Electronic Supplementary Information

Synthesis of amino acid-derivatives of 5-alkoxy-3,4-dihalo-2(5*H*)-furanones and their preliminary bioactivity investigation as linker

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General procedure for compounds O1-O27

According to previous work,[1] the mixture of 3,4-dihalo-2(5*H*)-furanone **1** (0.30 mmol) and DABCO (1.2 eq.) in alkyl alcohol (3.0 mL) was stirred at room temperature for 9 h. Once the reaction completed, the mixture was treated with saturated brine, and extracted with CH_2Cl_2. The obtained organic layer was washed with distilled water and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the residue was purified by column chromatography to give the expected product (**O1-O27**).

General procedure for compounds S1-S16

According to previous work,[2] the mixture of 3,4-dihalo-2(5*H*)-furanone **1** (0.30 mmol), CuI (10 mol%), and proline sodium salt (80%, added in batches) in sulfoxide (1 mL) was stirred at the required temperature (oil bath temperature, set as needed, usually 95 ^oC) under air for 12 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The organic extracts were dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel to afford desired product (**S1-S16**).

General procedure for compounds SO1-SO16

According to previous work,[3] the mixture of 3,4-dihalo-2(5*H*)-furanone **1** (0.30 mmol), sodium sulfinate 2 (0.60 mmol) and *n*-Bu_4NBr (3 mol %) in DCE: H_2O (v:v = 5:1, 3 mL) was stirred at 90 °C under air for 8 h. At ambient temperature, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (3 × 15 mL). The organic extracts were dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, the crude product was purified by column chromatography on silica gel to afford desired product (**SO1-SO16**).

