

## Supplementary Information

### Synthesis of New *trans*-Dehydrocrotonin Nitrogenated Derivatives and their Cytotoxic and DNA-Topoisomerase I Inhibitory Activities

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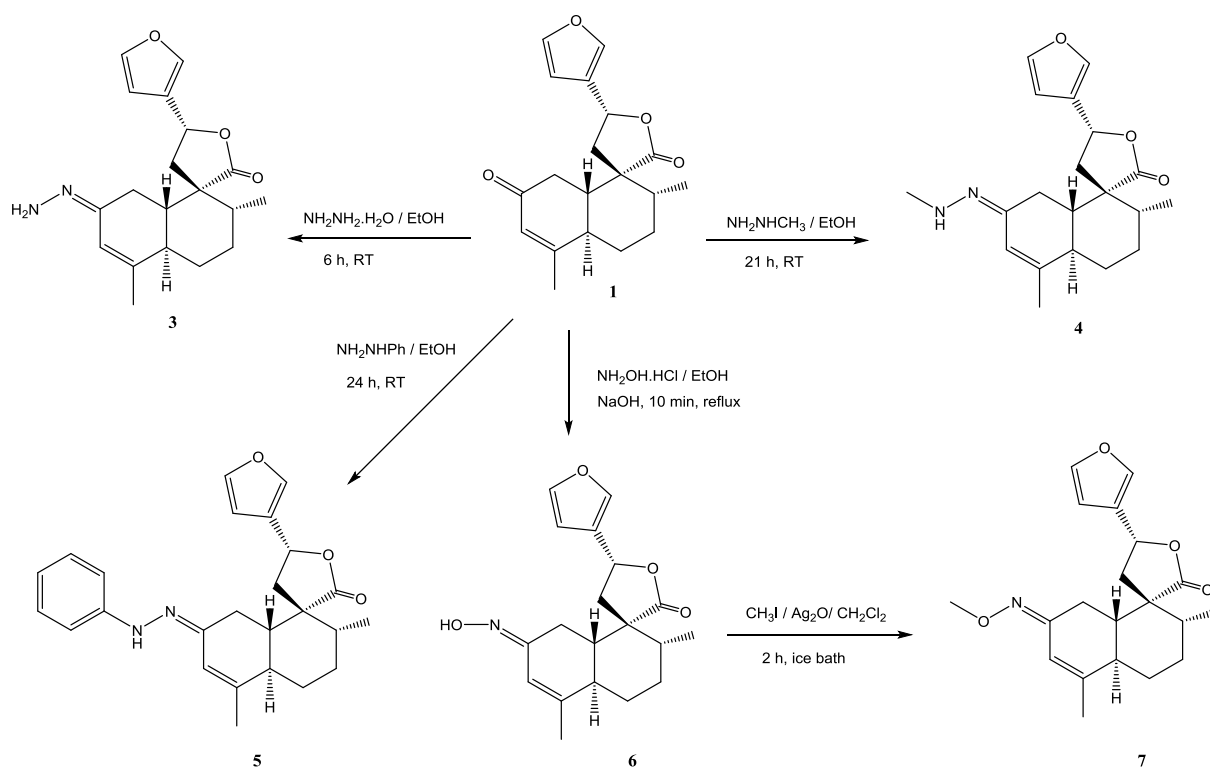


Figure S1. Semi-synthetic clerodanes 3-7.

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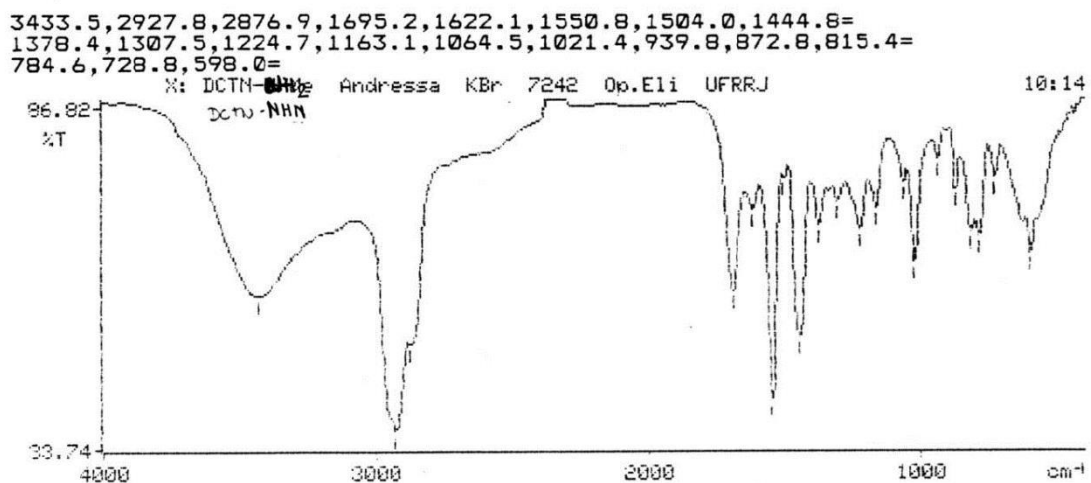


Figure S2. Infrared spectrum (KBr) of compound 3.

