Supporting Information

Discovery of 29-*O*-acyl-toosendanin-based derivatives as potent anti-cancer agents

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1. **Figures S1-S6.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **1**.

Figure S1. ^{1}H NMR (400 MHz) spectrum of **1** in $CDCl_3$.

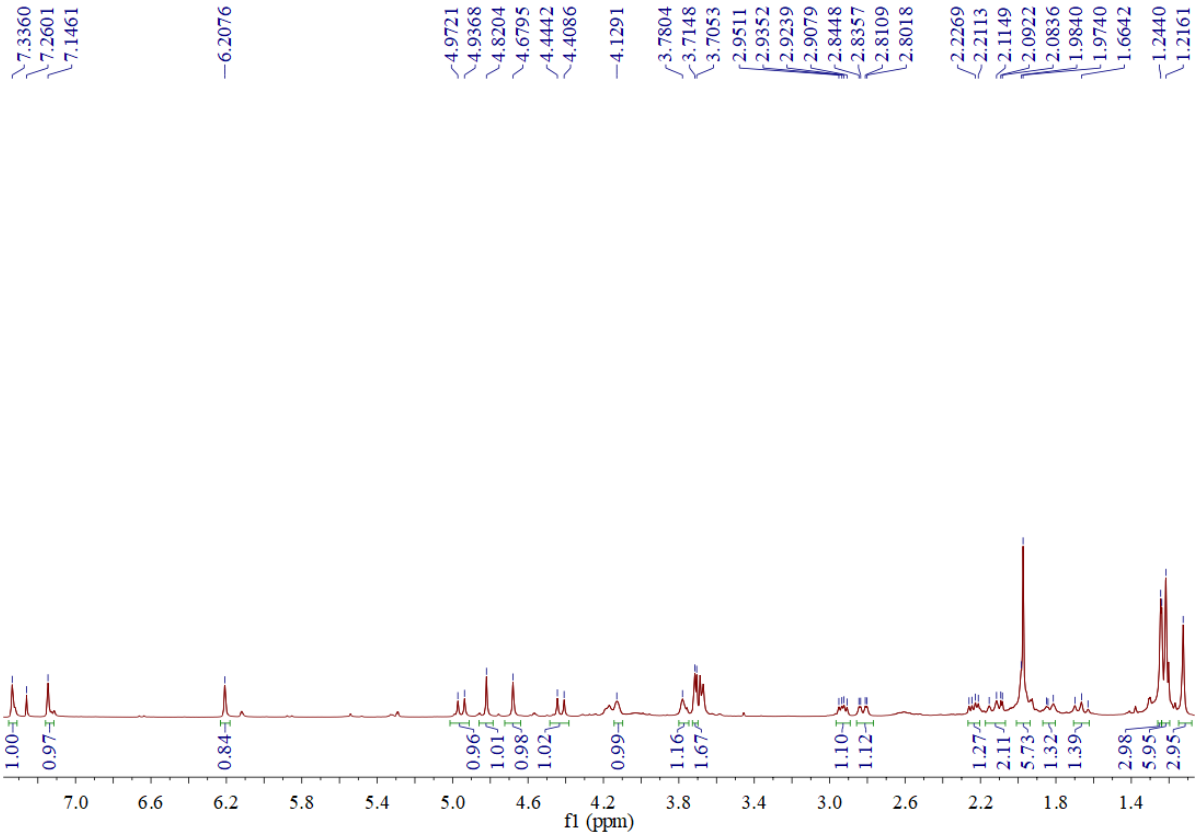


Figure S2. ^{13}C NMR (100 MHz) spectrum of **1** in $CDCl_3$.

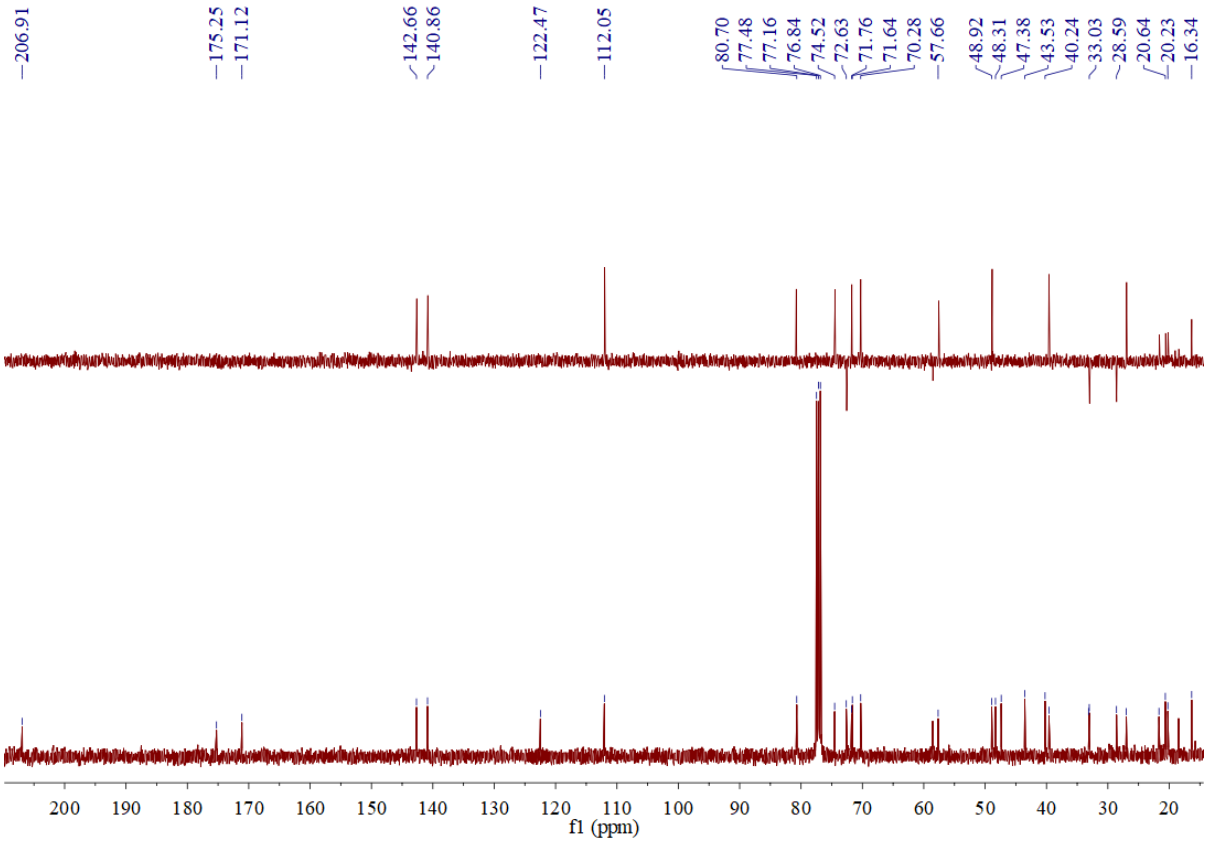


Figure S3. HSQC spectrum of **1** in $CDCl_3$.

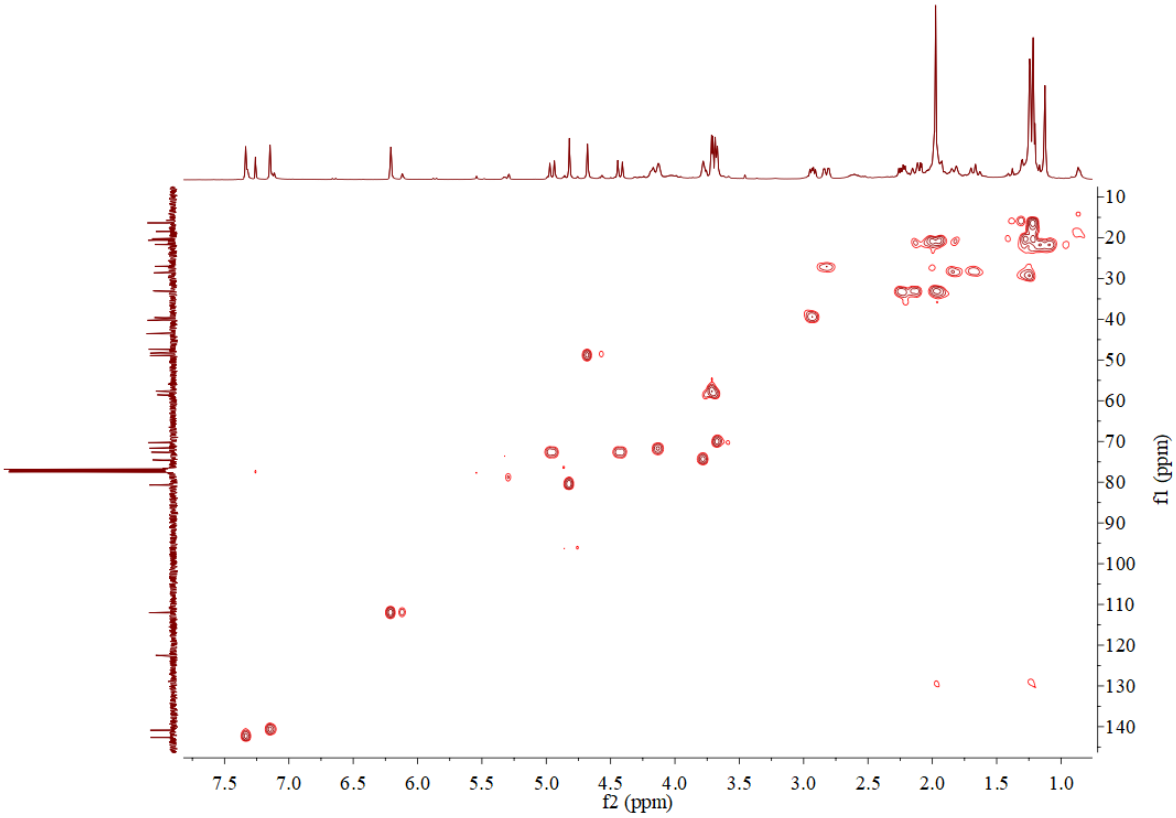


Figure S4. ^{1}H–^{1}H COSY spectrum of **1** in $CDCl_3$.

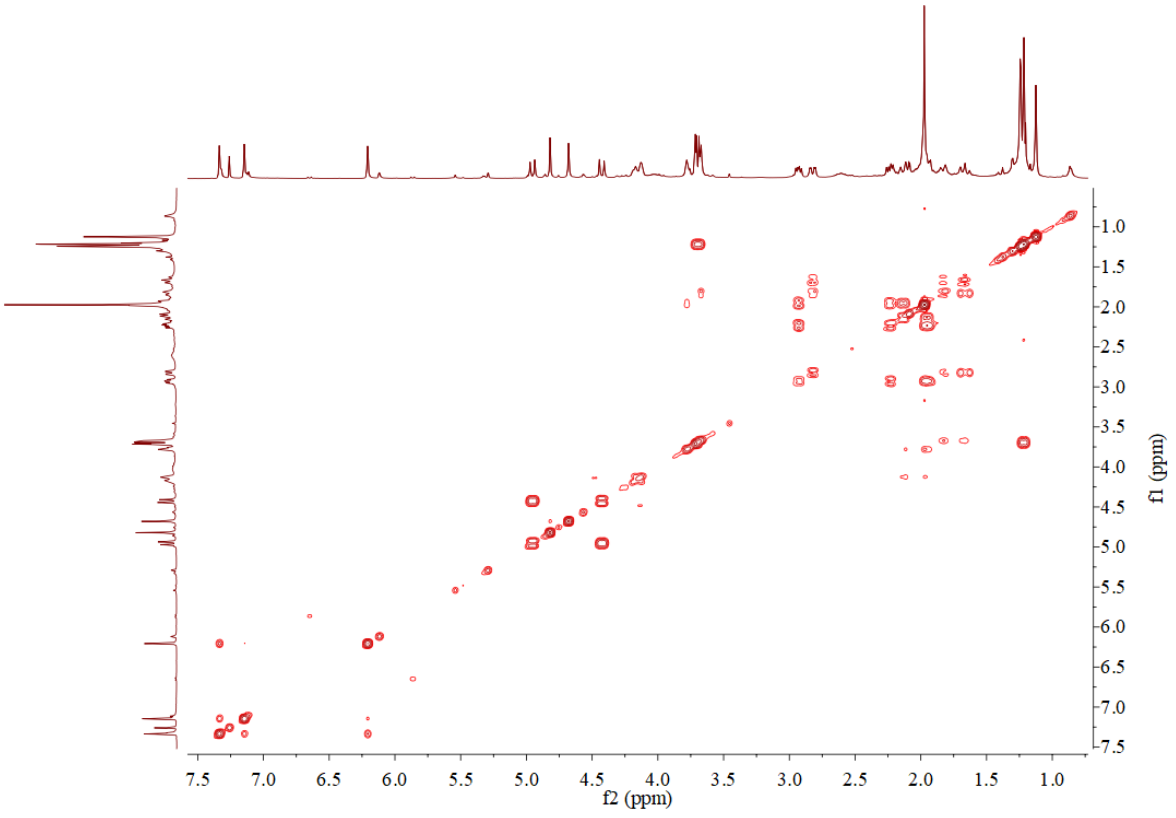


Figure S5. HMBC spectrum of **1** in $CDCl_3$.

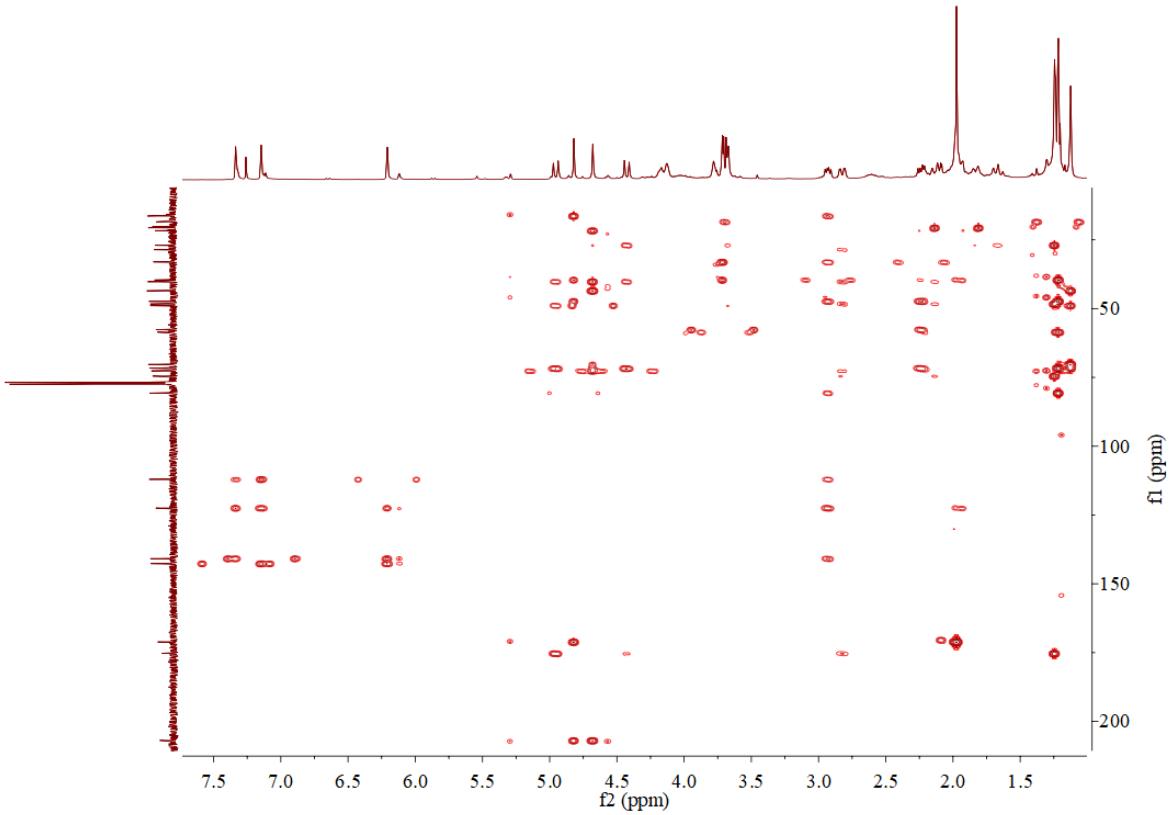
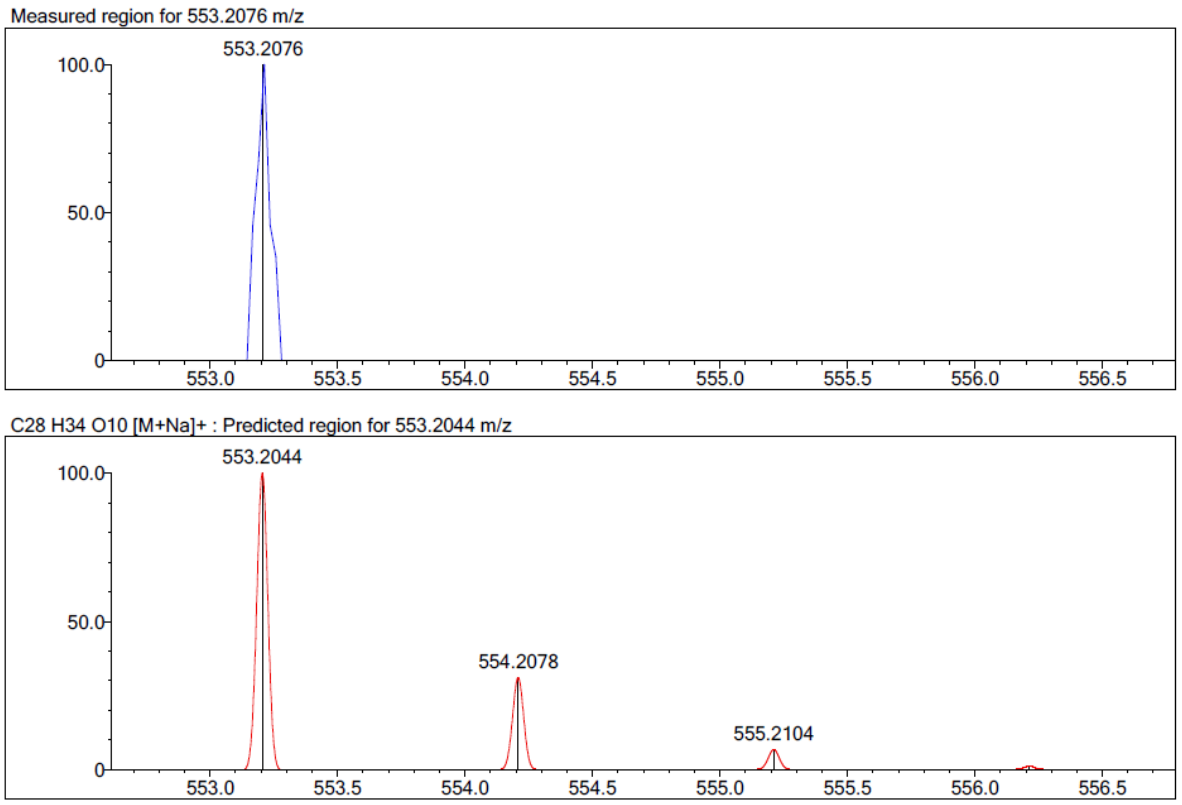


Figure S6. HRESIMS spectrum of **1**



2. **Figures S7–S8.** ^{1}H NMR and ^{13}C NMR spectra of **2**.

Figure S7. ^{1}H NMR (400 MHz) spectrum of **2** in $CDCl_3$&CD_3OD.

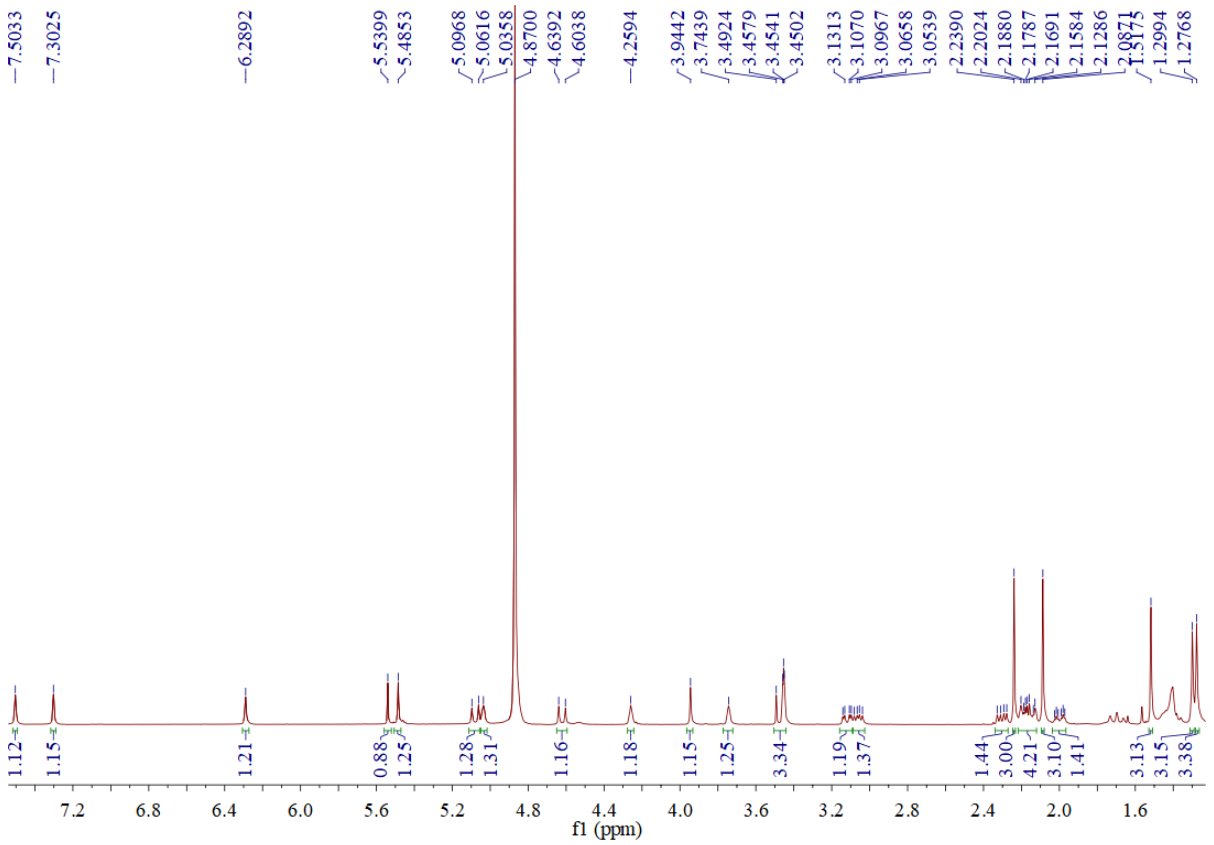
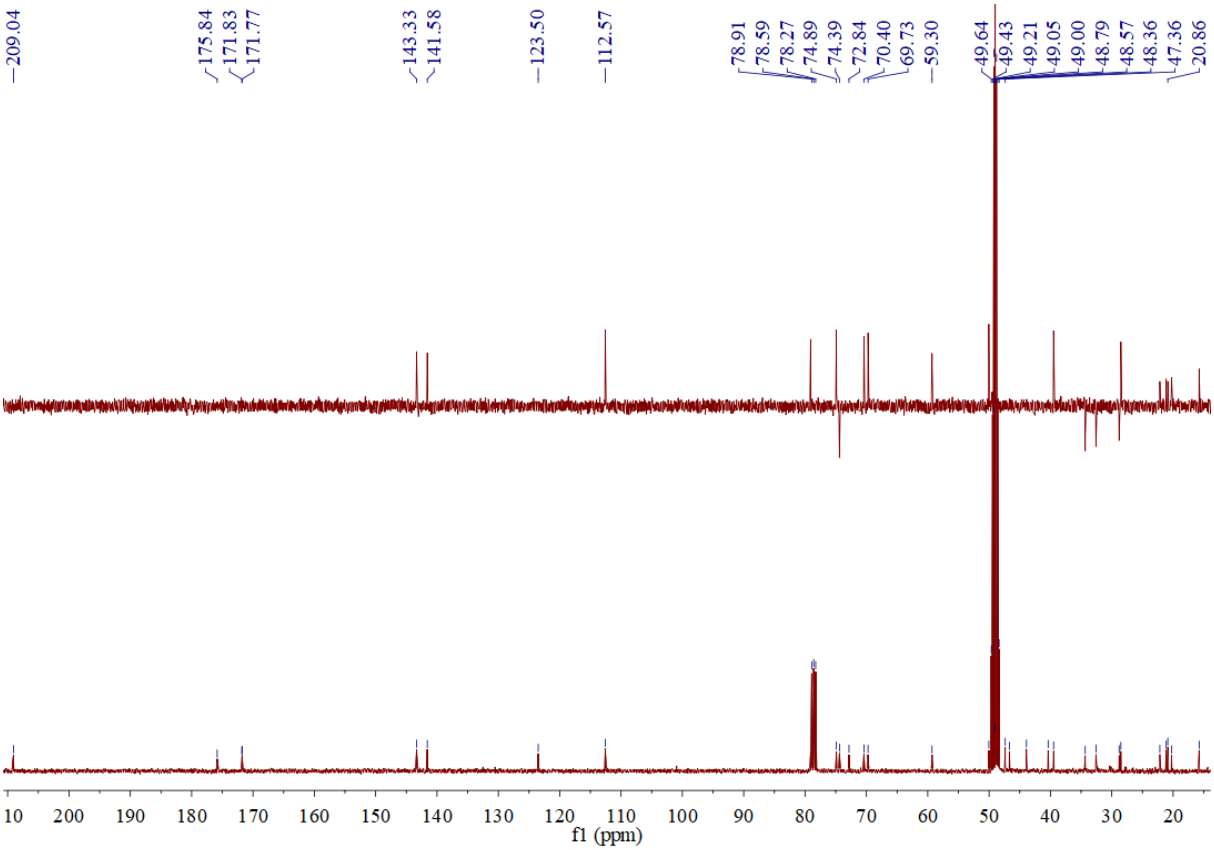


Figure S8. ^{13}C NMR (100 MHz) spectrum of **2** in $CDCl_3$&CD_3OD.



3. **Figures S9–S14.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **3**.

Figure S9. ^{1}H NMR (400 MHz) spectrum of **3** in $CDCl_3$.

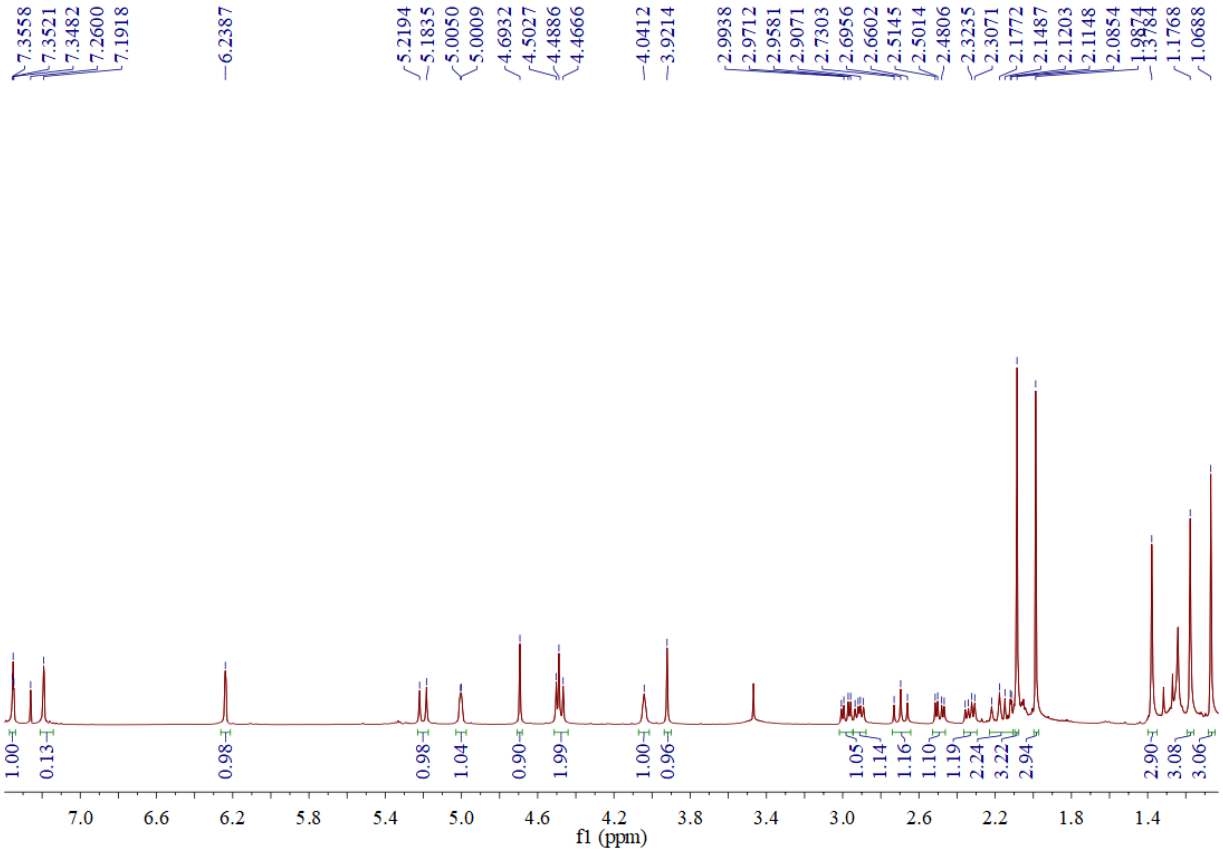


Figure S10. ^{13}C NMR (100 MHz) spectrum of **3** in $CDCl_3$.

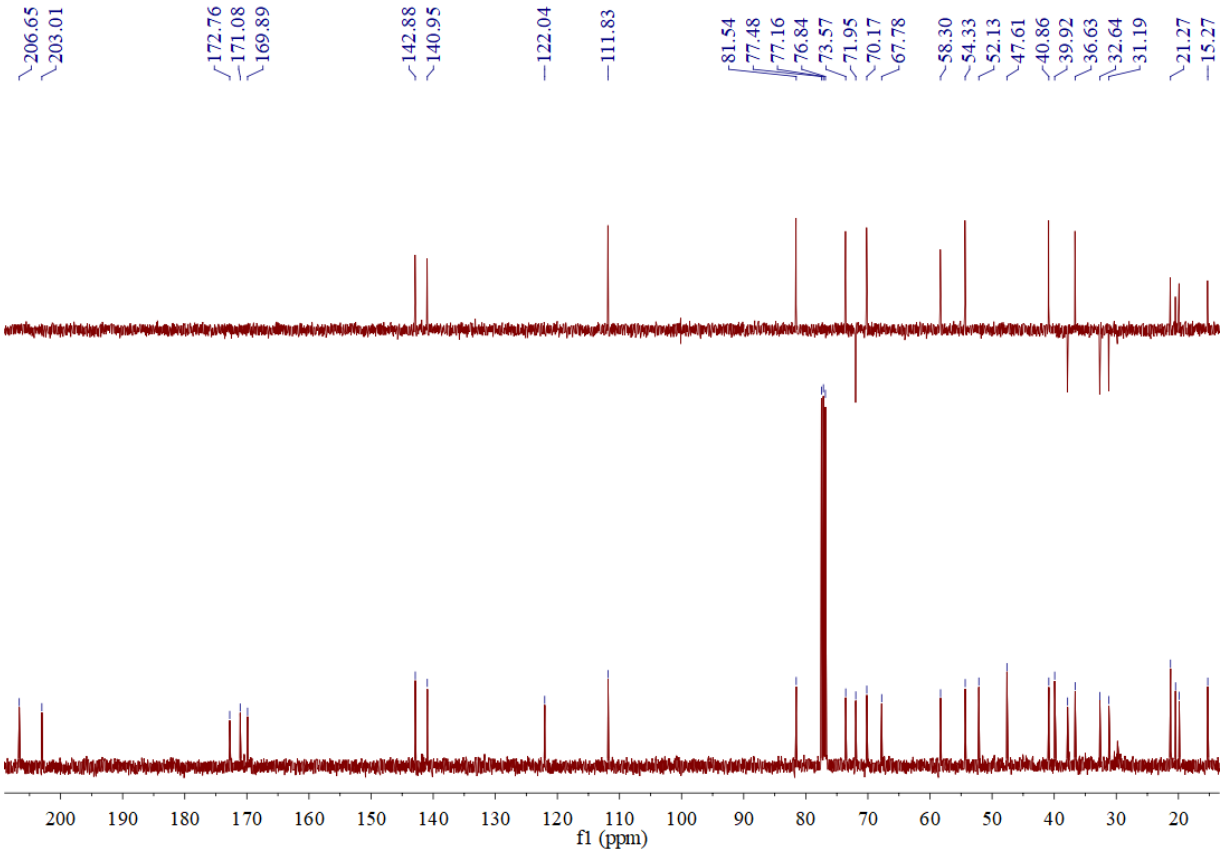


Figure S11. HSQC spectrum of **3** in $CDCl_3$.

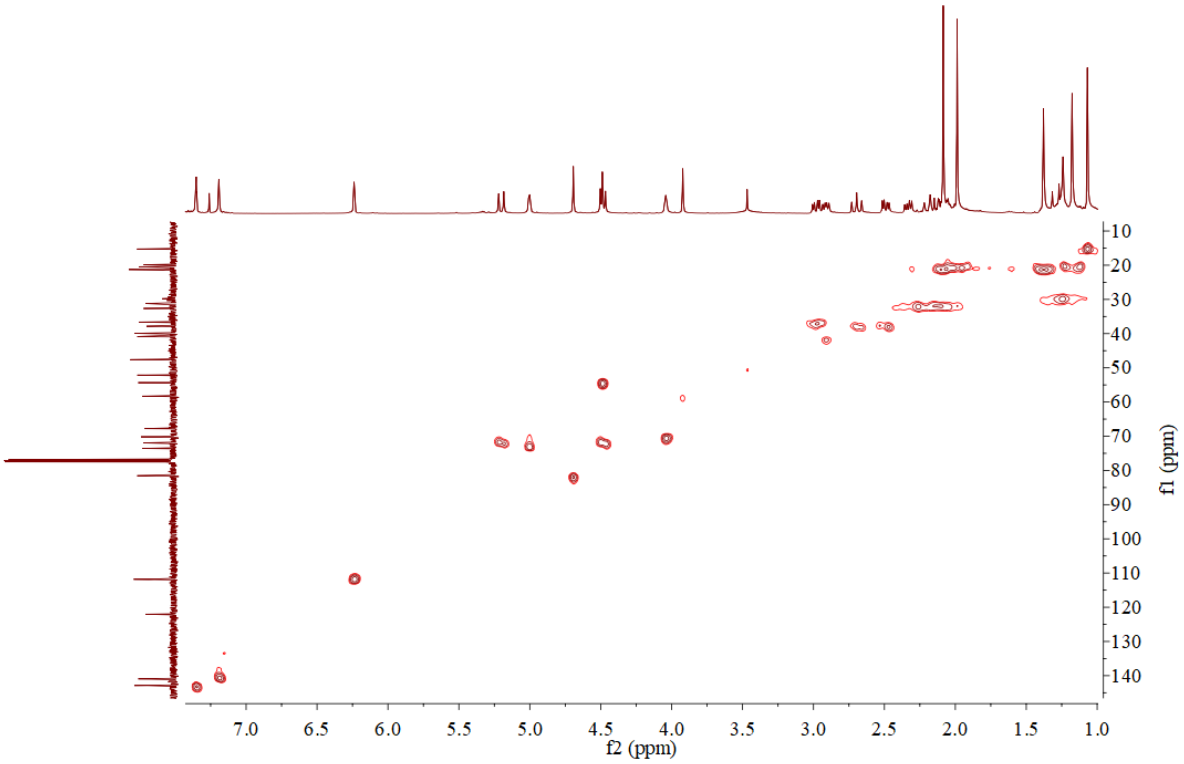


Figure S12. $^{1}H–^{1}H$ COSY spectrum of **3** in $CDCl_3$.

