Supporting Information

Synthesis of novel pentacyclic triterpene-Neu5Ac2en derivatives and investigation of their in vitro anti-influenza entry activity

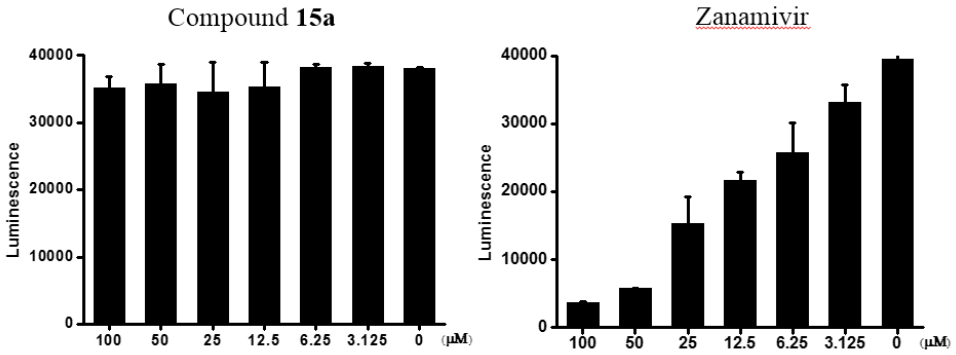
Yongying Shi[a,1], Longlong Si[a,1], Xu Han[a,1], Zibo Fan[a], Shouxin Wang[a,c], Man Li[a], Jiaqi Sun[a], Yongmin Zhang[b], Demin Zhou[a], Sulong Xiao[a,*]

Dedicated to Professor Lihe Zhang on the Occasion of His 80th Birthday.

[a]*State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing 100191, China*

[b]*Institut Parisien de Chimie Moléculaire, CNRS UMR 8232, Université Pierre & Marie Curie-Paris 6, 4 Place Jussieu, 75005 Paris, France*

1. **SI Figure 1.** The NA inhibition assay of compound **15a**.



SI Figure 1. Compounds **15a** had no inhibitory effect on the influenza virus NA activity. Compound or zanamivir 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 ℃. NA activity was measured by fluorescence of 4-methylumbelliferone with fluorescence spectrophotometer. Each point represents the mean ± S.E.M. for three independent experiments.

2. Selected ^{1}H, ^{13}C NMR and HRMS spectra

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

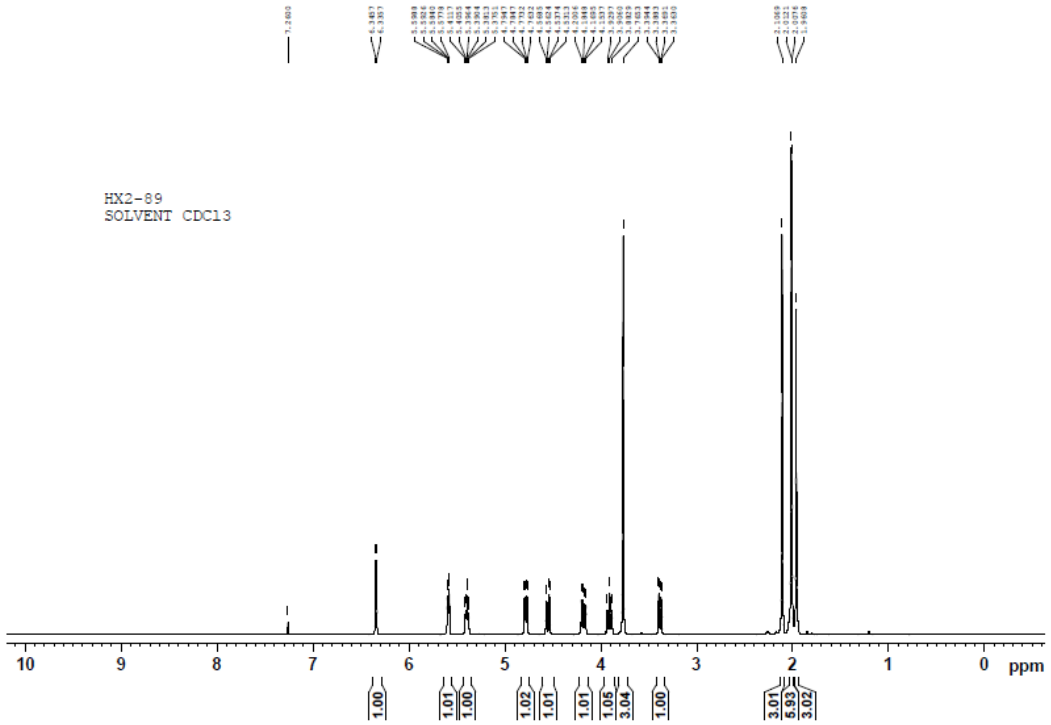


Figure 2. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **6**

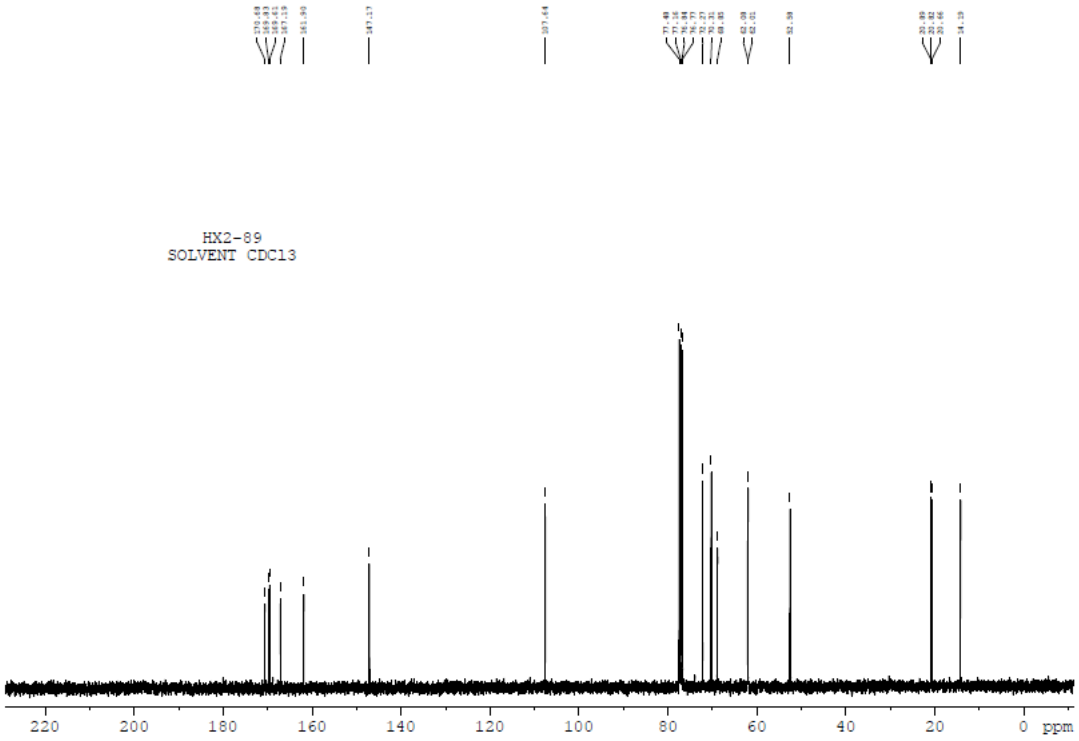


Figure 3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **7**

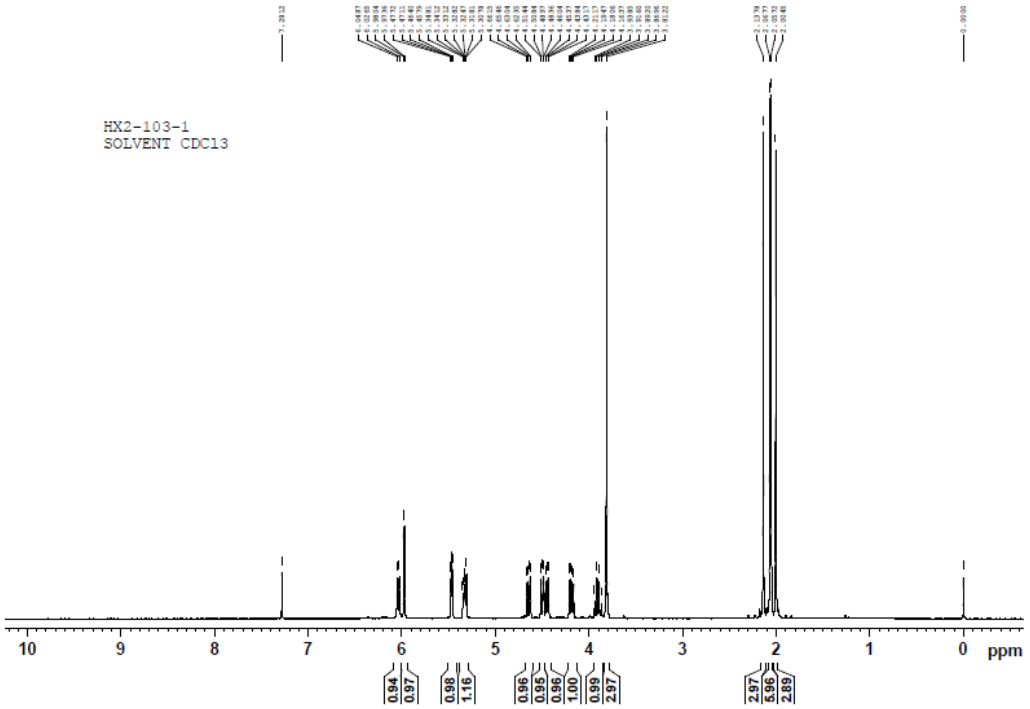


Figure 4. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **7**

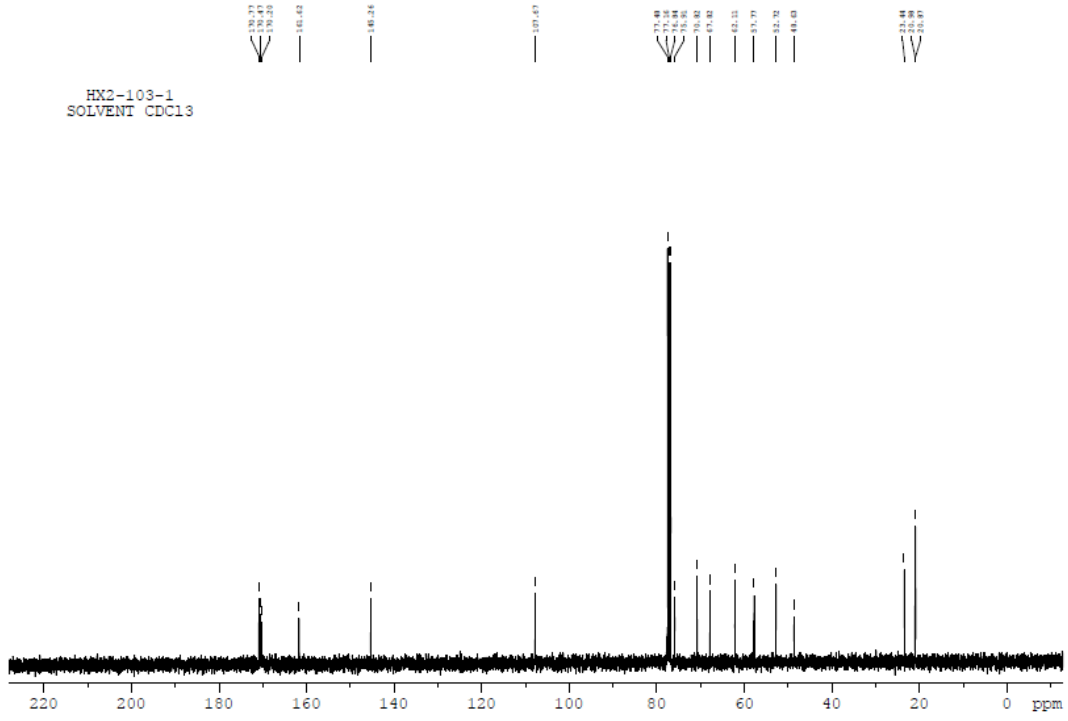


Figure 5. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8a**

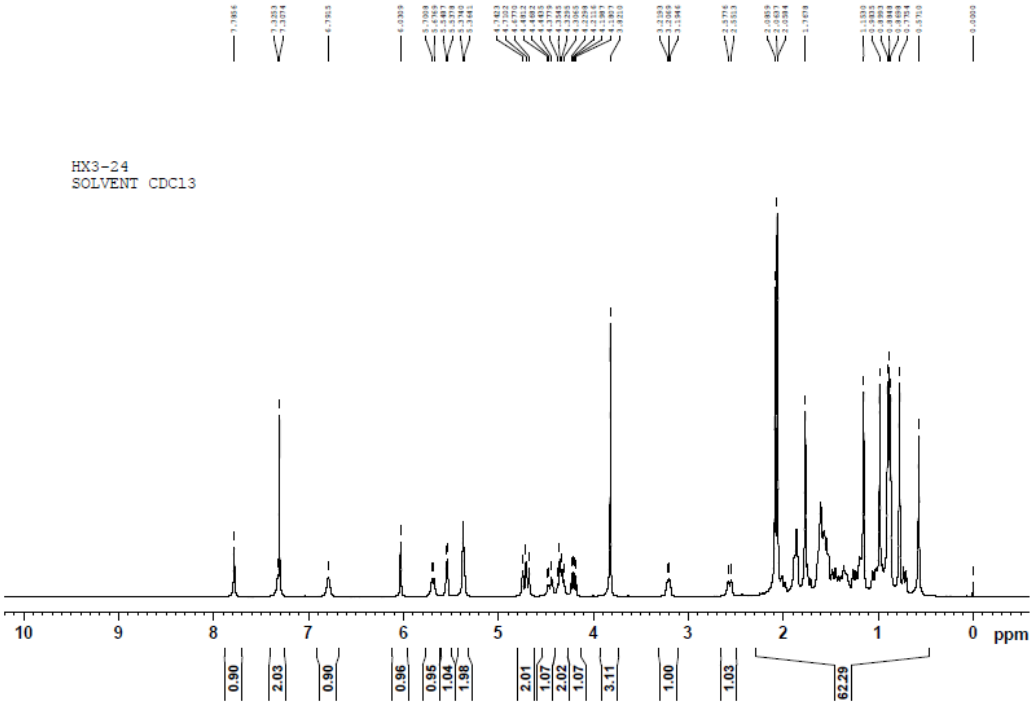


Figure 6. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8a**

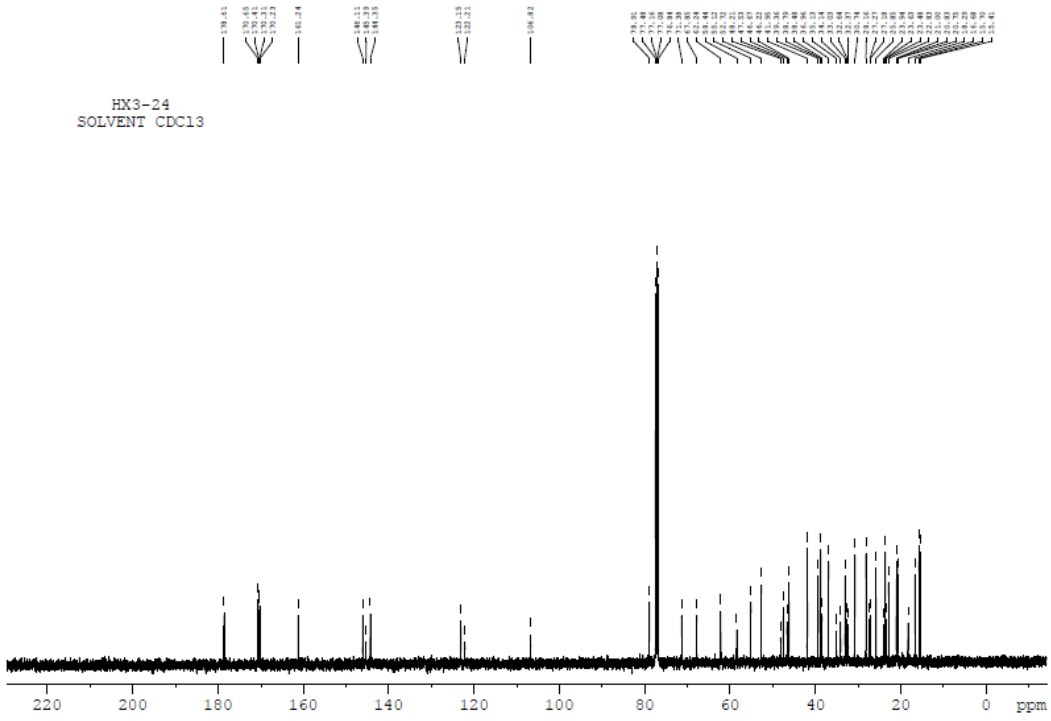


Figure 7. HR-ESI-MS spectrum of compound **8a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-24	C51 H75 N5 O12	C51 H75 N5 Na O12	972.5309	972.5304	-0.39

