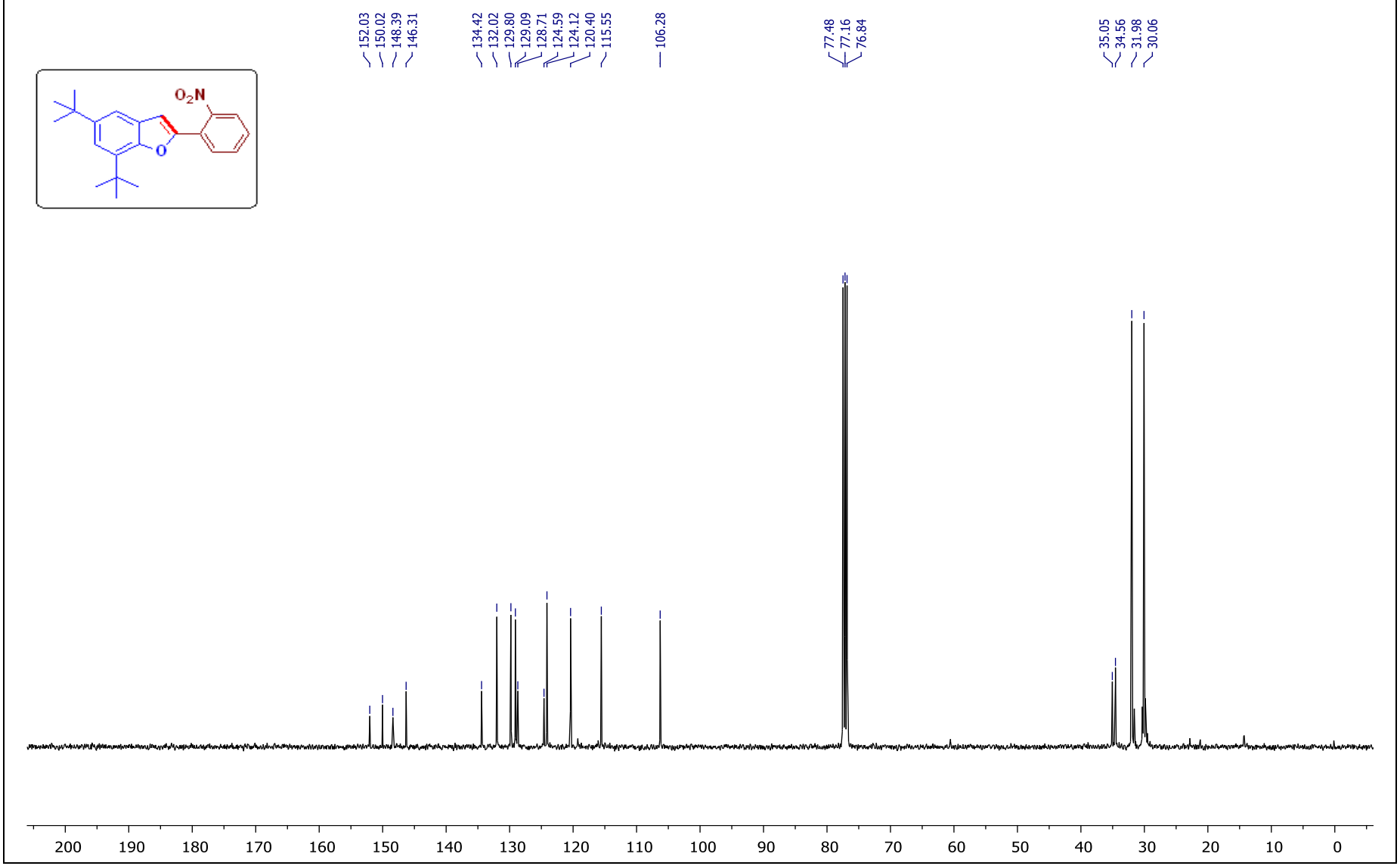
$^{13}C\{^{1}H\}$-NMR of 4d (101 MHz, $CDCl_3$)



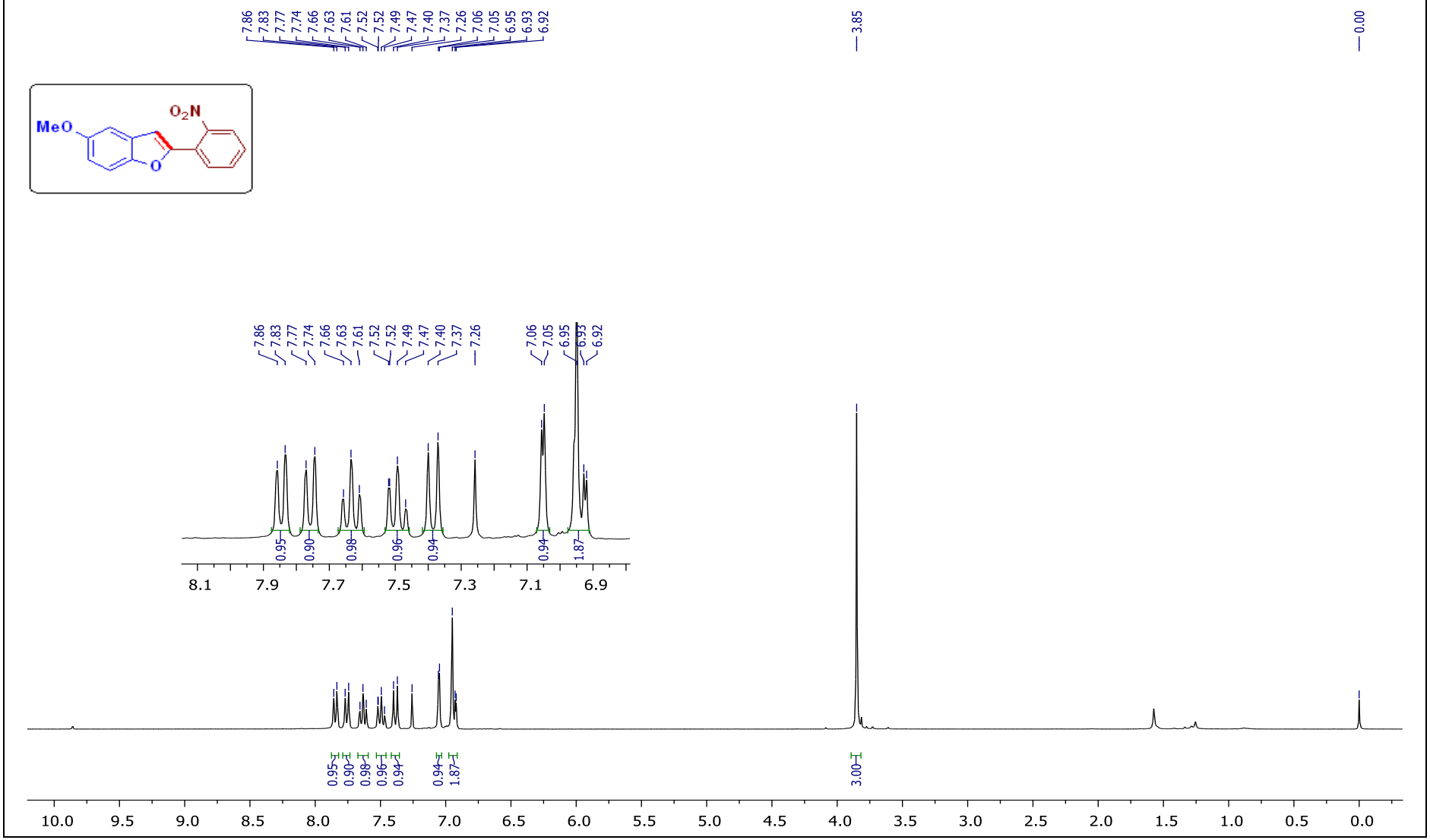
^{1}H-NMR of 4e (400 MHz, $CDCl_3$)



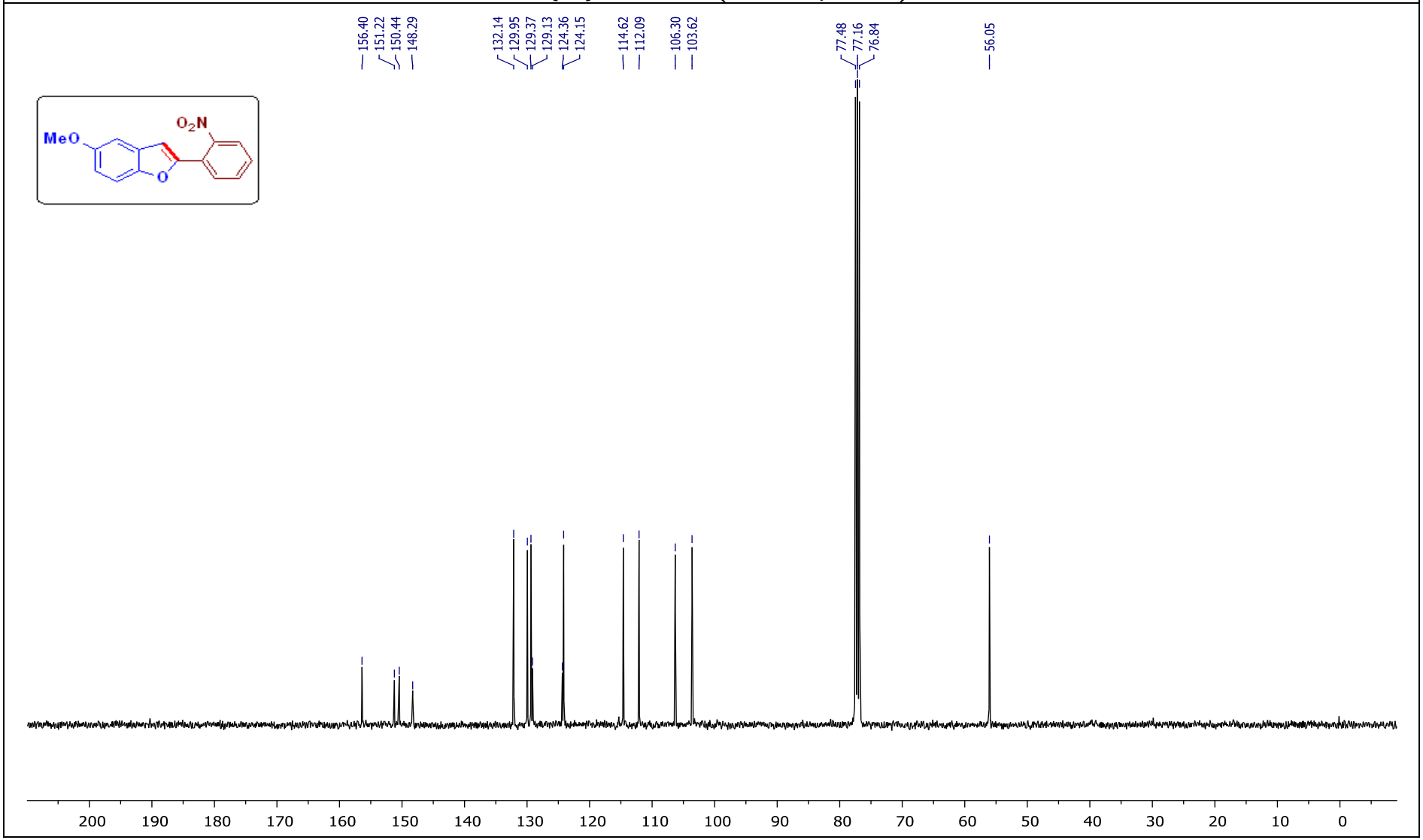
$^{13}C\{^{1}H\}$-NMR of 4e (101 MHz, $CDCl_3$)



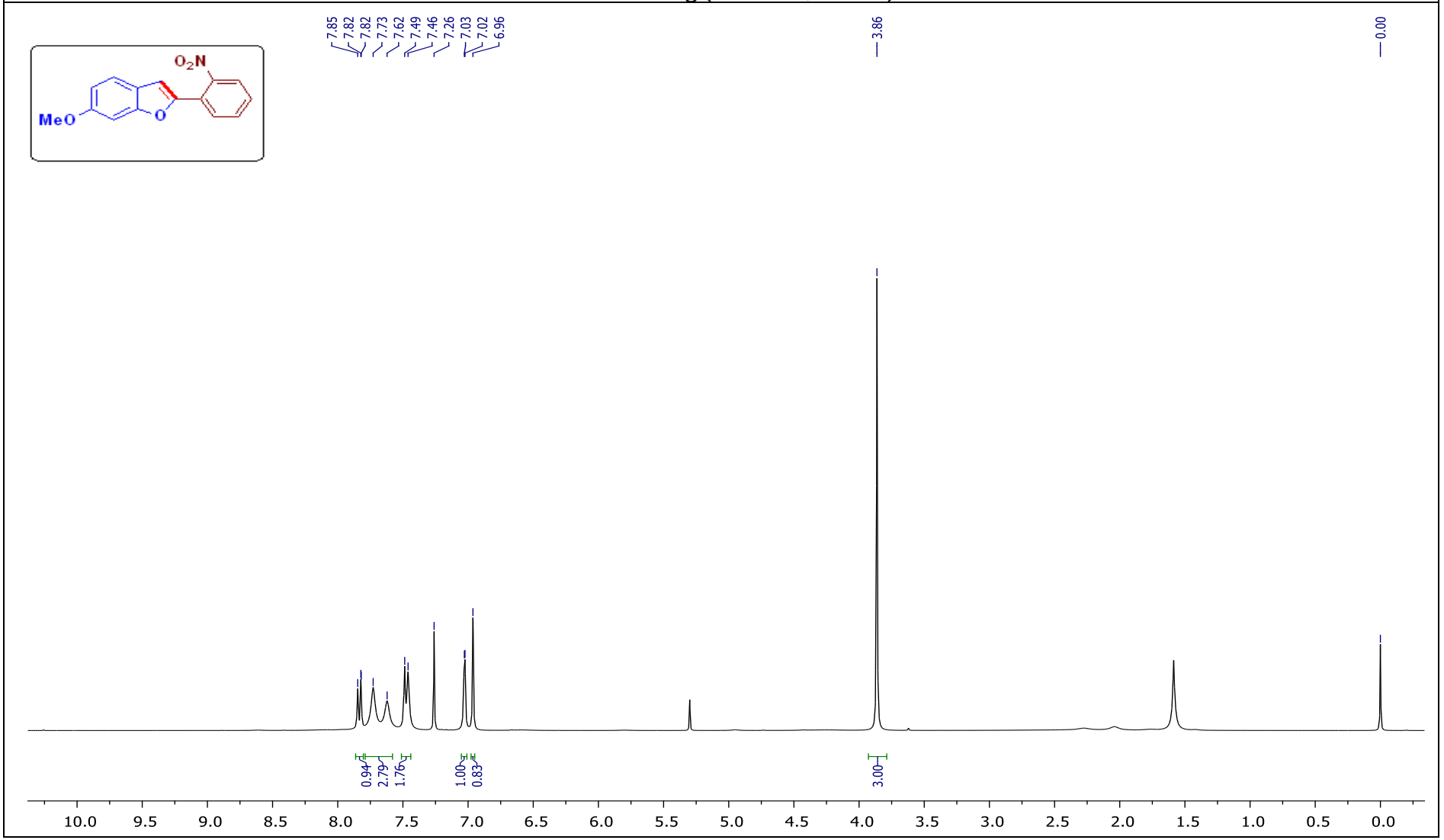
^{1}H-NMR of 4f (300 MHz, $CDCl_3$)



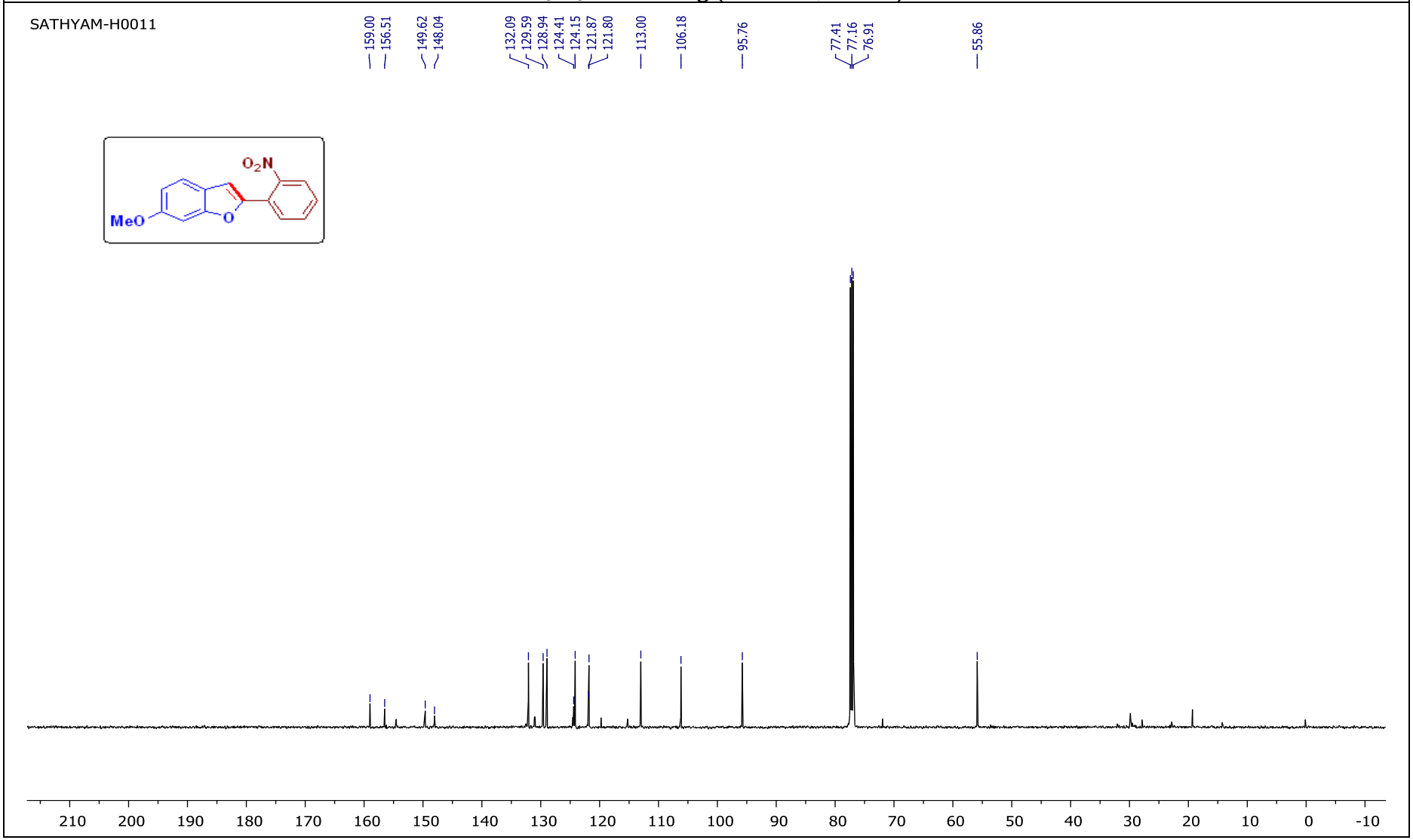
$^{13}C\{^{1}H\}$-NMR of 4f (101 MHz, $CDCl_3$)



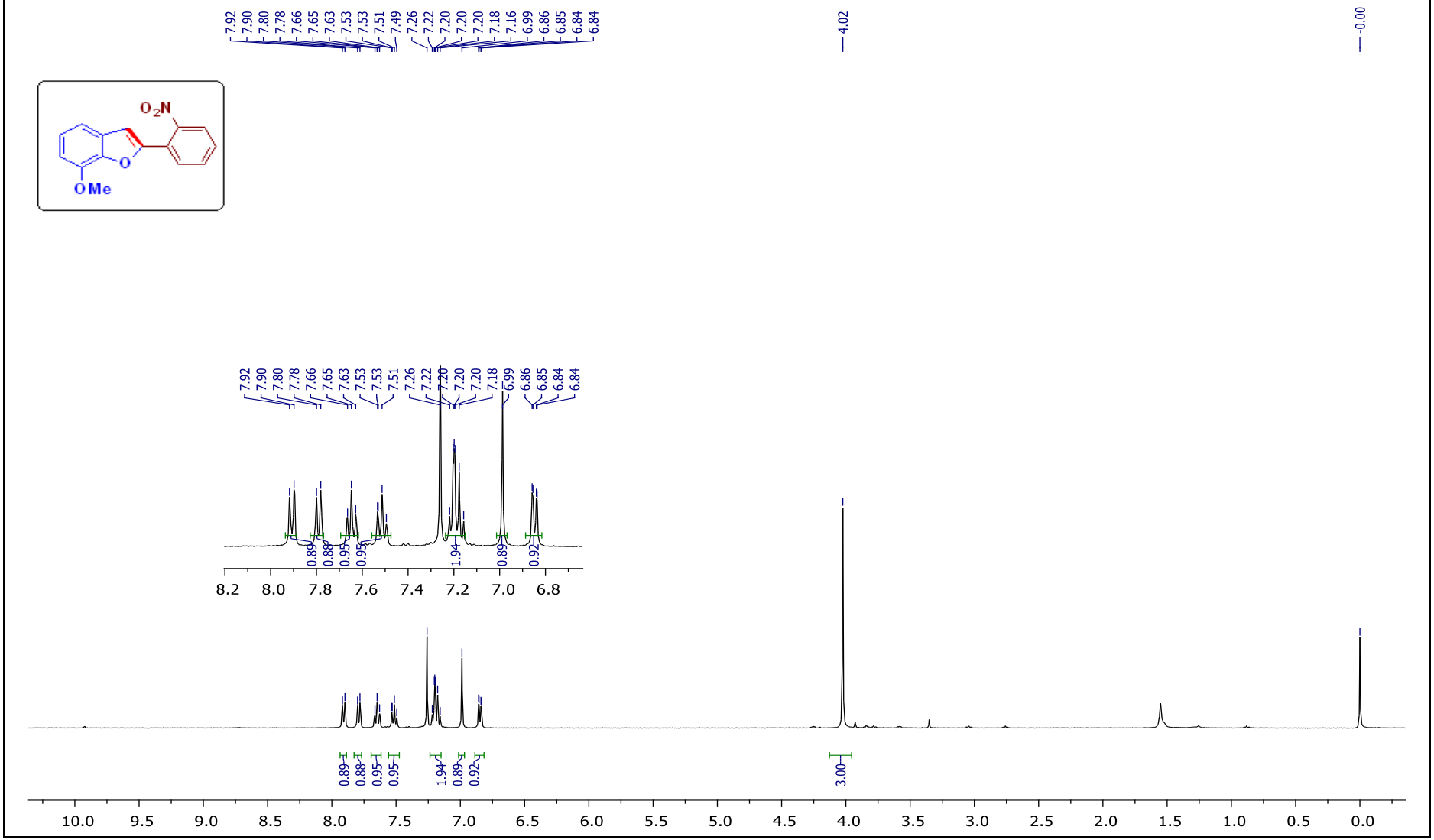
^{1}H-NMR of 4g (300 MHz, $CDCl_3$)



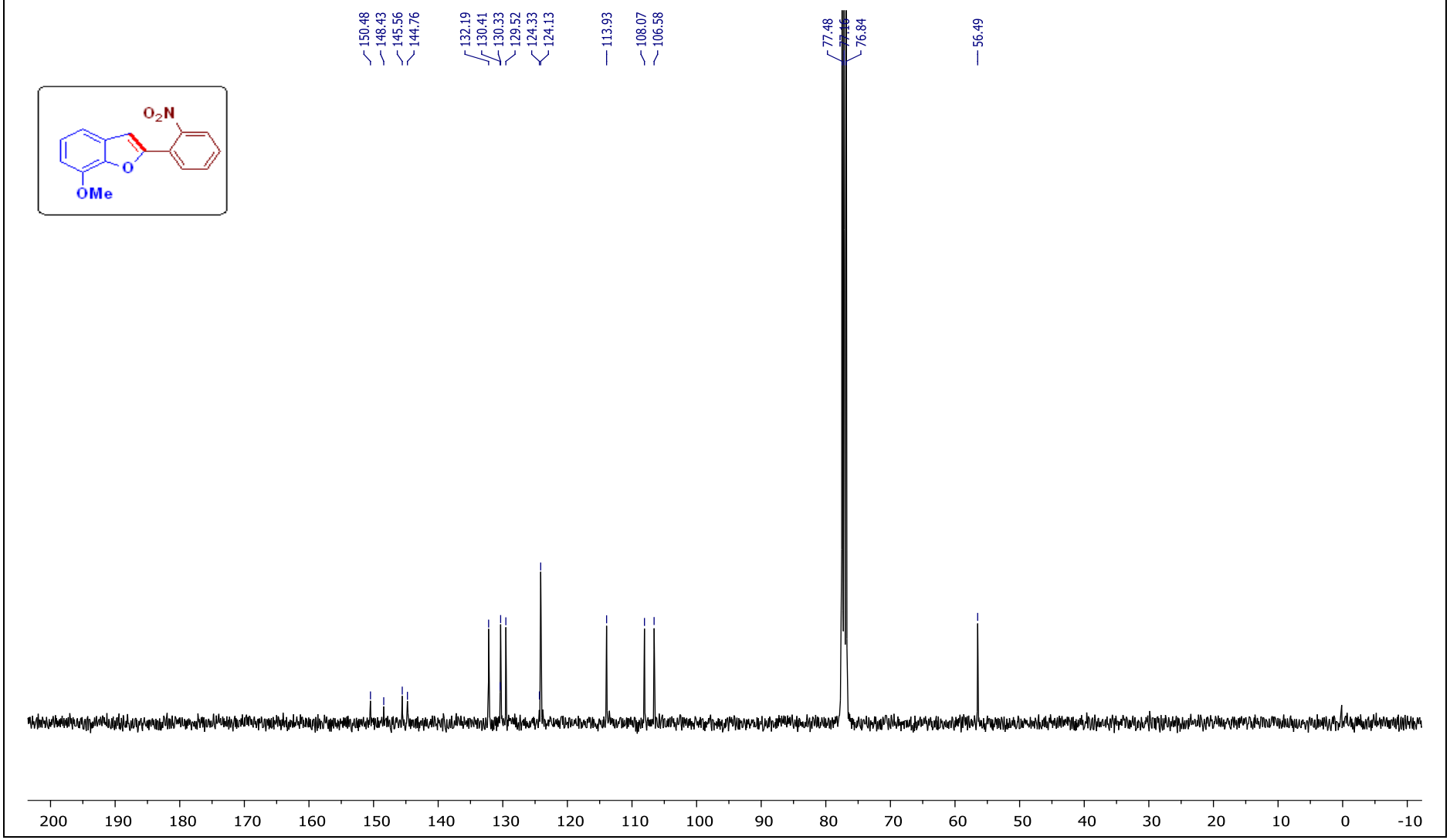
$^{13}C\{^{1}H\}$-NMR of 4g (101 MHz, $CDCl_3$)



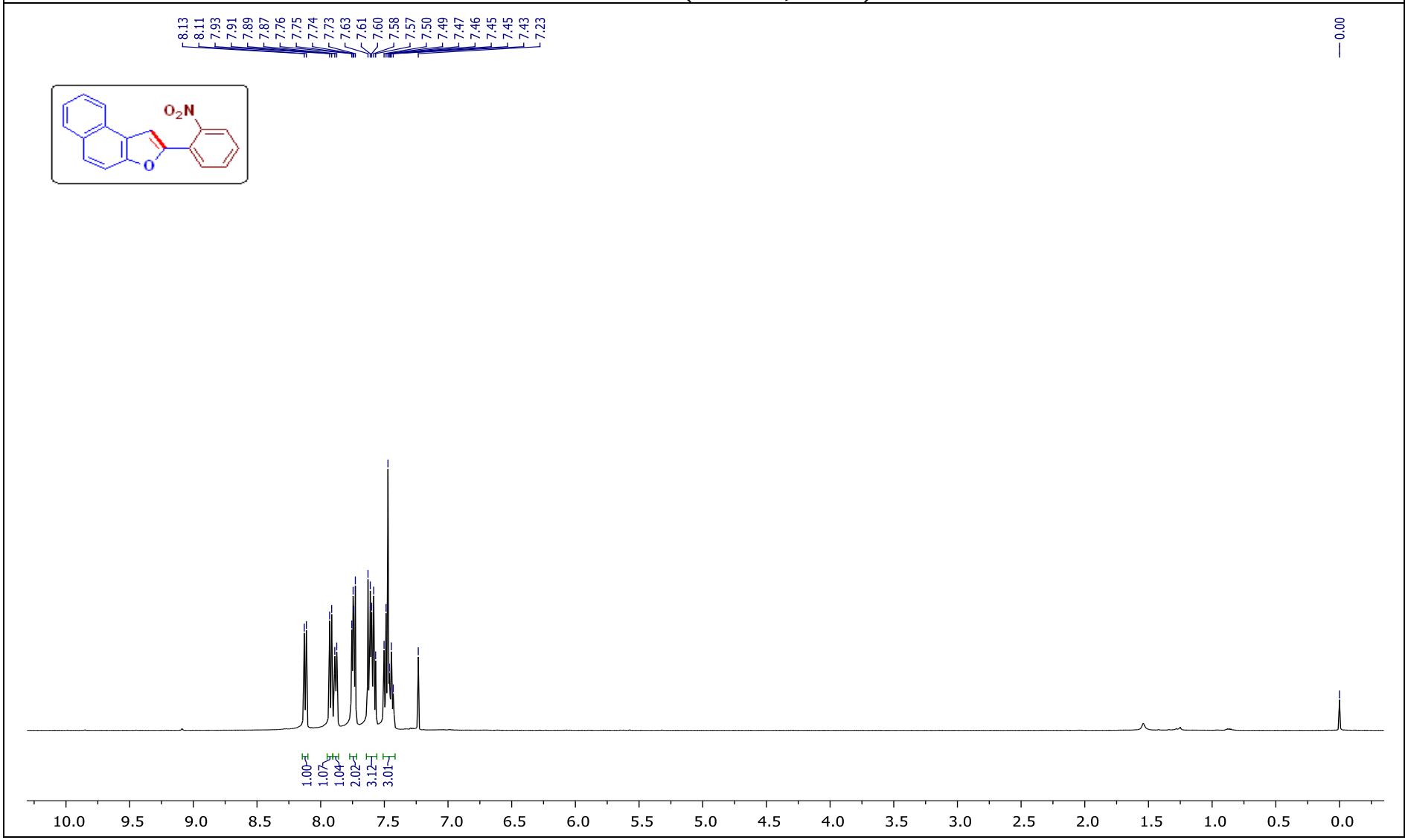
^{1}H-NMR of 4h (400 MHz, $CDCl_3$)



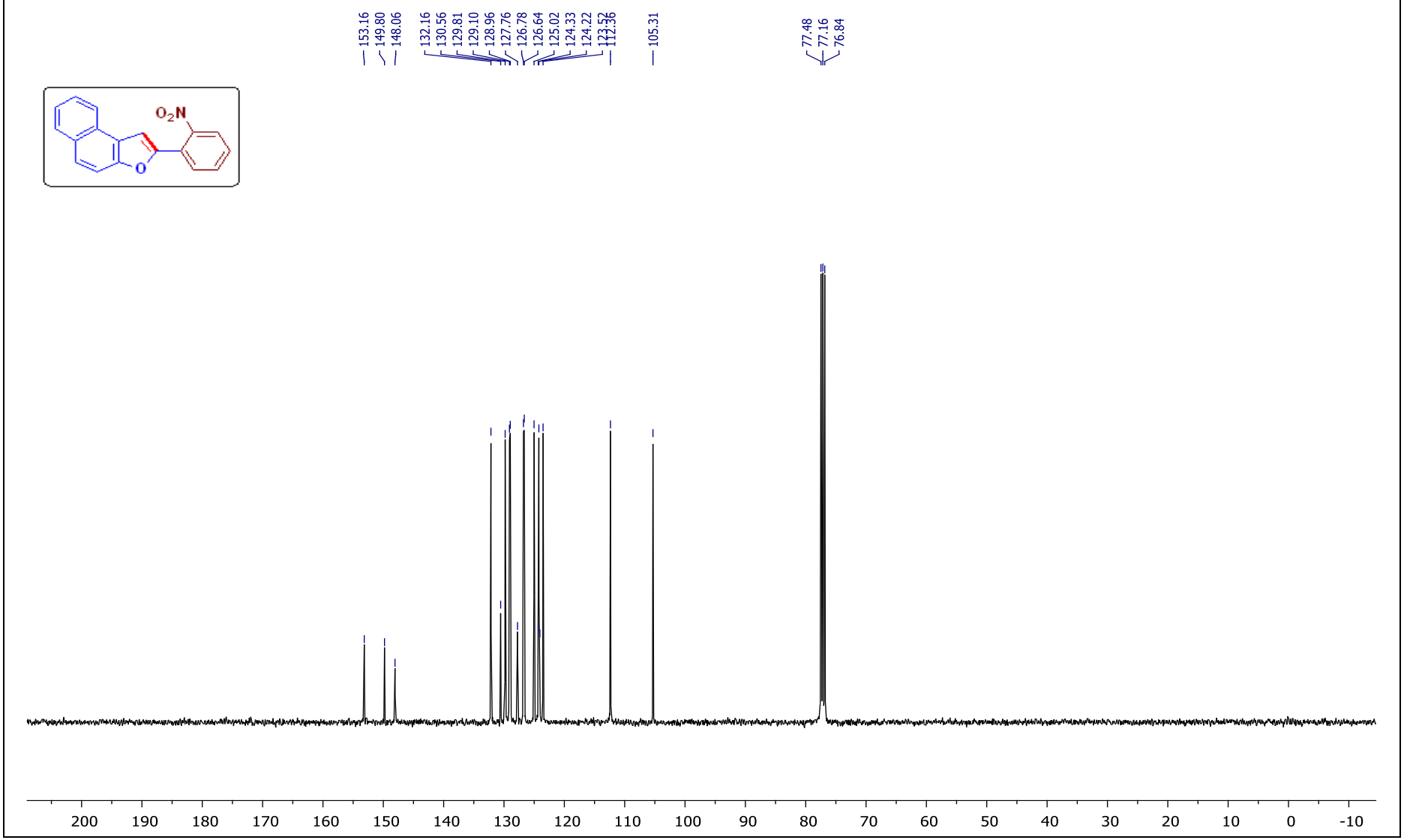
$^{13}C\{^{1}H\}$-NMR of 4h (101 MHz, $CDCl_3$)



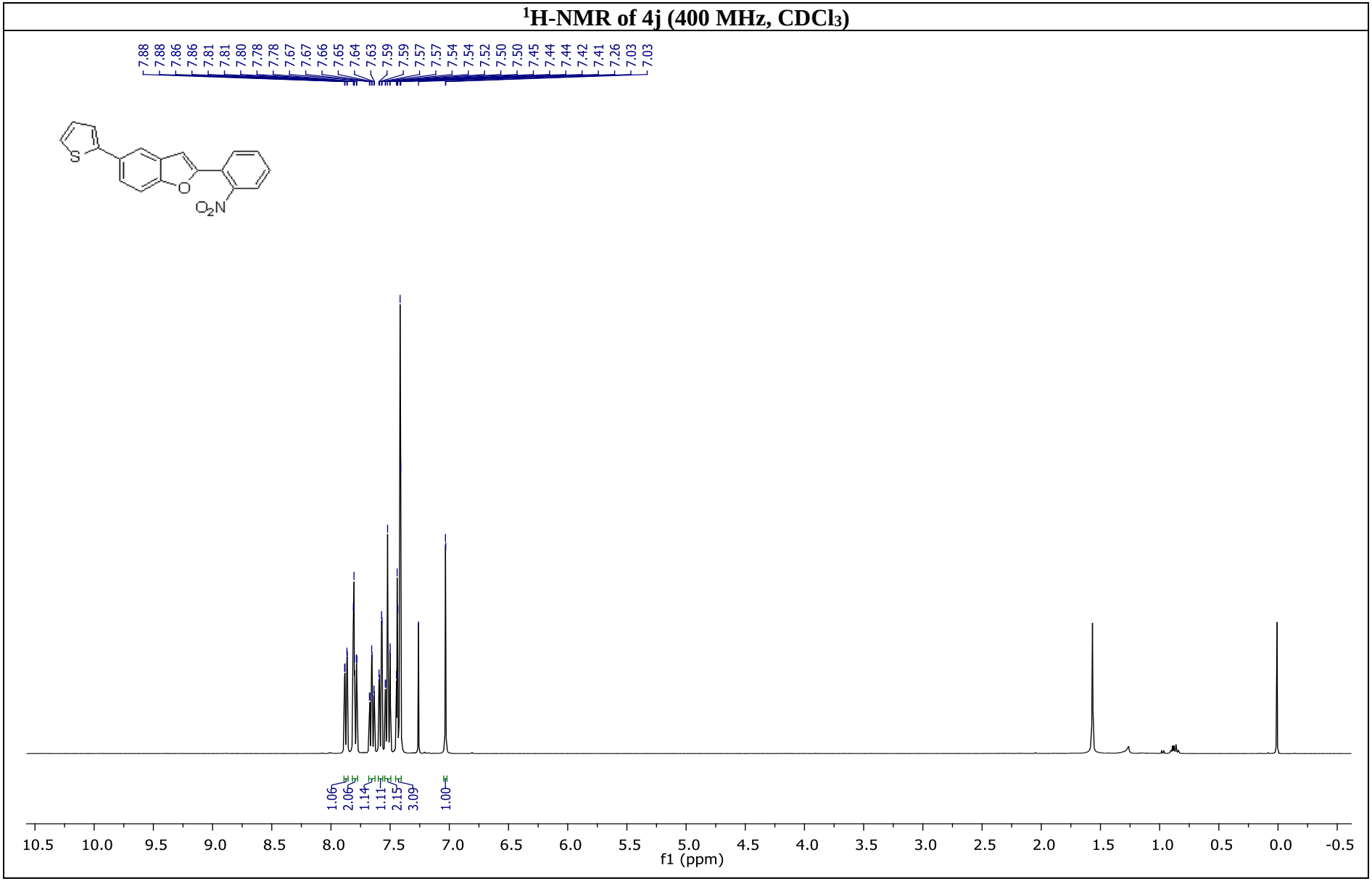
^{1}H-NMR of 4i (500 MHz, $CDCl_3$)



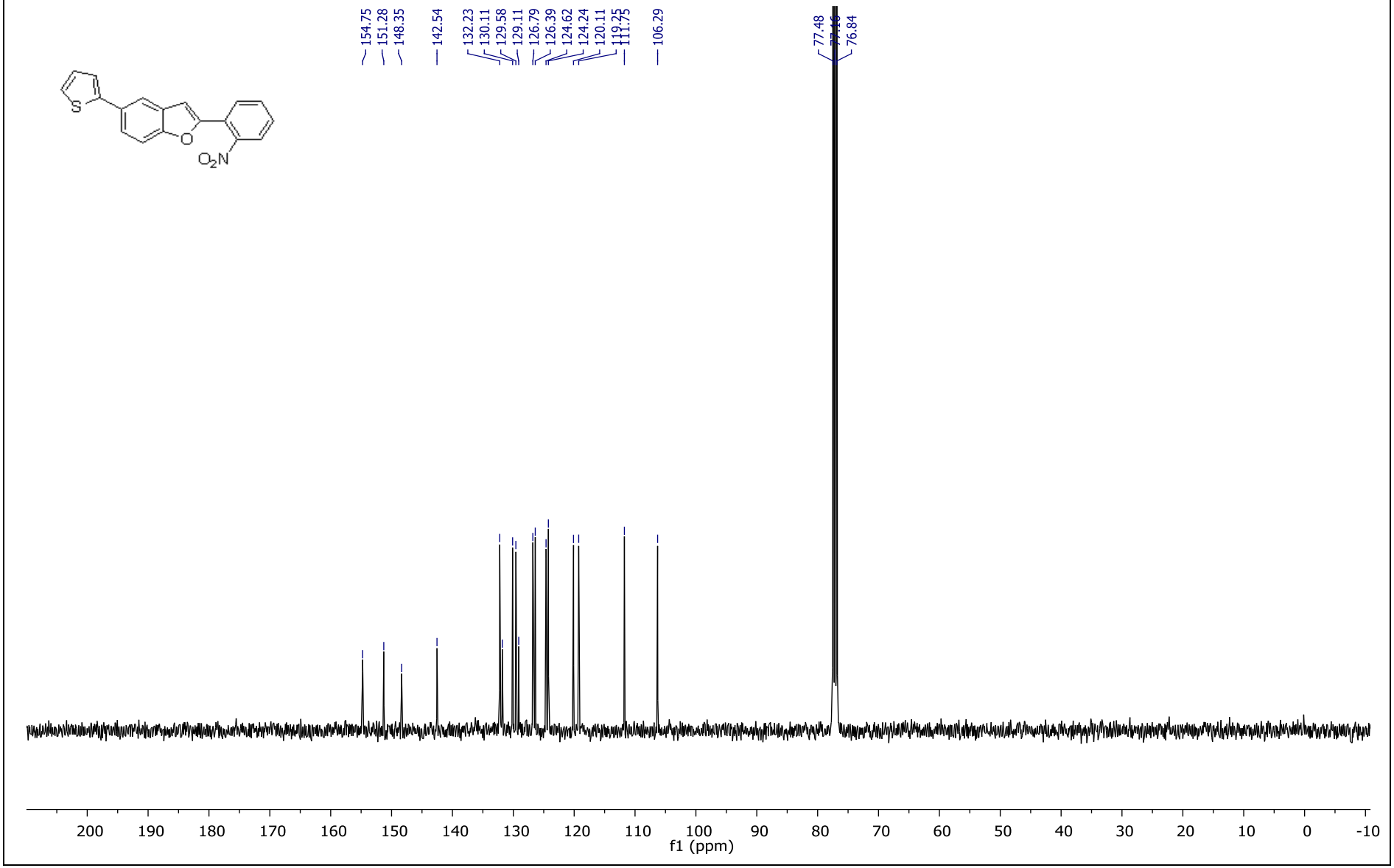
$^{13}C\{^{1}H\}$-NMR of 4i (101 MHz, $CDCl_3$)



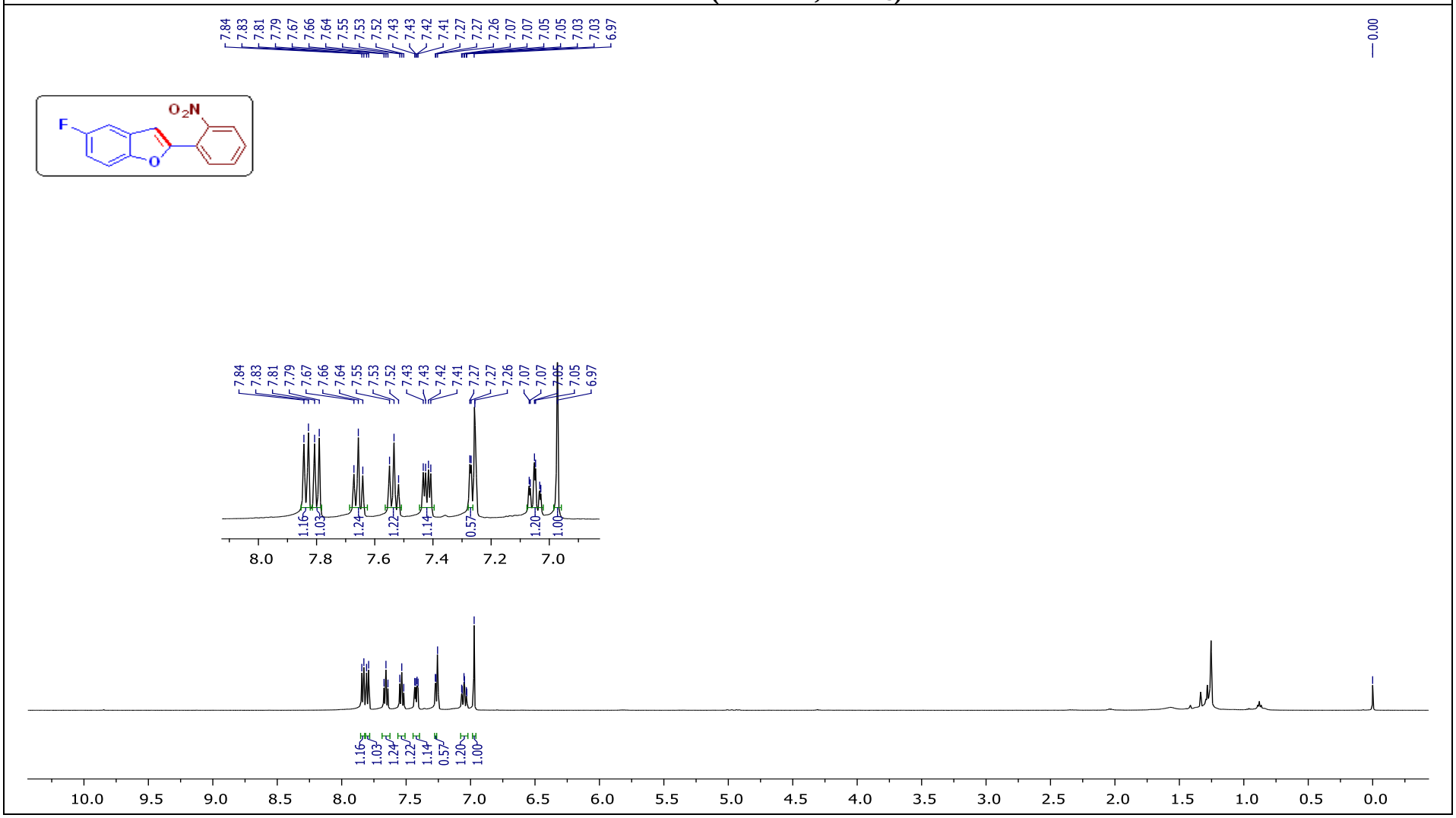
^{1}H-NMR of 4j (400 MHz, $CDCl_3$)



