Electronic Supplementary Material (ESI) for RSC Advances.

Three new cardiac glycosides from the roots of *Streblus asper* Lour. and their cytotoxic and melanogenesis-inhibitory activities

Dan Miao,[a] Tengqian Zhang,[a] Jian Xu,[a] Congyu Ma,[d] Wenyuan Liu,[d] Takashi Kikuchi,[e] Toshihiro Akihisa,[f] Masahiko Abe,[f] Feng Feng*[abc] and Jie Zhang*[ab]

[a] *School of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing 211198, P. R. China*

[b] *Key Laboratory of Biomedical Functional Materials, China Pharmaceutical University, Nanjing 211198, P. R. China*

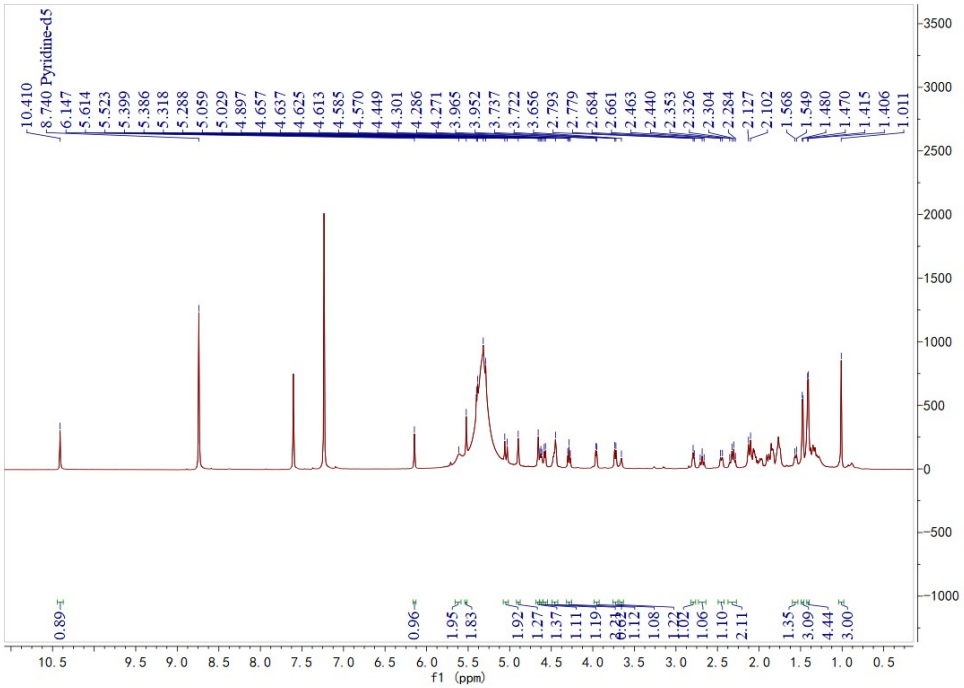
[c] *Jiangsu Food and Pharmaceutical Science College, Huaian, Jiangsu, 223003, China*

[d] *Department of Pharmaceutical Analysis, China Pharmaceutical University, Nanjing 210009, China*

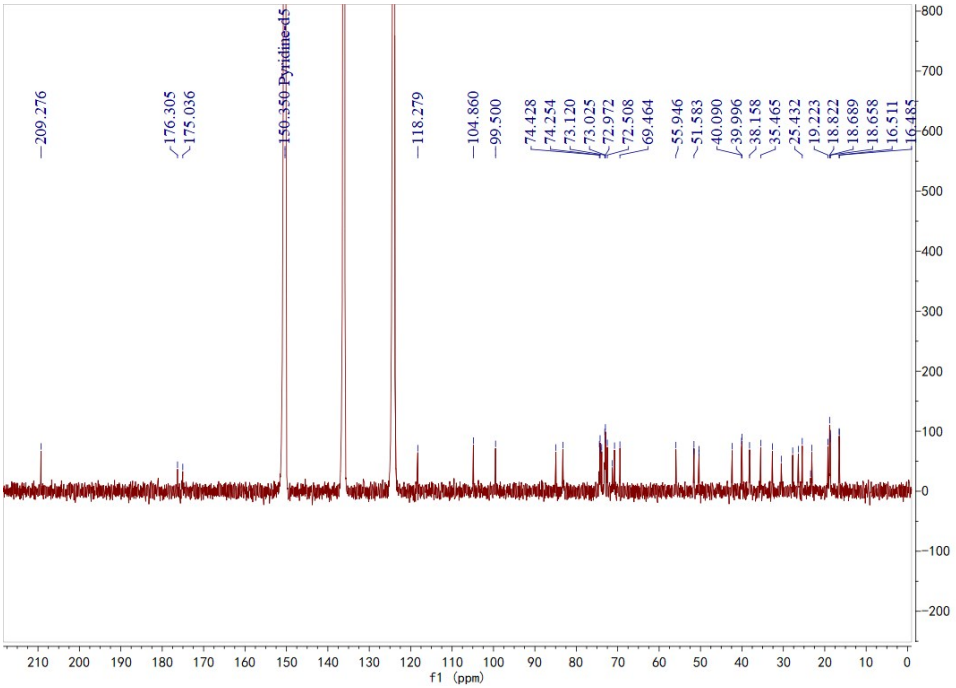
[e] *Osaka University of Pharmaceutical Sciences, 4-20-1 Nasahara, Takatsuki, Osaka 569-1094, Japan*

[f] *Research Institute for Science and Technology, Tokyo University of Science, 2641*

