

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 CH₂Cl₂. The obtained organic layer was washed with distilled water and dried over anhydrous Na₂SO₄. 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 °C) under air for 12 h. At ambient temperature, the reaction mixture was diluted with H₂O (15 mL) and extracted with EtOAc (3 × 15 mL). The organic extracts were dried over anhydrous Na₂SO₄. 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*-Bu₄NBr (3 mol %) in DCE: H₂O (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 H₂O (15 mL) and extracted with EtOAc (3 × 15 mL). The organic extracts were dried over anhydrous Na₂SO₄. 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**).

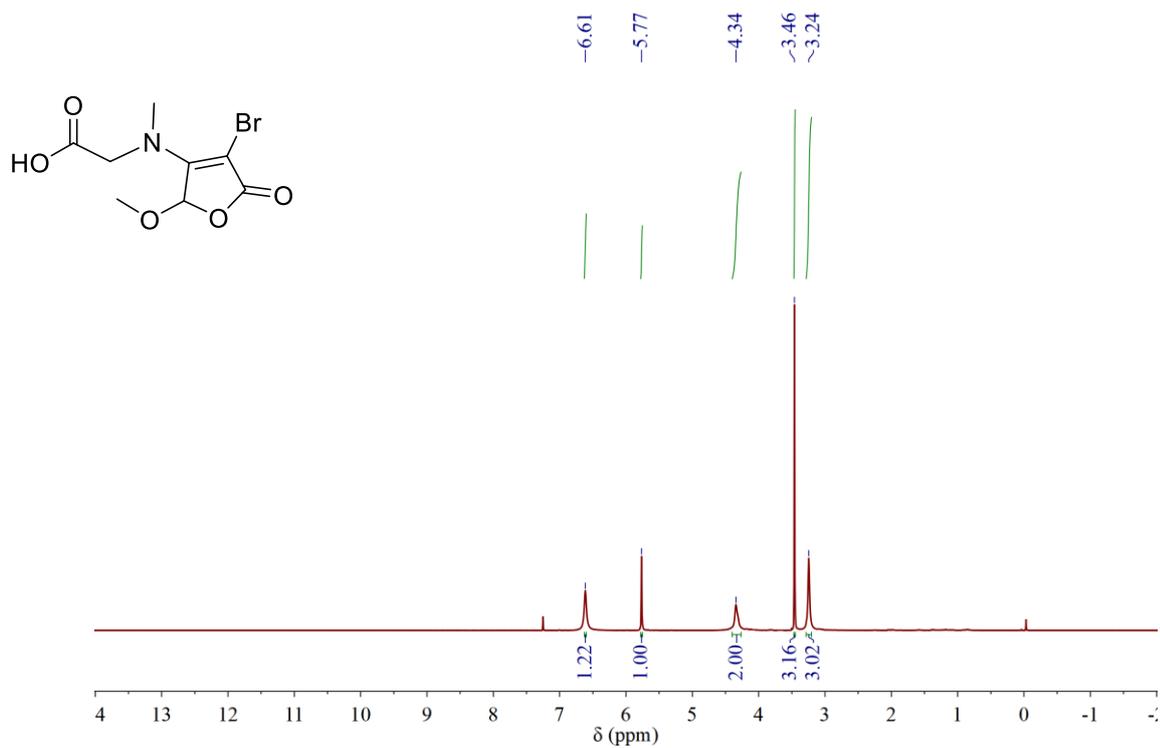


Figure 1. ¹H NMR spectrum of compound N1

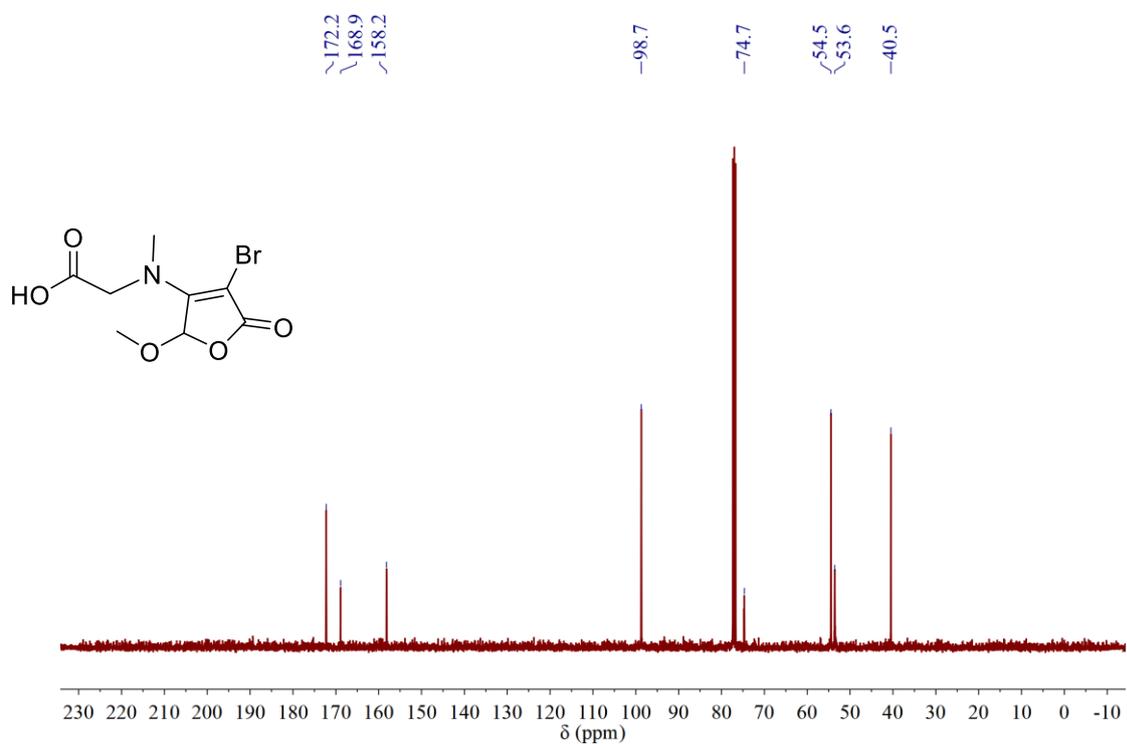


Figure 2. ¹³C NMR spectrum of compound N1

2-2_170320110141 #14 RT: 0.12 AV: 1 NL: 3.66E7
T: - c ESI Full ms [150.00-500.00]

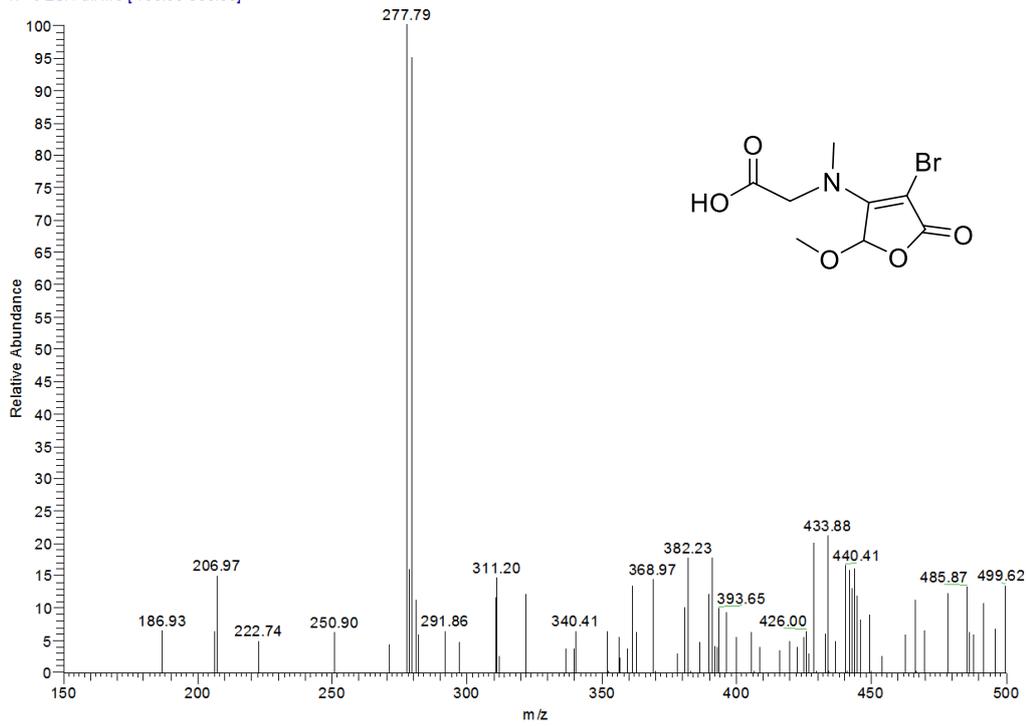


Figure 3. ESI-MS spectrum of compound N1

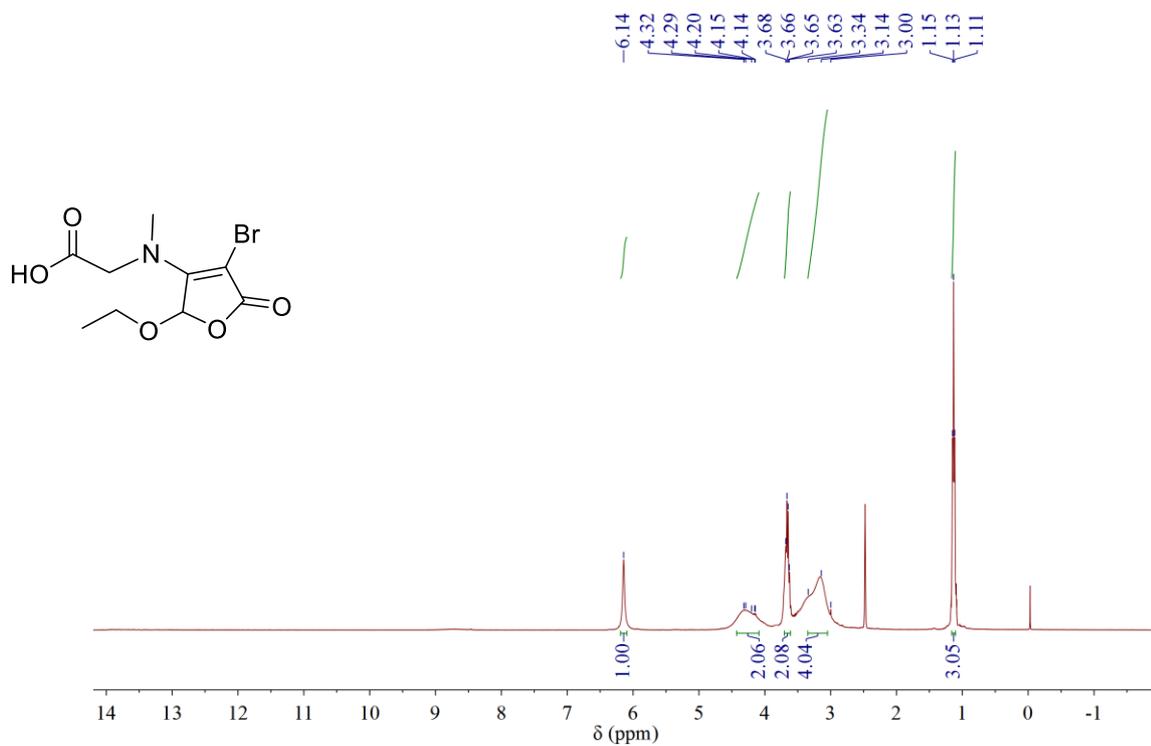


Figure 4. ¹H NMR spectrum of compound N2

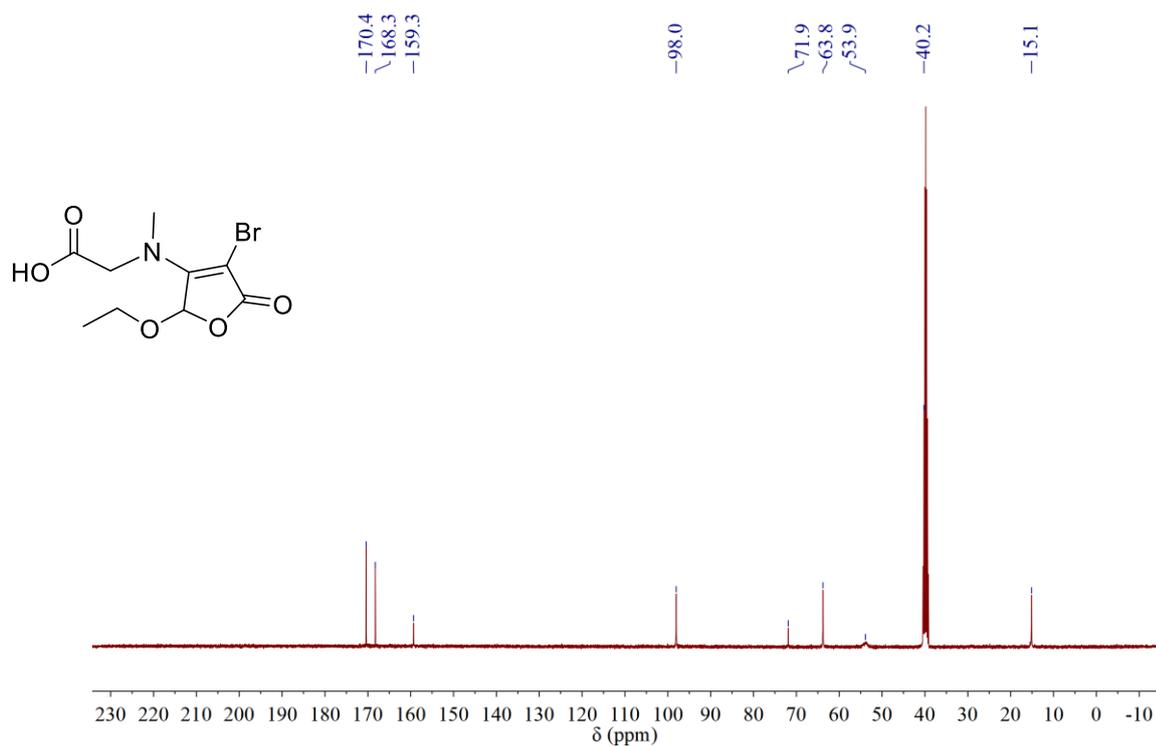


Figure 5. ^{13}C NMR spectrum of compound N2

2-2_170320110730 #15 RT: 0.13 AV: 1 NL: 4.92E7
T: - c ESI Full ms [150.00-500.00]