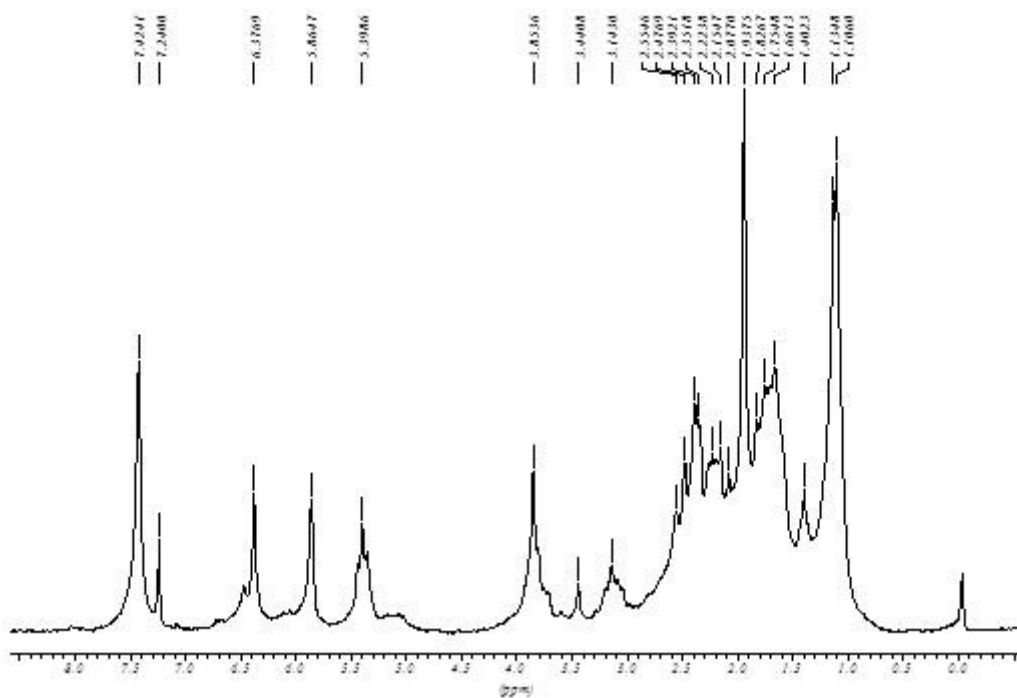


Figure S3. <sup>1</sup>H NMR spectrum (200 MHz, CDCl<sub>3</sub>) of compound 3.

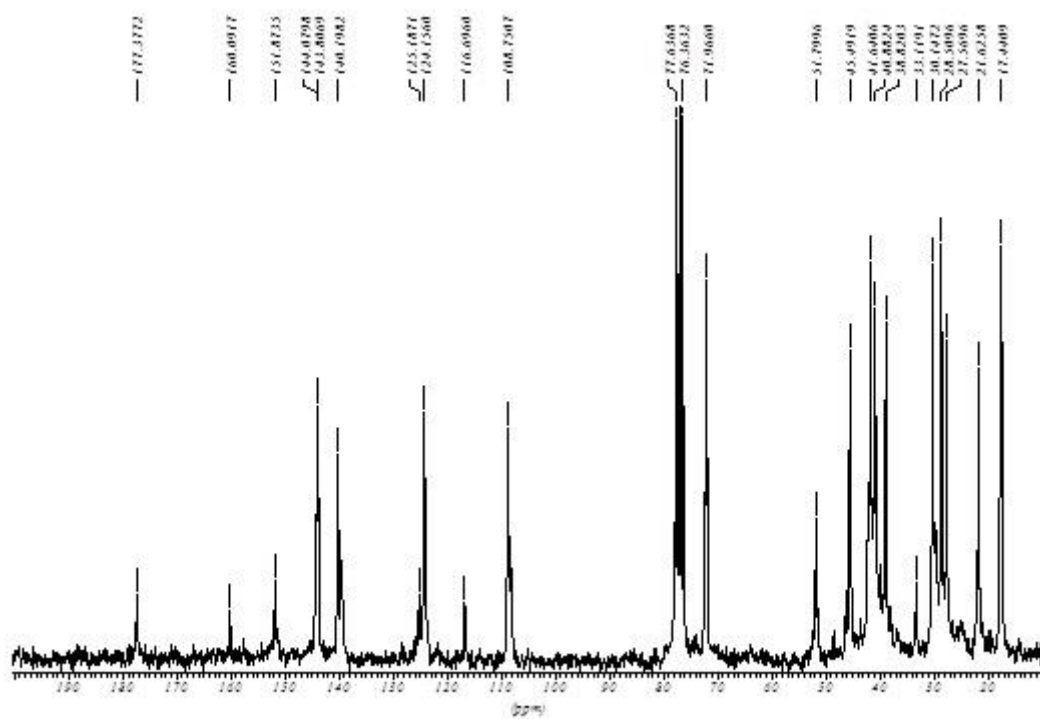


Figure S4.  $^{13}\text{C}$  NMR spectrum (50 MHz,  $\text{CDCl}_3$ ) of compound 3.

