

Synthesis and biological evaluation of novel triple-modified Colchicine derivatives as potent tubulin-targeting anticancer agents

Urszula Majcher¹, Greta Klejborowska¹, Magdalena Kaik¹, Ewa Maj², Joanna Wietrzyk², Mahshad Moshari³, Jordane Preto⁴, Jack A. Tuszynski^{4,5} and Adam Huczynski^{1,*}

¹ Department of Bioorganic Chemistry, Faculty of Chemistry, Adam Mickiewicz University, Umultowska 89b, 61-614 Poznan, Poland.

² Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Rudolfa Weigla 12, 53-114 Wrocław, Poland.

³ Department of Chemistry, University of Alberta, Edmonton, Alberta T6G 1Z2, Canada.

⁴ Department of Oncology, University of Alberta, Edmonton, Alberta T6G 1Z2, Canada.

⁵ DIMEAS, Politecnico di Torino, Corso Duca degli Abruzzi 24, Turin, Italy.

* Correspondence: adhucz@amu.edu.pl; Tel.: +48-61-829-1673

Supplementary Materials

Figure S1. The ¹³C NMR spectrum of **2** in CDCl₃.

Figure S2. The ¹H NMR spectrum of **2** in CDCl₃.

Figure S3. The ¹³C NMR spectrum of **3** in CDCl₃.

Figure S4. The ¹H NMR spectrum of **3** in CDCl₃.

Figure S5. The ¹³C NMR spectrum of **4** in CDCl₃.

Figure S6. The ¹H NMR spectrum of **4** in CDCl₃.

Figure S7. The ¹³C NMR spectrum of **5** in CDCl₃.

Figure S8. The ¹H NMR spectrum of **5** in CDCl₃.

Figure S9. The ¹³C NMR spectrum of **6** in CDCl₃.

Figure S10. The ¹H NMR spectrum of **6** in CDCl₃.

Figure S11. The ¹³C NMR spectrum of **7** in CDCl₃.

Figure S12. The ¹H NMR spectrum of **7** in CDCl₃.

Figure S13. The ¹³C NMR spectrum of **8** in CDCl₃.

Figure S14. The ¹H NMR spectrum of **8** in CDCl₃.

Figure S15. The ¹⁹F NMR spectrum of **8** in CDCl₃.

Figure S16. The ¹³C NMR spectrum of **9** in CDCl₃.

Figure S17. The ¹H NMR spectrum of **9** in CDCl₃.

Figure S18. The ¹³C NMR spectrum of **10** in CDCl₃.

Figure S19. The ¹H NMR spectrum of **10** in CDCl₃.

Figure S20. The ¹³C NMR spectrum of **11** in CDCl₃.

Figure S21. The ¹H NMR spectrum of **11** in CDCl₃.

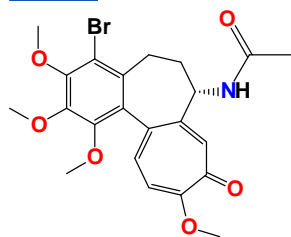
Figure S22. The ¹³C NMR spectrum of **12** in CDCl₃.

Figure S23. The ¹H NMR spectrum of **12** in CDCl₃.

Figure S24. 3D plots of the linear regression results for the binding energies (BE) vs MlogP vs log IC₅₀ [μM] values for LoVo cell line.



Figure S25. 3D plots of the linear regression results for the binding energies (BE) vs MlogP vs log IC₅₀ [μM] values for LoVo/DX cell line.



Chemical formula: $C_{22}H_{24}BrNO_6$, MW = 478.3 g/mol

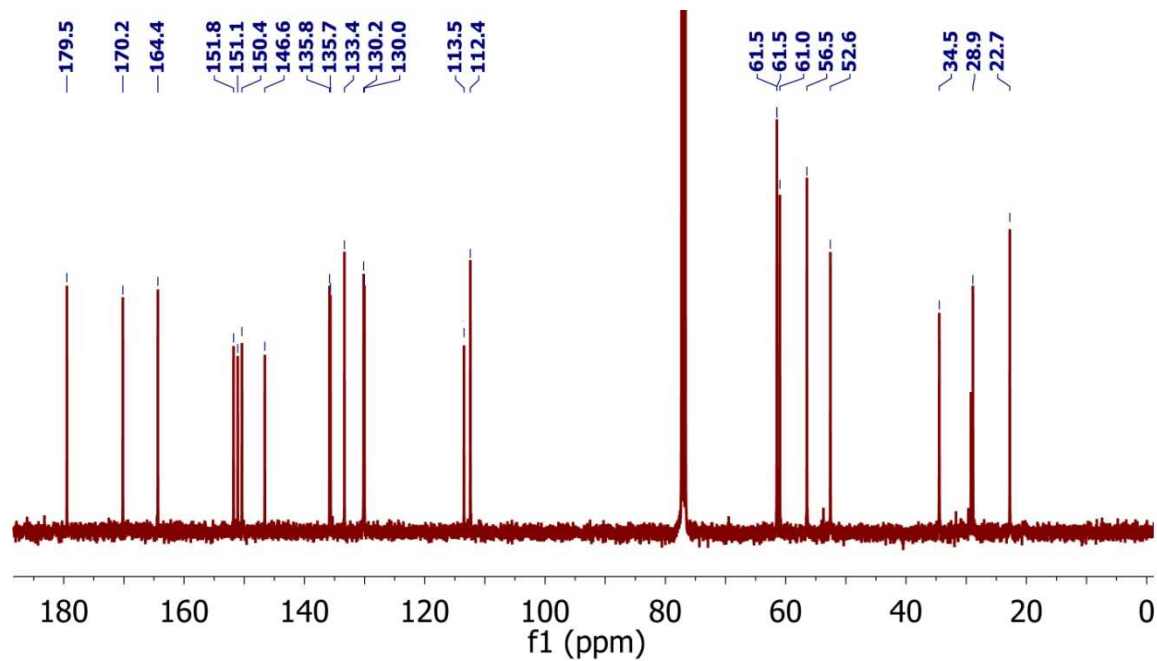


Figure S1. The ^{13}C NMR spectrum of **2** in $CDCl_3$.

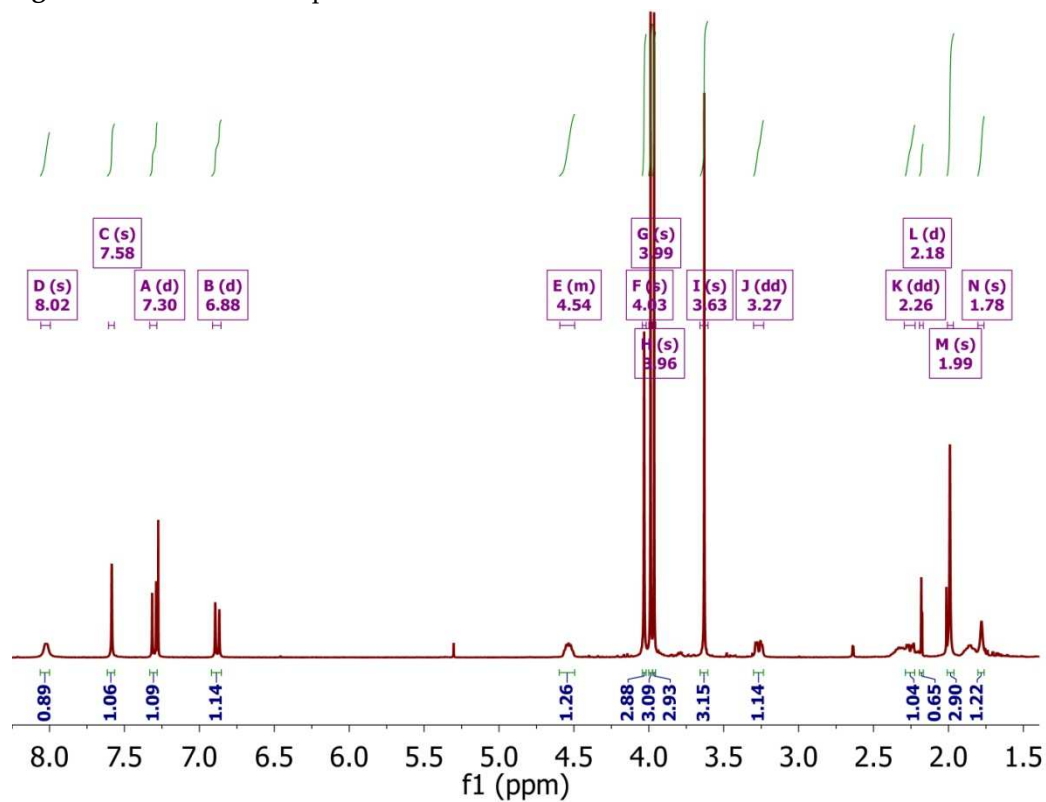
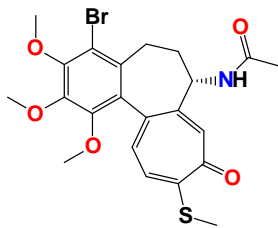


Figure S2. The 1H NMR spectrum of **2** in $CDCl_3$.



