Palladium Catalyzed, Multicomponent Synthesis of Fused-Ring Pyrroles from Aryl Iodides, Carbon Monoxide and Alkyne-Tethered Imines

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Supporting Information

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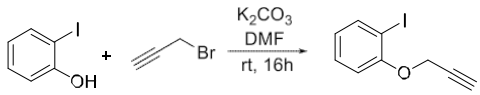
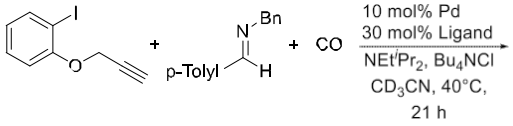
I. Use of ortho-Alkyne-Tethered Aryl Iodides

Substrate Synthesis



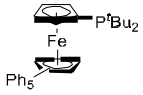
In analogy to literature reports,[1] solution of 2-iodophenol (858 mg, 3.9 mmol) and K_2CO_3 (815 mg, 5.9 mmol) in DMF (15 ml) was prepared in a 100 mL round bottom flask equipped with a magnetic stir bar. The solution was allowed to stir for 20 minutes at room temperature. To the solution was added a propargyl bromide solution in toluene 80% w/w (758 mg, 5.1 mmol). The reaction mixture was stirred overnight at room temperature. Water (20 mL) was then added and the resulting mixture was extracted three times with diethyl ether (15 mL portions). The ether fractions were combined and filtered through $MgSO_4$. The solvent was removed *in vacuo* and the crude residue was purified by column chromatography on silica gel (eluent: n-hexane/ethyl acetate 10:1) to afford 1-iodo-2-(prop-2-yn-1-yloxy)benzene as a colorless liquid in 80% yield (798 mg, 3.1 mmol).

Attempted Synthesis of Pyrrole with *ortho*-Alkyne-Tethered Aryl Iodide, Imine, and CO



In a glovebox, *ortho*-alkyne tethered aryl iodide (12 mg, 0.045 mmol), (p-tolyl)HC=NBn (6.3 mg, 0.03 mmol), NEt^iPr_2 (7.8 mg, 0.06 mmol), $[Pd(allyl)Cl]_2$ (0.5 mg, 0.0015 mmol), Bu_4NCl (17 mg, 0.06 mmol), P^tBu_3 (1.8 mg, 0.009 mmol) (or other ligands, see Table S1 below) and BnOBz internal standard (3.2 mg, 0.015 mmol) were transferred to a J-Young NMR with three 0.25 mL portions of CD_3CN. The NMR tube was then sealed with a screw-cap, taken out of the glovebox, and charged with 4 atm of CO. The tube was then heated in an oil bath at 40 ºC. The reaction was analyzed by ^1H NMR over the course of 21 h, and the consumption of starting material was quantified via integration against the internal standard. ^1H NMR analysis reveals the protonation of the base and the partial disappearance of the aryl iodide. In most cases, imine is left intact and there is no evidence of pyrrole formation.

Table S1. Reactivity of *ortho*-alkyne tethered aryl iodide, imine, and CO

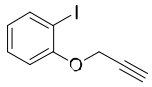
Entry	Pd Cat.	PR_3	Remaining Aryl Iodide (%)[c]	Remaining Imine (%)	Pyrrole (%)
1	$Pd(OAc)_2$	PPh_3	34	94	-
2	$Pd_2dba_3.CH_3Cl$	-	38	96	-
3	$[\{Pd(allyl)Cl\}_2]$	P^tBu_3	5	94	-
4	$[\{Pd(allyl)Cl\}_2]$	P(*o*-tolyl)$_3$	67	87	-
5	$[\{Pd(allyl)Cl\}_2]$		5	49	-

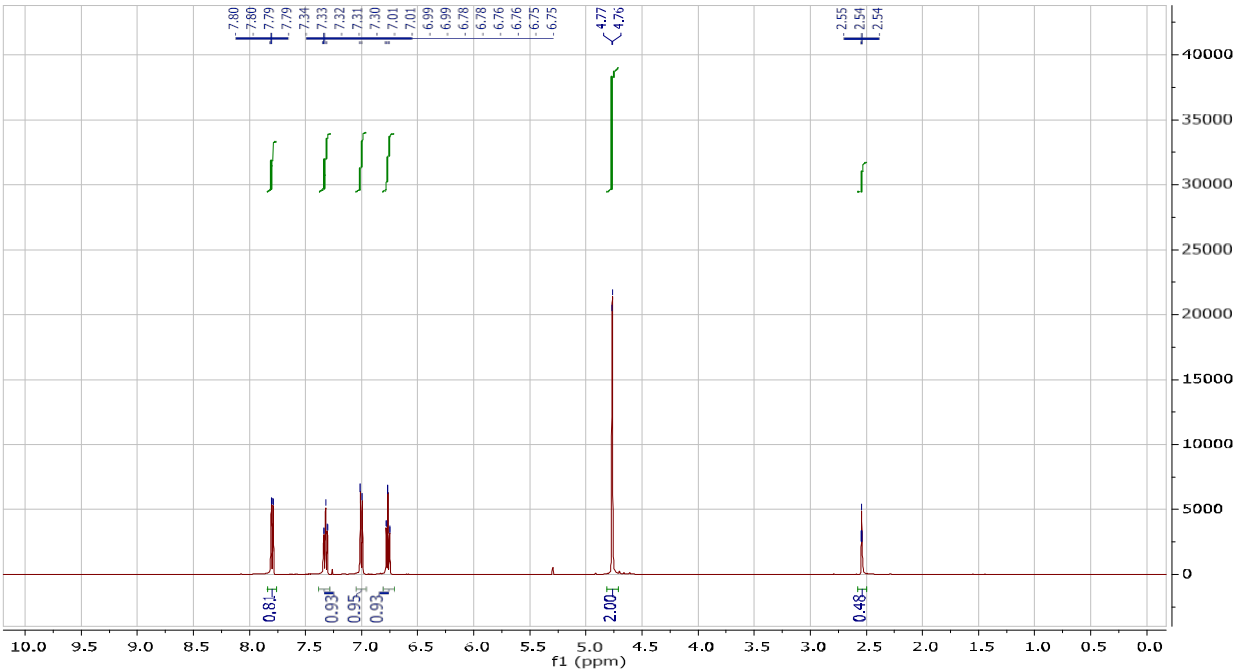
II. References

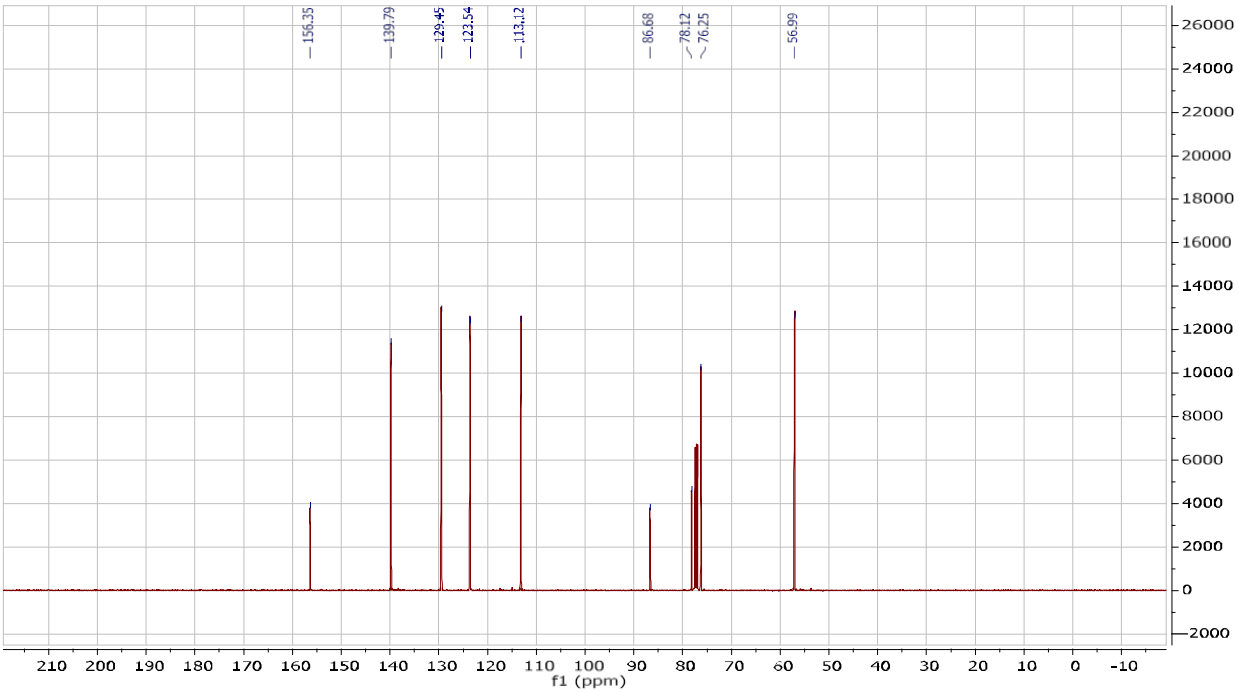
(1) Hadden, M.; Goodman, A.; Guo, C.; Guzzo, P. R.; Henderson, A. J.; Pattamana, K.; Ruenz, M.; Sargent, B. J.; Swenson, B.; Yet, L. *Bioorg. Med. Chem. Lett.* **2010,** *20*, 2912.

III. NMR Spectra

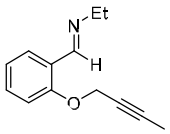
^{1}H and ^{13}C NMR spectra of Alkyne-tethered Aryl Iodide

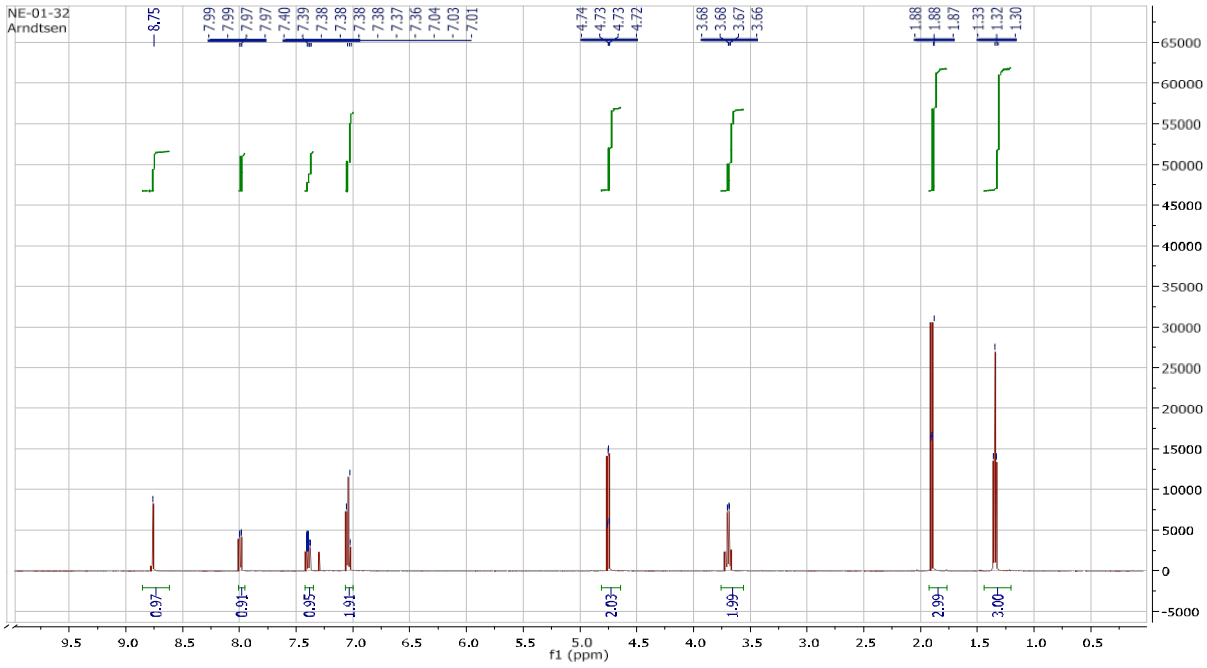


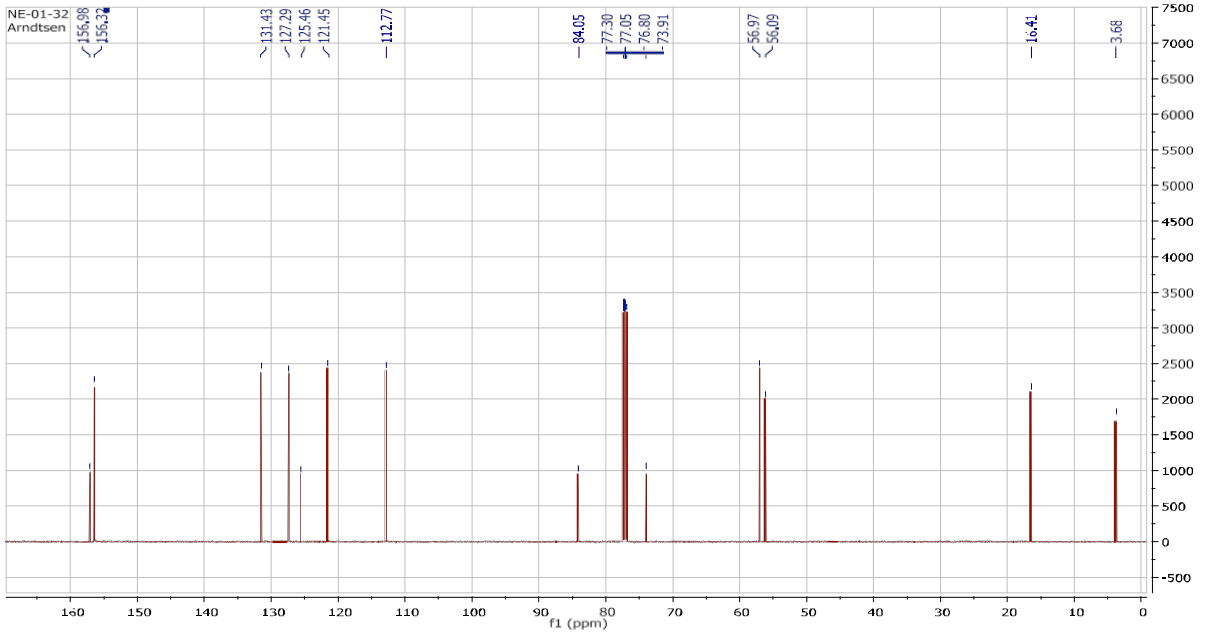




^{1}H and ^{13}C NMR spectra of 1a







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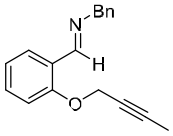

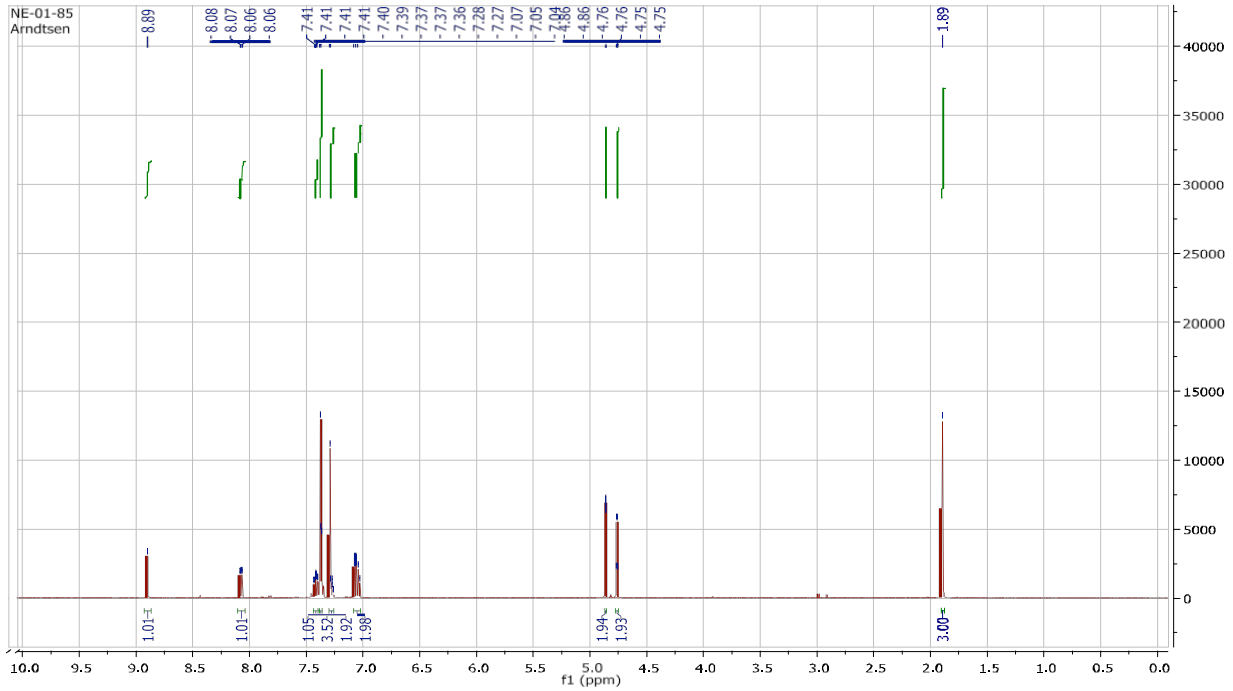

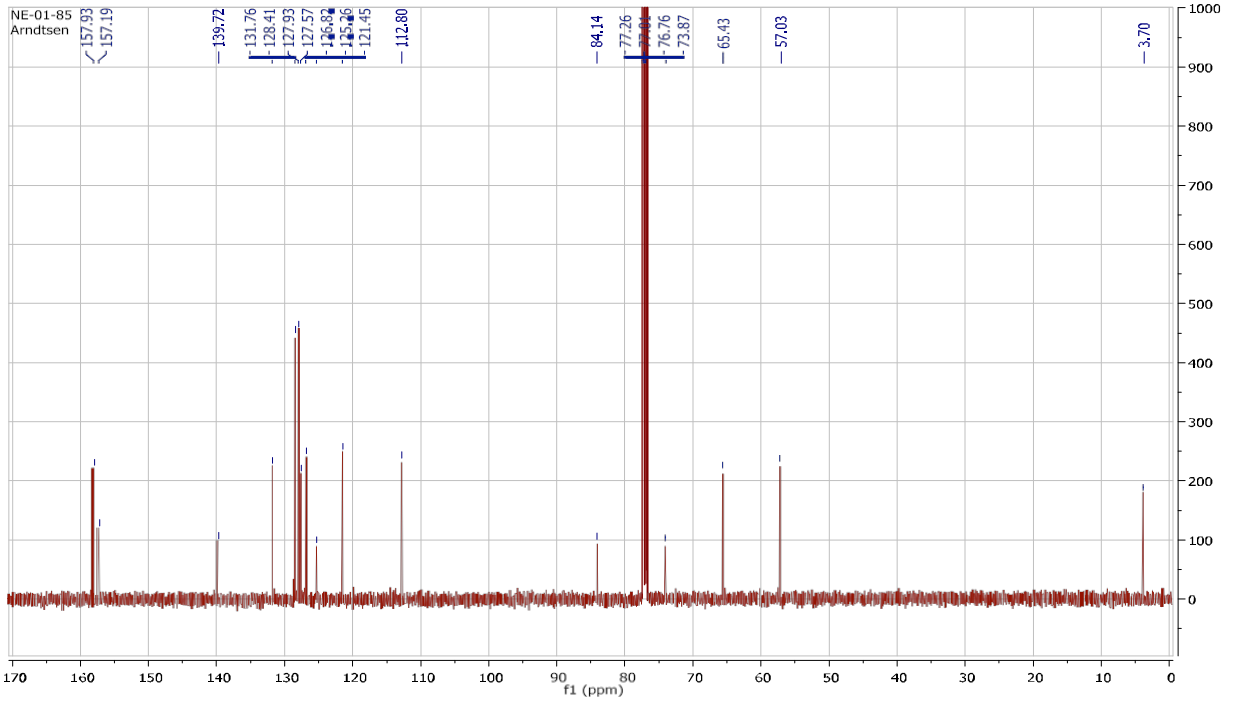

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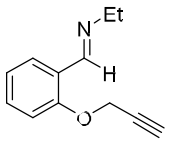