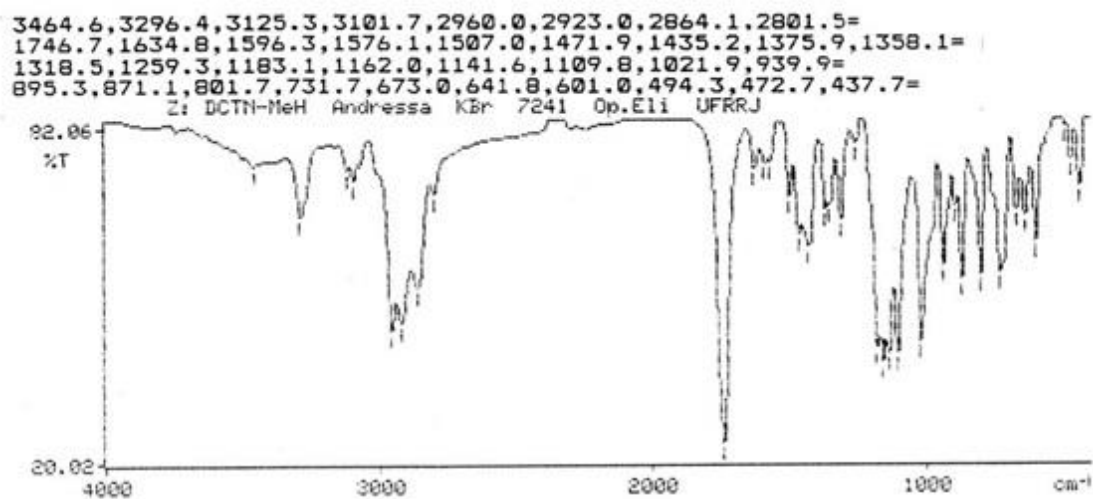
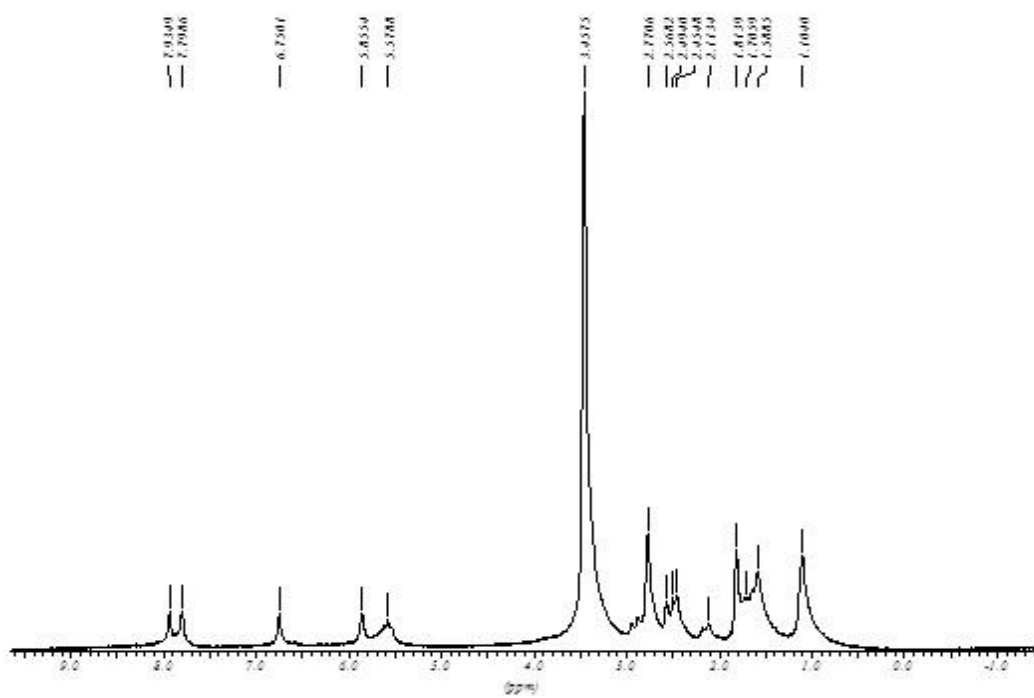
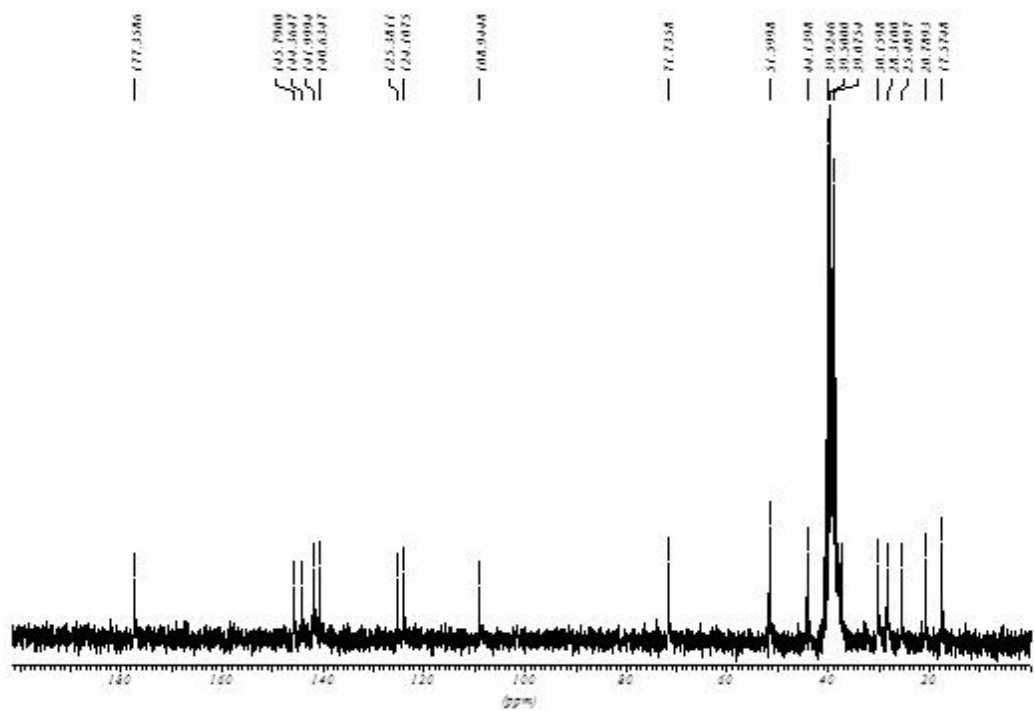


Figure S5. Infrared spectrum (KBr) of compound 4.



