

# ***Supporting Information***

## **Intramolecular Nicholas Reaction Enables the Synthesis of Strained Cyclooctynes**

Diego Manuel Monzón, Juan Manuel Betancort, Tomás Martín, Miguel Ángel Ramírez, Víctor S. Martín\*  
and David Díaz Díaz\*

## NMR spectra of compounds

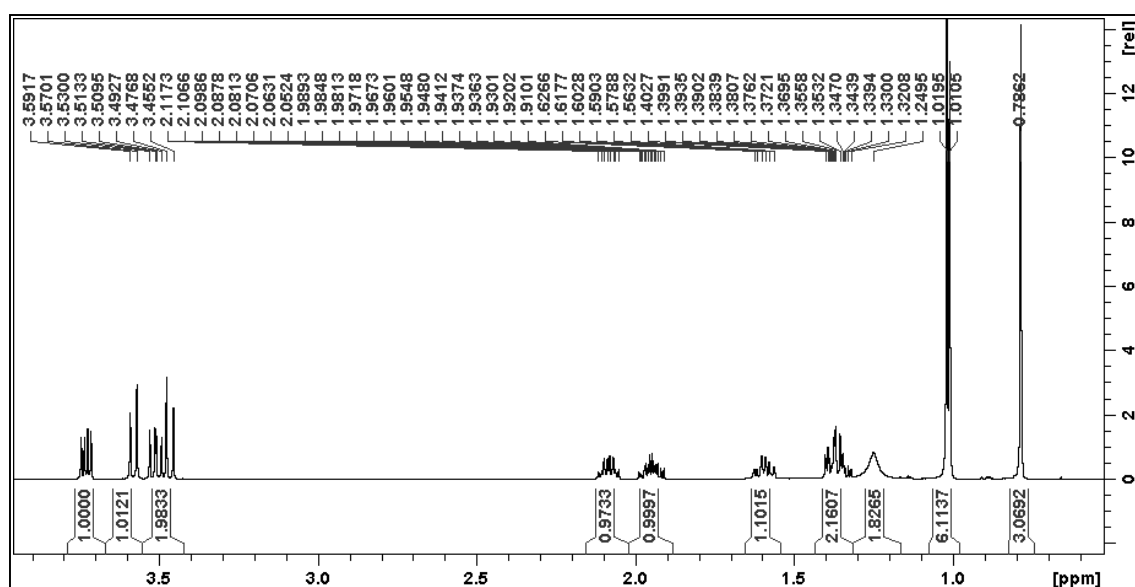


Figure S1.  $^1\text{H}$  NMR spectrum of compound 2

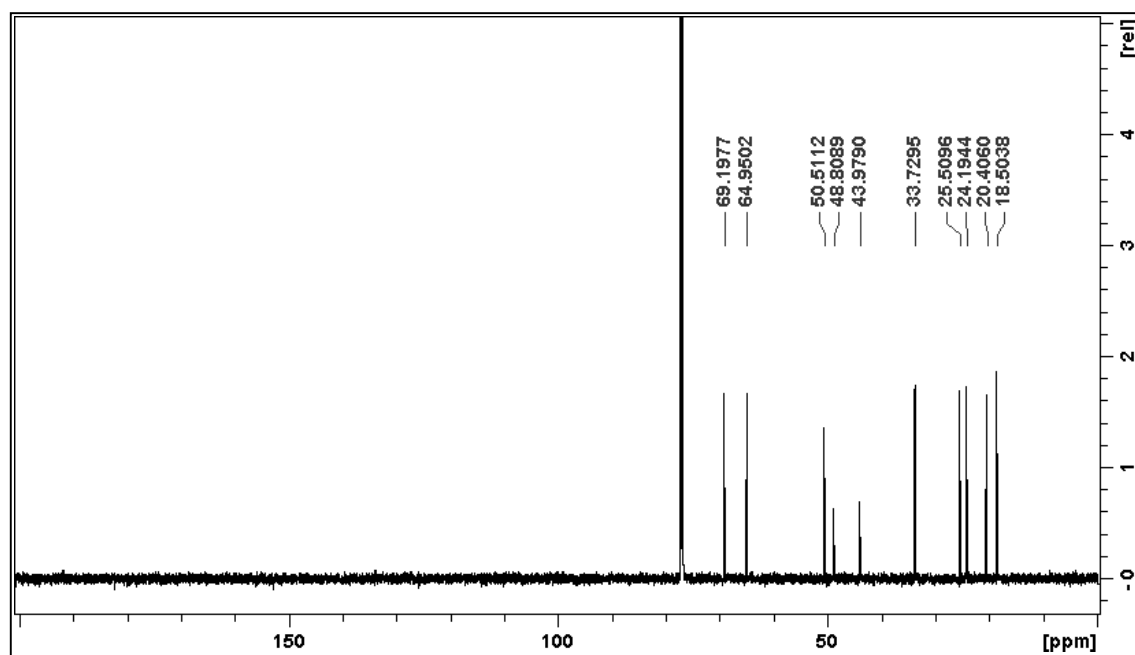


Figure S2.  $^{13}\text{C}$  NMR spectrum of compound 2

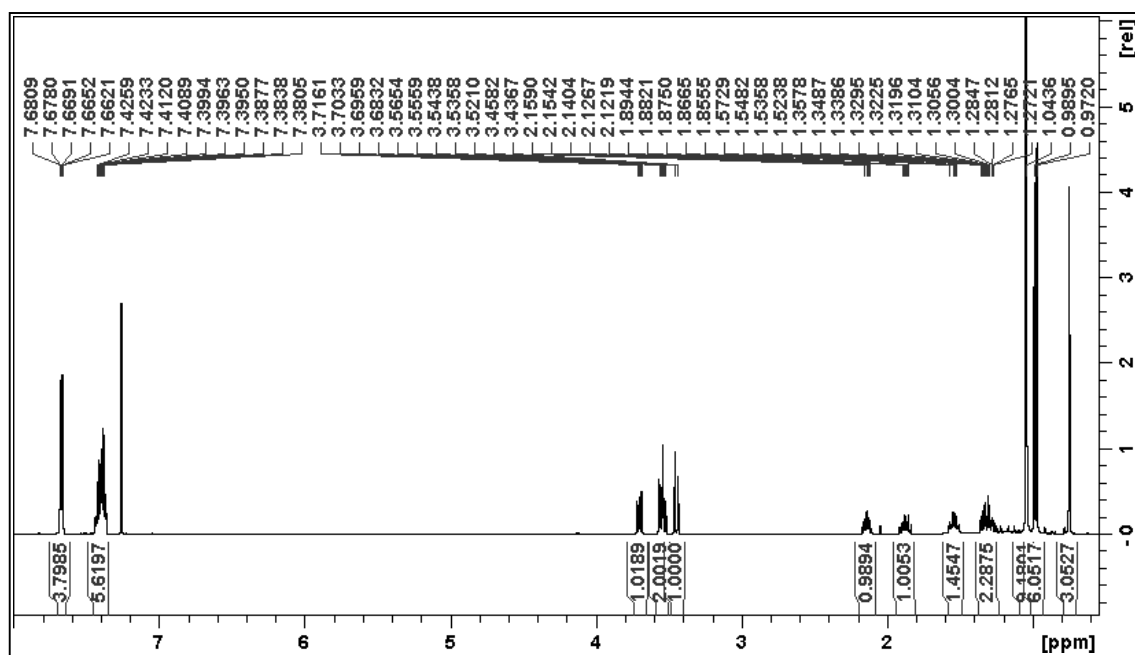


Figure S3. <sup>1</sup>H NMR spectrum of compound 3

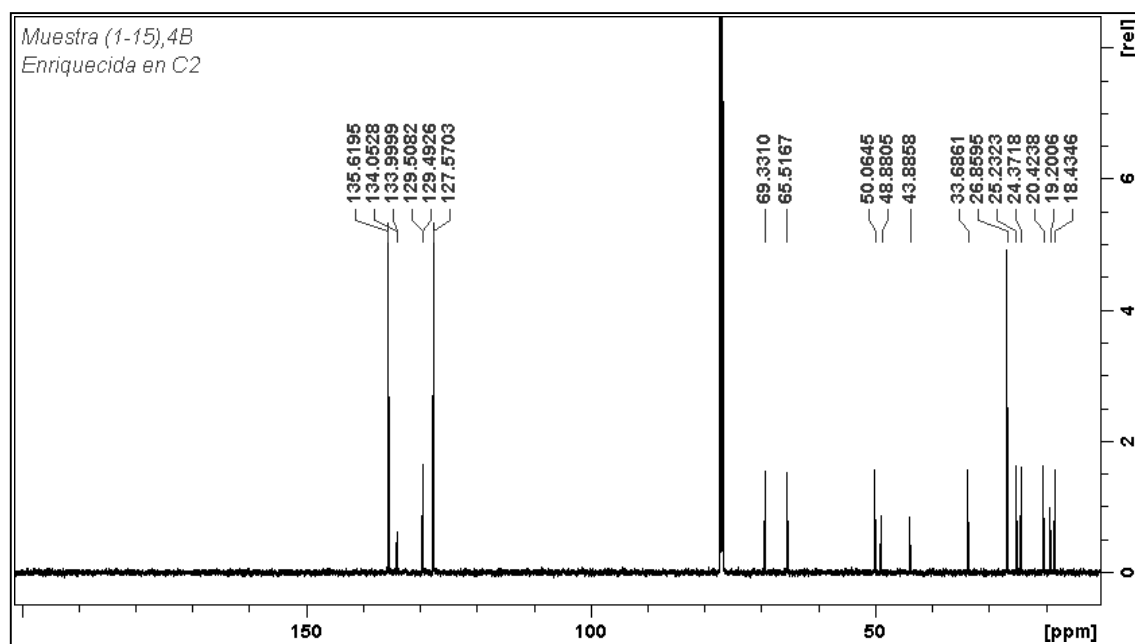


Figure S4. <sup>13</sup>C NMR spectrum of compound 3

