Supplementary Materials

Anti-proliferative effects on cancer stem cells of derivatives of iridoid glucosides isolated from *Valeriana fauriei*

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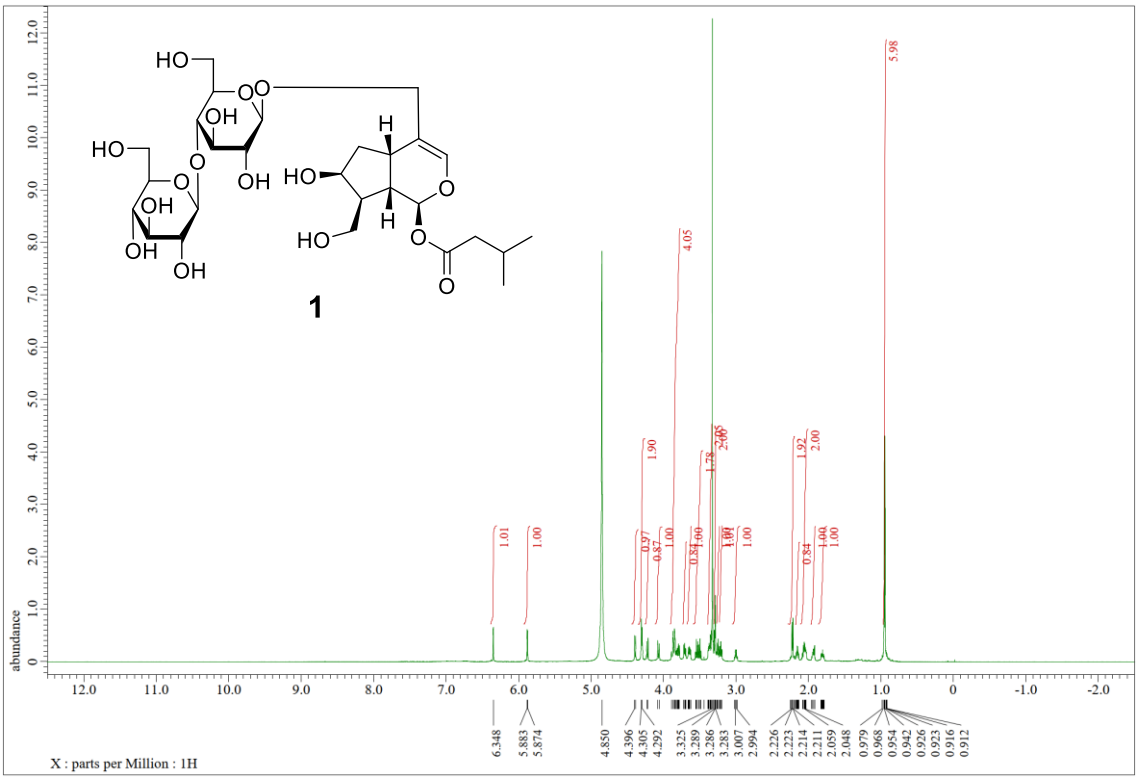
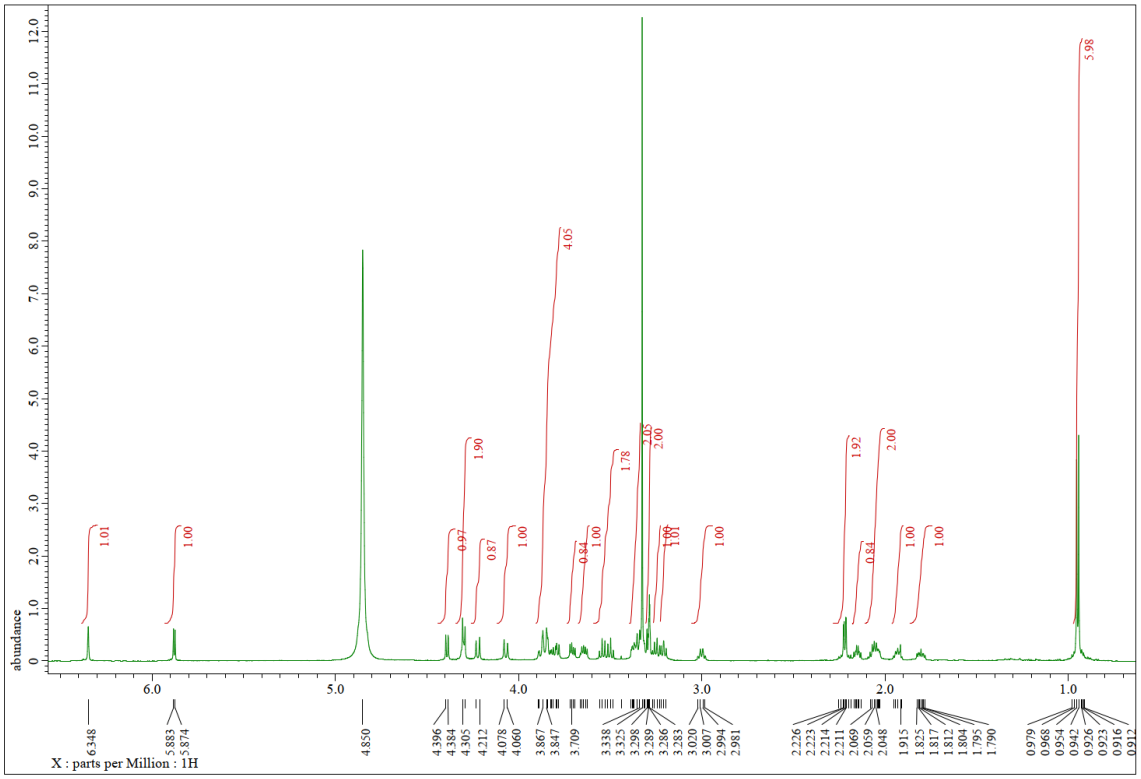
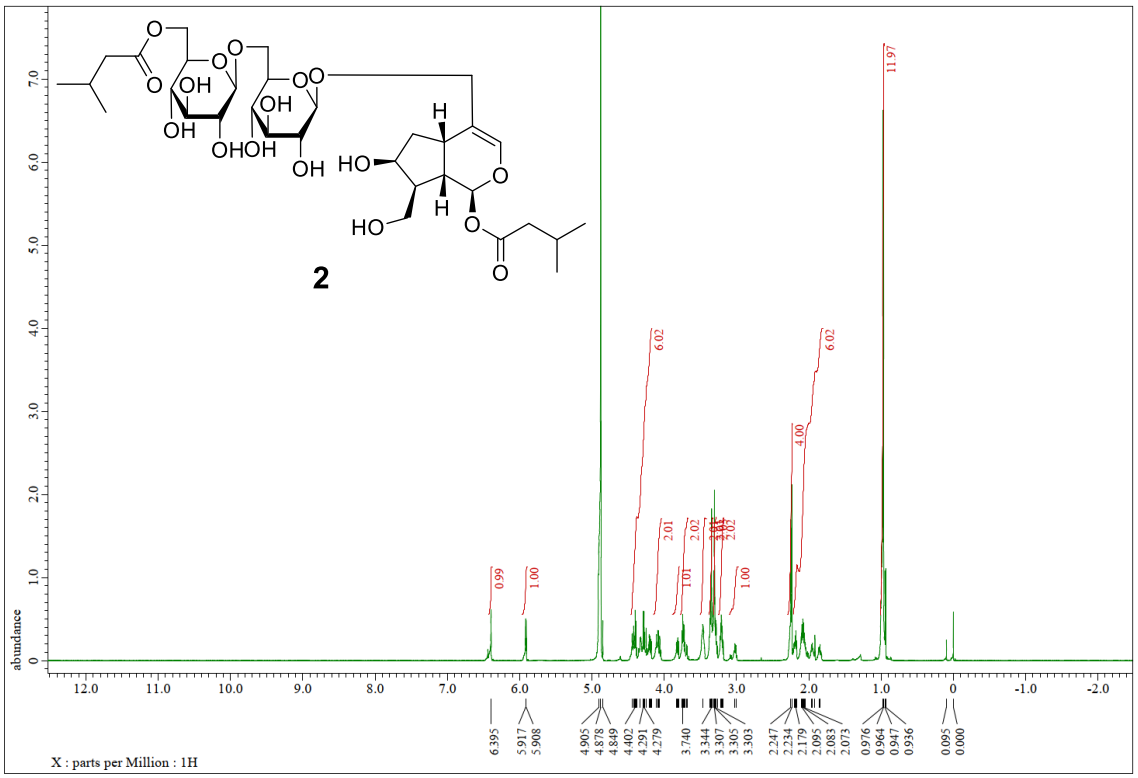
List of Supplementary Materials

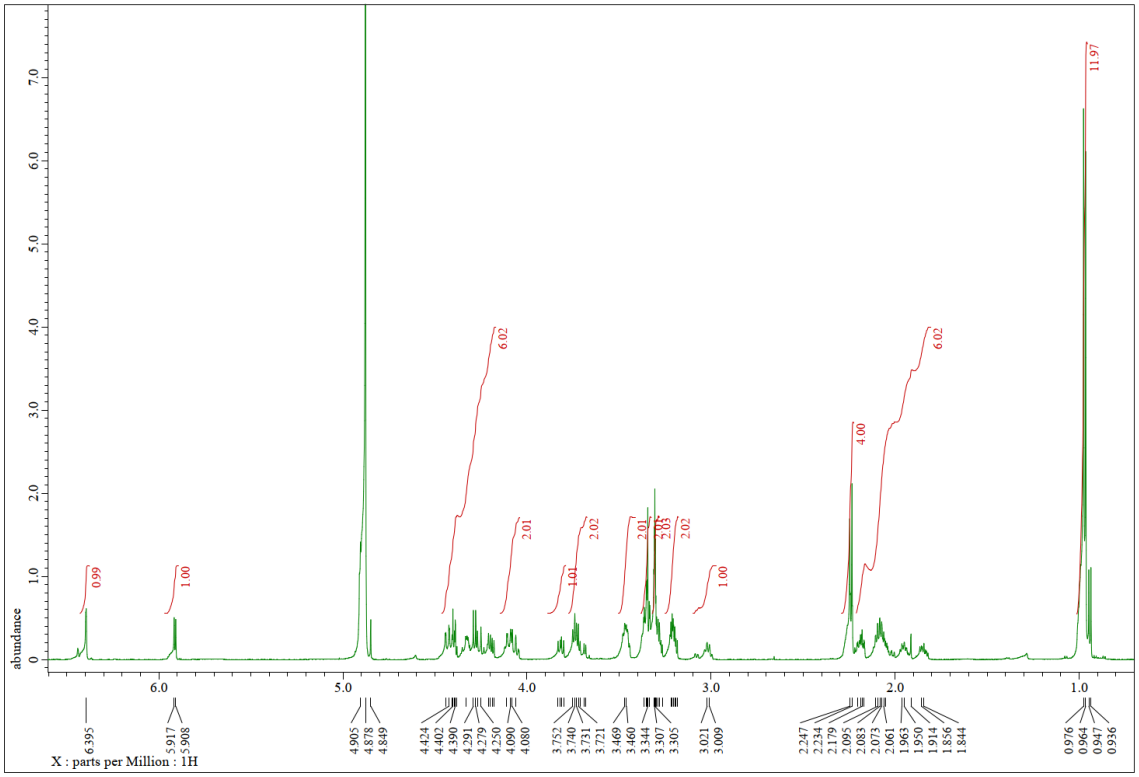
S1. ^{1}H NMR spectra of new compounds 1–3, 6, 6a, 7, 9, and 12