**Figure S6.**  $^1\text{H}$  NMR spectrum (200 MHz,  $\text{DMSO-}d_6$ ) of compound **4**.



**Figure S7.**  $^{13}\text{C}$  NMR spectrum (50 MHz,  $\text{DMSO-}d_6$ ) of compound **4**.

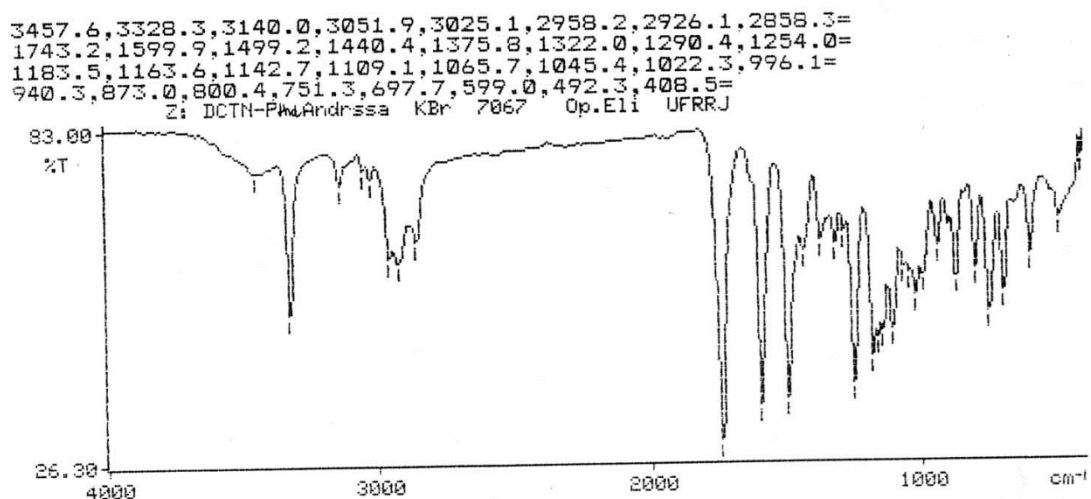


Figure S8. Infrared spectrum (KBr) of compound 5.

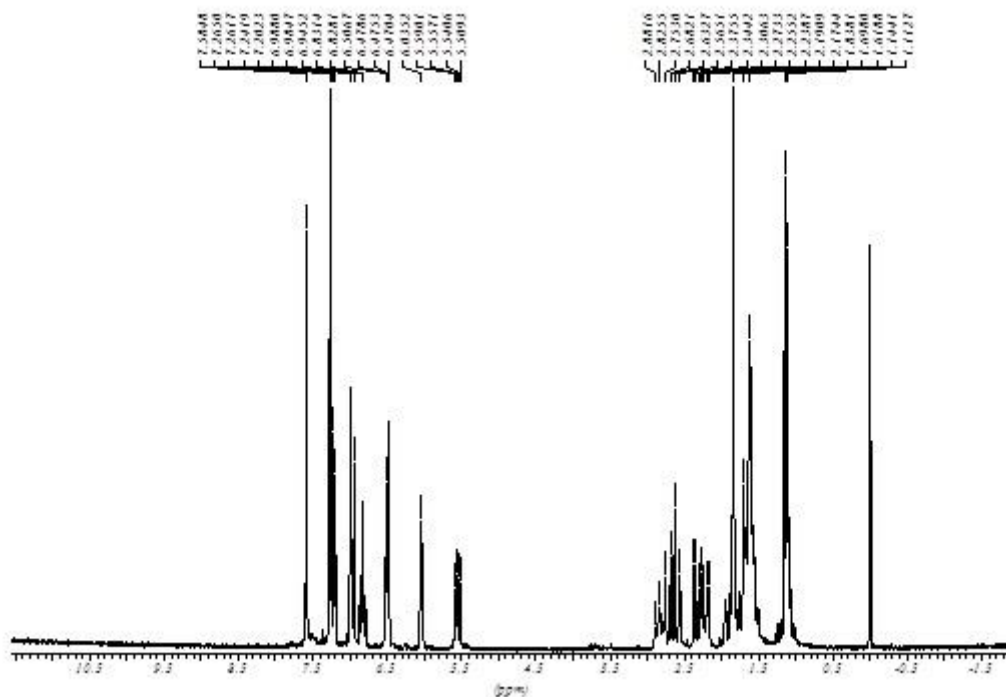


Figure S9. <sup>1</sup>H NMR spectrum (200 MHz, CDCl<sub>3</sub>) of compound 5.