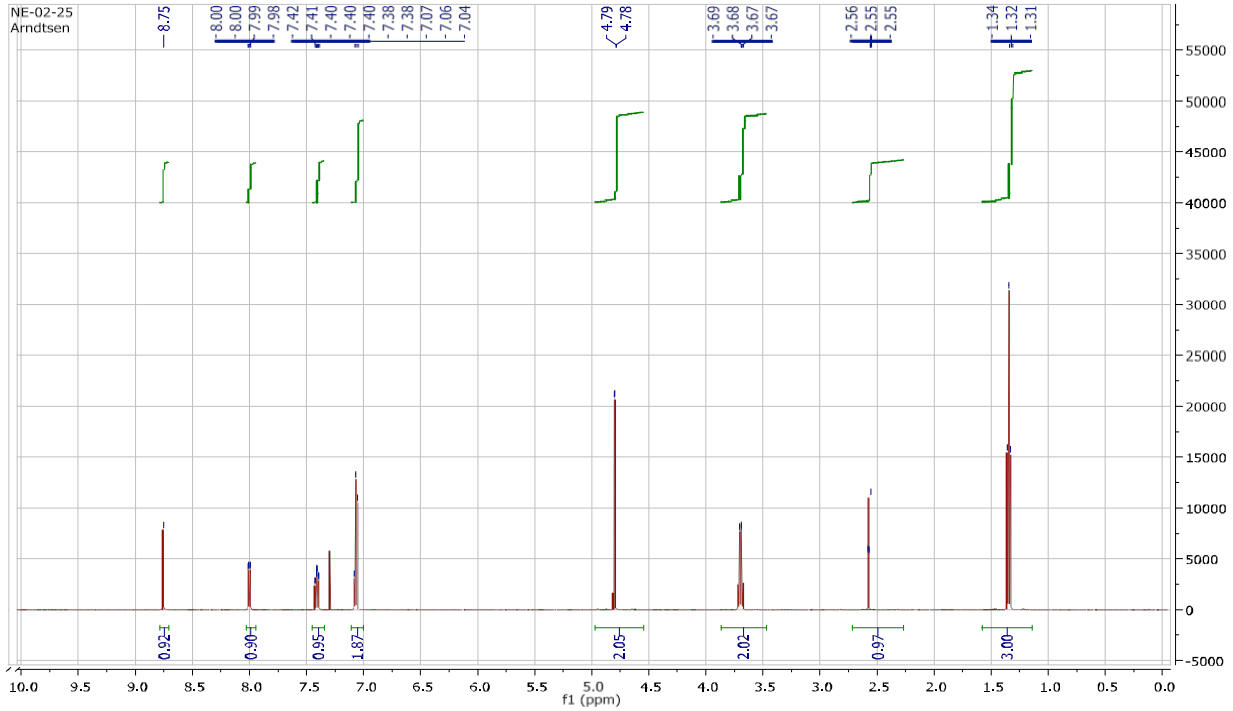

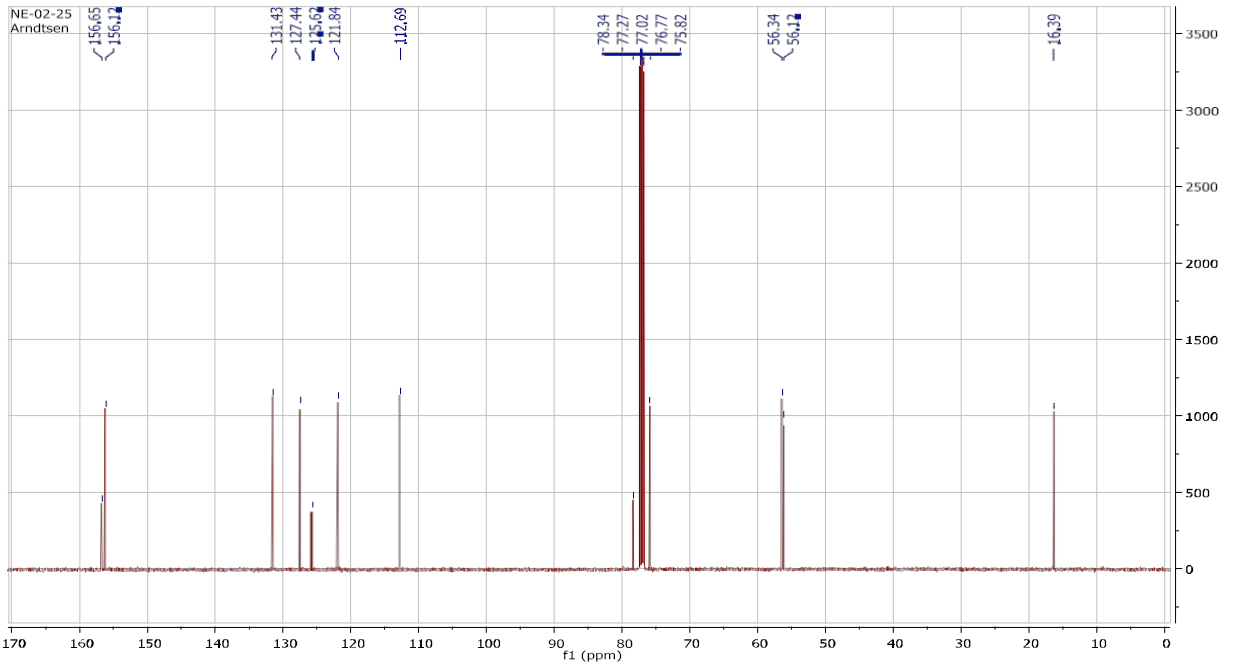

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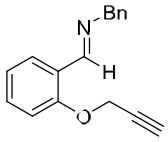
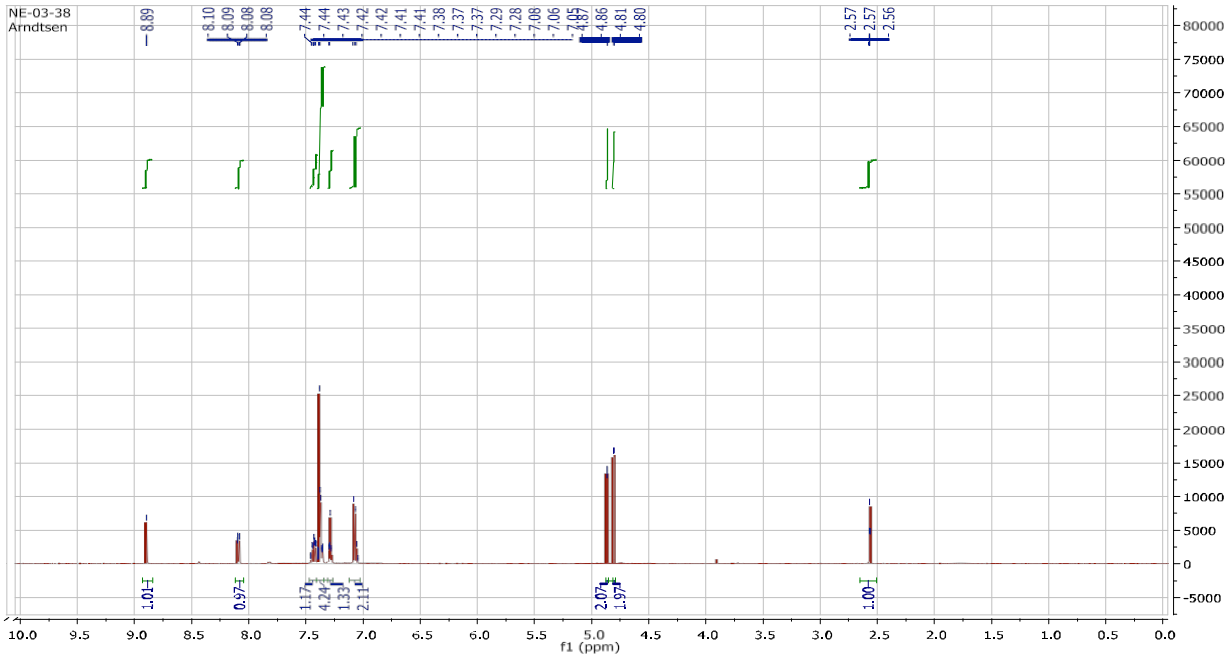
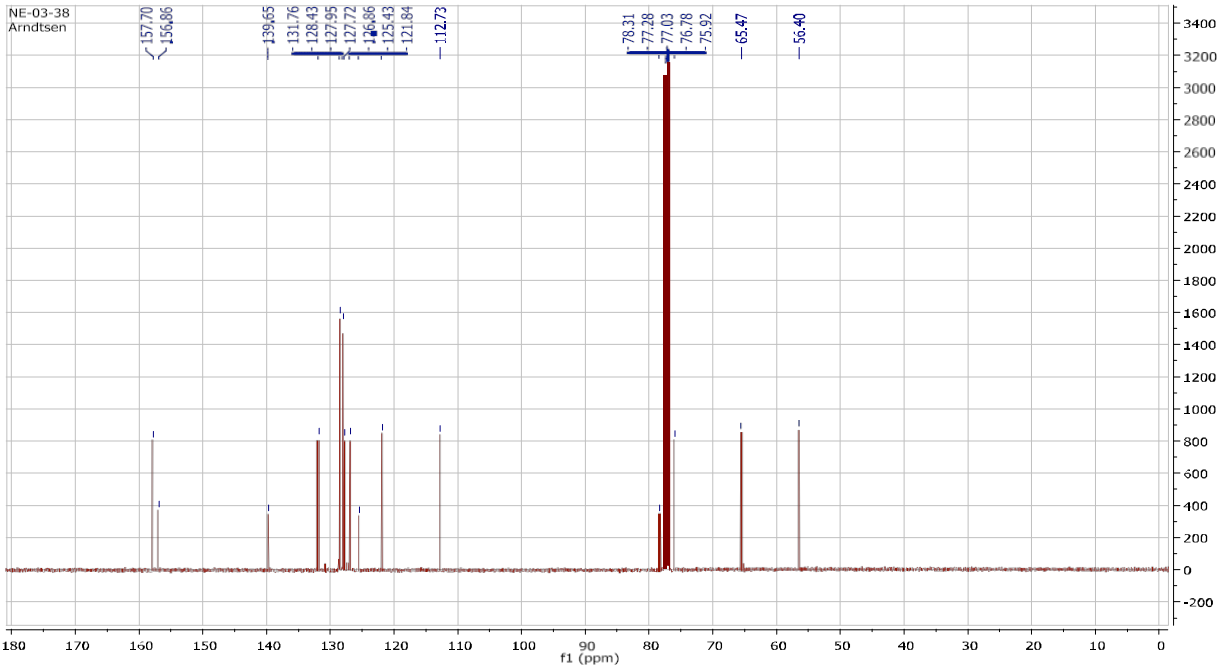
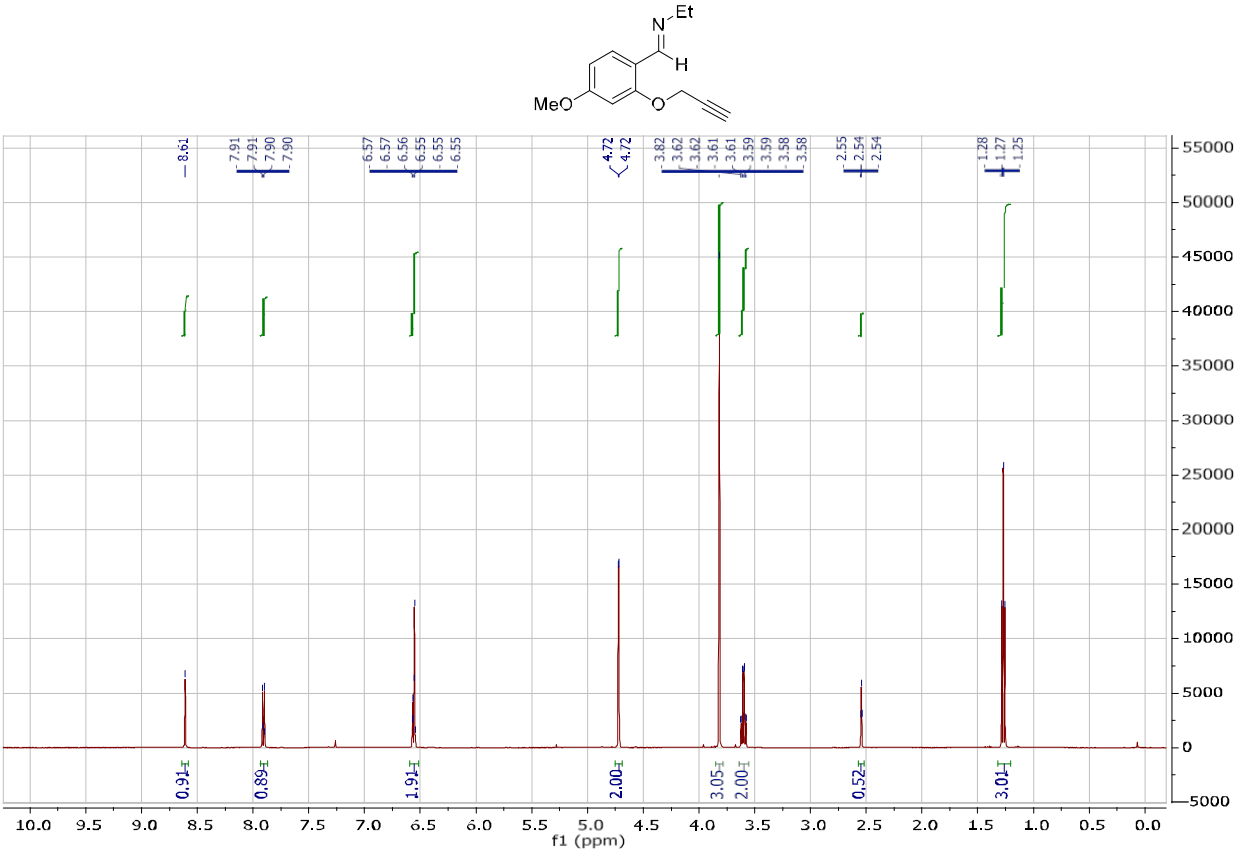
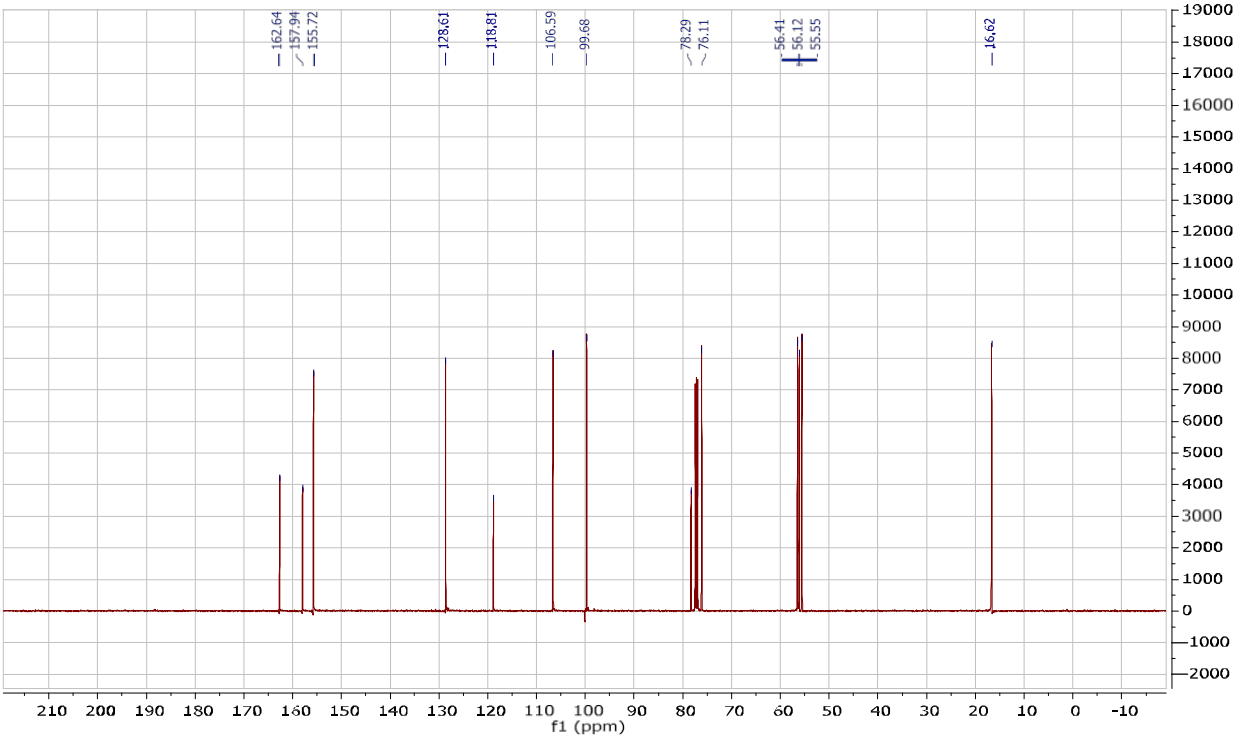




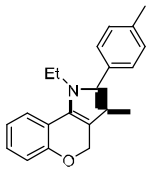


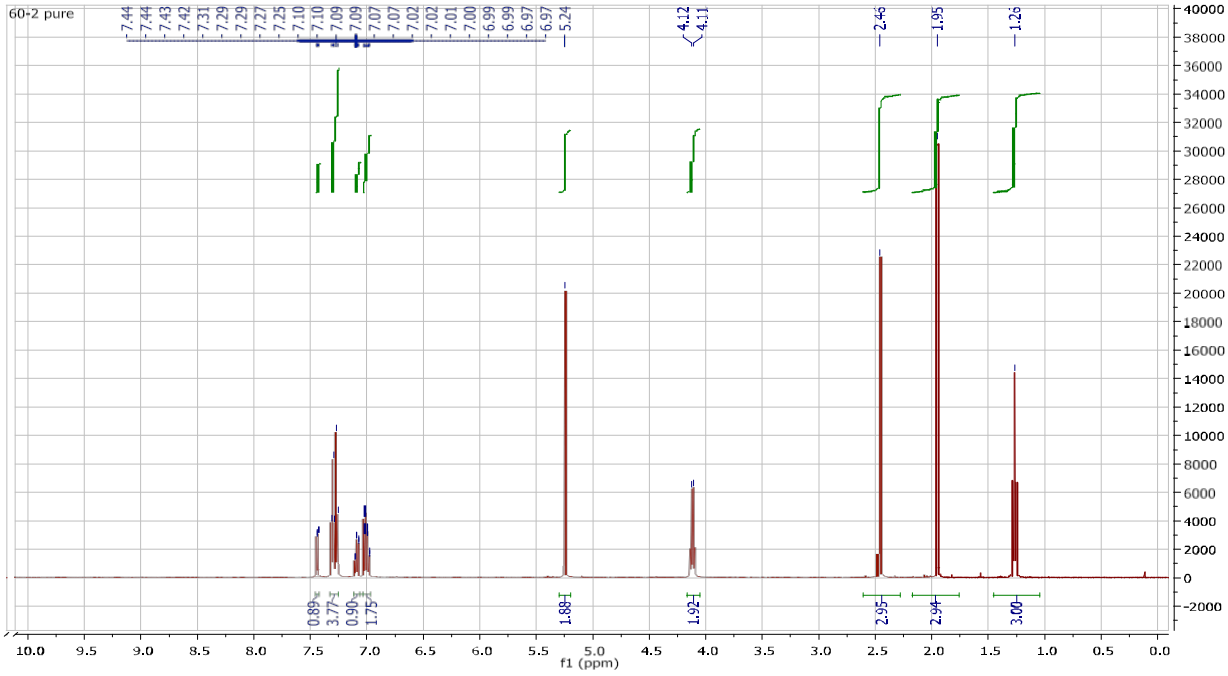
^{1}H and ^{13}C NMR spectra of 1e

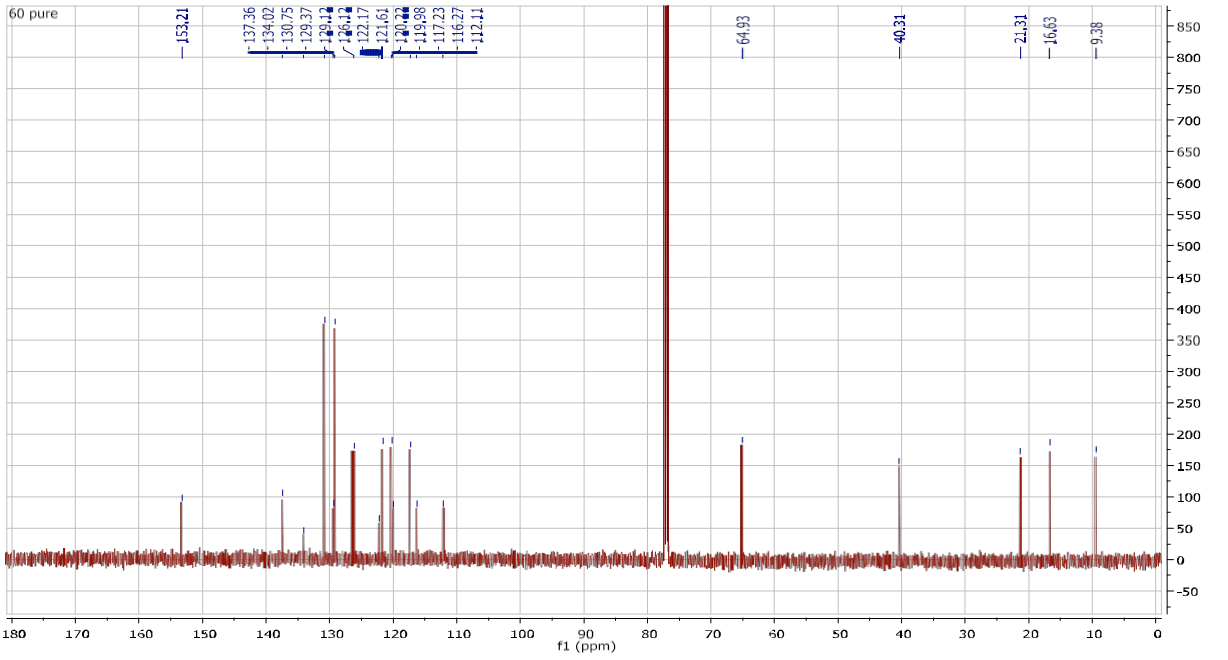




^{1}H and ^{13}C NMR spectra of 3a







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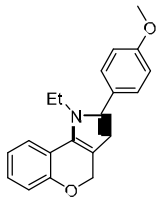