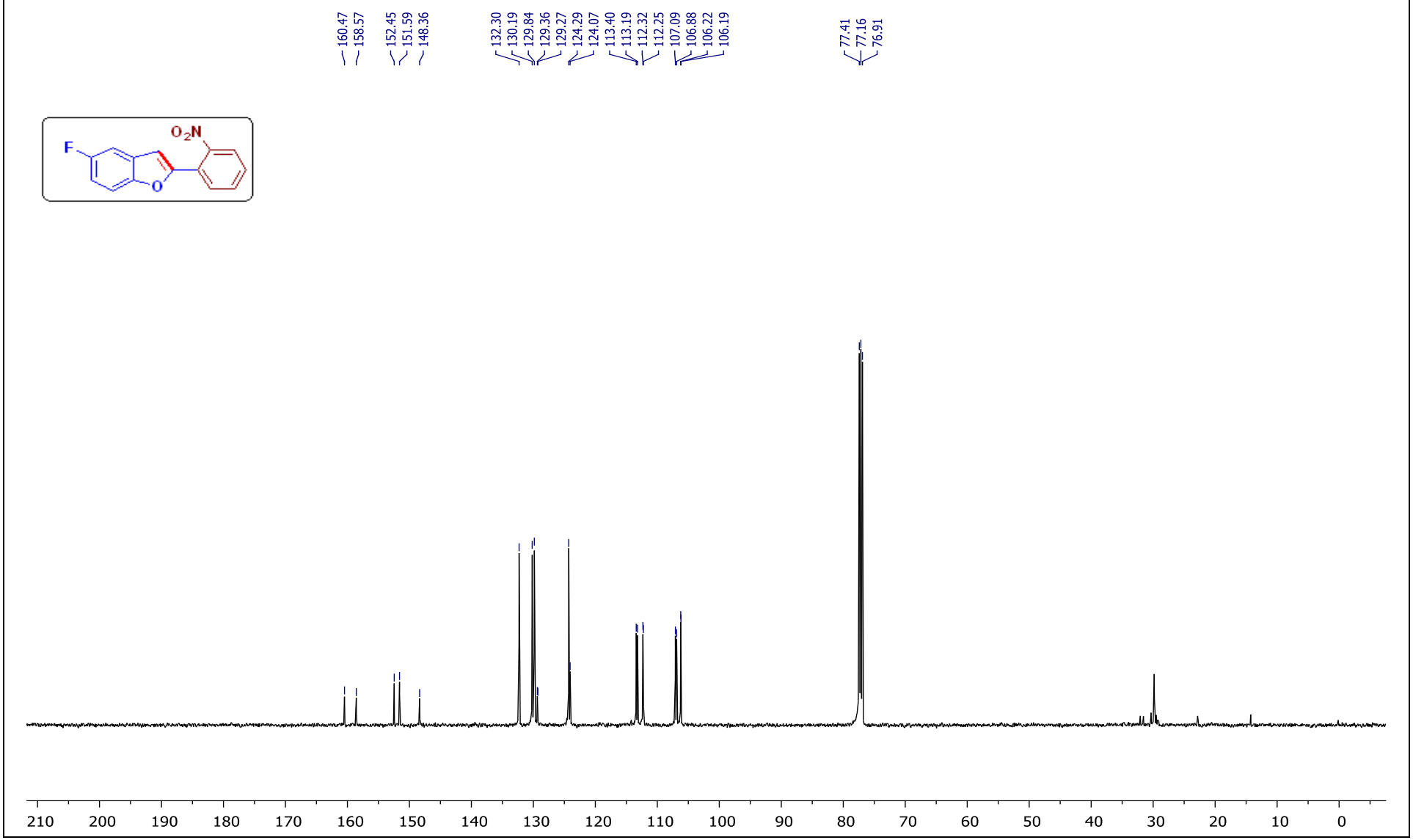
$^{13}C\{^{1}H\}$-NMR of 4j (101 MHz, $CDCl_3$)



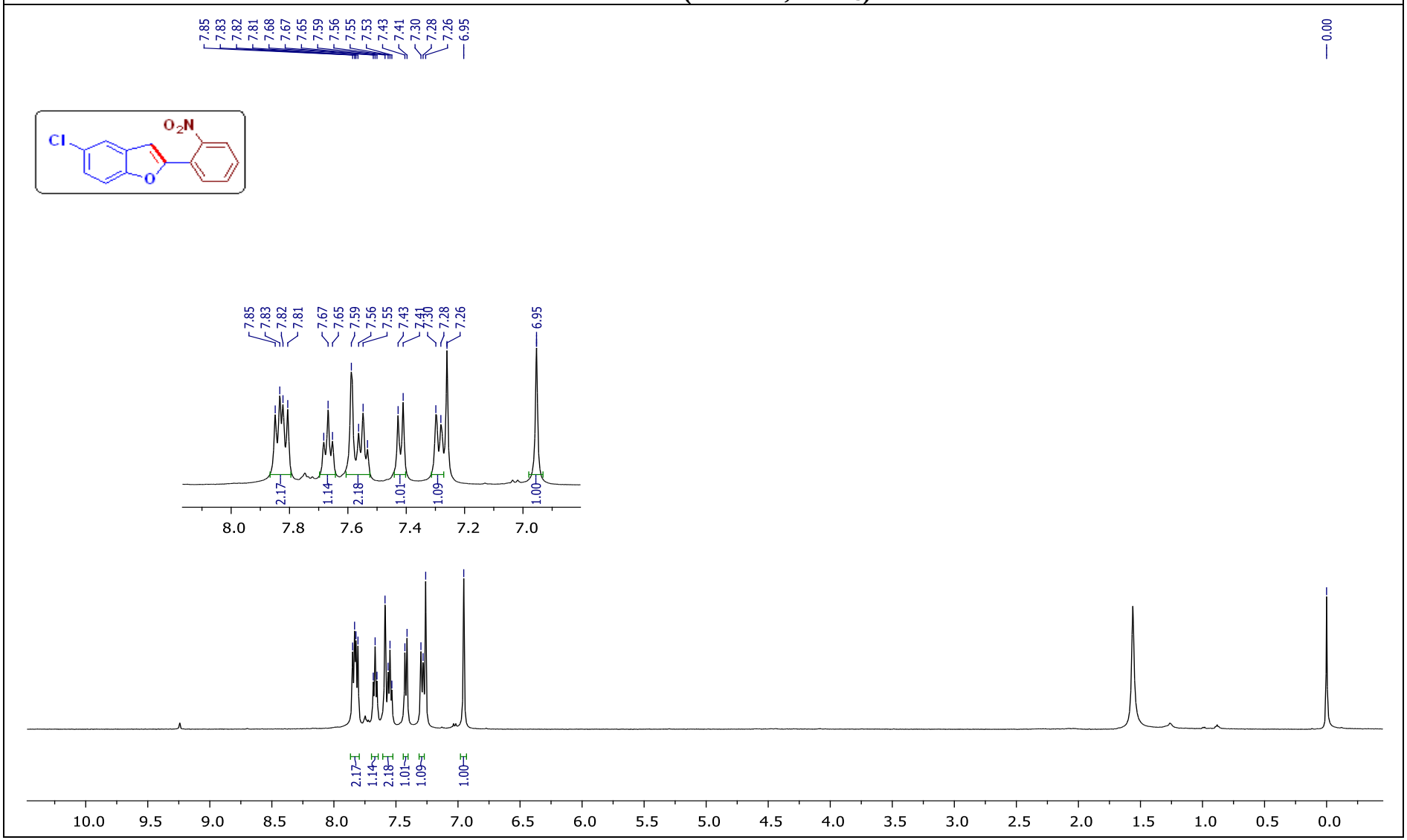
^{1}H-NMR of 4k (500 MHz, $CDCl_3$)



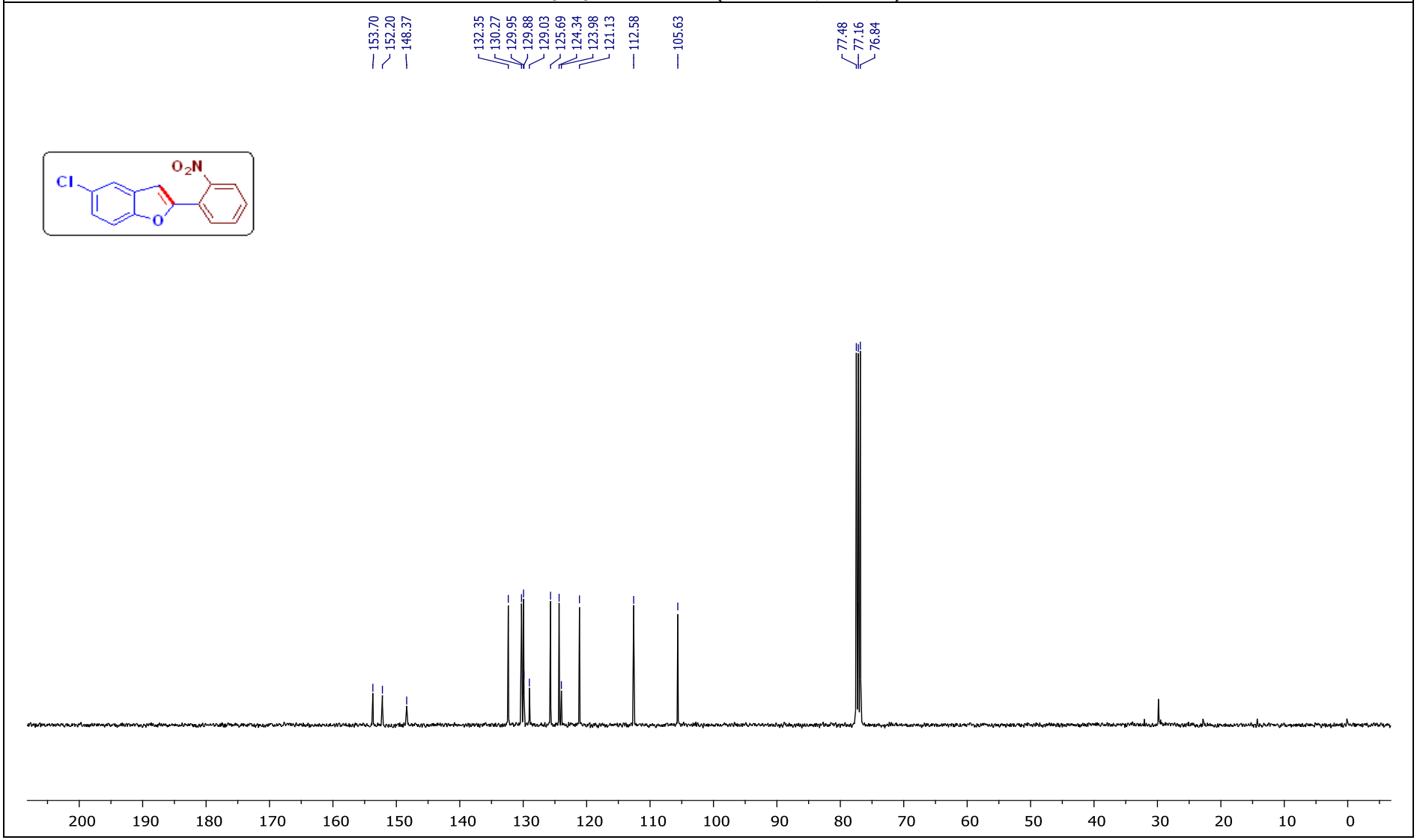
$^{13}C\{^{1}H\}$-NMR of 4k (126 MHz, $CDCl_3$)



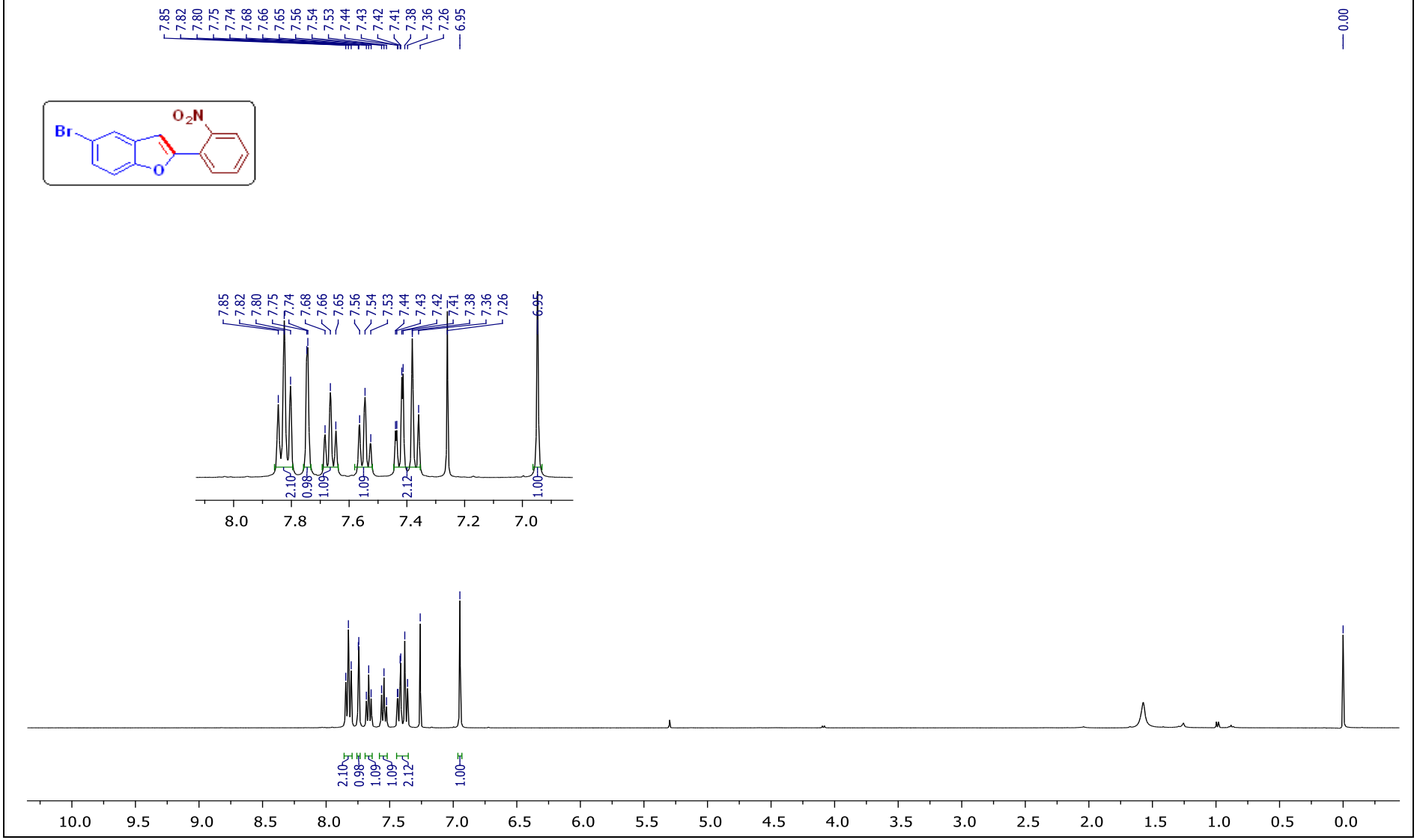
^{1}H-NMR of 4l (500 MHz, $CDCl_3$)



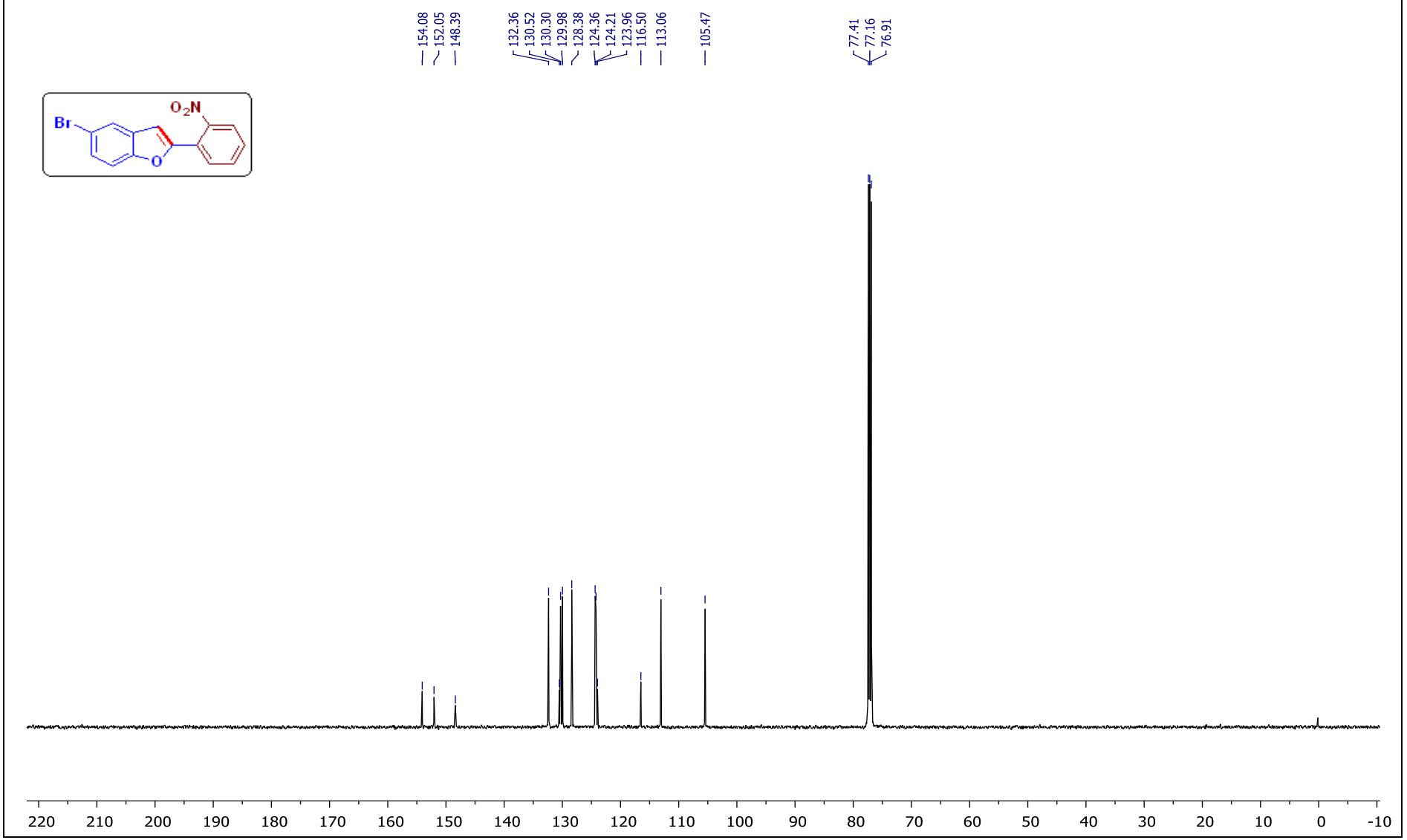
$^{13}C\{^{1}H\}$-NMR of 4l (101 MHz, $CDCl_3$)



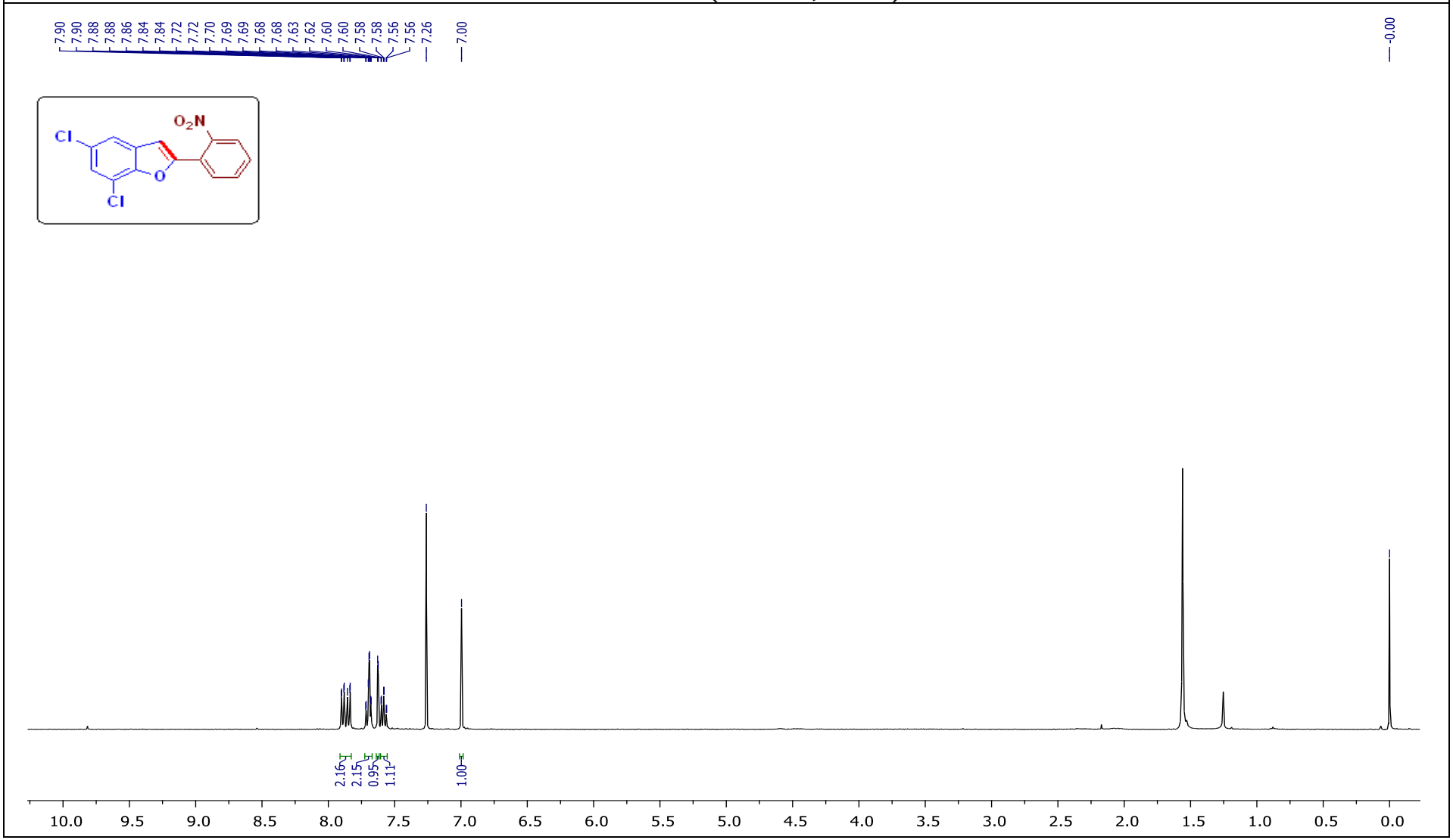
^{1}H-NMR of 4m (400 MHz, $CDCl_3$)



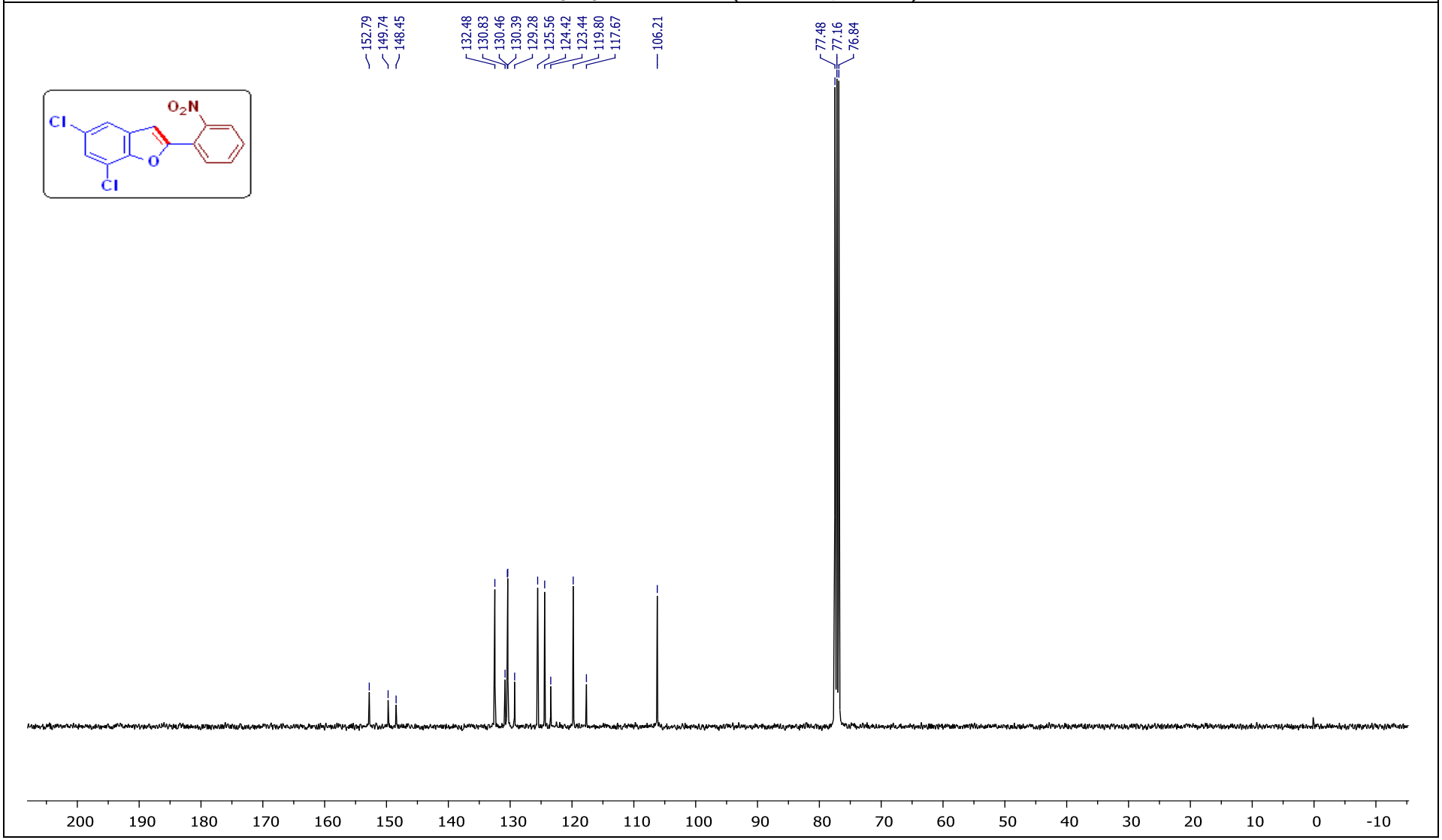
$^{13}C\{^{1}H\}$-NMR of 4m (126 MHz, $CDCl_3$)



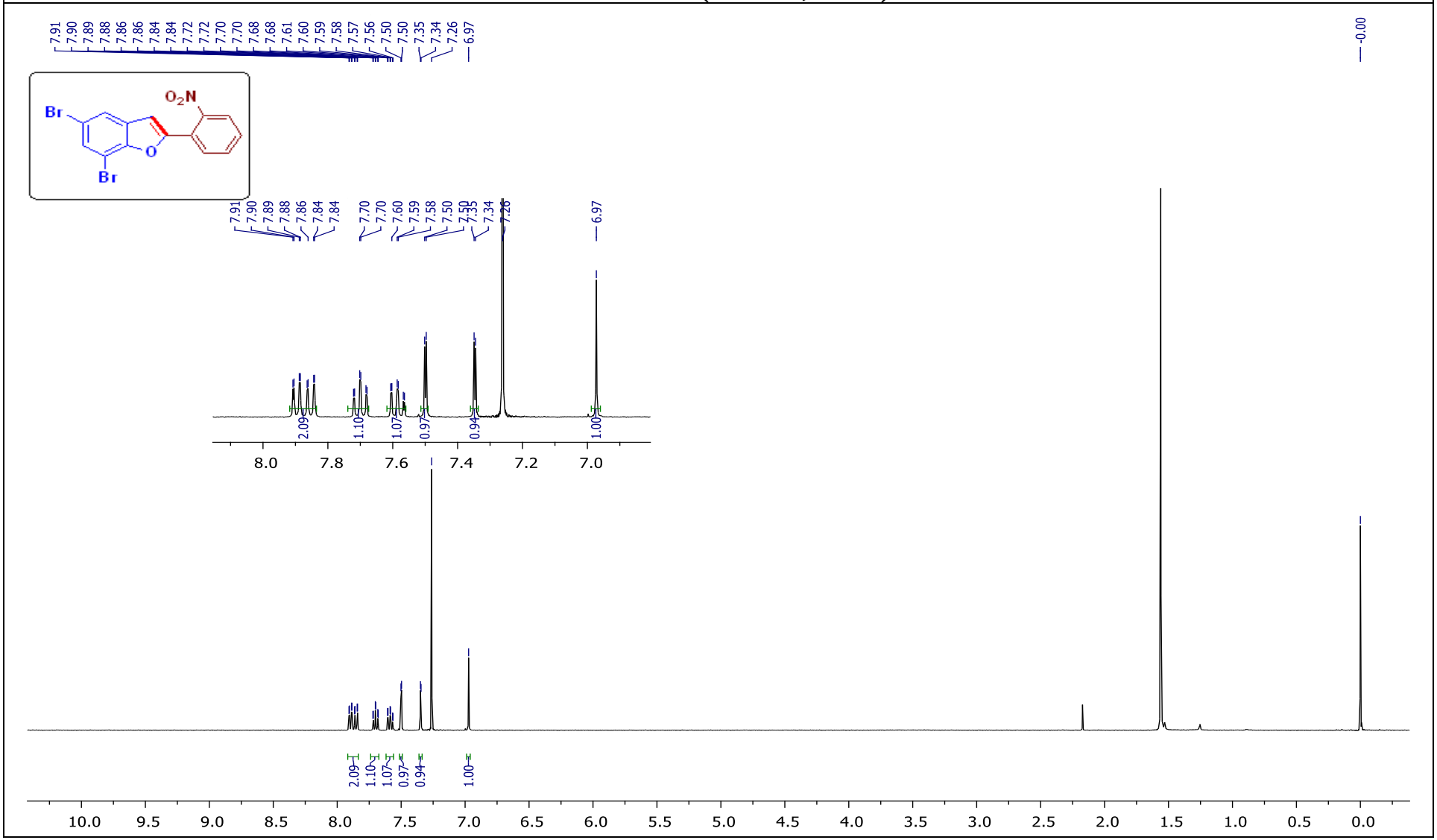
^{1}H-NMR of 4n (400 MHz, $CDCl_3$)



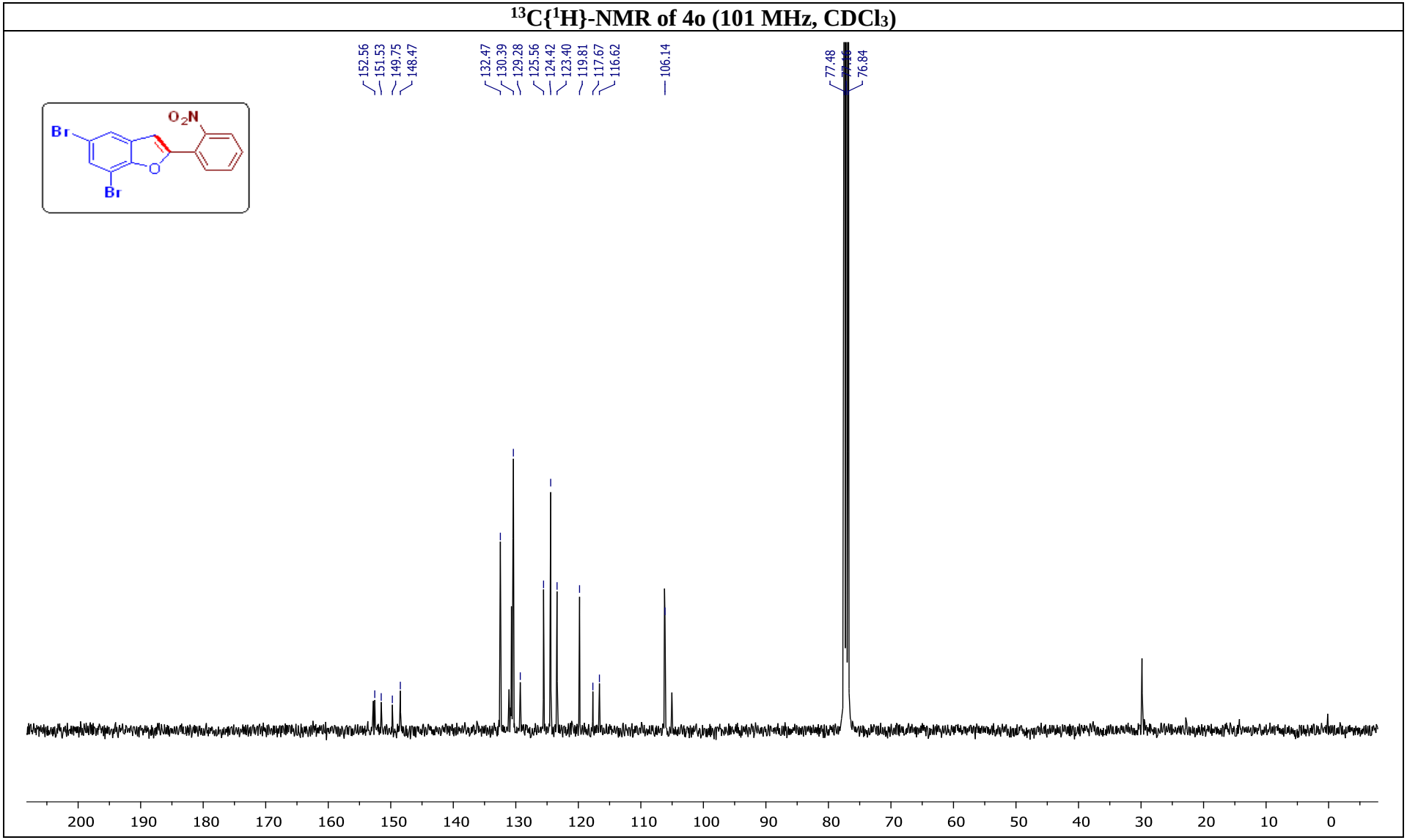
$^{13}C\{^{1}H\}$-NMR of 4n (126 MHz, $CDCl_3$)



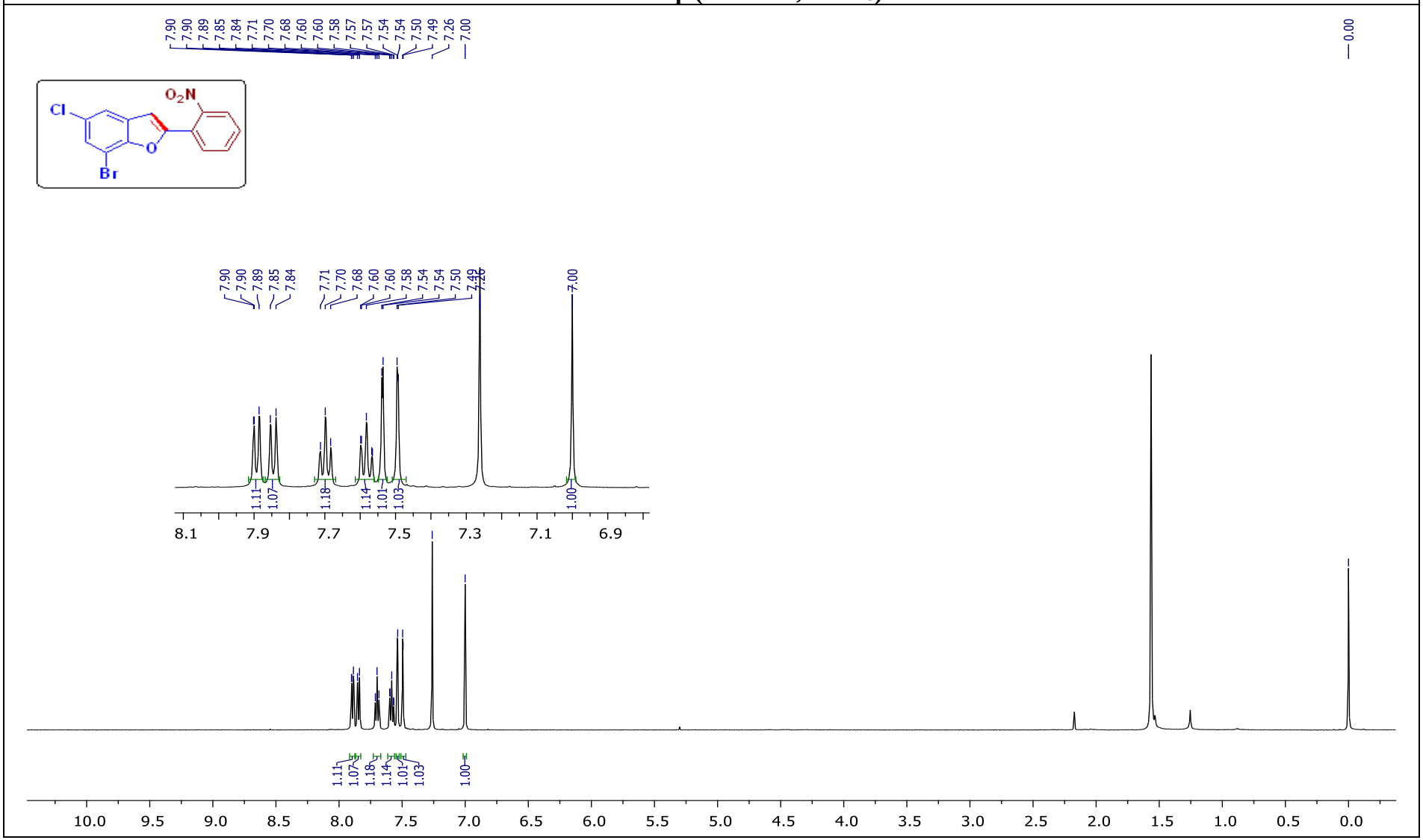
^{1}H-NMR of 4o (400 MHz, $CDCl_3$)



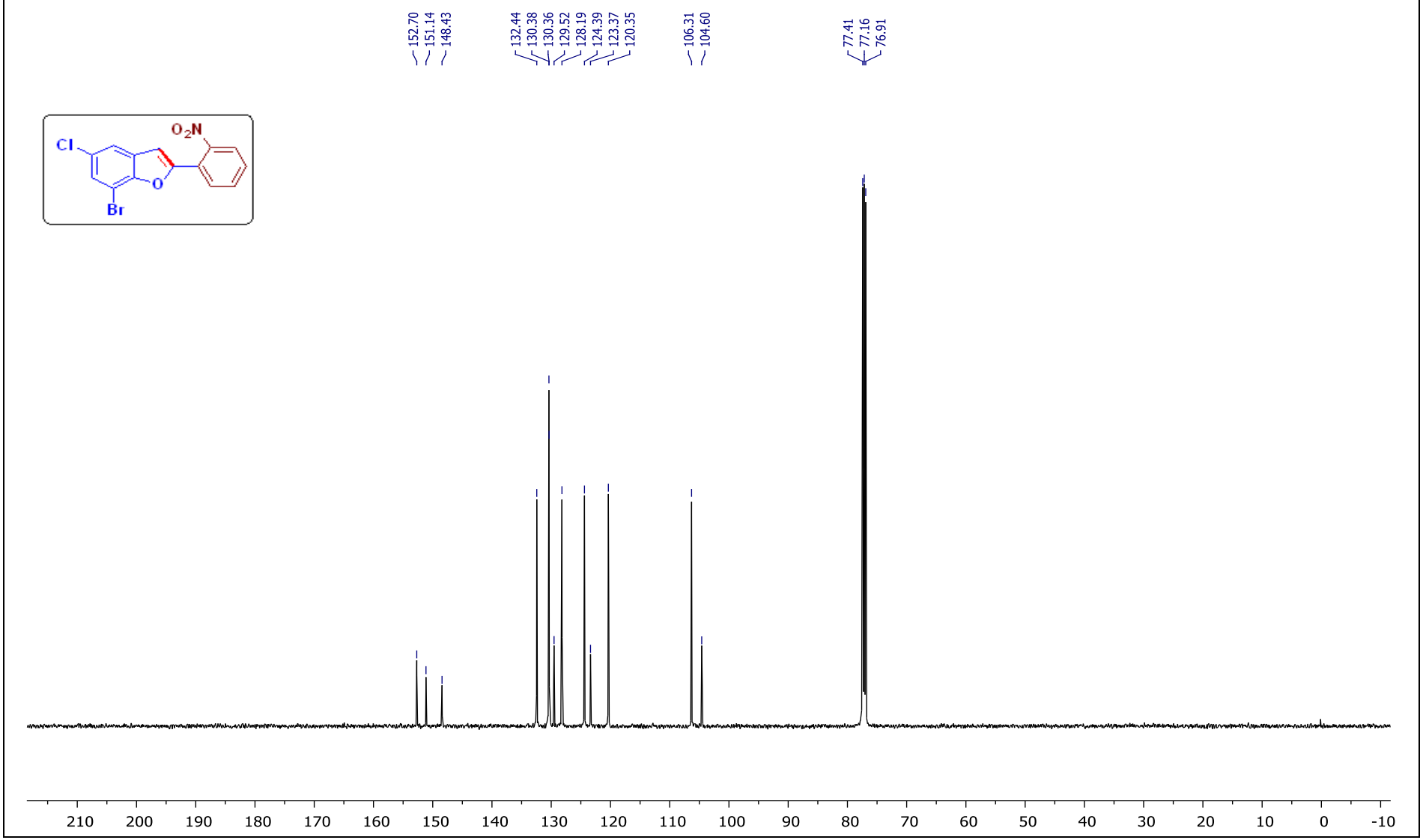
$^{13}C\{^{1}H\}$-NMR of 4o (101 MHz, $CDCl_3$)