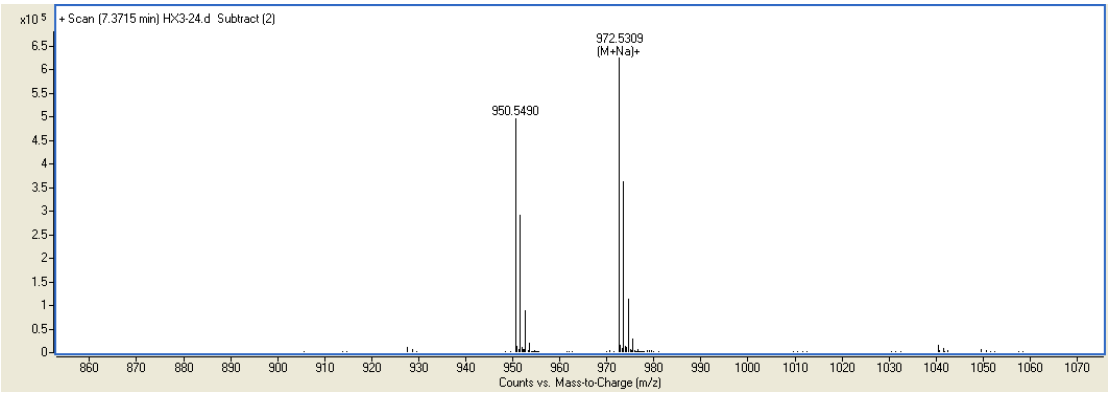


Figure 8. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8b**

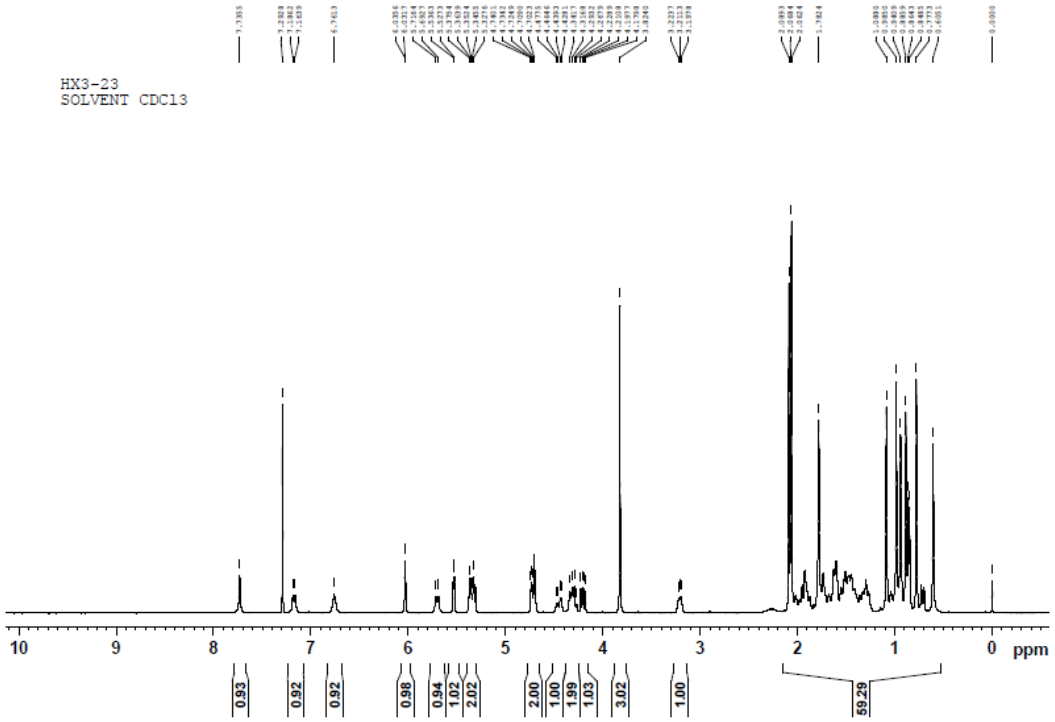


Figure 9. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8b**

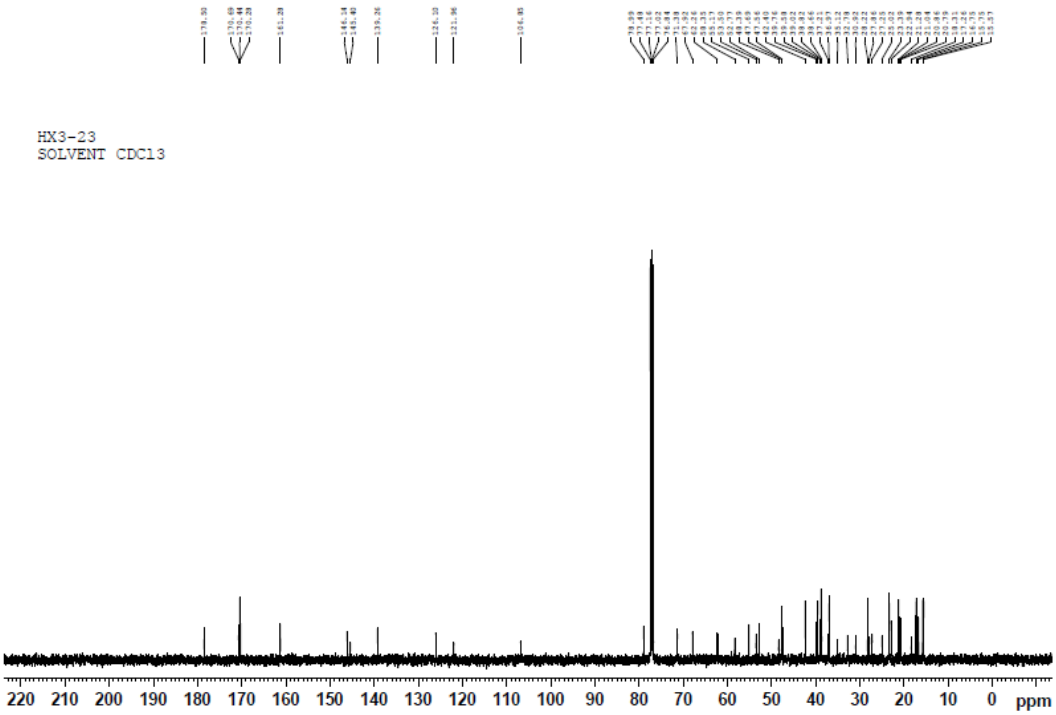


Figure 10. HR-ESI-MS spectrum of compound **8b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-23	C51 H75 N5 O12	C51 H76 N5 O12	950.5493	950.5485	-0.97

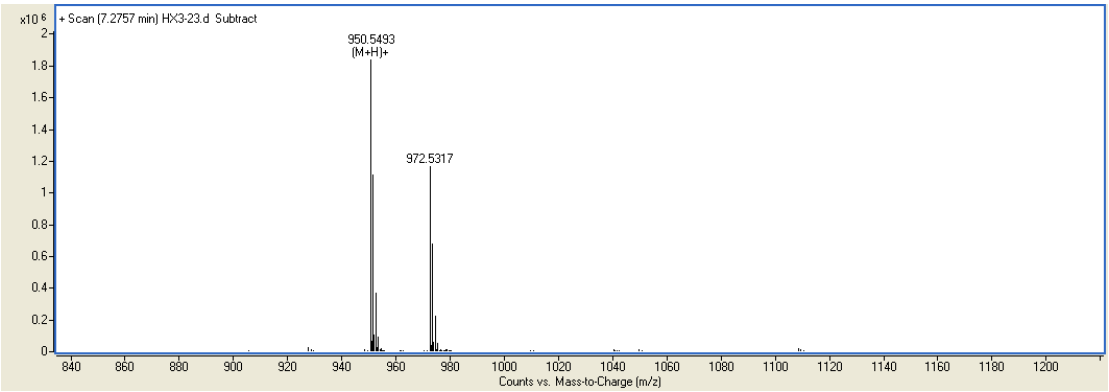


Figure 11. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8c**

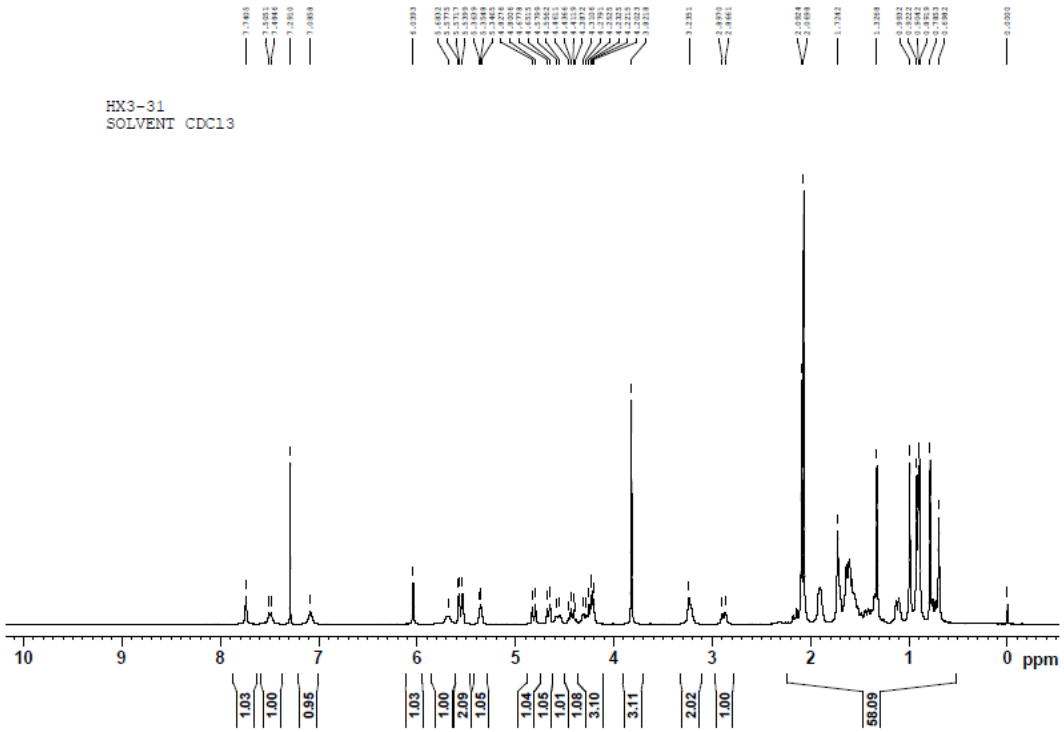


Figure 12. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8c**

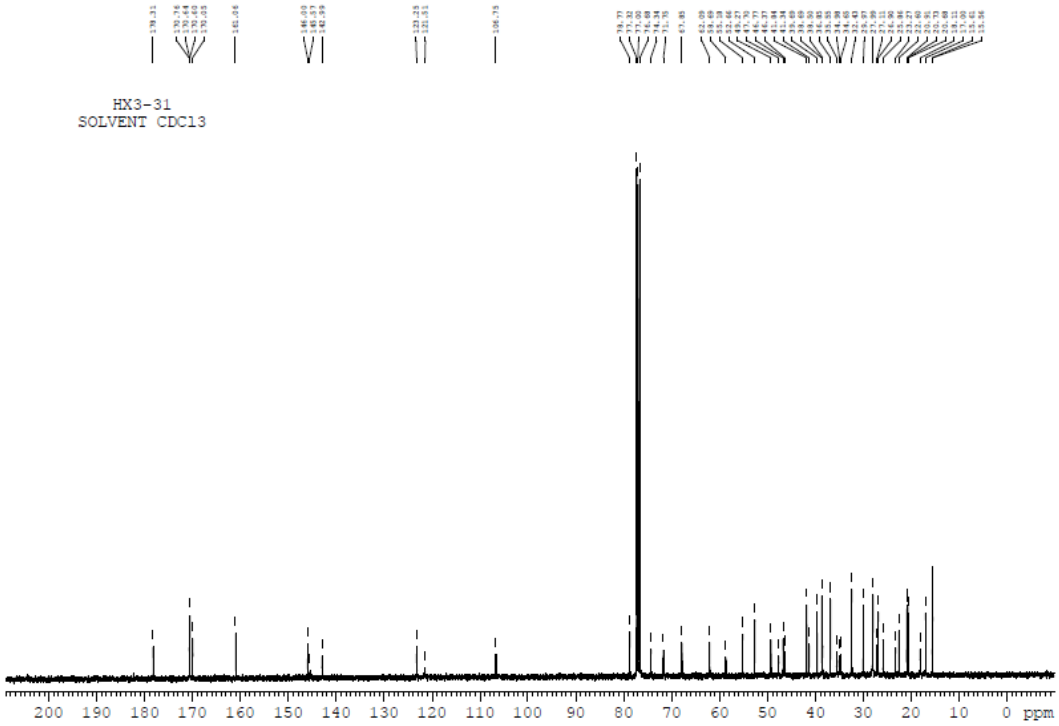


Figure 13. HR-ESI-MS spectrum of compound **8c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-31	C51 H75 N5 O13	C51 H76 N5 O13	966.5440	966.5434	-0.68