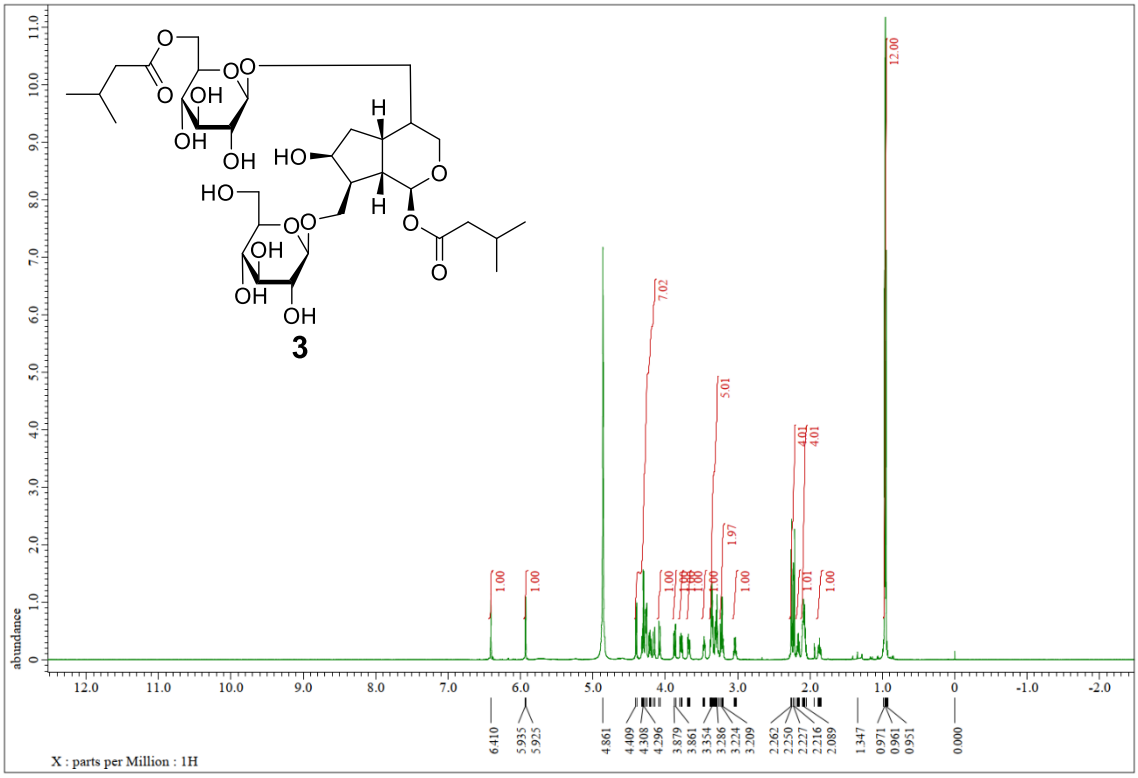


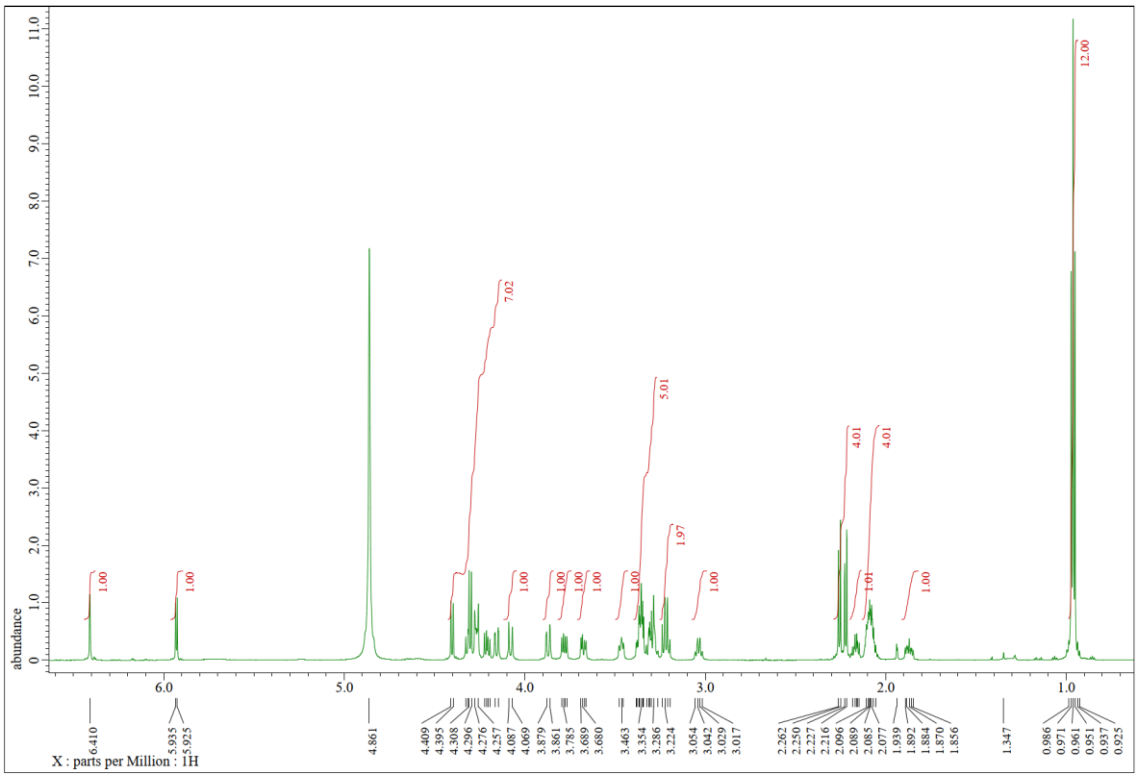
^{1}H NMR spectrum of **1**



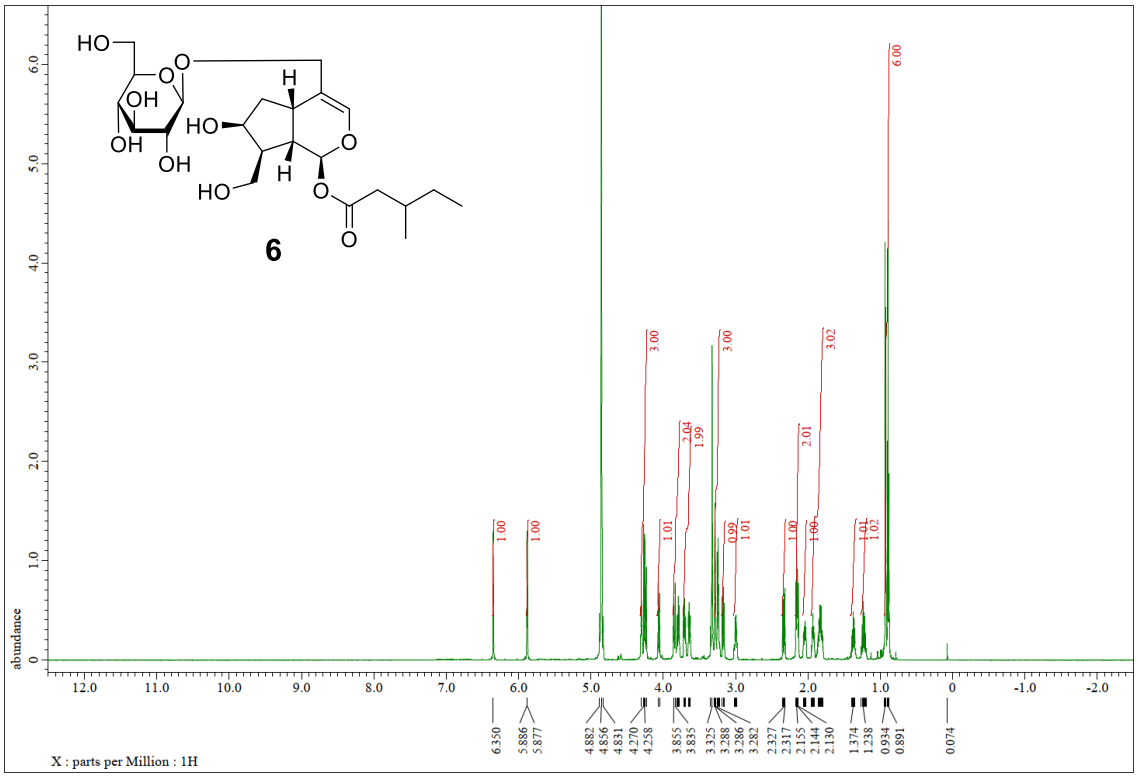


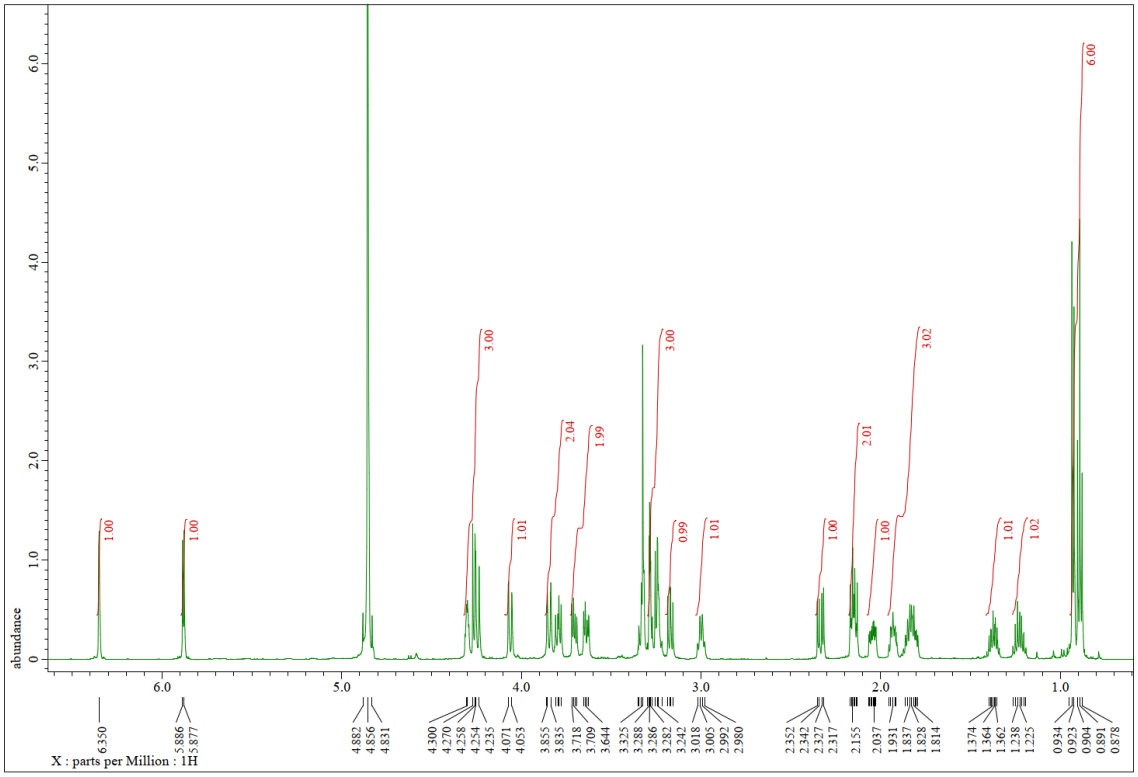
^{1}H NMR spectrum of **2**



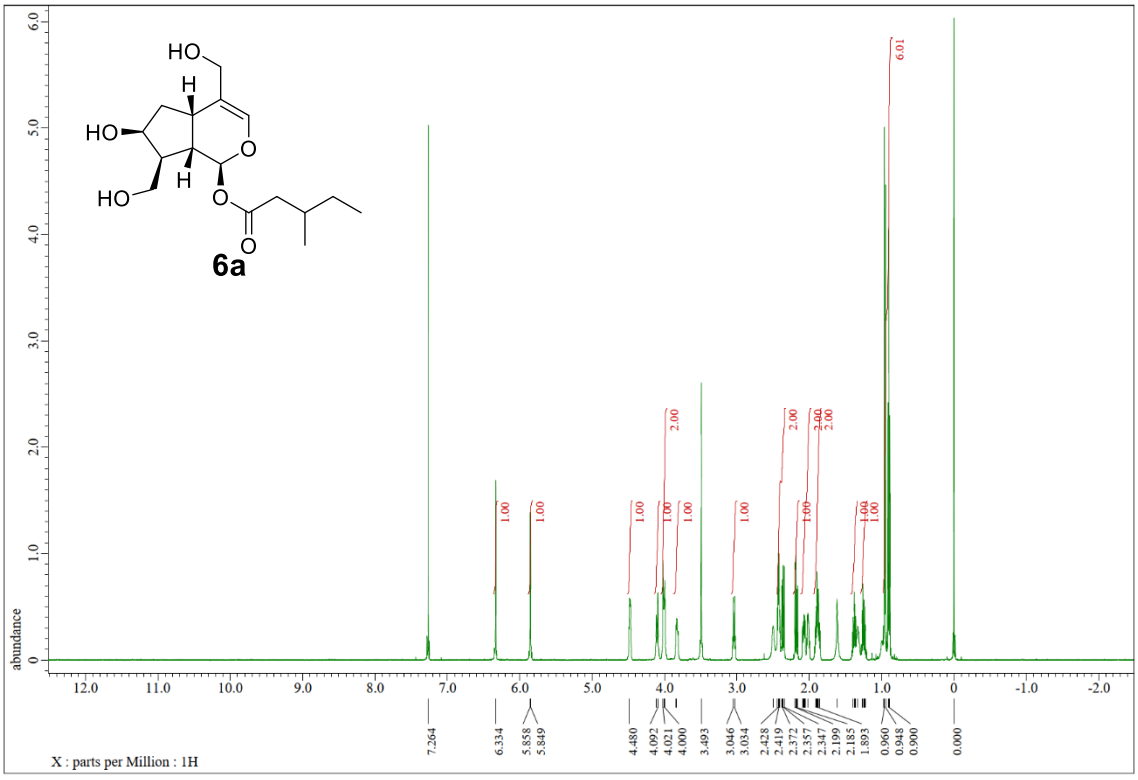


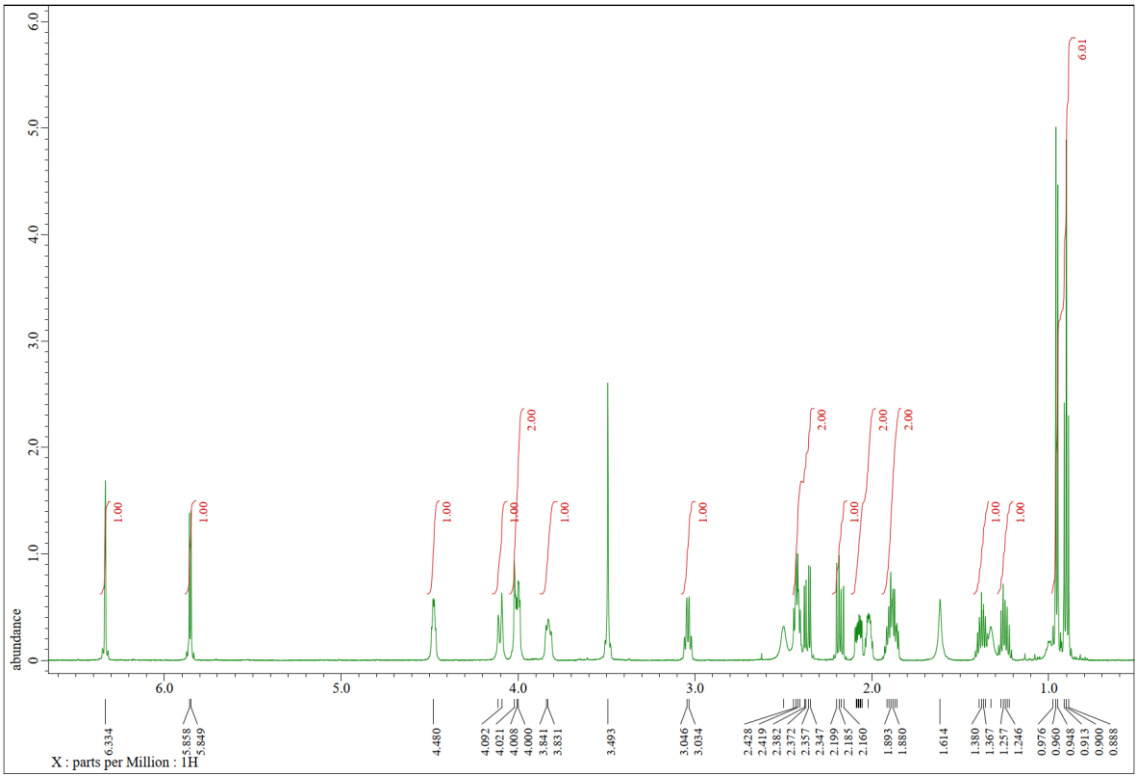
^{1}H NMR spectrum of **3**



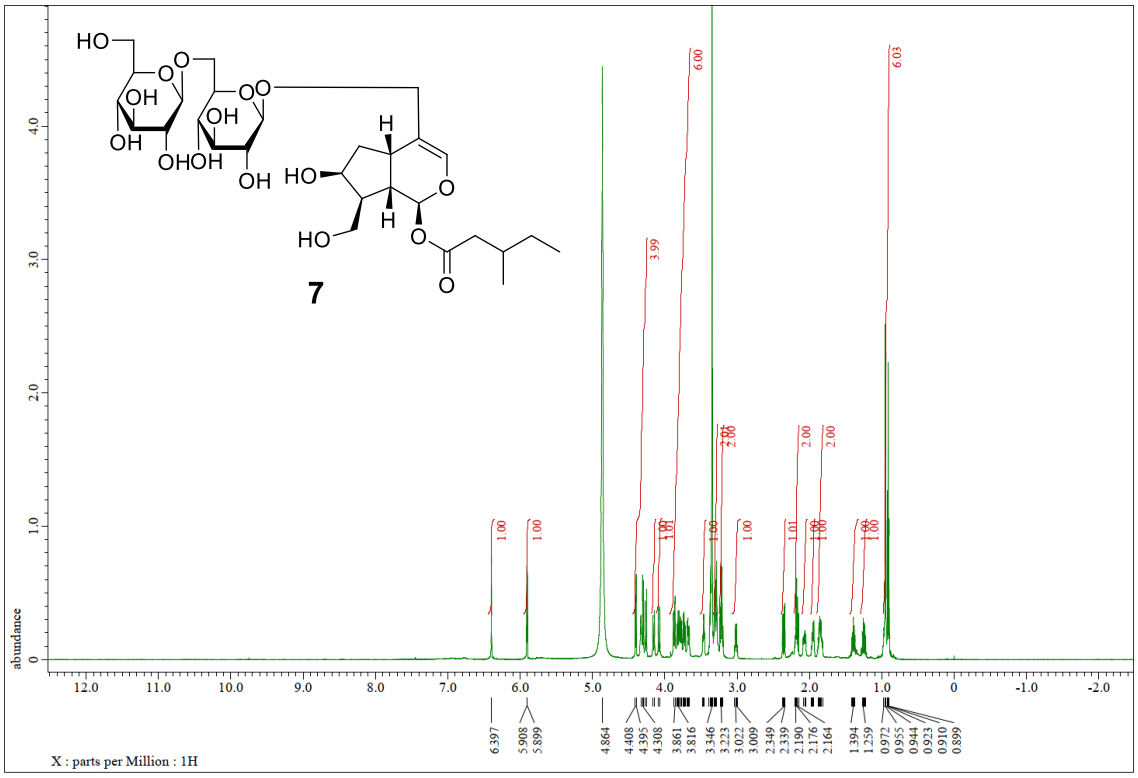


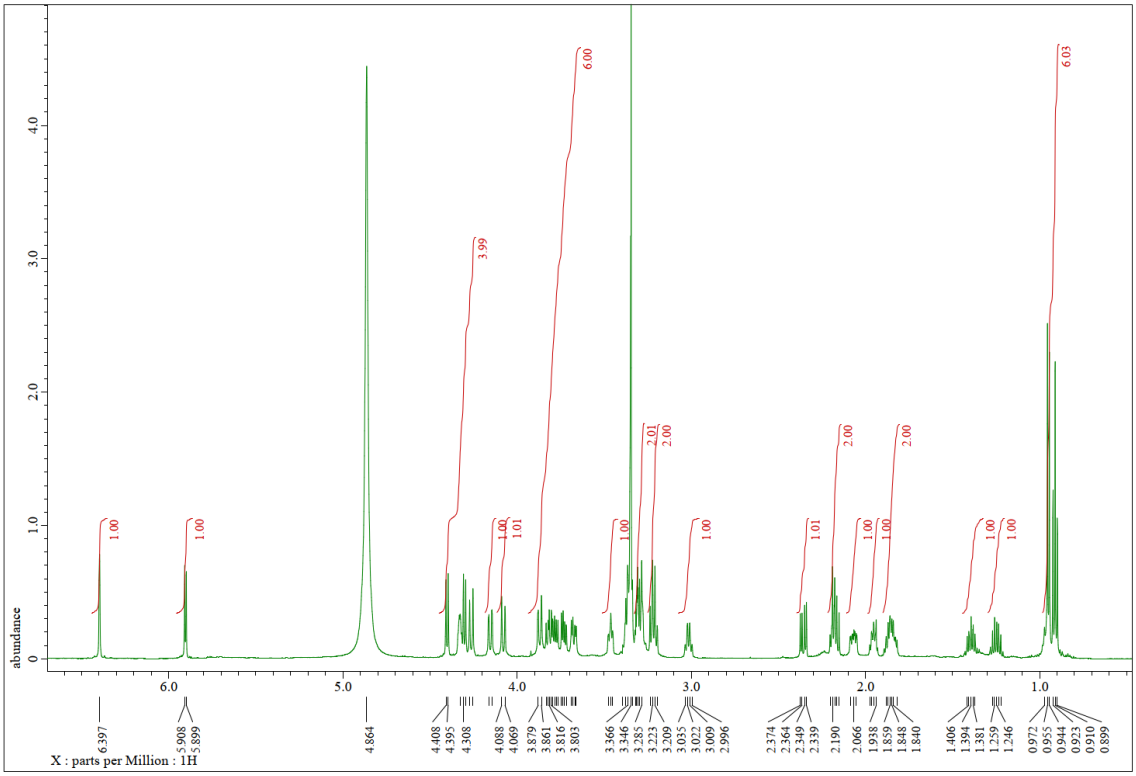
^{1}H NMR spectrum of **6**