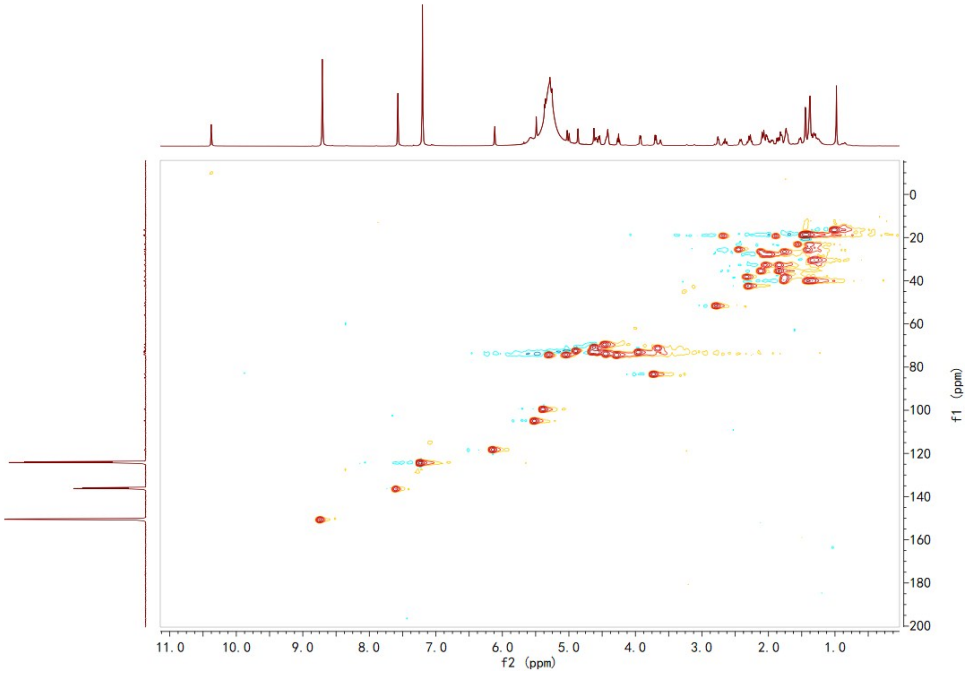
Yamazaki, Noda, Chiba 278-8510, Japan



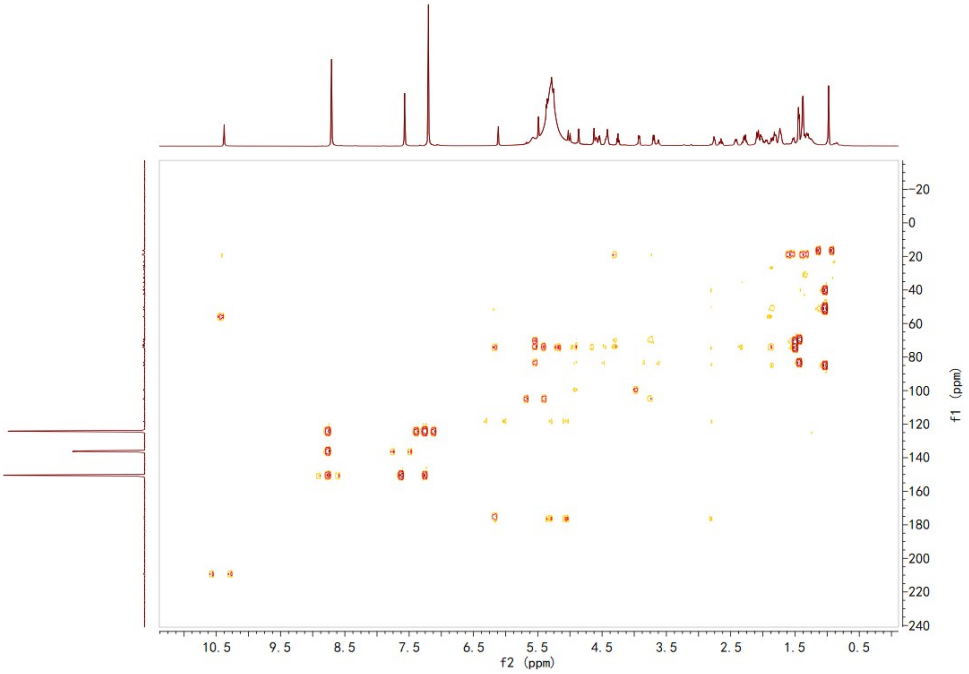
S1. ^{1}H-NMR spectrum of compound **1**



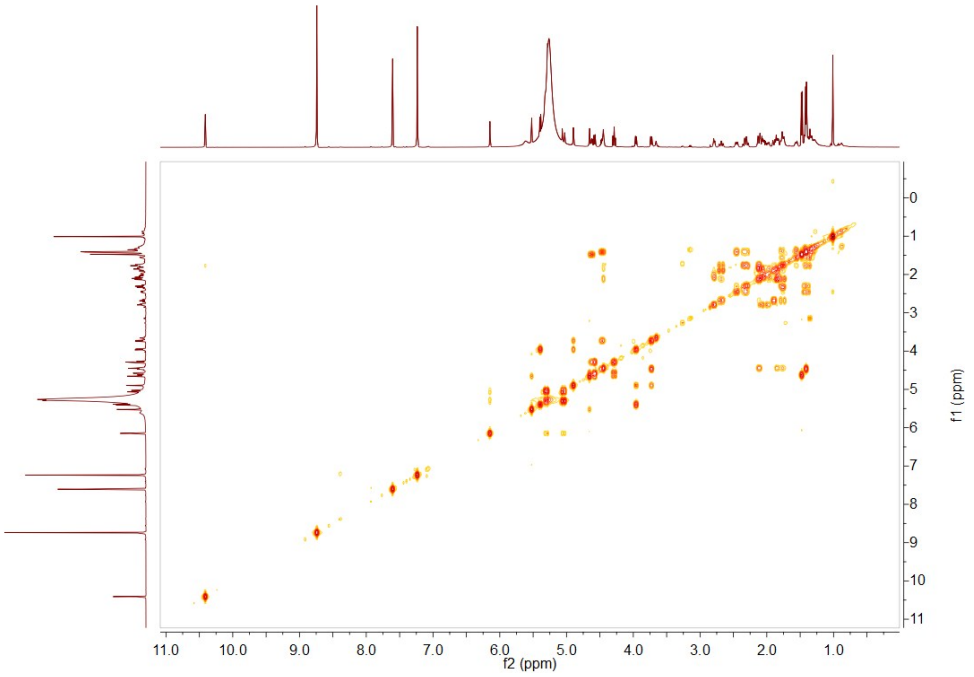
S2. ^{13}C-NMR spectrum of compound **1**