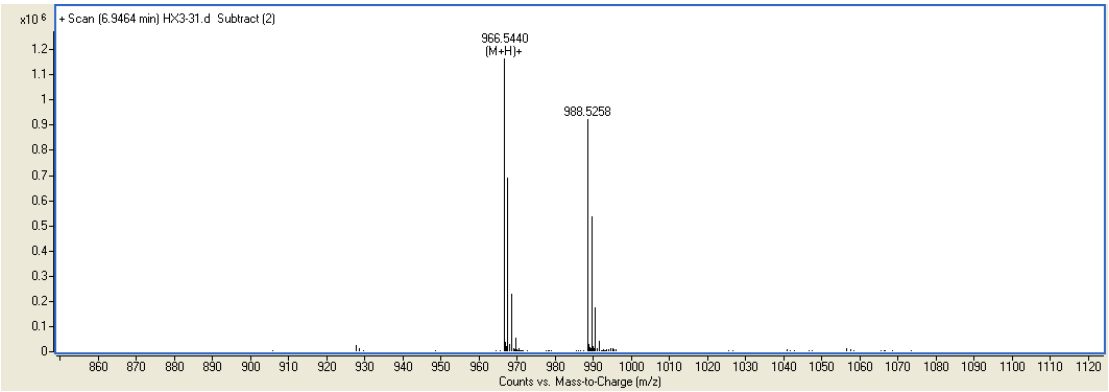


Figure 14. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **8d**

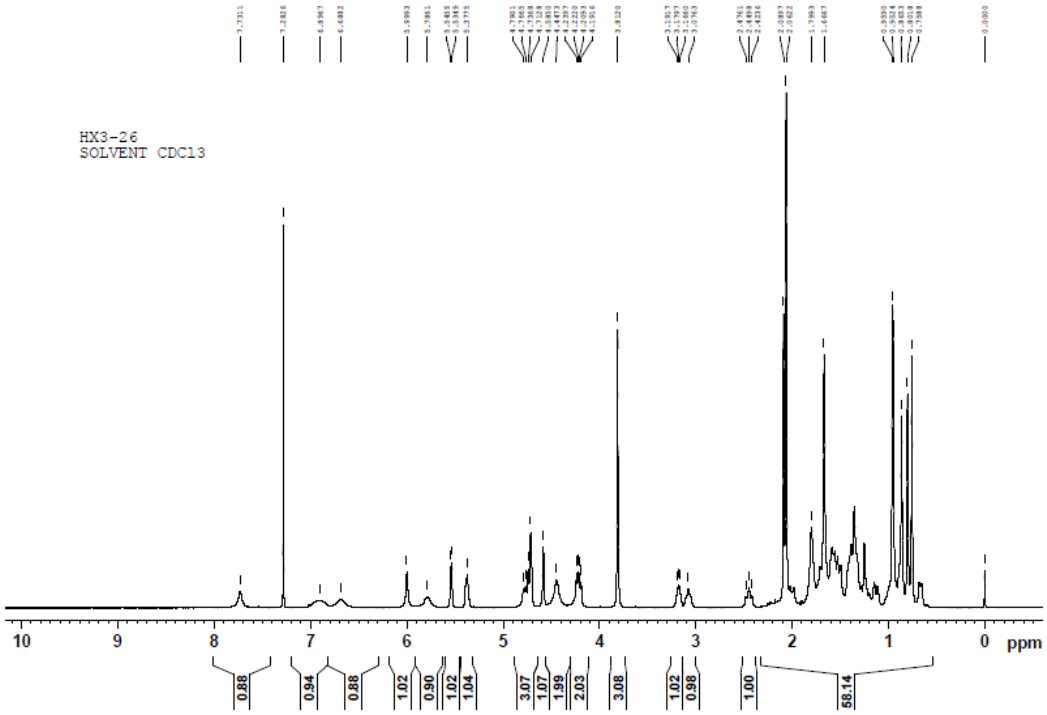


Figure 15. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **8d**

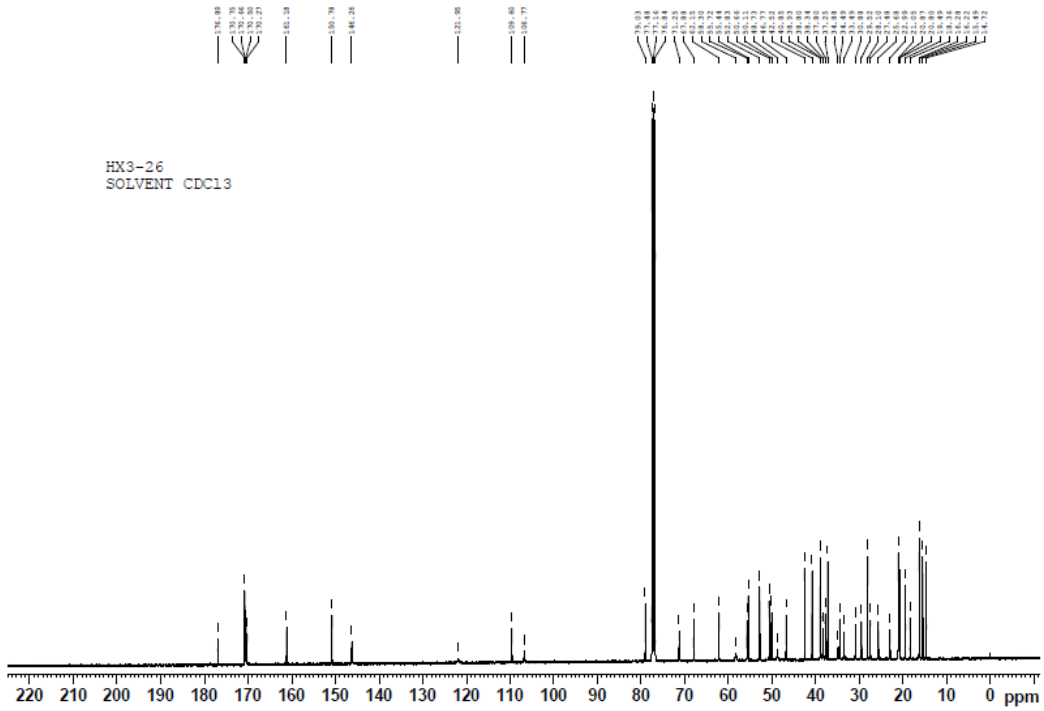


Figure 16. HR-ESI-MS spectrum of compound **8d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-26	C51 H75 N5 O12	C51 H75 N5 Na O12	972.5298	972.5304	0.85

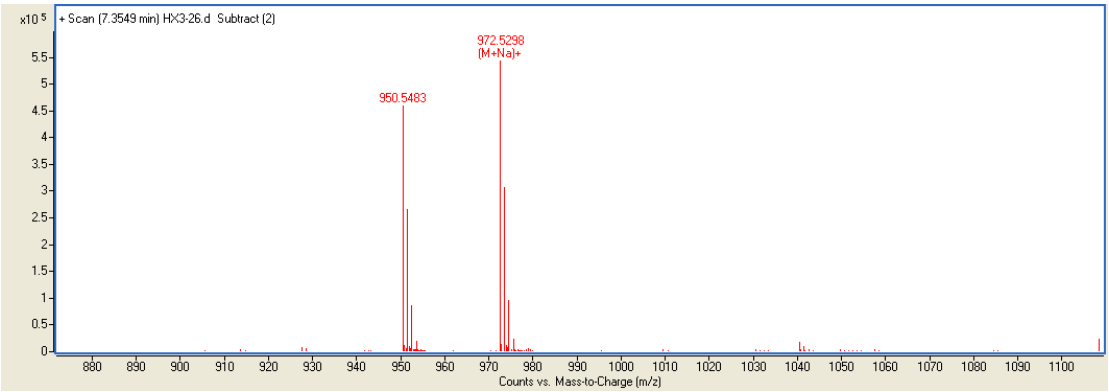


Figure 17. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9a**

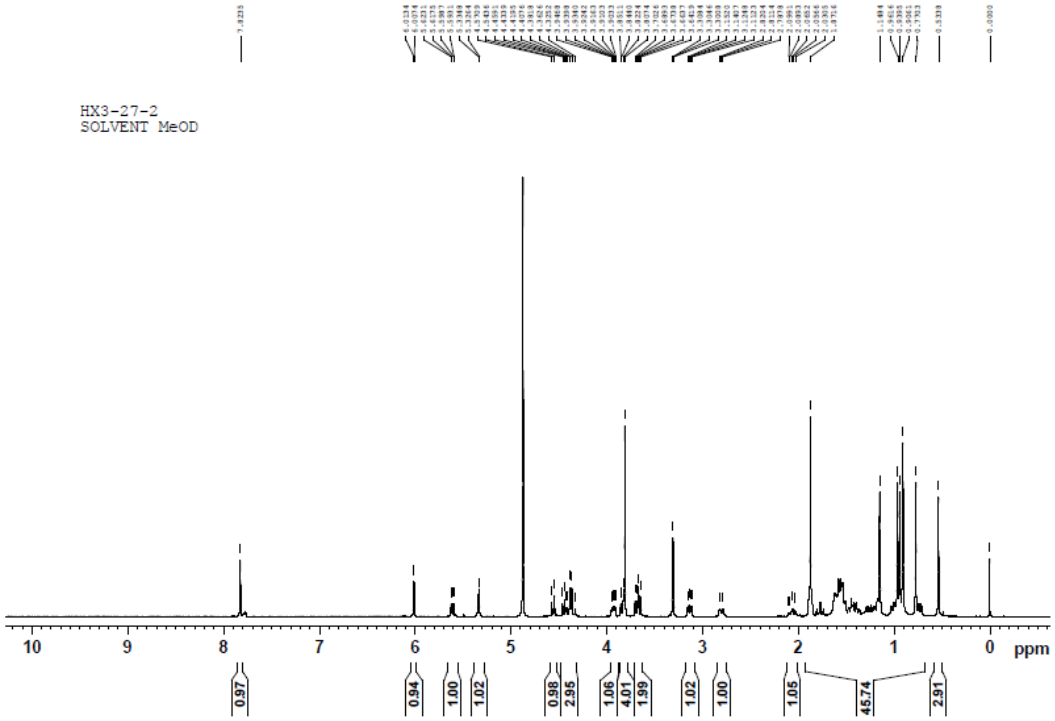


Figure 18. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9a**

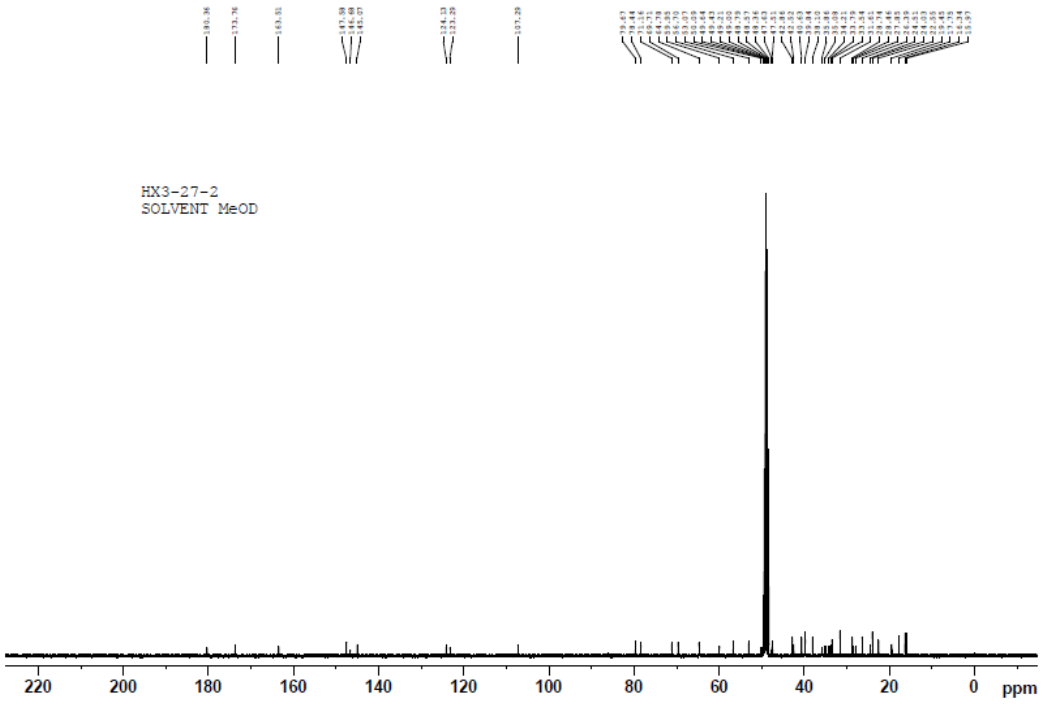


Figure 19. HR-ESI-MS spectrum of compound **9a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-27-2	C45 H69 N5 O9	C45 H70 N5 O9	824.5174	824.5168	-0.82

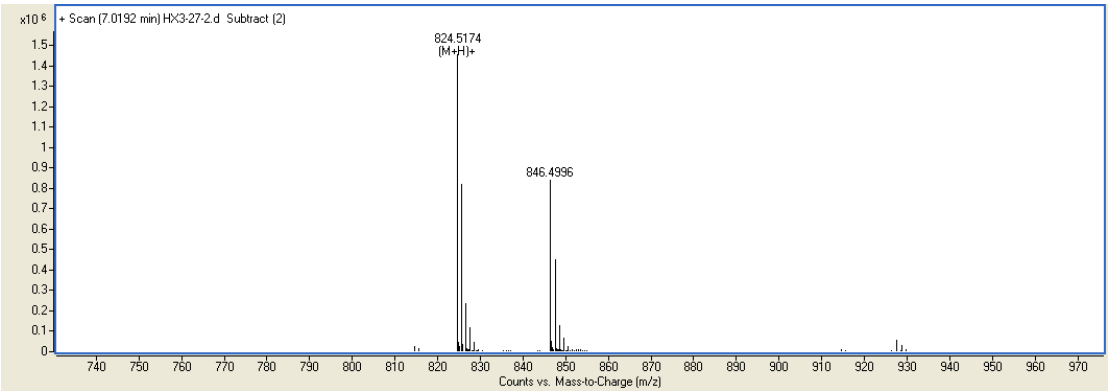


Figure 20. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9b**

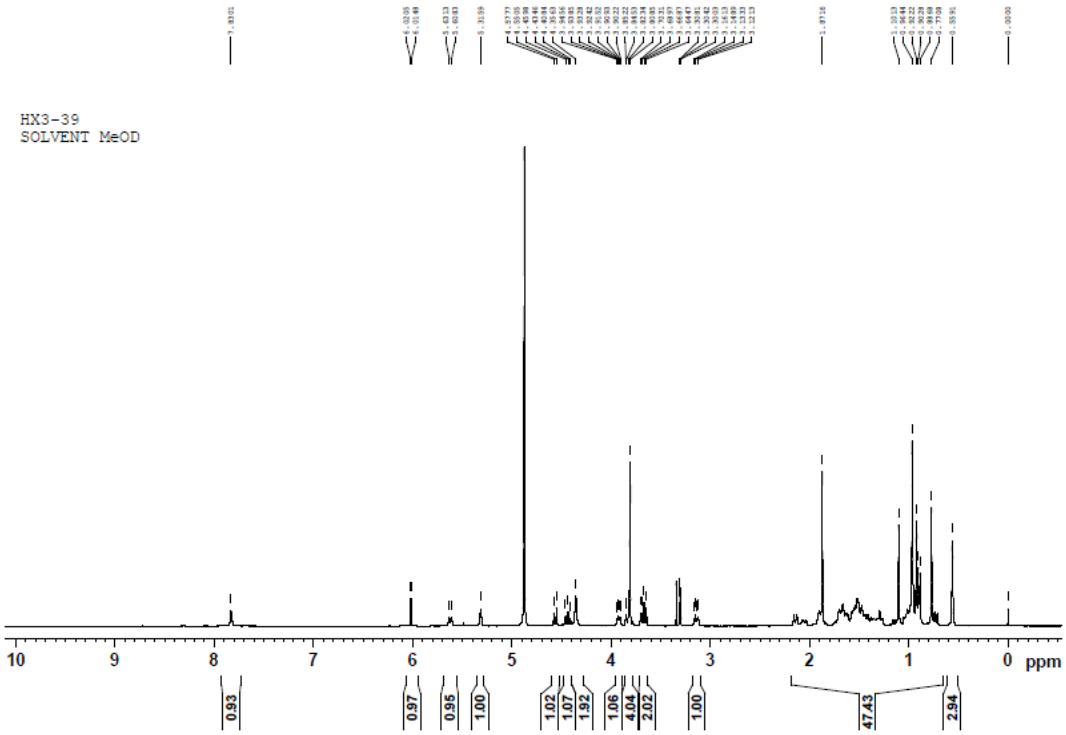


Figure 21. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9b**

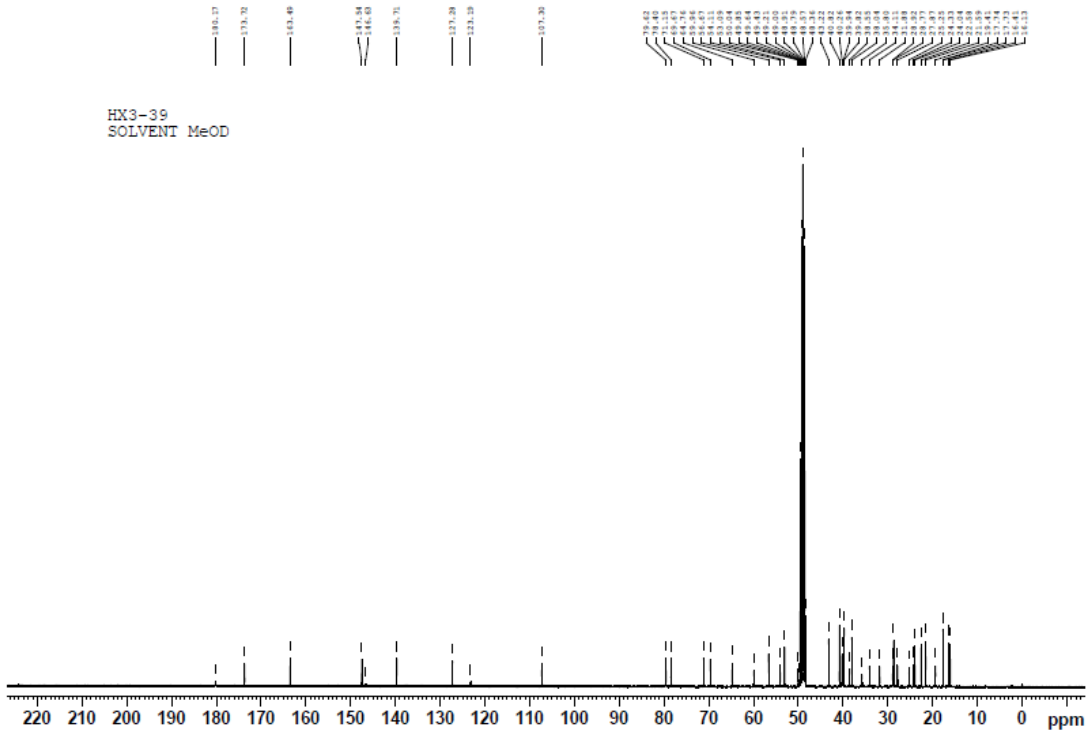


Figure 22. HR-ESI-MS spectrum of compound **9b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-39	C45 H69 N5 O9	C45 H70 N5 O9	824.5163	824.5168	0.47

