

## Appendix A

### **Synthesis of new phosphazine and triazole derivatives for treatment of Alzheimer's disease: modulating ROS/JNK and Wnt/β-catenin signaling pathways**

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## Experimental

### Chemistry

All chemicals were supplied by either Fluka or Aldrich chemical companies and were used without further purification. All melting points are uncorrected and were taken in open capillary tubes using Electrothermal apparatus 9100. Elemental microanalyses were carried out at Microanalytical Unit, Central Services Laboratory, National Research Centre, Dokki, Giza, Egypt, using Vario Elementar and were found within  $\pm 0.4\%$  of the theoretical values. **FT-IR** spectra were recorded with a Perkin-Elmer Frontier. Routine **NMR** spectra were recorded at room temperature on a Bruker Avance TM 300 or 400 spectrometer as solutions in dimethyl sulfoxide (DMSO) or in chloroform ( $\text{CDCl}_3$ ). All chemical shifts are quoted in  $\delta$  relative to the trace resonance of protonated chloroform ( $\delta$  7.25 ppm),  $\text{CDCl}_3$  ( $\delta$  77.0 ppm) or dimethyl sulfoxide ( $\delta$  2.50 ppm), DMSO ( $\delta$  39.51 ppm) and external 85% aqueous  $\text{H}_3\text{PO}_4$  ( $\delta$  0.0 ppm). The mass spectra were measured with a GC Finnigan MAT SSQ-7000 mass spectrometer. Follow up of the reactions and checking the purity of the compounds were made by Thin Layer Chromatography (TLC) on silica gel-precoated aluminum sheets (Type 60, F 254, Merck, Darmstadt, Germany) with eluent of petroleum ether (b.r. 60-80°C)/ethyl acetate and the spots were detected by exposure to UV lamp at  $\lambda_{254}$  nanometer for a few seconds. The chemical names given for the prepared compounds are according to the IUPAC system. The reported yields are based upon pure materials isolated by column chromatography with eluent of petroleum ether (b.r. 60-80°C)/ethyl acetate. Solvents were dried/purified according to conventional procedures.

### Experimental: Spectral Data

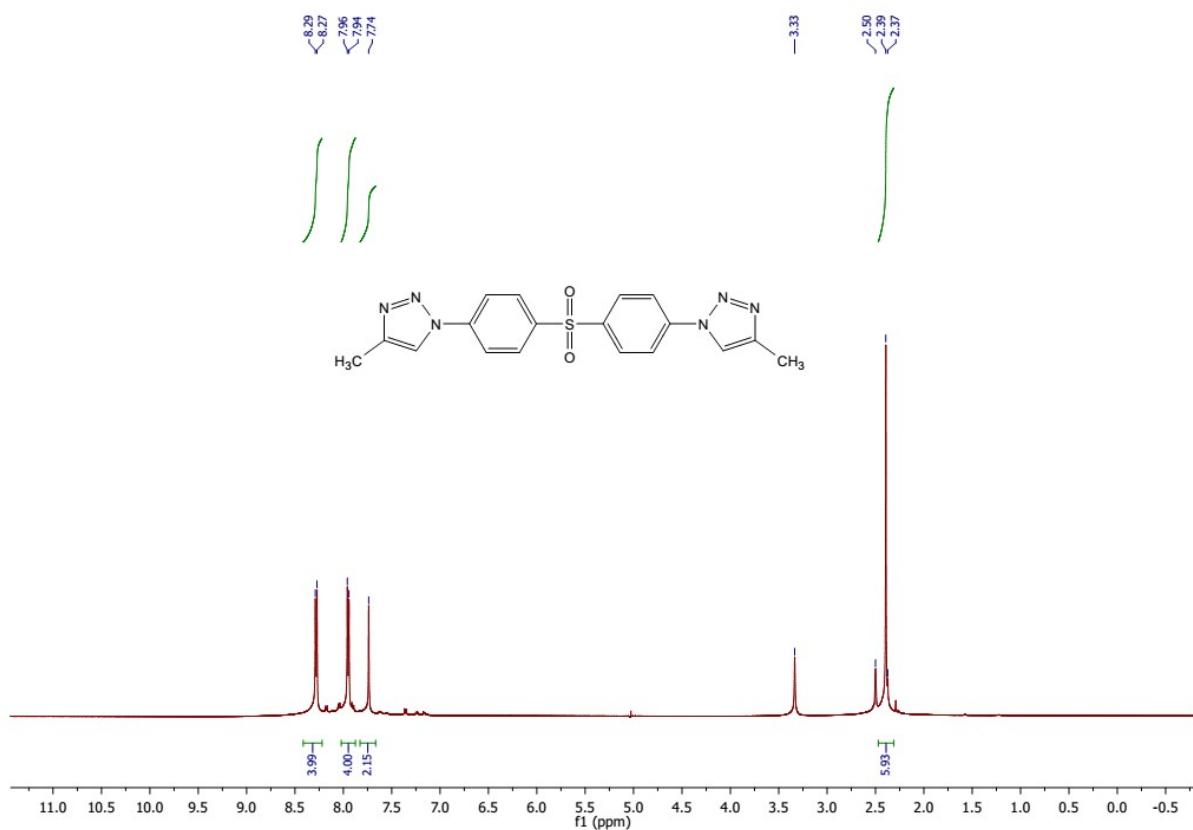


Figure : <sup>1</sup>H NMR of compound 3a

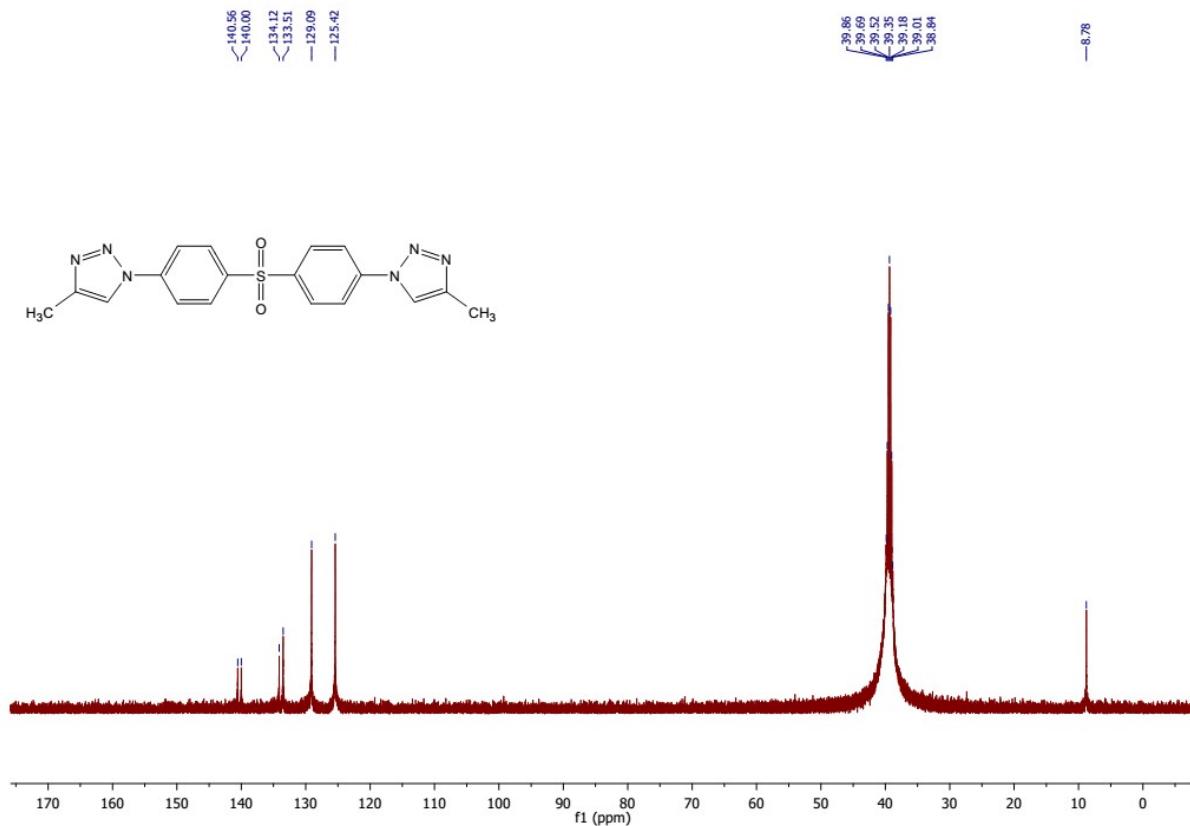
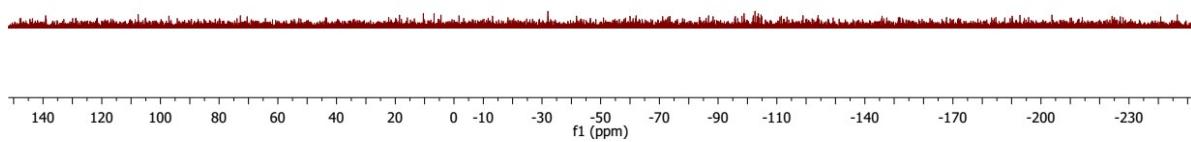


Figure :  $^{13}\text{C}$  NMR of compound 3a



**Figure : 13P NMR of compound 3a**

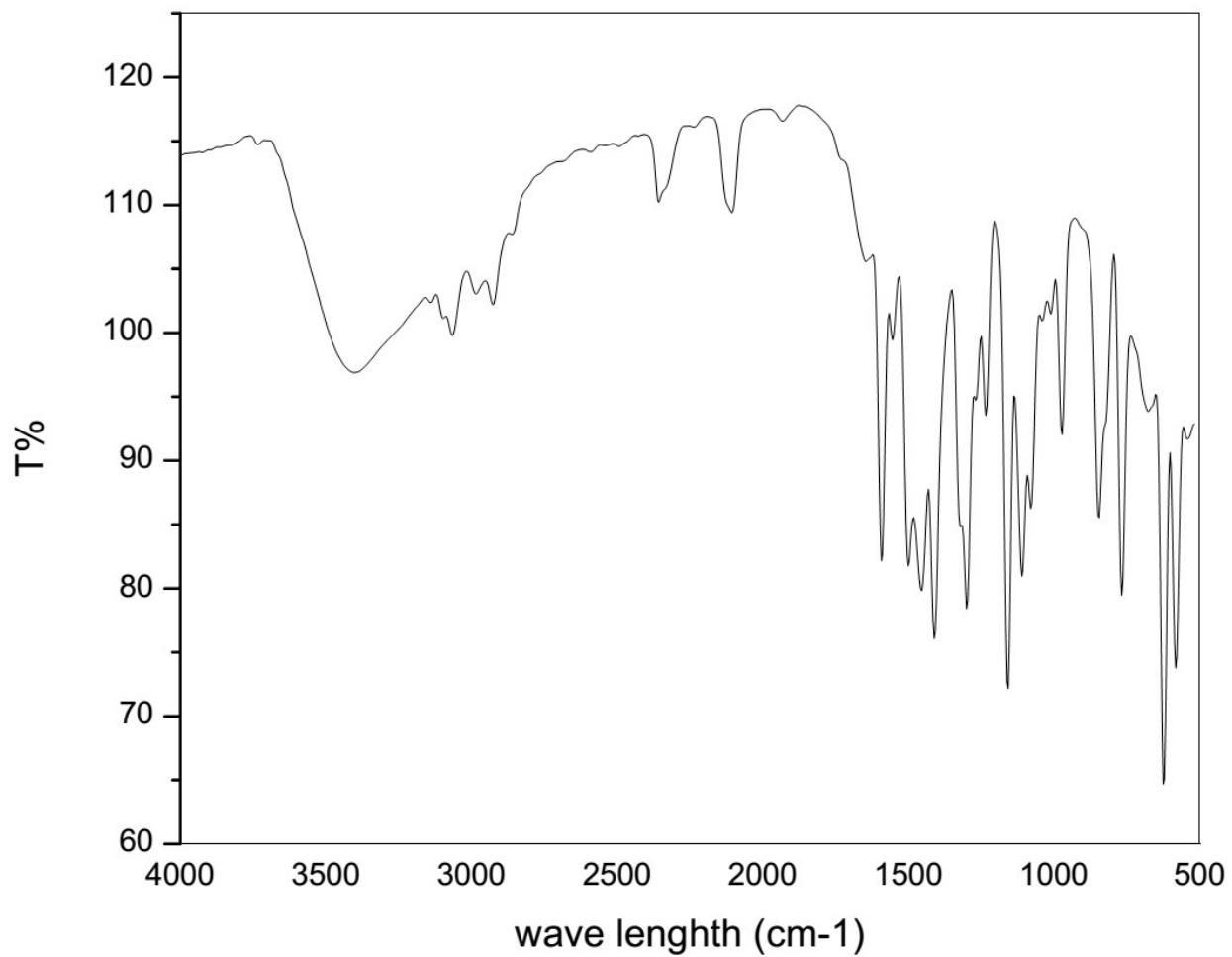


Figure : IR chart of compound 3a

Ewis-3a #1094 RT: 3.75 AV: 1 NL: 2.32E4  
T: {0,0} + c El Full ms [50.00-650.00]

