Supporting Information

Design, synthesis and biological activity evaluation of novel conjugated sialic acid and pentacyclic triterpene derivatives as anti-influenza entry inhibitors

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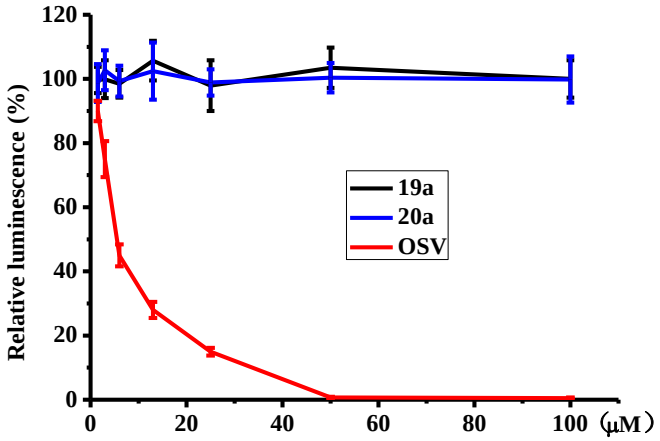
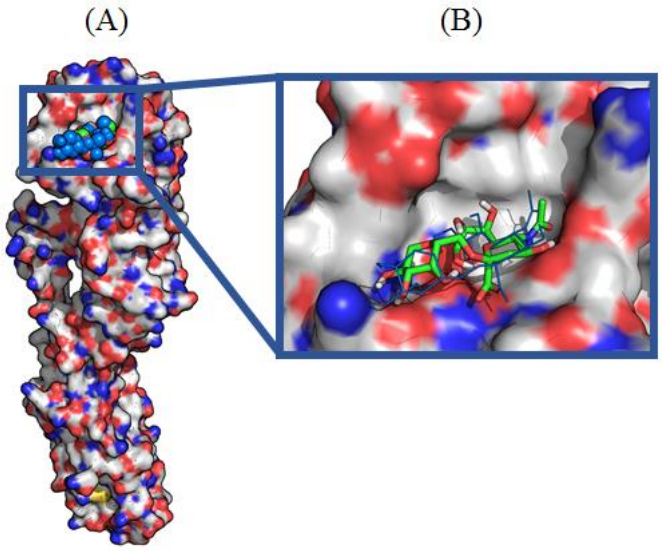


SI Figure 1. Compounds **19a** and **20a** had no inhibitory effect on the influenza virus neuraminidase activity. Compounds or OSV-P with two-fold serial dilution with PBS were mixed with influenza virus. The substrate solution (4-MUNANA) was mixed with the test compounds/virus mixture and incubated for 30 min at 37 ℃. Neuraminidase activity was measured by fluorescence of 4-methylumbelliferone with fluorescence spectrophotometer. Each point represents the mean ± S.E.M. for three independent experiments.



SI Figure 2. Docking structure of the original ligand Gal-2-Sia binding with a single chain of HA protein (Protein Data Bank: 1RVT) according to docking calculation. (A) Overview of the protein surface. The binding pocket is highlighted in the blue square. Gal-2-Sia from docking data is shown as green spheres and Gal-2-Sia in the X-ray crystal structure PDBid 1RVT is shown as blue spheres. (B) Closer view of the binding pocket. Gal-2-Sia from docking data is shown as green sticks and Gal-2-Sia in the X-ray crystal structure PDBid 1RVT is shown as blue lines.

Figure 1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **7**

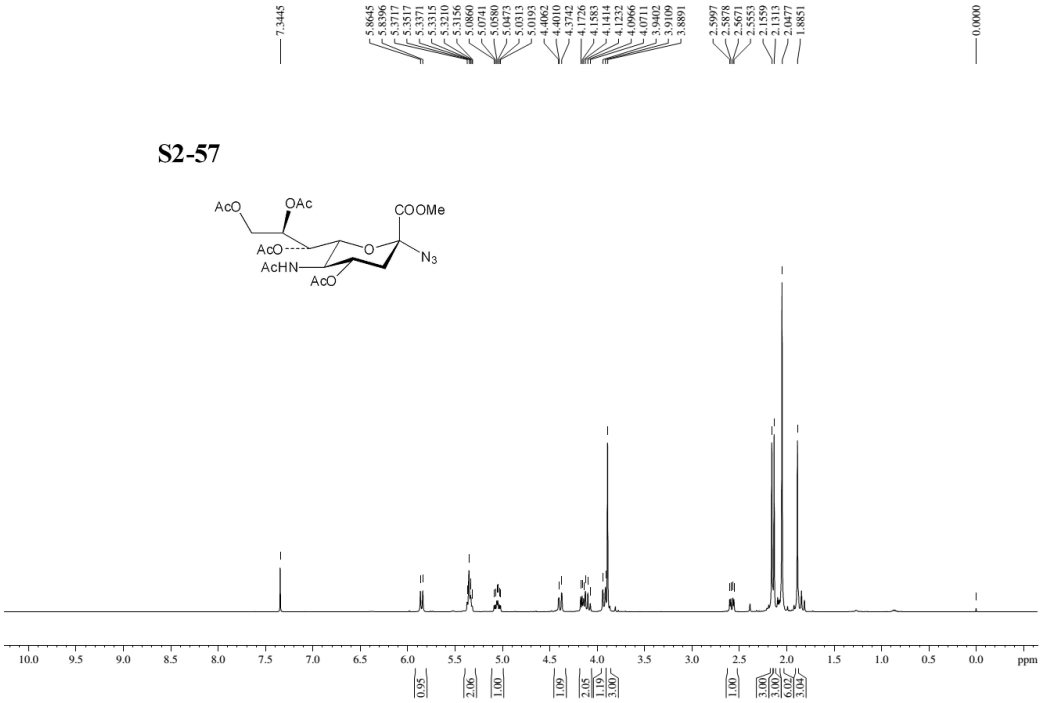


Figure 2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **7**

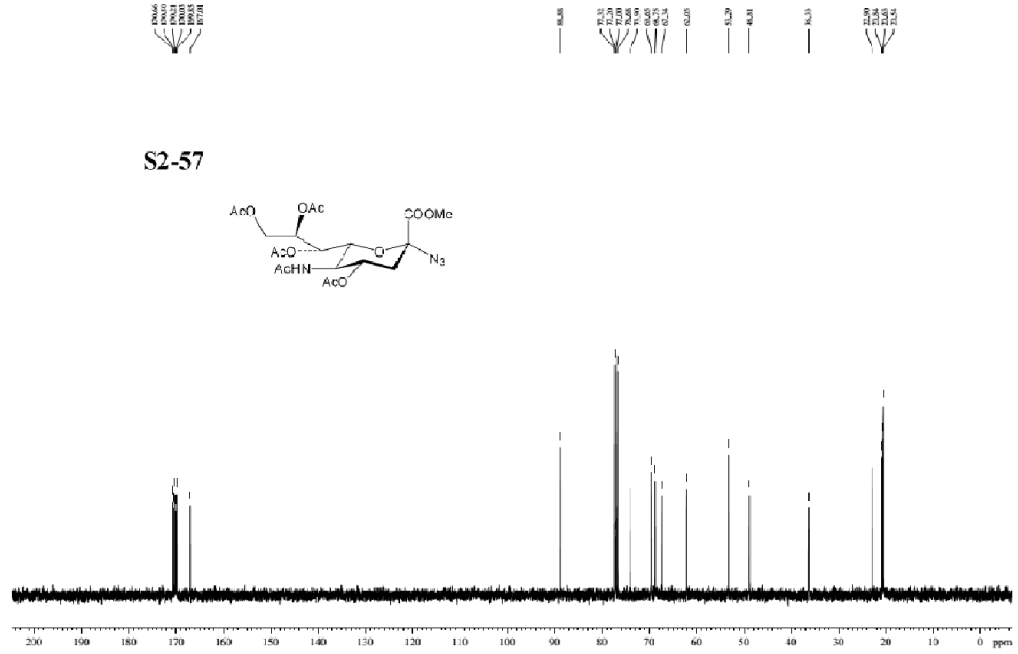


Figure 3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8a**

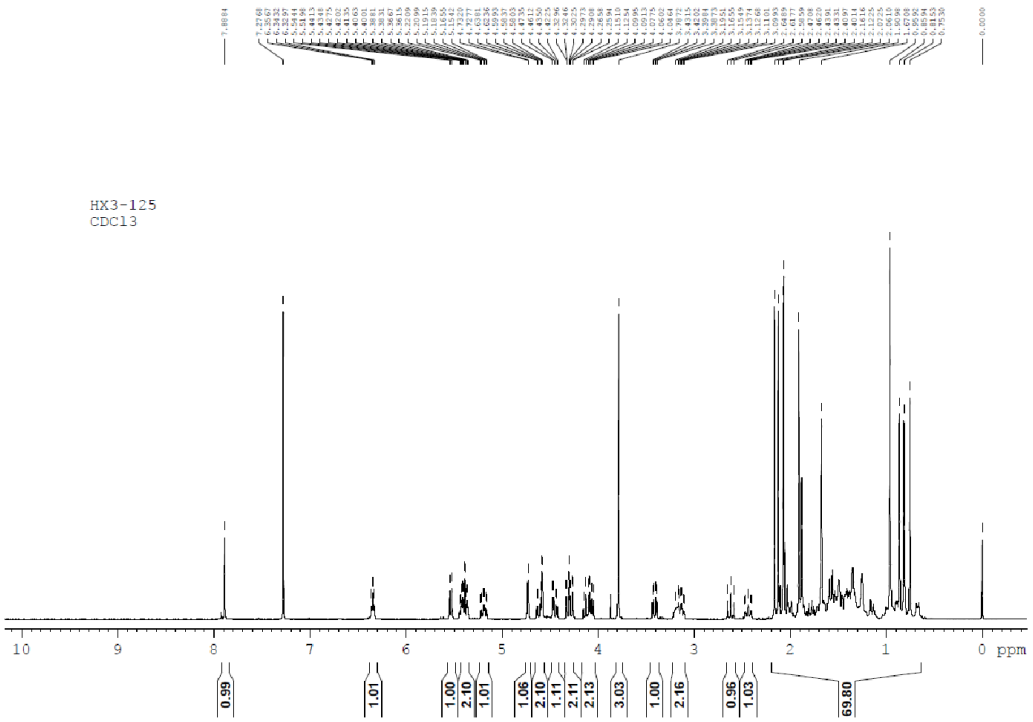


Figure 4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8a**

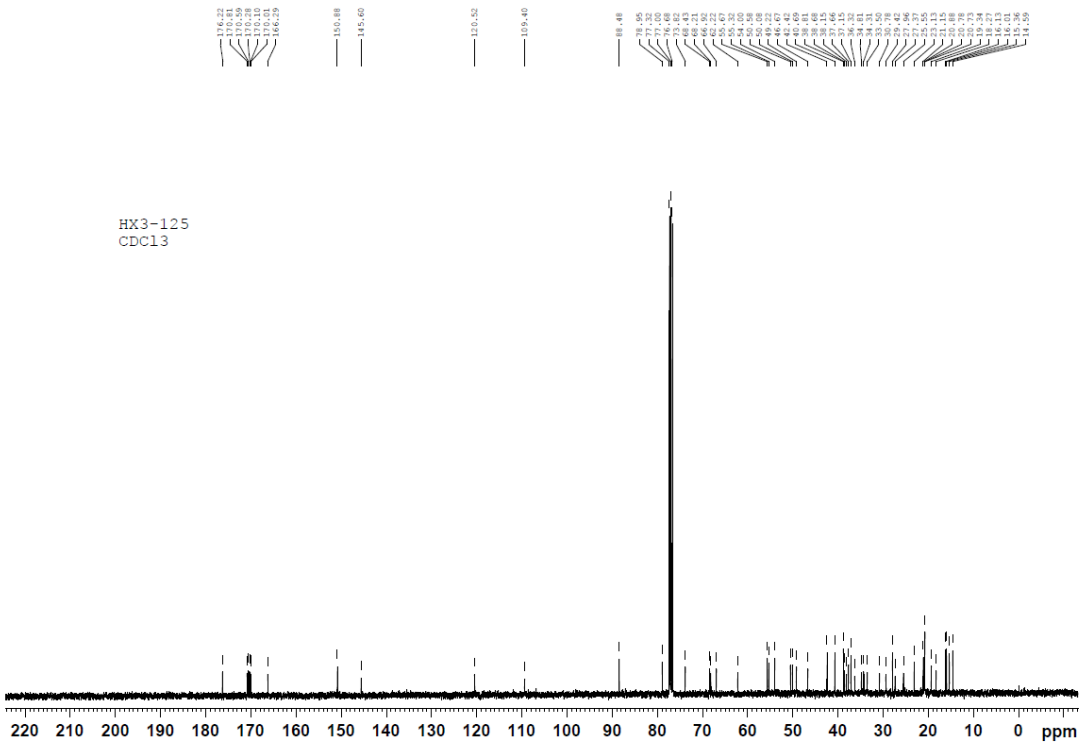


Figure 5. HR-ESI-MS spectrum of compound **8a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-125	C53 H79 N5 O14	C53 H79 N5 Na O14	1032.5523	1032.5516	-0.75

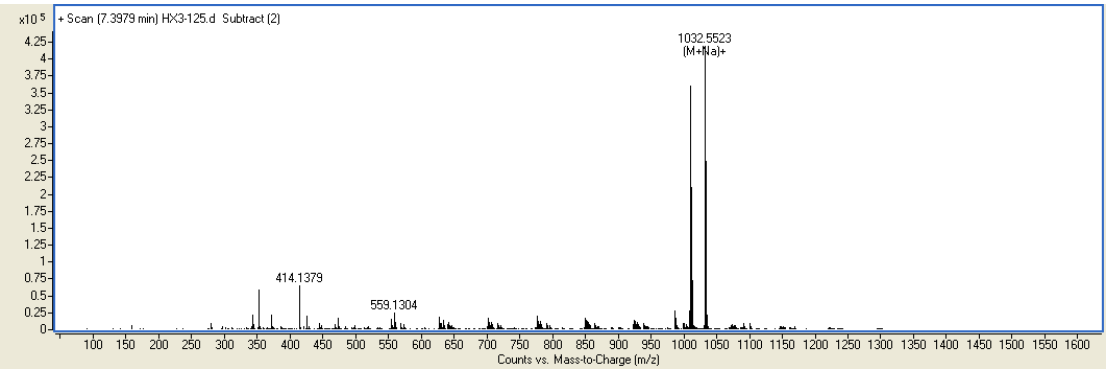


Figure 6. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8b**

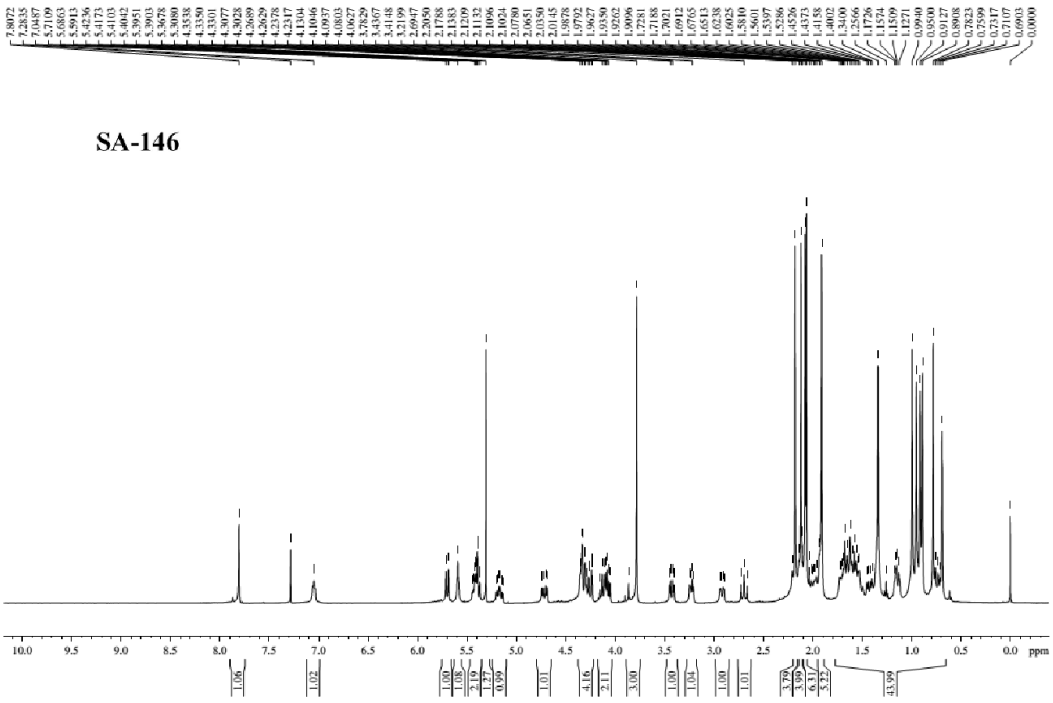


Figure 7. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8b**

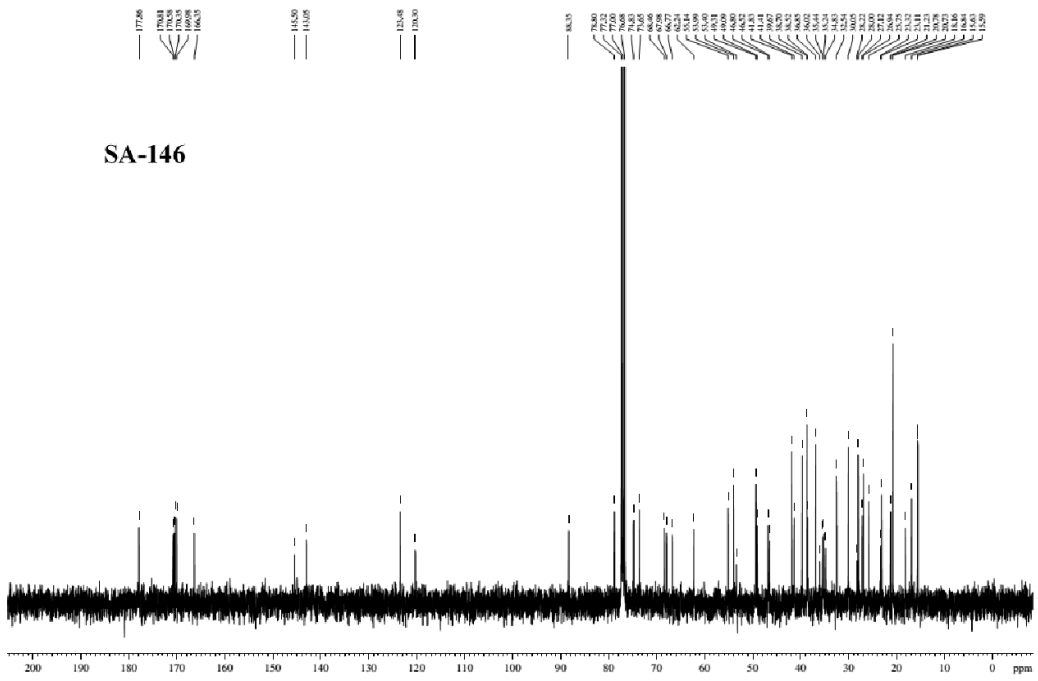


Figure 8. HR-ESI-MS spectrum of compound **8b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Measured Mass	Exact Mass	Delta (m/z)	Delta (ppm)	Description
SA-146	1010.57043	1010.56963	0.00080	0.79163	

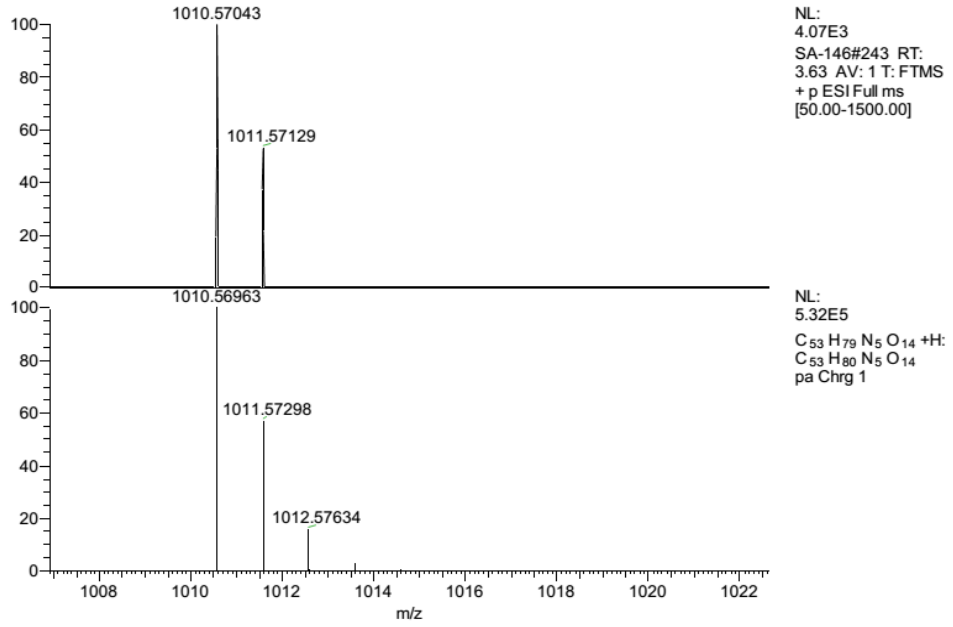


Figure 9. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8c**

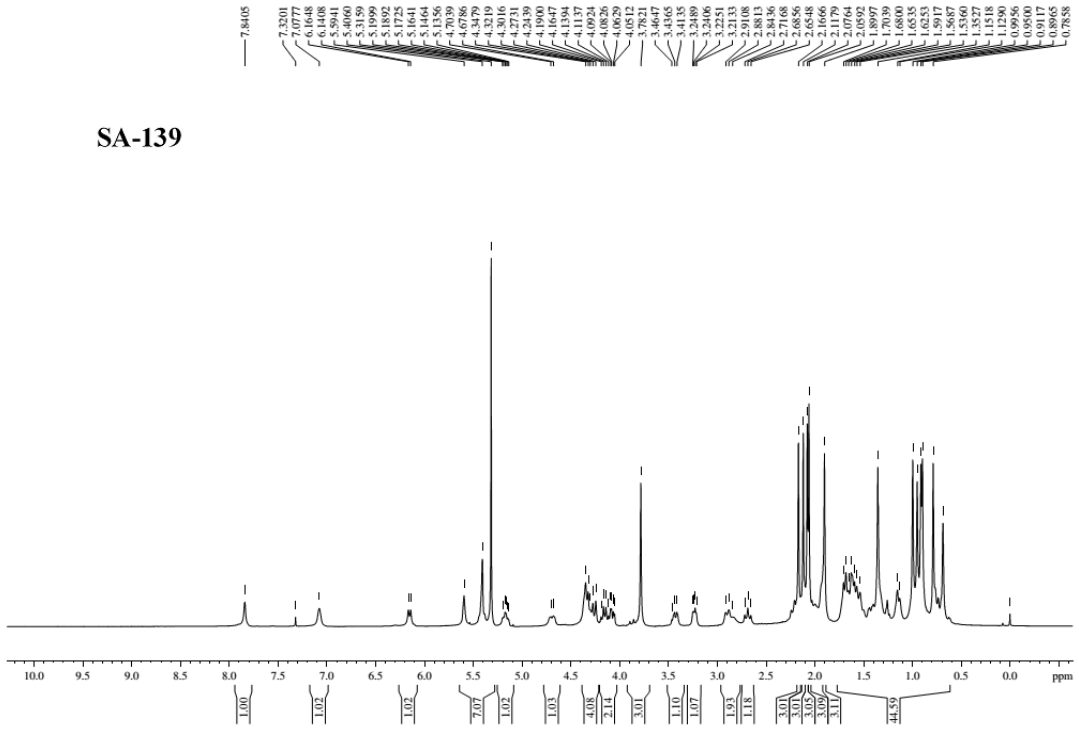


Figure 10. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8c**

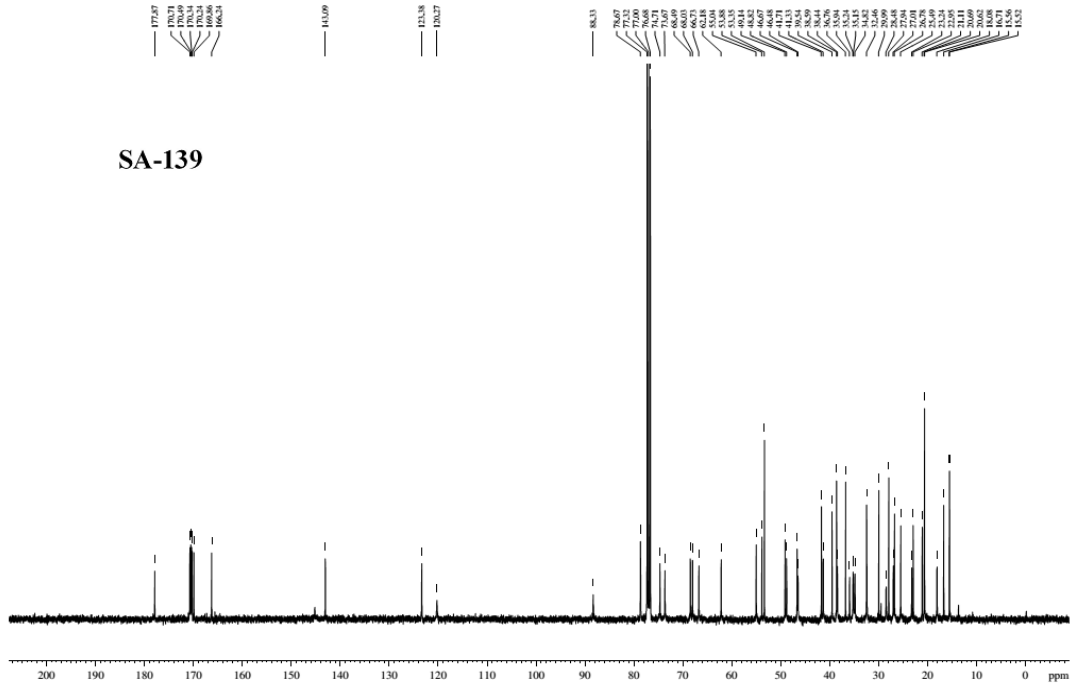


Figure 11. HR-ESI-MS spectrum of compound **8c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Measured Mass	Exact Mass	Delta (m/z)	Delta (ppm)	Description
SA-139	1026.56433	1026.56454	-0.00021	-0.20457	

