Supporting Information

Diastereoselective Synthesis of Fused Oxazolidines and Highly Substituted 1*H*-pyrrolo[2,1-*c*][1,4]oxazines via C–H functionalization

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General Information: Aldehydes, benzoic acid, 1,2,3,4-tertahydro- isoquinoline and trypoline were purchased from commercial sources and used as received. Amines were purchased from commercial sources unless otherwise stated and distilled prior to use. 3Å powdered molecular sieves were purchased from sigma aldrich and were activated before use by heating in a furnace to 300 ºC for 2 h and were stored in a desiccator. Reagent grade toluene was purchased from Sigma-Aldrich and distilled over sodium. Purification of reaction products was carried out by flash column chromatography using Sorbent Technologies Standard Grade silica gel (60 Å, 230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F254 plates. Visualization was accomplished with UV light, potassium permanganate and DragendorffMunier stains followed by heating. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra (^{1}HNMR) were recorded on Agilent-400 MHz and are reported in ppm using chloroform as the internal standard (7.24 ppm). Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = complex, br = broad; and coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (^{13}C-NMR) were recorded on a Agilent-400 MHz and are reported in ppm using chloroform as the internal standard (77.0 ppm). Mass spectra were recorded on Agilent mass spectrum

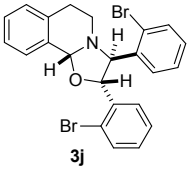
General procedure for the diastereoseletive intermolecular [3 + 2]-cycloaddition of benzylic amines or trypolines or THIQs (Scheme 2): To a solution of aldehyde (1.0 mmol, 2 equiv) in acetonitrile (10 mL) was added 3 Å molecular sieves (200 mg), amine (0.5 mmol, 1equiv) and benzoic acid (0.1 mmol, 0.2 equiv). The mixture was stirred at 50 ^{o}C and progress was monitored by TLC. When the aldehyde could no longer be detected, the reaction mixture was filtered through a plug of celite and rinsed with EtOAc (20 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (3 x 15 mL) and the combined aqueous layers were extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was then removed under reduced pressure and the residue purified by silica gel chromatography.

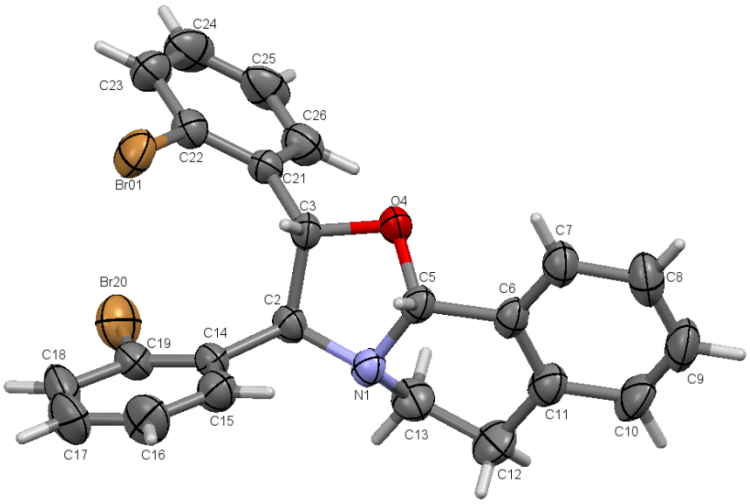
General procedure for the synthesis of substituted isoindoline derivatives (Scheme 3):

To a solution of aldehyde (1.0 mmol, 2 equiv) in acetonitrile (10 mL) was added 3 Å molecular sieves (200 mg), isoindoline (0.5 mmol, 1 equiv) and benzoic acid (0.1 mmol, 0.2 equiv). The mixture was stirred at 50 ^{o}C and progress was monitored by TLC. When the aldehyde could no longer be detected, the reaction mixture was filtered through a plug of celite and rinsed with EtOAc (20 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (3 x 15 mL) and the combined aqueous layers were extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was then removed under reduced pressure and the residue purified by silica gel chromatography

General procedure for the synthesis of substituted 1*H*-pyrrolo[2,1-*c*][1,4]oxazines (scheme 4): To a solution of aldehyde (2.0 mmol, 4 equiv) in acetonitrile (10 mL) was added 3Å molecular sieves (200 mg), pyrrolidine (0.5 mmol, 1equiv) and benzoic acid (0.1 mmol, 0.2 equiv). The mixture was stirred at reflux and progress was monitored by TLC. When the aldehyde could no longer be detected, the reaction mixture was filtered through a plug of celite and rinsed with EtOAc (20 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (3 x 15 mL) and the combined aqueous layers were extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was then removed under reduced pressure and the residue purified by silica gel chromatography

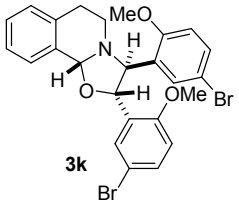
Crystals of **3j** were obtained from hexane/dichloromethane through slow diffusion at room temperature. The relative stereochemistry was assigned by X-ray crystallography.

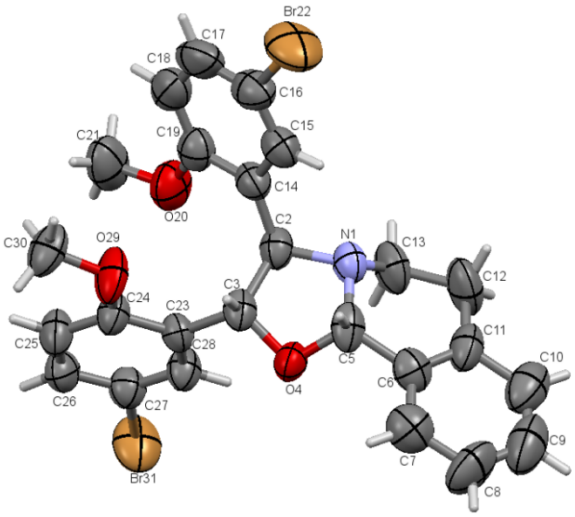




The requisite CIF was submitted to the journal and deposited with the CCDC (deposition # **1061480**)

Crystals of **3k** were obtained from hexane/dichloromethane through slow diffusion at room temperature. The relative stereochemistry was assigned by X-ray crystallography.





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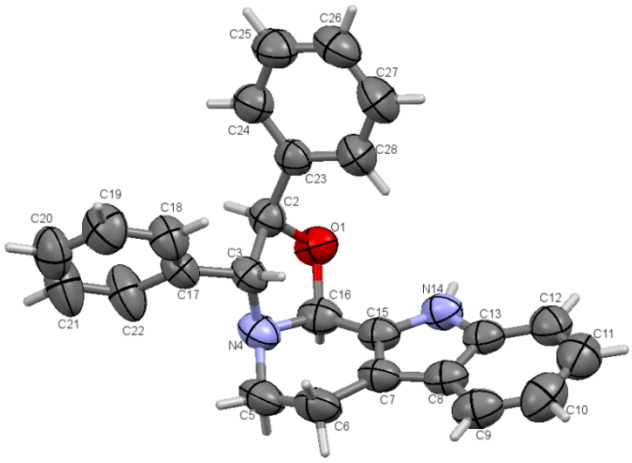
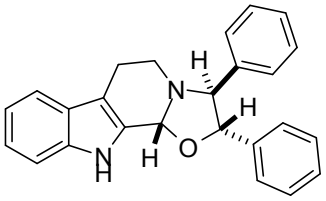
Crystals of **3o** were obtained from hexane/dichloromethane through slow diffusion at room temperature. The relative stereochemistry was assigned by X-ray crystallography.

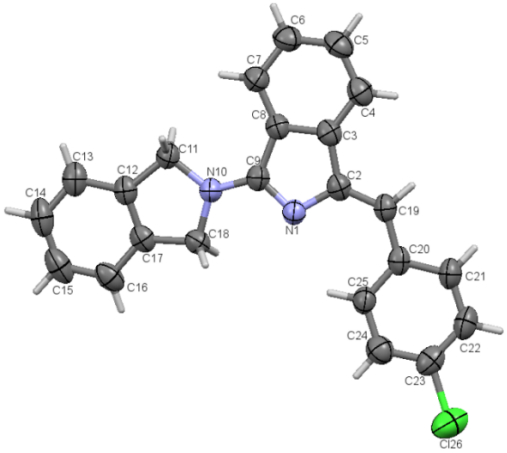


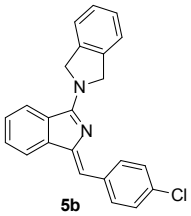


3o

The requisite CIF was submitted to the journal and deposited with the CCDC (deposition # **1061458**)

Crystals of **5b** were obtained from hexane/dichloromethane through slow diffusion at room temperature. The relative stereochemistry was assigned by X-ray crystallography.

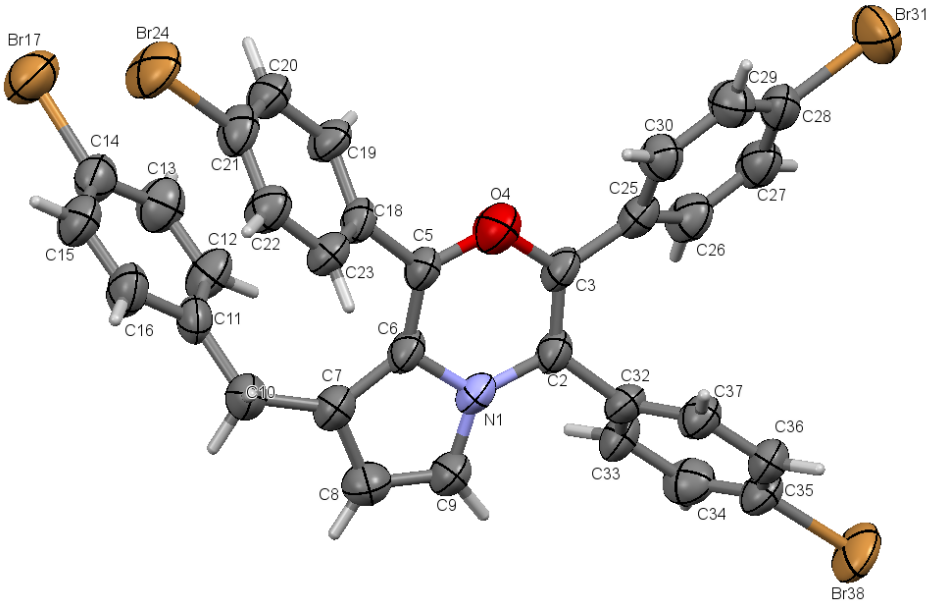




5b

The requisite CIF was submitted to the journal and deposited with the CCDC (deposition # **1061457**)

Crystals of **7a** were obtained from hexane/dichloromethane through slow diffusion at room temperature. The relative stereochemistry was assigned by X-ray crystallography.



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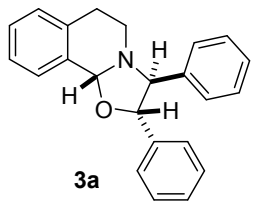
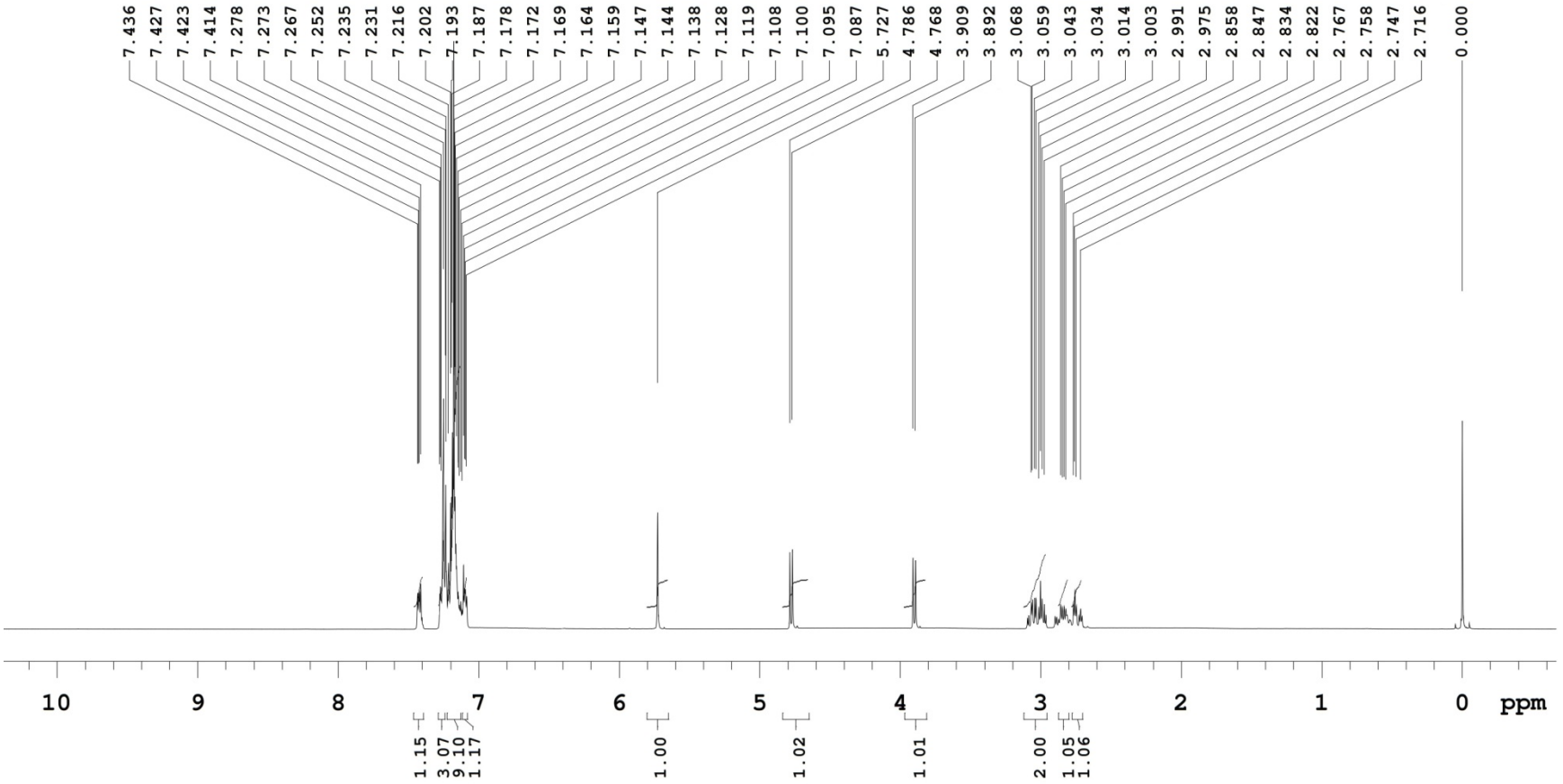
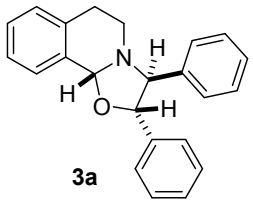
^{1}H NMR of **3a** in $CDCl_3$