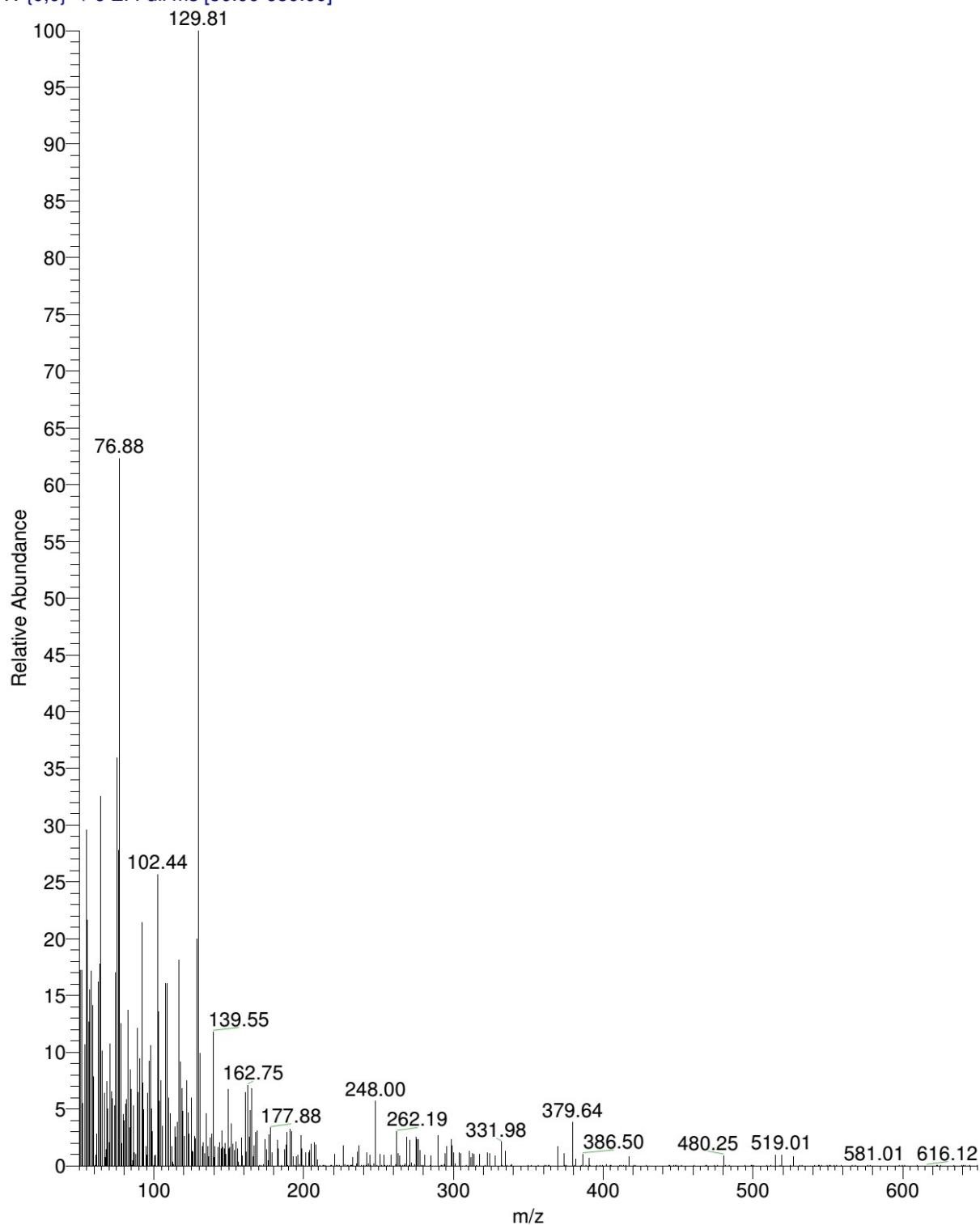


Figure : Mass spectrum of compound 3a

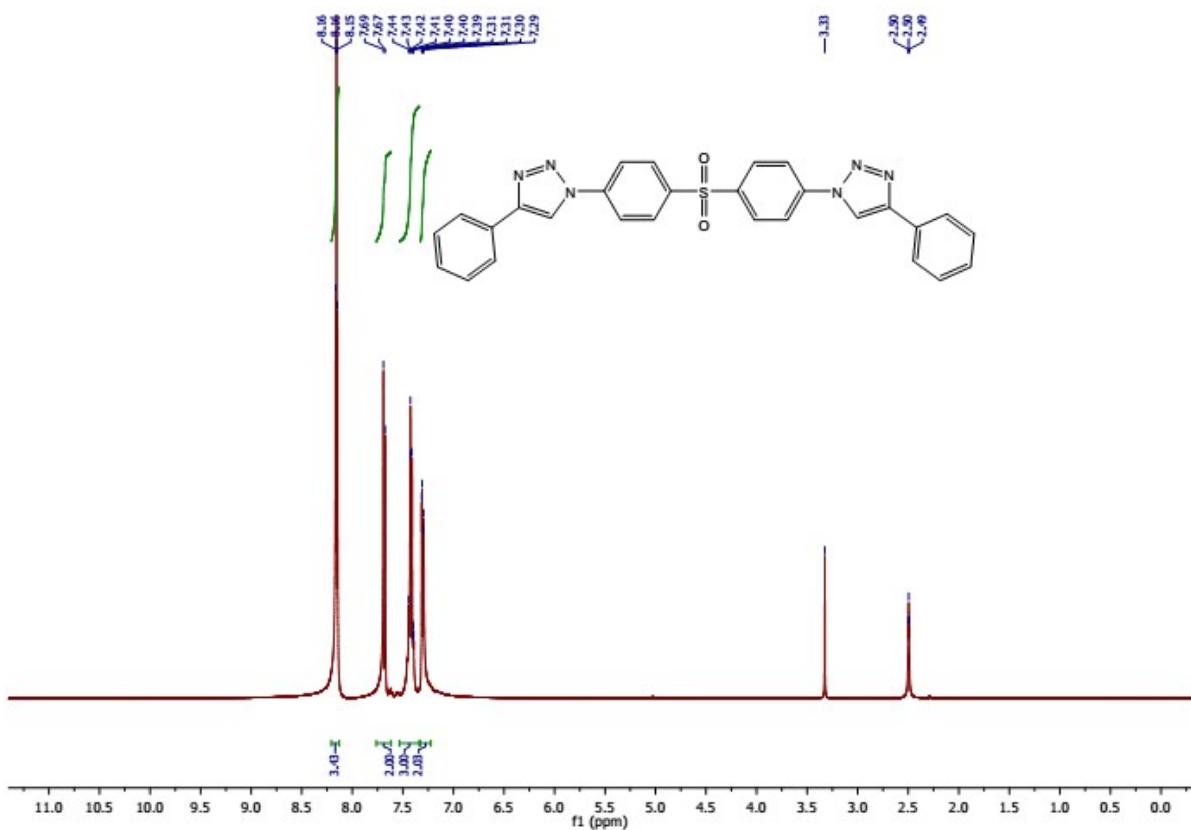


Figure : <sup>1</sup>H NMR of compound 3b

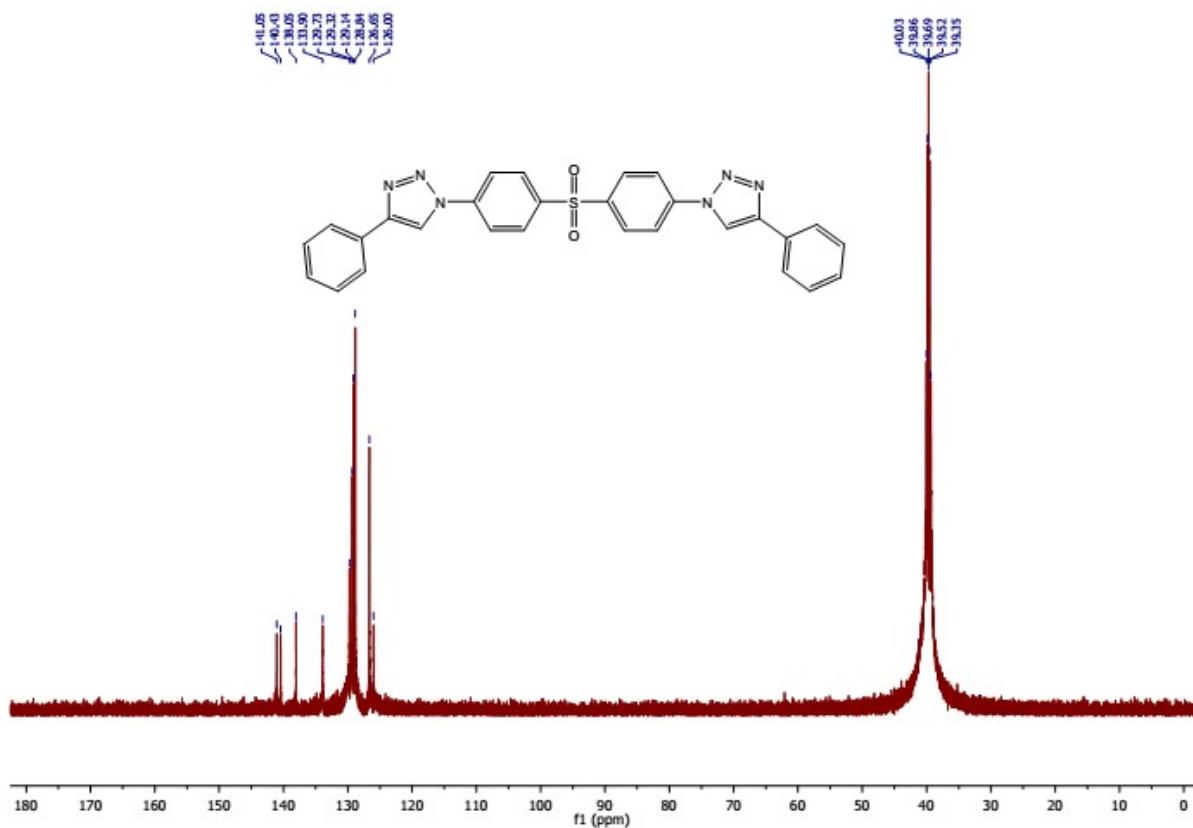
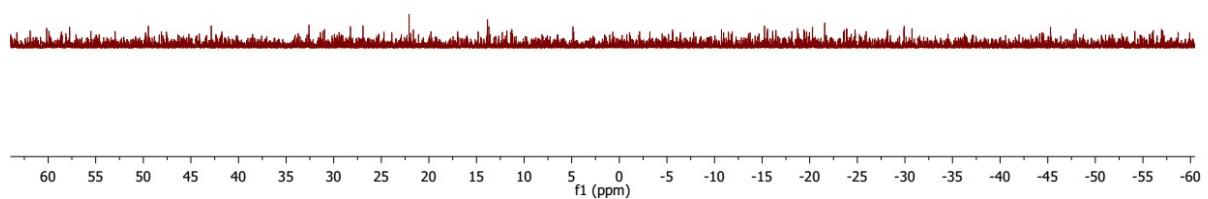
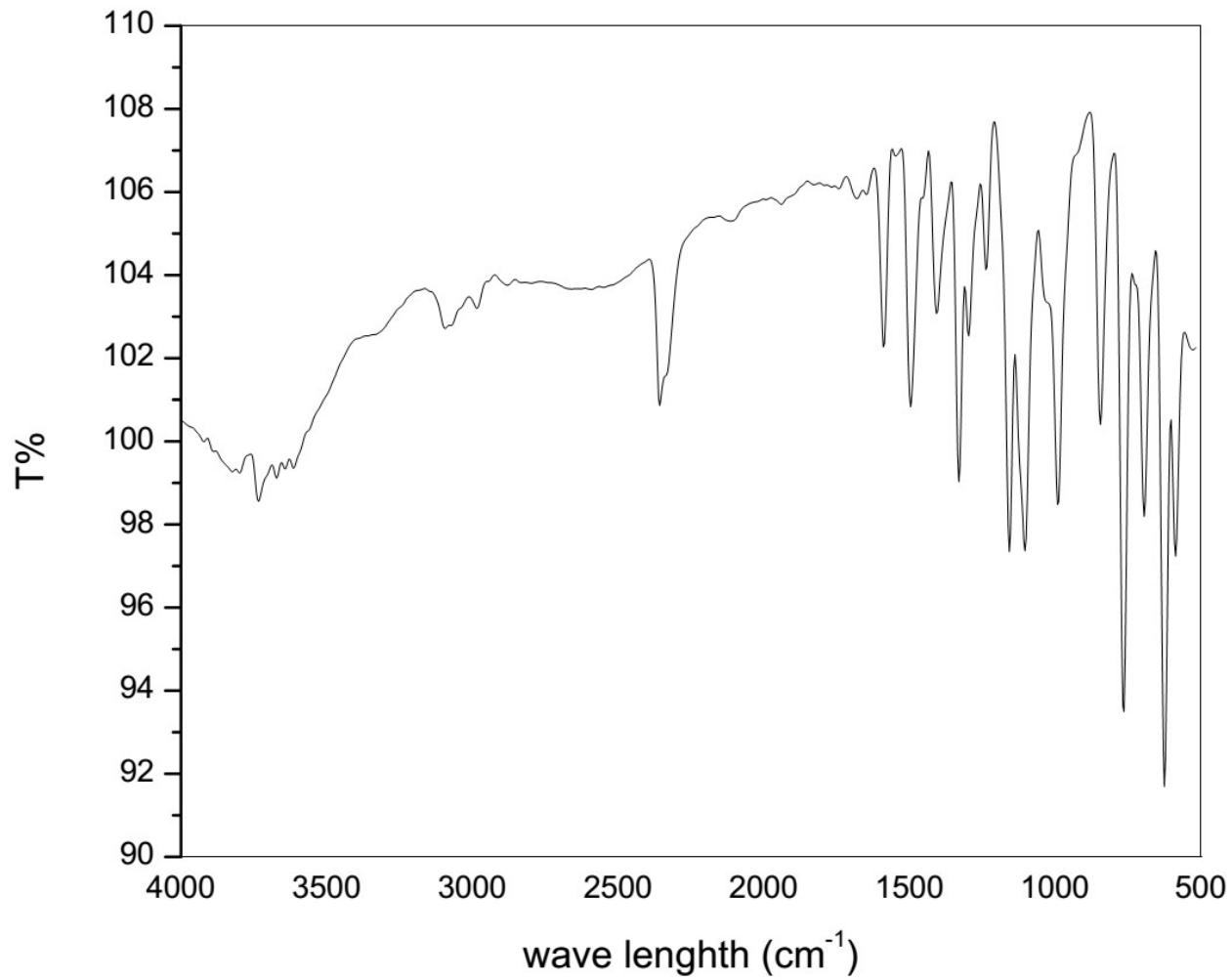


Figure :  $^{13}\text{C}$  NMR of compound 3b



**Figure : <sup>31</sup>P NMR of compound 3b**



**Figure : IR chart of compound 3b**

Ewis-3b #364 RT: 1.27 AV: 1 NL: 3.84E4  
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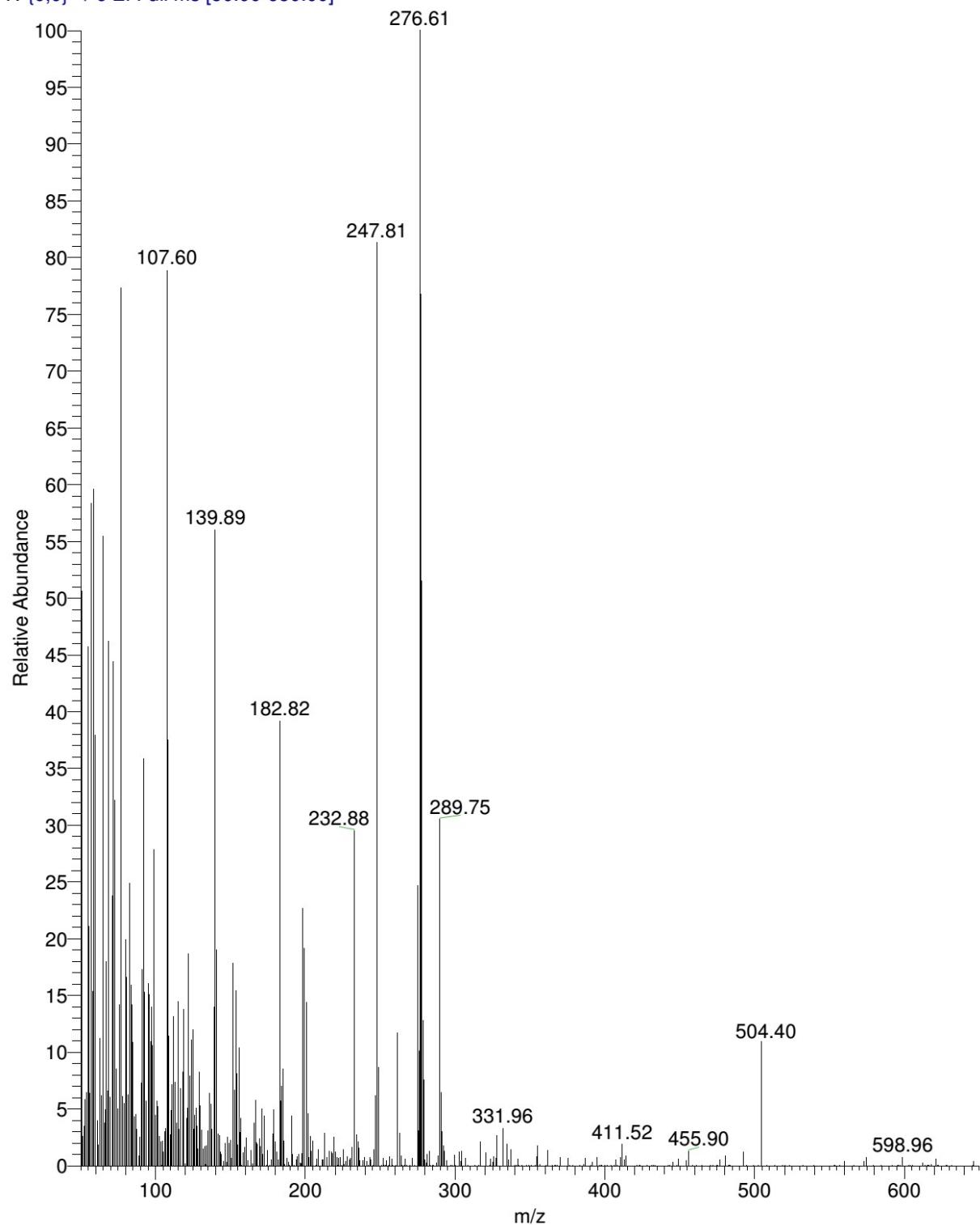