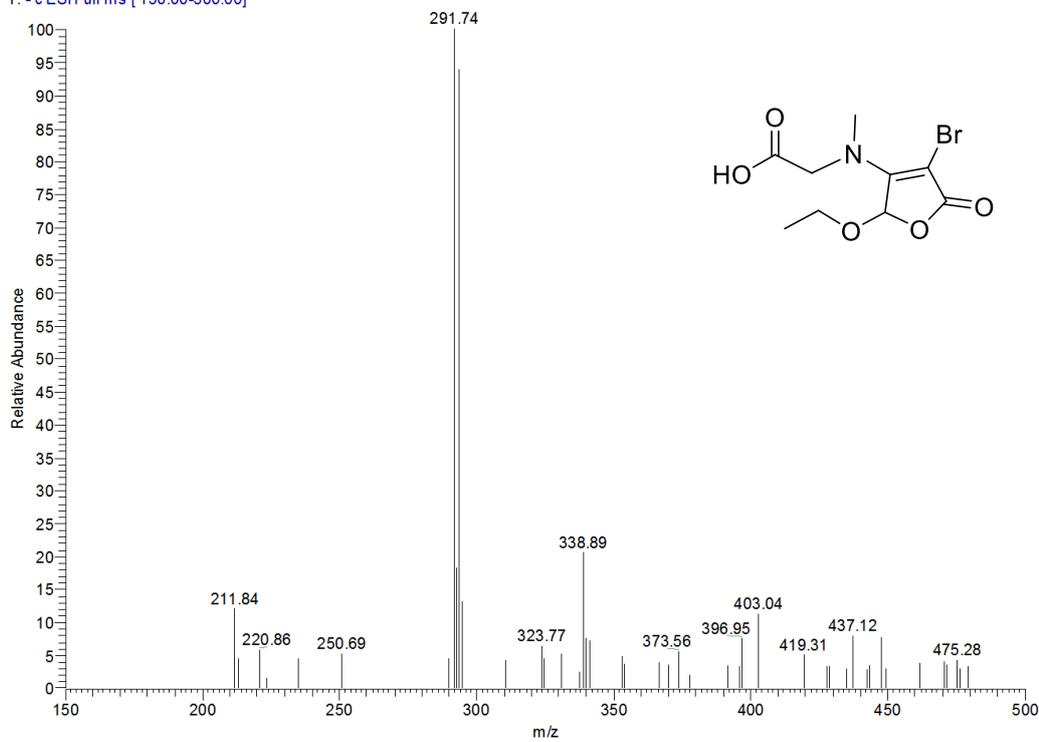


Figure 6. ESI-MS spectrum of compound N2

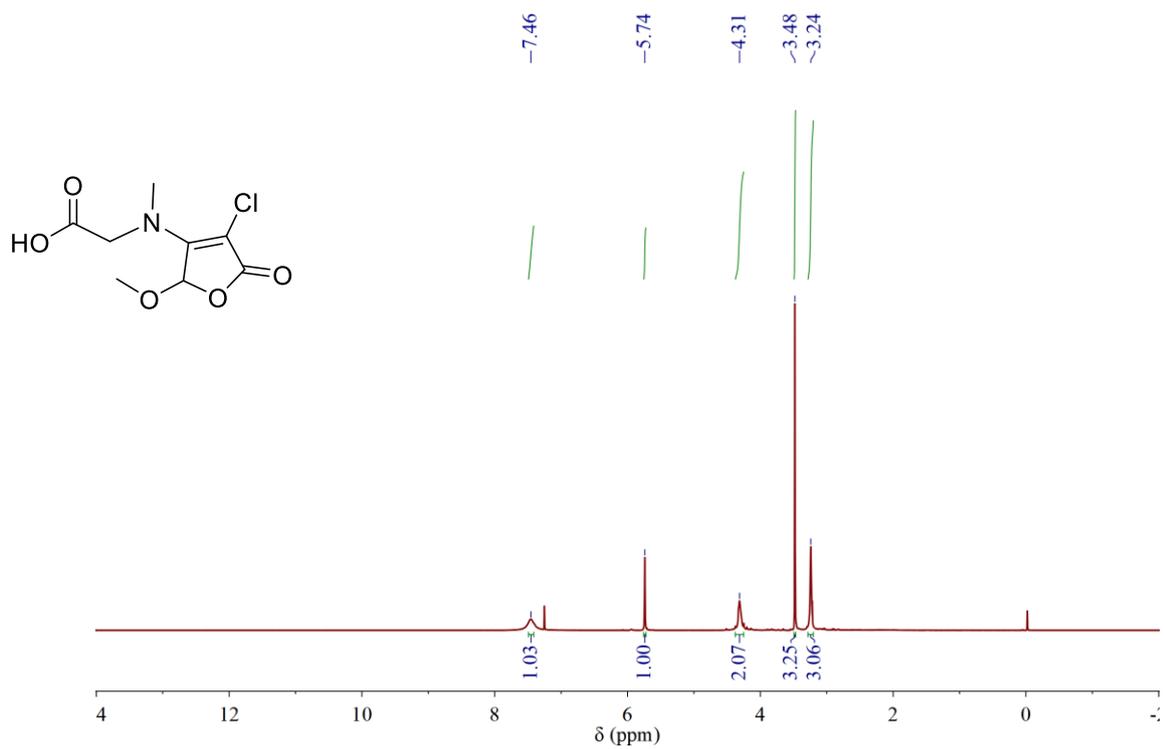


Figure 7. ^1H NMR spectrum of compound N3

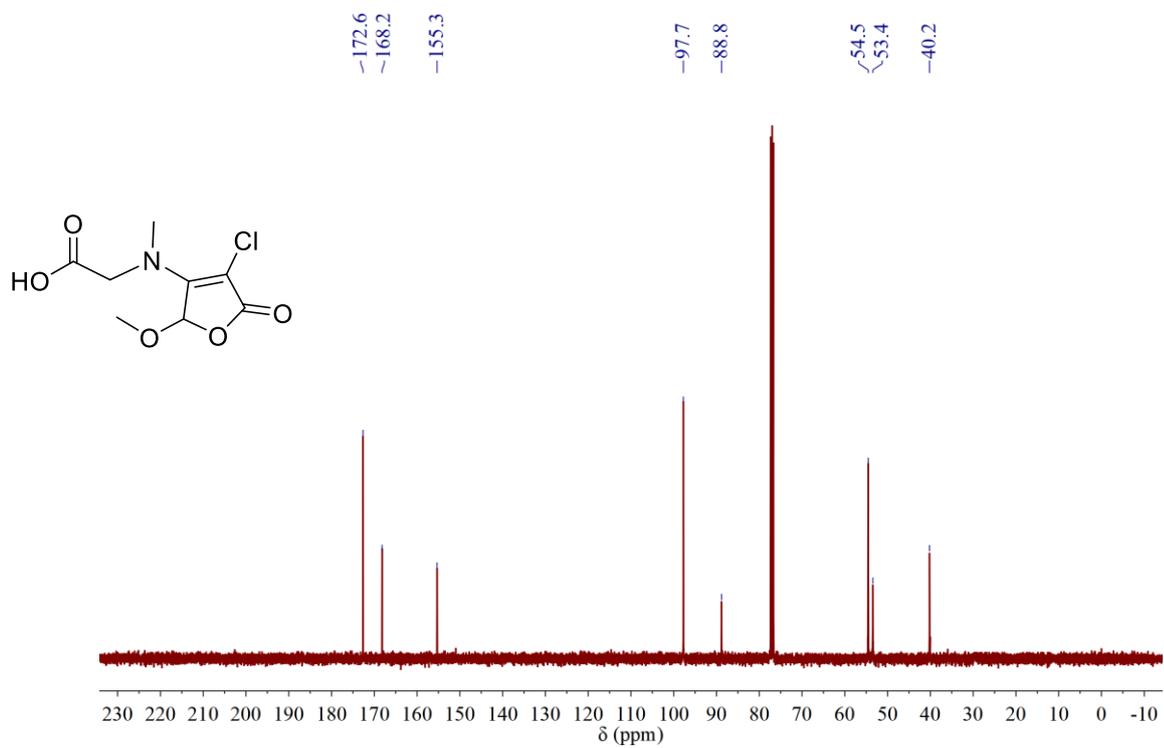


Figure 8. ^{13}C NMR spectrum of compound N3

so_180109121732 #20 RT: 0.14 AV: 1 NL: 3.53E5
T: - c ESI Full ms [100.00-500.00]

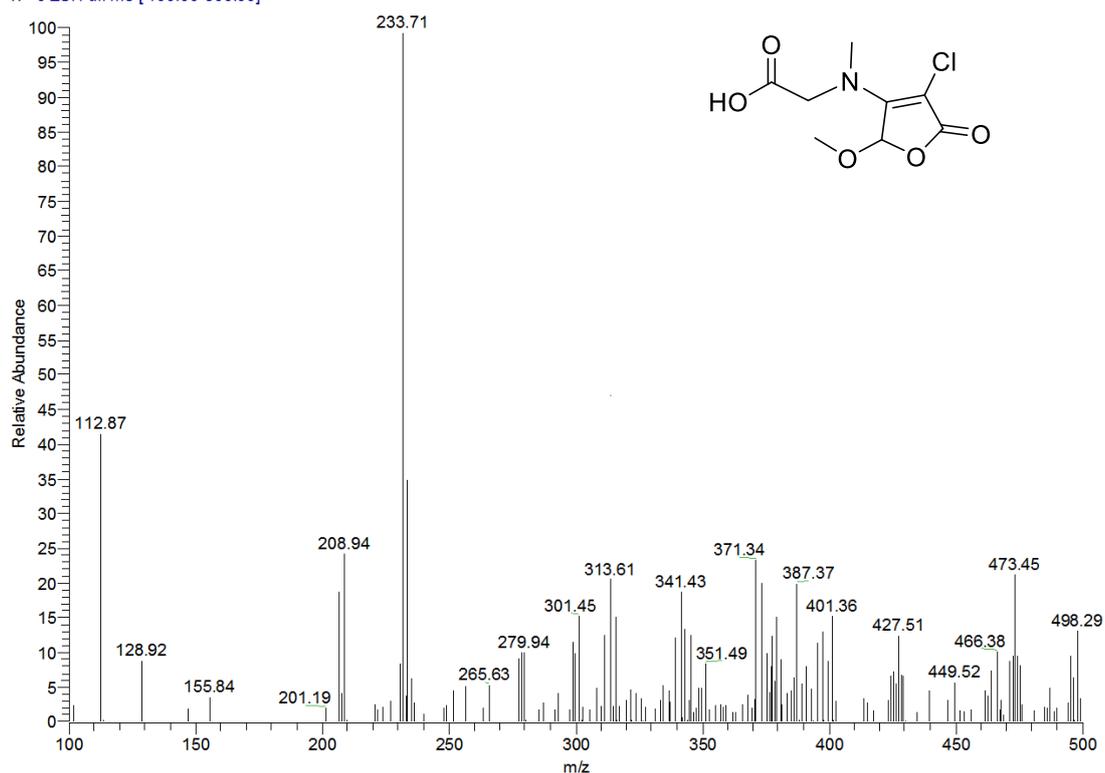


Figure 9. ESI-MS spectrum of compound N3

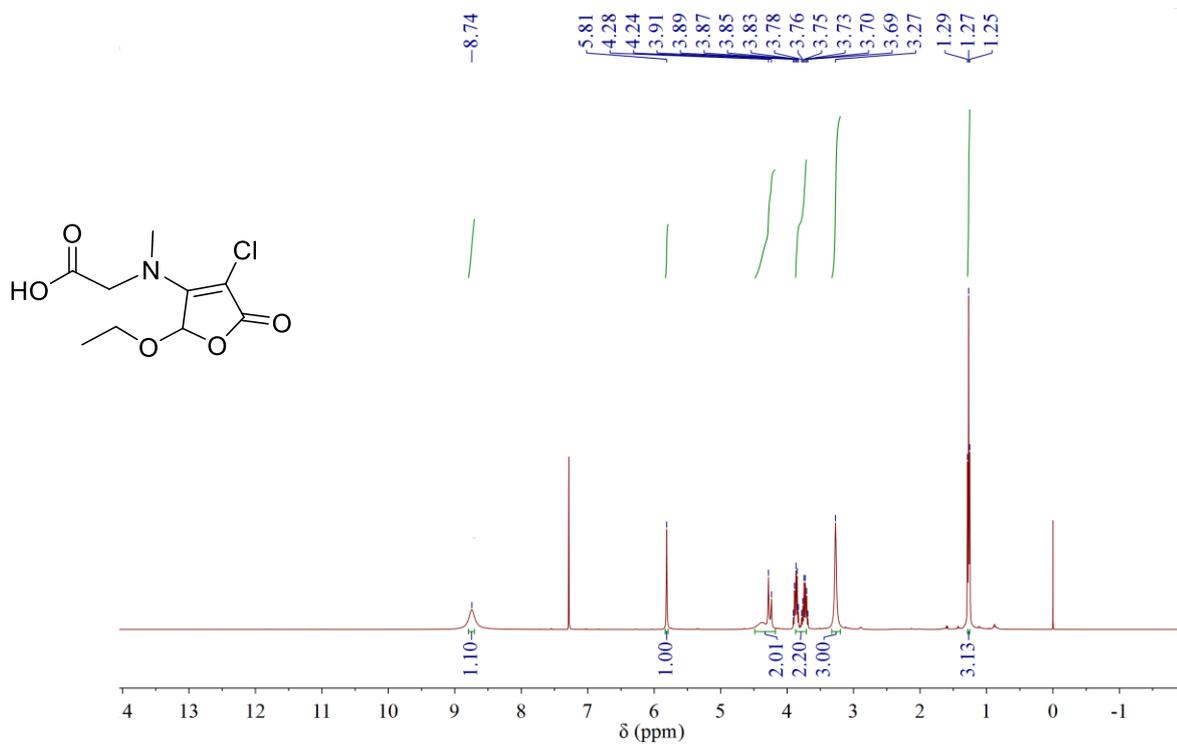


Figure 10. ¹H NMR spectrum of compound N4

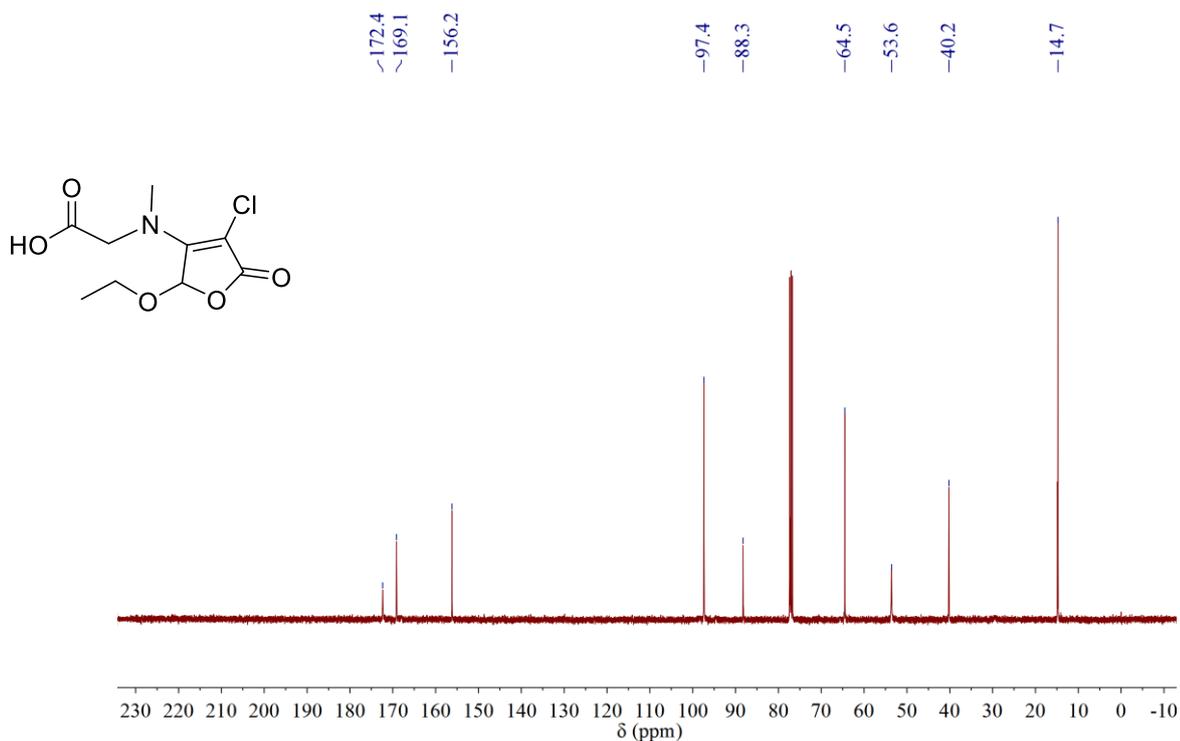


Figure 11. ^{13}C NMR spectrum of compound N4

so_180109121352#24 RT: 0.18 Av: 1 NL: 1.44E6
T: + c ESI Full ms [100.00-500.00]

