SUPPLEMENTARY MATERIAL

Three new phenylacetamide glycosides from *Dracocephalum tanguticum Maxim* and their anti-hyperglycemic activity

En-Guang Ma, Hai-Yan Wu, Li-Jiao Hu, Min Wei, Lin-Yun Mou, Gan-Peng Li*

Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission & Ministry of Education, Yunnan Minzu University, Kunming, Yunnan, 650500, P.R.China.

Correspondence

Prof. Gan-Peng Li, Key Laboratory of Chemistry in Ethnic Medicinal Resources, Yunnan Minzu University, Kunming, Yunnan, 650500, P.R.China. E-mail addresses: ganpeng_li@sina.com, Tel.: +86 0871 65936602

Acknowledgement

This work was financially supported by Technology Center, China Tobacco Yunnan Industrial Co., Ltd [grant number JSZX20151008-52].

ABSTRACT

Three new phenylacetamide glycosides (**1**–**3**) together with one known phenylacetamide glycoside (**4**) and two known flavonoid glycosides (**5**–**6**) were isolated from whole plants of *Dracocephalum tanguticum*. The structure of all compounds were elucidated based on spectroscopic data analysis and comparison with data reported in related literature. Compounds (**1**–**3**) were evaluated for their anti-hyperglycemic and anti-fungal (*Candida albicans*) activities, the results revealed that all of them showed moderate activity with 3T3-L1 adipocytes glucose consumption rate of 20.80±1.47%, 21.48±2.44%, and 21.57±1.35%, respectively at the final concentration of 25 μM. However, none of them showed obvious *Candida albicans* inhibitory activity.

Keywords：*Dracocephalum tanguticum*, phenylacetamide glycosides, anti-hyperglycemic activity

Table S1. ^{1}H and ^{13}C NMR data of **1**−**3** in Methanol-d_4 (400 and 100 MHz, *J* in Hz)

position	**1**		**2**		**3**	
	δ_C(mult.)	δ_H (mult, *J*, Hz)	δ_C(mult.)	δ_H (mult, *J*, Hz)	δ_C(mult.)	δ_H (mult, *J*, Hz)
1	134.3 s		134.5 s		134.4 s	
2,6	130.8 d	7.16 (d) 8.3	130.8 d	7.19 (d) 8.7	130.8 d	7.05 (d) 8.6
3,5	117.5 d	6.85 (d) 8.4	117.7 d	7.03 (d) 8.7	117.6 d	6.97 (d) 8.7
4	155.9 s		156.2 s		156.2 s	
7	35.7 t	2.88, overlap	35.7 t	2.82 (t) 7.3	35.7 t	2.65 (t) 7.2
8	42.8 t	3.59 (t) 7.4	42.3 t	3.51 (t) 7.3	42.1 t	3.30, overlap
1′	135.8 s		136.3 s		132.8 s	
2′,6′	128.2 d	7.77 (d) 7.5	128.8 d	7.53 (d) 8.5	130.4 d	7.01 (d) 8.6
3′,5′	129.6 d	7.43 (d) 7.4	129.9 d	7.36 (d) 8.5	116.2 d	6.70 (d) 8.4
4′	132.6 d	7.50 (d) 7.1	130.9 d	7.36 m	156.8s	
7′	170.3 s		141.7 d	7.50 (d) 15.8	32.2 t	2.78 (t) 7.5
8′			121.8 d	6.56 (d) 15.8	39.3 t	2.38 (t) 7.6
9′			168.6 s		175.4 s	
1′′	98.3 d	5.60 (d) 1.7	99.7 d	5.43 (d) 1.7	99.6 s	5.40 (d) 1.5
2′′	82.8 d	4.00, overlap	79.7 d	4.13 (dd) 9.8, 3.3	82.7 d	3.94 (dd) 9.1, 3.2
3′′	80.3 d	4.41, overlap	71.8 d	4.31 (dd) 3.2, 1.9	71.4 d	4.29 (dd) 3.0, 1.9
4′′	72.2 d	3.32, overlap	73.7 d	5.14 (t) 9.9	72.7 d	3.62, overlap
5′′	70.1 d	3.64, overlap	68.5 d	3.85, overlap	70.2 d	3.68, overlap
6′′	18.1 q	1.19 (d) 4.8	17.9 q	1.10 (d) 6.3	18.1 q	1.23 (d) 6.0
1′′′	105.7 d	4.52 (d) 7.6	106.2 d	4.47 (d) 7.8	105.8 d	4.60 (d) 7.6
2′′′	75.33 d	3.21, overlap	74.8 d	3.22, overlap	75.4 d	3.32, overlap
3′′′	77.9 d	3.27, overlap	77.9 d	3.34, overlap	77.6 d	3.40, overlap
4′′′	70.7 d	3.34, overlap	71.1 d	3.35, overlap	71.0 d	3.38, overlap
5′′′	77.5 d	2.89, overlap	77.7 d	3.30, overlap	77.7 d	3.33, overlap
6′′′a	61.8 t	3.49, overlap	62.3 t	3.83, overlap	62.2 t	3.85 (dd) 9.3, 2.4
6′′′b		3.38, overlap		3.73(dd) 11.9, 4.6		3.73 (dd) 10.6, 3.1
1′′′′	106.4 d	4.64 (d) 7.7	21.2 q	2.09 (s)		
2′′′′	75.3 d	3.36, overlap	172.6 s			
3′′′′	77.6 d	3.46, overlap				
4′′′′	72.3 d	3.63, overlap				
5′′′′	75.6 d	3.76, overlap				
6′′′′a	66.1 t	4.70 (d) 11.2				
6′′′′b		4.40, overlap				
1′′′′′	130.9 s					
2′′′′′, 6′′′′′	130.5 d	7.96 (d) 7.7				
3′′′′′, 5′′′′′	129.7 d	7.08 (t) 7.7				
4′′′′′	134.3 d	7.24 (t) 7.4				

7′′′′′	167.8 s

Table S2. Compounds (**1–3**) glucose consumption rate

Sample	Final concentration (μM)	glucose consumption rate (%)
insulin	0.1	27.45±1.63
1	25	20.80±1.47
2	25	21.48±2.44
3	25	21.57±1.35
insulin was used as positive control		

