

Structurally diverse biflavonoids from *Dysosma versipellis* and their bioactivity

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Five pairs of new biflavonoid enantiomers, (\pm)-dysosmabiflavonoids A–E (**1–5**), two new biflavonoids, dysosmabiflavonoids F–G (**6–7**), along with four biosynthetically related precursors (**8–11**) were isolated from the roots and rhizomes of *Dysosma versipellis*. Their structures were elucidated by extensive spectroscopic data, including HR-ESI-MS and 2D NMR. Their absolute configurations were determined by comparison of the calculated and experimental ECD spectra. All isolated compounds were evaluated for AChE inhibitory activity. Compounds **6** and **7** exhibited more potent inhibitory activities with IC₅₀ values of 1.42 and 0.73 μ M, respectively, than their biosynthetically related precursors kaemferol (**8**, 17.90 μ M) and quercetin (**9**, 3.96 μ M). The preliminary structure-activity relationship study indicated that the connection mode of biflavonoid subunits, oxidation degree of C ring, and 3,4-dihydroxy group of B ring were important structural factors for AChE inhibitory activity. Racemates **1–5** and their corresponding levorotatory and dextrorotatory enantiomers were tested for the potential to impede the generation of NO in lipopolysaccharide-stimulated RAW264.7 cells, and mushroom tyrosinase inhibitory effect. Racemate **1** displayed more potent mushroom tyrosinase inhibitory activity (IC₅₀, 28.27 μ M) than the positive control kojic acid (IC₅₀, 32.59 μ M). *D. versipellis* may have the therapeutic potential for melanogenesis disorders and neurodegenerative disease.

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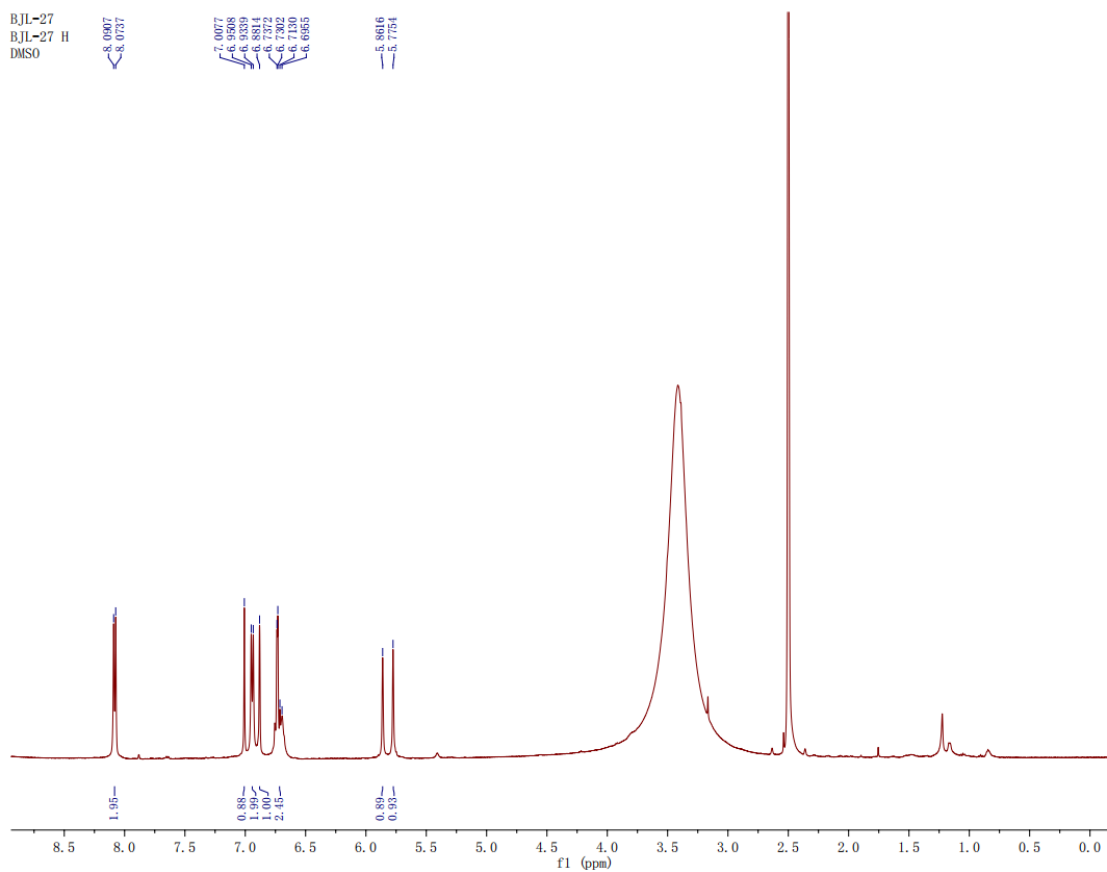