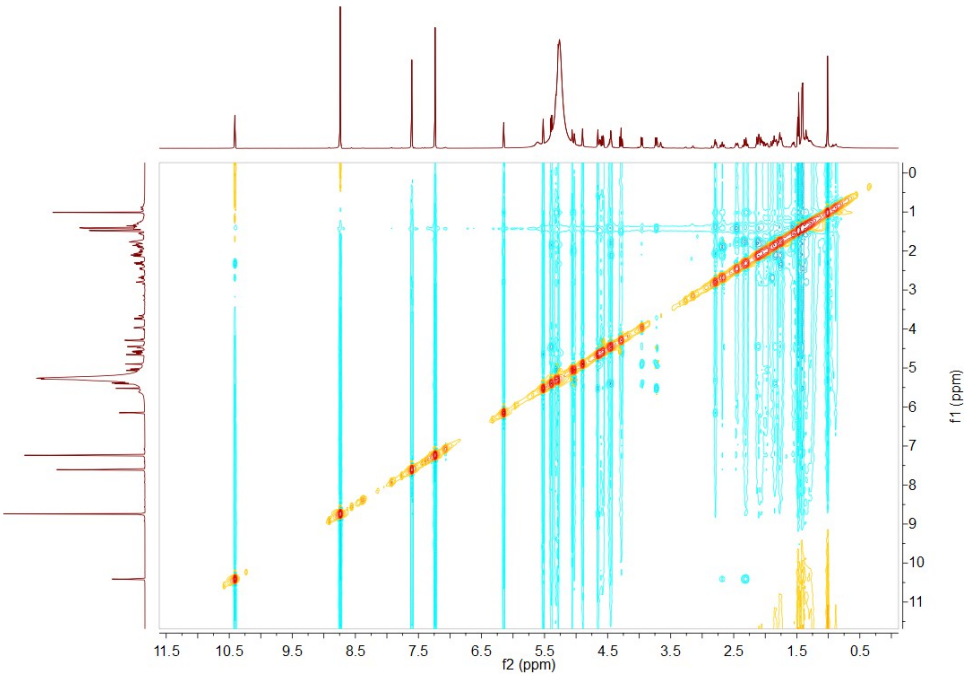
S3. HSQC spectrum of compound **1**



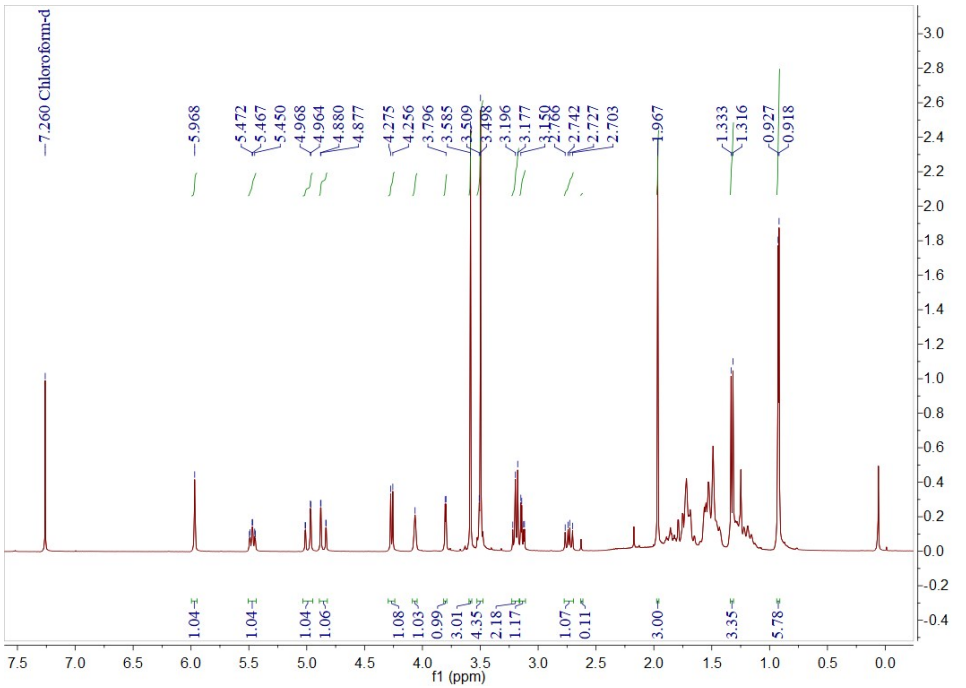
S4. HMBC spectrum of compound **1**



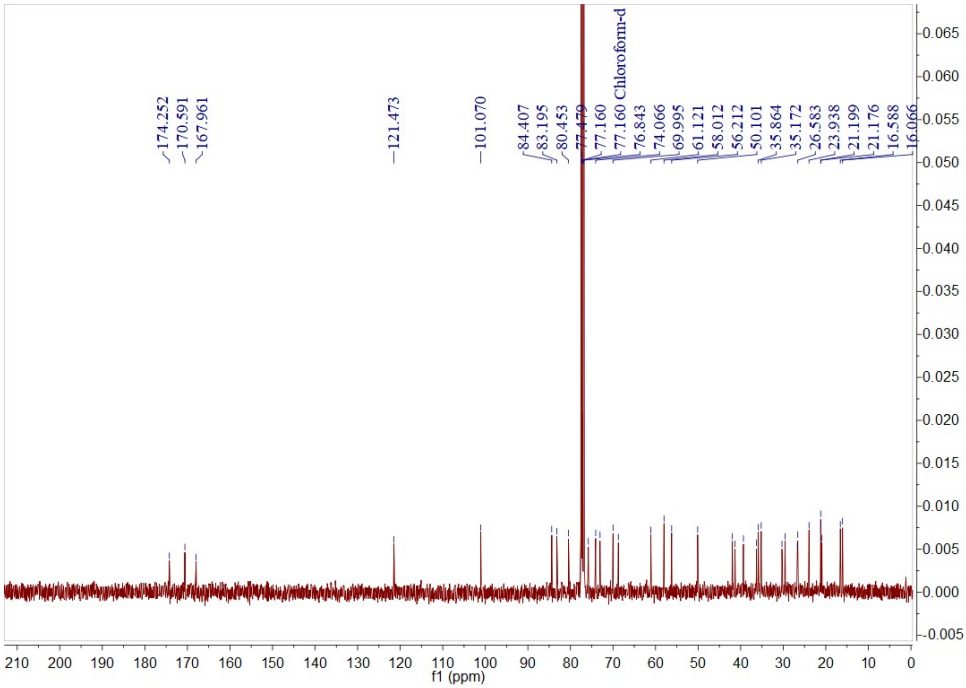
S5. ^{1}H-^{1}H COSY spectrum of compound **1**