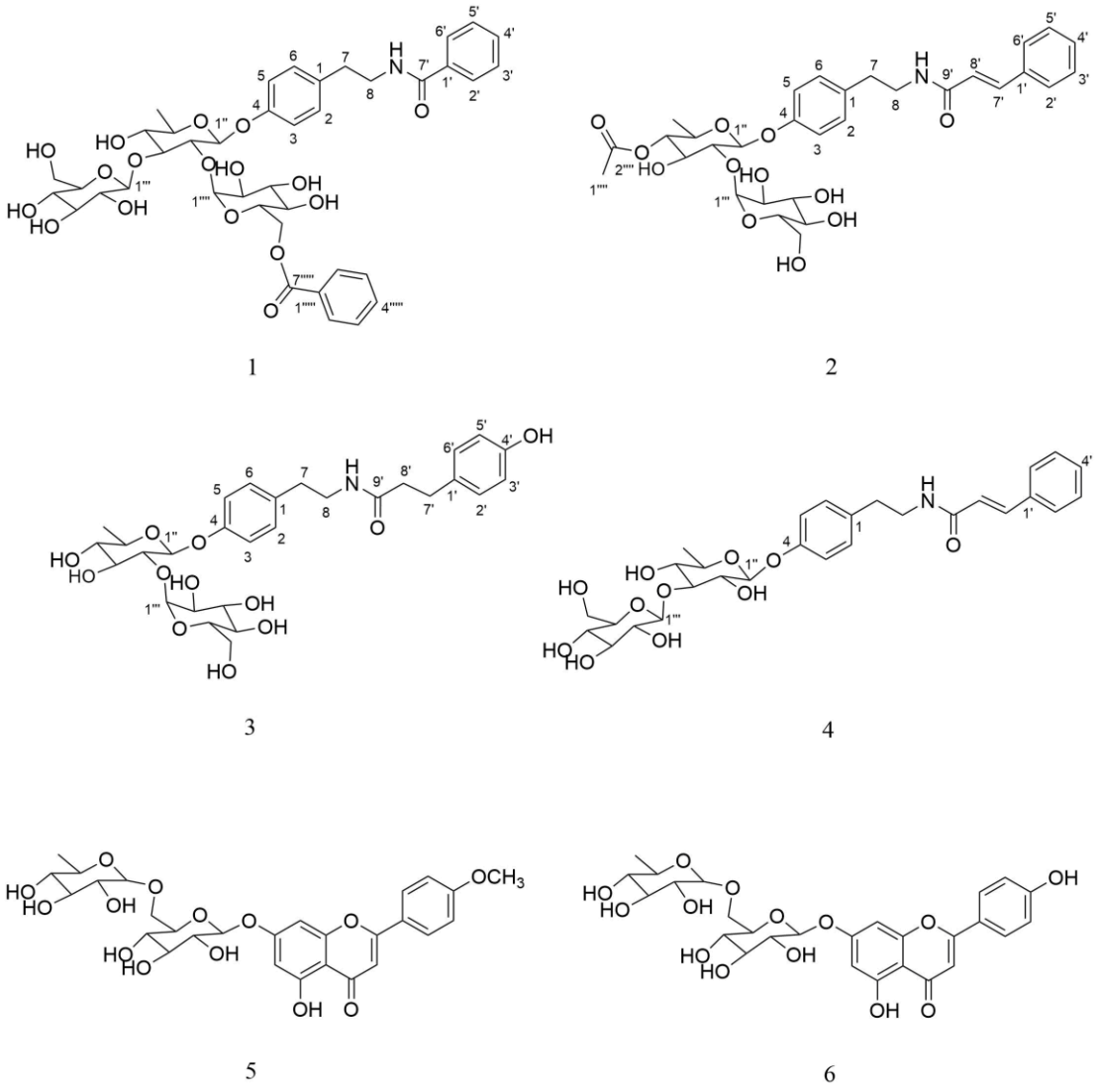


Figure 1. The structures of compounds **1–6**.

Supplemental file (Figure) Legend

Figure S1. ^{1}H NMR spectrum of compound **1** recorded in CD_3OD at 400 MHz

Figure S2. ^{13}C NMR spectrum of compound **1** recorded in CD_3OD at 100 MHz

Figure S3. Lift: ^{13}C NMR spectrum of compound **1** benzene ring enlarge

Right: ^{13}C NMR spectrum of compound **1** glycoside enlarge

Figure S4. HSQC spectrum of compound **1** recorded in CD_3OD at 500 MHz

Figure S5. HMBC spectrum of compound **1** recorded in CD_3OD at 500 MHz

Figure S6. COSY spectrum of compound **1** recorded in CD_3OD at 500 MHz

Figure S7. UV spectrum of compound **1** recorded in MeOH

Figure S8. IR spectrum of compound **1**

Figure S9. HR-ESI-MS spectrum of compound **1**

Figure S10. HPLC analysis of monosaccharide derivative of compound **1**

Figure S11. Key HMBC correlations of compound **1**.

Figure S12. ^{1}H NMR spectrum of compound **2** recorded in CD_3OD at 400 MHz

Figure S13. ^{13}C NMR spectrum of compound **2** recorded in CD_3OD at 100 MHz

Figure S14. HSQC spectrum of compound **2** recorded in CD_3OD at 500 MHz

Figure S15. HMBC spectrum of compound **2** recorded in CD_3OD at 500 MHz

Figure S16. HR- ESI-MS spectrum of compound **2**

Figure S17. Key HMBC correlations of compound **2**.

Figure S18. ^{1}H NMR spectrum of compound **3** recorded in CD_3OD at 400 MHz

Figure S19. ^{13}C NMR spectrum of compound **3** recorded in CD_3OD at 100 MHz

Figure S20. HR-ESI-MS spectrum of compound **3**

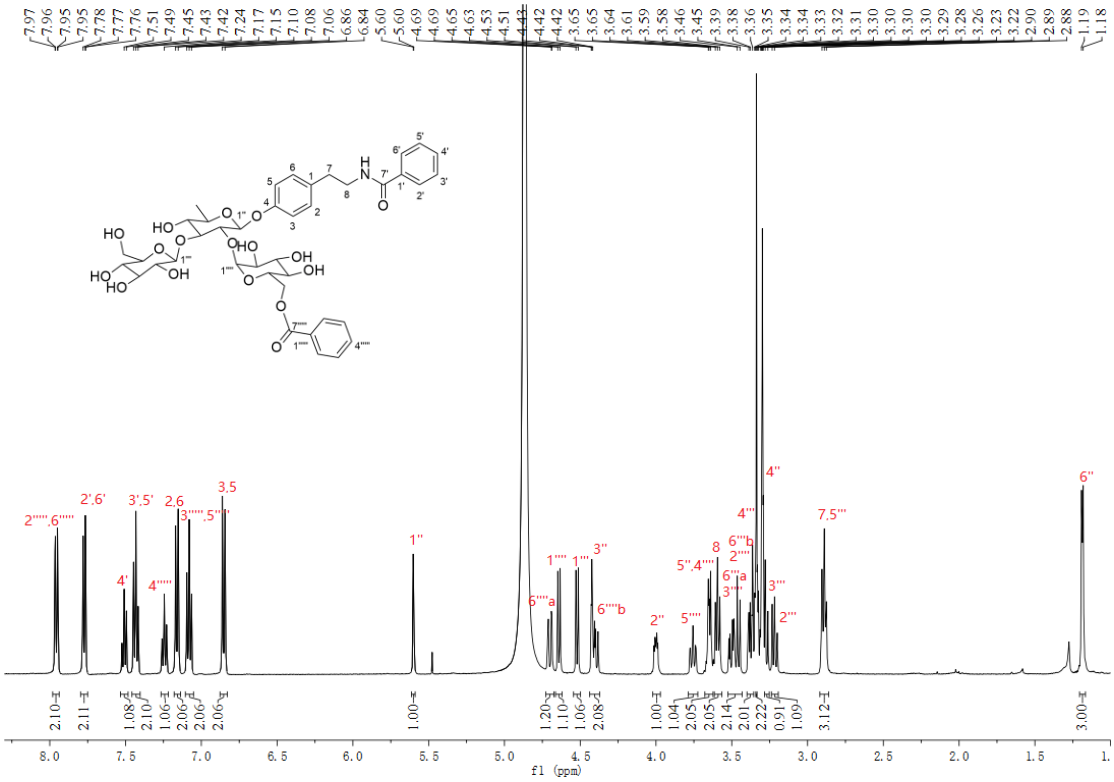


Figure S1. ^{1}H NMR spectrum of compound **1** recorded in CD_3OD at 400 MHz.

