Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Novel A-*seco*-nortriterpenoids from *Ganoderma cochlear* inhibiting Tau pathology by activating AMPK-ULK1-mediated autophagy

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1. Structural elucidation of compounds 5–10

The molecular formula of ganolearate E (**5**) (**Figure S1**) was determined to be $C_{28}H_{40}O_6$ on the basis of HRESIMS ion peak *m/z*: 490.3162 $[M + NH_4]^+$ (calcd. 490.3163). Its 1D NMR spectroscopic data (**Table S1**) showed similarity with those of cochlearic acid A with the only difference in the presence of an additional methoxyl at C-3, which was confirmed by the HMBC correlations (**Figure S2**) of OMe (δ_H 3.63, s) with C-3 (δ_C 174.1), of H_2-1 and H_2-2 with C-3, and of H_3-19 with C-1, C-5, and C-10. The further X-ray crystallographic analysis (**Figure S3**) proved that the absolute configuration of **5** was 5*S*,7*S*,10*S*,13*R*,14*R*,17*S*,20*S*. Thus, the structure of compound **5** was determined.

Comparison of molecular weight and 1D NMR spectroscopic data (**Table S1**) between **6** and **5** showed that compound **6** had a similar structure with **5**, except for the absence of the terminal double bond at C-4 and C-28 and the presence of an additional ketone carbonyl (δ_C 214.0). The HMBC correlations of H_3-29 with the ketone carbonyl and C-5 (δ_C 52.5), and of H_3-19 with C-1, C-5, and C-9 (δ_C 137.3) confirmed that C-4 was the ketone carbonyl. Subsequently, the ROESY correlation of H-7/H_3-30 proved that 7-OH was β-oriented. Finally, the structure of **6** (ganolearate F) was established.

Ganolearate G (**7**) had a molecular formula of $C_{28}H_{42}O_7$ determined by the HRESIMS *m/z*: 513.2821 $[M + Na]^+$ (calcd. 513.2823). Meanwhile, compound **7** showed similar 1D NMR spectra with those of compound **6**. However, an additional methoxyl group (δ_H 3.67, s; δ_C 51.4) was observed in 1D NMR spectra of **7**, rather than an oxygenated quaternary carbon in **6**. Furthermore, the methoxyl group showed HMBC correlation (**Figure S2**) with C-24 (δ_C 174.4), simultaneously, H_3-21 exhibited a doublet methyl signals at δ_H 0.89 (d, J = 6.4 Hz) in the ^{1}H NMR spectrum of **7**. Thus, we speculated that the methoxyl was connected to C-24 and the oxygenated quaternary carbon at C-20 was transformed into a methine. Therefore, the structure of **7** was confirmed.

According to the 1D NMR spectra (**Table S2**) of **8**, the structure of **8** resembled that of **7** except for the absence of a methoxyl at C-24 and a ketone carbonyl instead of the hydroxyl at C-7. The HMBC correlations of H_3-19 (δ_H 1.31, s) with C-5 (δ_C 52.5) and C-9 (δ_C 145.6), of H-5 (δ_H 3.05, t, J = 4.5 Hz) with C-10 (δ_C 39.2) and C-7 (δ_C 196.7), of H_3-21 (δ_H 0.88, d, J = 6.4 Hz) with C-20 (δ_C 35.6), C-17 (δ_C 49.0), and C-22 (δ_C 30.6), and of H_2-22 (δ_H 2.20, m; 2.46, m) with C-24 (δ_C 178.8) confirmed above deduction. Thus, the structure of **8** was determined and name as ganoclearic acid

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The molecular formula of compound **9** was determined to be $C_{26}H_{36}O_6$ based on the HRESIMS *m/z*: 445.2586 $[M + H]^+$ (calcd. 445.2585) with **9** degrees of unsaturation. Its ^1H NMR spectrum (**Table S2**) showed that three singlet methyl proton signals at δ_H 0.91 (s), δ_H 1.25 (s), δ_H 1.77 (s), one doublet methyl proton signal at δ_H 0.88 (d, J = 6.4 Hz), one methoxyl proton signal at δ_H 3.63 (s), one oxymethine proton signal at δ_H 4.59 (d, J = 5.2 Hz), and two terminal double bond proton signals at δ_H 4.84 (s) and δ_H 4.94 (s). except for the methoxyl, ^{13}C-DEPT NMR spectra of **9** showed 25 carbon resonances, which were assigned as four methyls, eight methylenes (one terminal double bond), four methines (one oxymethine), and nine quaternary carbons (one ester carbonyl, one carboxyl, one ketone, three olefiniccarbons, and one oxygenated carbon). These data suggested that compound **9** was a highly degraded lanostane triterpenoid and had a similar 7/6/5-tricyclo skeleton with that of cochlate B, which was confirmed by the HMBC correlations (**Figure S2**) of H_3-29 with C-4 (δ_C 145.8), C-28 (δ_C 114.7), and C-5 (δ_C 54.8), of H-5 (δ_H 2.75, m) with C-1 (δ_C 31.8), C-10 (δ_C 83.5), C-7 (δ_C 75.0), and C-19 (δ_C 36.0), of H-7 (δ_H 4.50, d, J = 5.2 Hz) with C-5, C-9, and C-10, C-14 (δ_C 50.8), and of H_2-19 with C-1, C-8 (δ_C 167.9), and C-11 (δ_C 201.2). However, combination the absence of two methylenes and the HMBC correlations (**Figure S2**) of H_3-21 (δ_H 1.16, d, J = 6.5 Hz) with C-17 (δ_C 47.7), C-20 (δ_C 45.1), and C-22 (δ_C 181.7), indicating that C-23 and C-24 were degraded. The ROESY correlations (**Figure S2**) of H-5/H_3-30/H-7, which demonstrated that H-7 was α-oriented. Therefore, the structure of **9** was established and named as ganoclearic acid I.

Ganolearate J (**10**) had a molecular formula of $C_{28}H_{40}O_7$ based on the HRESIMS *m/z*: 511.2673 $[M + Na]^+$ (calcd. 511.2666). Its 1D NMR spectroscopic data (**Table S2**) were similar with those of cochlate A with the difference in the absence of double bond at C-4 and C-28 and the presence of one oxygenated methylene (δ_H 3.77, d, J = 12.0 Hz, 4.21, d, J = 12.0 Hz; δ_C 64.9) and one quaternary carbon containing oxygen (δ_C 86.0). The detailed analysis of HMBC spectrum (**Figure S2**) of **10** showed the correlations of H_3-29 (δ_H 1.39, s) and H-5 (δ_H 2.36, d, J = 7.6 Hz) with the oxygenated methylene and quaternary carbons, suggesting that C-4 and C-28 were linked to hydroxyl group, respectively. Considering the molecular weight of **10** and the chemical shift of C-3 (δ_C 175.8), an ester bond between C-4 and C-3 was deduced. Finally, the structure of **10** was determined.

Table S1.[1]H and [13]C-DEPT NMR spectroscopic data of **1**–**7** (600/150 MHz,δ in *ppm*, *J* in Hz).

position	**1**[a]		**2**[a]		**3**[a]		**4**[a]		**5**[a]		**6**[b]		**7**[b]	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1			1.58, m	31.7 CH_2	1.86, m; 2.19, m	34.8 CH_2	2.60, m; 1.84, m	31.7 CH_2	1.94, m; 2.16, m	33.1 CH_2	1.89, m; 2.13, m	35.1 CH_2	1.70, m; 2.31, m	33.6 CH_2
2			2.49, m	31.2 CH_2	2.26, m; 2.46, m	29.3 CH_2	2.10, m; 1.46, m	29.0 CH_2	1.97, m; 2.21, m	29.4 CH_2	2.20, m; 2.33, m	30.2 CH_2	2.54, m; 1.36, m	29.4 CH_2
3				174.8 C		174.0 C		176.7 C		174.1 C		175.9 C		173.8 C
4		203.9 C				205.4 C				147.0 C		214.0 C		217.1 C
5		131.2 C	1.44, m	27.2 CH	1.62, m	35.7 CH	3.15, d (8.8)	48.5 CH	2.13, m	44.7 CH	2.83, m	52.5 CH	2.92, m	50.9 CH
6	7.54, d (7.9)	131.2 CH	1.09, dd, (7.8, 4.3); 0.29, dd, (7.2, 4.3)	17.3 CH_2	2.04, m	39.2 CH	1.78, m 2.52, m	38.5 CH_2	2.06, m; 2.14, m	32.4 CH_2	2.49, m; 2.67, m	32.1 CH_2	2.10, m	28.8 CH_2
7	7.47, d (7.9)	122.6 CH	1.85, m	22.5 CH	2.47, m	34.0 CH	5.36, t (7.3)	77.2 CH	4.29, t (6.0)	66.8 CH	4.23, t (6.0)	64.3 CH	4.03, dd (10.4, 4.0)	62.5 CH
8		152.8 C		174.5 C		171.8 C		174.1 C		160.7 C		160.5 C		158.6 C
9		140.7 C		137.7 C		135.6 C		133.7 C		137.2 C		137.3 C		135.1 C
10		138.1 C		48.8 CH		49.7 C		89.3 C		39.1 C		38.6 C		37.4 C
11		200.4 C		197.5 C		196.3 C		198.9 C		199.1 C		202.0 C		200.1 C
12	2.58, d (18.8); 2.91, d (18.8)	52.3 CH_2	2.43, d, (7.4)	50.1 CH_2	2.38, d (17.6); 2.54, d (17.6)	49.2 CH_2	2.58, d (16.6) 2.69, d (16.6)	49.6 CH_2	2.62, d (17.4); 2.74, d (17.4)	51.1 CH_2	2.51, d (18.0); 2.77, d (18.0)	52.3 CH_2	2.43, d (18.8) 2.59, d (18.8)	51.4 CH_2
13		45.2 C		48.1 C		48.0 C		49.7 C		45.6 C		46.5 C		44.1 C
14		52.3 C		48.2 C		49.7 C		49.8 C		51.9 C		52.8 C		51.2 C
15	5.60, dd (9.5, 5.1)	74.1 CH	2.27, dd, (12.8, 7.9); 1.88, dd, (12.8, 4.8)	40.9 CH_2	1.52, m; 1.72, m	29.5 CH_2	1.25, m; 2.15, m	29.3 CH_2	1.47, m; 2.56, m	30.2 CH_2	1.43, m; 2.20, m	30.7 CH_2	1.25, m; 2.15, m	29.5 CH_2
16	2.20, m; 1.94, m	39.0 CH_2	4.71, dd, (12.9, 5.9)	72.0 CH	2.12, m; 1.51, m	27.4 CH_2	1.45, m; 2.05, m	27.8 CH_2	1.71, m; 1.89, m	21.7 CH_2	1.95, m; 1.65, m	22.8 CH_2	1.45, m; 2.03, m	27.3 CH_2
17	1.90 m	49.0 CH	1.73, m	54.7 CH	1.76, m	49.2 CH	1.72, m	48.9 CH	2.19 m	52.9 CH	2.34, m	54.3 CH	1.63, m	50.5 CH
18	0.74, s	18.5 CH_3	1.05, s	17.7 CH_3	0.77, s	17.4 CH_3	0.87, s	17.2 CH_3	1.11, s	19.2 CH_3	1.15, s	19.7 CH_3	1.10, s	17.7 CH_3
19	2.57, s	18.3	1.21, s	24.5	1.30, s	22.5	1.50, s	27.7	1.25 s	22.4	1.23, s	22.4	1.17, s	21.2

		CH_3		CH_3		CH_3		CH_3		CH_3		CH_3	CH_3
20	1.40, m	35.4 CH	1.75, m	29.5 CH	1.46, m	35.7 CH	1.45, m	35.5 CH		87.7 C		90.1 C	1.43, m	35.6 CH
21	0.90, d (6.4)	17.7 CH_3	0.94, d (5.6)	18.0 CH_3	0.89, d (6.3)	17.8 CH_3	0.91, d (6.4)	18.1 CH_3	1.45, s	26.0 CH_3	1.46, s	26.3 CH_3	0.89, d (6.4)	17.7 CH_3
22	1.31, m; 1.82, m	30.7 CH_2	2.46, m	30.3 CH_2	1.33, m; 1.83, m	30.7 CH_2	1.84, m; 1.34, m	31.0 CH_2	2.03, m; 2.17, m	32.4 CH_2	1.98, m; 2.23, m	34.5 CH_2	1.84, m; 1.34, m	30.8 CH_2
23	2.27, m;		1.97, m	30.7 CH_2	2.27, m; 2.40, m	31.0 CH_2	2.24, m; 2.48, m	31.1 CH_2	2.49, m	27.9 CH_2	2.45, m; 2.69, m	28.6 CH_2	2.24, m; 2.48, m	31.1 CH_2
24	2.39, m	31.0 CH_2		176.2 C		178.7 C		174.4 C		177.1 C		180.1 C		174.4 C
28		174.2 C							4.82, s; 5.05, s	114.9 CH				
29					2.25, s	30.5 CH_3			1.83, s	24.0 CH_3	2.21, s	31.3 CH_3	2.28, s	33.5 CH_3
30	2.55, s	30.9 CH_3	1.11, s	26.3 CH_3	1.16, s	24.7 CH_3	1.13, s	24.4 CH_3	1.17, s	25.7 CH_3	1.13, s	26.6 CH_3	0.99, s	26.1 CH_3
3-OCH_3	1.21, s	19.3 CH_3	3.66, s	51.8 CH_3	3.63, s	51.6 CH_3	3.67, s	51.5 CH_3	3.63, s	51.5 CH_3	3.63, s	52.1 CH_3	3.67, s	51.7 CH_3
24-OCH_3	3.68, s	51.6 CH_3	3.71, s	52.3 CH_3									3.67, s	51.4 CH_3

[a]: $CDCl_3$; [b]: CD_3OD

Table S2.[1]H and [13]C-DEPT NMR spectroscopic data of **8–10** (600/150 MHz, δ in ppm, J in Hz).

position	**8**[b]		**9**[b]		**10**[a]	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	2.07, m; 2.38, m	33.4 CH_2	1.83, m	31.8 CH_2	1.86, m	32.6 CH_2
2	2.29, m; 2.38, m	29.4 CH_2	2.40, m; 2.45, m	29.5 CH_2	2.47, m; 2.84, m	27.7 CH_2
3		173.7 C		175.9 C		175.8 C
4		20.9 C		145.8 C		86.0 C
5	3.05, t (4.5)	52.5 CH	2.75, m	54.8 CH	2.36, d (7.6)	54.6 CH
6	2.52, m; 2.66, m	36.8 CH_2	2.28, m	42.1 CH_2	1.67, m 2.72, m	36.2 CH_2
7		196.7 C	4.59, d (5.2)	75.0 CH	4.64, t (8.9)	74.4 CH
8		152.3 C		167.9 C		168.8 C
9		145.6 C		126.5 C		127.3 C
10		39.2 C		83.5 C		86.3 C
11		202.3 C		201.2 C		199.1 C
12	2.50, d (18.0); 2.63, d (18.0)	51.1 CH_2	2.44, d (17.6); 2.78, d (17.6)	49.9 CH_2	2.56, d (18.8)	48.4 CH_2
13		45.2 C		48.8 C		45.8 C
14		48.4 C		50.8 C		51.0 C
15	2.18, m; 2.07, m	31.7 CH_2	1.27, m; 1.90, m	30.8 CH_2	1.51, m; 1.91, m	31.0 CH_2
16	1.43, m; 2.05, m	27.6 CH_2	1.53, m; 2.07, m	27.7 CH_2	1.51, m; 2.07, m	26.6 CH_2
17	1.62 m	49.0 CH	2.32, m	47.7 CH	1.73, m	49.6 CH
18	0.95, s	17.7 CH_3	0.91, s	17.8 CH_3	0.87, s	17.2 CH_3
19	1.31 s	22.0 CH_3	2.06, m; 2.32, m	36.0 CH_2	3.09, d (14.8); 3.24, d (14.8)	29.6 CH_3
20	1.45, m	35.6 CH	2.42, m	45.1 CH	1.45, m	35.7 CH
21	0.88, d (6.4)	17.6 CH_3	1.16, d (6.5)	17.8 CH_3	0.89, d (6.5)	17.5 CH_3
22	2.20, m; 2.46, m	30.6 CH_2		181.7 C	2.24, m; 2.48, m	30.7 CH_2
23	1.89, m;2.08, m	31.1 CH_2			1.84, m; 1.34, m	31.1 CH_2
24		178.8 C				174.4 C
28			4.84, s; 4.94, s	114.7 CH_2	3.77, d (12.0); 4.21, d (12.0)	64.9 CH_2
29	2.23, s	32.6 CH_3	1.77, s	22.4 CH_3	1.39, s	24.9 CH_3
30	1.08, s	24.4 CH_3	1.25, s	26.5 CH_3	1.11, s	25.7 CH_3
OCH_3	3.67, s	51.8 CH_3	3.63, s	52.1 CH_3	3.67, s	51.5 CH_3

[a]: $CDCl_3$; [b]: CD_3OD

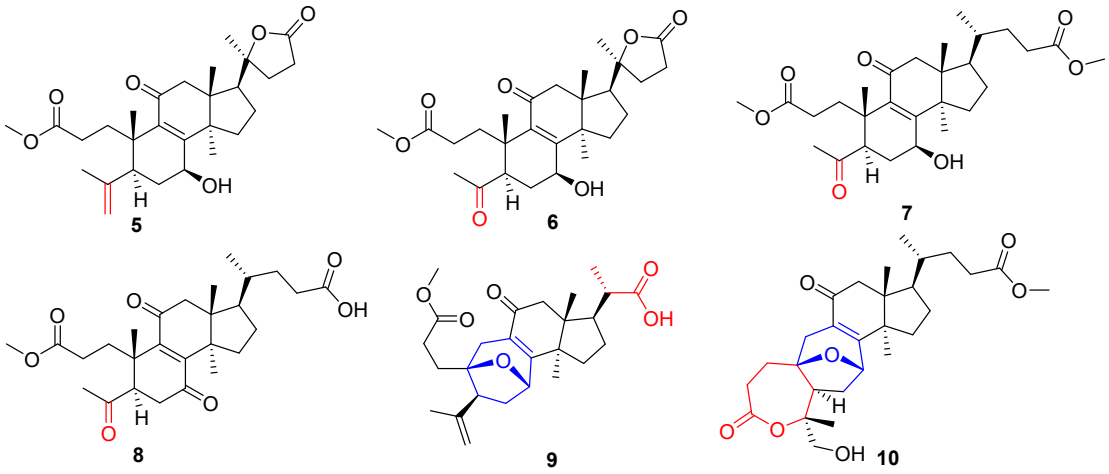

Figure S1. Structures of compounds **5**–**10**.

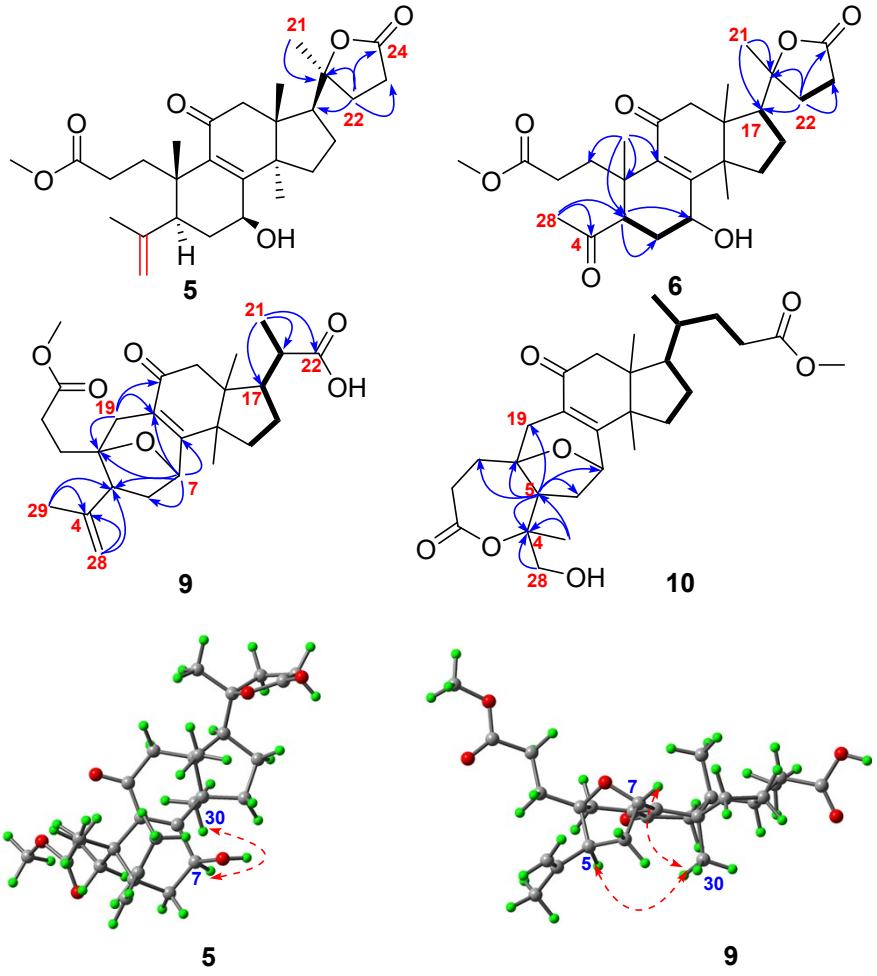

Figure S2. Selected HMBC (H→C), ^{1}H-^{1}H COSY (H-H) correlations of compounds **5, 6, 9, 10**, and ROESY (⇢⇠) correlations of compounds **5** and **9**.

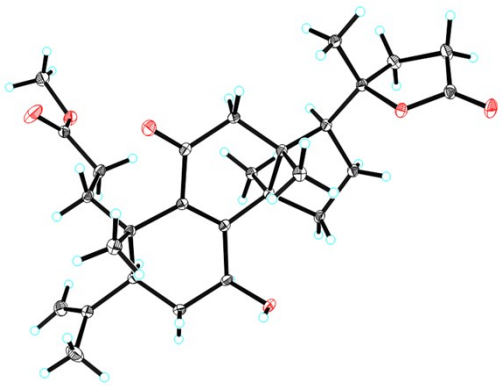

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Figure S3. X-ray crystallographic structure of compound **5**.

2. Autophagy activation of compounds 1–10

In order to test whether compounds**1**–**10** would affect autophagy, we used the SH-SY5Y mCherry-GFP-LC3 cell line, which contains thetandem monomeric mCherry-GFP-tagged LC3 (mCherry-GFP-LC3) reporter and was reported in our previous study.[1] The mCherry-GFP-LC3 in autolysosomes displayed more stable red mCherry fluorescence in the acidic lysosome while the GFP signal was sensitive to the acidic condition.[2] DMSO (dimethyl sulfoxide) and rapamycin were respectively as blank and positive controls.[3] The flow cytometry analysis results showed that compounds **1**–**10** significantly increased the autophagic flux (**FigureS4A–B**). Moreover, all of them displayed no toxicities in SH-SY5Y mCherry-GFP-LC3 cells by using the CCK-8 assay (**FigureS5A**). Compounds **1**–**4** with diverse rearranged skeleton were further investigated for their effect on autophagy and anti-ADs. Treatment with compounds **1**–**4** can increase autophagic flux in the SH-SY5Y mCherry-GFP-LC3 cells, similar as rapamycin (**Figure S5B–C**). Collectively, these results demonstrated that compounds **1**–**4** can activate autophagy.

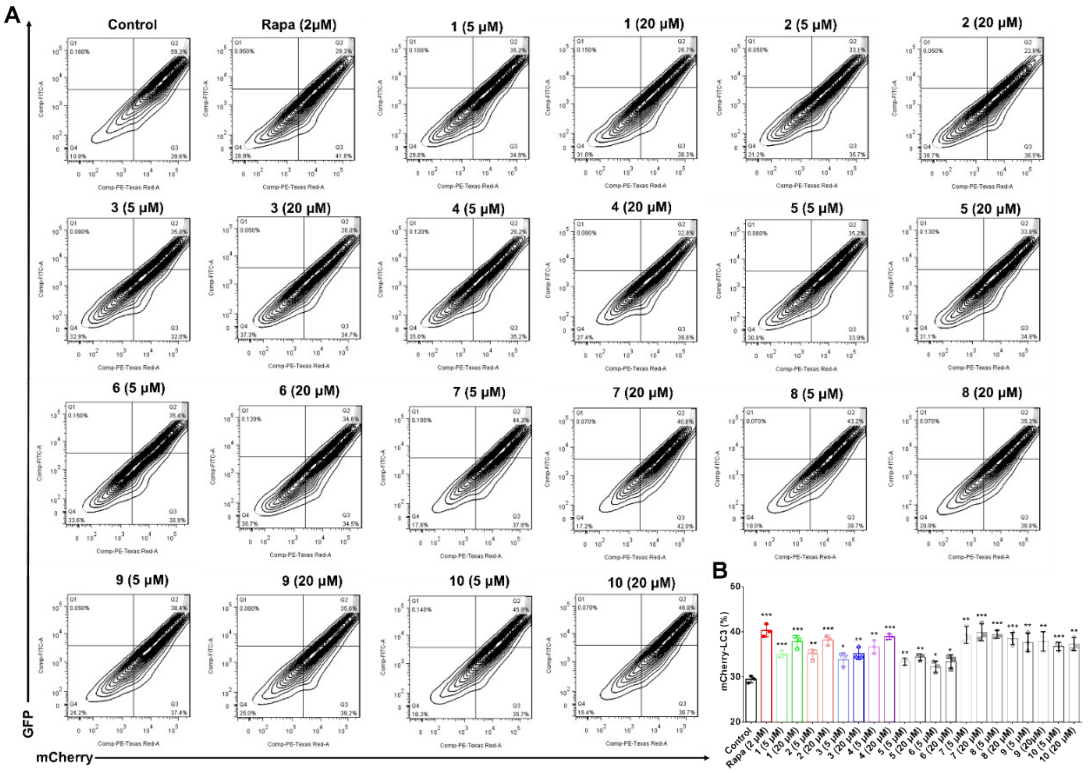


Figure S4. Compounds **1**–**10** induced autophagy in SH-SY5Y mCherry-GFP-LC3 cells by flow cytometry analysis. (A) Flow cytometry of SH-SY5Y mCherry-GFP-LC3 cells with or without drug treatment. The percentage of 10,000 cells expressing GFP or/and mCherry were counted. The Q1 area represents the proportion of cells with green fluorescence; the Q2 area represents the proportion of cells with yellow fluorescence; the Q3 area represents the proportion of cells with only red fluorescence; the Q4 area represents the proportion of cells showing no red and green fluorescence. (B) Quantification of the Q3 area in (A) based on 3 independent experiments. Record the proportion of cells that only emit red fluorescence in Q3 area under each treatment.

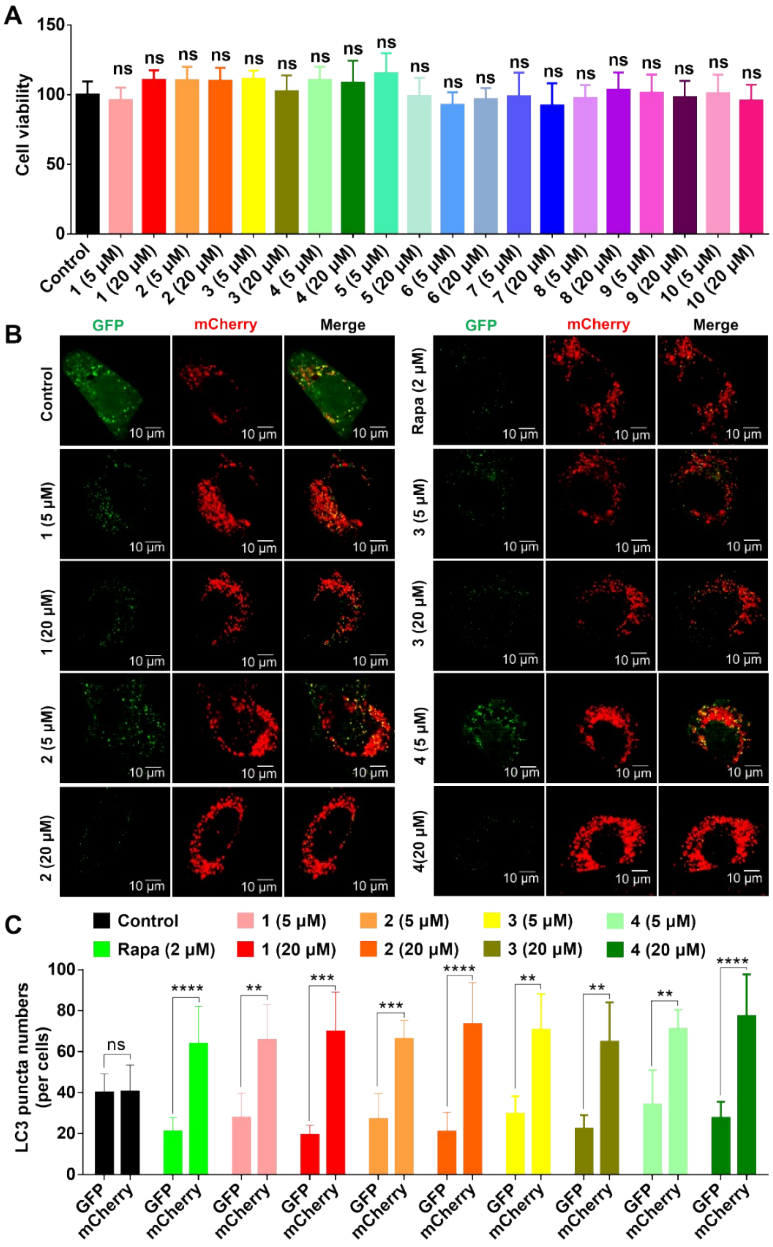


Figure S5. Increase of autophagic flux by compound **1**–**10** in SH-SY5Y mCherry-GFP-LC3 cells. (A) The CCK-8 assay showing the effects of compound **1**–**10** on cell viability. (B-C) Increased autophagic flux in response to **1**–**4** or Rapamycin (Rapa) treatment in SH-SY5Y mCherry-GFP-LC3 cells. (B) **1**–**4** treatment increased the maturation of autolysosomes as shown by the increased red puncta of mRFP-GFP-LC3 in cells, and this effect was similar to that of Rapamycin. (C) Quantification of LC3 puncta in (B) based on 3 independent experiments. ns, not significant; *, $P< 0.05$; **, $P< 0.01$; ***, $P< 0.001$; ****, $P< 0.0001$; one-way ANOVA with the Tukey's post-hoc test. Bars represent mean ± SD.

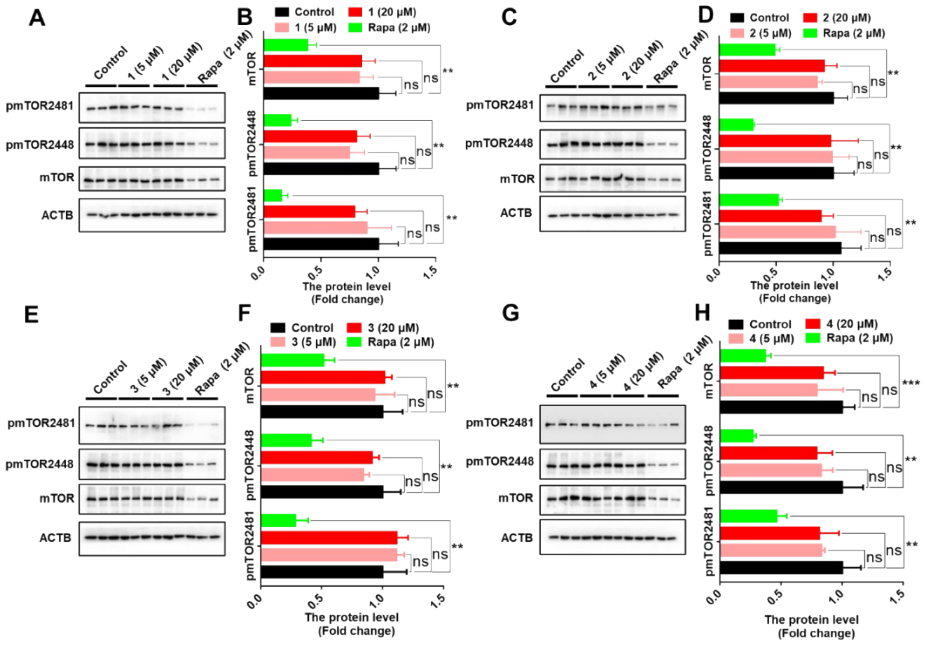


Figure S6. No inhibition effect of compounds **1**–**4** on mTOR. (A-H) Western blotting assays showing the protein levels of mTOR, pmTOR2448 and pmTOR2481 in the SH-SY5Y MAPT cells treated with or without compounds. Rapamycin (Rapa) as a positive control. (A-H) A representative Western blotting result (A, C, E, G) and quantification of respective protein levels (B, D, F, H) based on 3 independent experiments were presented. Relative protein abundance was normalized to ACTB. ns, not significant; **, $P< 0.01$; ***, $P< 0.001$; one-way ANOVA with the Tukey's post-hoc test. Bars represent mean ± SD.