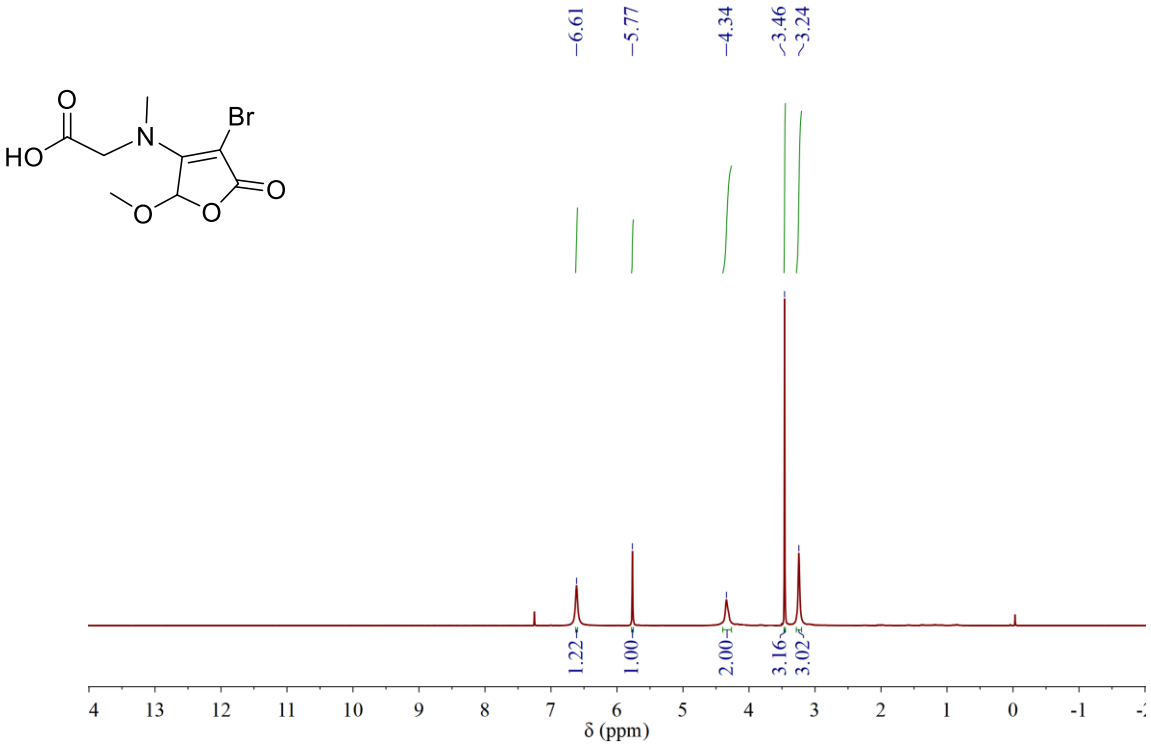


Figure 1. ^{1}H NMR spectrum of compound N1

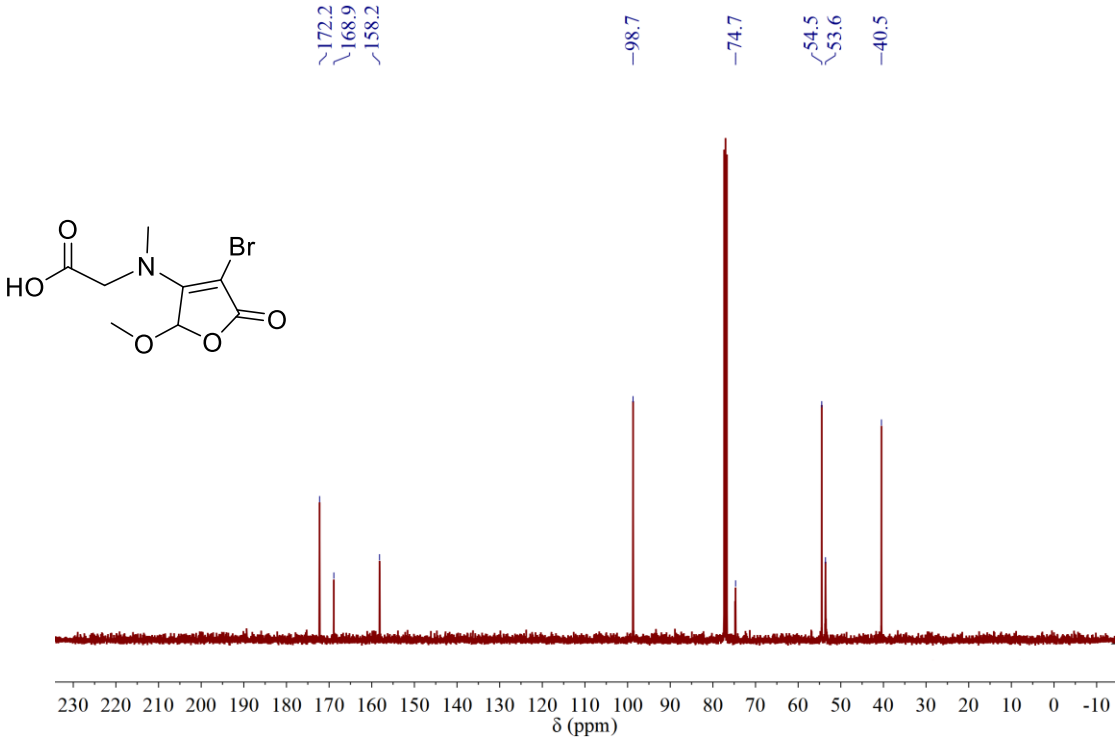


Figure 2. ^{13}C NMR spectrum of compound N1

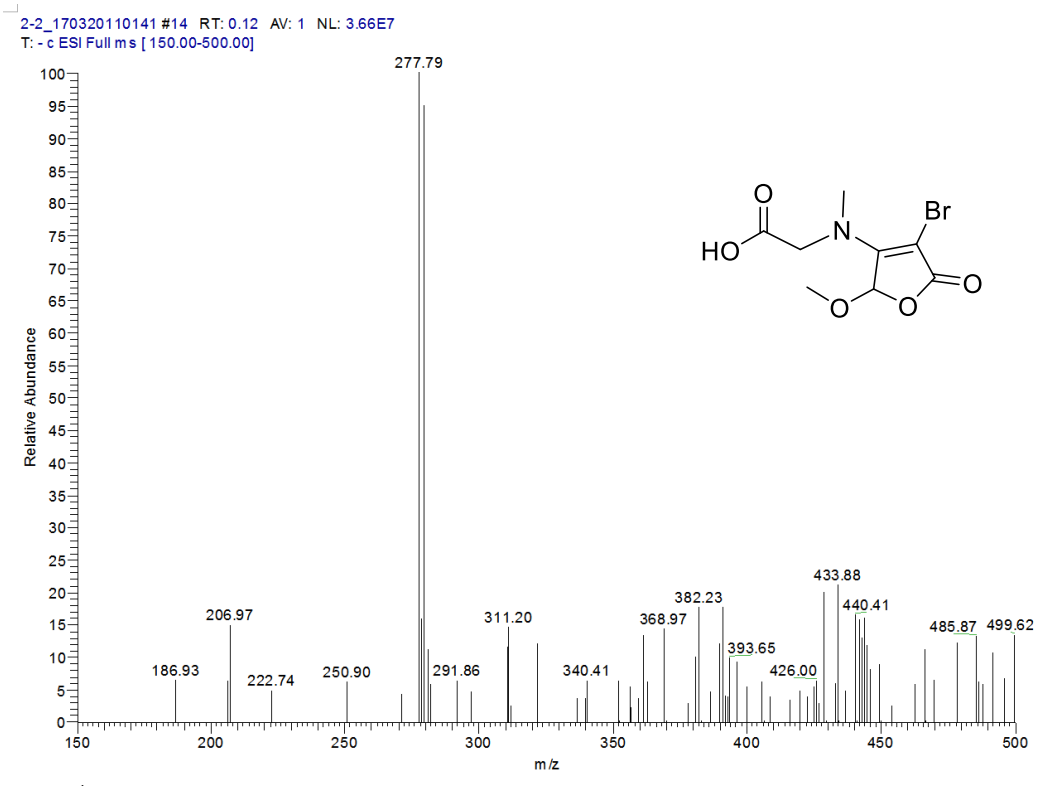


Figure 3. ESI-MS spectrum of compound N1

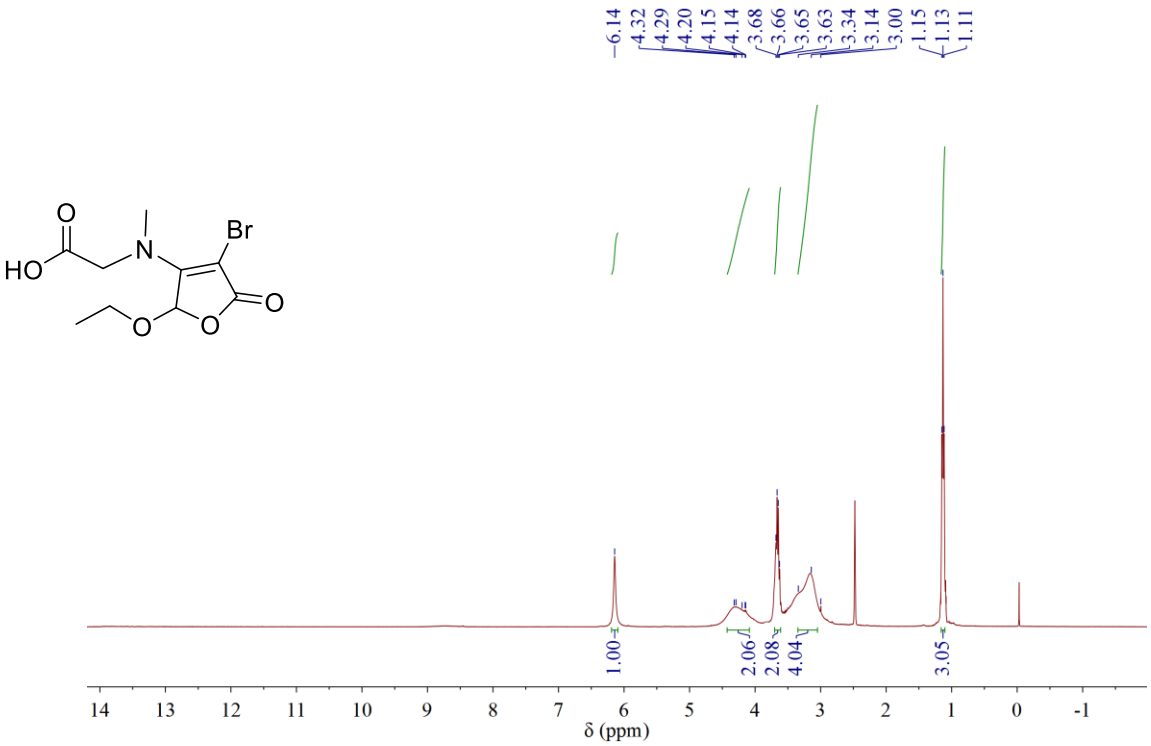


Figure 4. ^{1}H NMR spectrum of compound N2

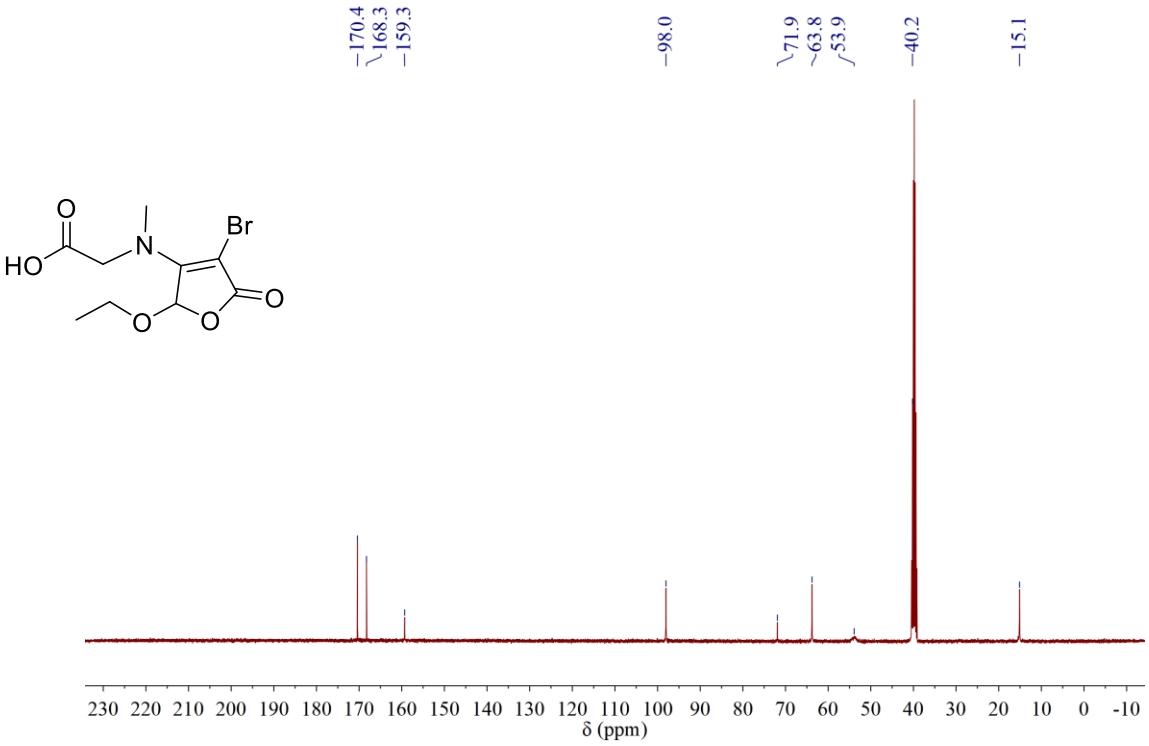


Figure 5. ^{13}C NMR spectrum of compound N2

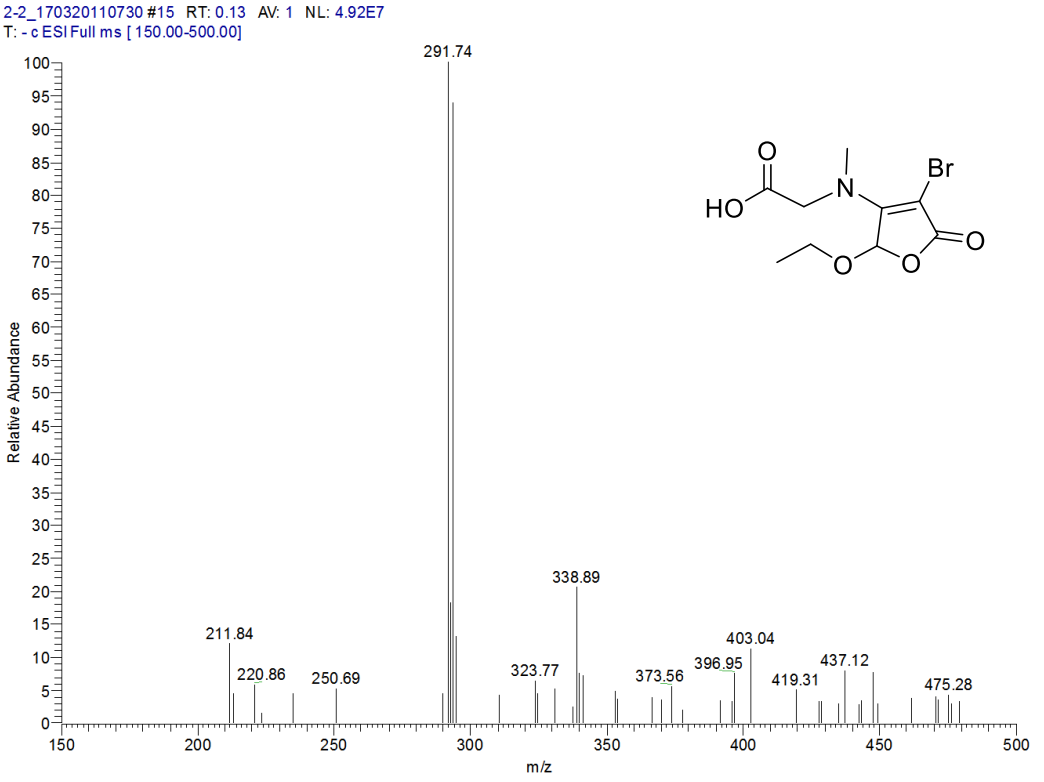


Figure 6. ESI-MS spectrum of compound N2

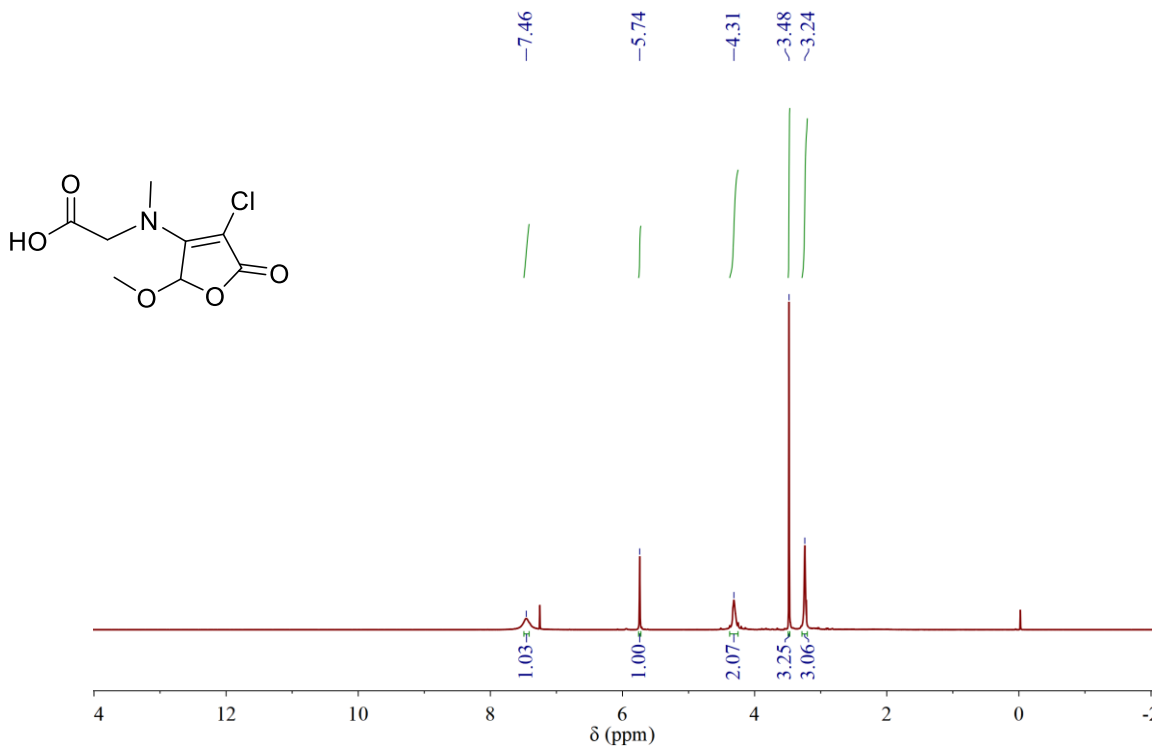


Figure 7. ^{1}H NMR spectrum of compound N3

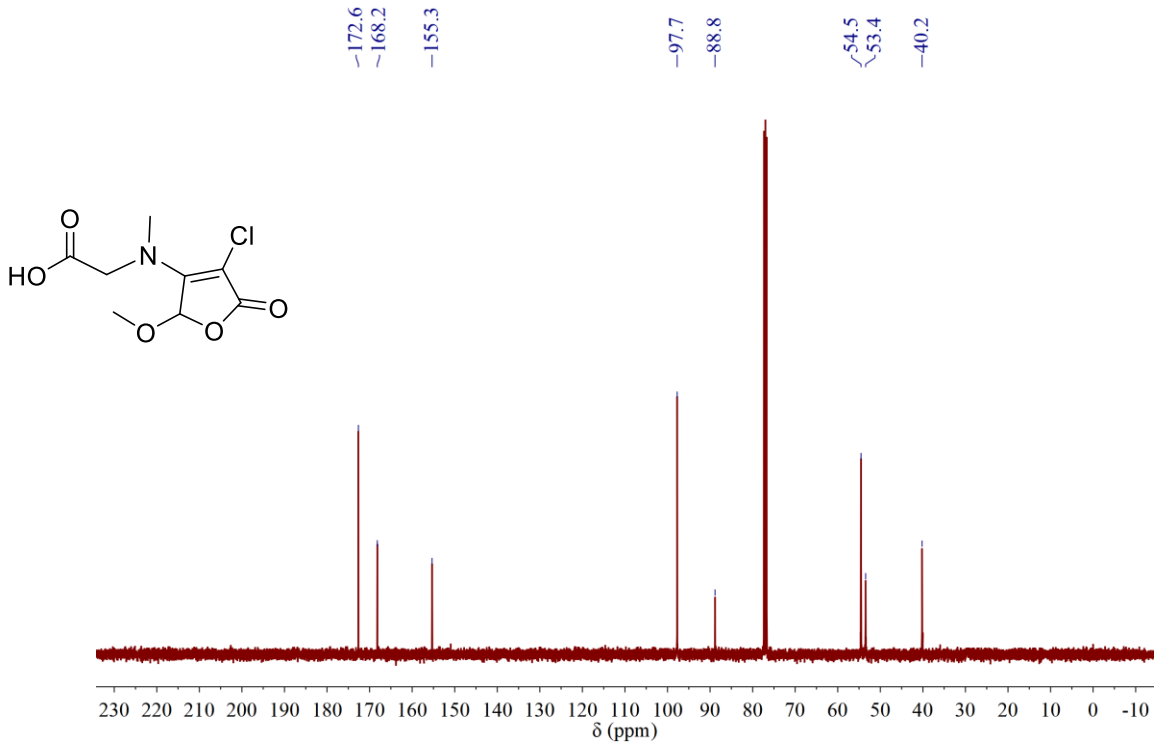


Figure 8. ^{13}C NMR spectrum of compound N3

