

Supporting Information

Loss of the phenolic hydroxyl group and aromaticity from the side chain of anti-proliferative 10-methyl-aplog-1, a simplified analog of aplysiatoxin, enhances its tumor-promoting and proinflammatory activities

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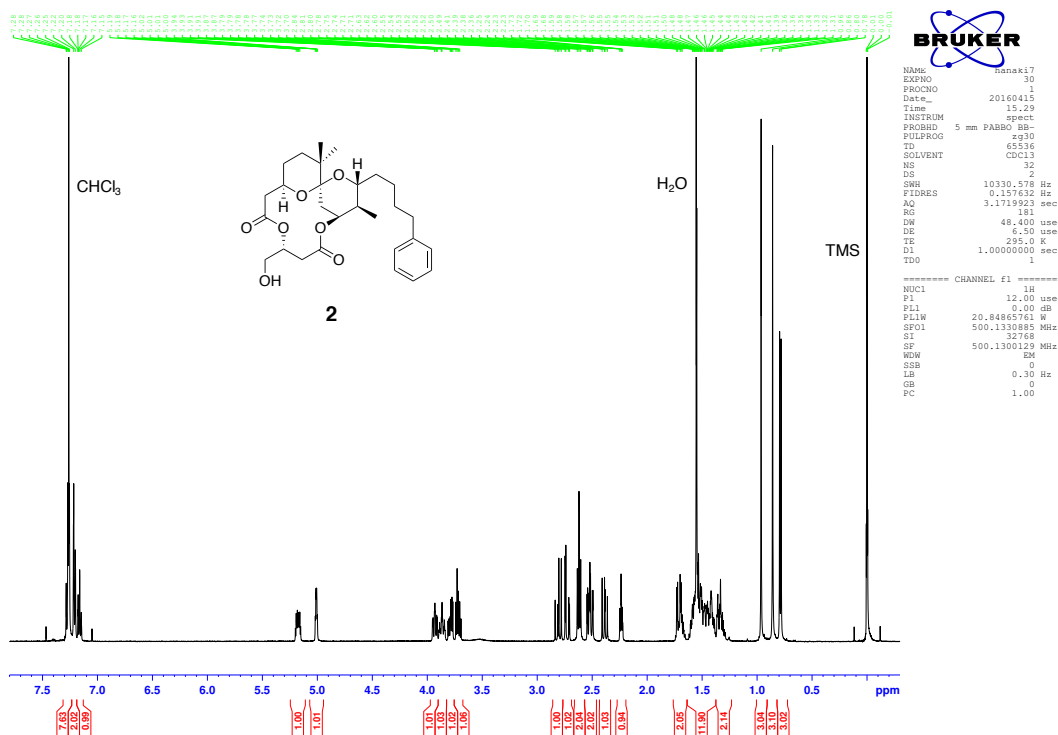
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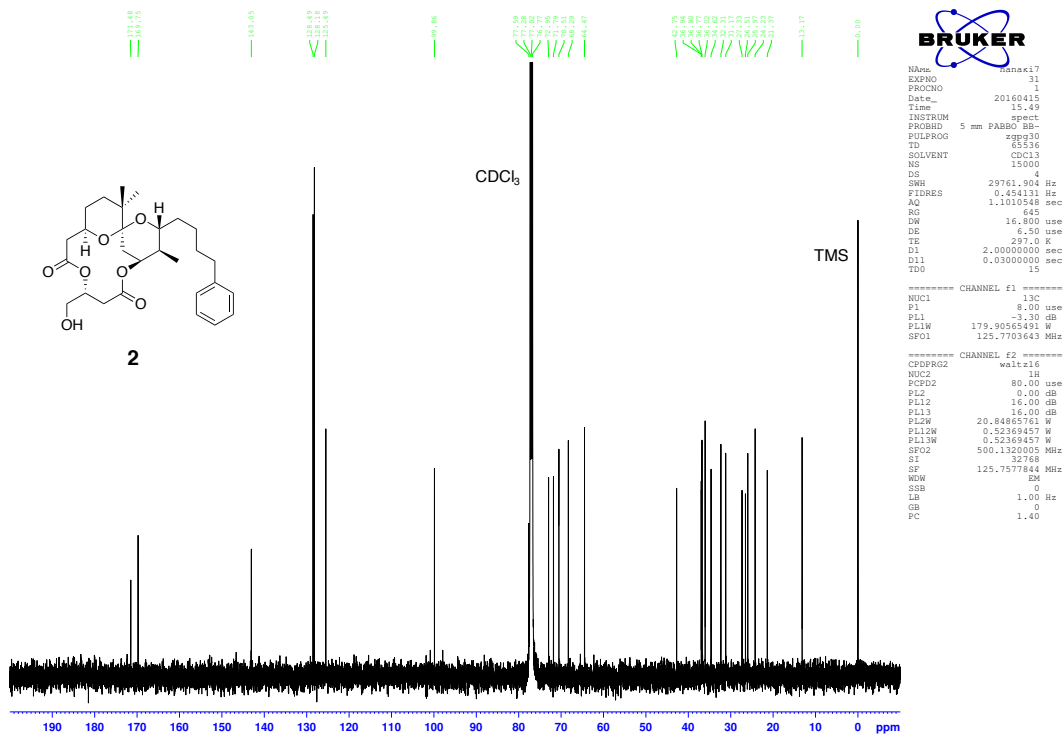
- I. ¹H and ¹³C NMR spectra of **2** and **3**
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I. ^1H and ^{13}C NMR spectra of **2** and **3**