Chemical formula: $C_{22}H_{24}BrNO_5S$, MW = 494.4 g/mol

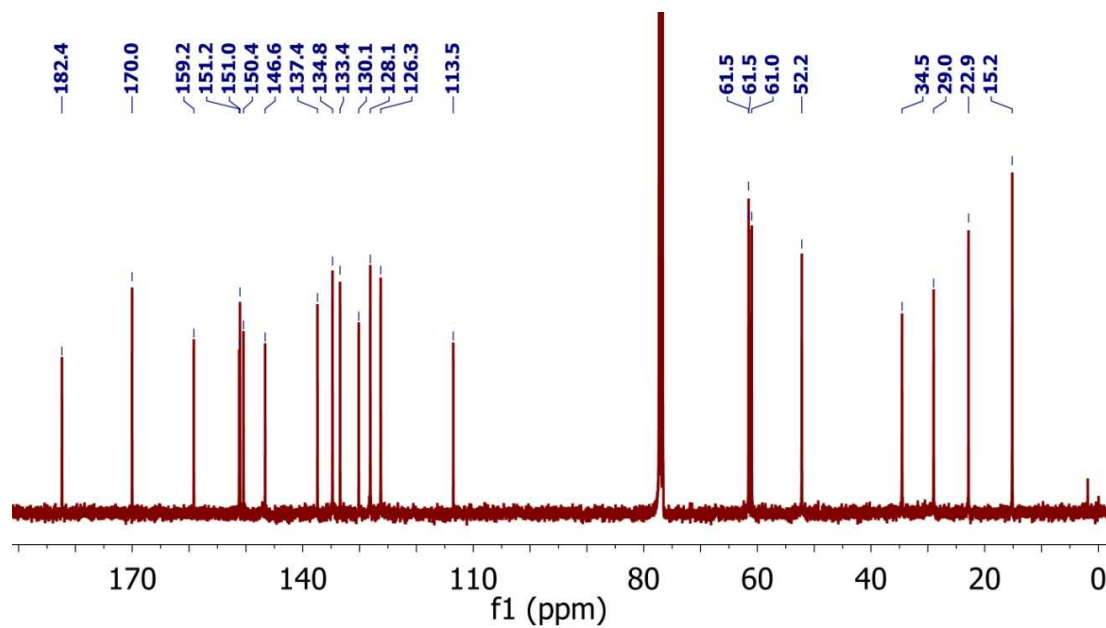


Figure S3. The ^{13}C NMR spectrum of 3 in $CDCl_3$.

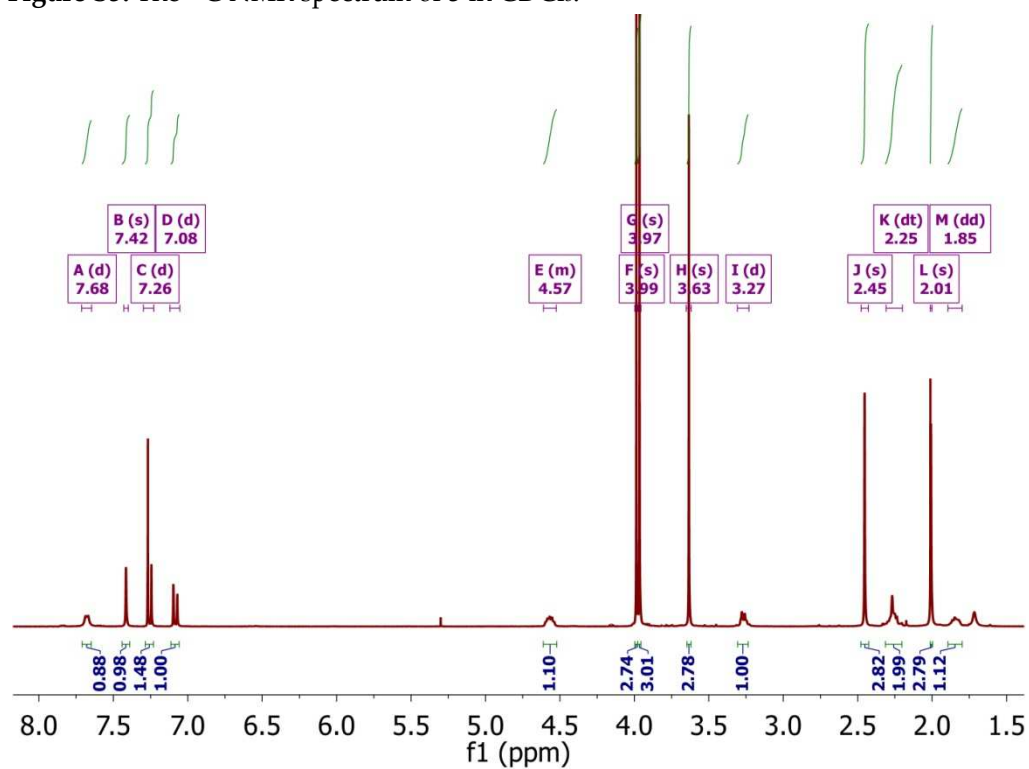
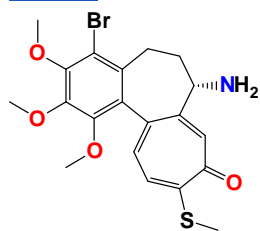


Figure S4. The 1H NMR spectrum of 3 in $CDCl_3$.



Chemical formula: $C_{20}H_{22}BrNO_4S$, MW = 452.4 g/mol

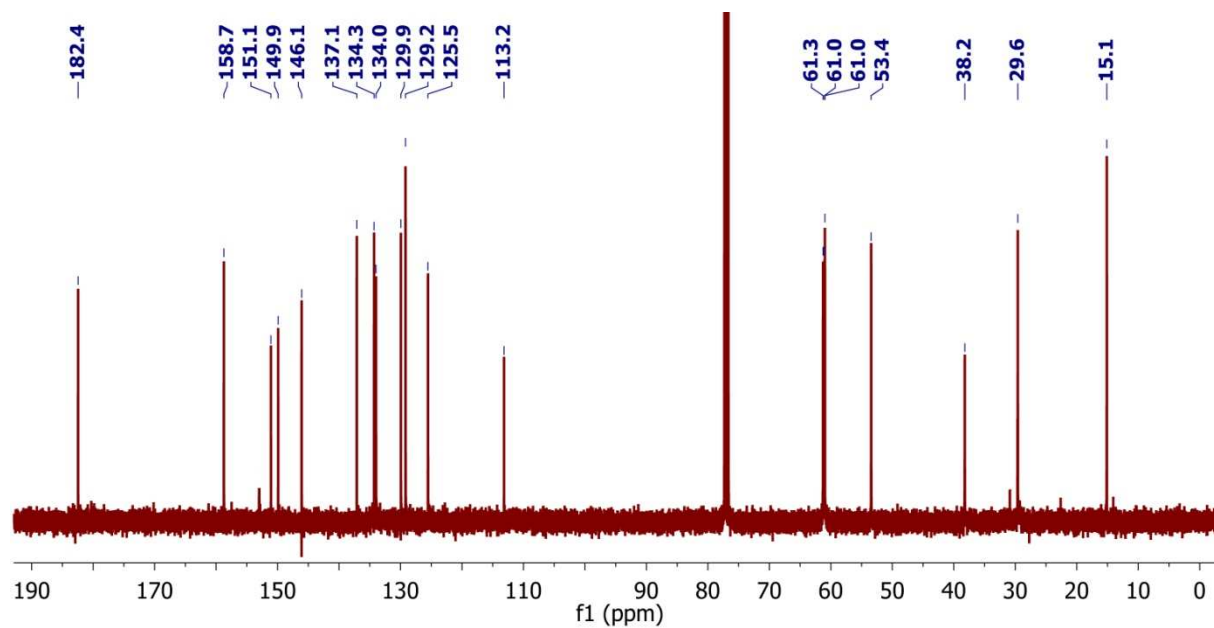


Figure S5. The ^{13}C NMR spectrum of **4** in $CDCl_3$.