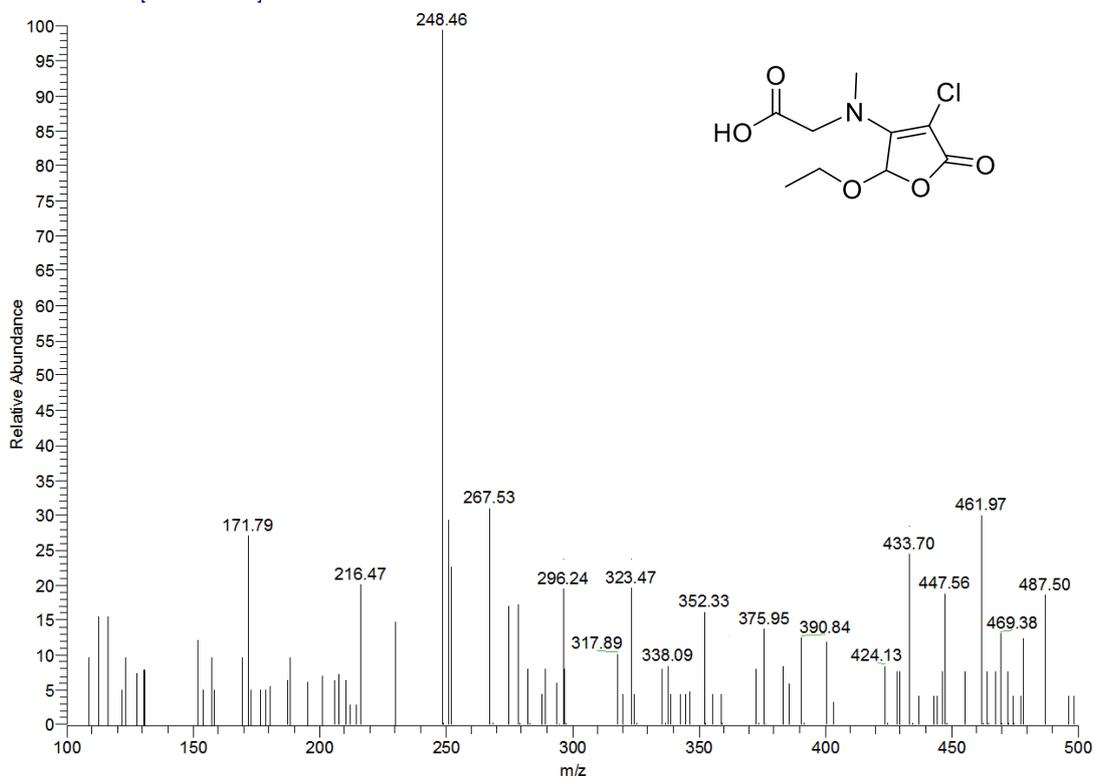


Figure 12. ESI-MS spectrum of compound N4

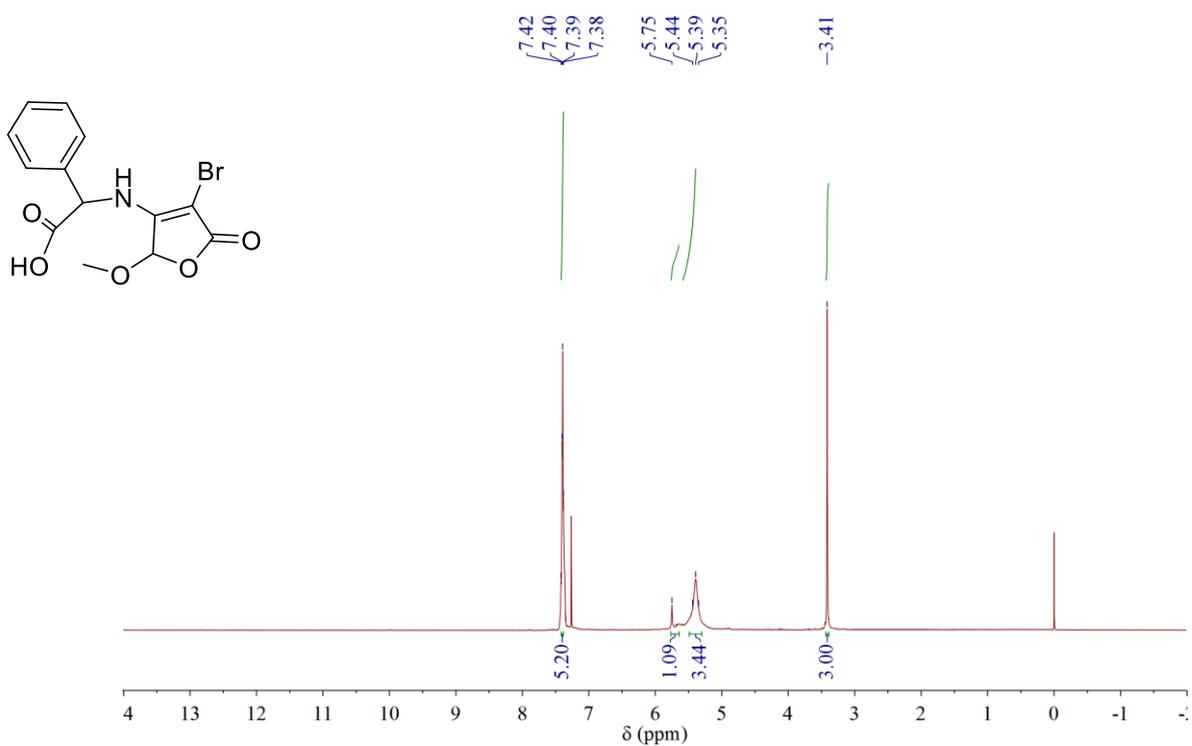


Figure 13. ¹H NMR spectrum of compound N5

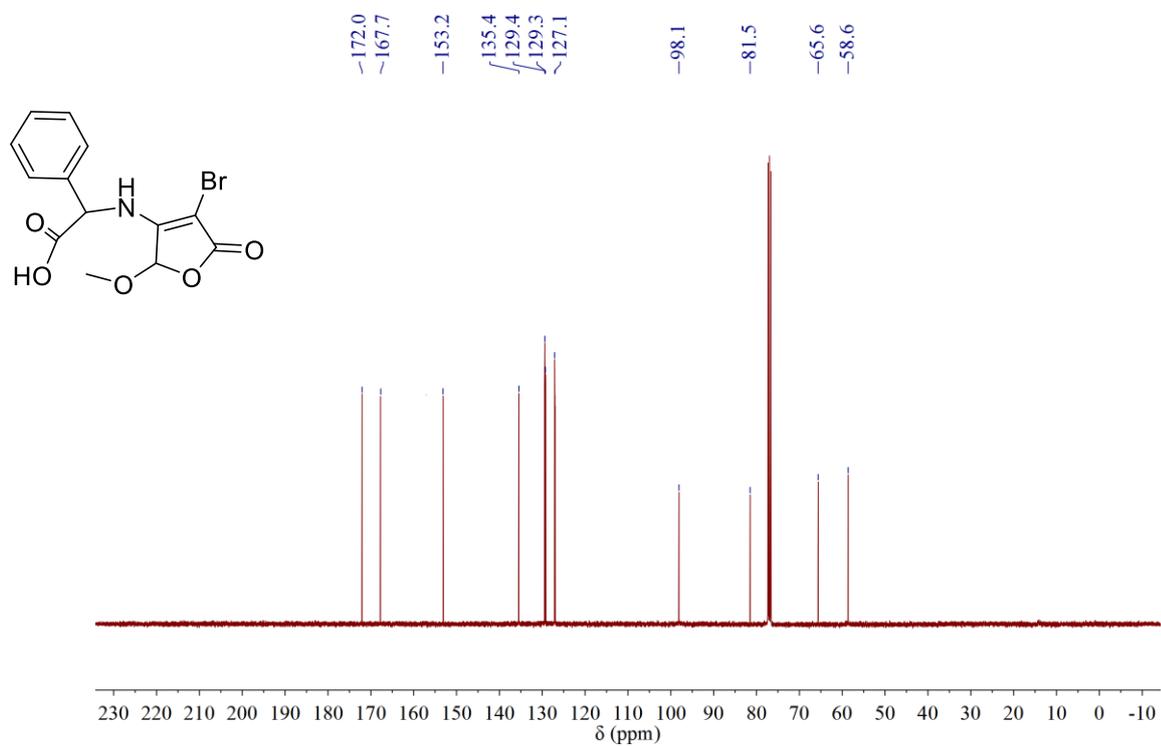


Figure 14. ¹³C NMR spectrum of compound N5

TPACO-1_170329111006 #112 RT: 0.93 AV: 1 NL: 1.33E8
T: + c ESI Full ms [100.00-500.00]

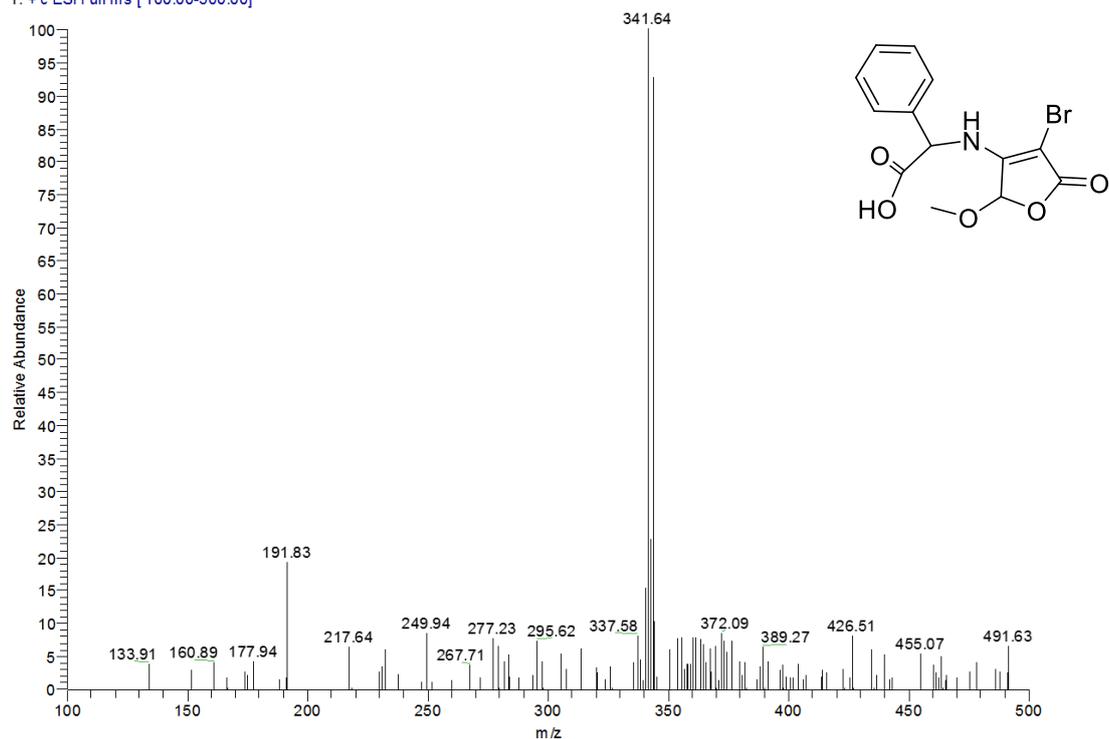


Figure 15. ESI-MS spectrum of compound N5

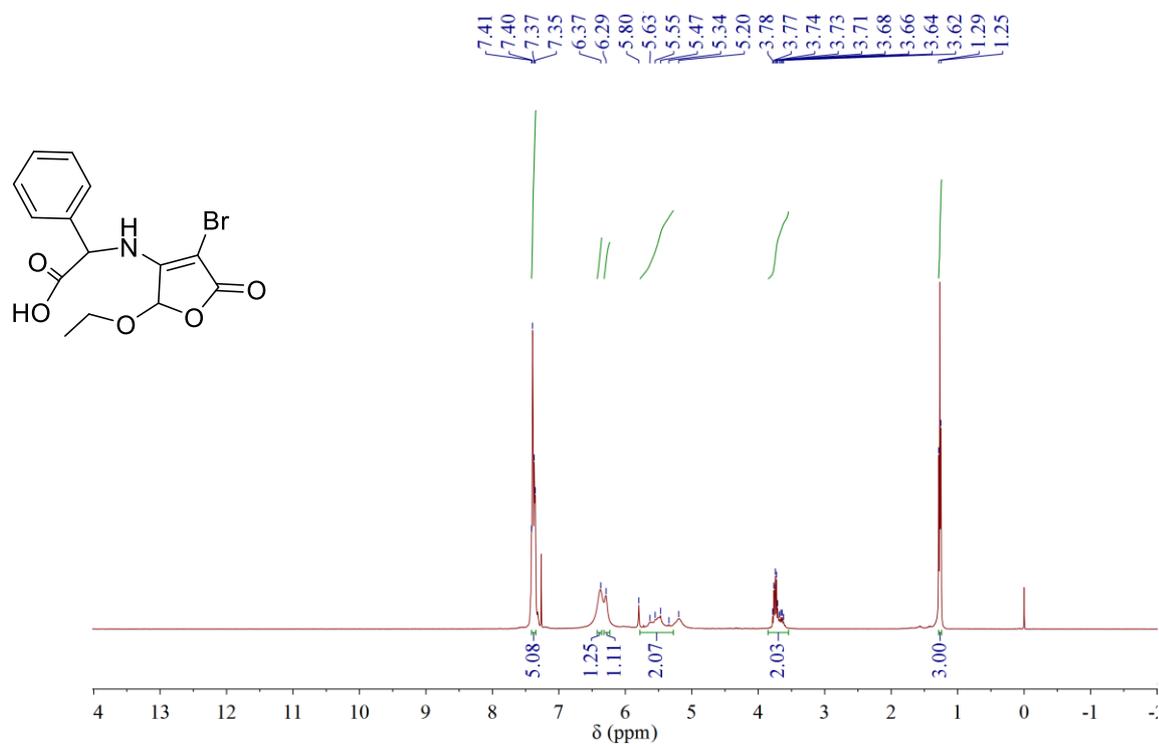


Figure 16. ¹H NMR spectrum of compound N6

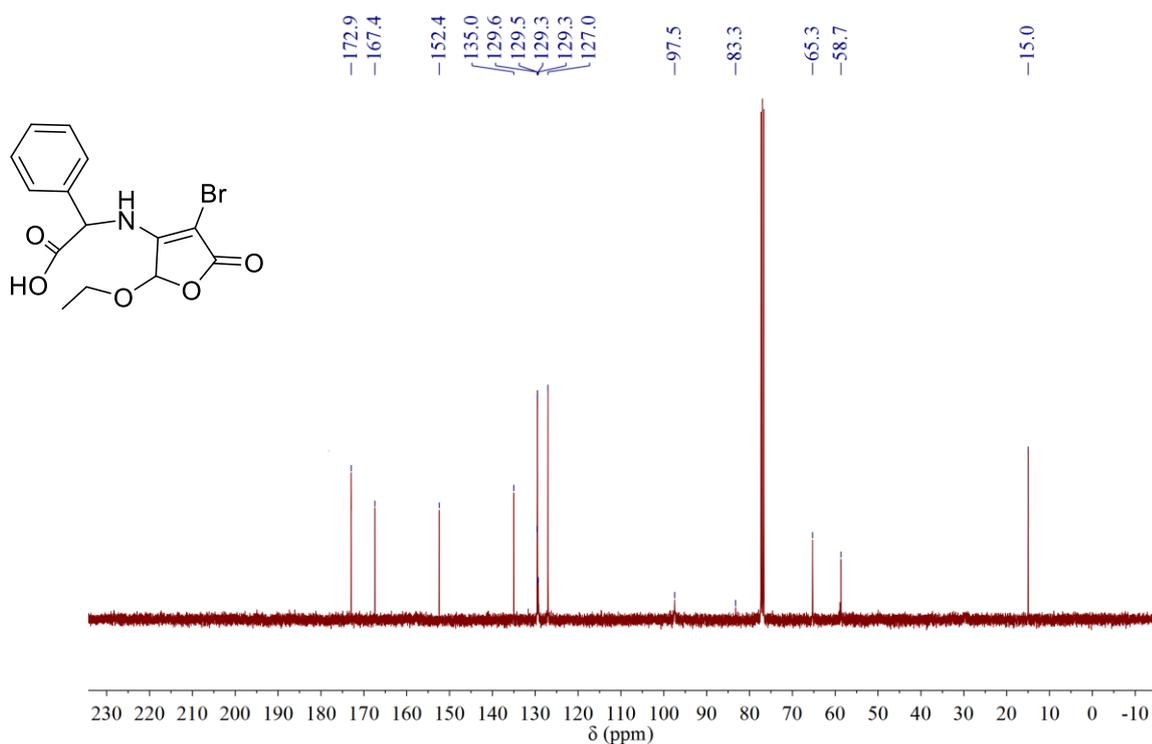


Figure 17. ^{13}C NMR spectrum of compound N6

TPACO-1_170329105542 #83 RT: 0.69 AV: 1 NL: 1.26E8
T: + c ESI Full ms [100.00-500.00]