Figure S1. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **1**

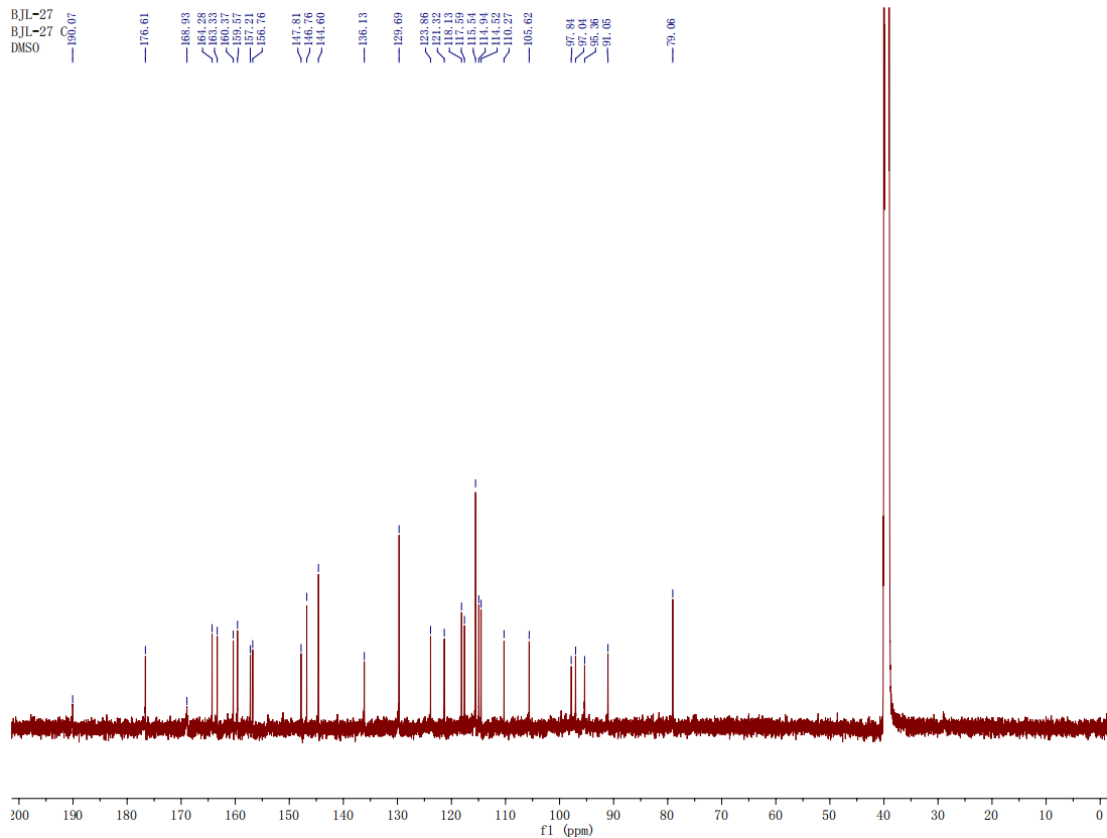


Figure S2. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **1**

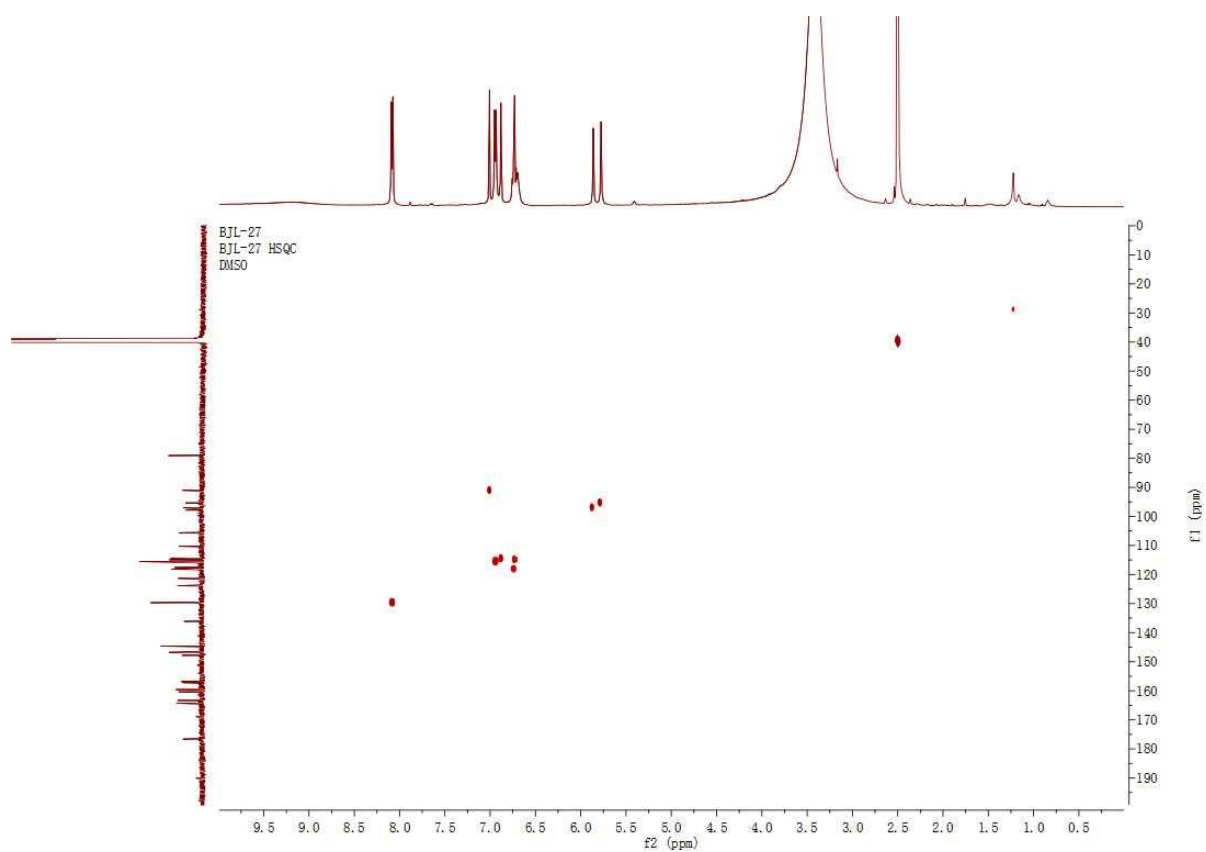


Figure S3. HSQC spectrum of (\pm) **1**

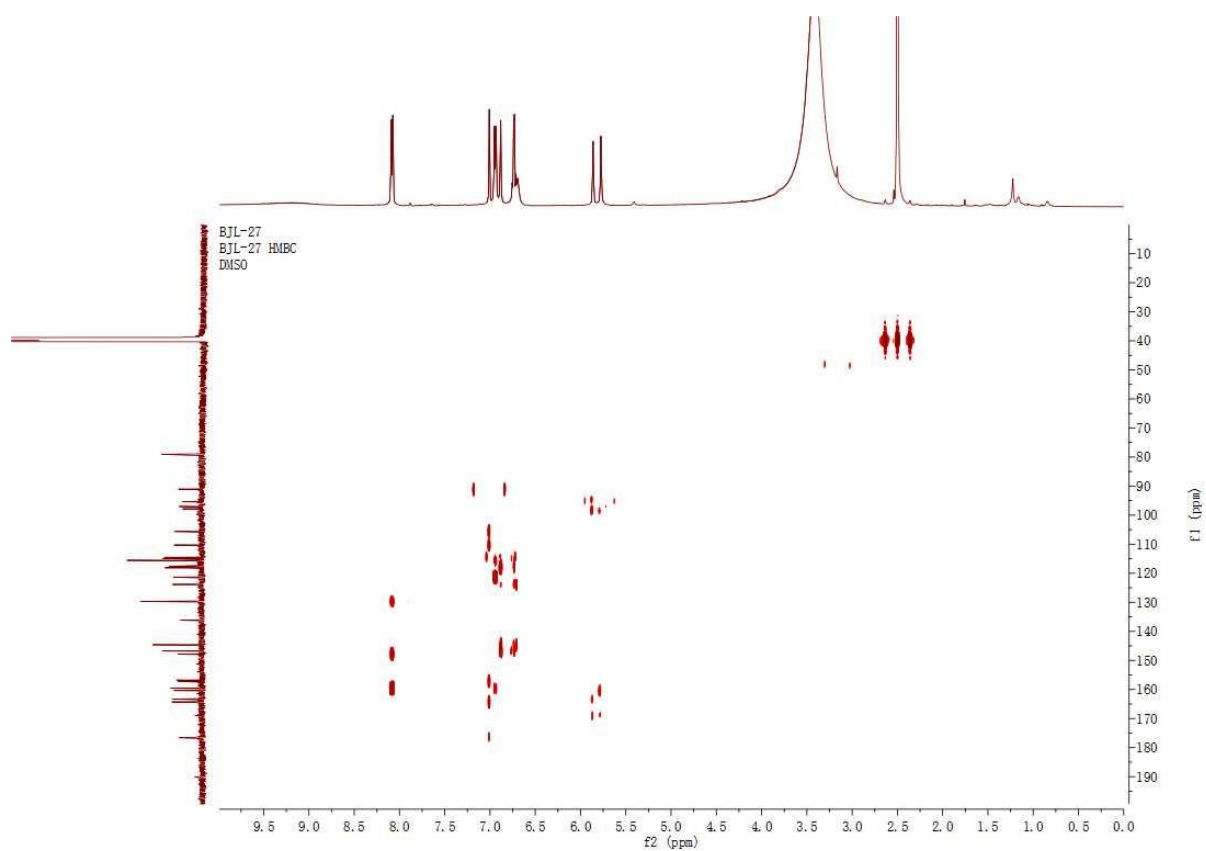


Figure S4. HMBC spectrum of (\pm) **1**

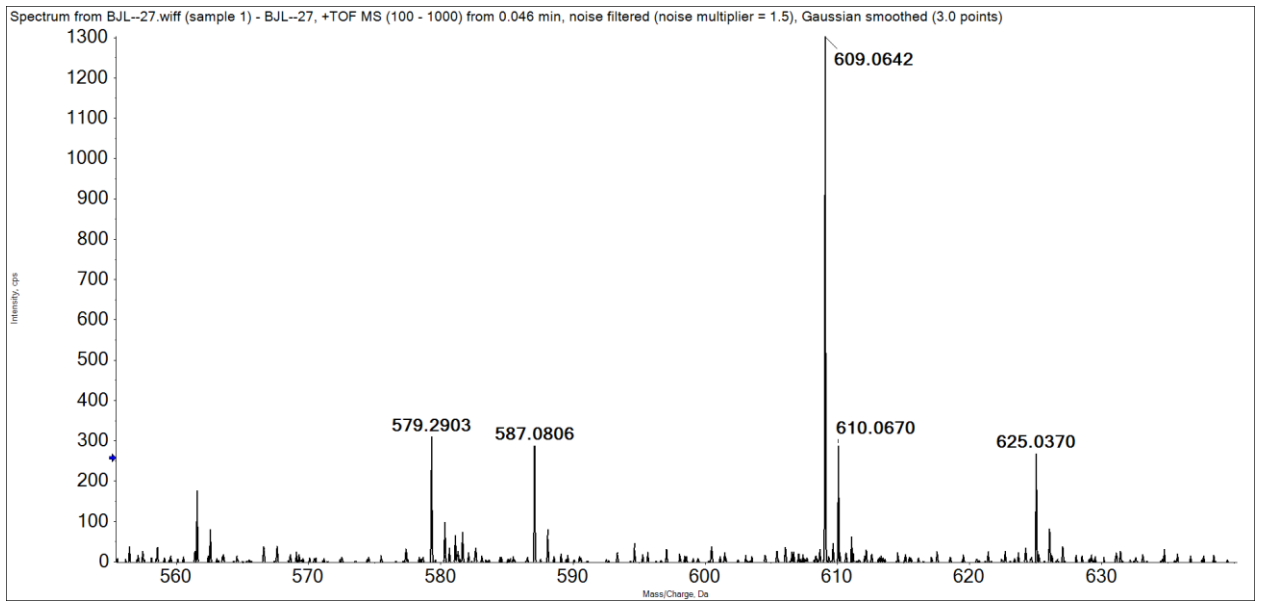


Figure S5. HR-ESI-MS spectrum of (\pm) 1

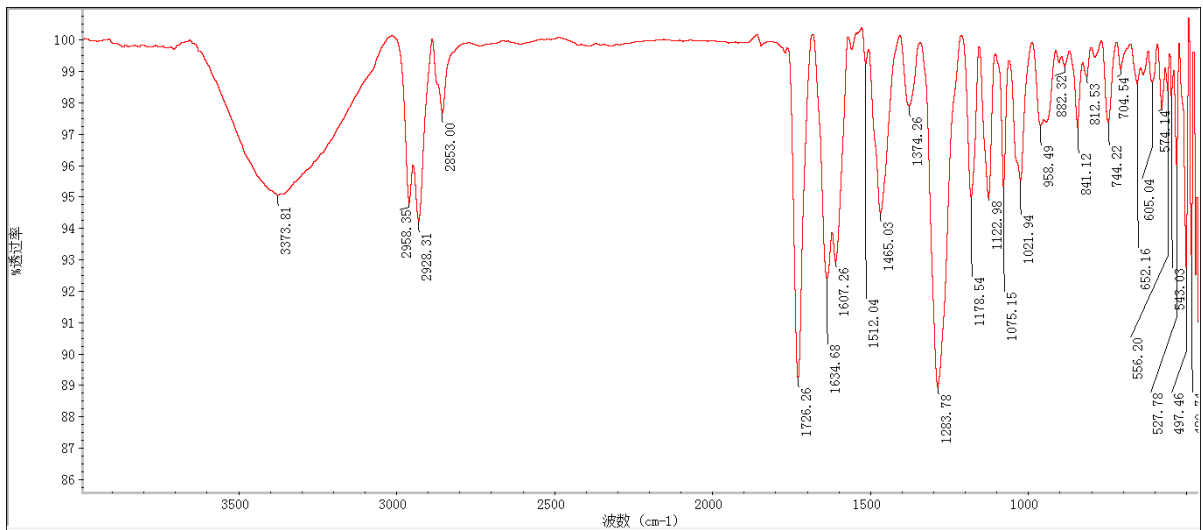


Figure S6. IR spectrum of (\pm) 1

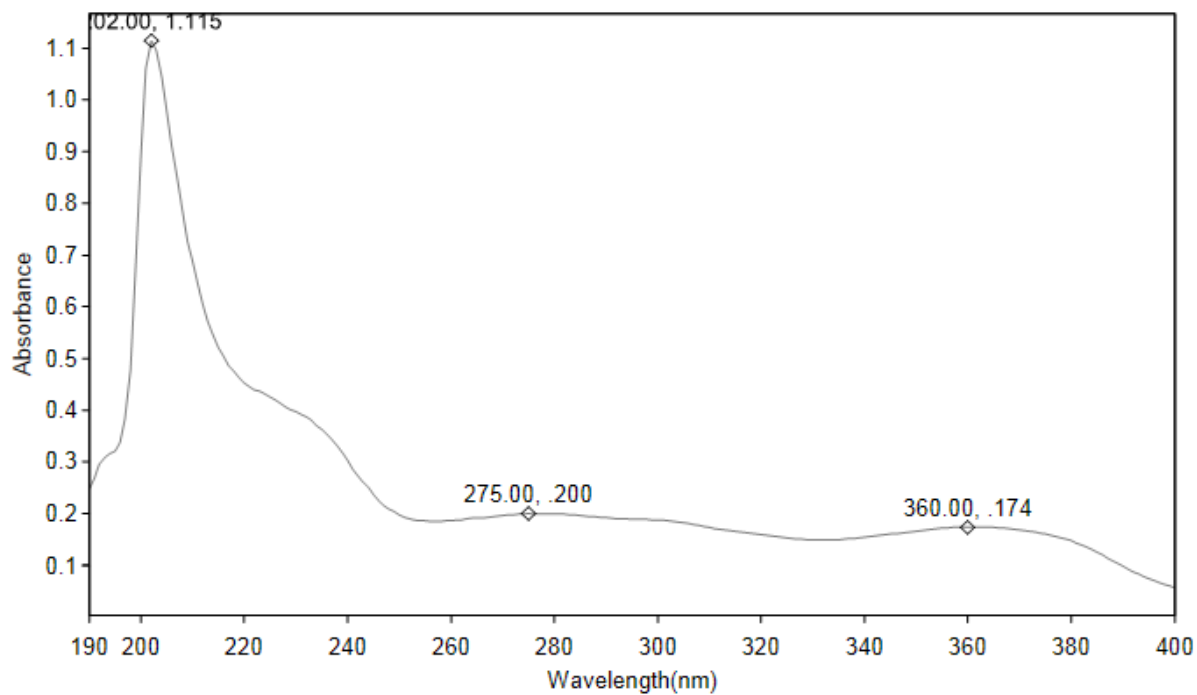


Figure S7. UV spectrum of (\pm) **1**

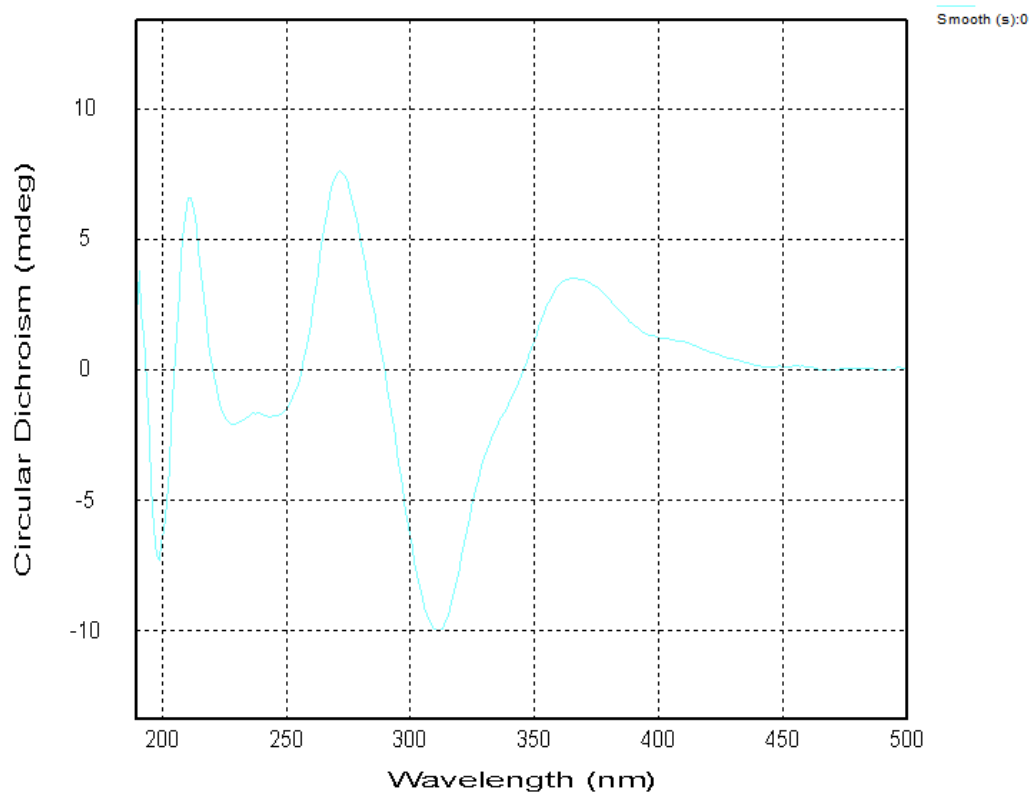


Figure S8. Experimental ECD spectrum of **1a**

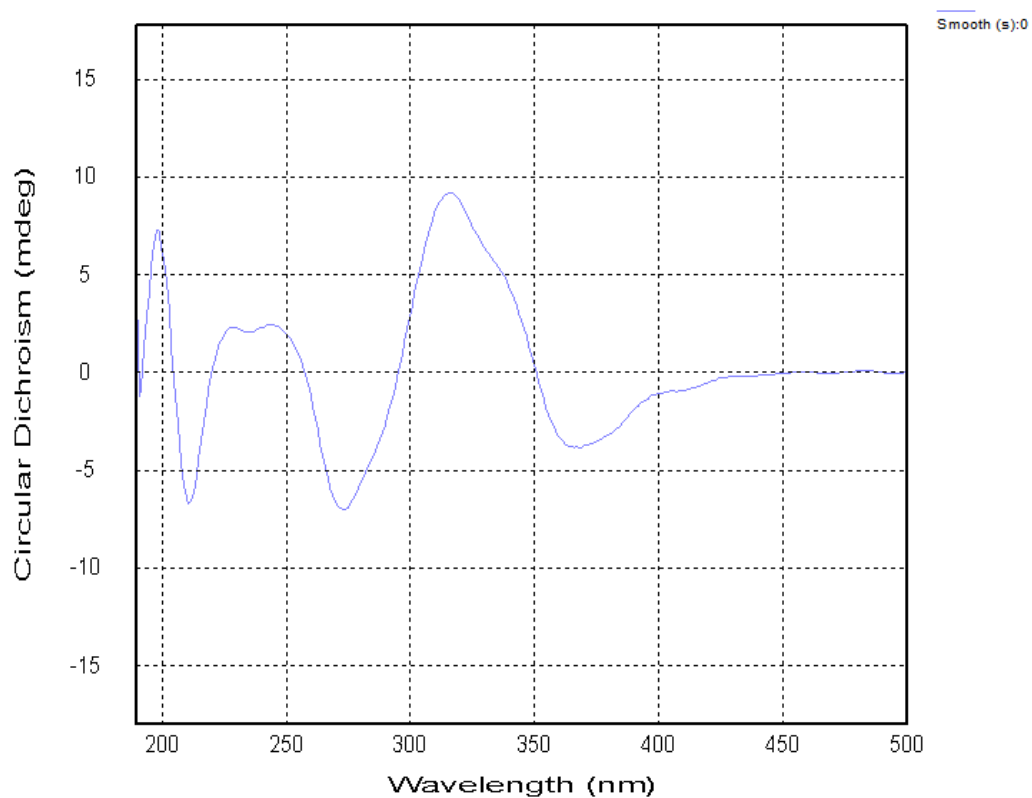


Figure S9. Experimental ECD spectrum of **1b**