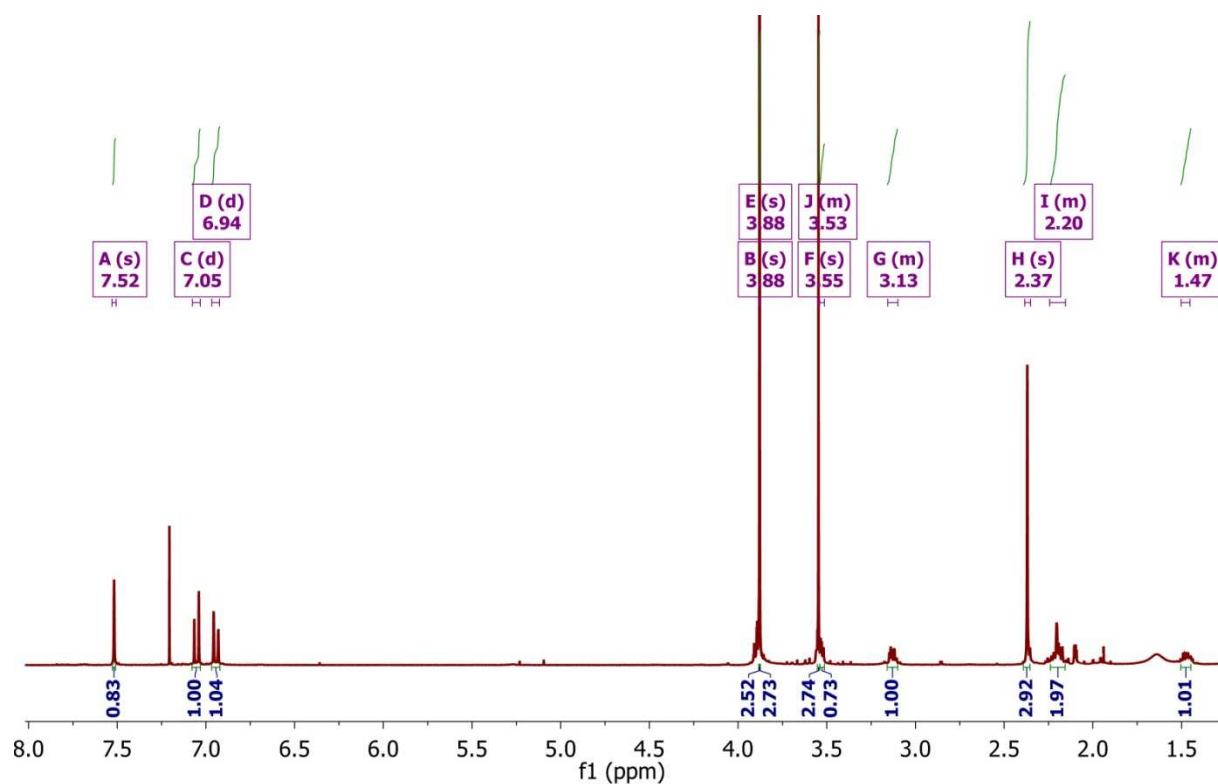
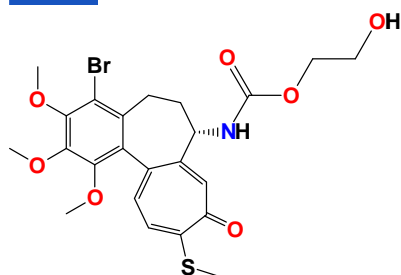


Figure S6. The 1H NMR spectrum of **4** in $CDCl_3$.



Chemical formula: $C_{23}H_{26}BrNO_7S$, MW = 539.1 g/mol

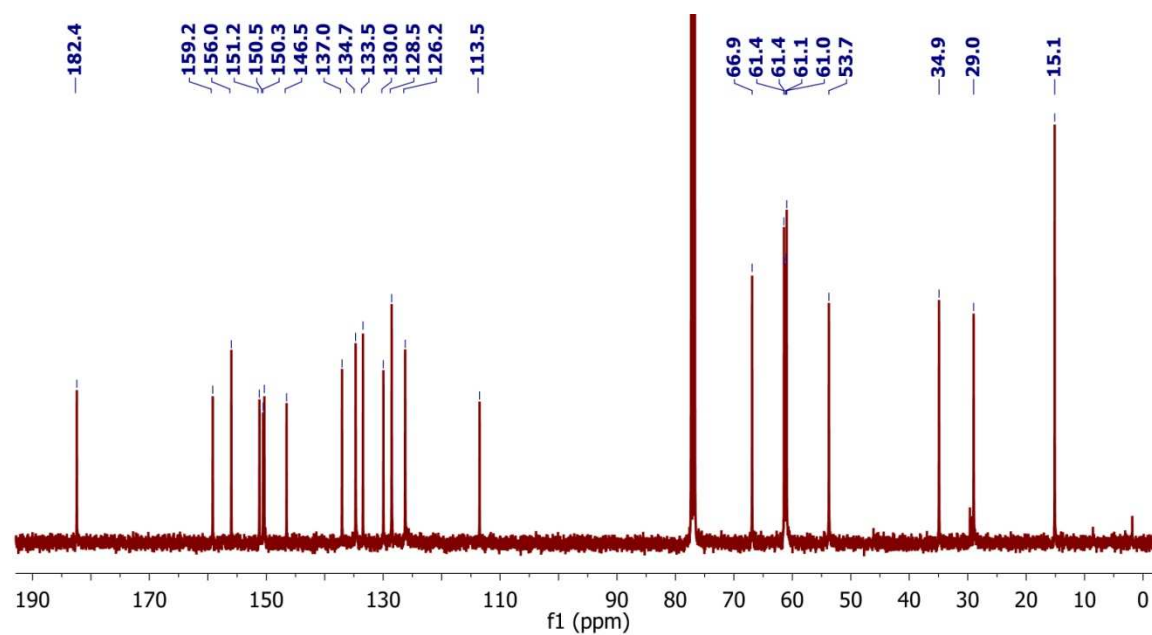


Figure S7. The ^{13}C NMR spectrum of **5** in $CDCl_3$.

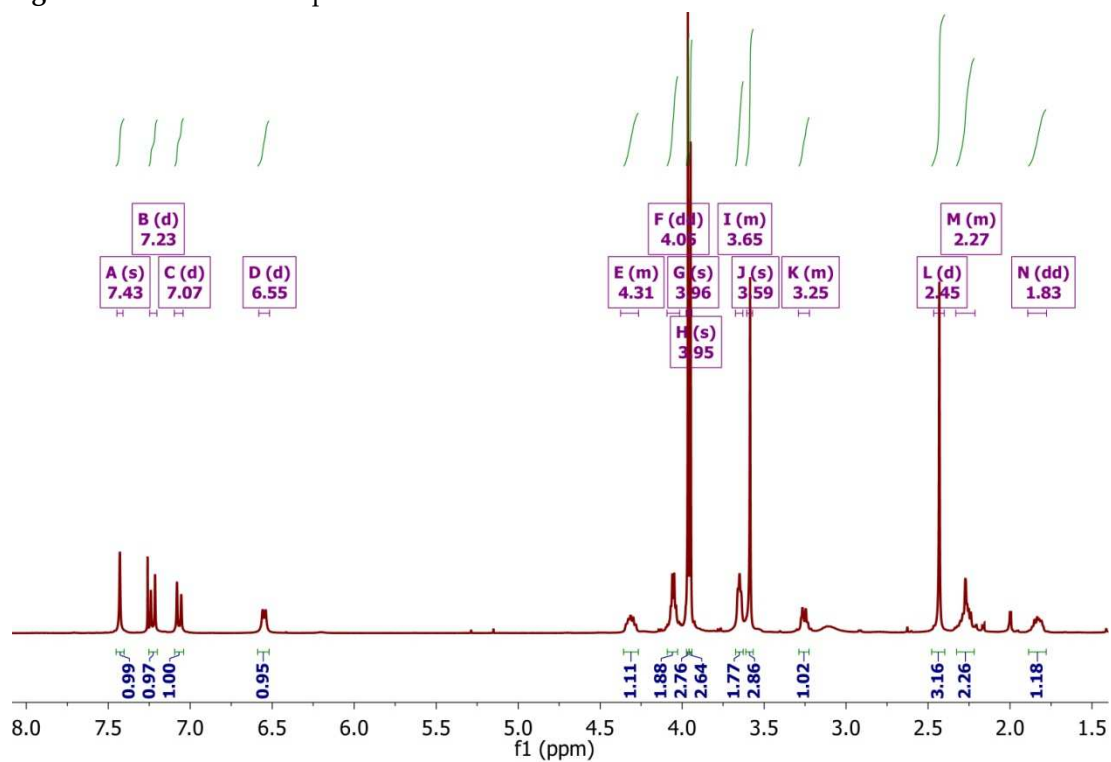
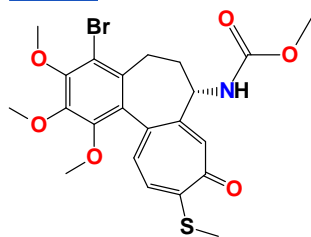


Figure S8. The 1H NMR spectrum of **5** in $CDCl_3$.