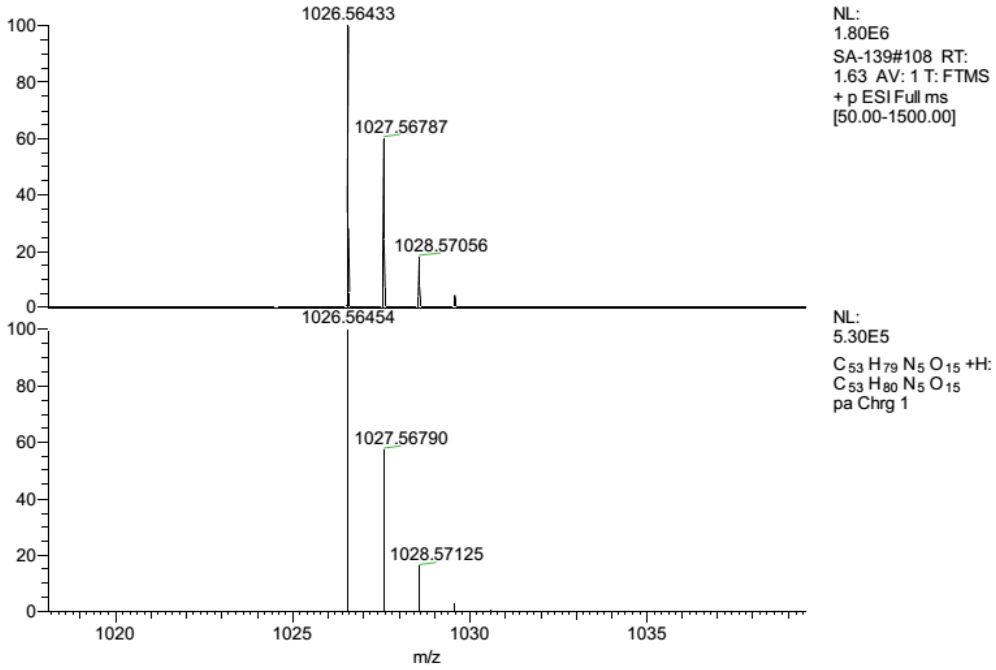
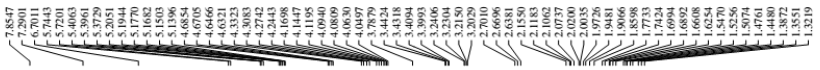


Figure 12. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8d**



S2-8

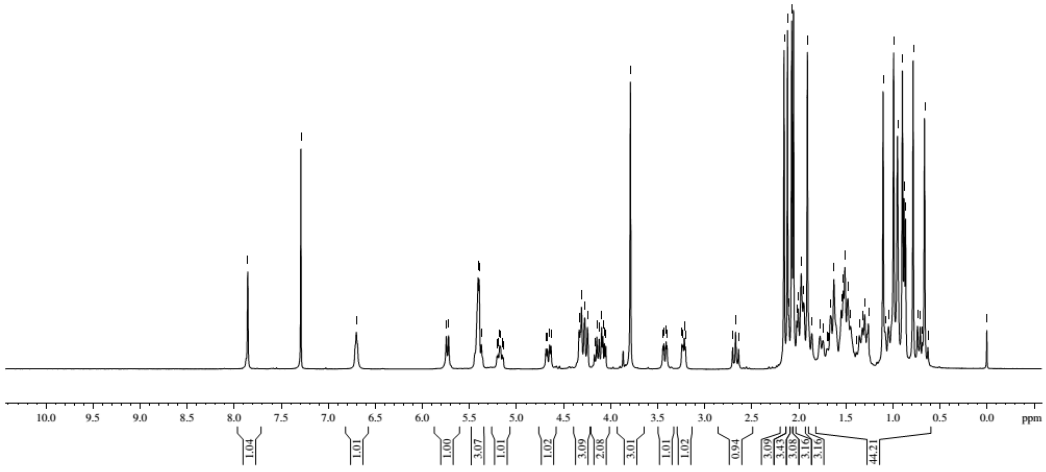


Figure 13. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8d**

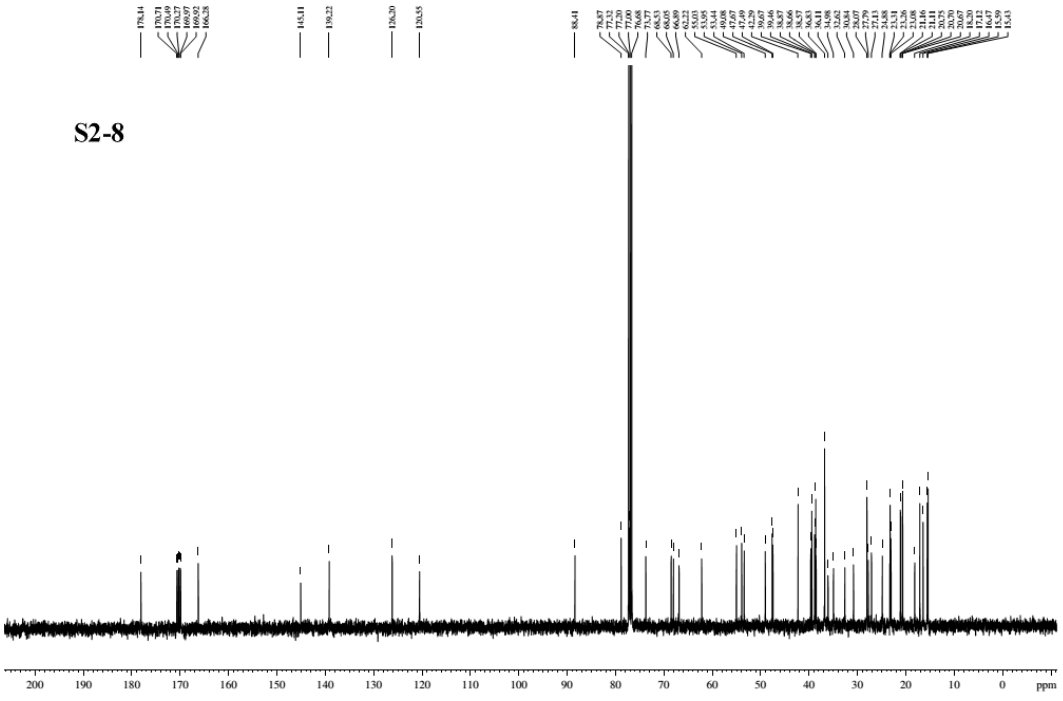


Figure 14. HR-ESI-MS spectrum of compound **8d**

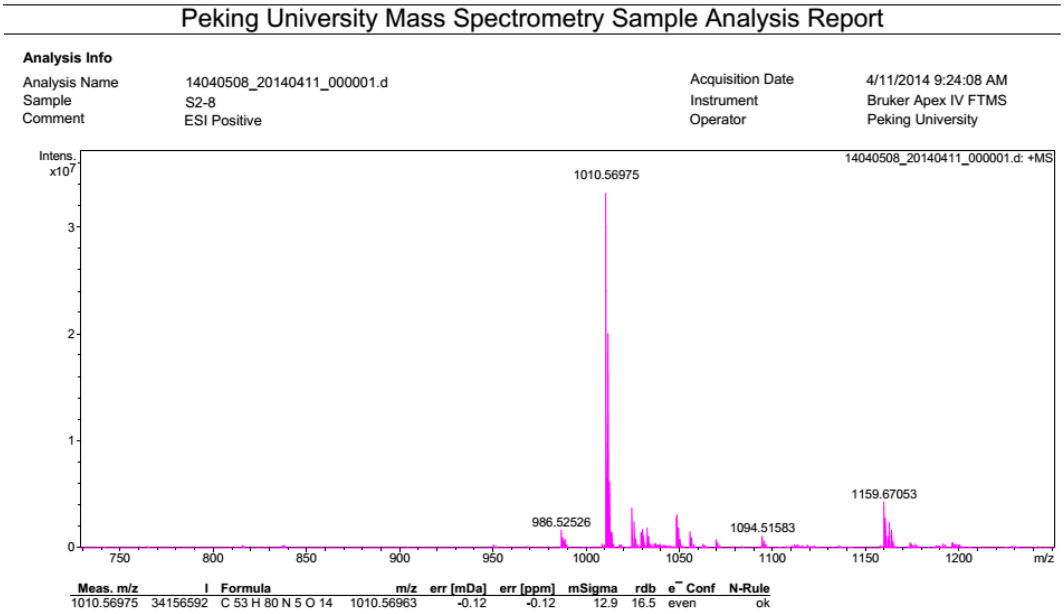


Figure 15. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9a**

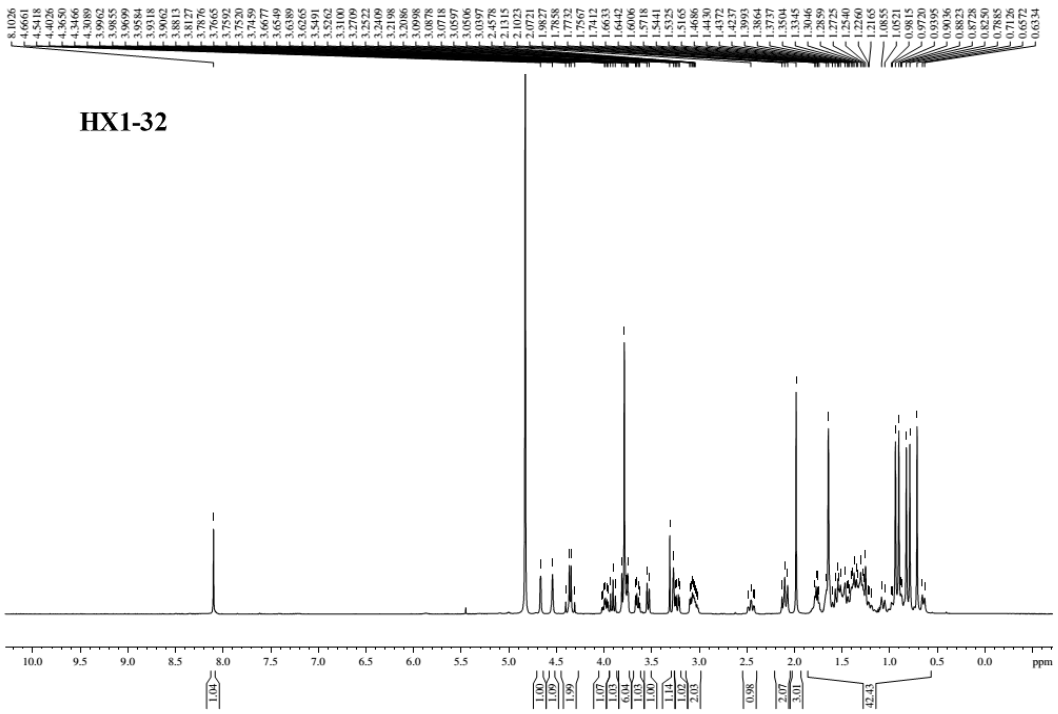


Figure 16. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9a**

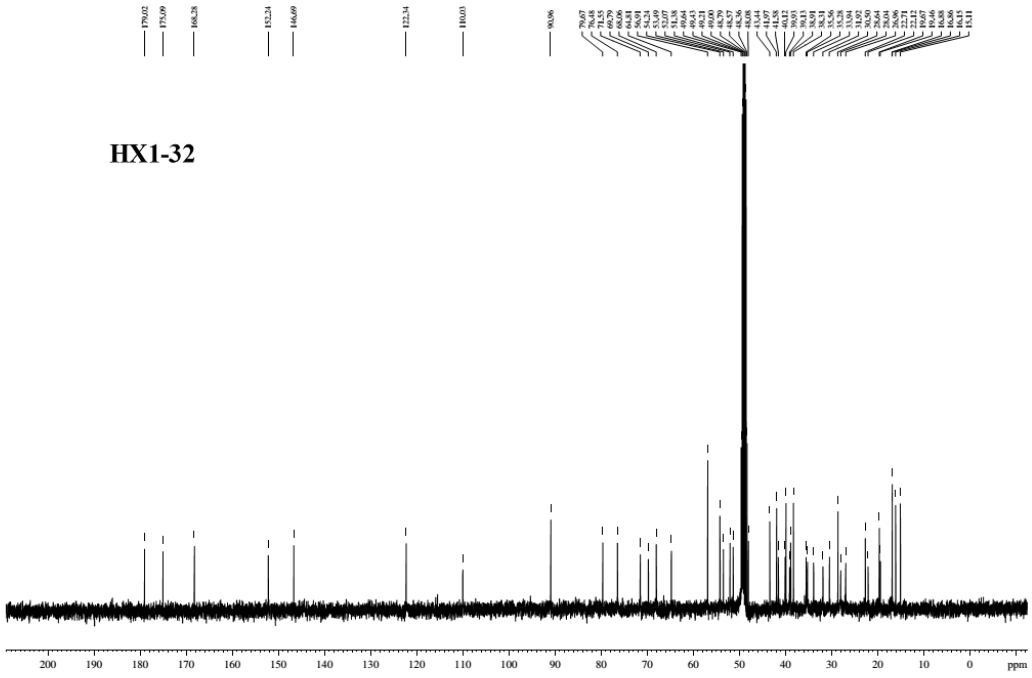


Figure 17. HR-ESI-MS spectrum of compound **9a**

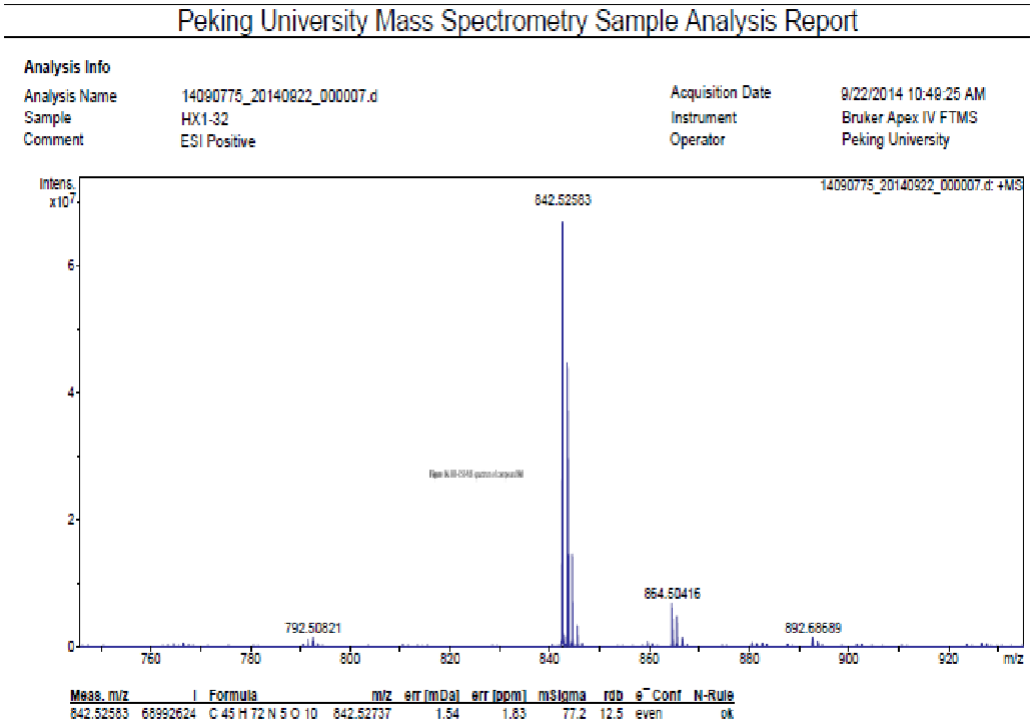


Figure 18. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9b**

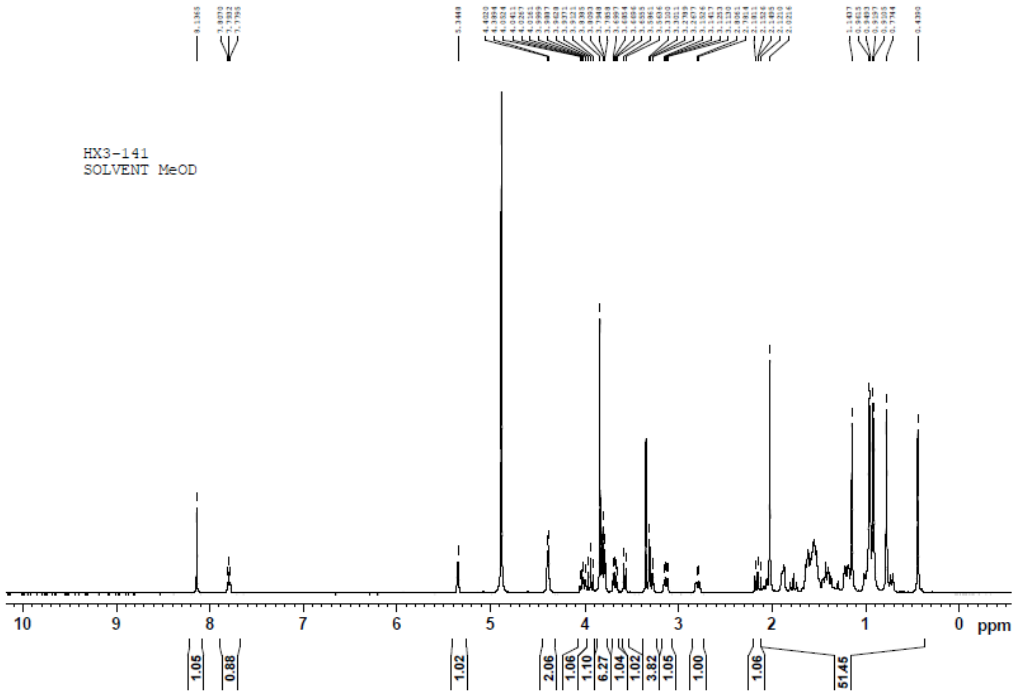


Figure 19. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9b**

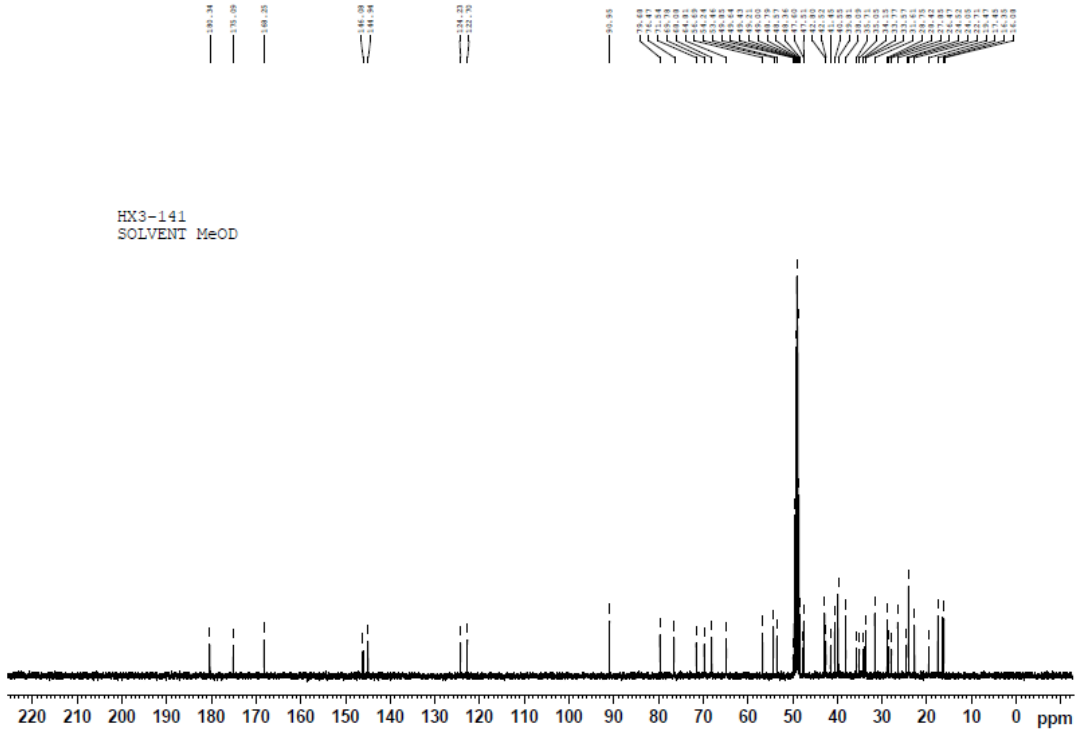


Figure 20. HR-ESI-MS spectrum of compound **9b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-141	C45 H71 N5 O10	C45 H71 N5 Na O10	864.5099	864.5093	-0.72

