Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Design and Development of Intramolecular Doubly Vinylogous Michael Addition to Access 3-Aryl Substituted 2-Alkenyl-Benzofurans and -Indoles

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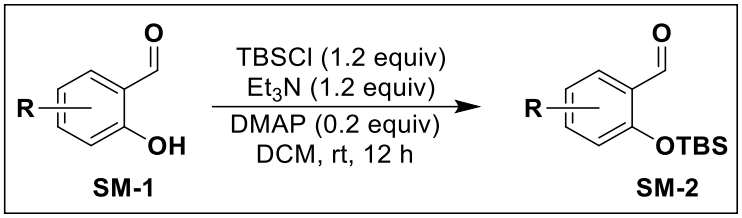
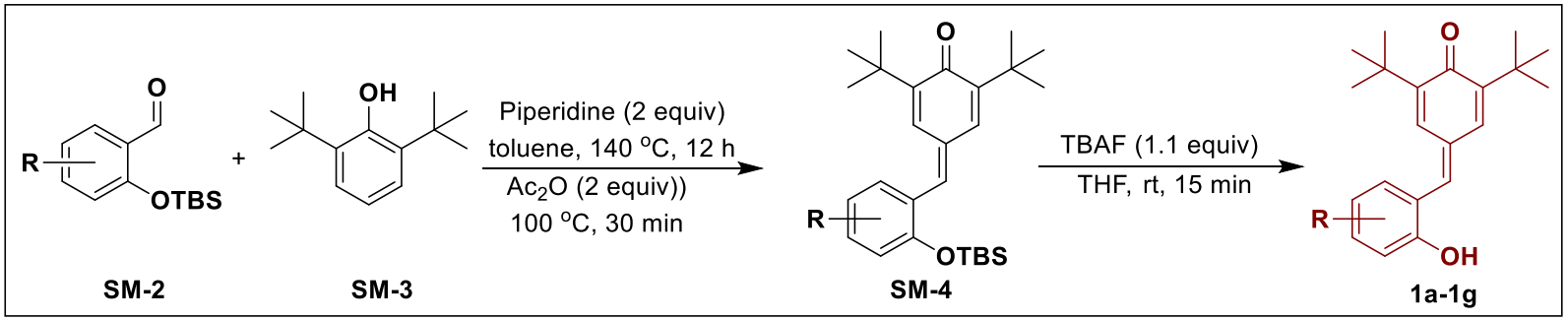
Table of Contents:

1. Synthesis of the starting materials

1.1. General procedure for synthesis of substrates 1a-1g:[1]

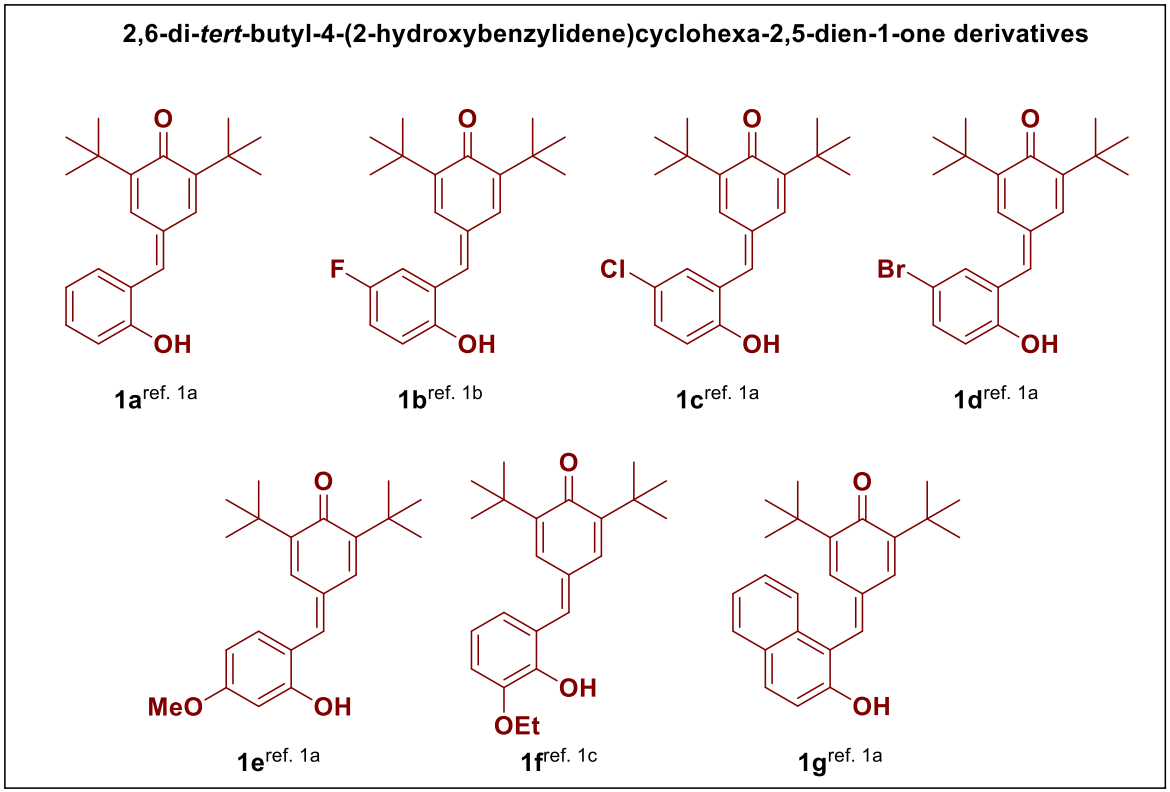


2-Hydroxybenzaldehyde derivatives **SM-1** (1 equiv, 10 mmol), TBSCl (1.2 equiv,12 mmol, 1.3 g) and DMAP (0.2 equiv,2 mmol, 0.24 g) were placed into a 50 mL reaction vial, and DCM (20 mL) was added, then Et_3N (1.2equiv,12 mmol, 1.7 mL) was added dropwise at 0 ^oC and the mixture was stirred overnight at room temperature. To the reaction mixture were added water (5mL) and DCM (5 mL). The resultant mixture was extracted with DCM (2 x 20 mL). The combined organic phase was dried over anhydrous Na_2SO_4, resulting in a white viscous liquid, which was used directly in the next step without further purification.



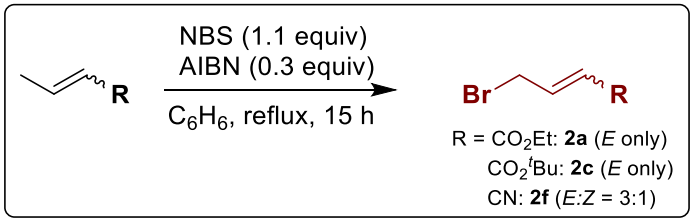
A solution of 2,6-di-*tert*-butylphenol **SM-3** (1.1 equiv, 11 mmol, 2.3 g) and benzaldehyde derivatives **SM-2** (1.0 equiv, 10 mmol) in toluene (40 mL) was placed in a Dean-Stark apparatus which was heated to reflux. Piperidine (2.0 equiv, 100 mmol, 9.9 mL) was added dropwise slowly. Then, the temperature was raised to 140 ^{o}C and stirred for 12 h. After that, the reaction mixture was cooled to 120 ^{o}C and acetic anhydride (2.0 equiv, 100 mmol, 9.4 mL) was added dropwise. The stirring was continued for 30 min and the solution was poured in icewater and extracted with EtOAc (3 x 100 mL). The organic phases were washed with brine and dried over anhydrous Na_2SO_4. Then the solvent was evaporated under reduced pressure to obtain the corresponding products **SM-4** after flash column chromatography (Hexane/EtOAc = 99/1).

To a solution of **SM-4** (1.0 equiv, 5 mmol) in THF (10 mL/mmol) at 0 ^{o}C was added TBAF (1.1 equiv, 1M in THF). The reaction mixture was stirred for 15 min at room temperature. Then saturated NH_4Cl solution was added dropwise to the reaction. The resulting solution was extracted with EtOAc (2 x 20 mL). Then the combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed to give the crude product which was purified by flash column chromatography (Hexane/EtOAc = 90/10) to afford the desired *ortho*-hydroxy *para*-quinone methide (*p*-QM) derivatives **1a- 1g**.[1]



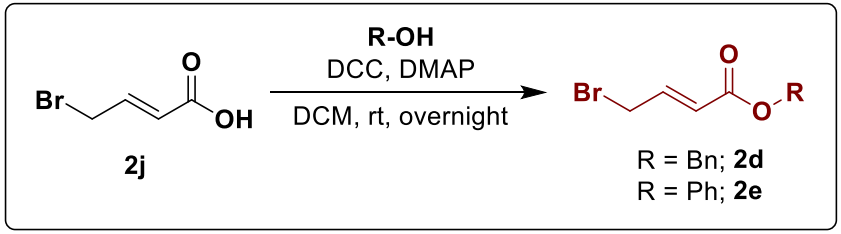
1.2. Synthesis of halo substituted allyl derivatives 2:

1.2.1. Synthesis of γ -bromocrotonoate derivatives [2a, 2c, 2f and 2j]:[2]



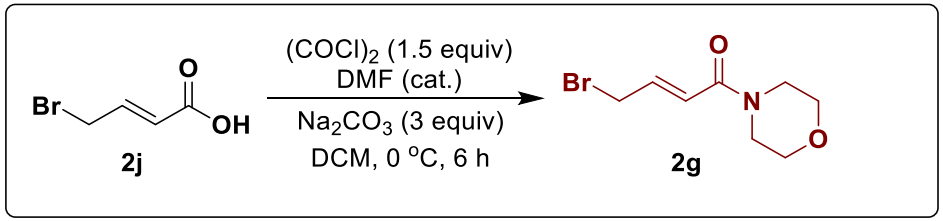
To a solution of crotonate/crotononitrile (1 equiv, 10 mmol), AIBN (0.3 equiv, 3 mmol, 492 mg) and *N*-bromosuccinimide (1.1 equiv, 11 mmol, 1.96 g) in benzene (50 mL) was stirred at reflux for 15 h under a nitrogen atmosphere. The mixture was allowed to cool to room temperature. The resulting mixture was filtered. The filtrate was washed with water (2 x 50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4.The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography, using Hexane/EtOAc (90:10) as eluent to afford **γ**–bromo crotonate/**γ**–bromo crotononitrile derivatives **2a, 2c, 2f** and **2j**.[2]

1.2.2. Phenyl/benzyl (*E*)-4-bromobut-2-enoate 2d-2e:[3a]



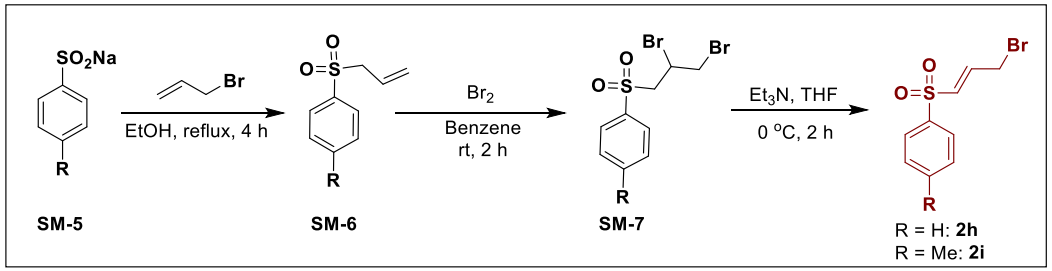
To a solution of 4-bromocrotonic acid **2j** (1.0 equiv, 10 mmol, 1.64 g) in DCM (40 mL) was added phenol/benzyl alcohol (1.1 equiv, 11 mmol) and DMAP (0.1 equiv, 1 mmol, 122 mg). The solution was cooled to 0 °C, then DCC (1.05 equiv, 10.5 mmol, 2.16 g) was added portion wise. The reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was filtered through a short celite-pad and the residue was washed with DCM (2 x 20 mL). The combined organic extract was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (Hexane: EtOAc = 20:80) to give the corresponding crotonates **2d-2e**.

1.2.3. Synthesis of (*E*)-4-bromo-1-morpholinobut-2-en-1-one 2g:[3b]



To a solution of (*E*)-4-bromobut-2-enoic acid **2d** (1 equiv, 3 mmol, 500 mg) in DCM (10 mL) under N_2 atmosphere at 0 ^oC. Then oxalyl chloride (1.5 equiv, 4.5 mmol, 571 mg) and DMF (0.1 mL) were added. The solution was stirred at 0 ^oC under N_2 atmosphere for 2 h, followed by the addition of Na_2CO_3 (3 equiv, 9 mmol, 954 mg) and morpholine (1.5 equiv, 4.5 mmol, l0.4 mL). The resulting reaction mixture1 was stirred at 0 ^oC for 6 h. To the reaction mixture were added water (10 mL) and DCM (10 mL). The resultant mixture was extracted with DCM (2 x 30 mL) The combined organic phase was dried over anhydrous Na_2SO_4, purified by column chromatography (Hexane/Ethyl acetate = 70:30) to obtain the title compound **2g** as a white solid (358 mg, 67% yield).[3b]

1.2.4. Synthesis of (*E*)-((3-bromoprop-1-en-1-yl)sulfonyl)benzene derivatives 2h-2i:[3c]

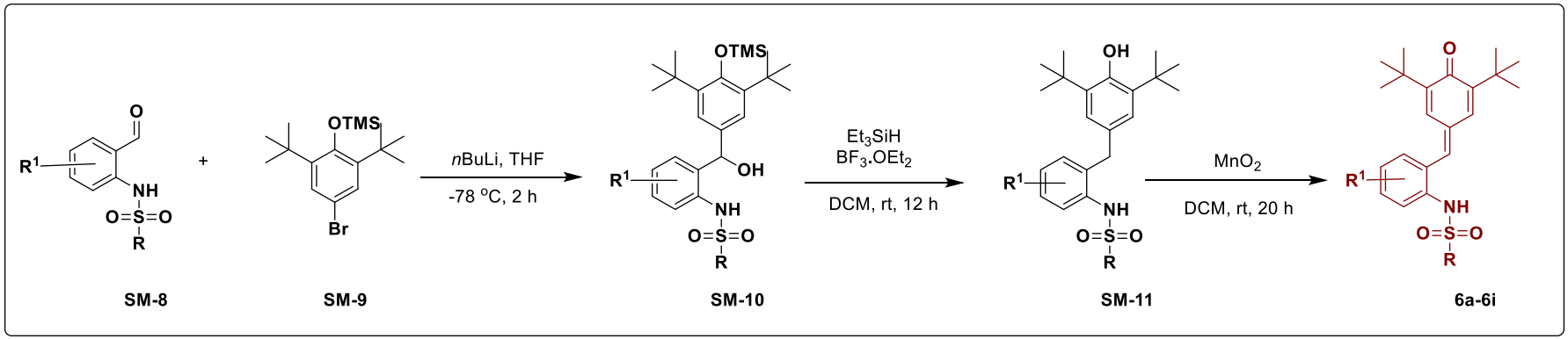


To a solution of substituted sodium benzenesulfinate **SM-5** (1 equiv, 10 mmol) in ethanol (40 mL) was added 3-bromoprop-1-ene (1.2 equiv, 12 mmol, 1.04 mL) under argon atmosphere. The reaction mixture was refluxed for 4 h and then the solvent was removed. The residue was added to water (30 mL) and then extracted with CH_2Cl_2 (3x10 mL). The combined organic phase were washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude residue **SM-6** was used in the next step directly without further purification.

To a solution of **SM-6** (1 equiv, 10 mmol) in benzene (15 mL) was added a solution of Br_2 (1. equiv, 11 mmol, 0.57 mL) in benzene (5 mL) dropwise. The reaction mixture was stirred at room temperature for 2 h. After the completion of the reaction, the reaction mixture was quenched with saturated aqueous $NaHSO_3$ solution and then extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The crude product **SM-7** was used in the next step without further purification.

Et_3N (1.1 equiv, 5.5 mmol) was added dropwise to a stirred solution of **SM-7** (1 equiv, 5 mmol) in dry THF (30 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 2 h. After completion of the reaction, the solvent was removed. The residue was added to water (25 mL) and then extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by flash chromatography (Hexane/Ethyl acetate = 30:1) to give the desire compounds **2h-2i**.[3c]

1.3. General procedure for the synthesis of 6a- 6i:[4]

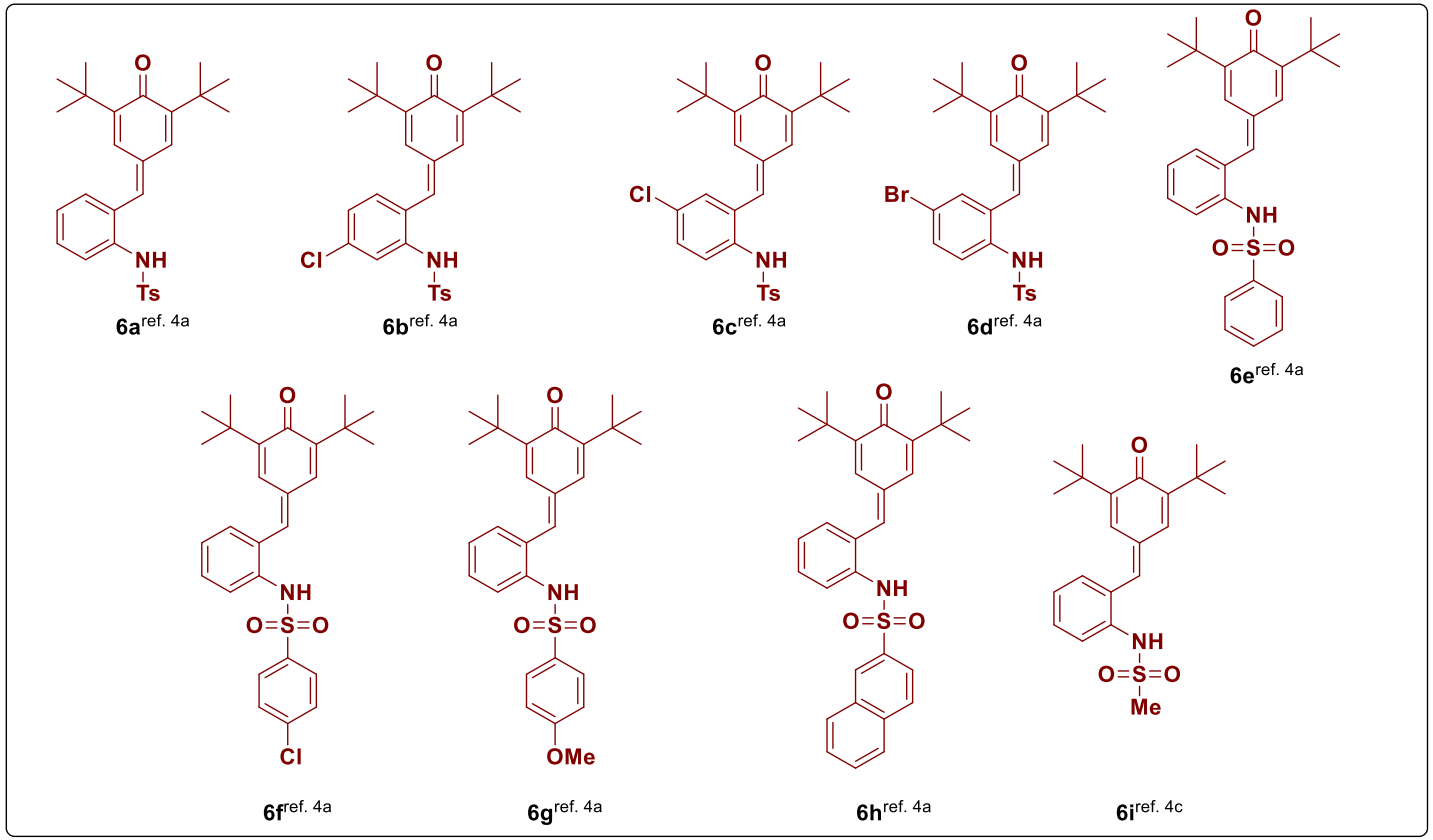


To a solution of (4-bromo-2,6-di-*tert*-butylphenoxy)trimethylsilane **SM-9** (1 equiv, 5 mmol, 1.78 g) in anhydrous THF (25 mL) at -78 °C was added *n*-butyllithium 2.5 M (1.2 equiv, 6 mmol, 2.4 mL) slowly in a dropwise manner. After finishing the addition, the reaction mixture was stirred at the same temperature for 30 min. Then, a solution of aldehyde **SM-8** (1.2 equiv, 6 mmol) in anhydrous THF (5 mL) was dropwise added. The reaction mixture was stirred at -78 °C for 2 h and saturated NH_4Cl solution was added to quench the reaction. Then the resulting solution was extracted with Et_2O (3 x 30 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to obtained the crude **SM-10**, which was directly used in the next step without further purification.

To a solution of substrate **SM-10** (1 equiv, 5 mmol) and triethylsilane (1.5 equiv, 7.5 mmol, 1.2 mL) in CH_2Cl_2 (25 mL) at 0 °C under nitrogen atmosphere was slowly added boron trifluoride etherate (1.5 equiv, 7.5 mmol, 0.89 mL). The reaction mixture was stirred at room temperature overnight, and then the reaction was quenched with saturated aqueous $NaHCO_3$ and stirred for 30 minutes. The resulting solution was extracted

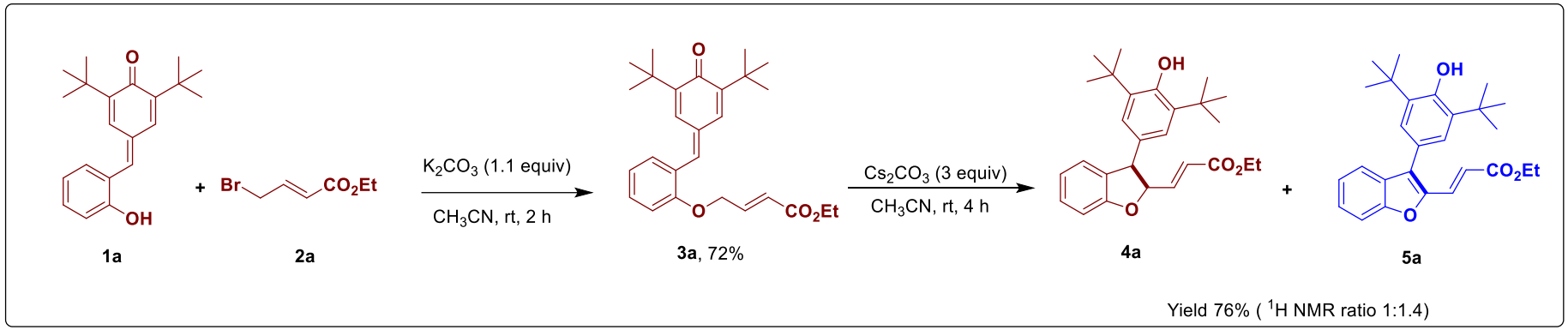
with EtOAc (3 x 30 mL). Then the combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed to give the crude product which was purified by silica gel flash chromatography (Hexane:EtOAc = 90:10) to give compounds **SM-11**.

A 25 mL glass tube equipped with a stirring bar was charged with the precursors **SM-11** (1equiv, 1 mmol), MnO_2 (5 equiv, 5 mmol, 435 mg), and CH_2Cl_2 (5 mL). The resulting solution was stirred at room temperature for 20 h. Then the solvent was evaporated under reduced pressure to give a residue, which was directly purified by flash column chromatography (Hexane:EtOAc = 85:15) to provide *p*-QMs **6a-6i** as a yellow solids.[4]



2. Step-wise and one-pot reactions of *p*-QM 1a and ethyl 4-bromocrotonoate 2a

2.1. Sequential reaction of 1a and 2a:

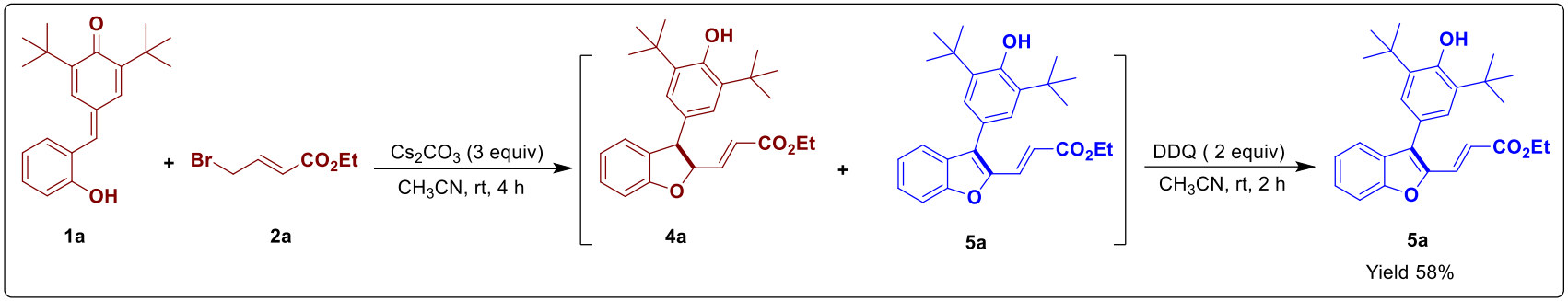


To a 15 mL clean and dry screw cap vial, a mixture of *p*-QM **1a** (1 equiv, 1 mmol, 310 mg) and anhydrous K_2CO_3 (1.1 equiv, 1.1 mmol, 152 mg) and CH_3CN (10 mL) were added and the reaction mixture was stirred at 0 ^oC for 15 min. To this reaction mixture was added a solution of ethyl 4-bromobut-2-enoate **2a** (1.3 equiv, 1.3 mmol, 0.18 mL) in CH_3CN (5 mL) dropwise over 10 min, the temperature of the reaction mixture was maintained at 0 ^oC during addition. After complete addition, the reaction mixture was allowed to stir at 0 ^oC for 2 h. After the of the reaction, the reaction mixture was concentrated under reduced pressure. The resulting residue was extracted with EtOAc (2 x 20 mL) the combined organic phase was washed with water (20 mL) and dried over anhydrous Na_2SO_4 and filtered. The organic phase was concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford the desired product **3a** in 72% yield.

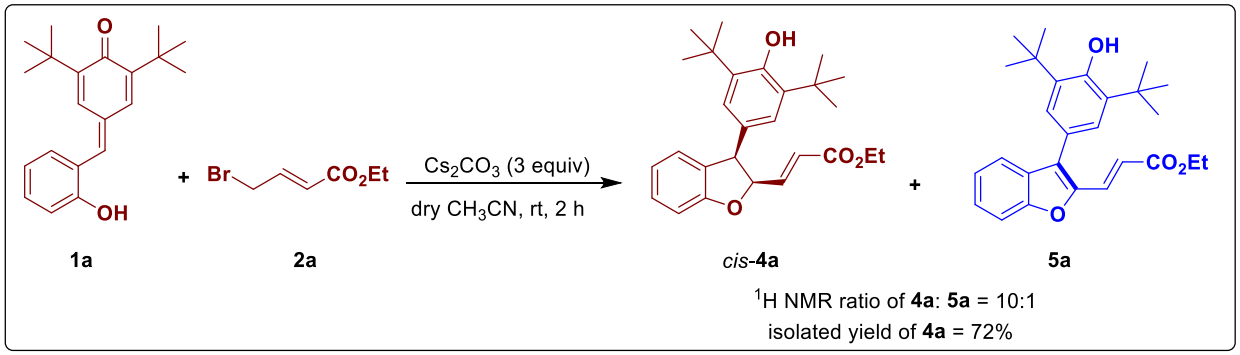
To a 15 mL clean and dry screw cap vial, Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg) was added followed by a solution of *para*-quinone methide-allyl derivative **3a** (1 equiv, 0.5 mmol, 211 mg) in CH_3CN (5 mL). The reaction vial was closed and the reaction mixture was allowed to stir at room

temperature for 4 h. The reaction mixture was quenched with water (10 mL), diluted with EtOAc (20 mL), and washed with water (10 mL) and brine (10 mL). Then the organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford a mixture of compounds **4a** and **5a** in a 1:1.4 ratio.

2.2. One pot reaction of 1a and 2a followed by oxidation to access 2-alkenyl benzofuran 5a:

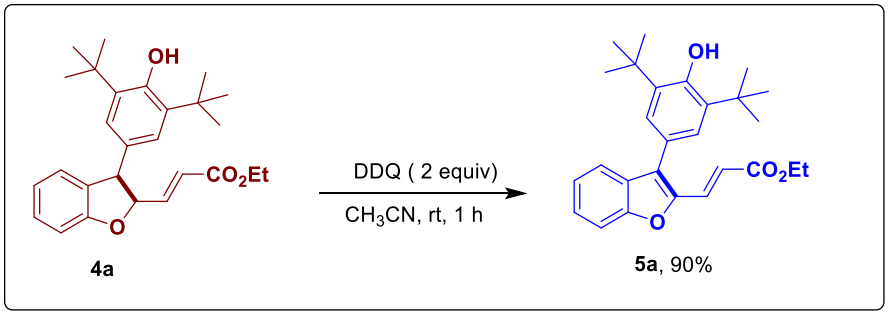


To a solution of *p*-QM **1a** (1 equiv, 0.5 mmol, 155 mg) in dry CH_3CN (4 mL) was added anhydrous Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg) followed by of 4-bromobut-2-enoate **2a** (1.3 equiv, 0.65 mmol,125 mg) in CH_3CN (5 mL) was added. Then, the reaction mixture was allowed stir at rt for 4 h. Followed by DDQ (2 equiv, 1 mmol, 227 mg) was added. This reaction mixture stirred for 2 h. The reaction mixture was quenched with water (10 mL), diluted with EtOAc (20 mL) the resulting mixture was washed with water (10 mL) and brine (10 mL). Then the organic extract was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford benzofuran **5a** in 58% yield.



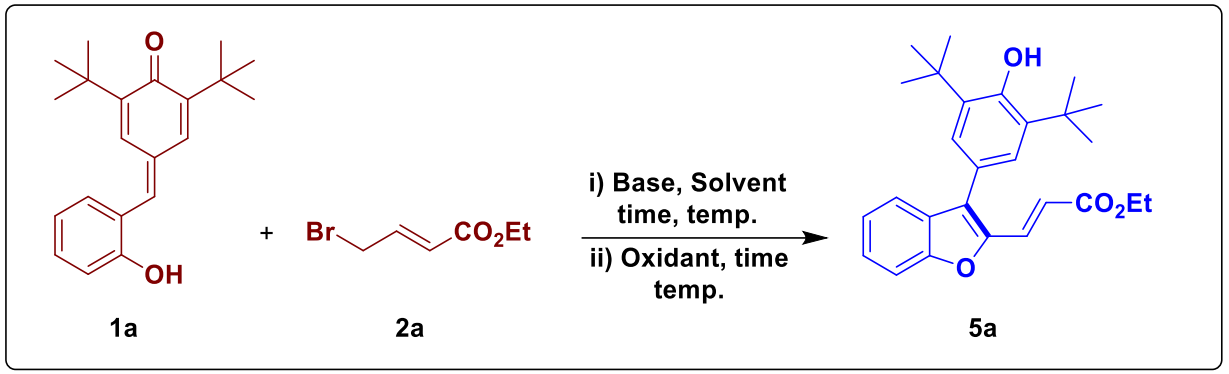
To a solution of *p*-QM **1a** (1 equiv, 0.5 mmol, 155 mg) in dry CH_3CN (5 mL) were added anhydrous Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg) and 4-bromobut-2-enoate **2a** (1.3 equiv, 0.65 mmol, 125 mg) in dry acetonitrile (5 mL) under argon atmosphere. After the addition, the reaction mixture was allowed to stir at rt for 2 h. After this time, the reaction mixture was concentrated under reduced pressure. The resulting residue was extracted with EtOAc (2 x 20 mL) the combined organic phase was washed with water (20 mL) and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford the desired dihydrobenzofuran **4a** in 72% yield. The relative configuration of *cis*-dihydrobenzofuran **4a** was confirmed by NOE.

2.3. Conversion of 4a to 5a by using the oxidant DDQ:



To a 15 mL clean and dry screw cap vial, a solution of ethyl (*E*)-3-(3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2,3-dihydrobenzofuran-2-yl)acrylate **4a** (1 equiv, 0.25 mmol, 106 mg) in acetonitrile (3 mL) followed by DDQ (2 equiv, 0.5 mmol, 113 mg) was added. The reaction mixture was stir, at room temperature for 2 h. To this reaction mixture were added water (5 mL), and EtOAc (5 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). Then the combined organic phase was washed with water (5 mL) and brine (5 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford 2-alkenyl benzofuran **5a** in 90% yield.

3. General experimental procedure for the optimization study

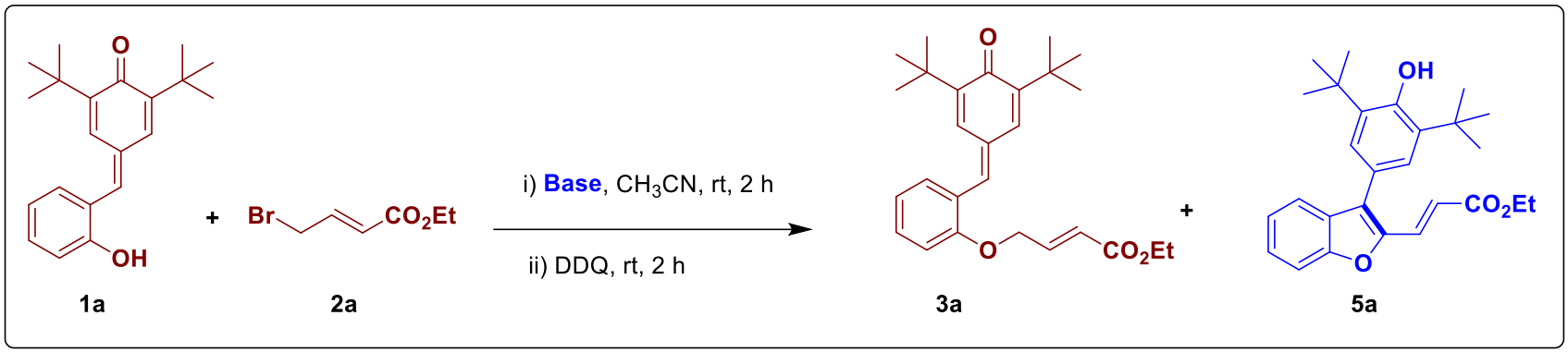


To a 15 mL clean and dry screw cap vial, *p*-QMs **1** (0.5 equiv, 0.5 mmol), γ-halo substituted activated allyl derivative **2** (1.3 equiv, 0.65 mmol) and solvent (5 mL) were added followed by base (3 equiv). The reaction mixture was allowed to stir at the indicated time and temperature. Upon completion of the starting material, the oxidant (2 equiv, 1 mmol) was added and the reaction contents were allowed to stir at the indicated time and temperature. To the cooled reaction mixture were added water (5 mL) and EtOAc (5 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). Then the combined organic phase was washed with water (5 mL) and brine (5 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a crude residue. The resulting residue was purified by column chromatography using ethyl acetate in hexane as eluent to isolate the products **5a** and **3a**.

Note: **please see tables T1-T5, for a screening of various bases, solvents, leaving group and their ratios/quantities, time and temperature reaction conditions**

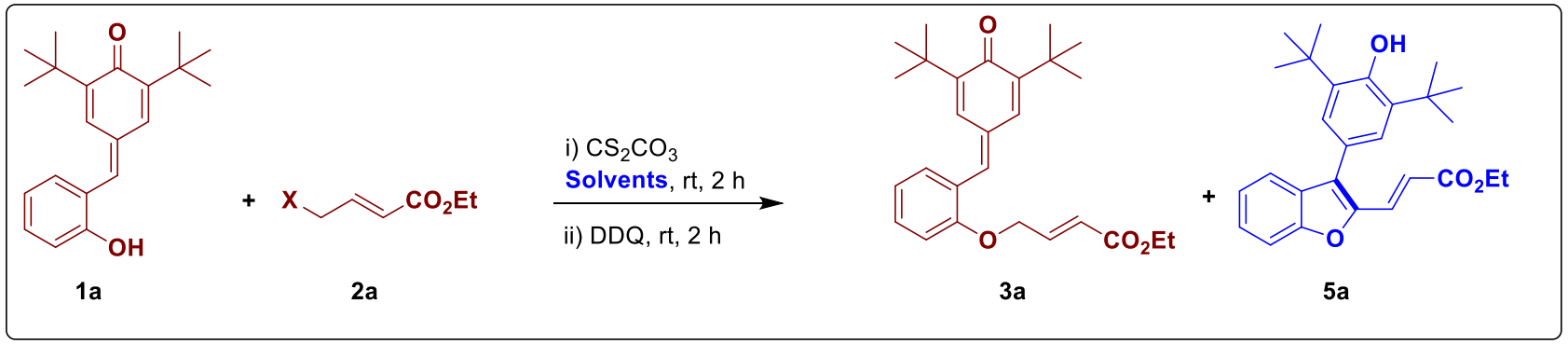
4. Optimization survey

Table T1: Screening of various bases



Entry	Base (3 equiv)	% Yield of 3a	% Yield of 5a
1	K_2CO_3	76	-
2	K_3PO_4	56	-
3	**Cs_2CO_3**	**-**	**76**
4	1,4-Diazabicyclo[2.2.2]octane (DABCO)	75	-
5	1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD	trace	14
6	NaH	trace	-
7	1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)	-	32
8	KO^tBu	-	29
9	NaOH	65	Trace
10	Et_3N	-	-
11	-	-	-

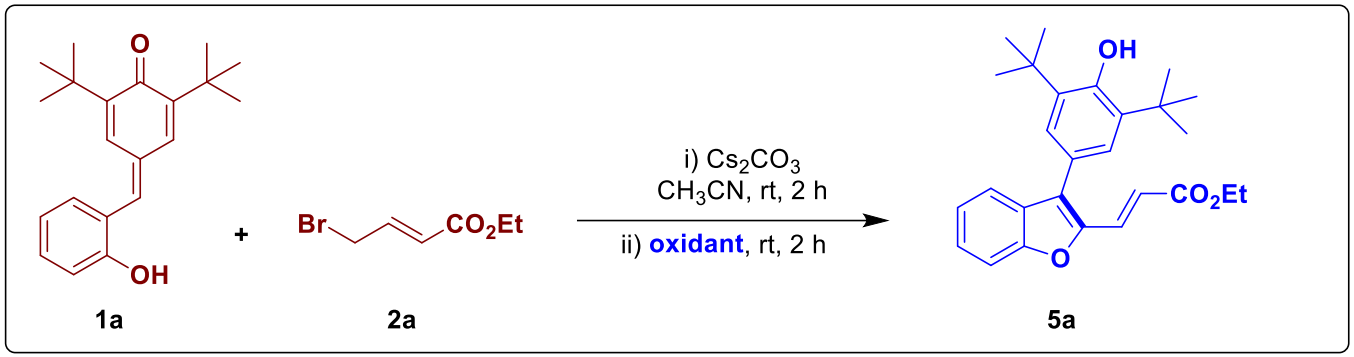
Table S2: Screening of various Solvents and leaving group (X)



Entry	Solvents (5 mL)	Leaving Group (X)	% Yield of 3a	% Yield of 5a
1.	**CH_3CN**	**Br**	-	**76**
2.	Dimethyl sulfoxide (DMSO)	Br	29	20
3.	Toluene	Br	24	-
4.	EtOH	Br	-	25
5.	1,4-Dioxane	Br	trace	-
6.	Tetrahydrofuran (THF)	Br	-	32
7.	Dimethylformamide (DMF)	Br	-	48
8.	Water	Br	NR	NR
9.	CH_3CN	Cl	-	42
10.	CH_3CN	I	-	58
11.	CH_3CN	OBoc	-	34

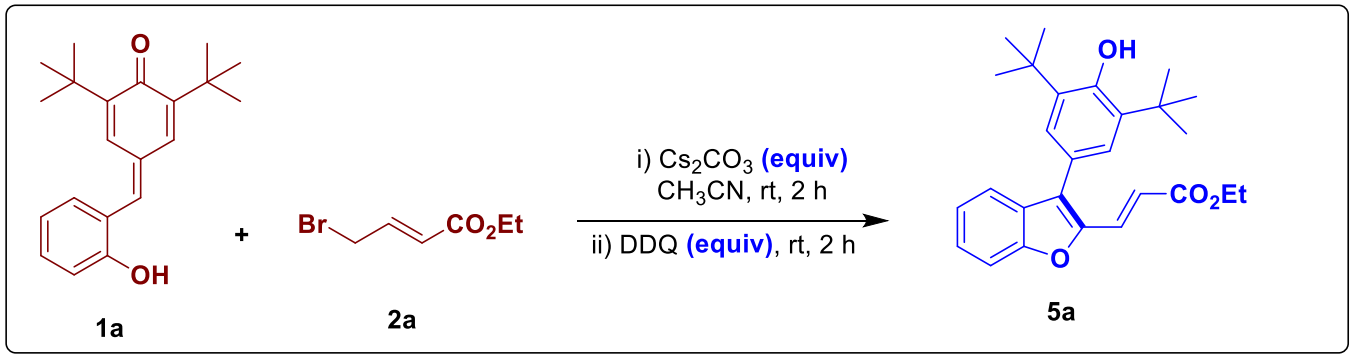
In DCM and DCE solvents the starting materials were found to be decomposed

Table T3: Optimization of oxidant



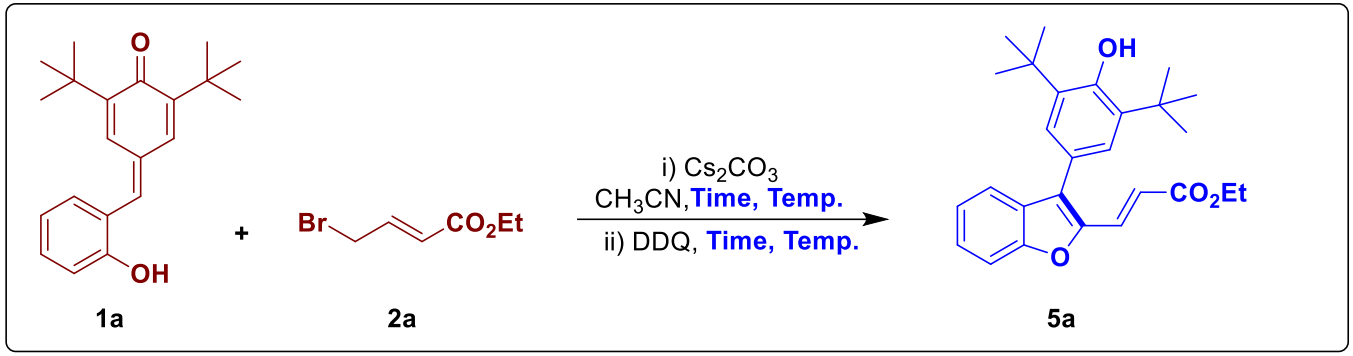
Entry	Oxidant (2 equiv)	% Yeild of 5a
1	(Diacetoxyiodo)benzene	20%
2	3,3',5,5'-Tetra-tert-butyl-[1,1'-bi(cyclohexylidene)]-2,2',5,5'-tetraene-4,4'-dione	Trace
3	MnO_2	28%
4	**DDQ**	**76%**

Table T4: Optimization of amount of base and oxidant



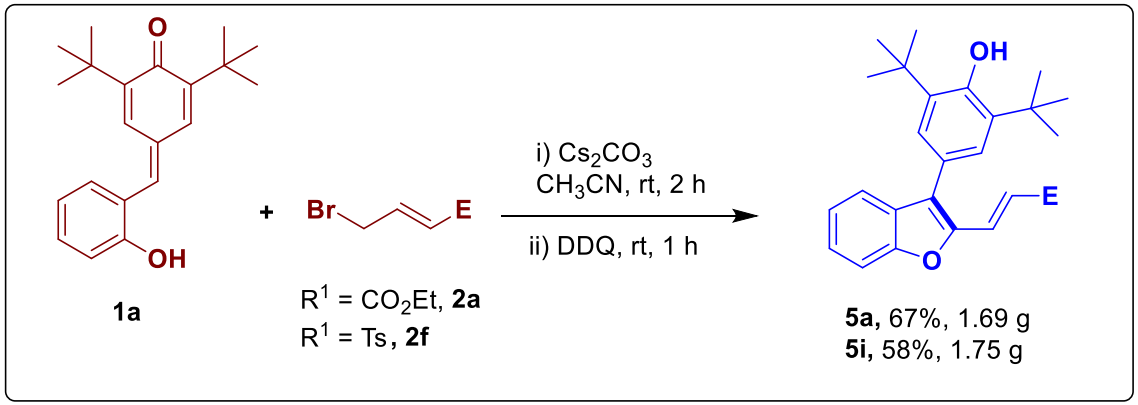
Entry.	Cs_2CO_3 (equiv)	DDQ (equiv)	% Yield of 5a
1	5	2	68
2	**3**	**2**	**76**
3	1	2	NR
4	3	1	68

Table T5: Optimization of Time and Temp.



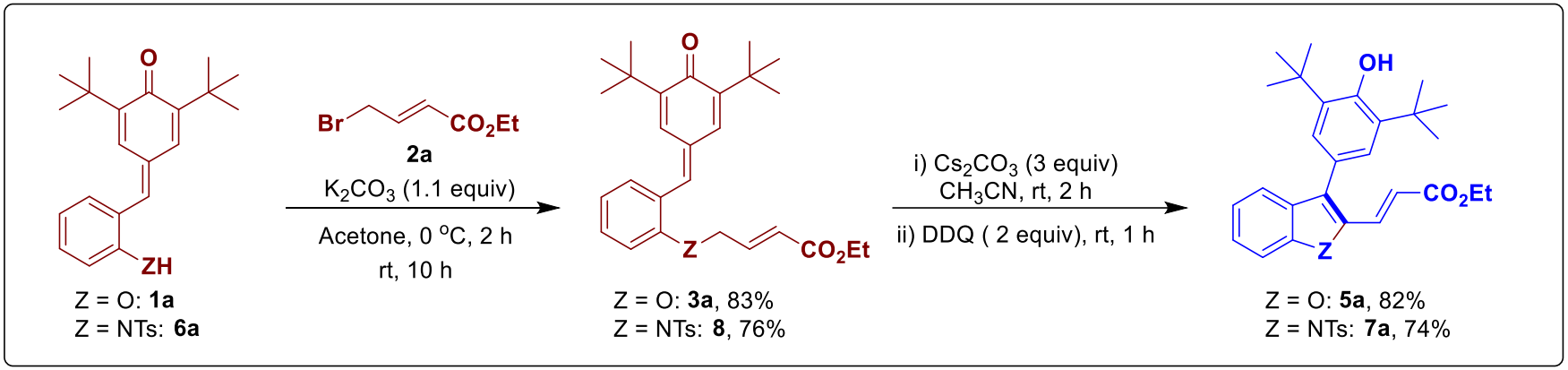
Entry.	Temp	Time (h)	% Yield of 5a
1	rt	1+2	48
2	rt	2+2	76
3	**rt**	**2+1**	**80**
4	50 ^{o}C	2+1	62

5. Experimental procedure for the gram-scale syntheses of 5a and 5i



To a clean and oven-dried 100 mL round bottom flask were added *p*-QM **1a** (1 equiv, 6 mmol, 1.86 g) and ethyl (*E*)-4-bromobut-2-enoate **2a** (1.3 equiv, 7.8 mmol, 1.07 mL) (or) (*E*)-1-((3-bromoprop-1-en-1-yl)sulfonyl)-4-methylbenzene **2f** (1.3 equiv, 7.8 mmol, 2.14 g), CH_3CN (30 mL) and Cs_2CO_3 (3 equiv, 18 mmol, 5.89 g). The reaction was stirred at room temperature for 2 h. Subsequently, DDQ (2 equiv, 12 mmol, 2.72 g) was added to the reaction mixture was allowed to stir at the same temperature for 1 h. To this reaction mixture were added water (30 mL) and EtOAc (30 mL). The resulting mixture was extracted with EtOAc (2 x 50 mL). Then the combined organic phase was washed with water (30 mL) and brine (30 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a crude residue. The resulting residue was purified by column chromatographyon silica gel to afford substituted benzofuran derivative **5a** (or) **5i** in 67% (or) 58% yield, respectively.

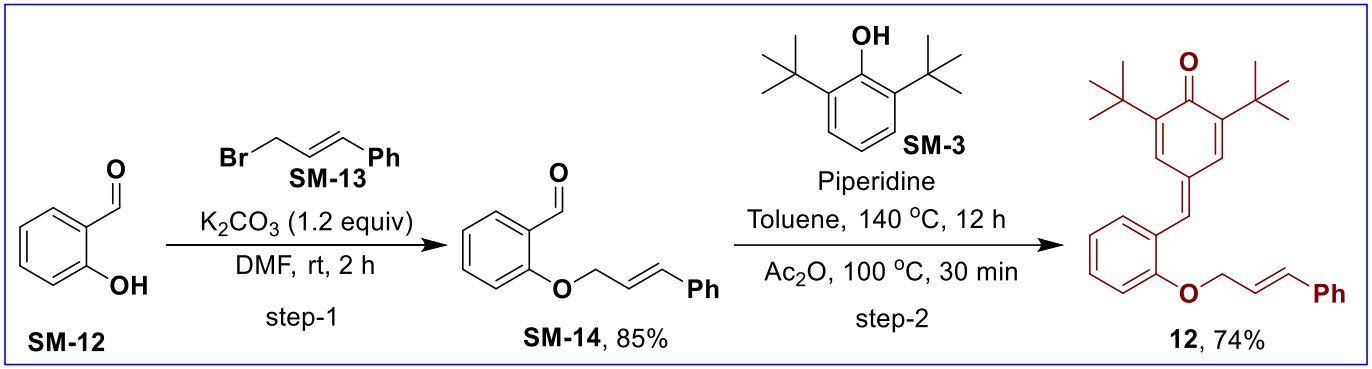
6. Control experiments and mechanistic studies



To a clean and oven dried round bottom flask (10 mL) were added *p*-QM **1a** (or) **6a** (1 equiv, 1 mmol), anhydrous K_2CO_3 (1.1 equiv, 1.1 mmol, 152 mg) and dry acetone (10 mL). The reaction mixture was stirred at 0 °C for 15 min. To this reaction mixture was added a solution of ethyl 4-bromobut-2-enoate **2a** (1.3 equiv, 1.3 mmol, 0.18 mL) in acetone (3 mL) dropwise over 10 min the temperature of the reaction mixture was maintained at 0 °C during the addition. After the addition, the reaction mixture was allowed to stir at 0 °C for 2 h, then at room temperature for another period of 10 h. After this time, the reaction mixture was concentrated under reduced pressure. The resulting residue was extracted with EtOAc (2 x 20 mL). The combined organic phase was washed with water (20 mL), 2 N NaOH solution (10 mL), brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel to afford the desired products **3a** (or) **8** in 83% (or) 76% yield, respectively.