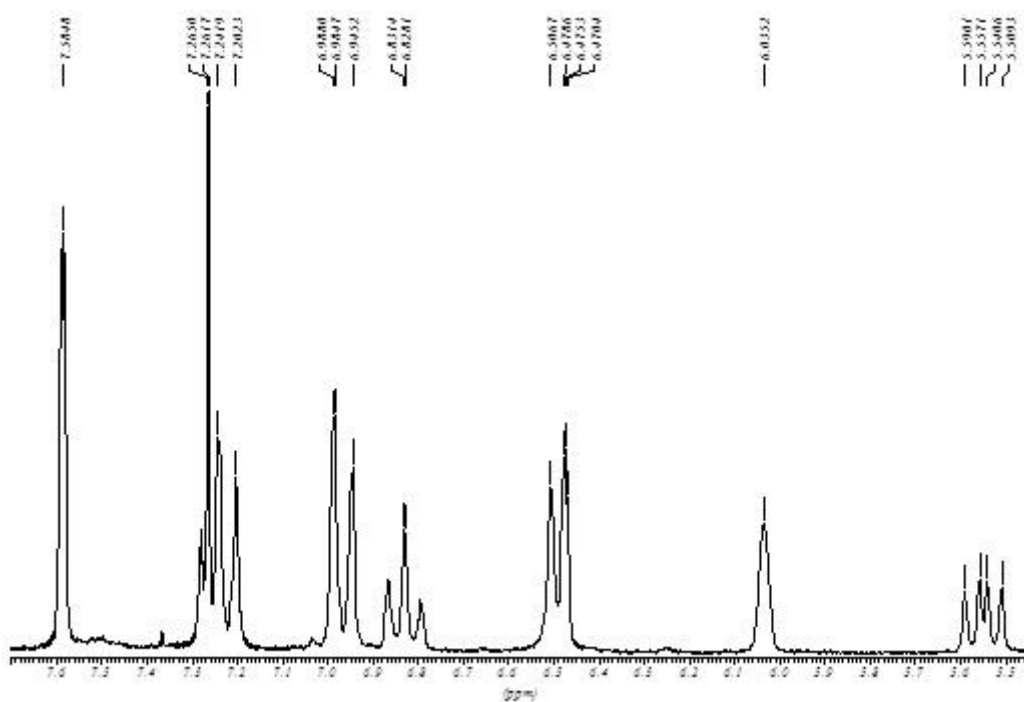


Figure S10. <sup>1</sup>H NMR spectrum (200 MHz, CDCl<sub>3</sub>) of compound **5** (expansion 1).

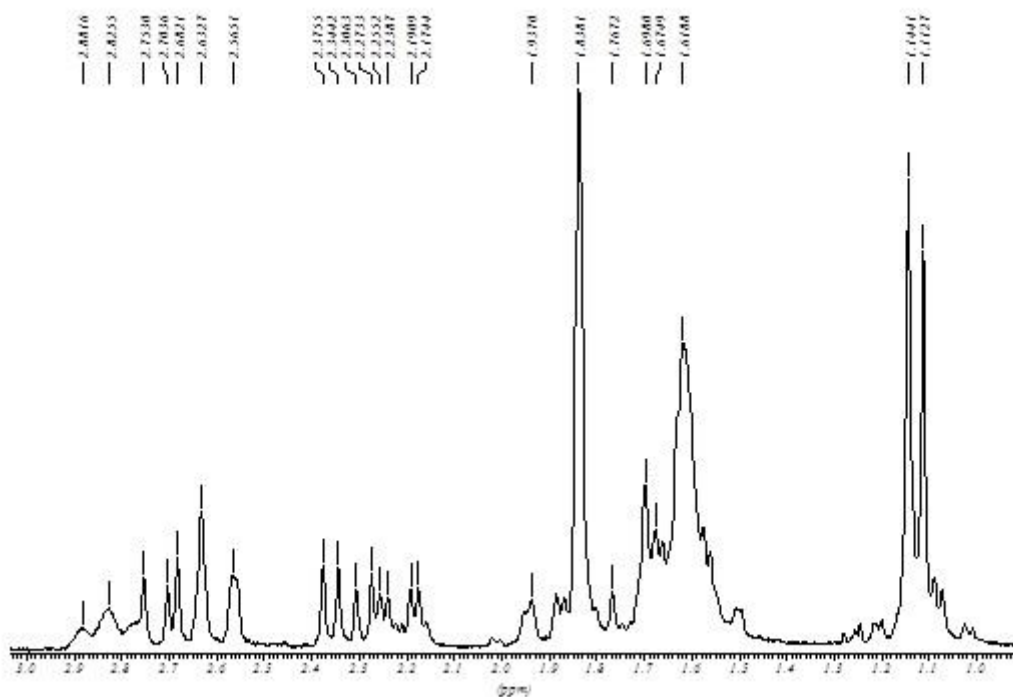


Figure S11. <sup>1</sup>H NMR spectrum (200 MHz, CDCl<sub>3</sub>) of compound **5** (expansion 2).

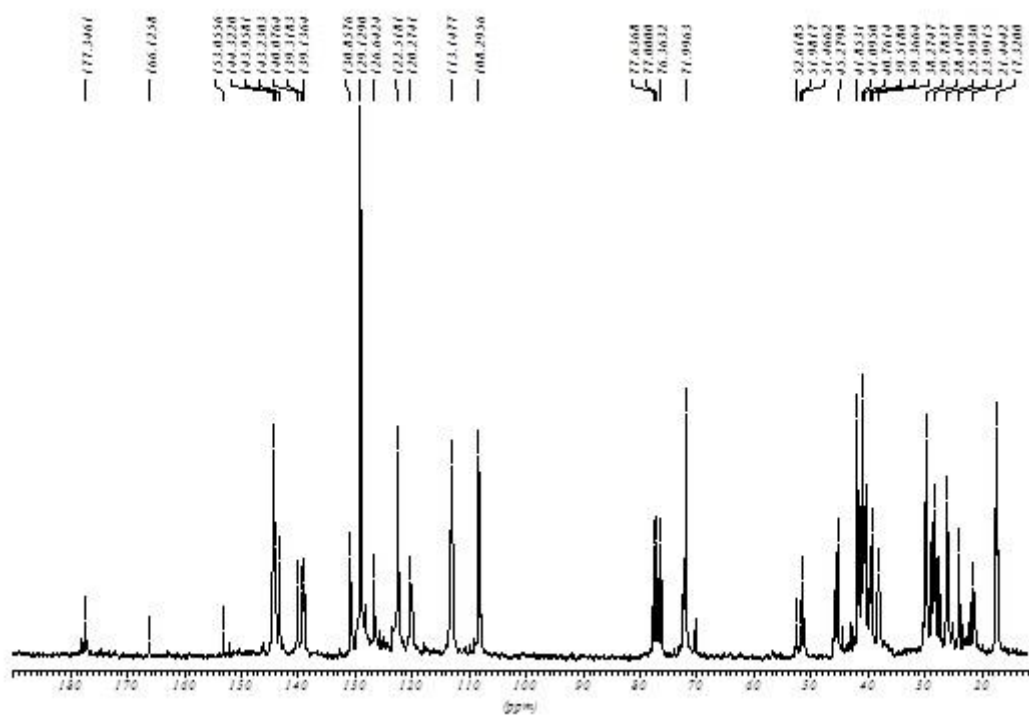


Figure S12.  $^{13}\text{C}$  NMR spectrum (50 MHz,  $\text{CDCl}_3$ ) of compound 5.