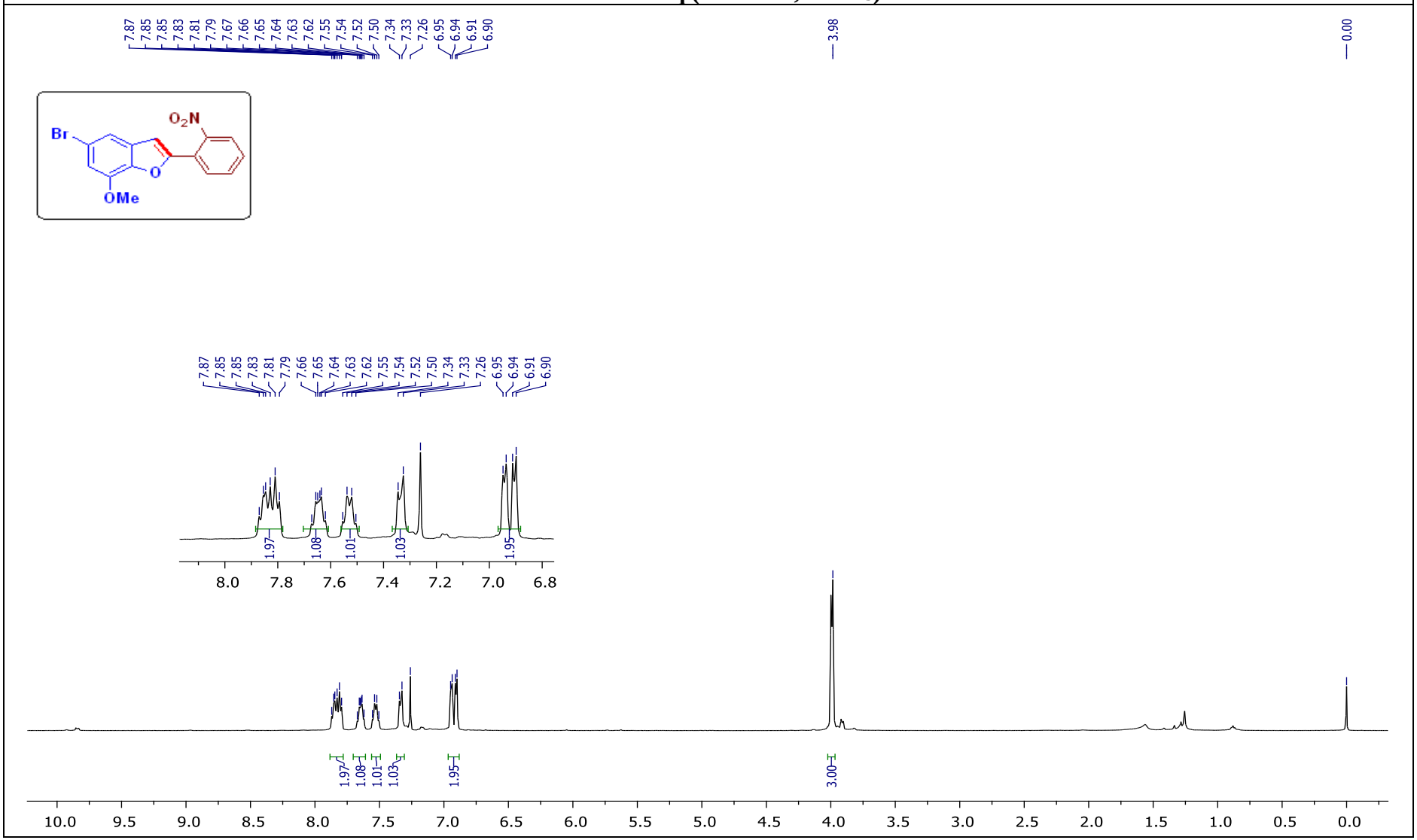
^{1}H-NMR of 4p (400 MHz, $CDCl_3$)



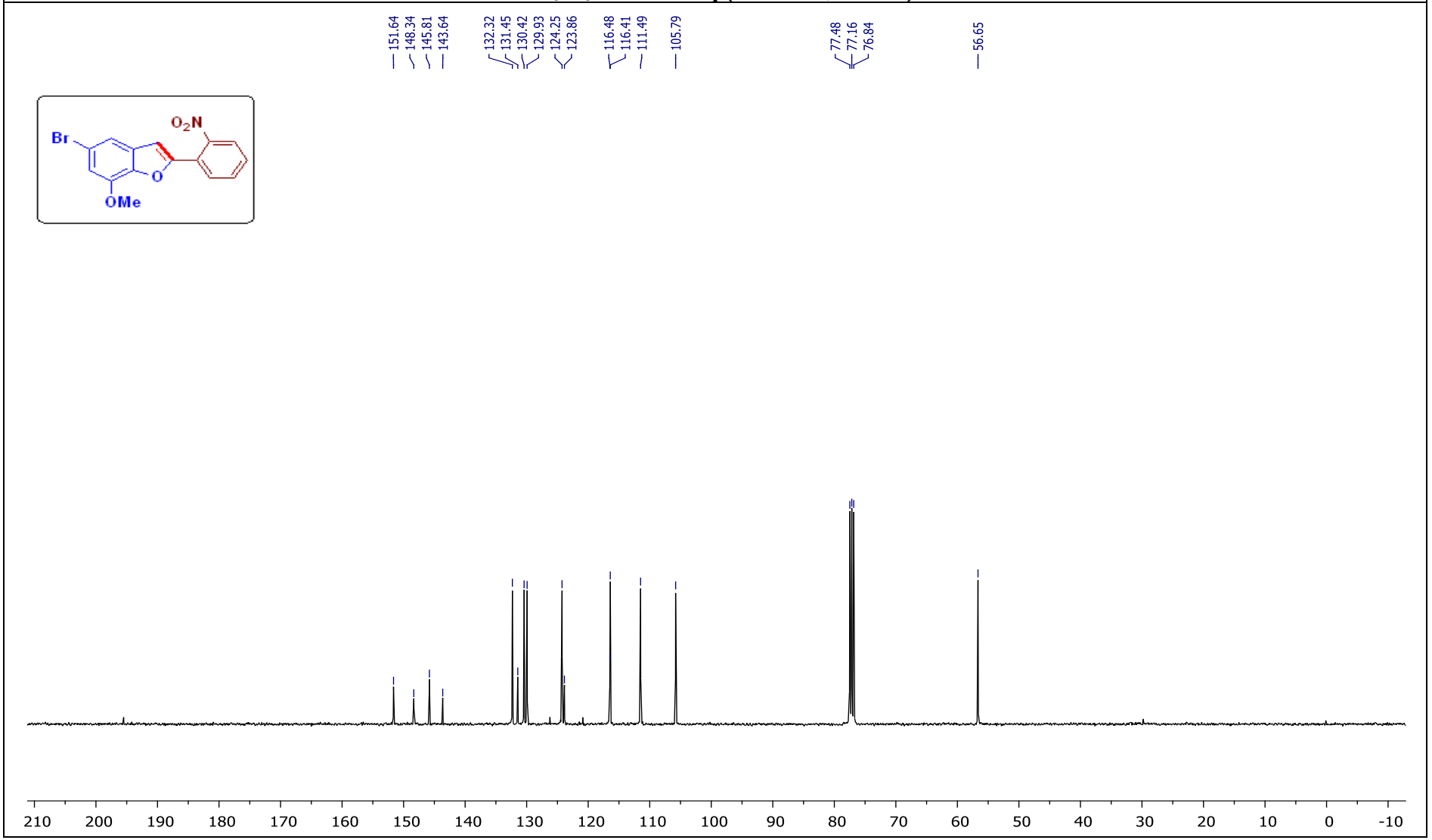
$^{13}C\{^{1}H\}$-NMR of 4p (101 MHz, $CDCl_3$)



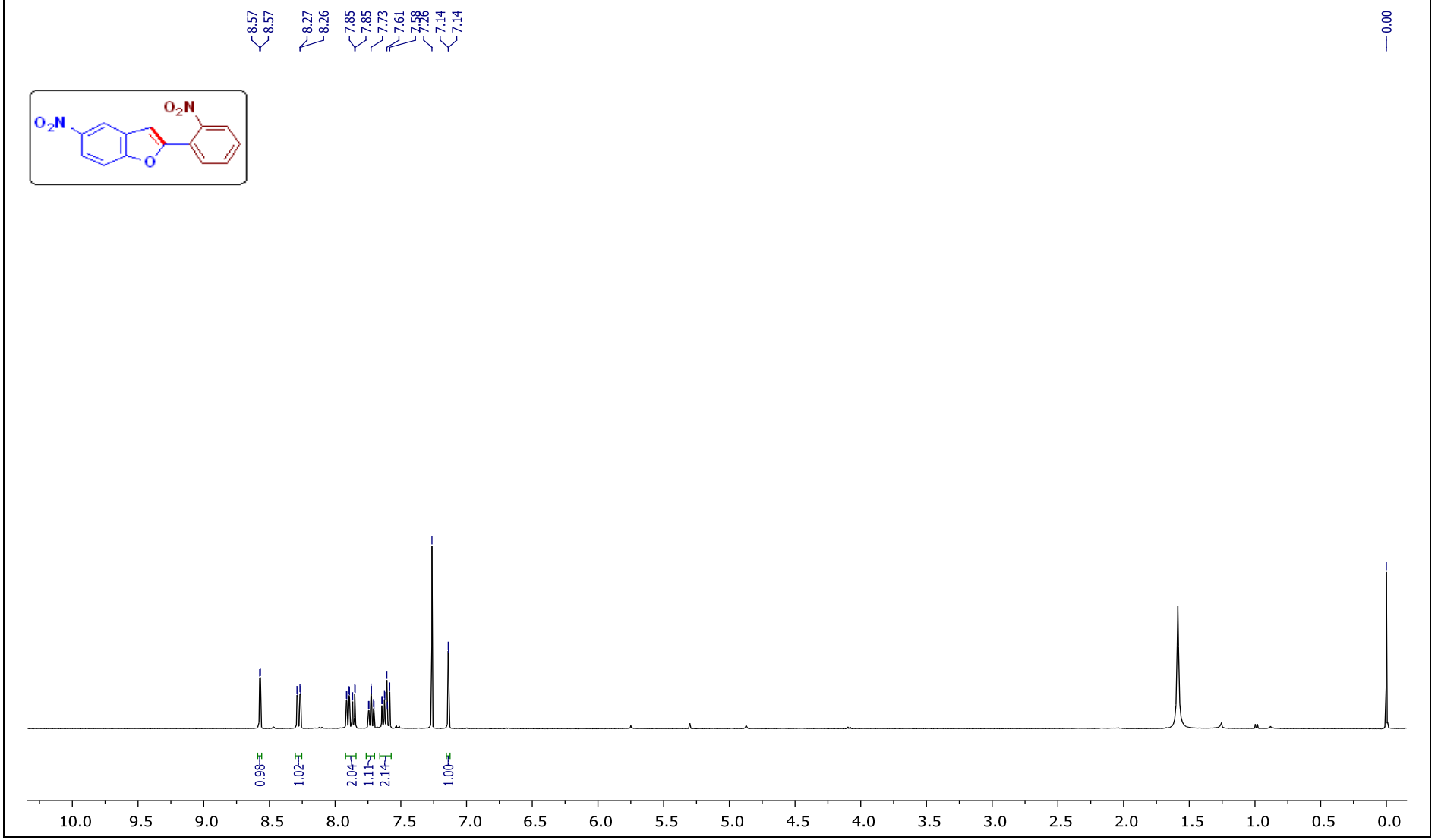
^{1}H-NMR of 4q (500 MHz, $CDCl_3$)



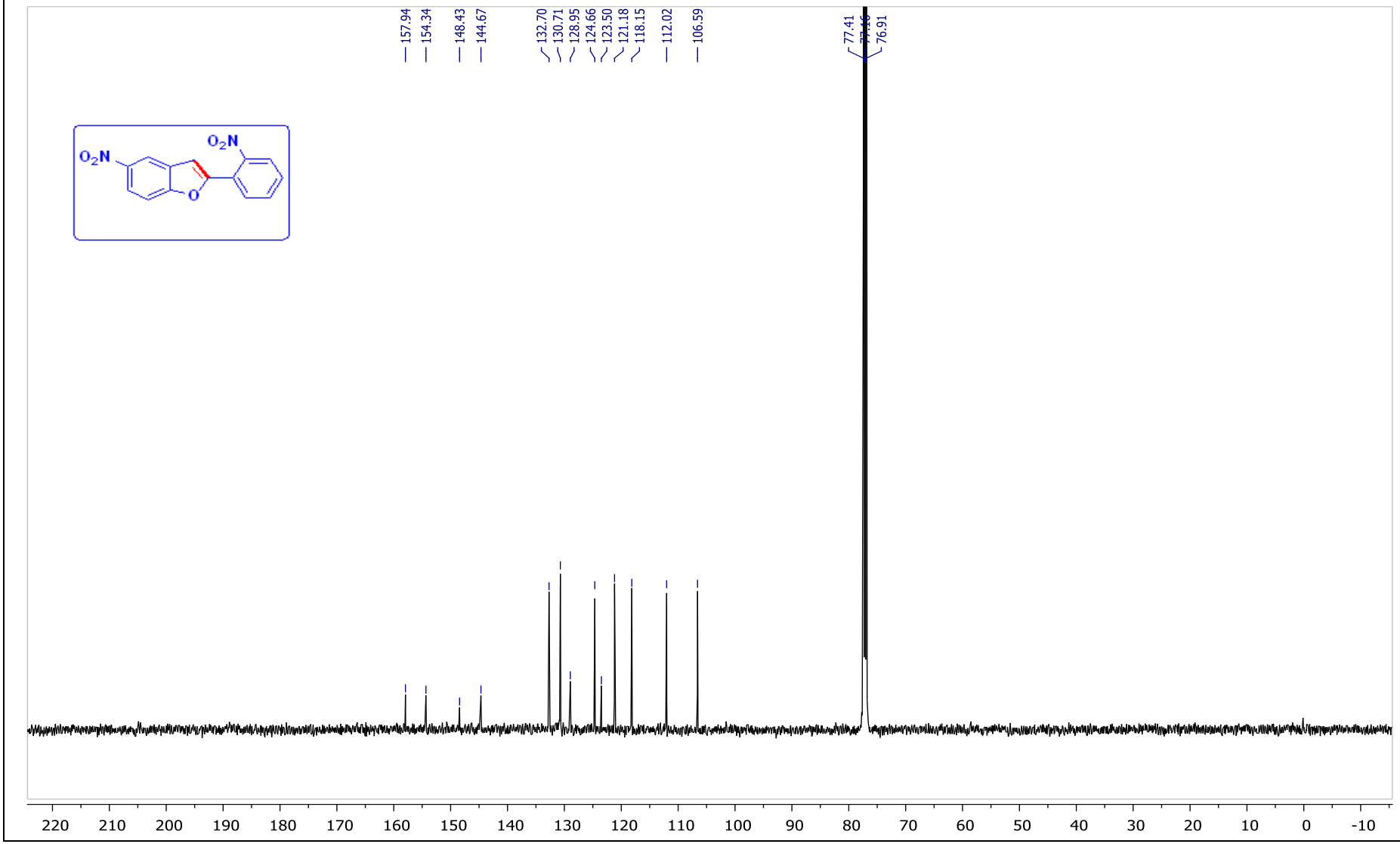
$^{13}C\{^{1}H\}$-NMR of 4q (126 MHz, $CDCl_3$)



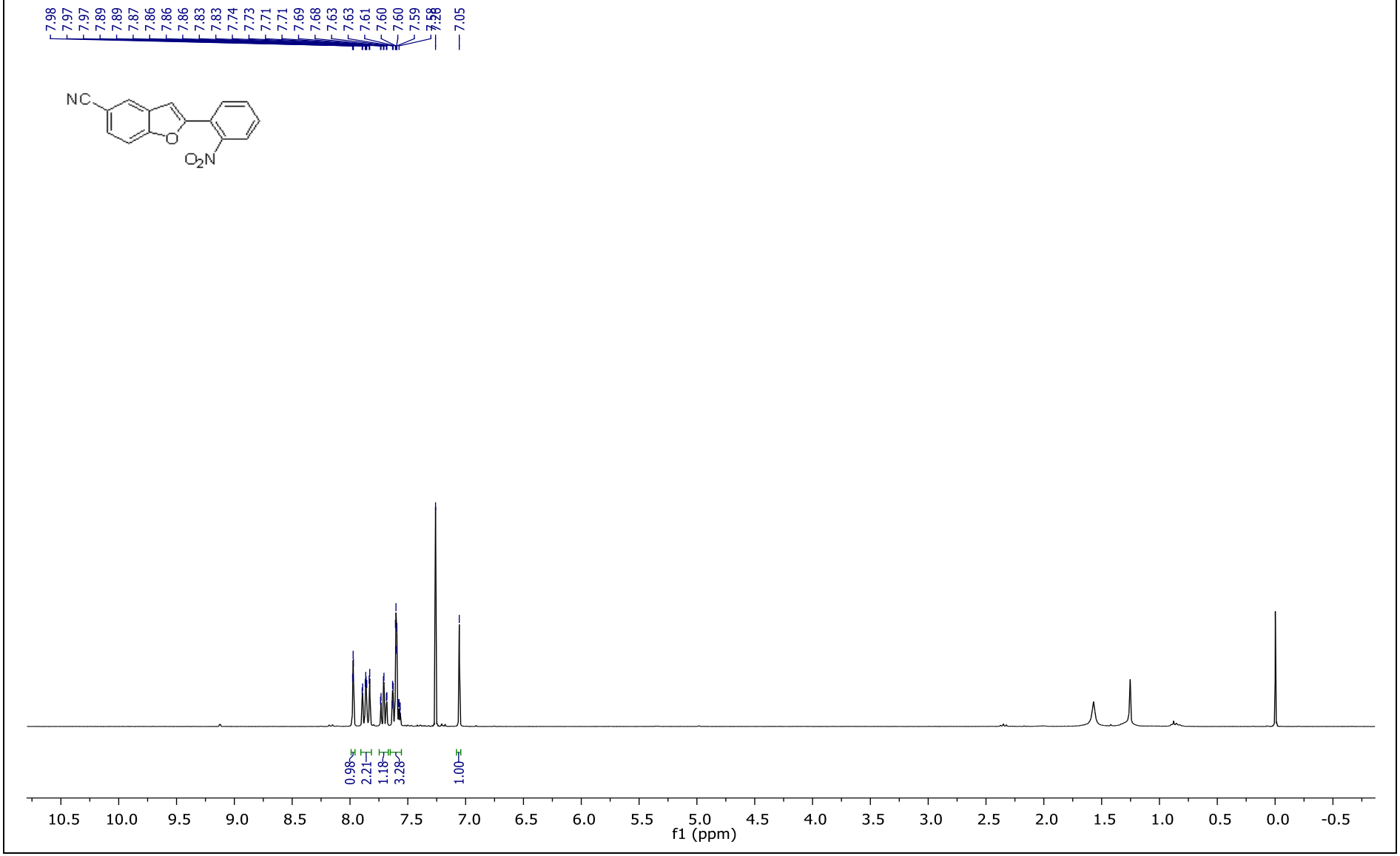
^{1}H-NMR of 4r (400 MHz, $CDCl_3$)



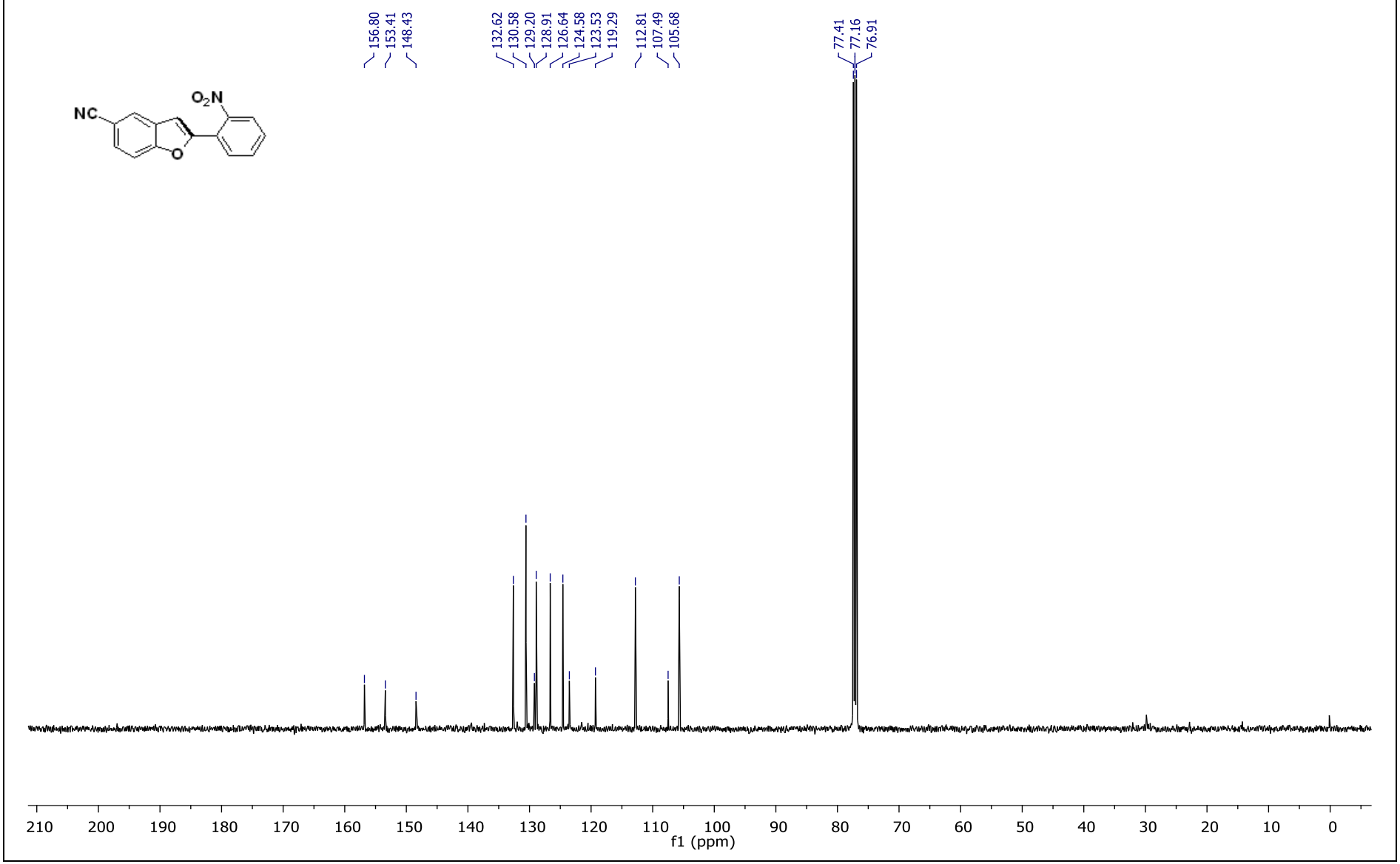
$^{13}C\{^{1}H\}$-NMR of 4r (126 MHz, $CDCl_3$)



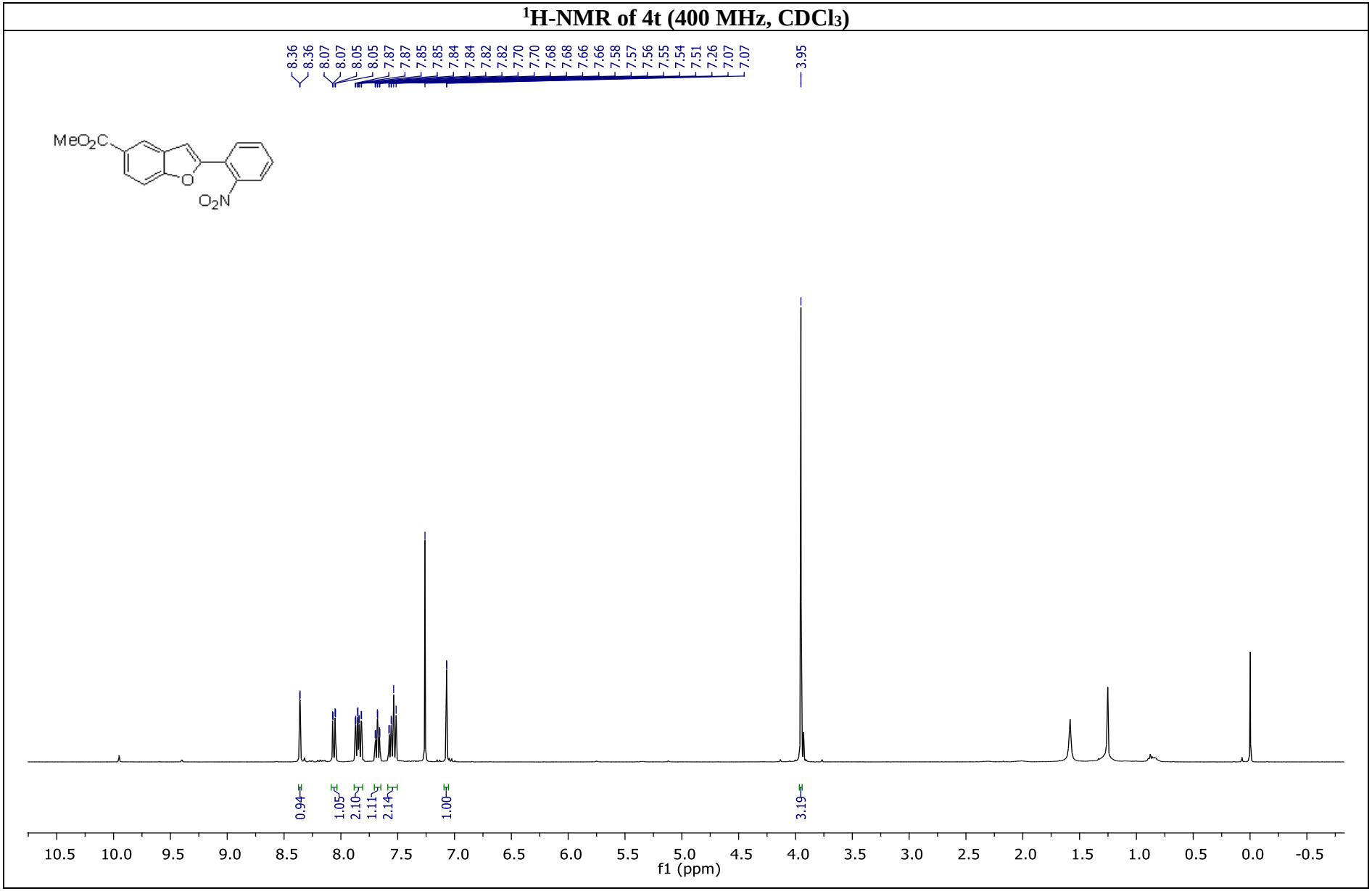
^{1}H-NMR of 4s (300 MHz, $CDCl_3$)



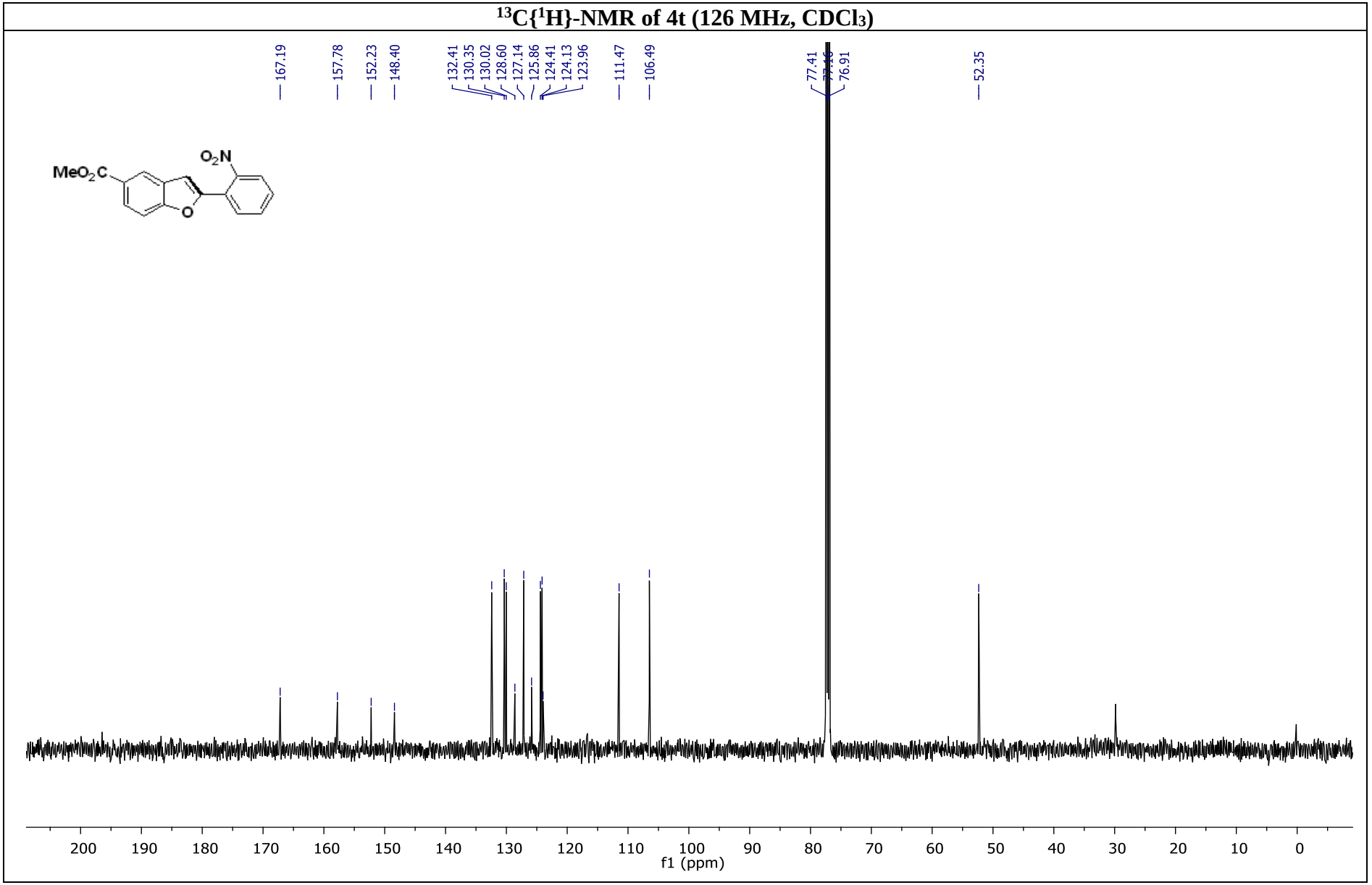
$^{13}C\{^{1}H\}$-NMR of 4s (126 MHz, $CDCl_3$)



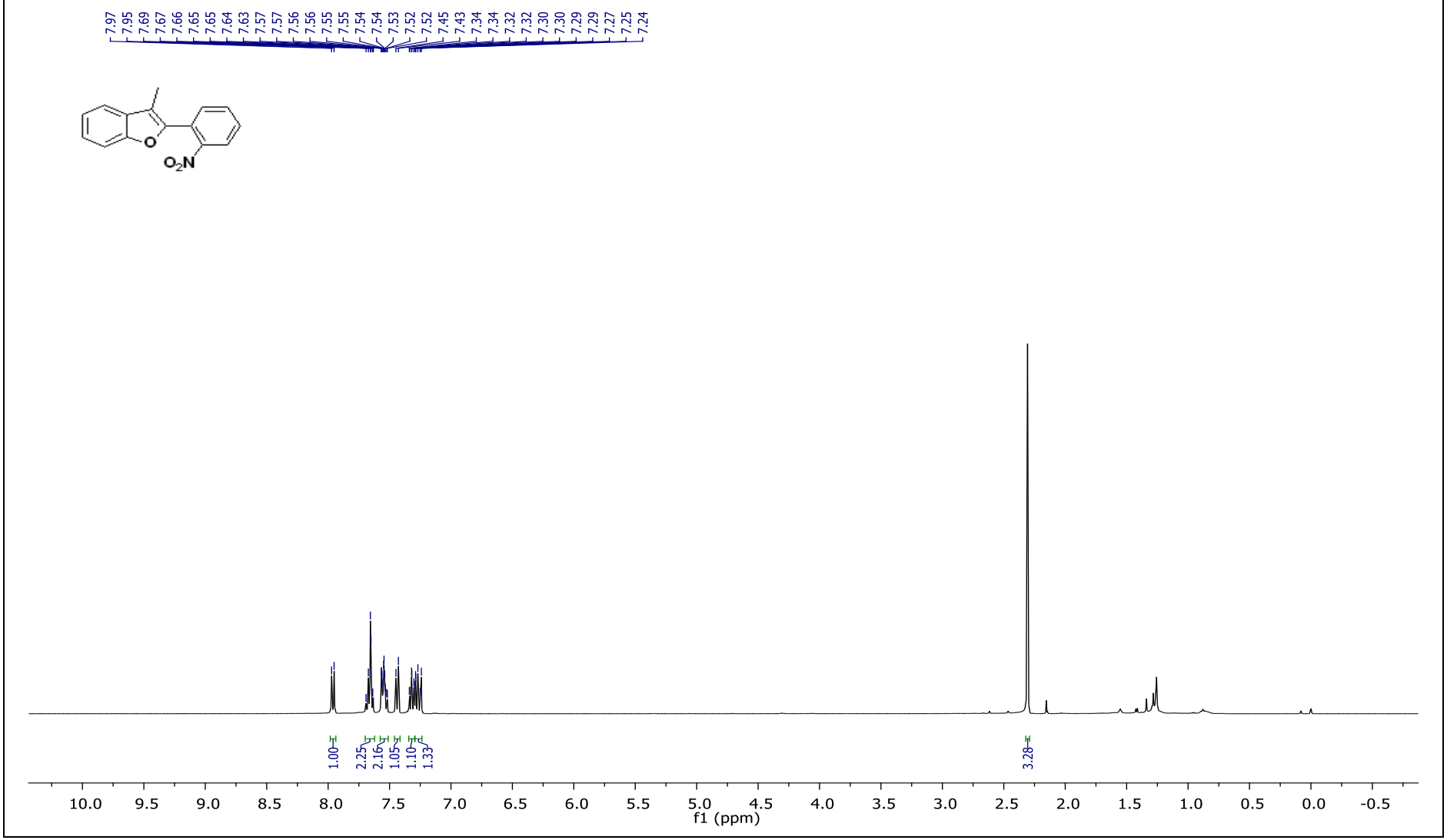
^{1}H-NMR of 4t (400 MHz, $CDCl_3$)



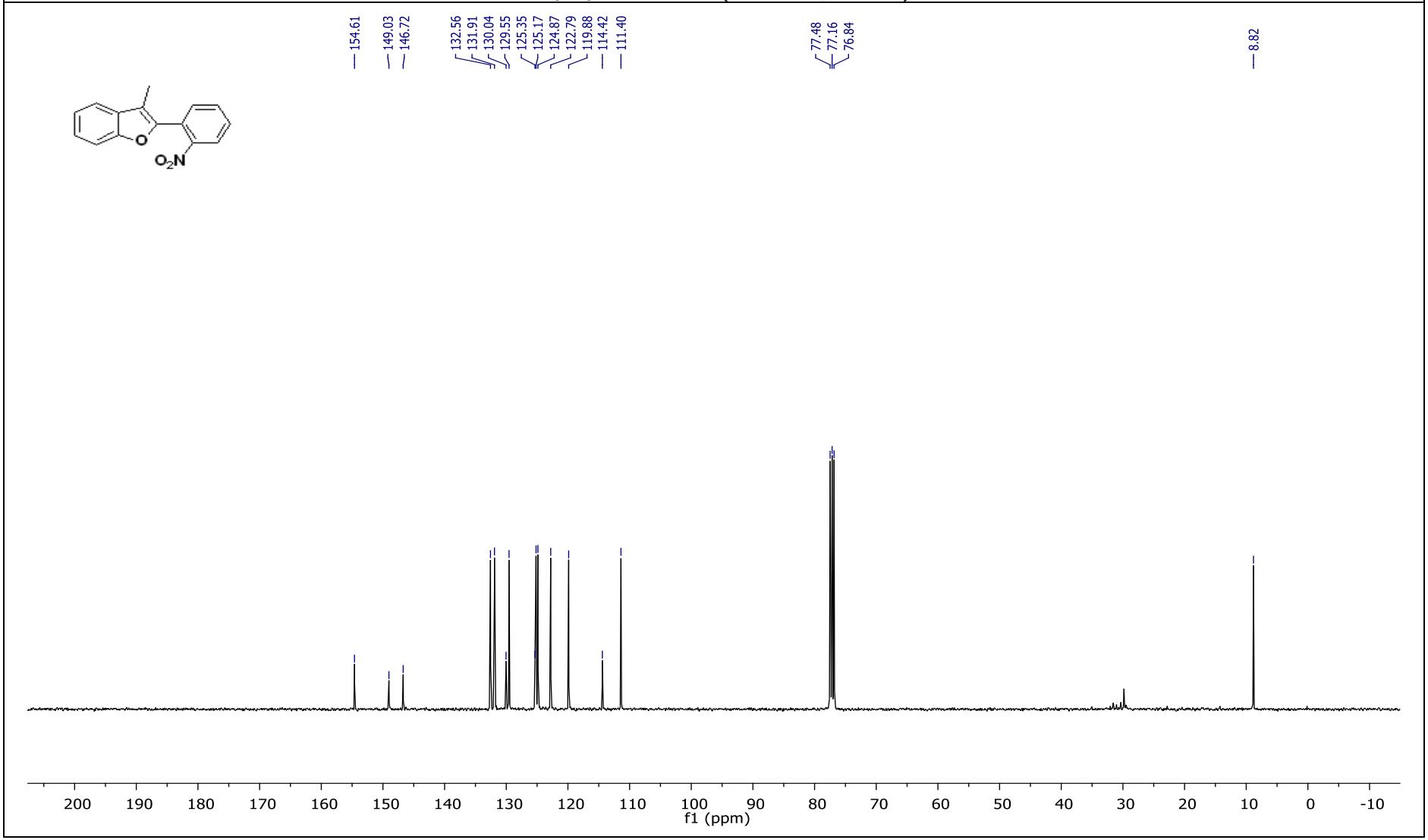
$^{13}C\{^{1}H\}$-NMR of 4t (126 MHz, $CDCl_3$)



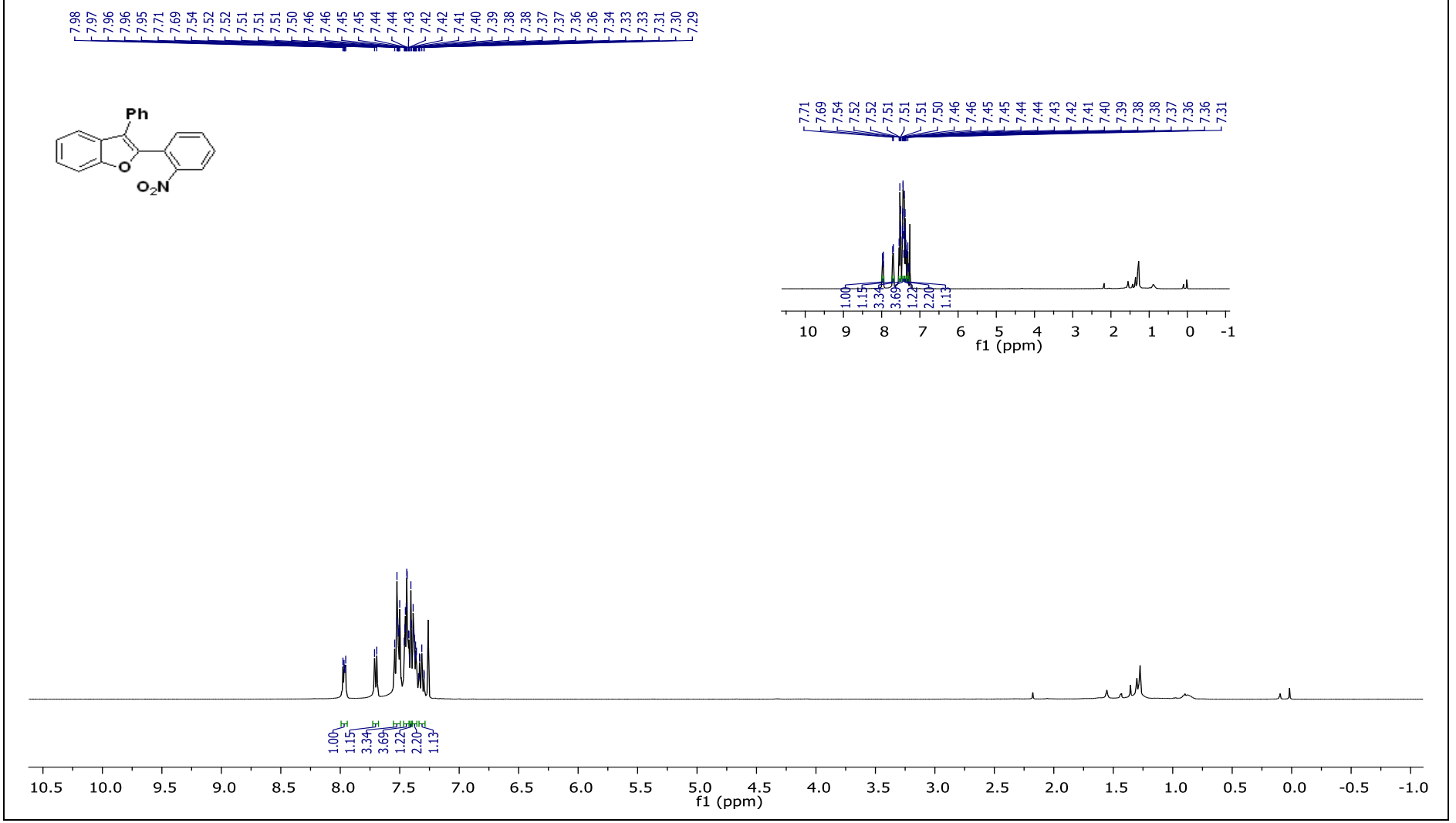
^{1}H-NMR of 4u (400 MHz, $CDCl_3$)



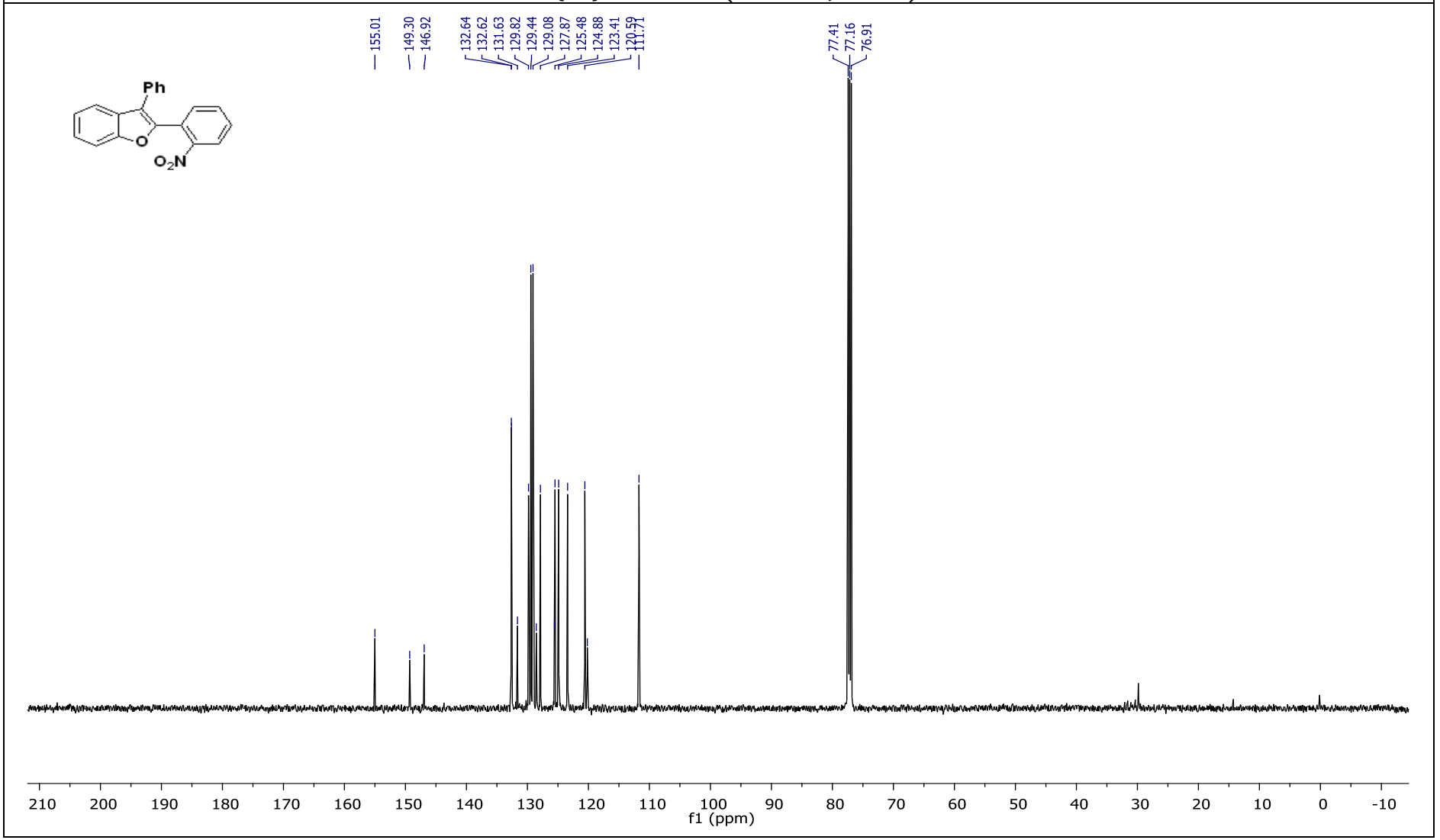
$^{13}C\{^{1}H\}$-NMRof 4u (101 MHz, $CDCl_3$)