To a 15 mL clean and dry screw cap vial, Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg) was added followed by the addition of a solution of *para*-quinone methide-allylcinnamate derivative **3a** (or) **8** (0.5 equiv, 0.5 mmol) in CH_3CN (5 mL). The reaction vial was closed and allowed to stir, at room temperature for 2 h. Subsequently, DDQ (2 equiv, 1 mmol, 227 mg) was added to the reaction mixture at the same temperature for and allowed

the reaction mixture to stir for 1 h. To this reaction mixture were added water (5 mL) and EtOAc (5 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). Then the combined organic phase was washed with water (5 mL) and brine (5 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford 2-alkenyl benzofuran **5a** (or) 2-alkenylindole **7a** in 82% (or) 74% yield, respectively.

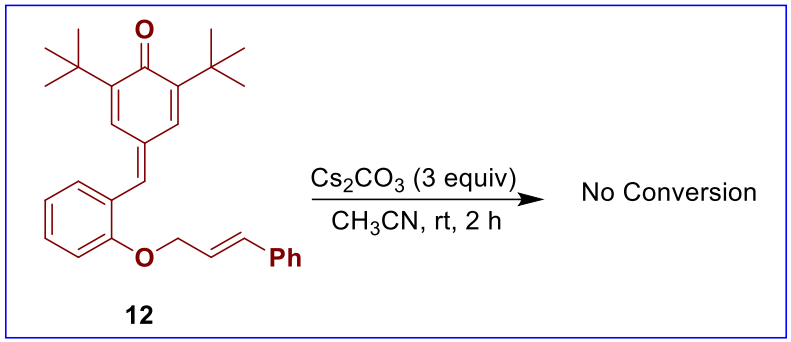


Step-1: In a reaction vial, to a solution of salicylaldehyde **SM-12** (1 equiv, 5 mmol, 0.52 mL) with cinnamyl bromide **SM-13** (1.2 equiv, 6 mmol, 0.89 mL) in DMF (10 mL) was added a suspension of K_2CO_3(1.2 equiv, 6 mmol, 828 mg) in DMF (20 mL) at room temperature and the reaction mixture was stirred for 2 h. To the reaction mixture were added water (20 mL) and EtOAc (20 mL). The resulting mixture was extracted with EtOAc (2 x 30 mL). Then the combined organic phase was washed with water (20 mL) and brine (20 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel to afford the O-allylated derivative **SM-14** in 85% yield.[5]

Step-2: A solution of phenol **SM-3** (1.1 equiv, 4.4 mmol) and aldehyde **SM-14** (1 equiv, 4 mmol) in toluene (16 mL) was placed in a Dean-Stark apparatus which was heated to reflux. Piperidine (2 equiv, 8 mmol) was added slowly in a dropwise manner. Then, the temperature was raised to 140 °C and stirred for 12 h. After that, the reaction mixture was cooled to 120 °C and acetic anhydride (2.0 equiv, 8 mmol) was dropwise added.

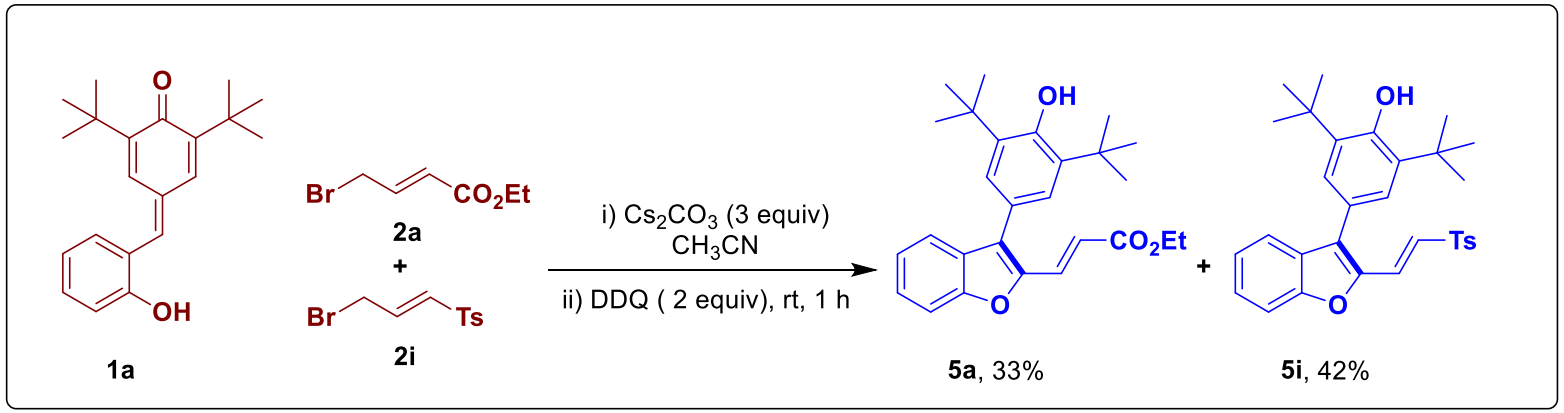
The stirring was continued for 30 min and the solution was poured in ice-water and extracted with EtOAc (3 x 20 mL). The organic phases were combined, washed with brine and dried over anhydrous Na_2SO_4. Then the solvent was evaporated under reduced pressure to afford the corresponding *p*-QM **12** after flash column chromatography (Hexane/EtOAc = 95/5).

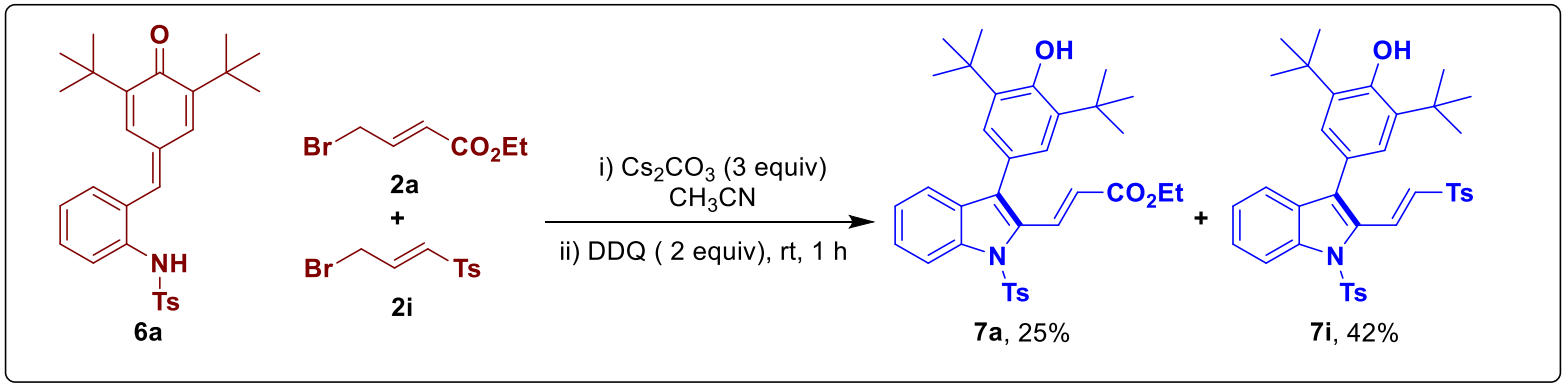
Spectral data for compound **12**: Yellow solid, 315 mg (0.74 mmol), 74%, R_f = 0.4 (EtOAc/Hex, 10:90); **MP** 193-195 ^oC; **IR** ($CHCl_3$) 2999, 2956, 2863, 1639, 1615, 1487, 1457, 1364 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.45 (m, 2H), 7.44 – 7.38 (m, 3H), 7.37 – 7.32 (m, 2H), 7.28 (dt, *J* = 4.9, 1.9 Hz, 1H), 7.10 (d, *J* = 2.3 Hz, 1H), 7.04 (dd, *J* = 17.1, 7.9 Hz, 2H), 6.74 (d, *J* = 16.0 Hz, 1H), 6.44 (dt, *J* = 16.0, 5.8 Hz, 1H), 4.79 (dd, *J* = 5.8, 1.3 Hz, 2H), 1.35 (s, 9H), 1.29 (s, 9H); **^{13}C{^{1}H}NMR** (101 MHz, $CDCl_3$) δ 186.7, 157.4, 149.0, 147.4, 138.9, 136.2, 135.4, 133.4, 132.0, 131.7, 130.8, 128.7, 128.4, 128.1, 126.6, 126.0, 125.4, 124.1, 120.8, 112.3, 69.3, 35.4, 35.1, 29.6; **MS** (ESI,*m/z*): $[M+Na]^+$ 449.



To a 15 mL clean screw cap vial, Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg) was added followed by a solution of *p*-QM **10** (0.5 equiv, 0.5 mmol, 213 mg) in a CH_3CN (5 mL). The reaction vial was closed and the reaction mixture was allowed to stir at room temperature for 2 h. The reaction was monitoring by TLC and found that starting material remained unreacted.

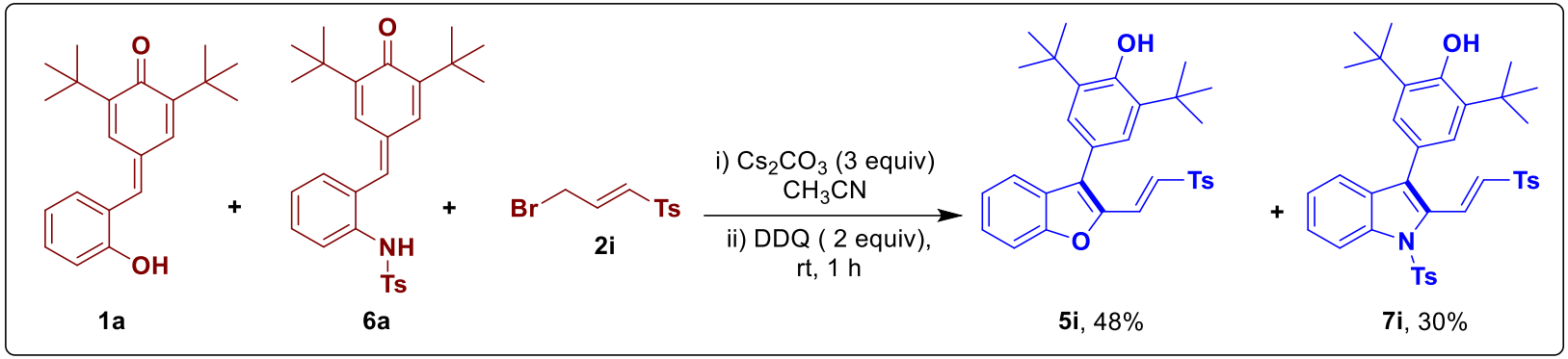
Cross-over experiments:





In a 15 mL clean and dry screw cap vial, *p*-QM **1a** (or) **6a** (1 equiv, 0.5 mmol), ethyl (*E*)-4-bromobut-2-enoate **2a**(1 equiv, 0.5 mmol, 96 mg) and (*E*)-1-((3-bromoprop-1-en-1-yl)sulfonyl)-4-methylbenzene **2f** (1 equiv, 0.5 mmol, 137 mg) in CH_3CN (5 mL) were taken followed by the addition of Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg). The reaction mixture was stirred at room temperature for 2 h. Subsequently, DDQ (2 equiv, 1 mmol, 227 mg) was added to the reaction mixture at the same temperature and the reaction mixture was allowed to stir for 1 h. To the reaction mixture were added water (10 mL) and EtOAc (10 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). Then the combined organic phase was washed with water (10 mL) and brine (5 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a

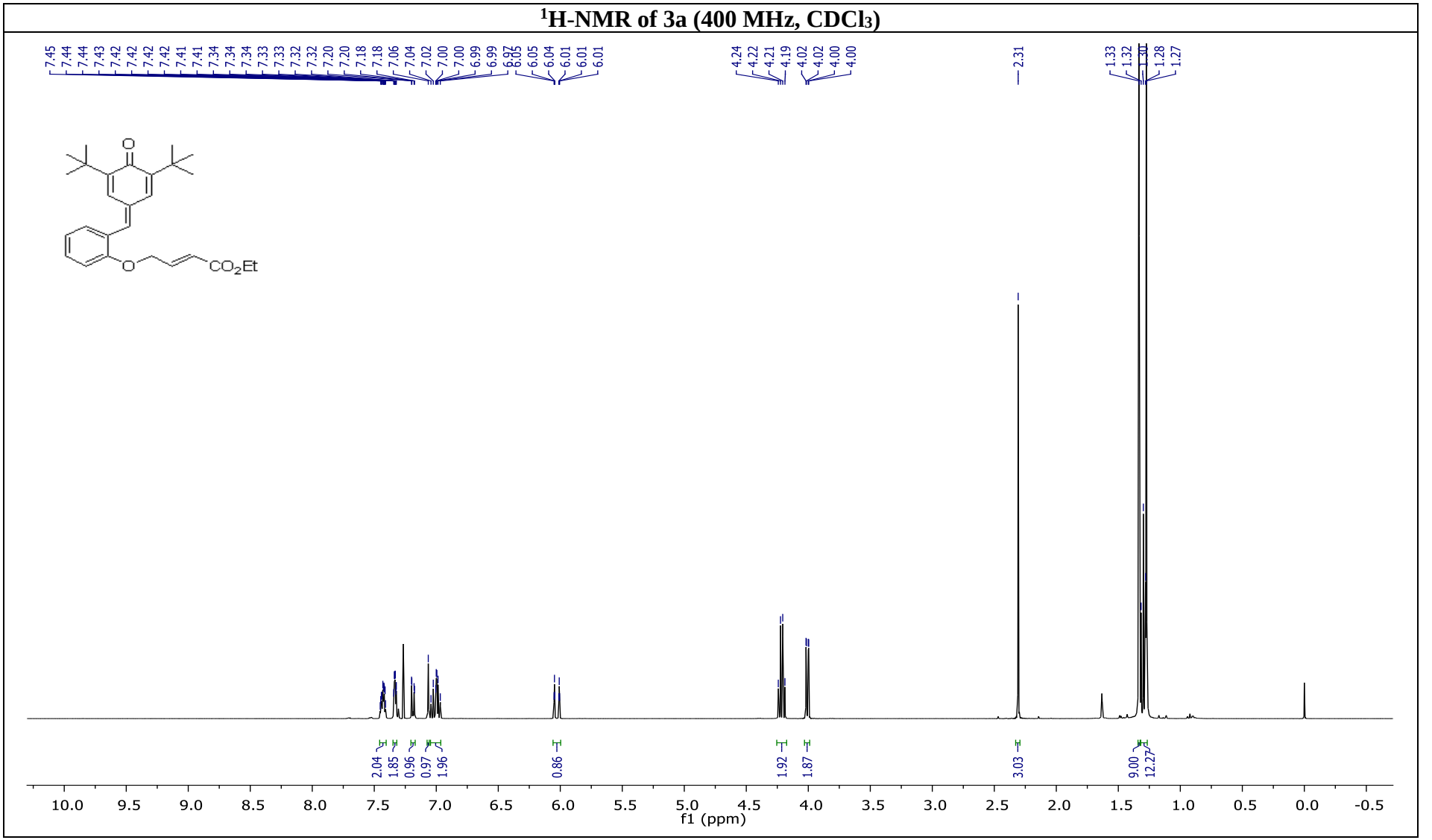
crude residue. The resulting residue was purified by column chromatography on silica gel to afford the substituted benzofuran derivatives **5a** and **5i** in 33% and 45% yield, respectively (or) indole derivatives **7a** and **7i** in 25% and 42% yield, respectively.



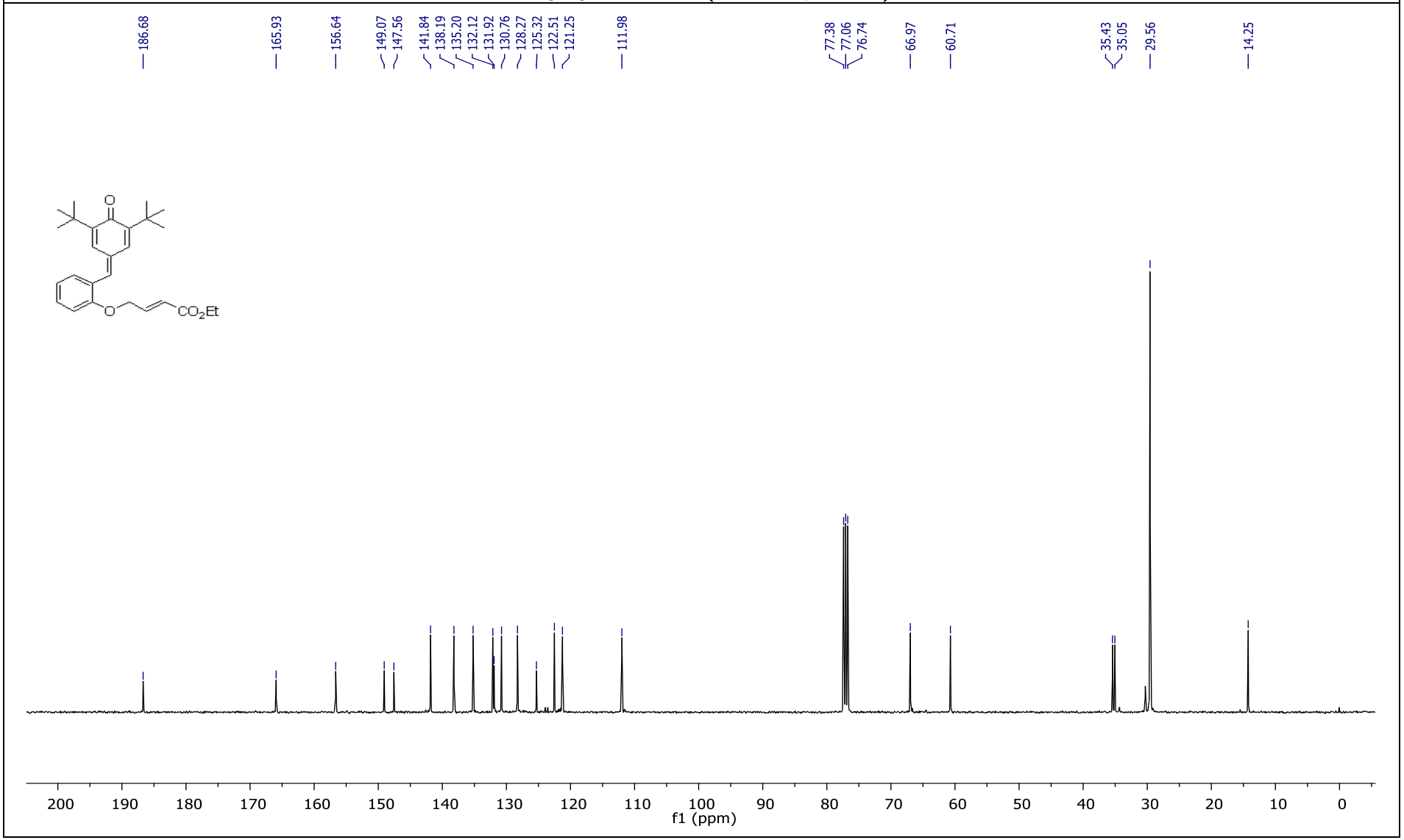
In a 15 mL clean and dry screw cap vial, *p*-QMs **1a** (or) **6a** (1 equiv, 0.5 mmol) and ethyl (*E*)-1-((3-bromoprop-1-en-1-yl)sulfonyl)-4-methylbenzene **2f** (1 equiv, 0.5 mmol, 137 mg) in CH_3CN (5 mL) were taken followed by the addition of Cs_2CO_3 (3 equiv, 1.5 mmol, 489 mg). The reaction mixture was stirred at room temperature for 2 h. Subsequently, DDQ (2 equiv, 1 mmol, 227 mg) was added to the reaction mixture at the same temperature and allowed the reaction mixture to stir for 1 h. To the reaction mixture were added water (10 mL) and EtOAc (10 mL). The resulting mixture was extracted with EtOAc (2 x 10 mL). Then the combined organic phase was washed with water (10 mL) and brine (5 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a crude residue. The resulting residue was purified by column chromatography on silica gel to afford the products **5i** and **7i** in 48%, 30% yield, respectively.

7. Copies of ^{1}H-NMR, ^{13}C{^{1}H}NMR and ^{19}F-NMR spectra

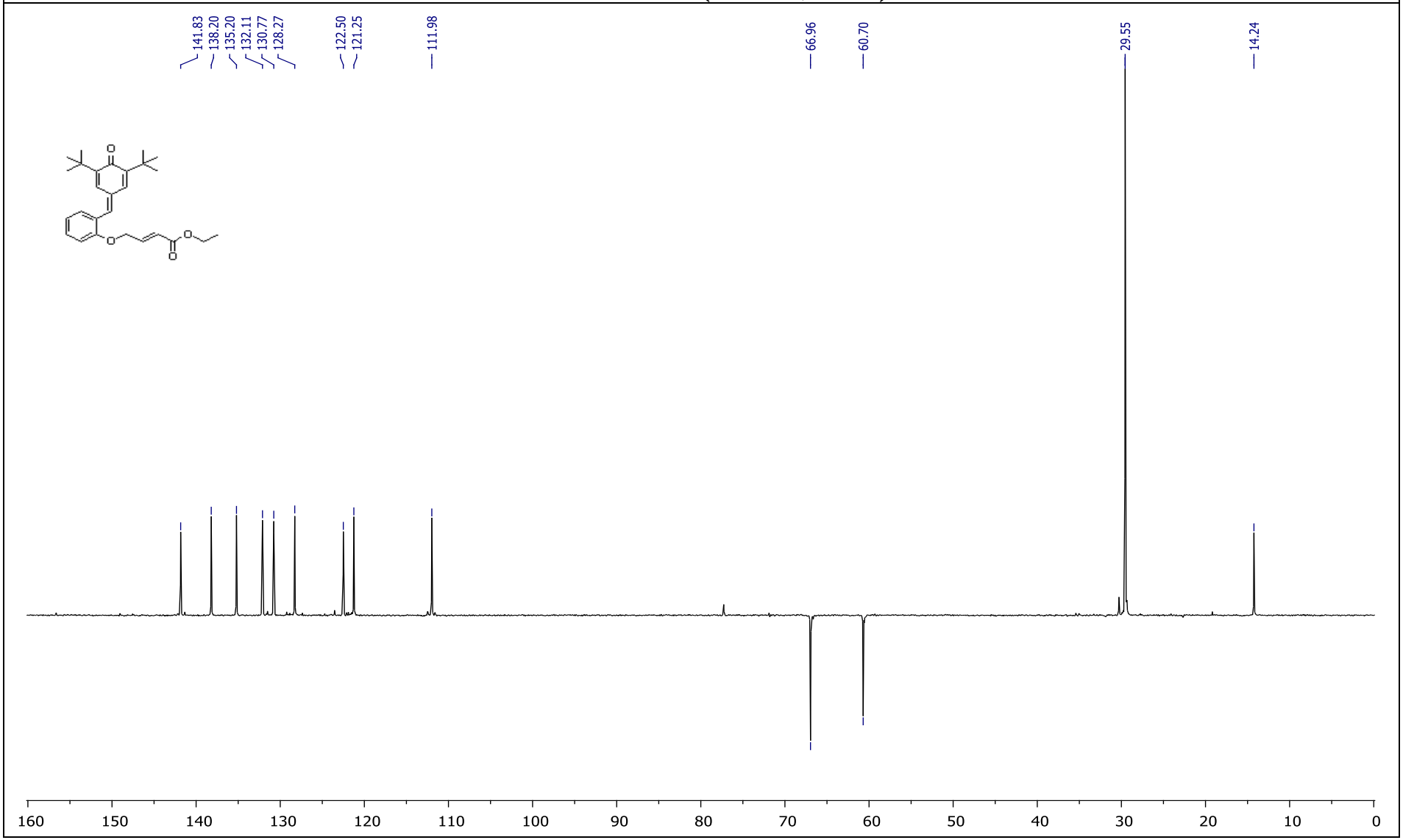
^{1}H-NMR of 3a (400 MHz, $CDCl_3$)



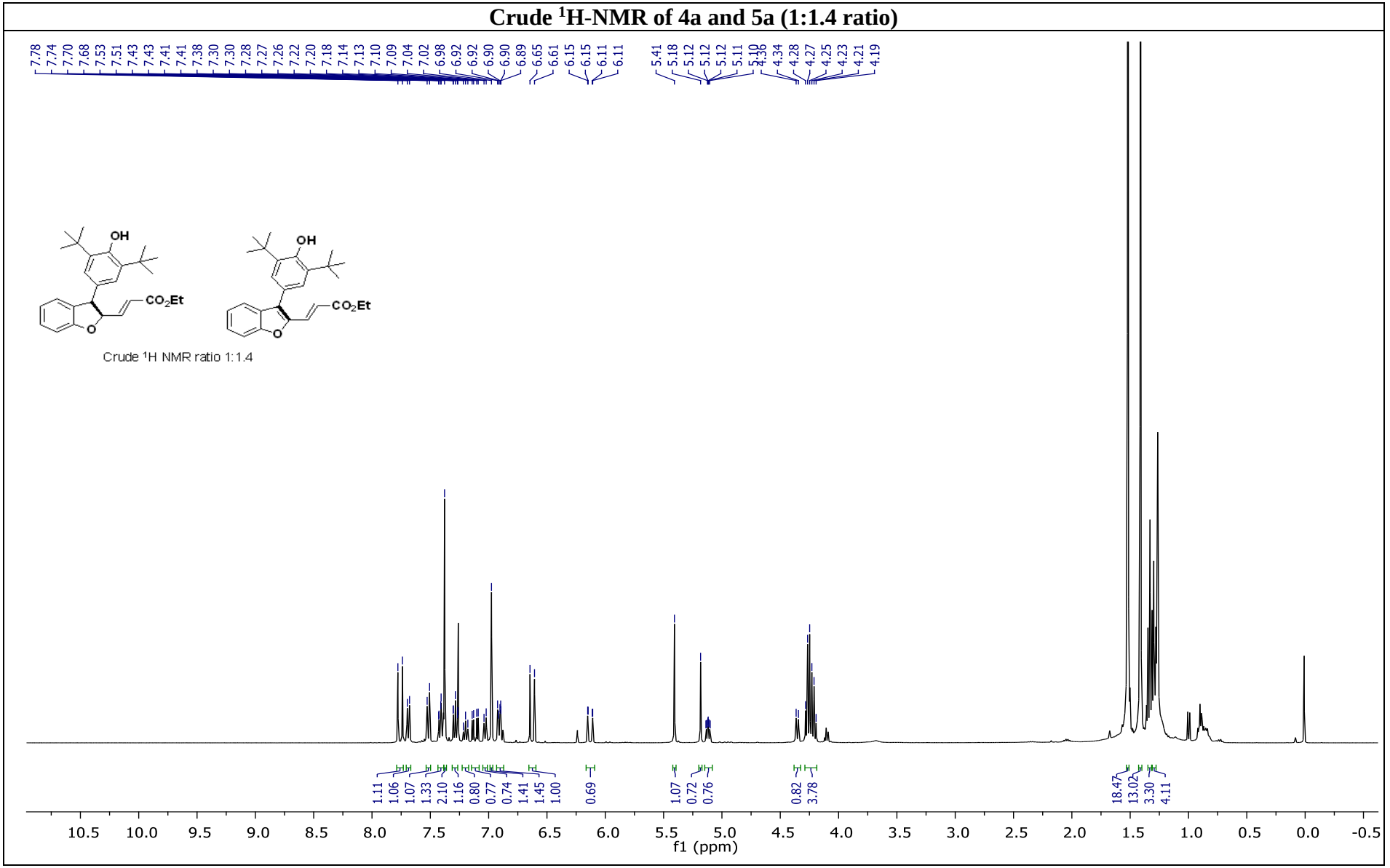
$^{13}C\{^{1}H\}$NMR of 3a (101 MHz, $CDCl_3$)



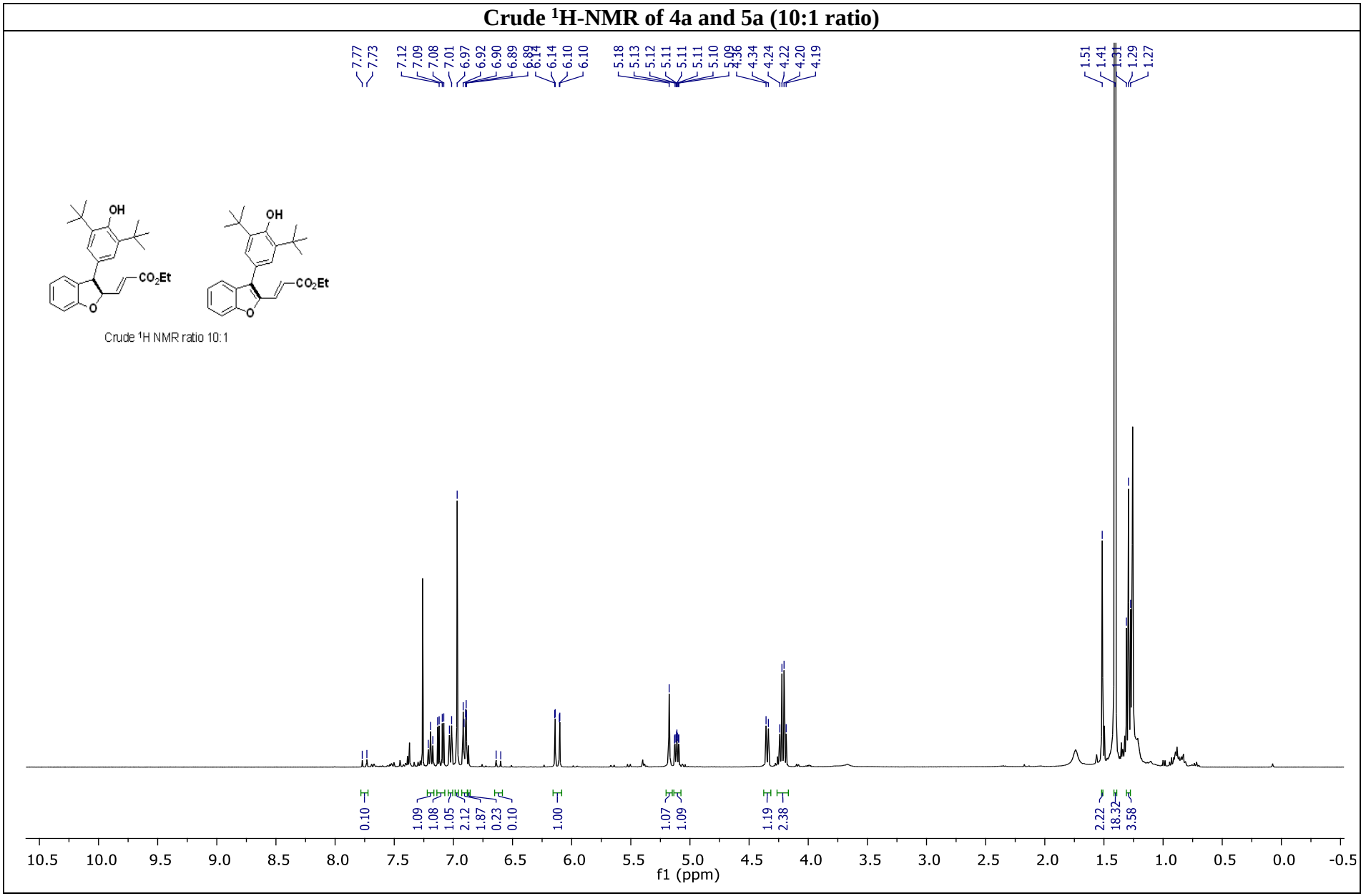
DEPT-NMR of 3a (135 MHz, $CDCl_3$)



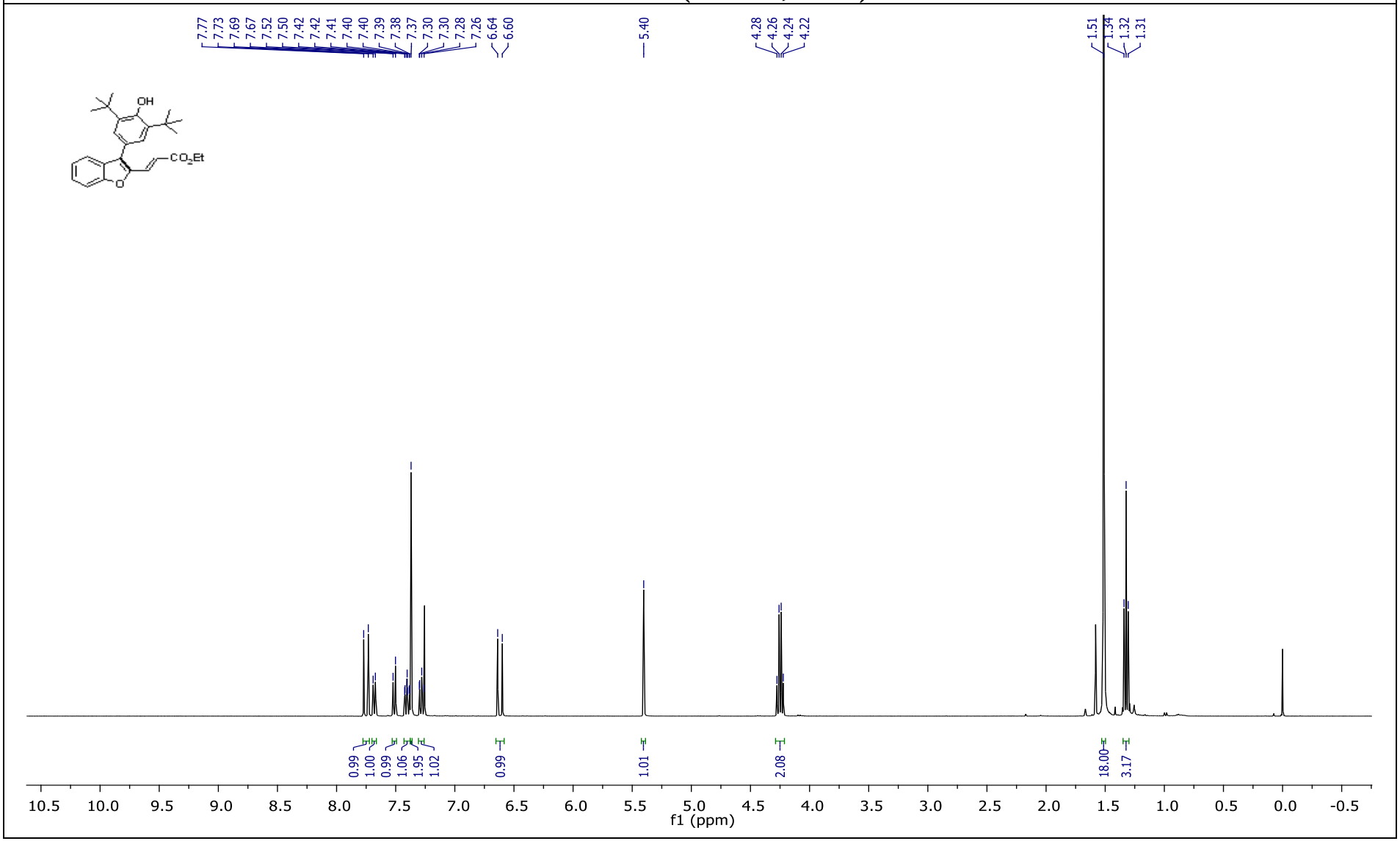
Crude ^{1}H-NMR of 4a and 5a (1:1.4 ratio)



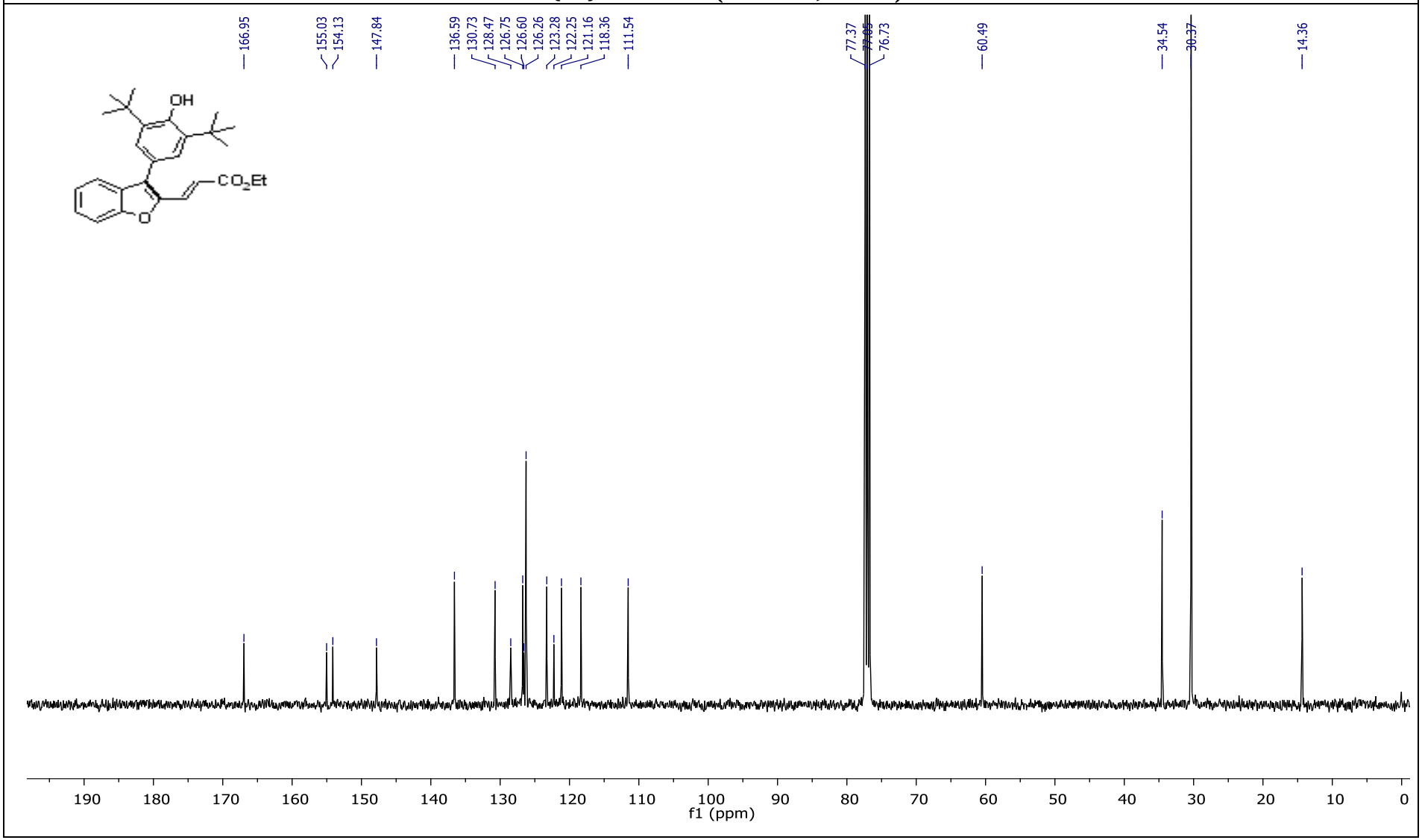
Crude ^{1}H-NMR of 4a and 5a (10:1 ratio)



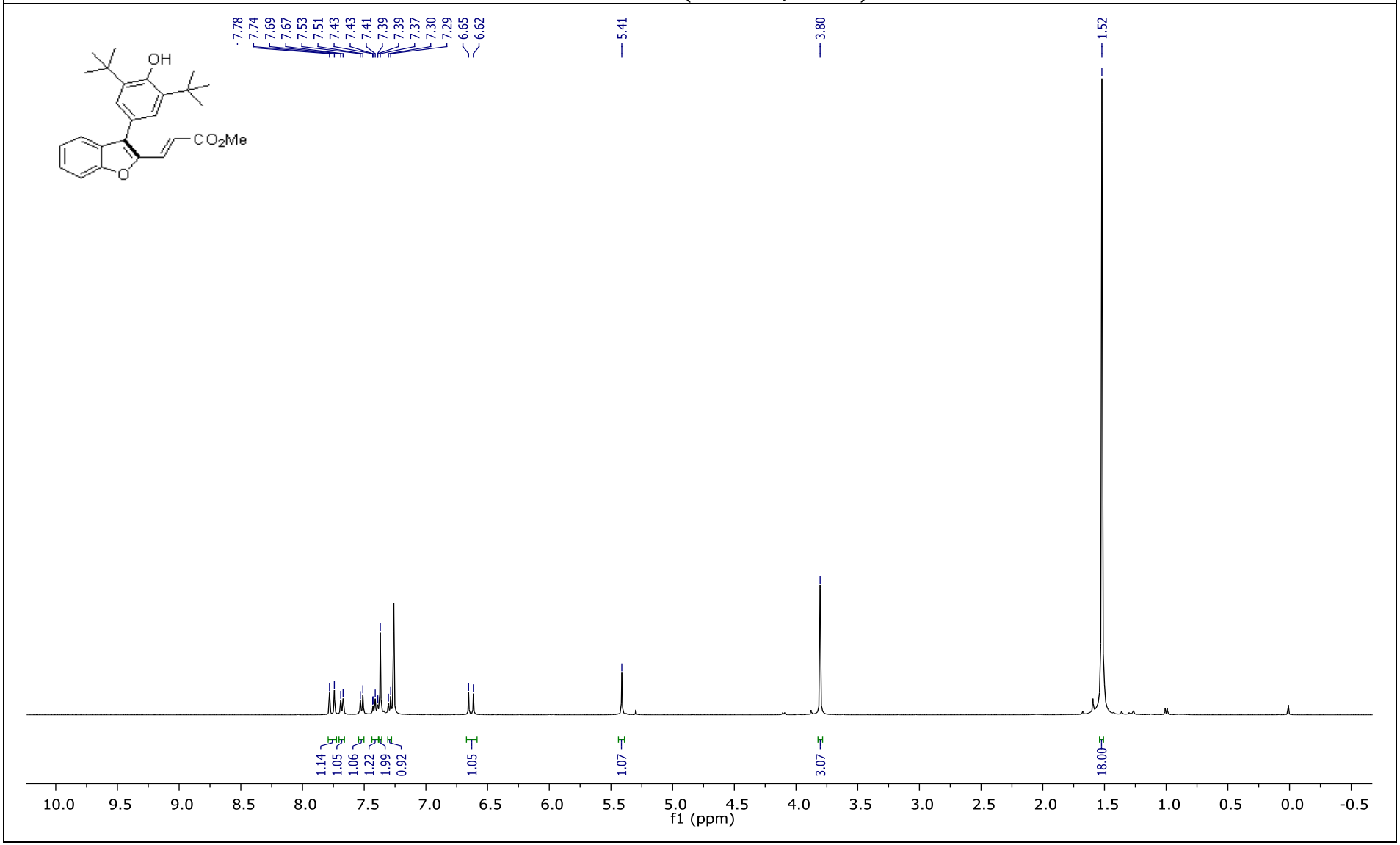
^{1}H-NMR of 5a (400 MHz, $CDCl_3$)



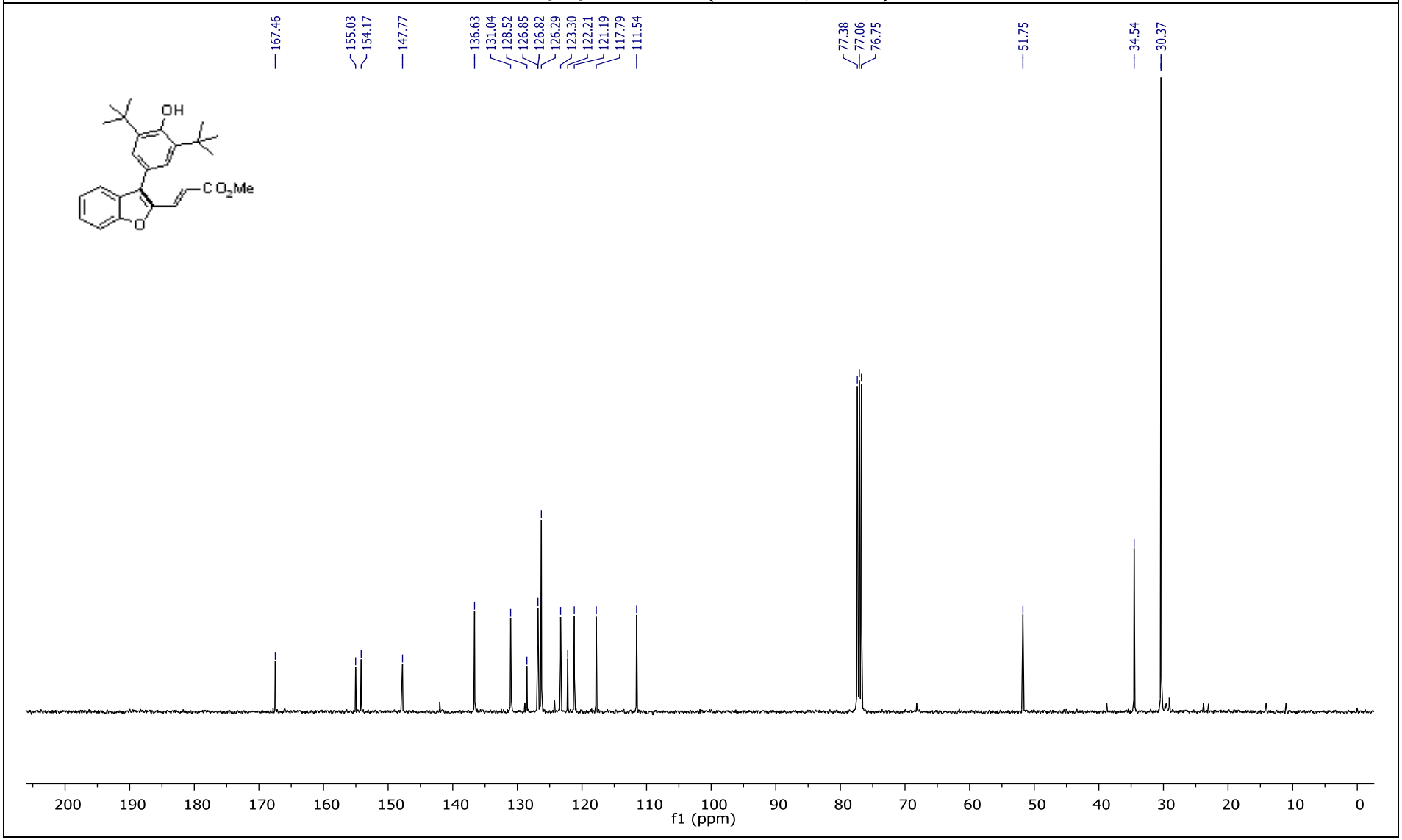
$^{13}C\{^{1}H\}$NMR of 5a (101 MHz, $CDCl_3$)



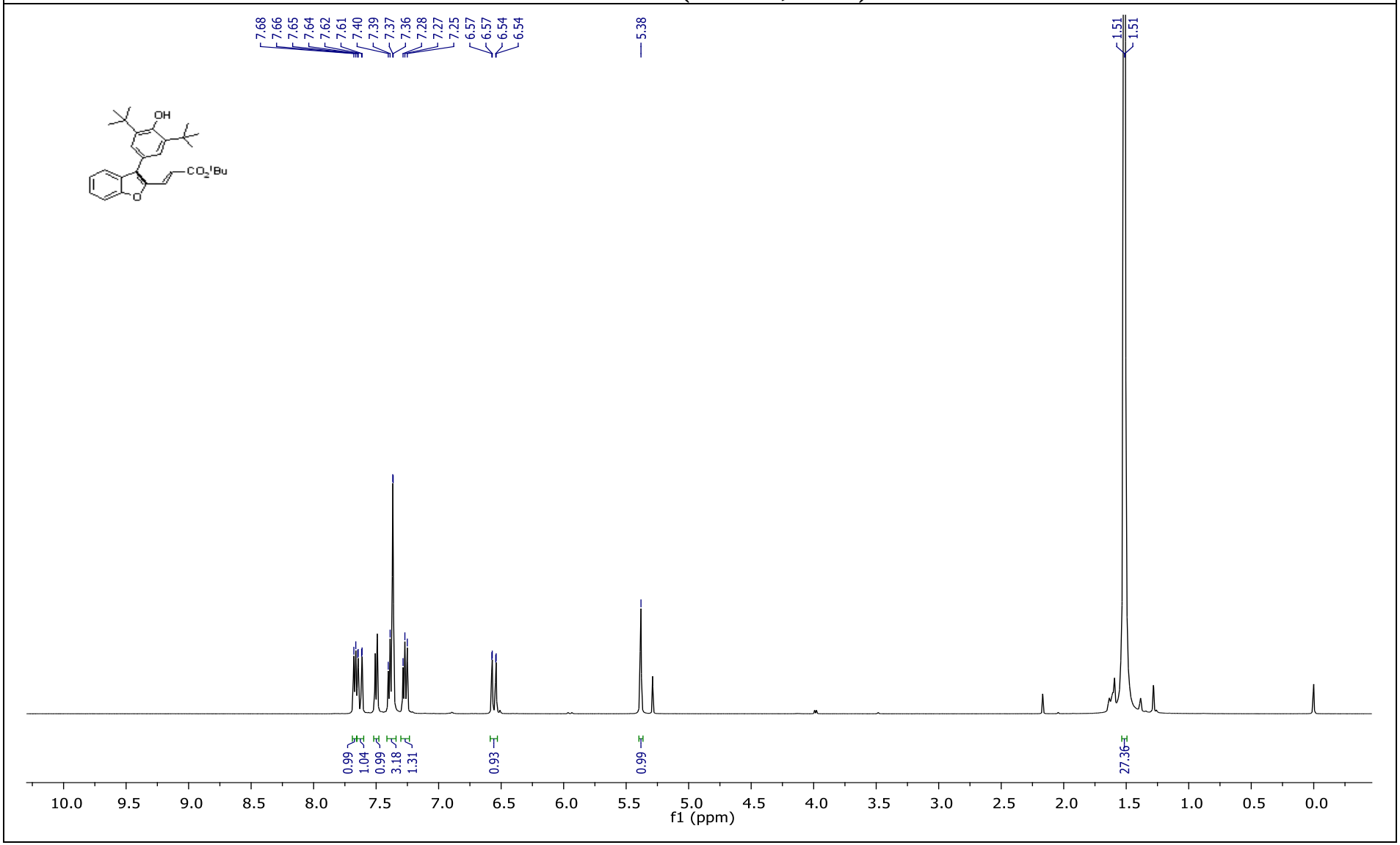
^{1}H-NMR of 5b (400 MHz, $CDCl_3$)