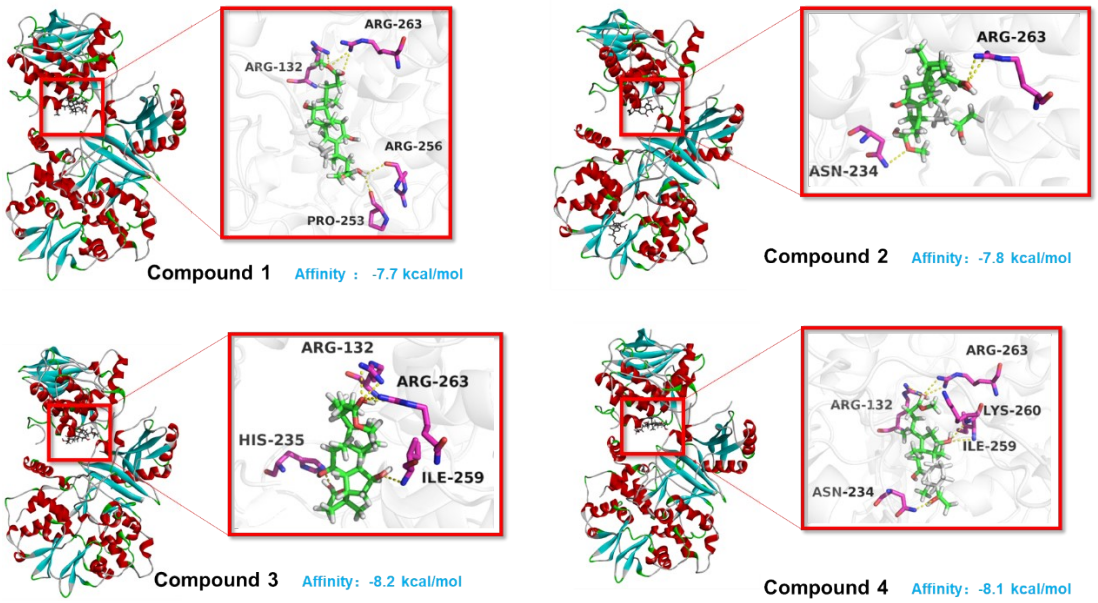


Figure S7. The molecular docking results of compounds **1**–**4** with AMPK (PDB: 4CFH).

NMR spectra of new compounds 1–10

Figure S8. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 1.

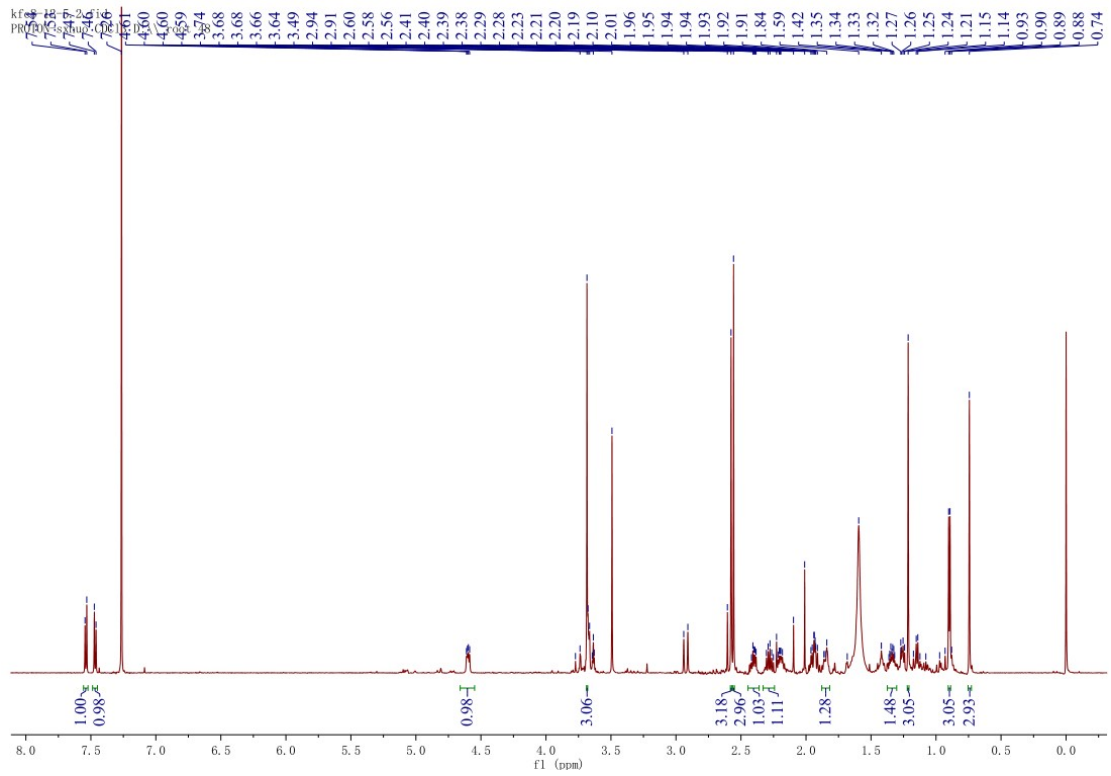


Figure S9. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 1.

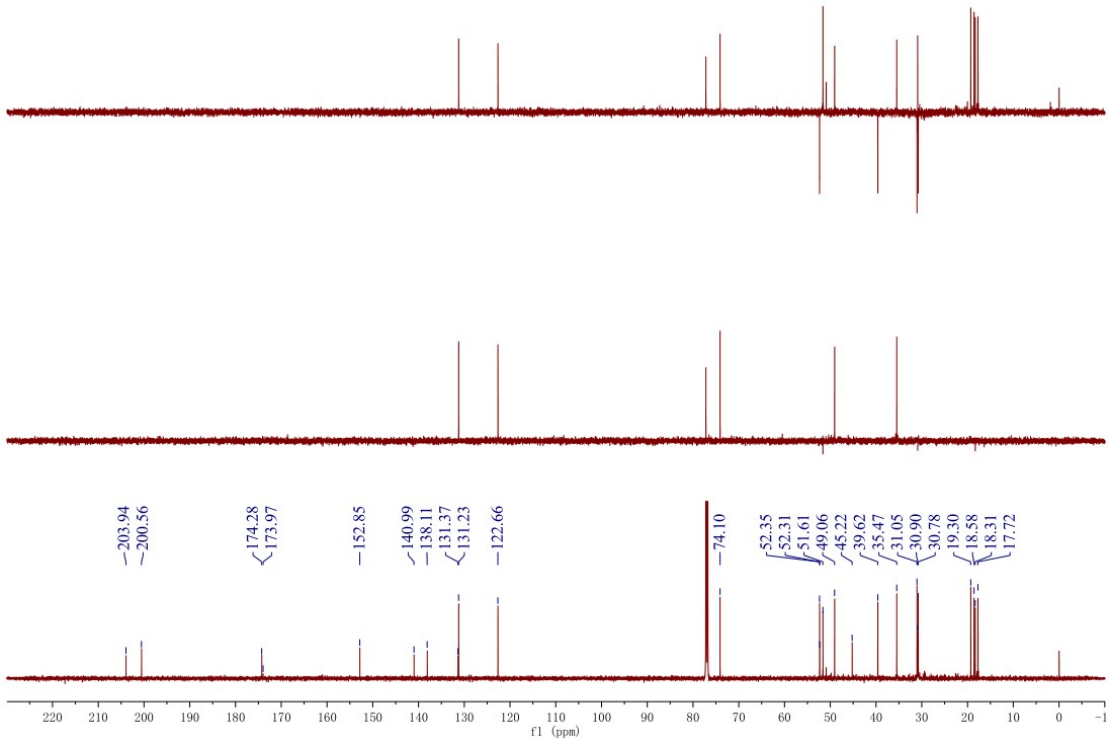


Figure S10. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 1.

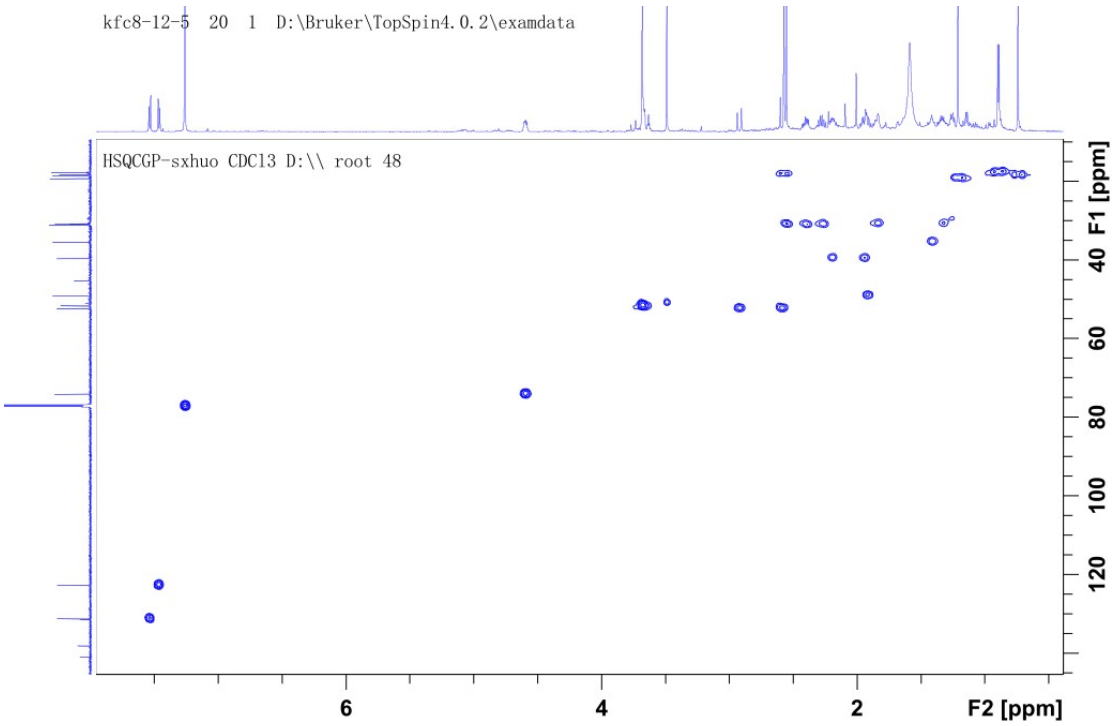


Figure S11. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 1.

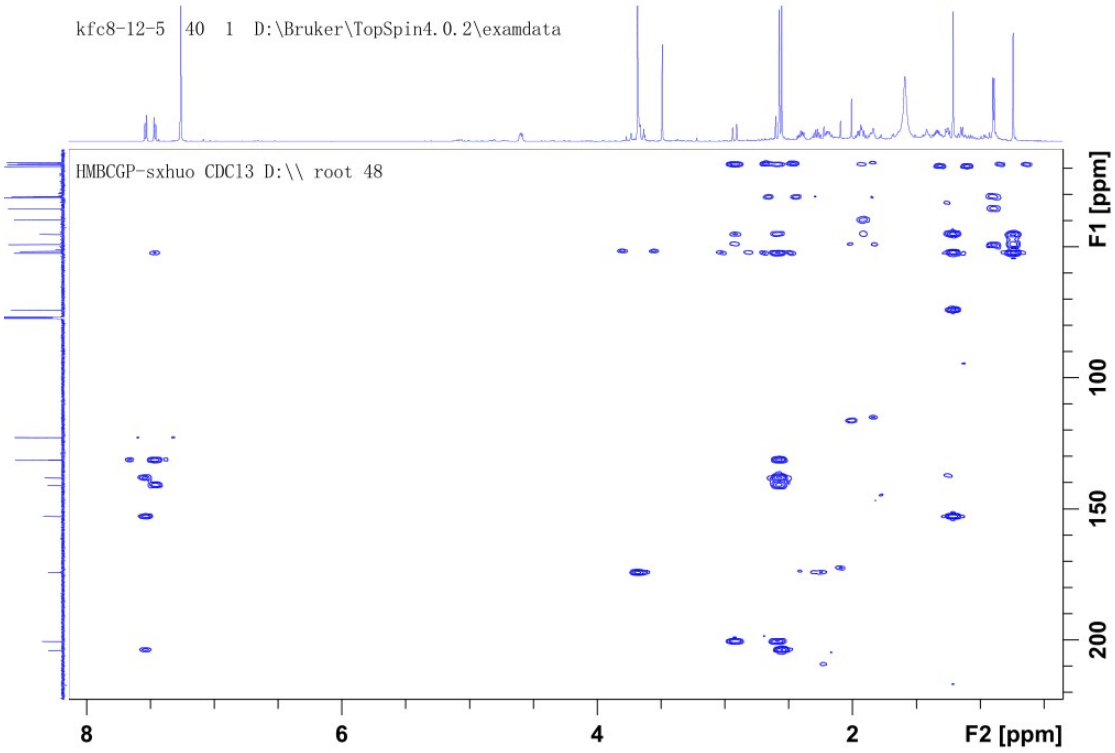


Figure S12. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 1.

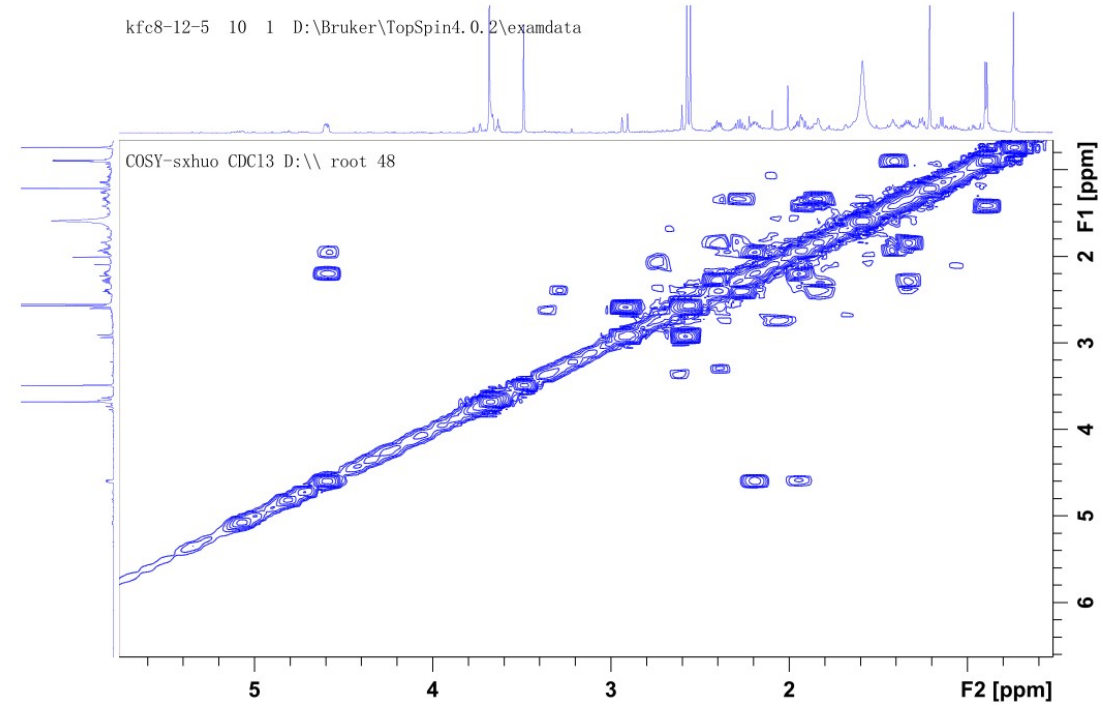


Figure S13. ROESY spectrum (600 MH, $CDCl_3$) of compound 1.

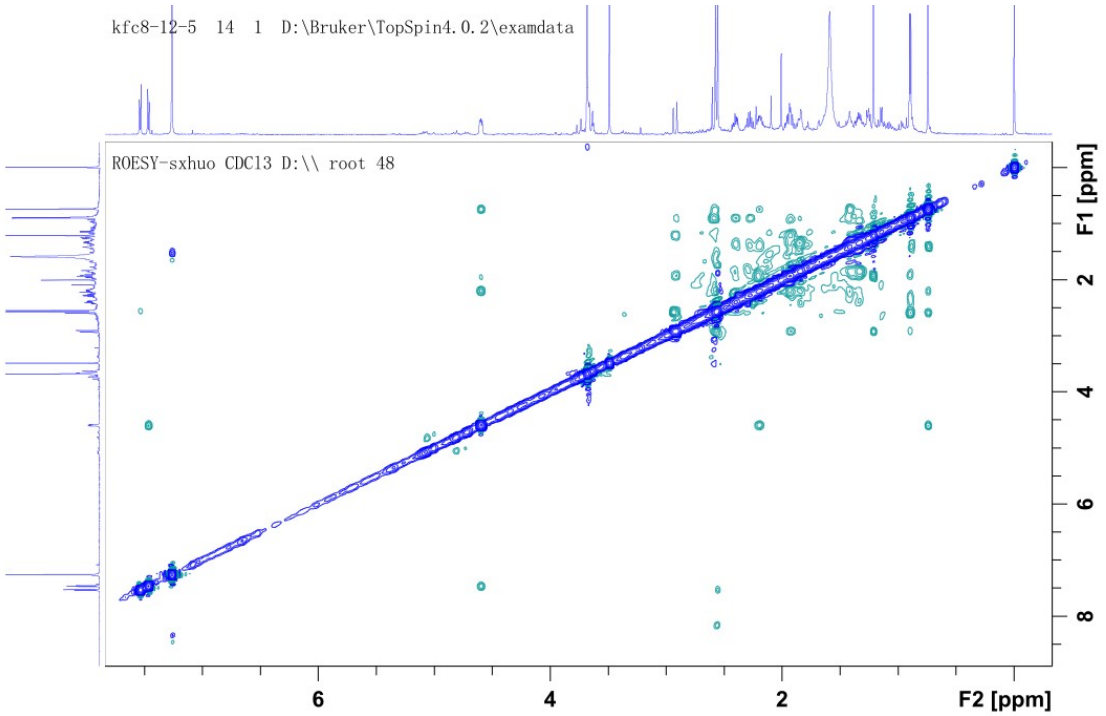


Figure S14. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 2.

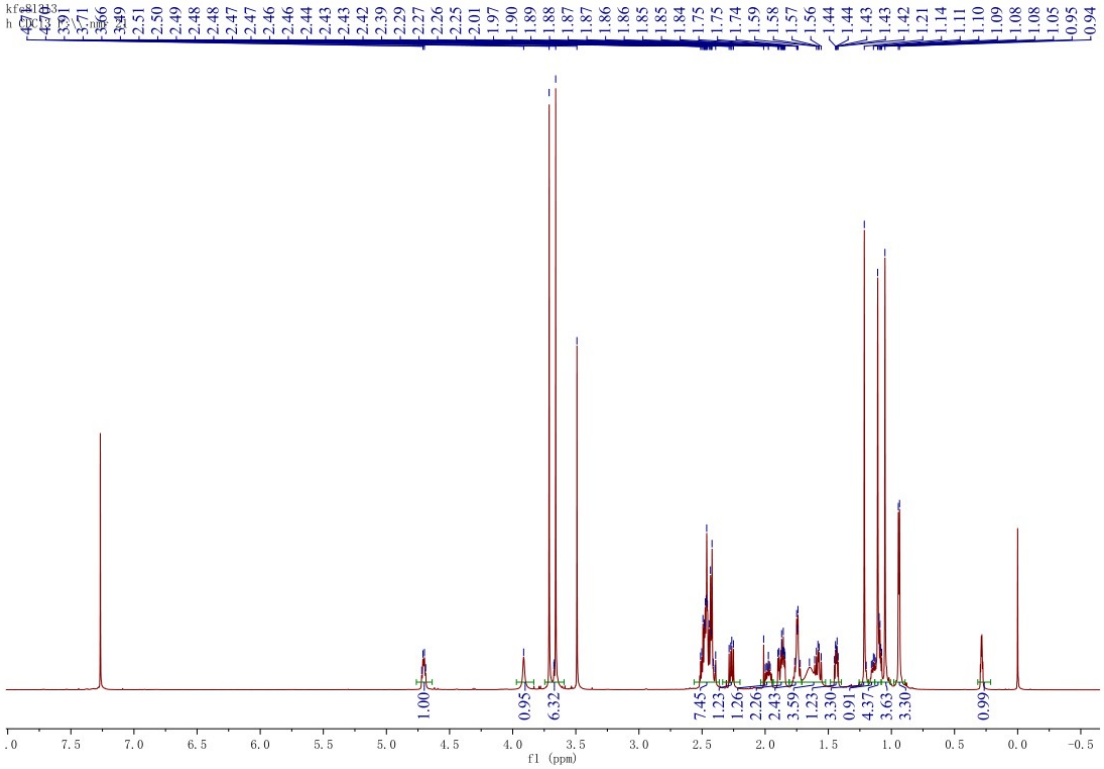


Figure S15. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 2.

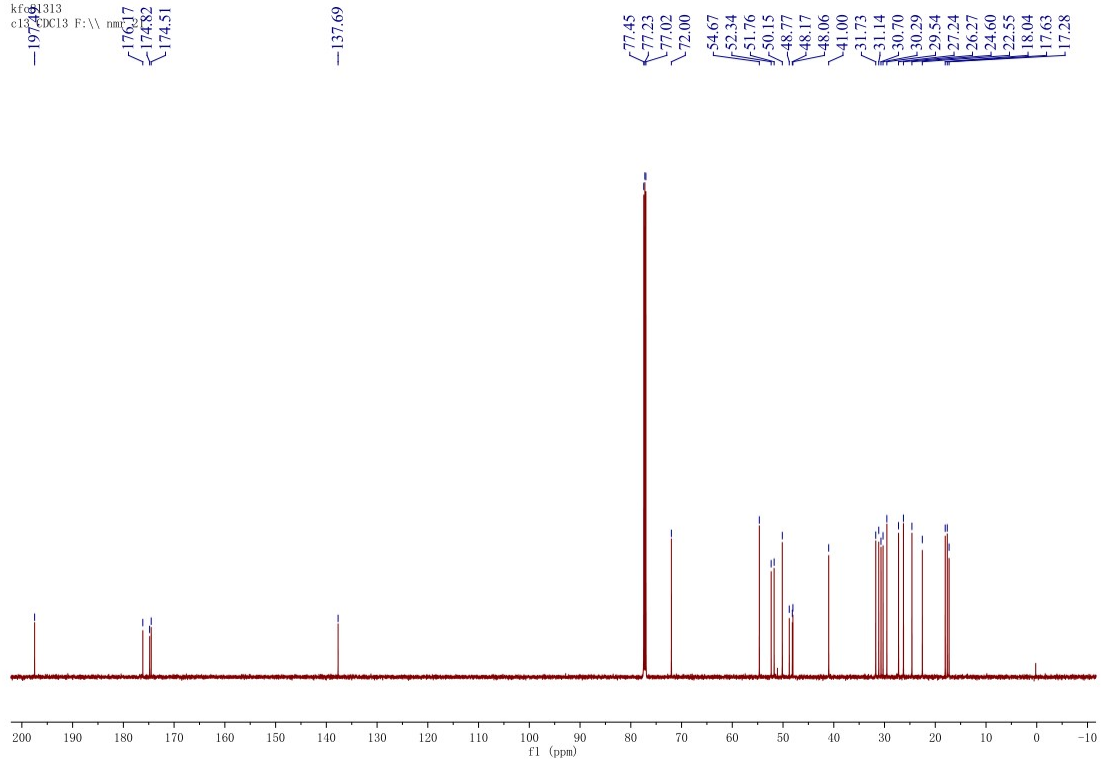


Figure S16. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 2.

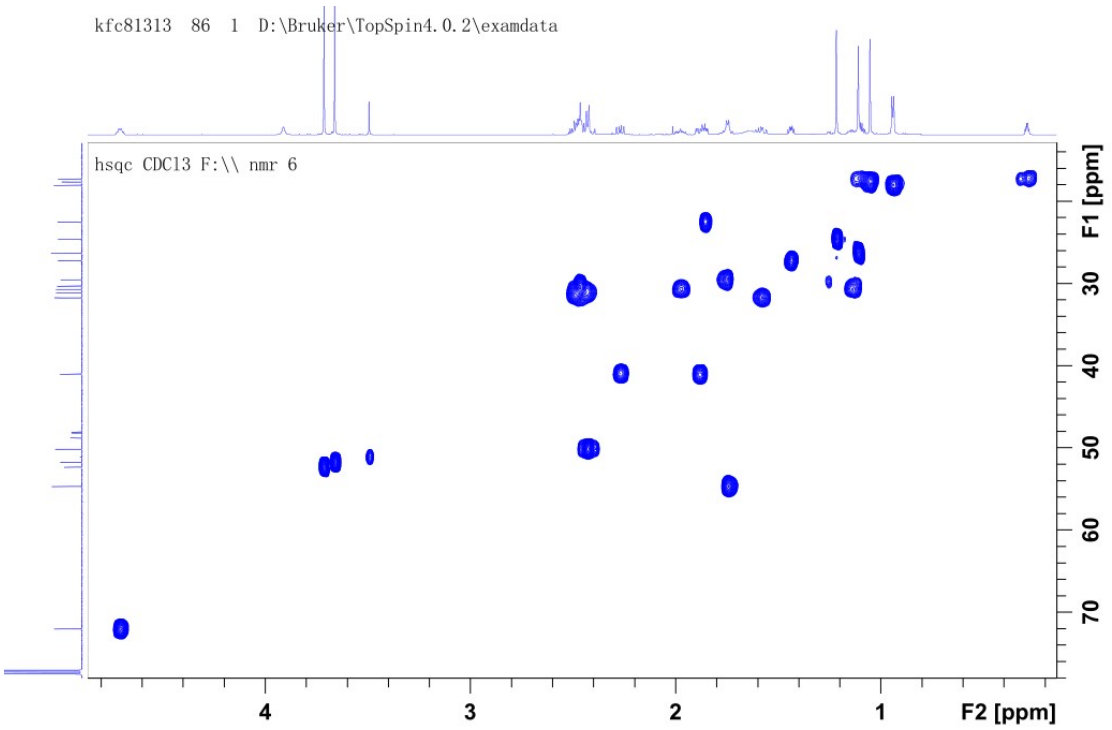


Figure S17. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 2.

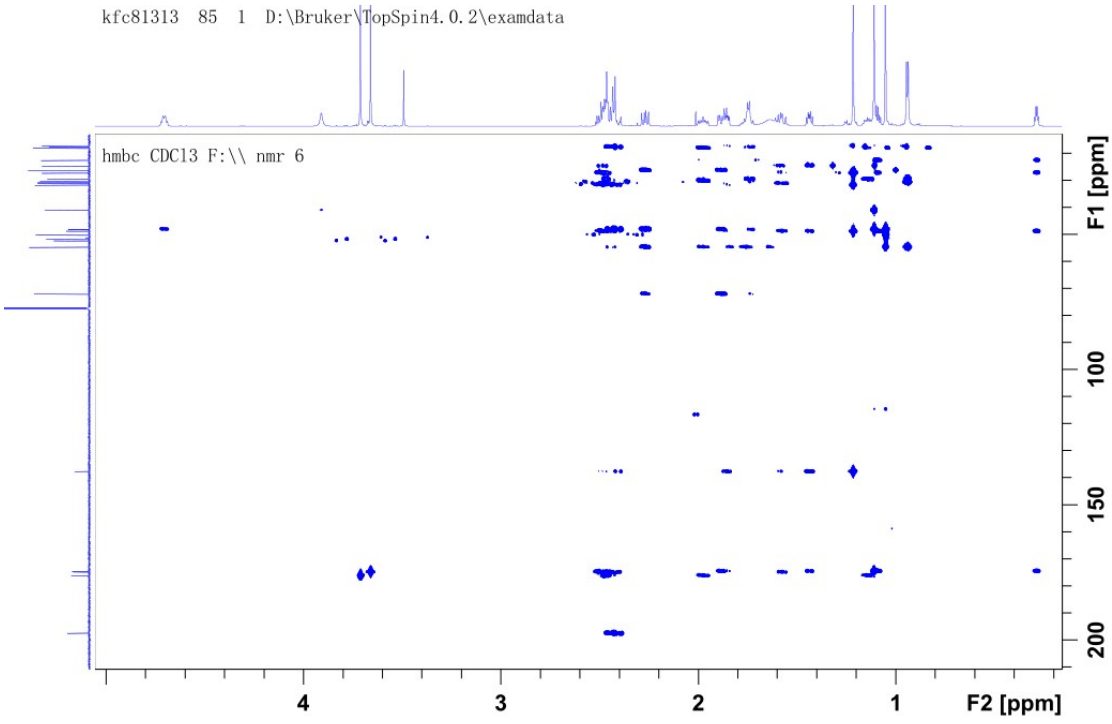


Figure S18. ^{1}H-^{1}H COSY spectrum (150 MH, $CDCl_3$) of compound 2.

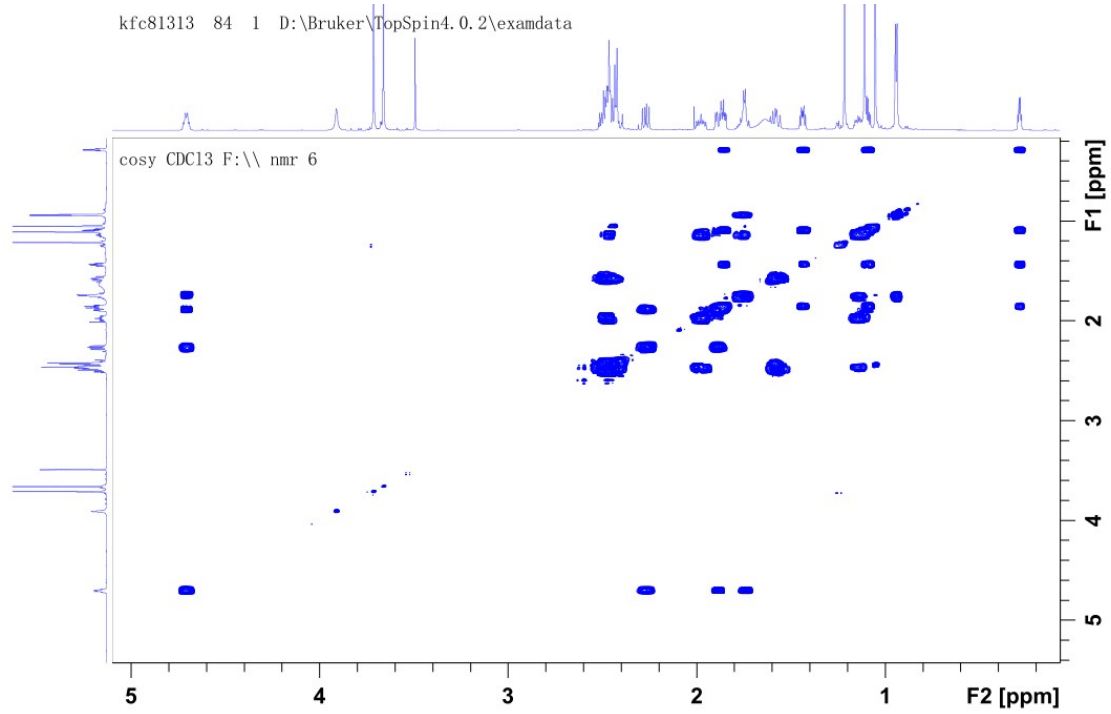


Figure S19. ROESY spectrum (150 MH, $CDCl_3$) of compound 2.

