

Supplementary Materials: Synthesis and Biochemical Evaluation of Baicalein Prodrugs

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General Method of Purity Determination Using RP-HPLC

The purity of all final compounds was measured by analytical reverse-phase HPLC on an Agilent 1260 Infinity (Agilent) with a C18 column (Phenomenex, 150 mm × 4.6 mm, 3 µm, 110 Å). RP-HPLC was performed using the following isocratic conditions: for method A, the mobile phase was acetonitrile and water with 0.1% trifluoroacetic acid (TFA) (30:70, *v/v*); for method B, the mobile phase was acetonitrile and water with 0.1% trifluoroacetic acid (TFA) (35:65, *v/v*); for method C, the mobile phase was acetonitrile and water with 0.1% trifluoroacetic acid (TFA) (40:60, *v/v*). All compounds were eluted with a flow rate of 1 mL/min and monitored at UV detector (220 nm or 254 nm). The purity of the tested compounds was >95%.

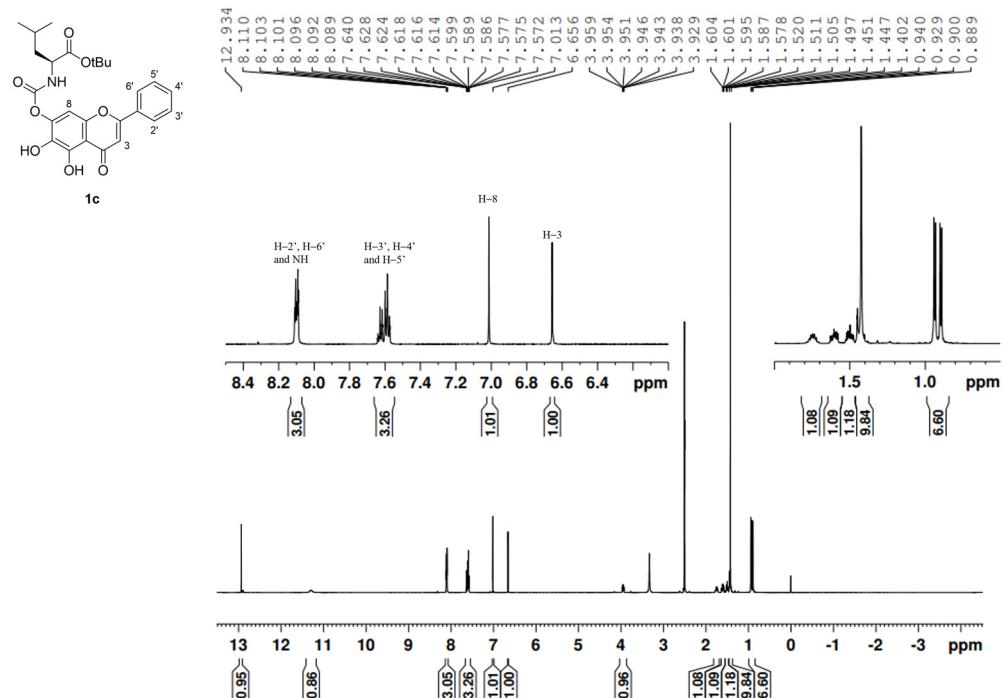


Figure S1. ^1H NMR spectra of compound **1c**.

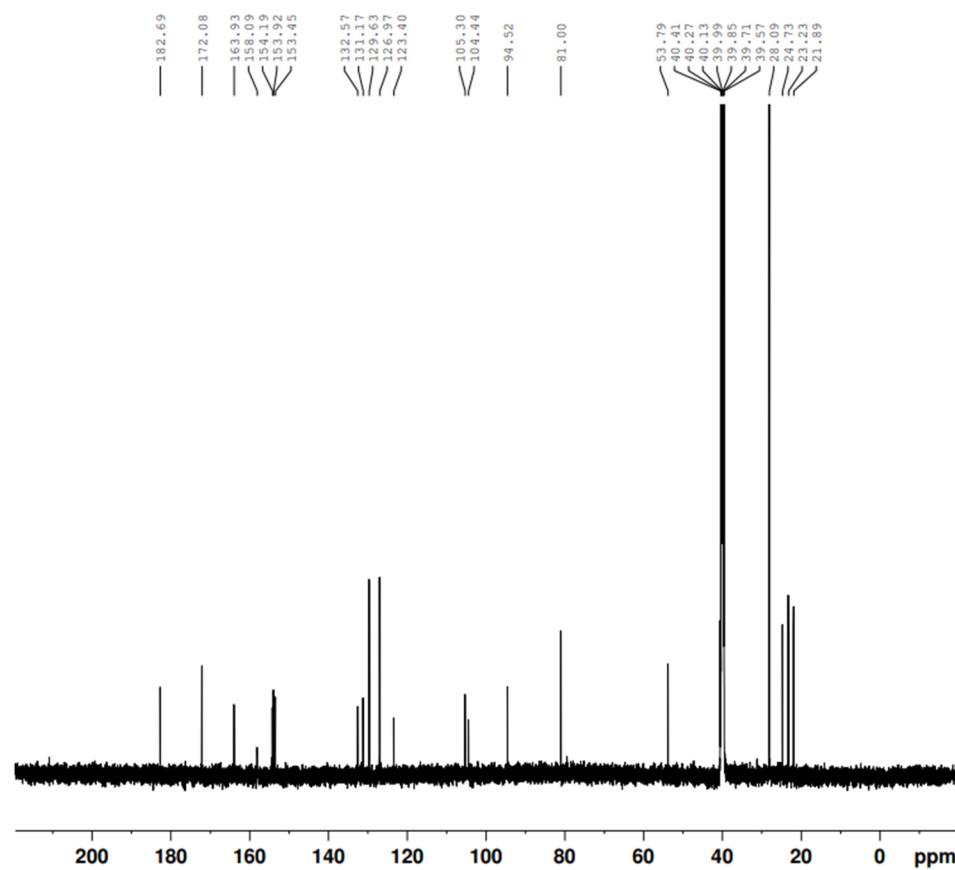


Figure S2. ^{13}C NMR spectra of compound **1c**.

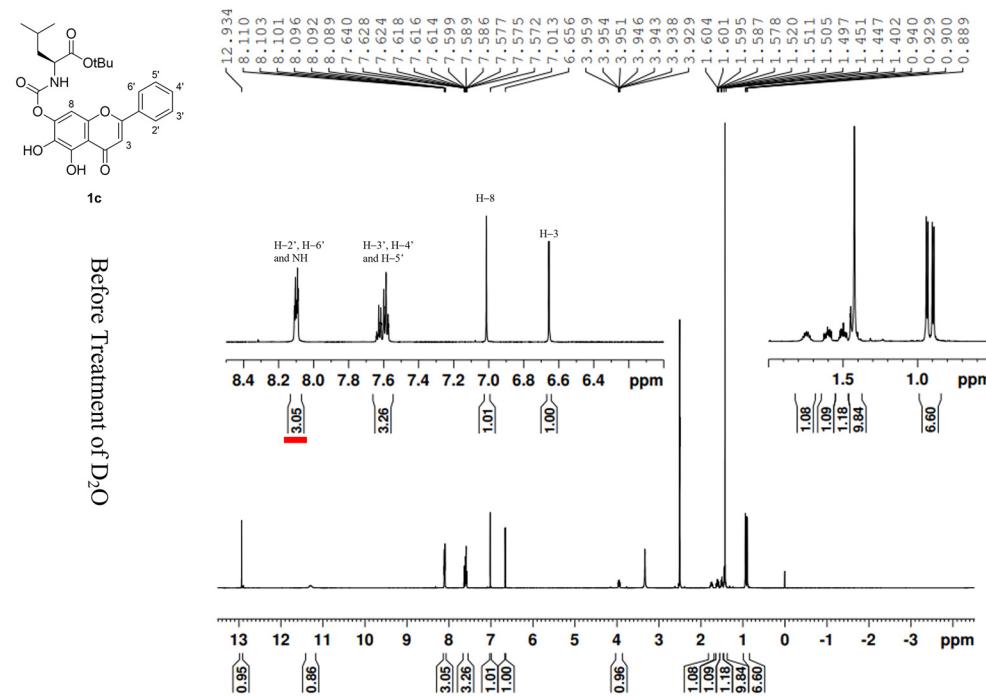


Figure S3. ^1H NMR spectra of compound **1c** measured in DMSO before the treatment of D_2O at 600 MHz.

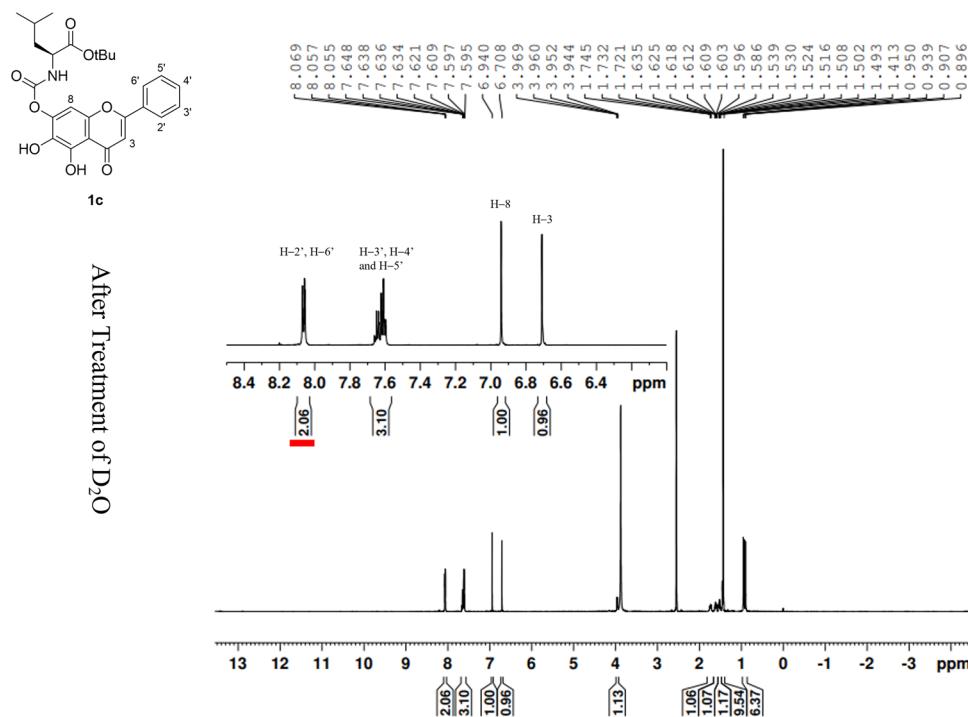


Figure S4. ^1H NMR spectra of compound **1c** measured in DMSO after the treatment of D_2O at 600 MHz.