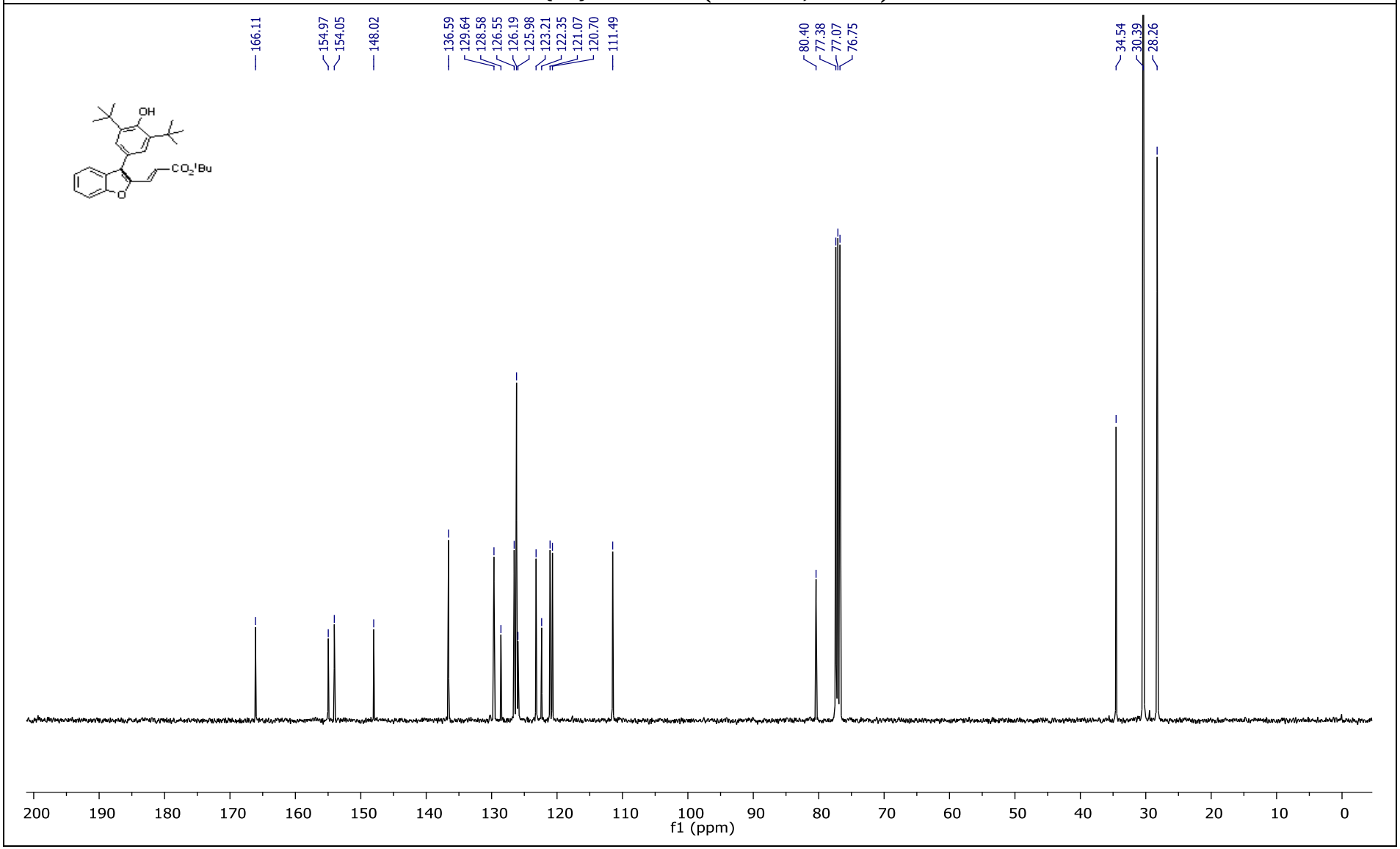
$^{13}C\{^{1}H\}$NMR of 5b (101 MHz, $CDCl_3$)



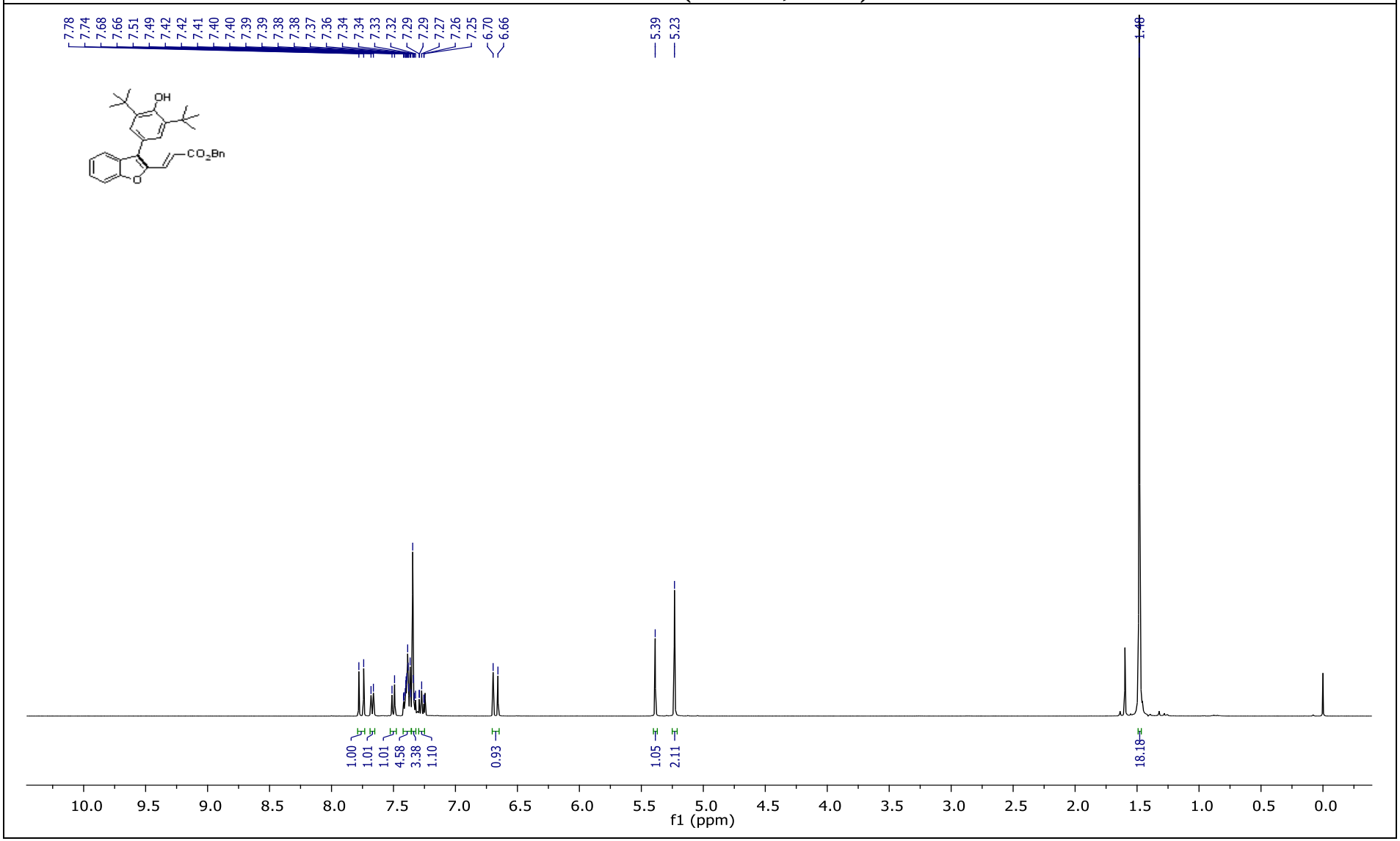
^{1}H-NMR of 5c (500 MHz, $CDCl_3$)



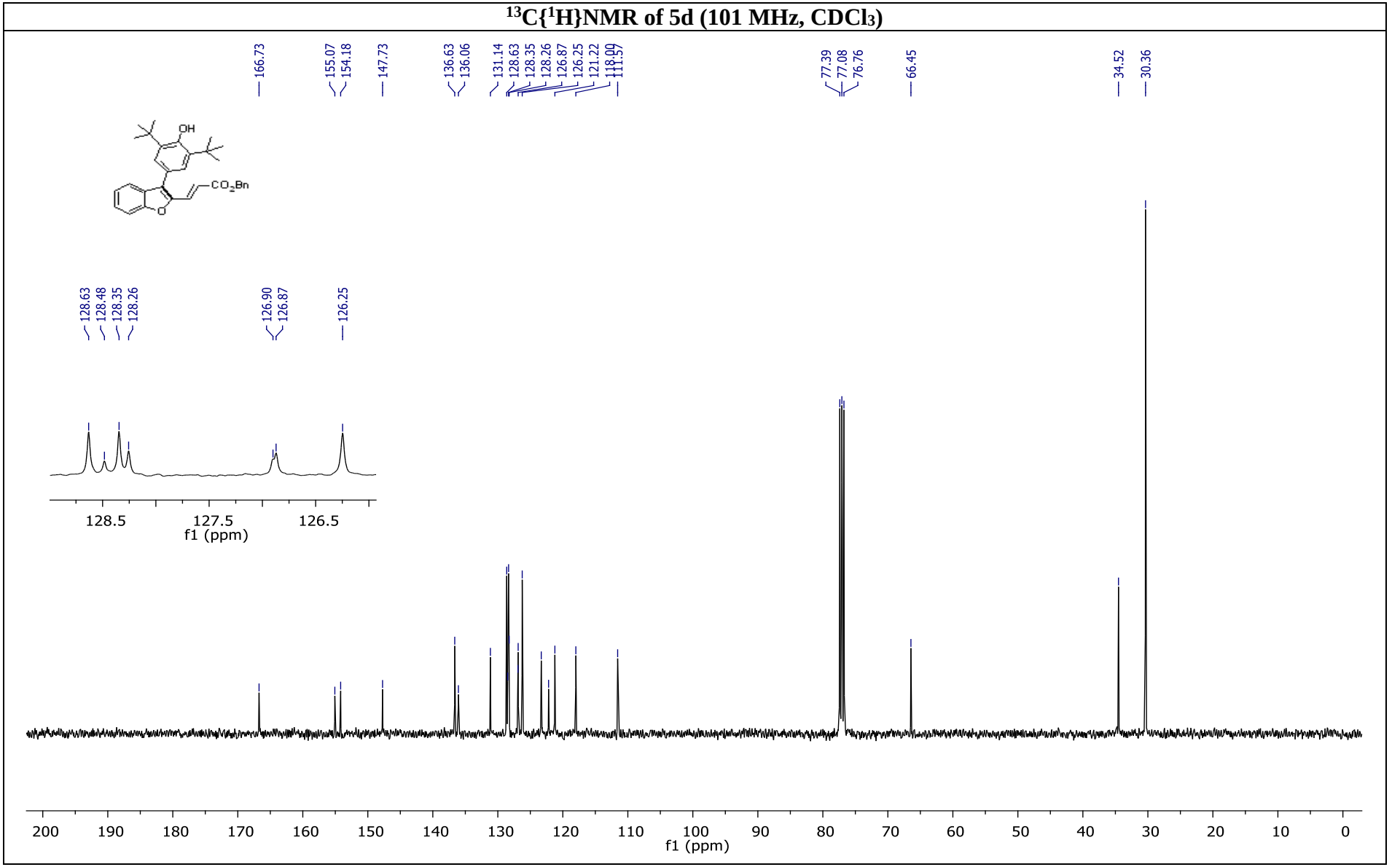
$^{13}C\{^{1}H\}$NMR of 5c (101 MHz, $CDCl_3$)



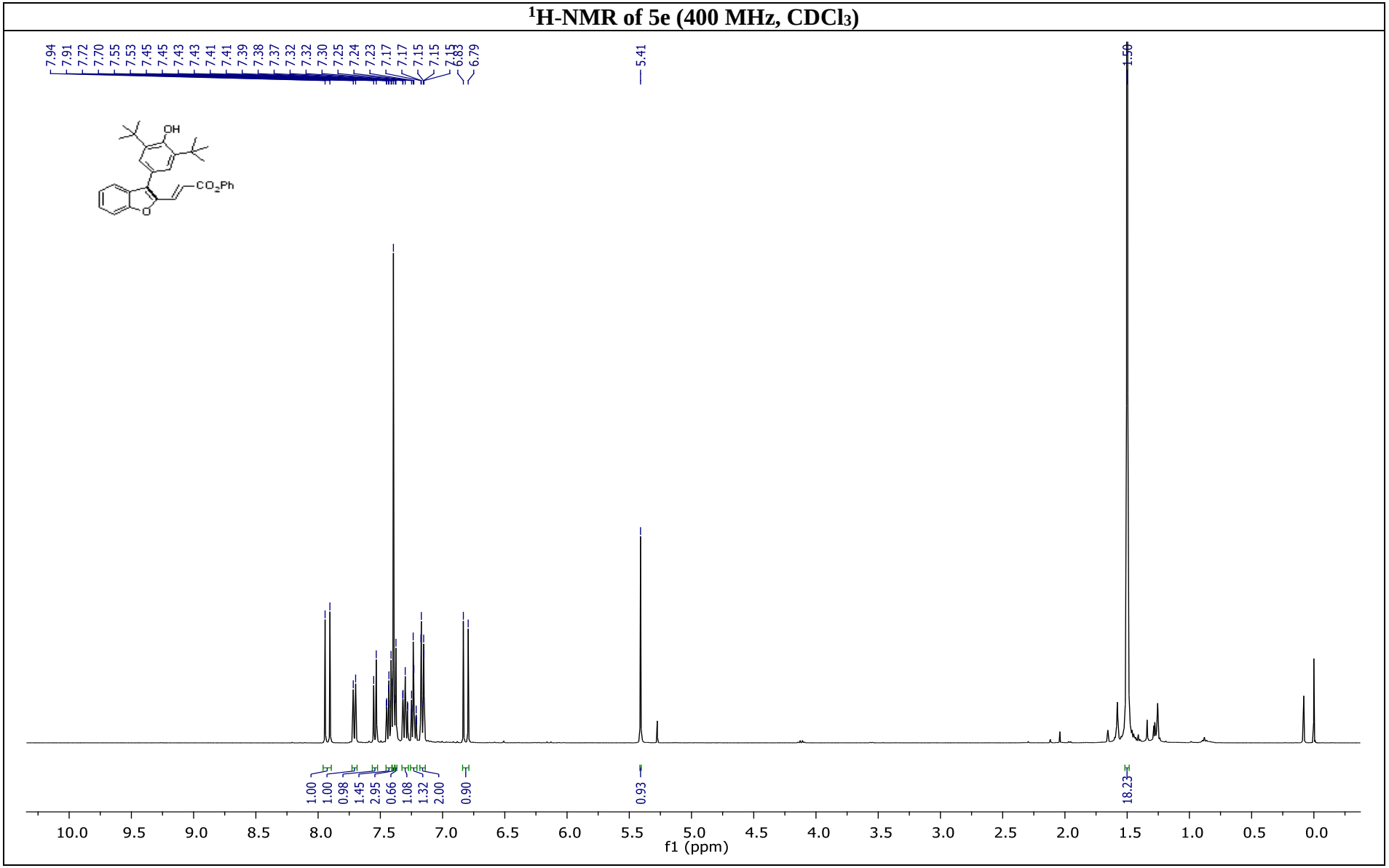
^{1}H-NMR of 5d (400 MHz, $CDCl_3$)



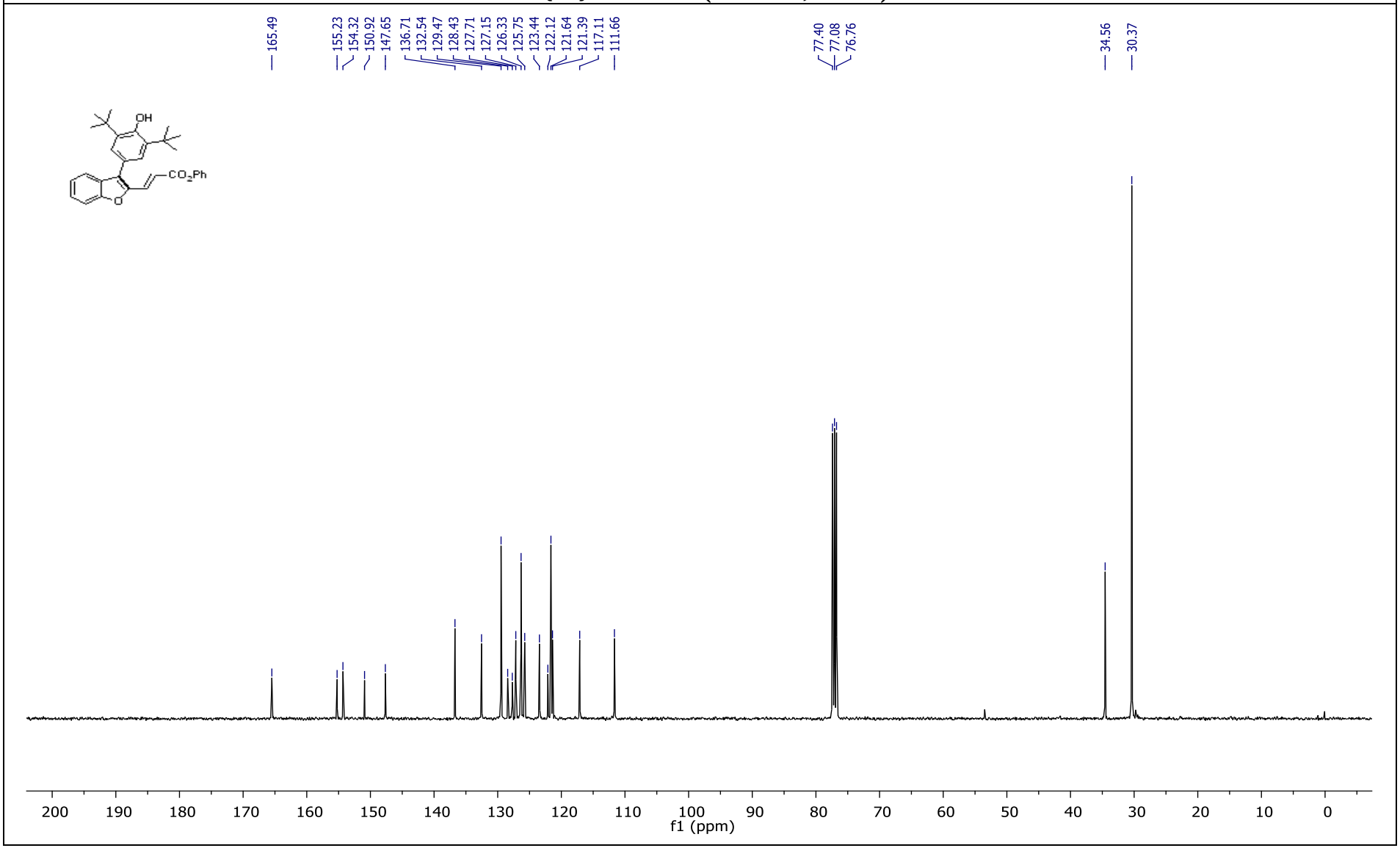
$^{13}C\{^{1}H\}$NMR of 5d (101 MHz, $CDCl_3$)



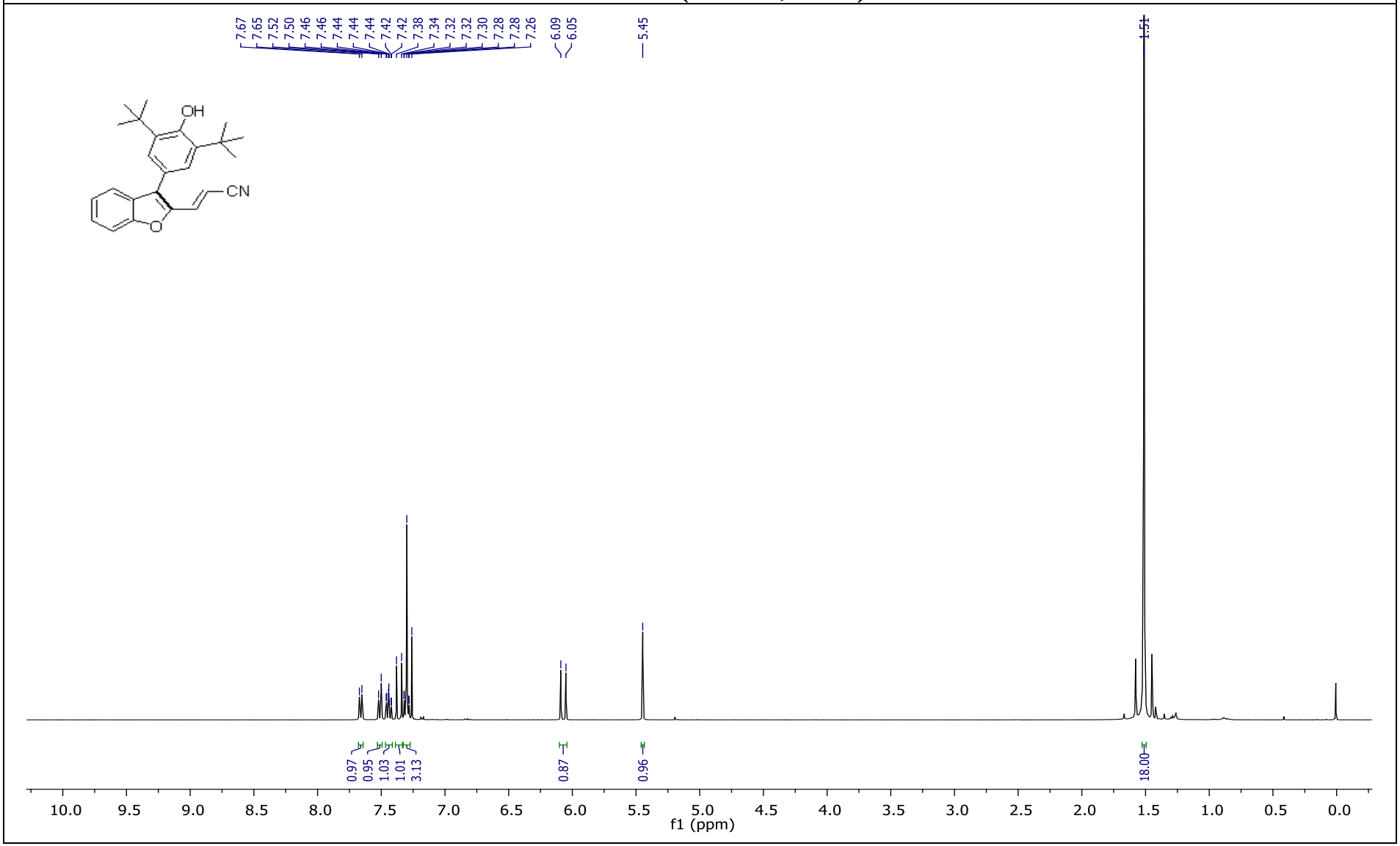
^{1}H-NMR of 5e (400 MHz, $CDCl_3$)



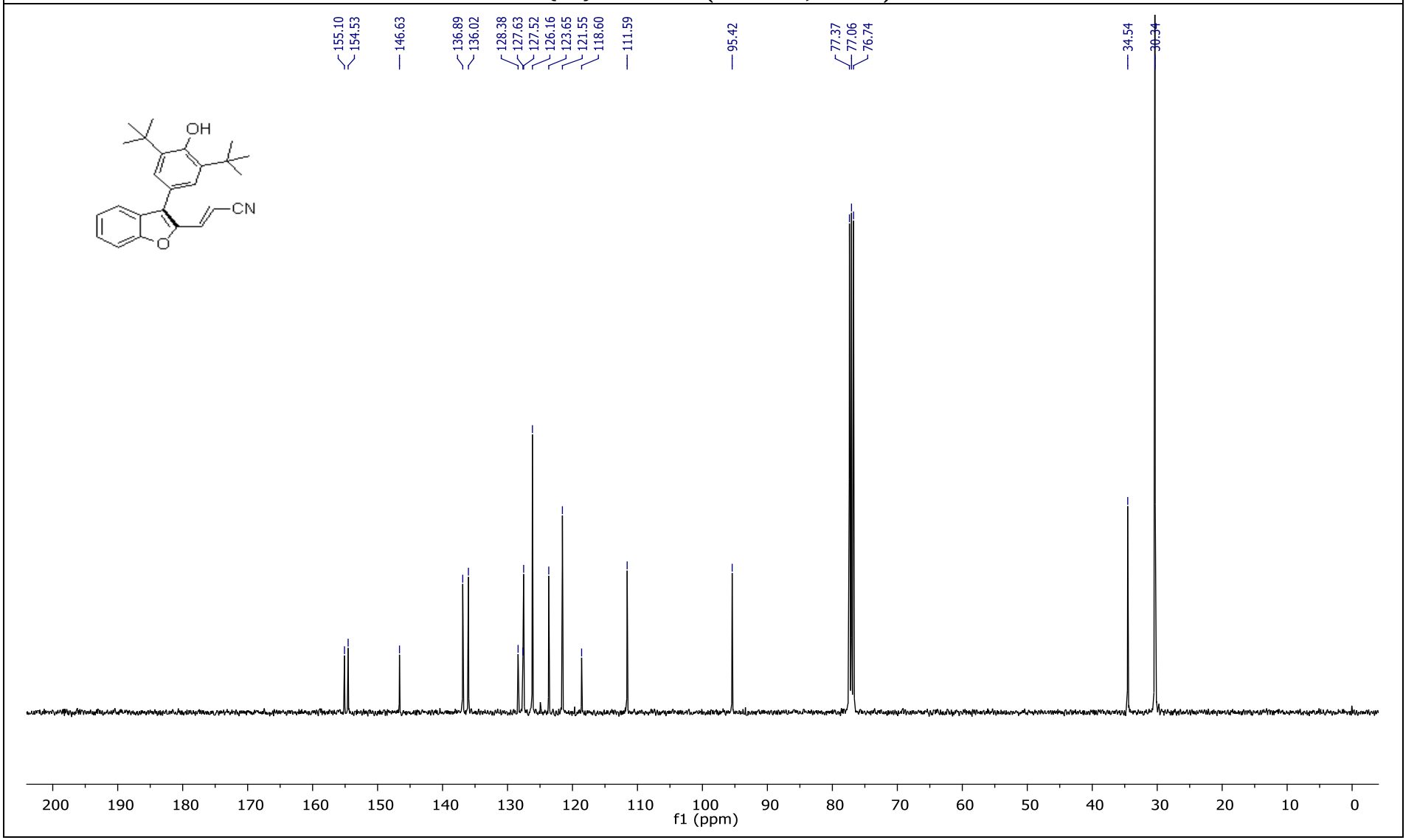
$^{13}C\{^{1}H\}$NMR of 5e (101 MHz, $CDCl_3$)



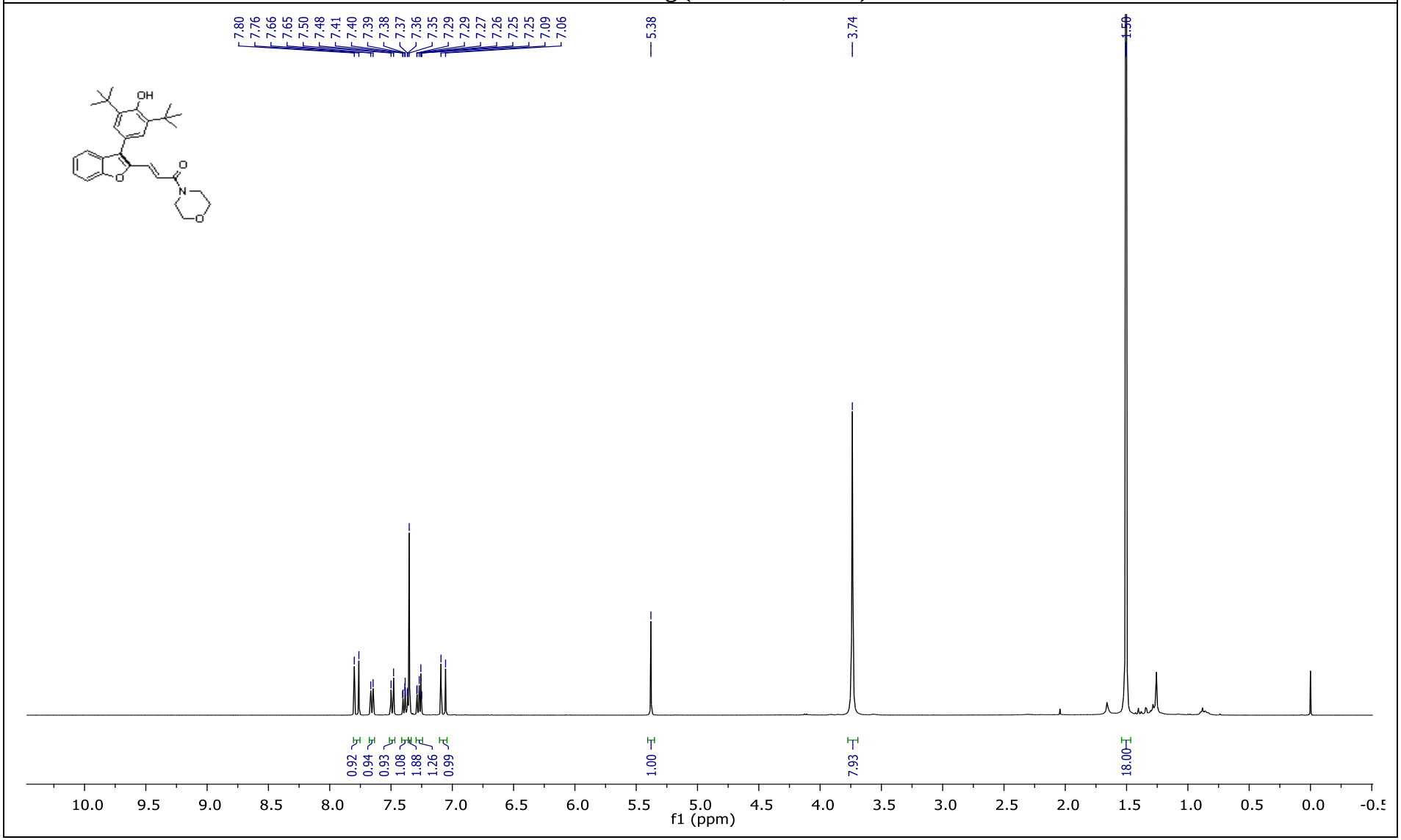
^{1}H-NMR of 5f (400 MHz, $CDCl_3$)



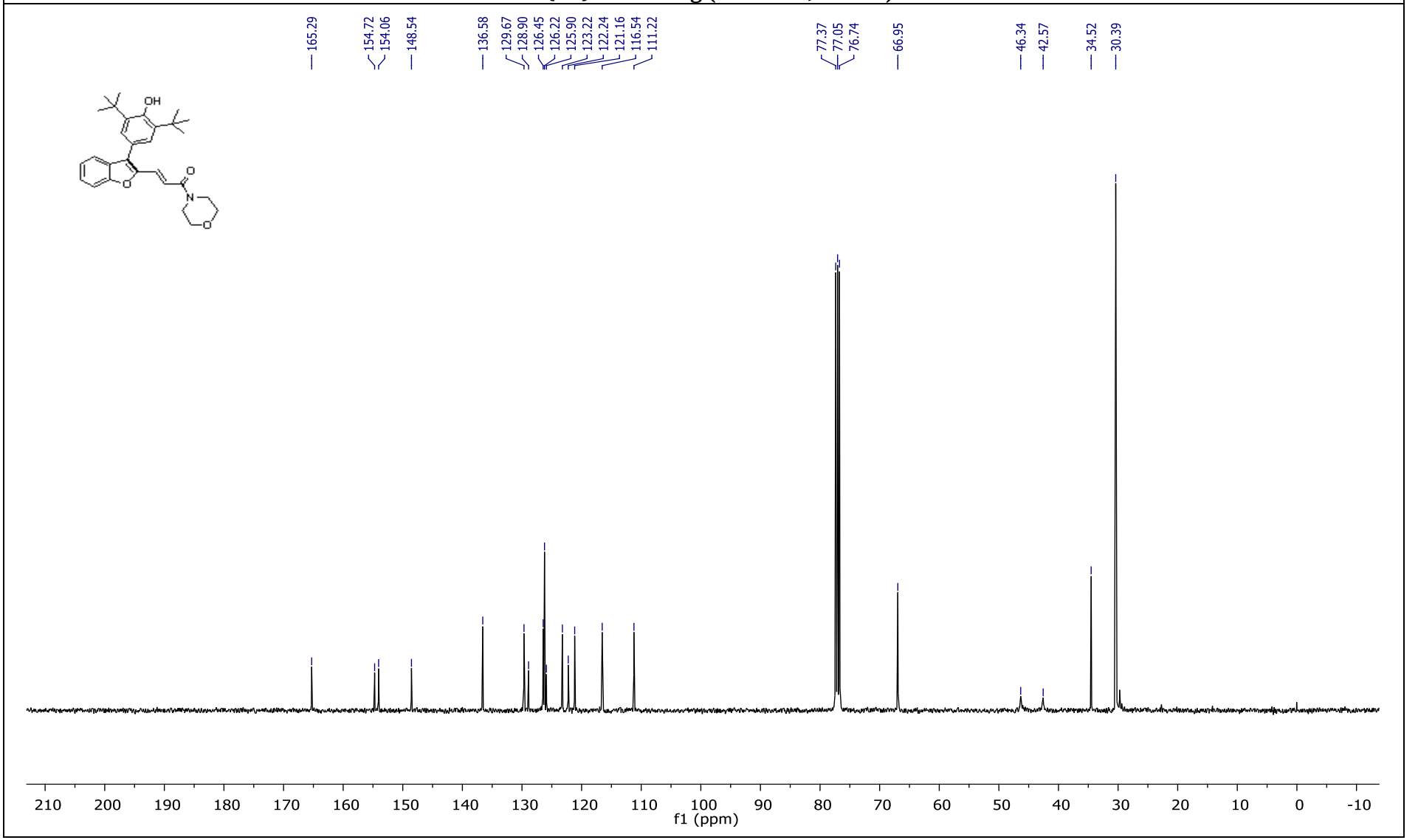
$^{13}C\{^{1}H\}$NMR of 5f (101 MHz, $CDCl_3$)



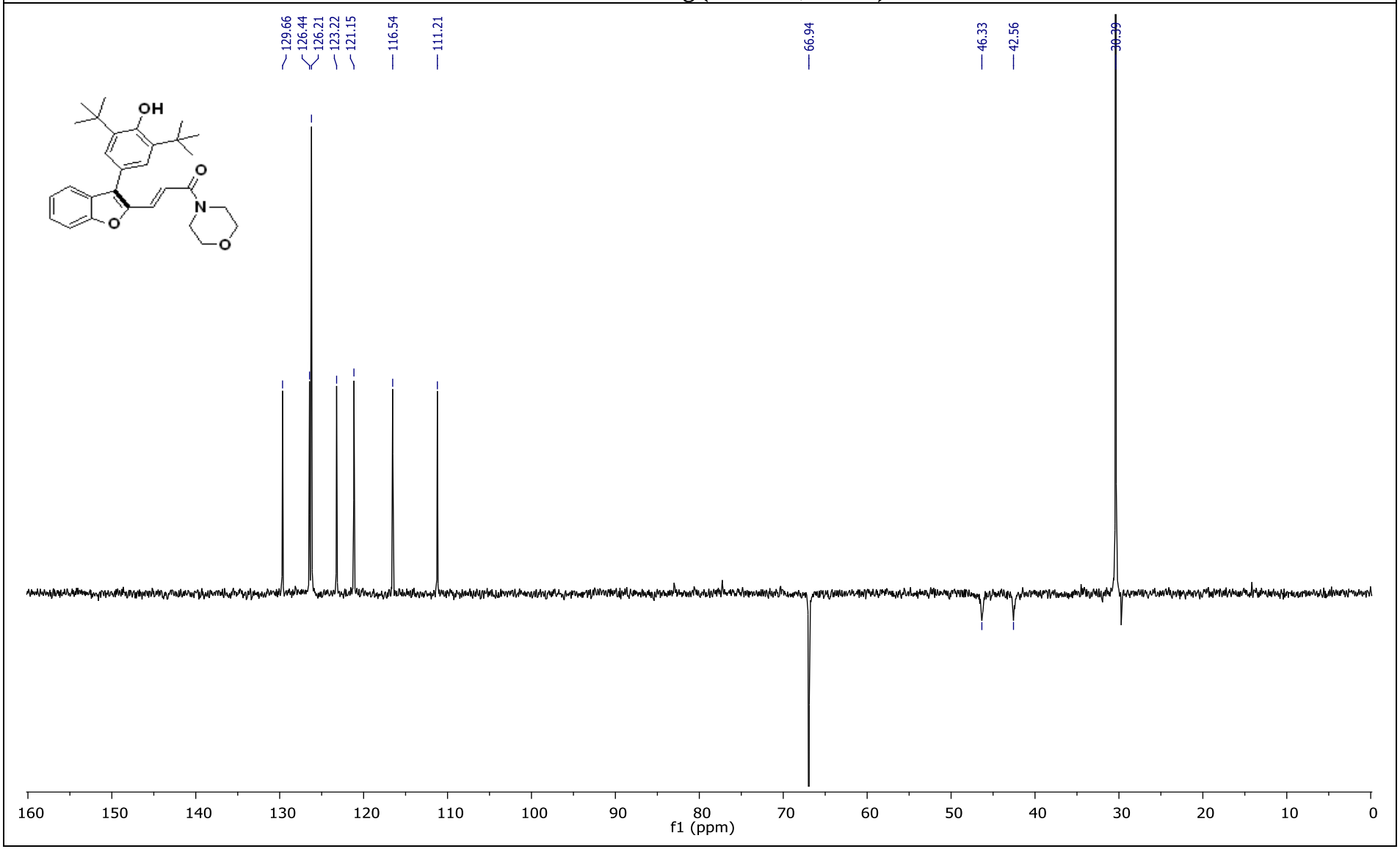
^{1}H-NMR of 5g (400 MHz, $CDCl_3$)



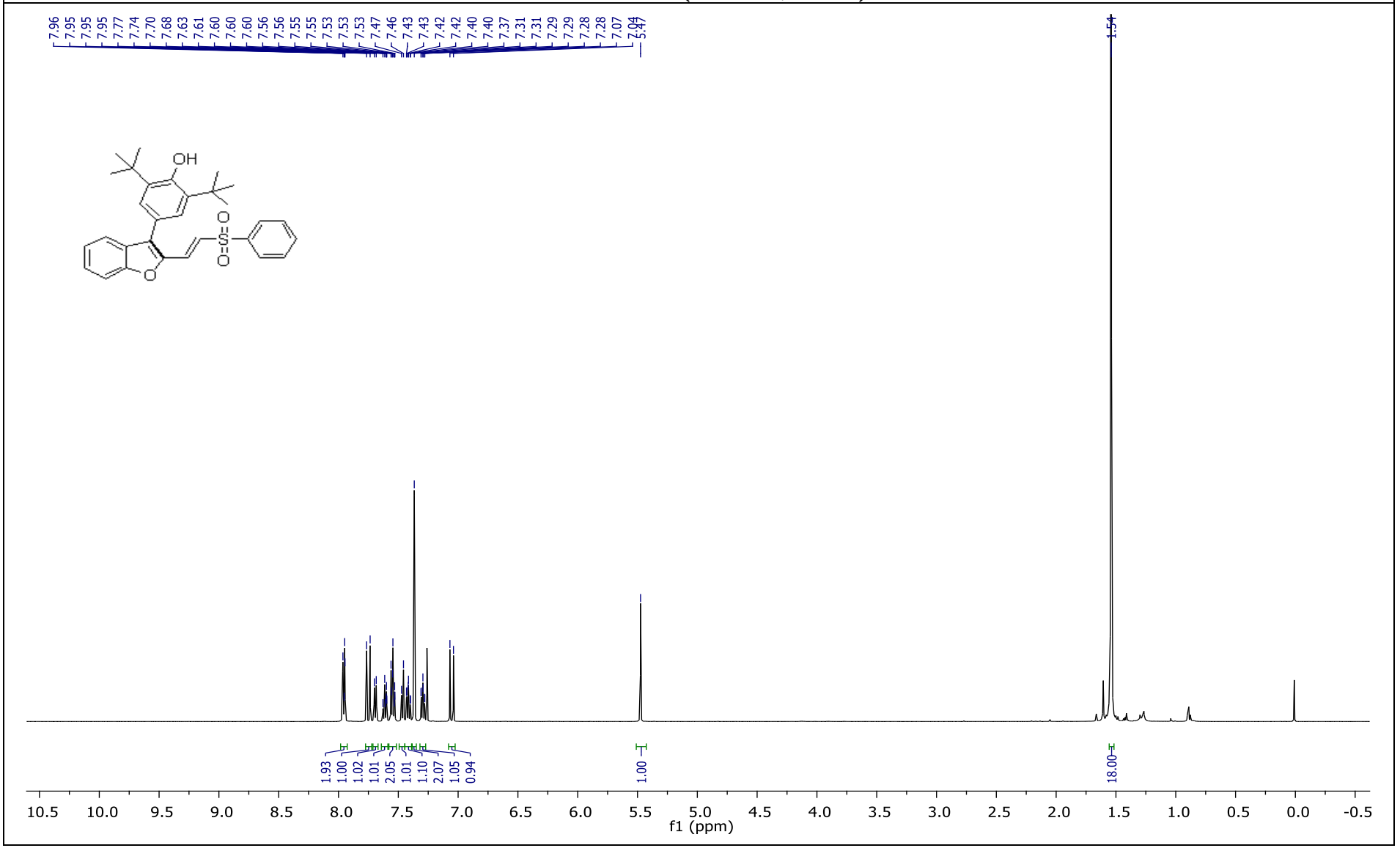
$^{13}C\{^{1}H\}$NMR of 5g (101 MHz, $CDCl_3$)



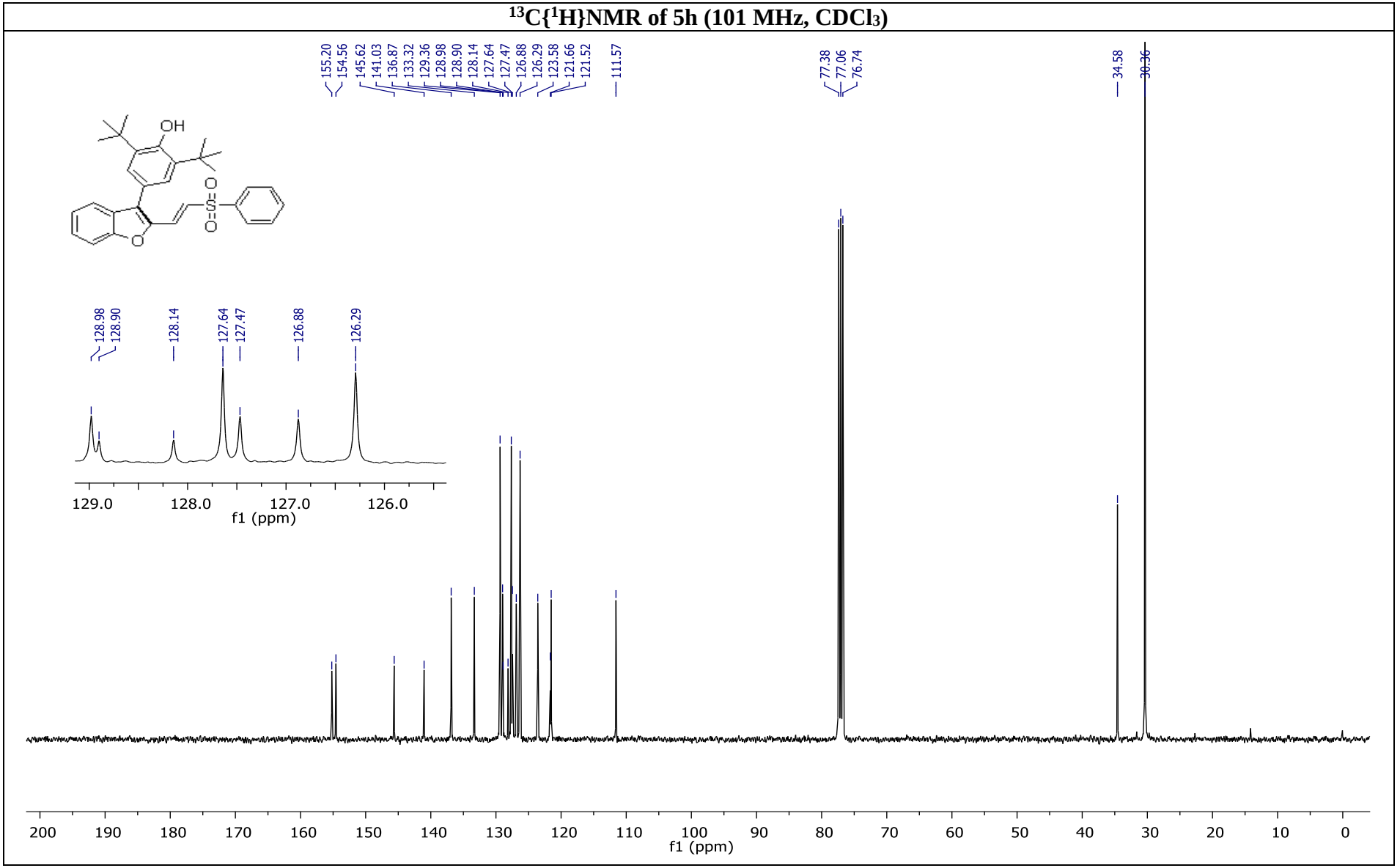
DEPT-NMR of 5g (135 MHz, $CDCl_3$)



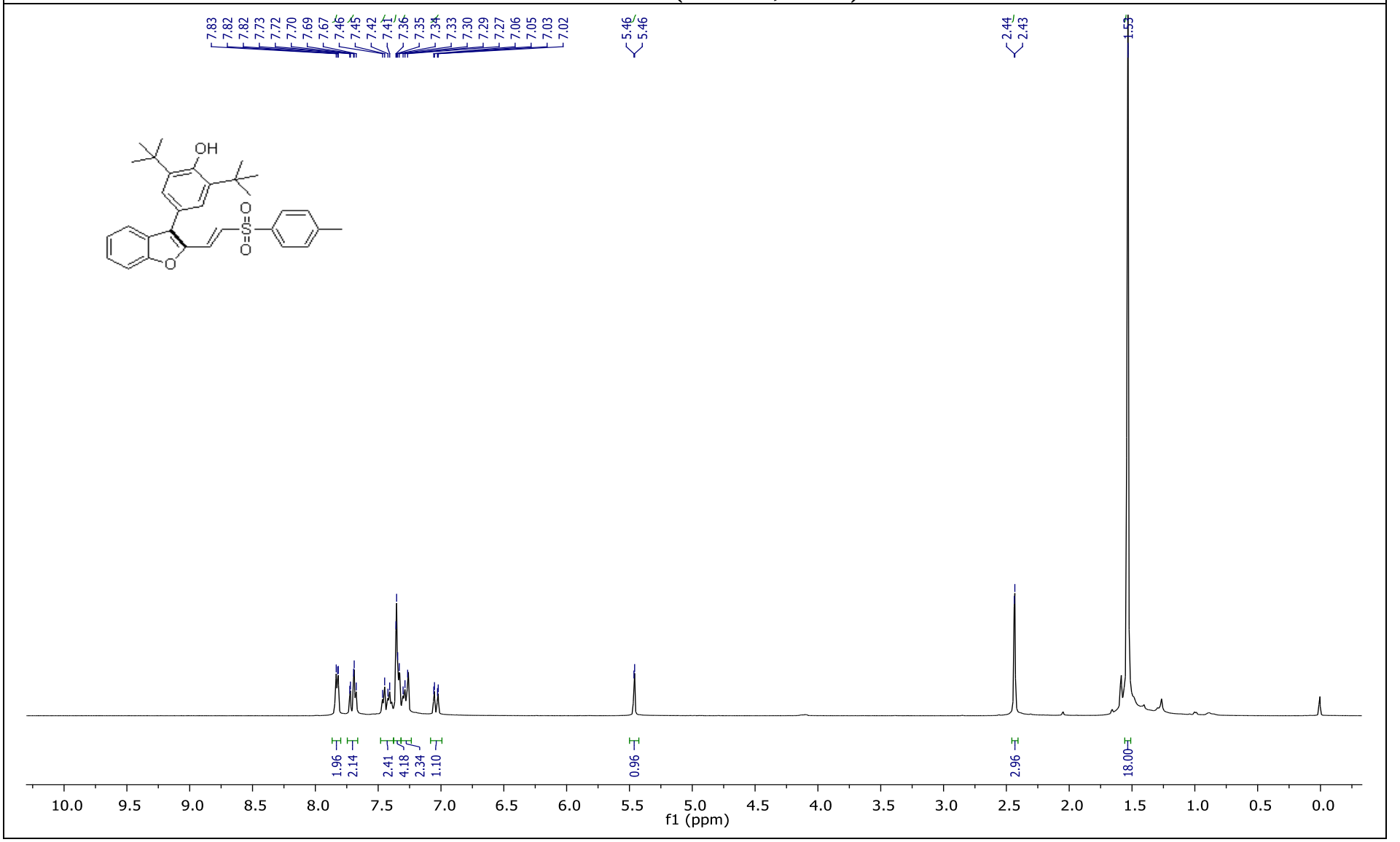
^{1}H-NMR of 5h (500 MHz, $CDCl_3$)