Chemical formula: $C_{22}H_{24}BrNO_6S$, MW = 509.1 g/mol

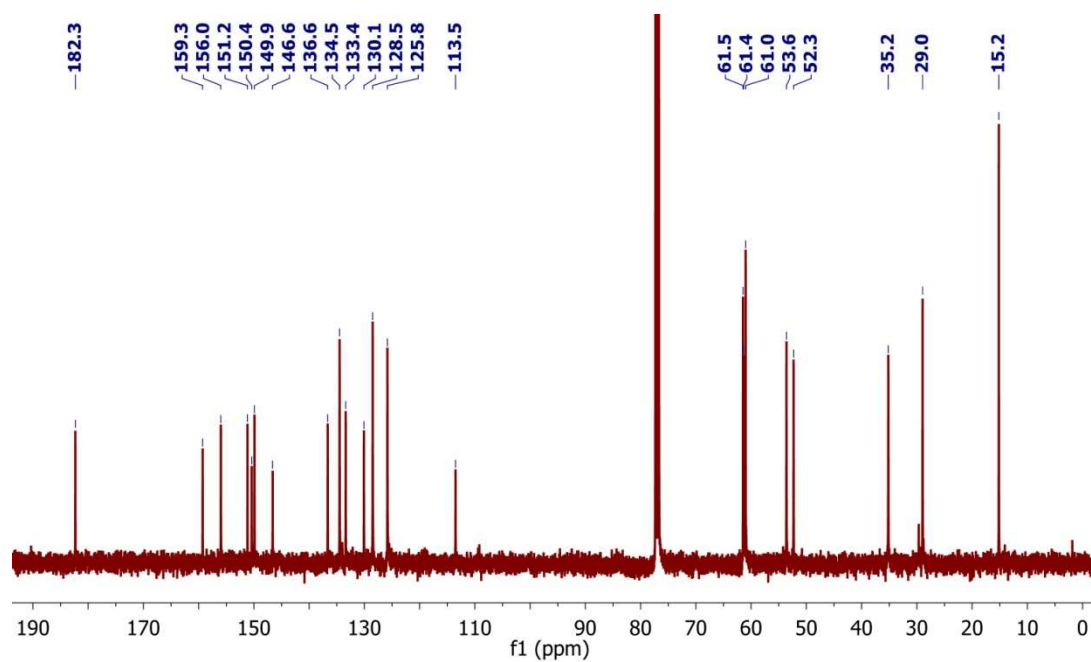


Figure S9. The ^{13}C NMR spectrum of 6 in $CDCl_3$.

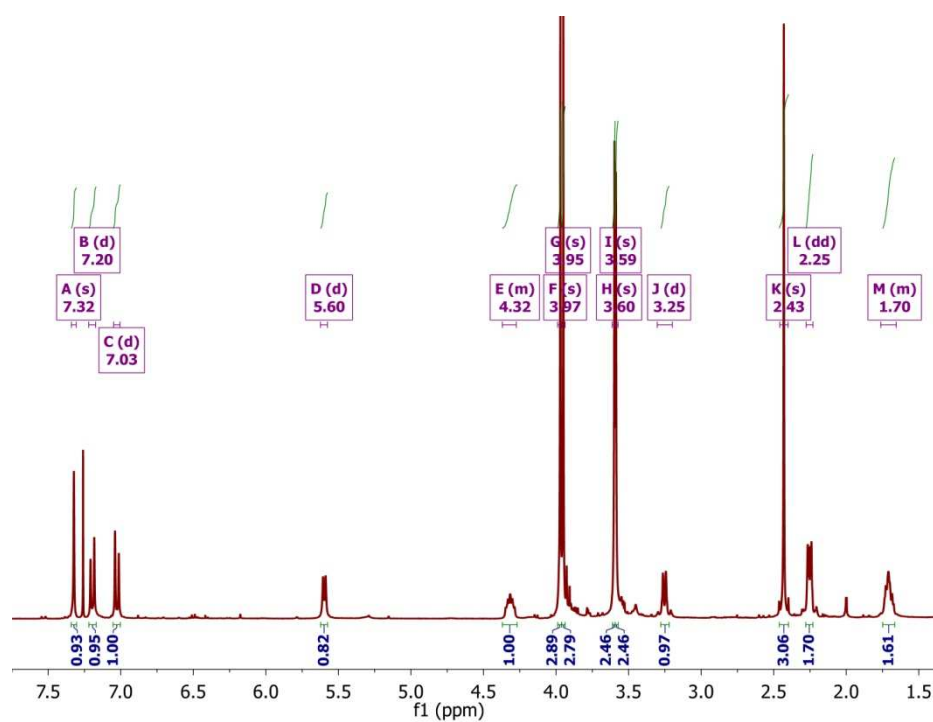
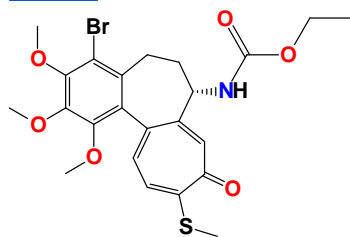


Figure S10. The 1H NMR spectrum of 6 in $CDCl_3$.



Chemical formula: $C_{23}H_{26}BrNO_6S$, MW = 524.4 g/mol

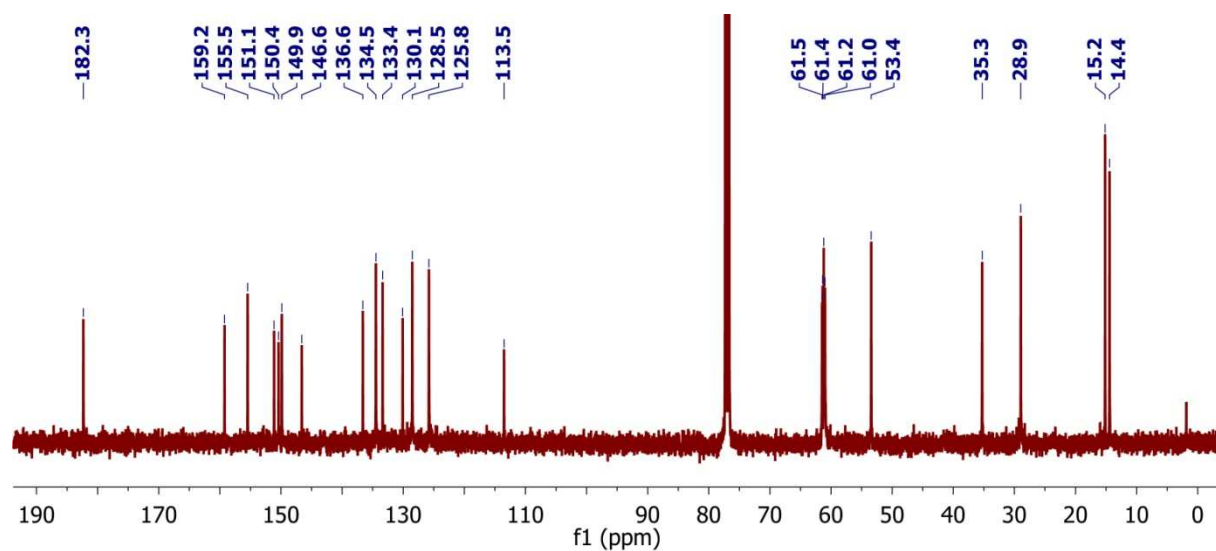


Figure S11. The ^{13}C NMR spectrum of 7 in $CDCl_3$.

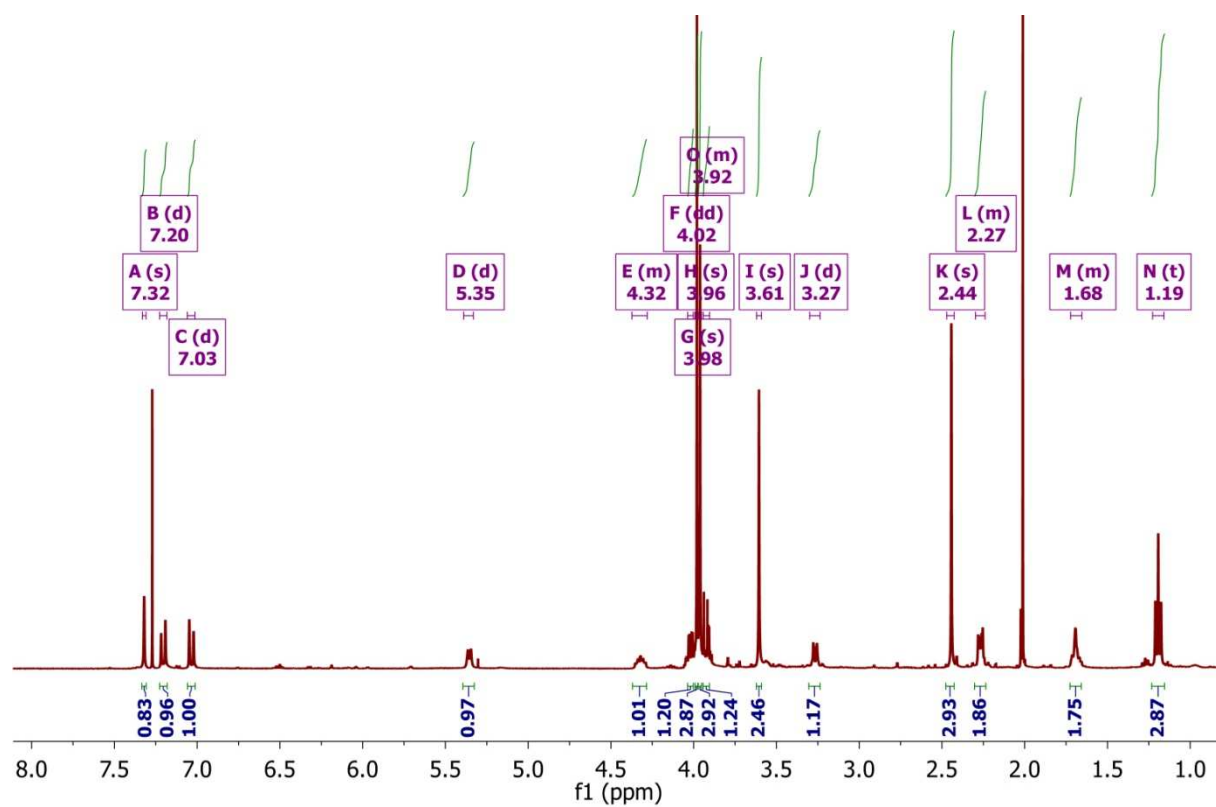
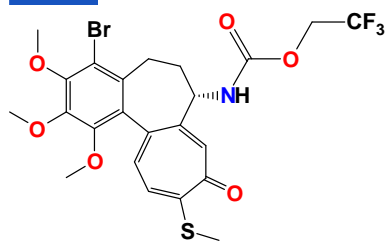


Figure S12. The 1H NMR spectrum of 7 in $CDCl_3$.