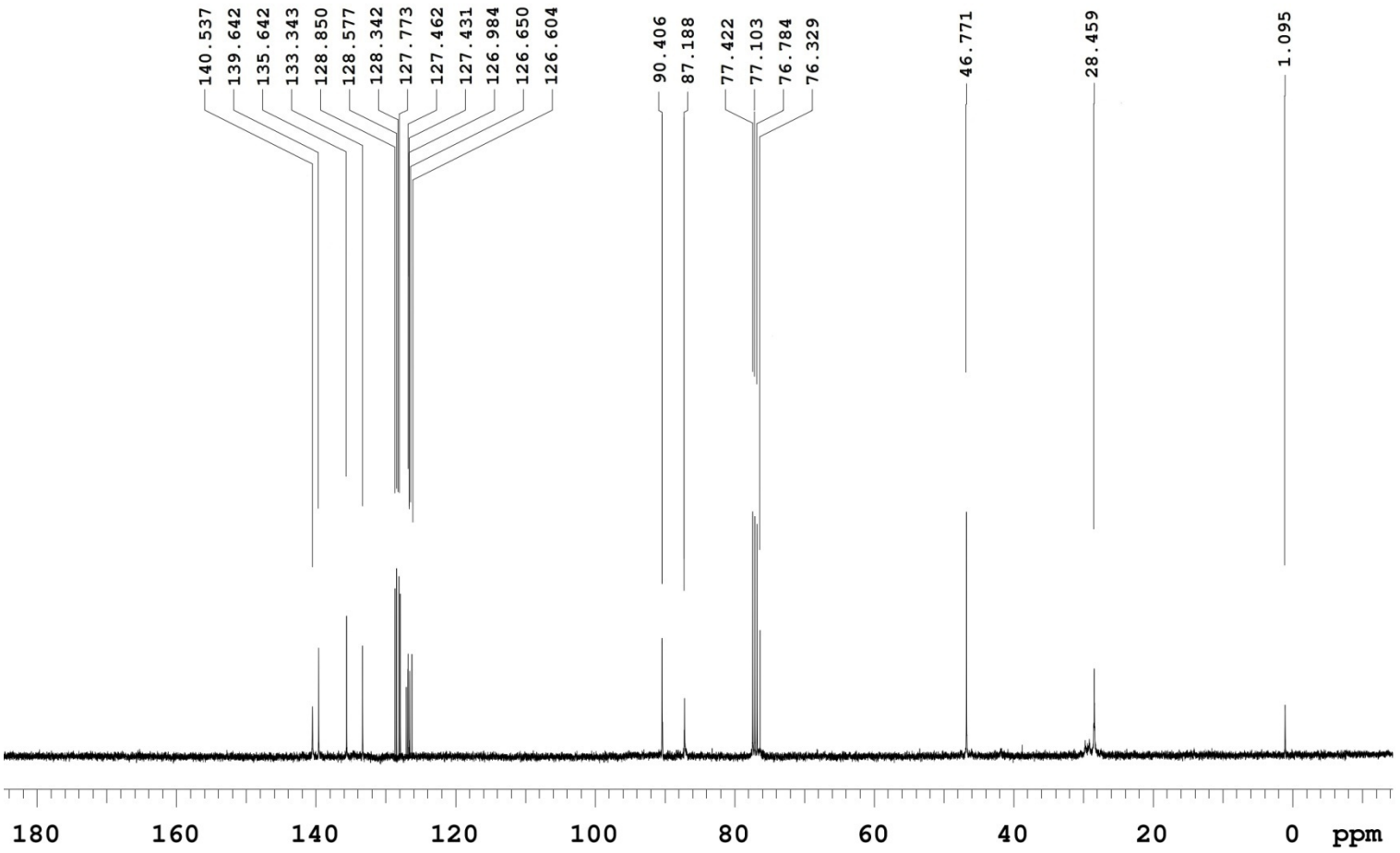
3a



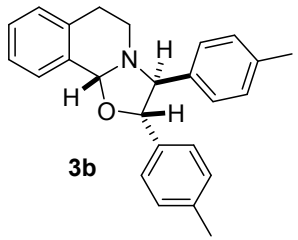
^{13}C NMR of **3a** in $CDCl_3$



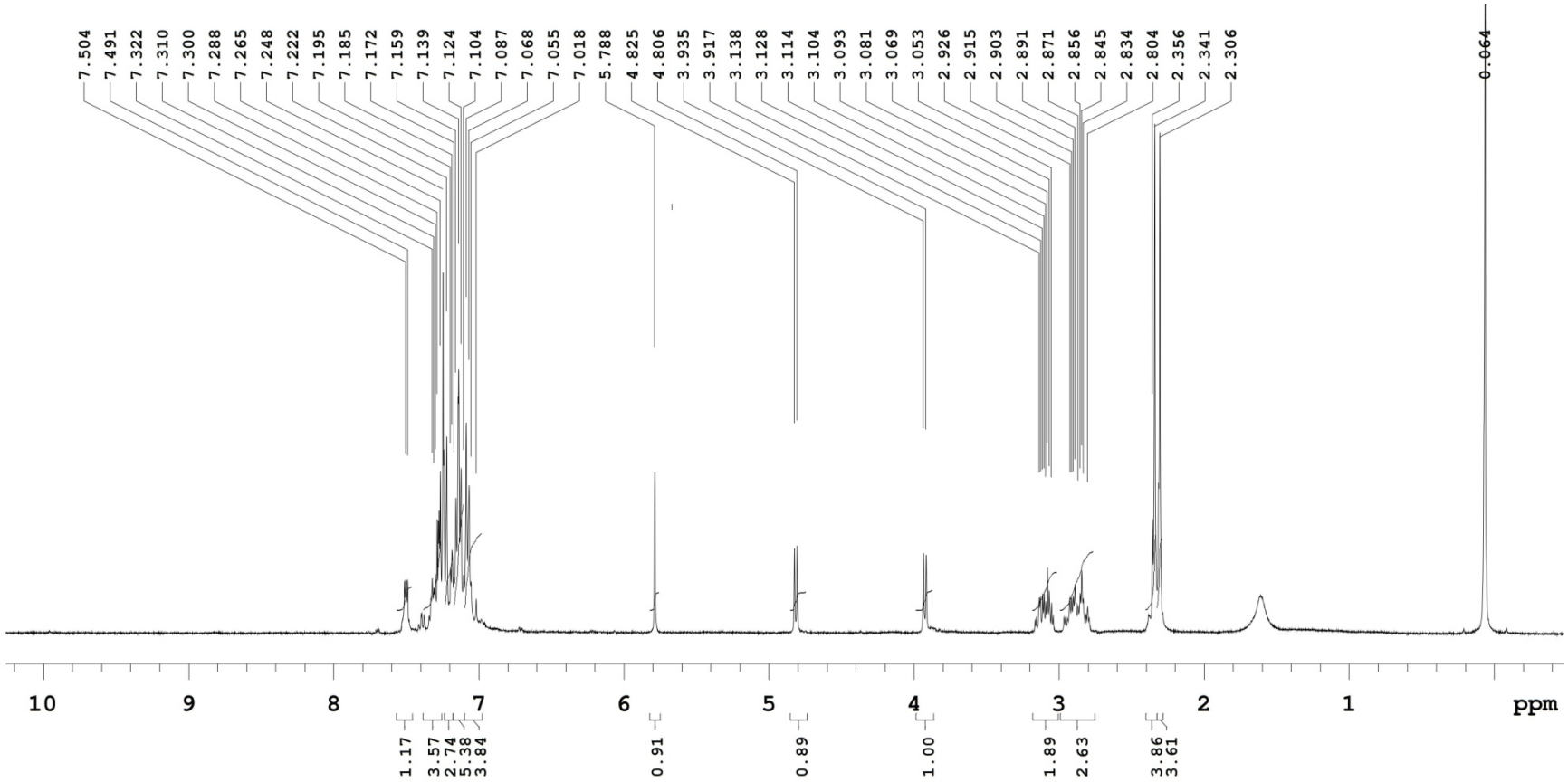
3a

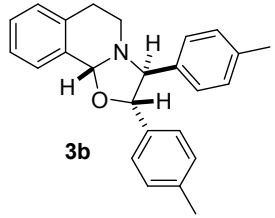


^{1}H NMR of **3b** in $CDCl_3$



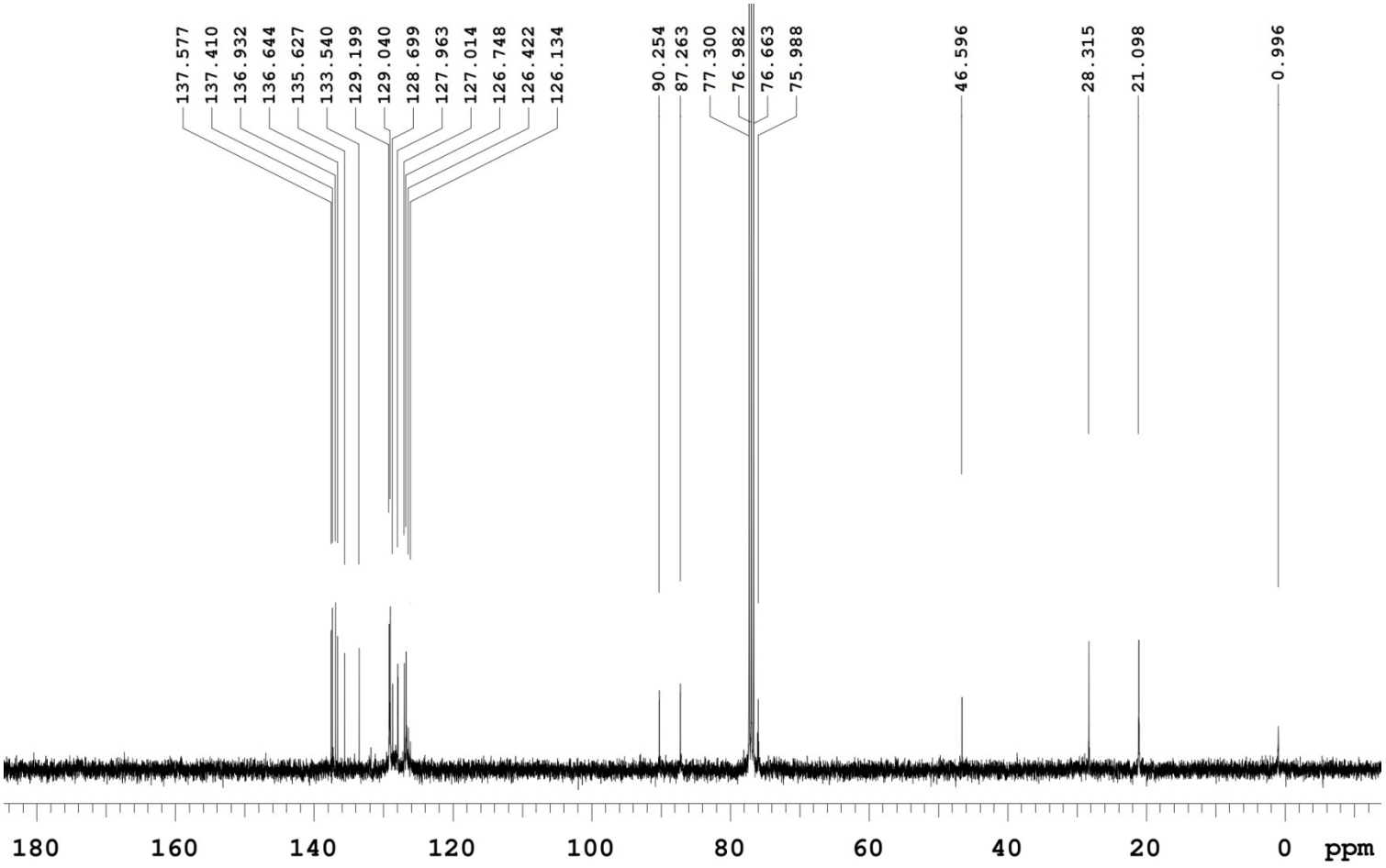
3b

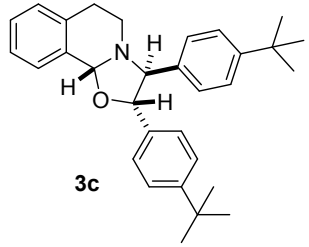




3b

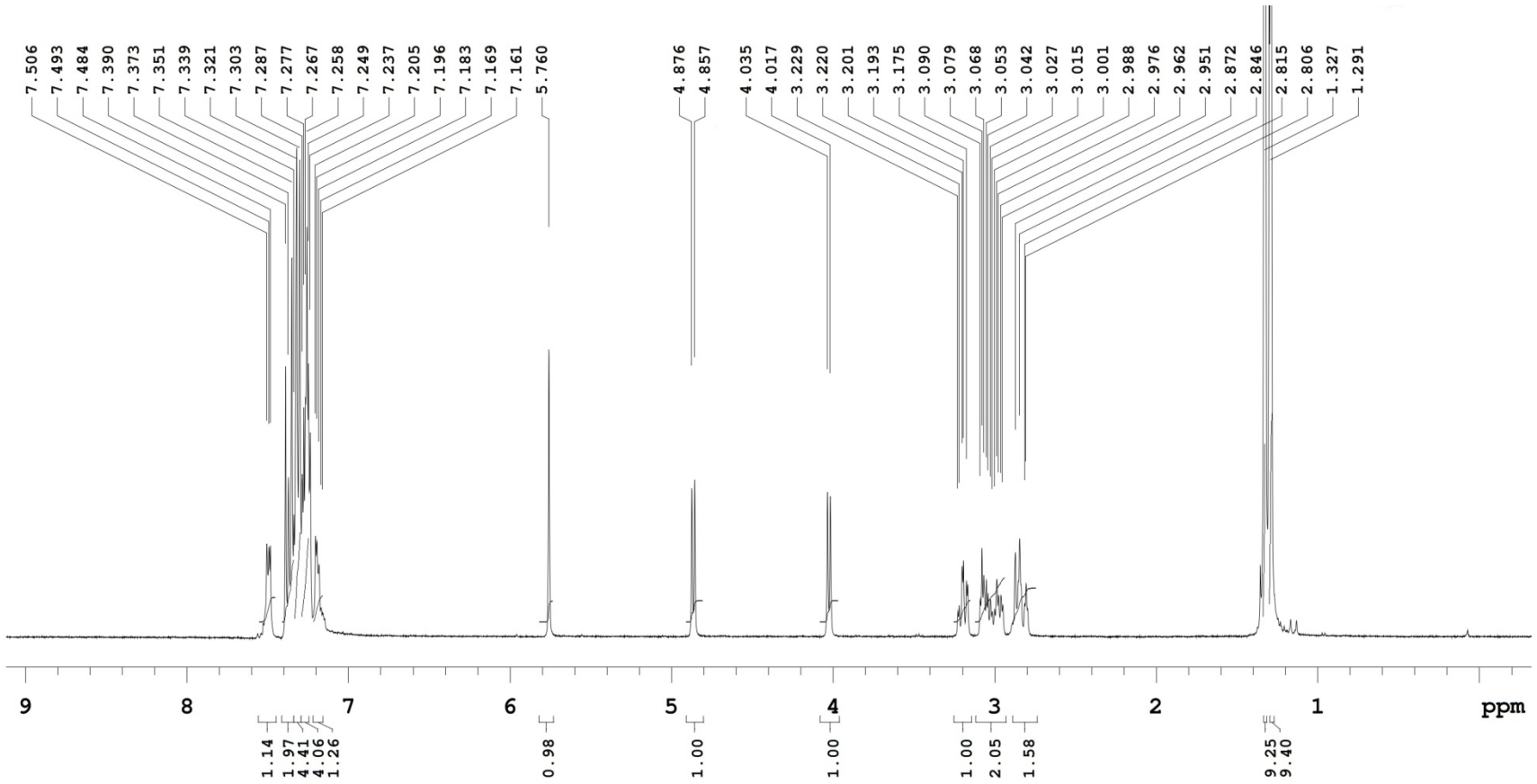
^{13}C NMR of **3b** in $CDCl_3$





3c

^{1}H NMR of **3c** in $CDCl_3$



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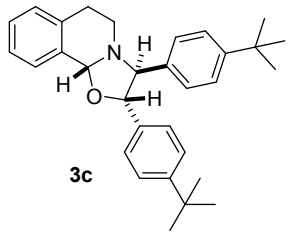
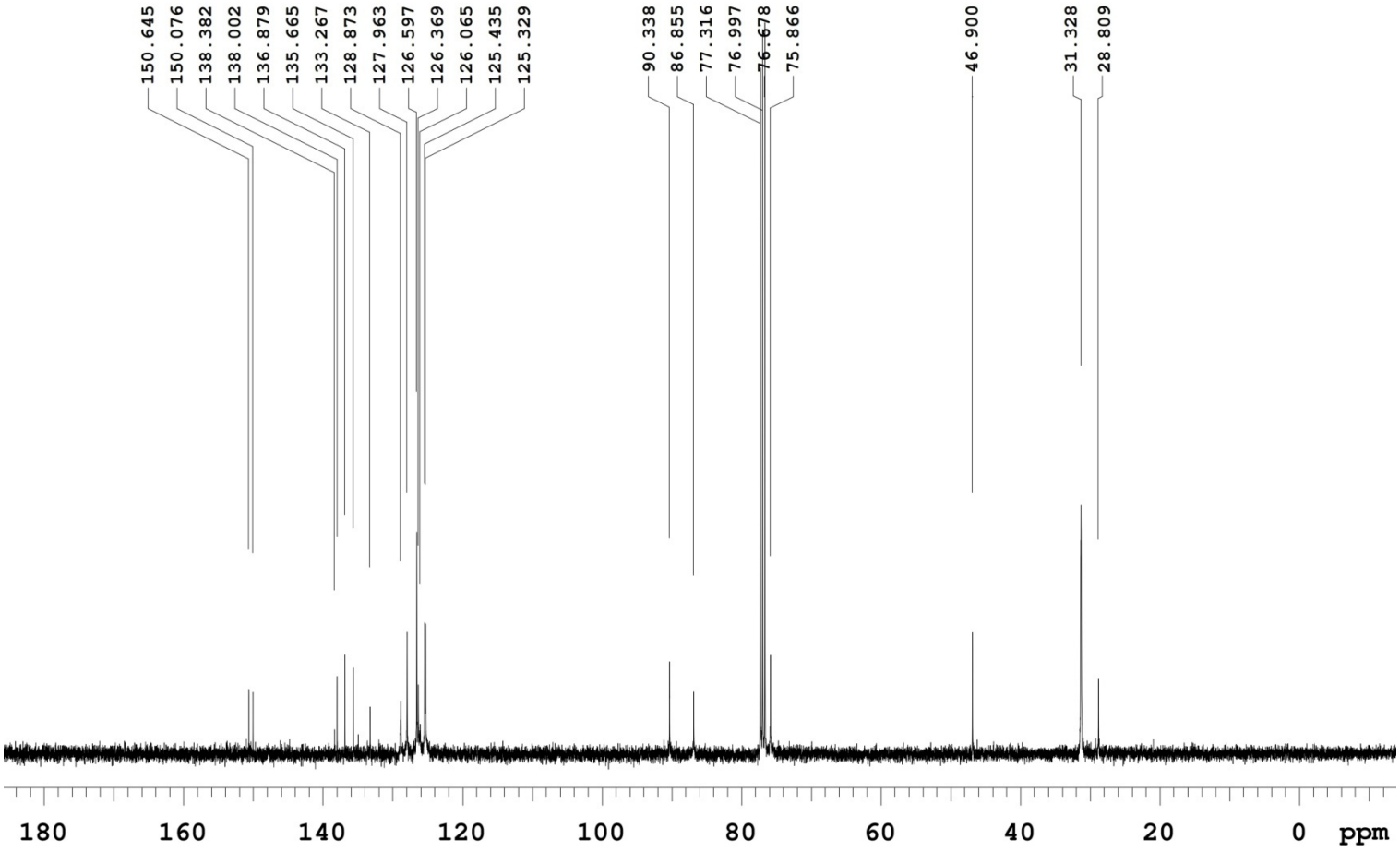
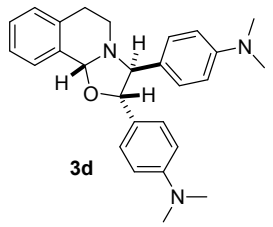
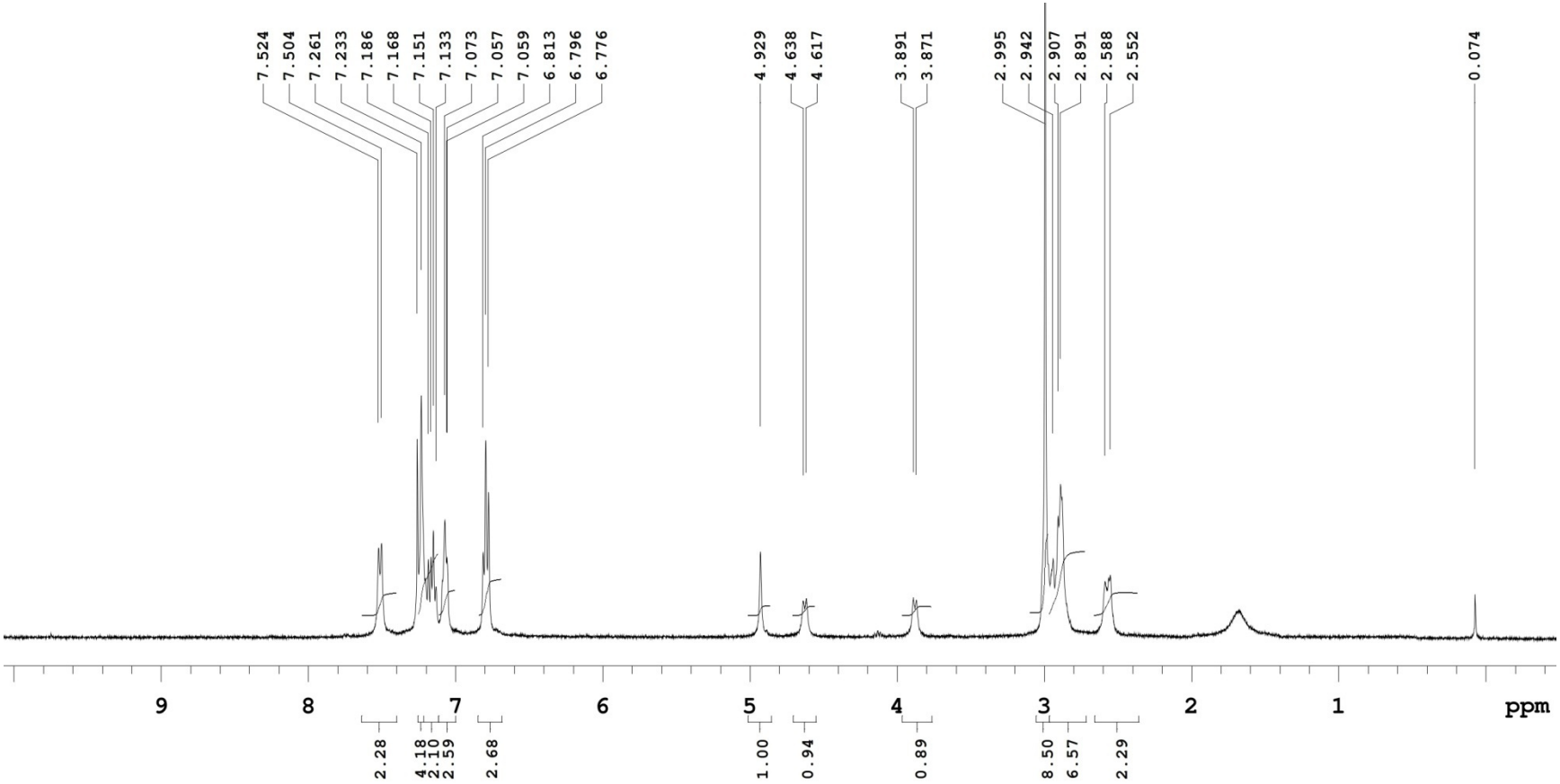


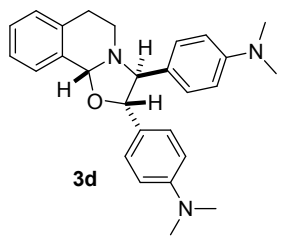
3c





^{1}H NMR of **3d** in $CDCl_3$





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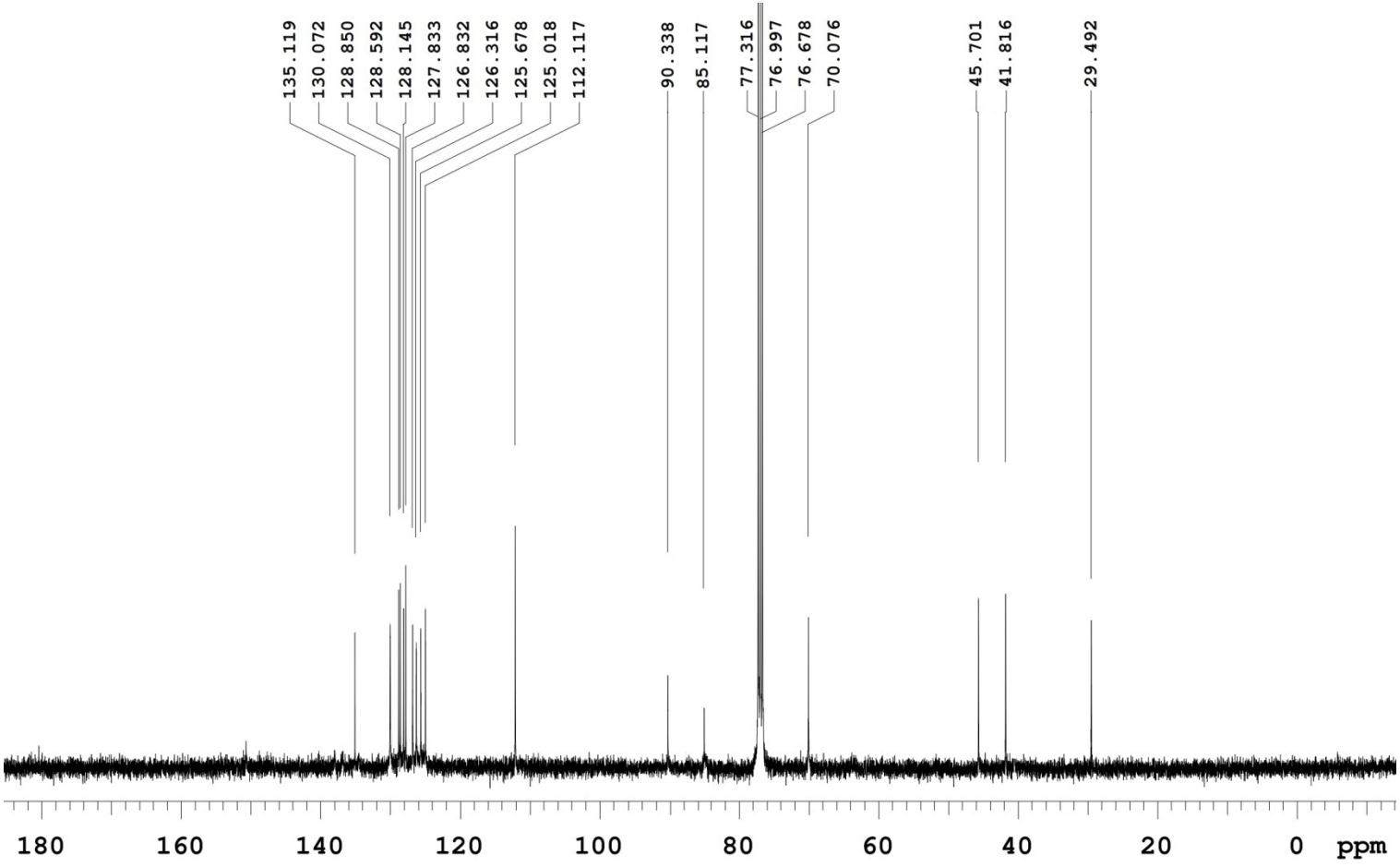
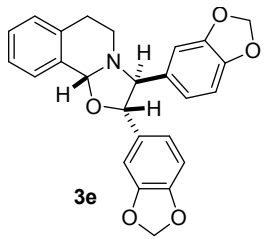
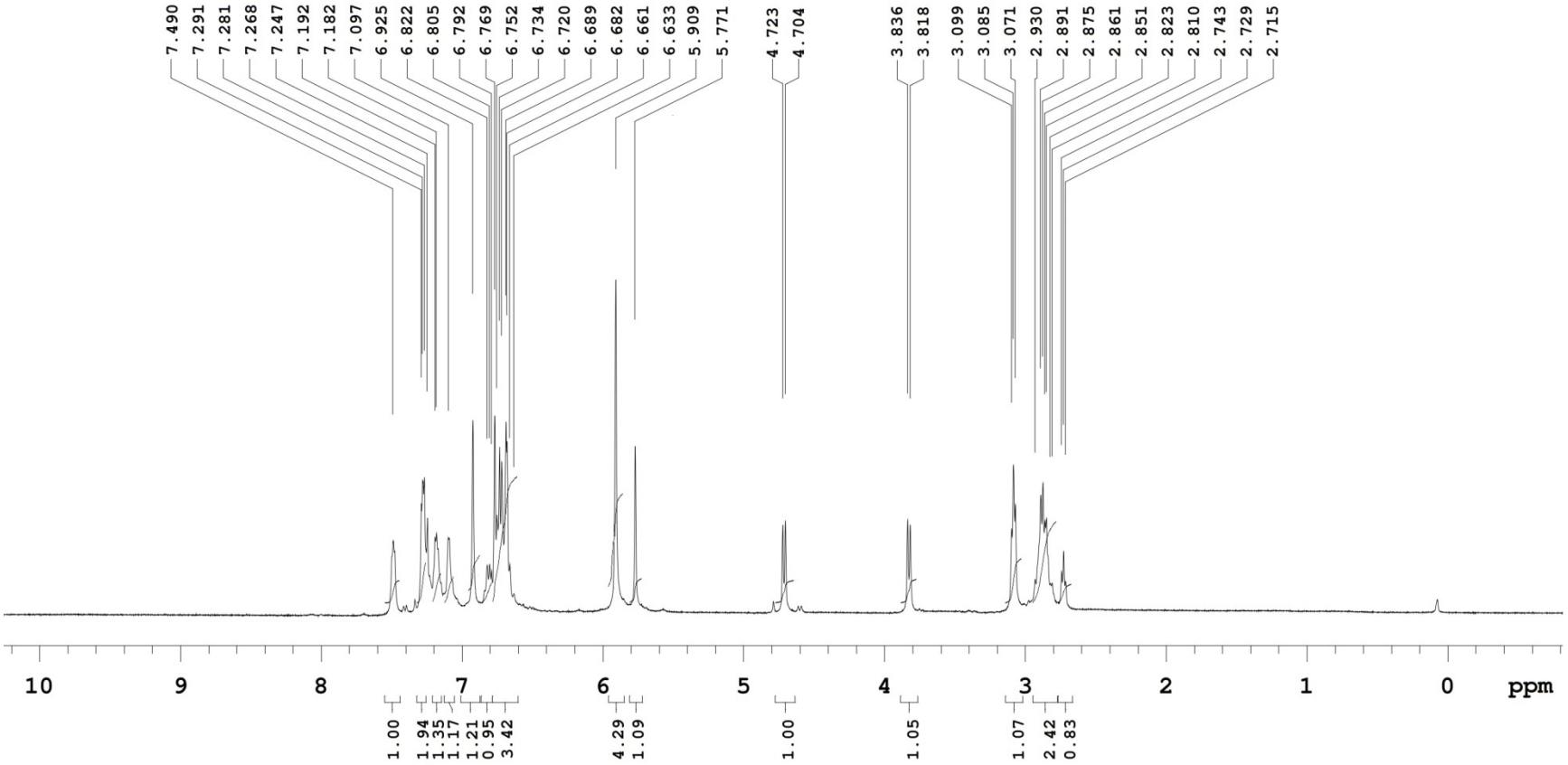