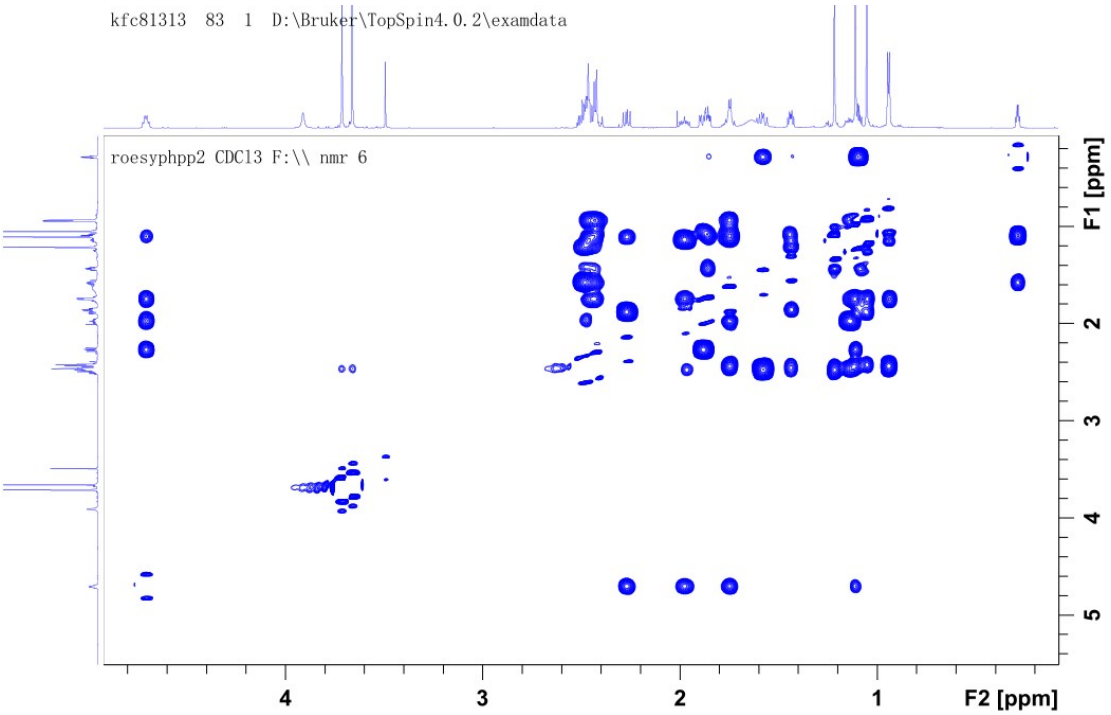


Figure S20. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 3.

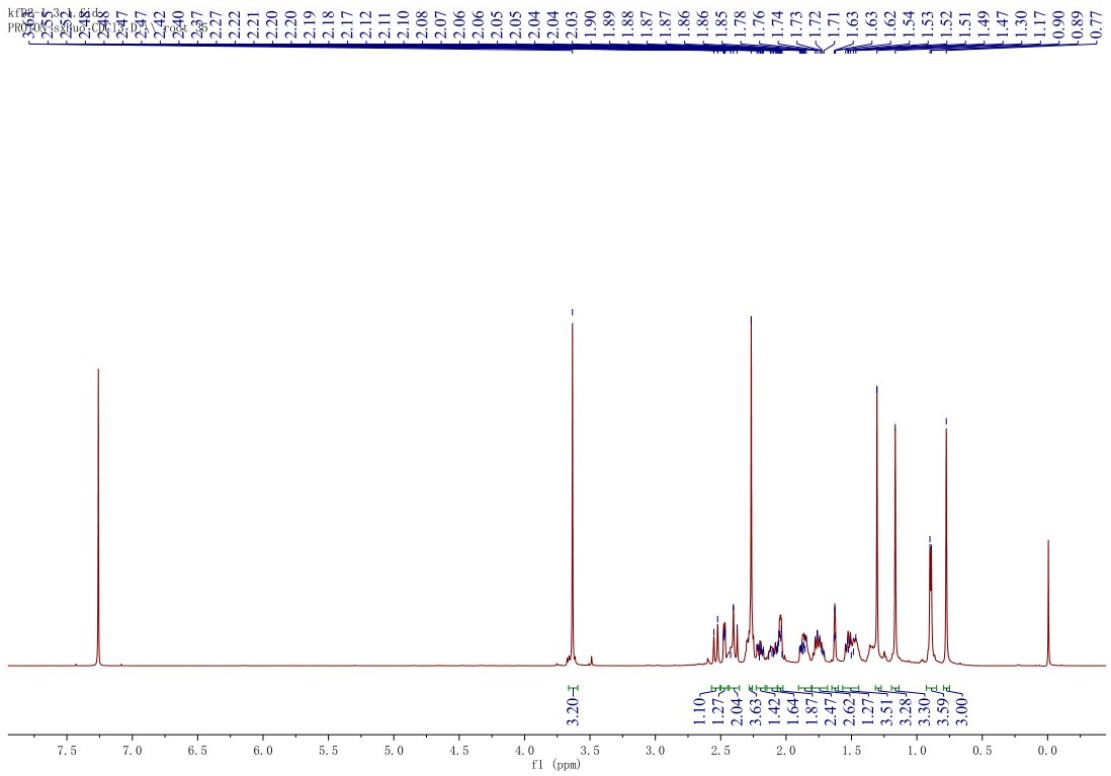


Figure S21. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 3.

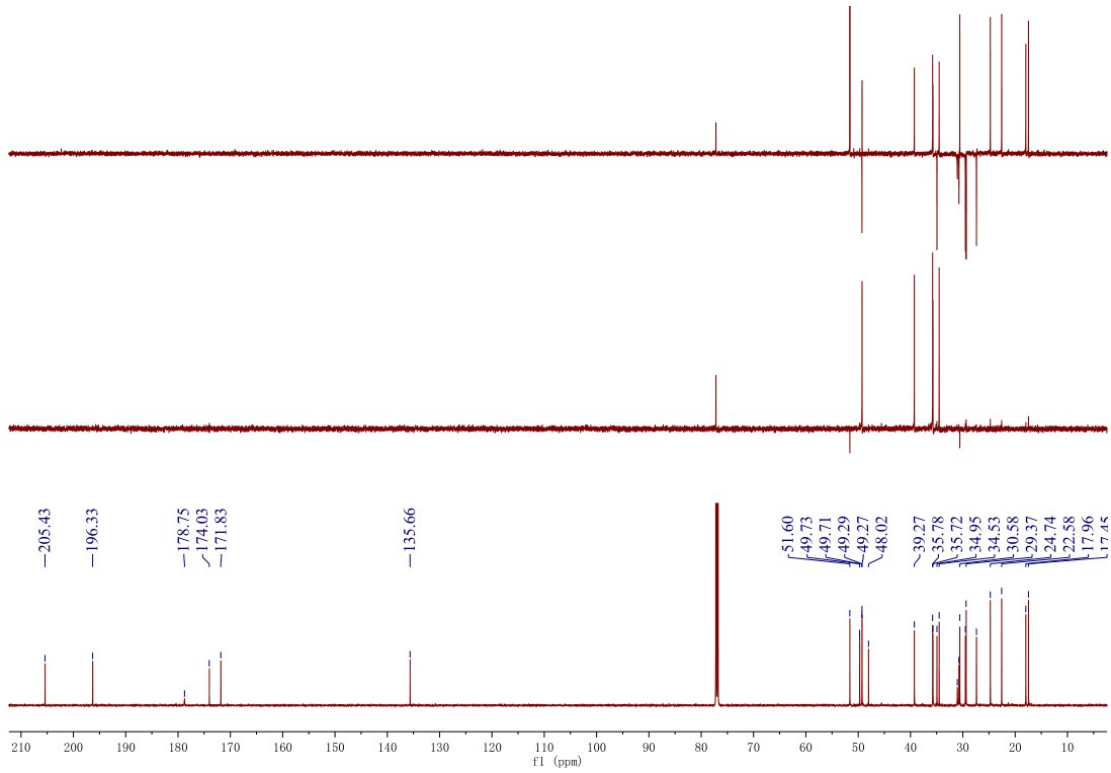


Figure S22. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 3.

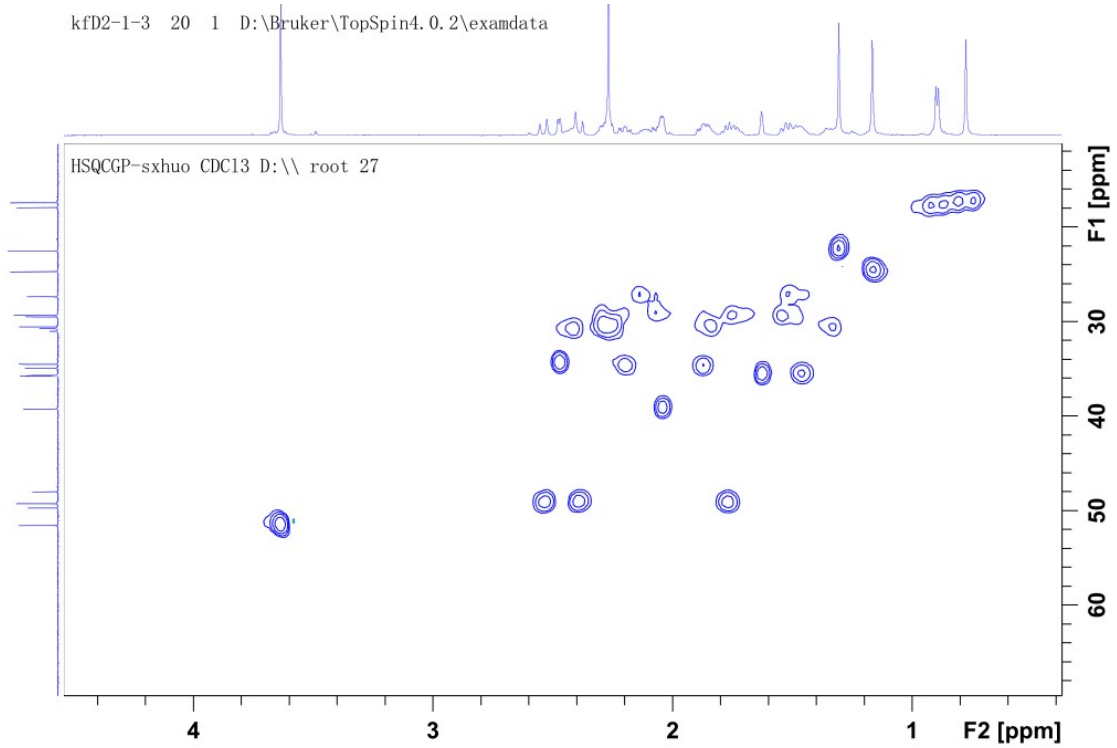


Figure S23. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 3.

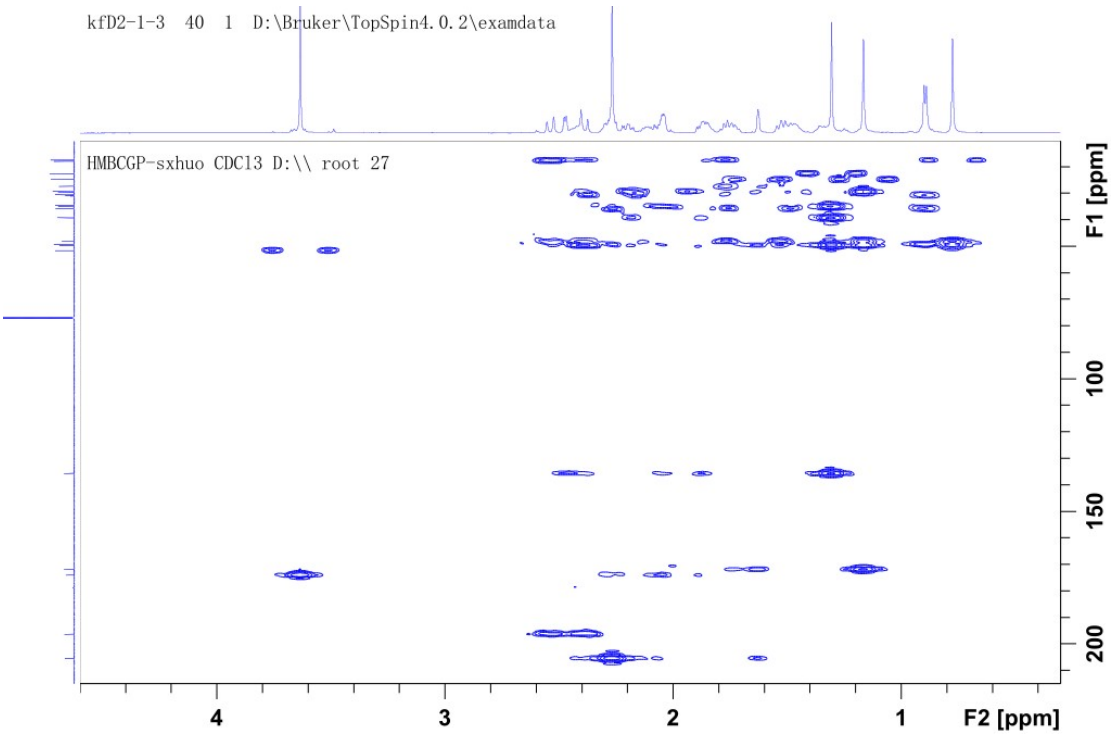


Figure S24. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 3.

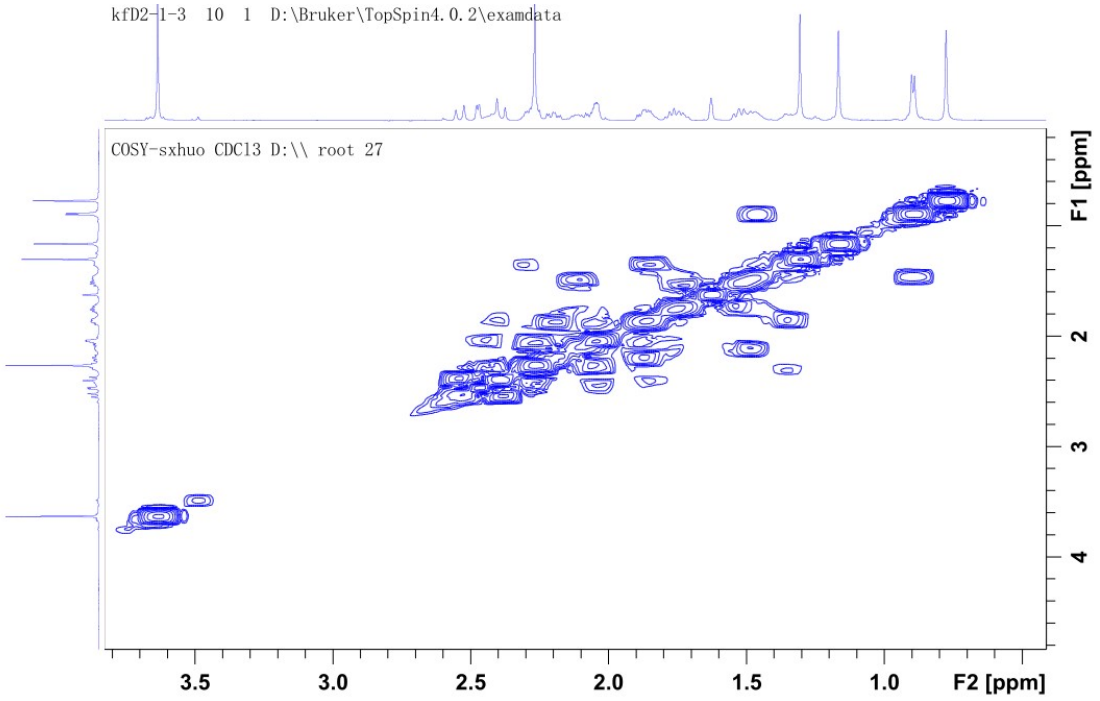


Figure S25. ROESY spectrum (600 MH, $CDCl_3$) of compound 3.

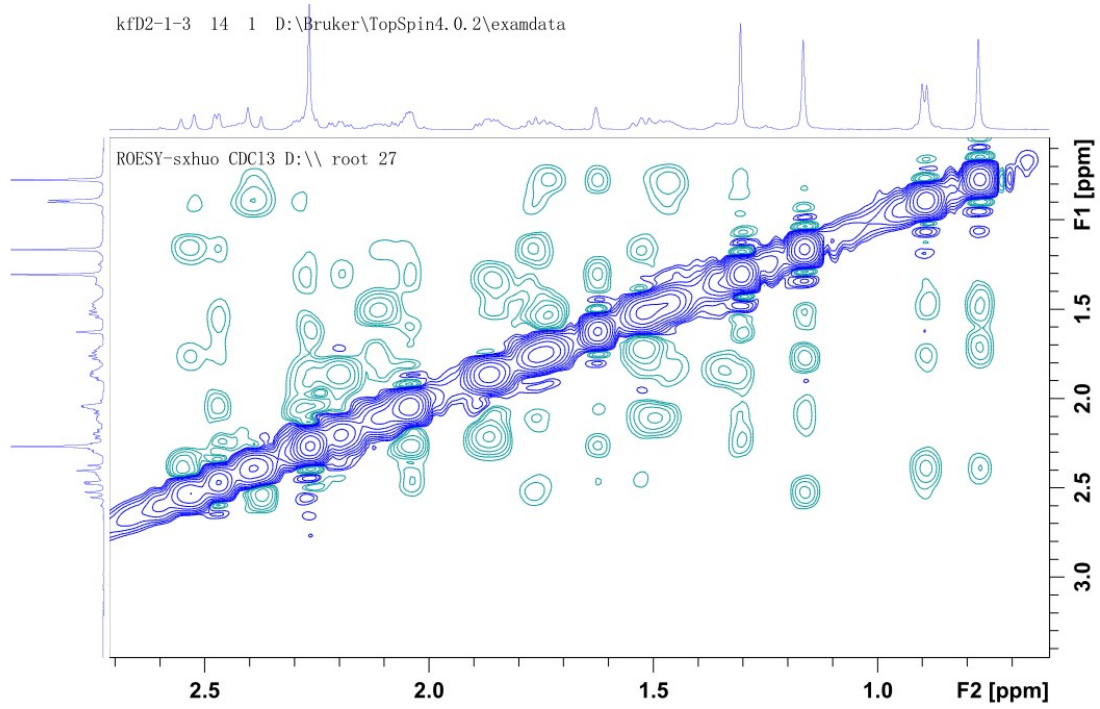


Figure S26. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 4.

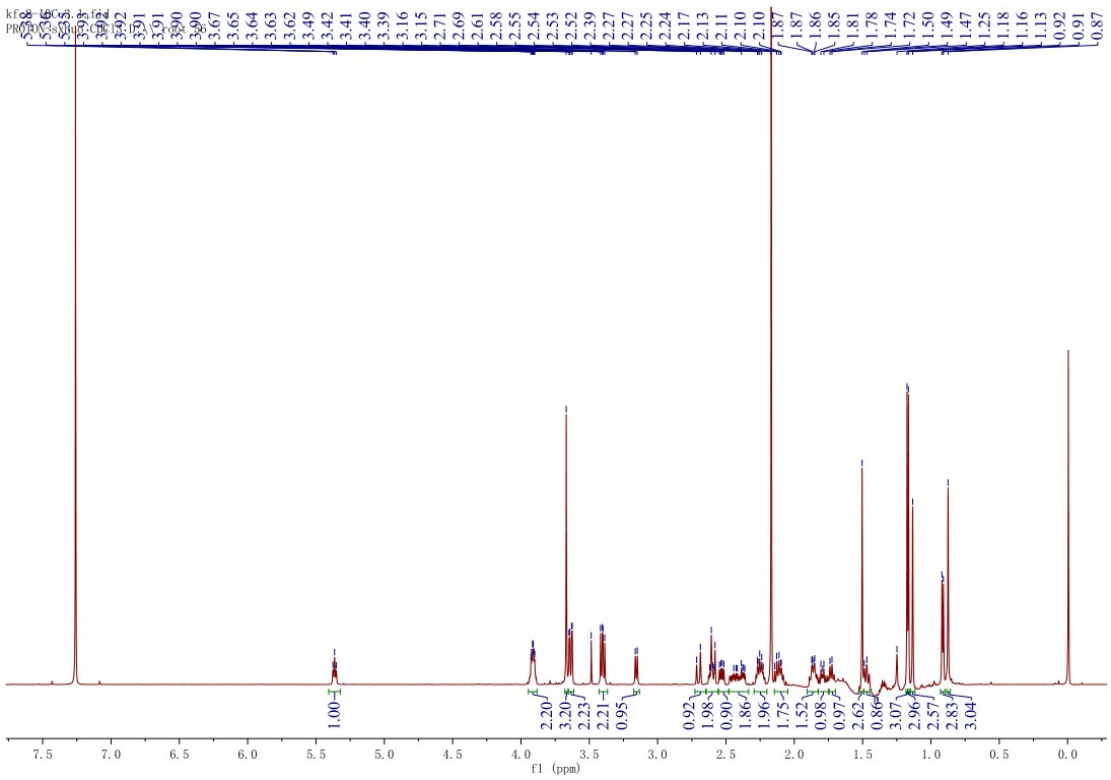


Figure S27. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 4.

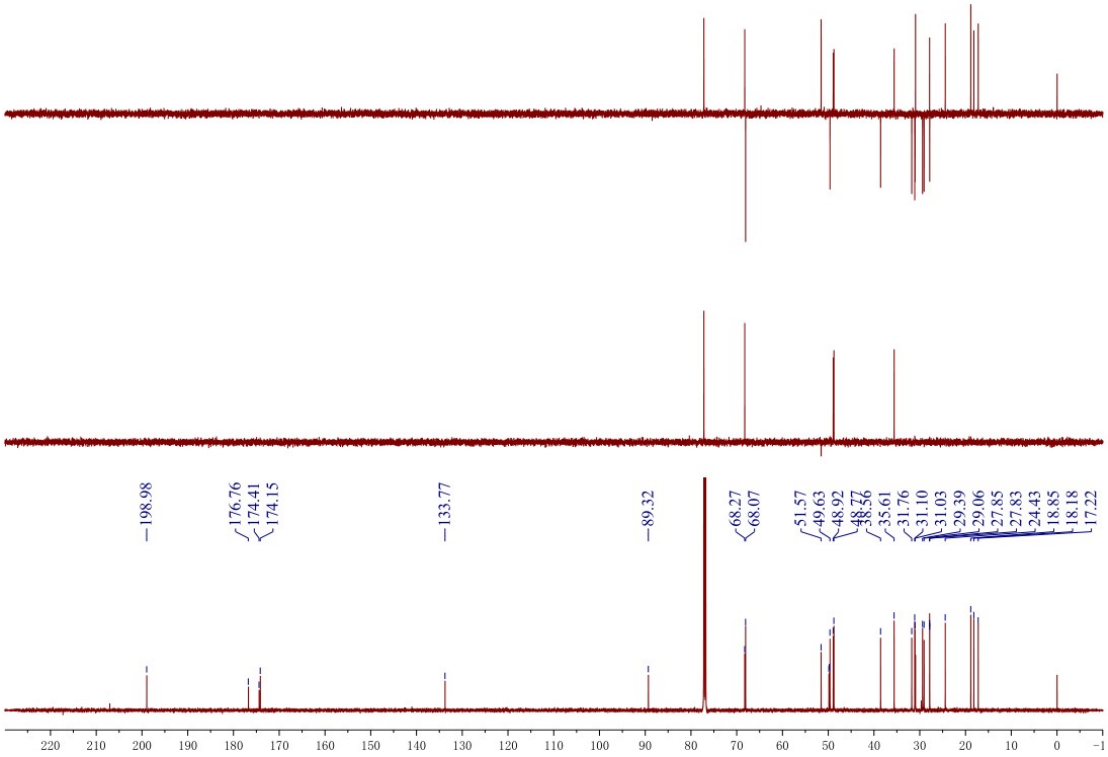


Figure S28. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 4.

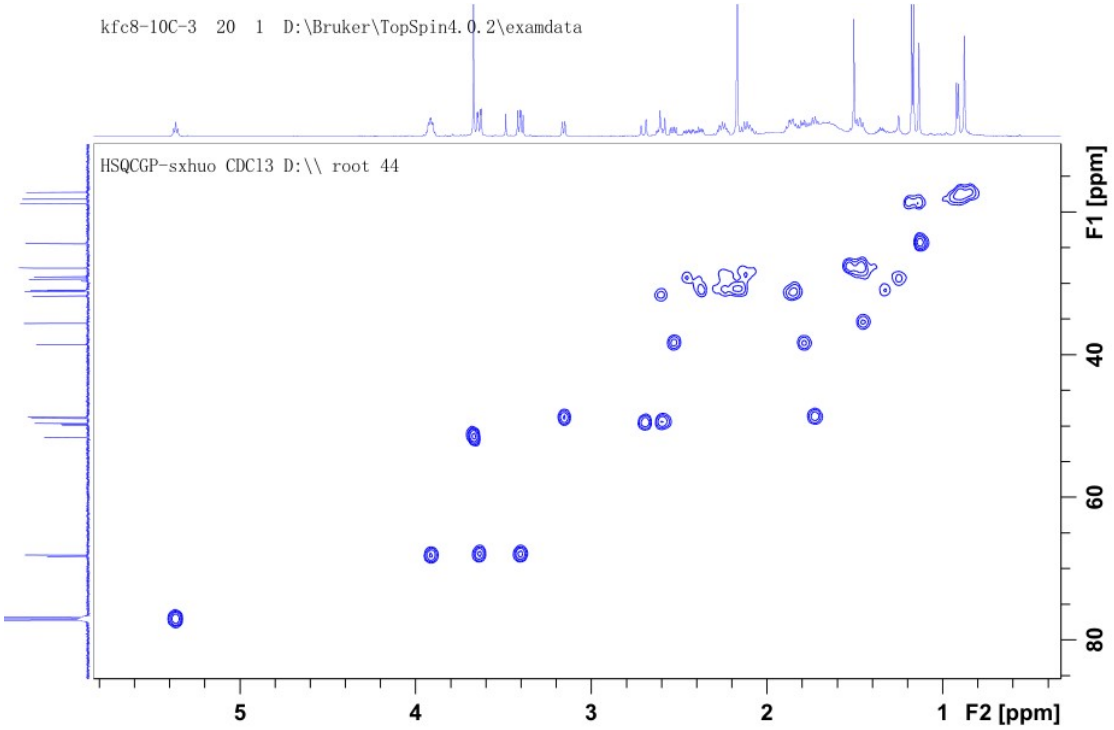


Figure S29. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 4.

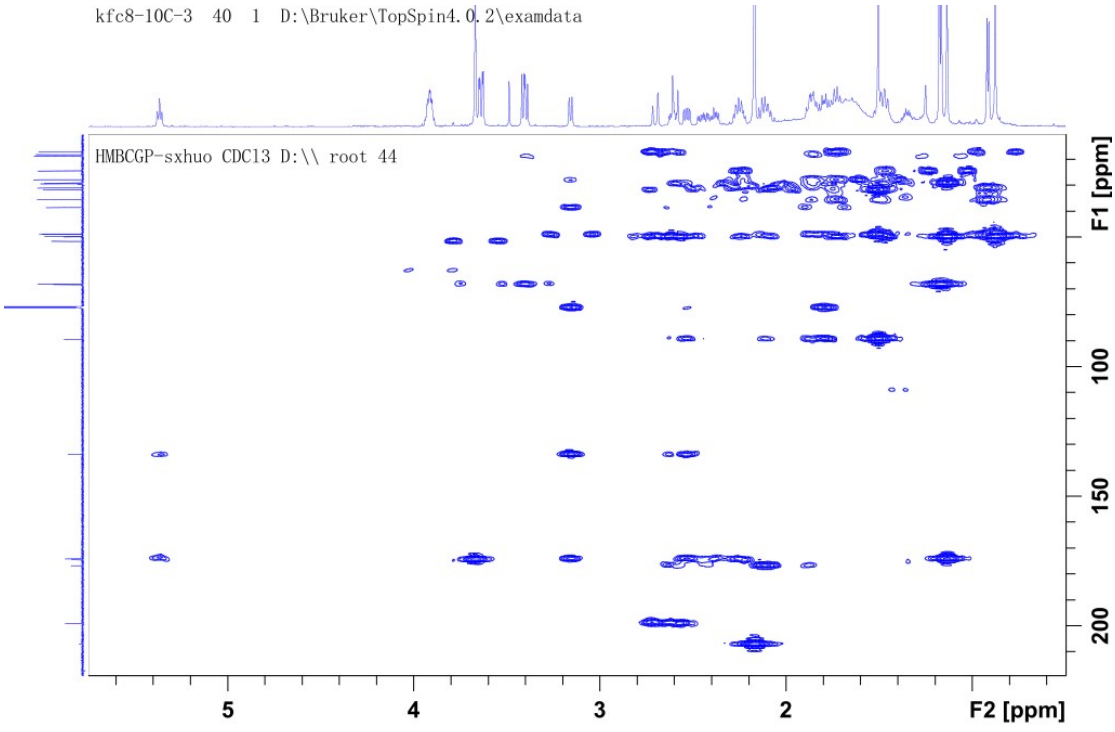


Figure S30. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 4.

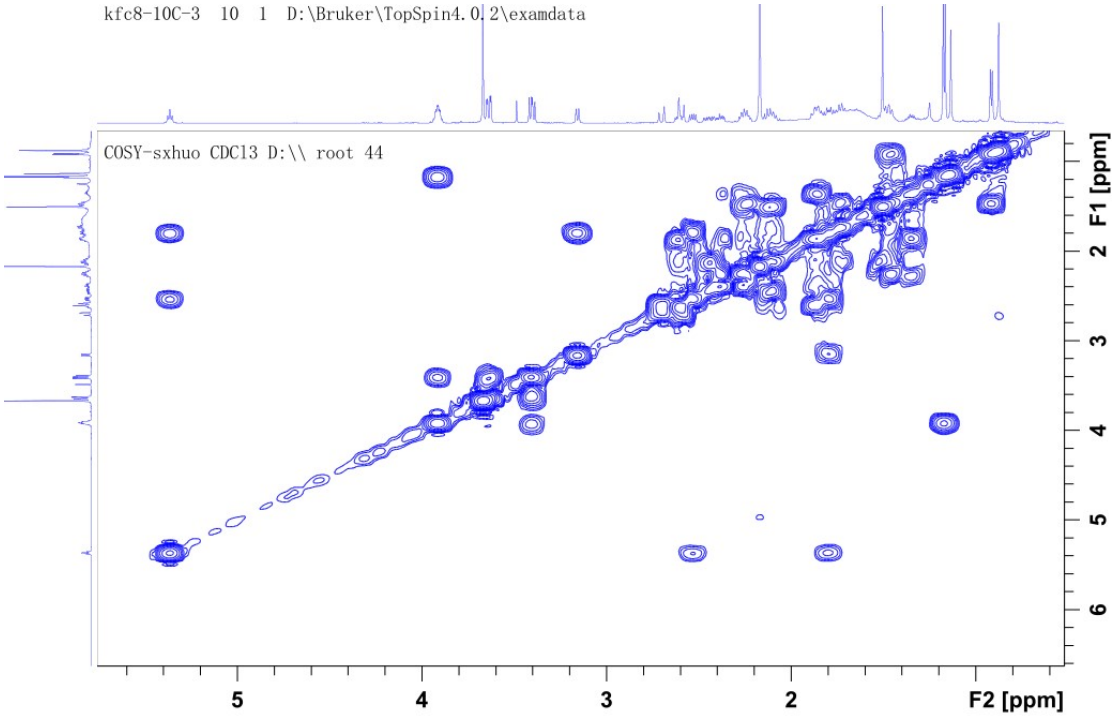


Figure S31. ROESY spectrum (600 MH, $CDCl_3$) of compound 4.

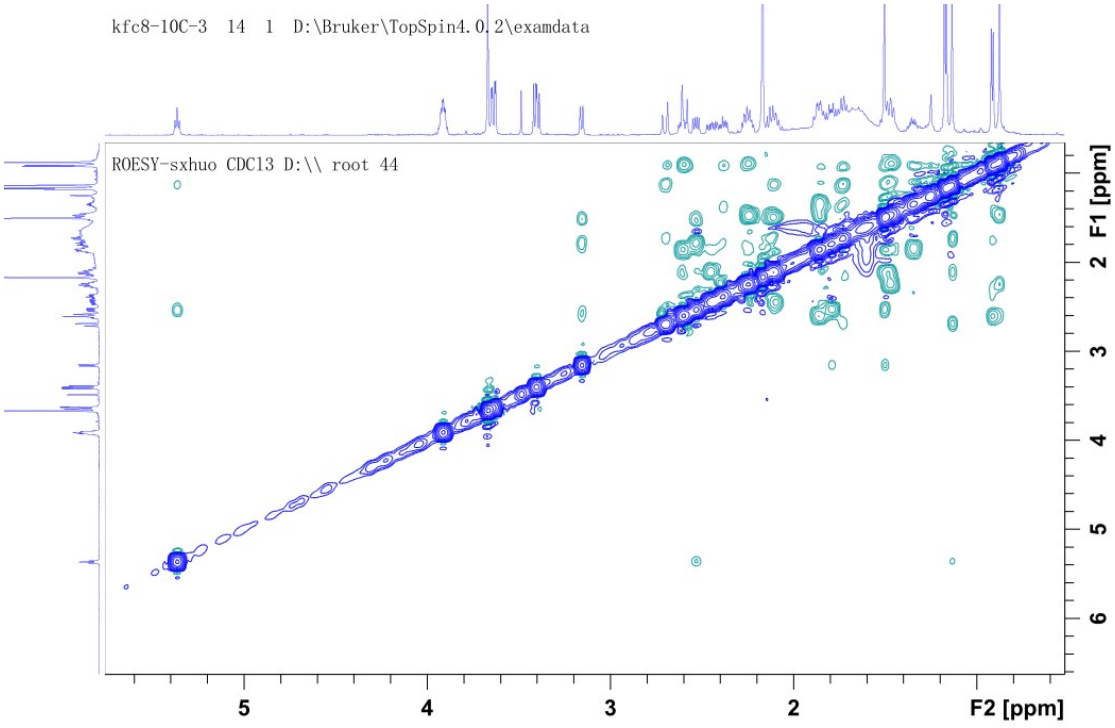


Figure S32. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 5.