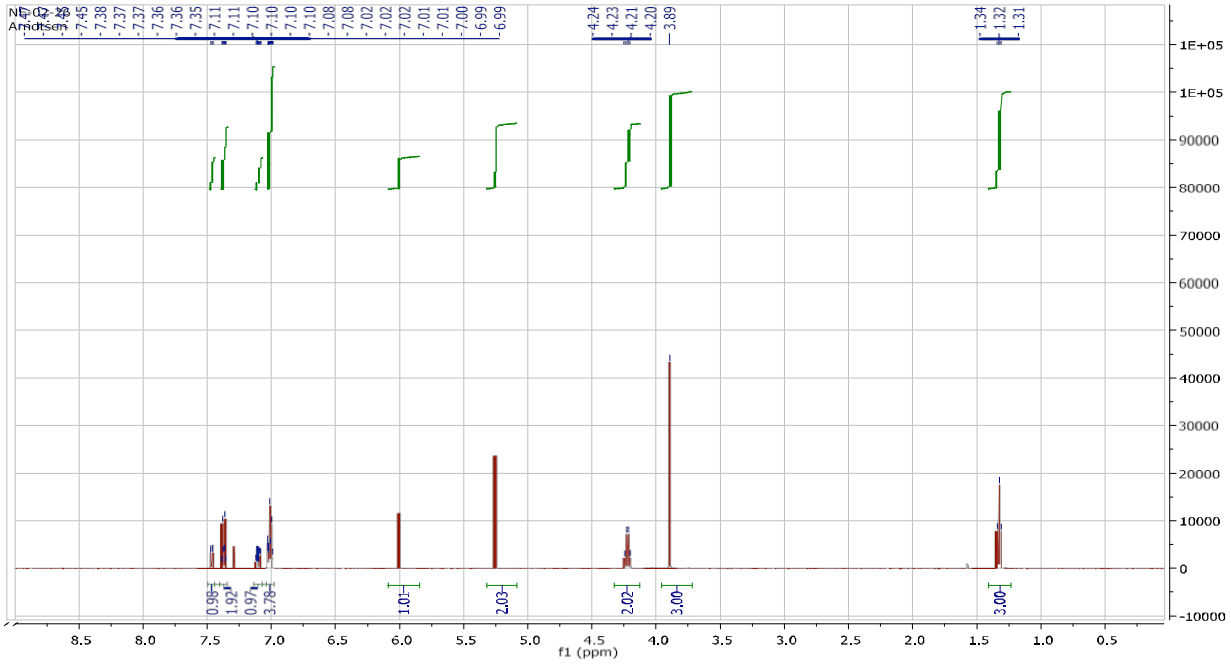

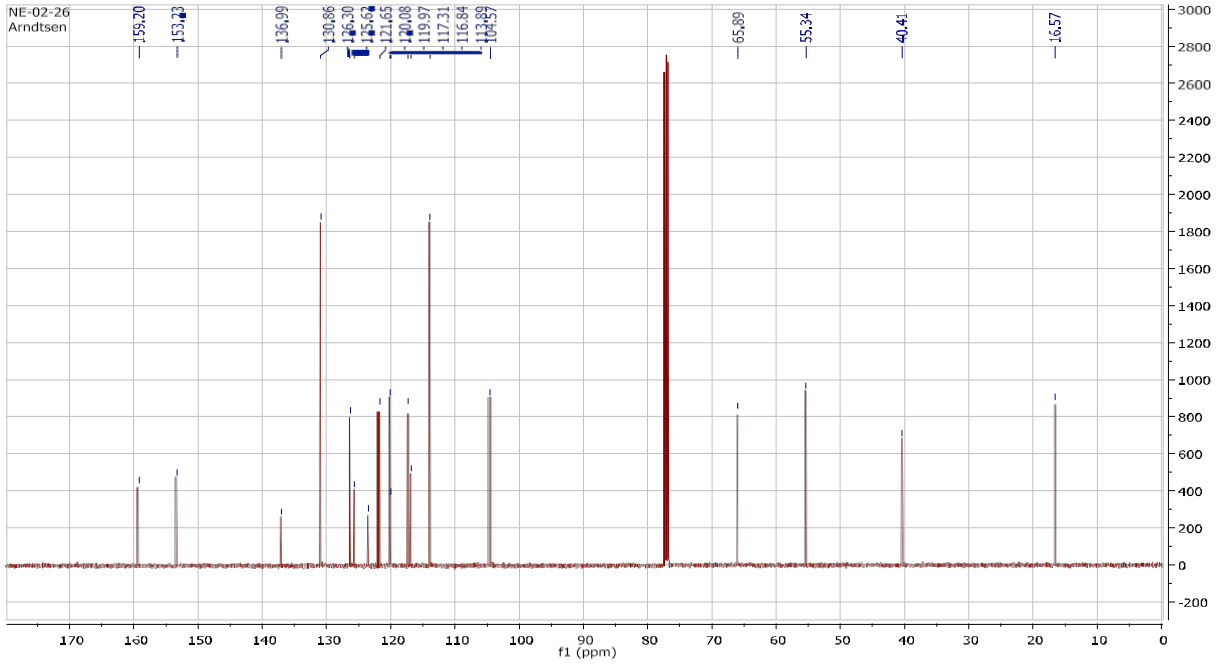

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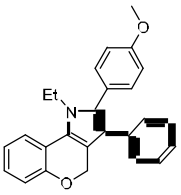

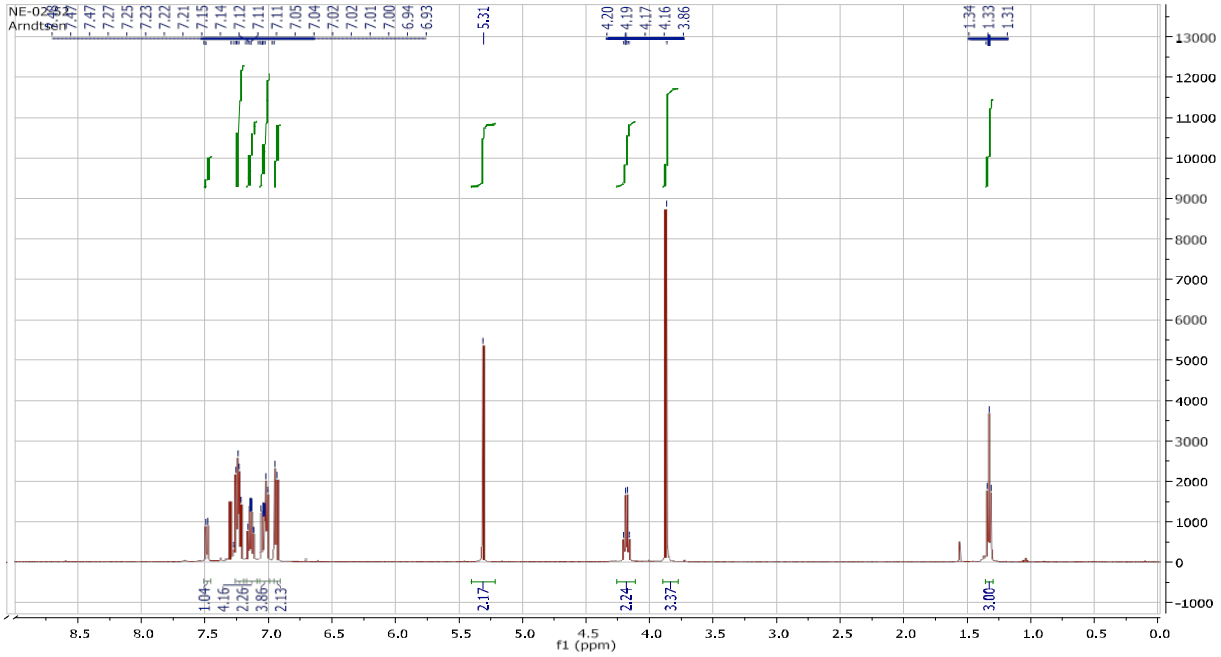

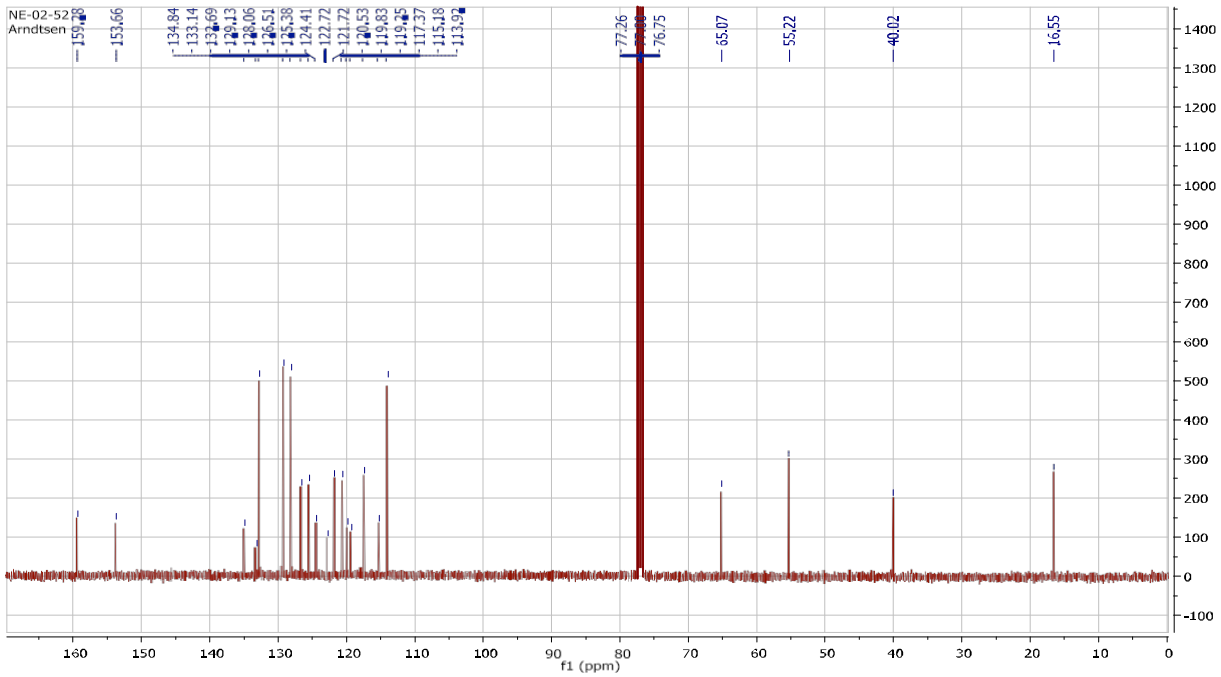

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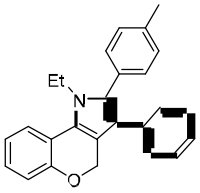

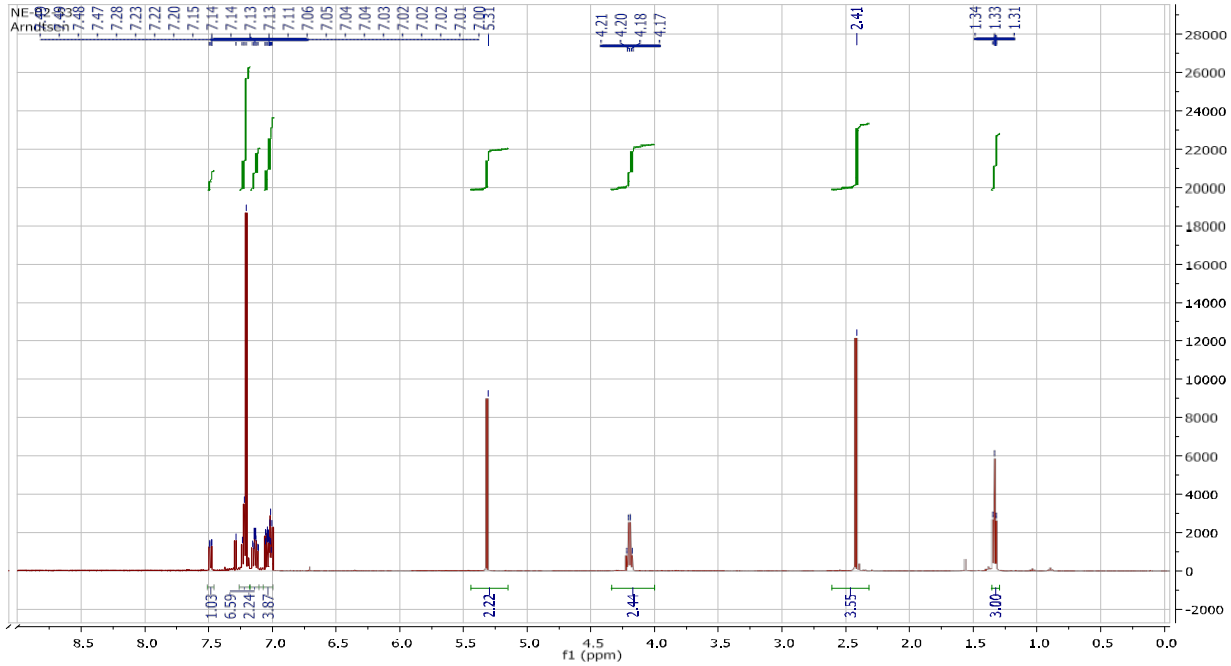

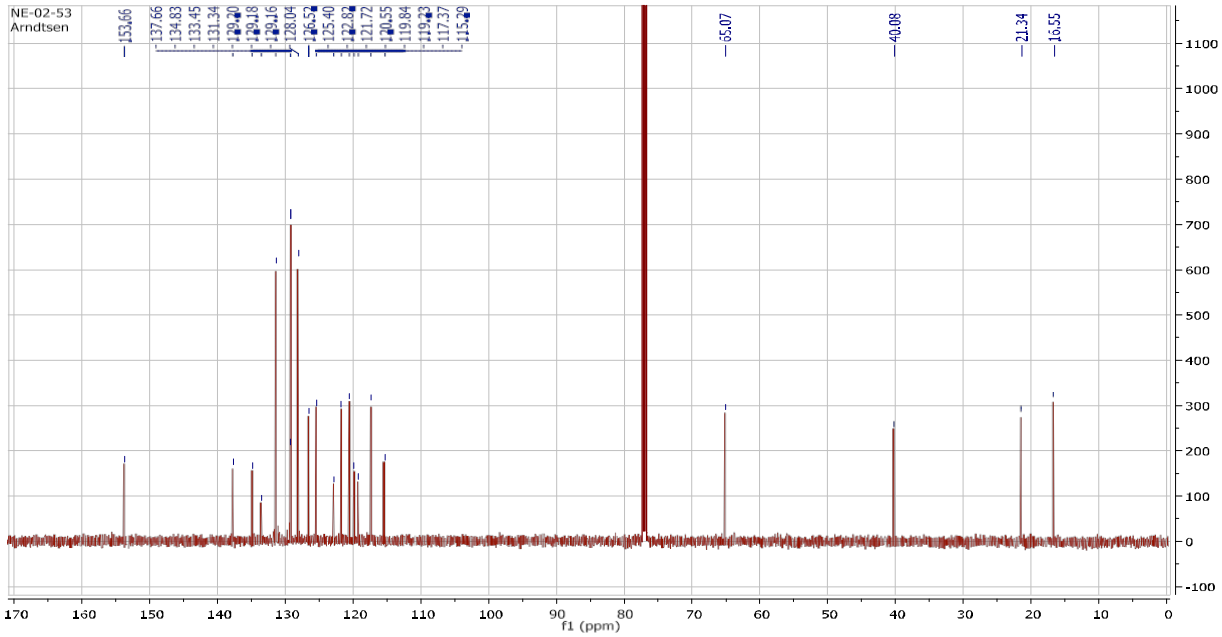

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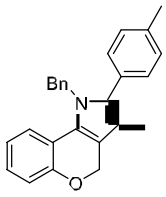
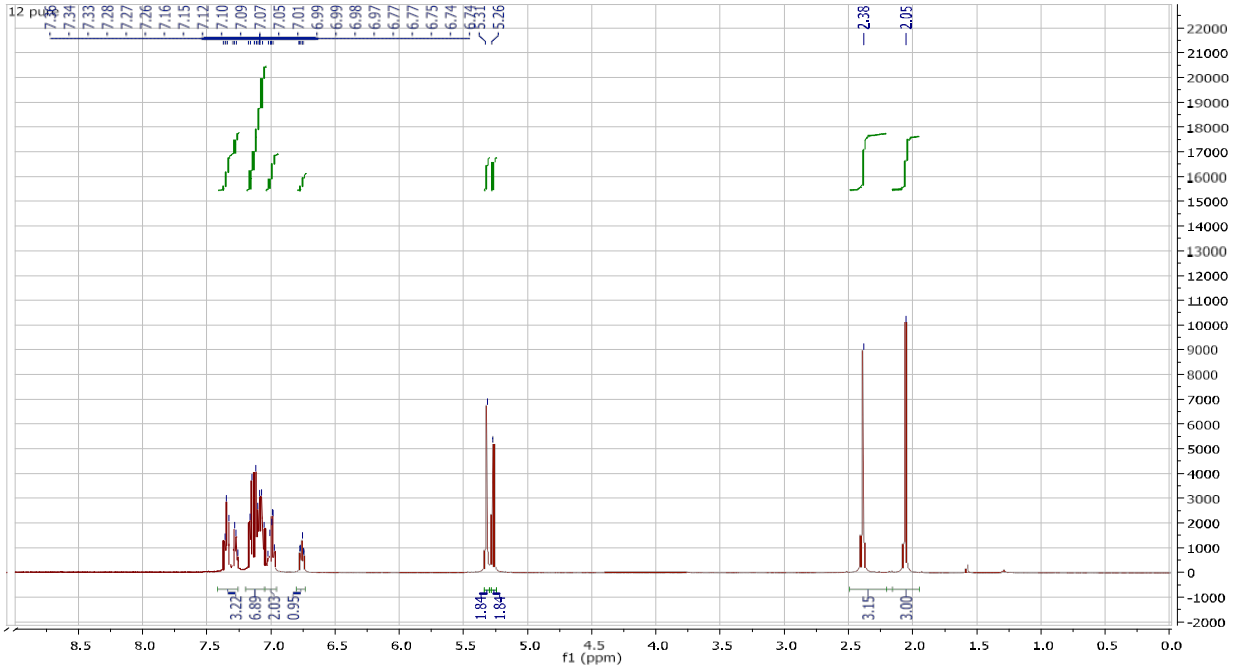
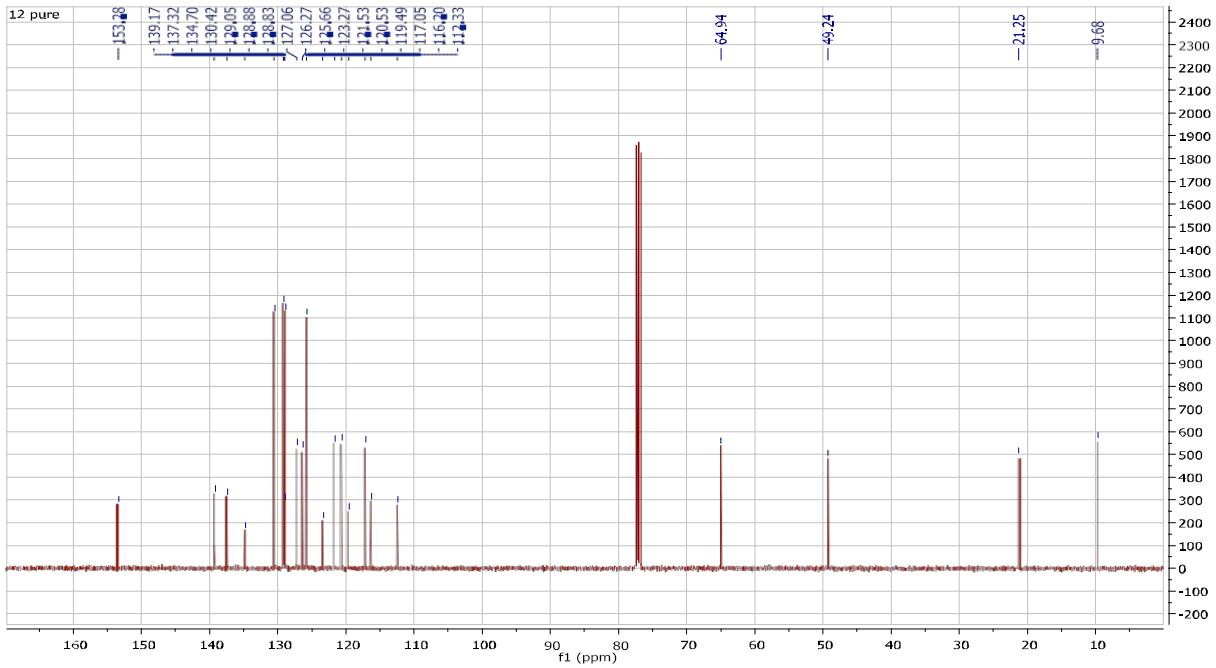
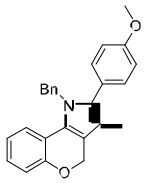
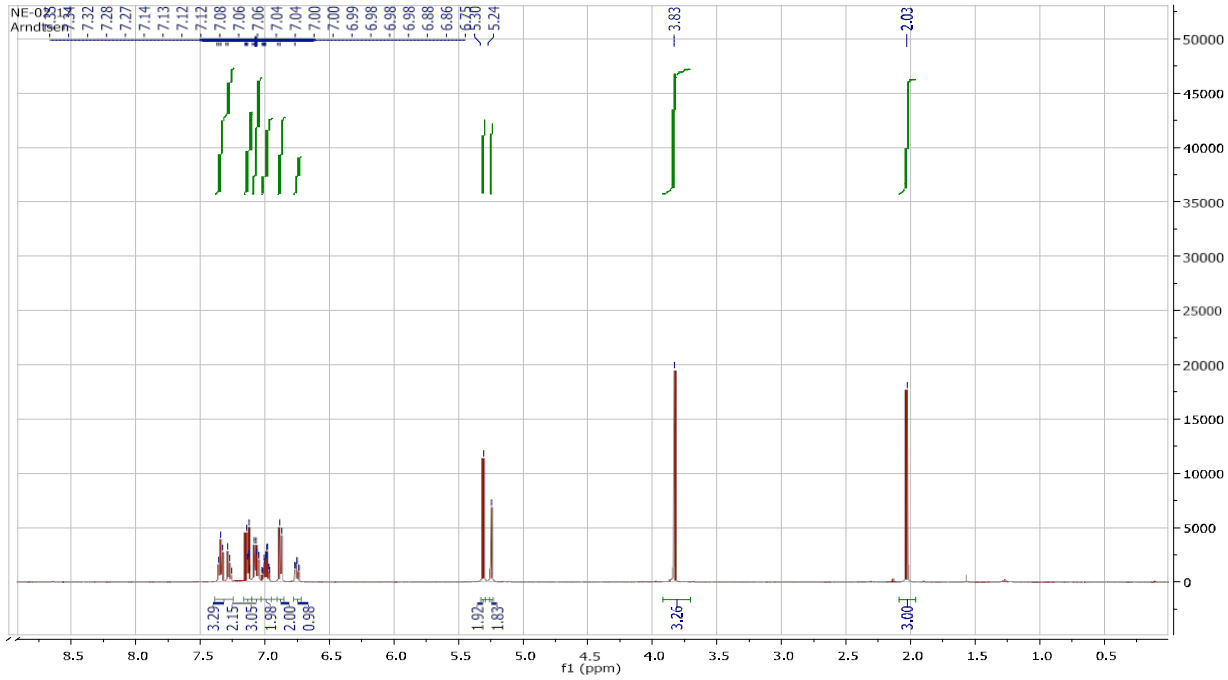