^{1}H NMR of **3e** in $CDCl_3$



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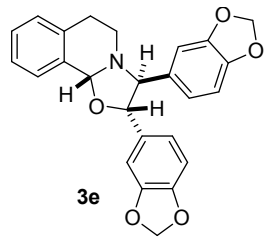

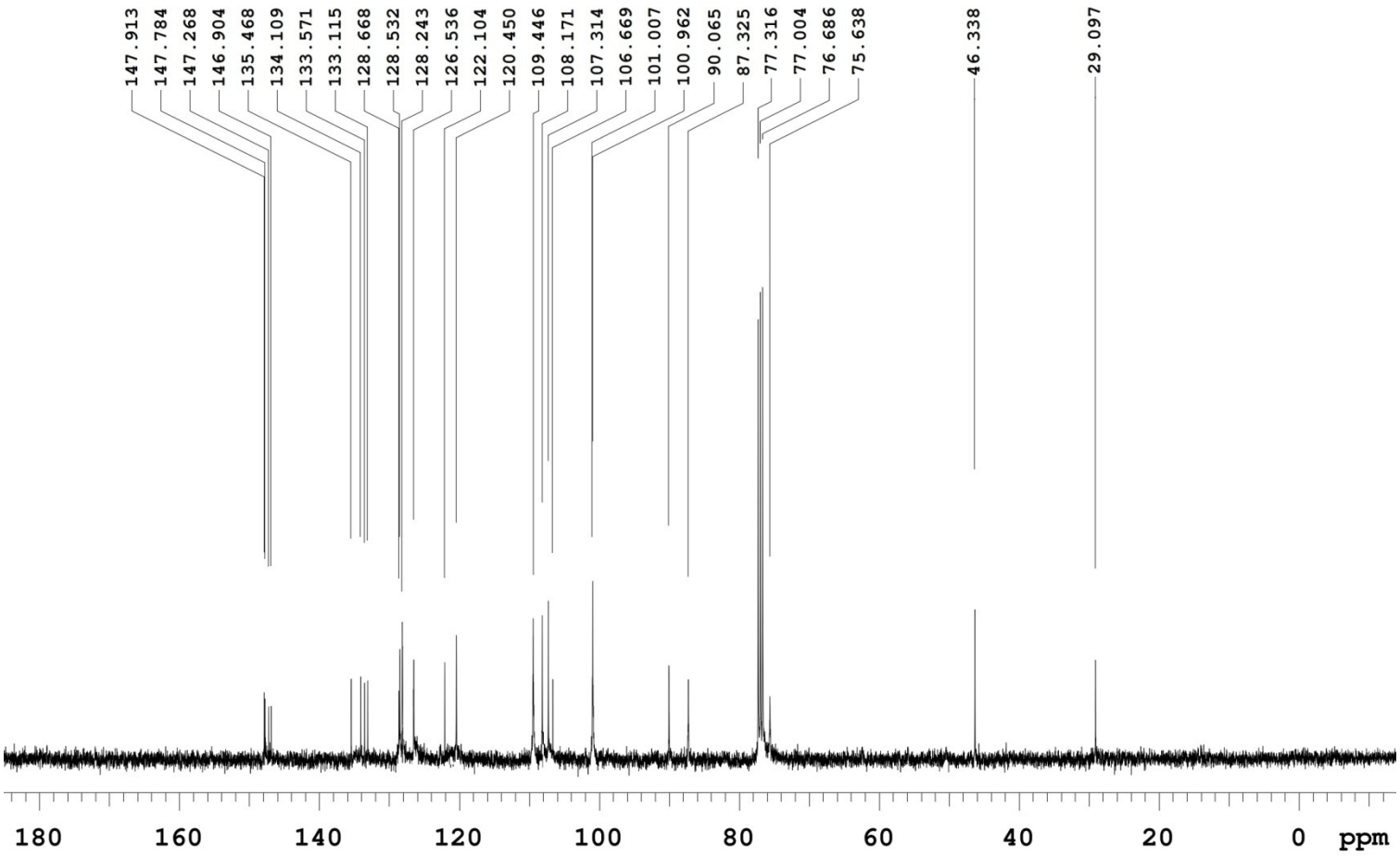

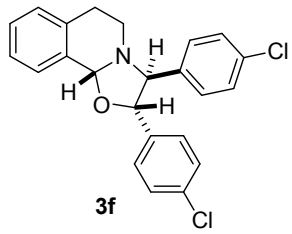

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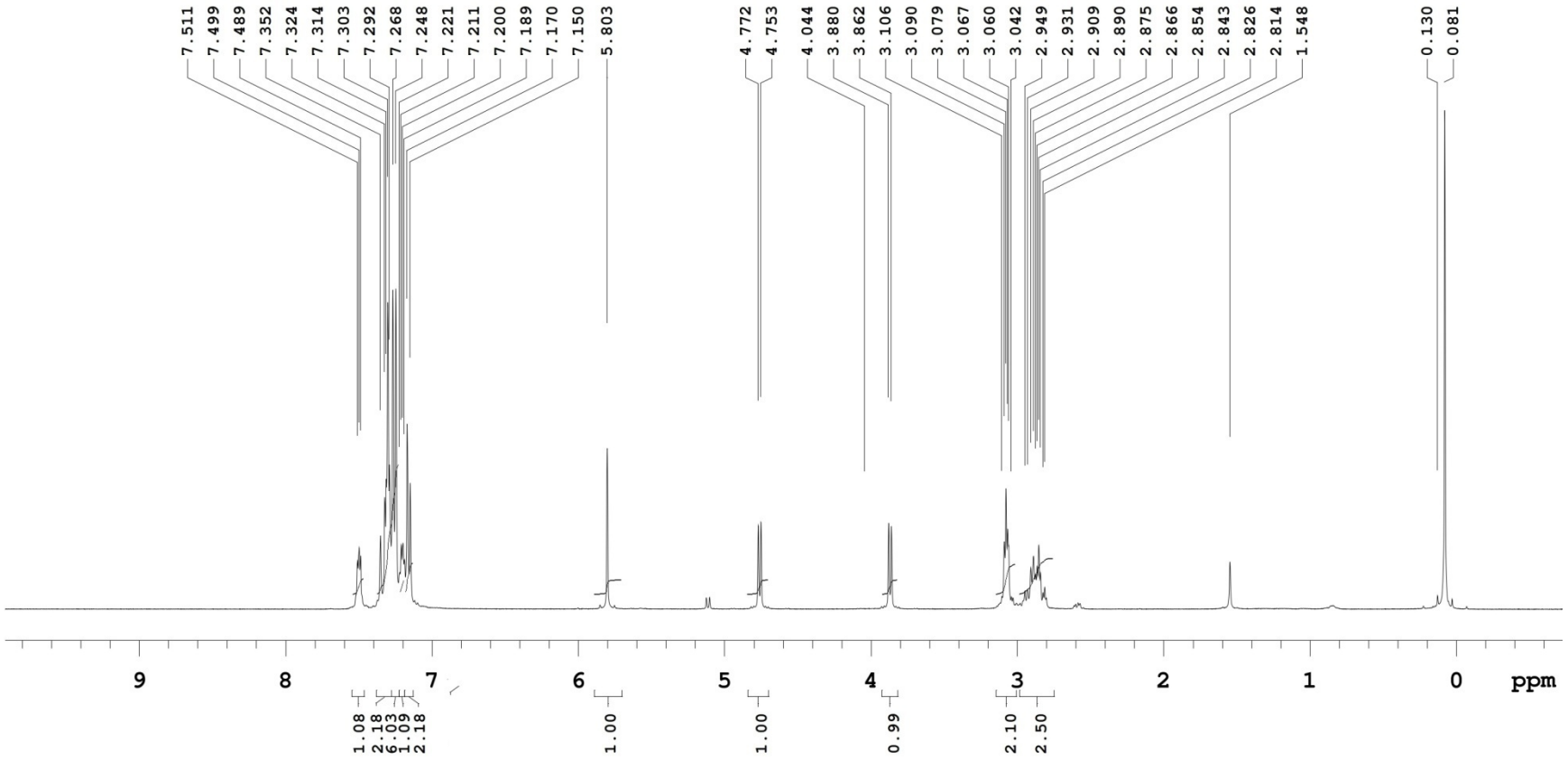

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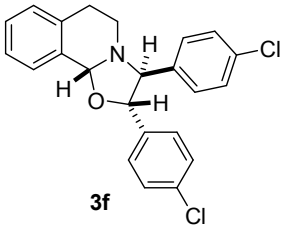

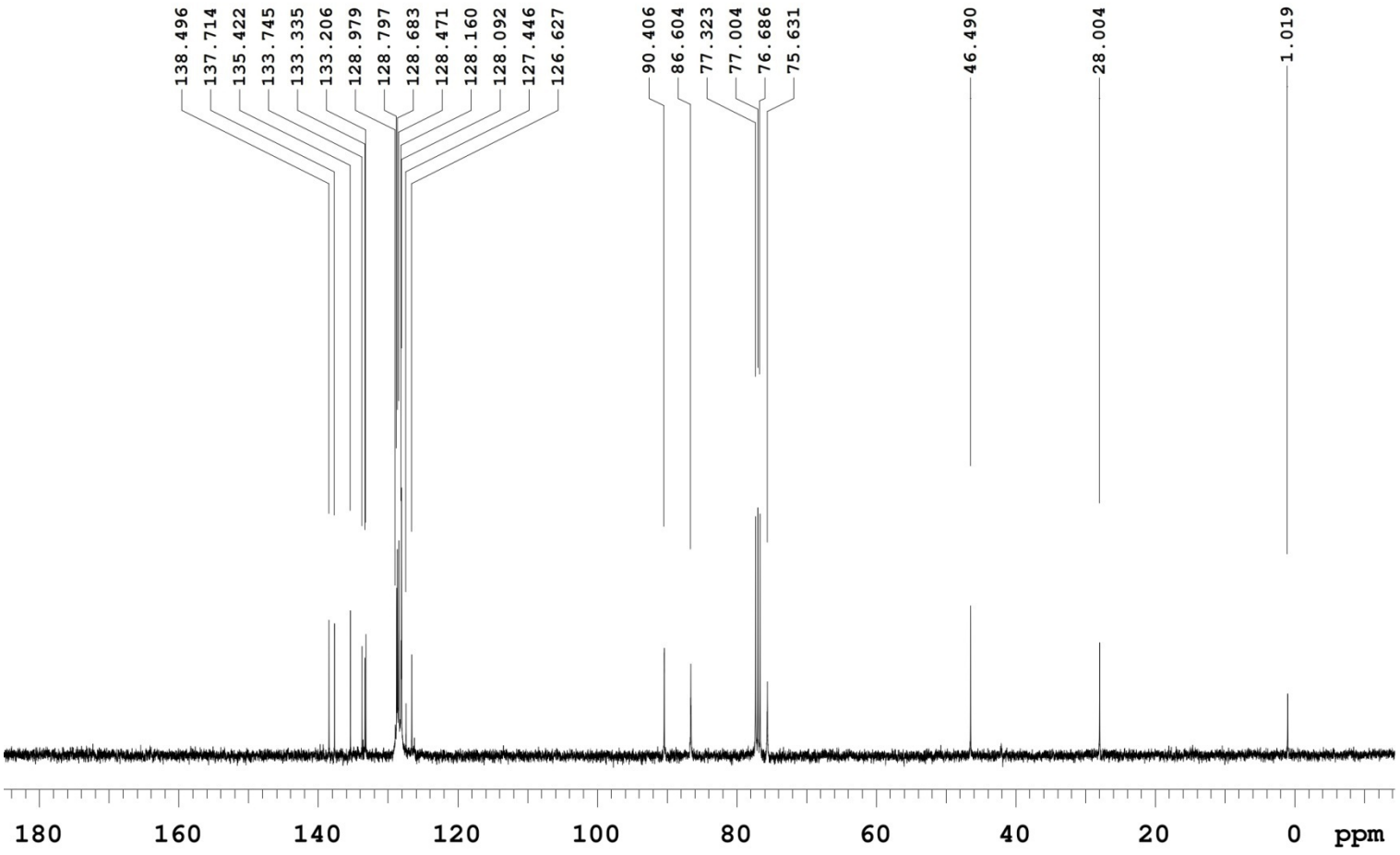

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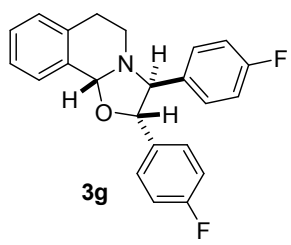

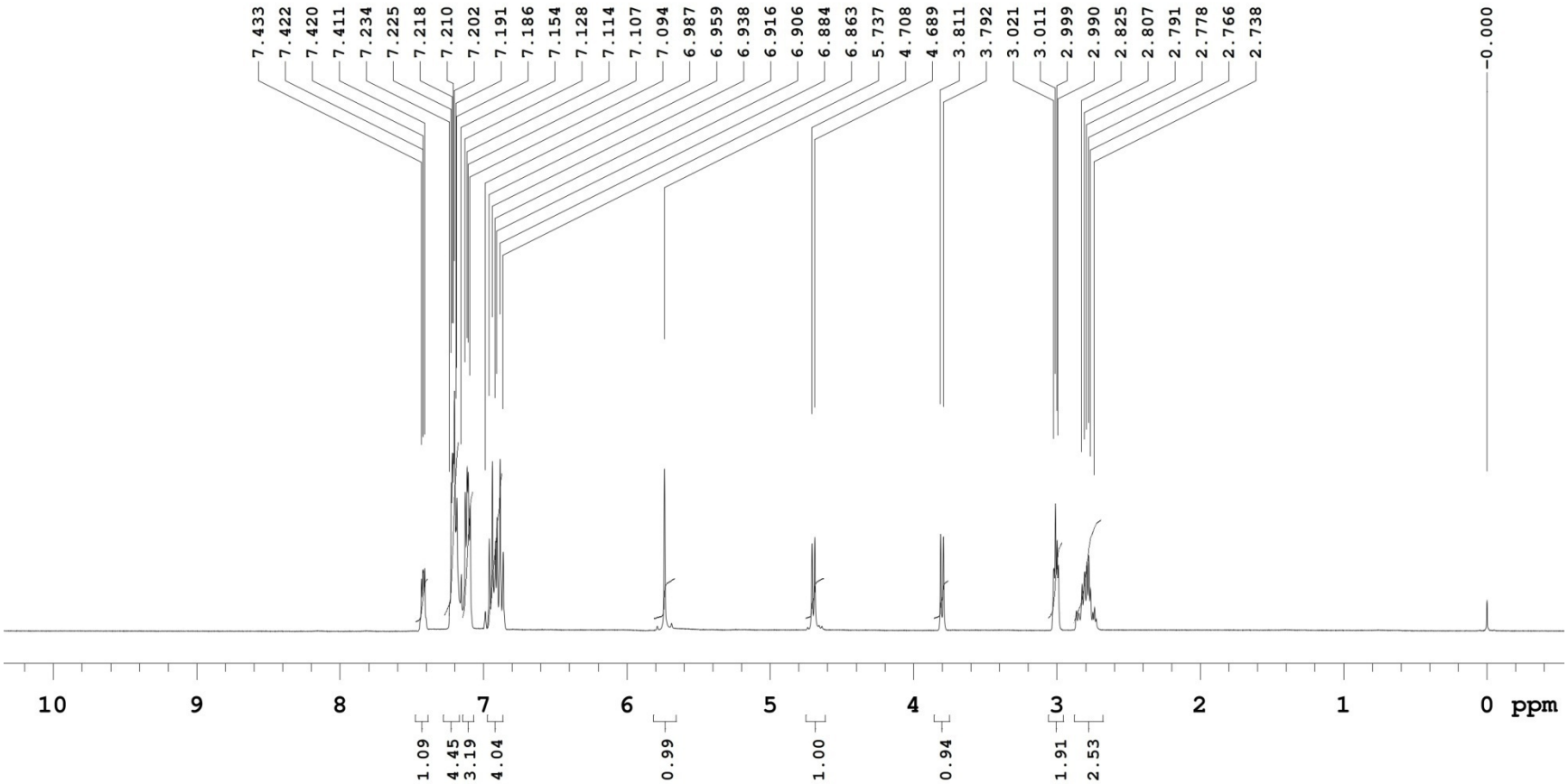

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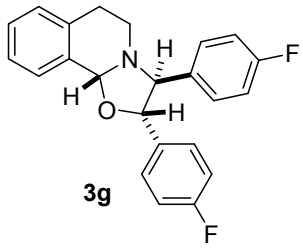