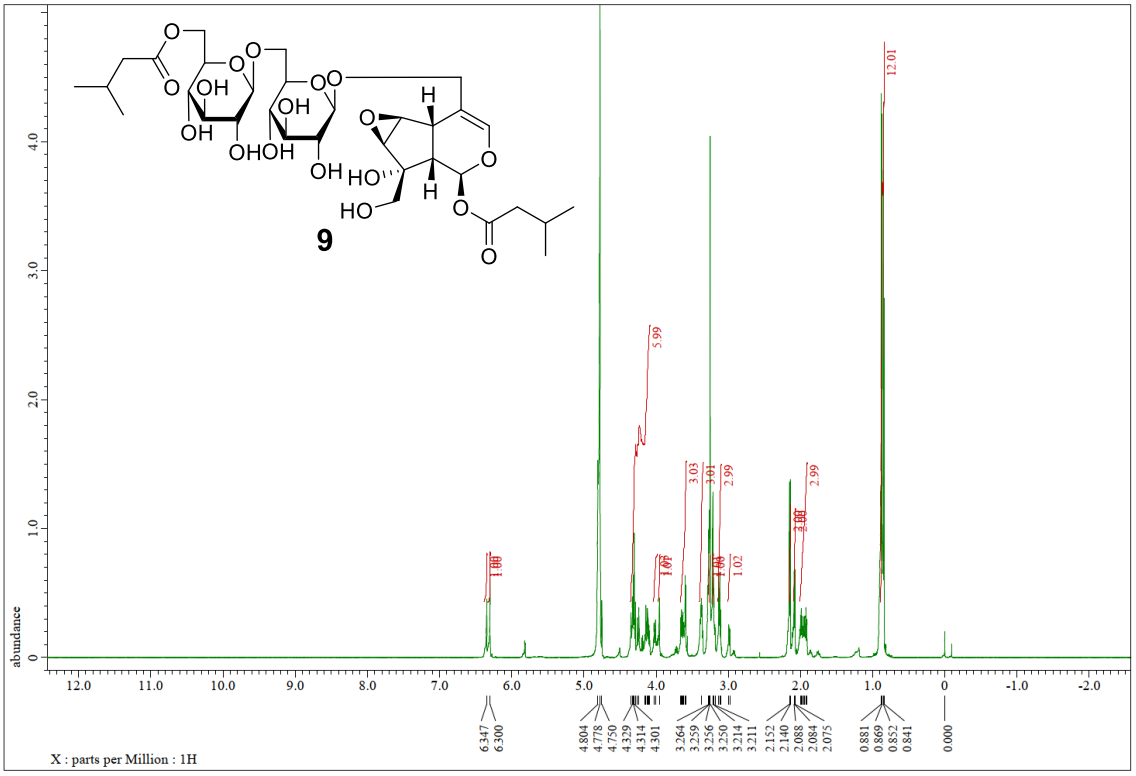


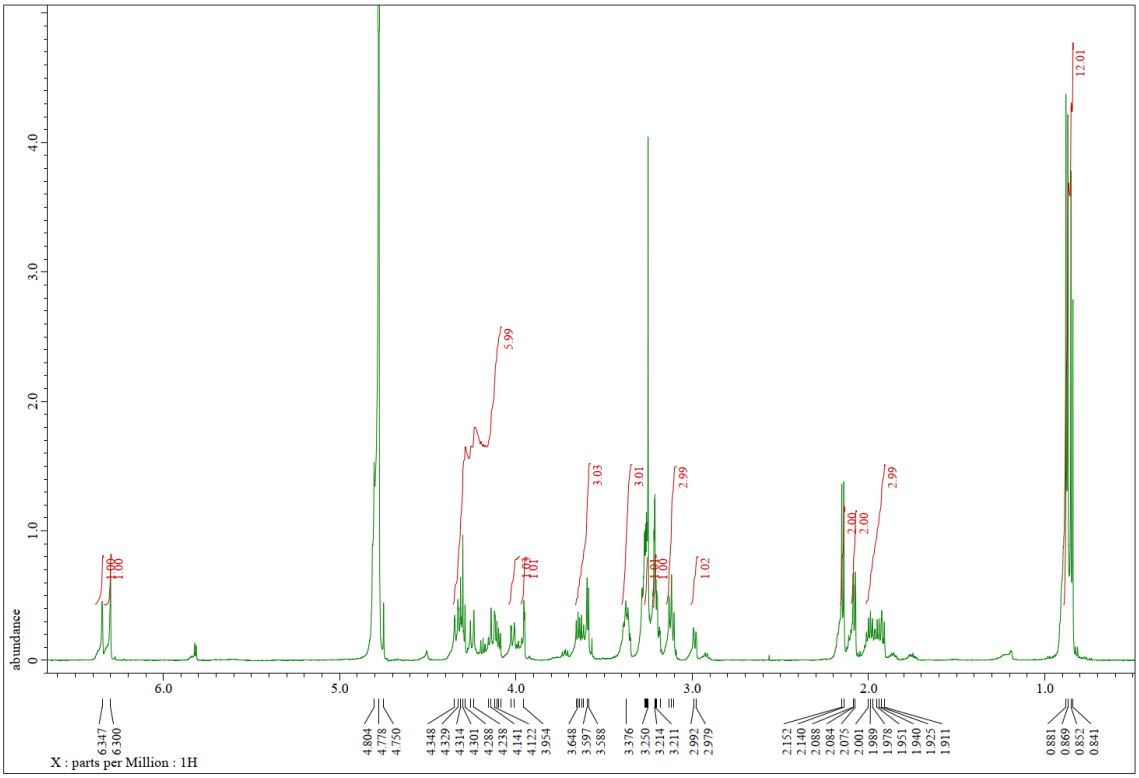
^{1}H NMR spectrum of **6a**



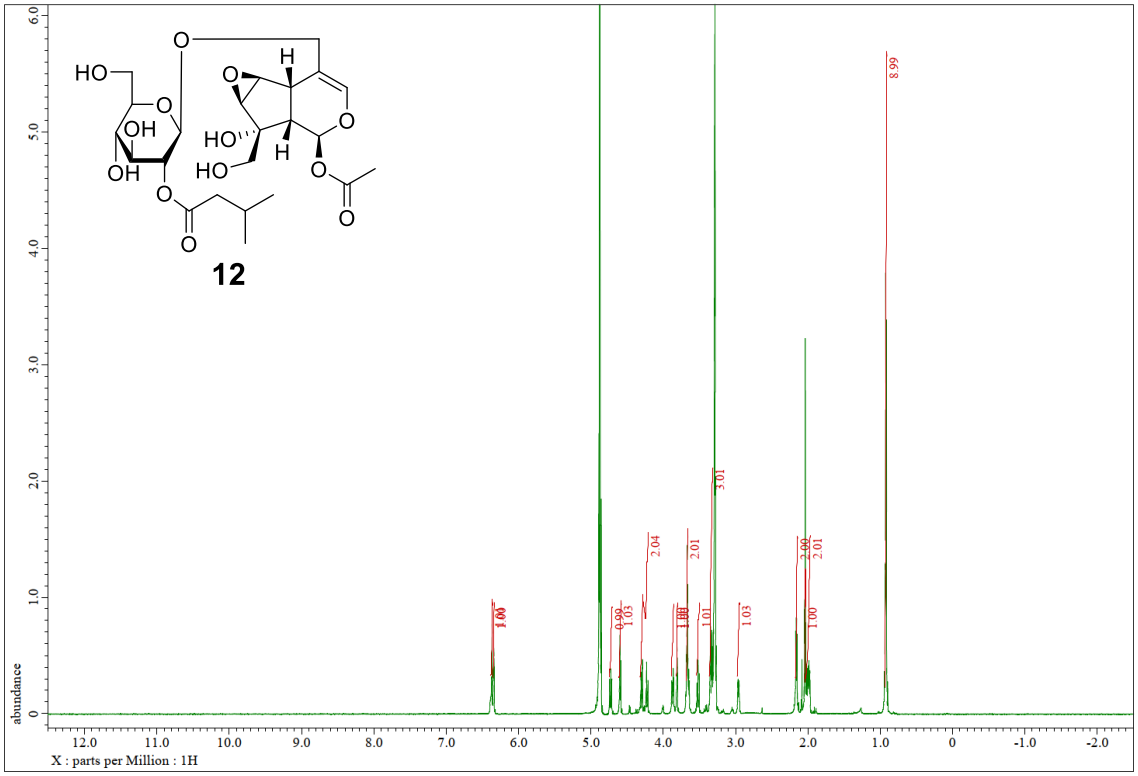


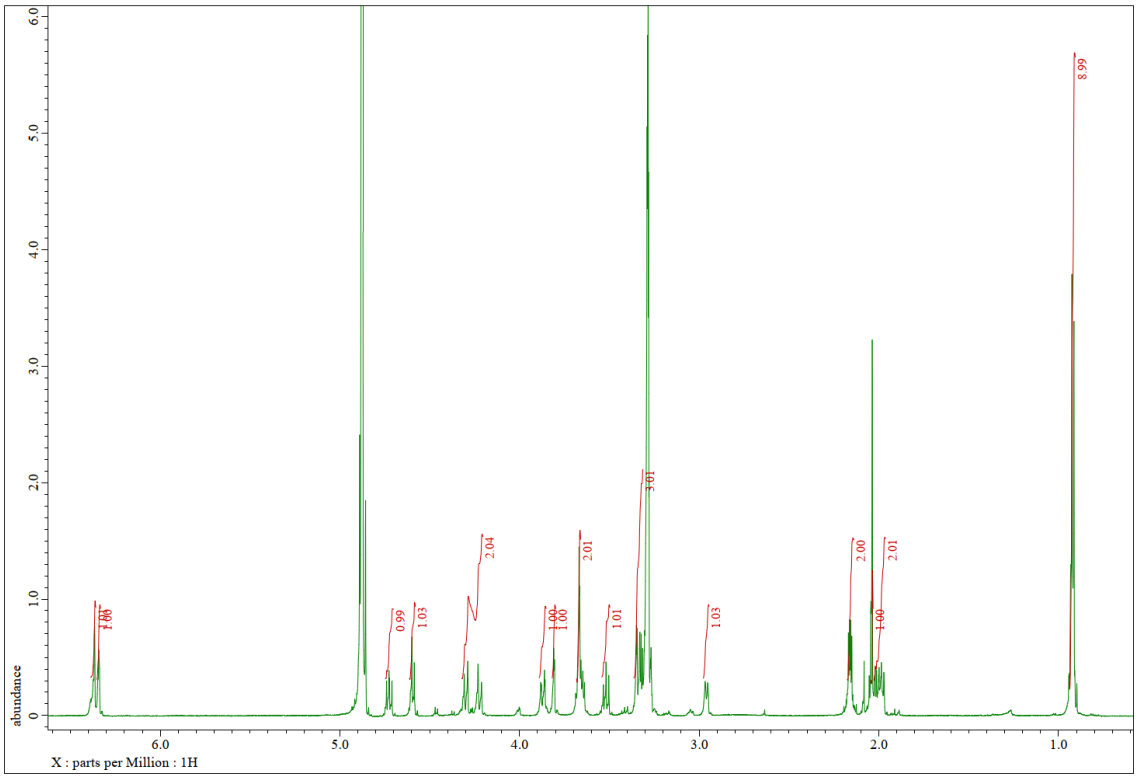
^{1}H NMR spectrum of **7**





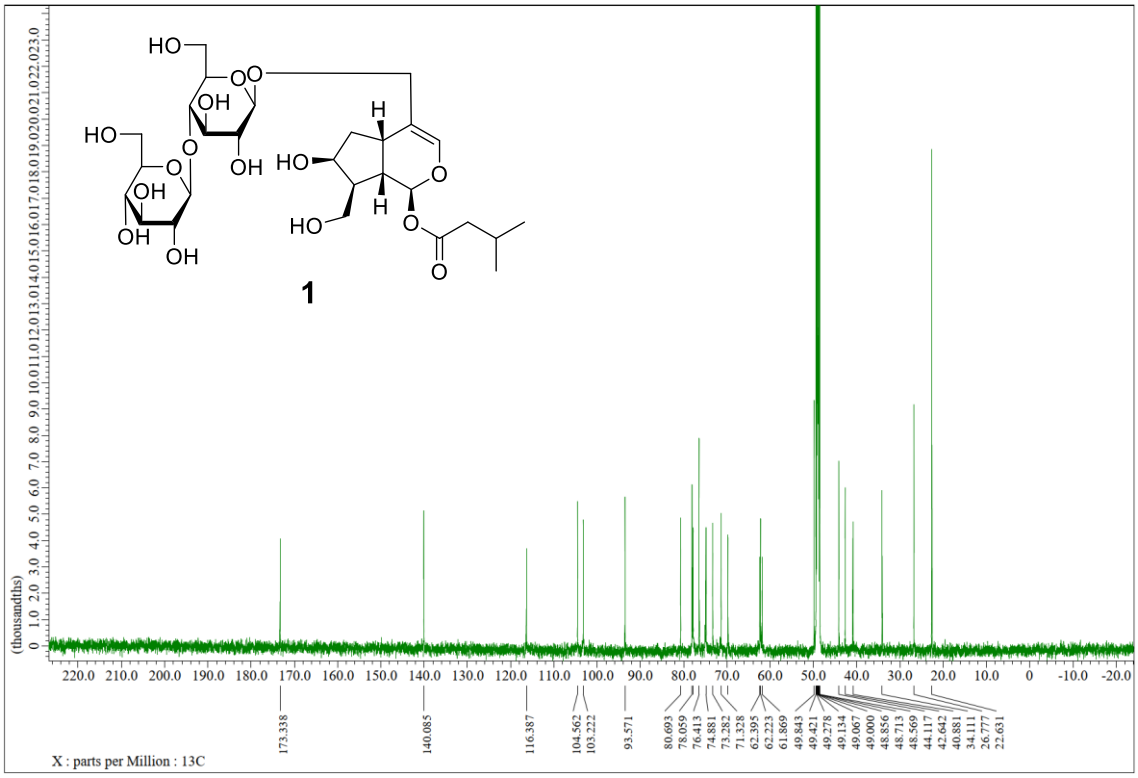
^{1}H NMR spectrum of **9**



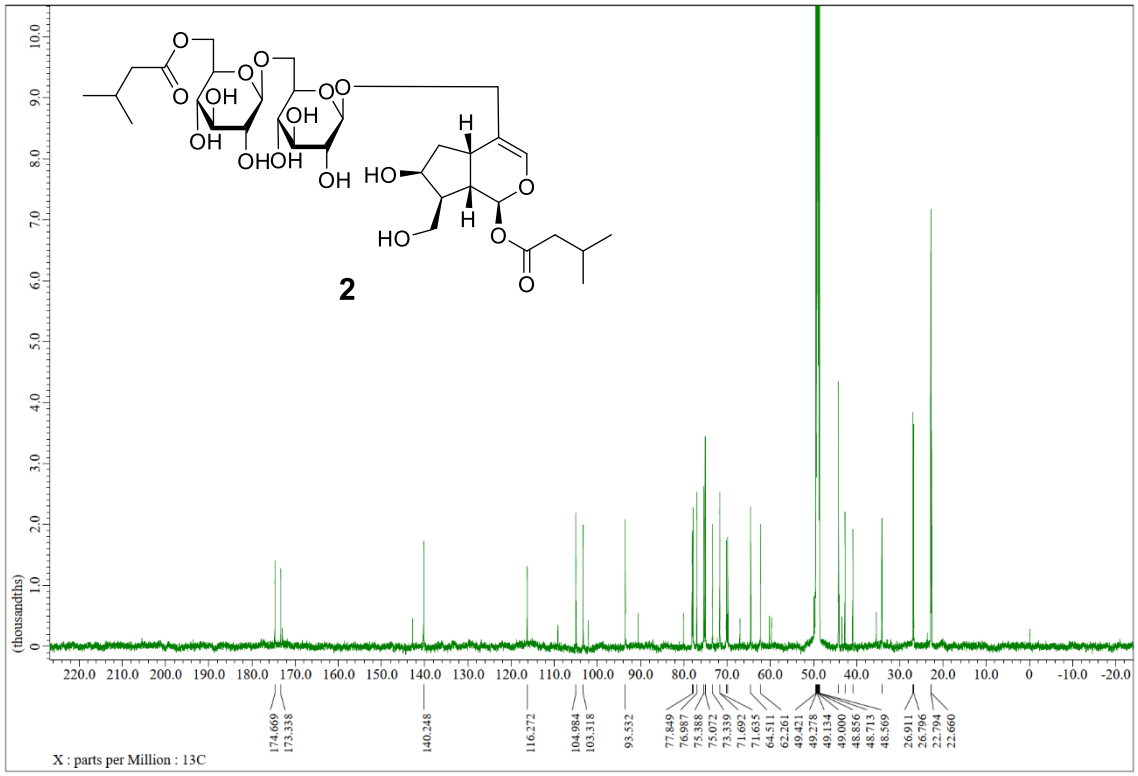


^{1}H NMR spectrum of **12**

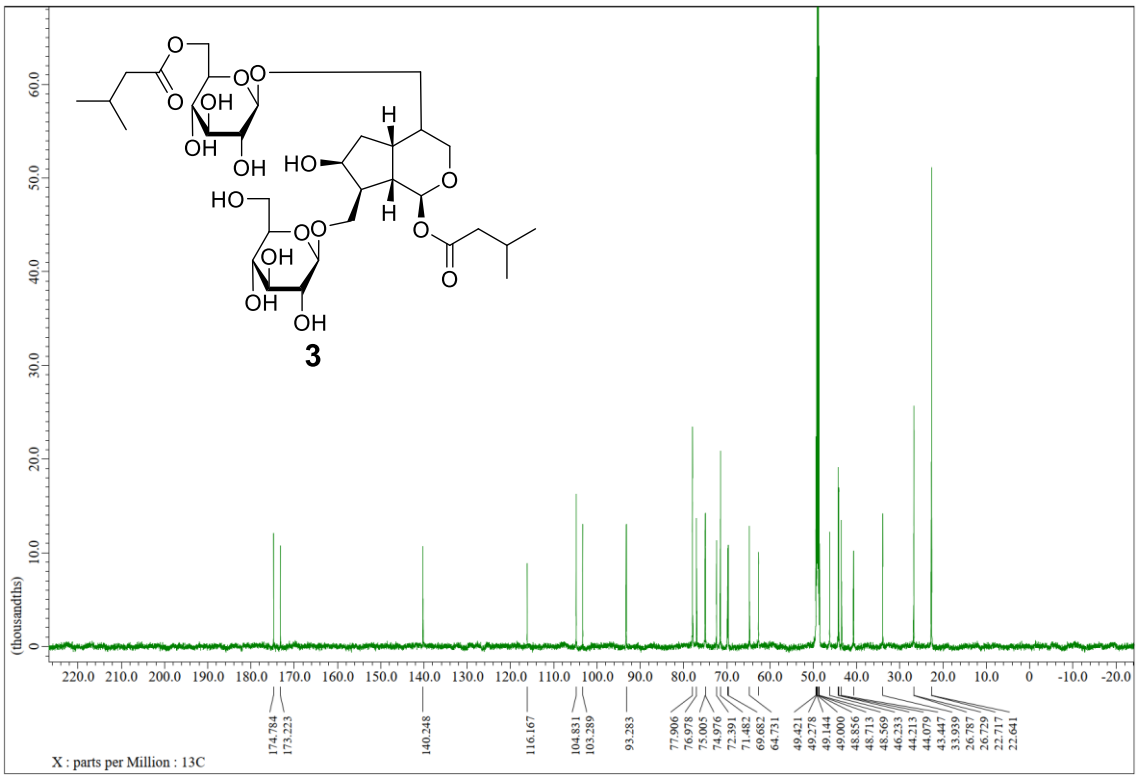
S2. ^{13}C NMR spectra of new compounds 1–3, 6, 6a,7, 9, and 12



