

Synthesis, and QSAR analysis of anti-oncological active spiro-alkaloids

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Supporting Information

Table titles

Table 1. Observed and predicted property (μM) for respective cell lines using CODESSA-III QSAR models.

Figure captions

Figure 1. Dose-response curve for the synthesized compounds **24-48** against HELA (cervical cancer) cell line.

Figure 2. Dose-response curve for the synthesized compounds **24-48** against HEPG2 (liver cancer) cell line.

Figure 3. Dose-response curve for the synthesized compounds **24-48** against T-47D (breast cancer) cell line.

Figure 4. Dose-response curve for the synthesized compounds **24-48** against MCF7 (breast cancer) cell line.

Figure 5. Dose-response curve for the synthesized compounds **24-48** against HCT116 (colon cancer) cell line.

Figure 6. Scatter plots of BMLR for HELA (A), HEPG2 (B), T47D (C), MCF7 (D), HCT116 (E) QSAR models.

Figures 7–25. IR Spectra of the synthesized compounds.

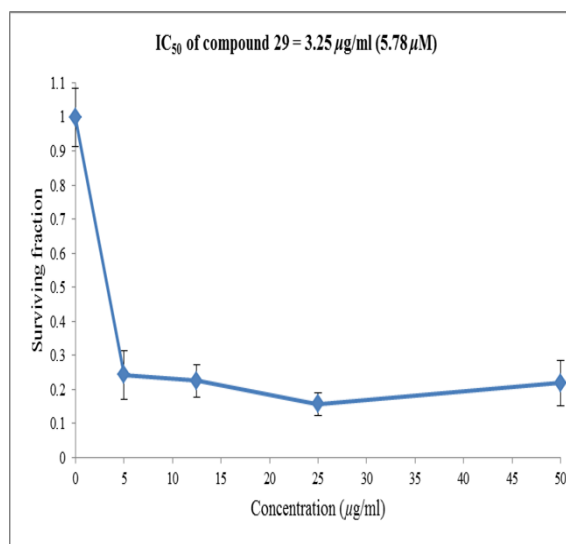
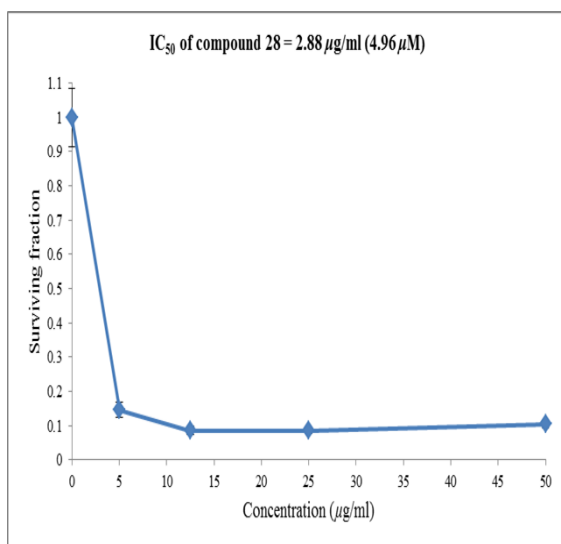
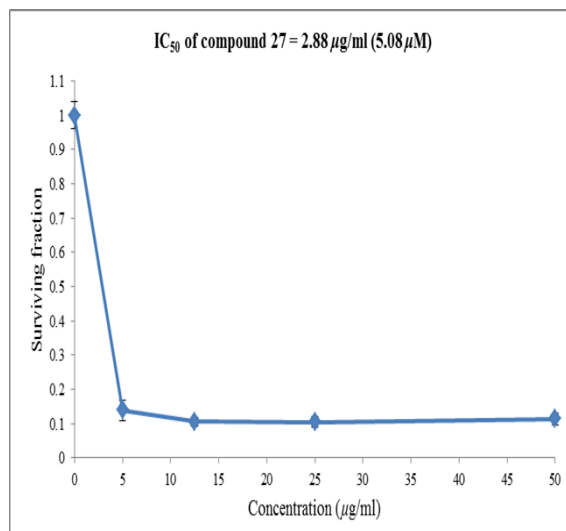
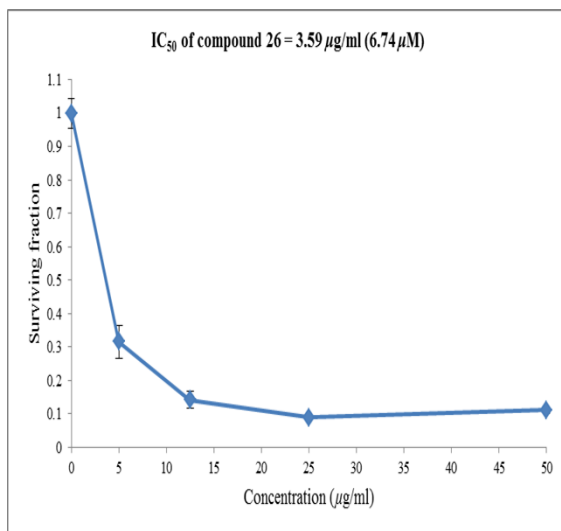
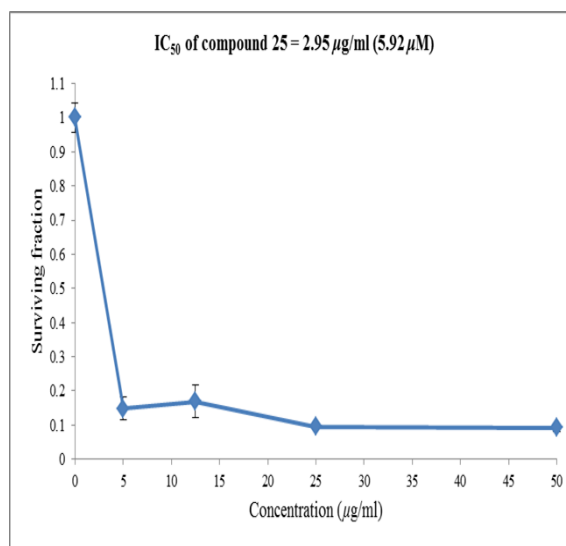
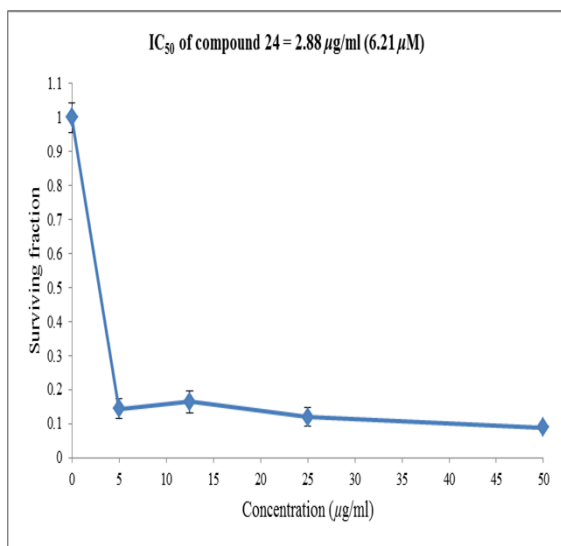
Figures 26–44. ^1H -NMR spectra of the synthesized compounds.

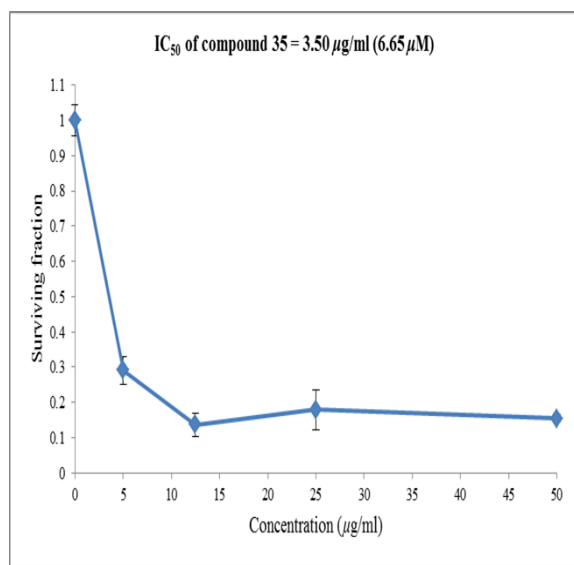
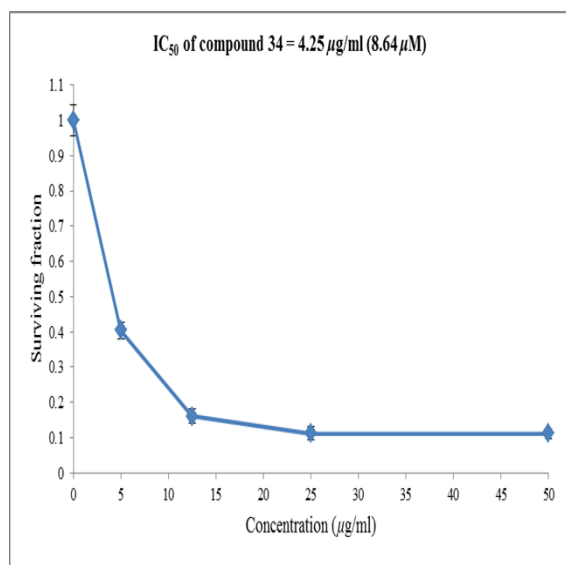
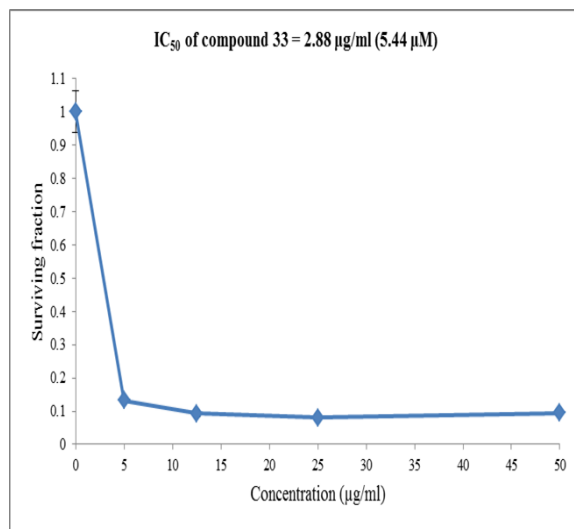
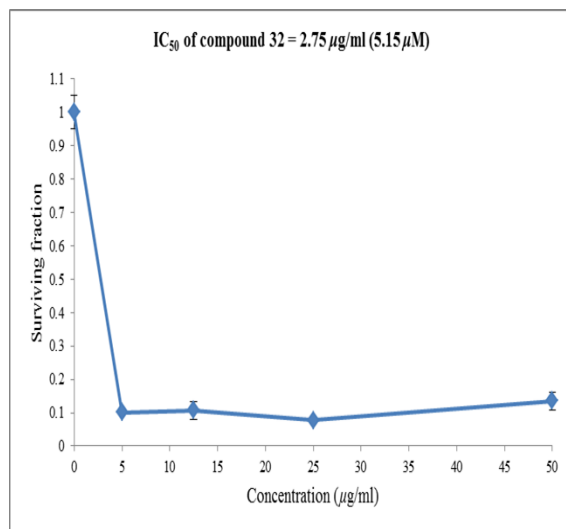
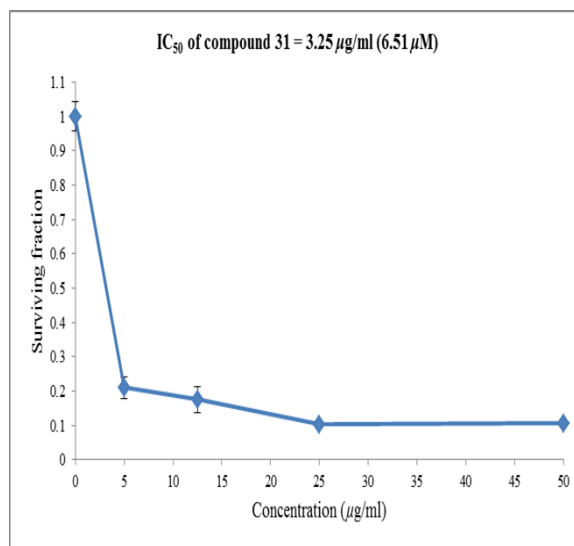
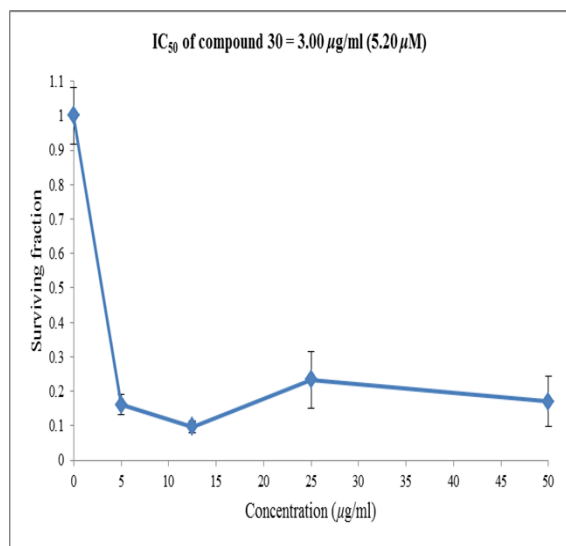
Figures 45–75. ^{13}C -NMR spectra of the synthesized compounds.

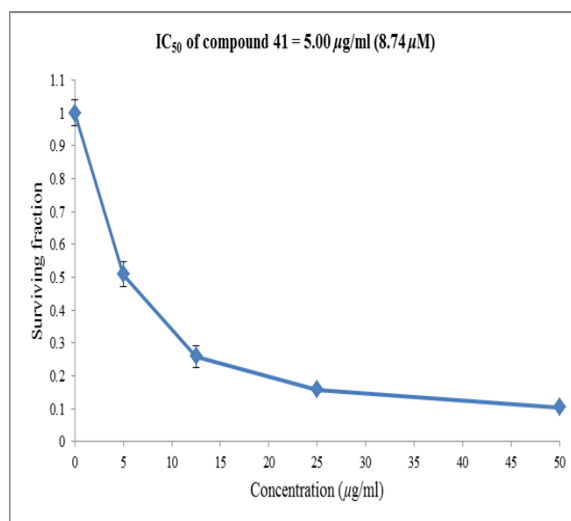
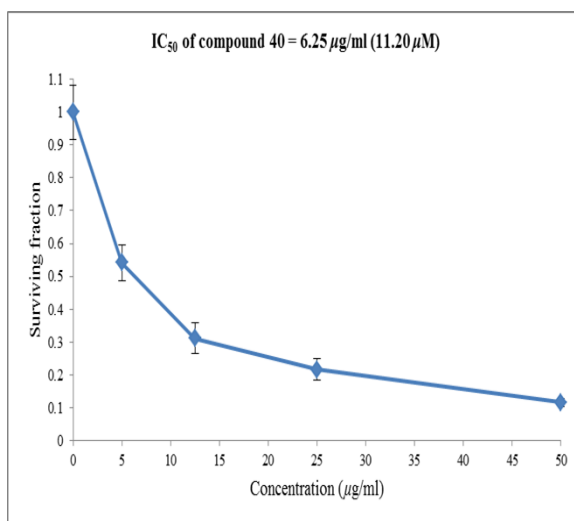
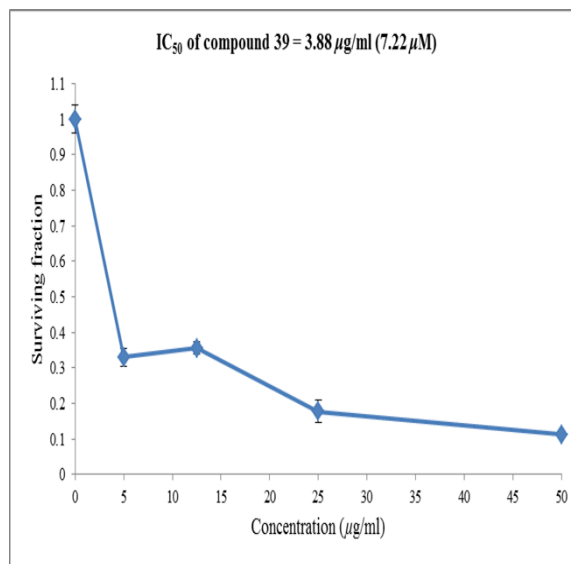
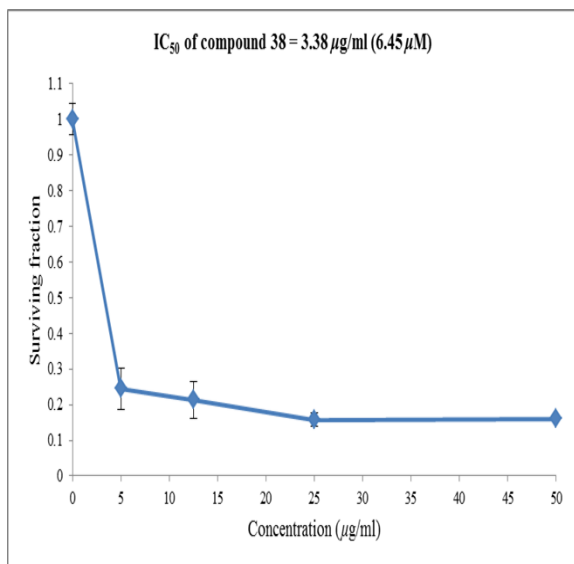
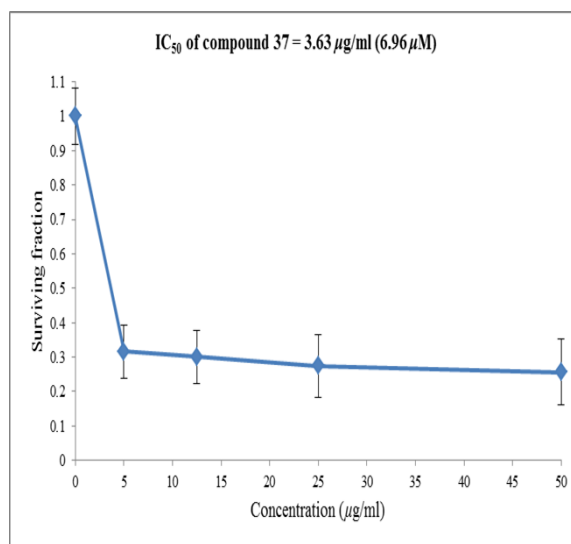
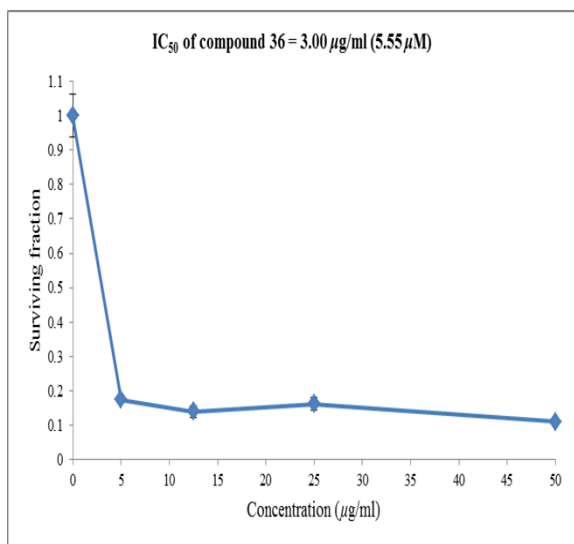
Figures 76–95. HRMS spectra of the synthesized compounds.

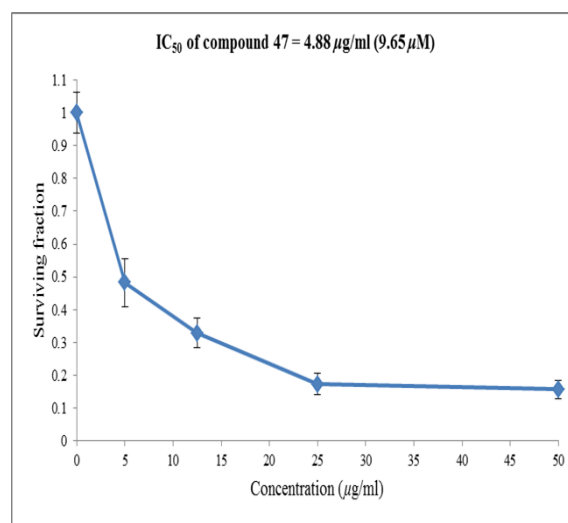
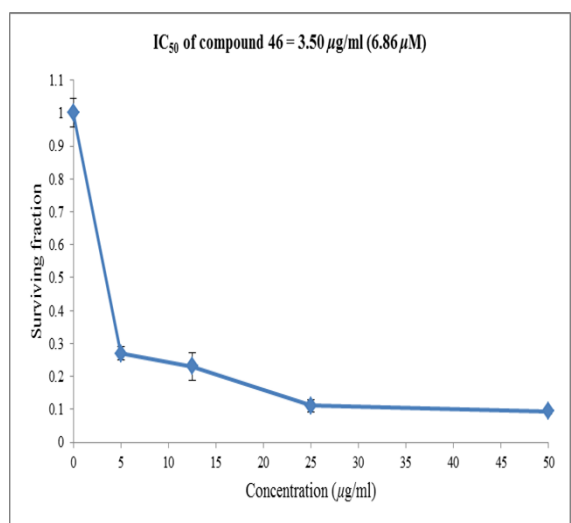
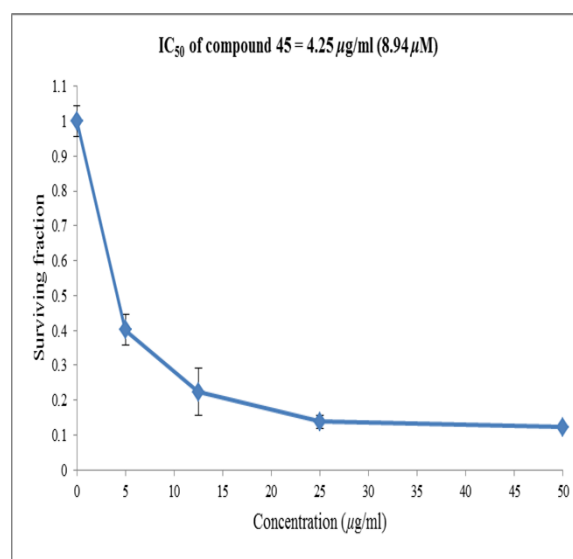
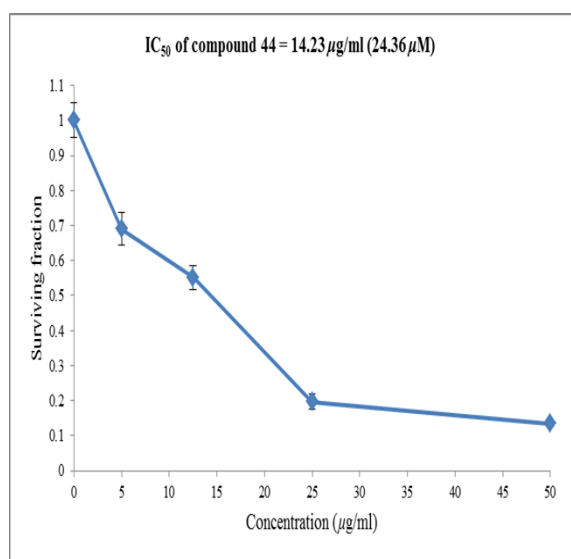
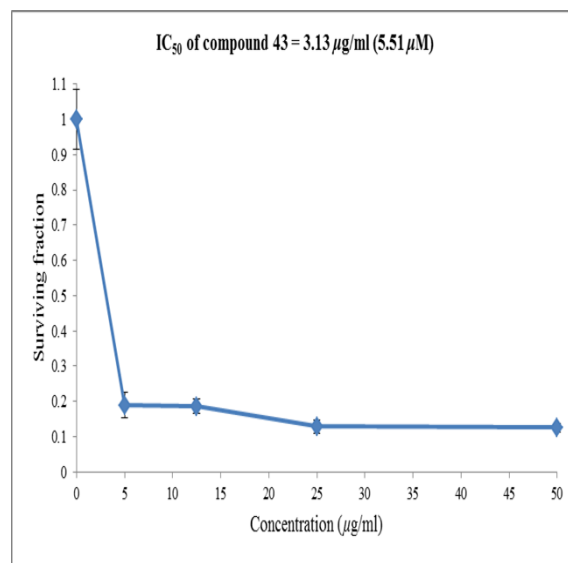
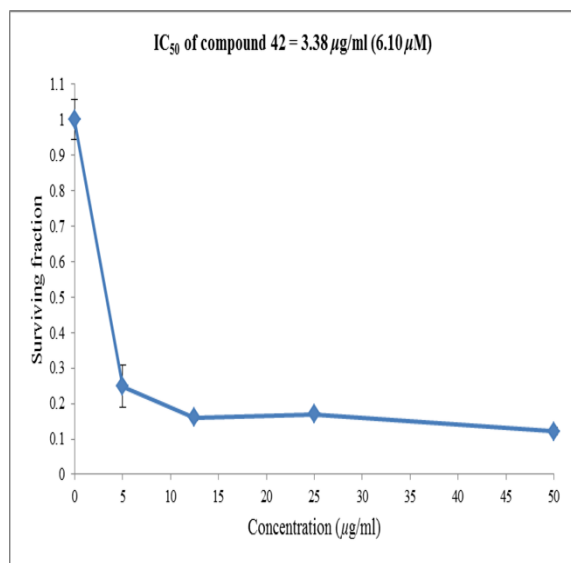
Table 1. Observed and predicted property (μM) for respective cell lines using CODESSA-III QSAR models.

Compd.	IC ₅₀ HELA obs.	IC ₅₀ HELA pred.	Error	IC ₅₀ HEPG2 obs.	IC ₅₀ HEPG2 pred.	Error	IC ₅₀ T47D obs.	IC ₅₀ T47D pred.	Error	IC ₅₀ MCF7 obs.	IC ₅₀ MCF7 pred.	Error	IC ₅₀ HCT116 obs.	IC ₅₀ HCT116 pred.	Error
24	6.210	6.120	0.090	7.460	6.169	1.291	16.440	19.242	2.802	7.010	6.168	0.842	1.335	1.204	0.131
25	5.920	5.865	0.055	5.660	6.890	-1.230	7.930	6.740	1.190	6.020	7.261	1.241	1.272	1.259	0.013
26	6.740	6.203	0.537	6.030	7.304	-1.274	13.410	19.402	5.992	5.630	7.002	1.372	1.110	1.126	0.017
27	5.080	5.976	0.896	6.260	7.253	-0.993	21.330	18.579	2.751	6.610	6.850	0.240	1.061	1.100	0.039
28	4.960	5.143	0.183	5.730	6.236	-0.506	9.810	11.252	1.442	5.390	5.657	0.267	1.133	1.180	0.047
29	5.780	5.573	0.207	8.890	7.452	1.438	22.130	18.234	3.896	7.110	6.231	0.879	1.363	1.264	0.099
30	5.200	4.666	0.534	5.430	5.156	0.274	14.450	15.051	0.601	6.730	6.409	0.321	1.328	1.447	0.119
31	6.510	6.165	0.345	8.730	6.739	1.991	16.750	9.265	7.485	9.770	6.866	2.904	1.567	1.416	0.150
32	5.150	5.996	0.846	5.770	6.711	-0.941	5.810	8.884	3.074	5.580	6.669	1.089	1.532	1.516	0.016
33	5.440	6.241	0.801	5.820	6.476	-0.656	5.630	5.566	0.064	5.850	7.190	1.340	1.279	1.261	0.018
34	8.640	7.374	1.266	14.18	12.72	1.460	22.760	17.950	4.810	17.04	17.092	0.052	1.066	1.174	0.108
35	6.650	6.329	0.321	7.320	7.112	0.208	10.640	10.518	0.122	7.600	6.433	1.167	1.417	1.308	0.109
36	5.550	5.502	0.048	5.460	6.663	-1.203	17.020	16.371	0.649	5.550	7.125	1.575	1.090	1.094	0.004
37	6.960	6.513	0.447	6.150	6.755	-0.605	13.230	13.661	0.431	6.710	6.245	0.465	1.061	1.027	0.033
38	6.450	8.847	2.397	6.680	7.720	-1.040	7.770	9.358	1.588	6.210	6.259	0.049	1.092	1.169	0.077
39	7.220	6.891	0.329	6.680	7.099	-0.419	12.760	11.608	1.152	7.220	5.673	1.547	1.122	1.117	0.005
40	11.20	10.235	0.965	13.67	8.846	4.824	21.250	19.269	1.981	8.300	6.878	1.422	1.223	1.207	0.015
41	8.740	7.924	0.816	5.910	6.838	-0.928	13.000	15.015	2.015	7.660	7.079	0.581	1.215	1.088	0.127
42	6.100	7.500	1.400	6.950	7.749	-0.799	9.030	11.701	2.671	5.200	6.806	1.606	1.052	1.200	0.147
43	5.510	5.892	0.382	7.490	6.283	1.207	19.080	17.223	1.857	6.610	6.947	0.337	1.139	1.119	0.020
44	24.36	22.006	2.354	23.71	25.344	-1.634	28.470	29.284	0.814	29.96	27.57	2.390	1.155	1.185	0.030
45	8.940	10.751	1.811	14.020	15.441	-1.421	19.530	19.209	0.321	10.26	9.241	1.019	1.315	1.326	0.011
46	6.860	6.493	0.367	9.290	7.952	1.338	20.080	22.197	2.117	7.840	9.027	1.187	1.294	1.250	0.044
47	9.650	7.134	2.516	8.400	7.565	0.835	26.600	22.463	4.137	8.900	8.941	-0.041	1.187	1.305	0.118
48	9.880	10.085	0.205	9.370	8.410	0.960	24.700	24.384	0.316	15.810	15.751	0.059	1.335	1.204	-0.131









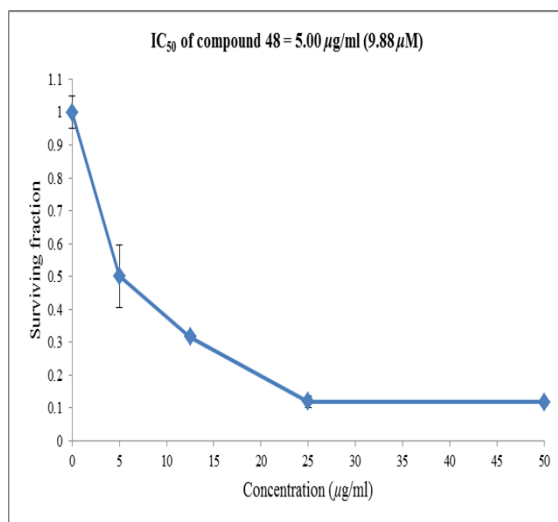
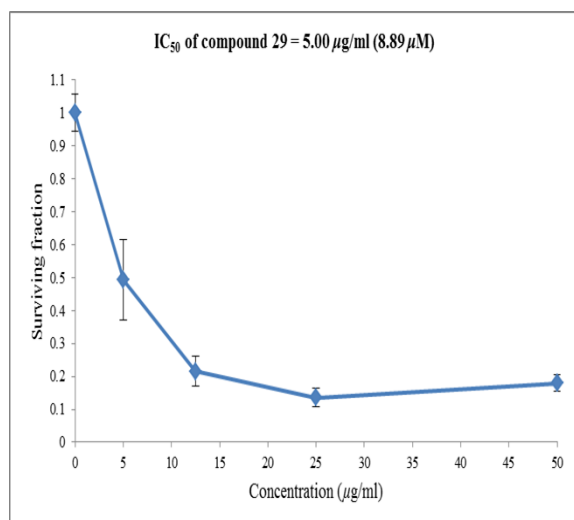
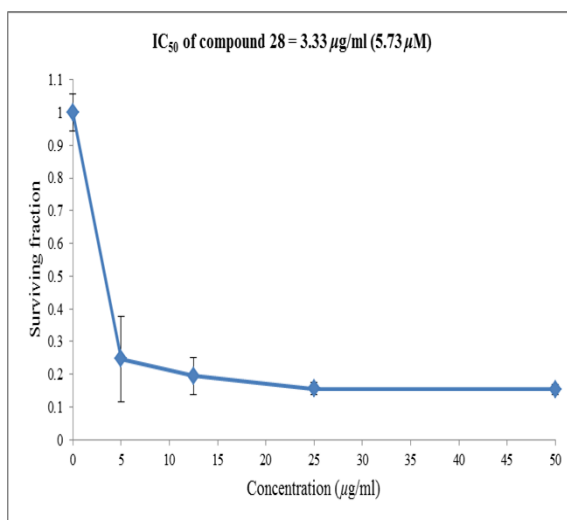
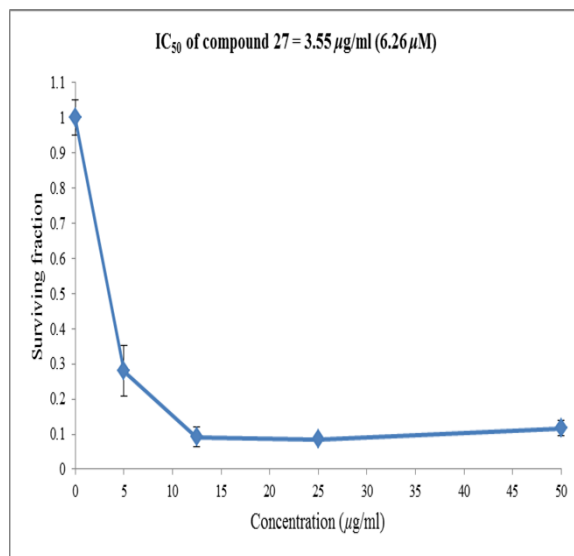
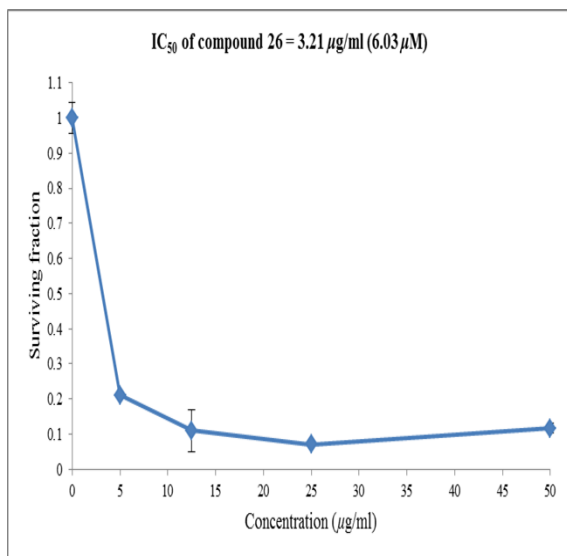
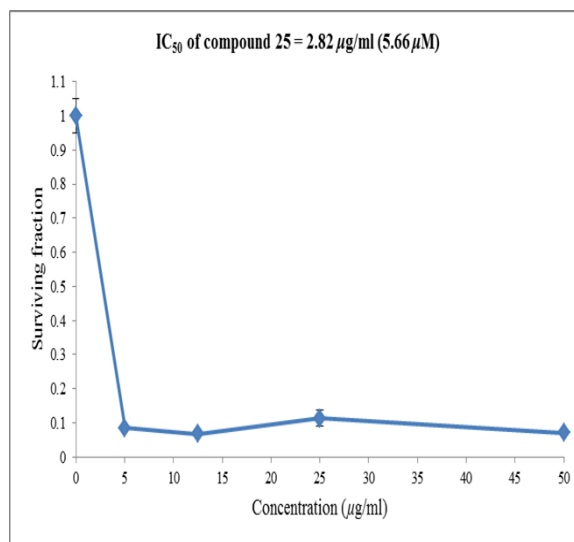
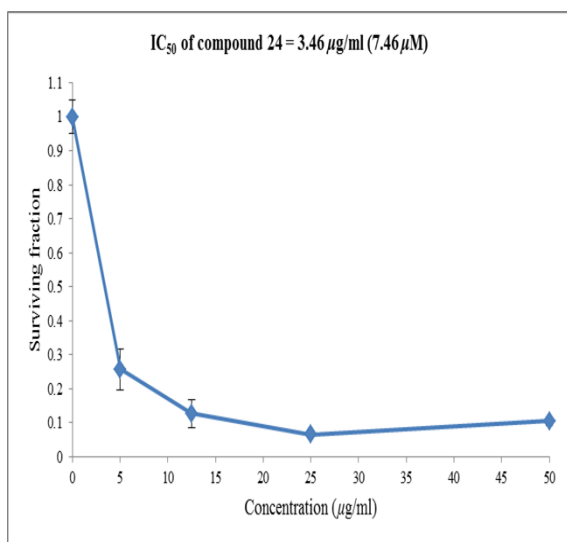
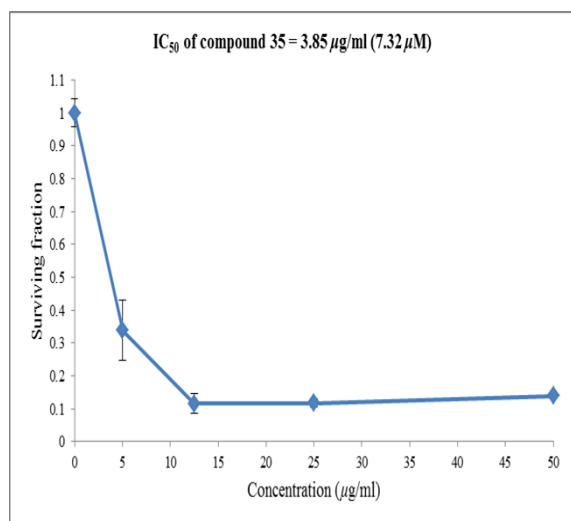
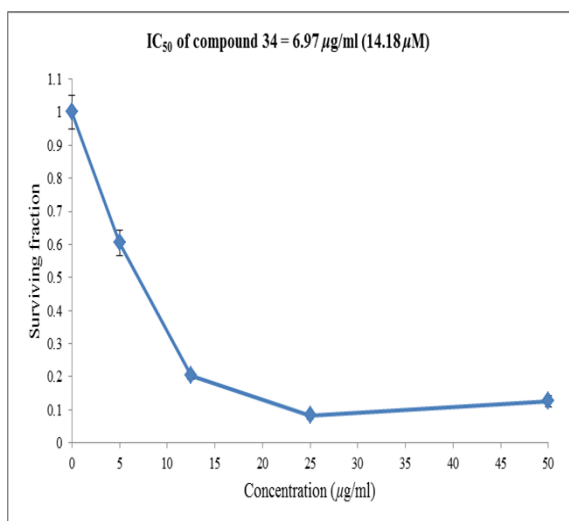
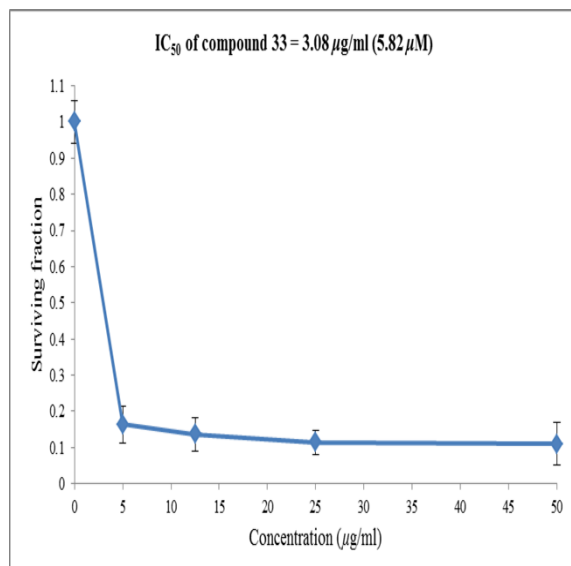
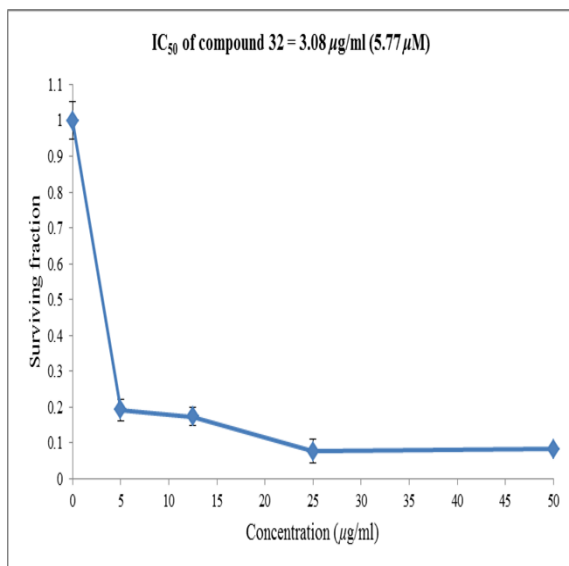
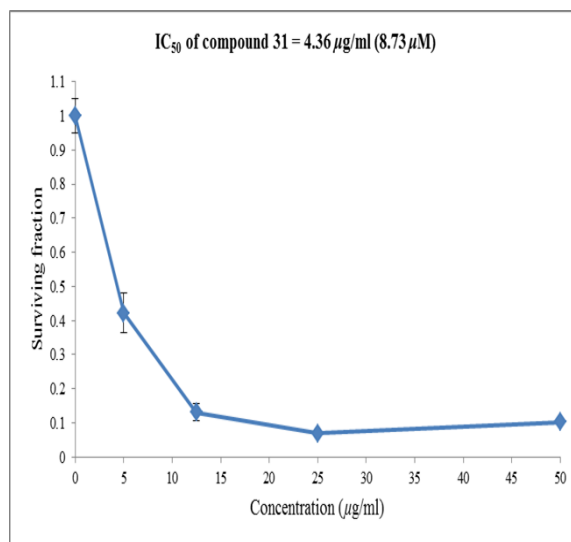
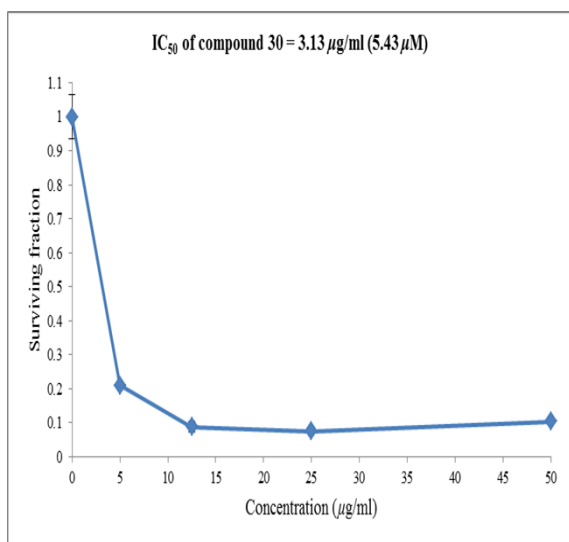
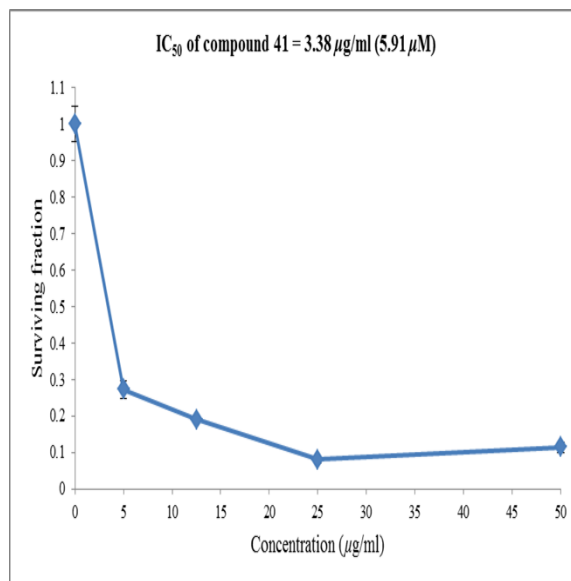
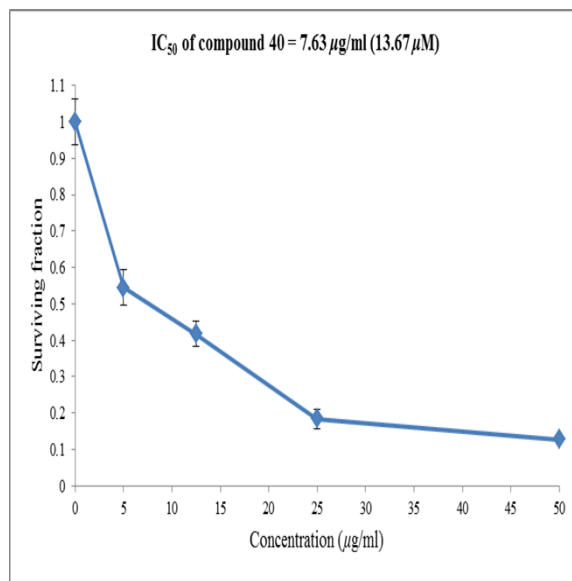
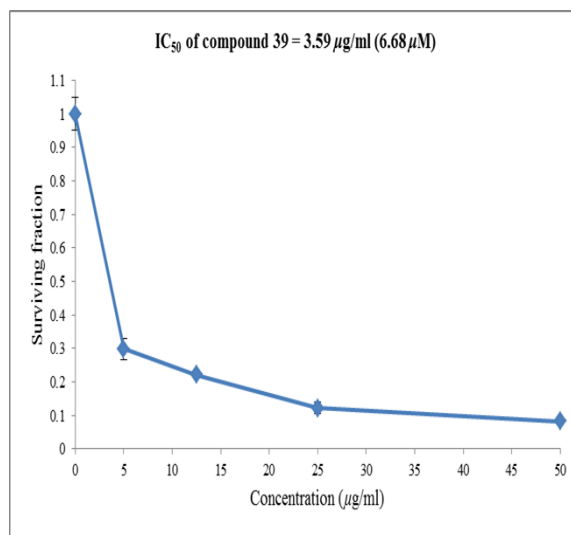
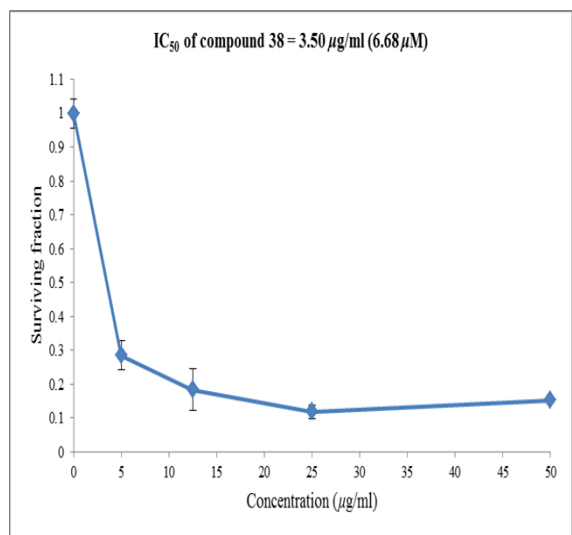
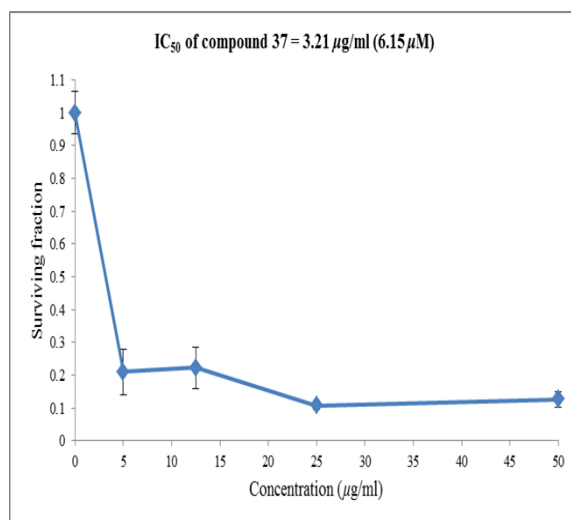
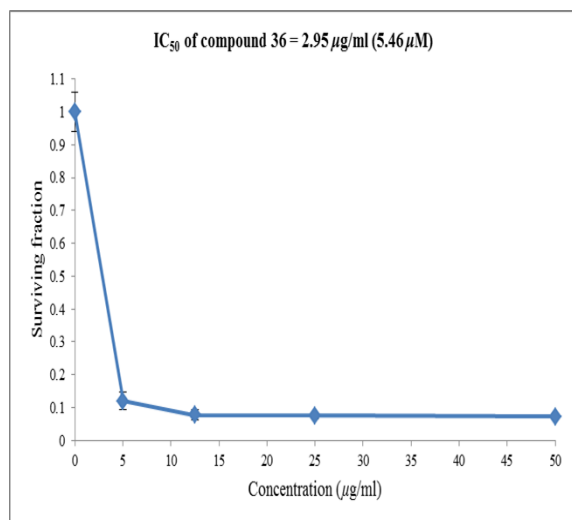
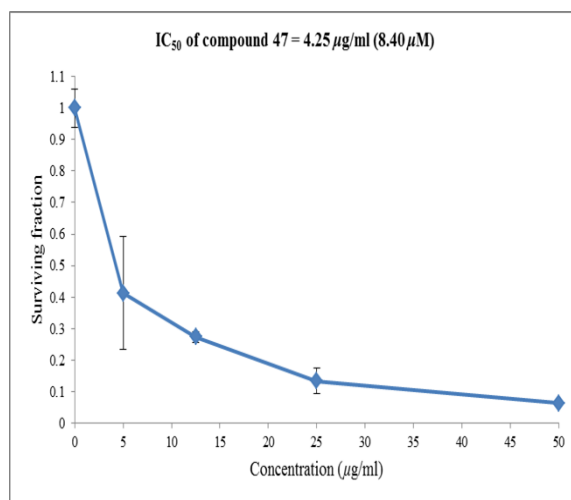
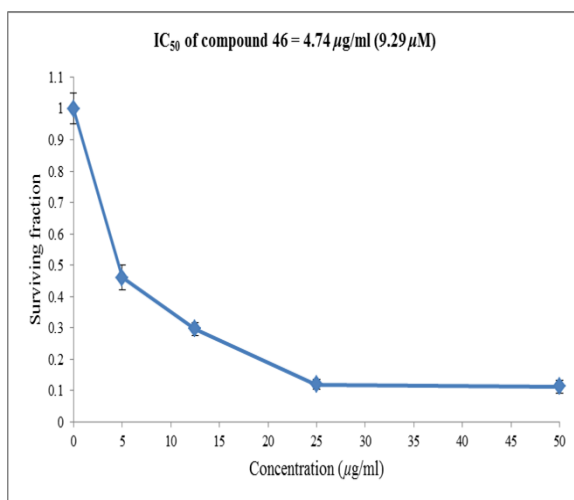
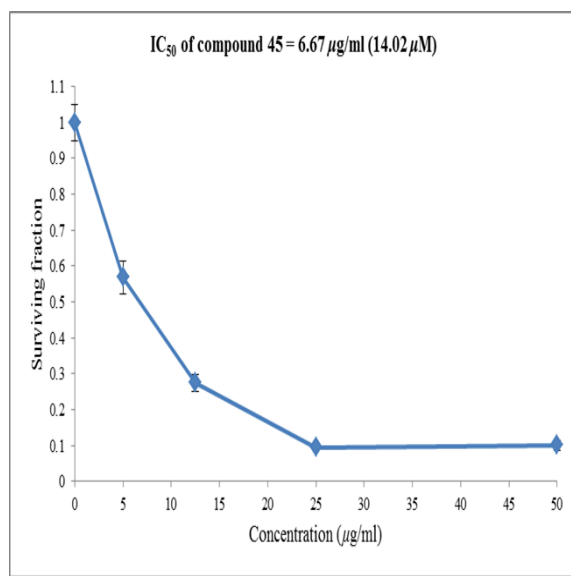
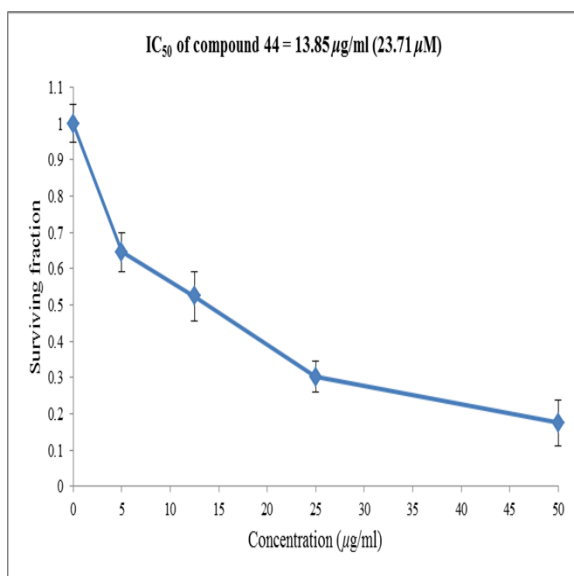
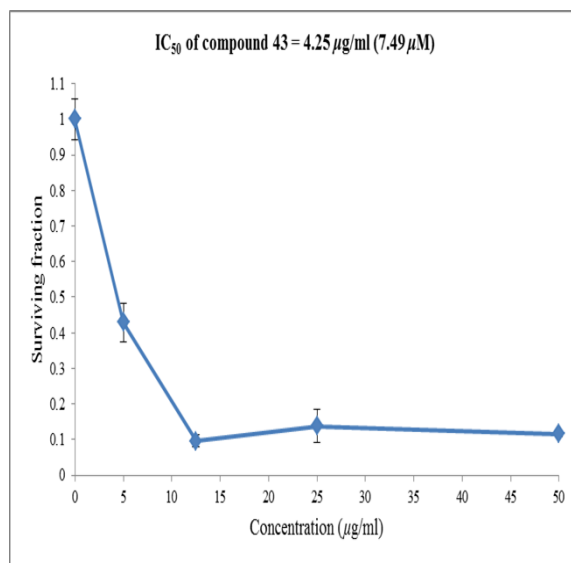
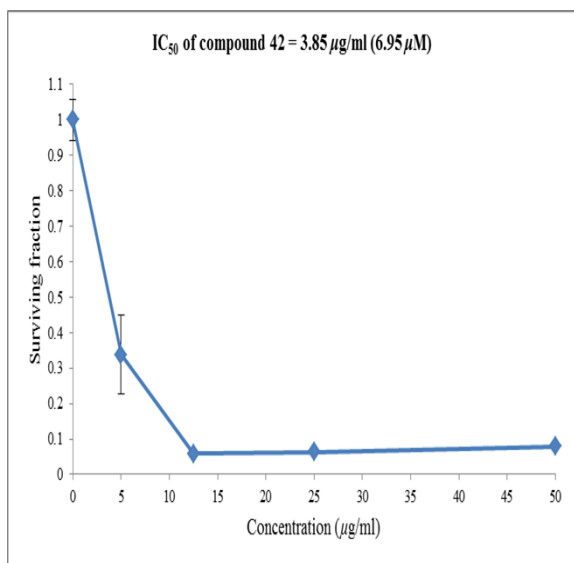