Chemical formula: $C_{23}H_{23}BrF_3NO_6S$, MW = 578.4 g/mol

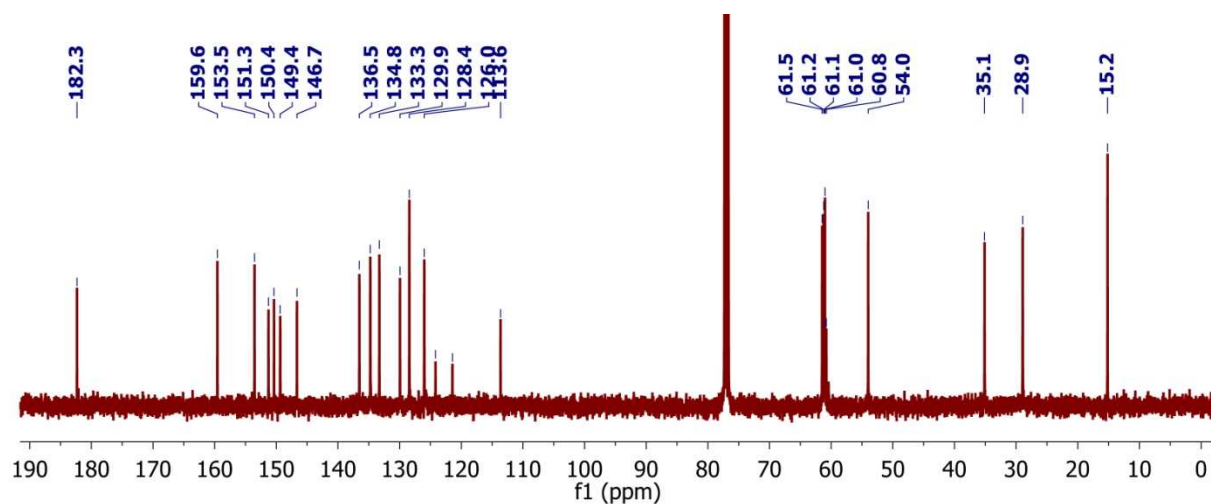


Figure S13. The ^{13}C NMR spectrum of 8 in $CDCl_3$.

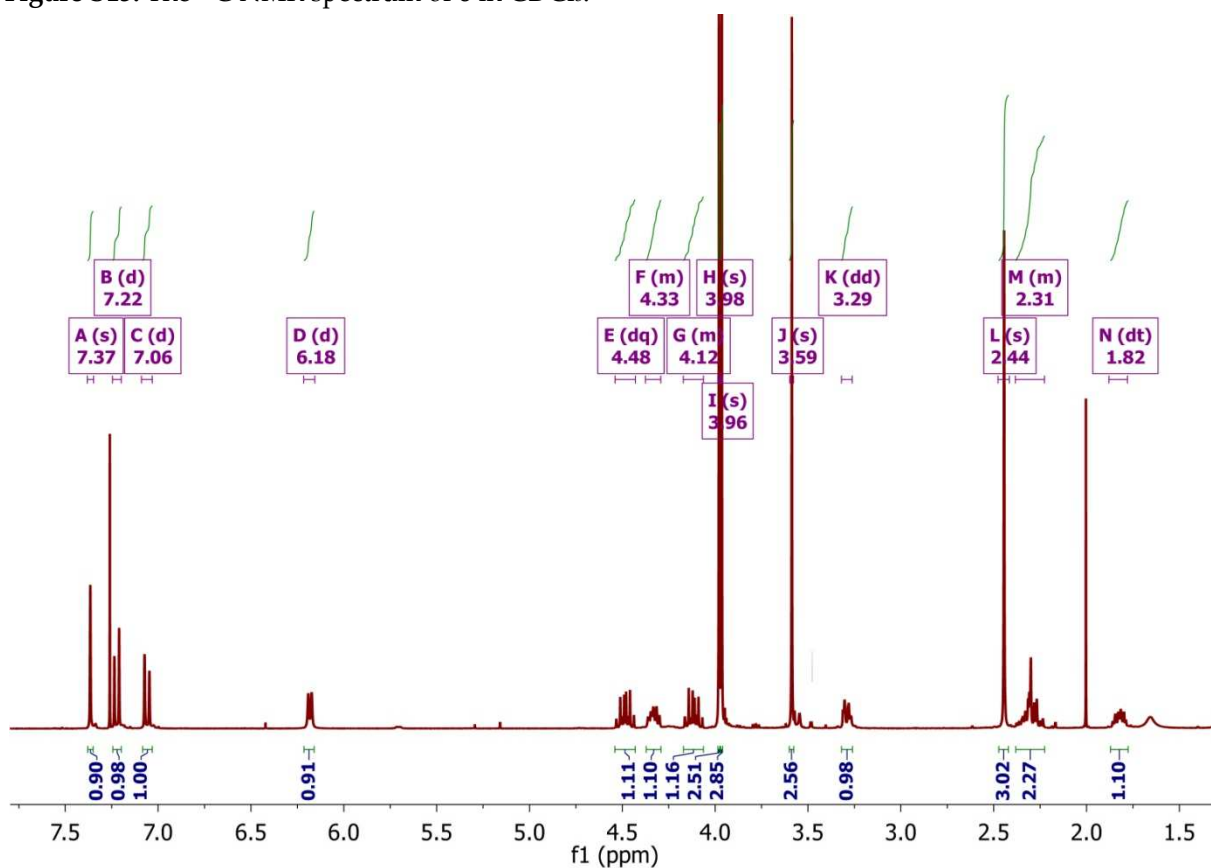


Figure S14. The 1H NMR spectrum of 8 in $CDCl_3$.

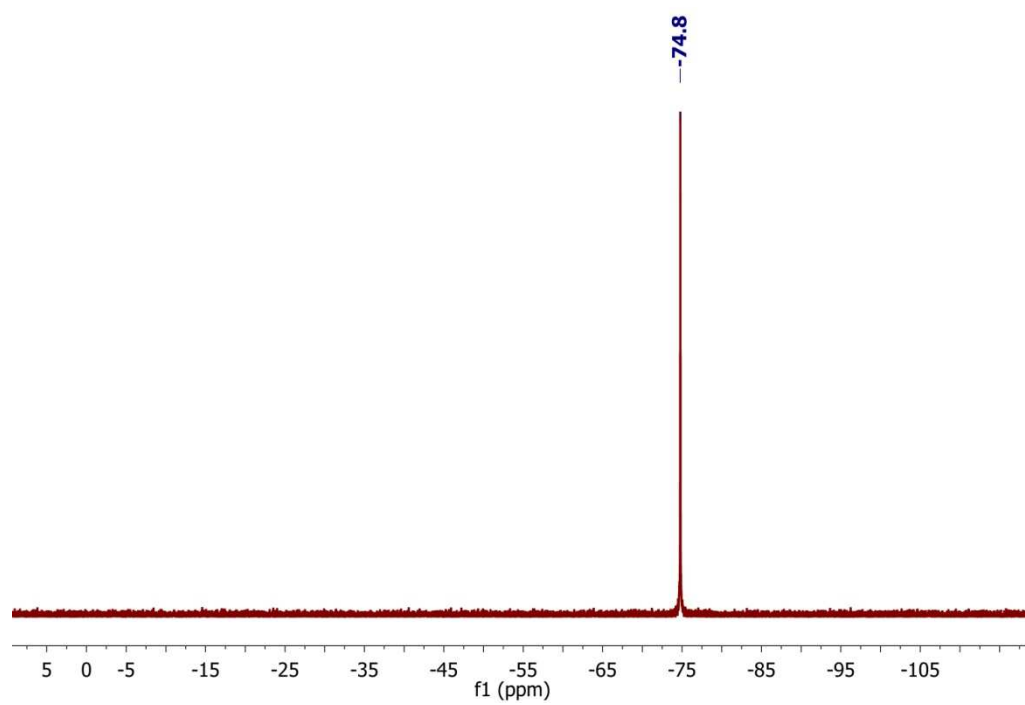
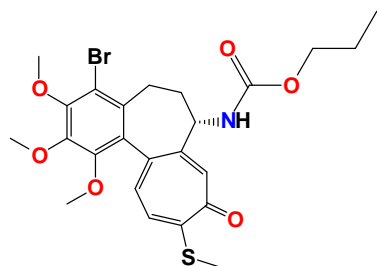


Figure S15. The ^{19}F NMR spectrum of **8** in CDCl_3 .