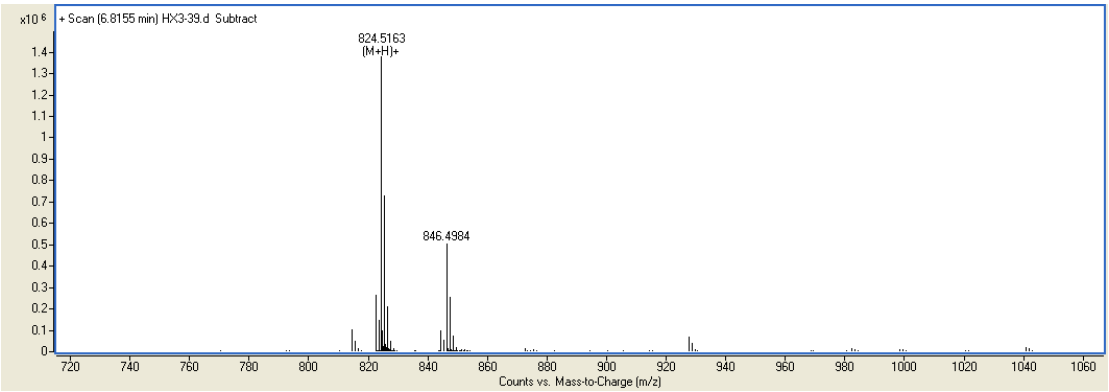


Figure 23. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9c**

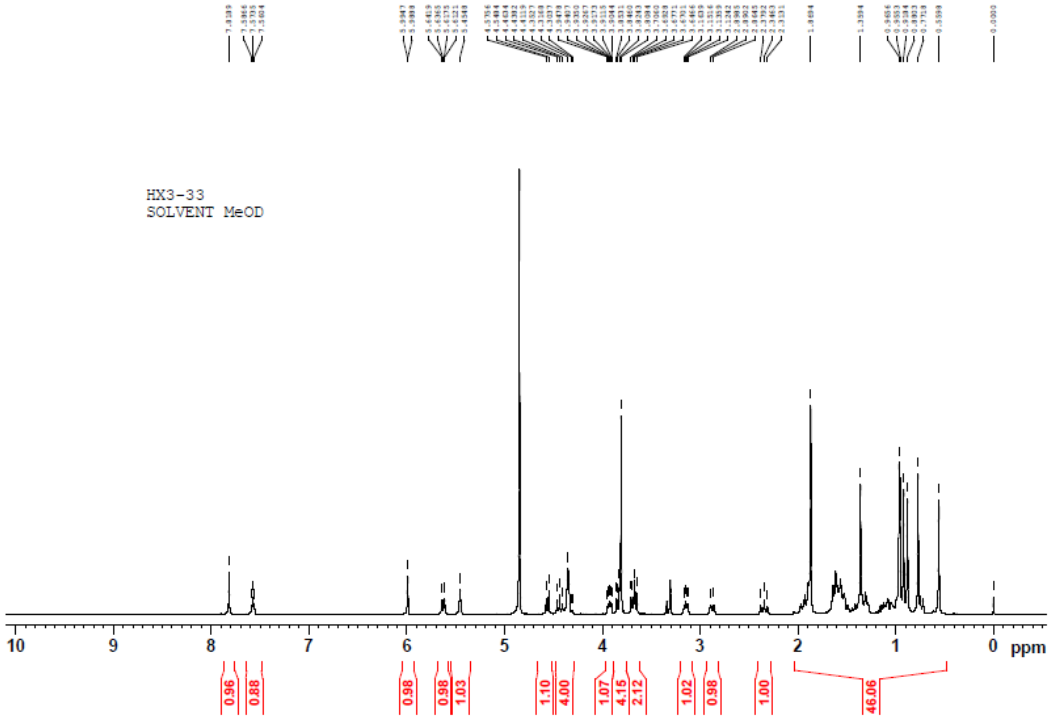


Figure 24. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9c**

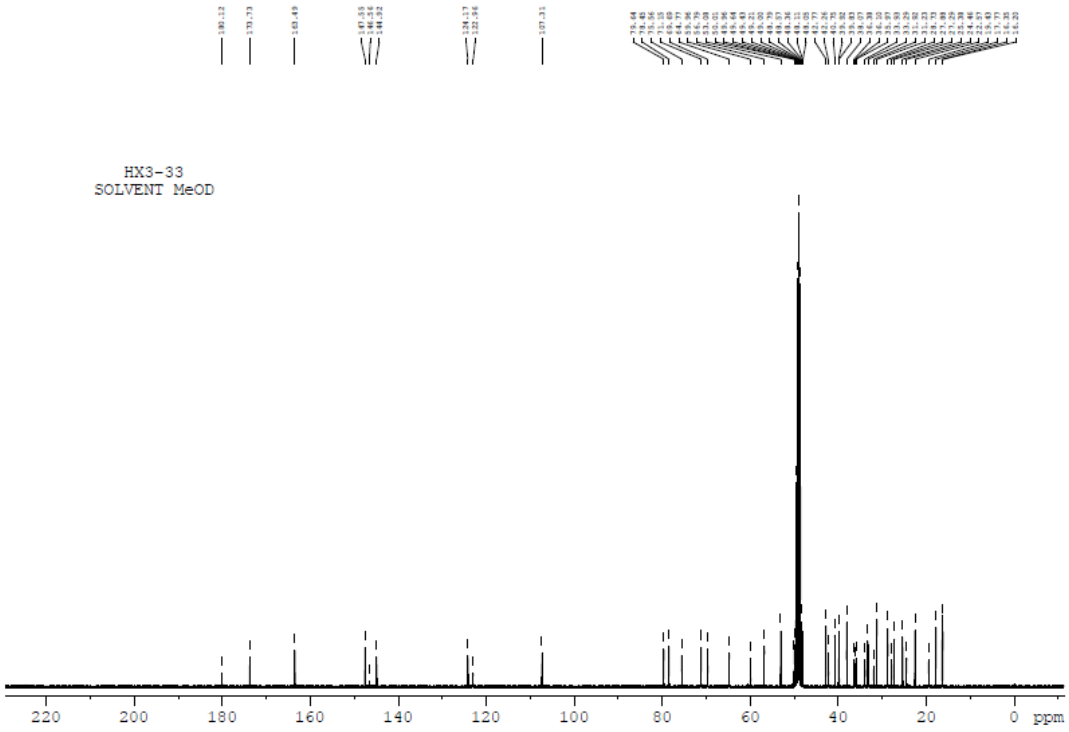


Figure 25. HR-ESI-MS spectrum of compound **9c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-33	C45 H69 N5 O10	C45 H70 N5 O10	840.5125	840.5117	-0.82

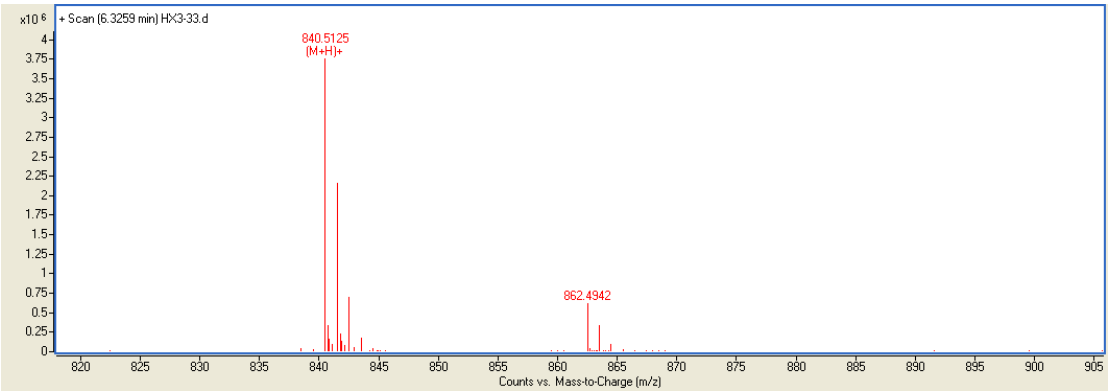


Figure 26. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **9d**

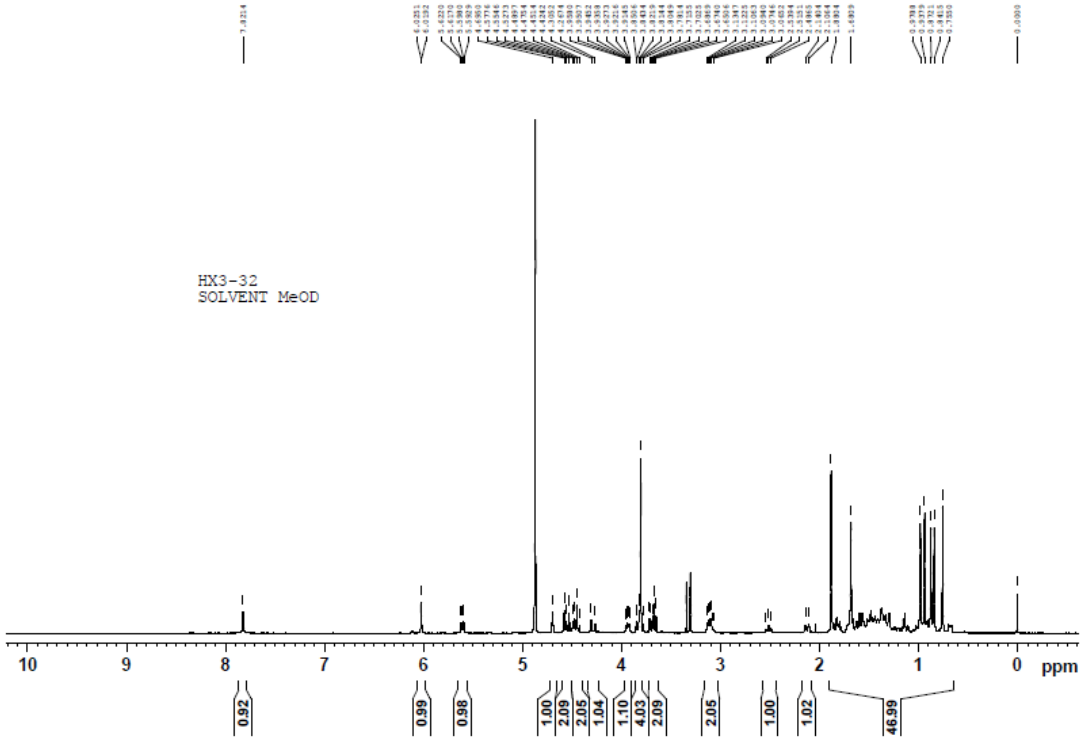


Figure 27. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **9d**

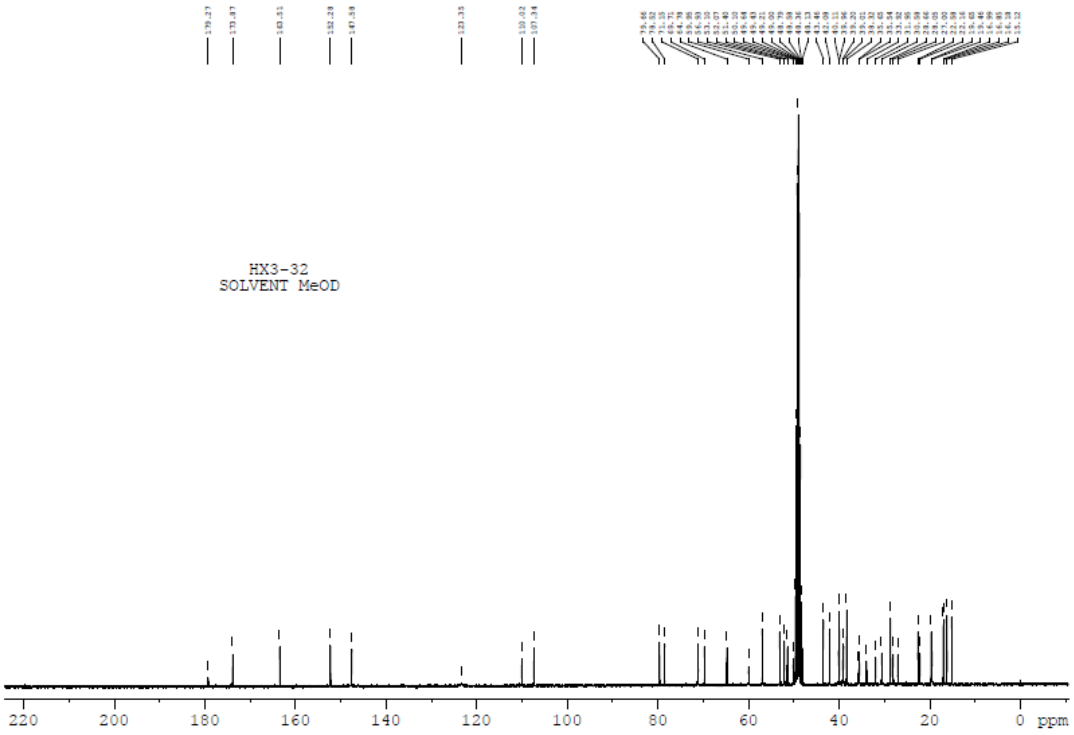


Figure 28. HR-ESI-MS spectrum of compound **9d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-32	C45 H69 N5 O9	C45 H70 N5 O9	824.5173	824.5168	-0.49