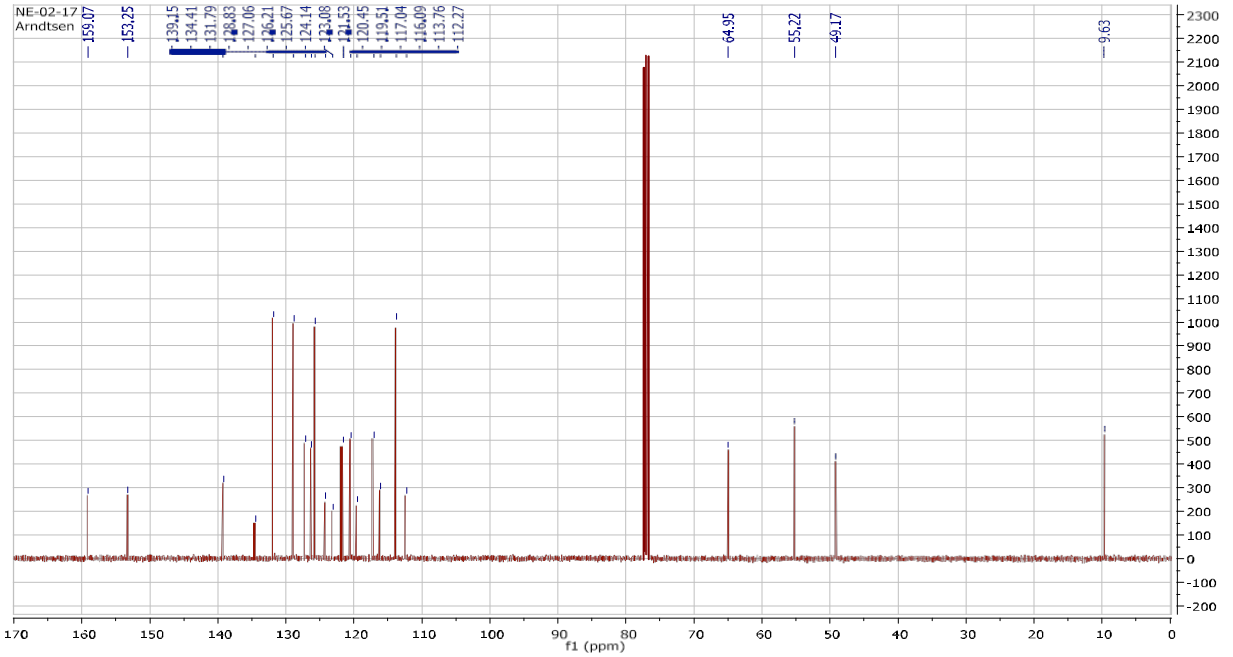




^{1}H and ^{13}C NMR spectra of 3f







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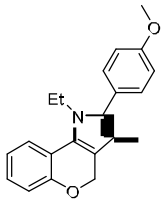
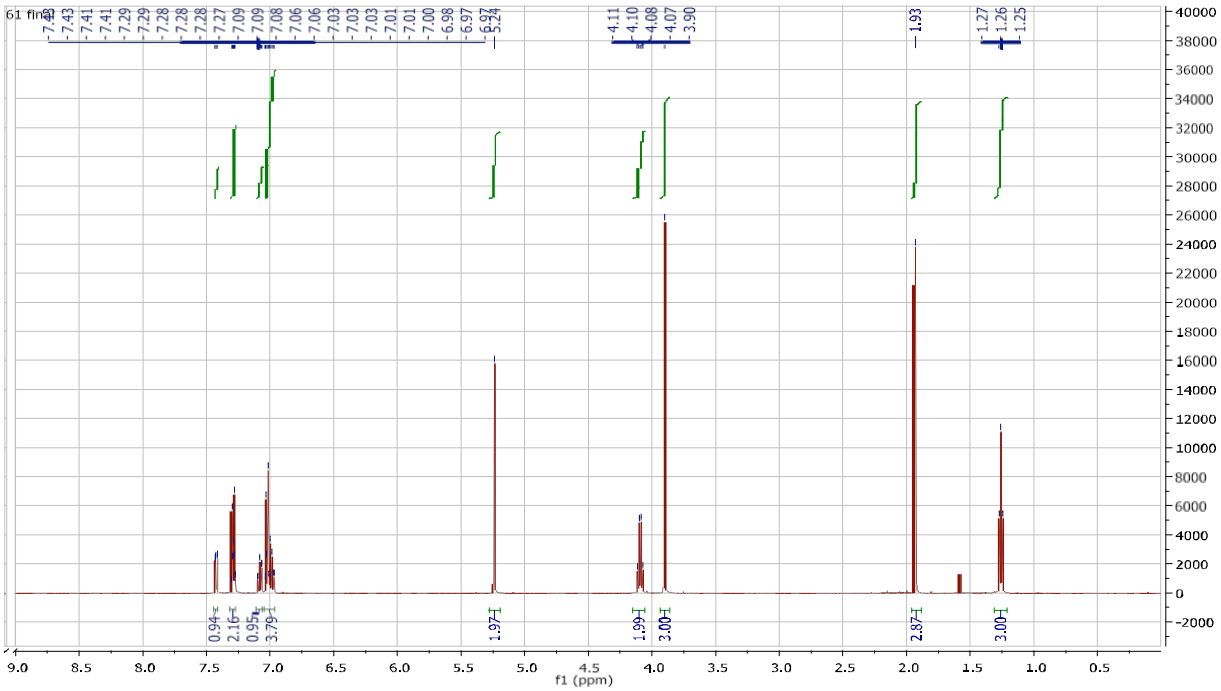
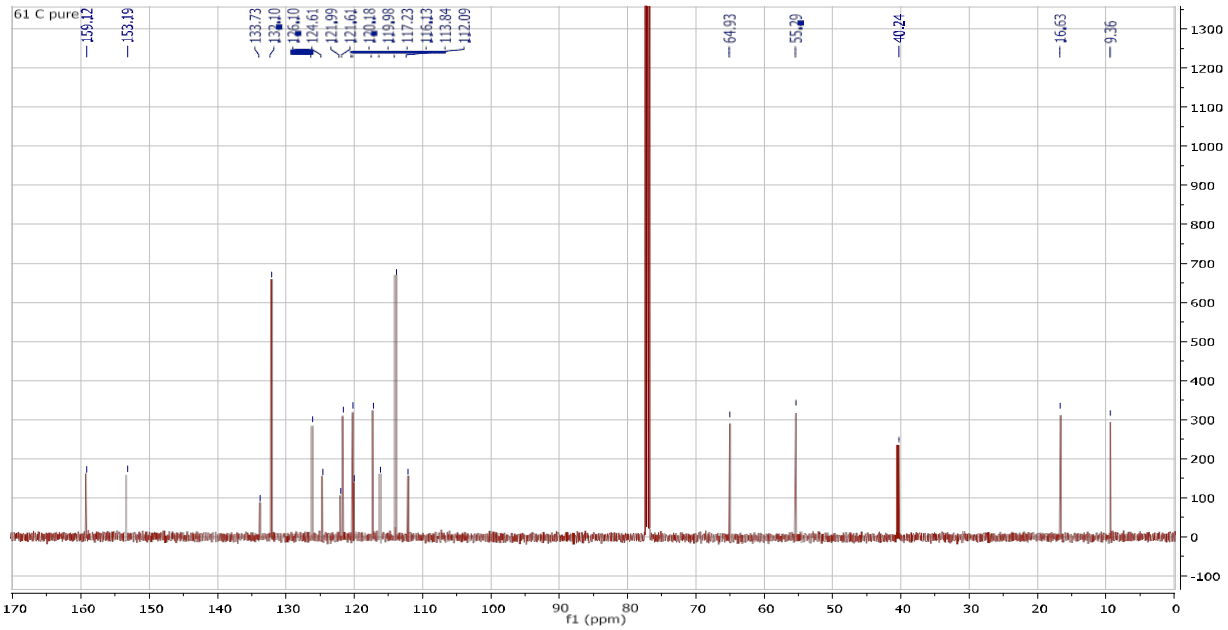
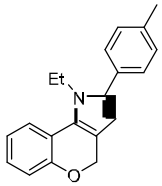
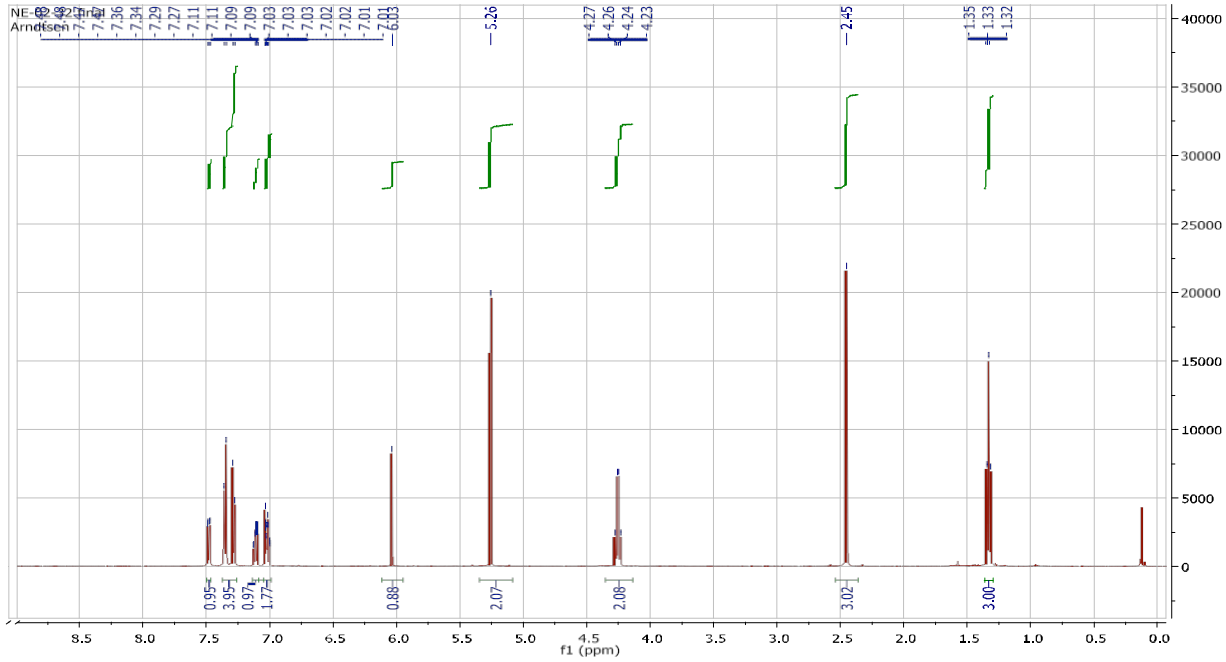