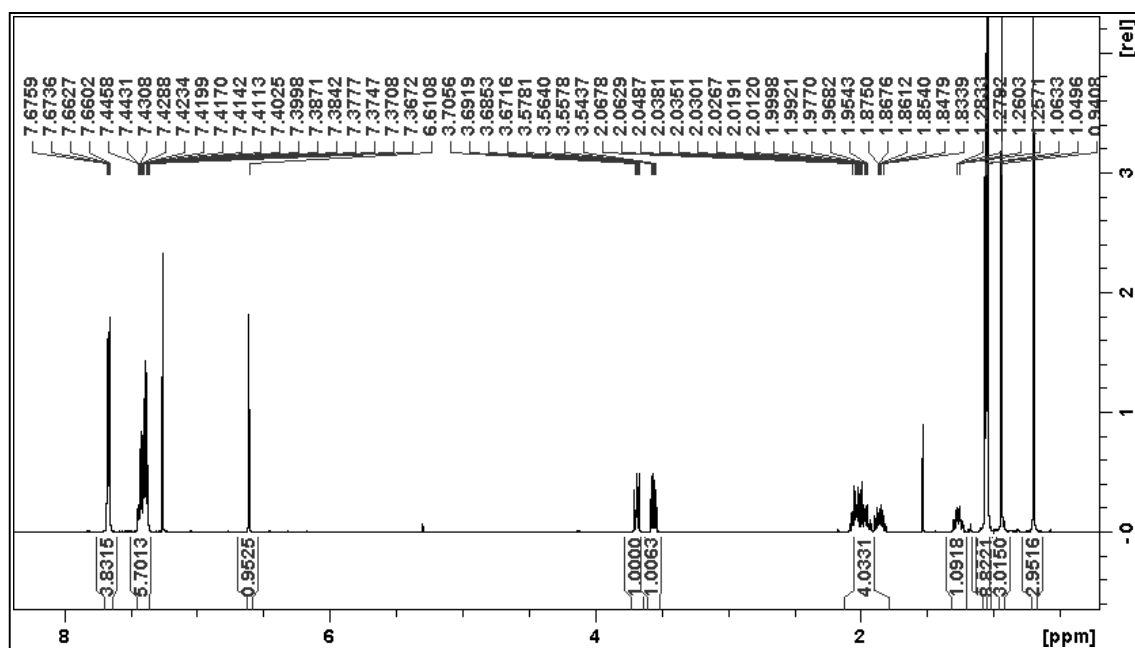


Figure S5.  $^1\text{H}$  NMR spectrum of compound 4

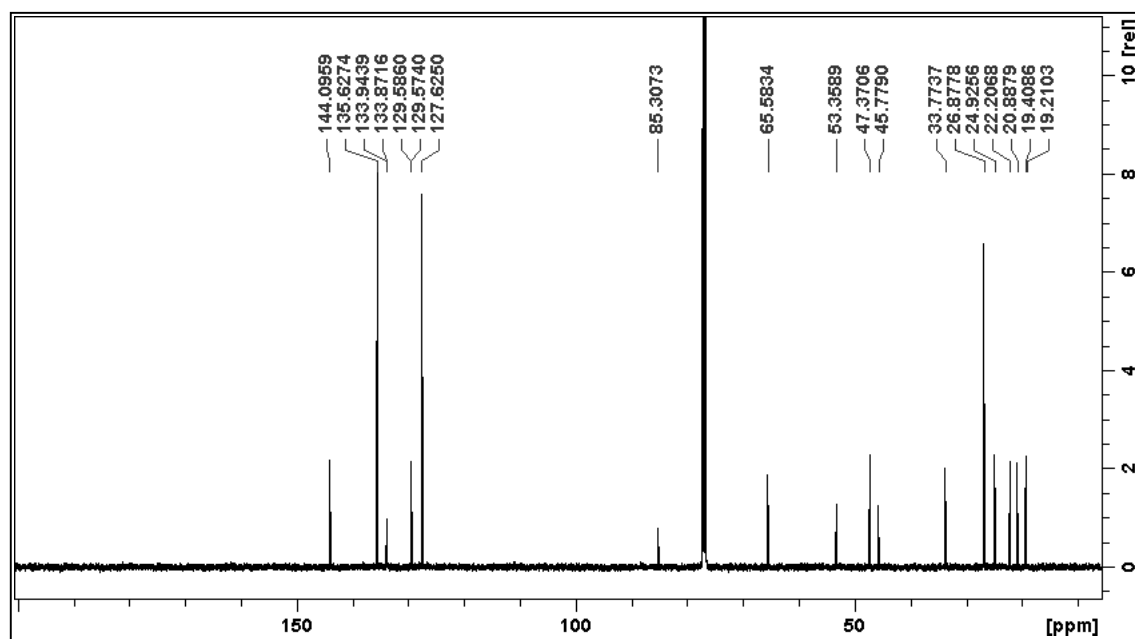


Figure S6.  $^{13}\text{C}$  NMR spectrum of compound 4

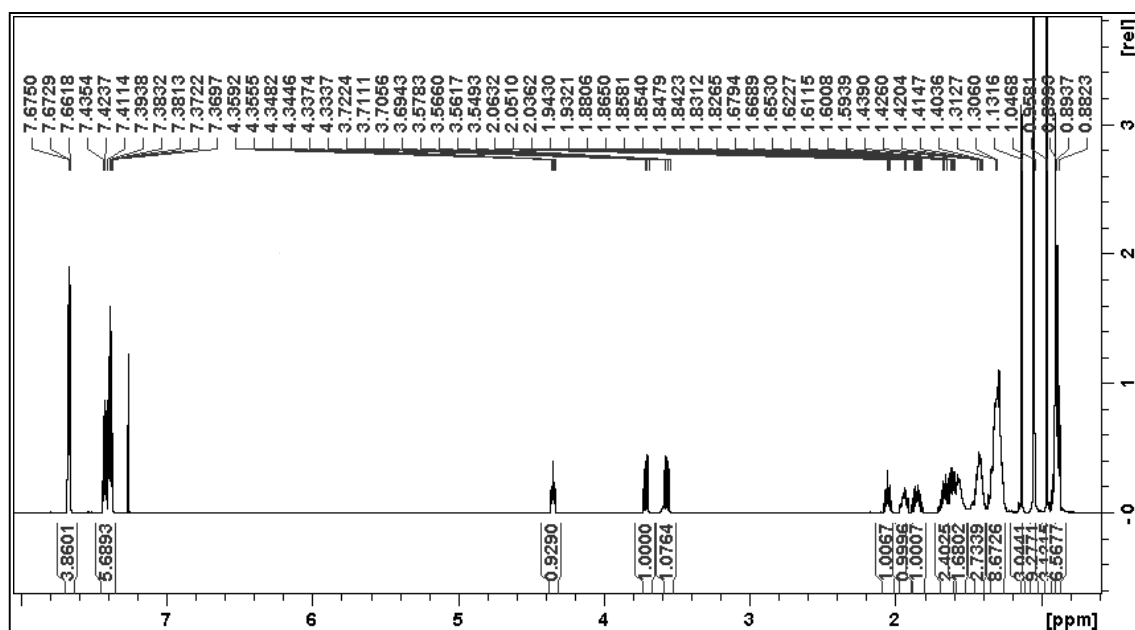


Figure S7. <sup>1</sup>H NMR spectrum of compound 5

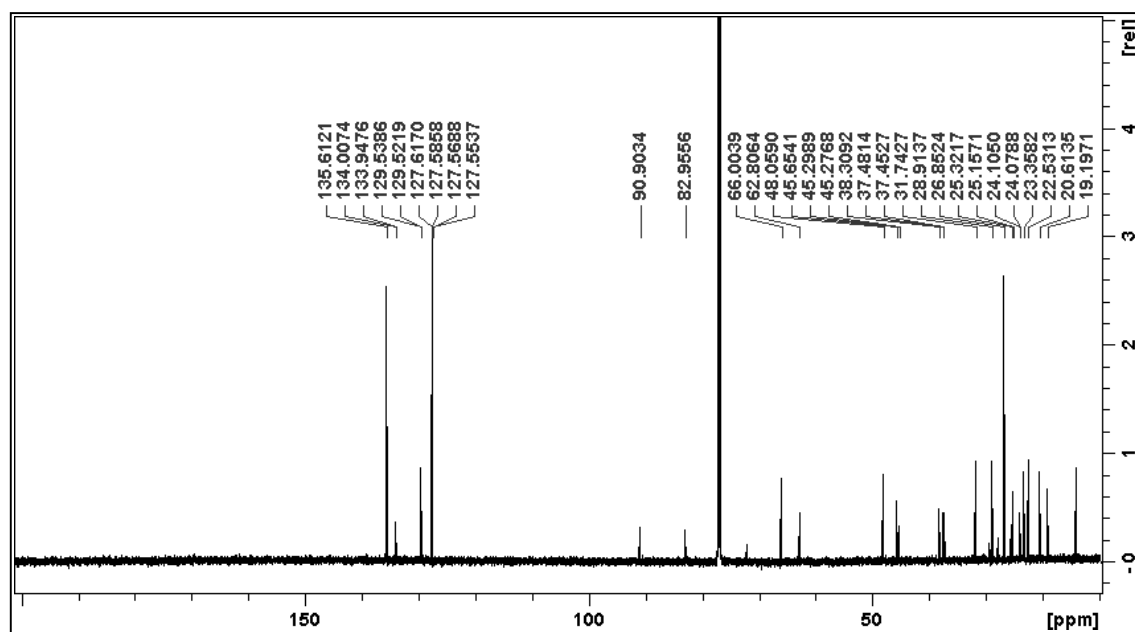


Figure S8. <sup>13</sup>C NMR spectrum of compound 5

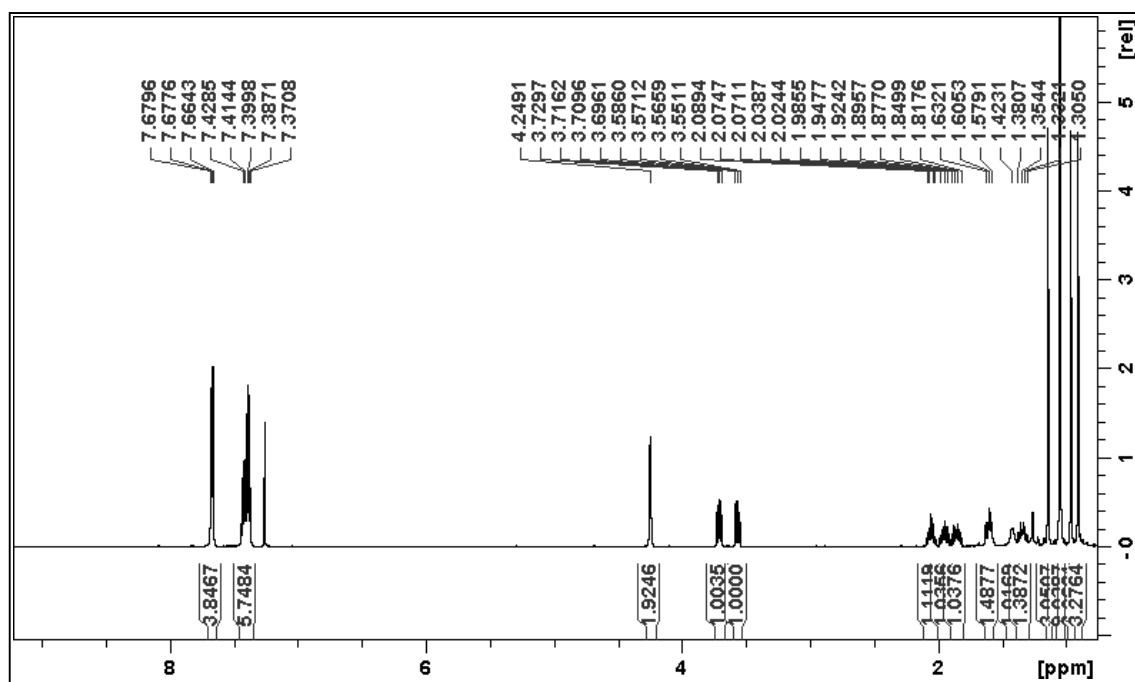


Figure S9. <sup>1</sup>H NMR spectrum of compound 6

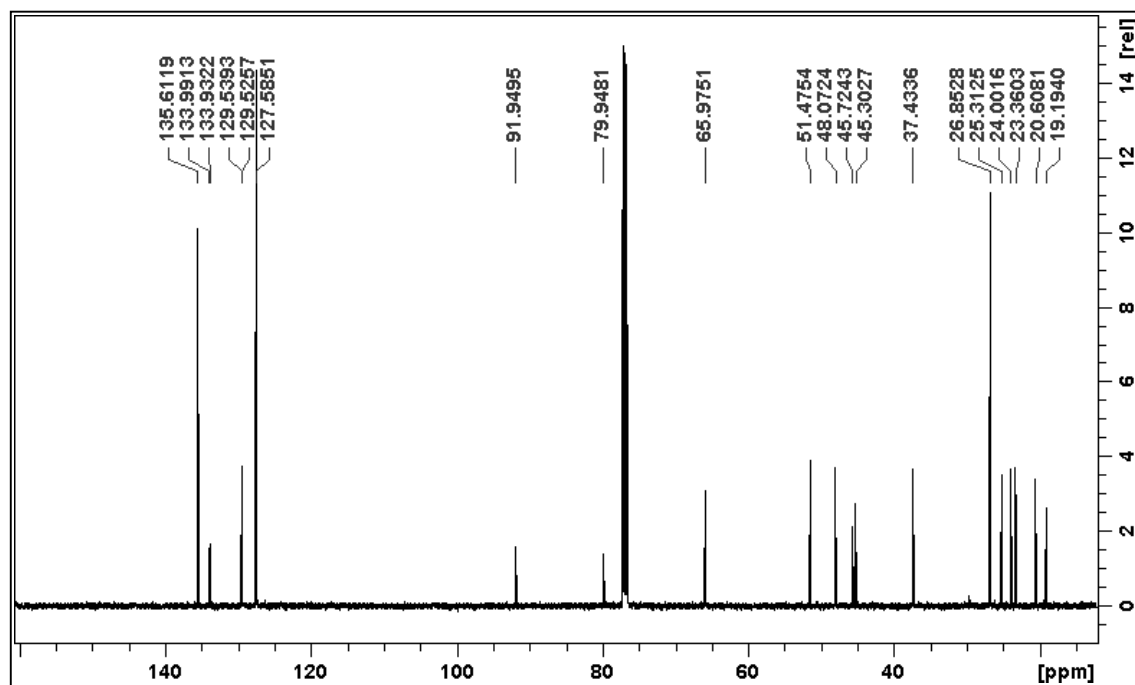


Figure S10. <sup>13</sup>C NMR spectrum of compound 6

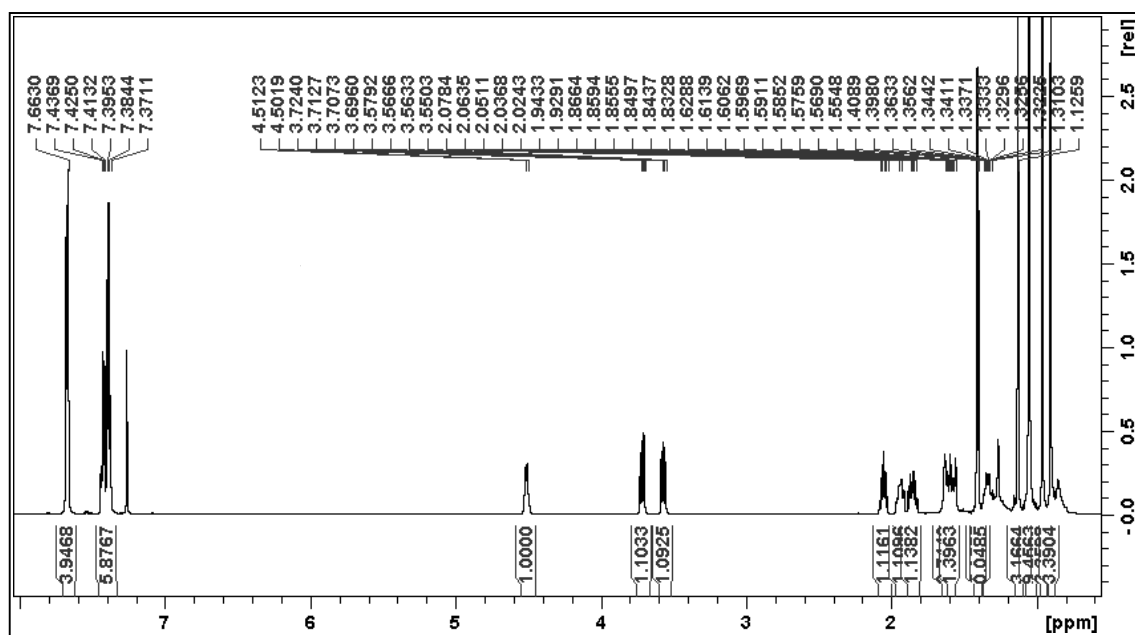