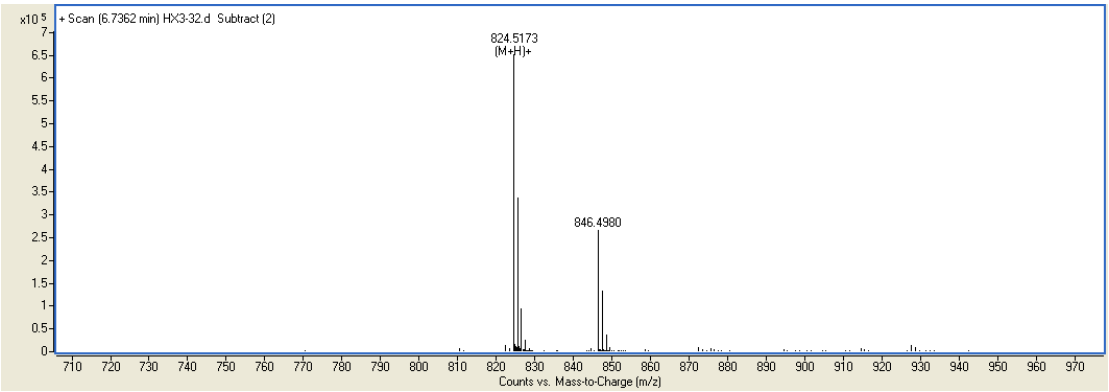


Figure 29. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **10a**

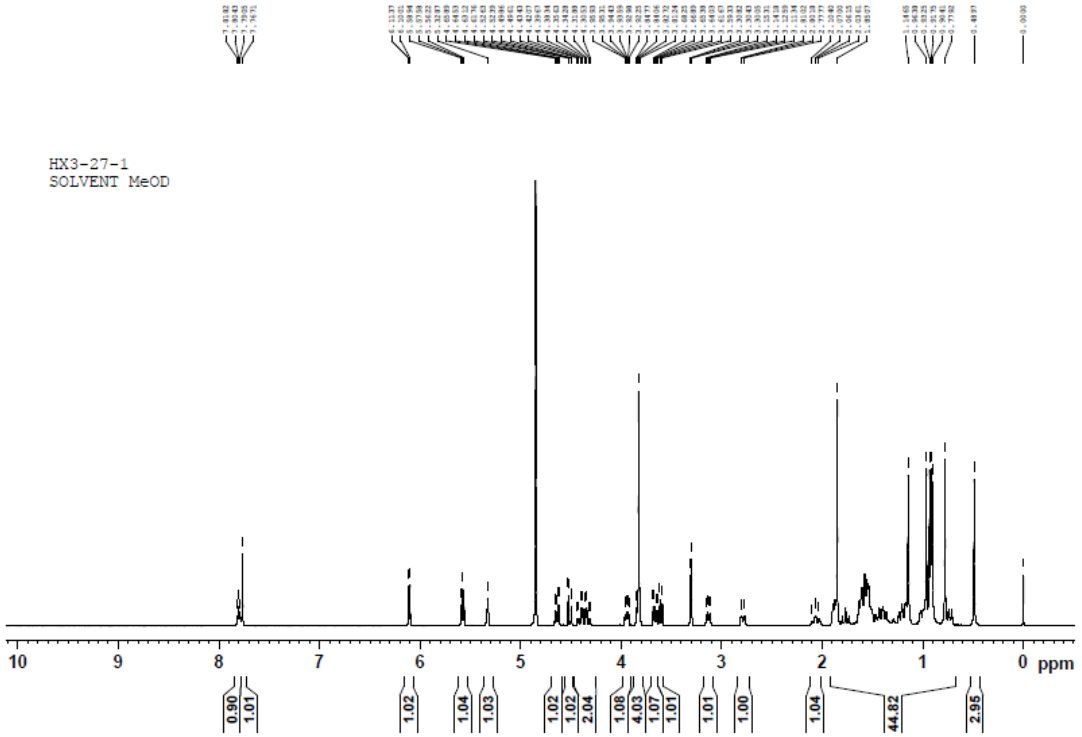


Figure 30. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **10a**

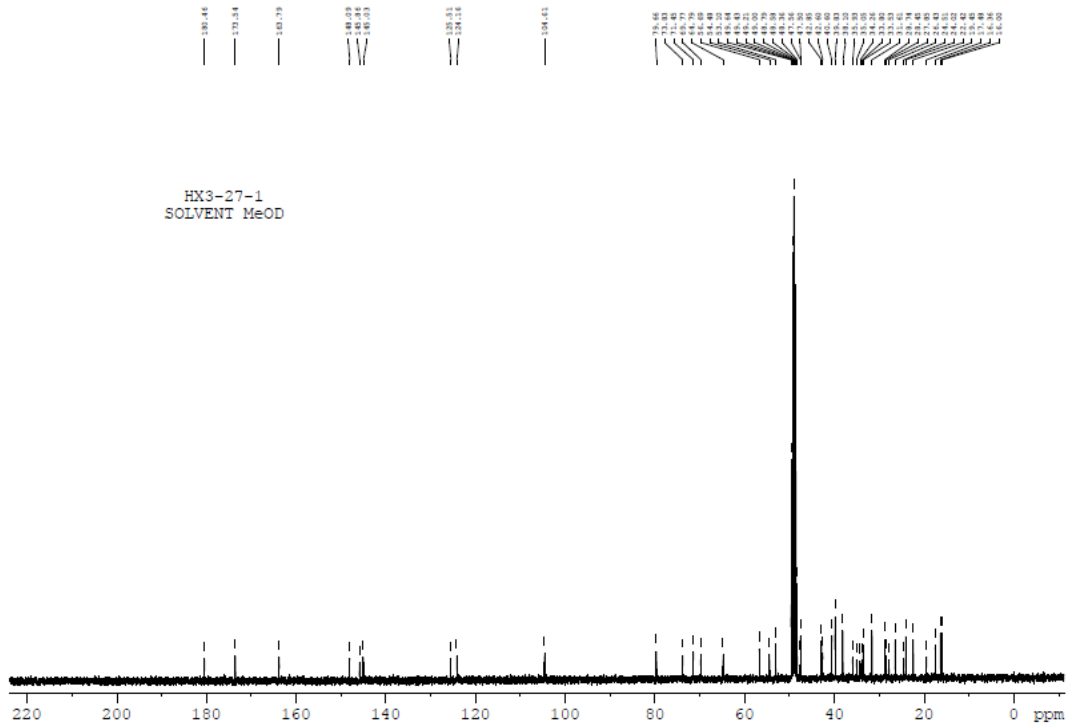


Figure 31. HR-ESI-MS spectrum of compound **10a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-27-1	C45 H69 N5 O9	C45 H69 N5 Na O9	846.4993	846.4987	-0.7

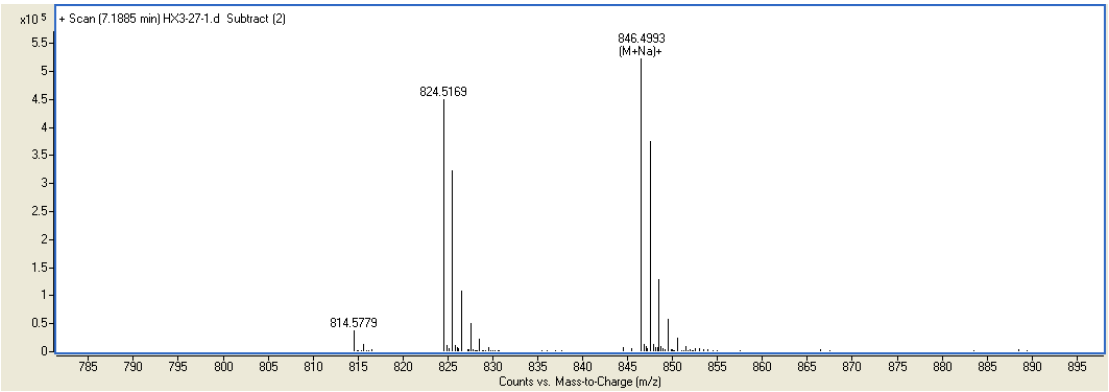


Figure 32. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **10b**

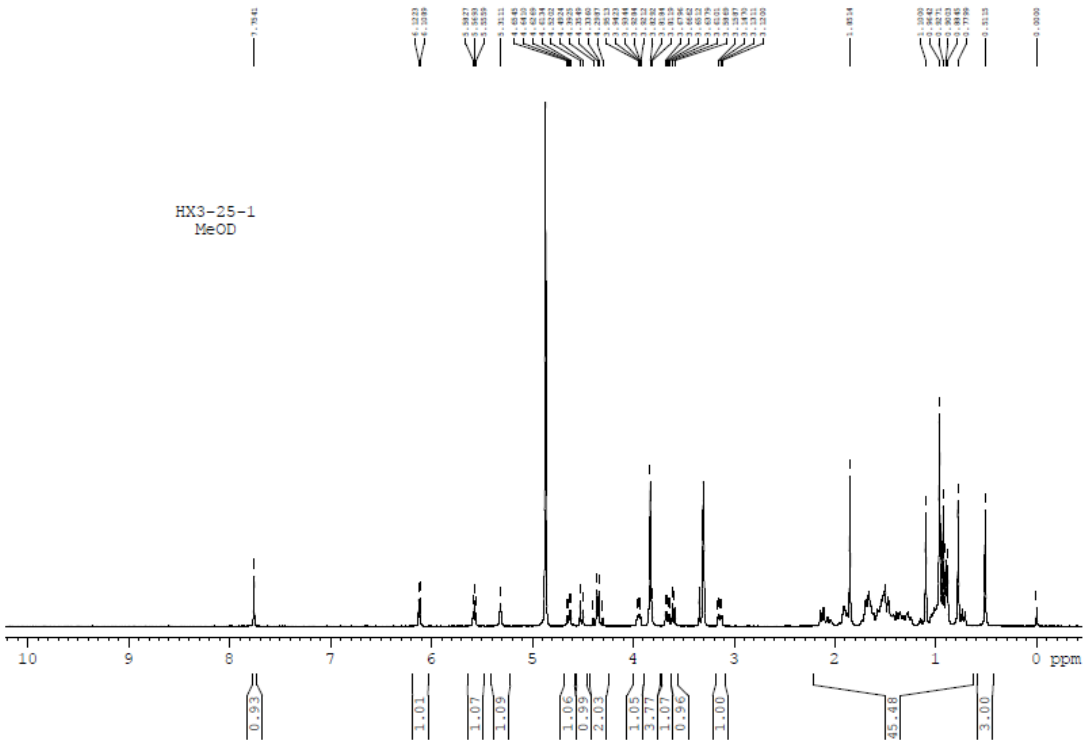


Figure 33. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **10b**

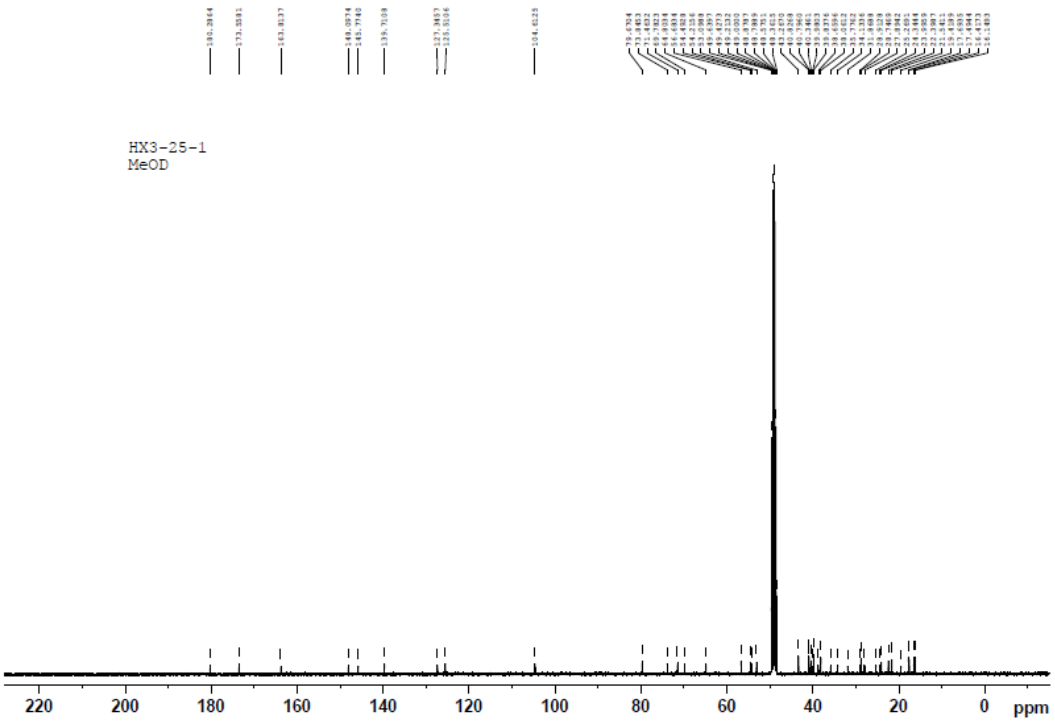


Figure 34. HR-ESI-MS spectrum of compound **10b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-25-1	C45 H69 N5 O9	C45 H69 N5 Na O9	846.4988	846.4987	-0.69