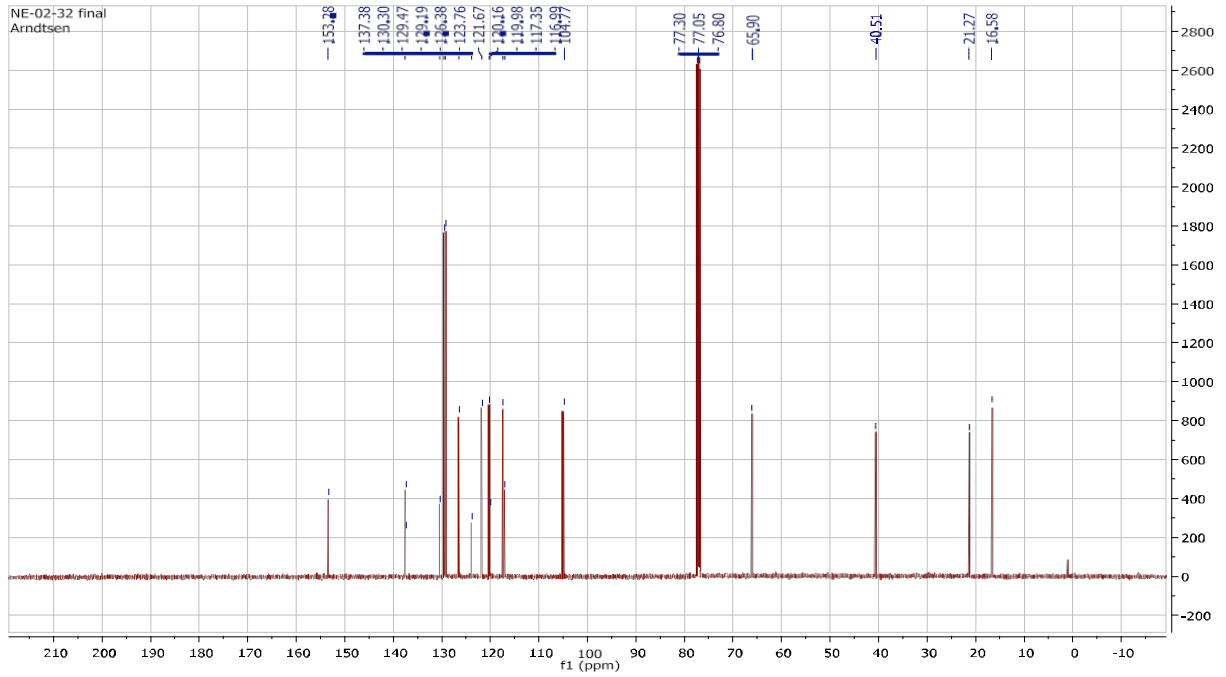




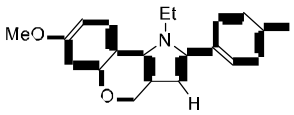
^{1}H and ^{13}C NMR spectra of 3h

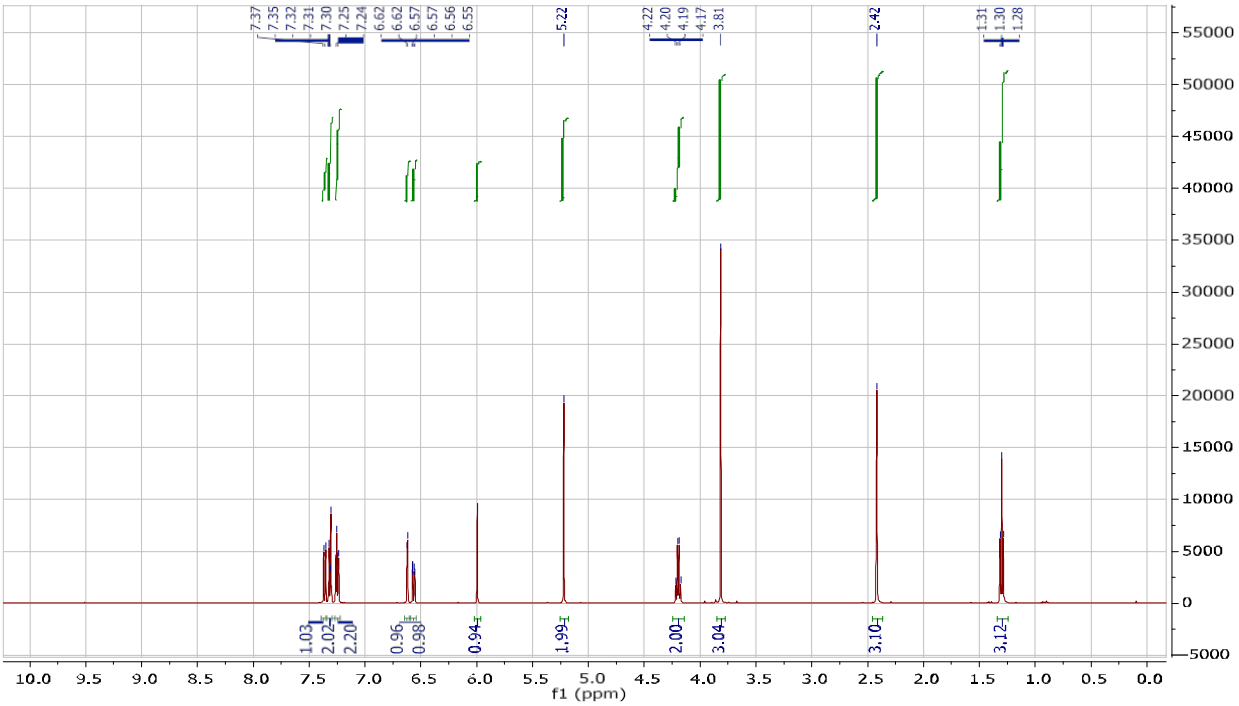


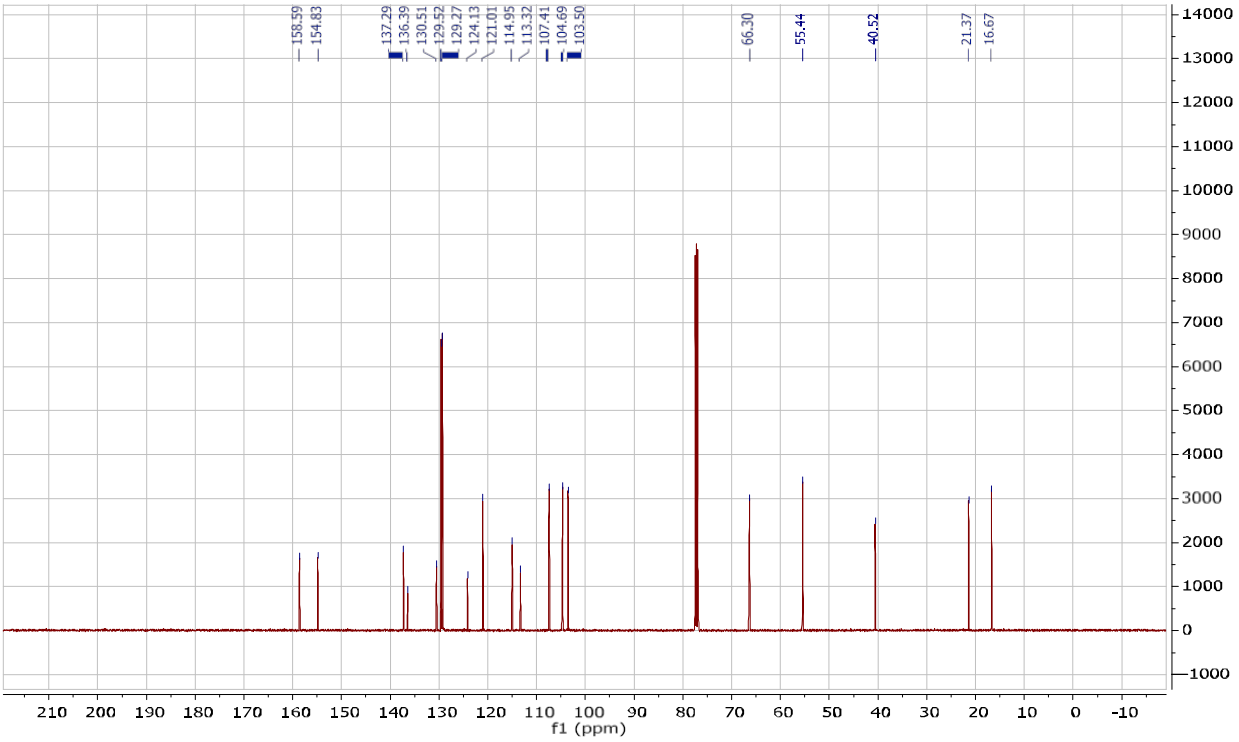




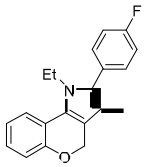
^{1}H and ^{13}C NMR spectra of 3i

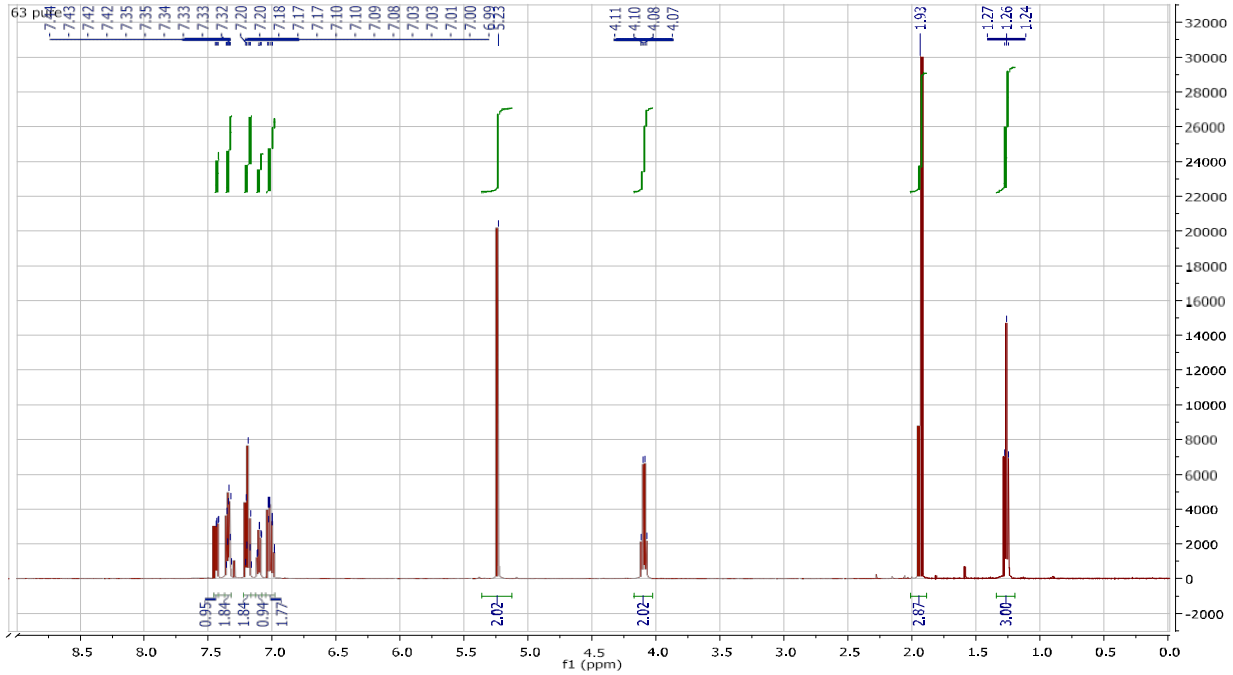


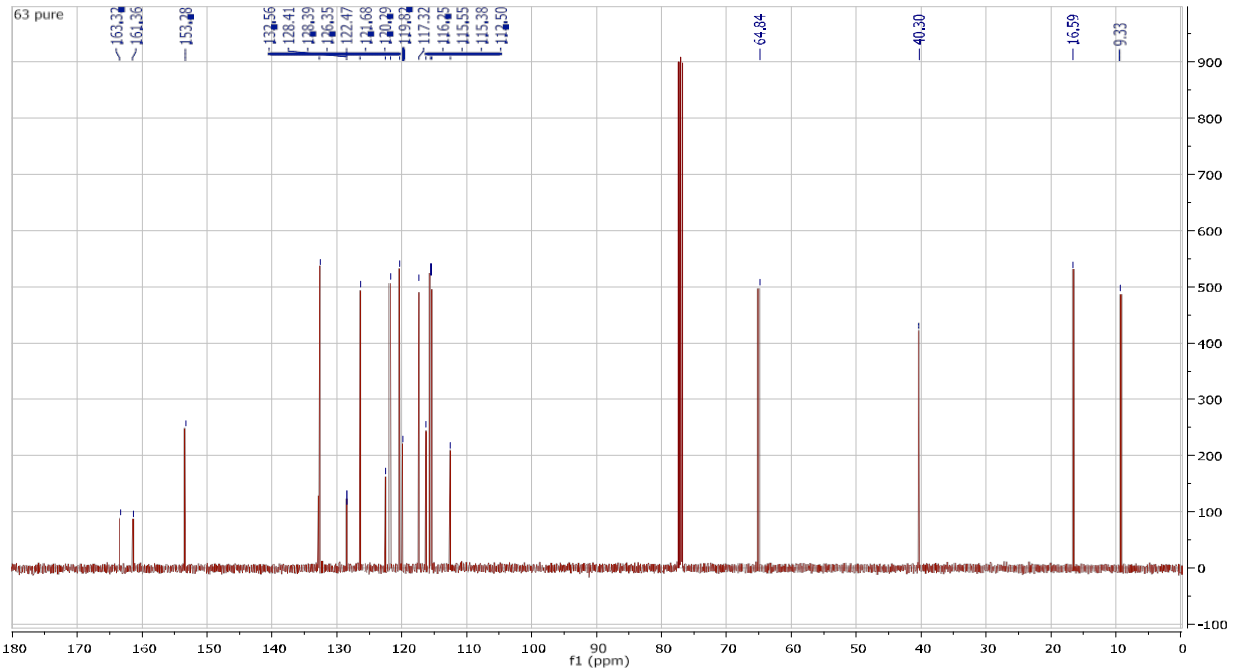




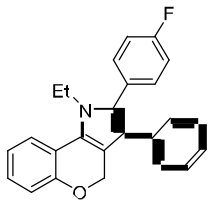
^{1}H and ^{13}C NMR spectra of 3j

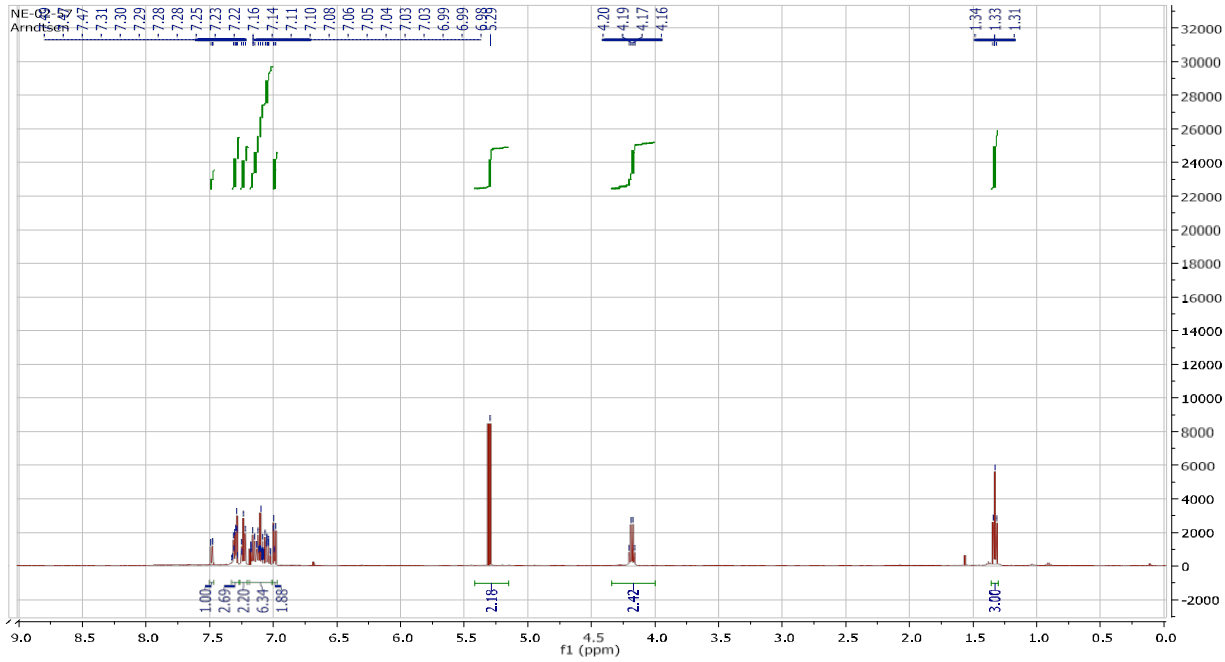


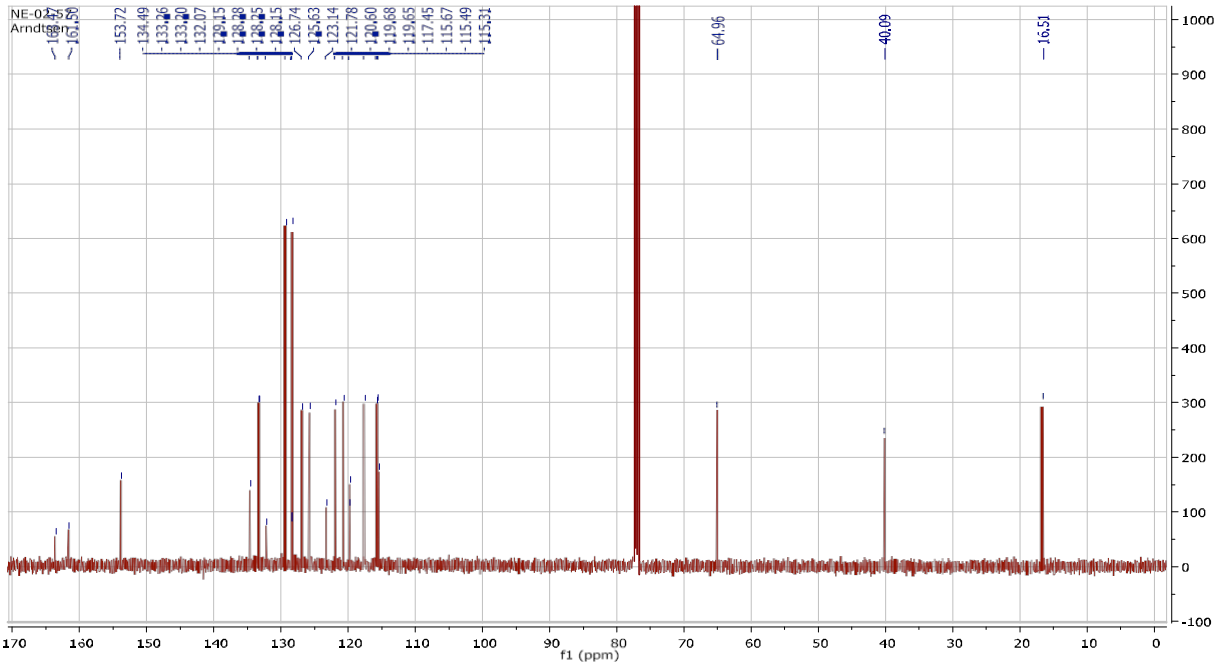




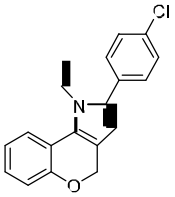
^{1}H and ^{13}C NMR spectra of 3k

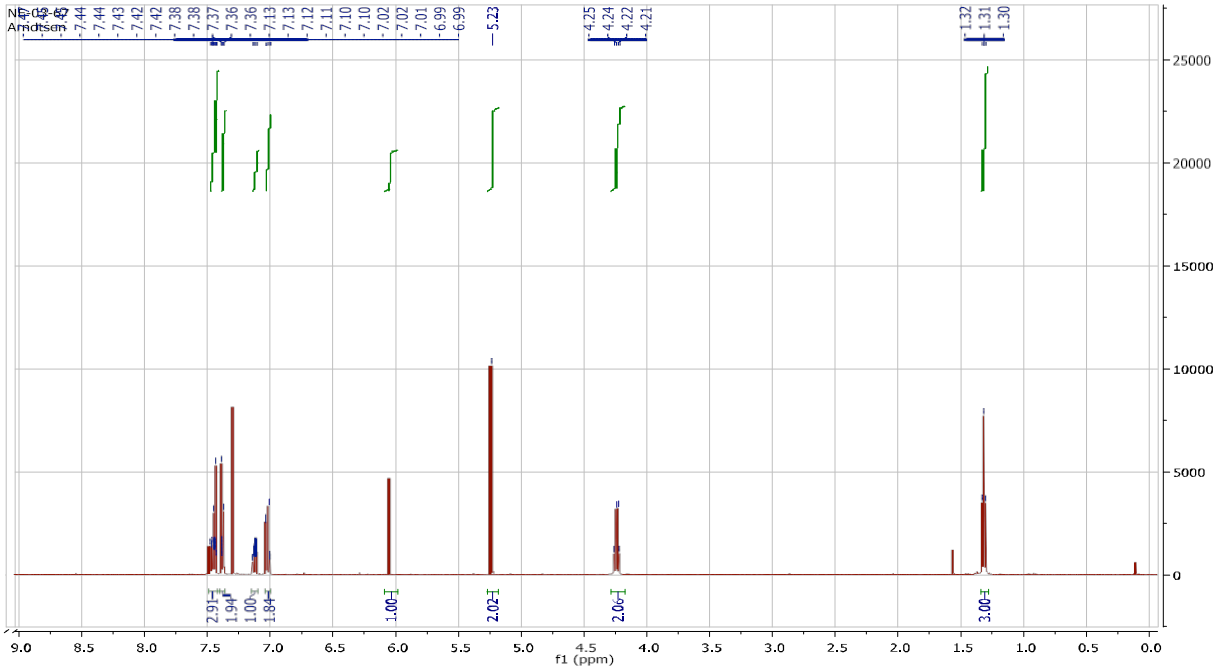


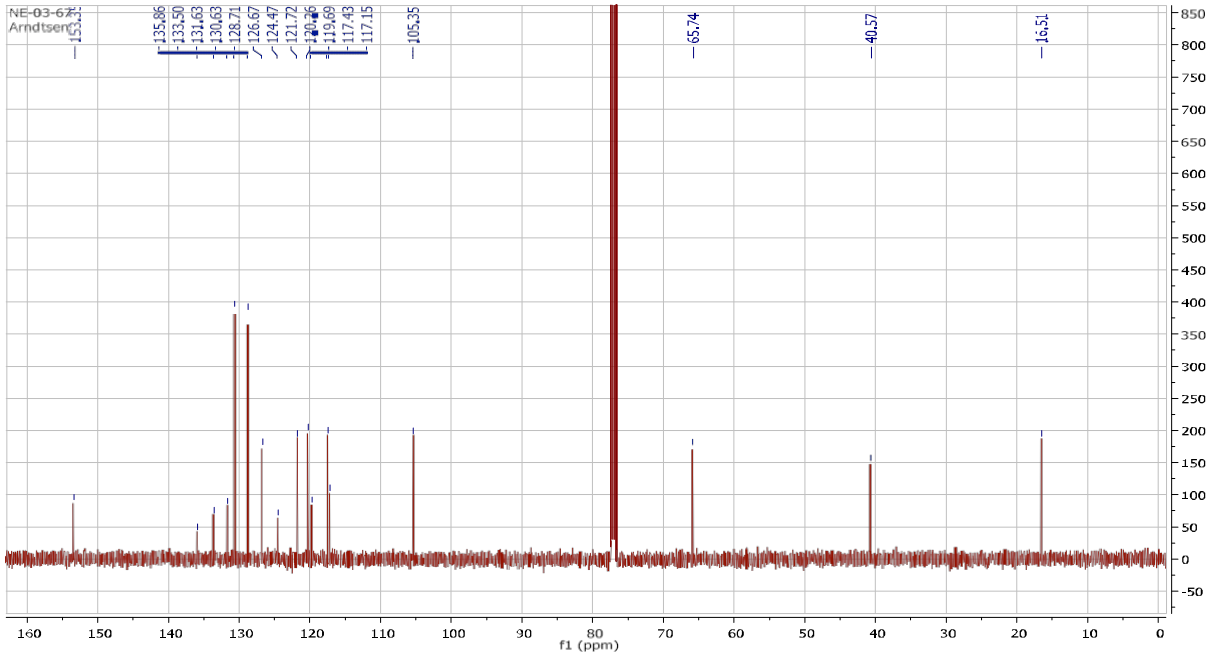




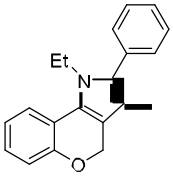