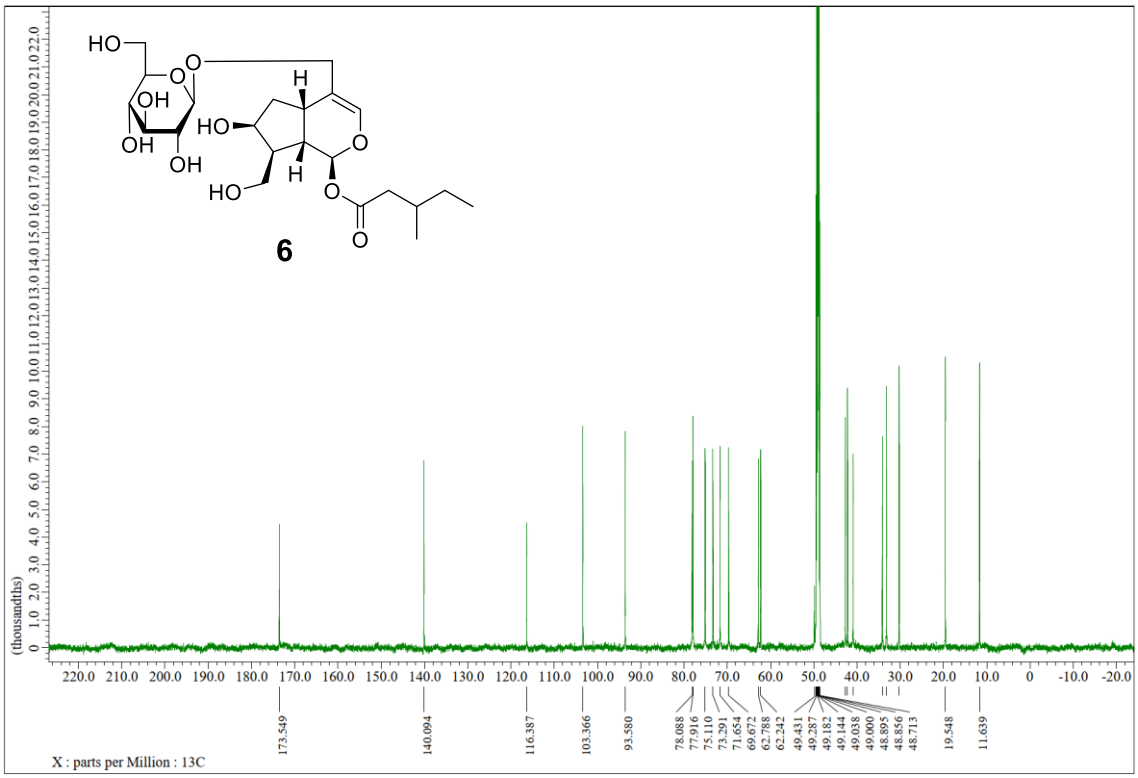
^{13}C NMR spectrum of **1**



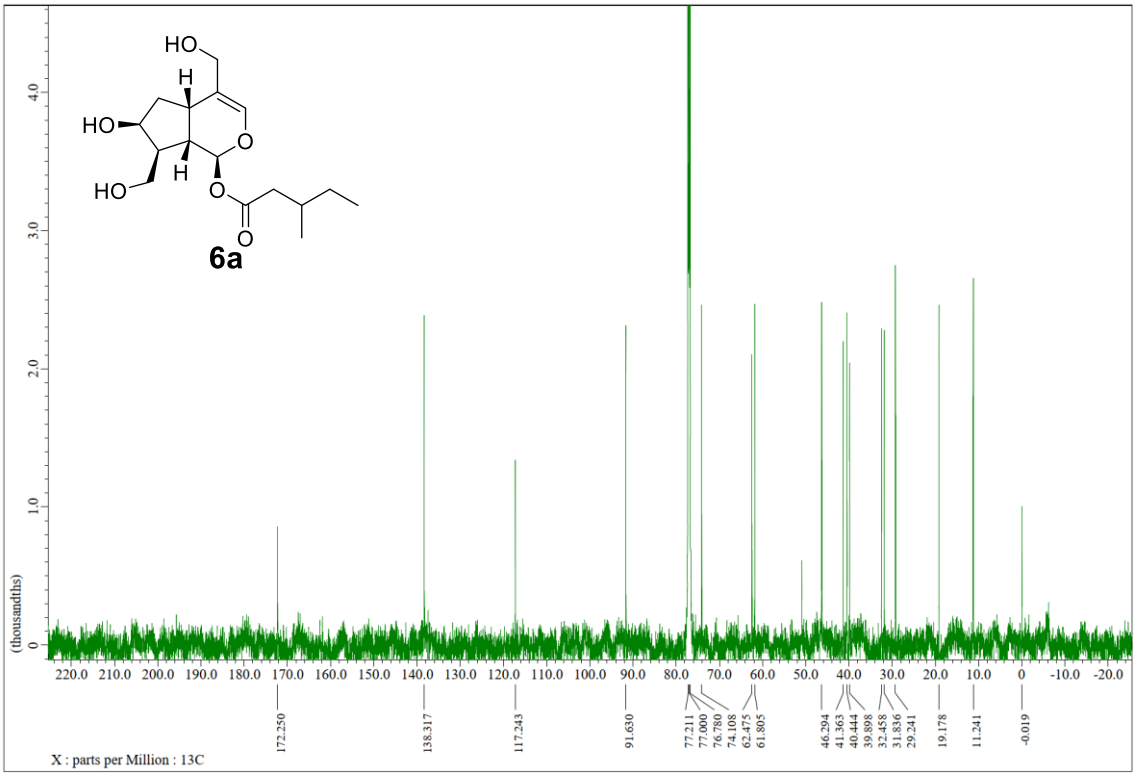
^{13}C NMR spectrum of **2**



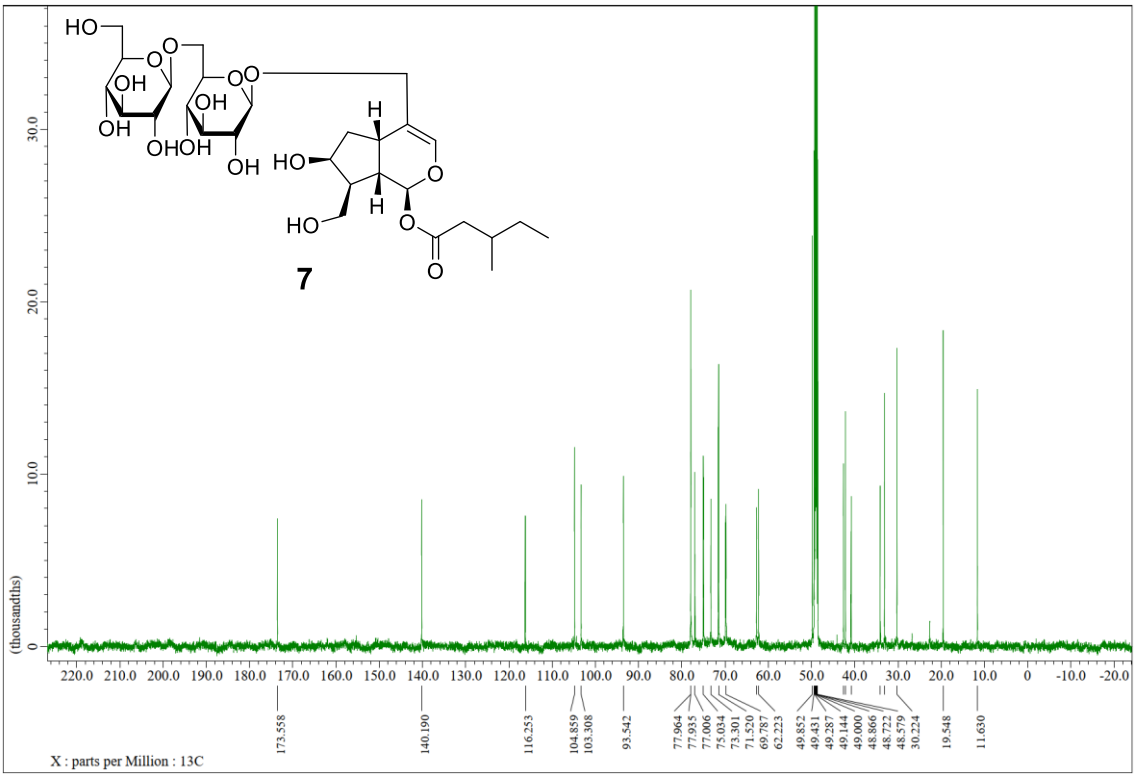
^{13}C NMR spectrum of **3**



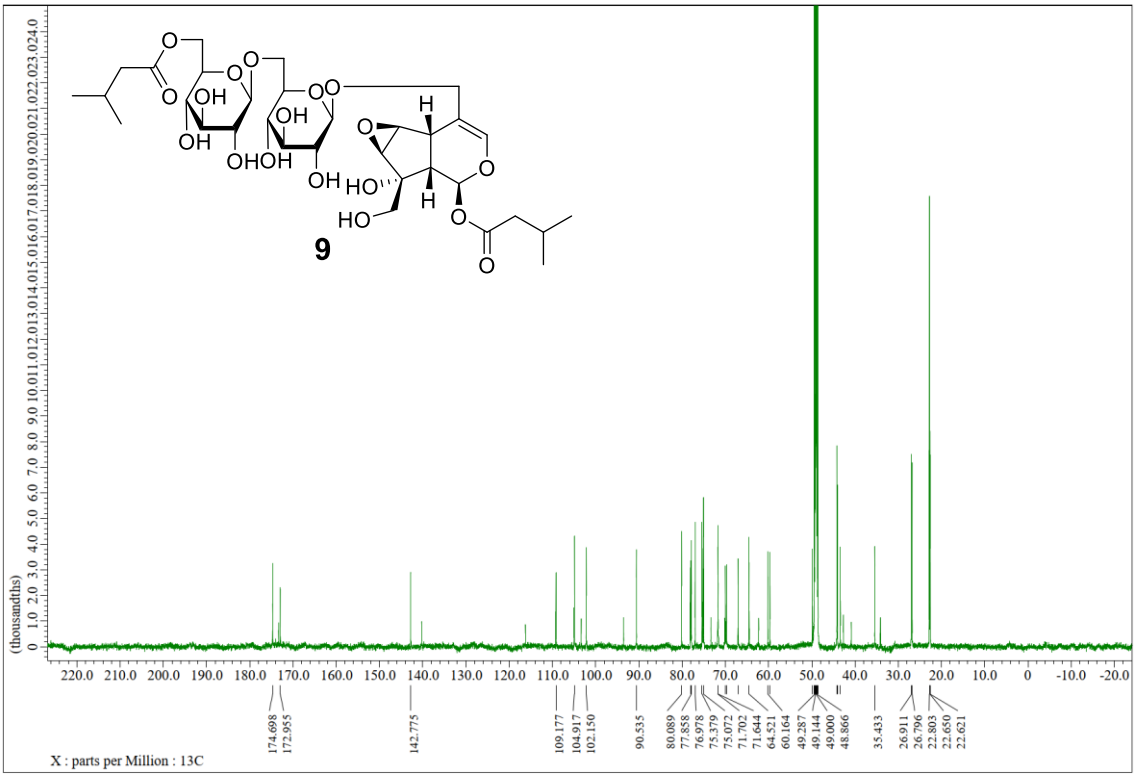
^{13}C NMR spectrum of **6**



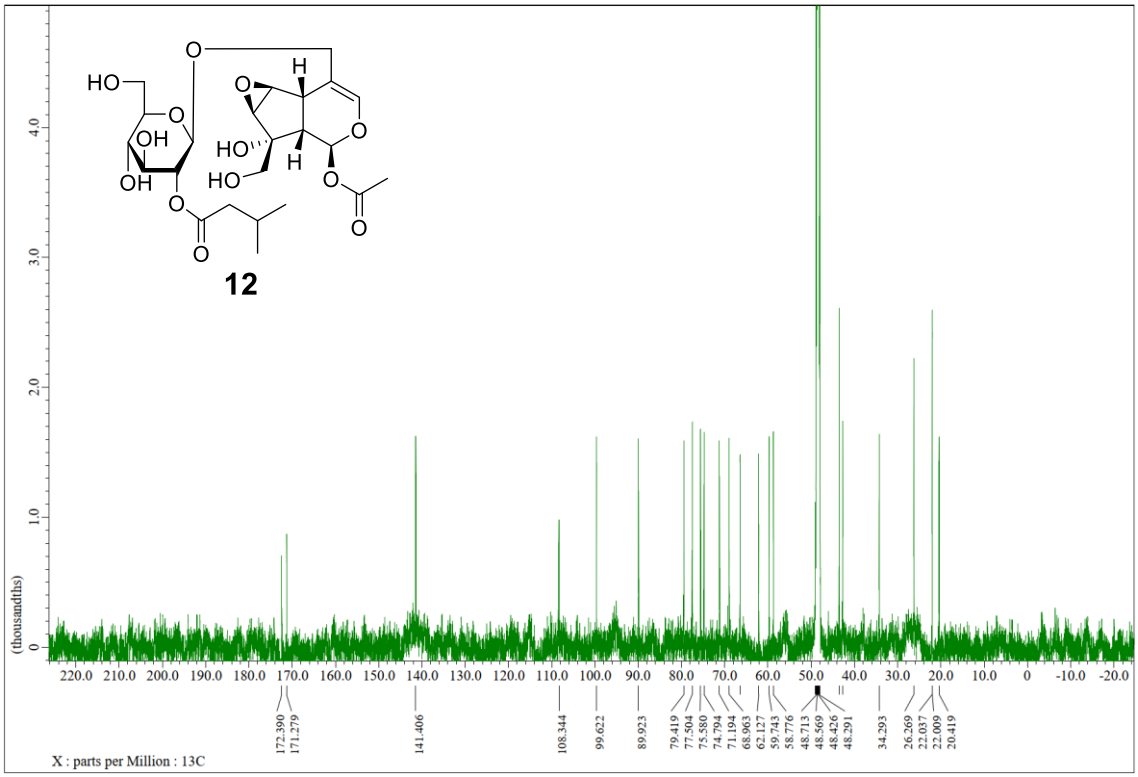
^{13}C NMR spectrum of **6a**



^{13}C NMR spectrum of **7**

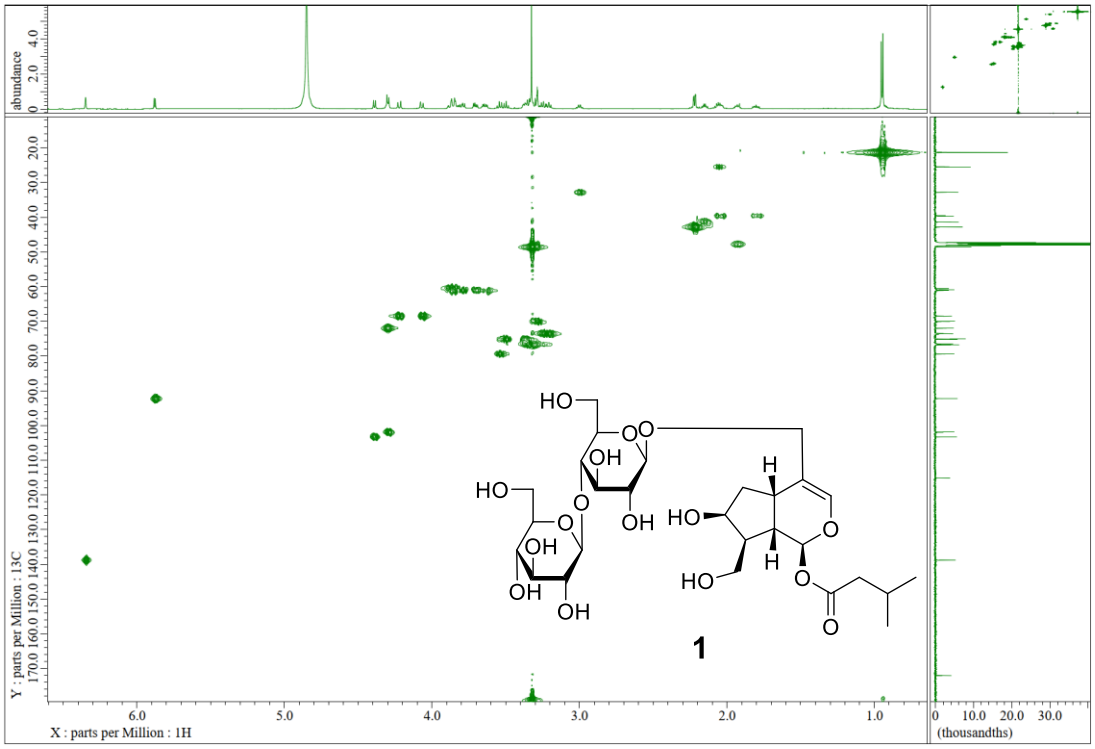


^{13}C NMR spectrum of **9**

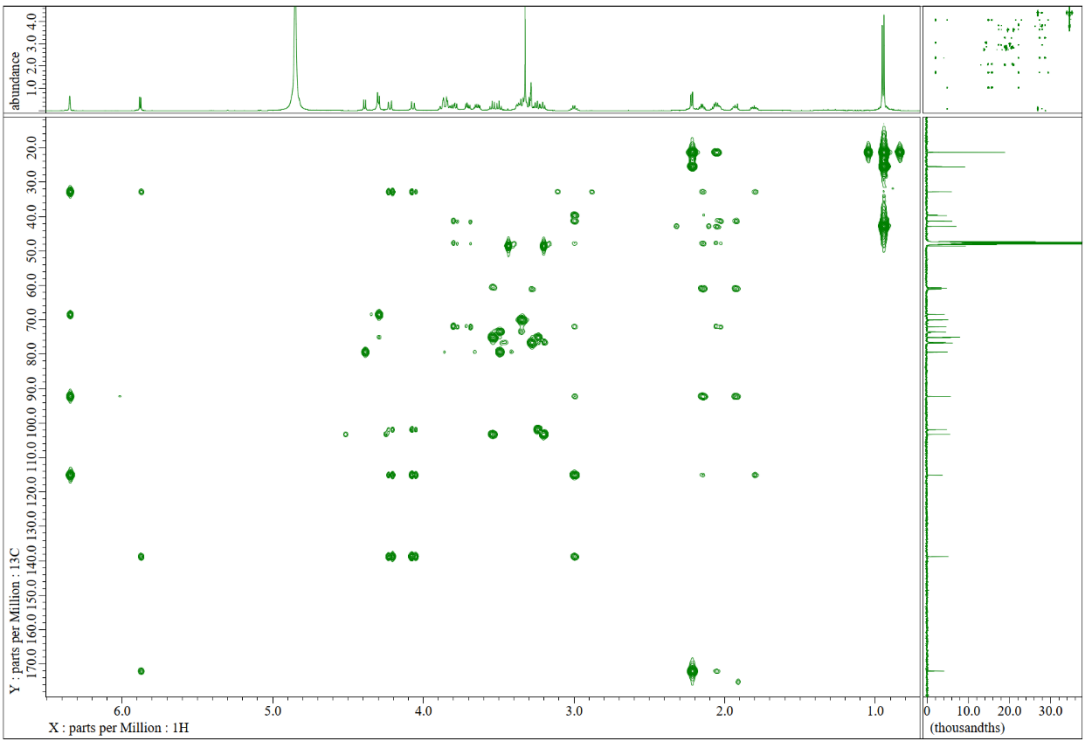


^{13}C NMR spectrum of **12**

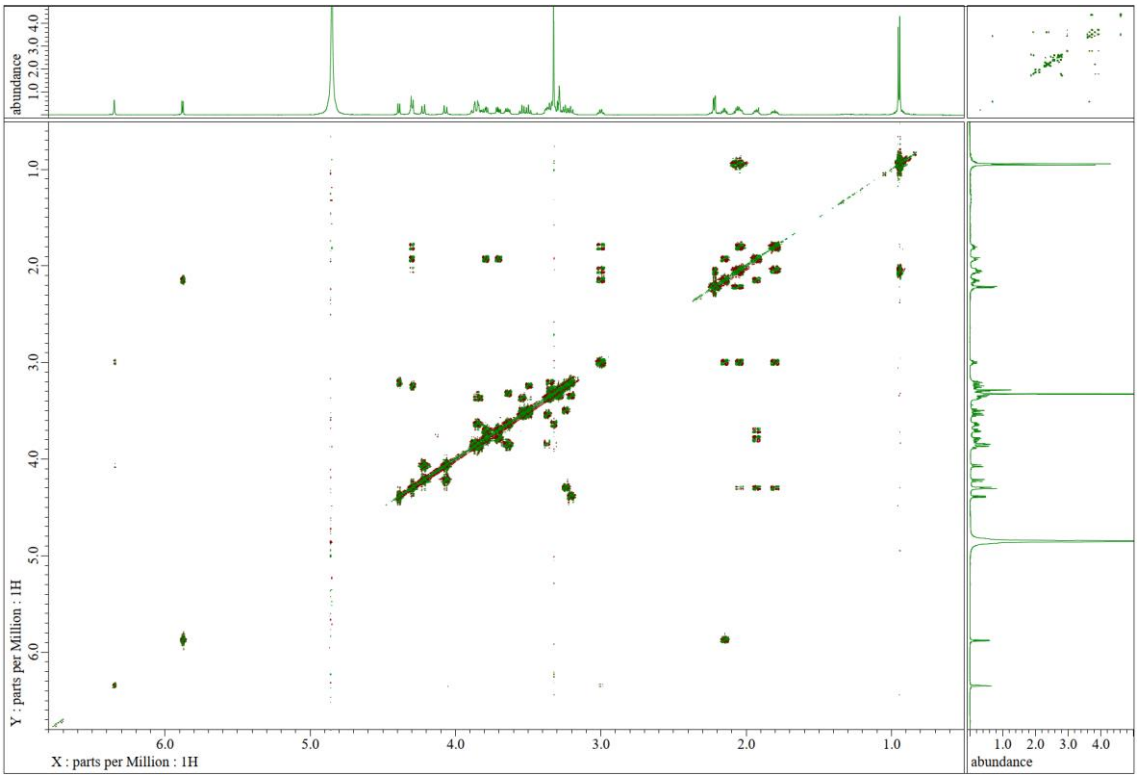
S3. 2DNMR spectra of new compounds 1–3, 6, 6a, 7, 9, and 12