Figure : Mass spectrum of compound 3b

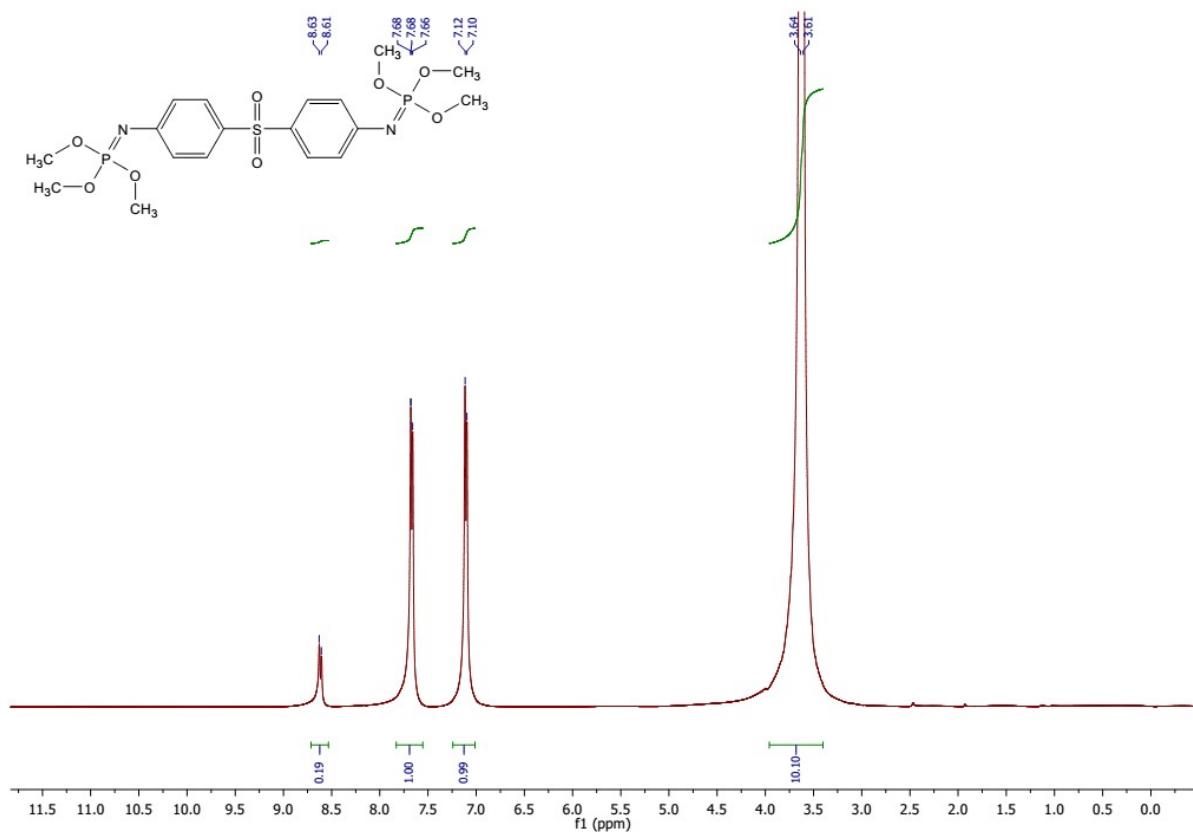


Figure :  $^1\text{H}$  NMR of compound 5a

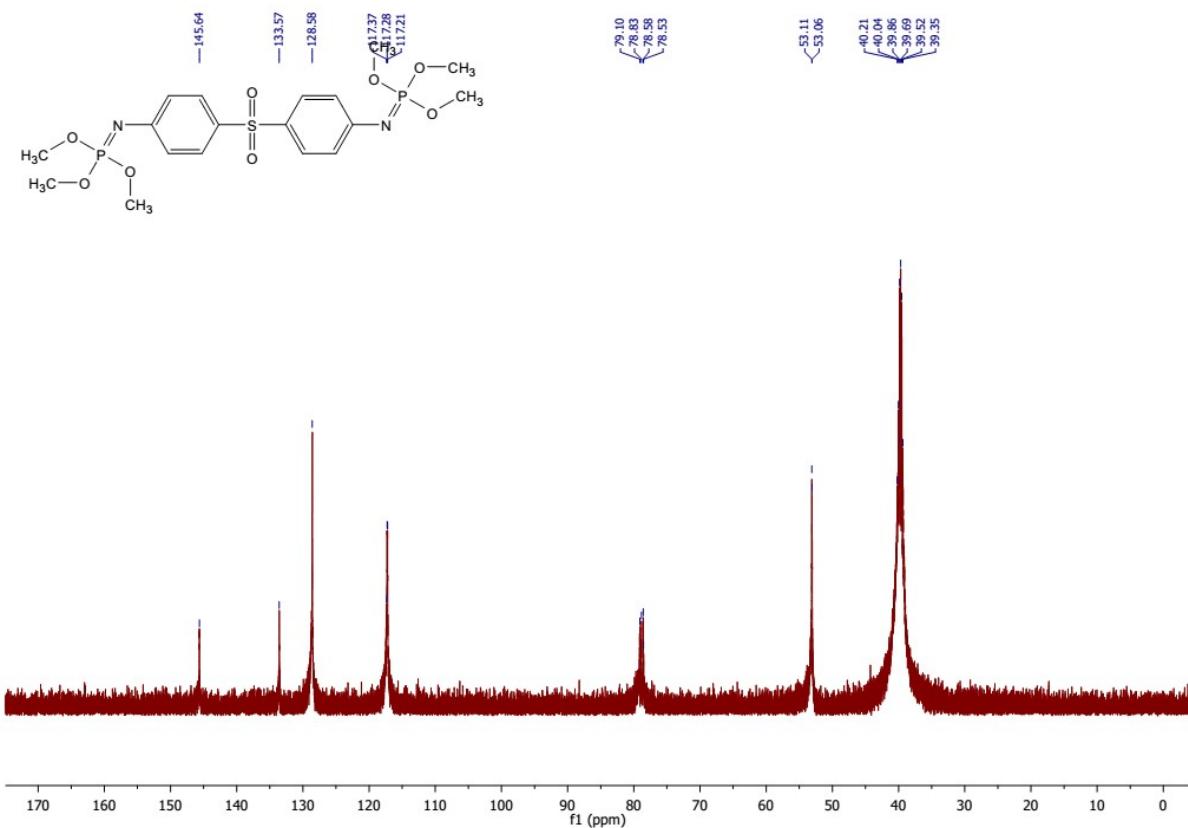
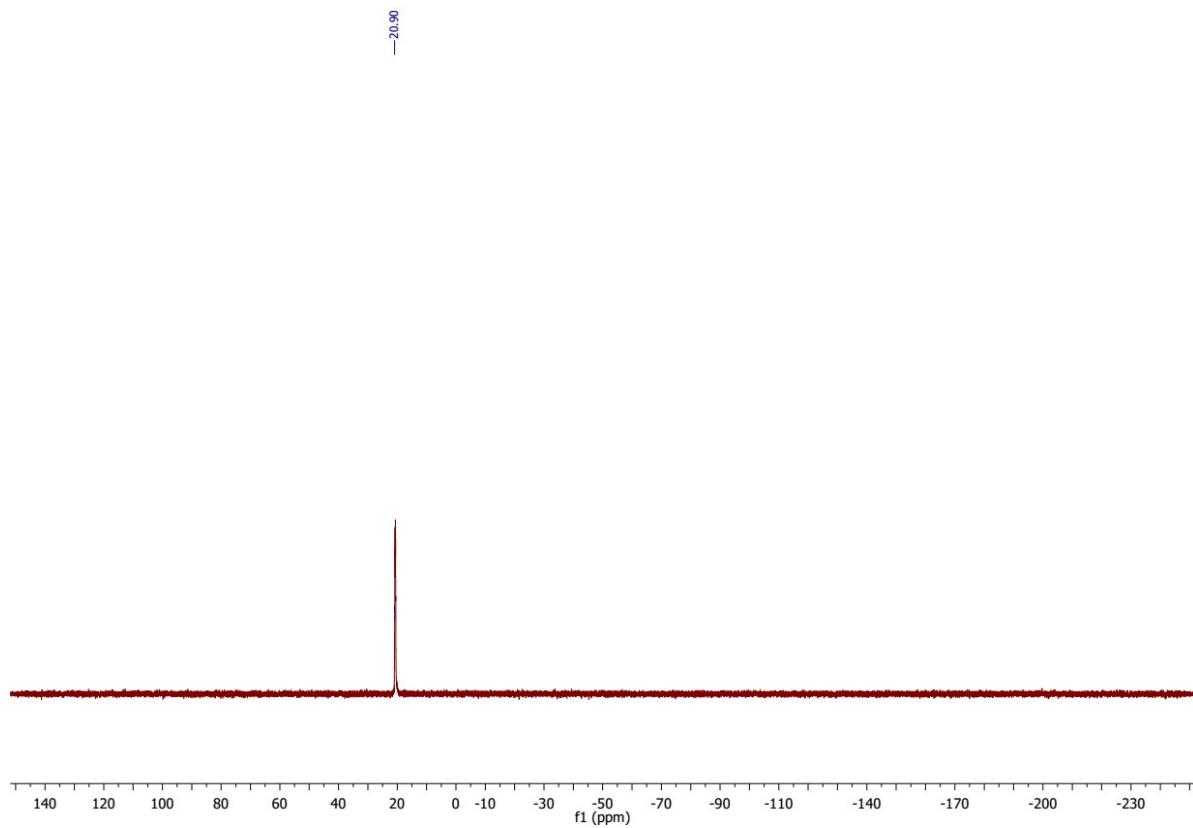


Figure :  $^{13}\text{C}$  NMR of compound 5a



**Figure :  $^{13}\text{P}$  NMR of compound 5a**

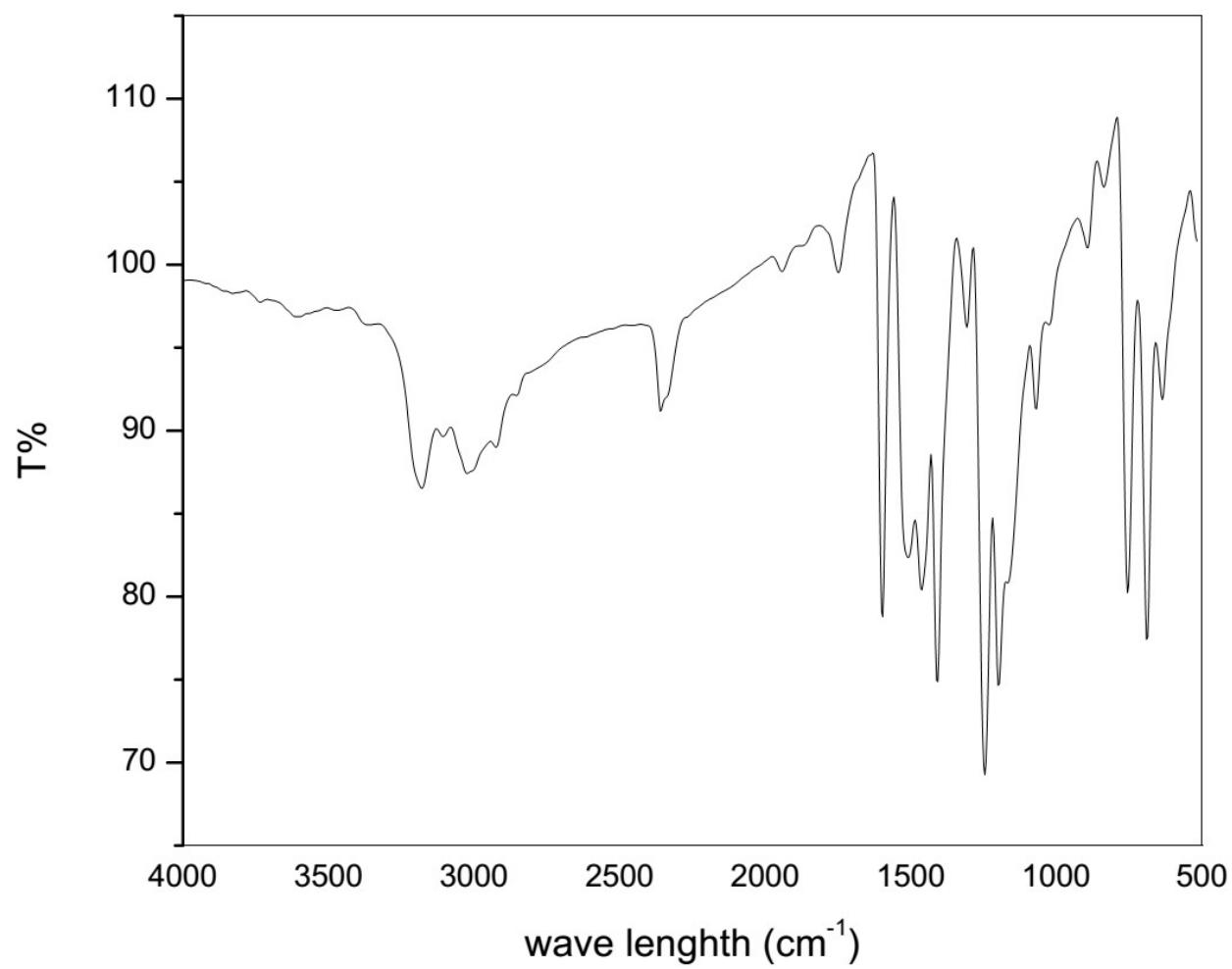


Figure : IR chart of compound 5a

Ewis-5a #745 RT: 2.56 AV: 1 NL: 1.03E4  
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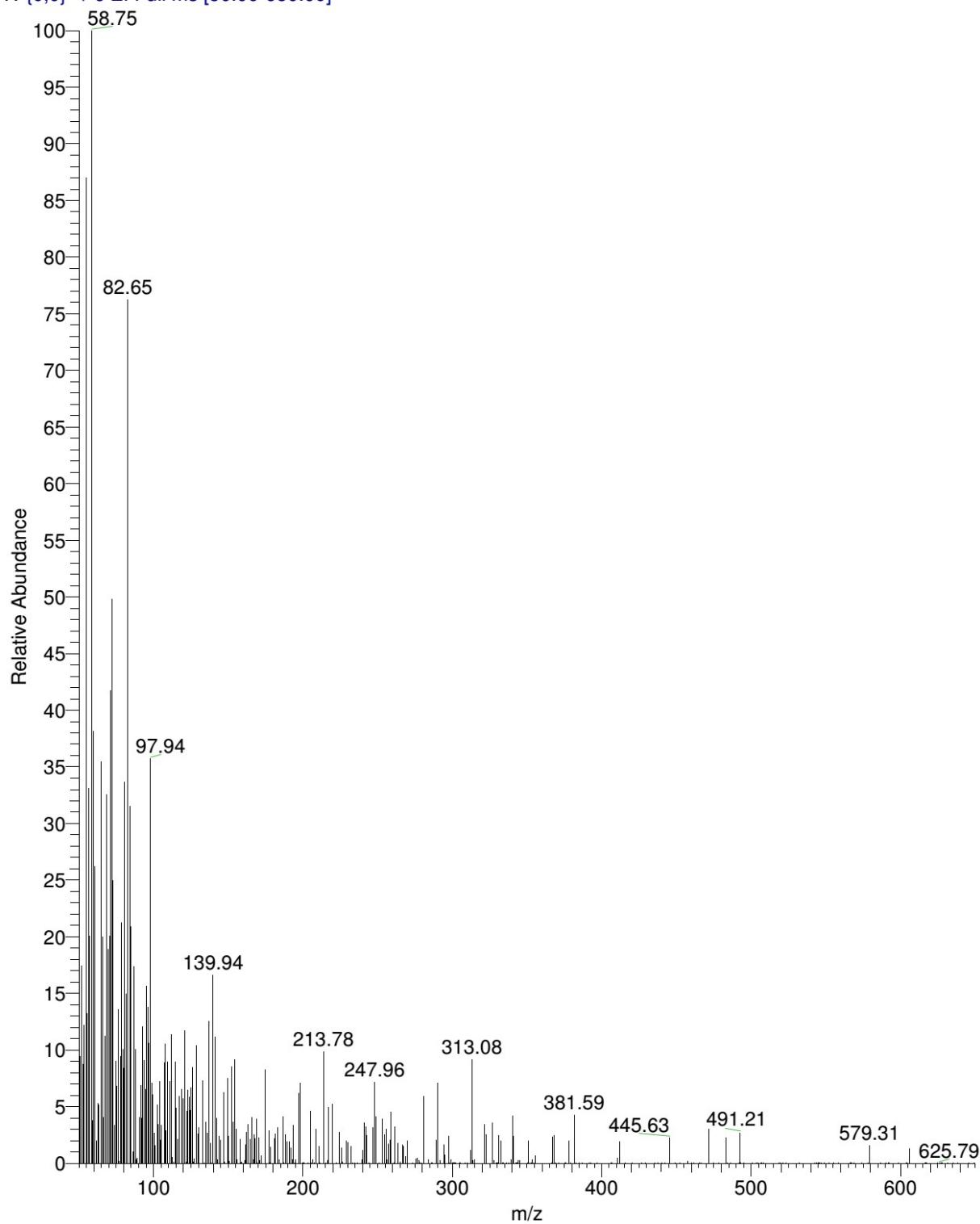