^{1}H and ^{13}C NMR spectra of 3l

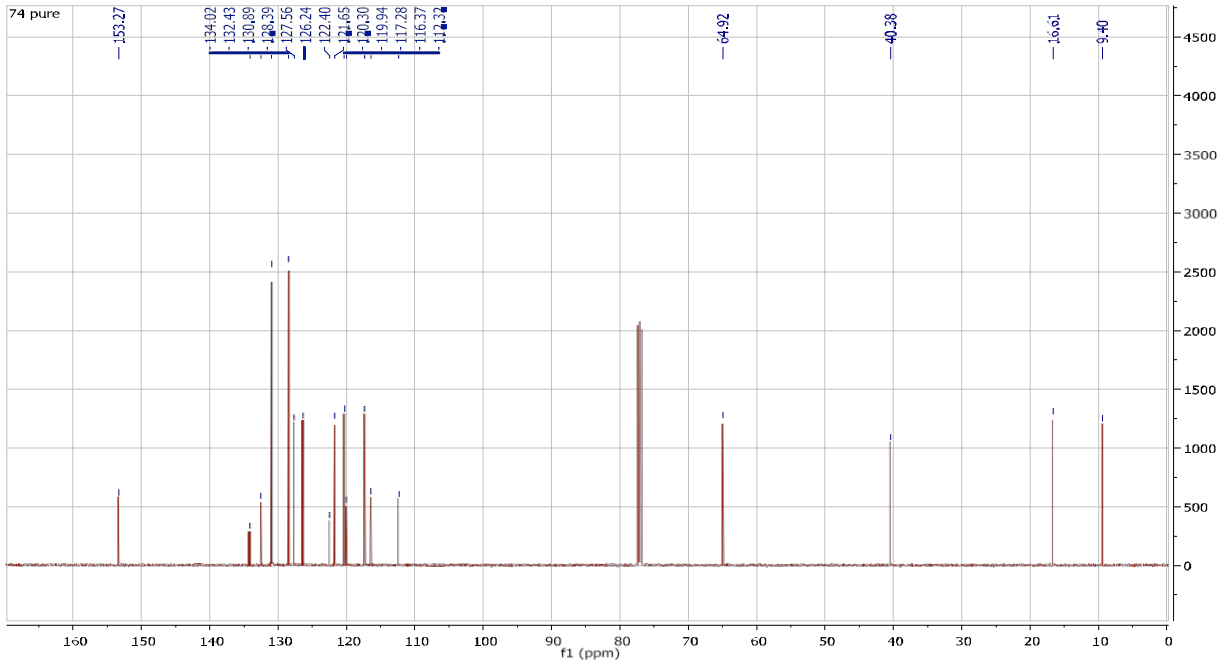




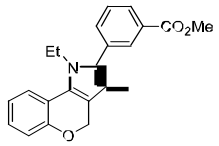


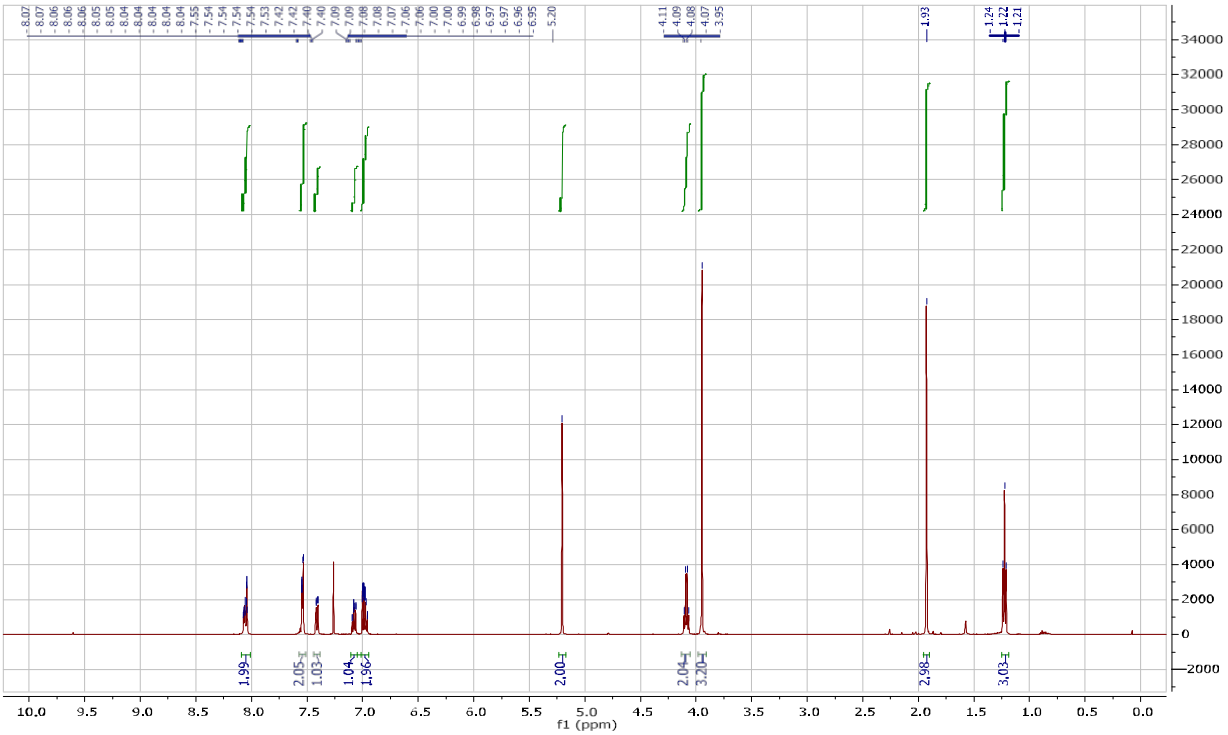
^{1}H and ^{13}C NMR spectra of 3m

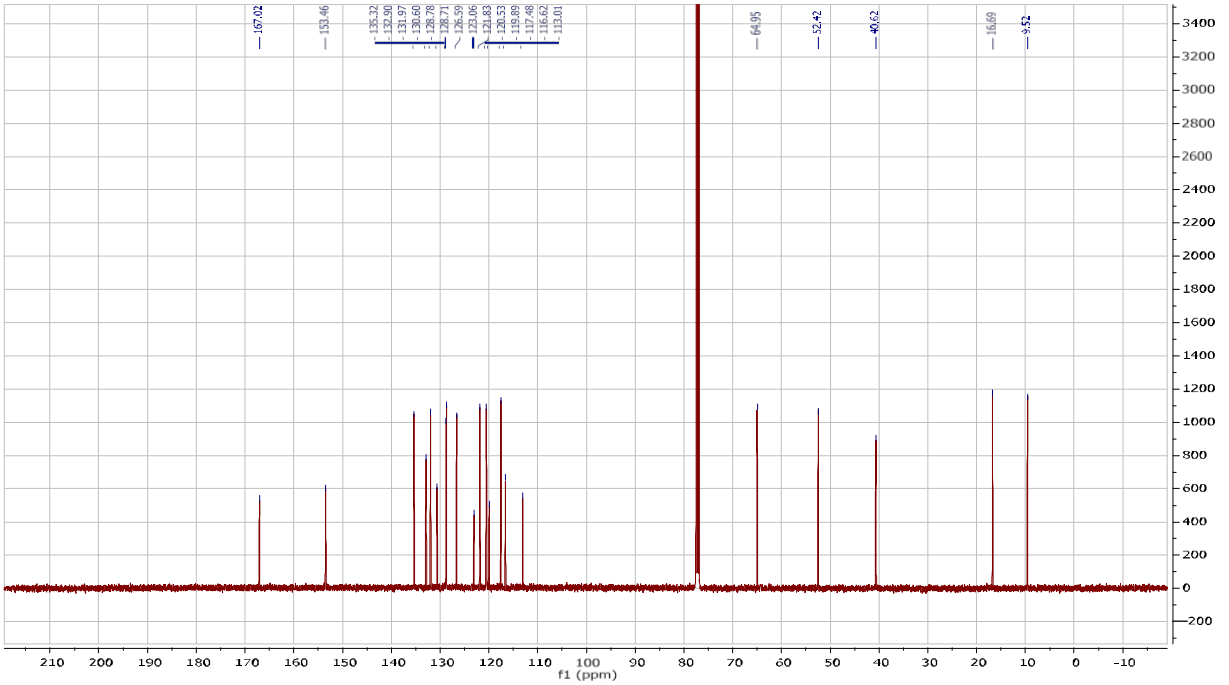




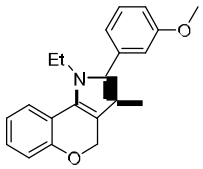
^{1}H and ^{13}C NMR spectra of 3n

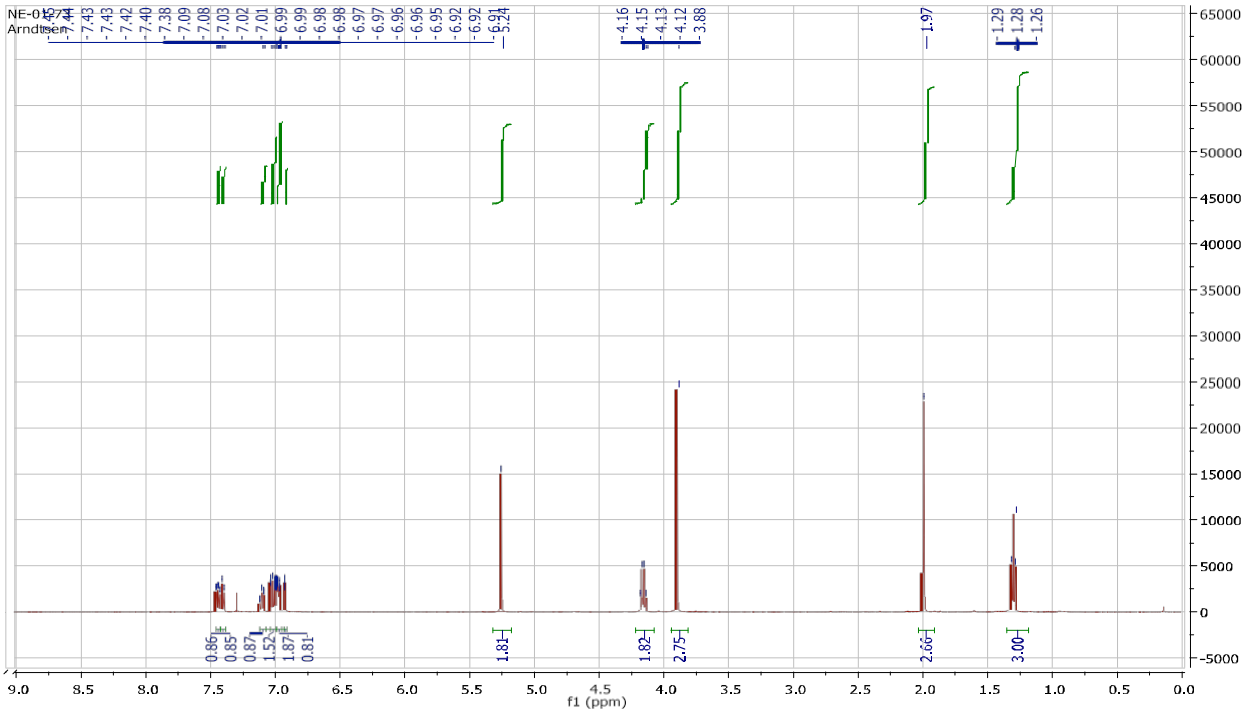


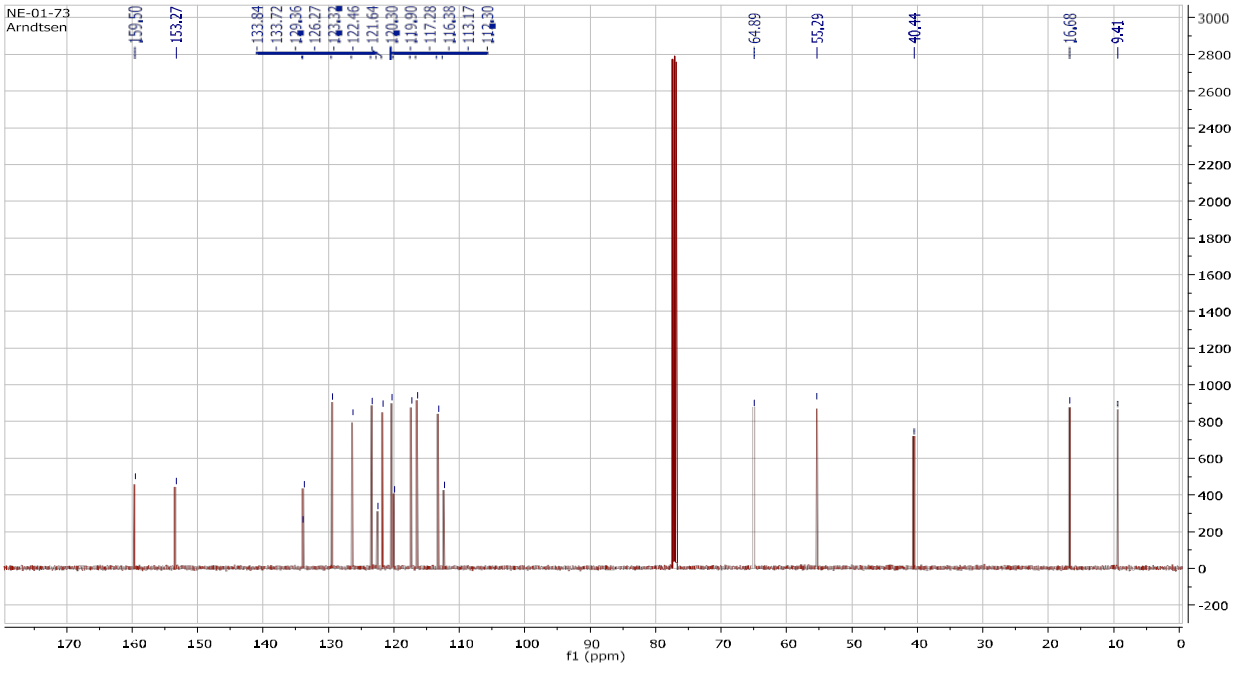




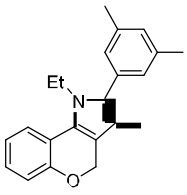
^{1}H and ^{13}C NMR spectra of 3o

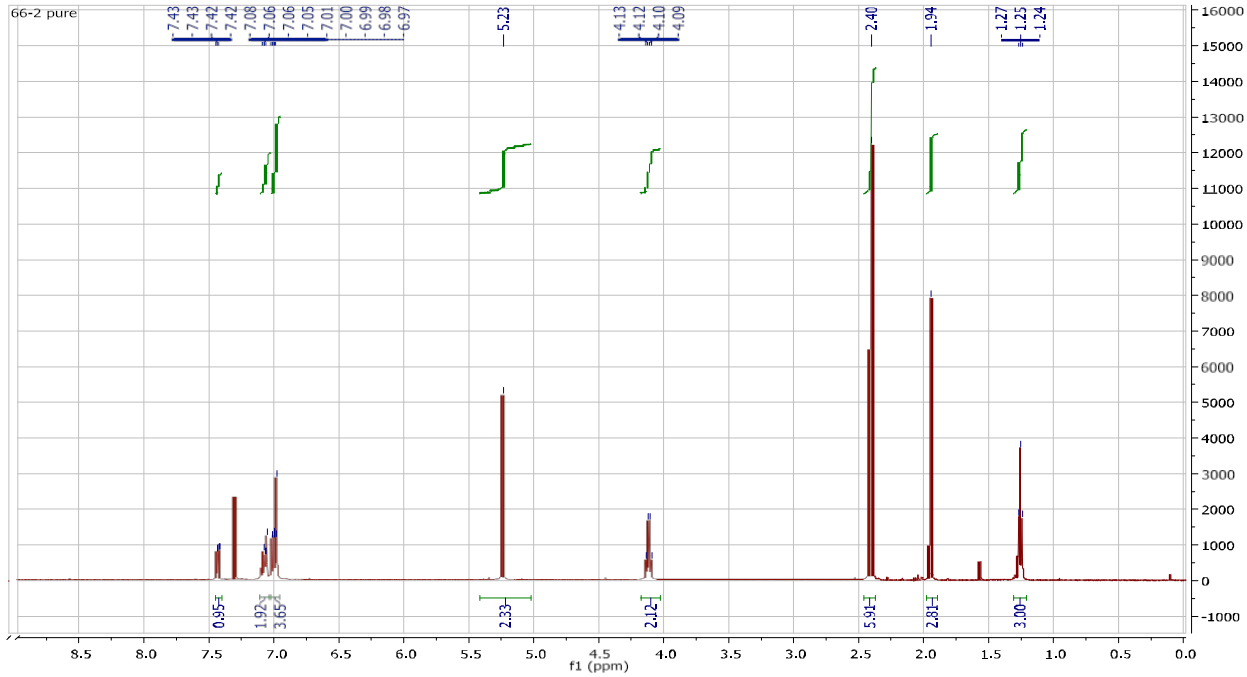


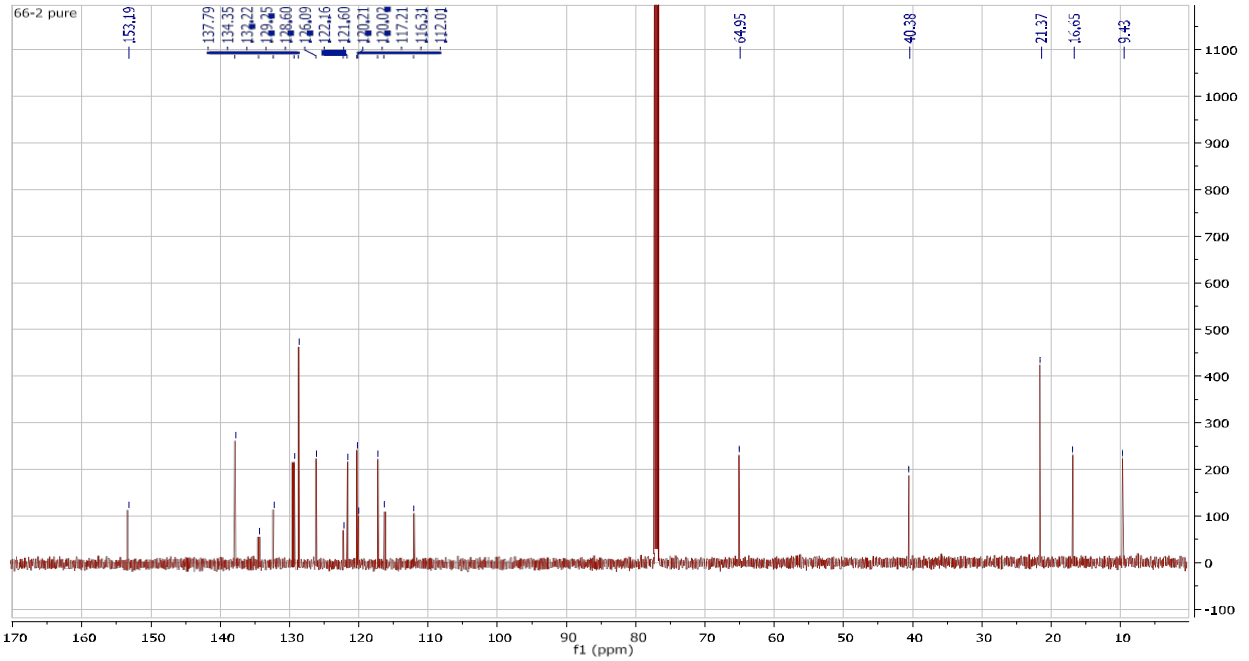




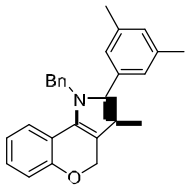
^{1}H and ^{13}C NMR spectra of 3p

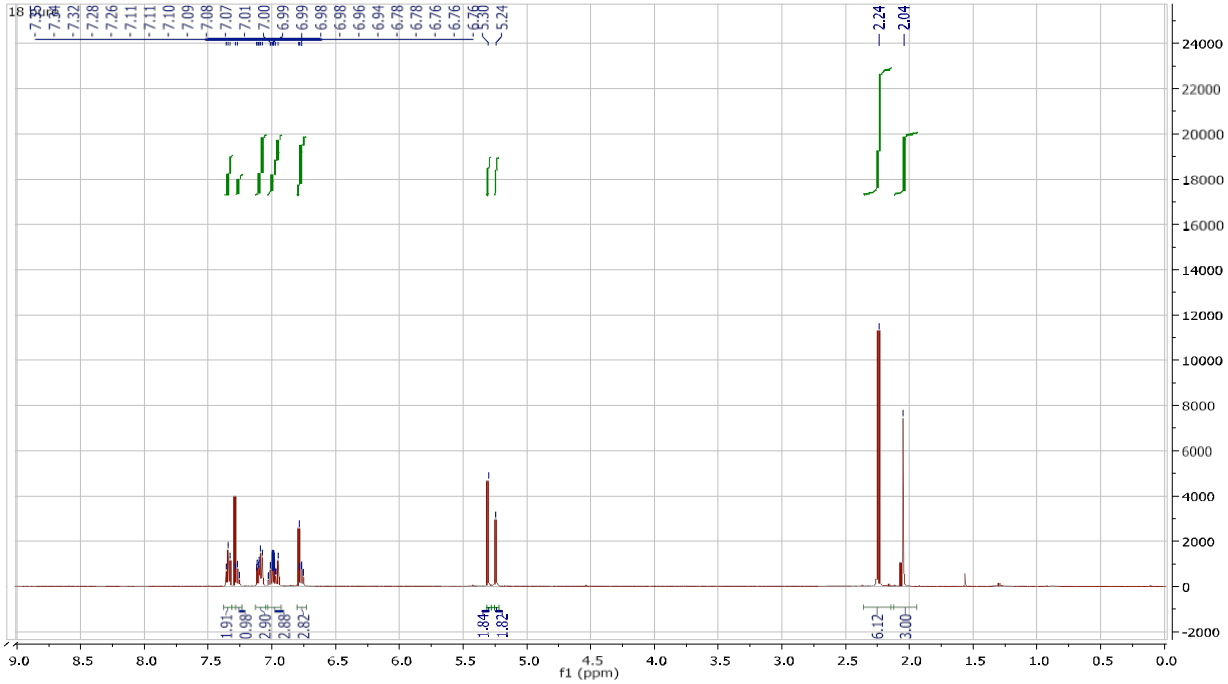


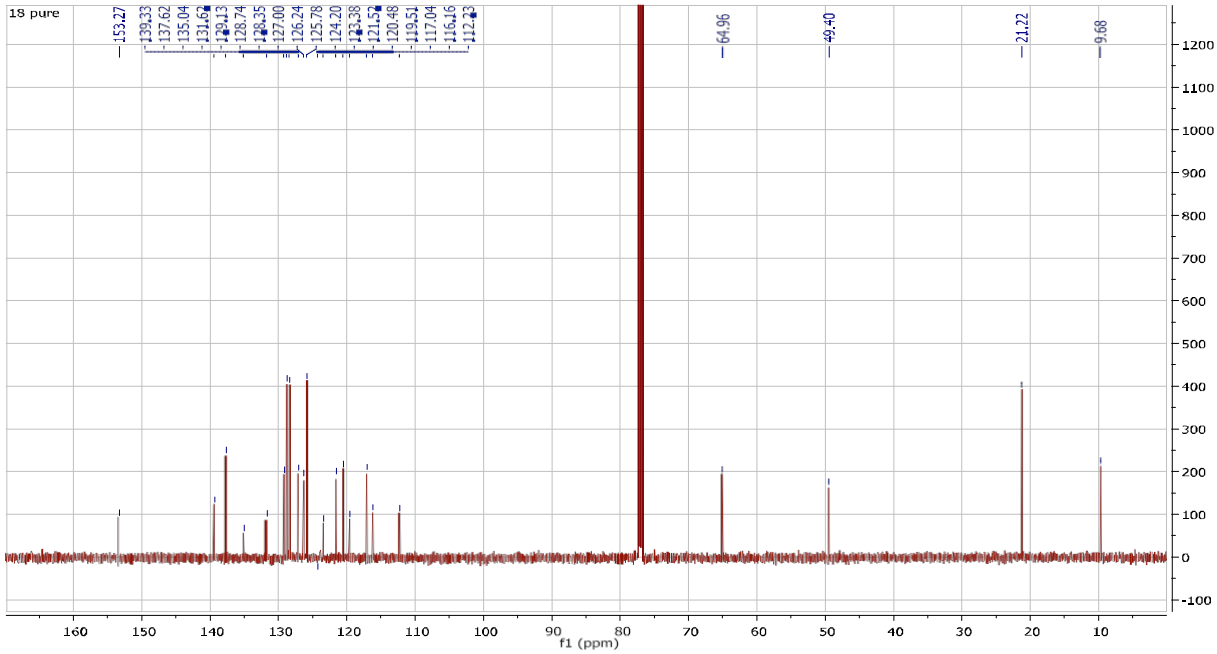