Figure 1. Dose-response curve for the synthesized compounds **24-48** against HELA (cervical cancer) cell line.









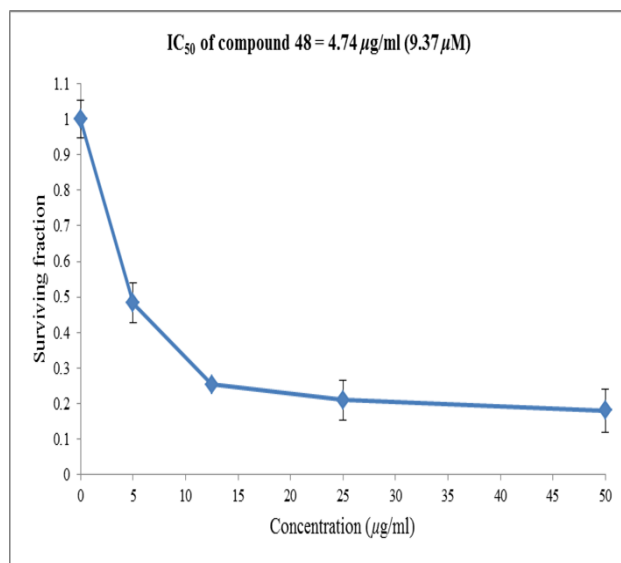
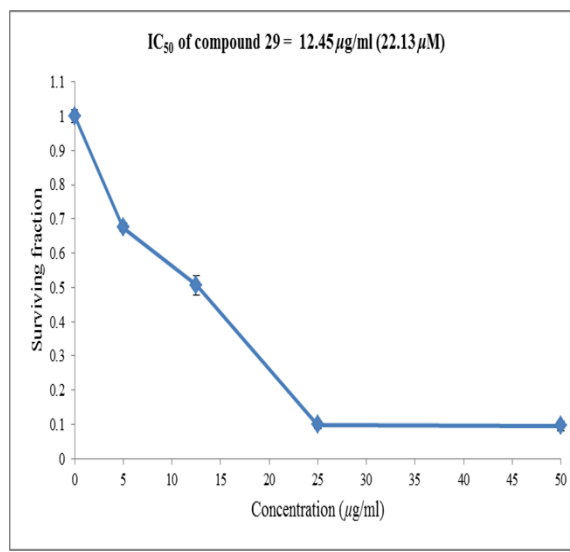
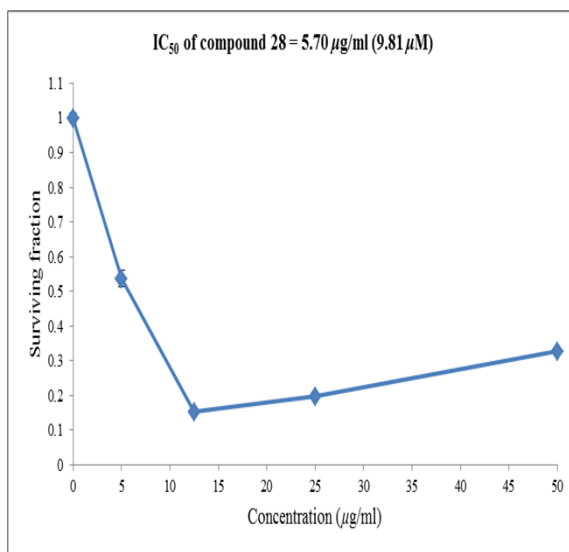
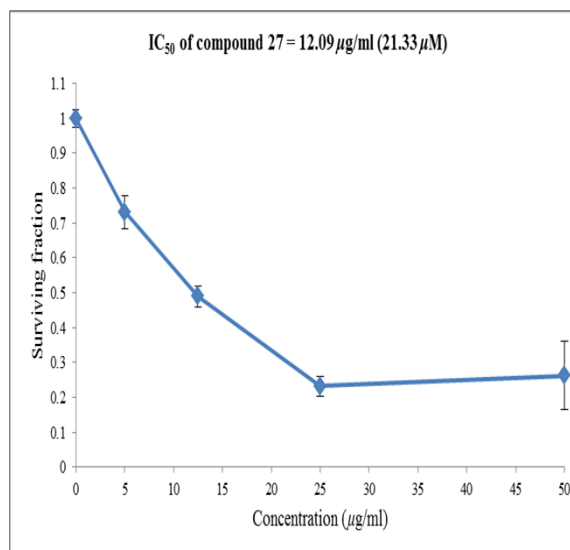
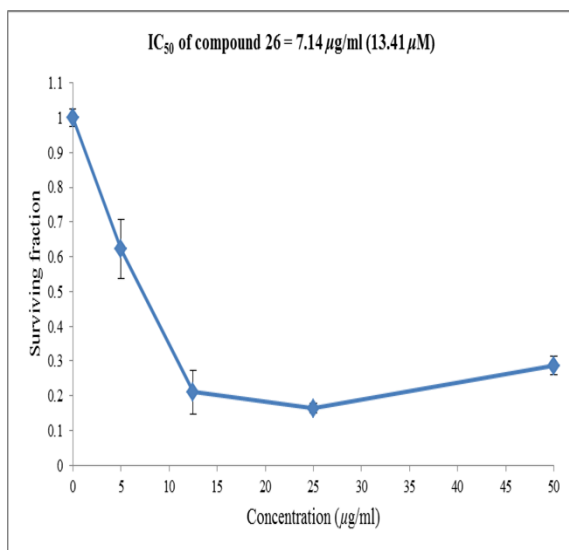
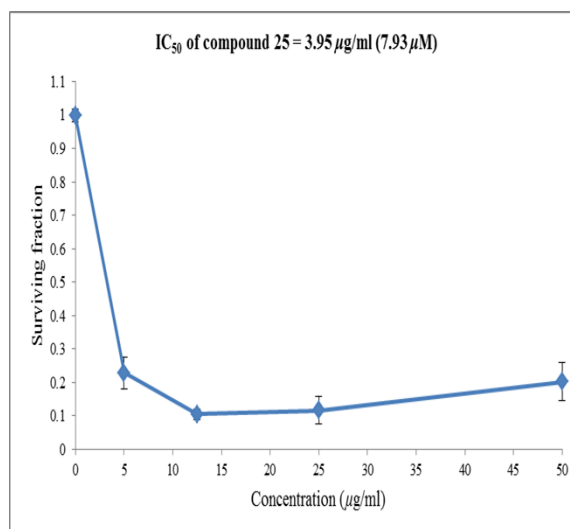
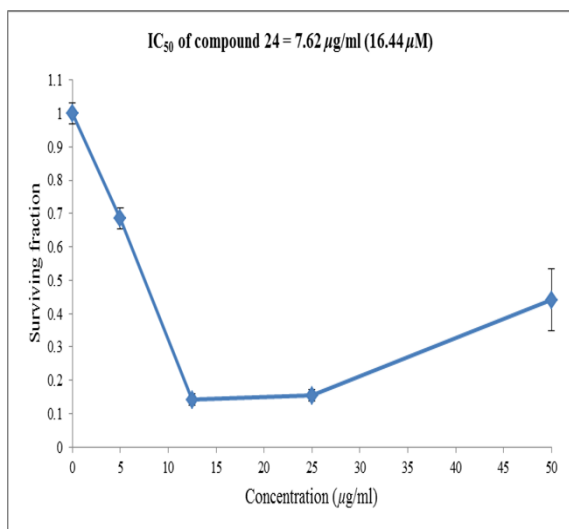
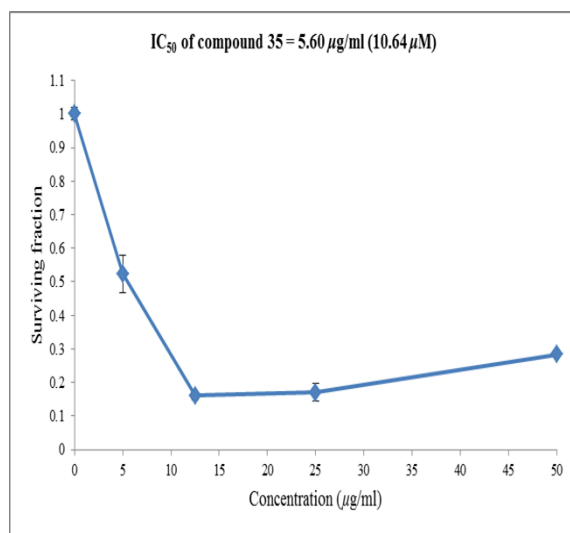
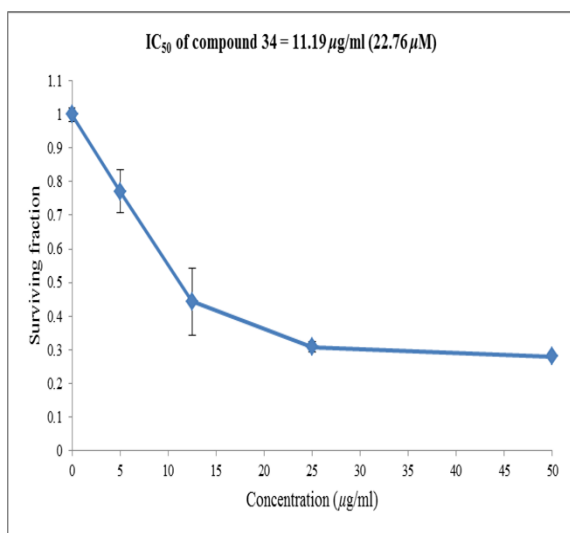
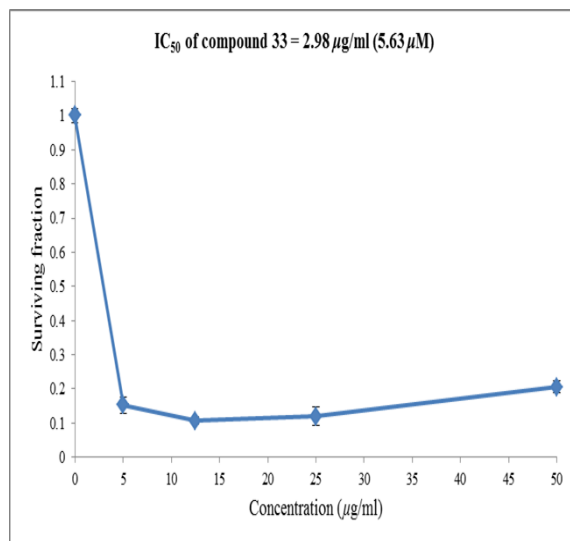
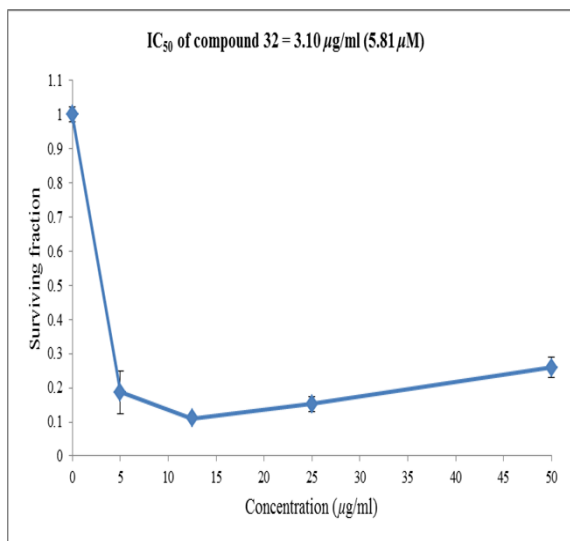
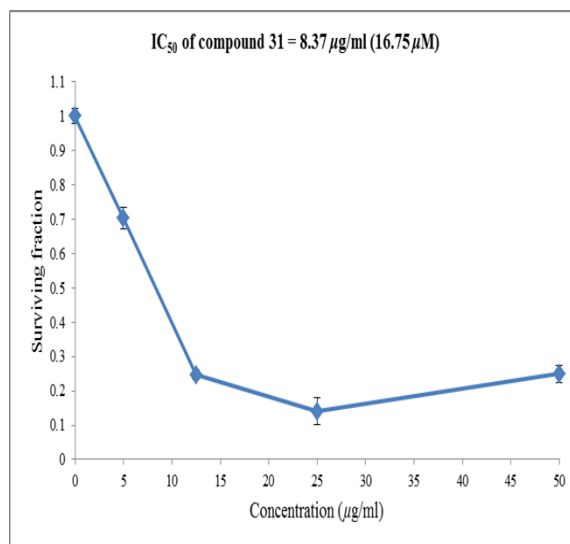
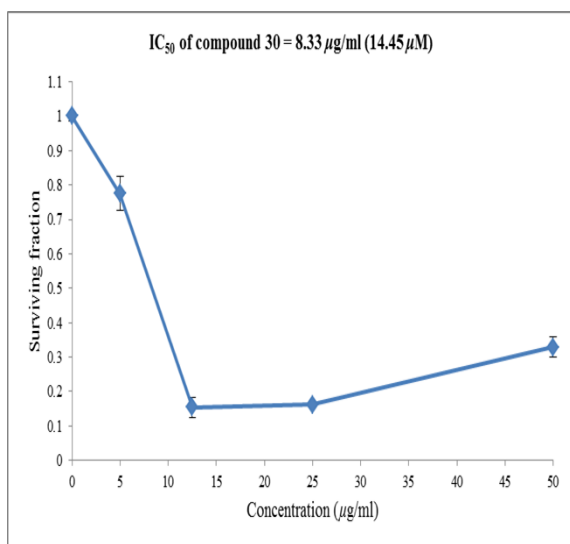
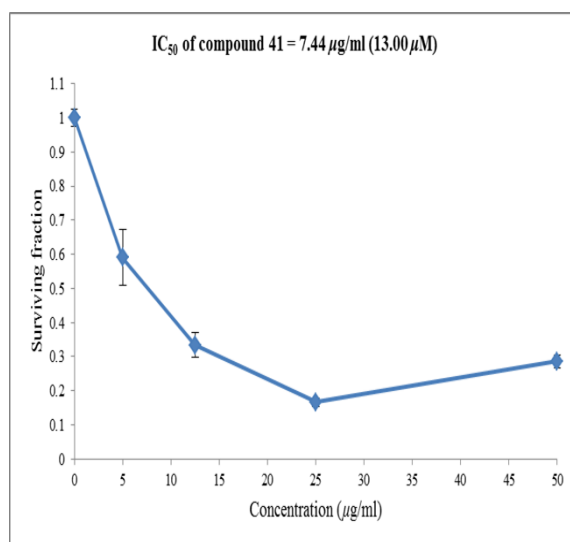
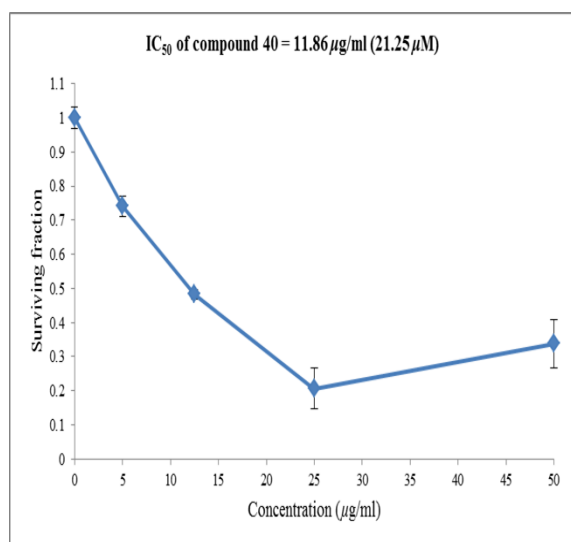
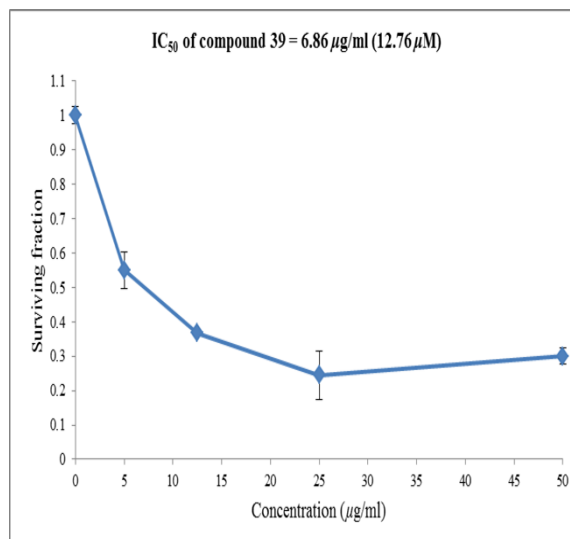
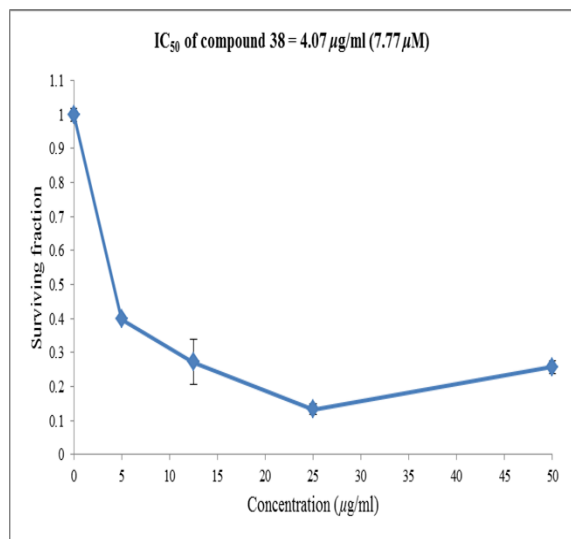
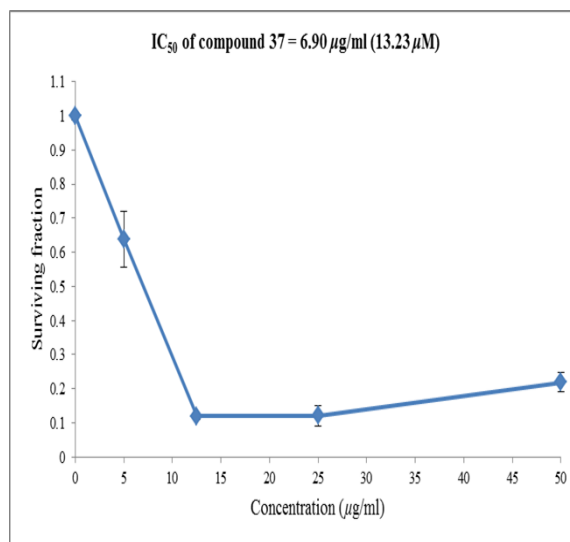
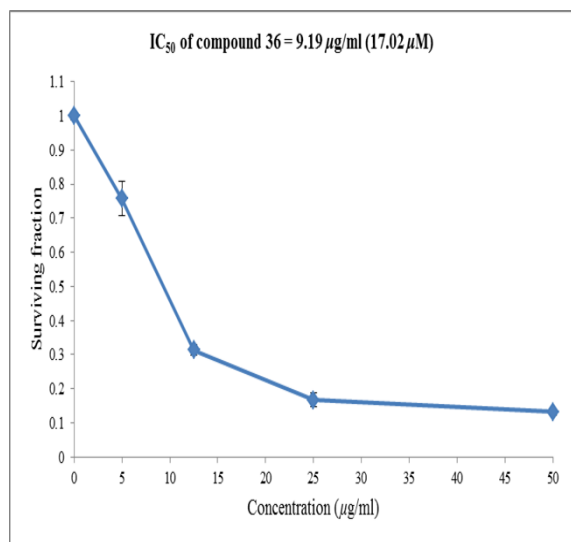
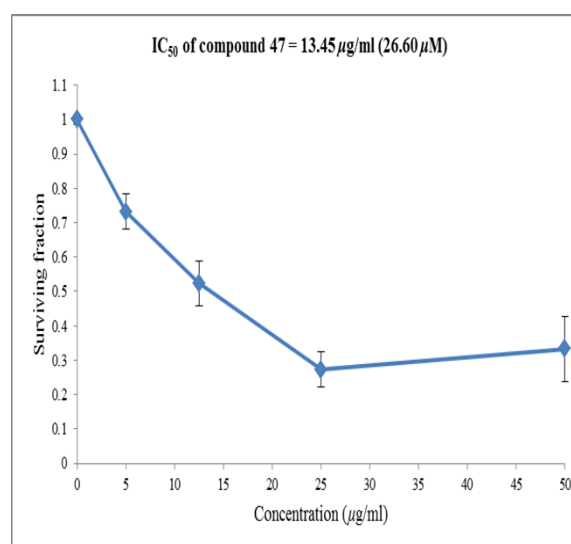
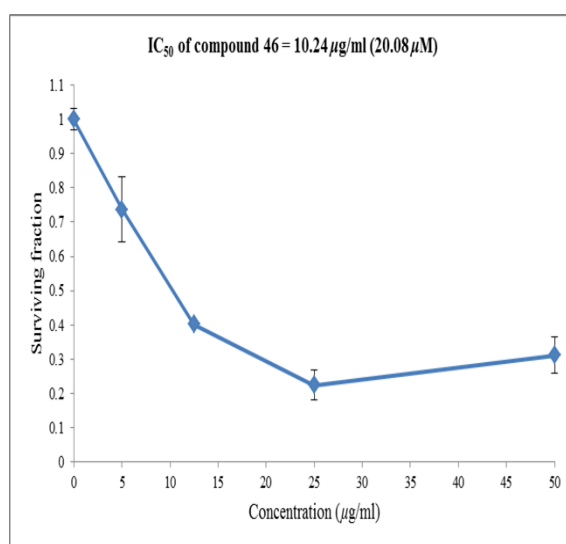
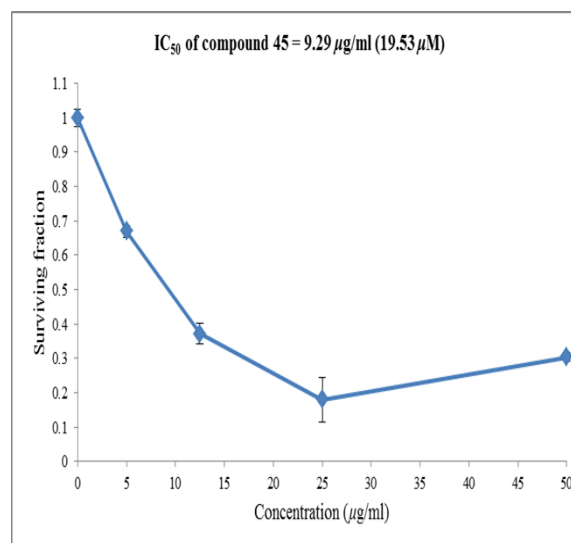
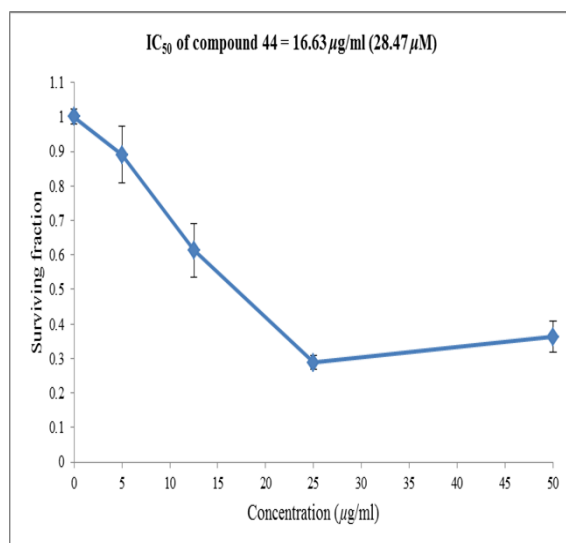
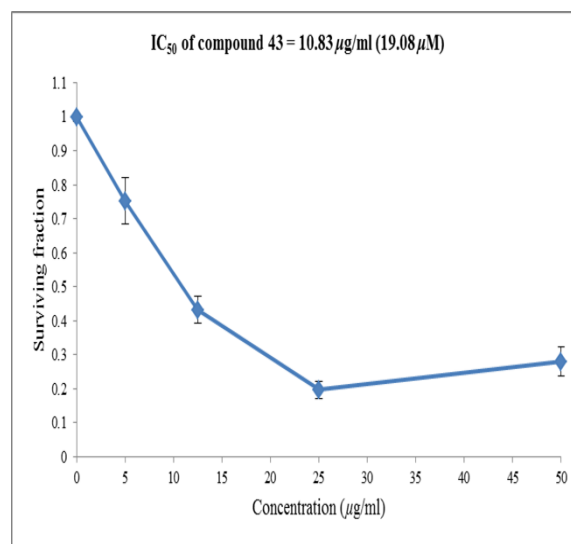
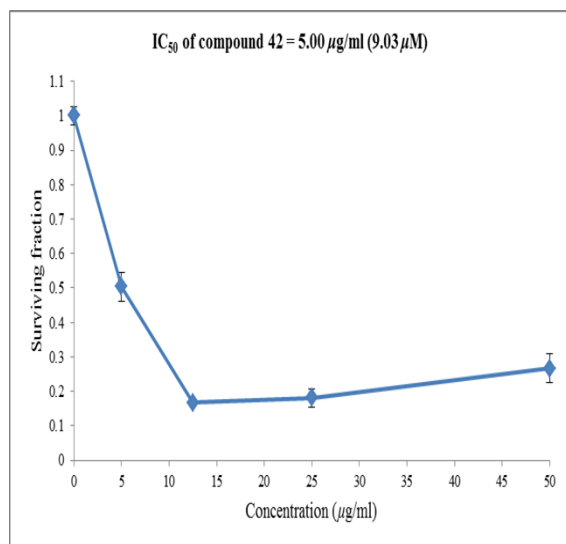


Figure 2. Dose-response curve for the synthesized compounds **24-48** against HEPG2 (liver cancer) cell line.