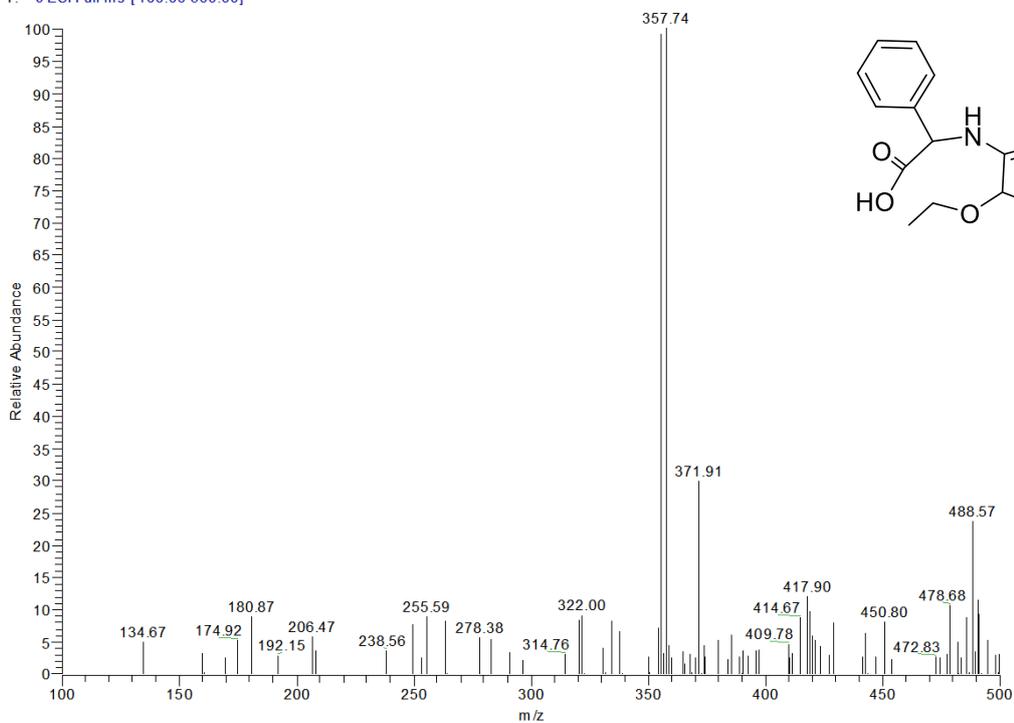


Figure 18. ESI-MS spectrum of compound N6

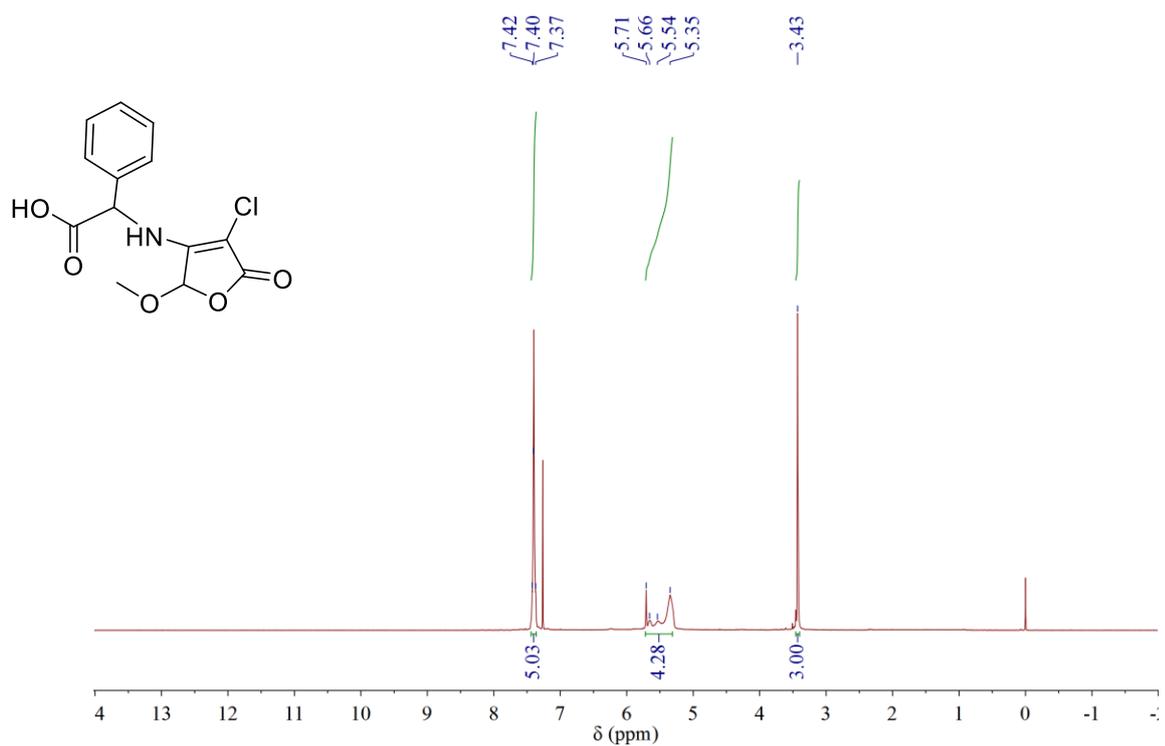


Figure 19. ¹H NMR spectrum of compound N7

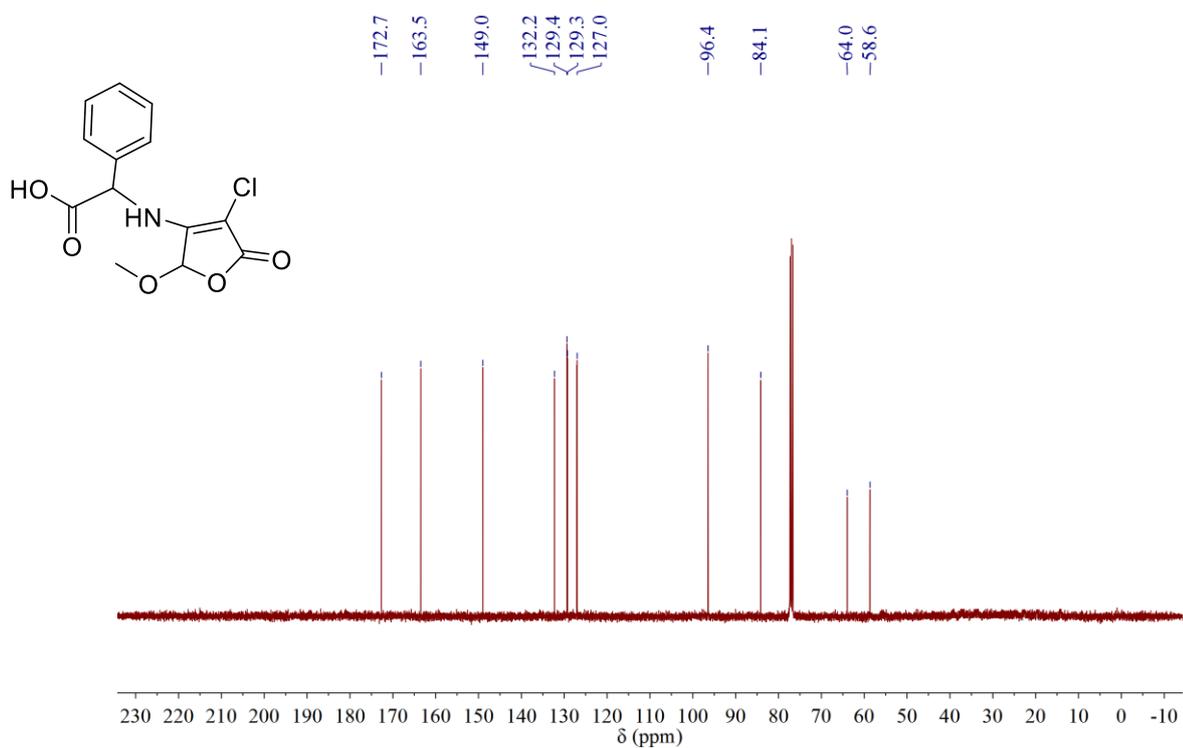


Figure 20. ¹³C NMR spectrum of compound N7

TPACO-1_170329112318 #110 RT: 0.91 AV: 1 NL: 5.04E6
T: + c ESI Full ms [100.00-500.00]

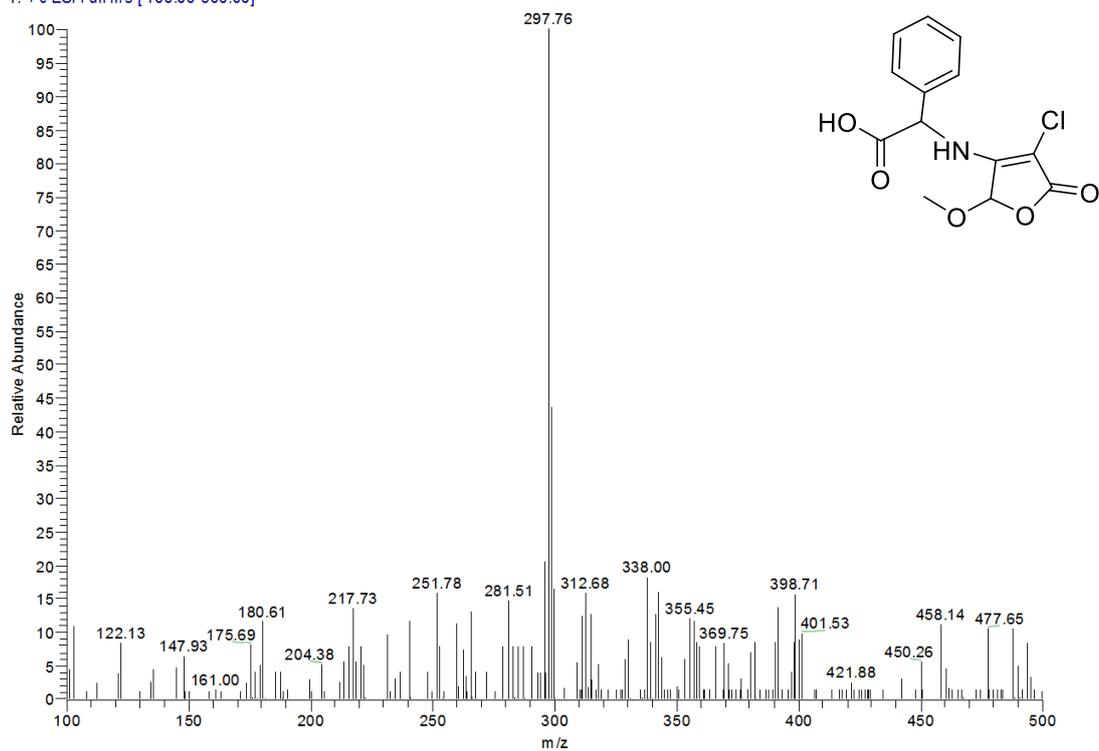


Figure 21. ESI-MS spectrum of compound N7

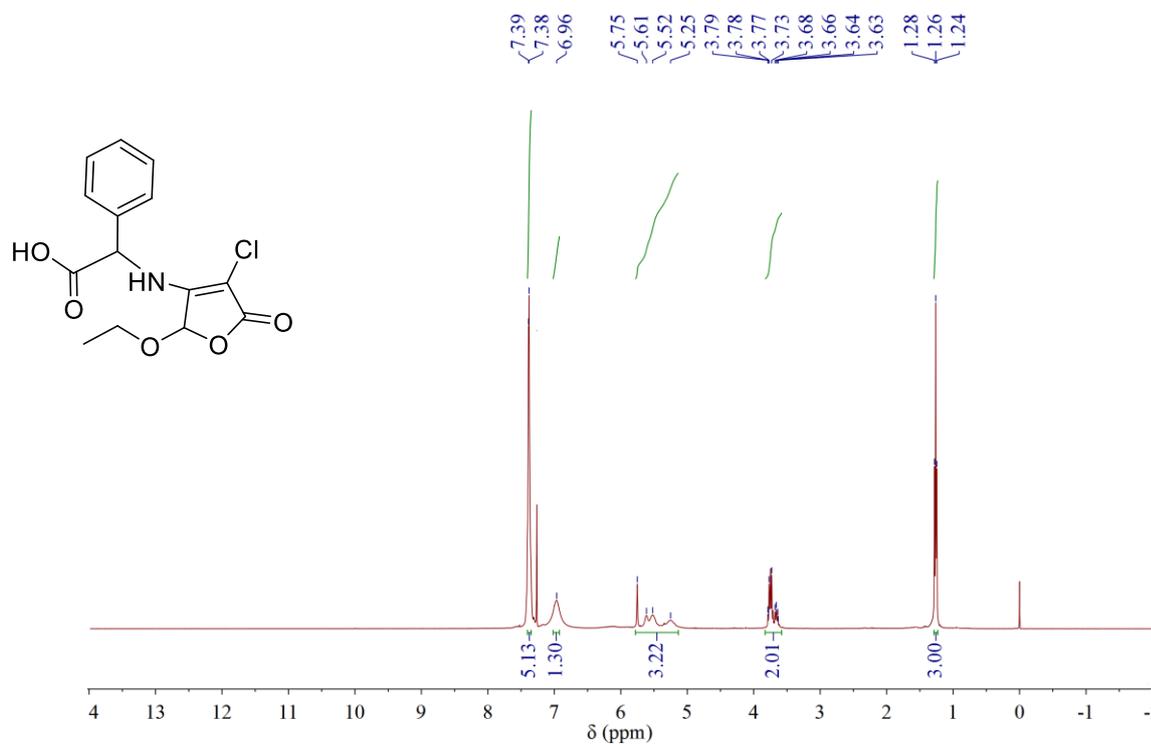


Figure 22. ¹H NMR spectrum of compound N8

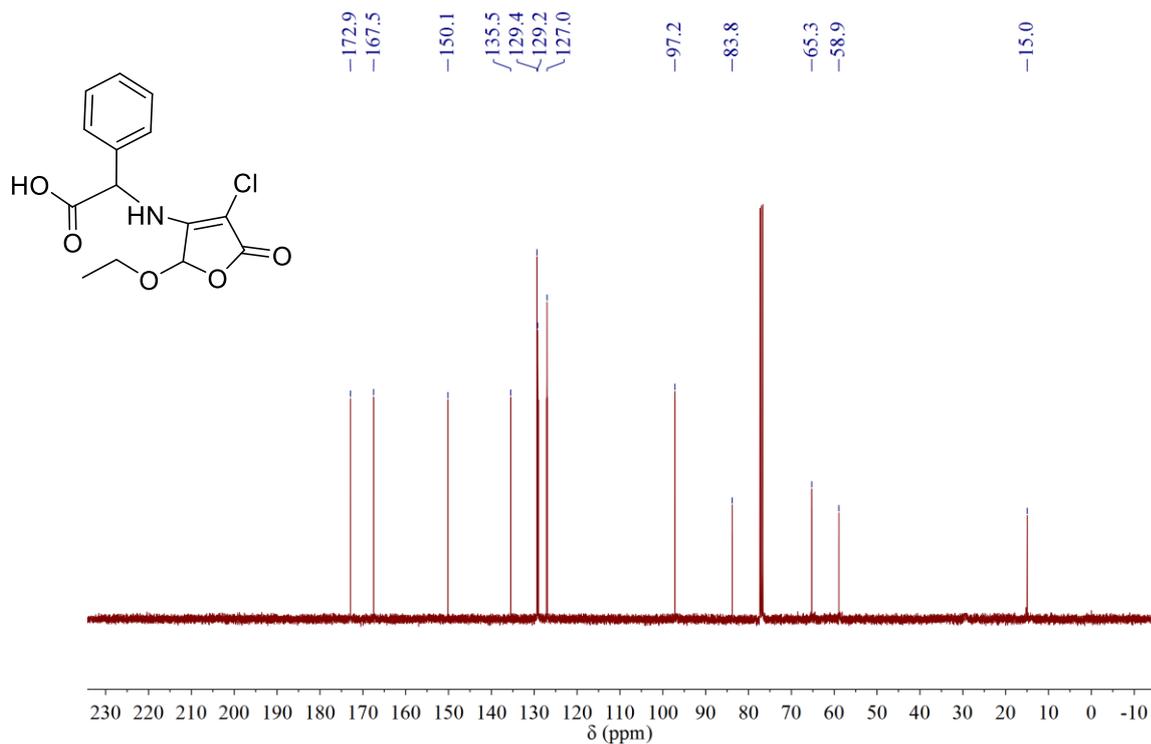


Figure 23. ^{13}C NMR spectrum of compound N8

TPACO-1_170329111955 #87 RT: 0.71 AV: 1 NL: 2.32E7
T: + c ESI Full ms [100.00-500.00]