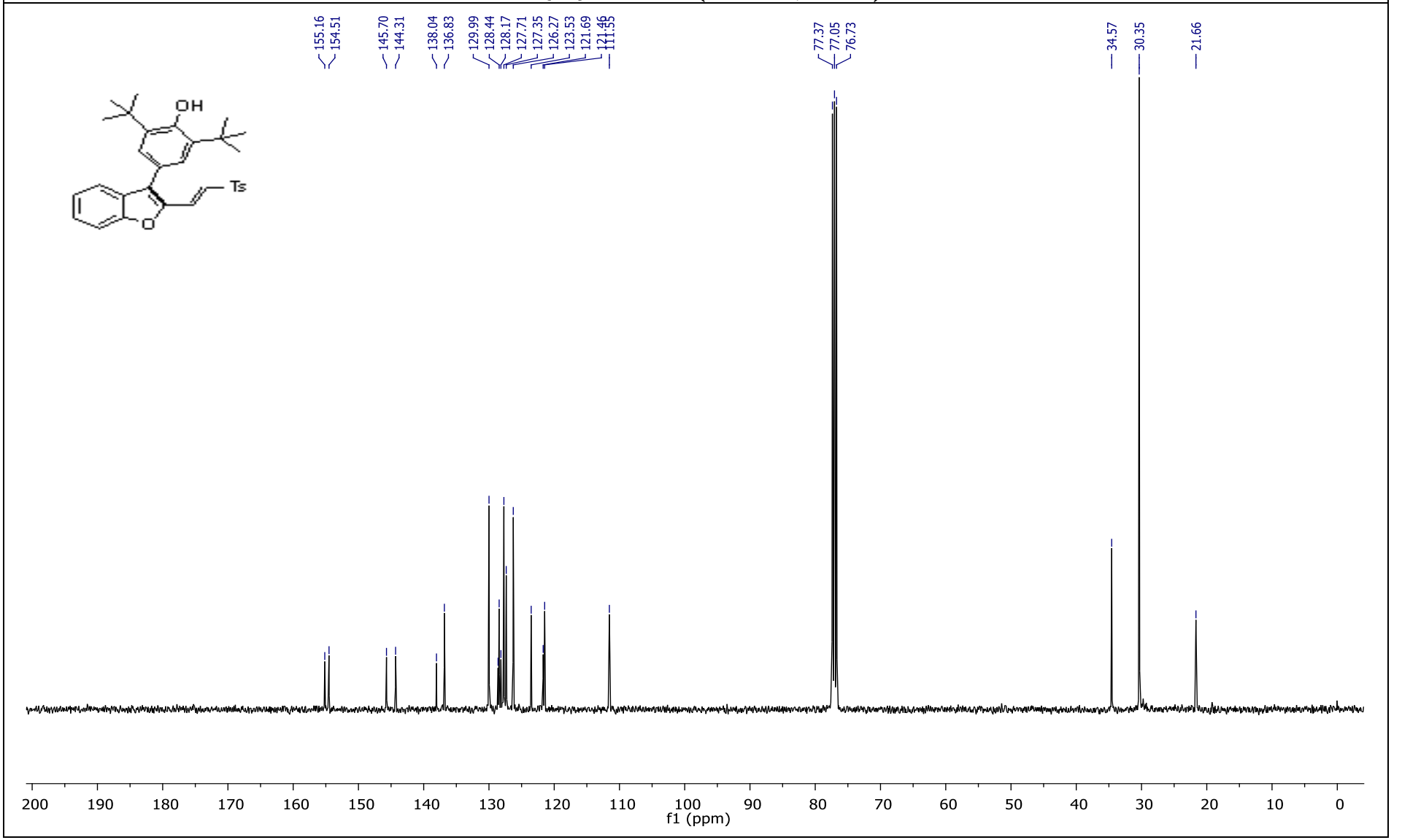
$^{13}C\{^{1}H\}$NMR of 5h (101 MHz, $CDCl_3$)



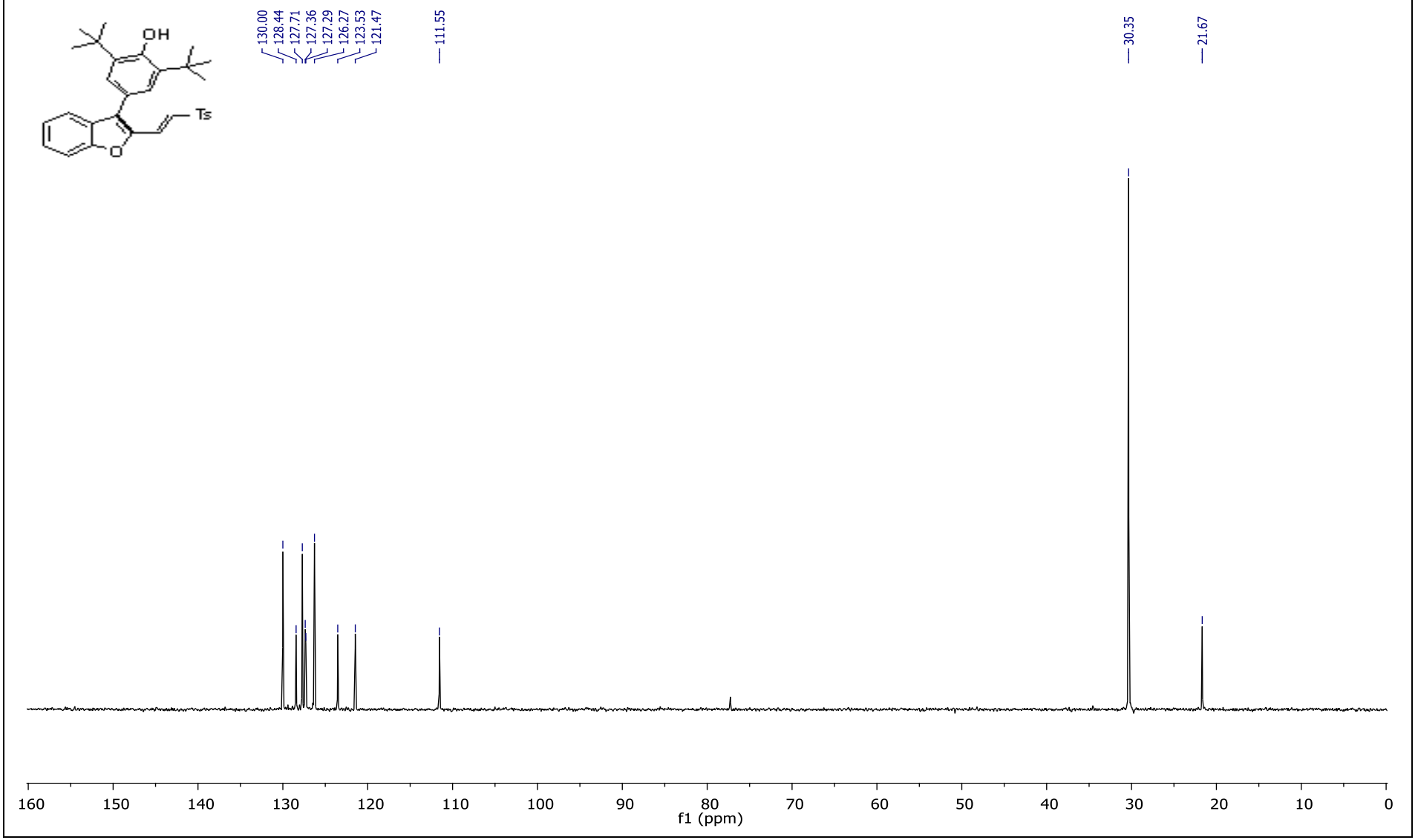
^{1}H-NMR of 5i (500 MHz, $CDCl_3$)



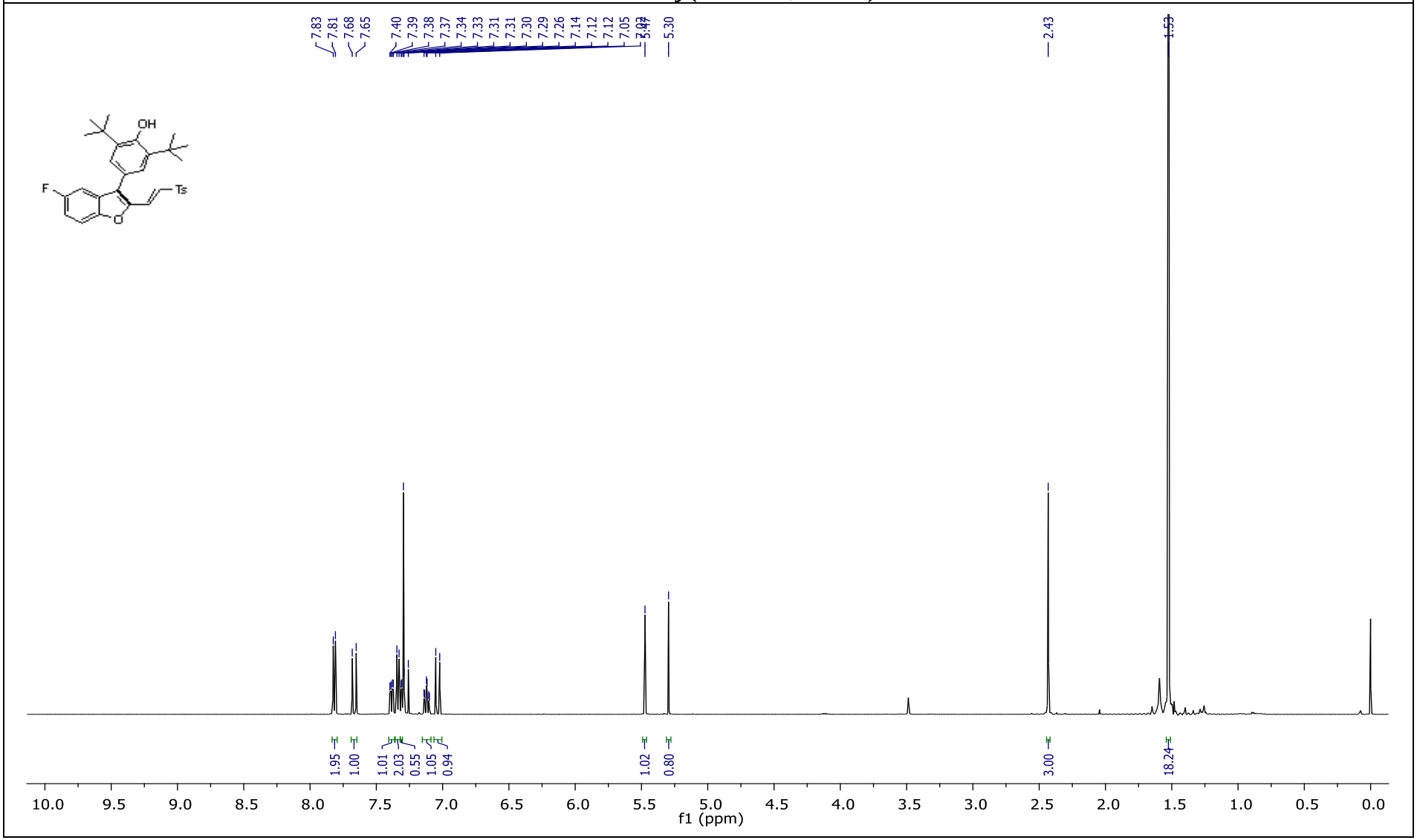
$^{13}C\{^{1}H\}$NMR of 5i (101 MHz, $CDCl_3$)



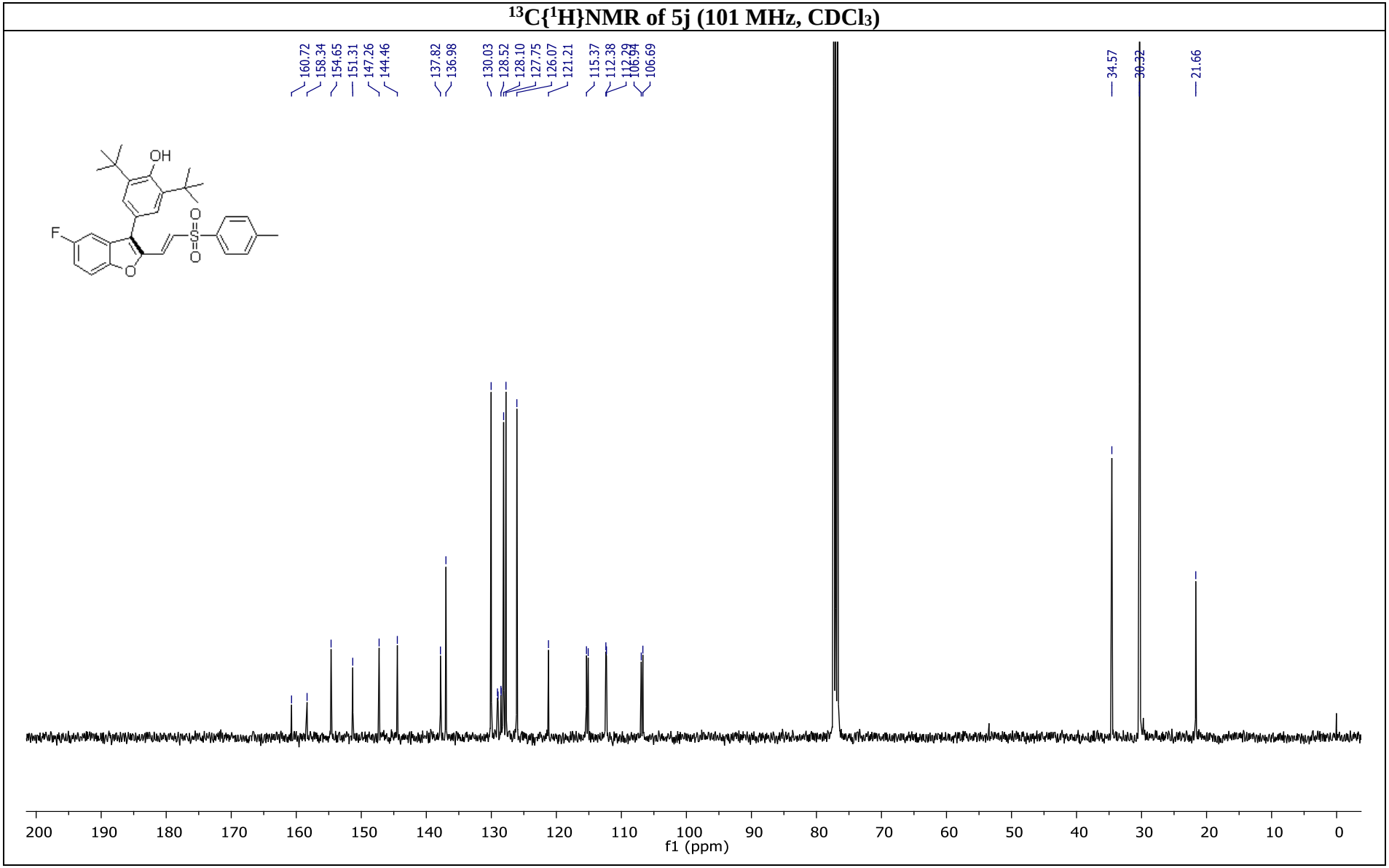
DEPT-NMR of 5i (135 MHz, $CDCl_3$)



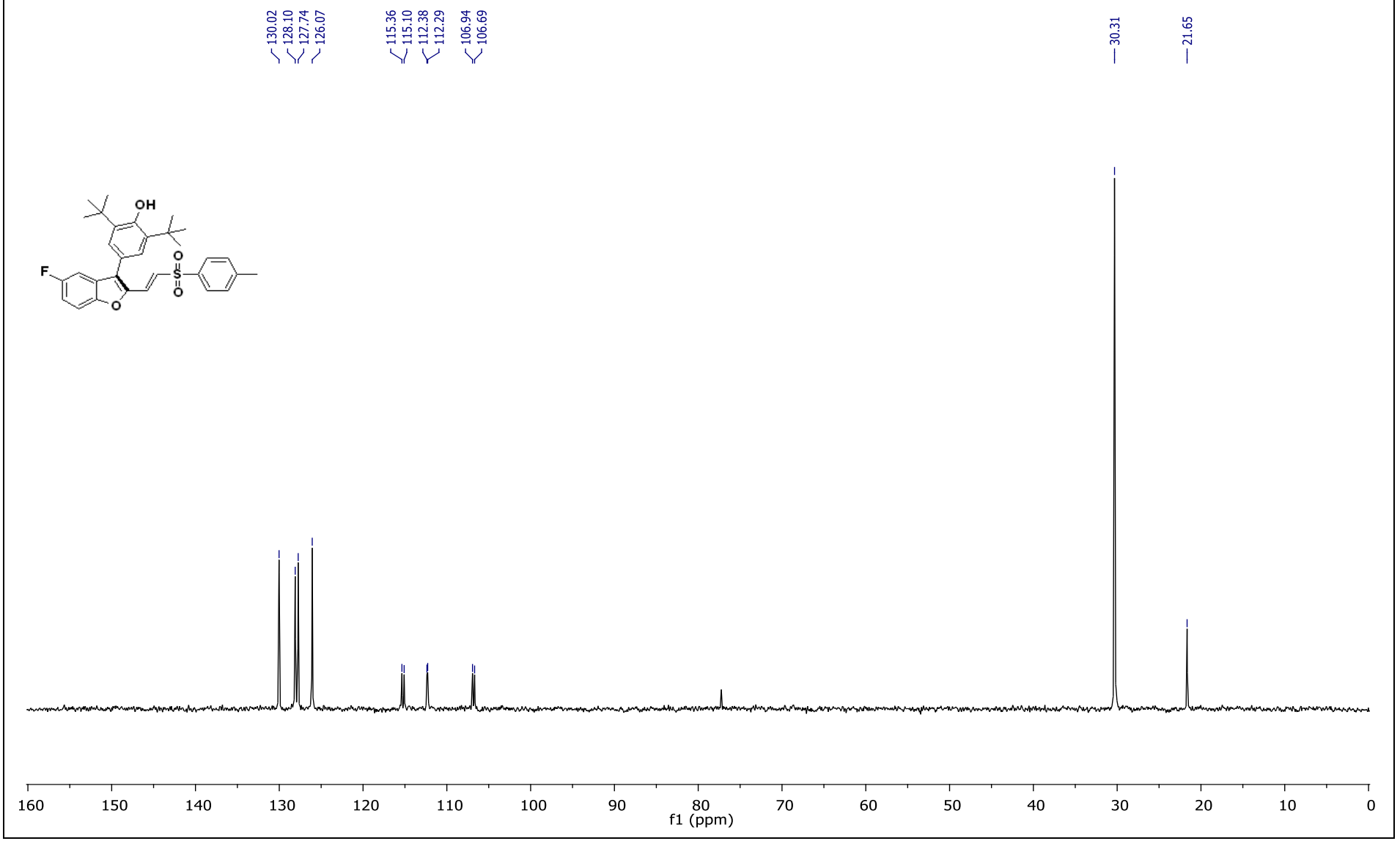
^{1}H-NMR of 5j (500 MHz, $CDCl_3$)



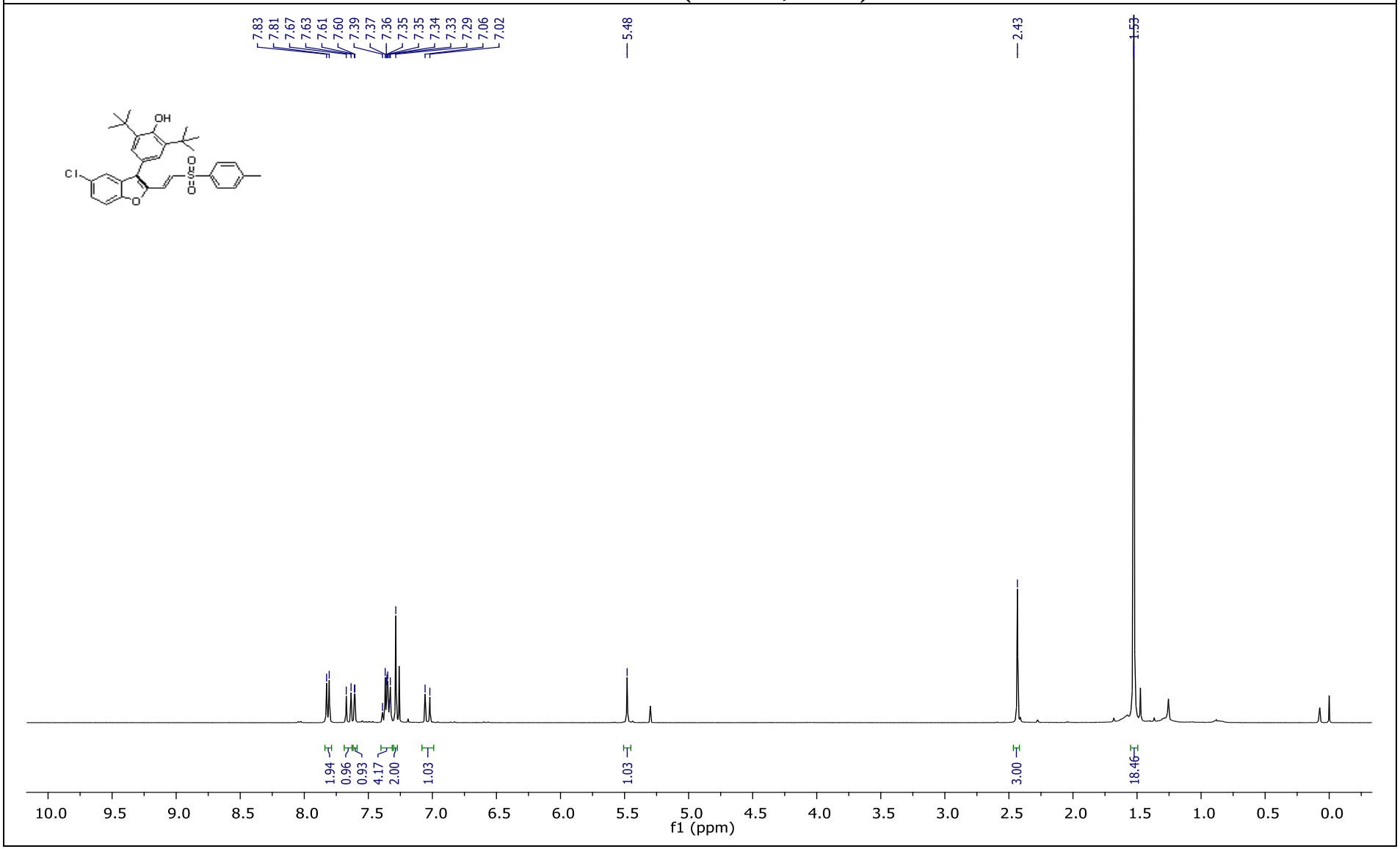
$^{13}C\{^{1}H\}$NMR of 5j (101 MHz, $CDCl_3$)



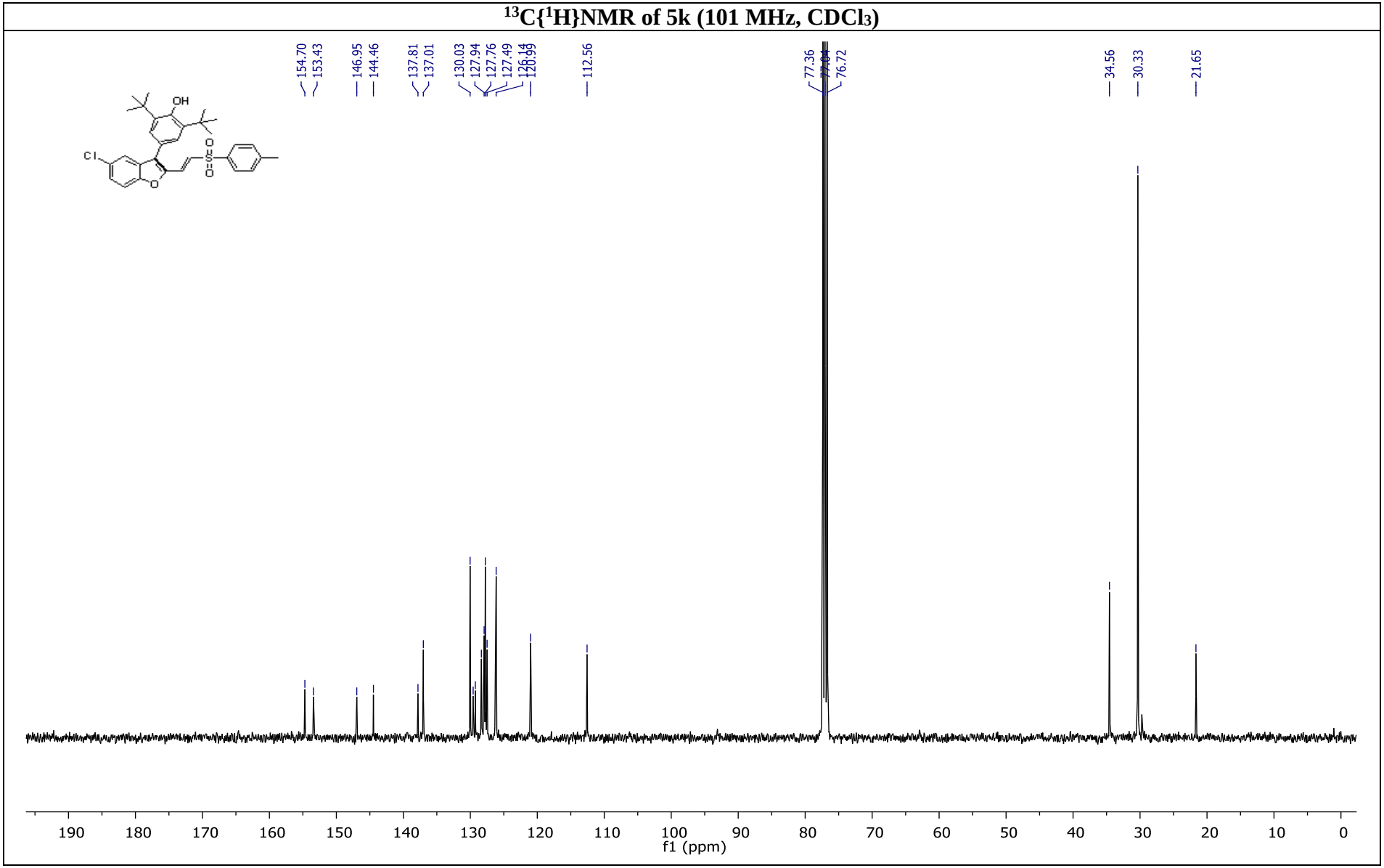
DEPT-NMR of 5j (135 MHz, $CDCl_3$)



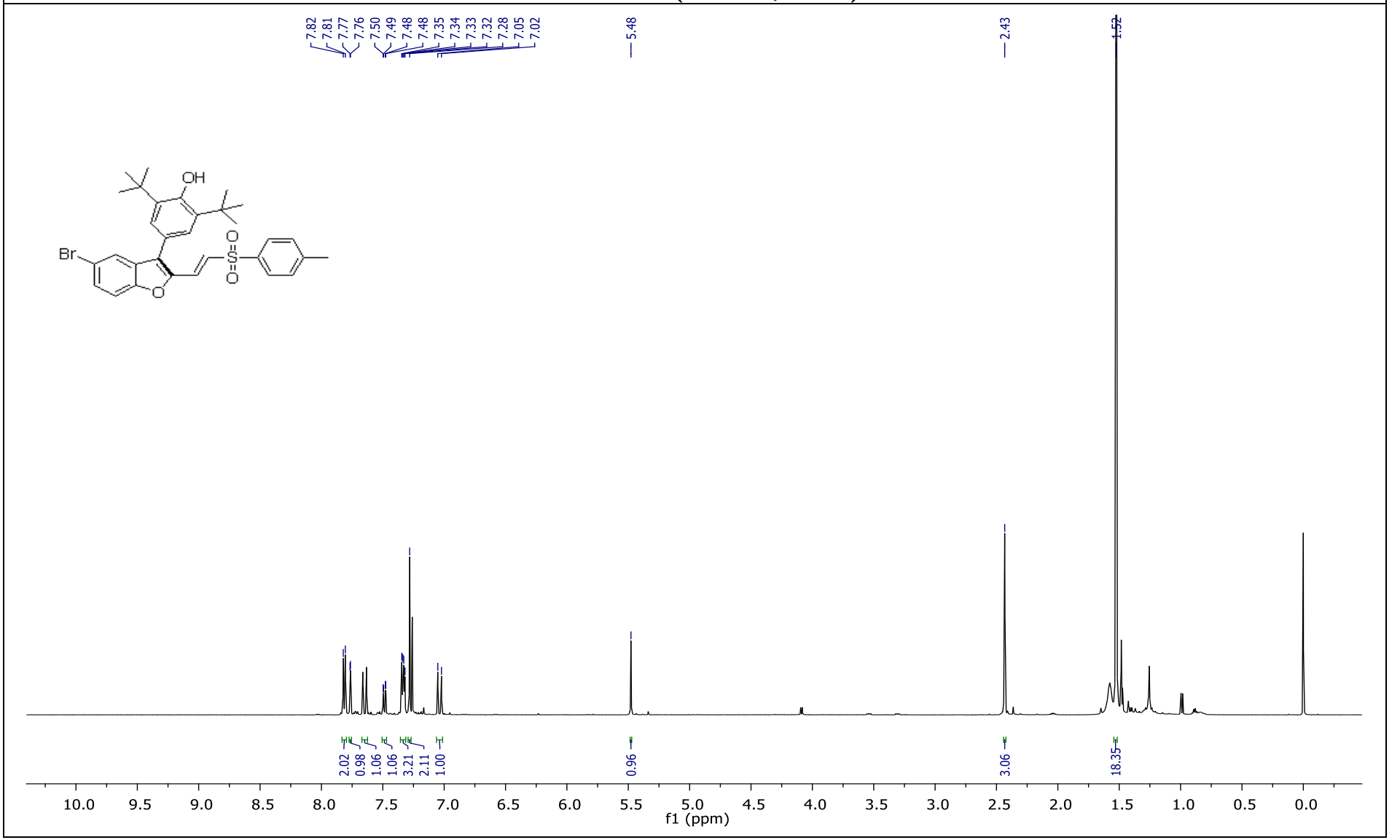
^{1}H-NMR of 5k (400 MHz, $CDCl_3$)



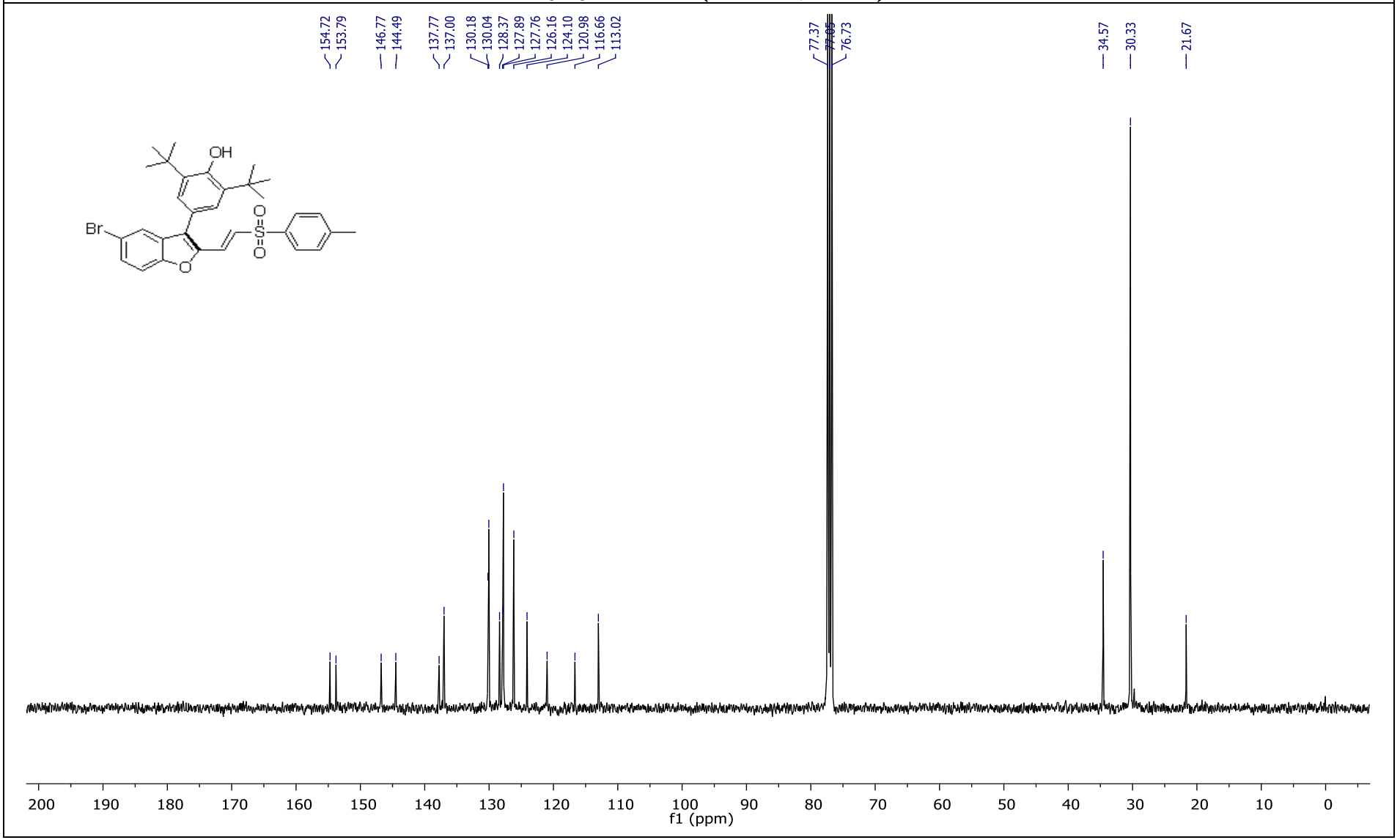
$^{13}C\{^{1}H\}$NMR of 5k (101 MHz, $CDCl_3$)



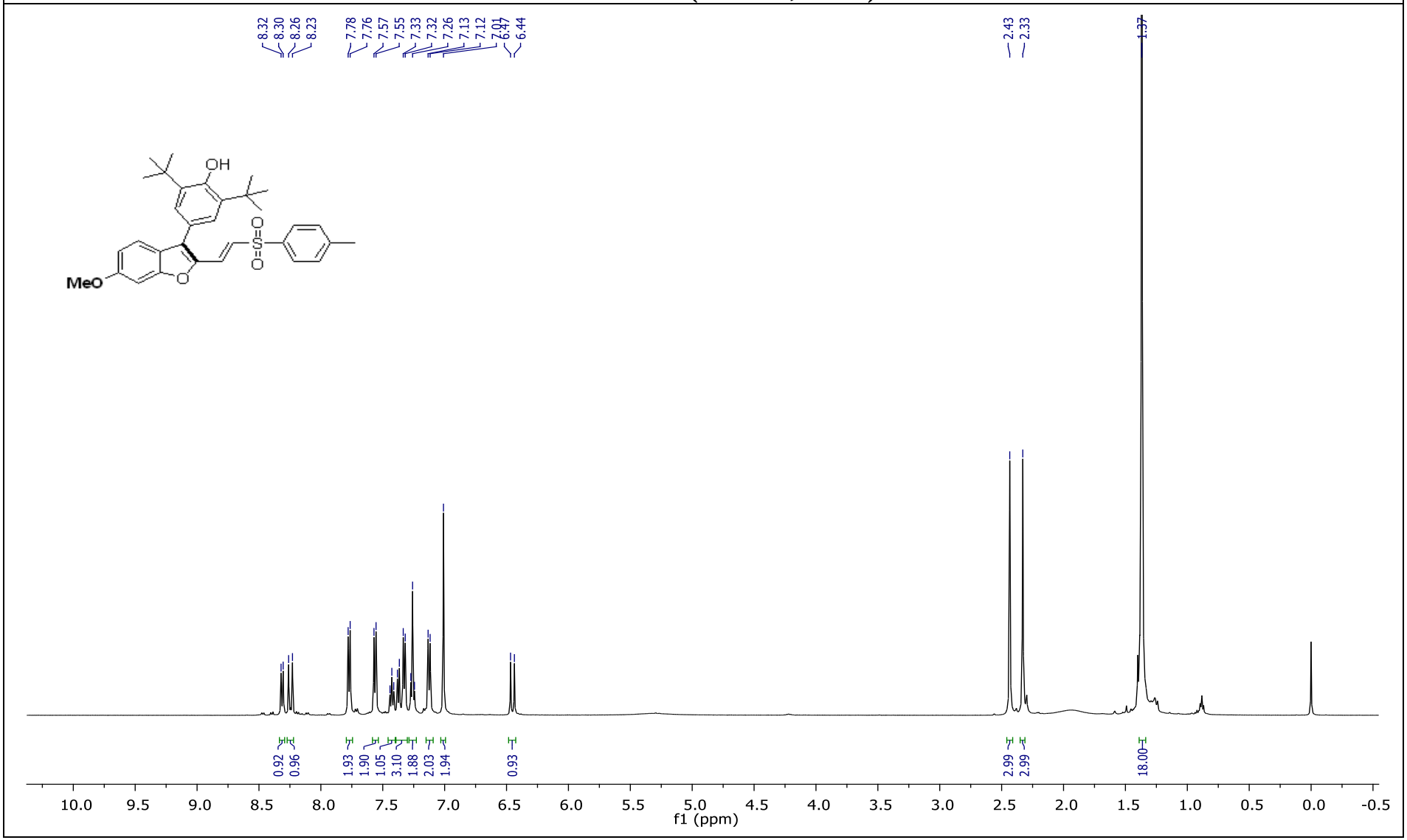
^{1}H-NMR of 5l (500 MHz, $CDCl_3$)



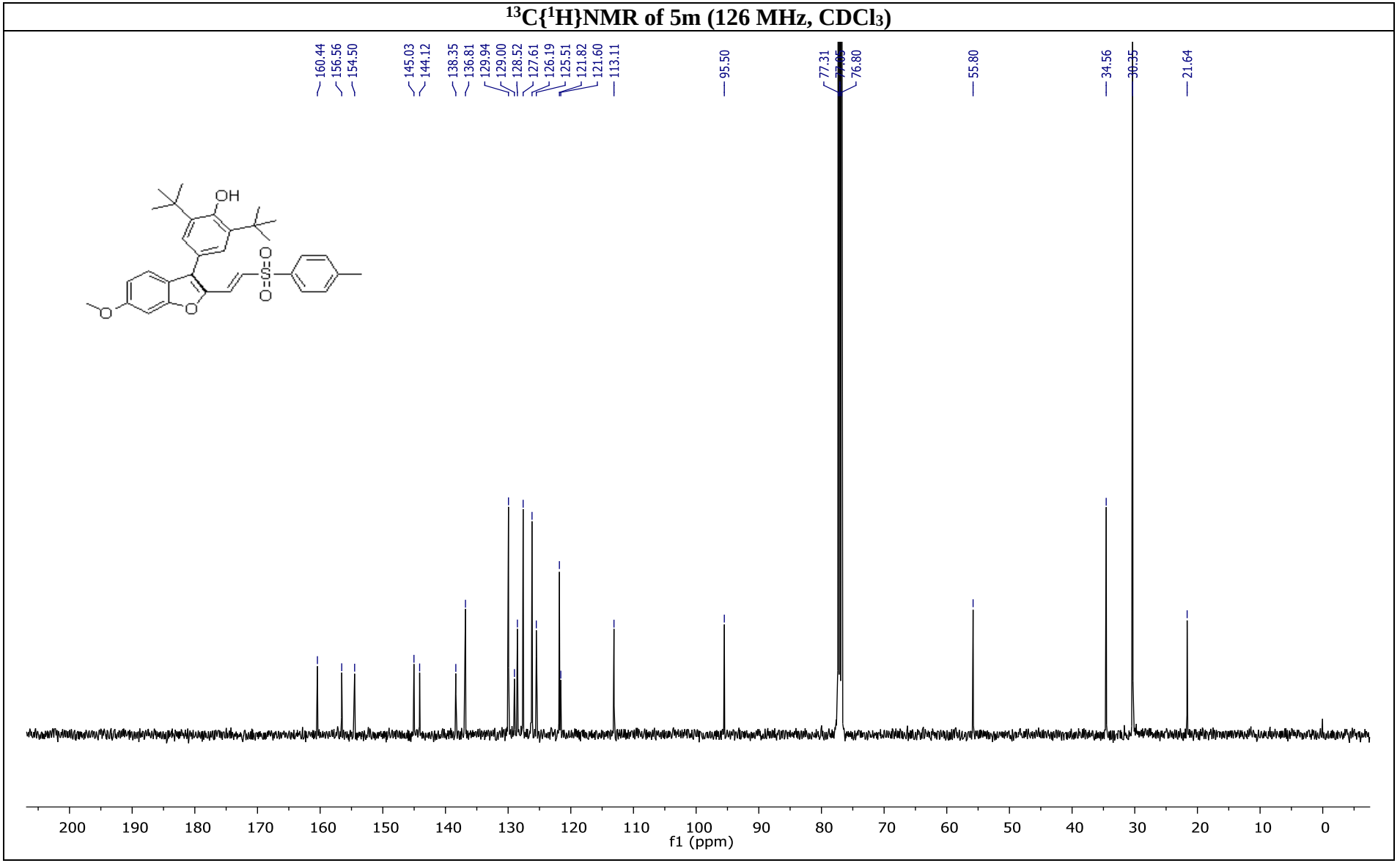
$^{13}C\{^{1}H\}$NMR of 5l (101 MHz, $CDCl_3$)



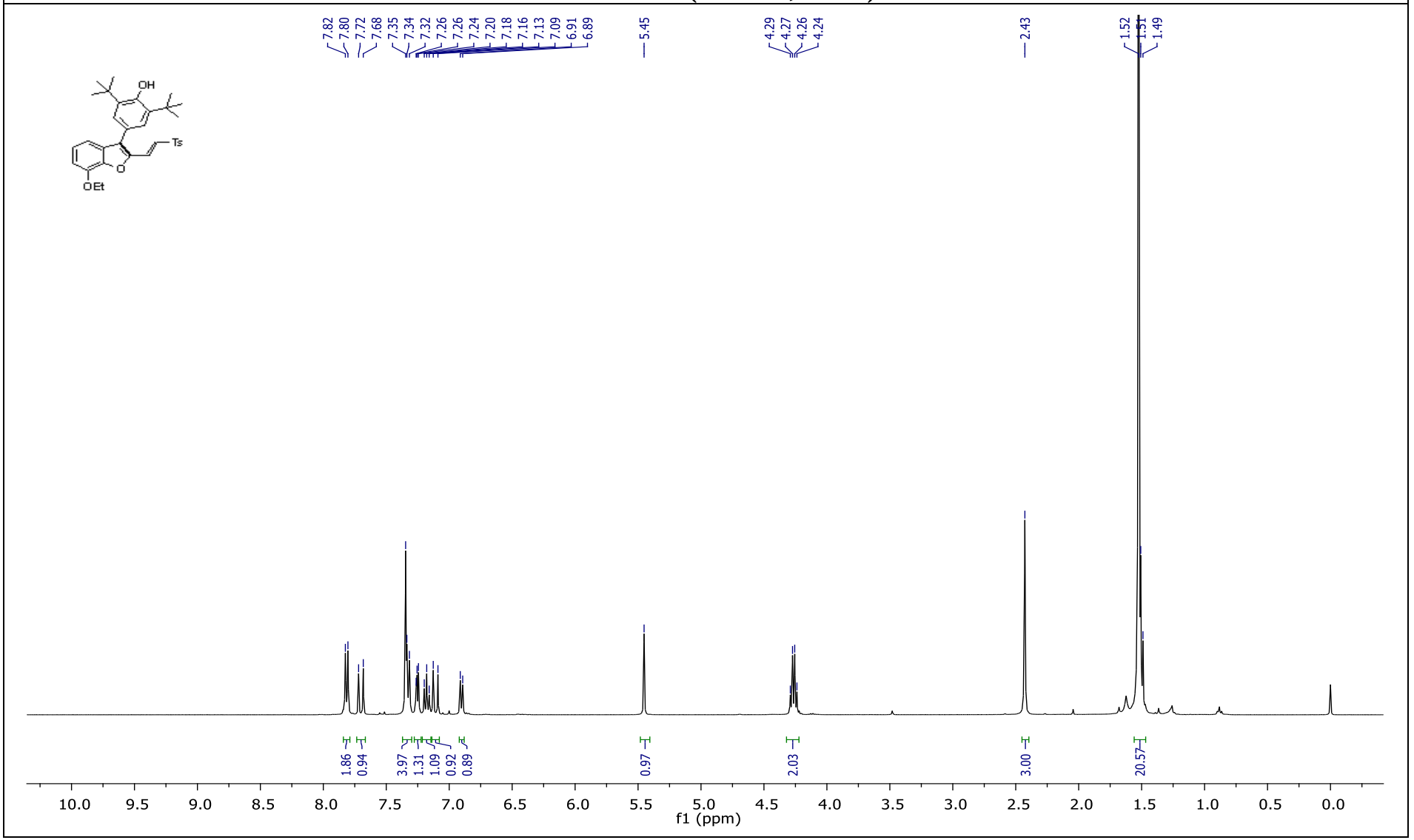
^{1}H-NMR of 5m (500 MHz, $CDCl_3$)



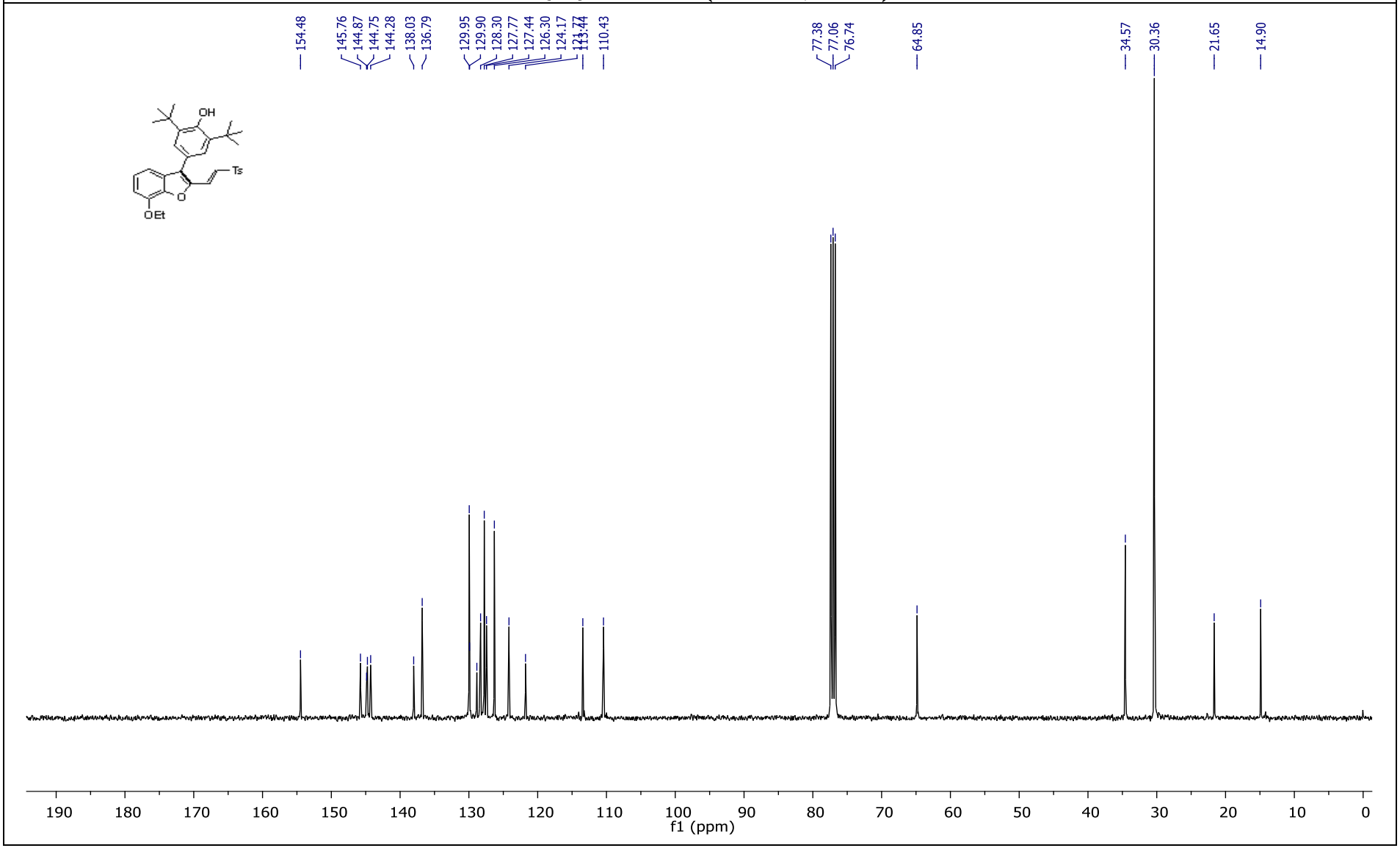
$^{13}C\{^{1}H\}$NMR of 5m (126 MHz, $CDCl_3$)