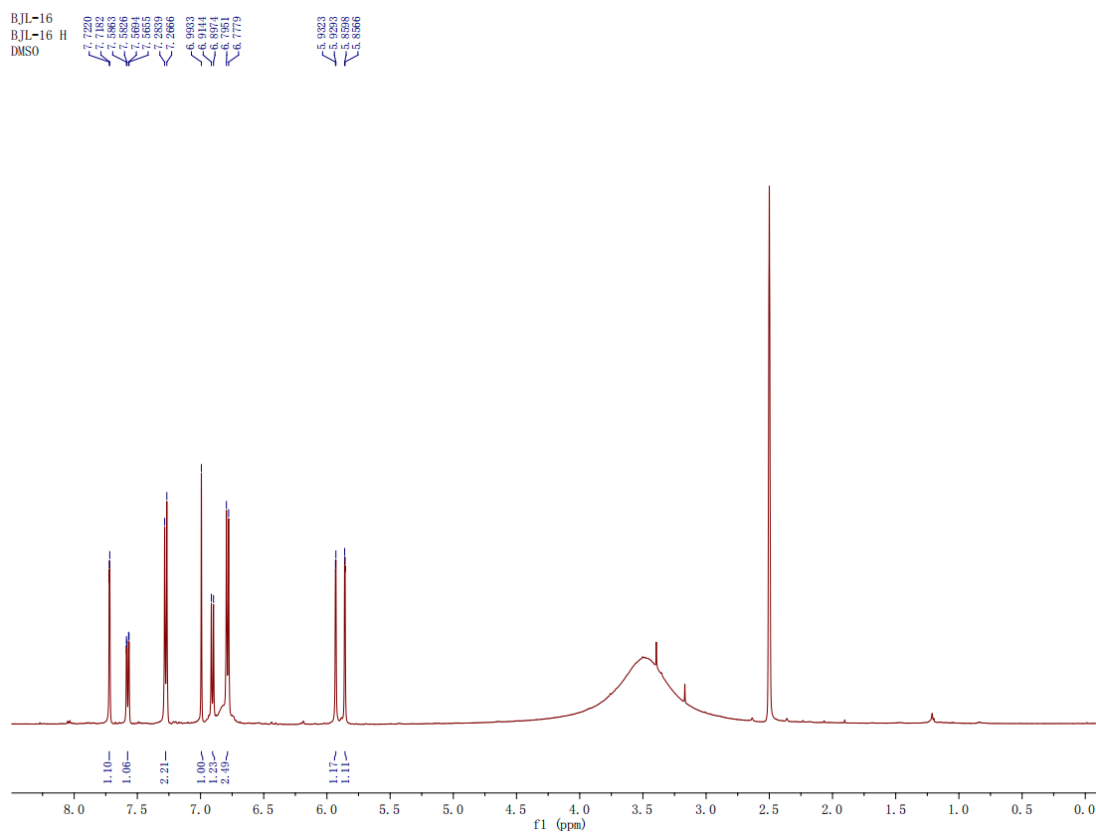


Figure S10. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **2**

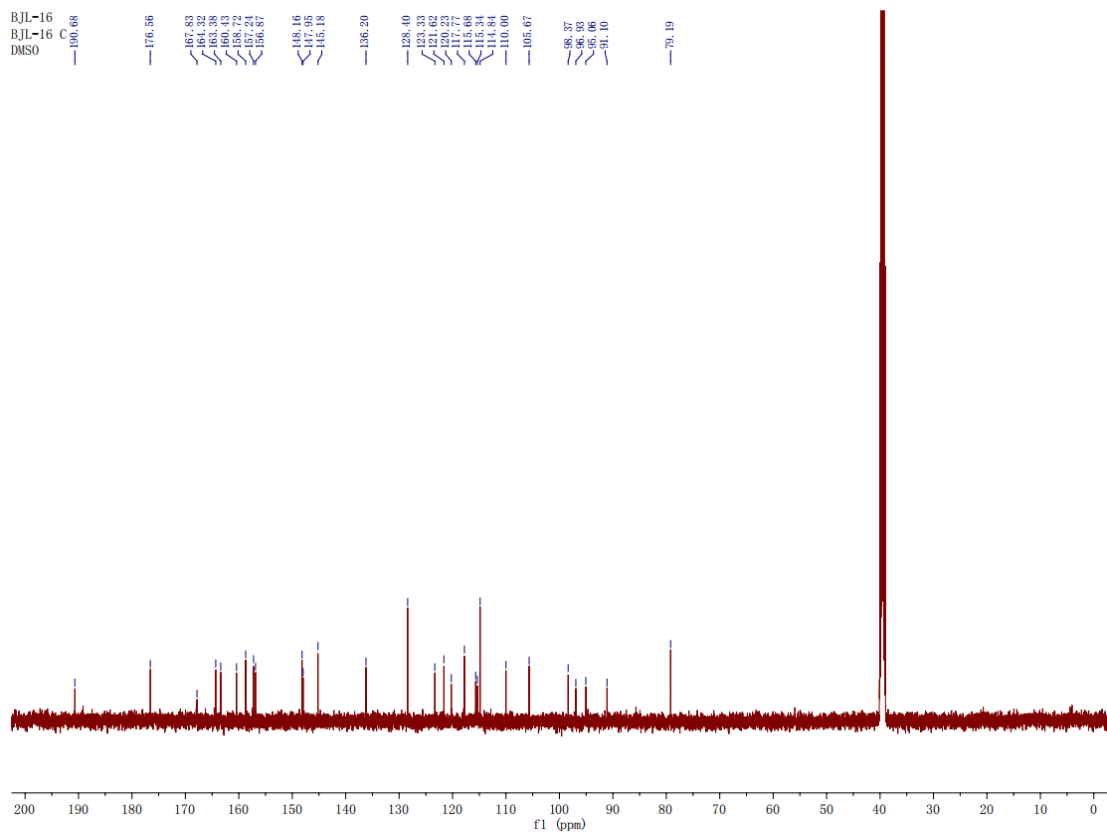


Figure S11. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **2**

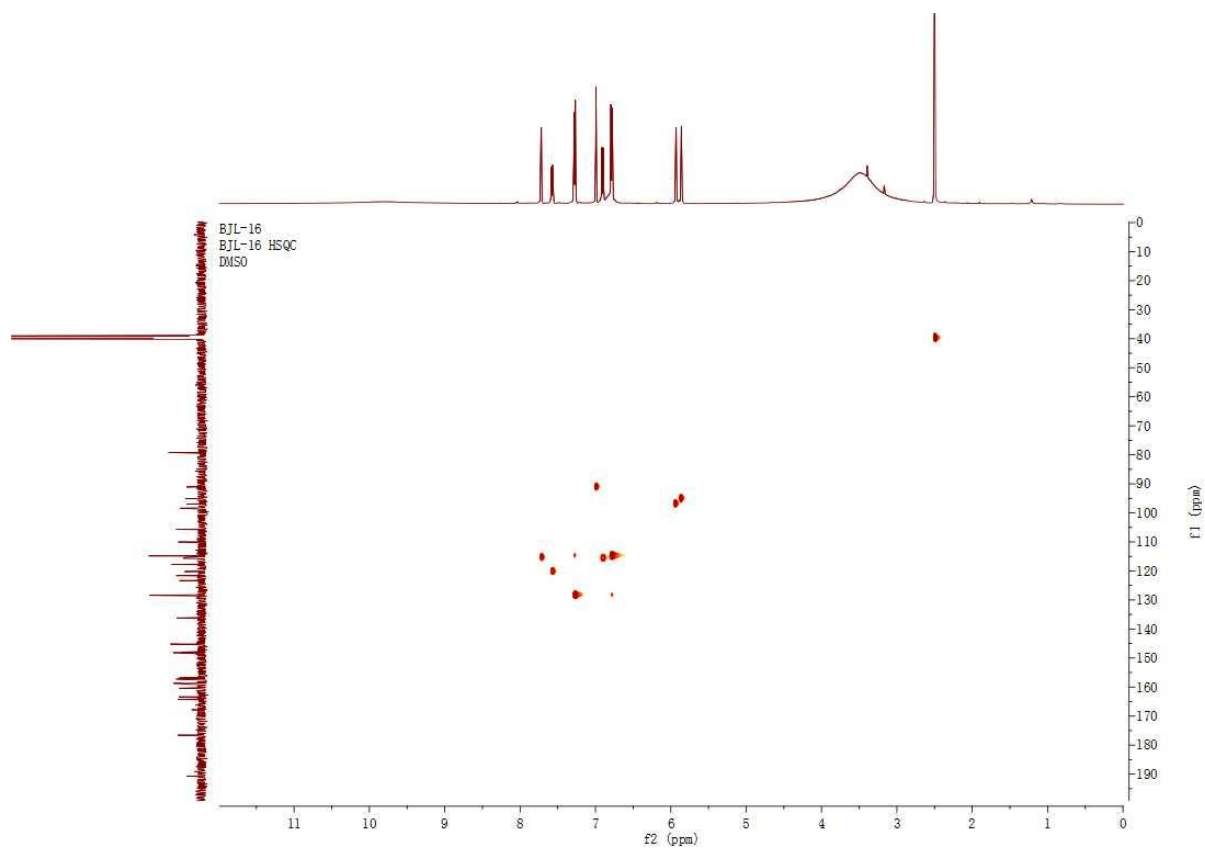


Figure S12. HSQC spectrum of (\pm) **2**

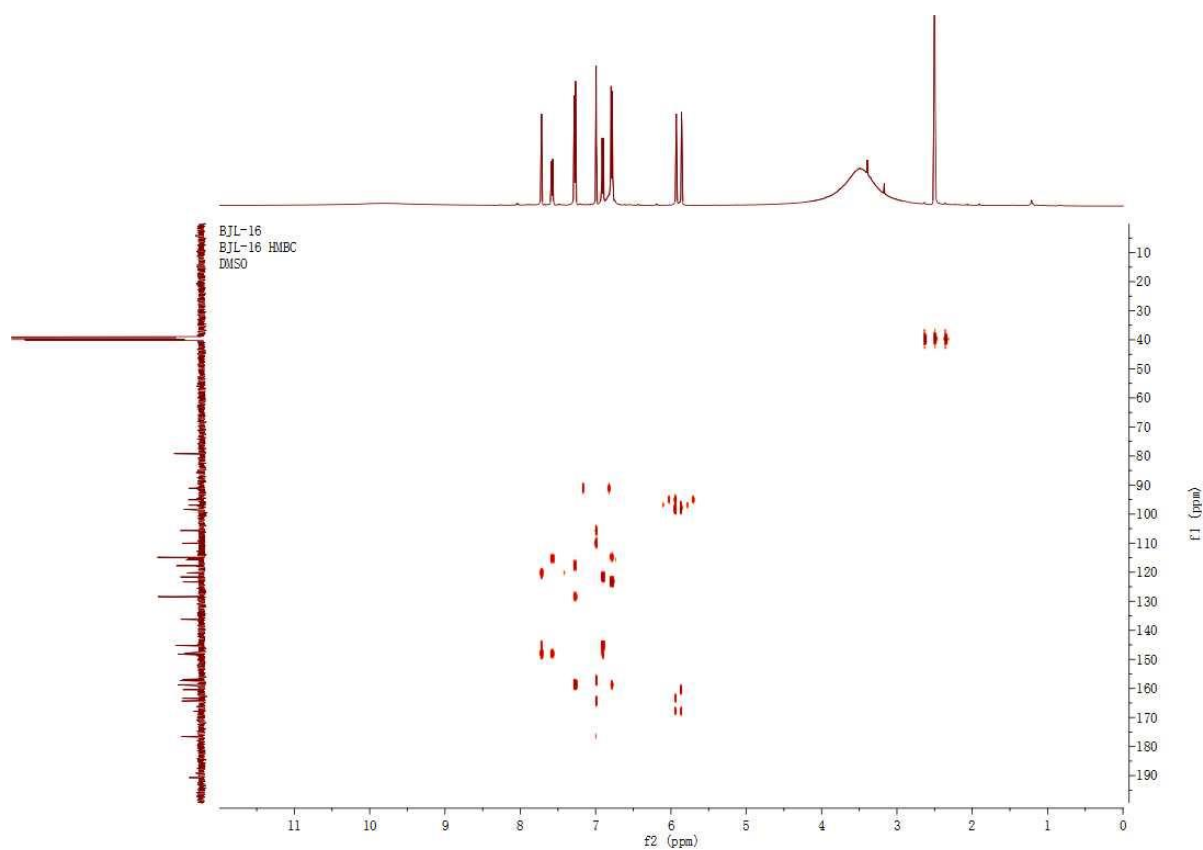


Figure S13. HMBC spectrum of (\pm) **2**

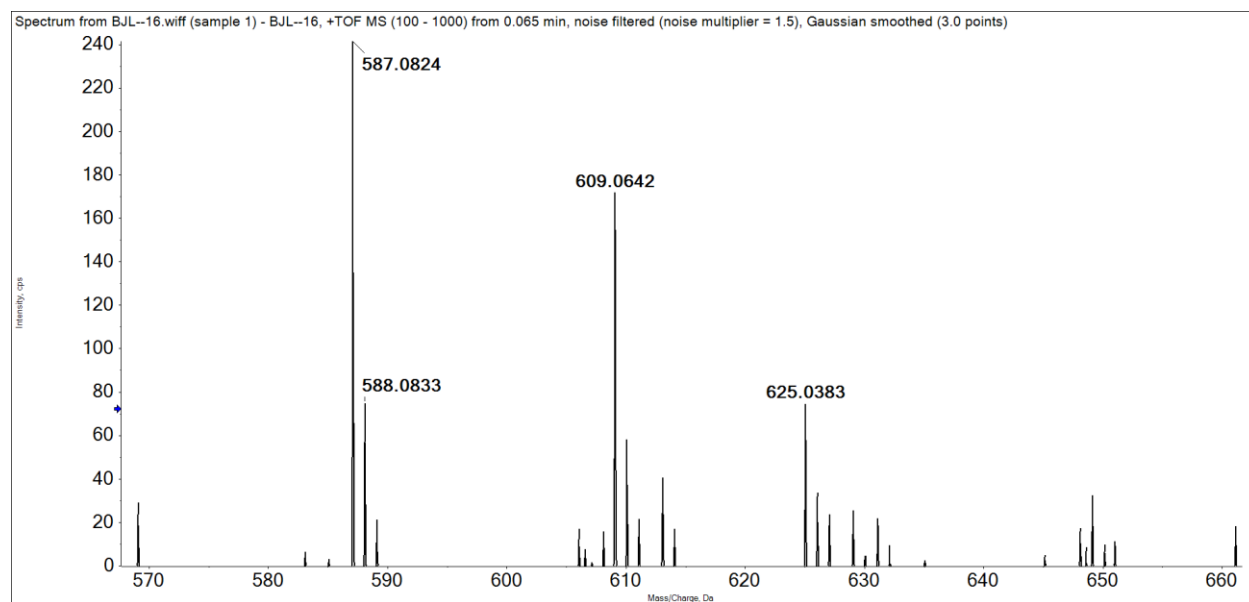


Figure S14. HR-ESI-MS spectrum of (\pm) **2**

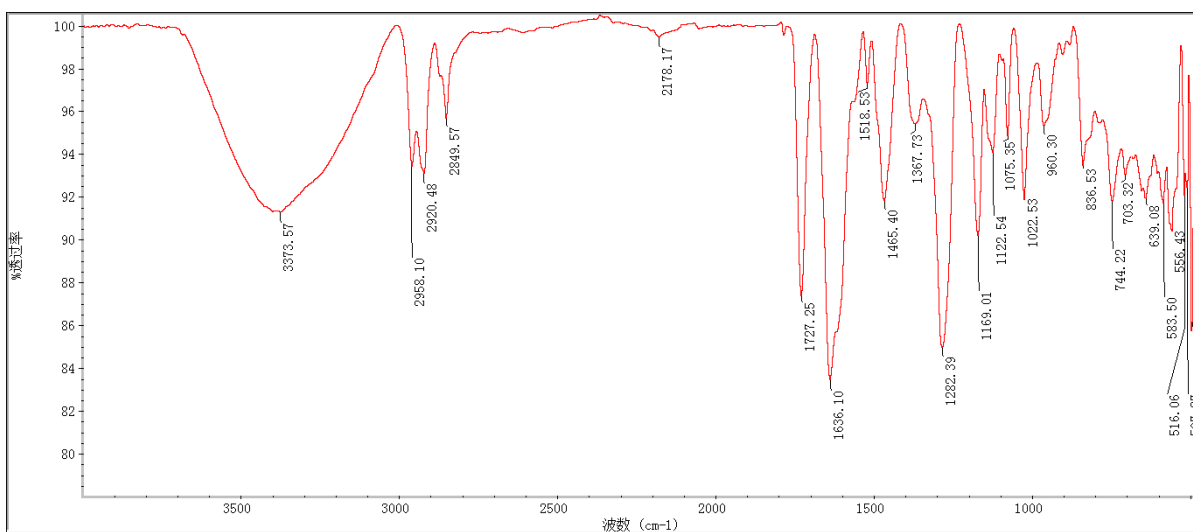


Figure S15. IR spectrum of (\pm) **2**

Scan Graph

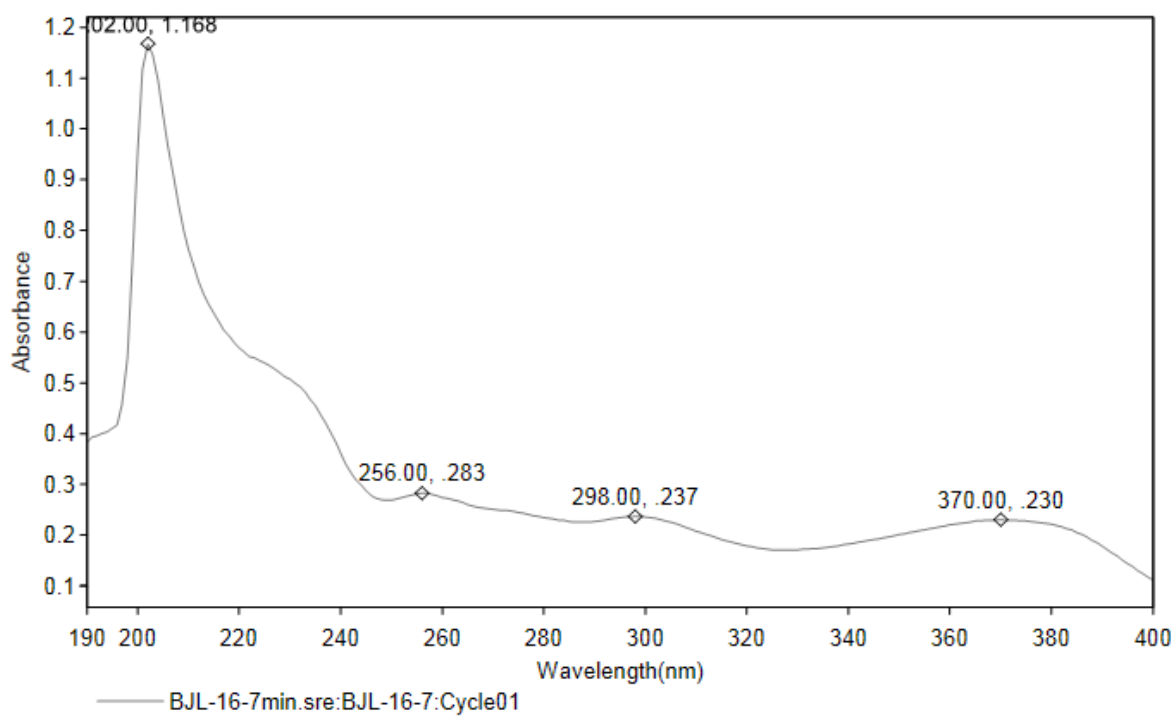


Figure S16. UV spectrum of (\pm) **2**

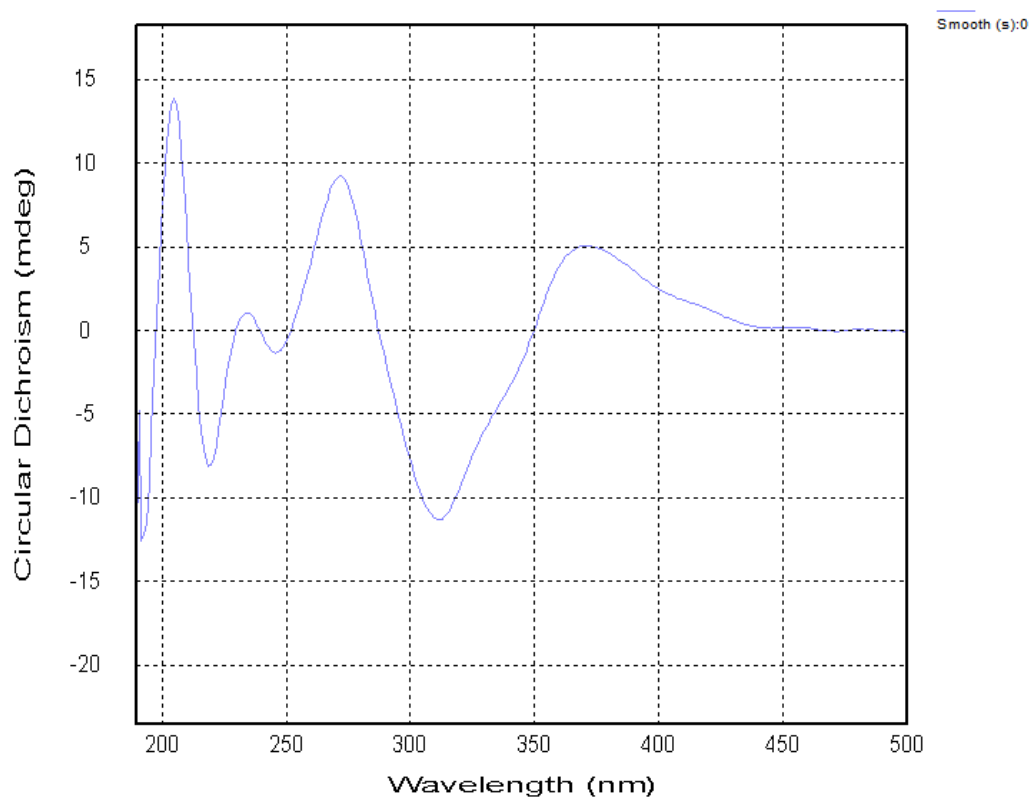


Figure S17. Experimental ECD spectrum of **2a**