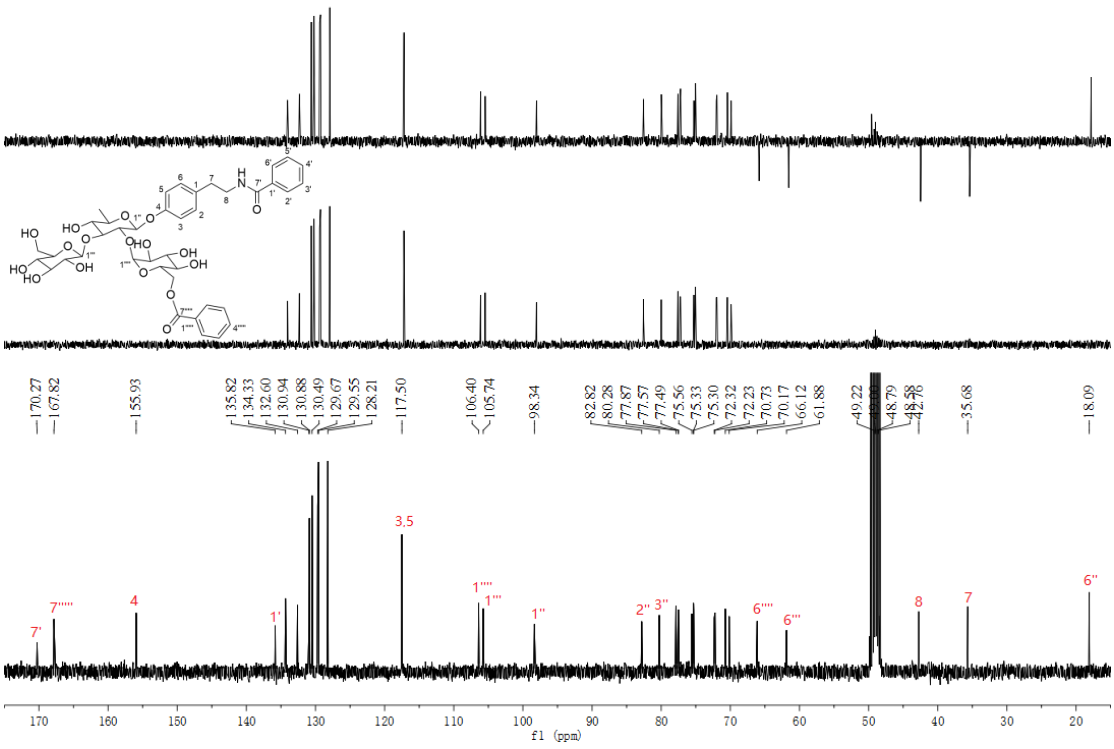


Figure S2. ^{13}C NMR spectrum of compound **1** recorded in CD_3OD at 100 MHz.

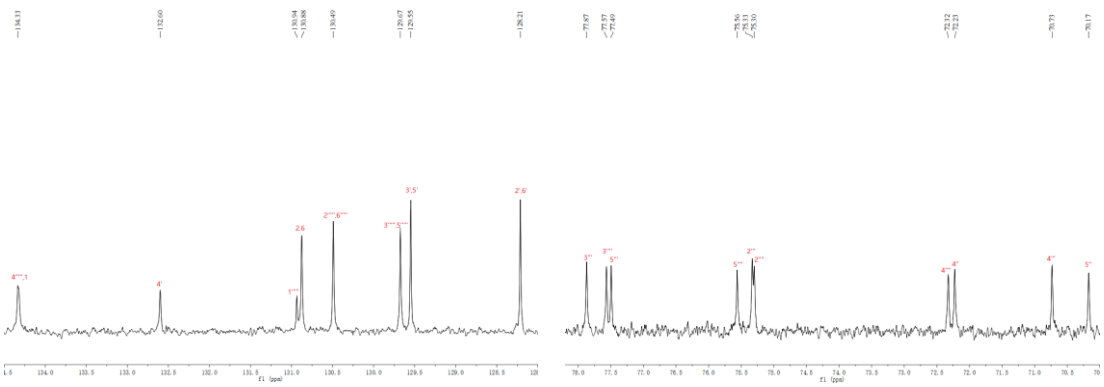


Figure S3. Lift: ^{13}C NMR spectrum of compound **1** benzene ring enlarge.

Right: ^{13}C NMR spectrum of compound **1** glycoside enlarge.

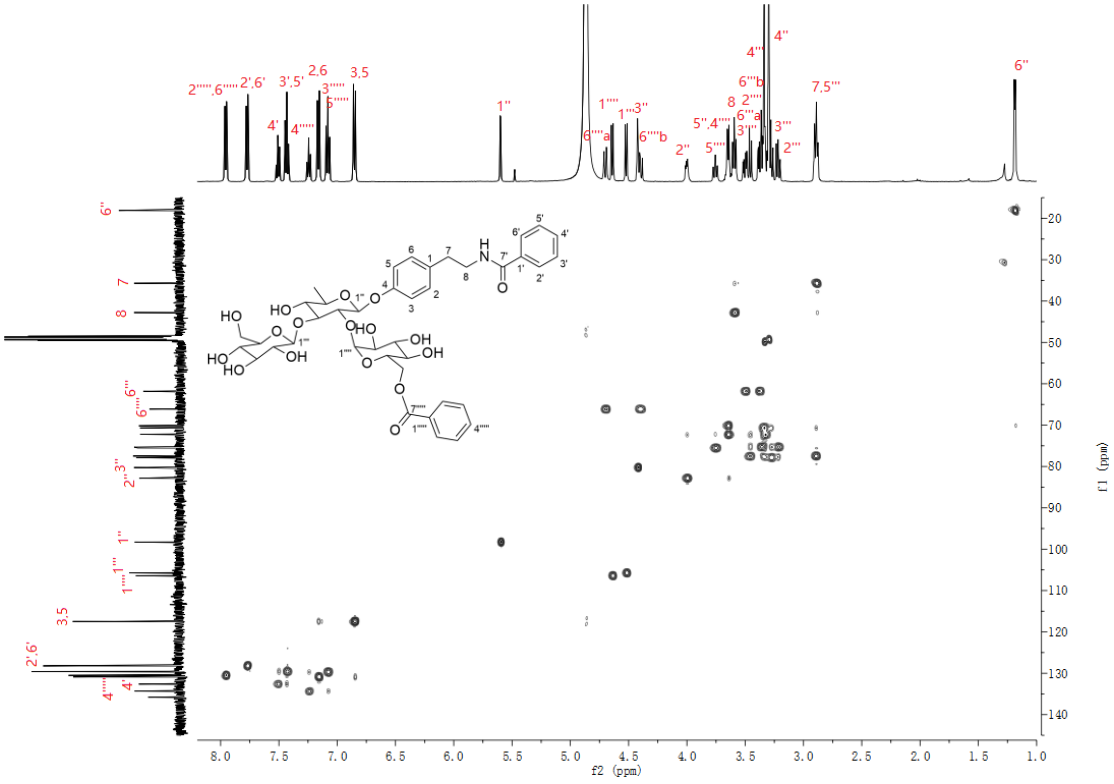


Figure S4. HSQC spectrum of compound **1** recorded in CD_3OD at 500 MHz.