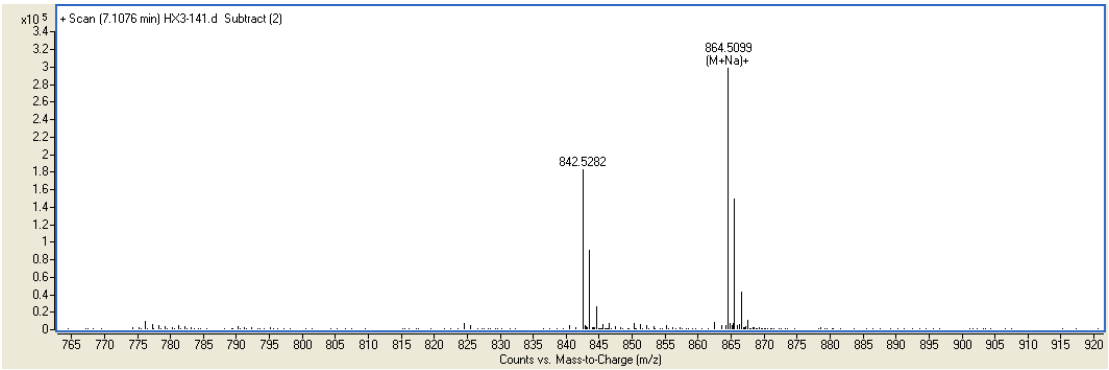


Figure 21. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9c**

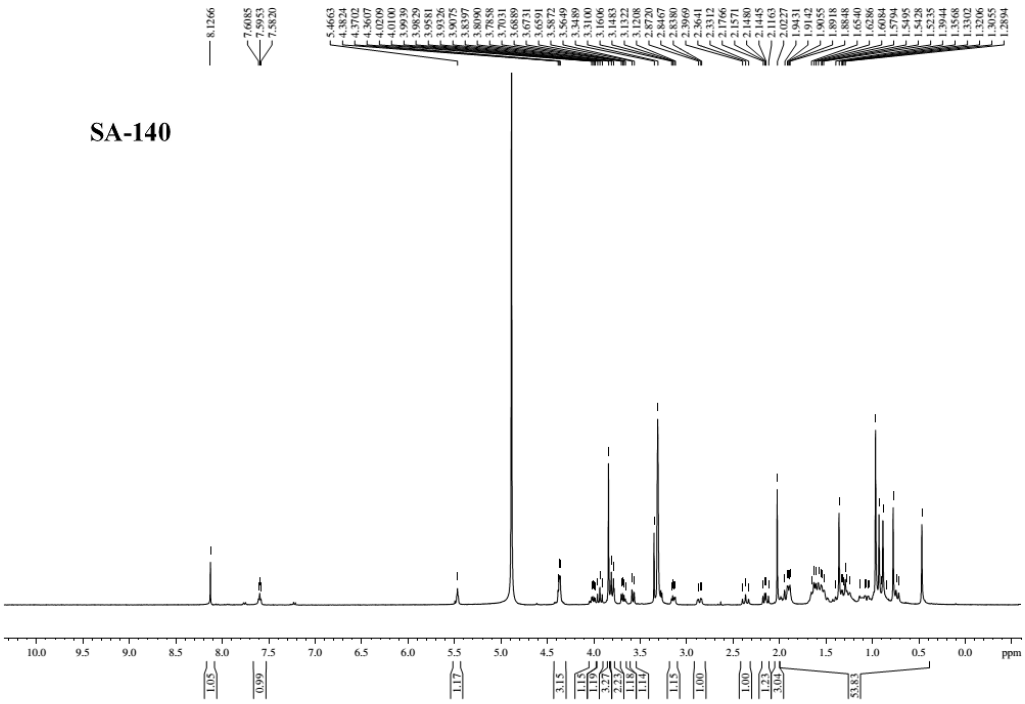


Figure 22. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9c**

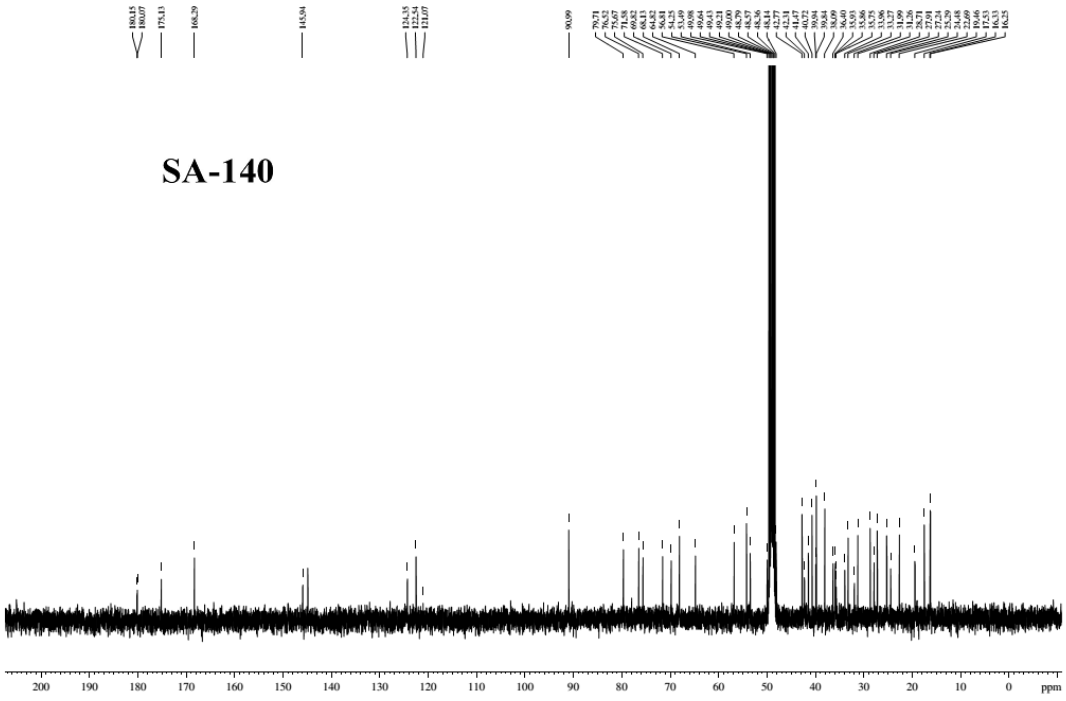


Figure 23. HR-ESI-MS spectrum of compound **9c**

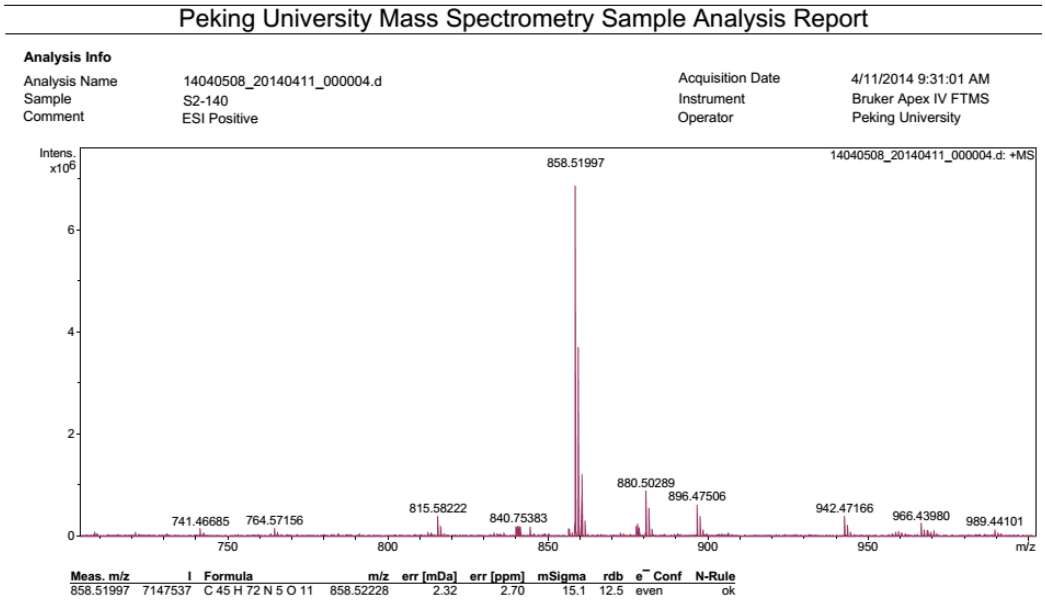


Figure 24. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9d**

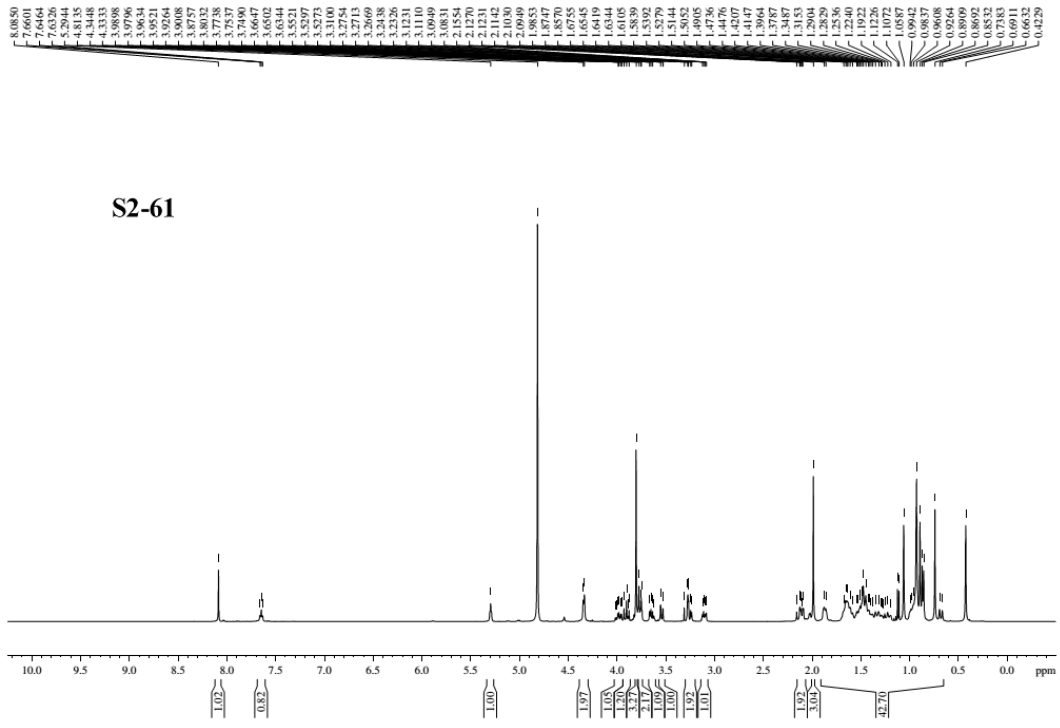


Figure 25. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9d**

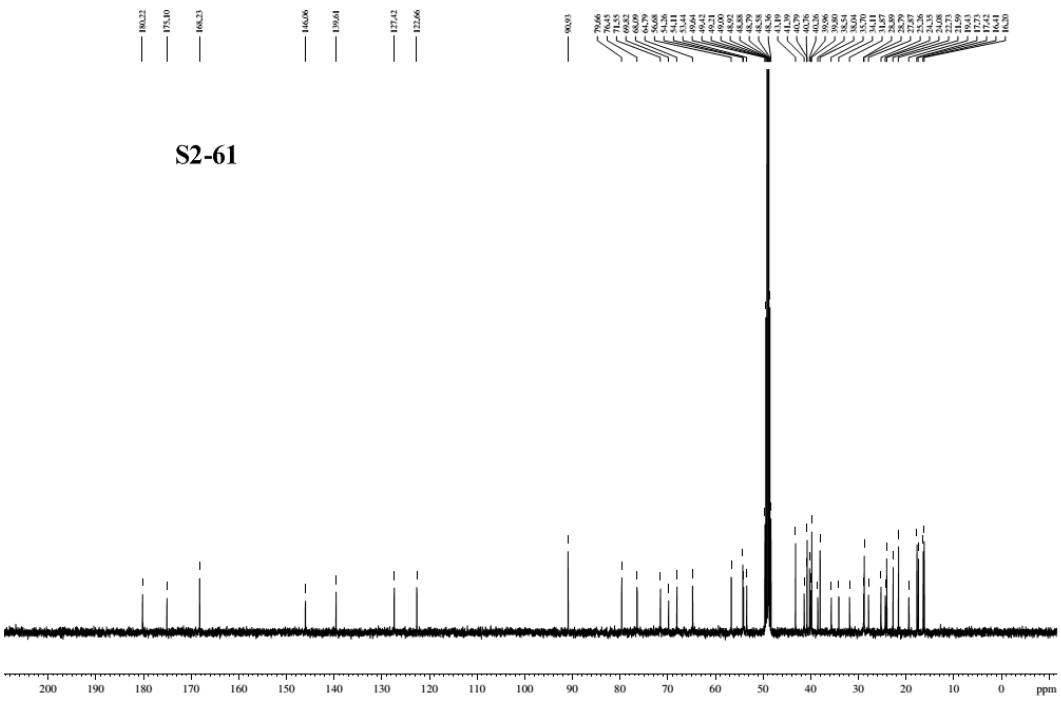


Figure 26. HR-ESI-MS spectrum of compound **9d**

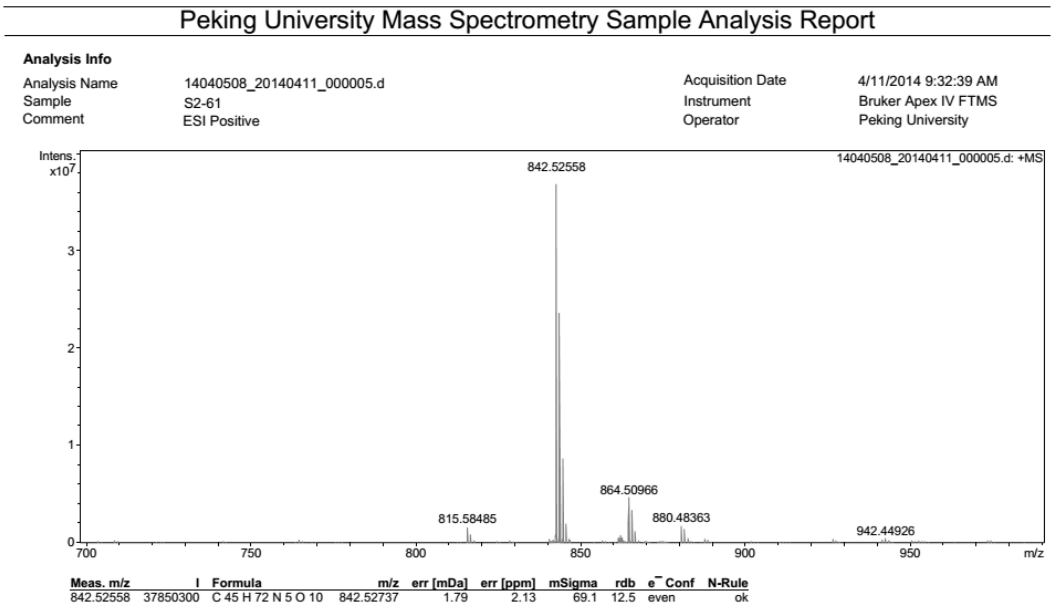


Figure 27. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **10**

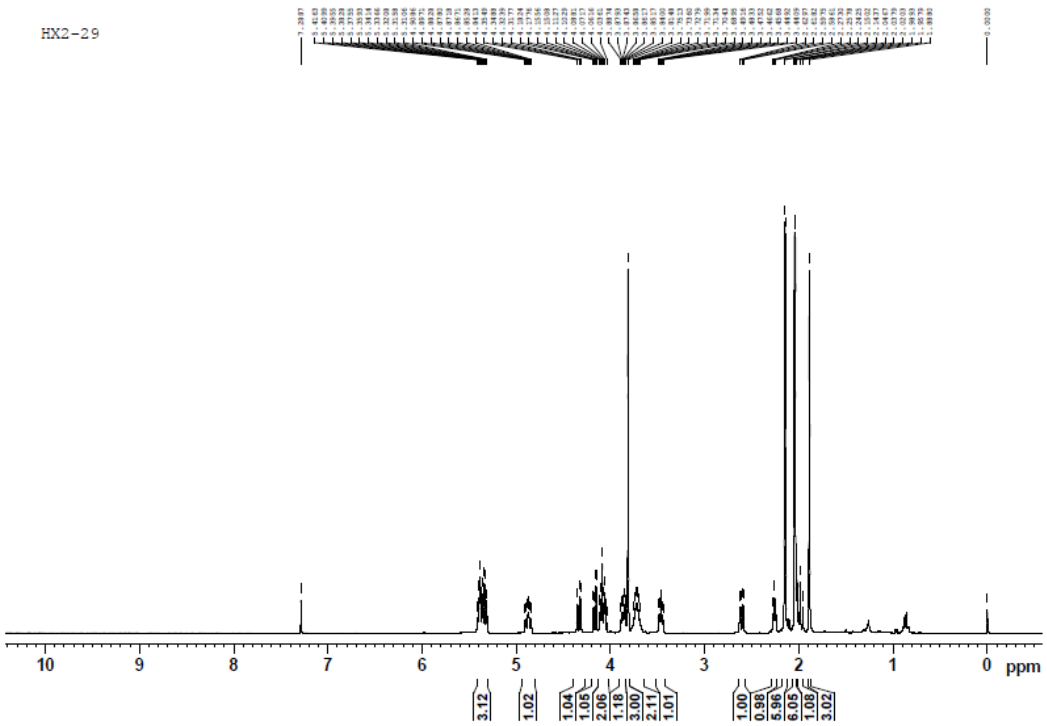


Figure 28. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **10**

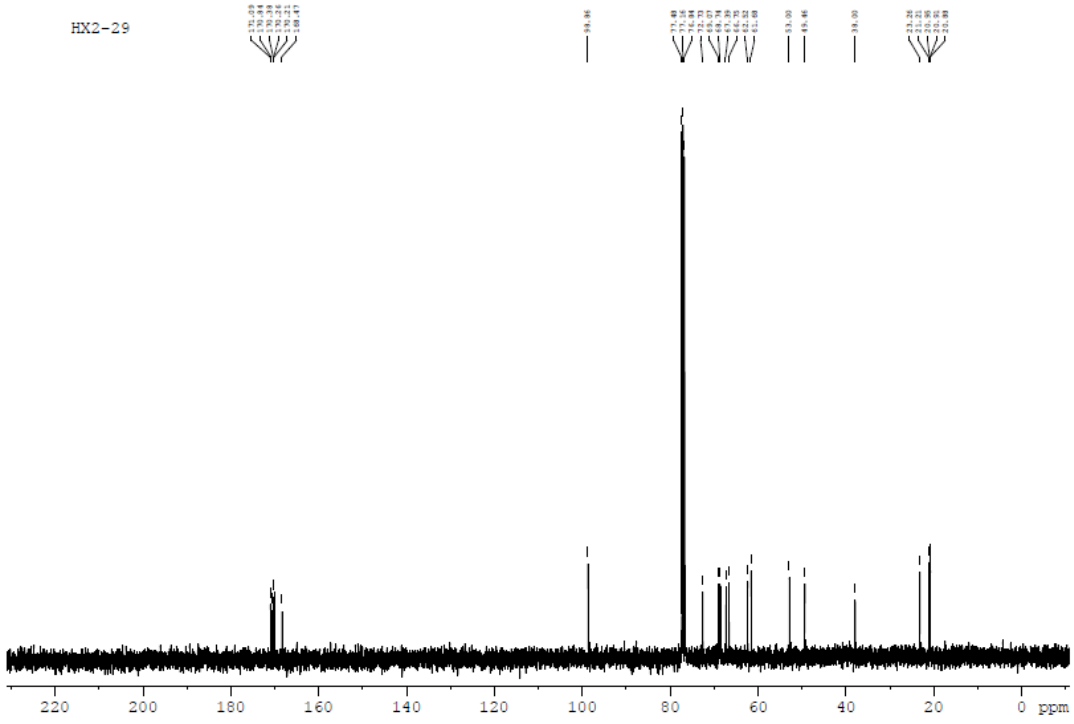


Figure 29. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **11**

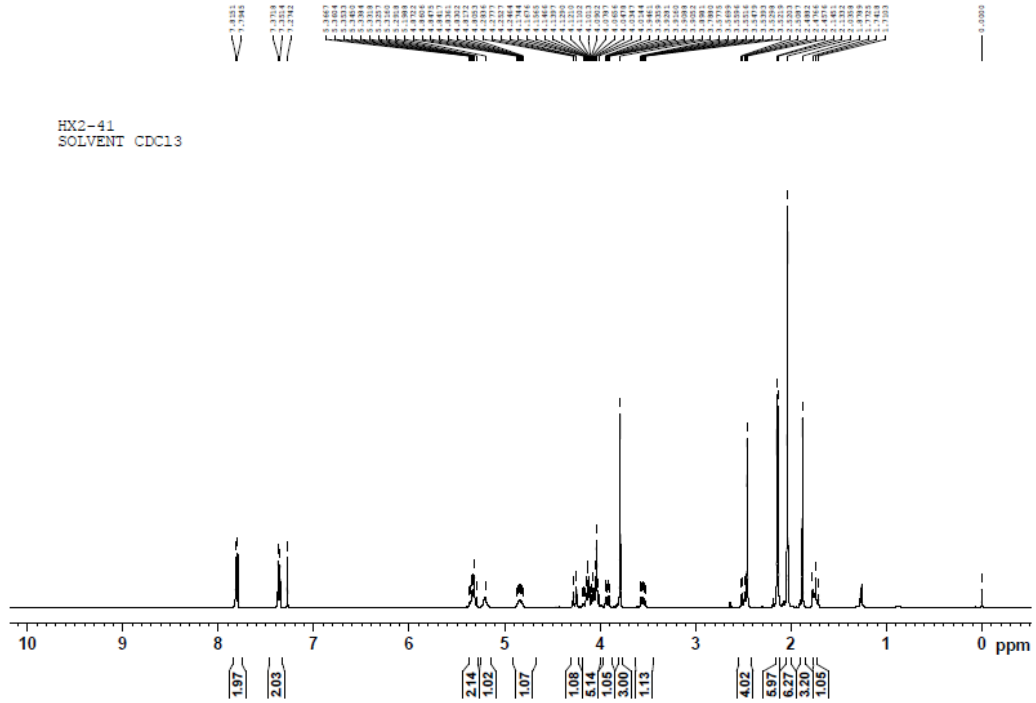


Figure 30. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **11**

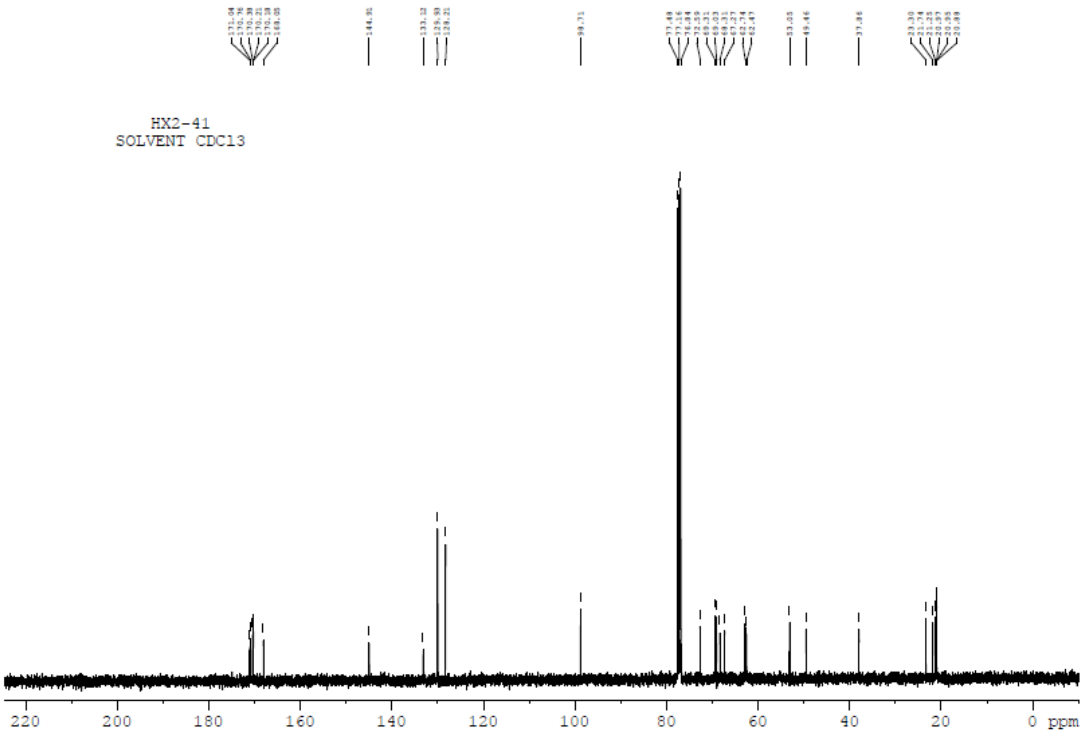


Figure 31. HR-ESI-MS spectrum of compound **11**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-41	C29 H39 N O16 S	C29 H39 N Na O16 S	712.1879	712.1882	0.38

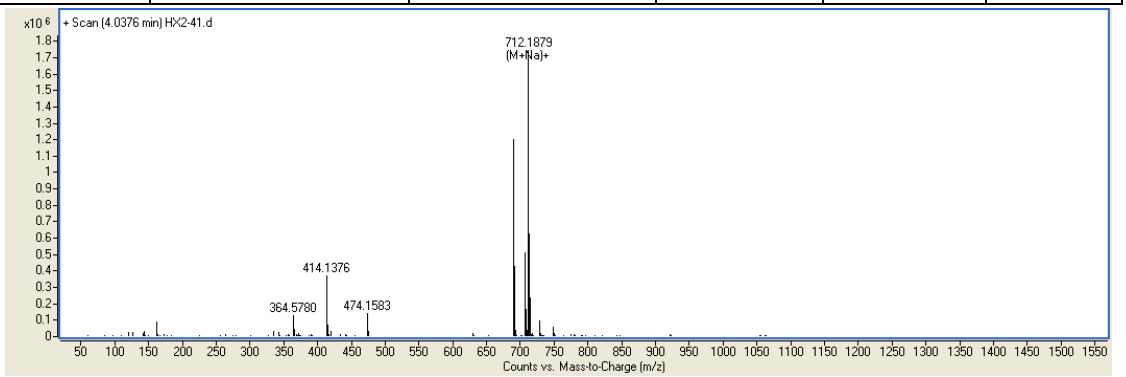


Figure 32. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **12**

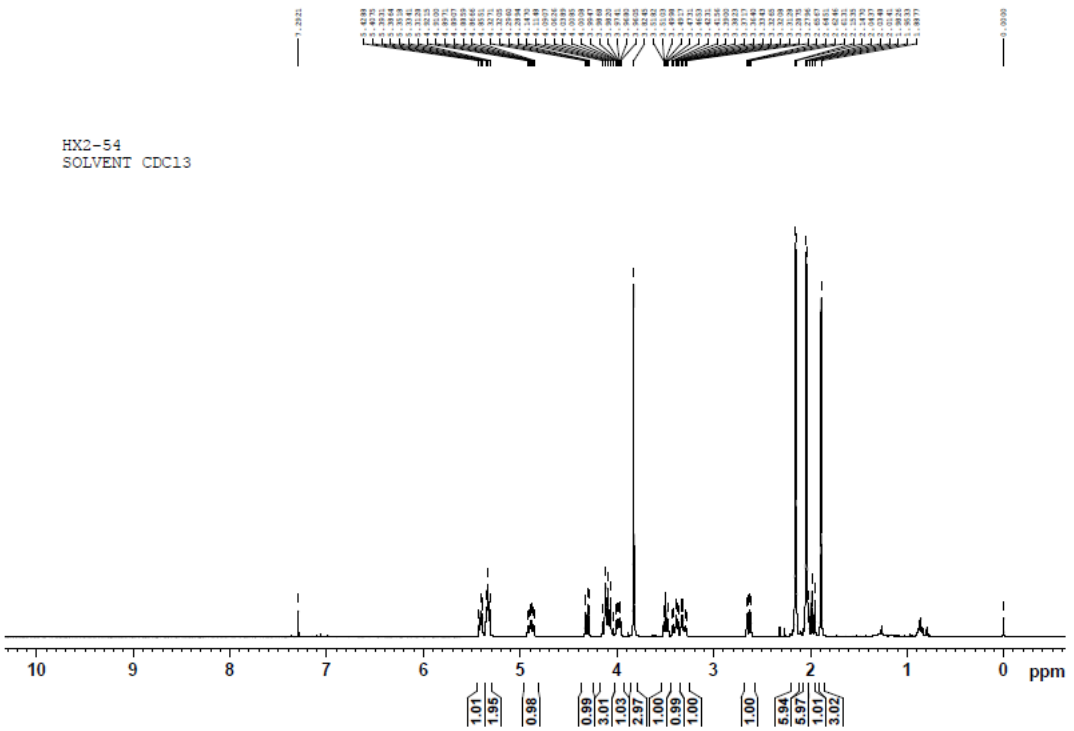


Figure 33. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **12**

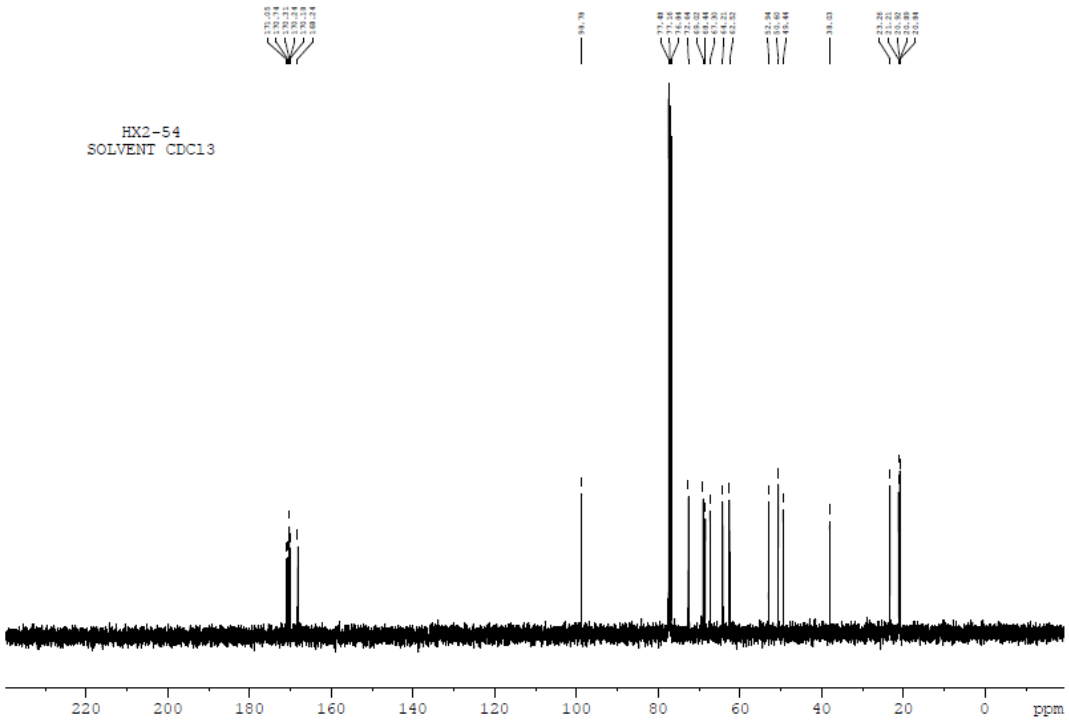


Figure 34. HR-ESI-MS spectrum of compound **12**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-54	C22 H32 N4 O13	C22 H33 N4 O13	561.204	561.2039	-0.09