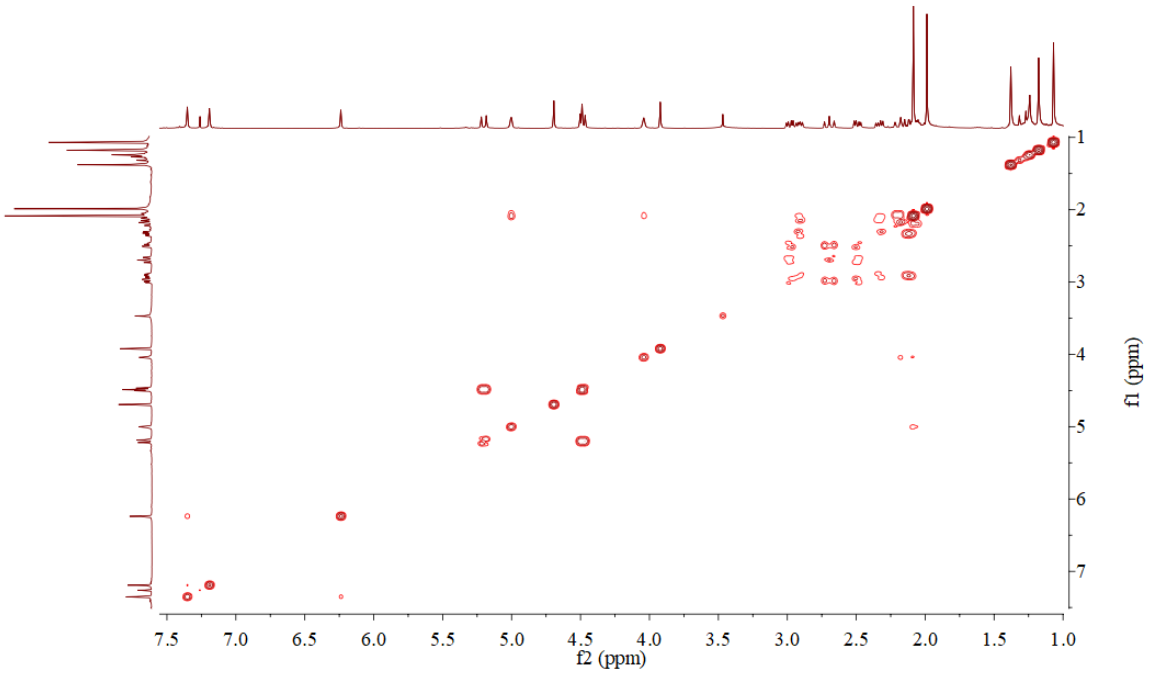


Figure S13. HMBC spectrum of **3** in $CDCl_3$.

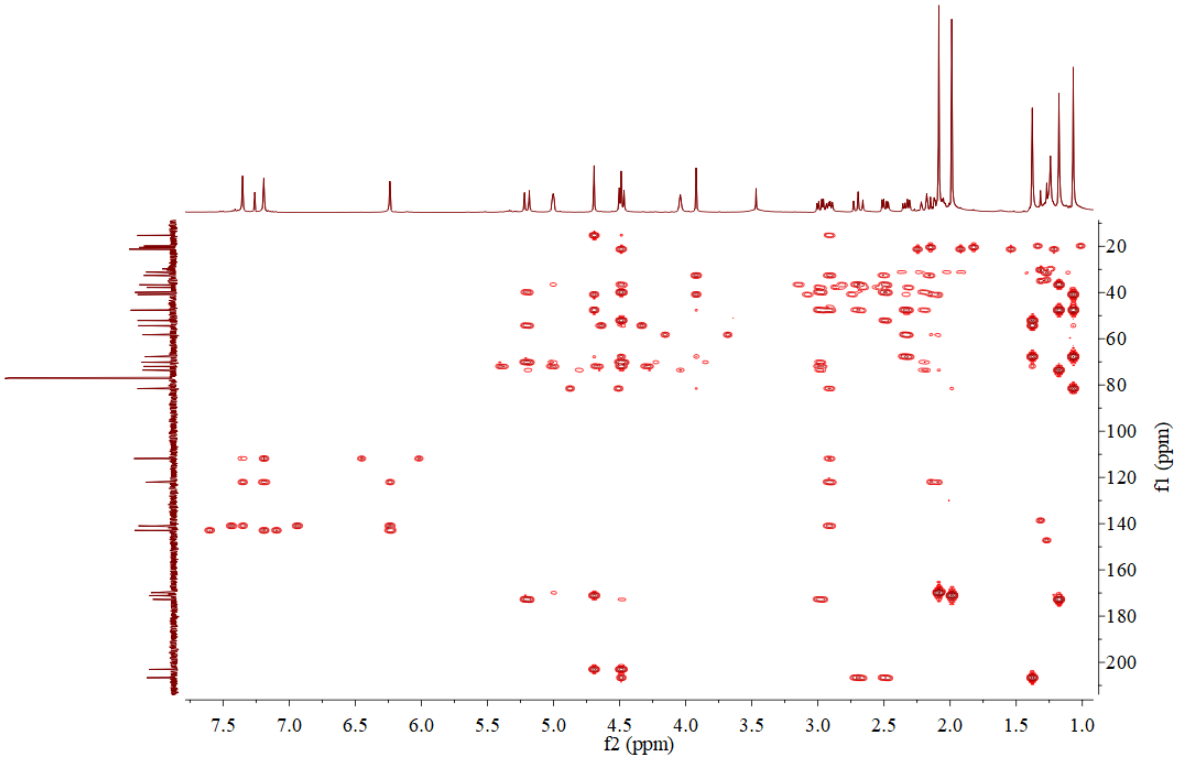
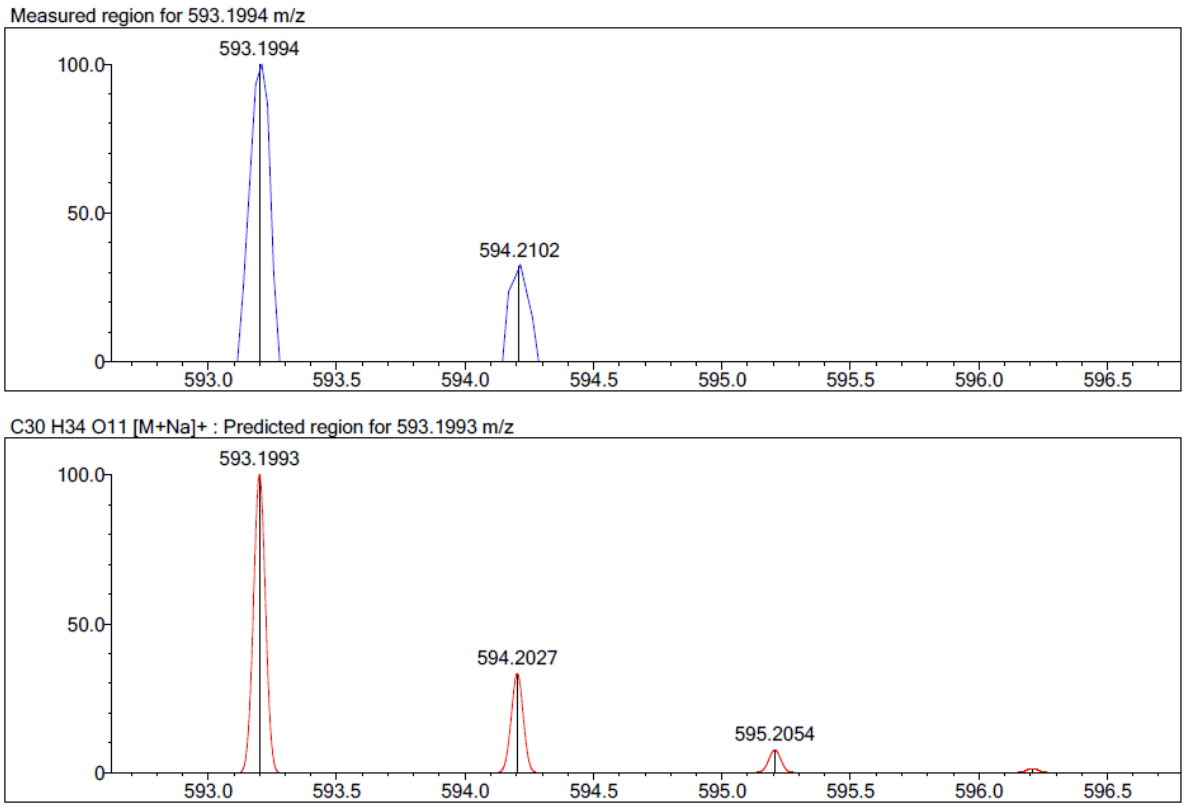


Figure S14. HRESIMS spectrum of **3**.



4. **Figures S15–S20.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **4**.

Figure S15. ^{1}H NMR (400 MHz) spectrum of **4** in pyridine-d_5.

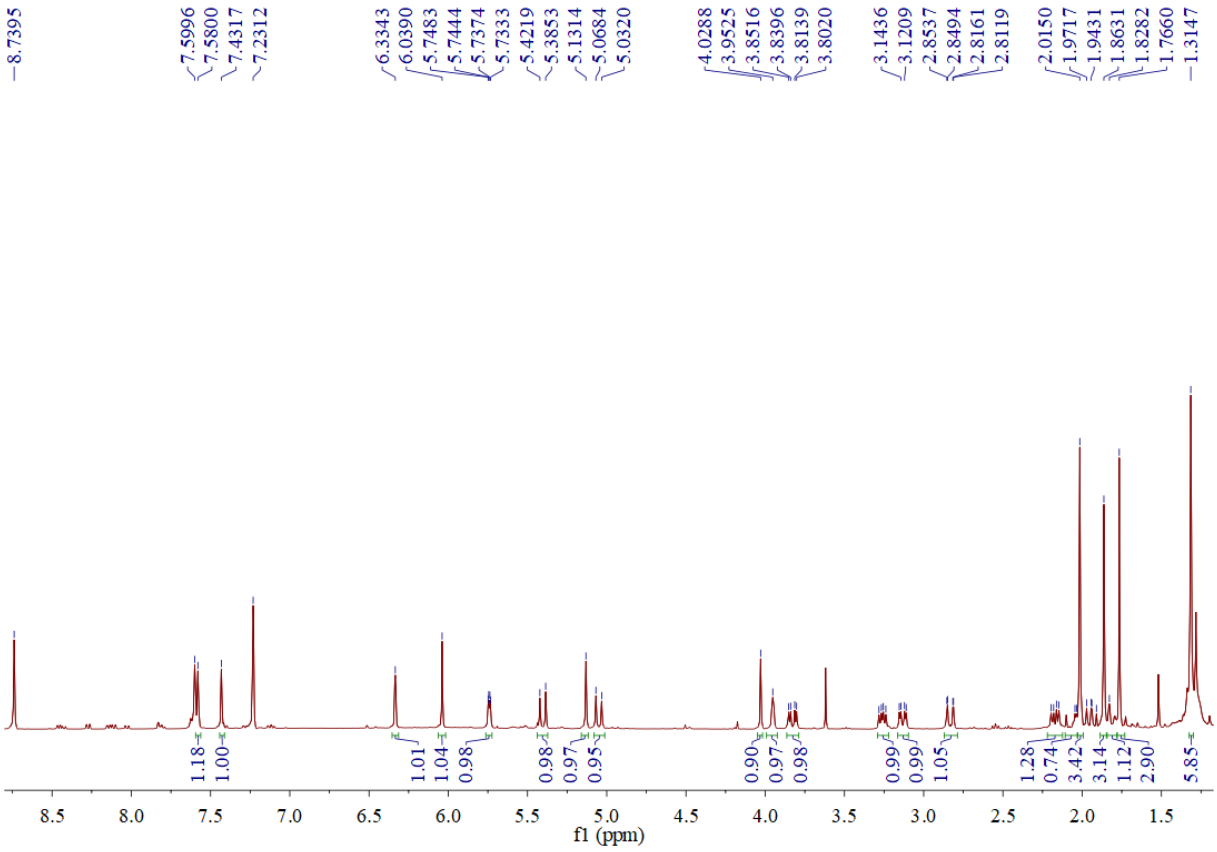


Figure S16. ^{13}C NMR (100 MHz) spectrum of **4** in pyridine-d_5.

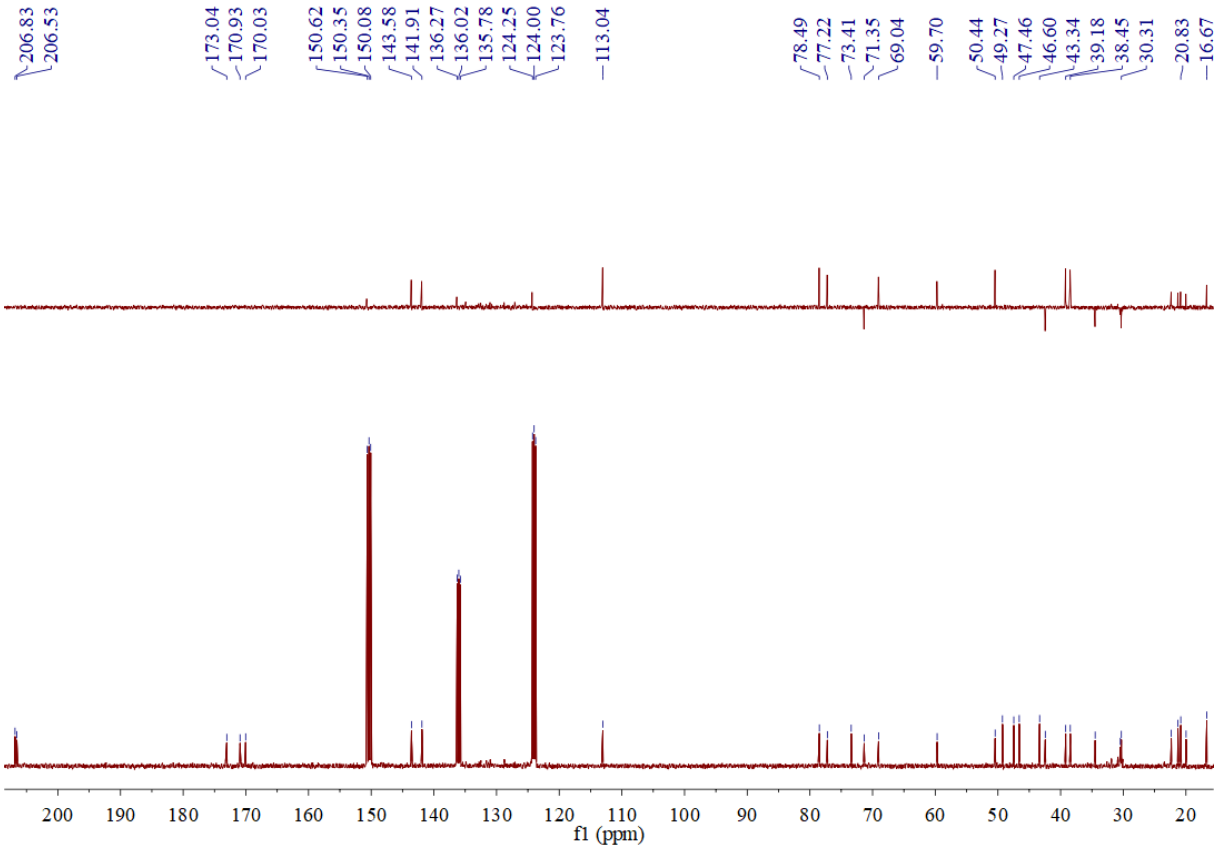


Figure S17. HSQC spectrum of **4** in pyridine-d_5.

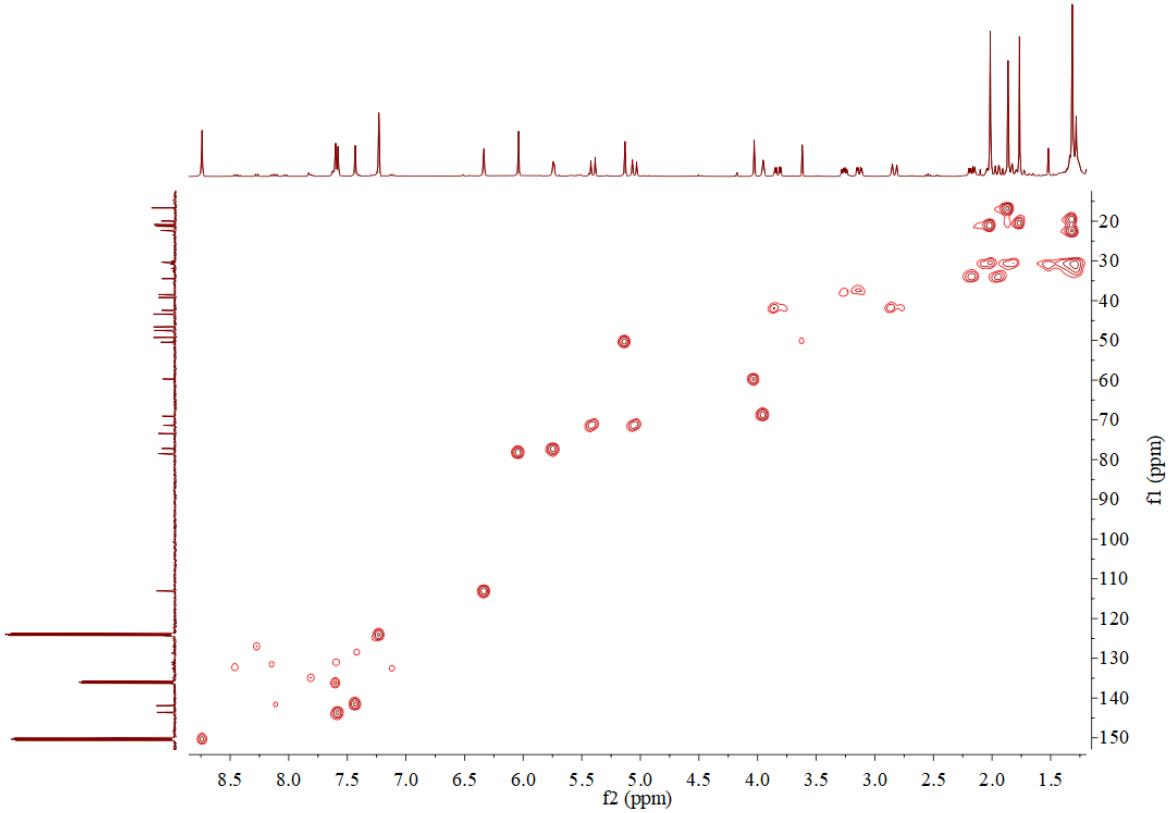


Figure S18. ^{1}H–^{1}H COSY spectrum of **4** in pyridine-d_5.

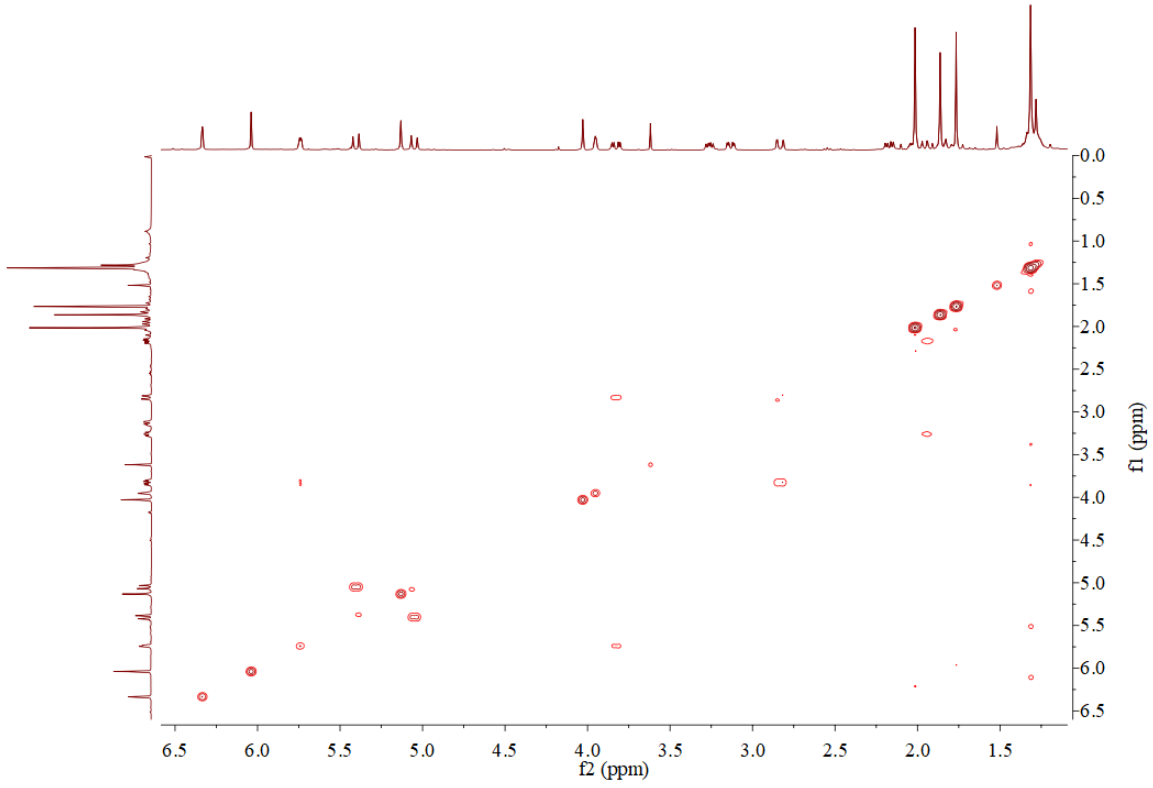


Figure S19. HMBC spectrum of **4** in pyridine-d_5.

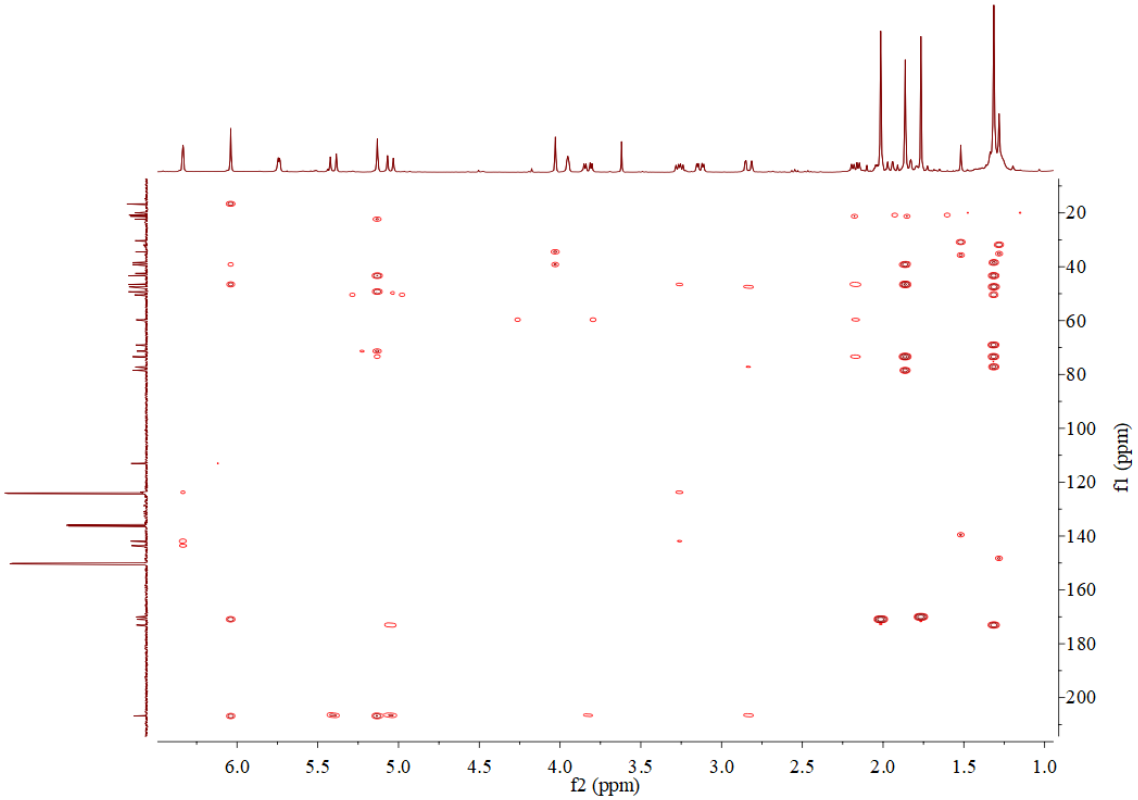
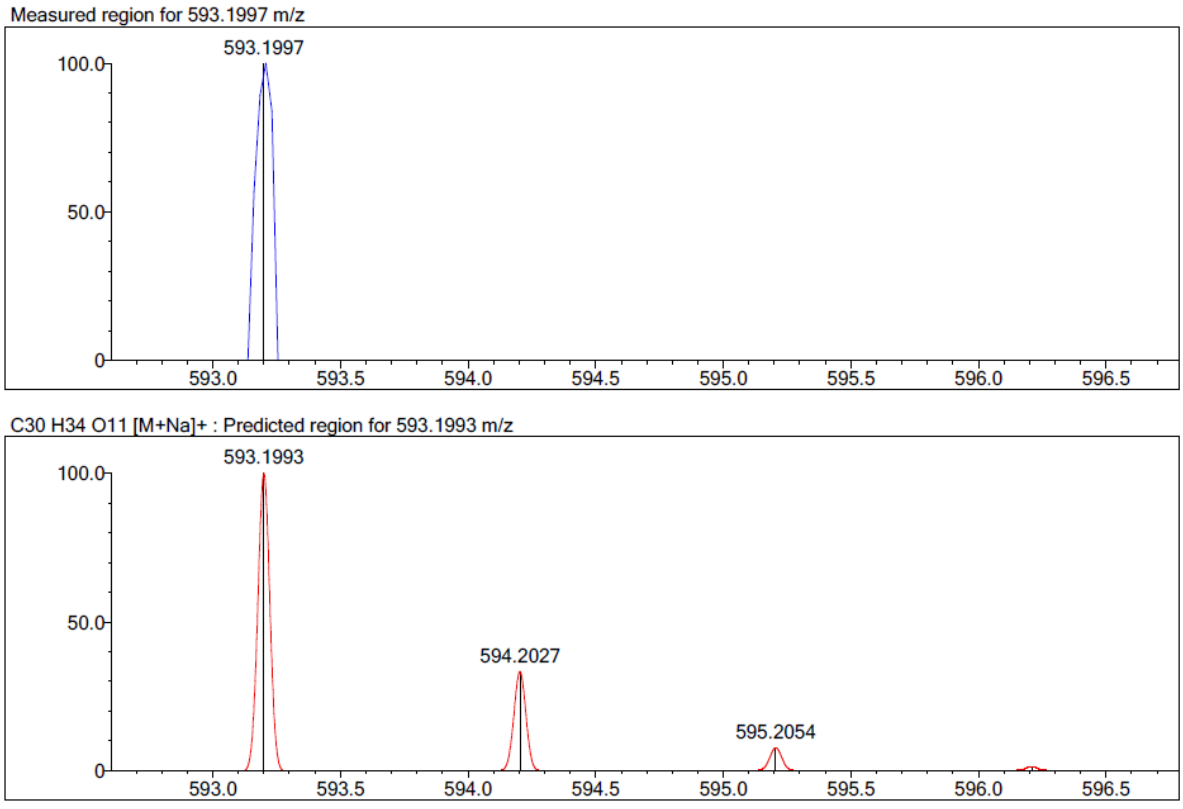


Figure S20. HRESIMS spectrum of **4**.



5. **Figures S21–S26.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **5**.

Figure S21. ^{1}H NMR (400 MHz) spectrum of **5** in $CDCl_3$.

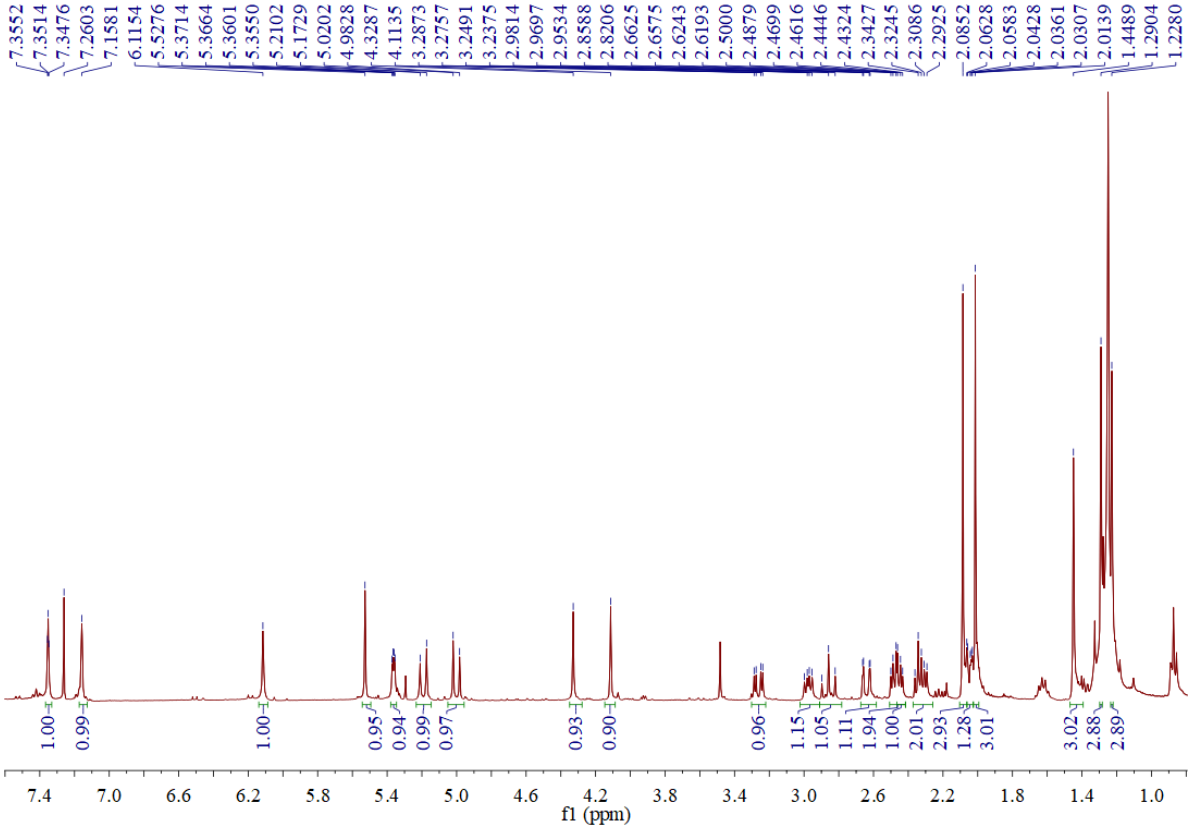


Figure S22. ^{13}C NMR (100 MHz) spectrum of **5** in $CDCl_3$.

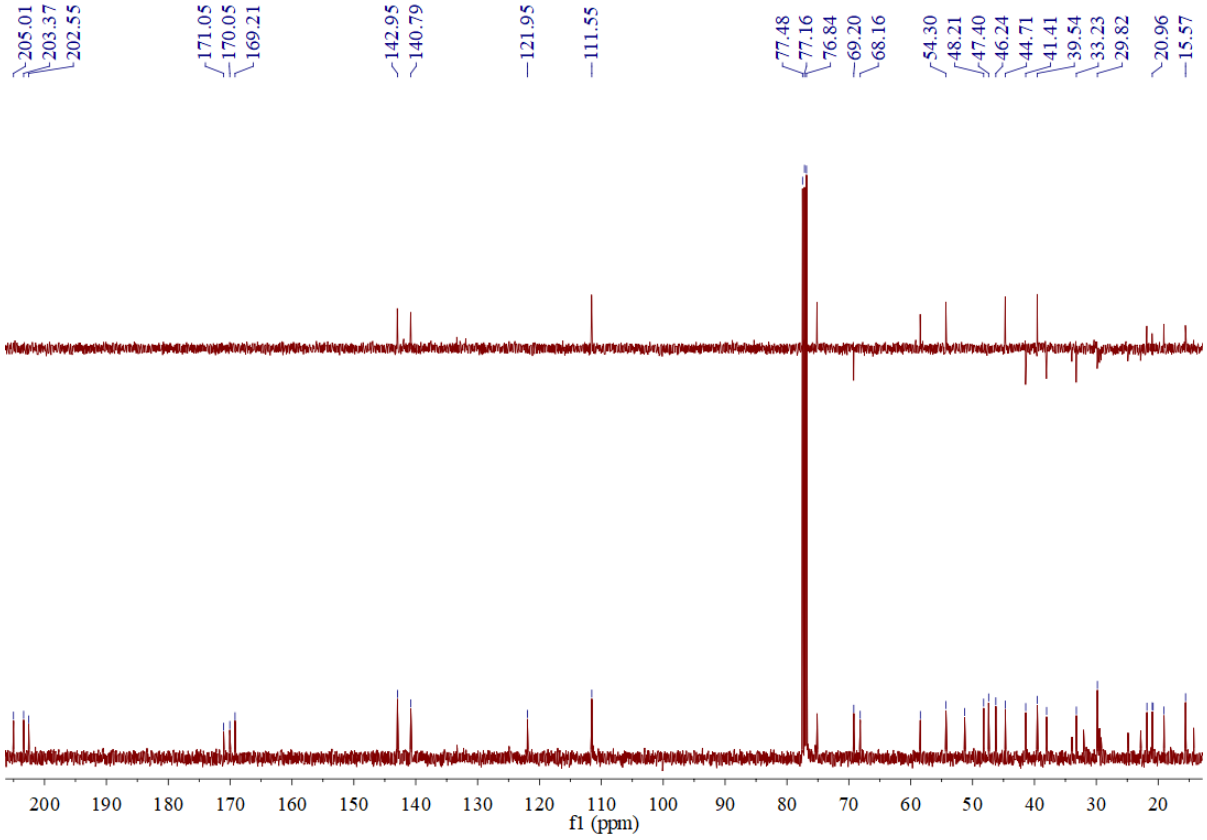


Figure S23. HSQC spectrum of **5** in $CDCl_3$.