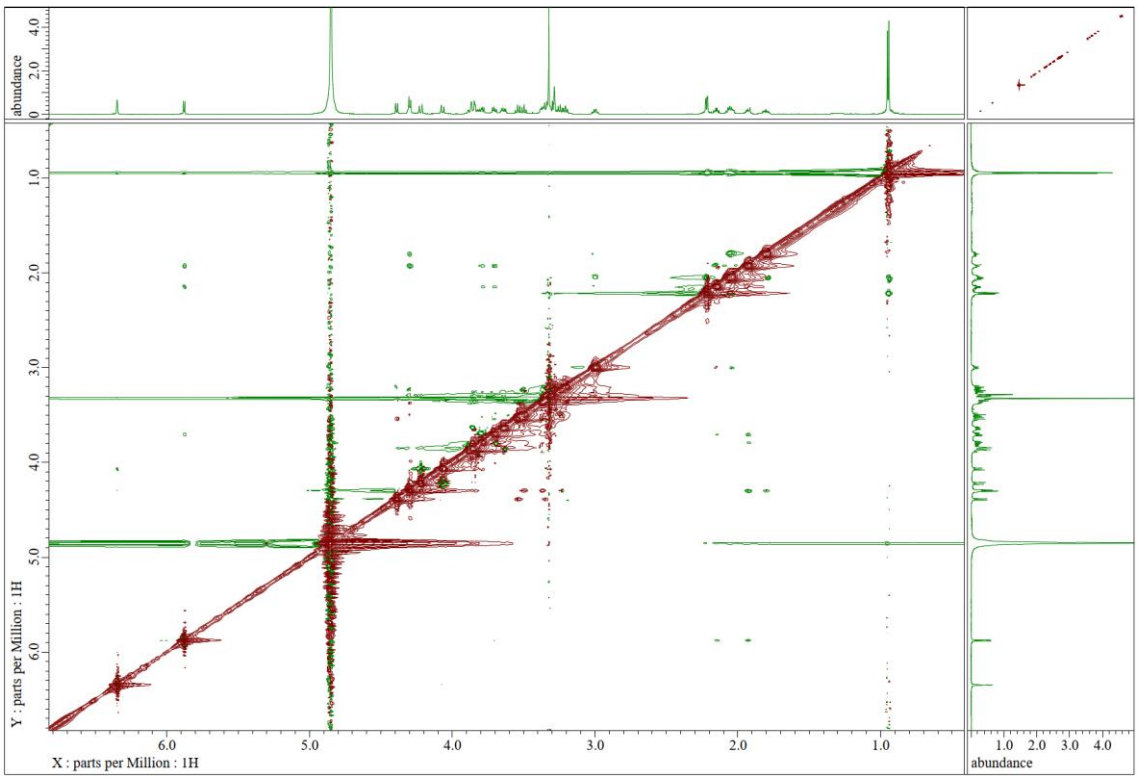
HMQC spectrum of **1**



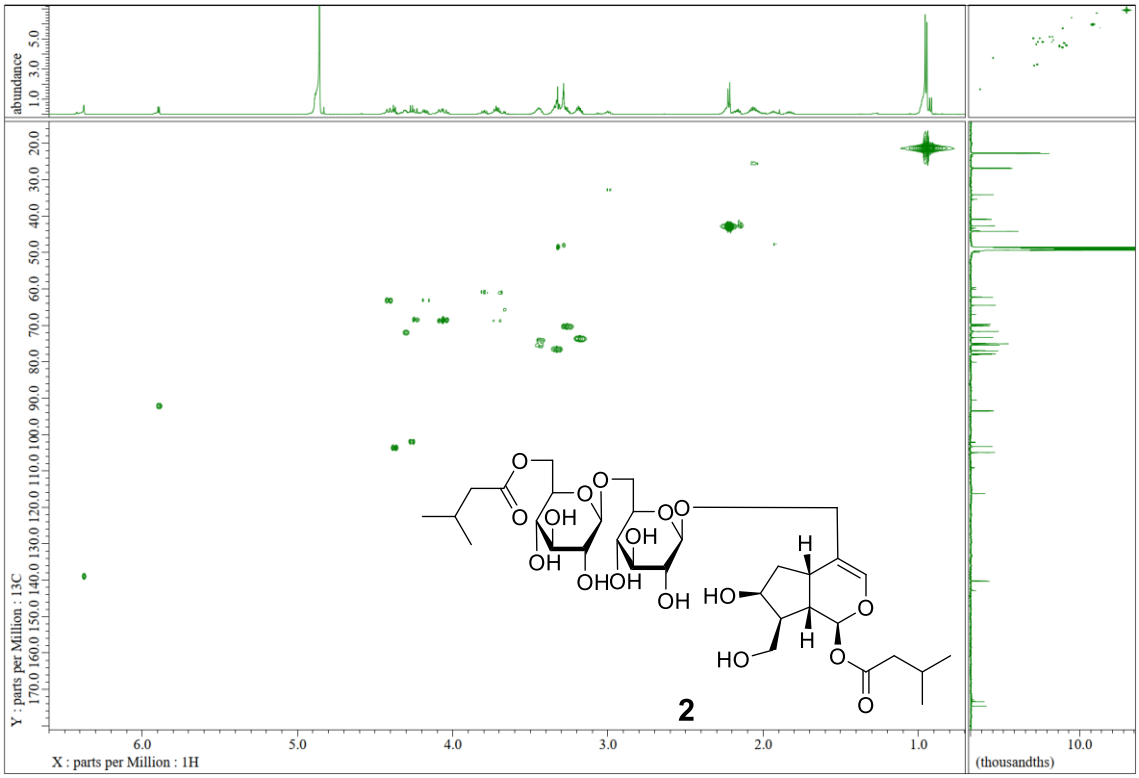
HMBC spectrum of **1**



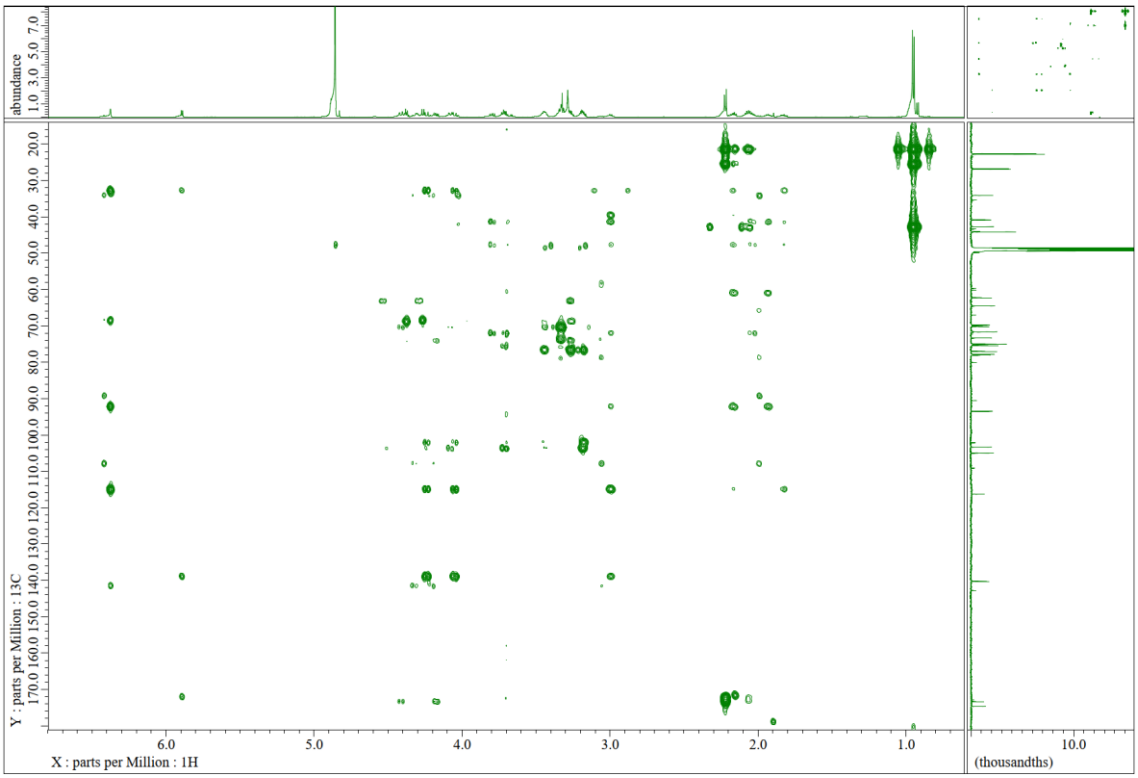
DQF spectrum of **1**



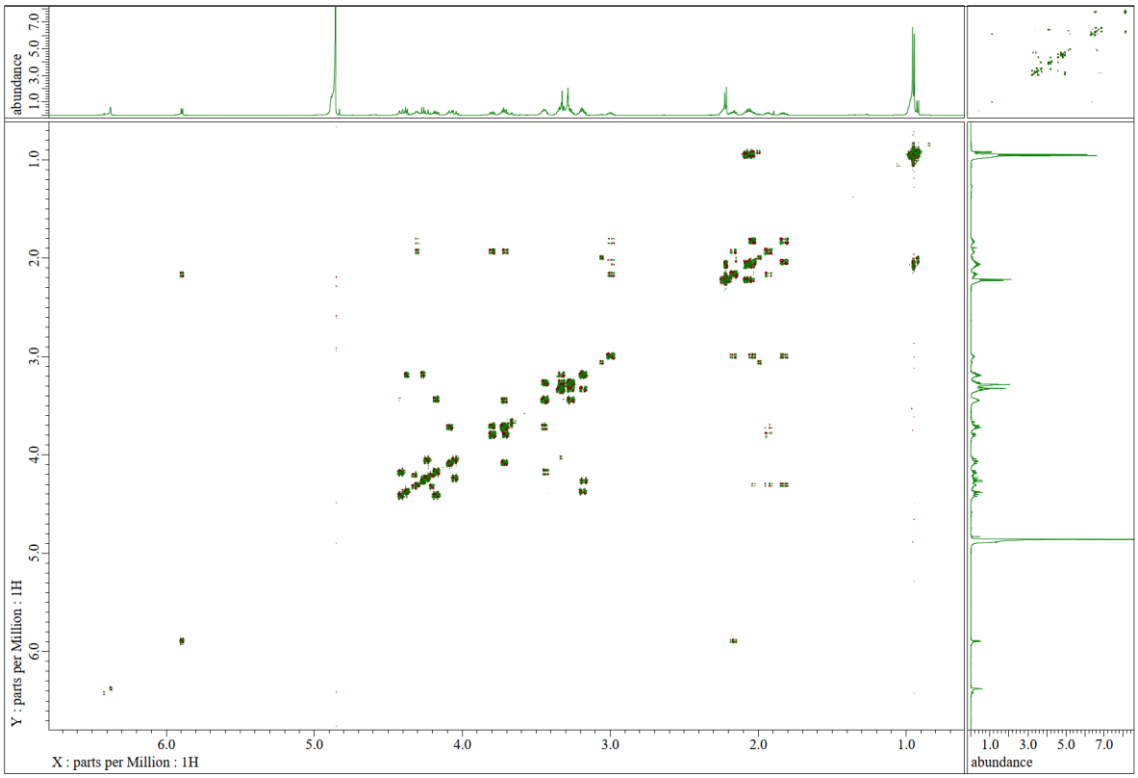
NOESY spectrum of **1**



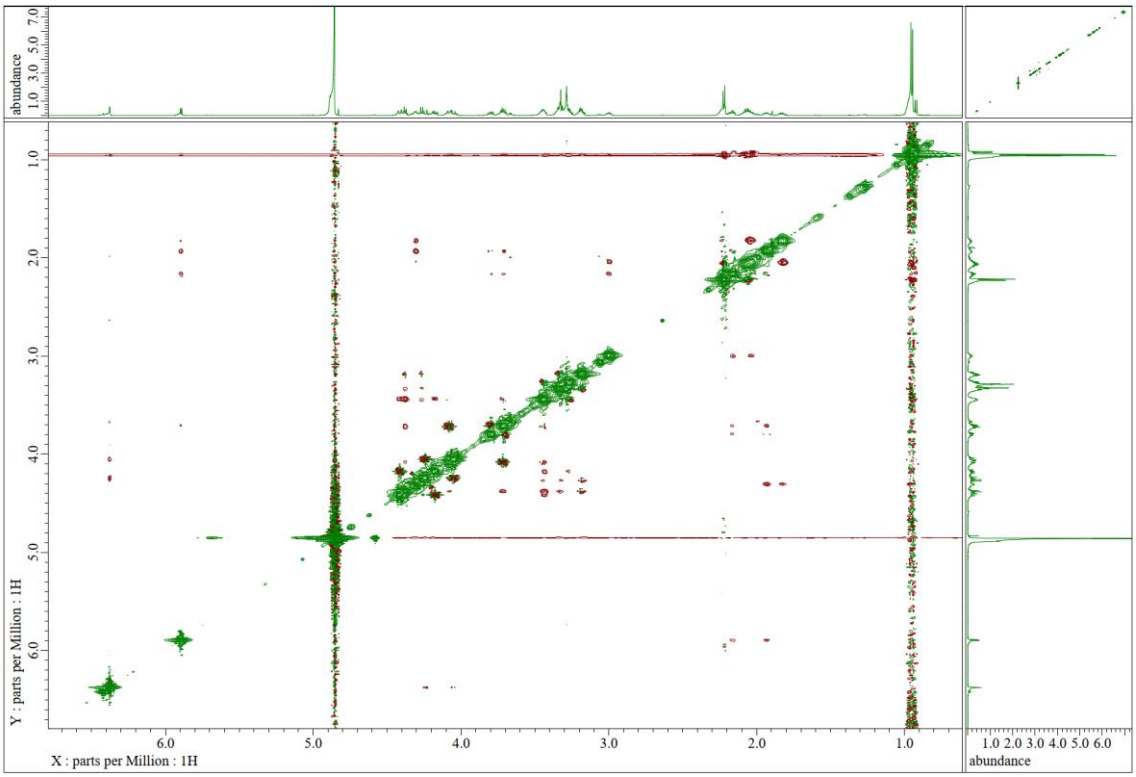
HMQC spectrum of **2**



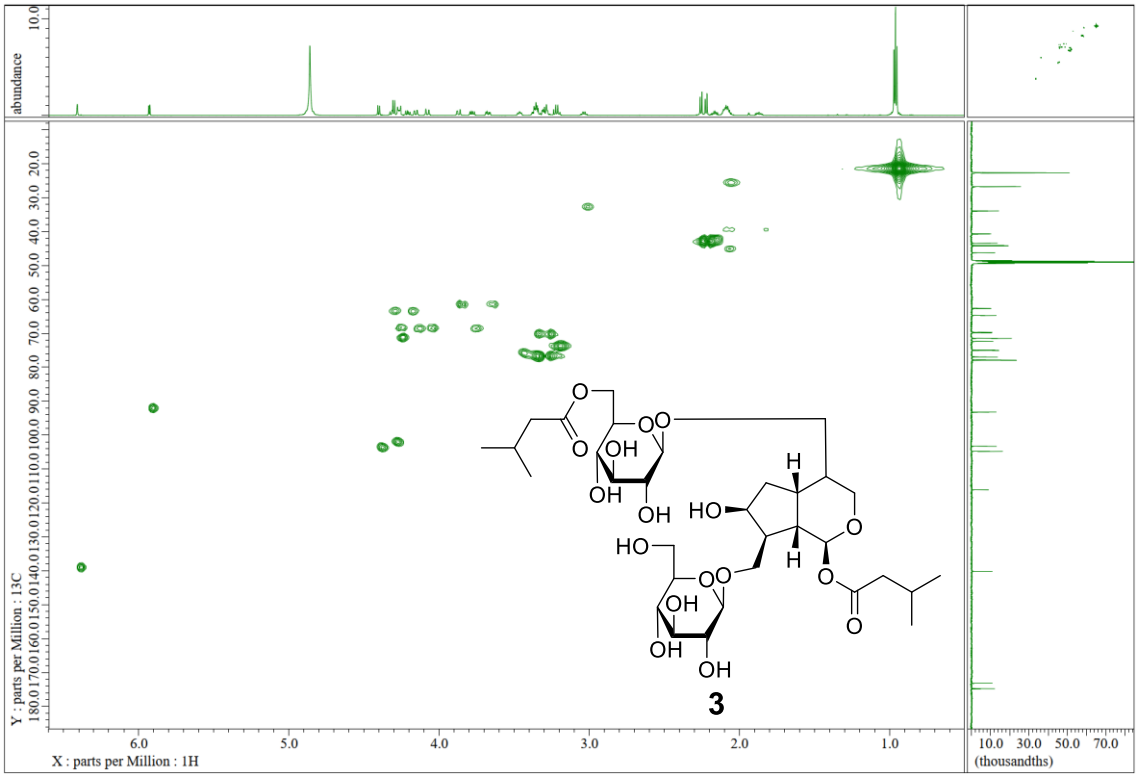
HMBC spectrum of **2**



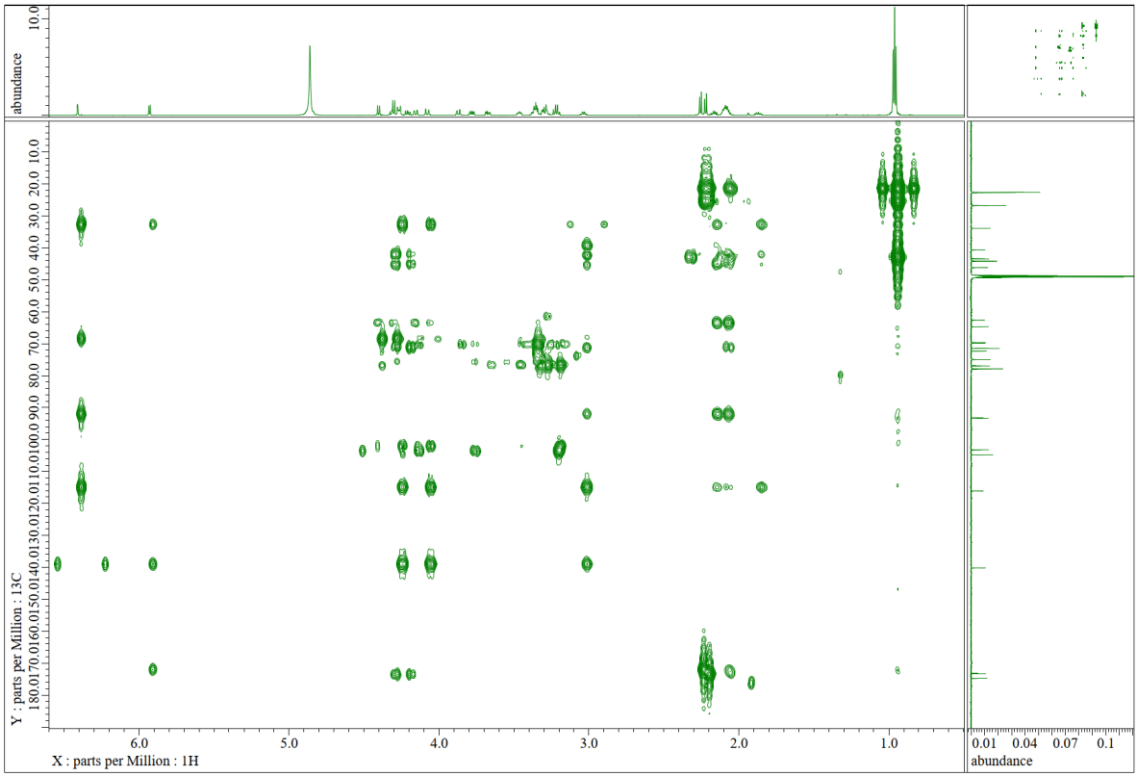
DQF spectrum of **2**



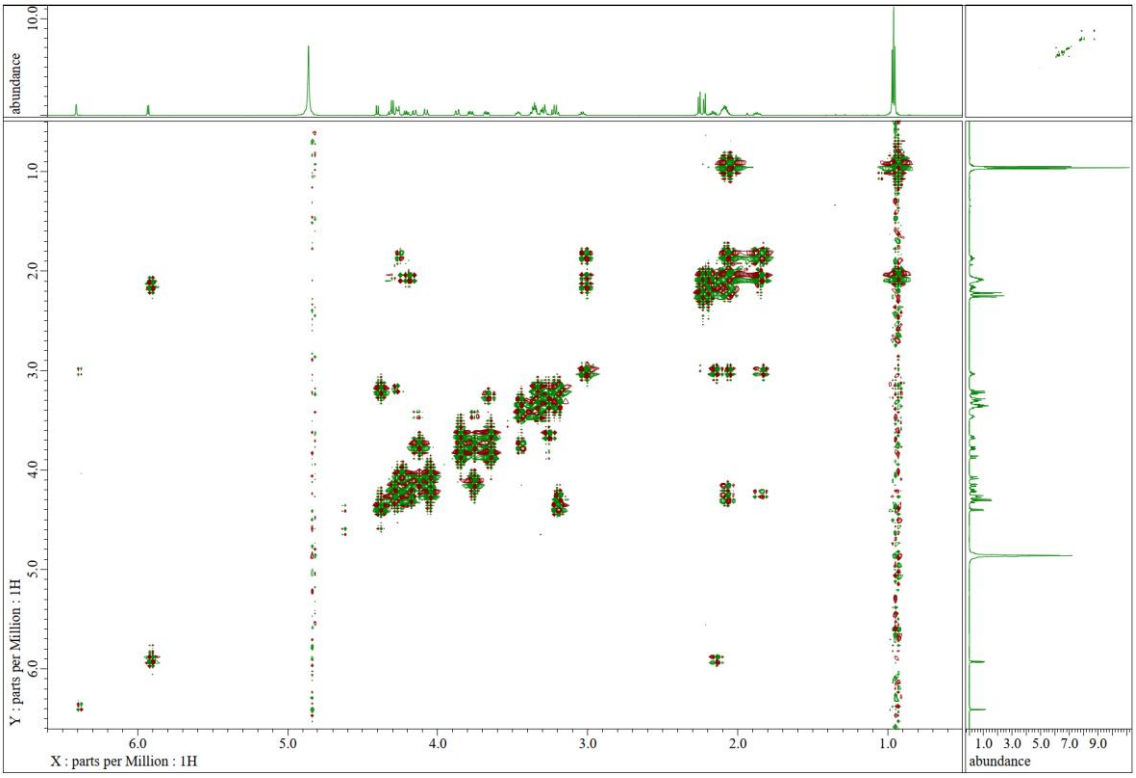
NOESY spectrum of **2**



HMQC spectrum of **3**



HMBC spectrum of **3**



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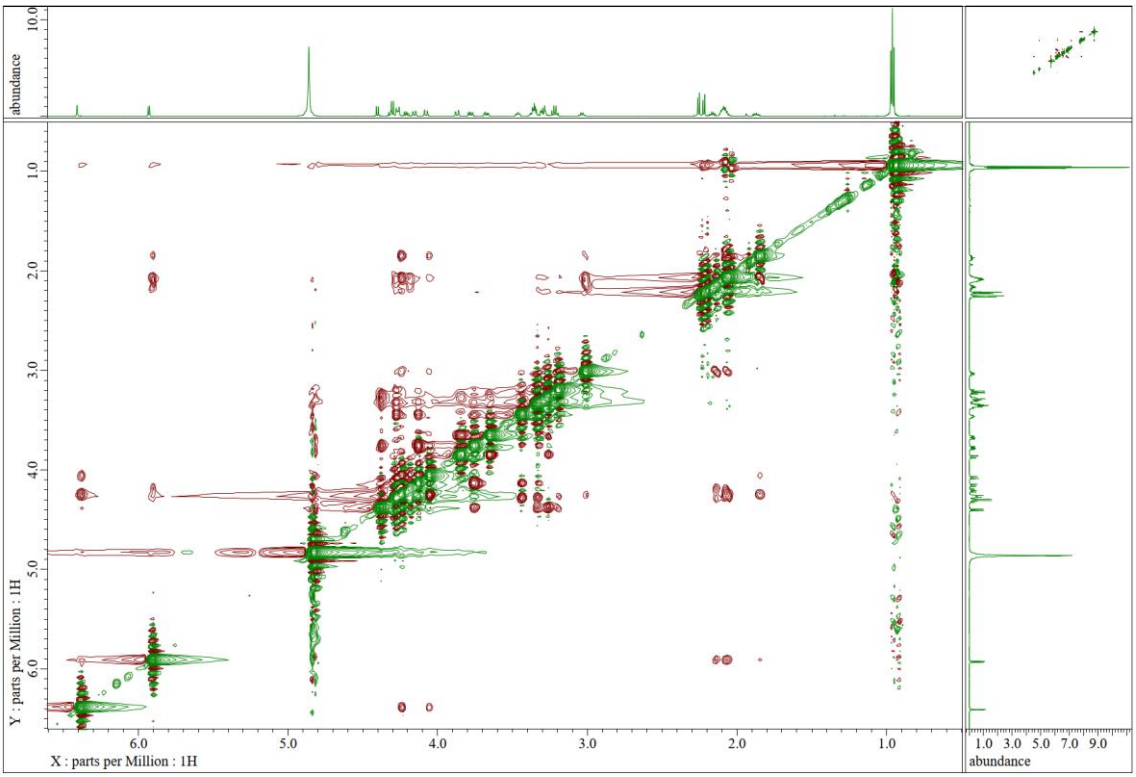
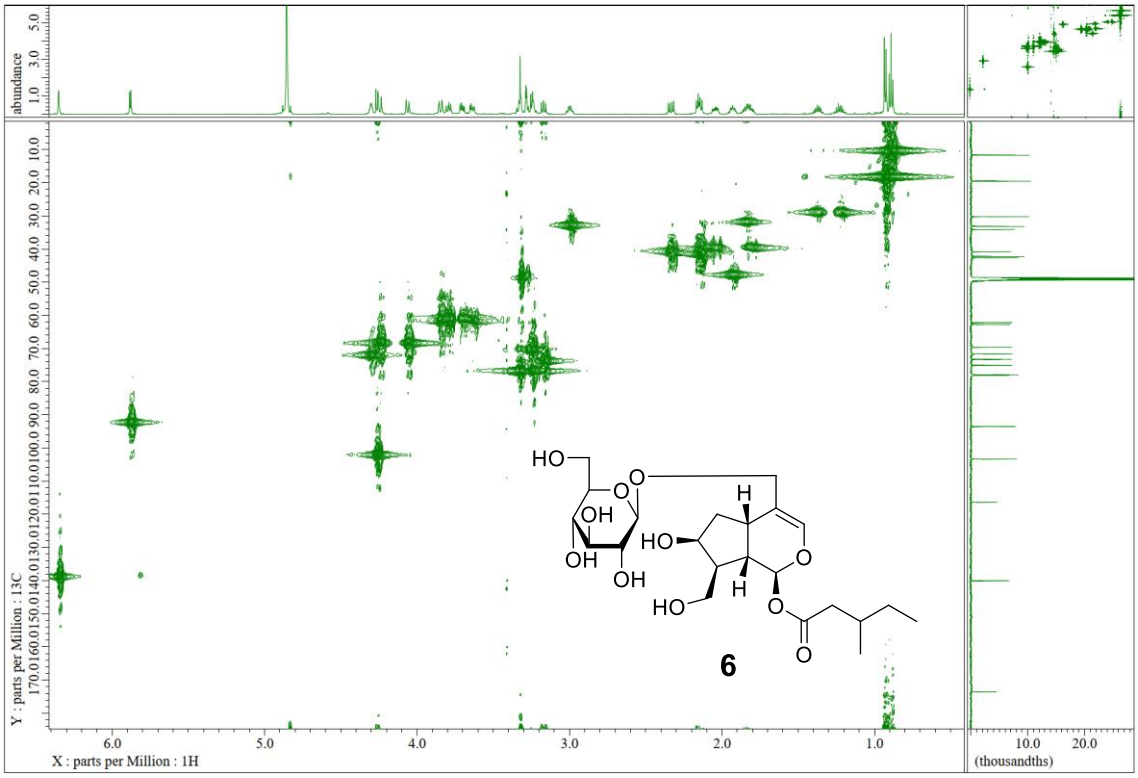
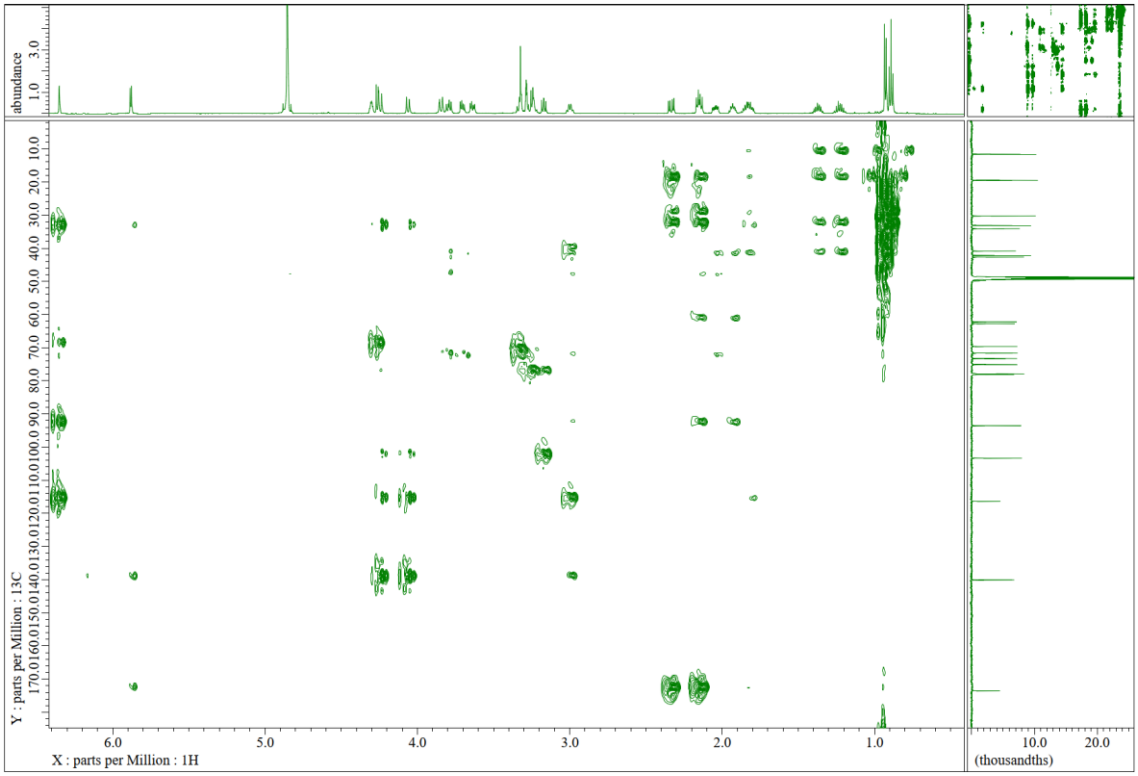