¹H-1D NMR spectrum of **2** (500 MHz, CDCl₃, 0.0049 M)



¹³C-1D NMR spectrum of **2** (125 MHz, CDCl₃, 0.0049 M)



Chemical structure of compound 3:

C[C@H]1CC[C@H]2[C@@H](C)[C@H](OCC(=O)O[C@H]3C[C@@H](C)[C@H](O)[C@H]3C)[C@H](C)[C@H]2O1

¹H NMR spectrum (CDCl₃):

Chemical shift (ppm): 8.00, 7.99, 7.98, 7.97, 7.96, 7.95, 7.94, 7.93, 7.92, 7.91, 7.90, 7.89, 7.88, 7.87, 7.86, 7.85, 7.84, 7.83, 7.82, 7.81, 7.80, 7.79, 7.78, 7.77, 7.76, 7.75, 7.74, 7.73, 7.72, 7.71, 7.70, 7.69, 7.68, 7.67, 7.66, 7.65, 7.64, 7.63, 7.62, 7.61, 7.60, 7.59, 7.58, 7.57, 7.56, 7.55, 7.54, 7.53, 7.52, 7.51, 7.50, 7.49, 7.48, 7.47, 7.46, 7.45, 7.44, 7.43, 7.42, 7.41, 7.40, 7.39, 7.38, 7.37, 7.36, 7.35, 7.34, 7.33, 7.32, 7.31, 7.30, 7.29, 7.28, 7.27, 7.26, 7.25, 7.24, 7.23, 7.22, 7.21, 7.20, 7.19, 7.18, 7.17, 7.16, 7.15, 7.14, 7.13, 7.12, 7.11, 7.10, 7.09, 7.08, 7.07, 7.06, 7.05, 7.04, 7.03, 7.02, 7.01, 7.00, 6.99, 6.98, 6.97, 6.96, 6.95, 6.94, 6.93, 6.92, 6.91, 6.90, 6.89, 6.88, 6.87, 6.86, 6.85, 6.84, 6.83, 6.82, 6.81, 6.80, 6.79, 6.78, 6.77, 6.76, 6.75, 6.74, 6.73, 6.72, 6.71, 6.70, 6.69, 6.68, 6.67, 6.66, 6.65, 6.64, 6.63, 6.62, 6.61, 6.60, 6.59, 6.58, 6.57, 6.56, 6.55, 6.54, 6.53, 6.52, 6.51, 6.50, 6.49, 6.48, 6.47, 6.46, 6.45, 6.44, 6.43, 6.42, 6.41, 6.40, 6.39, 6.38, 6.37, 6.36, 6.35, 6.34, 6.33, 6.32, 6.31, 6.30, 6.29, 6.28, 6.27, 6.26, 6.25, 6.24, 6.23, 6.22, 6.21, 6.20, 6.19, 6.18, 6.17, 6.16, 6.15, 6.14, 6.13, 6.12, 6.11, 6.10, 6.09, 6.08, 6.07, 6.06, 6.05, 6.04, 6.03, 6.02, 6.01, 6.00, 5.99, 5.98, 5.97, 5.96, 5.95, 5.94, 5.93, 5.92, 5.91, 5.90, 5.89, 5.88, 5.87, 5.86, 5.85, 5.84, 5.83, 5.82, 5.81, 5.80, 5.79, 5.78, 5.77, 5.76, 5.75, 5.74, 5.73, 5.72, 5.71, 5.70, 5.69, 5.68, 5.67, 5.66, 5.65, 5.64, 5.63, 5.62, 5.61, 5.60, 5.59, 5.58, 5.57, 5.56, 5.55, 5.54, 5.53, 5.52, 5.51, 5.50, 5.49, 5.48, 5.47, 5.46, 5.45, 5.44, 5.43, 5.42, 5.41, 5.40, 5.39, 5.38, 5.37, 5.36, 5.35, 5.34, 5.33, 5.32, 5.31, 5.30, 5.29, 5.28, 5.27, 5.26, 5.25, 5.24, 5.23, 5.22, 5.21, 5.20, 5.19, 5.18, 5.17, 5.16, 5.15, 5.14, 