Figure S11. <sup>1</sup>H NMR spectrum of compound 7

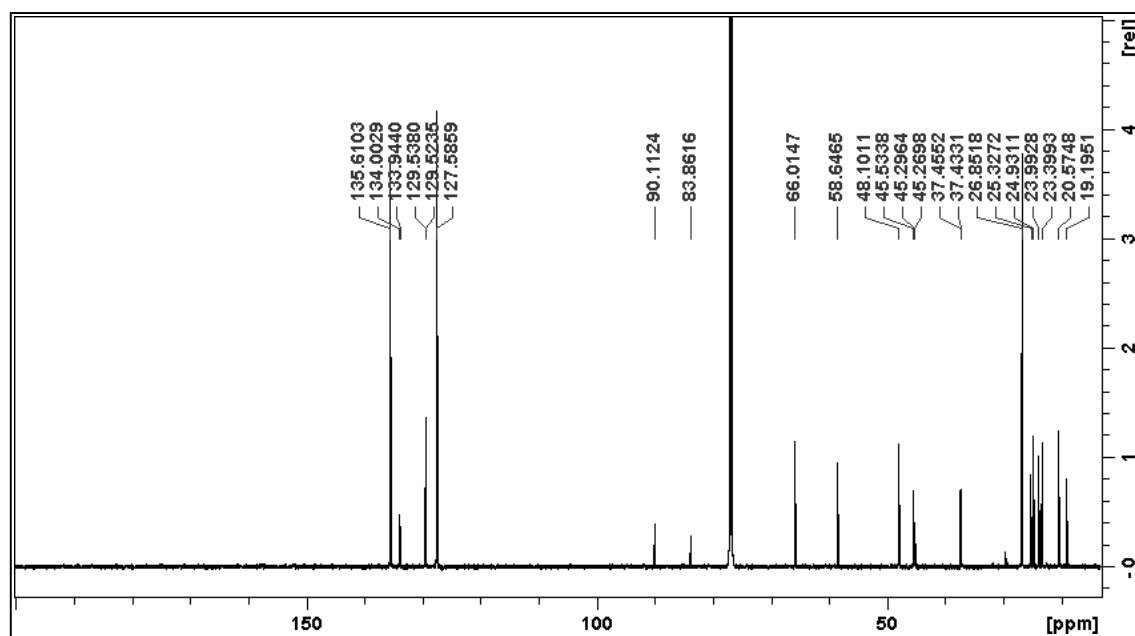


Figure S12. <sup>13</sup>C NMR spectrum of compound 7

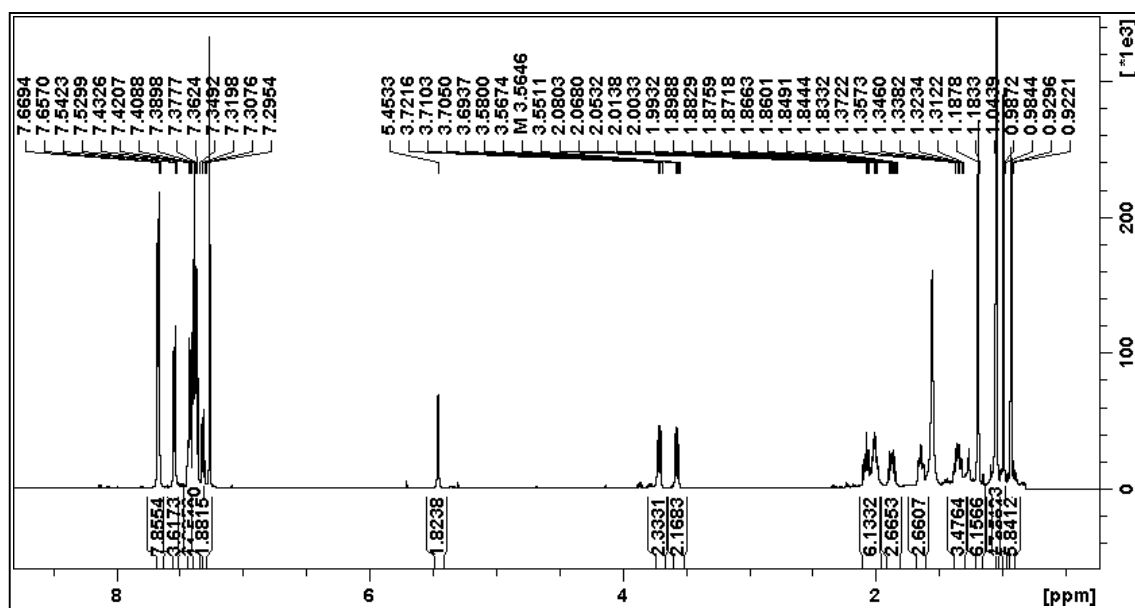


Figure S13.  $^1\text{H}$  NMR spectrum of compound 8

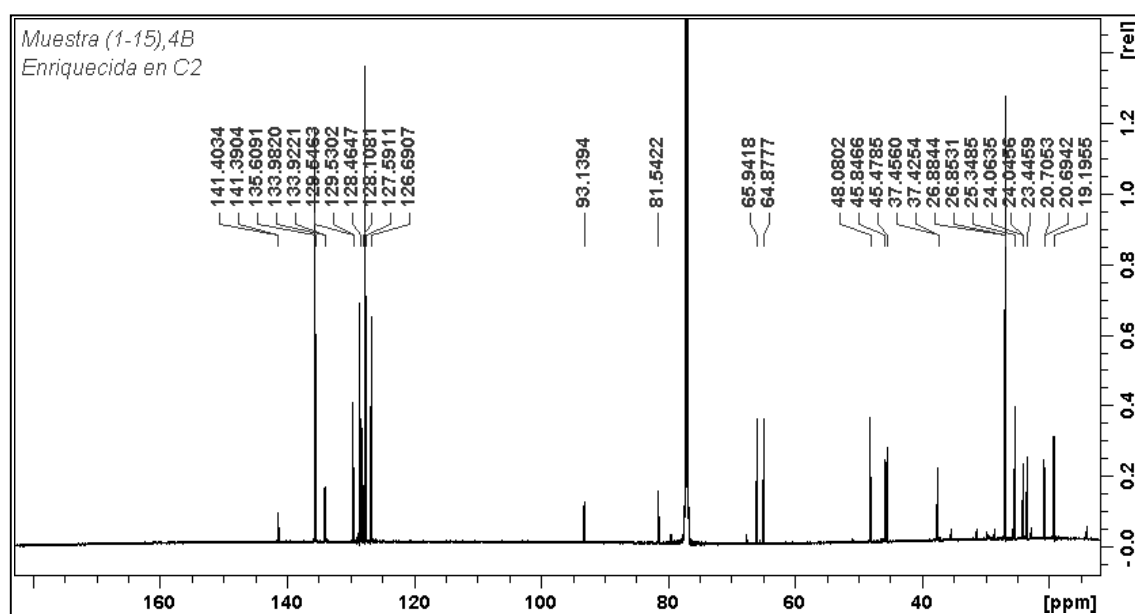


Figure S14.  $^{13}\text{C}$  NMR spectrum of compound 8



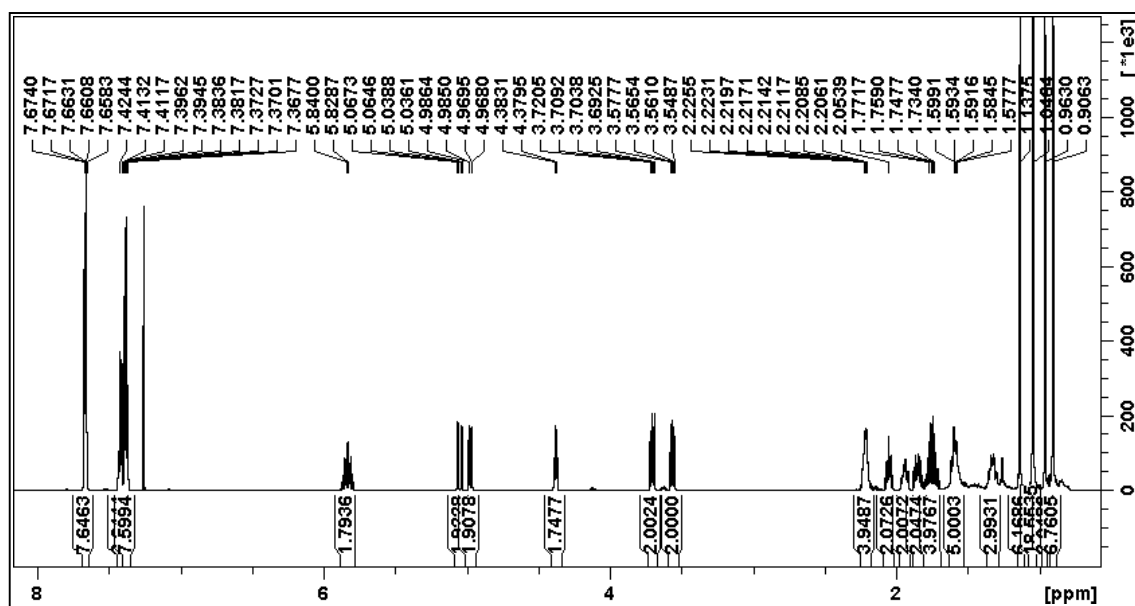


Figure S15.  $^1\text{H}$  NMR spectrum of compound 9

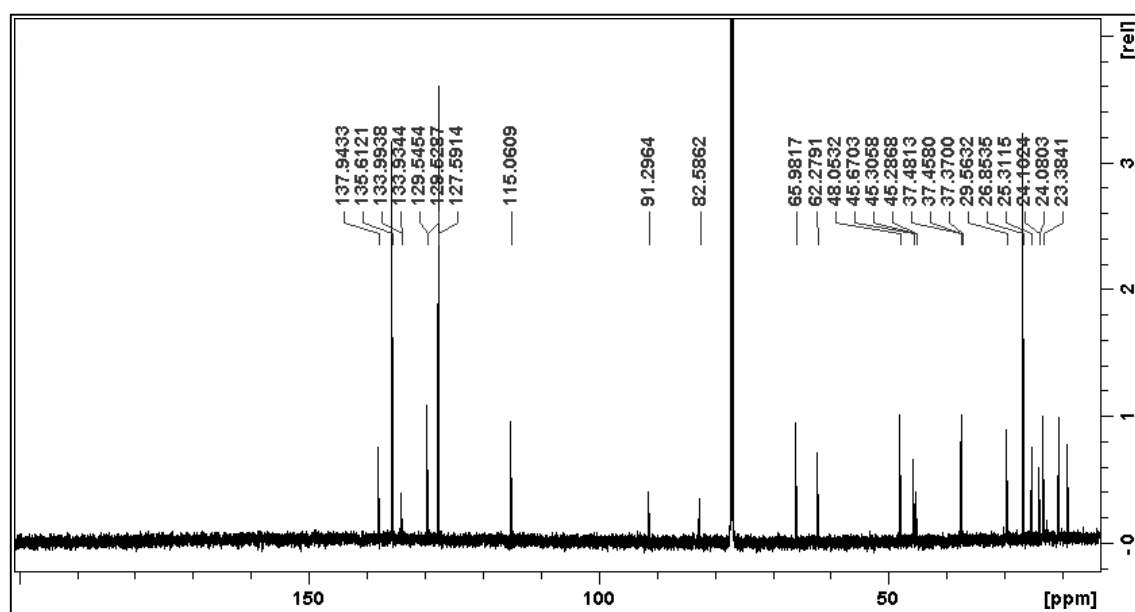


Figure S16.  $^{13}\text{C}$  NMR spectrum of compound 9

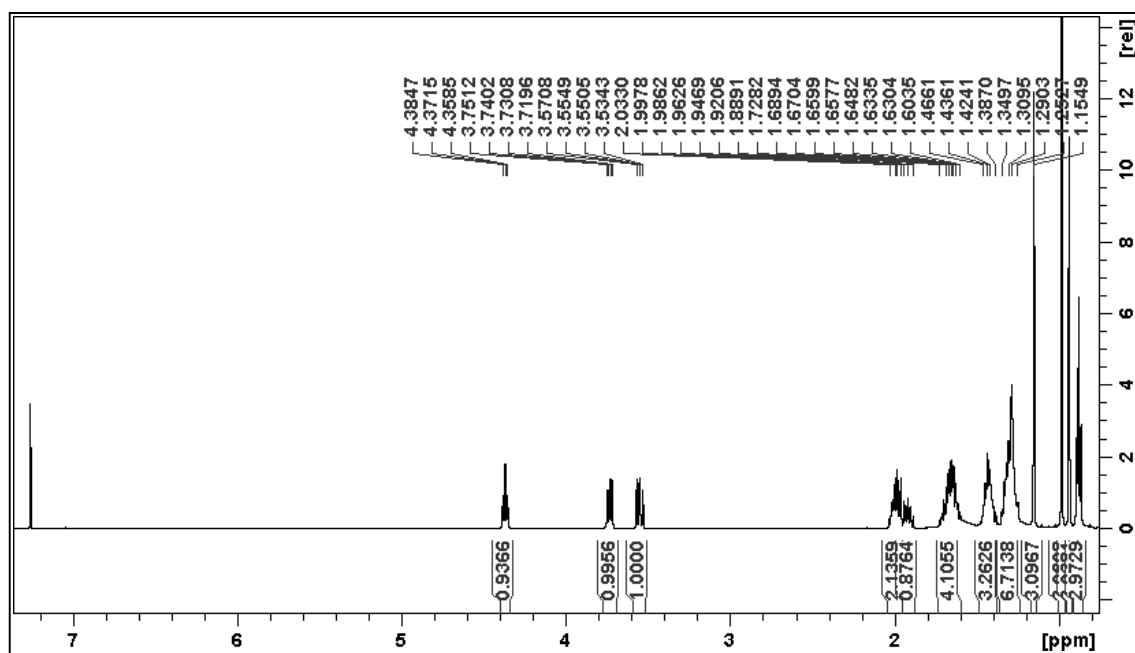


Figure S17. <sup>1</sup>H NMR spectrum of compound **10**