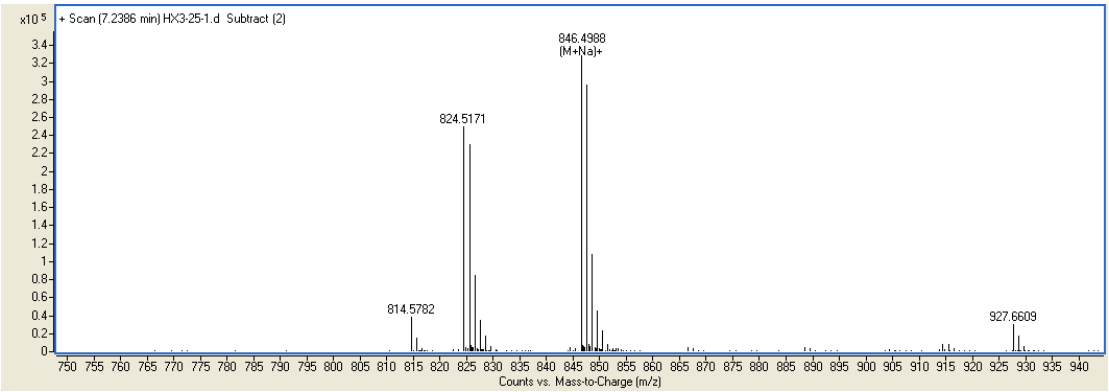


Figure 35. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **11**

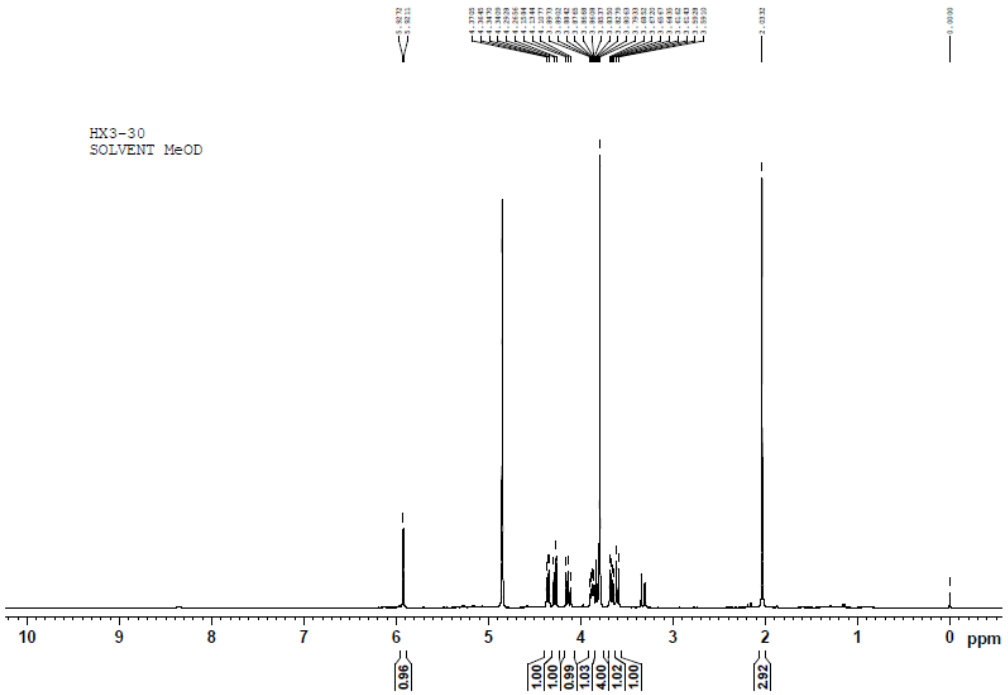


Figure 36. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **11**

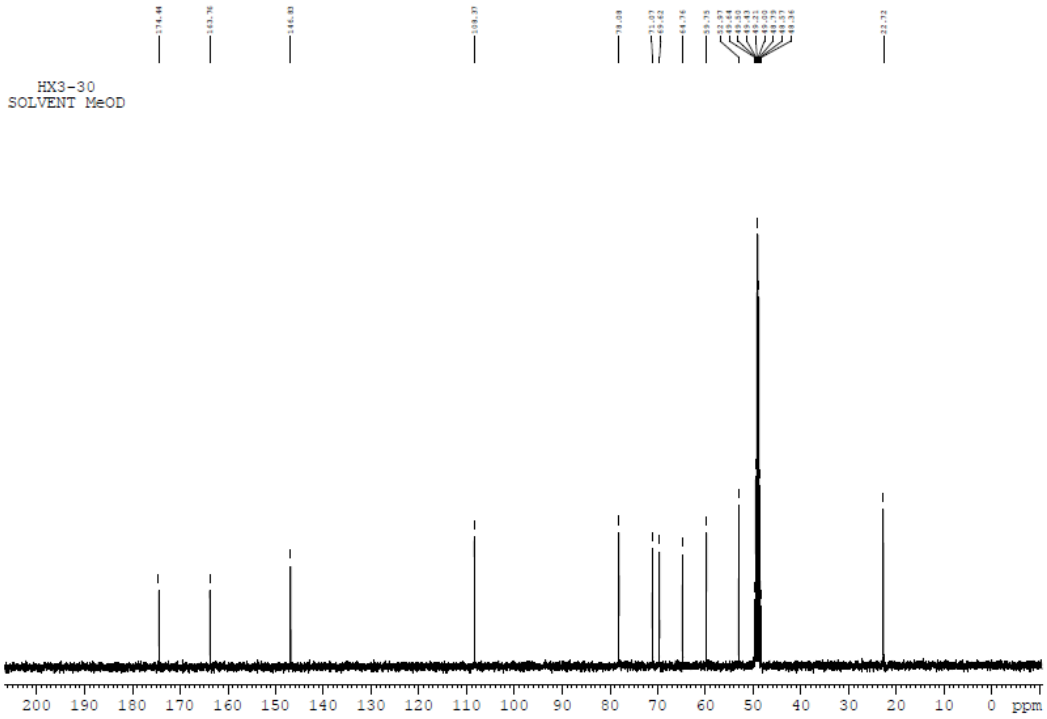


Figure 37. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15a**

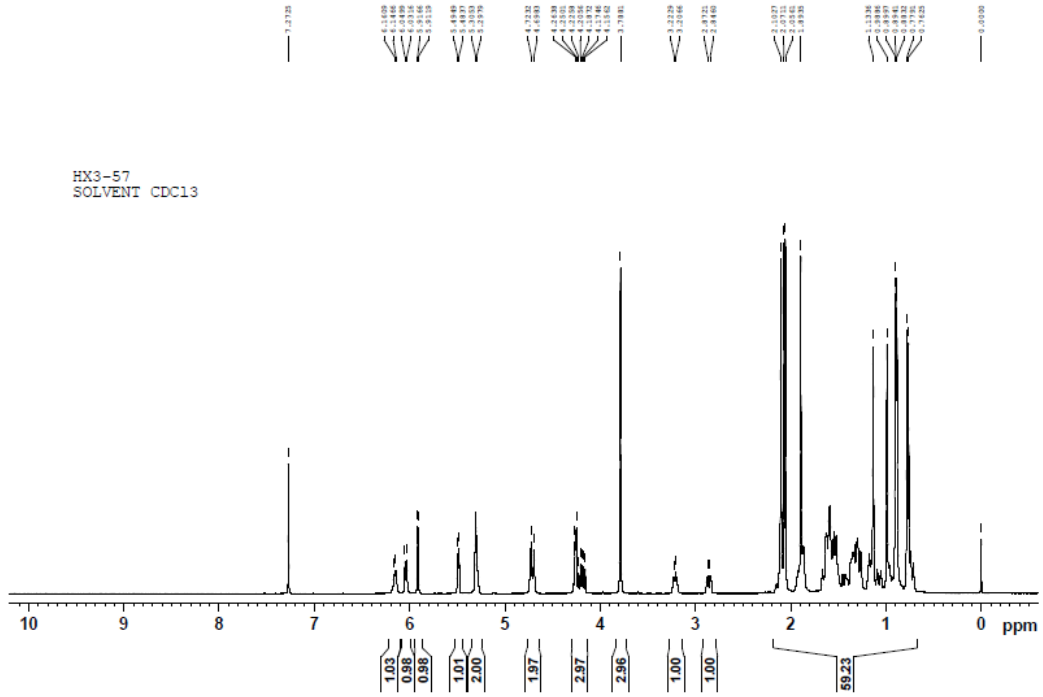


Figure 38. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **15a**

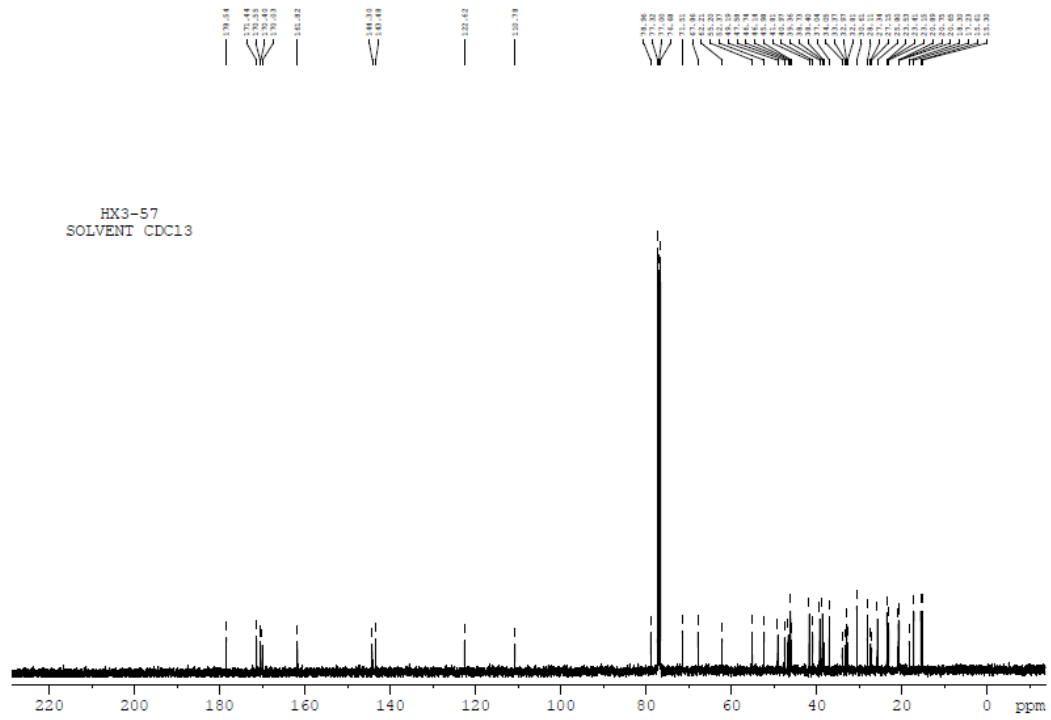


Figure 39. HR-ESI-MS spectrum of compound **15a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-57	C48 H72 N2 O12	C48 H72 N2 Na O12	891.4984	891.4977	-0.66

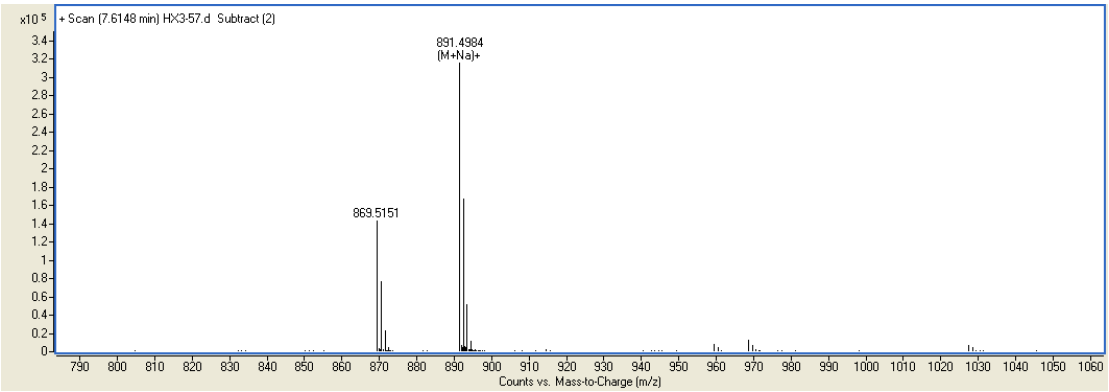


Figure 40. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15b**

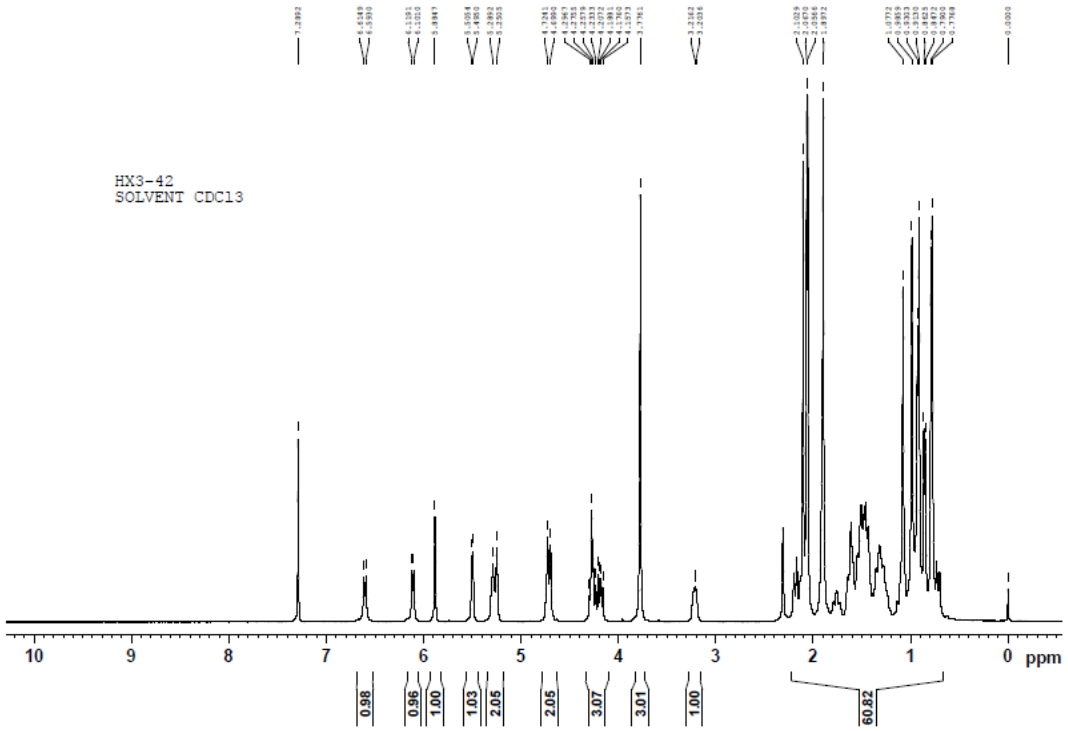


Figure 41. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **15b**

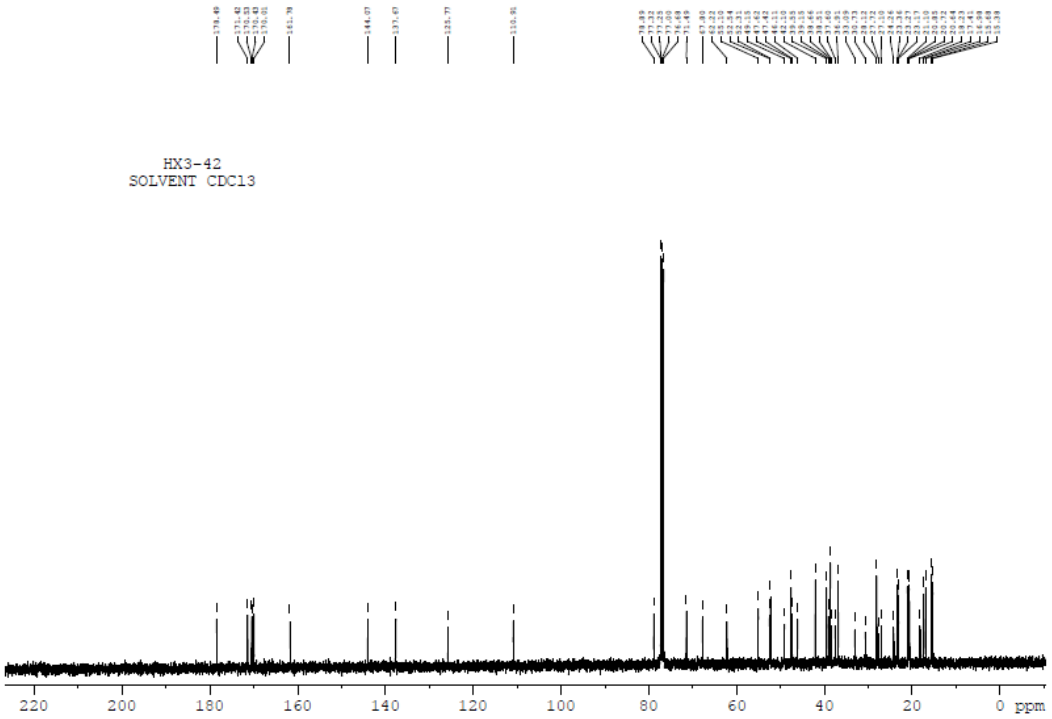


Figure 42. HR-ESI-MS spectrum of compound **15b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-42	C48 H72 N2 O12	C48 H73 N2 O12	869.5150	869.5158	0.86

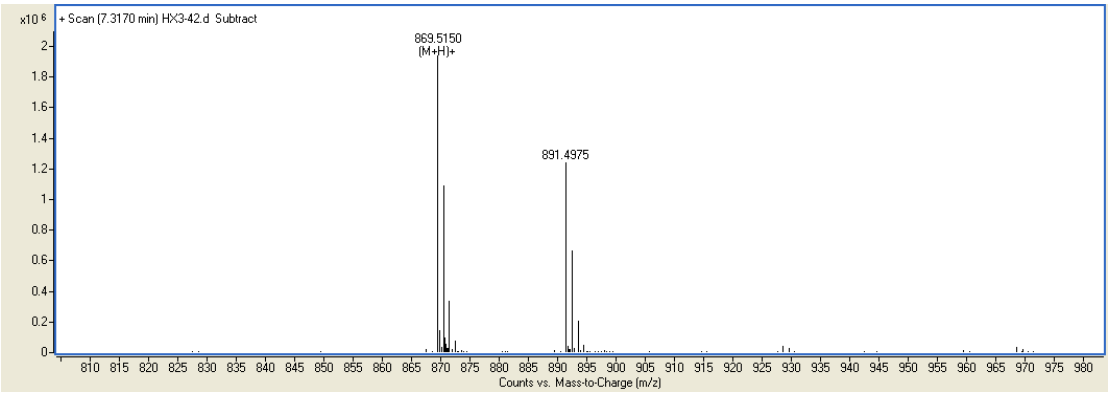


Figure 43. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15c**

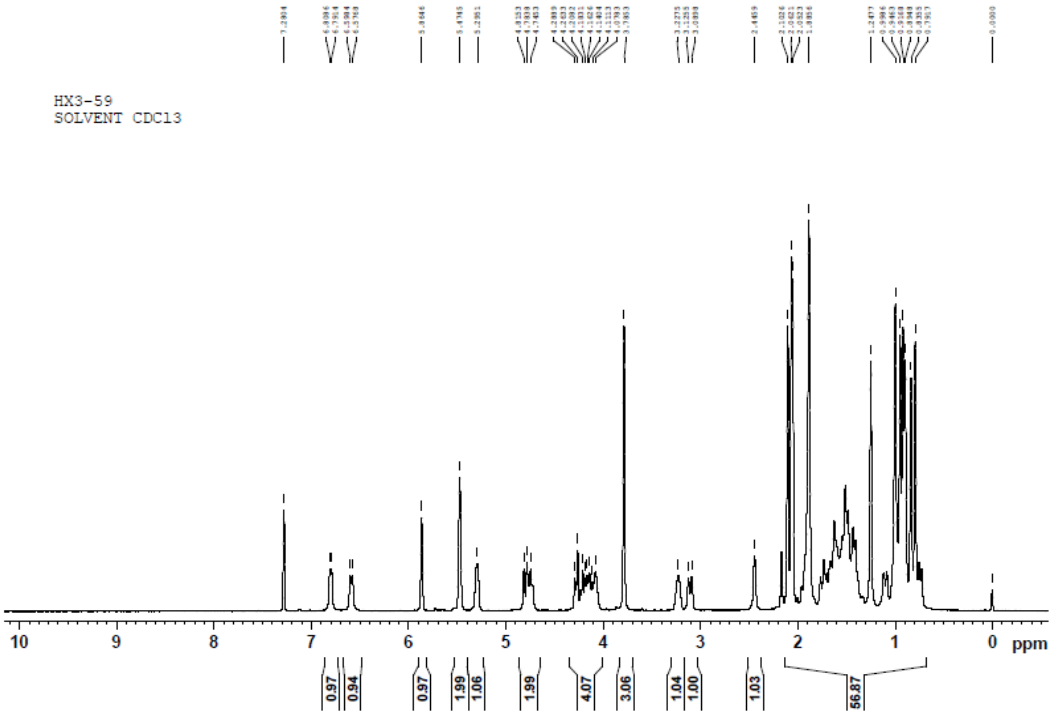


Figure 44. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **15c**

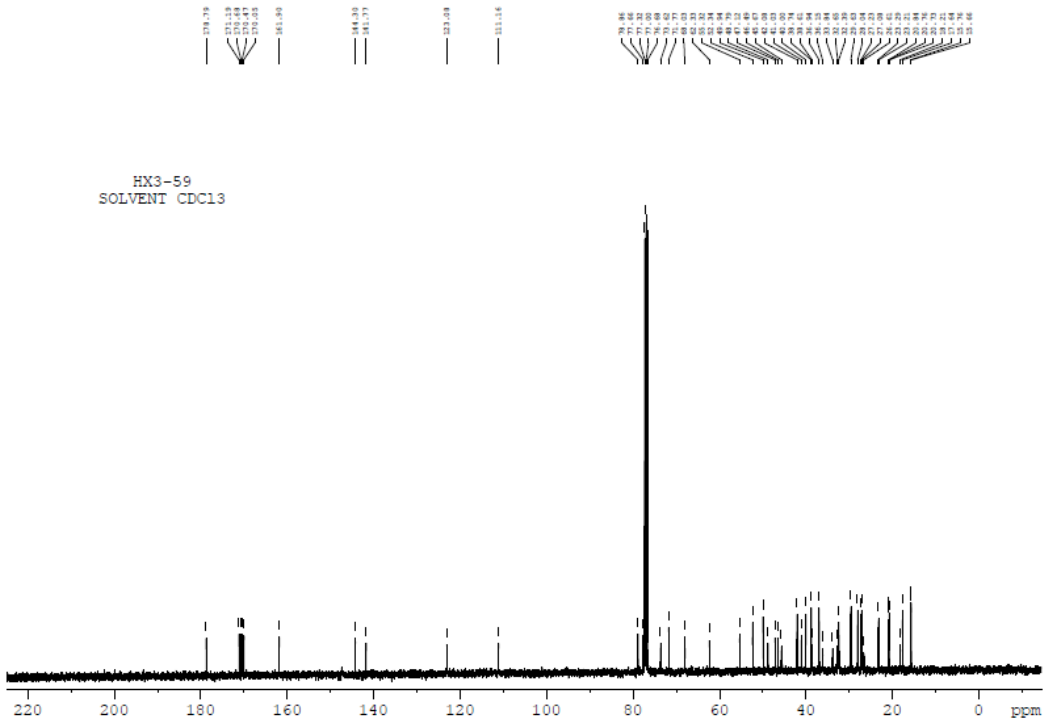


Figure 45. HR-ESI-MS spectrum of compound **15c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-59	C48 H72 N2 O13	C48 H73 N2 O13	885.5108	885.5107	-0.01