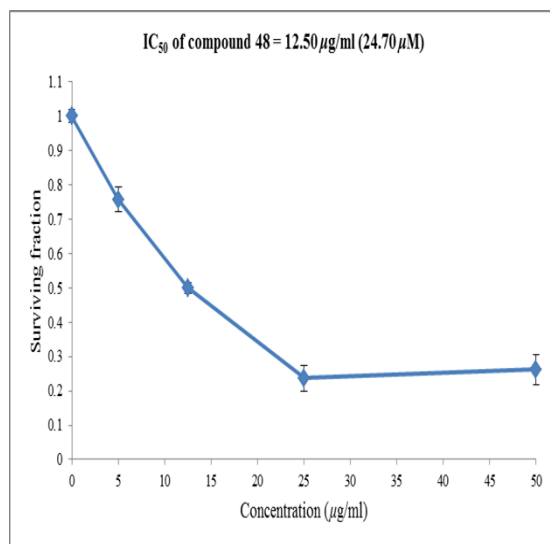
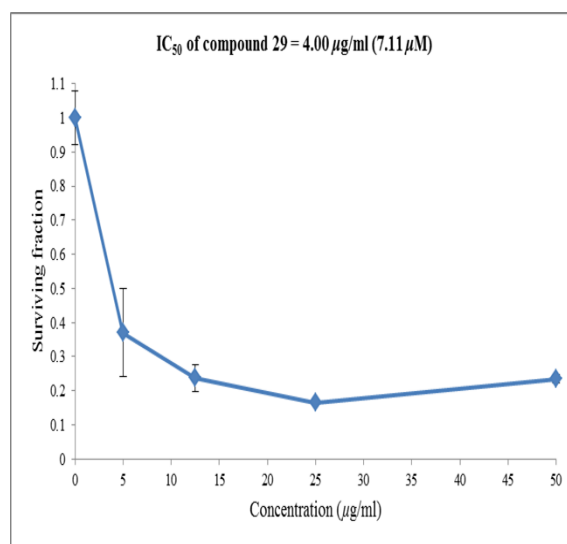
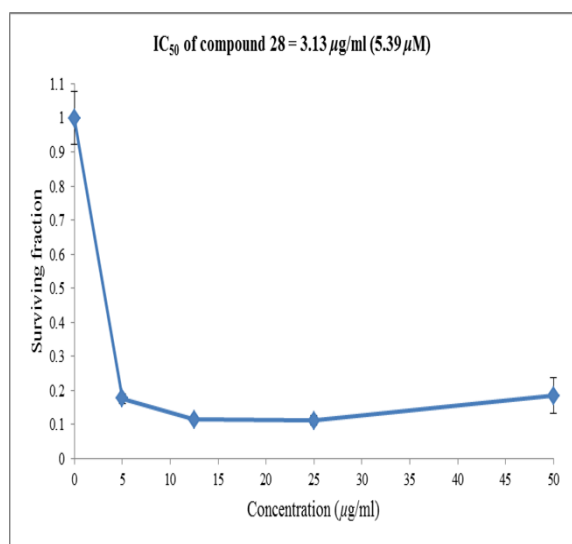
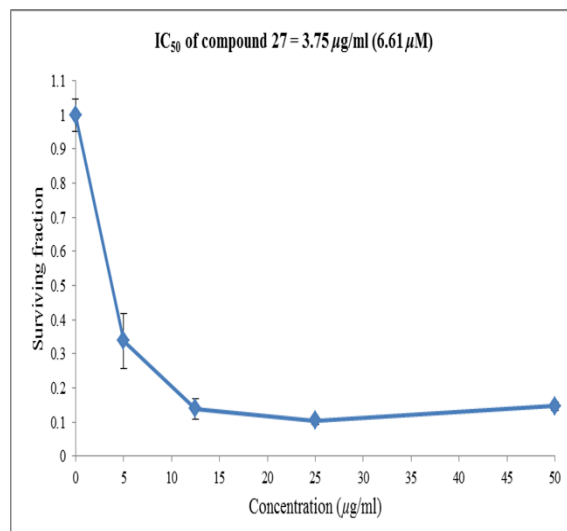
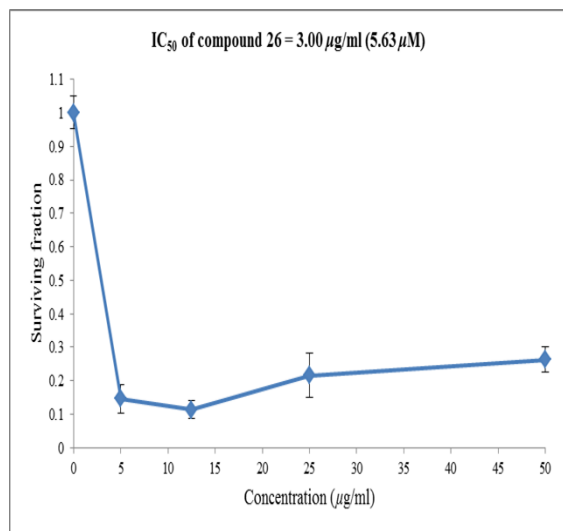
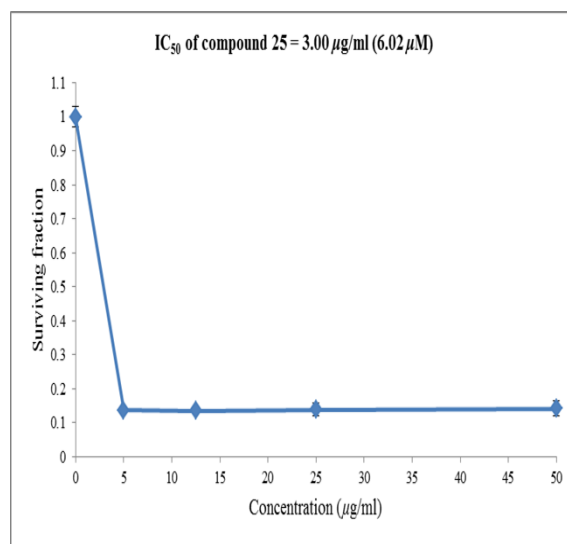
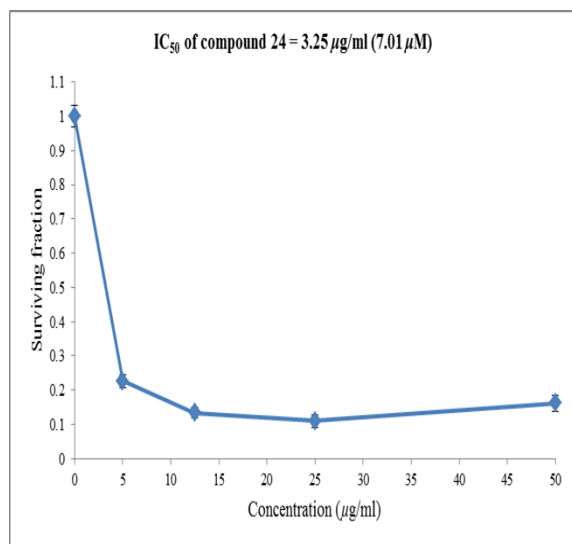
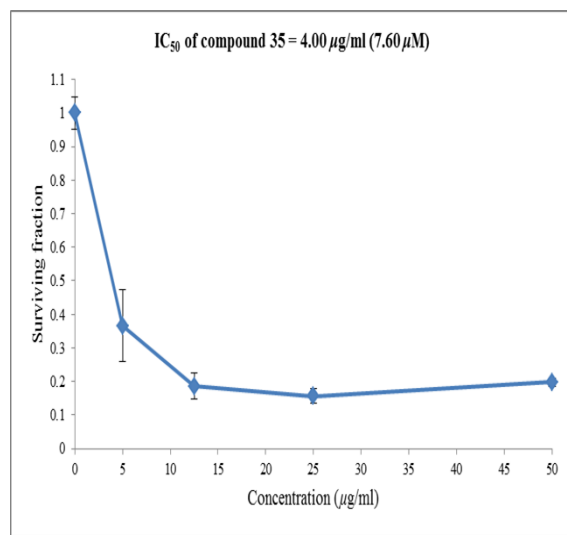
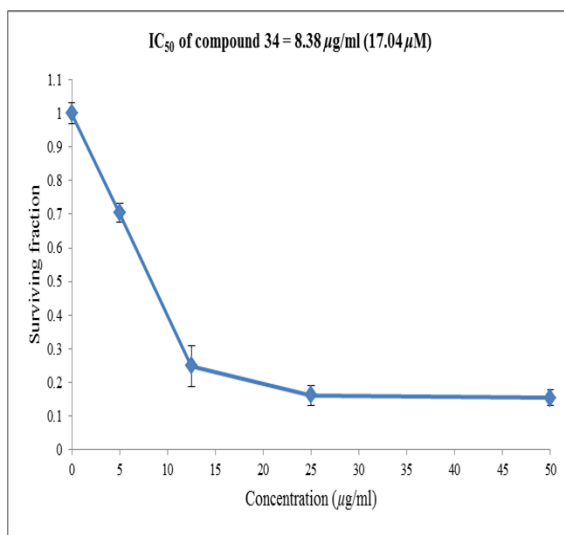
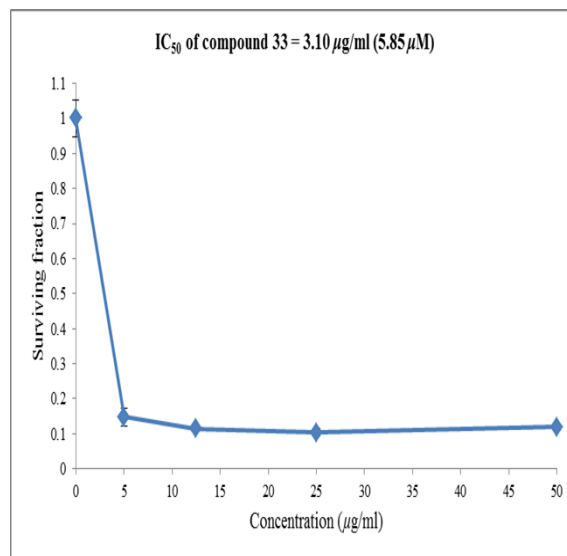
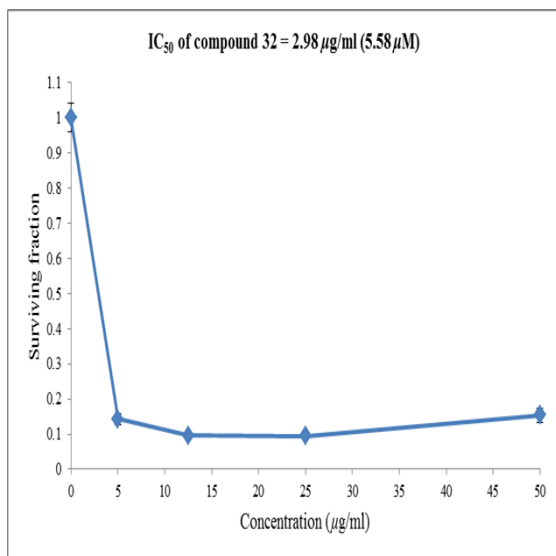
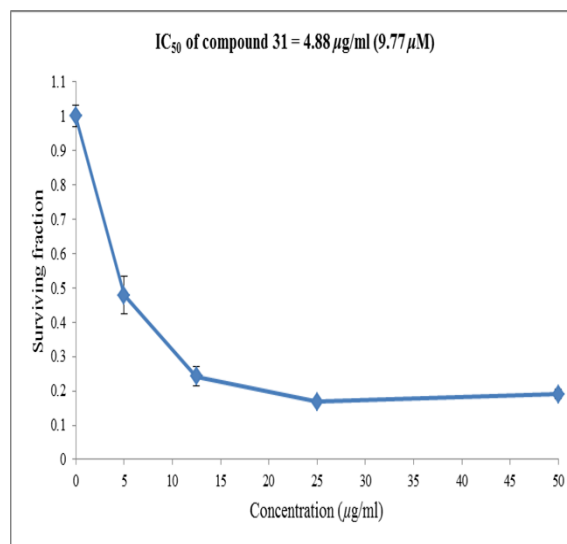
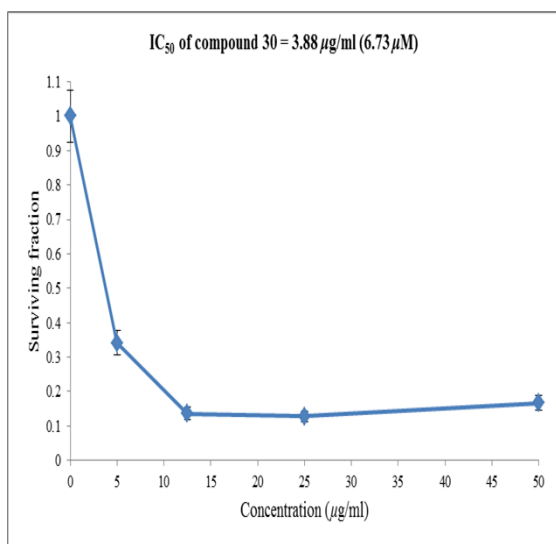
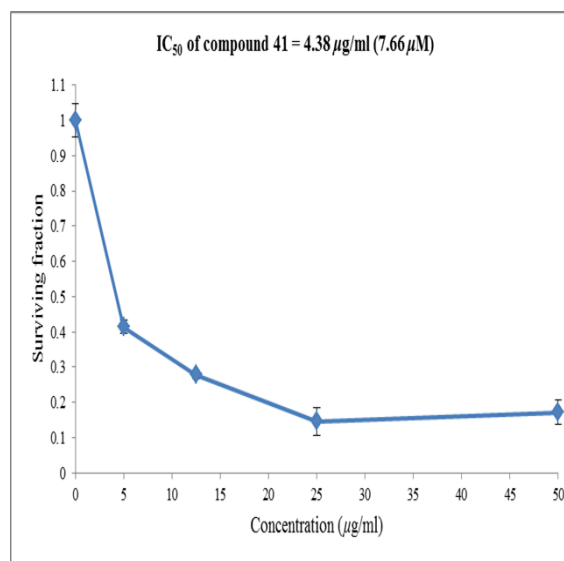
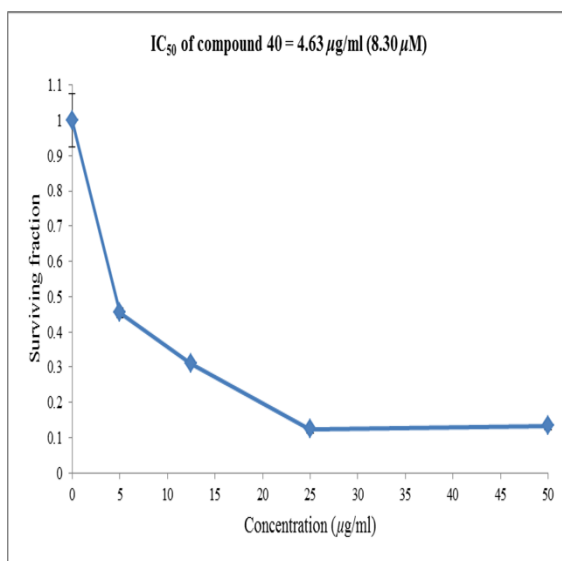
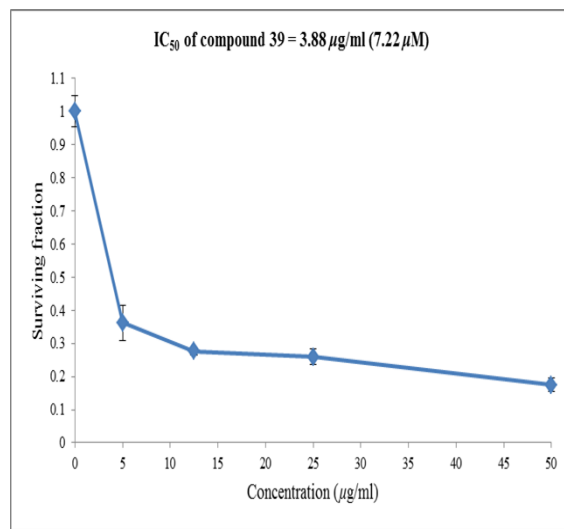
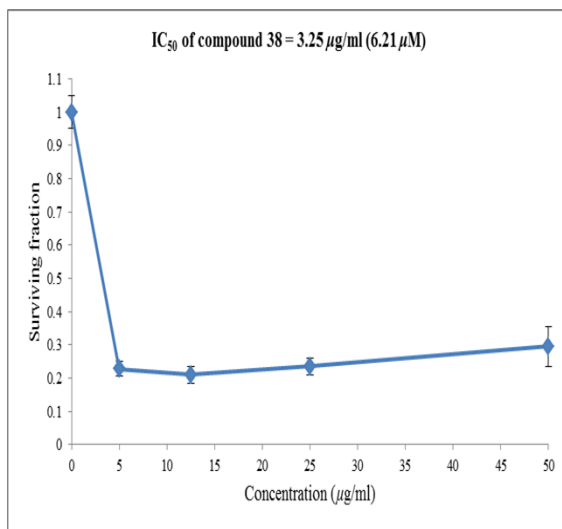
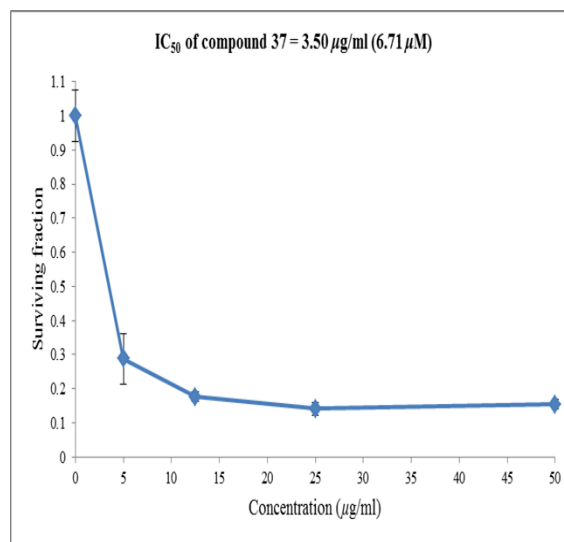
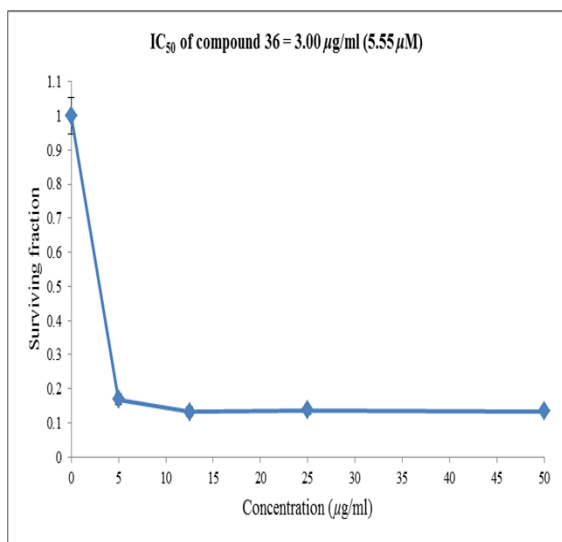
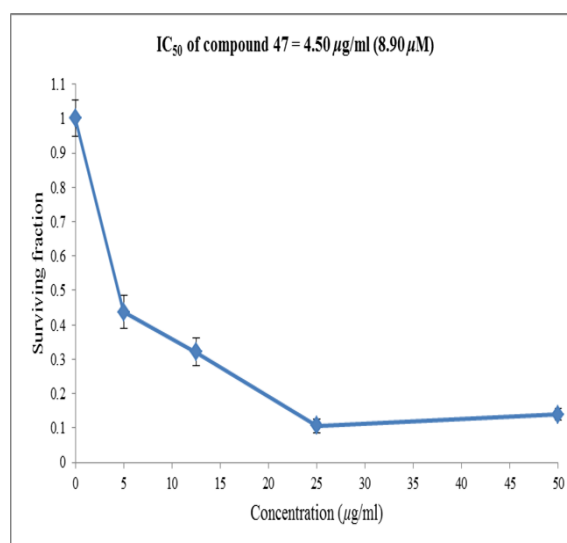
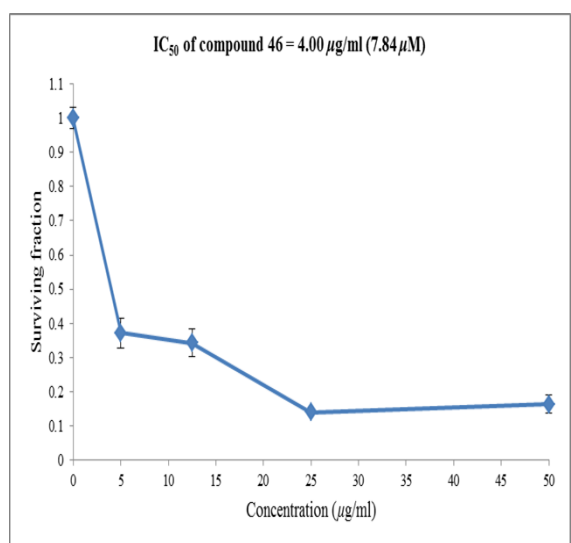
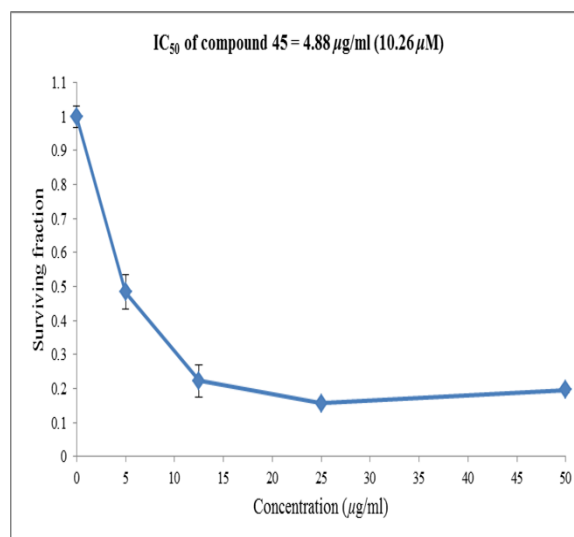
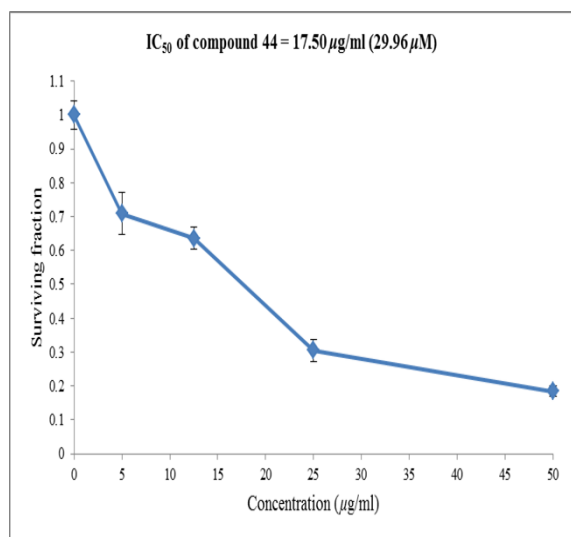
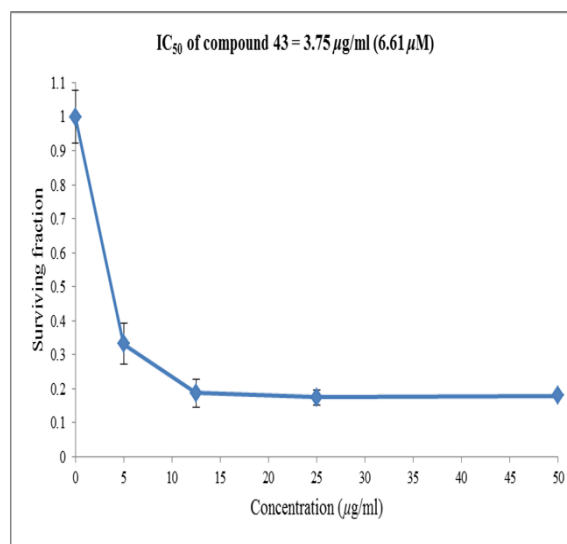
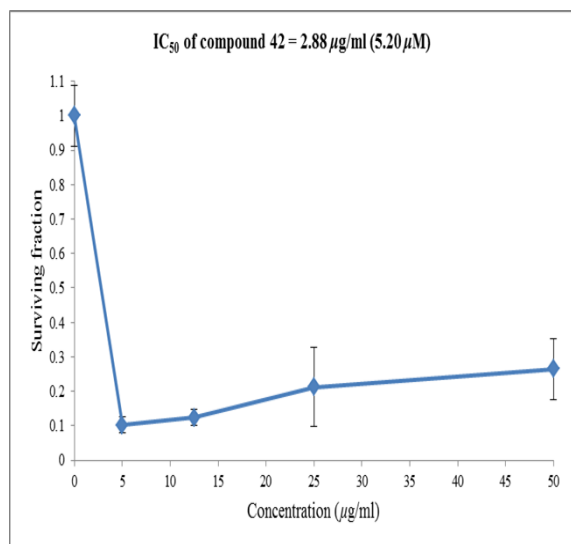


Figure 3. Dose-response curve for the synthesized compounds **24-48** against T-47D (breast cancer) cell line.









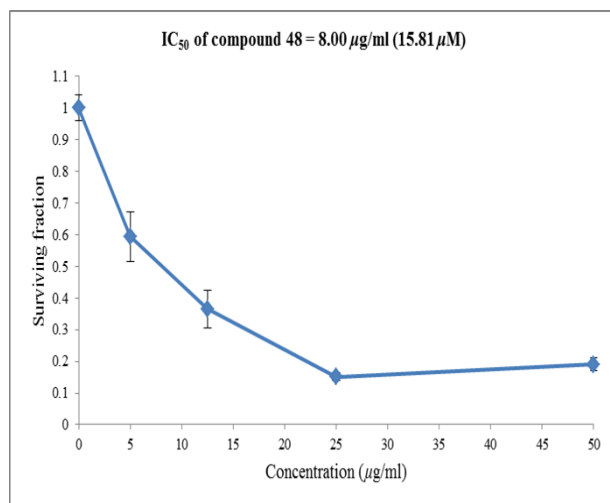
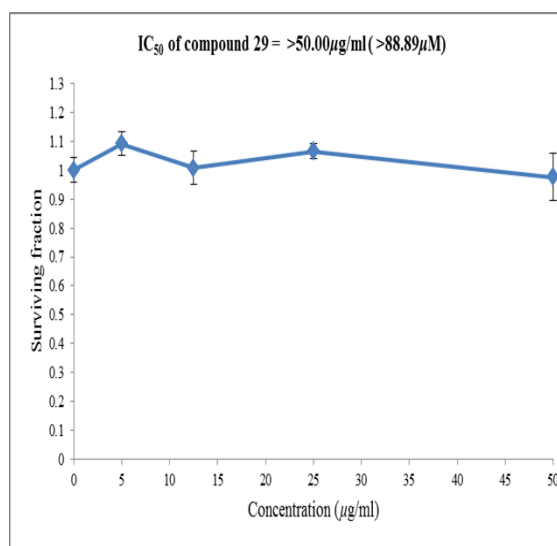
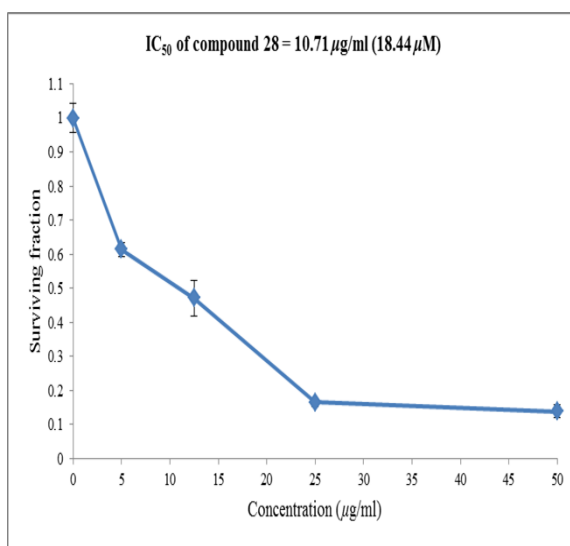
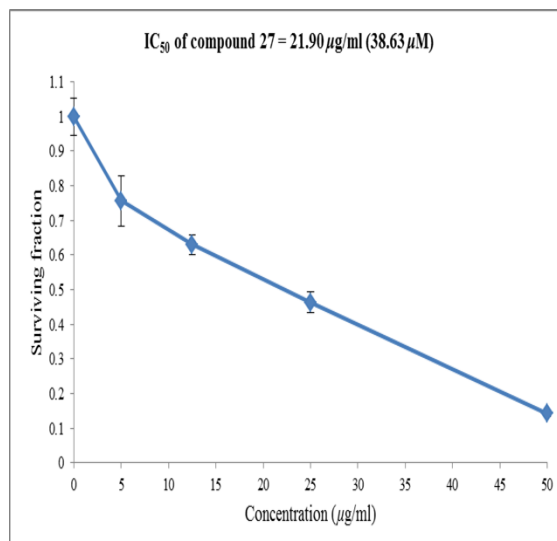
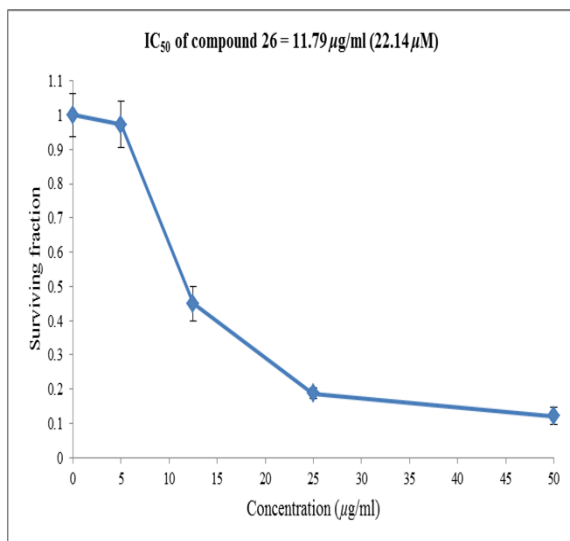
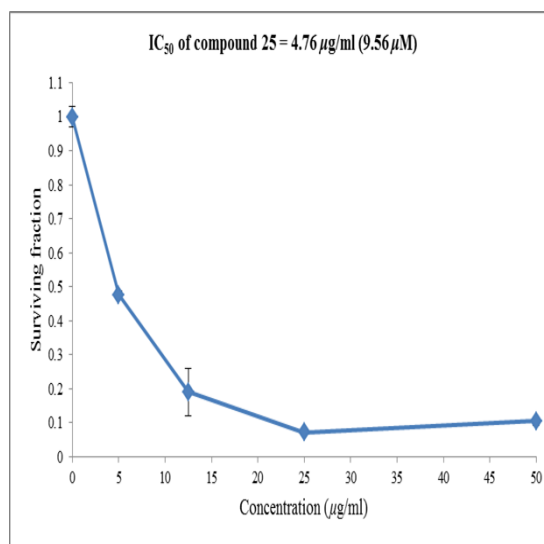
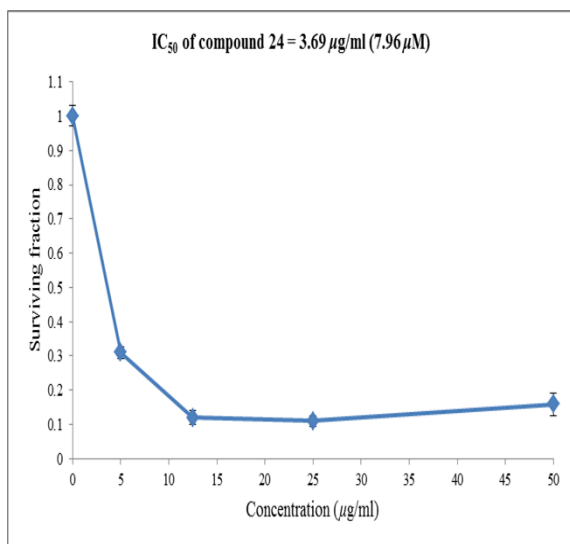
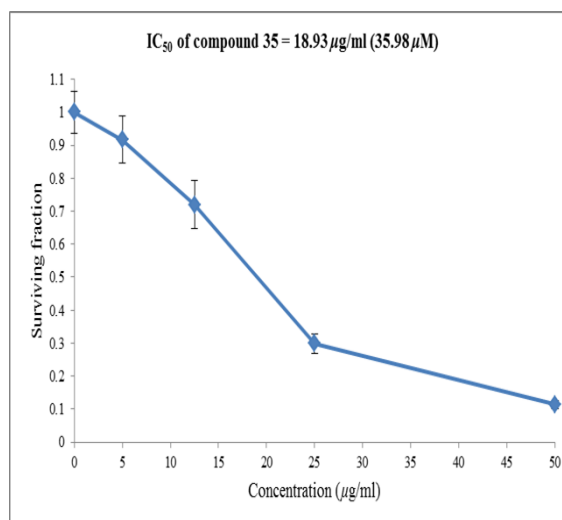
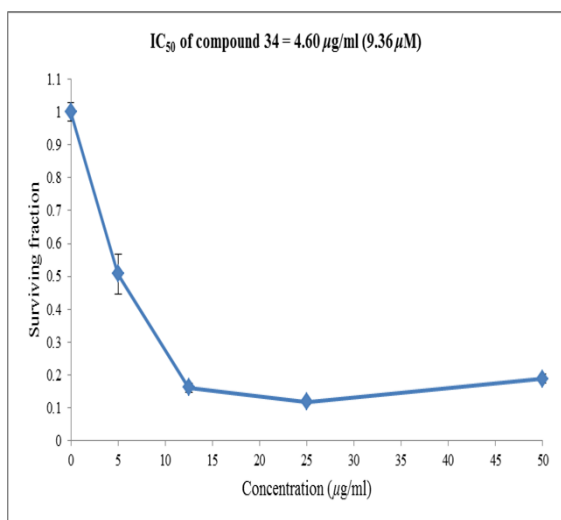
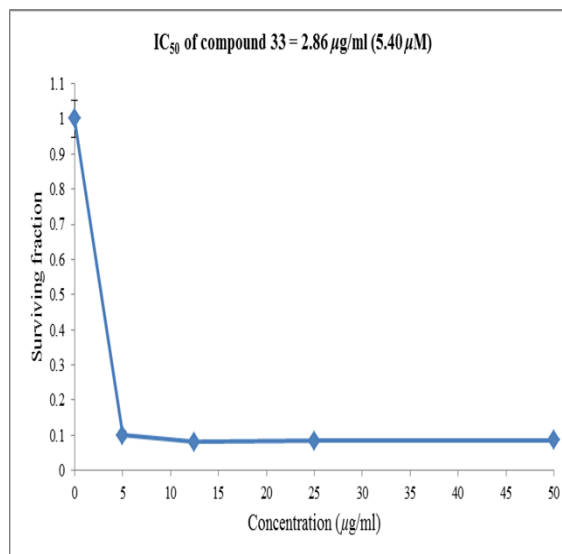
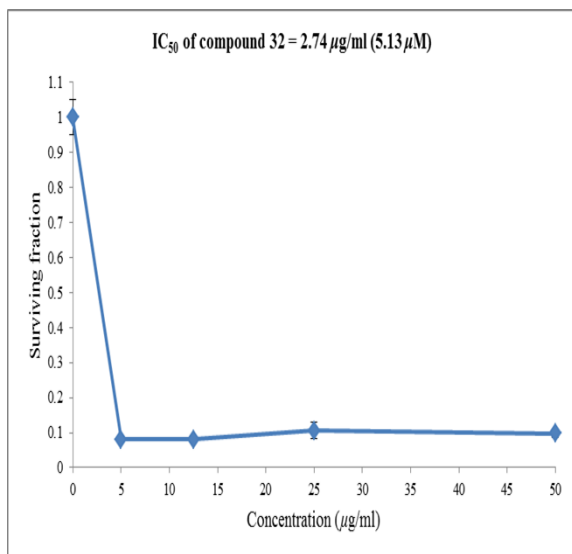
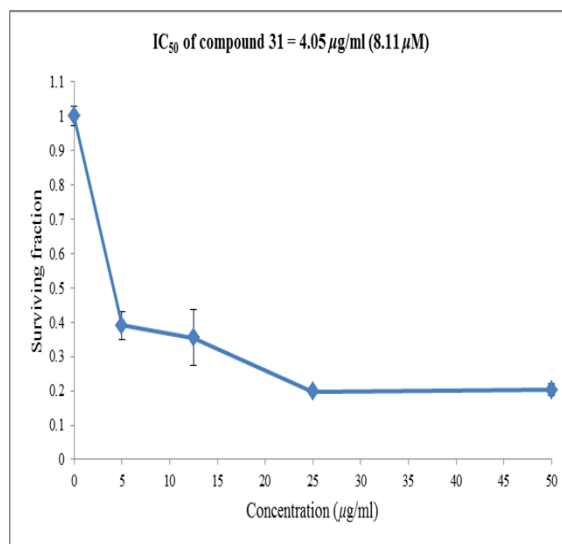
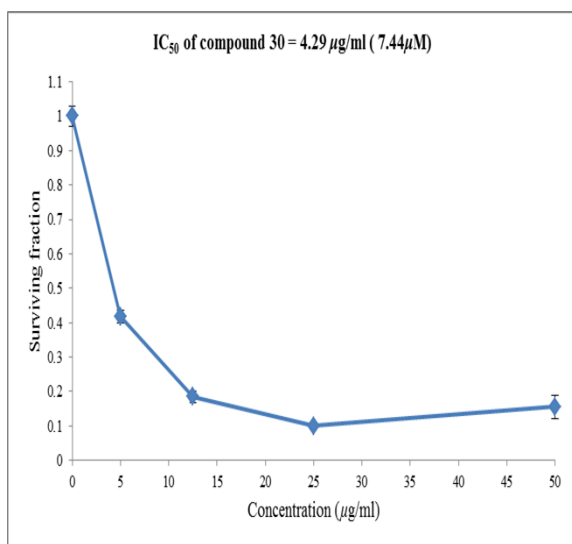
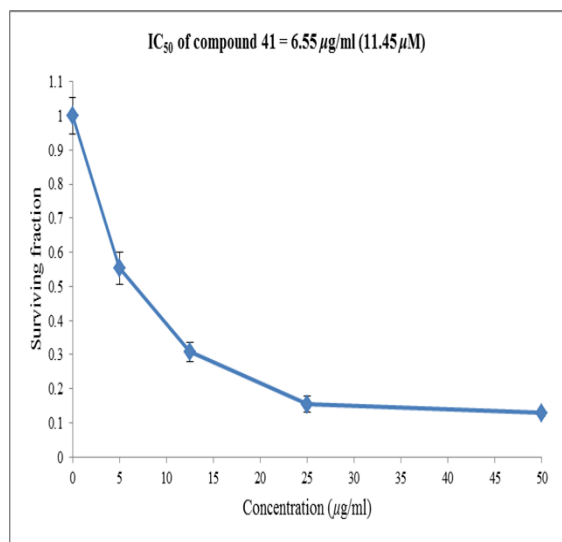
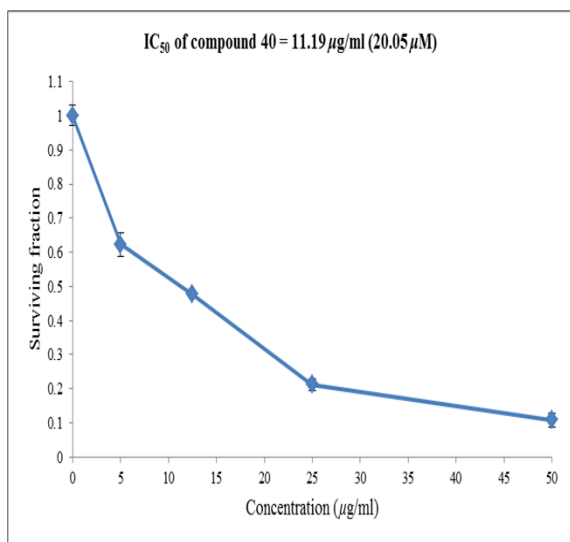
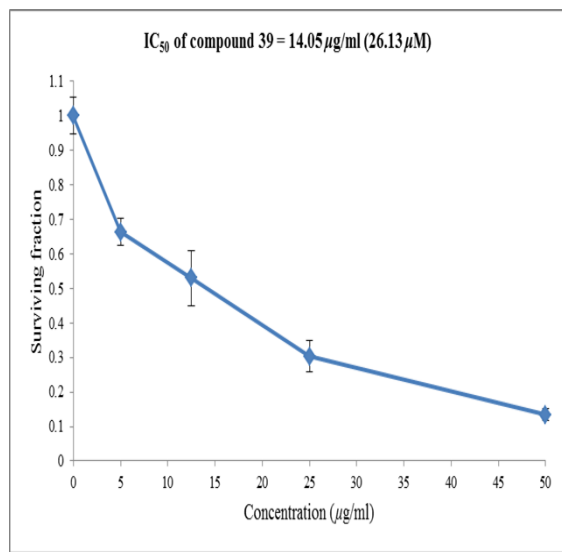
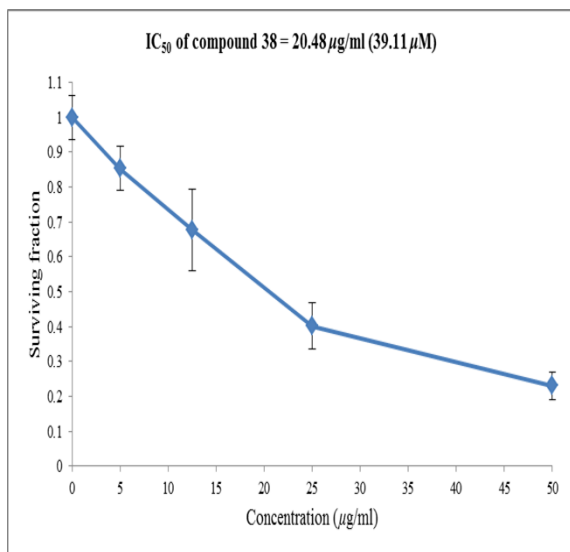
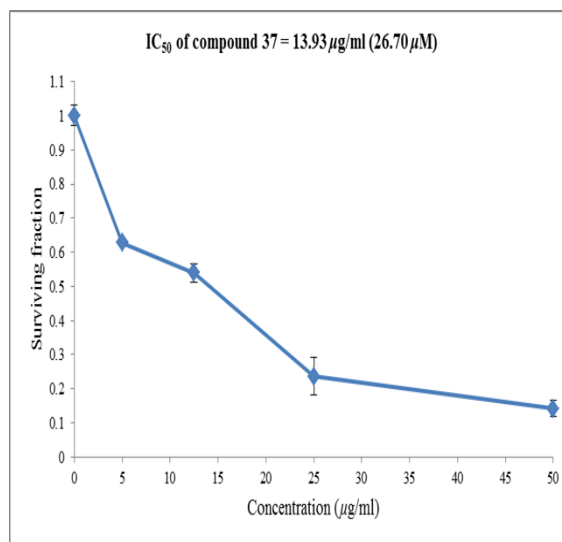
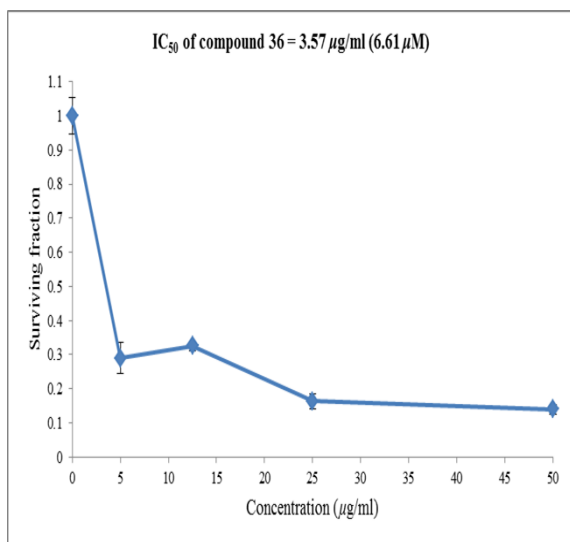
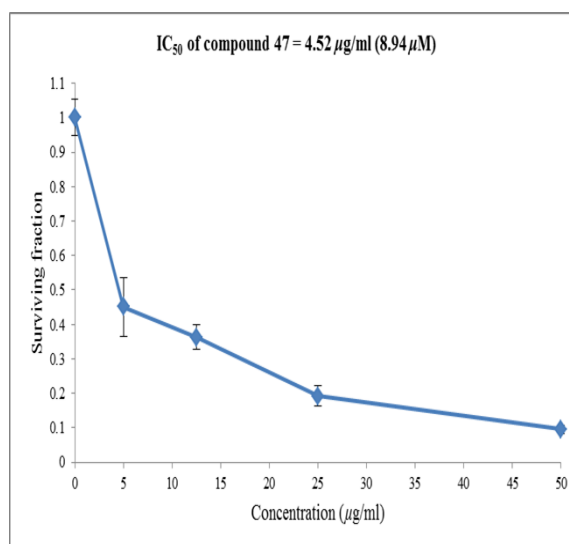
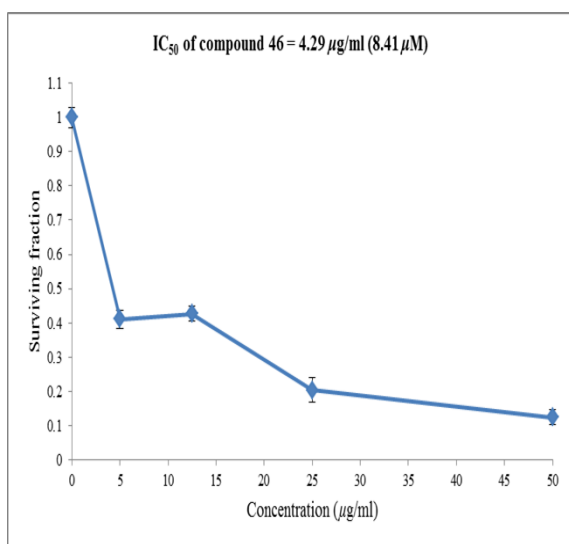
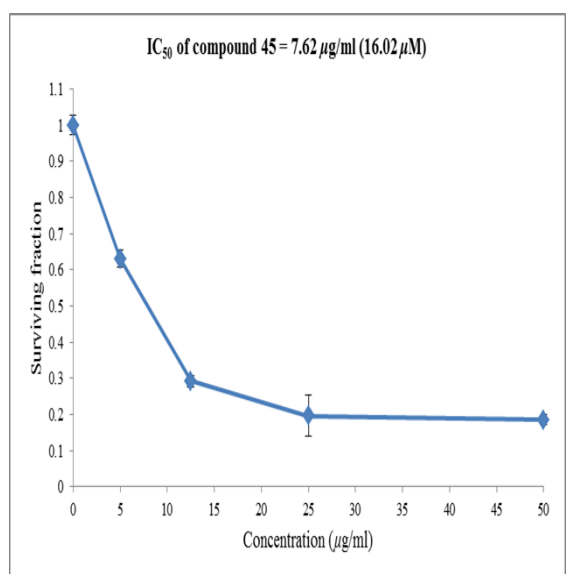
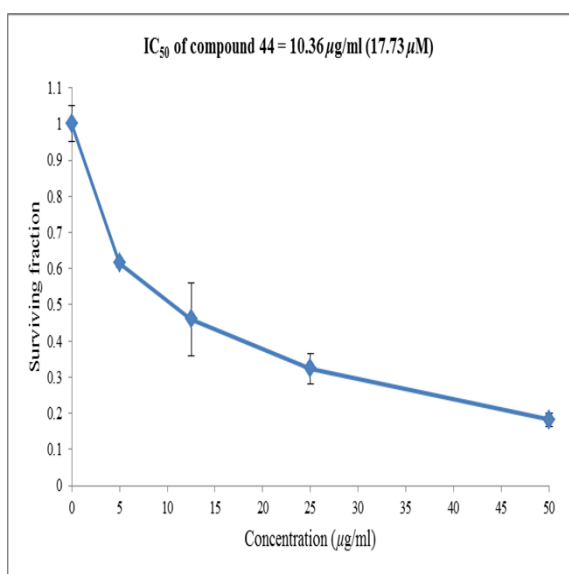
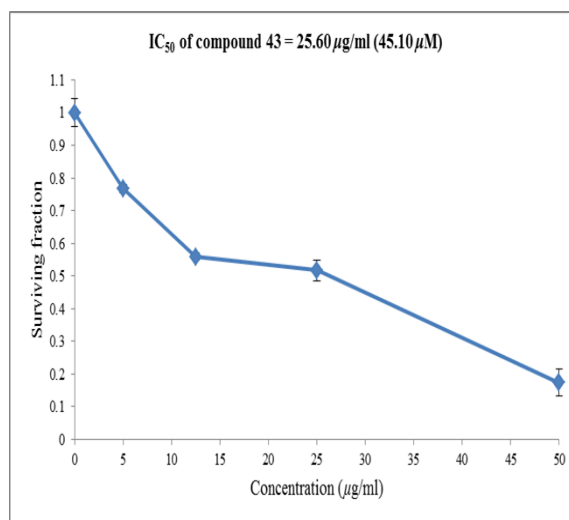
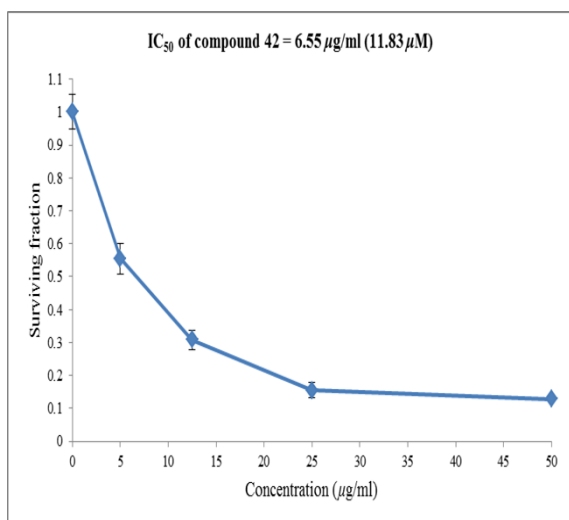


Figure 4. Dose-response curve for the synthesized compounds **24-48** against MCF7 (breast cancer) cell line.









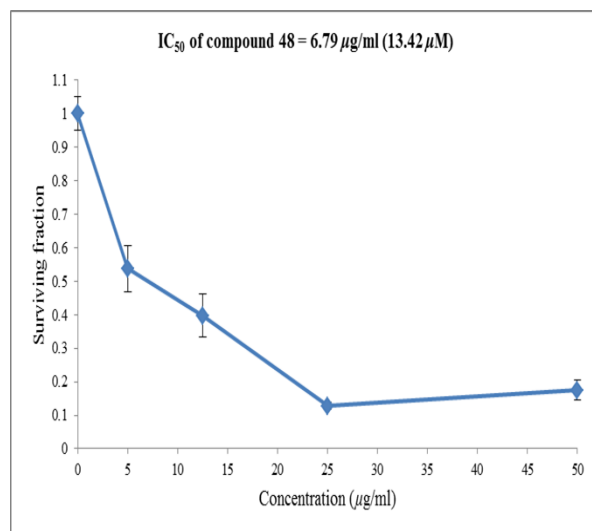
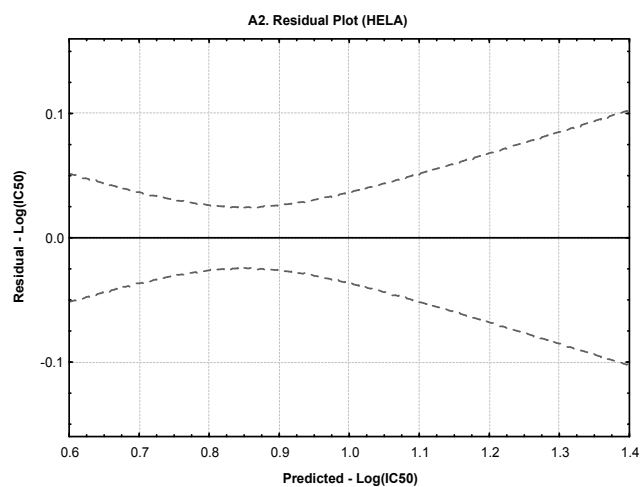
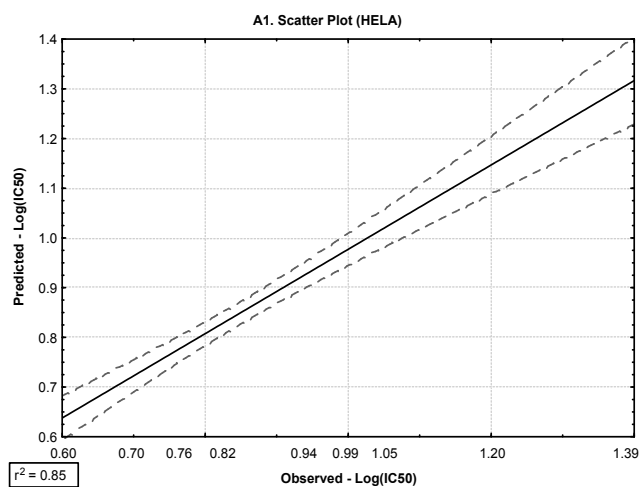


Figure 5. Dose-response curve for the synthesized compounds **24-48** against HCT116 (colon cancer) cell line.