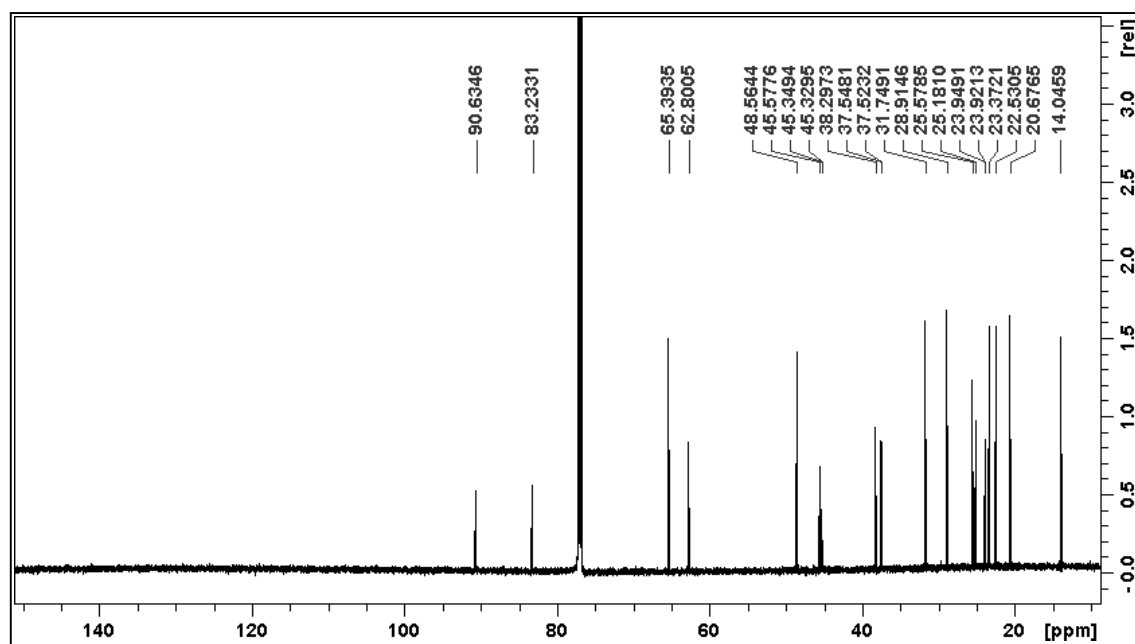


Figure S18. <sup>13</sup>C NMR spectrum of compound **10**

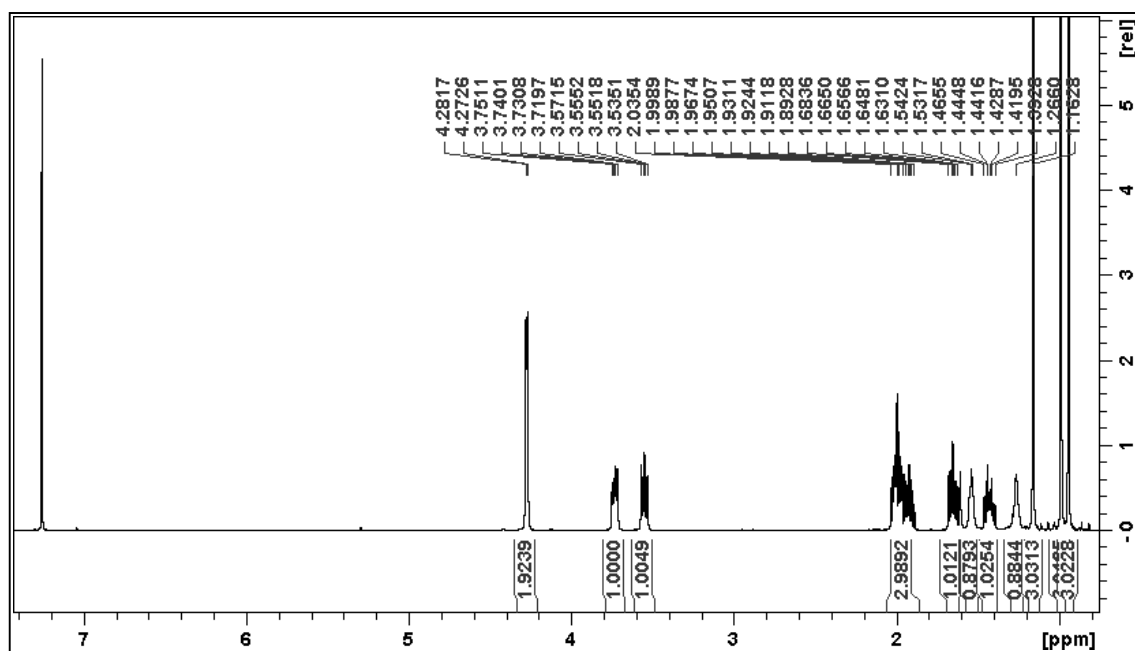


Figure S19. <sup>1</sup>H NMR spectrum of compound 11

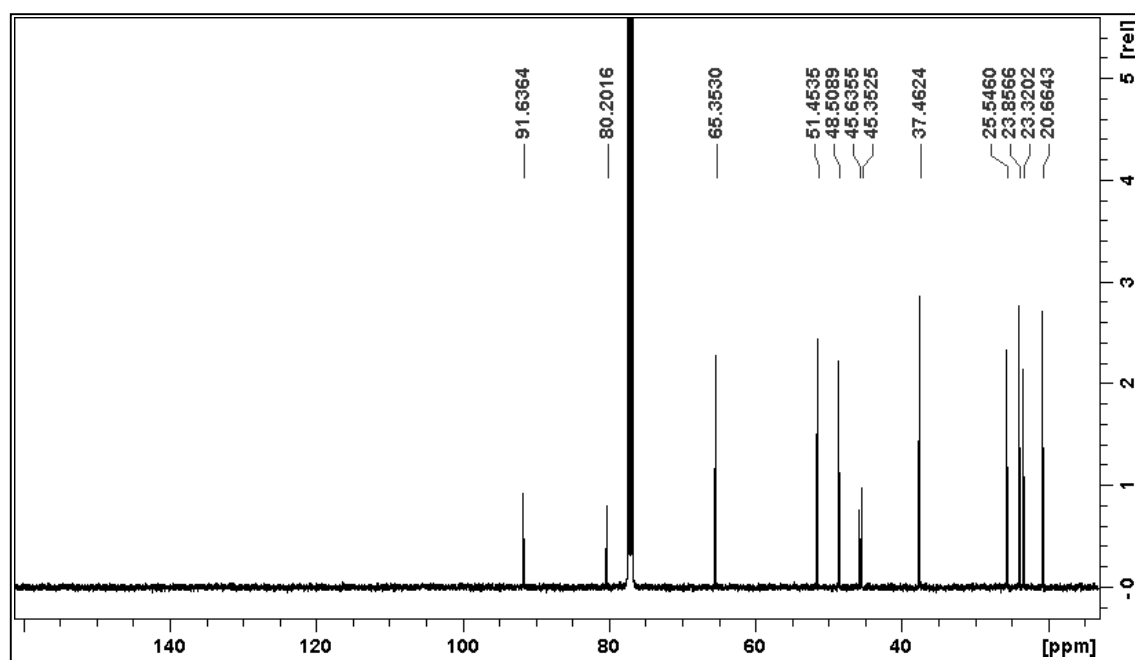


Figure S20. <sup>13</sup>C NMR spectrum of compound 11

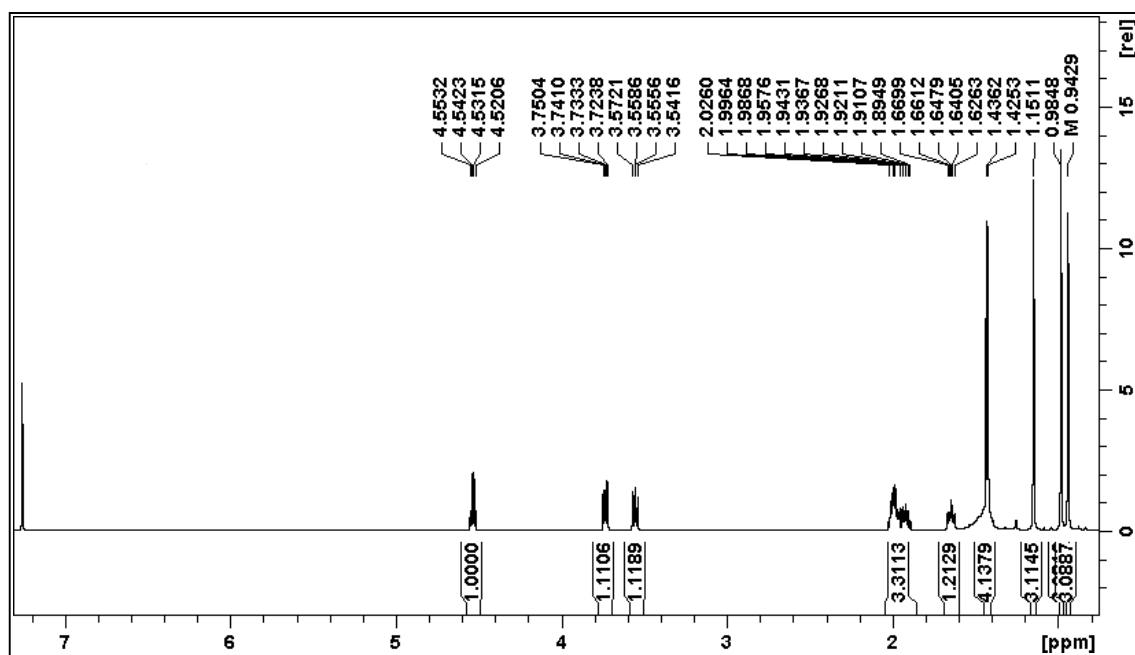


Figure S21. <sup>1</sup>H NMR spectrum of compound 12

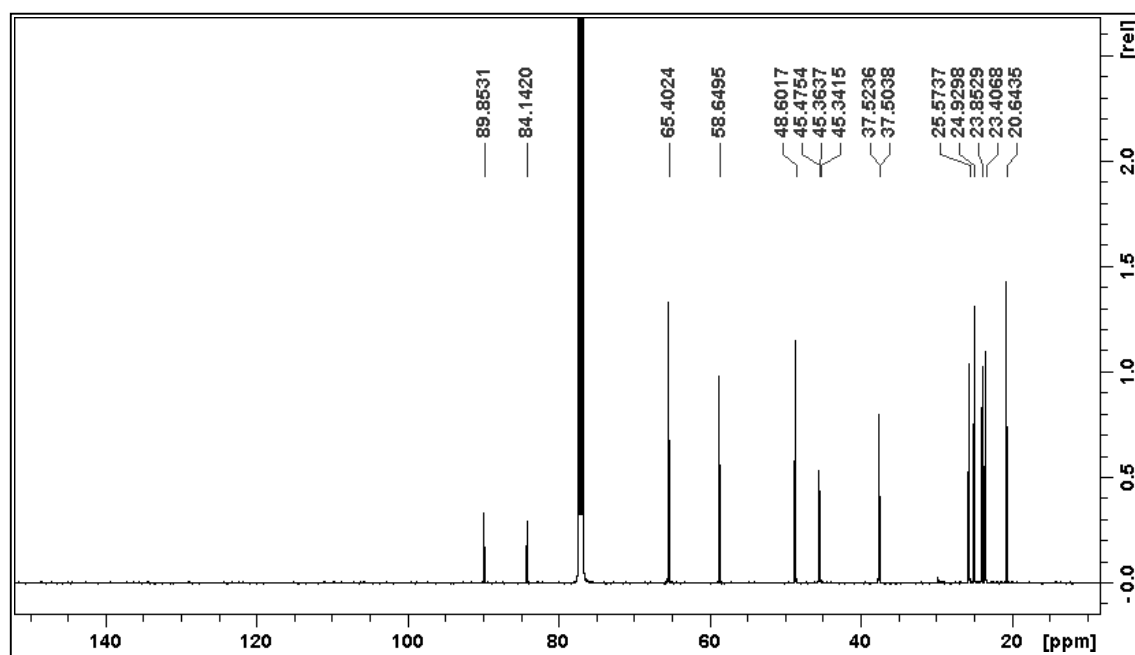


Figure S22. <sup>13</sup>C NMR spectrum of compound 12

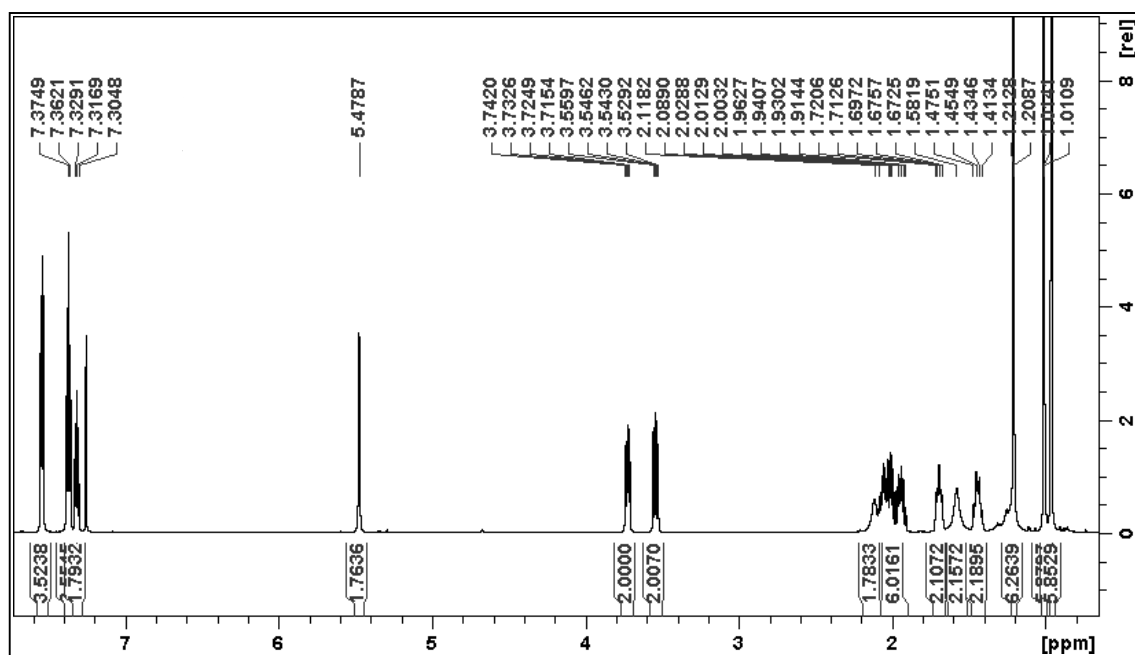


Figure S23. <sup>1</sup>H NMR spectrum of compound 13

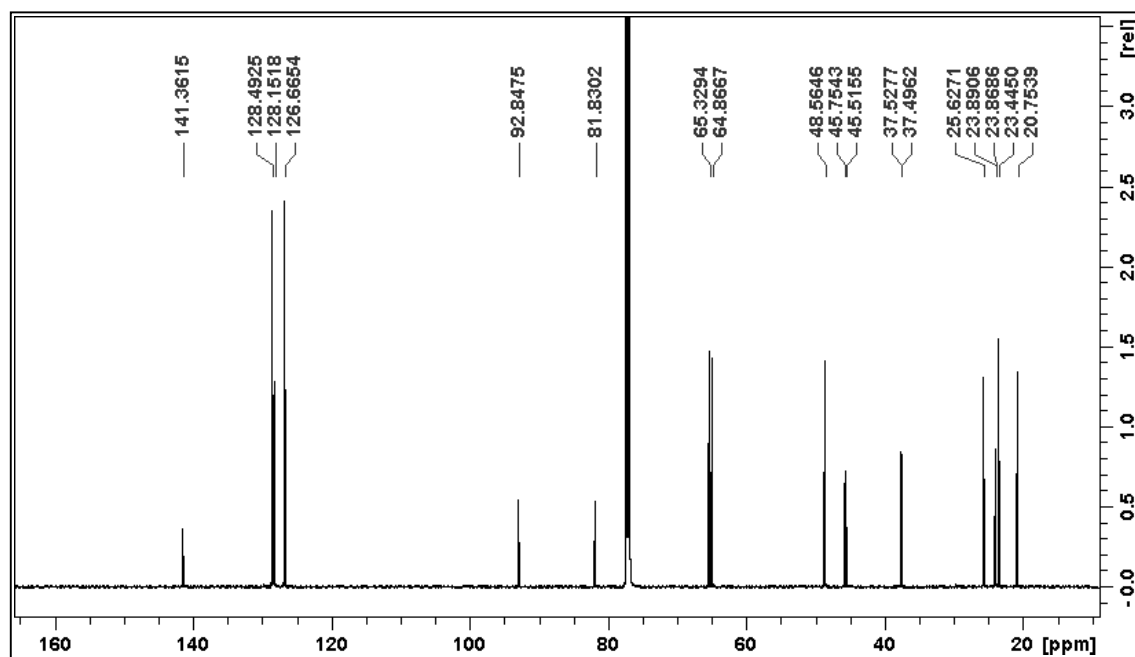