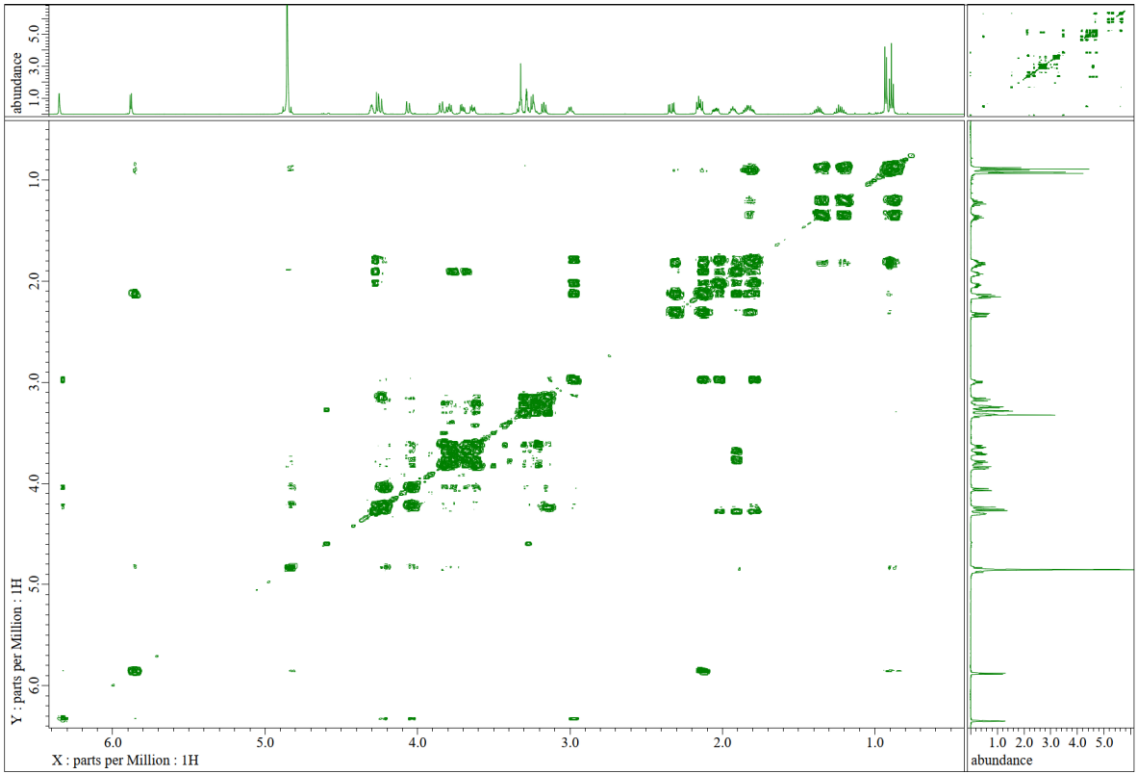
NOESY spectrum of **3**



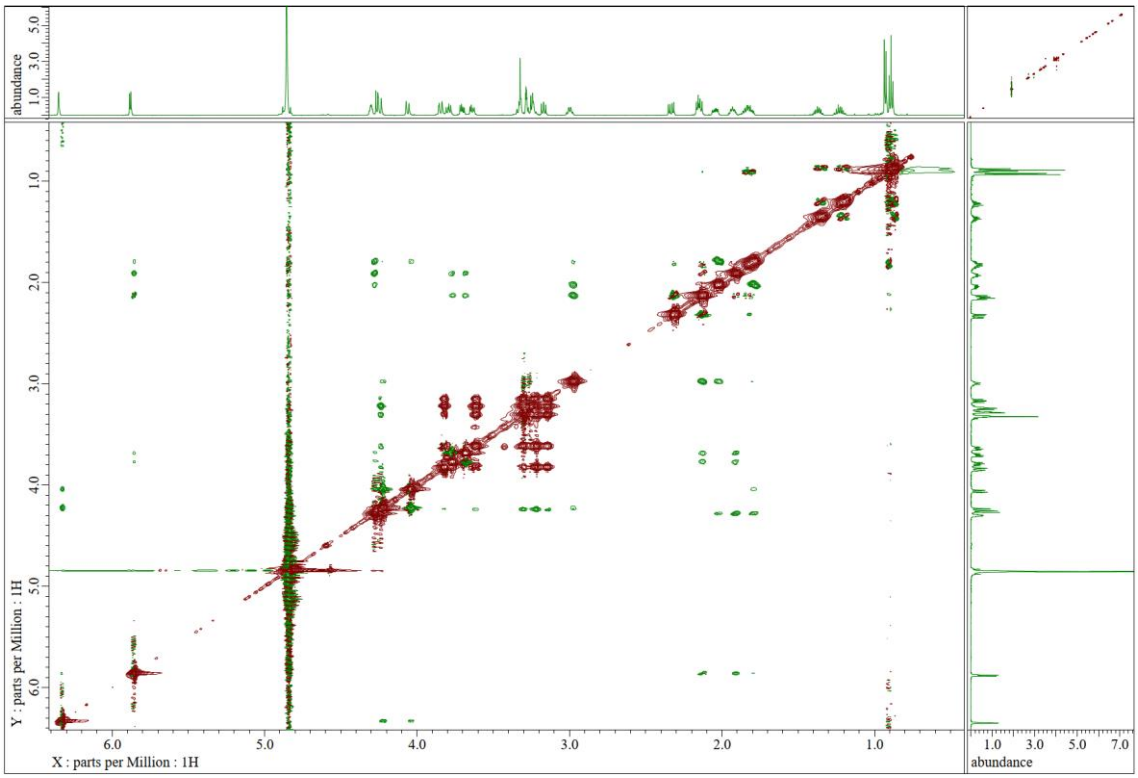
HMQC spectrum of **6**



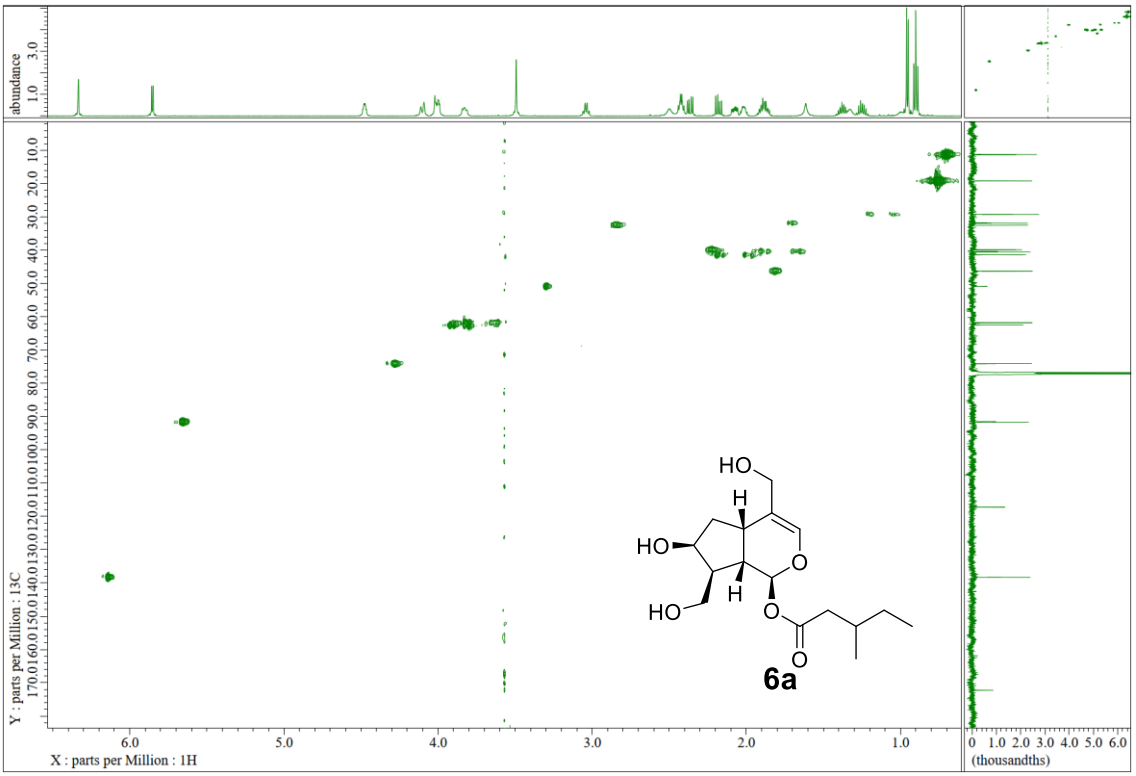
HMBC spectrum of **6**



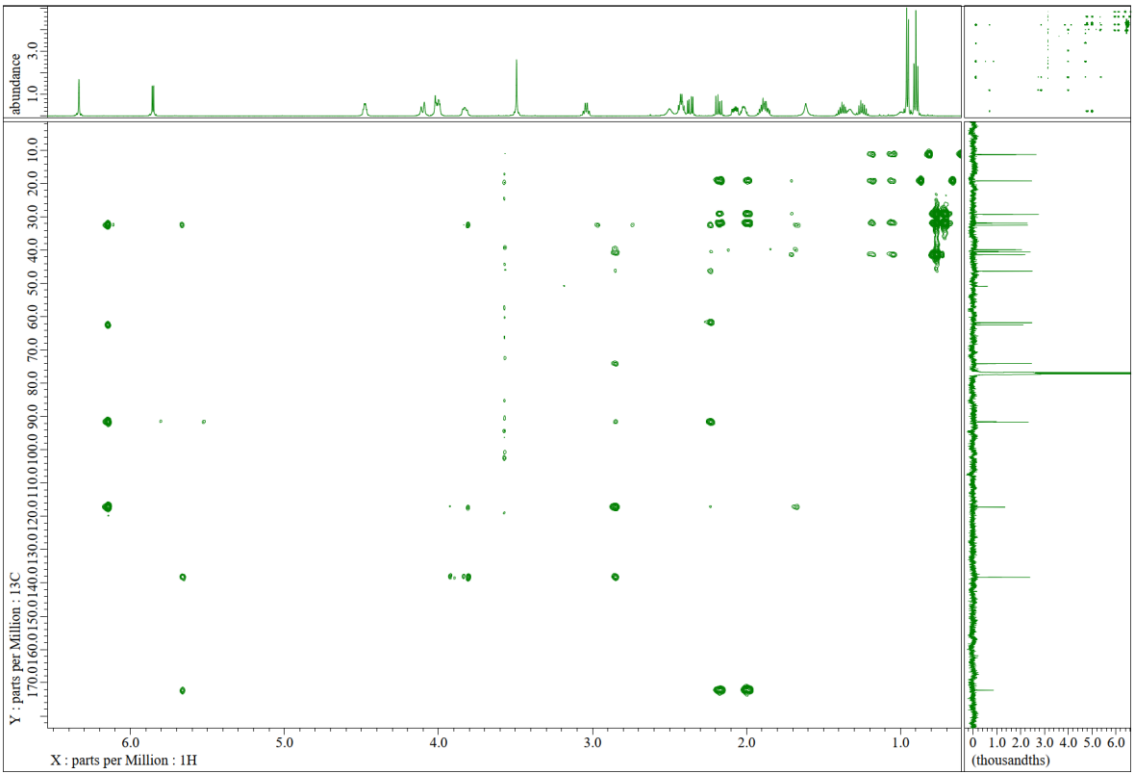
DQF spectrum of **6**



NOESY spectrum of **6**



HMQC spectrum of **6a**



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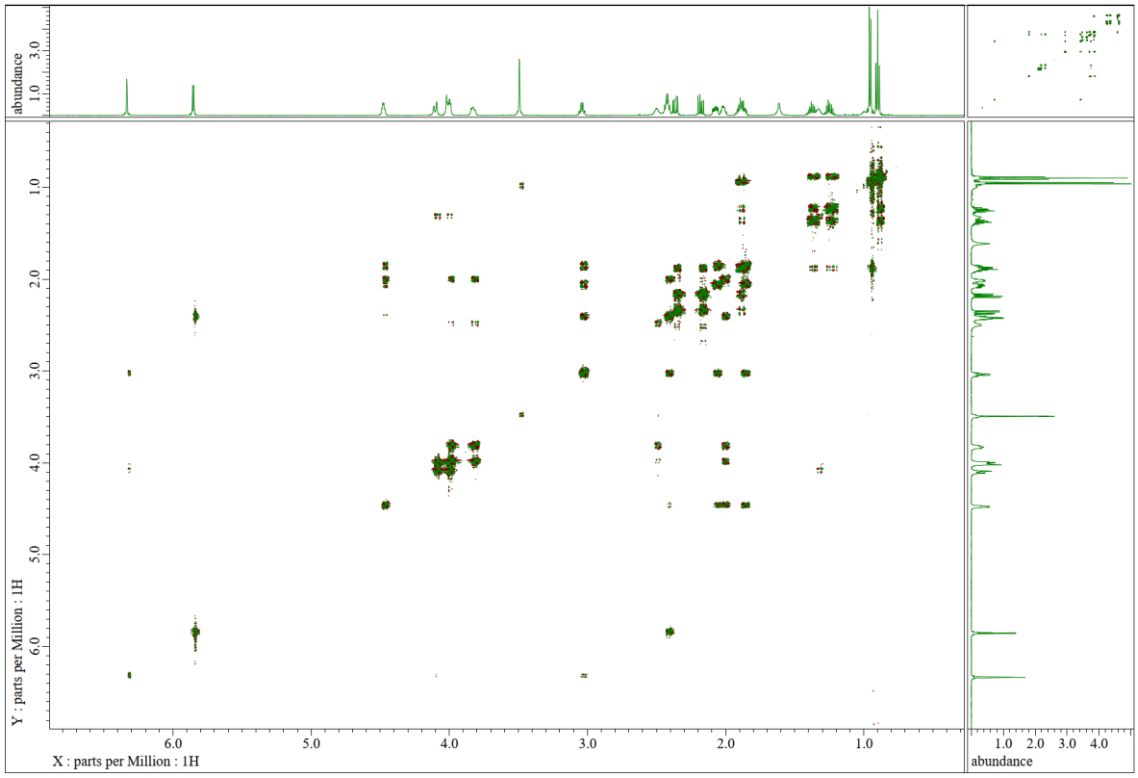
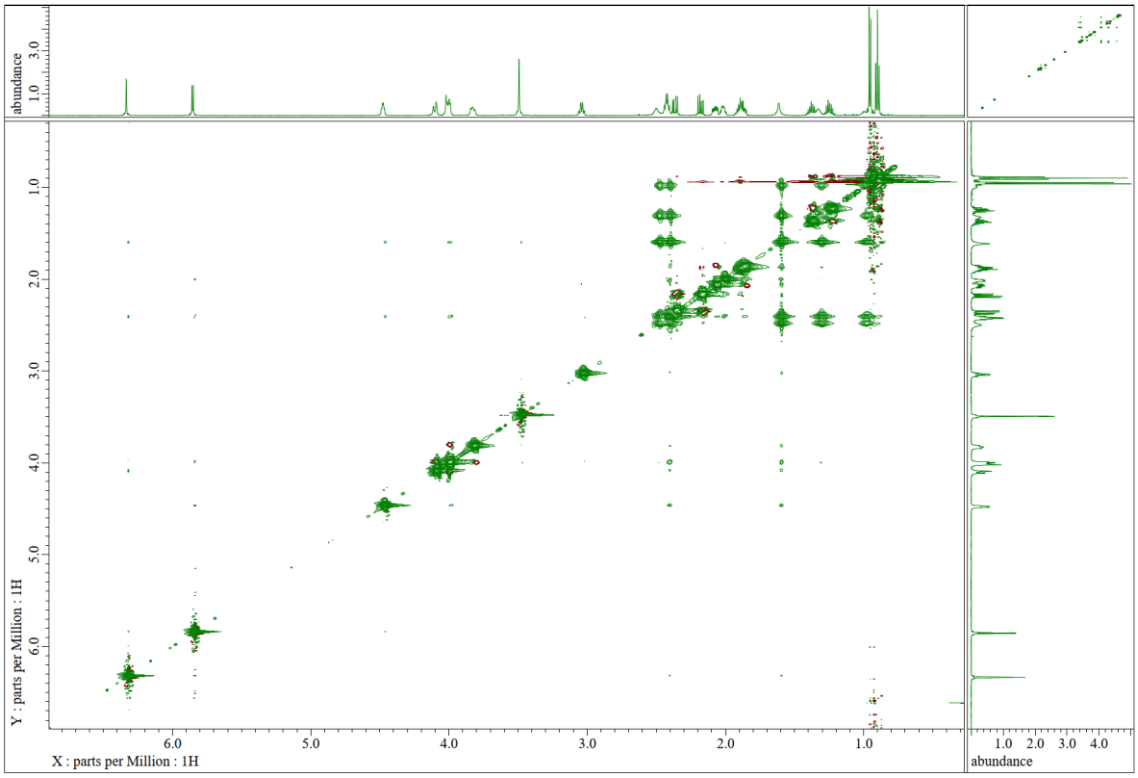
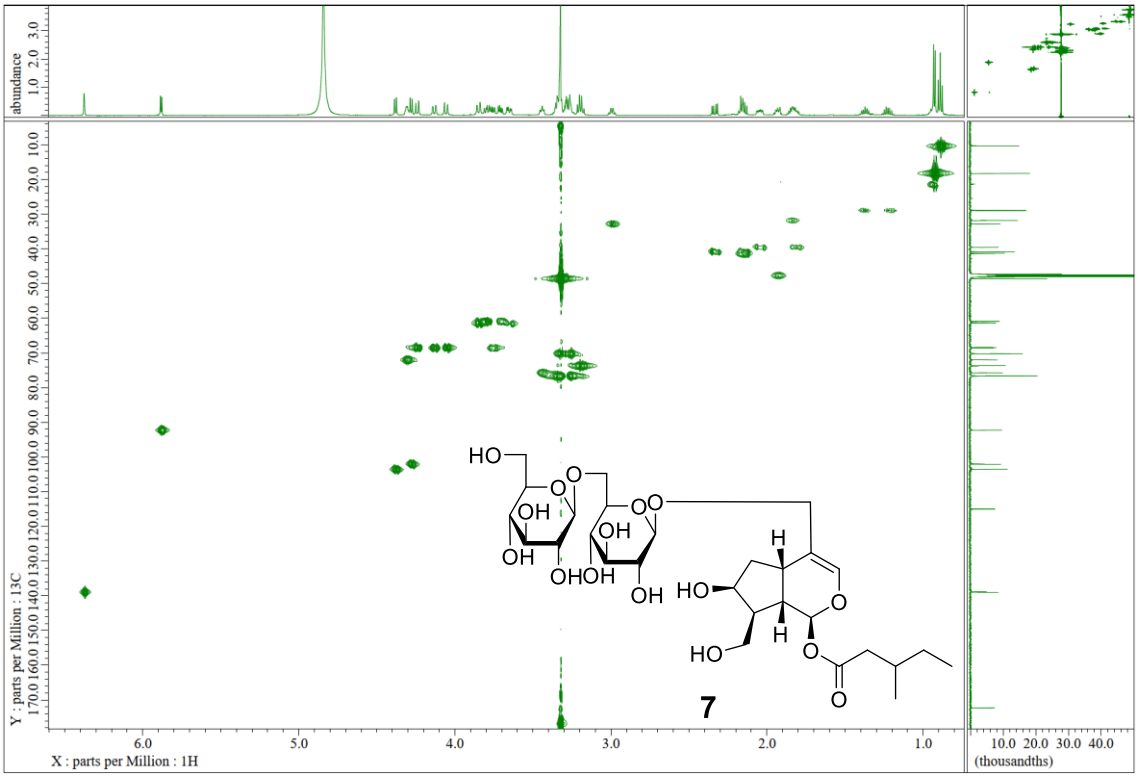