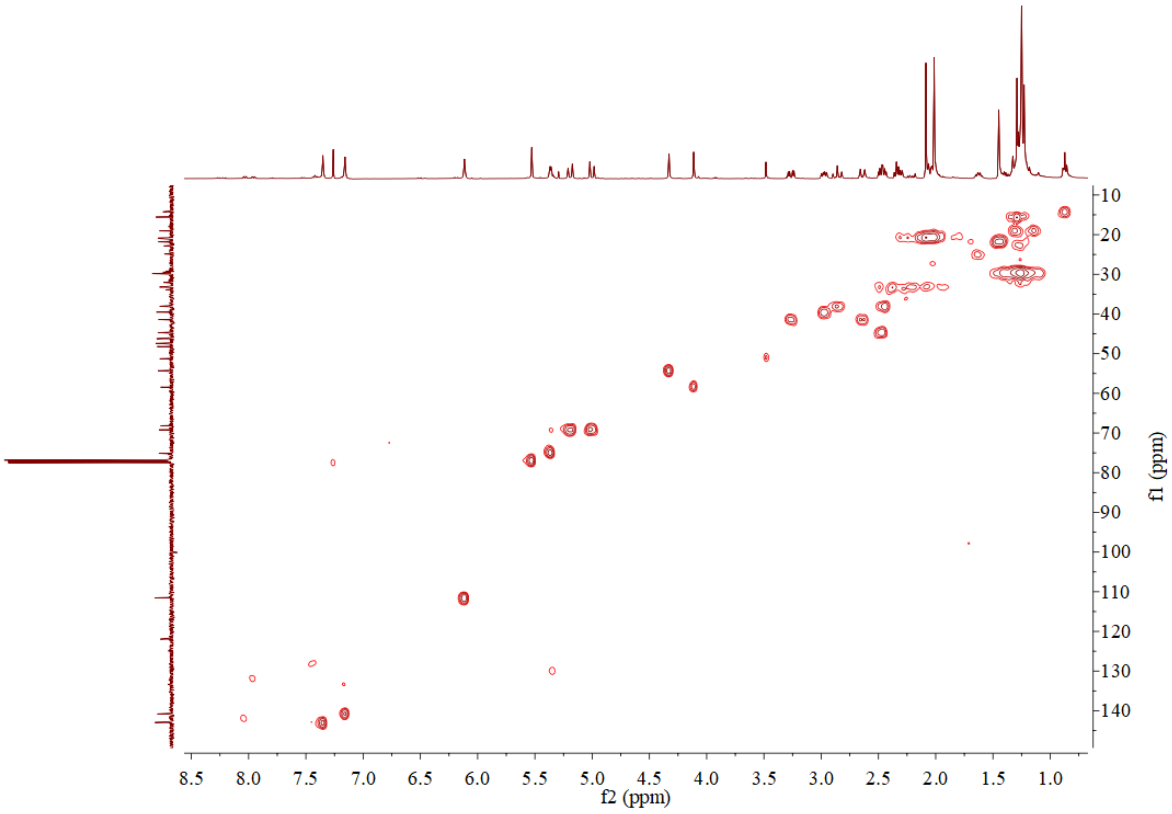


Figure S24. $^{1}H–^{1}H$ COSY spectrum of **5** in $CDCl_3$.

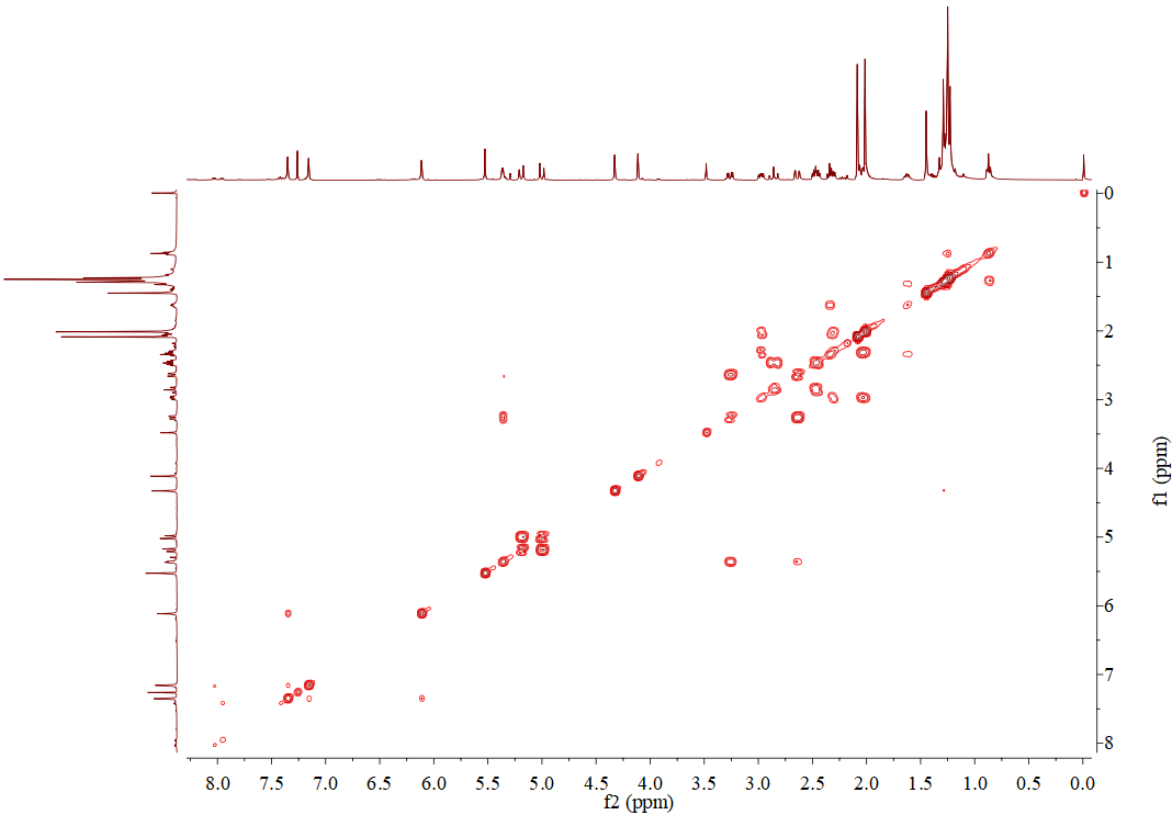


Figure S25. HMBC spectrum of **5** in $CDCl_3$.

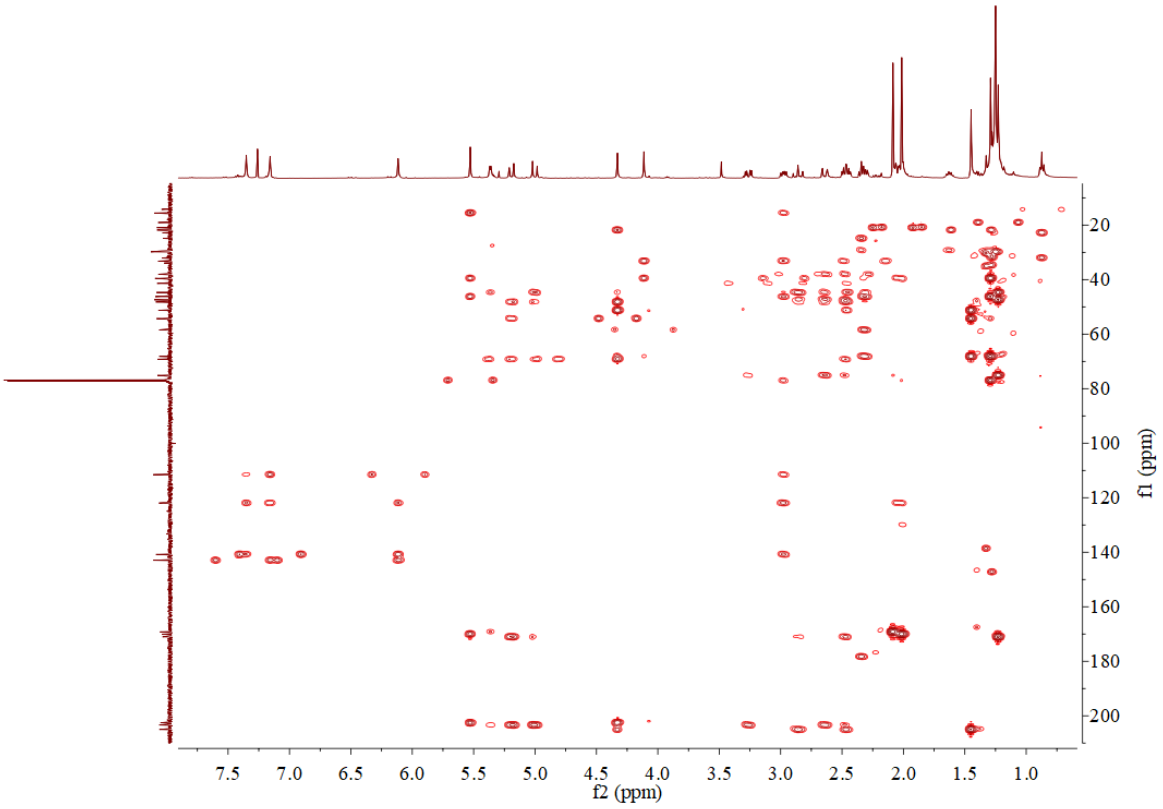
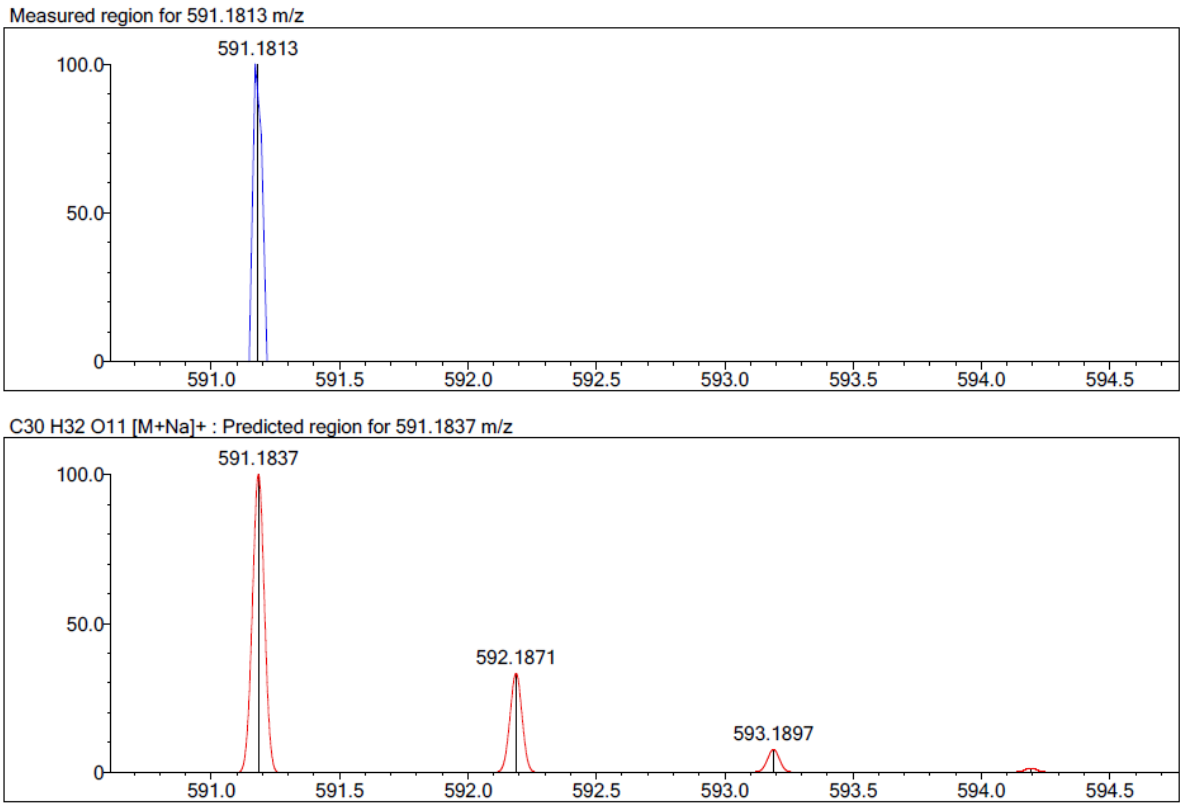


Figure S26. HRESIMS spectrum of **5**.



6. **Figures S27–S28.** ^{1}H NMR and ^{13}C NMR spectra of **6**.

Figure S27. ^{1}H NMR (500 MHz) spectrum of **6** in $CDCl_3$.

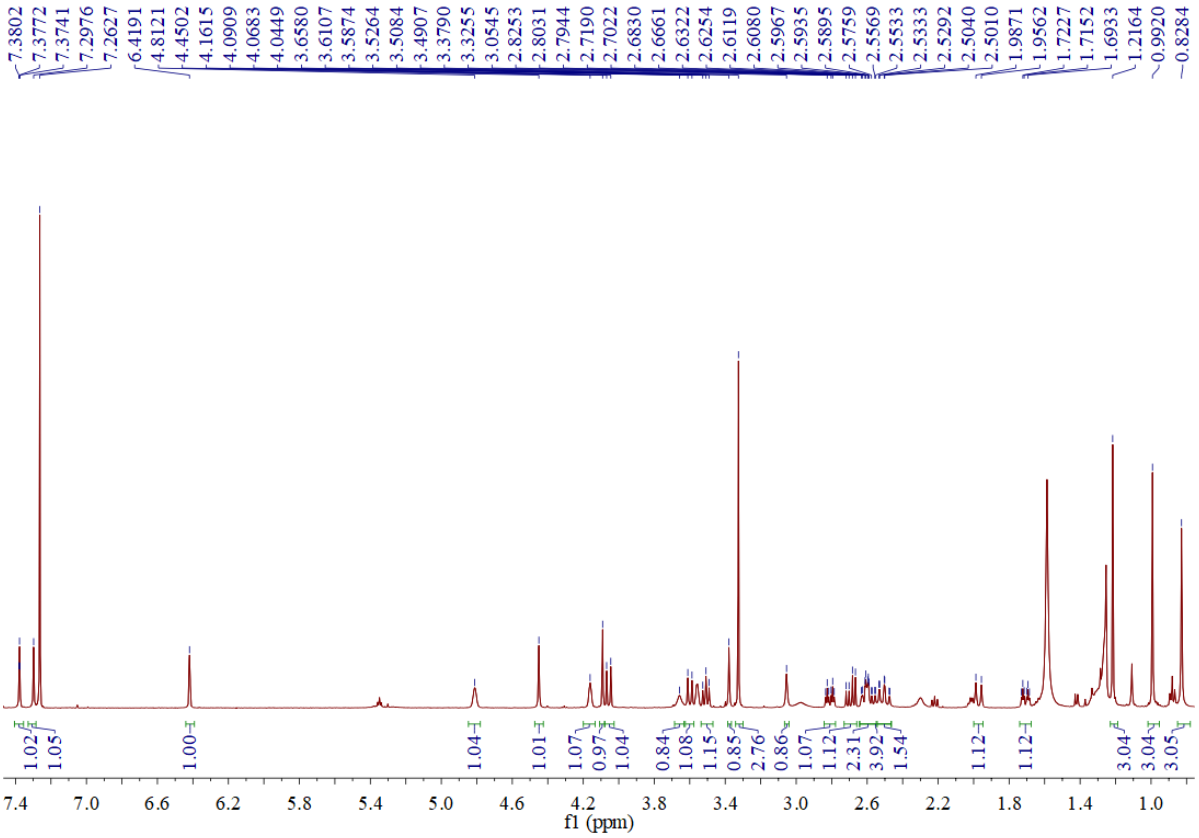
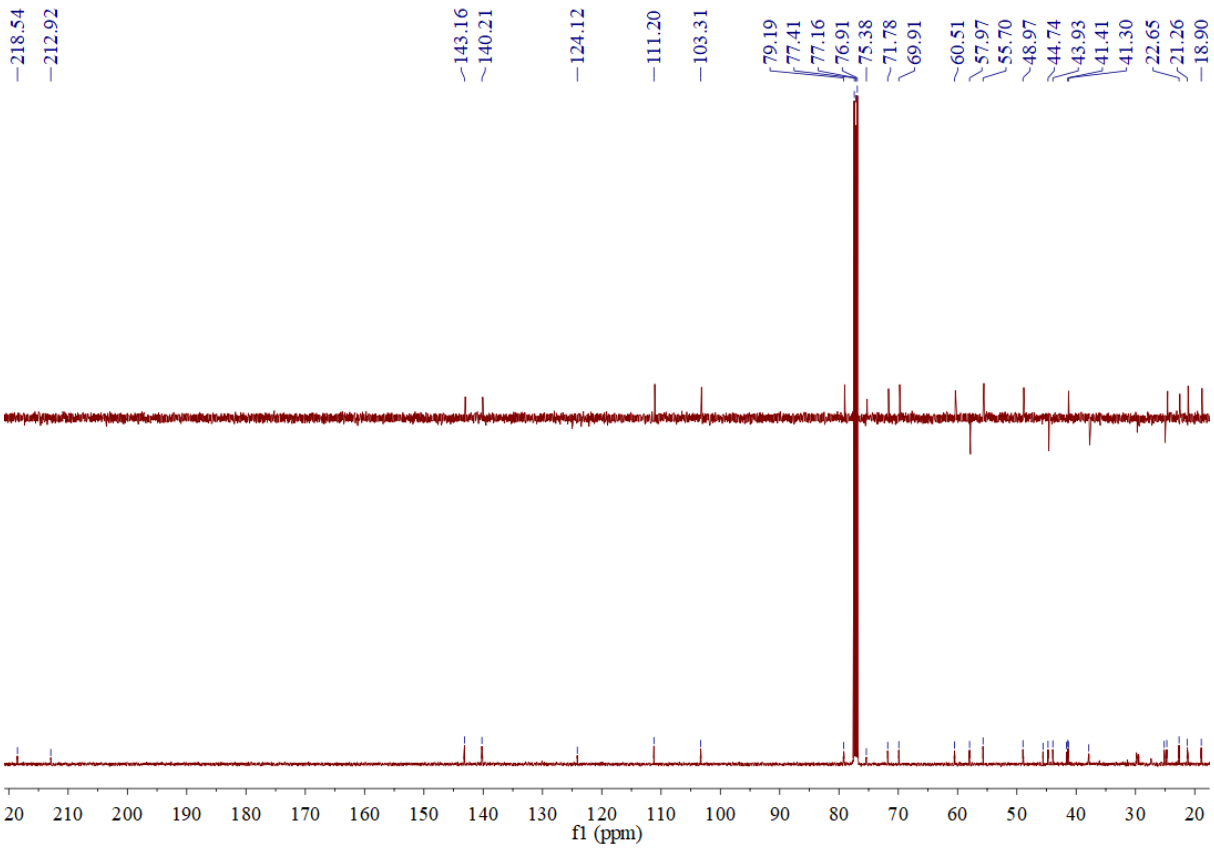


Figure S28. ^{13}C NMR (125 MHz) spectrum of **6** in $CDCl_3$.



7. **Figures S29–S30.** ^{1}H NMR and ^{13}C NMR spectra of **7**.

Figure S29. ^{1}H NMR (400 MHz) spectrum of **7** in pyridine-d_5.

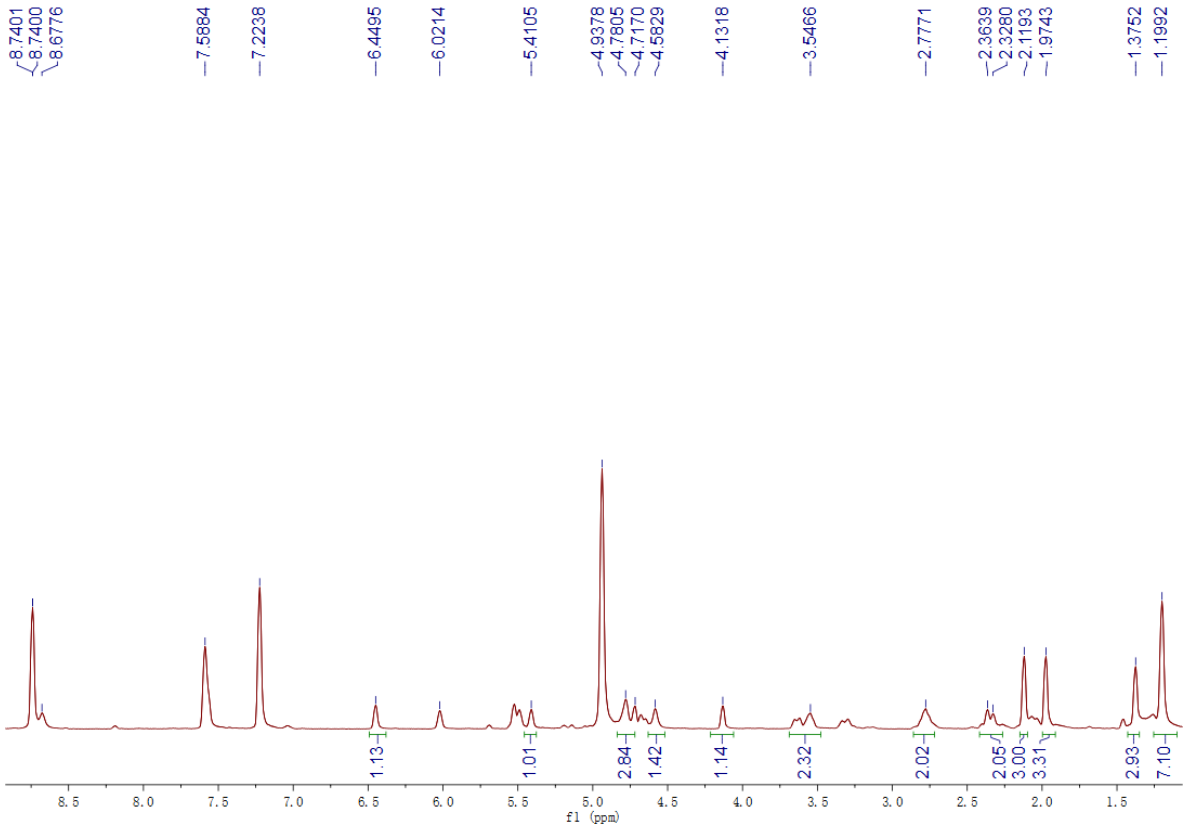
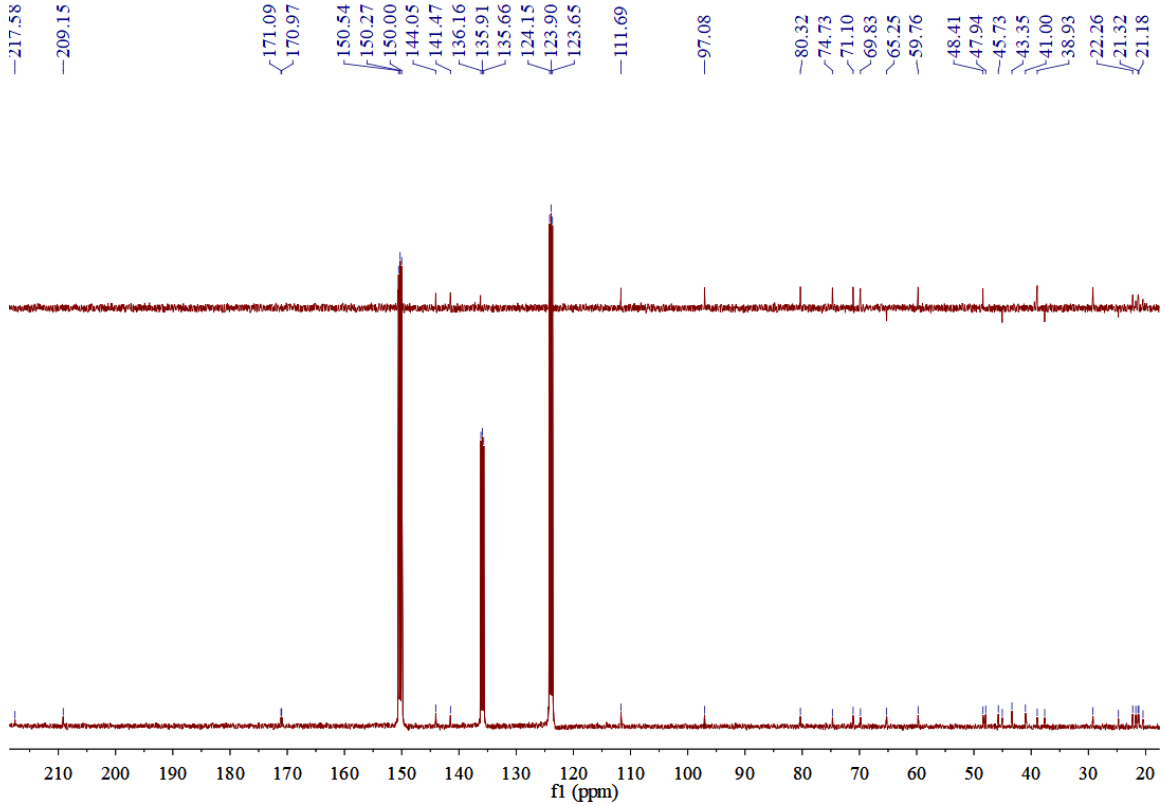


Figure S30. ^{13}C NMR (100 MHz) spectrum of **7** in pyridine-d_5.



8. **Figures S31–S32.** ^{1}H NMR and ^{13}C NMR spectra of **8**.

Figure S31. ^{1}H NMR (400 MHz) spectrum of **8** in $CDCl_3$.

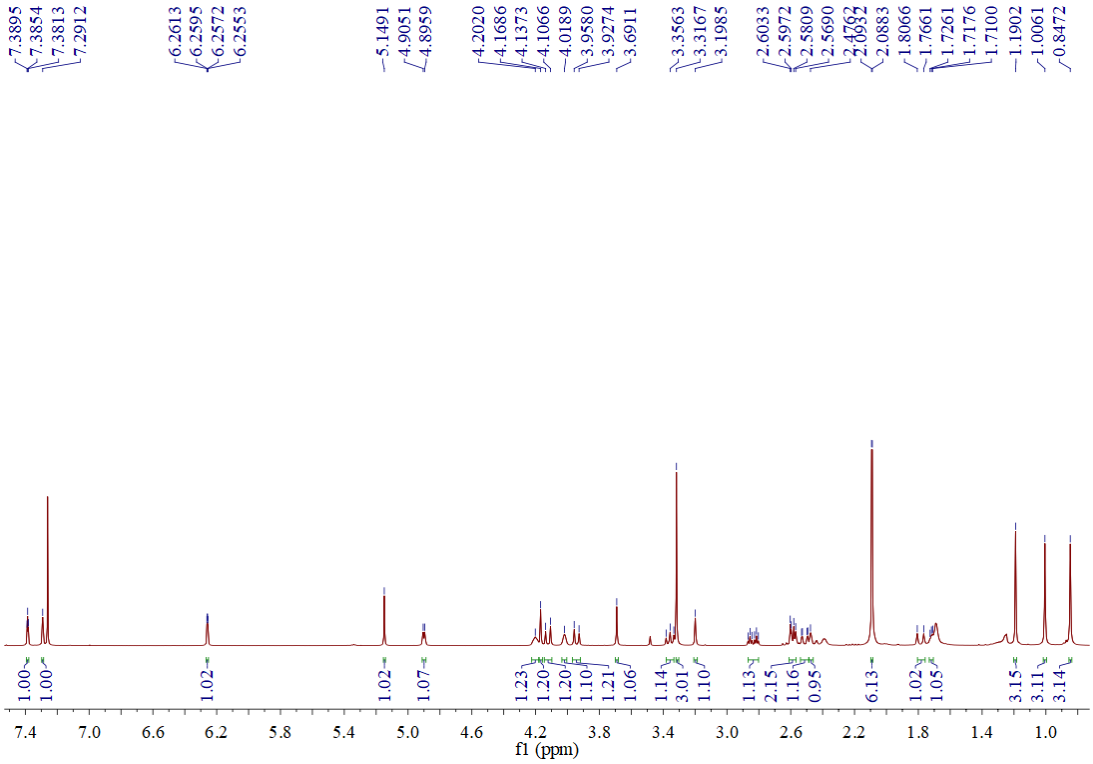
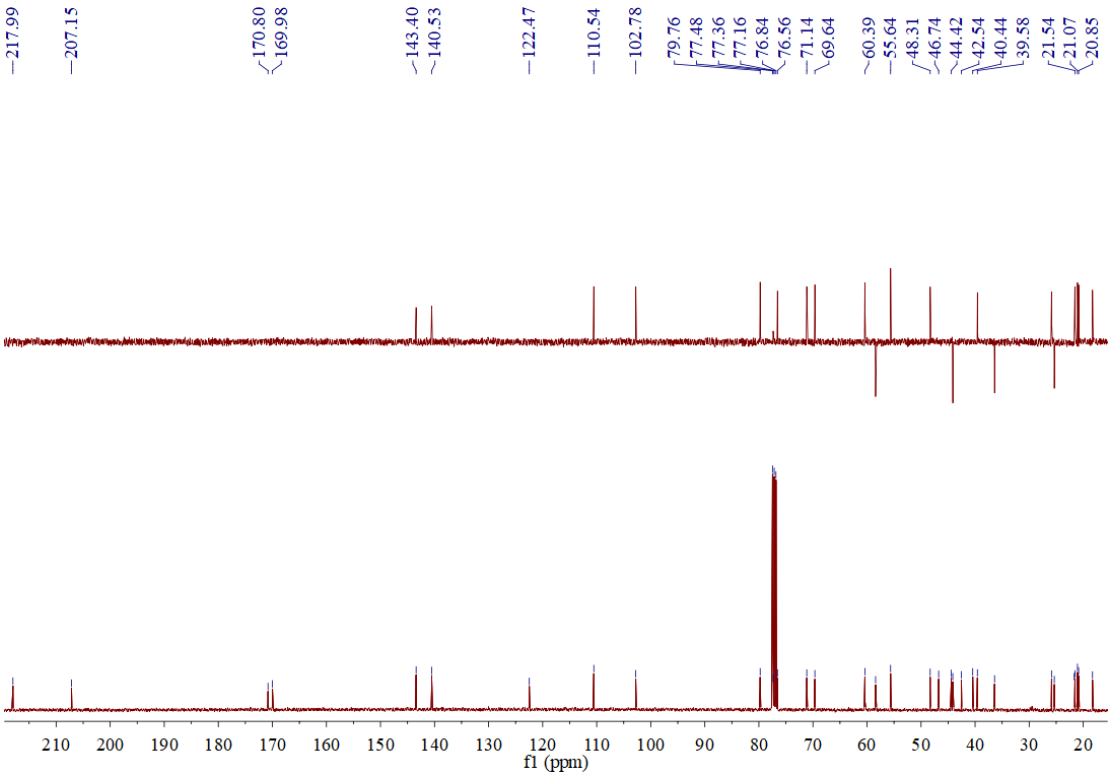


Figure S32. ^{13}C NMR spectra of **8** in $CDCl_3$.



9. **Figures S33–S38.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **9**.

Figure S33. ^{1}H NMR (400 MHz) spectrum of **9** in $CDCl_3$.

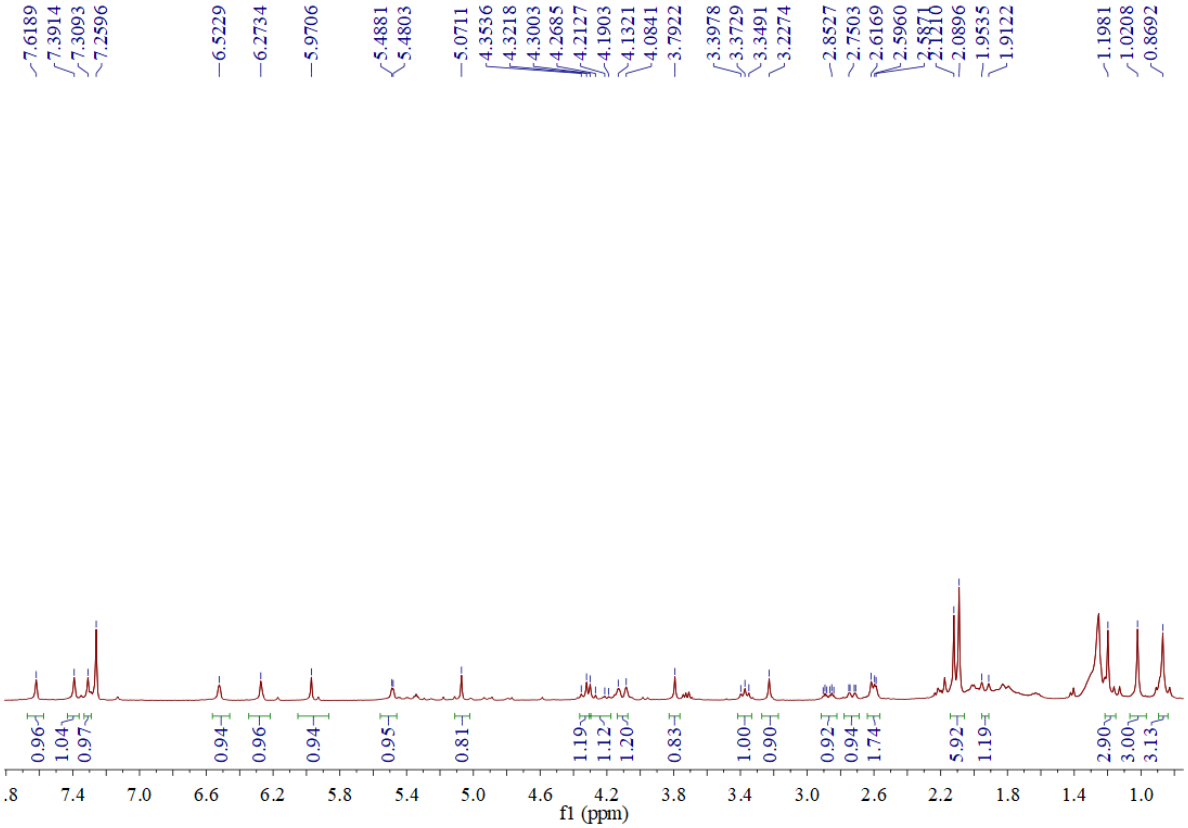


Figure S34. ^{13}C NMR (100 MHz) spectrum of **9** in $CDCl_3$.