Figure S24. <sup>13</sup>C NMR spectrum of compound 13

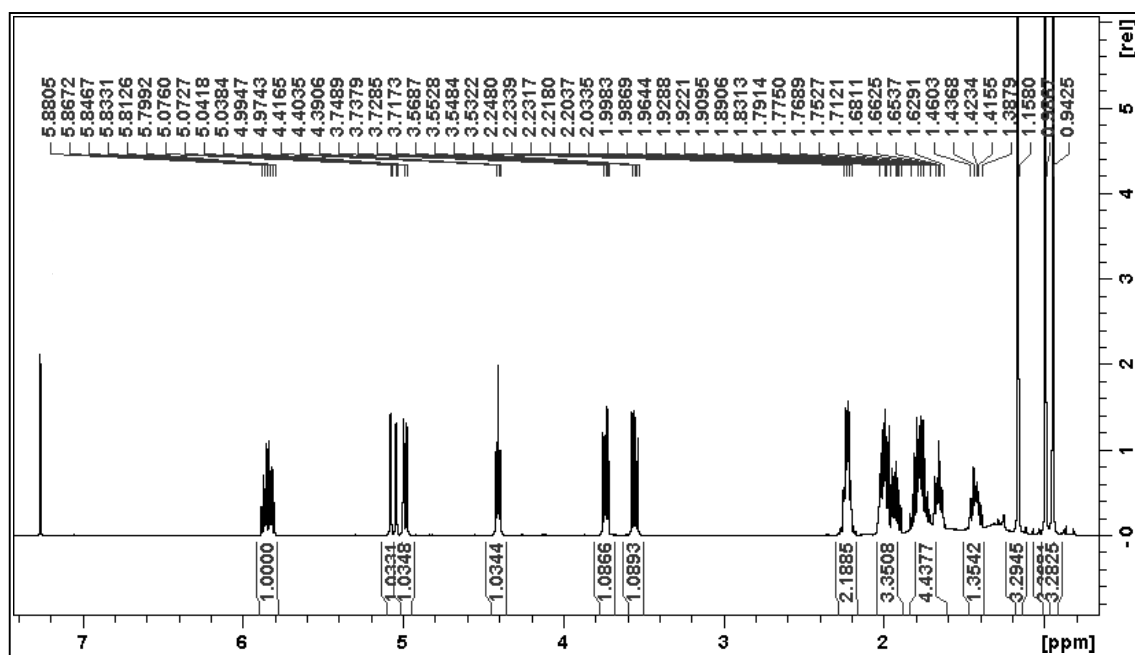


Figure S25.  $^1\text{H}$  NMR spectrum of compound **14**

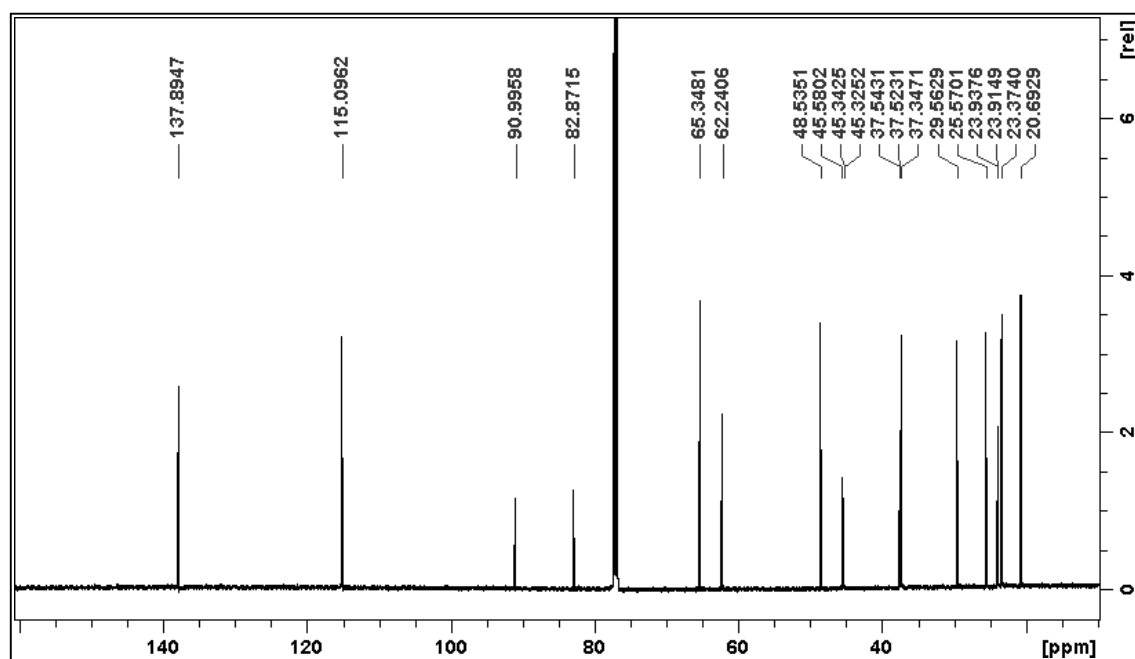


Figure S26.  $^{13}\text{C}$  NMR spectrum of compound **14**

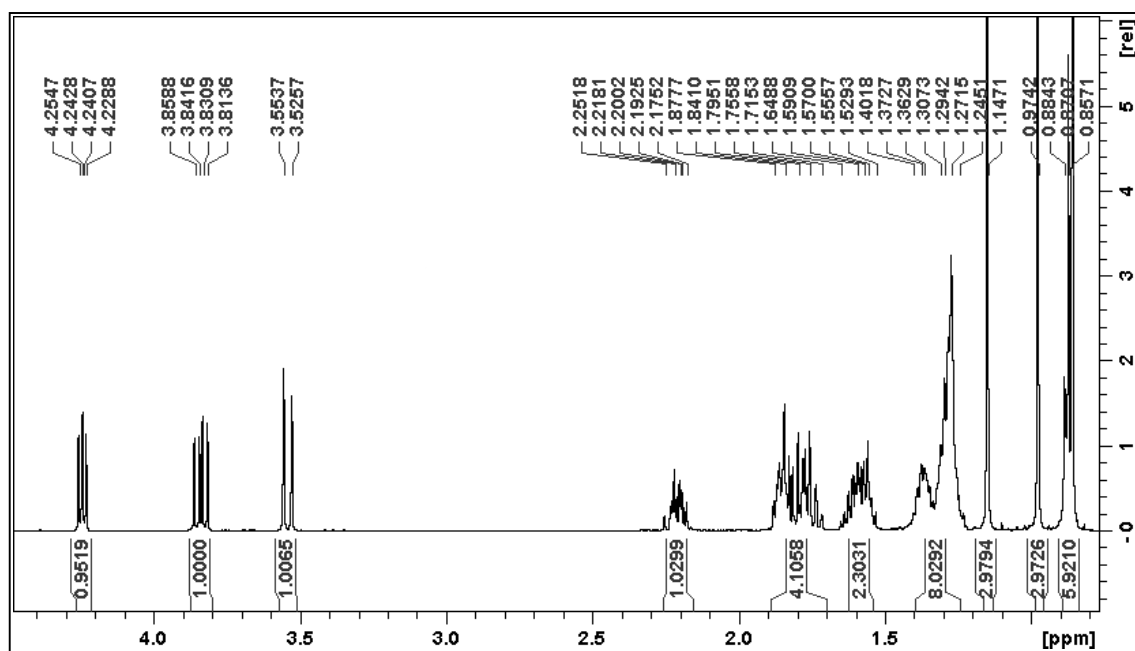


Figure S27. <sup>1</sup>H NMR spectrum of compound 1

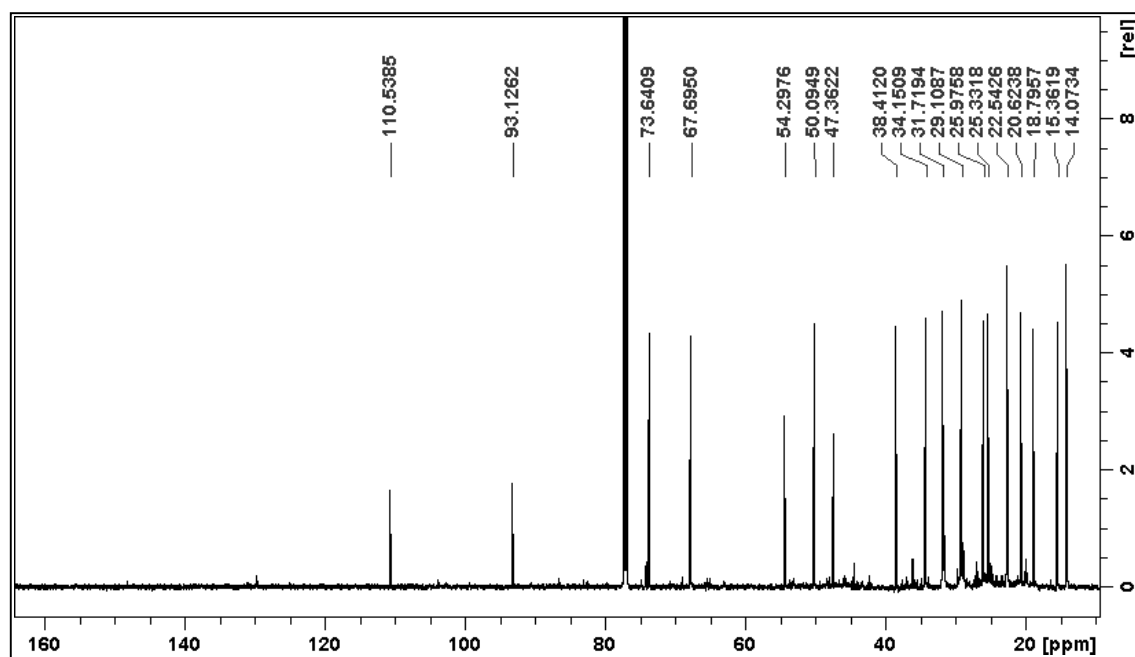


Figure S28. <sup>13</sup>C NMR spectrum of compound 1

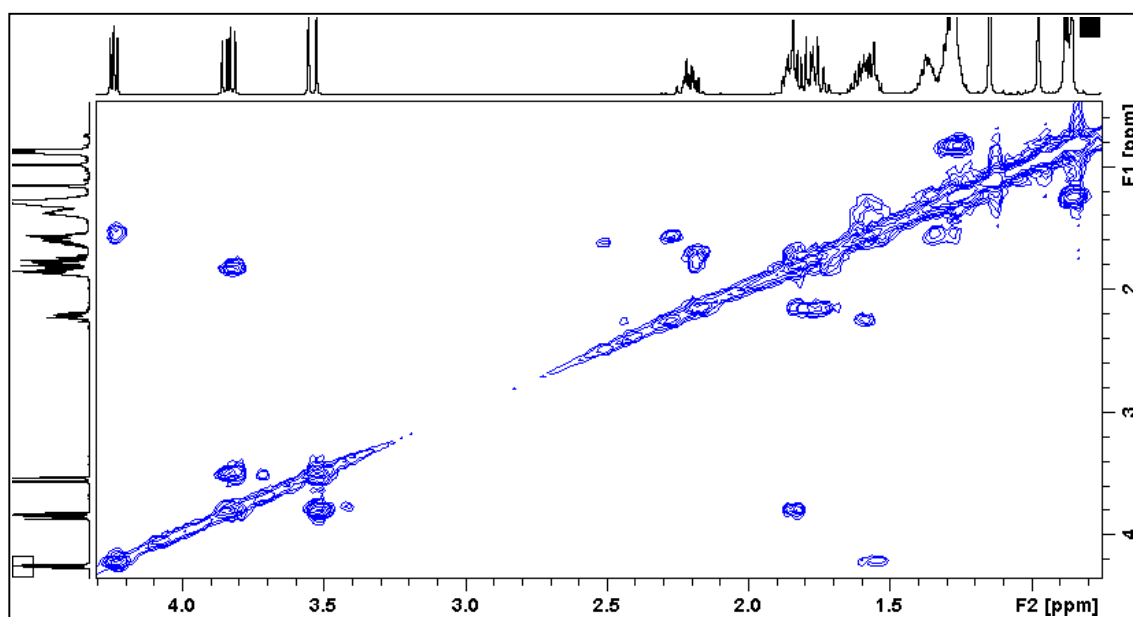


Figure S29. NMR-COSY spectrum of compound **1**

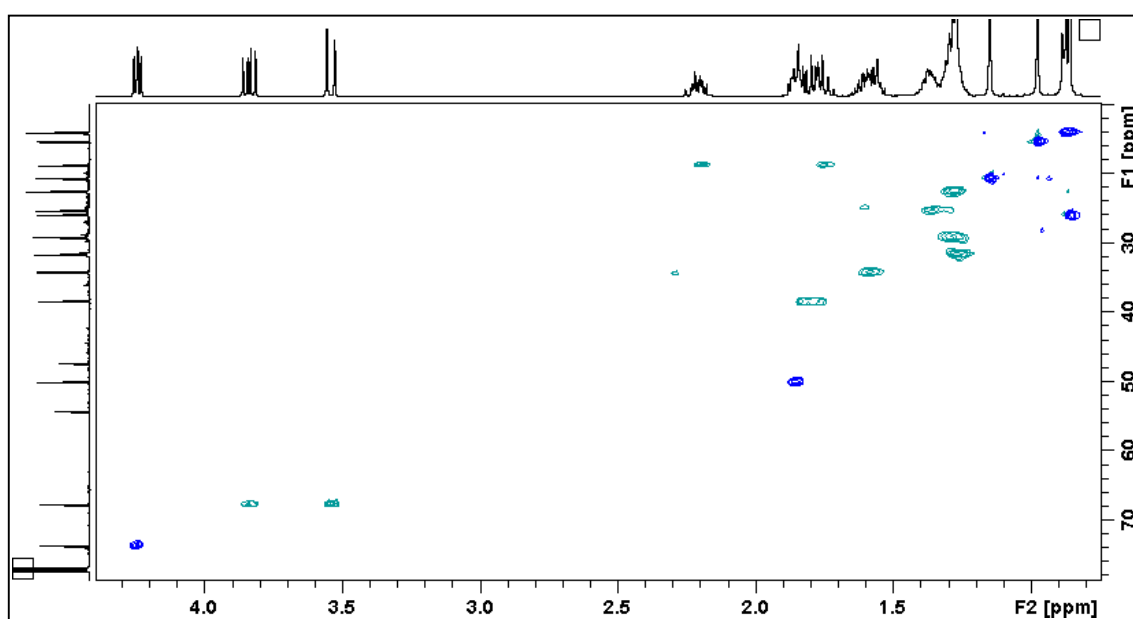
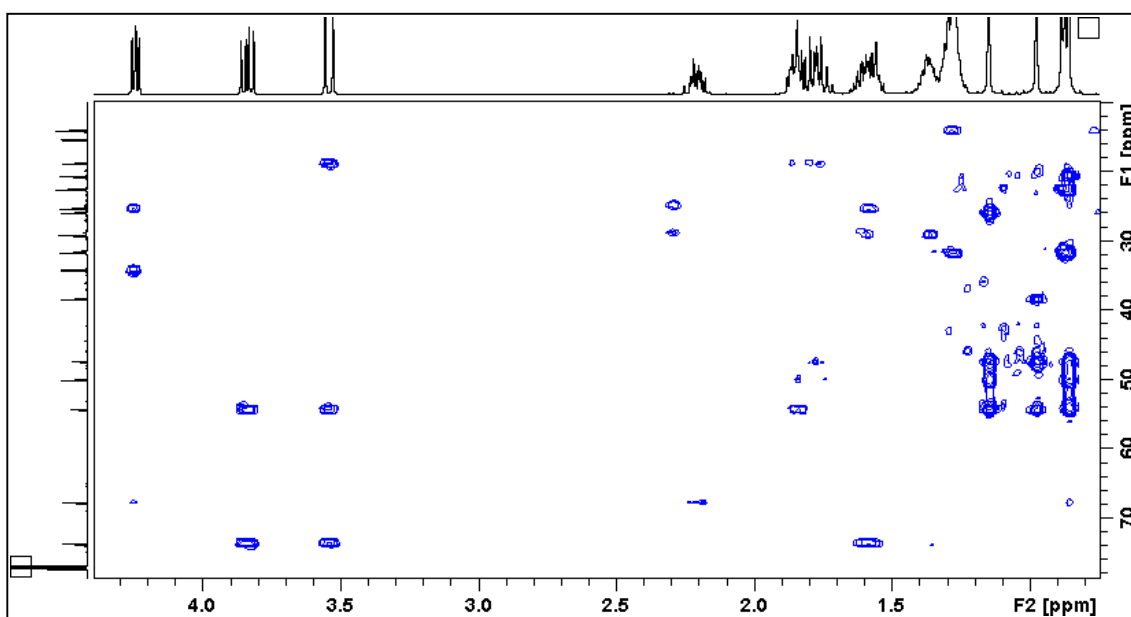
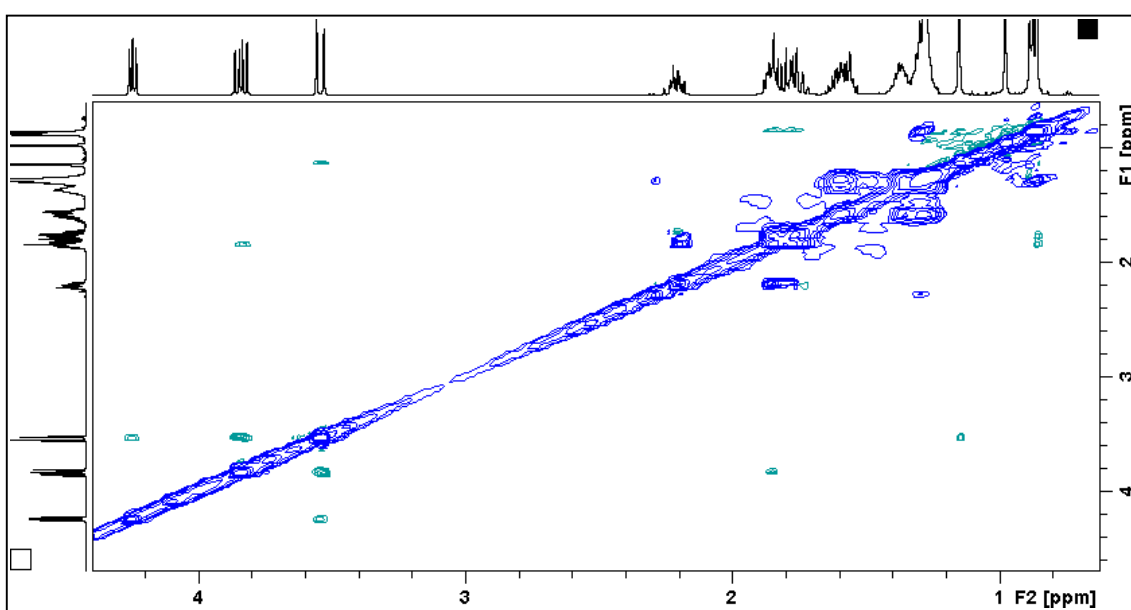