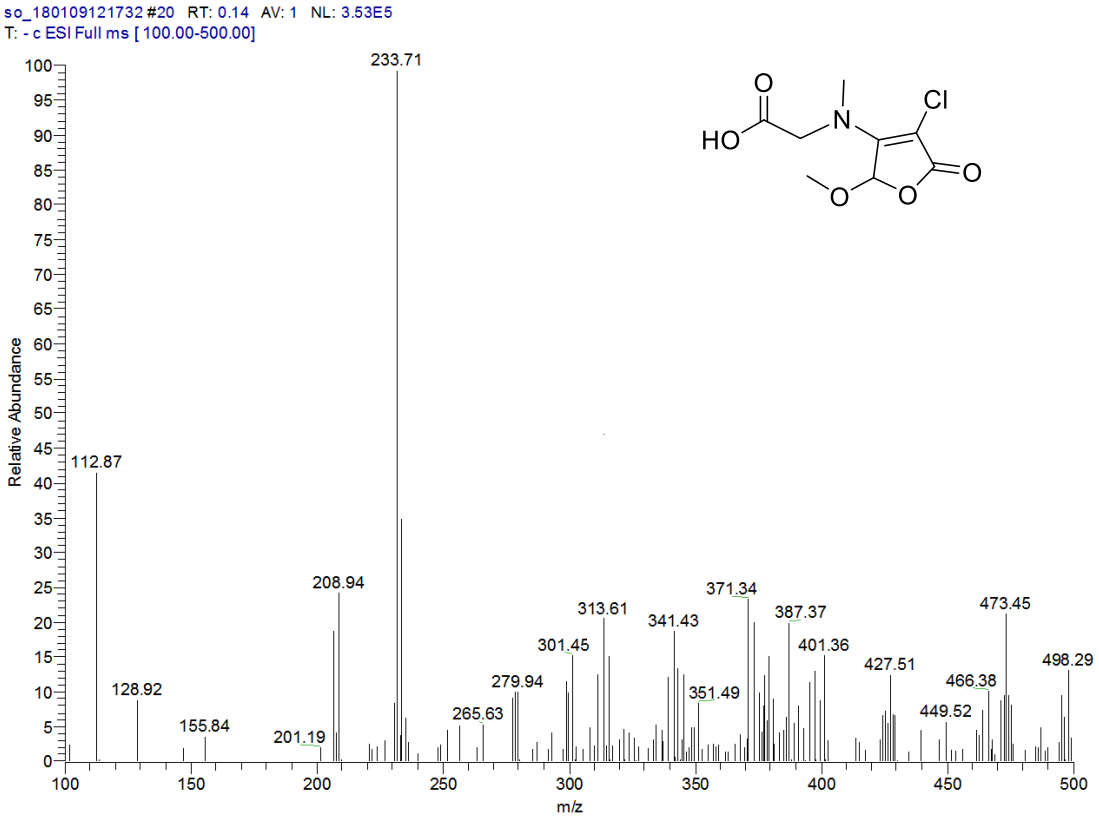


Figure 9. ESI-MS spectrum of compound N3

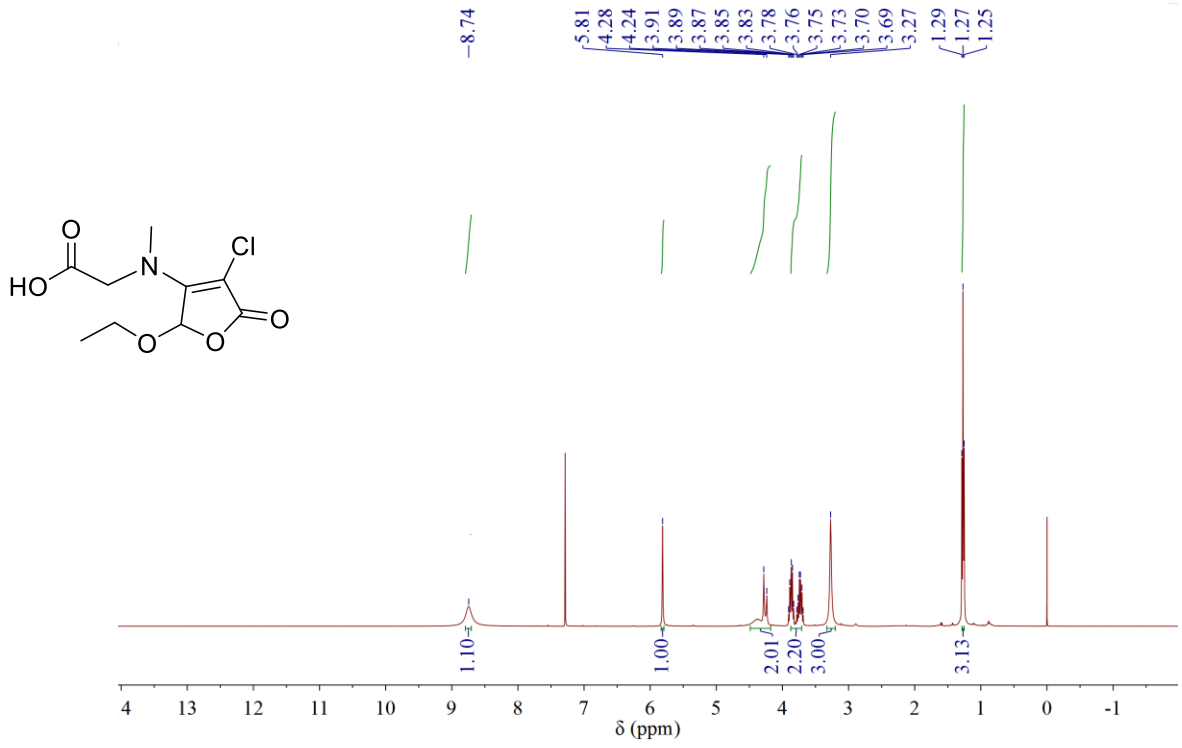


Figure 10. ^{1}H NMR spectrum of compound N4

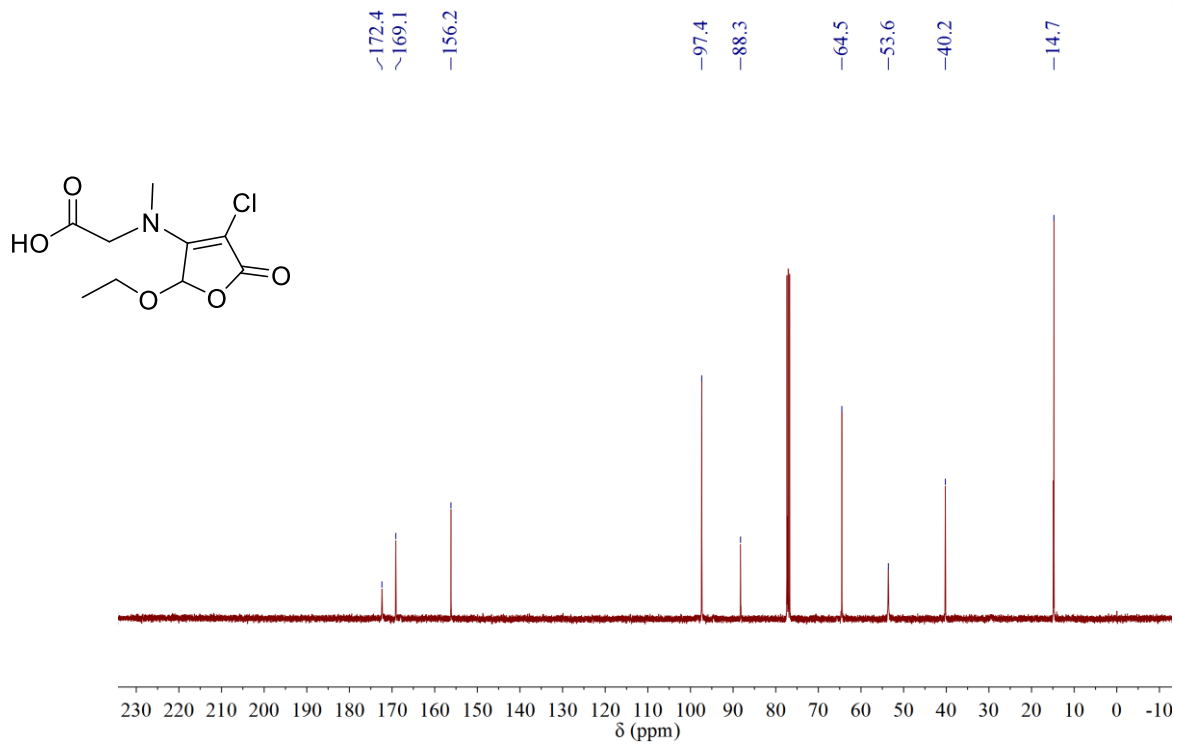


Figure 11. ^{13}**C NMR spectrum of compound N4**

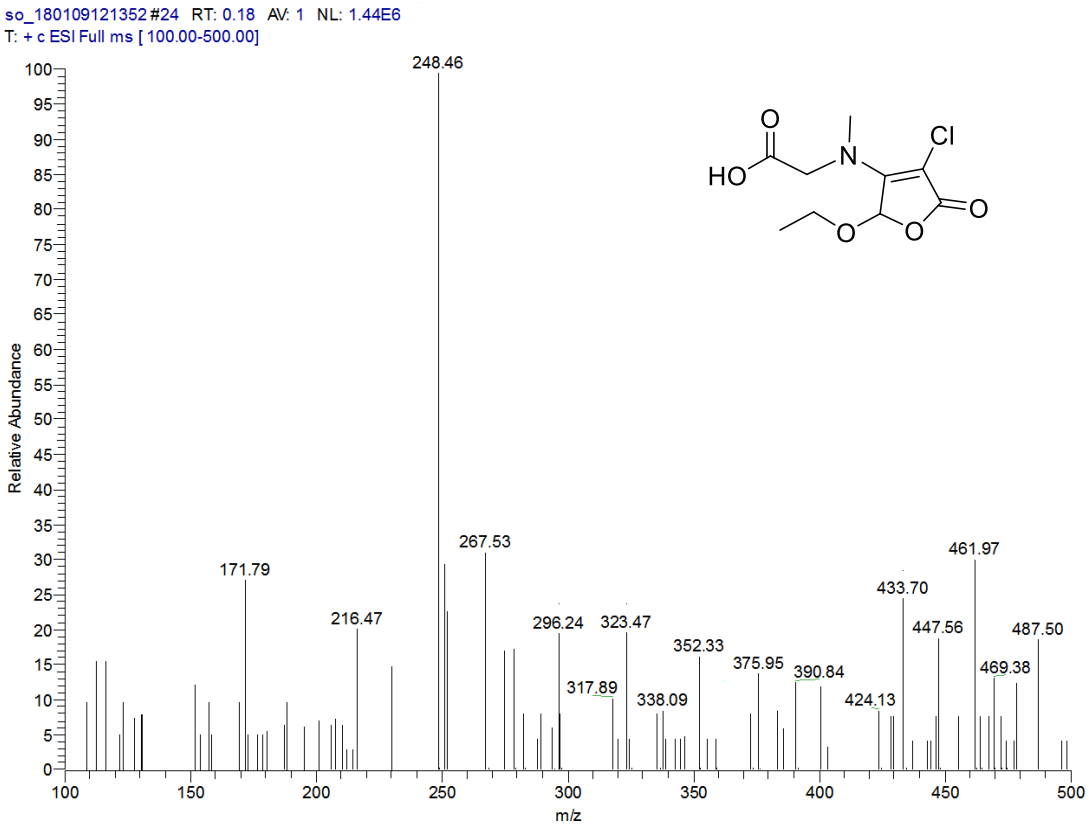


Figure 12. ESI-MS spectrum of compound N4

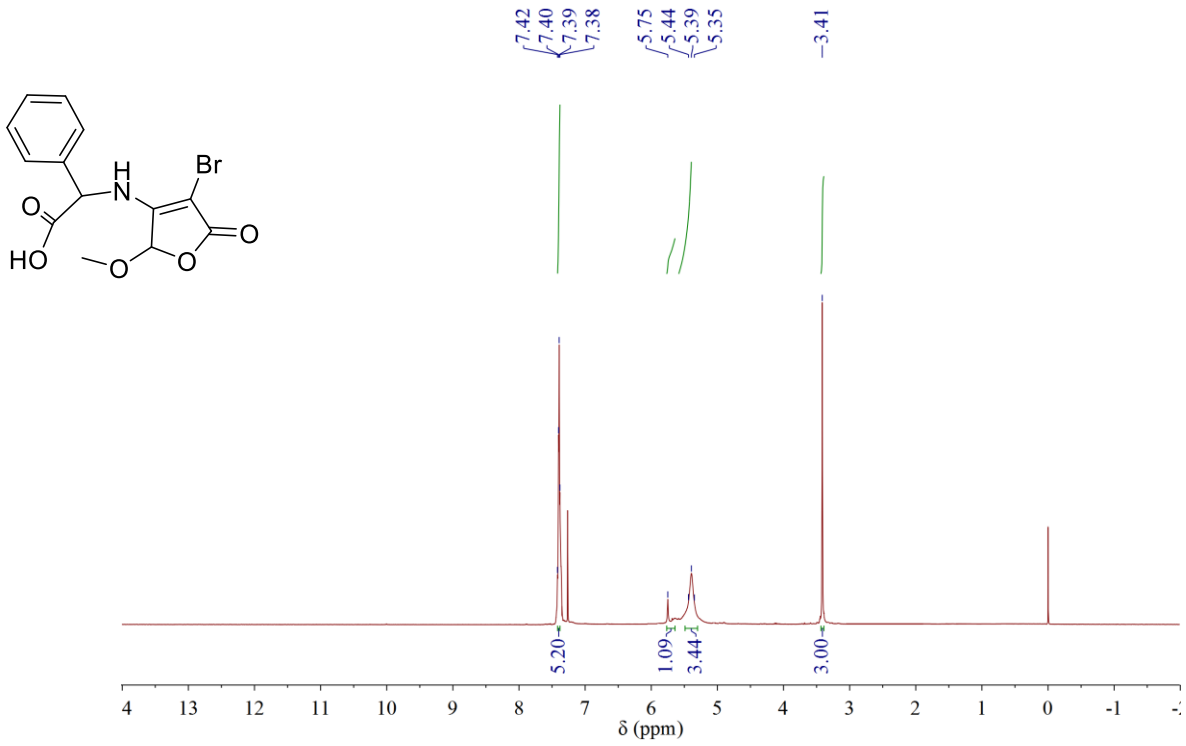


Figure 13. ^{1}H NMR spectrum of compound N5

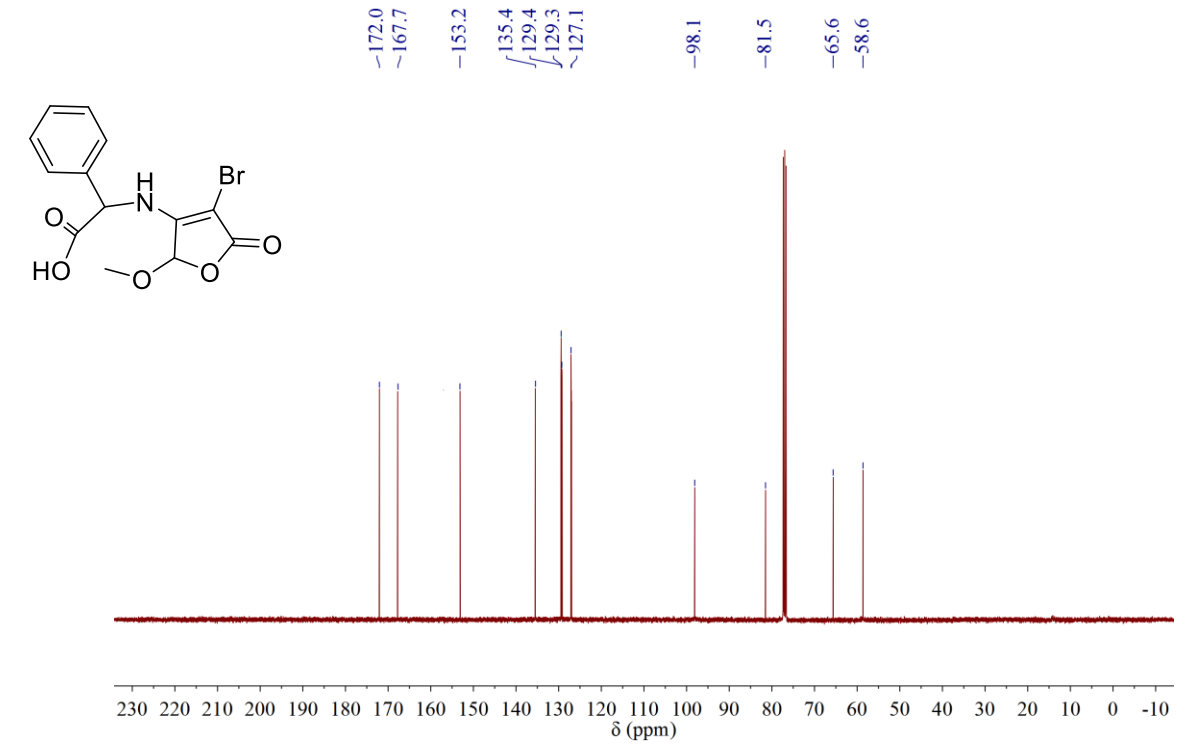
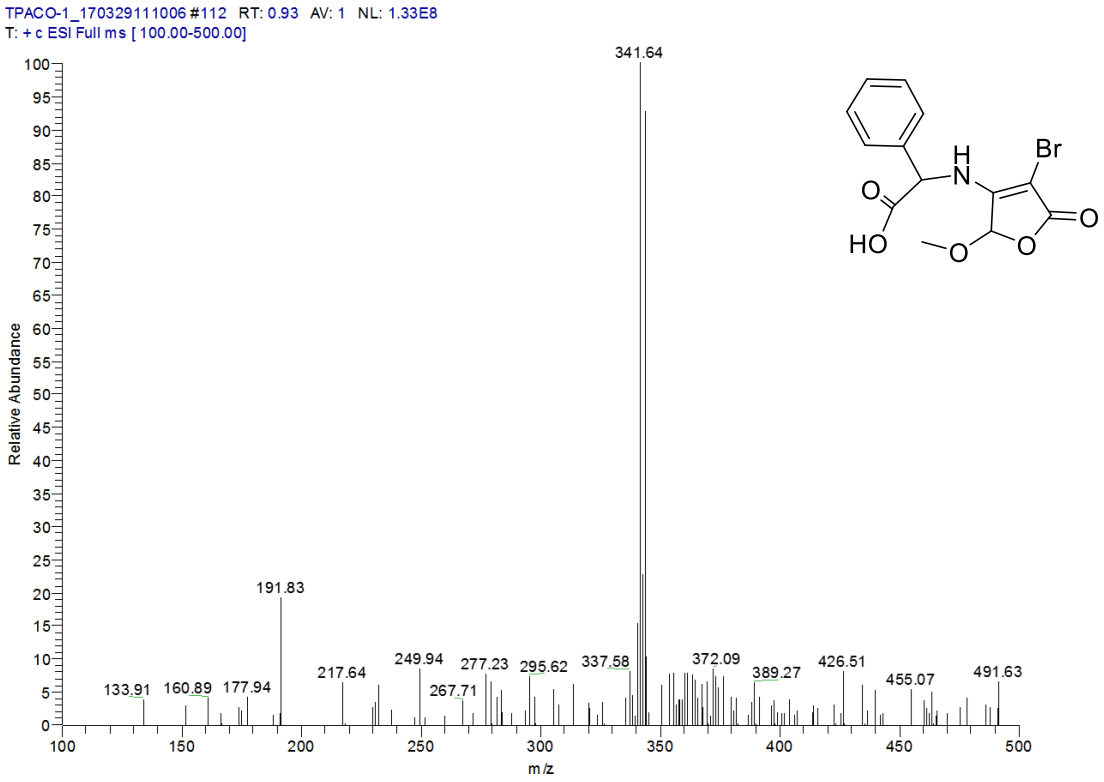


Figure 14. ^{13}C NMR spectrum of compound N5



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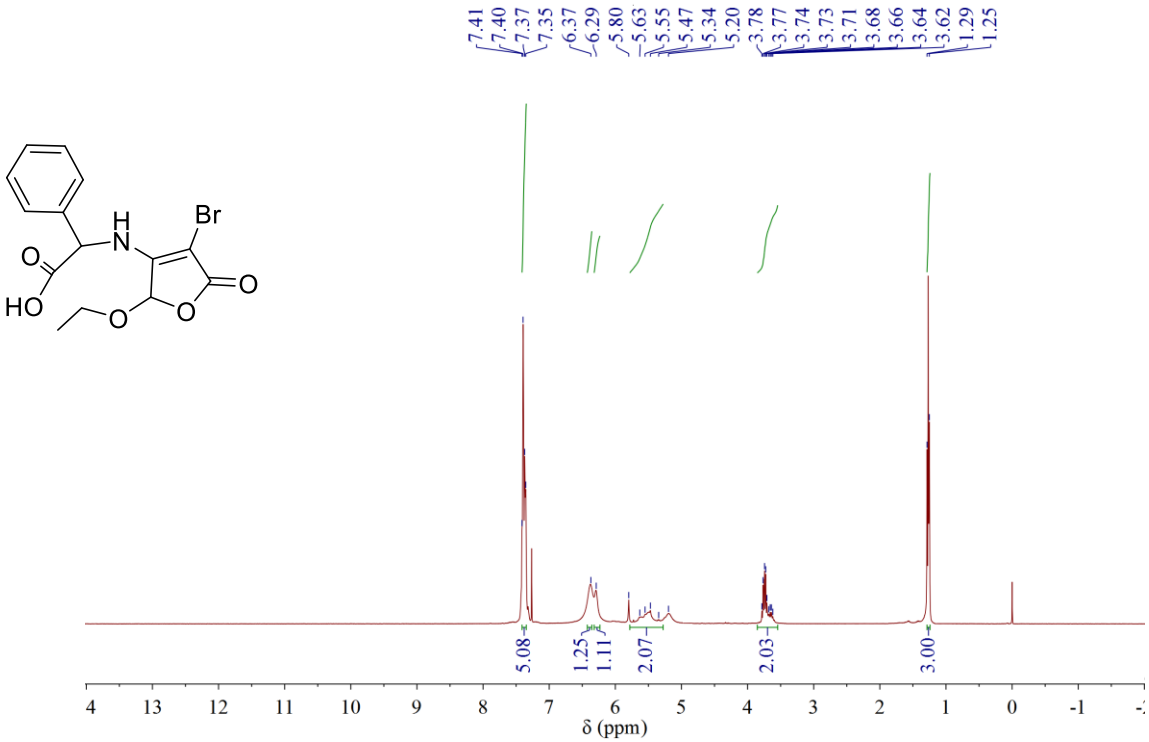