Figure : Mass spectrum of compound 5a

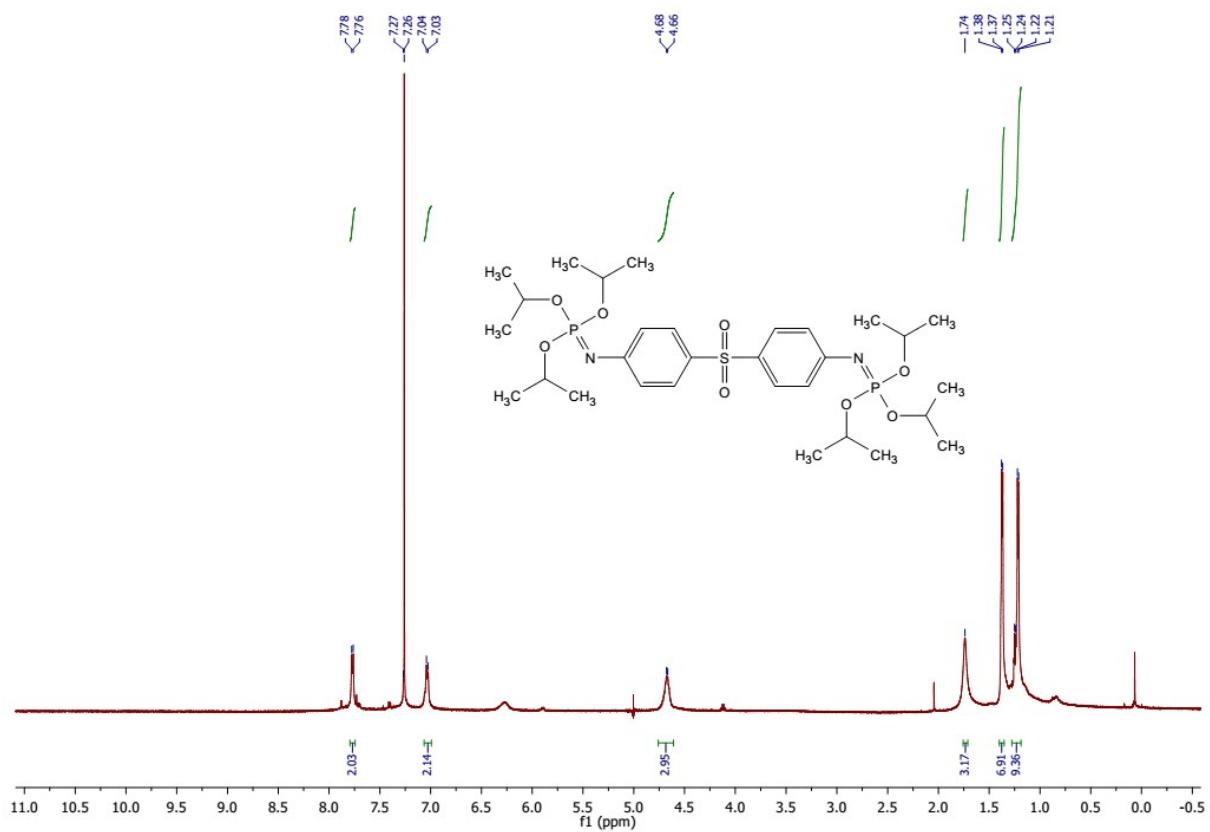
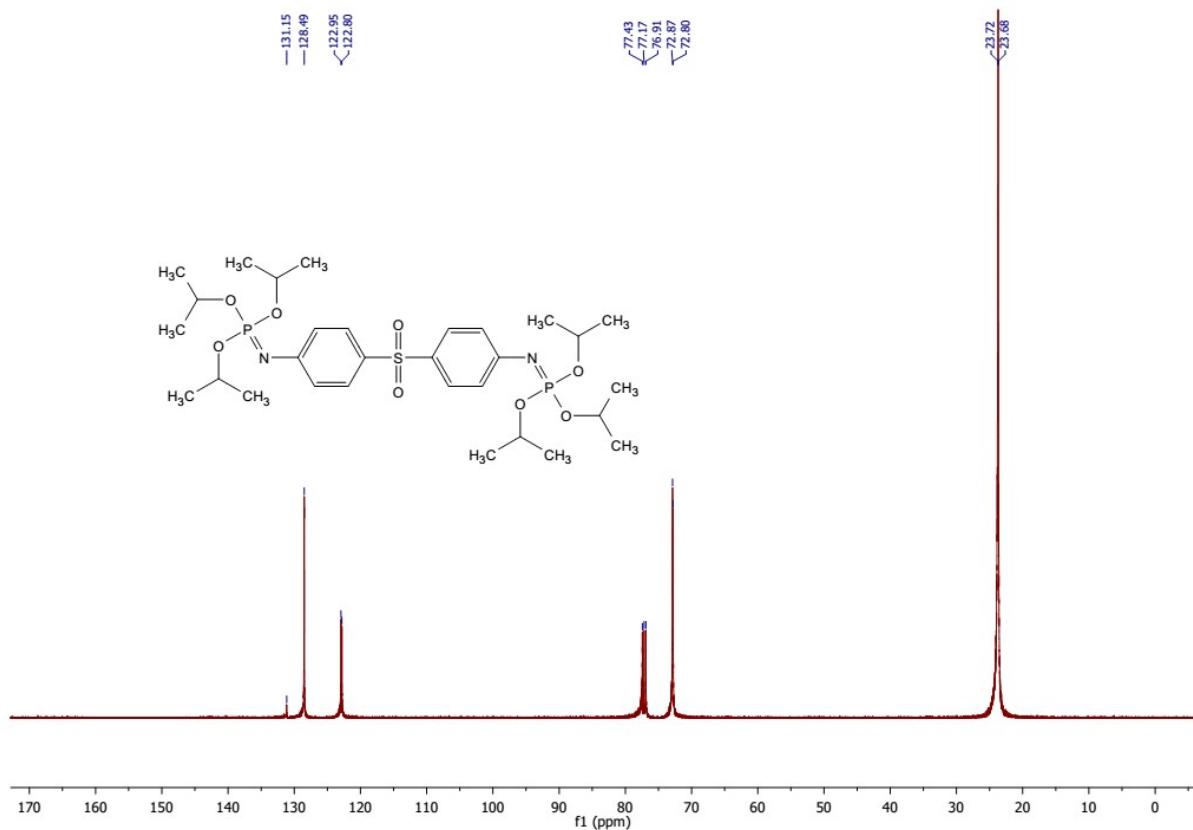
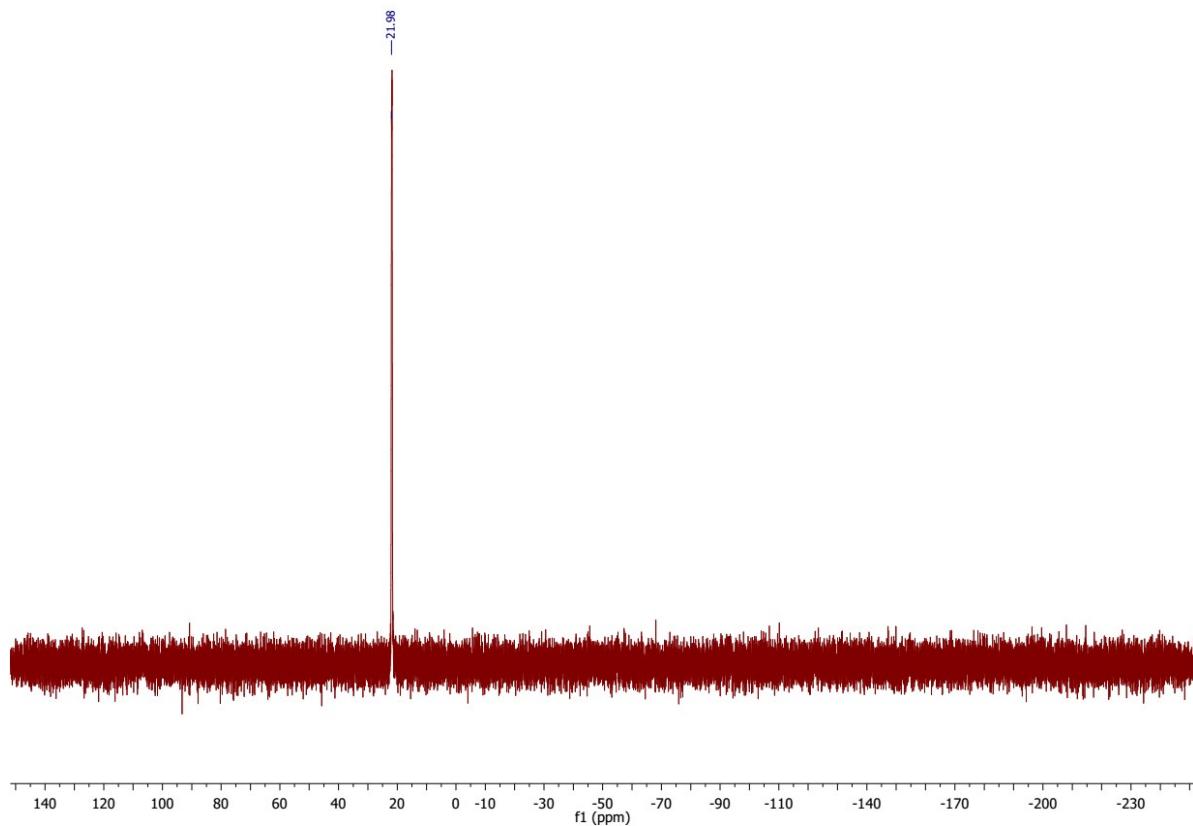


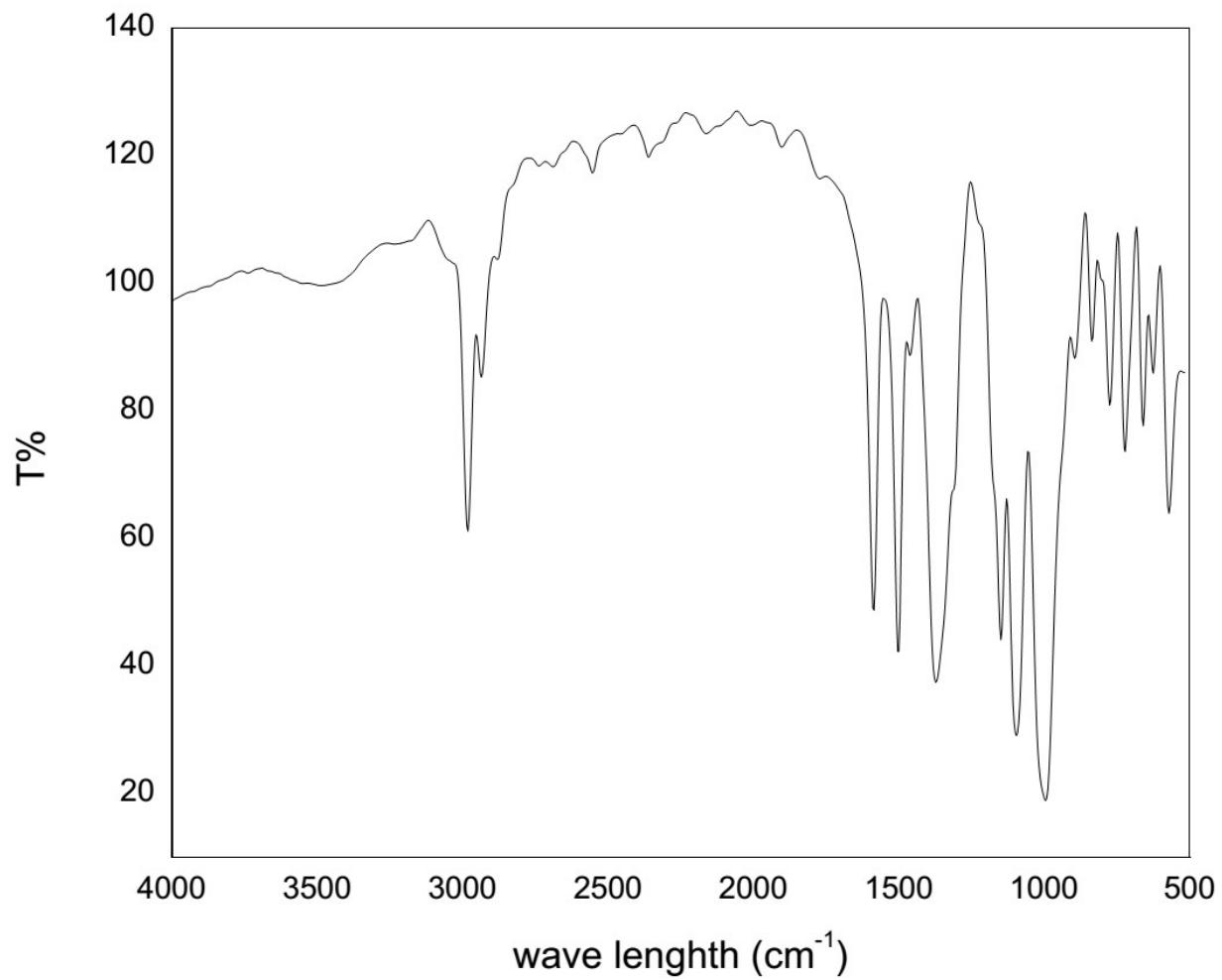
Figure :  $^1\text{H}$  NMR of compound 5b



**Figure :  $^{13}\text{C}$  NMR of compound 5b**



**Figure :  $^{13}\text{P}$  NMR of compound 5b**



**Figure : IR of compound 5b**

Ewis-5b\_250722101350 #830 RT: 2.85 AV: 1 NL: 6.09E4  
T: {0,0} + c EI Full ms [50.00-700.00]