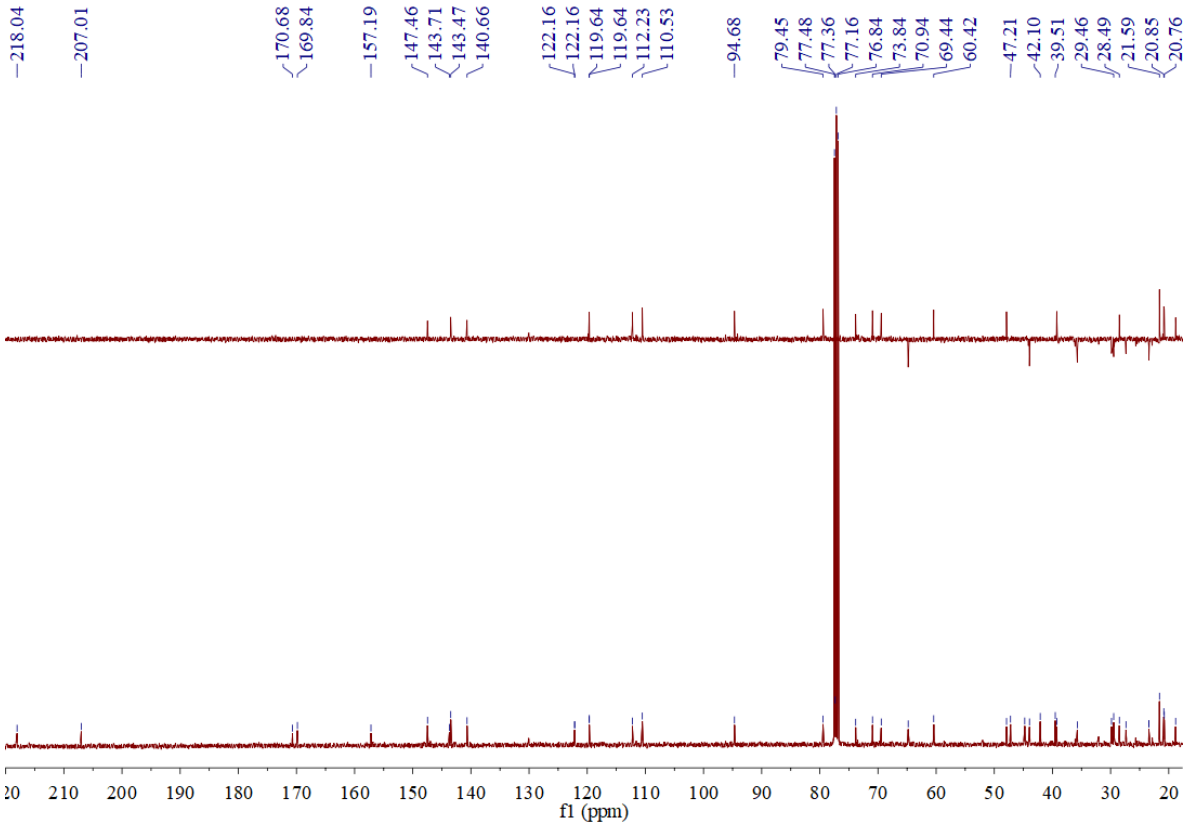


Figure S35. HSQC spectrum of **9** in $CDCl_3$.

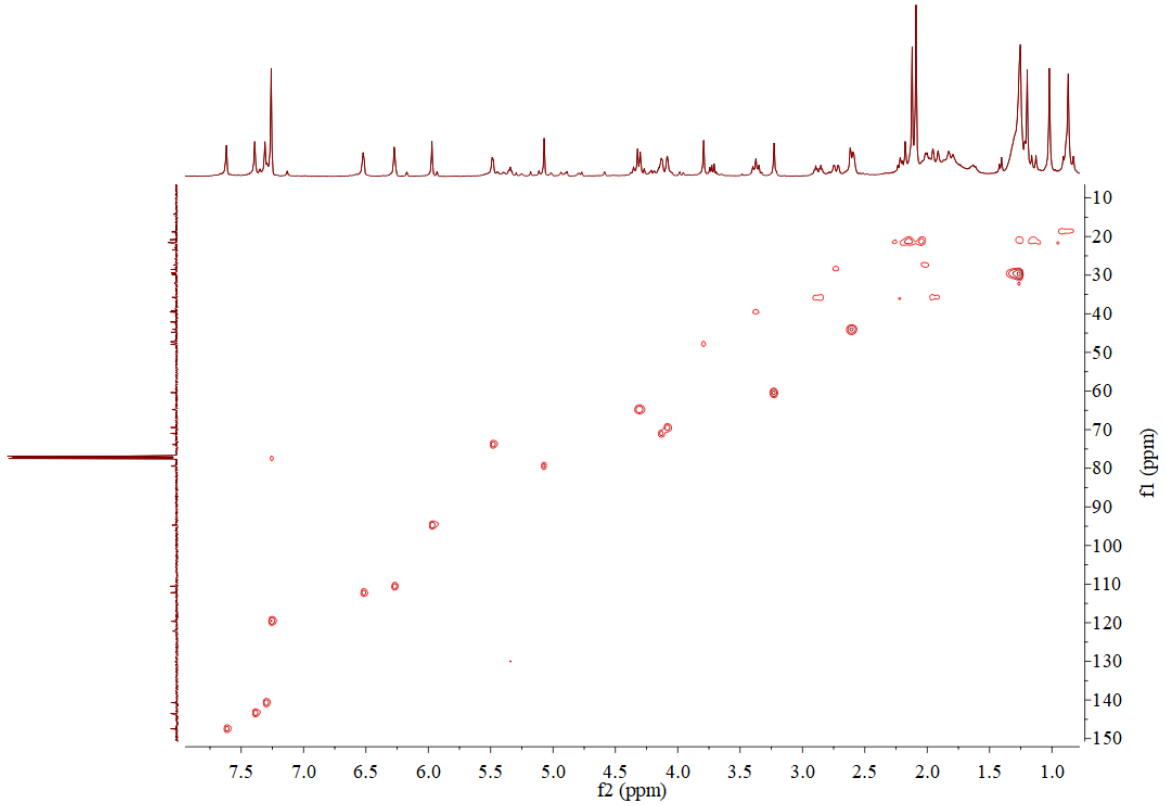


Figure S36. $^{1}H–^{1}H$ COSY spectrum of **9** in $CDCl_3$.

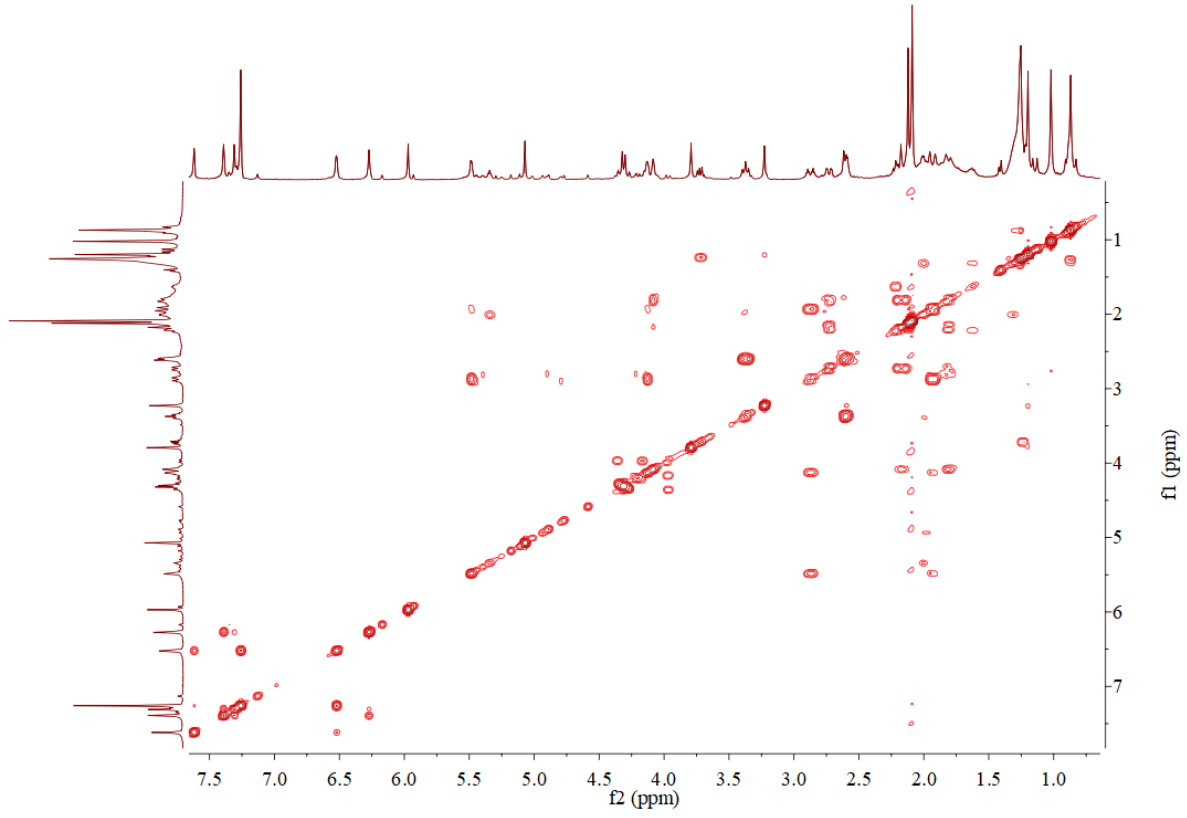


Figure S37. HMBC spectrum of **9** in $CDCl_3$.

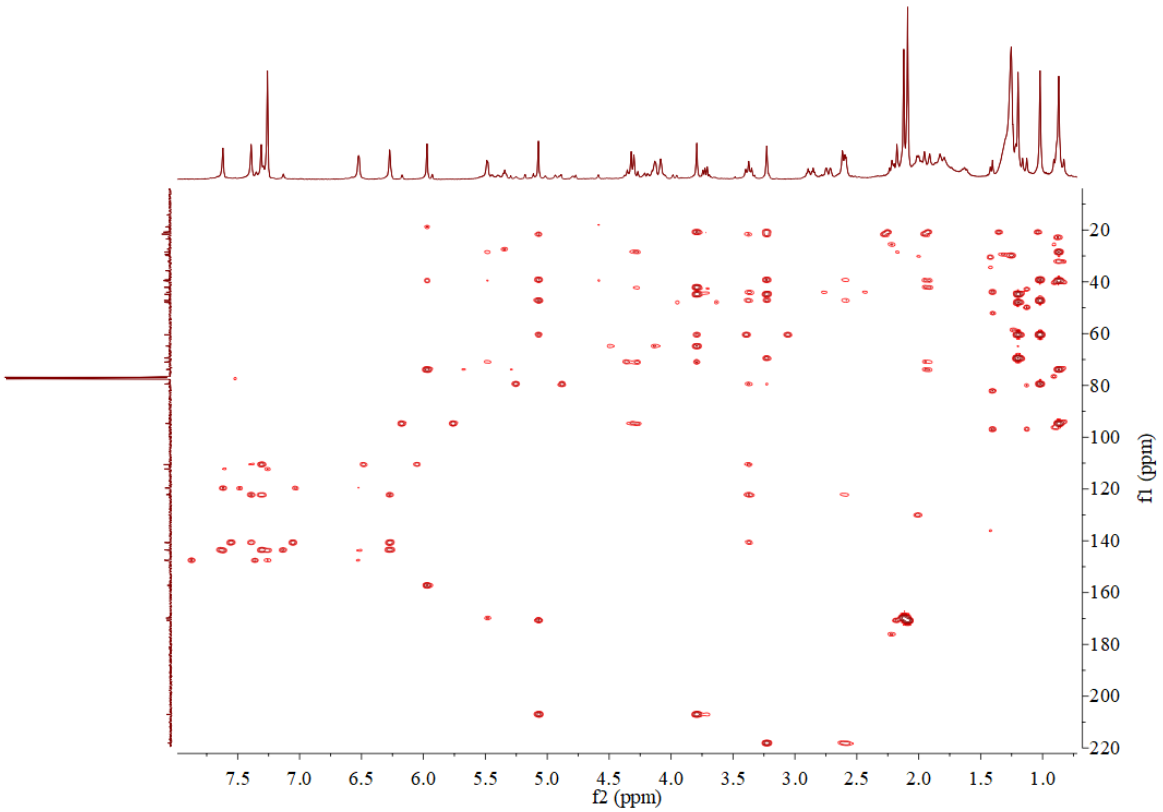
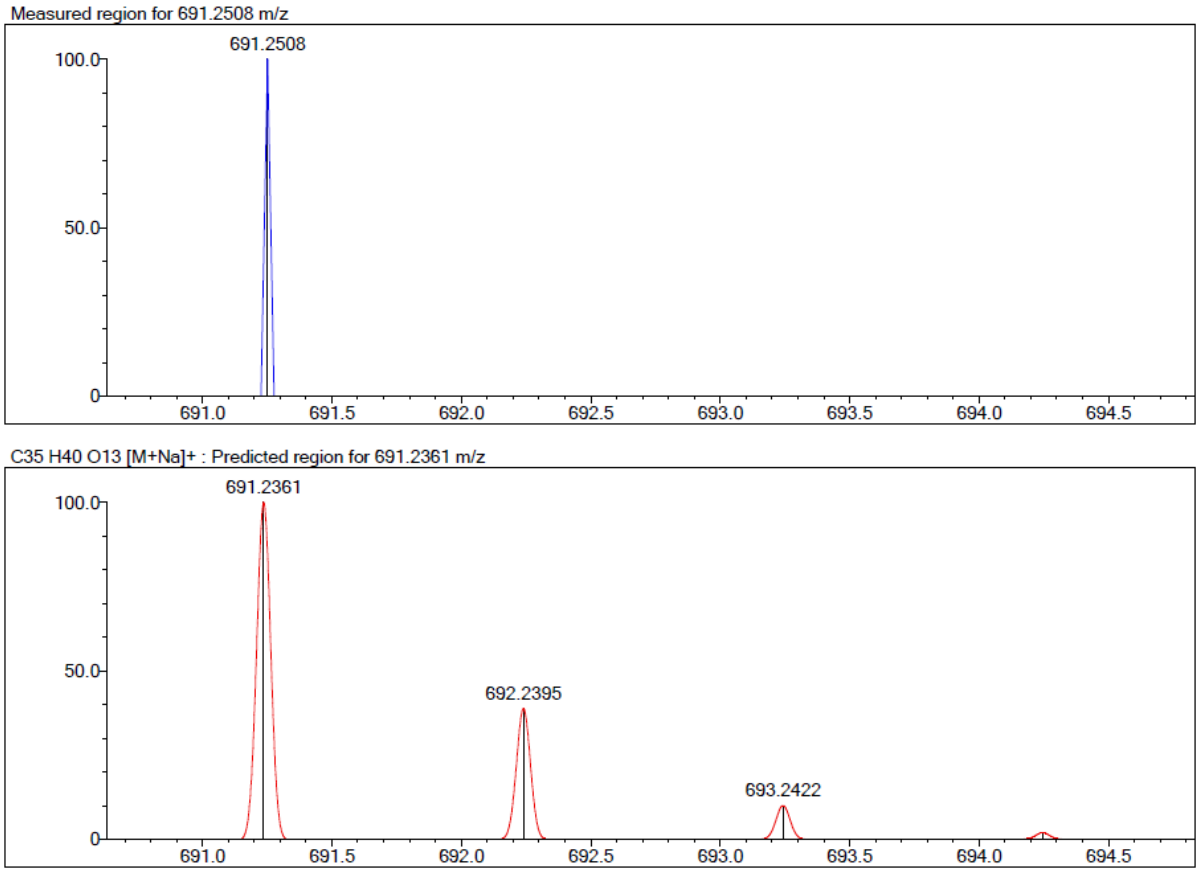


Figure S38. HRESIMS spectrum of **9**.



10. **Figures S39–S44.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **10**.

Figure S39. ^{1}H NMR (400 MHz) spectrum of **10** in $CDCl_3$.

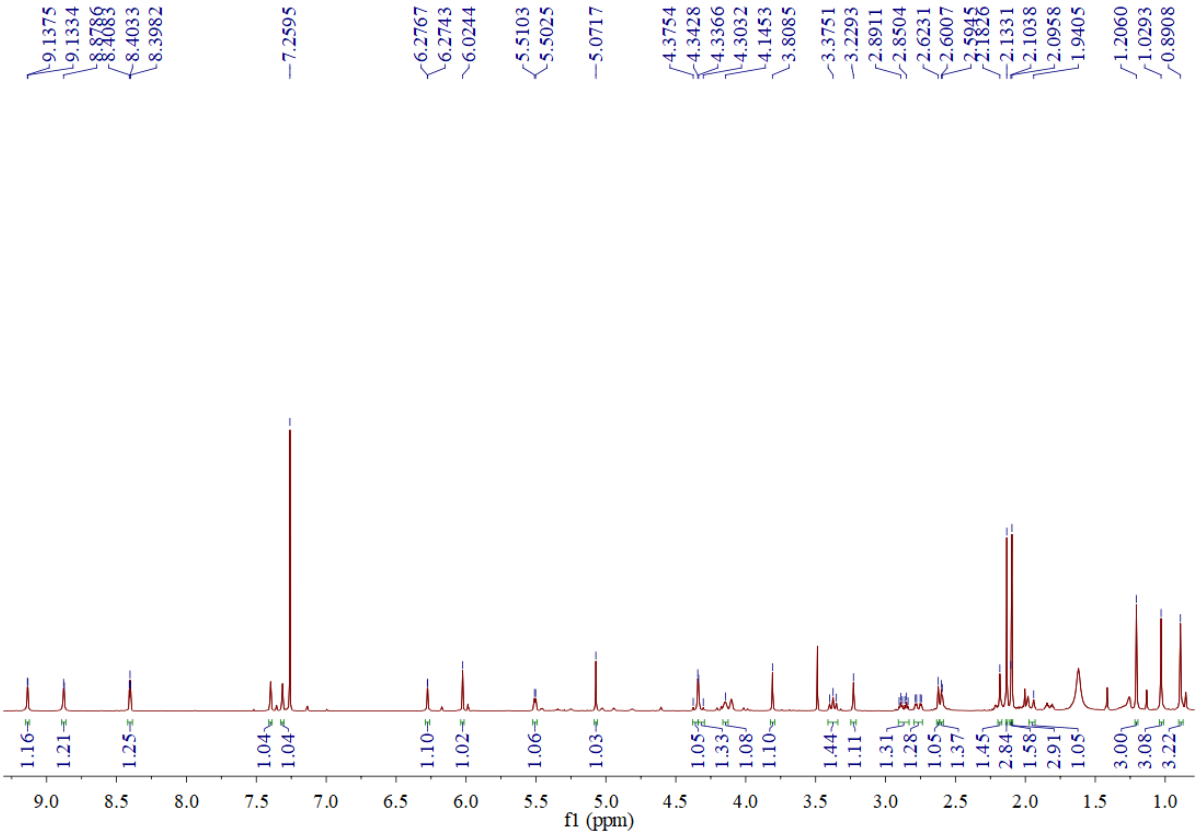


Figure S40. ^{13}C NMR (100 MHz) spectrum of **10** in $CDCl_3$.

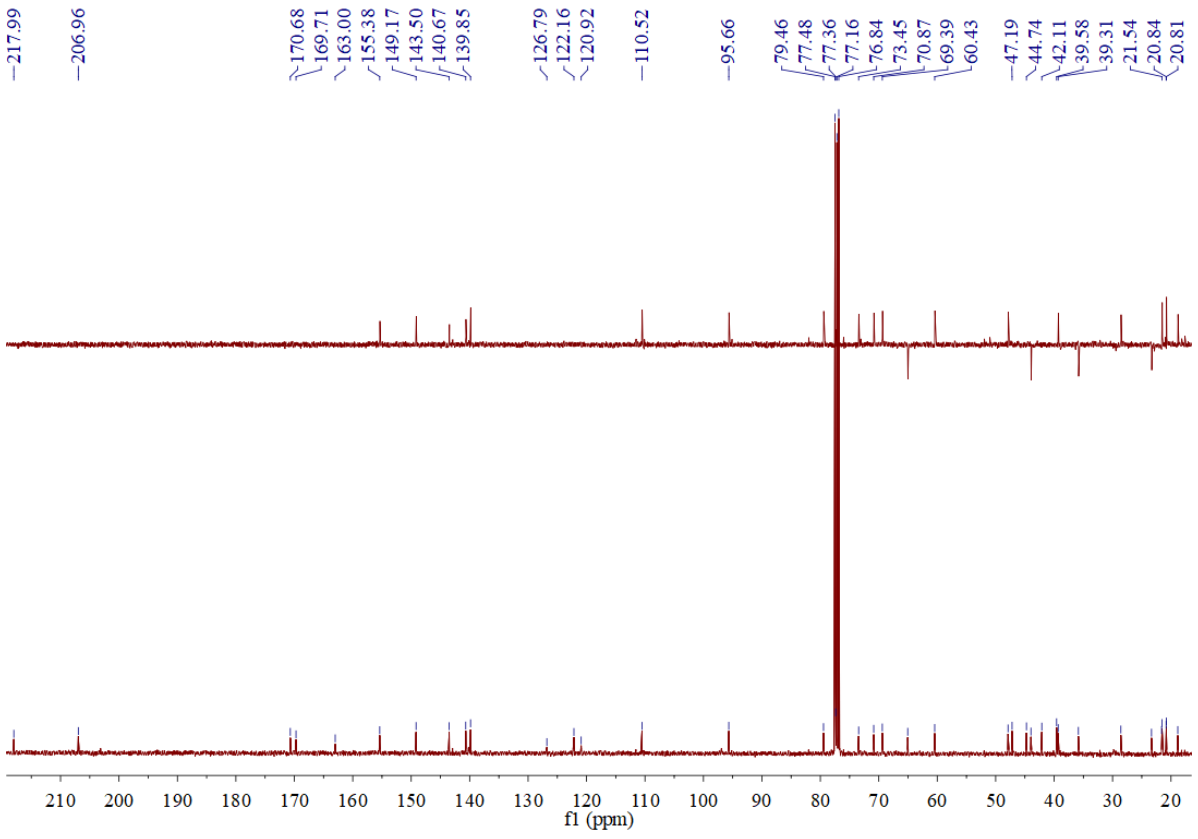


Figure S41. HSQC spectrum of **10** in $CDCl_3$.

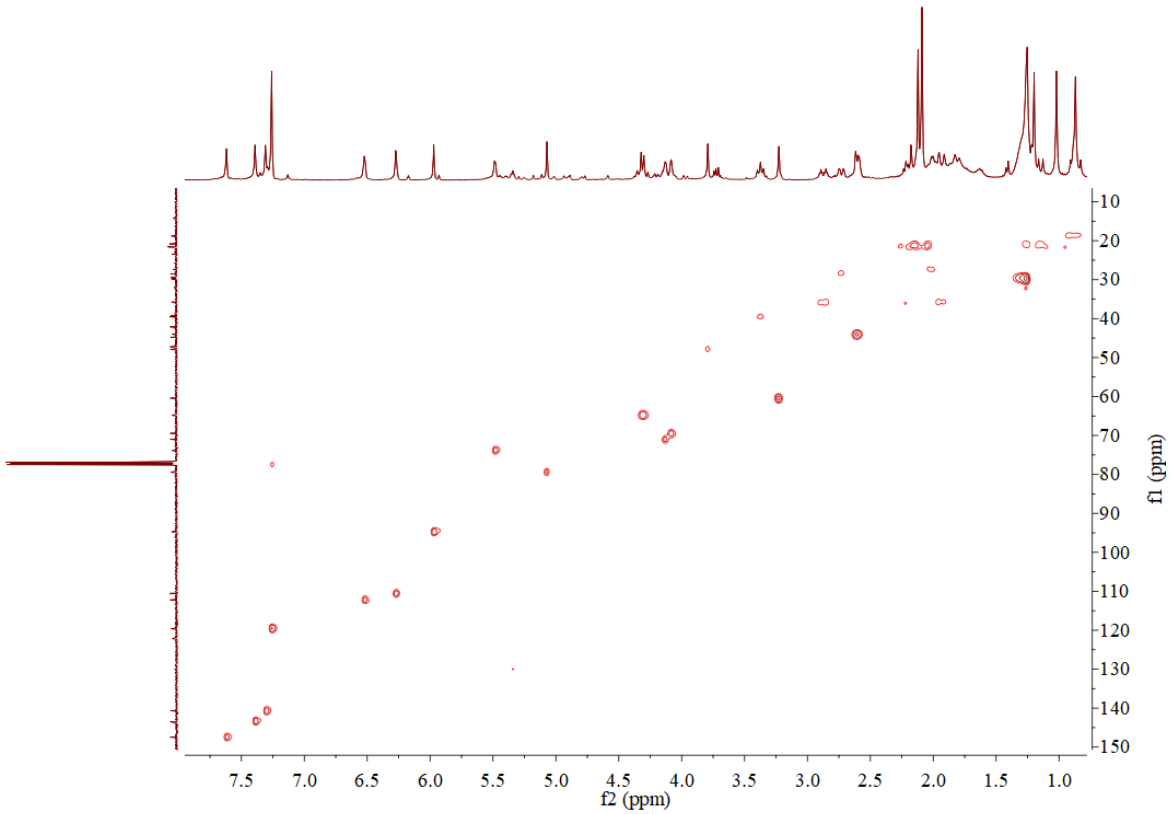


Figure S42. ^{1}H–^{1}H COSY spectrum of **10** in $CDCl_3$.

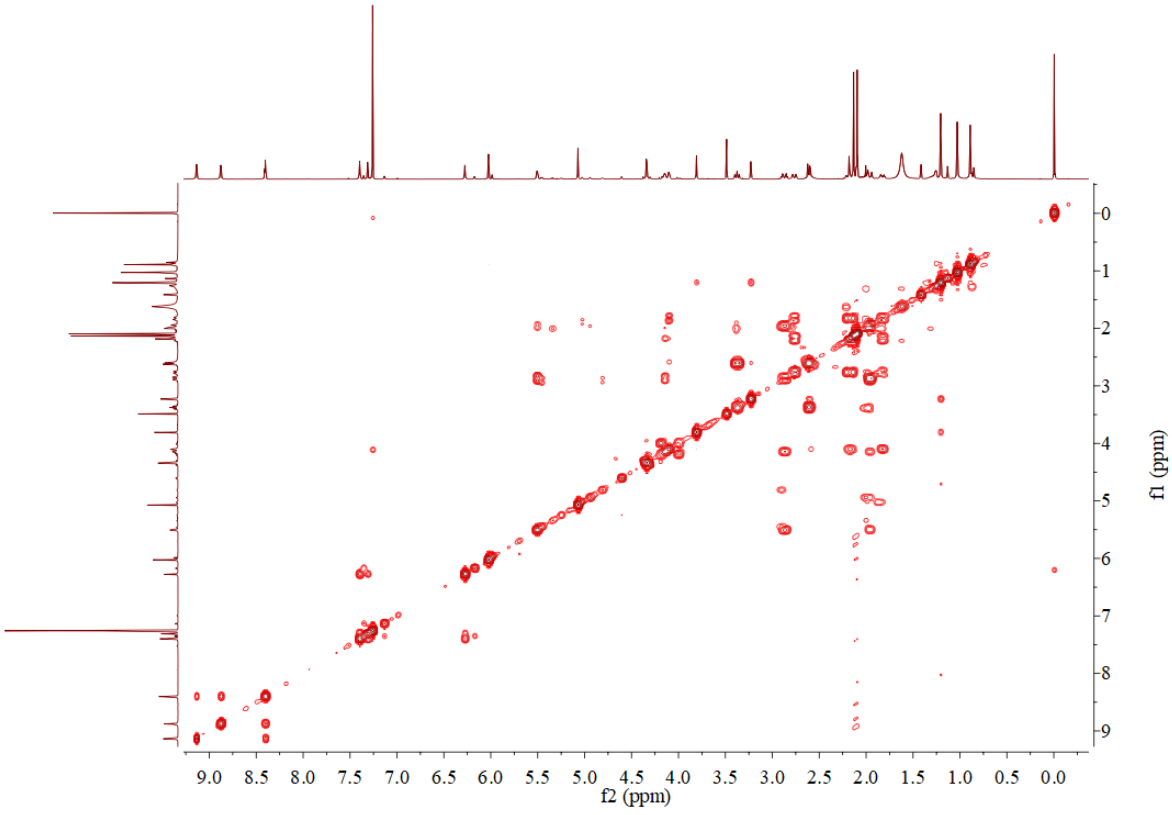


Figure S43. HMBC spectrum of **10** in $CDCl_3$.

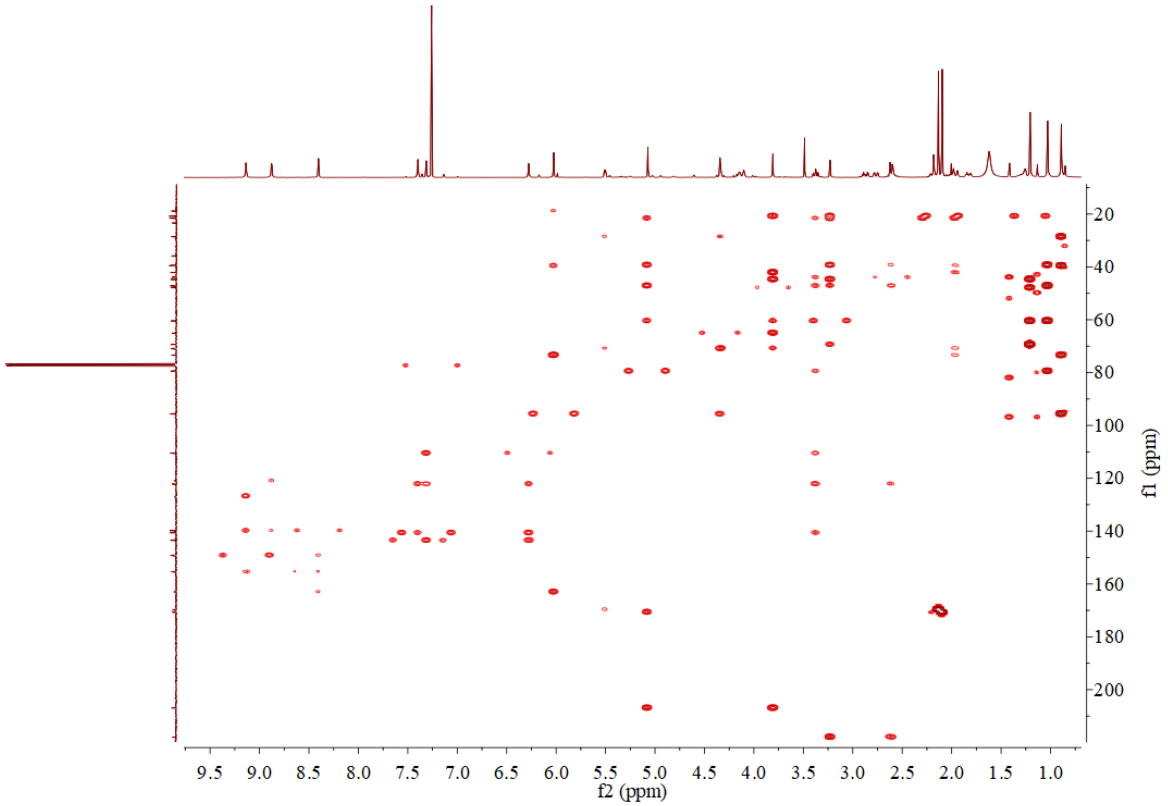
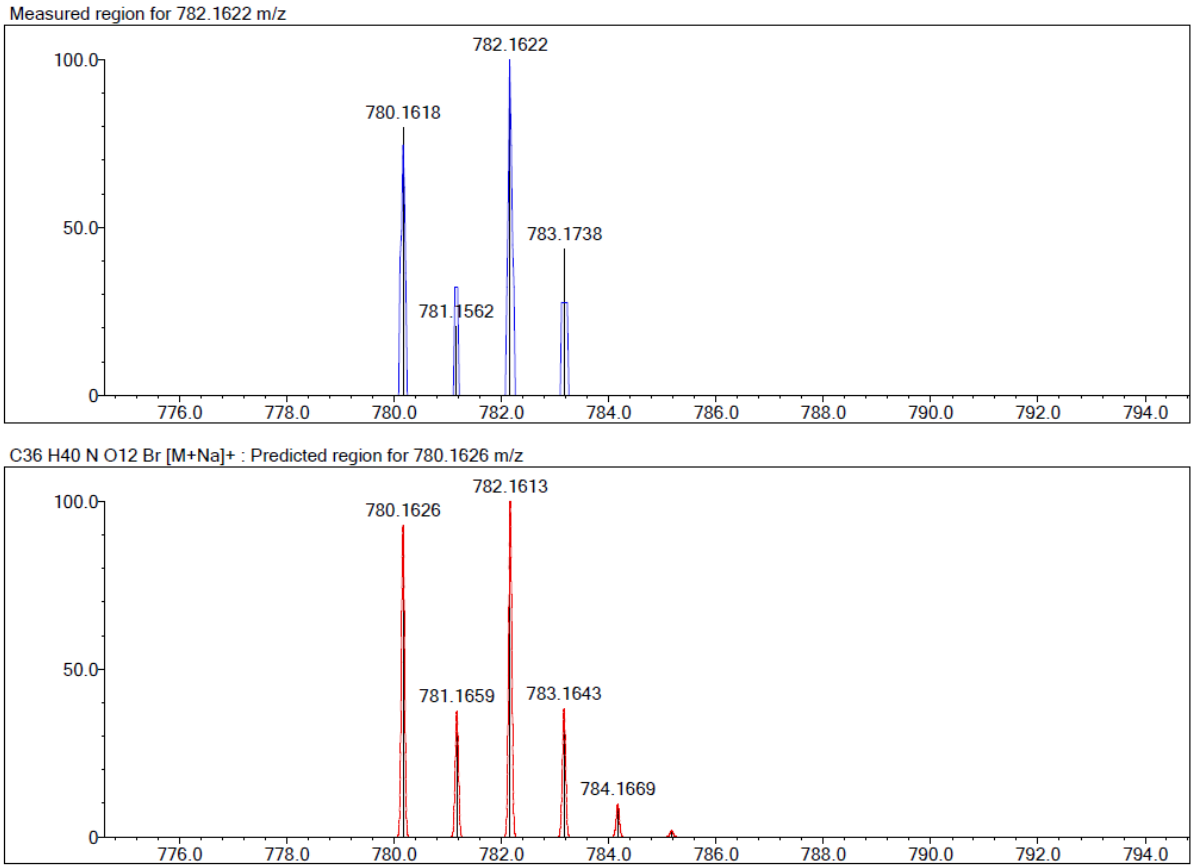


Figure S44. HRESIMS spectrum of **10**.



11. **Figures S45–S46.** ^{1}H NMR and ^{13}C NMR spectra of **11**.

Figure S45. ^{1}H NMR (400 MHz) spectrum of **11** in pyrdine-d_5.