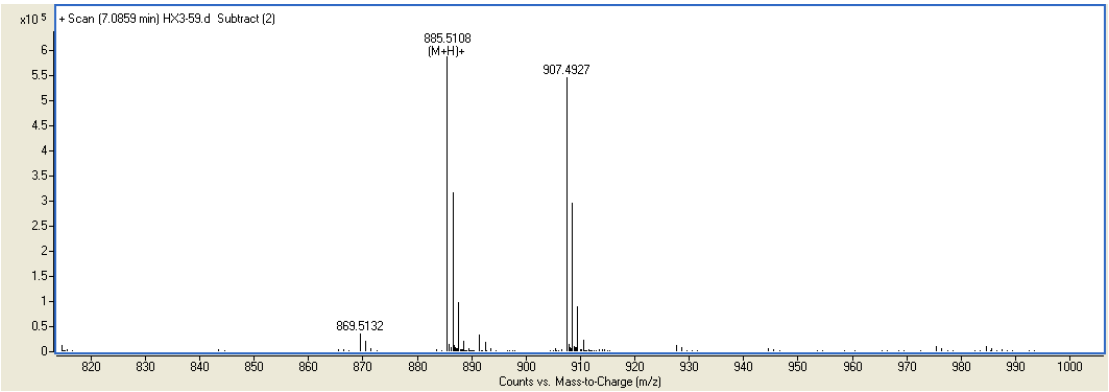


Figure 46. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of compound **15d**

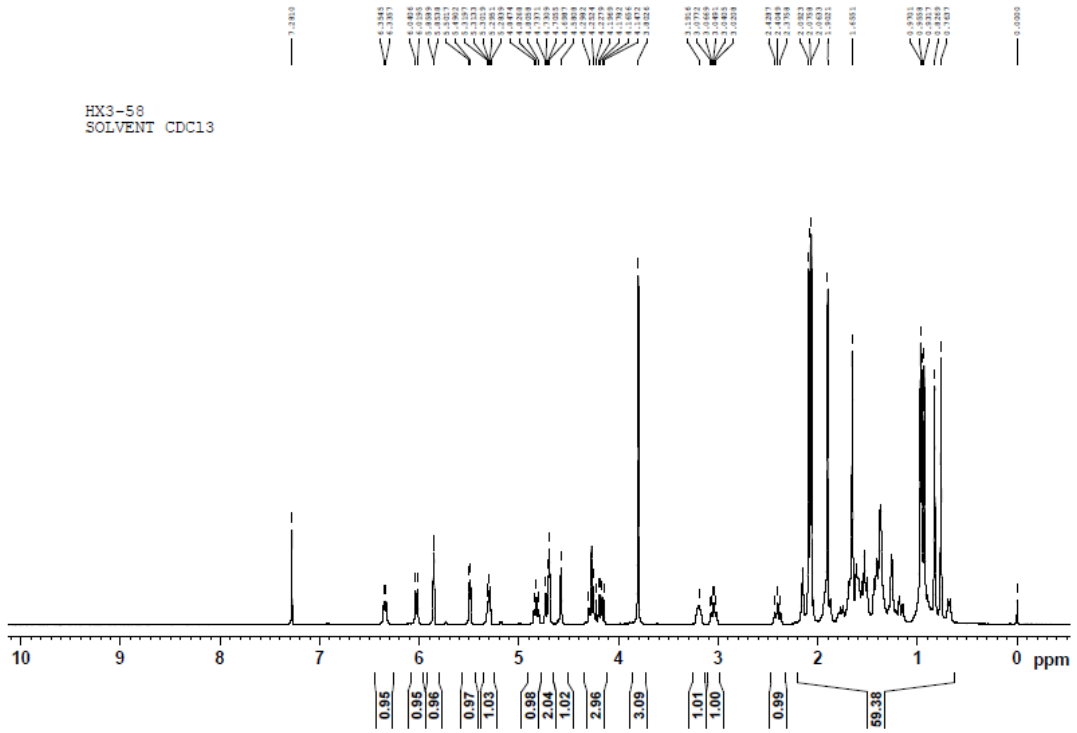


Figure 47. ^{13}C NMR (100 MHz, $CDCl_3$) spectrum of compound **15d**

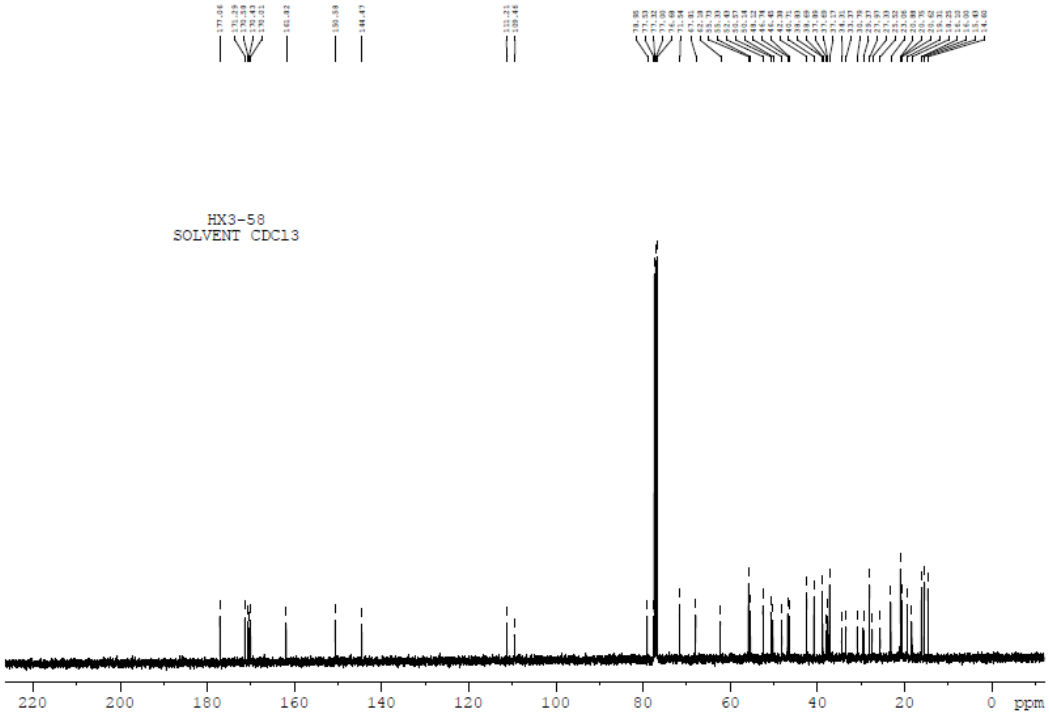


Figure 48. HR-ESI-MS spectrum of compound **15d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-58	C48 H72 N2 O12	C48 H73 N2 O12	869.5160	869.5158	-0.14

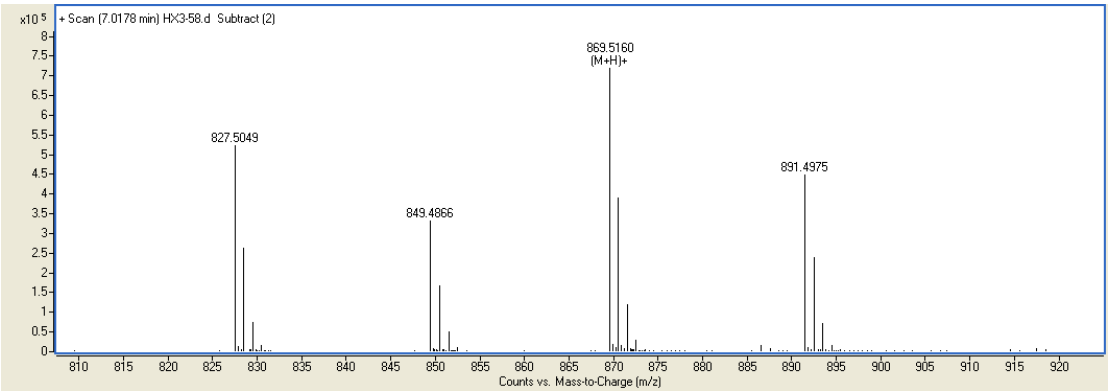


Figure 49. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **16a**

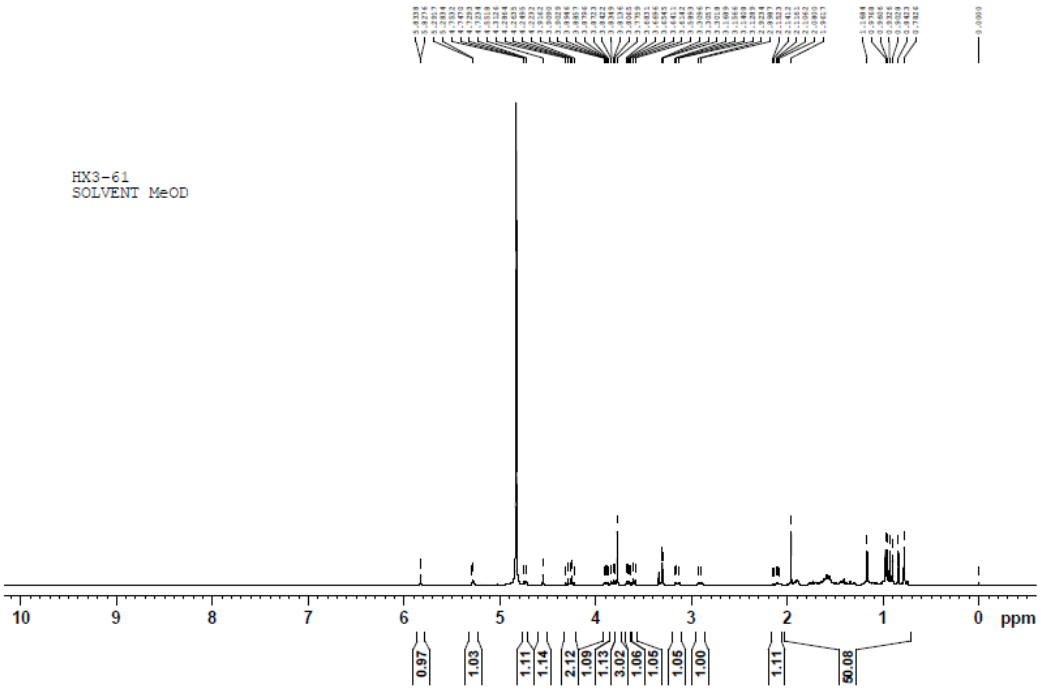


Figure 50. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **16a**

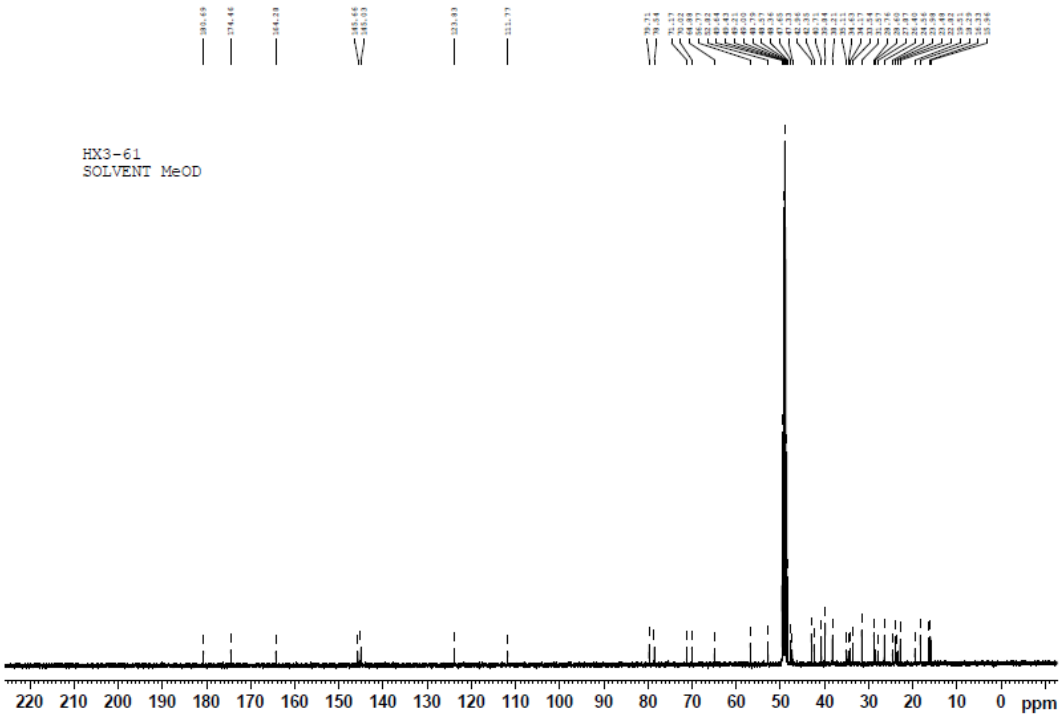


Figure 51. HR-ESI-MS spectrum of compound **16a**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-61	C42 H66 N2 O9	C42 H66 N2 Na O9	765.4669	765.4661	-1.61