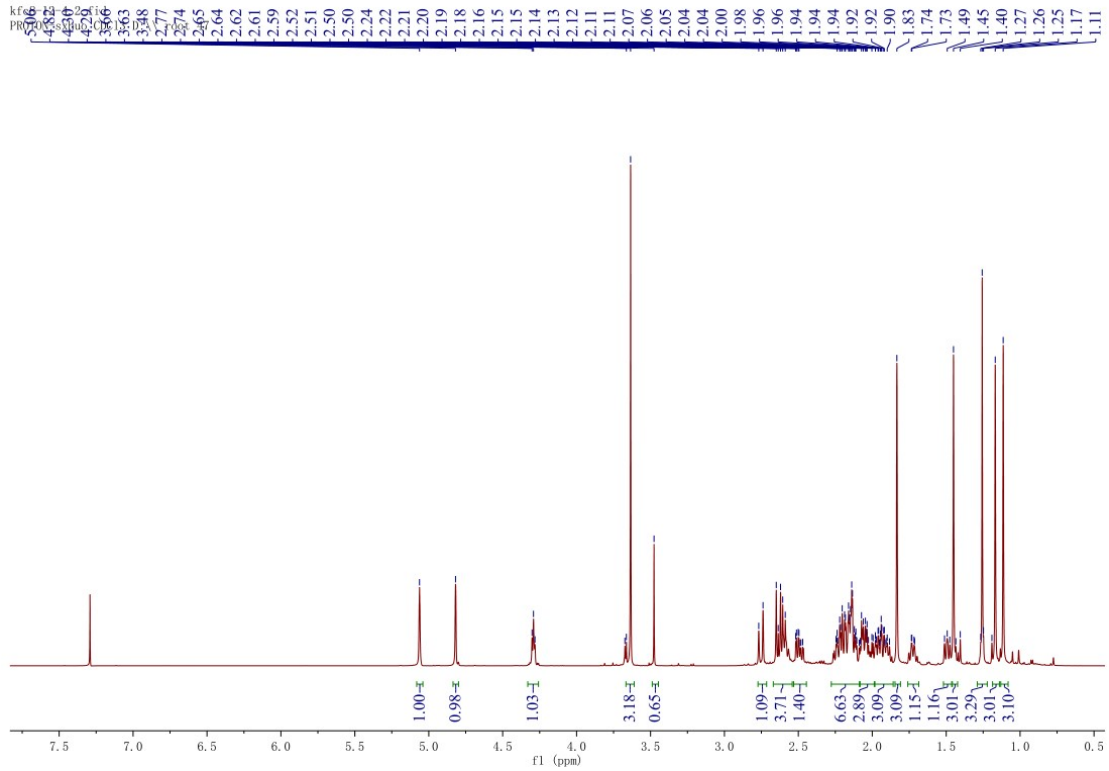


Figure S33. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 5.

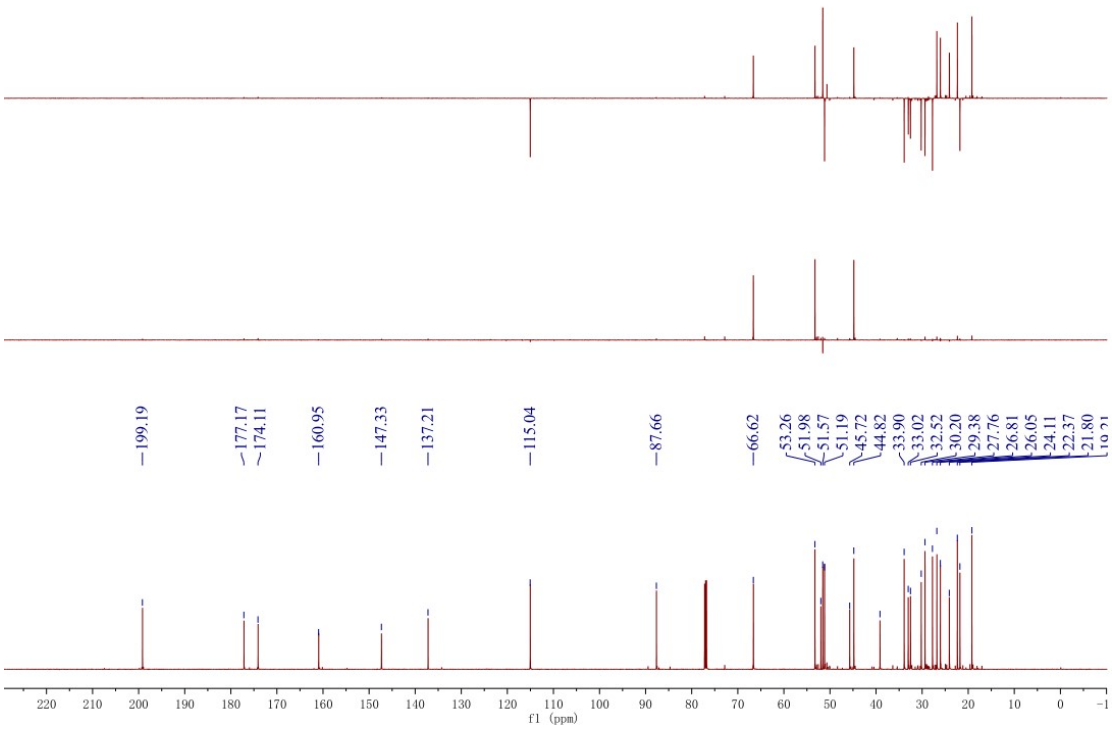


Figure S34. HSQC NMR spectrum (600/150 MH, $CDCl_3$) of compound 5.

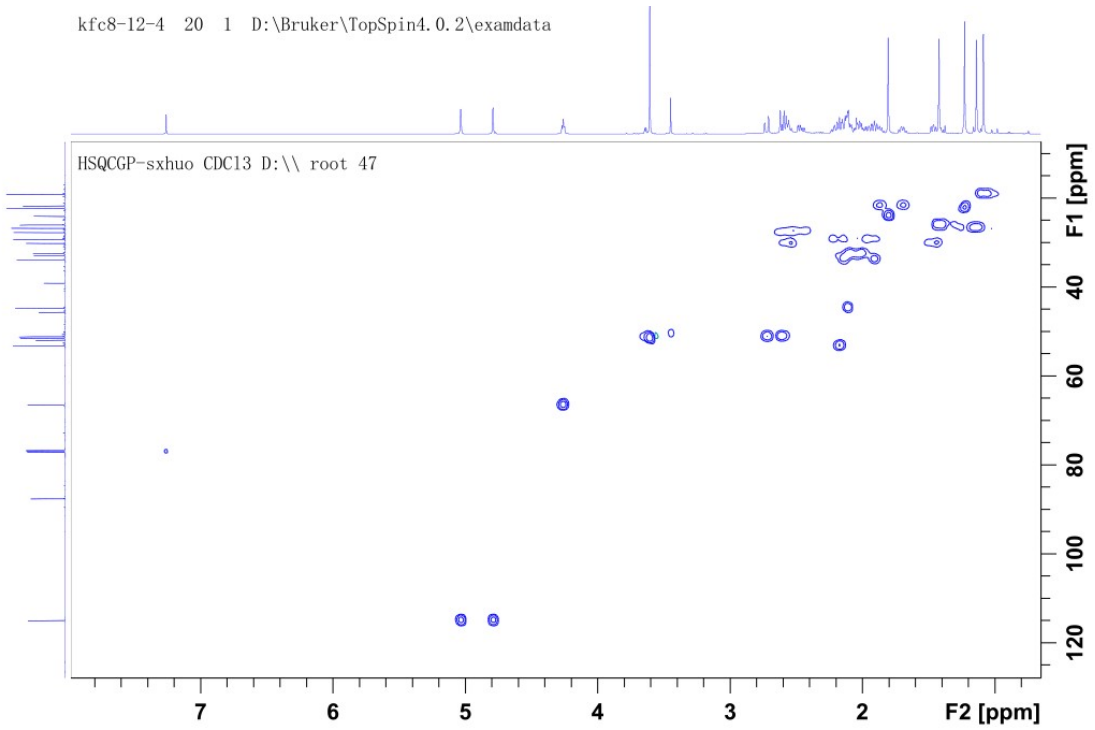


Figure S35. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 5.

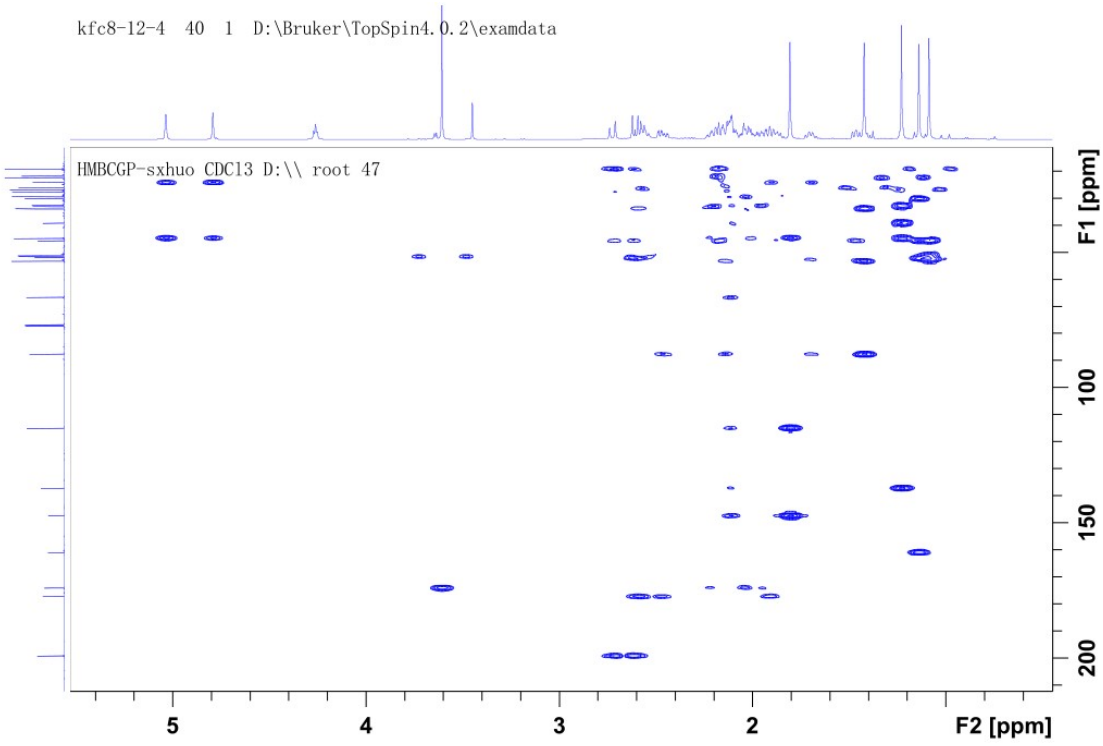


Figure S36. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 5.

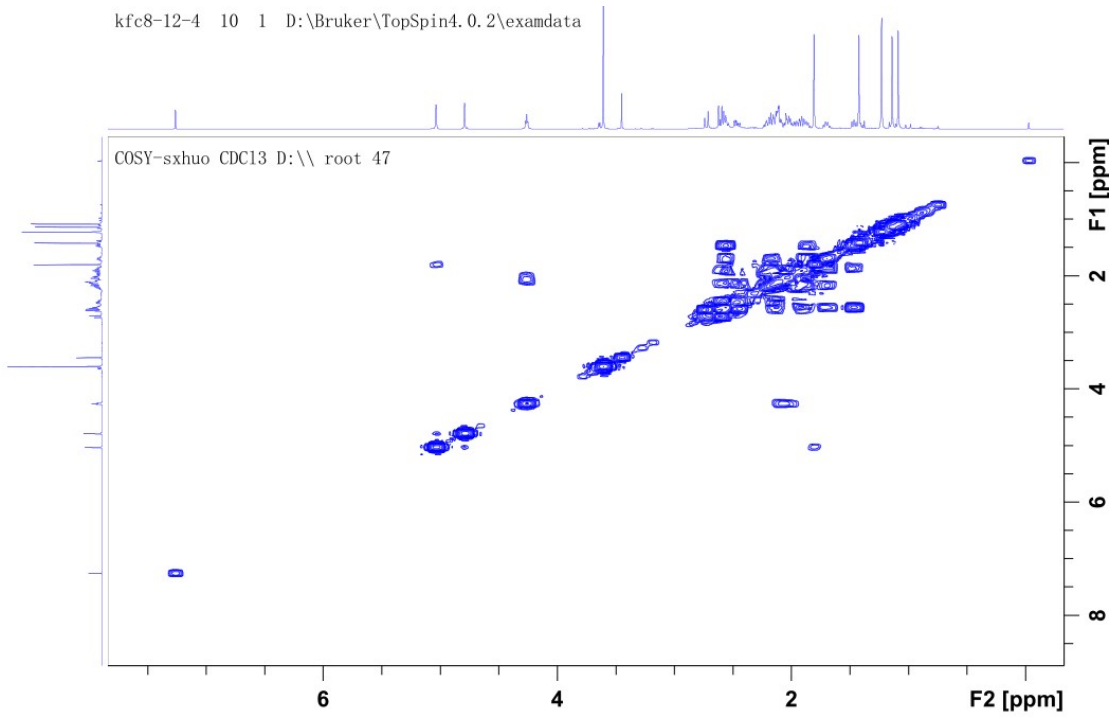


Figure S37. ROESY spectrum (600 MH, $CDCl_3$) of compound 5.

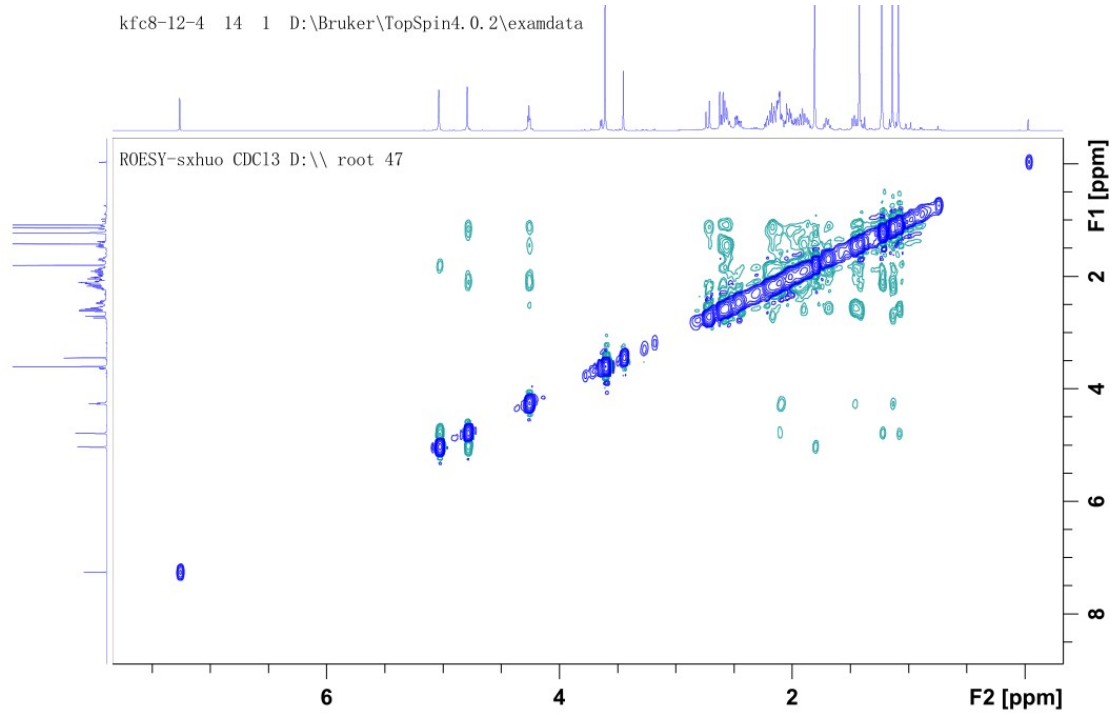


Figure S38. ^{1}H NMR spectrum (600 MH, CD_3OD) of compound 6.

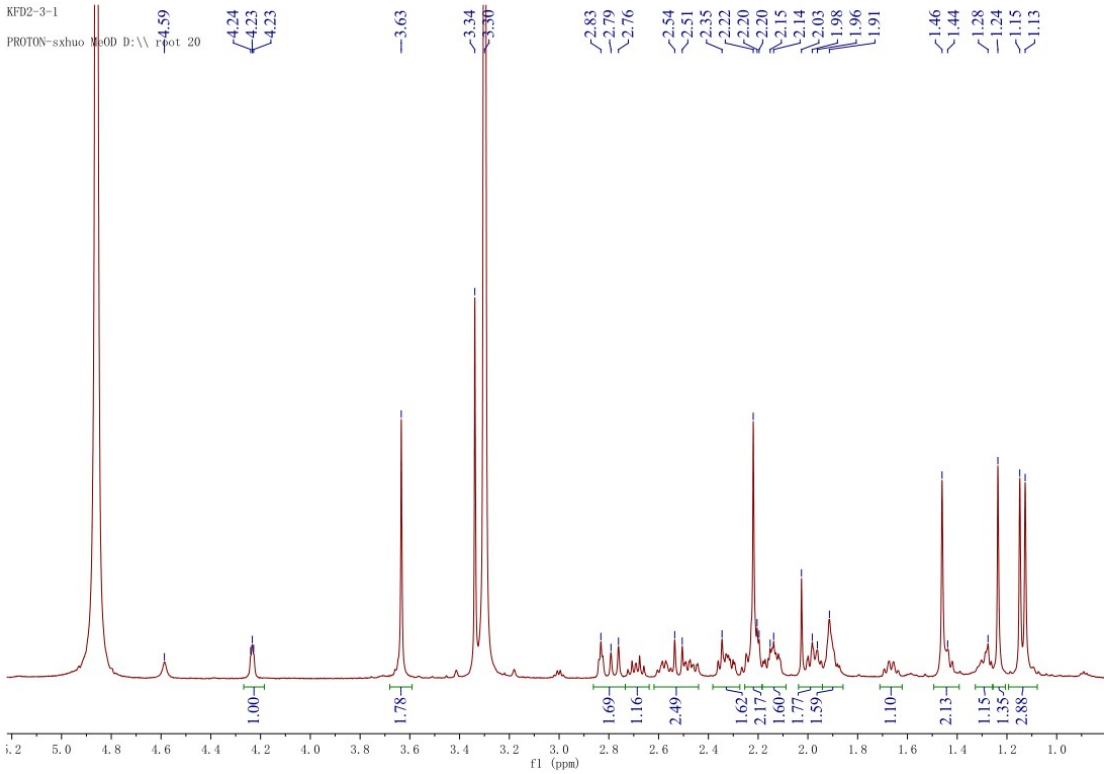


Figure S39. ^{13}C NMR spectrum (150 MH, CD_3OD) of compound 6.

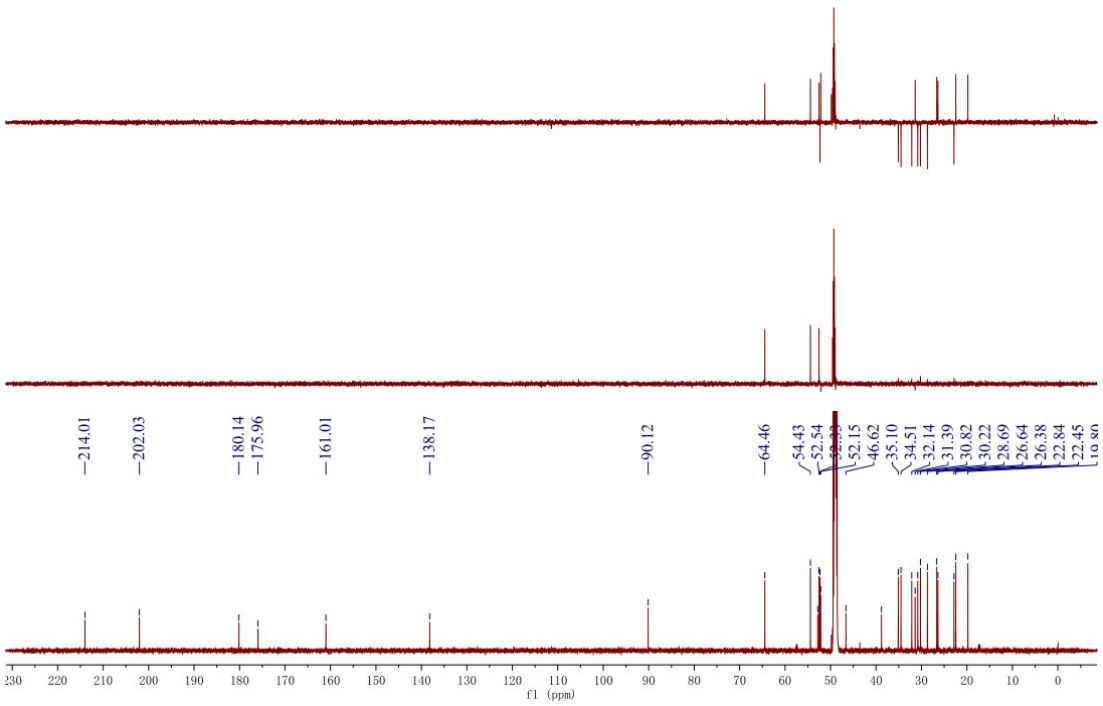


Figure S40. HSQC spectrum (600/150 MH, CD_3OD) of compound 6.

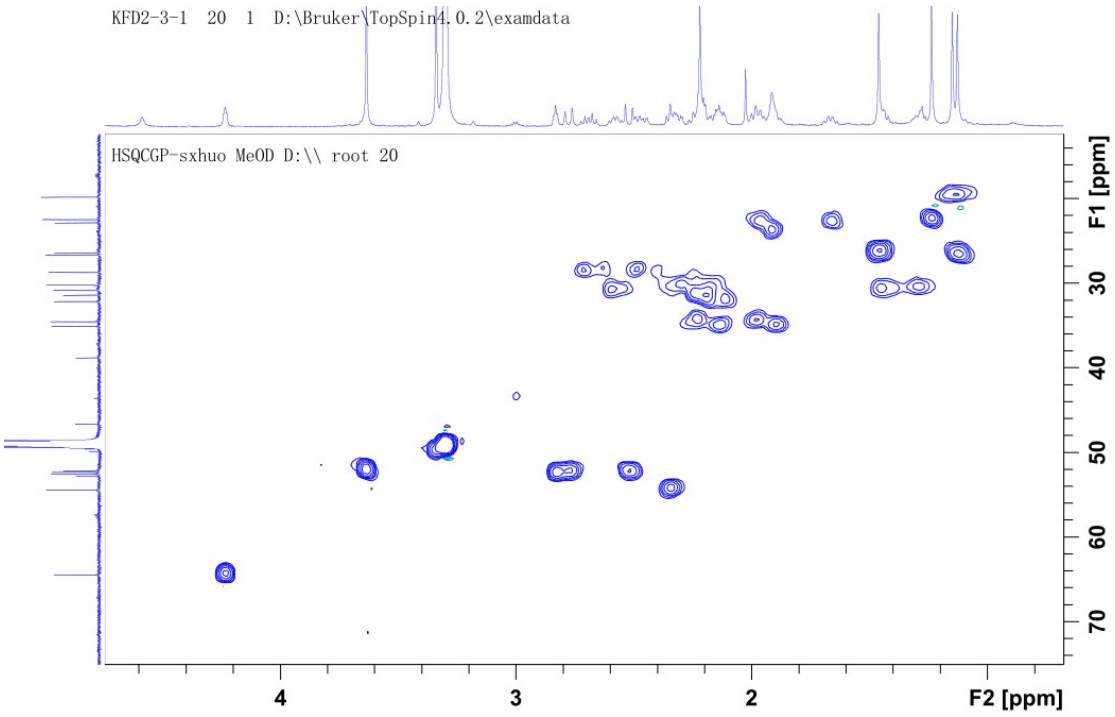


Figure S41. HMBC spectrum (600/150 MH, CD_3OD) of compound 6.

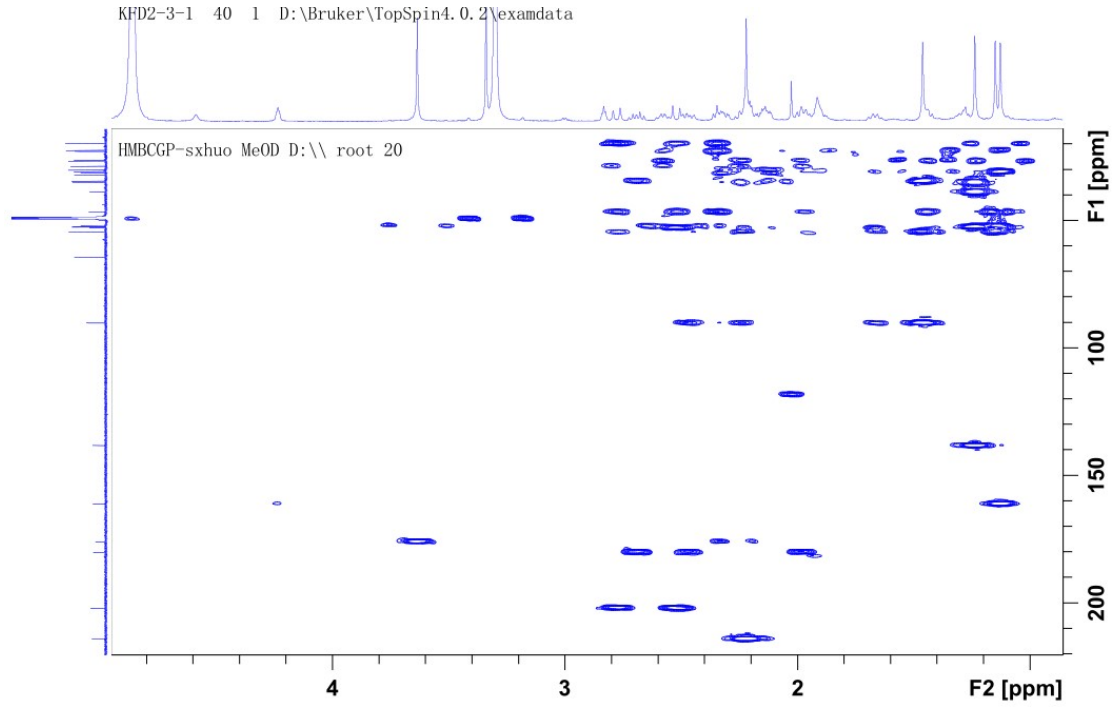


Figure S42. ^{1}H-^{1}H COSY spectrum (600 MH, CD_3OD) of compound 6.

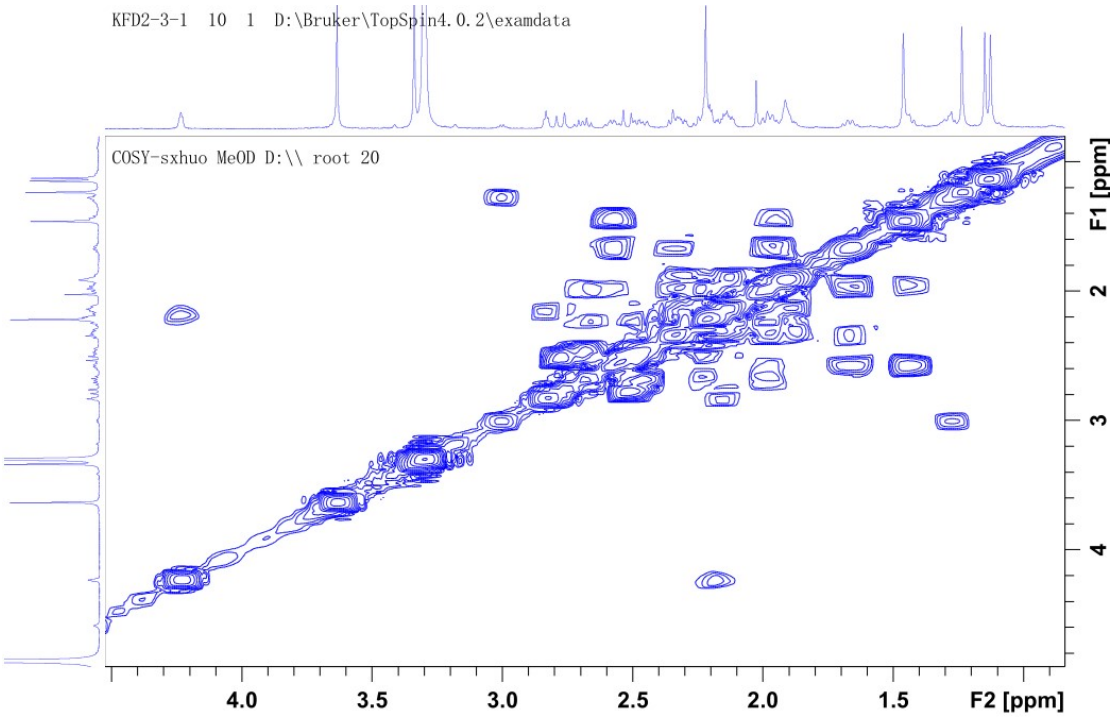


Figure S43. ^{1}H NMR spectrum (600 MH, $CDCl_3$) of compound 7.

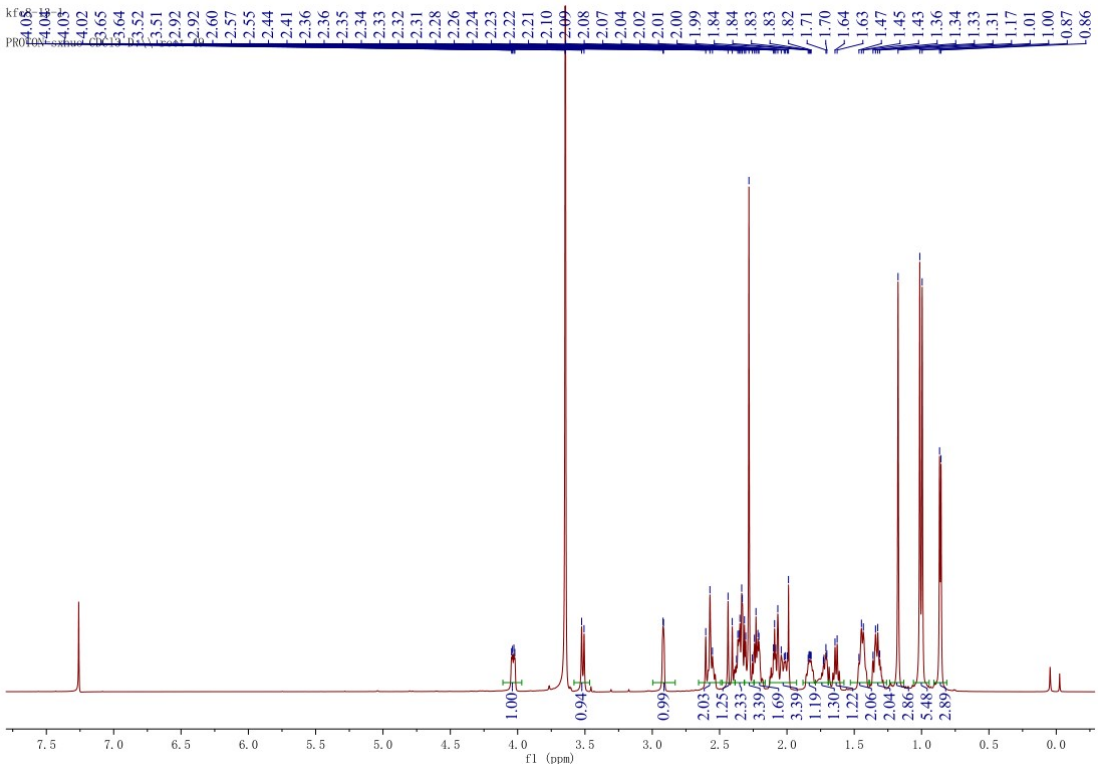


Figure S44. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 7.