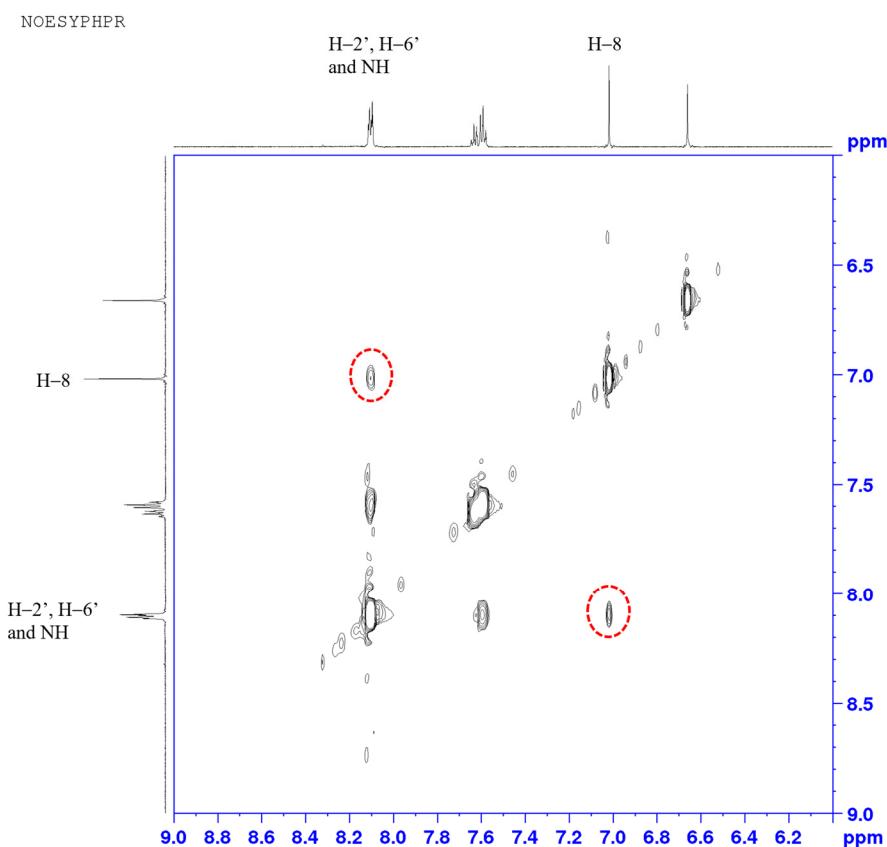


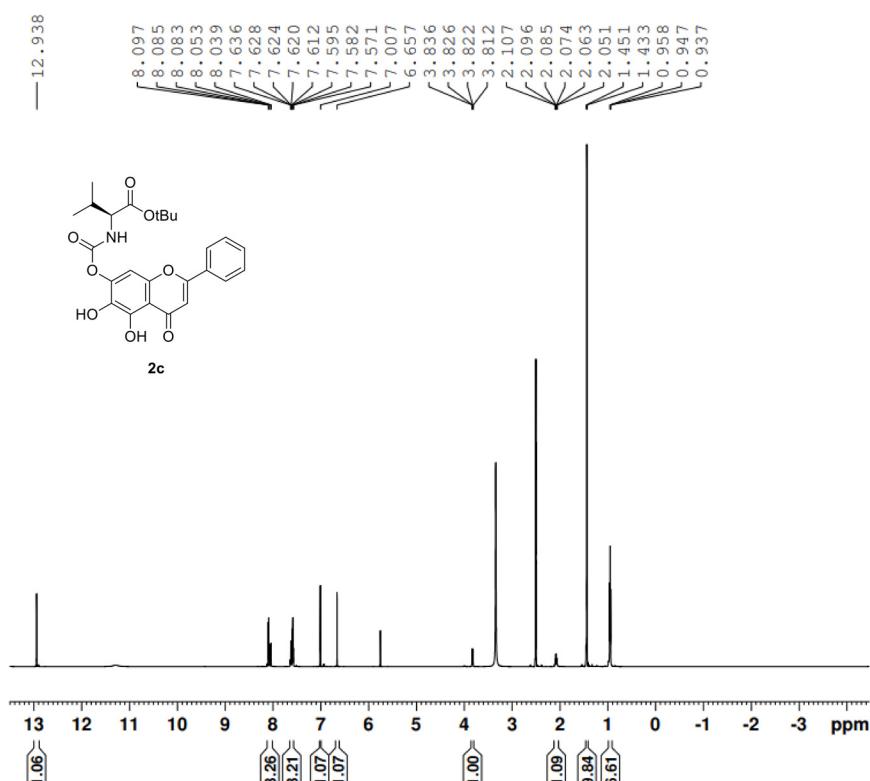
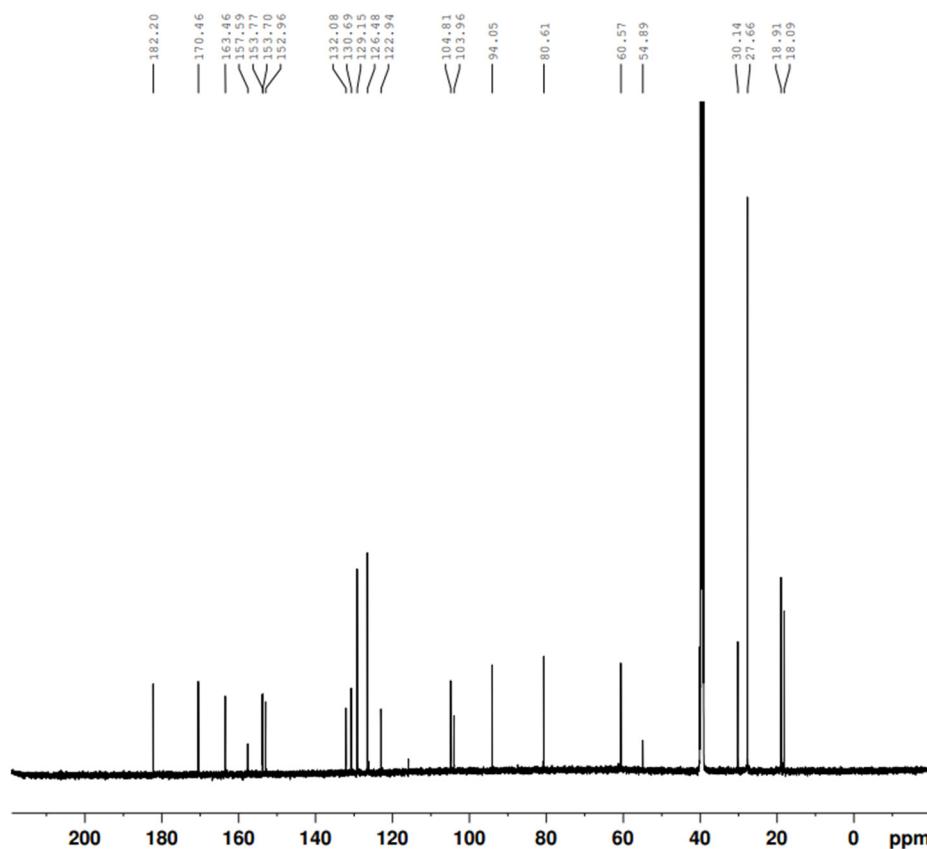
Figure S5. ^1H NOESY NMR spectra of compound **1c** measured in DMSO at 600 MHz.**Figure S6.** ^1H NMR spectra of compound **2c**.

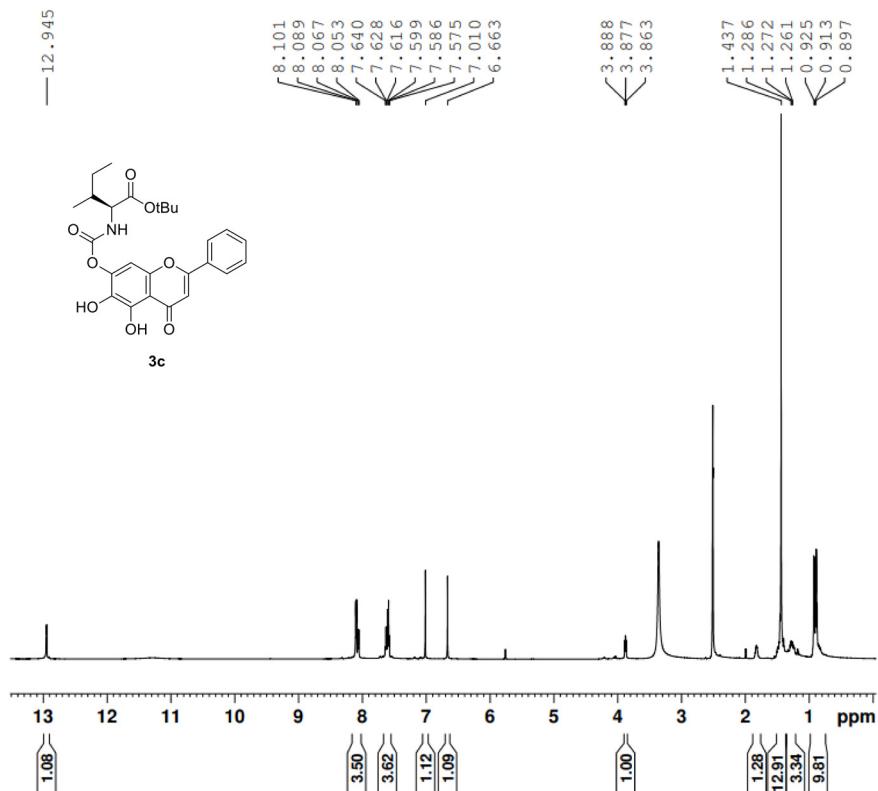
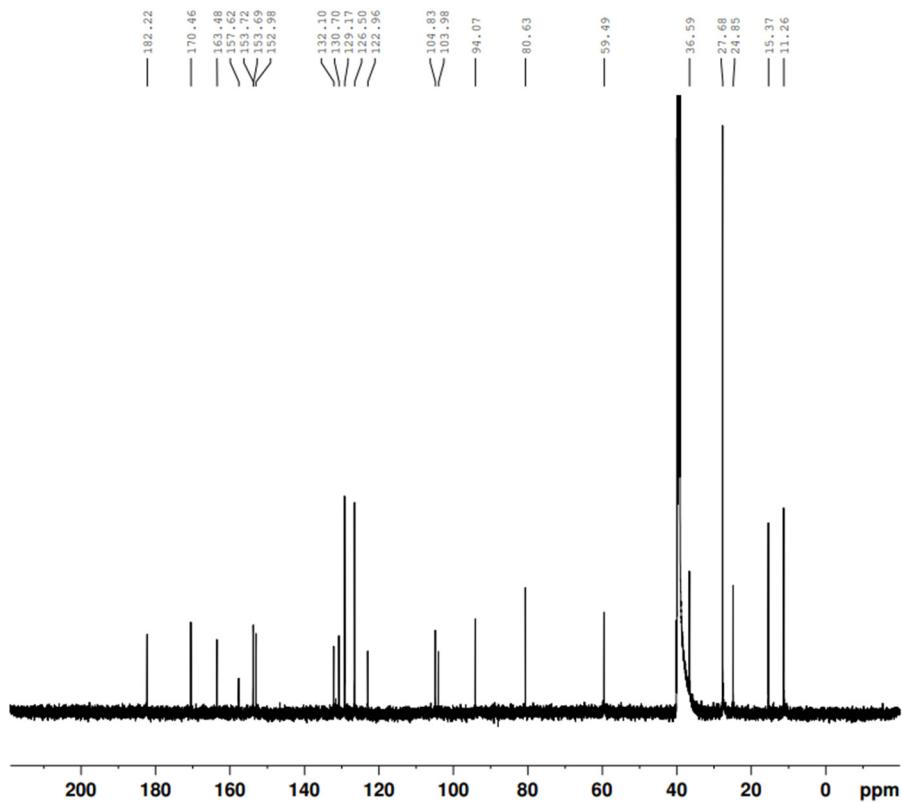
Figure S7. ^{13}C NMR spectra of compound 2c.**Figure S8.** ^1H NMR spectra of compound 3c.