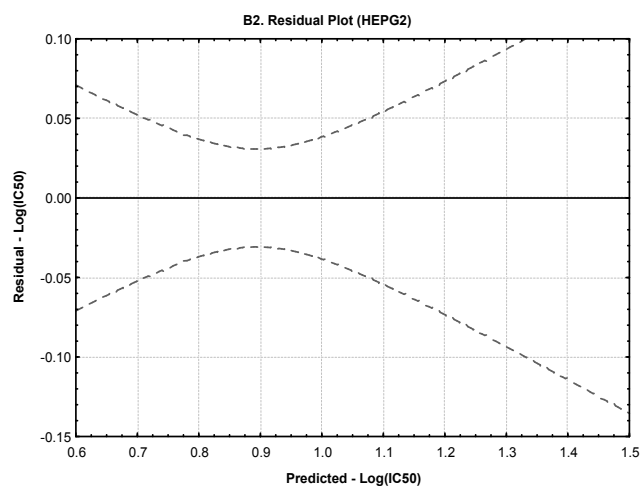
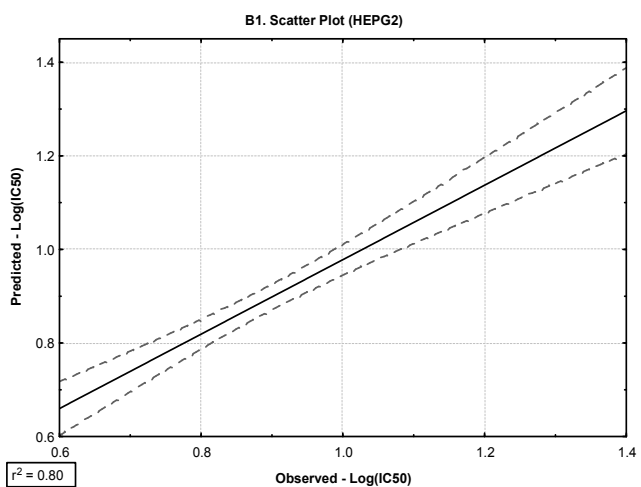
Scatter Plot – BMLR

Residual Plot

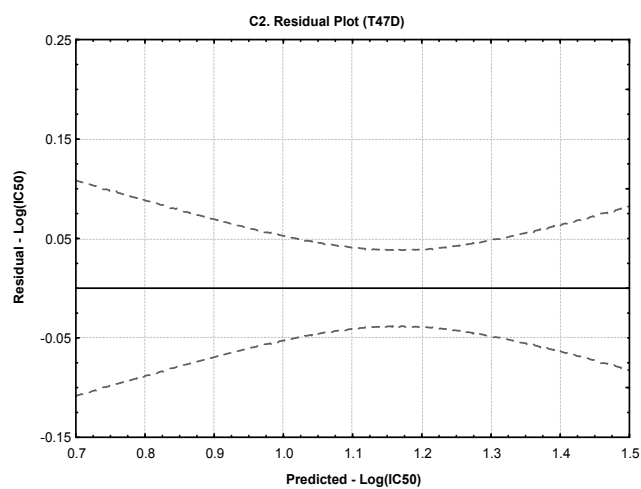
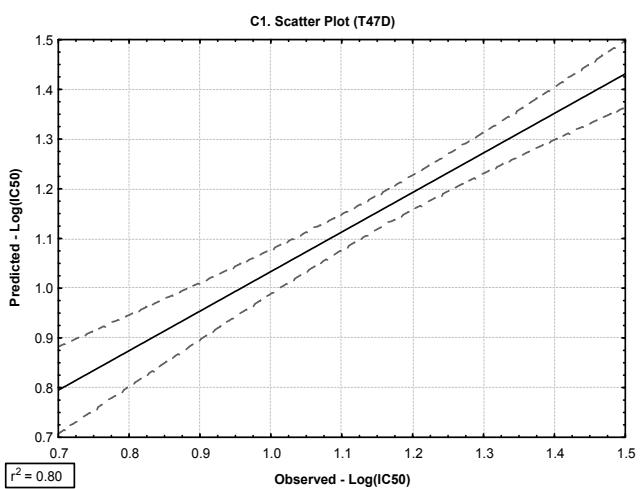
HELA - Cervical



HEPG2 - Liver



T47D - Breast



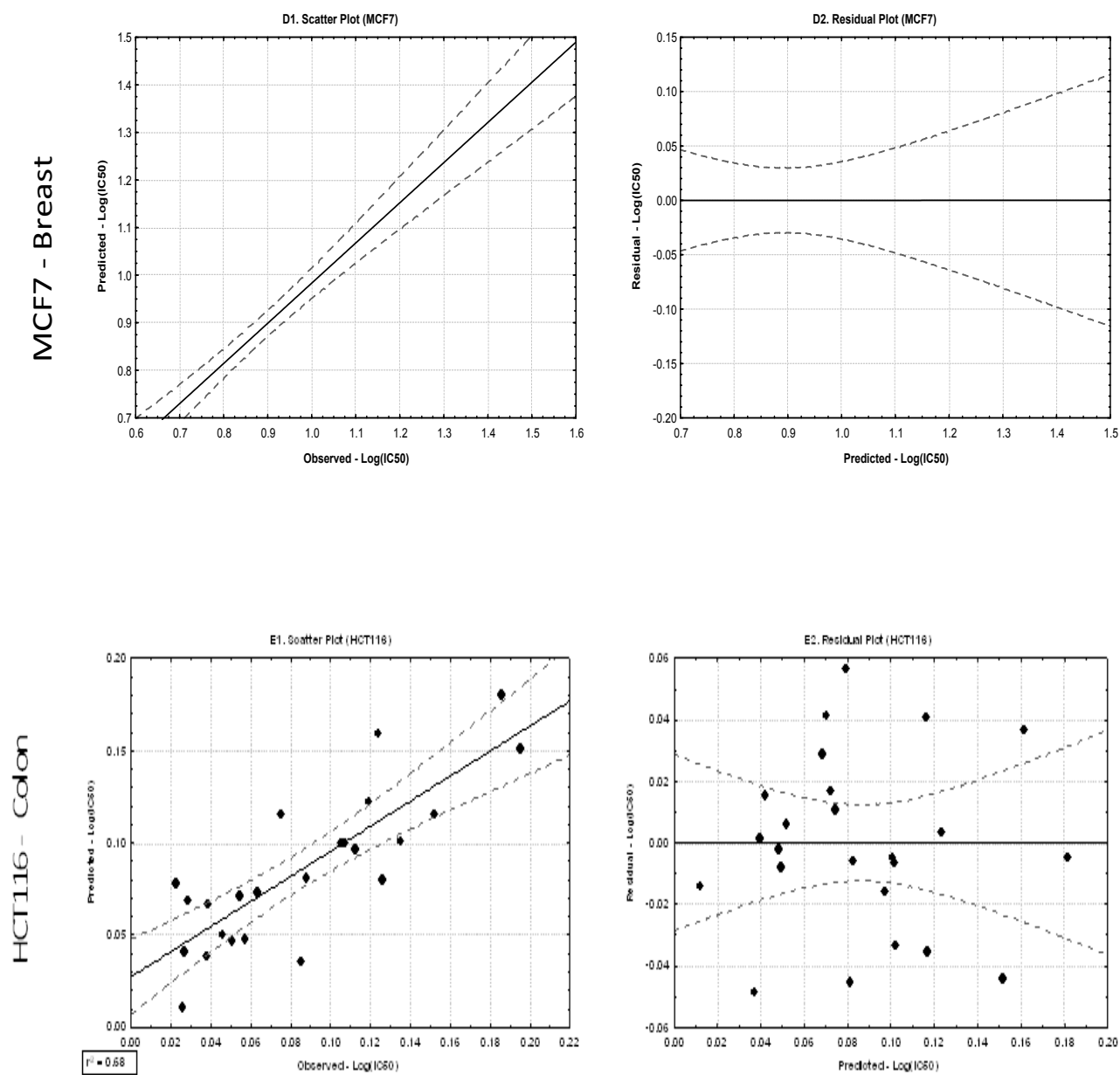


Figure 6. Scatter plots of BMLR for HELA (A), HEPG2 (B), T47D (C), MCF7 (D), HCT116 (E) QSAR models.

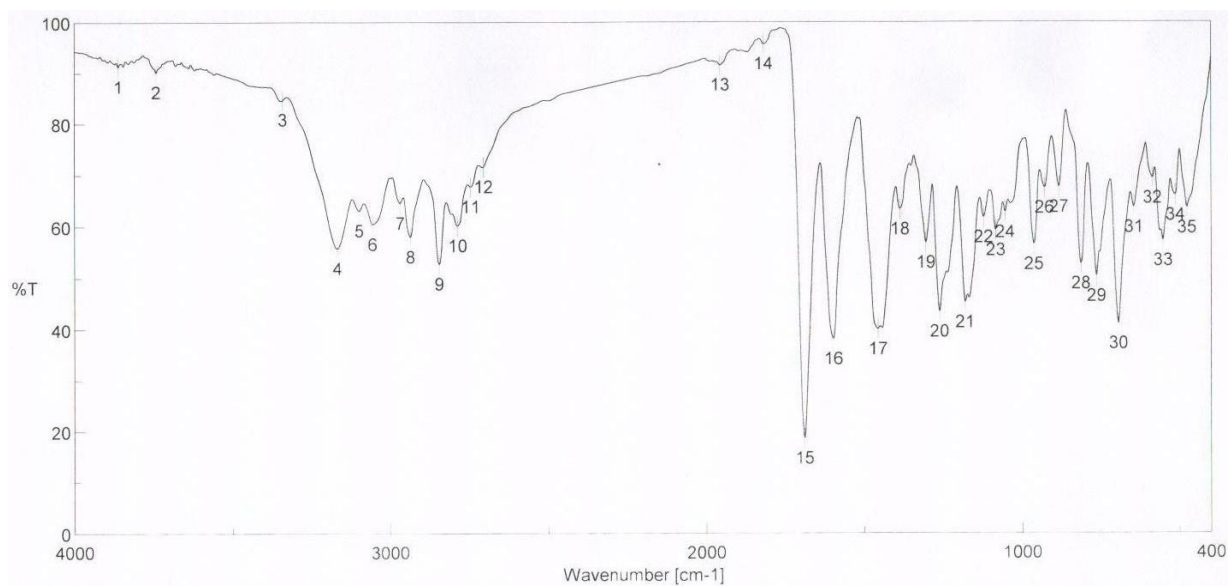


Figure 7. IR spectrum of compound 25.

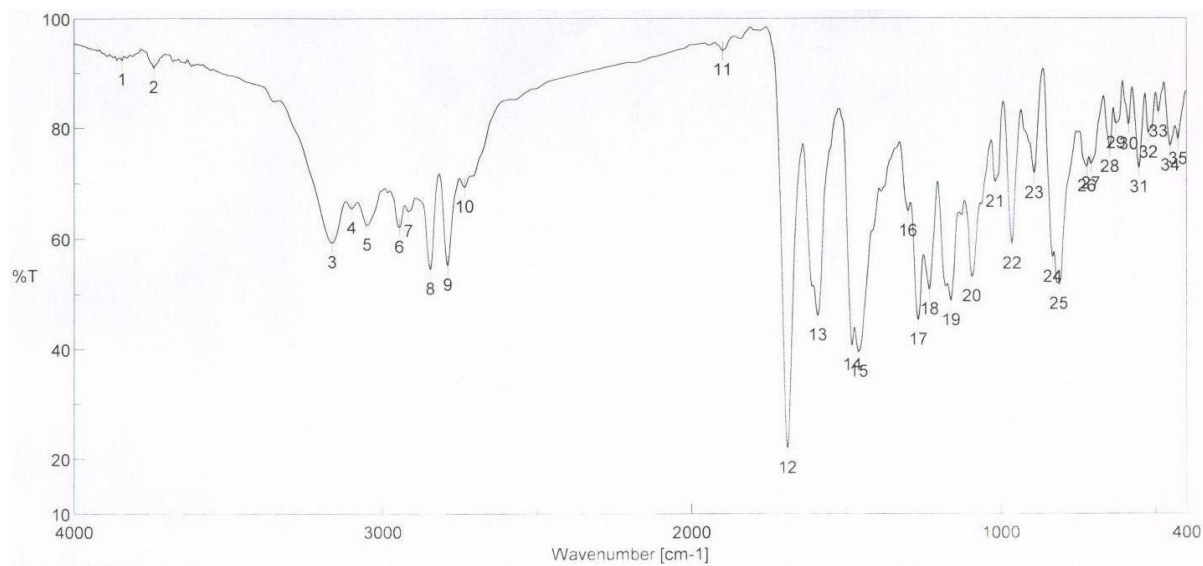


Figure 8. IR spectrum of compound 27.

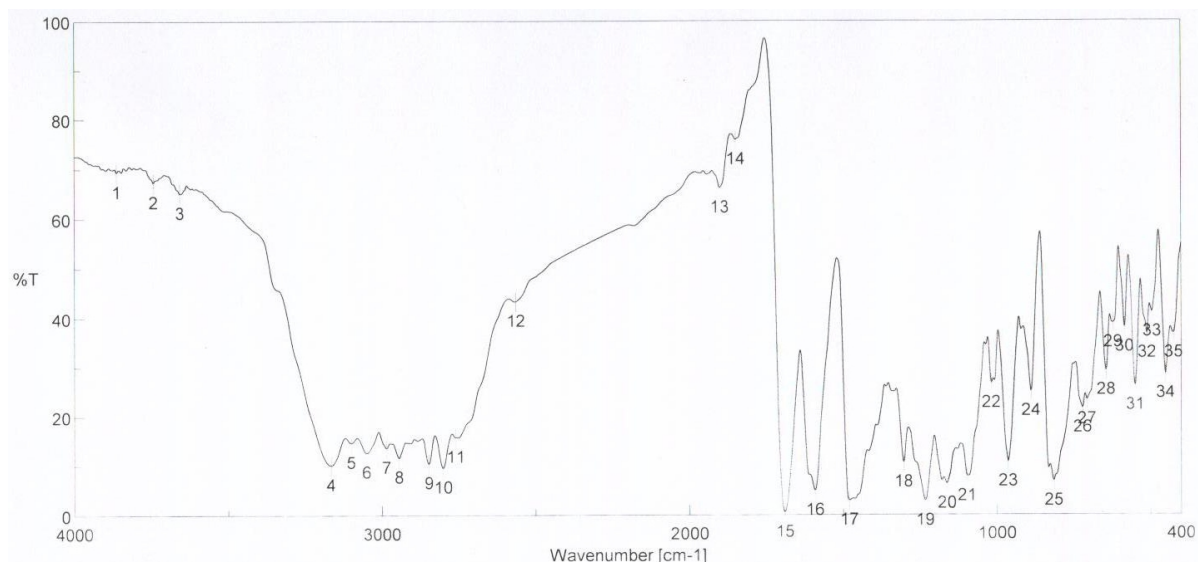


Figure 9. IR spectrum of compound 28.

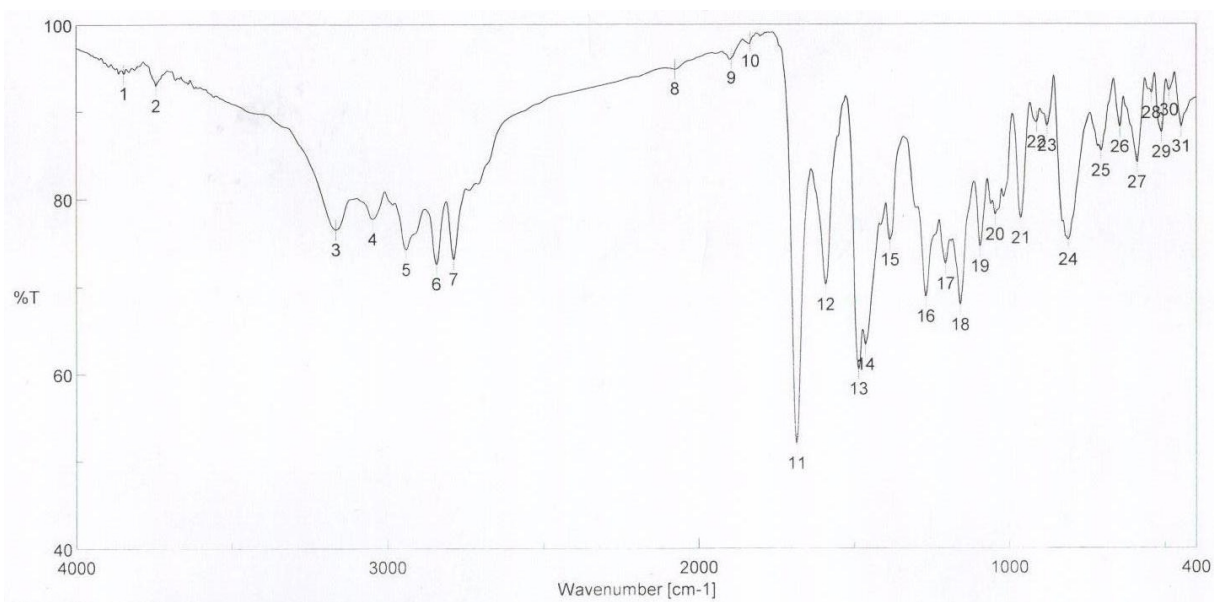


Figure 10. IR spectrum of compound 29.

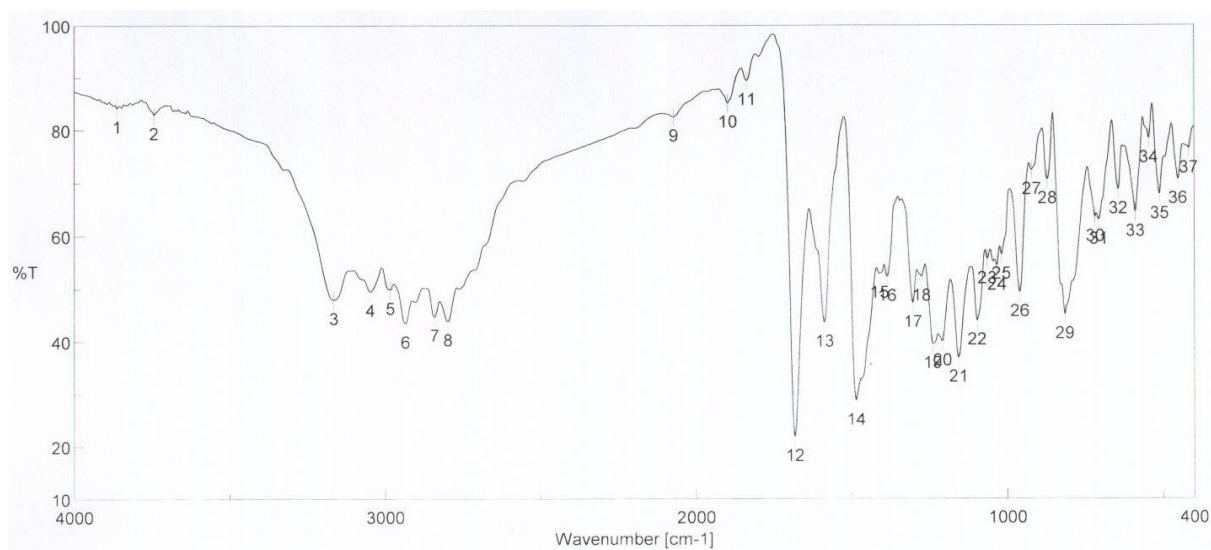


Figure 11. IR spectrum of compound **30**.

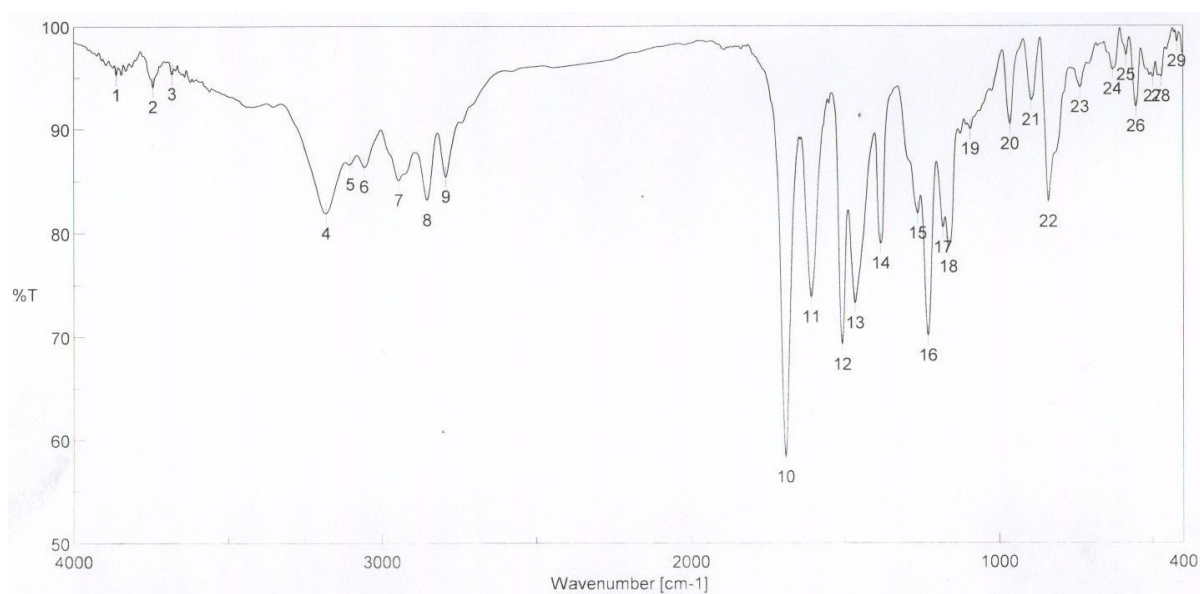


Figure 12. IR spectrum of compound **32**.

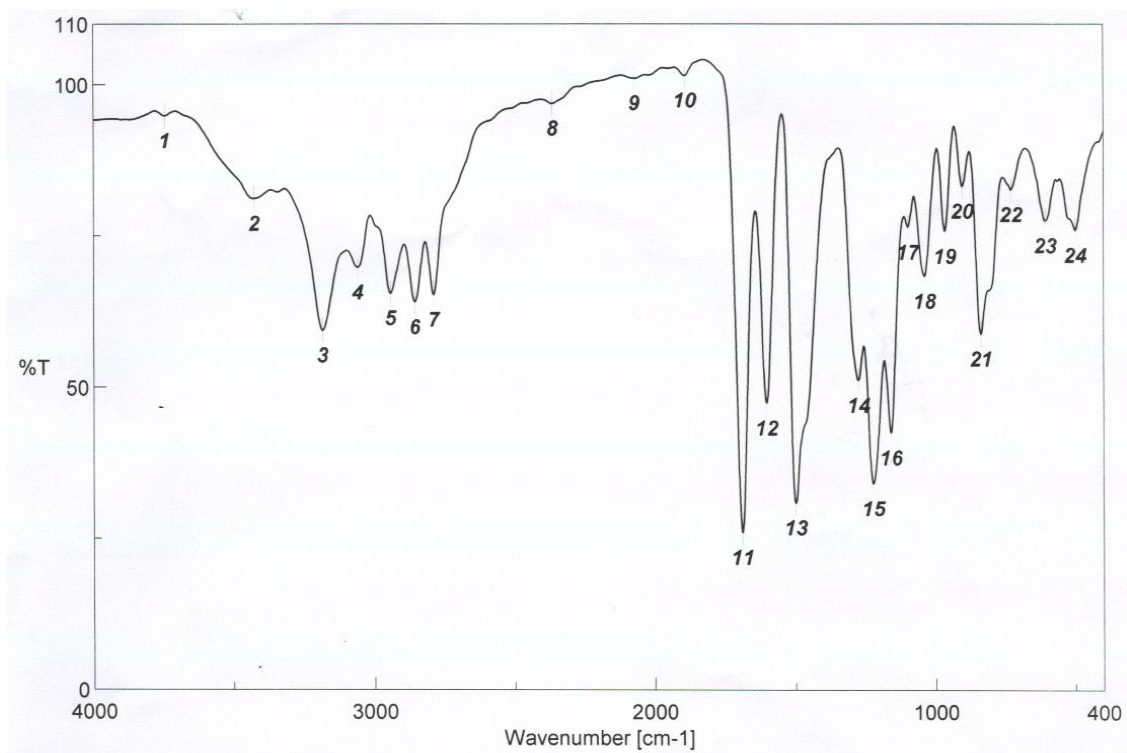


Figure 13. IR spectrum of compound 33.

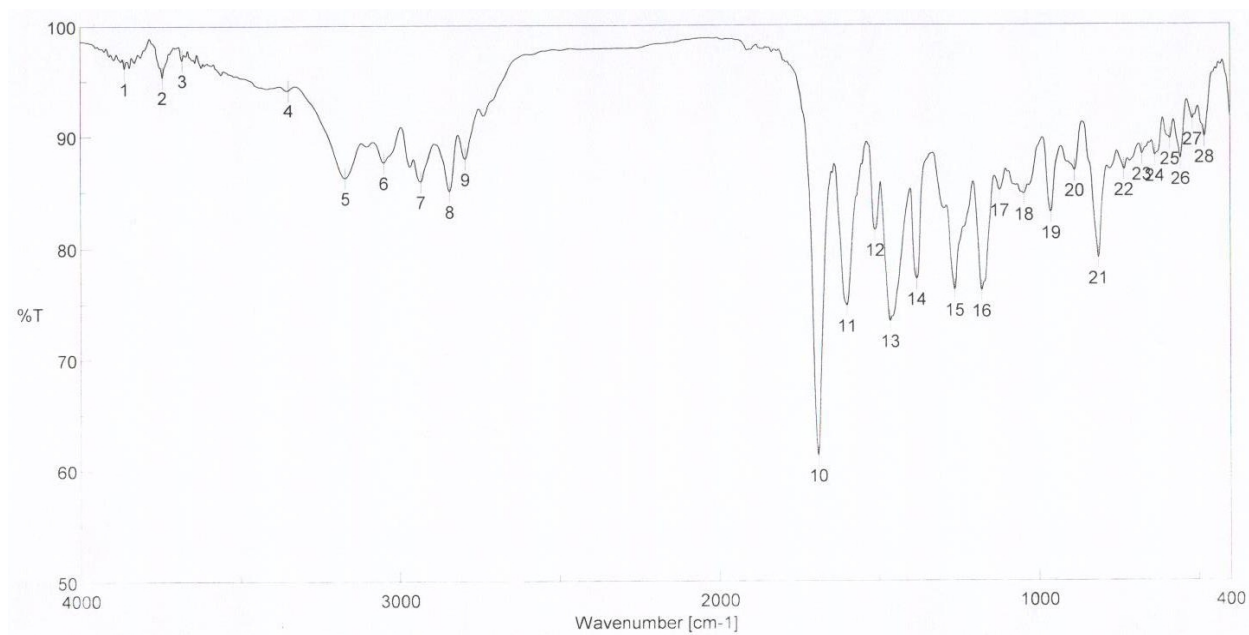


Figure 14. IR spectrum of compound 35.

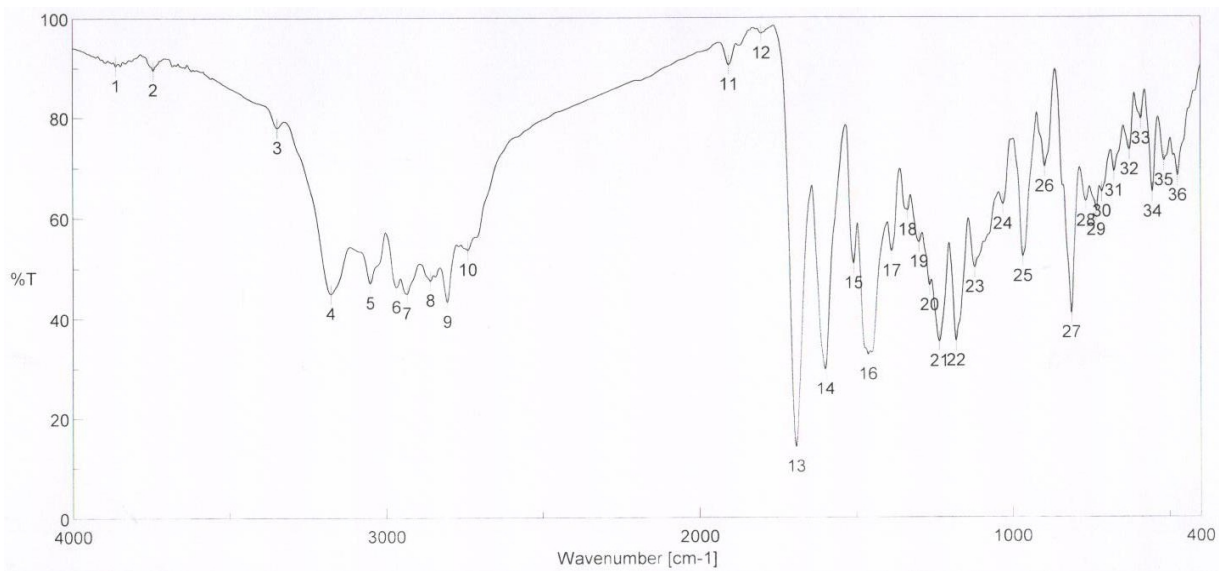


Figure 15. IR spectrum of compound 36.

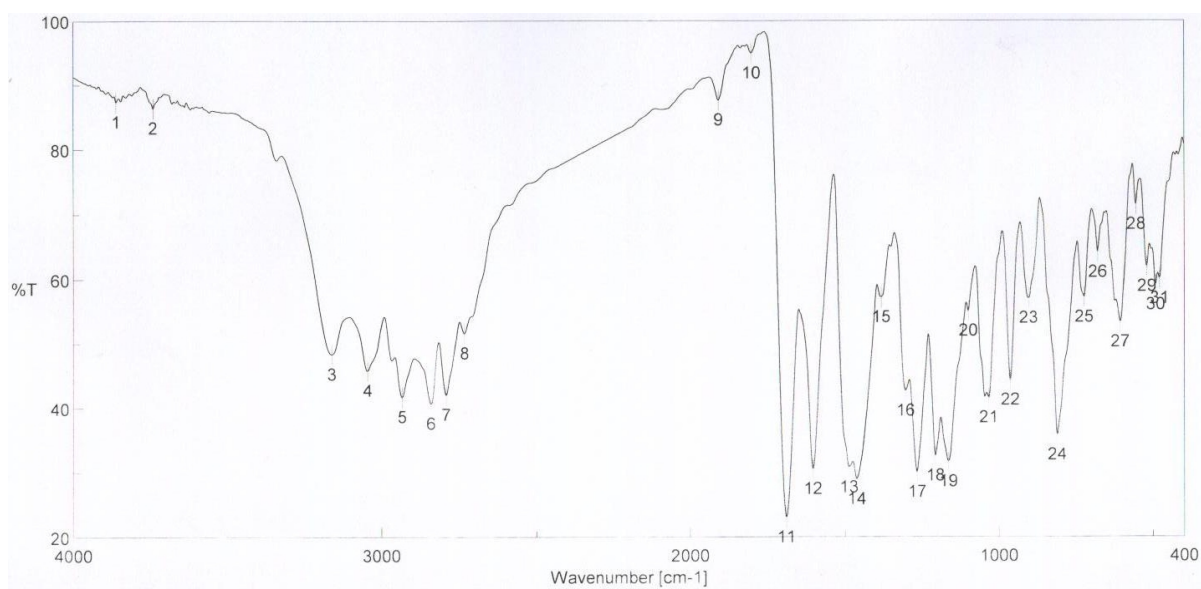


Figure 16. IR spectrum of compound 37.

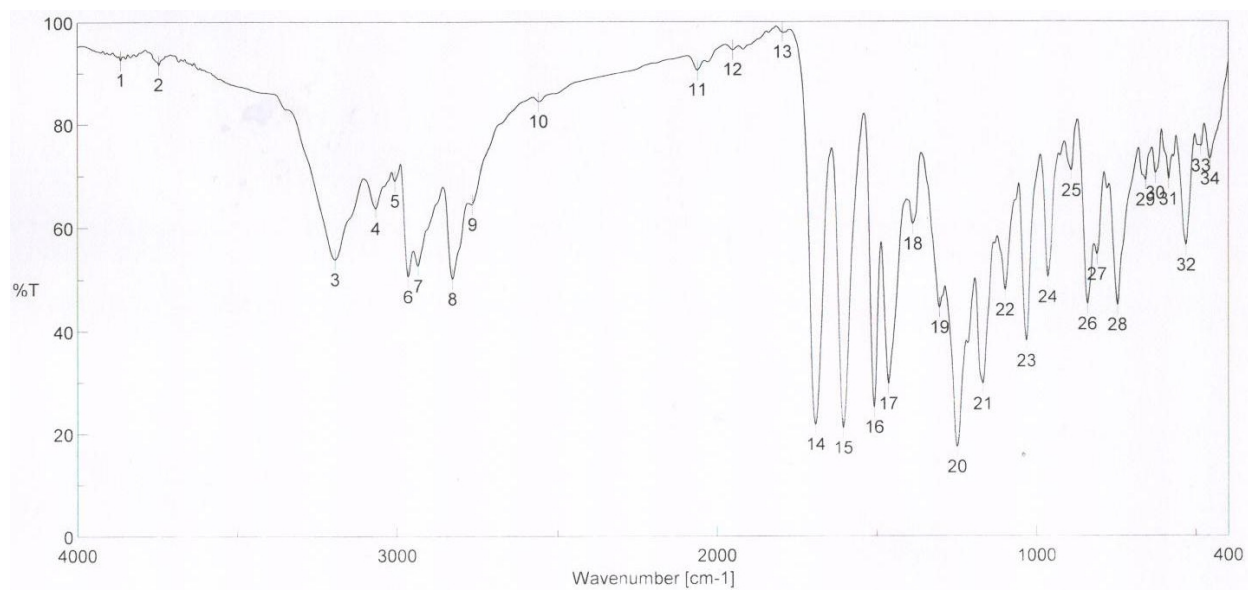


Figure 17. IR spectrum of compound **39**.

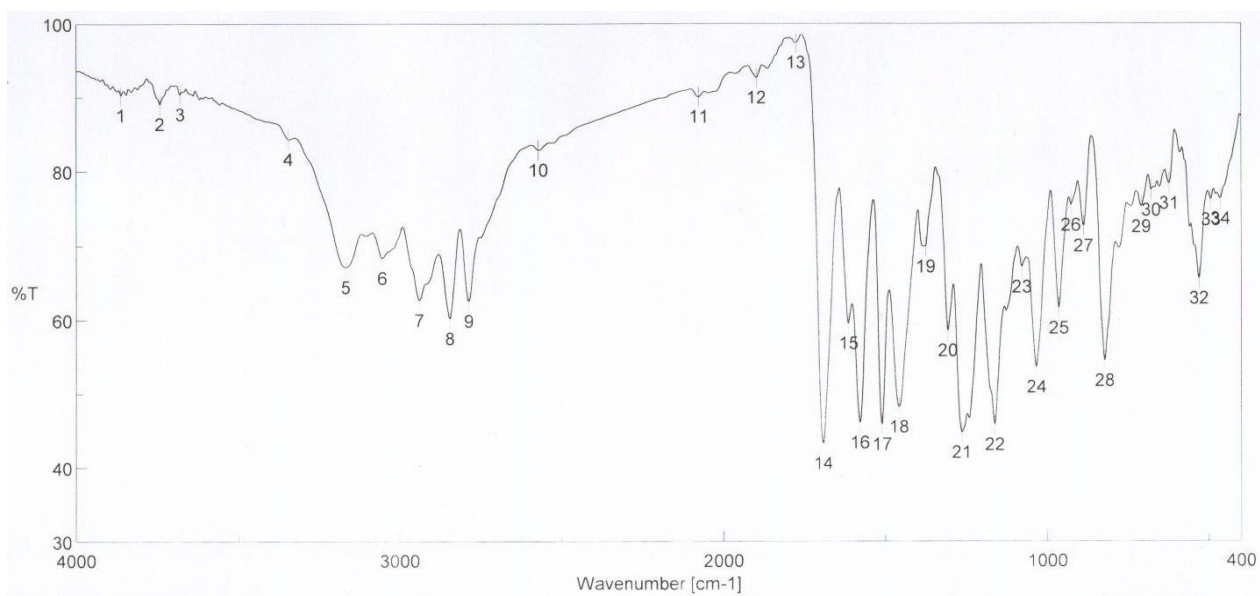


Figure 18. IR spectrum of compound **40**.

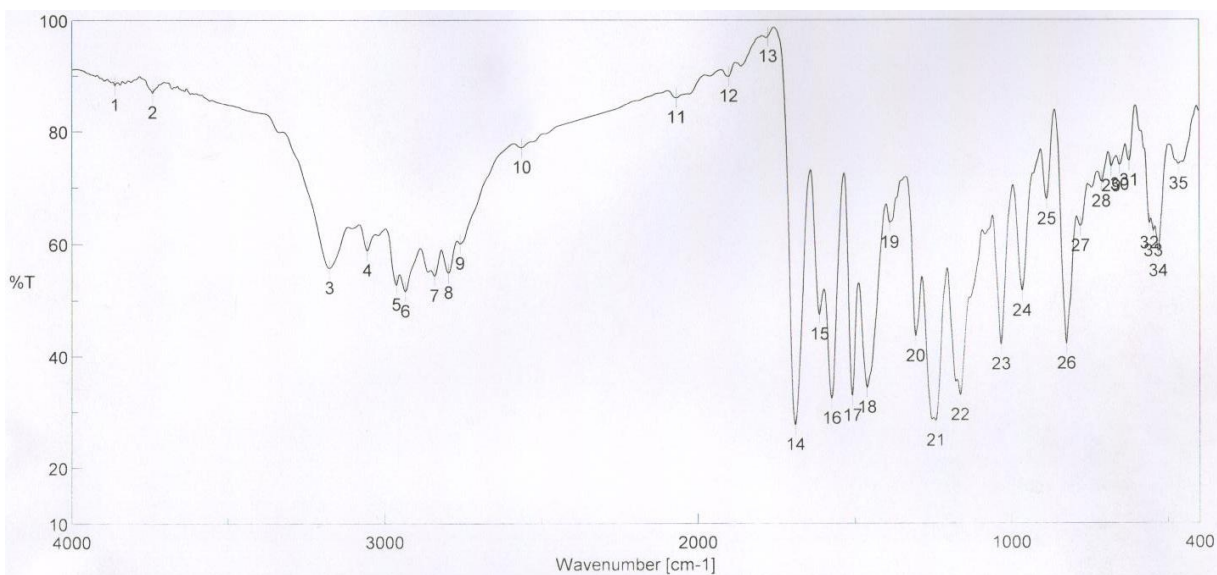


Figure 19. IR spectrum of compound **41**.

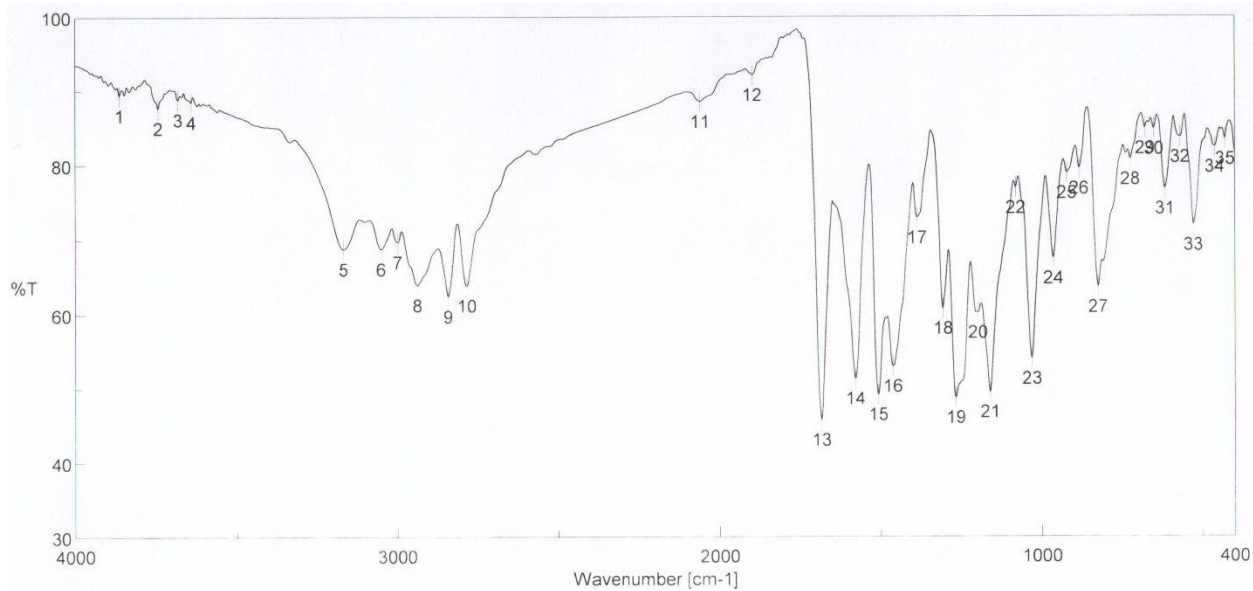


Figure 20. IR spectrum of compound **42**.

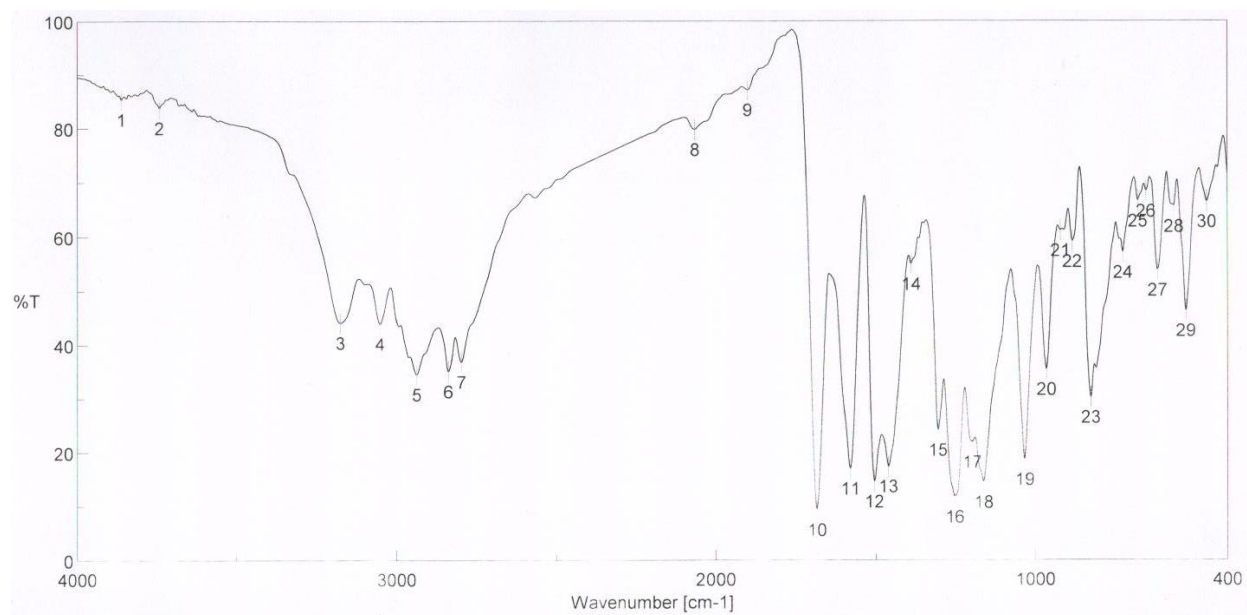


Figure 21. IR spectrum of compound 43.

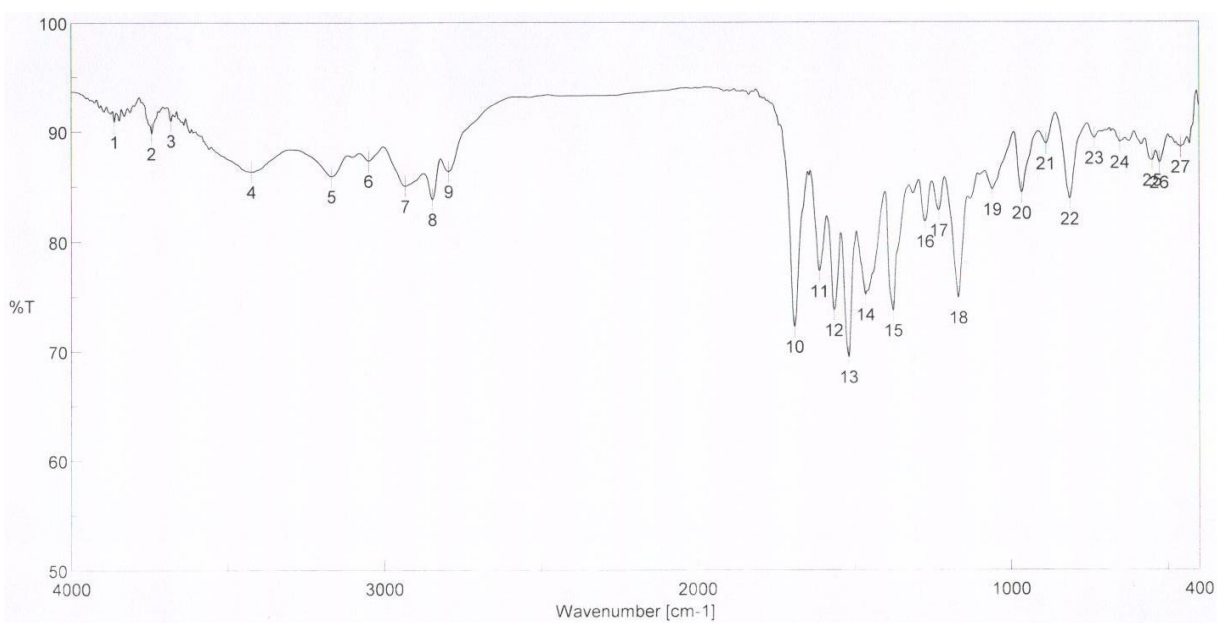


Figure 22. IR spectrum of compound 44.