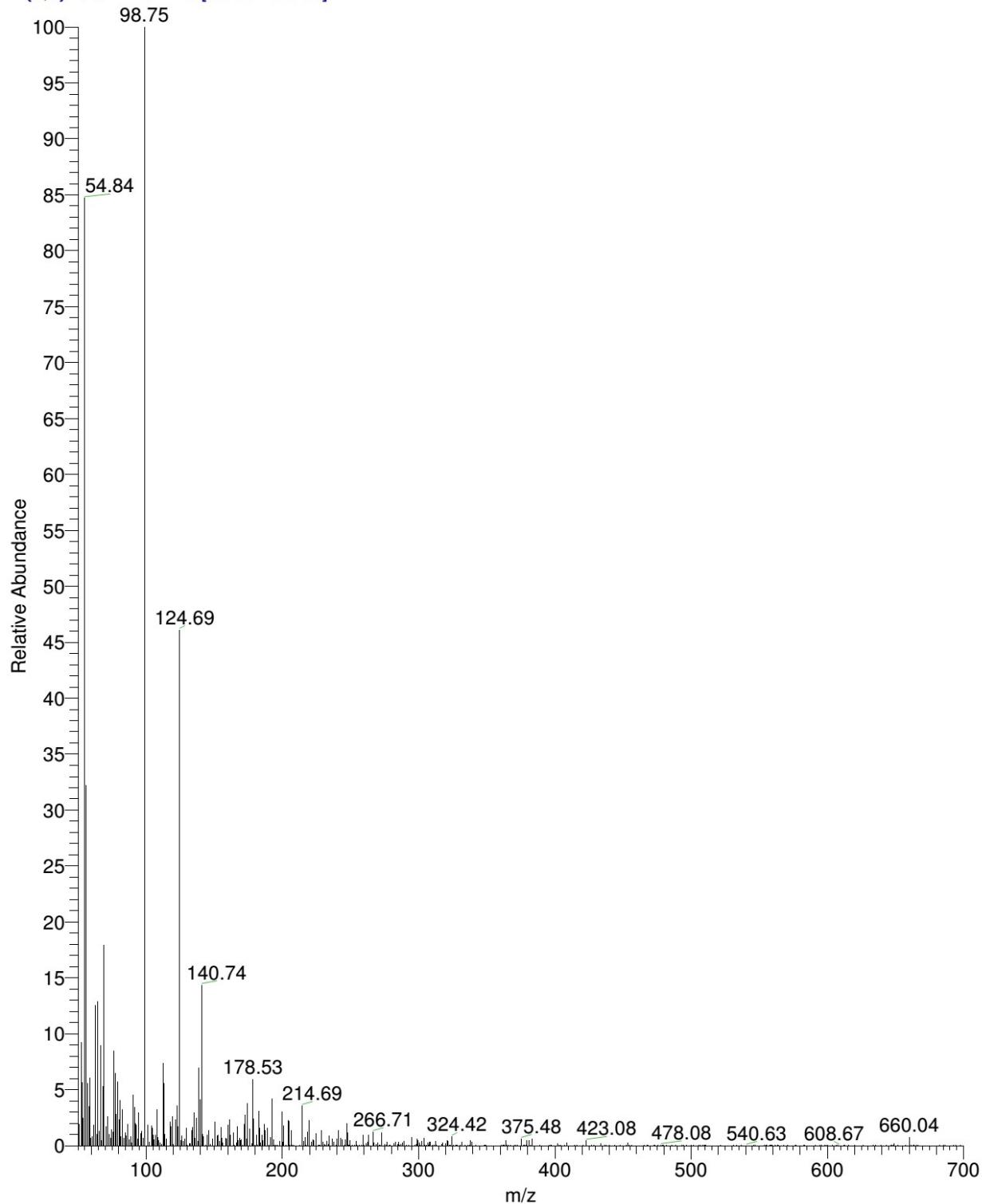


Figure : mass spectrum of compound 5b

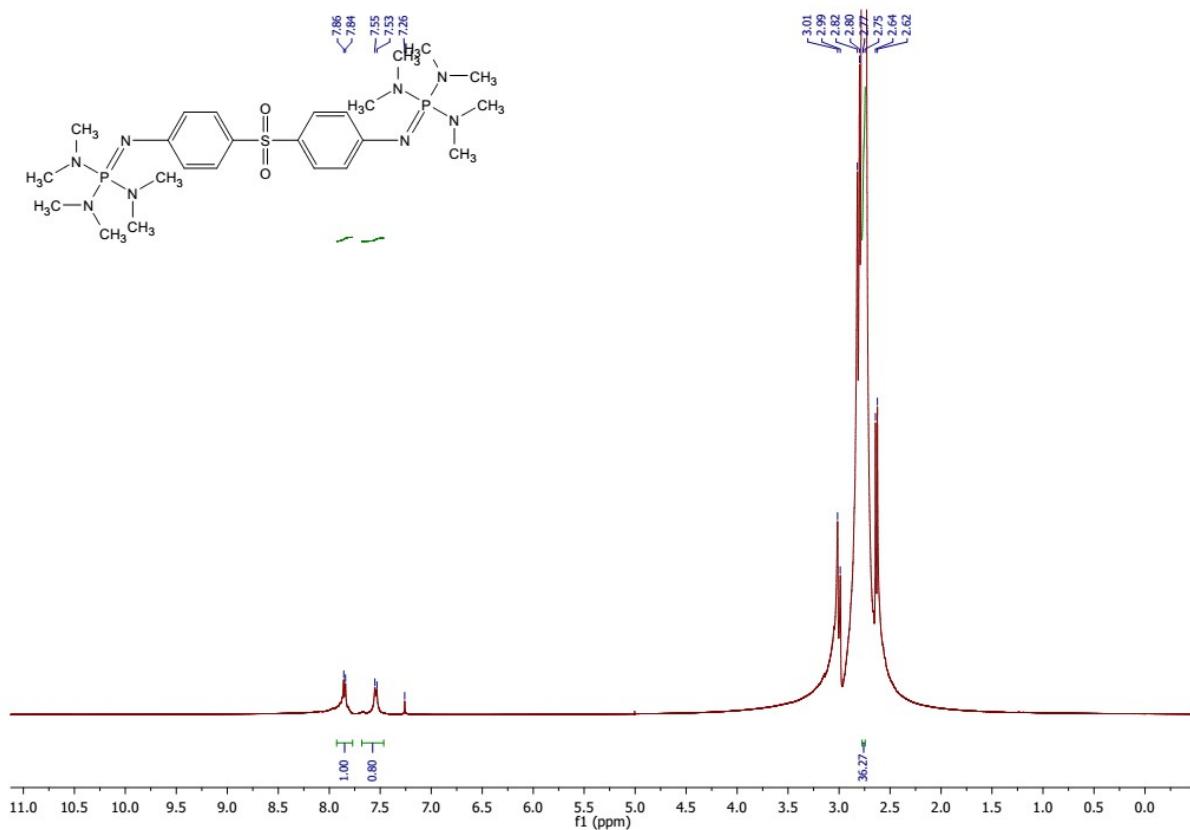


Figure :  $^1\text{H}$  NMR of compound **5c**

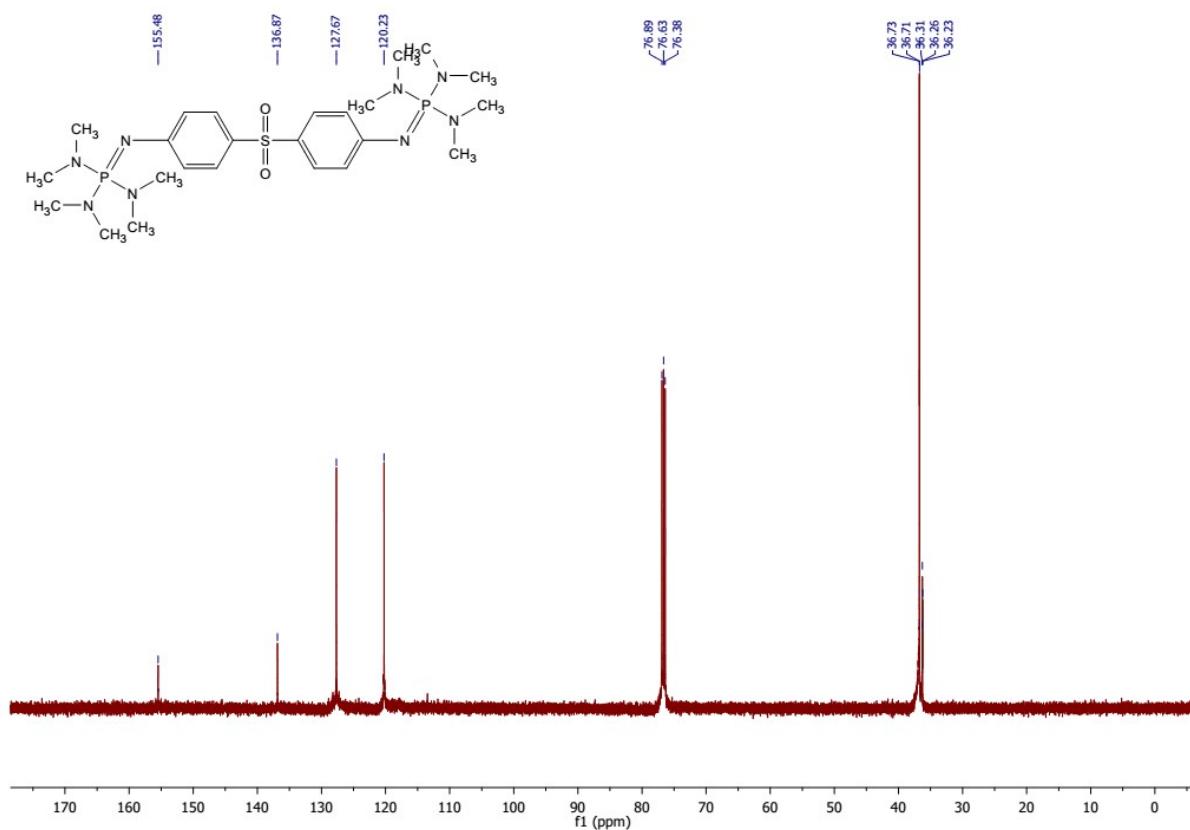
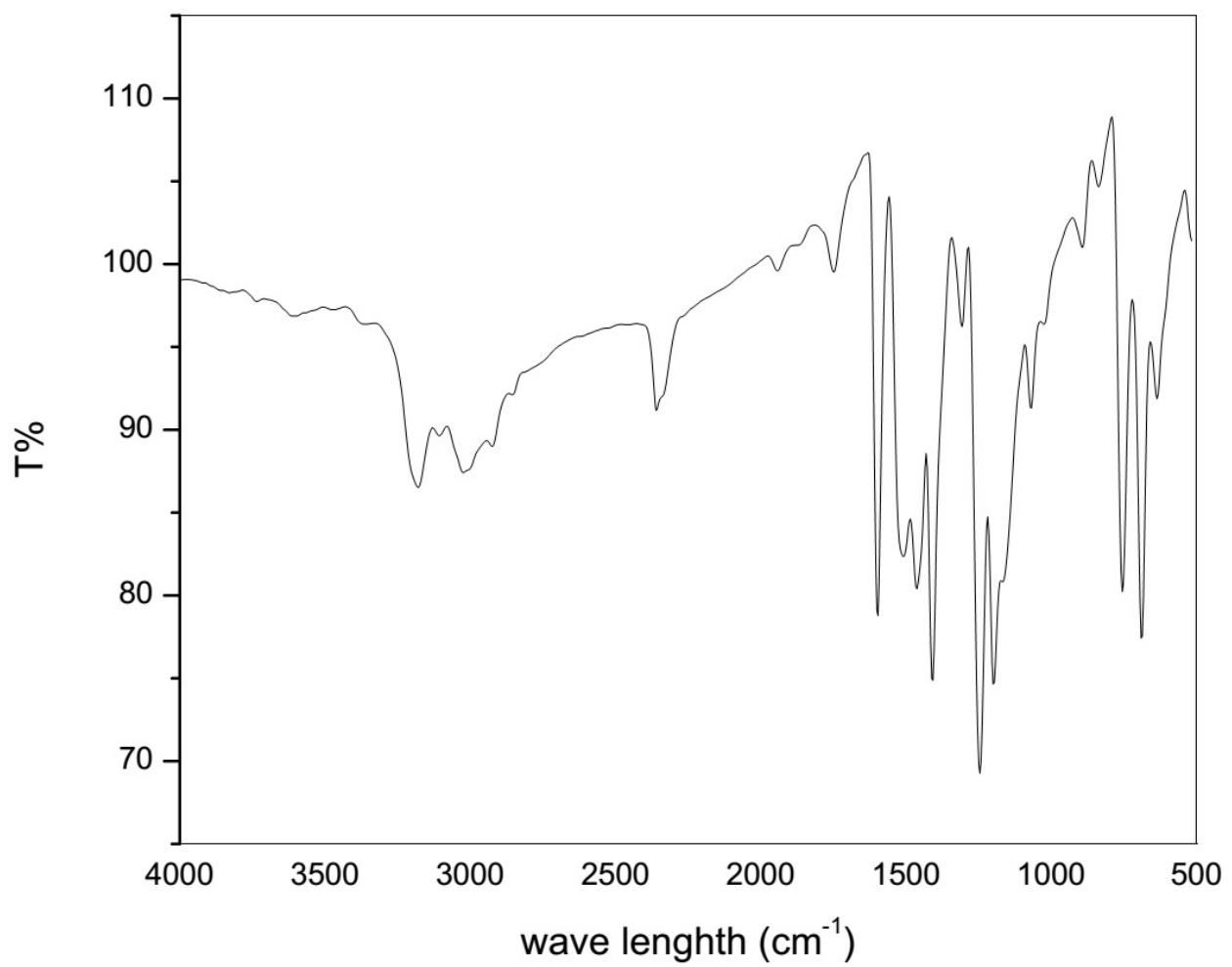


Figure :  $^{13}\text{C}$  NMR of compound 5c



**Figure : IR chart of compound 5c**

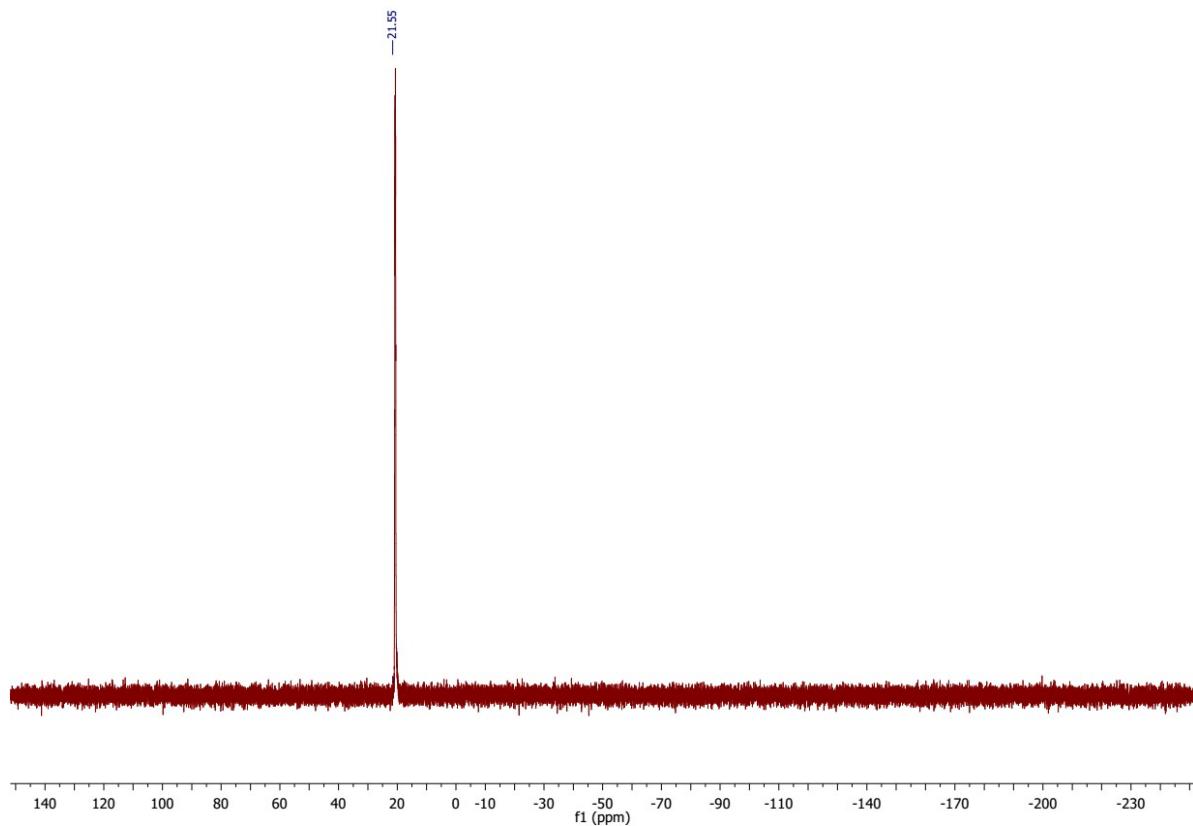


Figure :  $^{31}\text{P}$  NMR of compound 5c

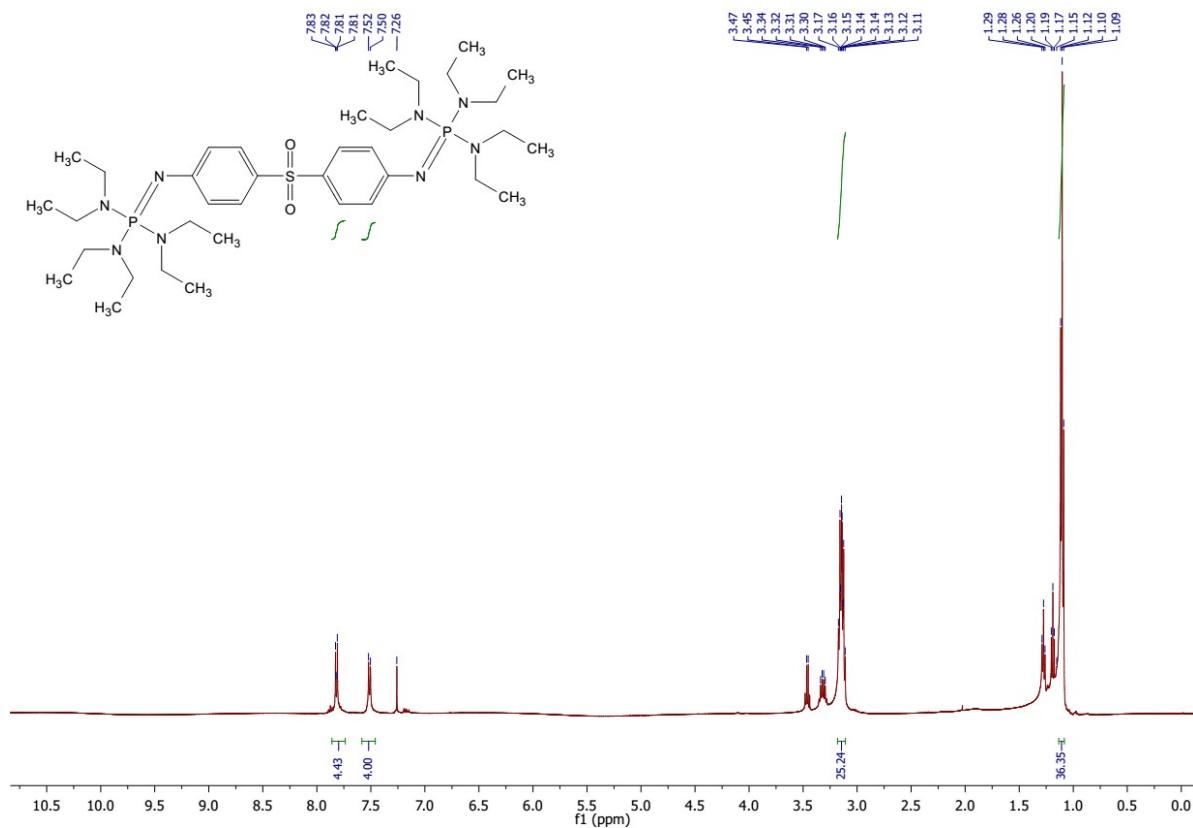


Figure :  $^1\text{H}$  NMR of compound 5d

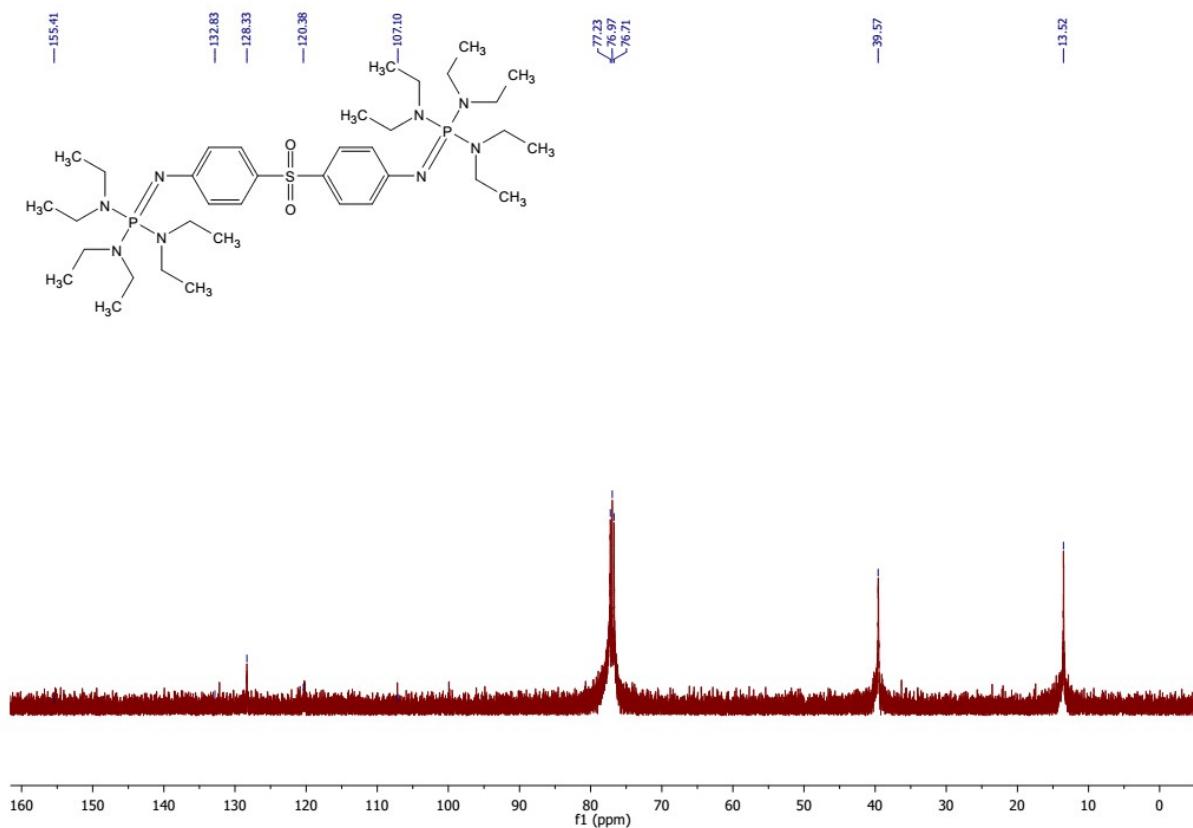
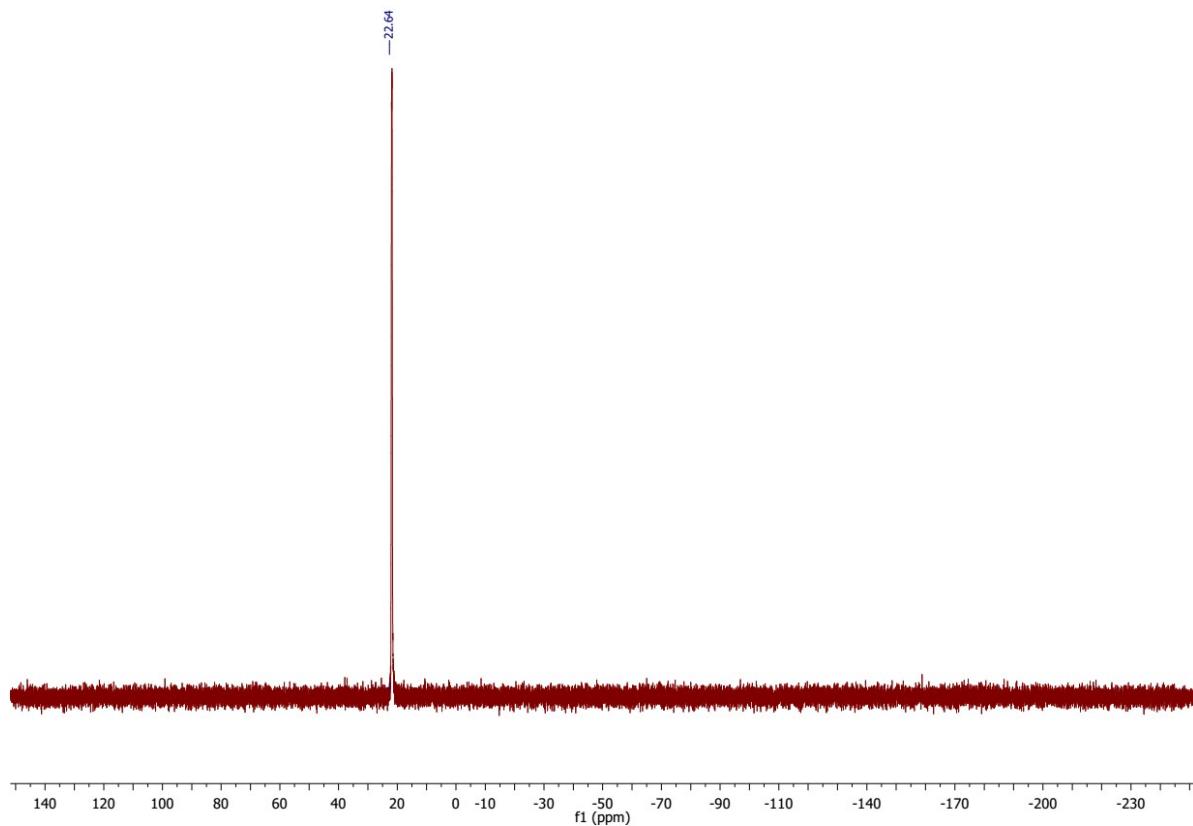


Figure :  $^{13}\text{C}$  NMR of compound 5d



**Figure :  $^{13}\text{P}$  NMR of compound 5d**

Ewis-5d #1154 RT: 3.96 AV: 1 NL: 1.16E4  
T: {0,0} + c El Full ms [50.00-850.00]