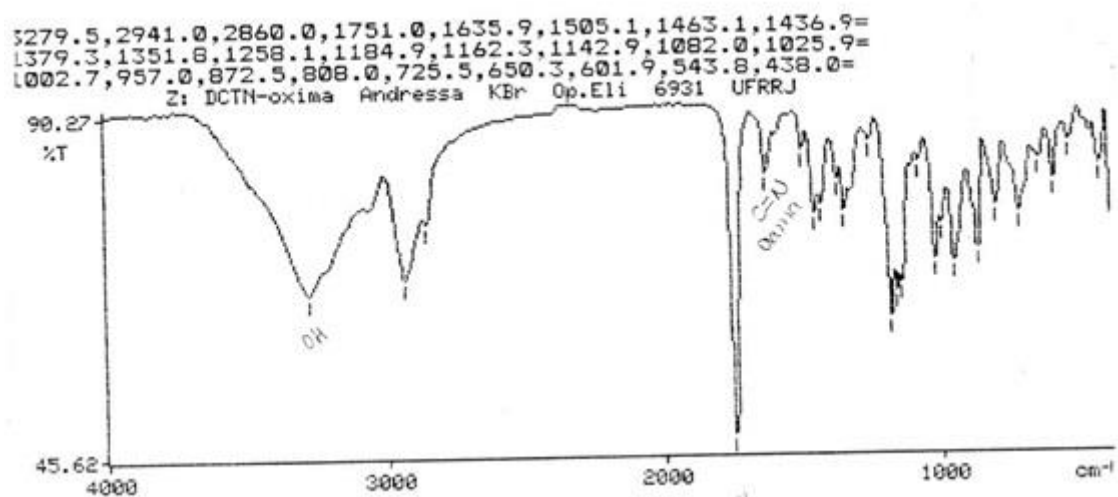


Figure S13. Infrared spectrum (KBr) of compound 6.

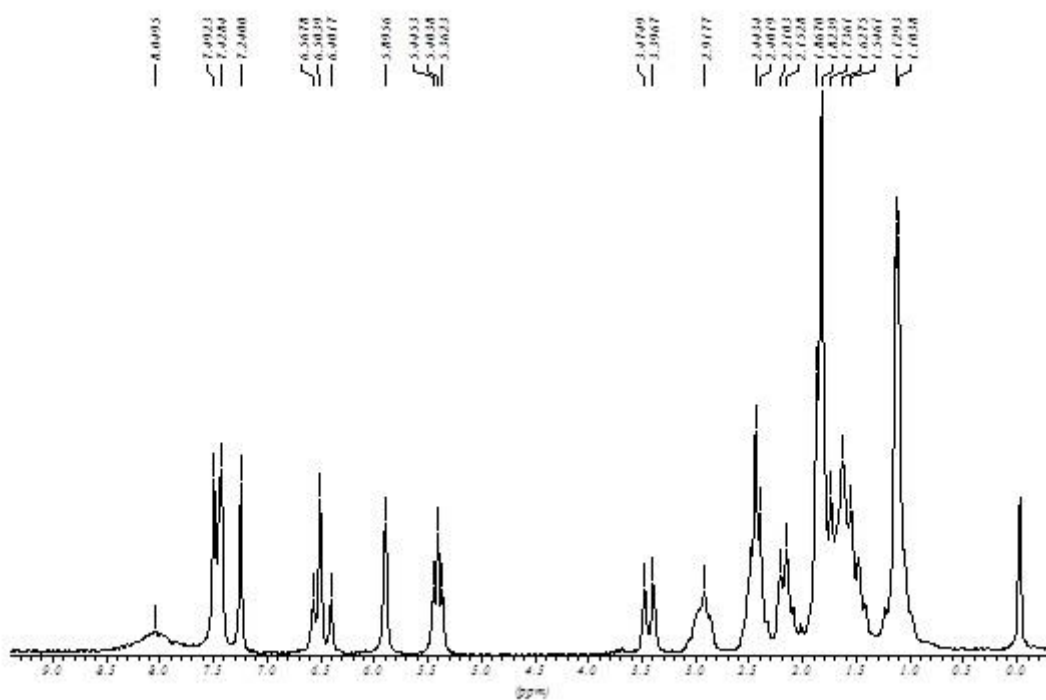


Figure S14.  $^1\text{H}$  NMR spectrum (200 MHz,  $\text{CDCl}_3$ ) of compound **6**.