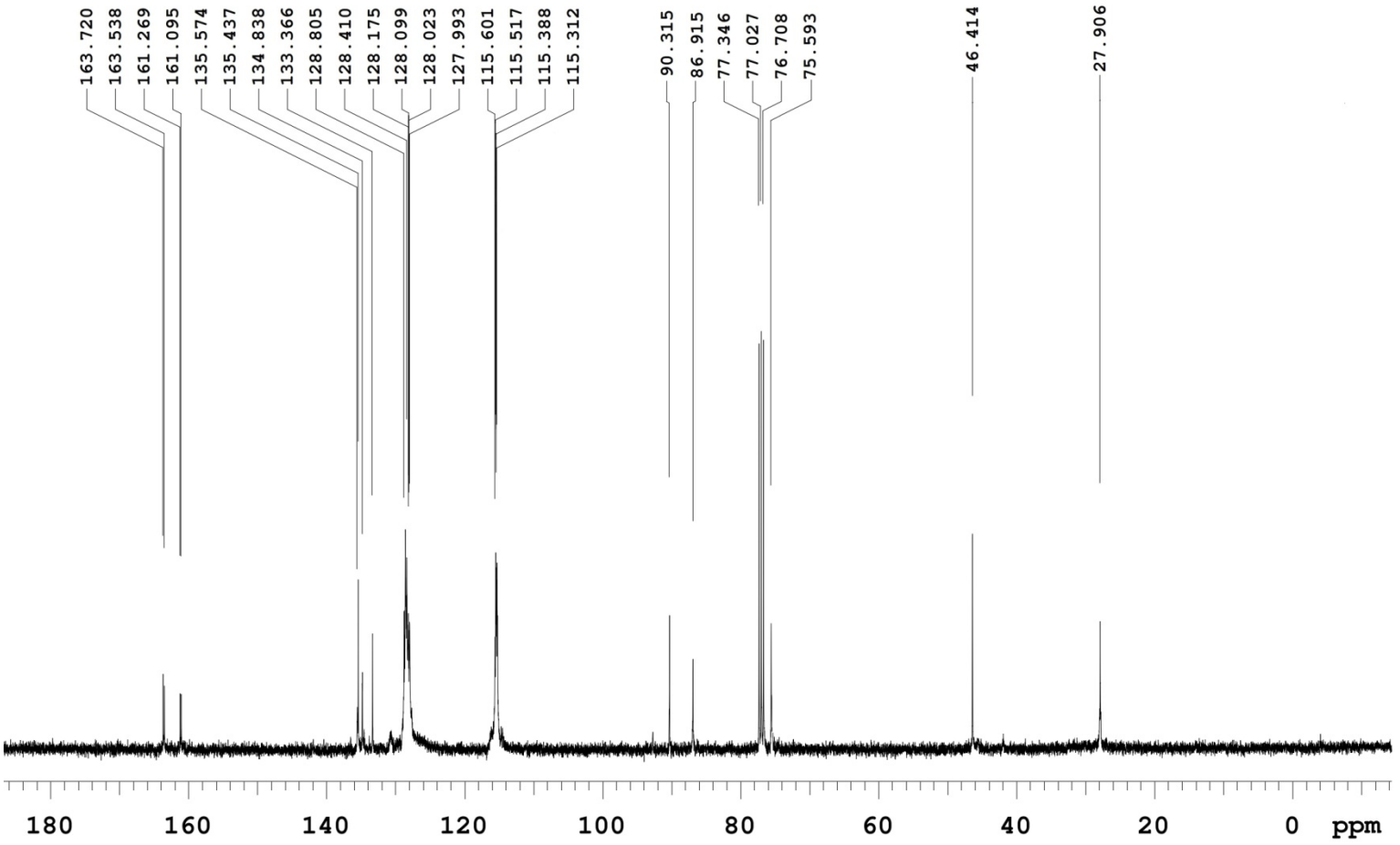

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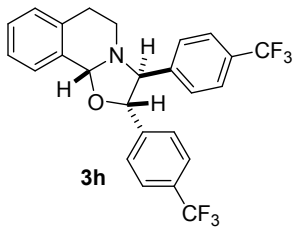
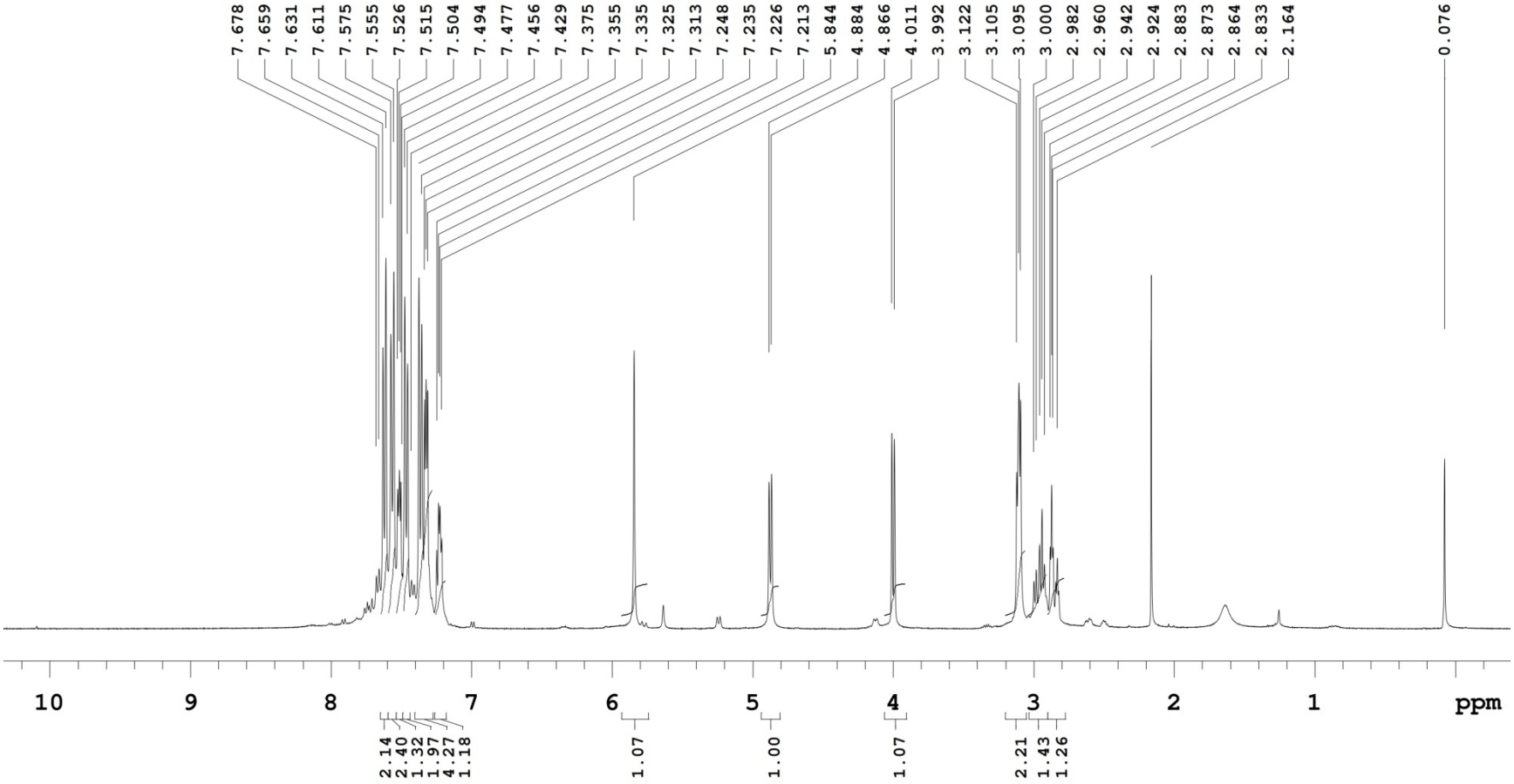
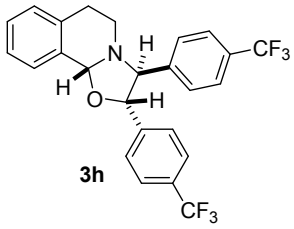
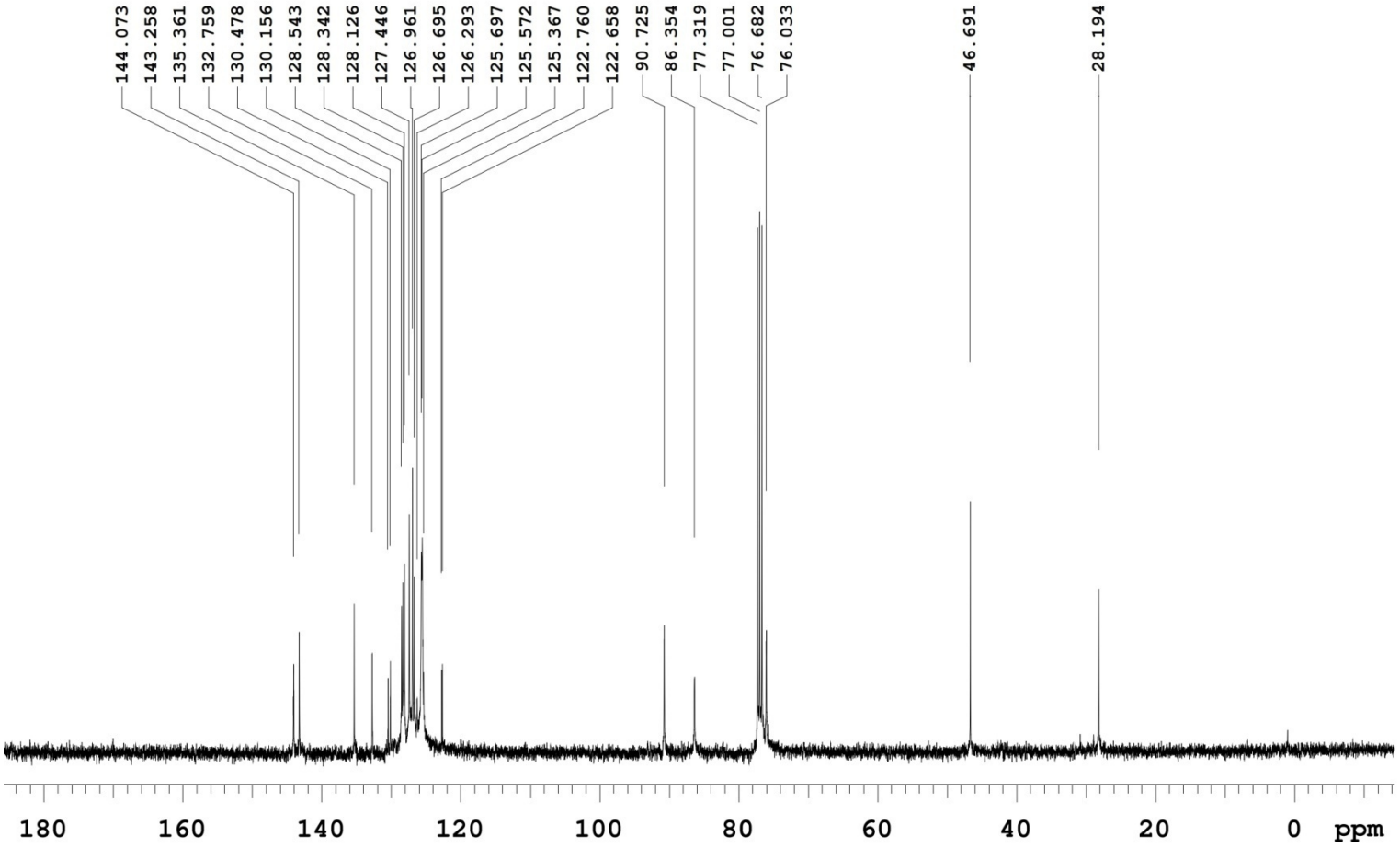