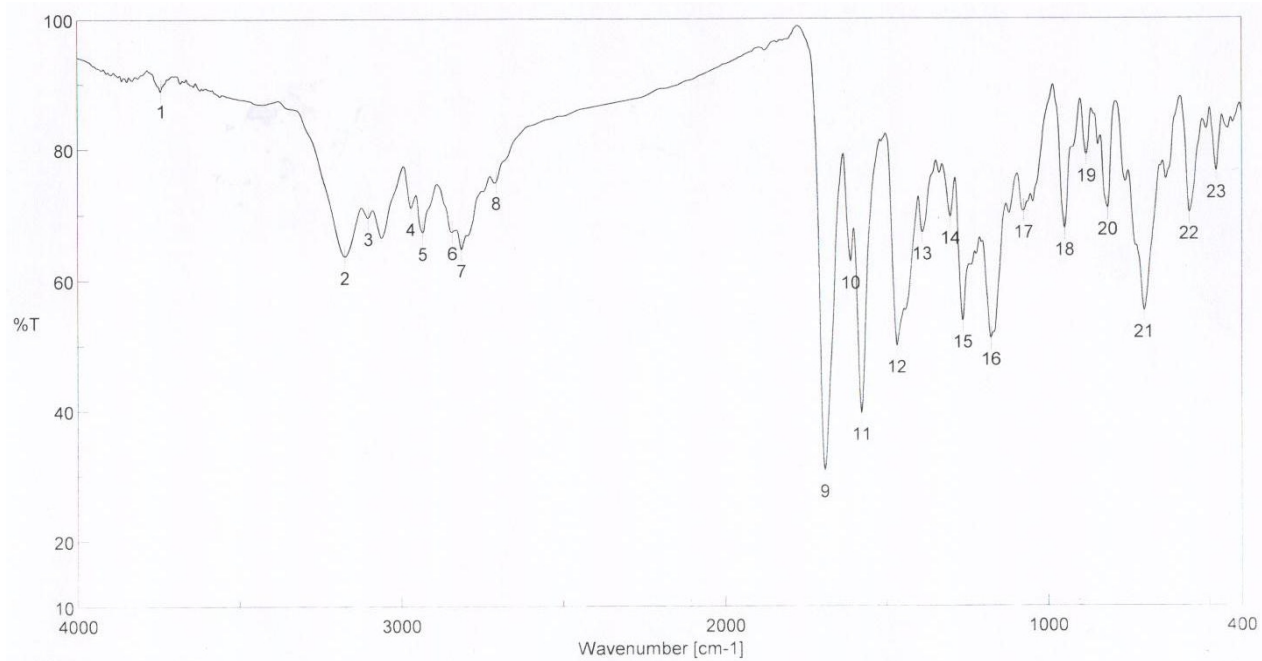


Figure 23. IR spectrum of compound 46.

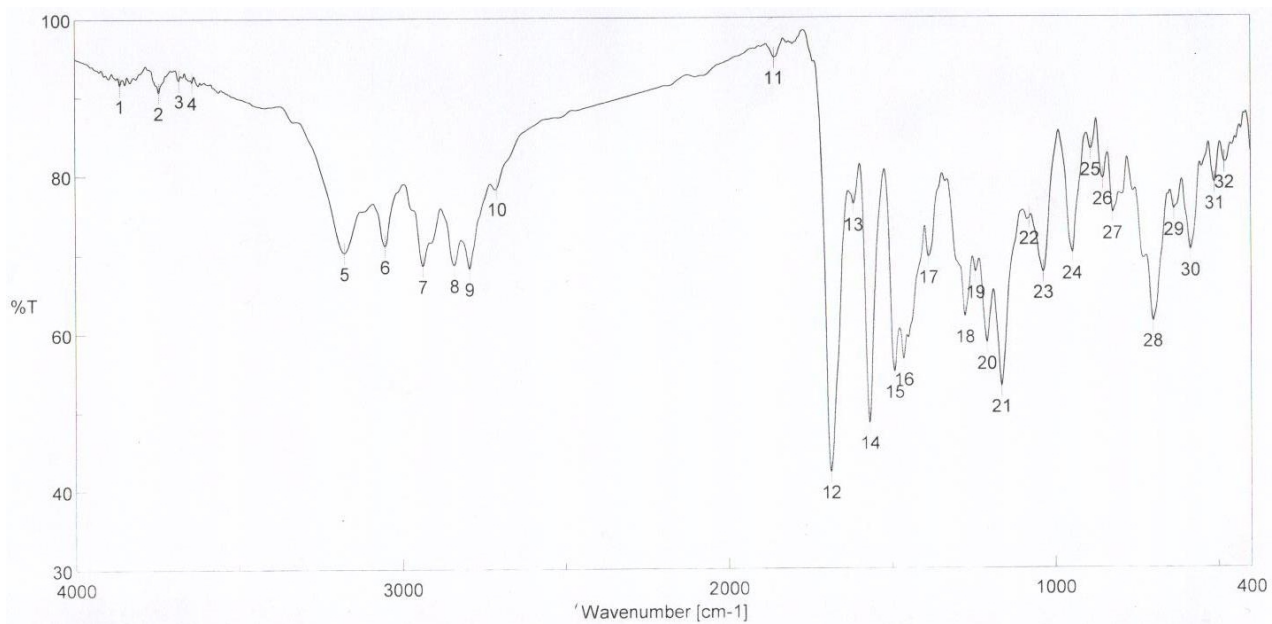


Figure 24. IR spectrum of compound 47.

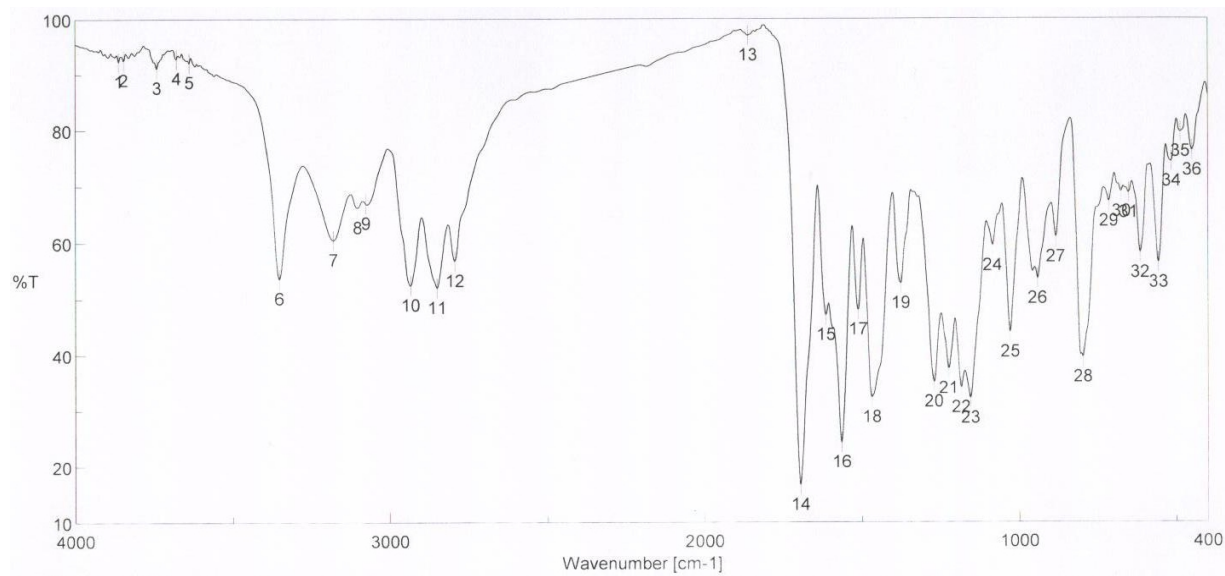


Figure 25. IR spectrum of compound **48**.

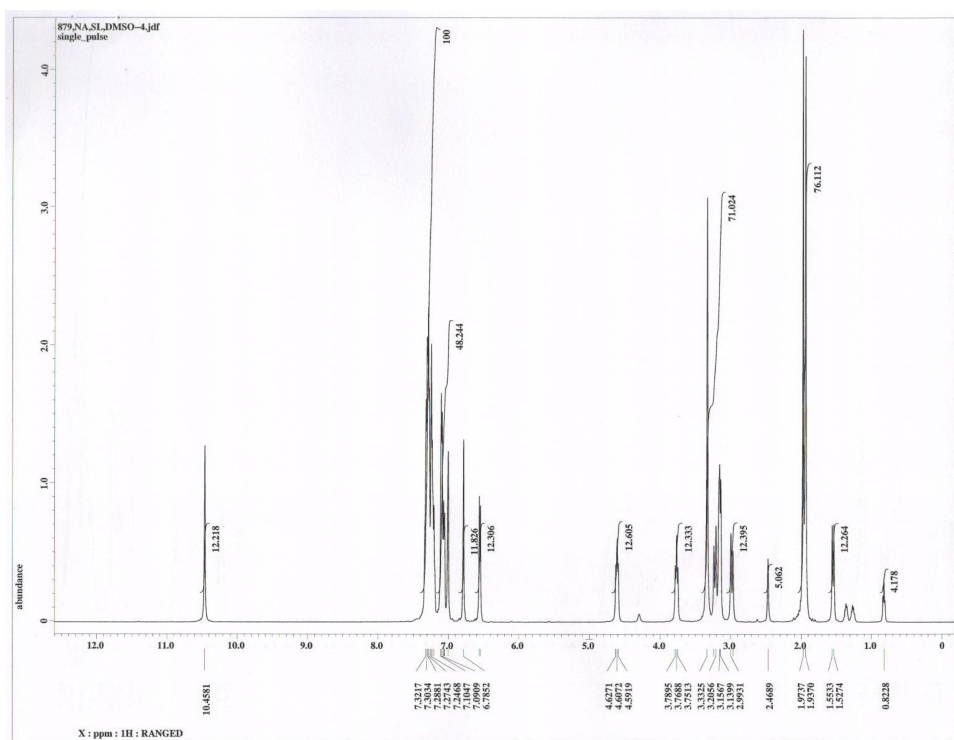


Figure 26. ^1H -NMR spectrum of compound **25**.

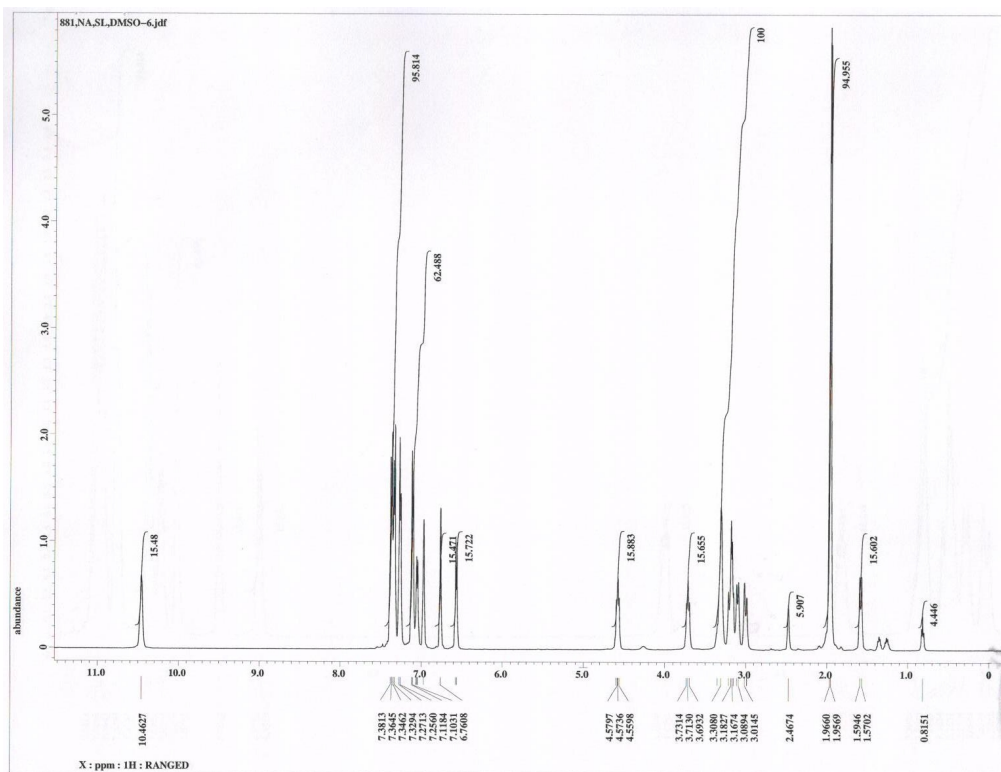


Figure 27. ^1H -NMR spectrum of compound 27.

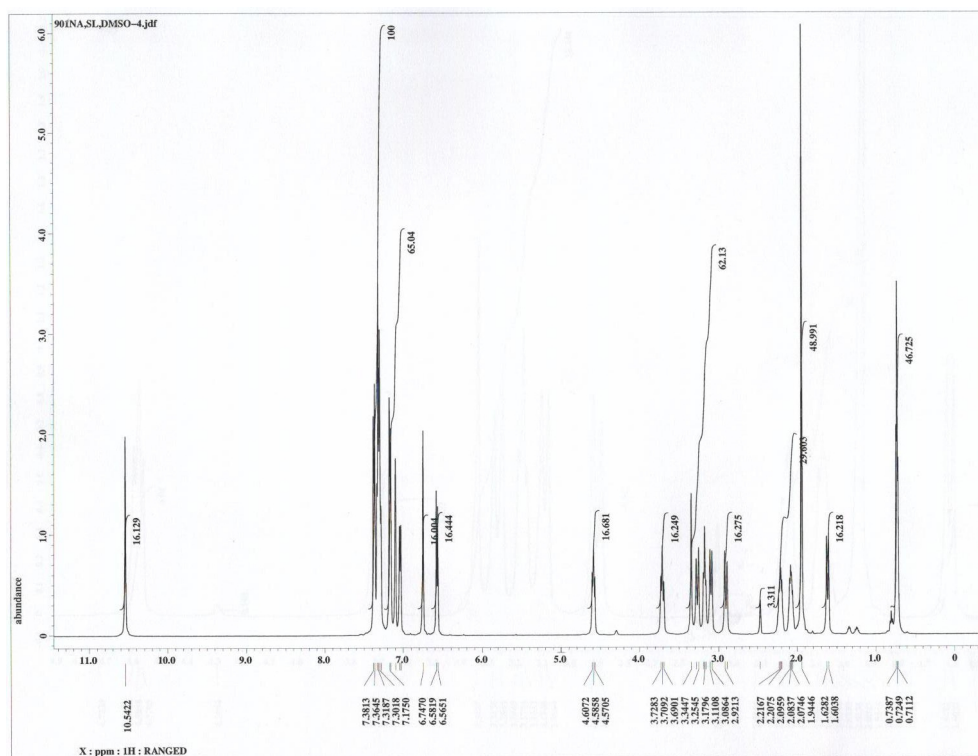
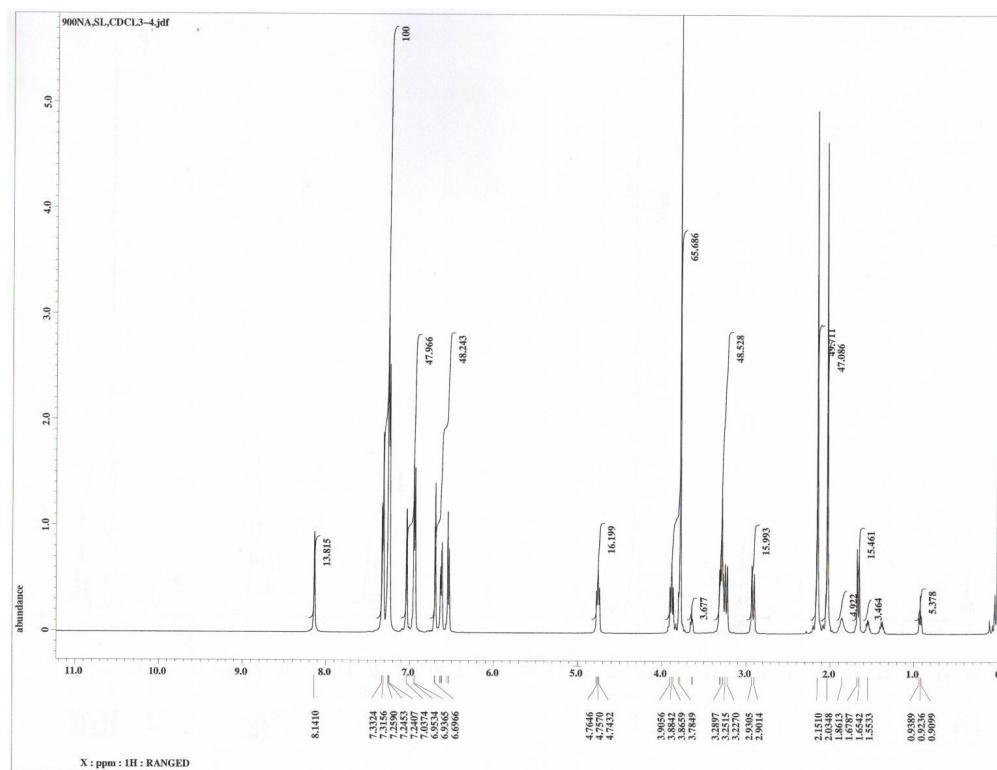


Figure 28. ^1H -NMR spectrum of compound 28.



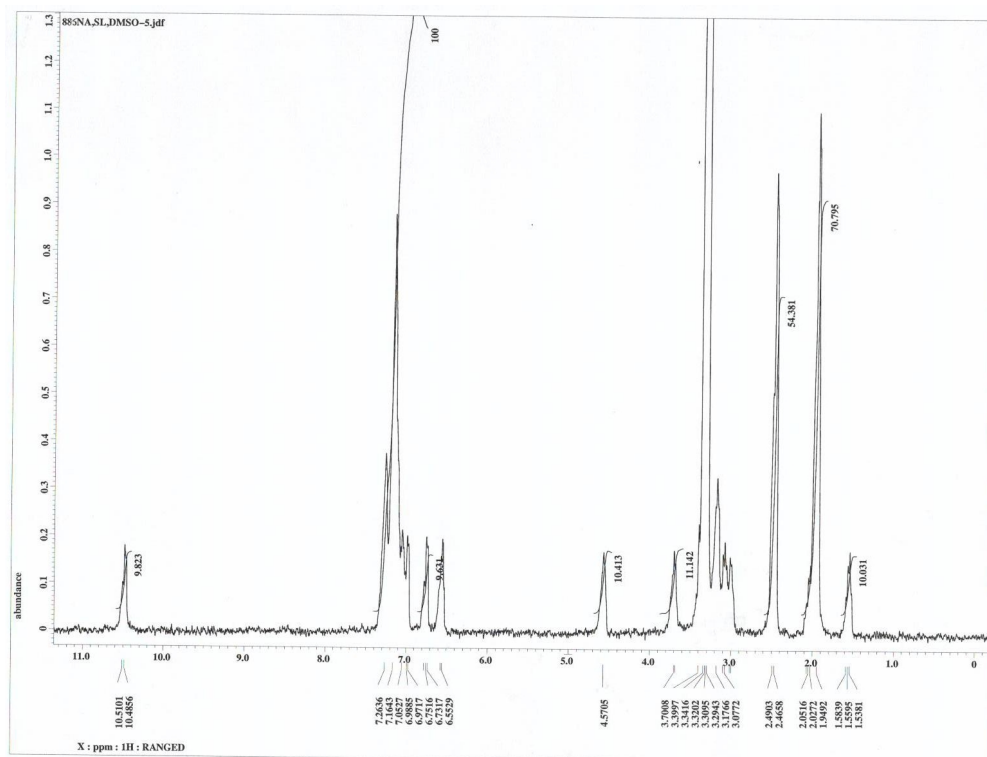


Figure 31. ^1H -NMR spectrum of compound **32**.

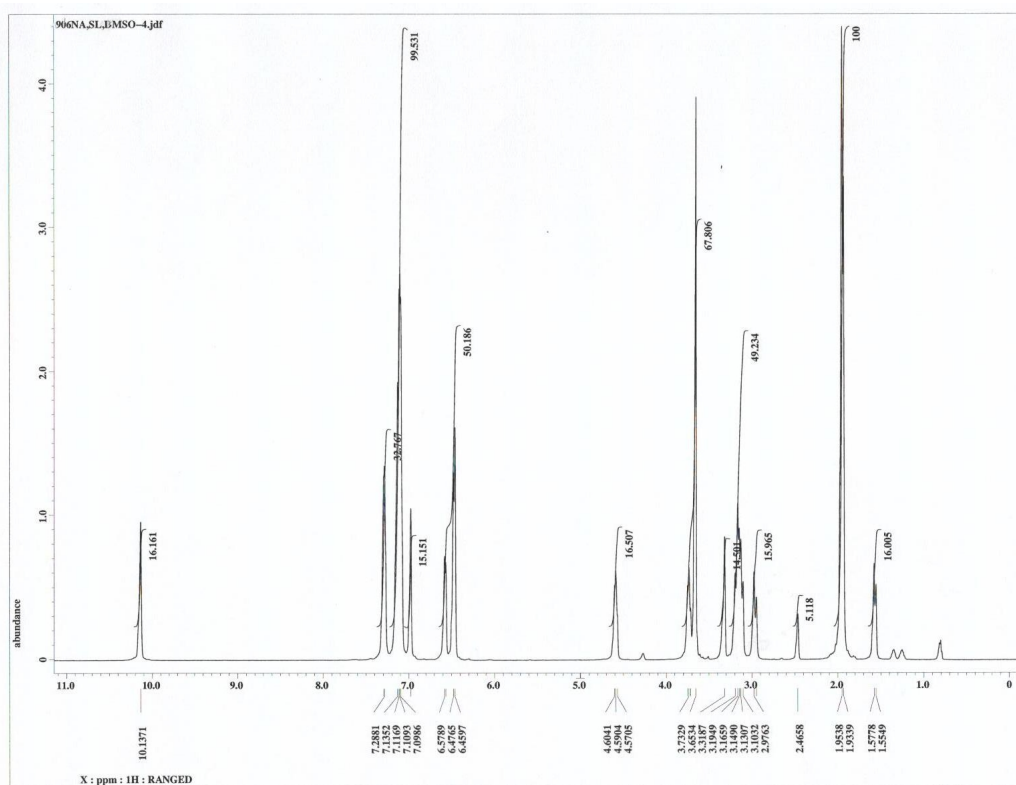


Figure 32. ^1H -NMR spectrum of compound **33**.

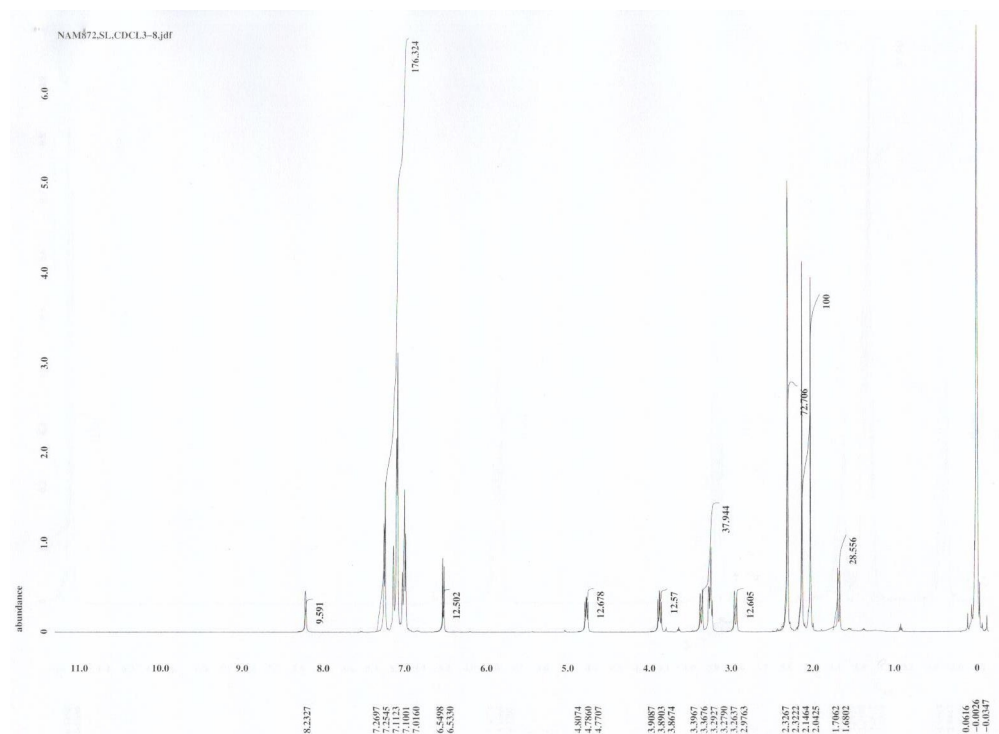


Figure 33. ^1H -NMR spectrum of compound 35.

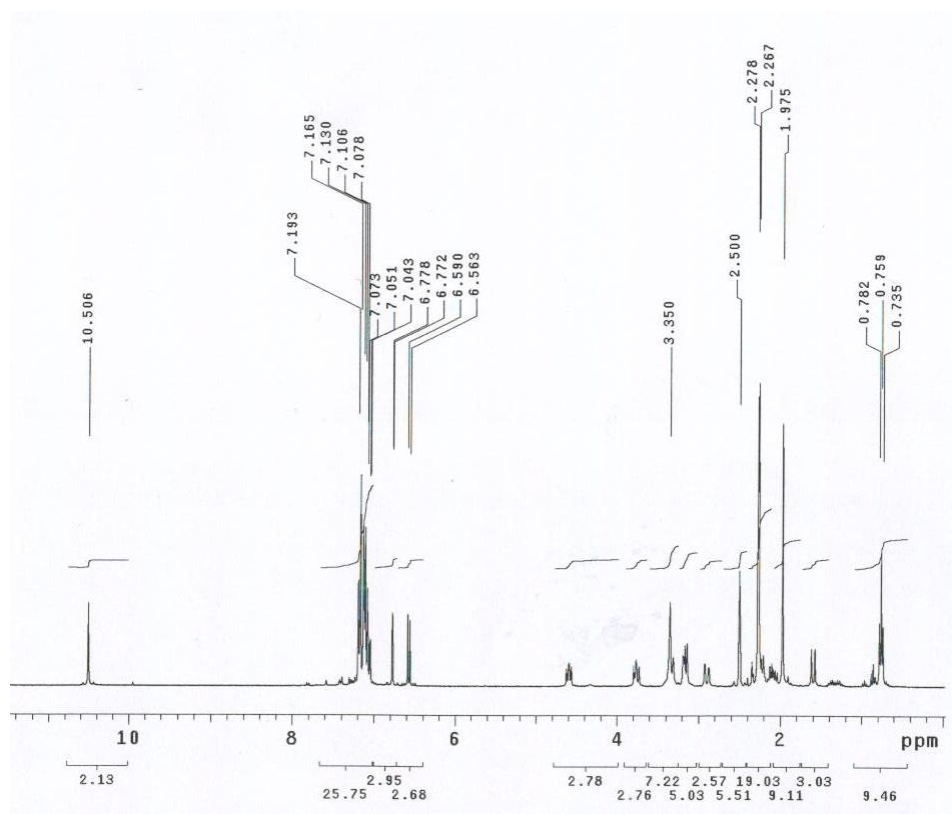


Figure 34. ^1H -NMR spectrum of compound 36.

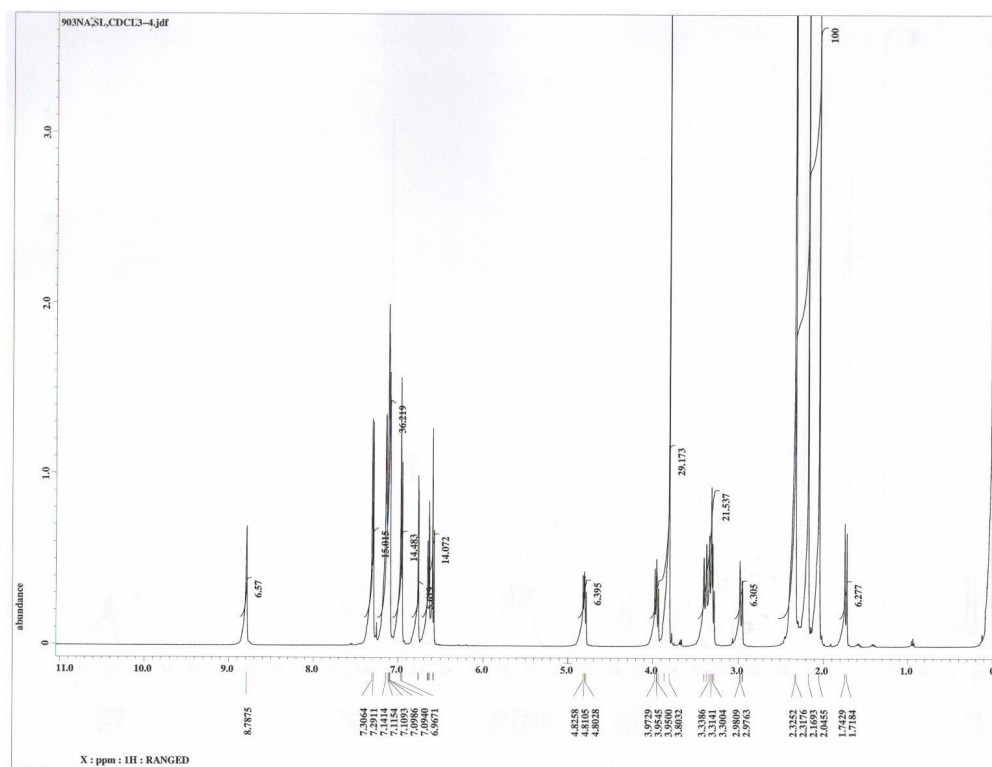


Figure 35. ^1H -NMR spectrum of compound **37**.

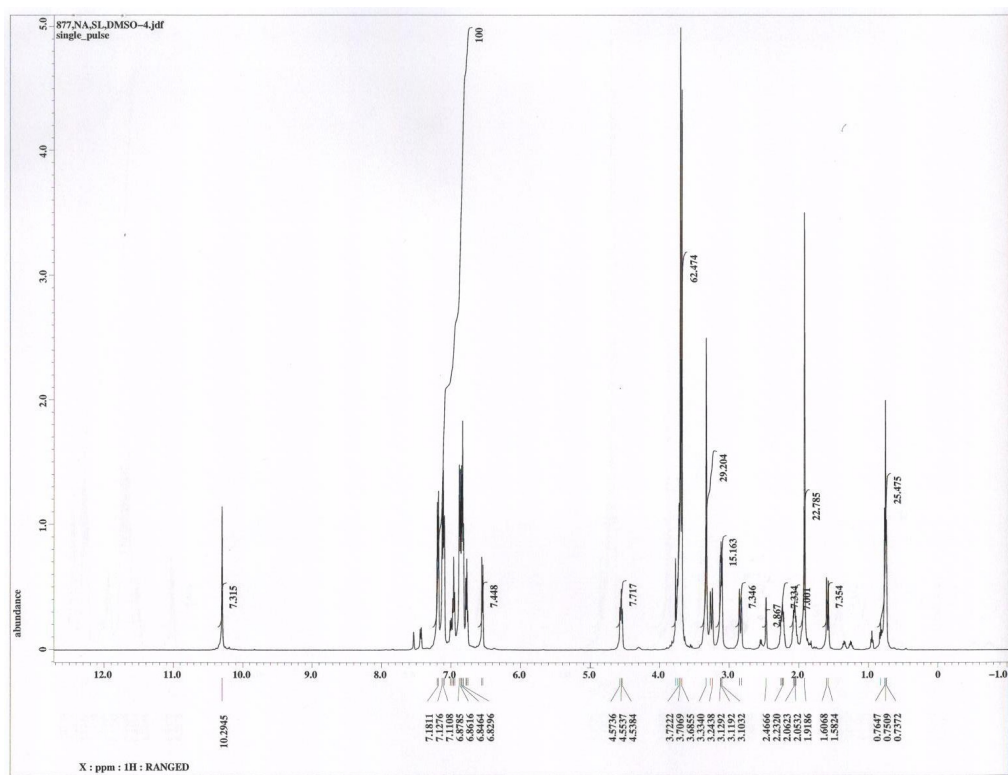


Figure 36. ^1H -NMR spectrum of compound **39**.

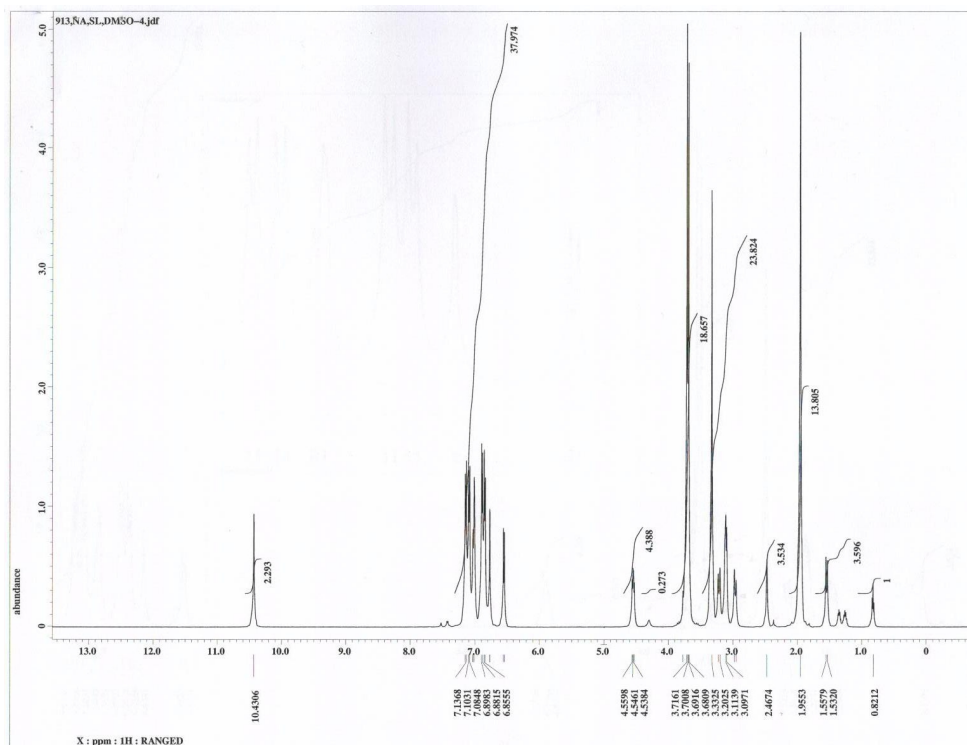


Figure 37. ^1H -NMR spectrum of compound 40.

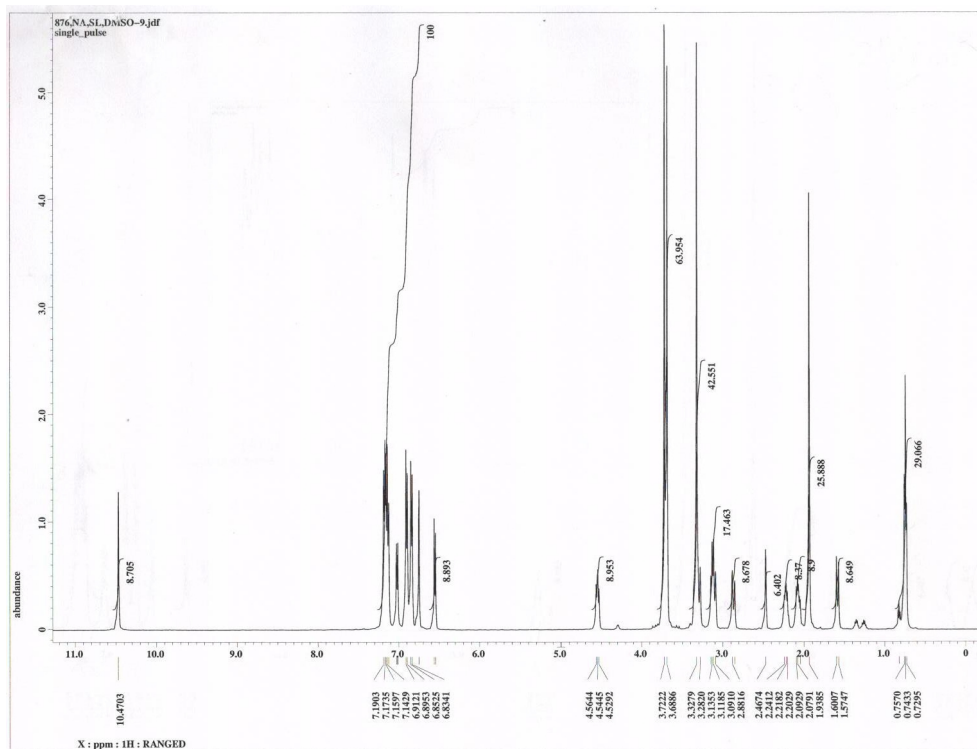


Figure 38. ^1H -NMR spectrum of compound 41.

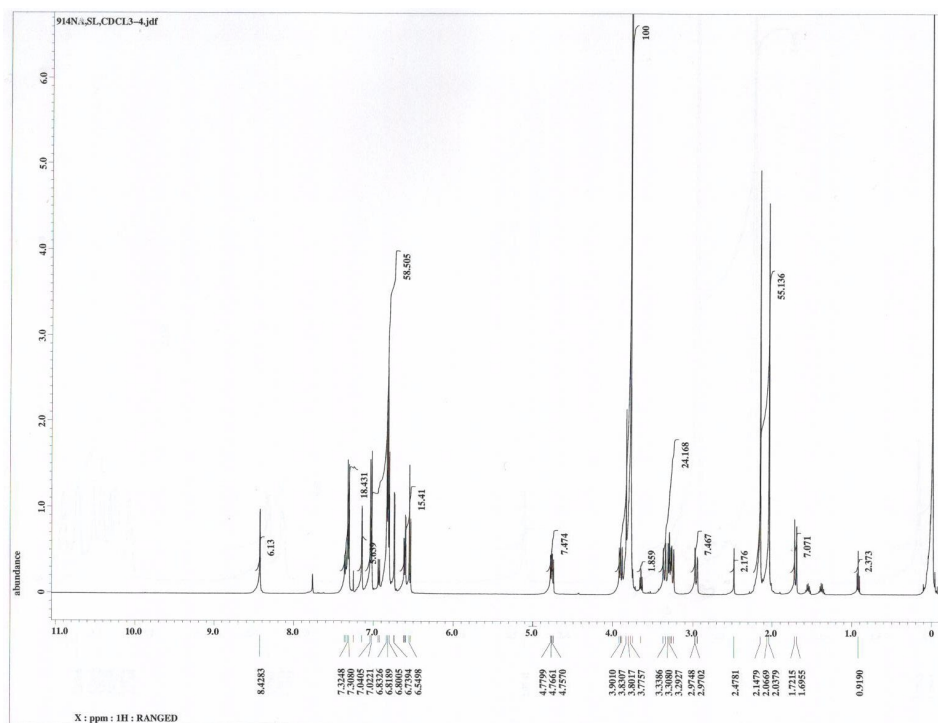


Figure 39. ^1H -NMR spectrum of compound 42.

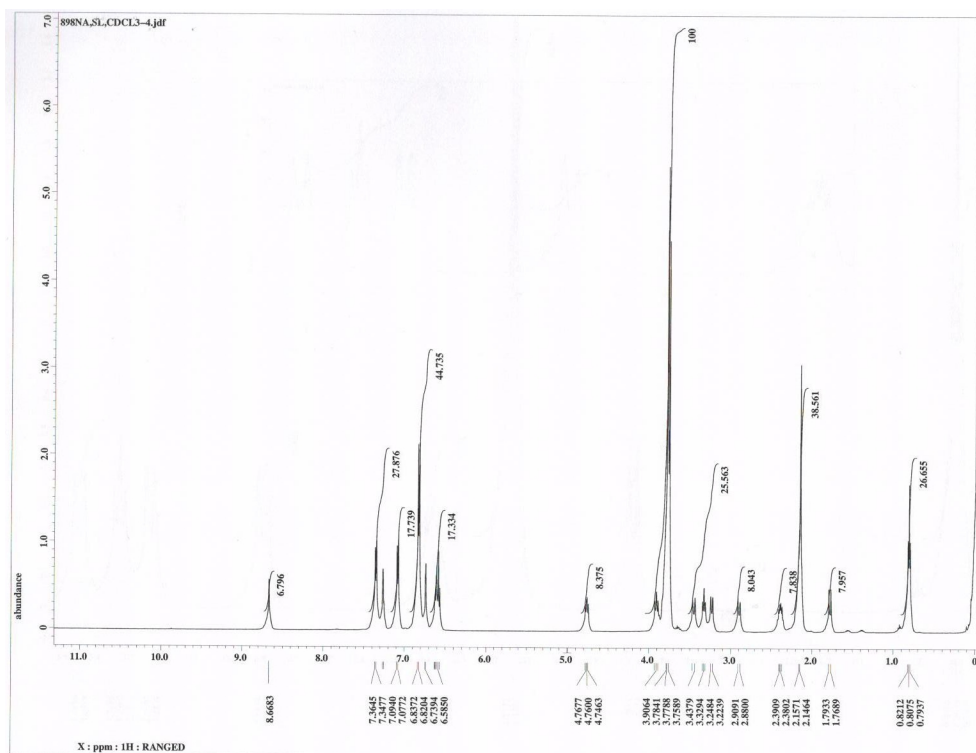


Figure 40. ^1H -NMR spectrum of compound 43.

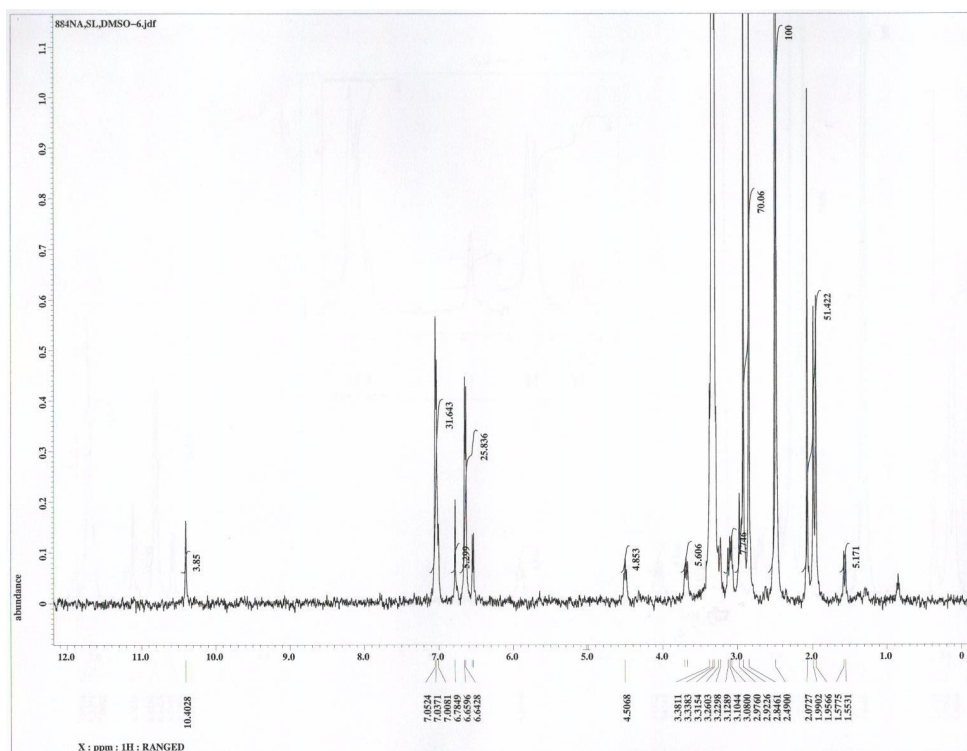


Figure 41. ^1H -NMR spectrum of compound 44.