Chemical formula: $C_{24}H_{28}BrNO_6S$, MW = 538.5 g/mol

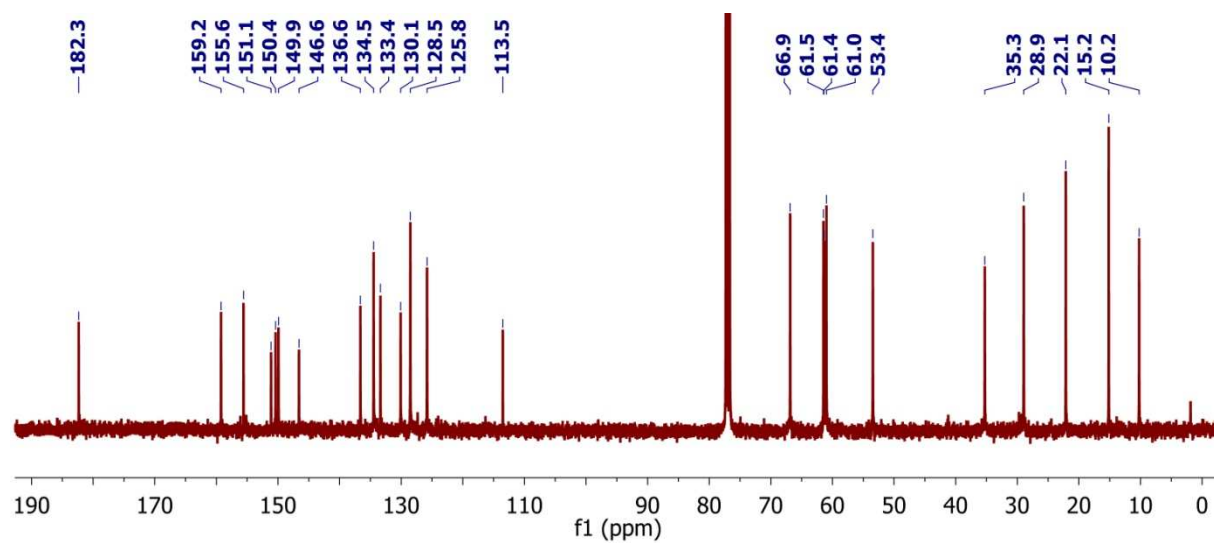


Figure S16. The ^{13}C NMR spectrum of **9** in $CDCl_3$.

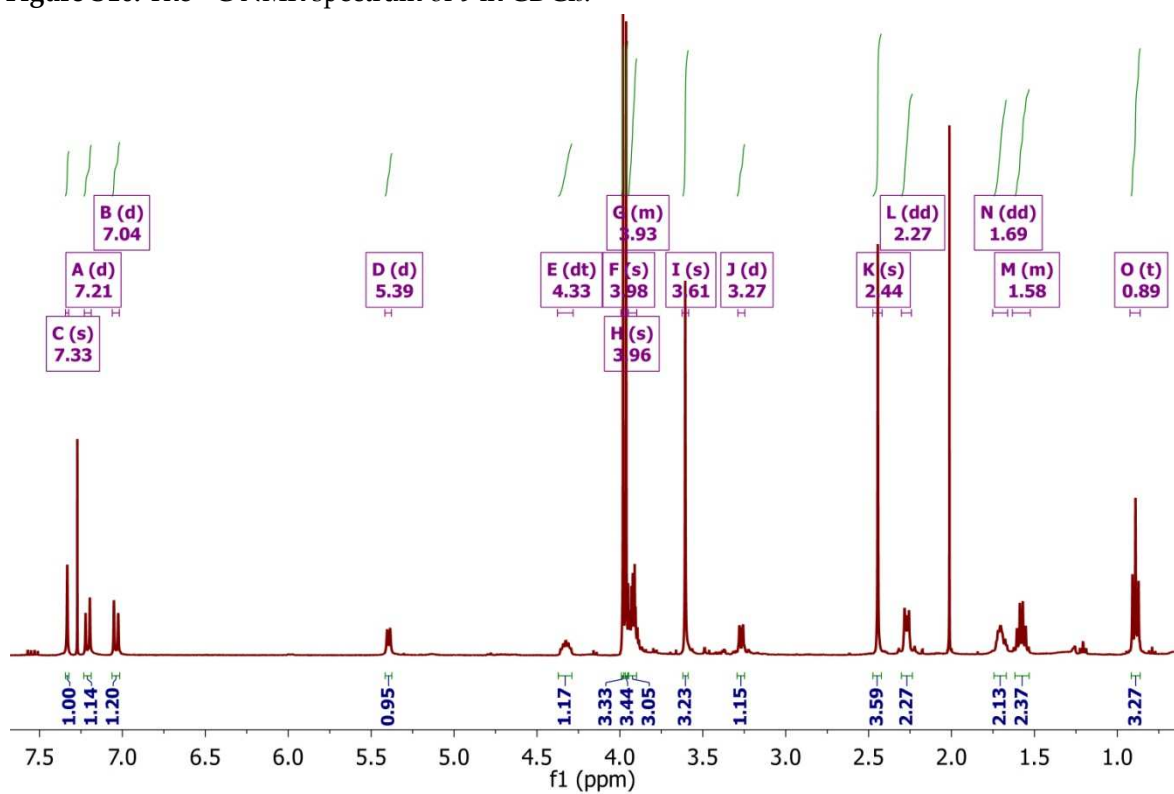
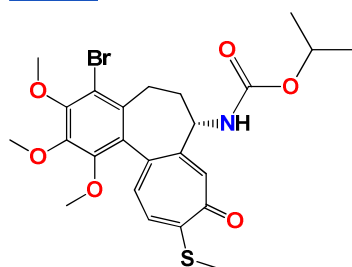


Figure S17. The 1H NMR spectrum of **9** in $CDCl_3$.



Chemical formula: $C_{24}H_{28}BrNO_6S$, MW = 538.5 g/mol

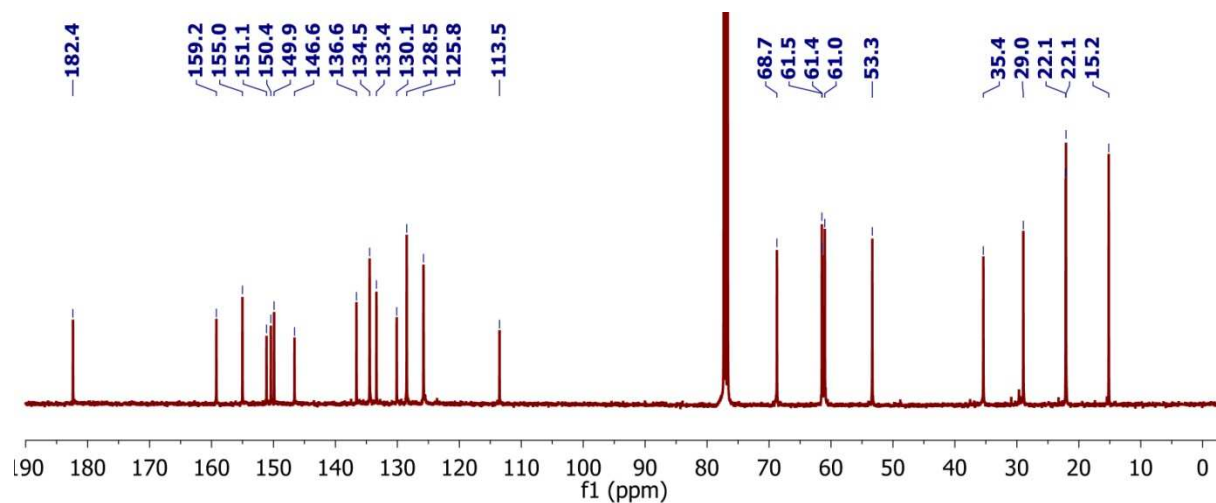


Figure S18. The ^{13}C NMR spectrum of 10 in $CDCl_3$.