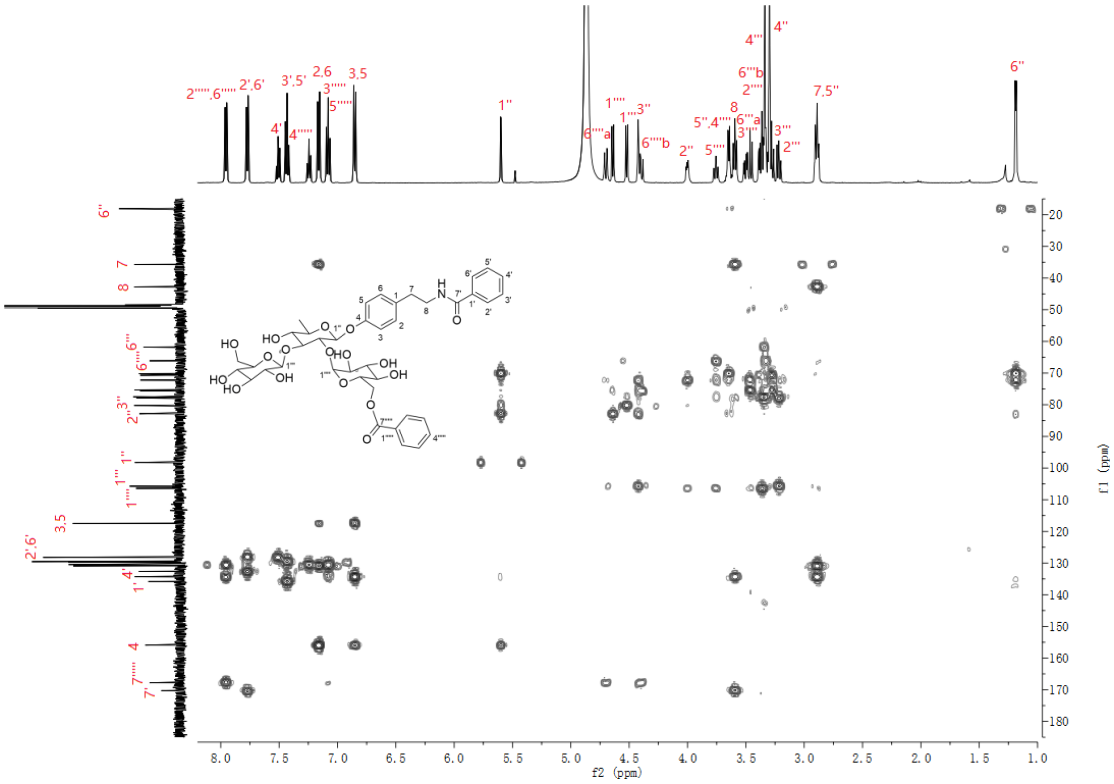


Figure S5. HMBC spectrum of compound **1** recorded in CD_3OD at 500 MHz.

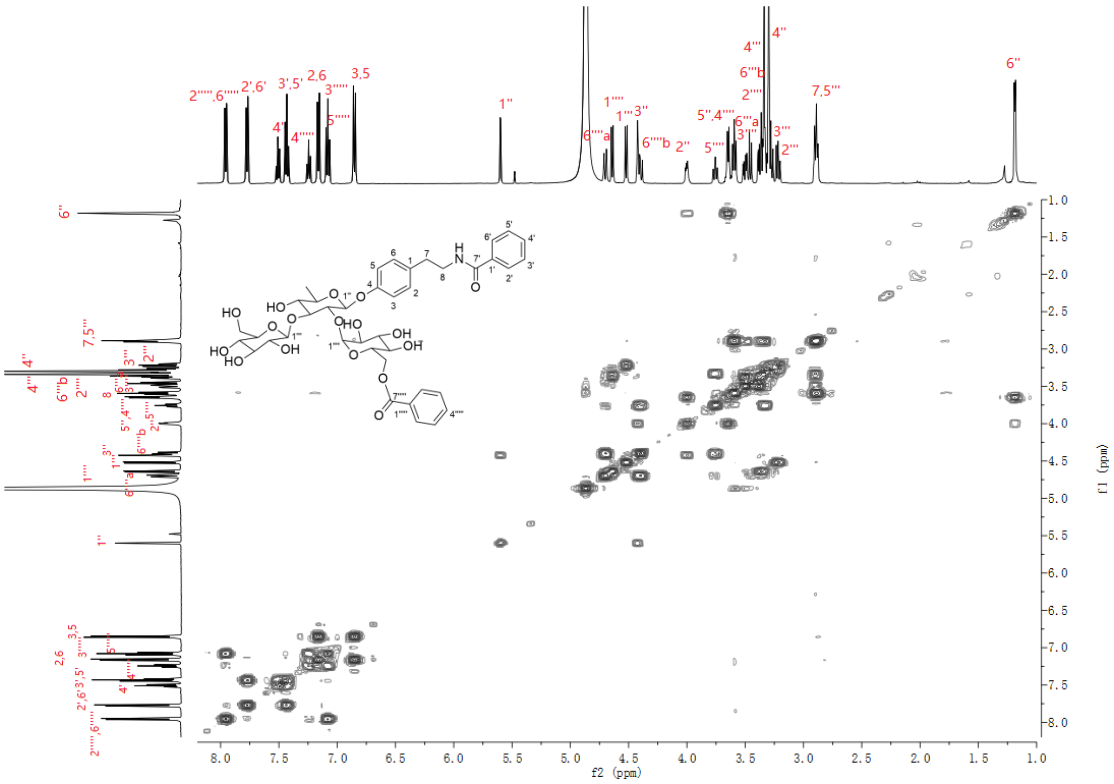


Figure S6. COSY spectrum of compound **1** recorded in CD_3OD at 500 MHz.

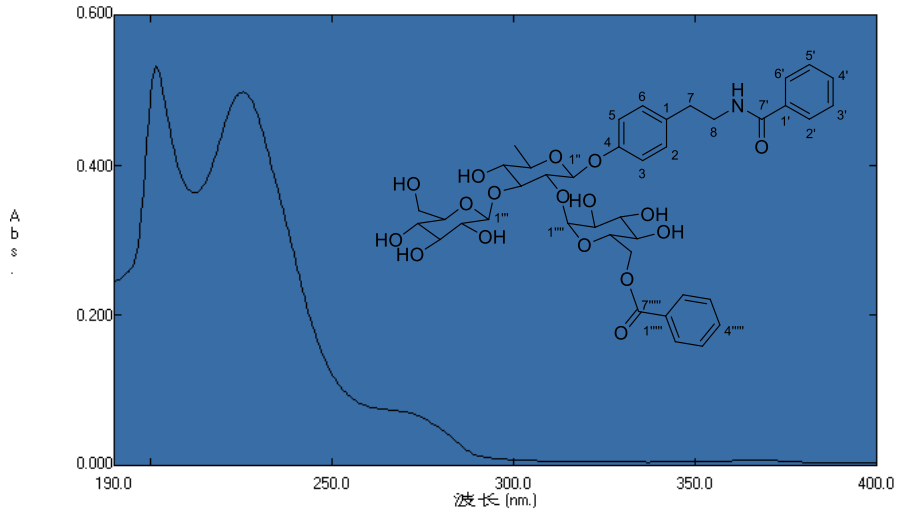


Figure S7. UV spectrum of compound **1** recorded in MeOH.