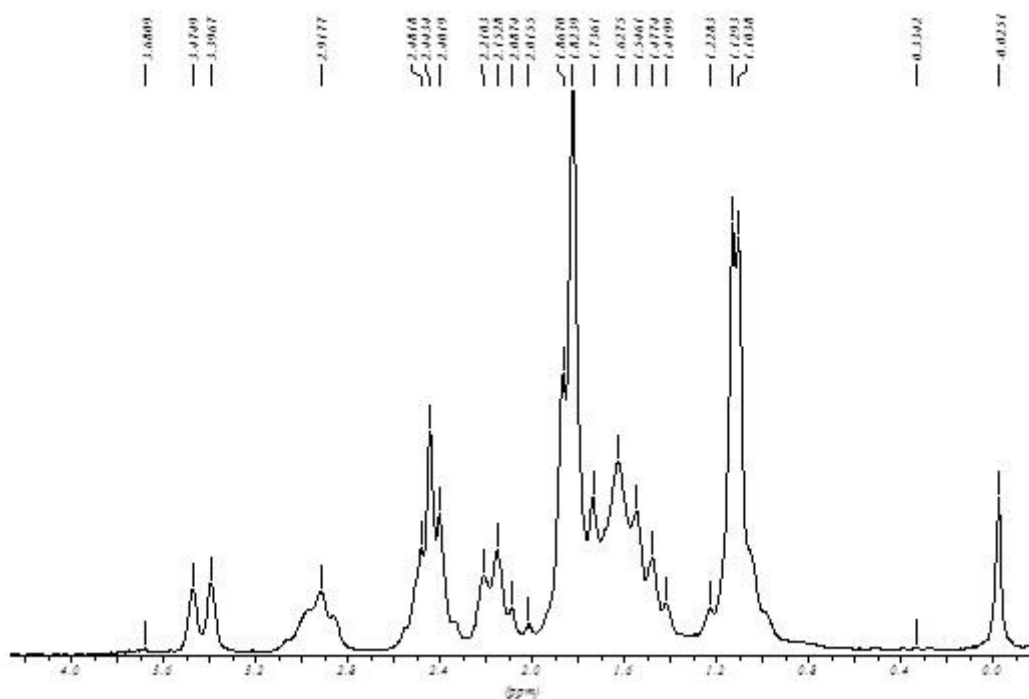


Figure S15.  $^1\text{H}$  NMR spectrum (200 MHz,  $\text{CDCl}_3$ ) of compound **6** (expansion).



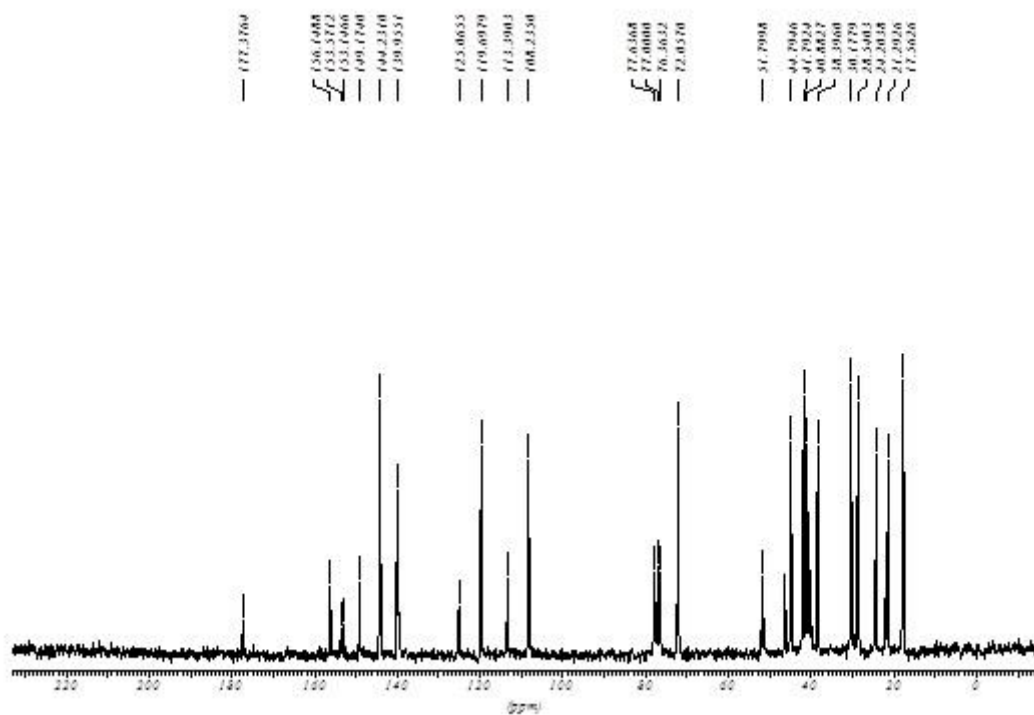


Figure S16.  $^{13}\text{C}$  NMR spectrum (50 MHz,  $\text{CDCl}_3$ ) of compound 6.