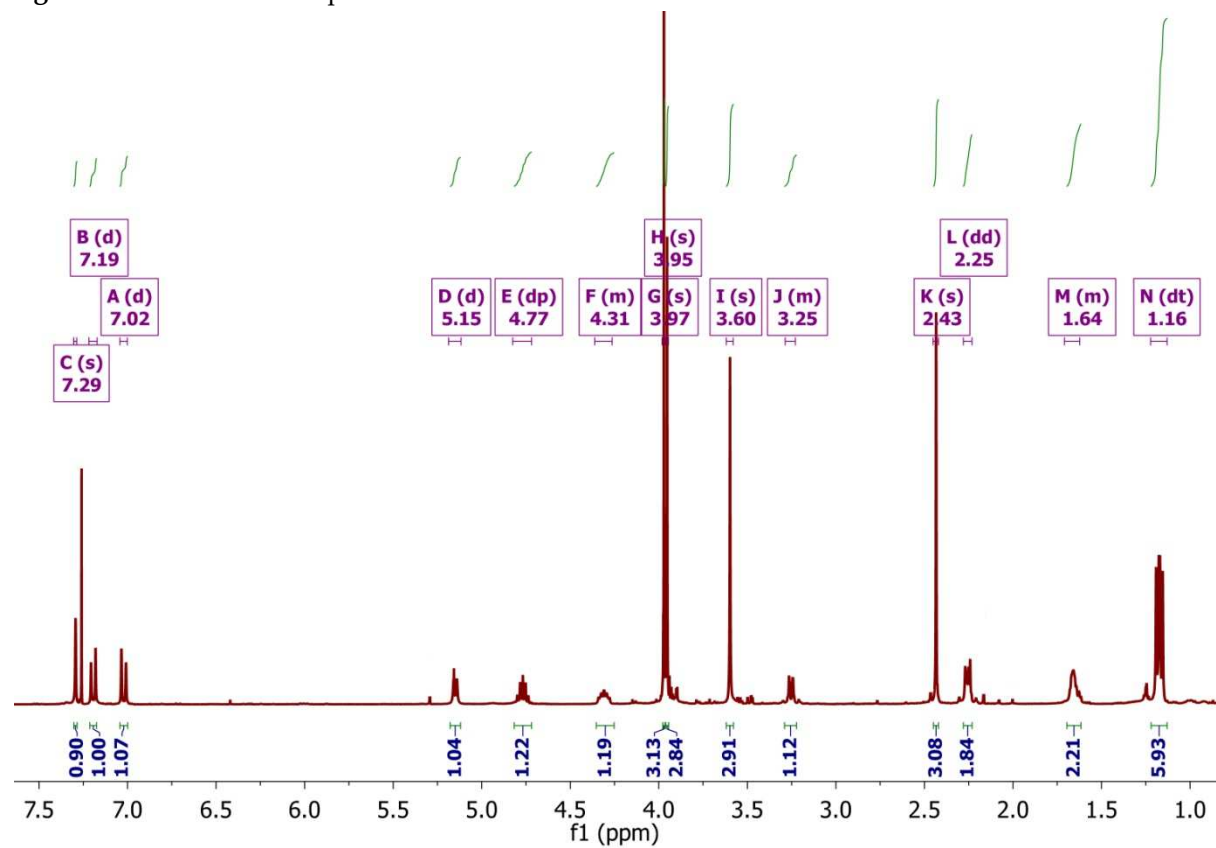
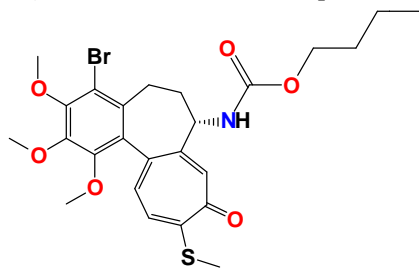


Figure S19. The ^1H NMR spectrum of **10** in CDCl_3 .



Chemical formula: $\text{C}_{25}\text{H}_{30}\text{BrNO}_6\text{S}$, MW = 551.1 g/mol

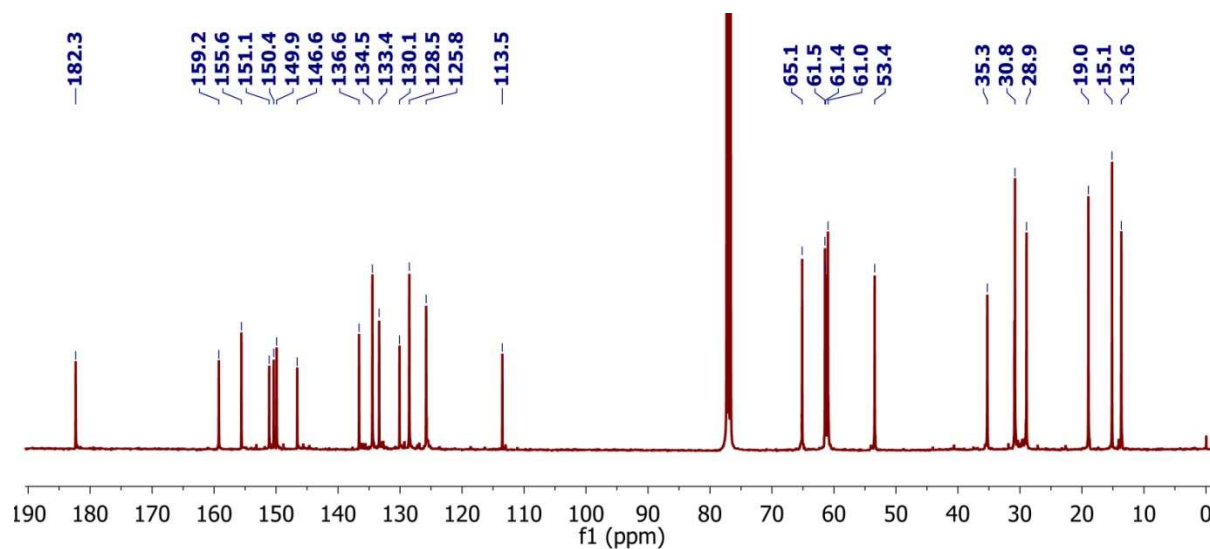


Figure S20. The ^{13}C NMR spectrum of **11** in CDCl_3 .

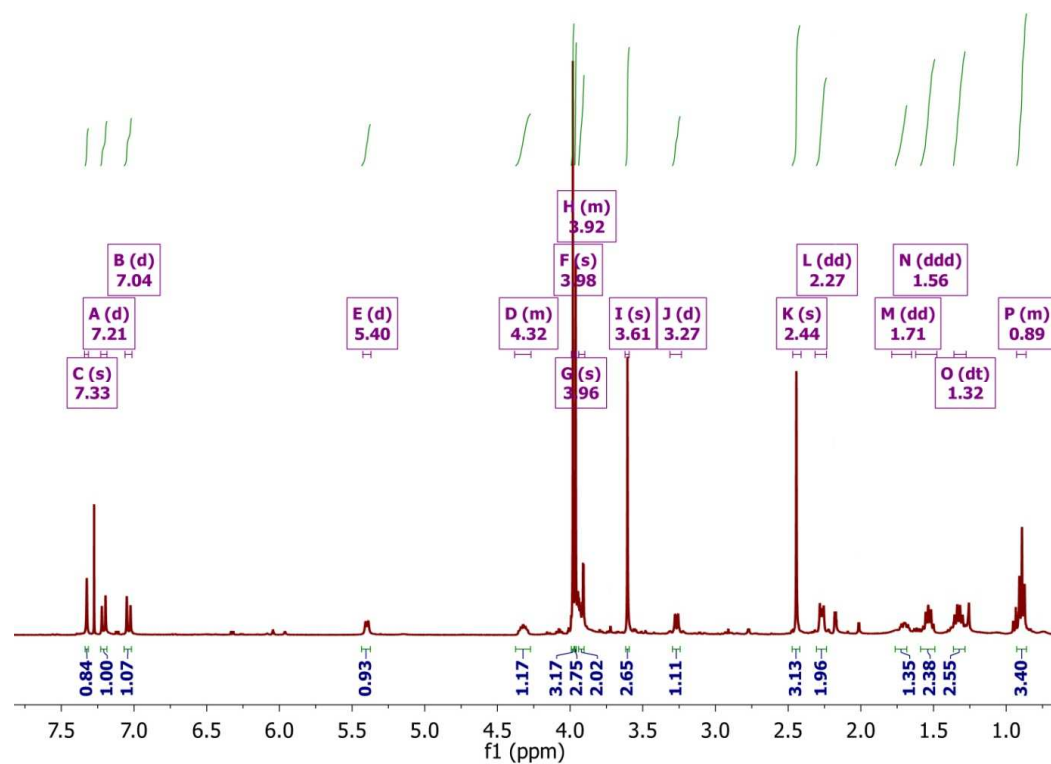
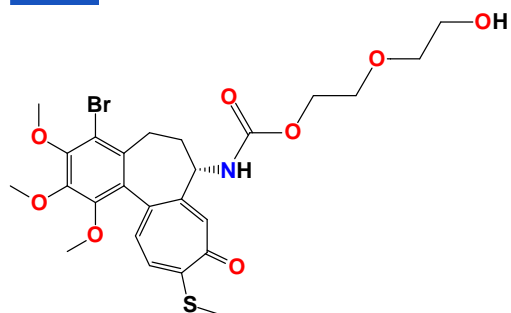


Figure S21. The ^1H NMR spectrum of **11** in CDCl_3 .