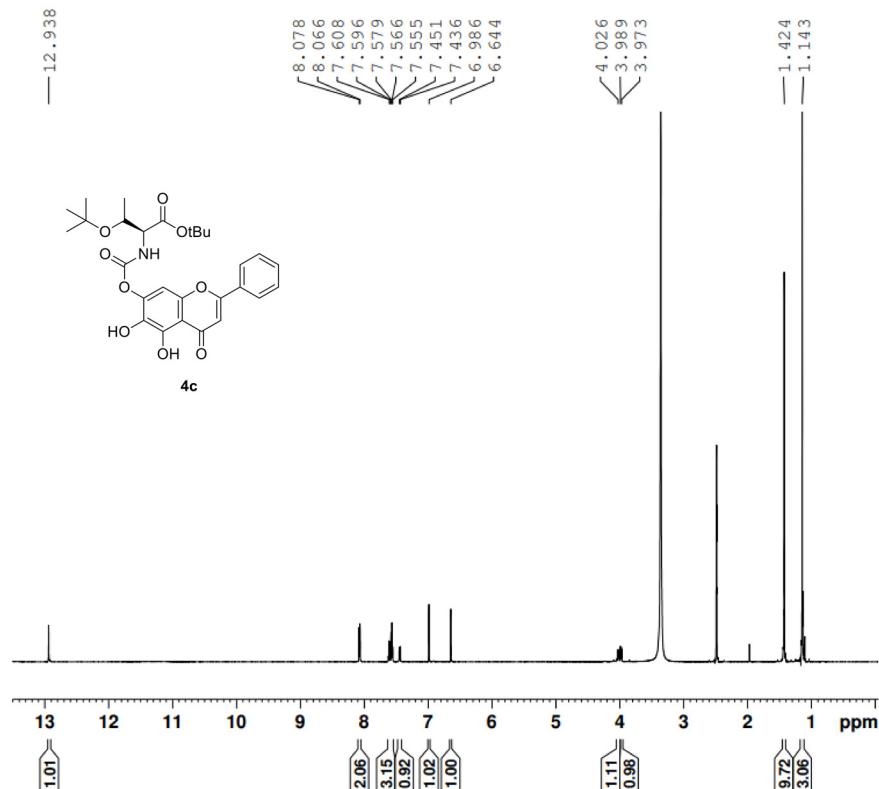
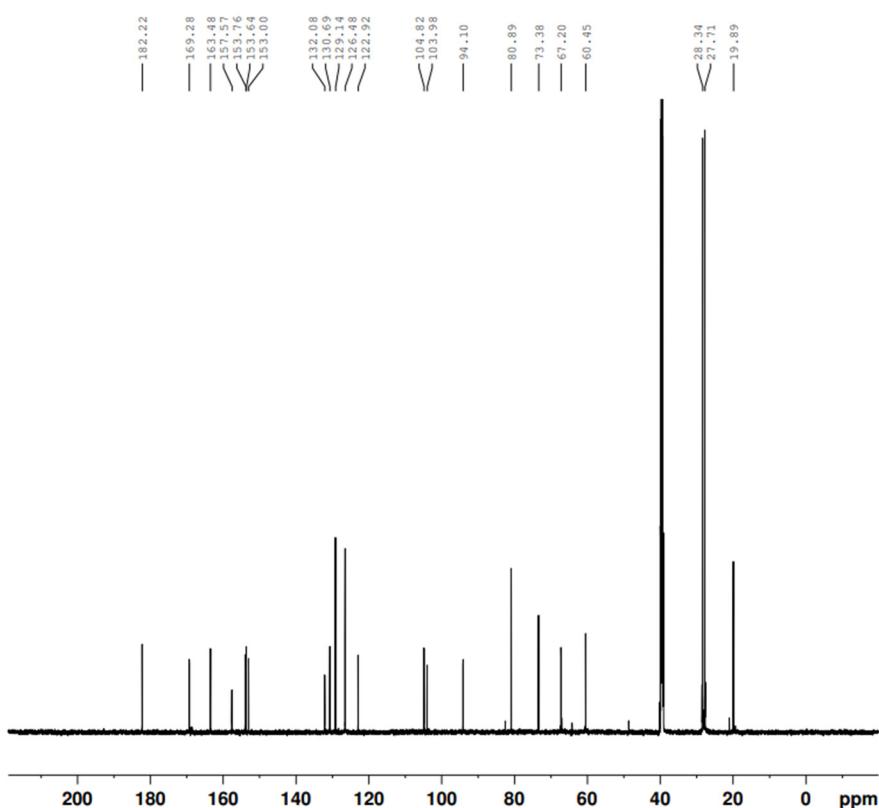
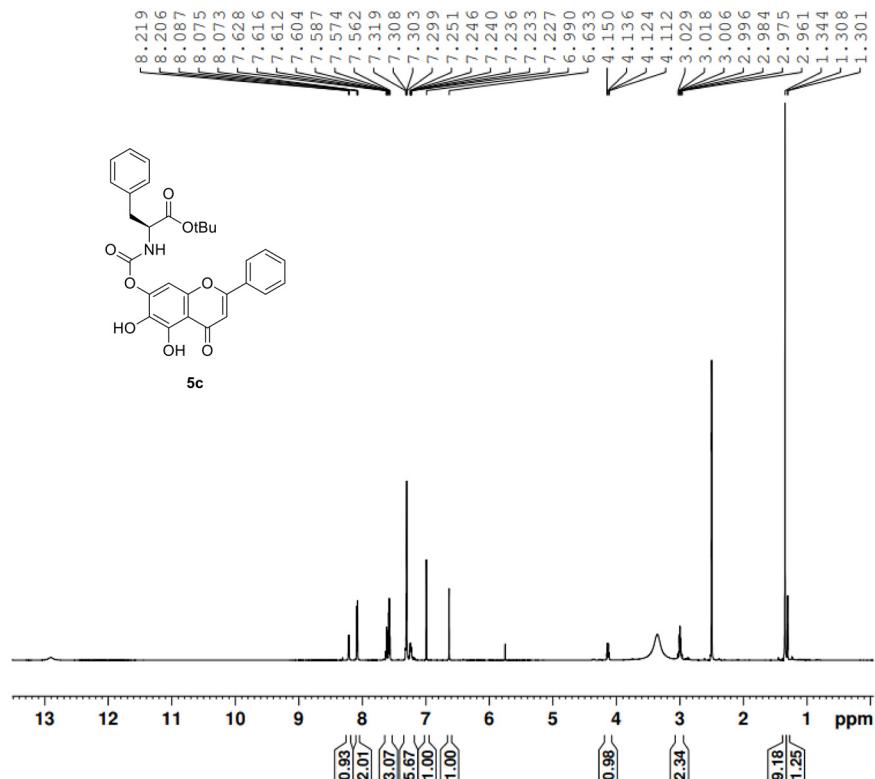
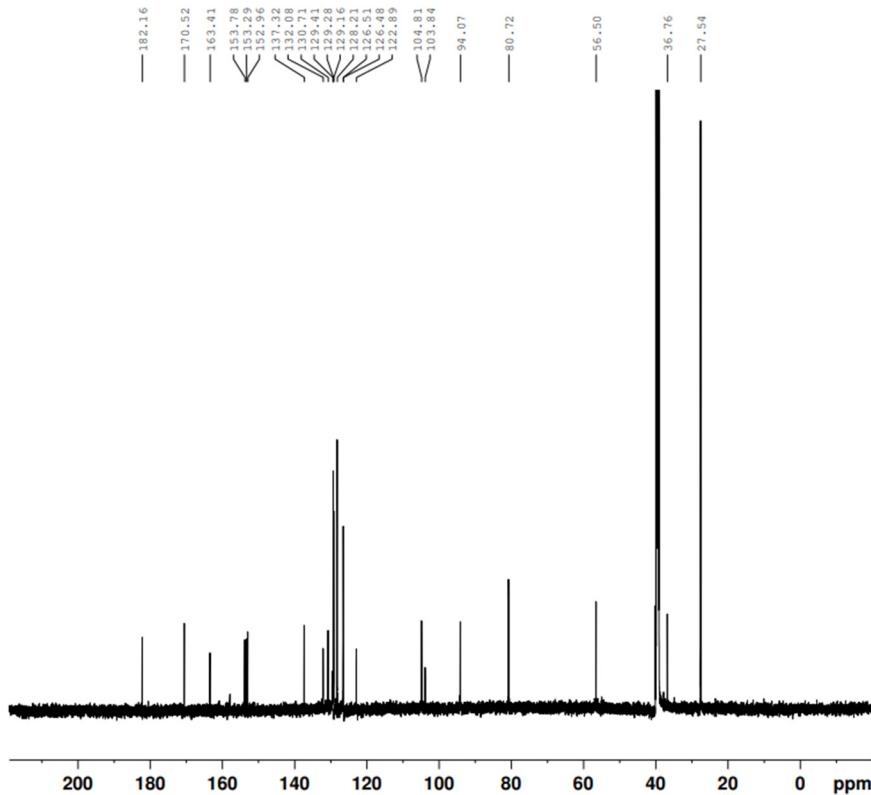
Figure S9. ^{13}C NMR spectra of compound 3c.**Figure S10.** ^1H NMR spectra of compound **4c**.