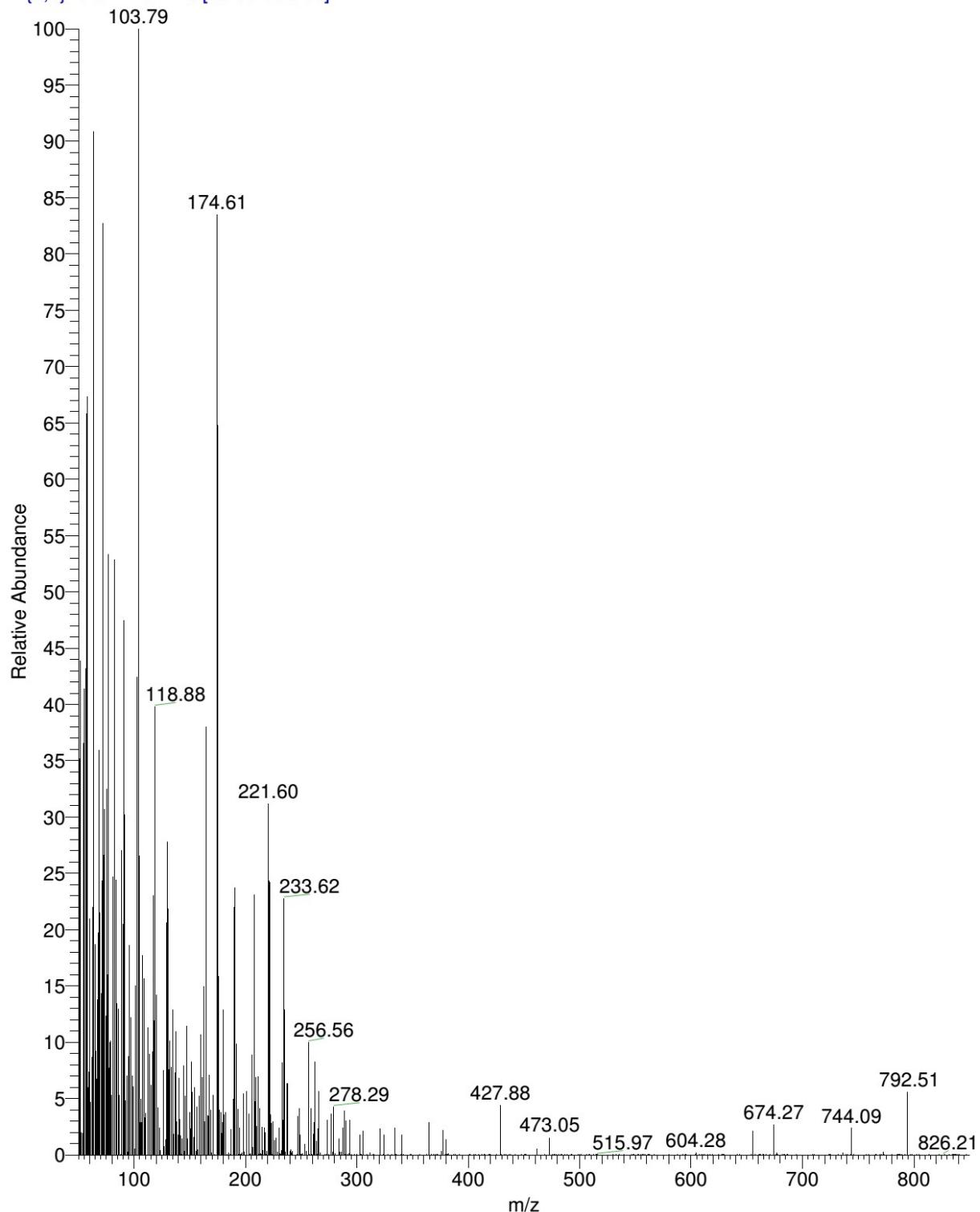
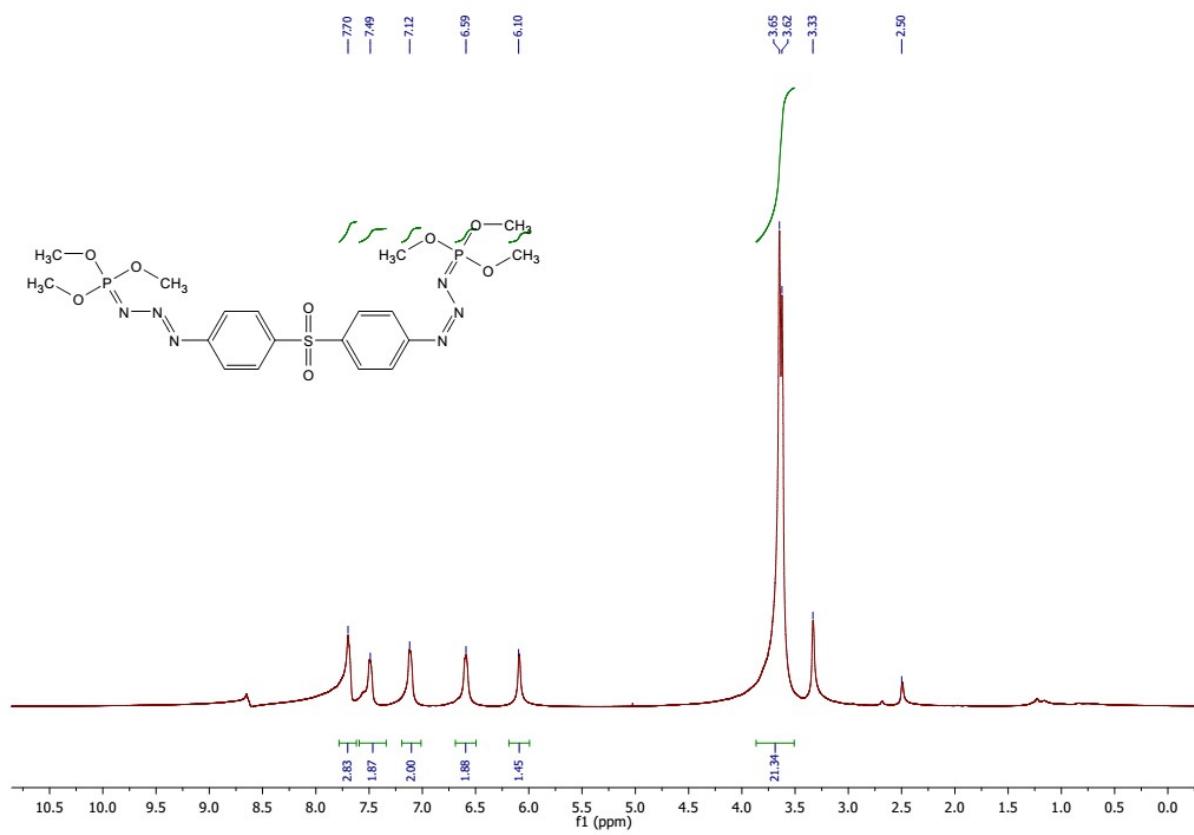
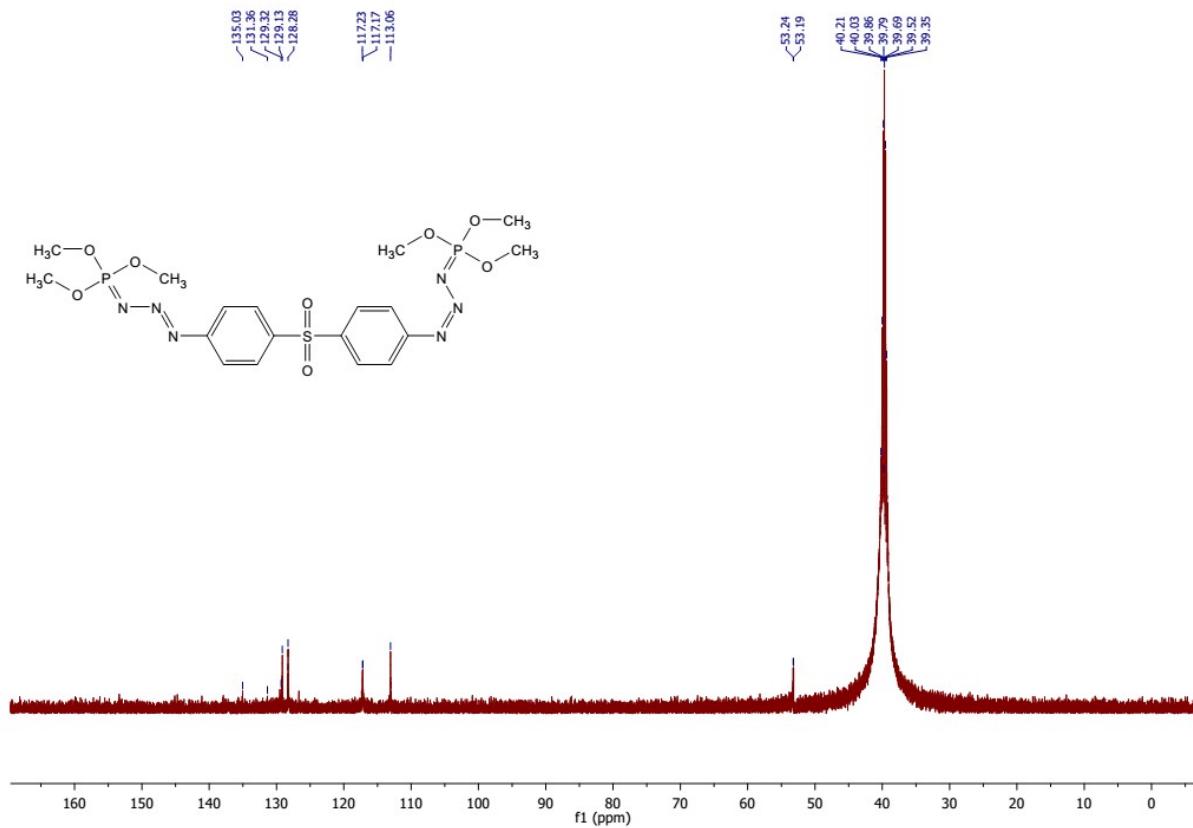


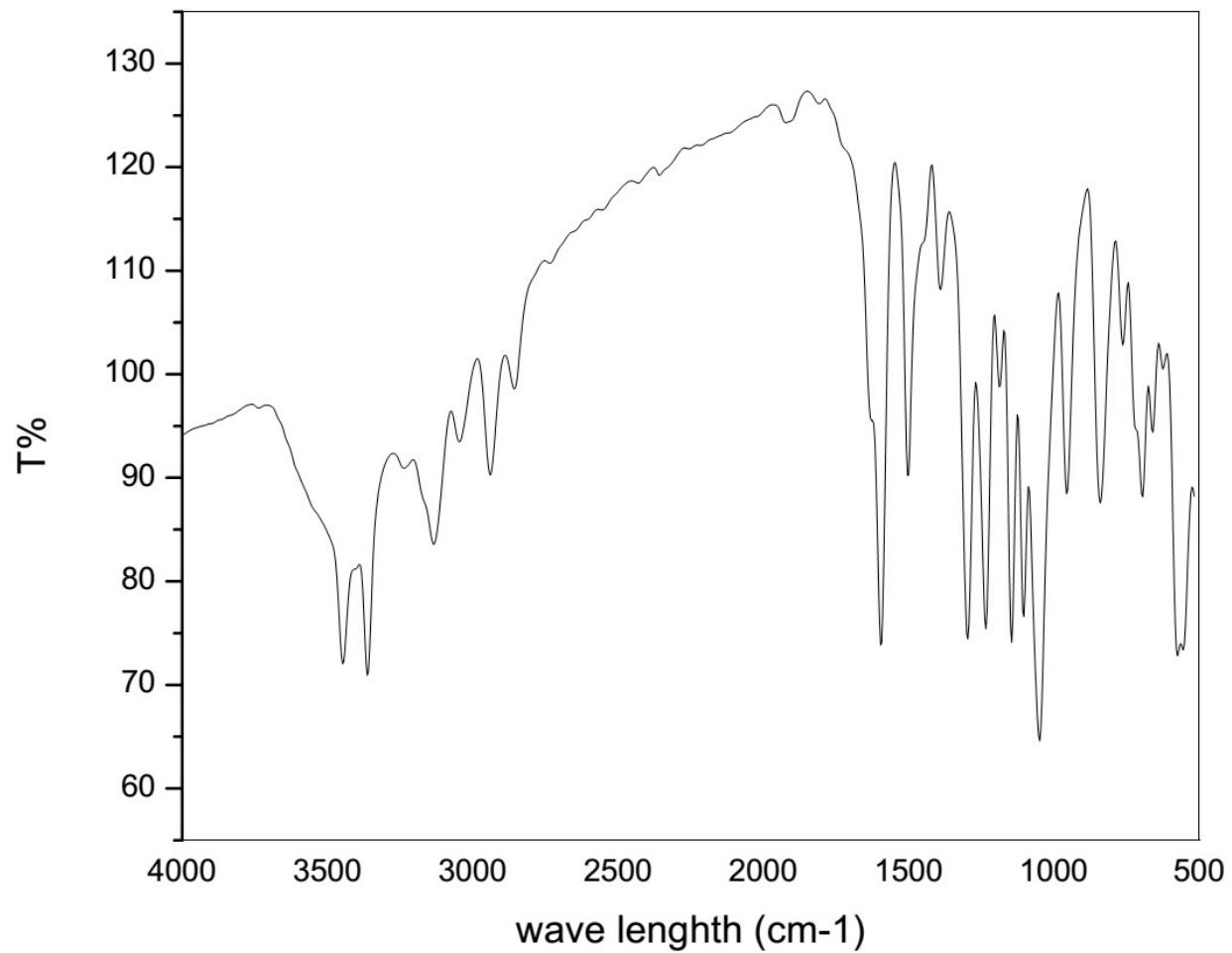
Figure : Mass spectrum of compound 5d



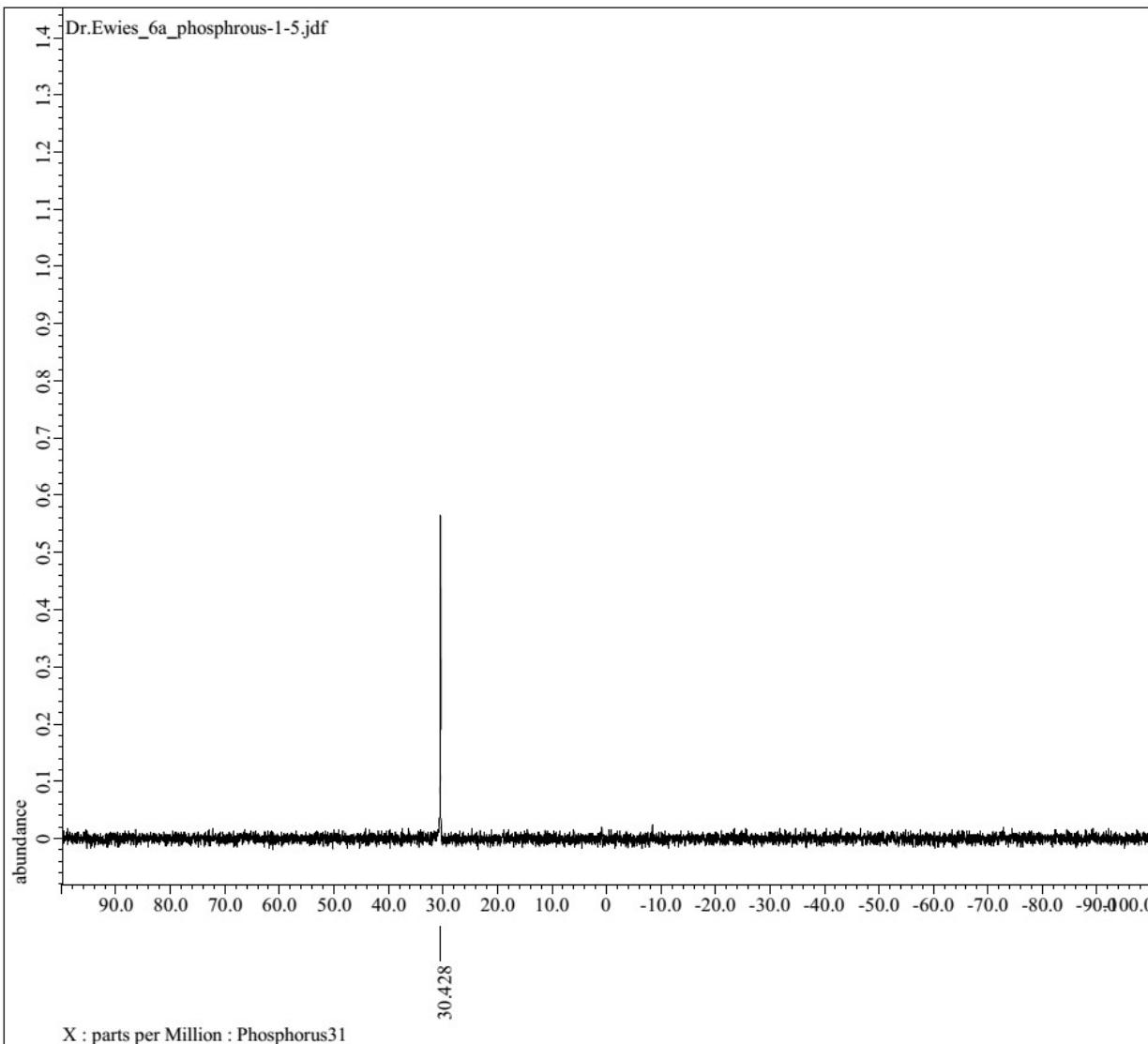
**Figure :  $^1\text{H}$  NMR of compound 6a**



**Figure : <sup>13</sup>C NMR of compound 6a**



**Figure : IR chart of compound 6a**



**Figure :  $^{31}\text{P}$  NMR of compound 6a**

Ewis-6a #844 RT: 2.90 AV: 1 NL: 2.28E5  
T: {0,0} + c El Full ms [50.00-650.00]