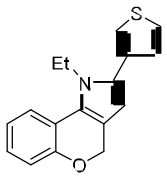
^{1}H and ^{13}C NMR spectra of 3q

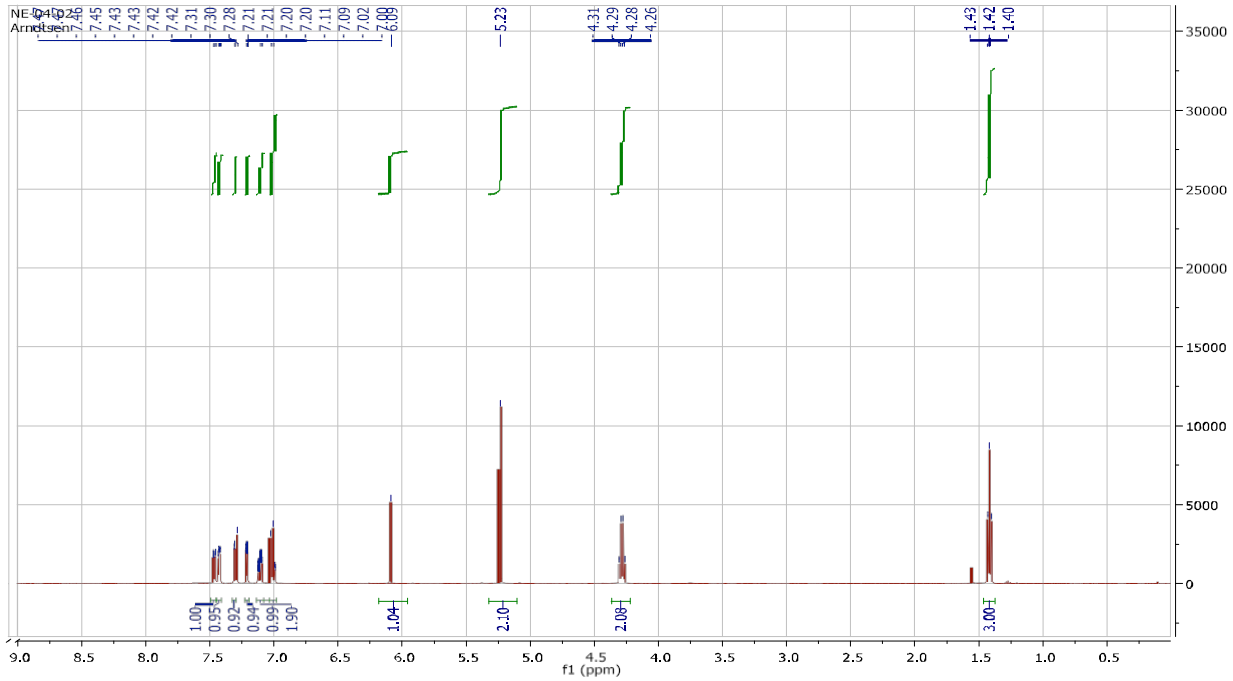


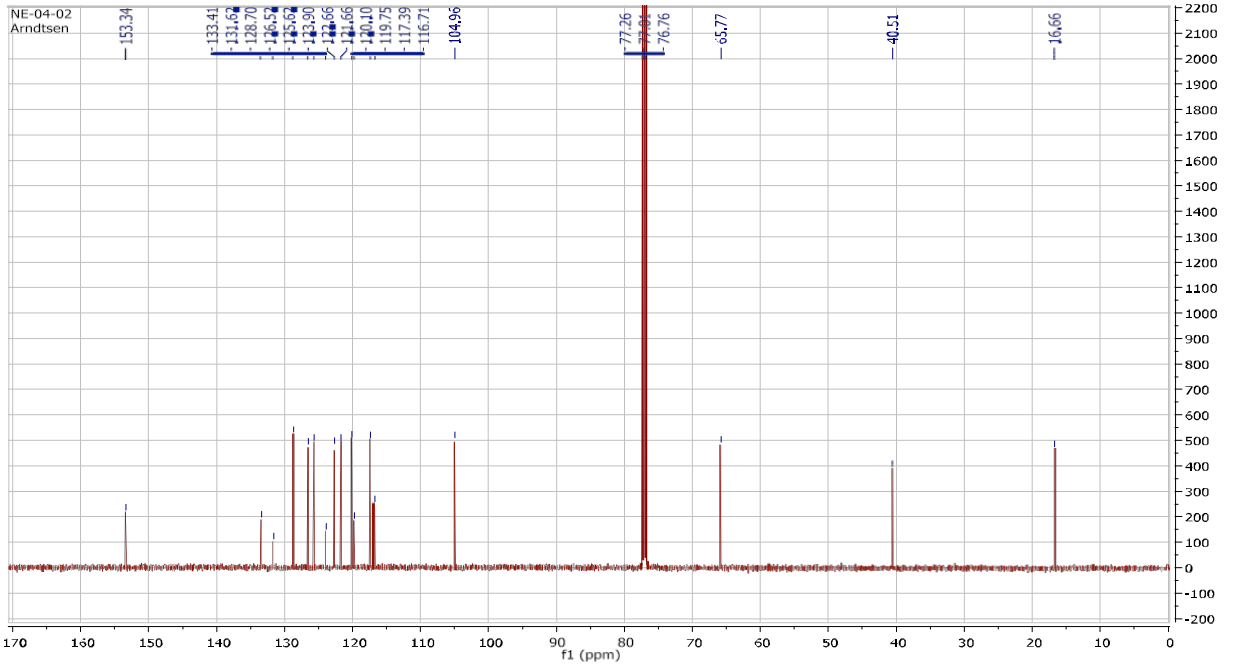




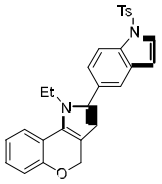
^{1}H and ^{13}C NMR spectra of 3r

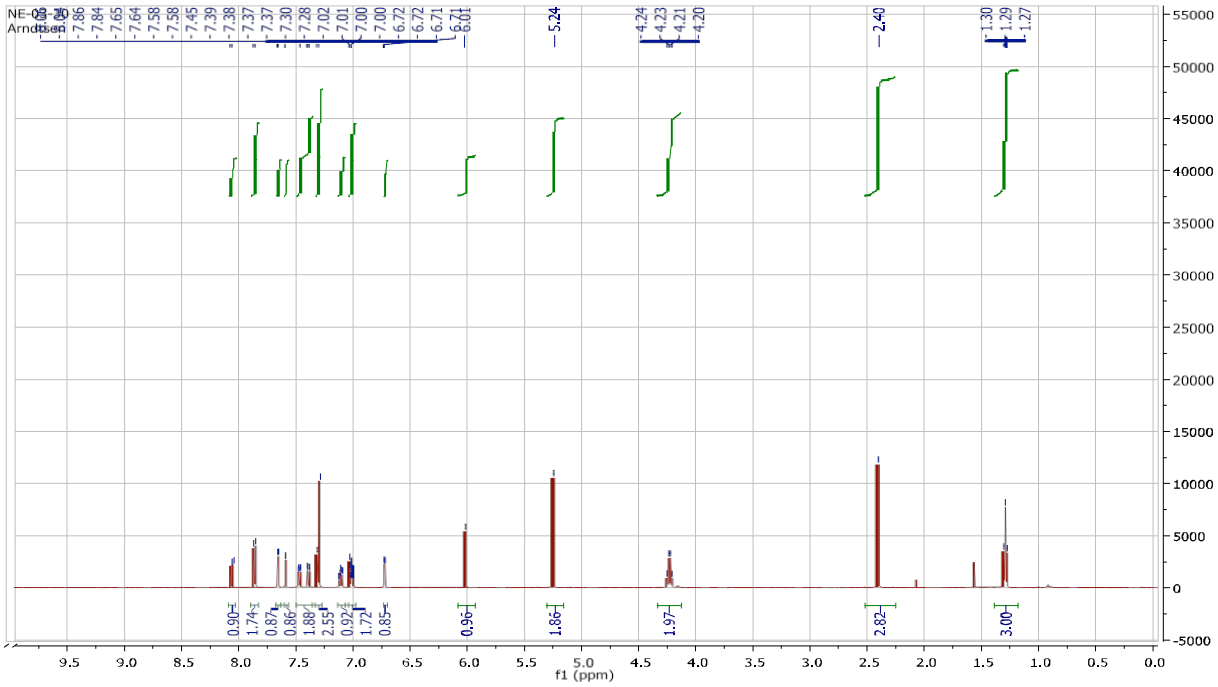


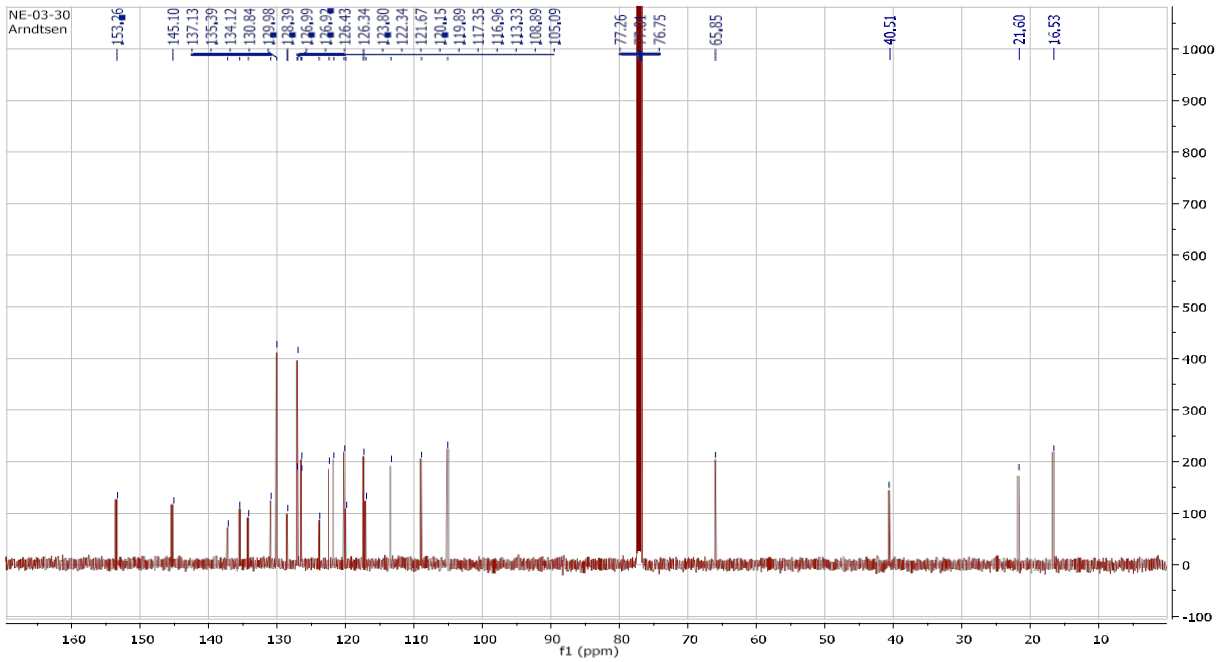




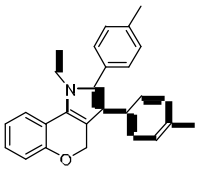
^{1}H and ^{13}C NMR spectra of 3s

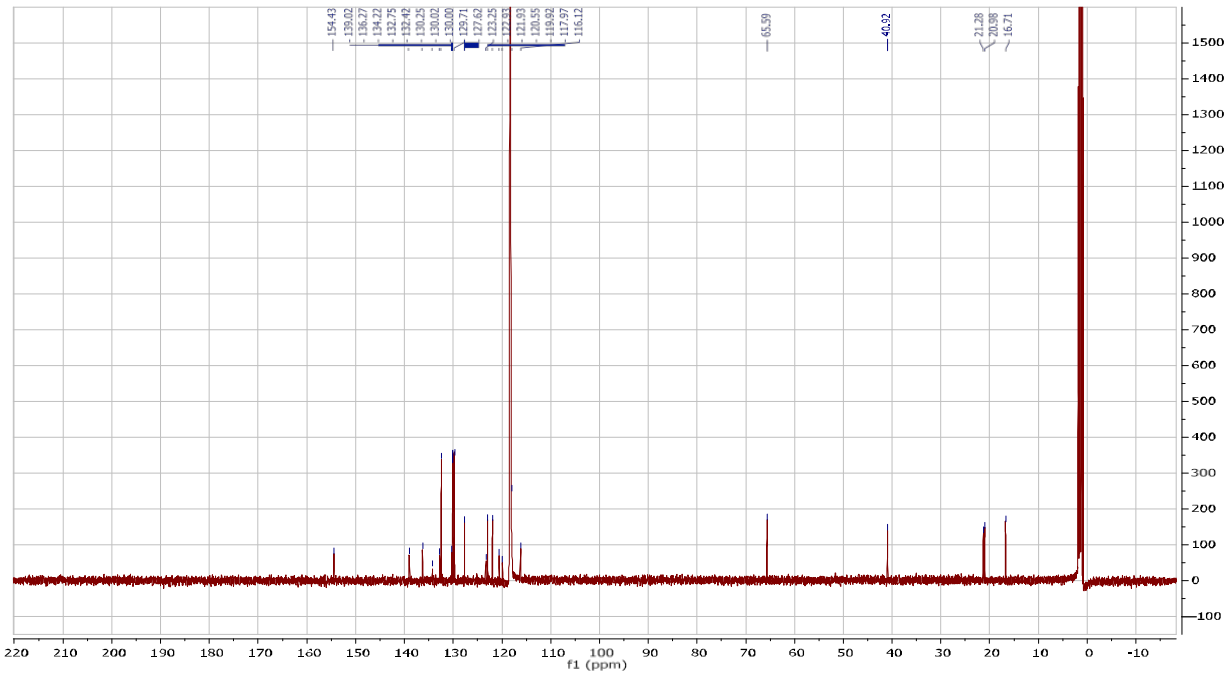




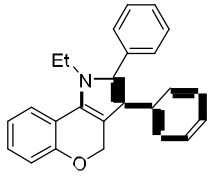


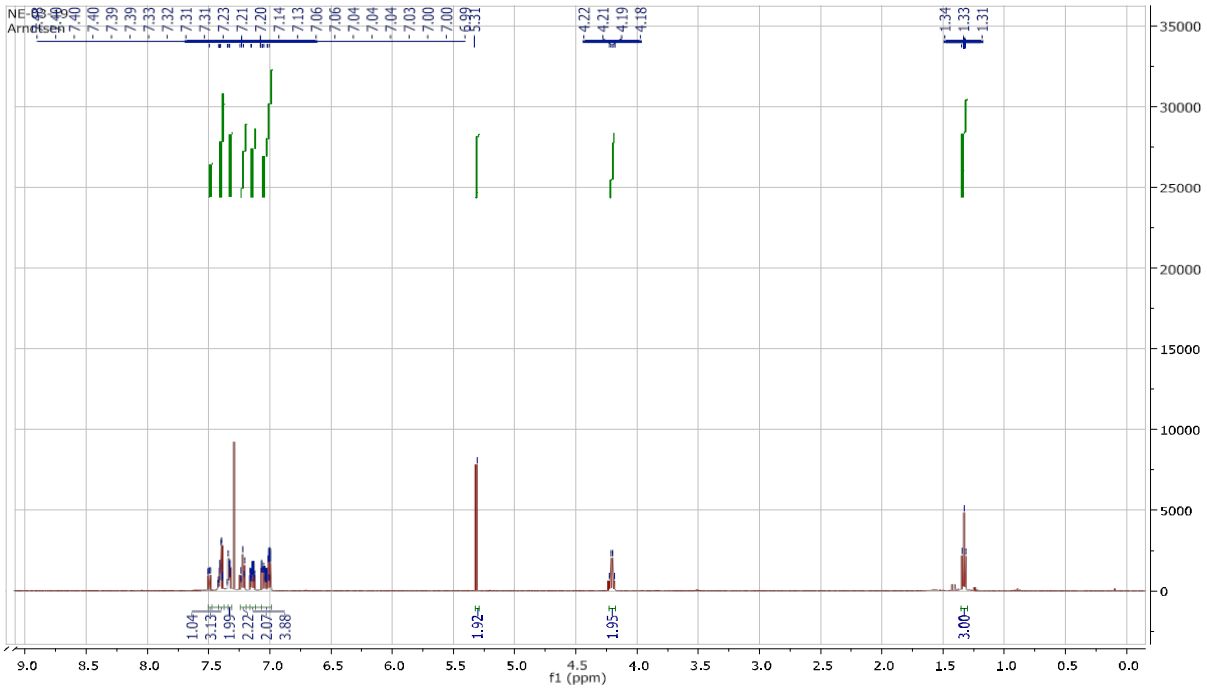
^{1}H and ^{13}C NMR spectra of 5a

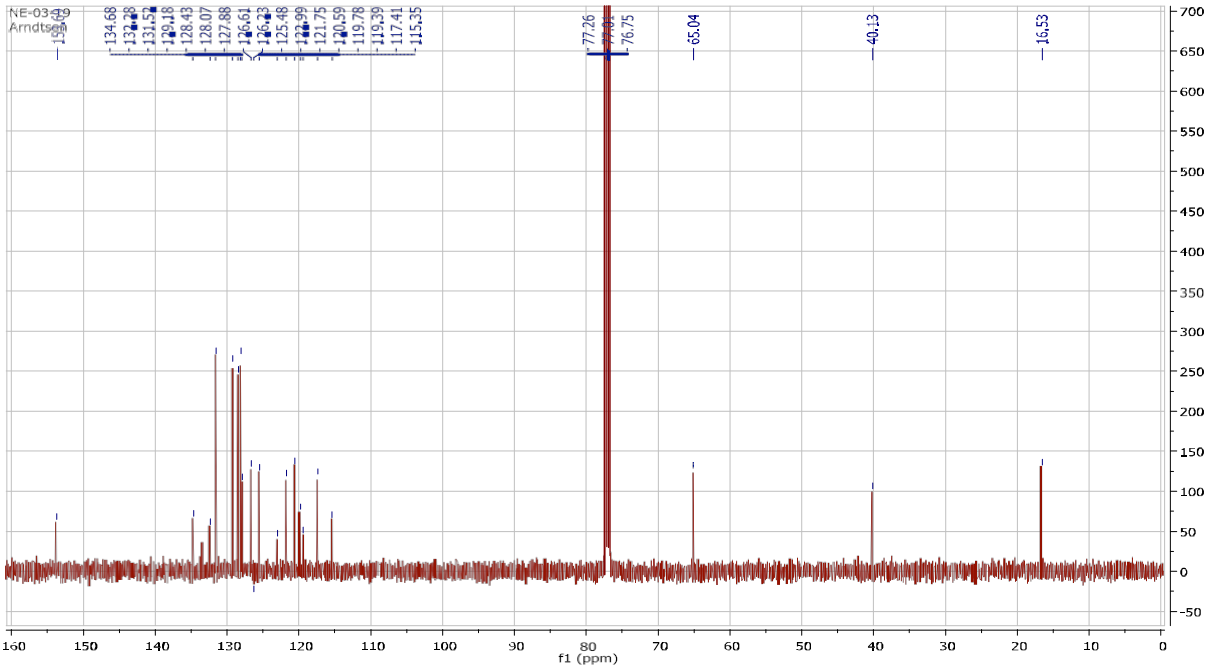




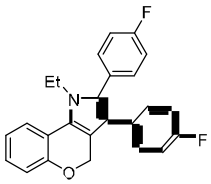
^{1}H and ^{13}C NMR spectra of 5b

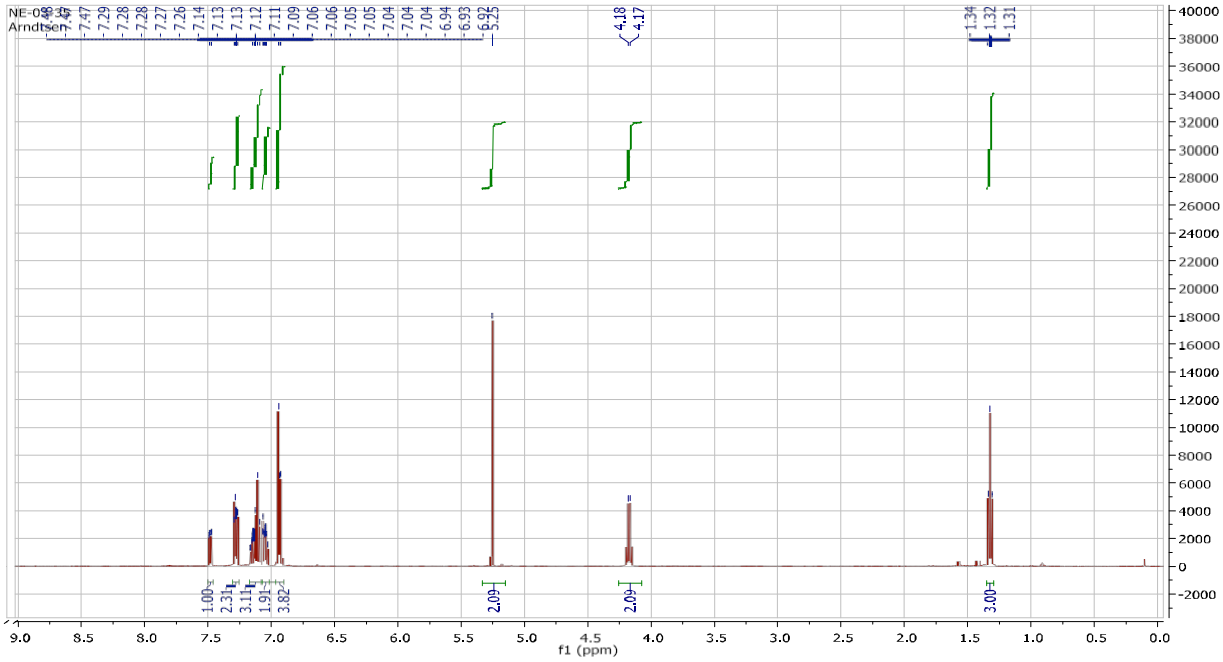


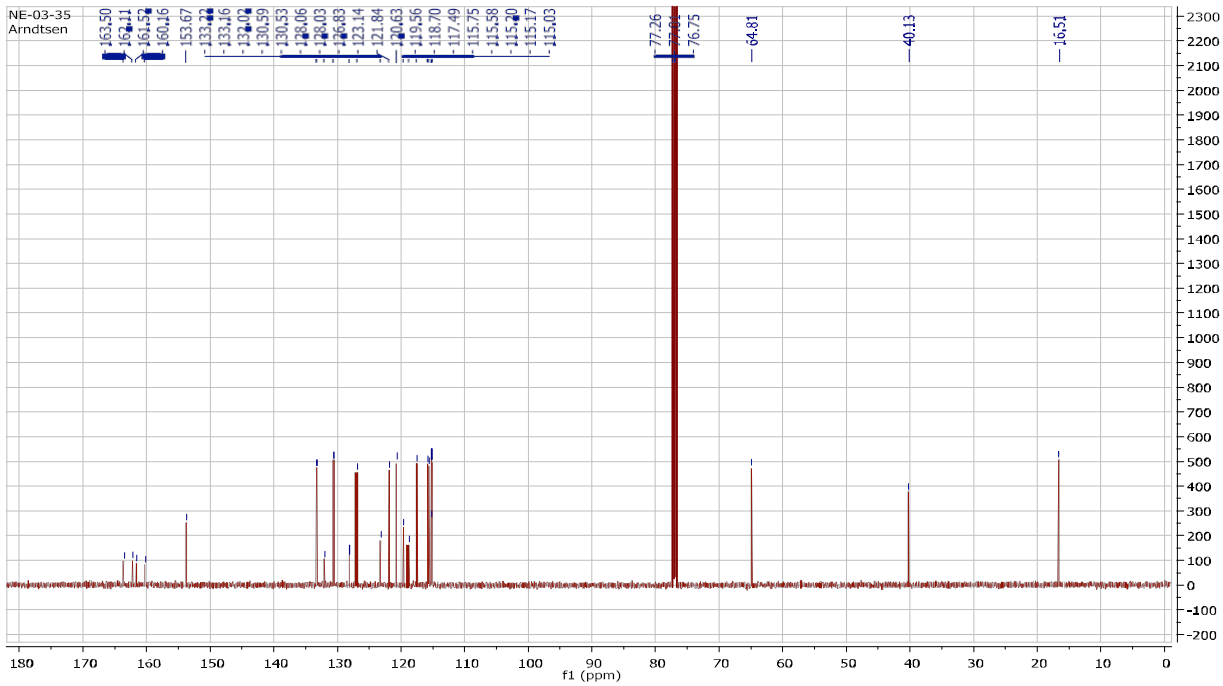