Figure S11. ^{13}C NMR spectra of compound **4c**.**Figure S12.** ^1H NMR spectra of compound **5c**.**Figure S13.** ^{13}C NMR spectra of compound **5c**.

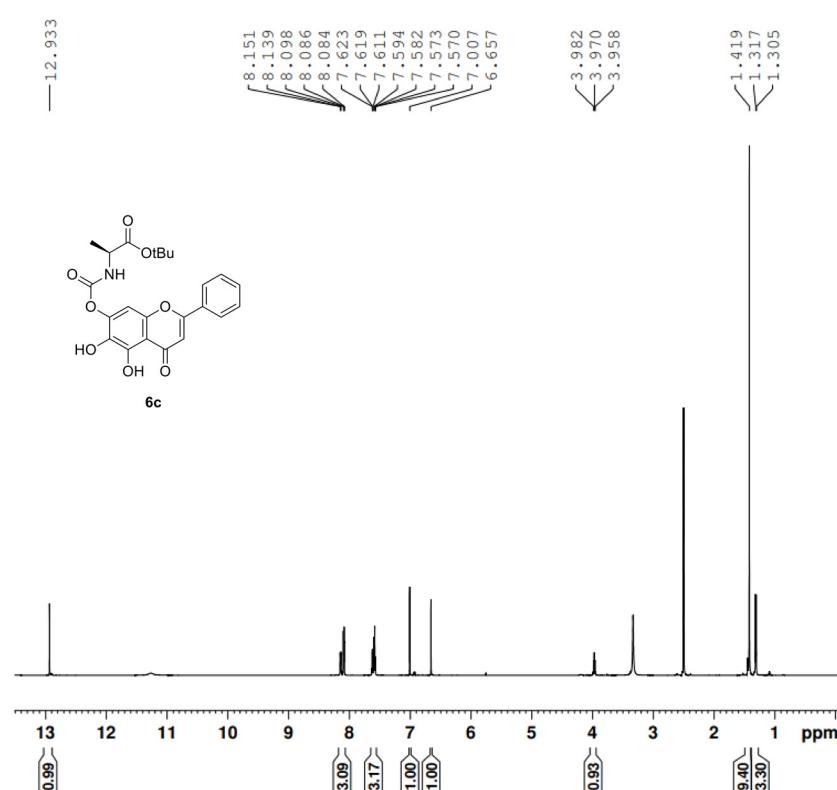


Figure S14. ¹H NMR spectra of compound 6c.

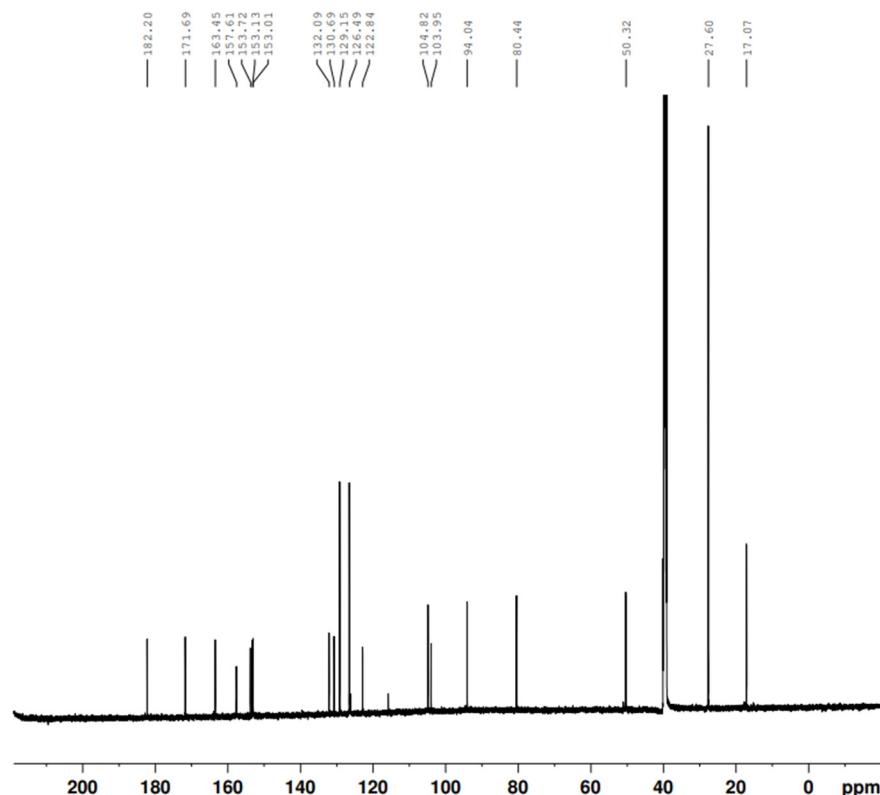


Figure S15. ¹³C NMR spectra of compound 6c.

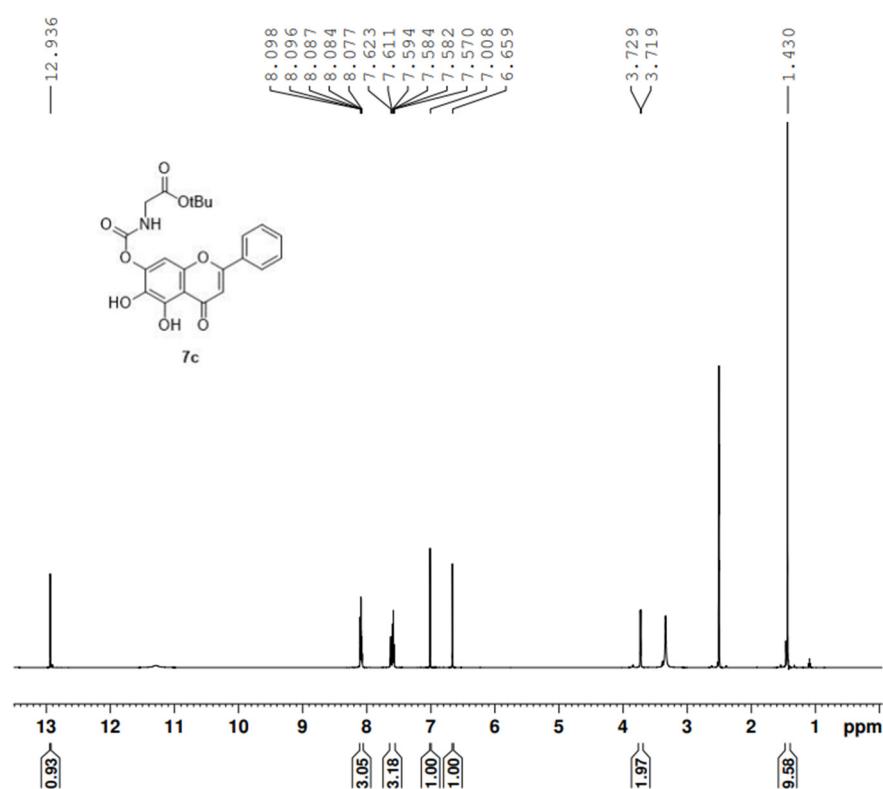


Figure S16. ¹H NMR spectra of compound 7c.

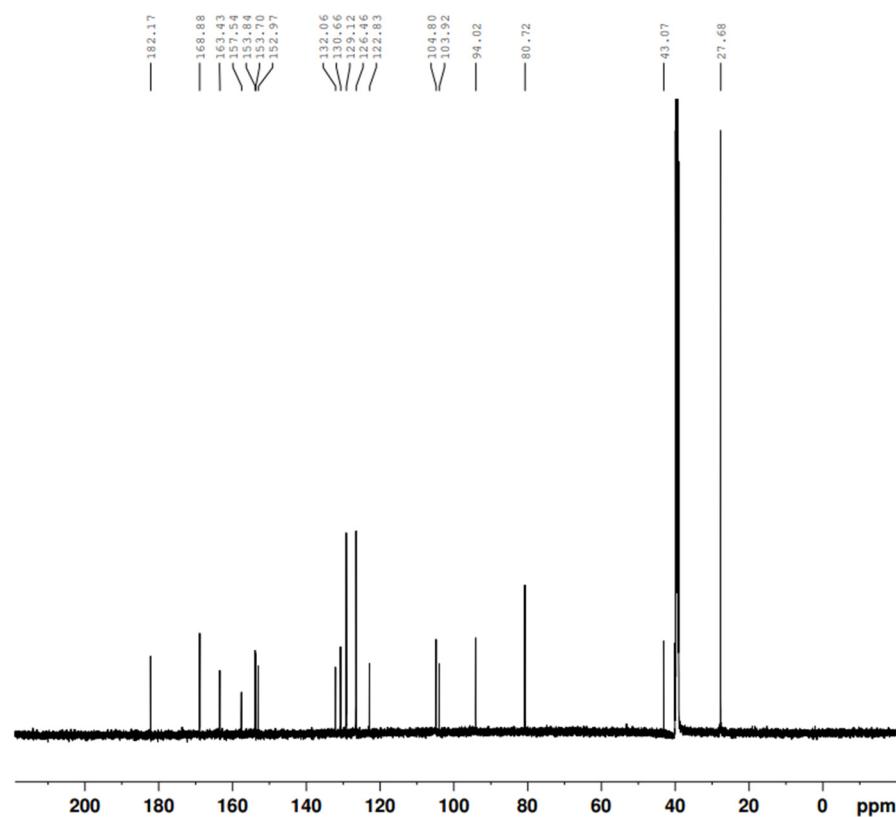


Figure S17. ¹³C NMR spectra of compound 7c.