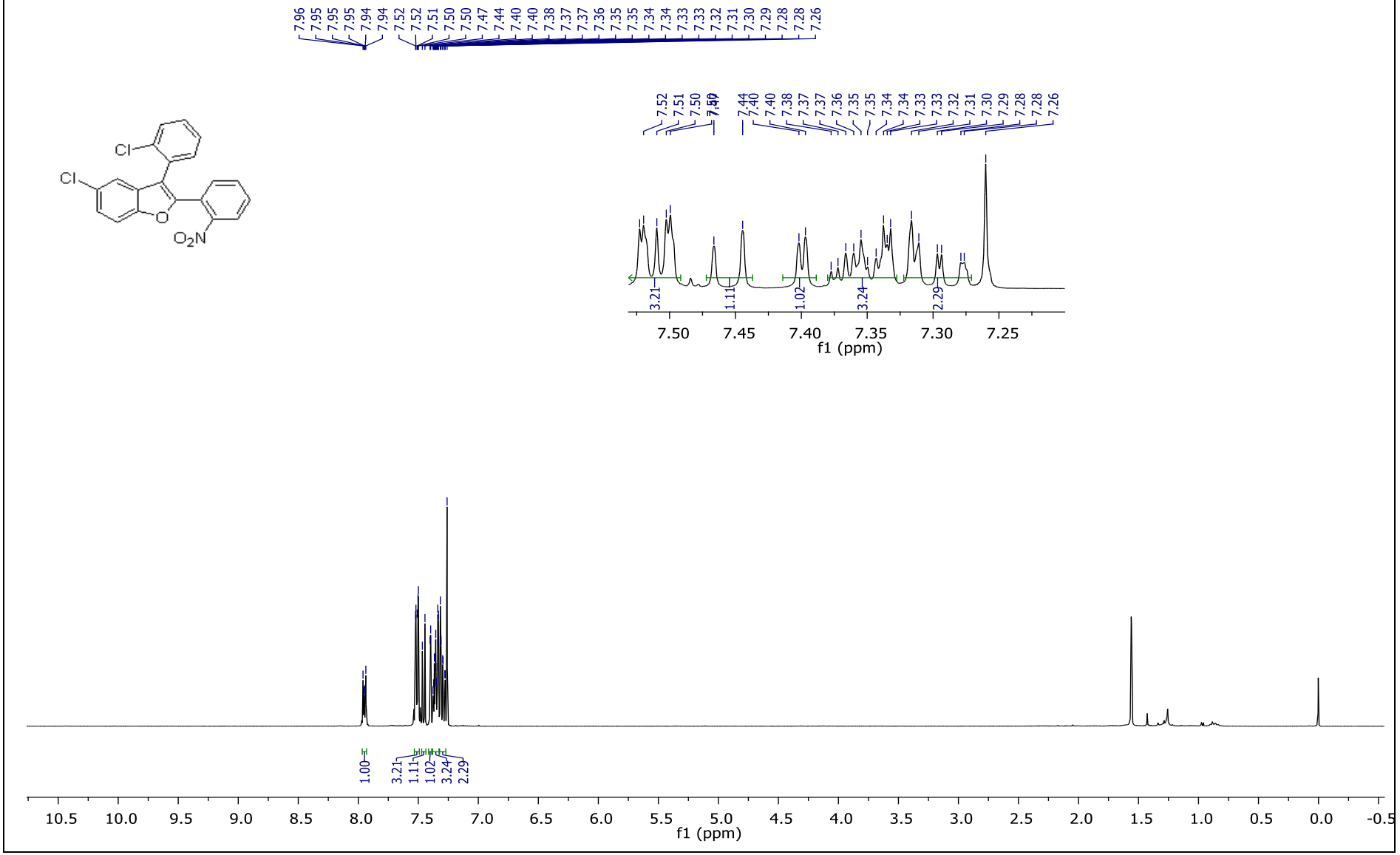
^{1}H-NMR of 4v (400 MHz, $CDCl_3$)



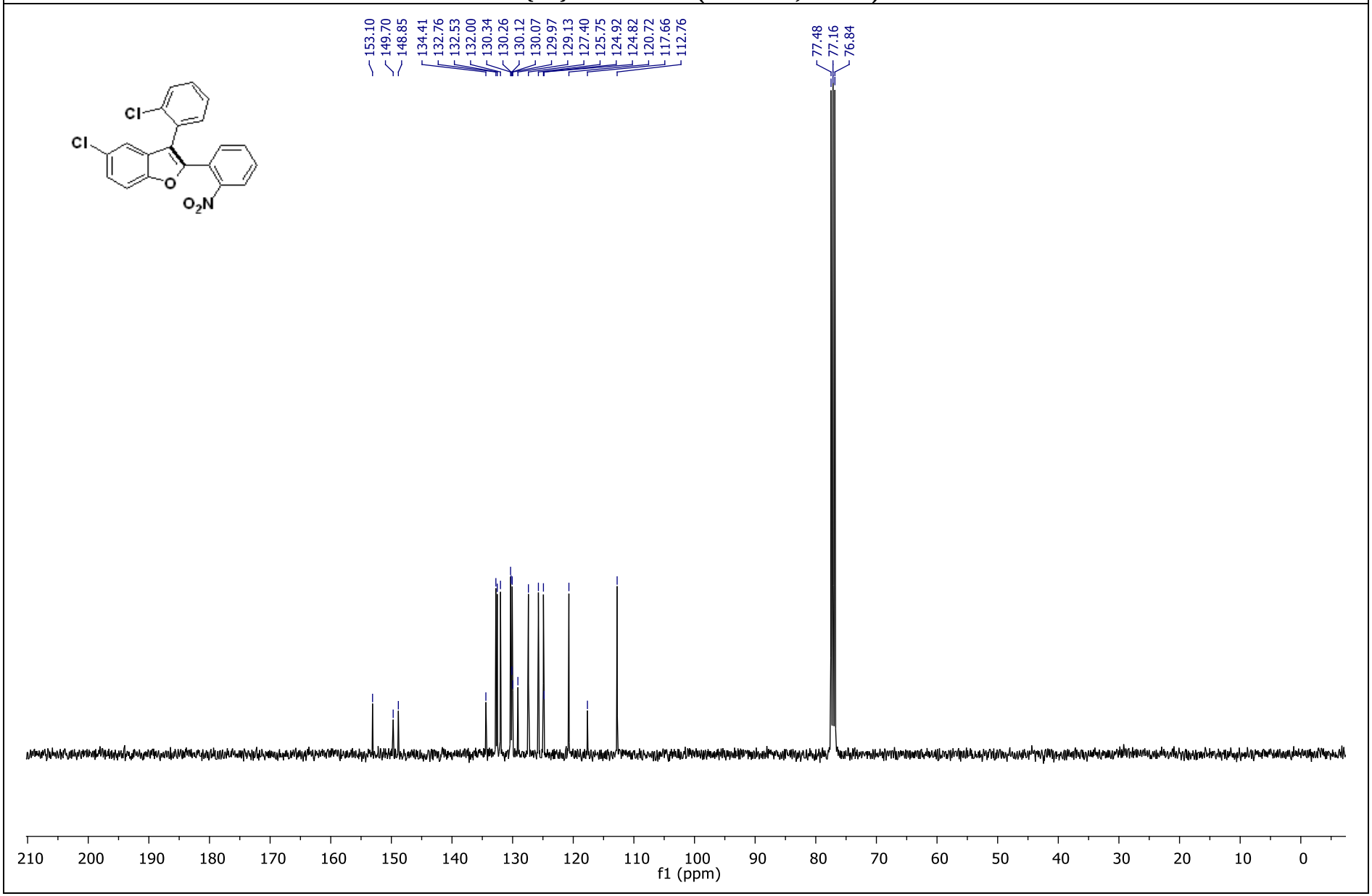
$^{13}C\{^{1}H\}$-NMRof 4v (126 MHz, $CDCl_3$)



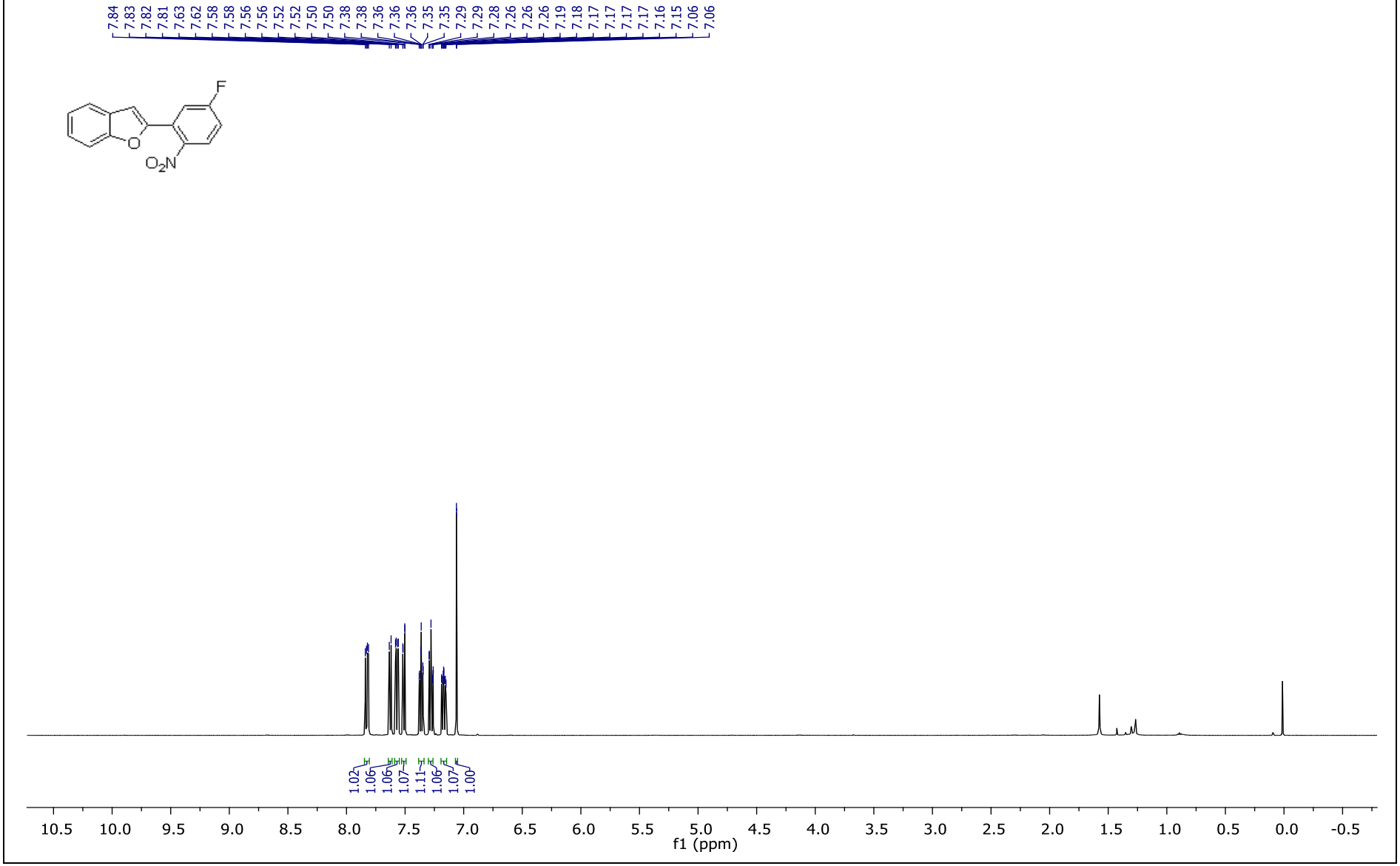
^{1}H-NMR of 4w (400 MHz, $CDCl_3$)



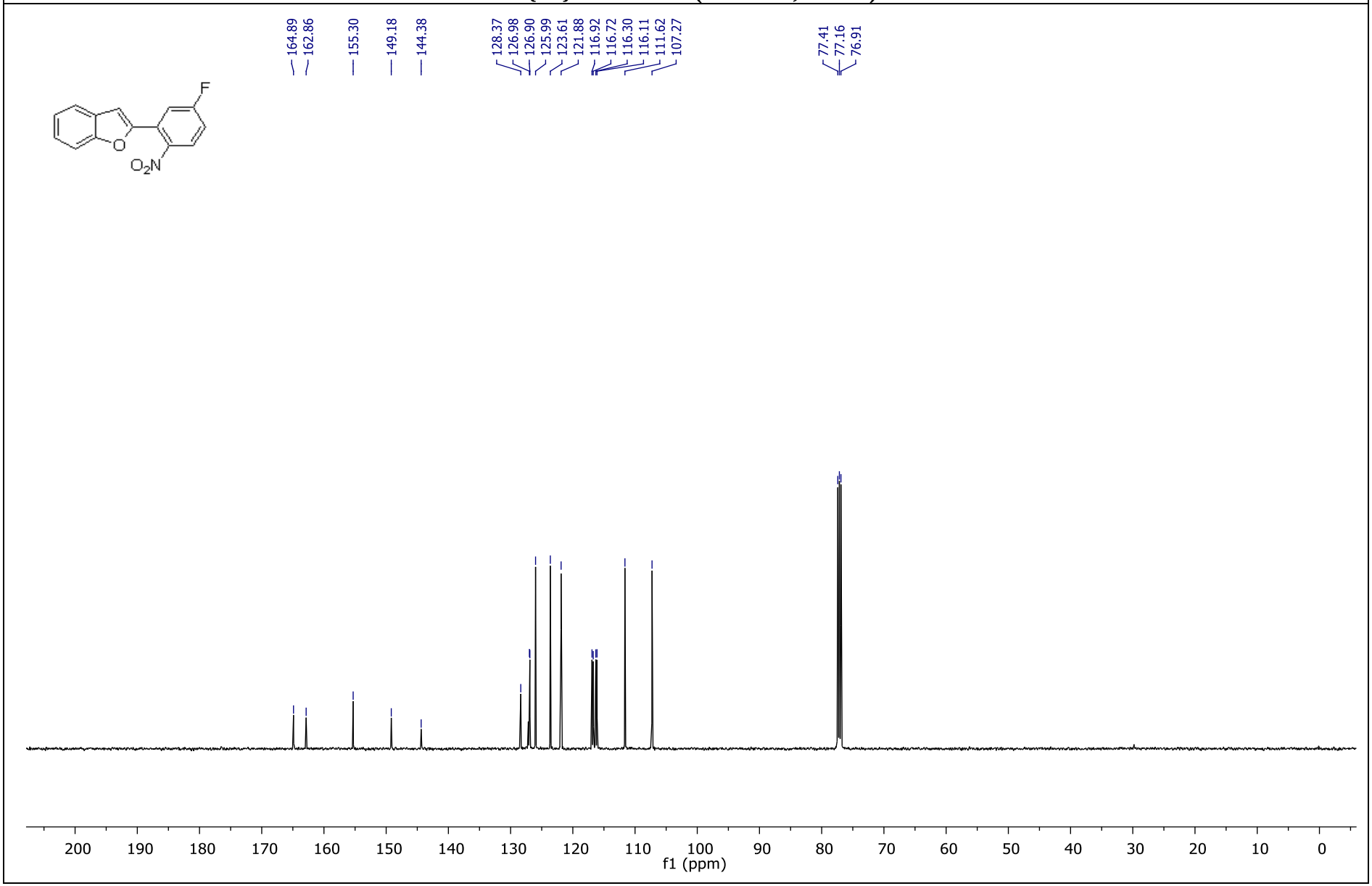
$^{13}C\{^{1}H\}$-NMR of 4w (101 MHz, $CDCl_3$)



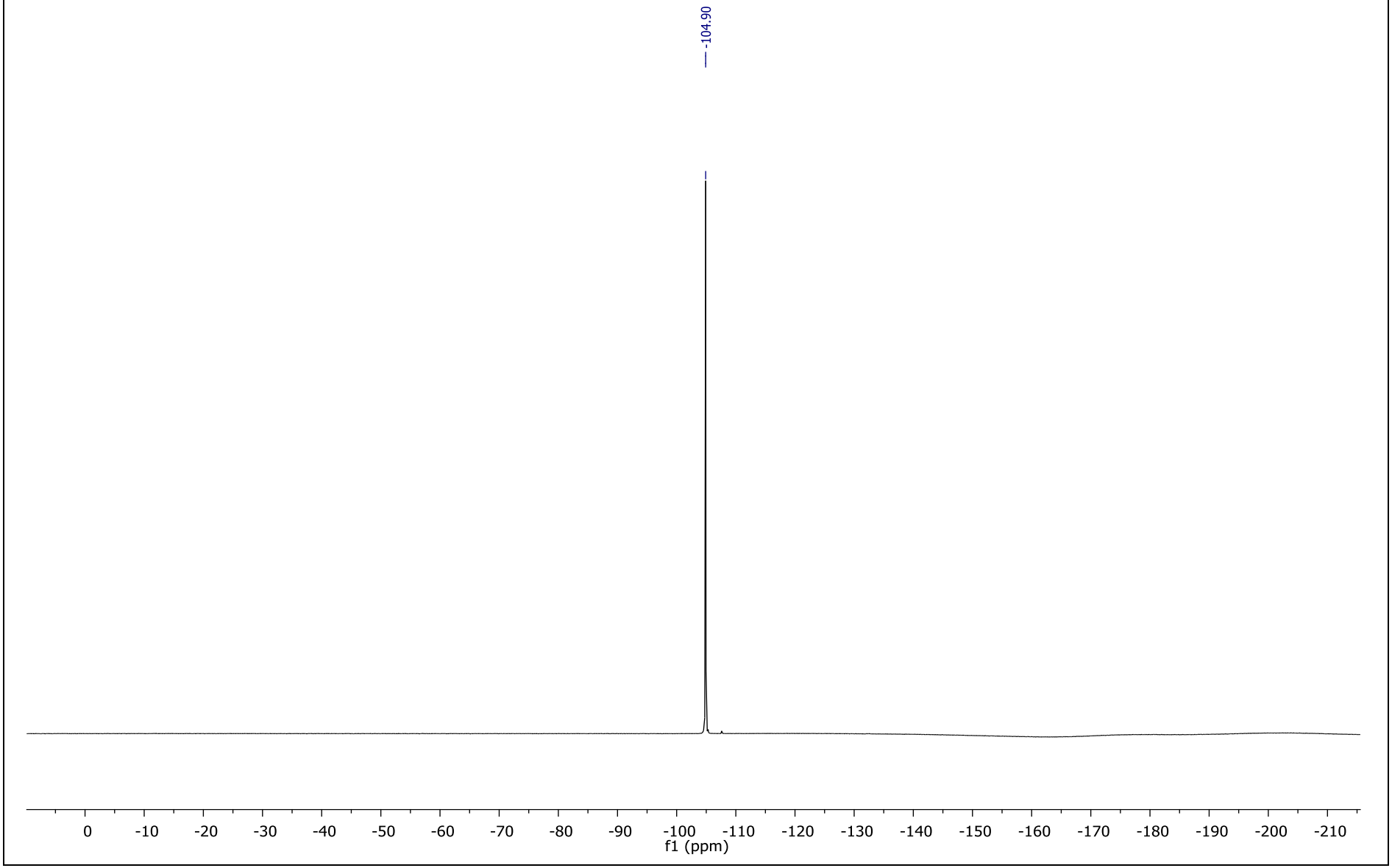
^{1}H-NMR of 4x (500 MHz, $CDCl_3$)



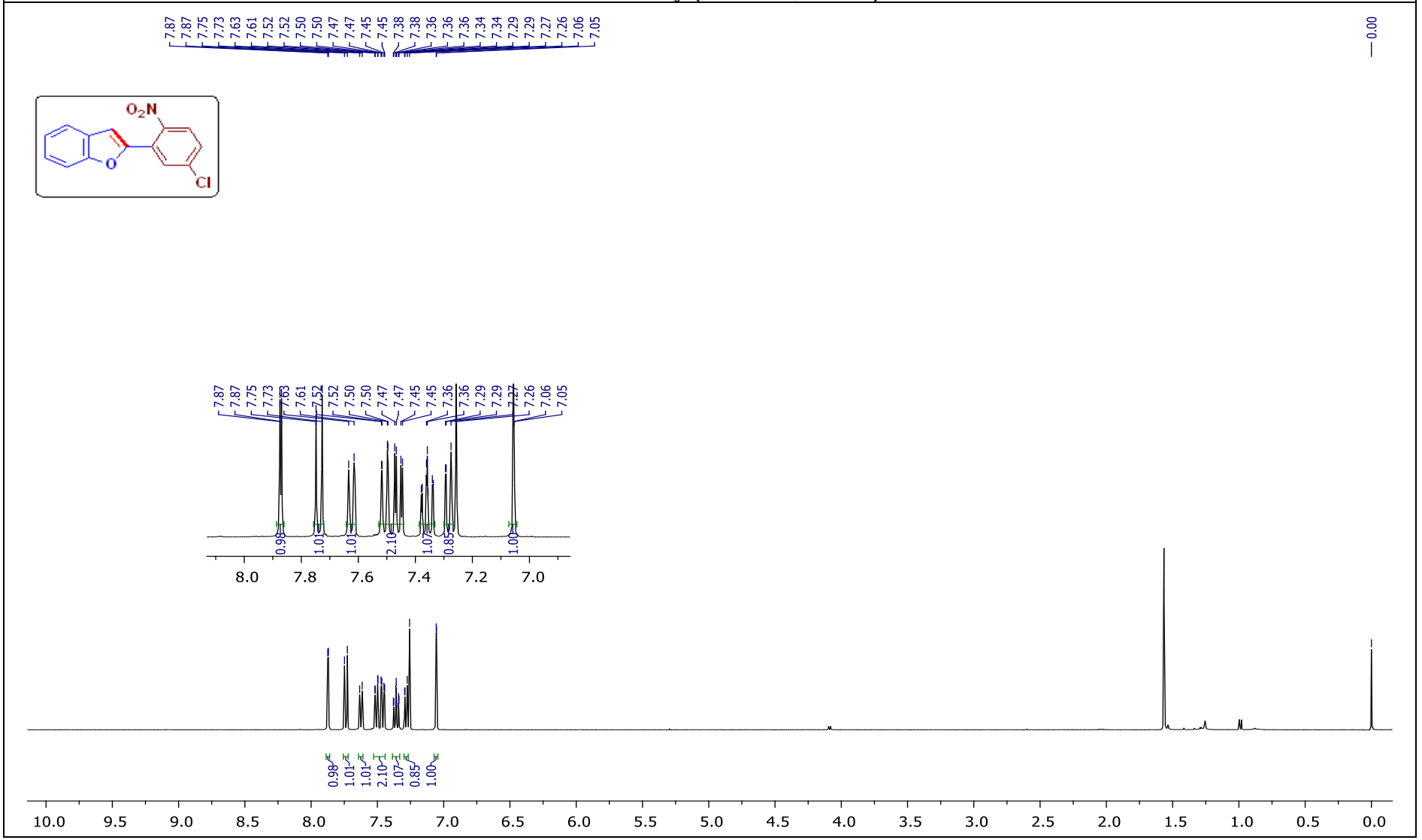
$^{13}C\{^{1}H\}$-NMR of 4x (126 MHz, $CDCl_3$)



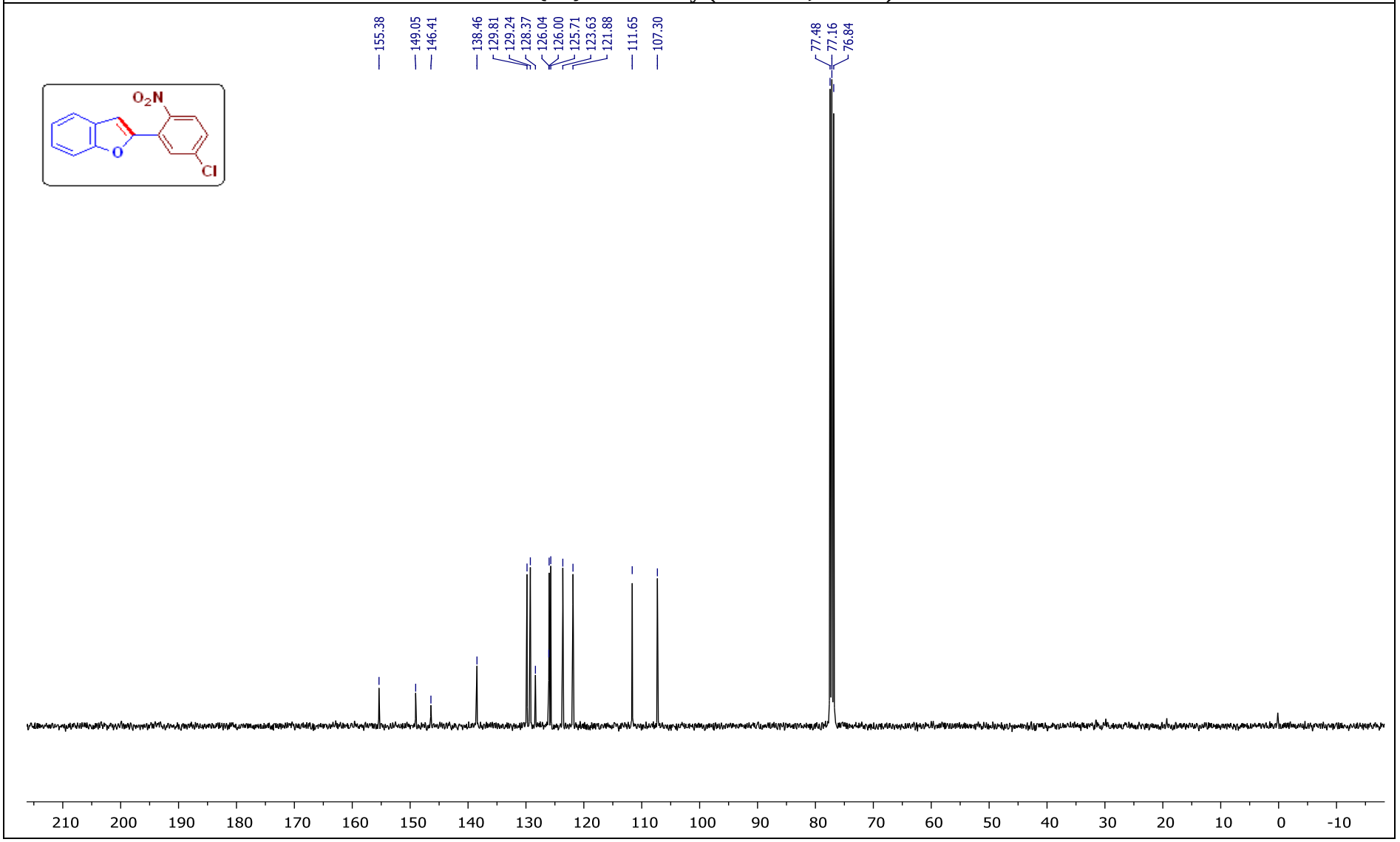
^{19}F-NMR of 4y (376 MHz, $CDCl_3$)



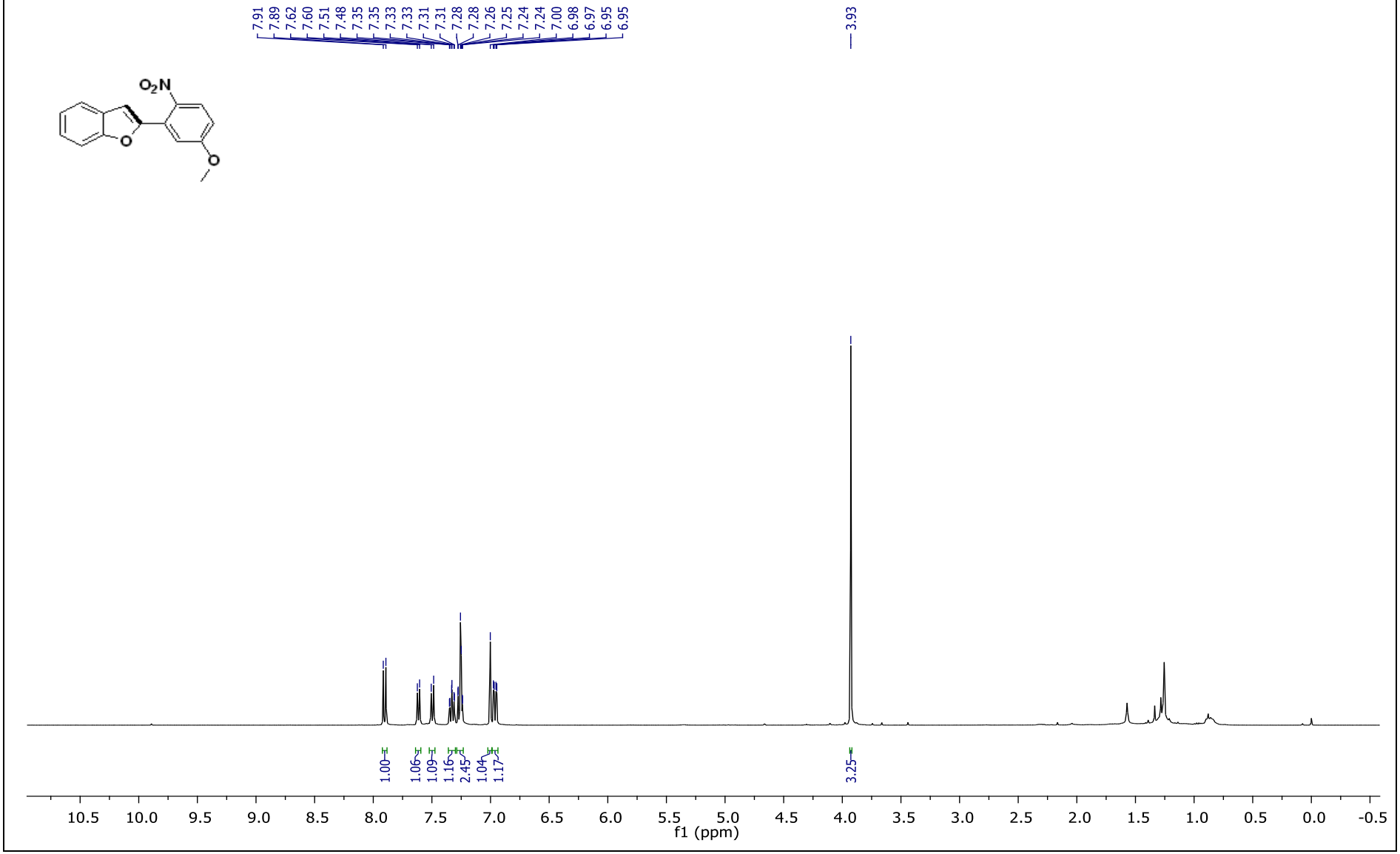
^{1}H-NMR of 4y (400 MHz, $CDCl_3$)



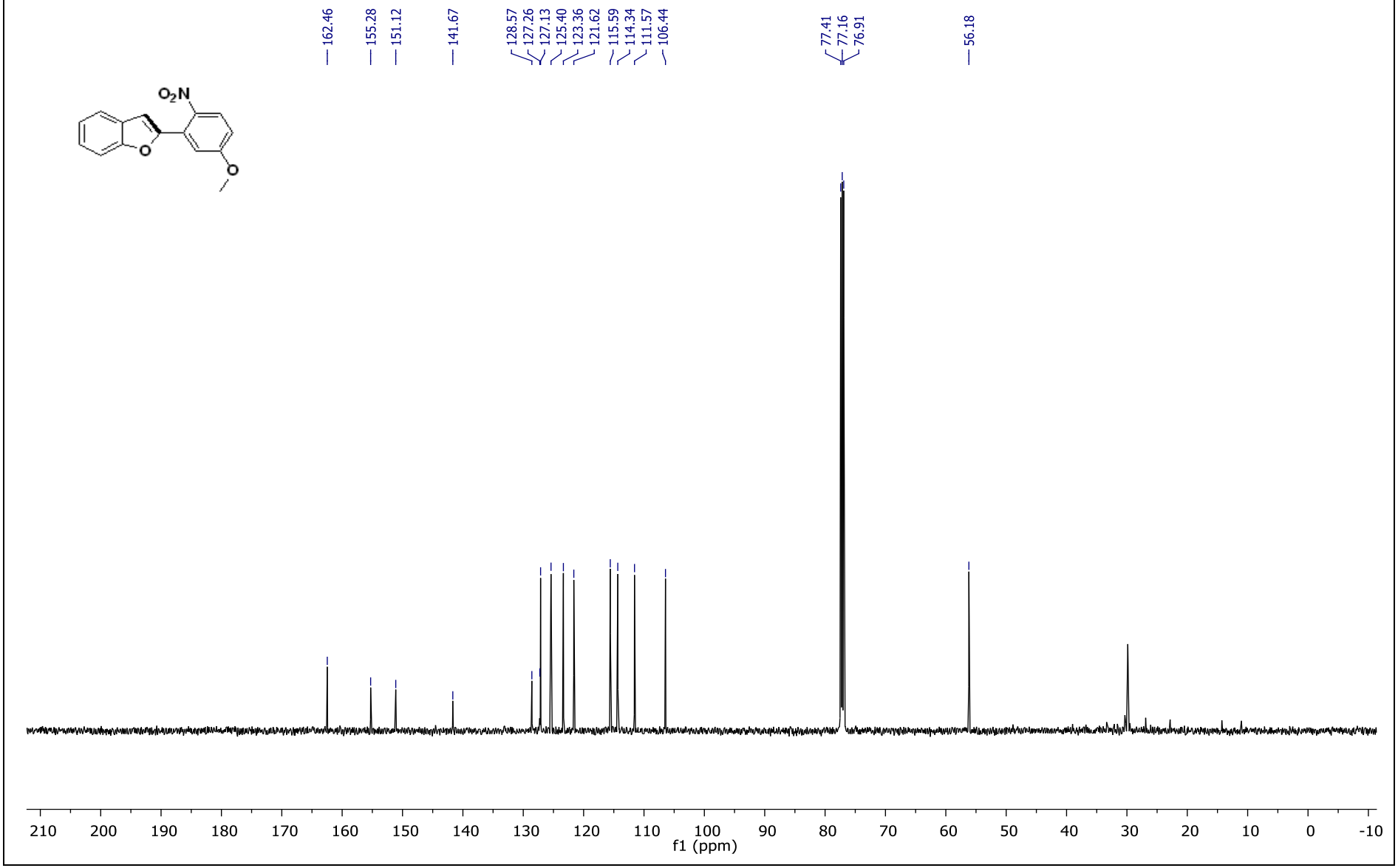
$^{13}C\{^{1}H\}$-NMR of 4y (126 MHz, $CDCl_3$)



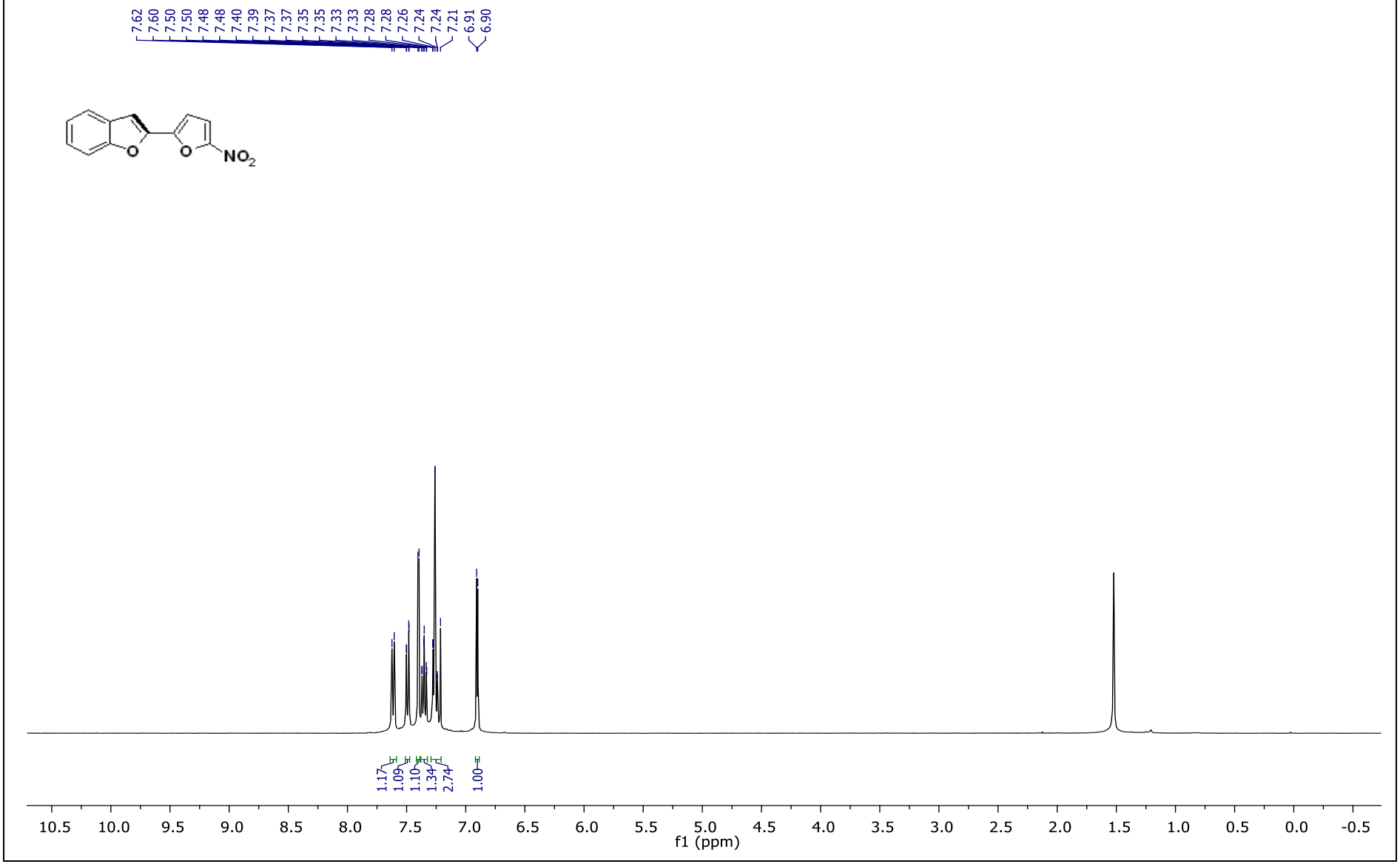
^{1}H-NMR of 4z (400 MHz, $CDCl_3$)



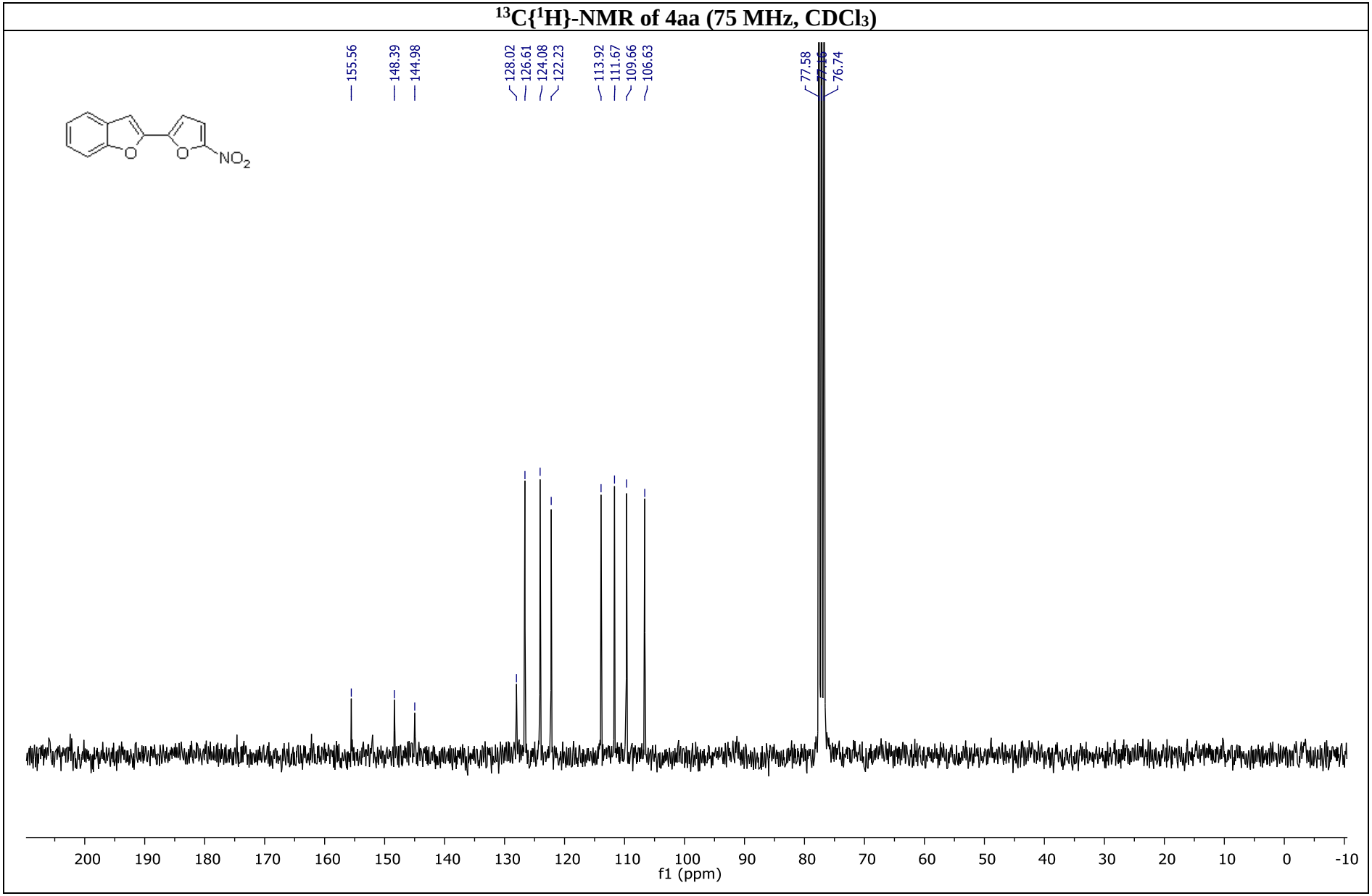
$^{13}C\{^{1}H\}$-NMR of 4z (126 MHz, $CDCl_3$)