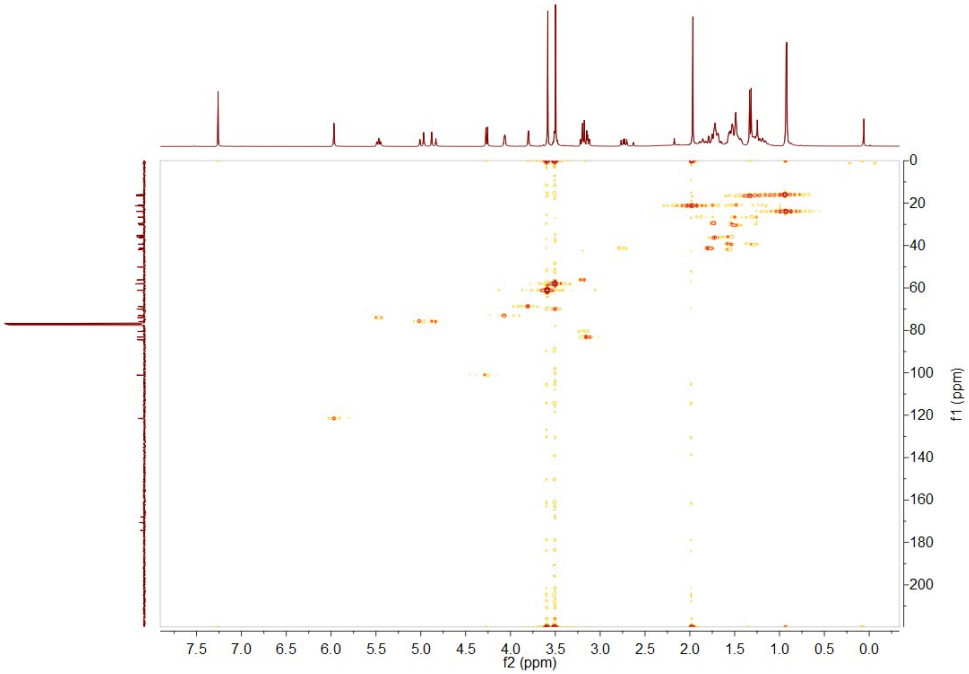
S6. ROESY spectrum of compound **1**



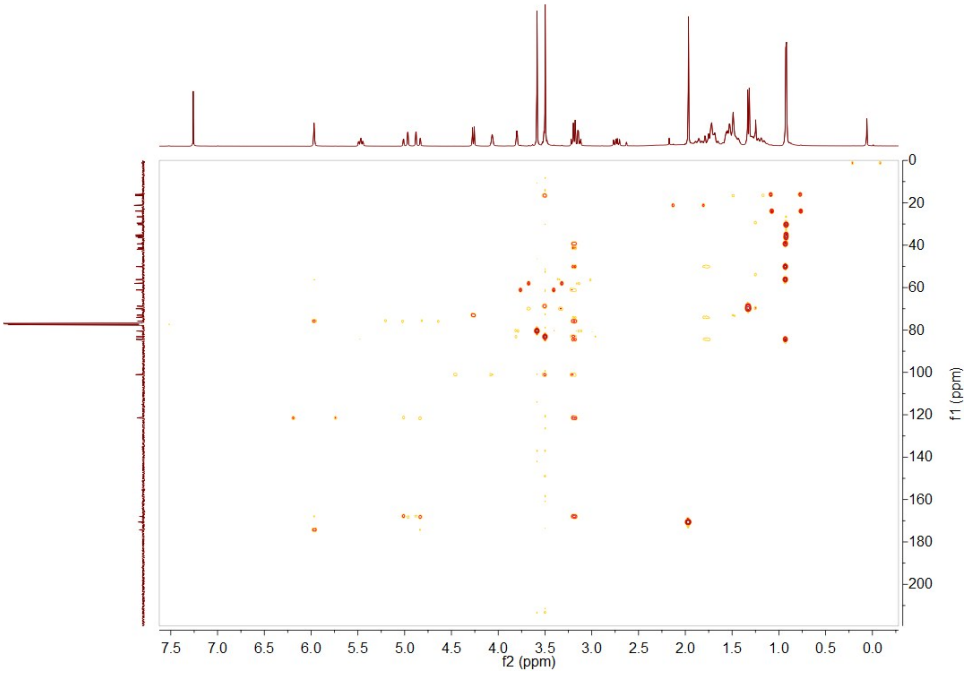
S7. ^{1}H-NMR spectrum of compound **2**



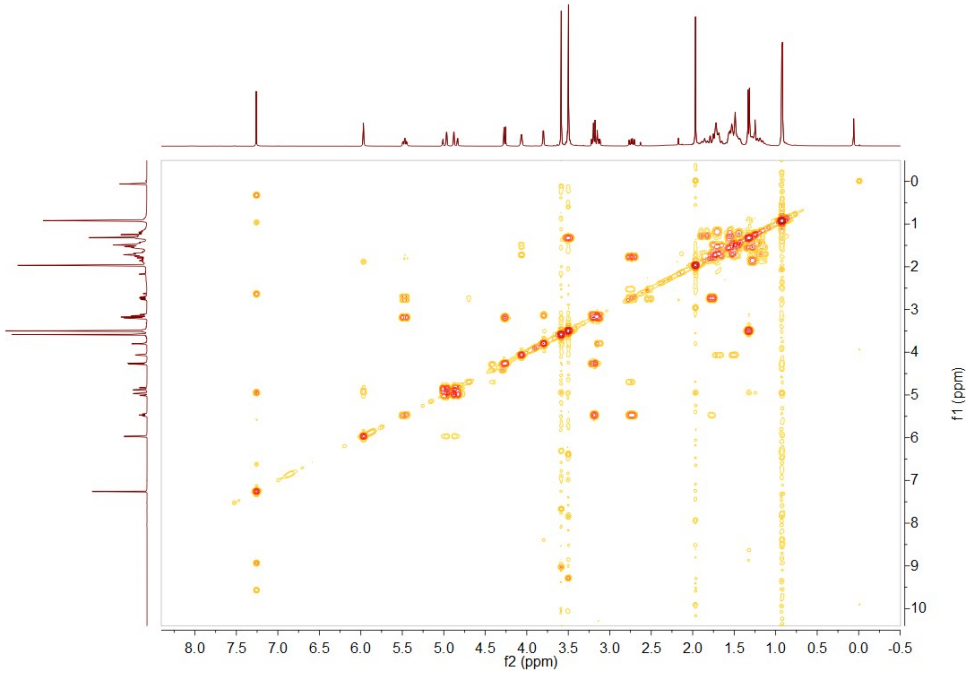
S8. ^{13}C-NMR spectrum of compound **2**