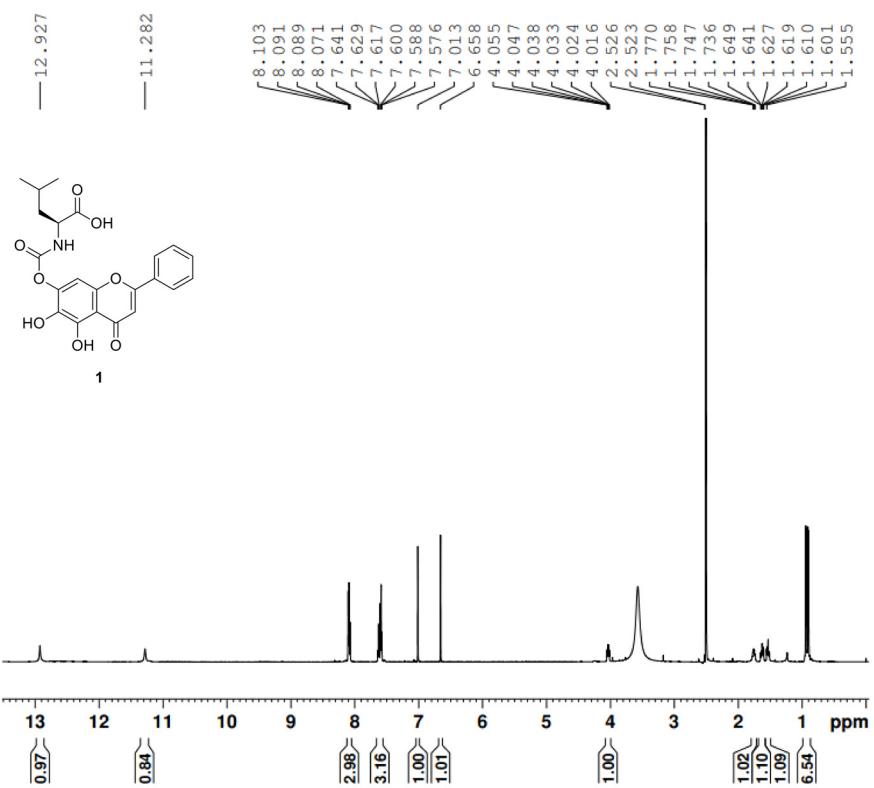


Figure S18. ^1H NMR spectra of compound 1.

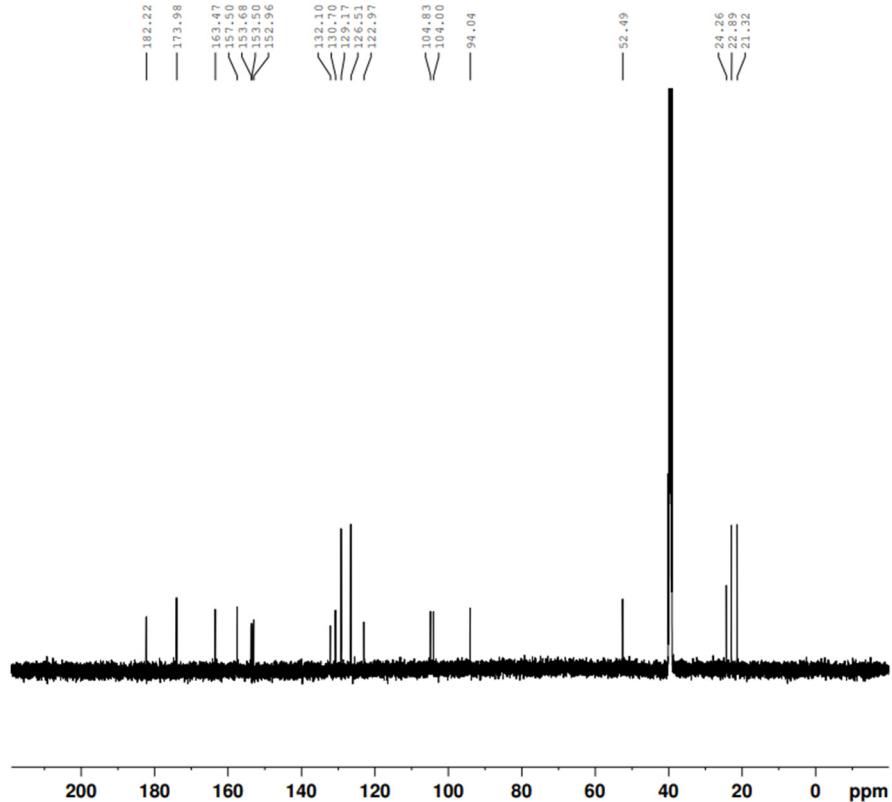


Figure S19. ^{13}C NMR spectra of compound 1.

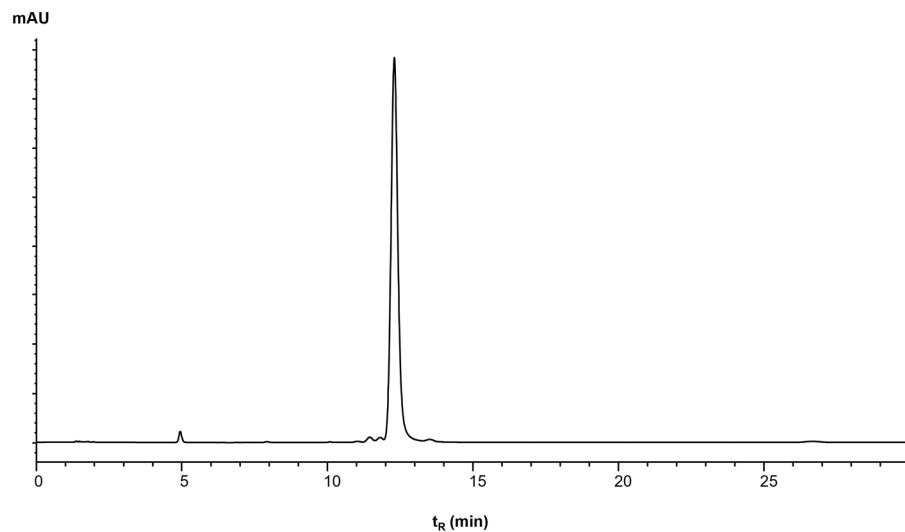


Figure S20. HPLC chromatogram of compound **1** eluted using Method C.

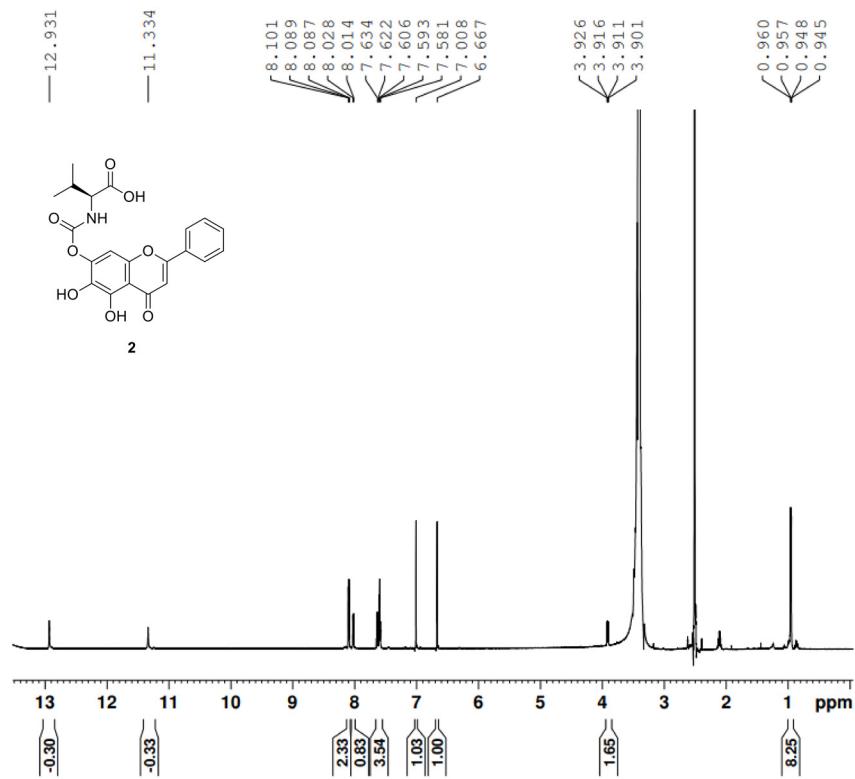


Figure S21. ^1H NMR spectra of compound **2**.

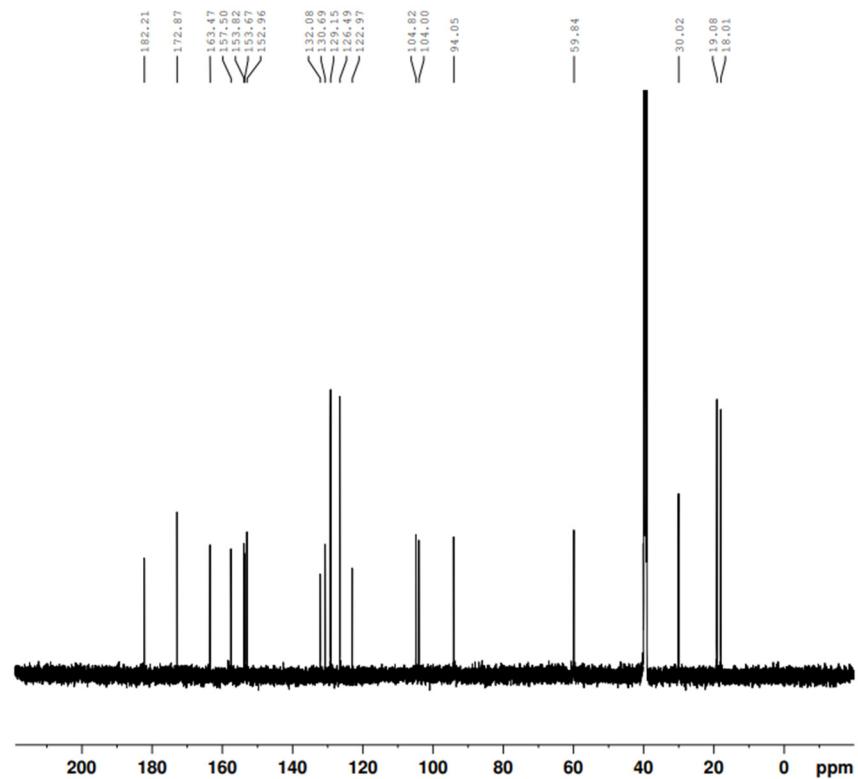


Figure S22. ¹³C NMR spectra of compound 2.

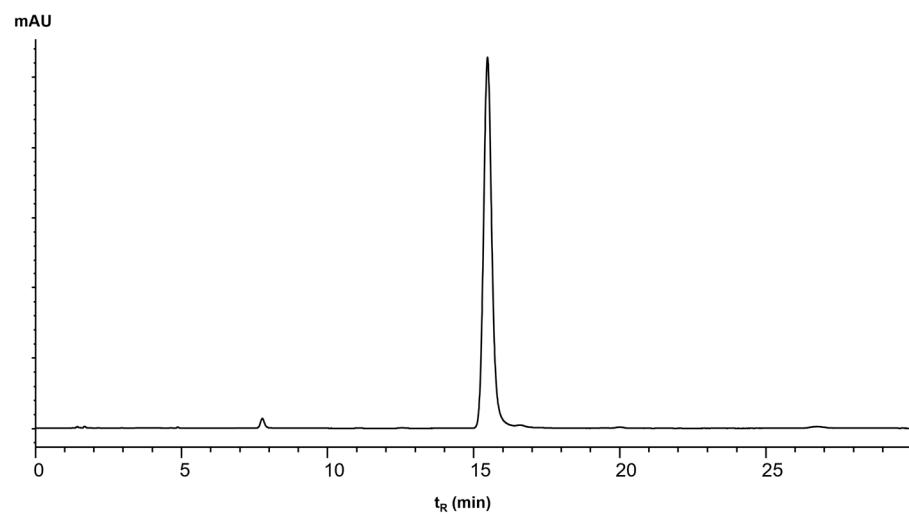


Figure S23. HPLC chromatogram of compound 2 eluted using Method C.