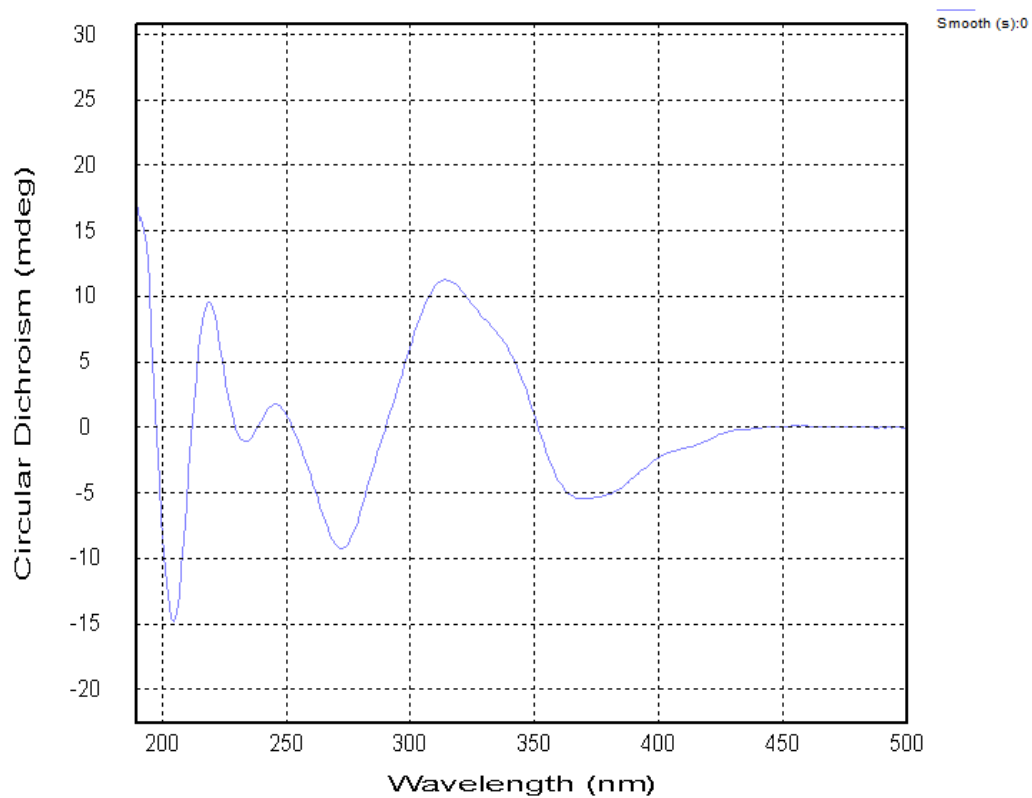


Figure S18. Experimental ECD spectrum of **2b**

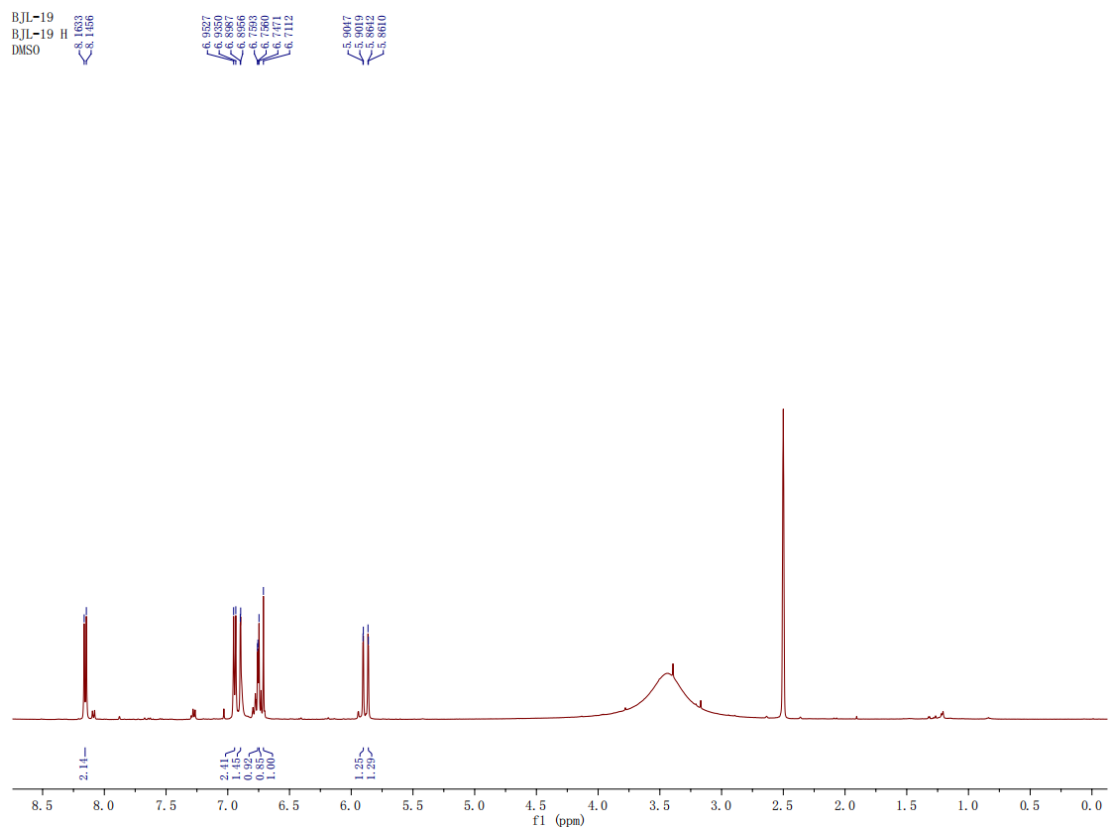


Figure S19. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **3**

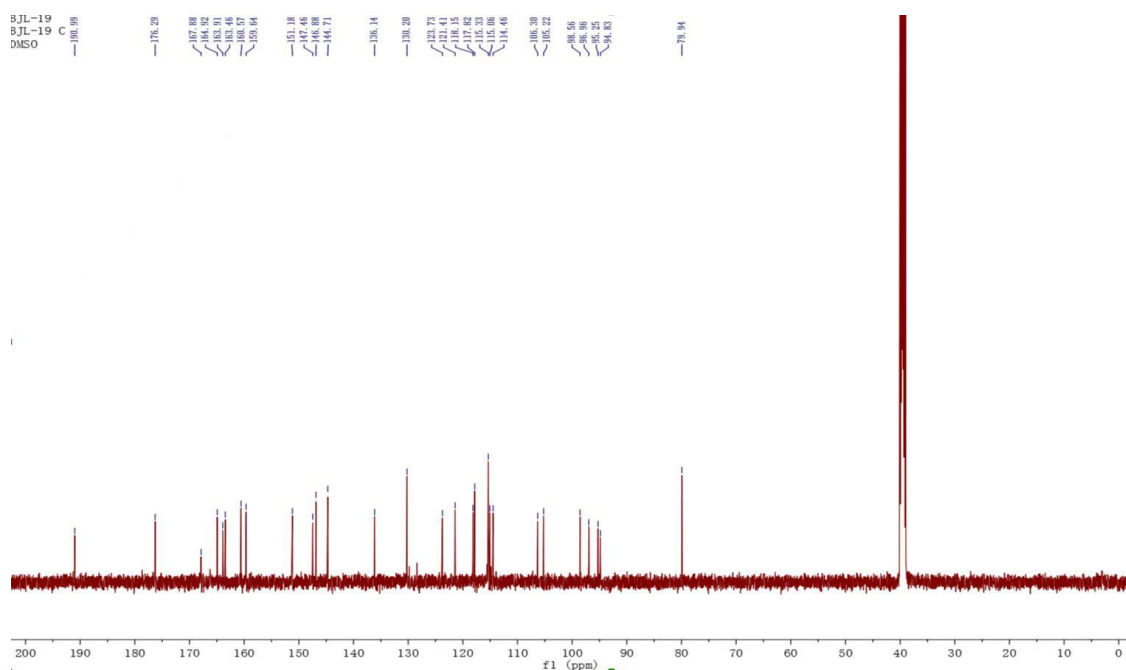


Figure S20. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **3**

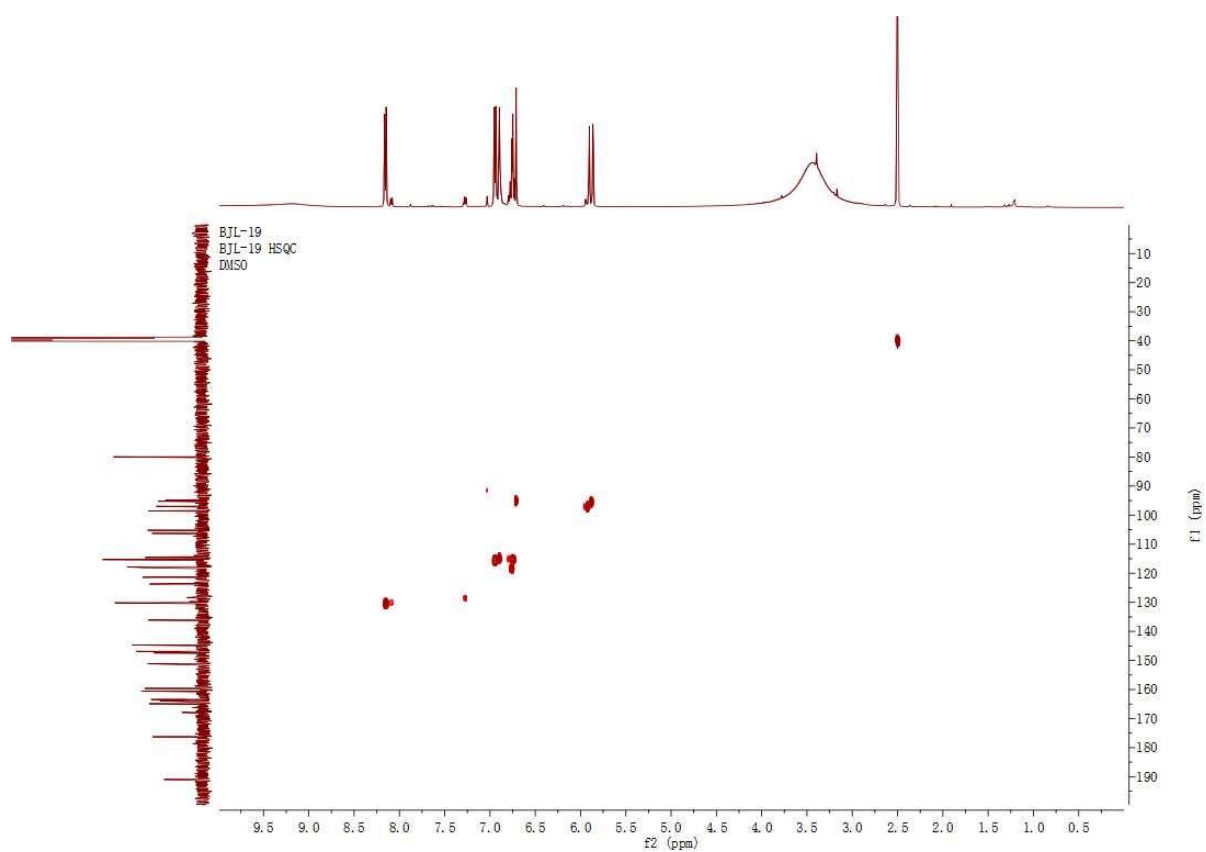


Figure S21. HSQC spectrum of (\pm) **3**

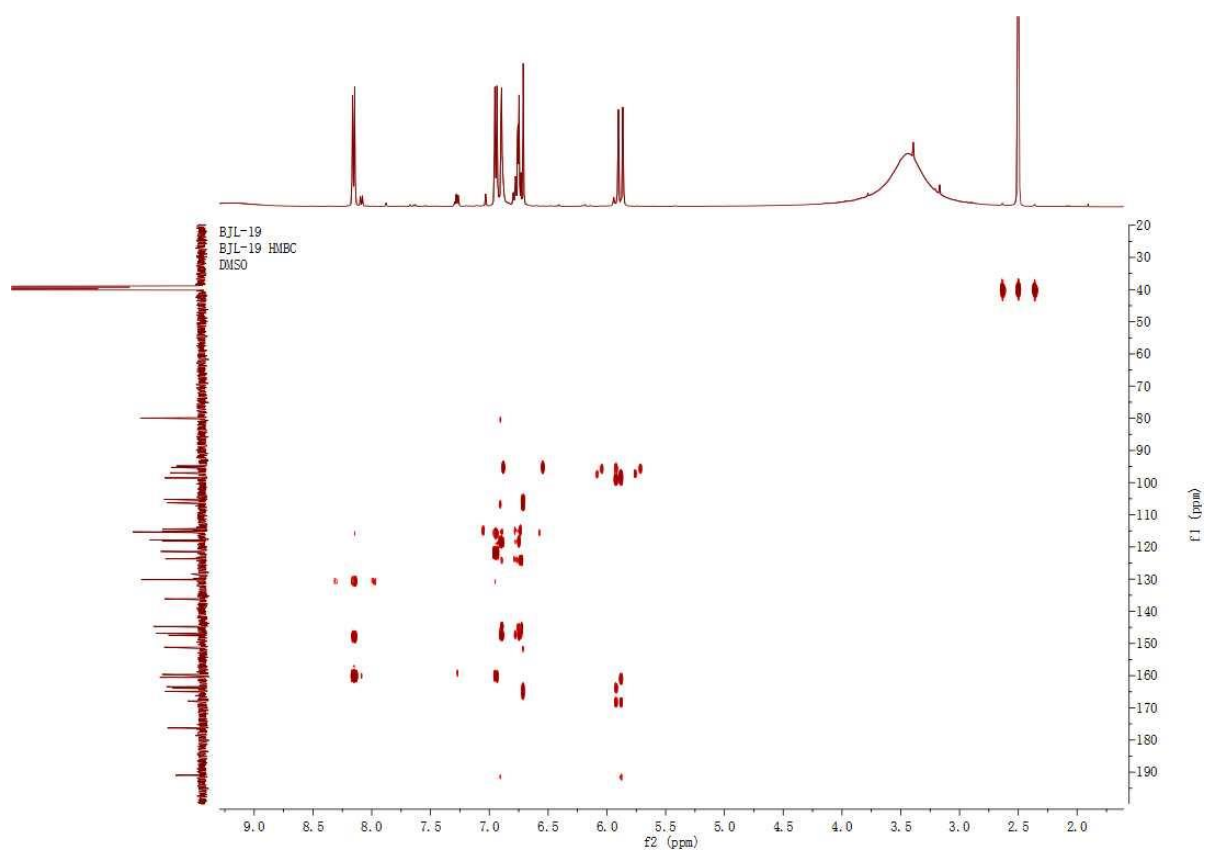


Figure S22. HMBC spectrum of (\pm) **3**

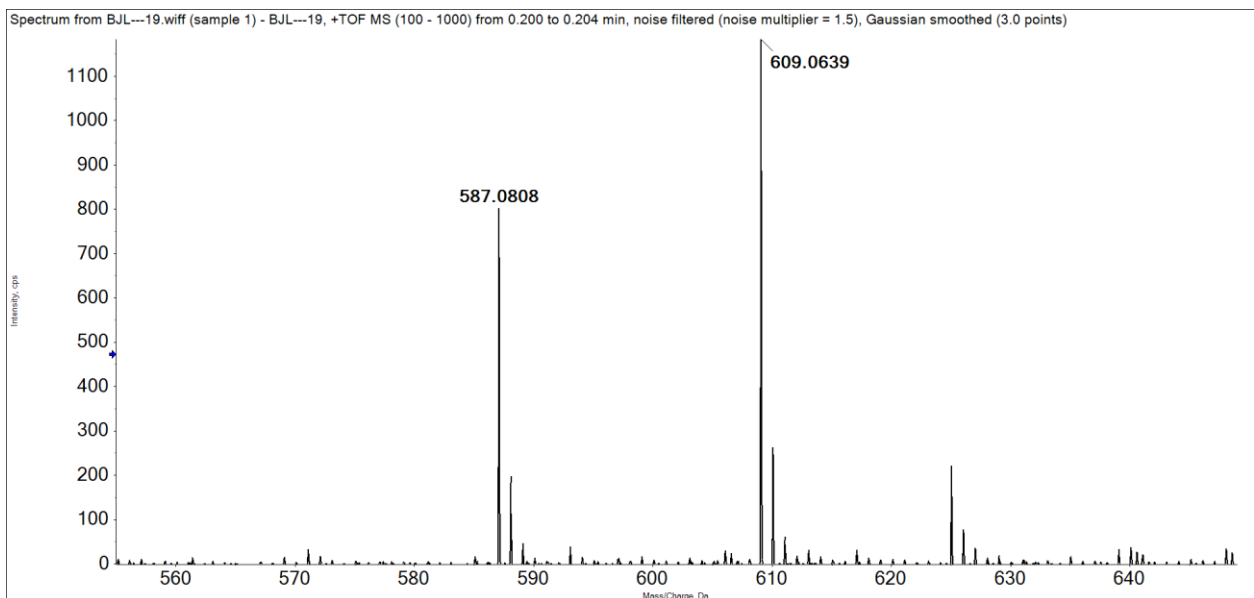


Figure S23. HRESIMS spectrum of (\pm) **3**

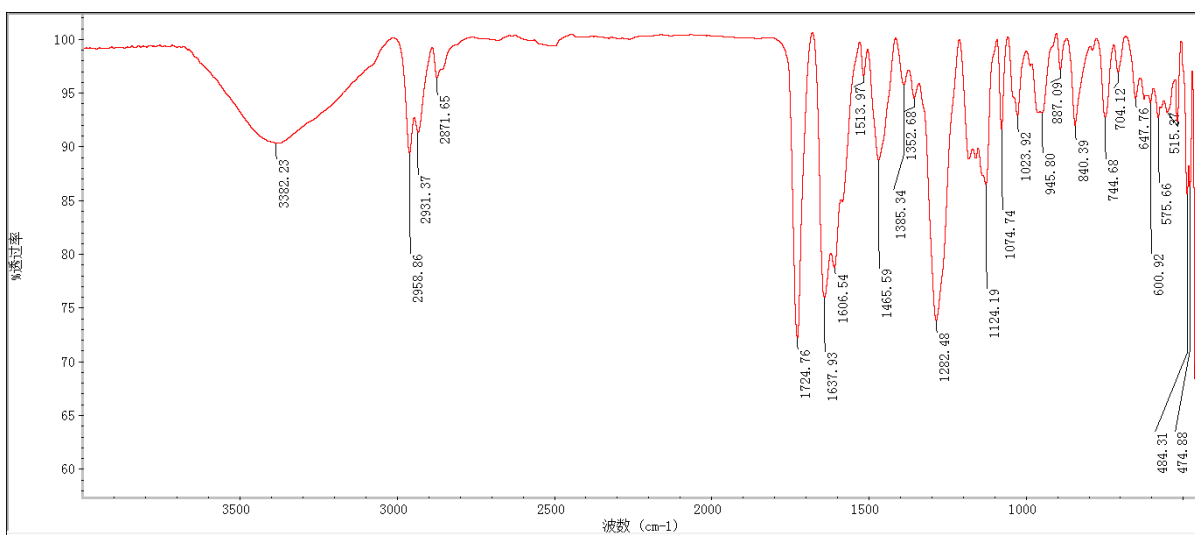


Figure S24. IR spectrum of (\pm) **3**

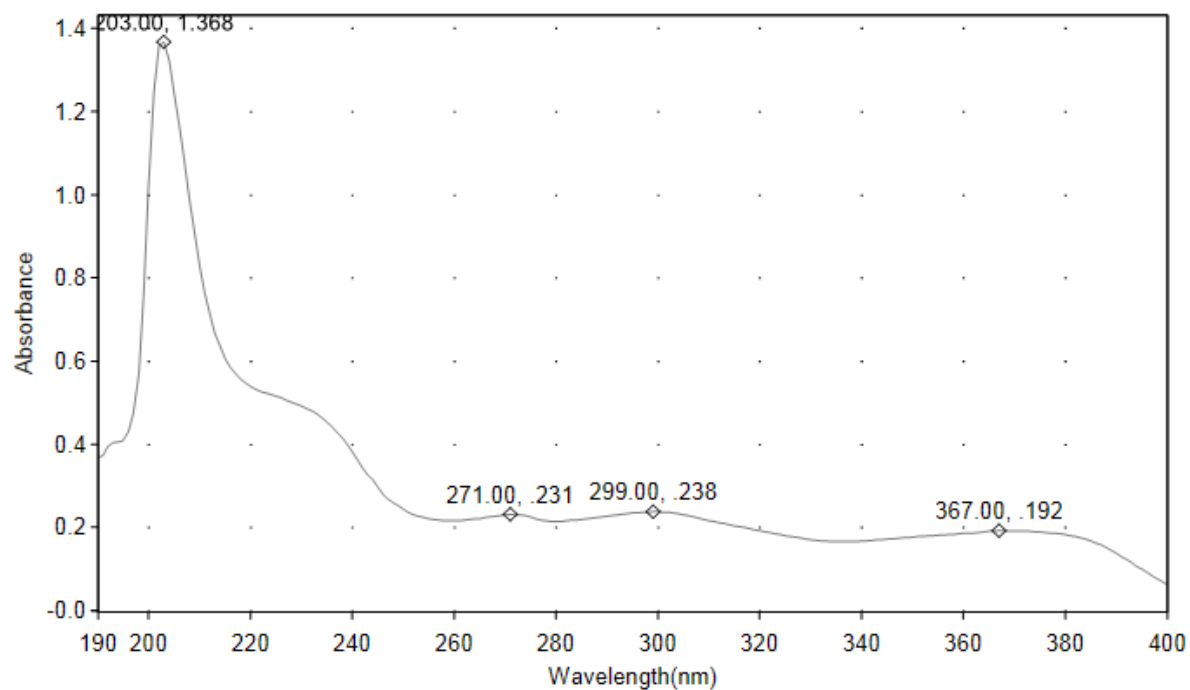


Figure S25. UV spectrum of (\pm) **3**

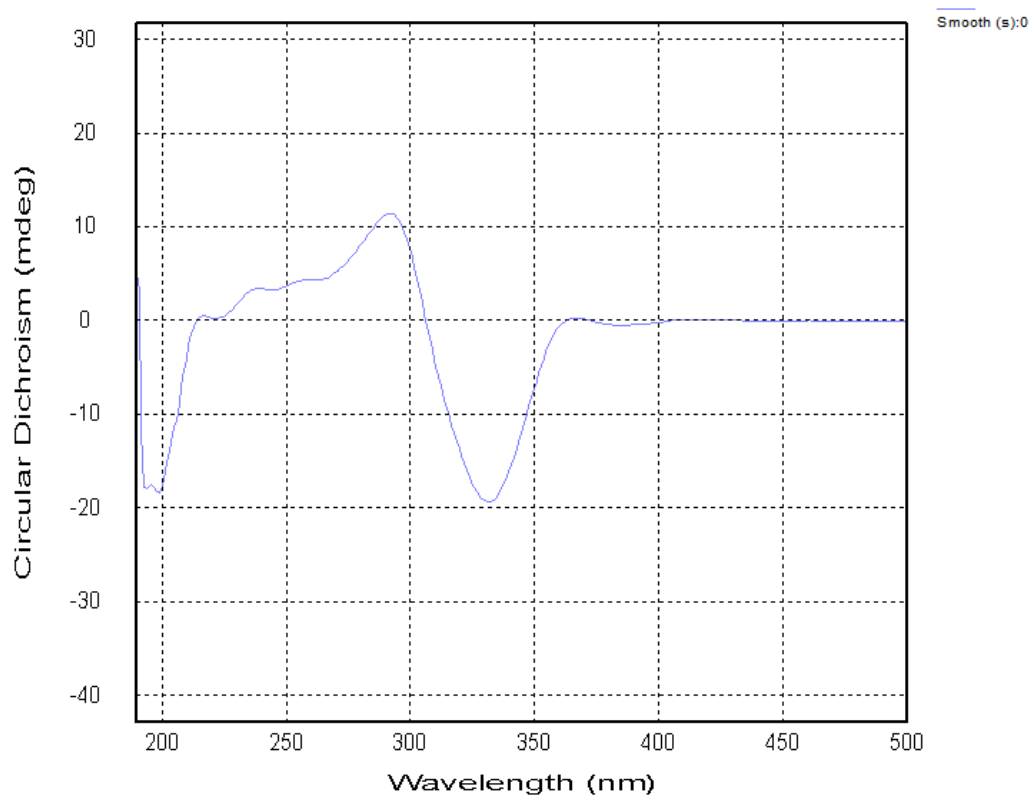