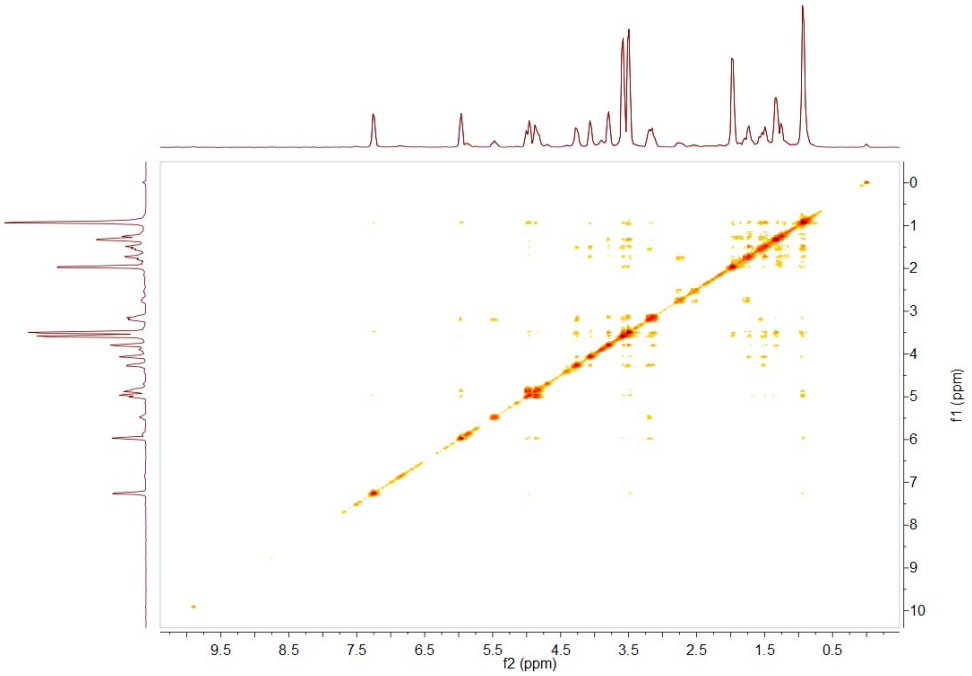
S9. HSQC spectrum of compound **2**



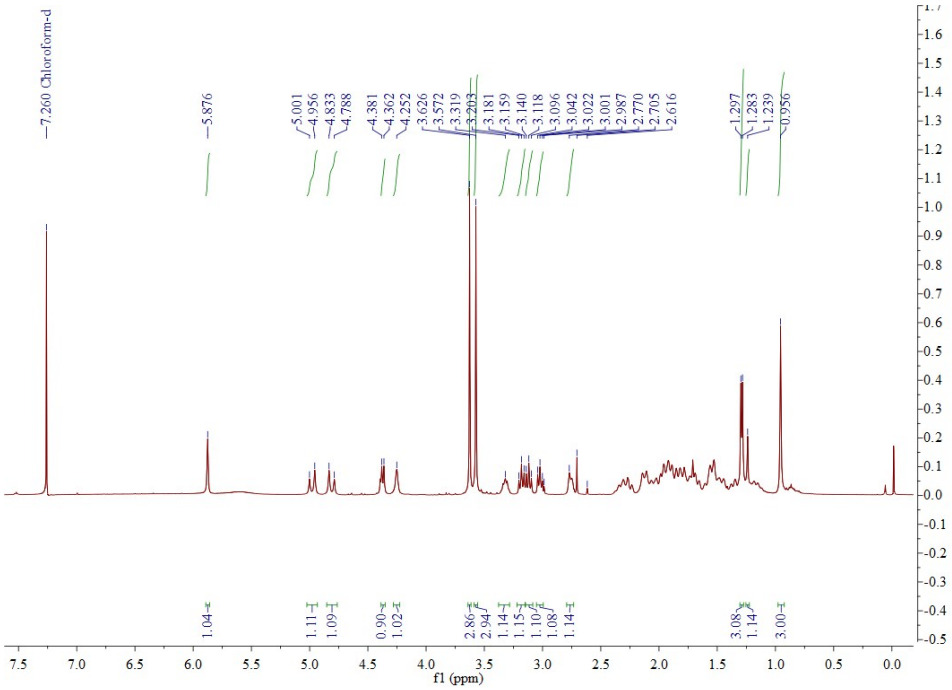
S10. HMBC spectrum of compound **2**



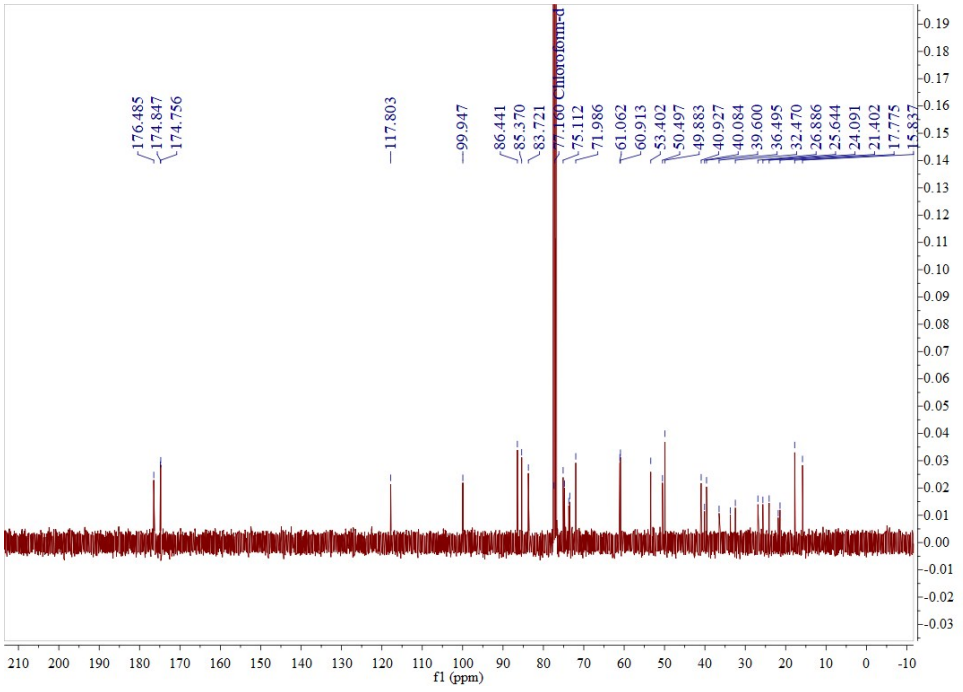
S11. ^{1}H-^{1}H COSY spectrum of compound **2**