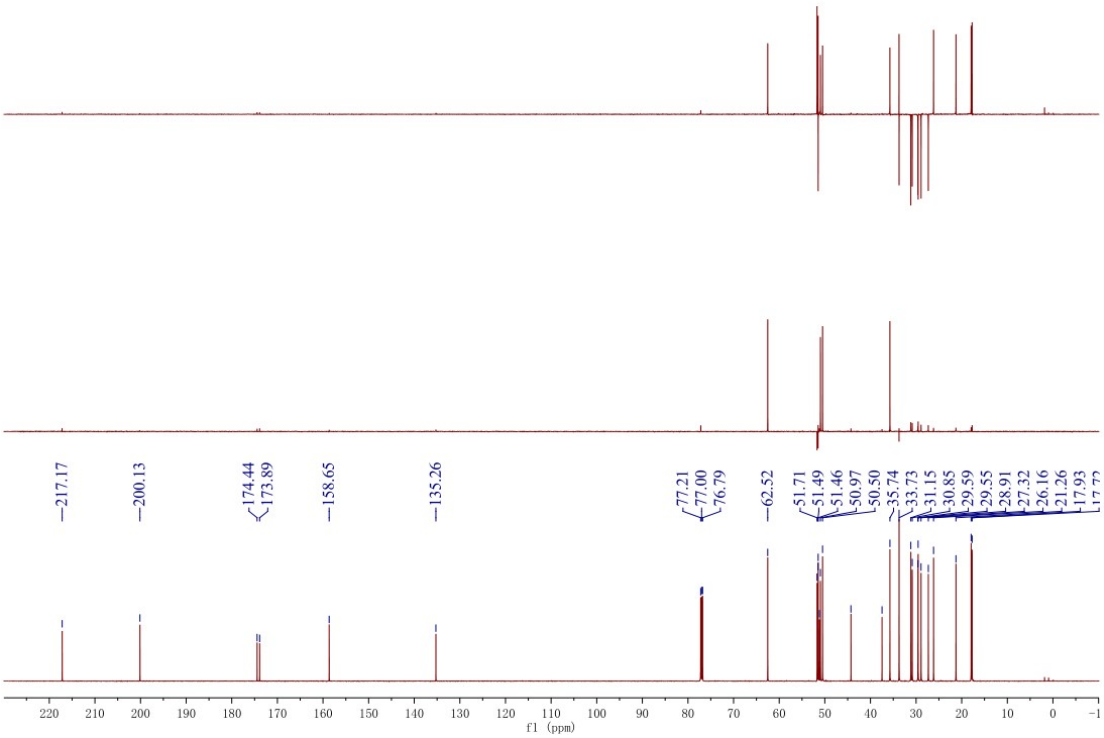


Figure S45. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 7.

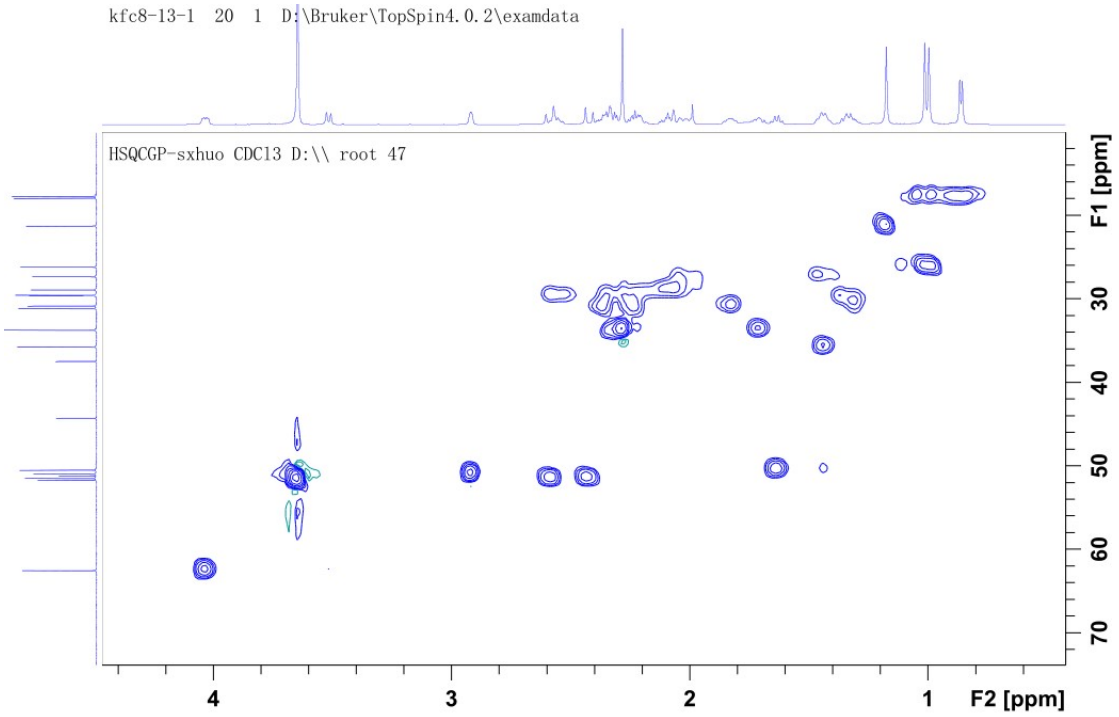


Figure S46. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 7.

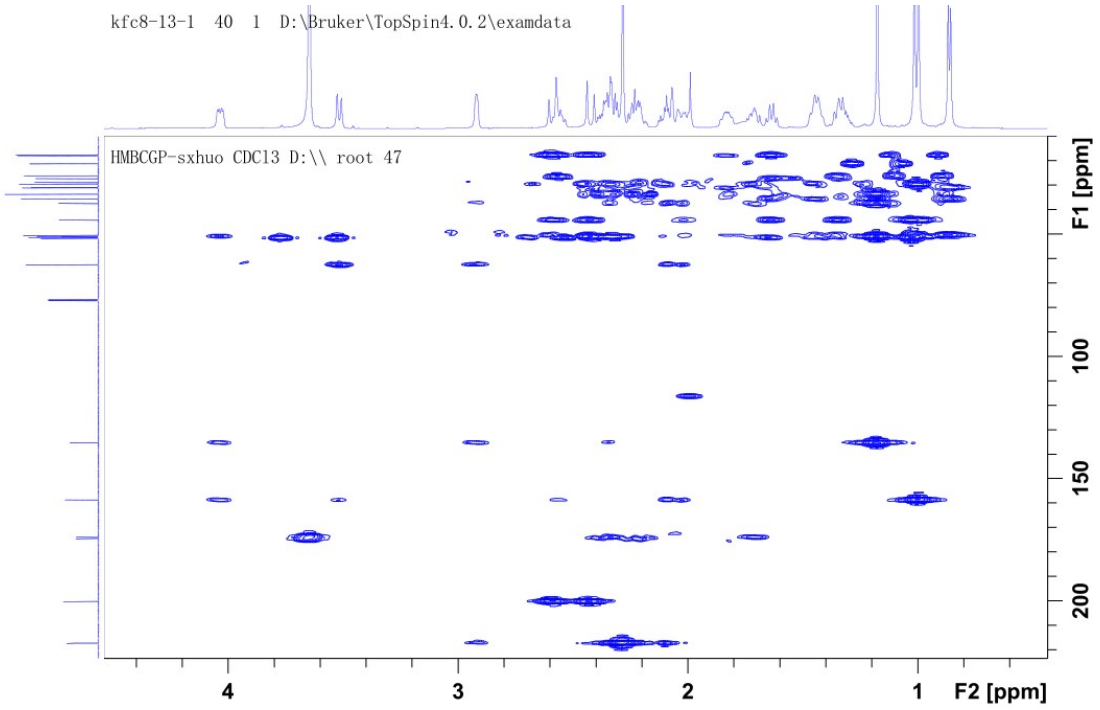


Figure S47. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 7.

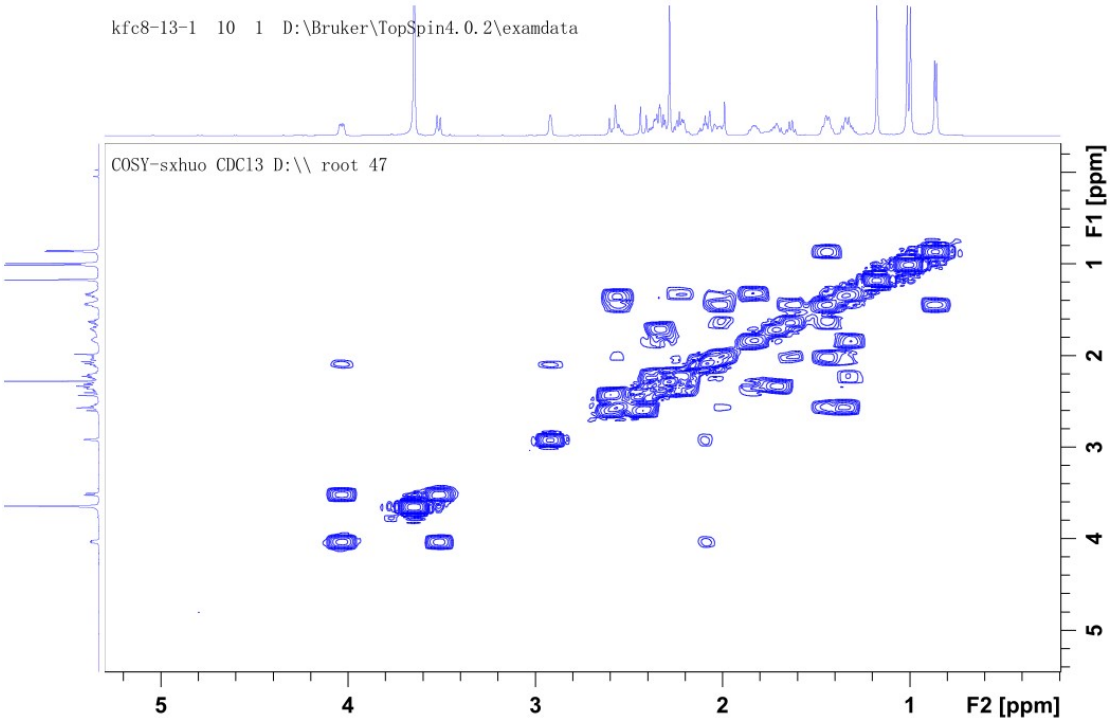


Figure S48. ROESY spectrum (600 MH, $CDCl_3$) of compound 7.

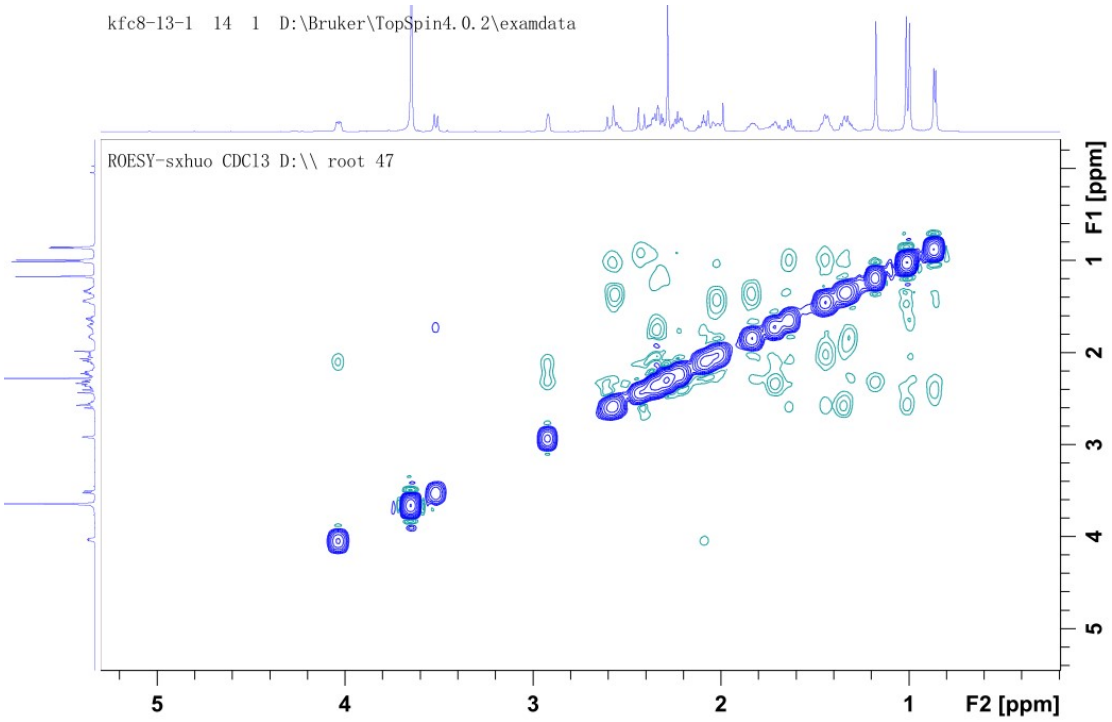


Figure S49. ^1H NMR spectrum (600 MH, $CDCl_3$) of compound 8.

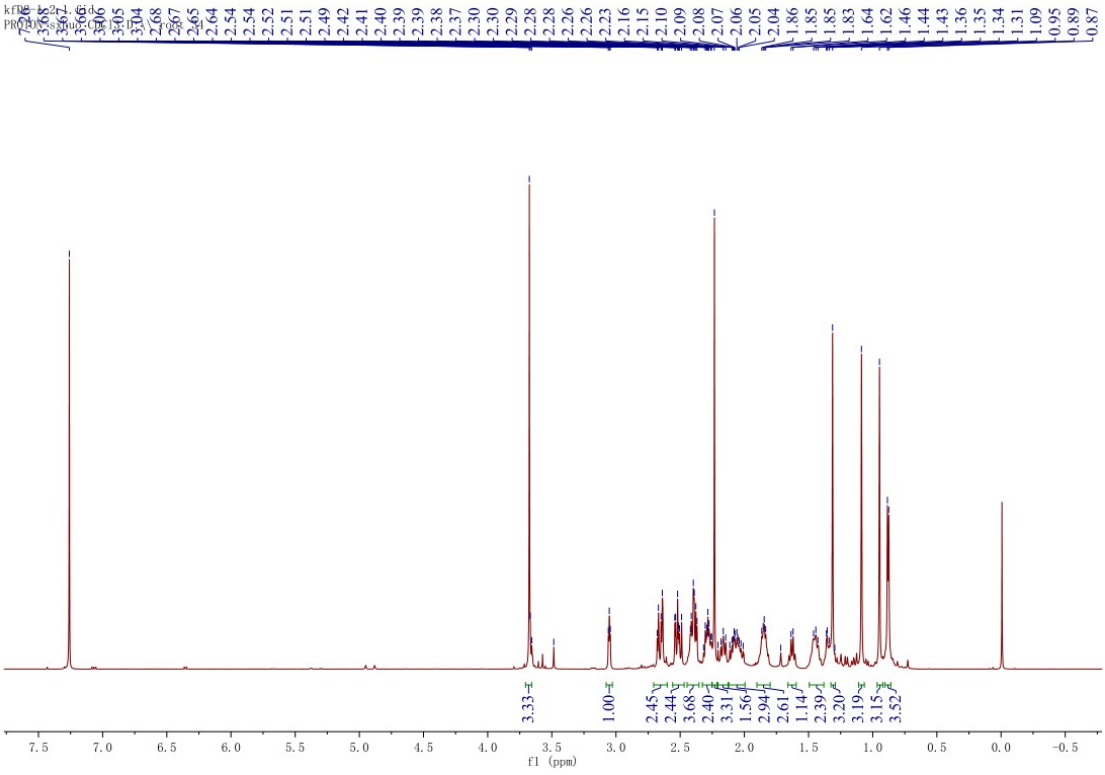


Figure S50. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 8.

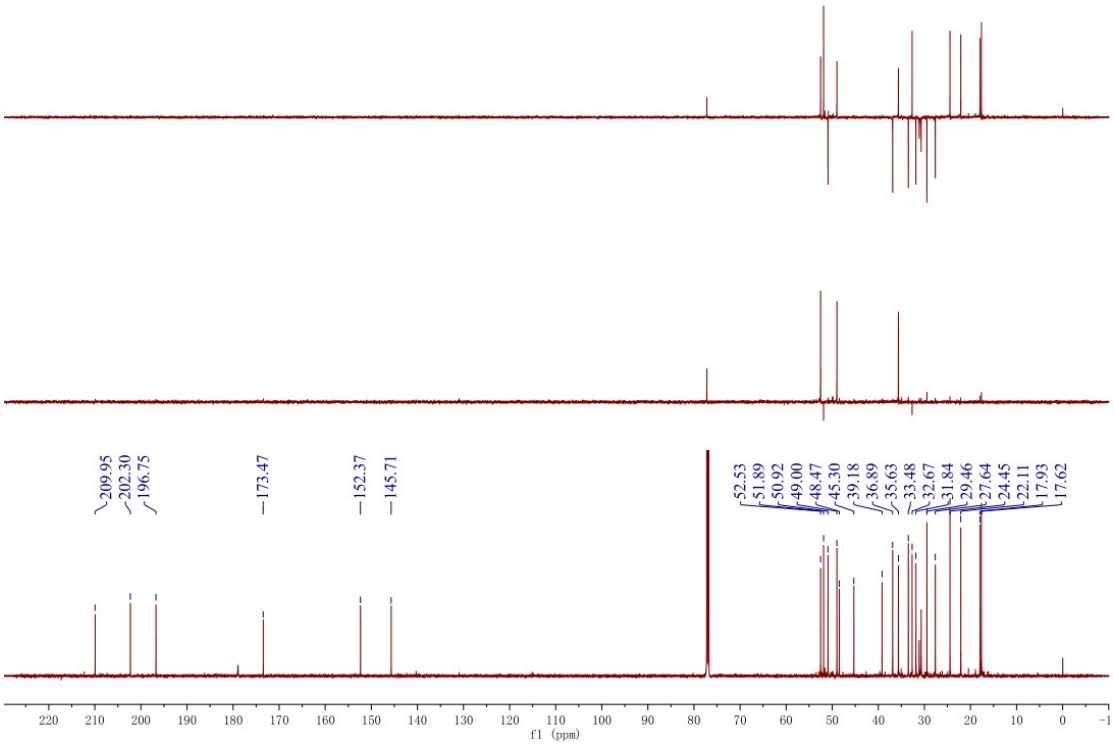


Figure S51. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 8.

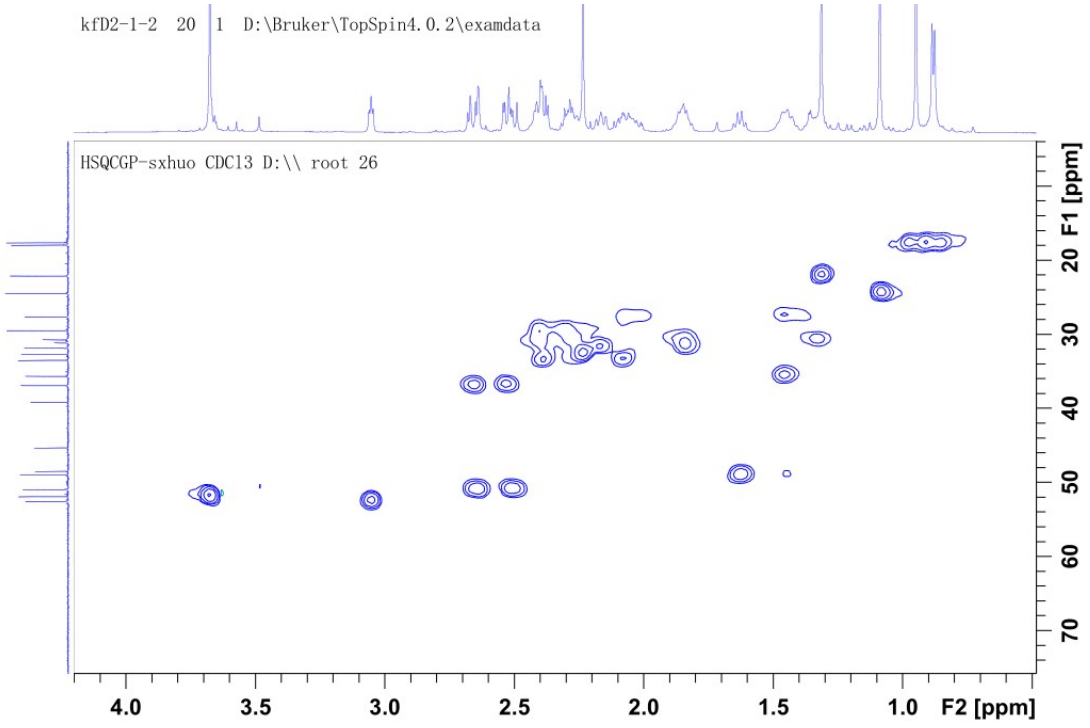


Figure S52. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 8.

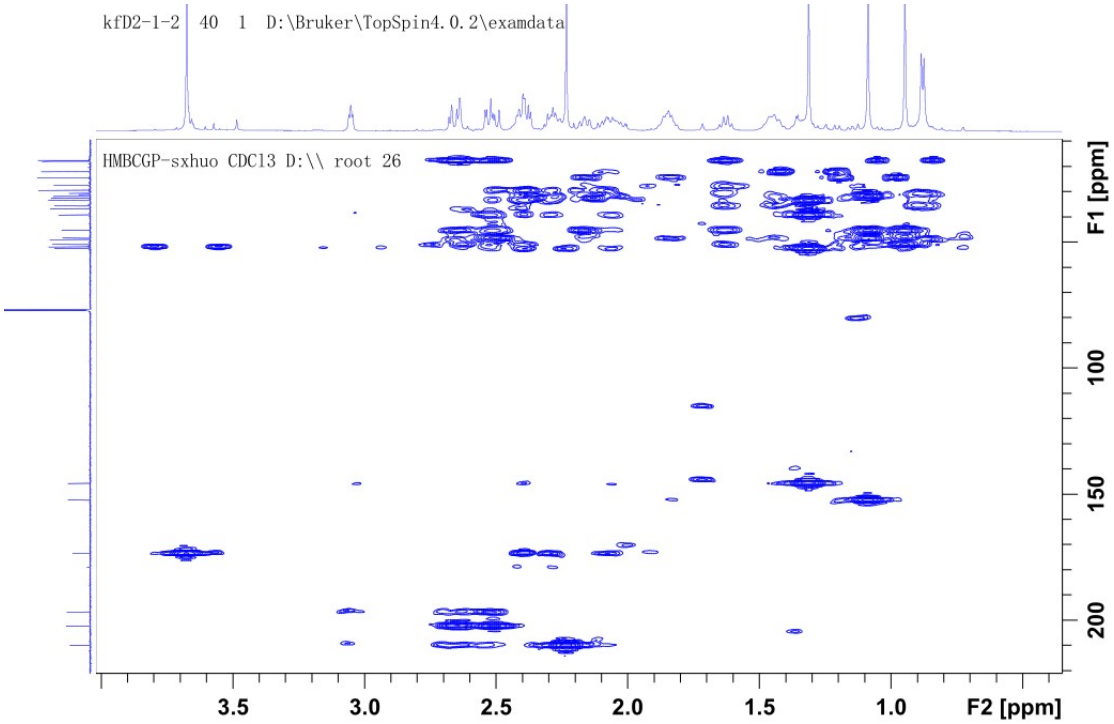


Figure S53.^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 8.

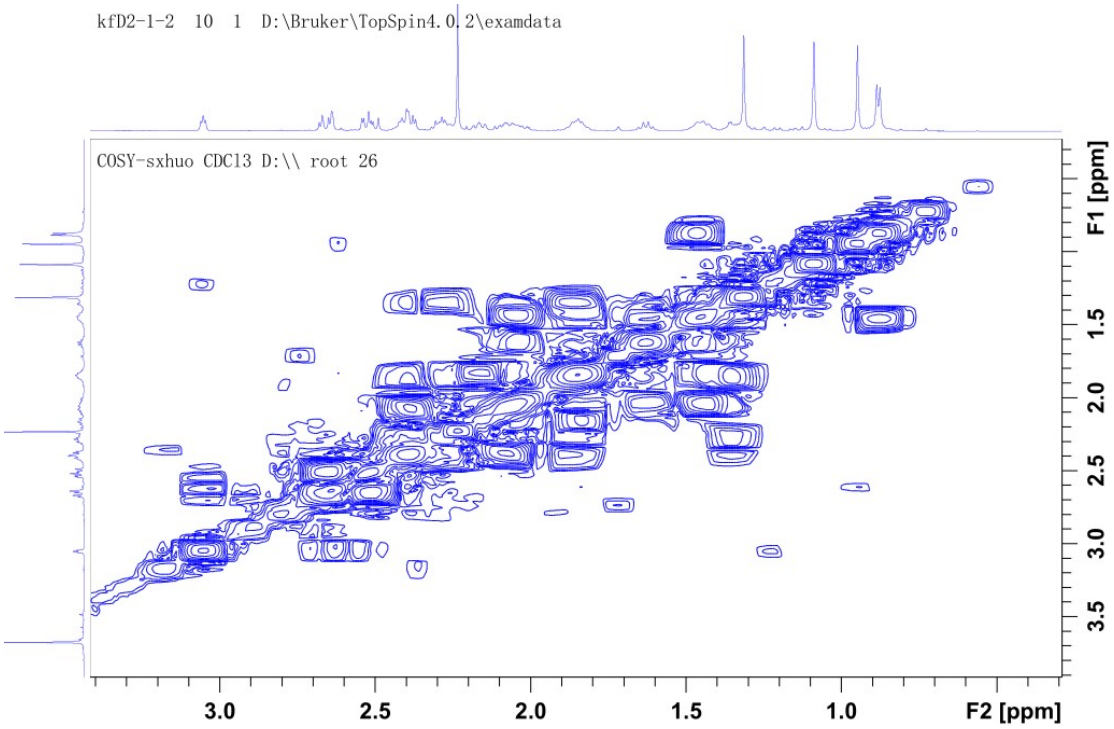


Figure S54. ROESY spectrum (600 MH, $CDCl_3$) of compound 8.

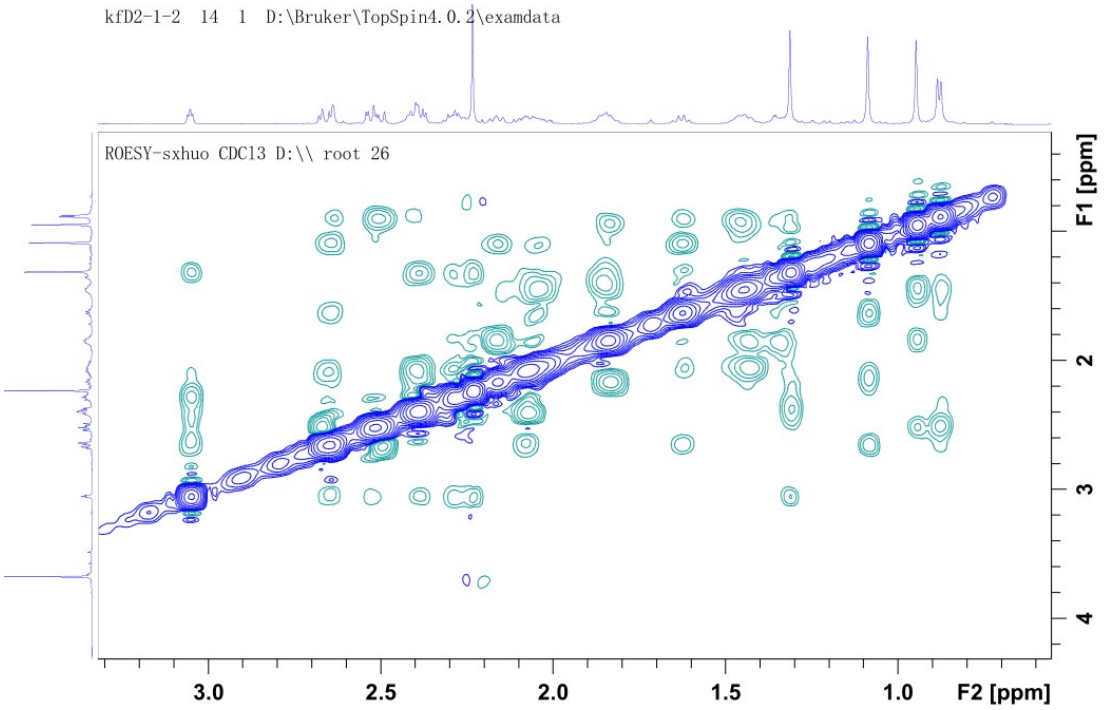


Figure S55. ^1H NMR spectrum (600 MH, $CDCl_3$) of compound 9.

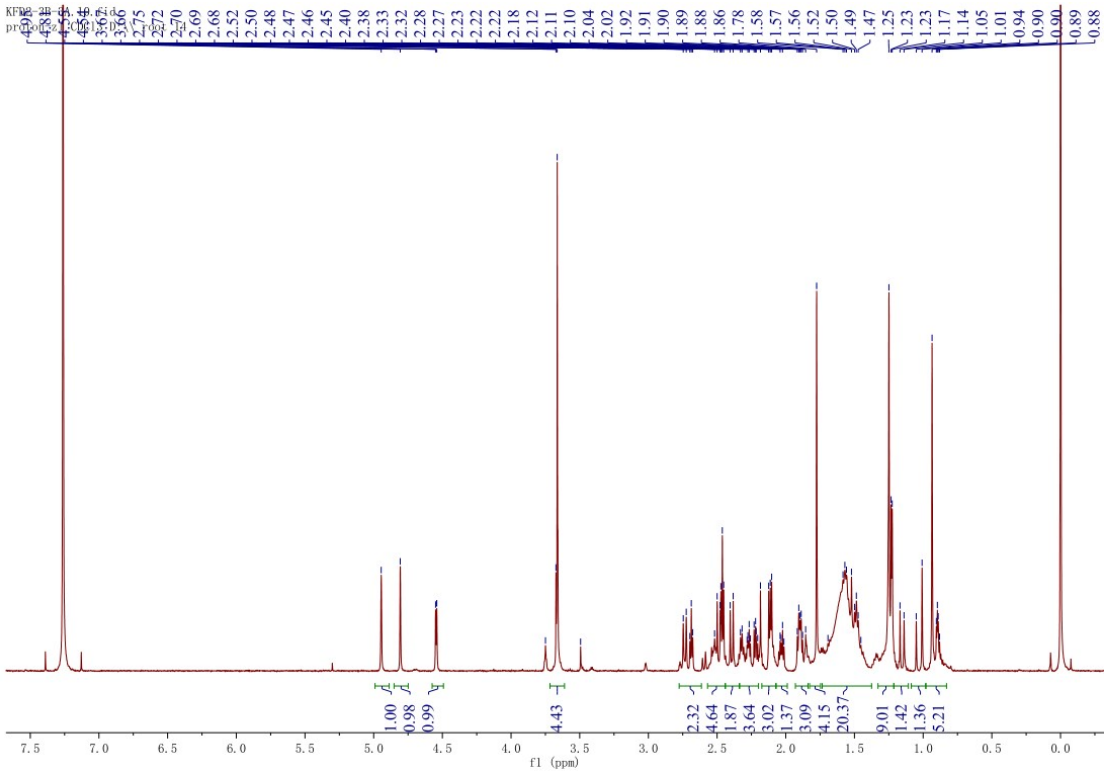


Figure S56. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 9.