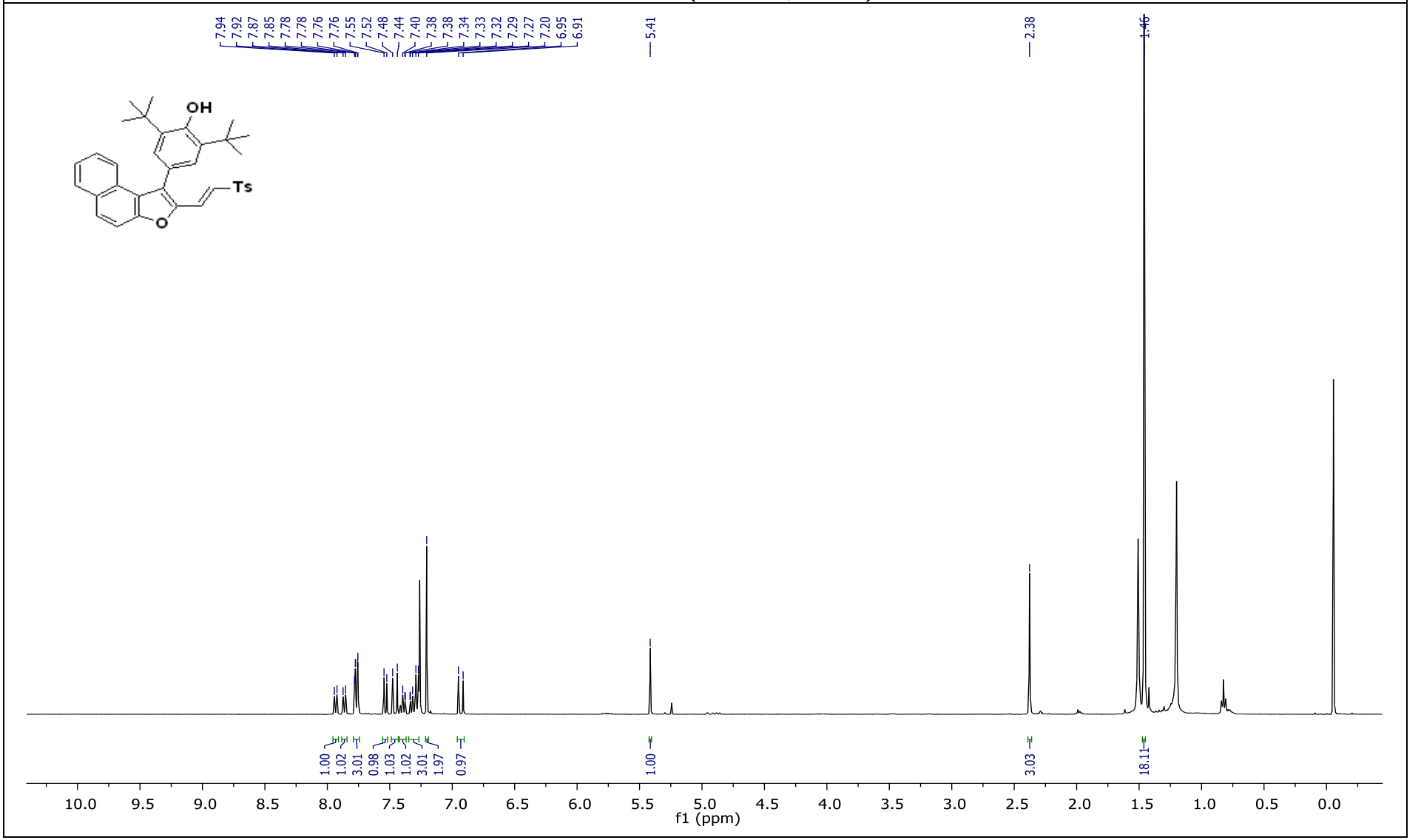
^{1}H-NMR of 5n (400 MHz, $CDCl_3$)



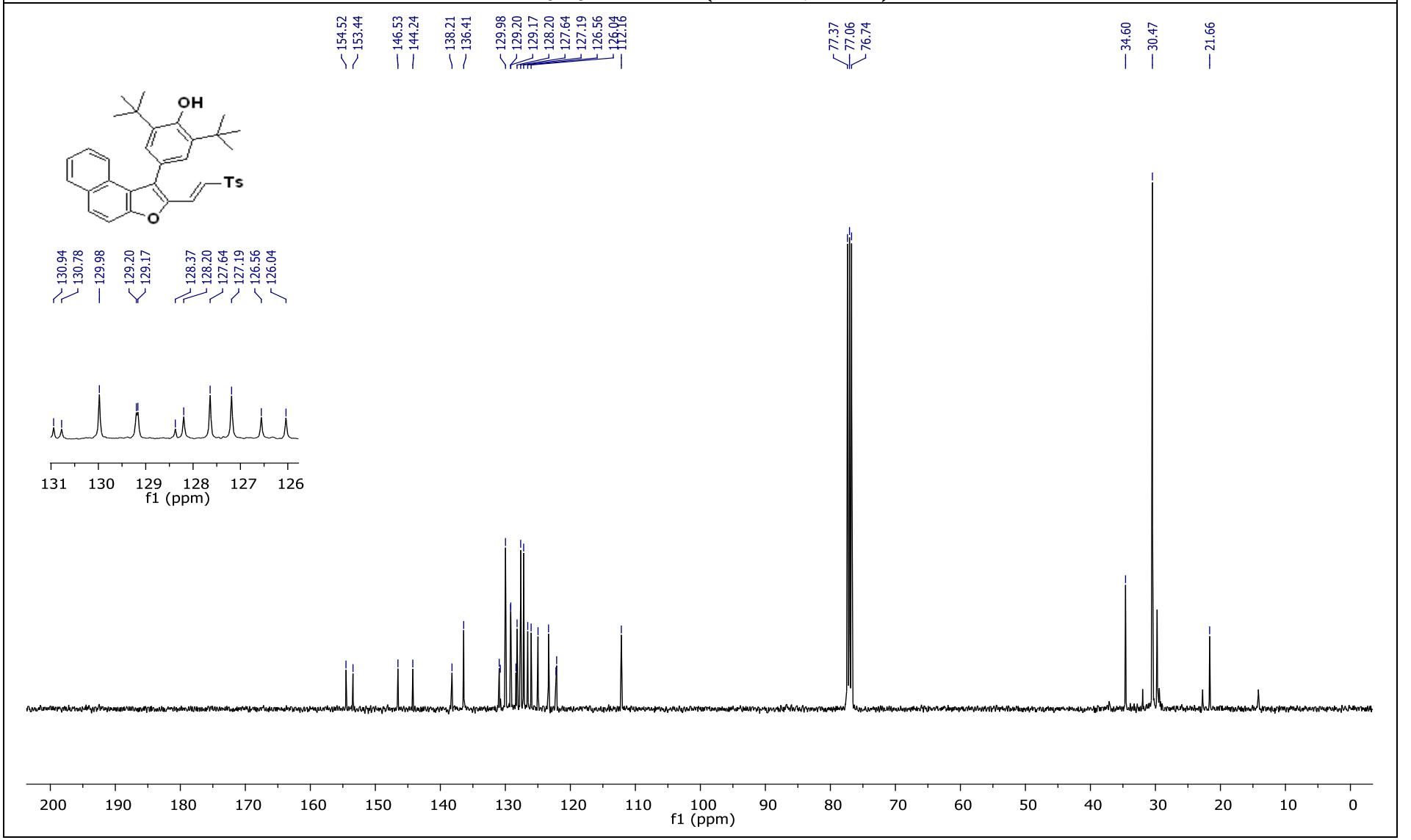
$^{13}C\{^{1}H\}$NMR of 5n (101 MHz, $CDCl_3$)



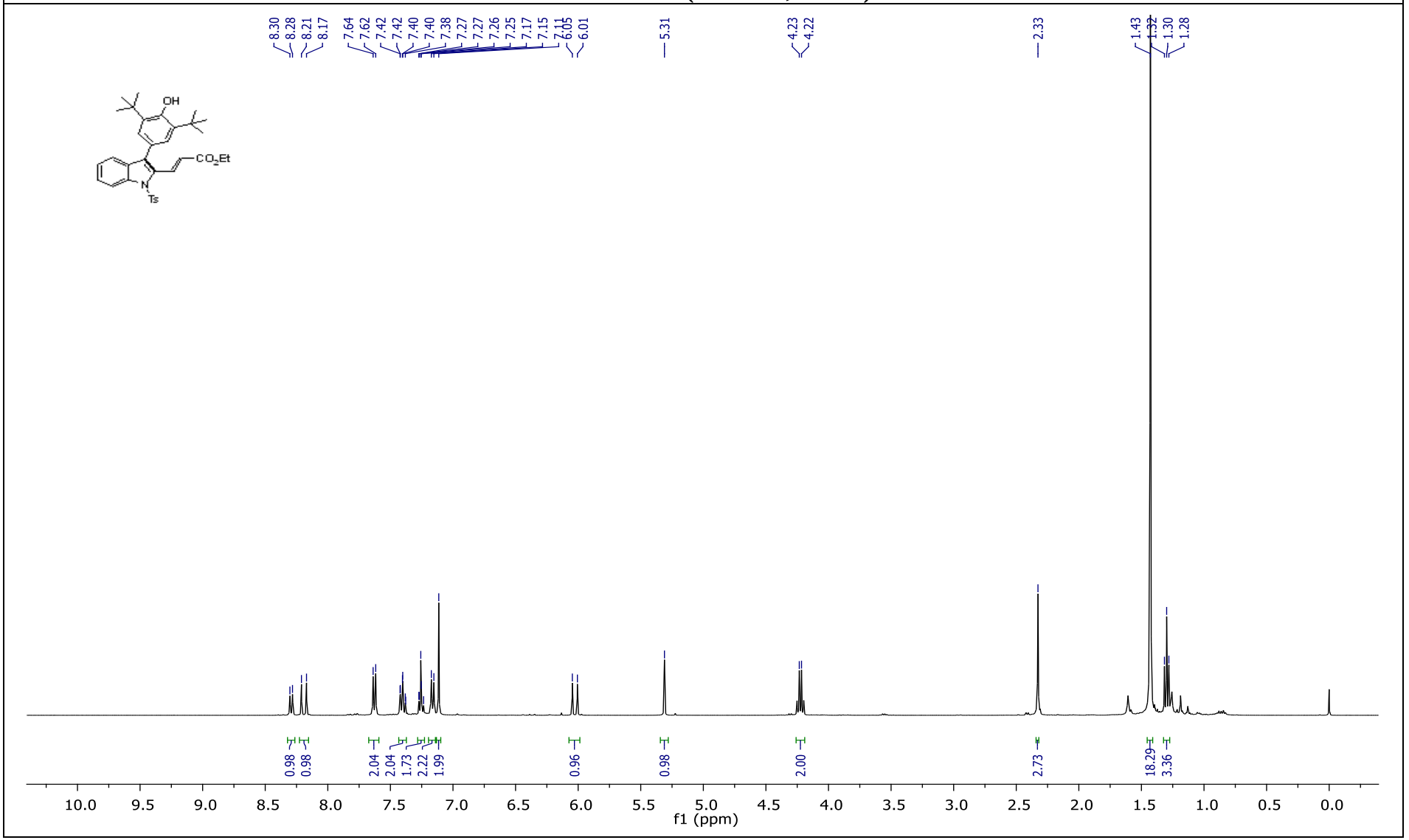
^{1}H-NMR of 5o (400 MHz, $CDCl_3$)



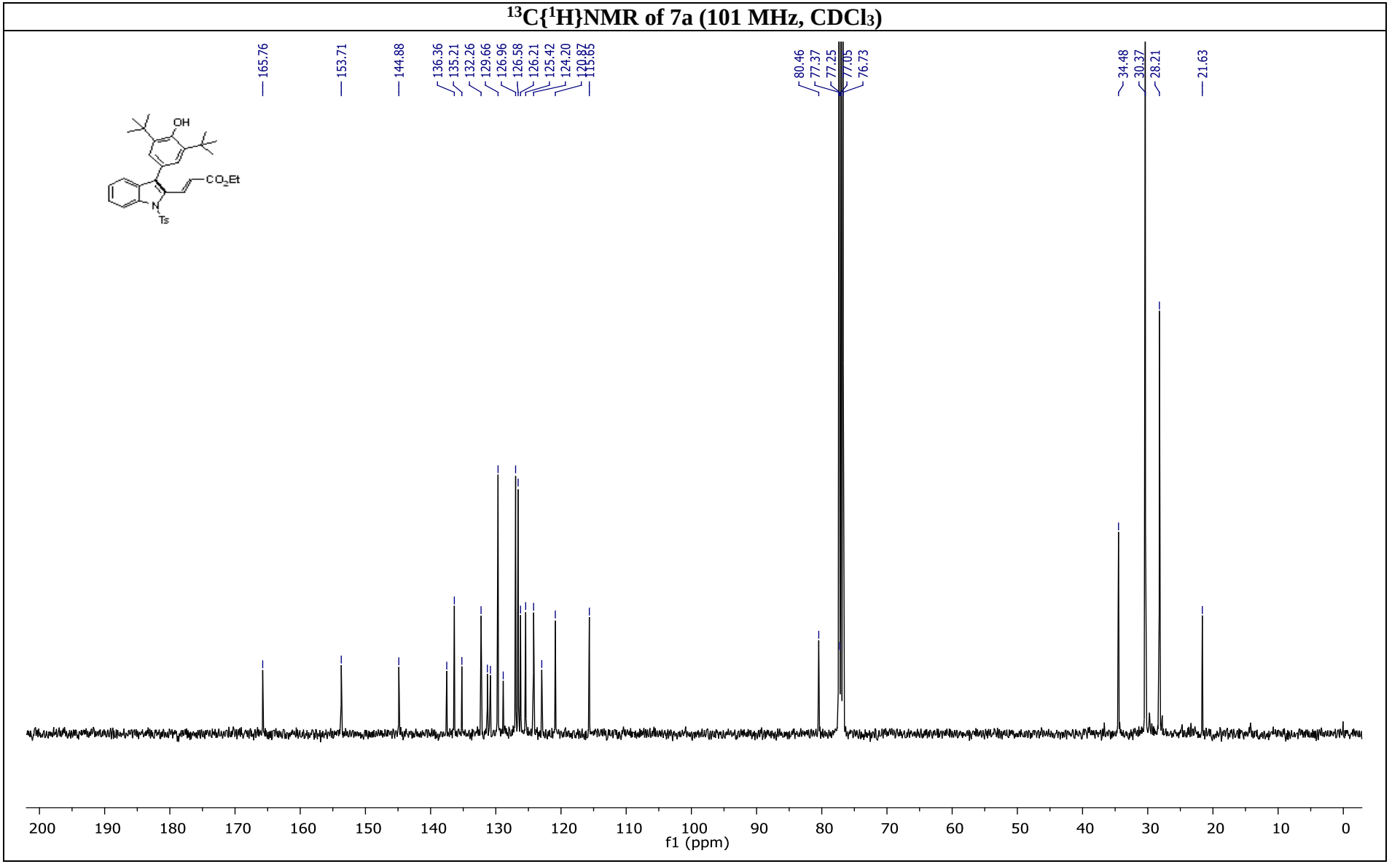
$^{13}C\{^{1}H\}$NMR of 5o (101 MHz, $CDCl_3$)



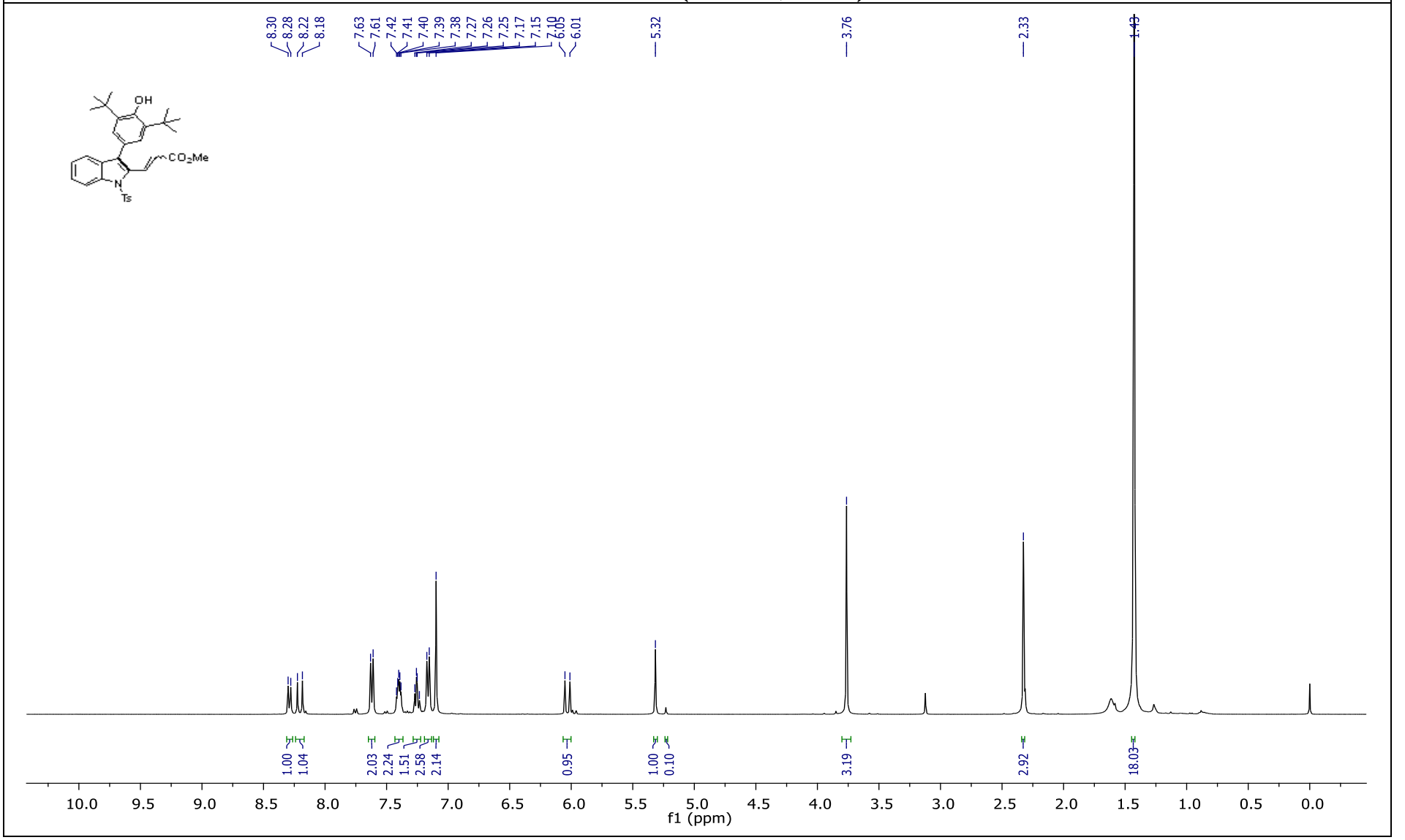
^{1}H-NMR of 7a (400 MHz, $CDCl_3$)



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



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



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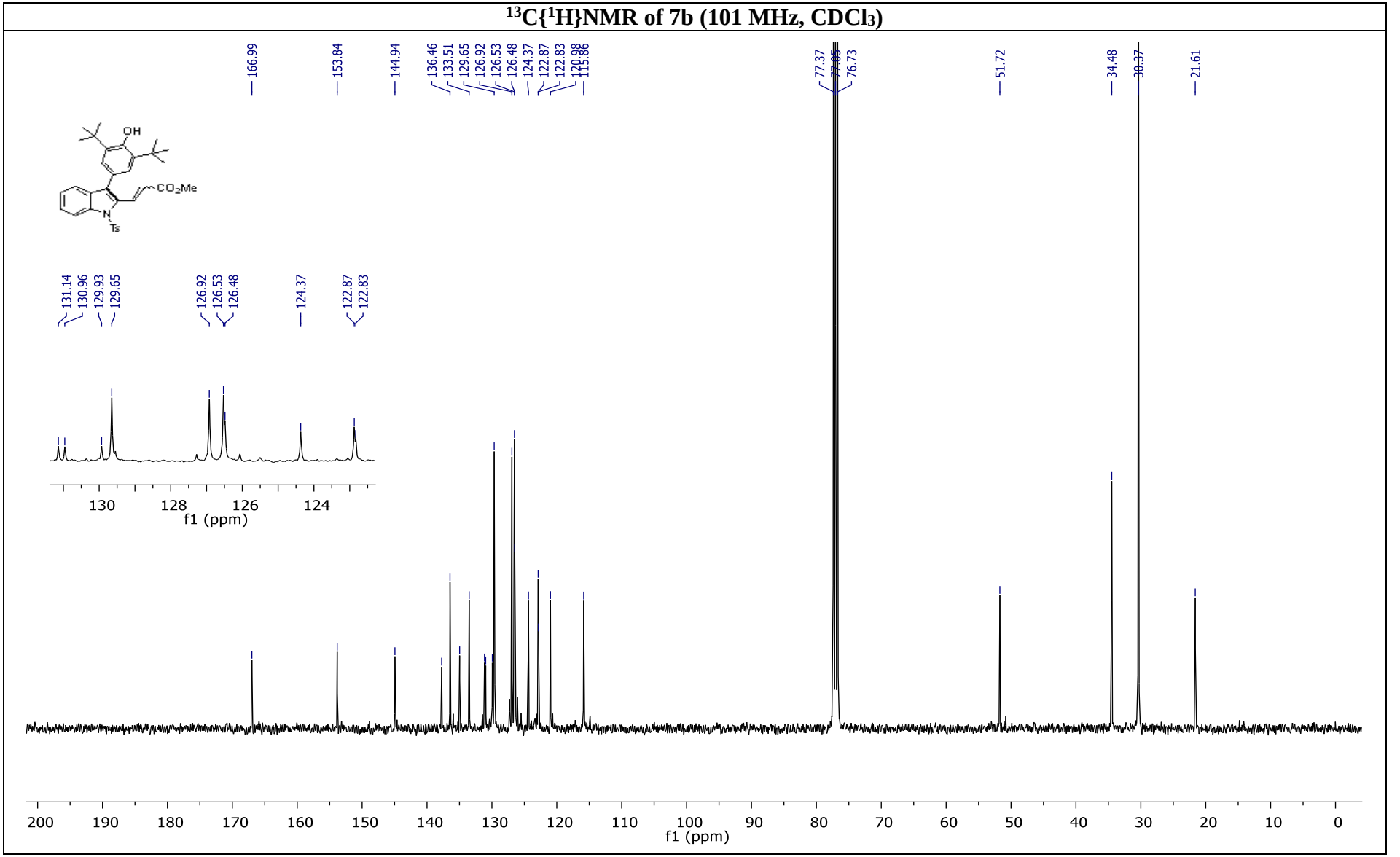
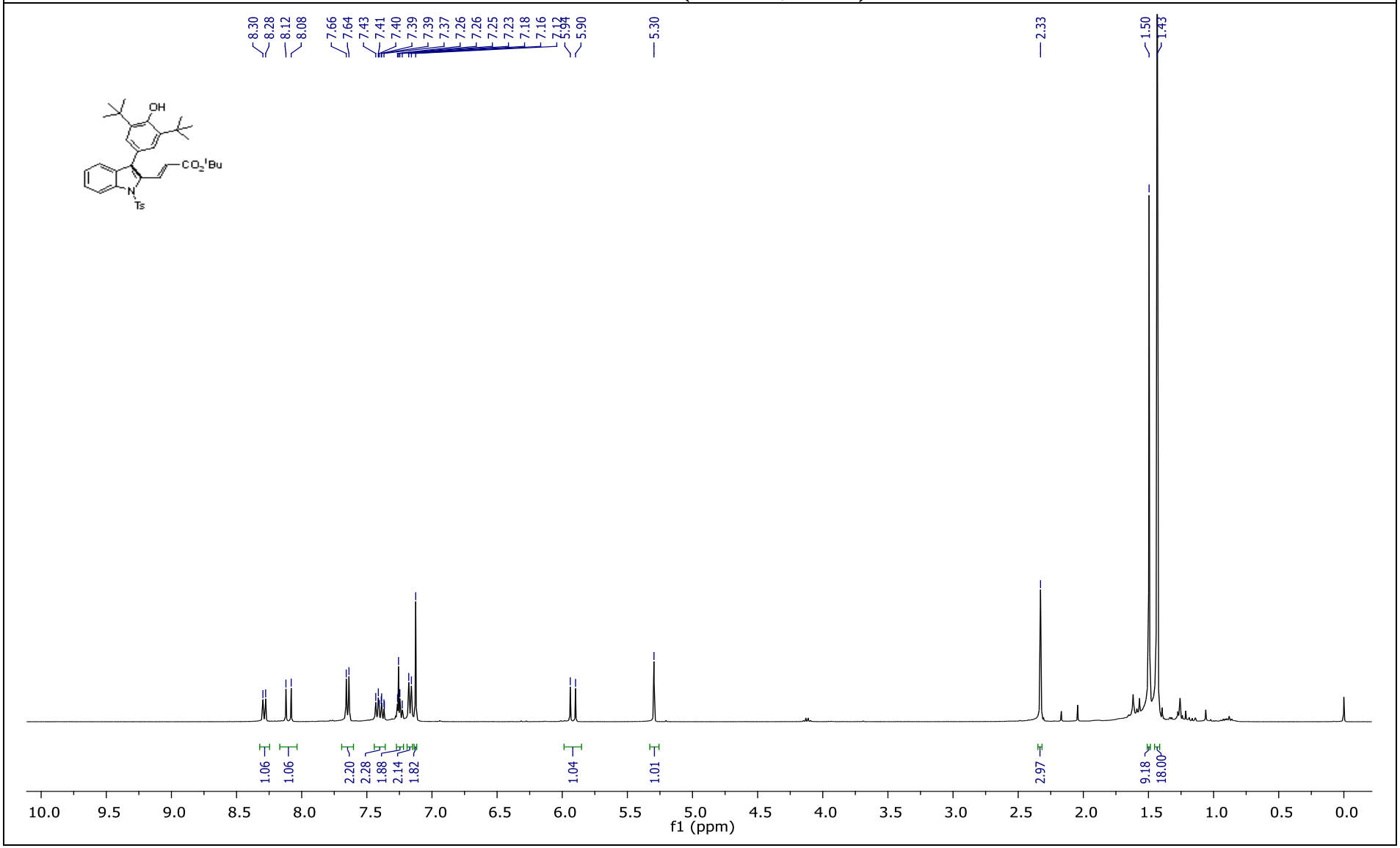
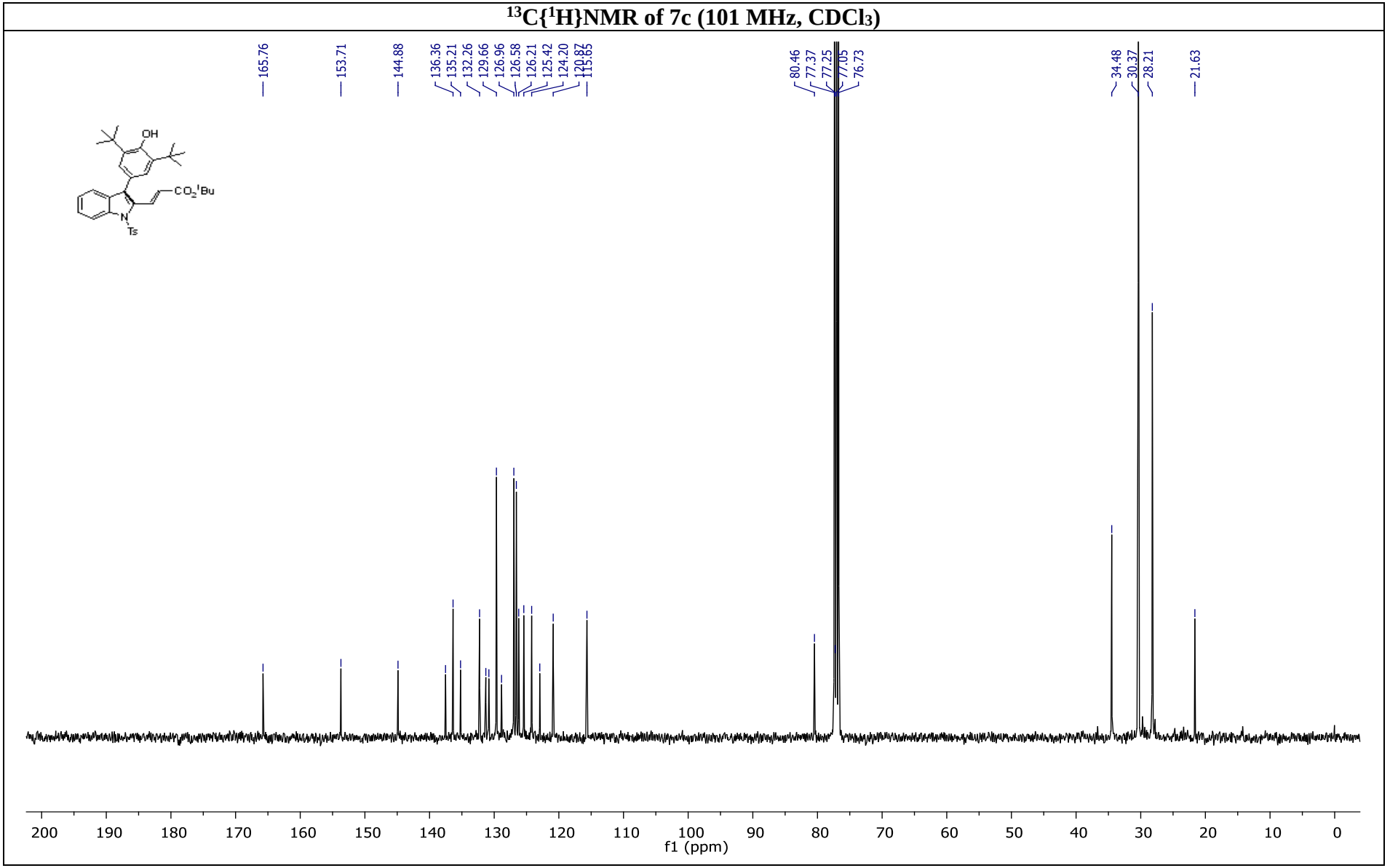


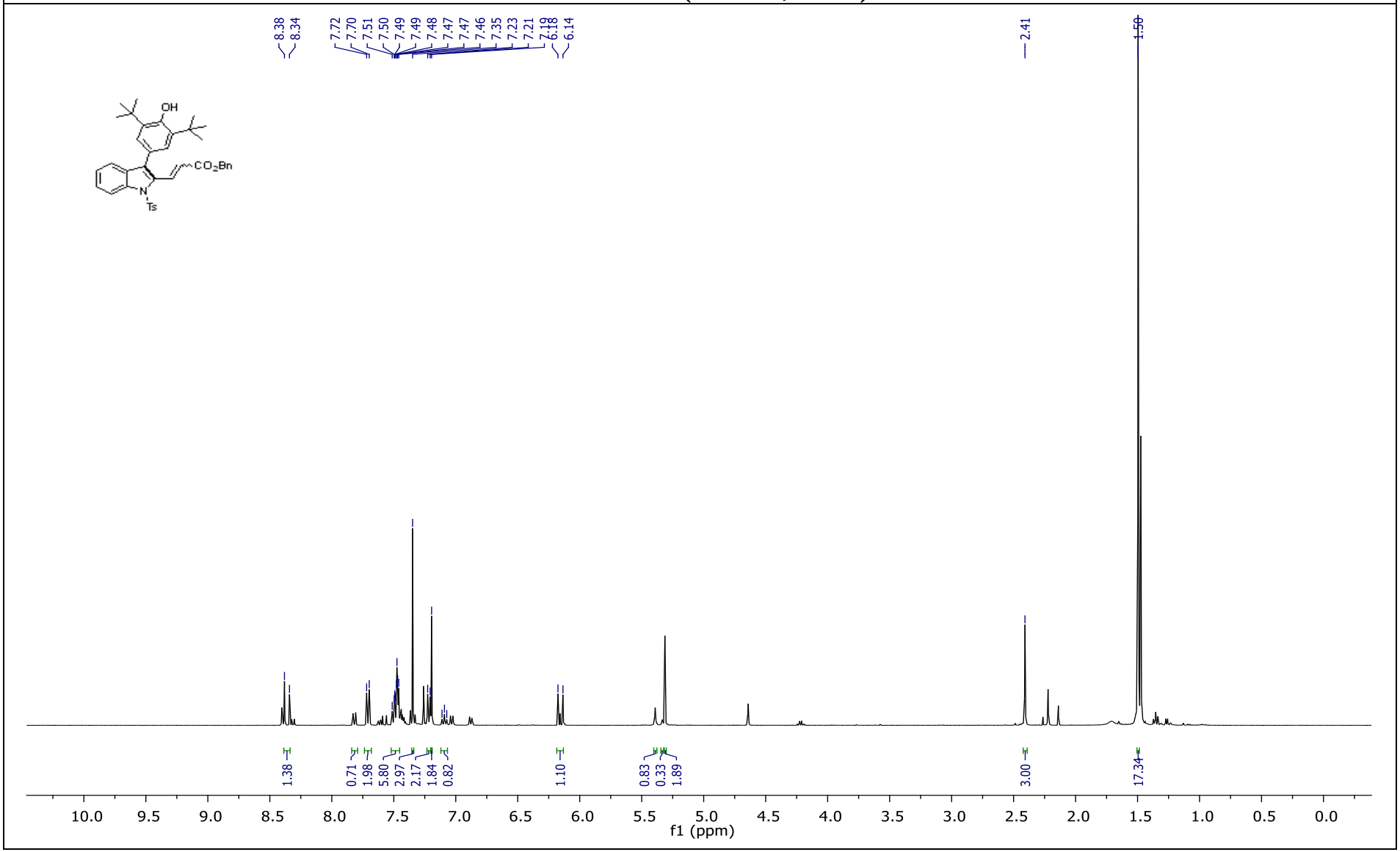
^{1}H-NMR of 7c (400 MHz, $CDCl_3$)



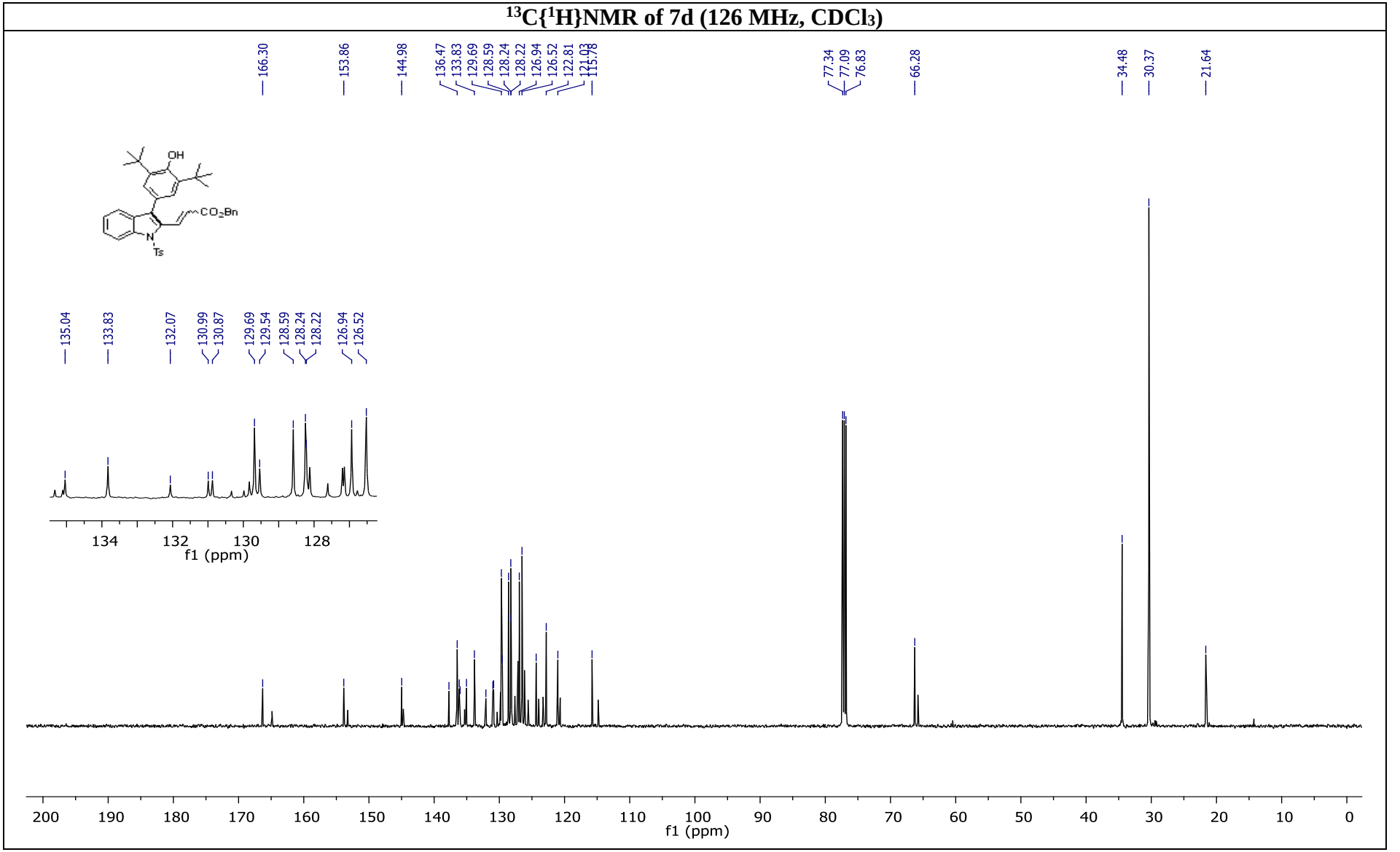
$^{13}C\{^{1}H\}$NMR of 7c (101 MHz, $CDCl_3$)



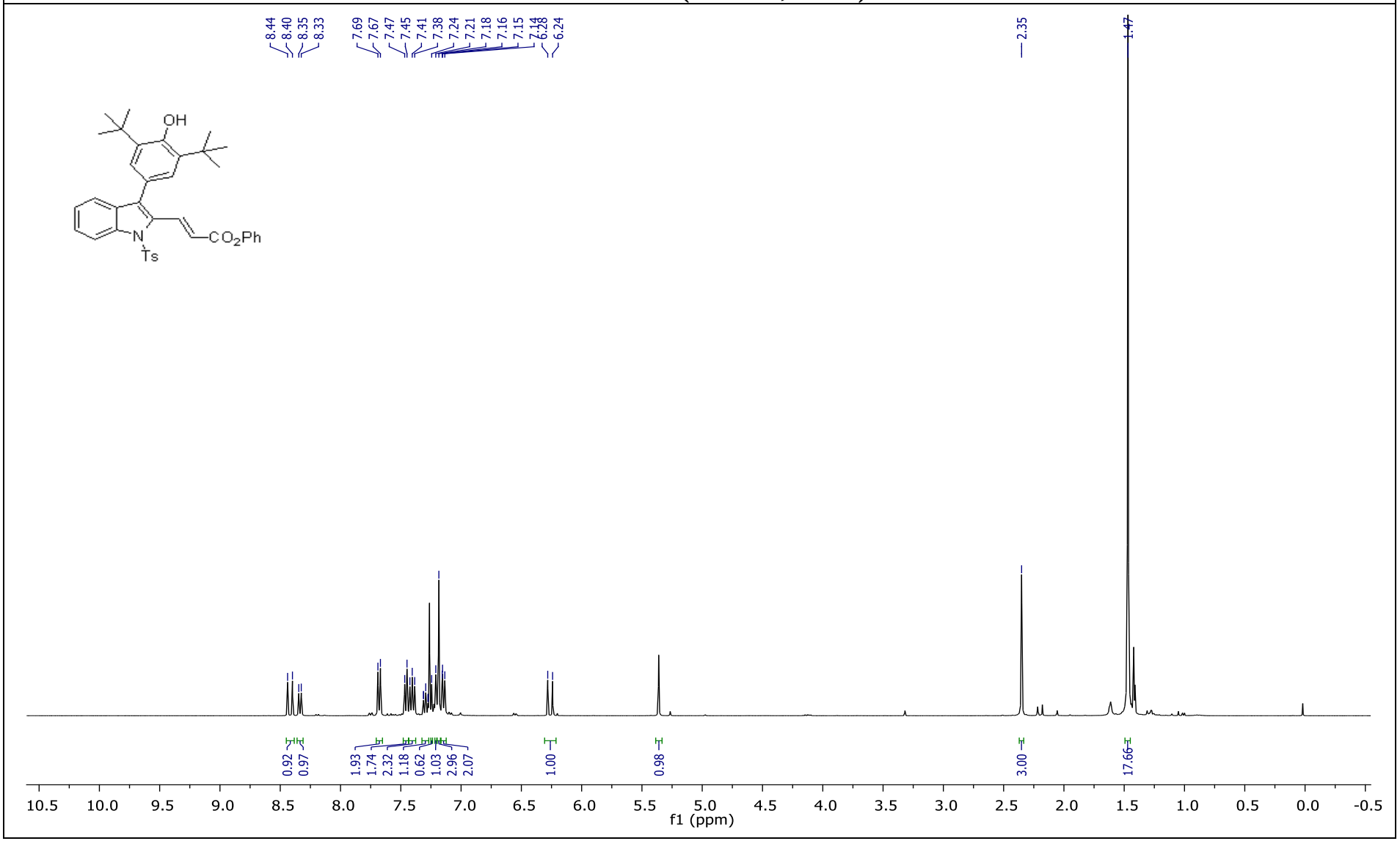
^{1}H-NMR of 7d (400 MHz, $CDCl_3$)



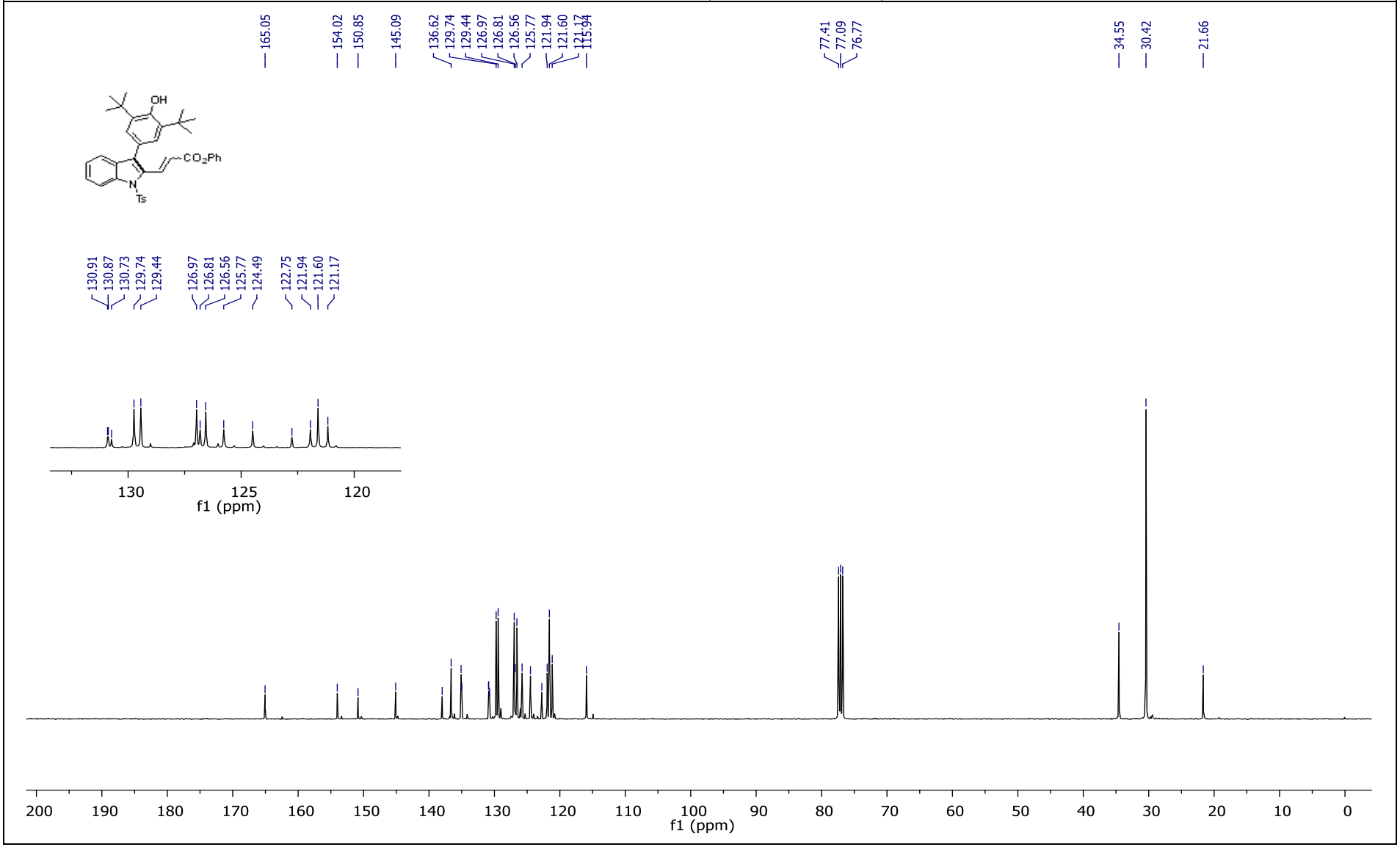
$^{13}C\{^{1}H\}$NMR of 7d (126 MHz, $CDCl_3$)



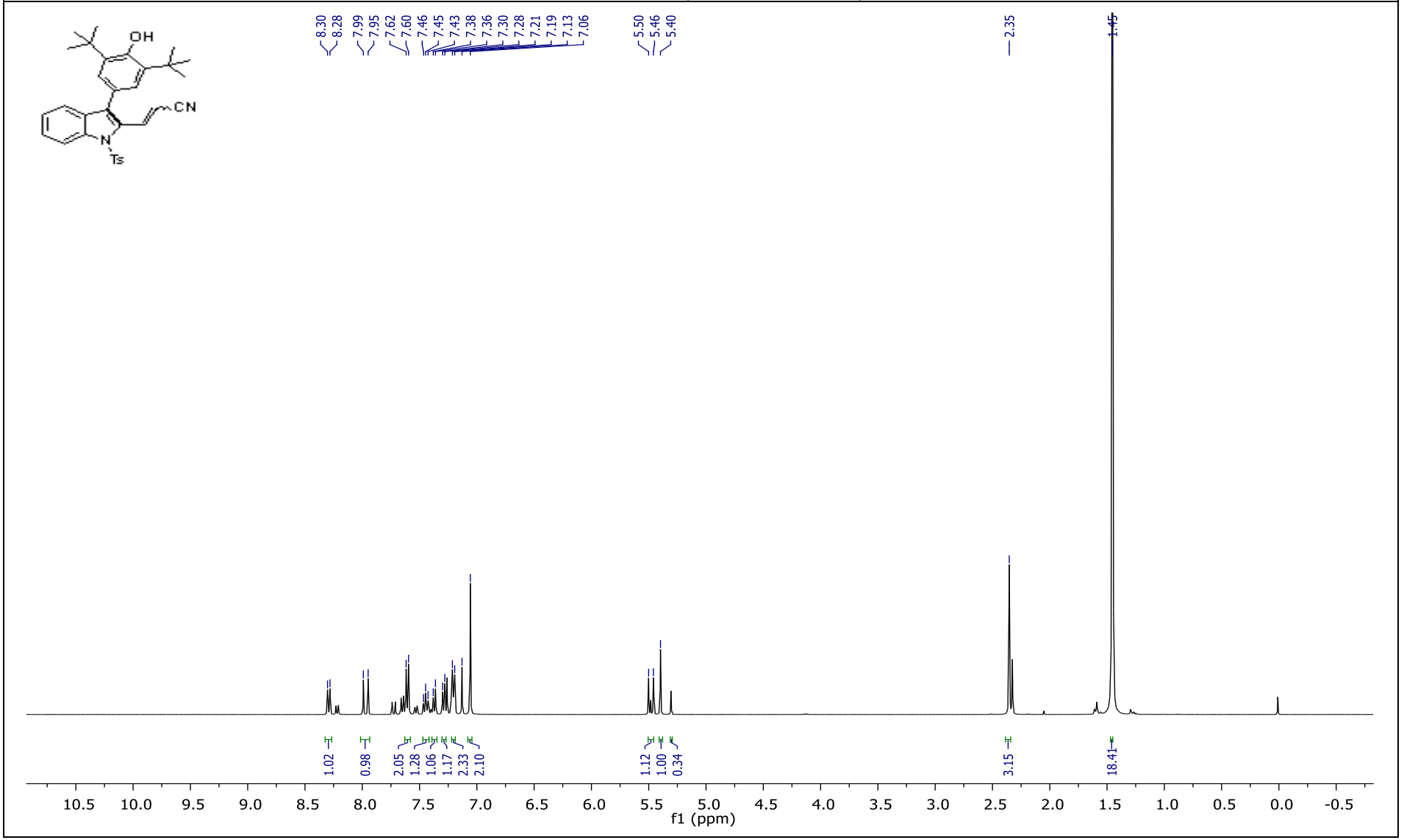
^{1}H-NMR of 7e (400 MHz, $CDCl_3$)



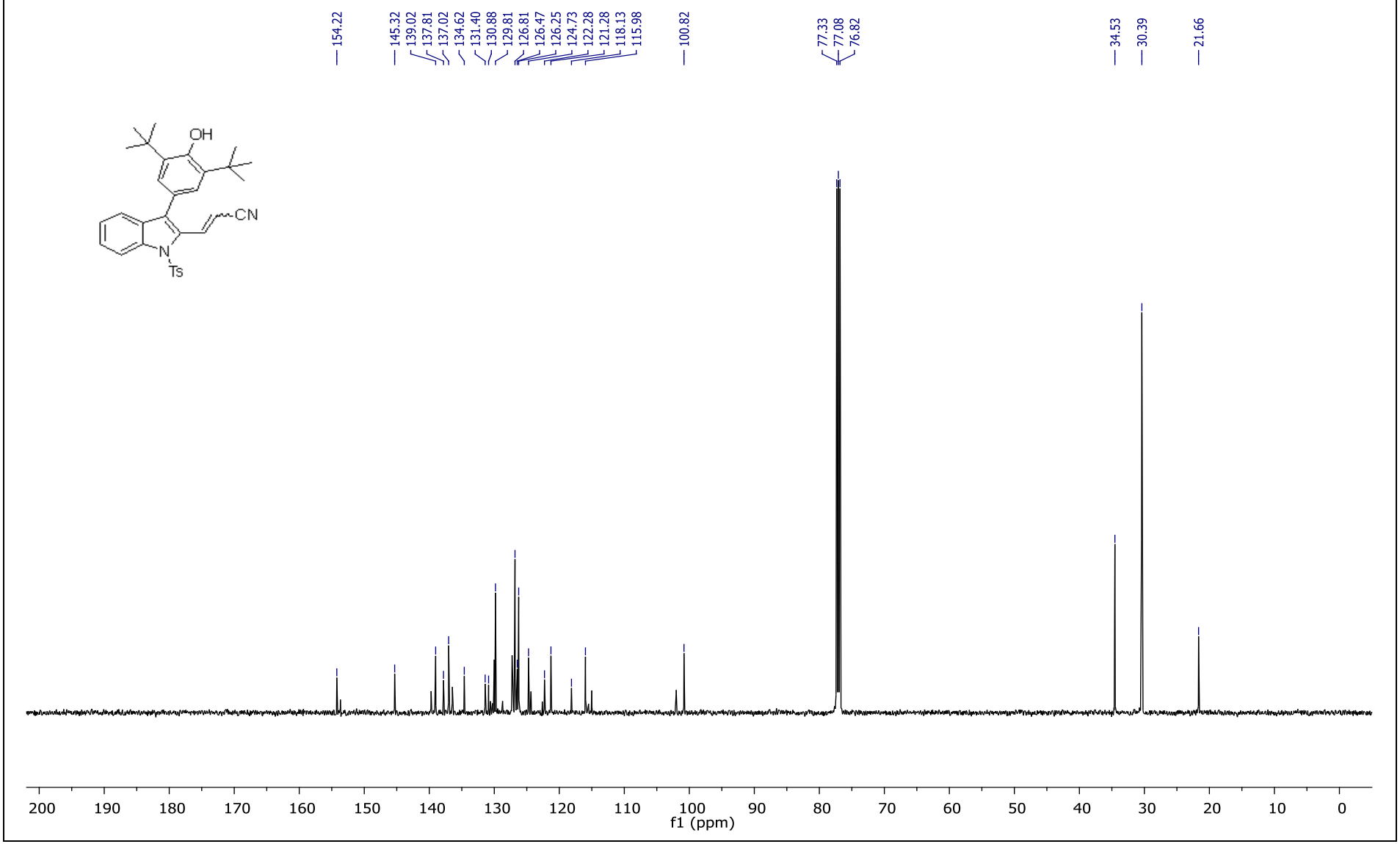
$^{13}C\{^{1}H\}$NMR of 7e (101 MHz, $CDCl_3$)