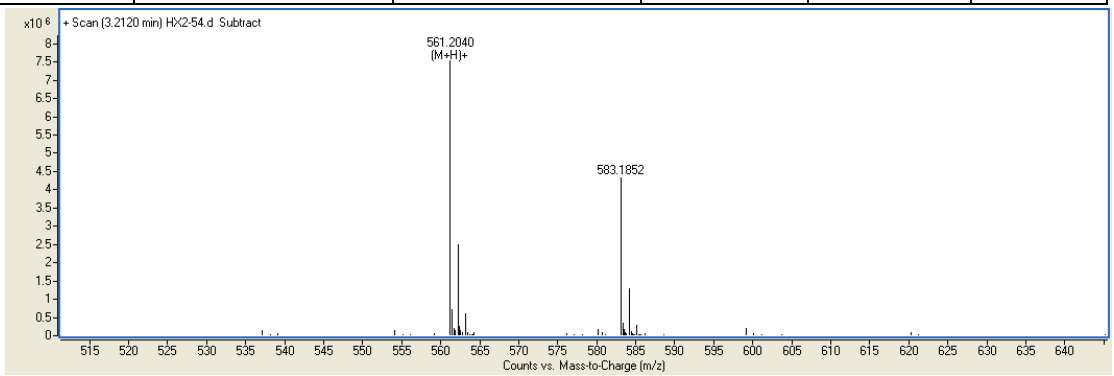


Figure 35. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13a**

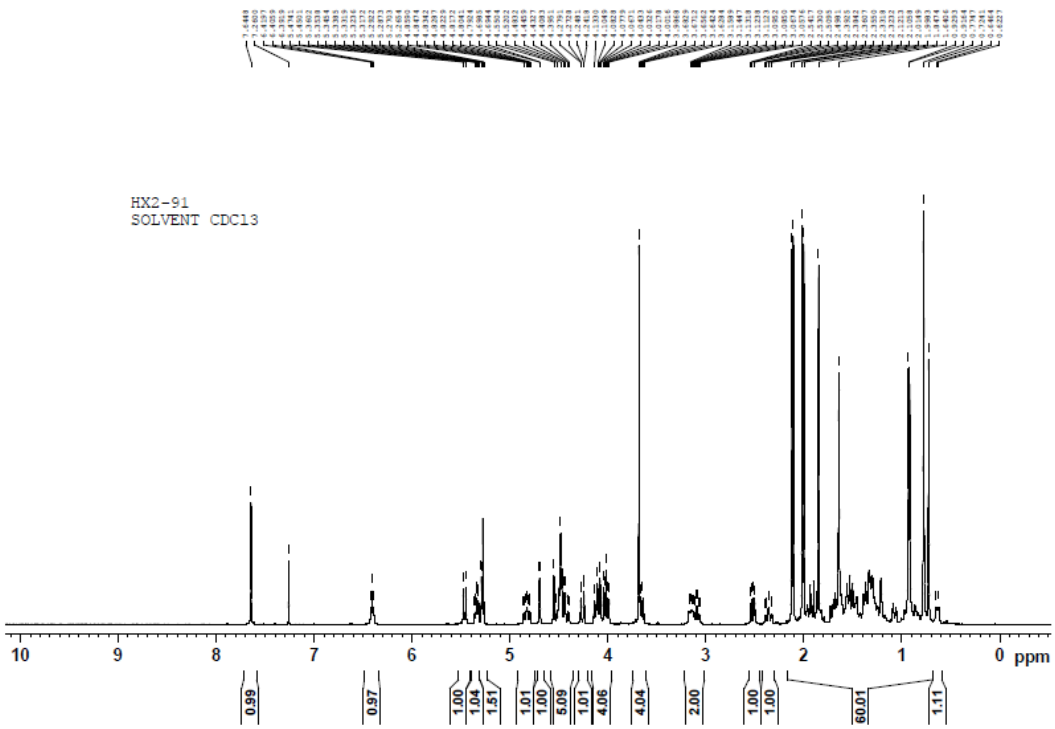


Figure 36. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **13a**

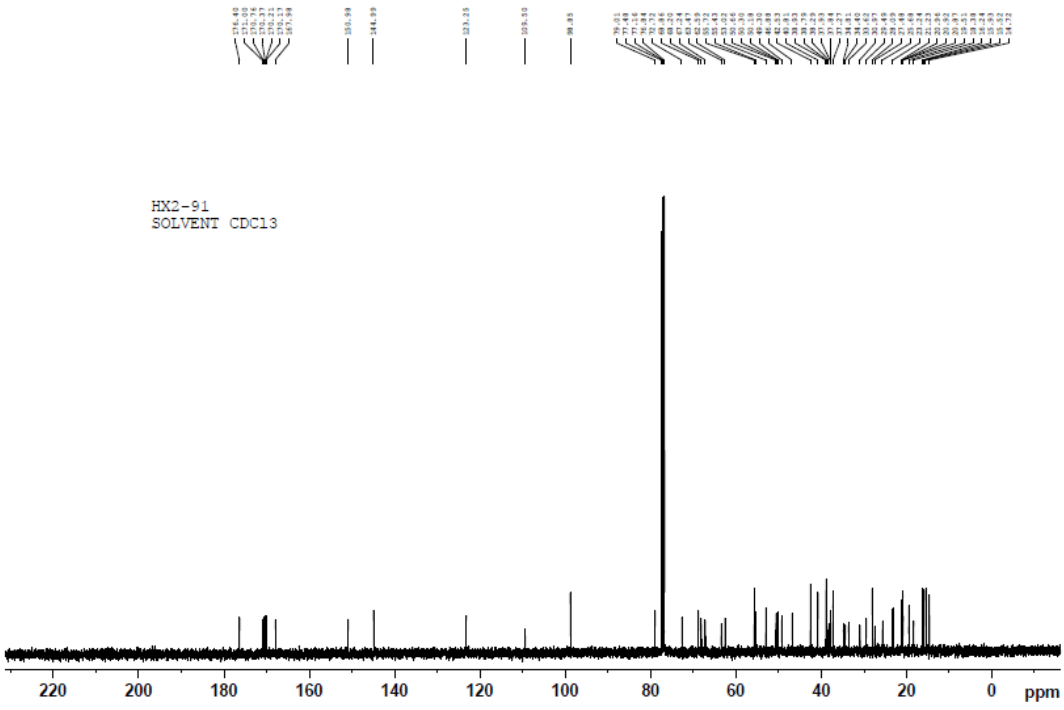


Figure 37. HR-ESI-MS spectrum of compound **13a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-91	C55 H83 N5 O15	C55 H84 N5 O15	1054.5967	1054.5958	-0.53

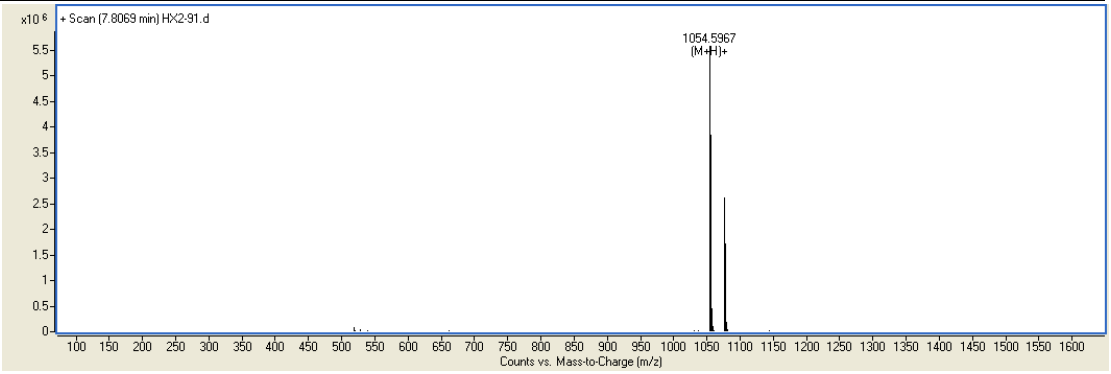


Figure 38. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13b**

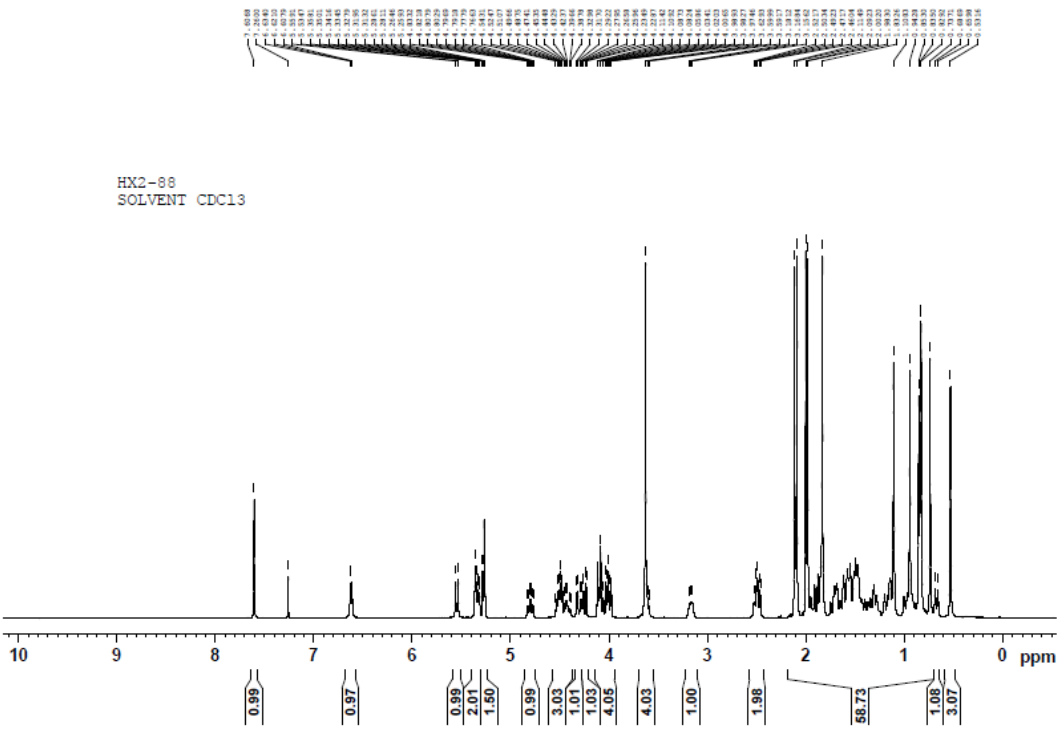


Figure 39. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **13b**

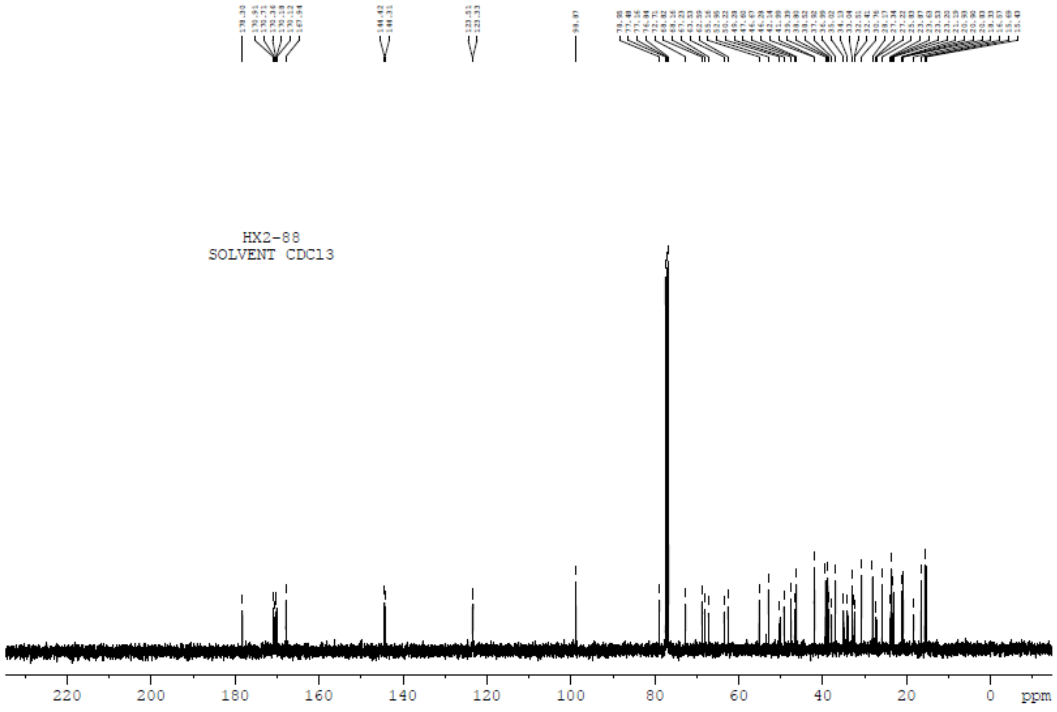


Figure 40. HR-ESI-MS spectrum of compound **13b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-88	C55 H83 N5 O15	C55 H84 N5 O15	1054.5959	1054.5958	0.42

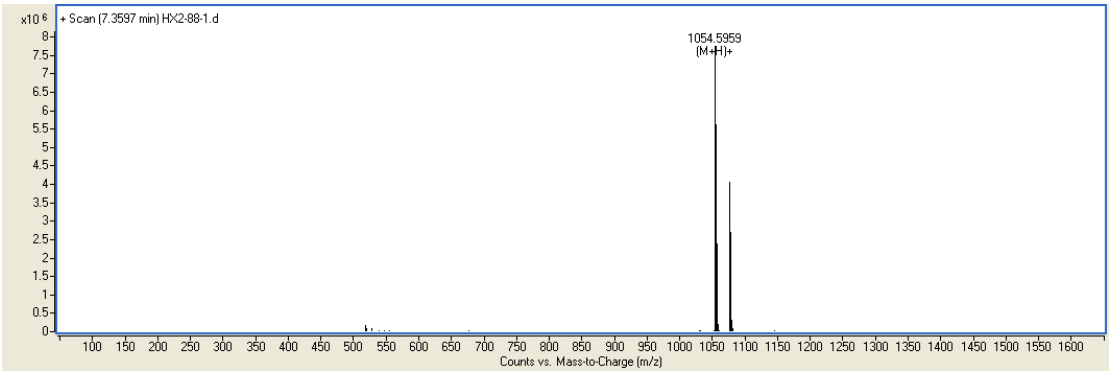


Figure 41. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13c**

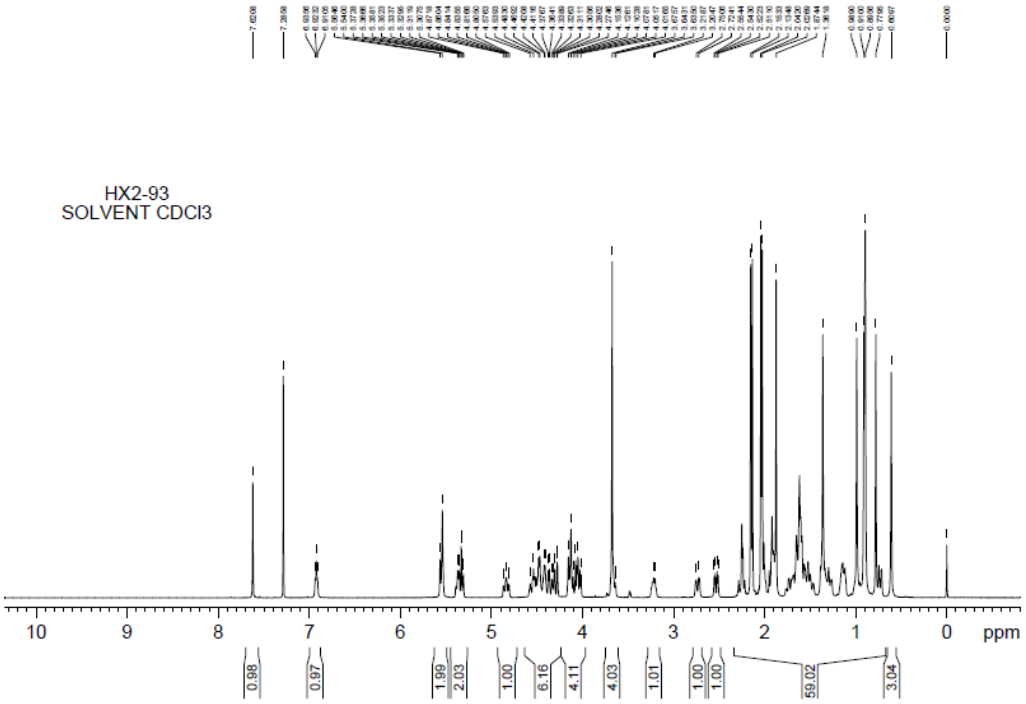


Figure 42. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **13c**

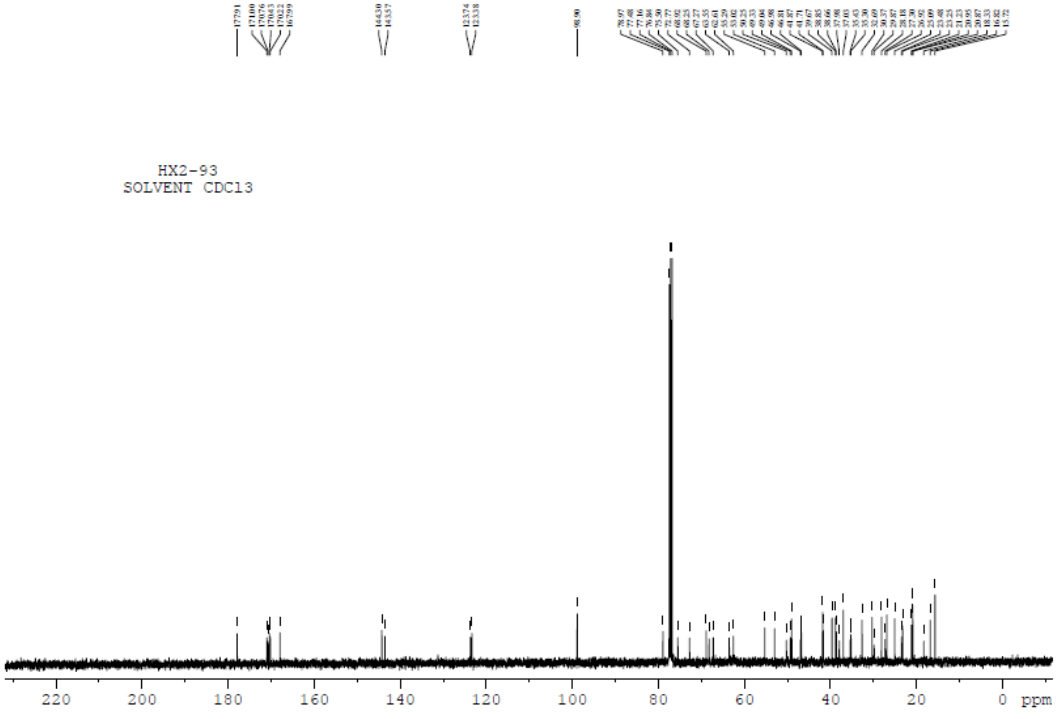


Figure 43. HR-ESI-MS spectrum of compound **13c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-93	C55 H83 N5 O16	C55 H83 N5 Na O16	1092.5736	1092.5727	-0.87