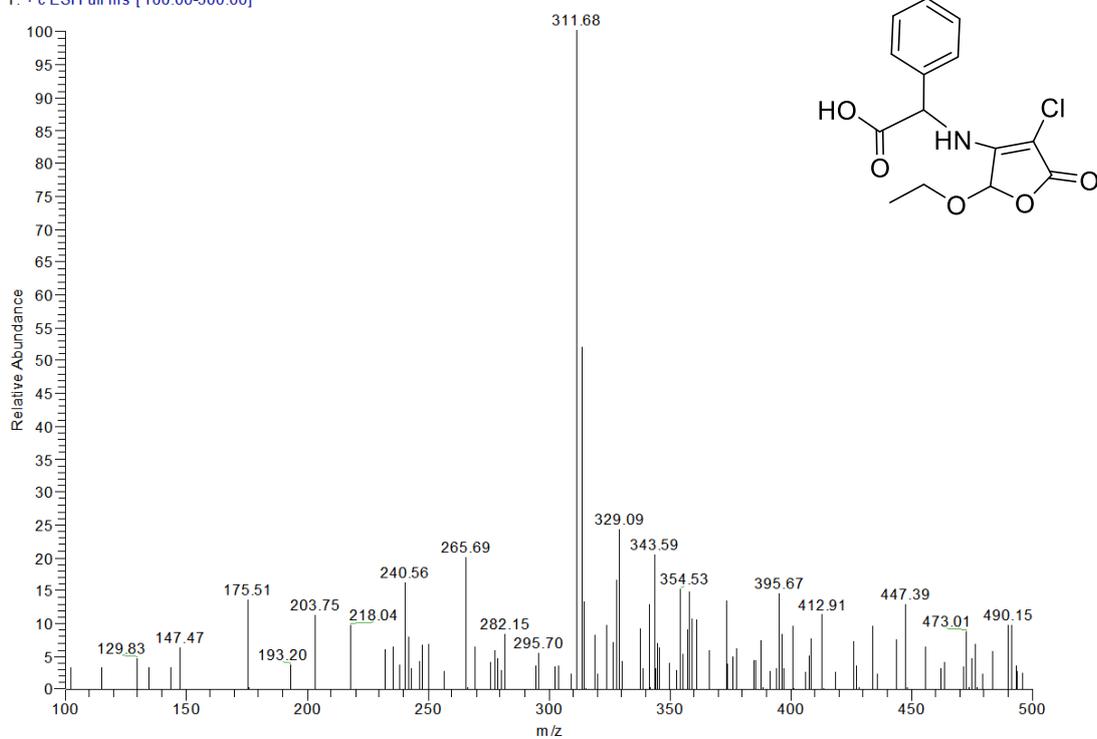


Figure 24. ESI-MS spectrum of compound N8

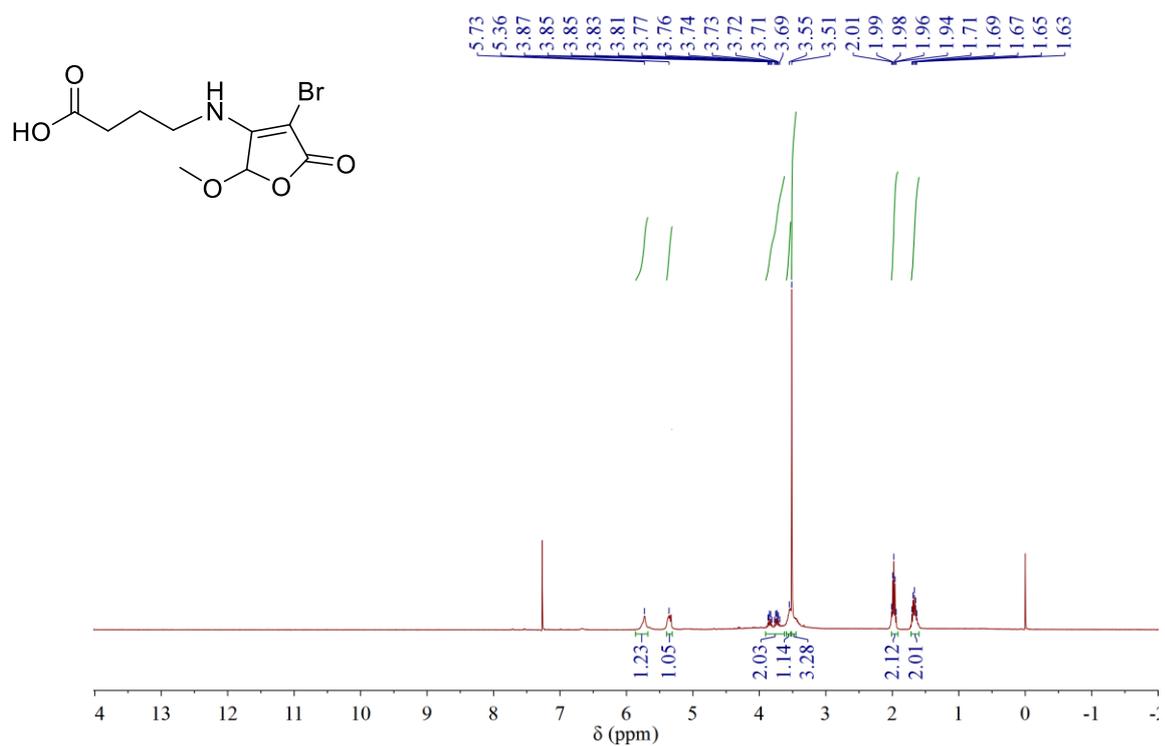


Figure 25. ¹H NMR spectrum of compound N9

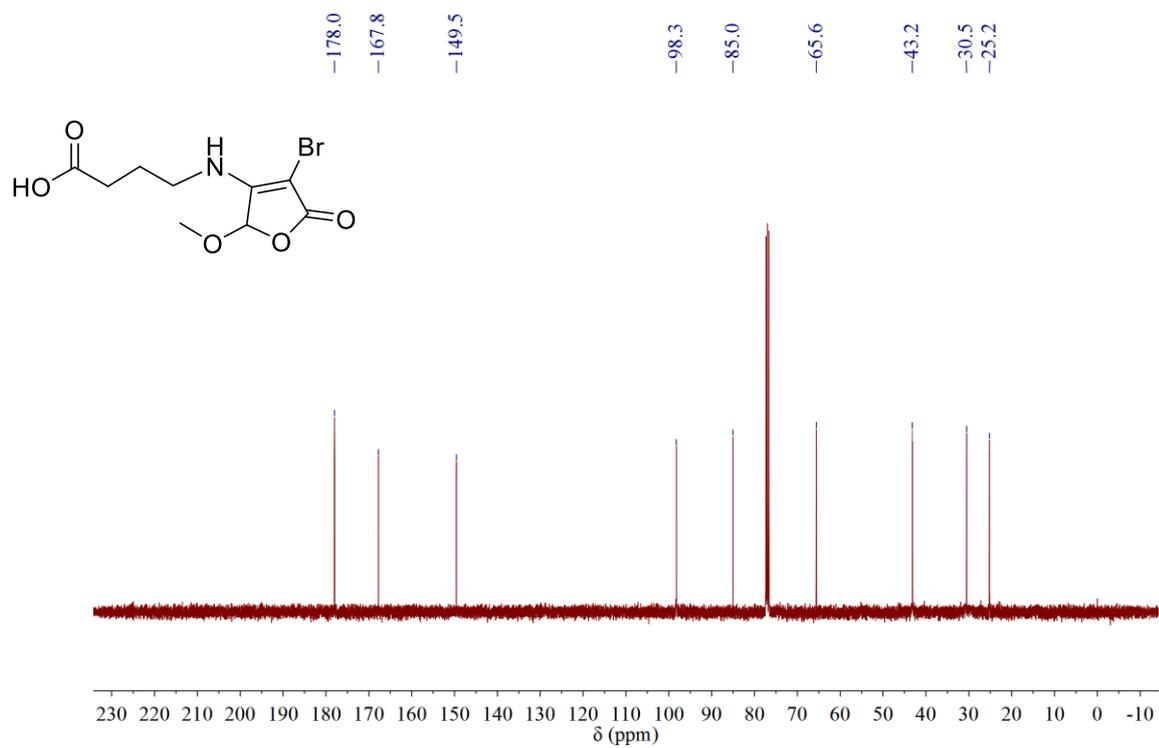


Figure 26. ¹³C NMR spectrum of compound N9

FILE_161228103150 #87 RT: 0.62 AV: 1 NL: 5.18E7
T: + c ESI Full ms [200.00-500.00]

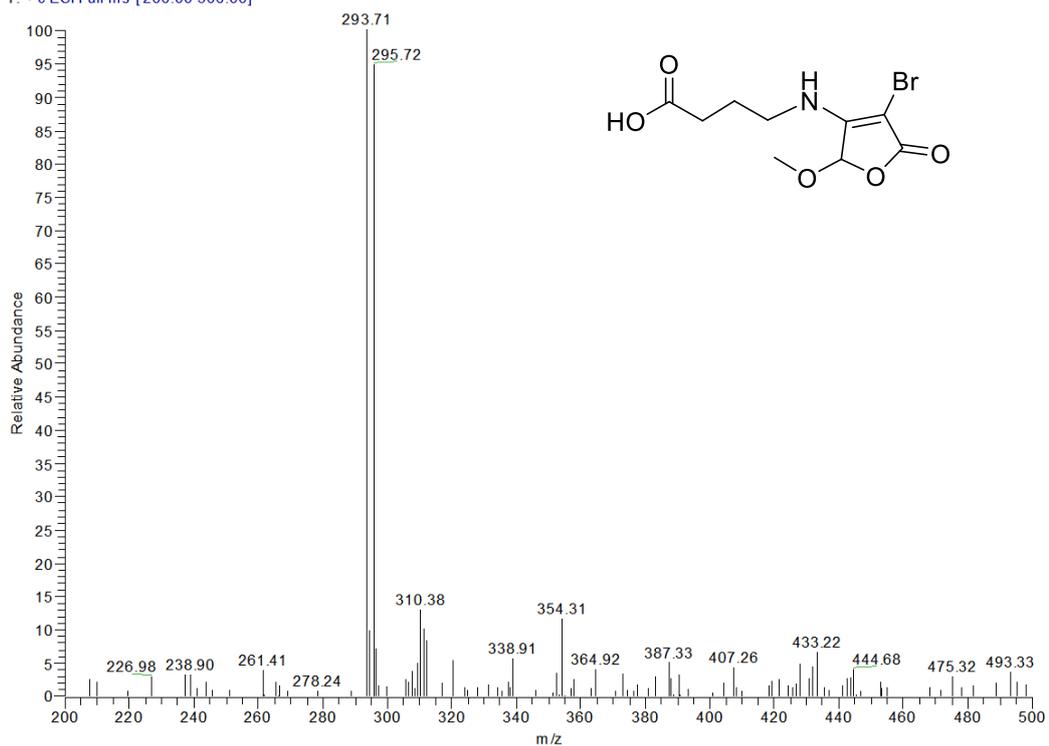


Figure 27. ESI-MS spectrum of compound N9

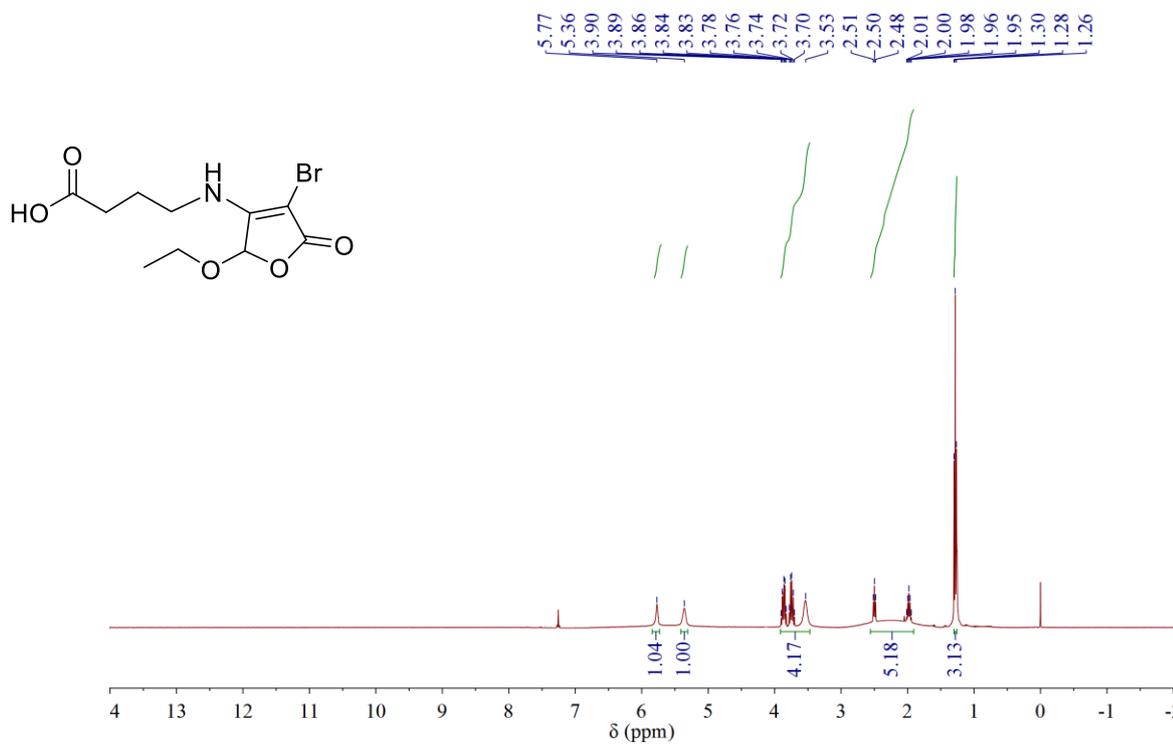


Figure 28. ¹H NMR spectrum of compound N10

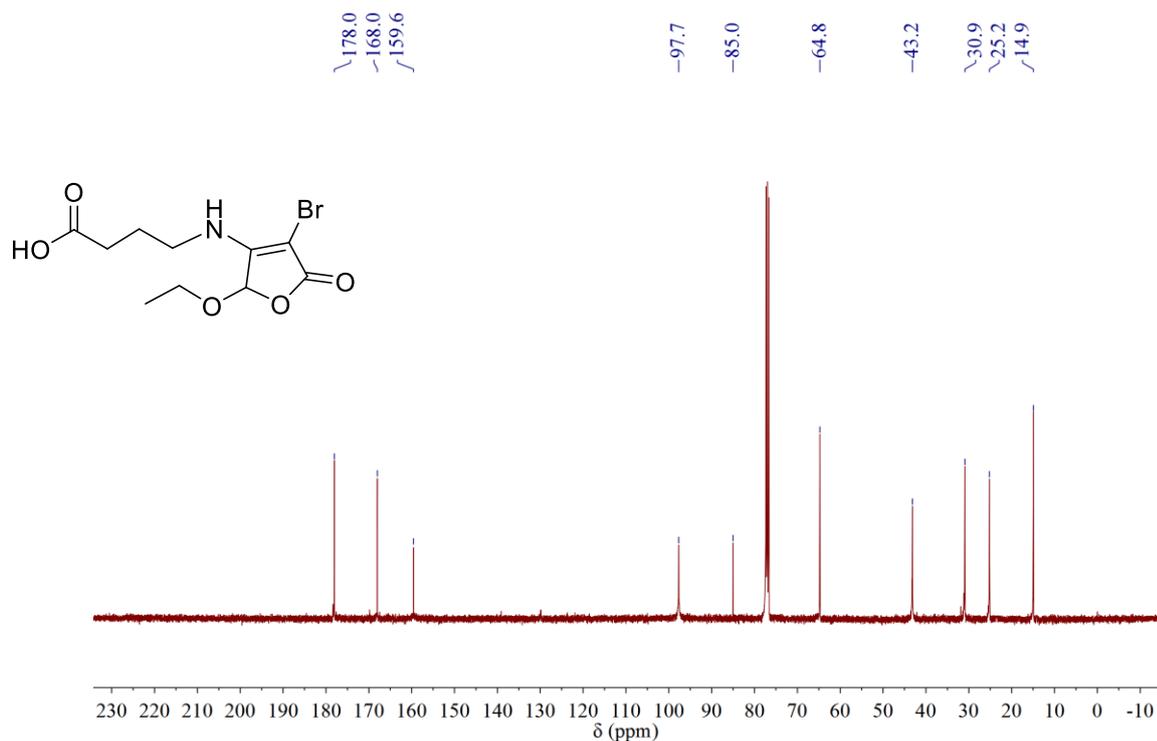


Figure 29. ¹³C NMR spectrum of compound N10

FILE_161228105509#17-19 RT: 0.12-0.13 AV: 3 NL: 2.38E8
T: + c ESI Full ms [200.00-500.00]