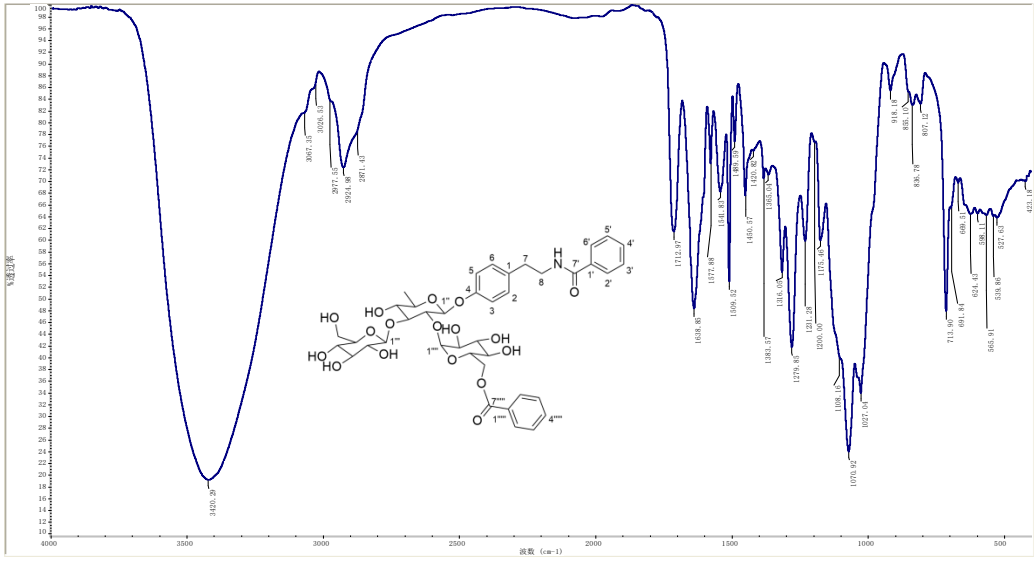
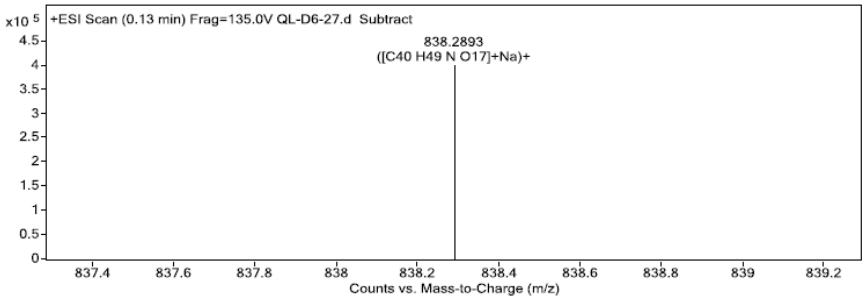


Figure S8. IR spectrum of compound **1**.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.128		48092.57		
104.1069	1	55043.7		
182.1537	1	58635.78		
427.6313	2	44751.8		
480.1996	1	130017.3		
838.2893	1	399292.59	C40 H49 N O17	(M+Na)+
839.2924	1	181276.81	C40 H49 N O17	(M+Na)+
840.2946	1	51811.96	C40 H49 N O17	(M+Na)+

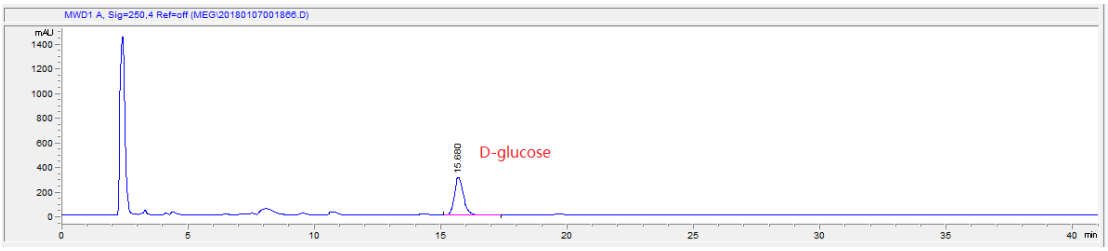
Formula Calculator Element Limits

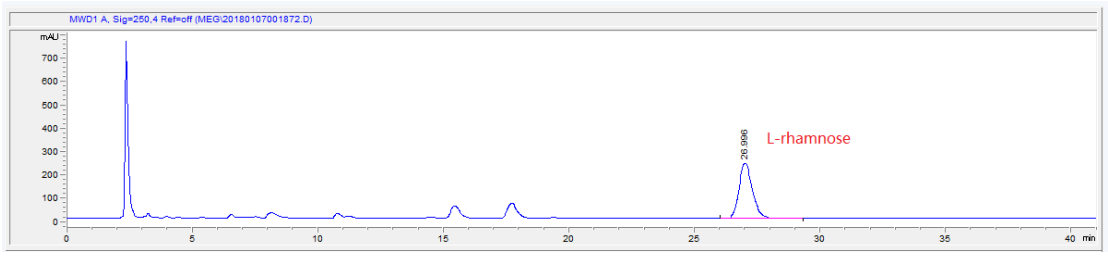
Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C40 H49 N O17	815.3001	838.2893	838.2893	0.00	0.00	17.0000

Figure S9. HR-ESI-MS spectrum of compound **1**.





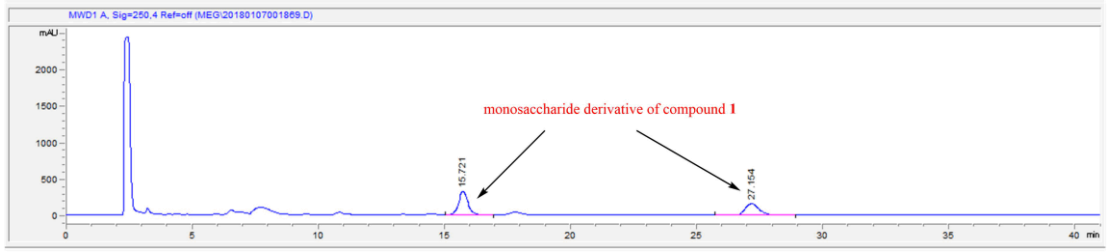


Figure S10. HPLC analysis of monosaccharide derivative of compound **1**.