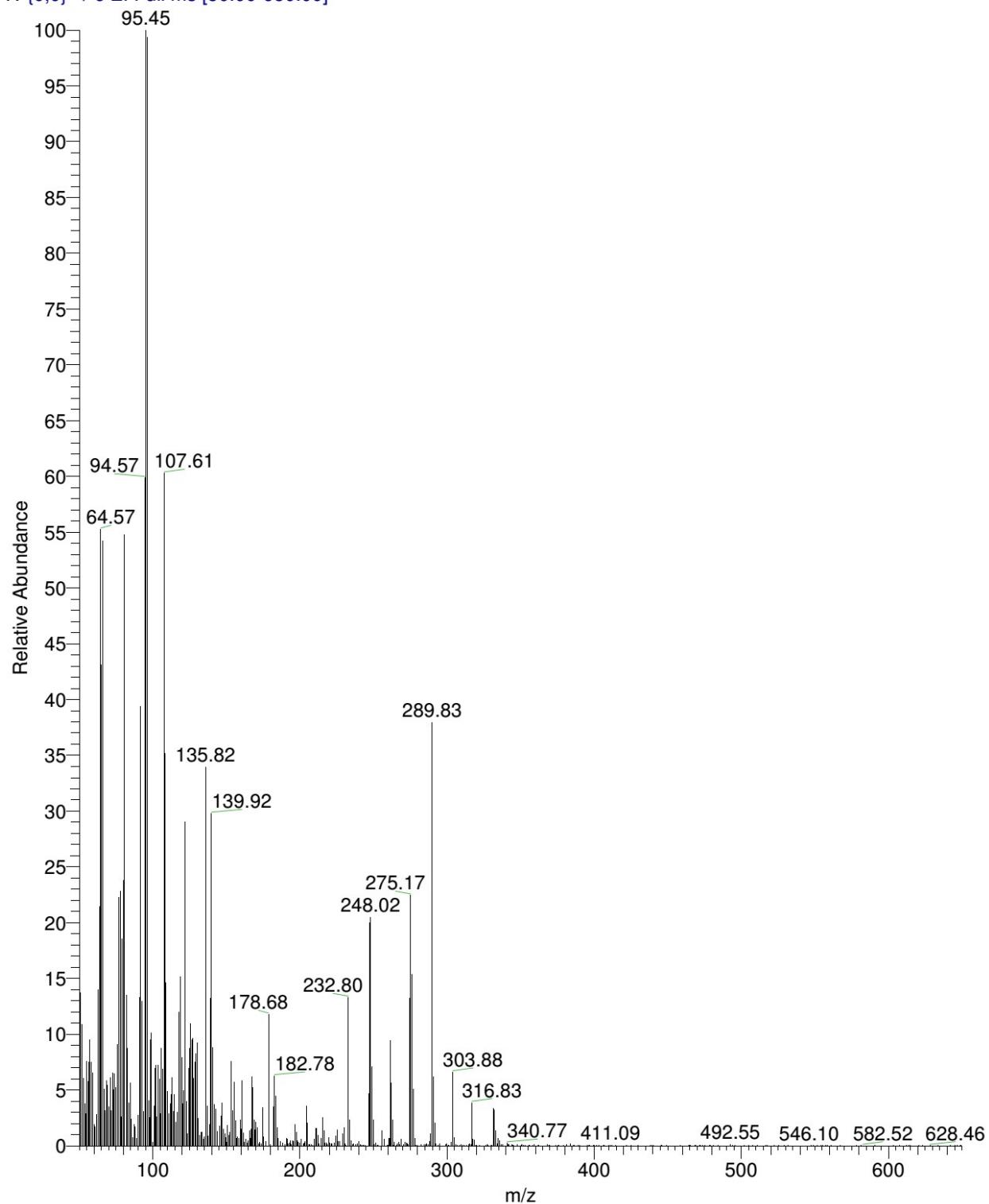


Figure : Mass spectrum of compound 6a

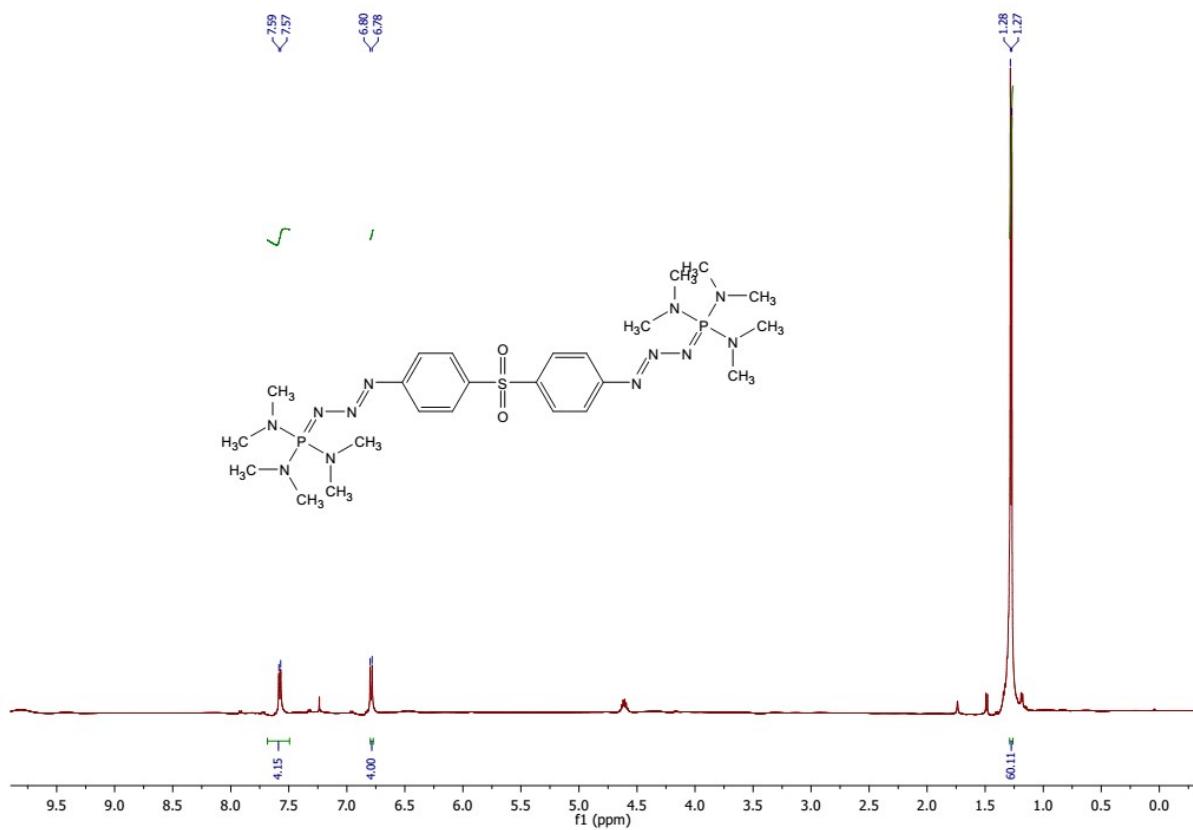


Figure : <sup>1</sup>H NMR of compound 6b

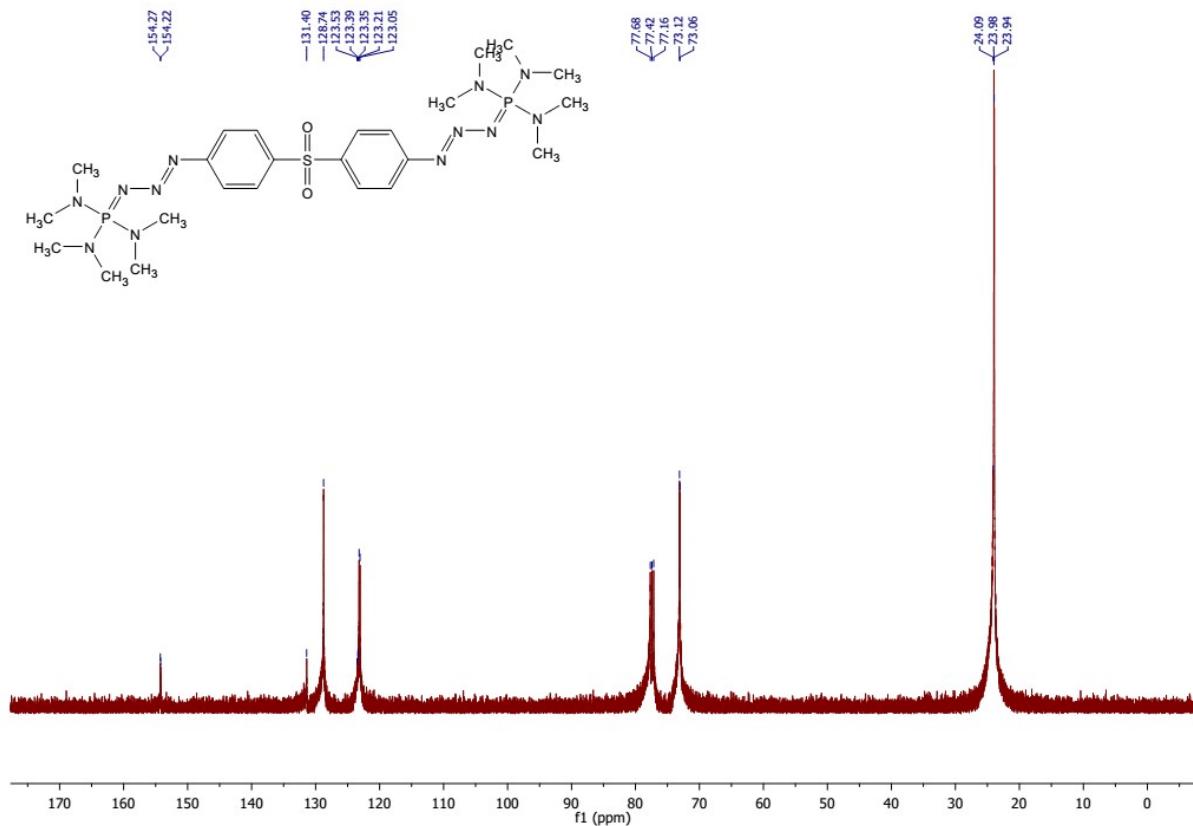
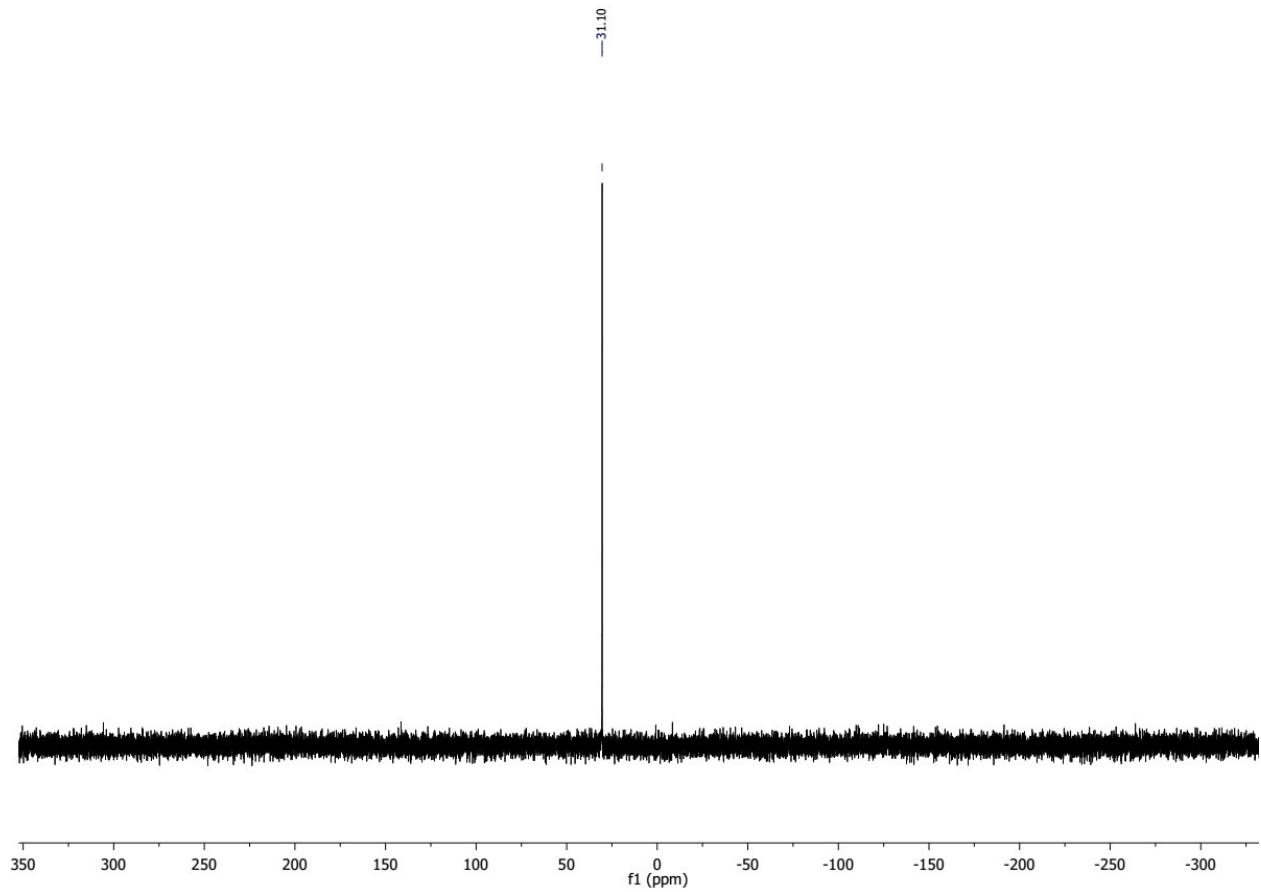


Figure :  $^{13}\text{C}$  NMR of compound 6b



**Figure :  $^{31}\text{P}$  NMR of compound 6b**

Ewis-6b #521 RT: 1.80 AV: 1 NL: 3.41E5  
T: {0,0} + c El Full ms [50.00-850.00]

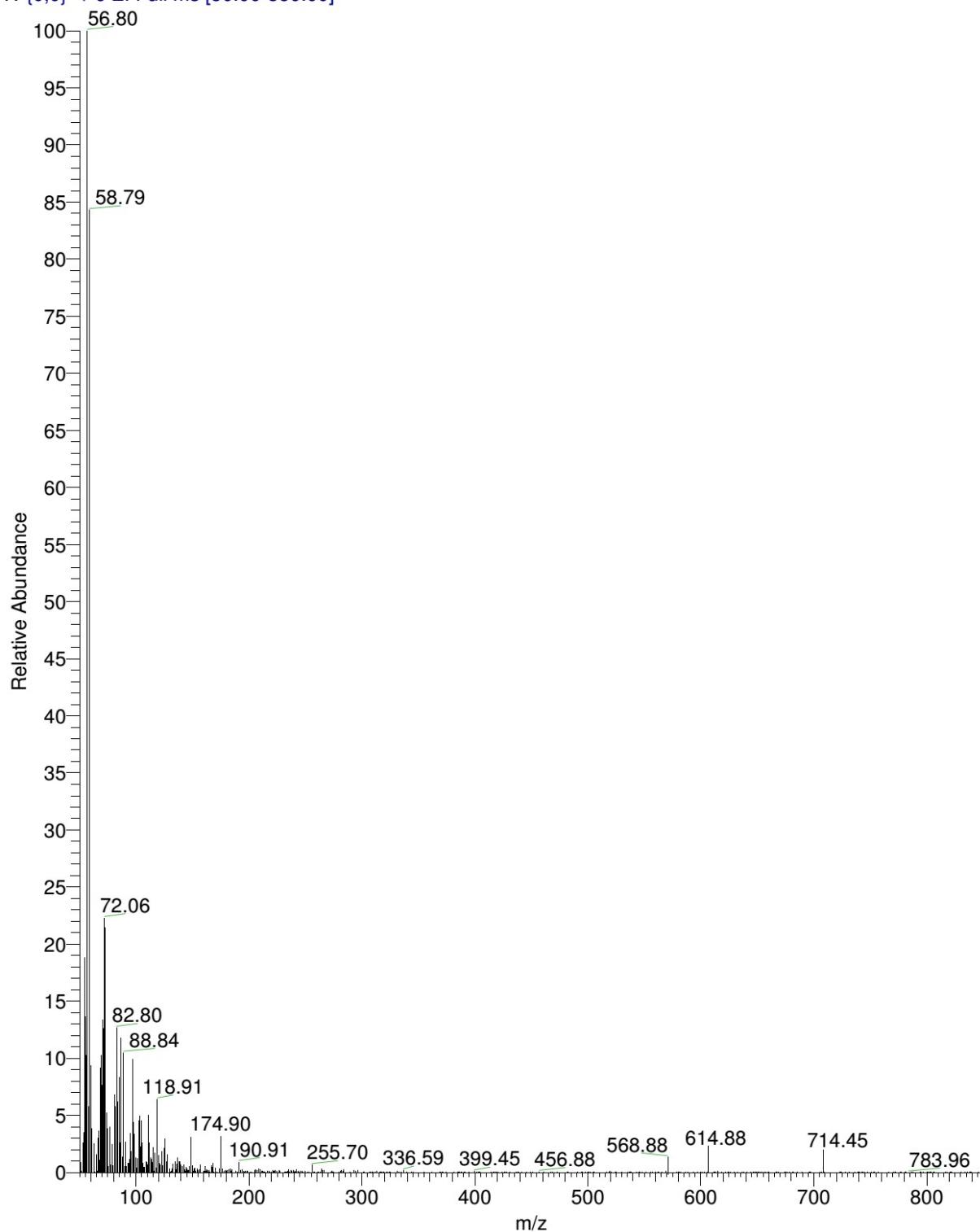
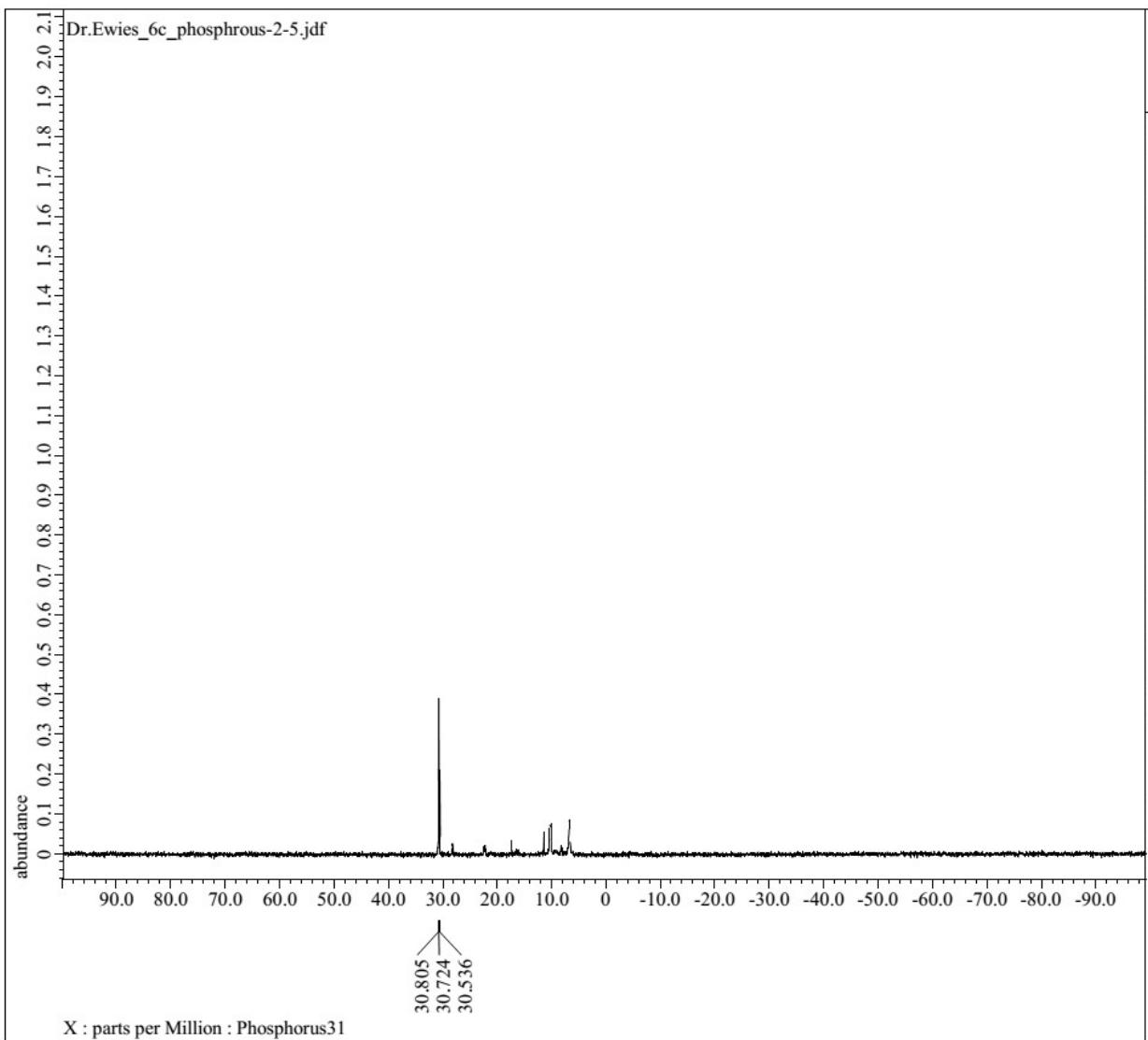