5.13, 5.12, 5.11, 5.10, 5.09, 5.08, 5.07, 5.06, 5.05, 5.04, 5.03, 5.02, 5.01, 5.00, 4.99, 4.98, 4.97, 4.96, 4.95, 4.94, 4.93, 4.92, 4.91, 4.90, 4.89, 4.88, 4.87, 4.86, 4.85, 4.84, 4.83, 4.82, 4.81, 4.80, 4.79, 4.78, 4.77, 4.76, 4.75, 4.74, 4.73, 4.72, 4.71, 4.70, 4.69, 4.68, 4.67, 4.66, 4.65, 4.64, 4.63, 4.62, 4.61, 4.60, 4.59, 4.58, 4.57, 4.56, 4.55, 4.54, 4.53, 4.52, 4.51, 4.50, 4.49, 4.48, 4.47, 4.46, 4.45, 4.44, 4.43, 4.42, 4.41, 4.40, 4.39, 4.38, 4.37, 4.36, 4.35, 4.34, 4.33, 4.32, 4.31, 4.30, 4.29, 4.28, 4.27, 4.26, 4.25, 4.24, 4.23, 4.22, 4.21, 4.20, 4.19, 4.18, 4.17, 4.16, 4.15, 4.14, 4.13, 4.12, 4.11, 4.10, 4.09, 4.08, 4.07, 4.06, 4.05, 4.04, 4.03, 4.02, 4.01, 4.00, 3.99, 3.98, 3.97, 3.96, 3.95, 3.94, 3.93, 3.92, 3.91, 3.90, 3.89, 3.88, 3.87, 3.86, 3.85, 3.84, 3.83, 3.82, 3.81, 3.80, 3.79, 3.78, 3.77, 3.76, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69, 3.68, 3.67, 3.66, 3.65, 3.64, 3.63, 3.62, 3.61, 3.60, 3.59, 3.58, 3.57, 3.56, 3.55, 3.54, 3.53, 3.52, 3.51, 3.50, 3.49, 3.48, 3.47, 3.46, 3.45, 3.44, 3.43, 3.42, 3.41, 3.40, 3.39, 3.38, 3.37, 3.36, 3.35, 3.34, 3.33, 3.32, 3.31, 3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00, 2.99, 2.98, 2.97, 2.96, 2.95, 2.94, 2.93, 2.92, 2.91, 2.90, 2.89, 2.88, 2.87, 2.86, 2.85, 2.84, 2.83, 2.82, 2.81, 2.80, 2.79, 2.78, 2.77, 2.76, 2.75, 2.74, 2.73, 2.72, 2.71, 2.70, 2.69, 2.68, 2.67, 2.66, 2.65, 2.64, 2.63, 2.62, 2.61, 2.60, 2.59, 2.58, 2.57, 2.56, 2.55, 2.54, 2.53, 2.52, 2.51, 2.50, 2.49, 2.48, 2.47, 2.46, 2.45, 2.44, 2.43, 2.42, 2.41, 2.40, 2.39, 2.38, 2.37, 2.36, 2.35, 2.34, 2.33, 2.32, 2.31, 2.30, 2.29, 2.28, 2.27, 2.26, 2.25, 2.24, 2.23, 2.22, 2.21, 2.20, 2.19, 2.18, 2.17, 2.16, 2.15, 2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00, 1.99, 1.98, 1.97, 1.96, 1.95, 1.94, 1.93, 1.92, 1.91, 1.90, 1.89, 1.88, 1.87, 1.86, 1.85, 1.84, 1.83, 1.82, 1.81, 1.80, 1.79, 1.78, 1.77, 1.76, 1.75, 1.74, 1.73, 1.72, 1.71, 1.70, 1.69, 1.68, 1.67, 1.66, 1.65, 1.64, 1.63, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53