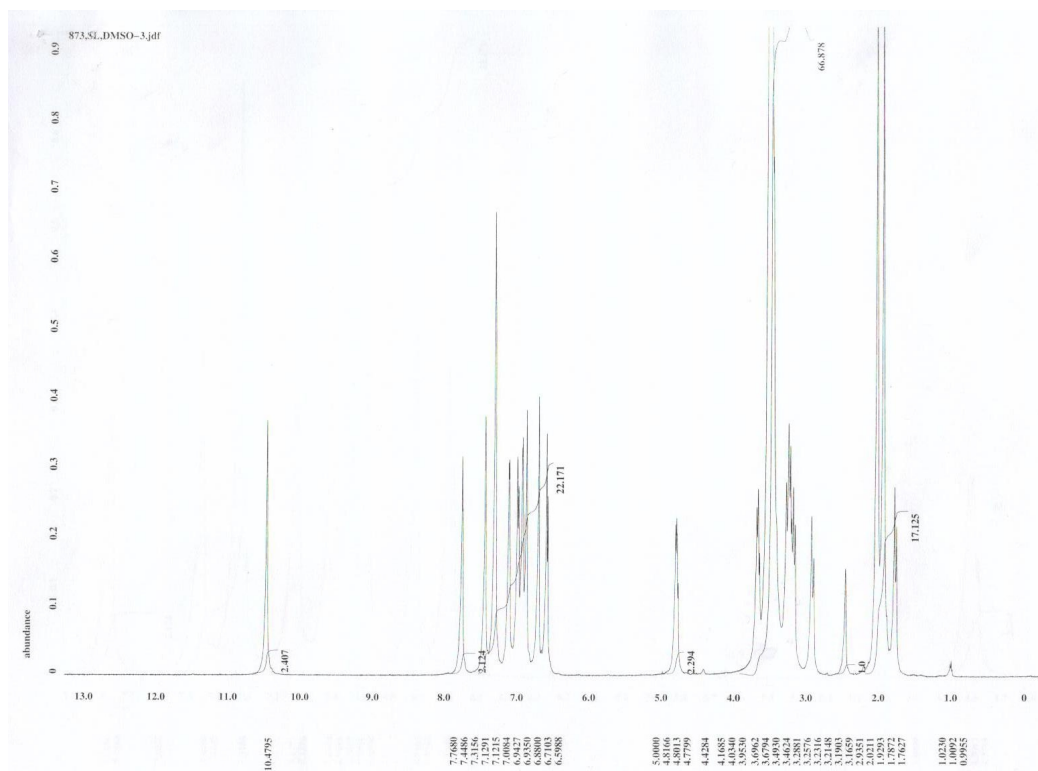


Figure 42. ^1H -NMR spectrum of compound 46.

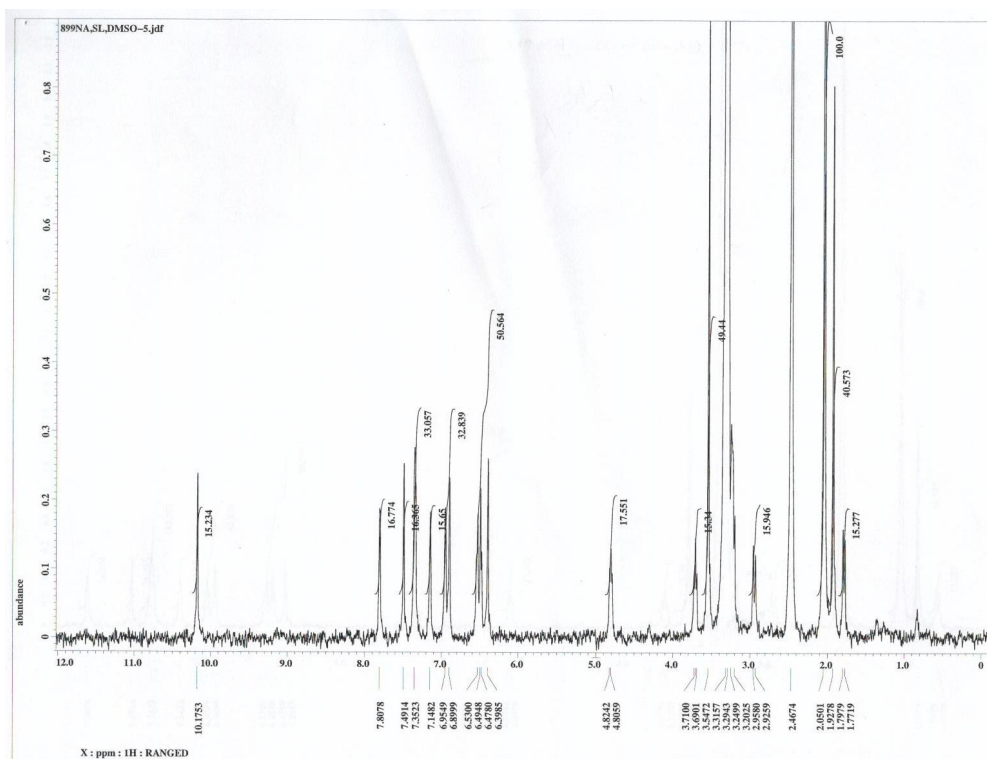


Figure 43. ^1H -NMR spectrum of compound **47**.

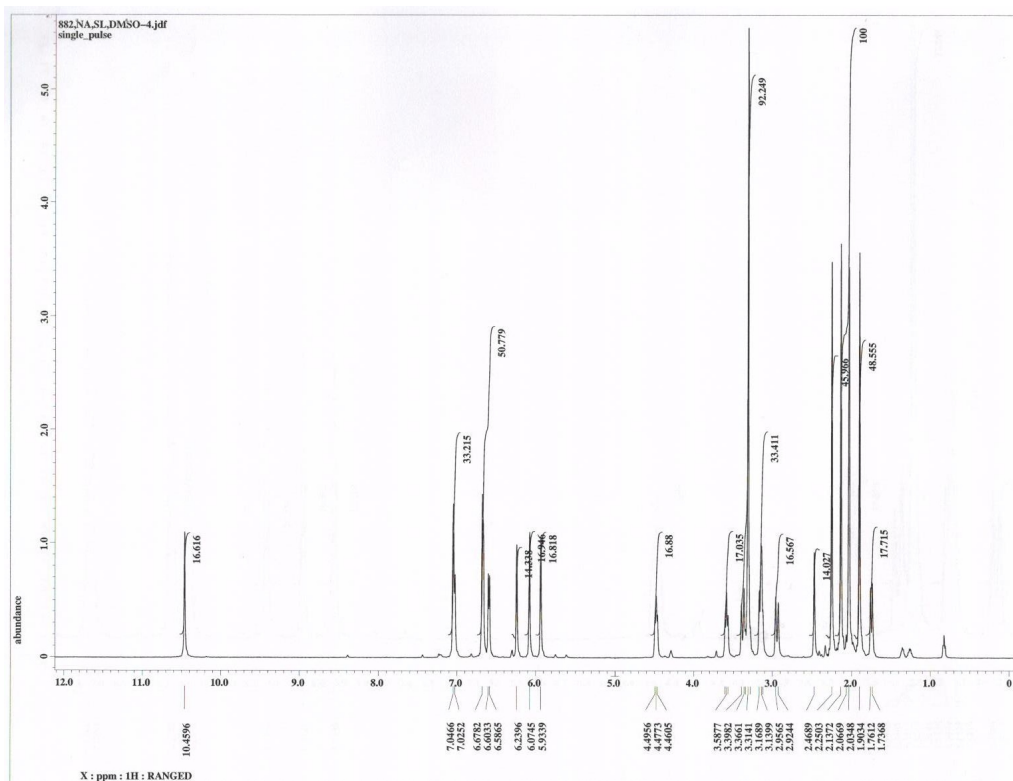


Figure 44. ^1H -NMR spectrum of compound **48**.

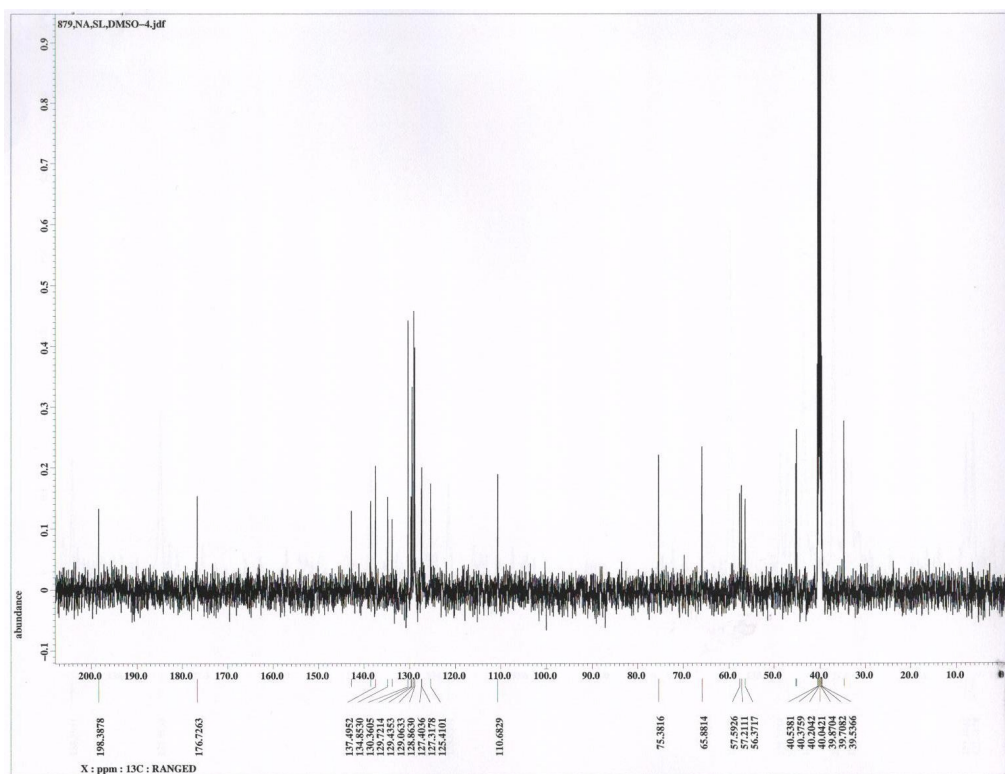


Figure 45. ^{13}C -NMR spectrum (on-resonance) of compound **25**.

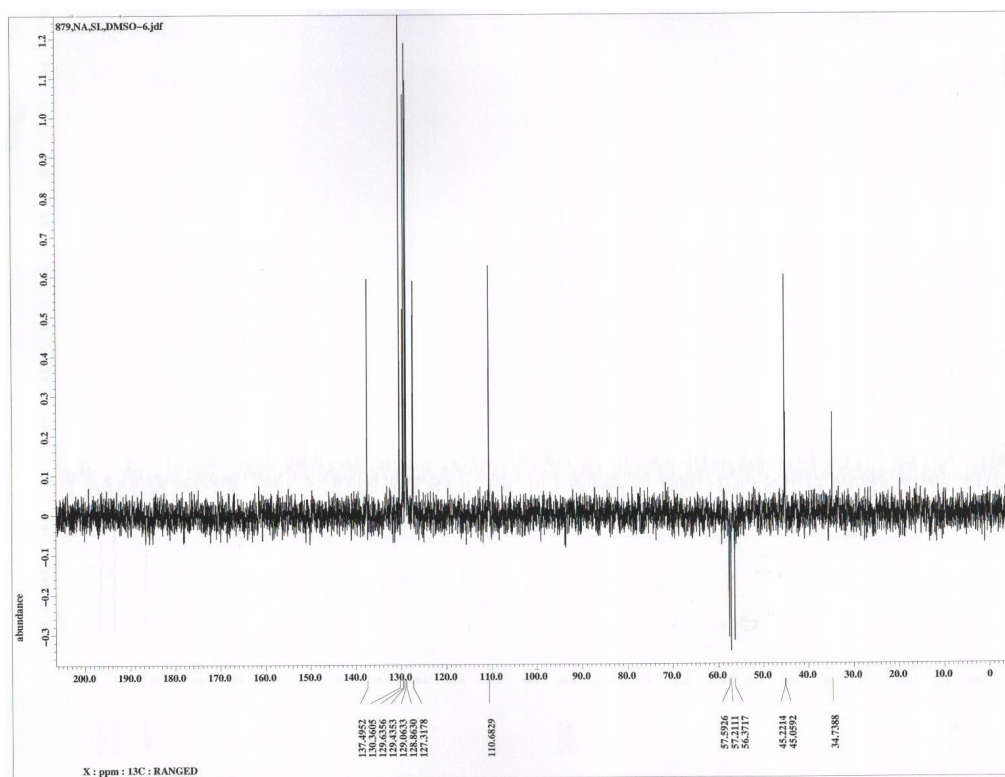


Figure 46. ^{13}C -NMR spectrum (DEPT) of compound **25**.

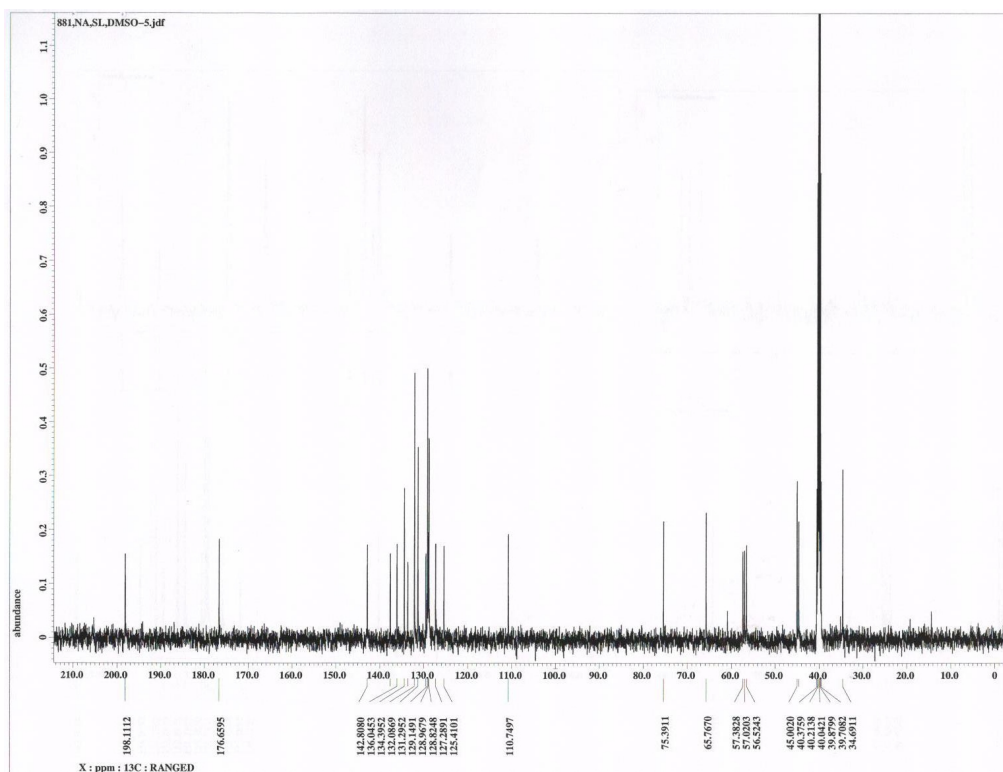


Figure 47. ^{13}C -NMR spectrum (on-resonance) of compound **27**.

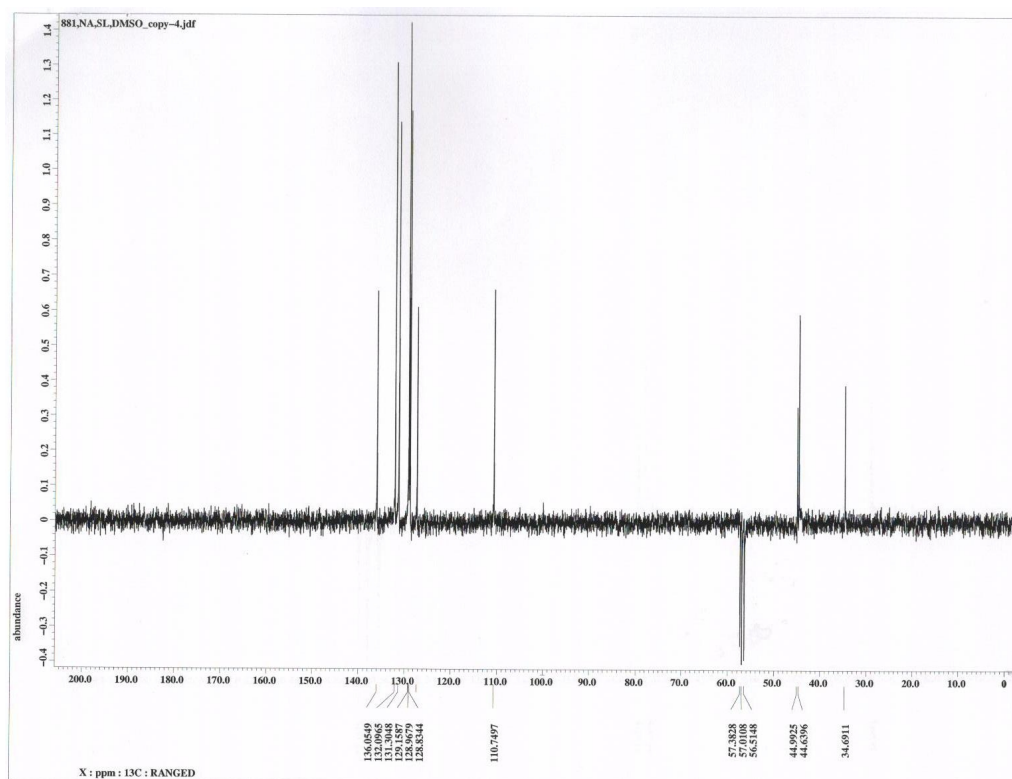


Figure 48. ^{13}C -NMR spectrum (DEPT) of compound **27**.

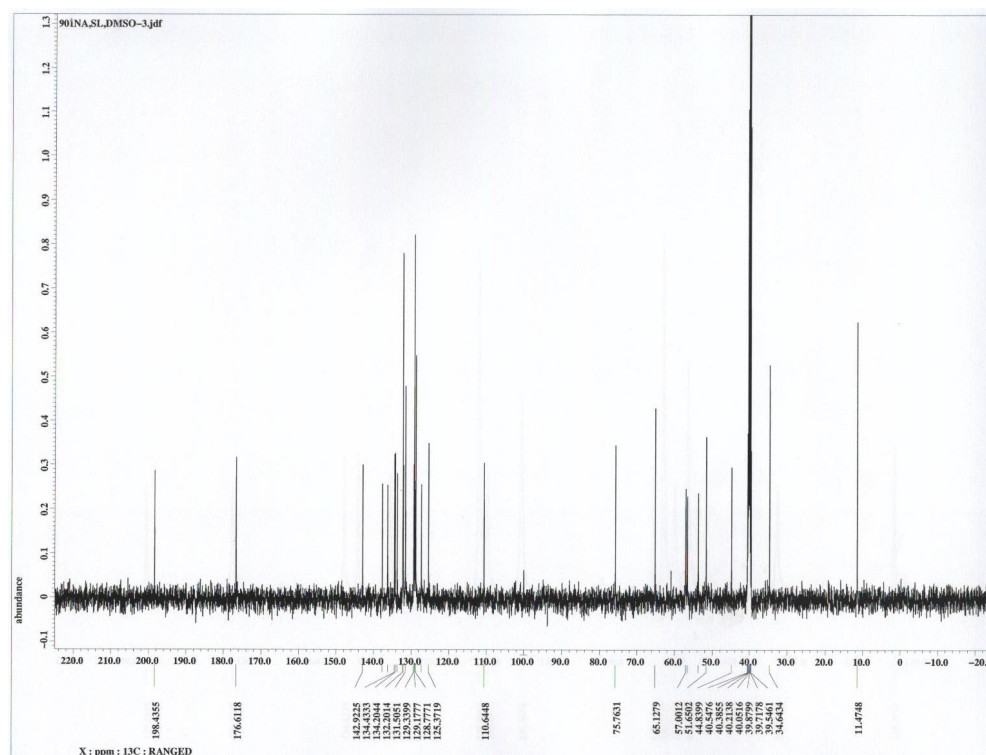


Figure 49. ^{13}C -NMR spectrum (on-resonance) of compound **28**.

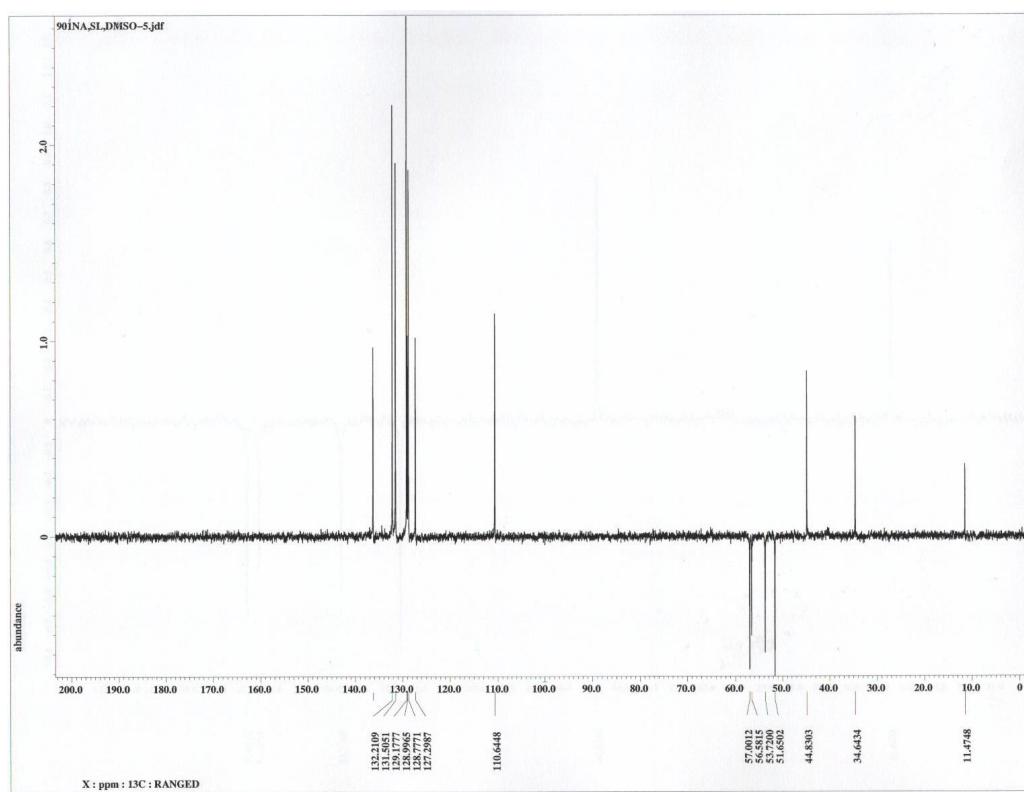


Figure 50. ^{13}C -NMR spectrum (DEPT) of compound **28**.

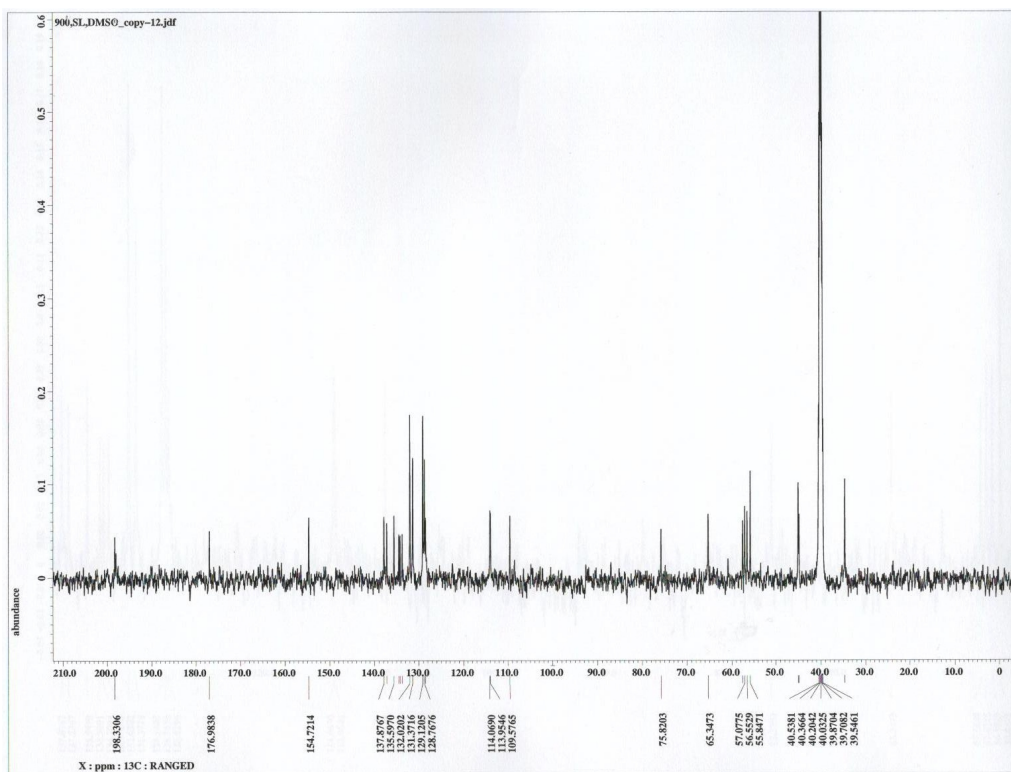


Figure 51. ^{13}C -NMR spectrum (on-resonance) of compound **29**.

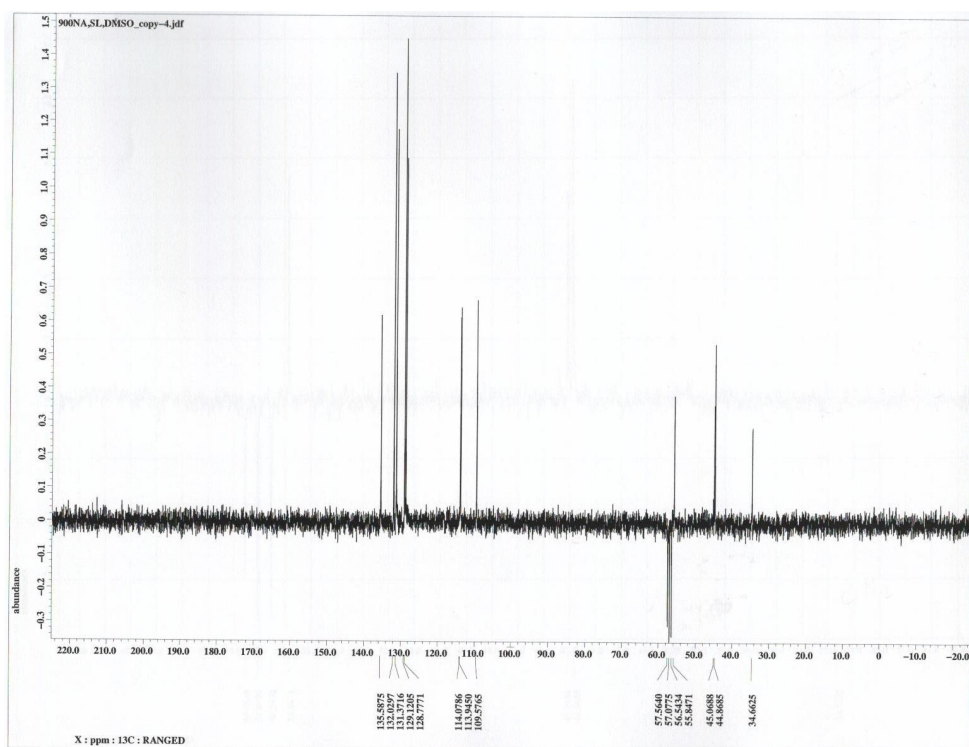


Figure 52. ^{13}C -NMR spectrum (DEPT) of compound **29**.

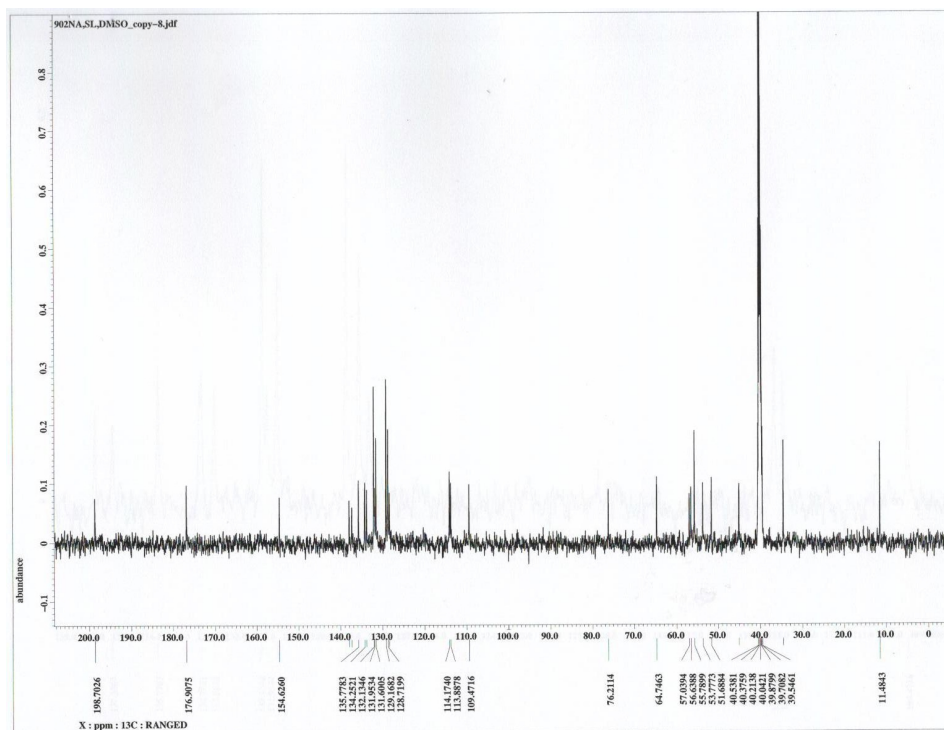


Figure 53. ^{13}C -NMR spectrum (on-resonance) of compound **30**.

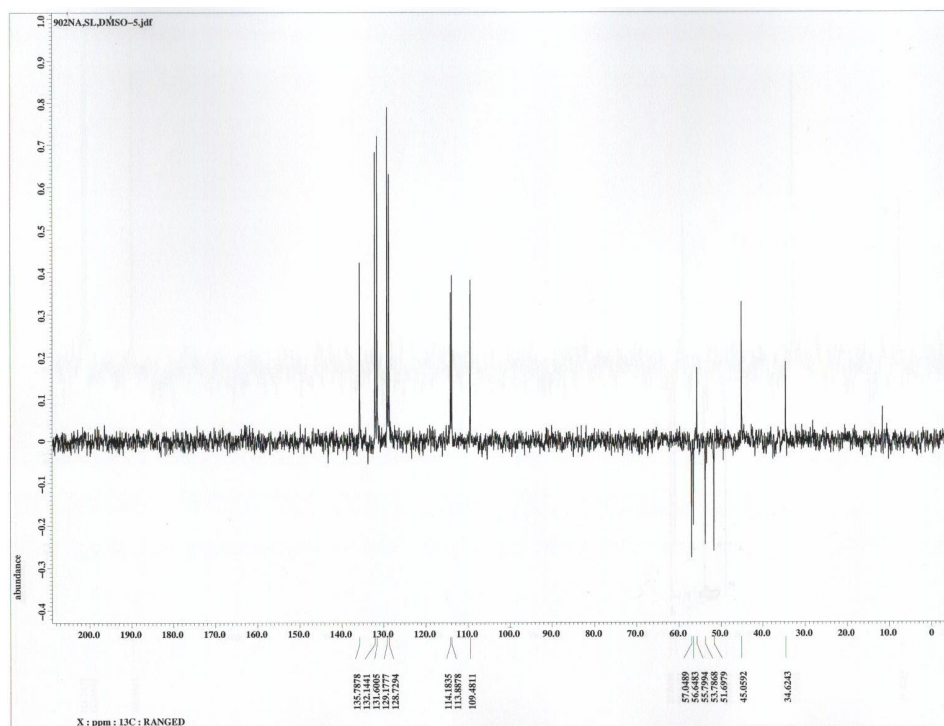


Figure 54. ^{13}C -NMR spectrum (DEPT) of compound **30**.

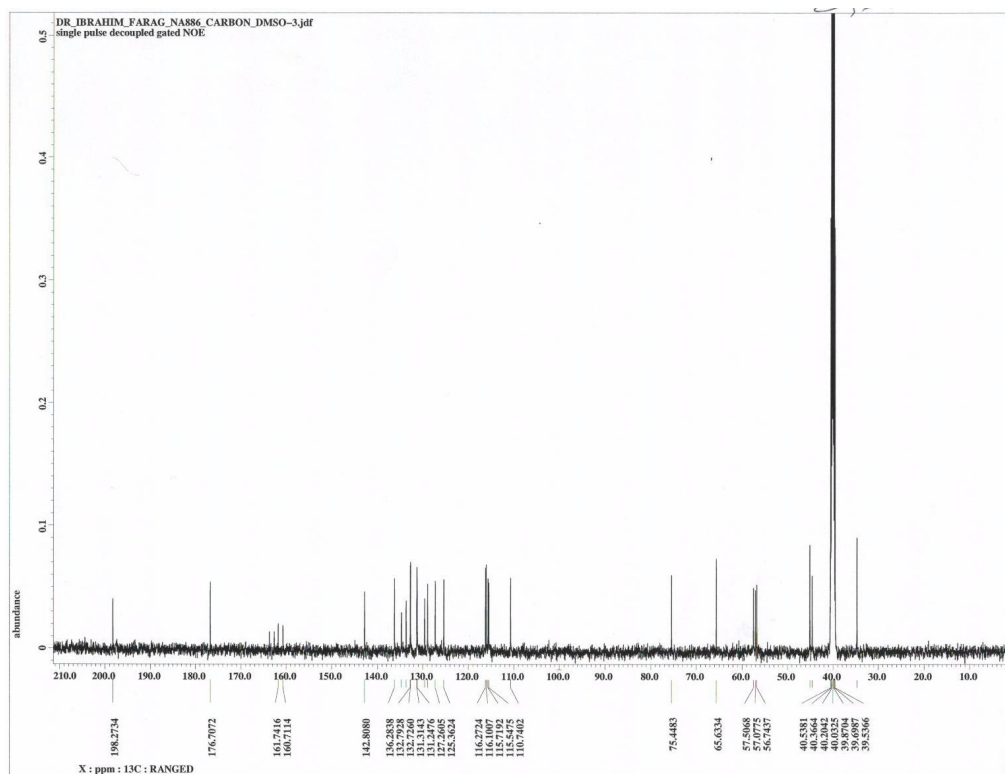


Figure 55. ^{13}C -NMR spectrum (on-resonance) of compound **32**.

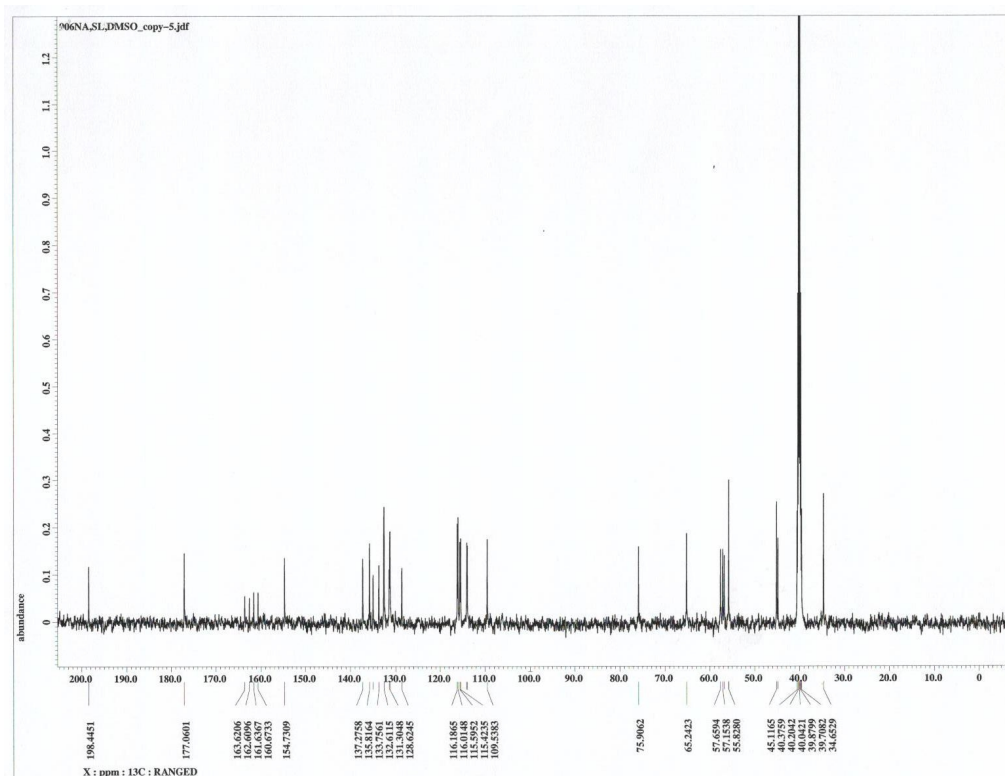


Figure 56. ^{13}C -NMR spectrum (on-resonance) of compound **33**.

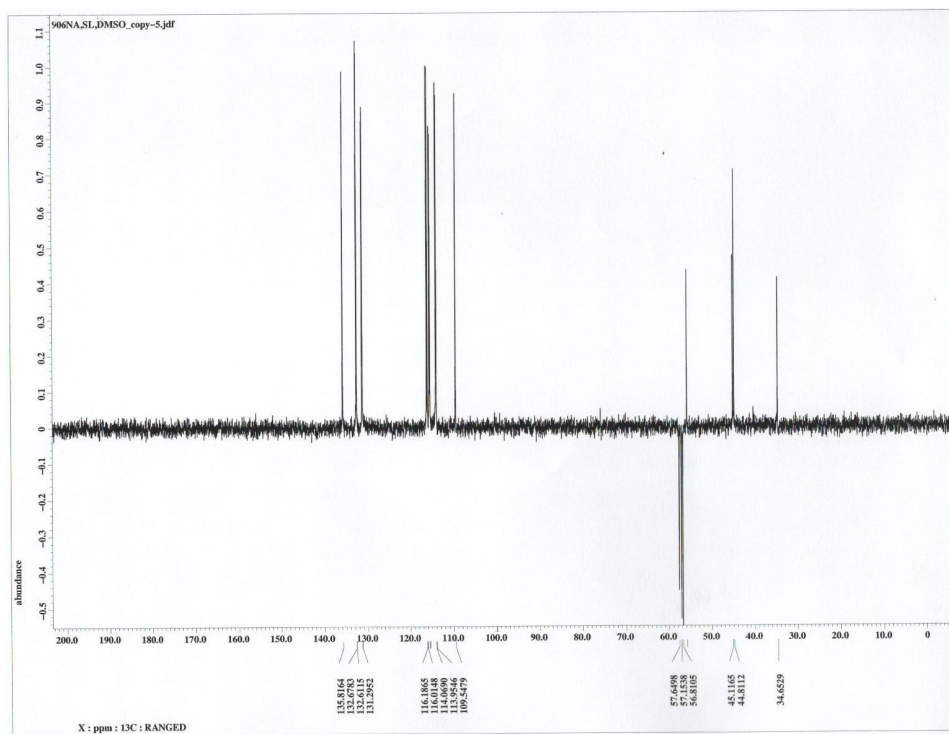


Figure 57. ^{13}C -NMR spectrum (DEPT) of compound **33**.

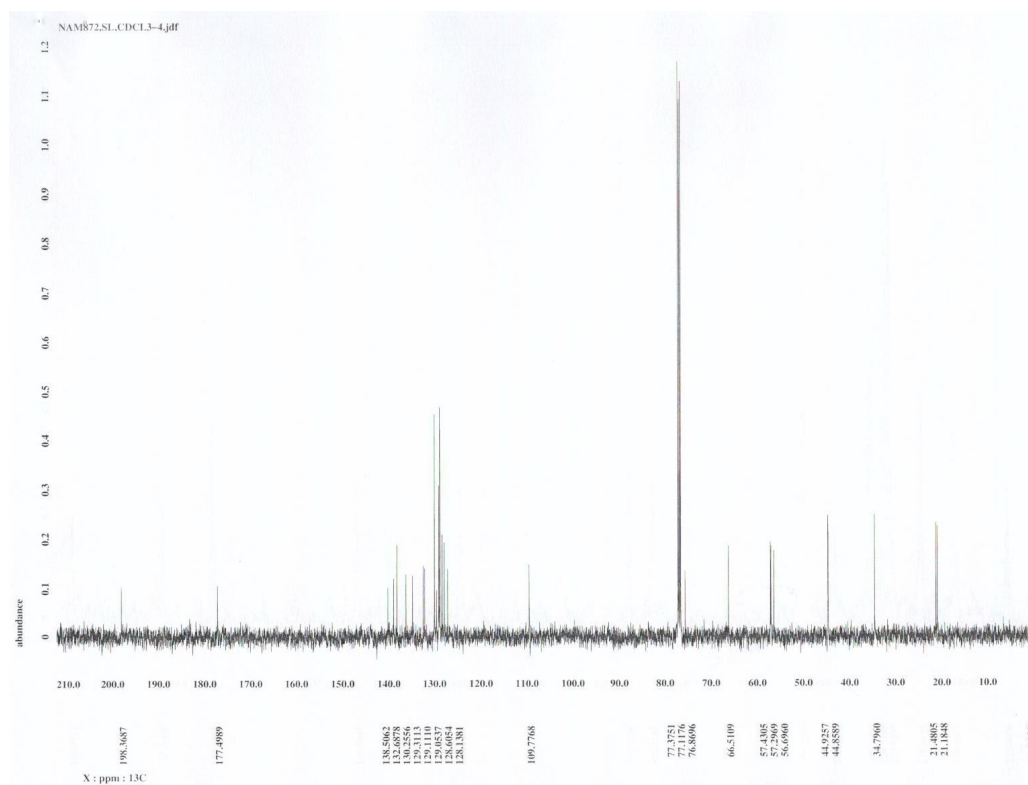


Figure 58. ^{13}C -NMR spectrum (on-resonance) of compound **35**.

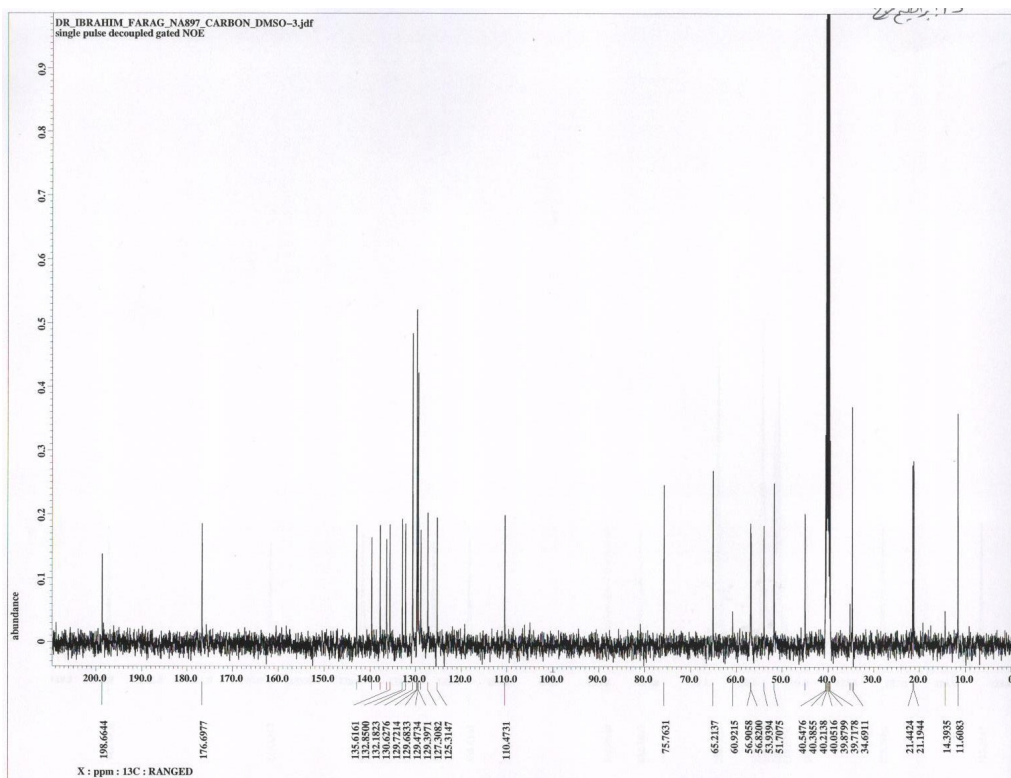


Figure 59. ^{13}C -NMR spectrum (on-resonance) of compound 36.