Figure : Mass spectrum of compound 6b



**Figure : 31P NMR of compound 6c**

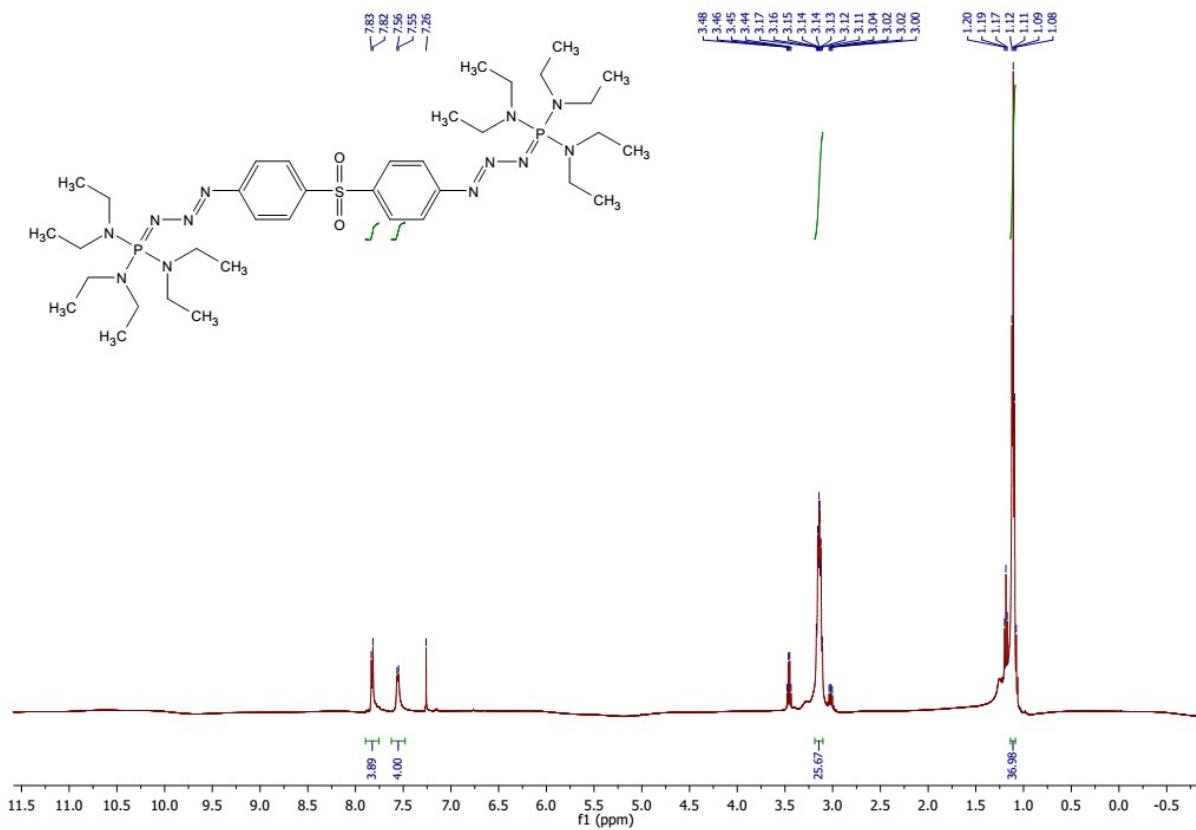


Figure :  $^1\text{H}$  NMR of compound 6d

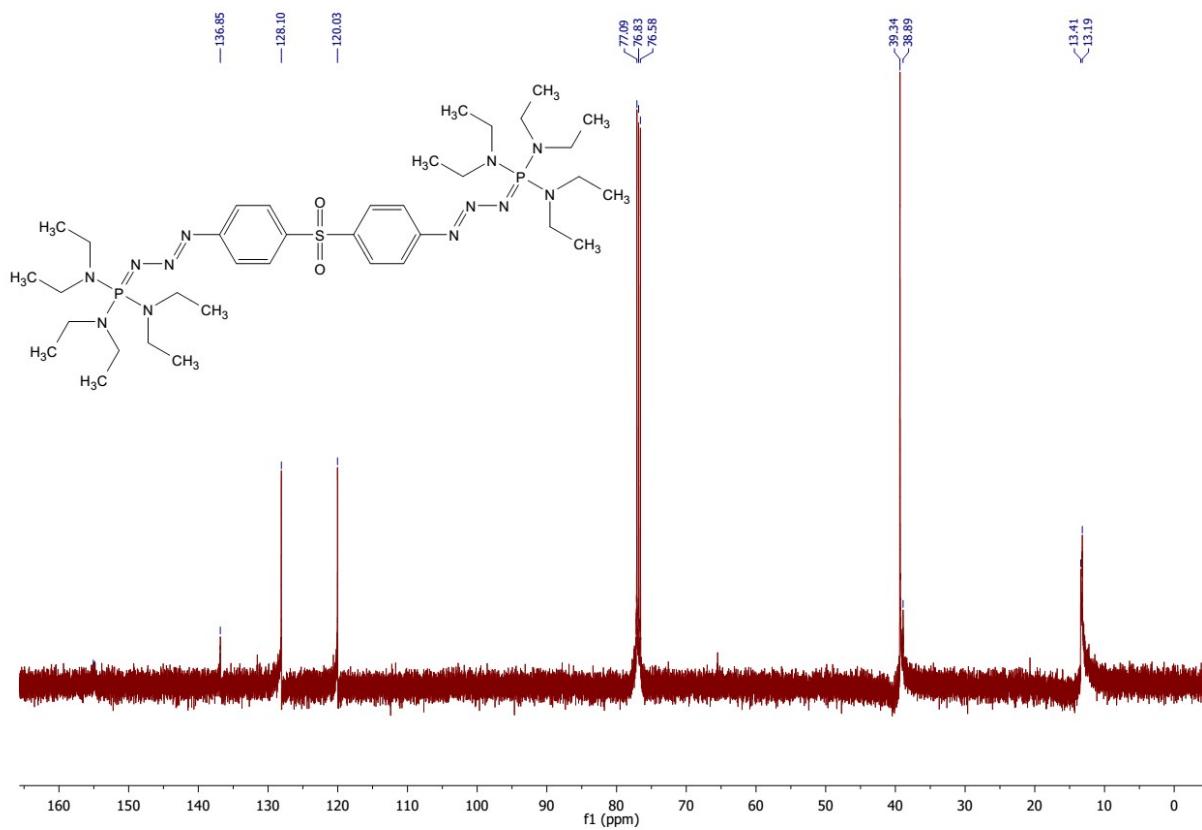
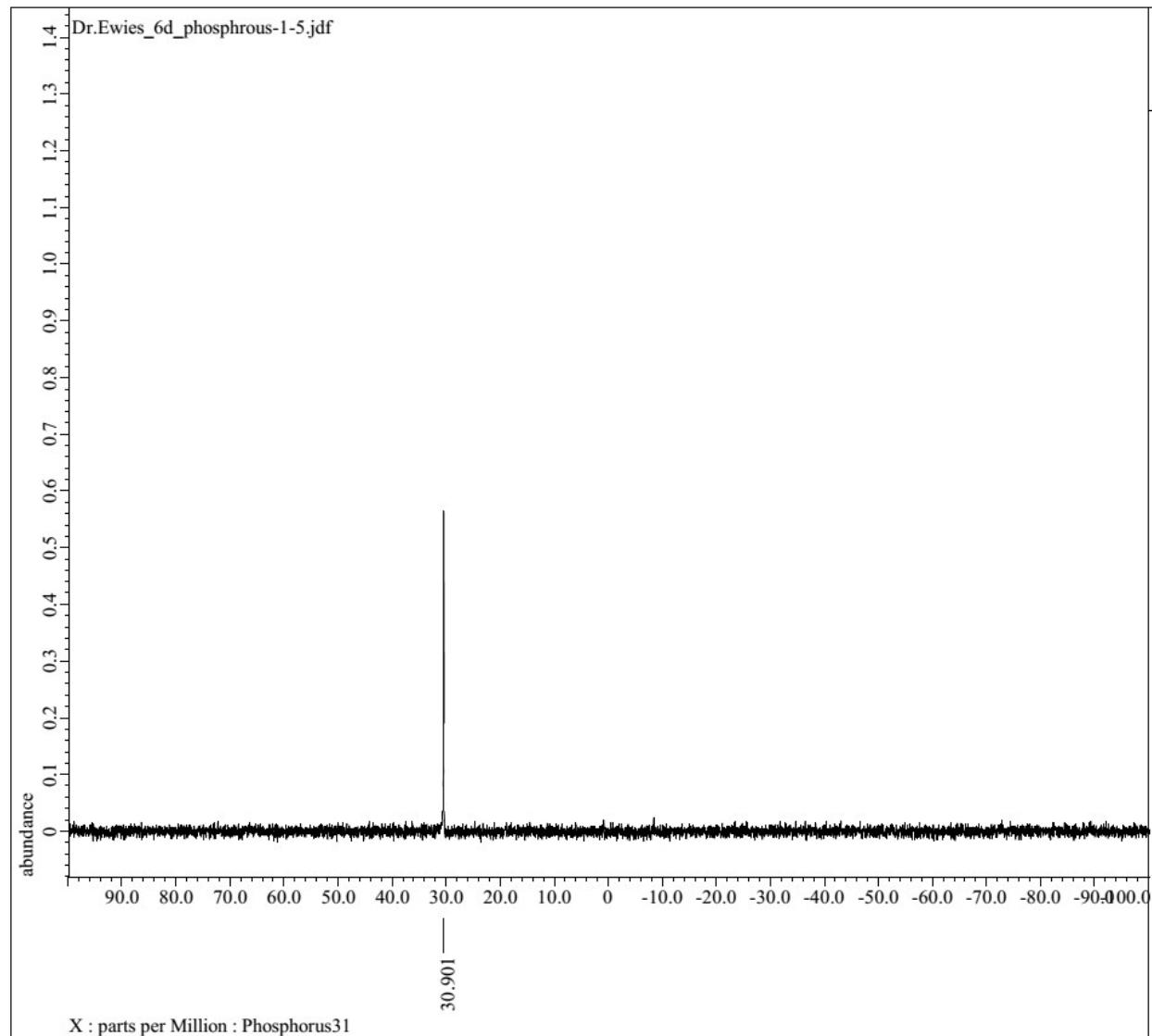


Figure :  $^{13}\text{C}$  NMR of compound 6d



**Figure :  $^{31}\text{P}$  NMR of compound 6d**



**Figure : IR chart of compound 6d**

Ewis-6d #1154 RT: 3.96 AV: 1 NL: 1.16E4  
T: {0,0} + c El Full ms [50.00-850.00]

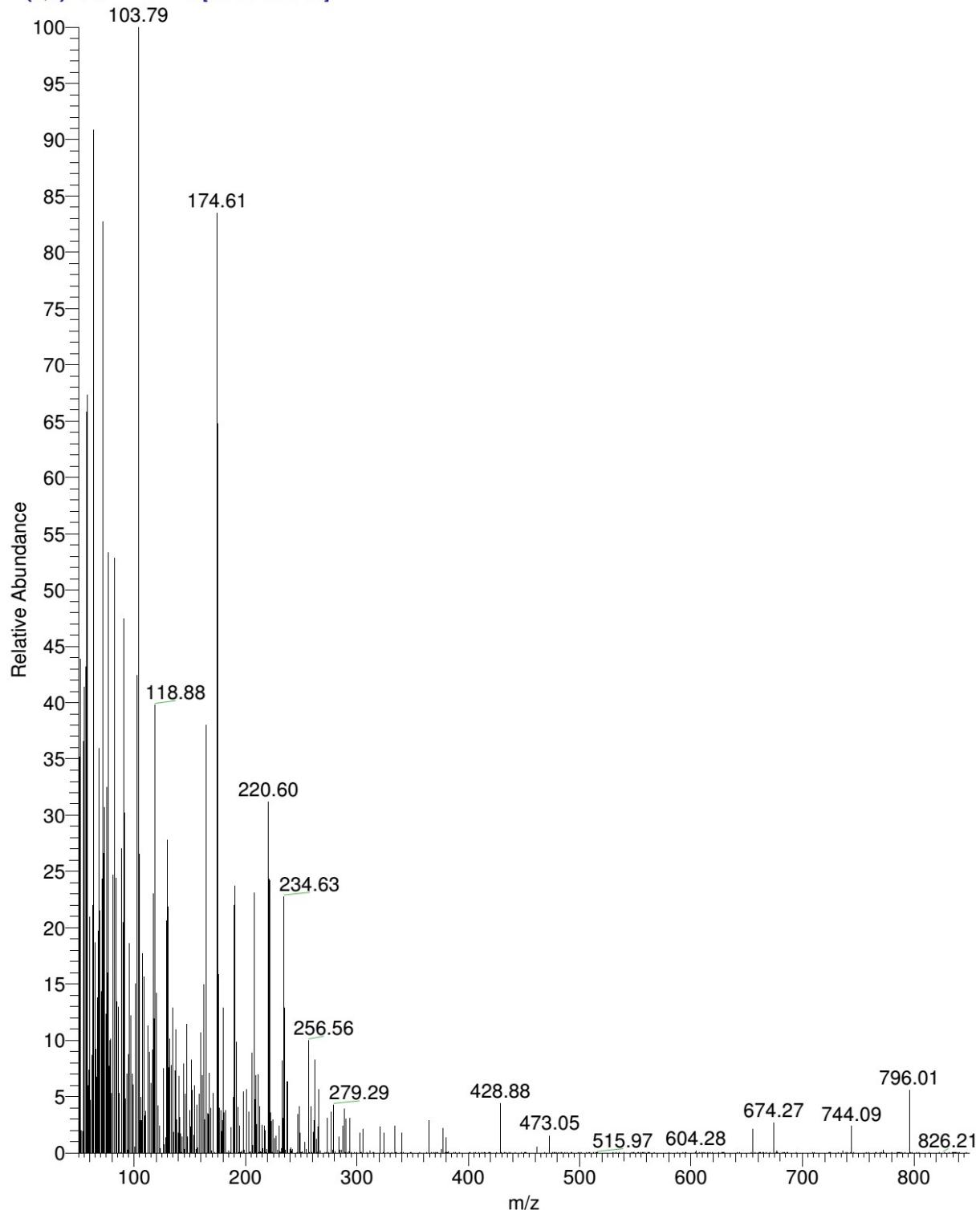


Figure : mass spectrum of compound 6d