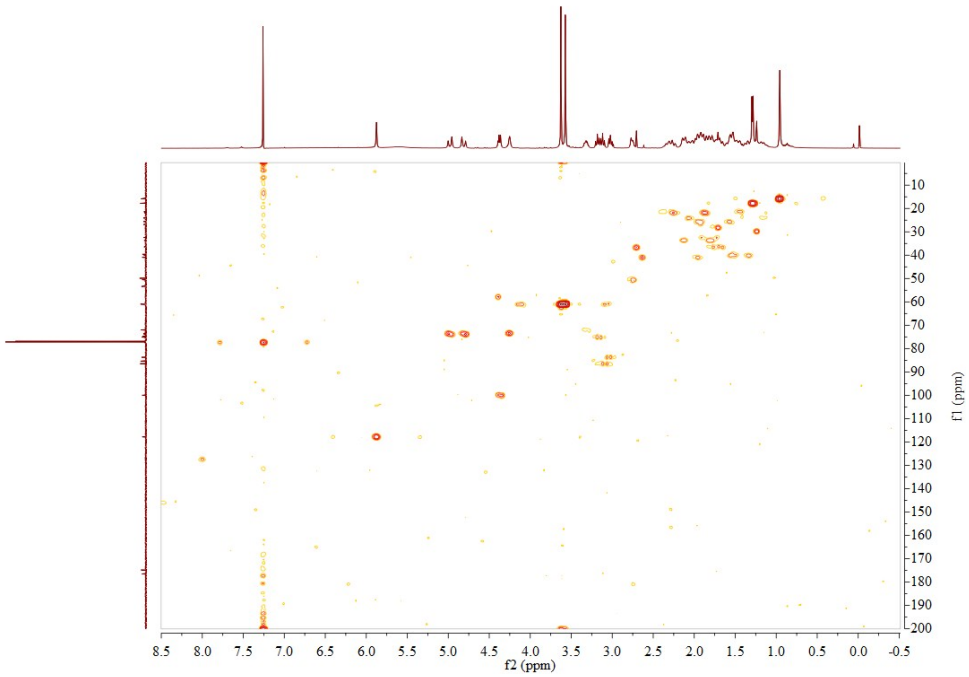
S12. NOESY spectrum of compound **2**



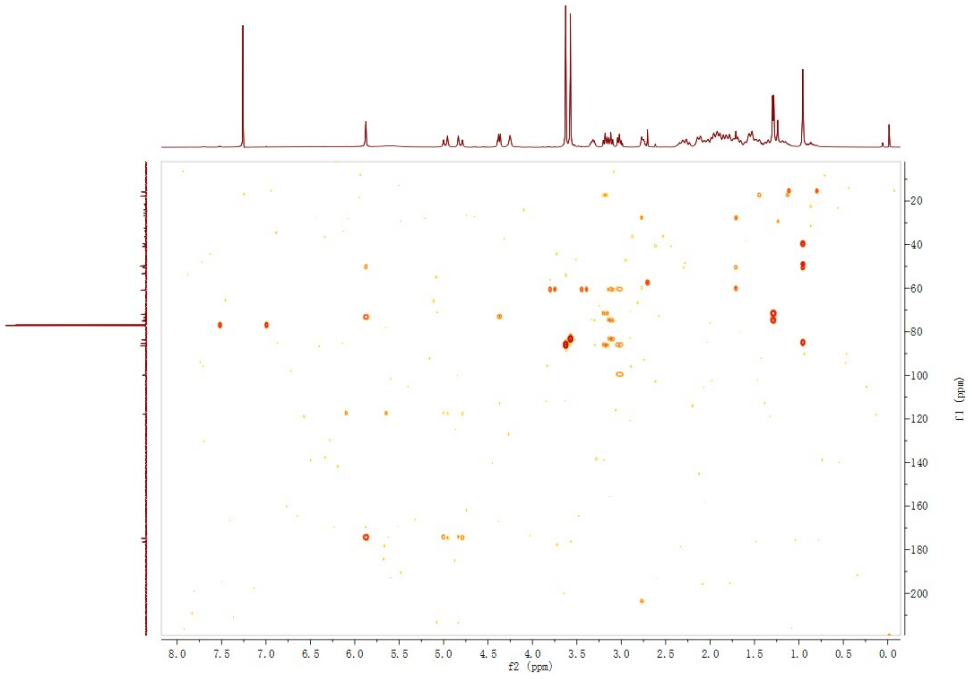
S13. [1]H-NMR spectrum of compound **3**



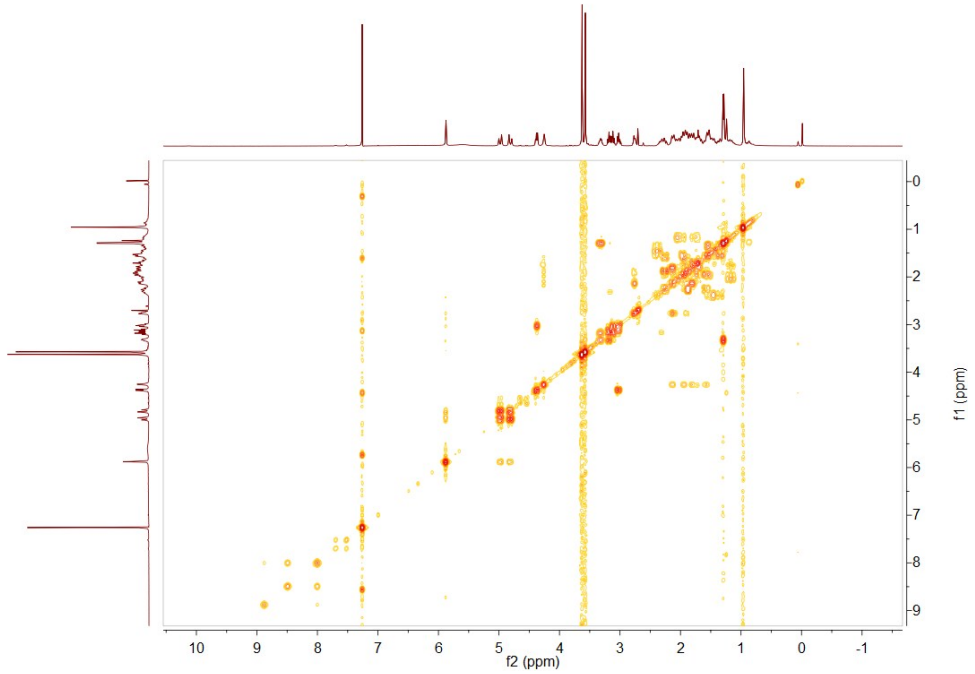
S14. [13]C-NMR spectrum of compound **3**