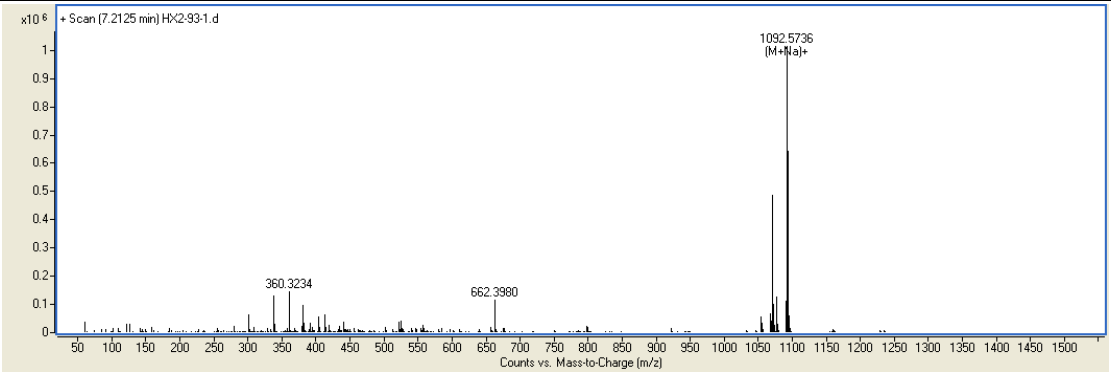


Figure 44. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **13d**

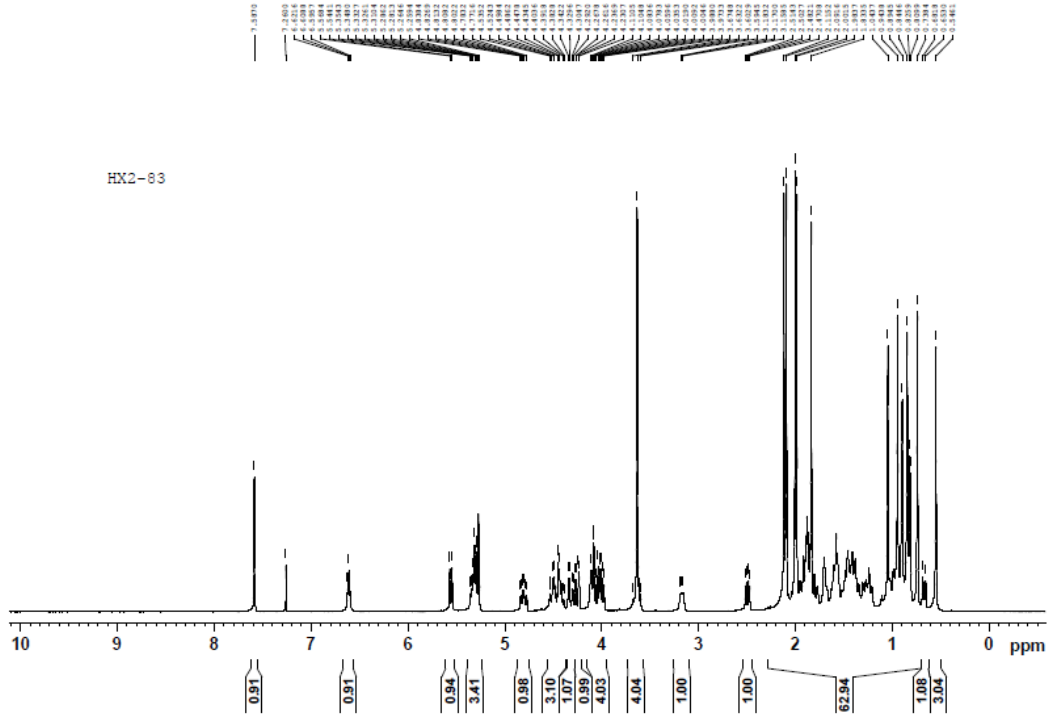


Figure 45. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **13d**

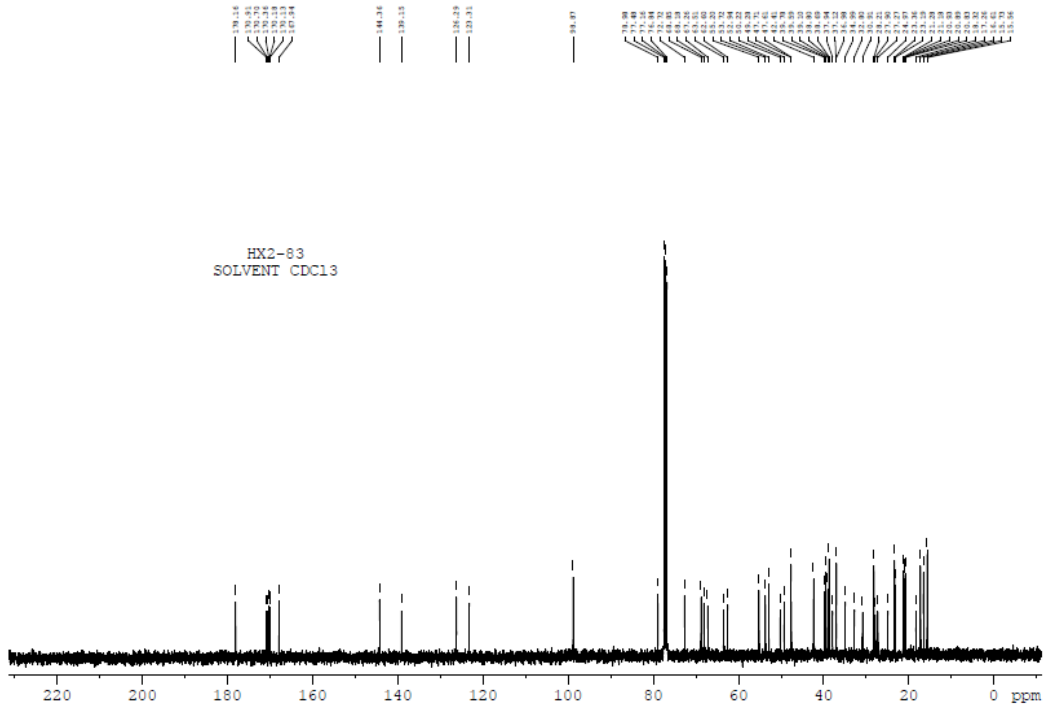


Figure 46. HR-ESI-MS spectrum of compound **13d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-83	C55 H83 N5 O15	C55 H83 N5 Na O15	1076.5784	1076.5778	-0.7

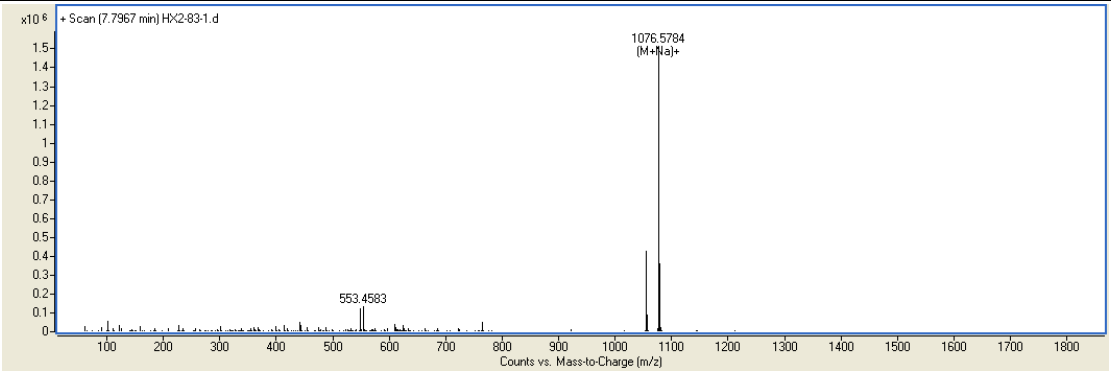


Figure 47. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **14a**

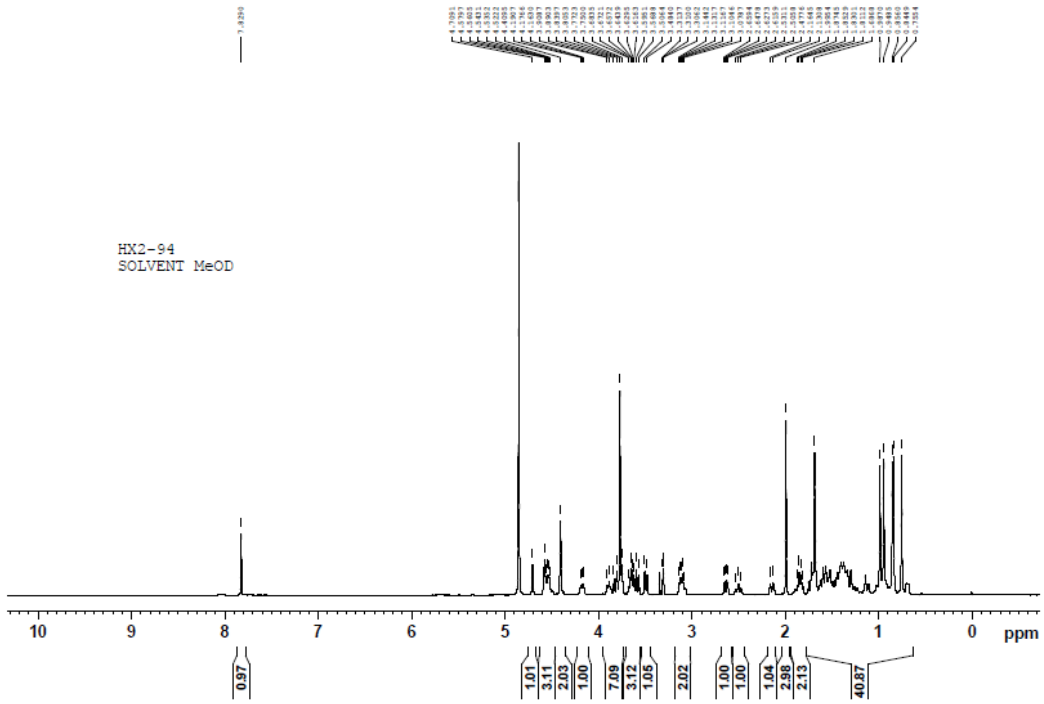


Figure 48. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **14a**

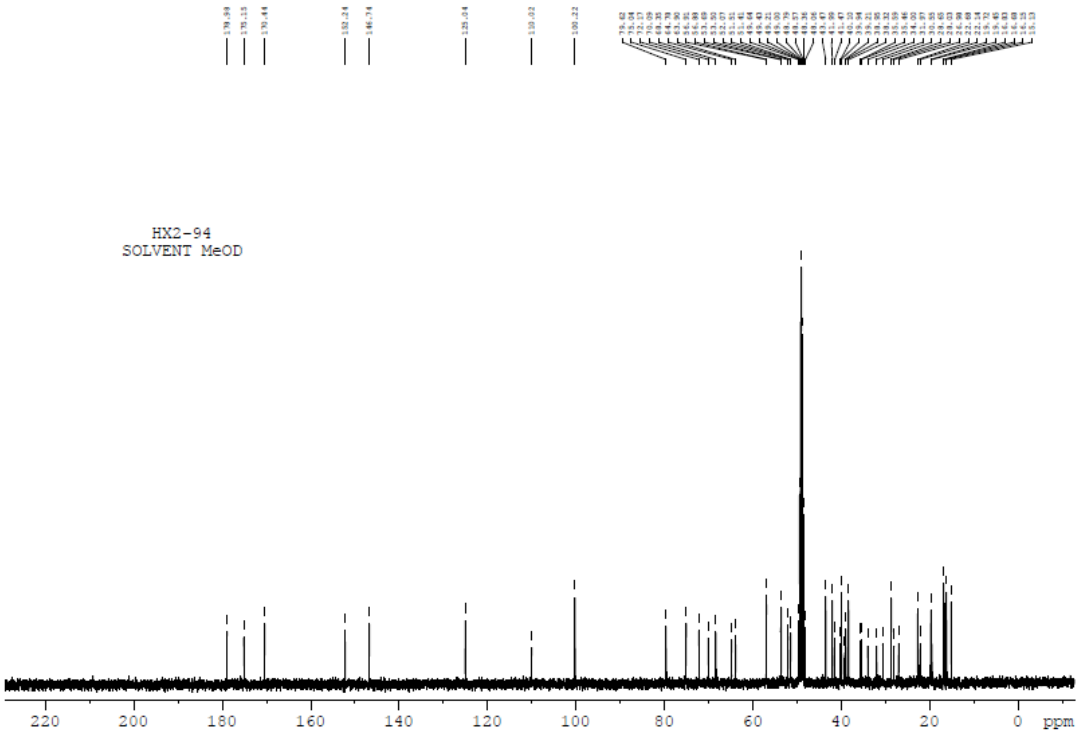


Figure 49. HR-ESI-MS spectrum of compound **14a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-94	C47 H75 N5 O11	C47 H75 N5 Na O11	908.5354	908.5355	0.11

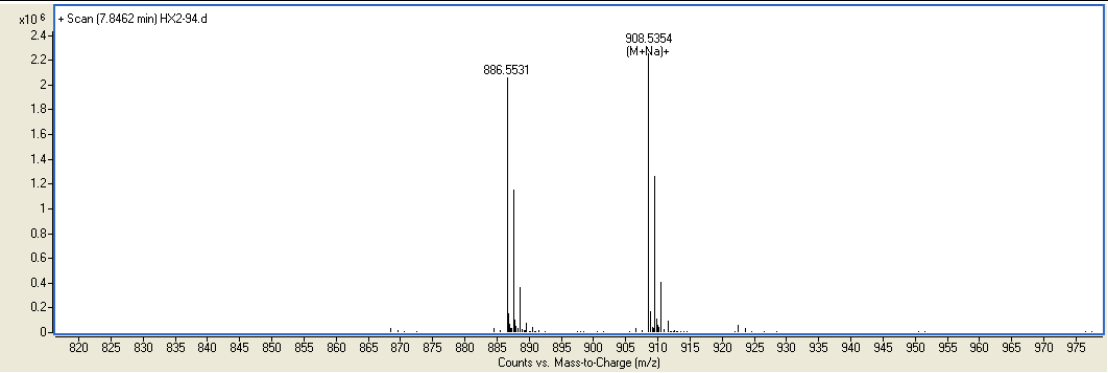


Figure 50. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **14b**

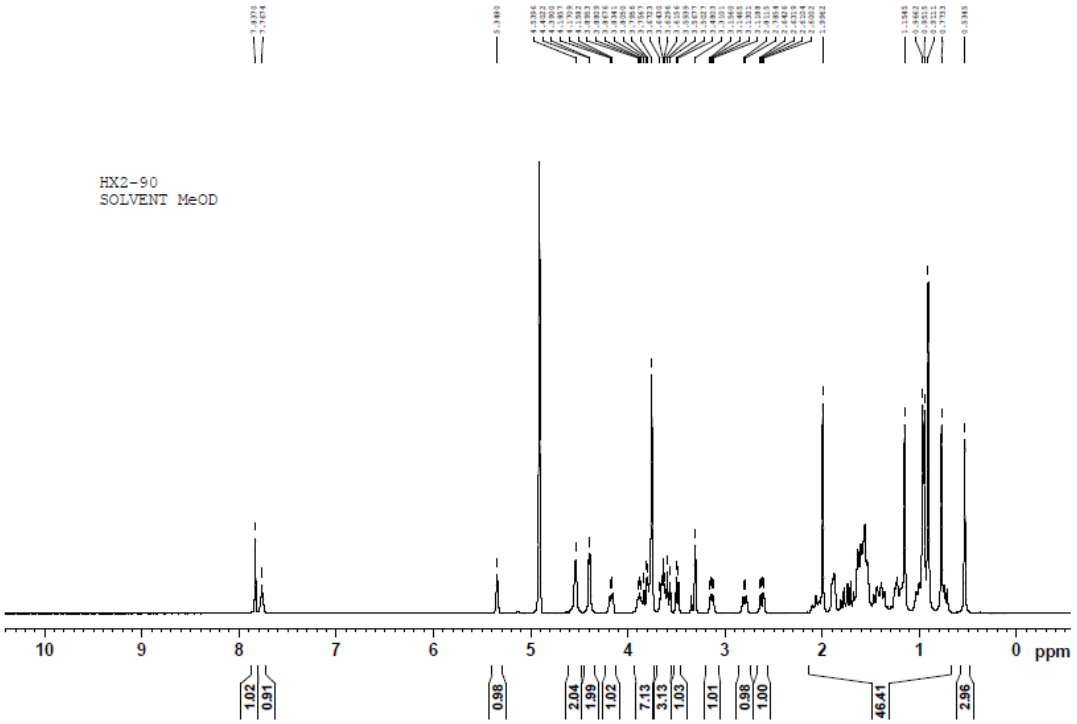


Figure 51. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **14b**

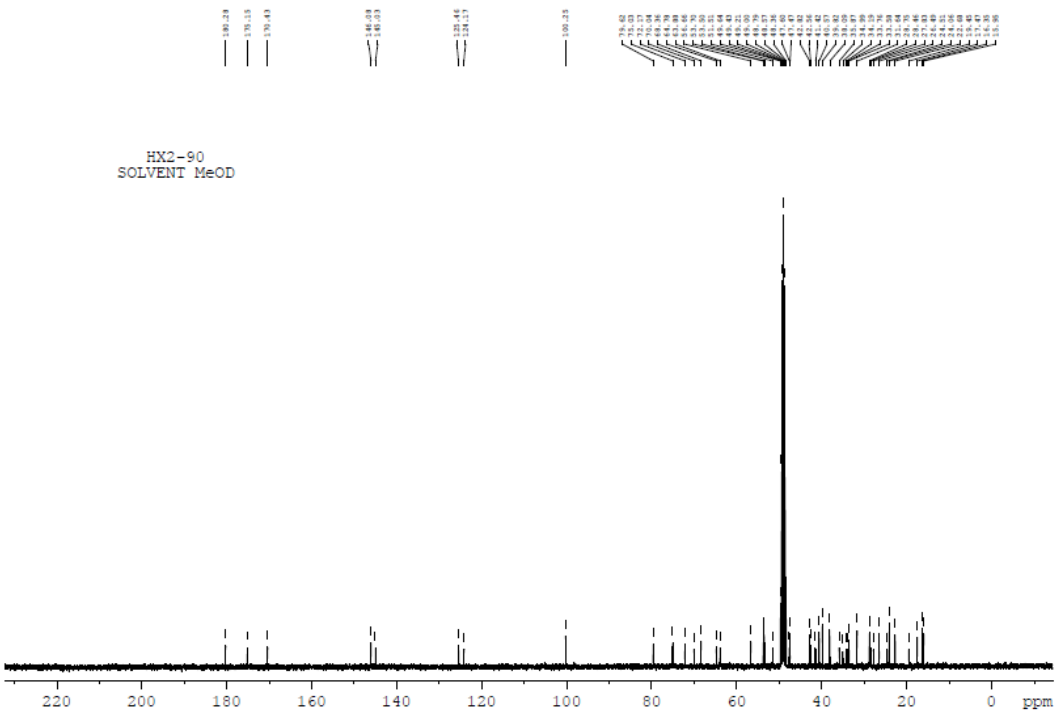


Figure 52. HR-ESI-MS spectrum of compound **14b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-90	C47 H75 N5 O11	C47 H76 N5 O11	886.5534	886.5536	0.11

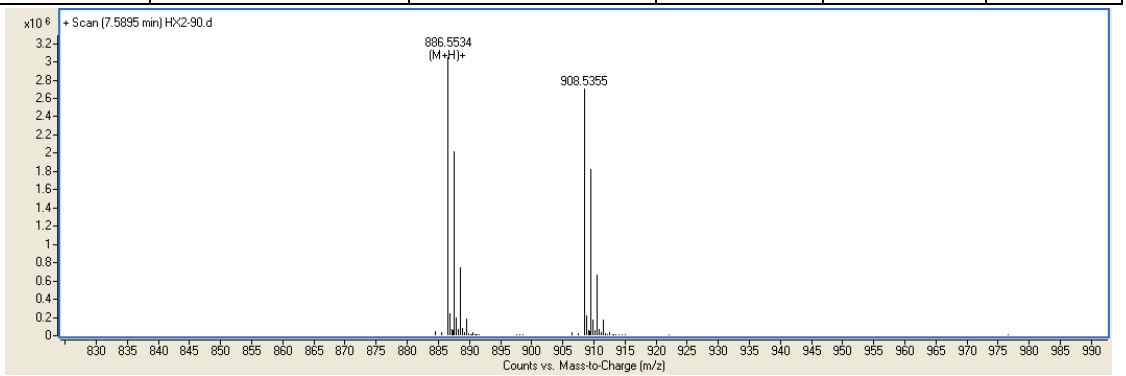


Figure 53. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **14c**

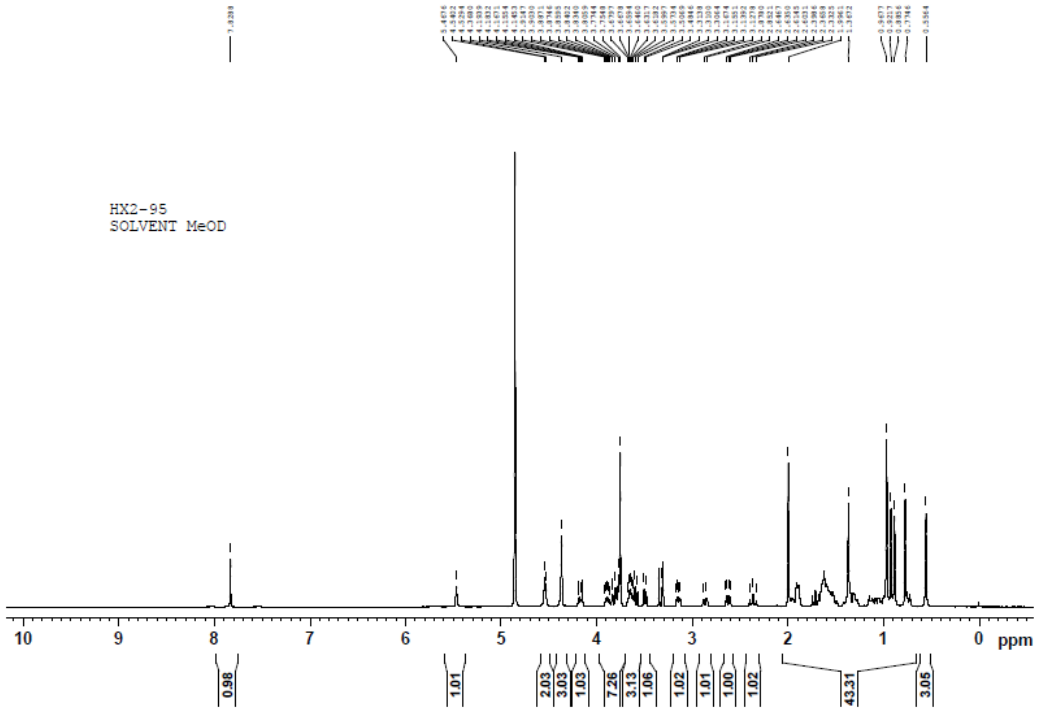


Figure 54. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **14c**

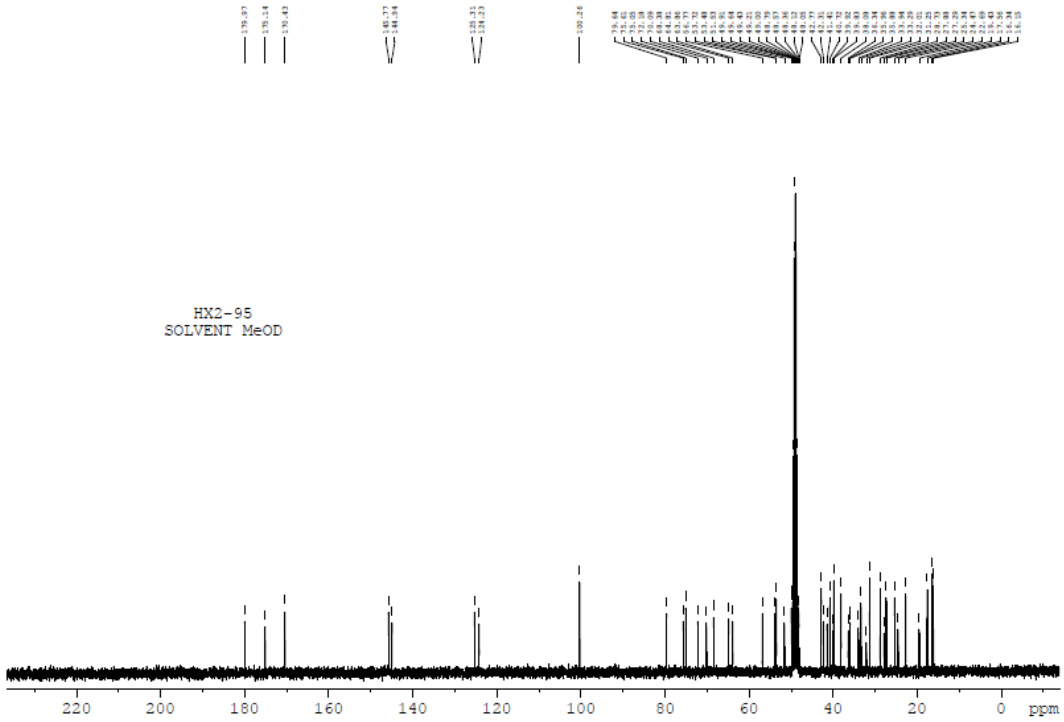


Figure 55. HR-ESI-MS spectrum of compound **14c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-95	C47 H75 N5 O12	C47 H75 N5 Na O12	924.5301	924.5304	0.14