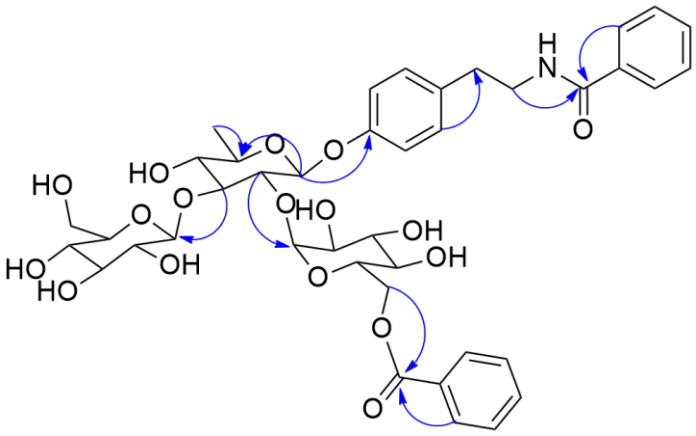


Figure S11. Key HMBC ( ) correlations compound **1**.

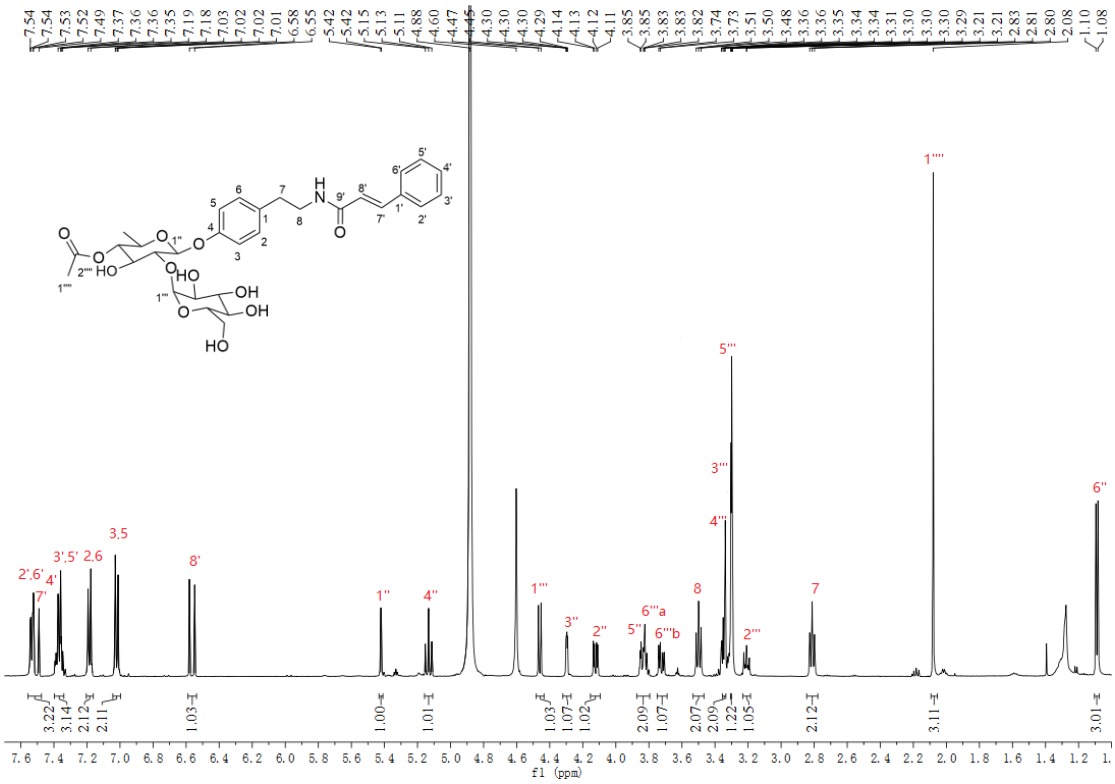


Figure S12. ^{1}H NMR spectrum of compound **2** recorded in CD_3OD at 400 MHz.

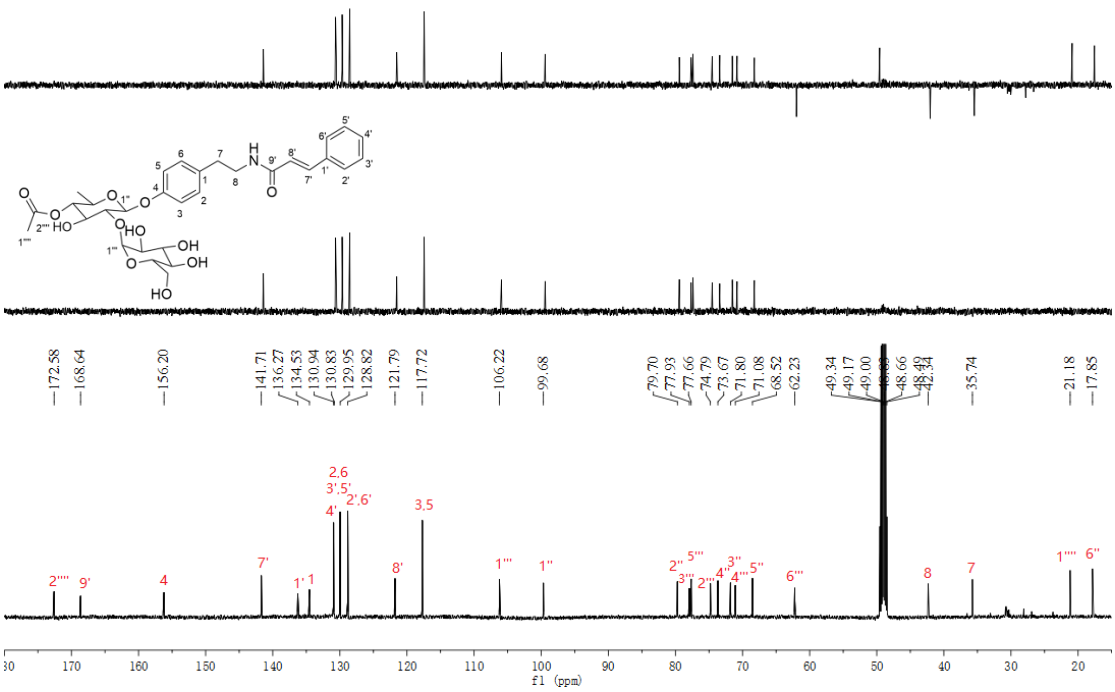


Figure S13. ^{13}C NMR spectrum of compound **2** recorded in CD_3OD at 100 MHz.