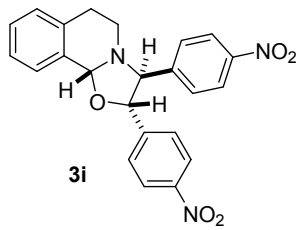


^{13}C NMR of **3h** in $CDCl_3$



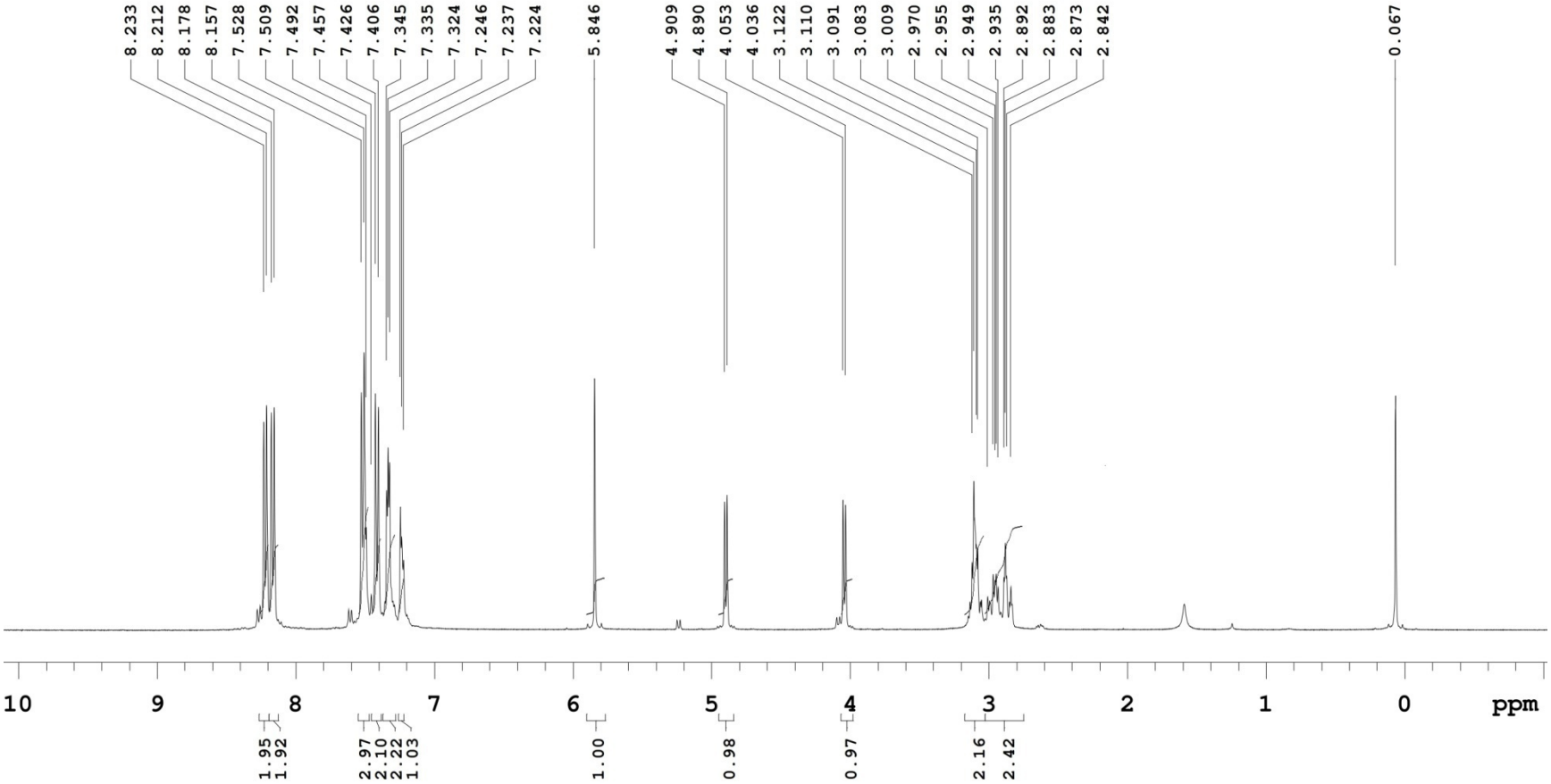
3h



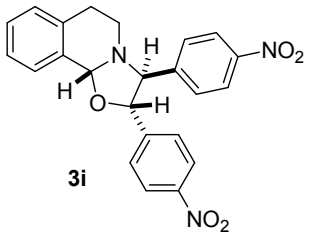


3i

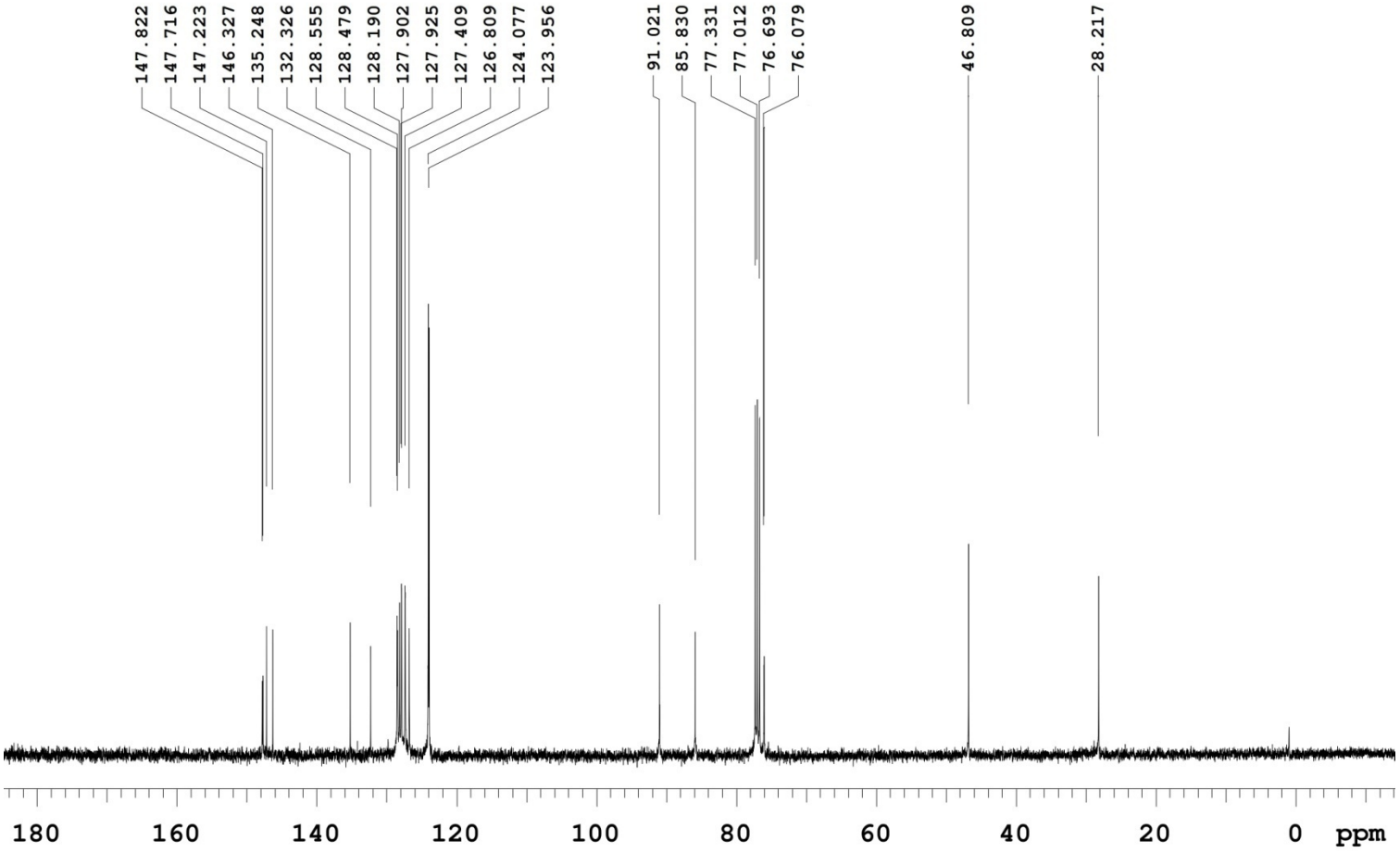
^{1}H NMR of **3i** in $CDCl_3$

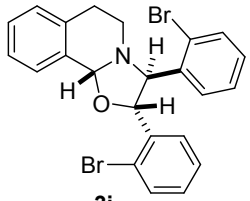


^{13}C NMR of **3i** in $CDCl_3$



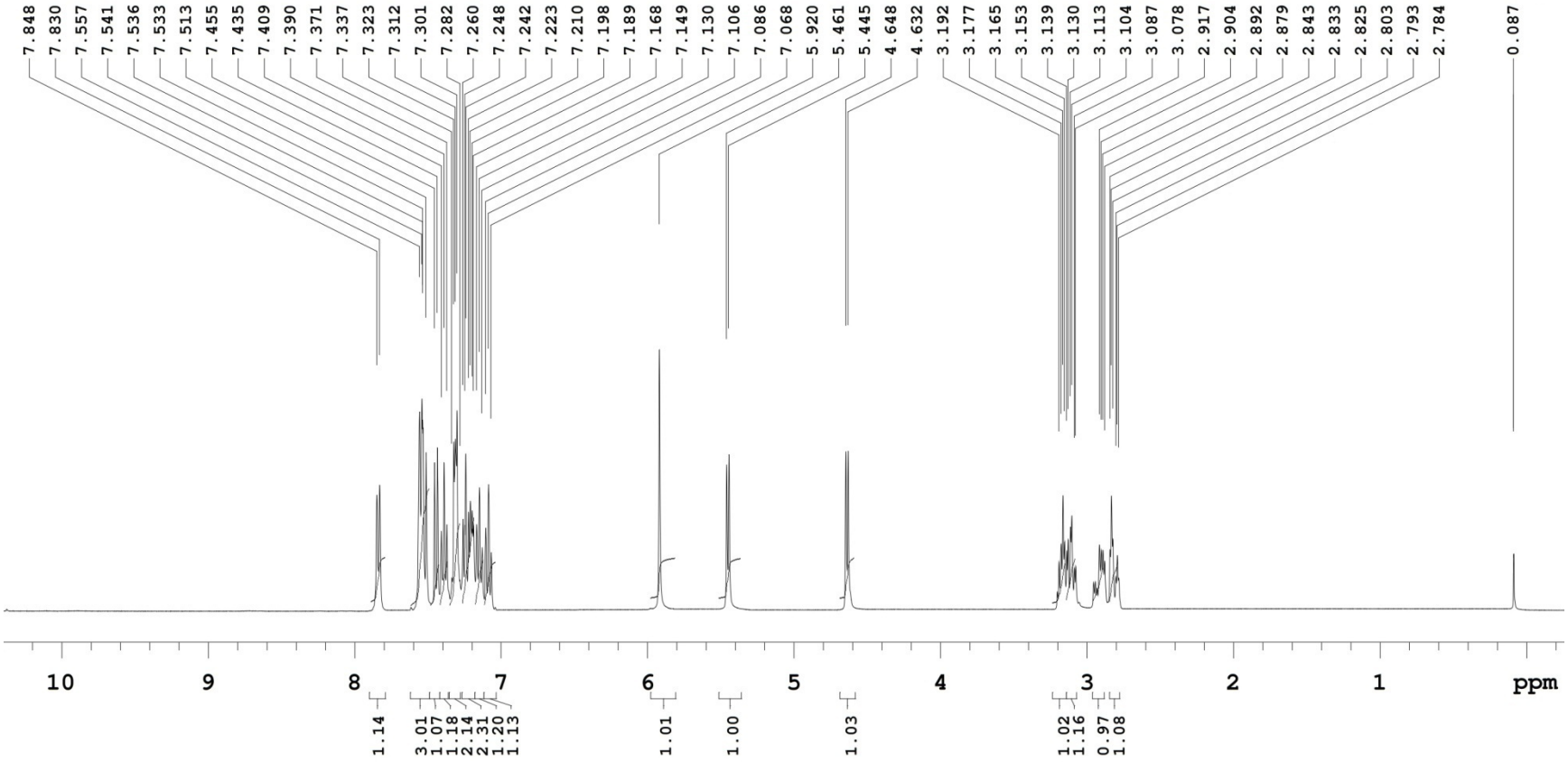
3i

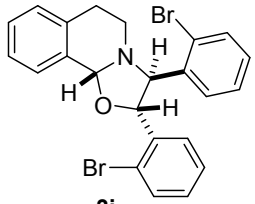




3j

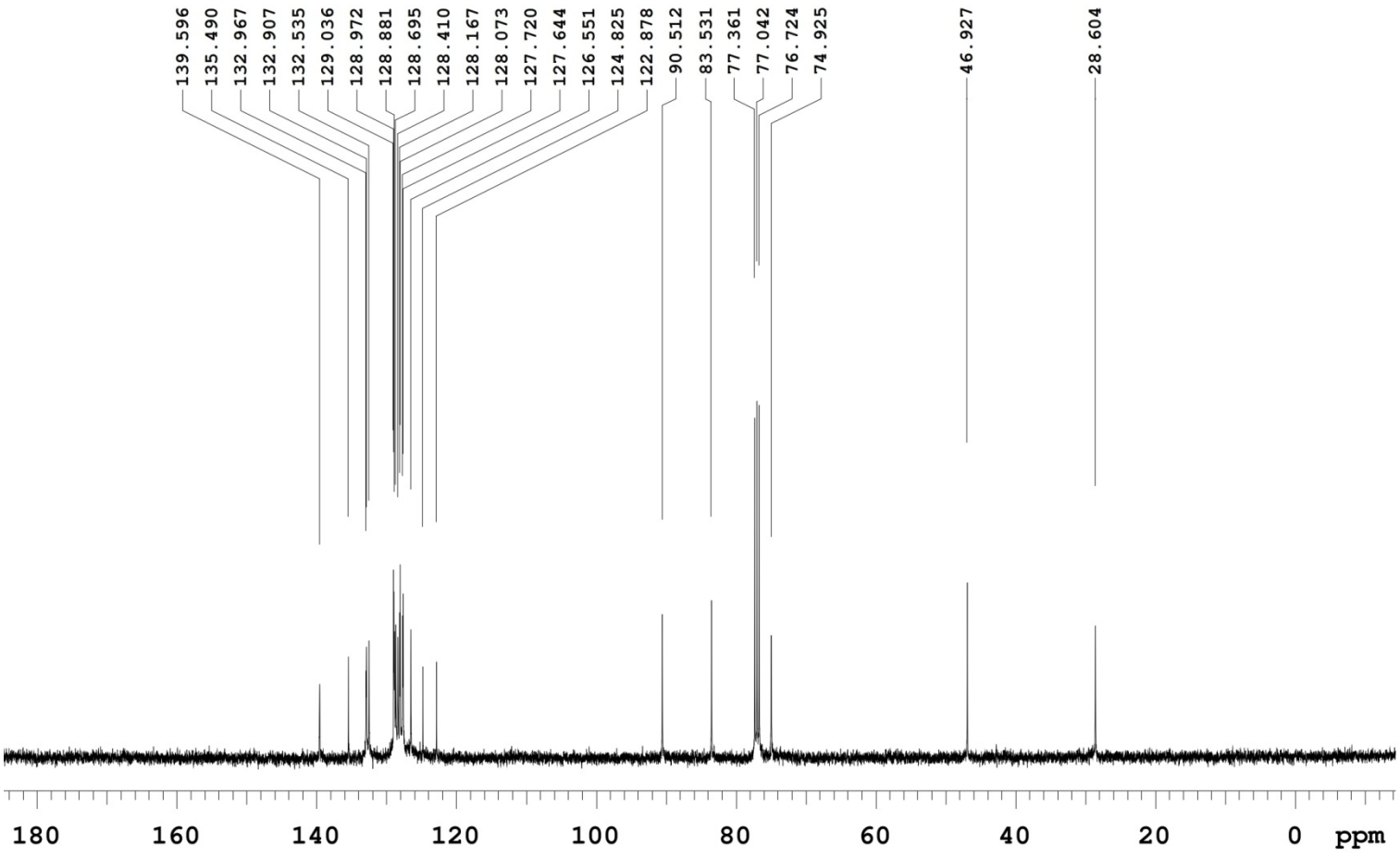
^{1}H NMR of **3j** in $CDCl_3$

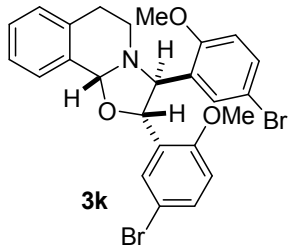




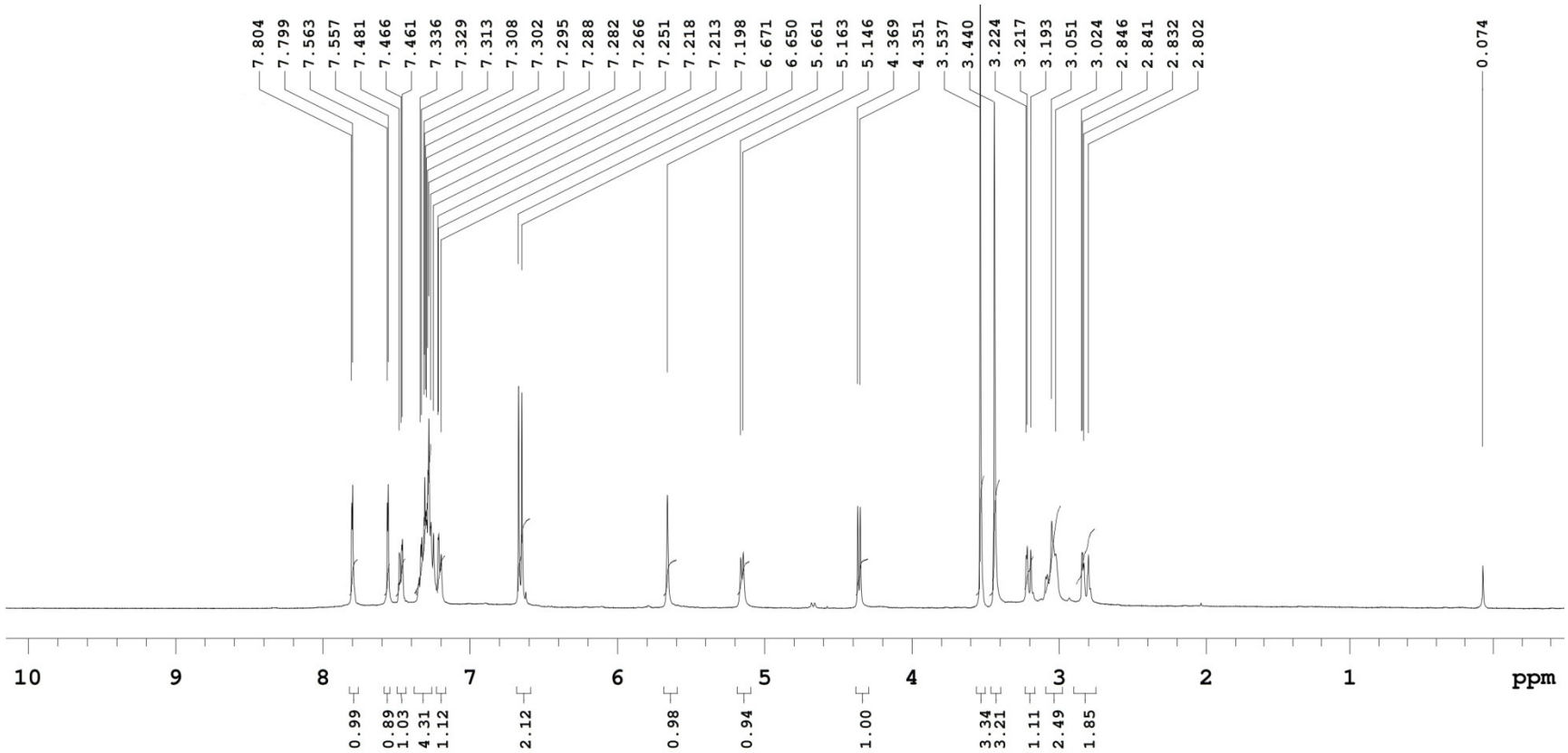
3j

^{13}C NMR of **3j** in $CDCl_3$

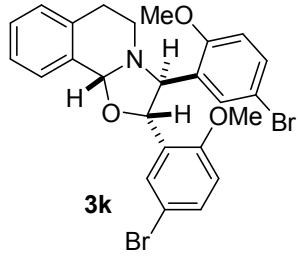


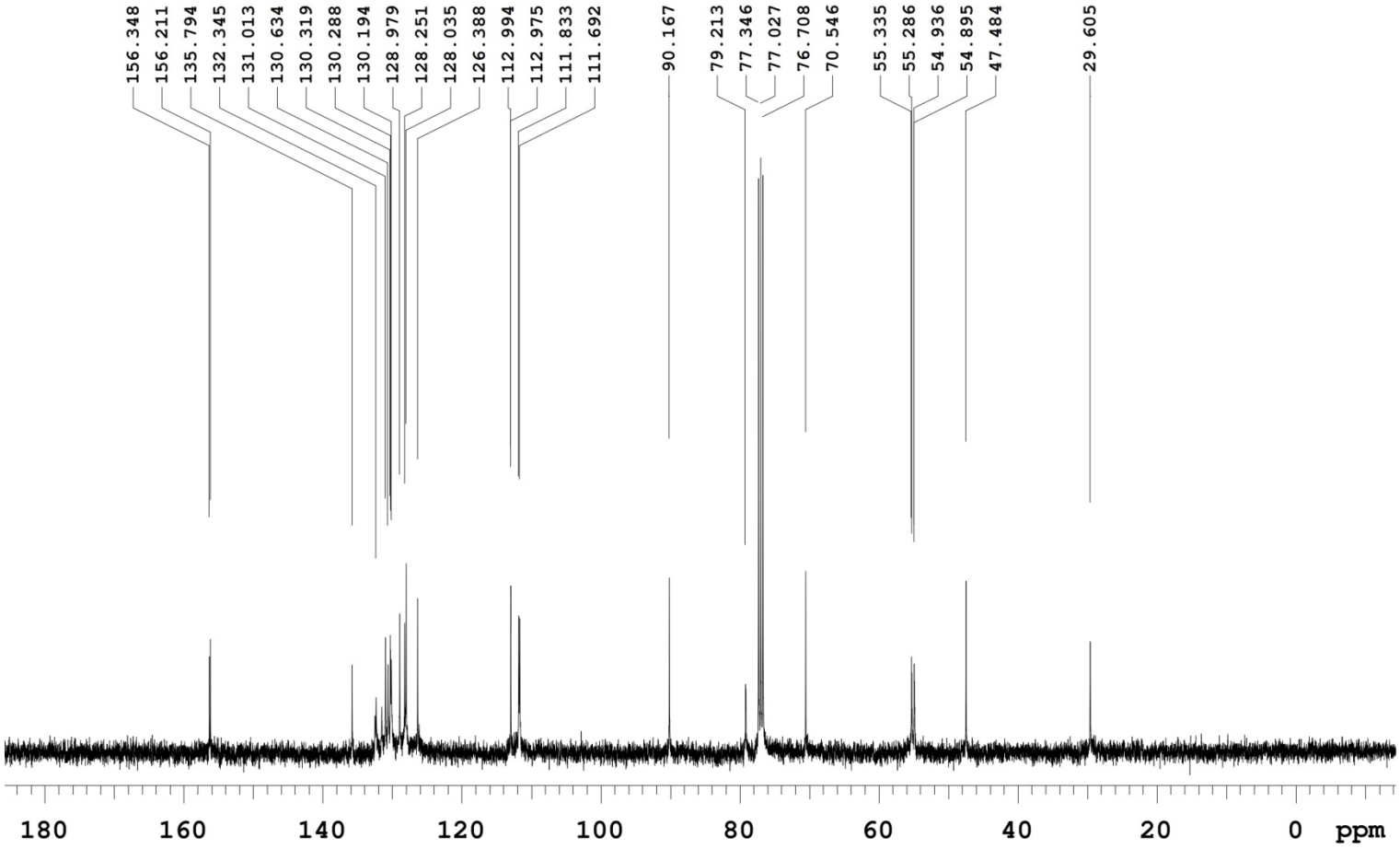


^{1}H NMR of **3k** in $CDCl_3$

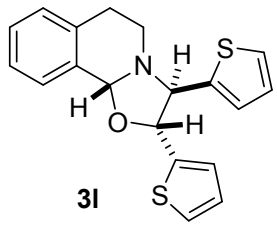


^{13}C NMR of **3k** in $CDCl_3$

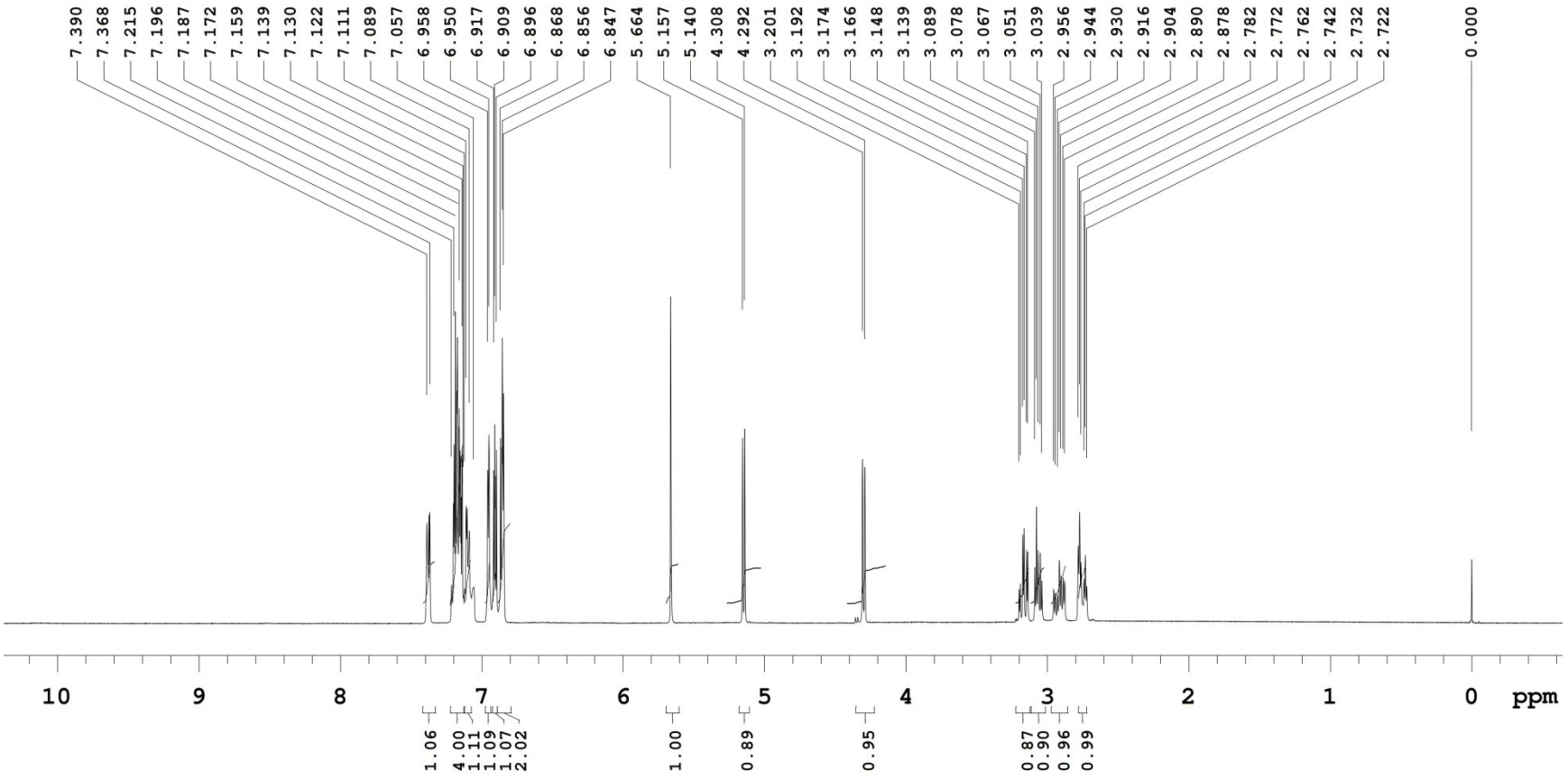