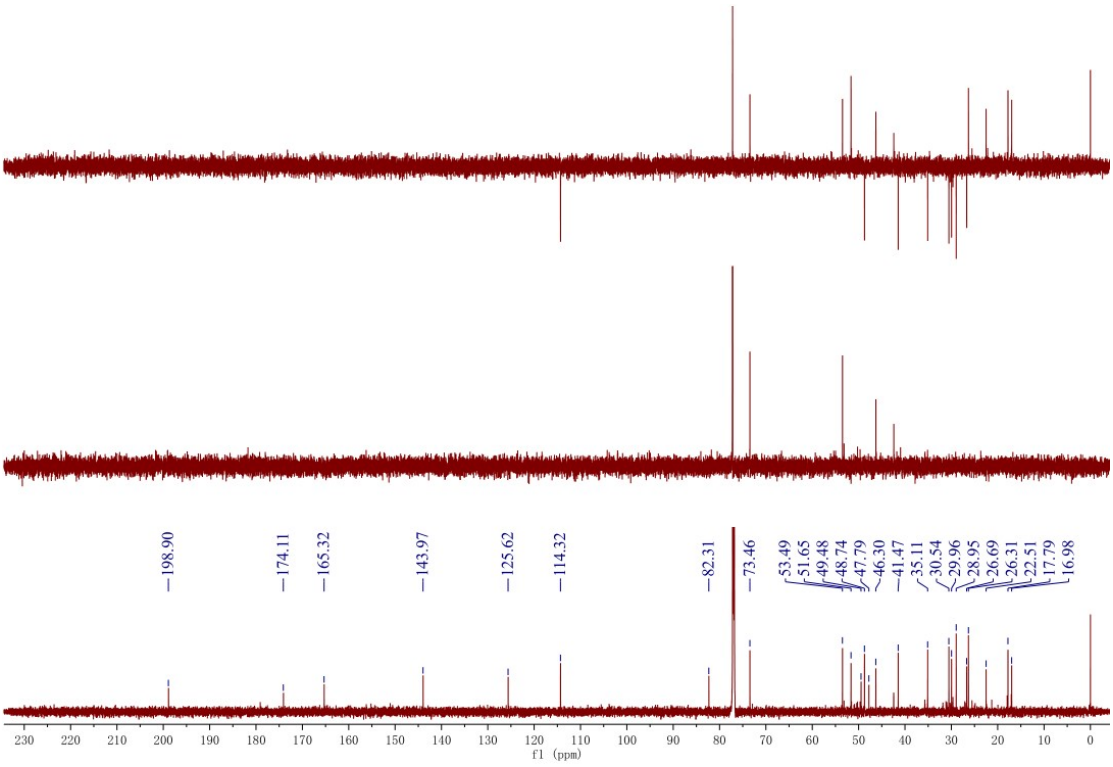


Figure S57. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 9.

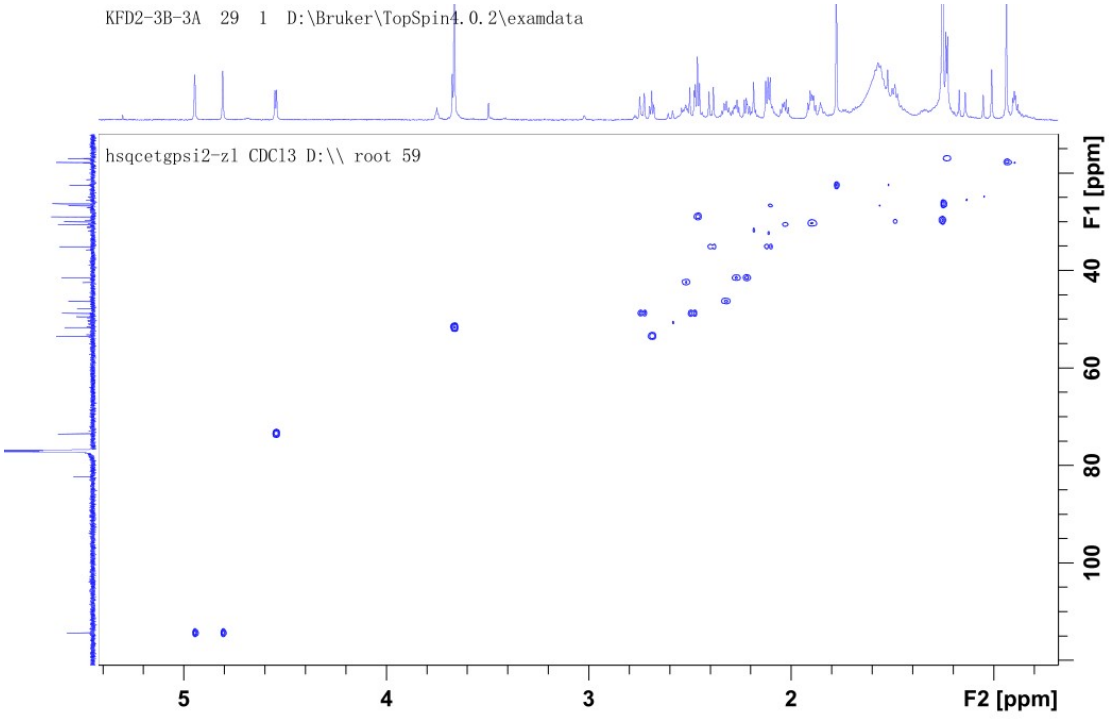


Figure S58. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 9.

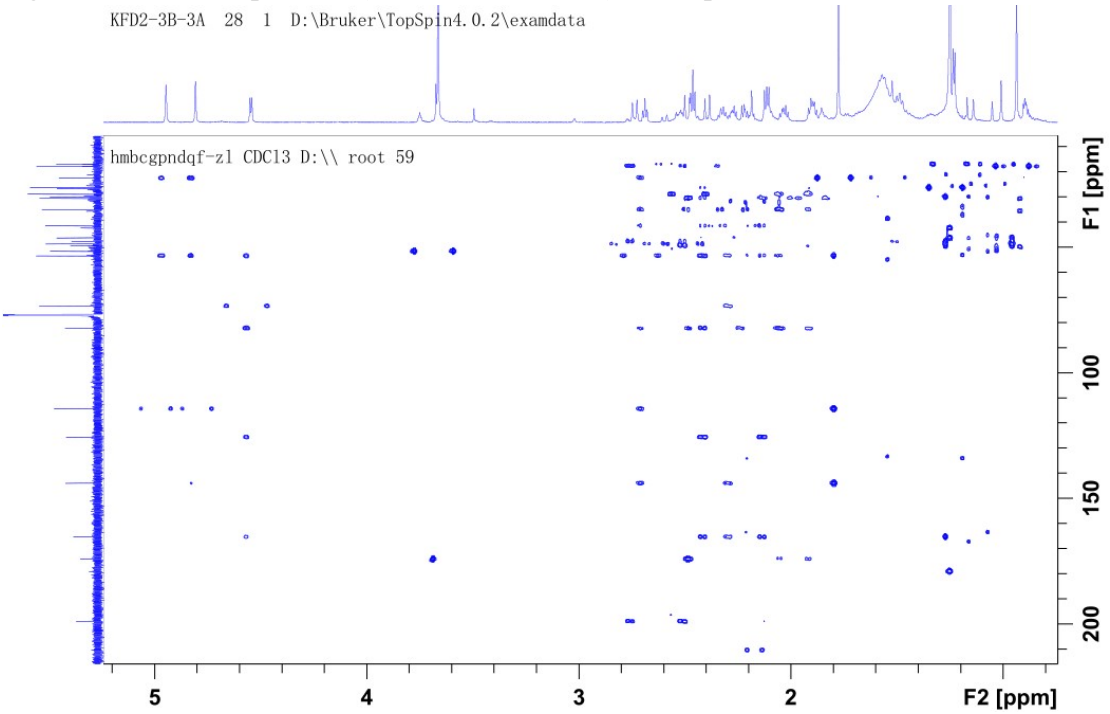


Figure S59. ^{1}H-^{1}H COSY spectrum (600 MH, $CDCl_3$) of compound 9.

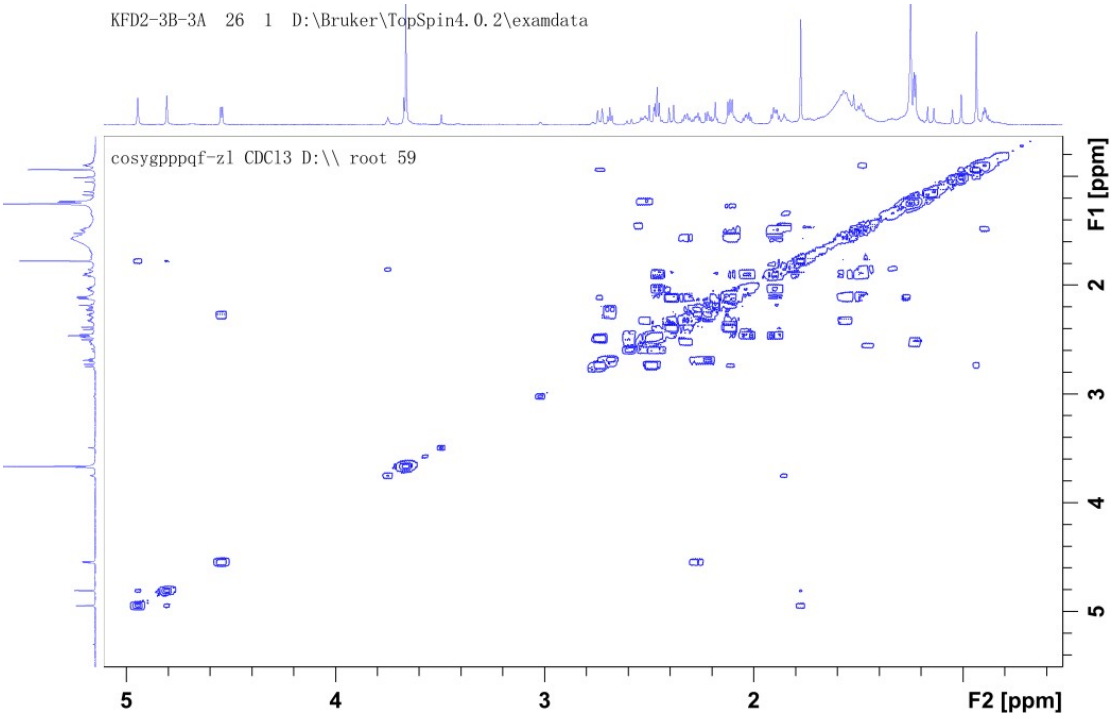


Figure S60. ROESY spectrum (600 MH, $CDCl_3$) of compound 9.

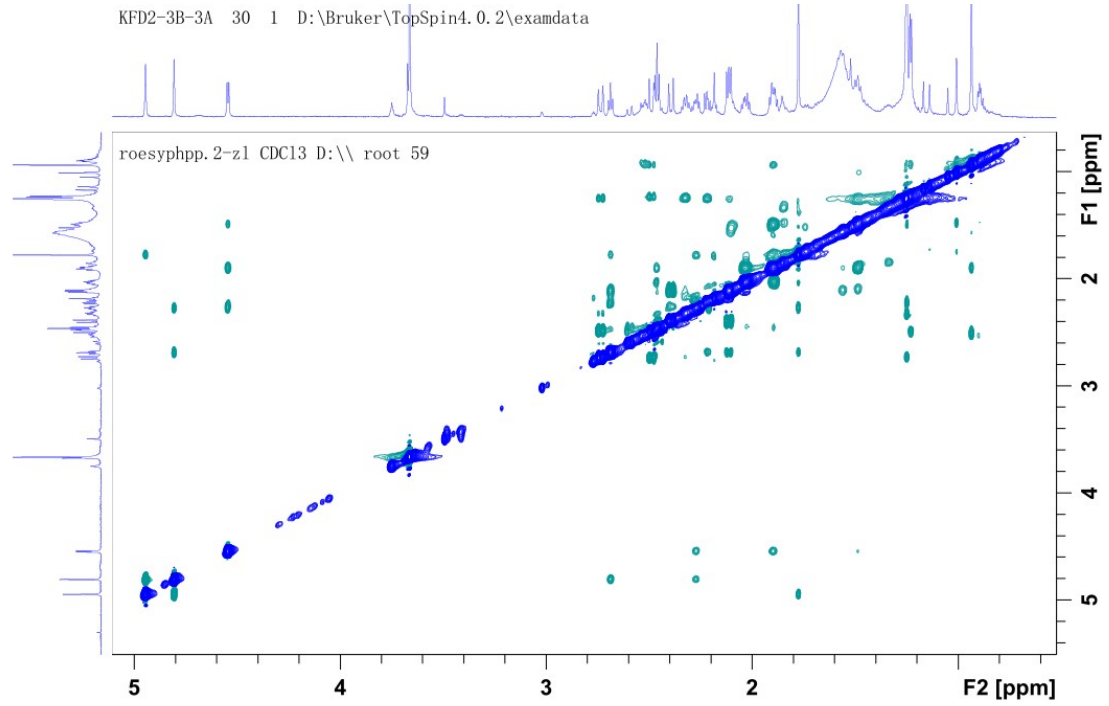


Figure S61. ^1H NMR spectrum (600 MH, $CDCl_3$) of compound 10.

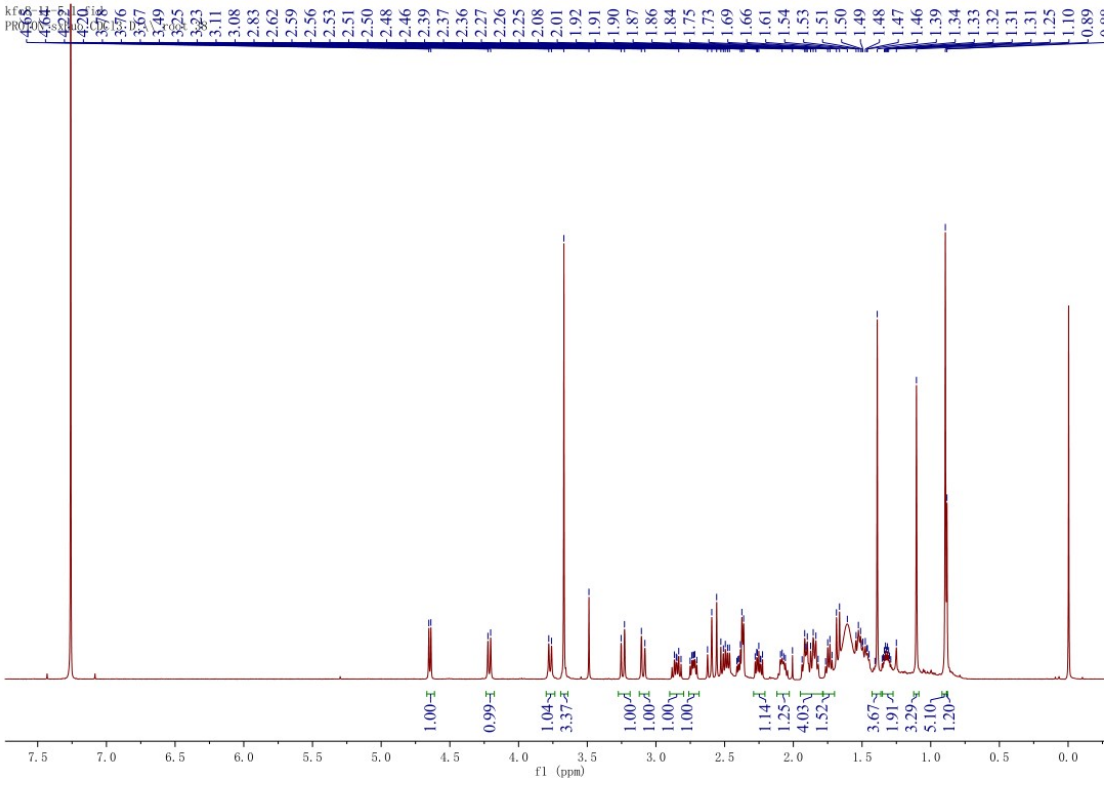


Figure S62. ^{13}C NMR spectrum (150 MH, $CDCl_3$) of compound 10.

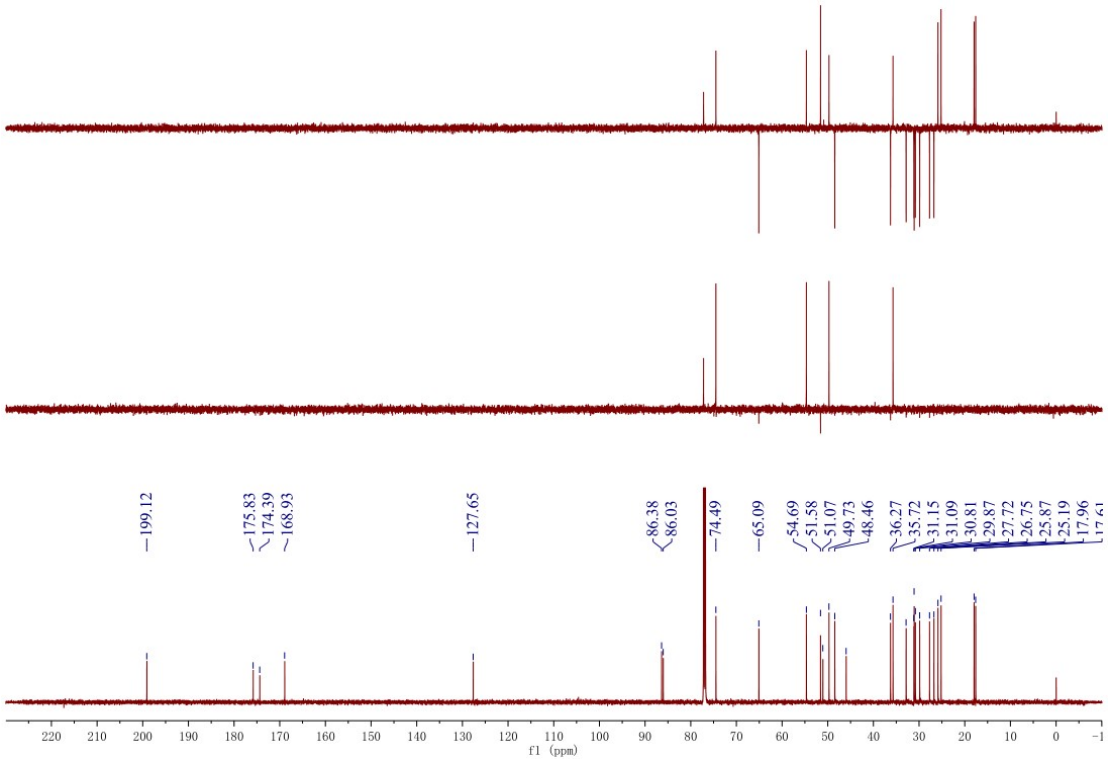


Figure S63. HSQC spectrum (600/150 MH, $CDCl_3$) of compound 10.

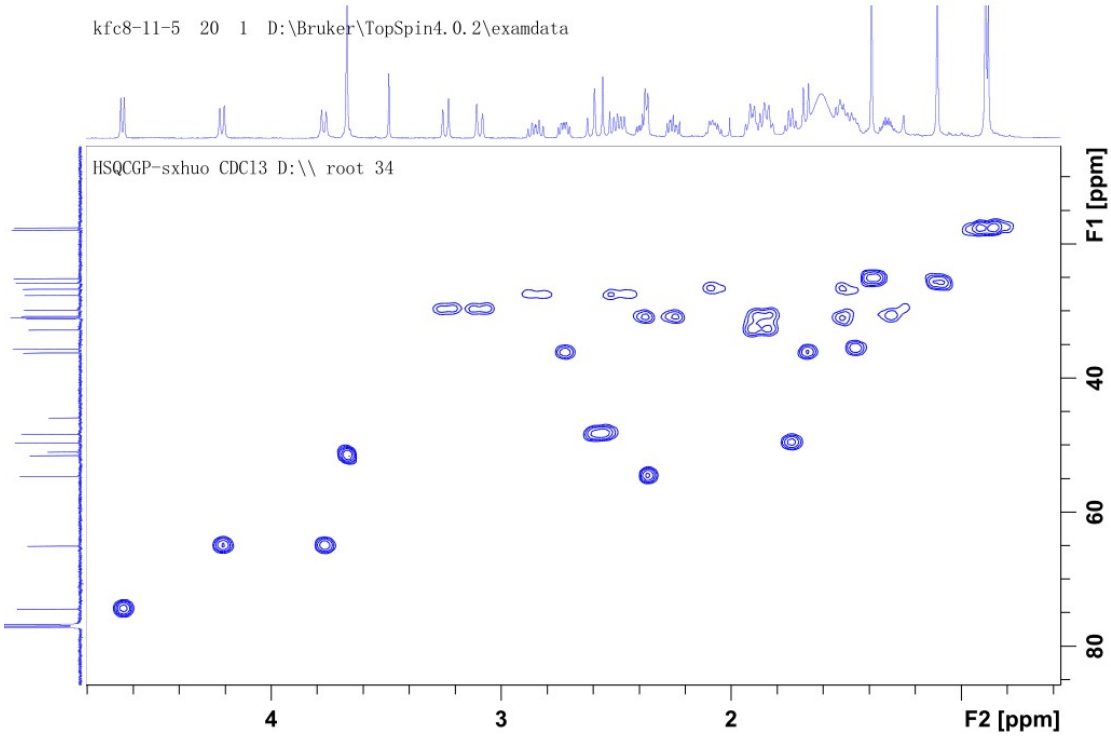


Figure S64. HMBC spectrum (600/150 MH, $CDCl_3$) of compound 10.

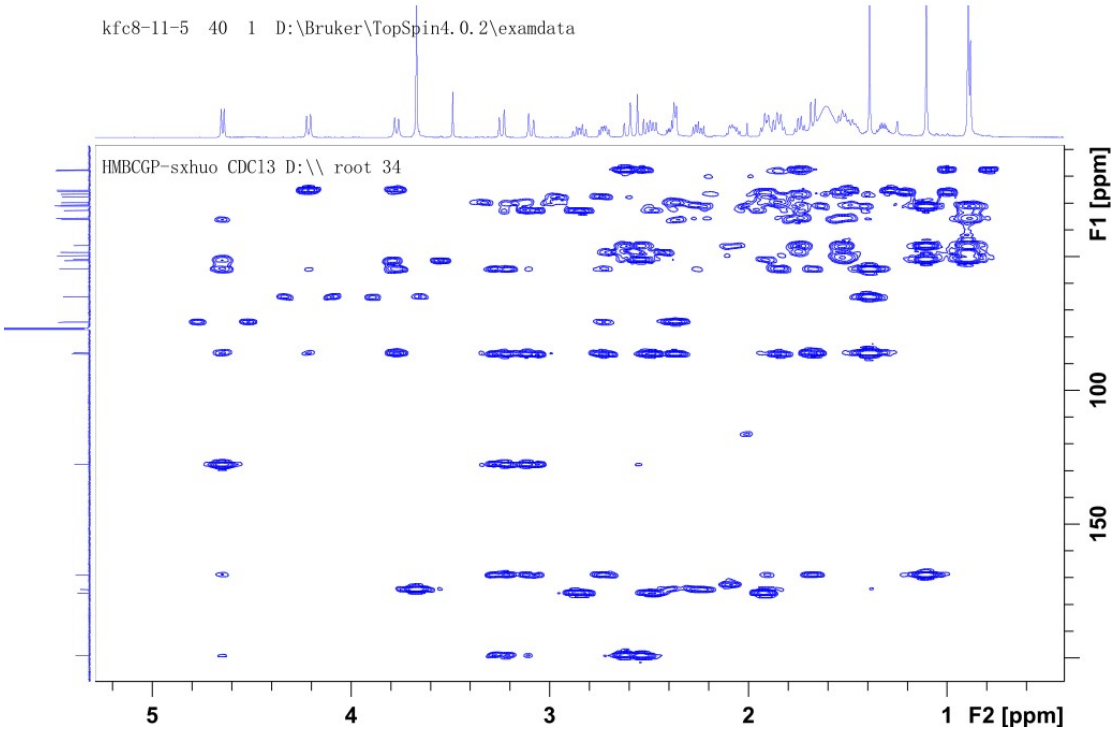


Figure S65. ^1H-^1H COSY spectrum (600 MH, $CDCl_3$) of compound 10.

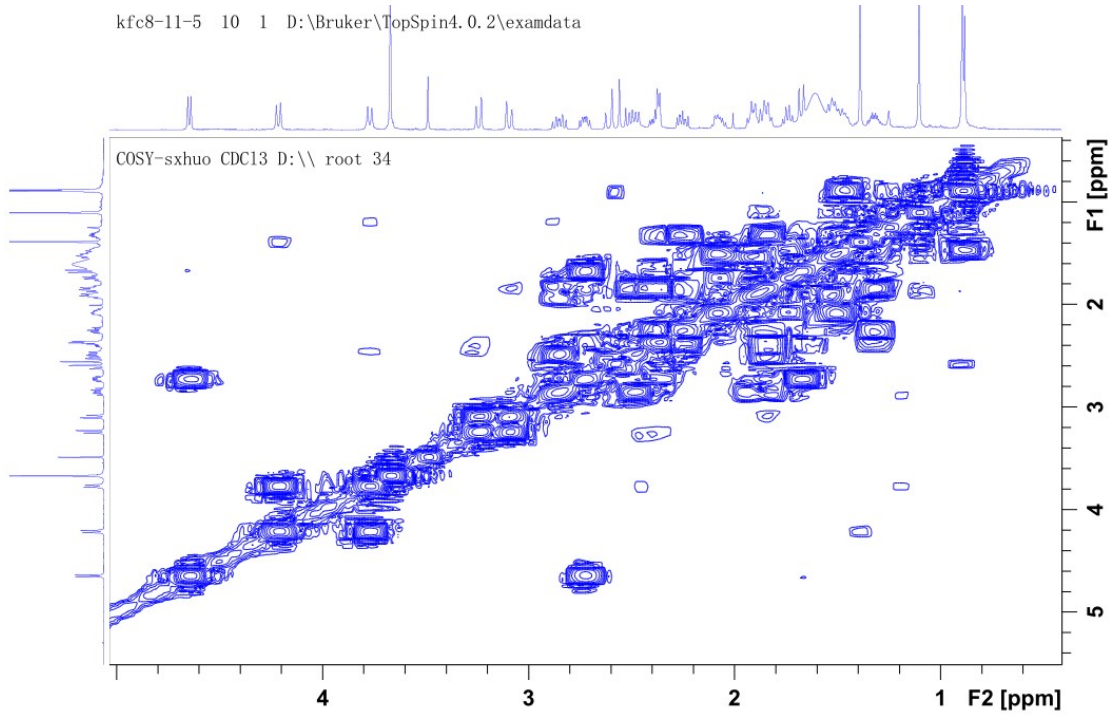
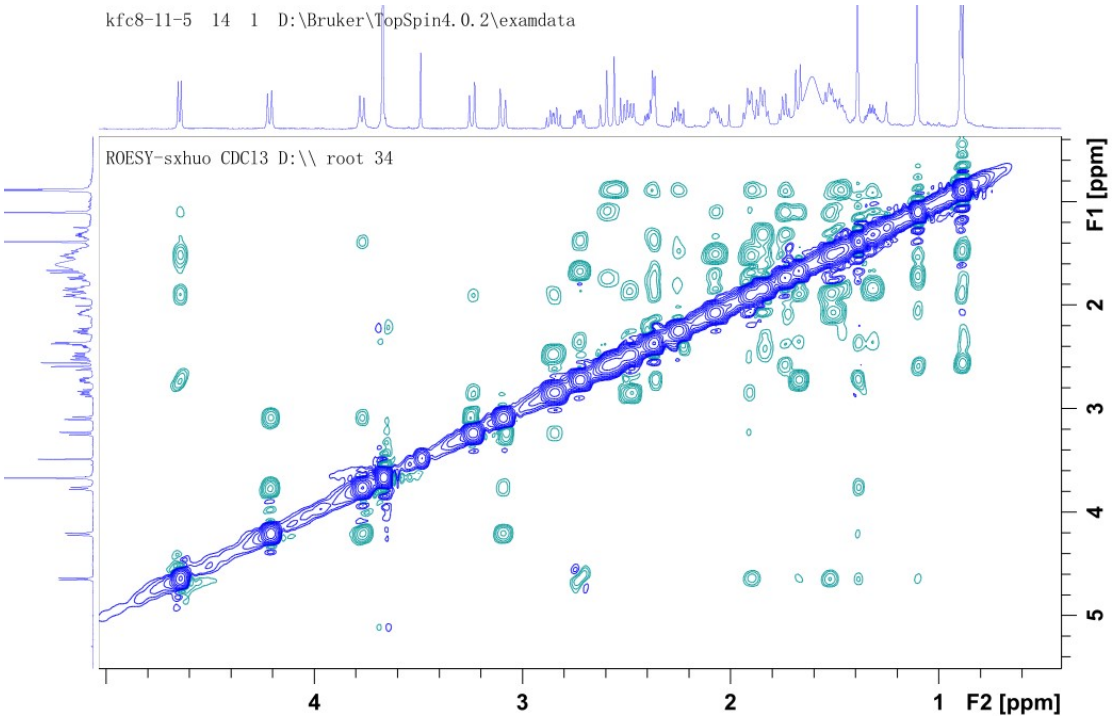


Figure S66. ROESY spectrum (600 MH, $CDCl_3$) of compound 10.



HRESIMS spectra of new compounds

Figure S67. **HRESIMS spectrum of compound 1.**

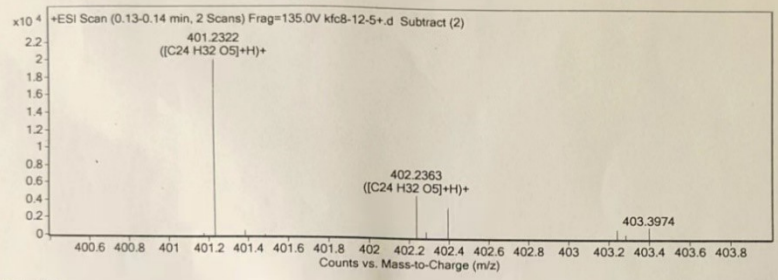
Qualitative Analysis Report

Data Filename	kfc8-12-5+.d	**Sample Name**	kfc8-12-5
Sample Type	Sample	**Position**	P1-C2
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	8/5/2022 7:10:04 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.2746	1	49620.82		
318.3008	1	46747.81		
401.2322	1	19914.69	C24 H32 O5	(M+H)+
437.1936	1	21394.35		
498.4422	1	53674.77		
499.4454	1	19708.68		
608.4251	1	47733.64		
609.4277	1	20782.95		
626.4351	1	42411.8		
627.4383	1	18953.54		

Formula Calculator Element Limits

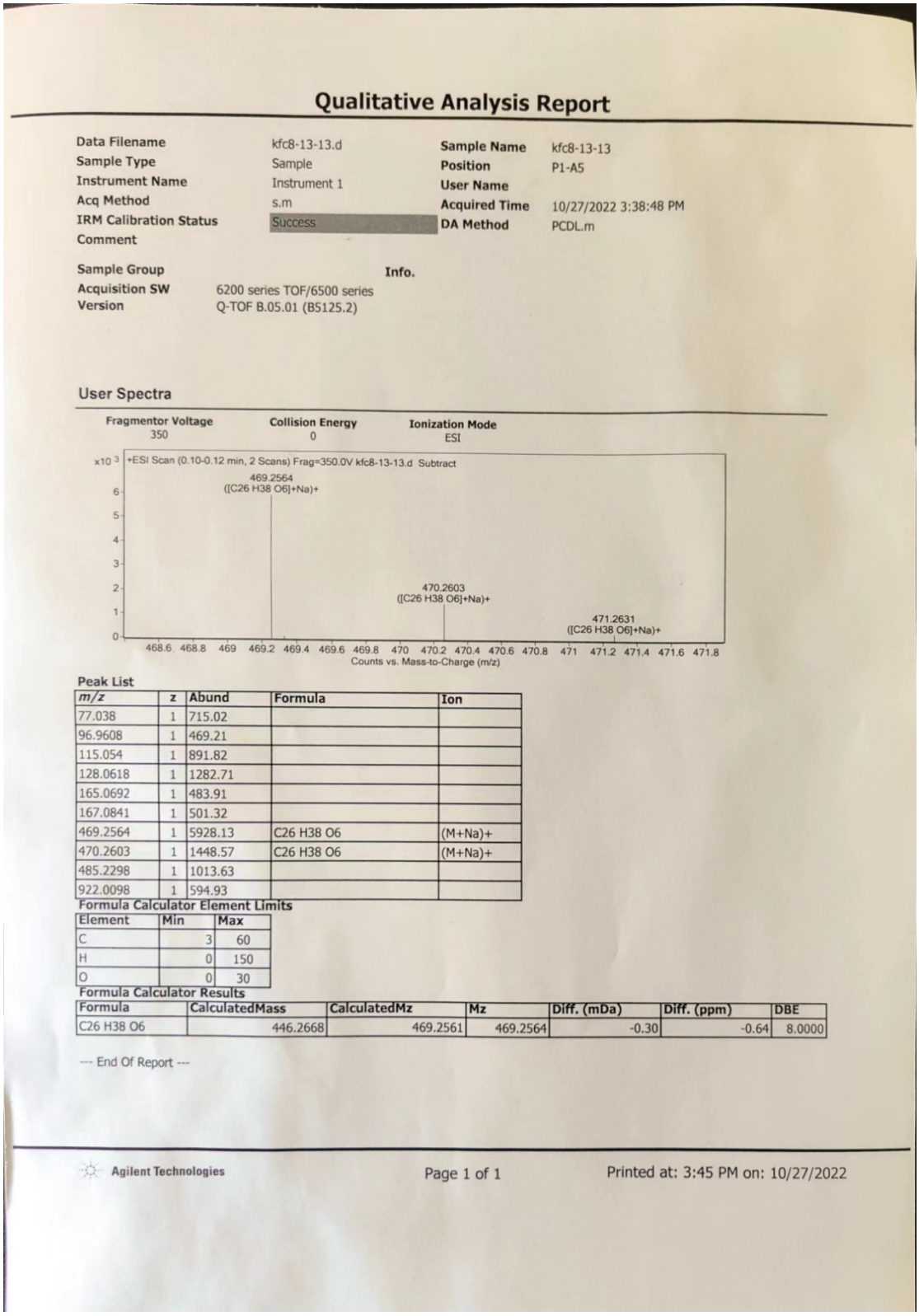
Element	Min	Max
C	3	60
H	0	300
O	0	30
Cl	0	1

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C24 H32 O5	400.2250	401.2323	401.2322	0.10	0.25	9.0000

--- End Of Report ---

Figure S68. HRESIMS spectrum of compound 2.