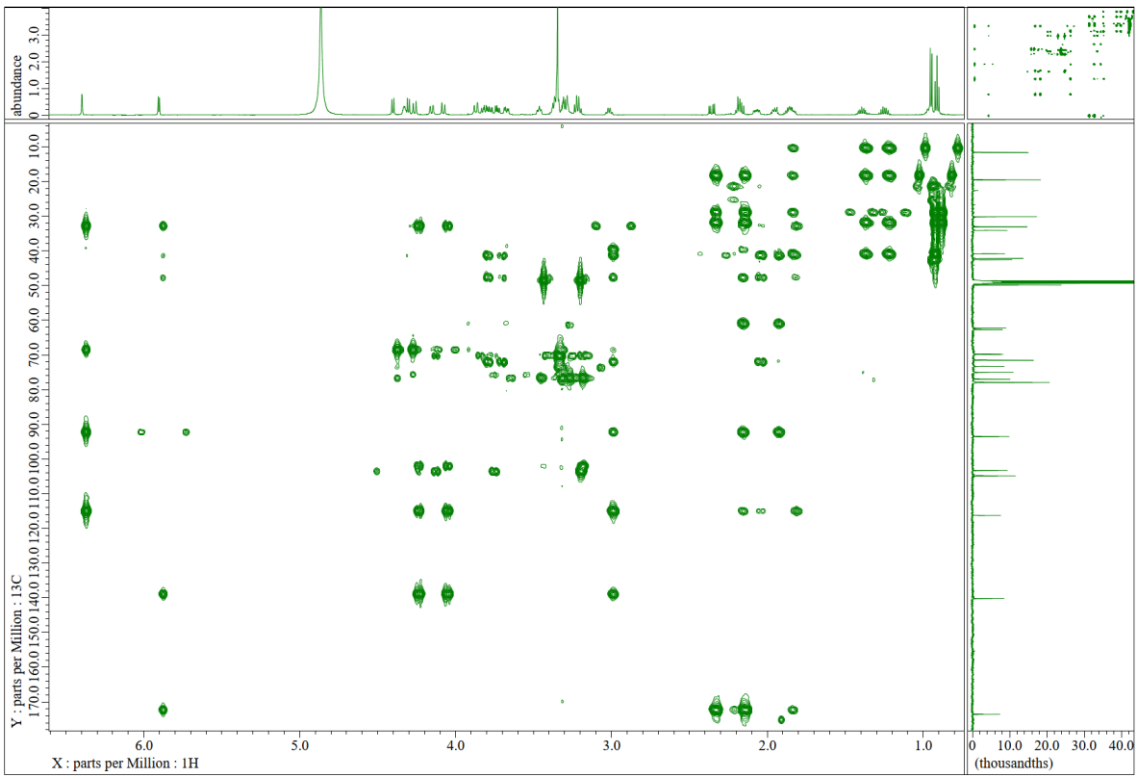
DQF spectrum of **6a**



NOESY spectrum of **6a**



HMQC spectrum of **7**



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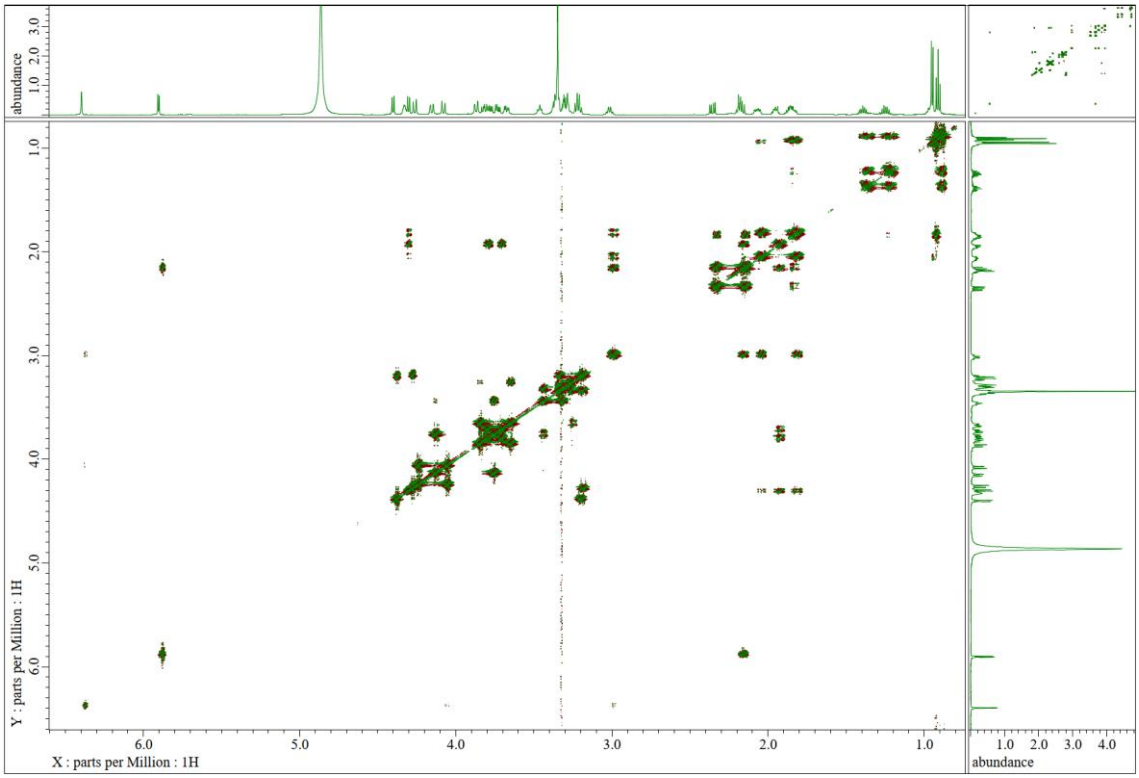
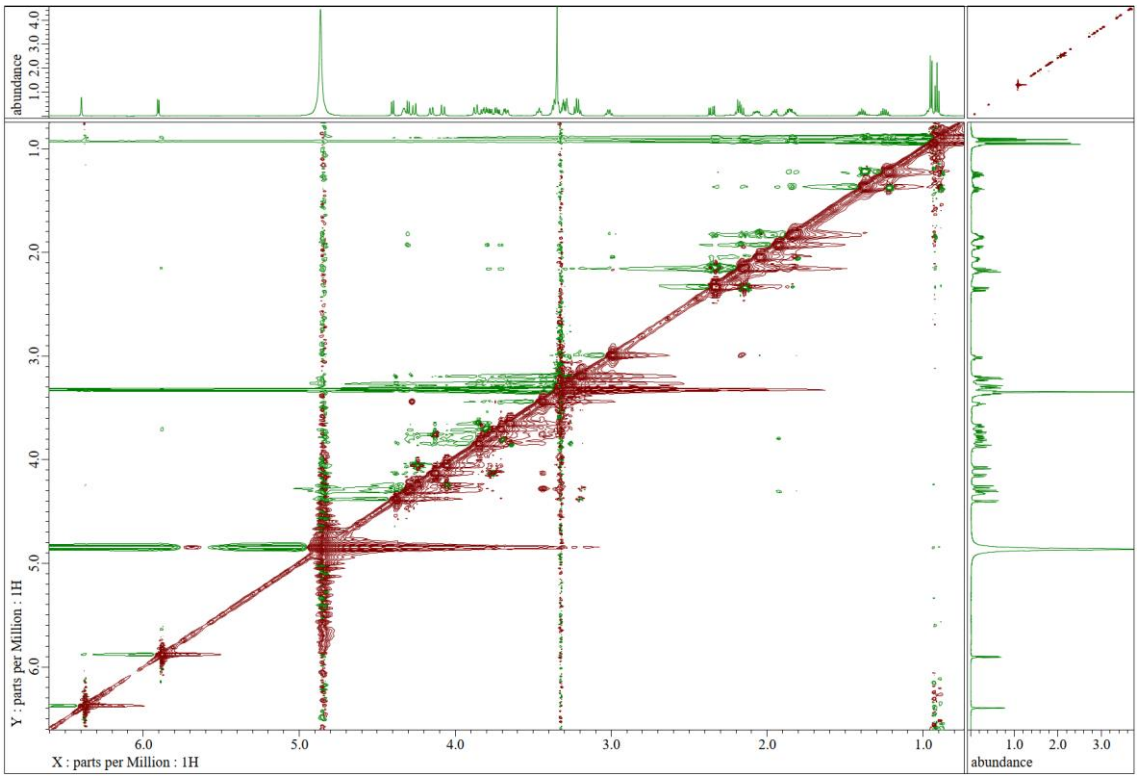
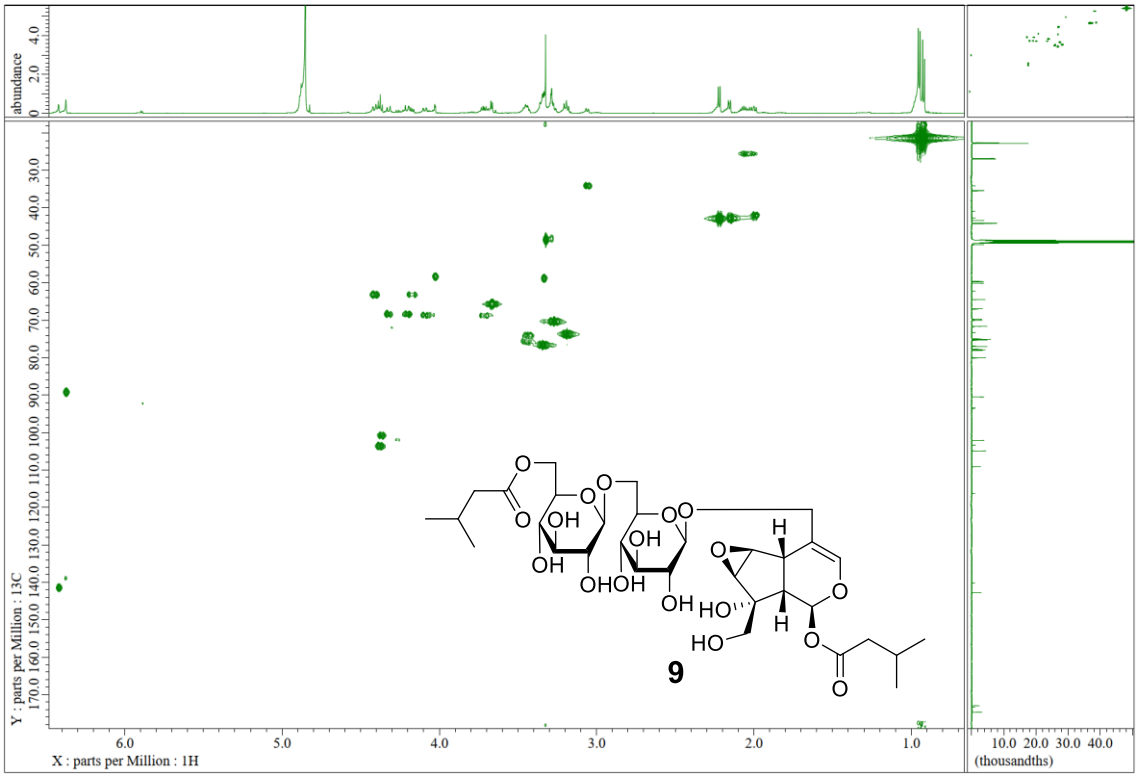