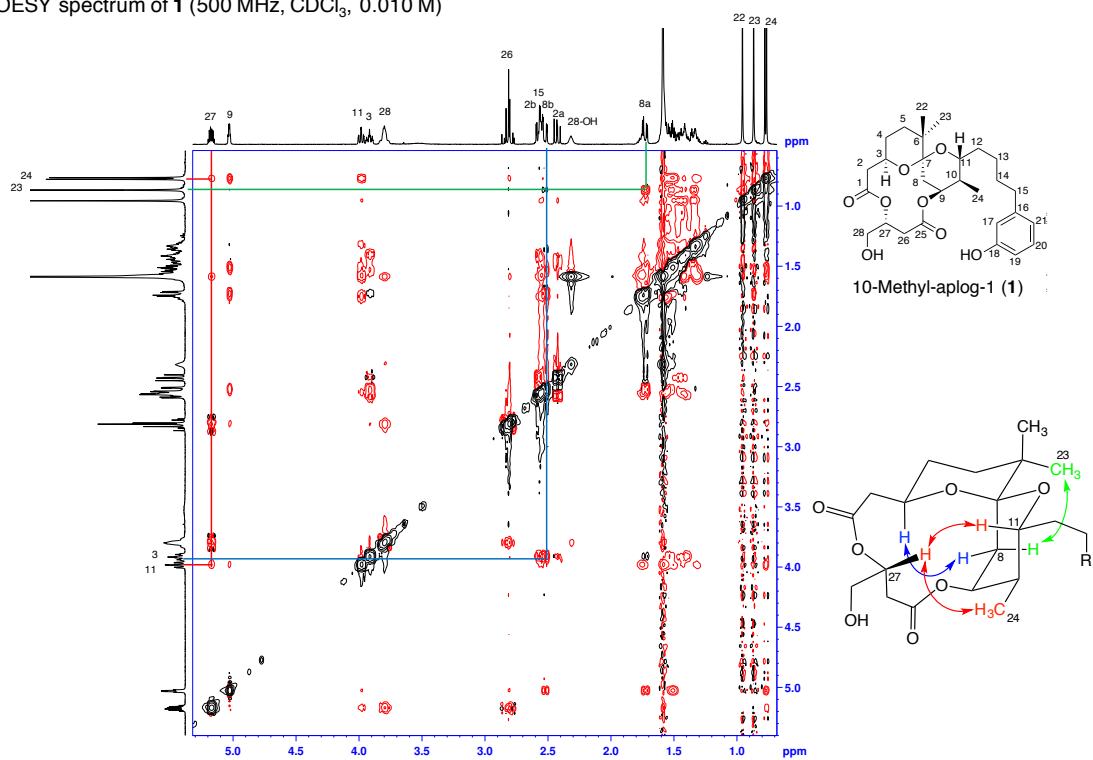
Chemical structure of compound **3** is shown. The ^1H NMR spectrum (CDCl₃) is displayed below the structure, showing peaks corresponding to the protons in the molecule. The x-axis represents the chemical shift in ppm, ranging from 0 to 10.