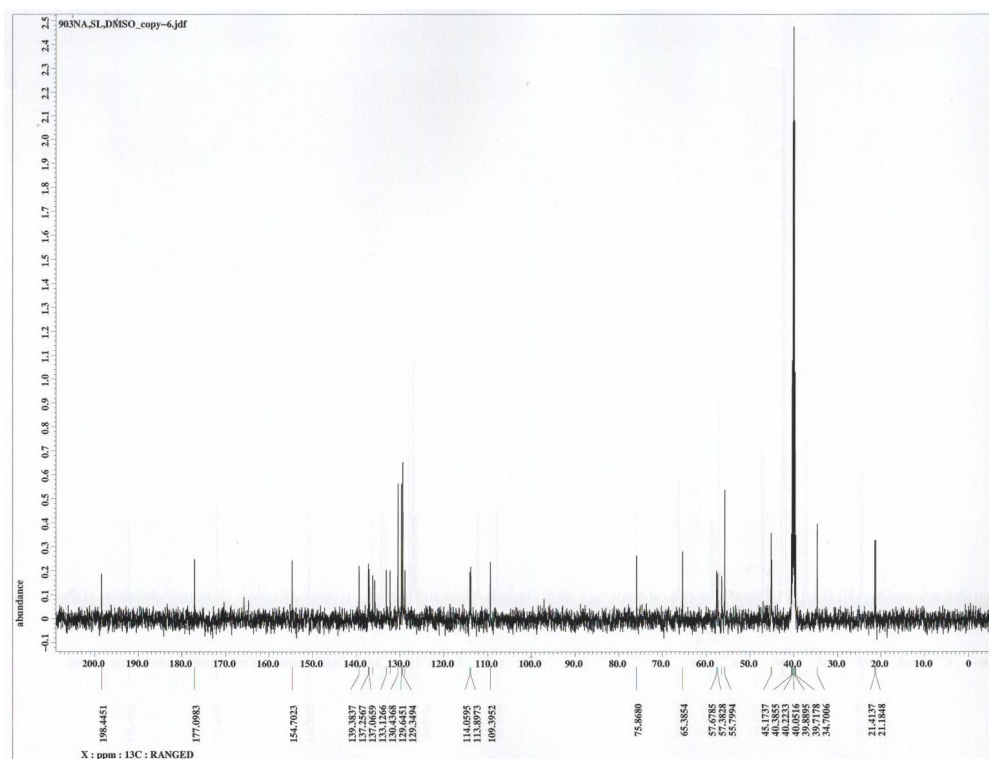


Figure 60. ^{13}C -NMR spectrum (on-resonance) of compound 37.

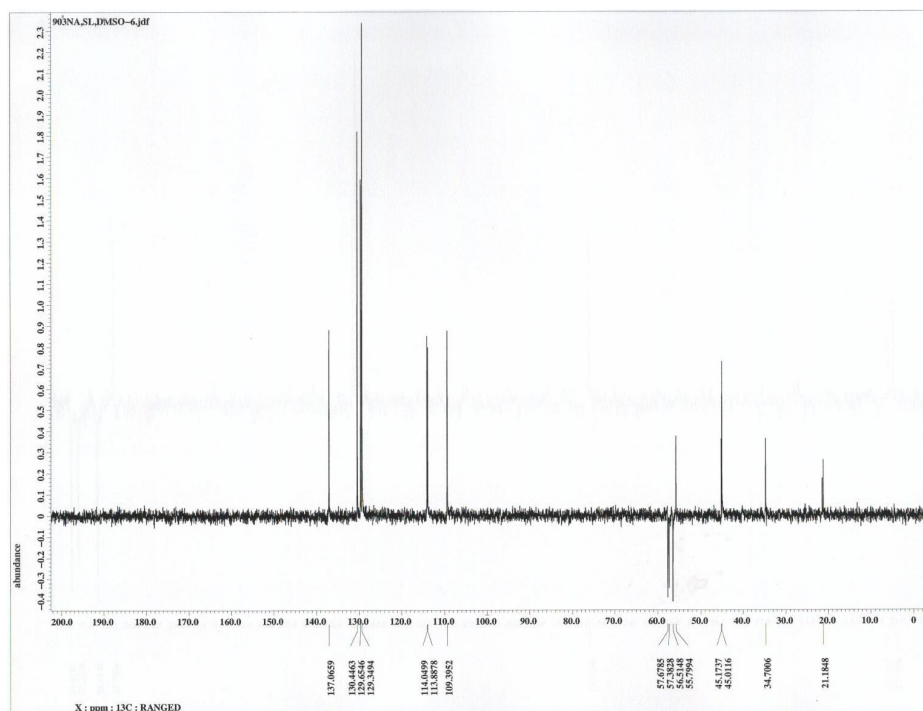


Figure 61. ^{13}C -NMR spectrum (DEPT) of compound **37**.

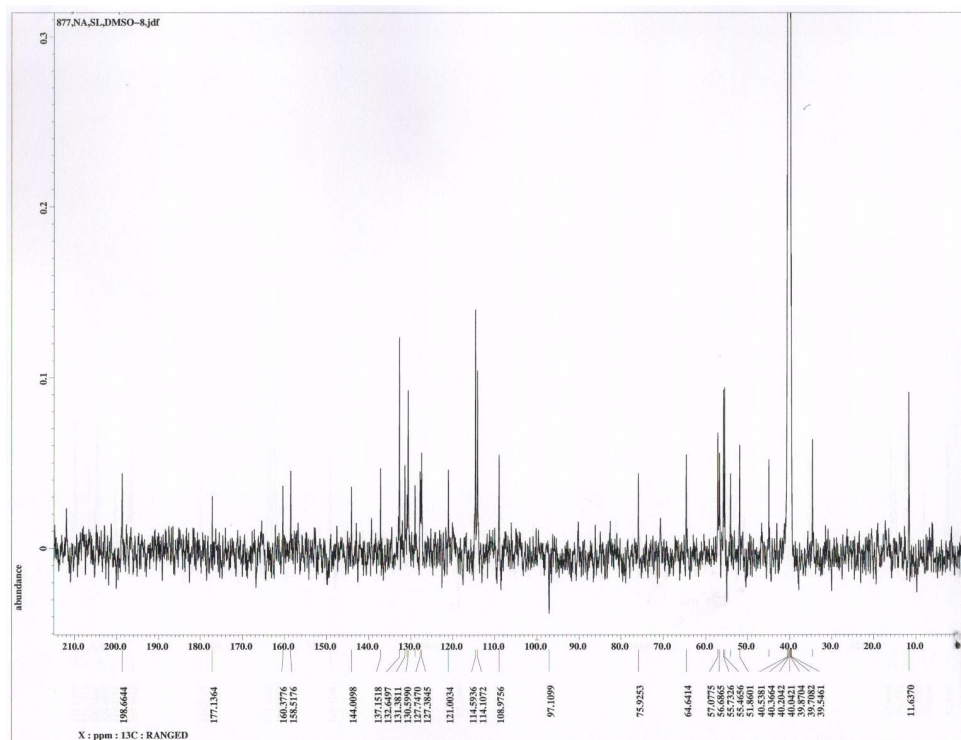
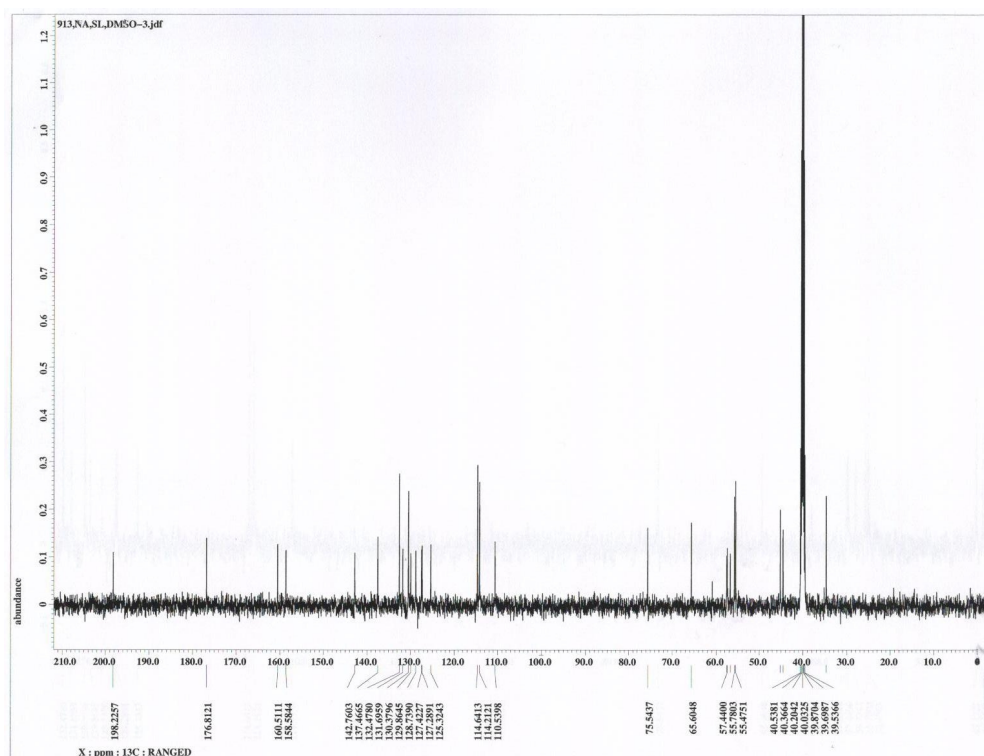
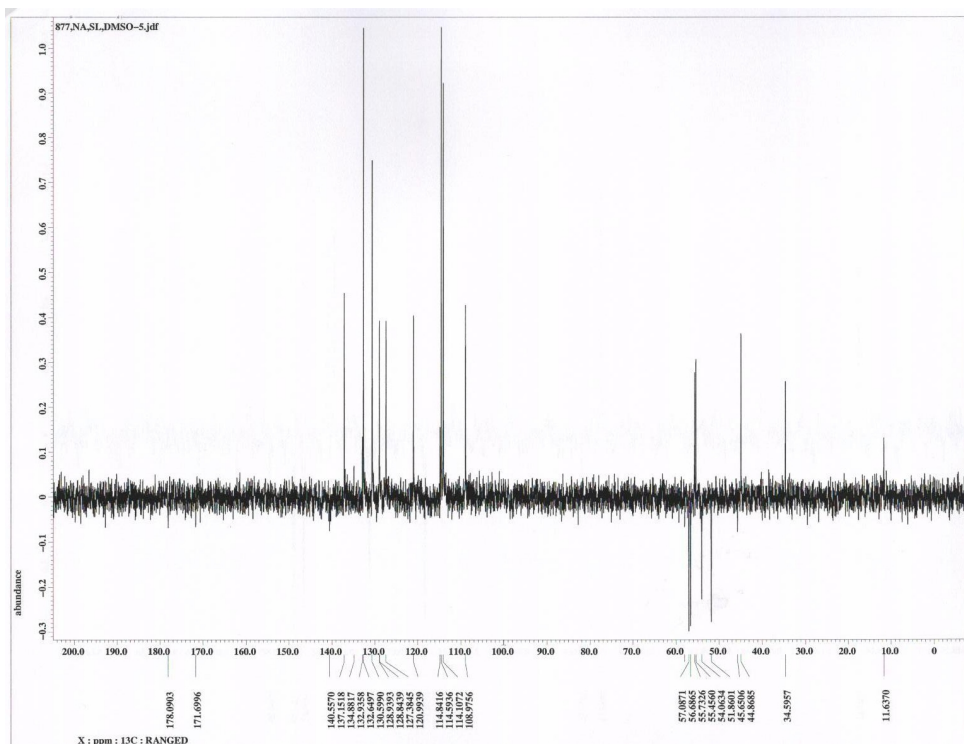


Figure 62. ^{13}C -NMR spectrum (on-resonance) of compound **39**.



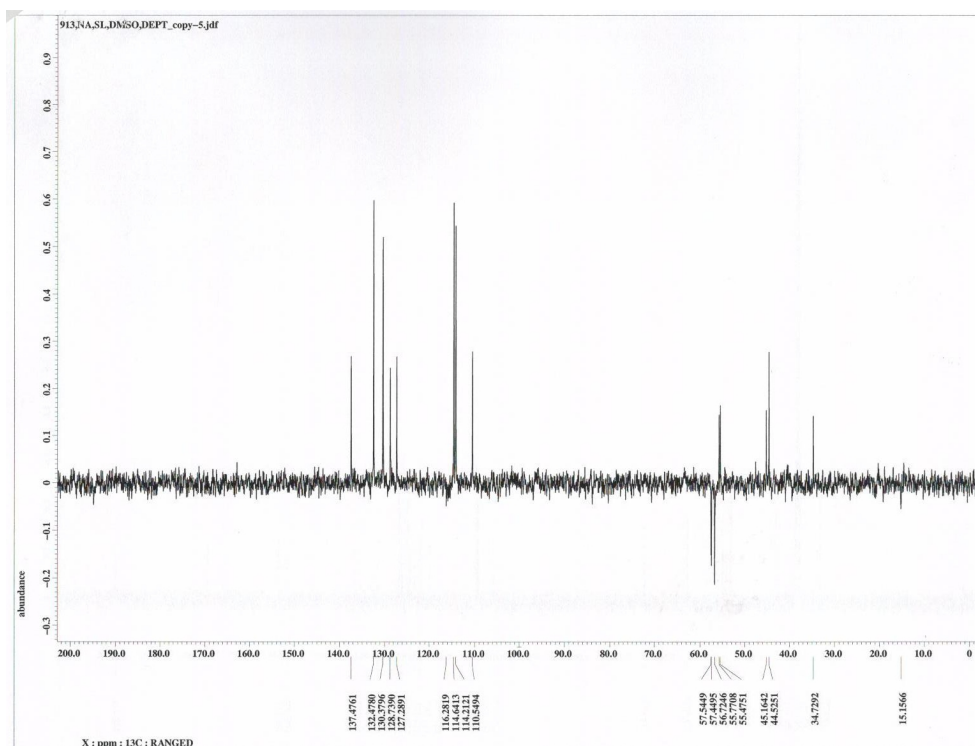


Figure 65. ^{13}C -NMR spectrum (DEPT) of compound **40**.

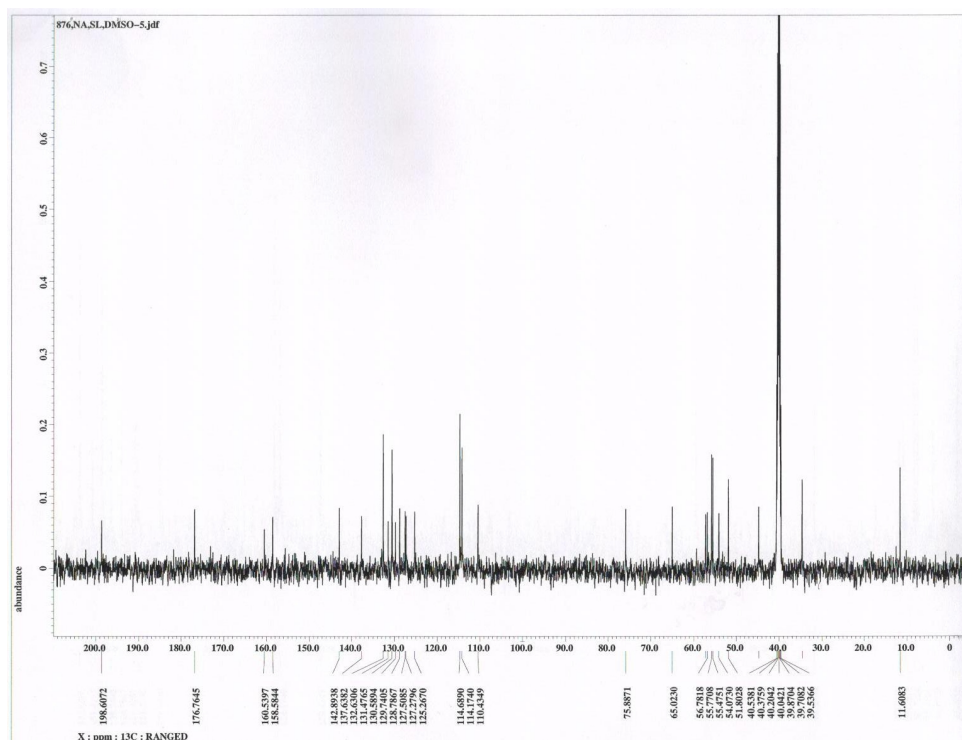


Figure 66. ^{13}C -NMR spectrum (on-resonance) of compound **41**.

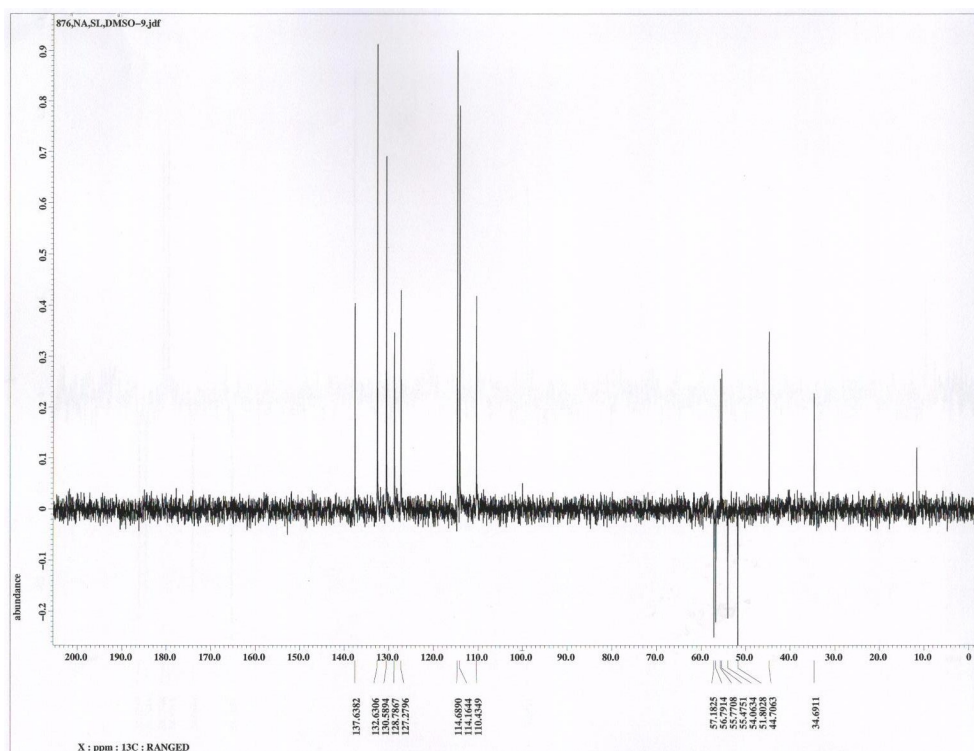


Figure 67. ^{13}C -NMR spectrum (DEPT) of compound **41**.

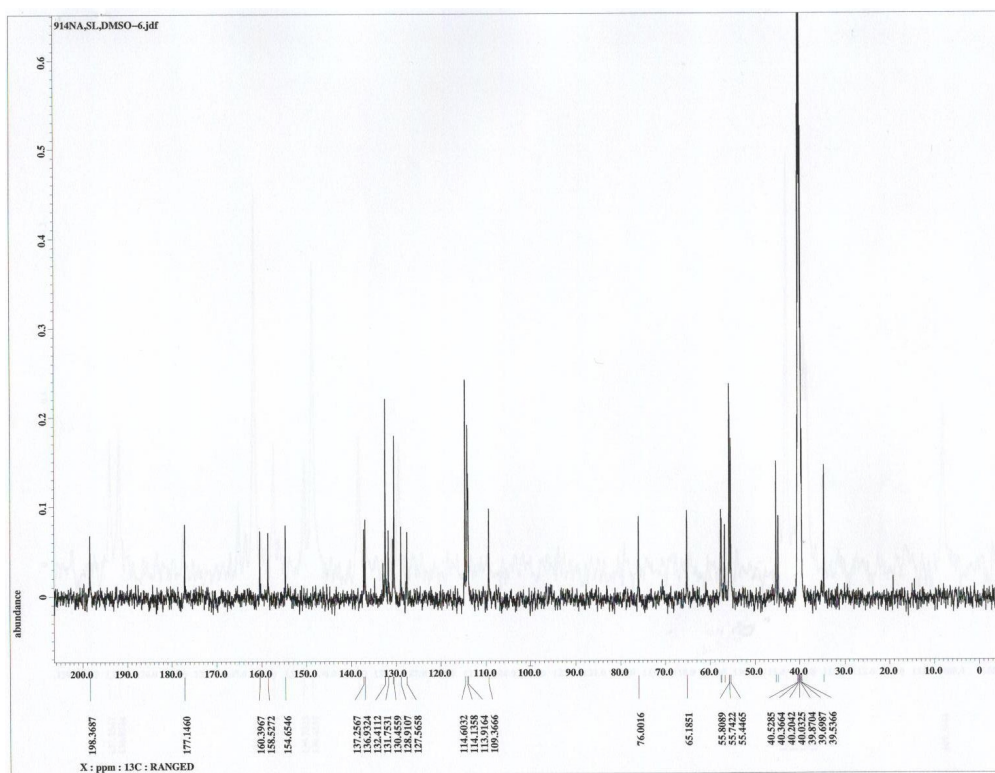


Figure 68. ^{13}C -NMR spectrum (on-resonance) of compound **42**.

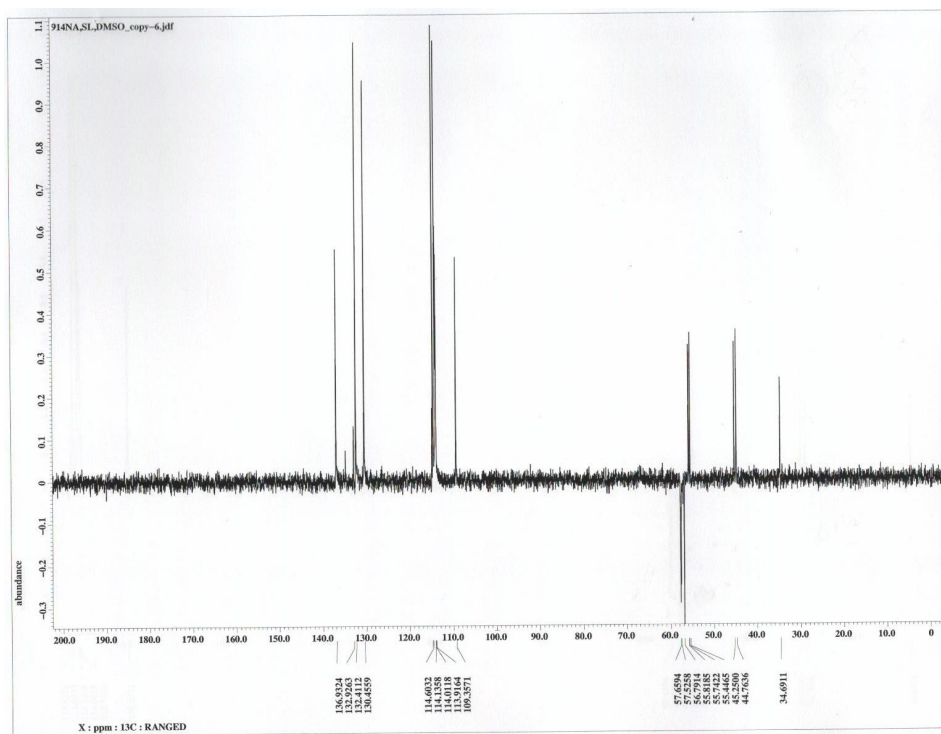


Figure 69. ^{13}C -NMR spectrum (DEPT) of compound **42**.

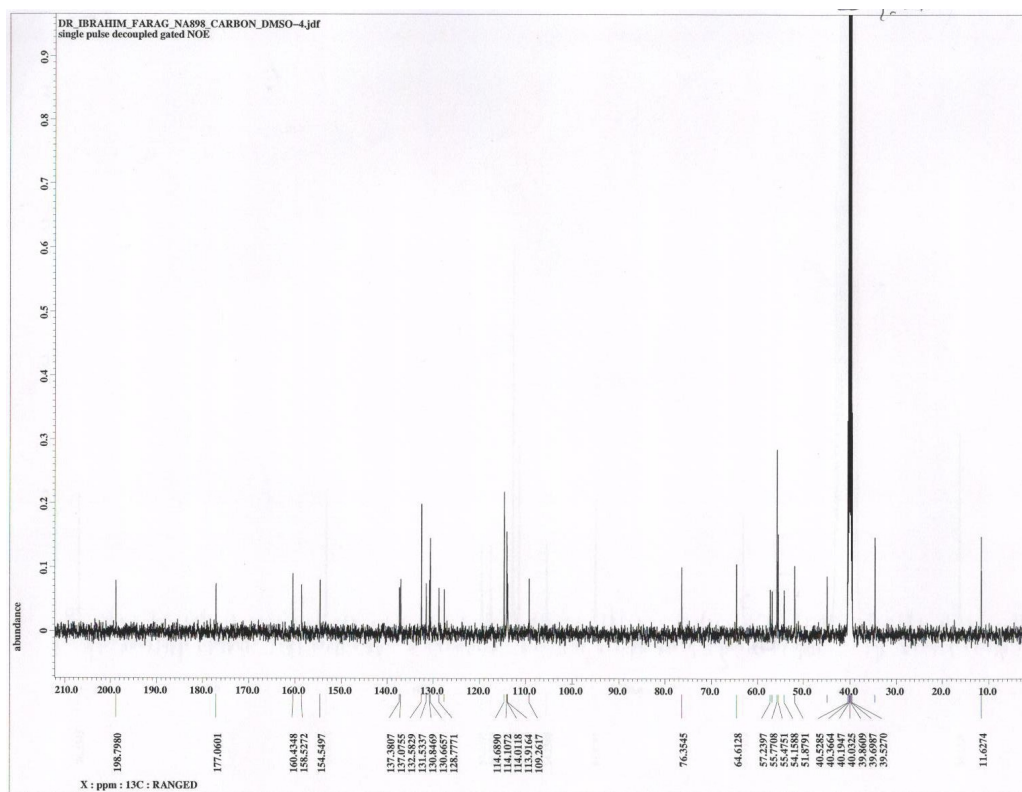


Figure 70. ^{13}C -NMR spectrum (on-resonance) of compound **43**.

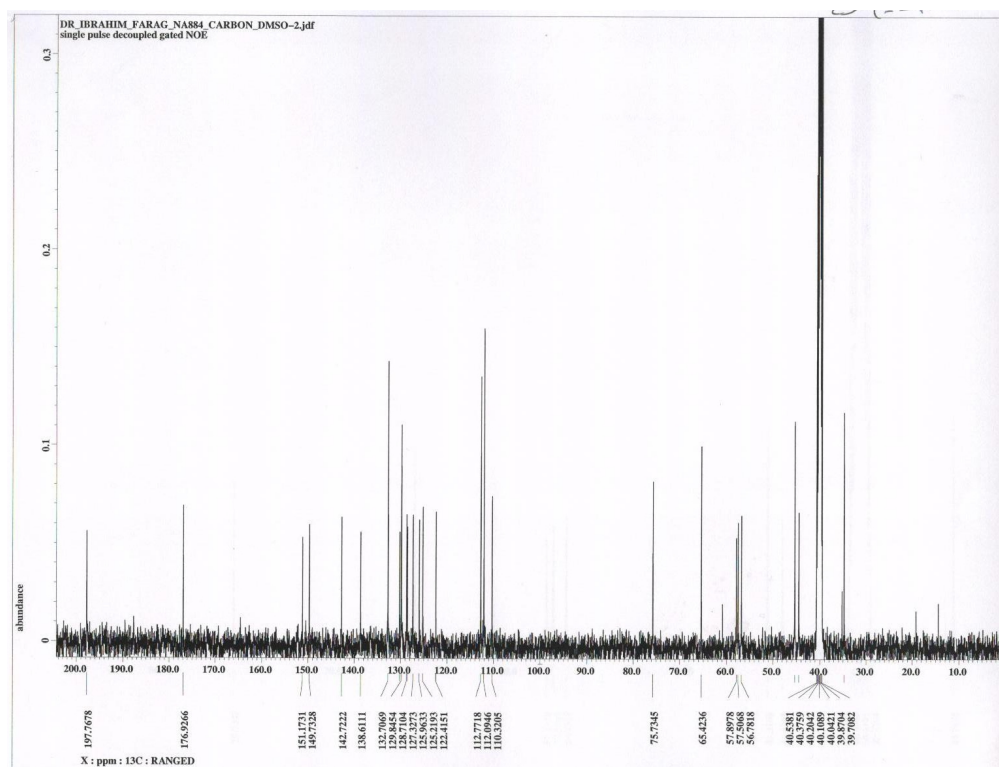


Figure 71. ^{13}C -NMR spectrum (on-resonance) of compound 44.

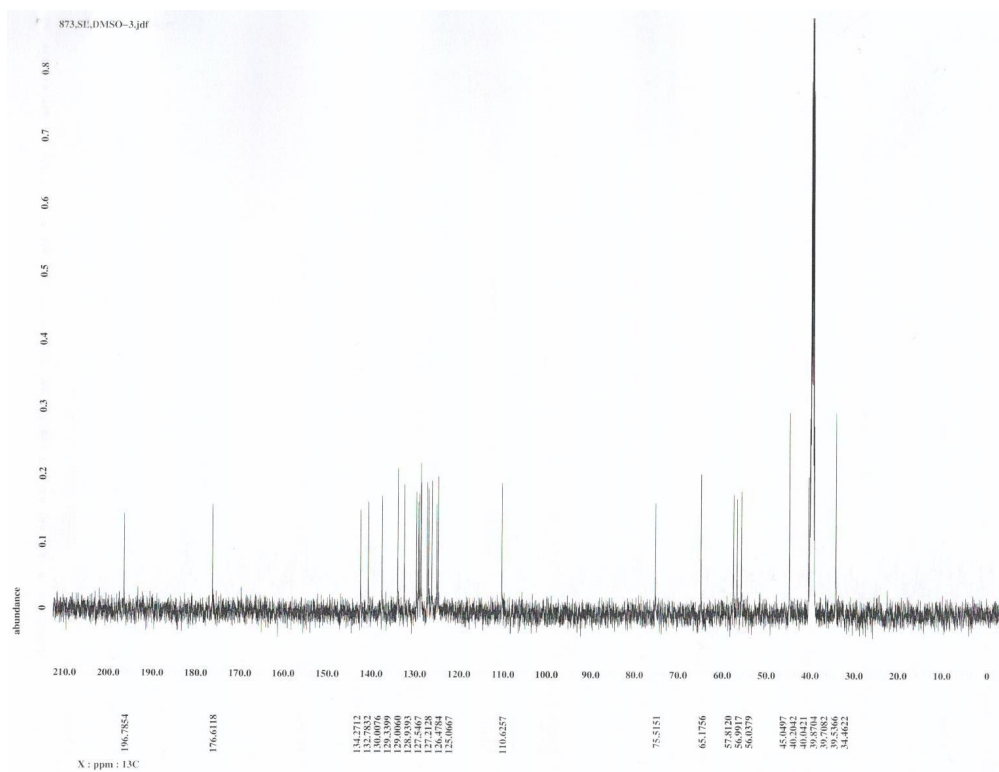


Figure 72. ^{13}C -NMR spectrum (on-resonance) of compound 46.

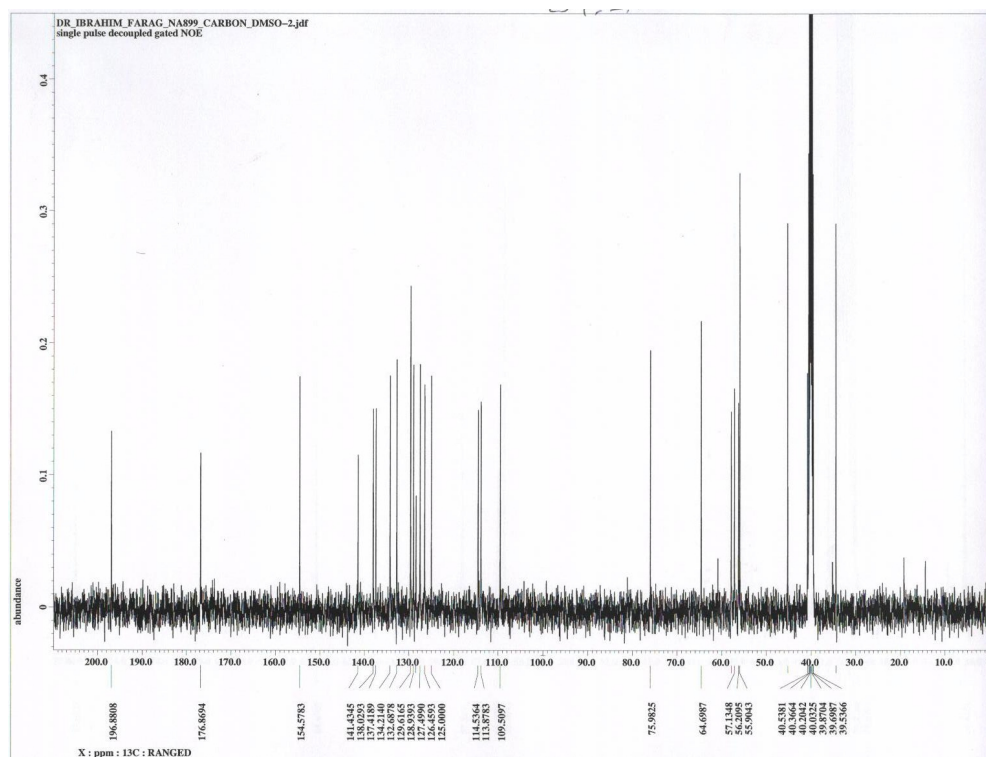


Figure 73. ^{13}C -NMR spectrum (on-resonance) of compound **47**.

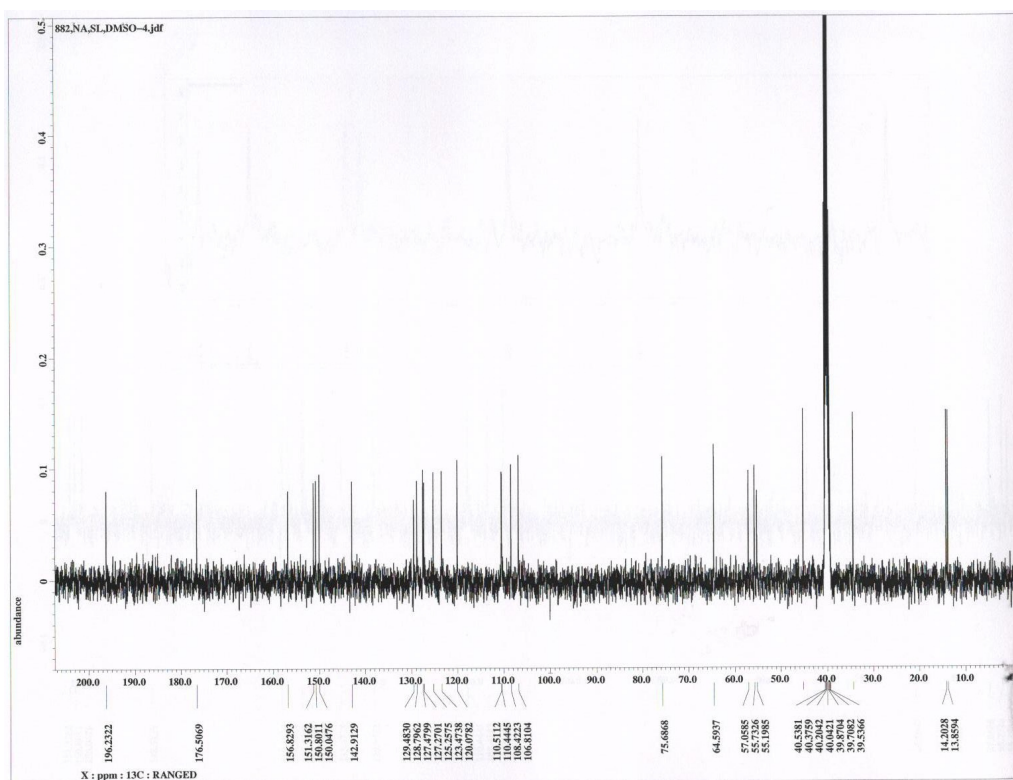


Figure 74. ^{13}C -NMR spectrum (on-resonance) of compound **48**.

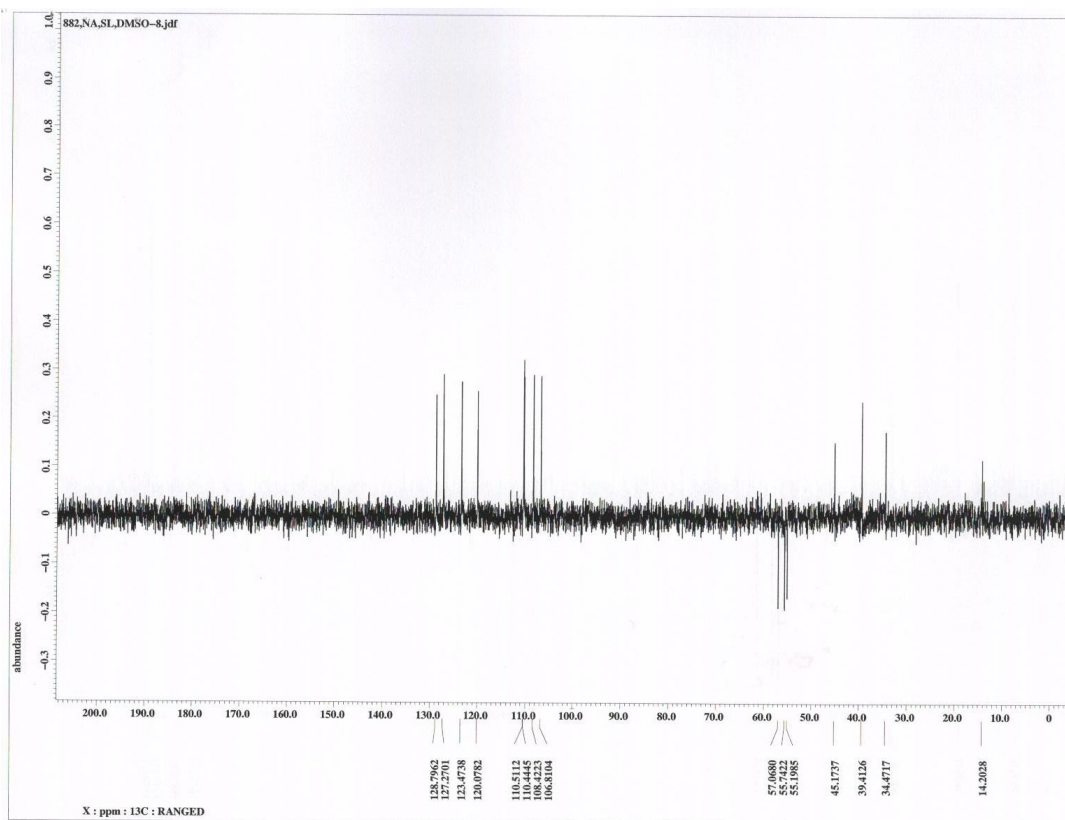


Figure 75. ^{13}C -NMR spectrum (DEPT) of compound **48**.

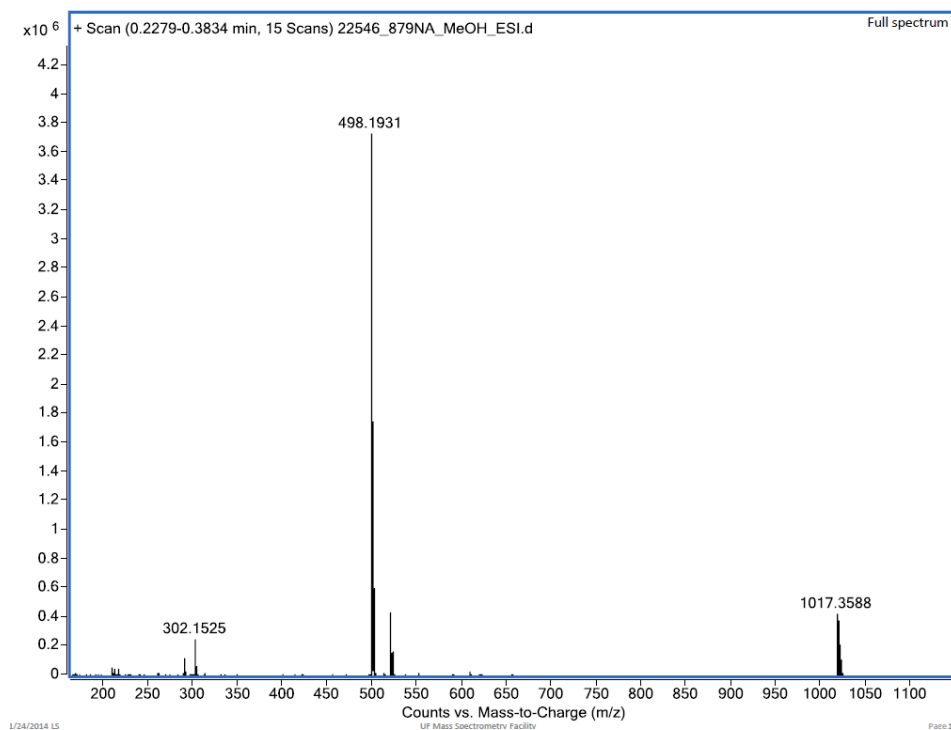


Figure 76. HRMS spectra of compound **25**.

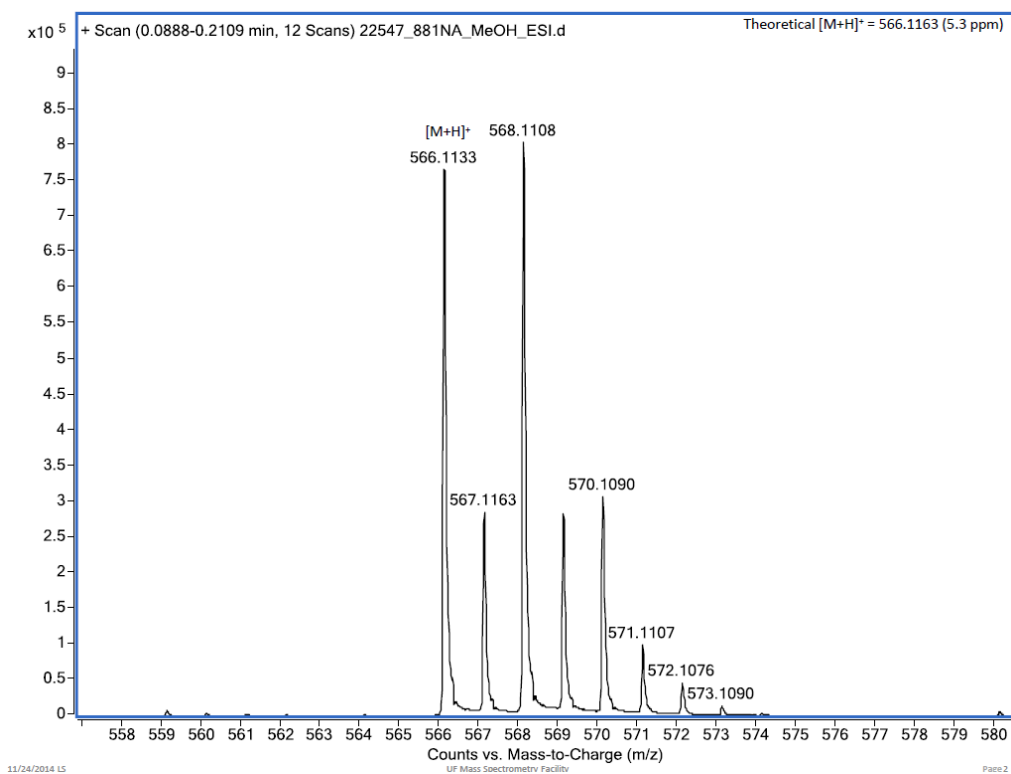


Figure 77. HRMS spectra of compound **27**.