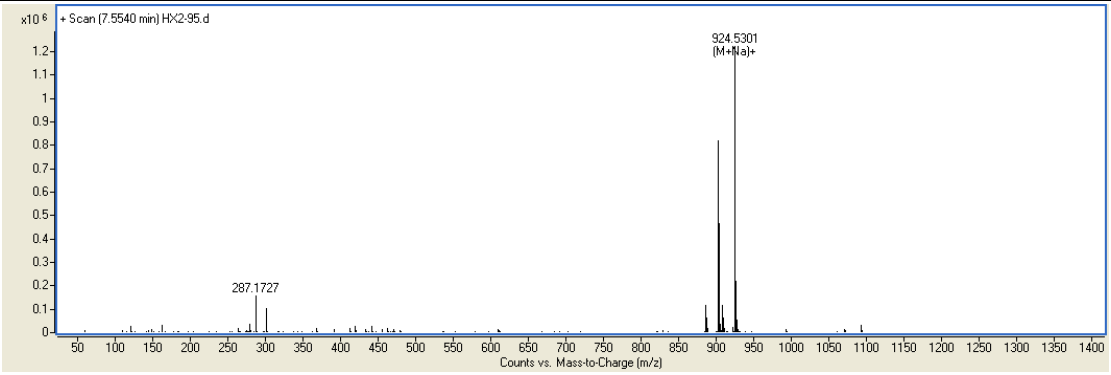


Figure 56. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **14d**

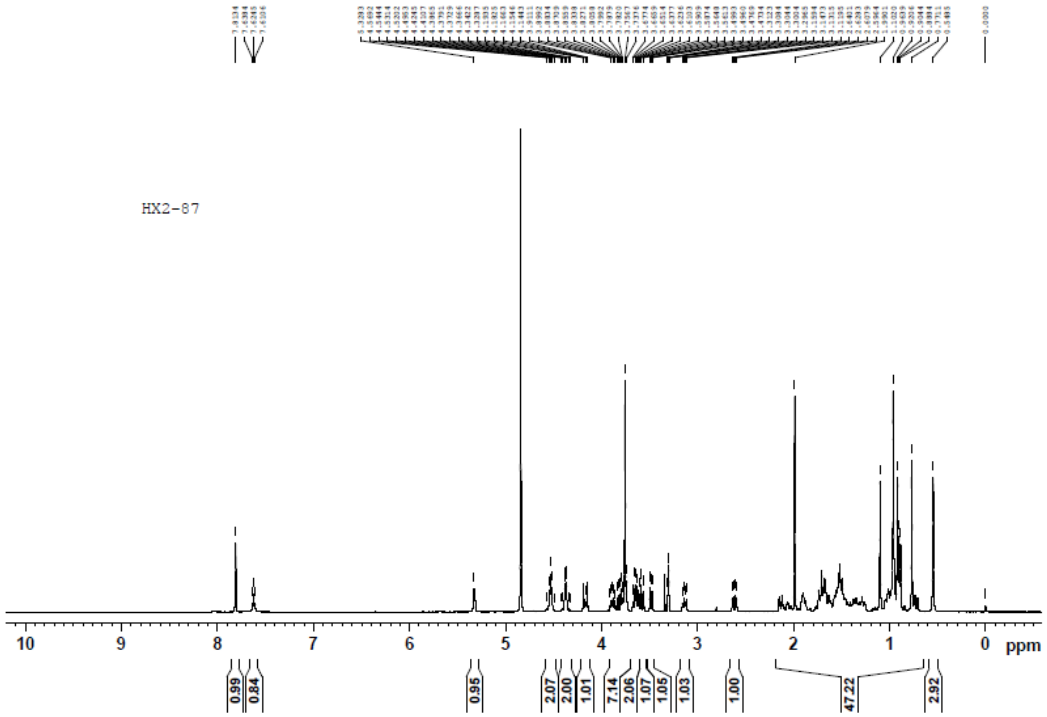


Figure 57. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **14d**

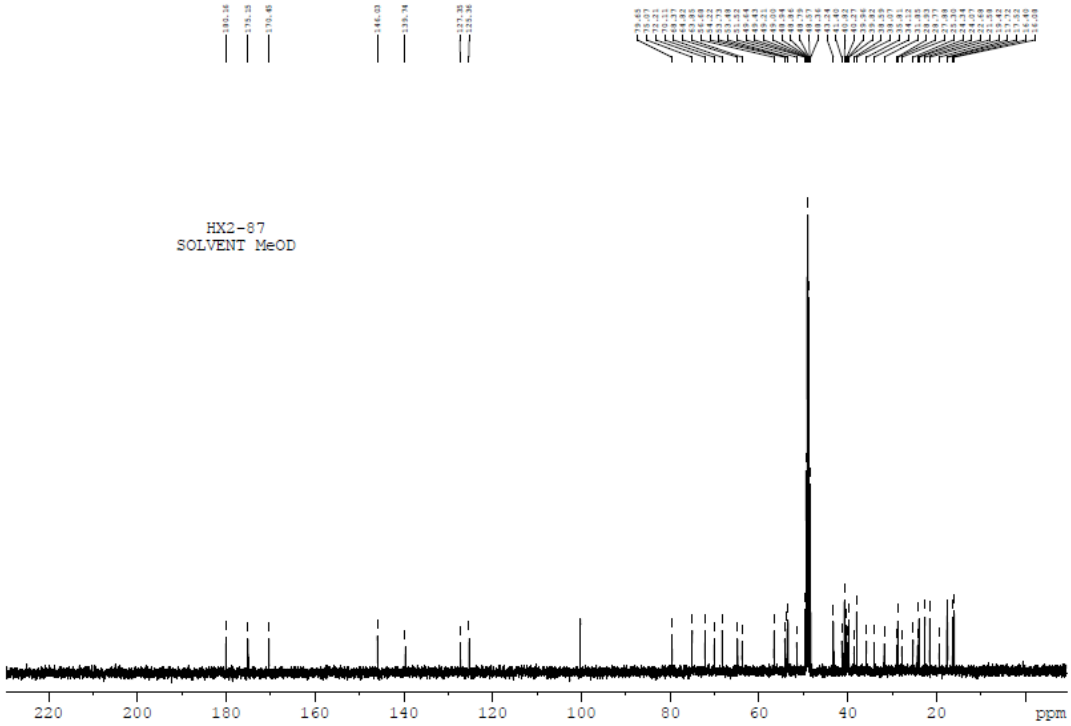


Figure 58. HR-ESI-MS spectrum of compound **14d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-87	C47 H75 N5 O11	C47 H75 N5 Na O11	908.5364	908.5355	-0.92

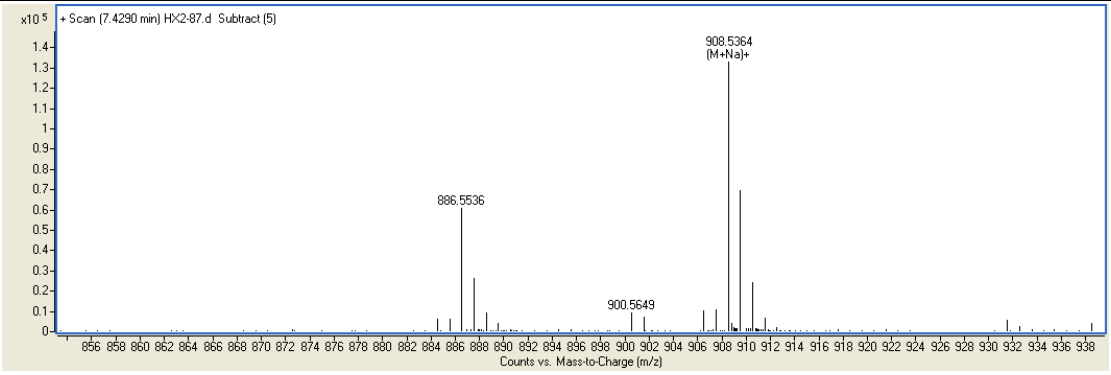


Figure 59. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **16**

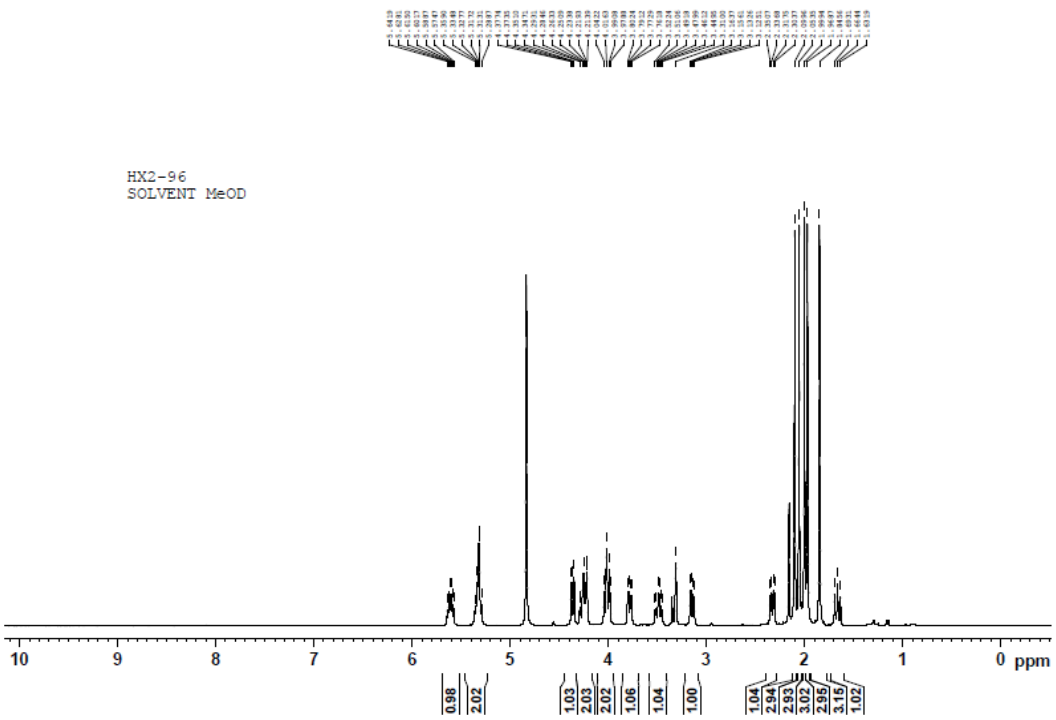


Figure 60. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **16**

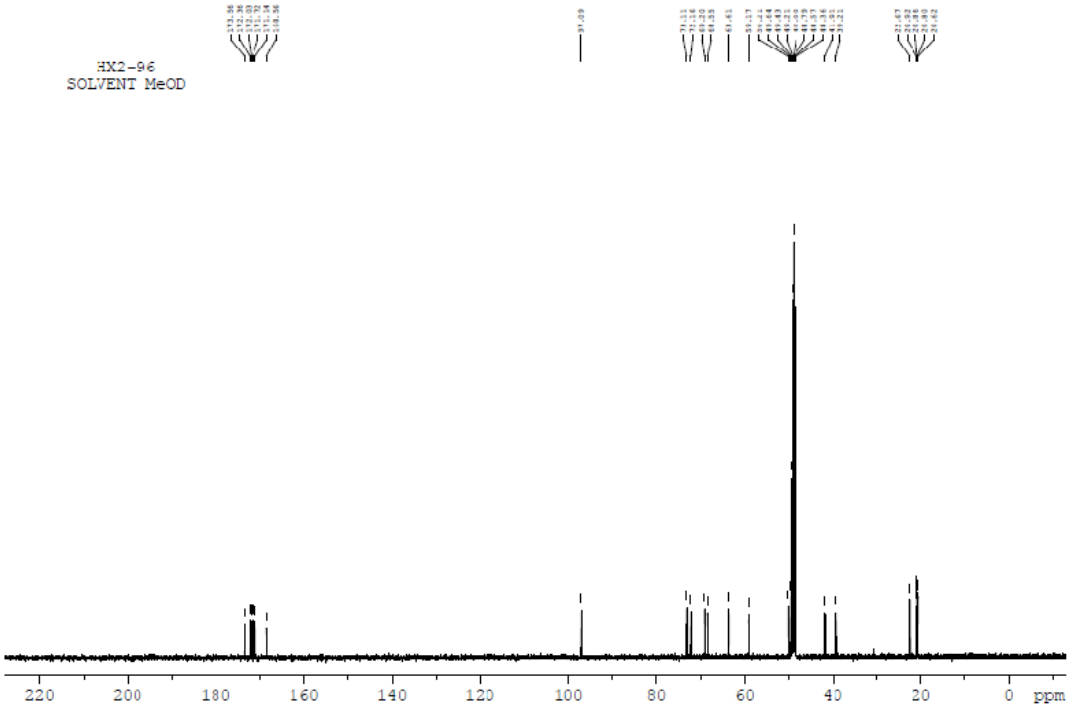


Figure 61. HR-ESI-MS spectrum of compound **16**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX2-96	C21 H30 N2 O12	C21 H31 N2 O12	503.1867	503.1872	0.97

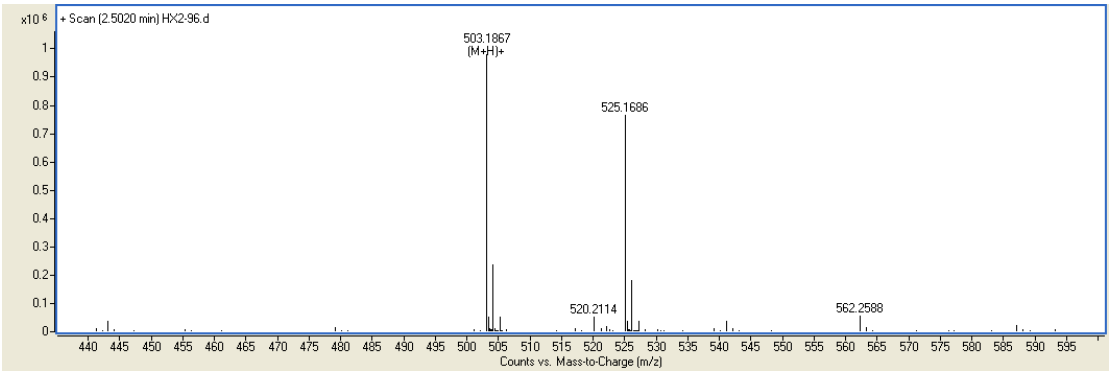


Figure 62. ^{1}H NMR (400 MHz, D_2O+CD_3OD) spectrum of compound **17**

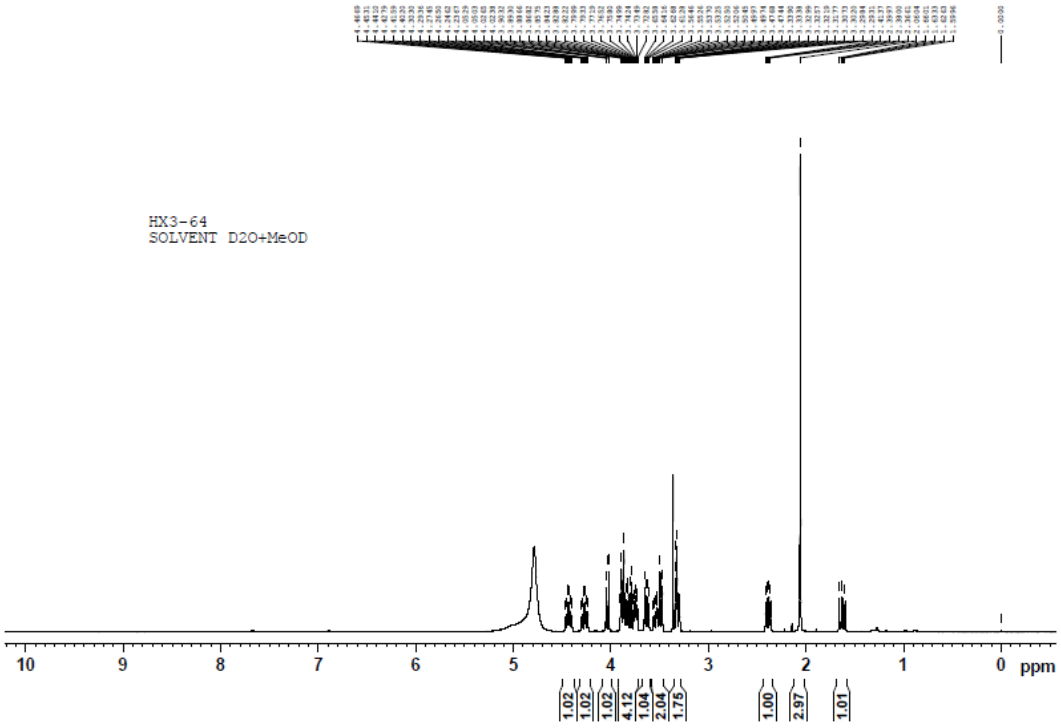


Figure 63. ^{13}C NMR (100 MHz, D_2O+ CD_3OD) spectrum of compound **17**

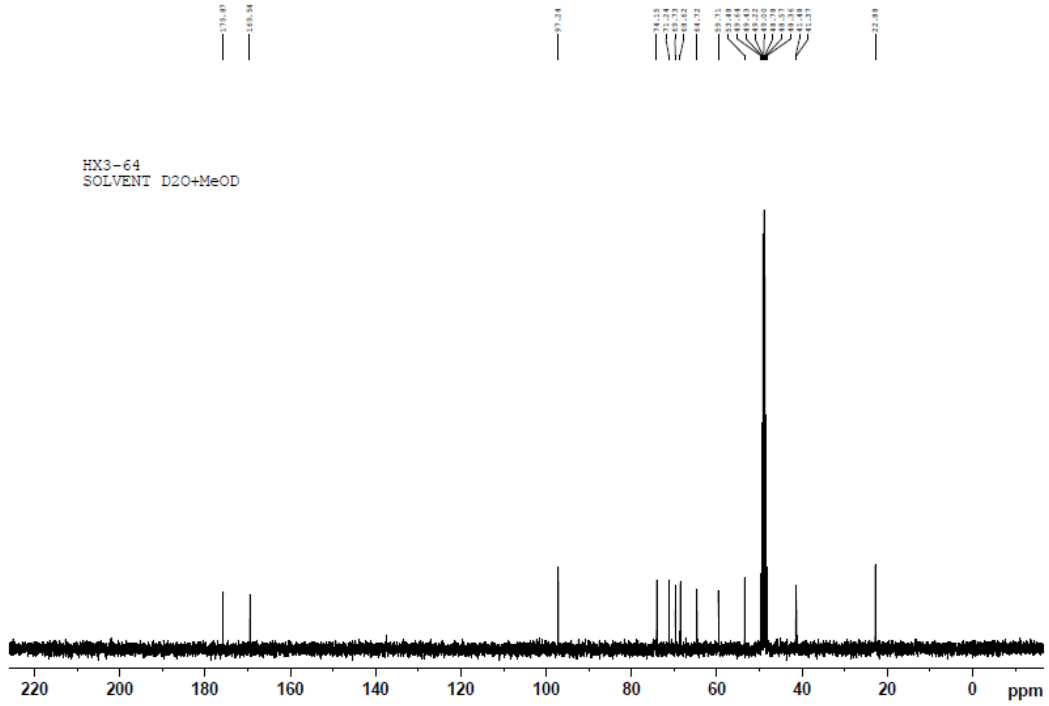


Figure 64. HR-ESI-MS spectrum of compound **17**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-64	C13 H22 N2 O8	C13 H23 N2 O8	335.1453	335.1449	-1.36

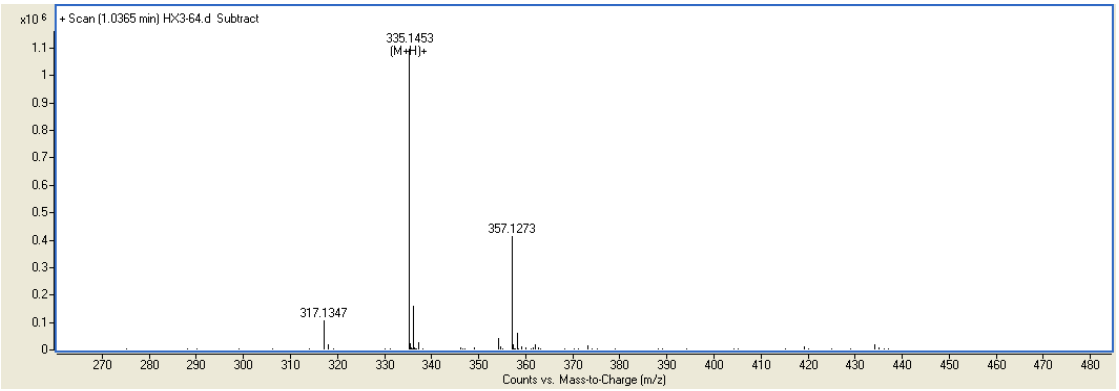


Figure 65. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **18**

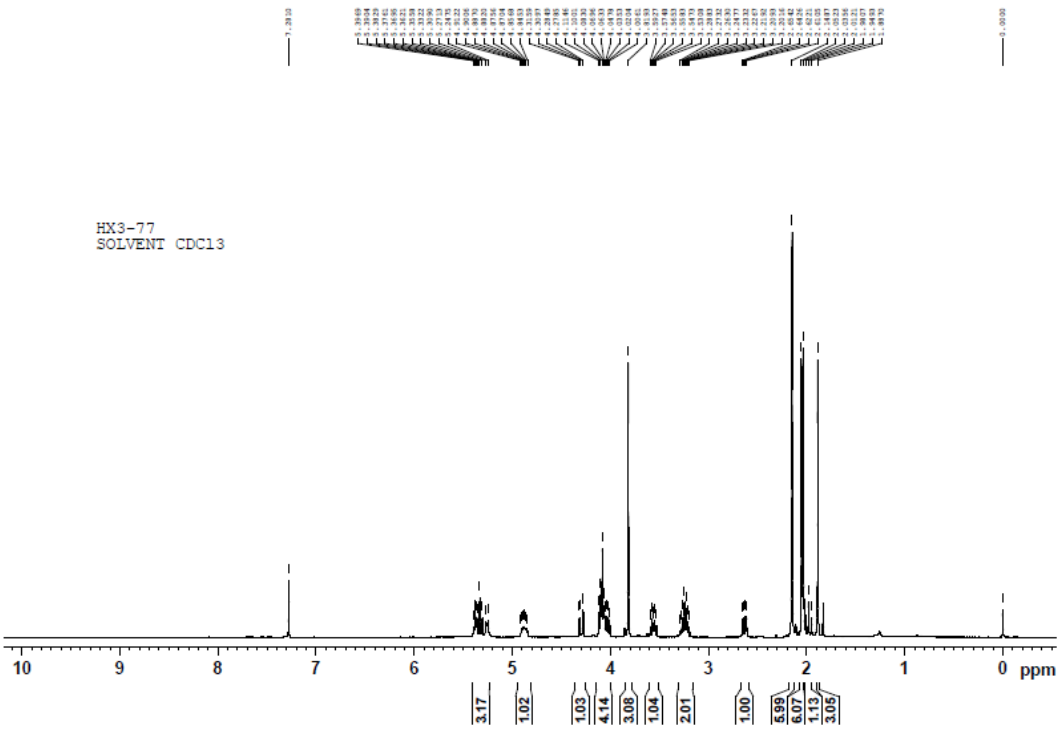


Figure 66. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **18**

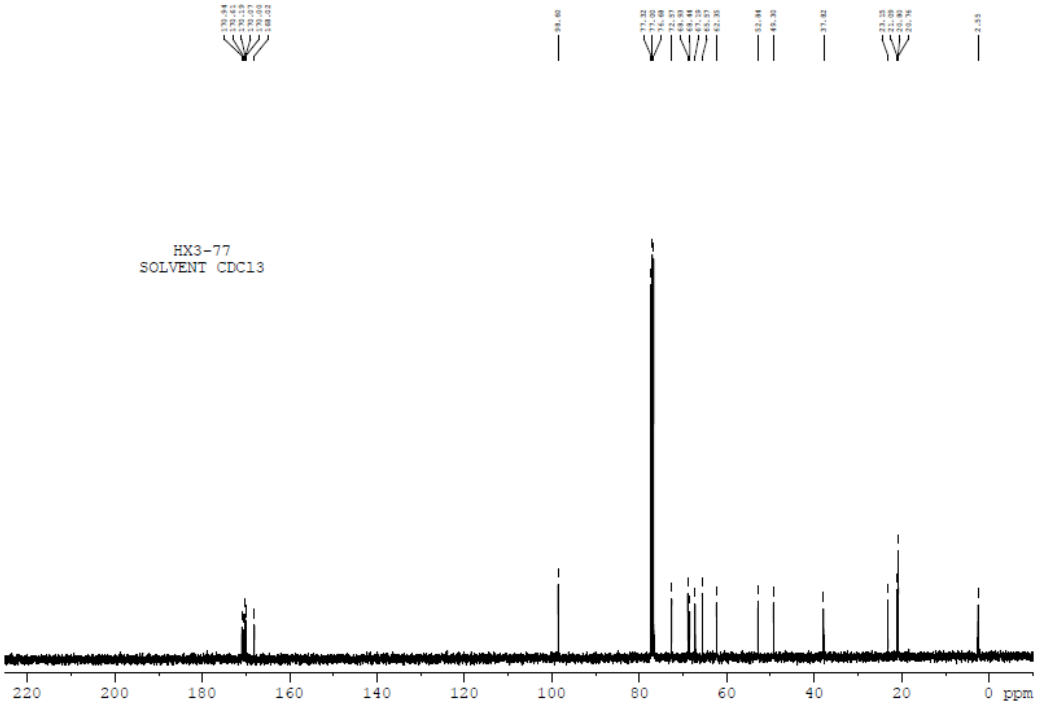


Figure 67. HR-ESI-MS spectrum of compound **18**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-77	C22 H32 I N O13	C22 H33 I N O13	646.0995	646.0991	-0.52