Figure S30. NMR-HSQC spectrum of compound **1**





**Figure S31.** NMR-HMBC spectrum of compound **1**



**Figure S32.** NMR-ROESY spectrum of compound **1**

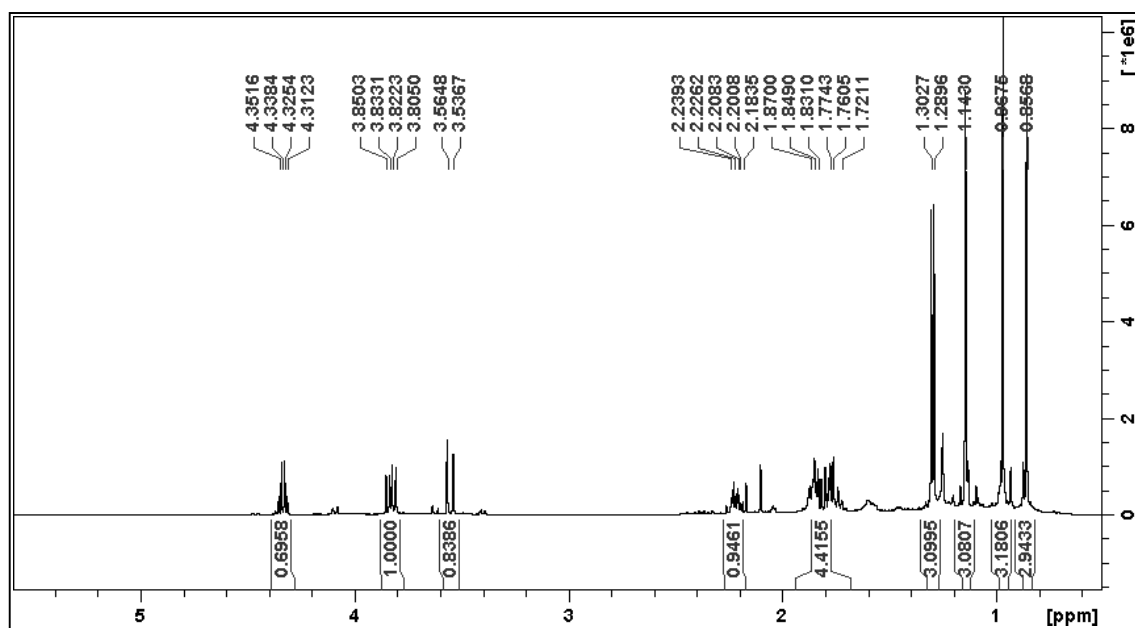


Figure S33. <sup>1</sup>H NMR spectrum of compound 21

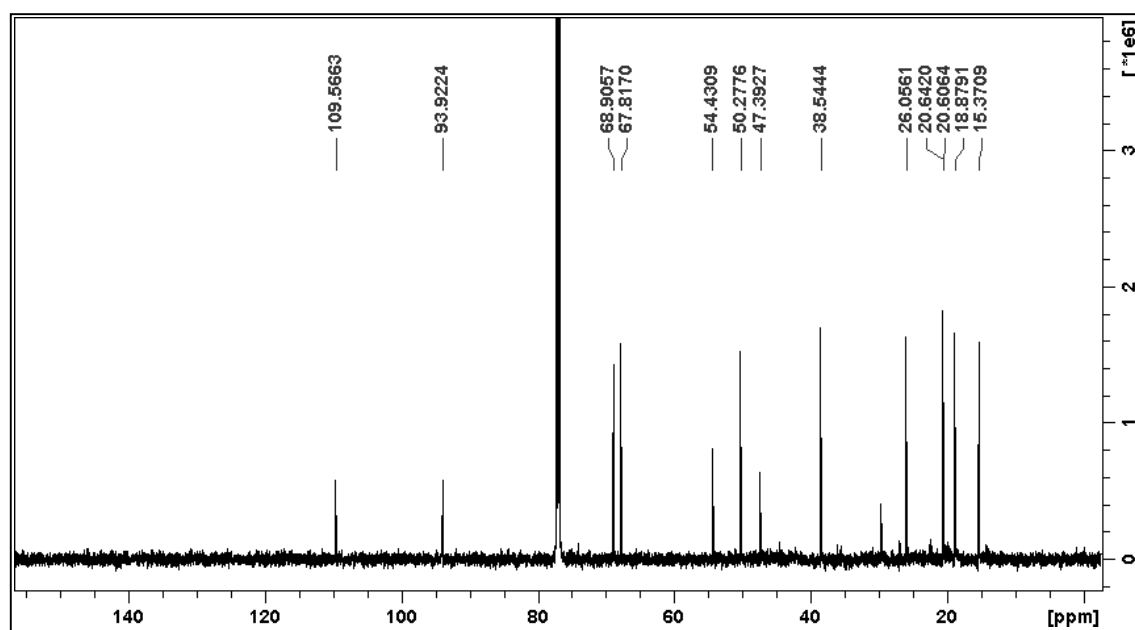


Figure S34. <sup>13</sup>C NMR spectrum of compound 21

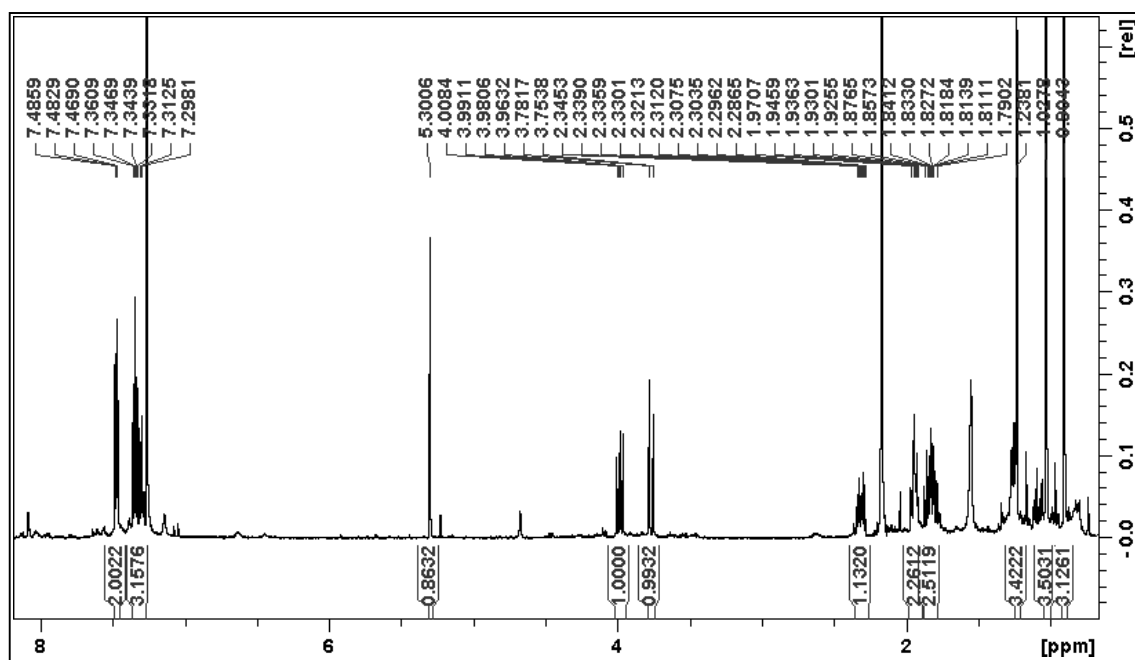


Figure S35. <sup>1</sup>H NMR spectrum of compound 22

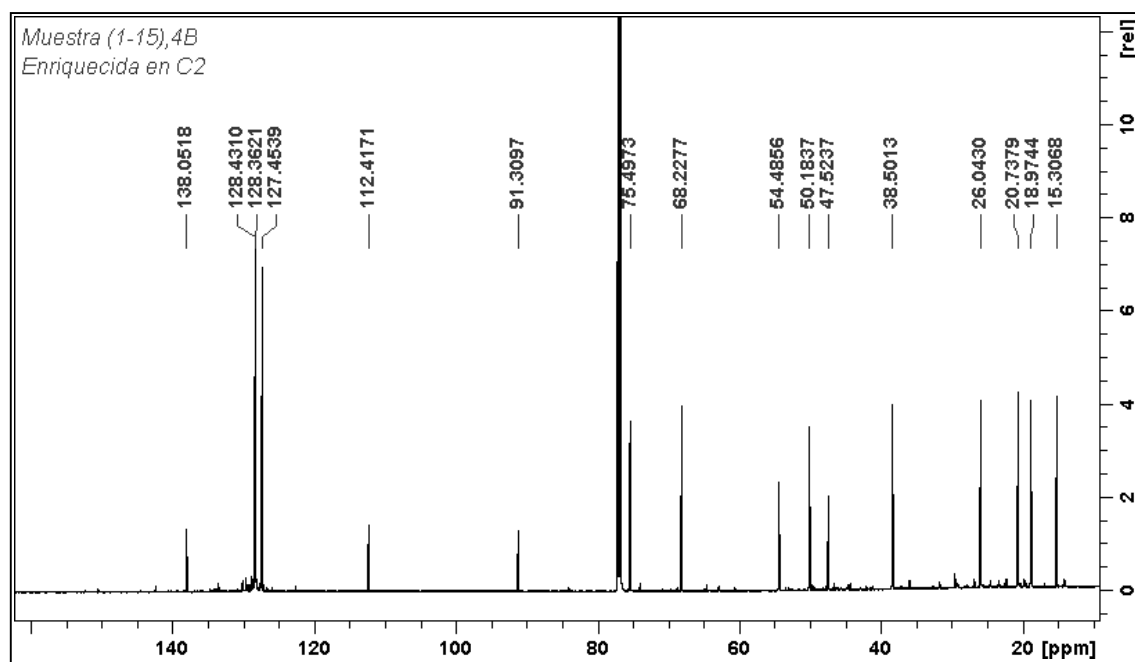
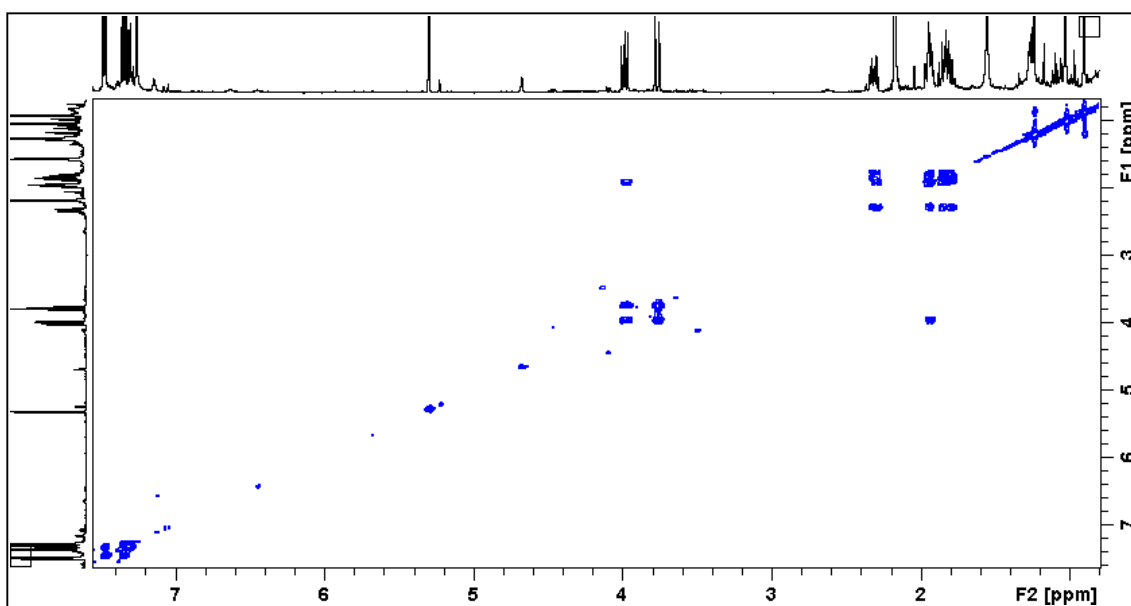
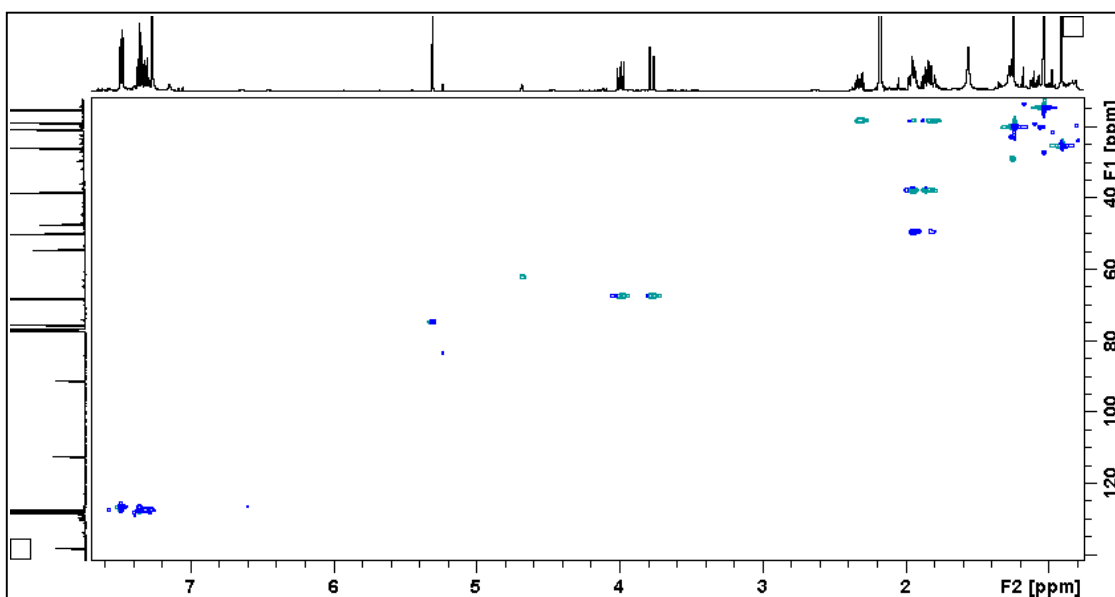