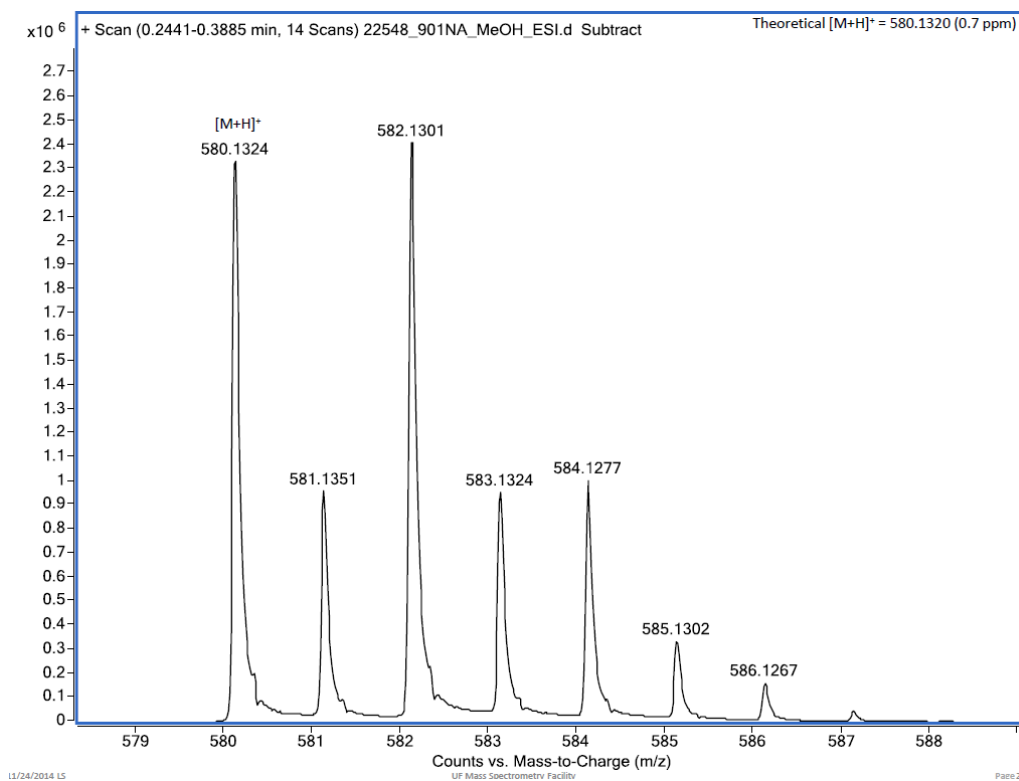


Figure 78. HRMS spectra of compound **28**.

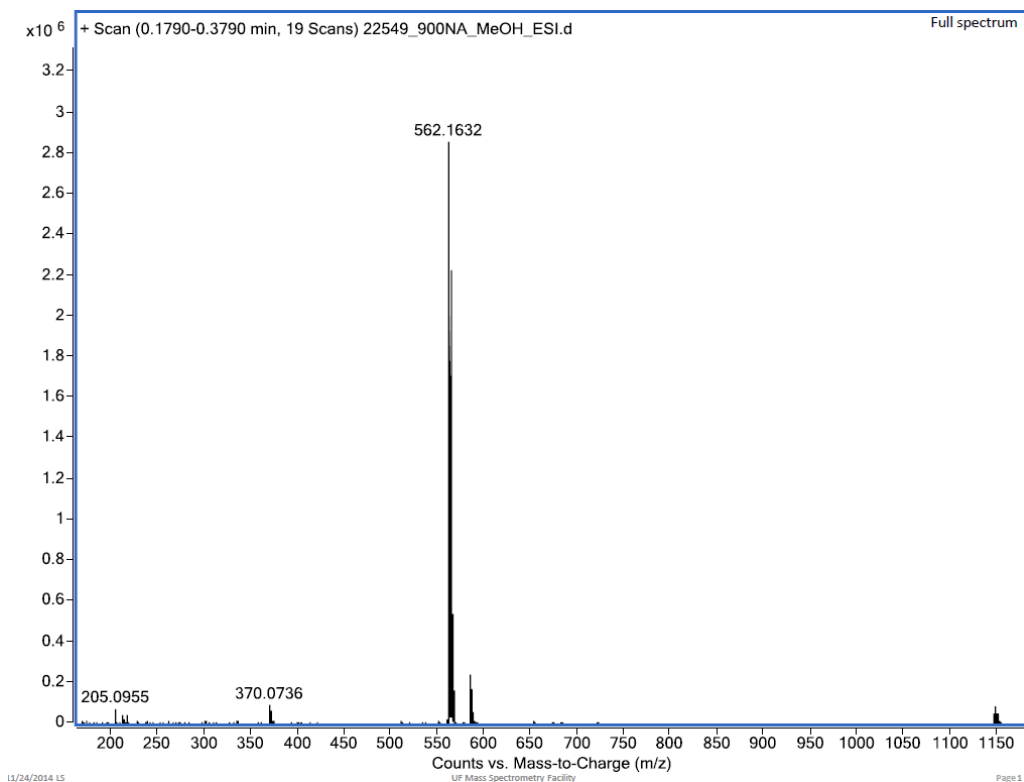


Figure 79. HRMS spectra of compound **29**.

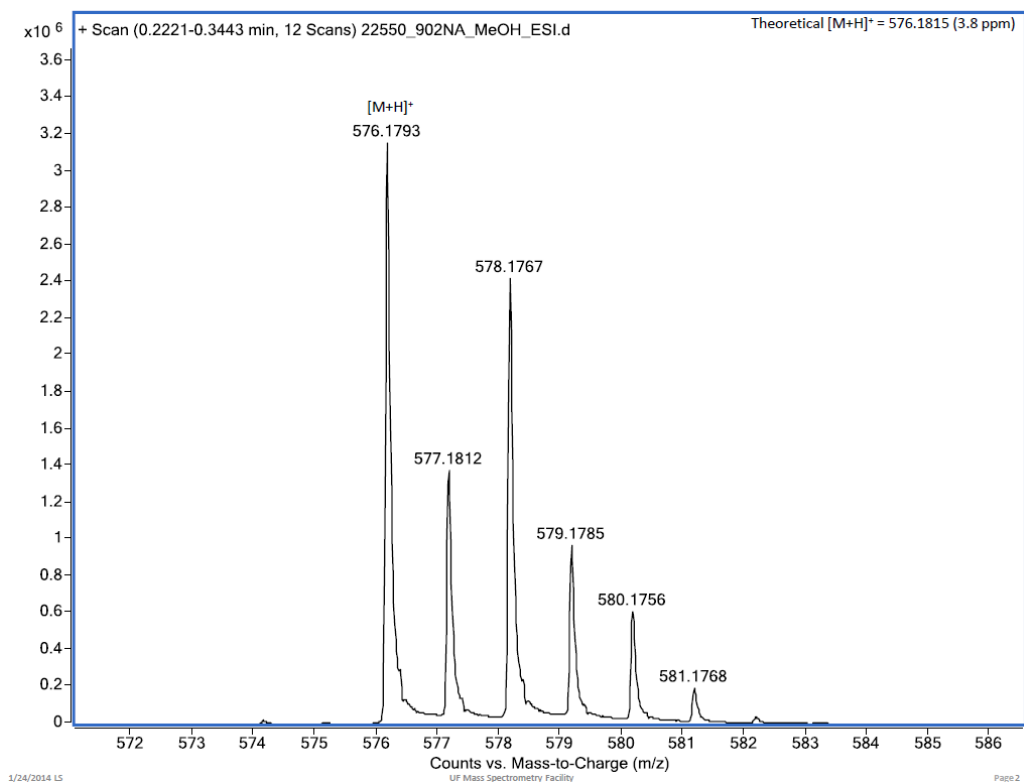


Figure 80. HRMS spectra of compound **30**.

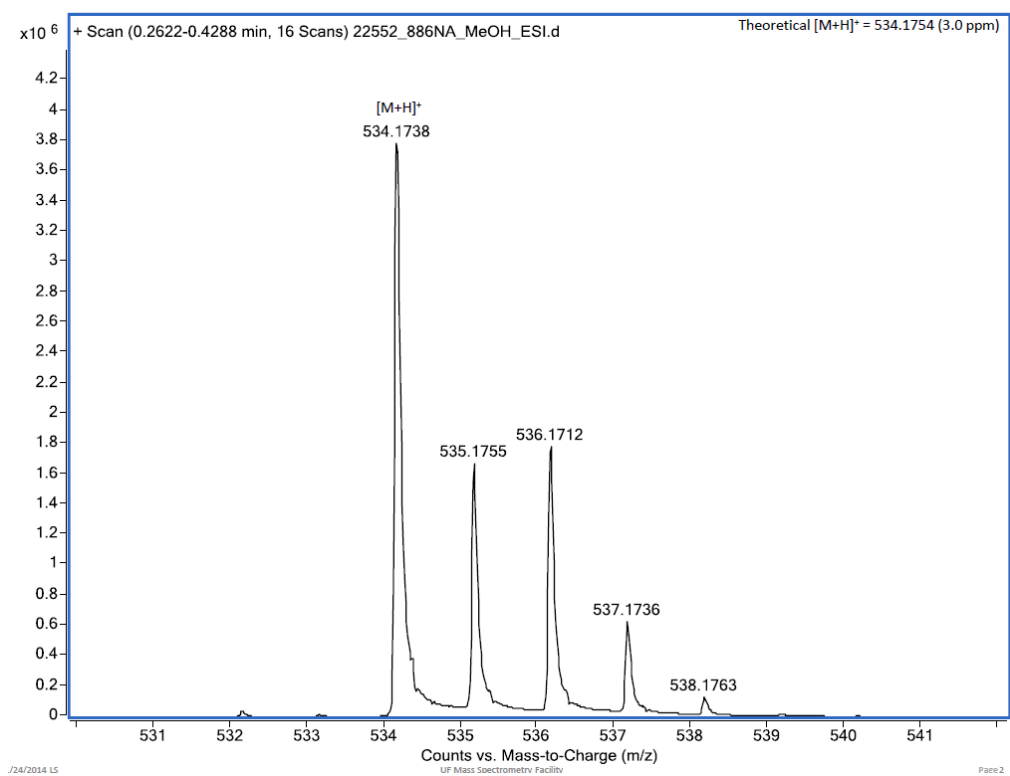


Figure 81. HRMS spectra of compound **32**.

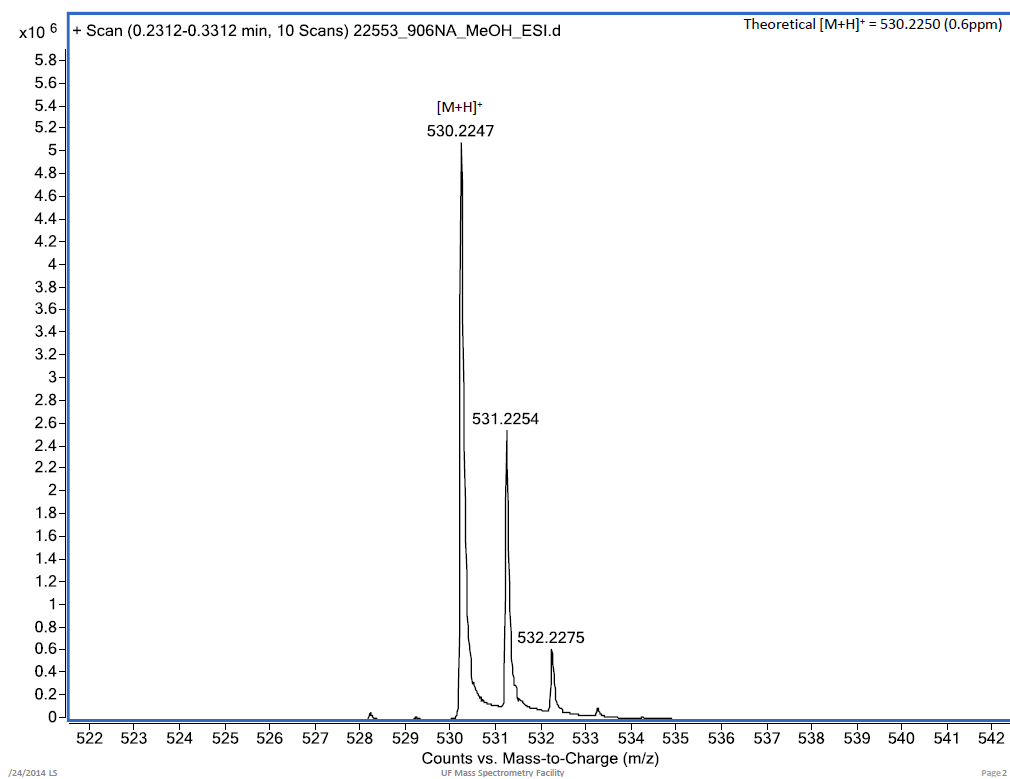


Figure 82. HRMS spectra of compound **33**.

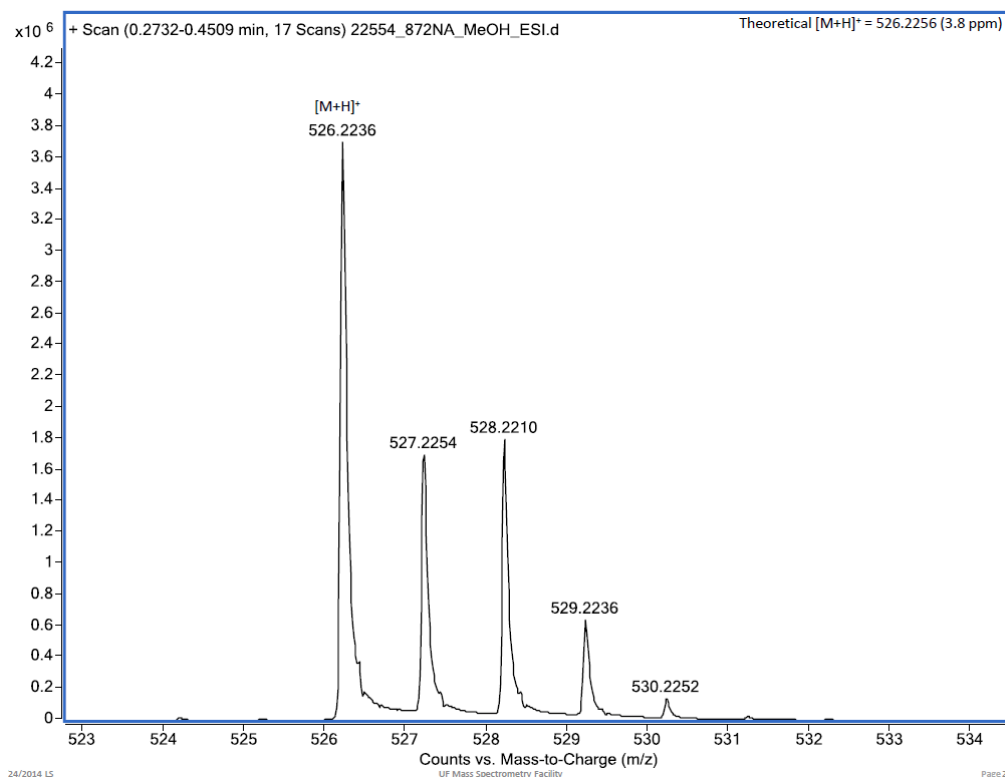


Figure 83. HRMS spectra of compound **35**.

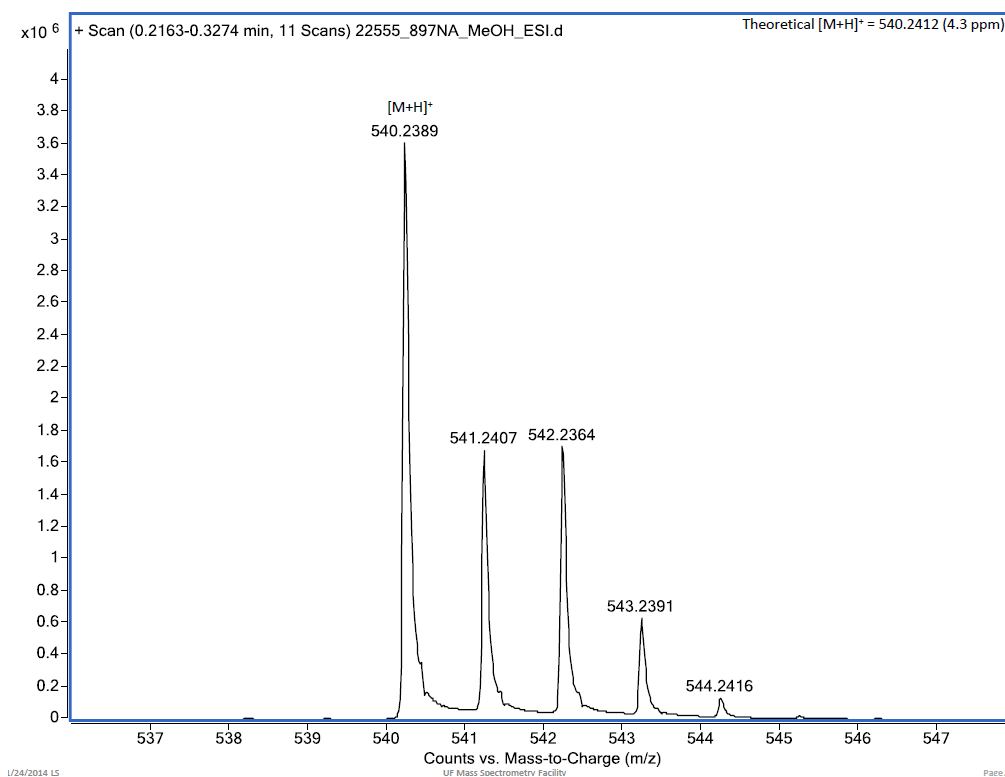


Figure 84. HRMS spectra of compound **36**.

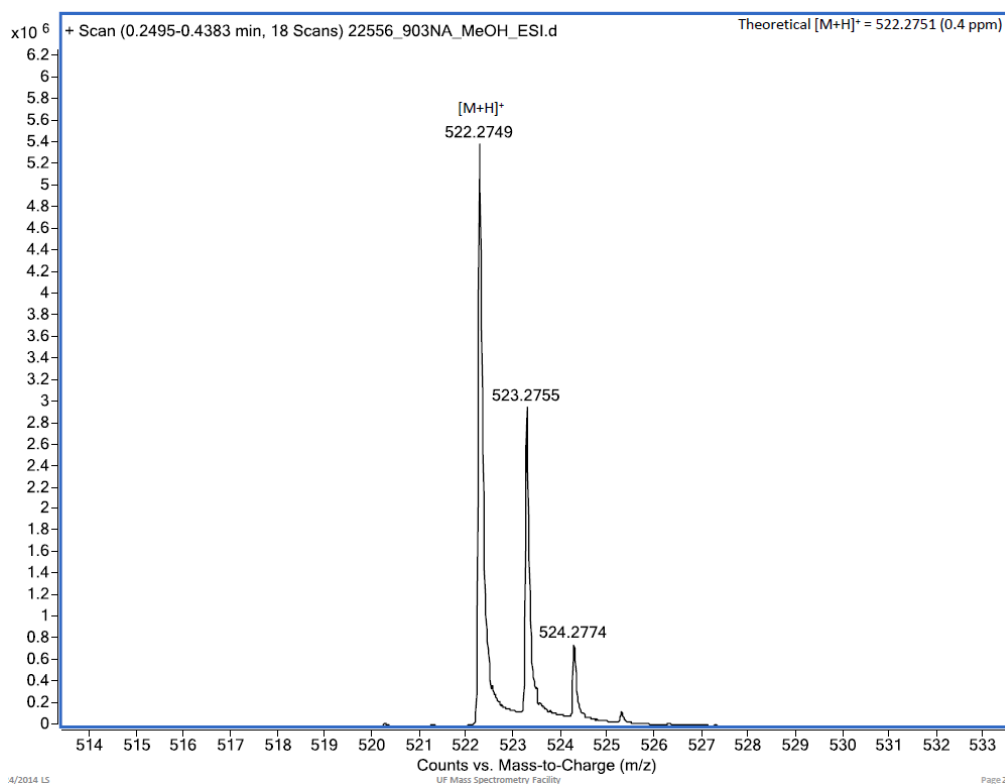


Figure 85. HRMS spectra of compound 37.

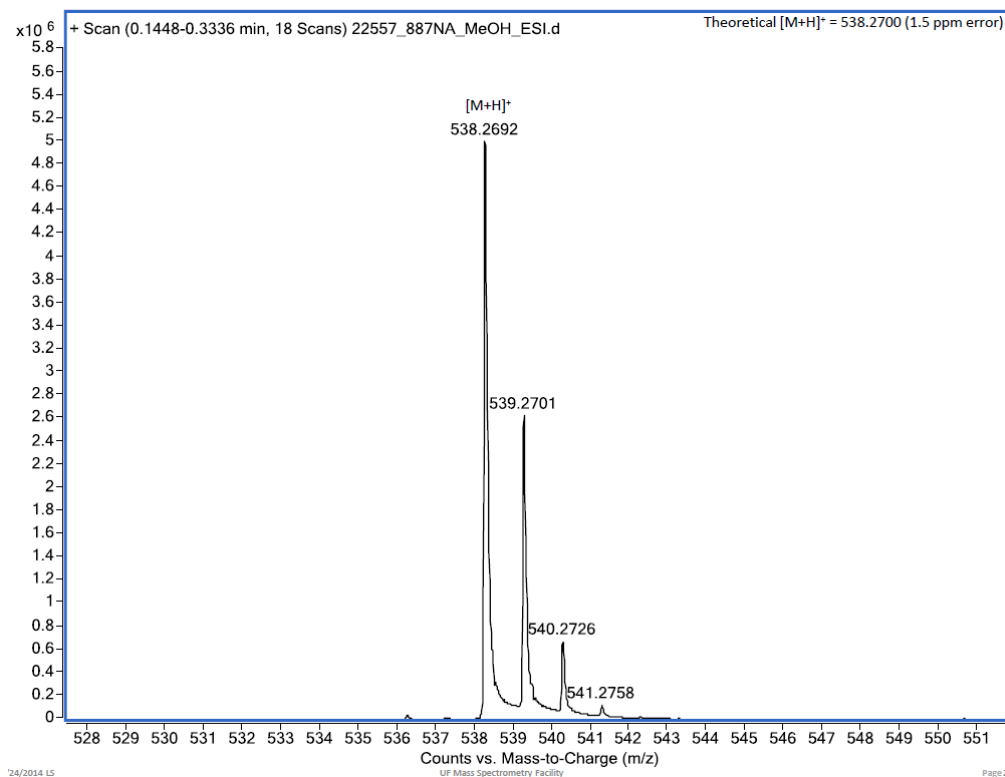


Figure 86. HRMS spectra of compound 39.

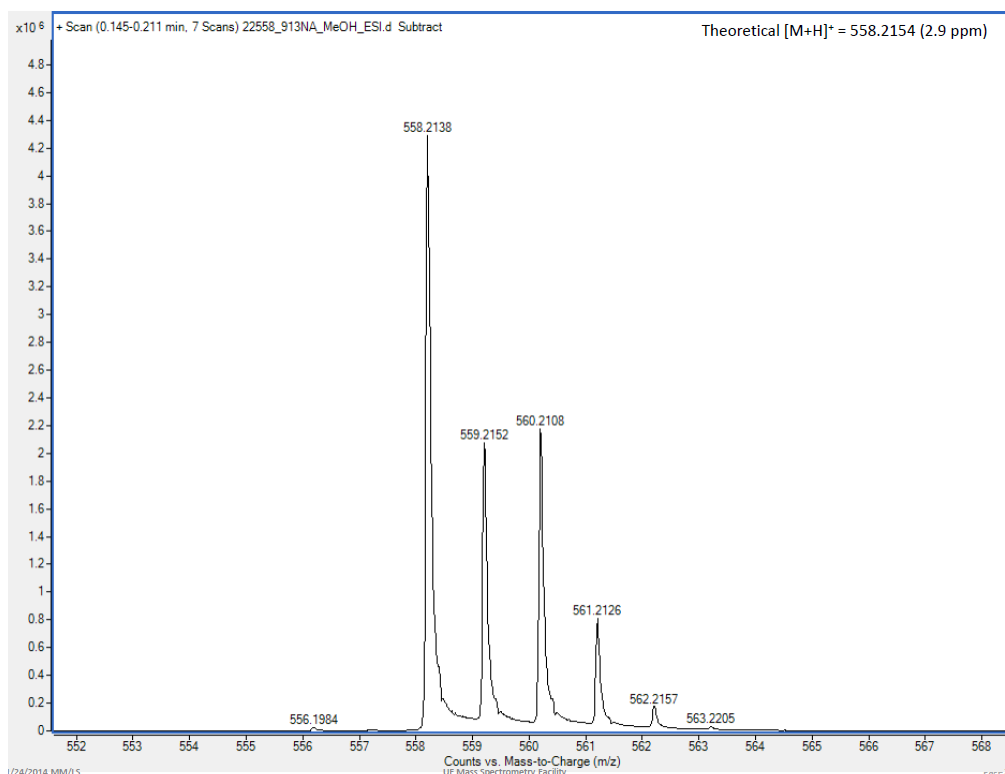


Figure 87. HRMS spectra of compound 40.

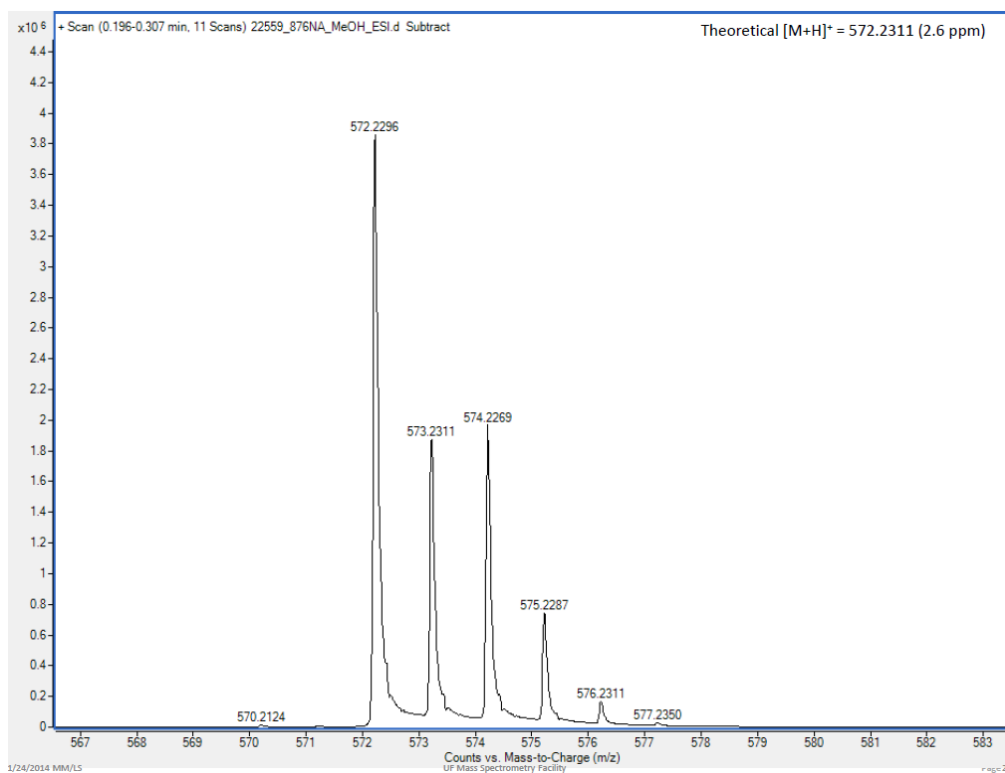


Figure 88. HRMS spectra of compound 41.

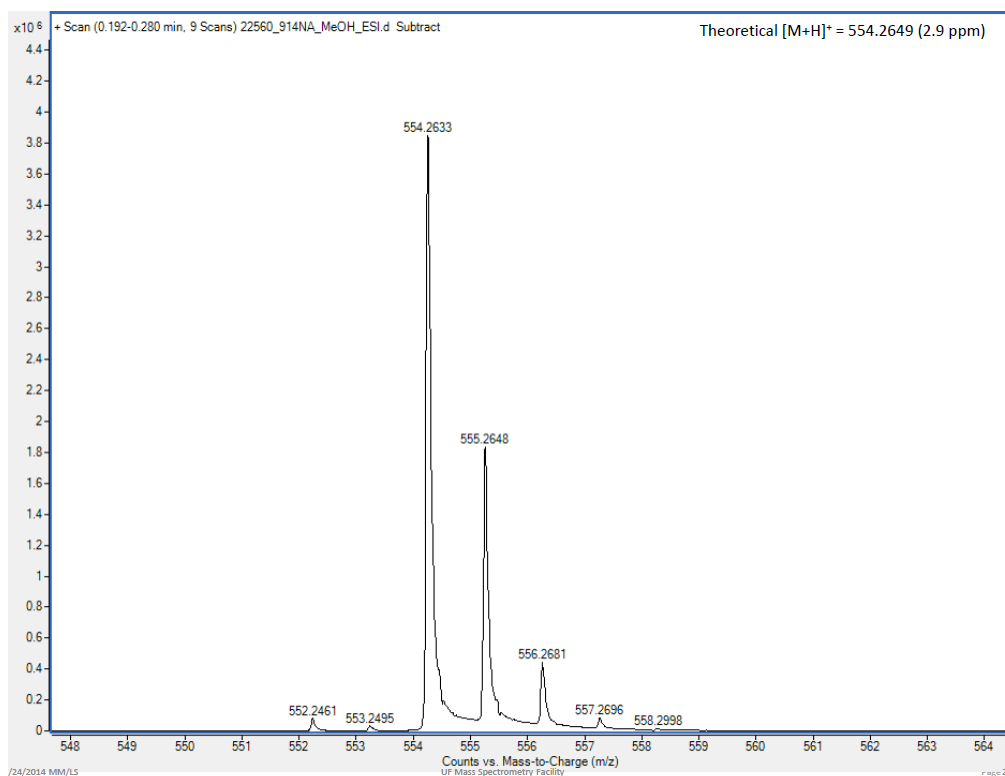


Figure 89. HRMS spectra of compound **42**.

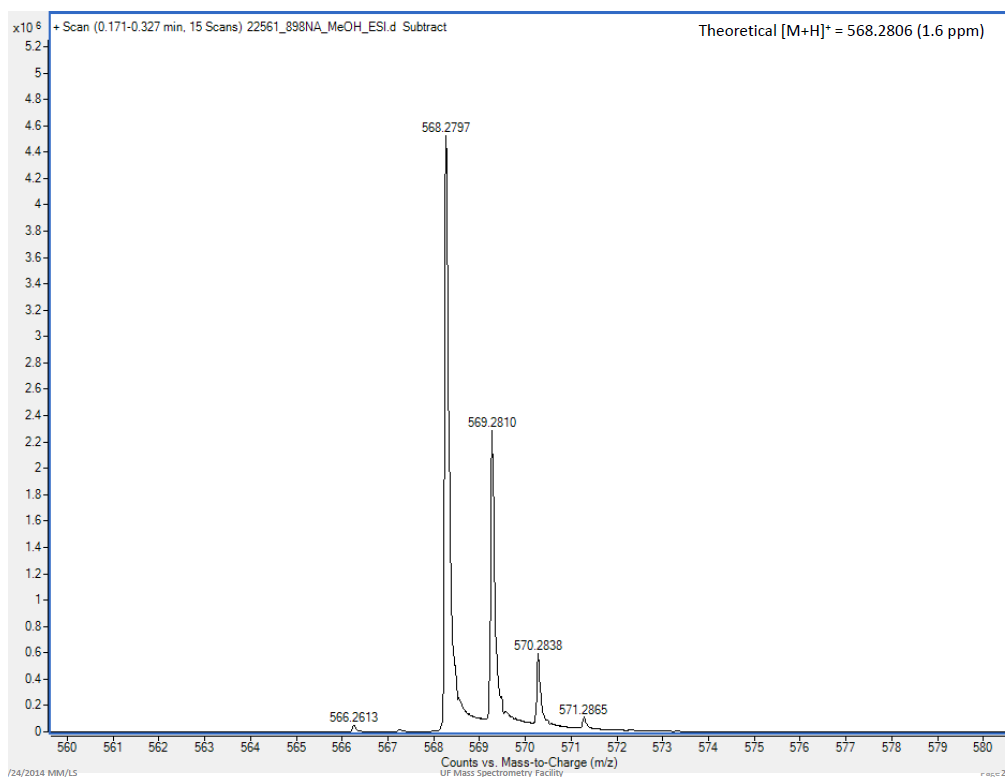


Figure 90. HRMS spectra of compound **43**.

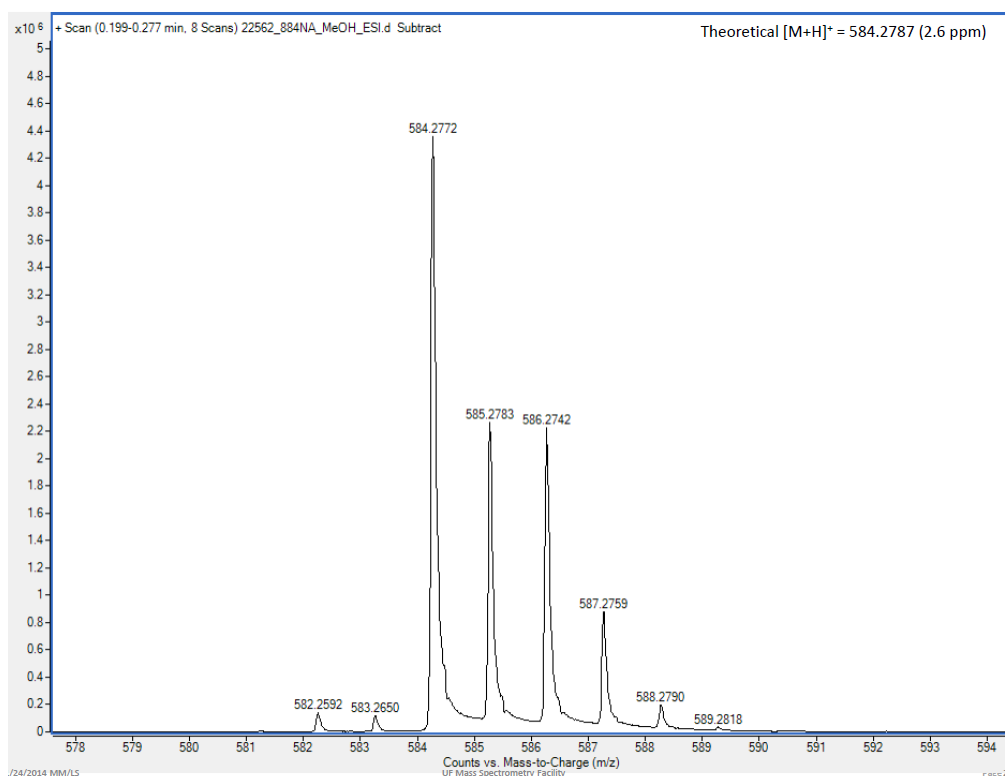


Figure 91. HRMS spectra of compound 44.

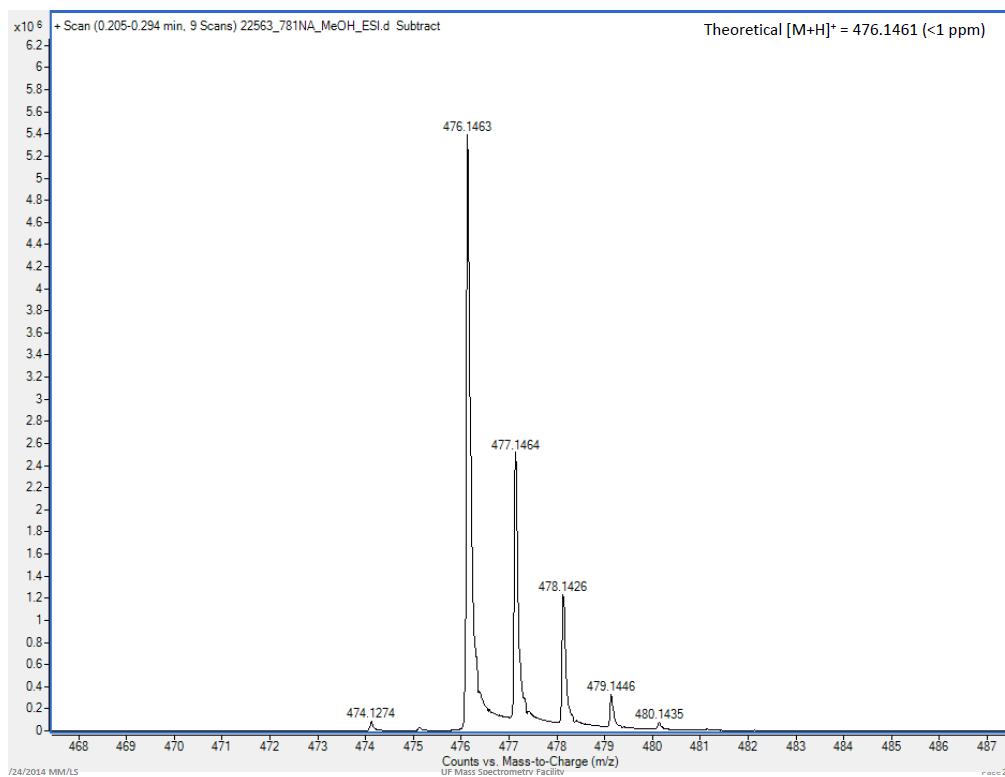


Figure 92. HRMS spectra of compound 45.

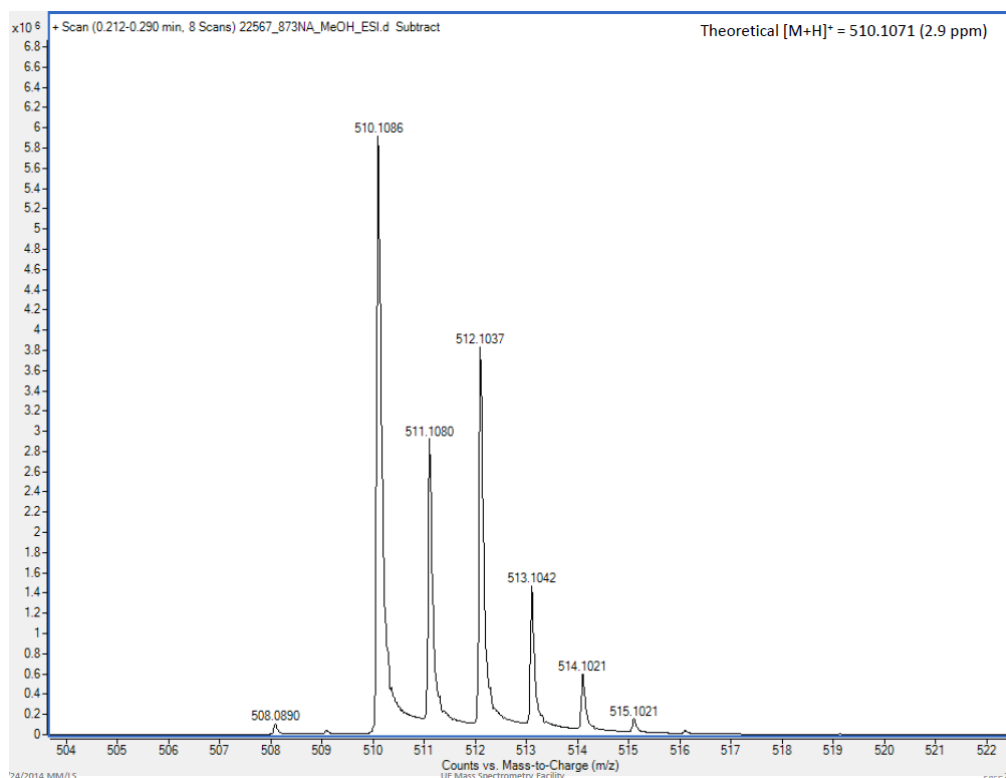


Figure 93. HRMS spectra of compound **46**.

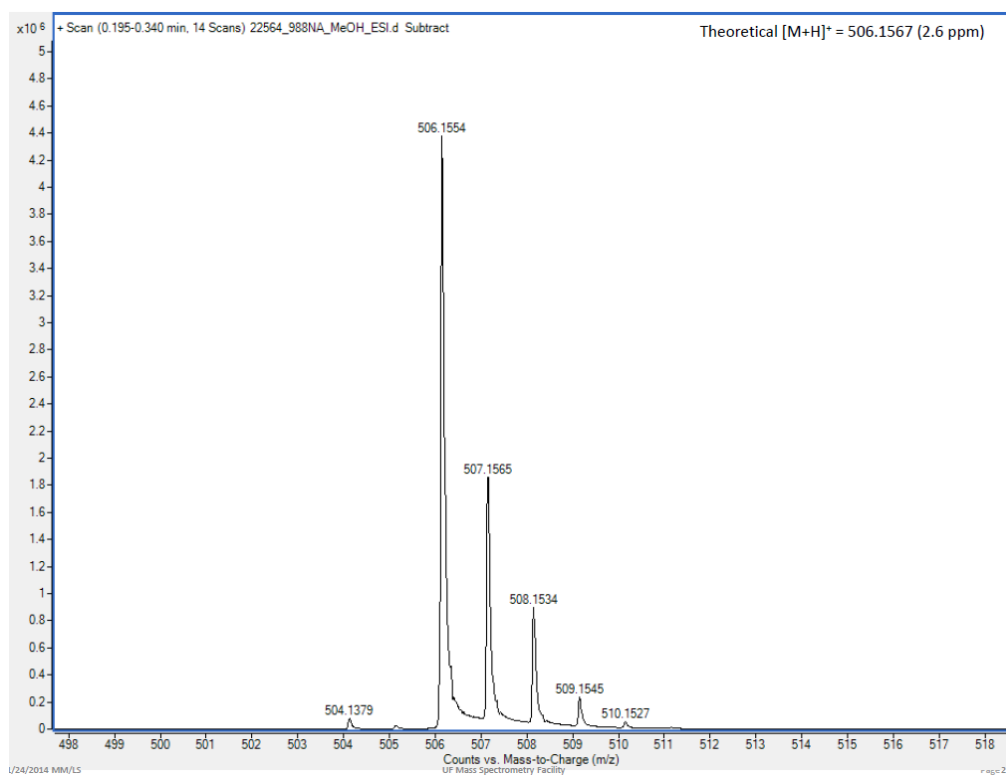


Figure 94. HRMS spectra of compound **47**.

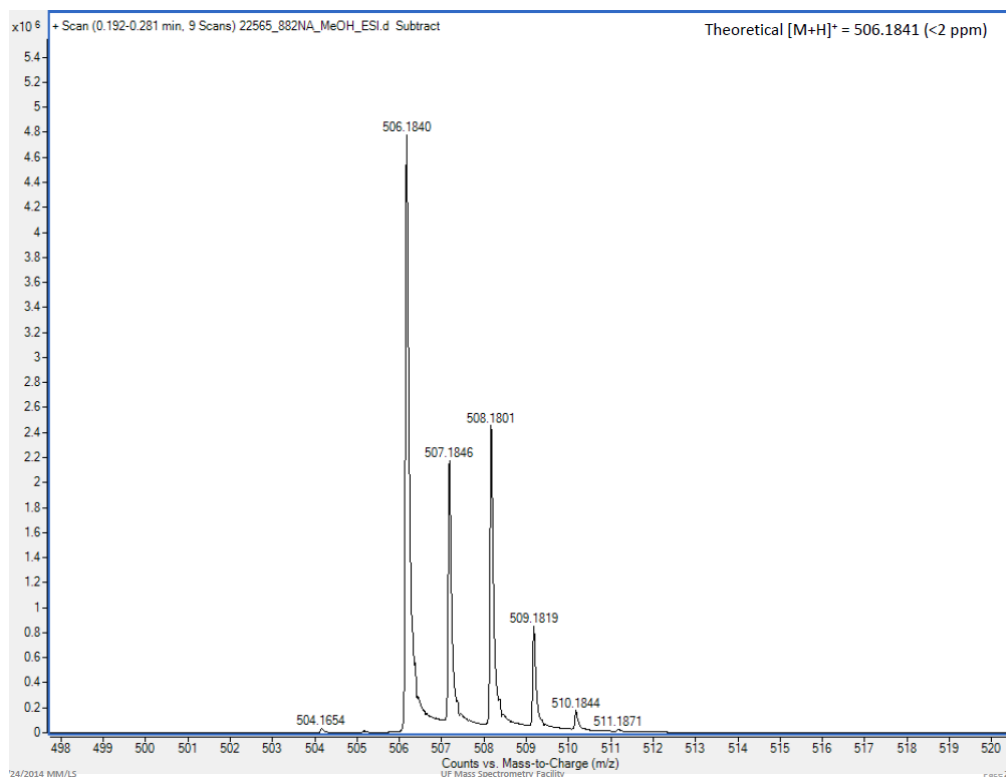


Figure 95. HRMS spectra of compound **48**.