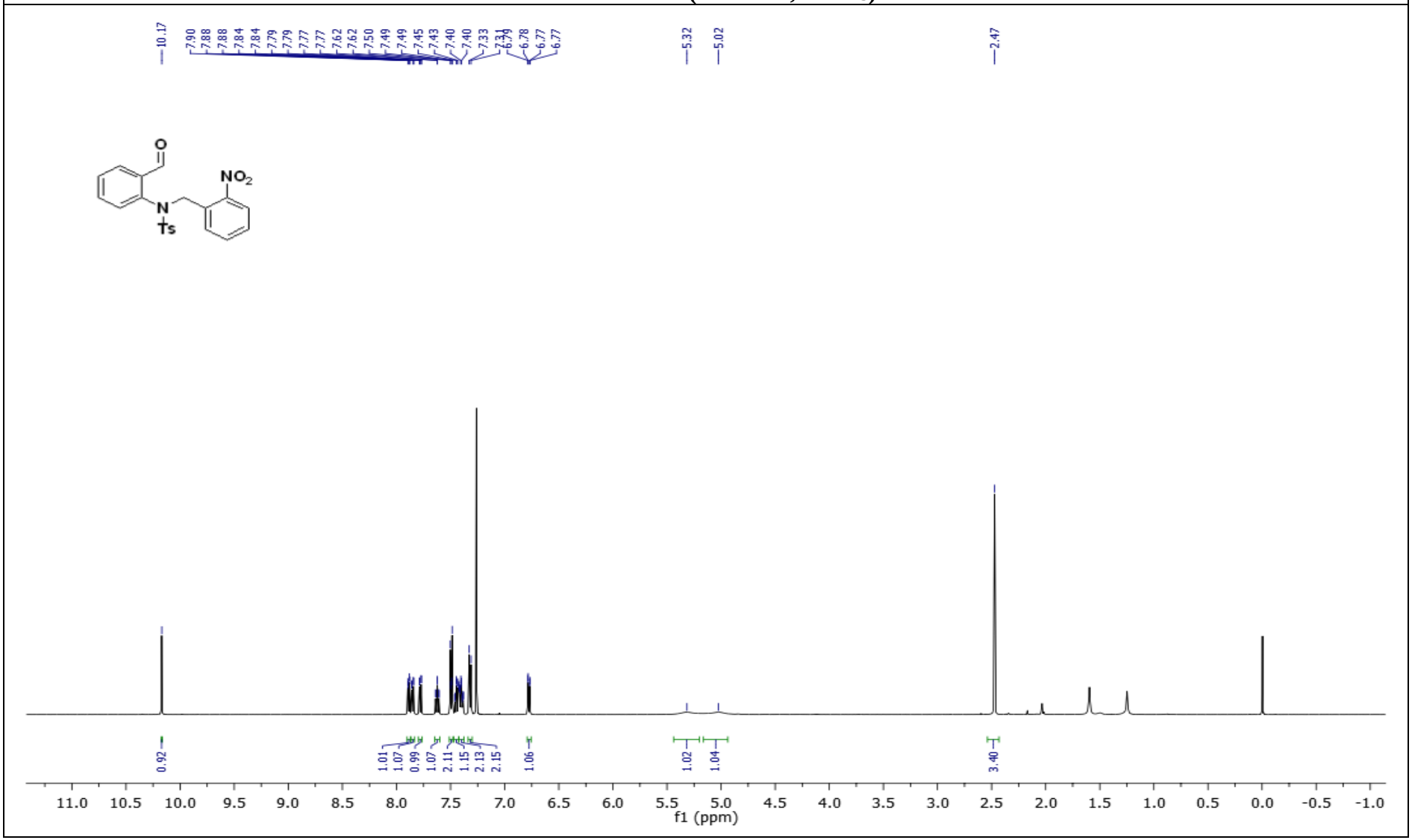
^{1}H-NMR of 4aa (400 MHz, $CDCl_3$)



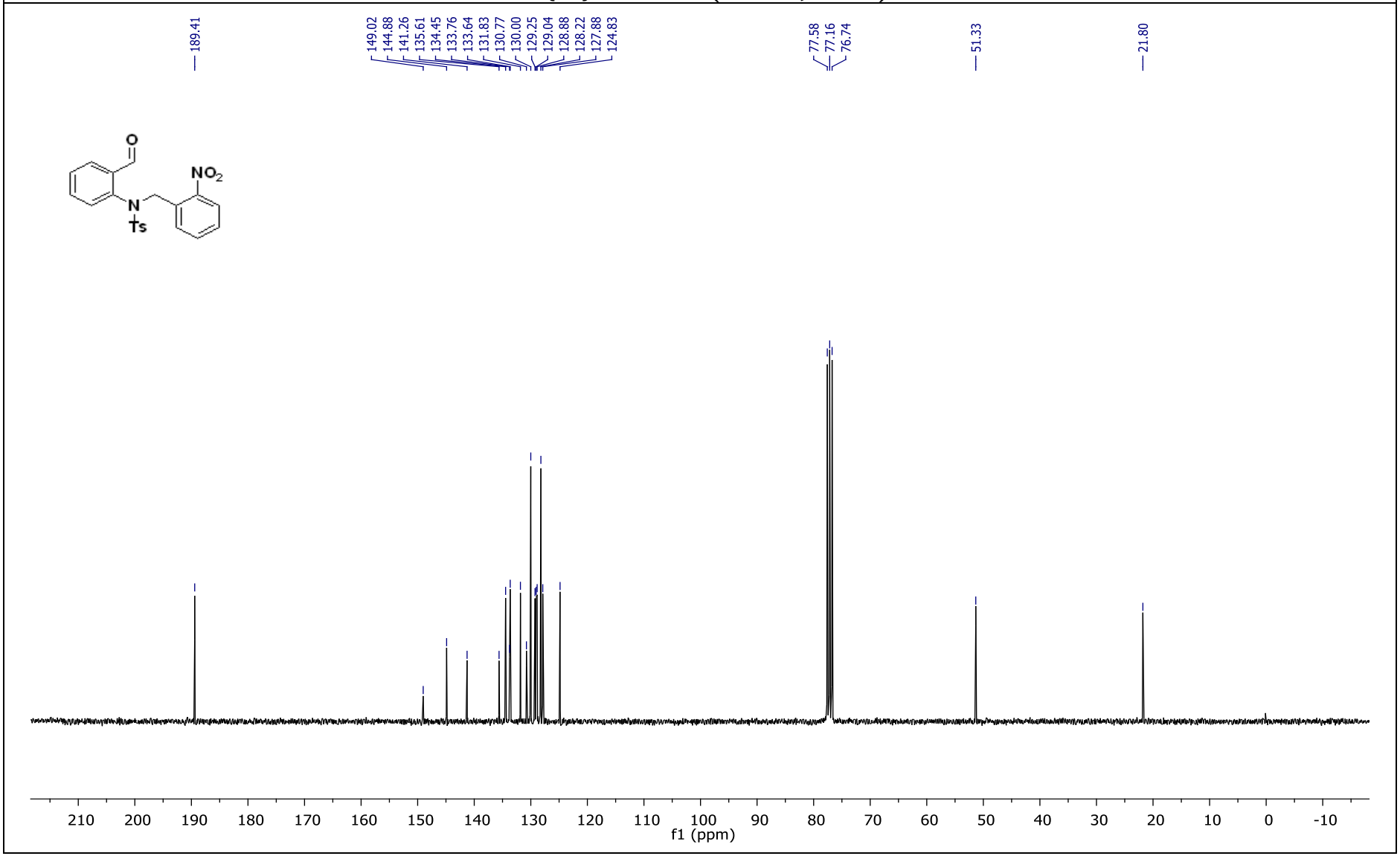
$^{13}C\{^{1}H\}$-NMR of 4aa (75 MHz, $CDCl_3$)



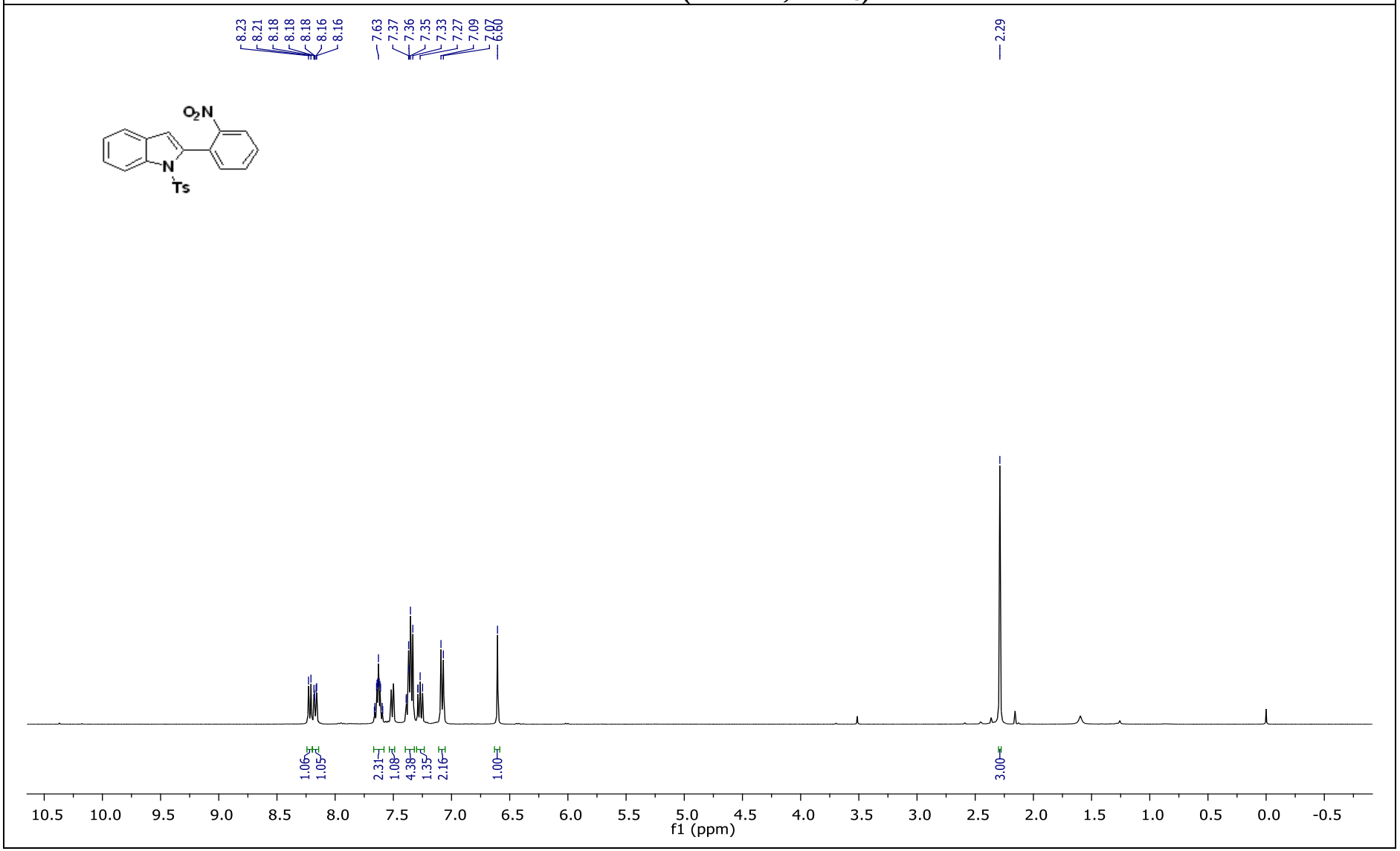
^{1}H-NMR of 6a (500 MHz, $CDCl_3$)



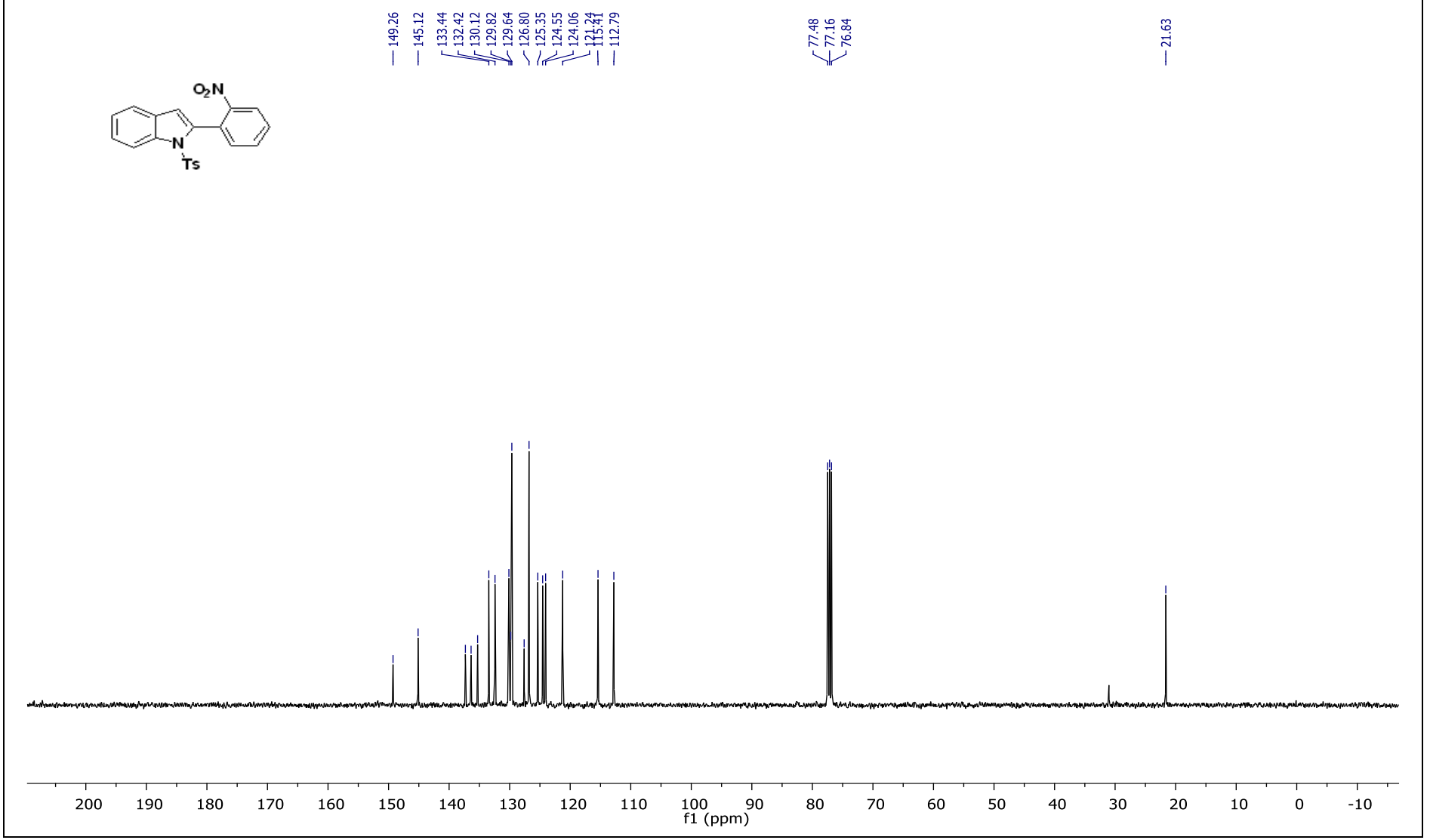
$^{13}C\{^{1}H\}$-NMRof 6a (75 MHz, $CDCl_3$)



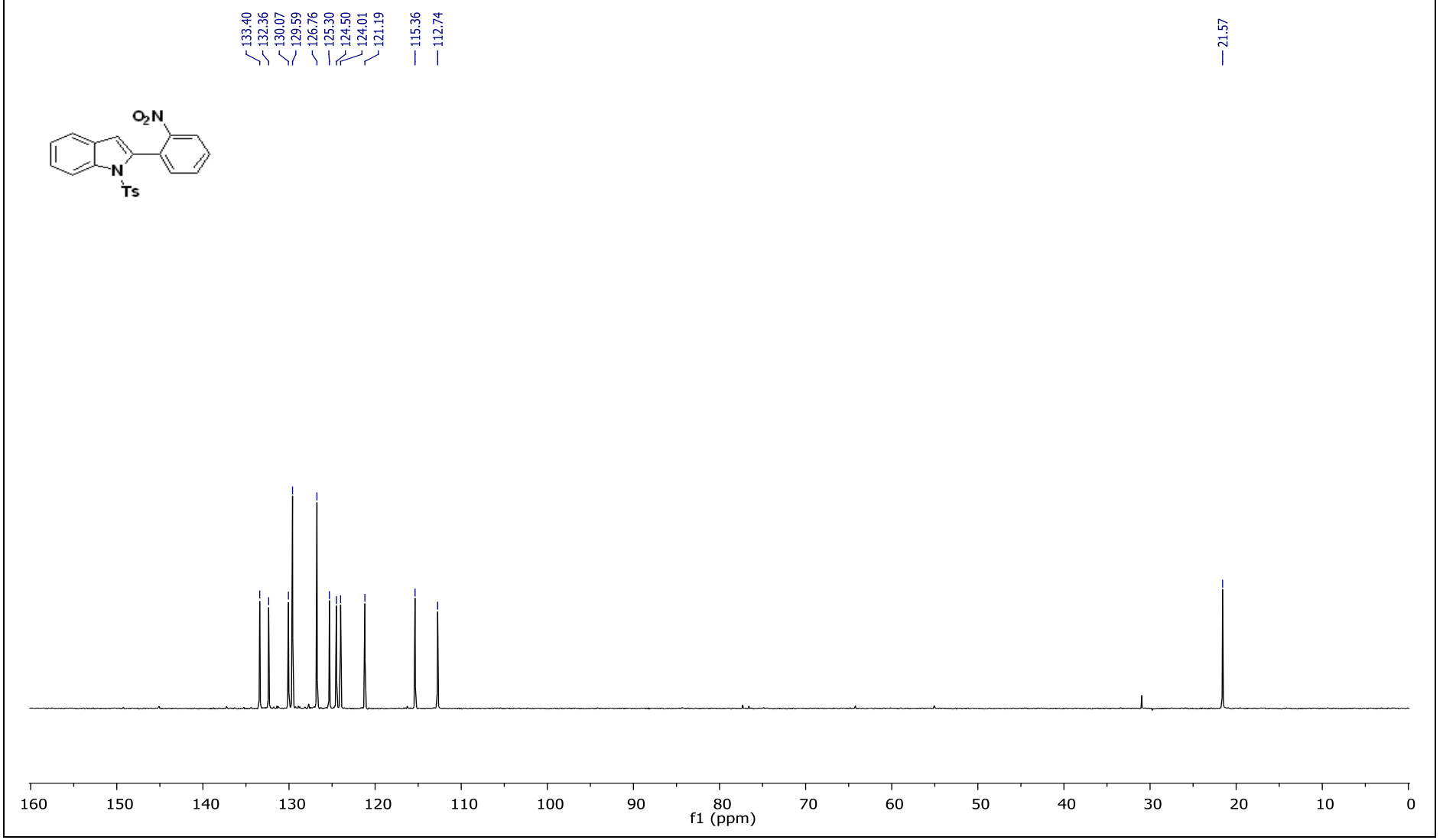
^{1}H-NMR of 7a (400 MHz, $CDCl_3$)



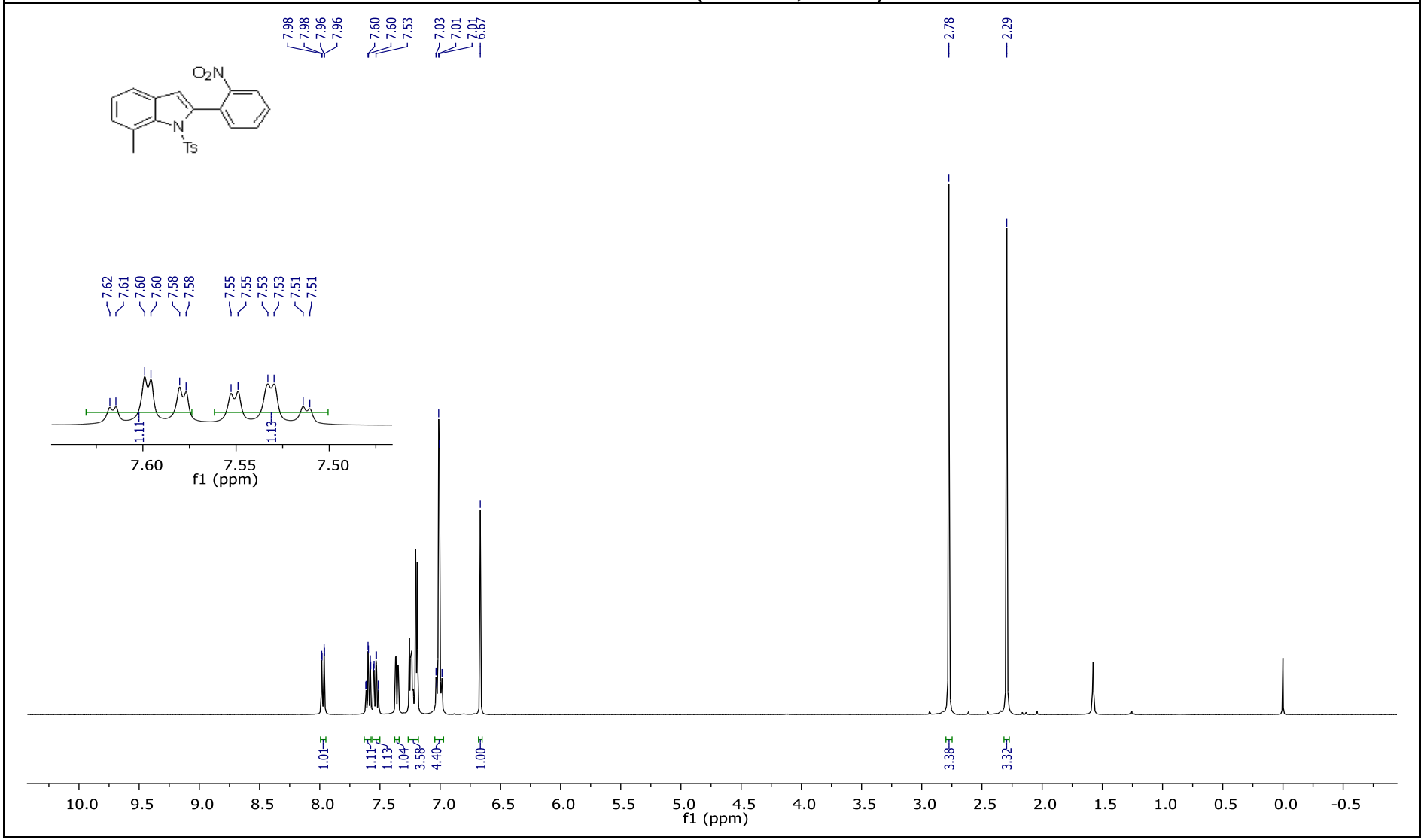
$^{13}C\{^{1}H\}$-NMR of 7a (101 MHz, $CDCl_3$)



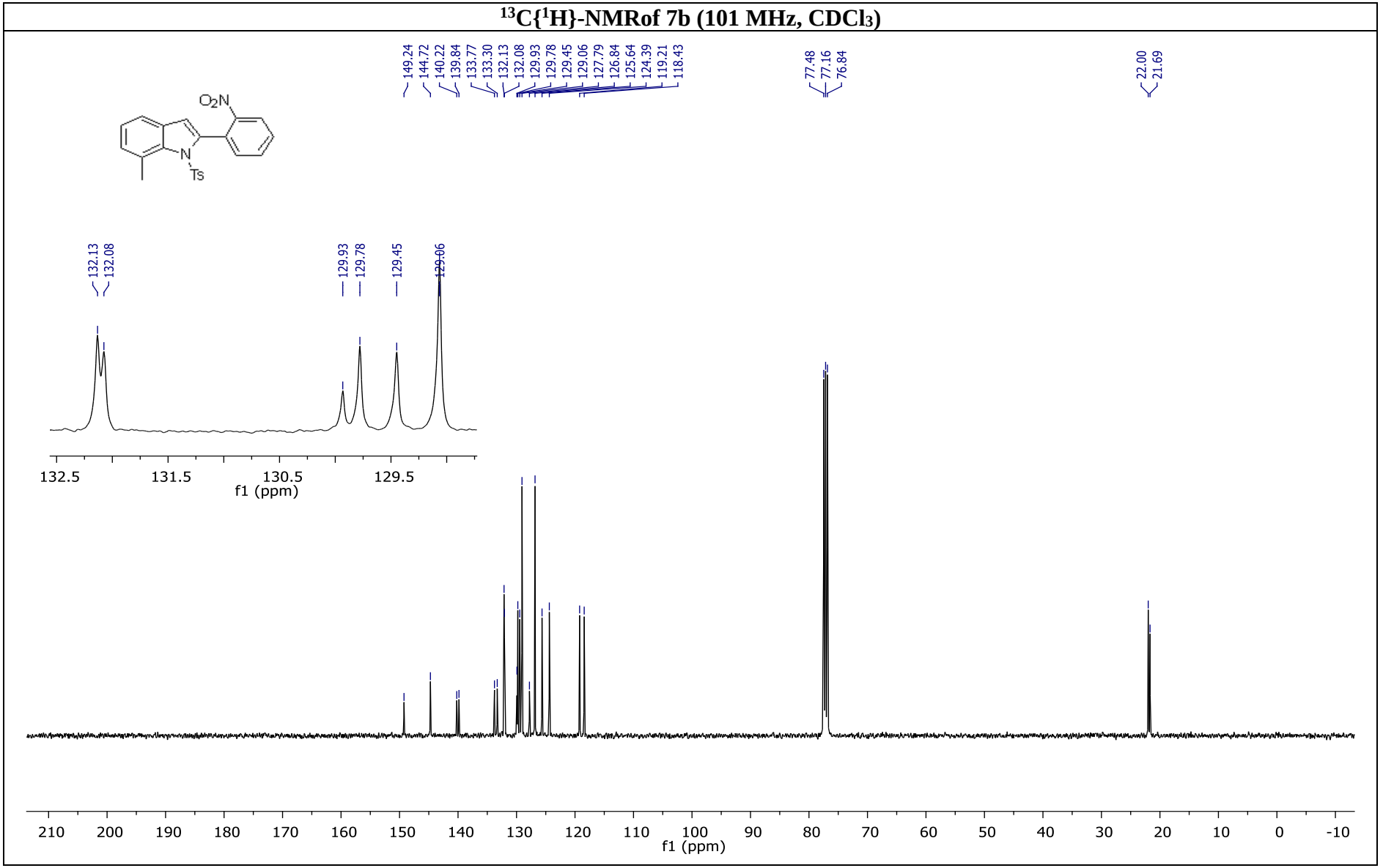
DEPT-135-NMR of 7a (101 MHz, $CDCl_3$)



^{1}H-NMR of 7b (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-NMRof 7b (101 MHz, $CDCl_3$)



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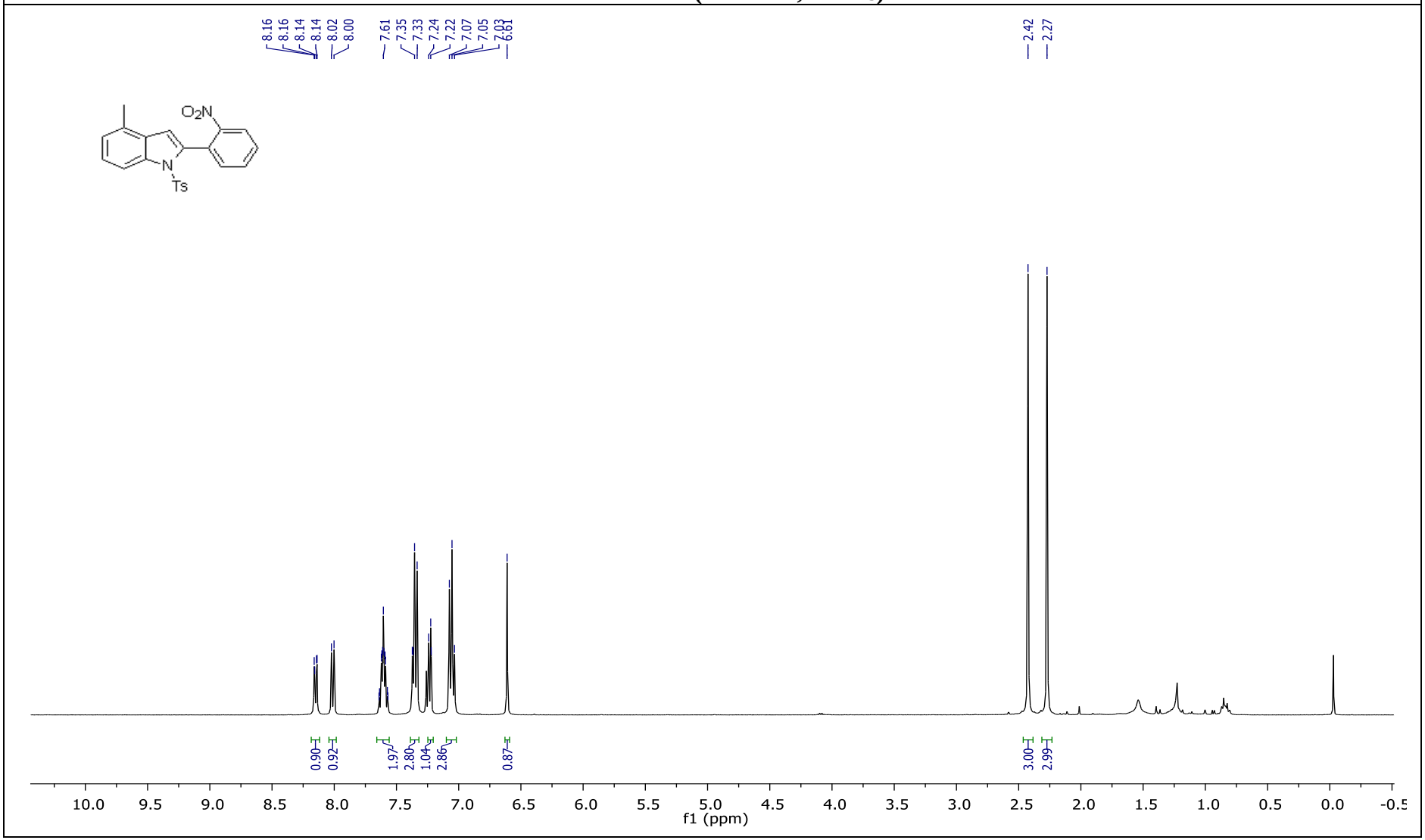

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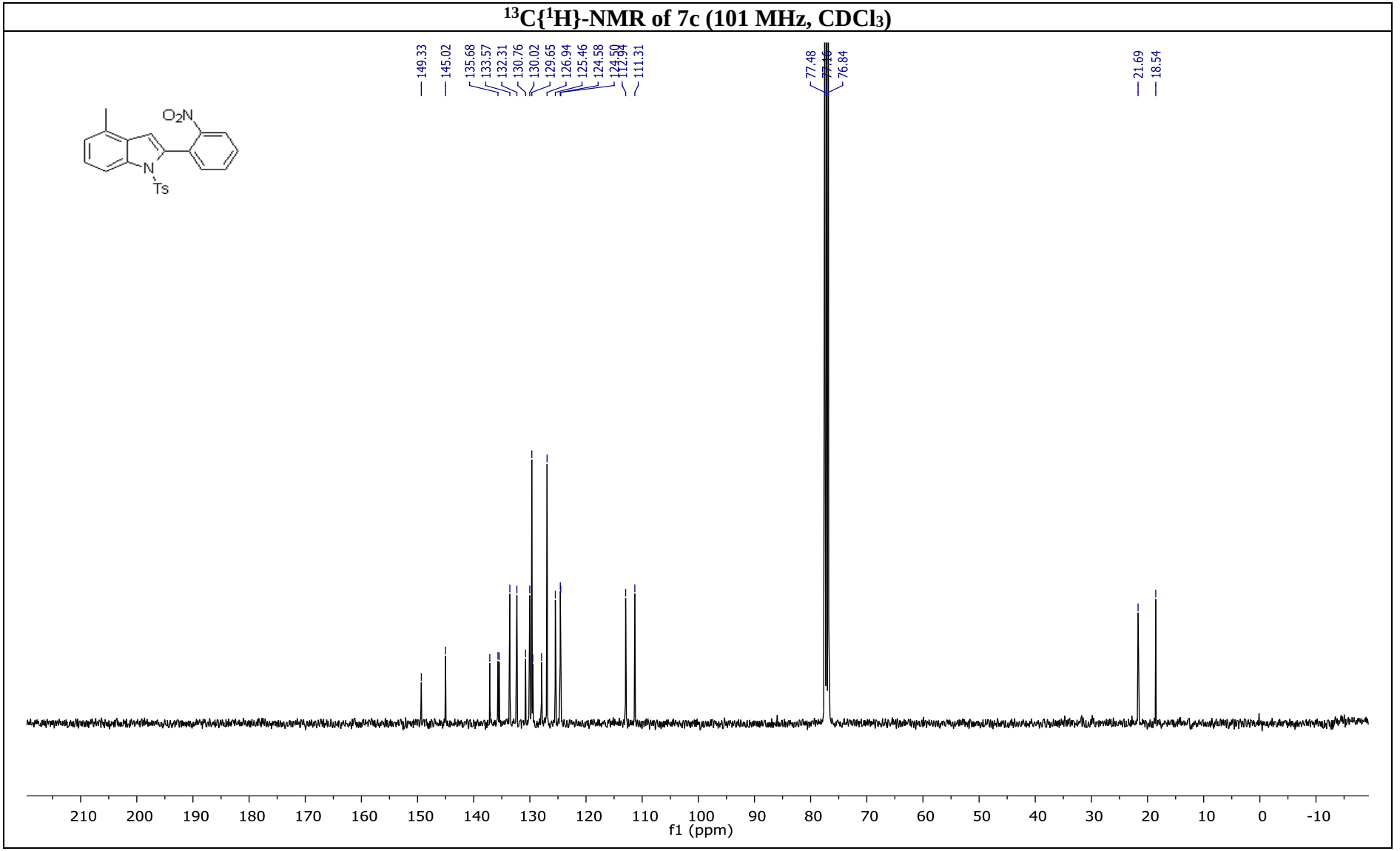

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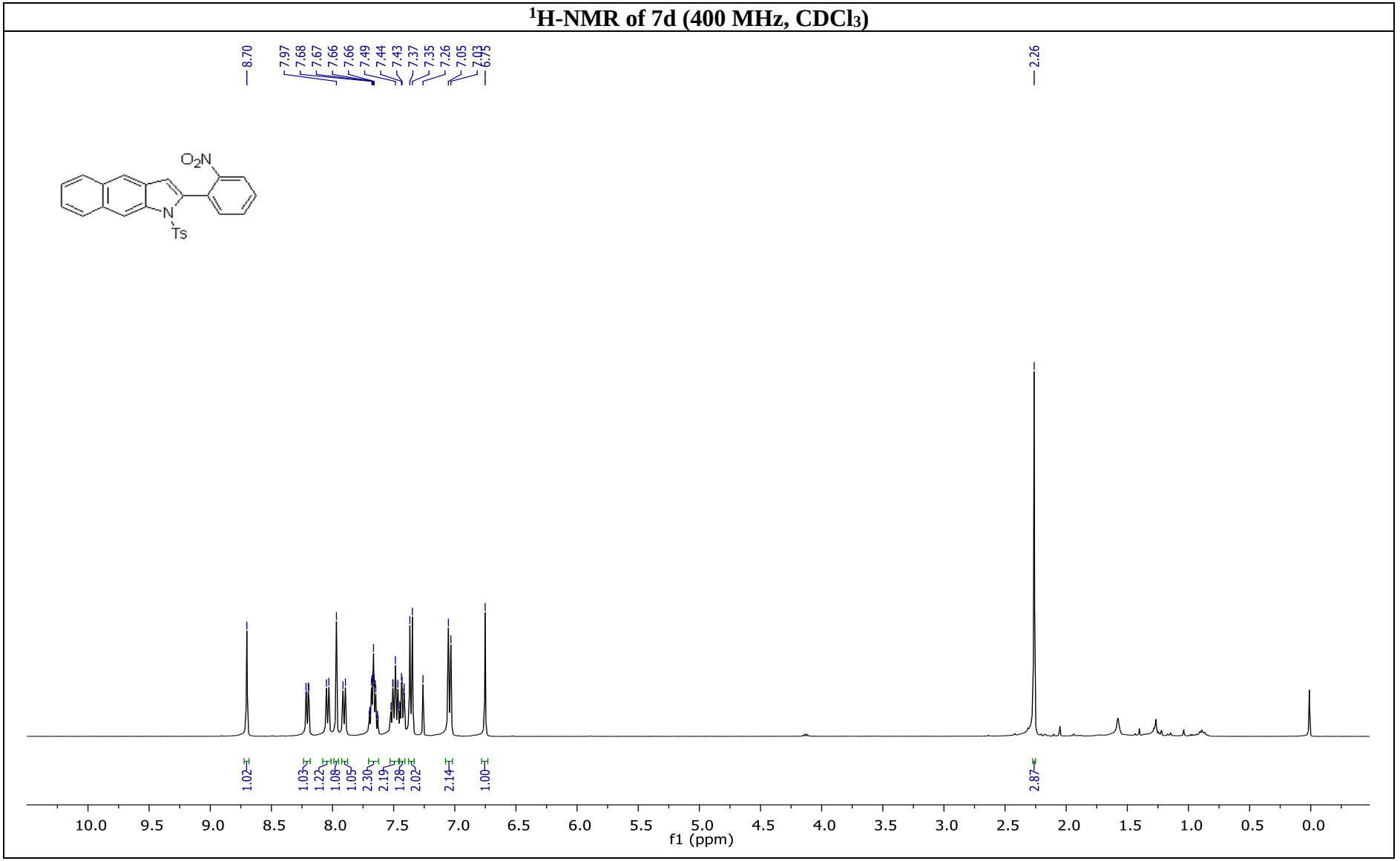

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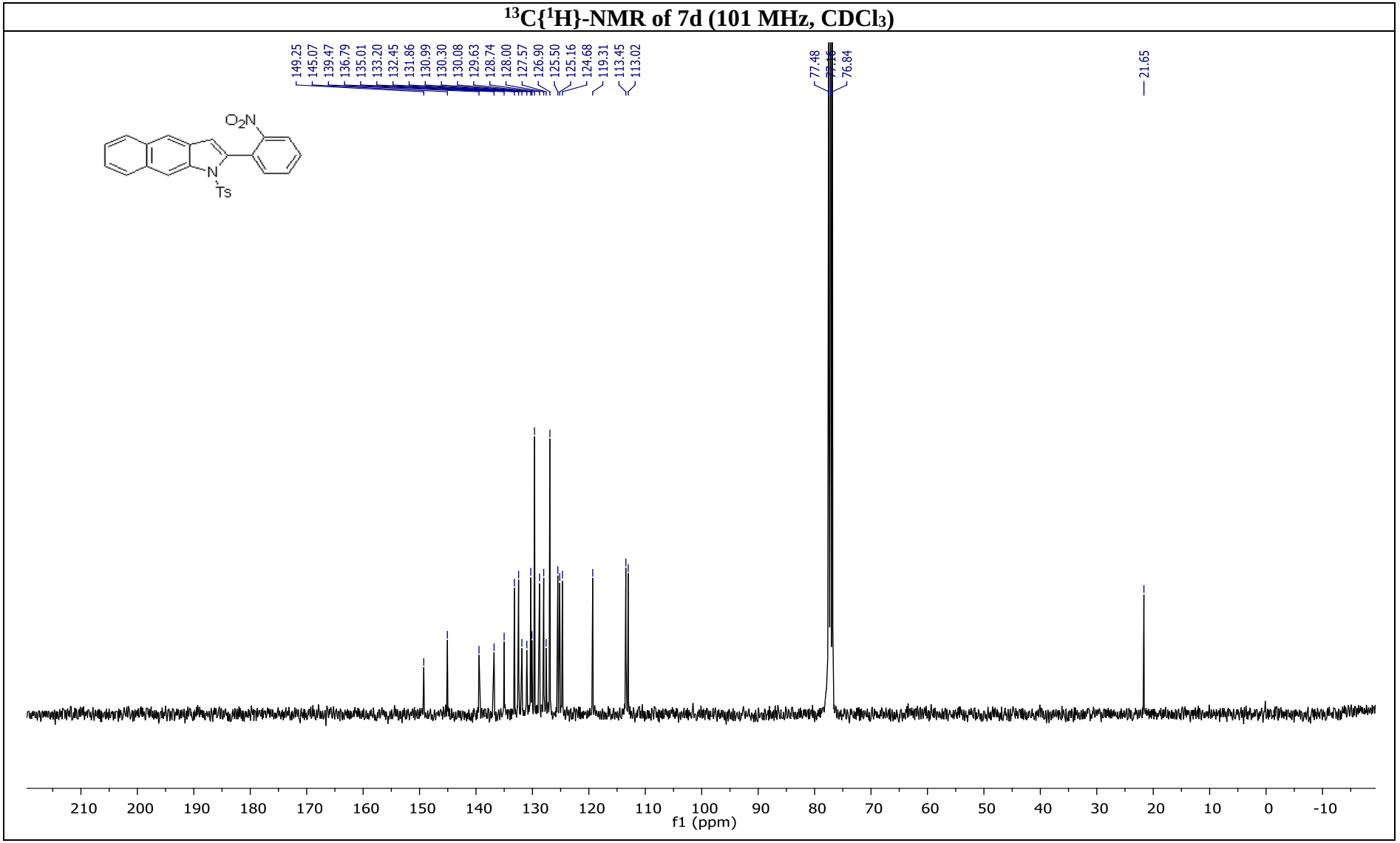

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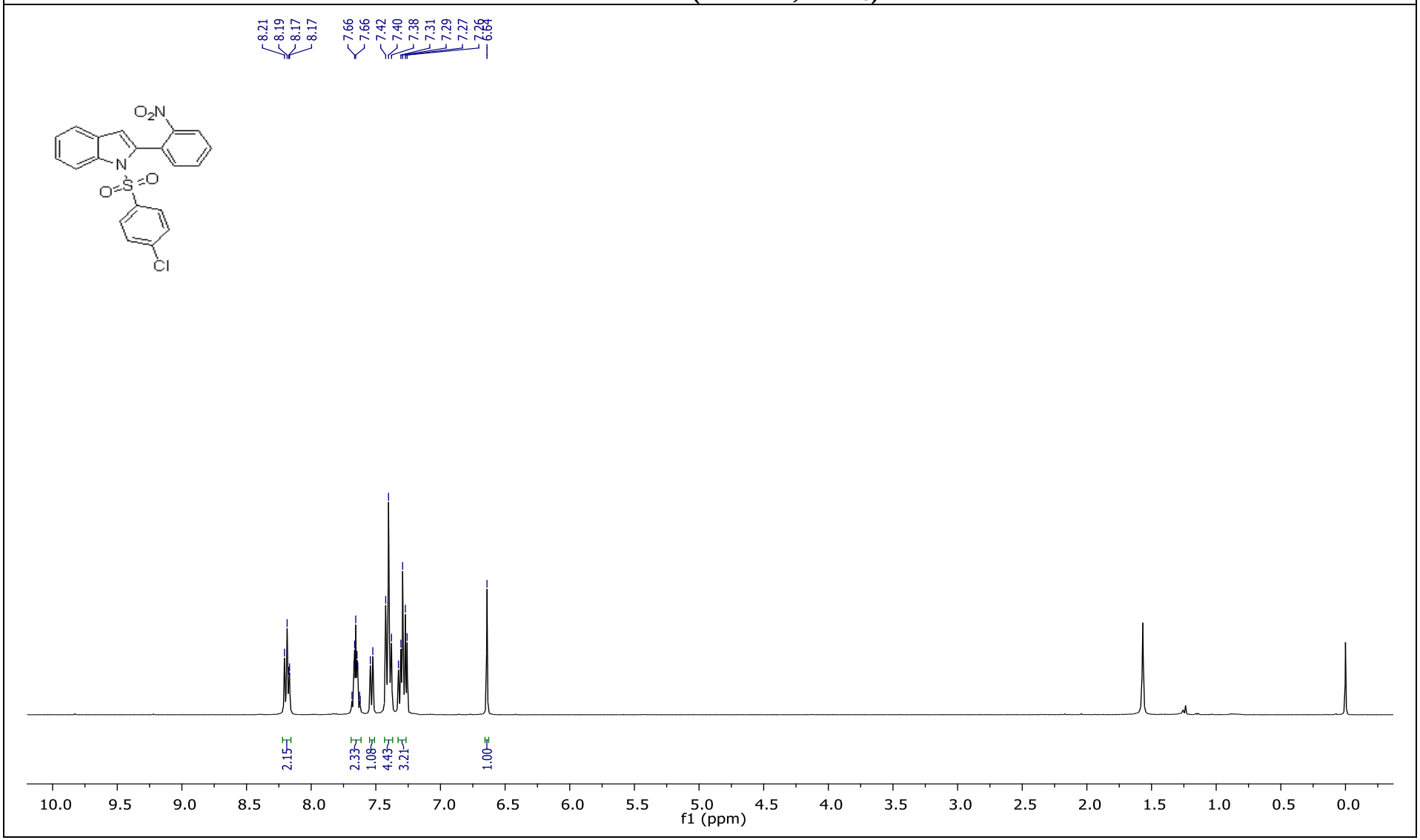