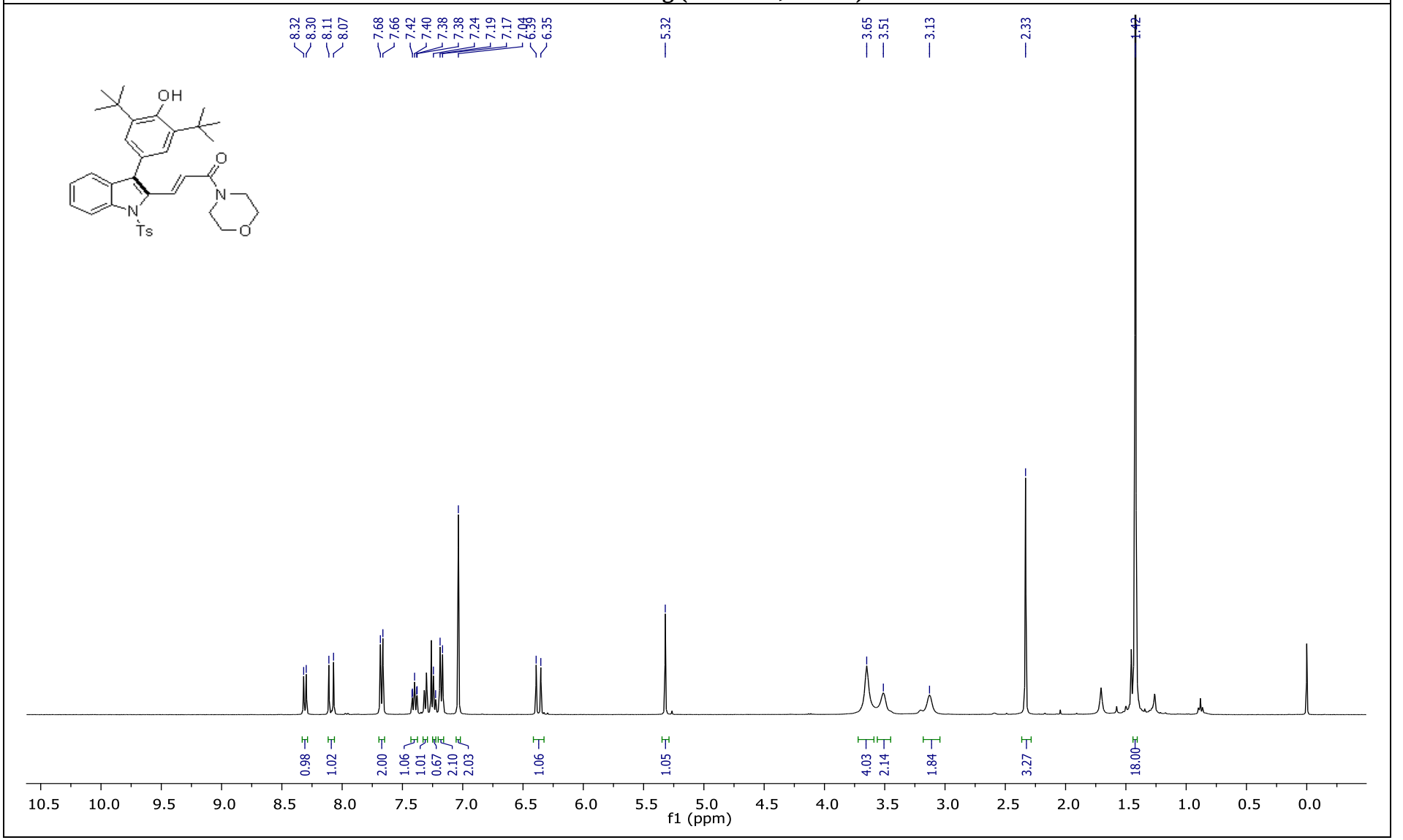
^{1}H-NMR of 7f (400 MHz, $CDCl_3$)



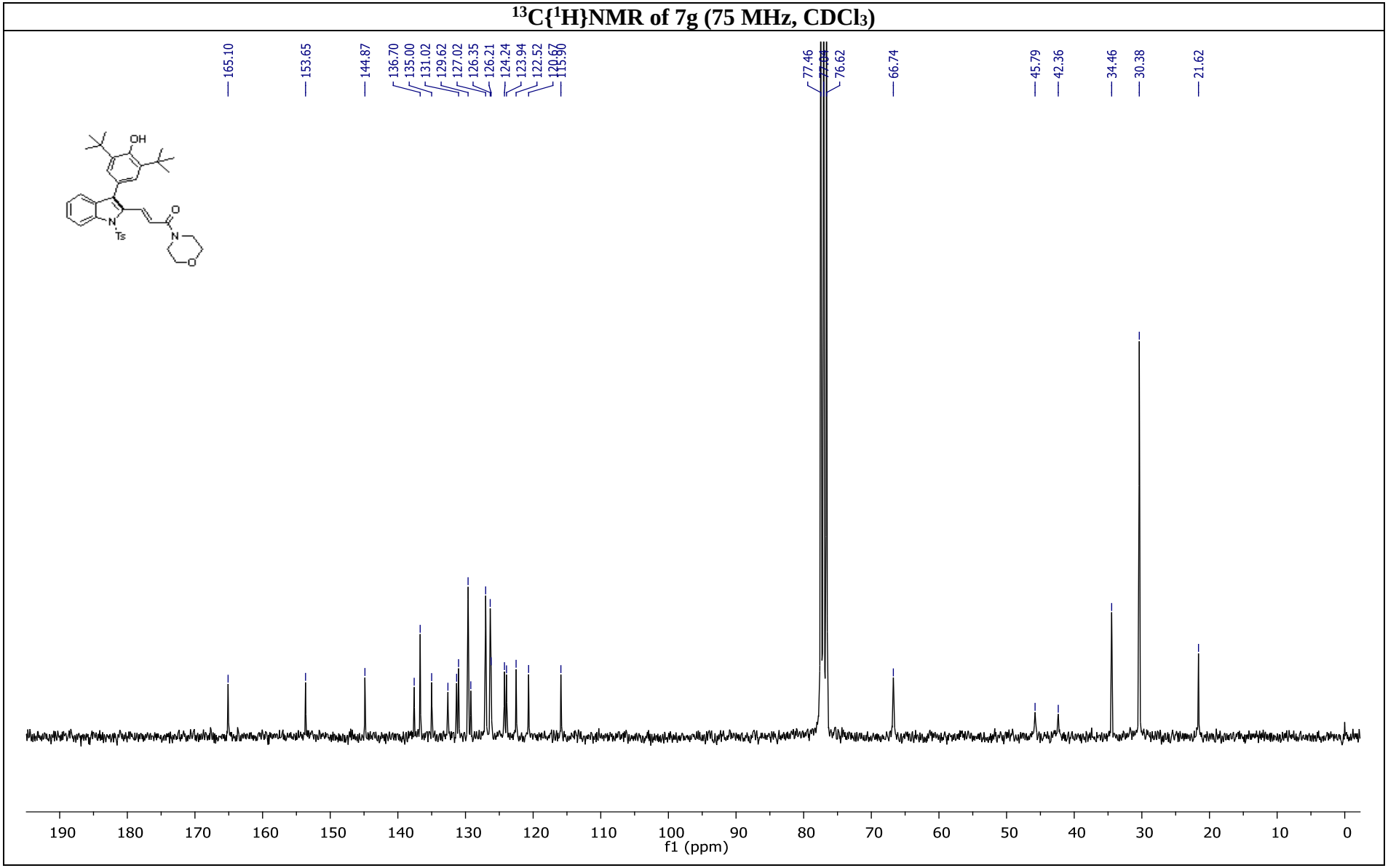
$^{13}C\{^{1}H\}$NMR of 7f (126 MHz, $CDCl_3$)



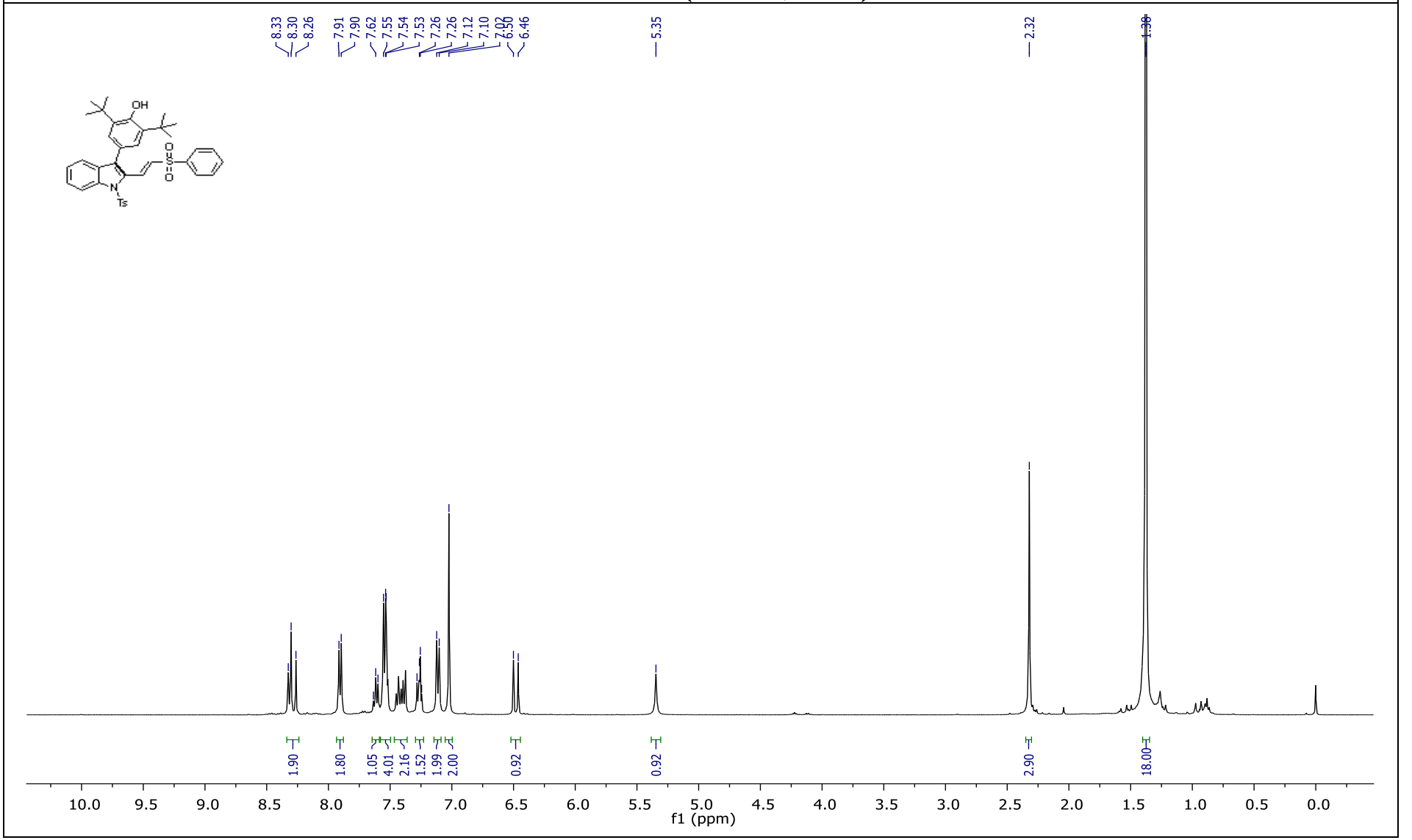
^{1}H-NMR of 7g (400 MHz, $CDCl_3$)



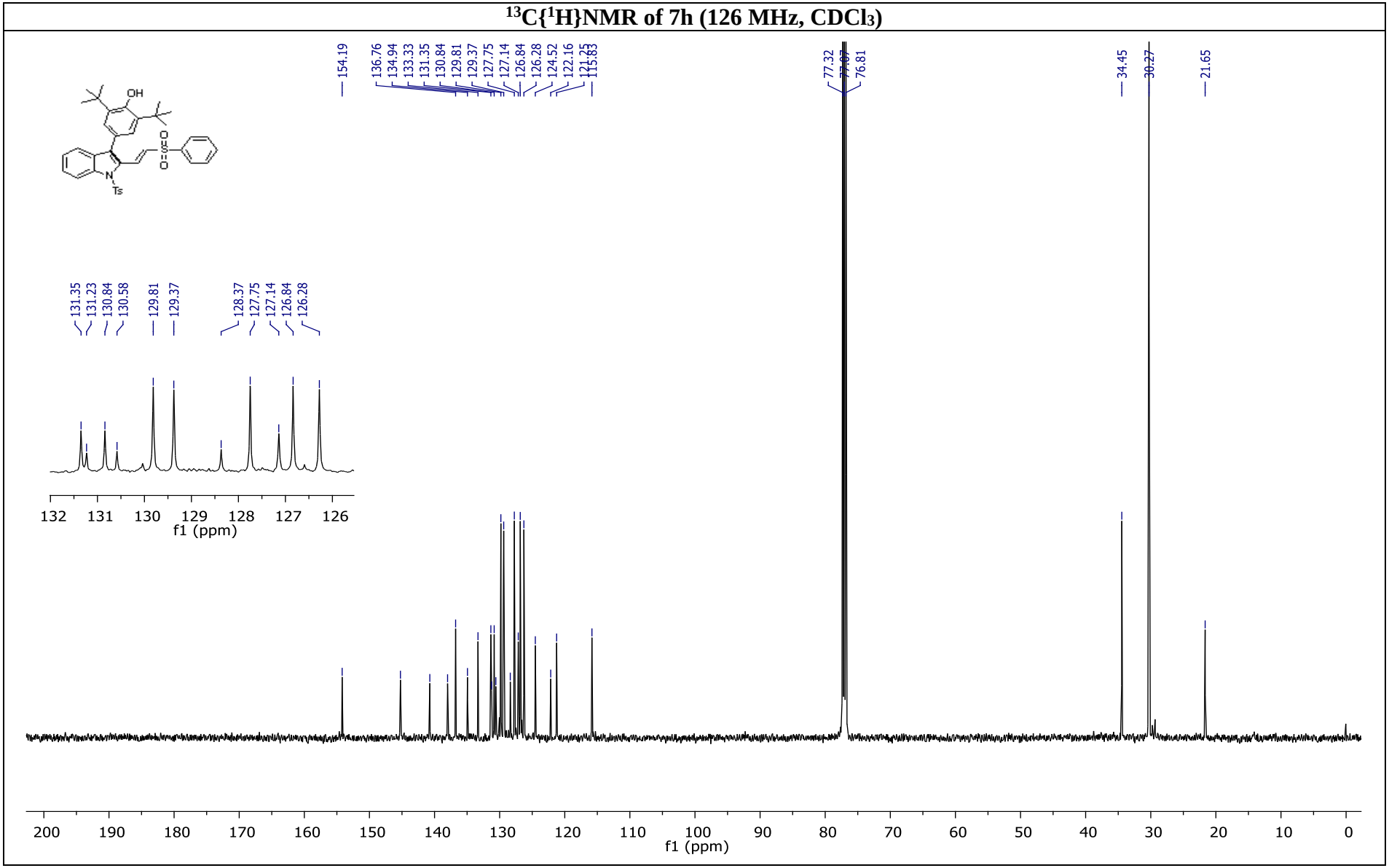
$^{13}C\{^{1}H\}$NMR of 7g (75 MHz, $CDCl_3$)



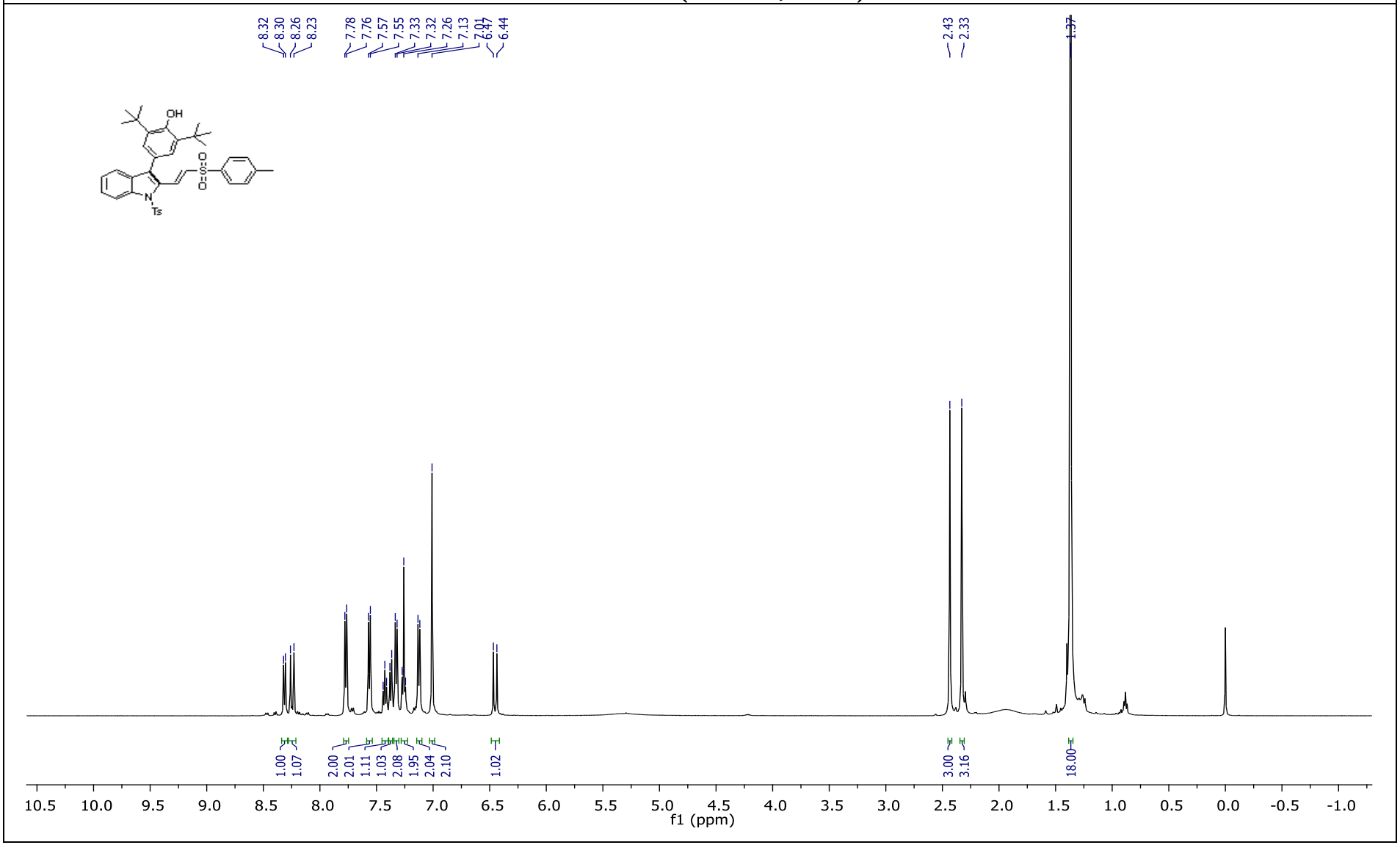
^{1}H-NMR of 7h (400 MHz, $CDCl_3$)



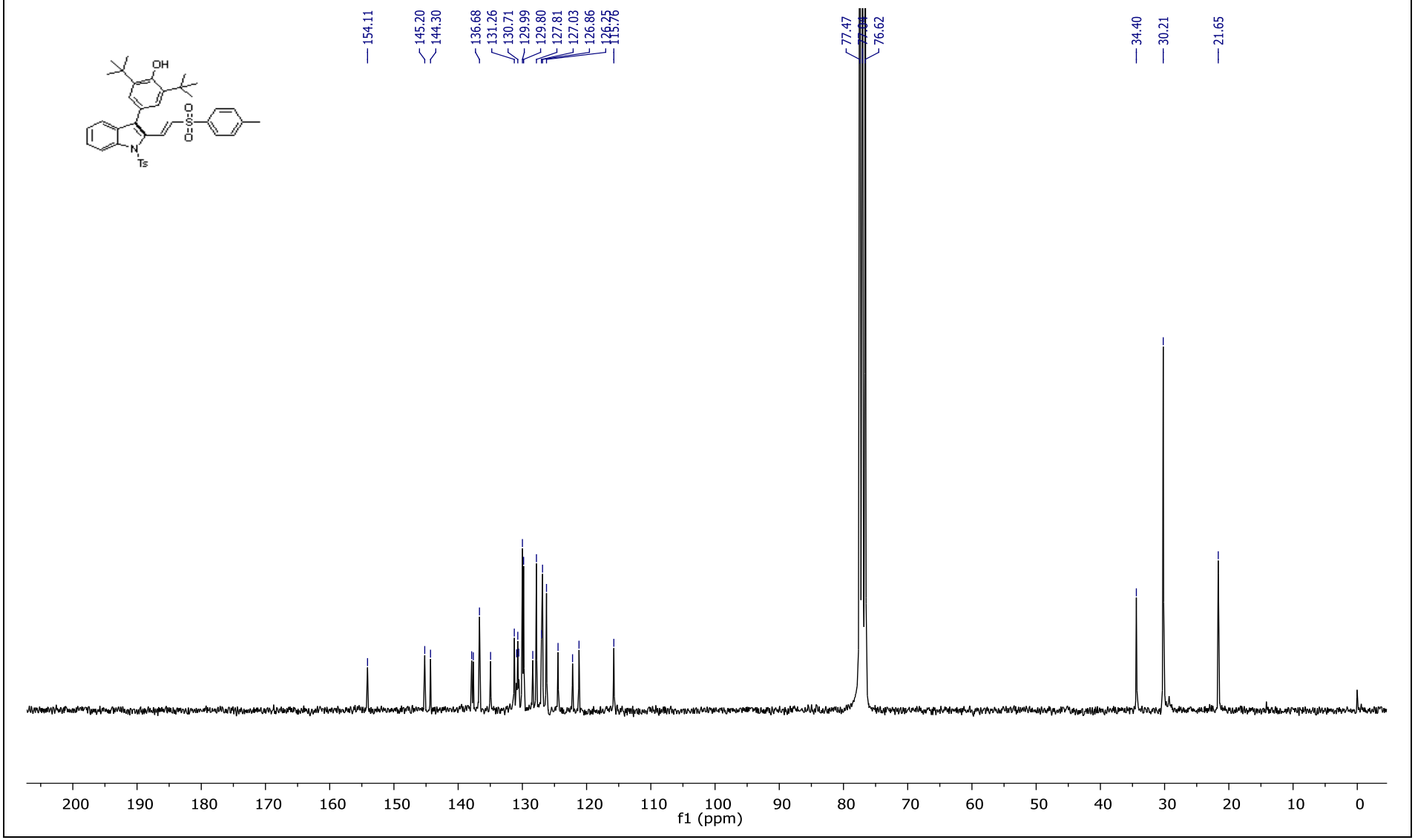
$^{13}C\{^{1}H\}$NMR of 7h (126 MHz, $CDCl_3$)



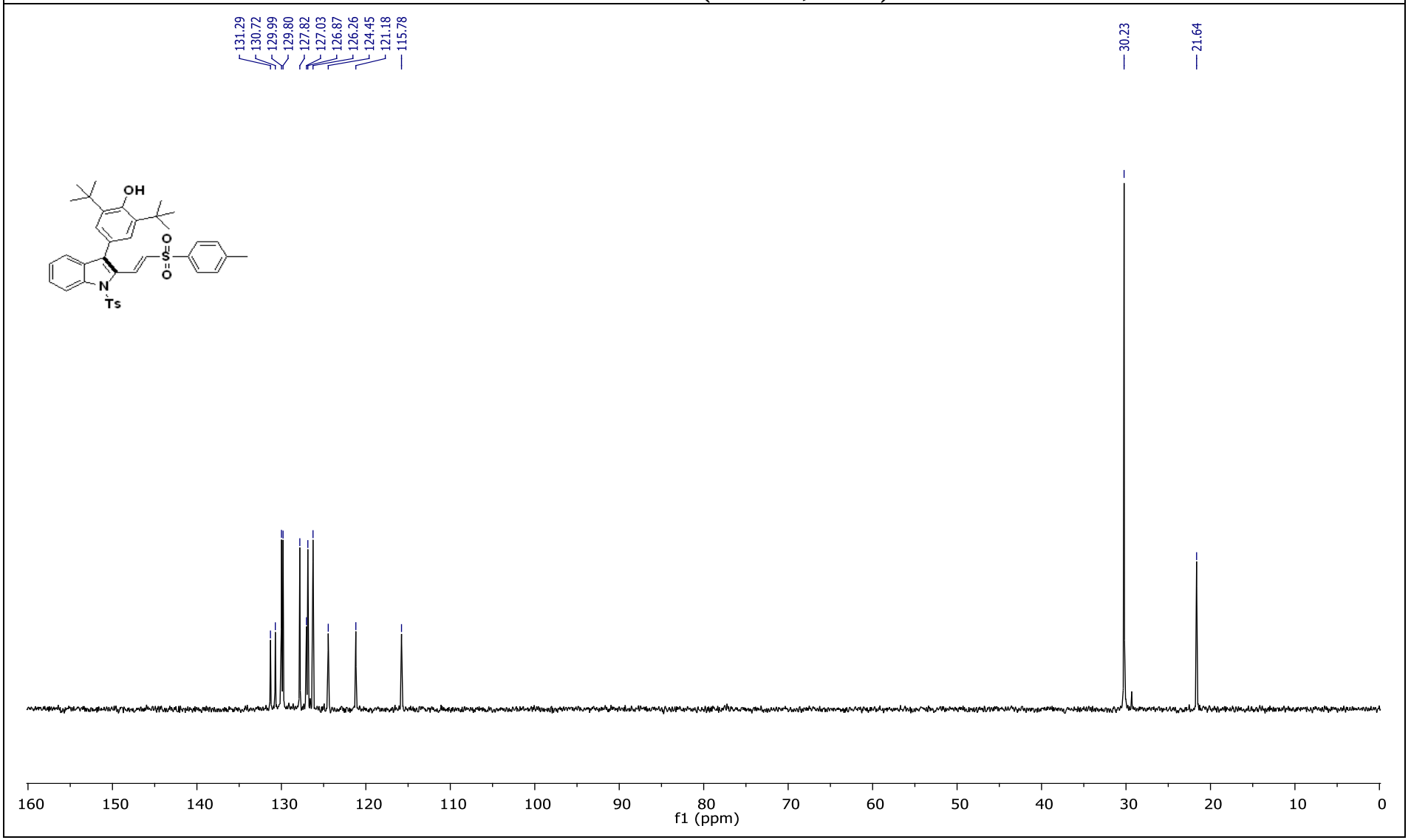
^{1}H-NMR of 7i (500 MHz, $CDCl_3$)



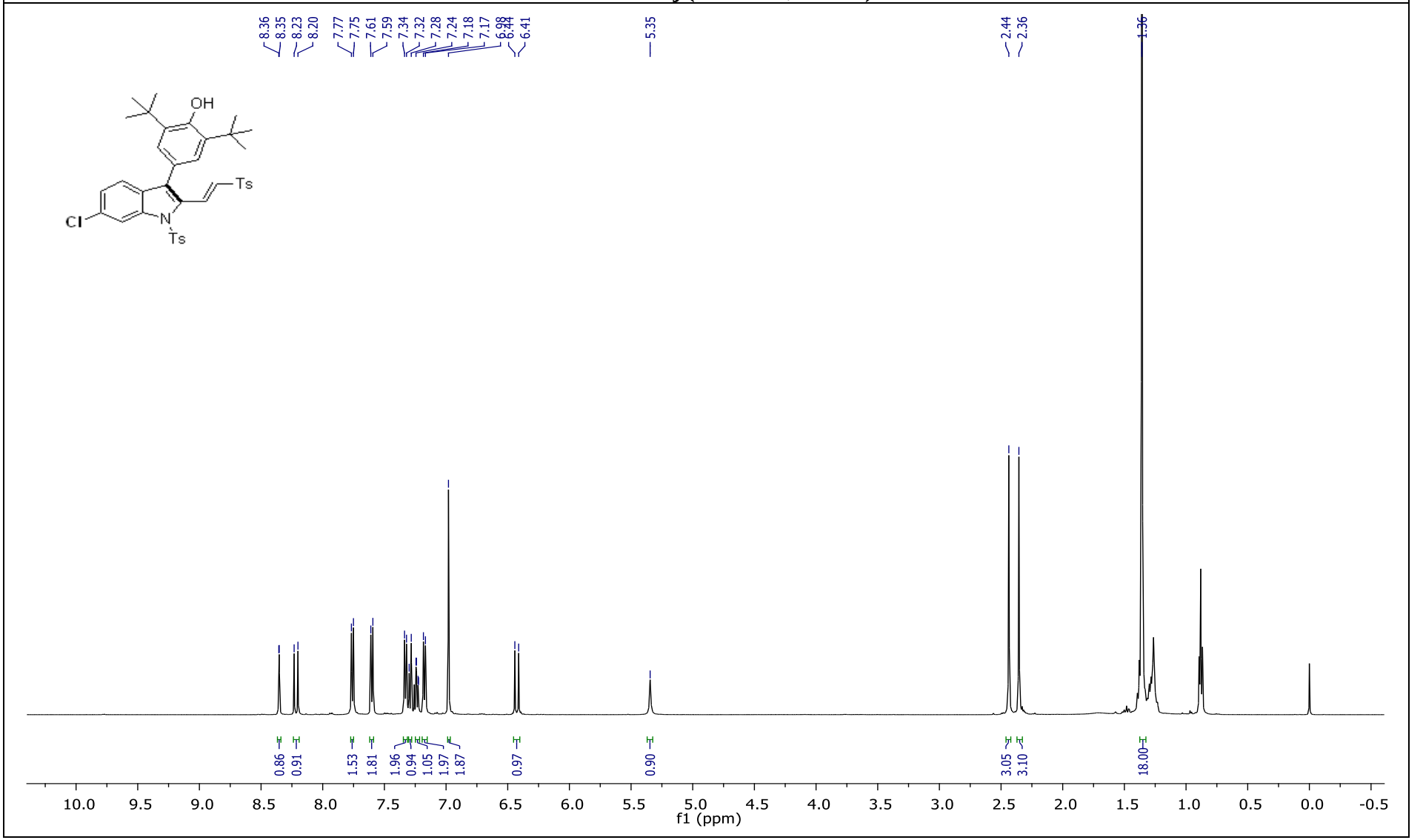
$^{13}C\{^{1}H\}$NMR of 7i (75 MHz, $CDCl_3$)



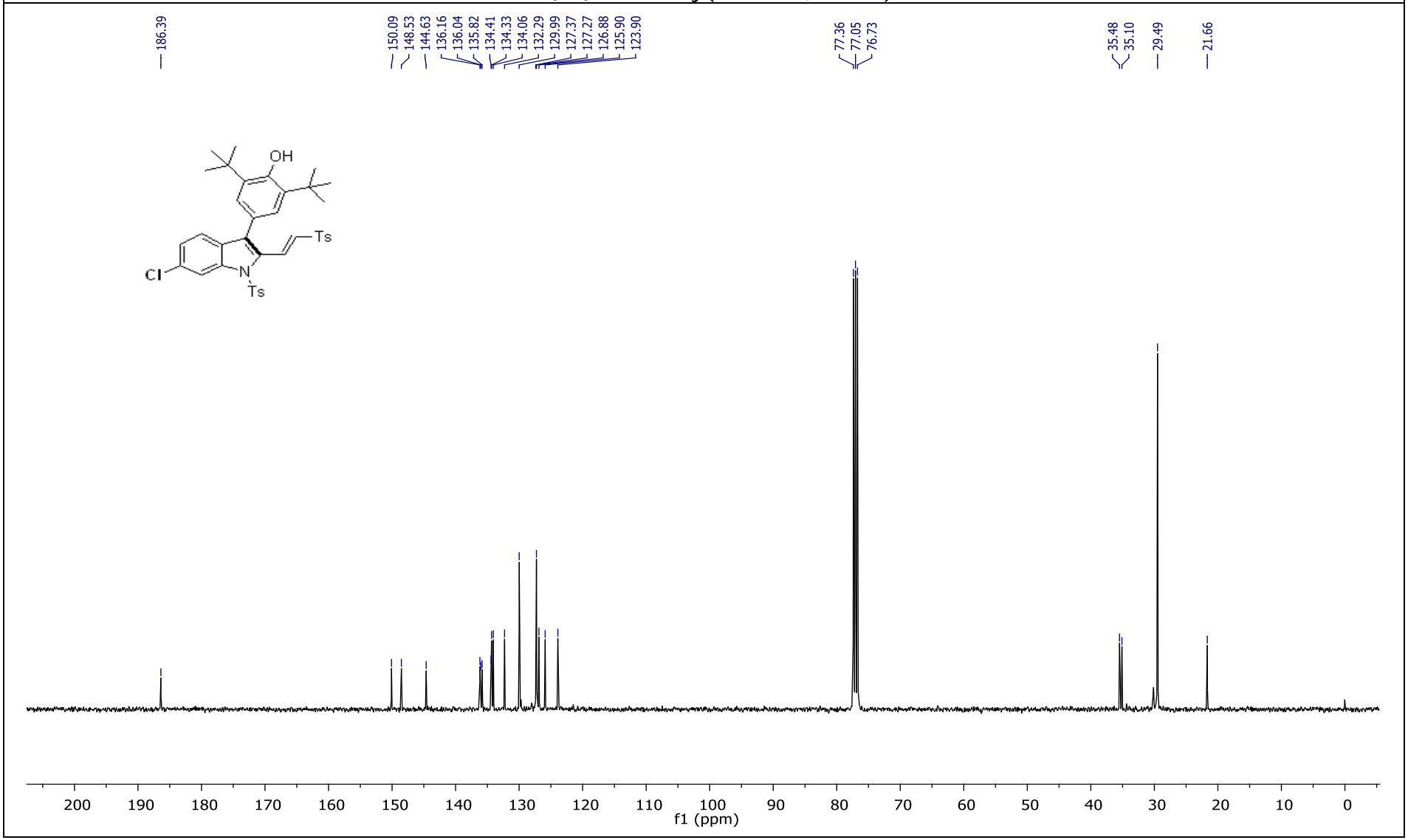
DEPT-NMR of 7i (135 MHz, $CDCl_3$)



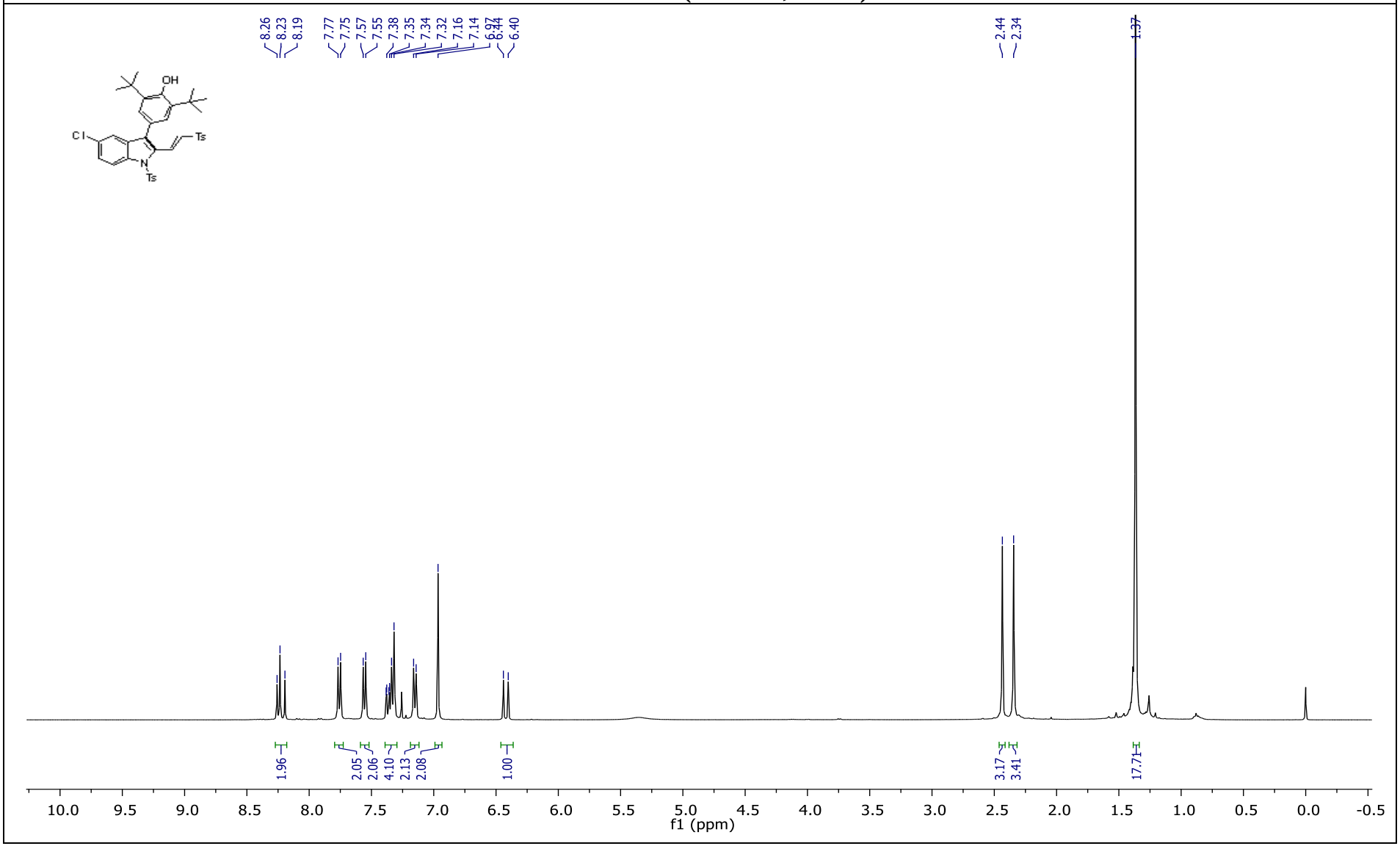
^{1}H-NMR of 7j (500 MHz, $CDCl_3$)



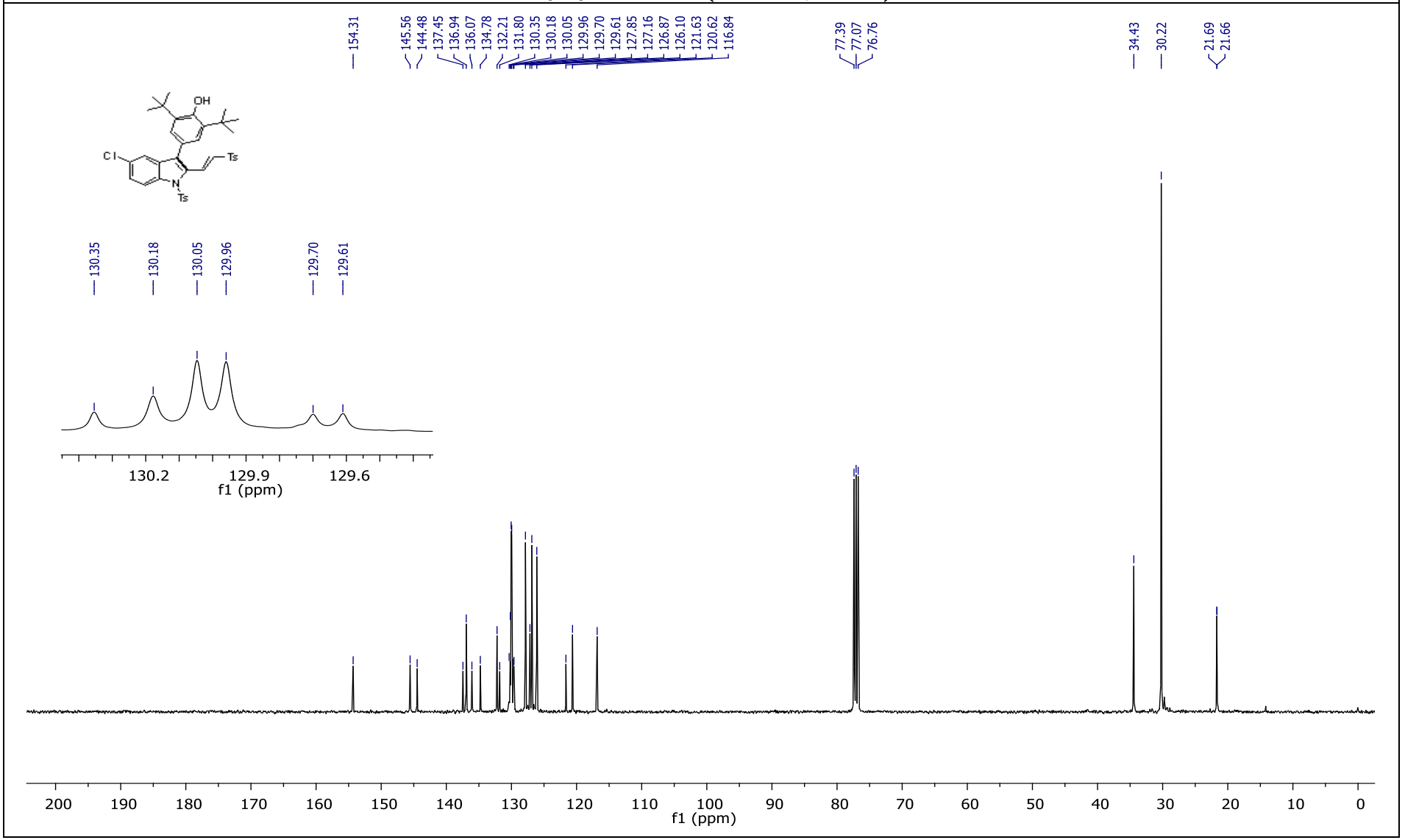
$^{13}C\{^{1}H\}$NMR of 7j (101 MHz, $CDCl_3$)



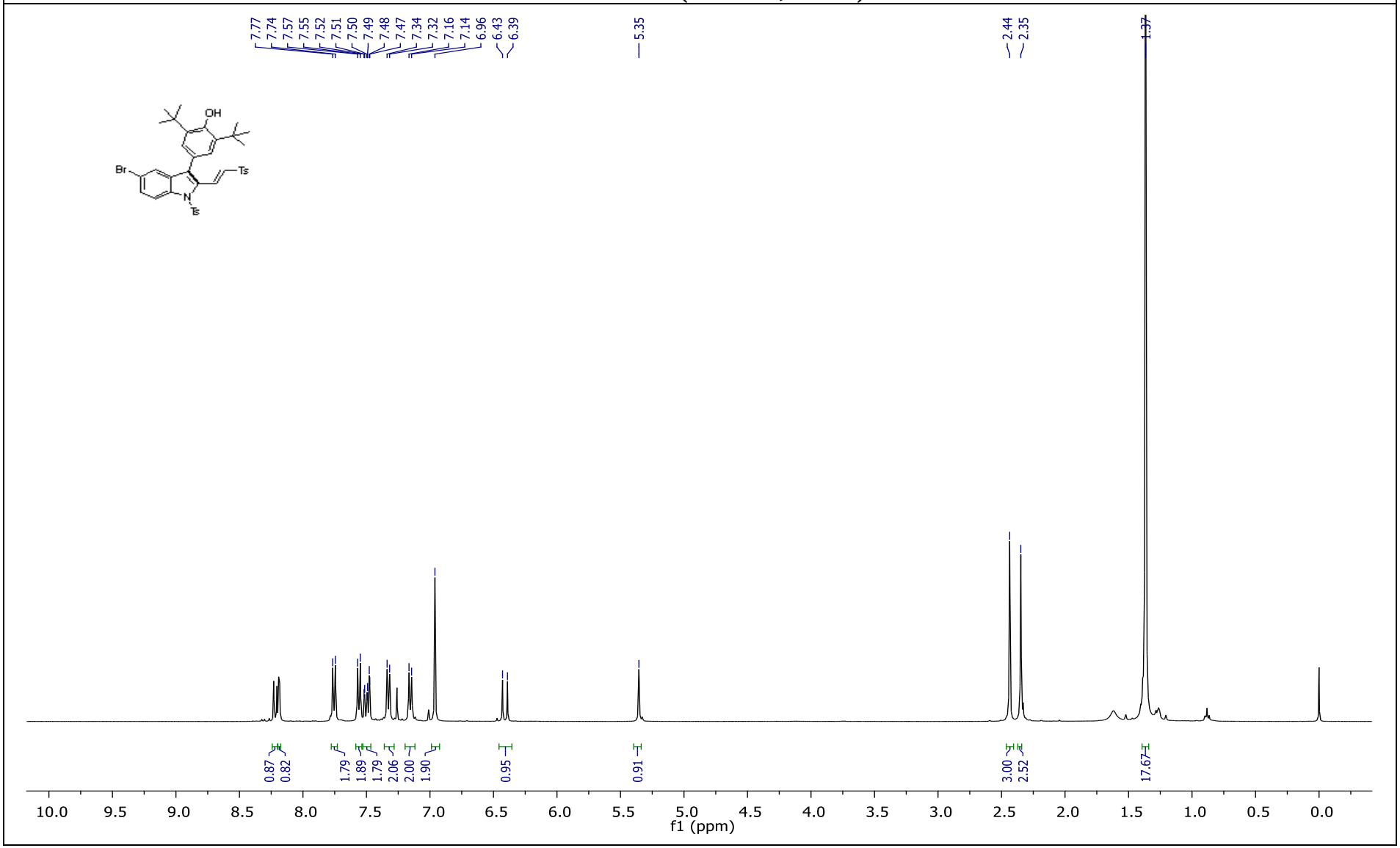
^{1}H-NMR of 7k (400 MHz, $CDCl_3$)



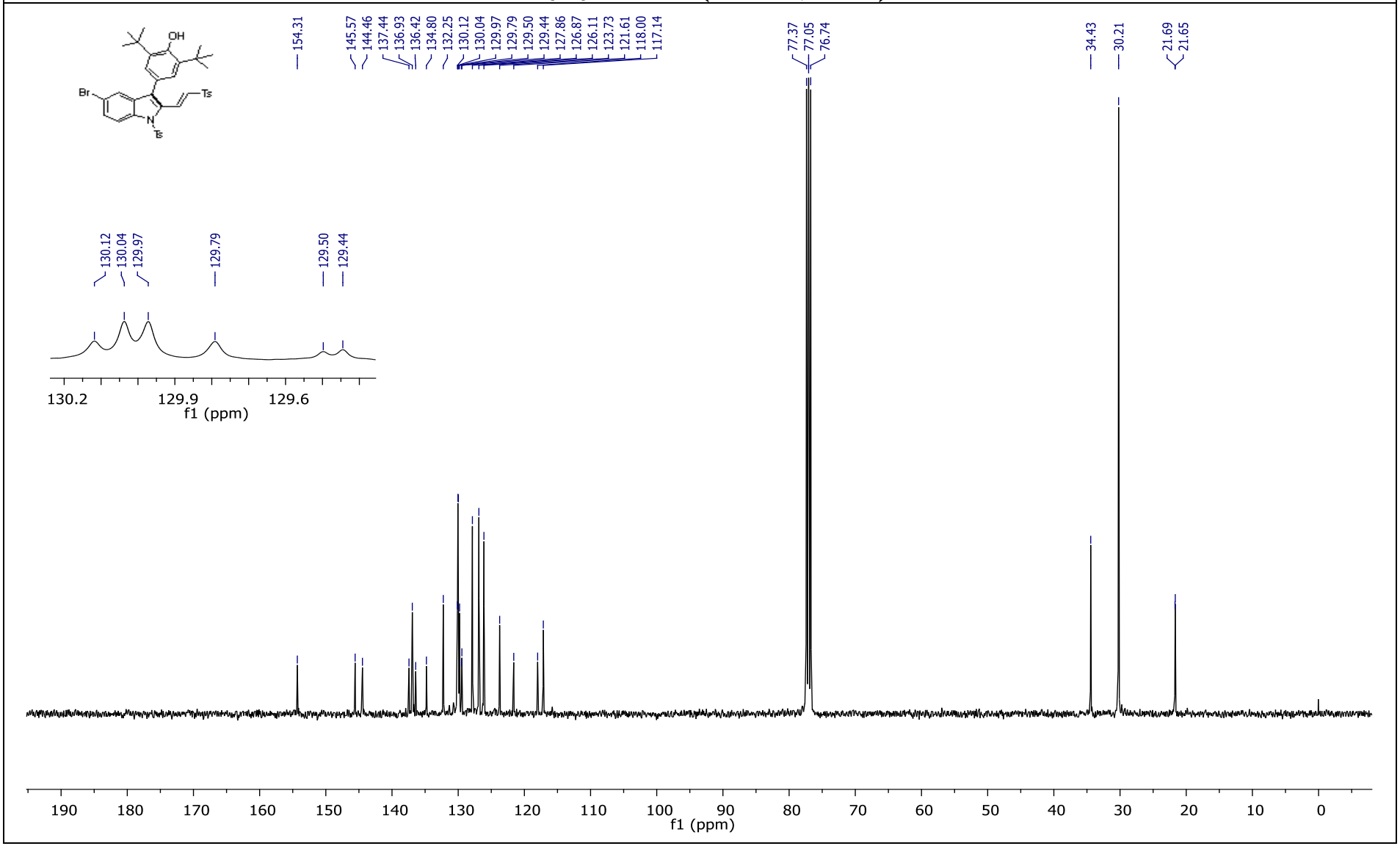
$^{13}C\{^{1}H\}$NMR of 7k (101 MHz, $CDCl_3$)