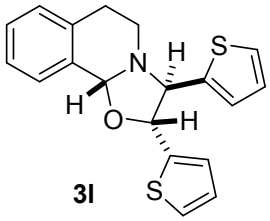
^{1}H NMR of **3l** in $CDCl_3$



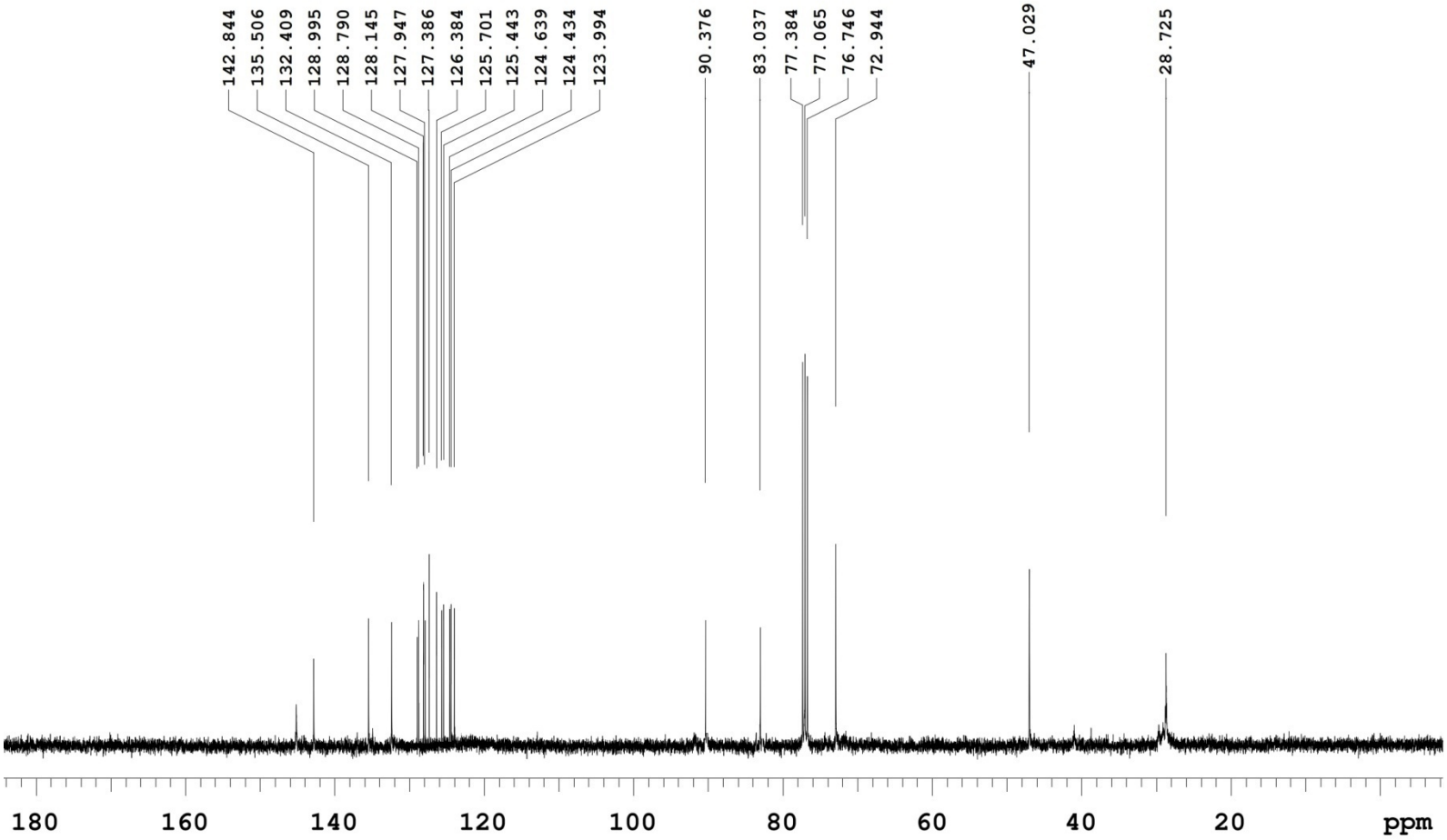
3l

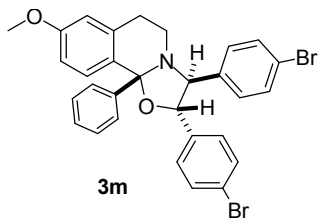


^{13}C NMR of **3l** in $CDCl_3$

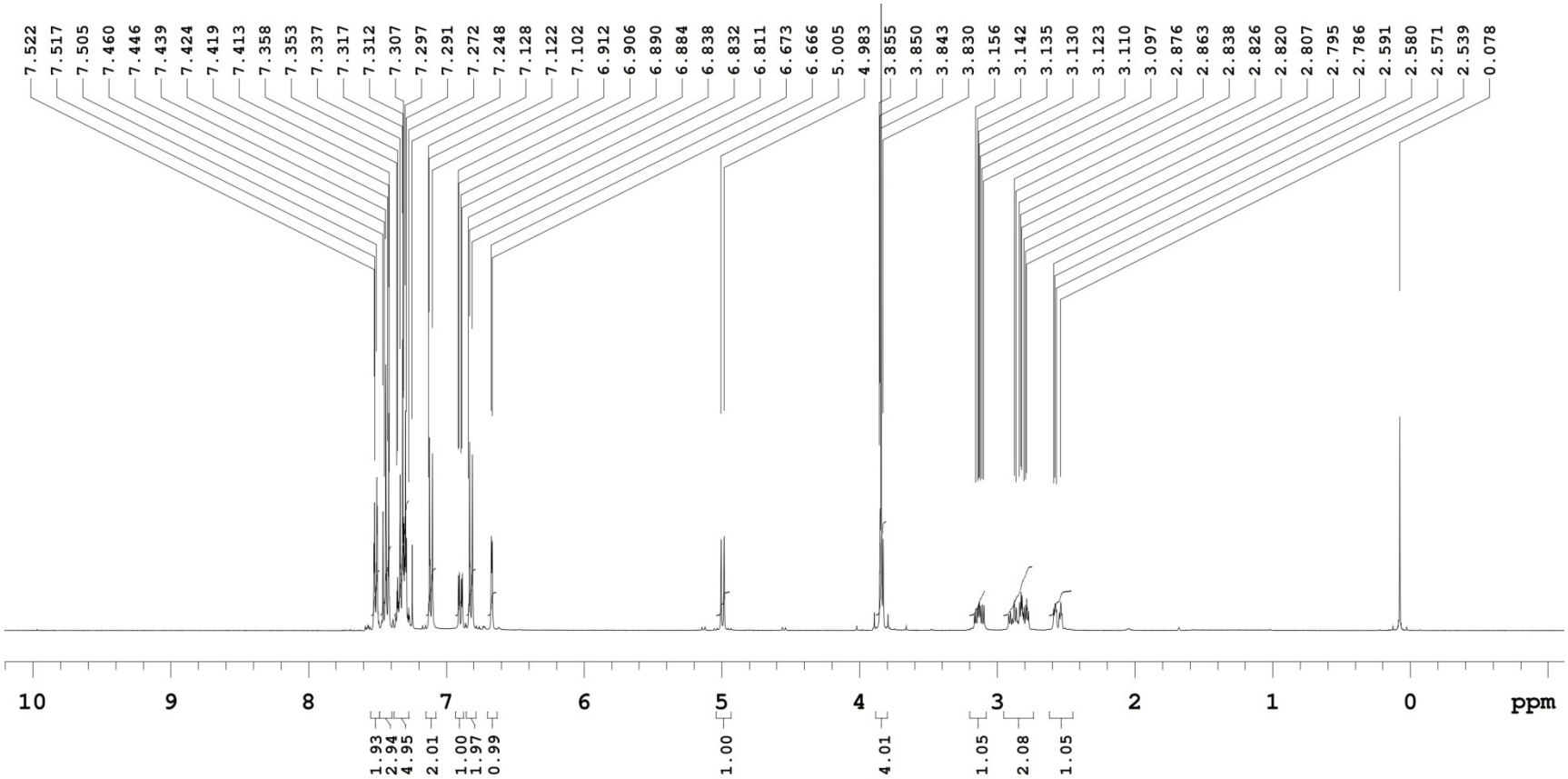


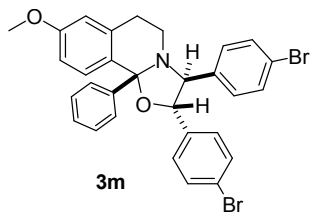
3l





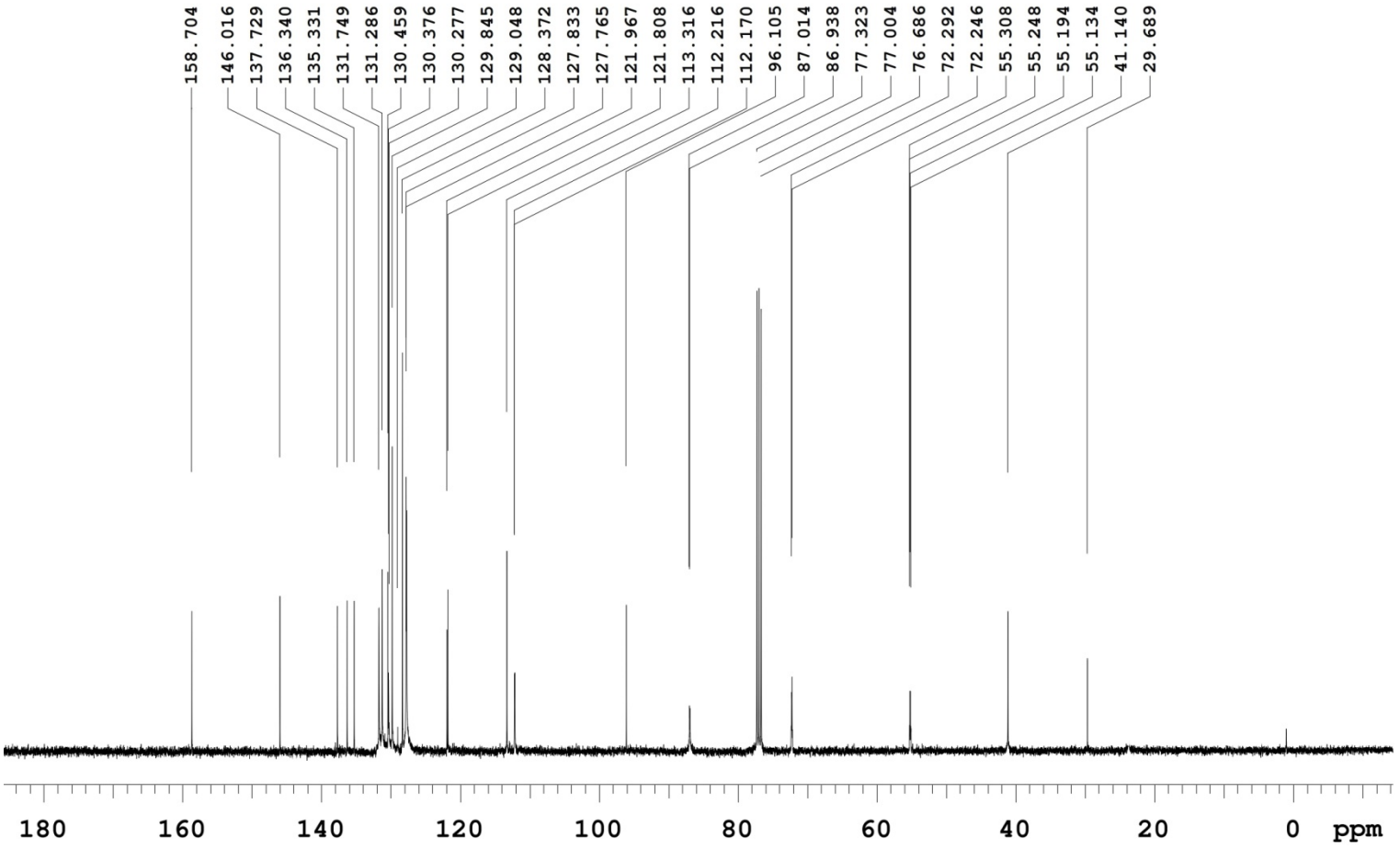
^{1}H NMR of **3m** in $CDCl_3$



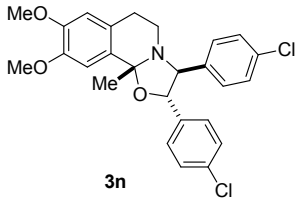


3m

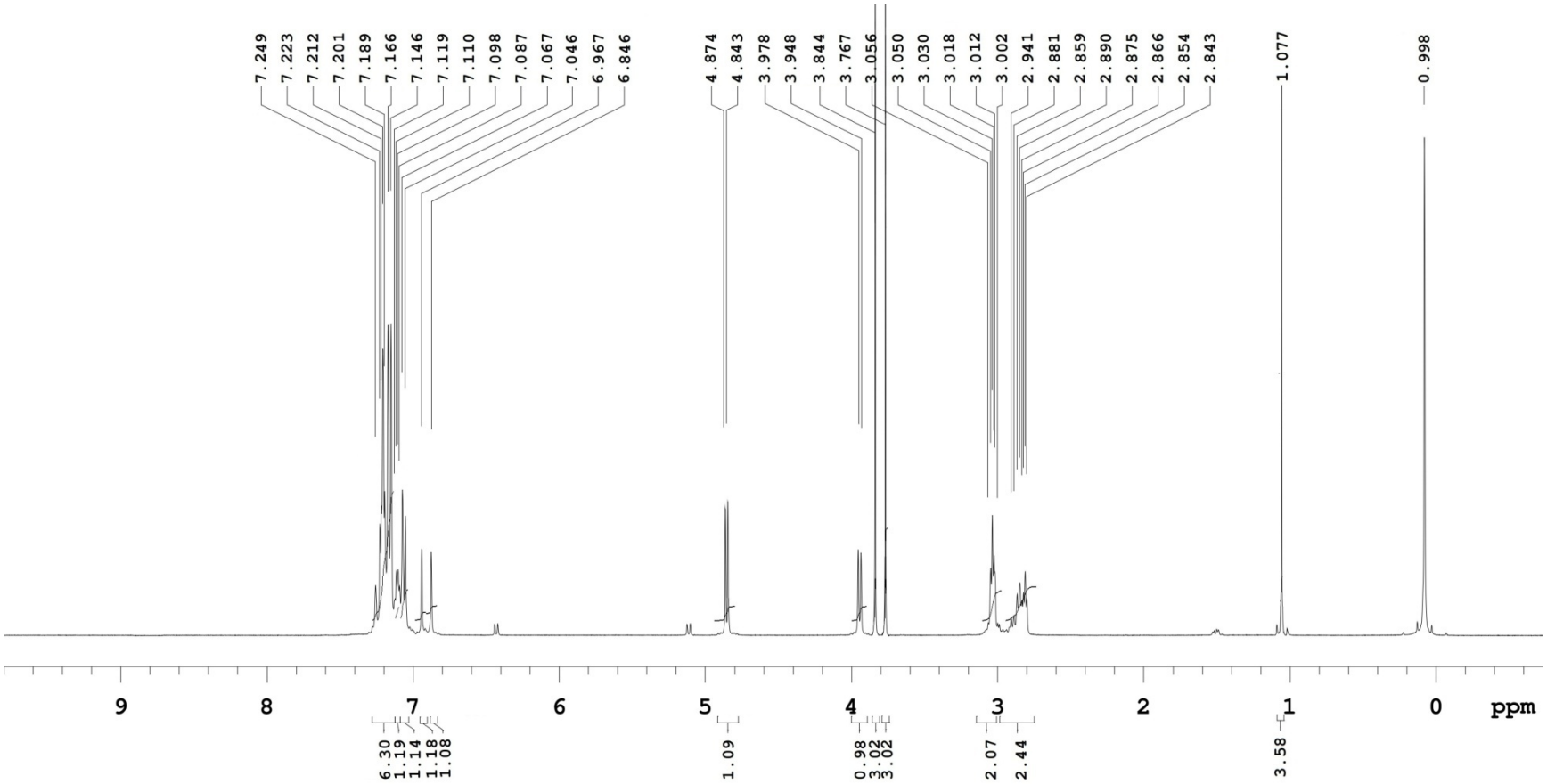
^{13}C NMR of **3m** in $CDCl_3$

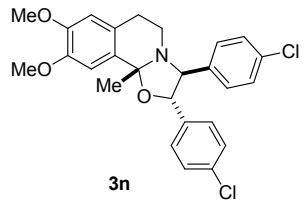


^{1}H NMR of **3n** in $CDCl_3$

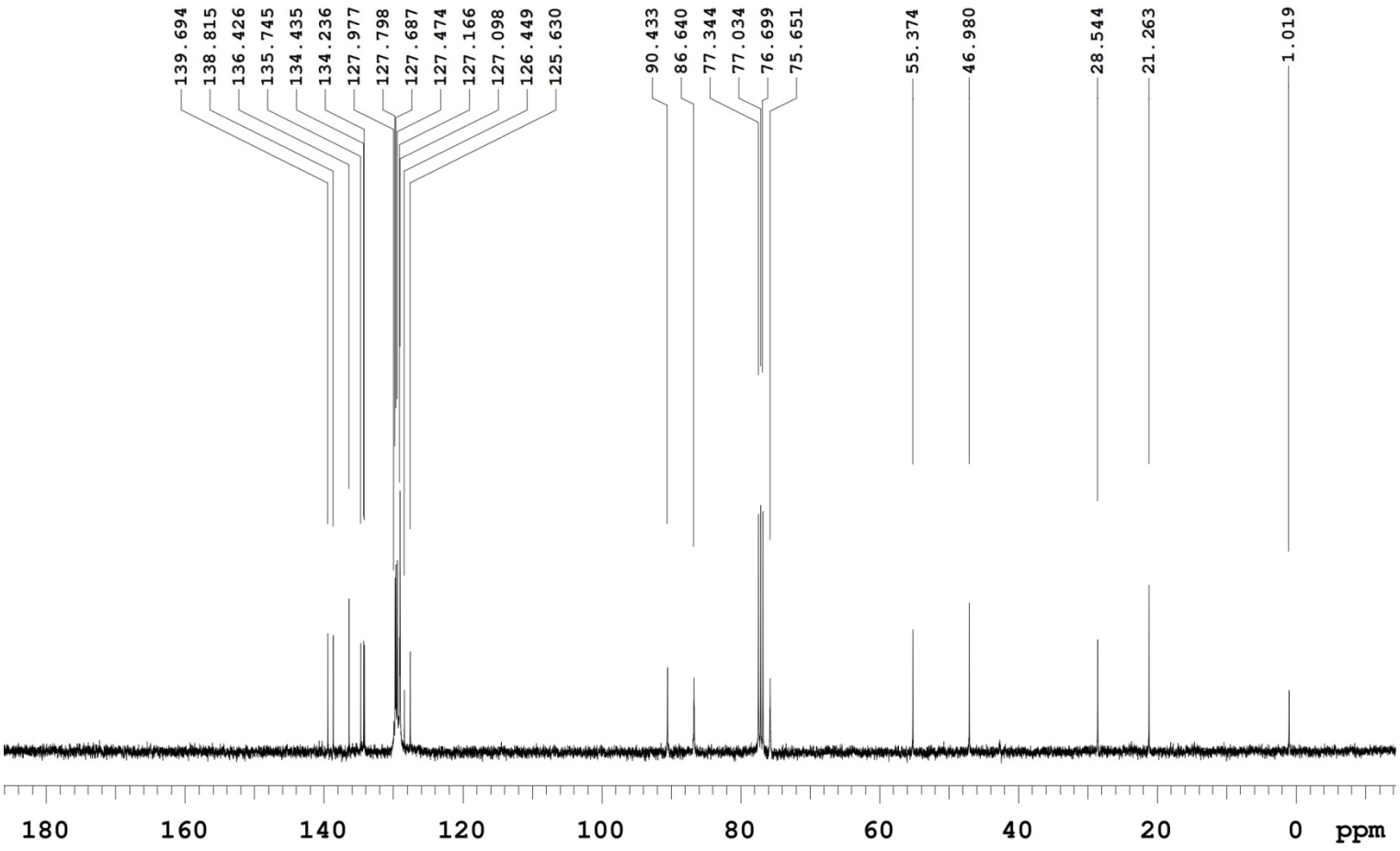


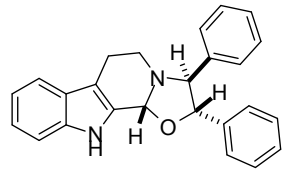
3n





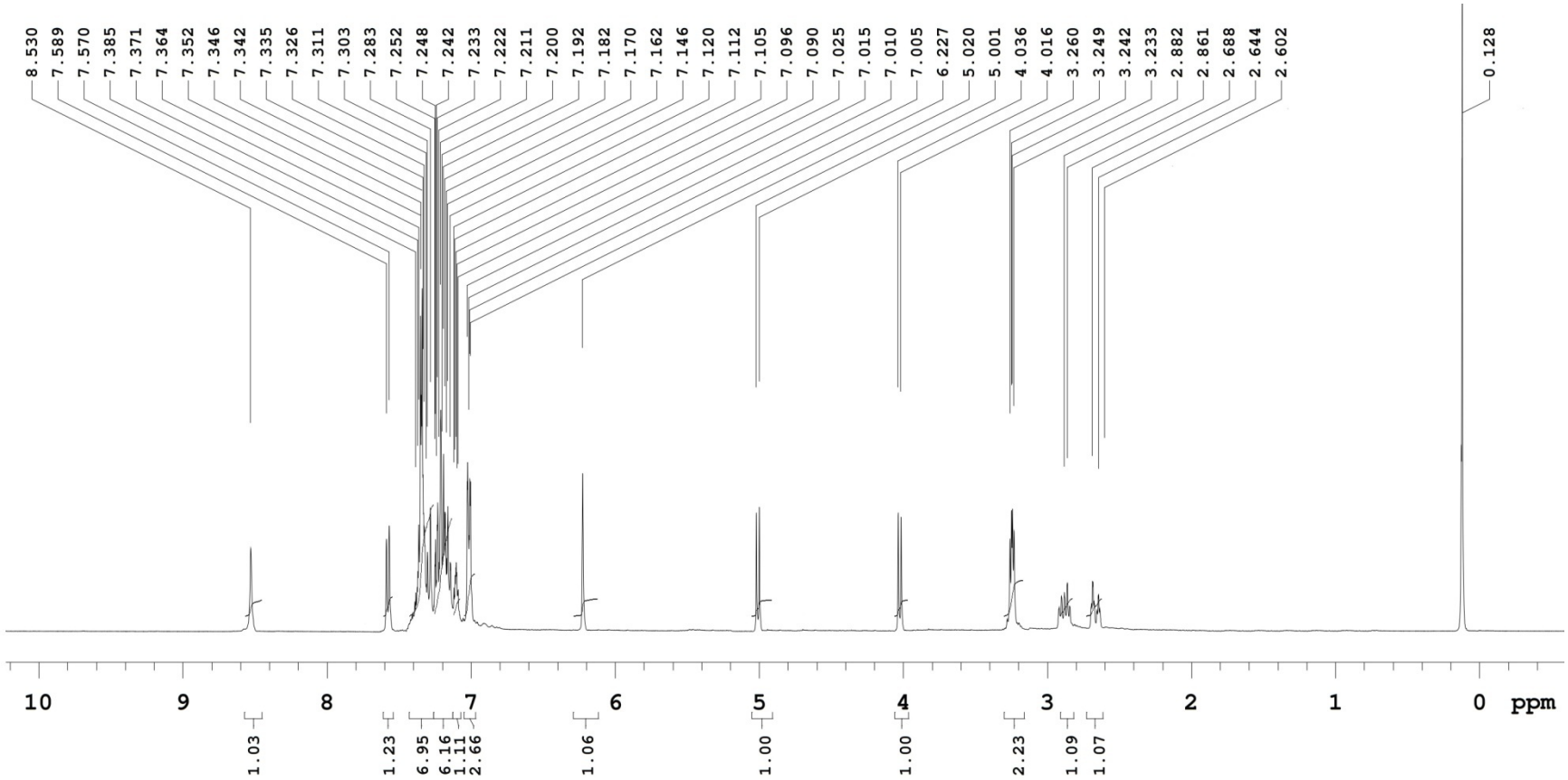
^{13}C NMR of **3n** in $CDCl_3$



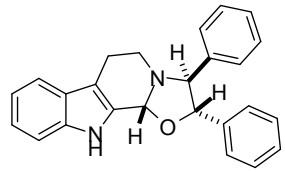


3o

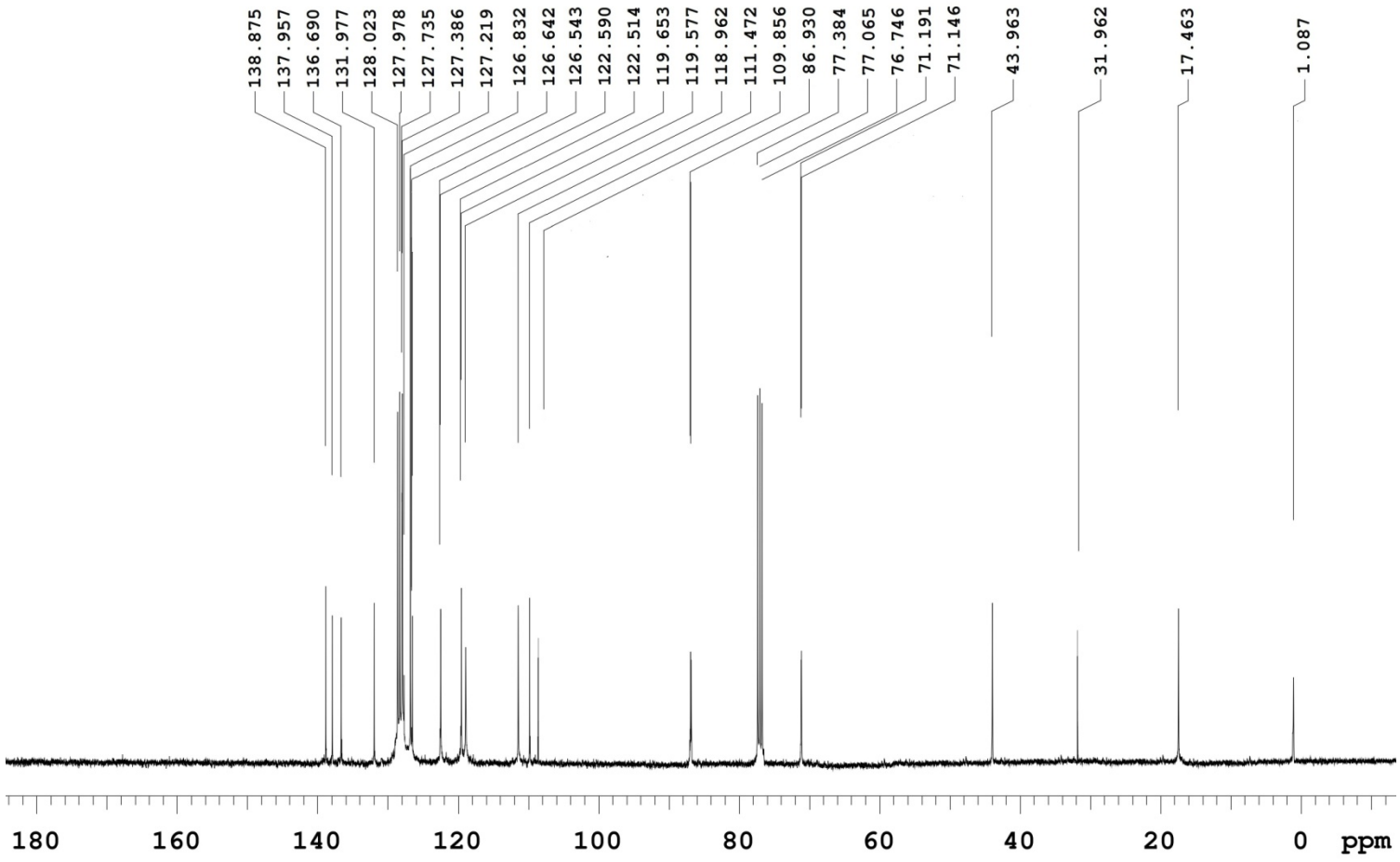
^{1}H NMR of **3o** in $CDCl_3$