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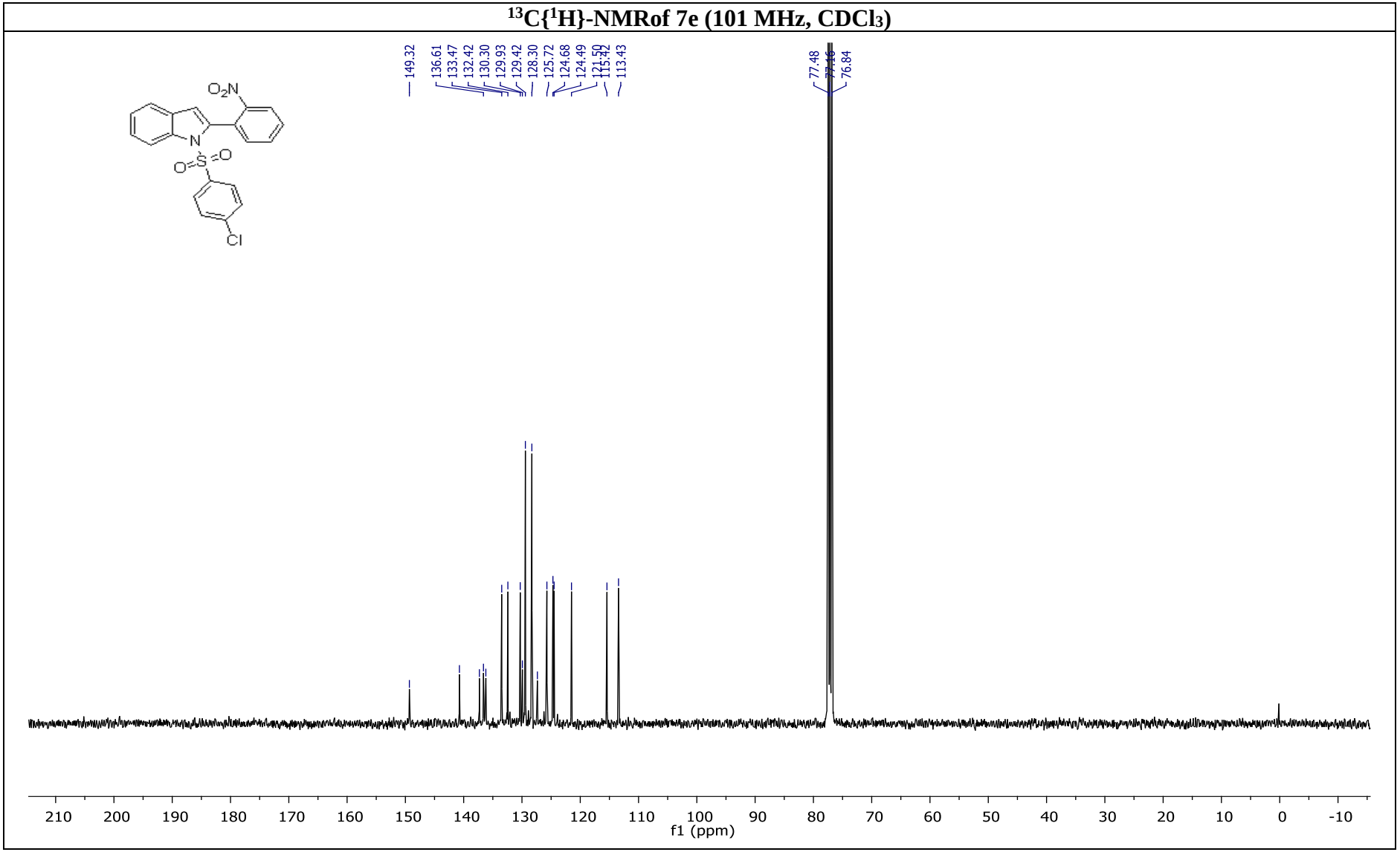
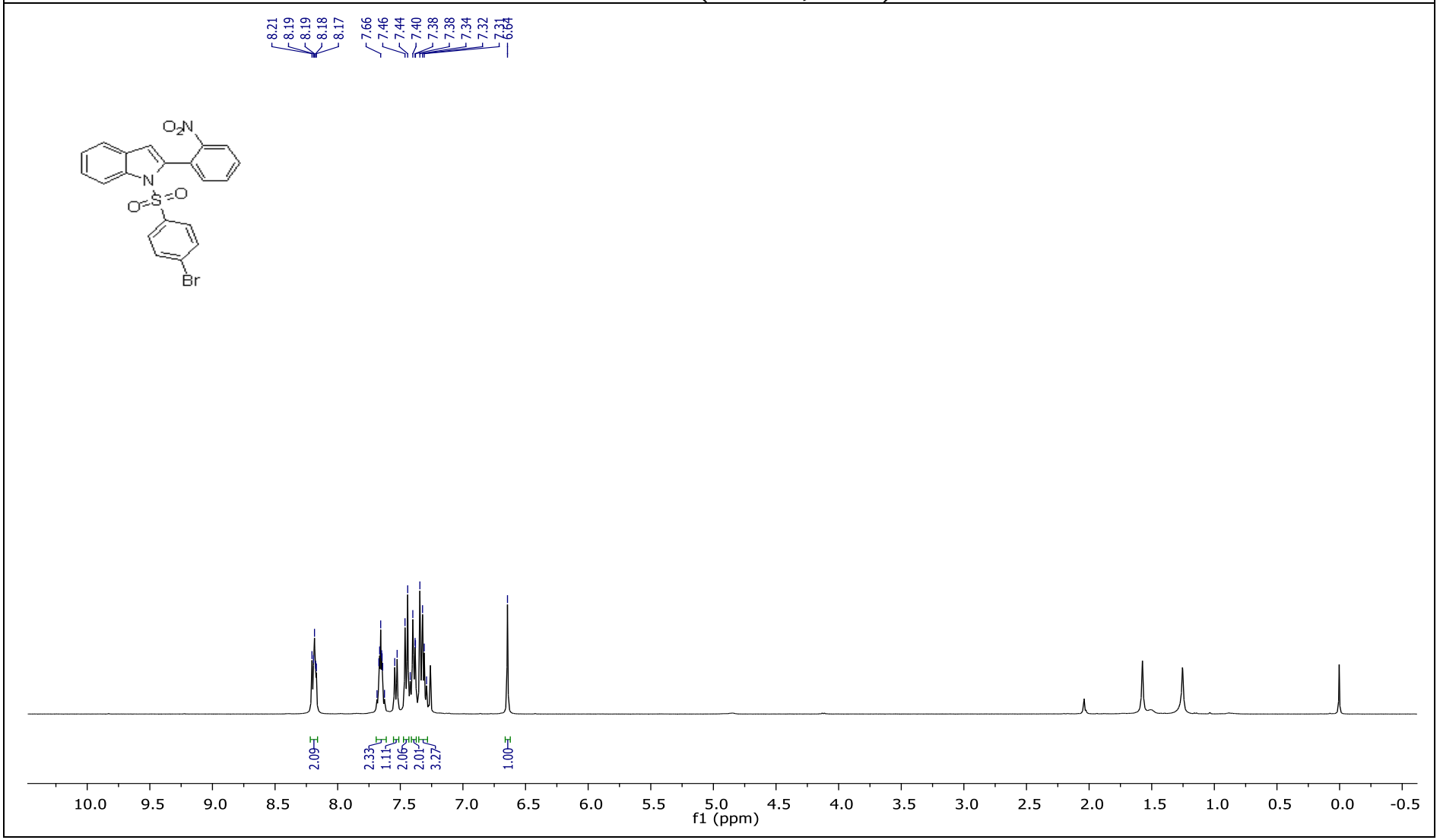


^{1}H-NMR of 7f (400 MHz, $CDCl_3$)



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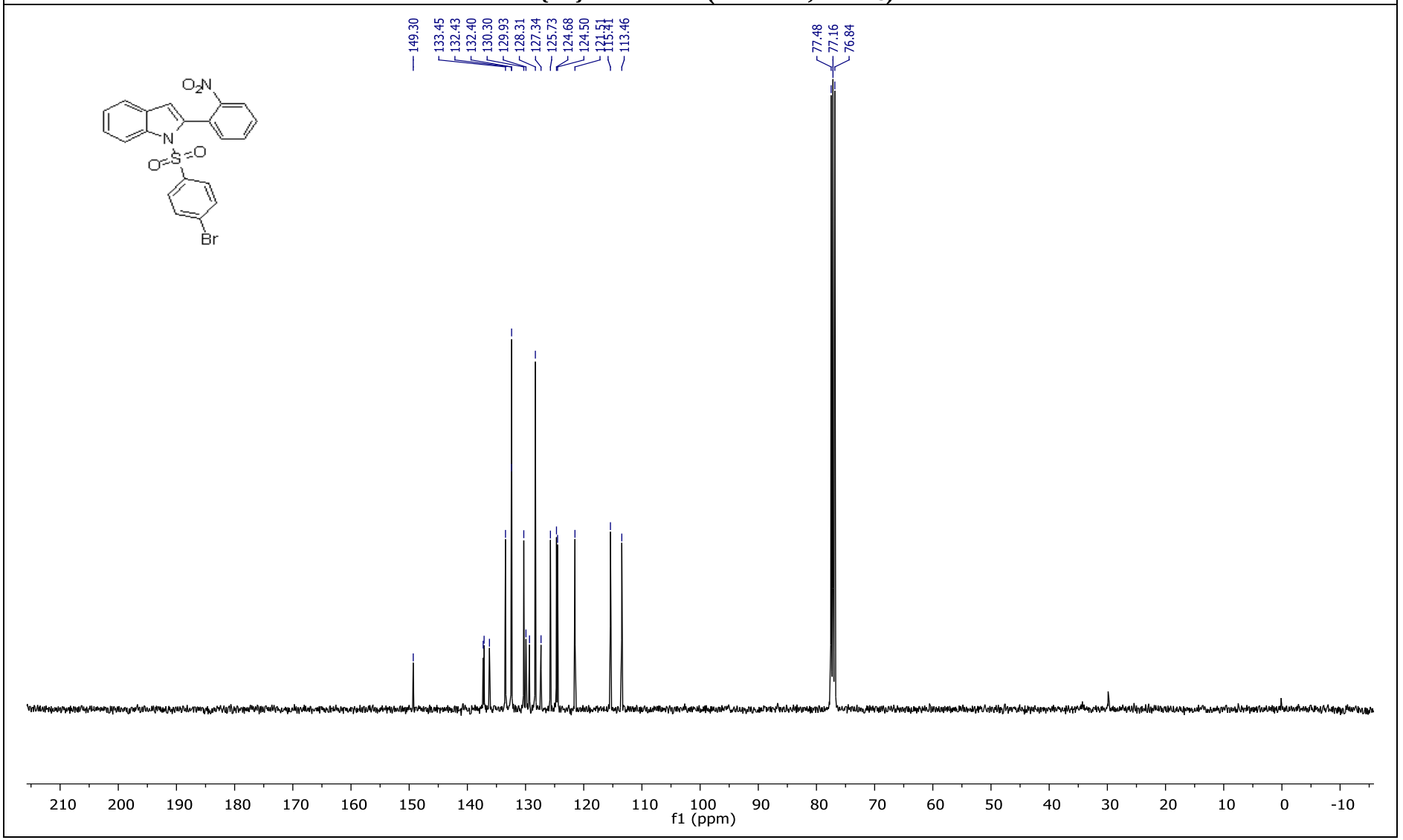
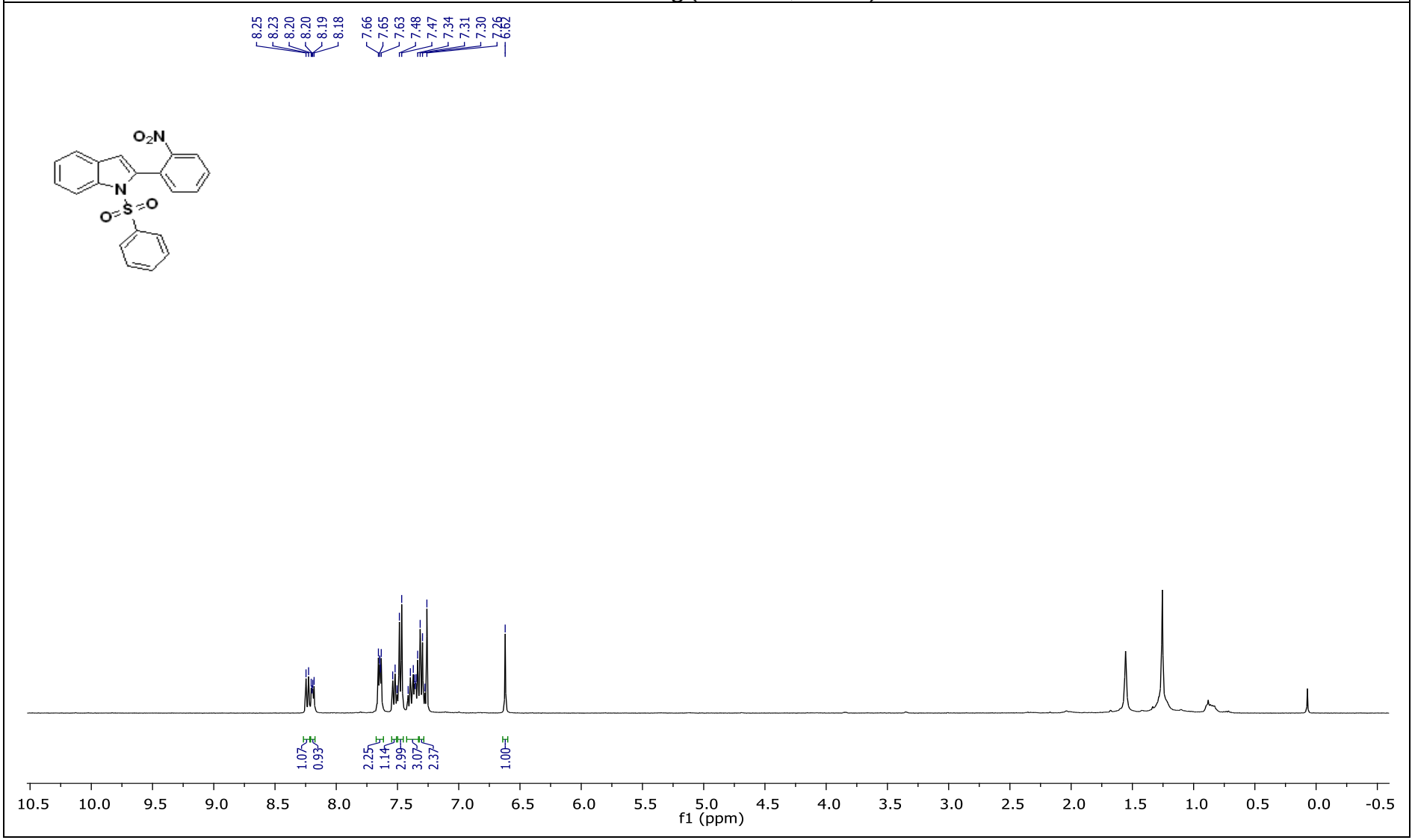


^{1}H-NMR of 7g (400 MHz, $CDCl_3$)



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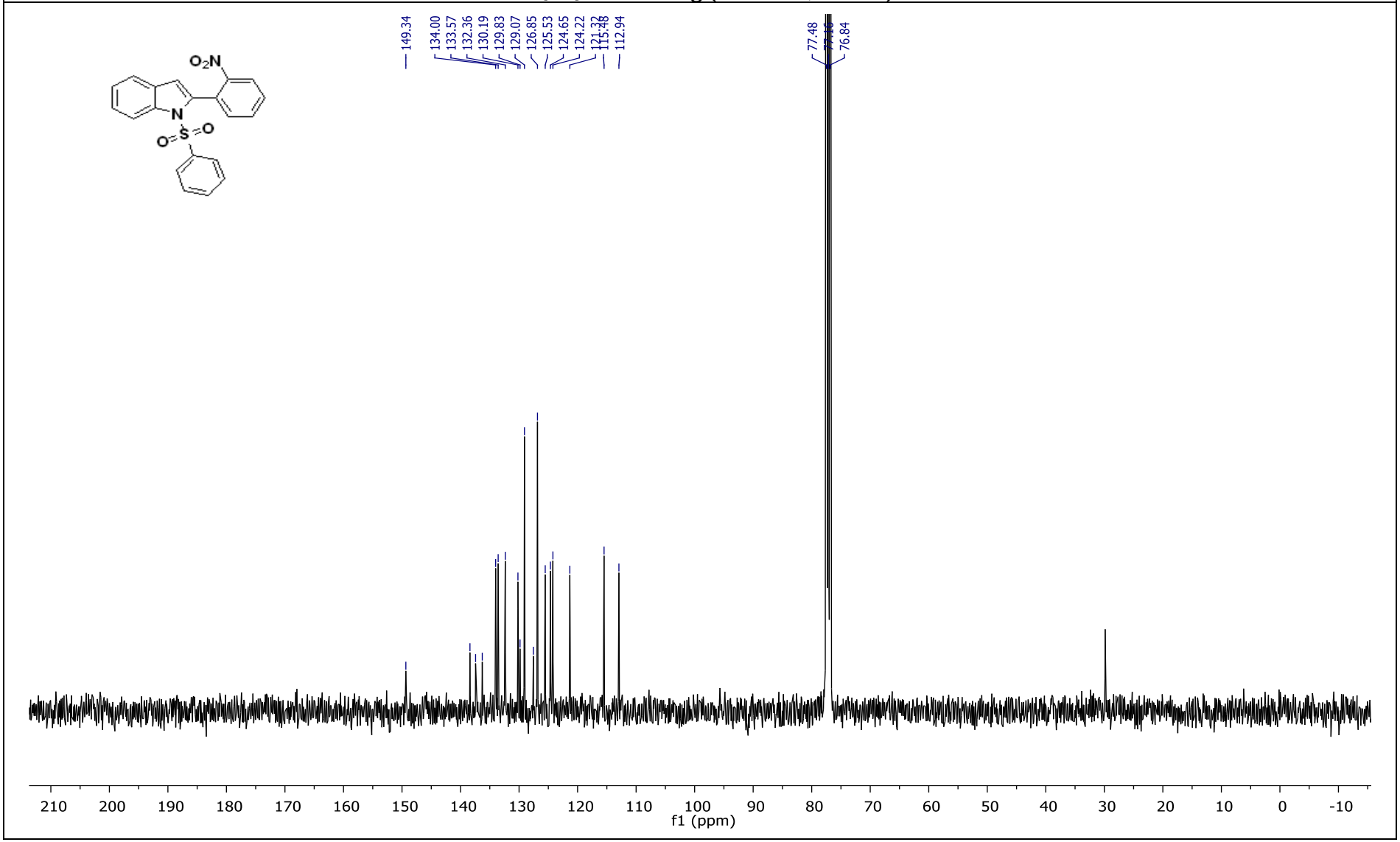
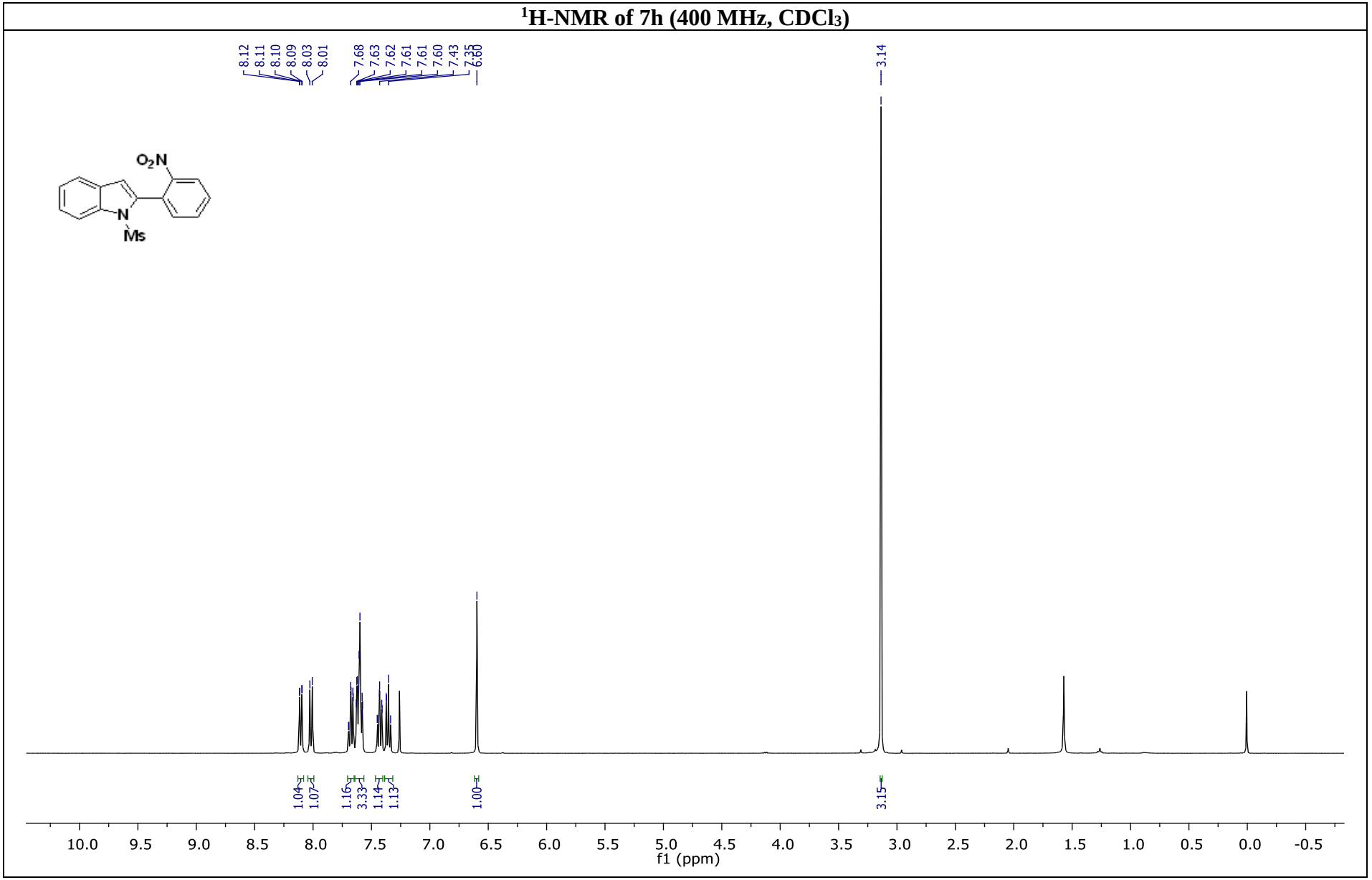
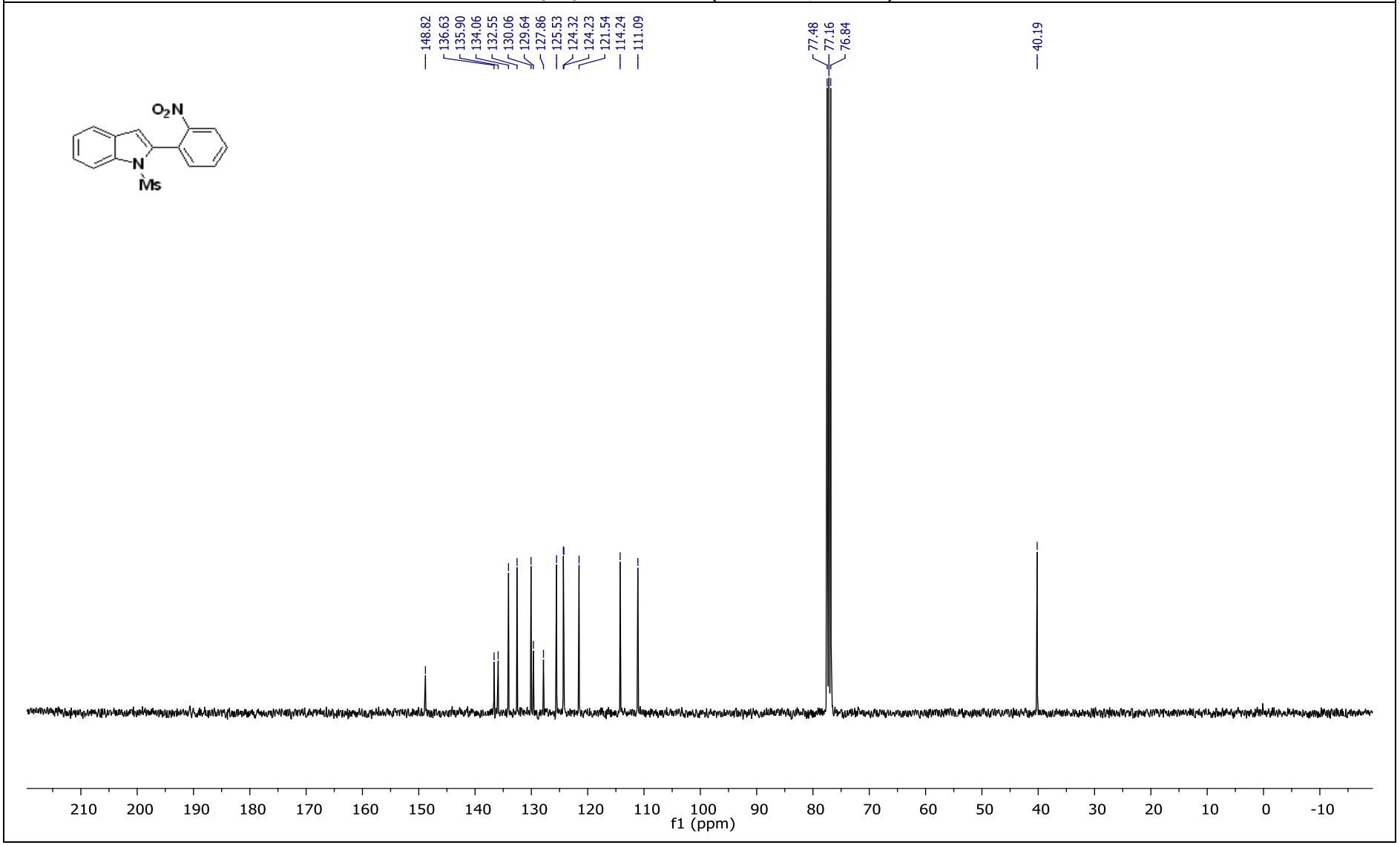


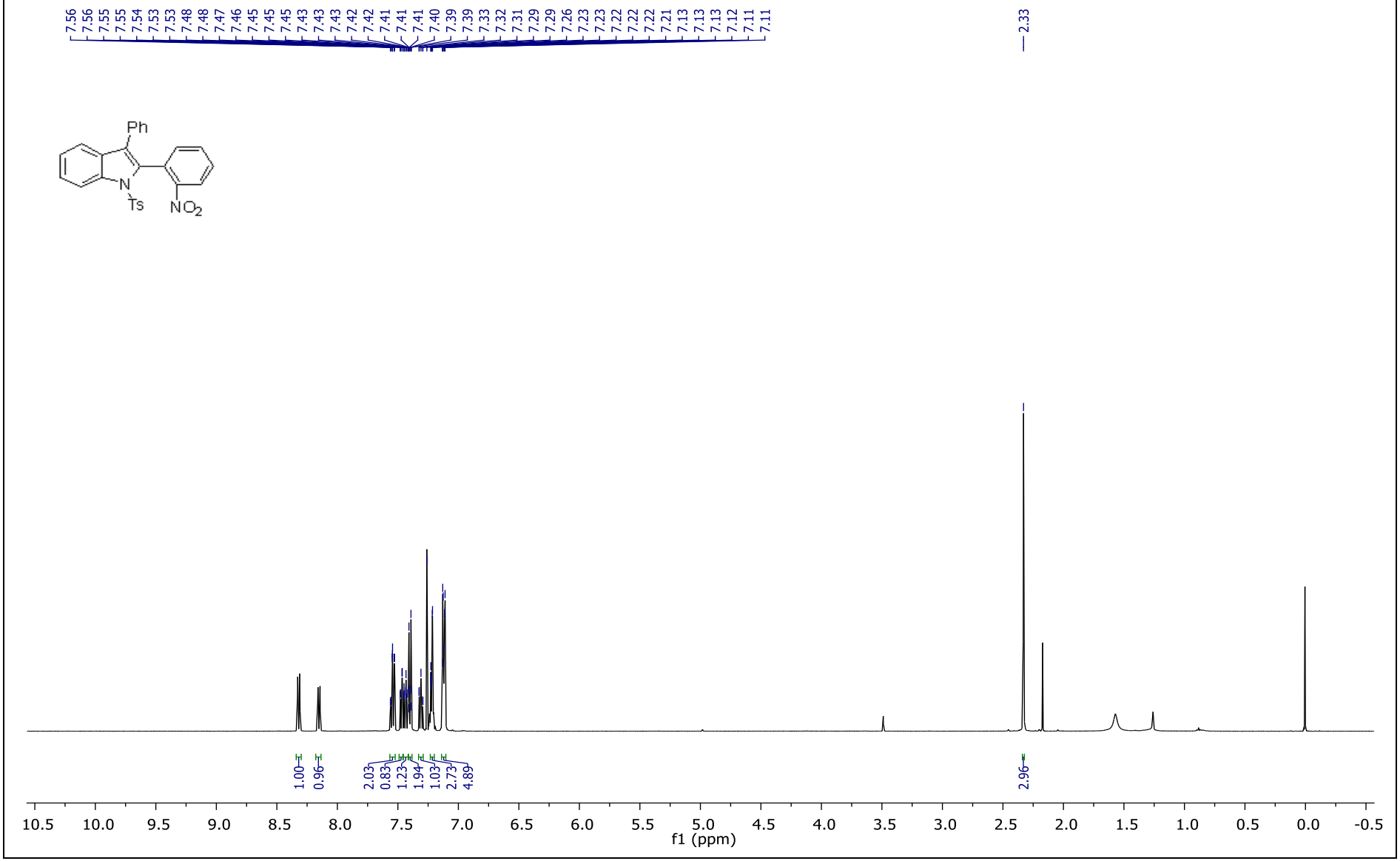
^{1}H-NMR of 7h (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-NMR of 7h (101 MHz, $CDCl_3$)



^{1}H-NMR of 7i (500 MHz, $CDCl_3$)



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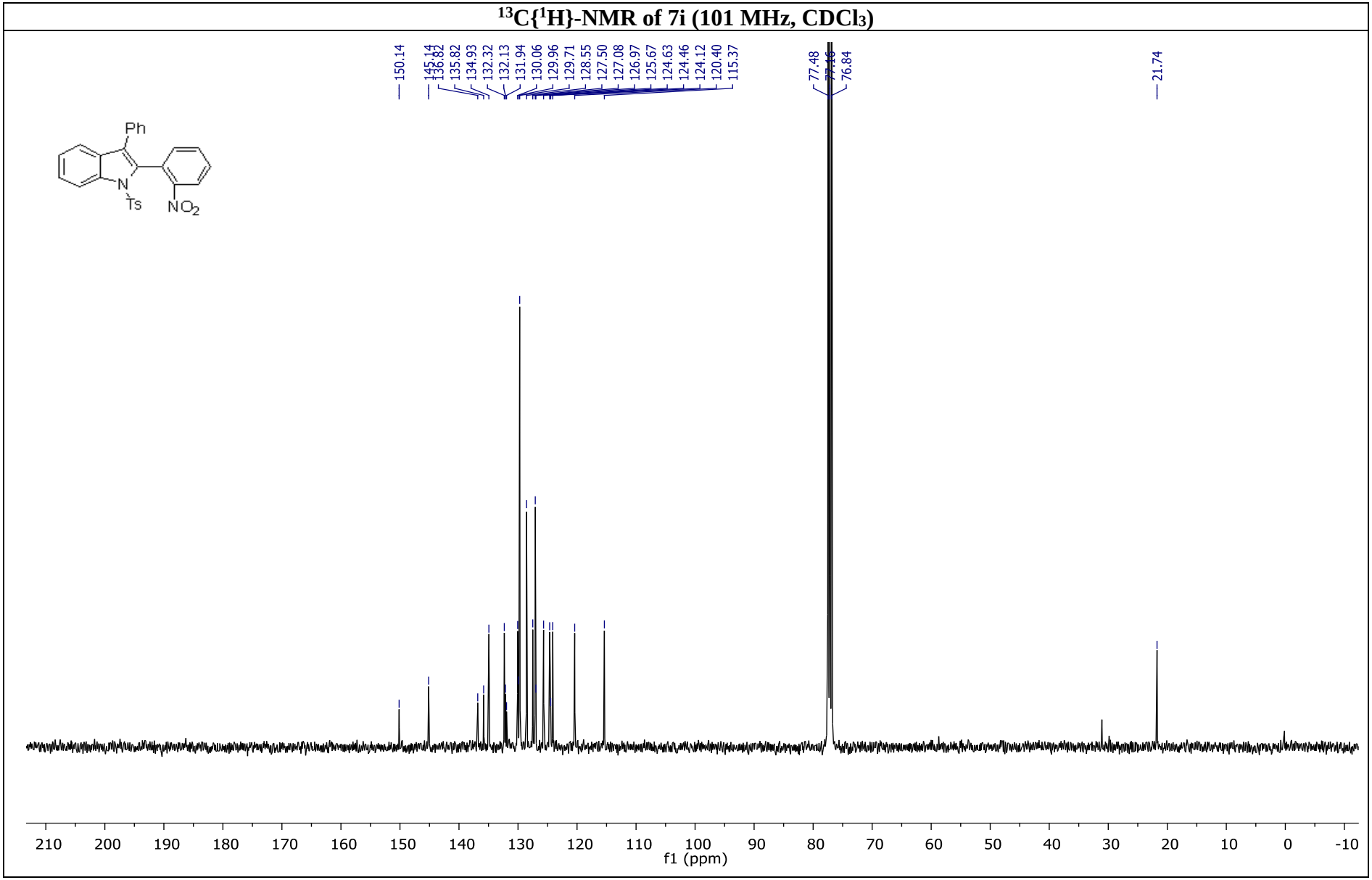
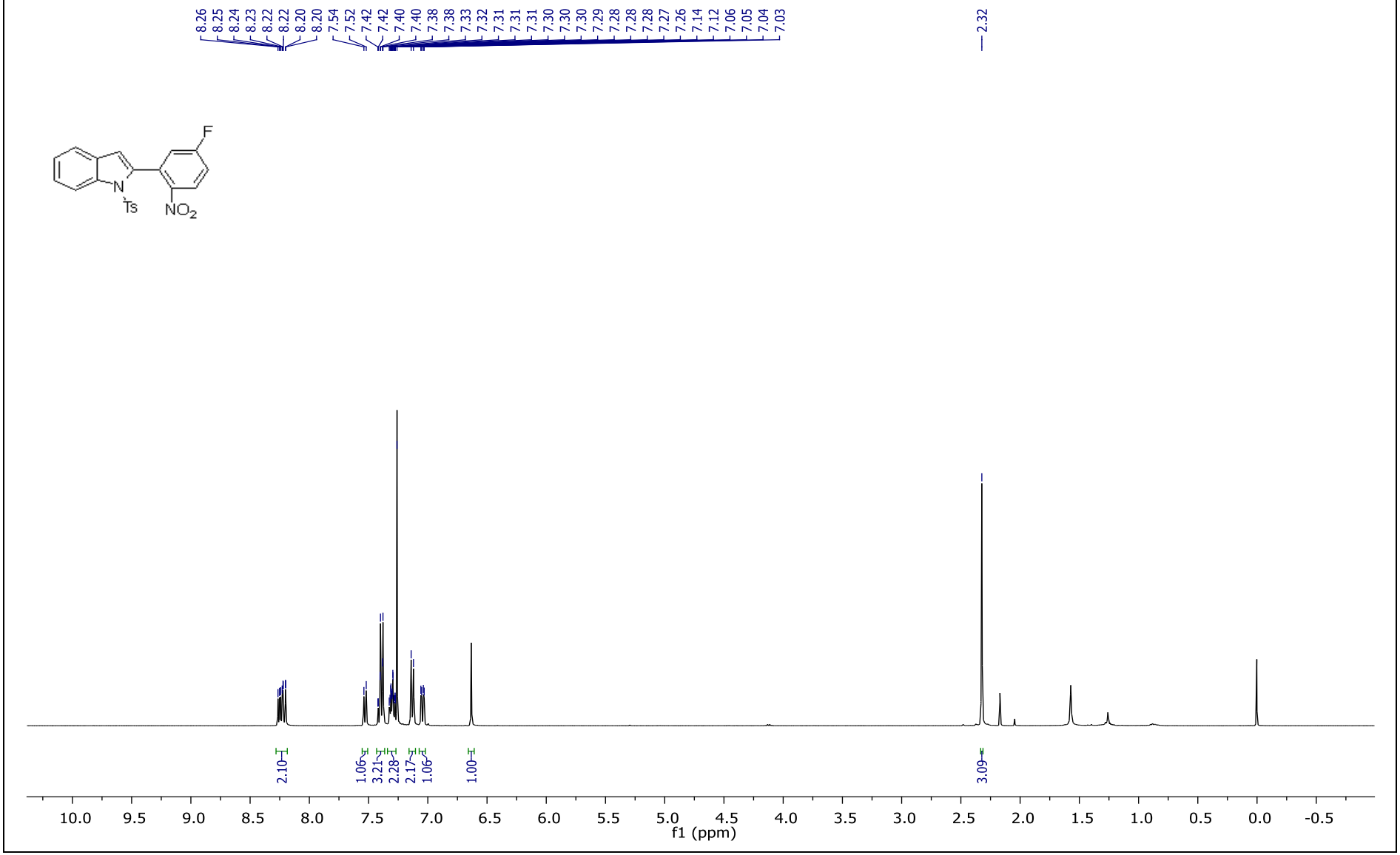
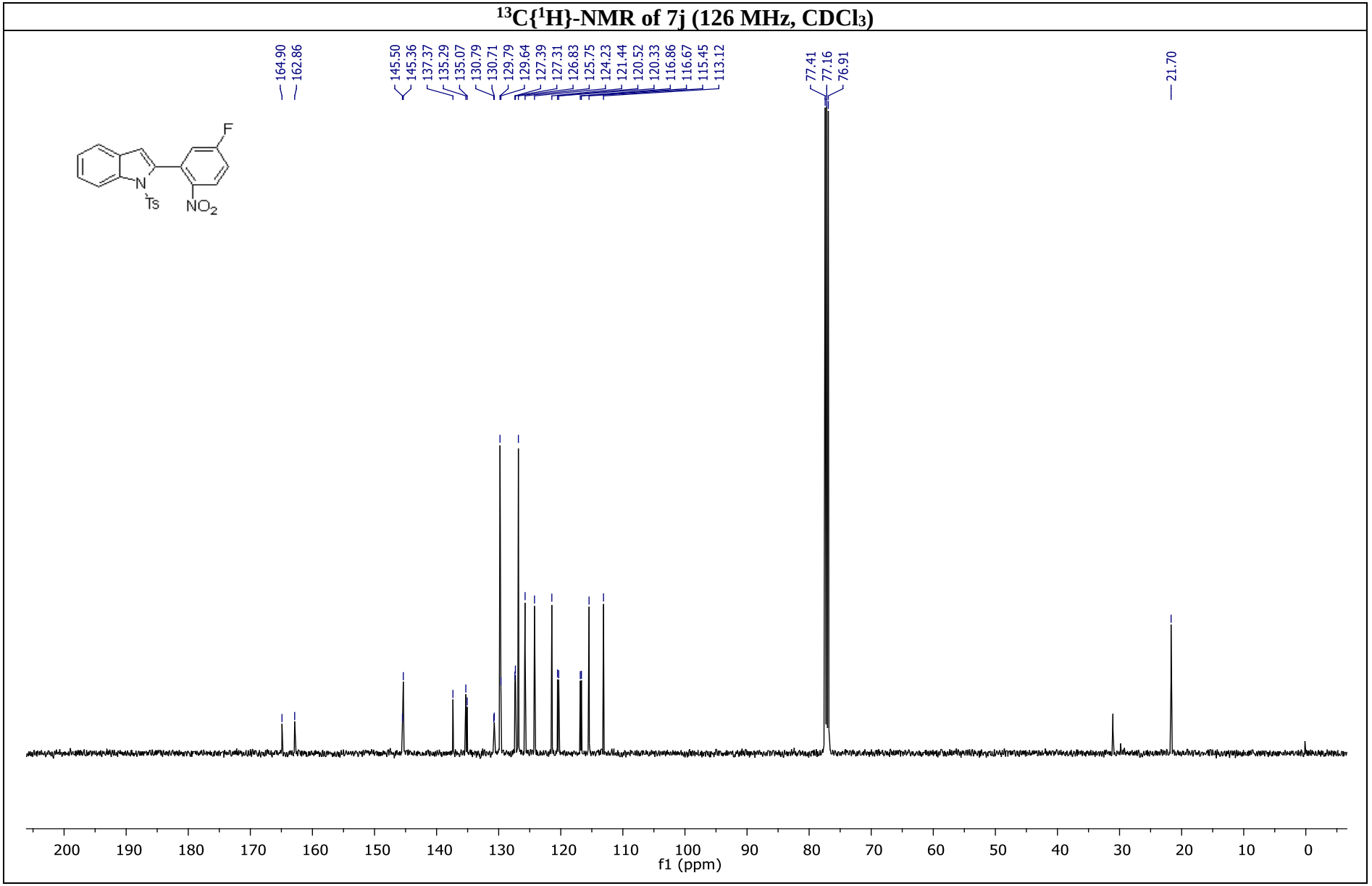


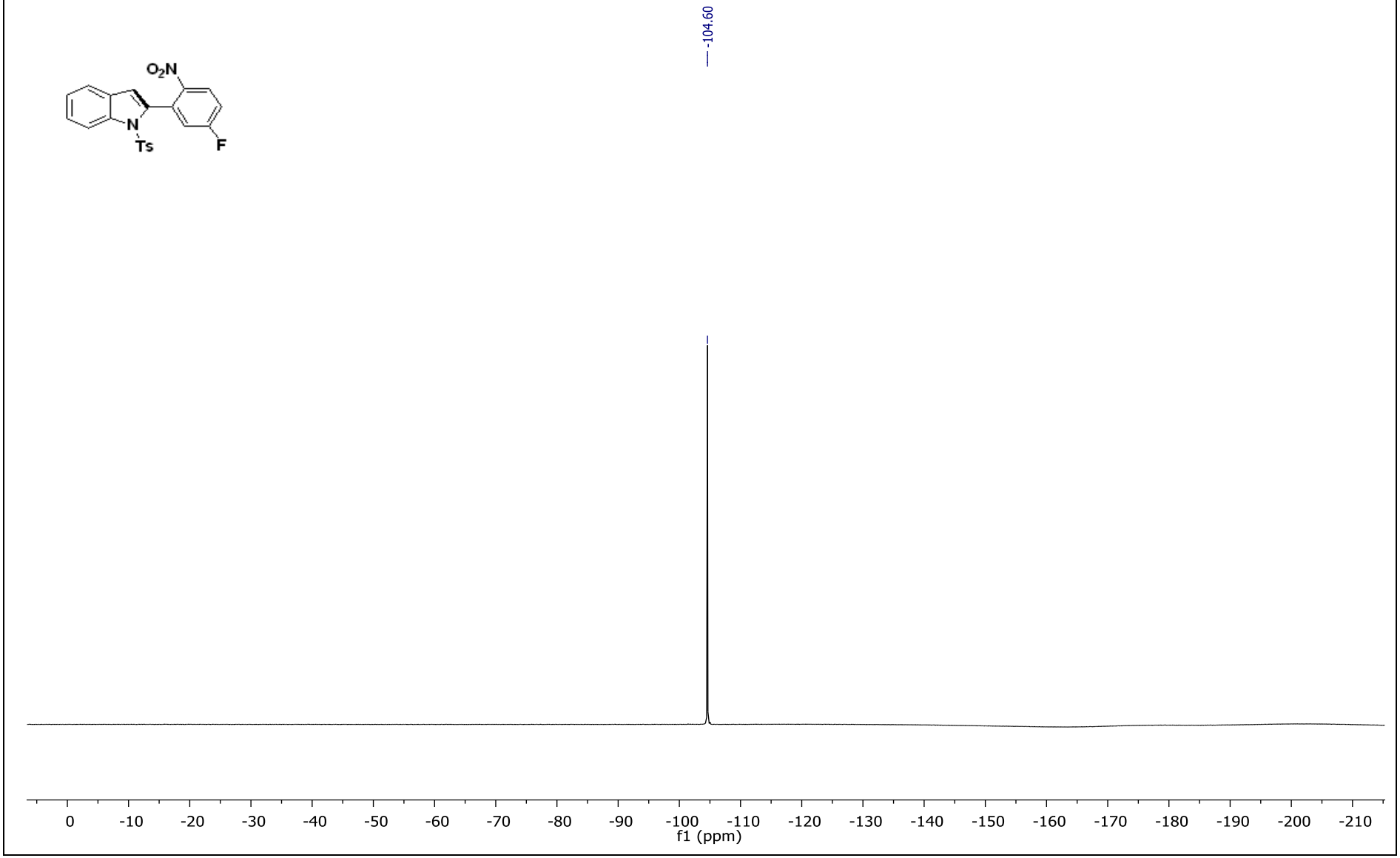
^{1}H-NMR of 7j (400 MHz, $CDCl_3$)