Figure S36. <sup>13</sup>C NMR spectrum of compound 22



**Figure S37.** NMR-COSY spectrum of compound **22**



**Figure S38.** NMR-HSQC spectrum of compound **22**

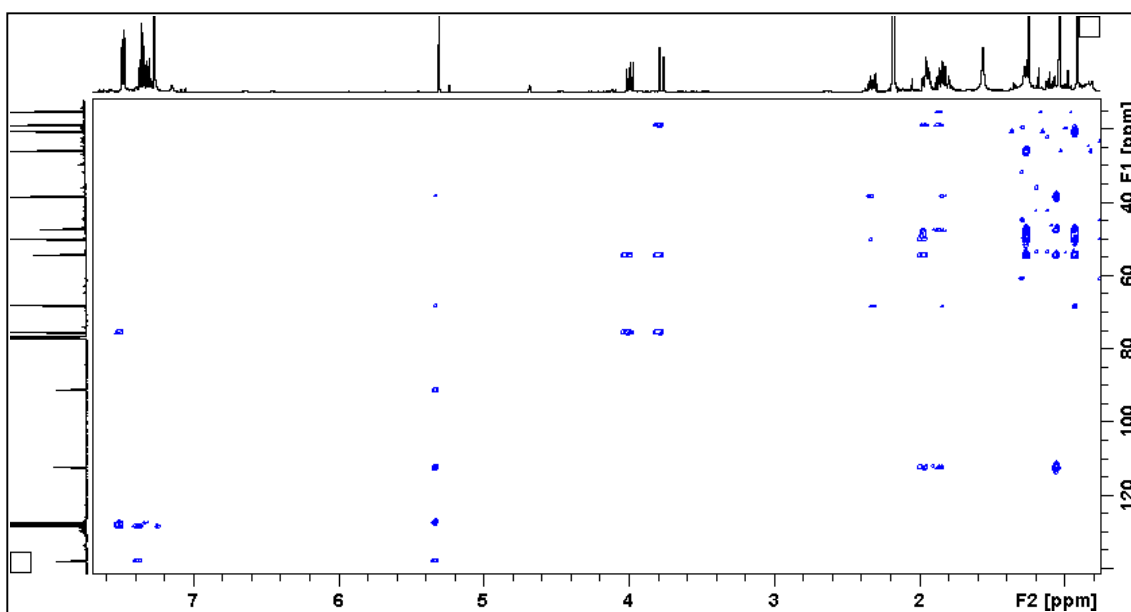


Figure S39. NMR-HMBC spectrum of compound 22

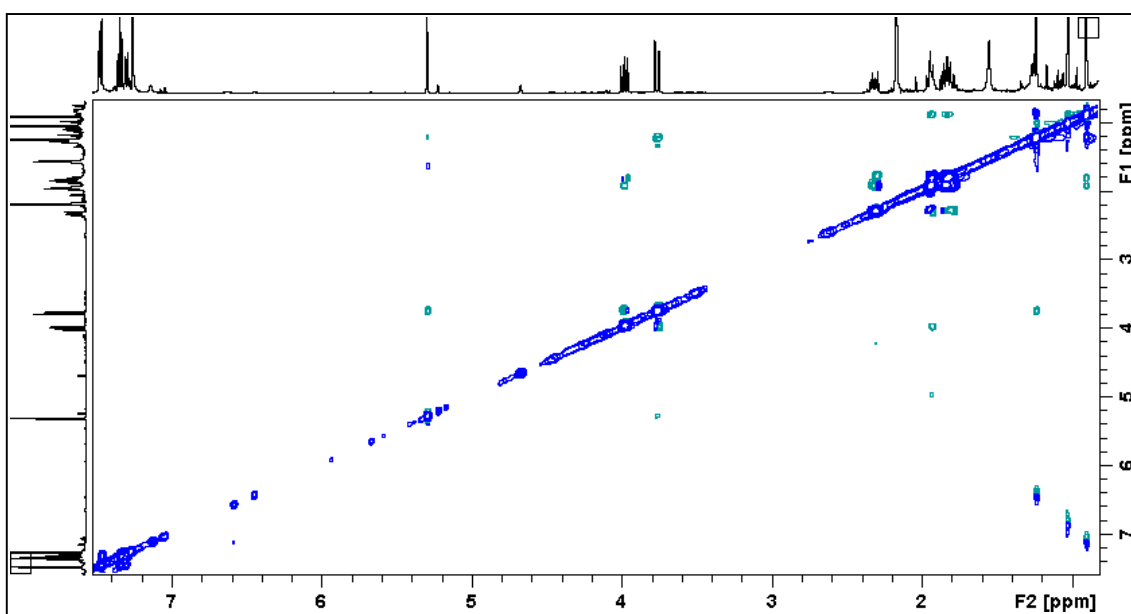


Figure S40. NMR-ROESY spectrum of compound 22

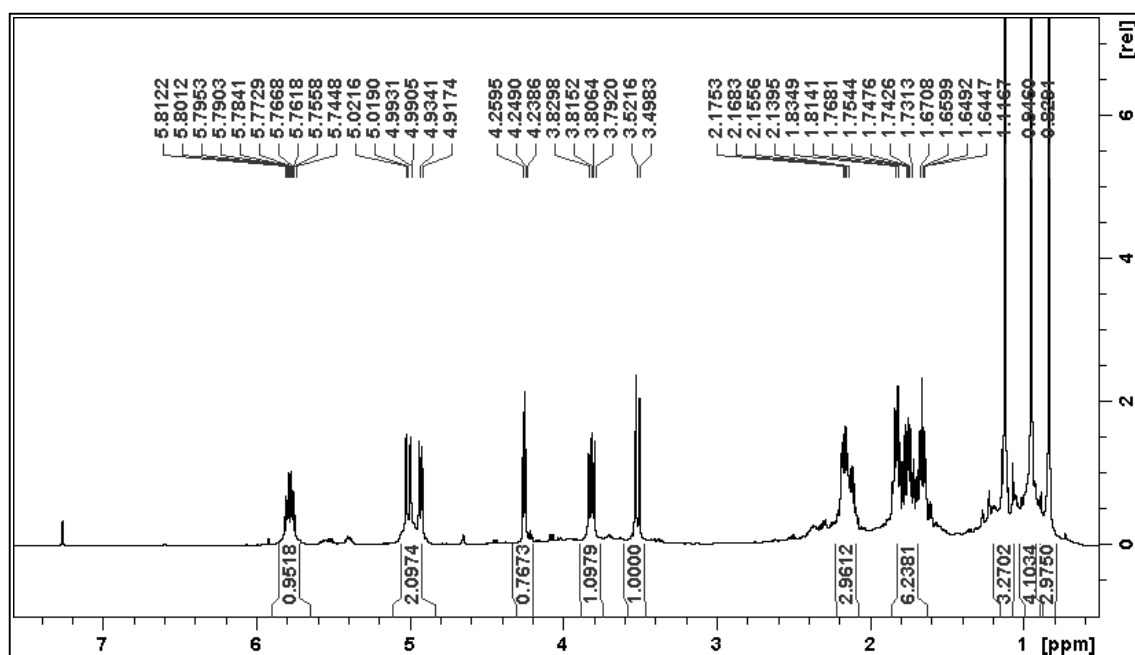


Figure S41. <sup>1</sup>H NMR spectrum of compound 23

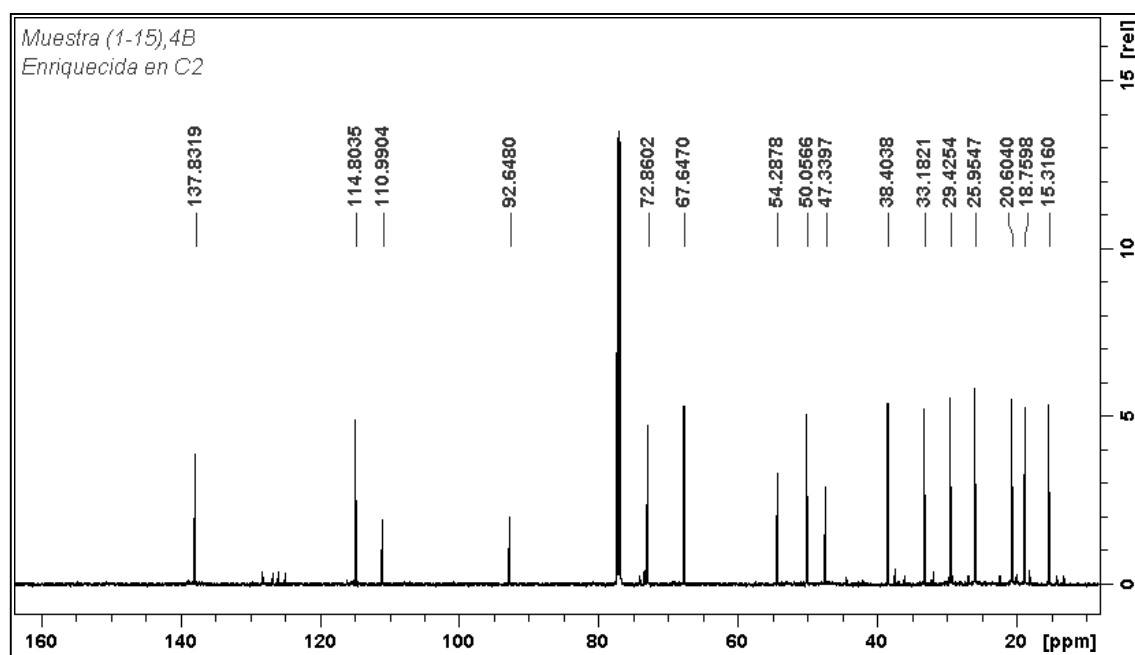
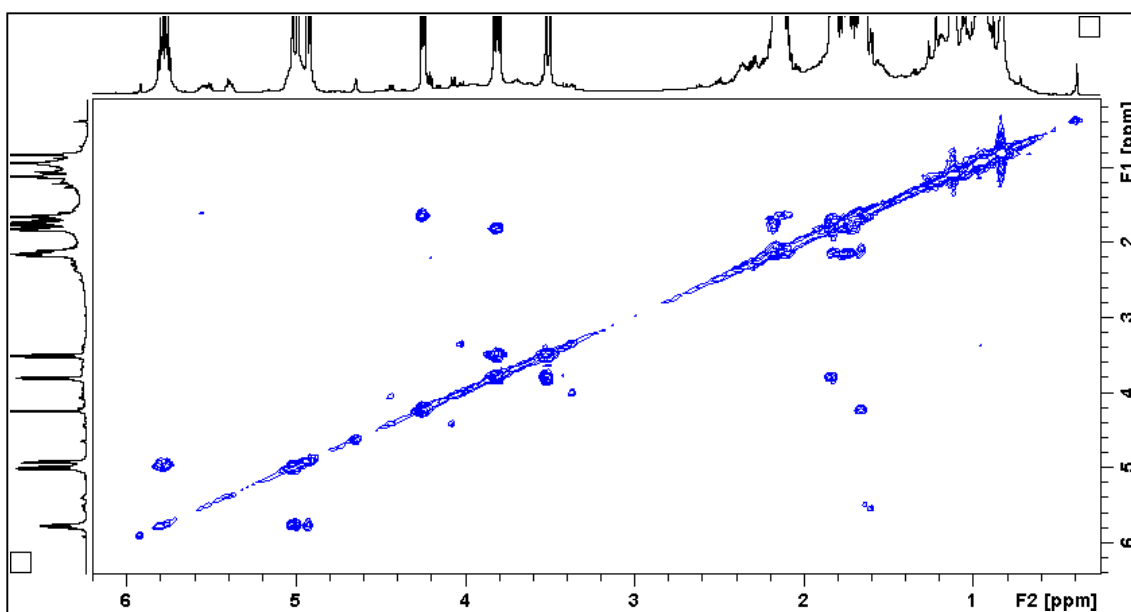
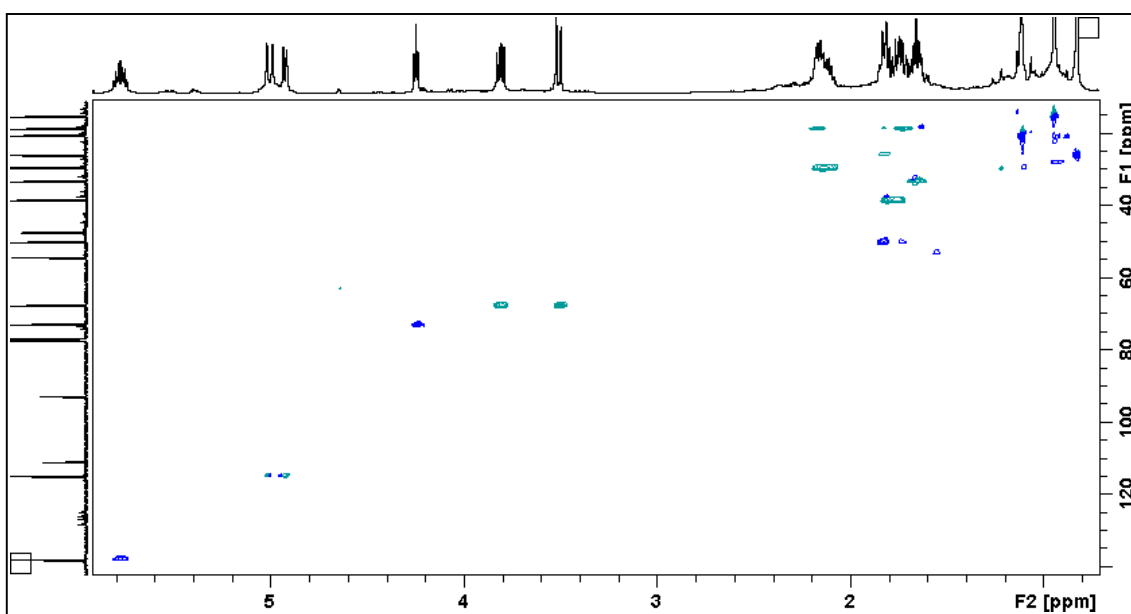


Figure S42. <sup>13</sup>C NMR spectrum of compound 23



**Figure S43.** NMR-COSY spectrum of compound **23**



**Figure S44.** NMR-HSQC spectrum of compound **23**

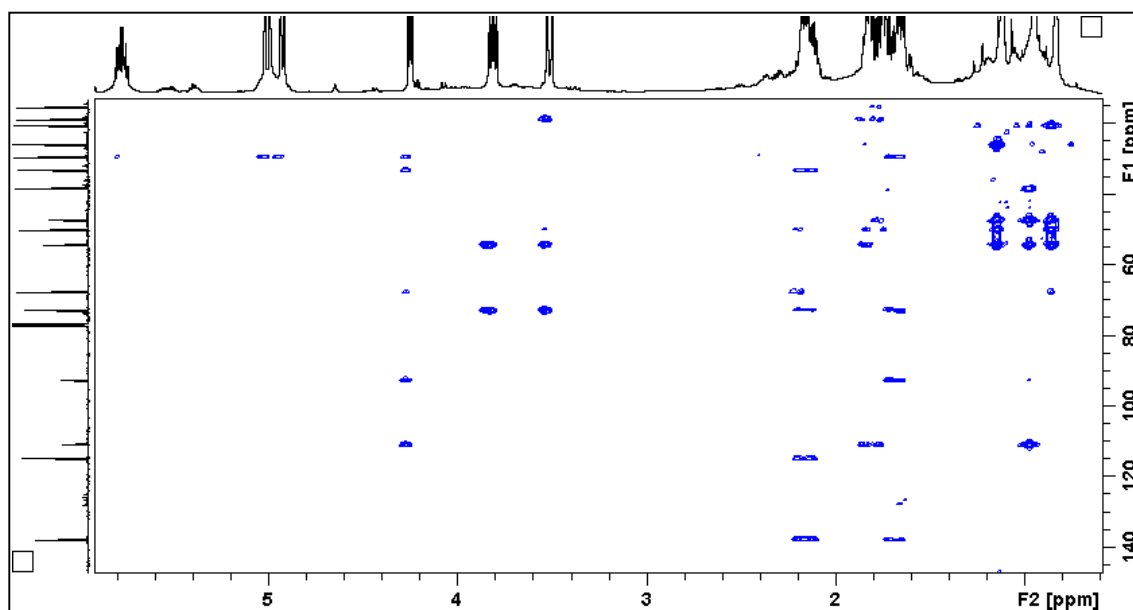