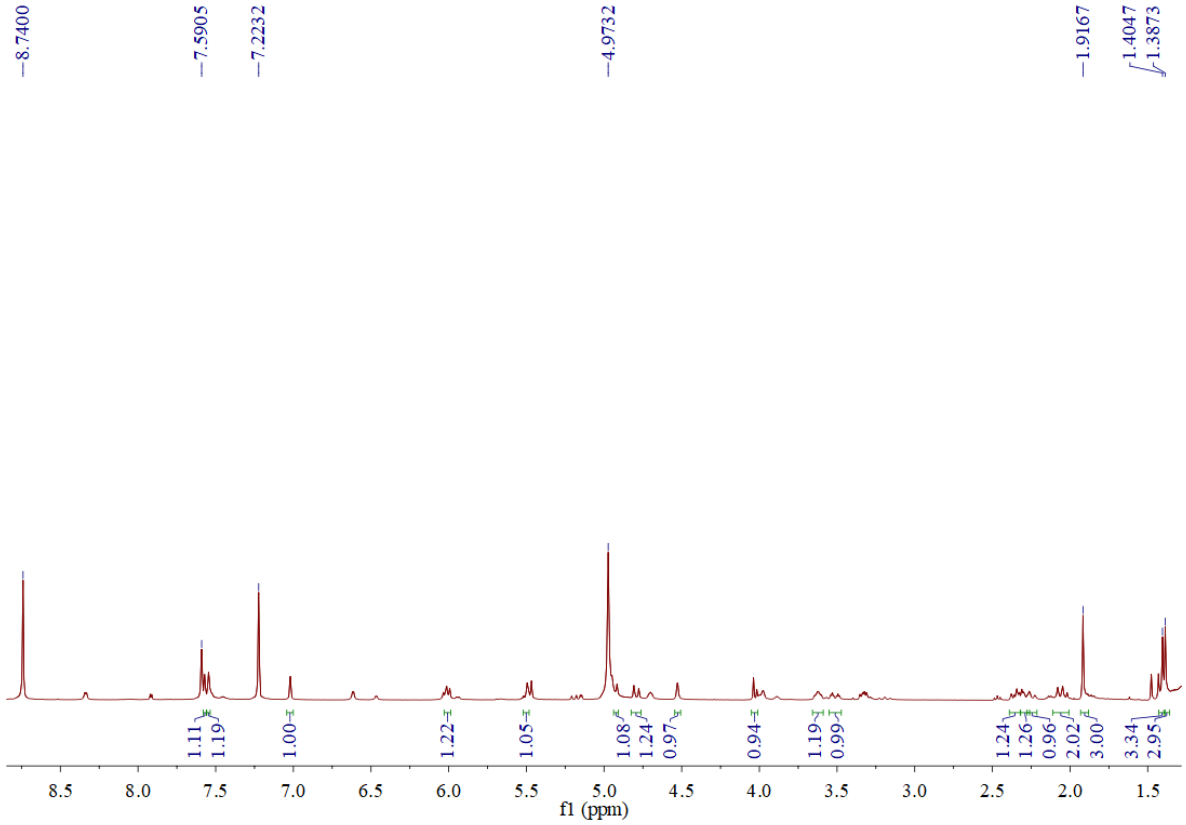
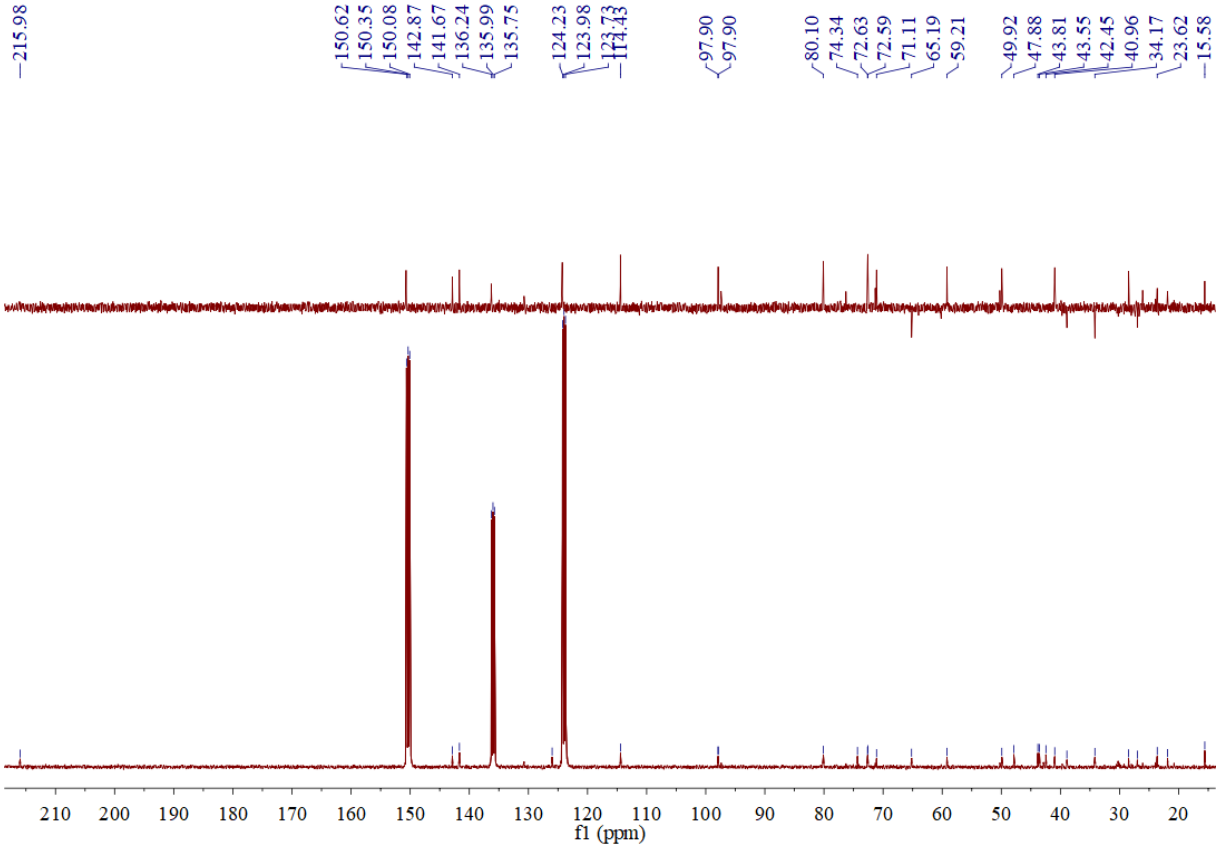


Figure S46. ^{13}C NMR (100 MHz) spectrum of **11** in pyrdine-d_5.



12. **Figures S47–S48.** ^{1}H NMR and ^{13}C NMR spectra of **12**.

Figure S47. ^{1}H NMR (400 MHz) spectrum of **12** in CD_3OD.

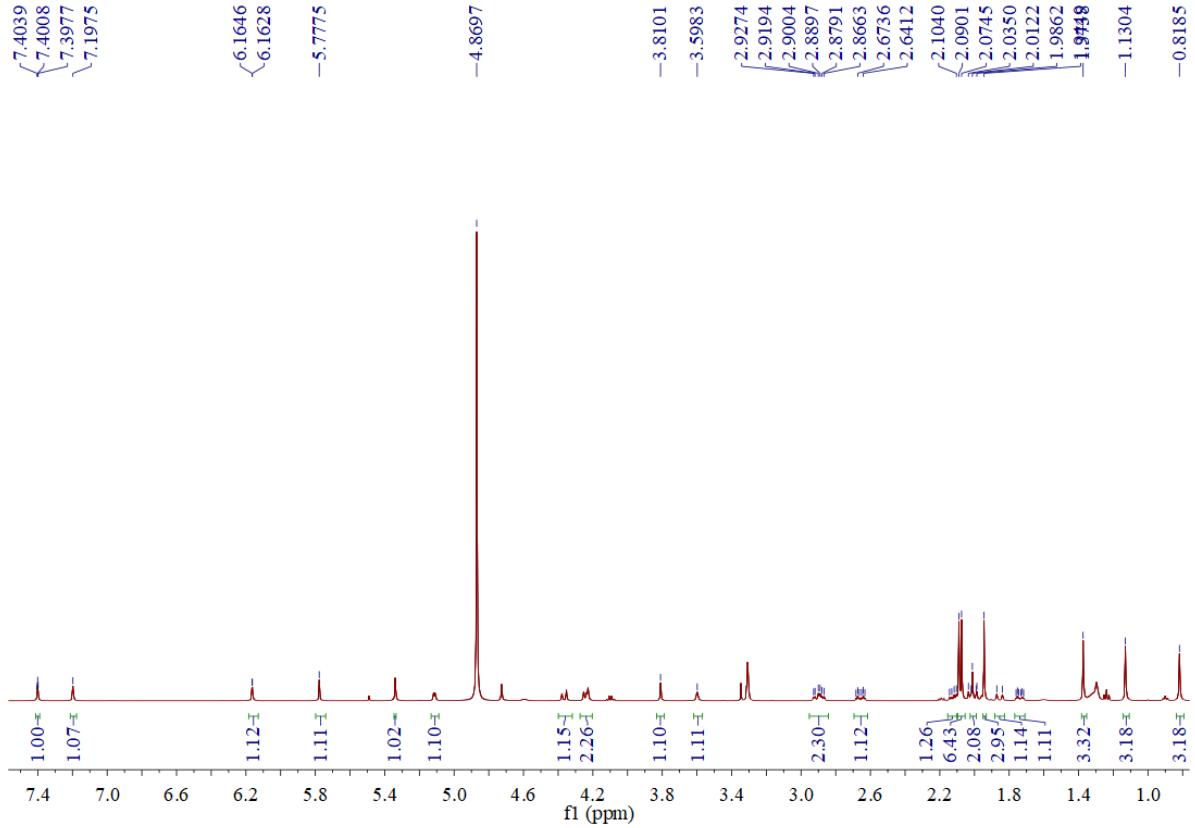
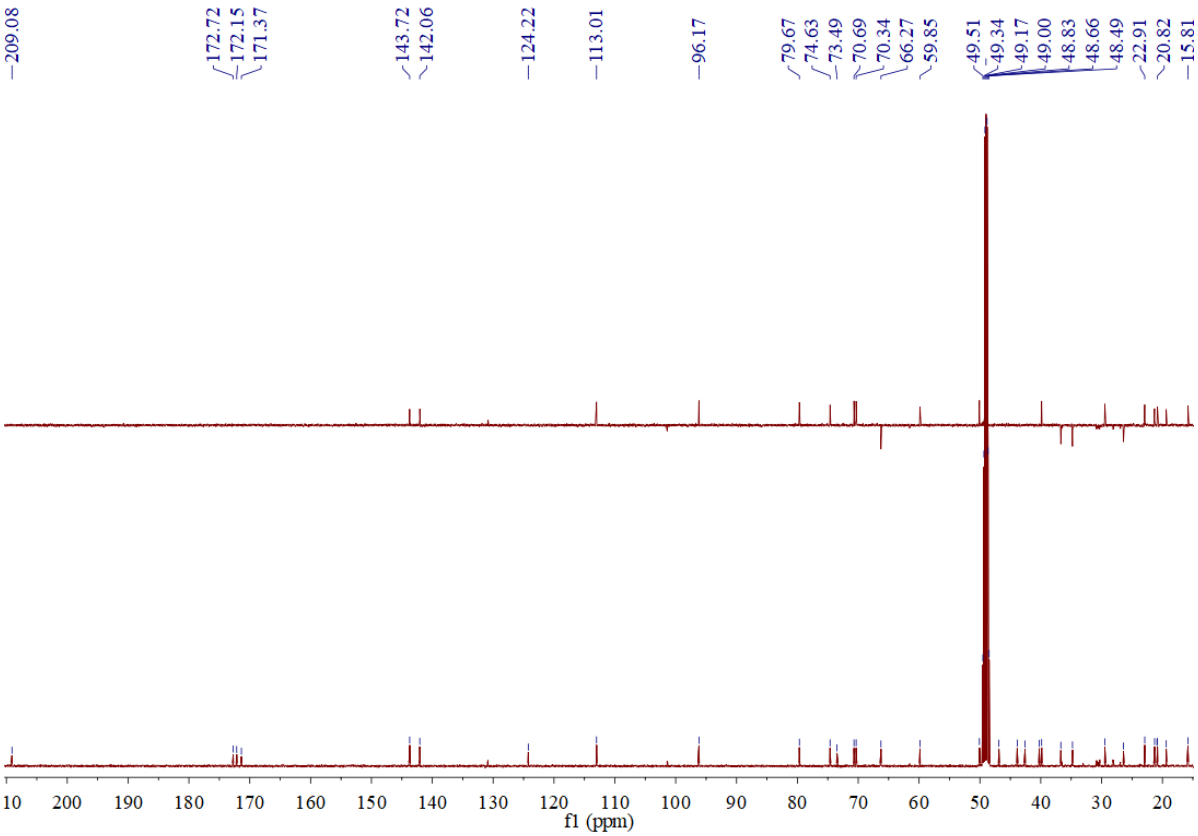


Figure S48. ^{13}C NMR (100 MHz) spectrum of **12** in CD_3OD.



13. **Figures S49–S50.** ^{1}H NMR and ^{13}C NMR spectra of **13**.

Figure S49. ^{1}H NMR (400 MHz) spectrum of **13** in $CDCl_3$.

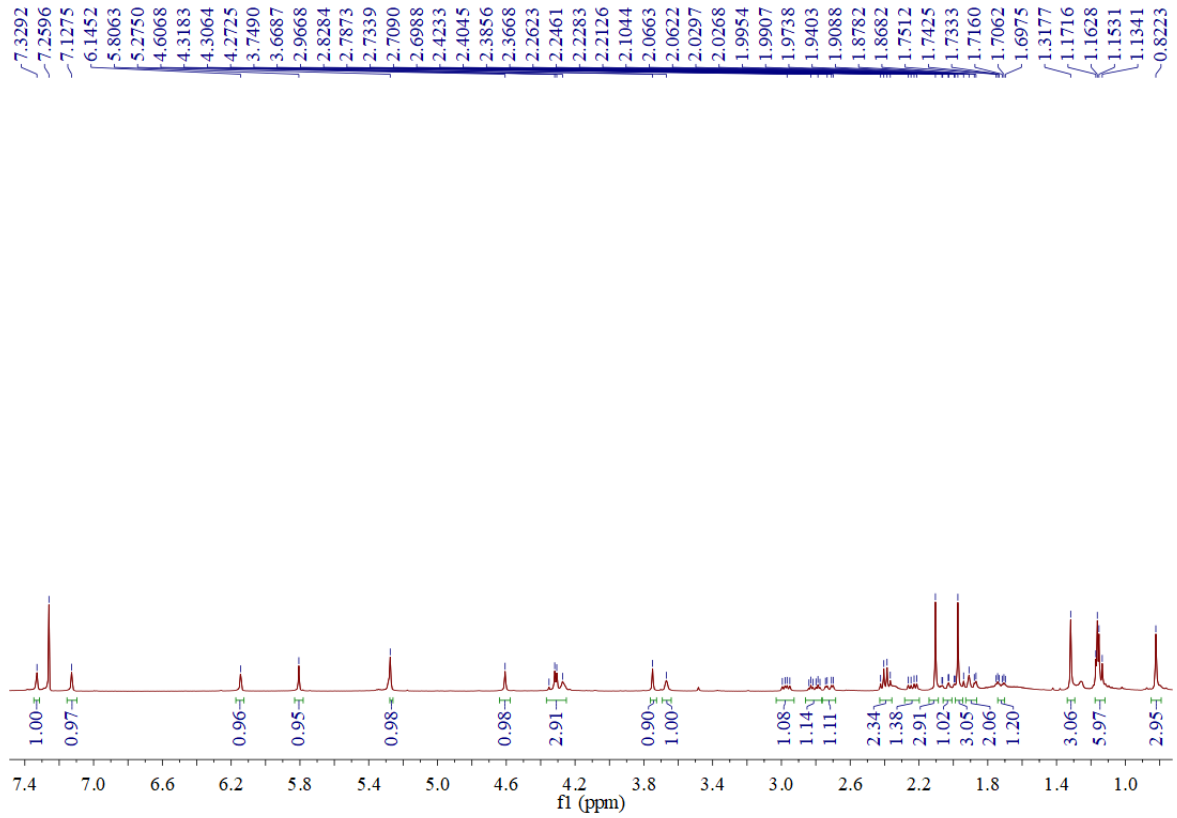
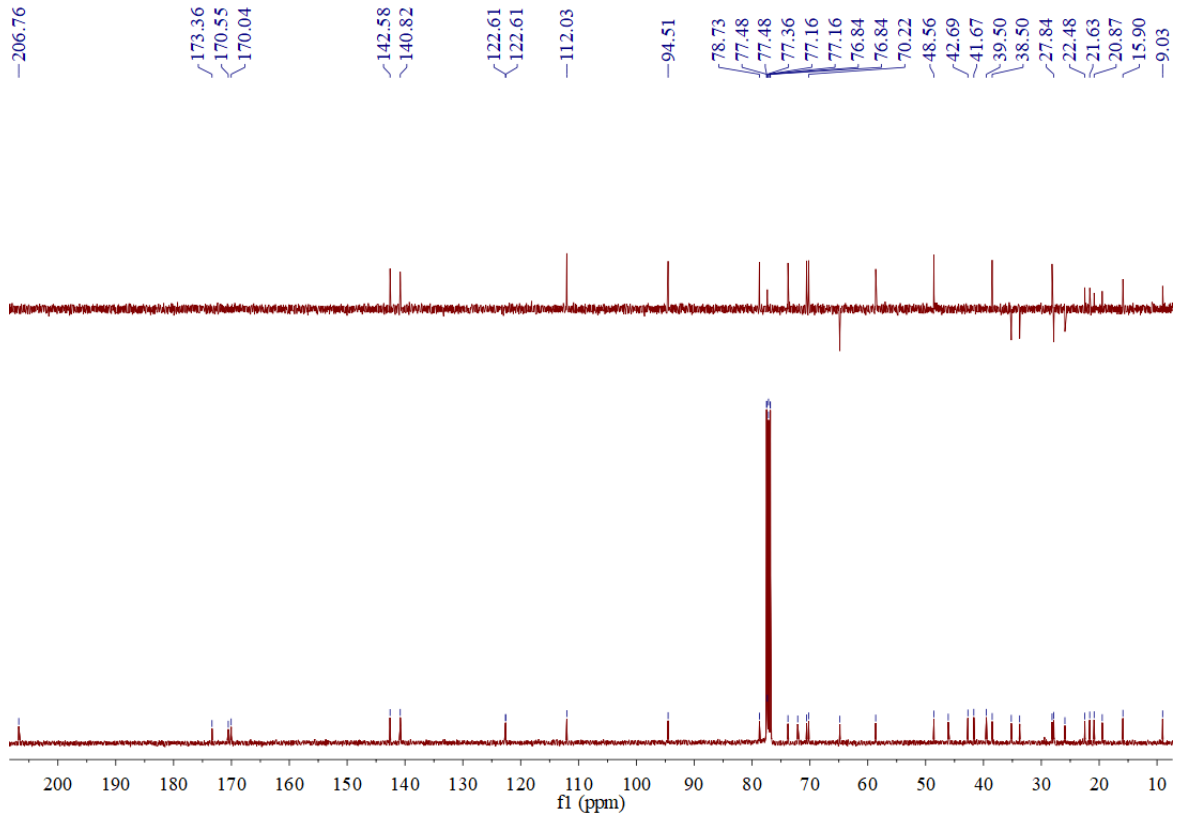


Figure S50. ^{13}C NMR (100 MHz) spectrum of **13** in $CDCl_3$.



14. **Figures S51–S52.** ^{1}H NMR and ^{13}C NMR spectra of **14**.

Figure S51. ^{1}H NMR (500 MHz) spectrum of **14** in $CDCl_3$.

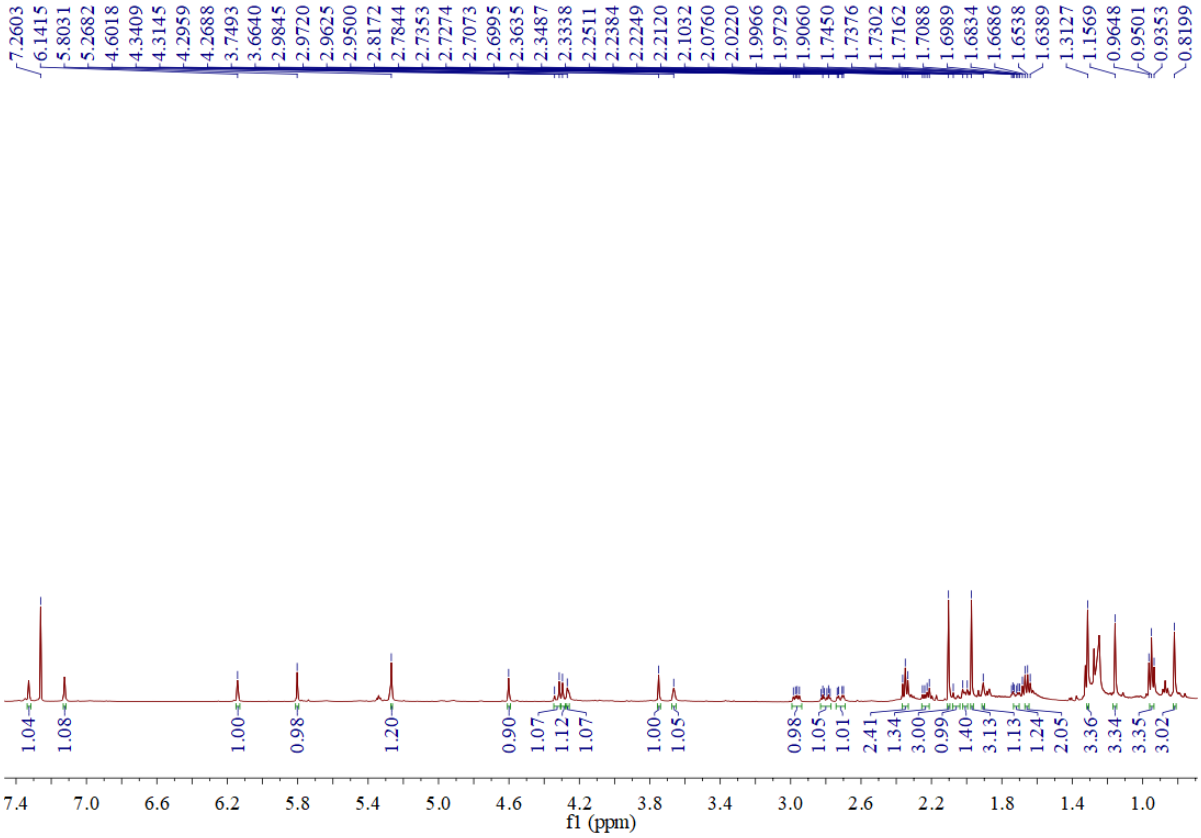
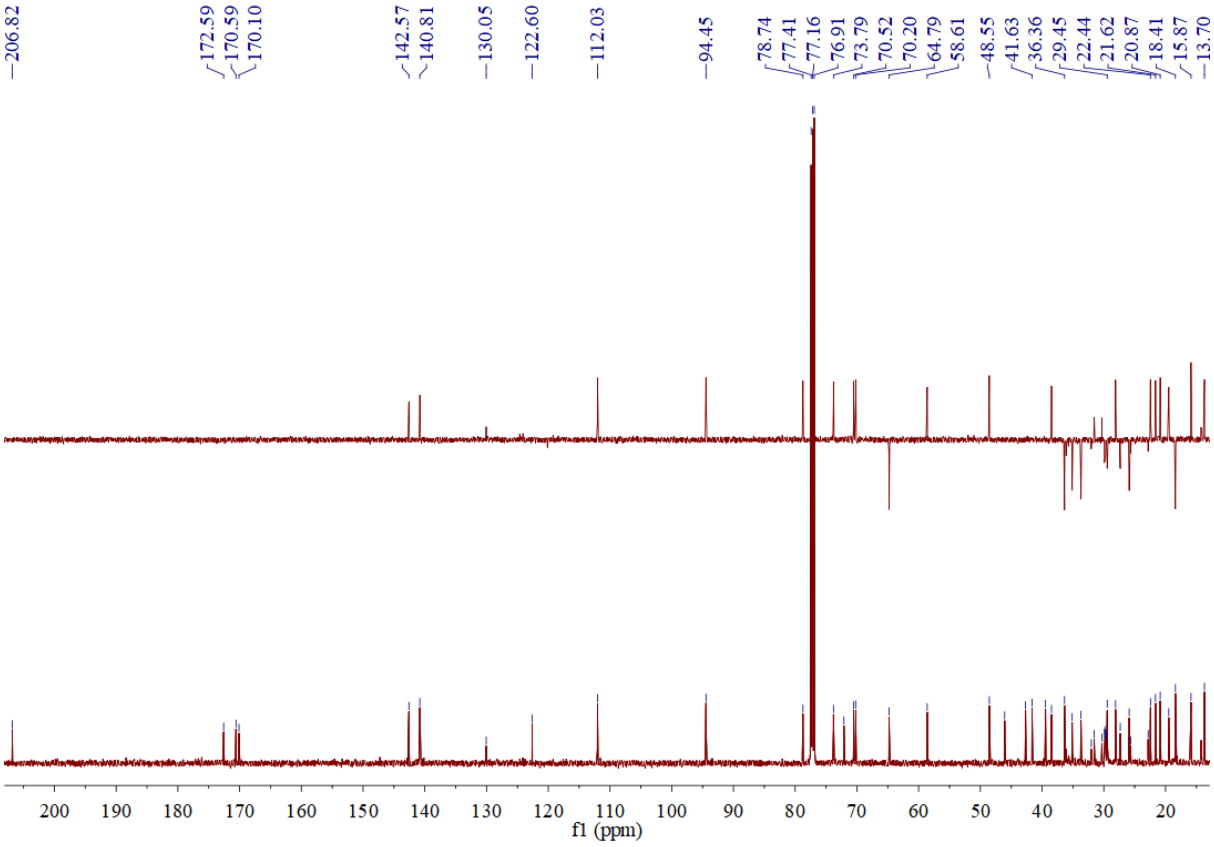


Figure S52. ^{13}C NMR (125 MHz) spectrum of **14** in $CDCl_3$.



15. **Figures S53–S54.** ^{1}H NMR and ^{13}C NMR spectra of **15**.

Figure S53. ^{1}H NMR (500 MHz) spectrum of **15** in $CDCl_3$.

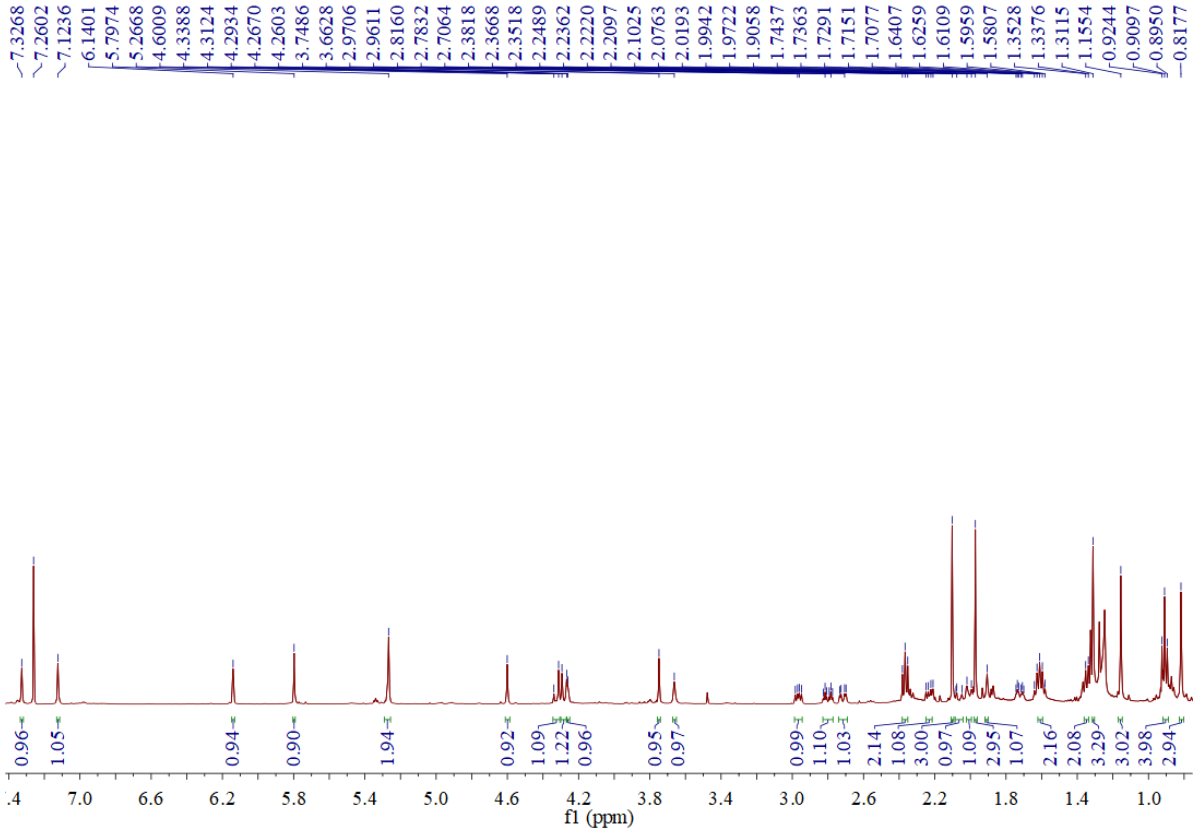
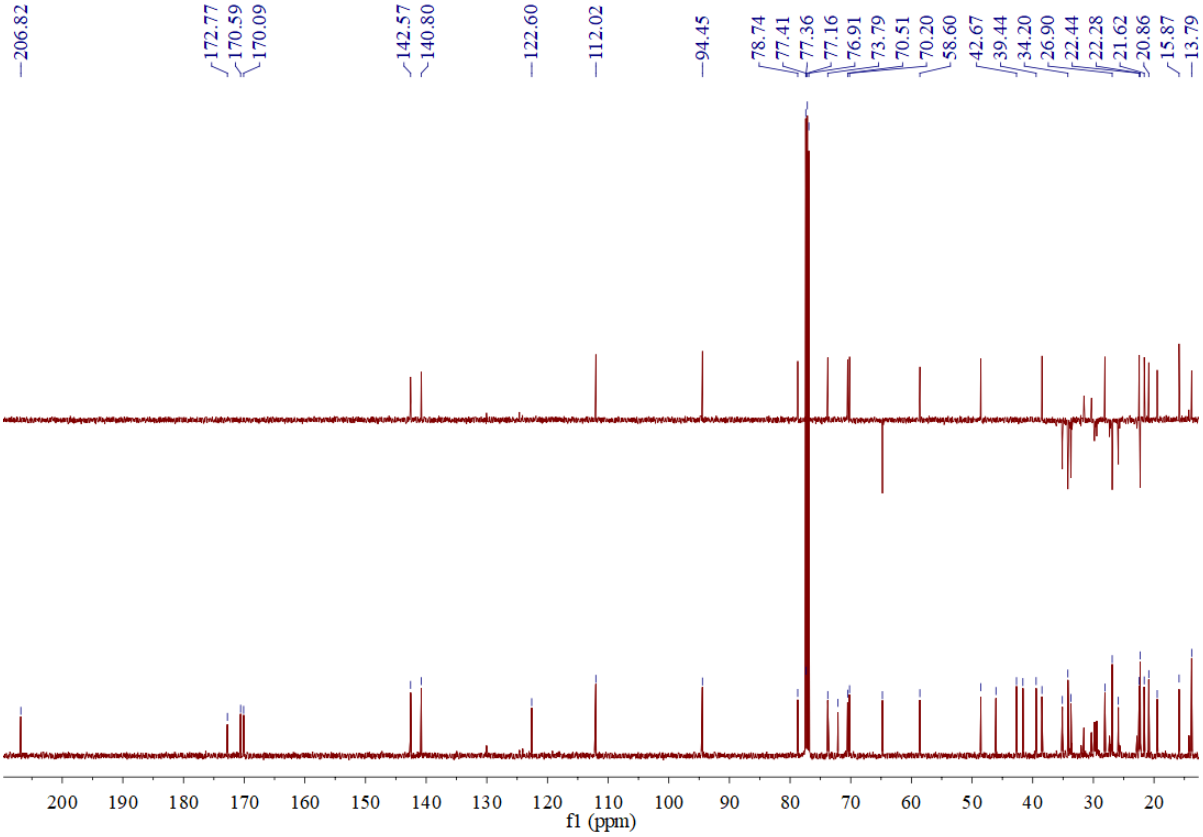


Figure S54. ^{13}C NMR (125 MHz) spectrum of **15** in $CDCl_3$.



16. **Figures S55–S60.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **16**.

Figure S55. ^{1}H NMR (400 MHz) spectrum of **16** in $CDCl_3$.

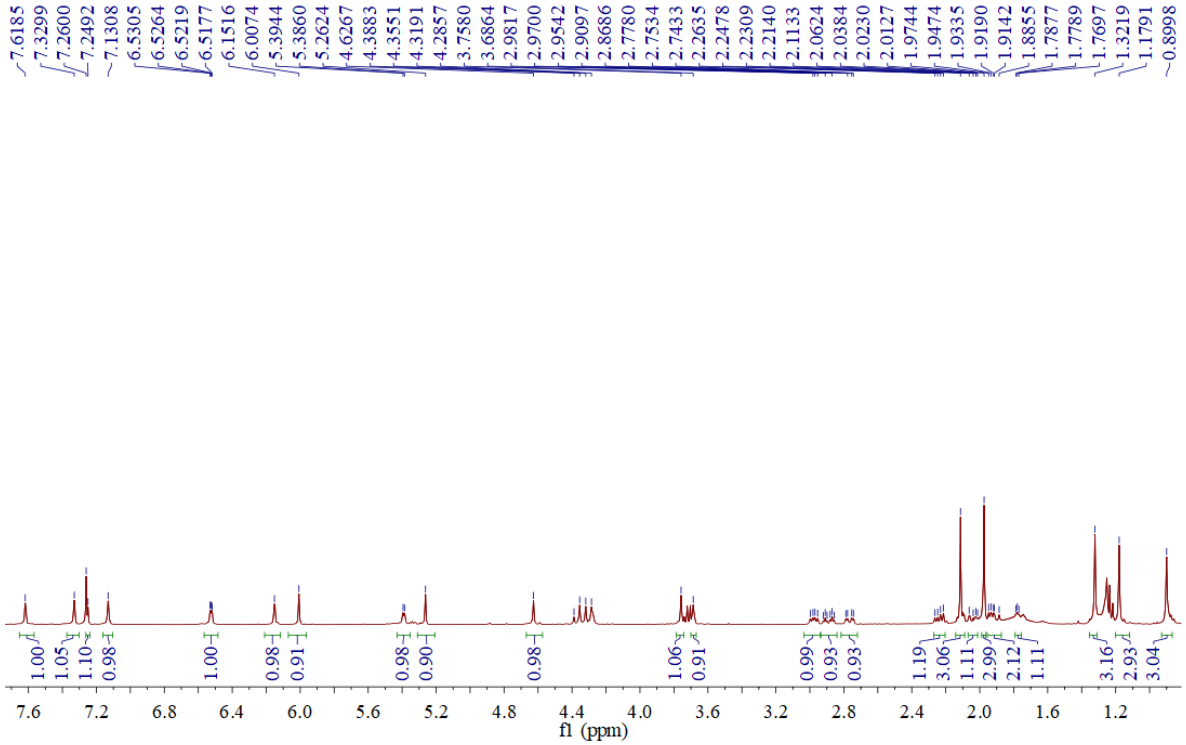


Figure S56. ^{13}C NMR (100 MHz) spectrum of **16** in $CDCl_3$.