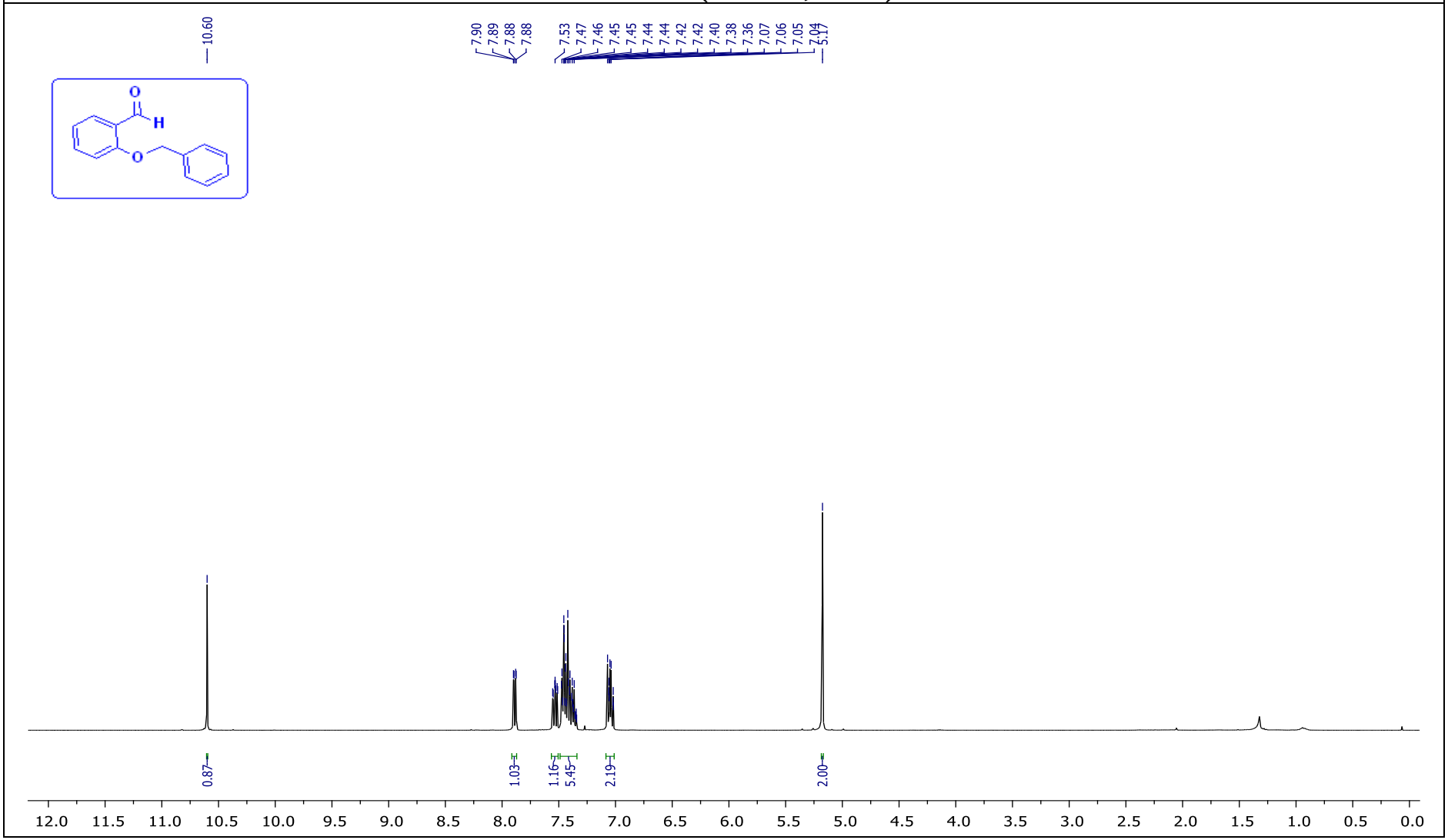
$^{13}C\{^{1}H\}$-NMR of 7j (126 MHz, $CDCl_3$)



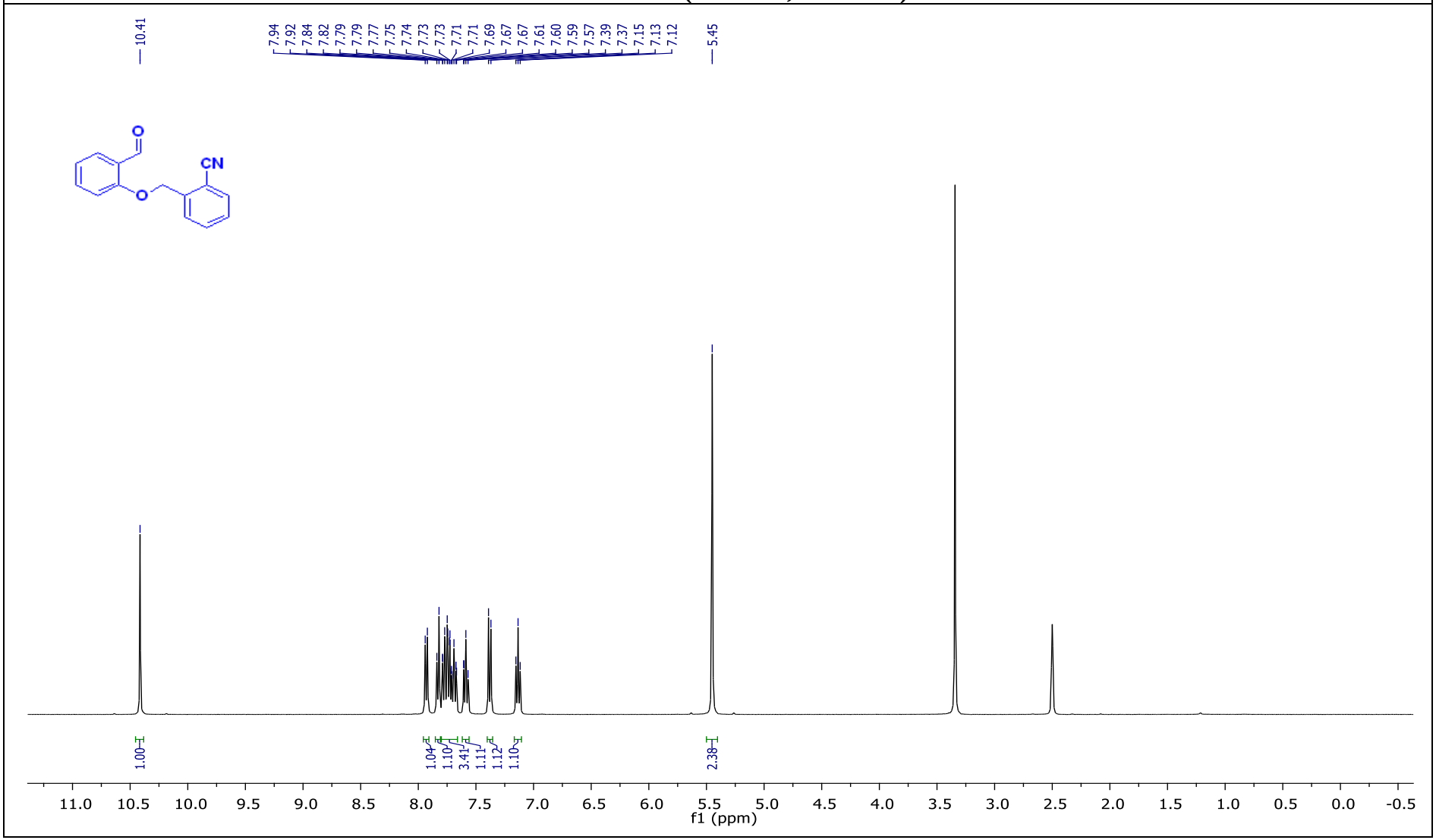
^{19}F-NMR of 7j (376 MHz, $CDCl_3$)



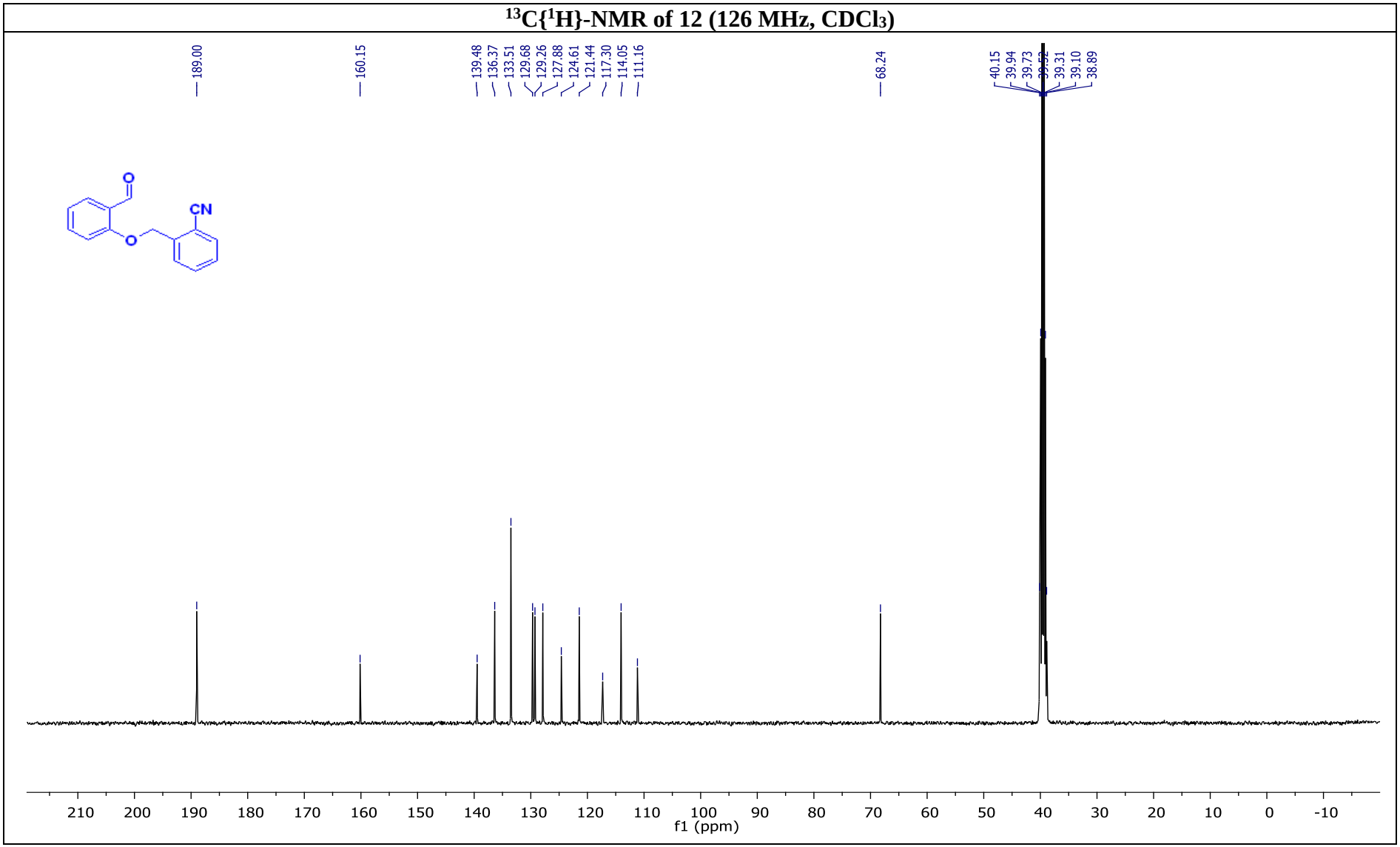
^{1}H-NMR of 9 (400 MHz, $CDCl_3$)



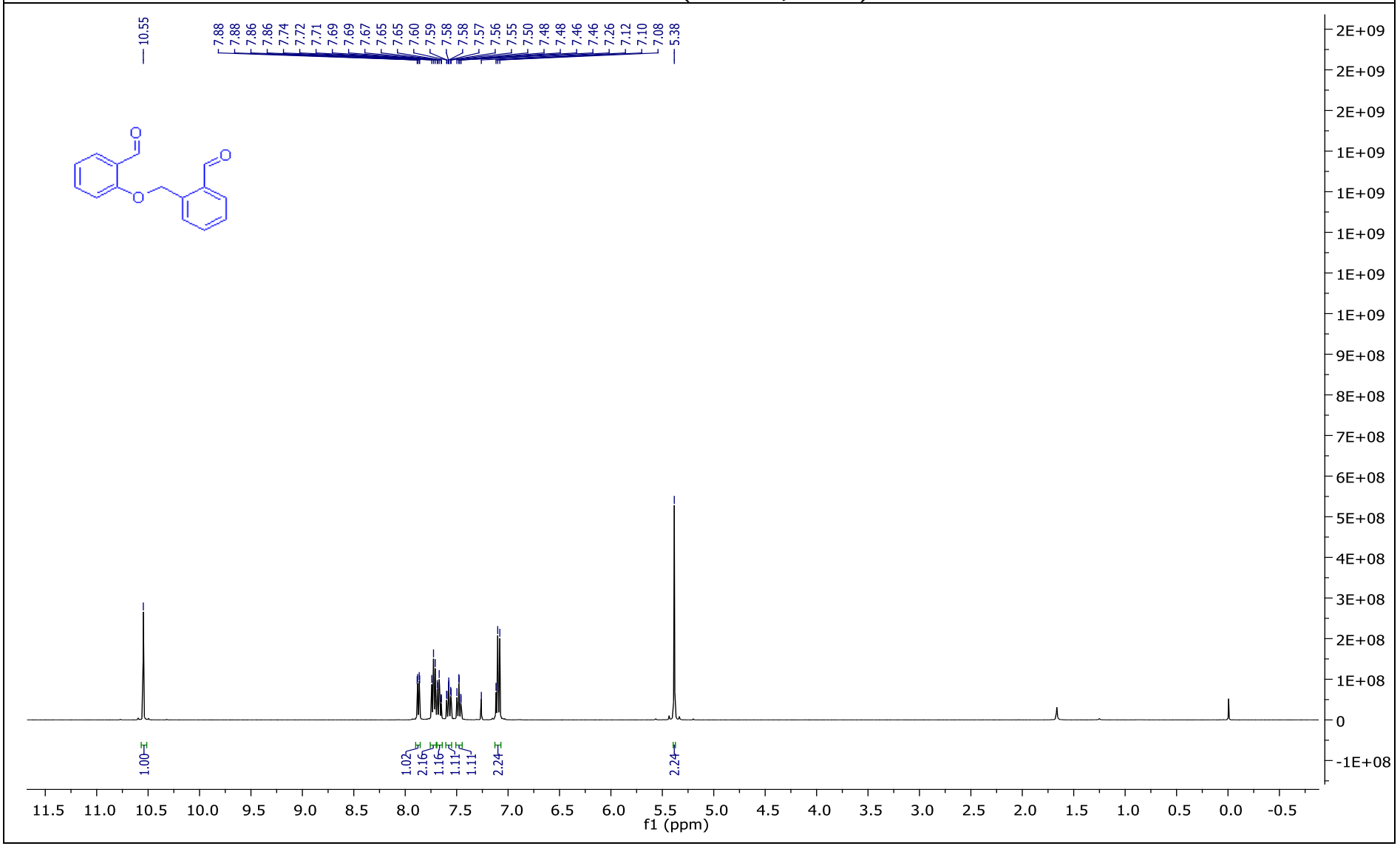
^{1}H-NMR of 12 (400 MHz, DMSO d_6)



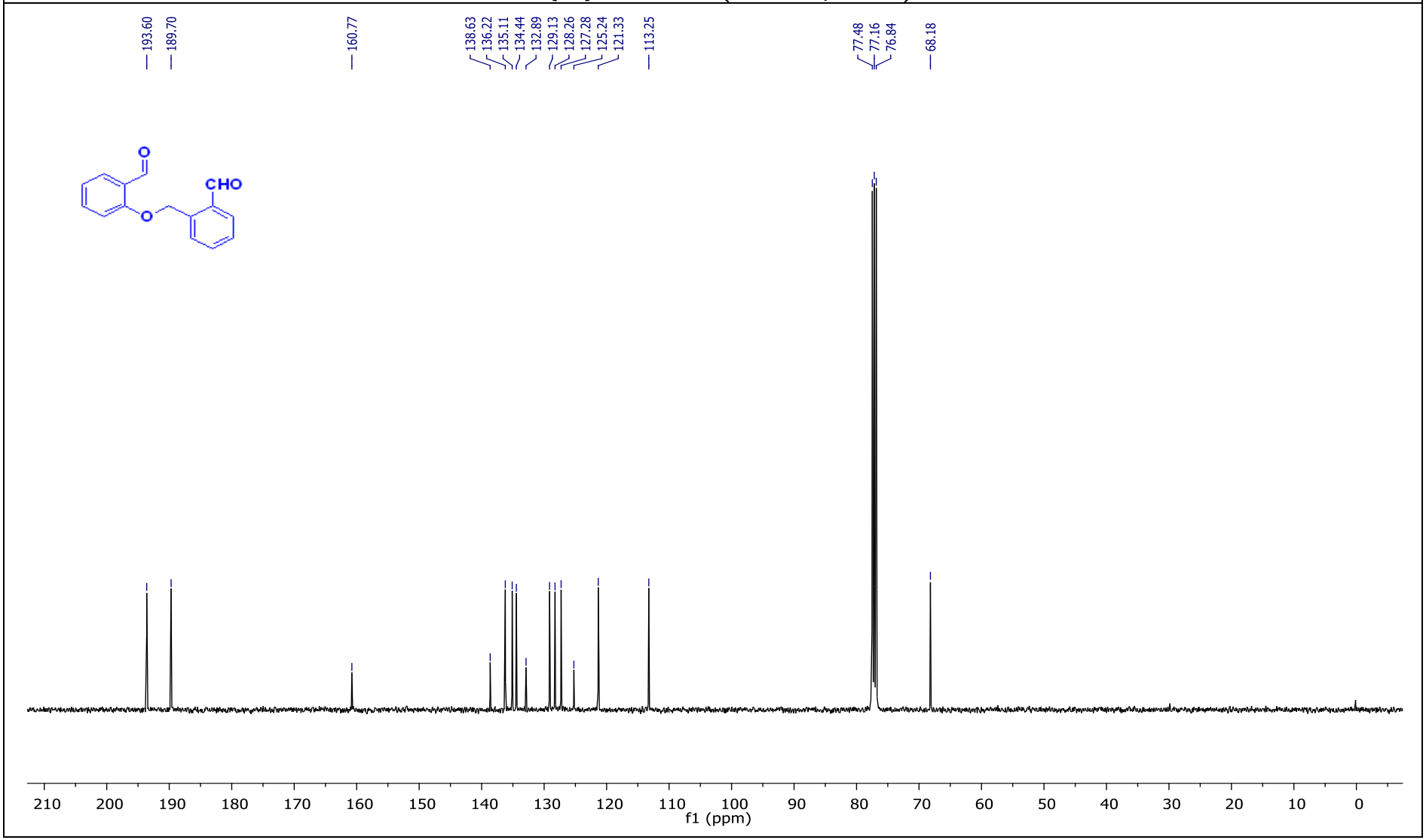
$^{13}C\{^{1}H\}$-NMR of 12 (126 MHz, $CDCl_3$)



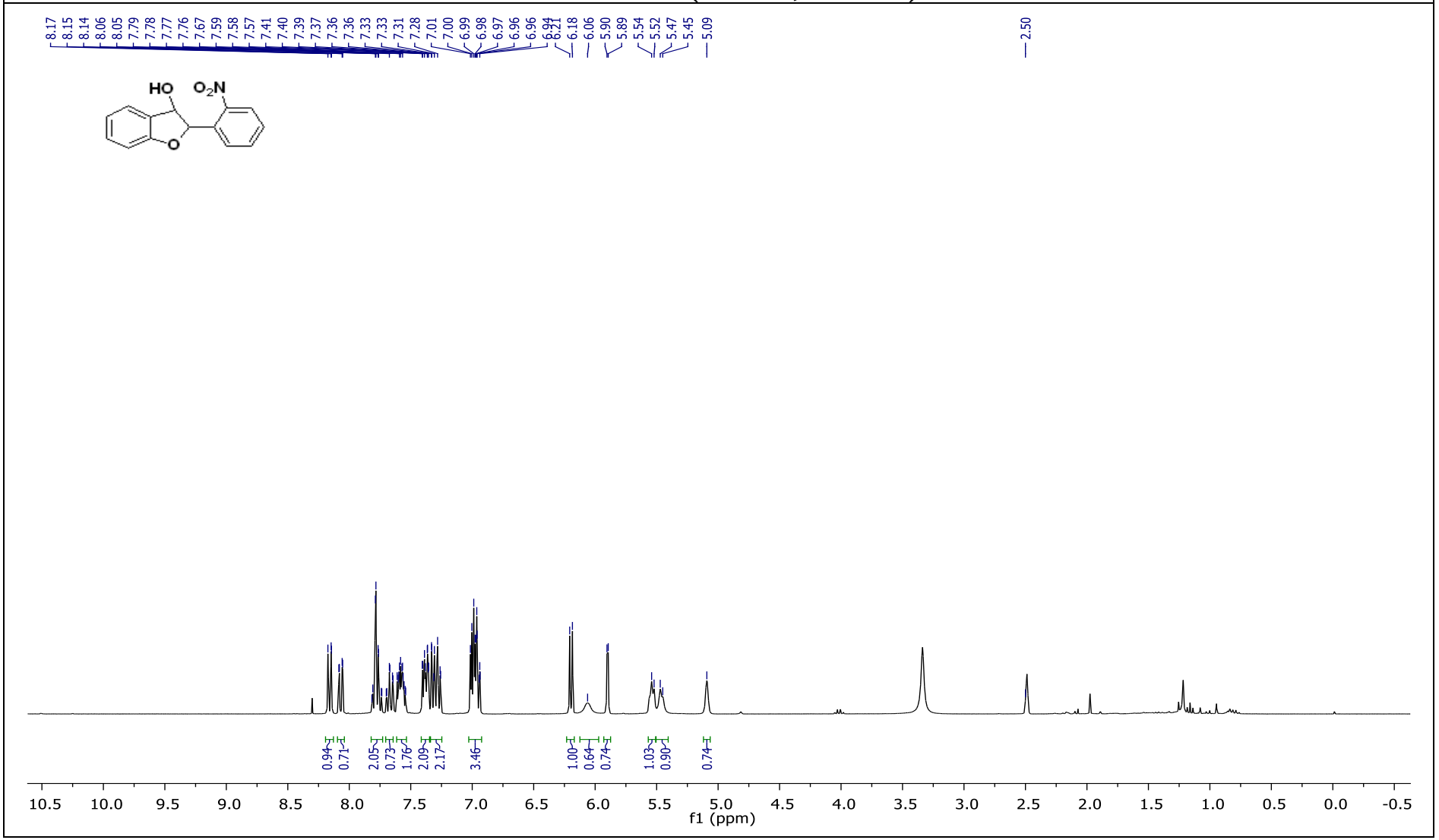
^{1}H-NMR of 13 (400 MHz, $CDCl_3$)



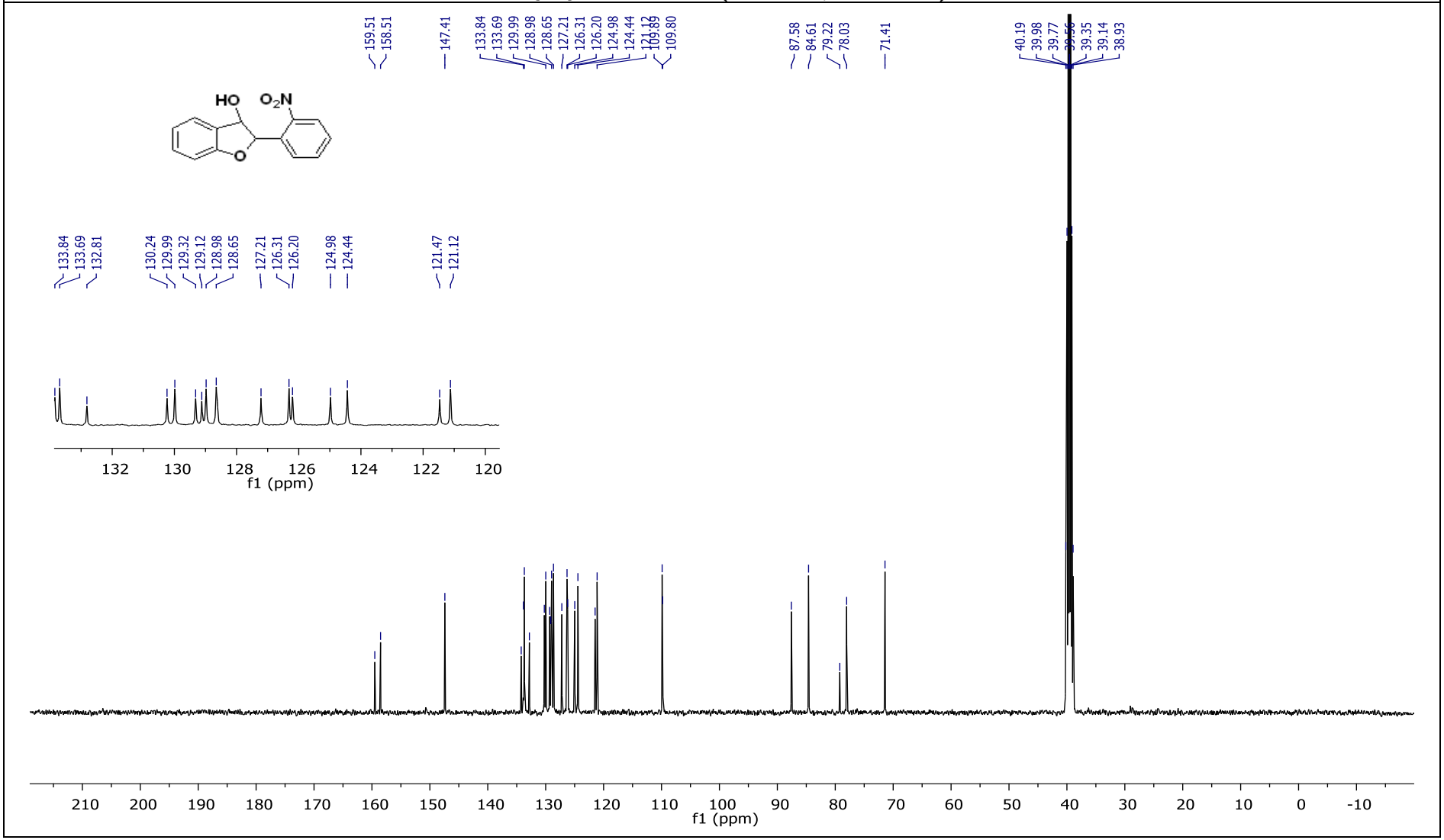
$^{13}C\{^{1}H\}$-NMR of 13 (101 MHz, $CDCl_3$)



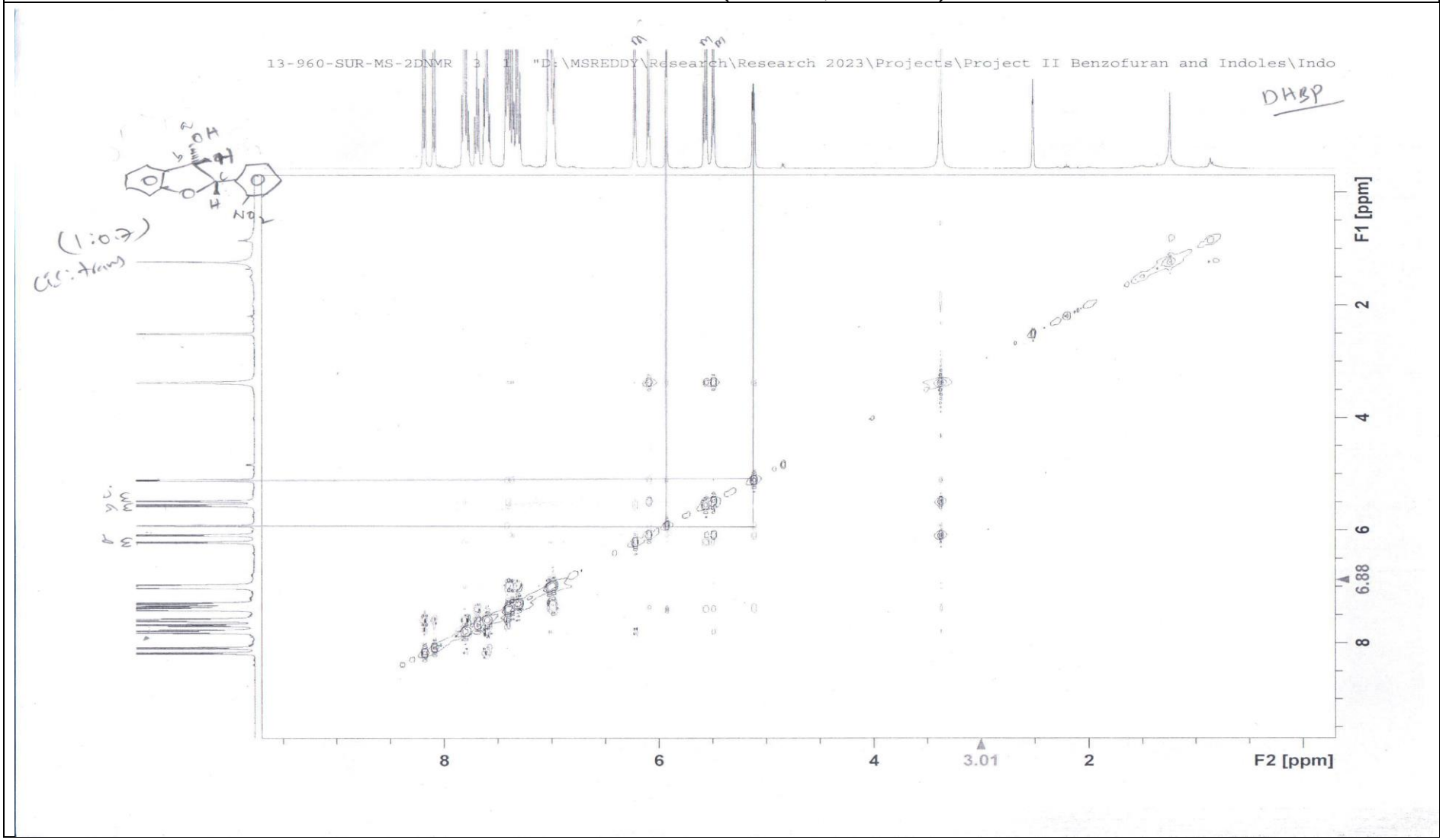
^{1}H-NMR of 4ab (400 MHz, DMSO-d$_6$)



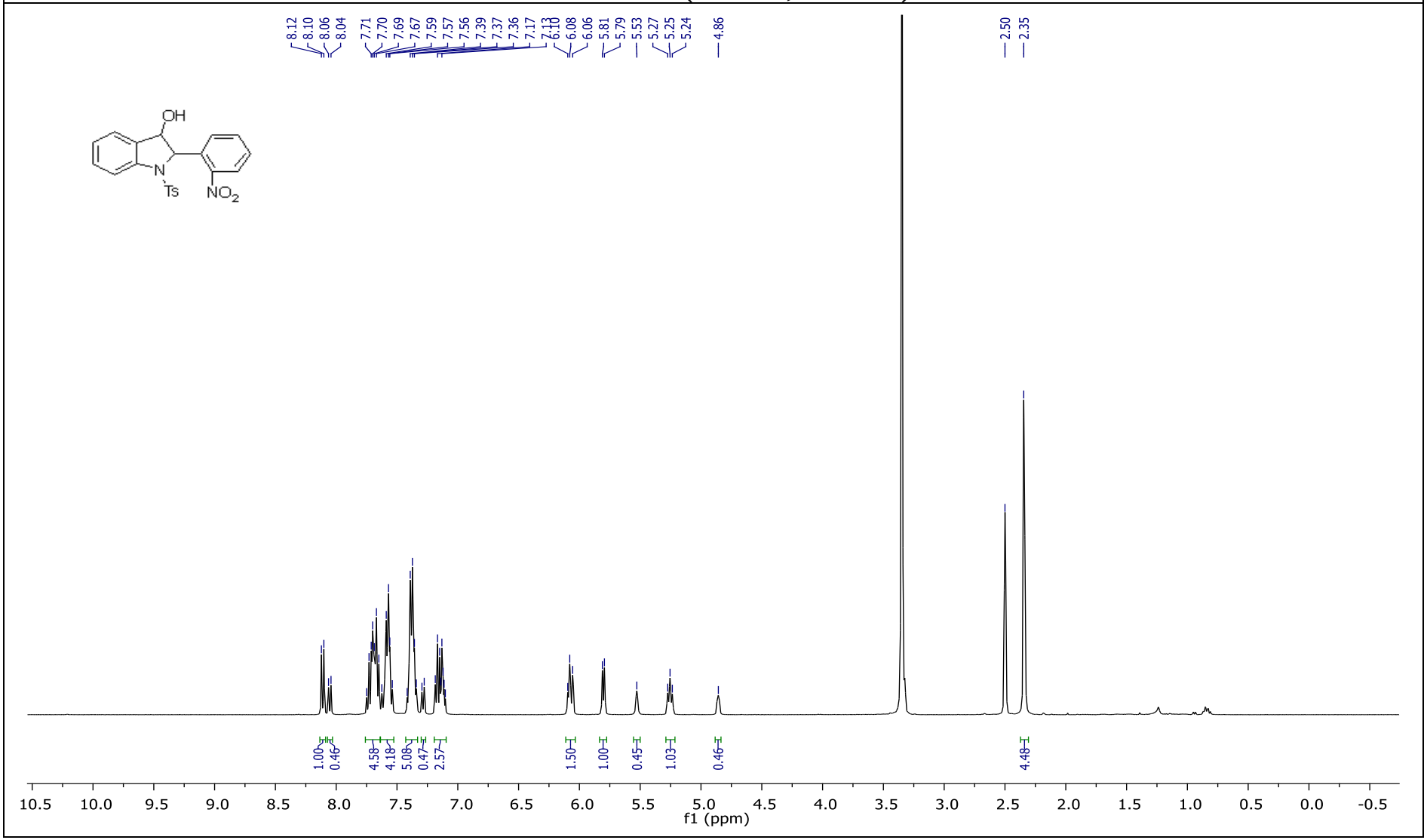
$^{13}C\{^{1}H\}$-NMR of 4ab (101 MHz, DMSO-d_6)



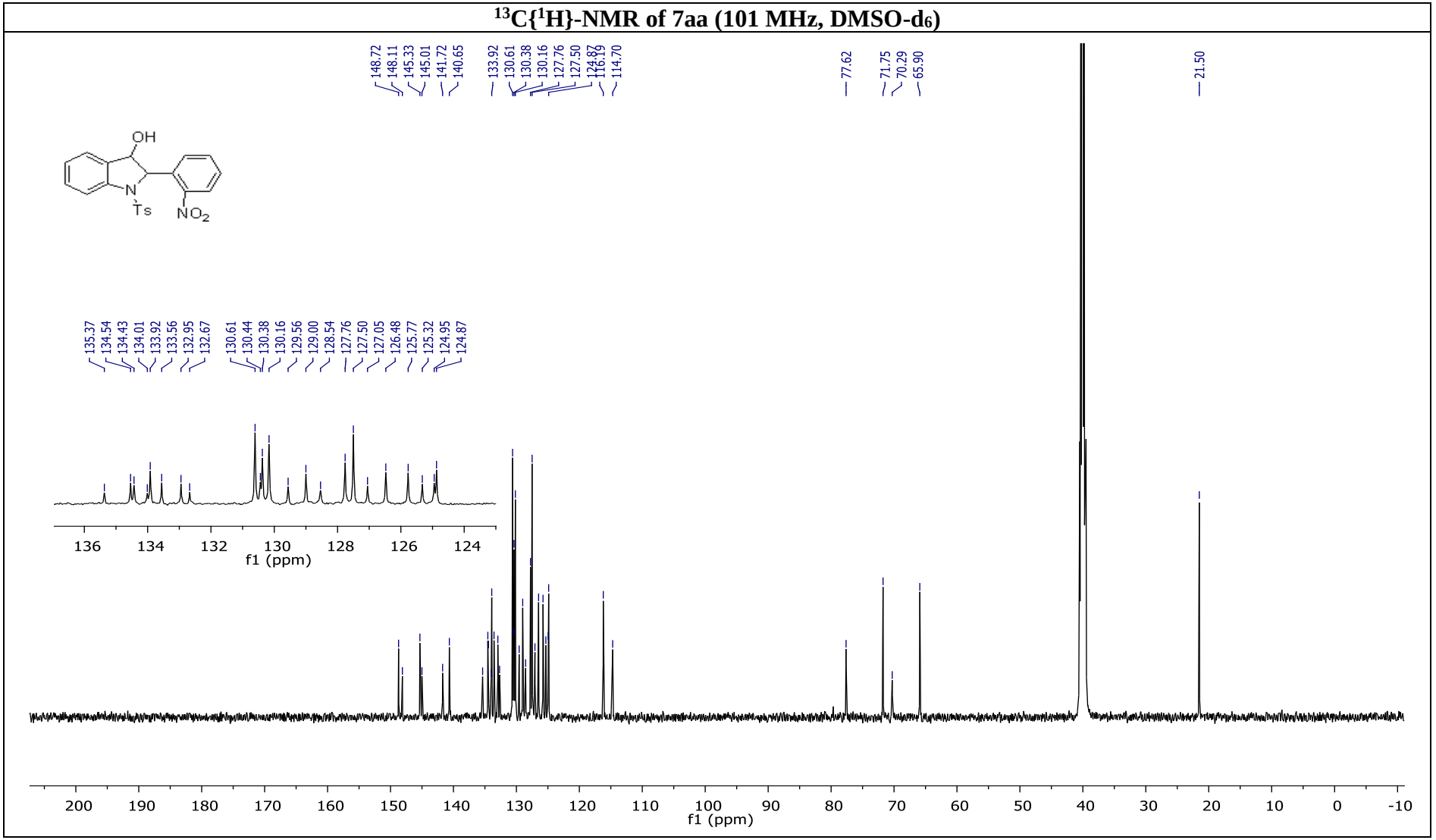
NOESY NMR of 4ab (400 MHz, DMSO d_6)



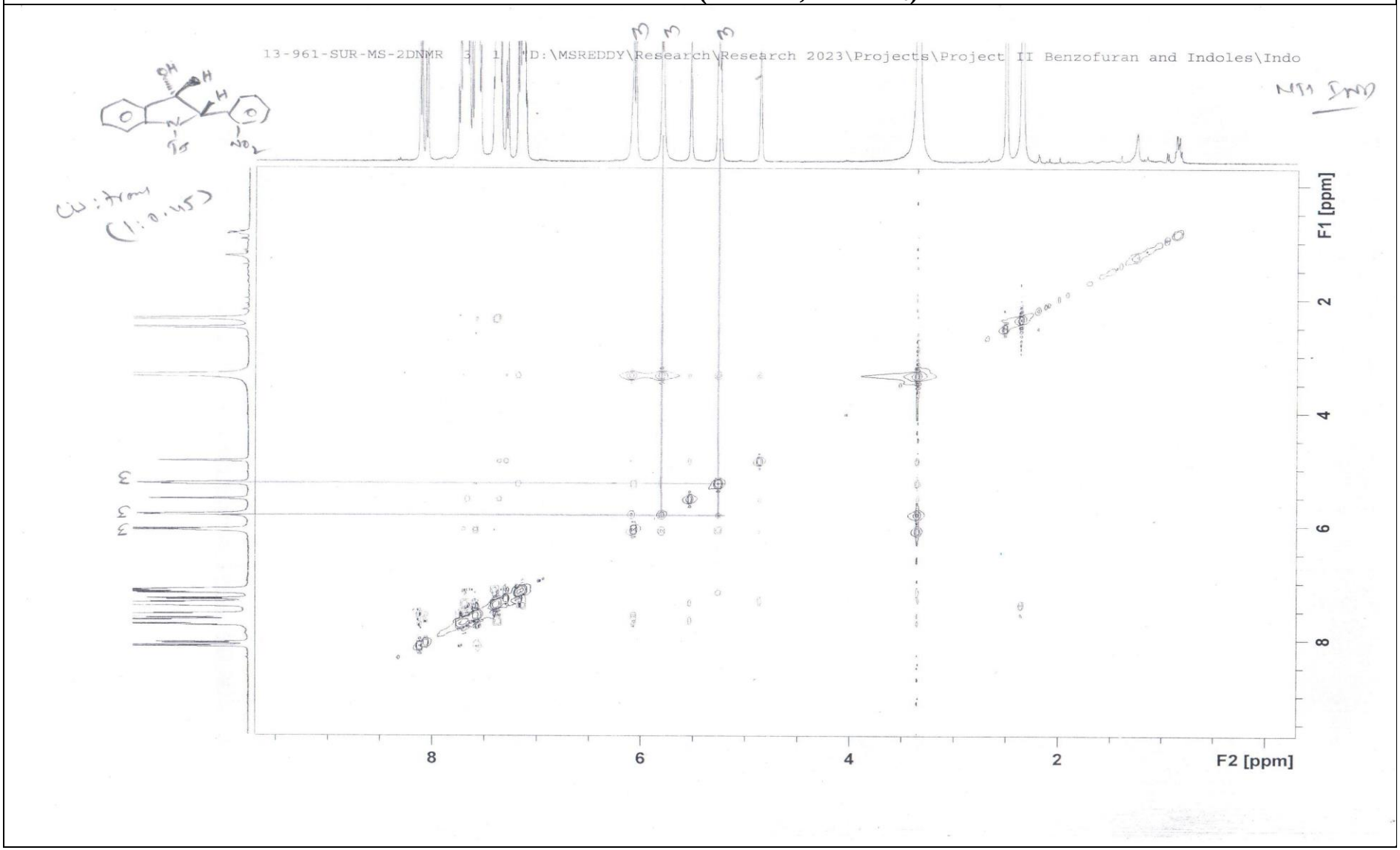
^{1}H-NMR of 7aa (400 MHz, DMSO-d$_6$)