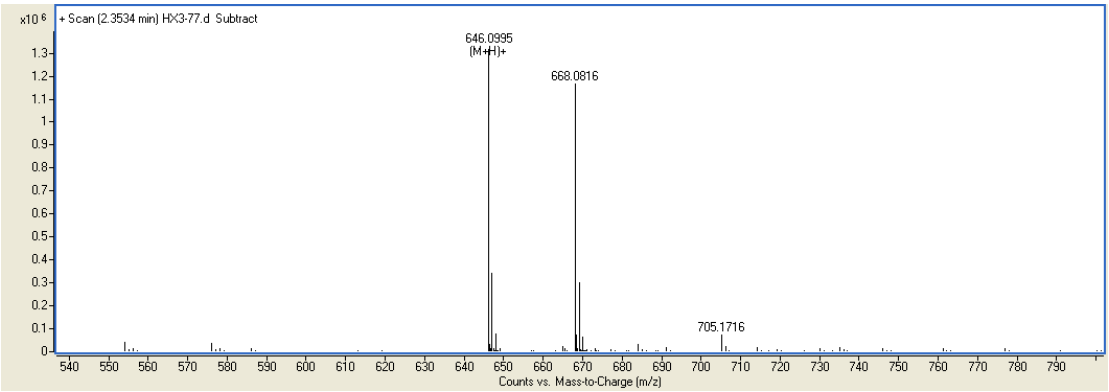


Figure 68. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **19a**

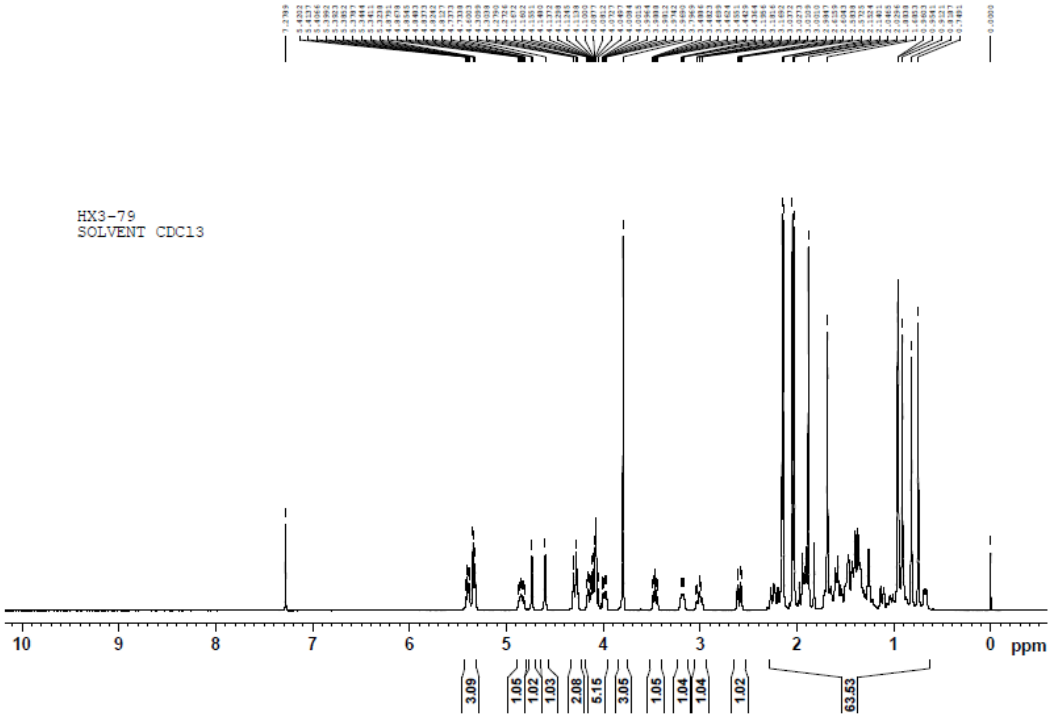


Figure 69. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **19a**

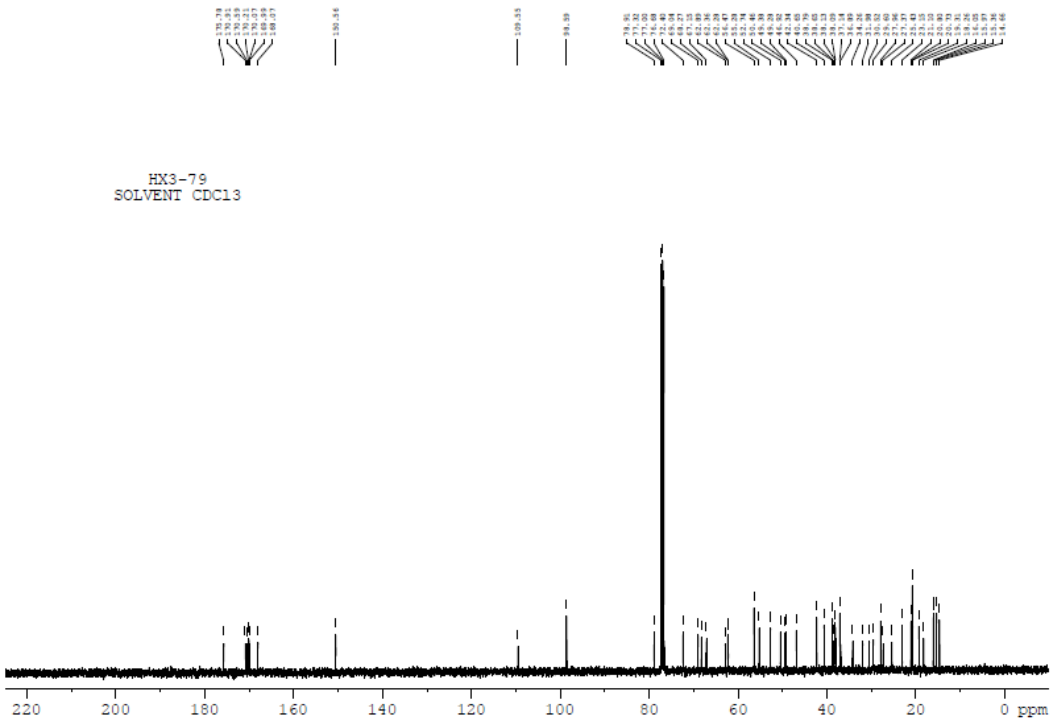


Figure 70. HR-ESI-MS spectrum of compound **19a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-79	C52 H79 N O16	C52 H79 N Na O16	996.5288	996.5291	0.23

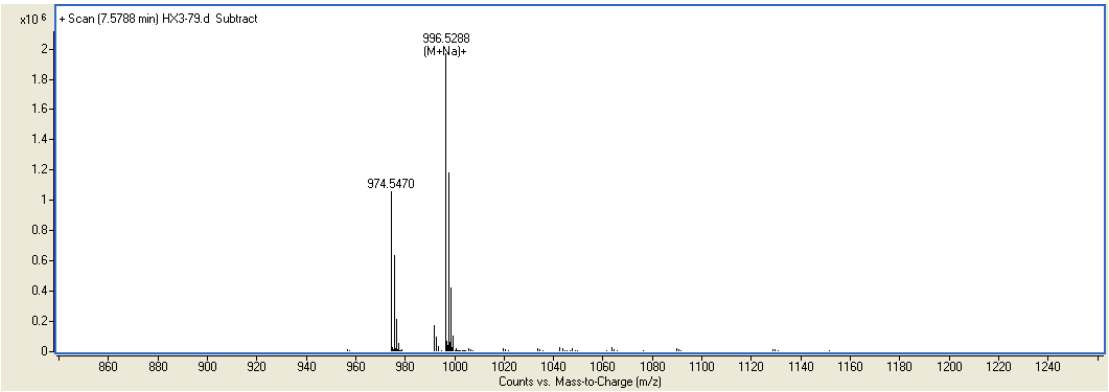


Figure 71. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **19b**

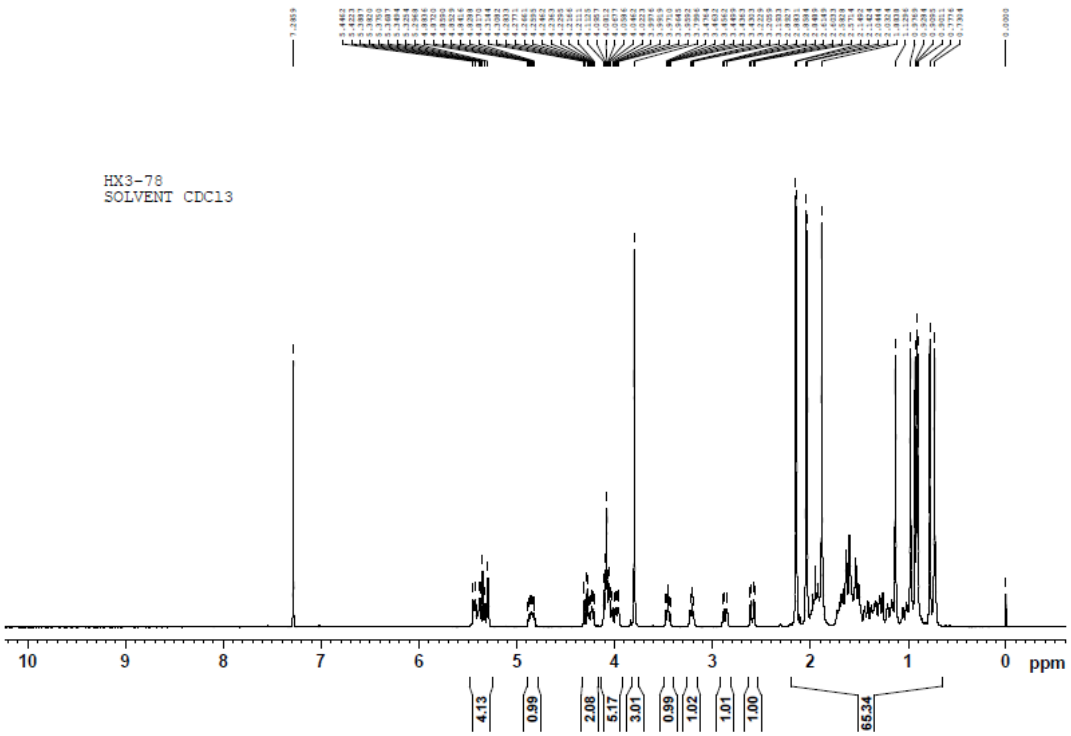


Figure 72. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **19b**

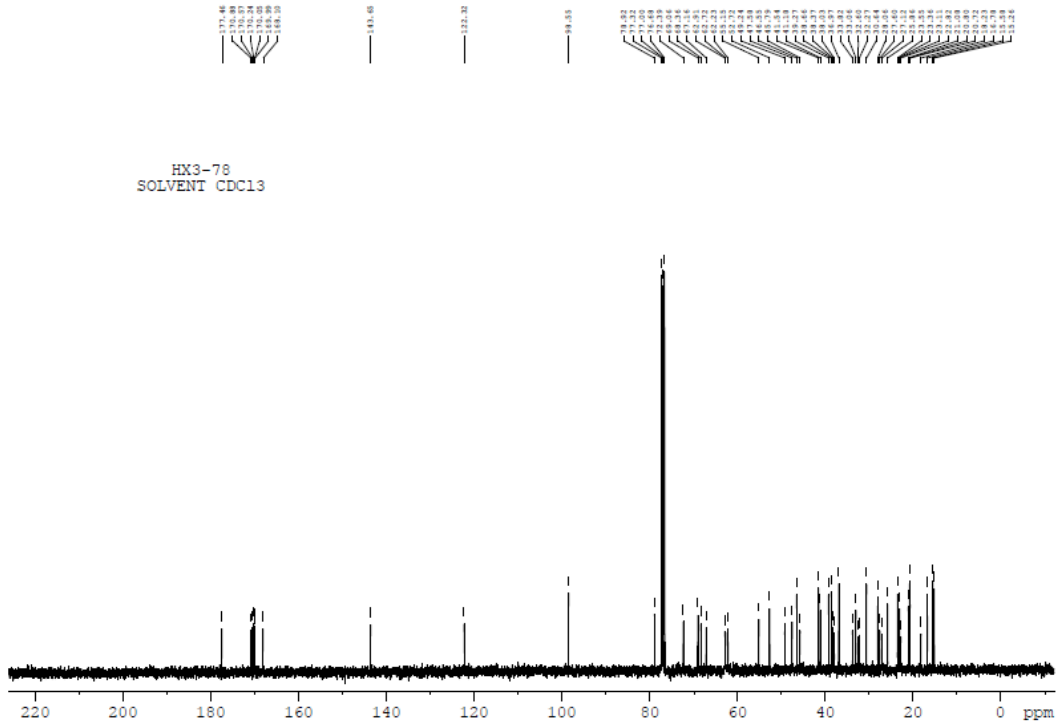


Figure 73. HR-ESI-MS spectrum of compound **19b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-78	C52 H79 N O16	C52 H79 N Na O16	996.5293	996.5291	-0.09

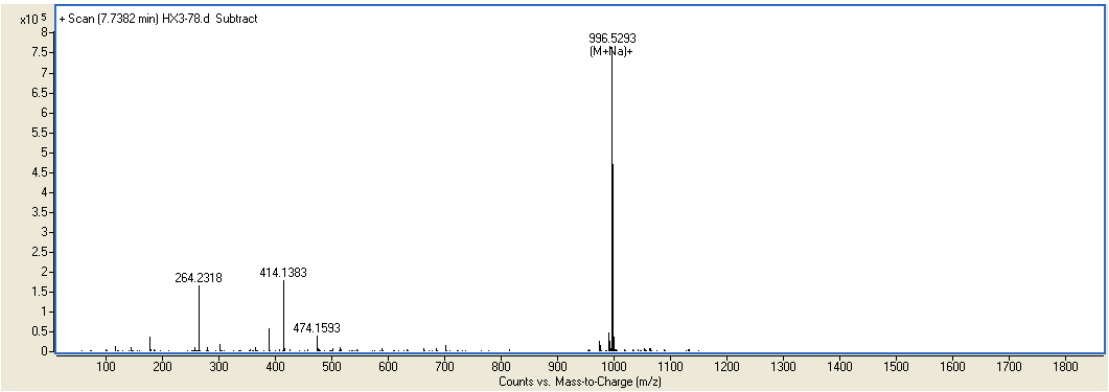


Figure 74. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **19c**

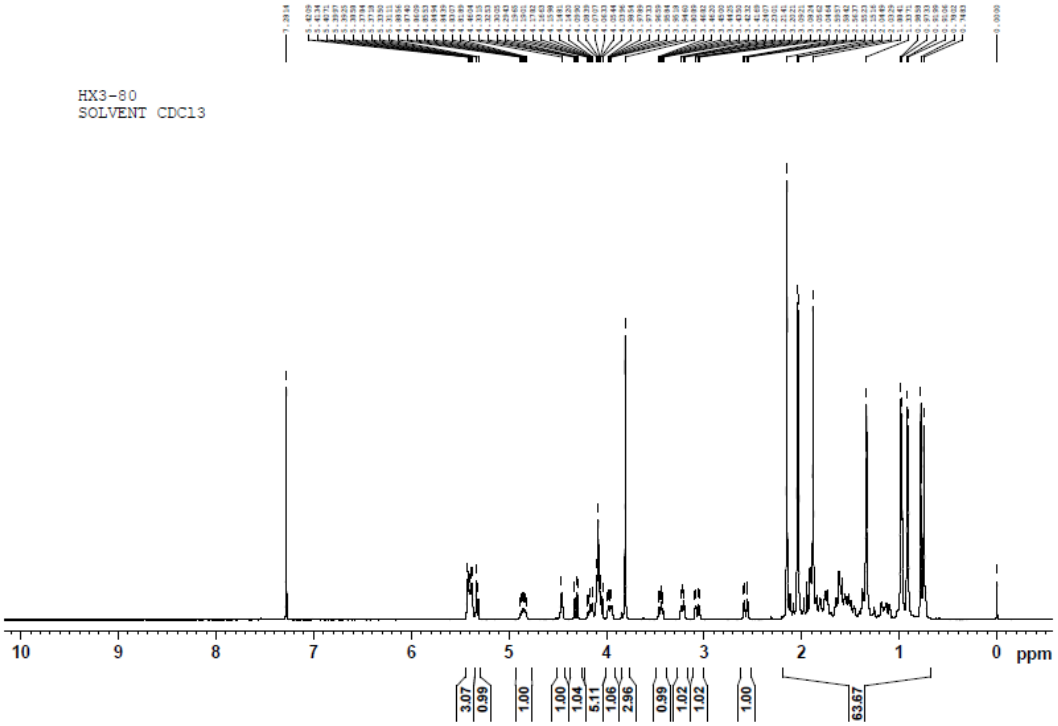


Figure 75. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **19c**

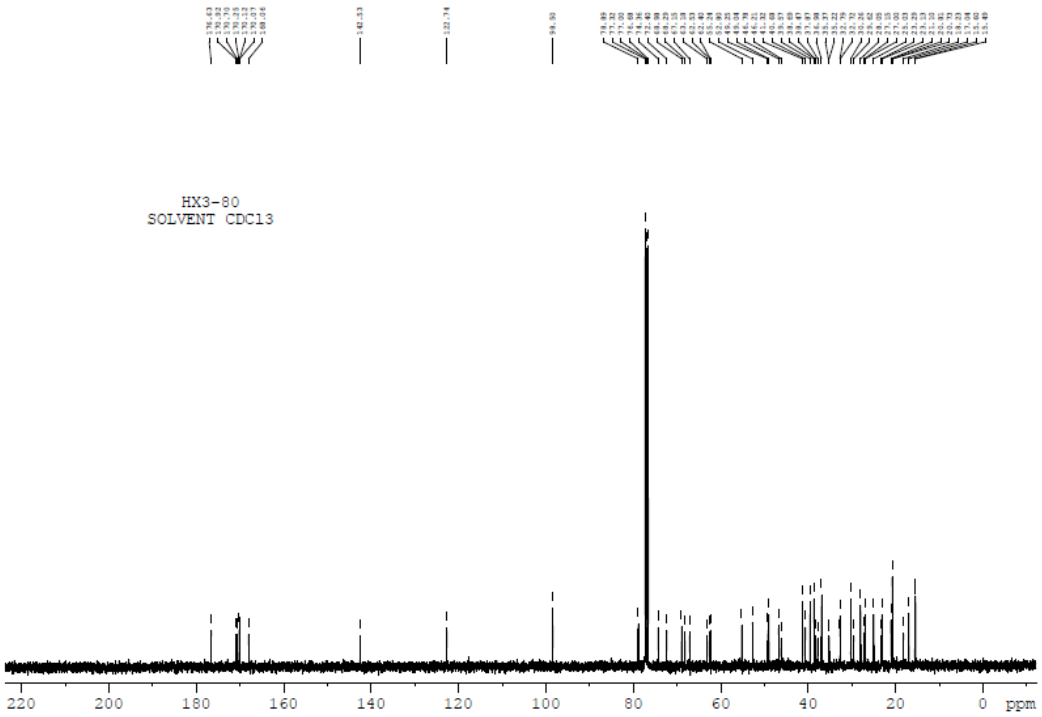


Figure 76. HR-ESI-MS spectrum of compound **19c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-80	C52 H79 N O17	C52 H79 N Na O17	1012.5241	1012.5240	0.03

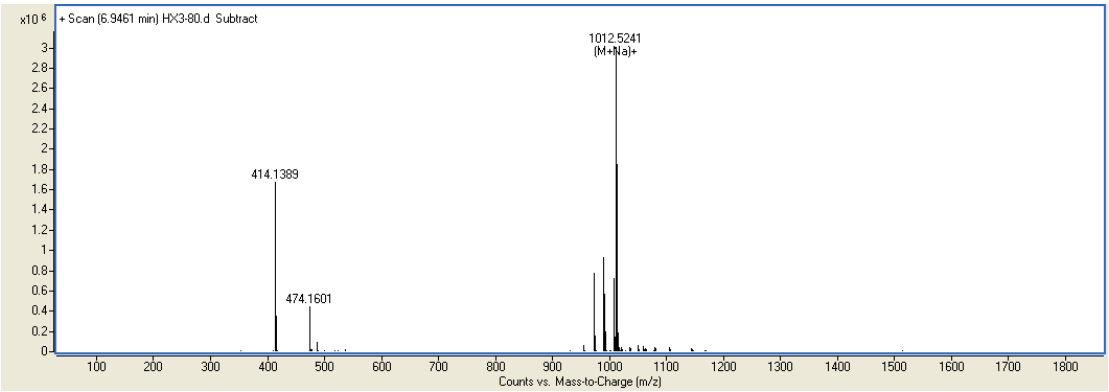


Figure 77. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **19d**

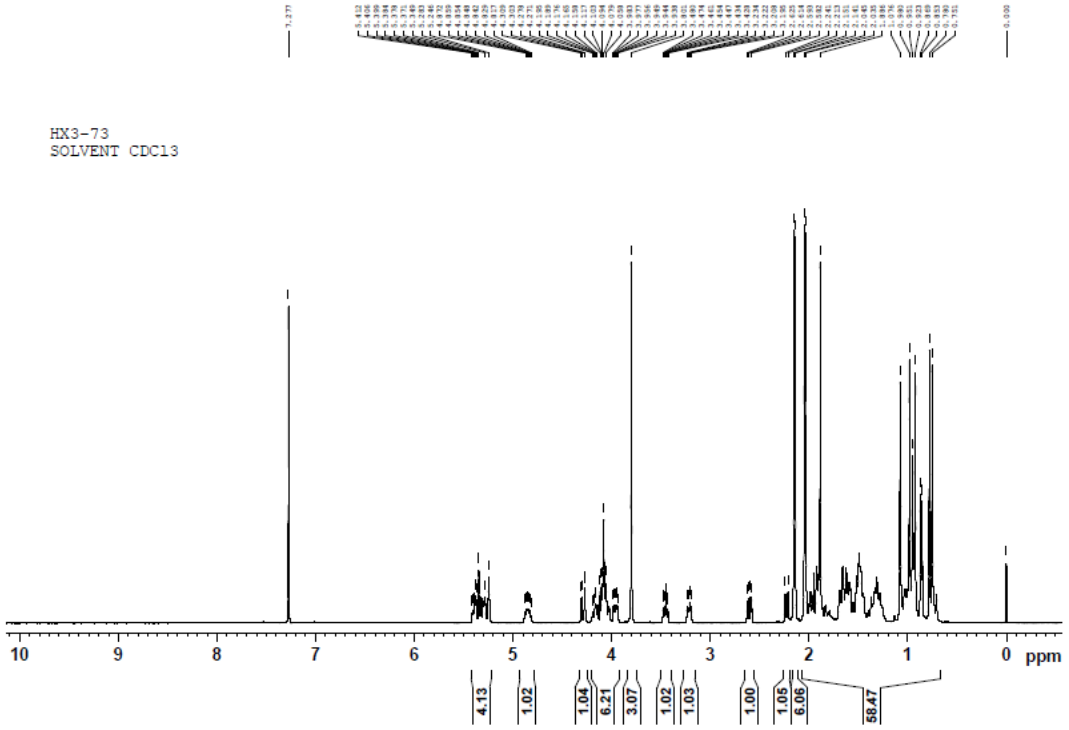


Figure 78. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **19d**

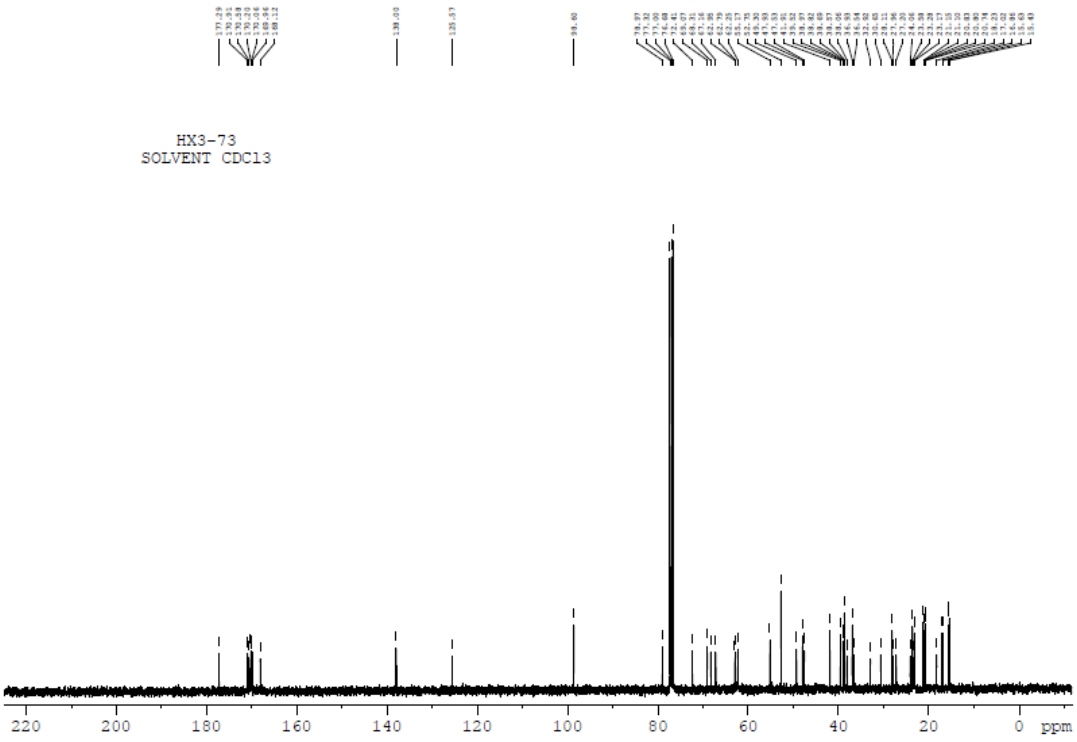


Figure 79. HR-ESI-MS spectrum of compound **19d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-73	C52 H79 N O16	C52 H79 N Na O16	996.5296	996.5291	-0.55