Figure 16. ^{1}H NMR spectrum of compound N6

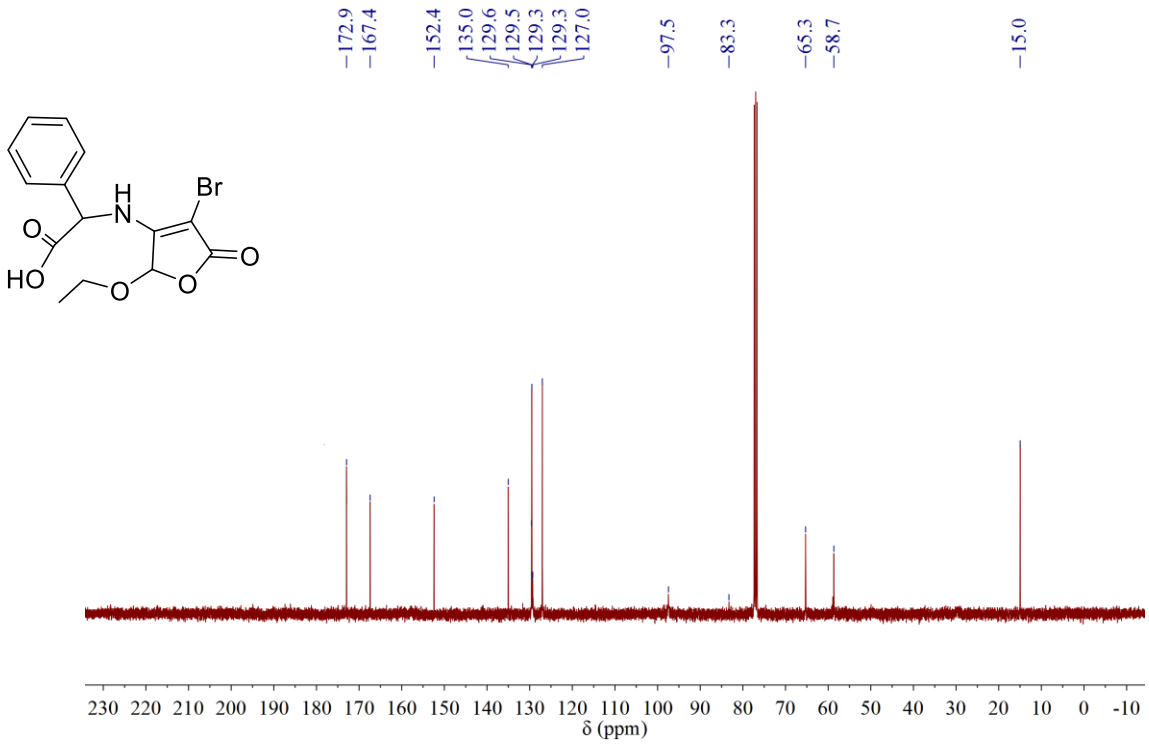


Figure 17. ^{13}C NMR spectrum of compound N6

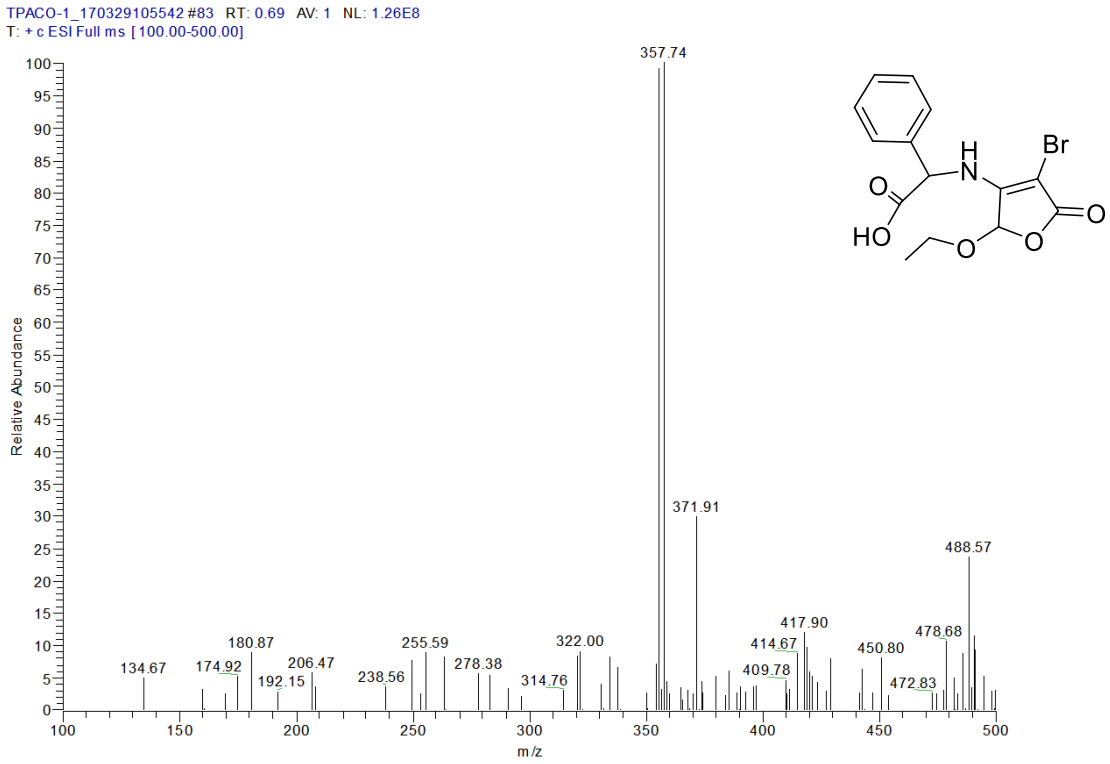


Figure 18. ESI-MS spectrum of compound N6

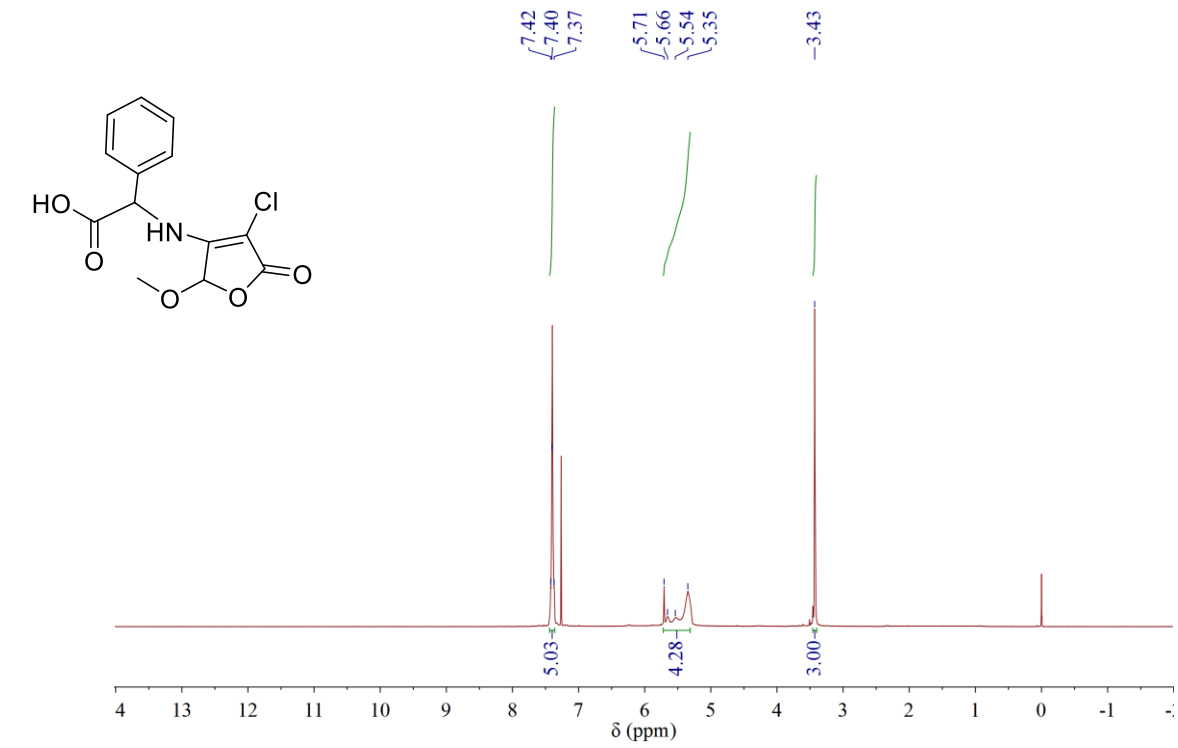


Figure 19. ^{1}H NMR spectrum of compound N7

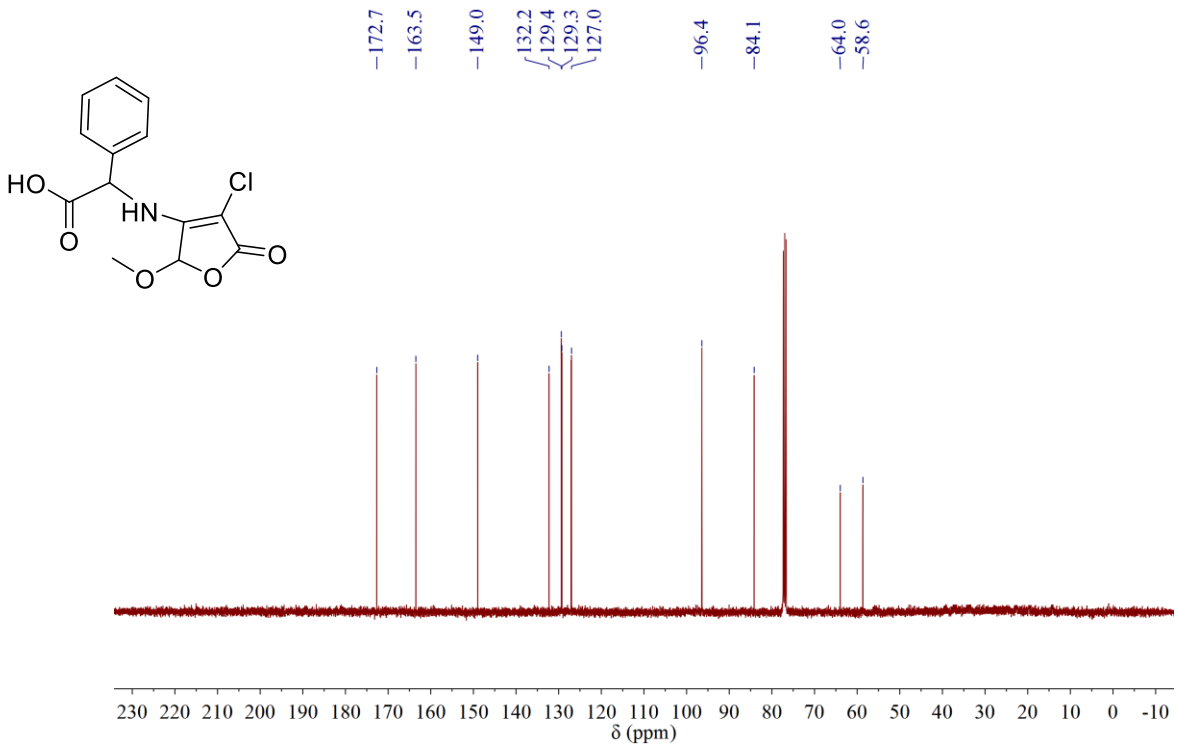
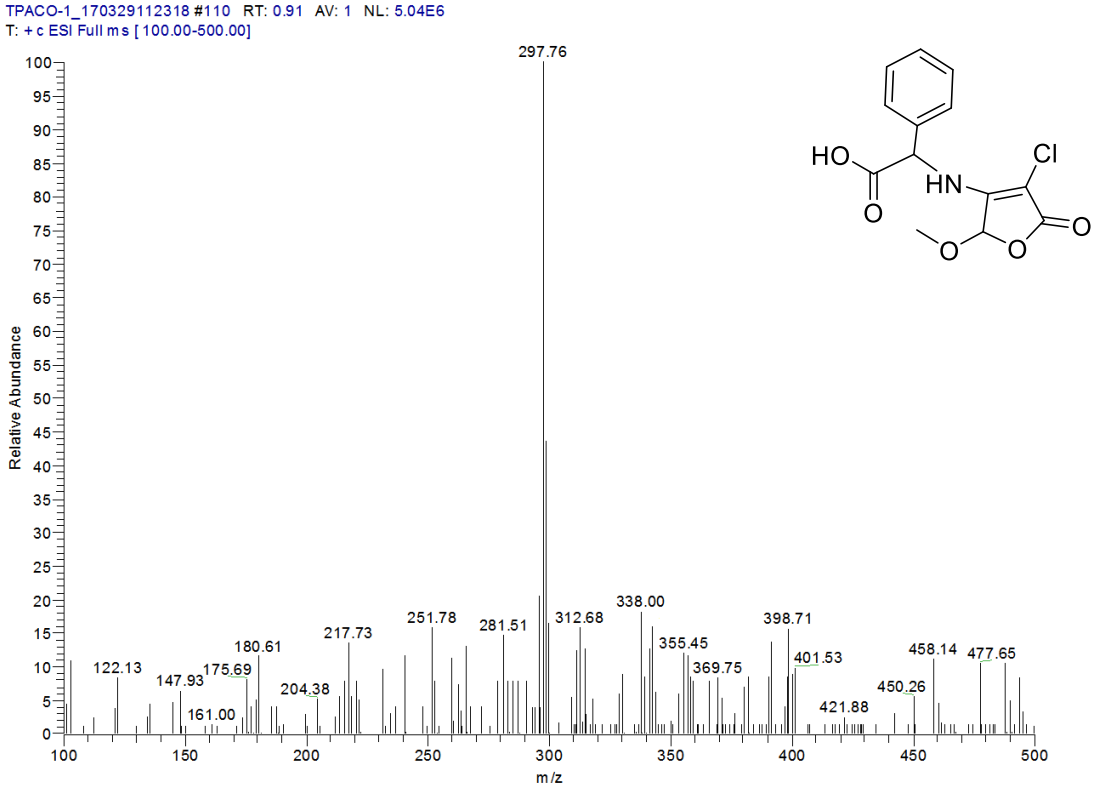


Figure 20. ^{13}C NMR spectrum of compound N7



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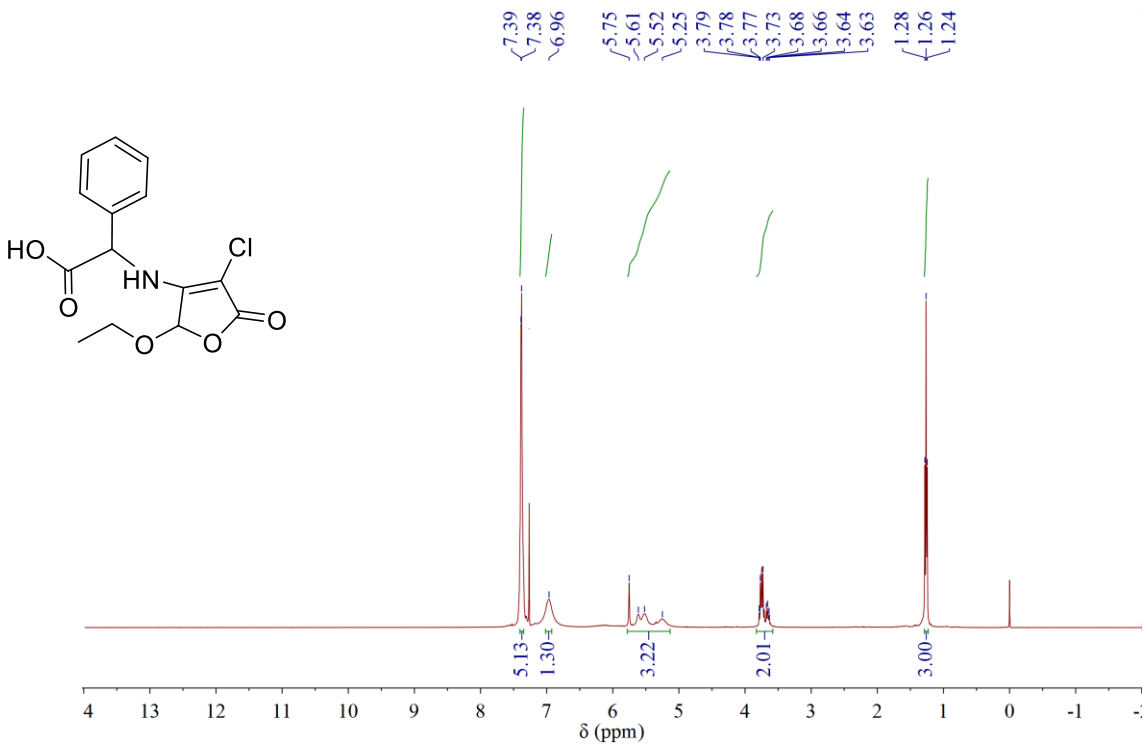