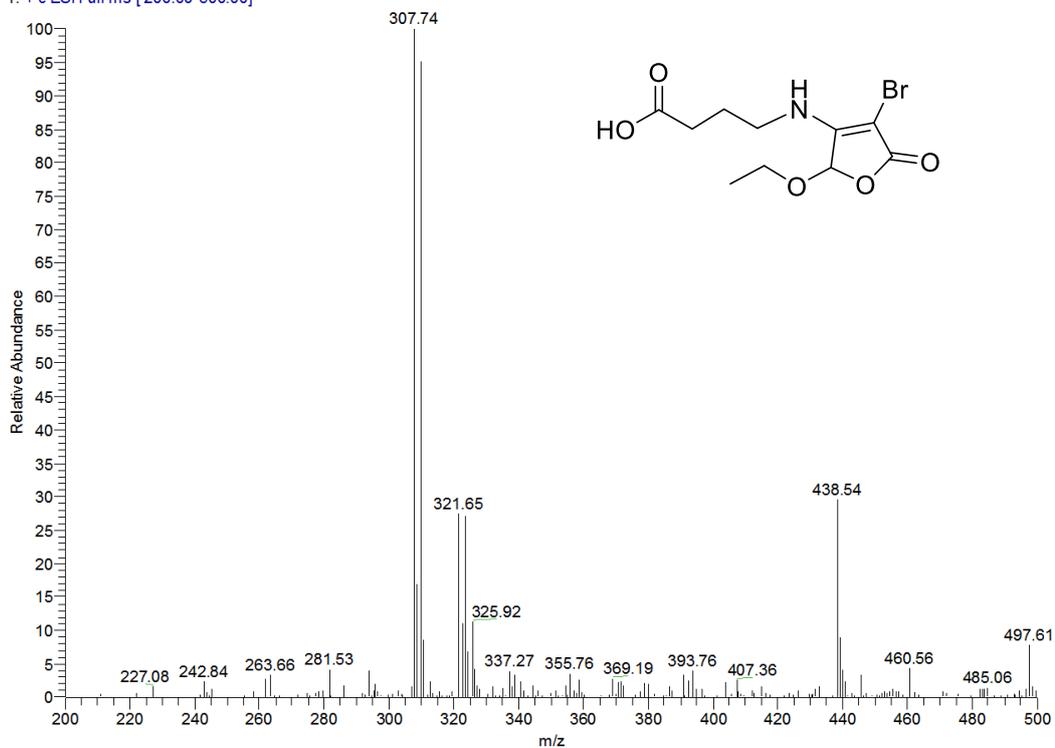


Figure 30. ESI-MS spectrum of compound N10

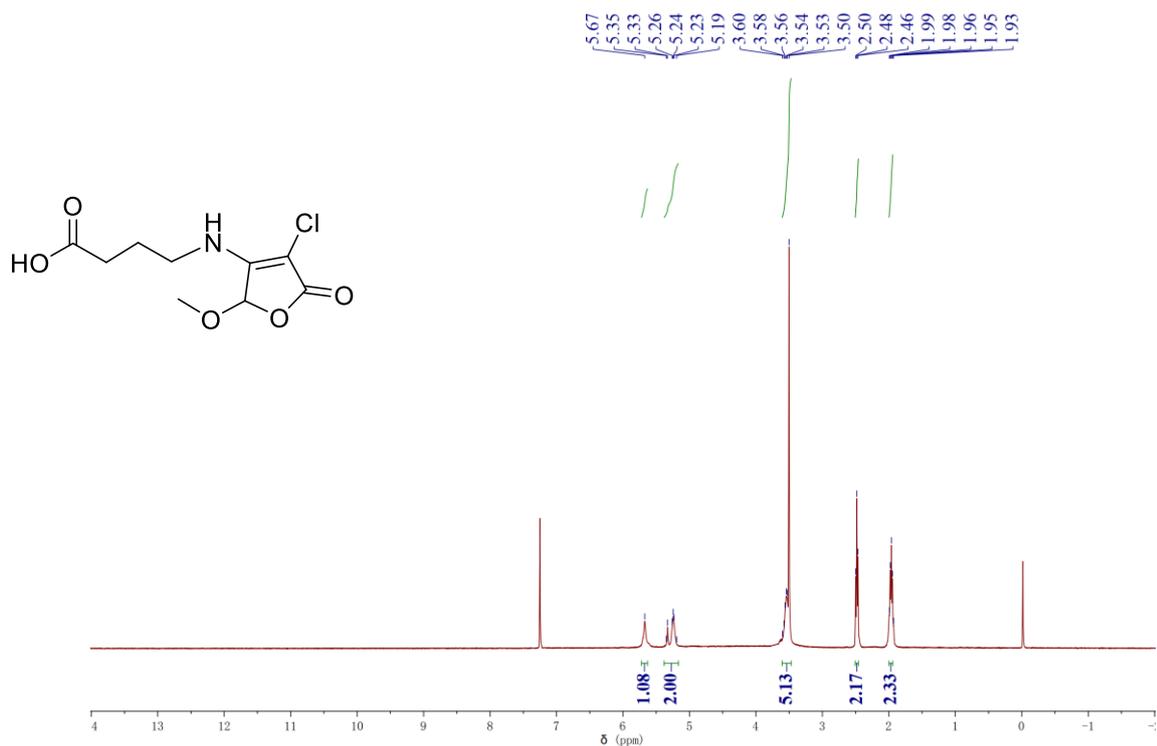


Figure 31. ¹H NMR spectrum of compound N11

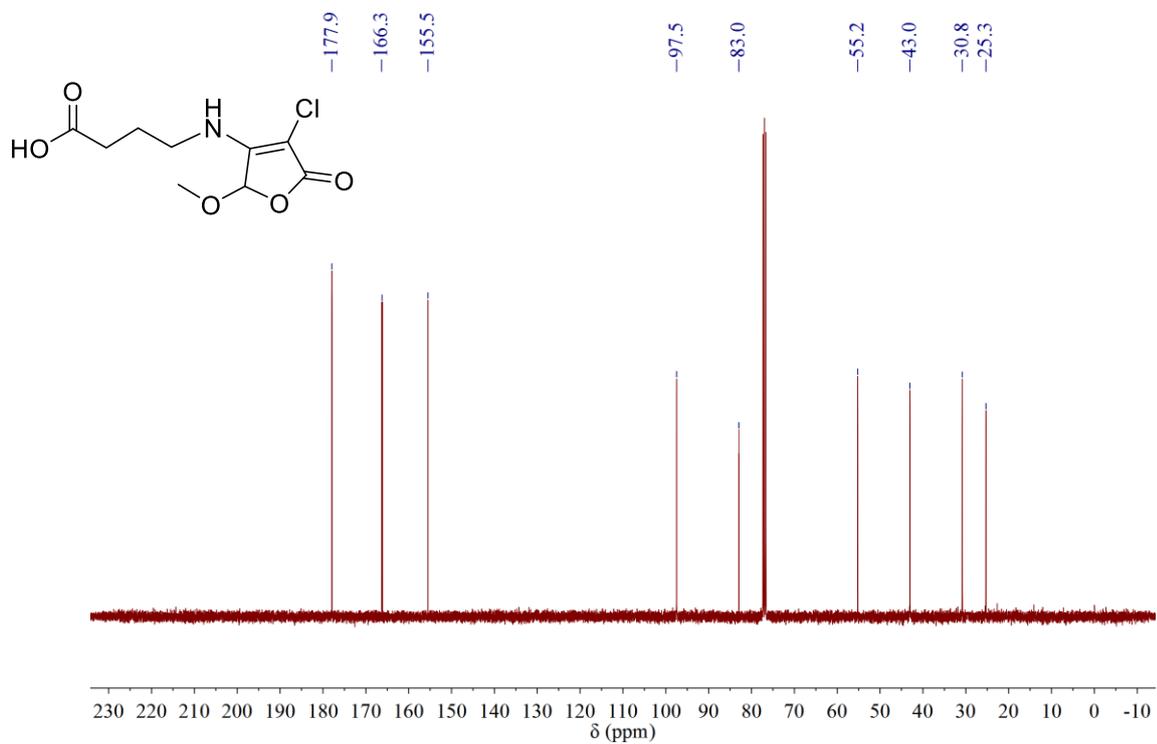


Figure 32. ¹³C NMR spectrum of compound N11

TPACO-1_170329104502 #78 RT: 0.66 AV: 1 NL: 7.03E6
T: + c ESI Full ms [100.00-500.00]

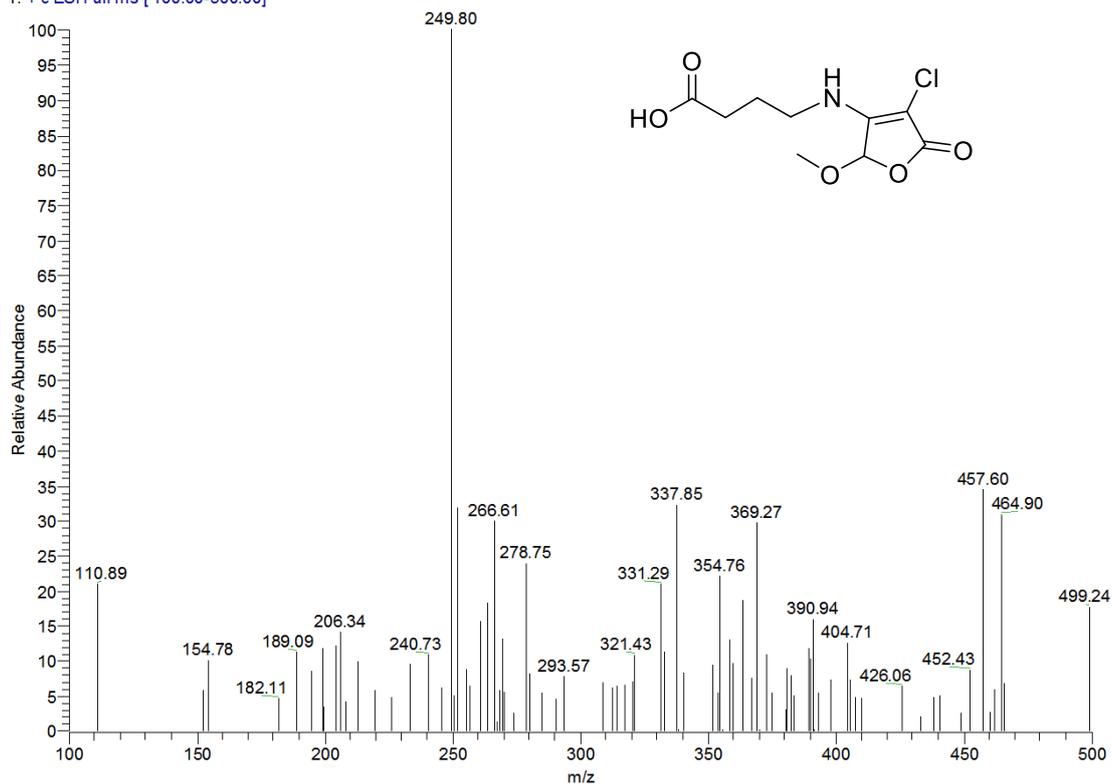


Figure 33. ESI-MS spectrum of compound N11

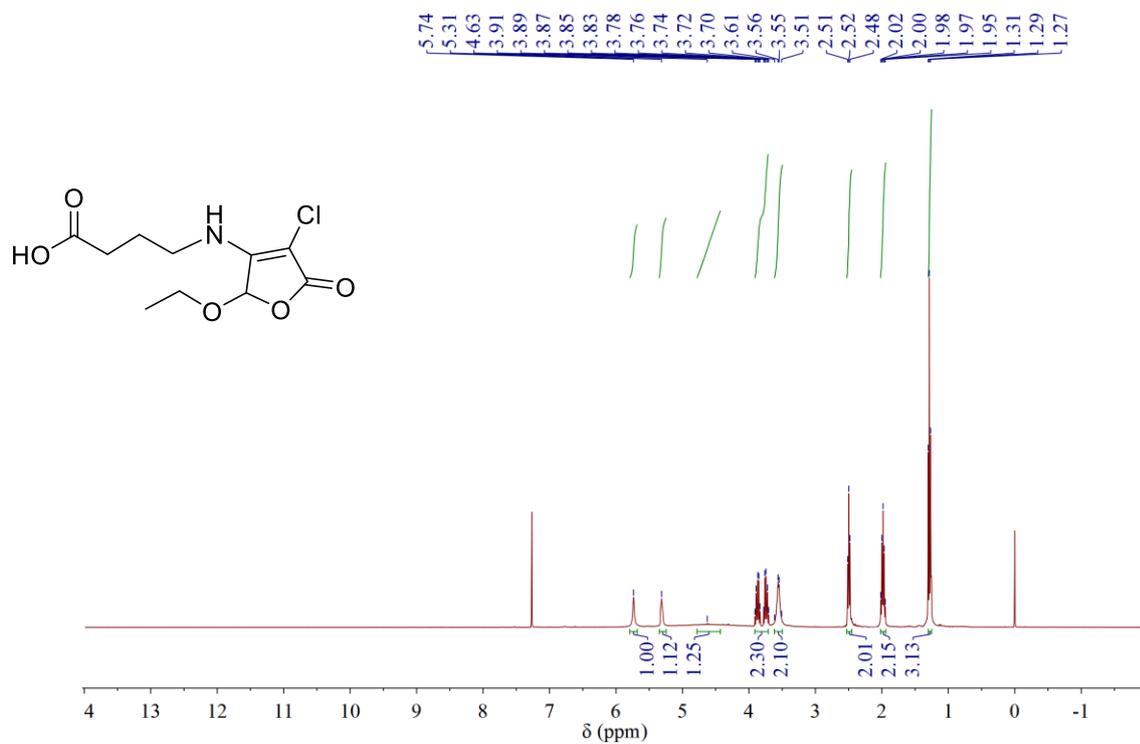


Figure 34. ¹H NMR spectrum of compound N12

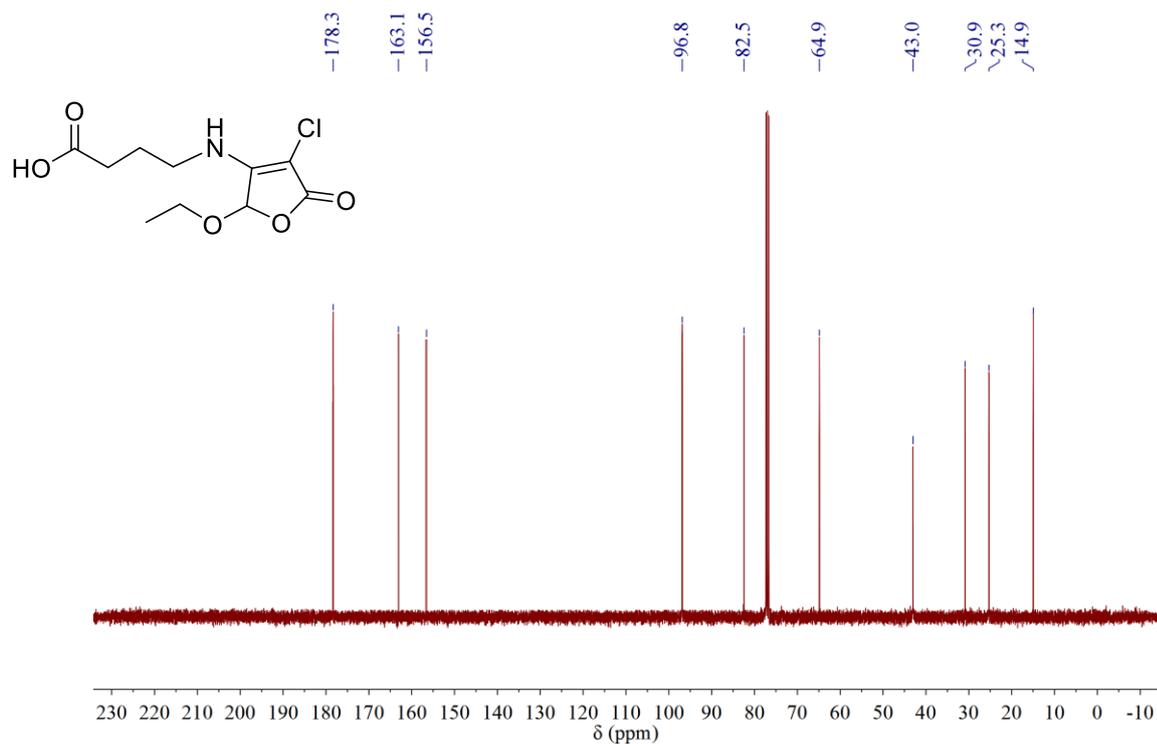


Figure 35. ¹³C NMR spectrum of compound N12

so_180109121208 #16 RT: 0.13 AV: 1 NL: 3.20E6
T: -c ESI Full ms [245.00-500.00]