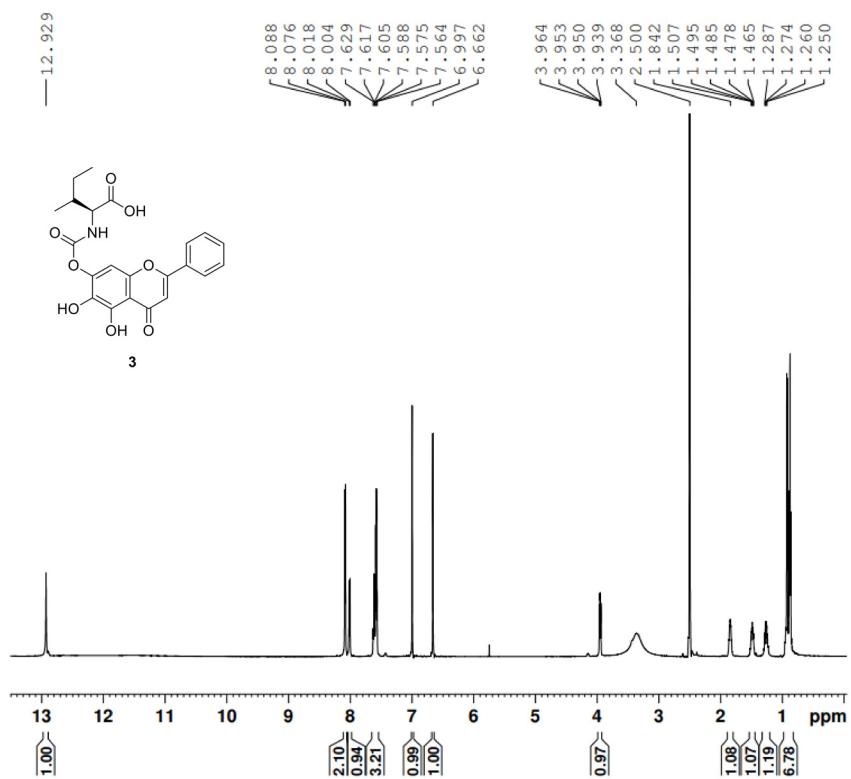


Figure S24. ^1H NMR spectra of compound 3.

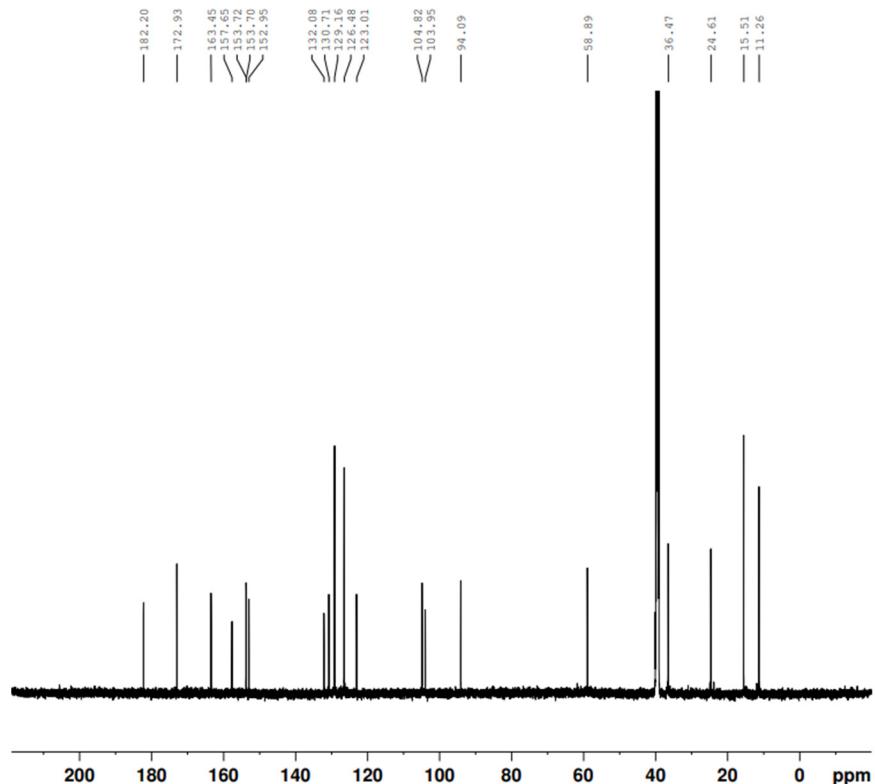


Figure S25. ^{13}C NMR spectra of compound 3.

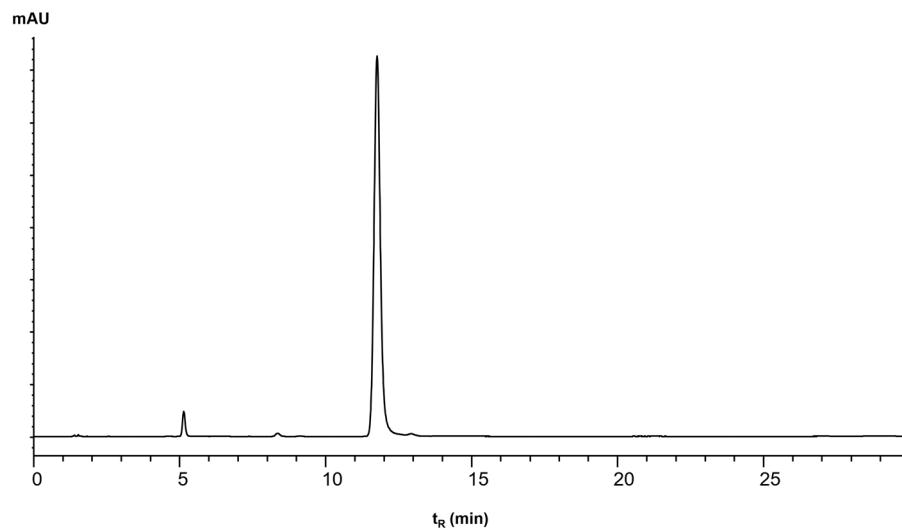


Figure S26. HPLC chromatogram of compound 3 eluted using Method C.

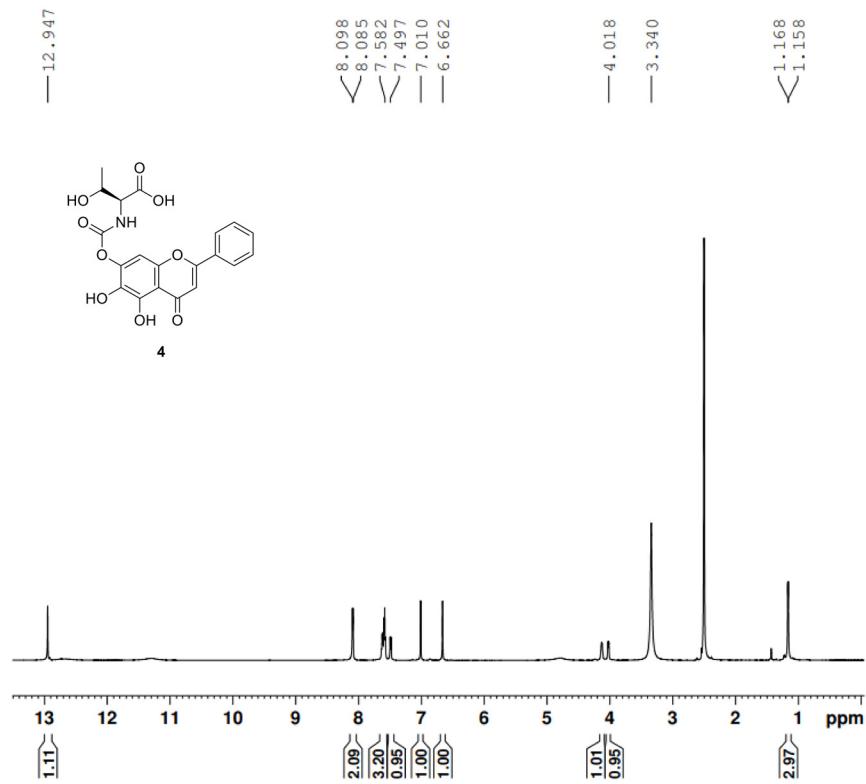


Figure S27. ^1H NMR spectra of compound 4.

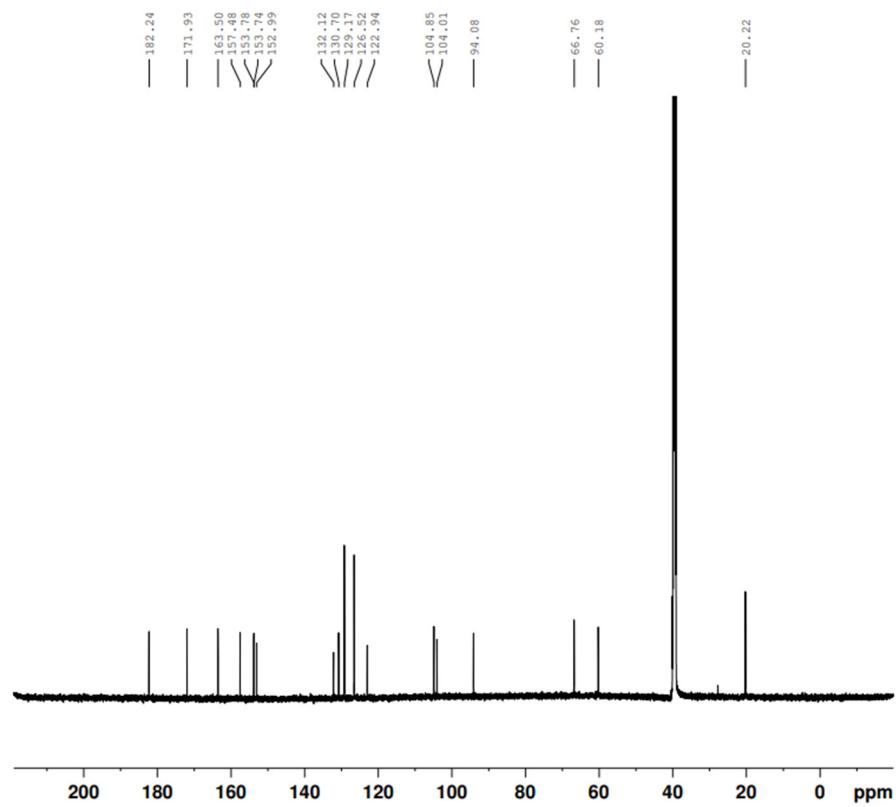


Figure S28. ^{13}C NMR spectra of compound 4.