Figure 22. ^{1}H NMR spectrum of compound N8

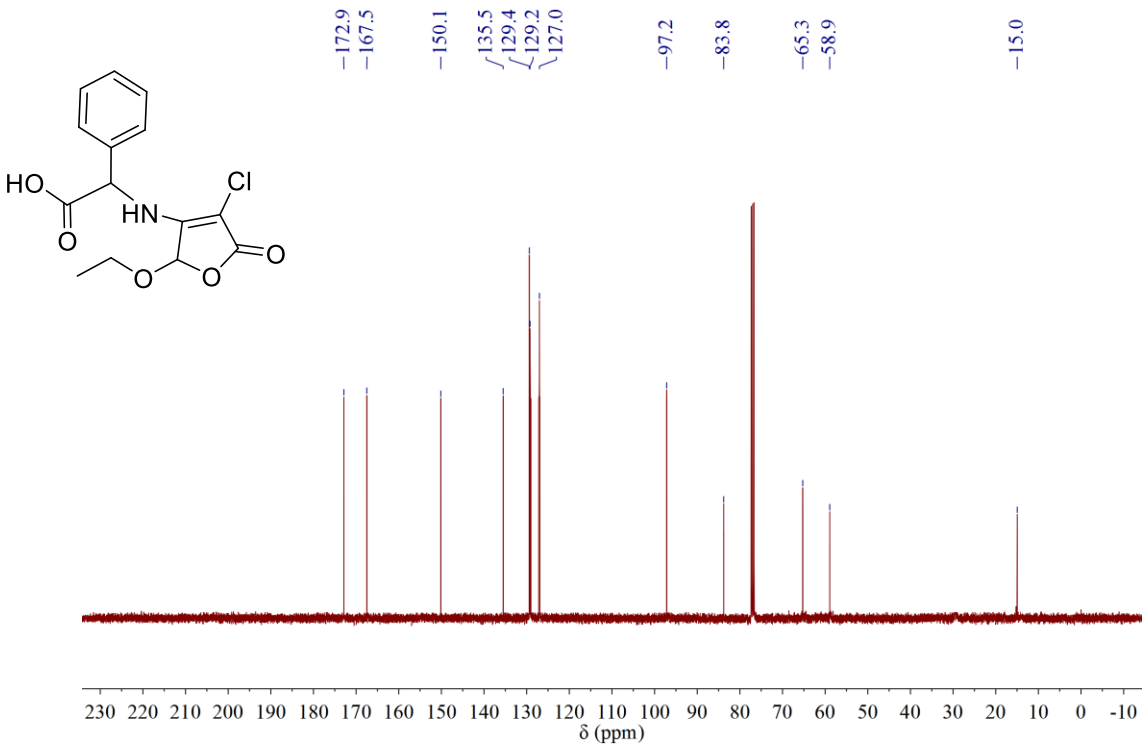

Figure 23. ^{13}C NMR spectrum of compound N8

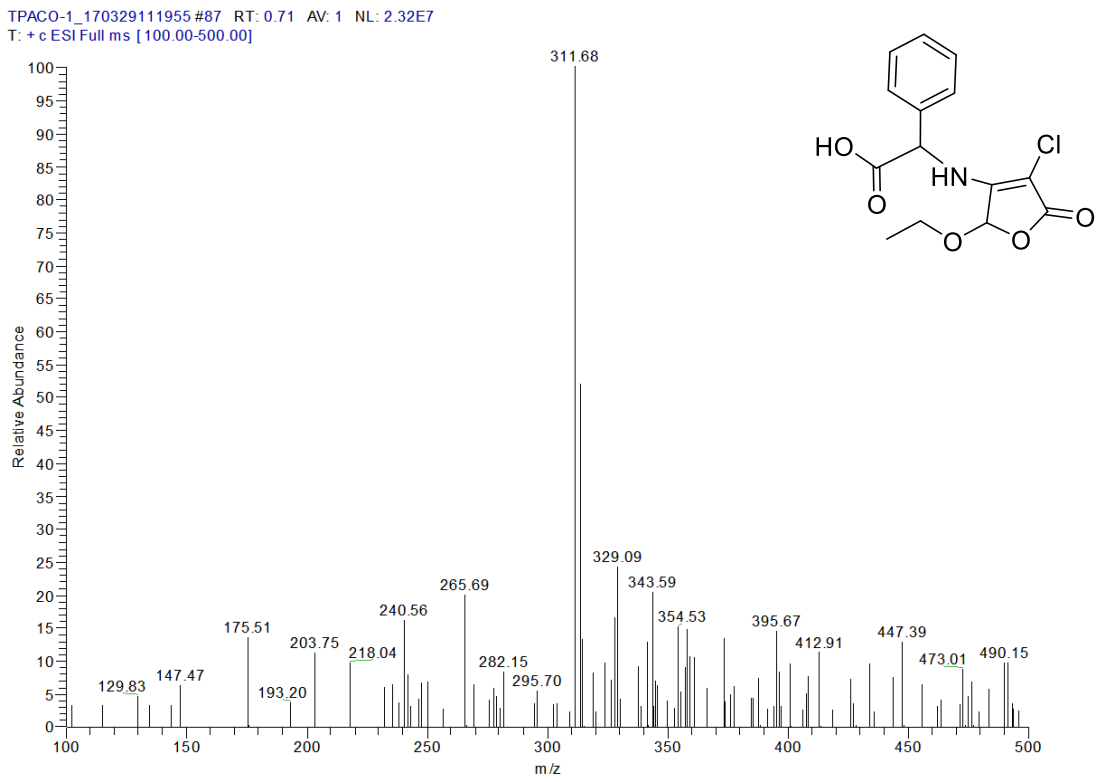

Figure 24. ESI-MS spectrum of compound N8

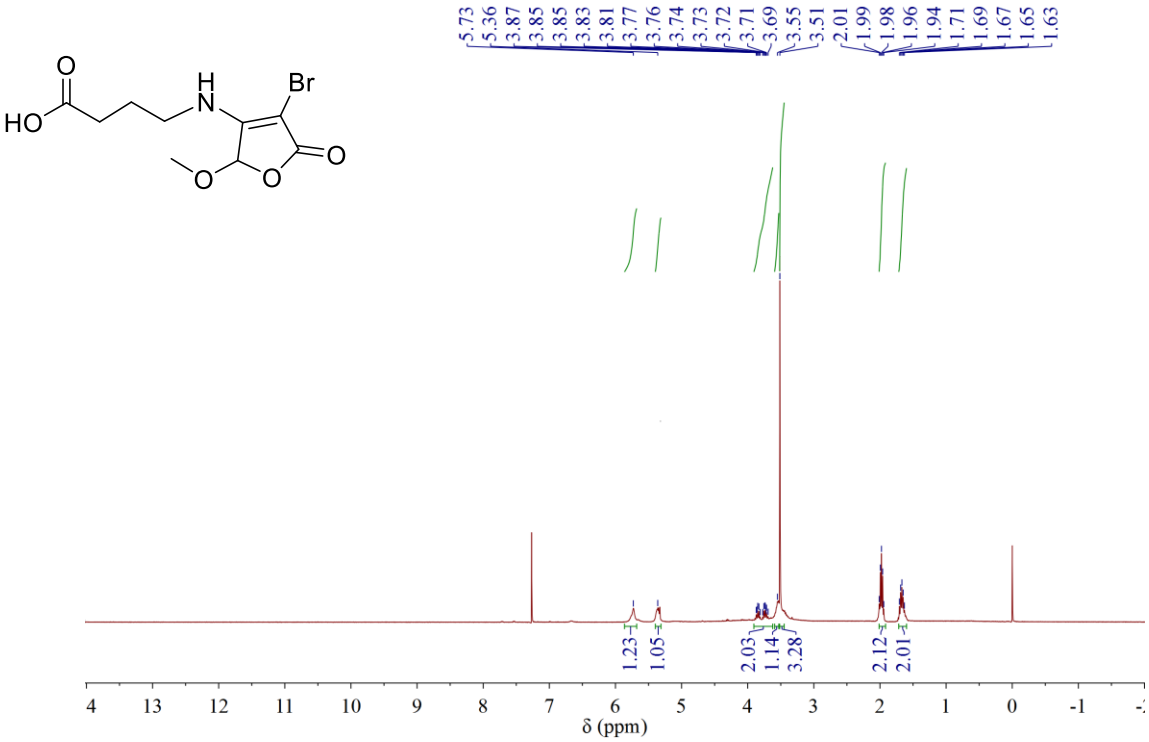

Figure 25. ^{1}H NMR spectrum of compound N9

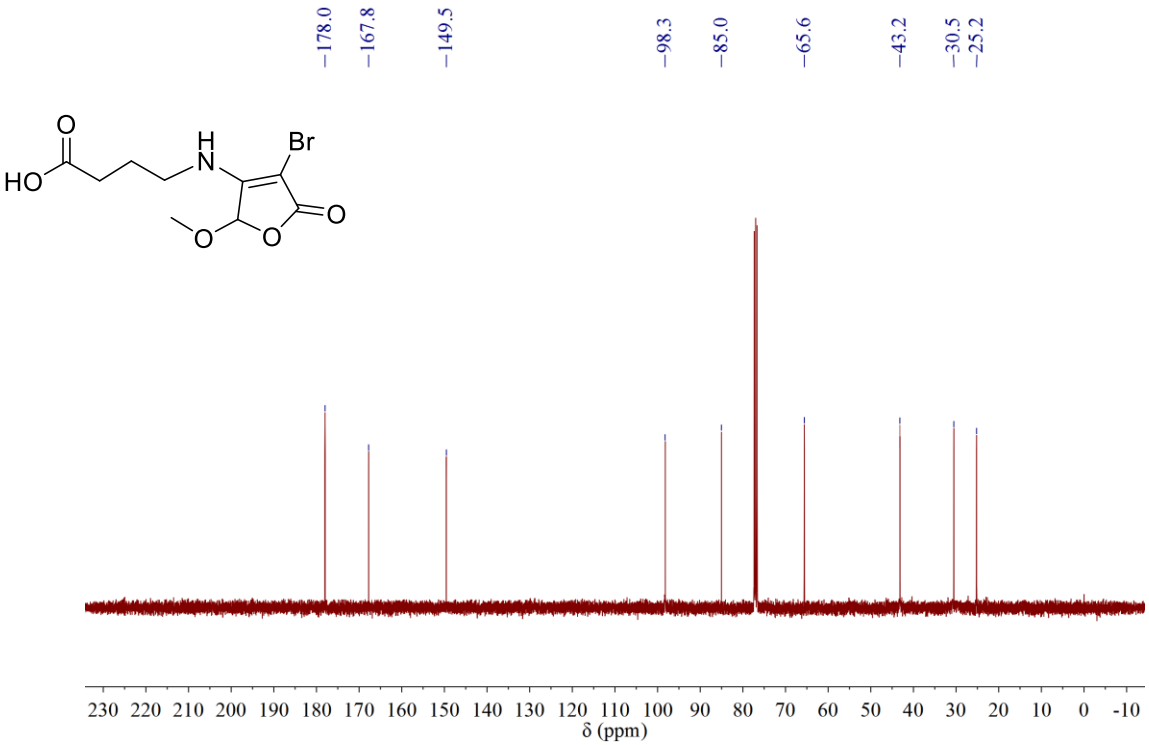

Figure 26. ^{13}C NMR spectrum of compound N9

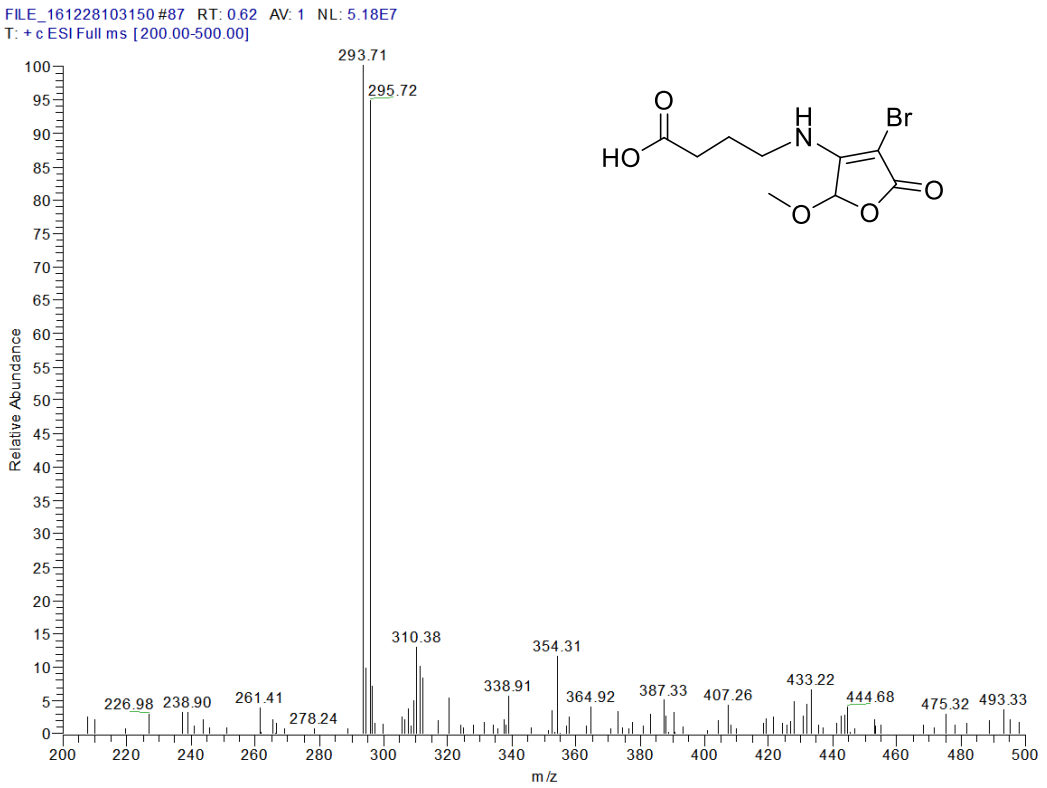

Figure 27. ESI-MS spectrum of compound N9

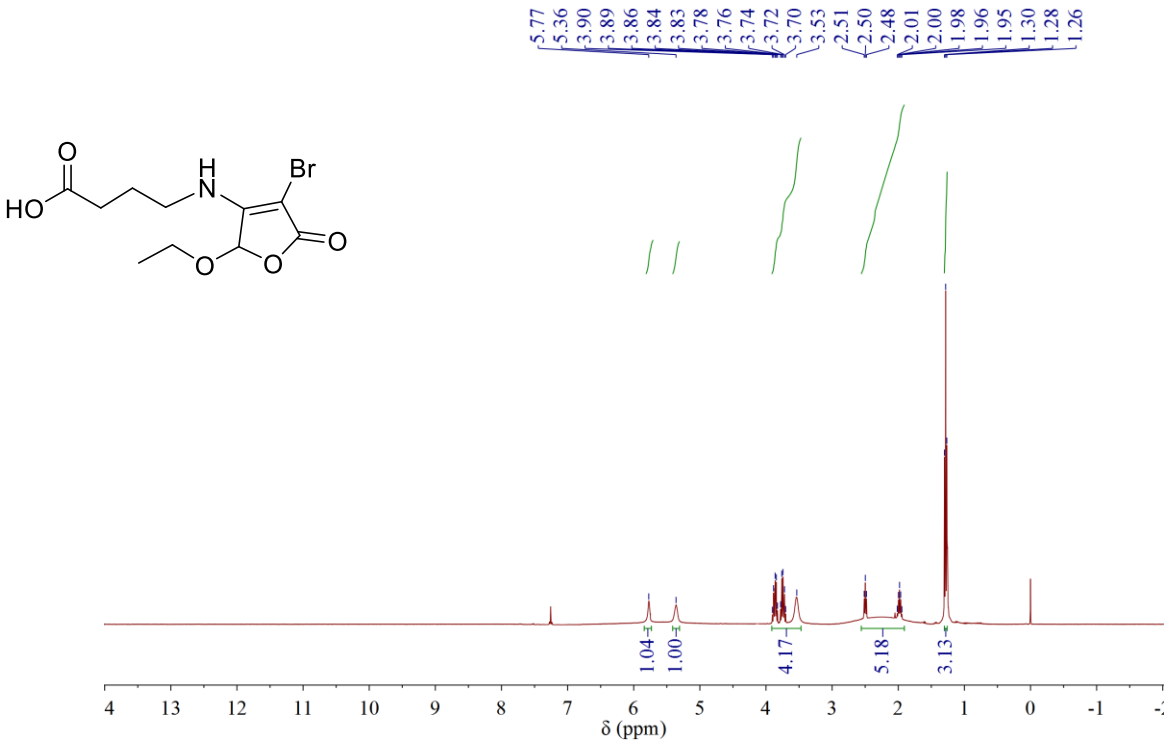

Figure 28. ^{1}H NMR spectrum of compound N10

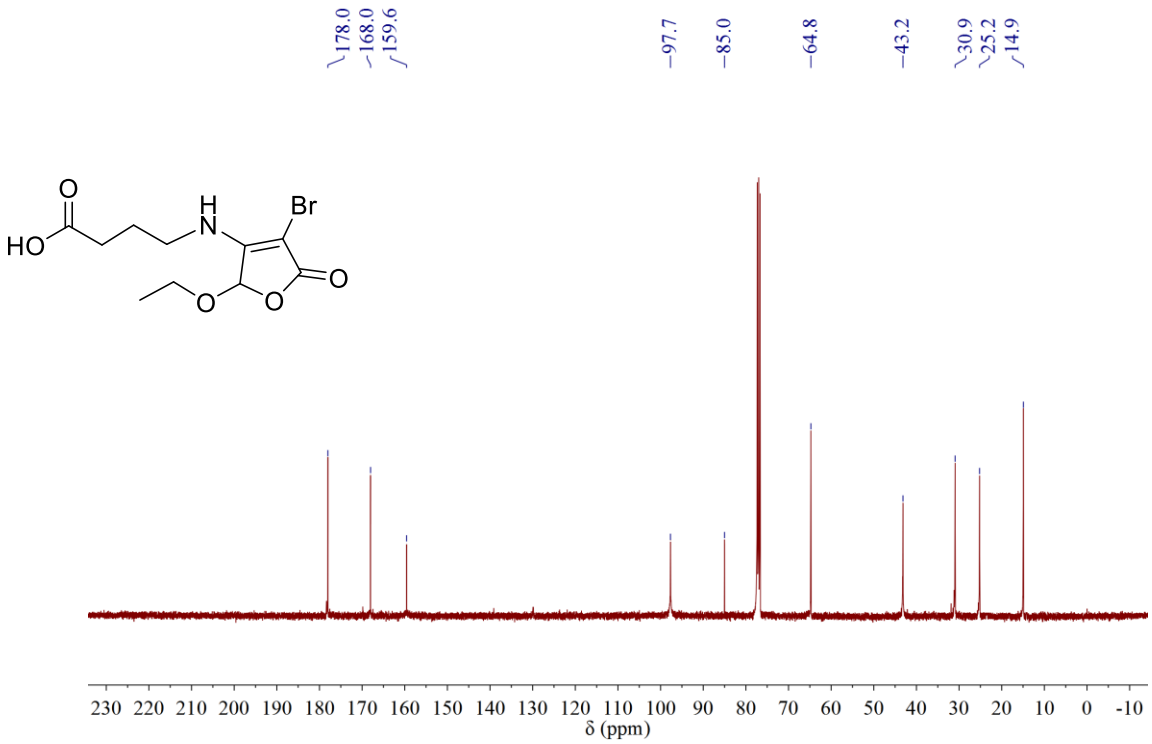

Figure 29. ^{13}C NMR spectrum of compound N10

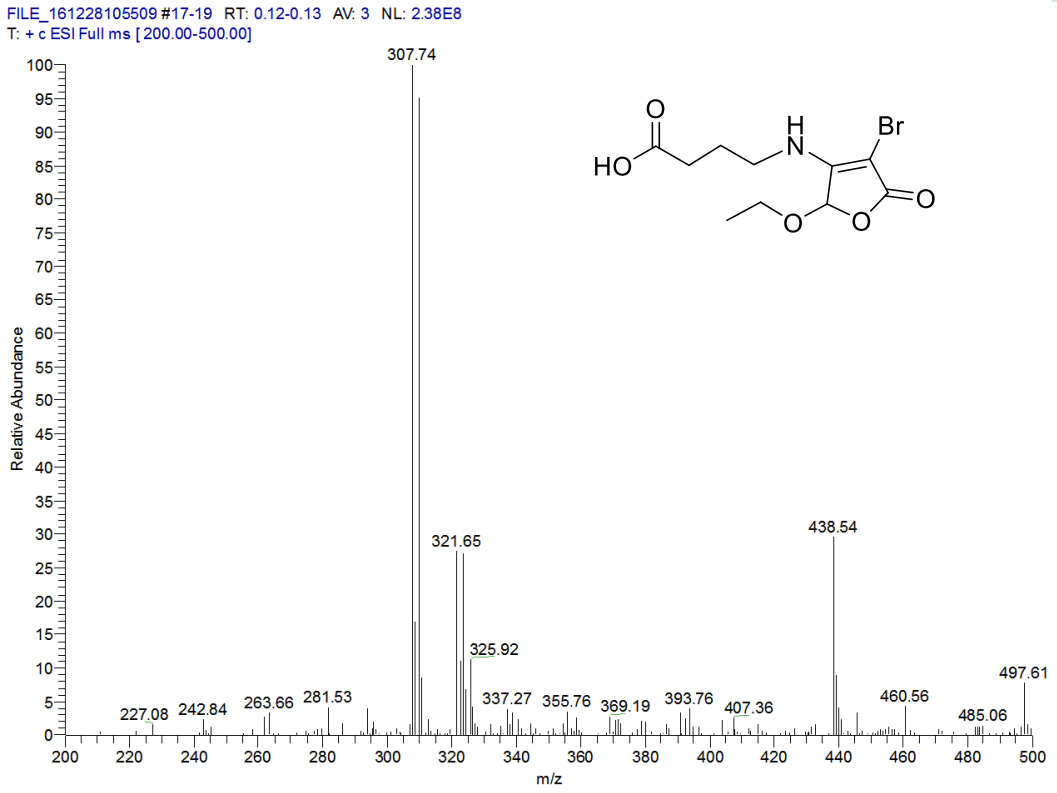

Figure 30. ESI-MS spectrum of compound N10

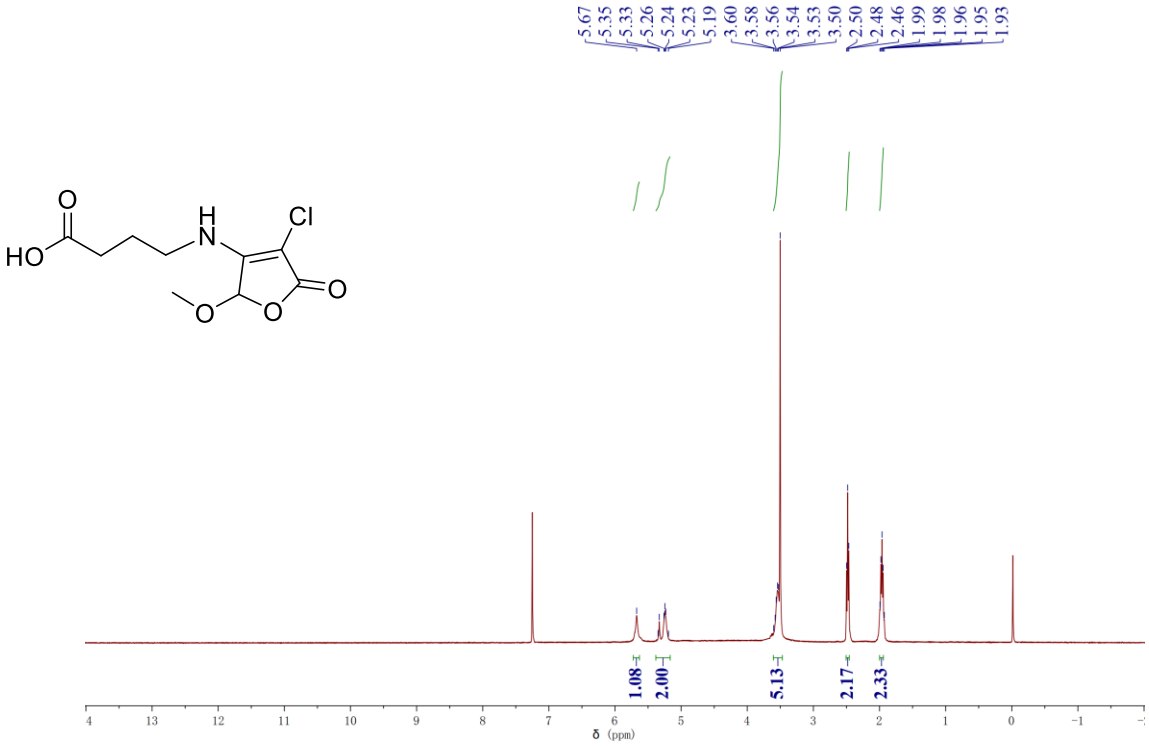