Figure S45. NMR-HMBC spectrum of compound 23

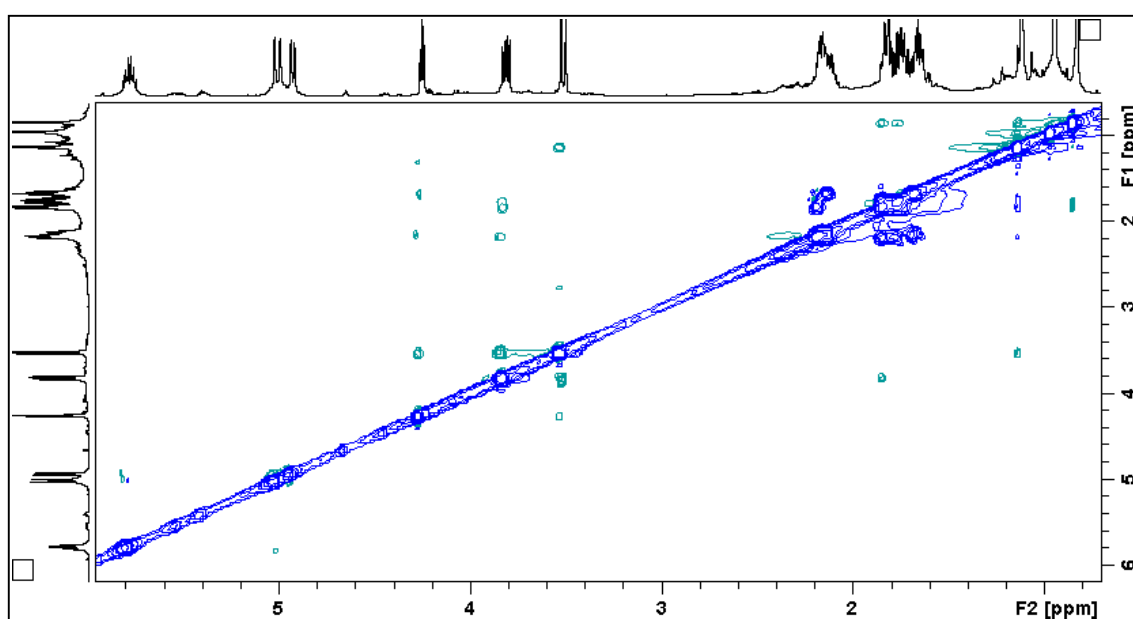
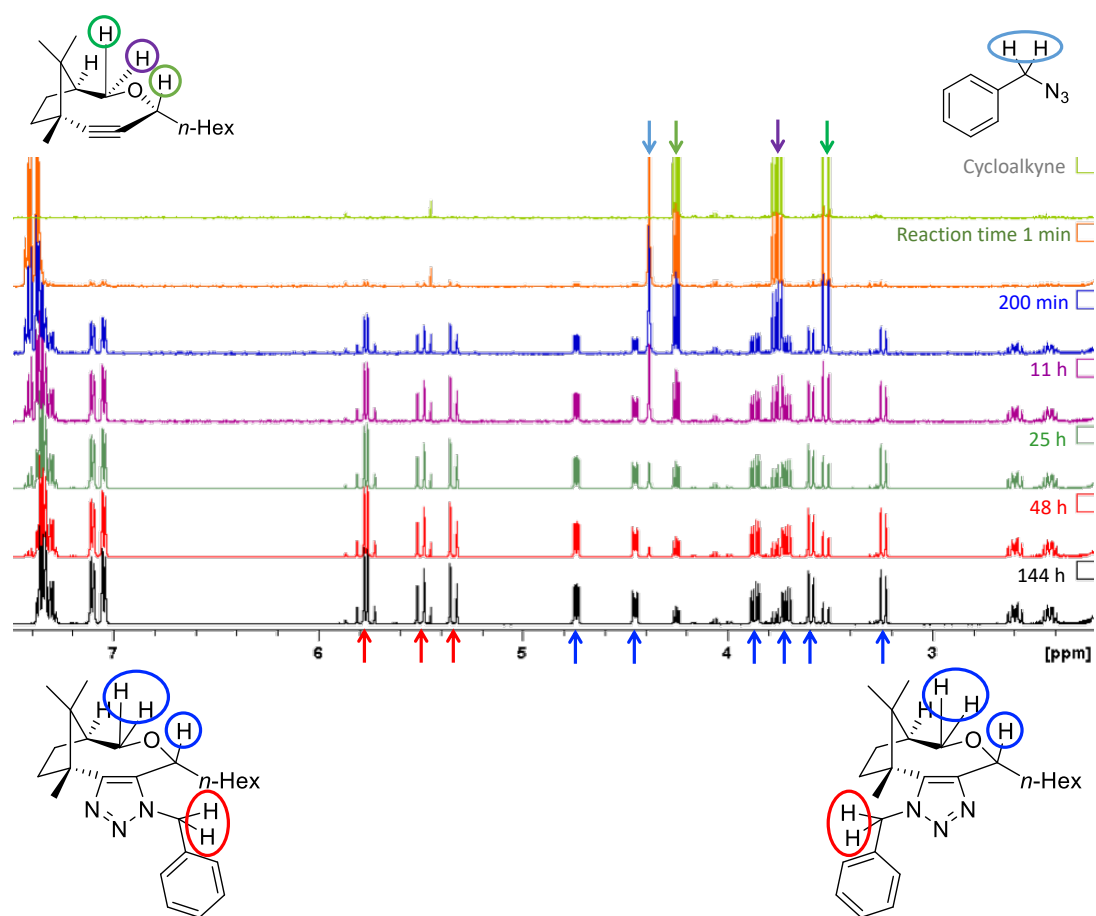
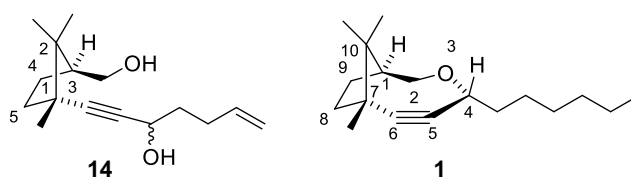


Figure S46. NMR-ROESY spectrum of compound 23





**Figure S47.** Monitoring SPAAC of cyclooctyne **1** and benzylazide by  $^1\text{H}$  NMR. The signals of the most relevant protons of each structure are indicated with colored arrows in the spectra, which match with the colored circles drawn on the structures



**Figure S48.** Numeration of atoms used for the nomenclature of acyclic precursors (e.g. compound **14**) and cyclic products (e.g. compound **1**)