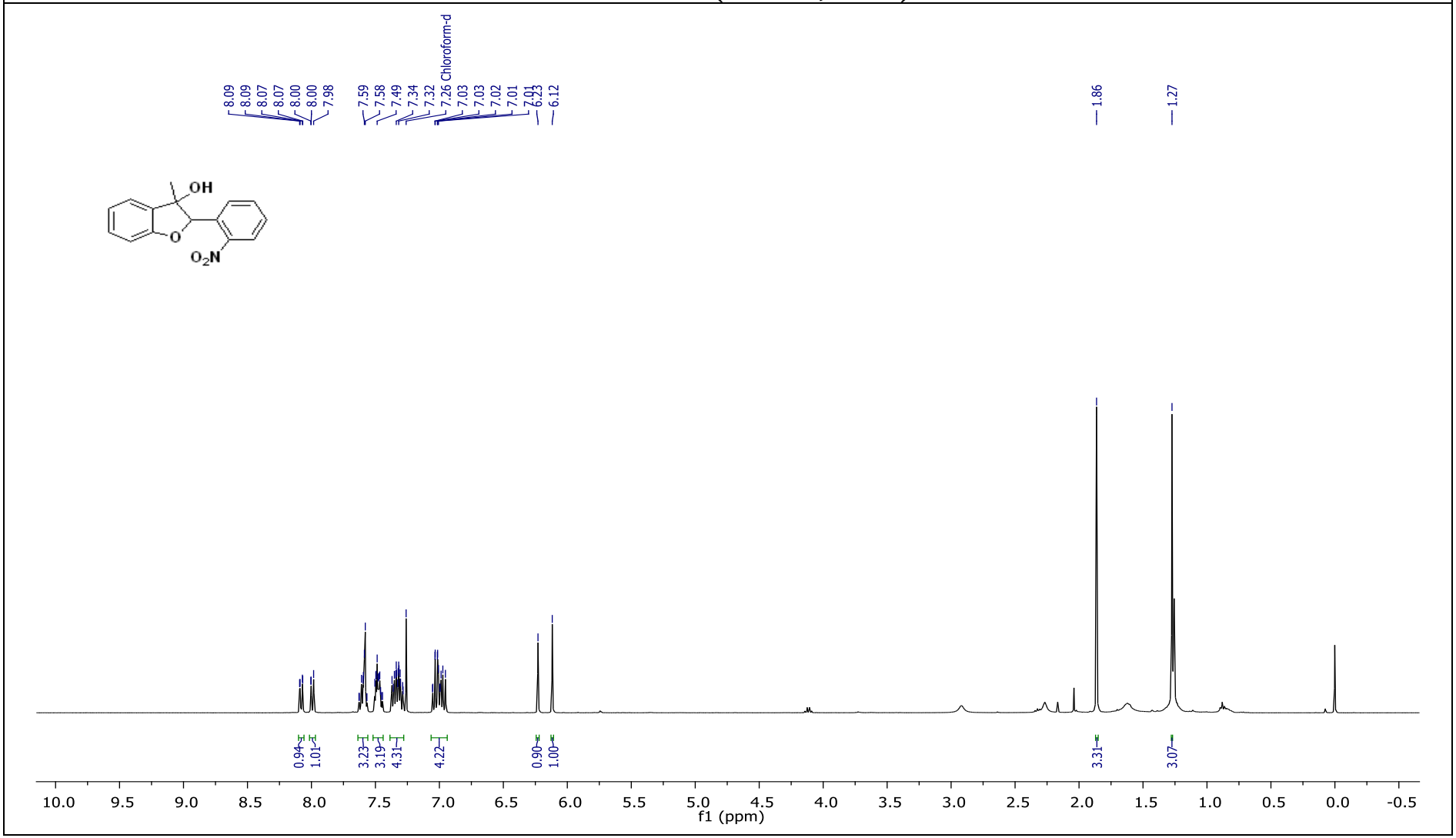
$^{13}C\{^{1}H\}$-NMR of 7aa (101 MHz, DMSO-d_6)



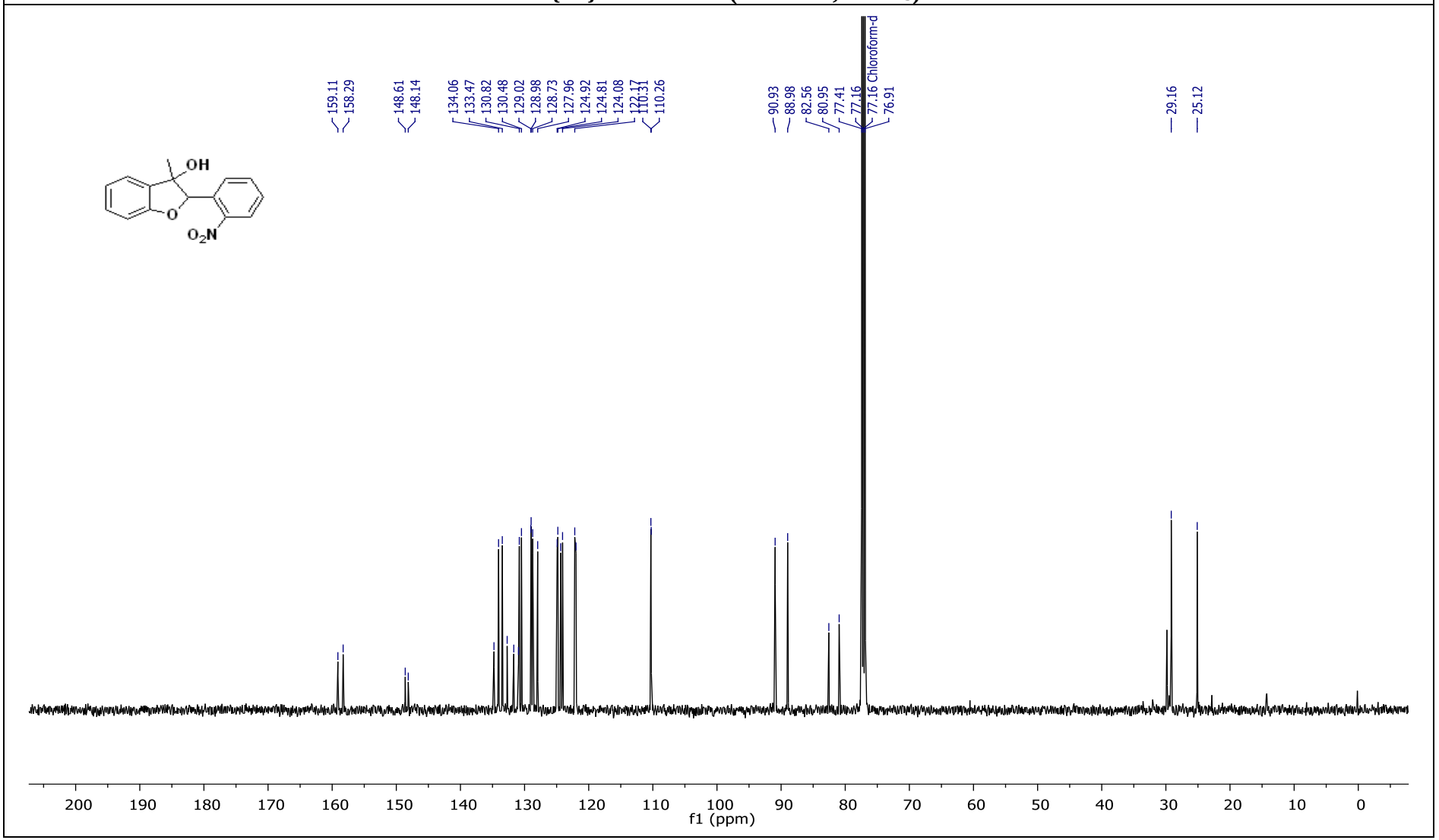
NOESY NMR of 7aa (101 MHz, DMSO d_6)



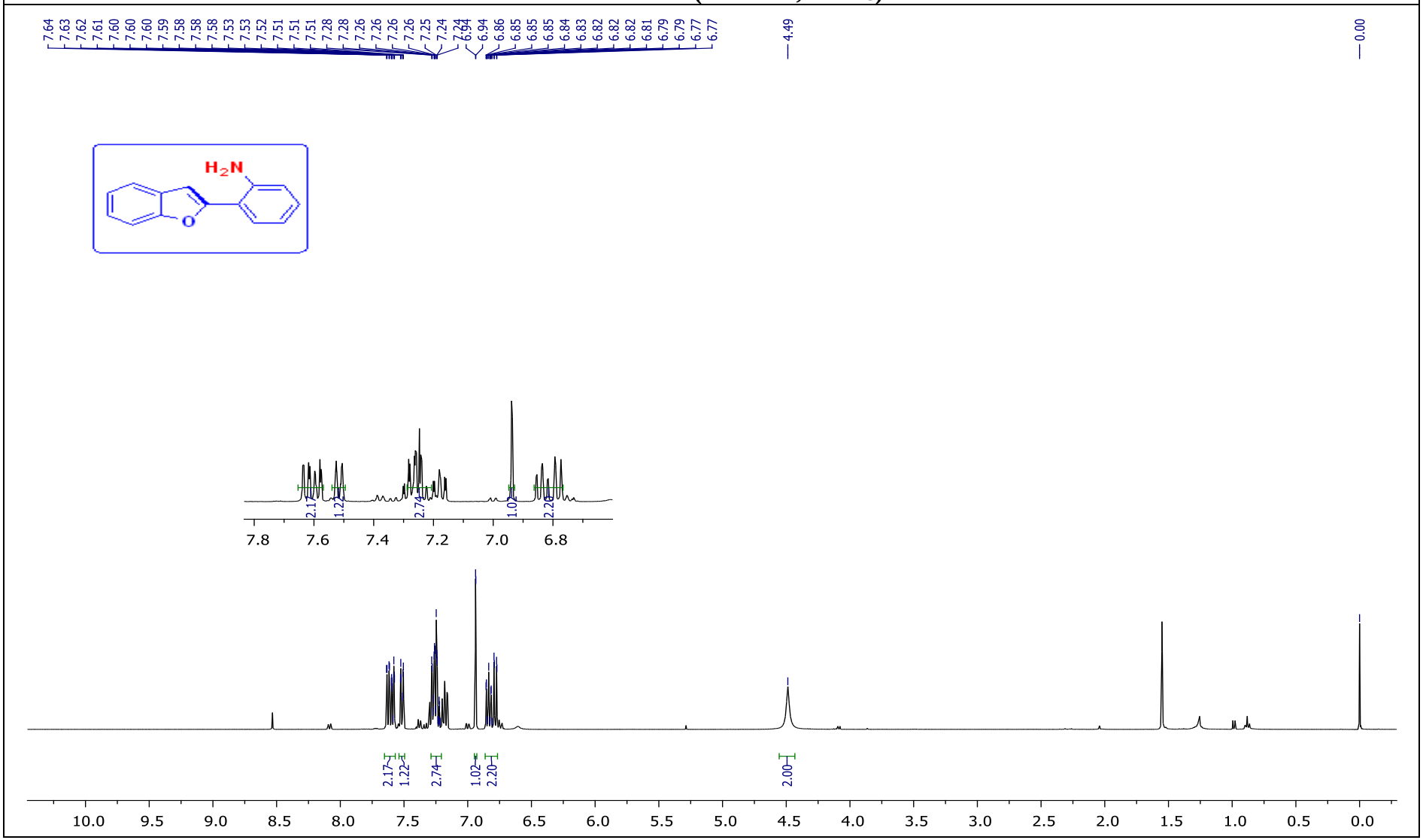
^{1}H-NMR of 4sa (400 MHz, $CDCl_3$)



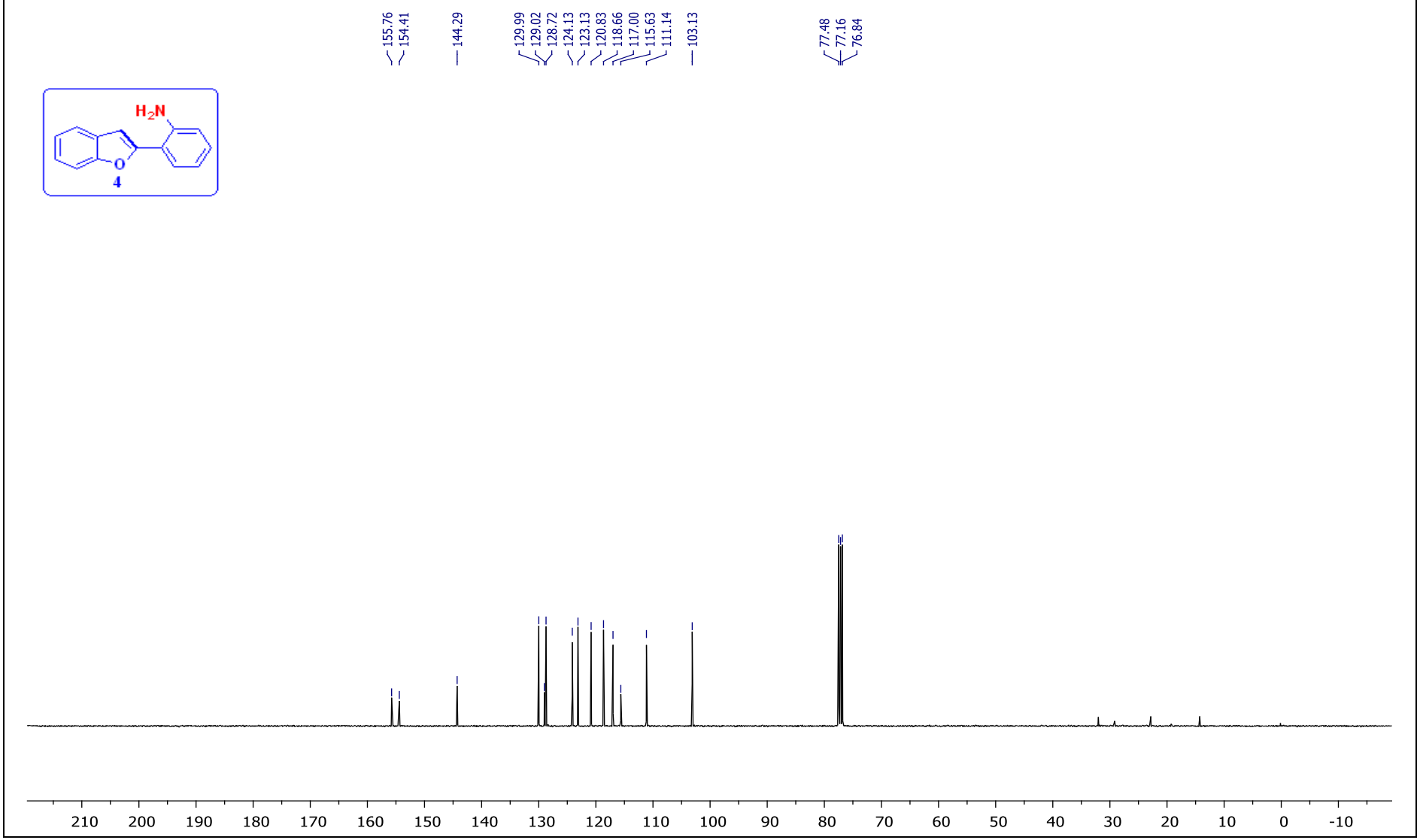
$^{13}C\{^{1}H\}$-NMRof 4sa (101 MHz, $CDCl_3$)



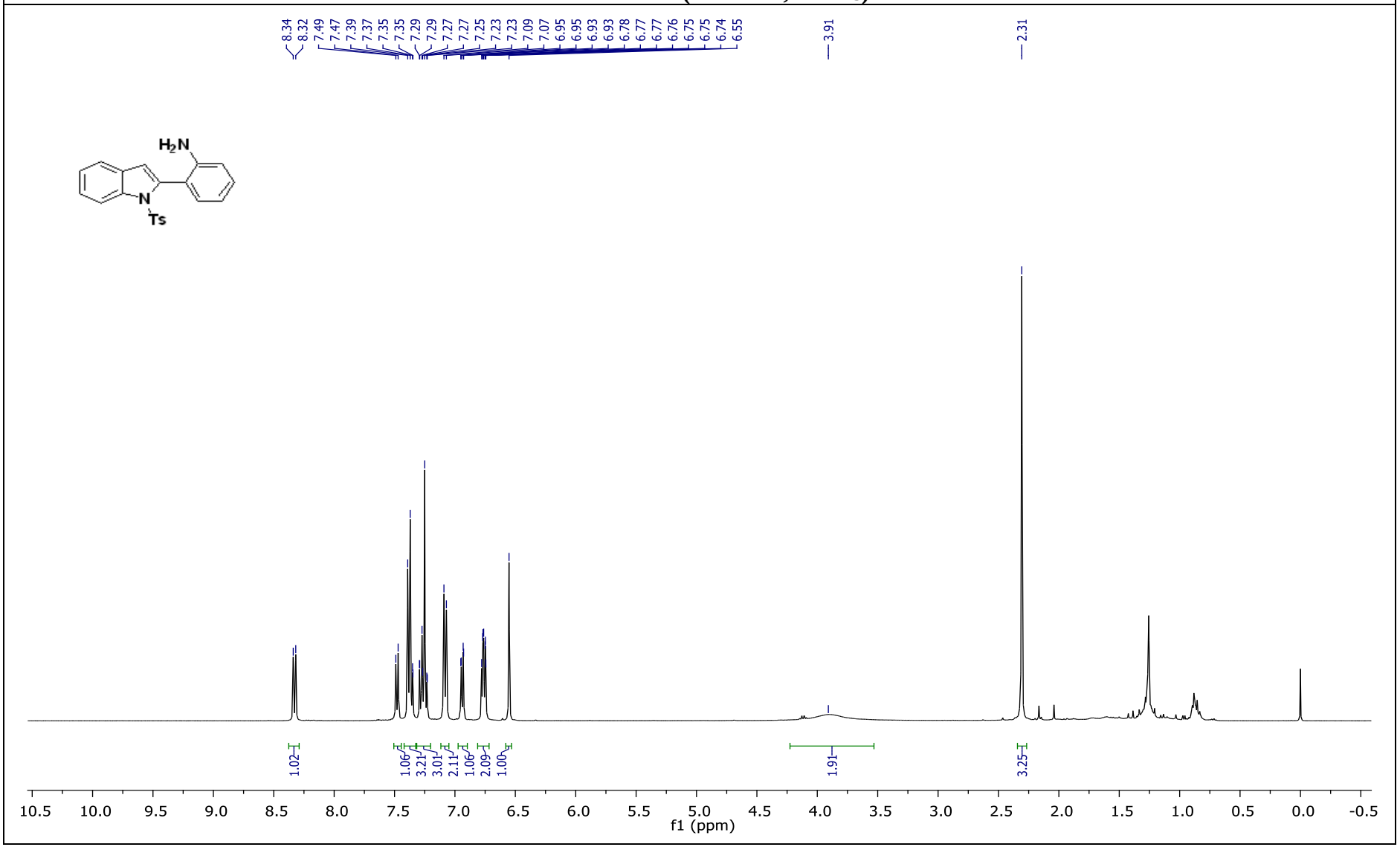
^{1}H-NMR of 14 (400 MHz, $CDCl_3$)



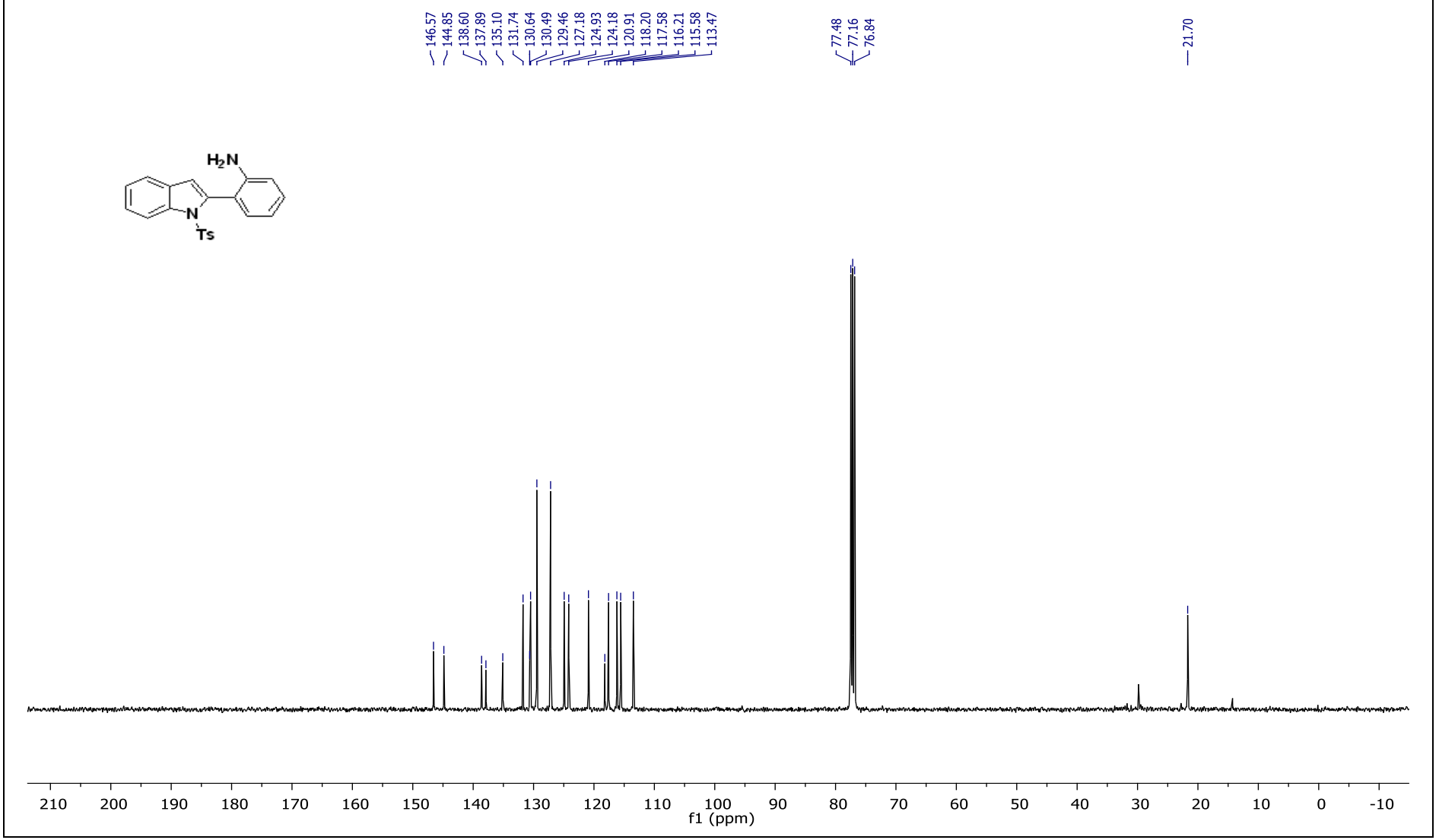
$^{13}C\{^{1}H\}$-NMR of 14 (126 MHz, $CDCl_3$)



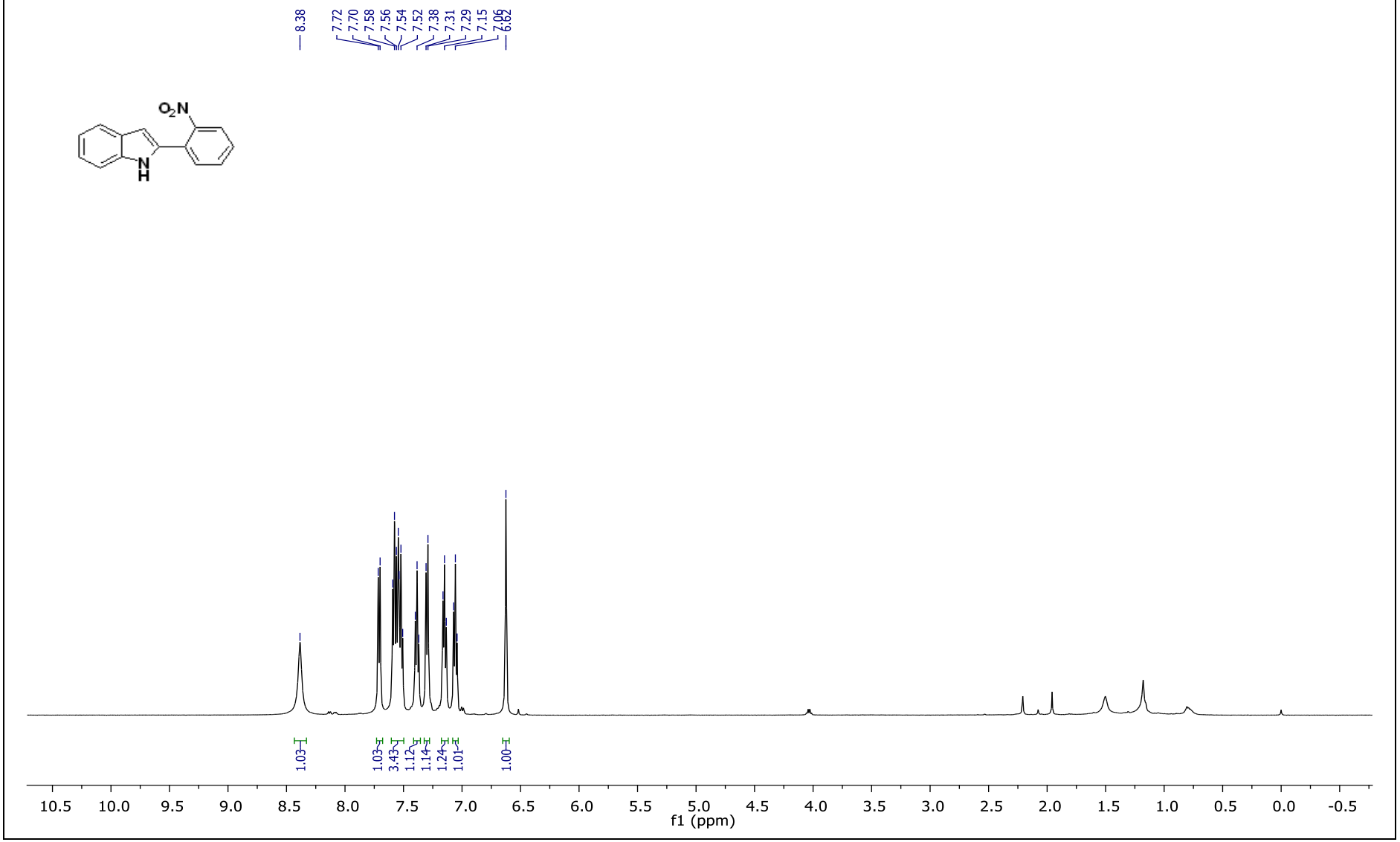
^{1}H-NMR of 15 (400 MHz, $CDCl_3$)



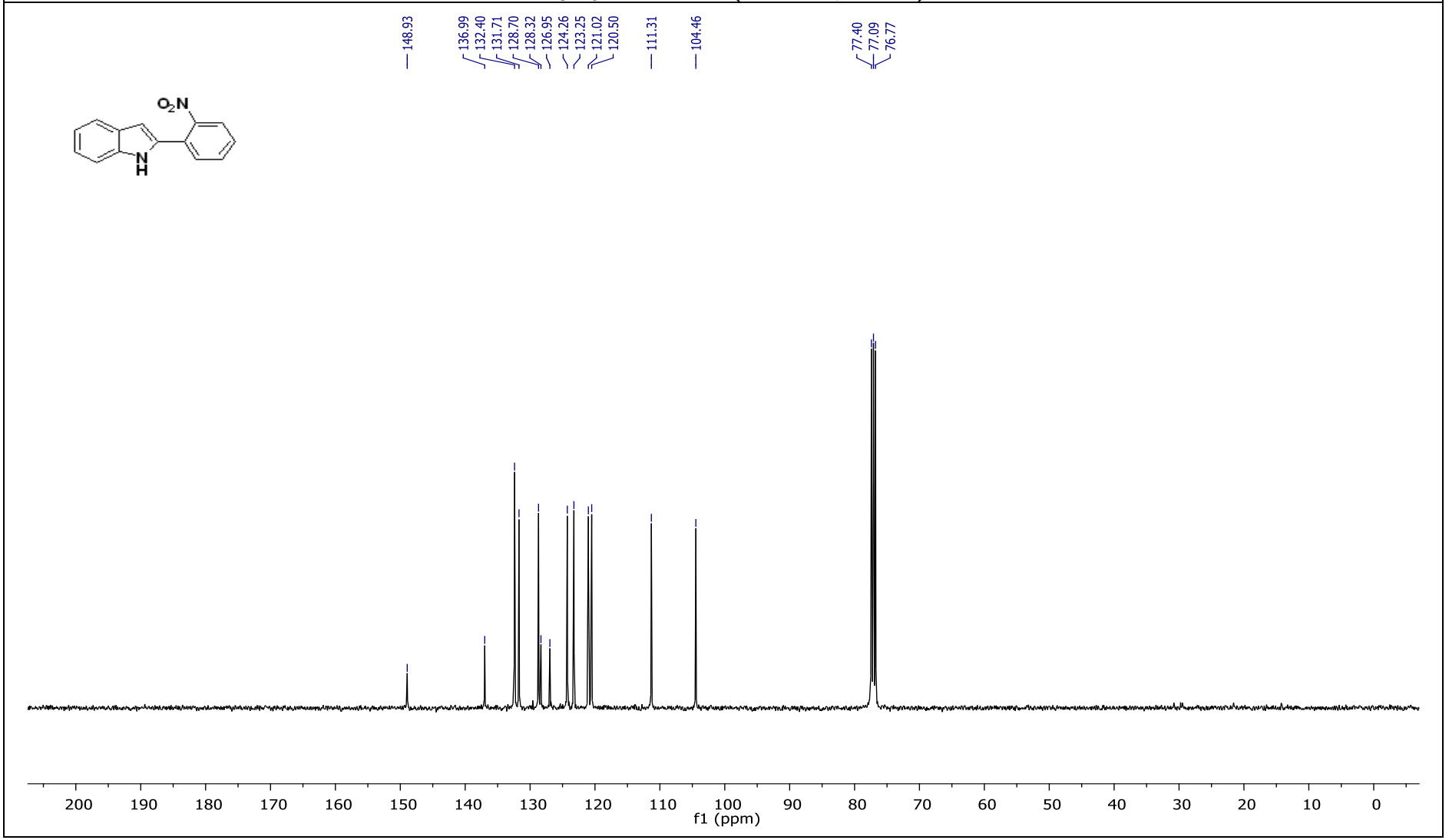
$^{13}C\{^{1}H\}$-NMR of 15 (101 MHz, $CDCl_3$)



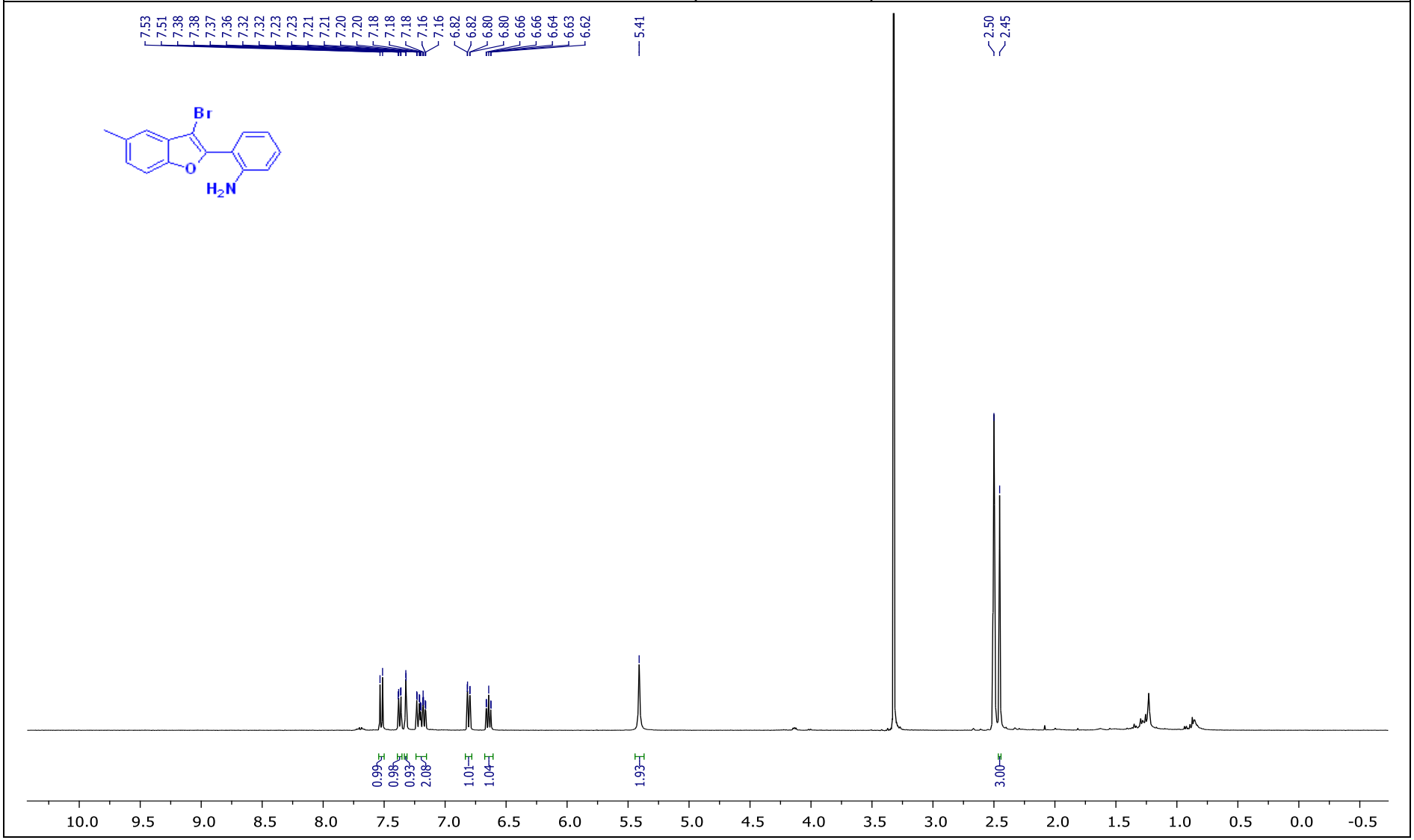
^{1}H-NMR of 16 (500 MHz, $CDCl_3$)



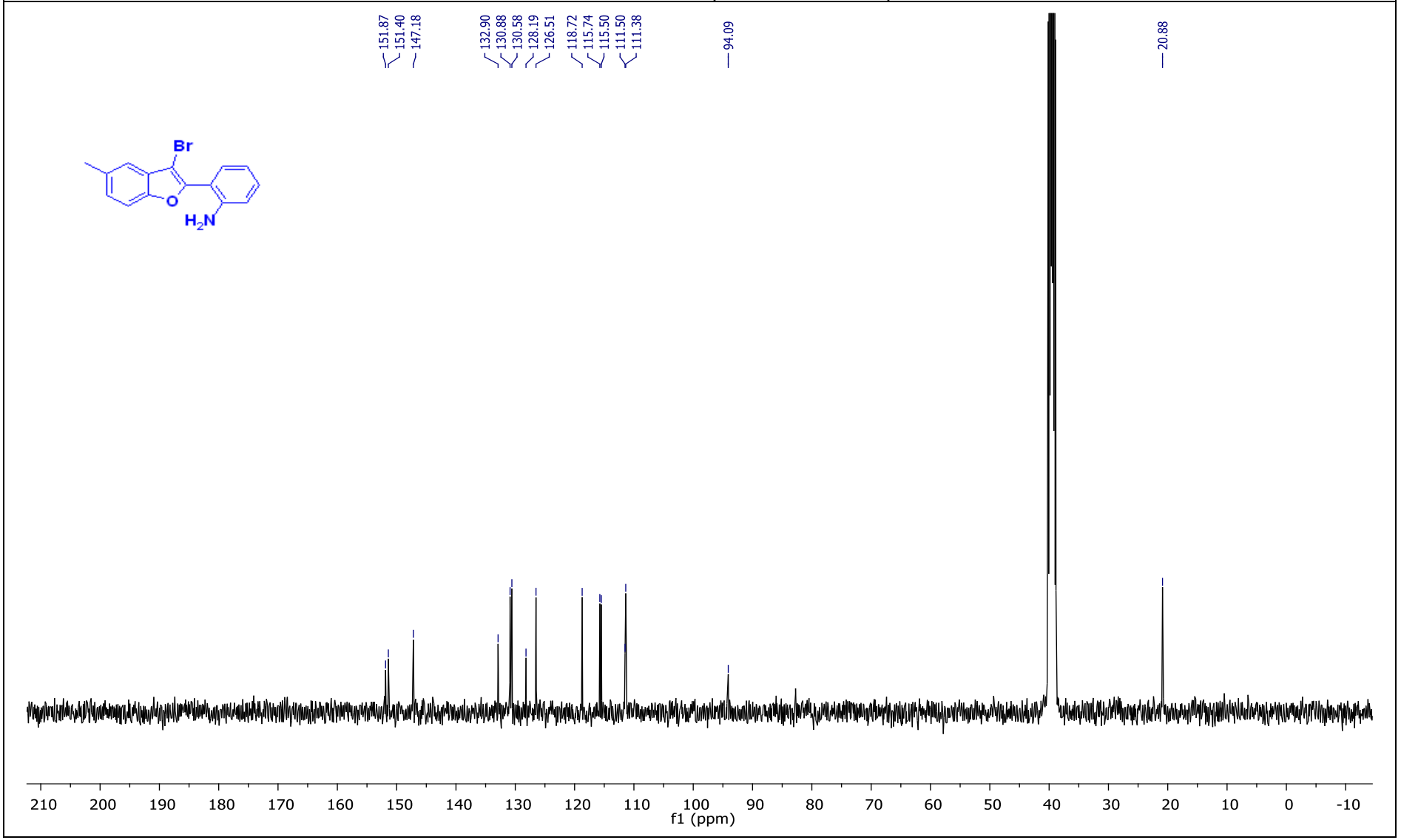
$^{13}C\{^{1}H\}$-NMR of 16 (101 MHz, $CDCl_3$)



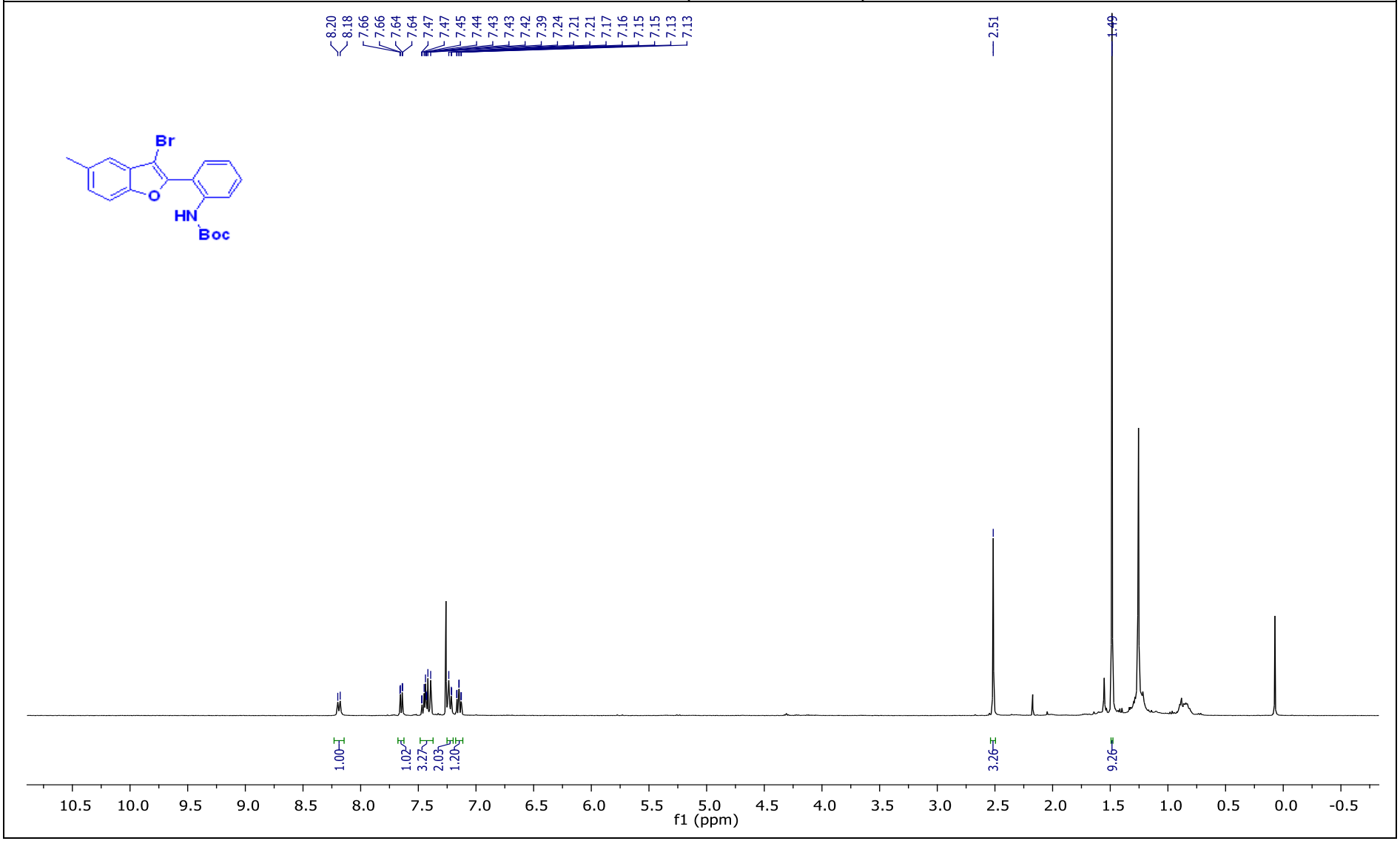
^{1}H-NMR of 17 (500 MHz, $CDCl_3$)



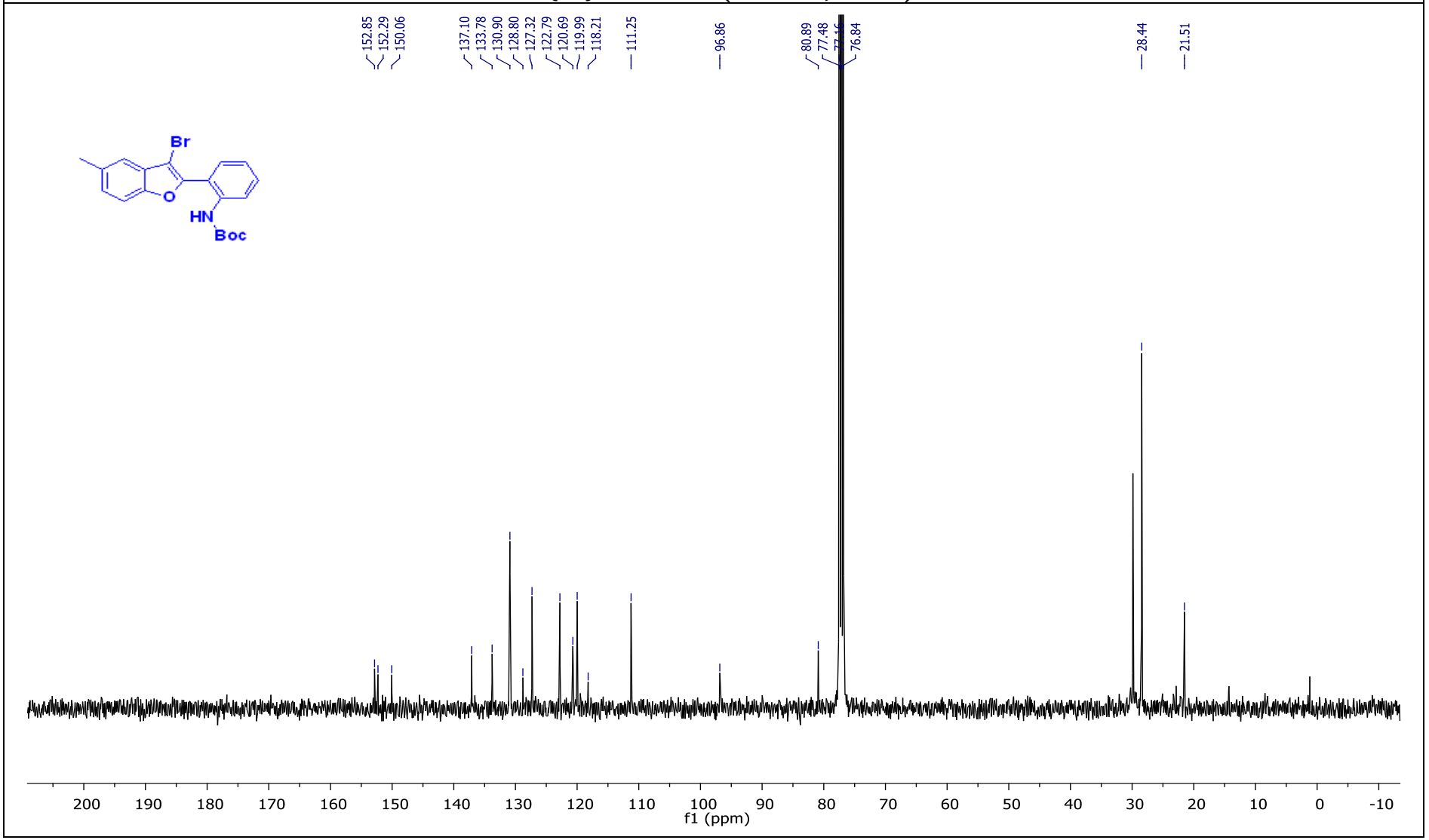
$^{13}C\{^{1}H\}$-NMR of 17 (101 MHz, $CDCl_3$)



^{1}H-NMR of 18 (500 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$-NMR of 18 (101 MHz, $CDCl_3$)



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