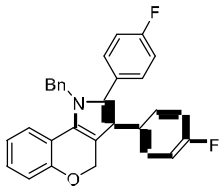
^{1}H and ^{13}C NMR spectra of 5c

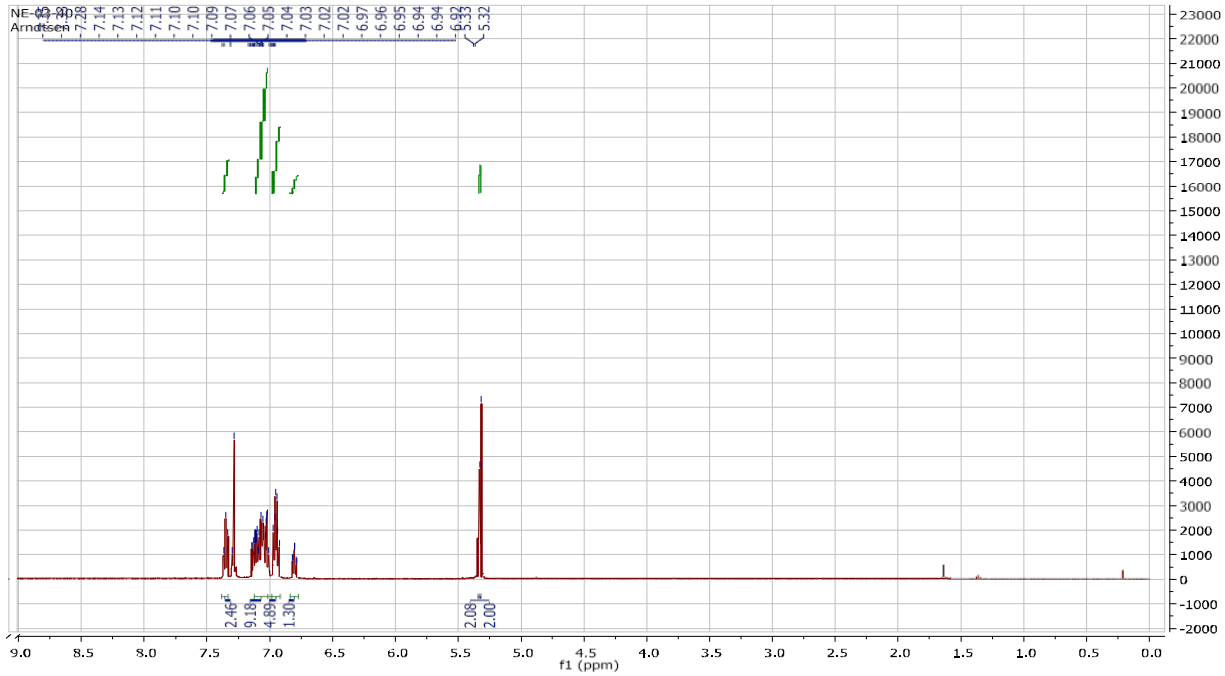


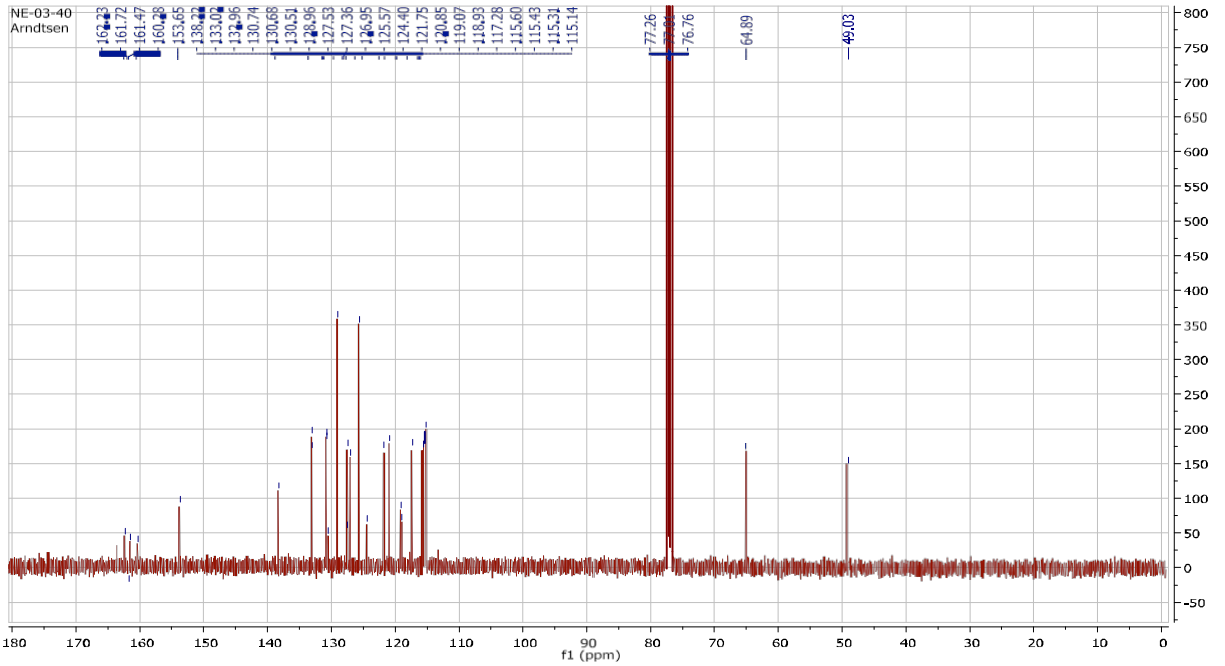




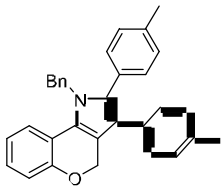
^{1}H and ^{13}C NMR spectra of 5d

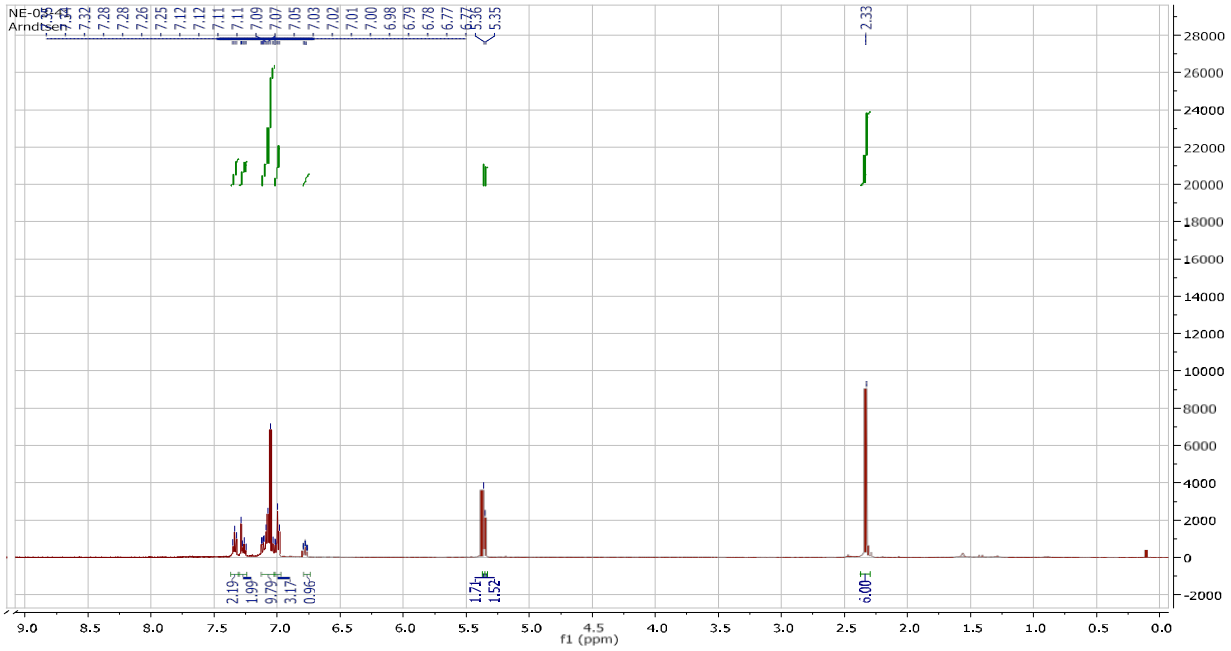


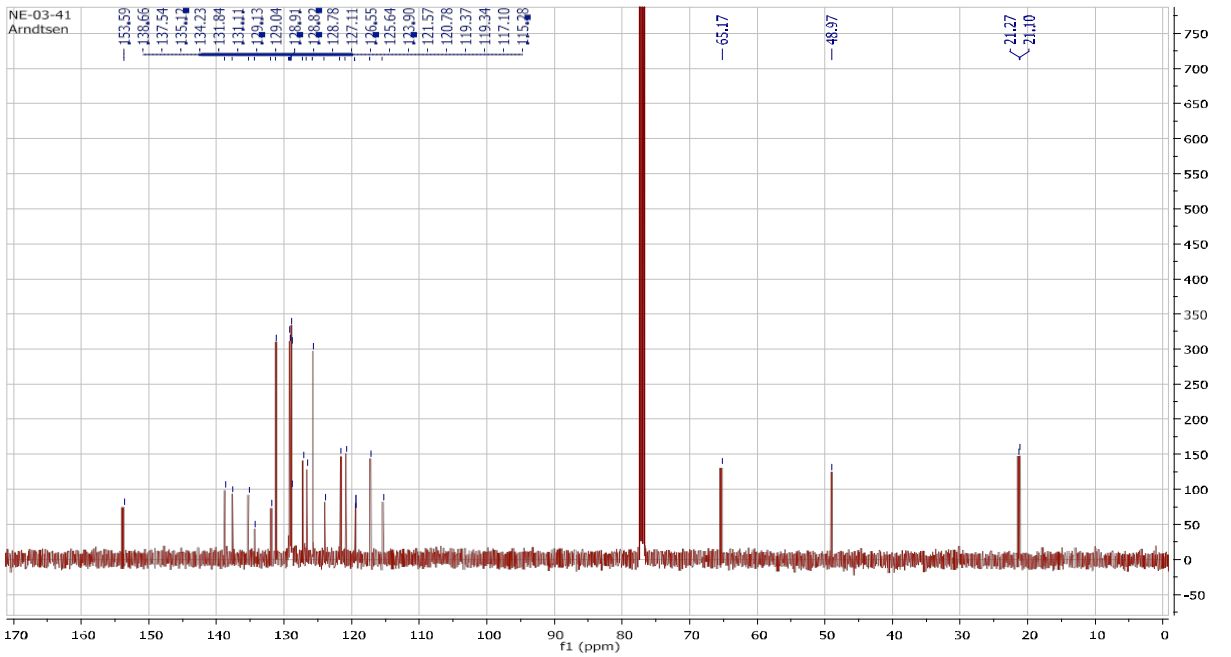




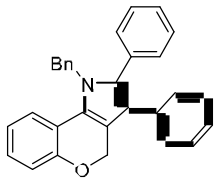
^{1}H and ^{13}C NMR spectra of 5e

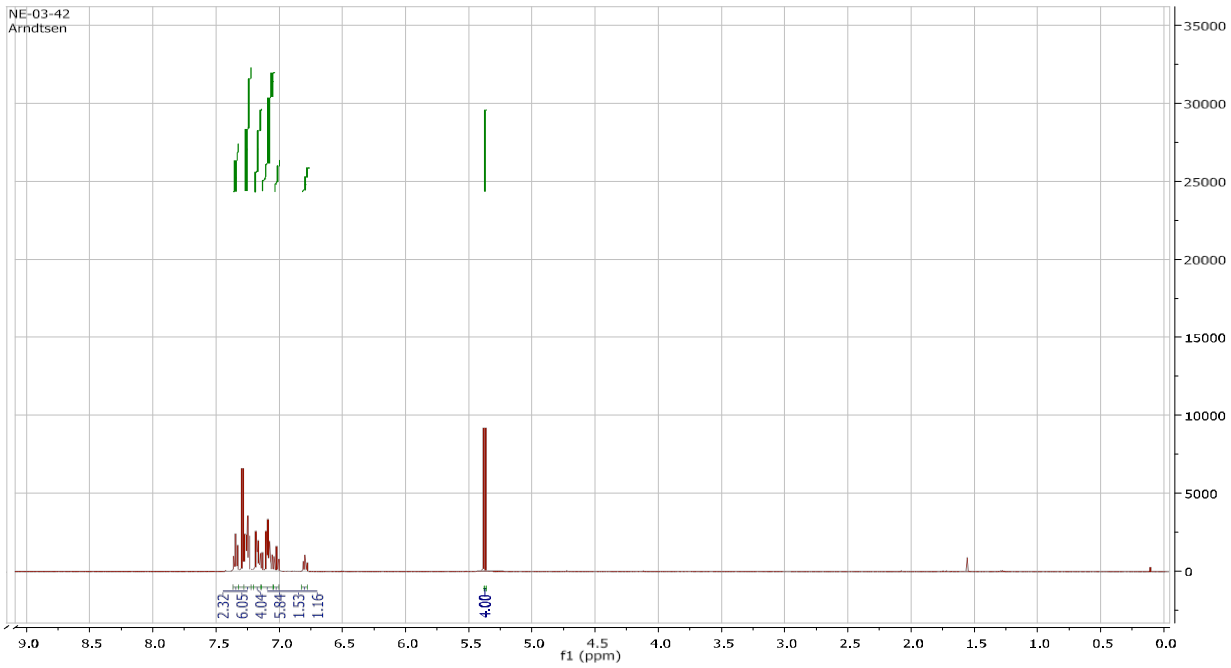


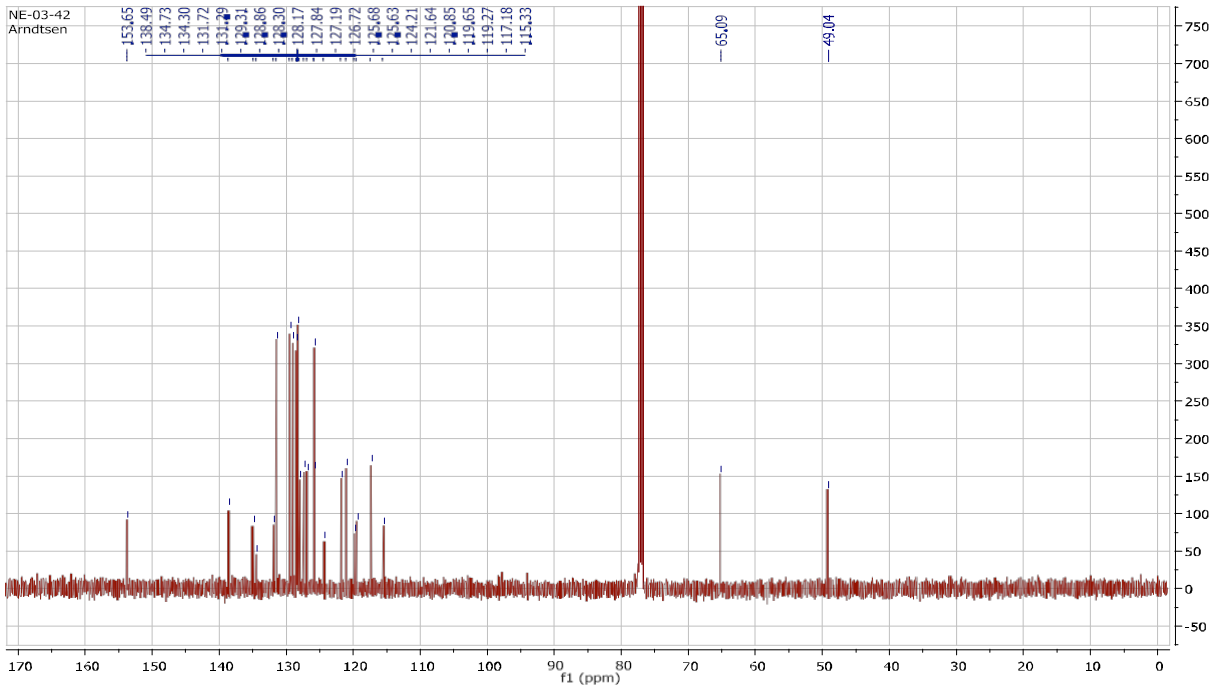




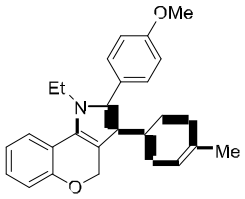
^{1}H and ^{13}C NMR spectra of 5f

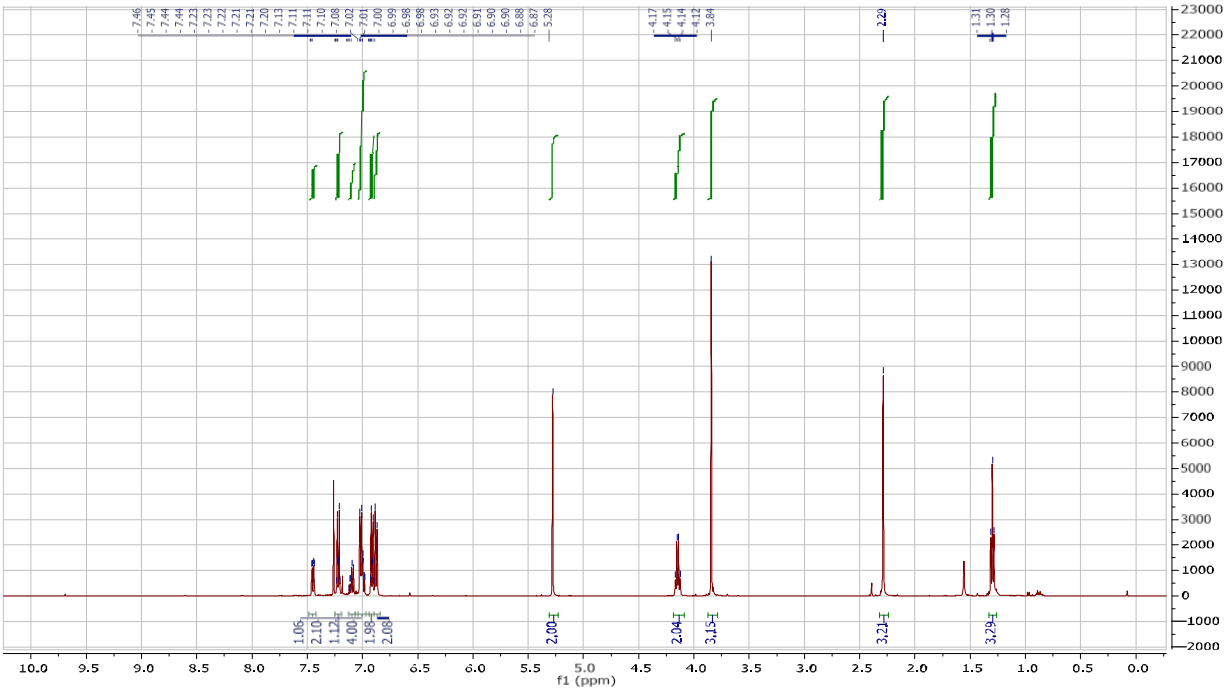


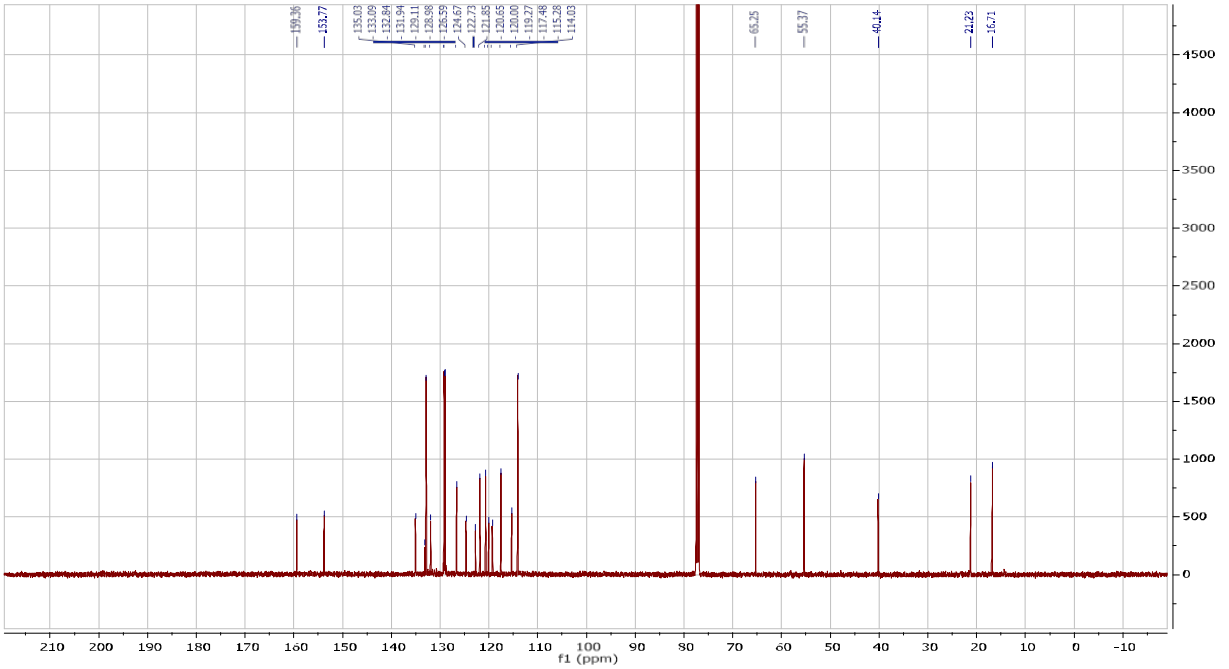




^{1}H and ^{13}C NMR spectra of 5g







^{1}H and ^{13}C NMR spectra of 5h