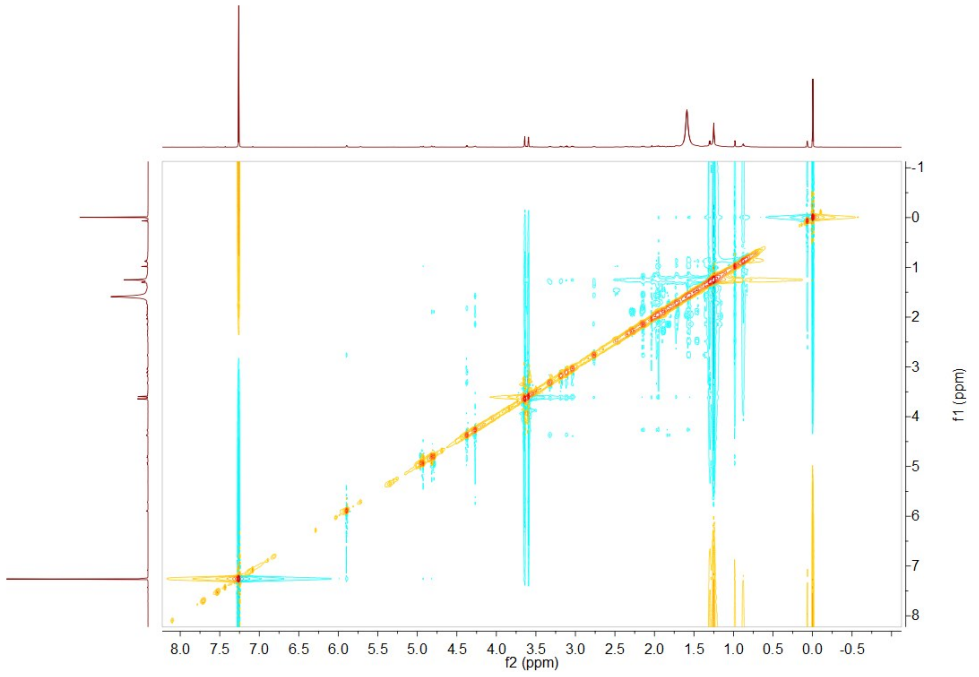
S15. HSQC spectrum of compound **3**



S16. HMBC spectrum of compound **3**

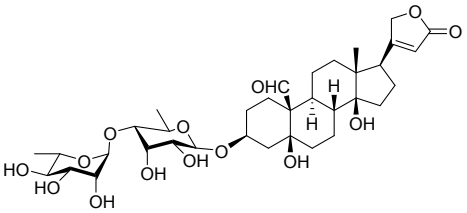
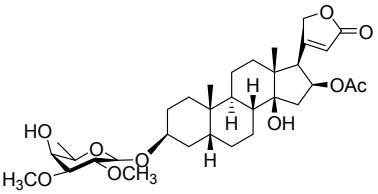
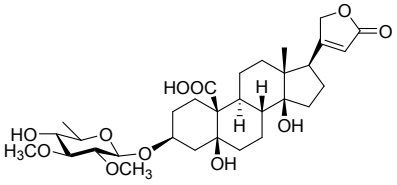
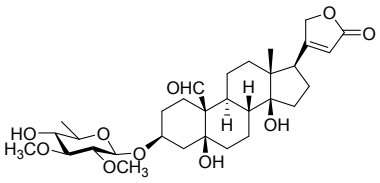
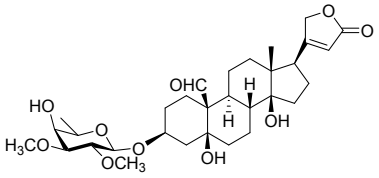
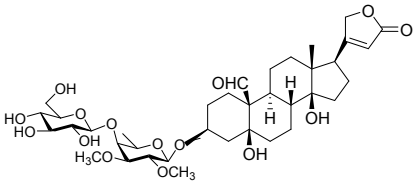


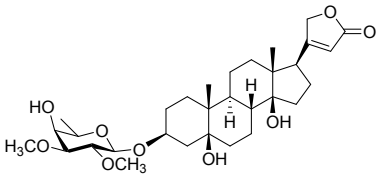
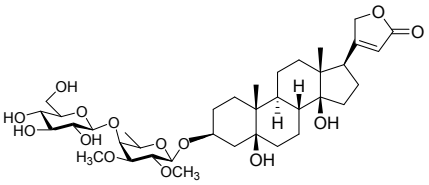
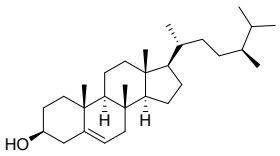
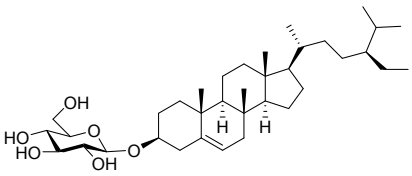
S17. ^{1}H-^{1}H COSY spectrum of compound **3**



S18. ROESY spectrum of compound **3**

S19. List of all compounds

No.	Name	Structure
1	Strophanthidin-3-*O*-α-L-rhamnopyranosyl-(1→4)-6-deoxy-β-D-allopyranoside	
2	5βH-16β-acetylkamaloside	
3	Mansonin-19-carboxylic acid	
4	Mansonin	
5	Strebloside	
6	Glucostrebloside	

7	Kamaloside	
8	Glucokamaloside	
9	β-sitosterol	
10	β-sitosterol-3-*O*-β-D-glucopyranoside	

S20. ^{1}H-NMR and ^{13}C-NMR spectroscopic data of compounds **1** and reference (δ in ppm, J in Hz)

	1[a]			**Reference: Strophanthidin-3-*O*-β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl-(1→4)-*O*-β-D-diginopyranosyl-(1→4)-*O*-β-D-oleandropyranosyl-(1→4)-*O*-β-D-digitoxopyranosyl-(1→4)-β-D-digitoxopyranoside**[b,1]	
Position	δ_C	δ_H	HMBC (H→C)	δ_C	δ_H
1	19.2	1.89, m 2.68, dd (13.8, 13.8)	10	18.5	1.89, m 2.57, ddd (14.6, 14.6, 3.2)
2	25.4	1.41, m 2.45, d (13.8)		25.6	1.66. m 2.18, dd (14.1, 2.6)
3	73.9	4.44, m		74.9	4.33, br s
4	35.5	1.84, m 2.12, m	5	36.2	1.70, m 2.17,
5	74.1			74.0	
6	42.4	1.55, m 2.29, d (12.0)	4, 5	36.9	1.77, m 2.29, m
7	23.1	1.37, m 1.56, d (5.4)	5	24.8	1.42, m 2.45, m
8	40.1	1.41, m	6	41.9	2.28, m
9	40.0	1.77, m	10, 11, 13	39.5	1.75, m
10	56.0			55.3	
11	26.4	1.76, m 2.11, m	13	22.6	1.37, m 1.56, m
12	38.2	1.76, m 2.34, d (16.2)		39.5	1.34, m 1.41, m
13	50.4			49.8	
14	84.9			84.4	
15	32.7	1.84, m 2.05, m	13, 14	32.1	1.83, m 2.06, m
16	27.7	1.99, m 2.07, m		27.2	

17	51.6	2.79, m	8, 13, 14, 20, 21, 22	51.1	2.78, br d (8.7)
18	16.5	1.01, s	8, 13, 14	16.0	1.00, s
19	209.3	10.41, s	1, 10	208.5	10.40, s
20	176.3			175.7	
21	74.3	5.04, d (18.0) 5.30, d (18.0)	20, 22	73.7	5.03, dd (18.0, 1.3) 5.29, dd (18.0, 1.3)
22	118.3	6.15, s	17, 20, 21	117.8	6.13, br s
23	175.0			174.5	
1′	99.5	5.39, d (7.8)	3	100.8	
2′	74.2	3.96, d (7.8)	1′	72.4	
3′	72.5	4.90, s	1′, 4′	72.9	
4′	83.2	3.73, d (9.0)	5′	83.9	
5′	69.5	4.46, m	6′	69.2	
6′	18.8	1.41, d (5.4)		18.6	
1″	104.9	5.52, s	4′, 2″, 5″	104.0	
2″	73.0	4.66, s	3″	72.4	
3″	74.4	4.29, dd (9.0, 9.0)	4″, 5″	72.2	
4″	73.1	4.58, d (9.0)	6″	73.7	
5″	70.8	4.63, m		70.3	
6″	18.7	1.48, d (6.0)	3″	18.4	

[a] ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectroscopic data in pyridine-d_5.