Qualitative Analysis Report

Data Filename	kfc8-13-13.d	**Sample Name**	kfc8-13-13
Sample Type	Sample	**Position**	P1-A5
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	10/27/2022 3:38:48 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
350	0	ESI

Peak List

m/z	z	Abund	Formula	Ion
77.038	1	715.02		
96.9608	1	469.21		
115.054	1	891.82		
128.0618	1	1282.71		
165.0692	1	483.91		
167.0841	1	501.32		
469.2564	1	5928.13	C26 H38 O6	(M+Na)+
470.2603	1	1448.57	C26 H38 O6	(M+Na)+
485.2298	1	1013.63		
922.0098	1	594.93		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	150
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C26 H38 O6	446.2668	469.2561	469.2564	-0.30	-0.64	8.0000

--- End Of Report ---

Figure S69. HRESIMS spectrum of compound 3.

Qualitative Analysis Report

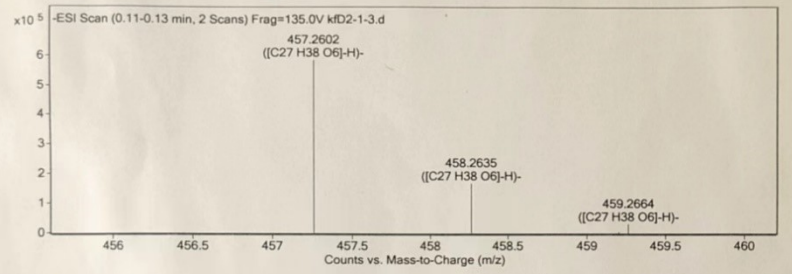
Data Filename	kfD2-1-3.d	**Sample Name**	kfD2-1-3
Sample Type	Sample	**Position**	P1-A2
Instrument Name	Instrument 1	**User Name**	
Acq Method	s-.m	**Acquired Time**	7/7/2022 3:49:00 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
112.9856		105301.97		
119.0365	1	129092.3		
457.2602	1	585371.81	C27 H38 O6	(M-H)-
458.2635	1	167561.88	C27 H38 O6	(M-H)-
503.2655	1	145443.75		
504.2686	1	45851.85		
525.2473	1	45404.75		
915.526	1	52806.61		
966.0004	1	46023.82		
1033.9881	1	97520.19		

Formula Calculator Element Limits

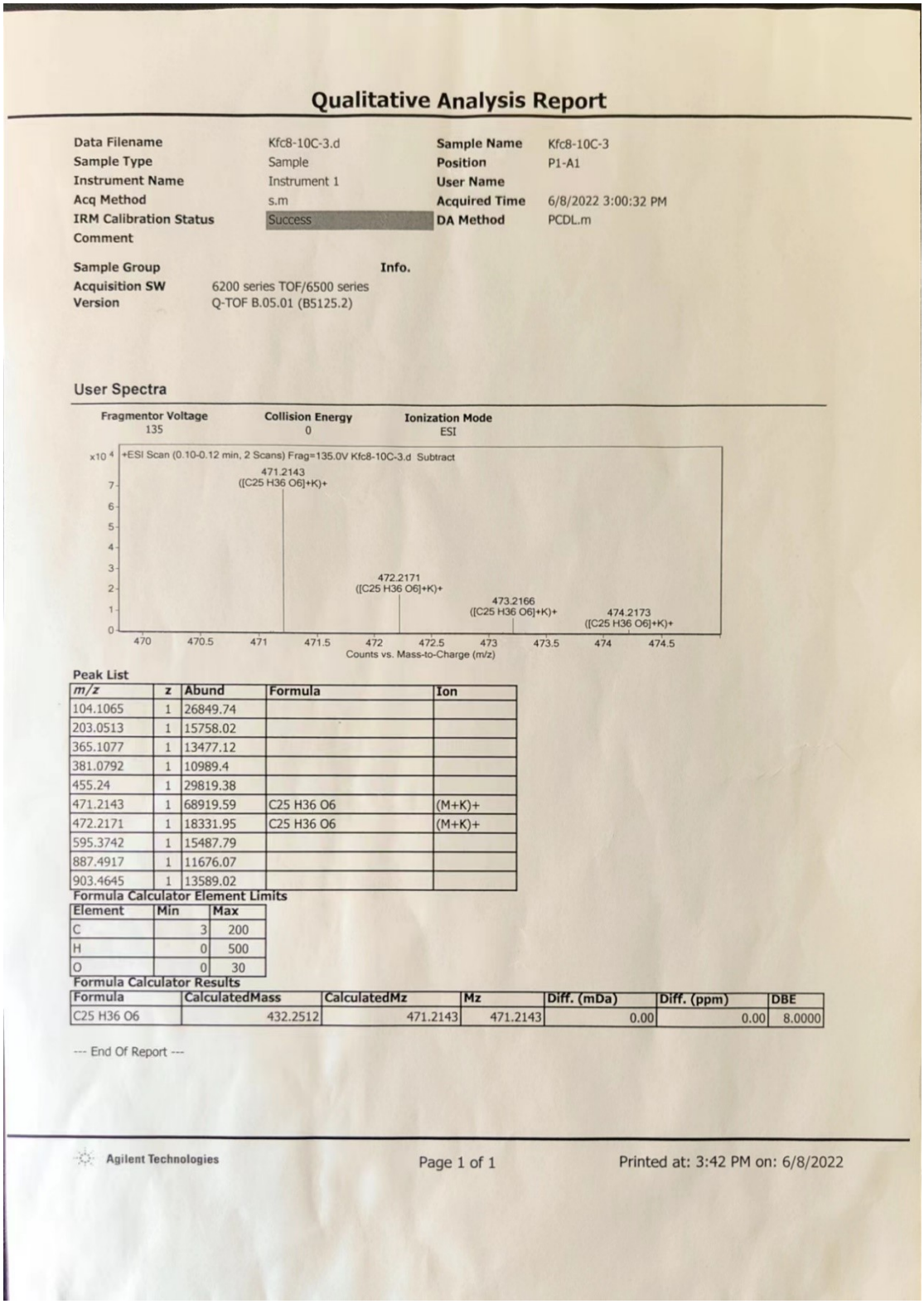
Element	Min	Max
C	3	120
H	0	250
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C27 H38 O6	458.2668	457.2596	457.2602	-0.60	-1.31	9.0000

--- End Of Report ---

Figure S70. HRESIMS spectrum of compound 4.



Qualitative Analysis Report

Data Filename	Kfc8-10C-3.d	**Sample Name**	Kfc8-10C-3
Sample Type	Sample	**Position**	P1-A1
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	6/8/2022 3:00:32 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI

Peak List

m/z	z	Abund	Formula	Ion
104.1065	1	26849.74		
203.0513	1	15758.02		
365.1077	1	13477.12		
381.0792	1	10989.4		
455.24	1	29819.38		
471.2143	1	68919.59	C25 H36 O6	(M+K)+
472.2171	1	18331.95	C25 H36 O6	(M+K)+
595.3742	1	15487.79		
887.4917	1	11676.07		
903.4645	1	13589.02		

Formula Calculator Element Limits

Element	Min	Max
C	3	200
H	0	500
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C25 H36 O6	432.2512	471.2143	471.2143	0.00	0.00	8.0000

--- End Of Report ---

Figure S71. HRESIMS spectrum of compound 5.

Qualitative Analysis Report

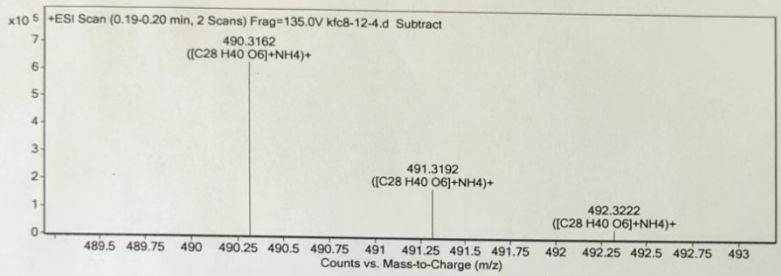
Data Filename	kfc8-12-4.d	**Sample Name**	kfc8-12-4
Sample Type	Sample	**Position**	P1-A2
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	8/3/2022 2:25:06 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
473.2897	1	173277.55		
490.3162	1	626633.81	C28 H40 O6	(M+NH4)+
491.3192	1	175515	C28 H40 O6	(M+NH4)+
495.2714	1	154990.91		
518.3472	1	119163.45		
962.5977	1	99514.55		
963.601	1	62775.43		
967.5539	1	490104.38		
968.5569	1	304059.59		
969.5595	1	98724.64		

Formula Calculator Element Limits

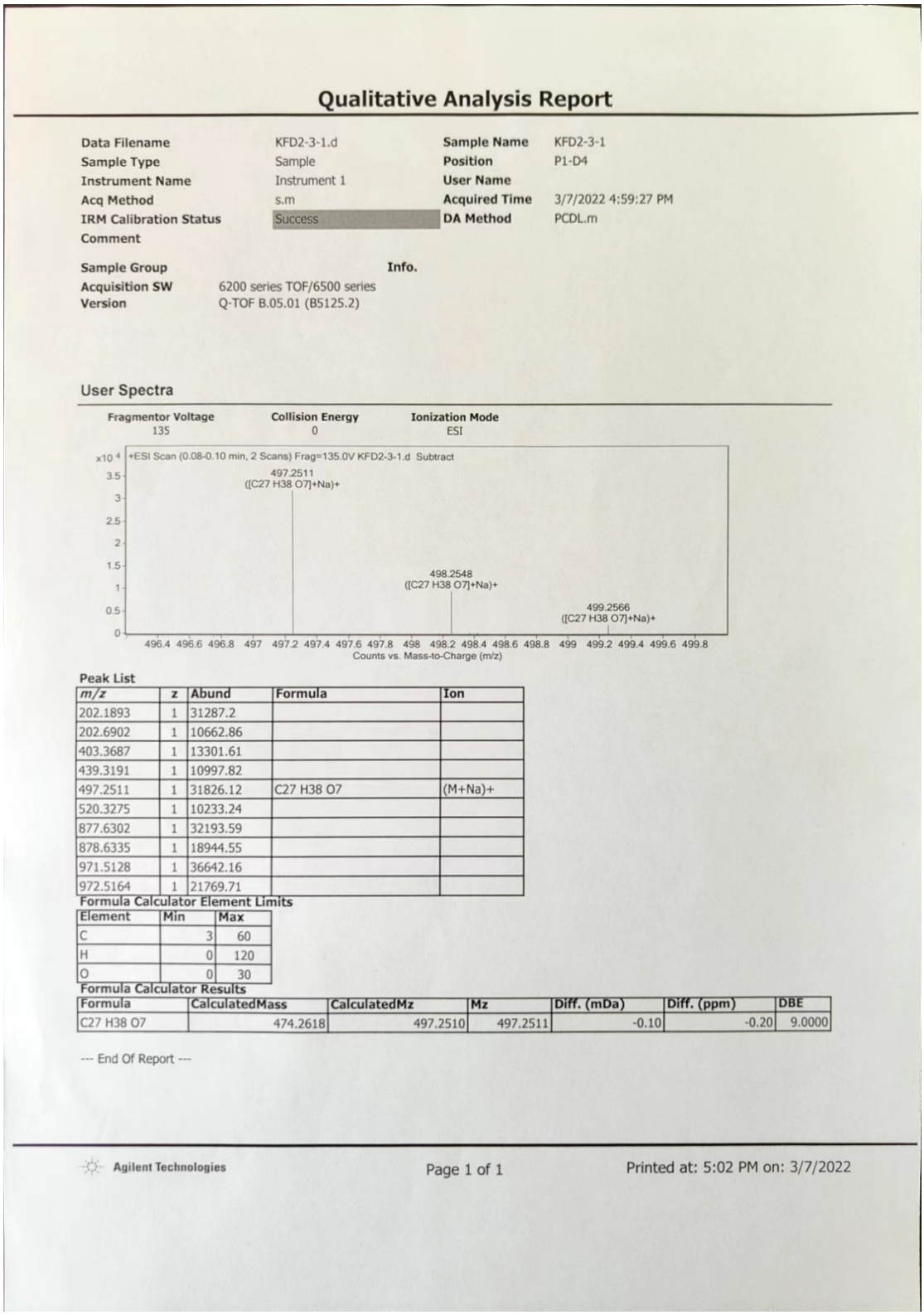
Element	Min	Max
C	3	60
H	0	300
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C28 H40 O6	472.2825	490.3163	490.3162	0.10	0.20	9.0000

--- End Of Report ---

Figure S72. HRESIMS spectrum of compound 6.



Qualitative Analysis Report

Data Filename	KFD2-3-1.d	**Sample Name**	KFD2-3-1
Sample Type	Sample	**Position**	P1-D4
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	3/7/2022 4:59:27 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI

Peak List

m/z	z	Abund	Formula	Ion
202.1893	1	31287.2		
202.6902	1	10662.86		
403.3687	1	13301.61		
439.3191	1	10997.82		
497.2511	1	31826.12	C27 H38 O7	(M+Na)+
520.3275	1	10233.24		
877.6302	1	32193.59		
878.6335	1	18944.55		
971.5128	1	36642.16		
972.5164	1	21769.71		

Formula Calculator Element Limits

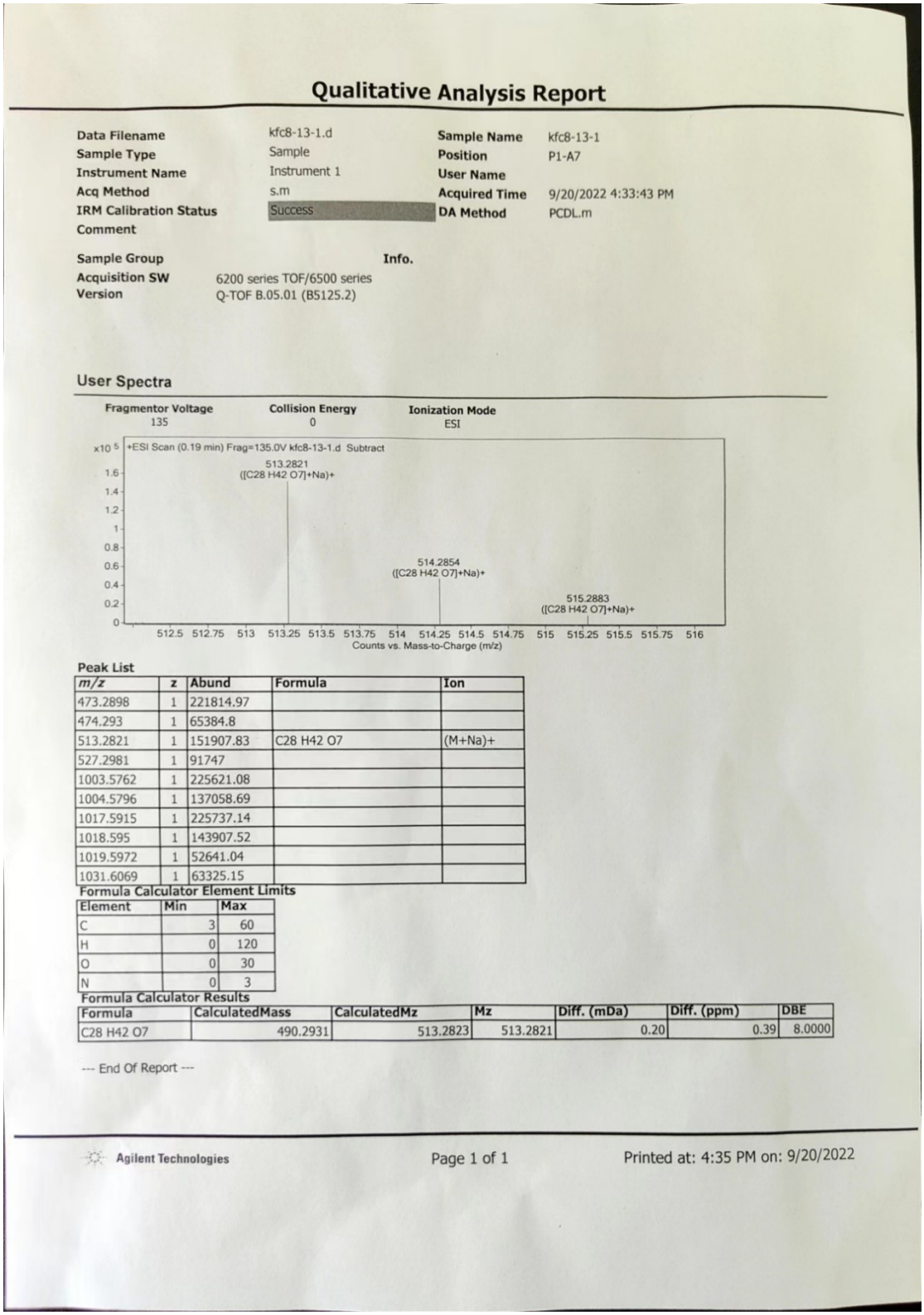
Element	Min	Max
C	3	60
H	0	120
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C27 H38 O7	474.2618	497.2510	497.2511	-0.10	-0.20	9.0000

--- End Of Report ---

Figure S73. HRESIMS spectrum of compound 7.



Qualitative Analysis Report

Data Filename	kfc8-13-1.d	**Sample Name**	kfc8-13-1
Sample Type	Sample	**Position**	P1-A7
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	9/20/2022 4:33:43 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI

Peak List

m/z	z	Abund	Formula	Ion
473.2898	1	221814.97		
474.293	1	65384.8		
513.2821	1	151907.83	C28 H42 O7	(M+Na)+
527.2981	1	91747		
1003.5762	1	225621.08		
1004.5796	1	137058.69		
1017.5915	1	225737.14		
1018.595	1	143907.52		
1019.5972	1	52641.04		
1031.6069	1	63325.15		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C28 H42 O7	490.2931	513.2823	513.2821	0.20	0.39	8.0000

--- End Of Report ---

Figure S74. HRESIMS spectrum of compound 8.

Qualitative Analysis Report

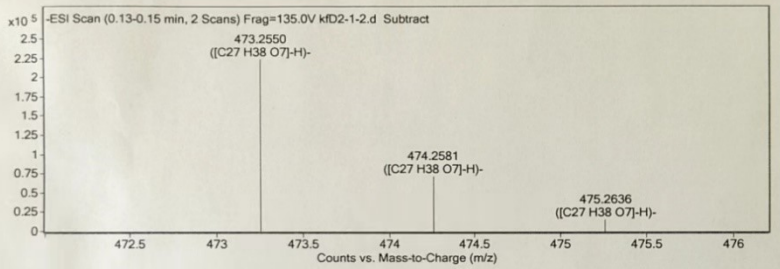
Data Filename	kfD2-1-2.d	**Sample Name**	kfD2-1-2
Sample Type	Sample	**Position**	P1-A1
Instrument Name	Instrument 1	**User Name**	
Acq Method	s-.m	**Acquired Time**	7/7/2022 3:47:48 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
112.9856		20192.06		
375.2756	1	9774.97		
473.255	1	223294.16	C27 H38 O7	(M-H)-
474.2581	1	71663.35	C27 H38 O7	(M-H)-
475.2636	1	14966.73	C27 H38 O7	(M-H)-
487.2702	1	12957.75		
519.2604	1	70048.14		
520.2635	1	21239.5		
541.2417	1	13120.13		
1033.9881	1	11821.45		

Formula Calculator Element Limits

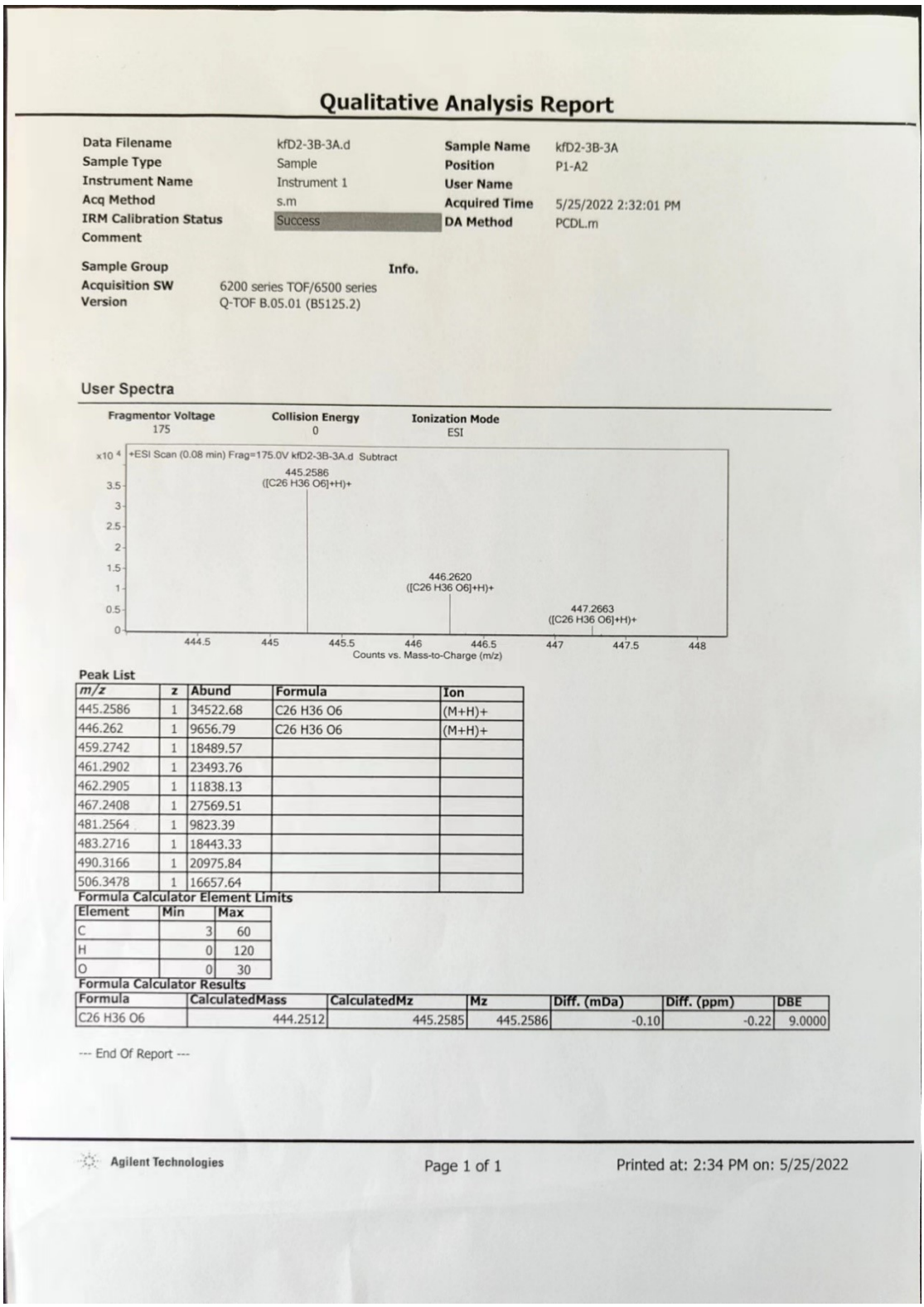
Element	Min	Max
C	3	120
H	0	250
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C27 H38 O7	474.2618	473.2545	473.2550	-0.50	-1.06	9.0000

--- End Of Report ---

Figure S75. HRESIMS spectrum of compound 9.



Qualitative Analysis Report

Data Filename	kfD2-3B-3A.d	**Sample Name**	kfD2-3B-3A
Sample Type	Sample	**Position**	P1-A2
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	5/25/2022 2:32:01 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI

Peak List

m/z	z	Abund	Formula	Ion
445.2586	1	34522.68	C26 H36 O6	(M+H)+
446.262	1	9656.79	C26 H36 O6	(M+H)+
459.2742	1	18489.57		
461.2902	1	23493.76		
462.2905	1	11838.13		
467.2408	1	27569.51		
481.2564	1	9823.39		
483.2716	1	18443.33		
490.3166	1	20975.84		
506.3478	1	16657.64		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C26 H36 O6	444.2512	445.2585	445.2586	-0.10	-0.22	9.0000

--- End Of Report ---

Figure S76. HRESIMS spectrum of compound 10.

Qualitative Analysis Report

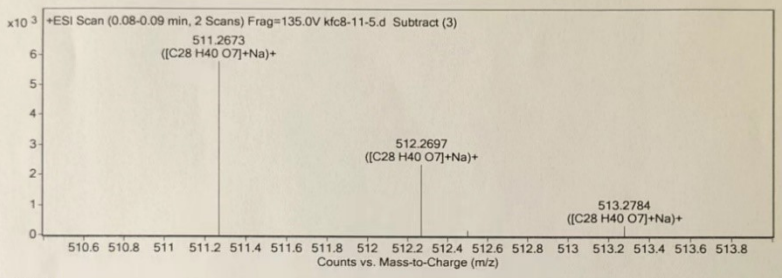
Data Filename	kfc8-11-5.d	**Sample Name**	kfc8-11-5
Sample Type	Sample	**Position**	P1-A6
Instrument Name	Instrument 1	**User Name**	
Acq Method	s.m	**Acquired Time**	7/18/2022 5:12:04 PM
IRM Calibration Status	Success	**DA Method**	PCDL.m
Comment			

Sample Group **Info.**

Acquisition SW Version 6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
274.2742	1	6710.53		
318.3016	1	4426.33		
340.2832	1	1683.01		
353.2664	1	2055.67		
437.1935	1	7427.04		
438.2055	1	1945.35		
506.3114	1	6683.55		
507.3167	1	2324.01		
511.2673	1	5780.68	C28 H40 O7	(M+Na)+
512.2697	1	2383.68	C28 H40 O7	(M+Na)+

Formula Calculator Element Limits

Element	Min	Max
C	3	120
H	0	200
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C28 H40 O7	488.2774	511.2666	511.2673	-0.70	-1.37	9.0000

--- End Of Report ---

X-ray crystallographic data of compounds 2, 4, and 5

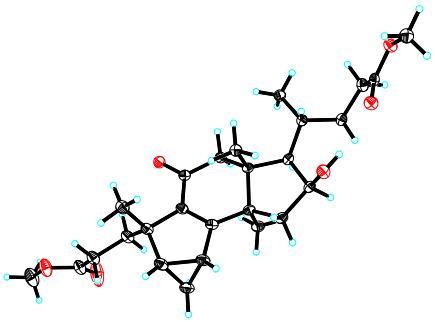


Figure S77. View of a molecule of compound **2** with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

Table S3. Crystal data and structure refinement for compound 2.

Identification code	global	
Empirical formula	$C_{26}\ H_{38}\ O_6$	
Formula weight	446.56	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P21212	
Unit cell dimensions	a = 10.8614(3) Å	α= 90°.
	b = 36.7053(9) Å	β= 90°.
	c = 6.0922(2) Å	γ = 90°.
Volume	2428.78(12) Å3	
Z	4	
Density (calculated)	1.221 mg/m^3	
Absorption coefficient	0.689 mm^{-1}	
F(000)	968	
Crystal size	0.250 × 0.120 × 0.070 mm^3	
Theta range for data collection	2.41 to 68.32°.	
Index ranges	-13<=h<=12, -44<=k<=34, -7<=l<=6	
Reflections collected	15579	
Independent reflections	4402 [R(int) = 0.0887]	
Completeness to theta = 68.32°	99.80%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.95 and 0.79	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4402 / 0 / 296	
Goodness-of-fit on F2	1.099	
Final R indices [I>2sigma(I)]	R1 = 0.0335, wR2 = 0.0856	
R indices (all data)	R1 = 0.0597, wR2 = 0.0960	
Absolute structure parameter	-0.05(6)	

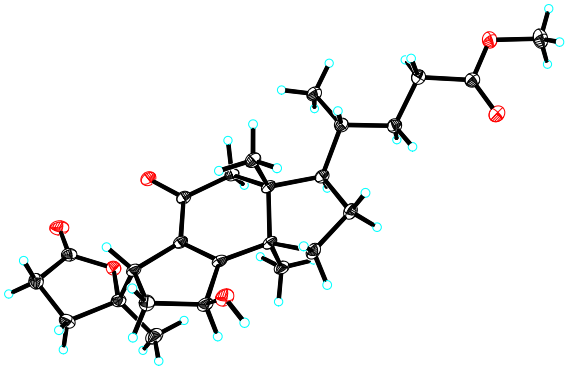


Figure S78. View of a molecule of compound **4** with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

Table S4. Crystal data and structure refinement for compound 4.

Identification code	global	
Empirical formula	$C_{25}H_{36}O_6$	
Formula weight	432.54	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P212121	
Unit cell dimensions	a = 7.7089(3) Å	α = 90°.
	b = 8.1588(3) Å	β = 90°.
	c = 36.7130(13) Å	γ = 90°.
Volume	2309.08(15) Å3	
Z	4	
Density (calculated)	1.244 mg/m^3	
Absorption coefficient	0.709 mm^{-1}	
F(000)	936	
Crystal size	0.680 × 0.190 × 0.040 mm^3	
Theta range for data collection	2.41 to 69.95°.	
Index ranges	-9<=h<=9, -7<=k<=9, -44<=l<=44	
Reflections collected	16444	
Independent reflections	4355 [R(int) = 0.0890]	
Completeness to theta = 69.95°	99.90%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.97 and 0.78	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4355 / 0 / 286	
Goodness-of-fit on F2	1.146	
Final R indices [I>2sigma(I)]	R1 = 0.0449, wR2 = 0.1142	
R indices (all data)	R1 = 0.0600, wR2 = 0.1190	
Absolute structure parameter	0.07(8)	
Largest diff. peak and hole	0.482 and -0.454 e.Å-3	

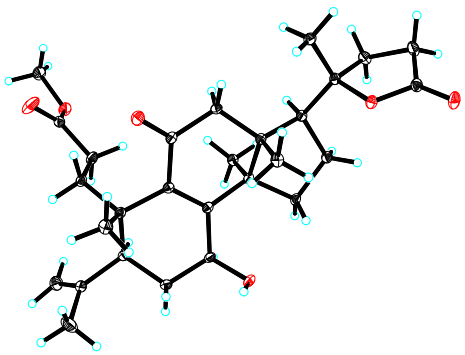
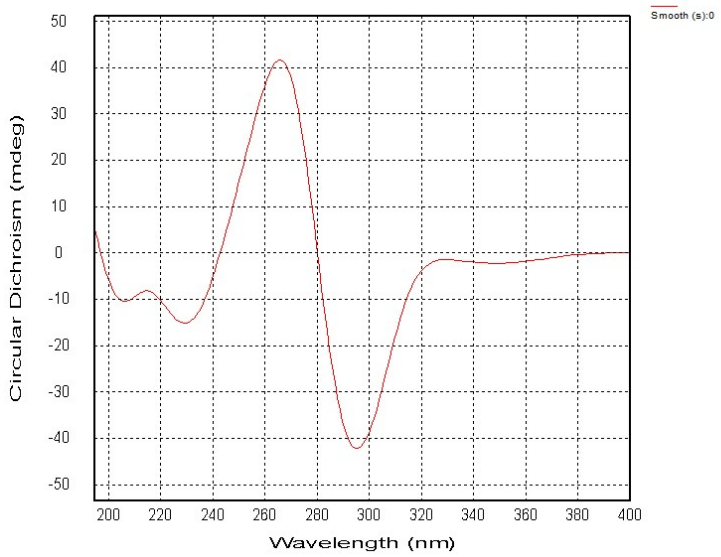


Figure S79. View of a molecule of compound **5** with the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

Table S5. Crystal data and structure refinement for compound 5.