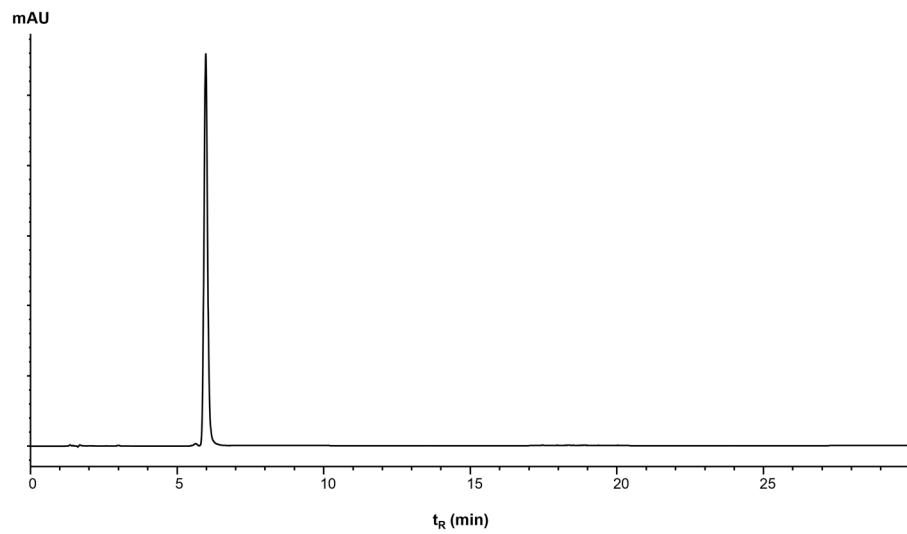


Figure S29. HPLC chromatogram of compound 4 eluted using Method B.

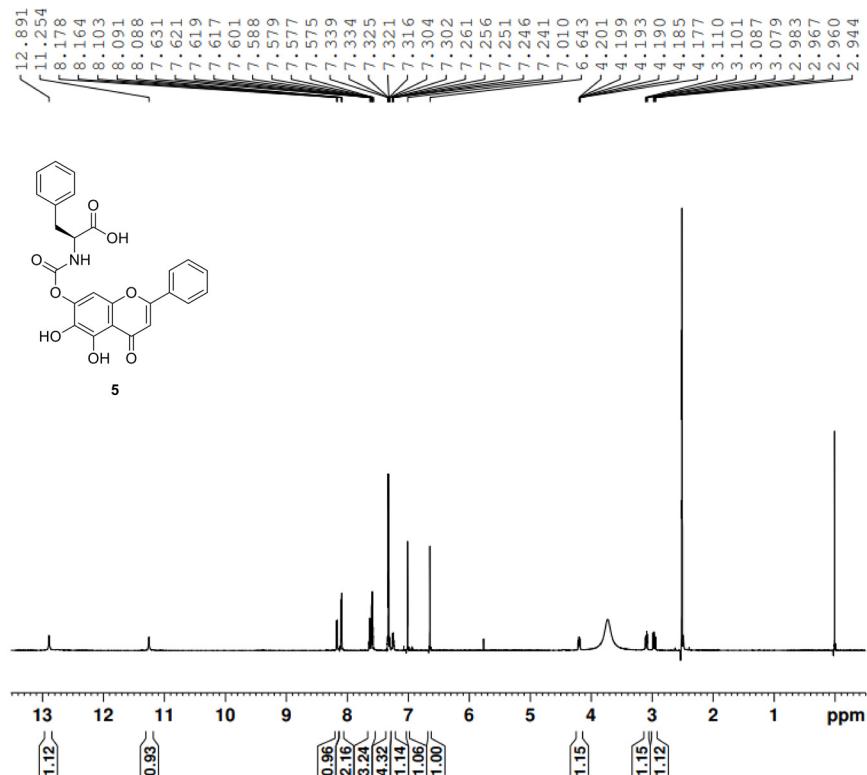


Figure S30. ¹H NMR spectra of compound 5.

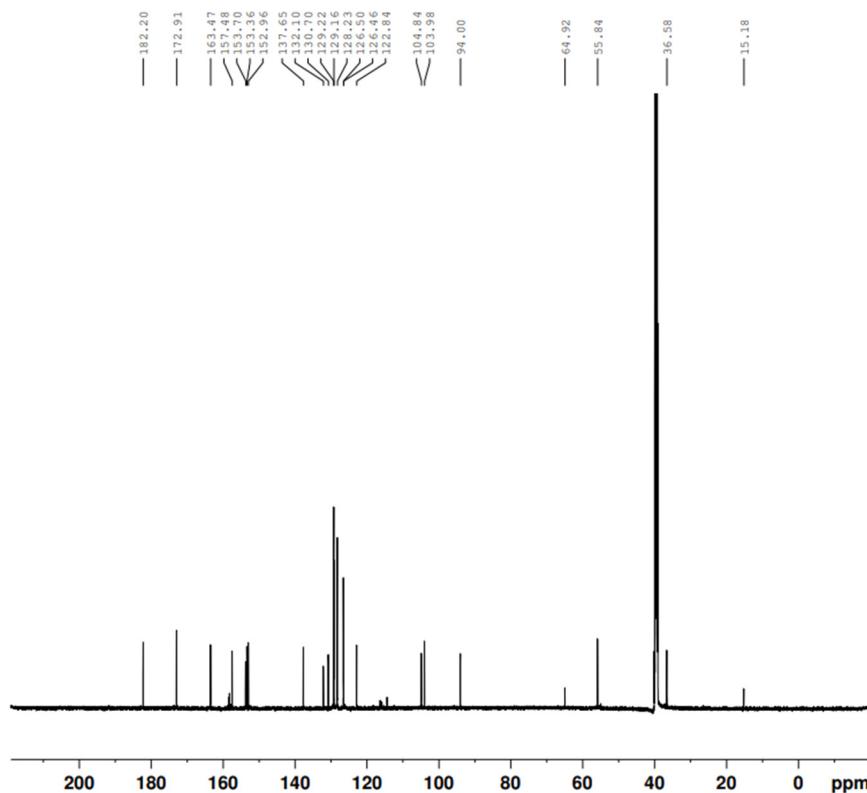


Figure S31. ¹³C NMR spectra of compound 5.

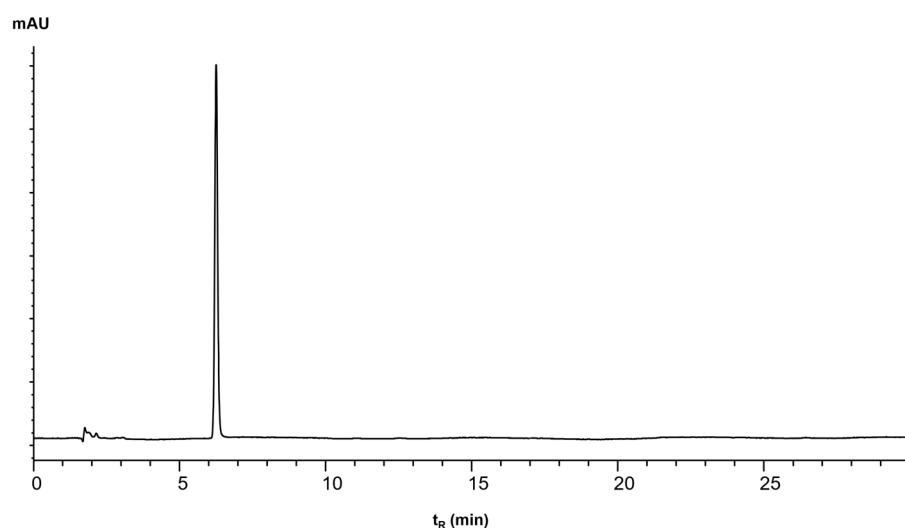


Figure S32. HPLC chromatogram of compound 5 eluted using Method A.

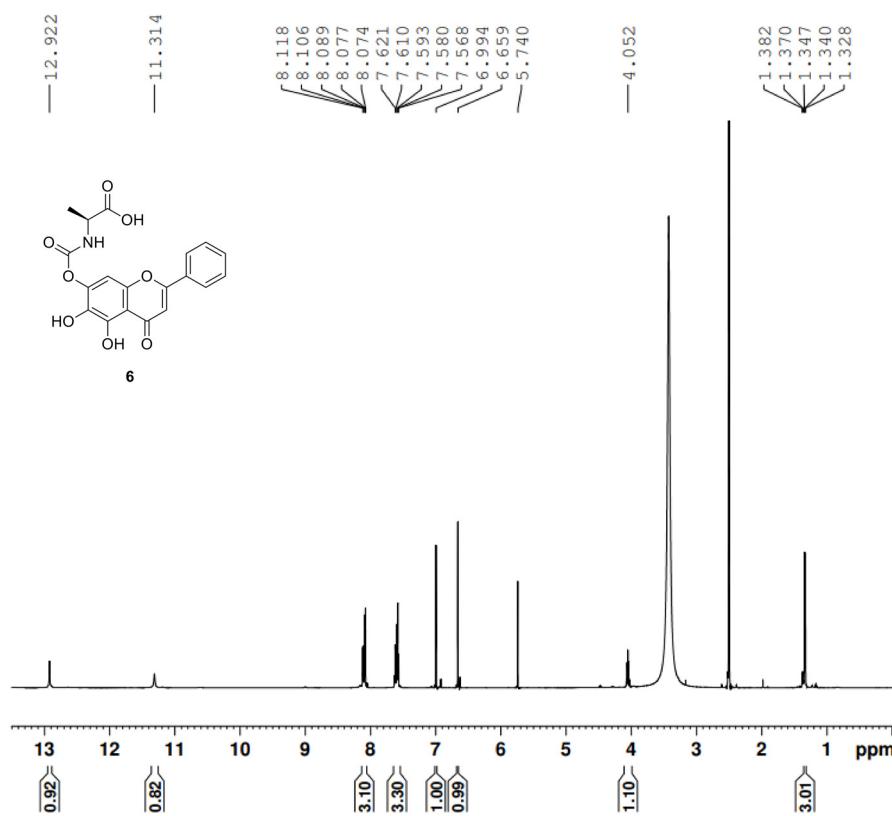


Figure S33. ^1H NMR spectra of compound 6.