Figure 31. ^{1}H NMR spectrum of compound N11

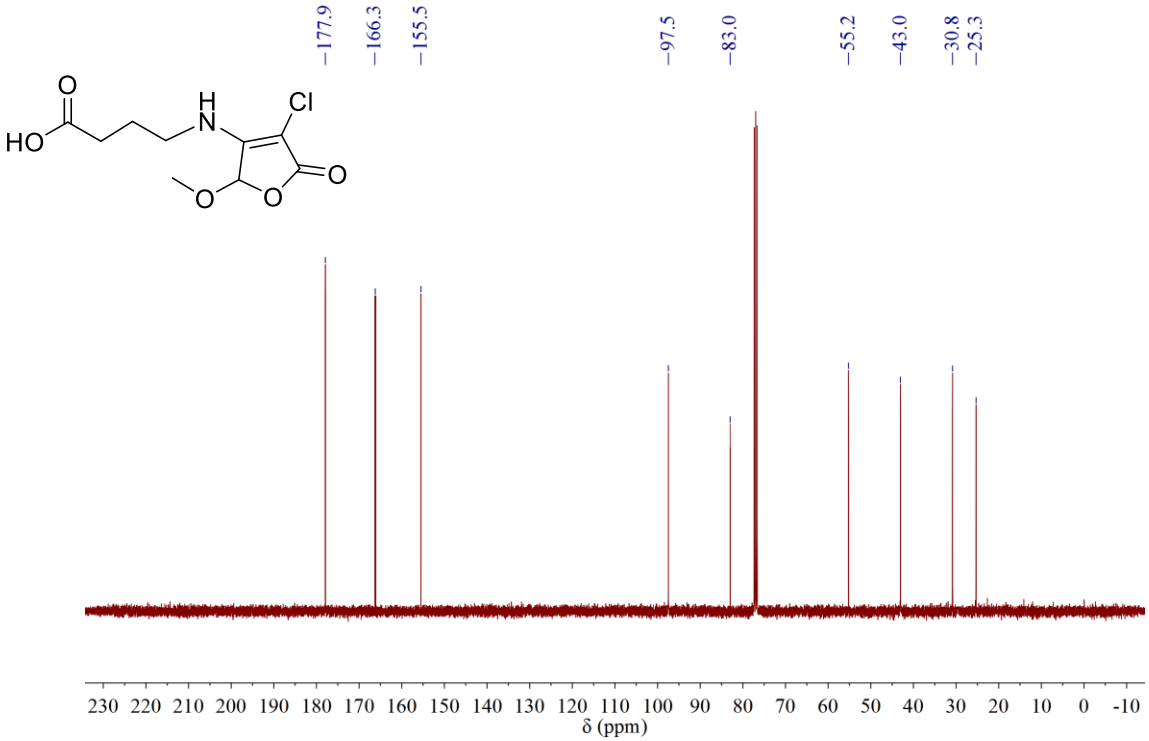

Figure 32. ^{13}C NMR spectrum of compound N11

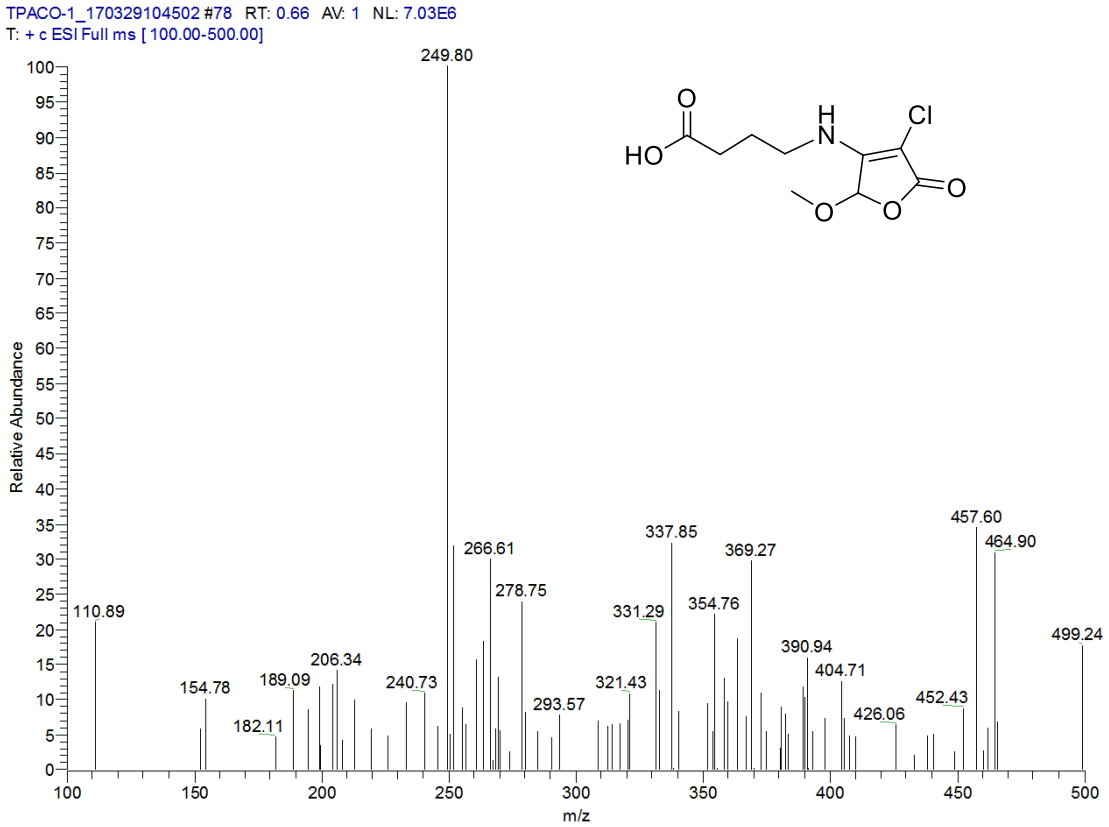

Figure 33. ESI-MS spectrum of compound N11

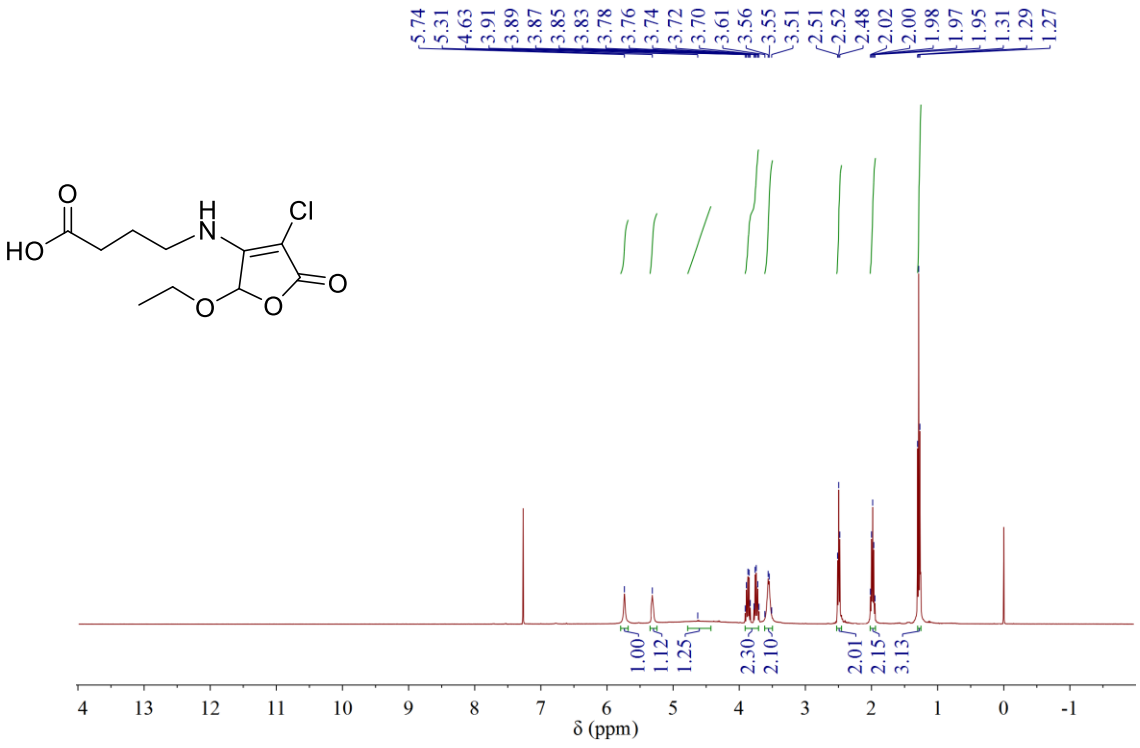

Figure 34. ^{1}H NMR spectrum of compound N12

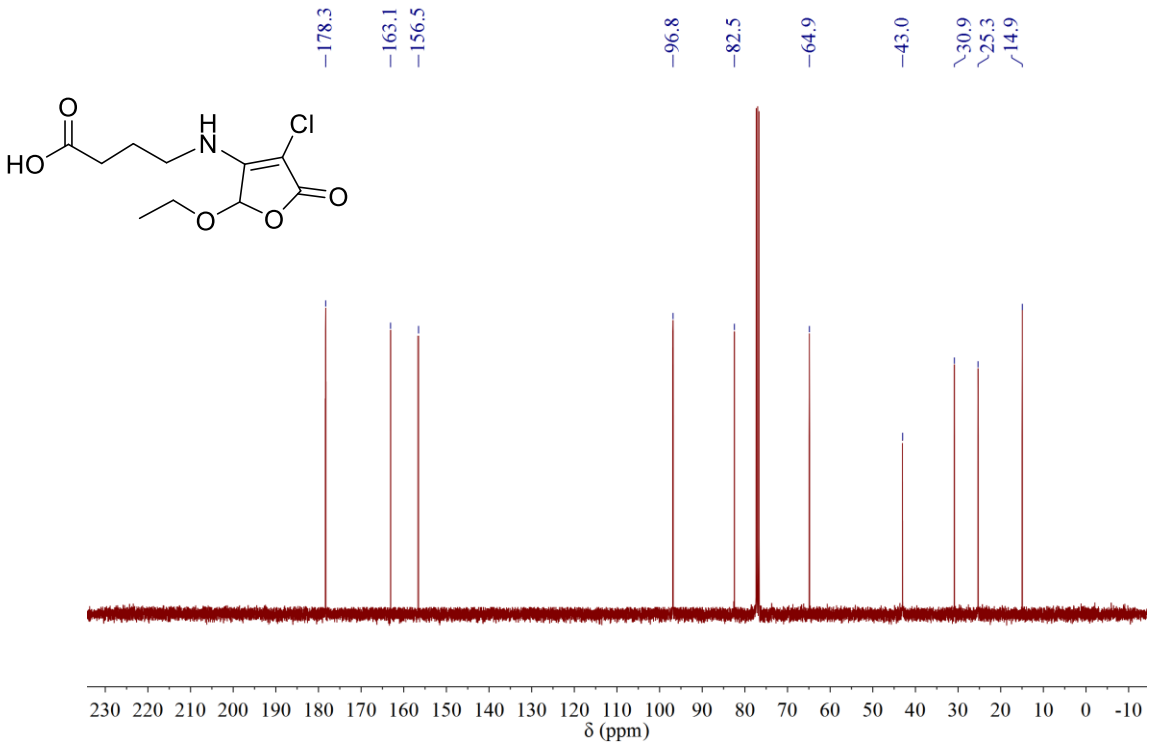

Figure 35. ^{13}C NMR spectrum of compound N12

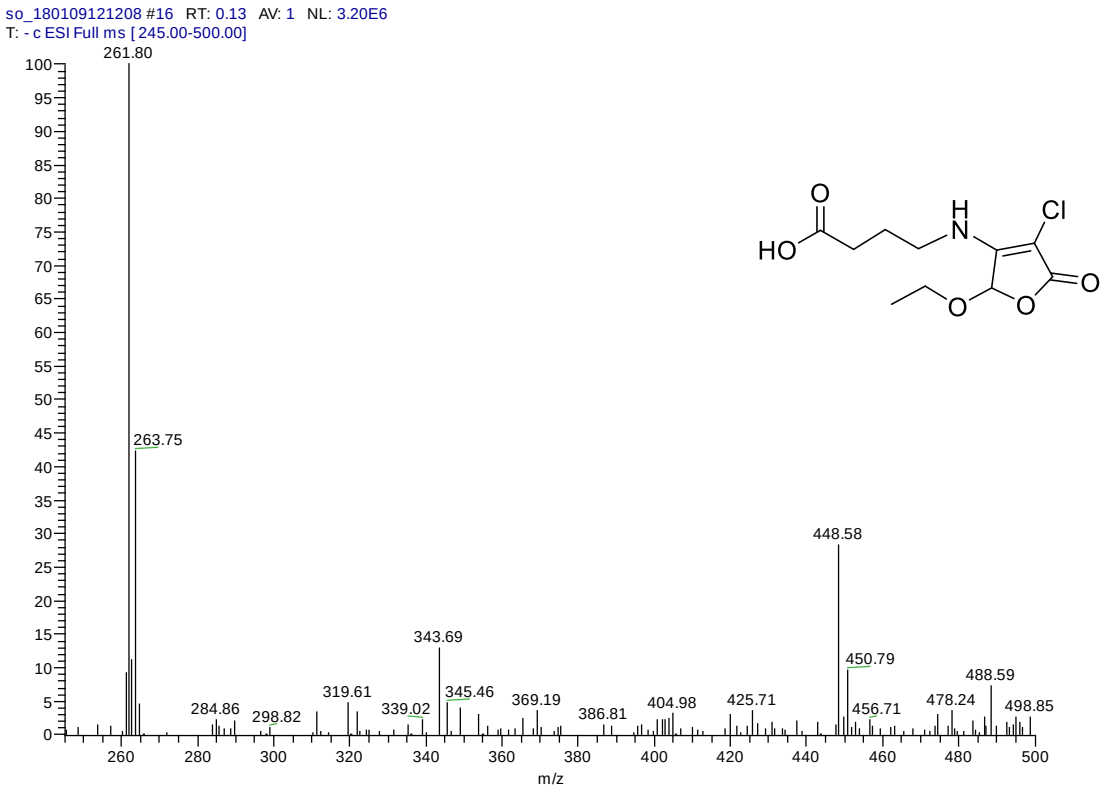

Figure 36. ESI-MS spectrum of compound N12

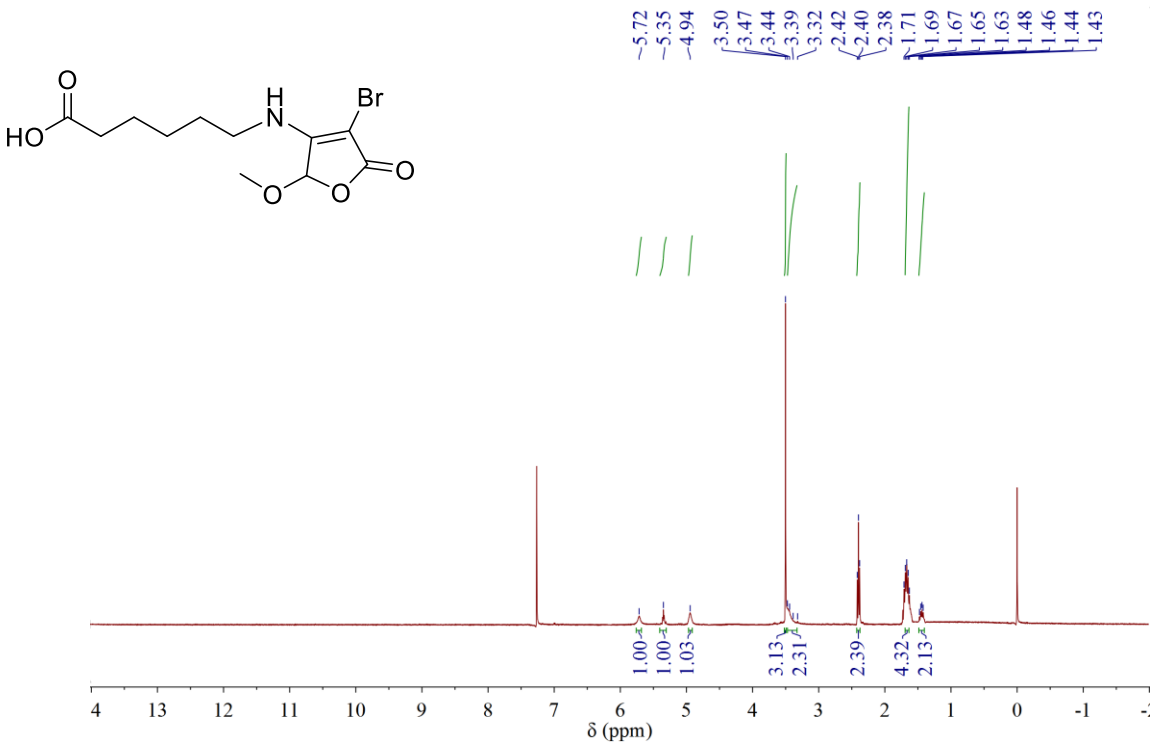

Figure 37. ^{1}H NMR spectrum of compound N13

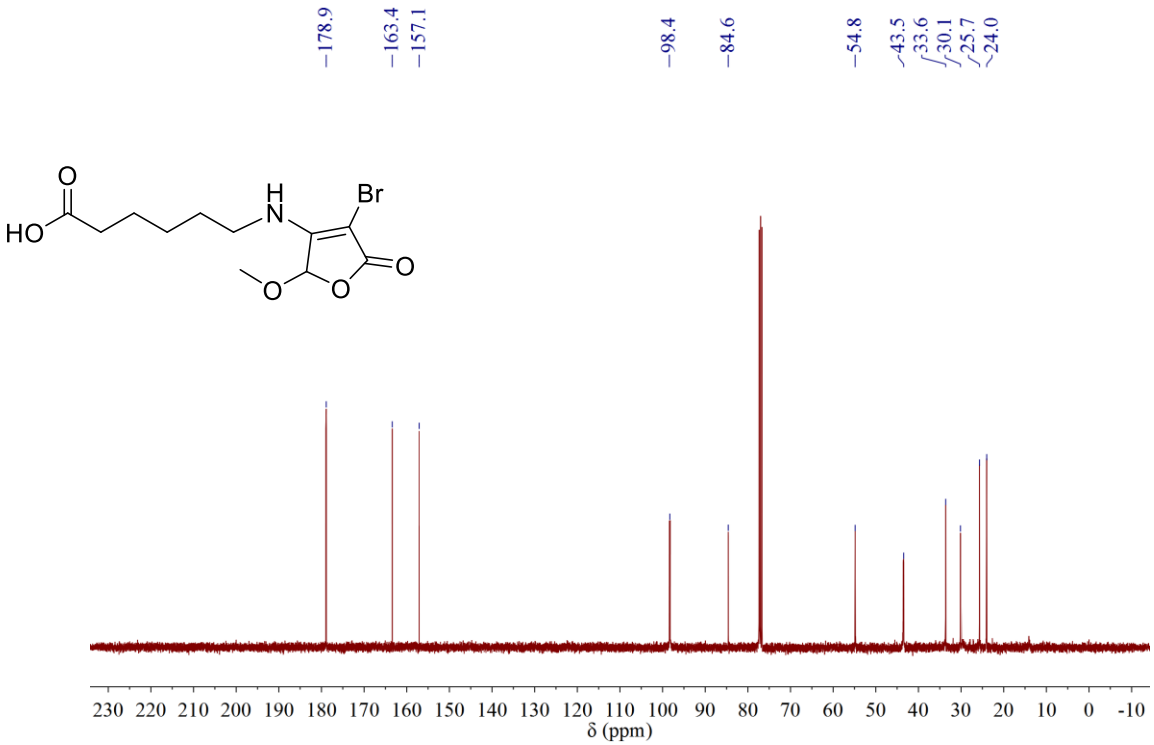

Figure 38. ^{13}C NMR spectrum of compound N13

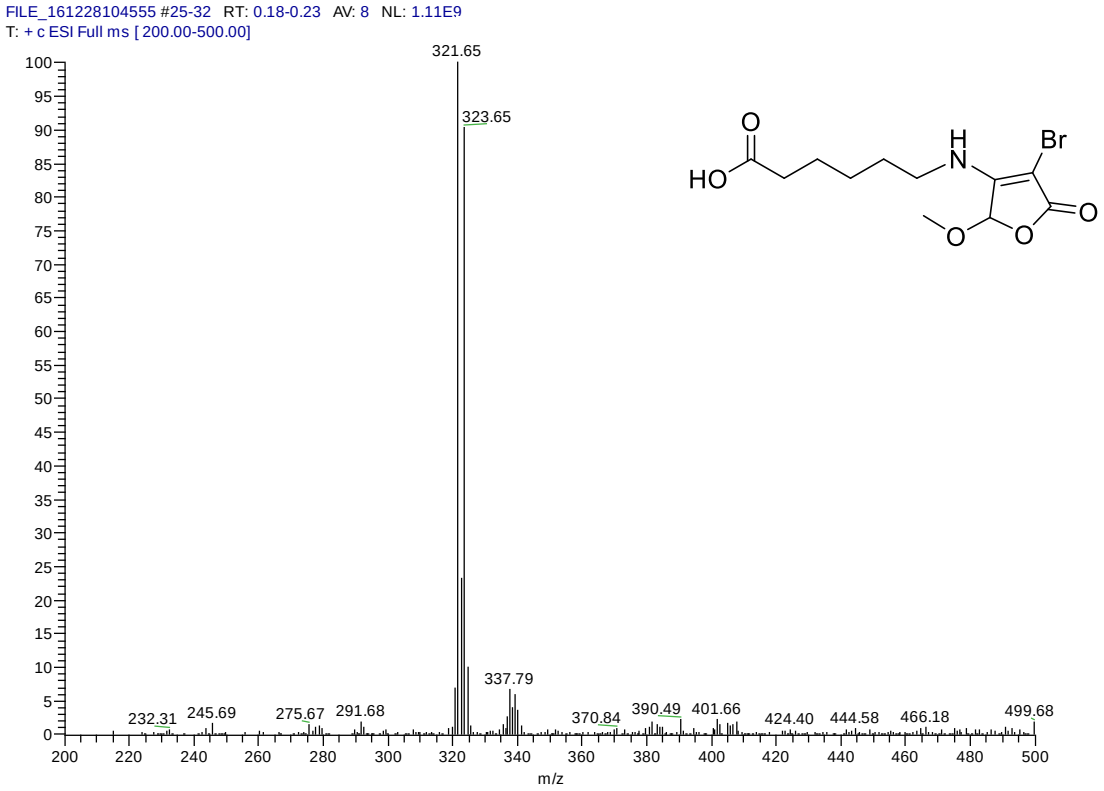

Figure 39. ESI-MS spectrum of compound N13