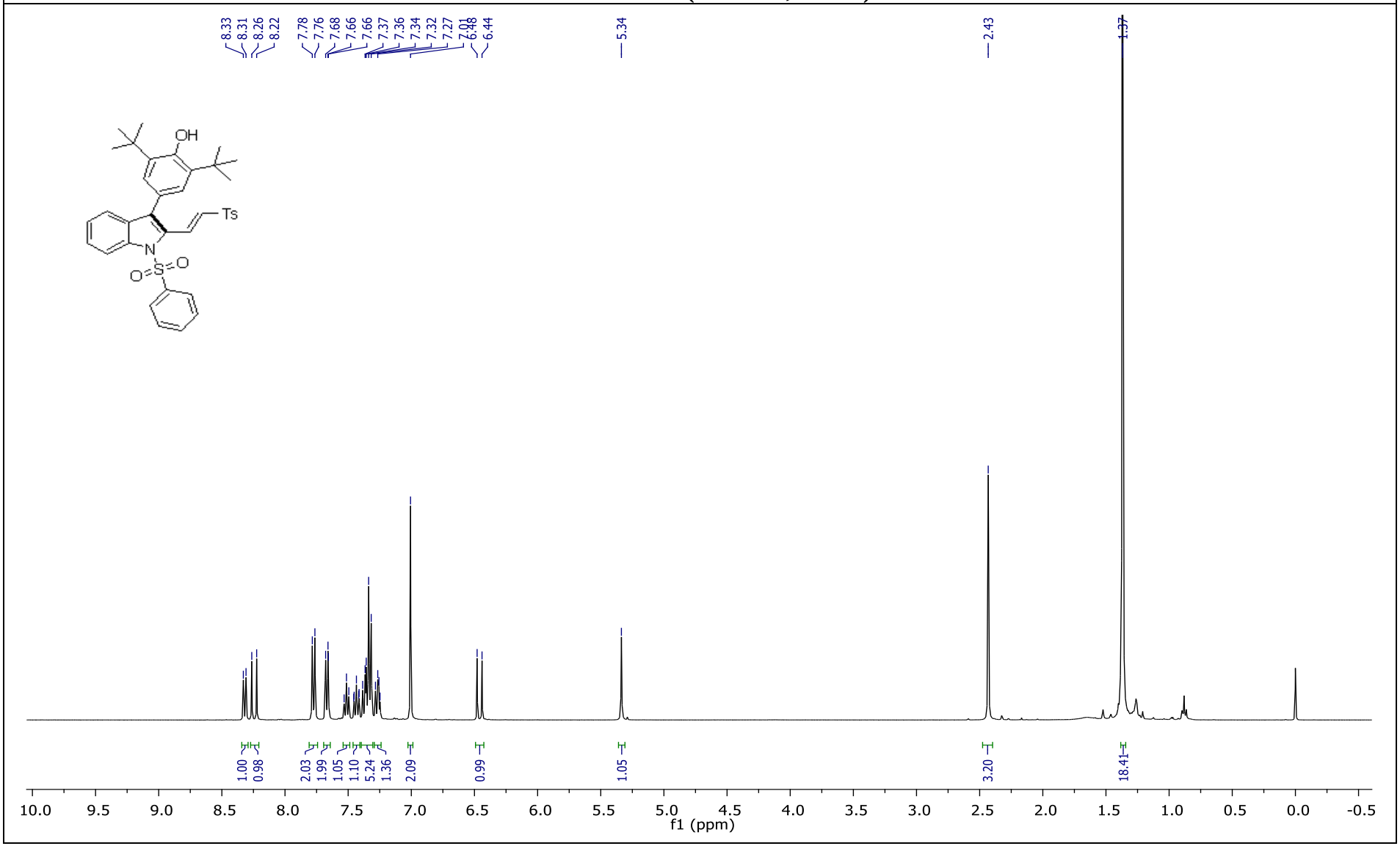
^{1}H-NMR of 7l (400 MHz, $CDCl_3$)



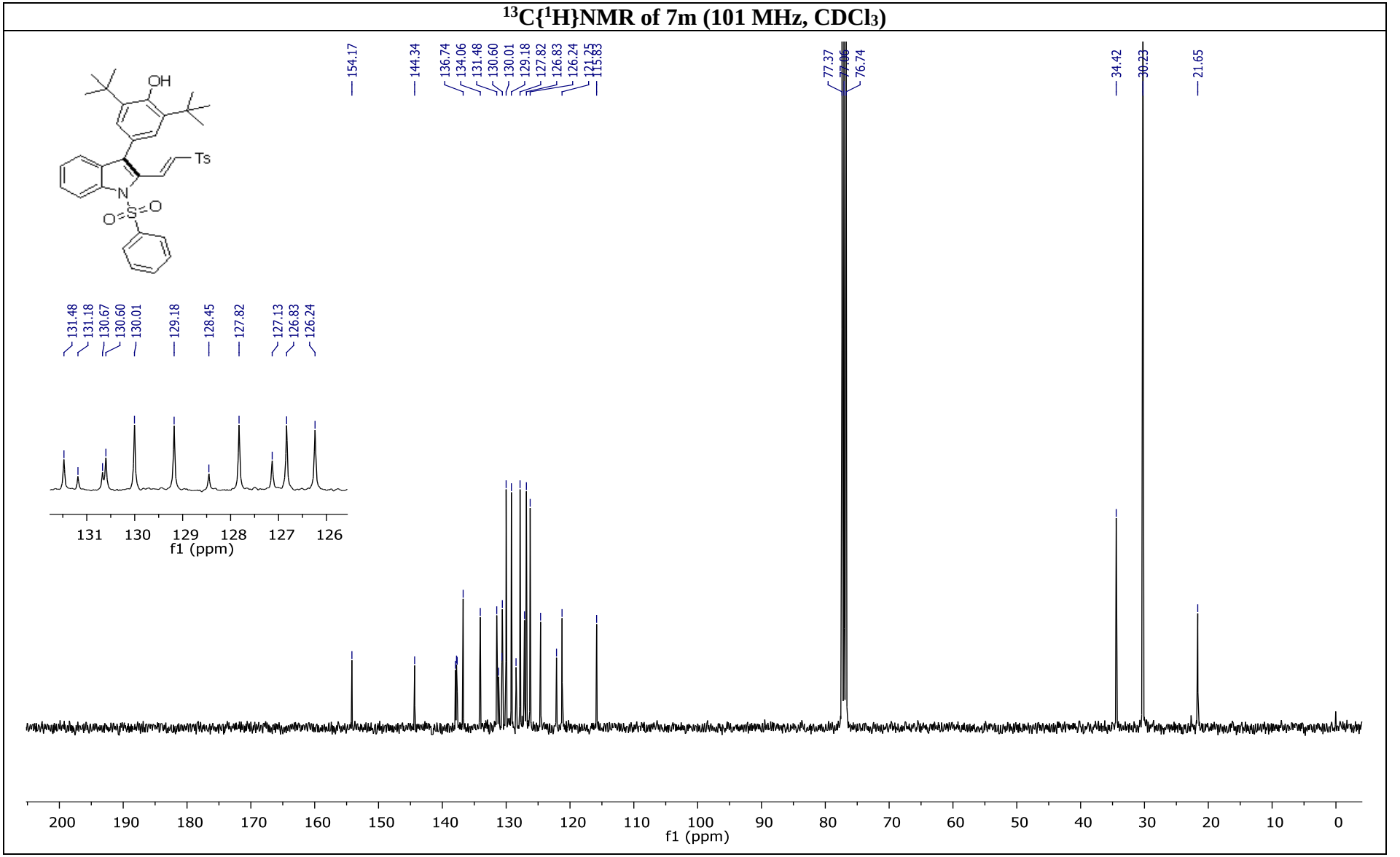
$^{13}C\{^{1}H\}$NMR of 7l (101 MHz, $CDCl_3$)



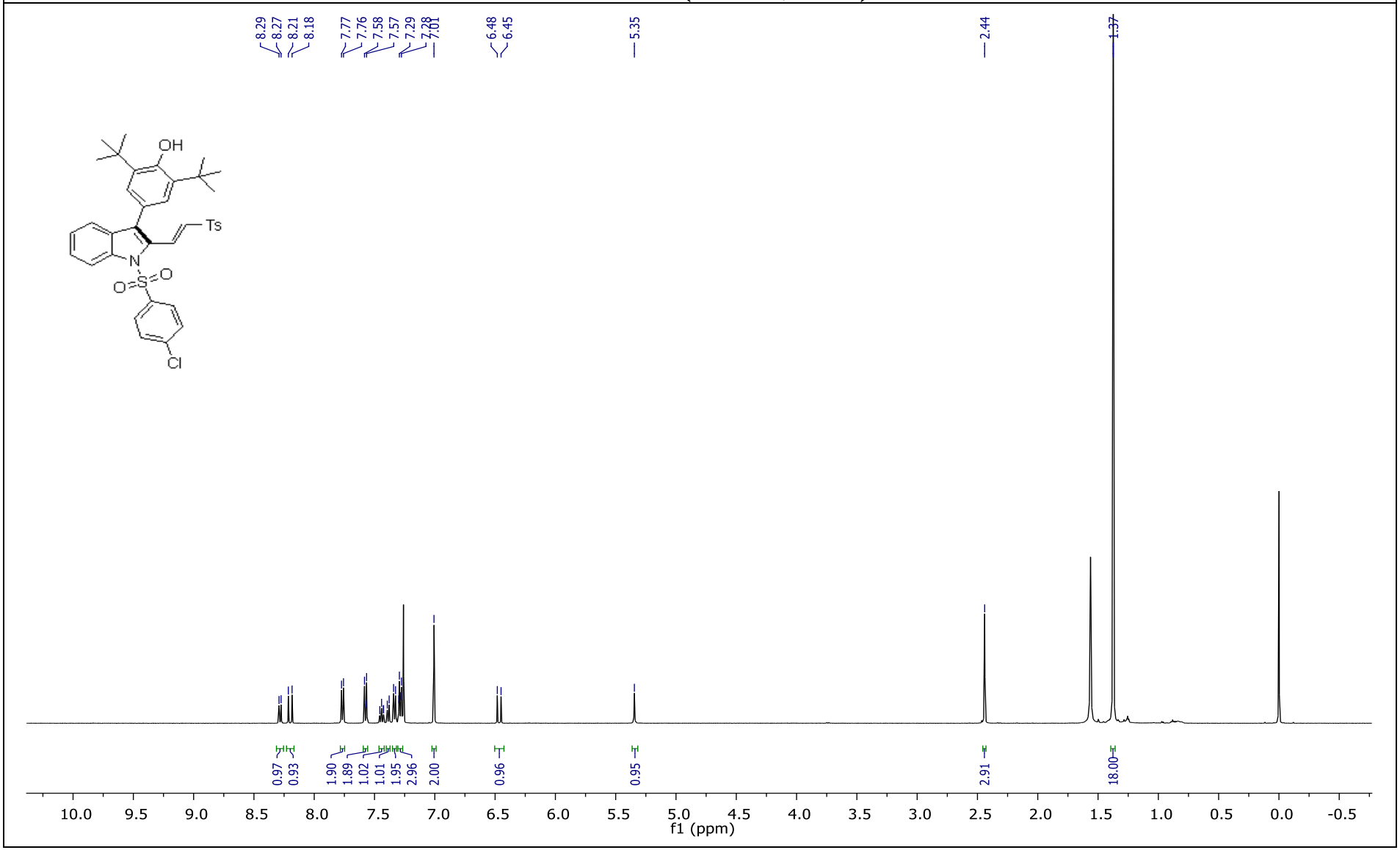
^{1}H-NMR of 7m (400 MHz, $CDCl_3$)



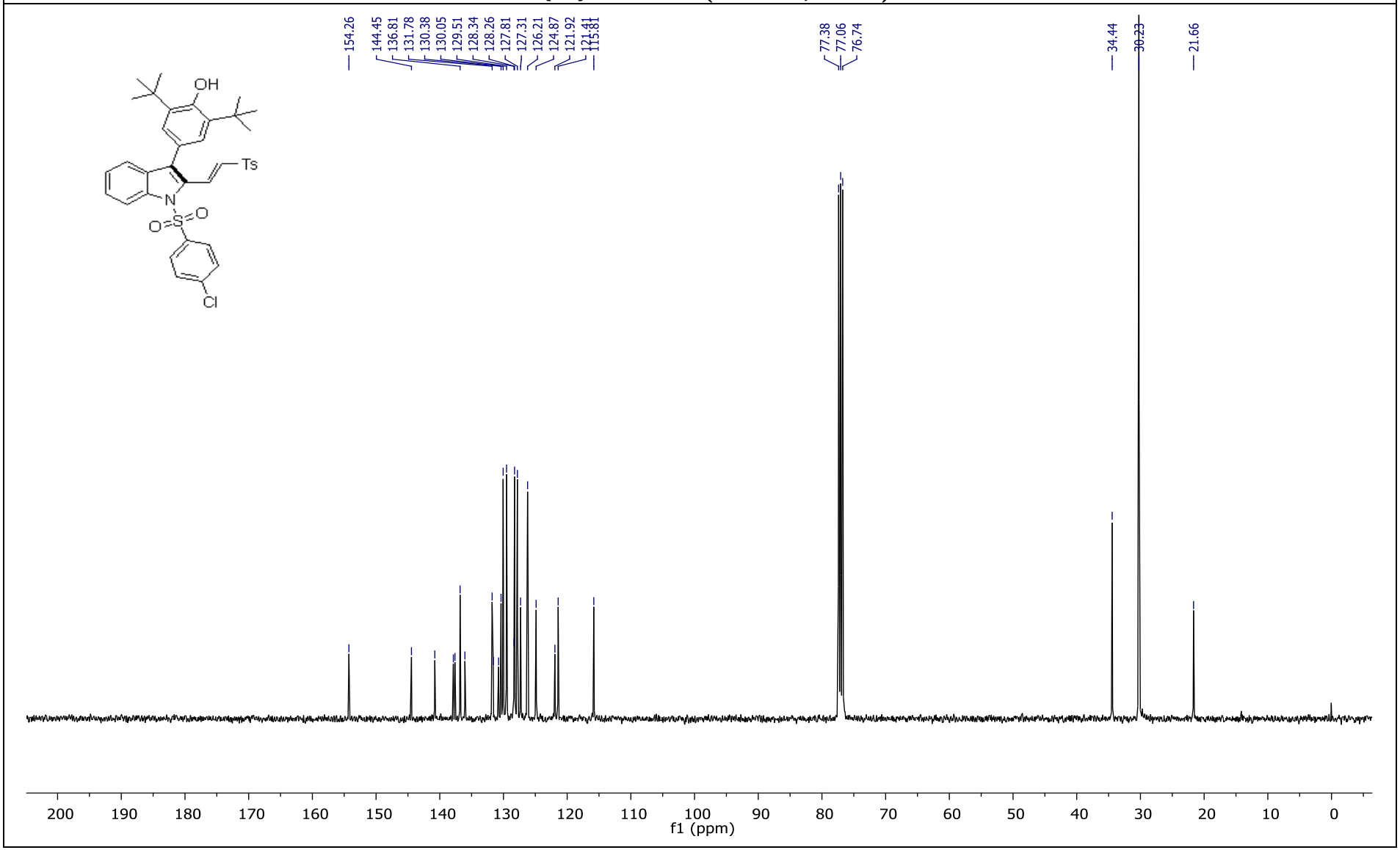
$^{13}C\{^{1}H\}$NMR of 7m (101 MHz, $CDCl_3$)



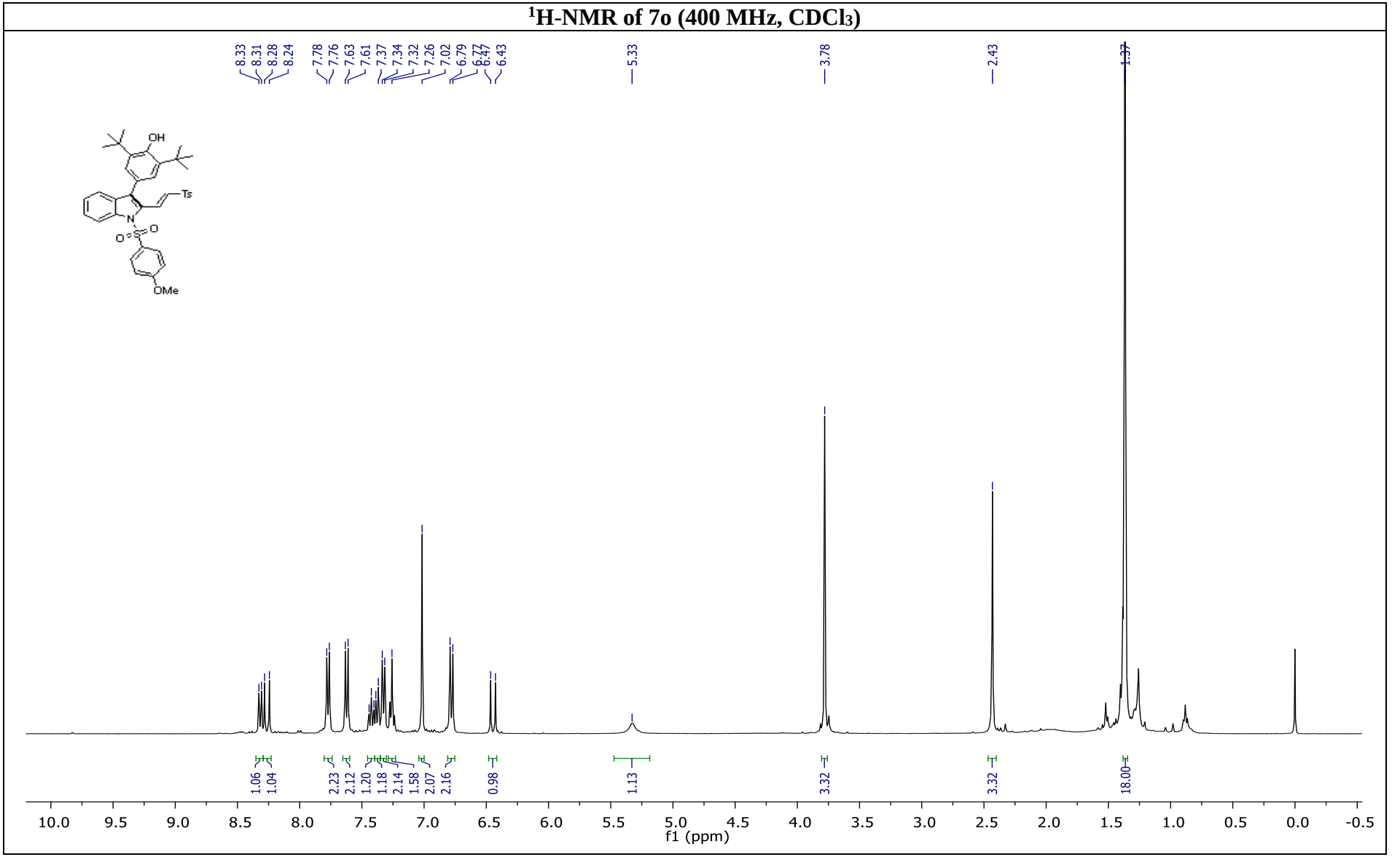
^{1}H-NMR of 7n (500 MHz, $CDCl_3$)



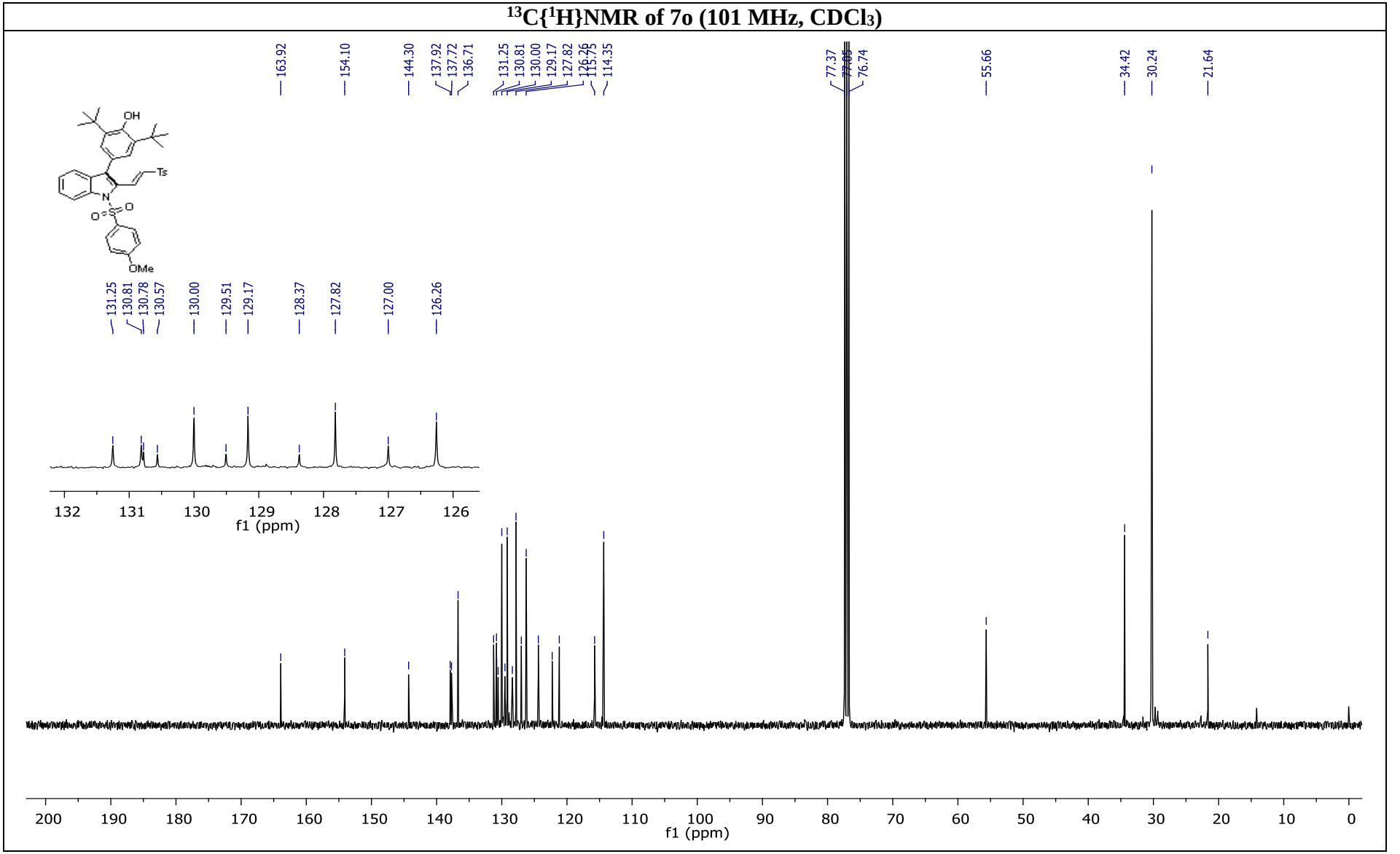
$^{13}C\{^{1}H\}$NMR of 7n (101 MHz, $CDCl_3$)



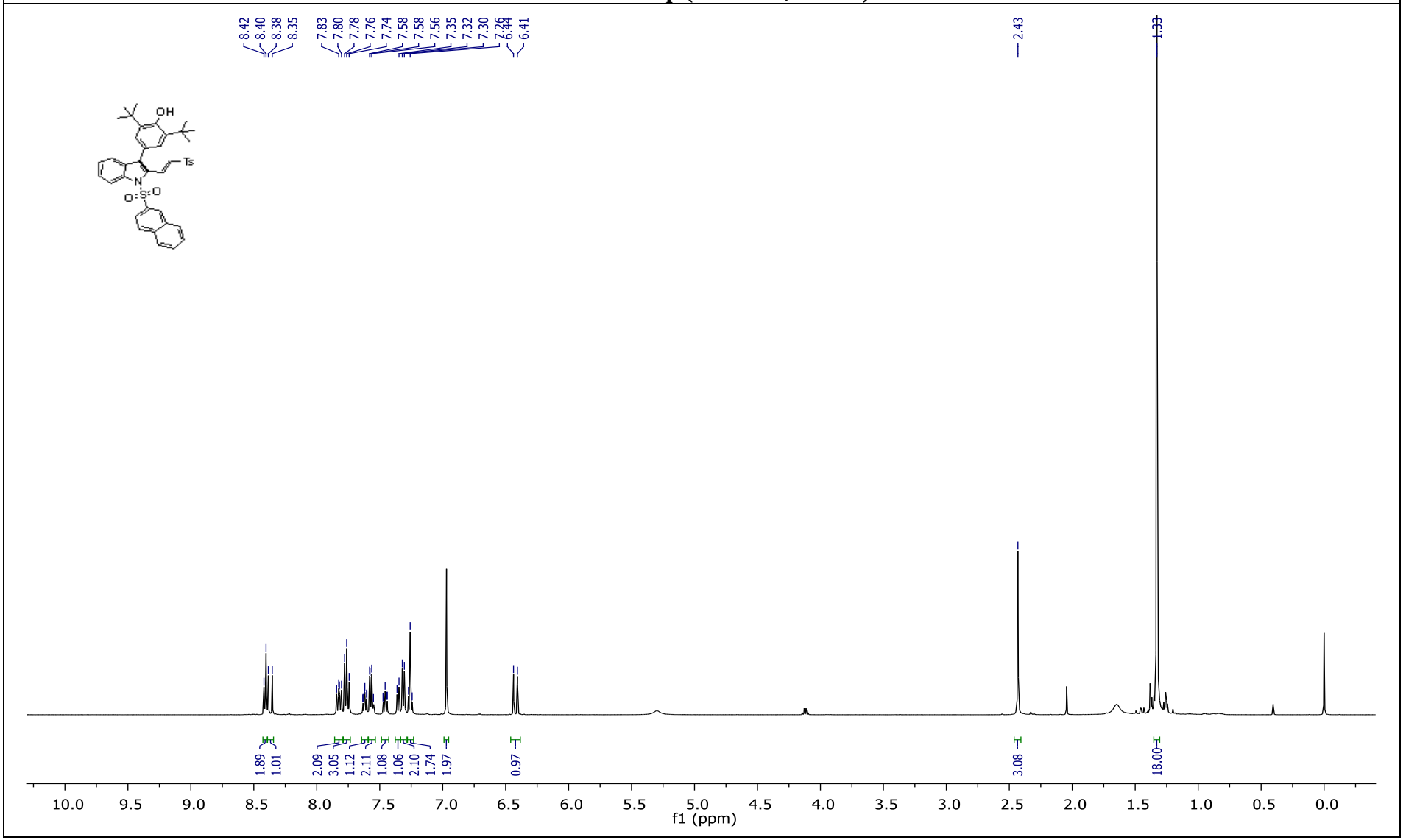
^{1}H-NMR of 7o (400 MHz, $CDCl_3$)



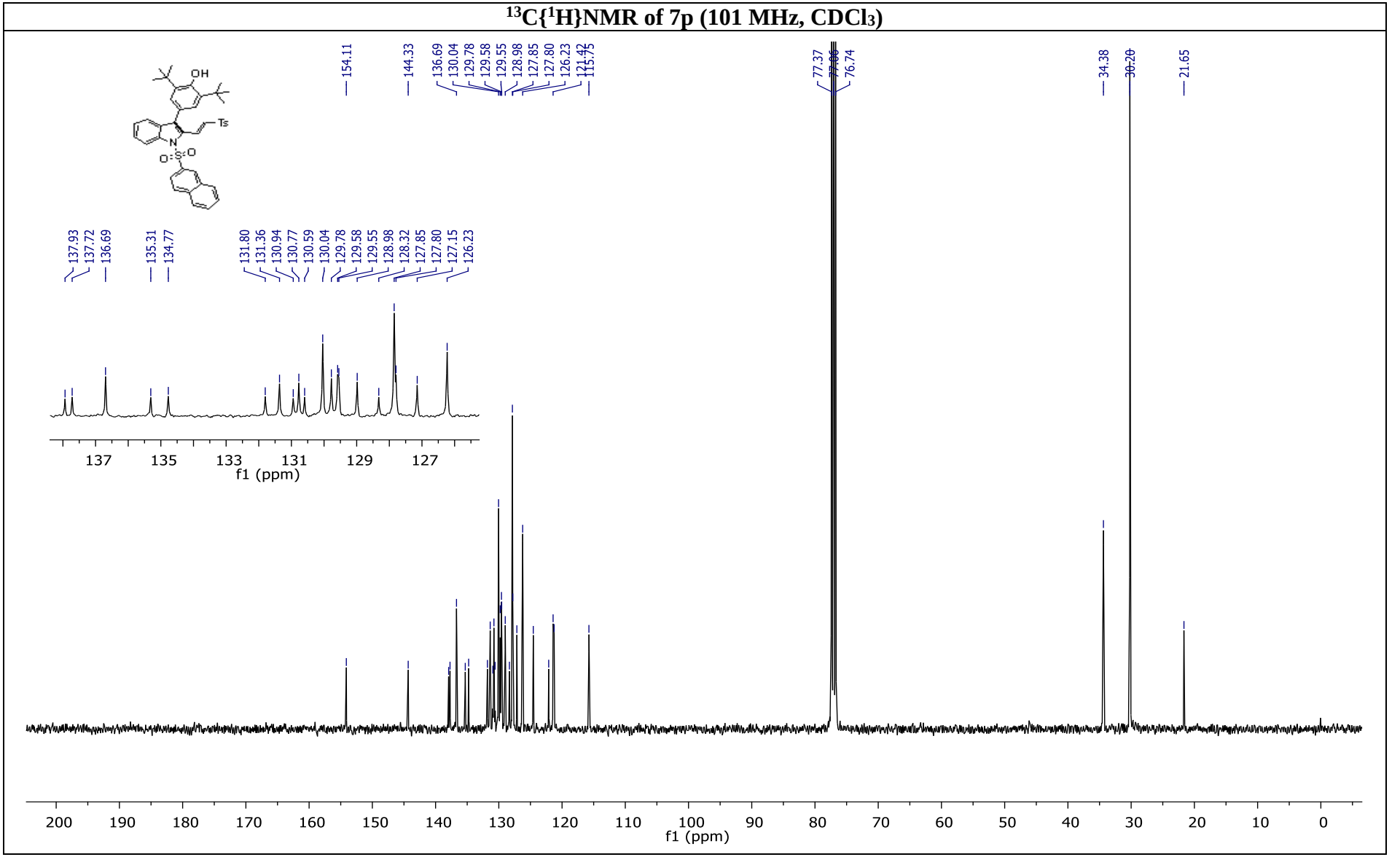
$^{13}C\{^{1}H\}$NMR of 7o (101 MHz, $CDCl_3$)



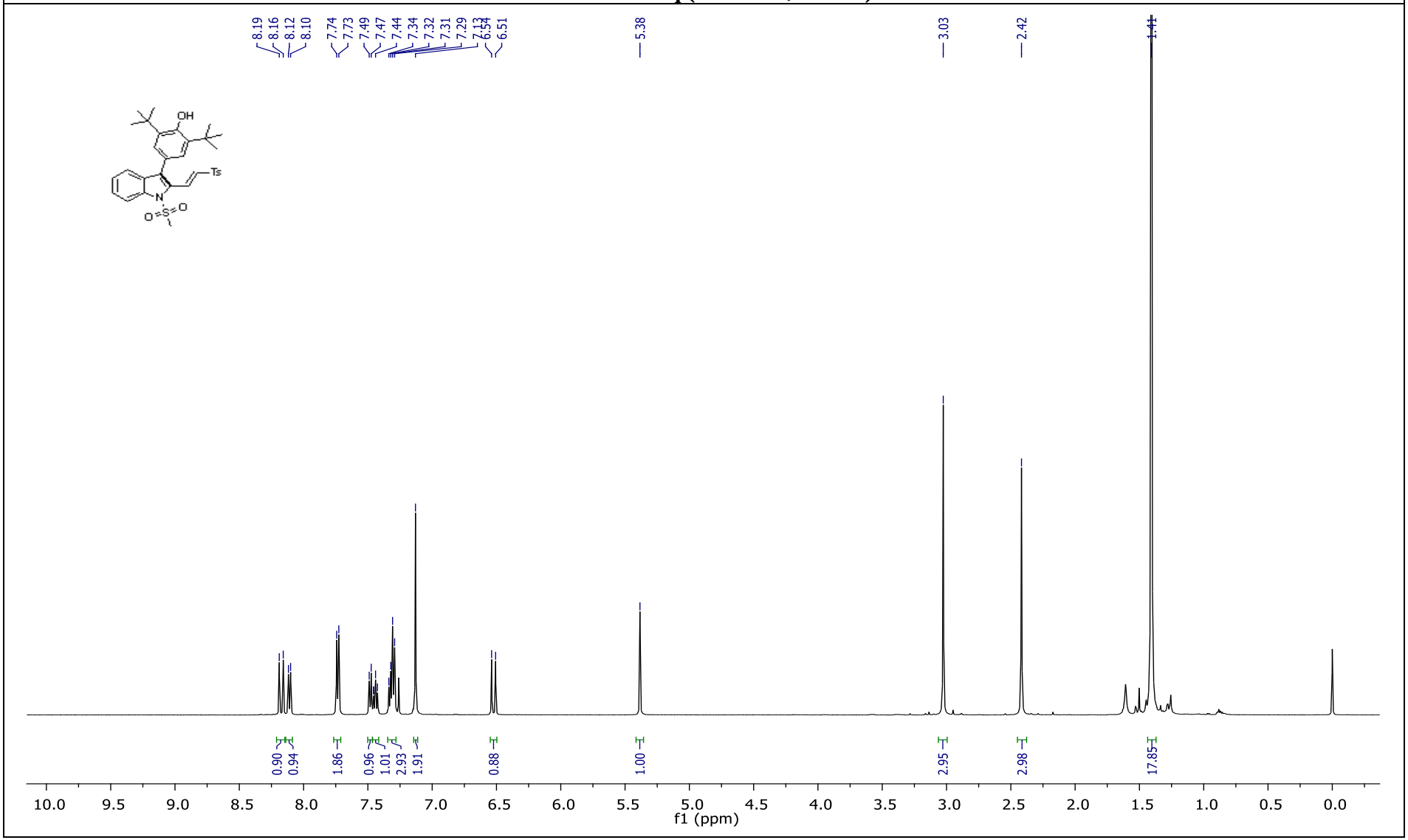
^{1}H-NMR of 7p (500 MHz, $CDCl_3$)



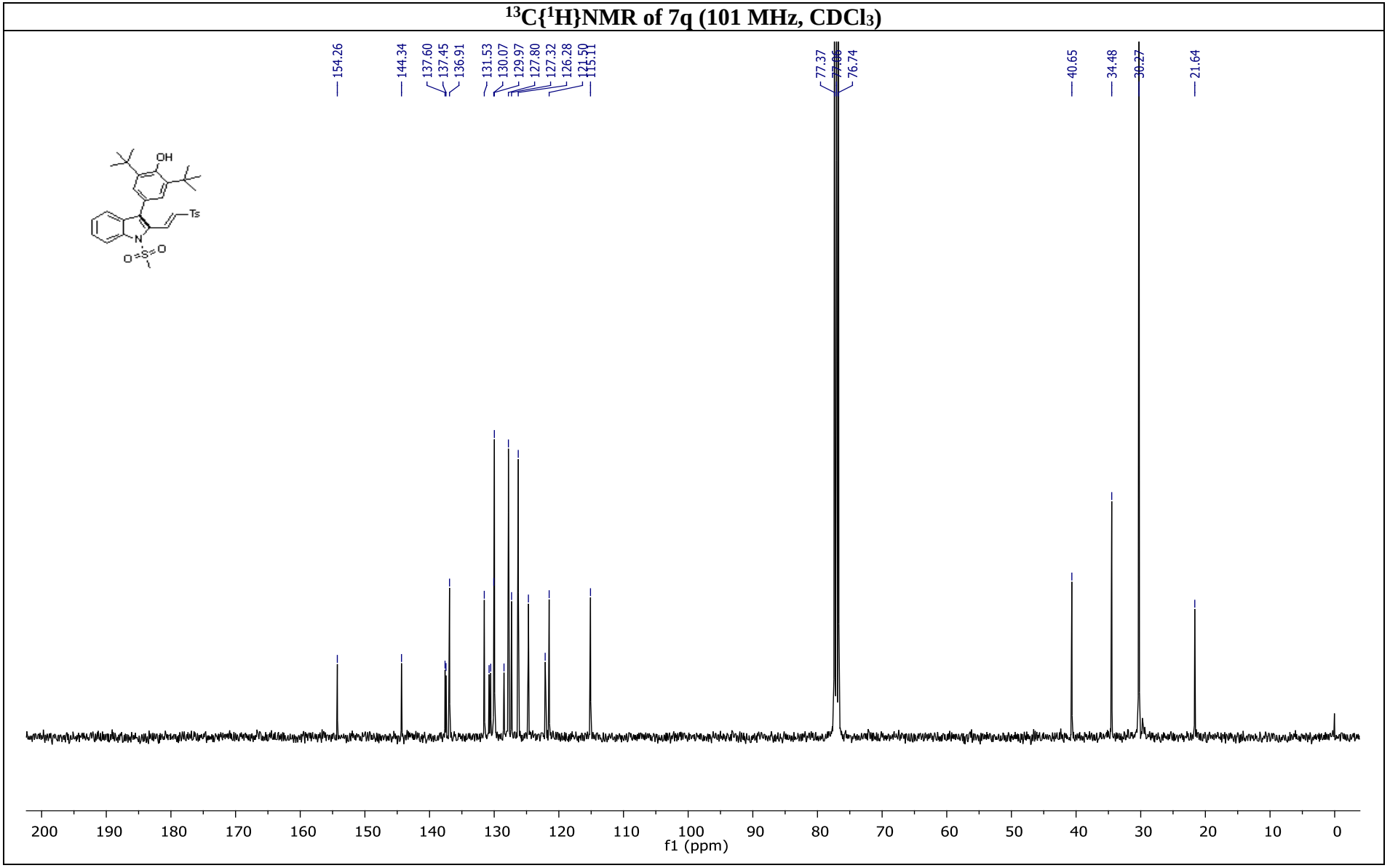
$^{13}C\{^{1}H\}$NMR of 7p (101 MHz, $CDCl_3$)



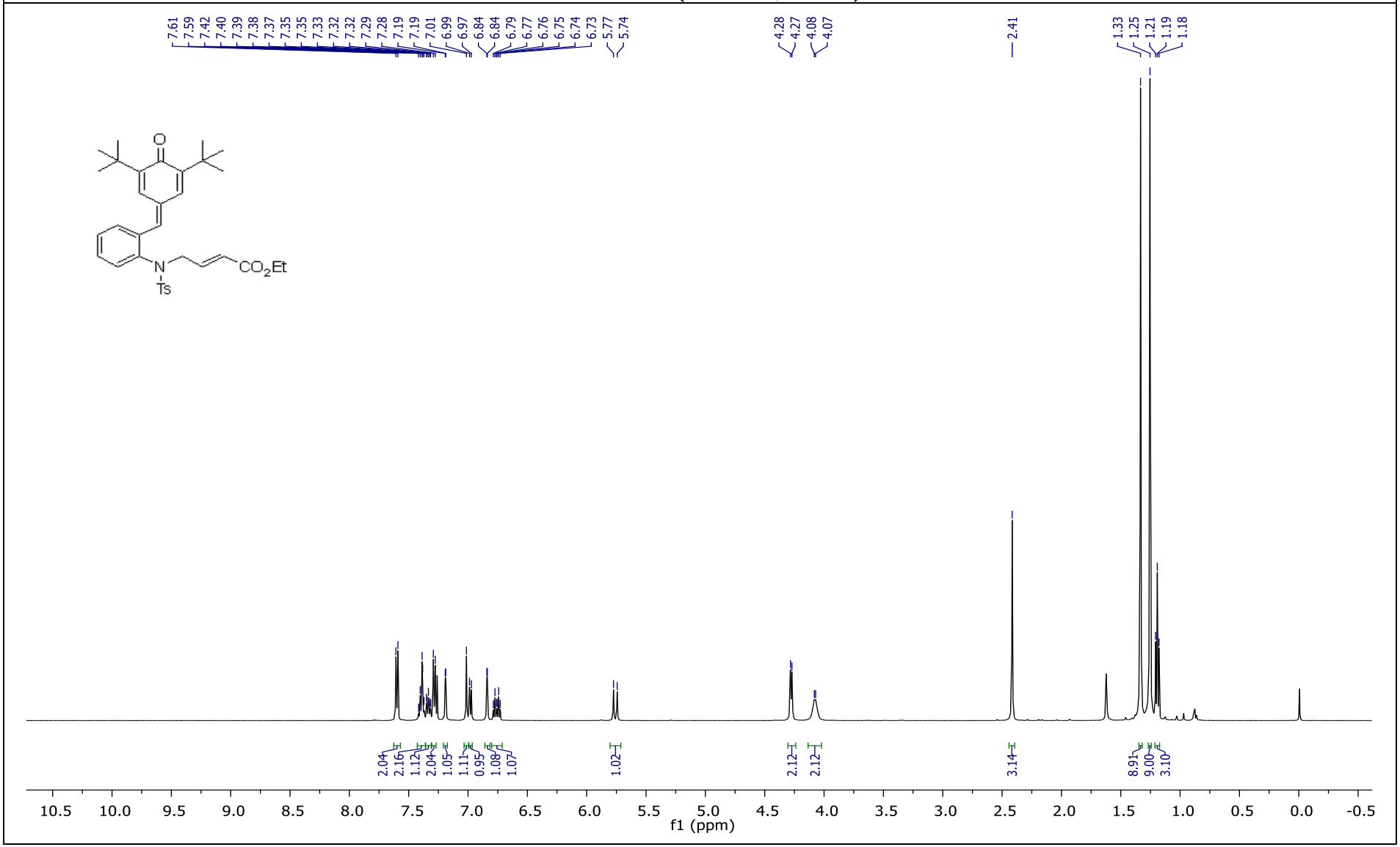
^{1}H-NMR of 7q (500 MHz, $CDCl_3$)



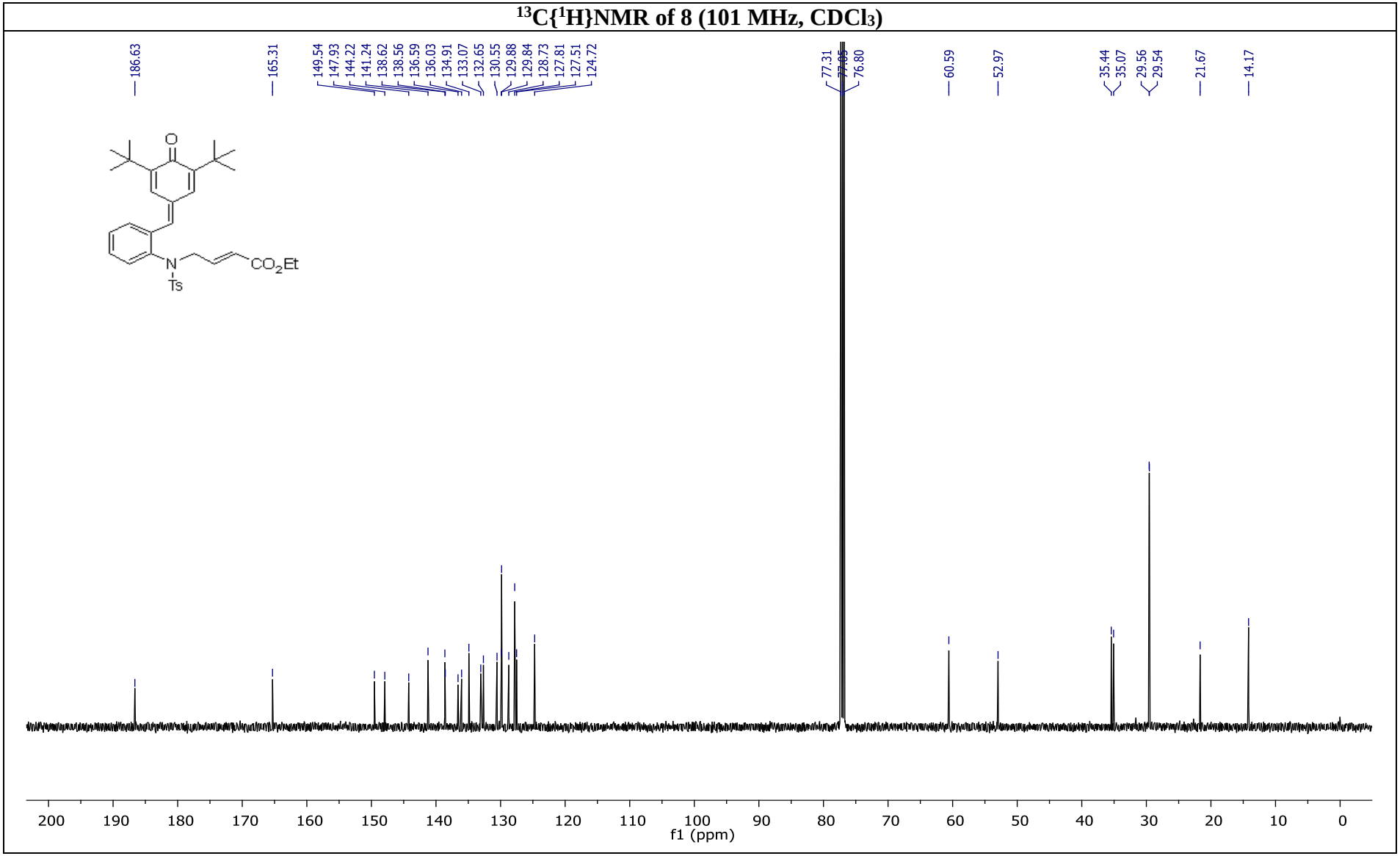
$^{13}C\{^{1}H\}$NMR of 7q (101 MHz, $CDCl_3$)



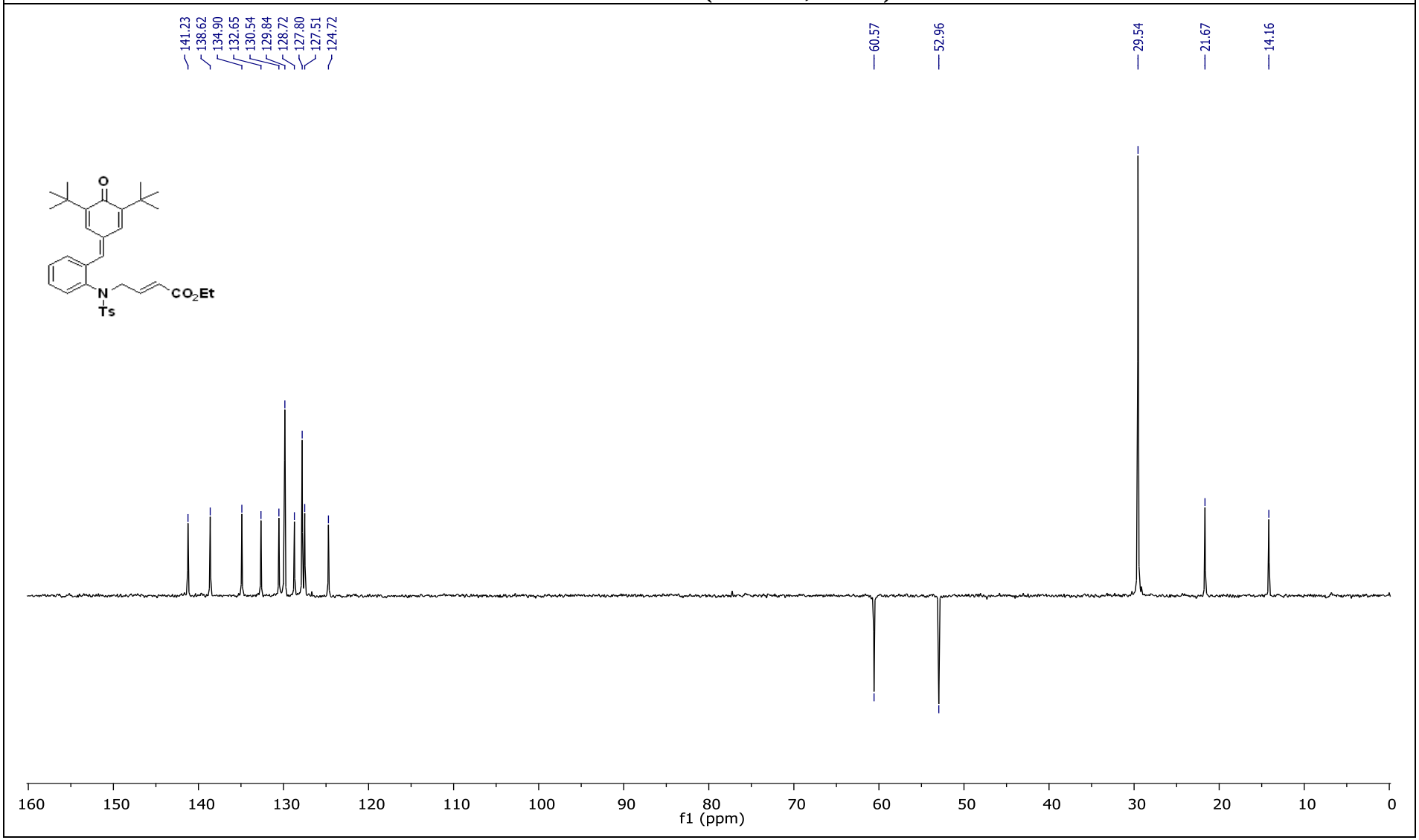
^{1}H-NMR of 8 (400 MHz, $CDCl_3$)