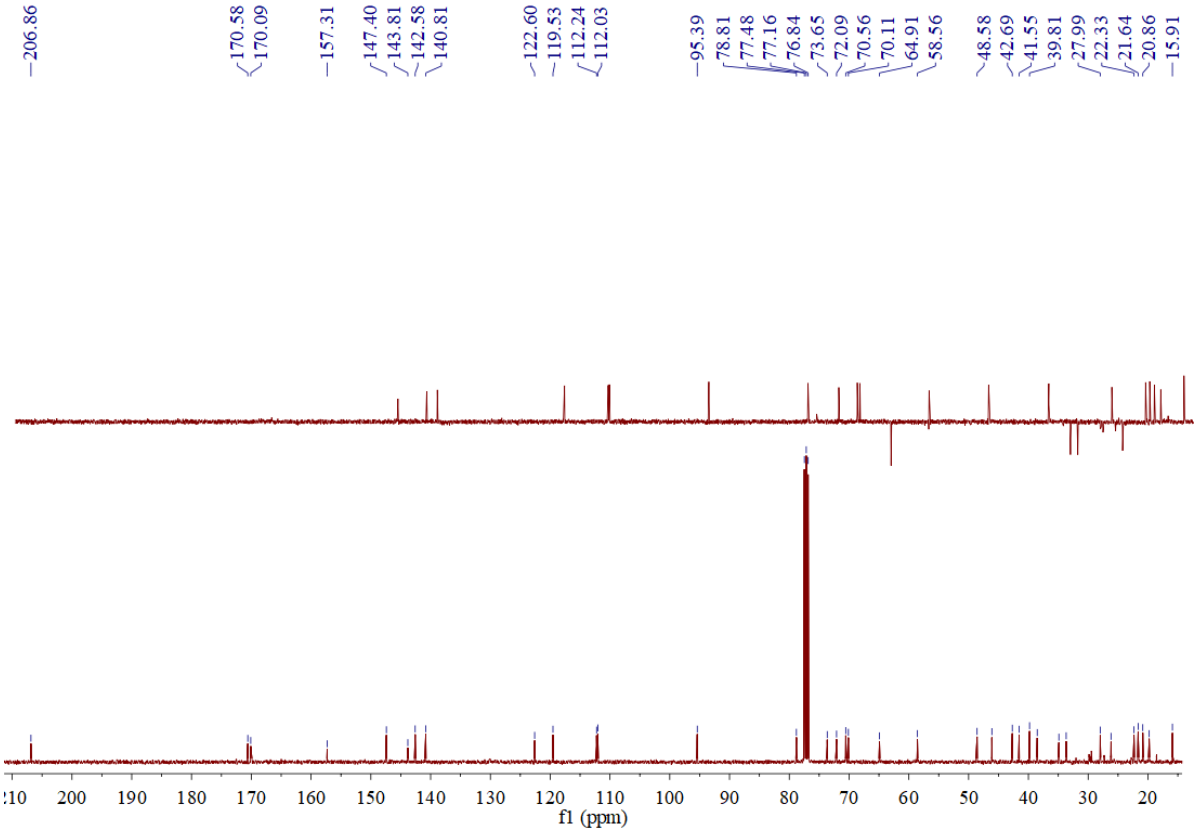


Figure S57. HSQC spectrum of **16** in $CDCl_3$.

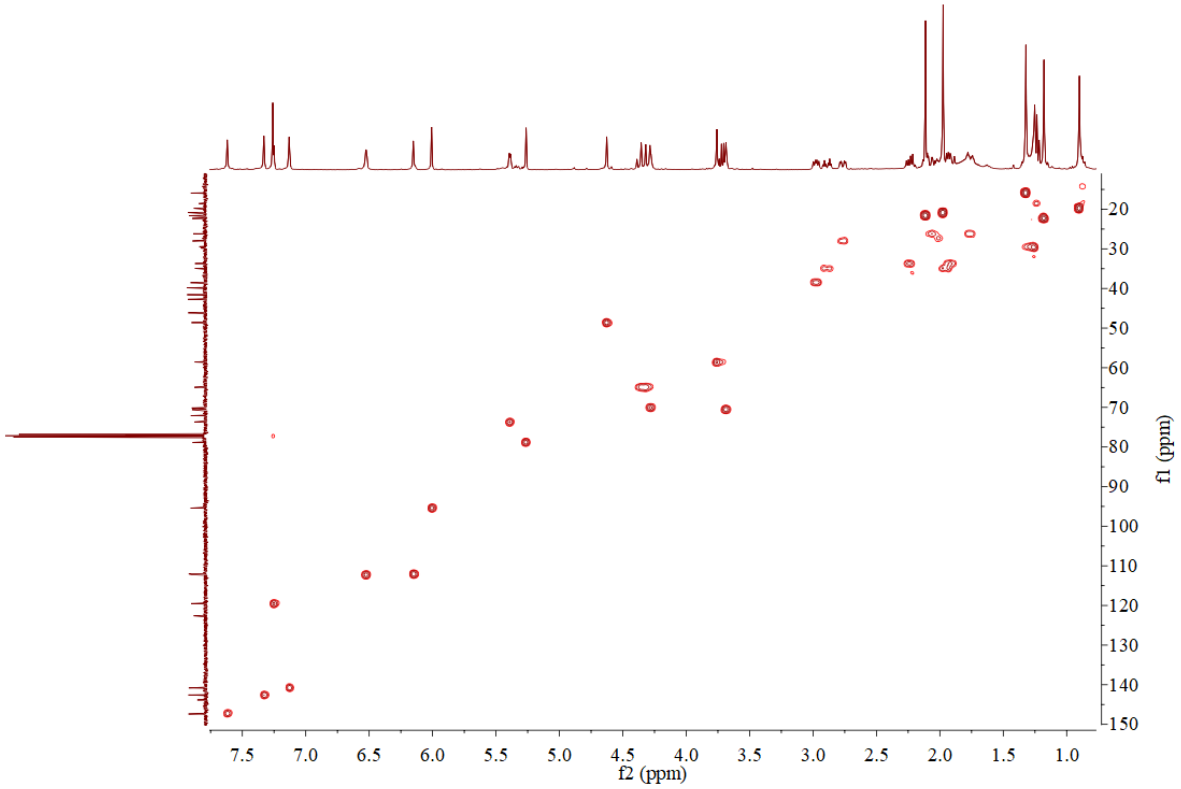


Figure S58. $^{1}H–^{1}H$ COSY spectrum of **16** in $CDCl_3$.

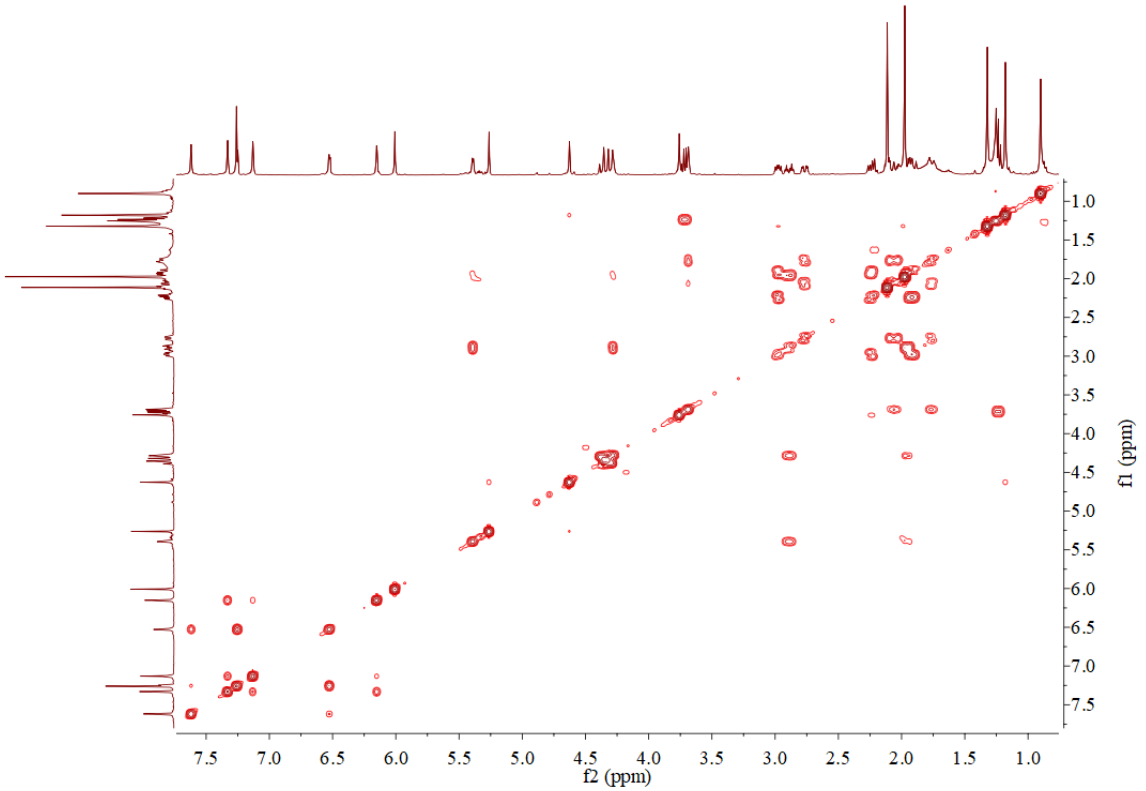


Figure S59. HMBC spectrum of **16** in $CDCl_3$.

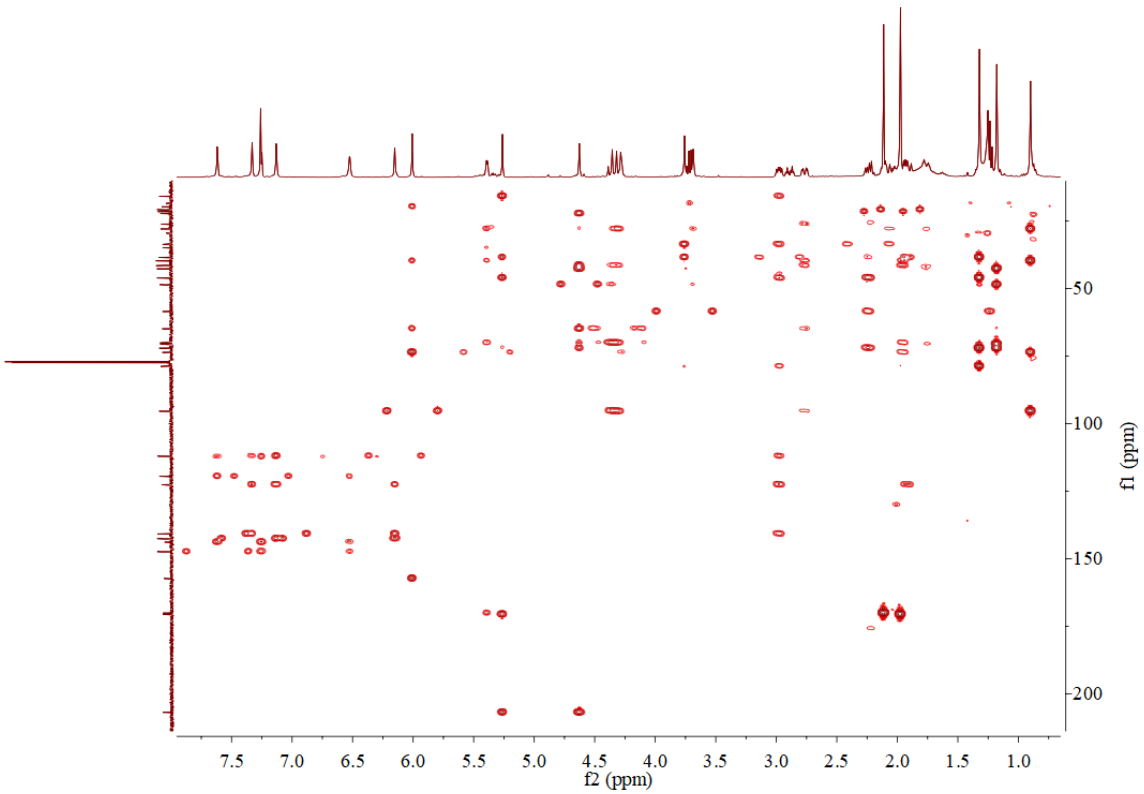
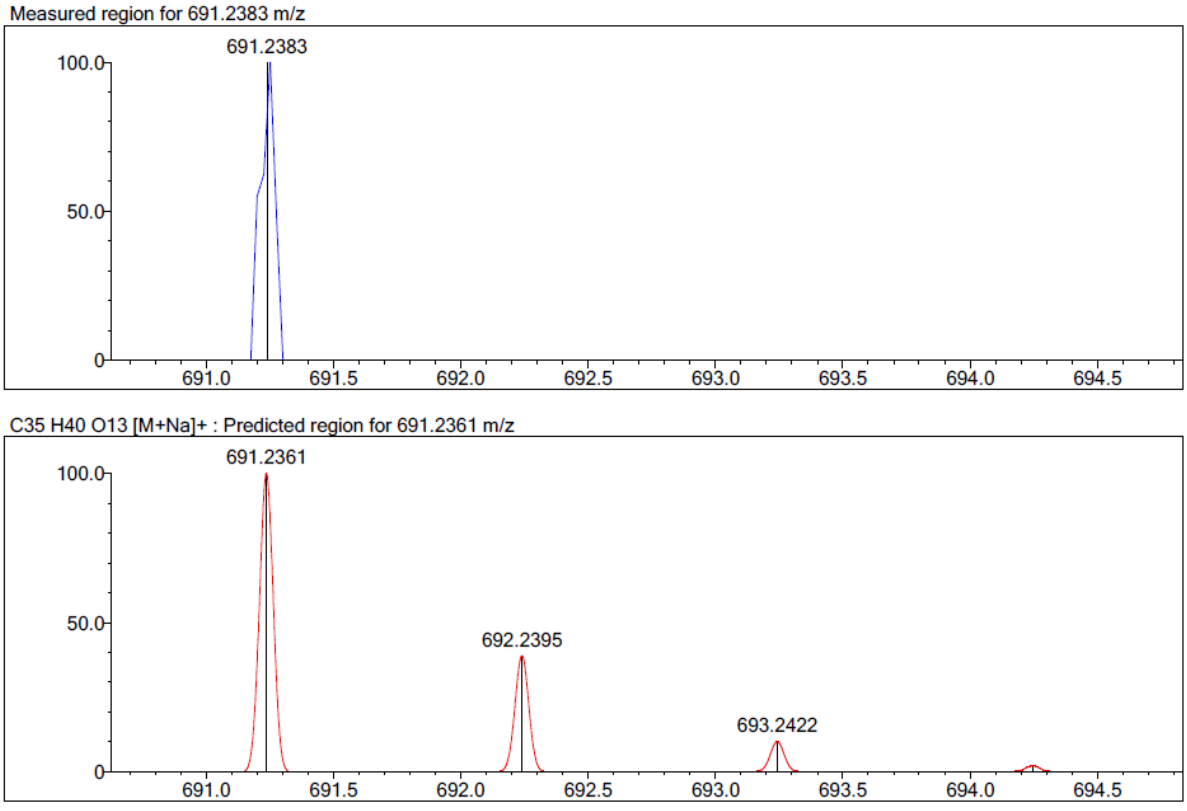


Figure S60. HRESIMS spectrum of **16**.



17. **Figures S61–S63.** ^{1}H NMR, ^{13}C NMR, and HRESIMS spectra of **17**.

Figure S61. ^{1}H NMR (400 MHz) spectrum of **17** in $CDCl_3$.

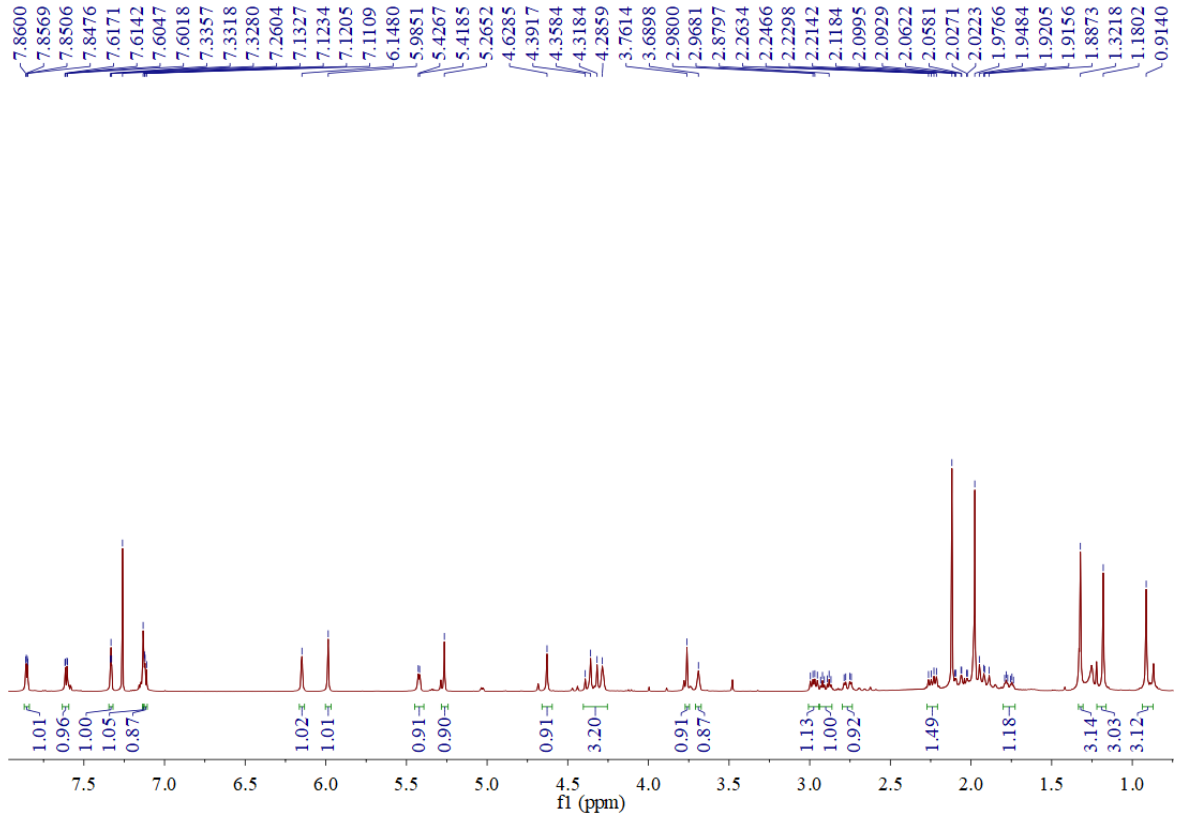


Figure S62. ^{13}C NMR (100 MHz) spectrum of **17** in $CDCl_3$.

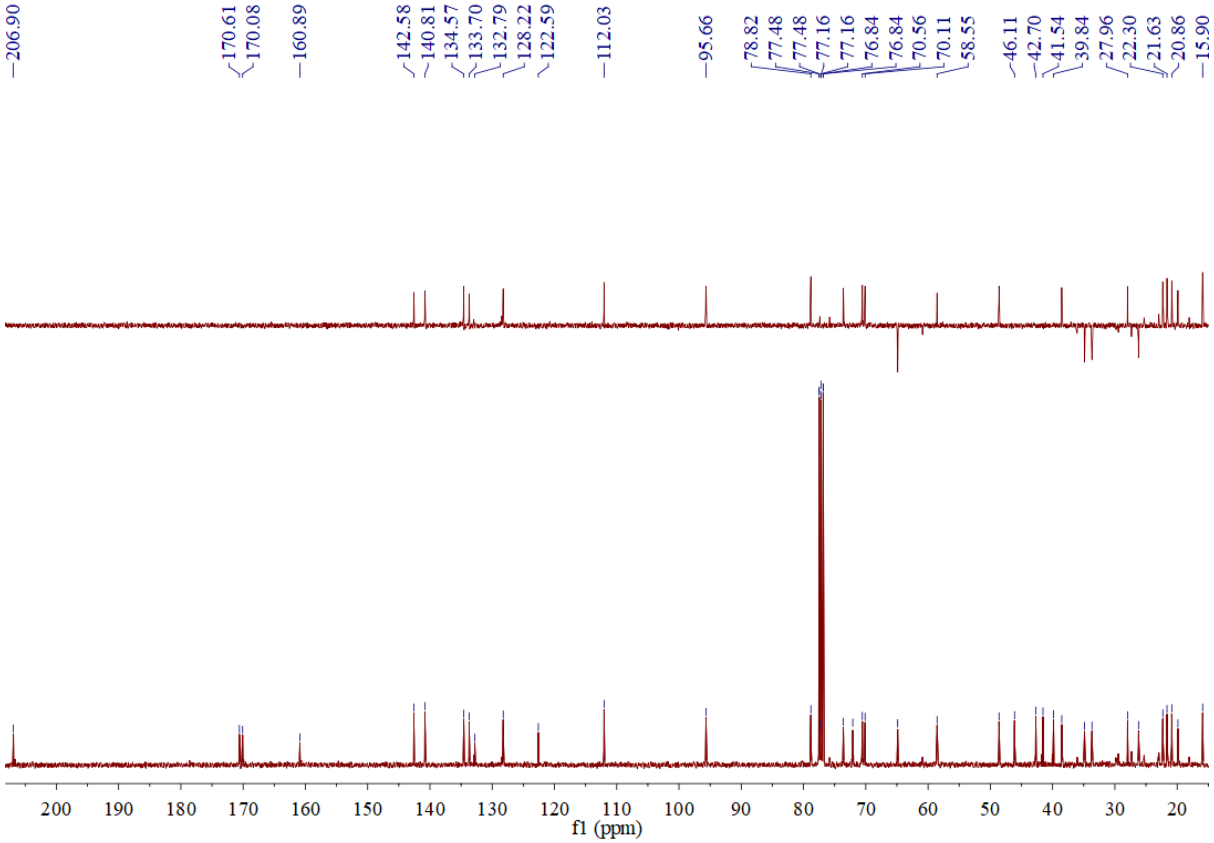
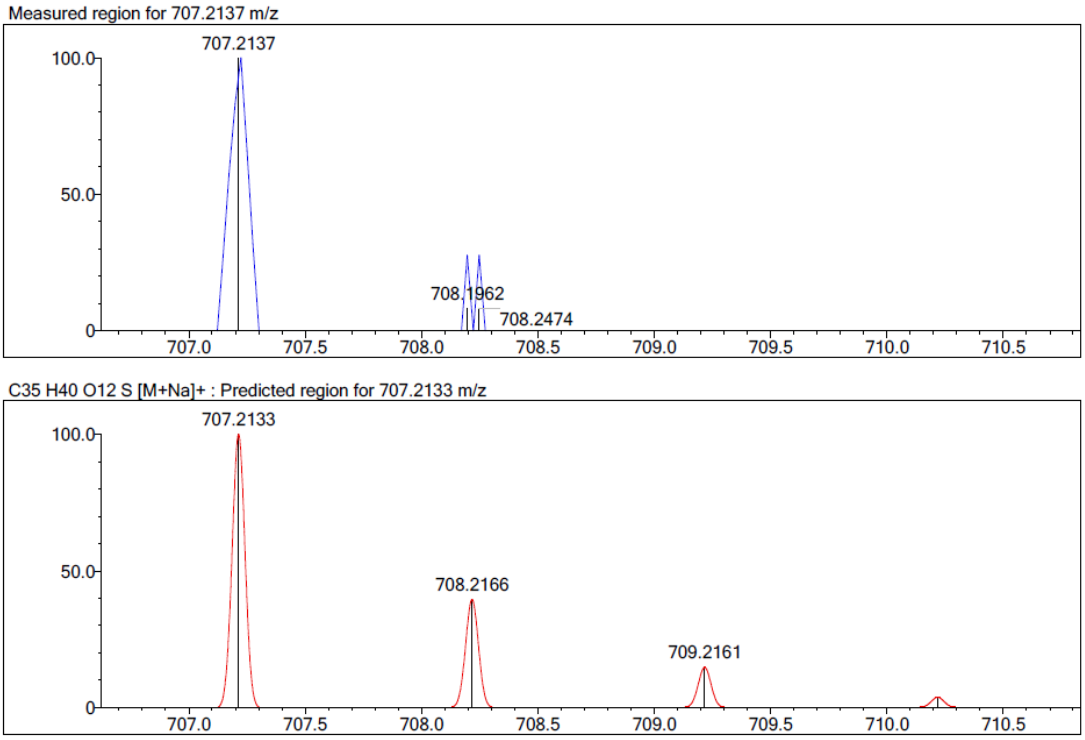


Figure S63. HRESIMS spectrum of **17**.



18. **Figures S64**–**S65.** ^{1}H NMR and ^{13}C NMR spectra of **18**.

Figure S64. ^{1}H NMR (400 MHz) spectrum of **18** in $CDCl_3$.

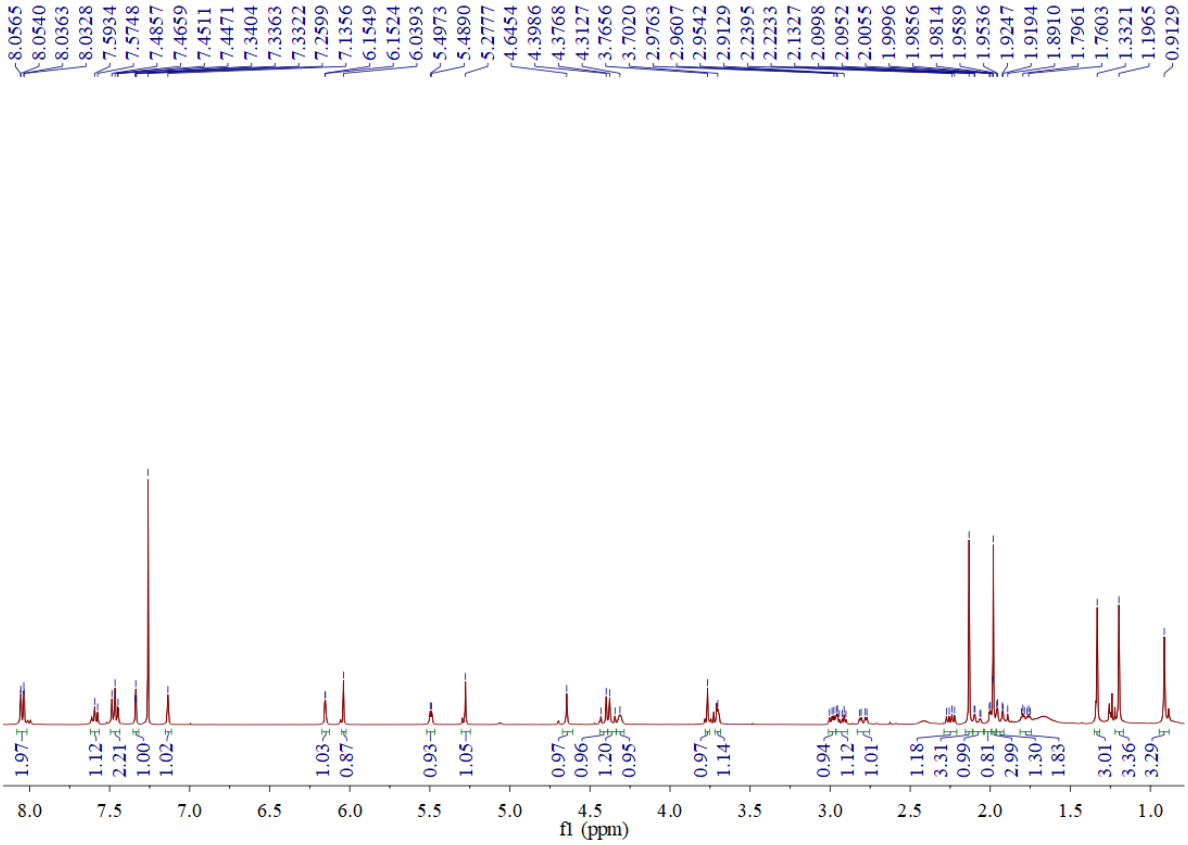
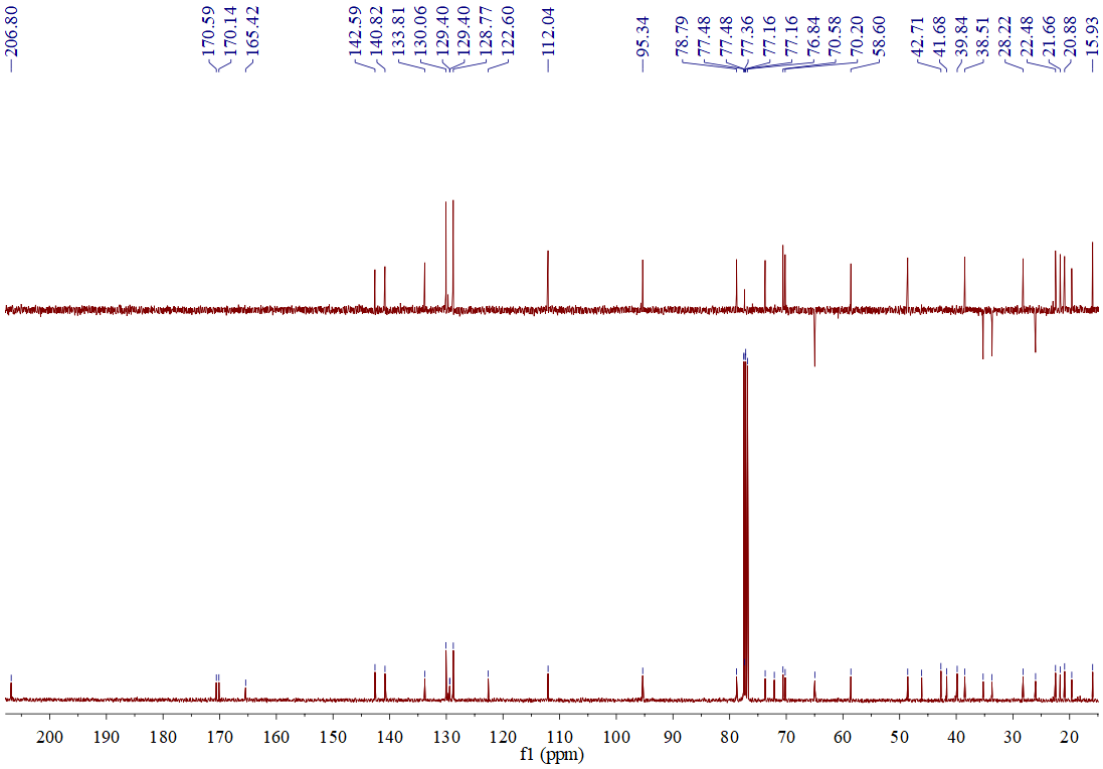


Figure S65. ^{13}C NMR (100 MHz) spectrum of **18** in $CDCl_3$.



19. **Figures S66**–**S71.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **19**.

Figure S66. ^{1}H NMR (400 MHz) spectrum of **19** in $CDCl_3$.

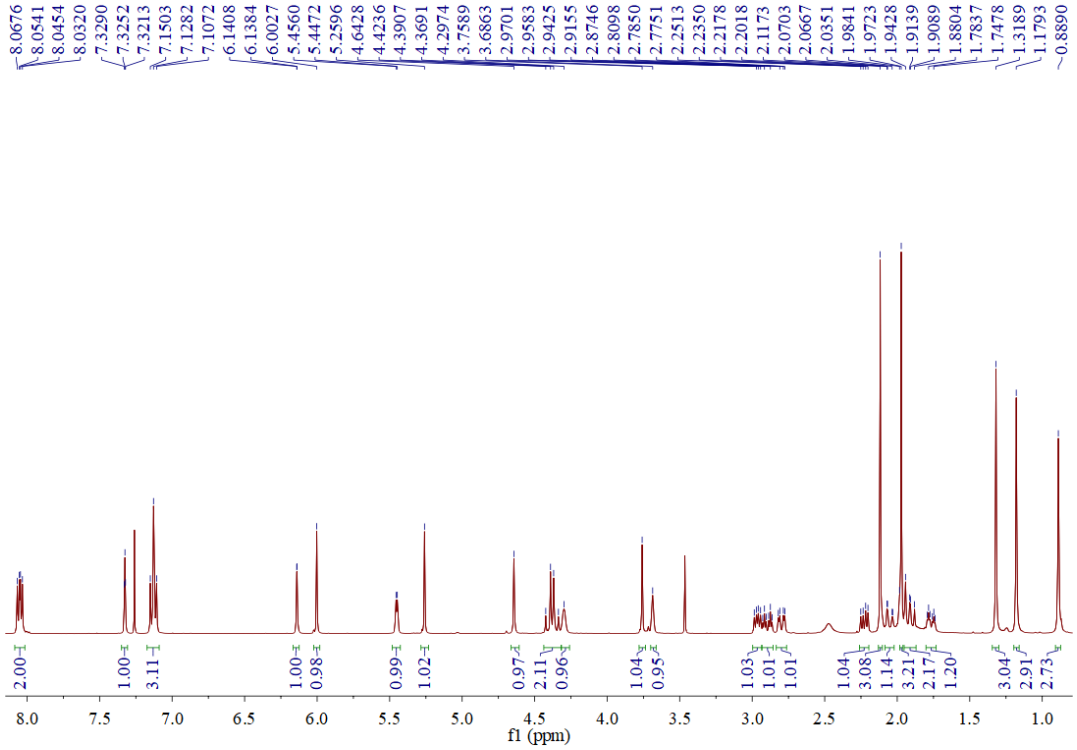


Figure S67. ^{13}C NMR (100 MHz) spectrum of **19** in $CDCl_3$.

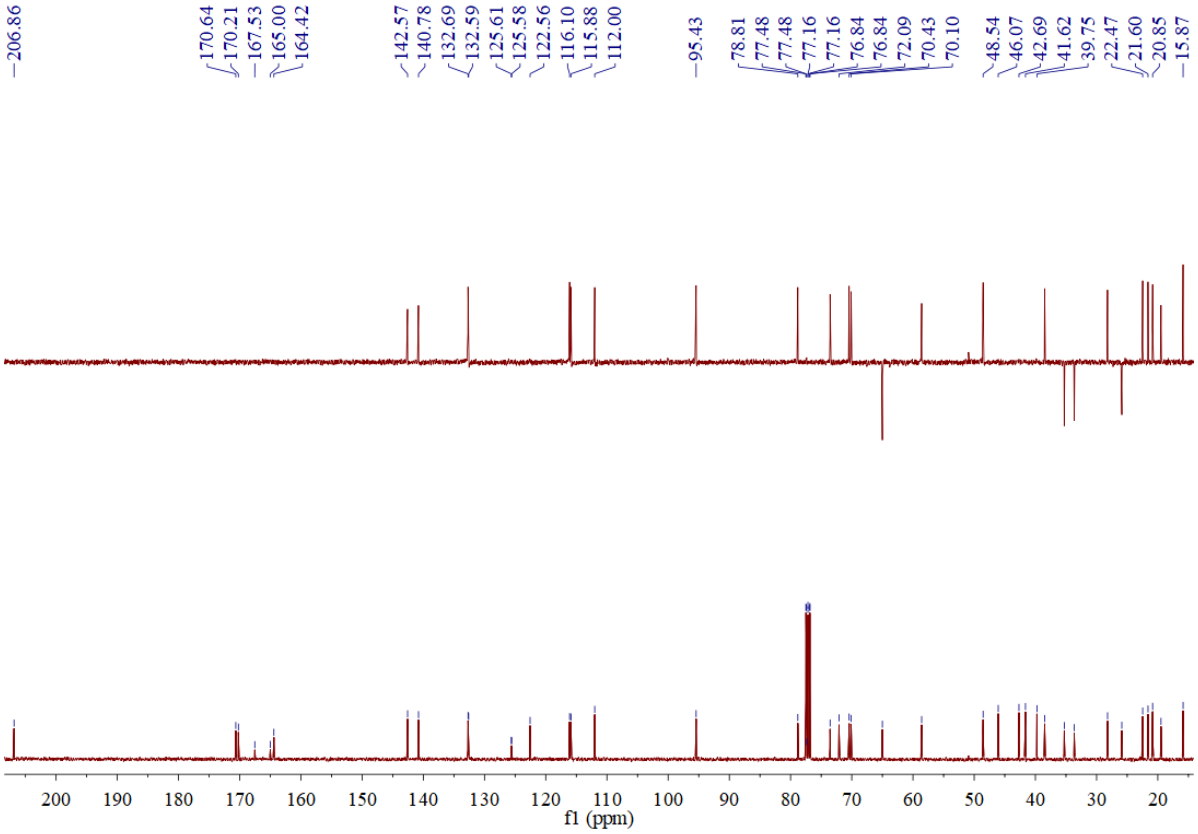


Figure S68. HSQC spectrum of **19** in $CDCl_3$.