Figure S26. Experimental ECD spectrum of **3a**

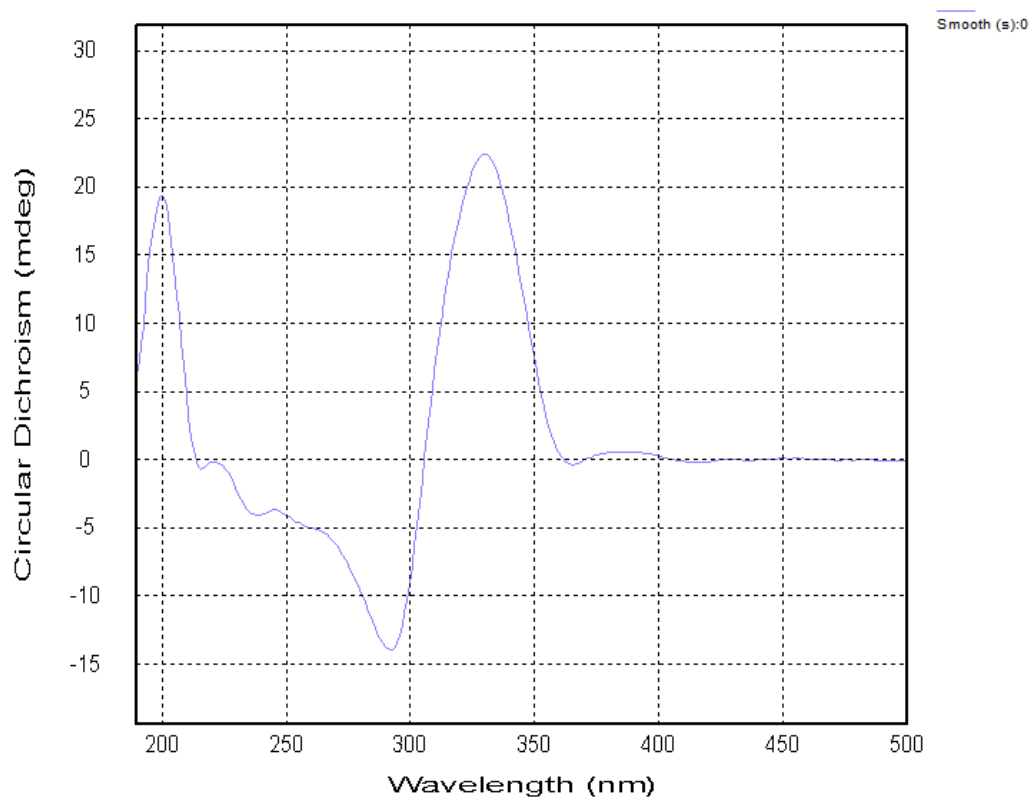


Figure S27. Experimental ECD spectrum of **3b**

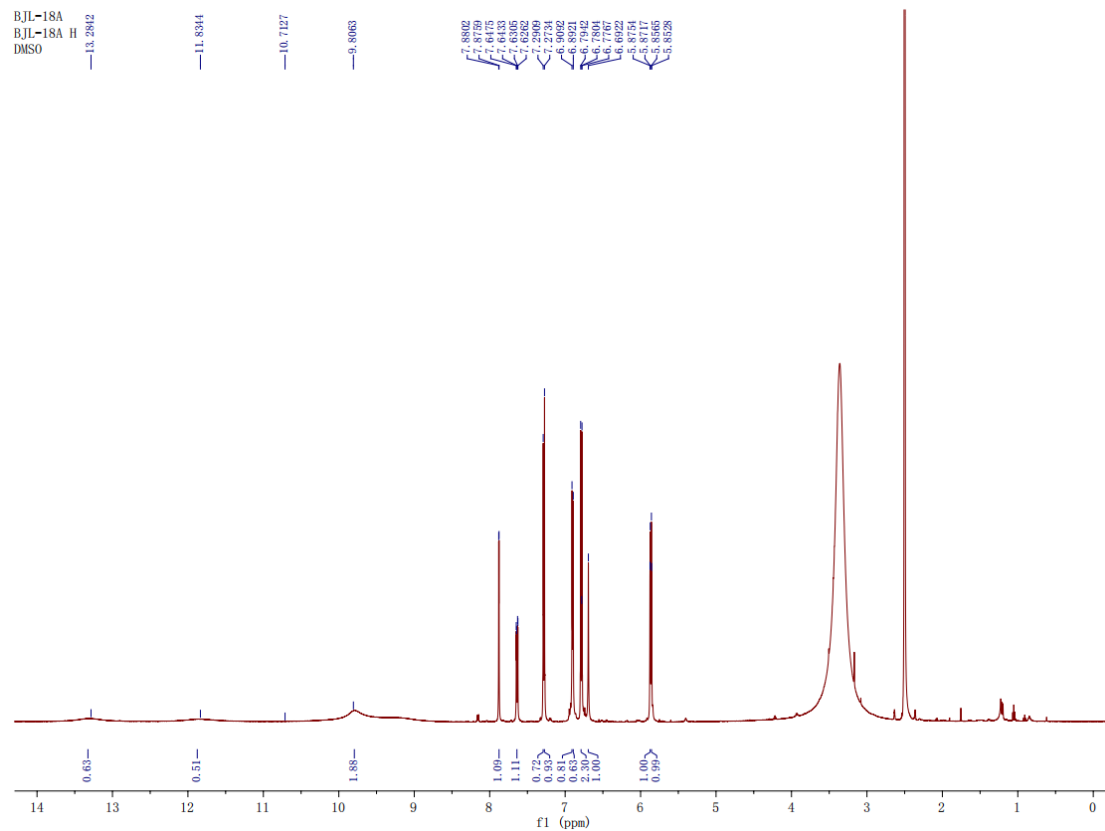


Figure S28. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **4**

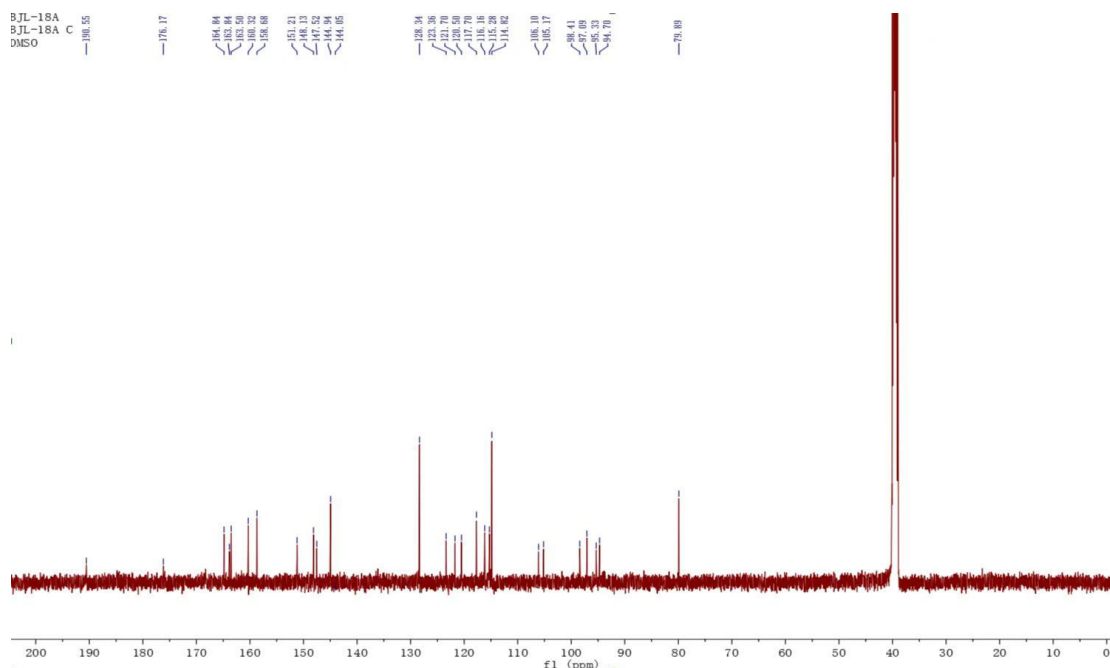


Figure S29. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **4**

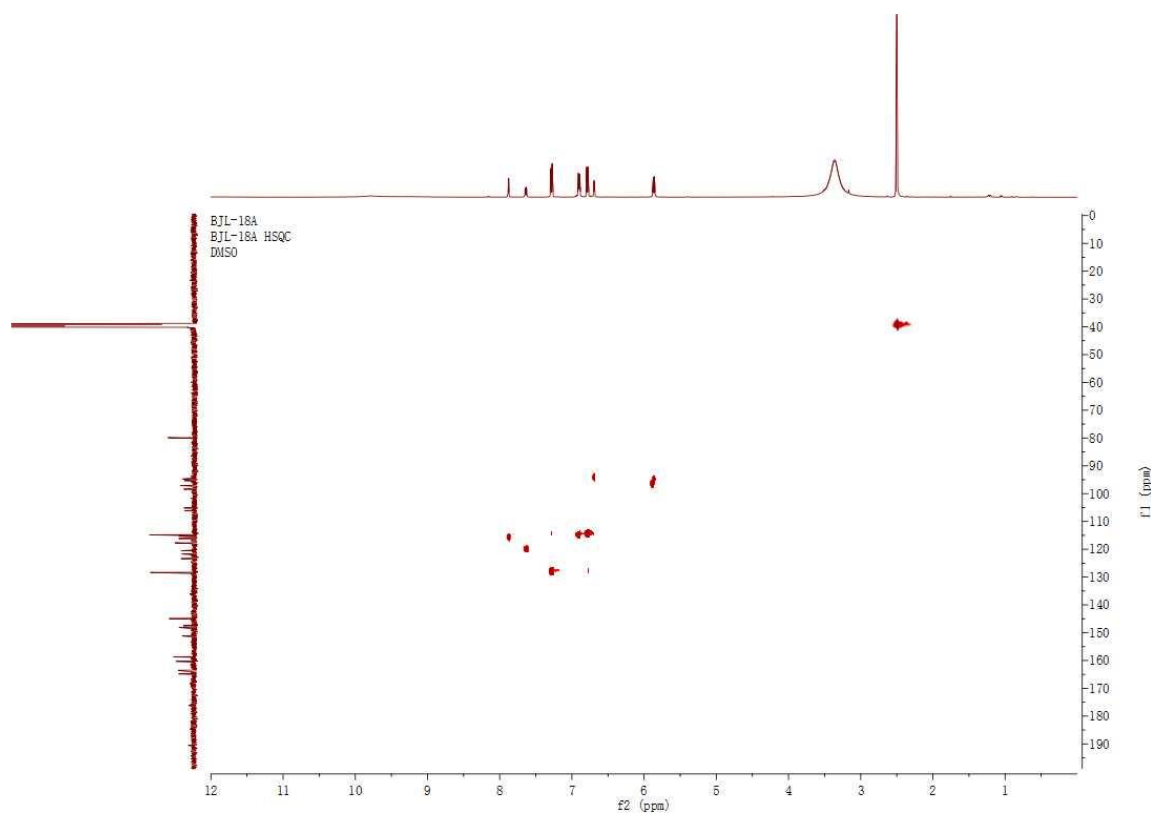


Figure S30. HSQC spectrum of (\pm) **4**

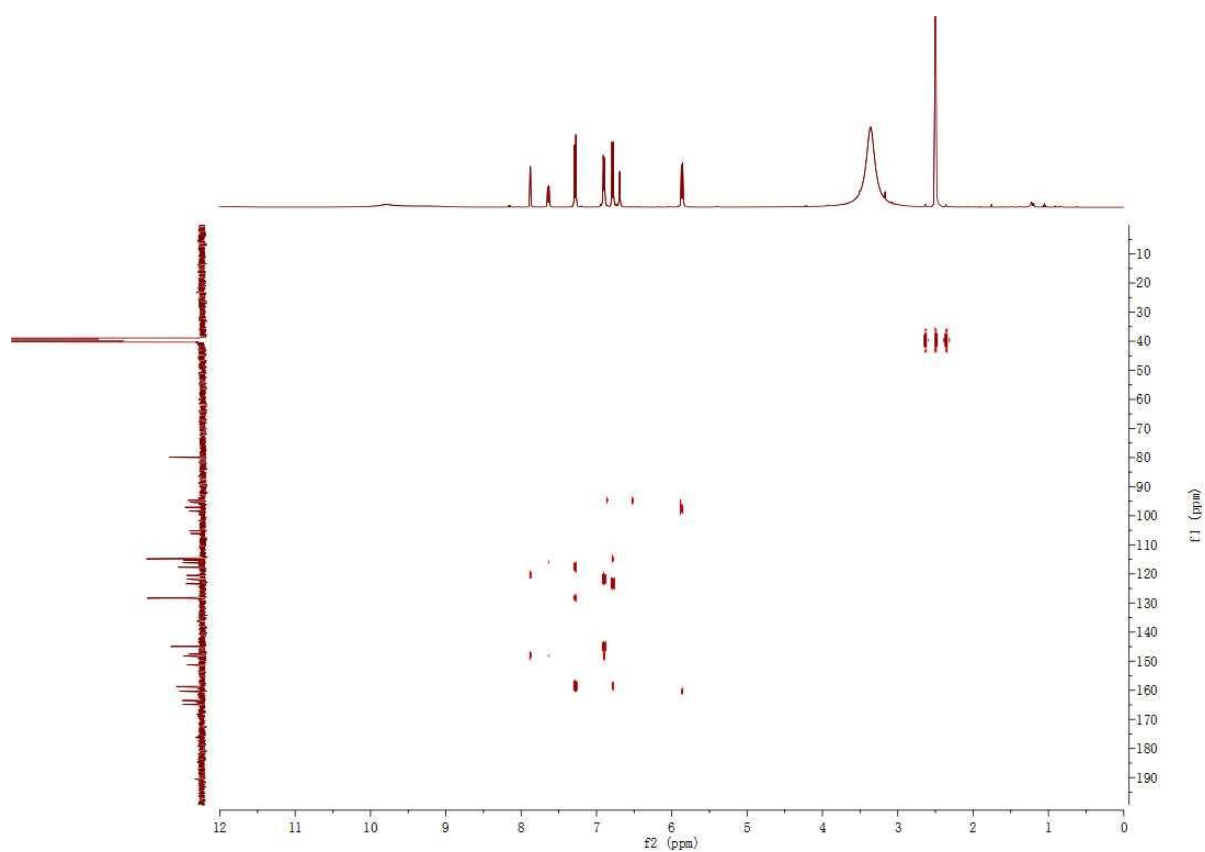


Figure S31. HMBC spectrum of (\pm) **4**

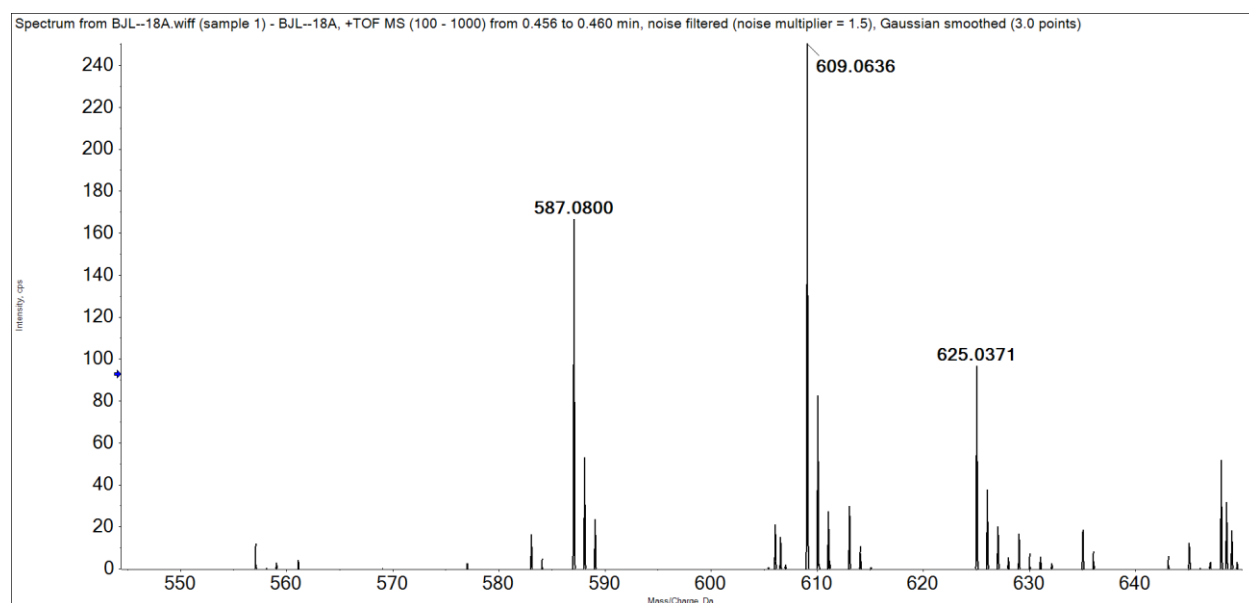


Figure S32. HR-ESI-MS spectrum of (\pm) **4**

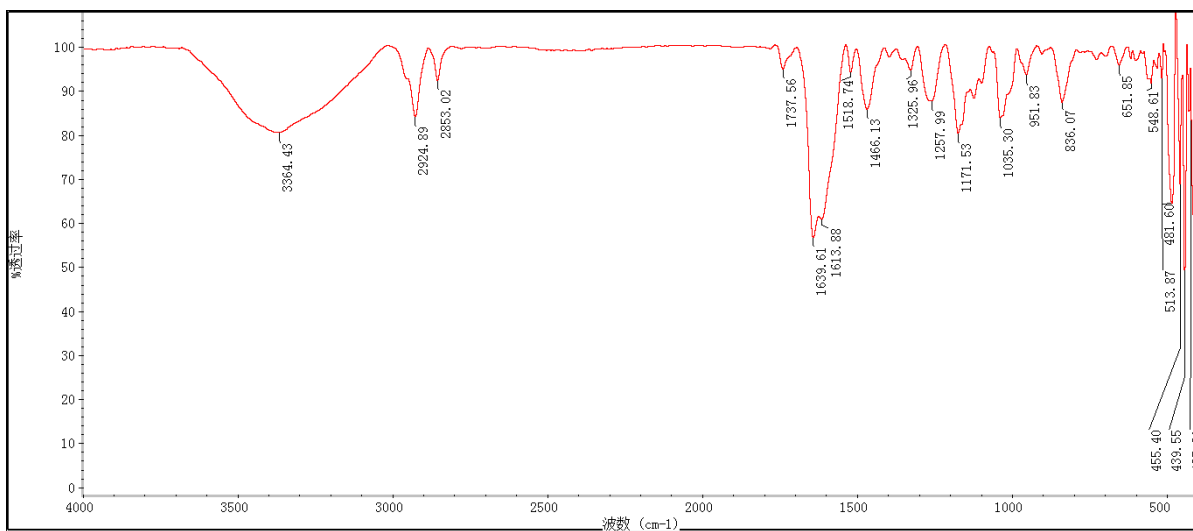


Figure S33. IR spectrum of (\pm) **4**

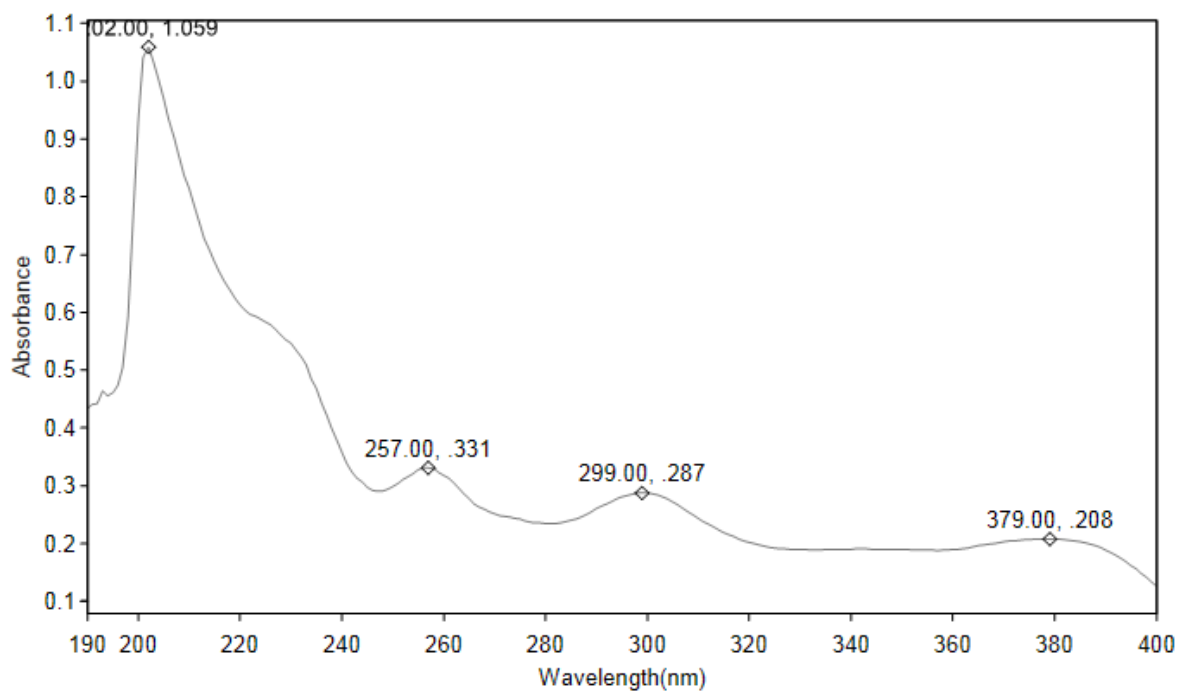