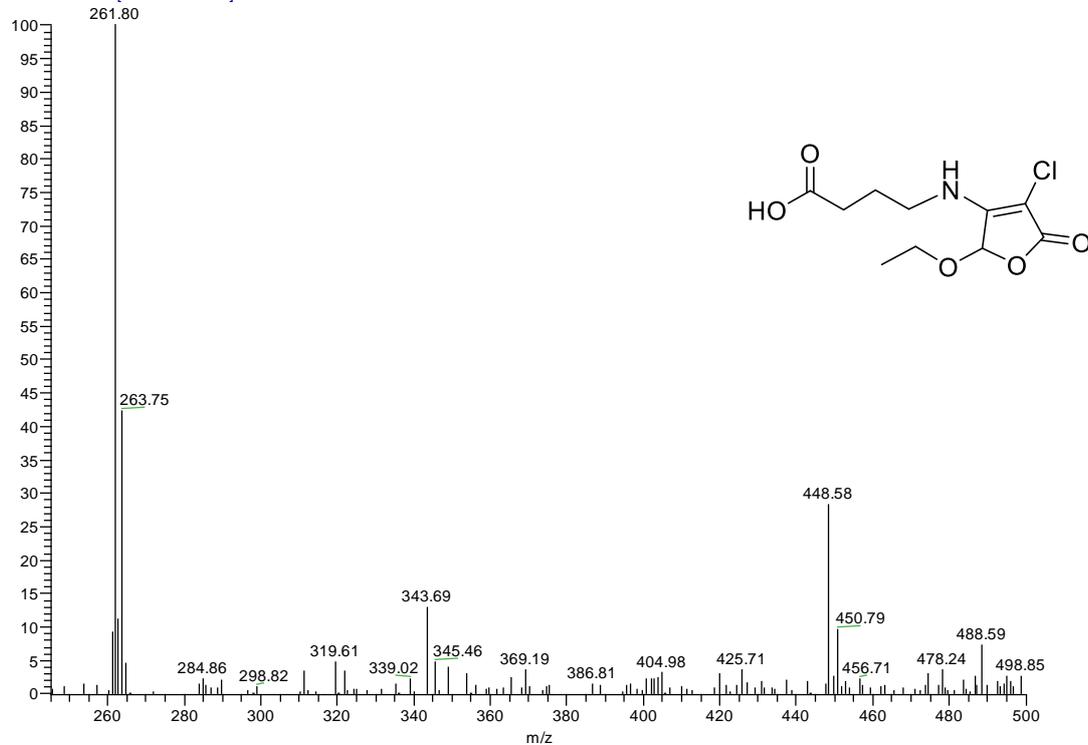


Figure 36. ESI-MS spectrum of compound N12

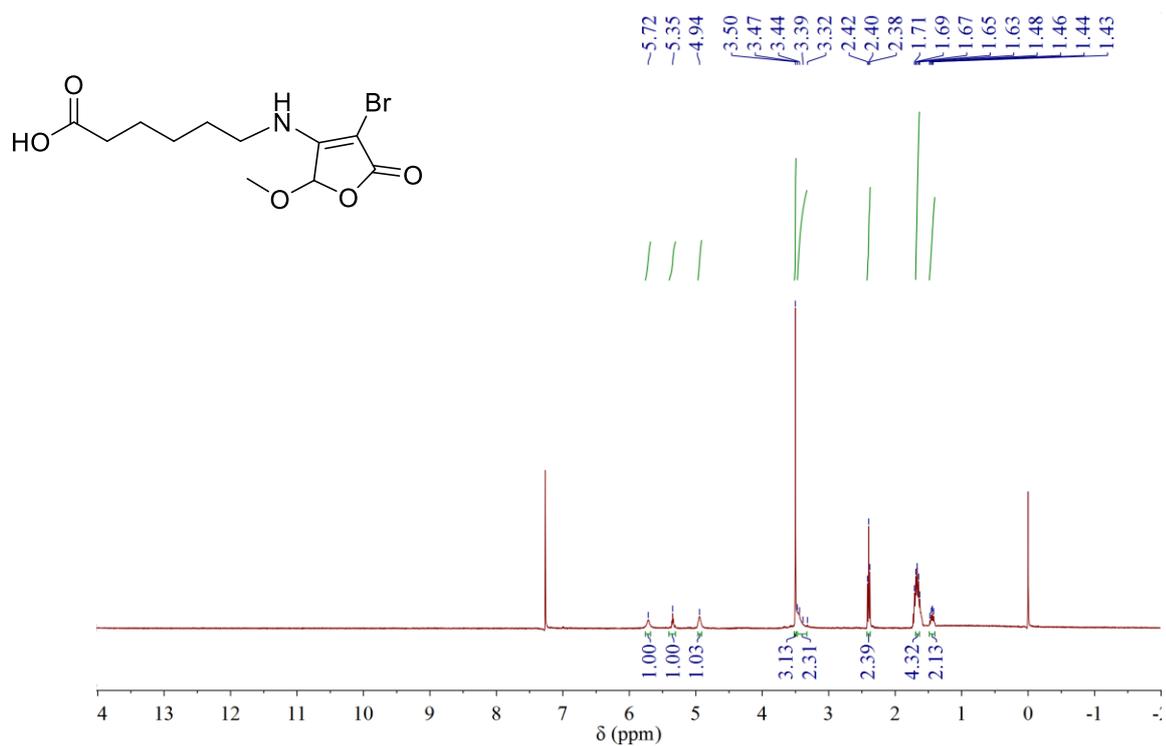


Figure 37. $^1\text{H NMR}$ spectrum of compound N13

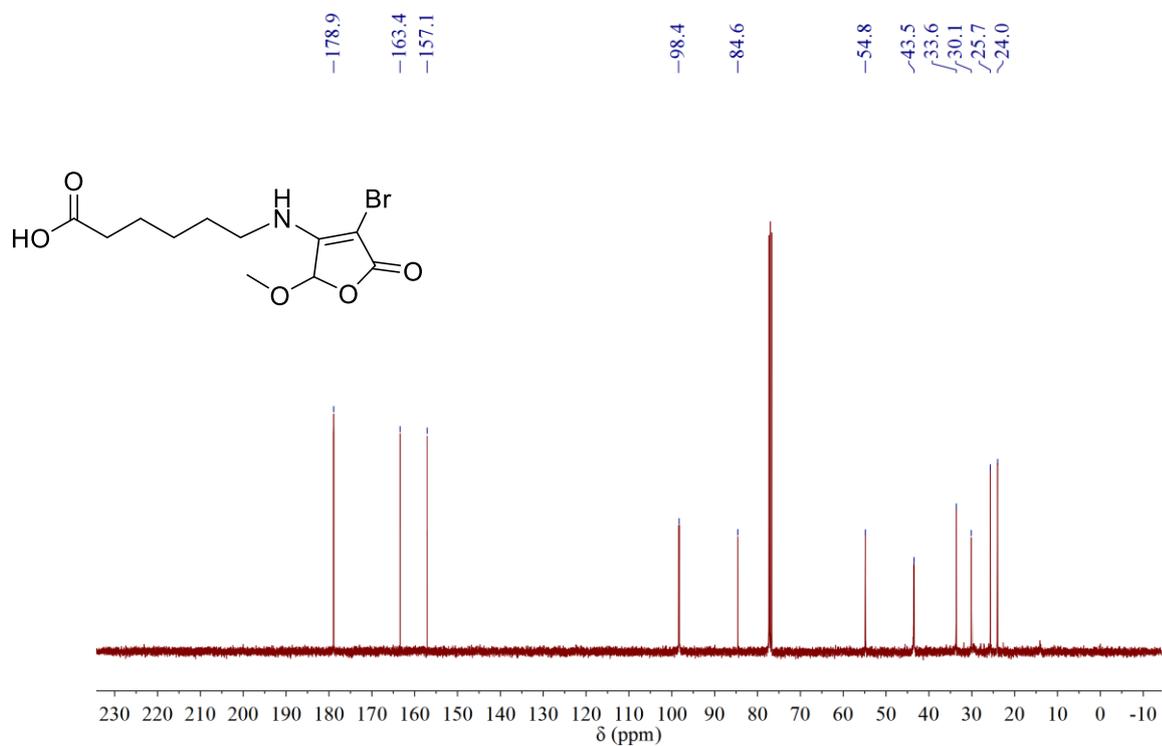


Figure 38. $^{13}\text{C NMR}$ spectrum of compound N13

FILE_161228104555 #25-32 RT: 0.18-0.23 AV: 8 NL: 1.11E9
 T: + c ESI Full ms [200.00-500.00]

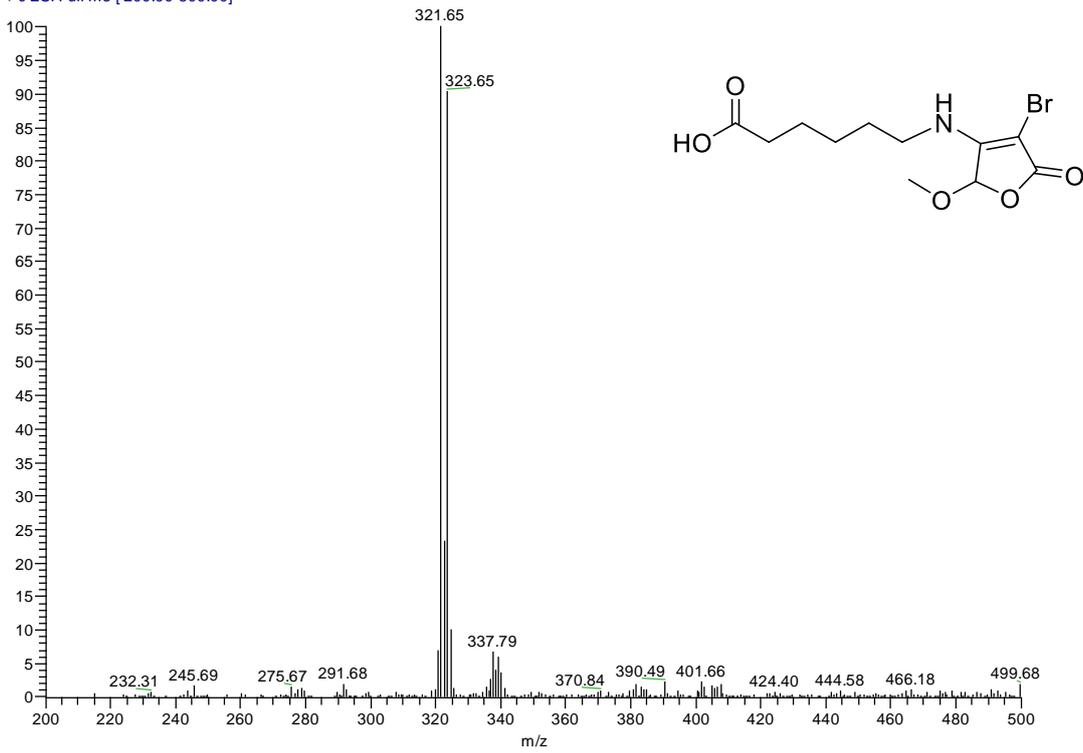


Figure 39. ESI-MS spectrum of compound N13

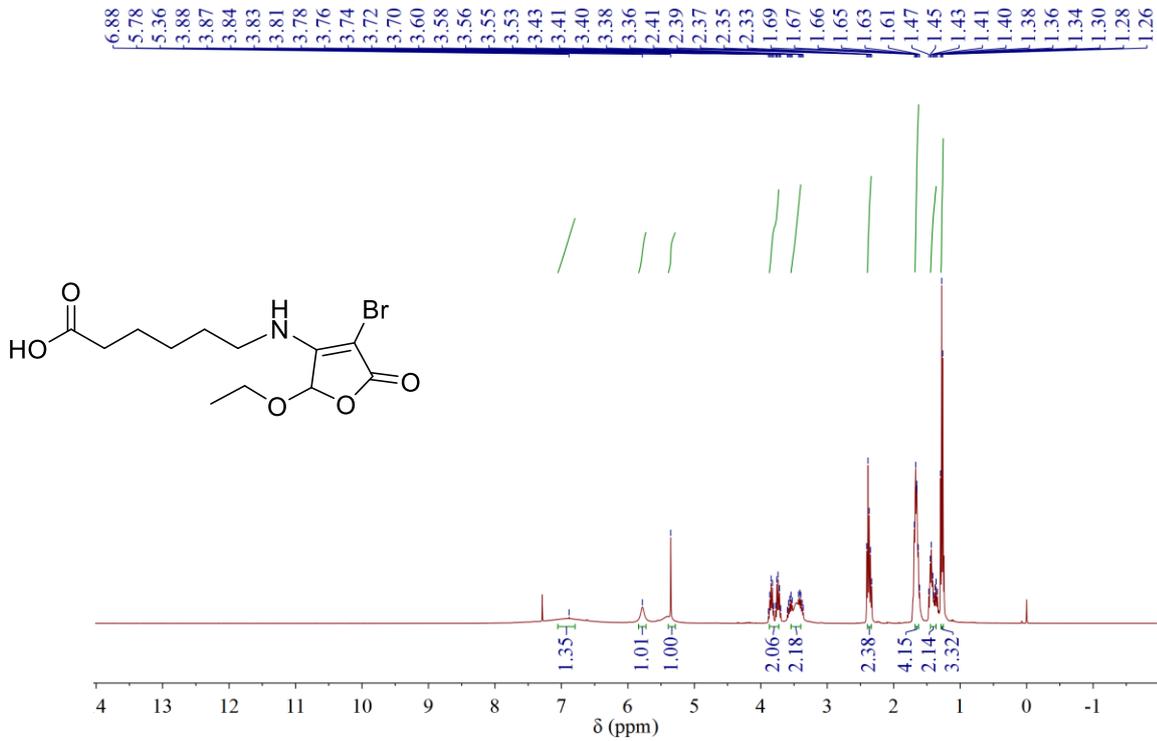


Figure 40. ¹H NMR spectrum of compound N14

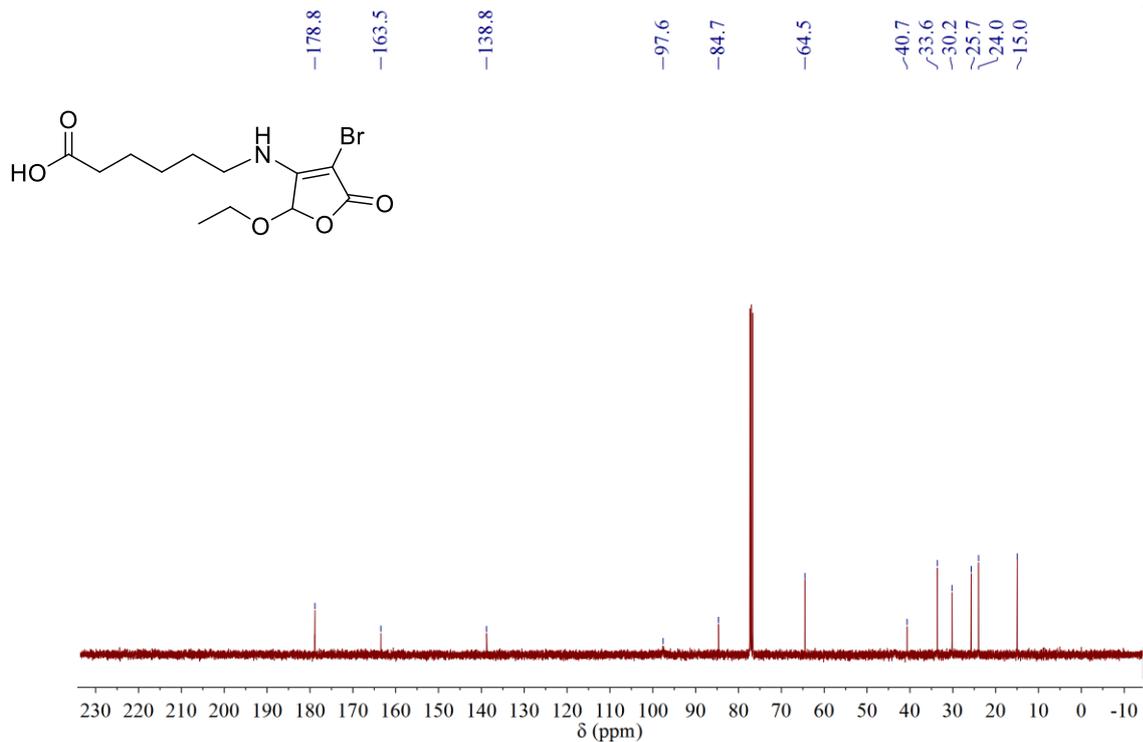


Figure 41. ¹³C NMR spectrum of compound N14

FILE_161228110003 #14 RT: 0.10 AV: 1 NL: 5.28E8
T: + c ESI Full ms [200.00-500.00]