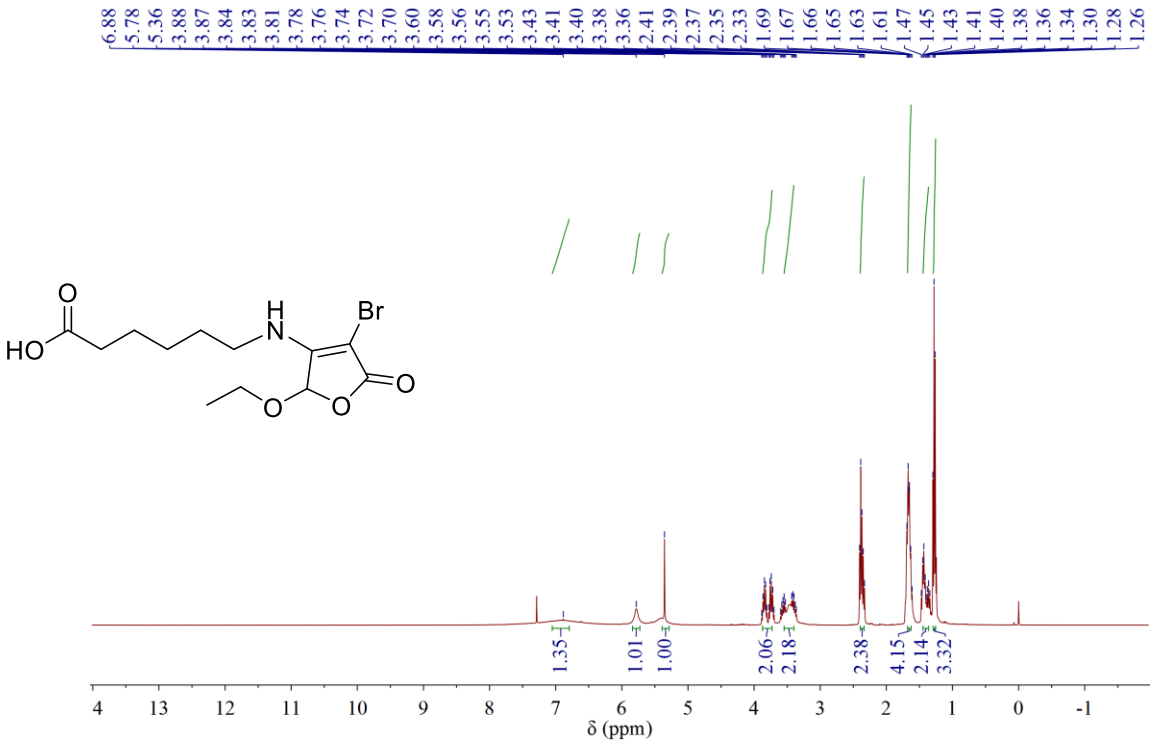

Figure 40. ^{1}H NMR spectrum of compound N14

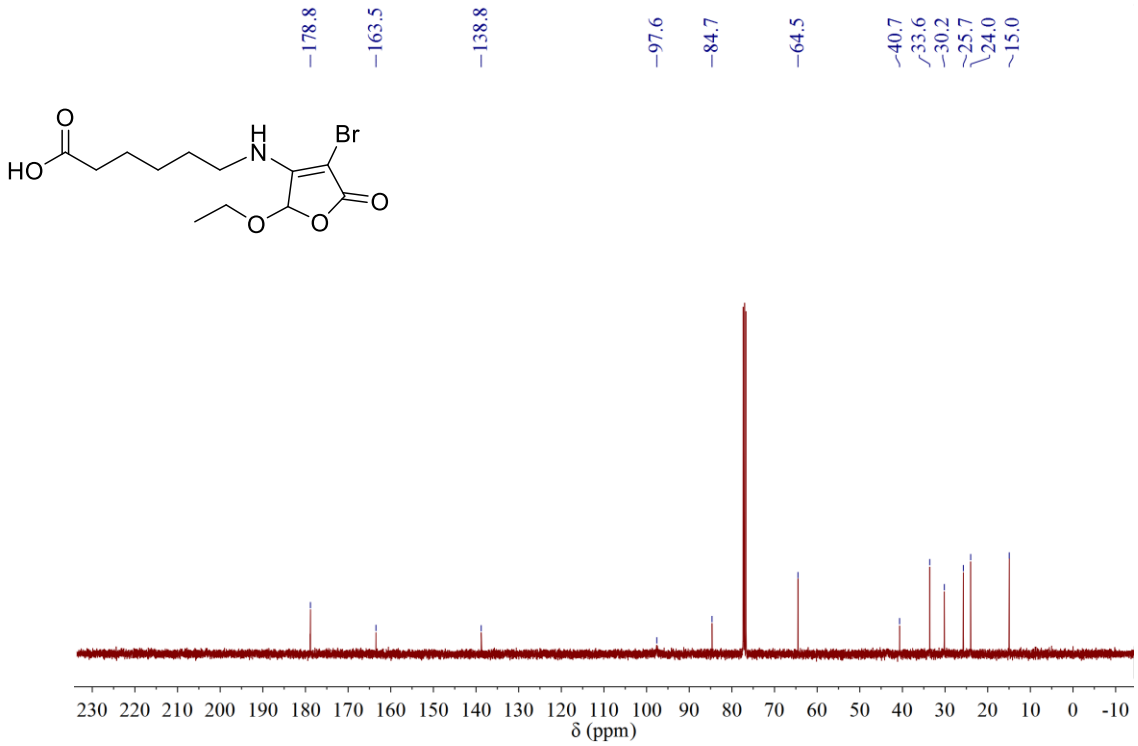

Figure 41. ^{13}C NMR spectrum of compound N14

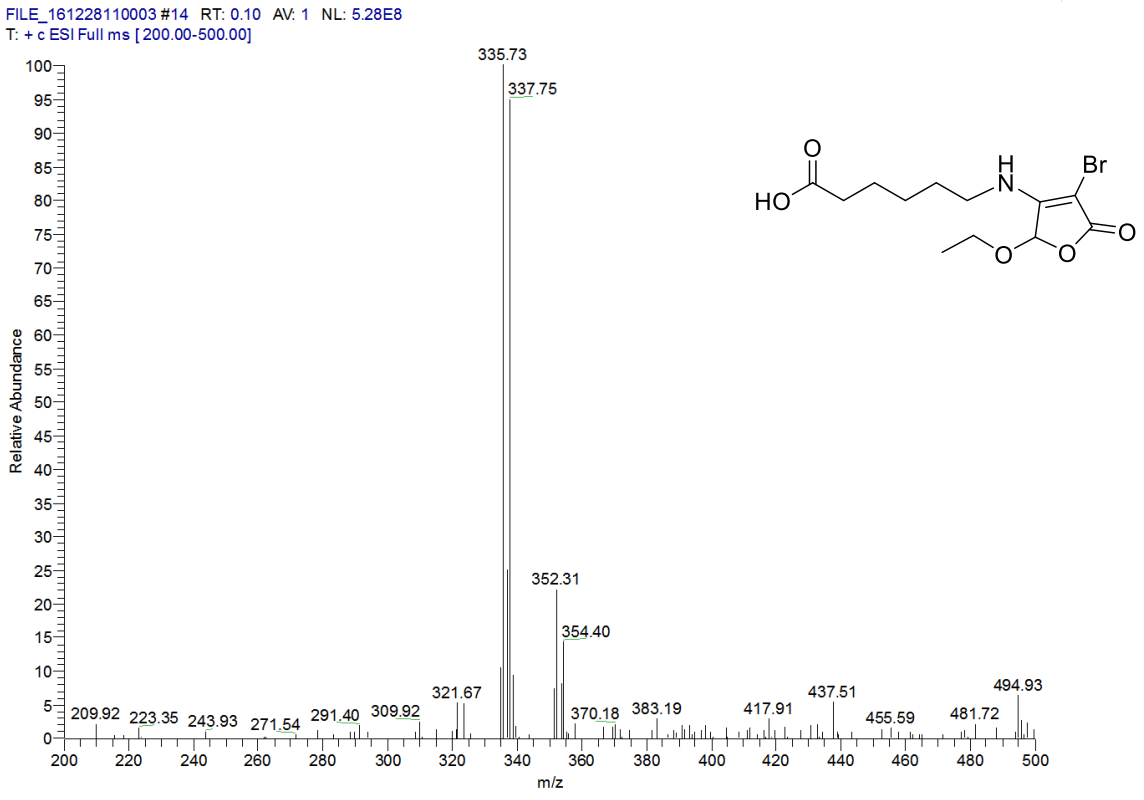

Figure 42. **ESI-MS spectrum of compound N14**

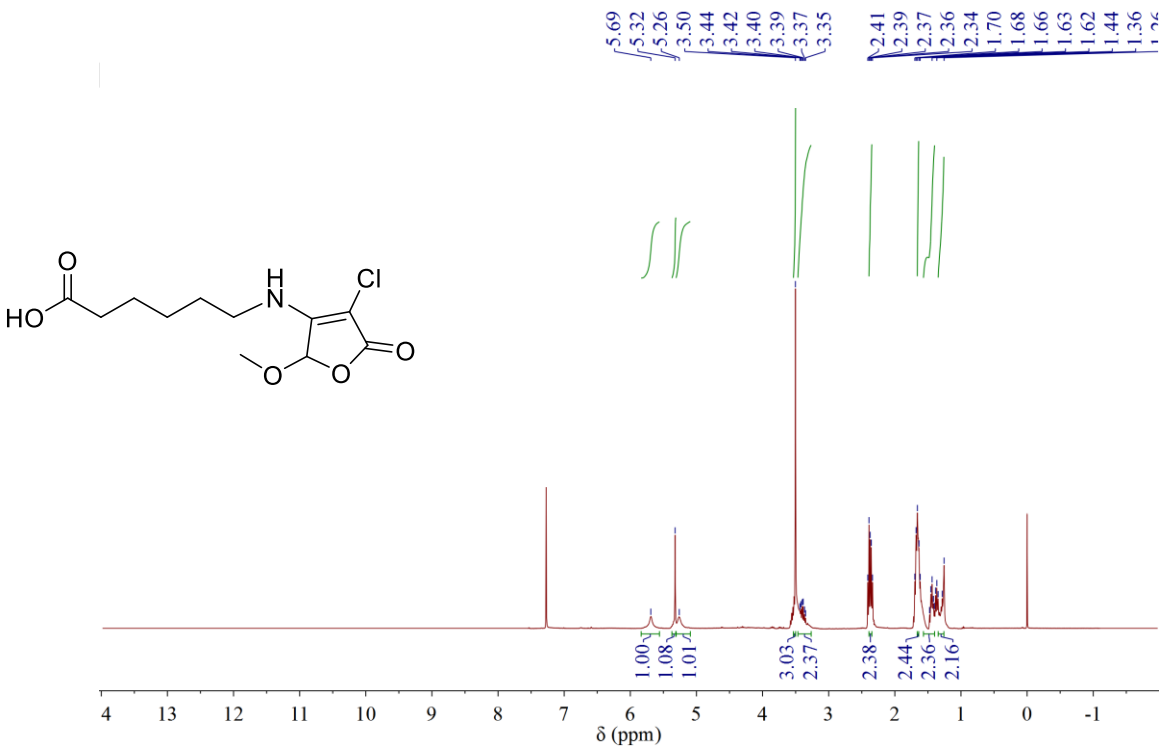

Figure 43. ^{1}H NMR spectrum of compound N15

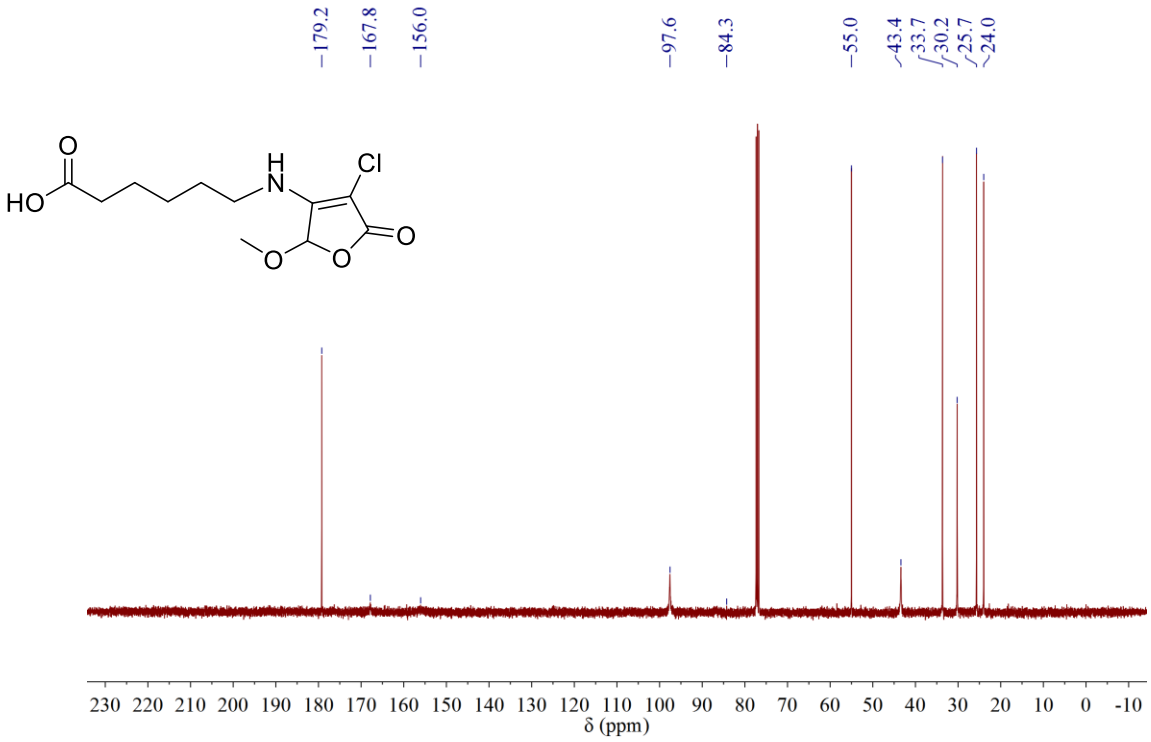

Figure 44. ^{13}C NMR spectrum of compound N15

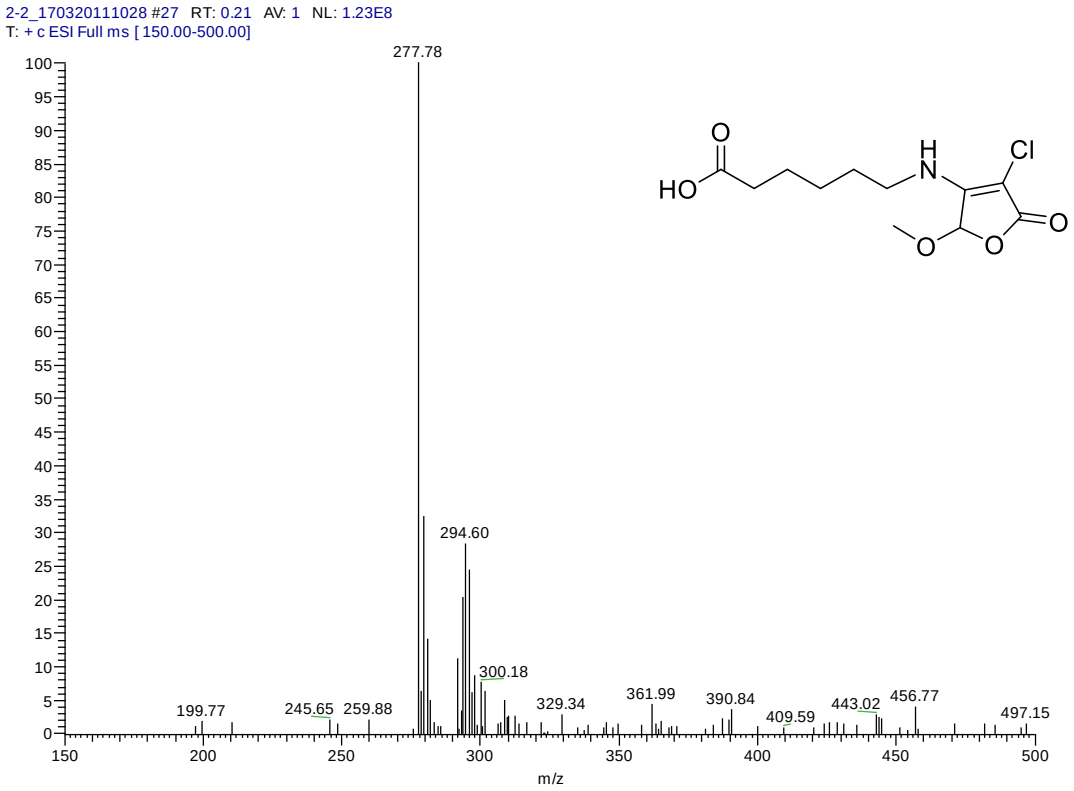

Figure 45. ESI-MS spectrum of compound N15

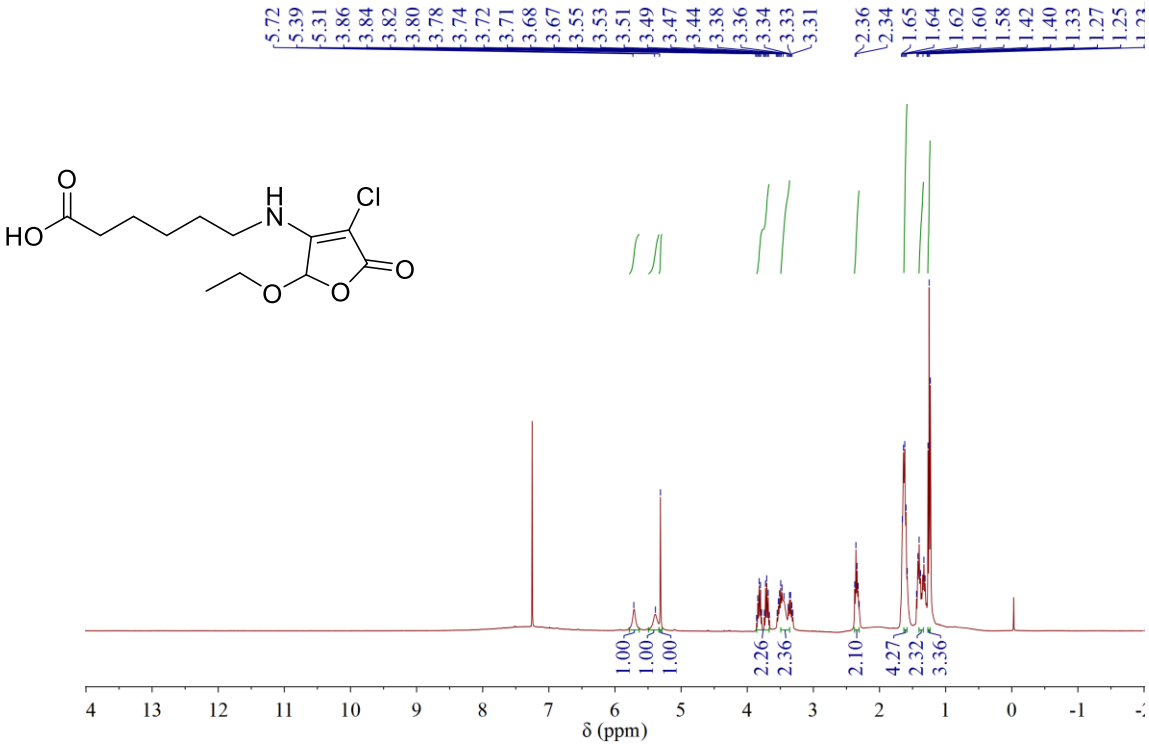

Figure 46. ^{1}H NMR spectrum of compound N16

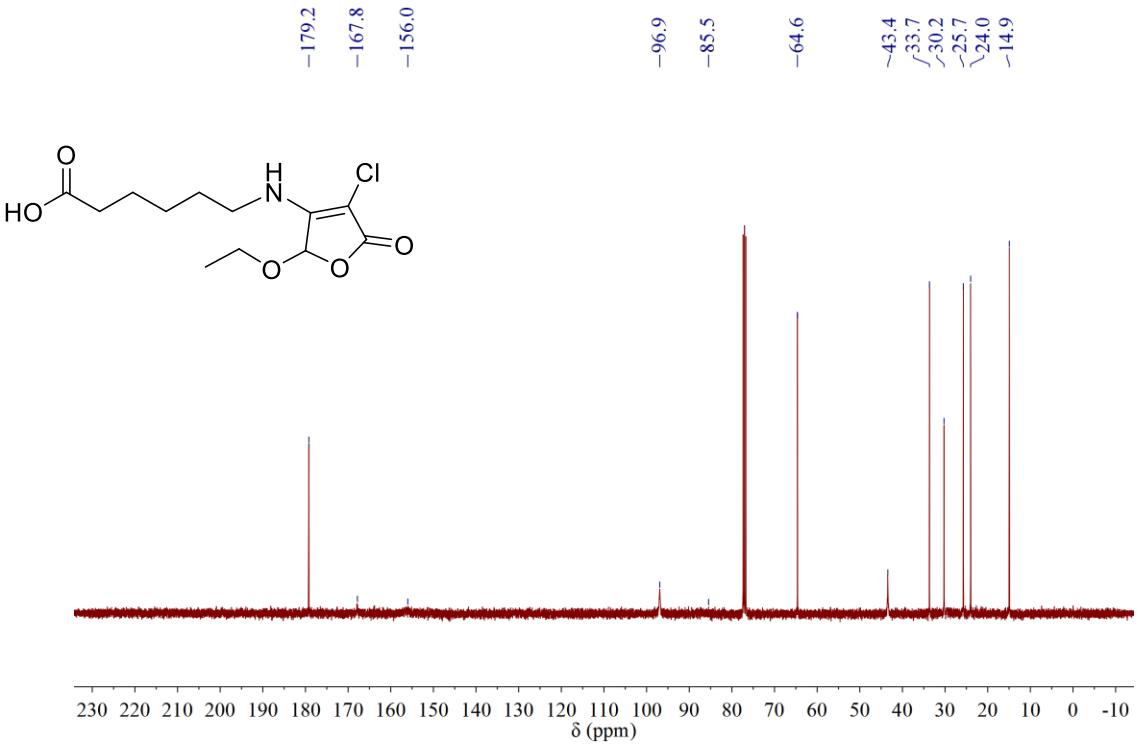

Figure 47. ^{13}C NMR spectrum of compound N16

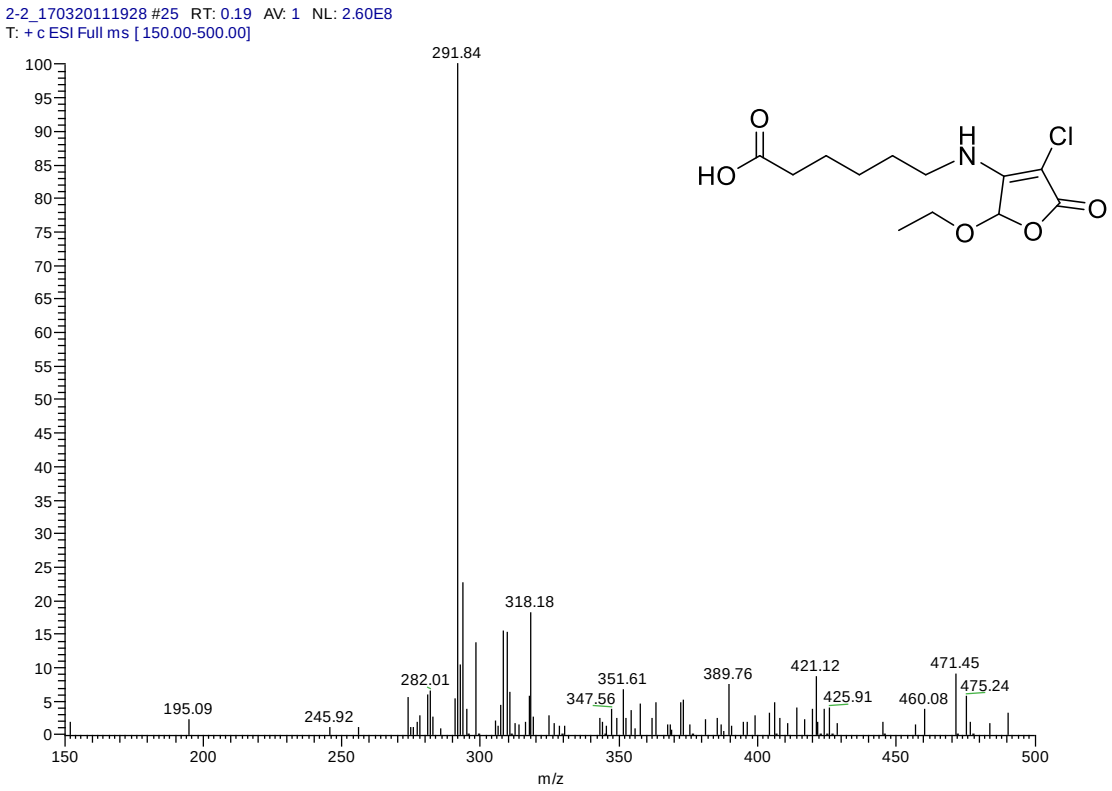

Figure 48. ESI-MS spectrum of compound N16

References

1. H.-Q. Wu, S.-H. Luo, L. Cao, H.-N. Shi, B.-W. Wang and Z.-Y. Wang, DABCO-mediated C-O bond formation from C_{sp2}-halogen bond-containing compounds and alkyl alcohols. *Asian J. Org. Chem.*, 2018, **7**, 2479.
2. L. Cao, S.-H. Luo, H.-Q. Wu, L.-Q. Chen, K. Jiang, Z.-F. Hao and Z.-Y. Wang, Copper(I)-catalyzed alkyl- and arylsulfenylation of 3,4-dihalo-2(5*H*)-furanones (X=Br, Cl) with sulfoxides under mild conditions. *Adv. Synth. Catal.*, 2017, **359**, 2961.
3. L. Cao, J.-X. Li, H.-Q. Wu, K. Jiang, Z.-F. Hao, S.-H. Luo and Z.-Y. Wang, Metal-free sulfonylation of 3,4-dihalo-2(5*H*)-furanones (X = Cl, Br) with sodium sulfinates under air atmosphere in aqueous media *via* a radical pathway. *ACS Sustainable Chem. Eng.*, 2018, **6**, 4147.