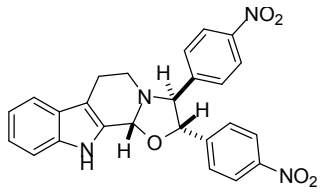


^{13}C NMR of **3o** in $CDCl_3$



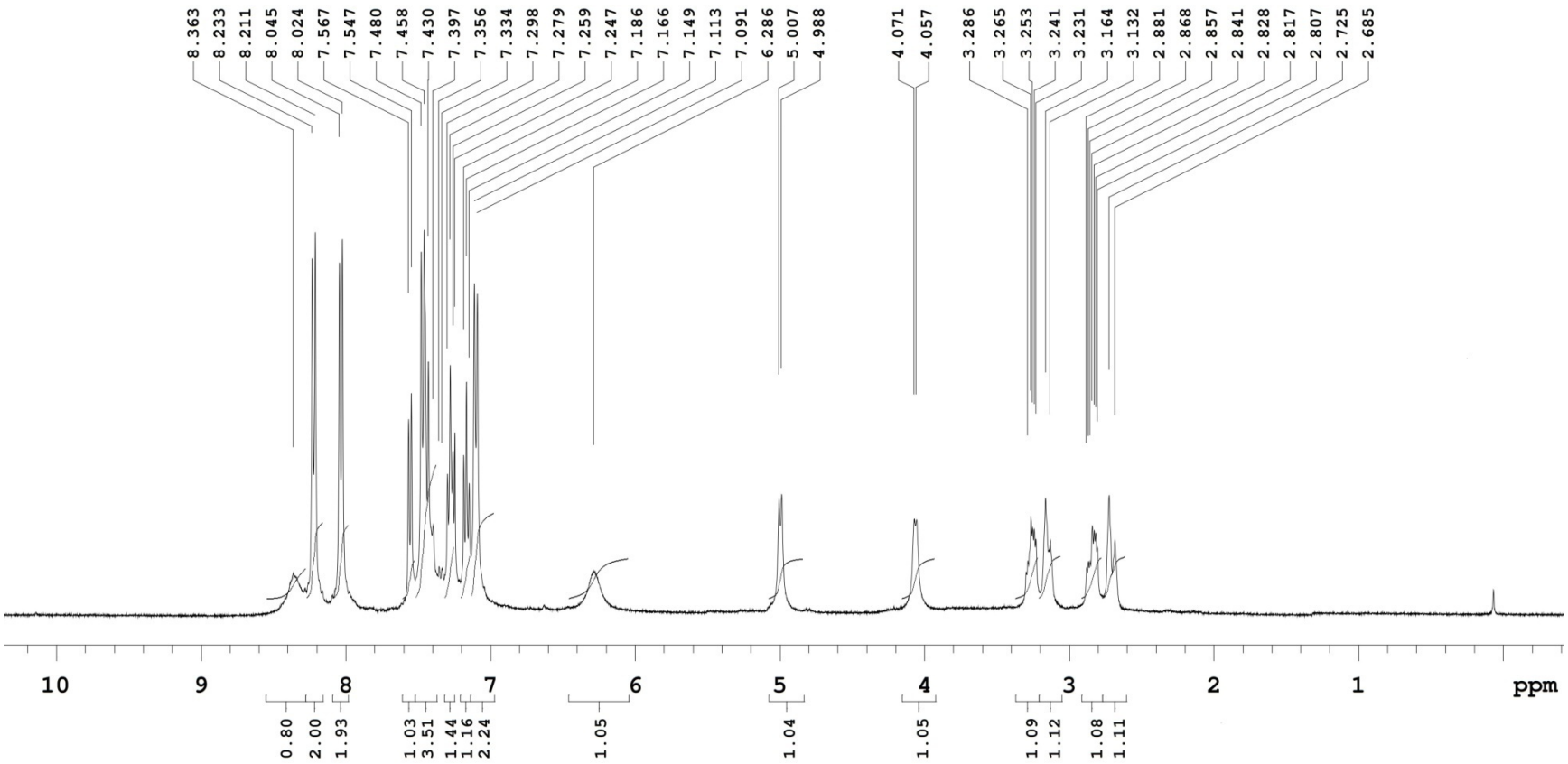
3o

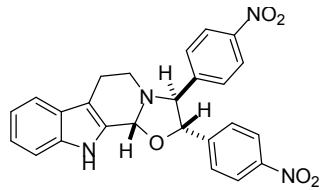




3p

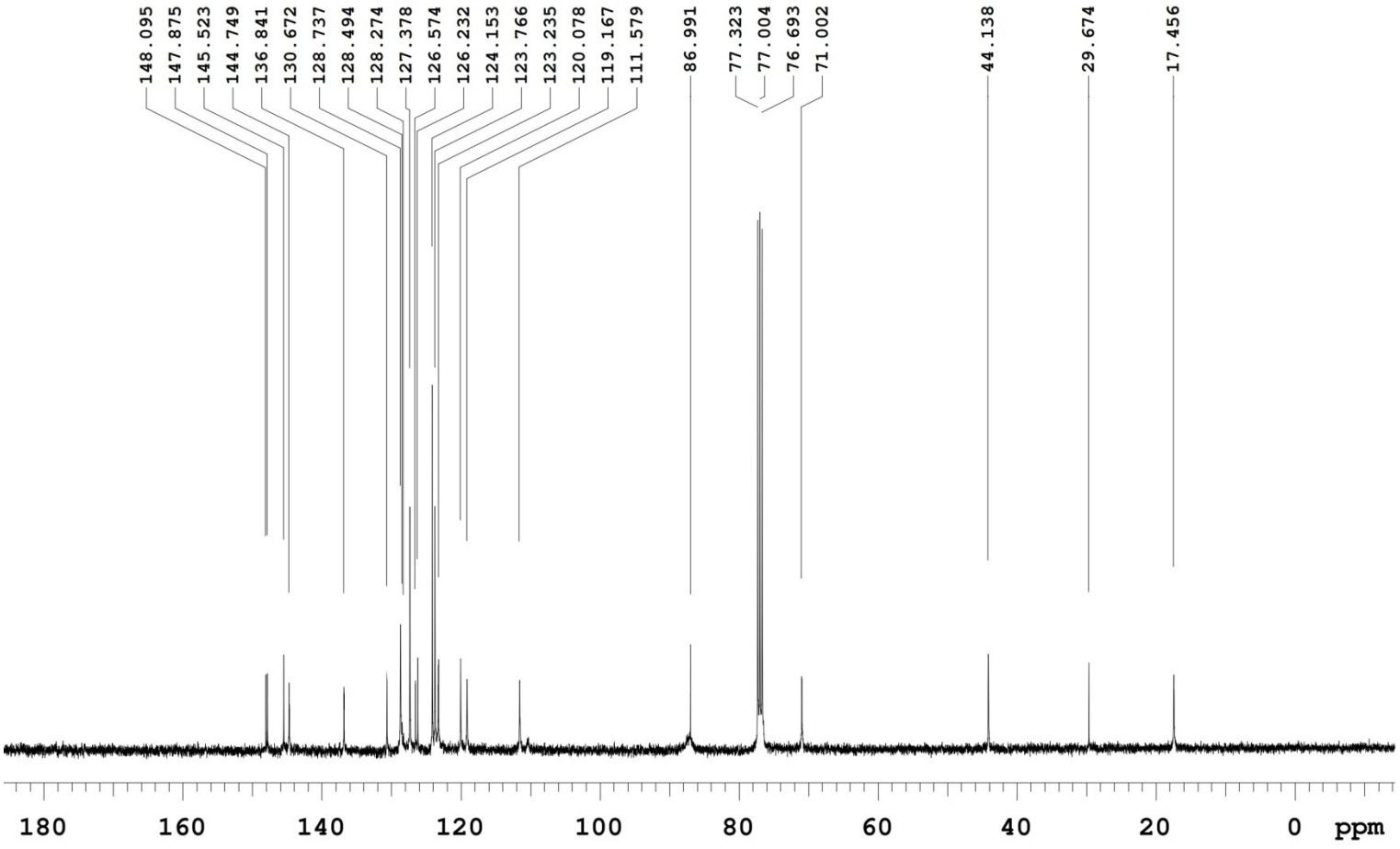
^{1}H NMR of **3p** in $CDCl_3$

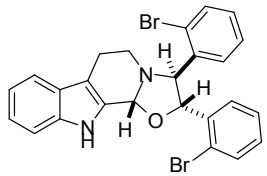




3p

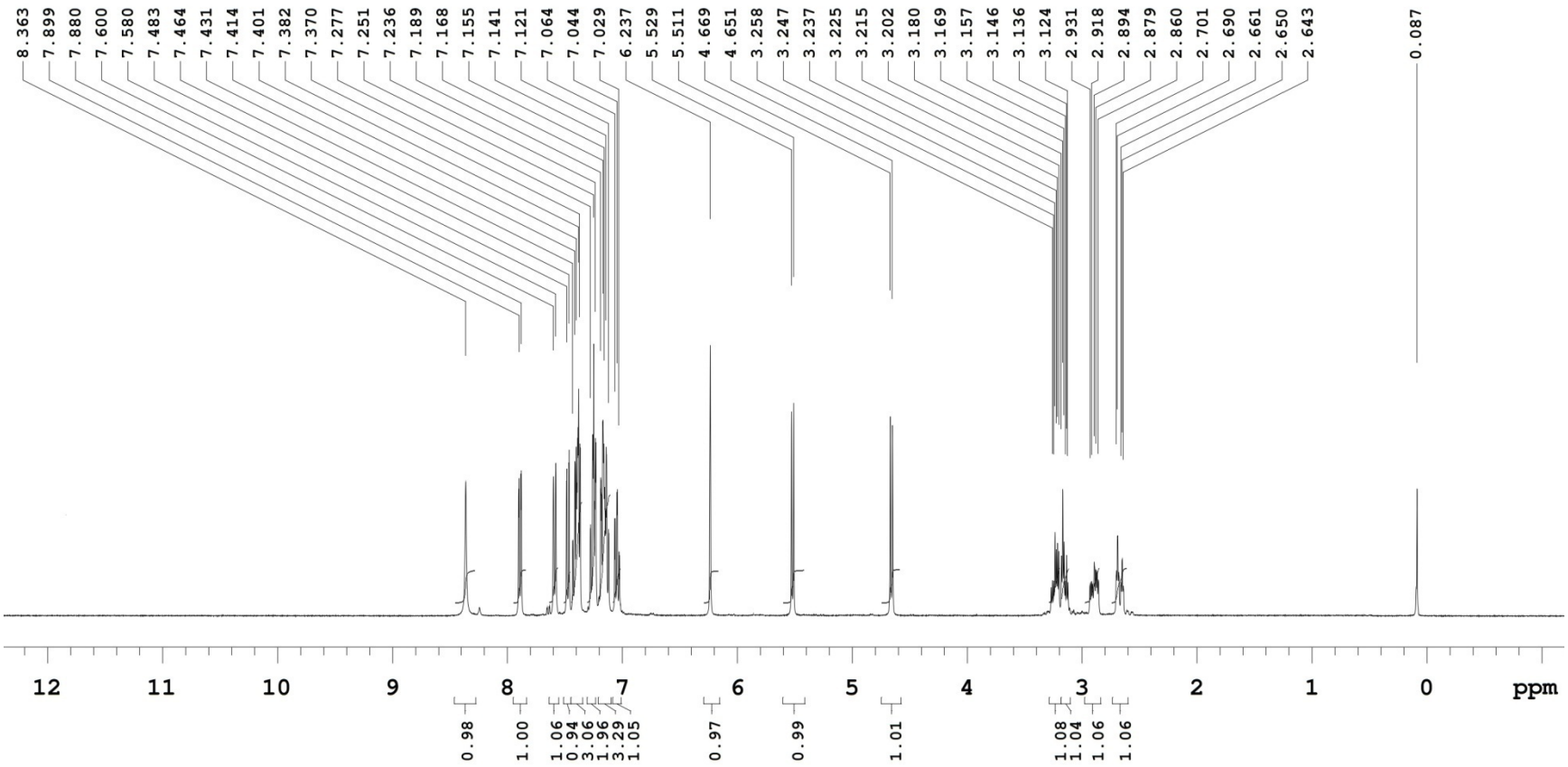
^{13}C NMR of **3p** in $CDCl_3$



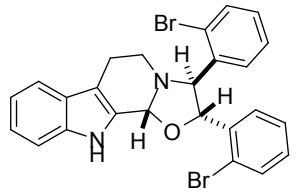


3q

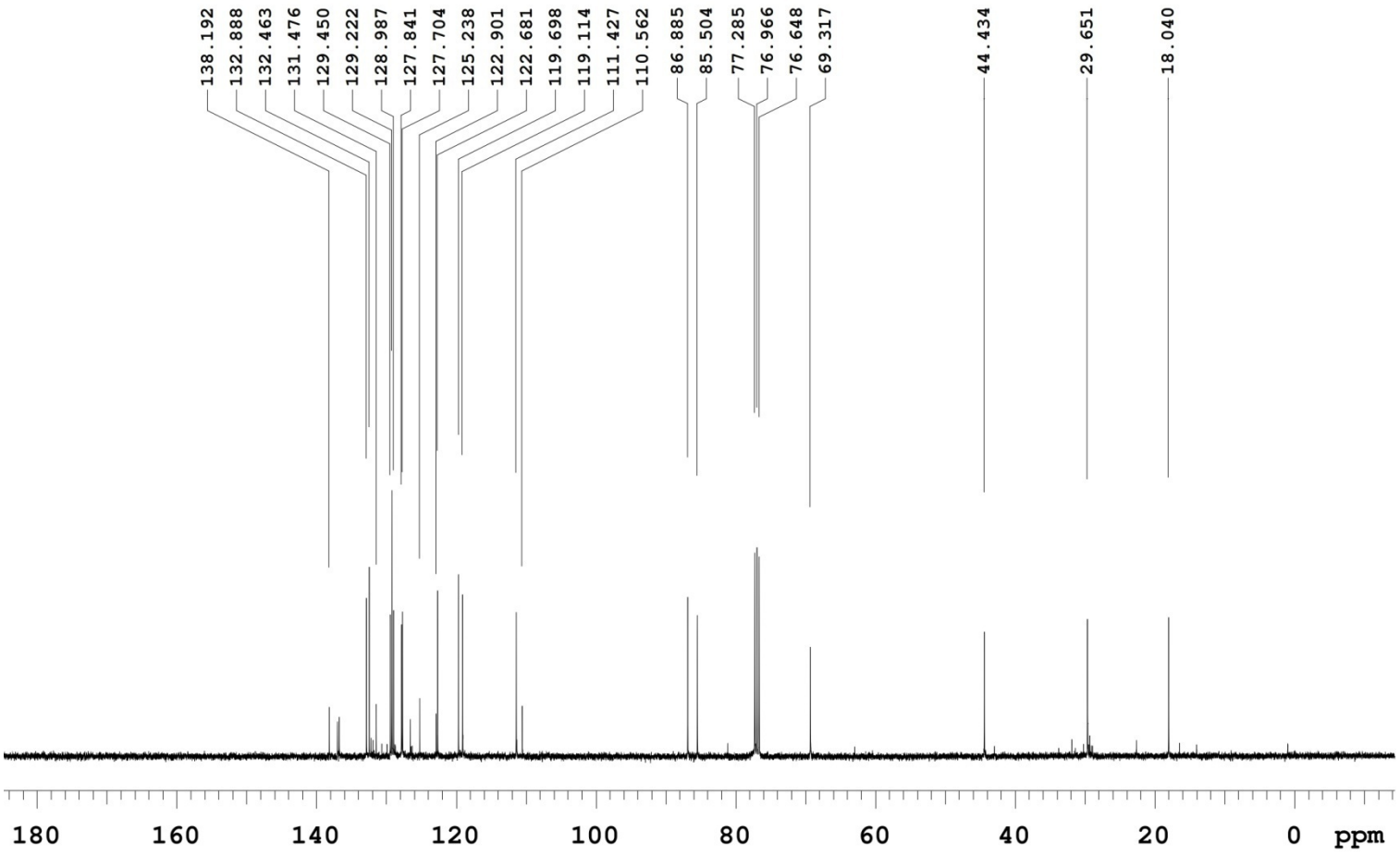
^{1}H NMR of **3q** in $CDCl_3$



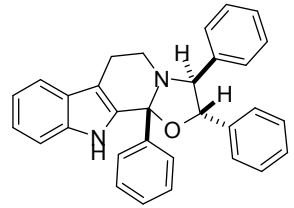
^{13}C NMR of **3q** in $CDCl_3$



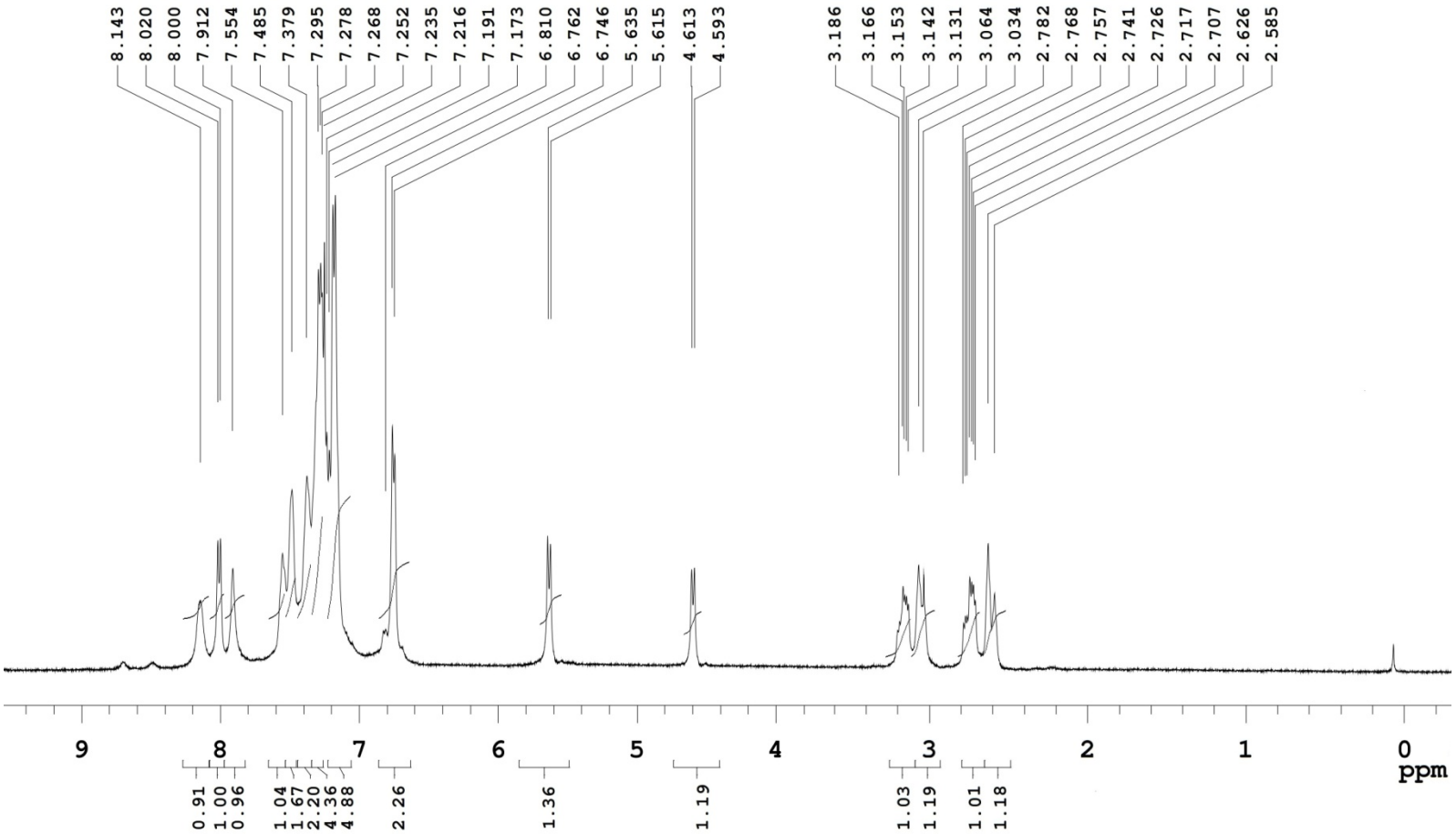
3q

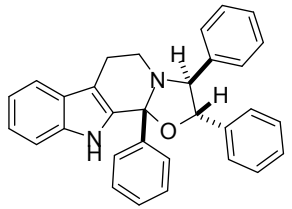


^{1}H NMR of **3r** in $CDCl_3$



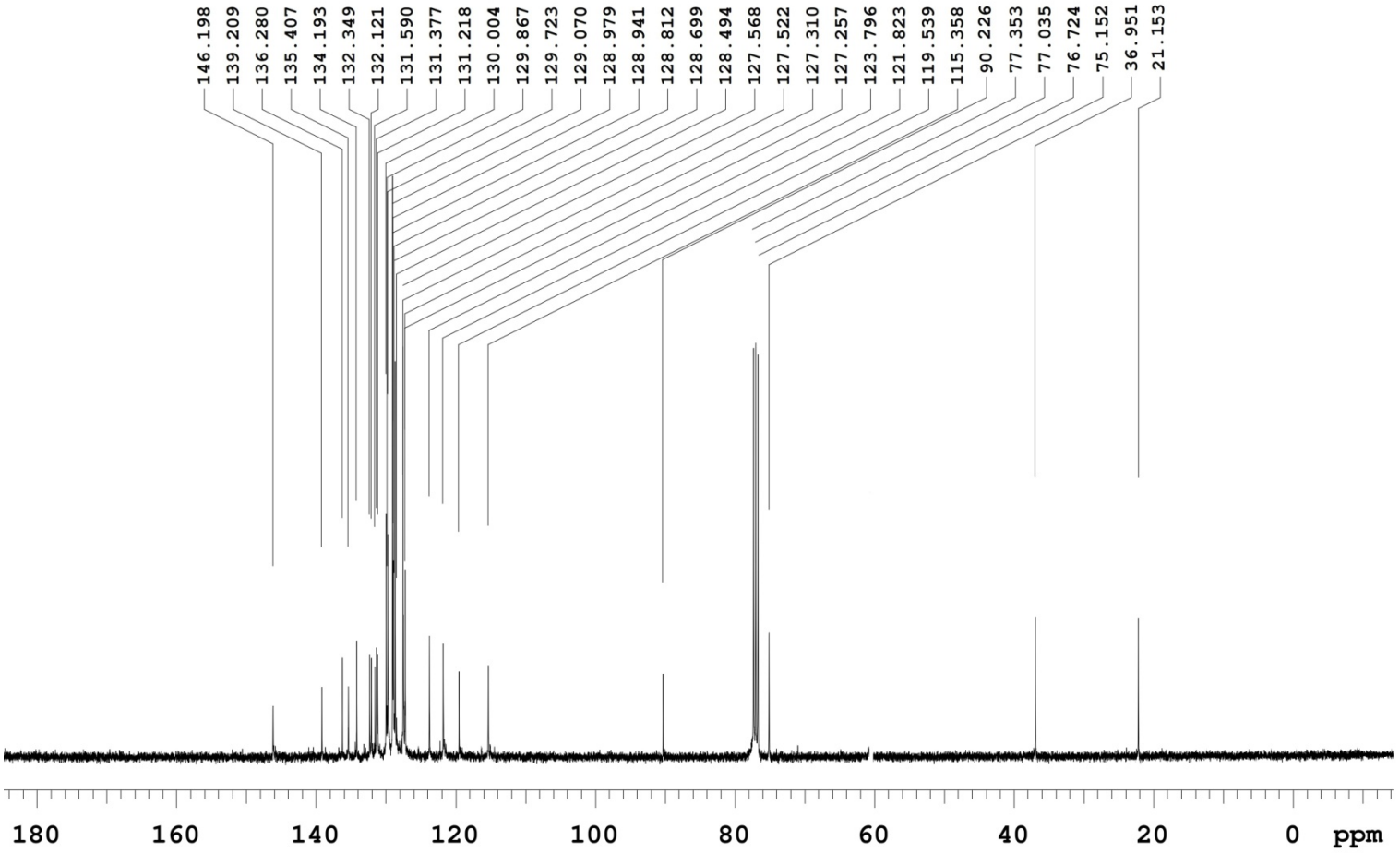
3r



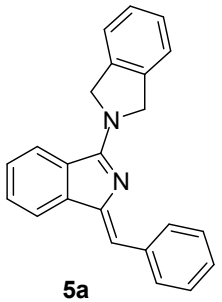


3r

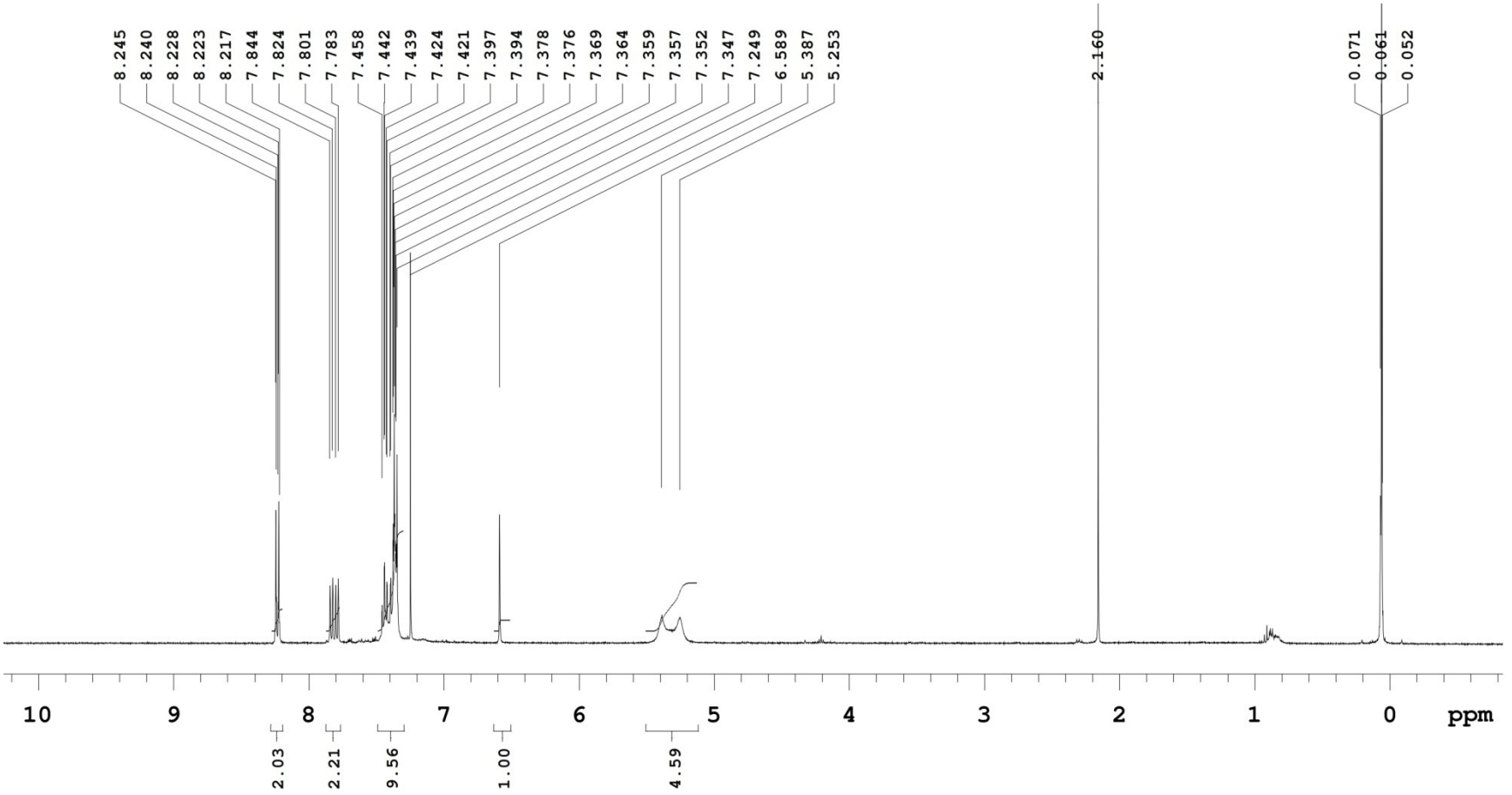
^{13}C NMR of **3r** in $CDCl_3$