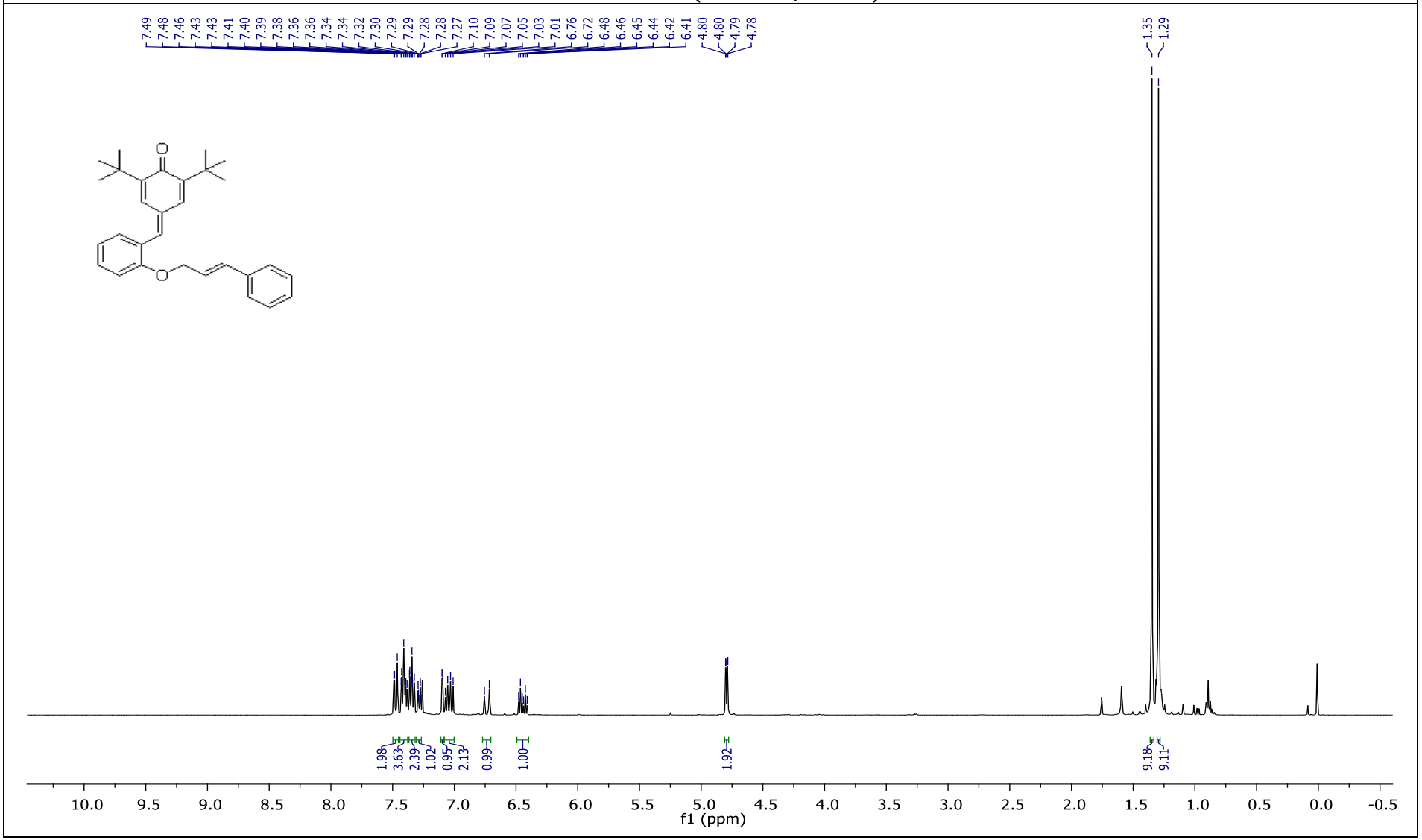
$^{13}C\{^{1}H\}$NMR of 8 (101 MHz, $CDCl_3$)



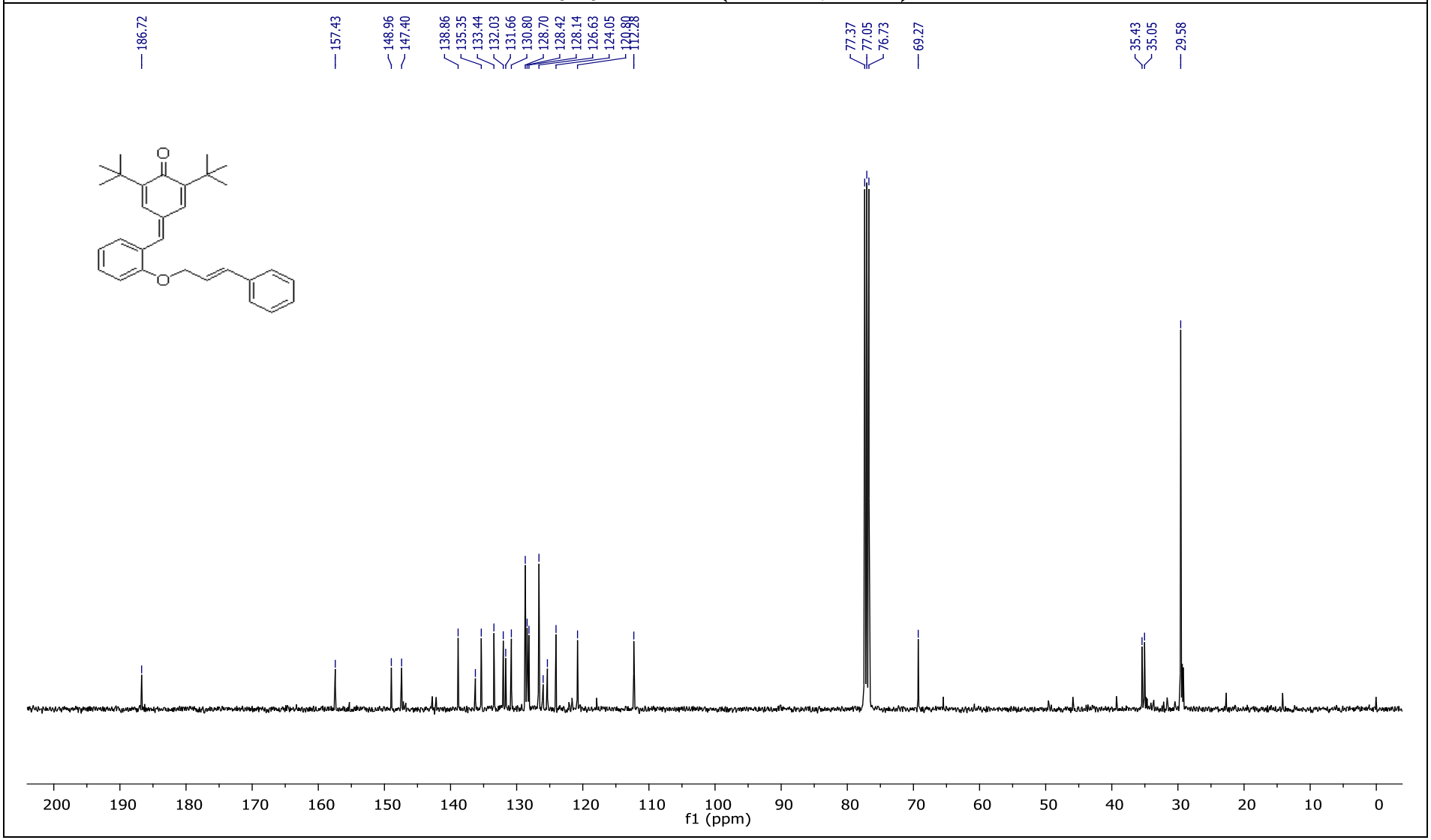
DEPT-NMR of 8 (135 MHz, $CDCl_3$)



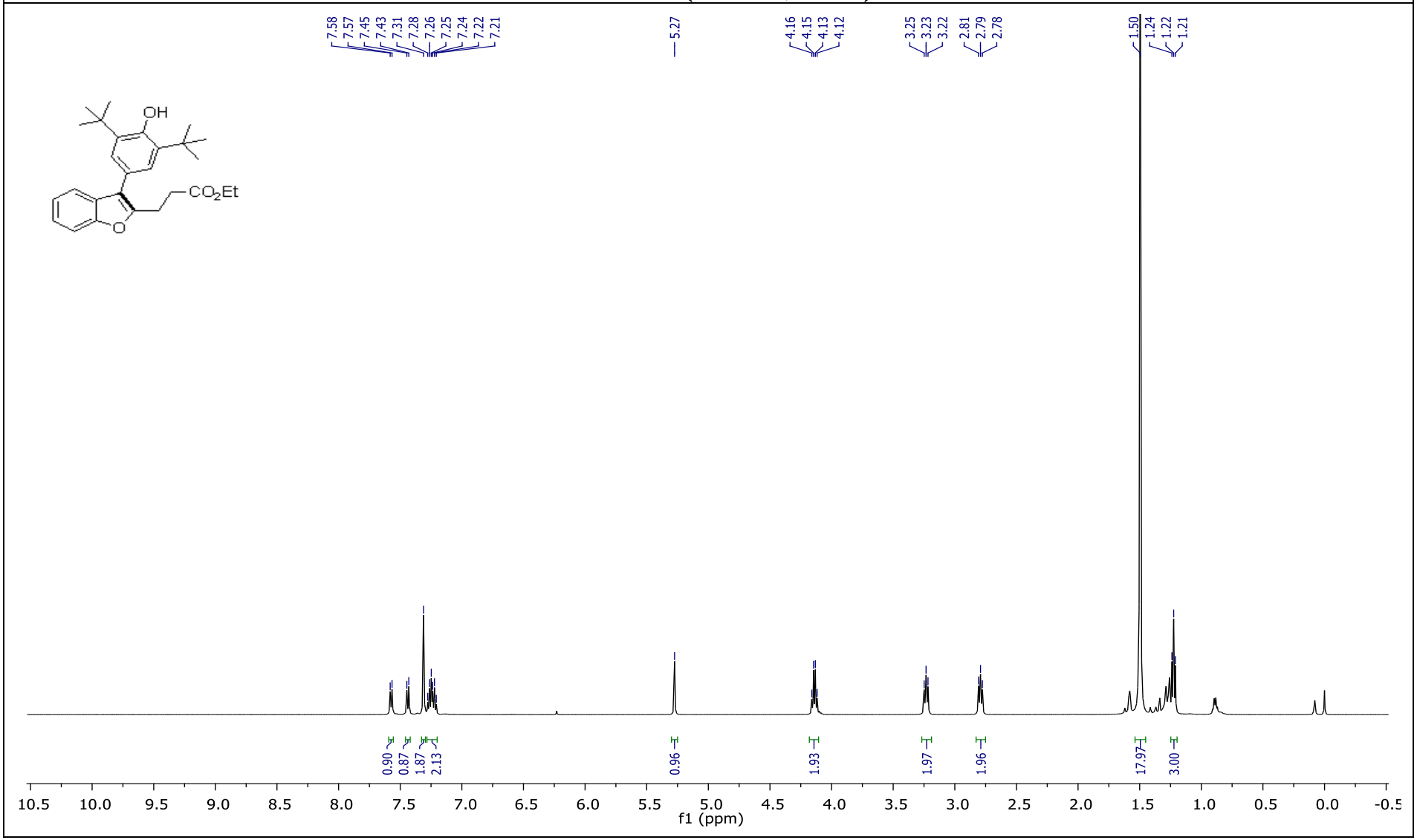
^{1}H-NMR of 12 (400 MHz, $CDCl_3$)



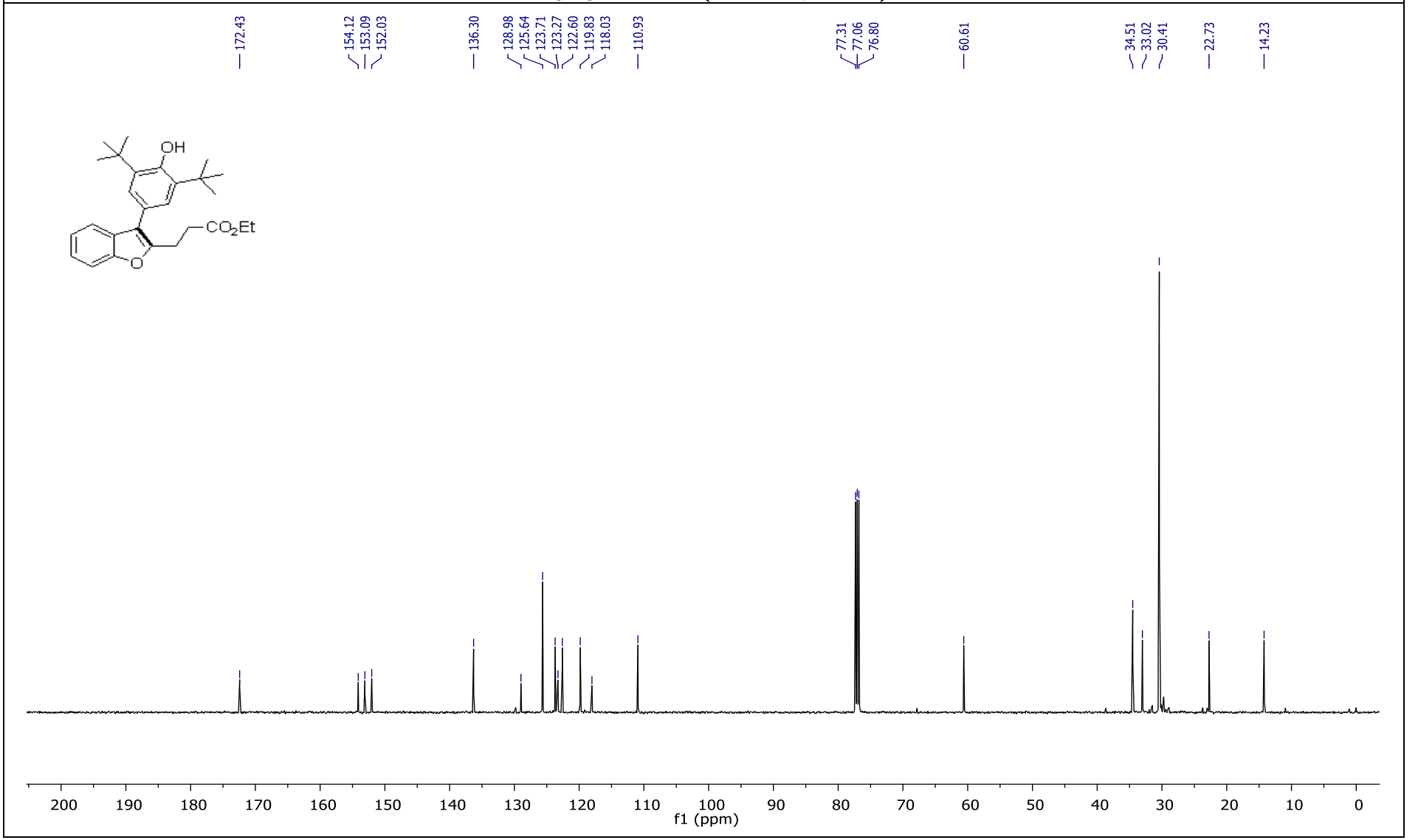
$^{13}C\{^{1}H\}$NMR of 12 (101 MHz, $CDCl_3$)



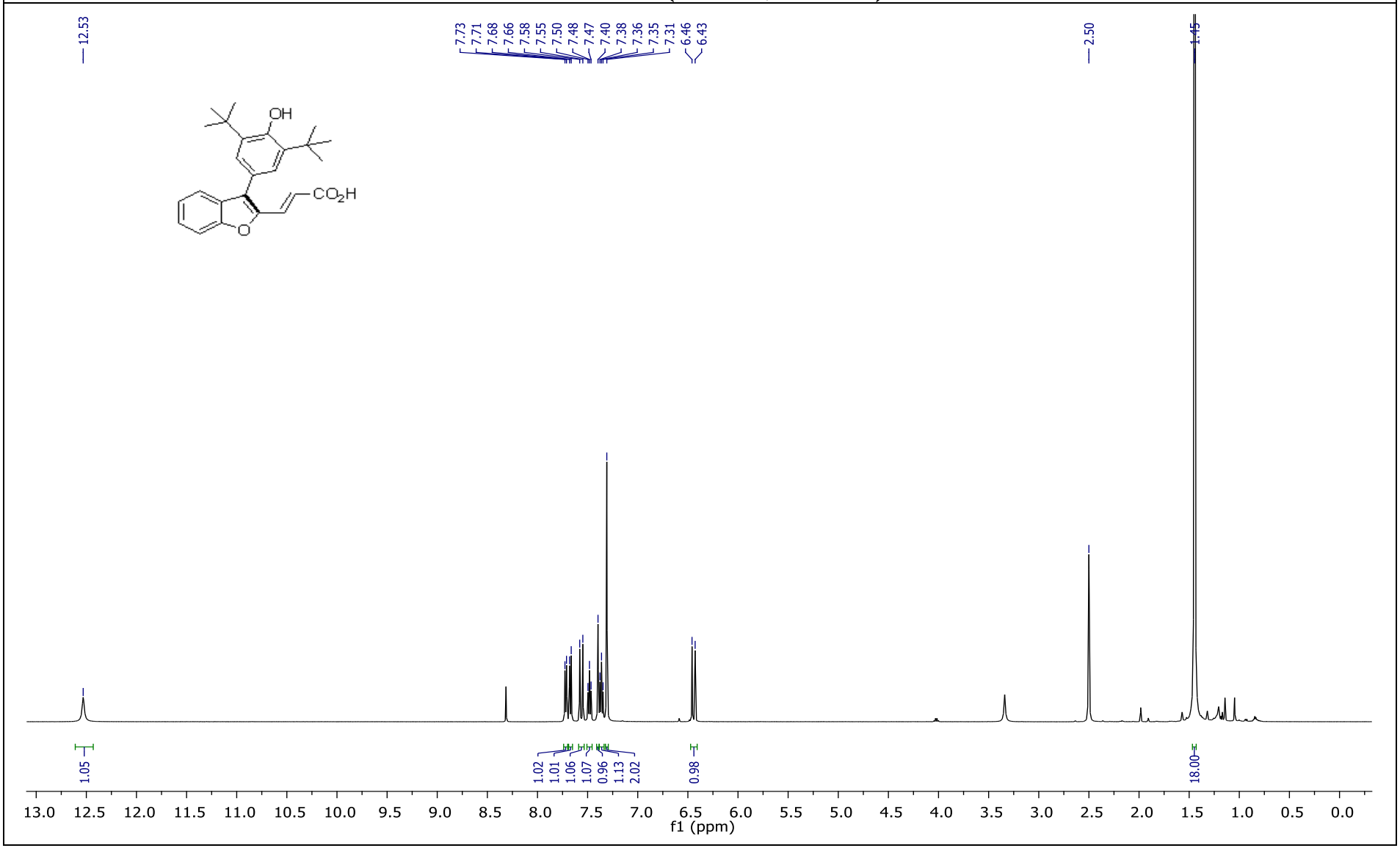
^{1}H-NMR of 9 (500 MHz, $CDCl_3$)



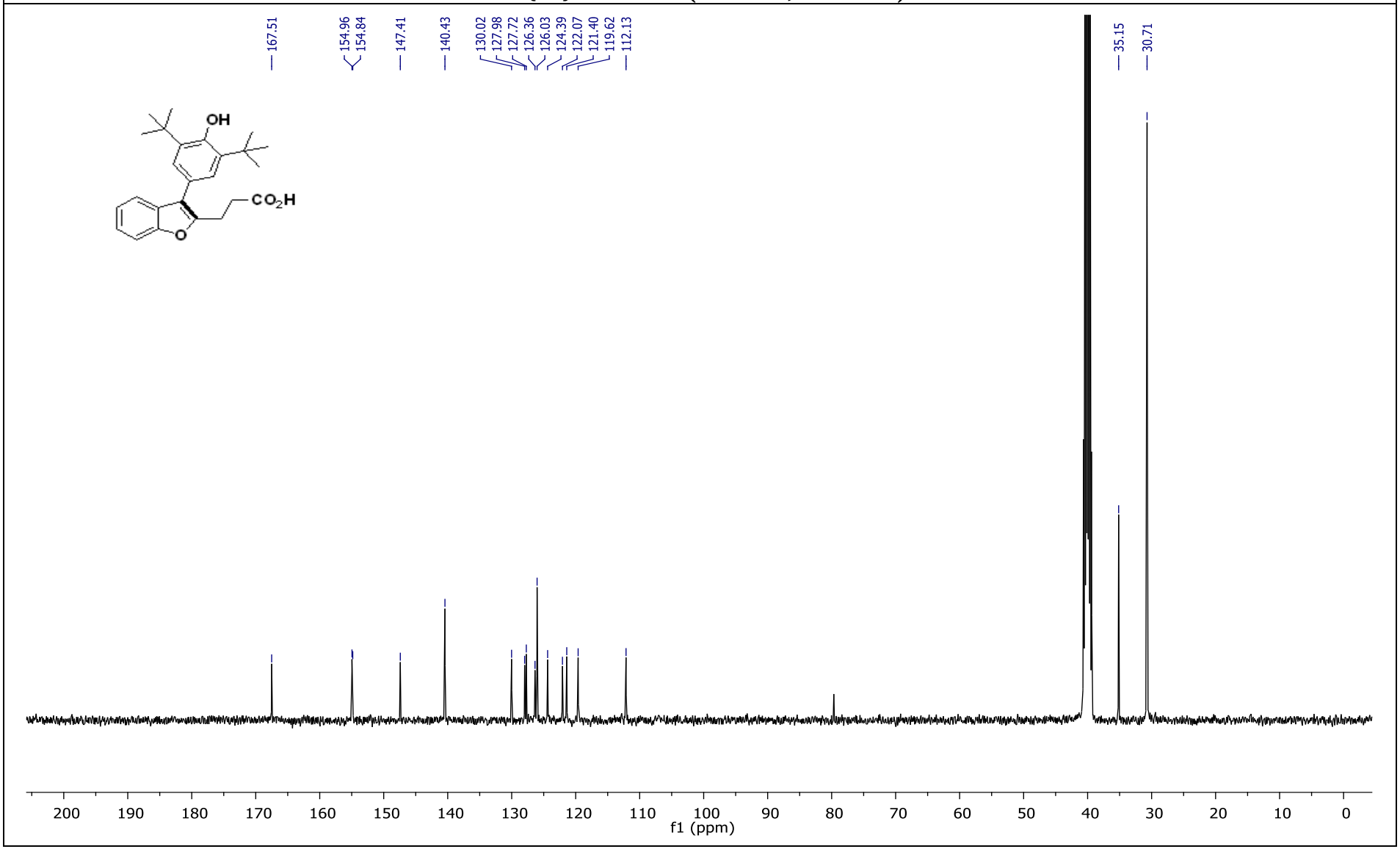
$^{13}C\{^{1}H\}$NMR of 9 (126 MHz, $CDCl_3$)



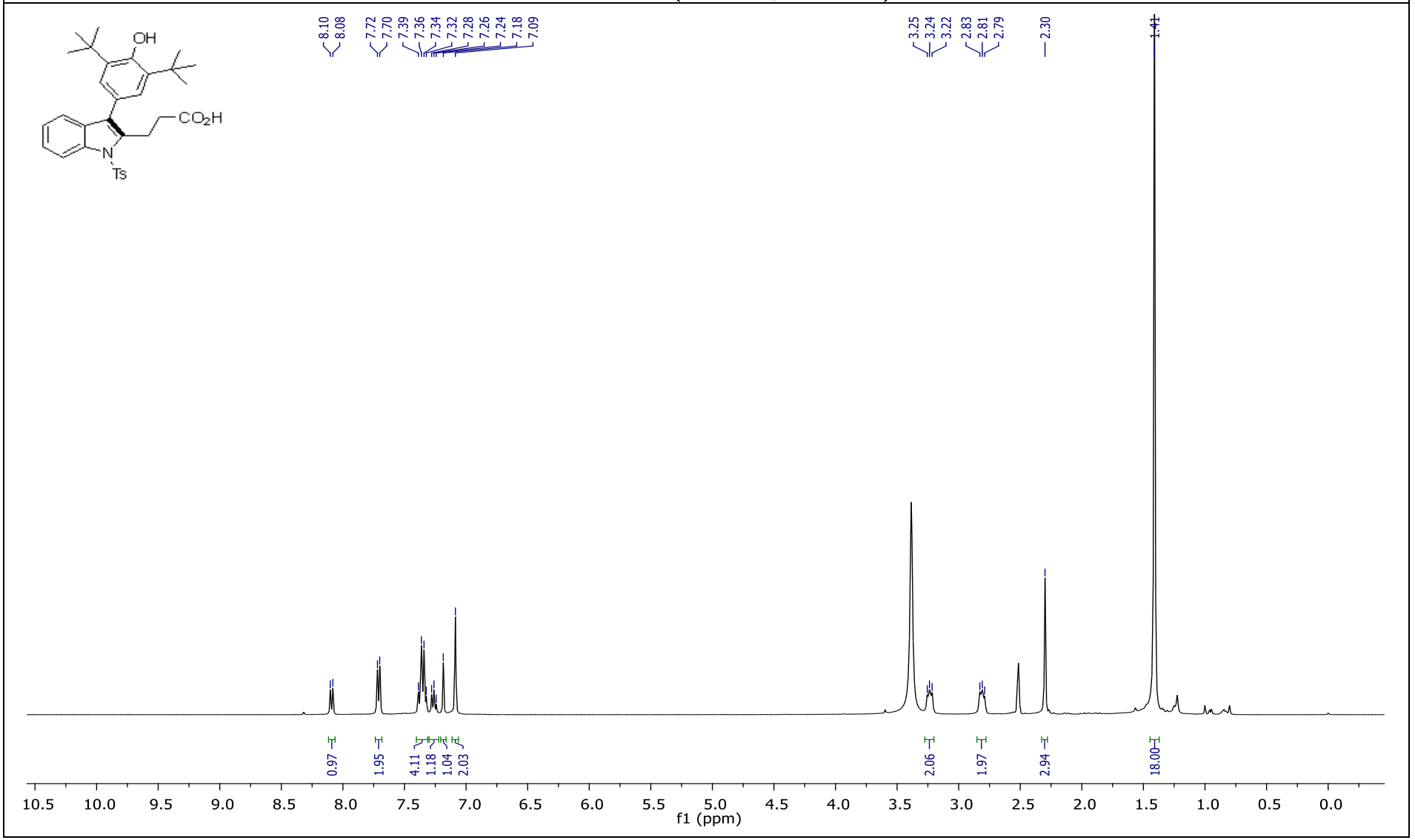
^{1}H-NMR of 10 (500 MHz, DMSO d_6)



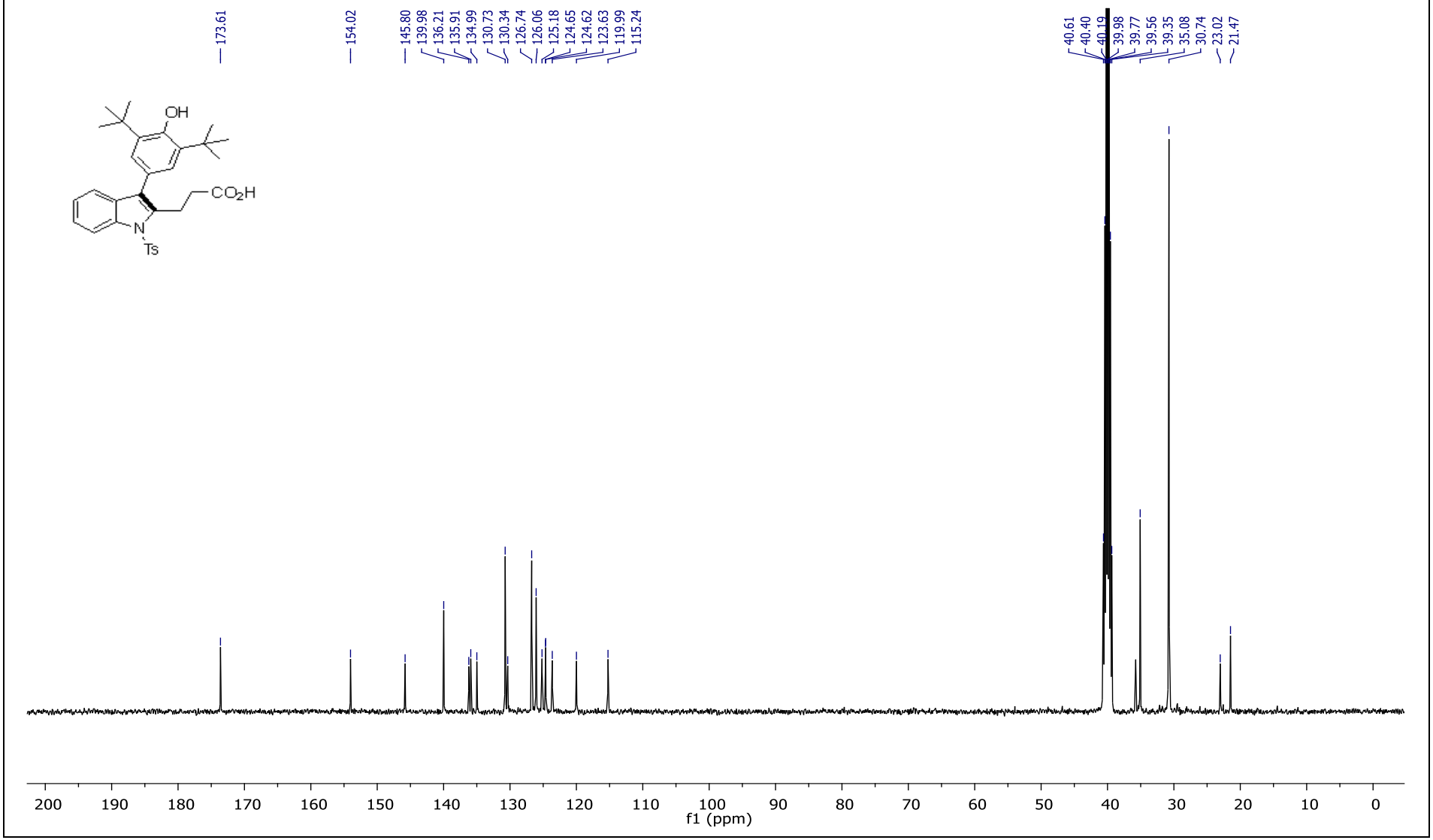
$^{13}C\{^{1}H\}$NMR of 10 (101 MHz, DMSO d_6)



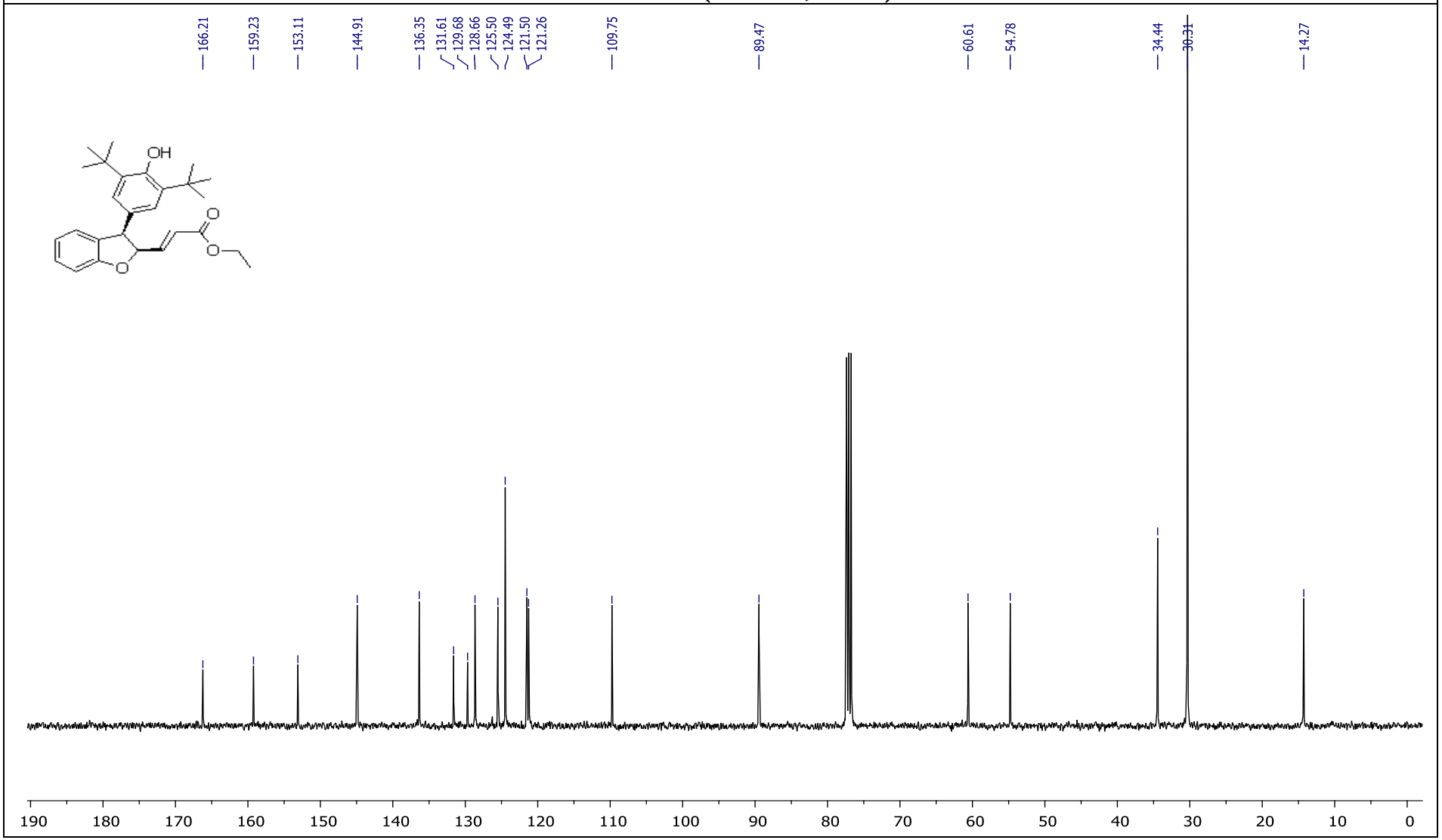
^{1}H-NMR of 11 (400 MHz, DMSO d_6)



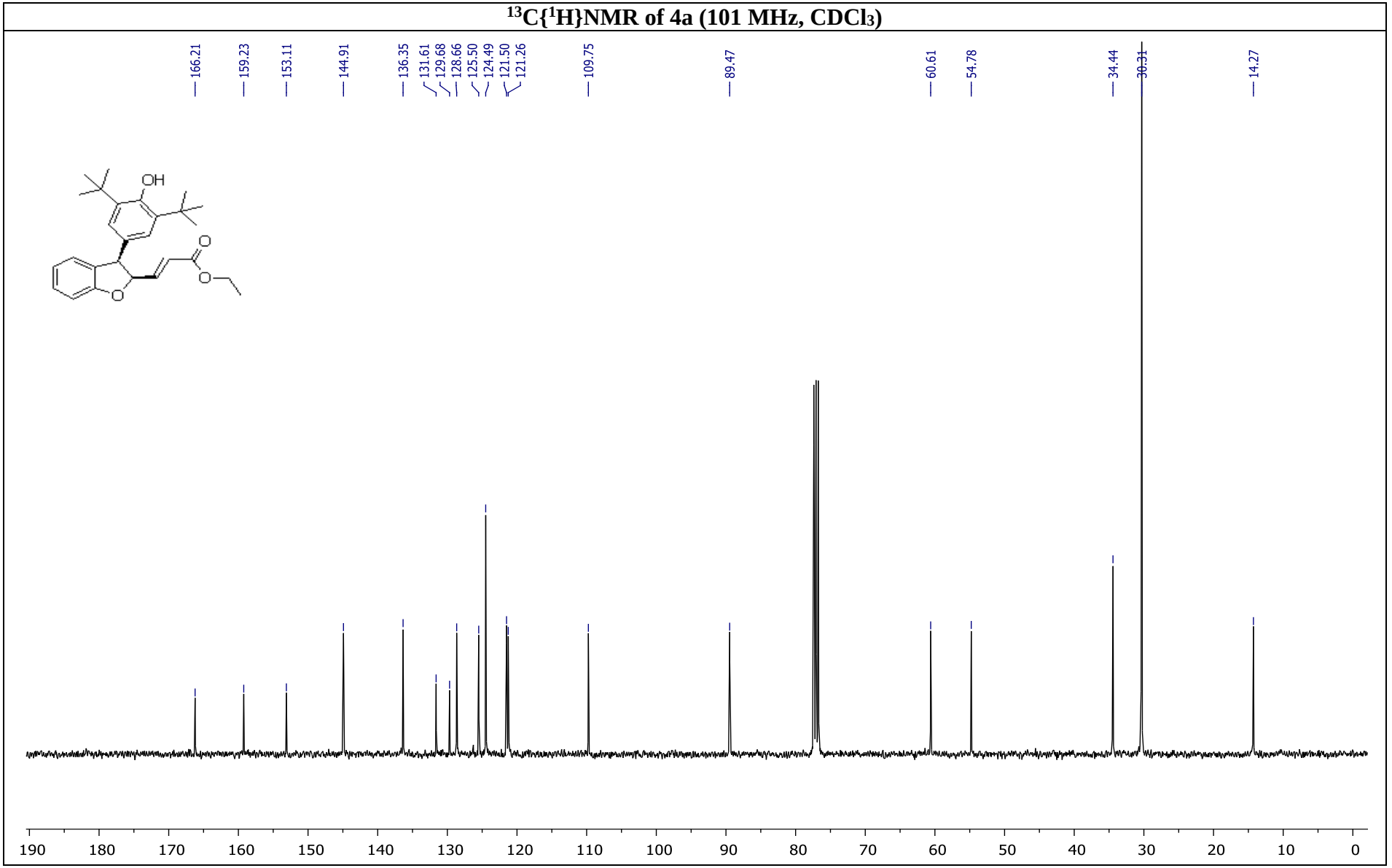
$^{13}C\{^{1}H\}$NMR of 11 (101 MHz, DMSO d_6)



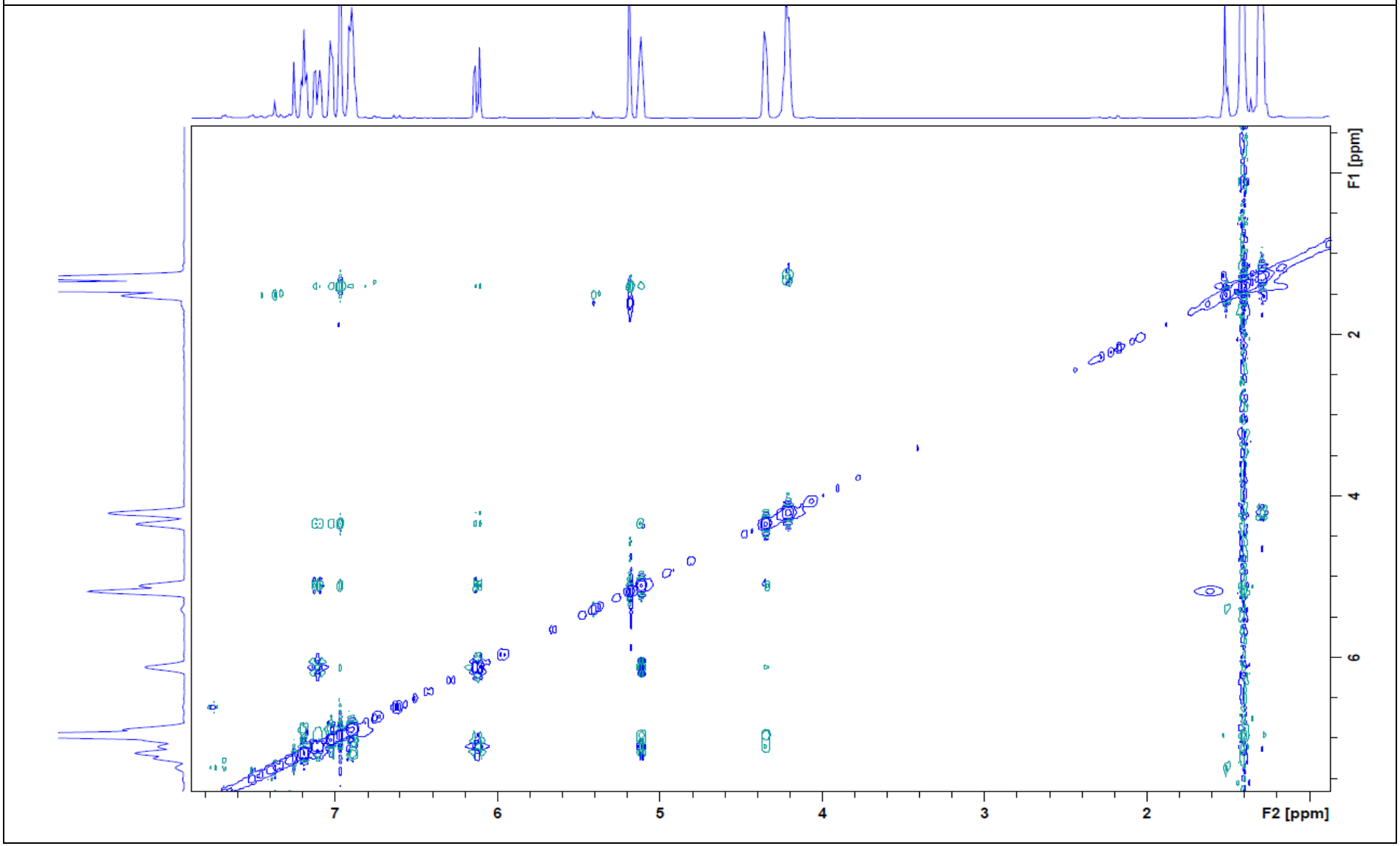
^{1}H-NMR of 4a (400 MHz, $CDCl_3$)



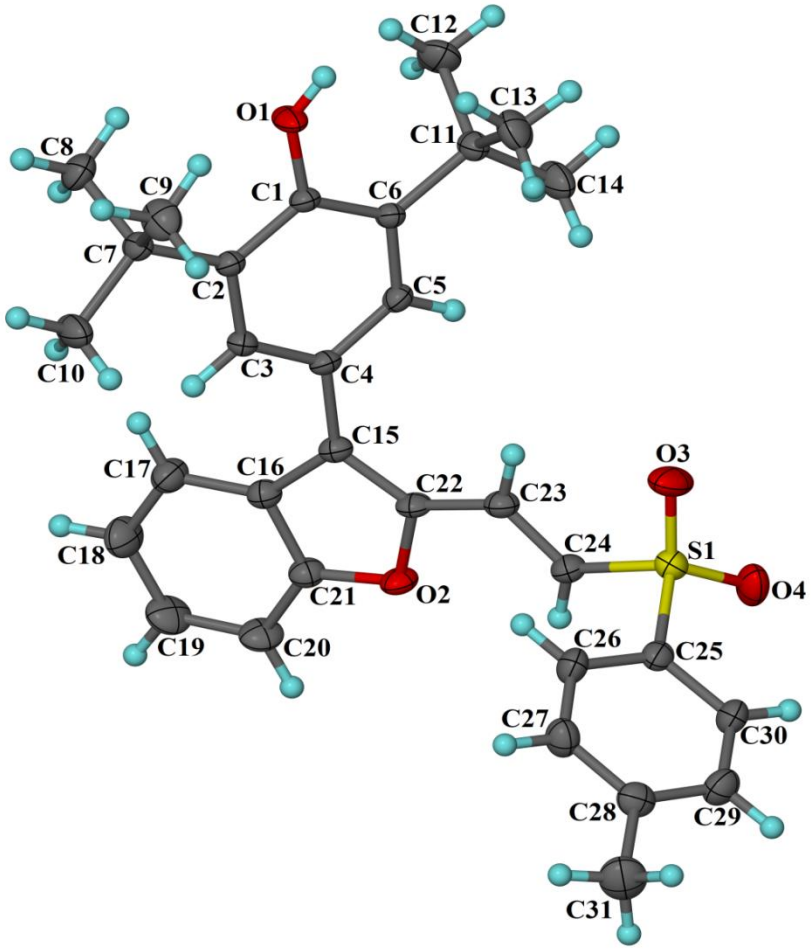
$^{13}C\{^{1}H\}$NMR of 4a (101 MHz, $CDCl_3$)



NOE-NMR of 4a



8. Crystallographic data for compounds 5i and 7m

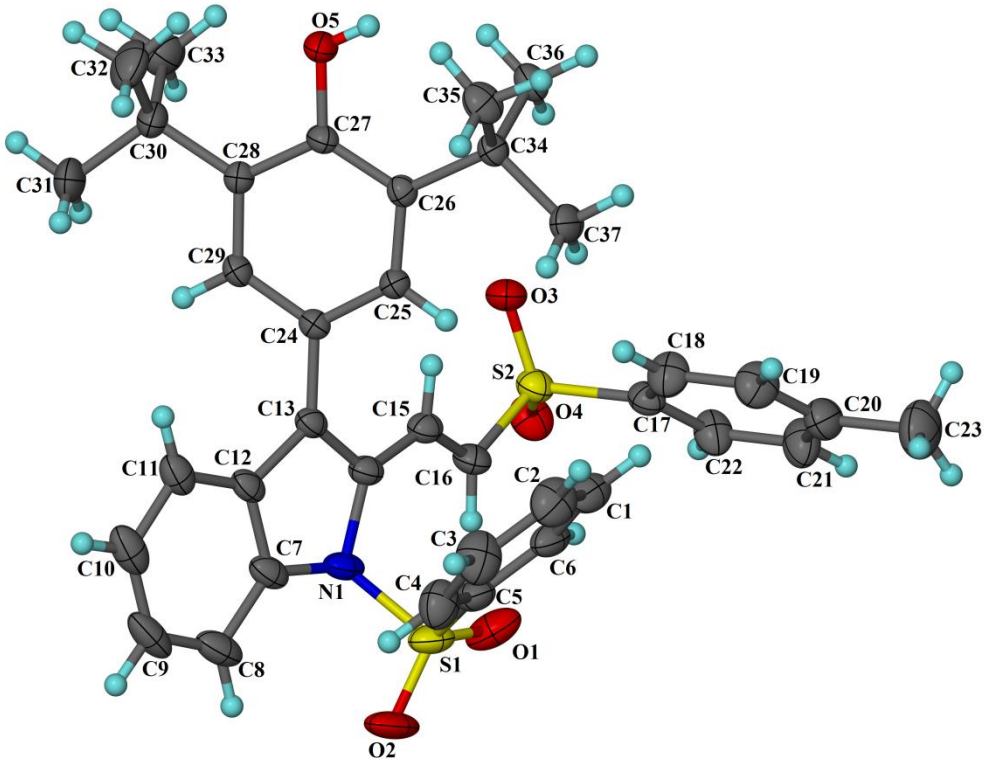


Compound 5i

Figure caption: ORTEP diagram of **5i** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius.

Crystal data for 5i: $C_{31}H_{34}O_4S+$ Solvent, M = 502.64, Monoclinic, space group $P2_1/c$ (No.14), a =17.6839(9)Å, b =11.2101(6)Å, c = 15.0773(7)Å, α = 90°, β = 106.593(2)°, γ = 90°, V = 2864.4(3)Å^3, Z = 4, D_c = 1.166 g/cm^3, F_{000} = 1072, Bruker D8 QUEST PHOTON-100, Mo-Kα radiation, λ = 0.71073 Å, T = 293(2)K, $2\theta_{max}$ = 55º, μ= 0.145 mm^{-1}, 55165 reflections collected, 6585 unique (R_{int} = 0.1018), 335 parameters, *R1* = 0.0571, *wR2* =0.1314, *R* indices based on 3360 reflections with I > 2σ(I) (refinement on F^2), Final *GooF* = 1.022, largest difference hole and peak = -0.4212 and 0.227 e.Å^{-3}. The **CCDC deposition number 2182173** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Data collection and Structure solution details for 5i: Single crystal X-ray data were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer and Photon 100 detector. An Iμs microfocus Mo source (λ=0.71073Å) supplied the multi-mirror monochromated incident beam. A combination of Phi and Omega scans were used to collect the necessary data. Integration and scaling of intensity data were accomplished using SAINT program.[6] The structures were solved by Direct Methods using SHELXS97[7] and refinement was carried out by full-matrix least-squares technique using SHELXL-2014/7.[7,8] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The compound crystallized with the solvent of crystallization dichloromethane; however, the solvent structure could not be resolved. Hence, the contributions of the solvent molecules were removed from the diffraction data using the SQUEEZE option in PLATON. The SQUEEZE estimated 83 electron counts in the voids of 257Å.[8] The files (.hkl and .ins) generated by PLATON after the SQUEEZE treatment were used for the final refinement of structure.[9] The **CCDC deposition number 2182173** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/



Compound 7m

Figure caption: ORTEP diagram of **7m** compound with the atom-numbering. Displacement ellipsoids are drawn at the 35% probability level and H atoms are shown as small spheres of arbitrary radius. The phenyl ring (C1-C6 atoms) is disordered over two sites and only major component of the disordered atoms are shown in ORTEP picture for clarity.

Crystal data for 7m: $C_{37}H_{39}NO_5S_2$, M = 641.81, Monoclinic, Space group $P2_1/c$(No.14), a =10.294(2)Å, b =19.579(4)Å, c = 17.114(3)Å, α = 90°, β = 99.109(8)°, γ = 90°, V = 3405.9(11)Å^3, Z = 4, D_c = 1.252 g/cm^3, F_{000} = 1360, Bruker D8 QUEST PHOTON III C7 HPAD detector, Mo-Kα radiation, λ = 0.71073 Å, T = 294(2)K, $2\theta_{max}$ = 50º, μ = 0.199 mm^{-1}, 37337 reflections collected, 7766 unique (R_{int} = 0.0710), 436 parameters, *R1* = 0.0523, *wR2* =0.1050, *R* indices based on 4068 reflections with I > 2σ(I) (refinement on F^2), Final *GooF* = 0.994, largest difference hole and peak = -0.293 and 0.185 e.Å^{-3}. **CCDC deposition number 2252885** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Data collection and Structure solution details for 7m: X-ray data for the compound were collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 Å) and a PHOTON-III C7 HPAD detector. The raw data frames were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [10]. The structure was solved using intrinsic phasing method [11] and further refined with the SHELXL [11-13] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. All C bound H atoms were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and Uiso(H) = 1.5Ueq(C) for methyl H or 1.2Ueq(C) for other H atoms]. The phenyl ring carbon atoms were disordered over two sites, with site occupancy factor of 0.53(2) for the major component of the disordered atoms (C1/C2/C3/C4/C5/C6) and 0.47(2) for the minor component of the disordered atoms (C1D/C2D/C3D/C4D/C5D/C6D). PART, FVAR, DELU, and SIMU instructions were utilized for modelling the structural disorder and structural refinement. **CCDC deposition number 2252885** contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

9. References

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