[b] ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectroscopic data in pyridine-d_5.

S21. ^{1}H-NMR and ^{13}C-NMR spectroscopic data of compounds **2** and reference (δ in ppm, J in Hz)

	2[a]			**Reference: oleandrigenin** [b,2]	**Reference: acoschimperoside P, 2′-acetate** [c,3]	
Position	δ_C	δ_H	HMBC (H→C)	δ_C	δ_C	δ_H
1	30.3	1.44, m 1.51, m		29.5	30.8	1.53, m 1.57, m
2	26.7	1.26, m 1.50, m		27.8	26.5	1.20, m 1.56, m
3	73.1	4.06, br s		66.6	73.3	4.15, br s
4	29.6	1.26, m 1.73, m		33.2	30.1	1.74, m 1.98, m
5	36.3	1.72, m		35.8	35.6	1.51, m
6	26.6	1.25, m 1.88, m		26.2	24.0	1.32, m 1.43, m
7	21.2	1.69, m 1.74, m		20.8	21.4	1.30, m 1.66, m
8	41.9	1.57, m		41.7	42.0	1.78, m
9	35.9	1.58, m		35.4	37.1	1.81, m
10	35.2			35.2	35.1	
11	20.9	1.20, m 1.48, m		21.0	21.0	1.30, m 1.66, m
12	39.4	1.32, m 1.54, m		41.2	38.7	1.32, m 1.43, m
13	50.1			49.9	50.4	
14	84.4			84.1	83.2	
15	41.3	1.77, dd (15.6, 2.4) 2.73, dd (15.6, 9.6)	13	39.2	41.2	2.12, br s 2.78, dd (9.7, 5.5)
16	74.1	5.47, td (9.2, 2.4)	16-OCOCH_3 20	73.8	74.8	5.68, dd (9.7, 8.9)
17	56.2	3.20, m	13, 20, 21	56.0	56.7	3.38, d (8.9)
18	16.1	0.93, s	12, 13, 14	15.9	16.3	1.07, s

19	23.9	0.92, s	1, 5	23.6	23.8	0.85, s
20	168.0			170.1	170.5	
21	75.8	4.85, dd (18.4, 1.6)	20	75.6	76.4	5.41, dd (18.1, 1.7)
		4.97, dd (18.4, 1.6)				5.54, dd (18.1, 1.7)
22	121.5	5.96, s	20	121.2	121.6	6.35, s
23	174.3		21	173.8	174.5	
16-OCOCH$_3$	21.2	1.97, s		21.0	21.6	2.04, s
	170.6			167.5	170.5	
1′	101.1	4.27, d (7.6)	3			
2′	80.5	3.19, d (7.6)	1′, 3′			
3′	83.2	3.13, dd (9.6, 3.2)	4′			
4′	68.7	3.80, d (3.2)				
5′	70.0	3.50, m	1', 4', 6'			
6′	16.6	1.33, d (6.8)	5′			
2′-OCH*3*	61.1	3.59, s	1′, 2′			
3′-OCH*3*	58.0	3.50, s	3′			

[a] ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectroscopic data in chloroform-*d*.

[b] ^{13}C (100 MHz) NMR spectroscopic data in chloroform-*d*.

[c] ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectroscopic data in pyridine-d_5.

S22. ^{1}H-NMR and ^{13}C-NMR spectroscopic data of compounds **3** and reference (δ in ppm, J in Hz)

Position	**3**[a]			**Reference: reevesioside D**[b,4]	
	δ_C	δ_H	HMBC (H→C)	δ_C	δ_H
1	21.4	1.44, m 2.39, m	19	21.3	1.46, m 2.36, m
2	25.6	1.57, m 1.93, m		25.7	1.59, m 1.94, m
3	73.5	4.25, br s		72.2	4.25, br s
4	33.7	1.81, m 2.12, m		33.2	1.79, m 2.08, m
5	75.1			74.6	
6	36.5	1.65, m 1.76, m		36.5	1.72, m 2.07, m
7	24.1	1.17, m 2.07, m		23.9	1.25, m 2.09, m
8	40.9	1.24, m		40.7	1.52, m
9	40.1	1.96, m		39.4	1.92, m
10	53.4			53.3	
11	21.9	1.86, m 2.25, m		21.8	1.31, m 1.54, m
12	39.6	1.34, m 1.56, m		40.0	1.33, m 1.52, m
13	49.9			49.8	
14	85.4			85.3	
15	32.5	1.73, m 1.93, m		32.3	1.68, m 2.01, m
16	26.9	2.09, m 2.20, m		26.8	1.85, m 2.01, m
17	50.5	2.75, m	16	50.4	2.75,dd (9.6, 5.2)
18	15.8	0.96, s	12, 13, 14,	15.7	0.86, s

19	176.5			176.6	
20	174.9			174.7	
21	73.7	4.81, d (18.0)		73.6	4.79, dd (18.2,1.6)
		4.98, d (18.0)			4.95, dd (18.2,1.6)
22	117.8	5.88, s	17, 21, 23	117.6	5.88, s
23	174.8			174.6	
1′	100.0	4.37, d (7.6)	3		
2′	83.7	3.02, dd (8.4, 8.0)	1′, 2′		
3′	86.4	3.12, dd (8.8, 8.8)	2′, 4′		
4′	74.8	3.18, dd (8.4, 8.0)	3′, 5′, 6′		
5′	72.0	3.33, m			
6′	17.8	1.29, d (5.6)	4′, 5′		
2′-OCH*3*	61.1	3.63, s	2′		
3′-OCH*3*	60.9	3.57, s	3′		

[a] ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectroscopic data in chloroform-*d*.

[b] ^{1}H (400 MHz) and ^{13}C (150 MHz) NMR spectroscopic data in chloroform-*d*.

Reference:

1 S. Kubo, M. Kuroda, Y. Matsuo, D. Masatani, H. Sakagami and Y. Mimakia, *Chemical & Pharmaceutical Bulletin*, 2012, **60**, 1275–1282.

2 G. M. Cabrera, M. E. Deluca, A. M. Seldes, E. G. Gros, J. C. Oberti, J. Crockett and M. L. Gross, *Phytochemistry*, 1993, **32**, 1253–1259.

3 Y. Rifai, M. A. Arai, T. Koyano, T. Kowithayakorn and M. Ishibashi, *J Nat Med*, 2011, **65**, 629–632.

4 H. S. Chang, M. Y. Chiang, H. Y. Hsu, C. W. Yang, C. H. Lin, S. J. Lee and I. S. Chen, *Phytochemistry*, 2013, **87**, 86–95.