Figure S34. UV spectrum of (\pm) **4**

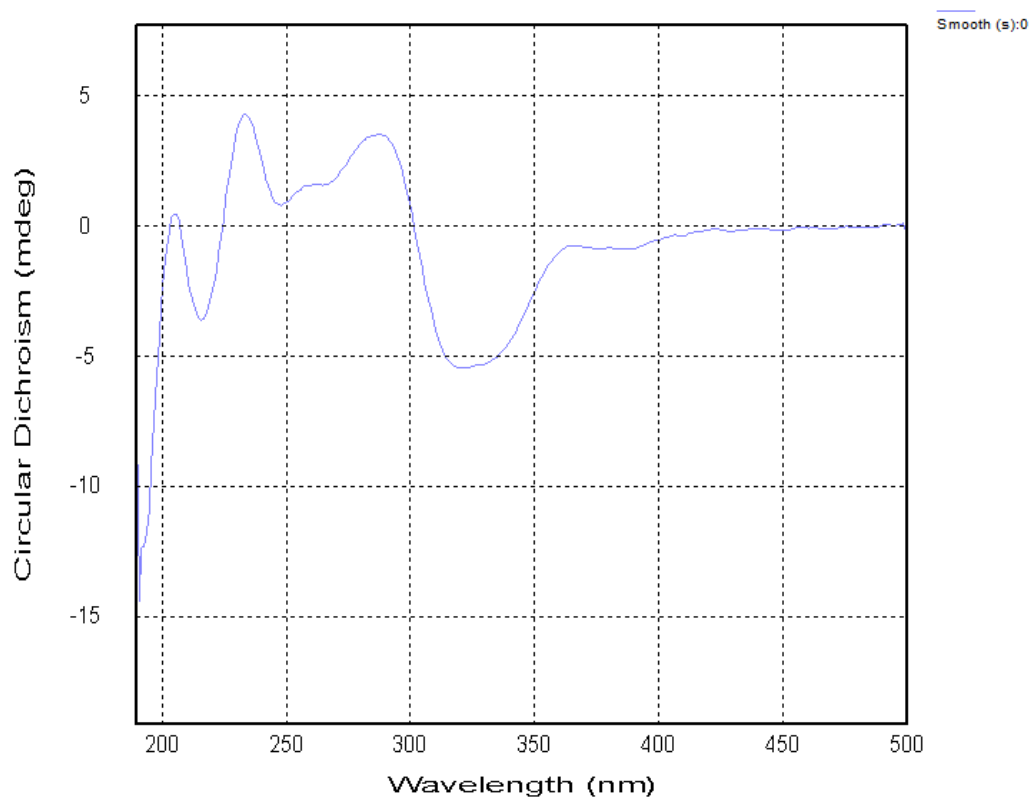


Figure S35. Experimental ECD spectrum of **4a**

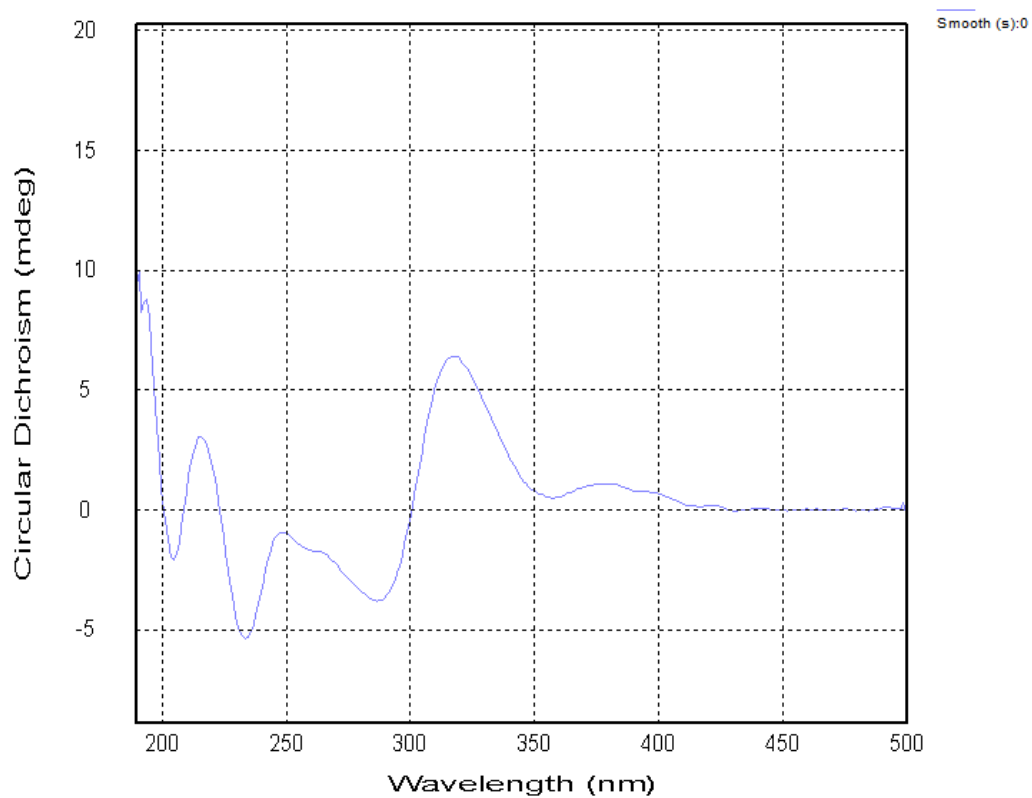


Figure S36. Experimental ECD spectrum of **4b**

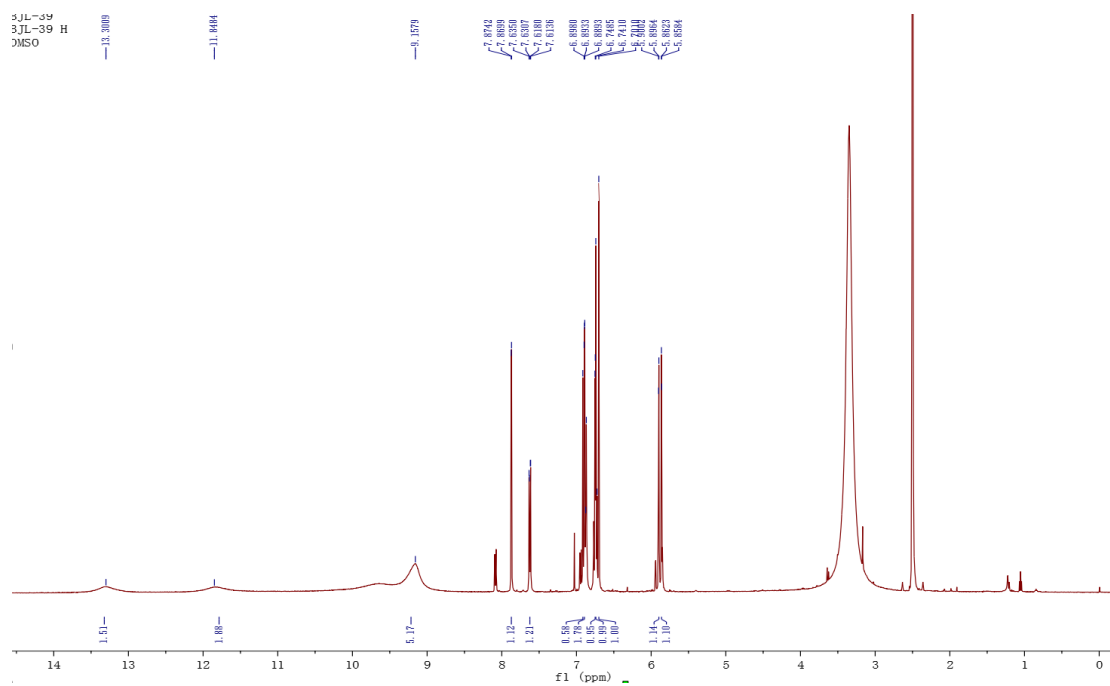


Figure S37. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **5**

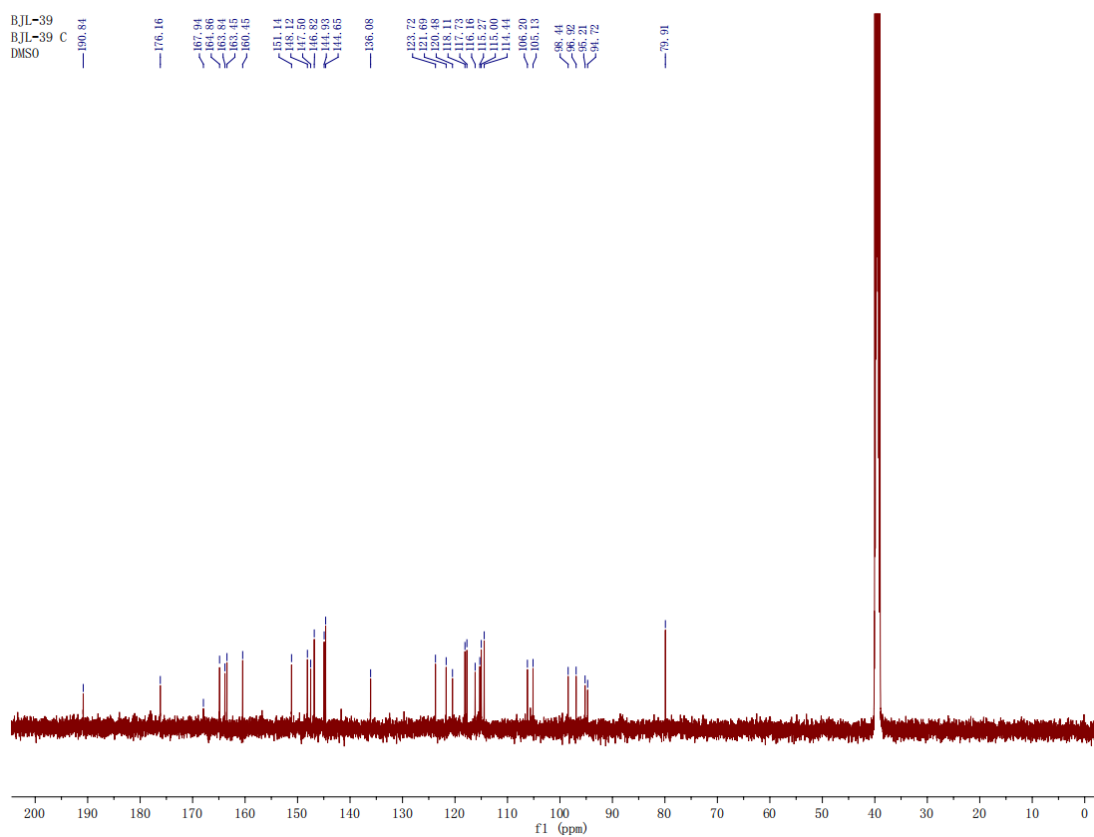


Figure S38. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (\pm) **5**

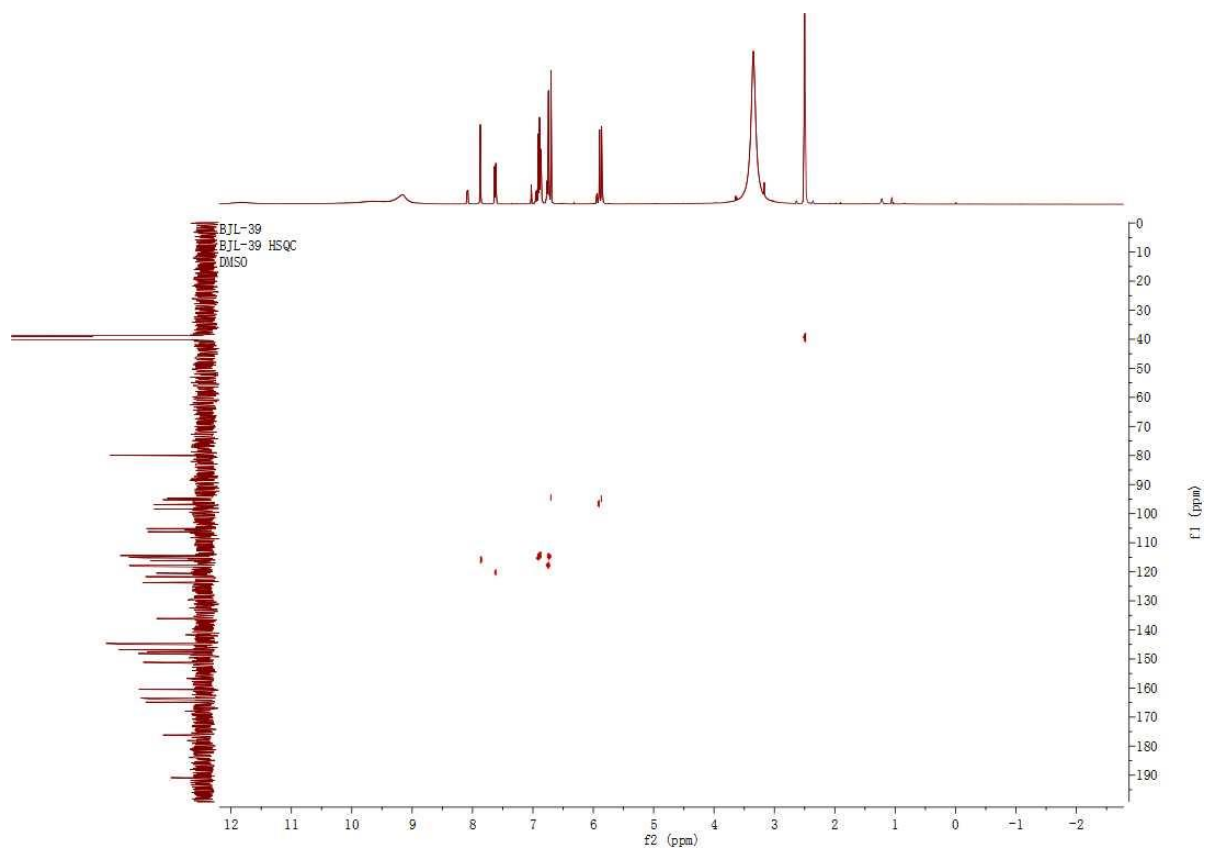


Figure S39. HSQC spectrum of (\pm) 5

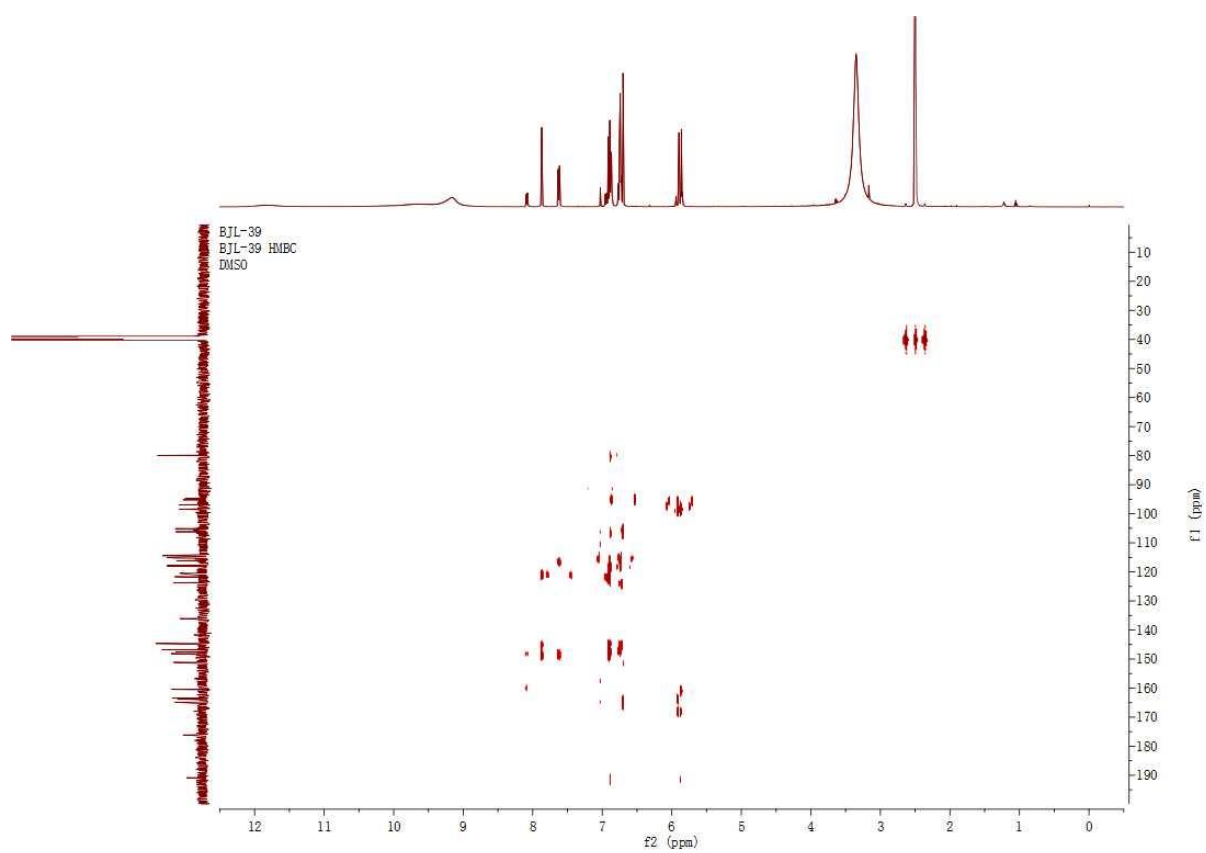


Figure S40. HMBC spectrum of (\pm) 5

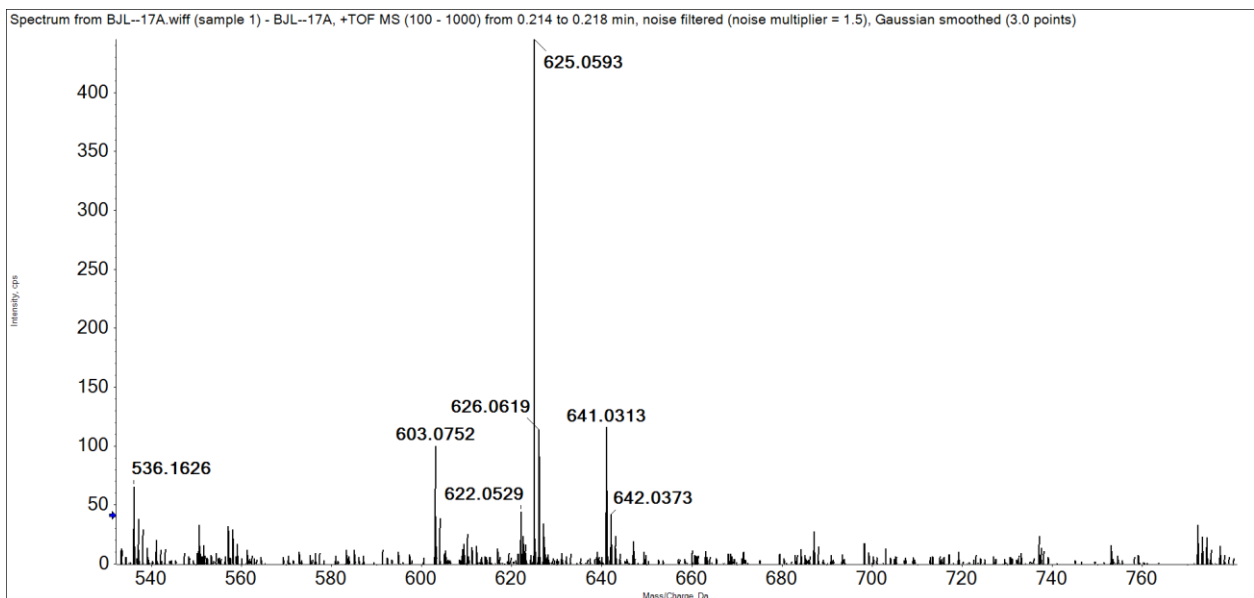


Figure S41. HRESIMS spectrum of (\pm) 5

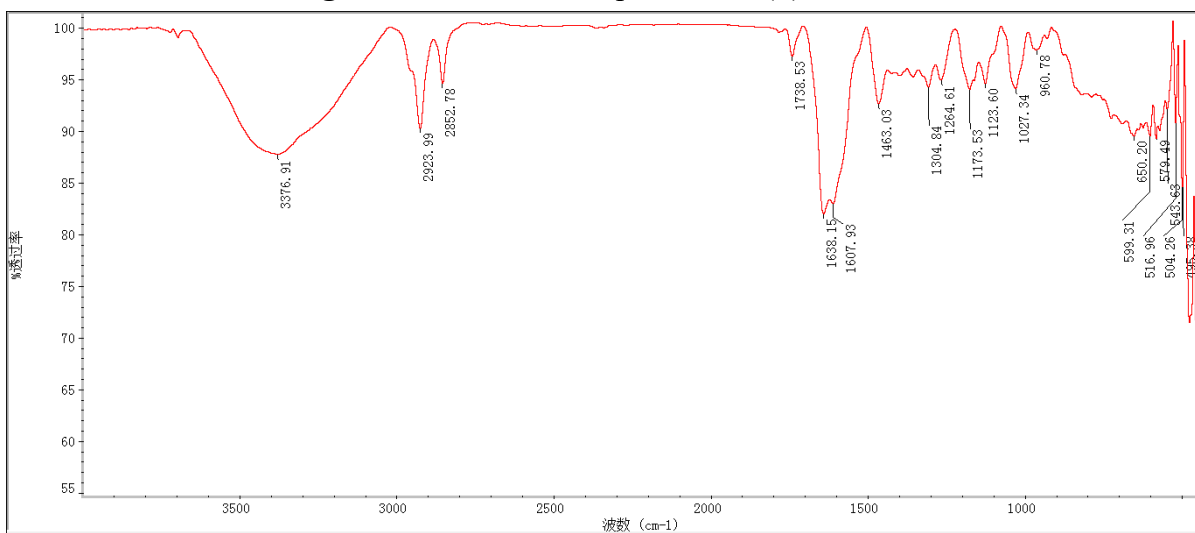


Figure S42. IR spectrum of (\pm) 5