Chemical formula: $C_{25}H_{30}BrNO_8S$, MW = 584.5 g/mol

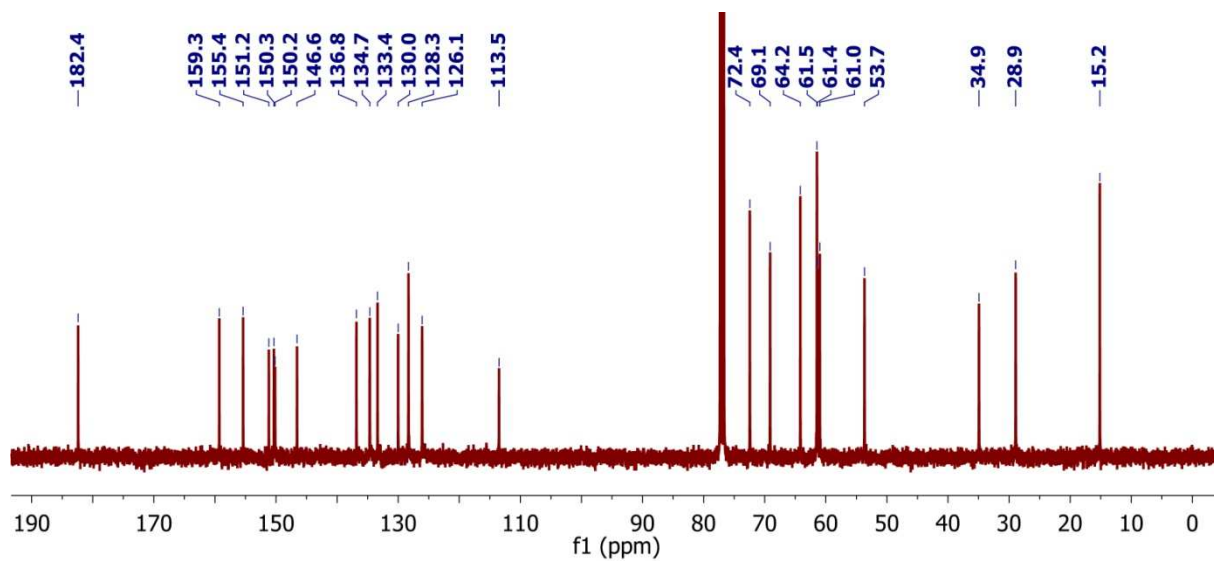


Figure S22. The ^{13}C NMR spectrum of **12** in $CDCl_3$.

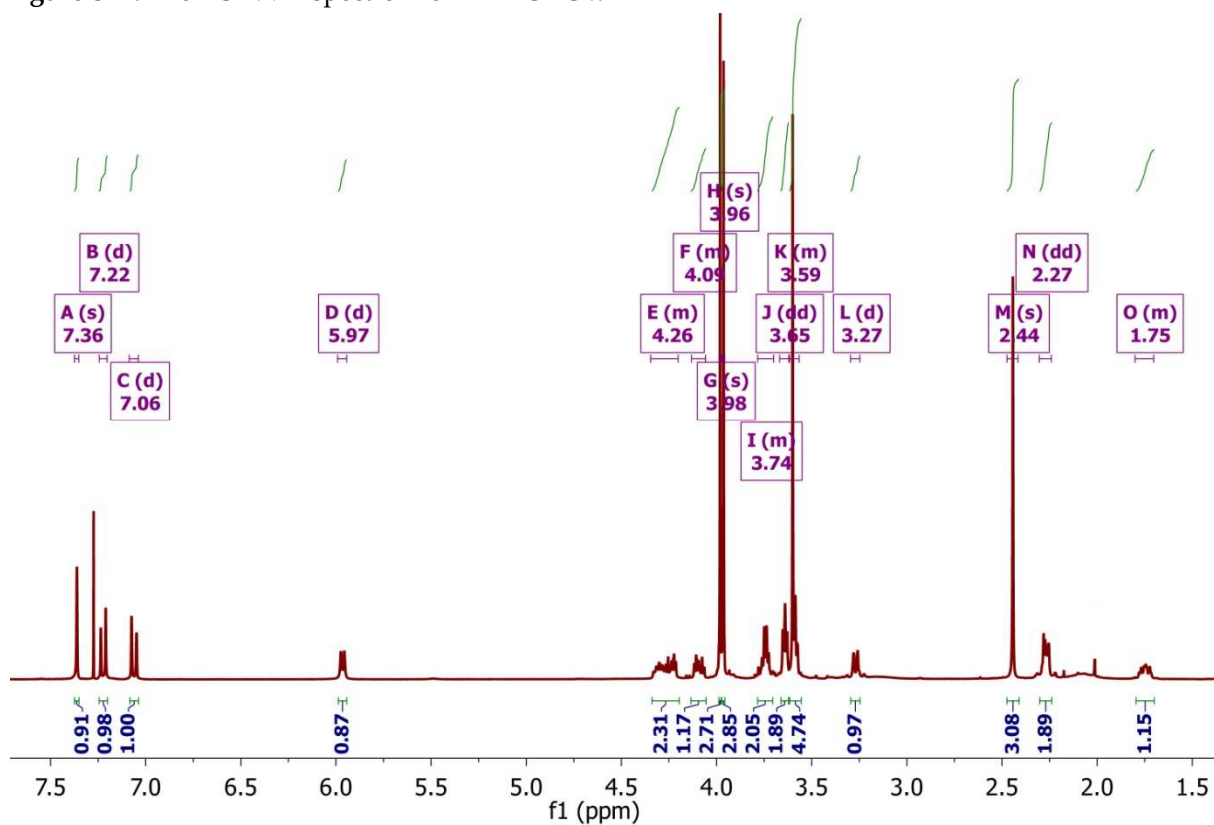


Figure S23. The 1H NMR spectrum of **12** in $CDCl_3$.

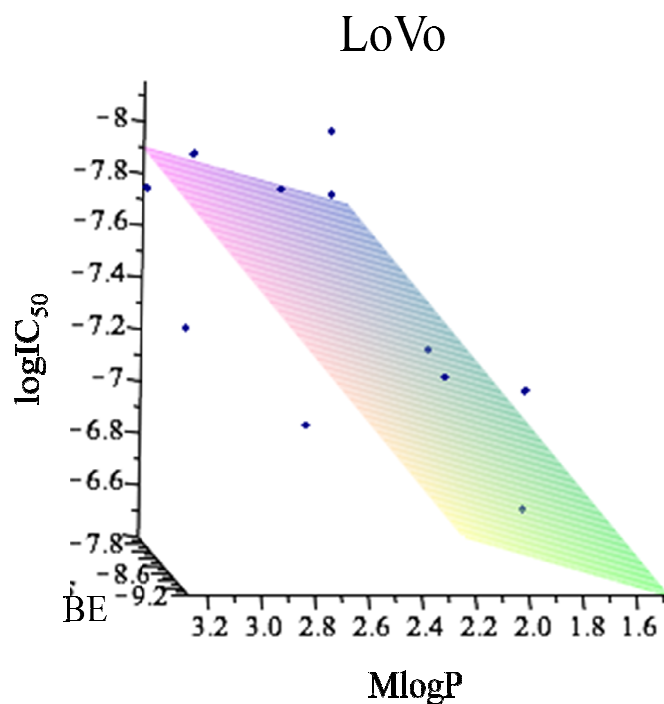


Figure S24. 3D plots of the linear regression results for the binding energies (BE) vs MlogP vs log IC₅₀ [μM] values for LoVo cell line.

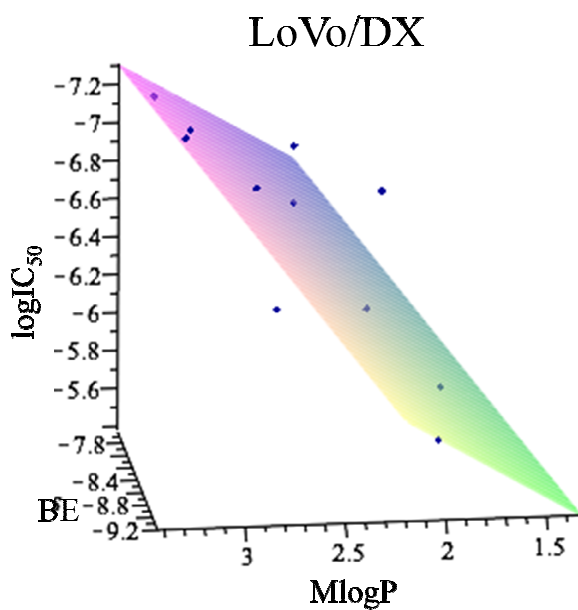


Figure S25. 3D plots of the linear regression results for the binding energies (BE) vs MlogP vs log IC₅₀ [μM] values for LoVo/DX cell line.