Peak list (ppm):

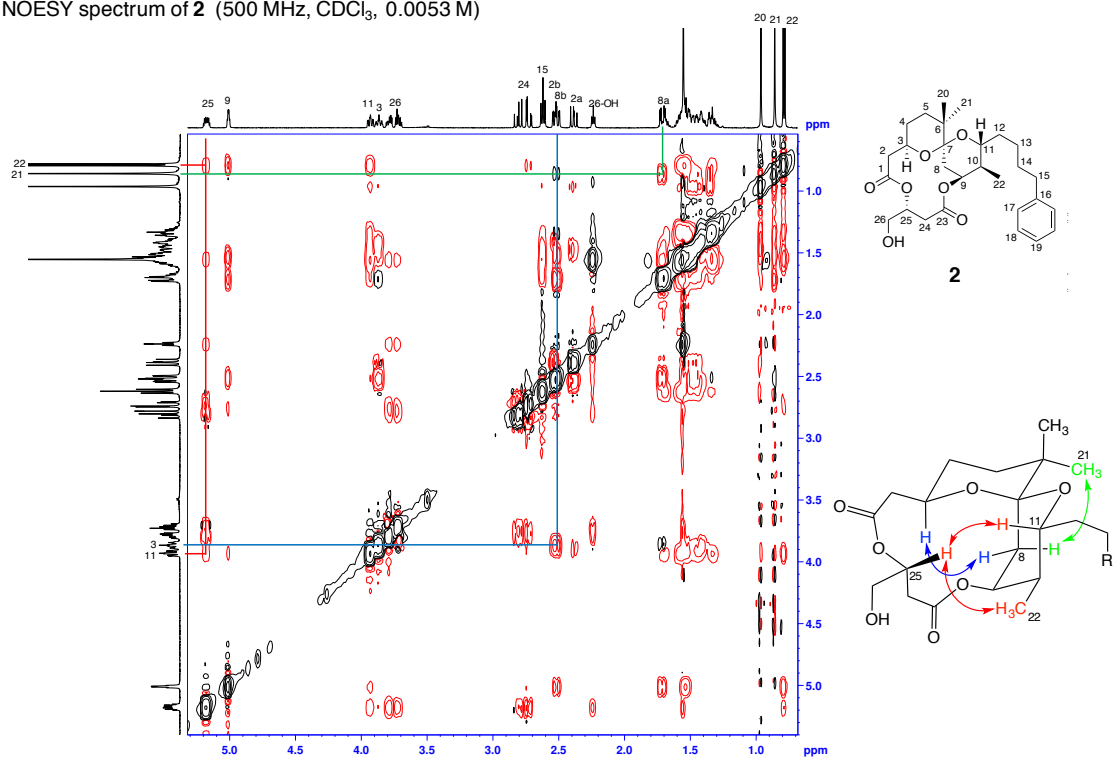
- 7.26, 7.22, 7.17, 7.12, 7.07, 7.02, 6.97, 6.92, 6.87, 6.82, 6.77, 6.72, 6.67, 6.62, 6.57, 6.52, 6.47
- 4.20, 4.15, 4.10, 4.05, 4.00, 3.95, 3.90, 3.85, 3.80, 3.75, 3.70, 3.65, 3.60, 3.55, 3.50, 3.45, 3.40, 3.35, 3.30, 3.25, 3.20, 3.15, 3.10, 3.05, 3.00, 2.95, 2.90, 2.85, 2.80, 2.75, 2.70, 2.65, 2.60, 2.55, 2.50, 2.45, 2.40, 2.35, 2.30, 2.25, 2.20, 2.15, 2.10, 2.05, 2.00, 1.95, 1.90, 1.85, 1.80, 1.75, 1.70, 1.65, 1.60, 1.55, 1.50, 1.45, 1.40, 1.35, 1.30, 1.25, 1.20, 1.15, 1.10, 1.05, 1.00, 0.95, 0.90, 0.85, 0.80, 0.75, 0.70, 0.65, 0.60, 0.55, 0.50, 0.45, 0.40, 0.35, 0.30, 0.25, 0.20, 0.15, 0.10, 0.05, 0.00
- 1.20