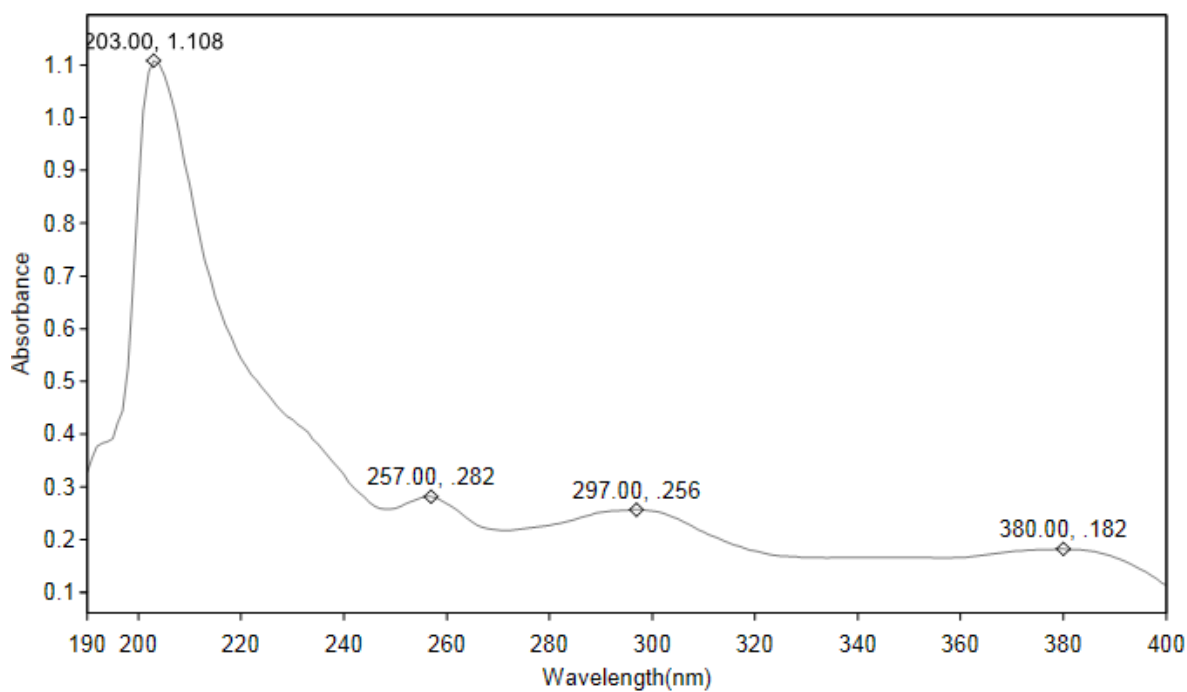


Figure S43. UV spectrum of (±) **5**

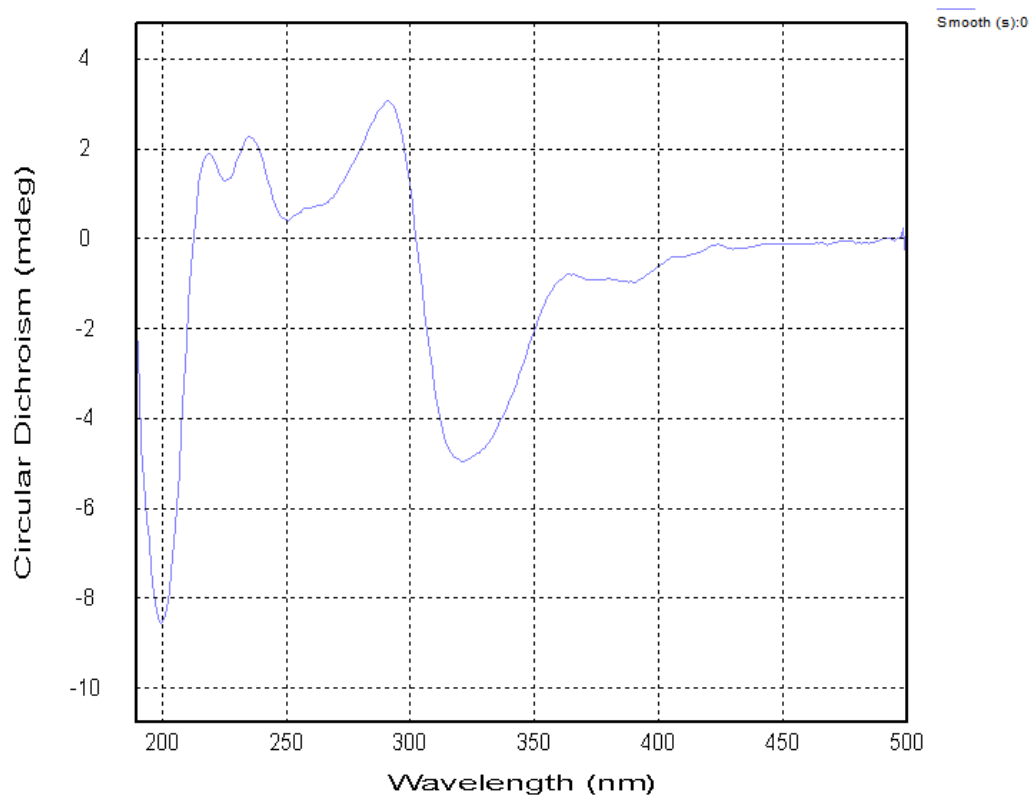


Figure S44. Experimental ECD spectrum of **5a**

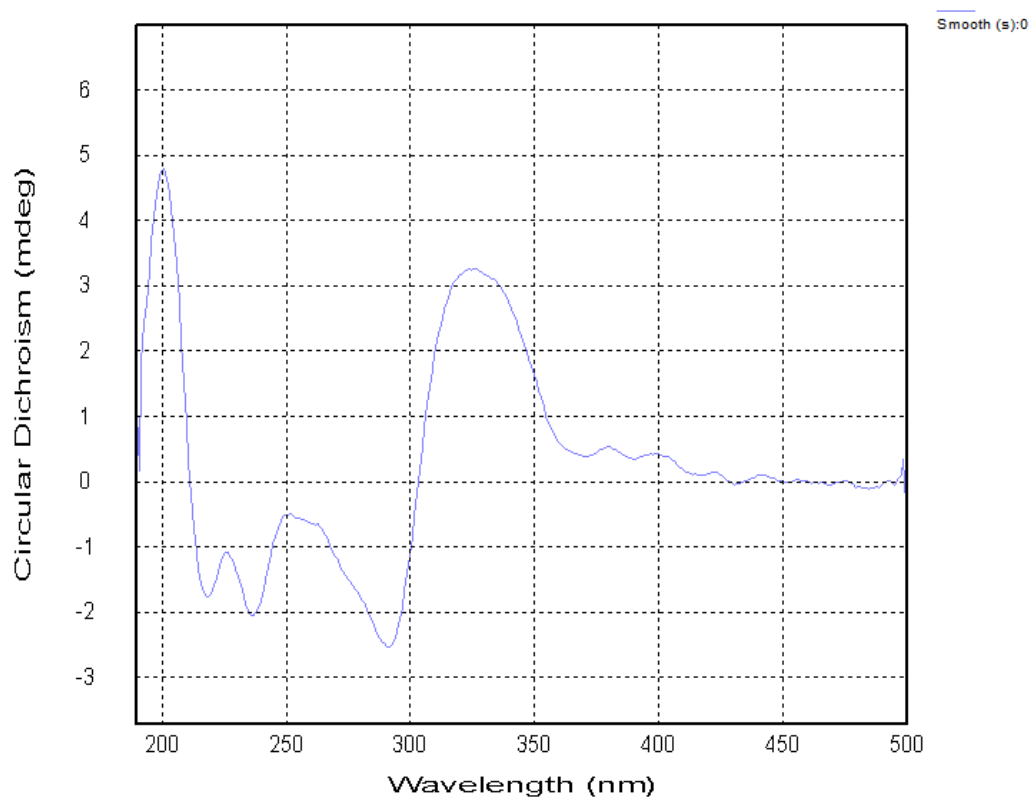


Figure S45. Experimental ECD spectrum of **5b**

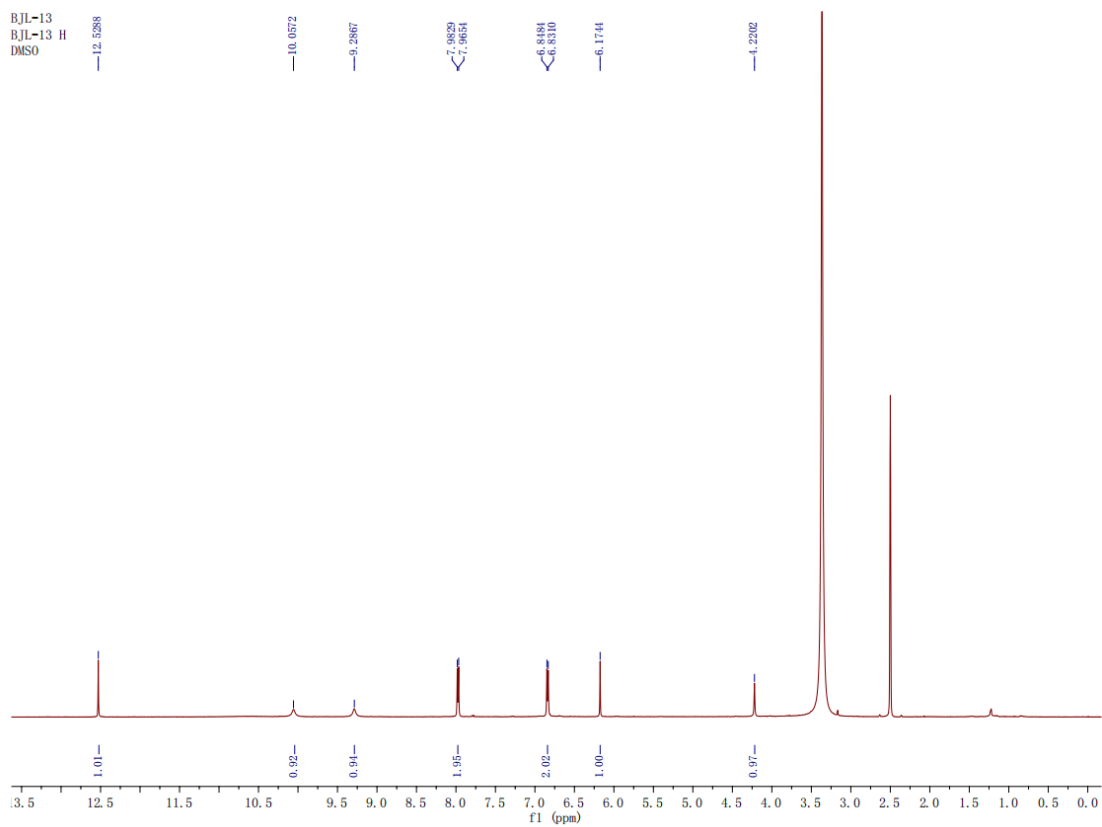


Figure S46. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of **6**

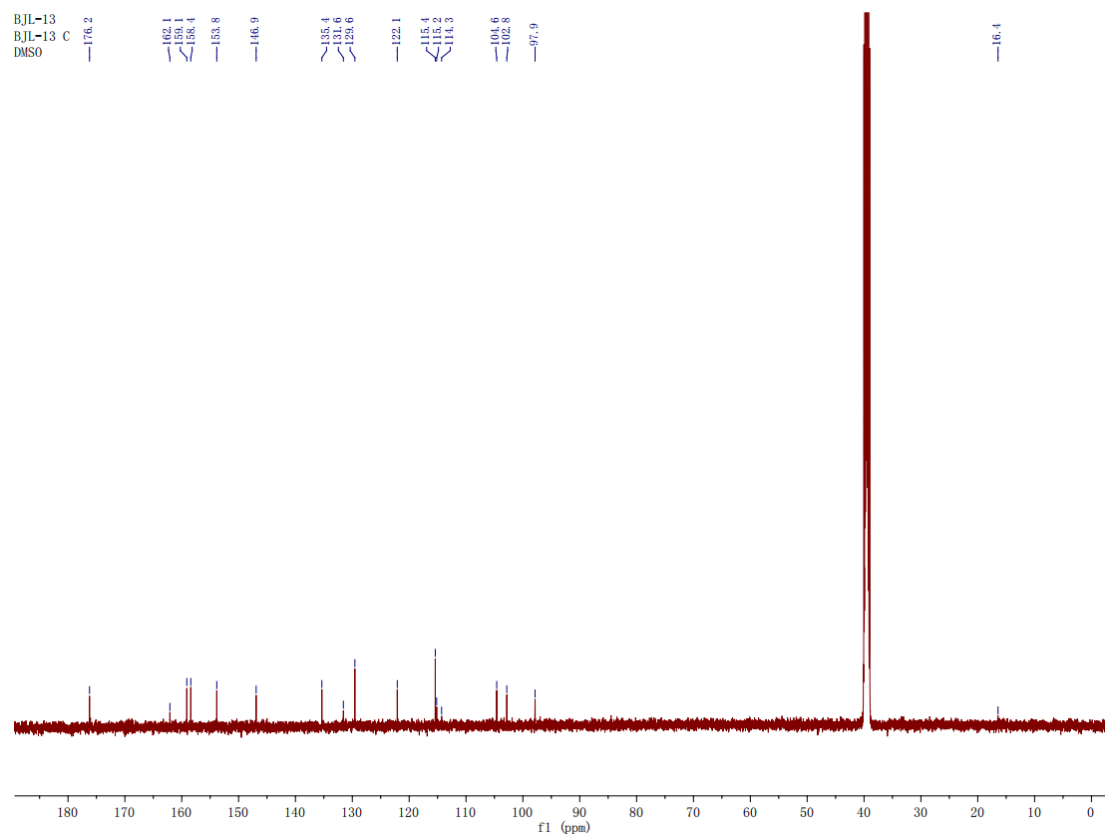


Figure S47. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of **6**

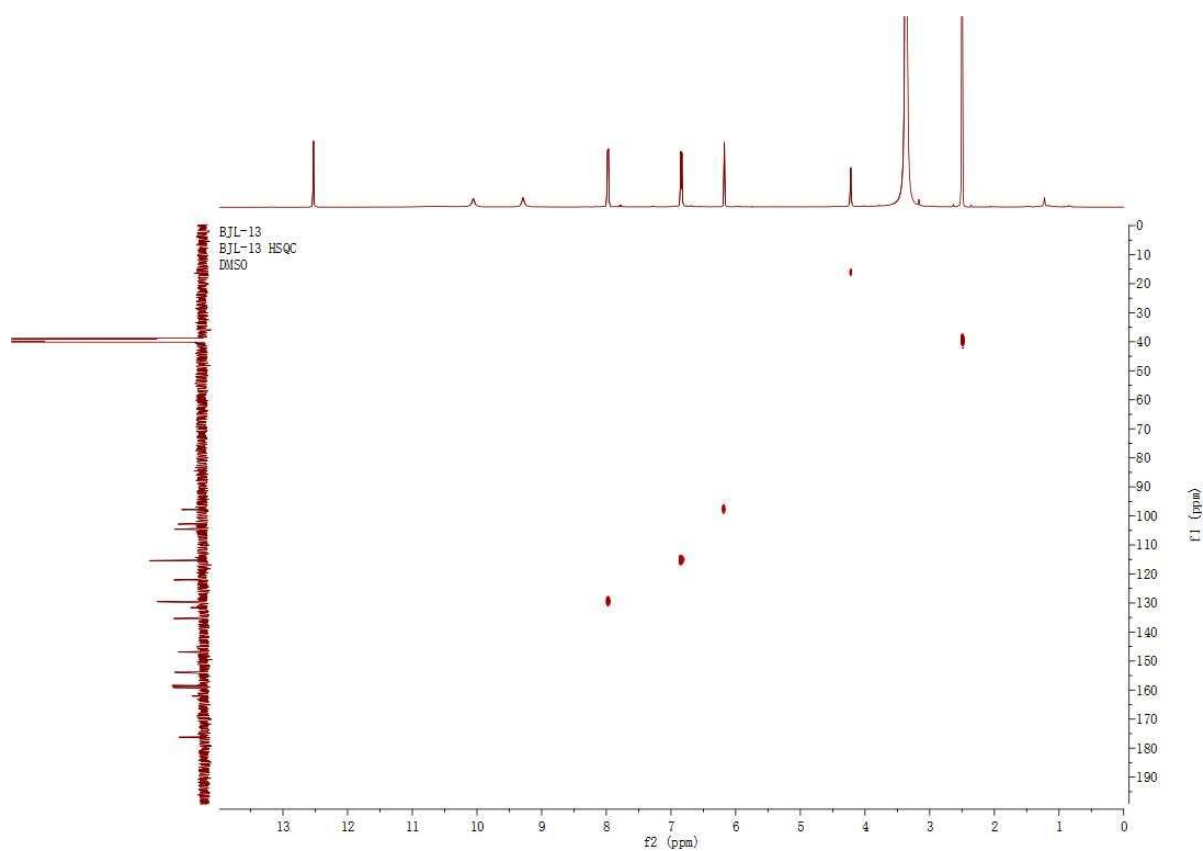


Figure S48. HSQC spectrum of **6**

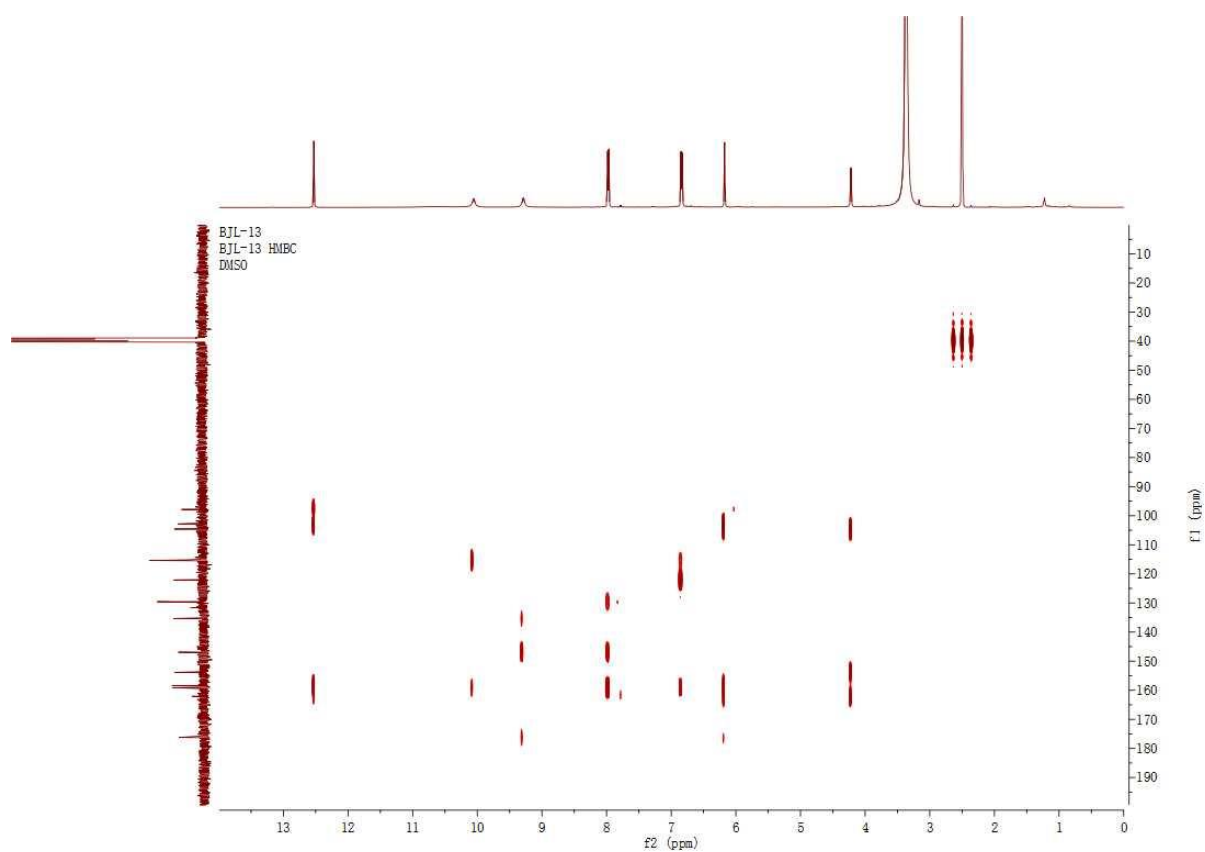


Figure S49. HMBC spectrum of **6**

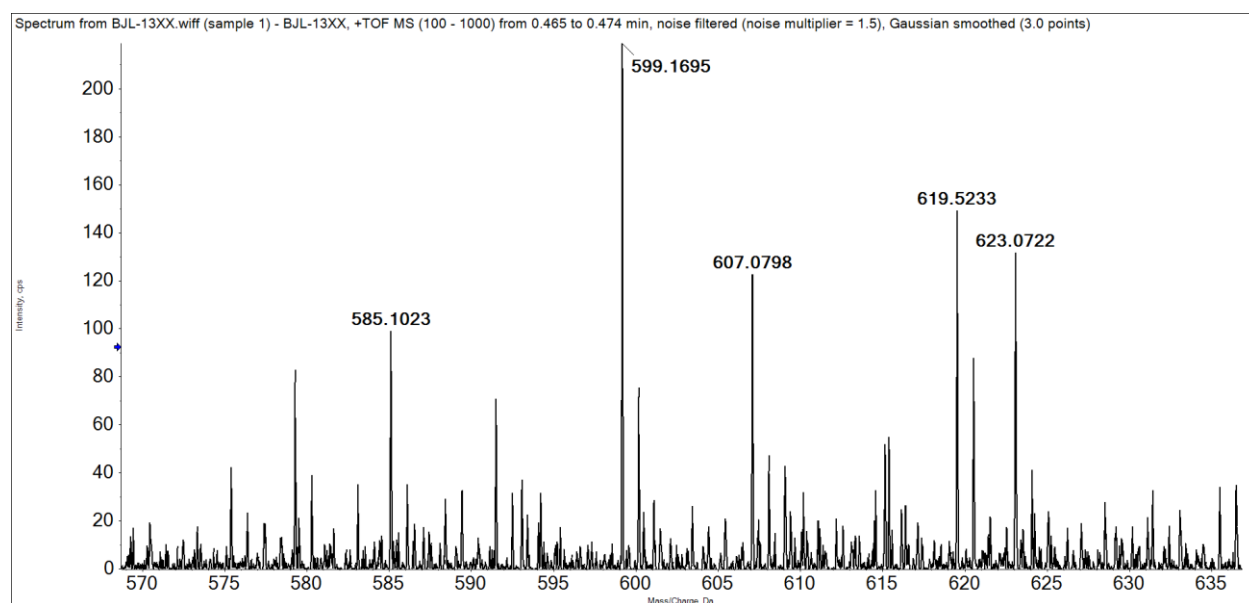


Figure S50. HRESIMS spectrum of **6**