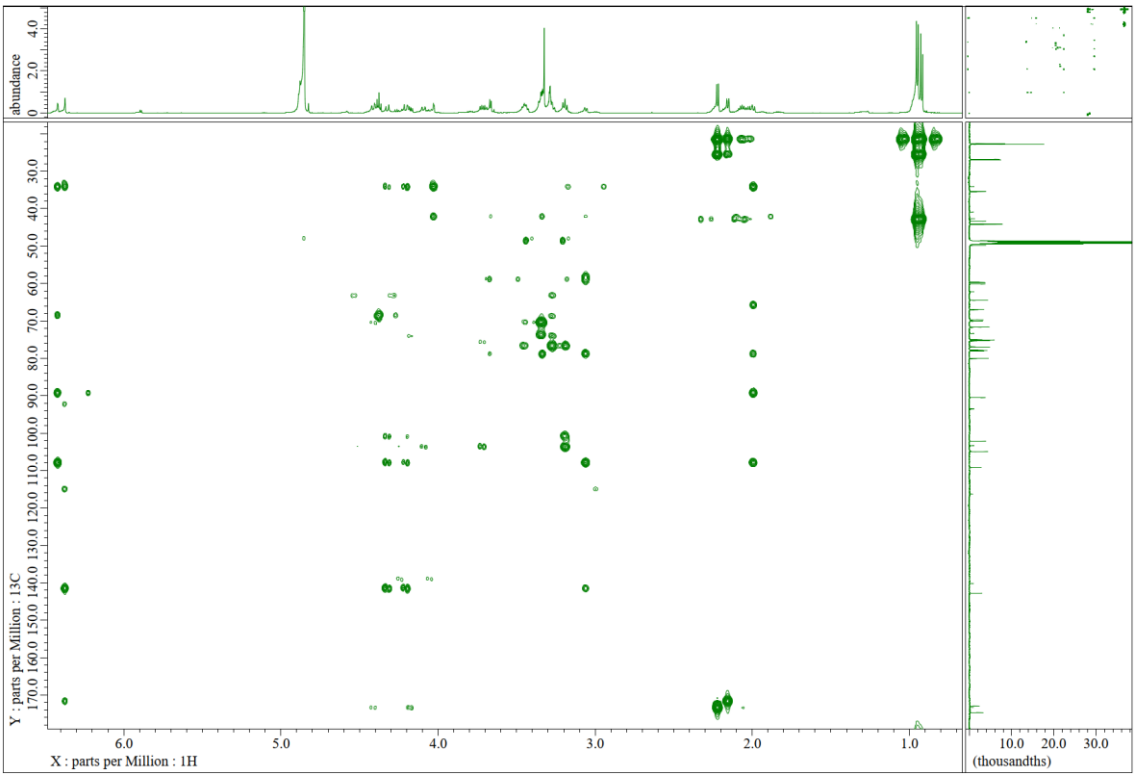
DQF spectrum of **7**



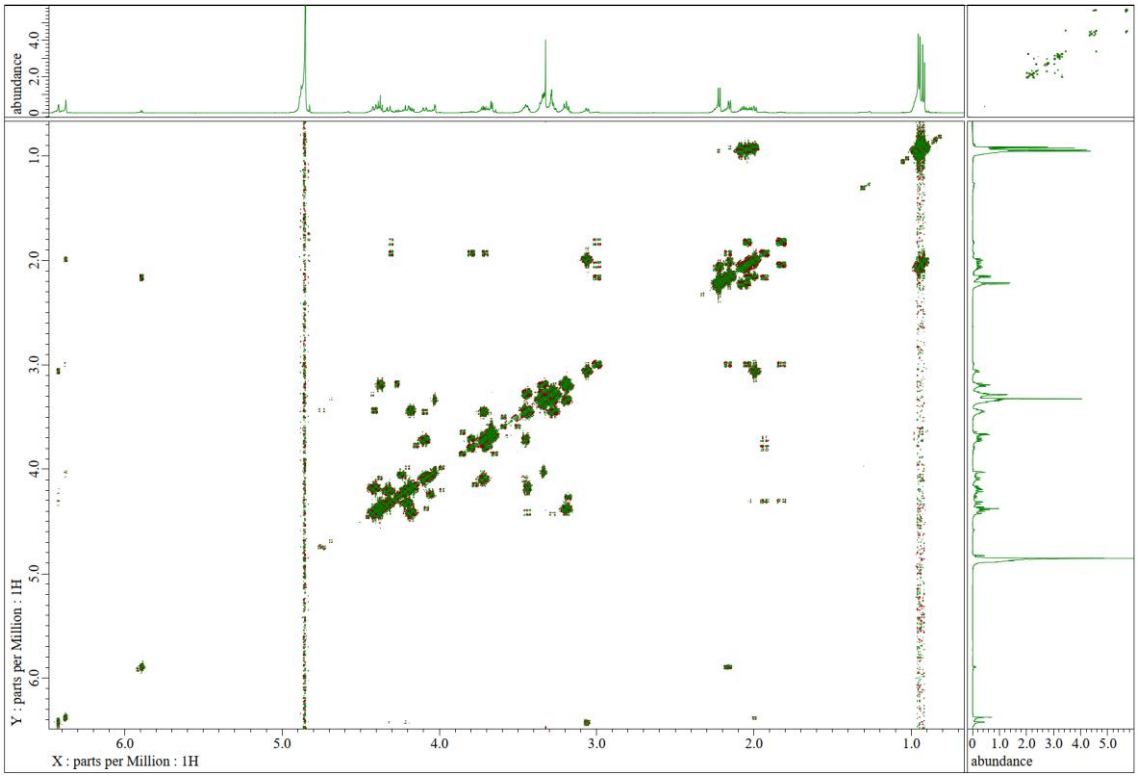
NOESY spectrum of **7**



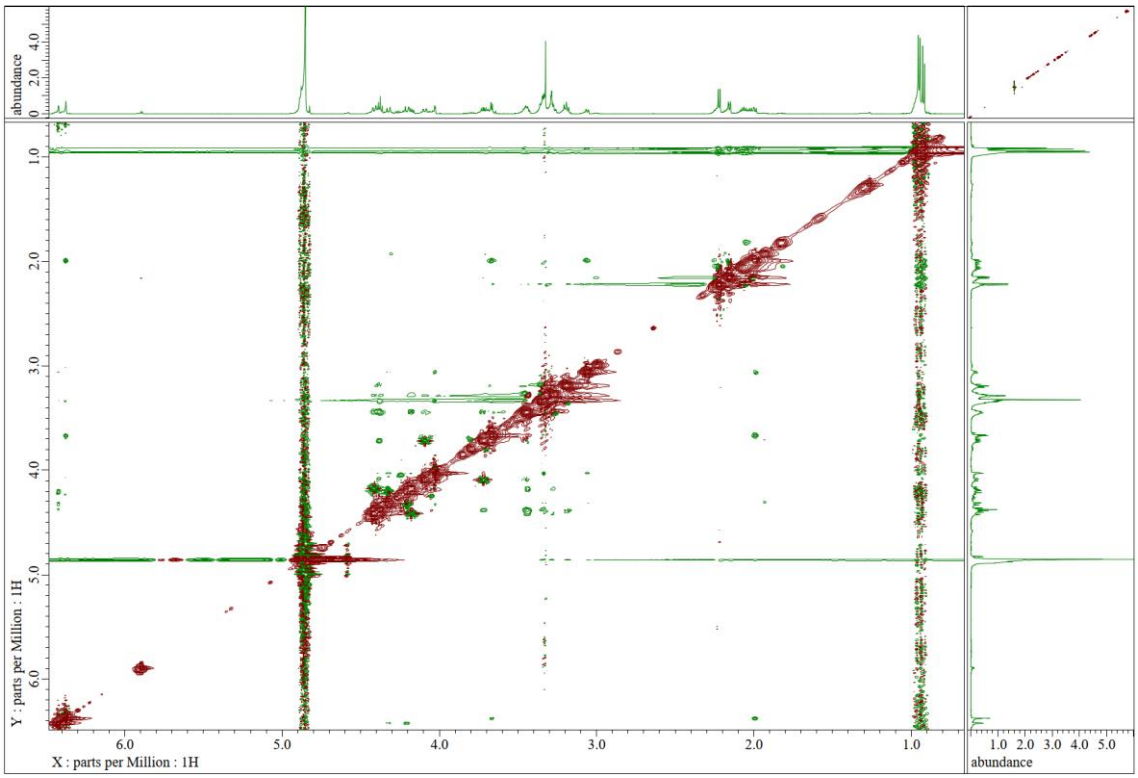
HMQC spectrum of **9**



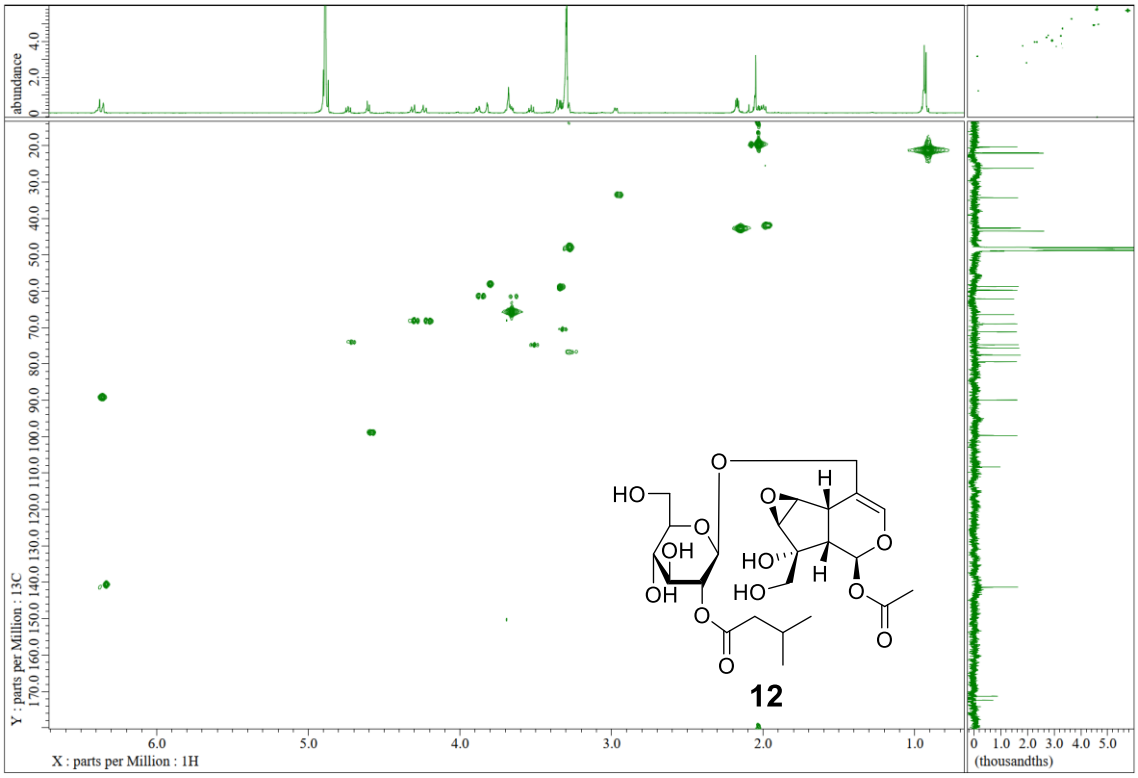
HMBC spectrum of **9**



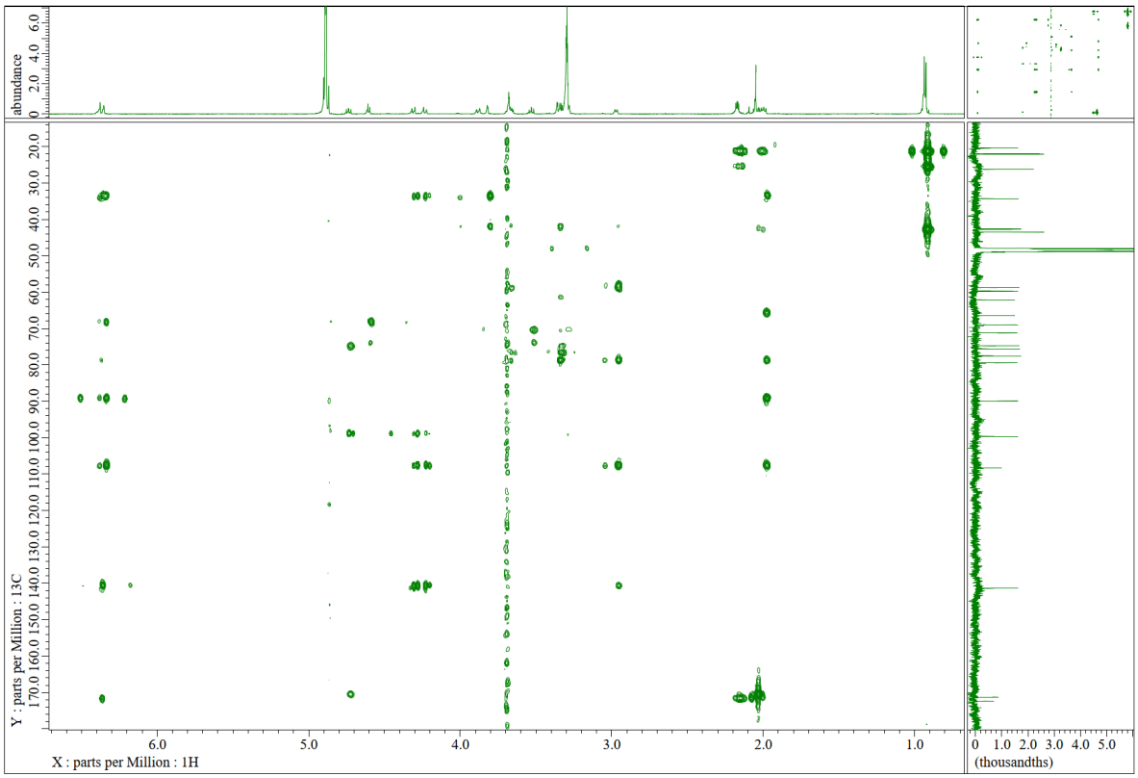
DQF spectrum of **9**



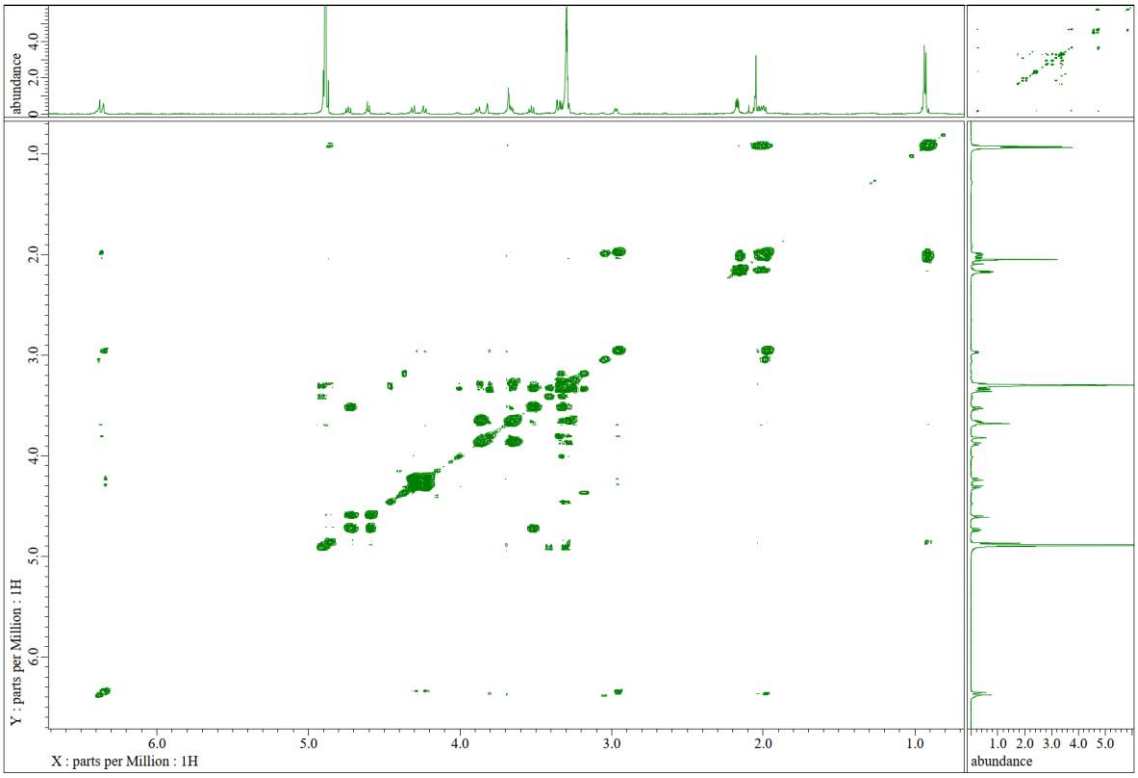
NOESY spectrum of **9**



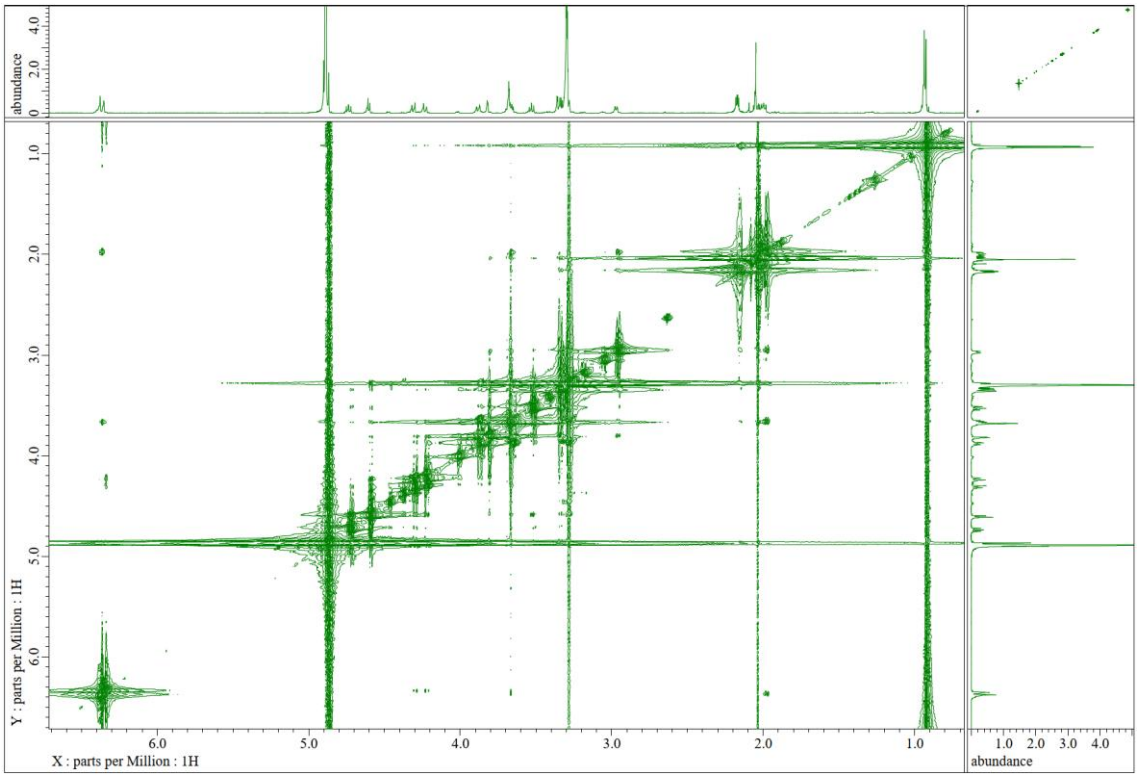
HMQC spectrum of **12**



HMBC spectrum of **12**

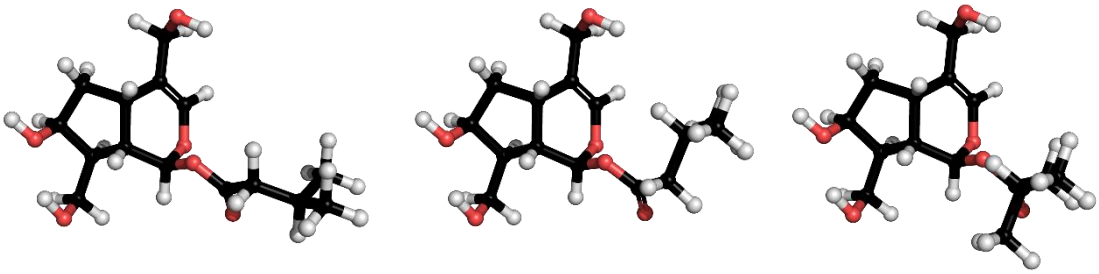


DQF spectrum of **12**



NOESY spectrum of **12**

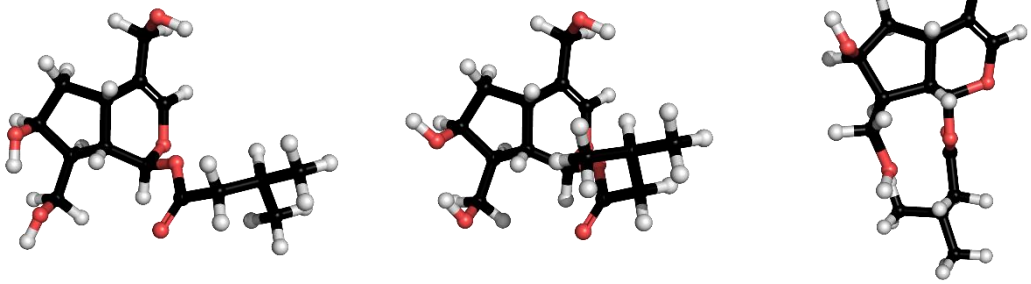
S4. Optimized geometries, the minimum value of frequency, relative free-energies, and Boltzmann distributions of conformers of 1a, 6a, and 9a.



Conf. 1
[10.50]
ΔG = 0.00
P = 52.76

Conf. 2
[15.47]
ΔG = 0.64
P = 18.03

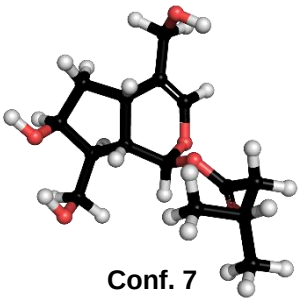
Conf. 3
[19.56]
ΔG = 0.89
P = 11.75



Conf. 4
[11.55]
ΔG = 1.41
P = 4.92

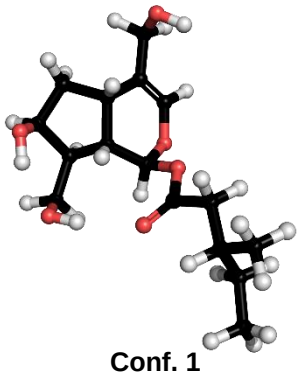
Conf. 5
[19.04]
ΔG = 1.45
P = 4.57

Conf. 6
[15.95]
ΔG = 1.55
P = 3.85

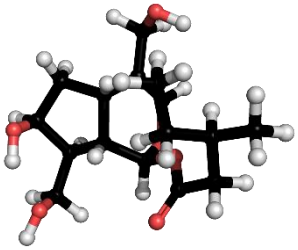


Conf. 7
[17.97]
ΔG = 2.22
P = 1.24

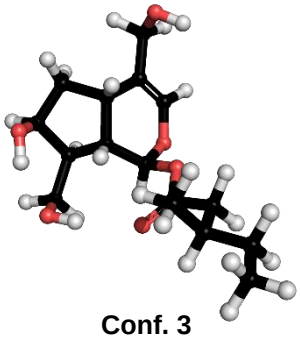
Figure S4-1 The optimized structures of 7 conformers of **1a** with the minimum value of frequency [in brackets, cm^{-1}], relative free-energy (ΔG, kcal/mol), and Boltzmann distribution (P, %), at 298.15 K, calculated at the CAM-B3LYP/def2-TZVP level in MeOH.



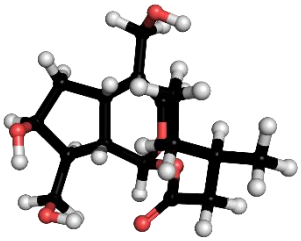
Conf. 1
[8.62]
ΔG = 0.00
P = 36.82



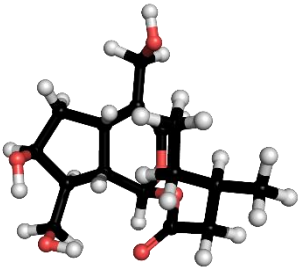
Conf. 2
[12.74]
ΔG = 0.10
P = 30.81



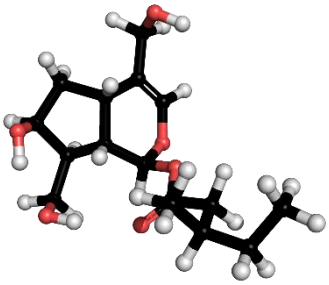
Conf. 3
[19.56]
ΔG = 0.77
P = 10.06



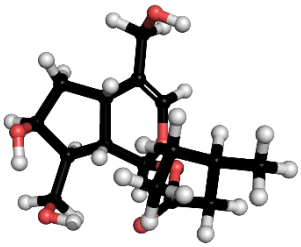
Conf. 4
[16.04]
ΔG = 0.82
P = 9.22



Conf. 5
[18.47]
ΔG = 1.26
P = 4.37

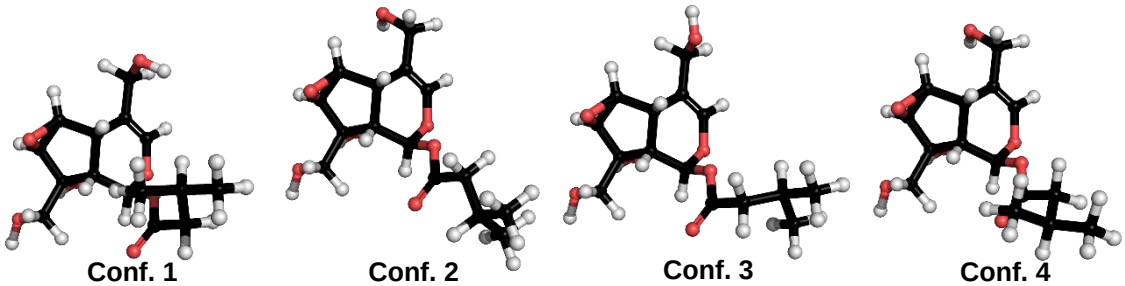


Conf. 6
[16.94]
ΔG = 1.34
P = 3.84



Conf. 7
[19.24]
ΔG = 1.91
P = 1.47

Figure S4-2 The optimized structures of 7 conformers of **6a** with the minimum value of frequency [in brackets, cm^{-1}], relative free-energy (ΔG, kcal/mol), and Boltzmann distribution (P, %), at 298.15 K, calculated at the CAM-B3LYP/def2-TZVP level in MeOH.

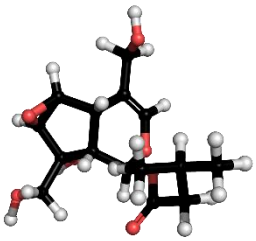


Conf. 1
[18.42]
ΔG = 0.00
P = 18.82

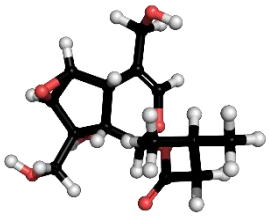
Conf. 2
[24.91]
ΔG = 0.14
P = 14.78

Conf. 3
[12.55]
ΔG = 0.16
P = 14.26

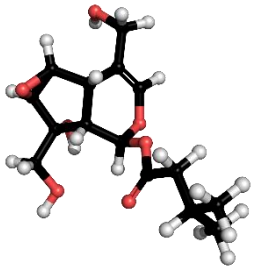
Conf. 4
[18.09]
ΔG = 0.23
P = 12.66



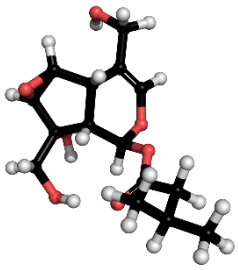
Conf. 5
[15.49]
ΔG = 0.25
P = 12.33



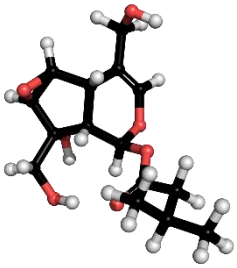
Conf. 6
[20.54]
ΔG = 0.55
P = 7.49



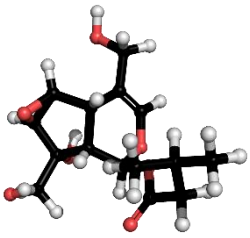
Conf. 7
[18.13]
ΔG = 1.01
P = 3.43



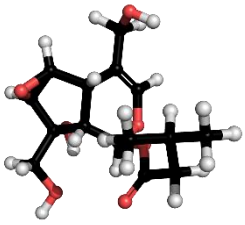
Conf. 8
[19.47]
ΔG = 1.01
P = 3.41



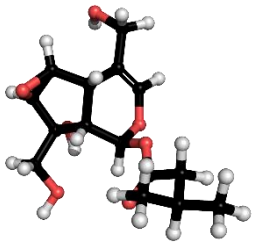
Conf. 9
[20.04]
ΔG = 1.13
P = 2.77



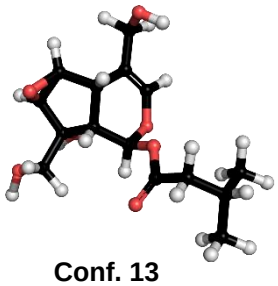
Conf. 10
[21.36]
ΔG = 1.14
P = 2.73



Conf. 11
[11.54]
ΔG = 1.31
P = 2.05



Conf. 12
[17.81]
ΔG = 1.34
P = 1.97



Conf. 13
[19.08]
ΔG = 1.52
P = 1.44

Figure S4-3 The optimized structures of 13 conformers of **9a** with the minimum value of frequency [in brackets, cm^{-1}], relative free-energy (ΔG, kcal/mol), and Boltzmann distribution (P, %), at 298.15 K, calculated at the CAM-B3LYP/def2-TZVP level in MeOH.

S5. Anti-proliferative activity of 1a, 6a, and 9a against non-CSCs and CSCs from MDA-MB-231 cells.

Table S5-1 Inhibition (%) of cell proliferation of **1a**, **6a**, and **9a** against non-CSCs (MDA-MB-231 calls). ADR (positive control) inhibited 27.9±6.7% at 0.05 μM. Inhibition ratio (%) of relative cell proliferation are shown as means ±SD of three replicates. Statical significance was analyzed using the Dunnett's test (*$P < 0.05$, **$P < 0.01$).

Compounds	Concentrations of test compounds (μM)							IC_{50} (μM)
	Control	20 μM	40 μM	60 μM	80 μM	100 μM	120 μM	
1a	0±5.7	-	-	16.0±4.3*	38.8±10.8**	48.6±6.8**	72.3±1.7**	> 100
6a	0±6.0	4.2±4.8	38.5±3.3**	64.3±3.6**	79.2±3.6**	77.7±3.0**		47.7±4.2
9a	0±5.7	-	-	8.7±11.4	46.5±6.8**	30.3±3.6**	70.9±5.3**	> 100

Table S5-2 Inhibition (%) of cell proliferation of **1a**, **6a**, and **9a** against CSCs from MDA-MB-231 cells. ADR (positive control) inhibited 50.3±2.4% at 0.05 μM. Inhibition ratio (%) of relative cell proliferation are shown as means ±SD of three replicates. Statical significance was analyzed using the Dunnett's test (*$P < 0.05$, **$P < 0.01$).

Compounds	Concentrations of test compounds (μM)								IC_{50} (μM)
	Control	10 μM	20 μM	40 μM	60 μM	80 μM	100 μM	120 μM	
1a	0±5.9	-	-	37.4±6.9**	70.5±2.1**	93.3±2.2**	94.3±0.1**	97.4±0.4**	45.0±5.3
6a	0±1.2	16.2±3.6**	60.4±1.9**	84.3±1.2**	96.5±0.4**	98.6±0.2**	98.1±4.6**		17.6±1.0
9a	0±5.9	-	-	38.1±6.1**	55.8±1.0**	91.8±2.5**	98.5±0.3**	98.5±0.3**	47.7±3.9