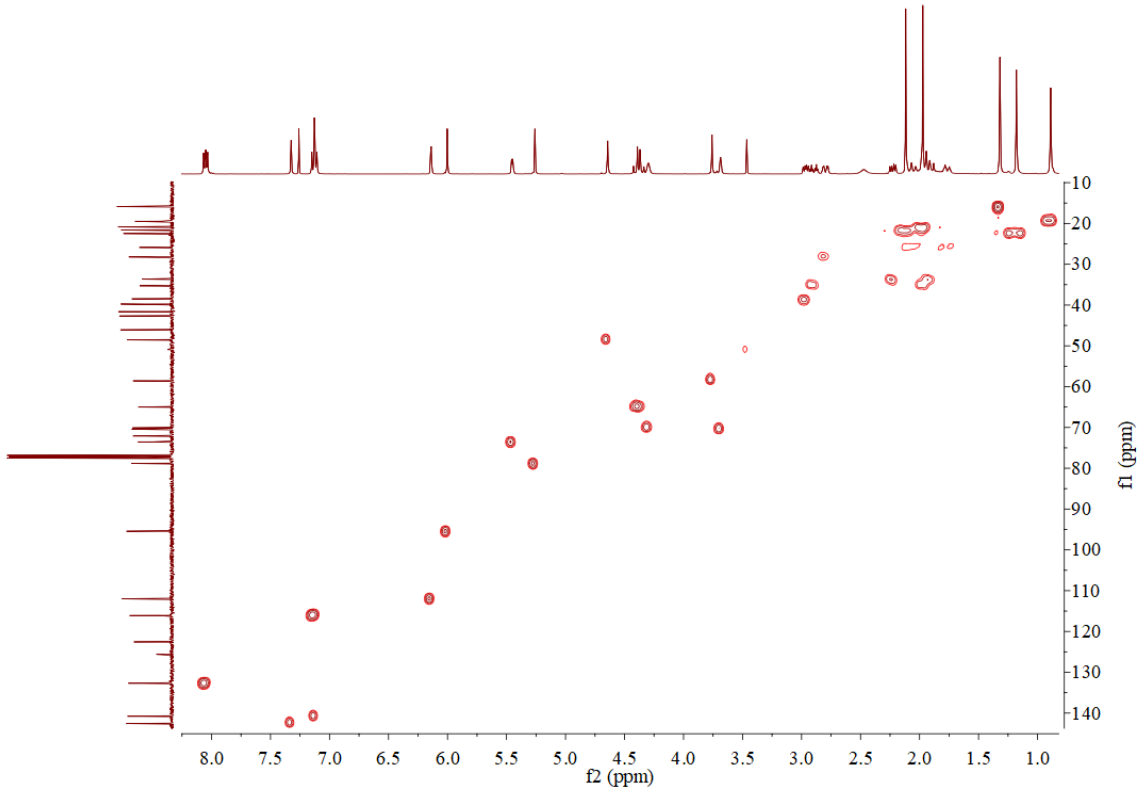


Figure S69. $^{1}H–^{1}H$ COSY spectrum of **19** in $CDCl_3$.

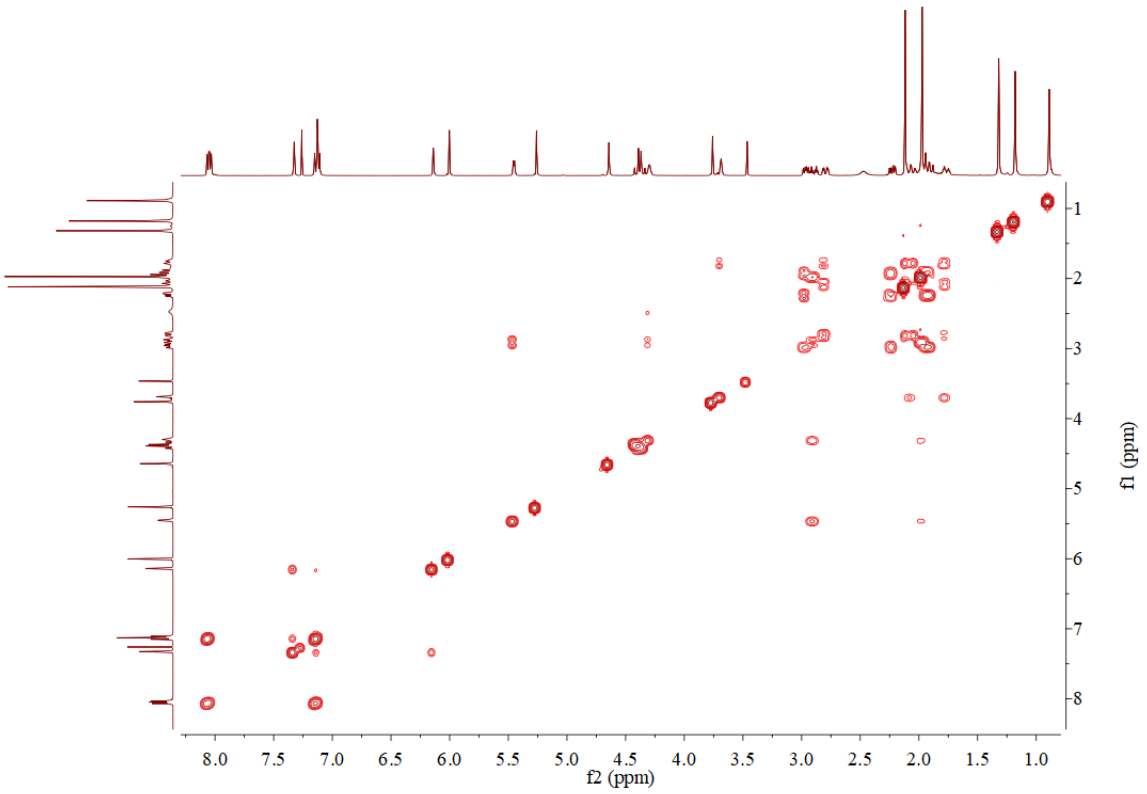


Figure S70. HMBC spectrum of **19** in $CDCl_3$.

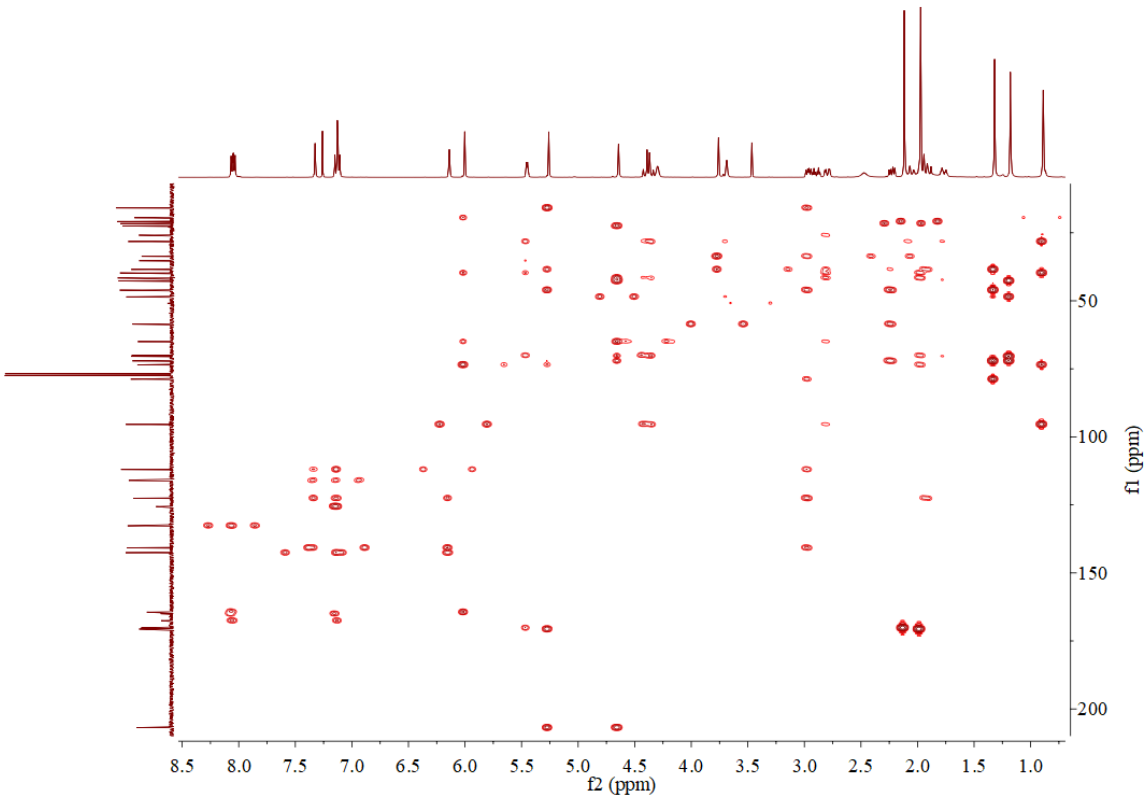
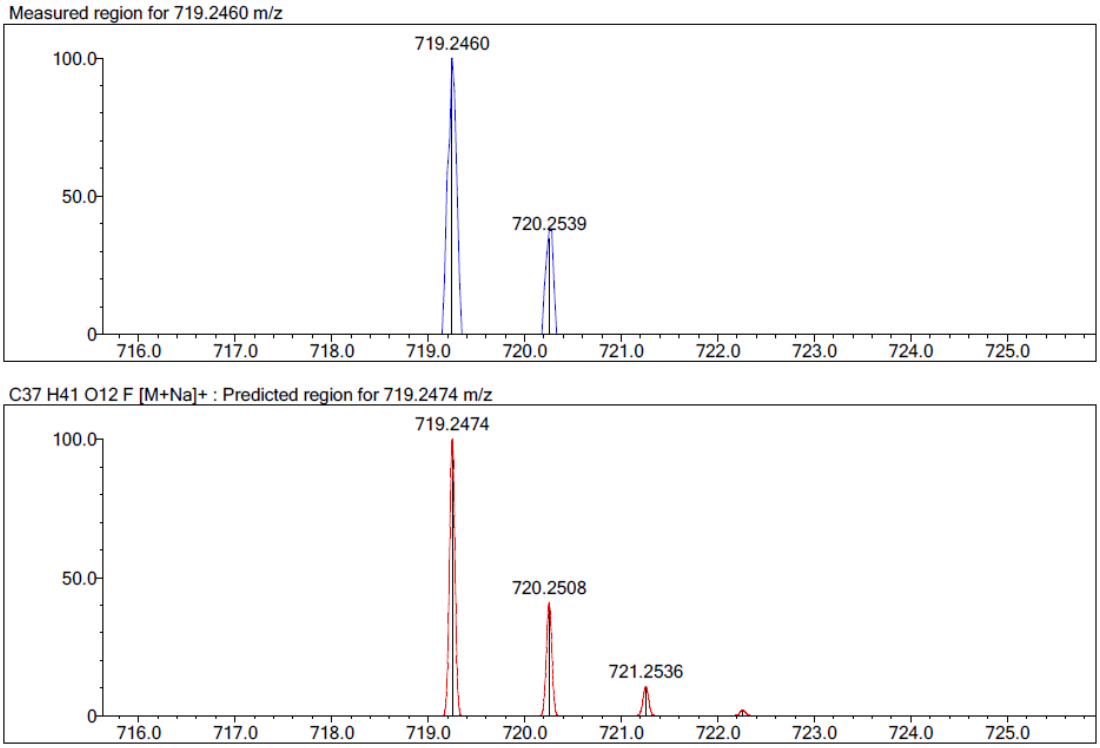


Figure S71. HRESIMS spectrum of **19**.



20. **Figures S72–S73.** ^{1}H NMR and ^{13}C NMR spectra of **20**.

Figure S72. ^{1}H NMR (400 MHz) spectrum of **20** in $CDCl_3$.

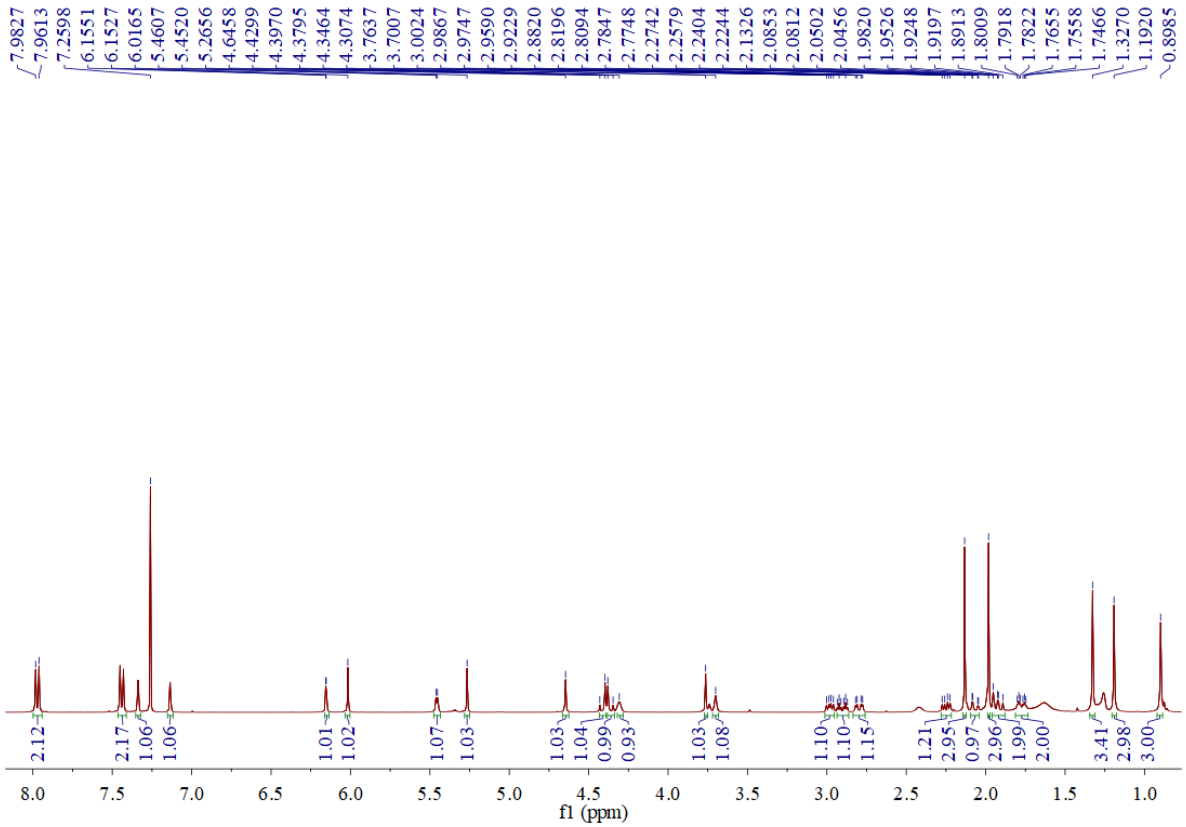
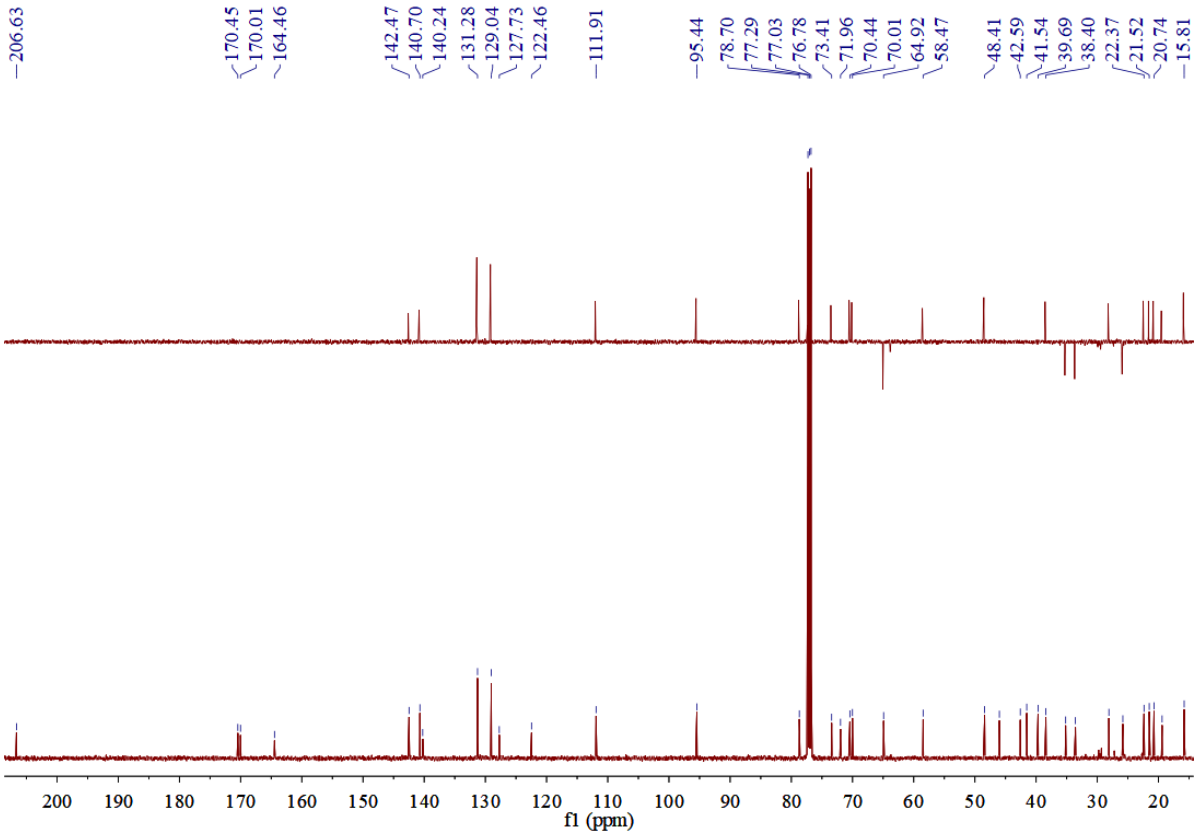


Figure S73. ^{13}C NMR (100 MHz) spectrum of **20** in $CDCl_3$.



21. **Figures S74–S79.** ^{1}H NMR, ^{13}C NMR, 2D NMR, and HRESIMS spectra of **21**.

Figure S74. ^{1}H NMR (500 MHz) spectrum of **21** in $CDCl_3$.

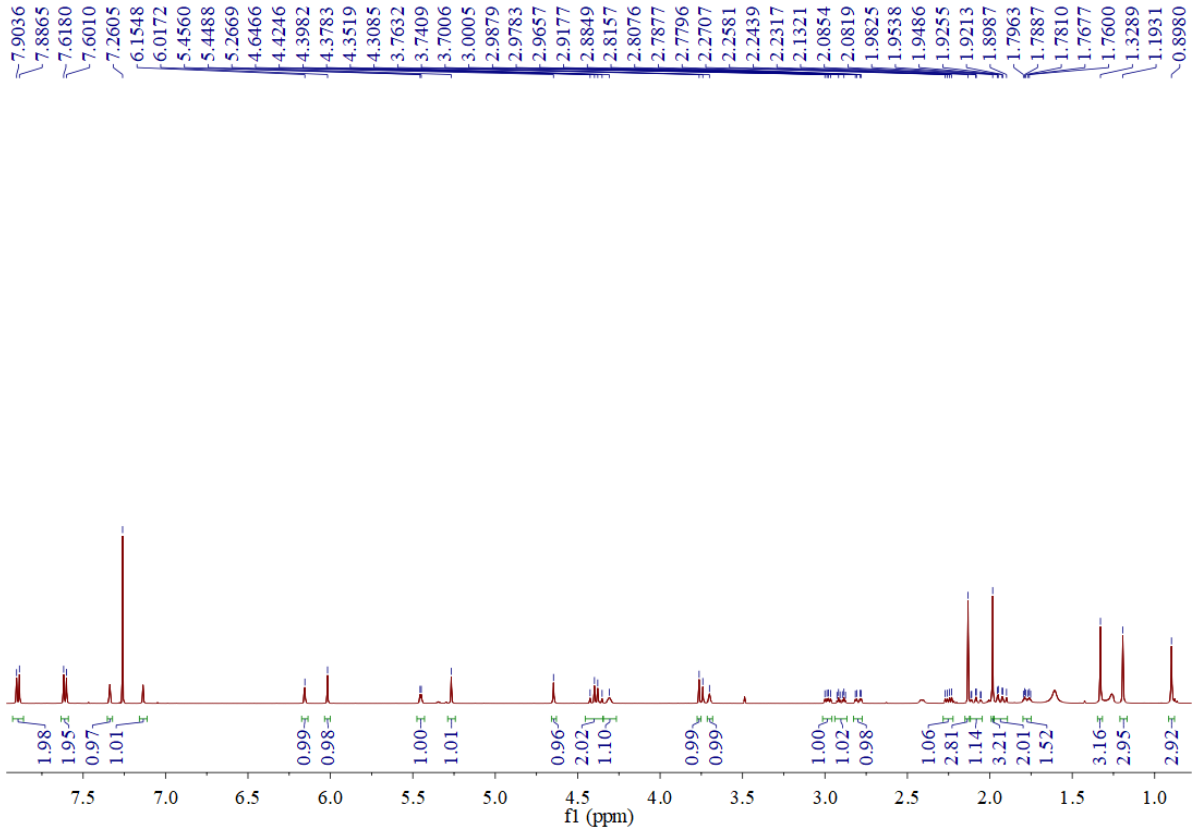


Figure S75. ^{13}C NMR (125 MHz) spectrum of **21** in $CDCl_3$.

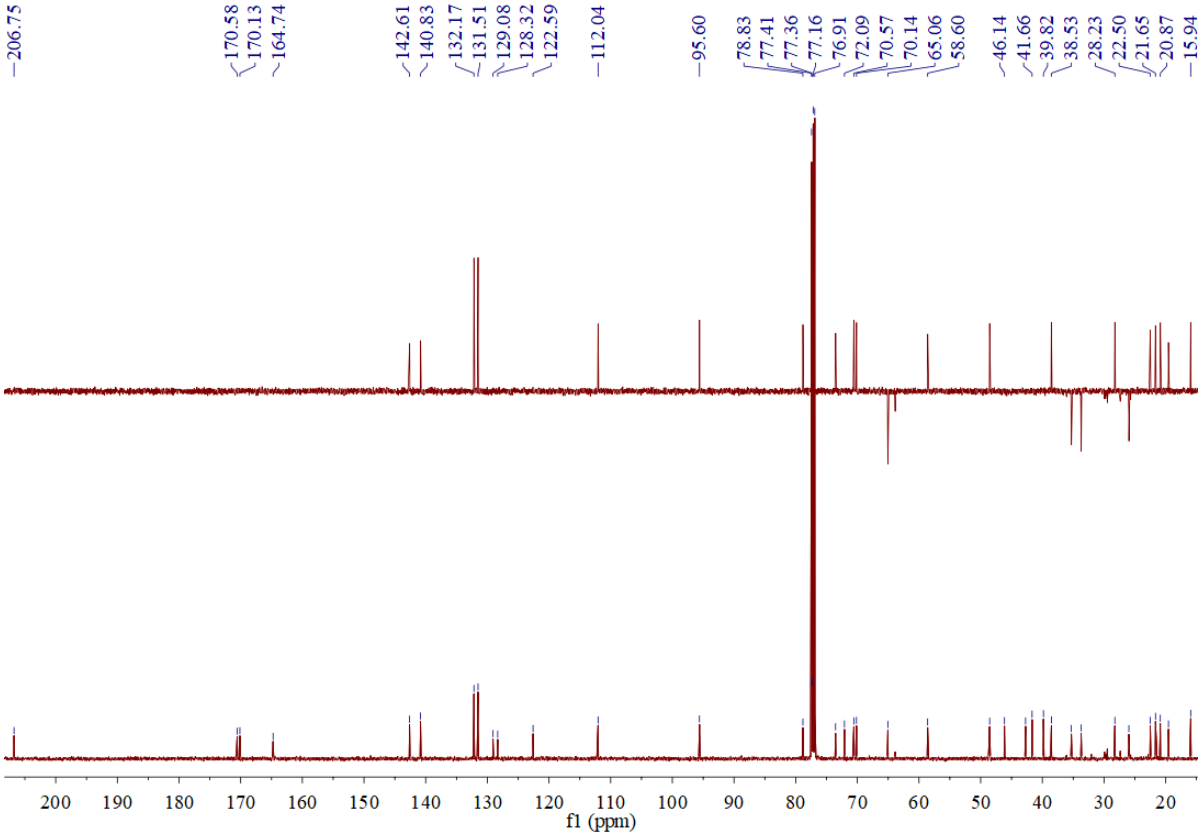


Figure S76. HSQC spectrum of **21** in $CDCl_3$.

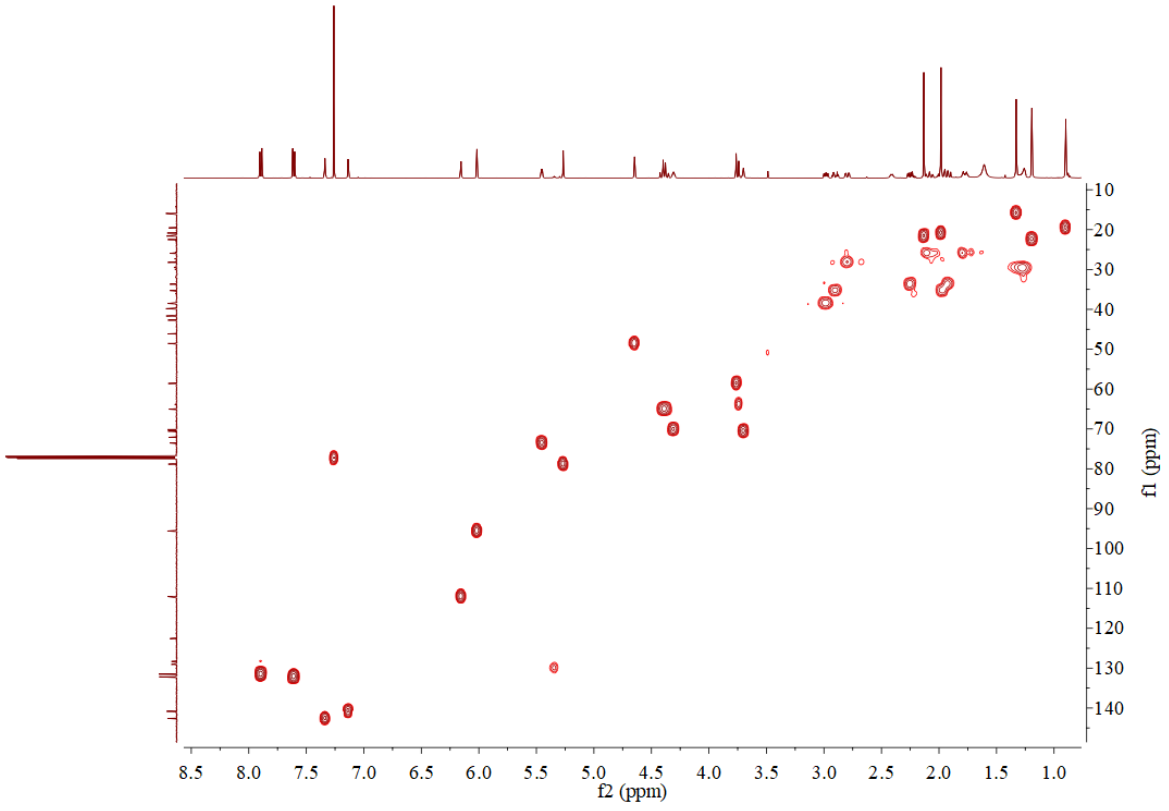


Figure S77. $^{1}H–^{1}H$ COSY spectrum of **21** in $CDCl_3$.

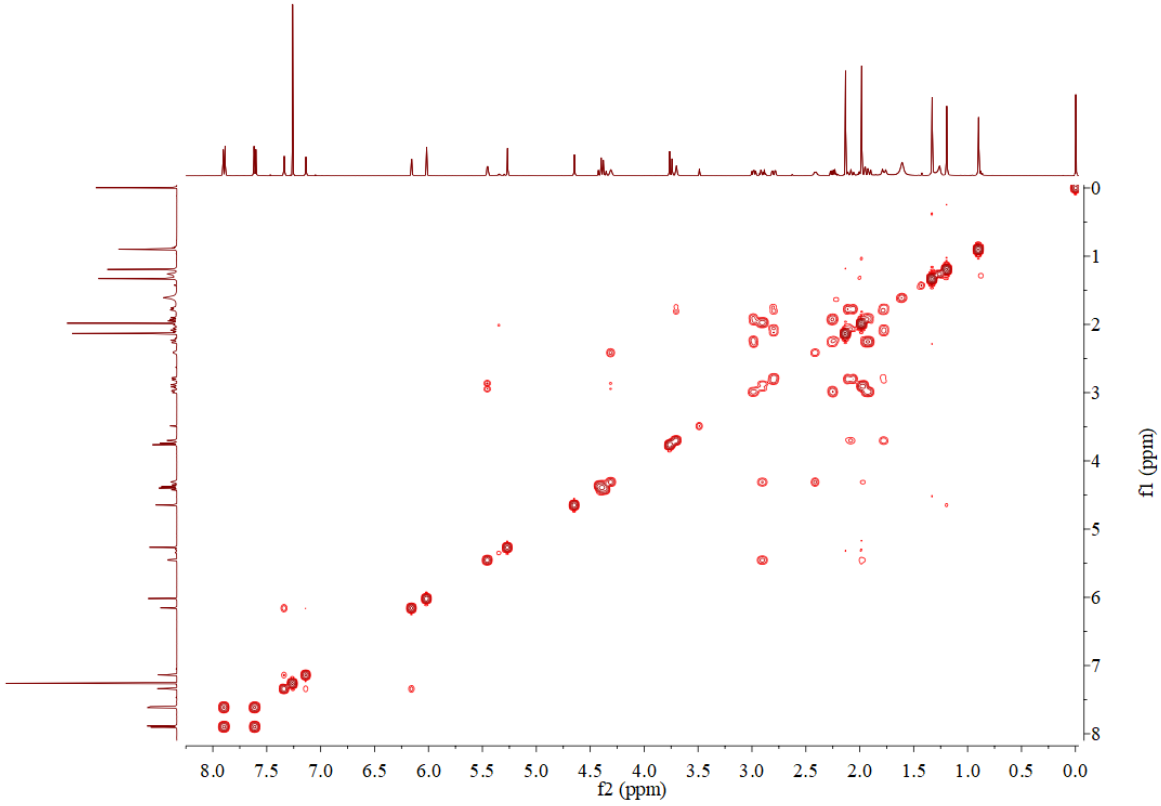


Figure S78. HMBC spectrum of **21** in $CDCl_3$.

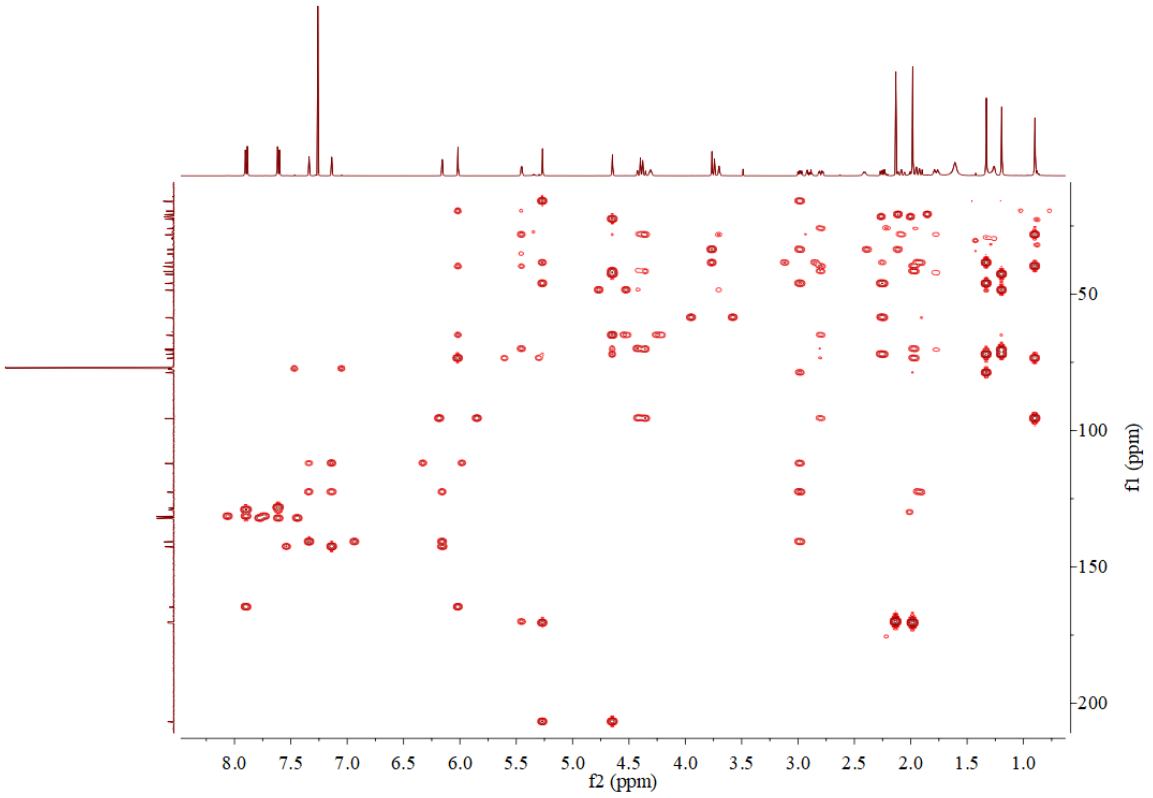
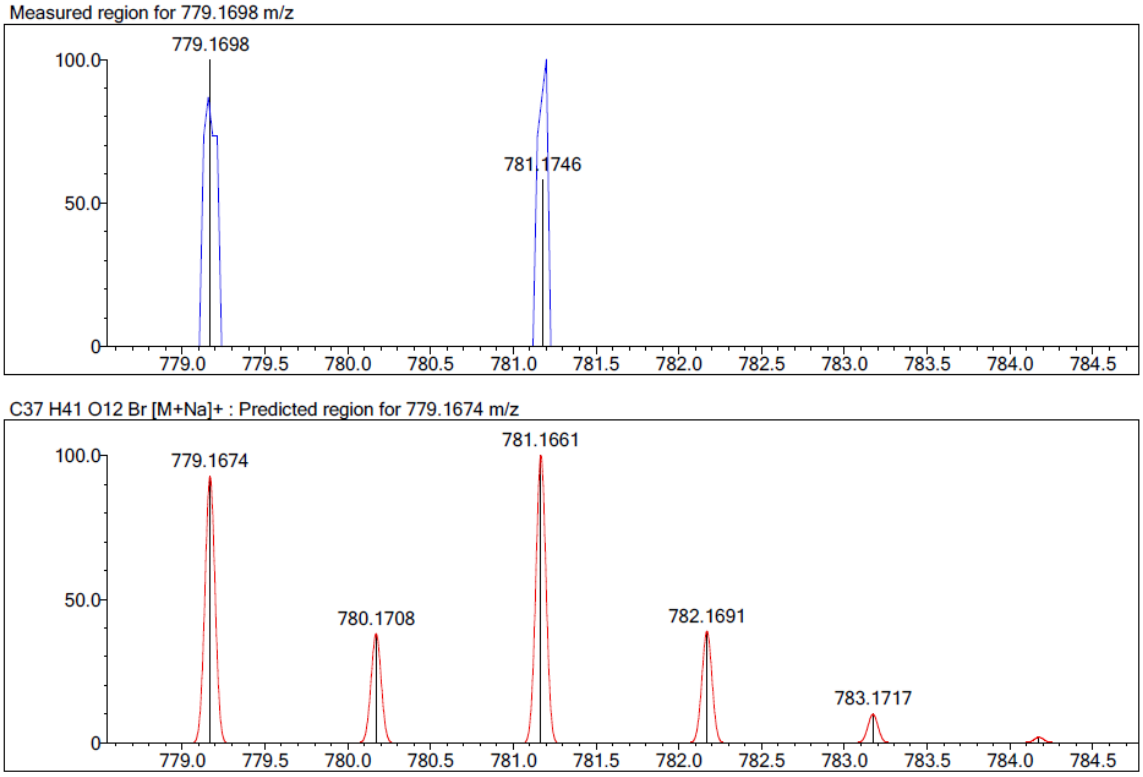


Figure S79. HRESIMS spectrum of **21**.