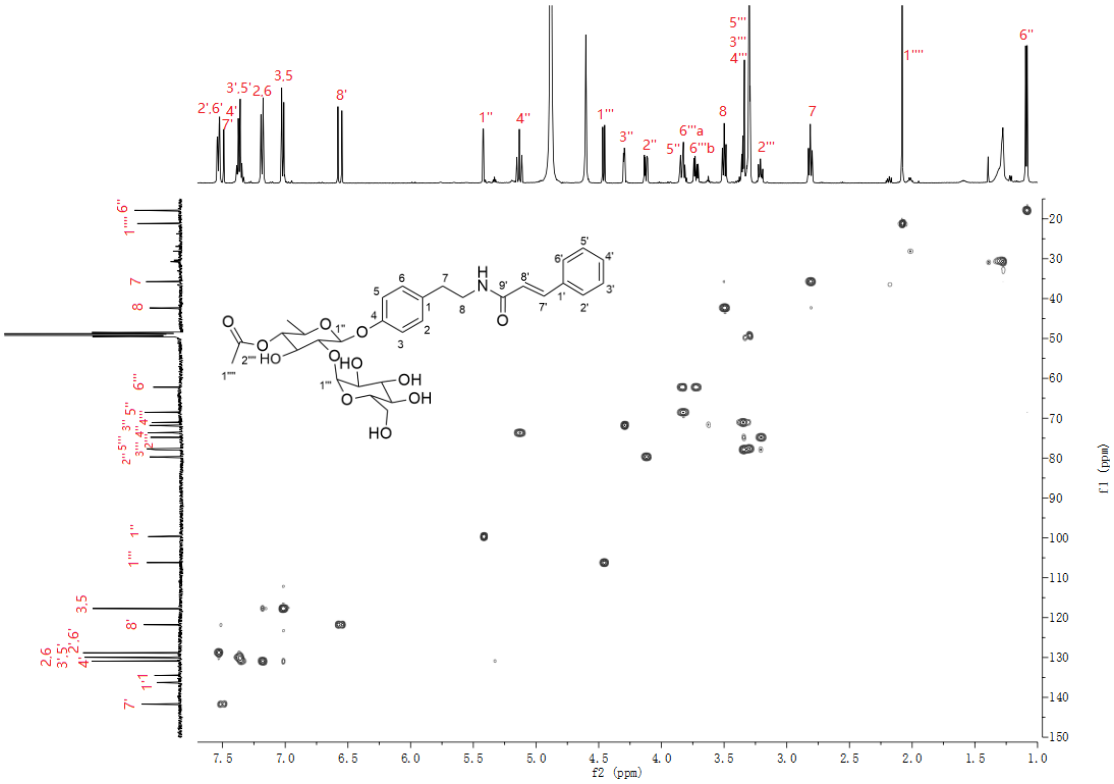


Figure S14. HSQC spectrum of compound **2** recorded in CD_3OD at 500 MHz.

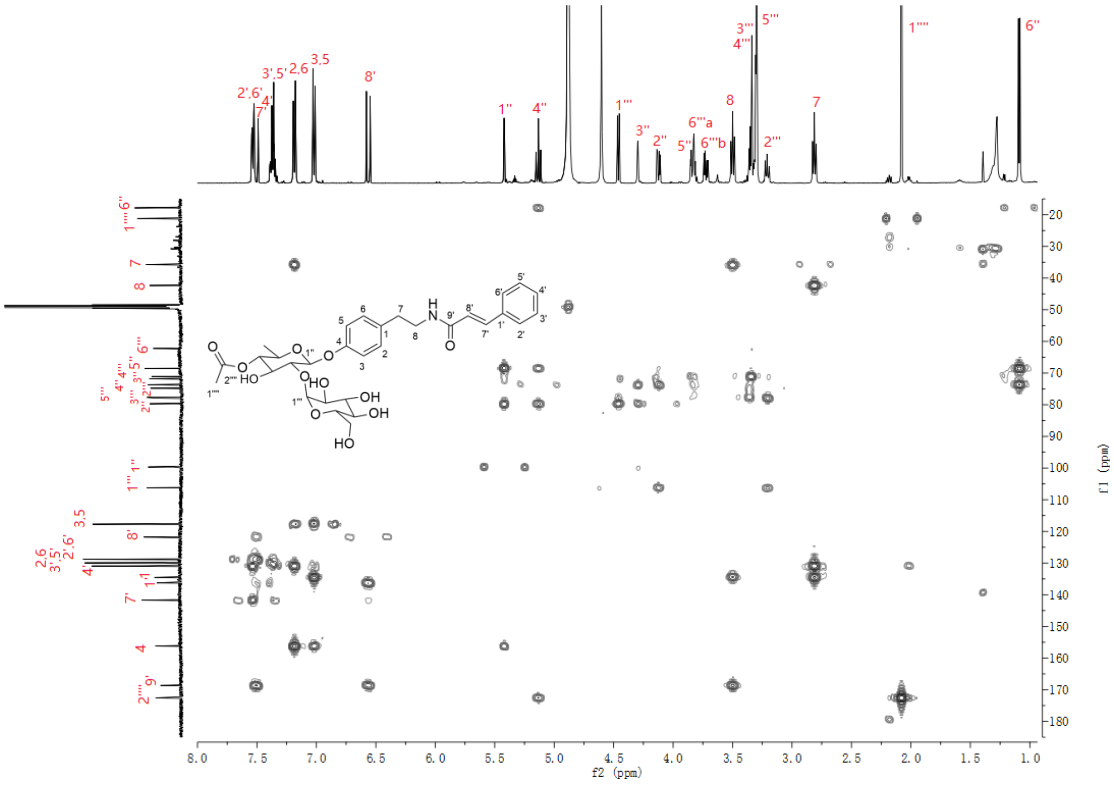
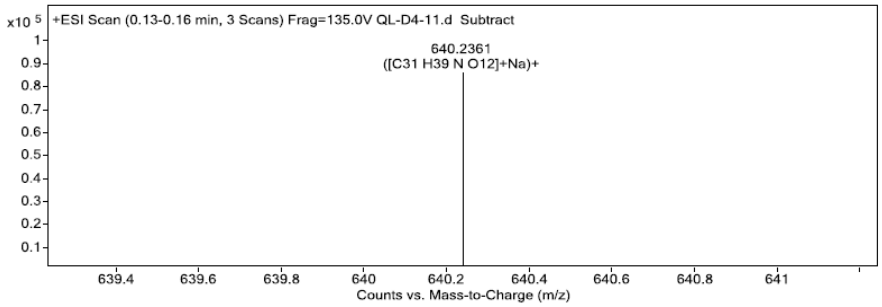


Figure S15. HMBC spectrum of compound **2** recorded in CD_3OD at 500 MHz.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
102.1275	1	199106.42		
103.1305	1	15556.78		
360.3229	1	16636.71		
422.2434	1	12925.4		
640.2361	1	85945.16	C31 H39 N O12	(M+Na)+
641.2397	1	30660.19	C31 H39 N O12	(M+Na)+
656.2099	1	22135.59		
1257.482	1	16198.41		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	10

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C31 H39 N O12	617.2472	640.2364	640.2361	0.30	0.47	13.0000

Figure S16. HR-ESI-MS spectrum of compound **2**.

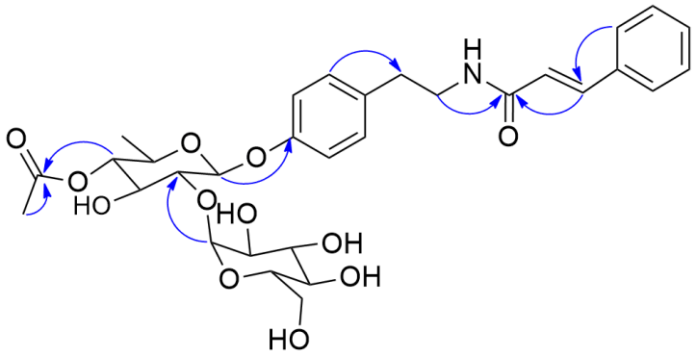


Figure S17. Key HMBC ( ) correlations of compound **2**.