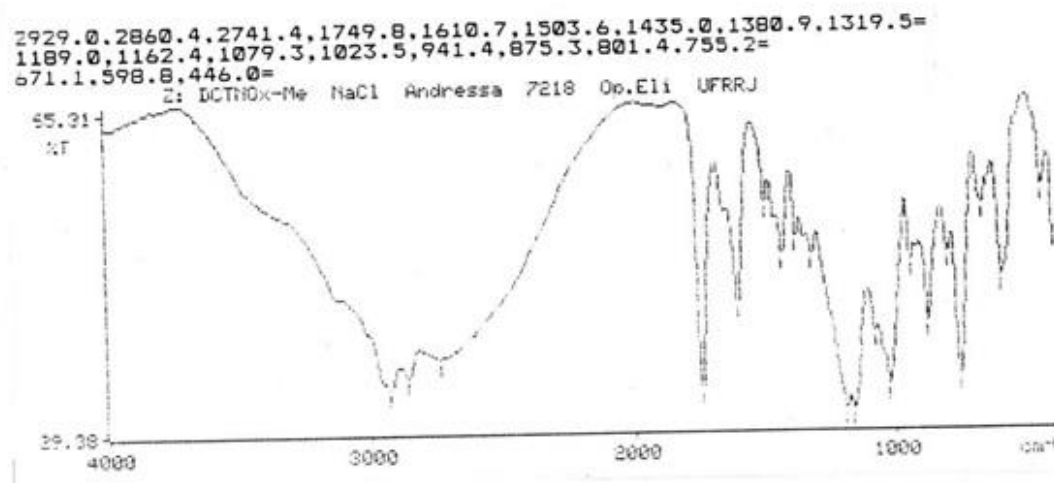
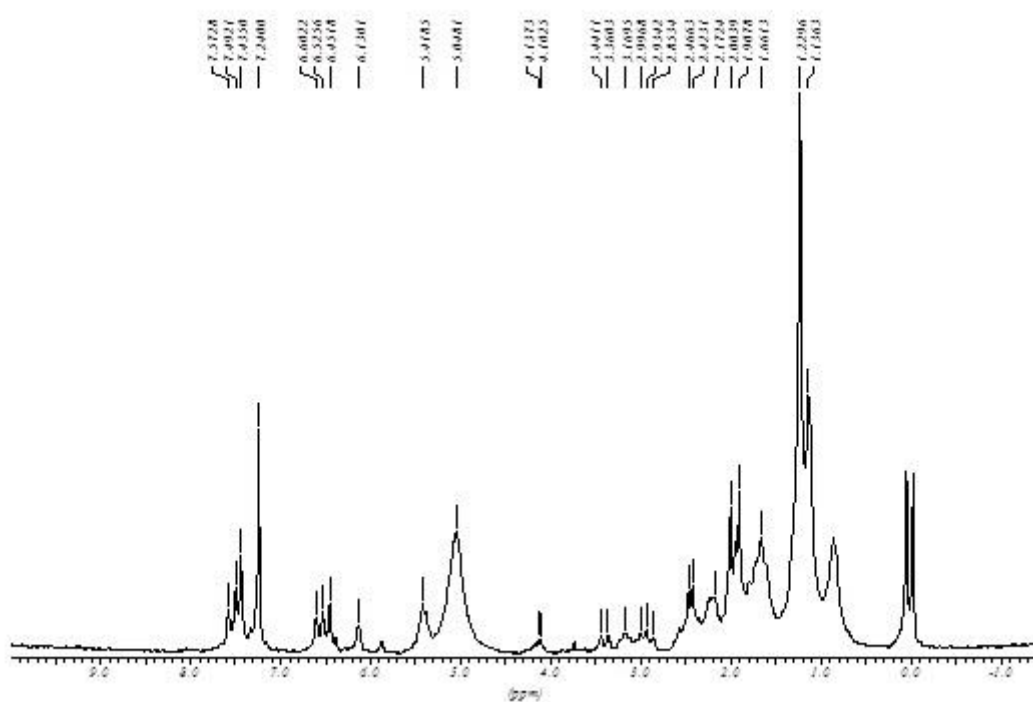
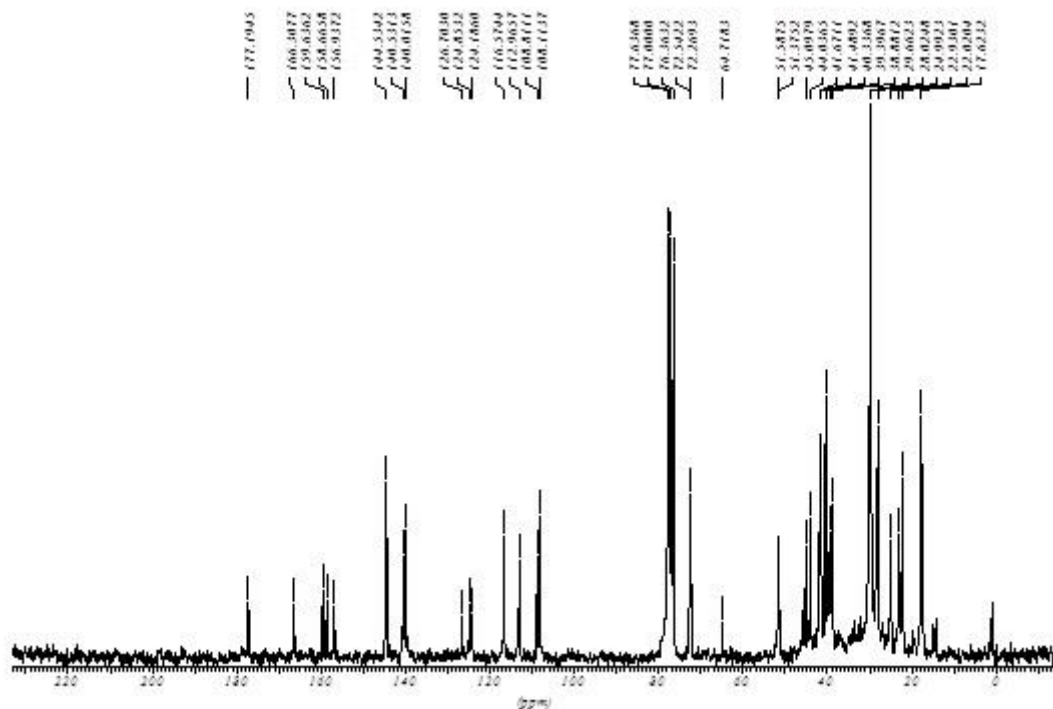


Figure S17. Infrared spectrum (KBr) of compound 7.



**Figure S18.**  $^1\text{H}$  NMR spectrum (200 MHz,  $\text{CDCl}_3$ ) of compound 7.



**Figure S19.**  $^{13}\text{C}$  NMR spectrum (50 MHz,  $\text{CDCl}_3$ ) of compound 7.