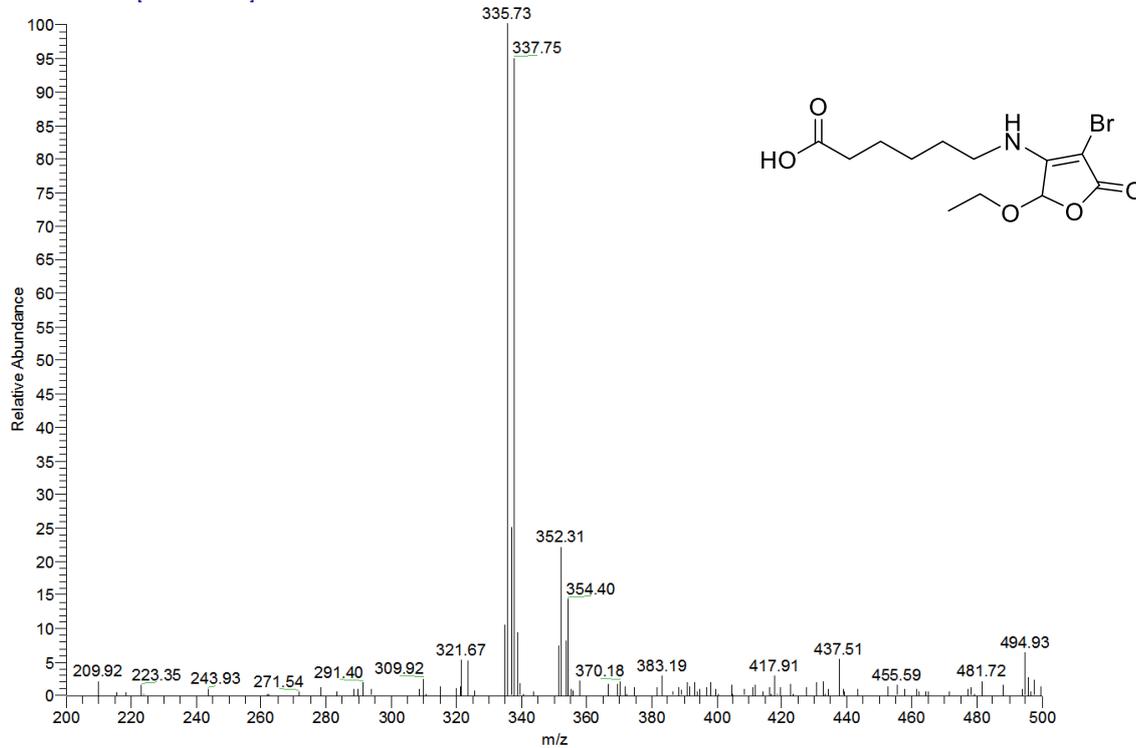


Figure 42. ESI-MS spectrum of compound N14

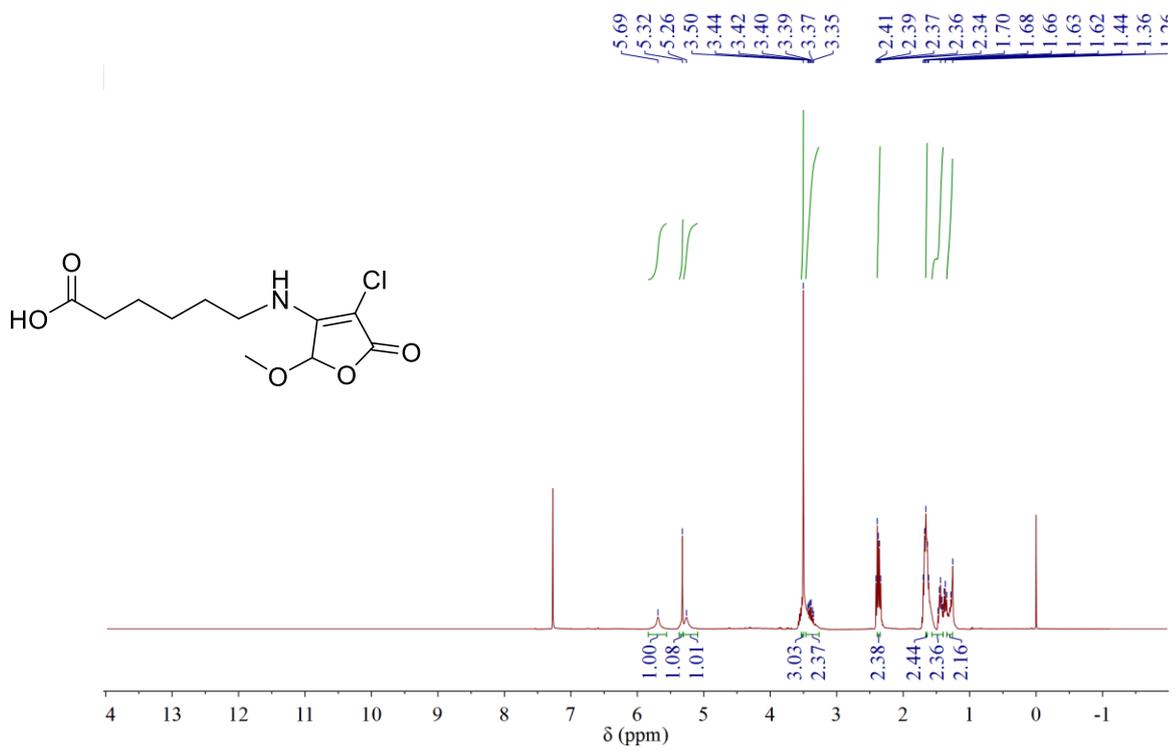


Figure 43. ¹H NMR spectrum of compound N15

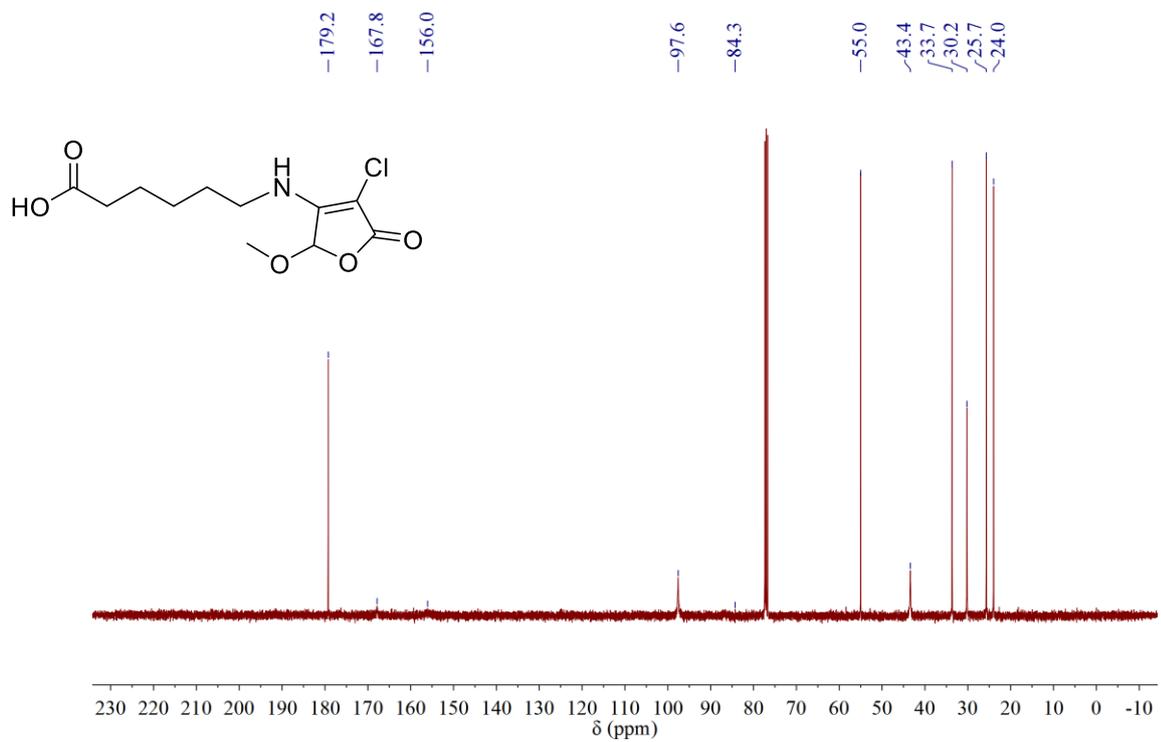


Figure 44. ¹³C NMR spectrum of compound N15

2-2_170320111028 #27 RT: 0.21 AV: 1 NL: 1.23E8
T: +c ESI Full ms [150.00-500.00]

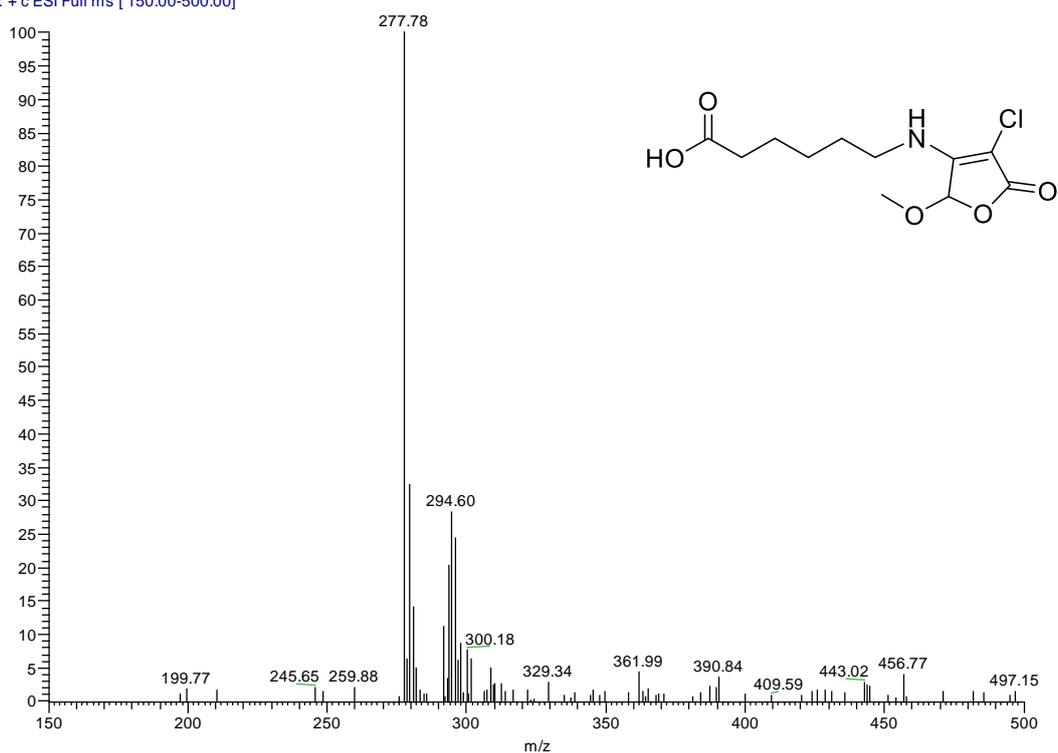


Figure 45. ESI-MS spectrum of compound N15

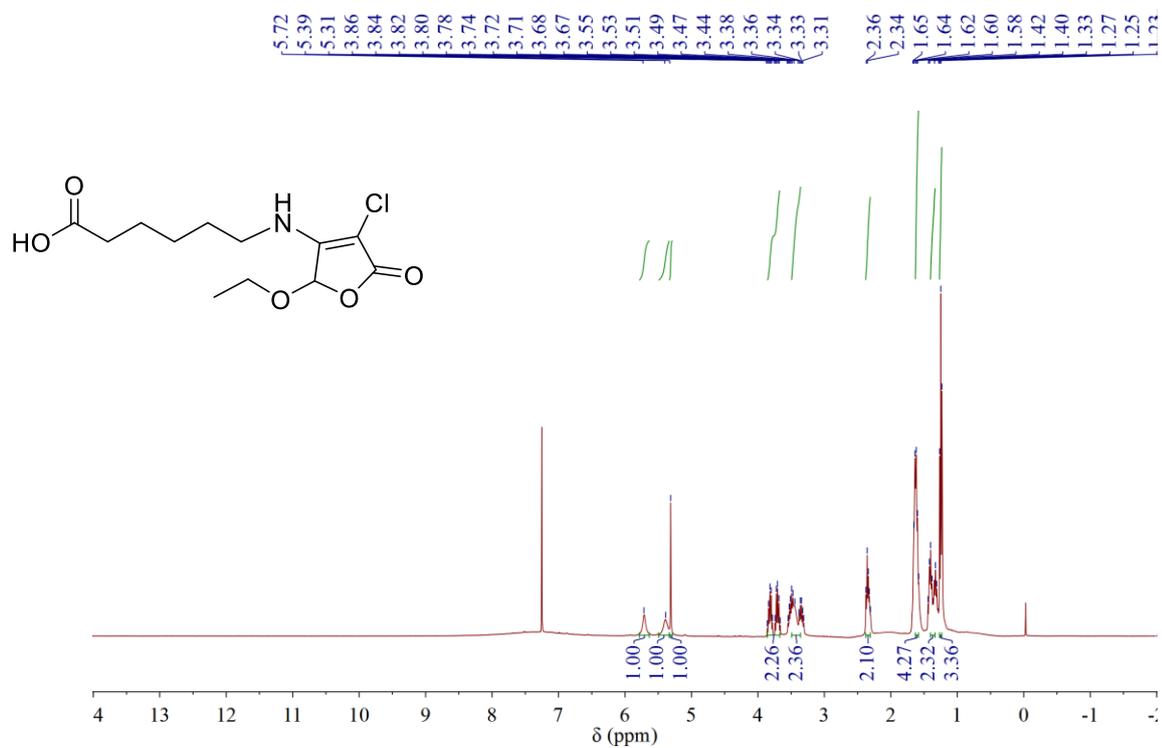


Figure 46. ¹H NMR spectrum of compound N16

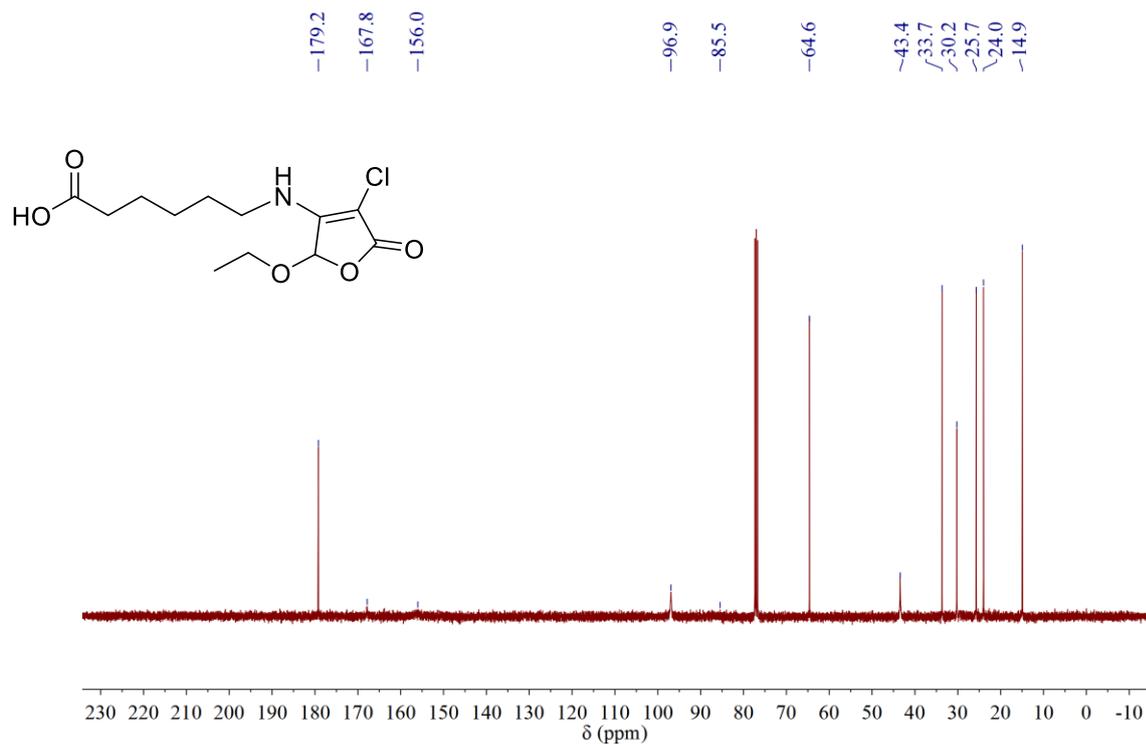


Figure 47. ^{13}C NMR spectrum of compound N16

2-2_170320111928 #25 RT: 0.19 AV: 1 NL: 2.60E8
T: + c ESI Full ms [150.00-500.00]

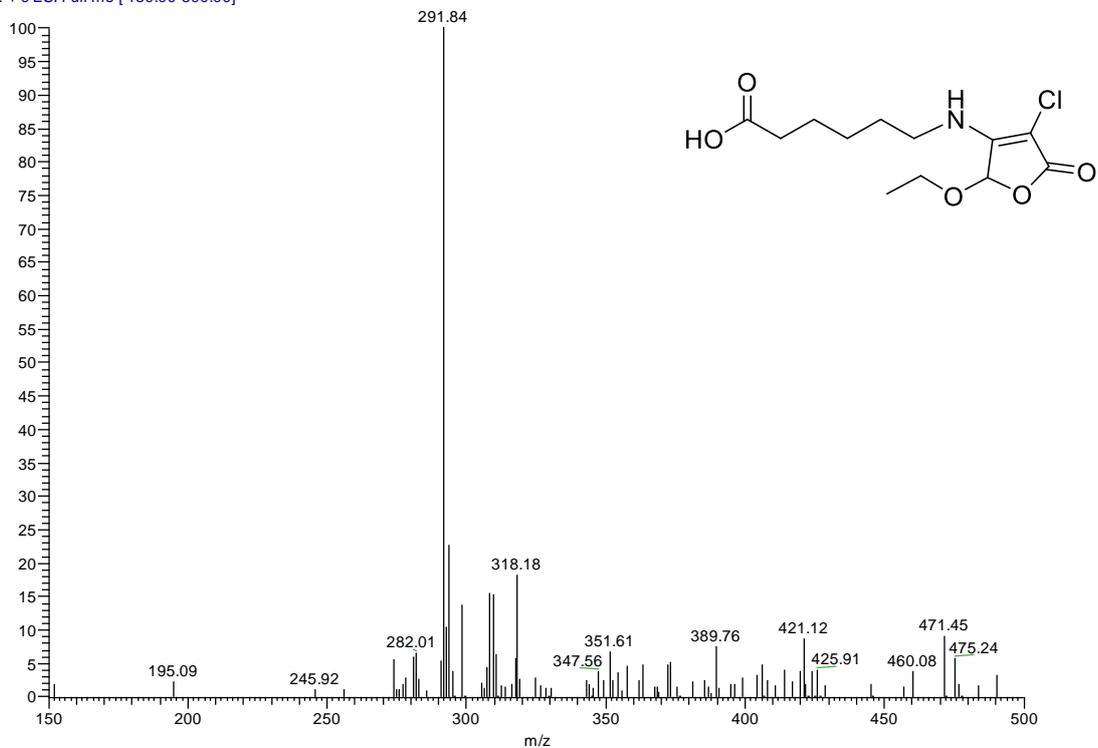


Figure 48. ESI-MS spectrum of compound N16

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.