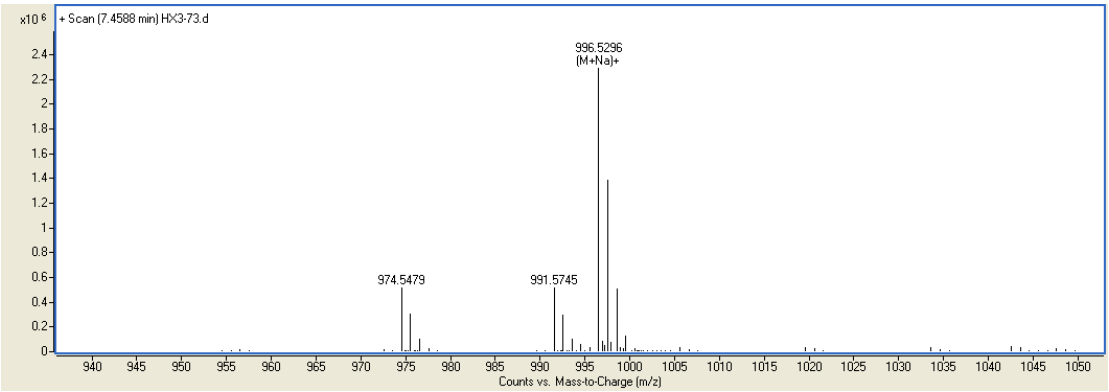


Figure 80. ^{1}H NMR (400 MHz, CD_3OD+$CDCl_3$) spectrum of compound **20a**

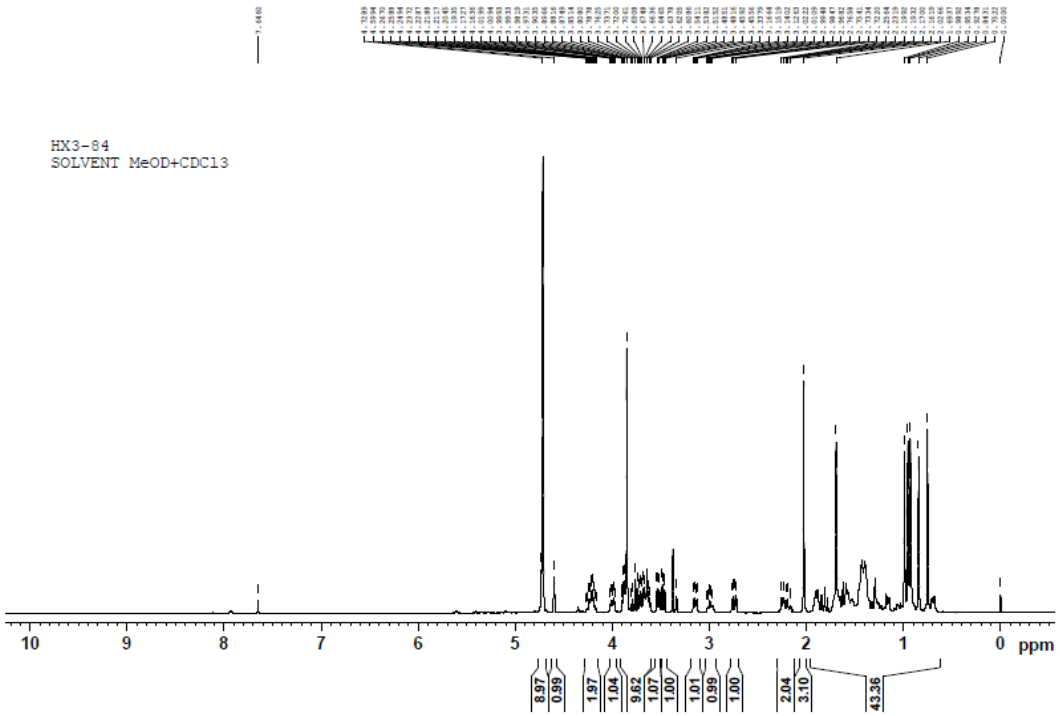


Figure 81. ^{13}C NMR (100 MHz, $CD_3OD+CDCl_3$) spectrum of compound **20a**

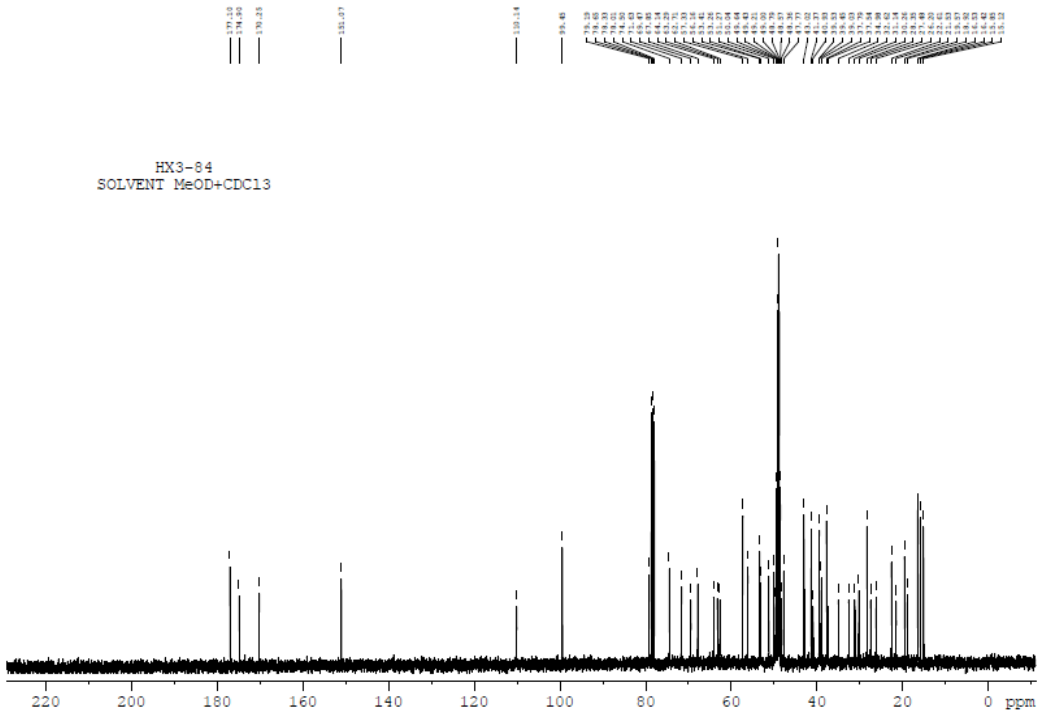


Figure 82. HR-ESI-MS spectrum of compound **20a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-84	C44 H71 N O12	C44 H71 N Na O12	828.4866	828.4868	0.3

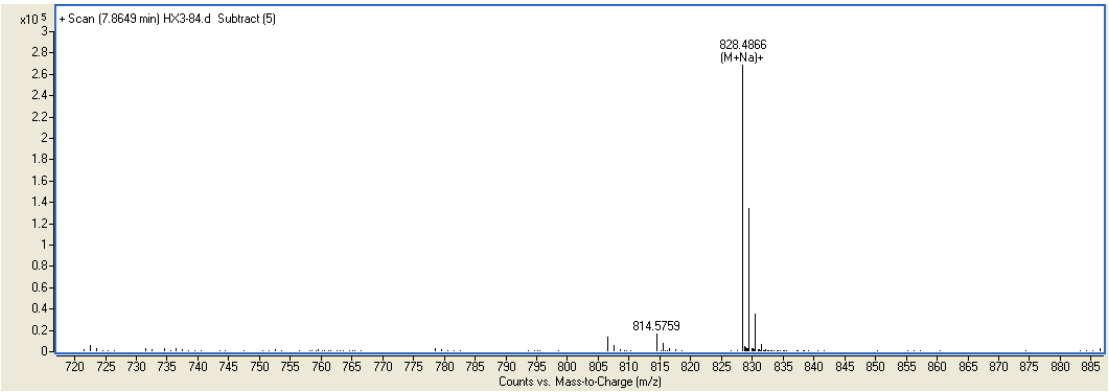


Figure 83. ^{1}H NMR (400 MHz, CD_3OD+$CDCl_3$) spectrum of compound **20b**

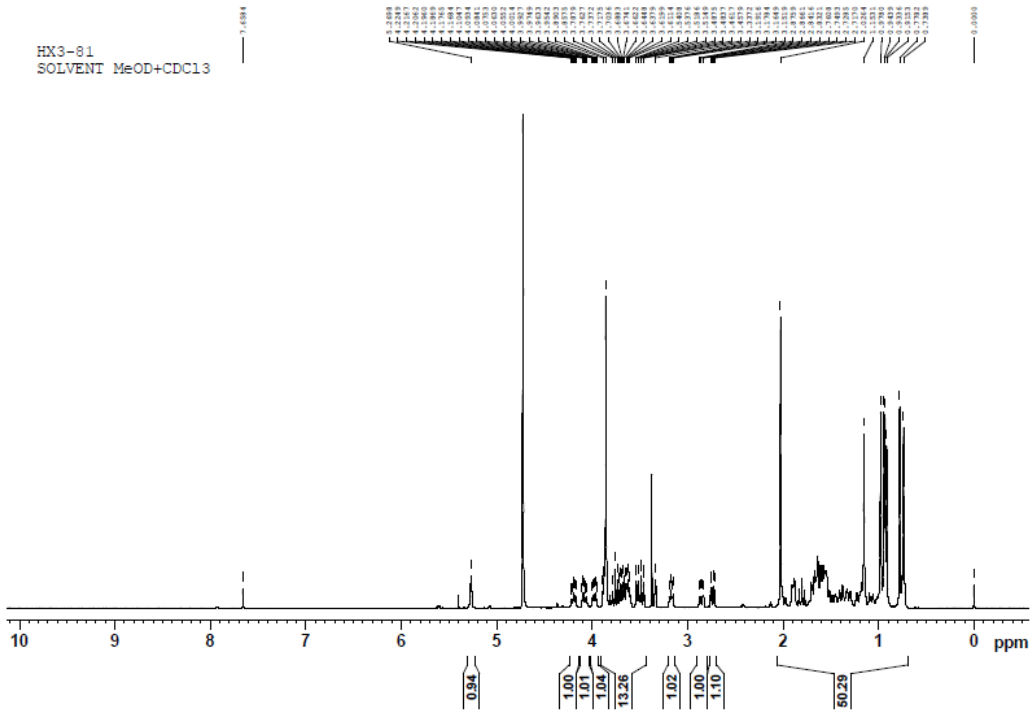


Figure 84. ^{13}C NMR (100 MHz, CD_3OD+$CDCl_3$) spectrum of compound **20b**

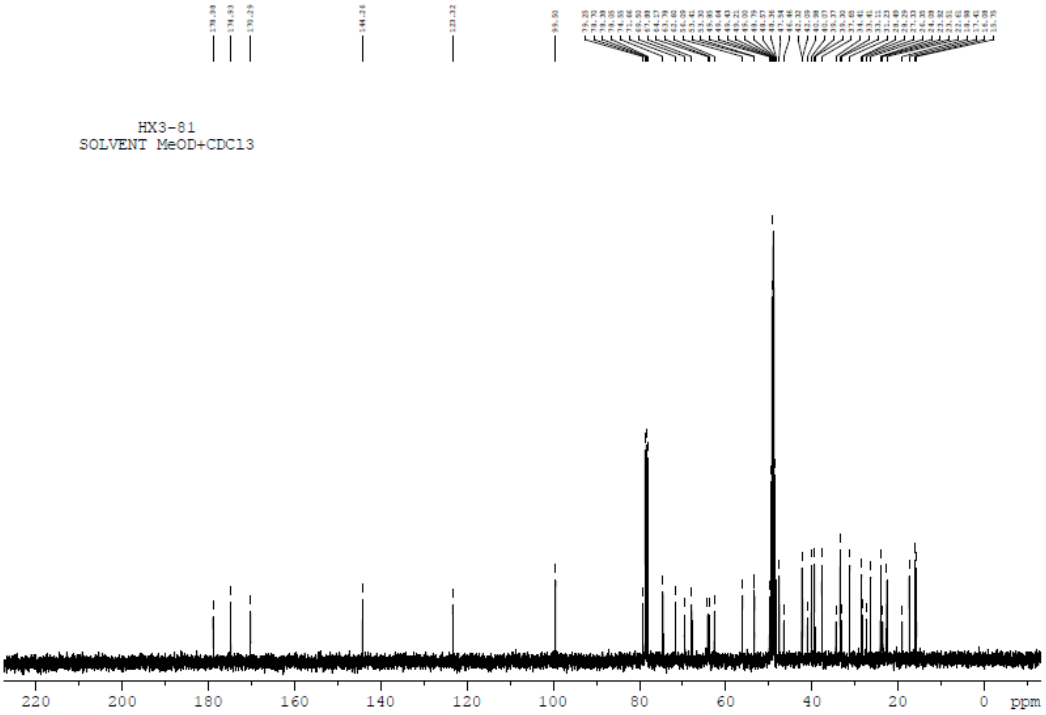


Figure 85. HR-ESI-MS spectrum of compound **20b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-81	C44 H71 N O12	C44 H71 N Na O12	828.4876	828.4868	-0.8

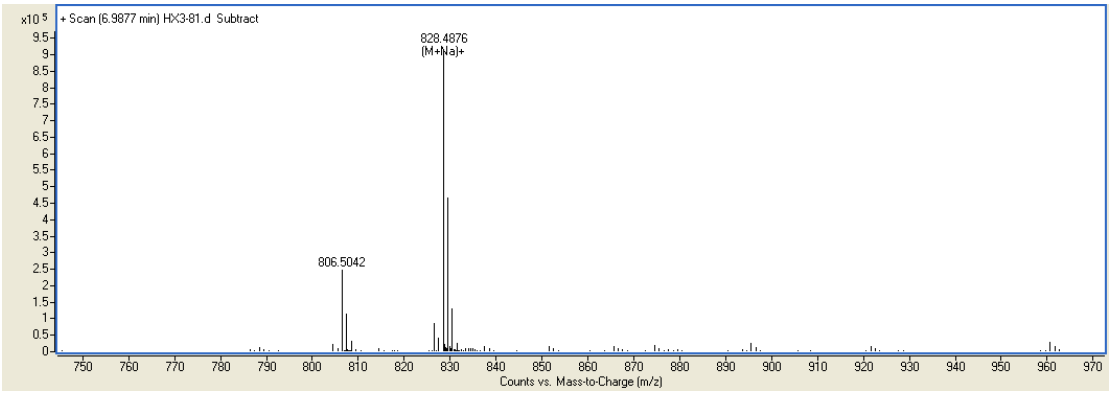


Figure 86. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **20c**

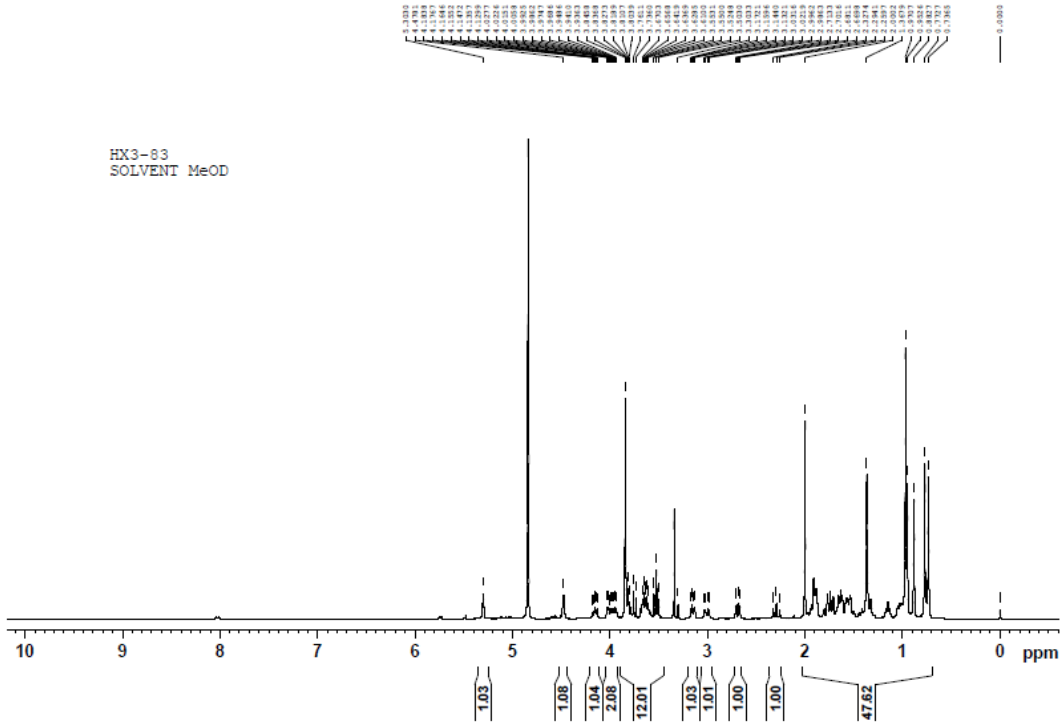


Figure 87. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **20c**

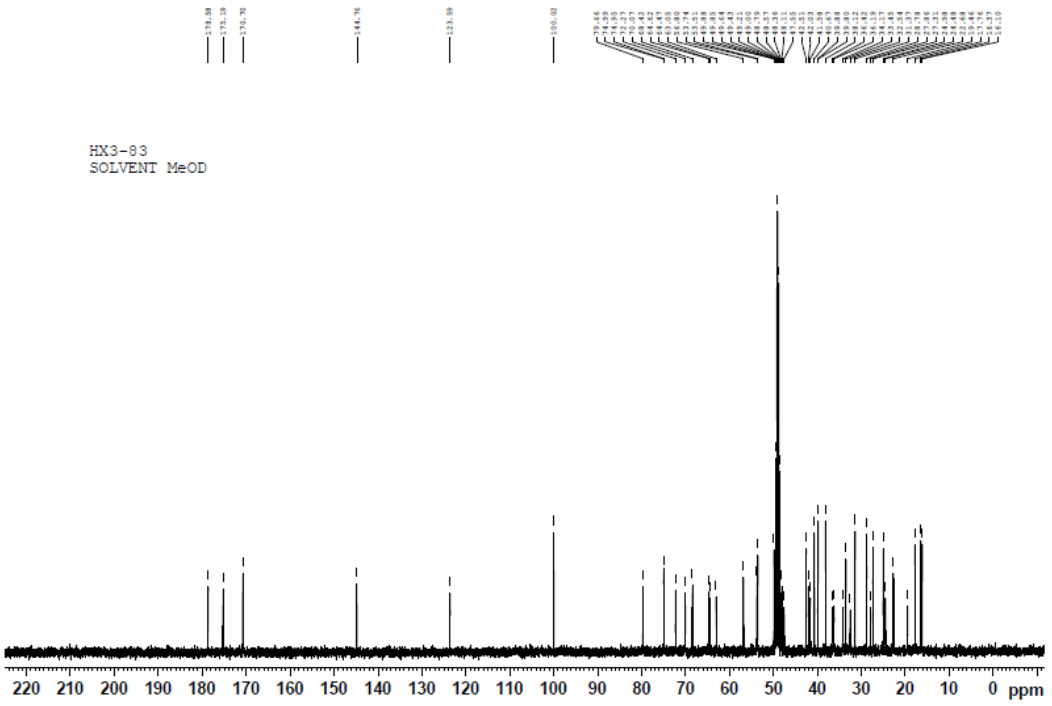


Figure 88. HR-ESI-MS spectrum of compound **20c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-83	C44 H71 N O13	C44 H72 N O13	822.5001	822.4998	-0.45

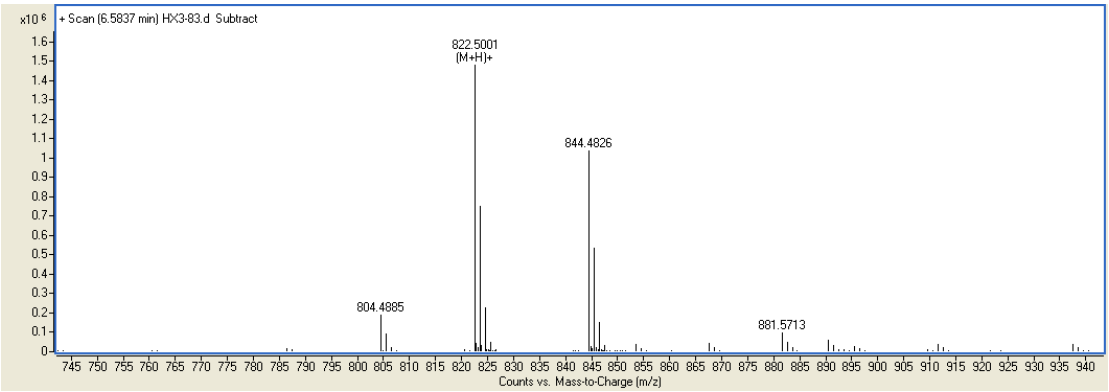


Figure 89. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **20d**

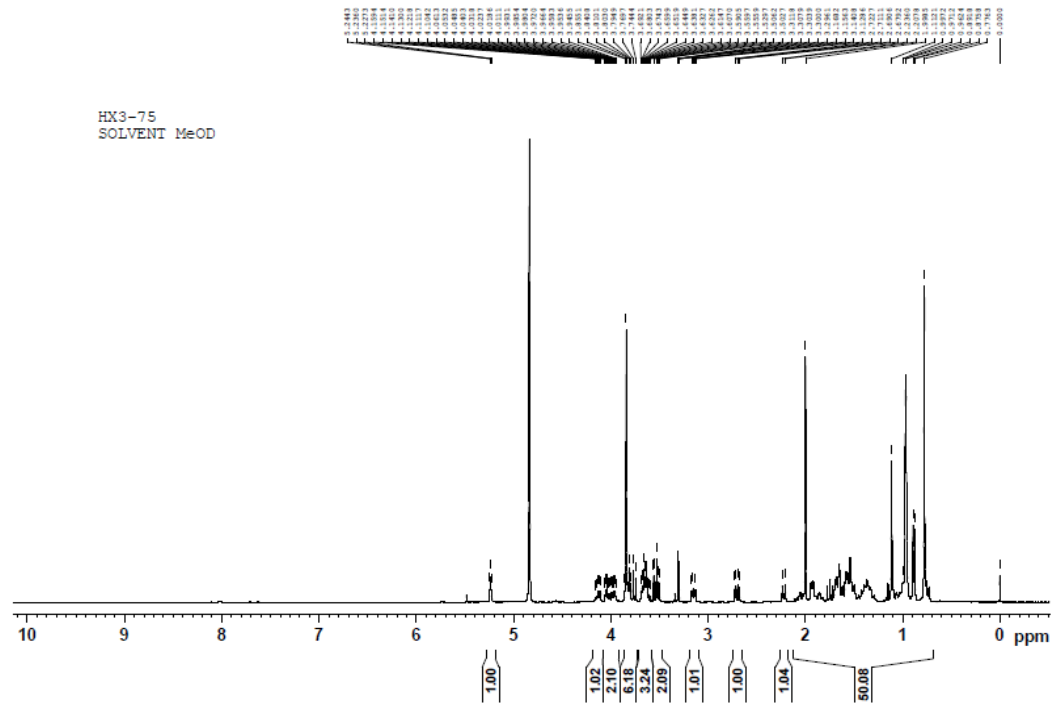


Figure 90. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **20d**

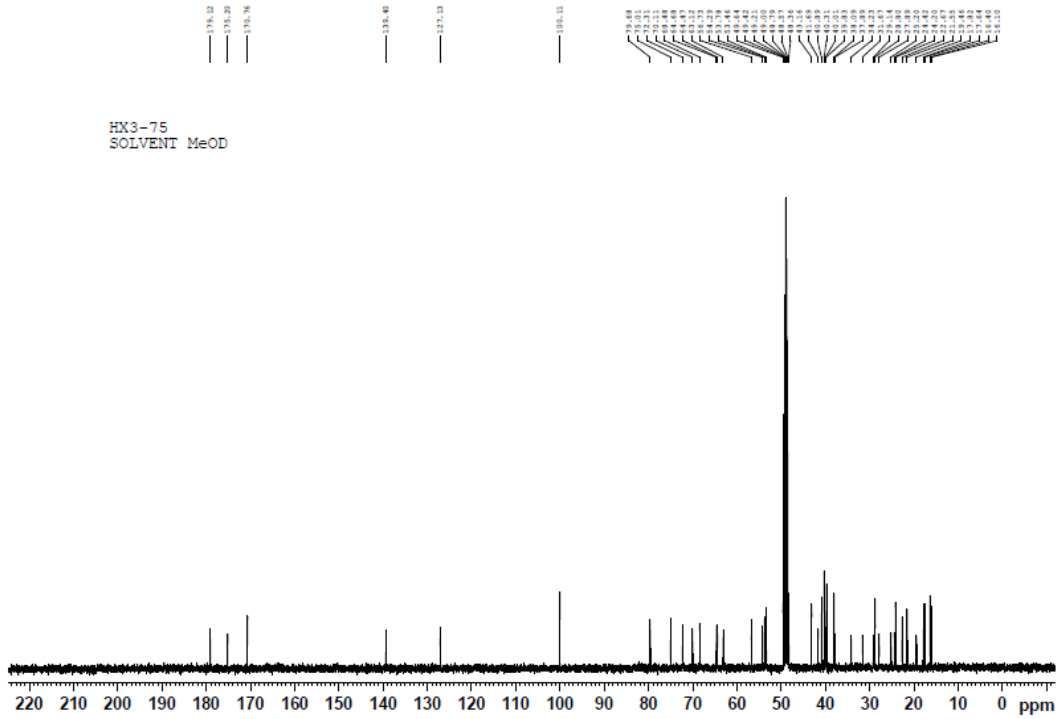


Figure 91. HR-ESI-MS spectrum of compound **20d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-75	C44 H71 N O12	C44 H71 N Na O12	828.4873	828.4868	-0.55