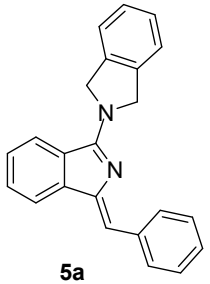
^{1}H NMR of **5a** in $CDCl_3$



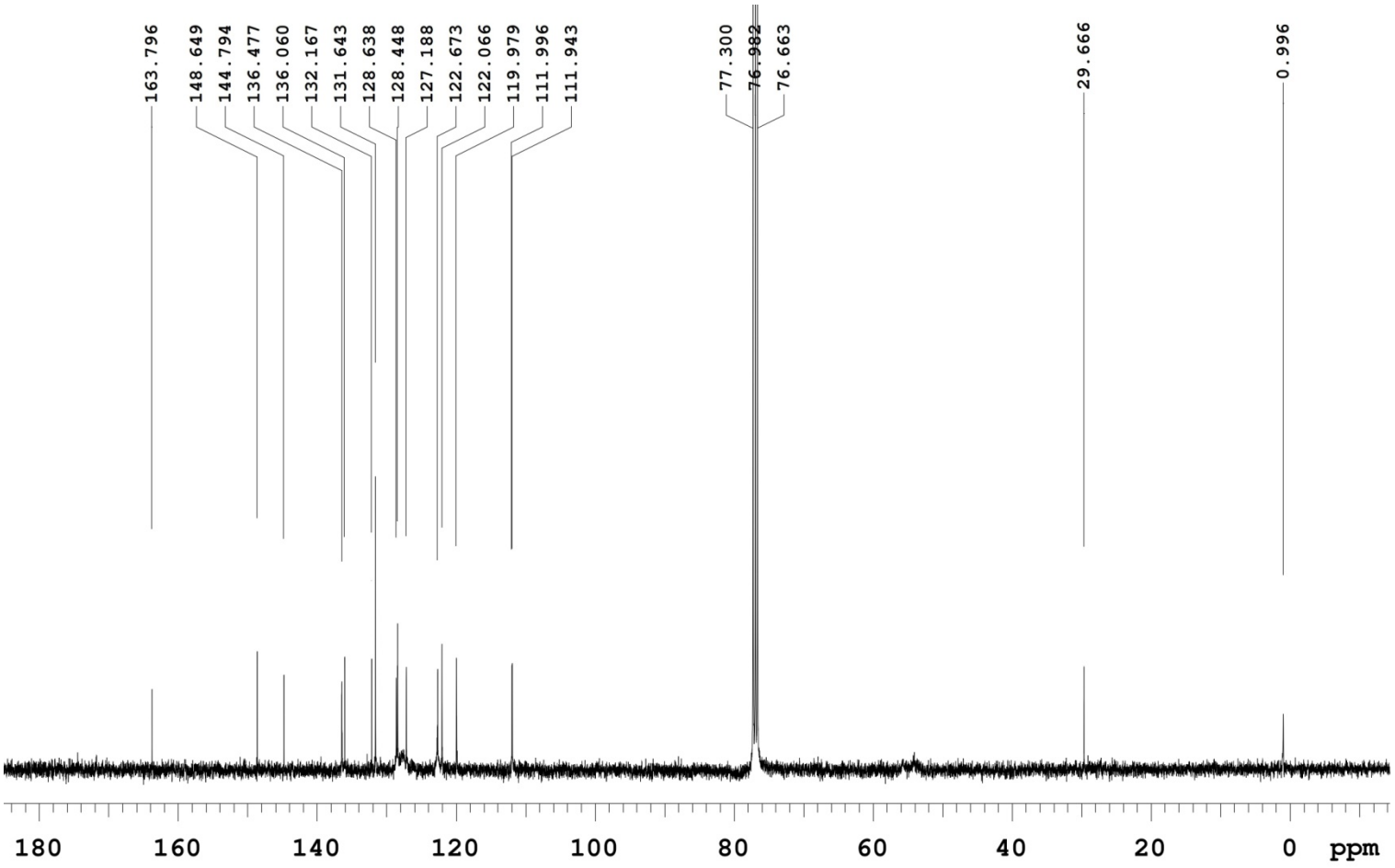
5a



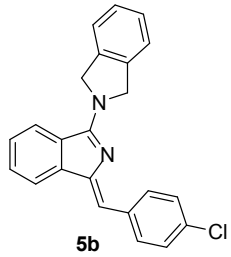
^{13}C NMR of **5a** in $CDCl_3$

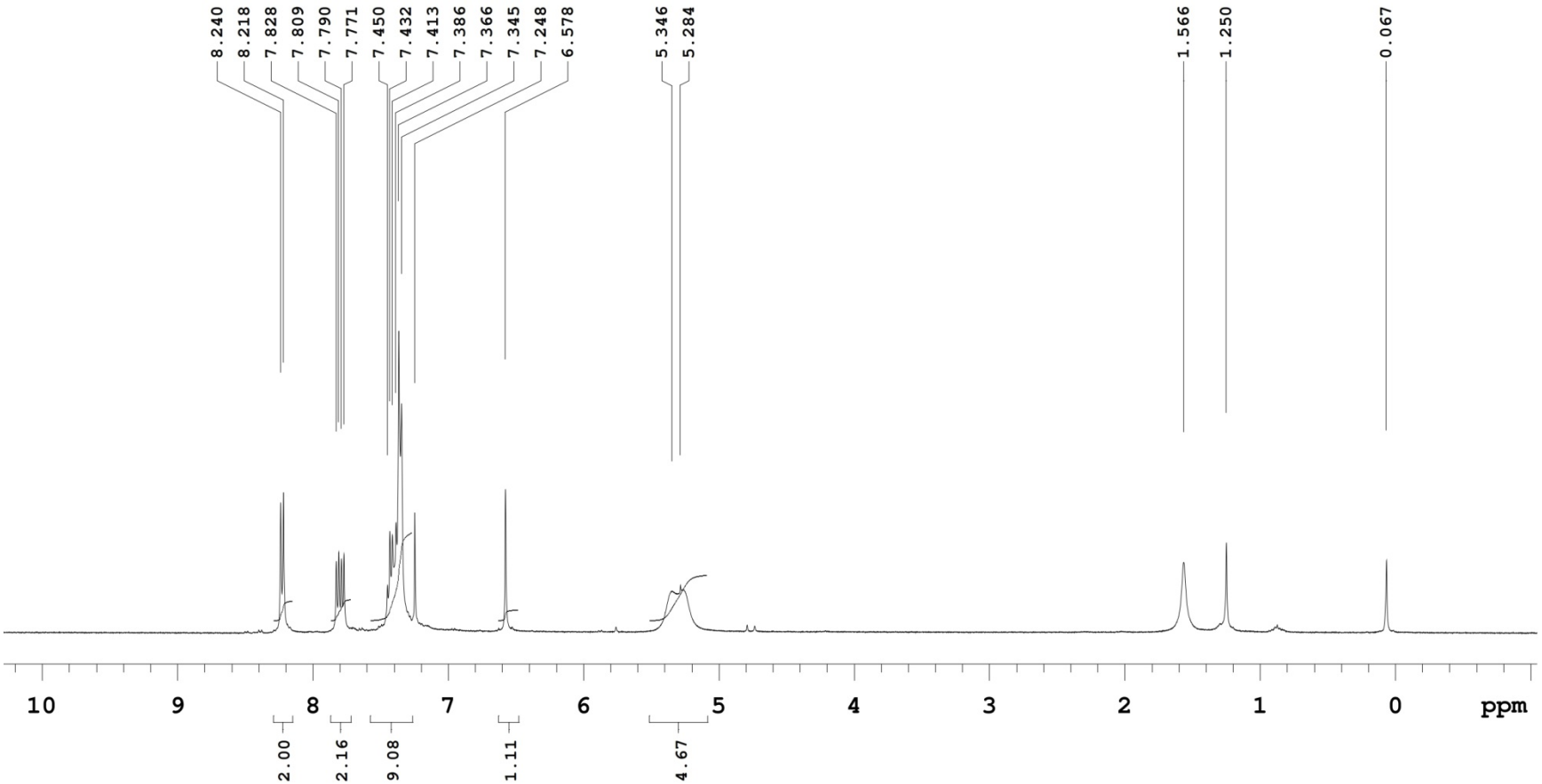


5a

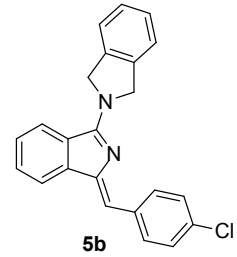


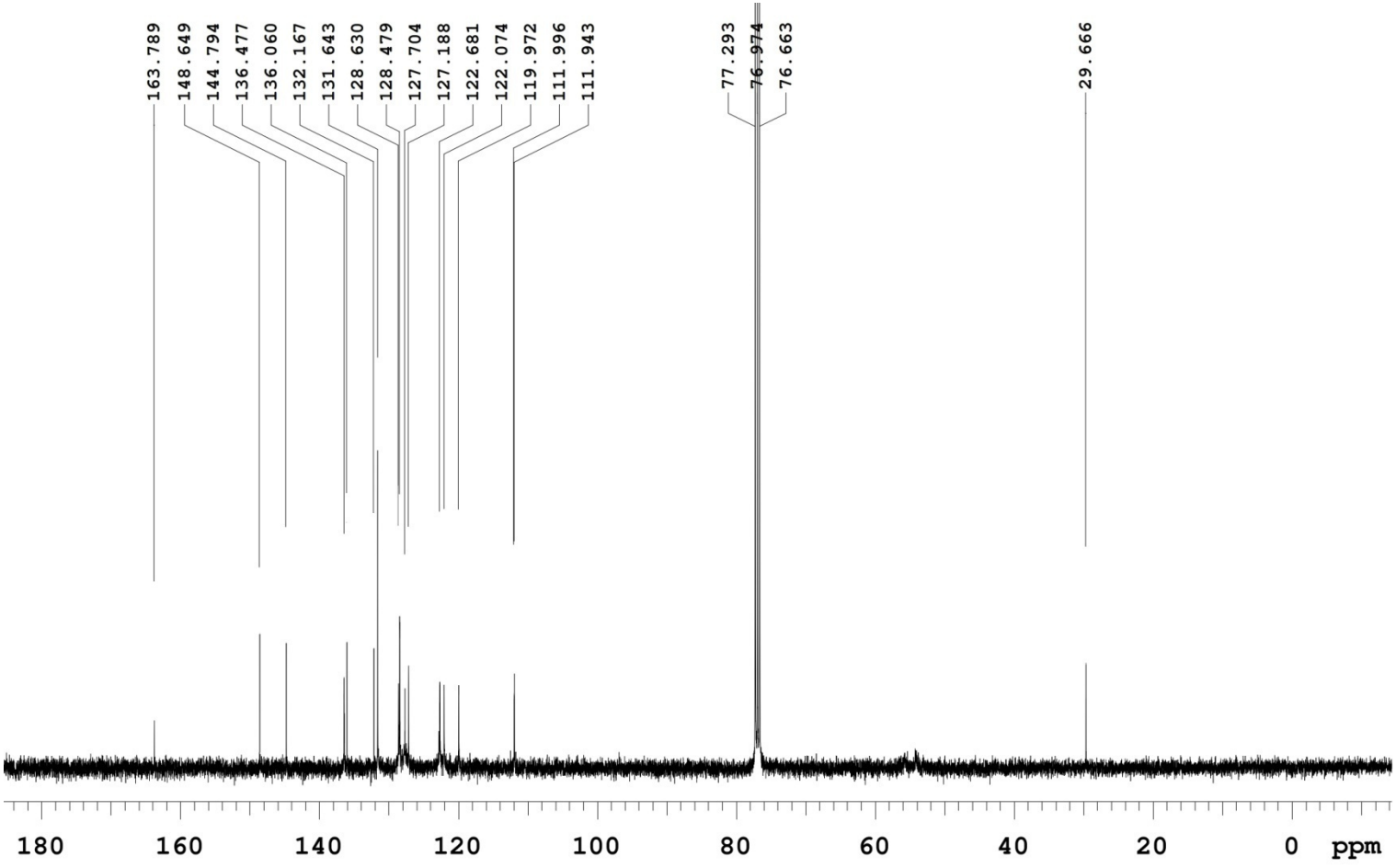
^{1}H NMR of **5b** in $CDCl_3$



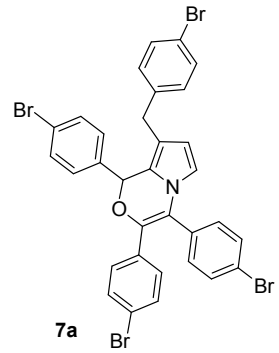


^{13}C NMR of **5b** in $CDCl_3$

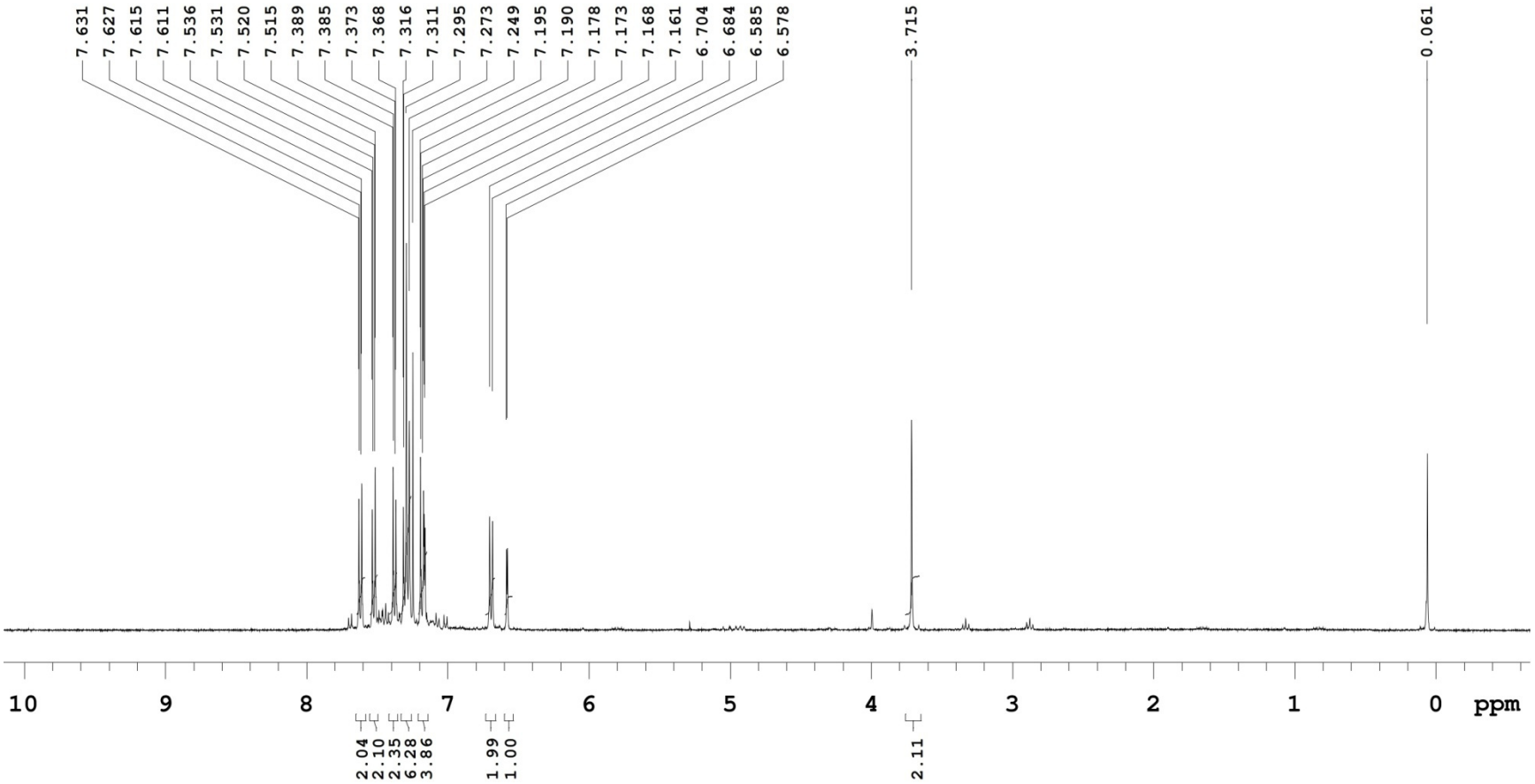




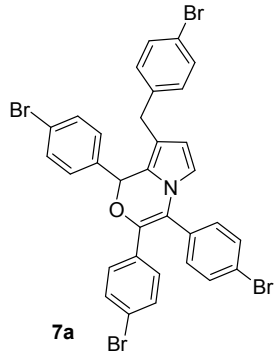
^{1}H NMR of **7a** in $CDCl_3$



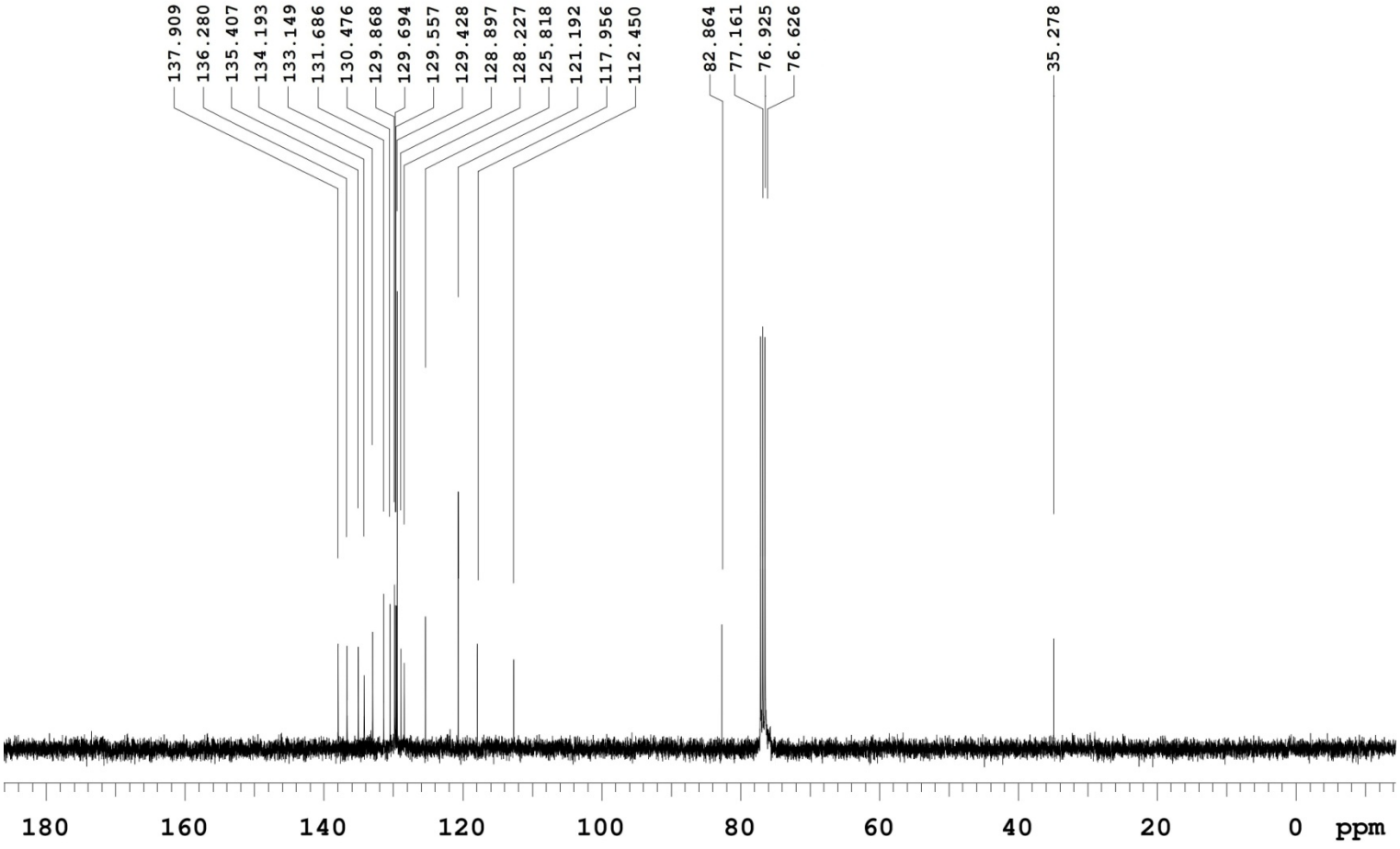
7a



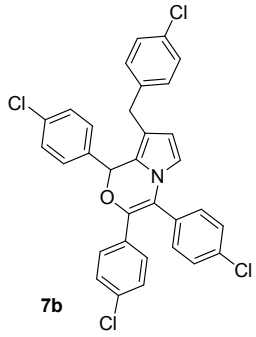
^{13}C NMR of **7a** in $CDCl_3$

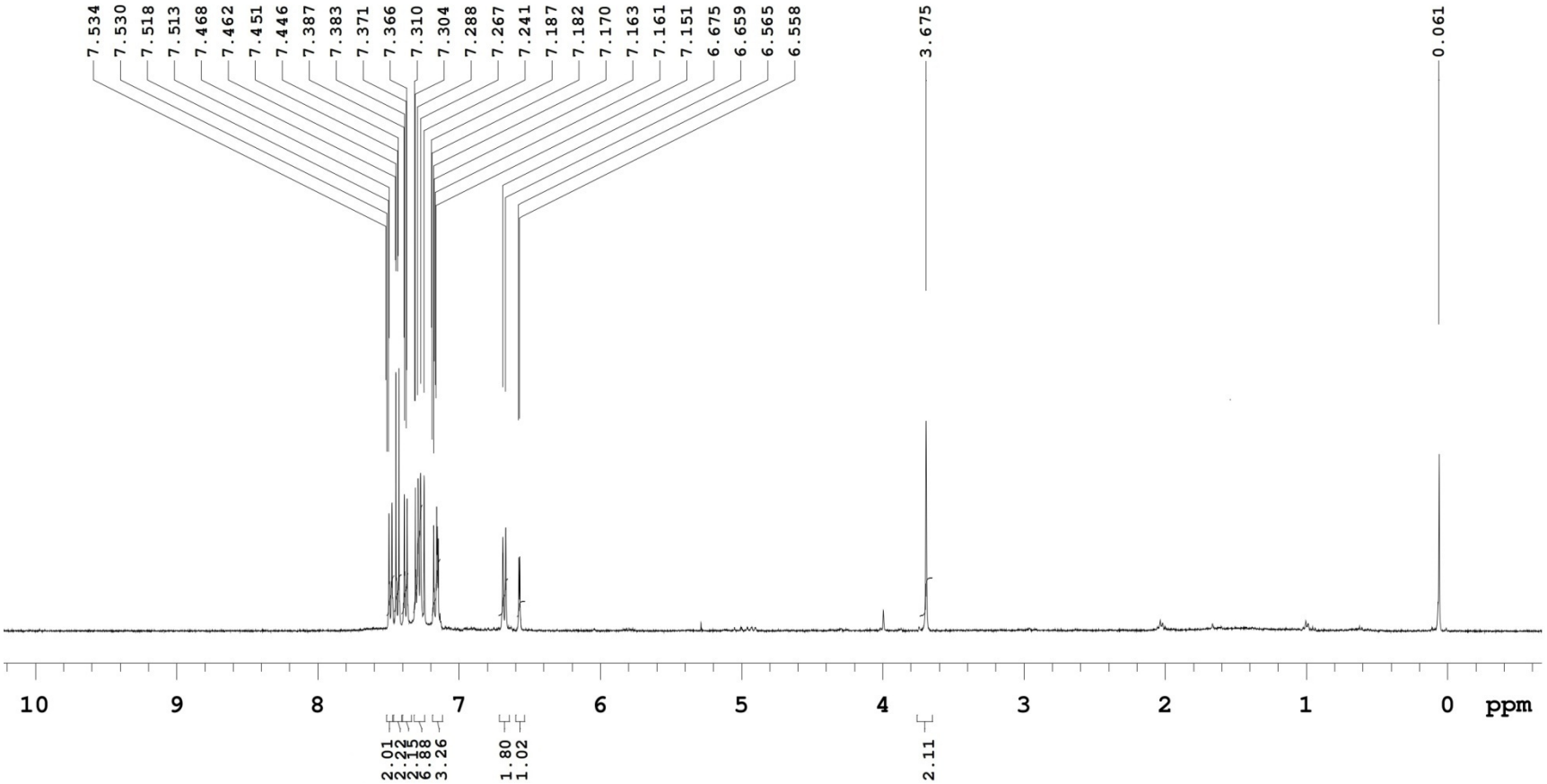


7a

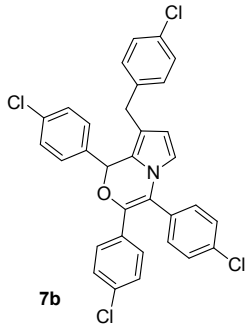


^{1}H NMR of **7b** in $CDCl_3$





^{13}C NMR of **7b** in $CDCl_3$



7b