Identification code	global	
Empirical formula	C_{28} $H_{40}O_6$	
Formula weight	472.6	
Temperature	150(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.1802(3) Å	α = 90°.
	b = 13.5202(4) Å	β = 90°.
	c = 11.2870(4) Å	γ = 90°.
Volume	1246.94(7) Å3	
Z	2	
Density (calculated)	1.259 mg/m^3	
Absorption coefficient	0.701 mm^{-1}	
F(000)	512	
Crystal size	0.540 × 0.450 × 0.280 mm^3	
Theta range for data collection	3.92 to 72.31°.	
Index ranges	-8<=h<=10, -16<=k<=16, -13<=l<=13	
Reflections collected	22359	
Independent reflections	4854 [R(int) = 0.0348]	
Completeness to theta = 69.95°	99.00%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.83 and 0.69	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4854 / 1 / 314	
Goodness-of-fit on F2	0.978	
Final R indices [I>2sigma(I)]	R1 = 0.0311, wR2 = 0.1015	
R indices (all data)	R1 = 0.0312, wR2 = 0.1017	
Absolute structure parameter	-0.09(3)	
Largest diff. peak and hole	0.213 and -0.214 e.Å-3	

Calculated ECD data of compound 3



File: compound 2-1mm (195-400) 22090803.dsx
ProBinaryX
Attributes :
- Time Stamp: Thu Sep 08 13:38:16 2022
- File ID : F361B51F-DFB3-4086-8AA1-5D9E05E7A180
- Is CFR Compliant: false
- Original data has not been modified.
Remarks:
- User: CD
- Date: 2022/09/08
- Instrument: 0547
- DetectorType: LAAPD
- DichOS Calibration Correction Curve: 0547/2
- HV (CDDC channel): 0 v
- Time per point: 1 s
- Description: Sample 1
- Concentration: 0.4600 mg/mL MeOH
- Pathlength: 1 mm
- Temperature: 20℃
Settings:
- Time-per-point: 1s (25us x 40000)
- SE
- Wavelength: 195nm - 400nm
- Step Size: 1nm
- Bandwidth: 1nm

Figure S80. The CD spectrum of compound 3.

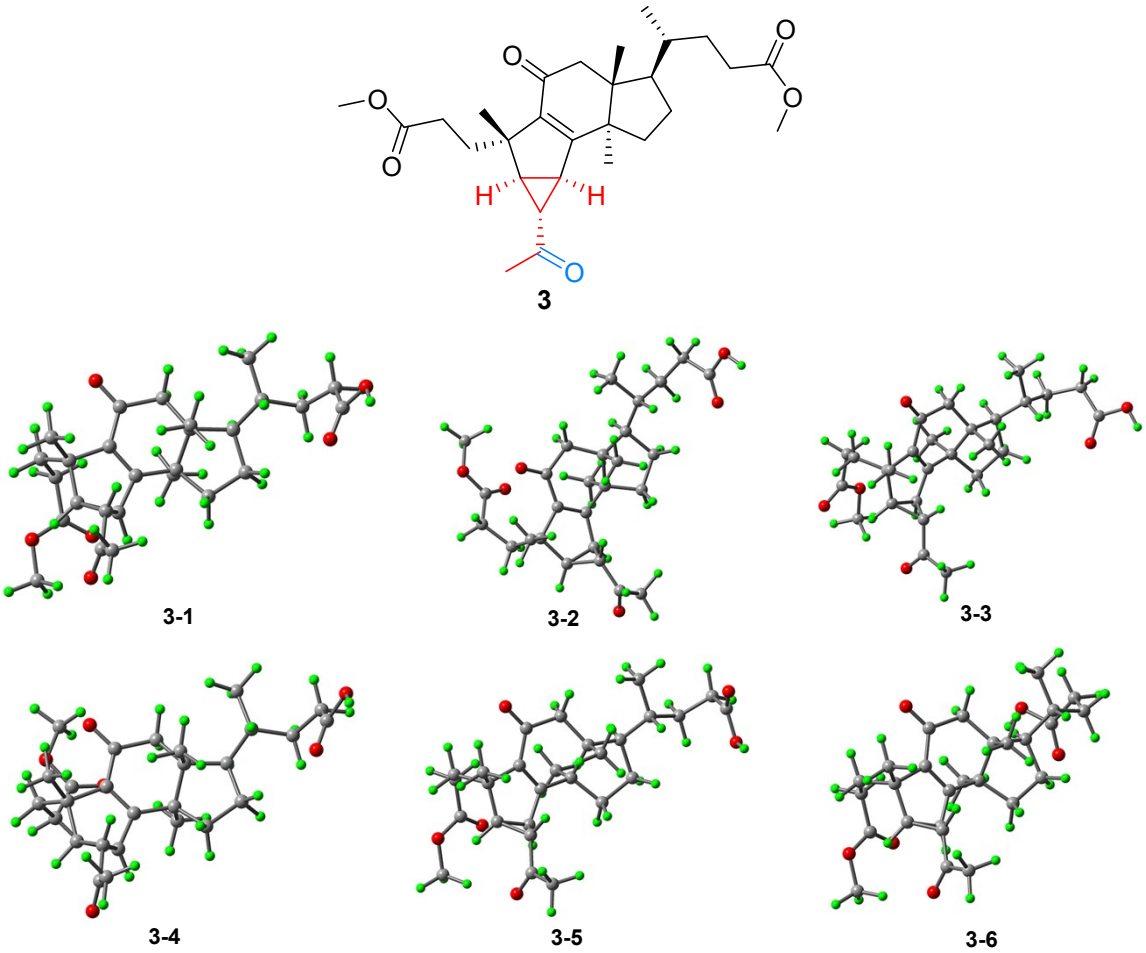


Figure S81. Six optimized conformers of 3.

Table S6. Conformational analysis of the six optimized conformers of 3 in the gas phase (T = 298.15 K)

Conformer	E (Hartree)	C (Hartree)	G (kcal/mol)	ΔG (kcal/mol)	Population
3-1	-1502.963528	0.537406	-942787.415691	0	50.38%
3-2	-1502.961835	0.536663	-942786.819782	0.595908597	18.42%
3-3	-1502.961967	0.537037	-942786.667542	0.748148798	14.24%
3-4	-1502.961837	0.537663	-942786.193728	1.221962773	6.40%
3-5	-1502.962021	0.537875	-942786.175875	1.239815433	6.21%
3-6	-1502.963046	0.539234	-942785.965986	1.449704978	4.35%

Electronic energy obtained at M062X/6-311+G(2d,p) EmpiricalDispersion=GD3 of theory; Thermal correction to Gibbs free energy obtained at B3LYP/6-31G(d) Scale=0.9813 SCRF=(IEFPCM,Solvent=Methanol) EmpiricalDispersion=GD3BJ of theory; Gibbs free energy (E + C); The relative Gibbs free energy; The Boltzmann distribution of each conformer.

Table S7. Atomic coordinates (Å) of 3-1 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	-3.23512	0.526145	-0.56739	H	0.119621	-2.313954	0.32708
C	-2.122056	2.896378	-0.333574	H	0.932854	1.843407	2.580452
C	-1.13449	0.773697	0.569663	H	1.159912	2.32409	0.903301
C	-1.824834	-0.010336	-0.300388	H	3.317207	1.374559	1.078659
C	0.19691	0.375992	1.122447	H	2.906236	0.525473	2.556464
C	1.018129	-0.352274	-0.001508	H	2.240756	-1.418372	1.42333
C	0.207584	-1.568463	-0.473631	H	1.875098	1.435588	-0.975986
C	-1.219404	-1.201115	-0.89923	H	1.752793	0.019954	-2.016593
C	1.178004	1.466868	1.582592	H	0.308422	0.950923	-1.62946
C	2.5539	0.744099	1.544493	H	-0.729933	-1.391108	2.084626
C	2.37444	-0.581764	0.725174	H	0.786959	-0.862865	2.855399
C	1.24866	0.574155	-1.219442	H	-0.695622	0.065459	3.074908
C	-0.12209	-0.524864	2.351256	H	3.808412	-0.068877	-0.792381
O	-1.811074	-1.911788	-1.716835	H	3.074056	-3.015872	-0.36453
C	-1.894902	1.997591	0.899677	H	4.370407	-2.489437	-1.446797
C	3.615907	-0.918382	-0.125625	H	2.708263	-2.027755	-1.78732
C	3.428958	-2.179904	-0.980128	H	4.840201	-0.320261	1.575478
C	4.850734	-1.078924	0.789155	H	4.800665	-2.054169	1.290153
C	6.187484	-0.969472	0.053952	H	7.015565	-1.257482	0.715448
C	6.485584	0.434647	-0.422474	H	6.250334	-1.643829	-0.806332
O	7.5108	0.453524	-1.303706	H	7.666171	1.387841	-1.542075
O	5.917714	1.449686	-0.0675	H	-4.587147	1.070781	-2.180456
C	-3.585291	0.643382	-2.058433	H	-3.554387	-0.332164	-2.546478
C	-4.320083	-0.278333	0.203834	H	-2.872753	1.295602	-2.573463
C	-3.173286	1.904277	0.119222	H	-4.073245	-0.255477	1.270618
C	-2.38695	4.33414	-0.060752	H	-5.263685	0.2677	0.081917
C	-1.86563	5.315466	-1.085307	H	-2.123343	6.336742	-0.798902
O	-2.990992	4.69569	0.942761	H	-0.776564	5.21837	-1.174124
C	-4.562293	-1.732381	-0.210113	H	-2.285984	5.088097	-2.072495
C	-3.570128	-2.718017	0.366447	H	-5.550165	-2.046474	0.15403
O	-3.611285	-3.887548	-0.295365	H	-4.58428	-1.858993	-1.294175
O	-2.850457	-2.523466	1.329283	H	-1.651088	-4.534083	-0.035085
C	-2.671157	-4.884598	0.141134	H	-2.804144	-5.10518	1.202588
H	-4.086743	2.334432	0.517025	H	-2.878612	-5.767613	-0.462583
H	-1.809333	2.499346	1.857341				
H	-1.539323	2.667968	-1.220473				
H	0.663282	-2.079206	-1.324518				

Table S8. Atomic coordinates (Å) of 3-2 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	2.79563	-0.680457	1.390819	H	-0.971786	-2.854745	0.019287
C	2.253769	1.860815	0.967764	H	-0.512386	1.333837	-2.353118
C	0.992294	-0.055739	-0.061568	H	-0.853291	1.911142	-0.726491
C	1.375258	-0.941184	0.894516	H	-3.119431	1.416268	-1.174525
C	-0.299256	-0.200235	-0.799252	H	-2.70924	0.467029	-2.589887
C	-1.396287	-0.716837	0.201496	H	-2.598587	-1.545554	-1.387277
C	-0.933739	-2.064621	0.779735	H	-2.328413	-0.135438	2.0802
C	0.501252	-2.030152	1.332218	H	-0.66748	0.431175	1.933556
C	-0.961535	1.0526	-1.395634	H	-1.961149	1.24348	1.047634
C	-2.450815	0.631029	-1.540007	H	0.237855	-2.187098	-1.617189
C	-2.657523	-0.683452	-0.709736	H	-0.860791	-1.257846	-2.654587
C	-1.593906	0.268625	1.377489	H	0.851171	-0.819779	-2.537107
C	-0.011174	-1.183595	-1.970829	H	-4.152325	0.141132	0.596154
O	0.880276	-2.912542	2.106212	H	-3.984226	-2.902256	0.252736
C	2.02811	0.980112	-0.272846	H	-5.279195	-2.099291	1.151181
C	-4.046809	-0.74386	-0.043294	H	-3.619491	-1.979677	1.719159
C	-4.239964	-1.998527	0.819845	H	-4.87735	0.052342	-1.894535
C	-5.15073	-0.67031	-1.121889	H	-5.233152	-1.6464	-1.616907
C	-6.524701	-0.274218	-0.579214	H	-7.295821	-0.403862	-1.3504
C	-6.591822	1.171867	-0.14129	H	-6.84135	-0.901106	0.260874
O	-7.711346	1.422968	0.573971	H	-7.702476	2.374237	0.795008
O	-5.777991	2.038676	-0.396402	H	2.250285	0.219608	3.305303
C	2.896829	-0.575603	2.921481	H	3.927143	-0.350532	3.219686
C	3.765093	-1.793494	0.908793	H	2.594346	-1.517018	3.386211
C	3.128508	0.65176	0.697344	H	4.78745	-1.502312	1.174859
C	2.874484	3.188217	0.708724	H	3.529027	-2.701568	1.471526
C	2.429324	4.322631	1.601415	H	1.346039	4.467469	1.507354
O	3.69805	3.346568	-0.186403	H	2.626073	4.073882	2.651334
C	3.710207	-2.156426	-0.586911	H	2.949992	5.244066	1.334669
C	4.115498	-1.061826	-1.549684	H	4.392114	-2.999647	-0.754726
O	5.314822	-0.535429	-1.22911	H	2.709619	-2.483114	-0.87513
O	3.46957	-0.699432	-2.515736	H	5.104361	1.451901	-1.812029
C	5.742739	0.589136	-2.022653	H	6.767096	0.791887	-1.711836
H	4.160319	0.87564	0.45736	H	5.702501	0.347191	-3.086178
H	2.199825	1.43578	-1.240555				
H	1.51023	1.812324	1.756957				
H	-1.568952	-2.407157	1.600183				

Table S9. Atomic coordinates (Å) of 3-3 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	-2.830567	-0.689934	-1.430543	H	0.892765	-2.84227	0.038079
C	-2.302268	1.857478	-1.056942	H	0.475589	1.427938	2.257021
C	-1.026725	-0.032334	0.008477	H	0.837853	1.941083	0.613658
C	-1.409647	-0.939055	-0.9275	H	3.094428	1.438762	1.105227
C	0.259729	-0.160121	0.75781	H	2.658246	0.54156	2.546426
C	1.359086	-0.721254	-0.214889	H	2.541277	-1.508739	1.410107
C	0.885565	-2.081511	-0.75289	H	1.959183	1.201644	-1.121502
C	-0.537057	-2.041249	-1.335537	H	2.30721	-0.215726	-2.107291
C	0.930152	1.106682	1.314781	H	0.655339	0.383143	-1.986073
C	2.413026	0.673549	1.488895	H	0.801507	-1.168878	2.647426
C	2.613471	-0.670252	0.704768	H	-0.894316	-0.685517	2.523304
C	1.576829	0.222927	-1.421219	H	-0.326404	-2.103802	1.647033
C	-0.047804	-1.095721	1.963396	H	4.126295	0.096507	-0.615448
O	-0.908871	-2.930915	-2.104524	H	3.924386	-2.932033	-0.174169
C	-2.063206	1.004648	0.199524	H	5.236512	-2.172262	-1.085105
C	4.007236	-0.765801	0.051932	H	3.58383	-2.054028	-1.673538
C	4.195208	-2.050011	-0.767817	H	4.829794	0.081772	1.884029
C	5.103201	-0.66705	1.136663	H	5.17363	-1.627662	1.662826
C	6.484558	-0.299443	0.592714	H	7.248947	-0.412112	1.373189
C	6.56757	1.131867	0.111187	H	6.801732	-0.954421	-0.225498
O	7.696778	1.352557	-0.598797	H	7.697539	2.296544	-0.849313
O	5.757537	2.012038	0.330116	H	-2.275607	0.182588	-3.356375
C	-2.925414	-0.605223	-2.963213	H	-3.954124	-0.382581	-3.268373
C	-3.789251	-1.809396	-0.942614	H	-2.622826	-1.55372	-3.413265
C	-3.171356	0.651513	-0.754291	H	-4.810628	-1.556317	-1.250216
C	-2.921677	3.189853	-0.819688	H	-3.508477	-2.729734	-1.462069
C	-2.517259	4.295465	-1.766348	H	-3.039765	5.220695	-1.516836
O	-3.713059	3.371713	0.09921	H	-1.433296	4.454845	-1.710918
C	-3.783964	-2.096906	0.568704	H	-2.742998	4.006658	-2.800061
C	-4.448425	-1.006365	1.377907	H	-4.359488	-3.013382	0.746868
O	-3.676955	-0.585561	2.398672	H	-2.771429	-2.2675	0.937886
O	-5.553022	-0.549193	1.146986	H	-5.166096	0.246913	3.60922
C	-4.205163	0.514614	3.164959	H	-3.464761	0.711762	3.939163
H	-4.201736	0.87365	-0.504086	H	-4.330334	1.389366	2.521302
H	-2.221685	1.492172	1.153875				
H	-1.567647	1.79206	-1.853187				
H	1.531188	-2.465897	-1.545966				

Table S10. Atomic coordinates (Å) of 3-4 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	-3.153679	0.39634	-0.869514	H	0.165579	-2.356128	0.316631
C	-2.25723	2.804436	-0.325539	H	0.830543	1.911184	2.428515
C	-1.158136	0.670856	0.445269	H	1.080915	2.31793	0.734748
C	-1.761872	-0.109811	-0.48915	H	3.265316	1.451443	1.011653
C	0.179718	0.347103	1.029811	H	2.840126	0.650505	2.511939
C	1.049861	-0.390264	-0.051639	H	2.271354	-1.360721	1.441925
C	0.288462	-1.64443	-0.509325	H	1.811142	-0.068956	-2.065501
C	-1.118181	-1.312966	-1.019991	H	0.354146	0.862516	-1.730203
C	1.110818	1.495965	1.455701	H	1.905356	1.377159	-1.06596
C	2.509419	0.816122	1.482791	H	-0.679563	-1.409939	2.073545
C	2.394537	-0.548252	0.714271	H	0.801346	-0.770312	2.830548
C	1.289163	0.504273	-1.29344	H	-0.723667	0.097268	2.983656
C	-0.115457	-0.504606	2.298342	H	3.8517	-0.045797	-0.785604
O	-1.68584	-2.065692	-1.816335	H	2.843399	-2.075192	-1.732524
C	-2.023106	1.81157	0.823414	H	3.201572	-2.997333	-0.263967
C	3.668281	-0.875044	-0.091571	H	4.509399	-2.468324	-1.331091
C	3.545924	-2.173363	-0.901354	H	4.826084	-0.170164	1.61498
C	4.881967	-0.959133	0.860964	H	4.8481	-1.914488	1.400225
C	6.234886	-0.836928	0.158195	H	7.052452	-1.071784	0.852909
C	6.503581	0.555165	-0.36826	H	6.342683	-1.54323	-0.671542
O	7.560356	0.572171	-1.211447	H	7.69287	1.500197	-1.485466
O	5.889047	1.564056	-0.079616	H	-2.551874	1.402438	-2.7229
C	-3.288561	0.670662	-2.379223	H	-4.287406	1.061137	-2.605877
C	-4.291388	-0.578107	-0.46373	H	-3.139199	-0.25503	-2.940208
C	-3.248552	1.690496	-0.035022	H	-5.227998	-0.008896	-0.472972
C	-2.660002	4.18243	0.065526	H	-4.385492	-1.350624	-1.229766
C	-2.175078	5.300231	-0.828482	H	-1.078728	5.300353	-0.864459
O	-3.345229	4.390386	1.060187	H	-2.526118	5.139874	-1.85516
C	-4.133573	-1.265266	0.908692	H	-2.532815	6.263637	-0.460703
C	-3.354691	-2.56227	0.841358	H	-3.645224	-0.615372	1.637995
O	-3.914723	-3.421221	-0.028025	H	-5.128533	-1.513837	1.296576
O	-2.359121	-2.834459	1.488555	H	-2.223254	-4.406064	-0.71987
C	-3.186715	-4.64079	-0.262524	H	-3.035051	-5.184615	0.672293
H	-4.214811	2.010564	0.341484	H	-3.804209	-5.221139	-0.947476
H	-2.032011	2.219882	1.82853				
H	-1.612736	2.715253	-1.193926				
H	0.796317	-2.181827	-1.312937				

Table S11. Atomic coordinates (Å) of 3-5 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	-2.741717	-0.666045	-1.438733	H	1.083615	-2.745604	-0.062543
C	-2.310669	1.87572	-0.90264	H	0.395446	1.312848	2.470357
C	-0.999385	-0.030994	0.081966	H	0.737608	1.979672	0.878608
C	-1.324888	-0.89213	-0.916478	H	3.006452	1.569902	1.327184
C	0.279491	-0.155577	0.845111	H	2.636284	0.557557	2.710401
C	1.41992	-0.585294	-0.149408	H	2.612853	-1.422983	1.440584
C	1.025244	-1.926744	-0.790438	H	1.91184	1.431506	-0.904371
C	-0.399133	-1.929626	-1.371615	H	2.377547	0.112321	-1.974998
C	0.873213	1.096836	1.509957	H	0.687019	0.591959	-1.859498
C	2.377934	0.738412	1.663529	H	-0.19585	-2.195056	1.567657
C	2.656637	-0.536561	0.794611	H	0.840718	-1.267746	2.668805
C	1.60352	0.453107	-1.28106	H	-0.883948	-0.892243	2.527304
C	0.004806	-1.198242	1.967806	H	4.159559	0.394443	-0.429606
O	-0.725929	-2.7986	-2.183496	H	5.365385	-1.69536	-1.130387
C	-2.079717	0.955225	0.307519	H	3.675929	-1.738039	-1.603678
C	4.068473	-0.52065	0.172456	H	4.212697	-2.665695	-0.195065
C	4.343733	-1.722454	-0.739982	H	4.888145	0.404642	1.956324
C	5.116664	-0.44118	1.302619	H	5.051538	-1.346039	1.920661
C	6.575923	-0.292119	0.825455	H	7.217864	-0.115102	1.695808
C	6.737985	0.861437	-0.133408	H	6.933734	-1.191238	0.321529
O	6.443674	2.047028	0.449834	H	6.540002	2.735044	-0.236373
O	7.063249	0.775866	-1.301526	H	-3.839492	-0.30849	-3.282996
C	-2.808691	-0.504198	-2.966383	H	-2.456885	-1.41385	-3.458944
C	-3.678603	-1.833706	-1.026834	H	-2.185505	0.330404	-3.302092
C	-3.143063	0.623687	-0.702258	H	-4.705085	-1.569566	-1.304961
C	-2.991121	3.166097	-0.608185	H	-3.395517	-2.707482	-1.621169
C	-2.577908	4.350426	-1.449973	H	-2.744731	4.132727	-2.511908
O	-3.837808	3.256555	0.274664	H	-3.142208	5.238674	-1.160352
C	-3.643038	-2.257679	0.453223	H	-1.503682	4.537042	-1.329234
C	-4.109555	-1.220394	1.450908	H	-4.296604	-3.13141	0.569828
O	-5.320633	-0.725182	1.12529	H	-2.637562	-2.559784	0.751013
O	-3.498354	-0.875867	2.445665	H	-6.831169	0.527228	1.628665
C	-5.807599	0.347491	1.955771	H	-5.783328	0.060354	3.008489
H	-4.188245	0.79773	-0.479434	H	-5.196455	1.24079	1.798604
H	-2.292345	1.364392	1.287827				
H	-1.547505	1.887842	-1.674279				
H	1.687545	-2.208879	-1.612406				

Table S12. Atomic coordinates (Å) of 3-6 obtained at the Cam-B3LYP/6-311+G(d,p) level of theory in the MeOH.

C	2.632342	0.016763	1.567426	H	-1.761599	-1.181504	1.800101
C	2.698618	1.835883	-0.334578	H	-0.71321	0.401955	-2.644578
C	0.806003	0.219608	0.026269	H	-0.549544	1.893254	-1.725449
C	1.124582	-0.005684	1.327335	H	-2.894586	2.031481	-1.740309
C	-0.596642	0.101818	-0.475209	H	-3.073982	0.382005	-2.311087
C	-1.572921	0.654939	0.62704	H	-3.183504	-0.521043	-0.139376
C	-1.372519	-0.161866	1.914092	H	-0.260255	2.286415	1.305477
C	0.101333	-0.278745	2.337009	H	-1.431554	2.790969	0.084368
C	-1.014466	0.903143	-1.719614	H	-1.955947	2.485149	1.738368
C	-2.559618	1.001834	-1.574575	H	-0.785573	-2.031133	0.09727
C	-2.929411	0.543835	-0.124816	H	-1.75713	-1.578605	-1.317405
C	-1.282621	2.139077	0.948554	H	-0.000112	-1.748233	-1.450244
C	-0.809911	-1.406451	-0.799109	H	-3.935299	2.365038	0.403628
O	0.382492	-0.60771	3.491964	H	-4.505179	-0.164055	2.038412
C	2.013701	0.530053	-0.771187	H	-5.45518	1.323647	2.185781
C	-4.156318	1.289563	0.435815	H	-3.73716	1.328079	2.584778
C	-4.478244	0.921686	1.892078	H	-6.16959	1.809769	-0.119322
C	-5.405761	1.100053	-0.457809	H	-5.174905	1.361496	-1.49529
C	-6.054249	-0.298982	-0.437171	H	-6.25544	-0.632422	0.58258
C	-5.258063	-1.352915	-1.169386	H	-7.018797	-0.236619	-0.955518
O	-4.99811	-2.435169	-0.400371	H	-4.495177	-3.064962	-0.953017
O	-4.88875	-1.276093	-2.326124	H	4.144859	0.962676	2.812782
C	3.053854	0.956603	2.70902	H	2.613184	0.627326	3.653049
C	3.166174	-1.407249	1.880625	H	2.724968	1.982328	2.515982
C	3.158131	0.494013	0.202944	H	4.26072	-1.367633	1.915157
C	3.583628	2.46848	-1.349988	H	2.818941	-1.675514	2.882828
C	3.643132	3.97784	-1.34129	H	3.974697	4.334405	-0.358455
O	4.224699	1.794395	-2.14951	H	4.324074	4.336772	-2.115132
C	2.72485	-2.534305	0.928602	H	2.640815	4.391348	-1.507168
C	3.197285	-2.415902	-0.503909	H	3.120035	-3.480435	1.319551
O	4.529886	-2.223934	-0.575717	H	1.637299	-2.620913	0.901155
O	2.486571	-2.504569	-1.488215	H	4.722579	-1.017811	-2.261367
C	5.063223	-1.990228	-1.894334	H	6.146142	-1.991055	-1.774798
H	4.1451	0.184396	-0.116784	H	4.74969	-2.778242	-2.581287
H	2.105256	0.248467	-1.813297				
H	2.137062	2.502906	0.311882				
H	-1.902682	0.267764	2.767534				

Uncropped images of western blot

Figure S82. Uncropped images of western blot in figure 5 of paper.

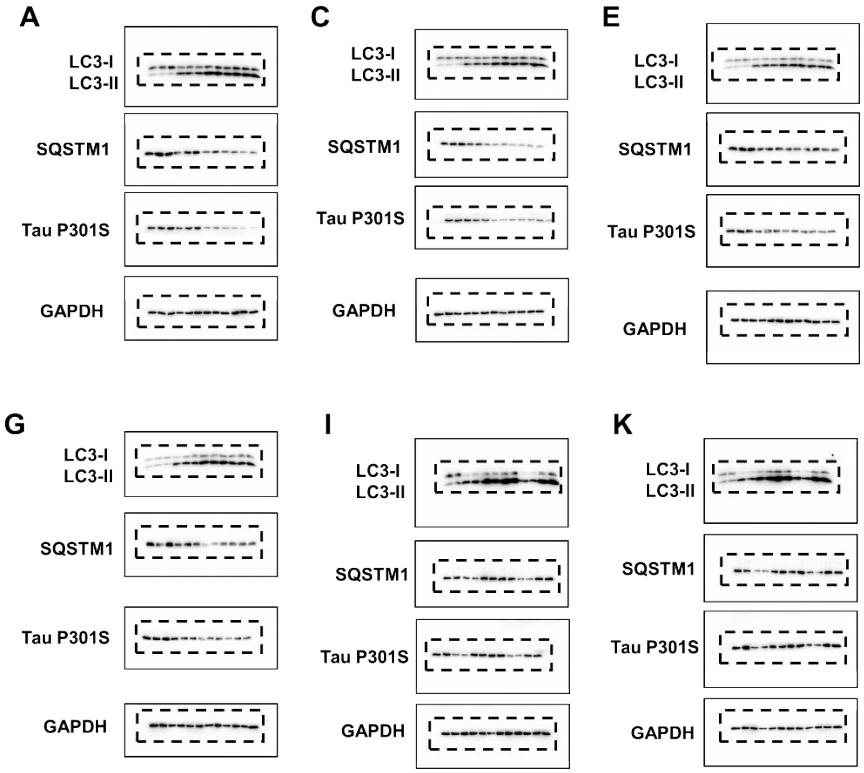


Figure S83. Uncropped images of western blot in figure S6 of Supplementary information.

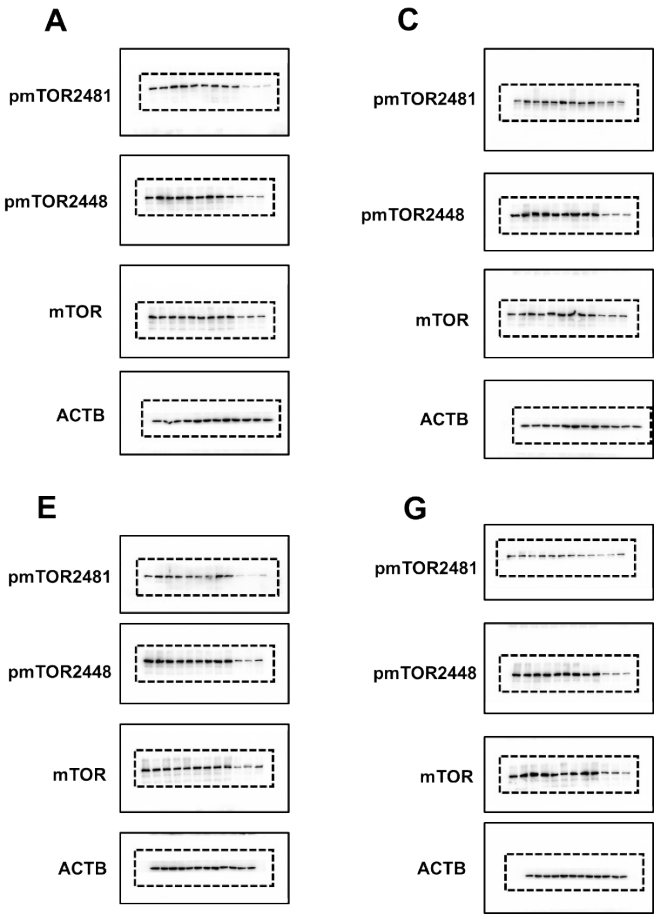
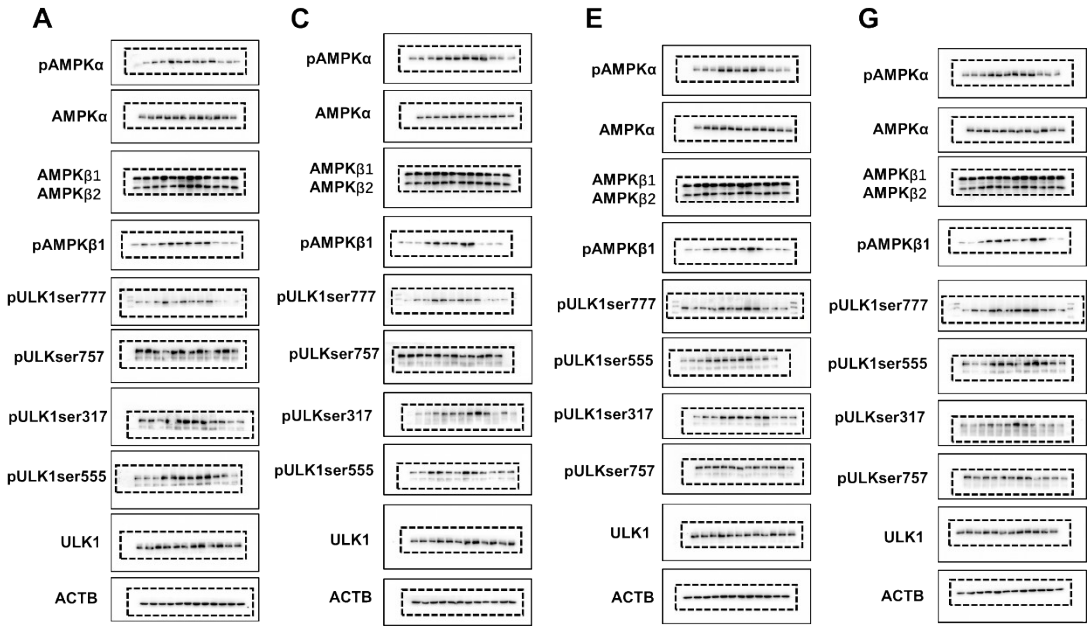


Figure S84. Uncropped images of western blot in figure 6 of paper.



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