22. **Figures S80**–**S82.** ^{1}H NMR, ^{13}C NMR, and HRESIMS spectra of **22**.

Figure S80. ^{1}H NMR (500 MHz) spectrum of **22** in $CDCl_3$.

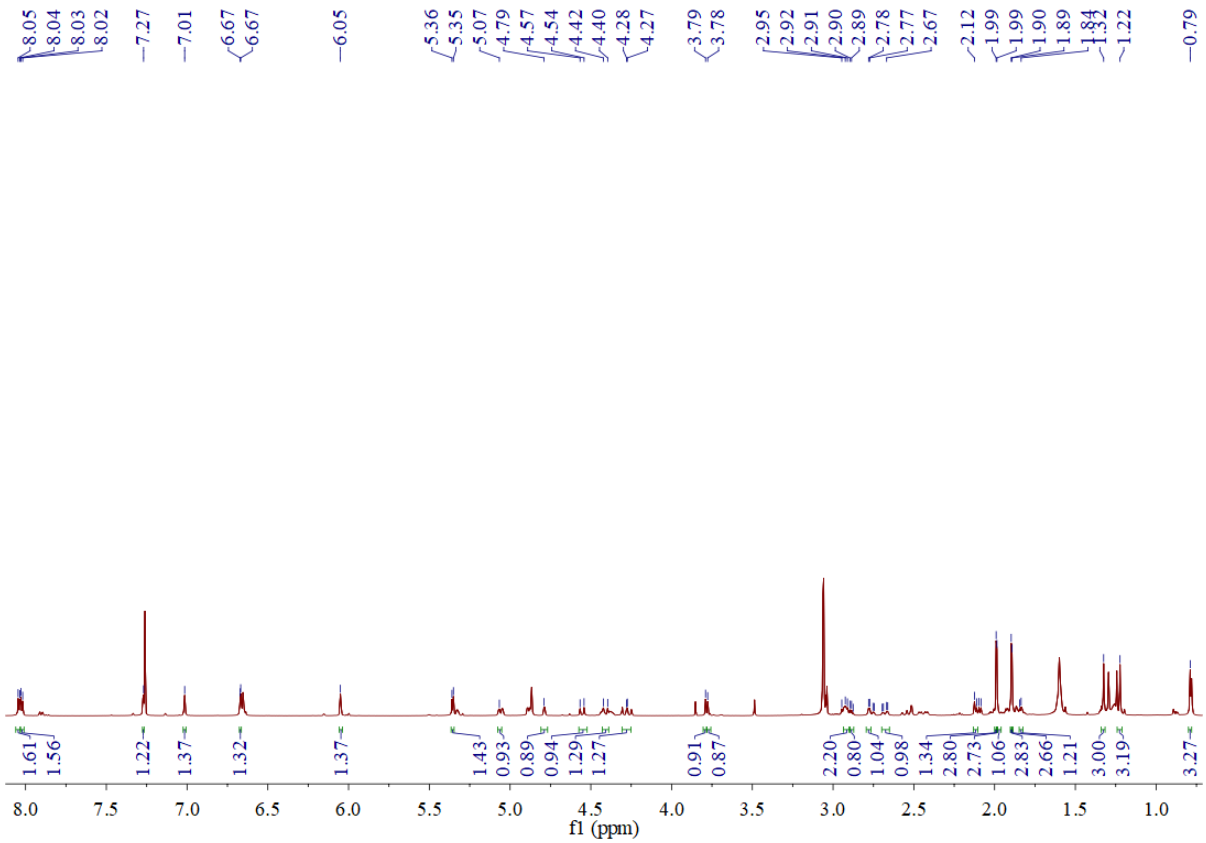


Figure S81. ^{13}C NMR (125 MHz) spectrum of **22** in $CDCl_3$.

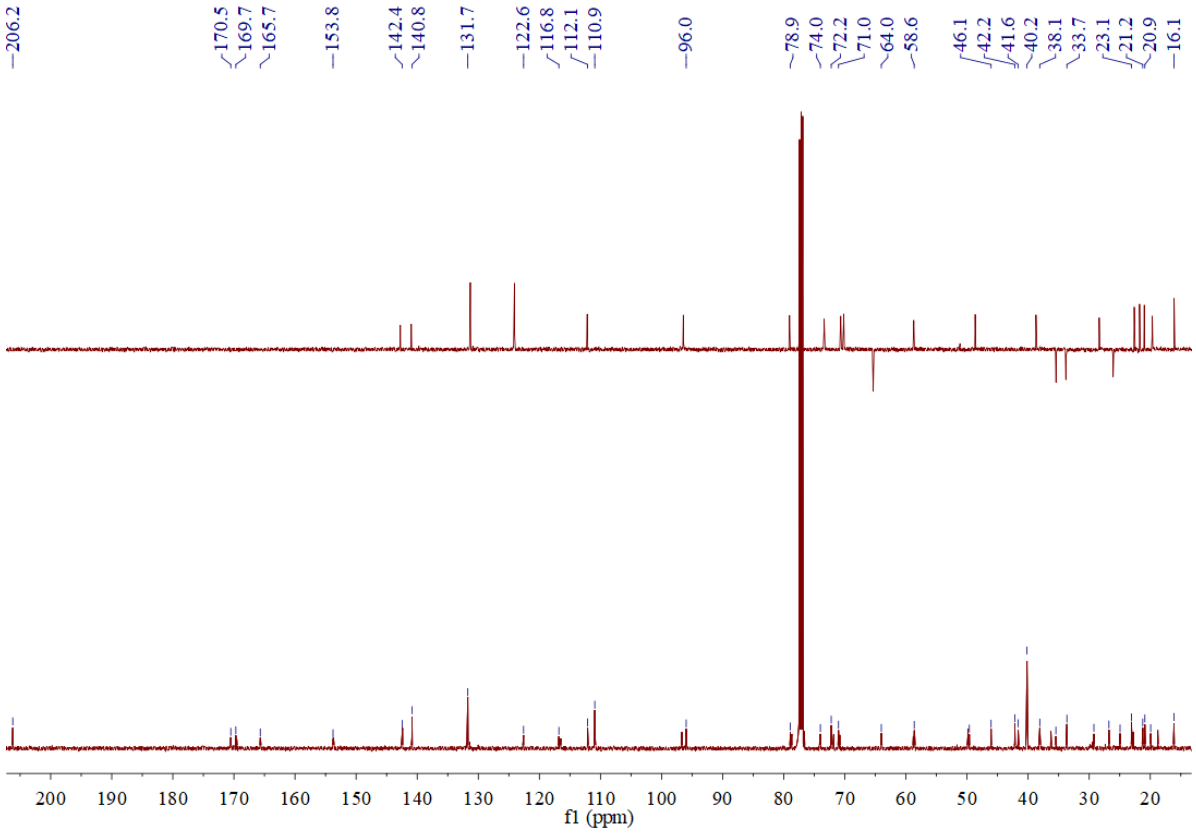
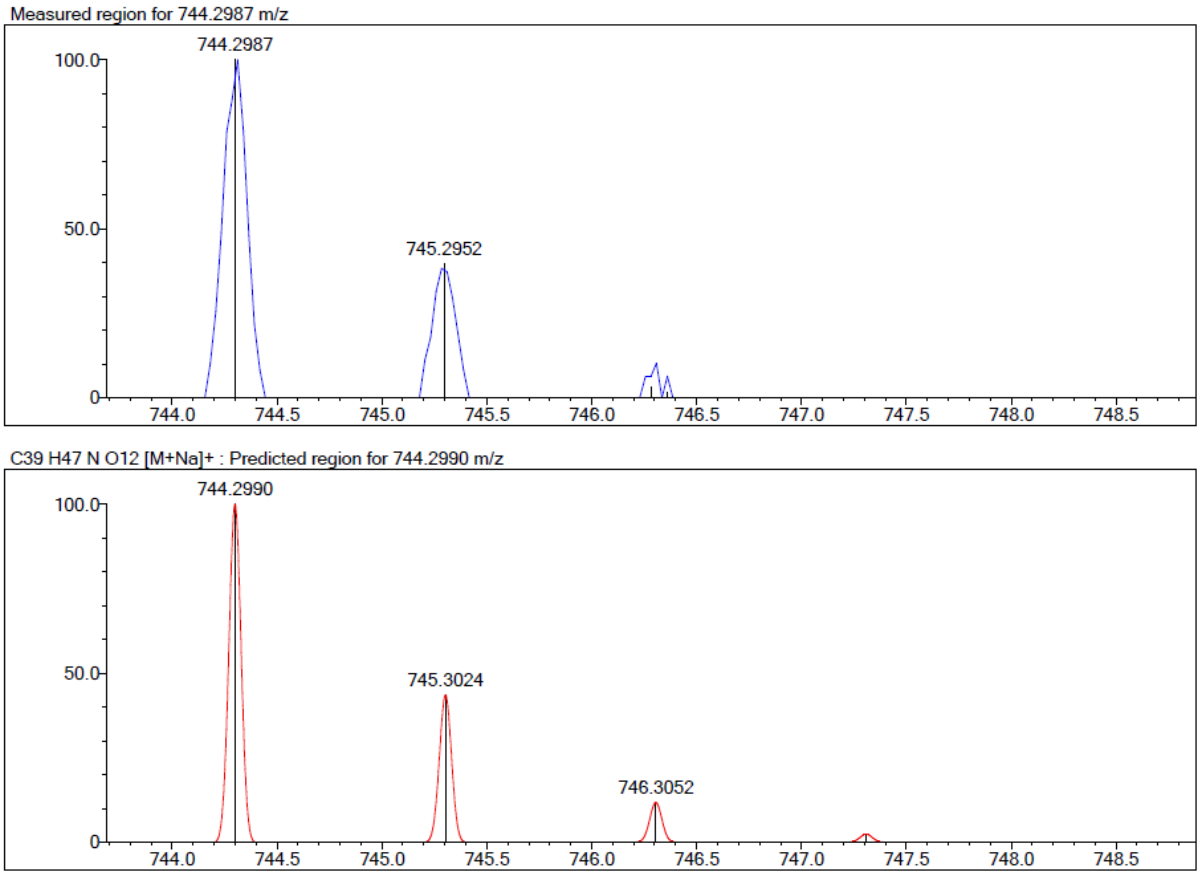


Figure S82. HRESIMS spectrum of **22**.



23. **Figures S83–S84.** ^{1}H NMR and ^{13}C NMR spectra of **23**.

Figure S83. ^{1}H NMR (400 MHz) spectrum of **23** in $CDCl_3$.

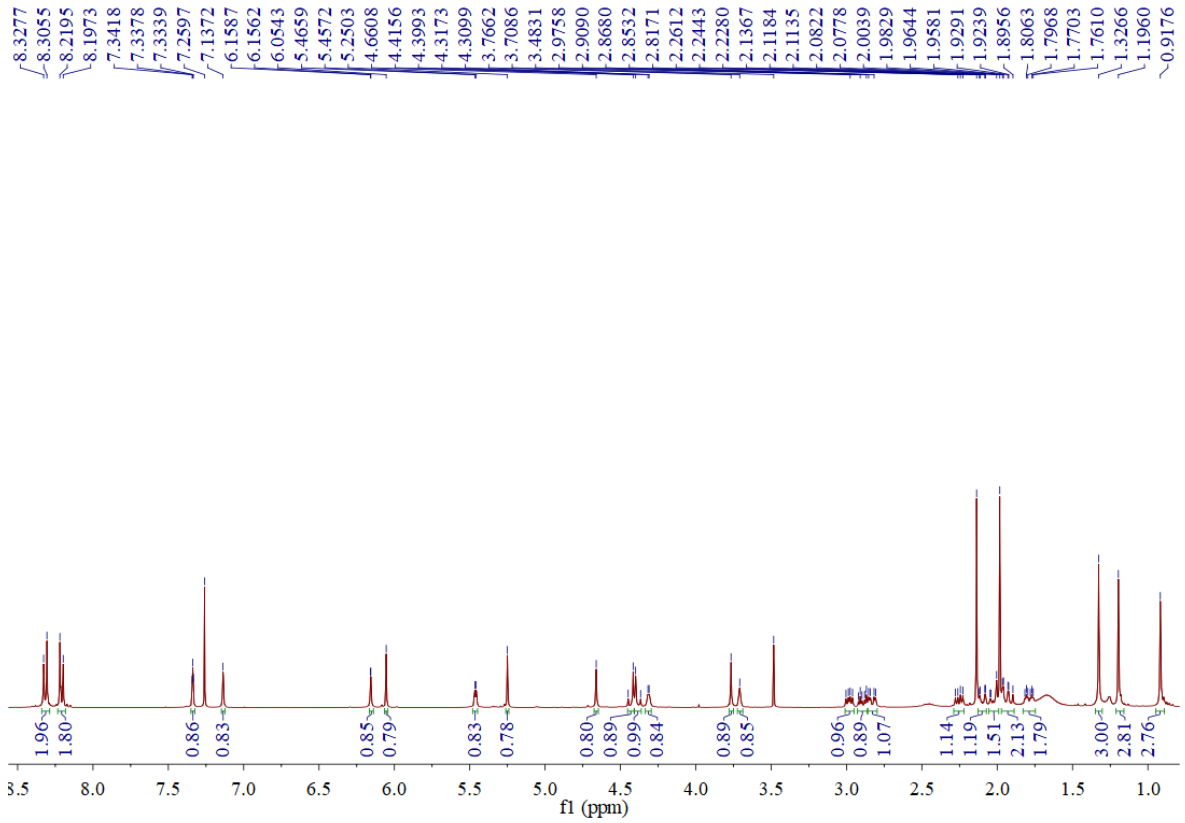
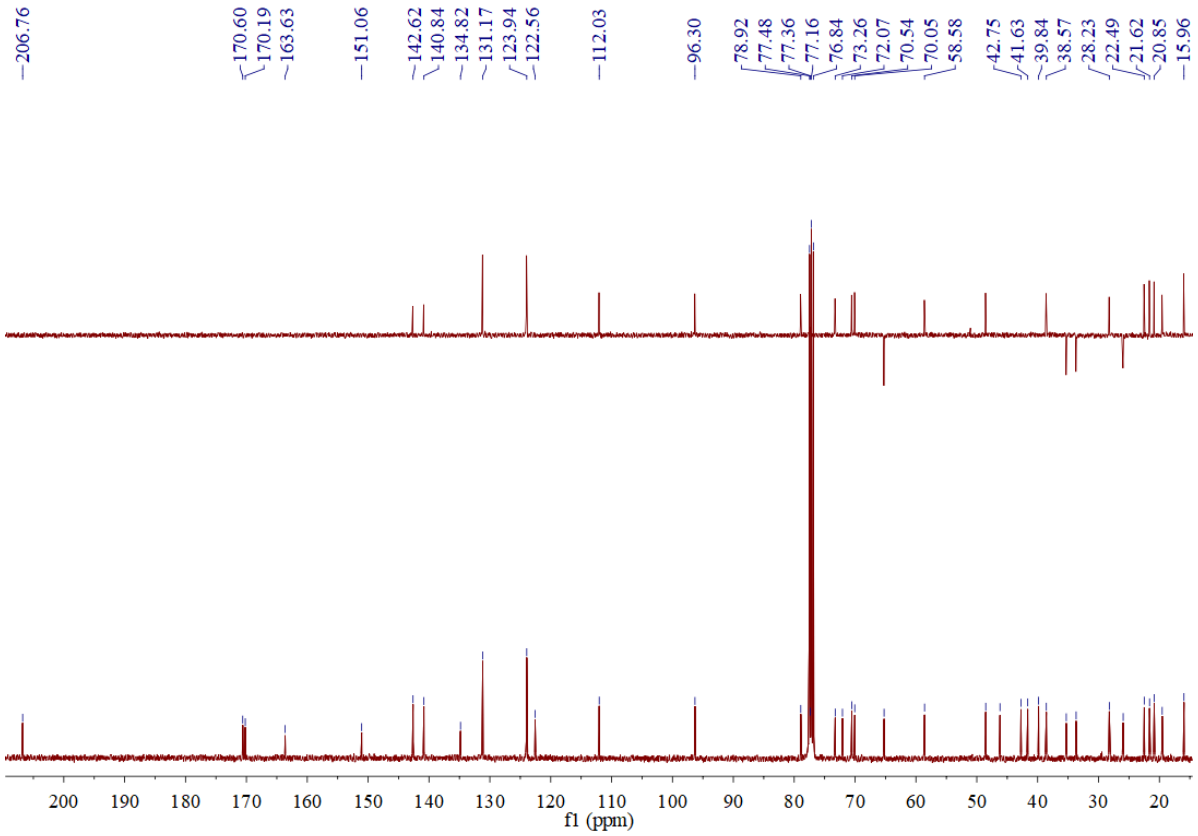


Figure S84. ^{13}C NMR (125 MHz) spectrum of **23** in $CDCl_3$.



24. **Figures S85–S86.** ^{1}H NMR and ^{13}C NMR spectra of **24**.

Figure S85. ^{1}H NMR (400 MHz) spectrum of **24** in $CDCl_3$.

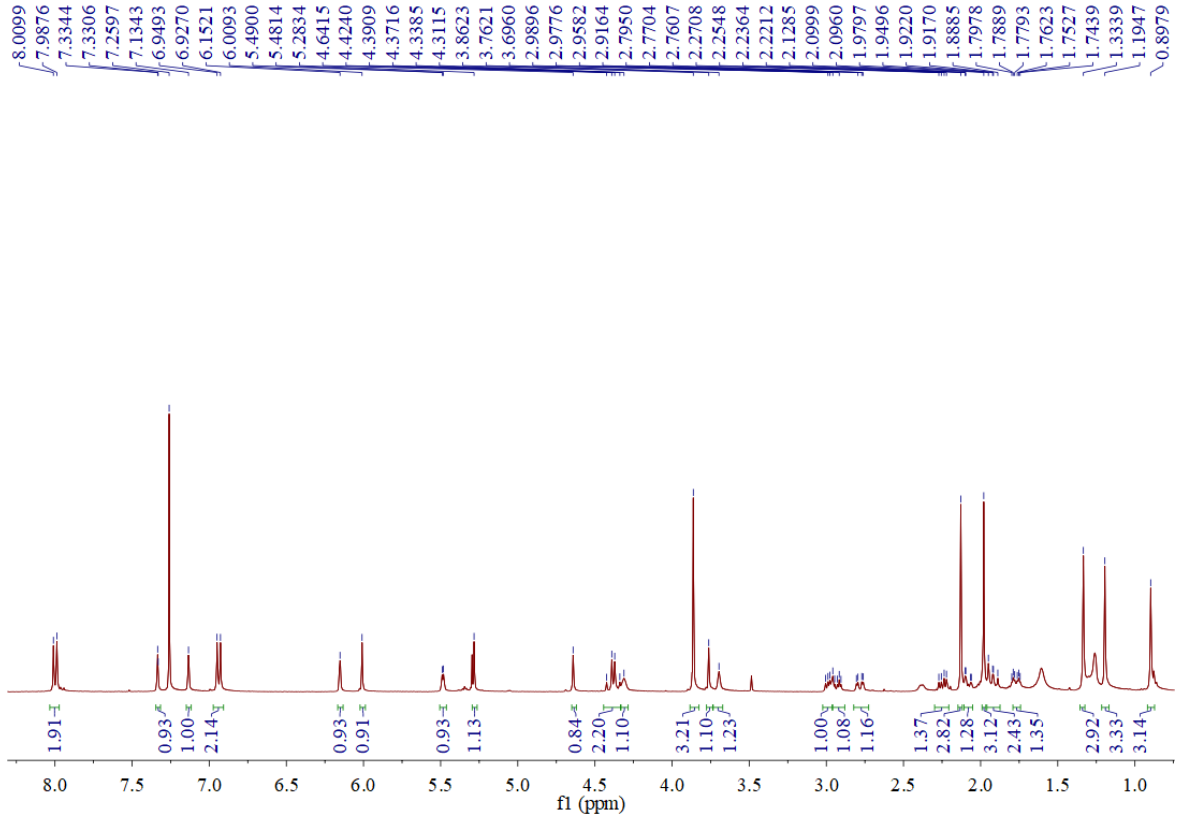
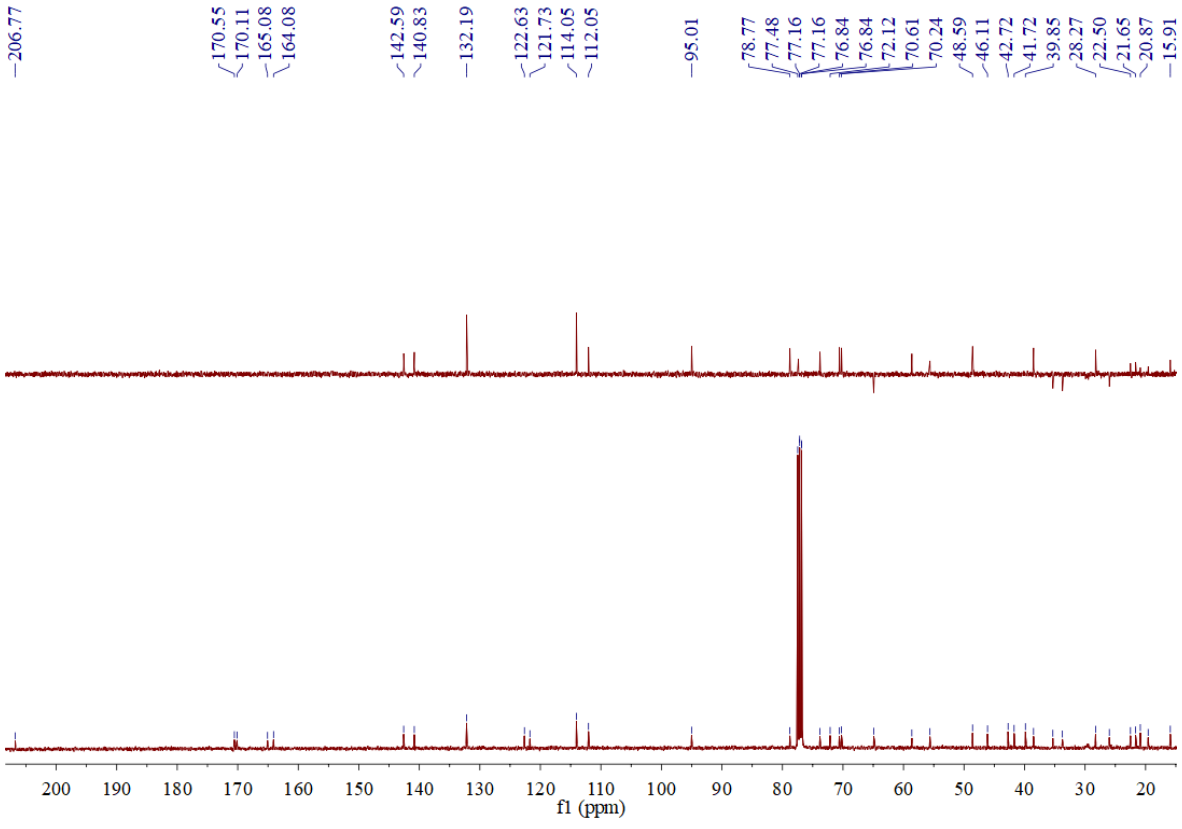


Figure S86. ^{13}C NMR (100 MHz) spectrum of **24** in $CDCl_3$.



25. **Figures S87–S89.** ^{1}H NMR, ^{13}C NMR, and HRESIMS spectra of **25**.

Figure S87. ^{1}H NMR (400 MHz) spectrum of **25** in $CDCl_3$.

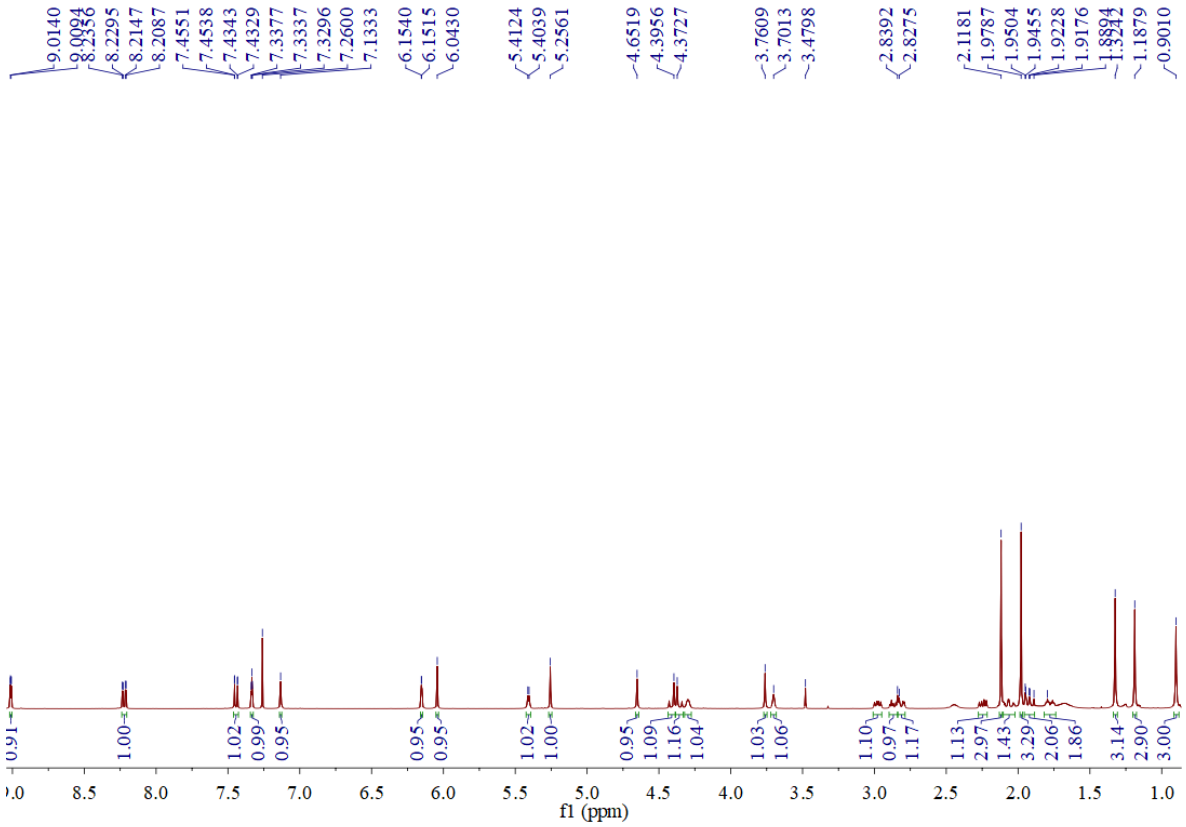


Figure S88. ^{13}C NMR (100 MHz) spectrum of **25** in $CDCl_3$.

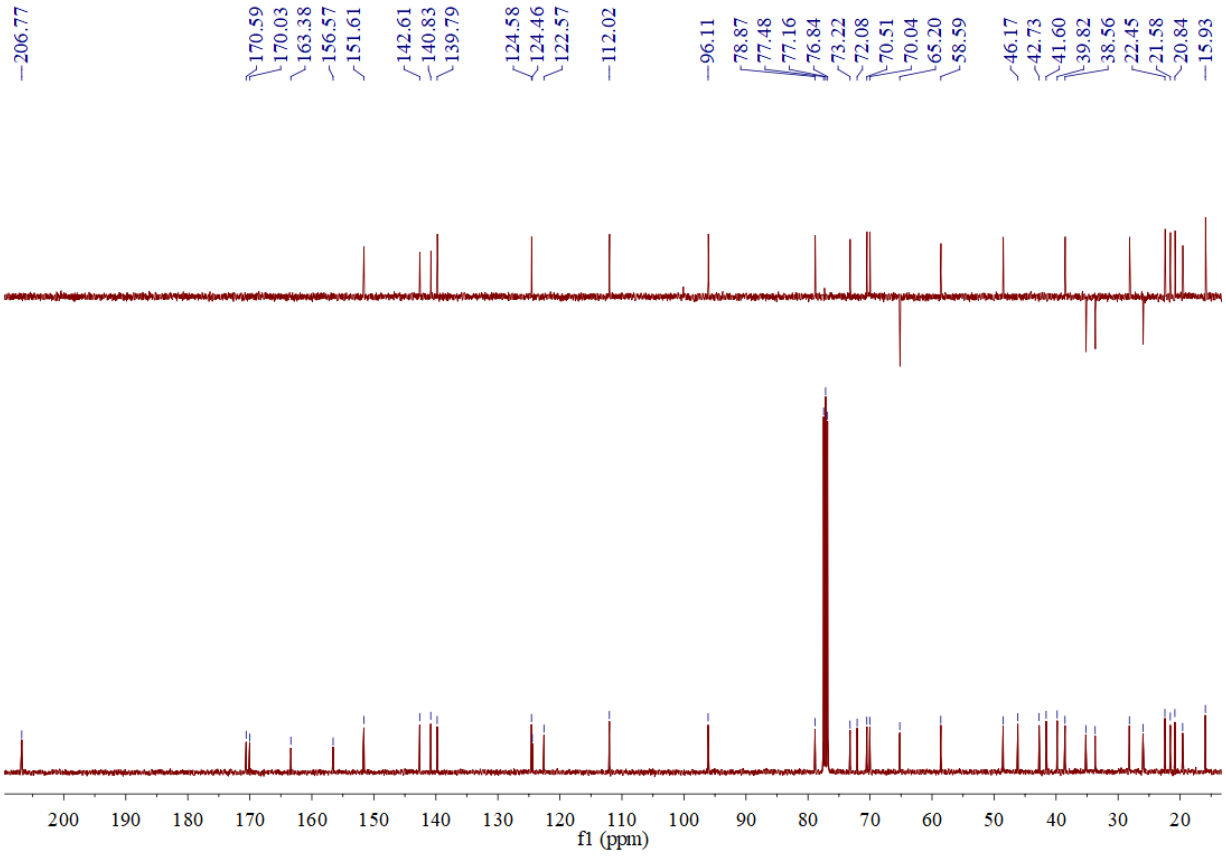
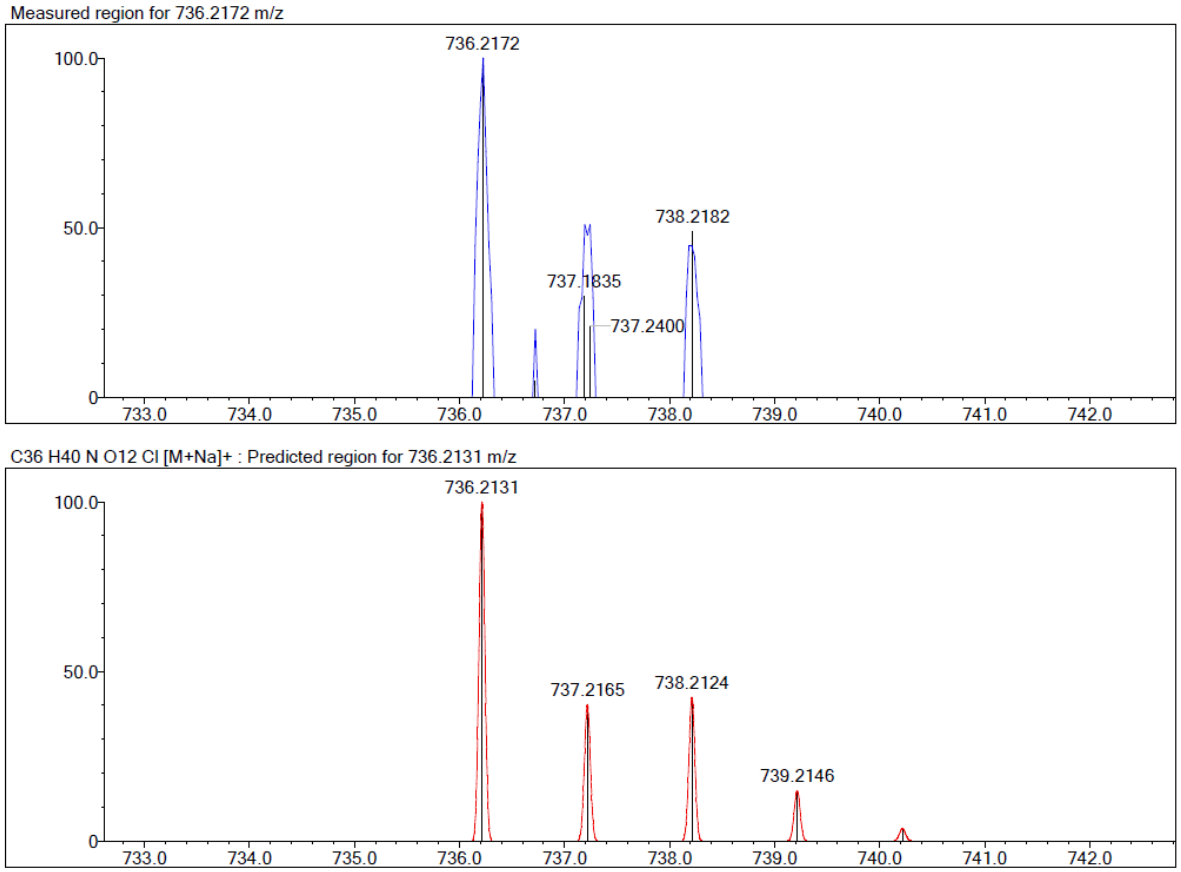


Figure S89. HRESIMS spectrum of **25**.



26. **Table S1.** The IC_{50} and folds values of compounds **14**, **17**–**19**, **21**, and **25** on HepG2 cell line.

Compd.	HepG2		Compd.	HepG2	
	IC_{50} (μM)	Folds[a]		IC_{50} (μM)	Folds[a]
14	0.0455 ± 0.00590	1.04 ↓	**21**	0.241 ± 0.0287	5.51 ↓
17	0.136 ± 0.00871	3.11 ↓	**25**	0.0352 ± 0.00264	1.24 ↑
18	0.0751 ± 0.00967	1.72 ↓	TSN	0.0437 ± 0.00443	-
19	0.0946 ± 0.0141	2.16 ↓			

[a] The increase (↑) or decrease (↓) fold values of the compounds are calculated by comparison their IC_{50} values with that of TSN in the same cancer cell model.

27. **Table S2.** The cell viability of compounds **14**, **17**–**19**, **21**, and **25** on normal cells (MCF10A) at the concentration of 0.3 μM.

Compd.	MCF10A	Compd.	MCF10A
	Cell viability (%)		Cell viability (%)
14	0.314	**21**	10.7
17	0.658	**25**	0.310
18	4.57	TSN	0.384
19	0.155		