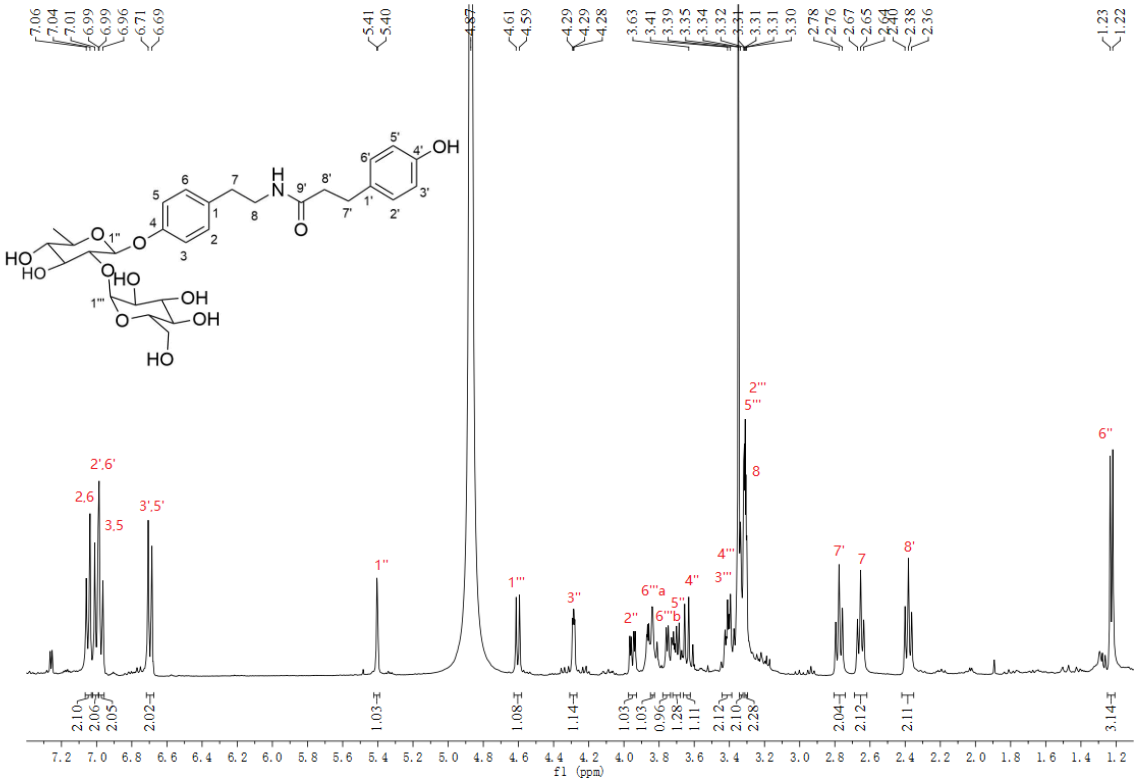


Figure S18. ^{1}H NMR spectrum of compound **3** recorded in CD_3OD at 400 MHz.

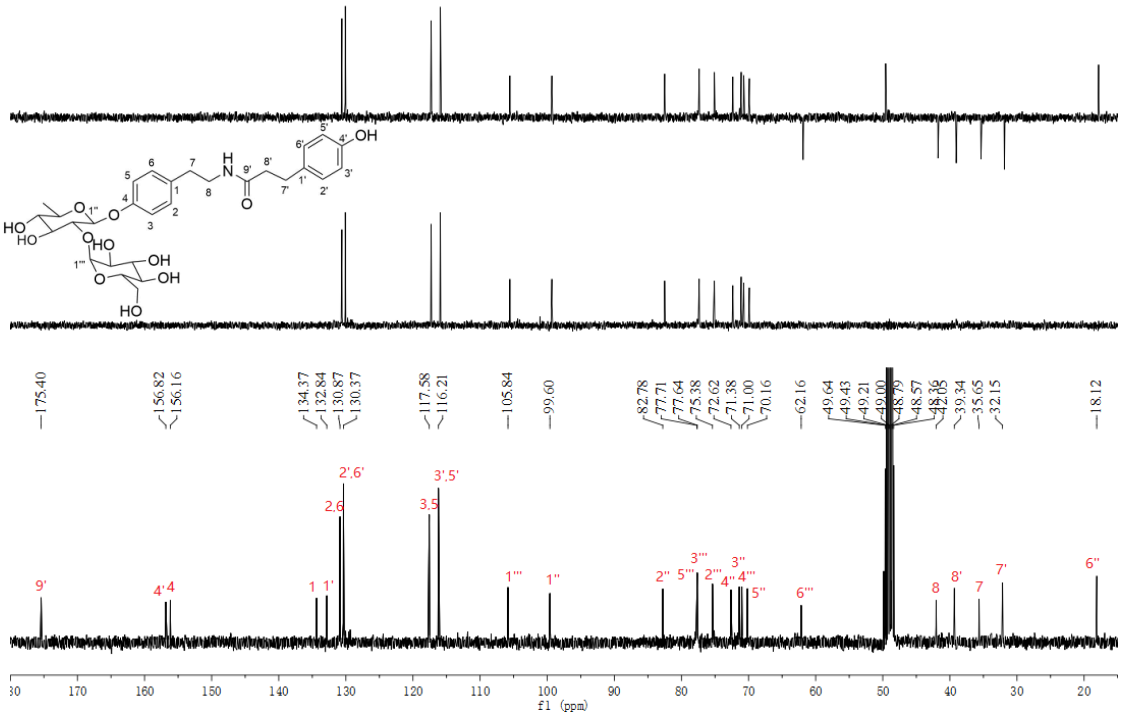
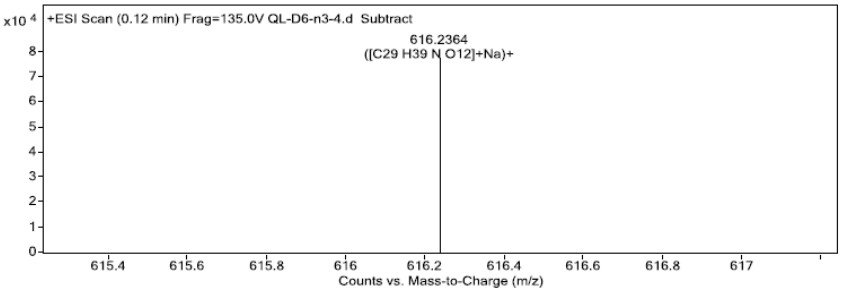


Figure S19. ^{13}C NMR spectrum of compound **3** recorded in CD_3OD at 100 MHz.

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
135	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
104.1069		8208.24		
182.1537	1	9764.07		
360.3237	1	8664.72		
480.1993	1	40792.4		
481.2018	1	7864.52		
616.2364	1	77657.05	C29 H39 N O12	(M+Na)+
617.2394	1	23722.42	C29 H39 N O12	(M+Na)+
638.2176	1	9670.18		

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
C29 H39 N O12	593.2472	616.2364	616.2364	0.00	0.00	11.0000

Figure S20. HR-ESI-MS spectrum of compound **3**.