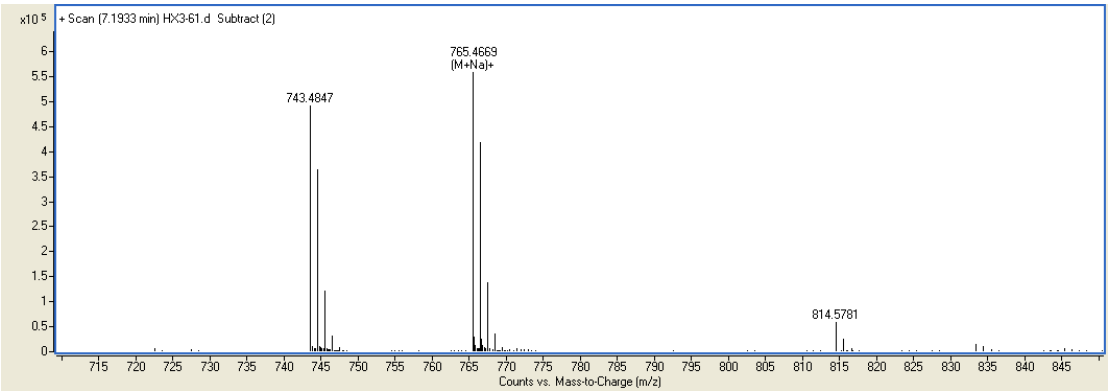


Figure 52. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **16b**

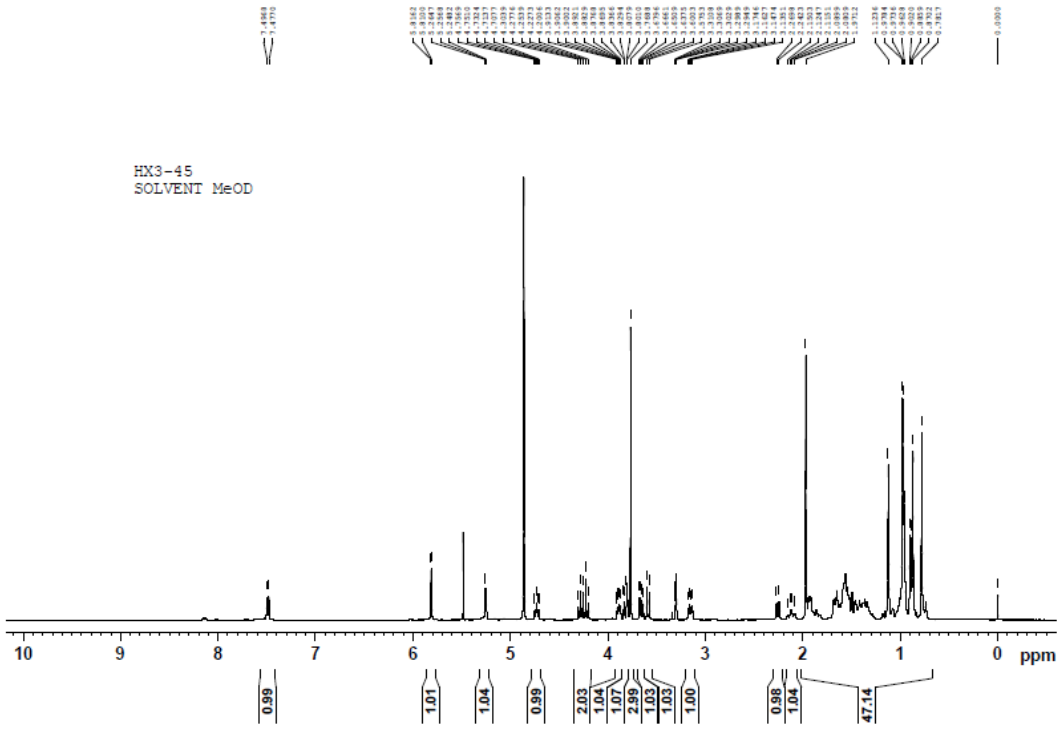


Figure 53. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **16b**

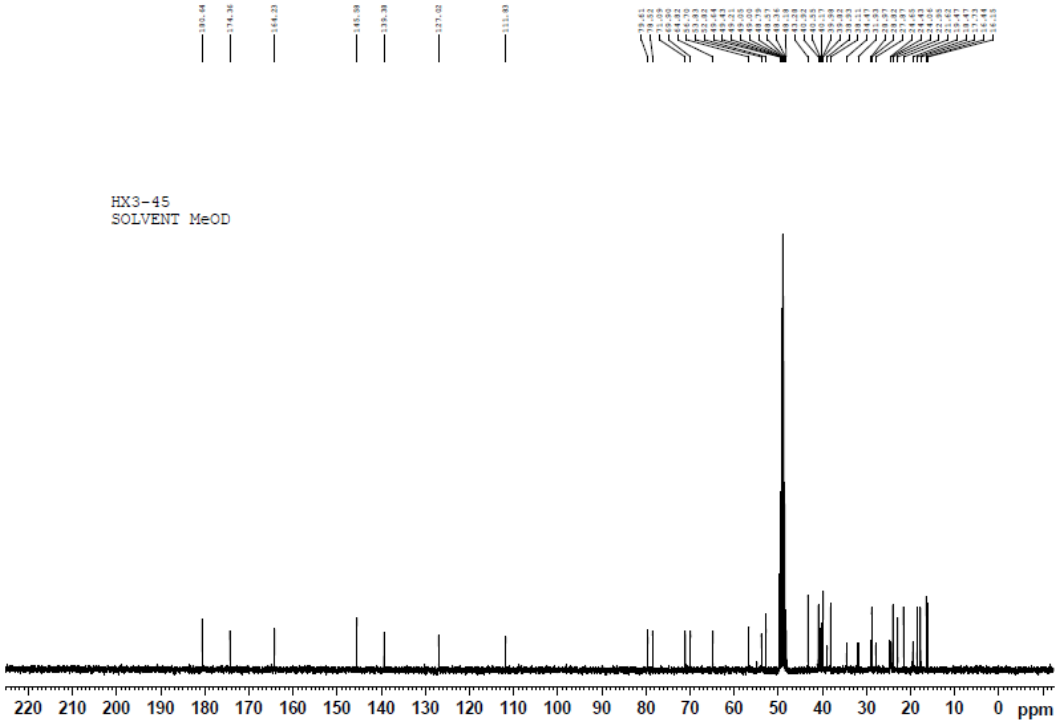


Figure 54. HR-ESI-MS spectrum of compound **16b**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-45	C42 H66 N2 O9	C42 H67 N2 O9	743.4846	743.4841	-0.94

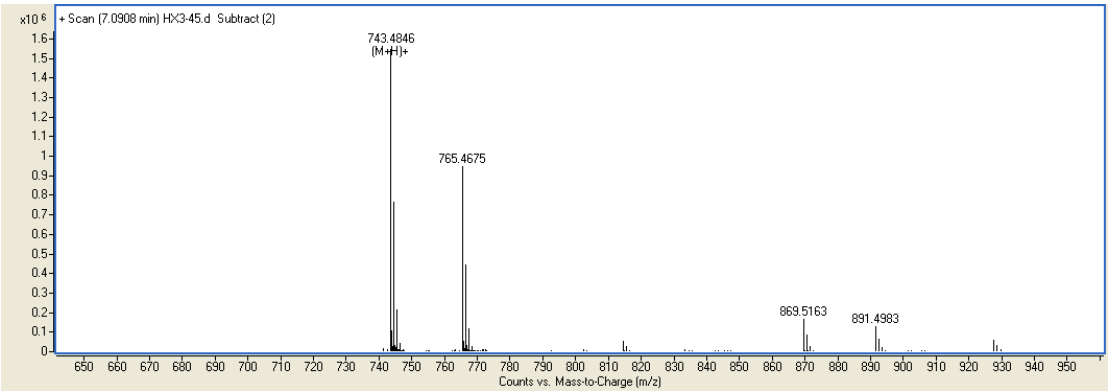


Figure 55. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **16c**

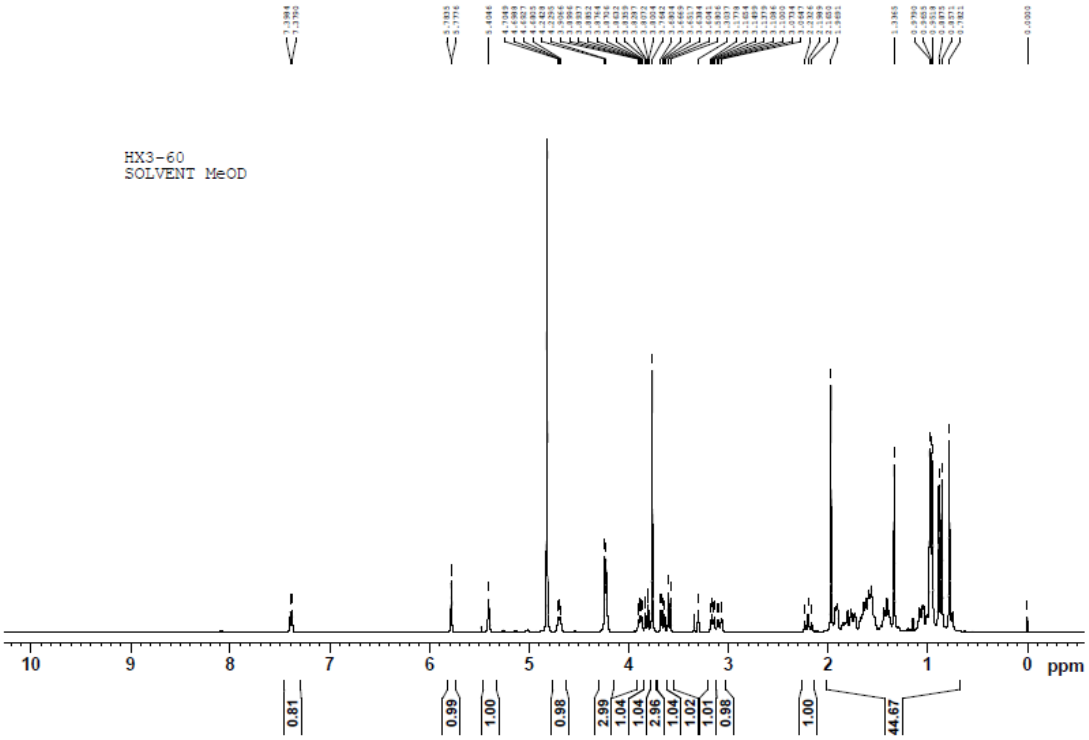


Figure 56. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **16c**

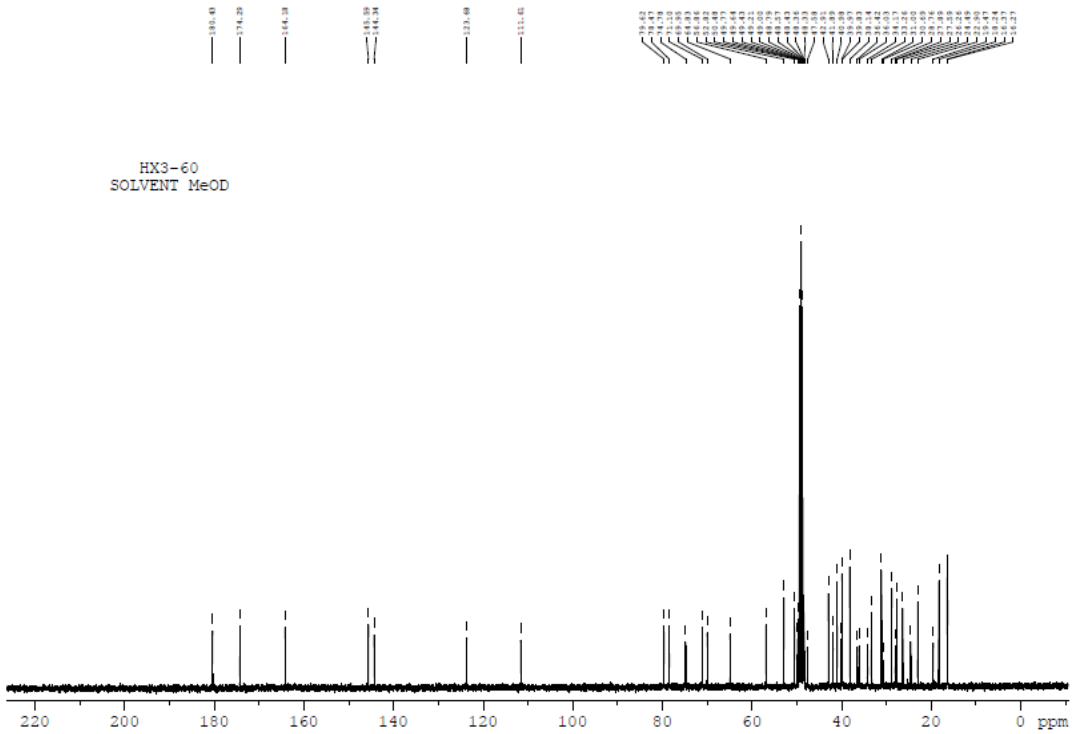


Figure 57. HR-ESI-MS spectrum of compound **16c**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-60	C42 H66 N2 O10	C42 H67 N2 O10	759.4787	759.4790	0.1

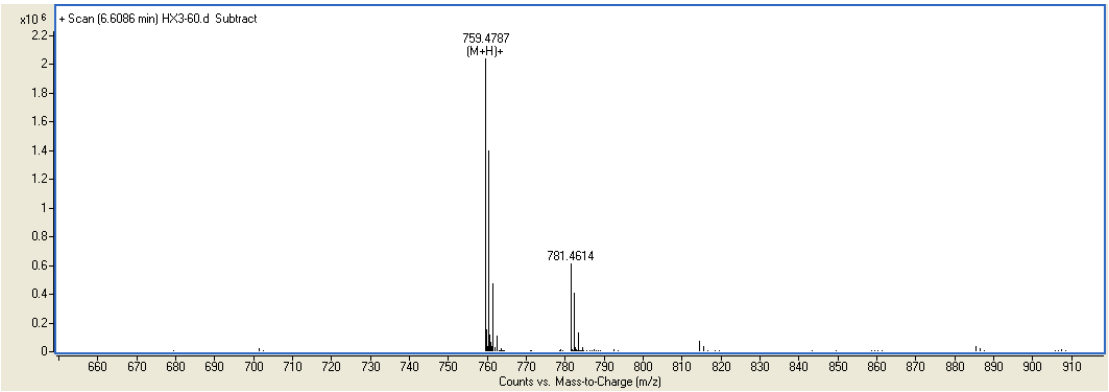


Figure 58. ^{1}H NMR (400 MHz, CD_3OD) spectrum of compound **16d**

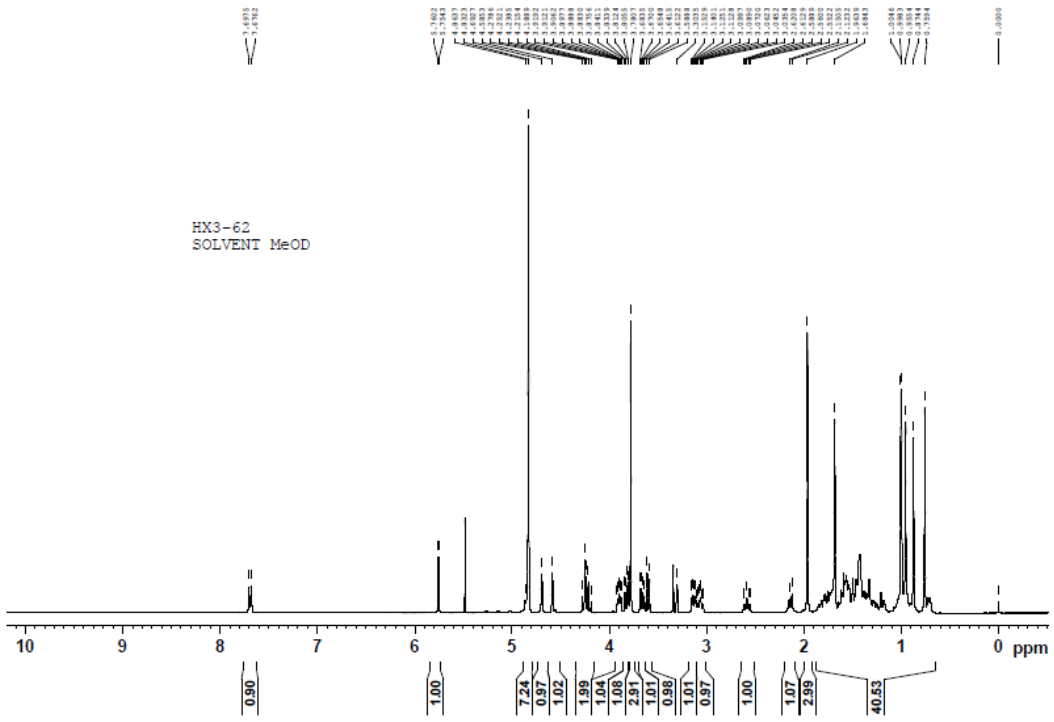


Figure 59. ^{13}C NMR (100 MHz, CD_3OD) spectrum of compound **16d**

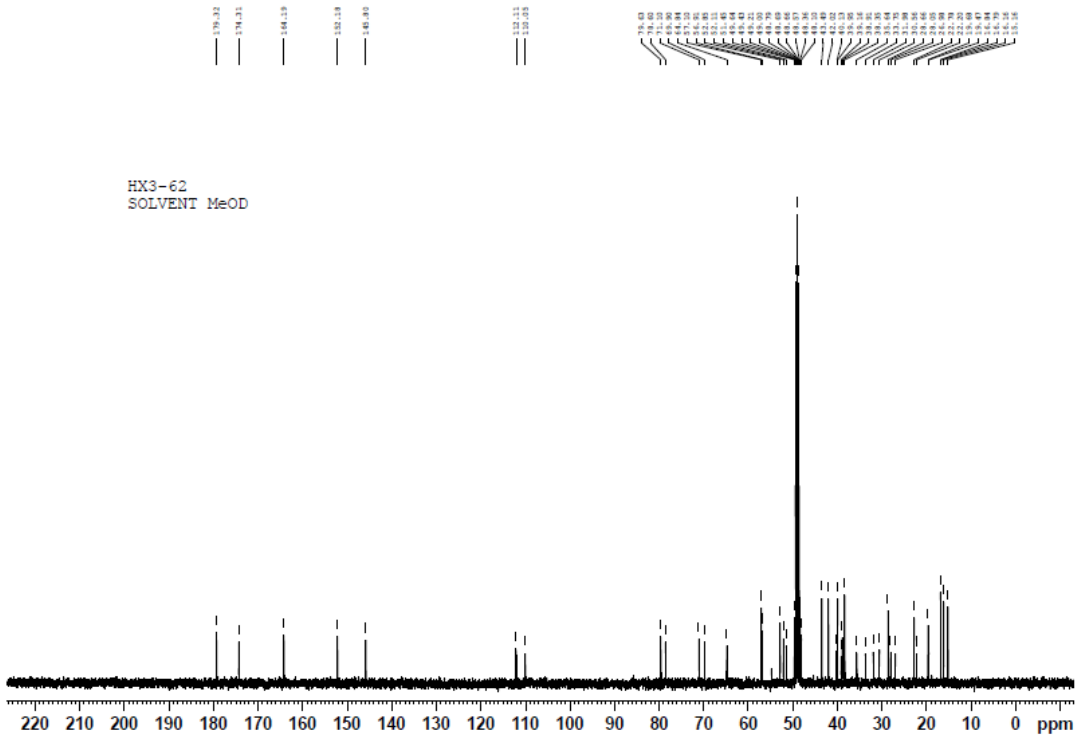


Figure 60. HR-ESI-MS spectrum of compound **16d**

HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
HX3-62	C42 H66 N2 O9	C42 H66 N2 Na O9	765.4667	765.4661	-0.82