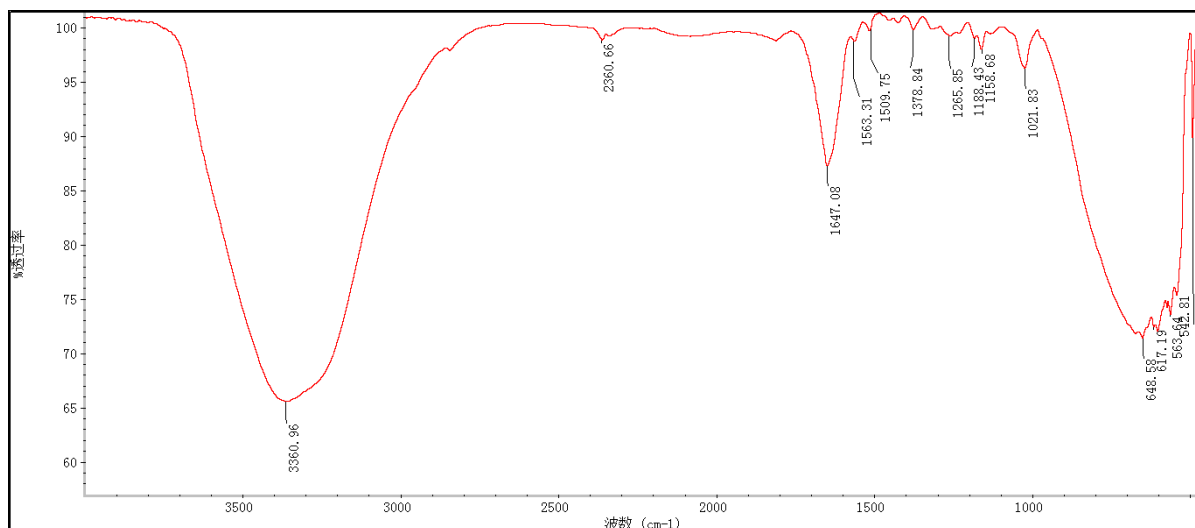


Figure S51. IR spectrum of 6

Scan Graph

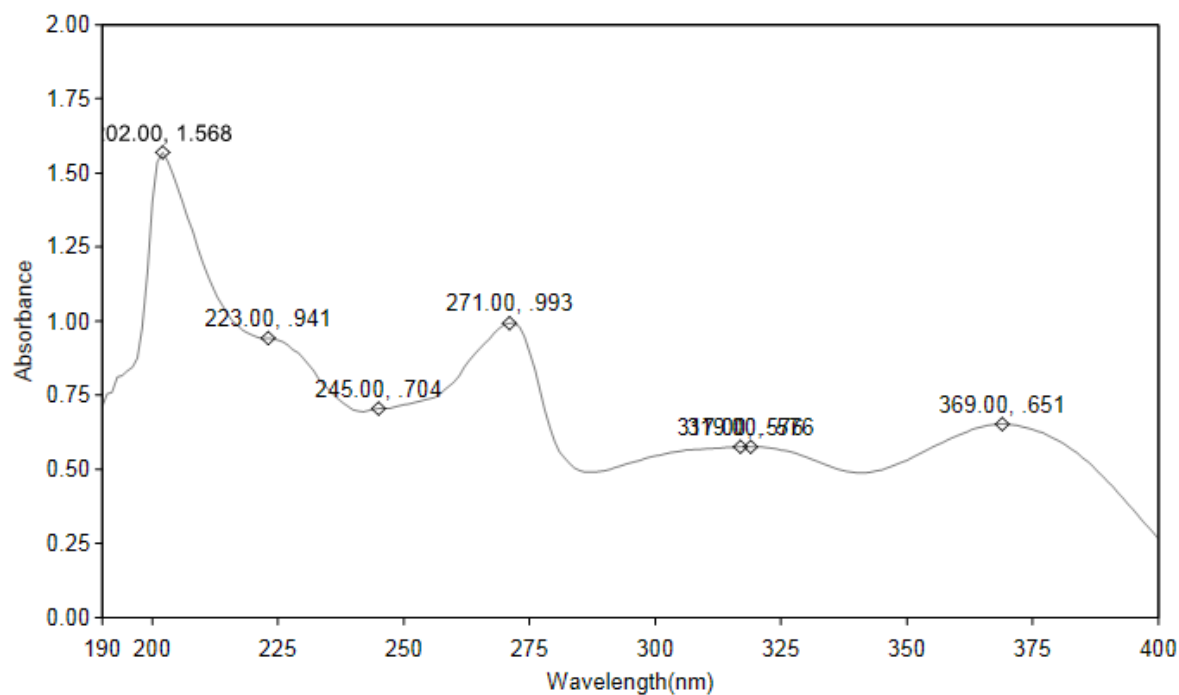


Figure S52. UV spectrum of 6

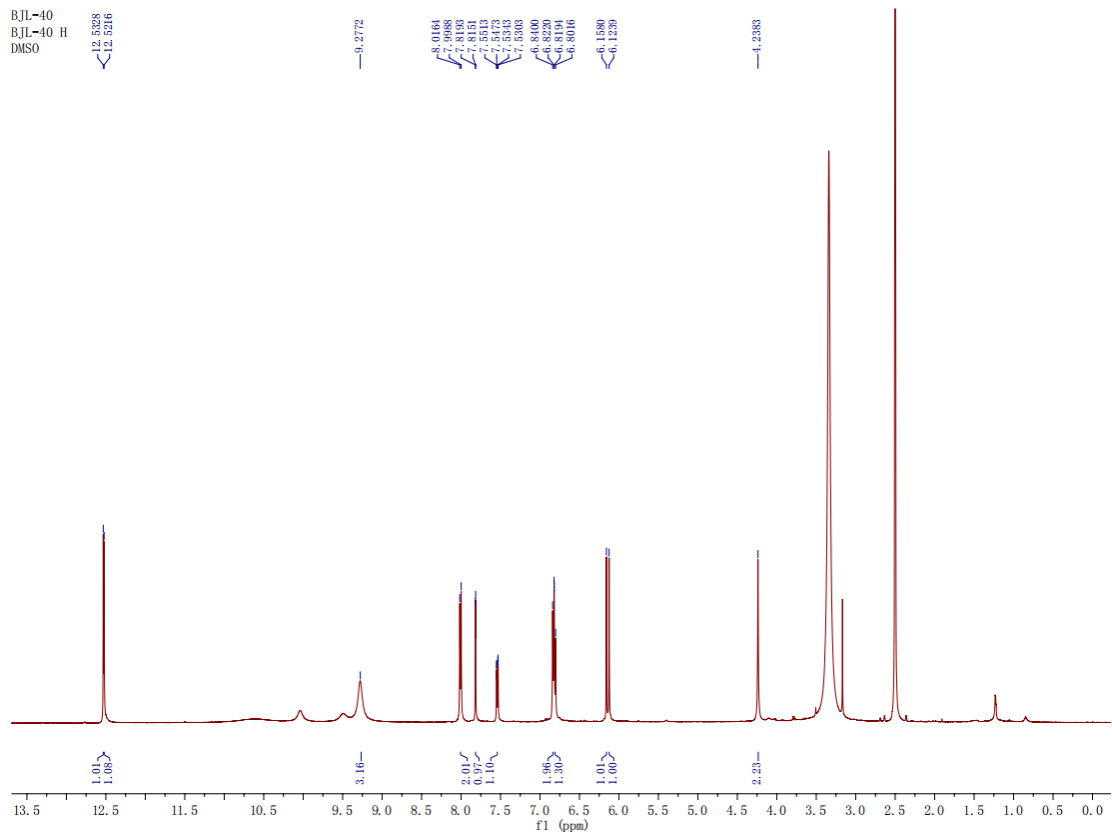


Figure S53. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of **7**

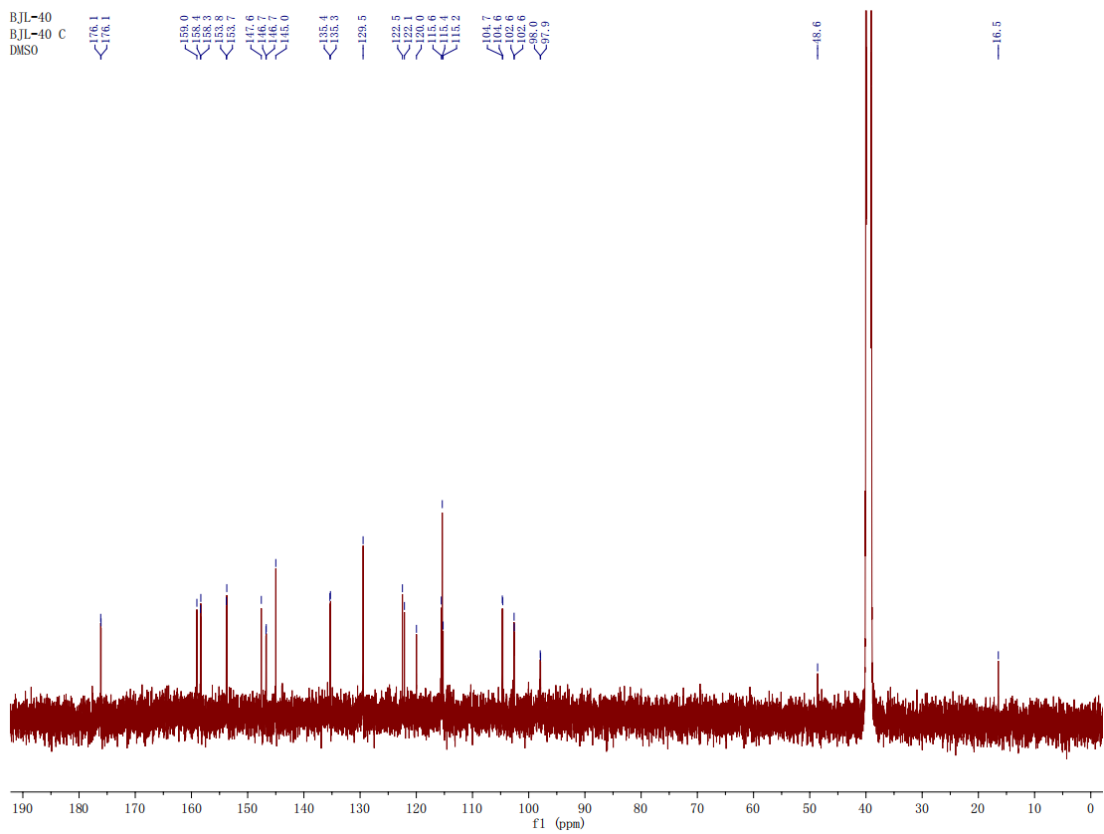


Figure S54. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of **7**

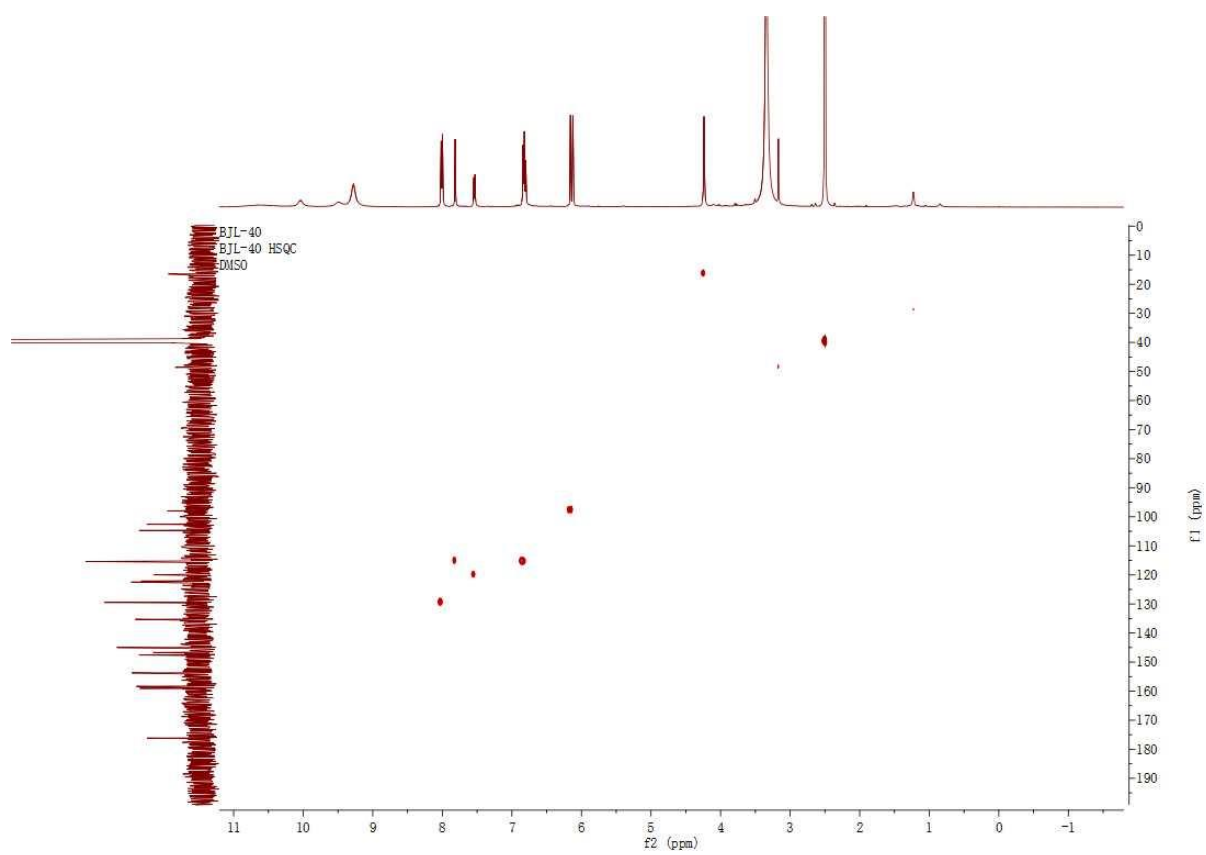


Figure S55. HSQC spectrum of **7**

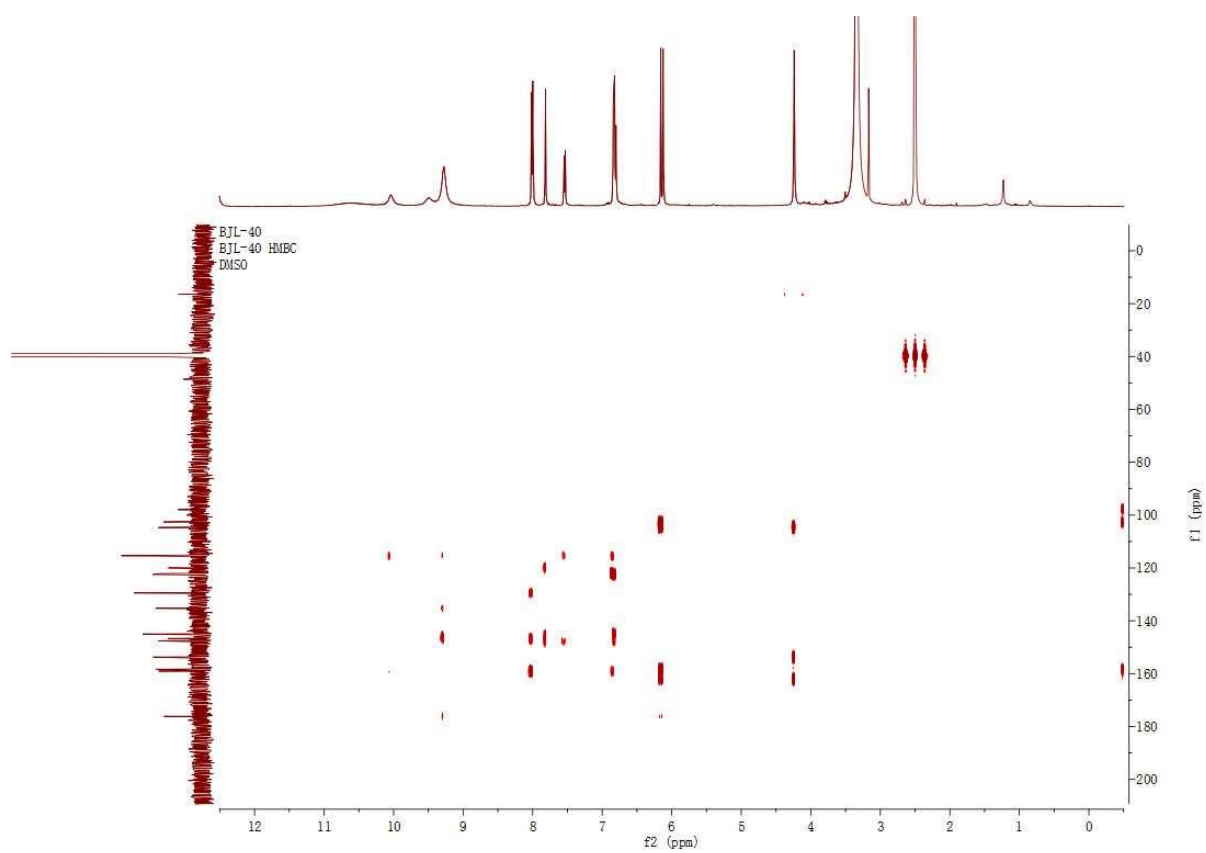


Figure S56. HMBC spectrum of **7**

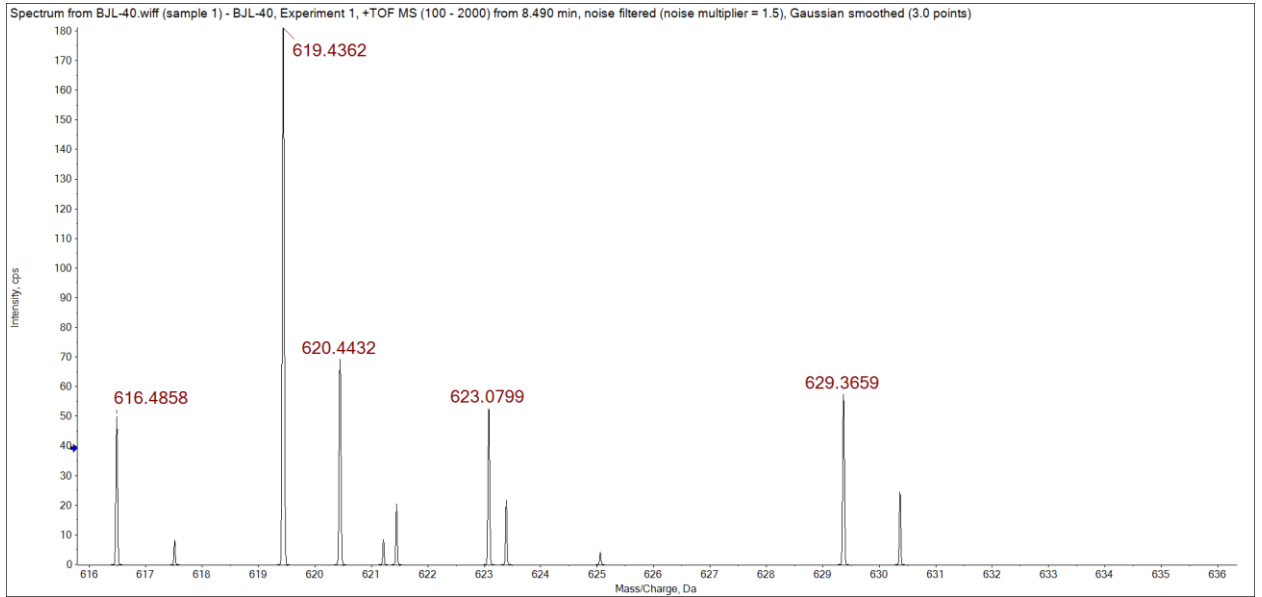


Figure S57. HRESIMS spectrum of 7

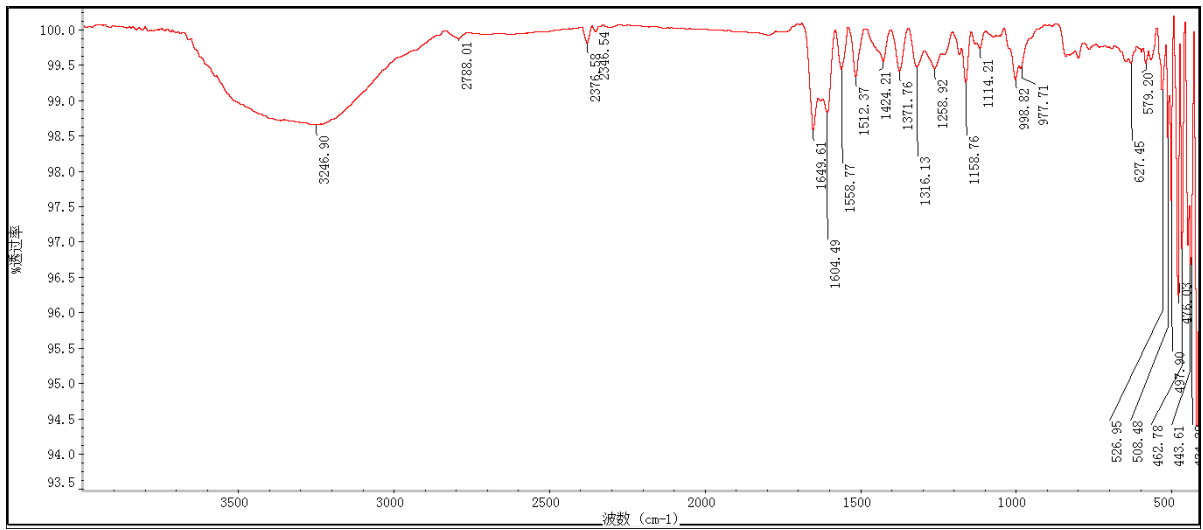


Figure S58. IR spectrum of 7

Scan Graph

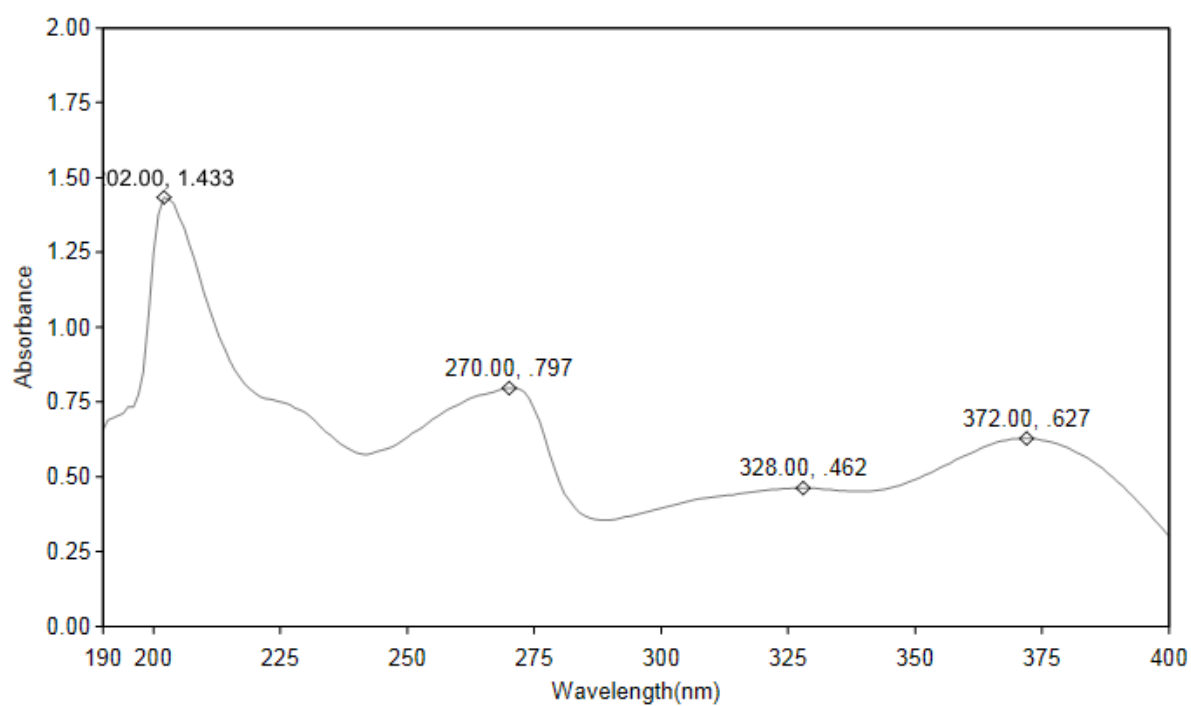


Figure S59. UV spectrum of 7