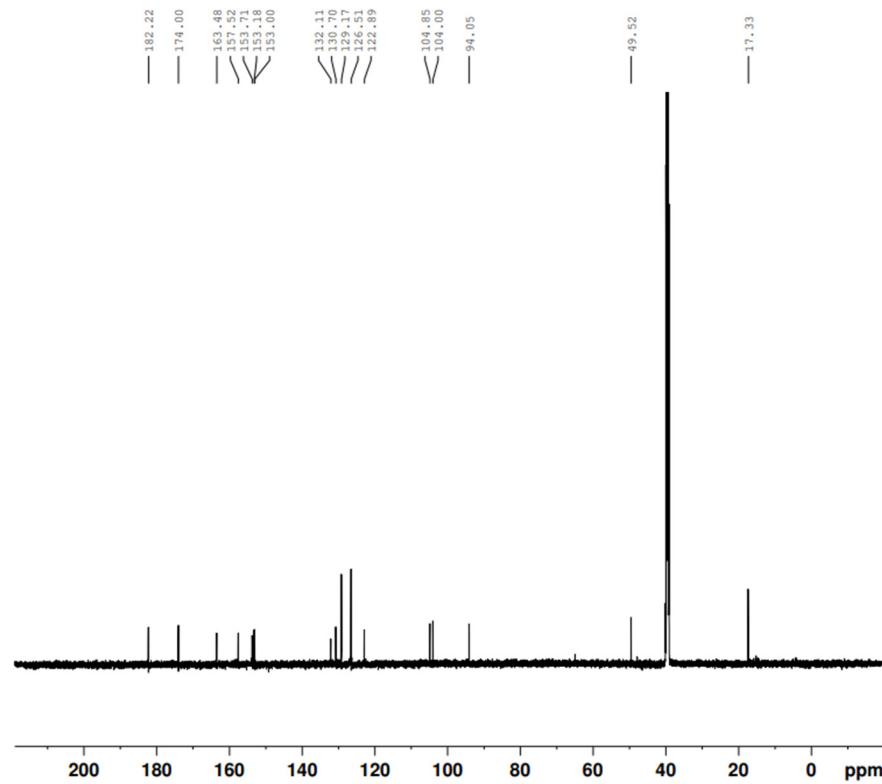


Figure S34. ^{13}C NMR spectra of compound 6.

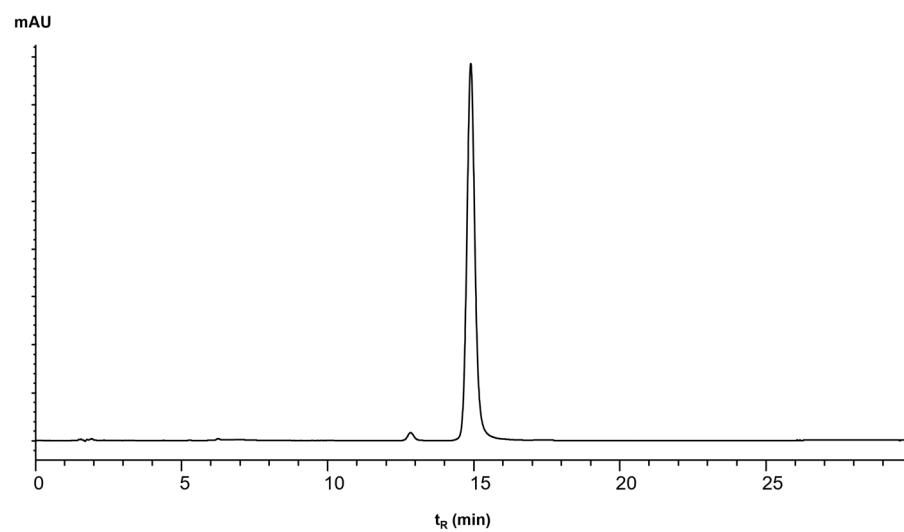


Figure S35. HPLC chromatogram of compound 6 eluted using Method A.

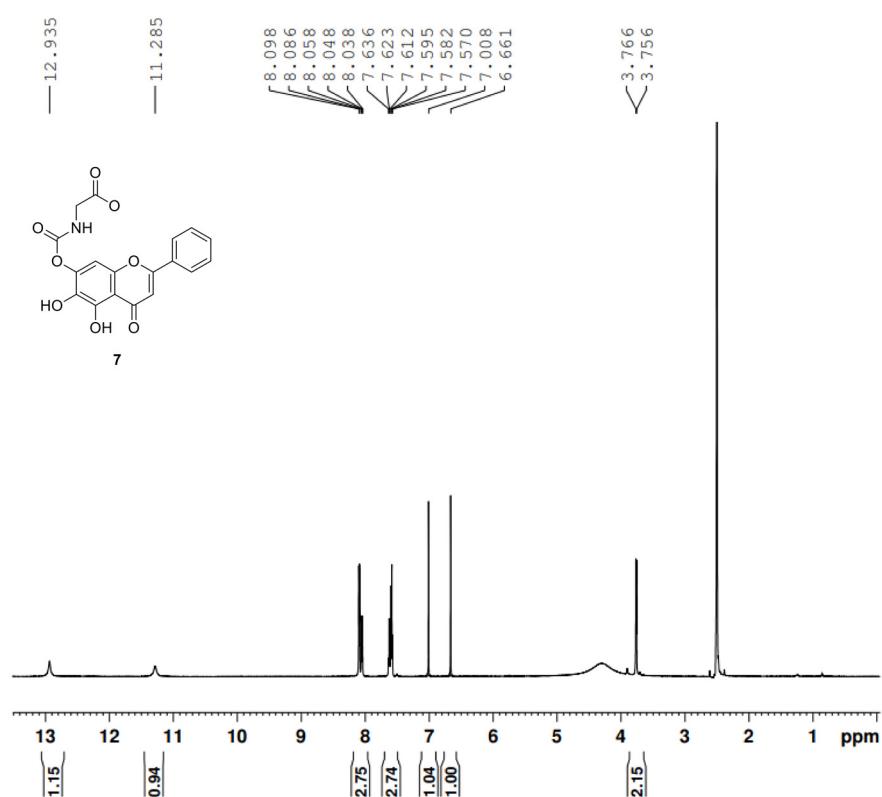


Figure S36. ¹H NMR spectra of compound 7.

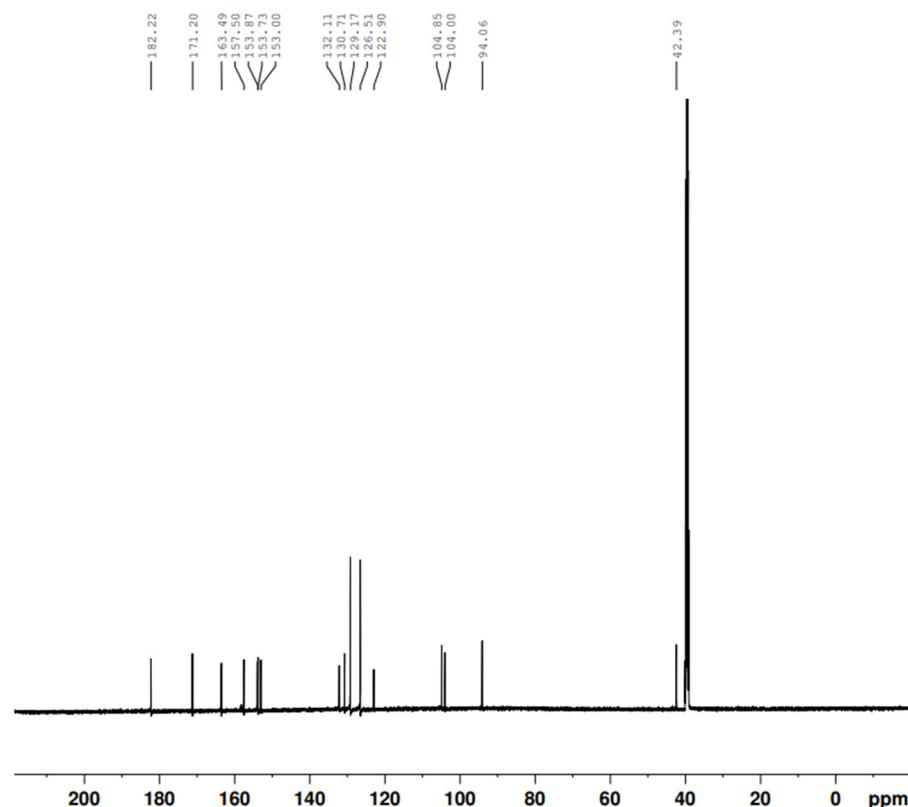


Figure S37. ¹³C NMR spectra of compound 7.

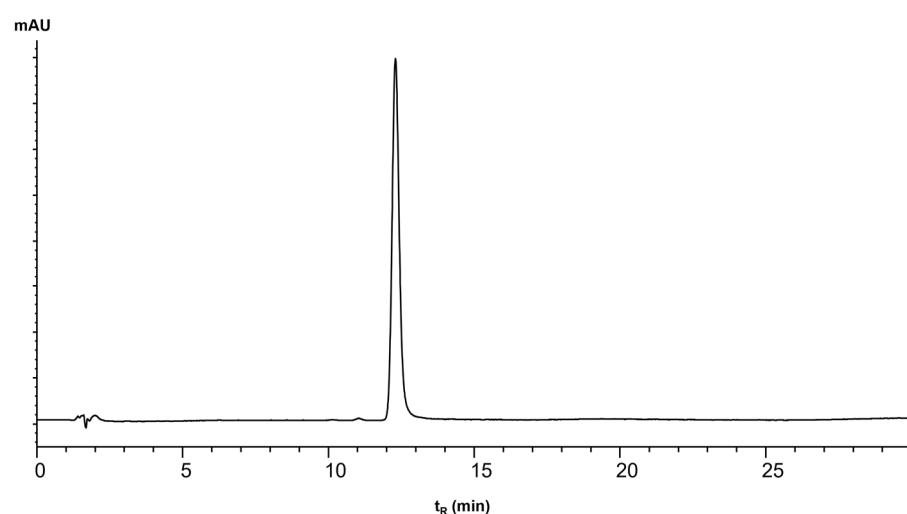


Figure S38. HPLC chromatogram of compound 7 eluted using Method A.