II. NOESY spectra of 1–3

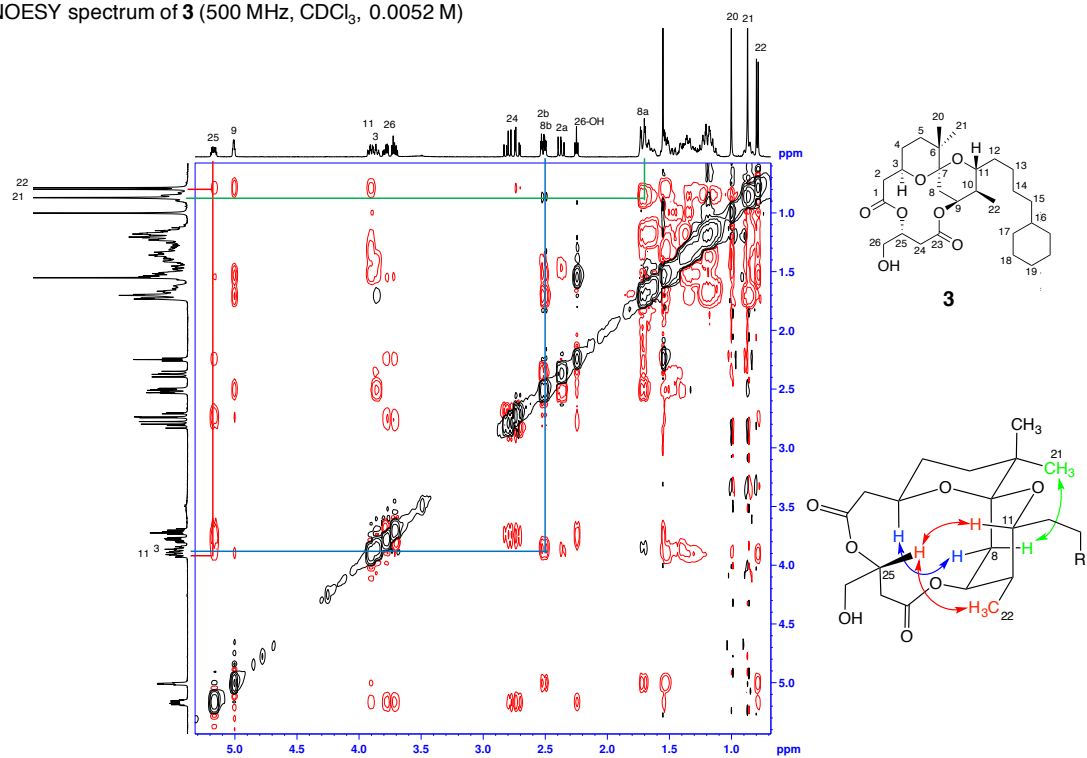
NOESY spectrum of **1** (500 MHz, CDCl_3 , 0.010 M)



NOESY spectrum of **2** (500 MHz, CDCl_3 , 0.0053 M)

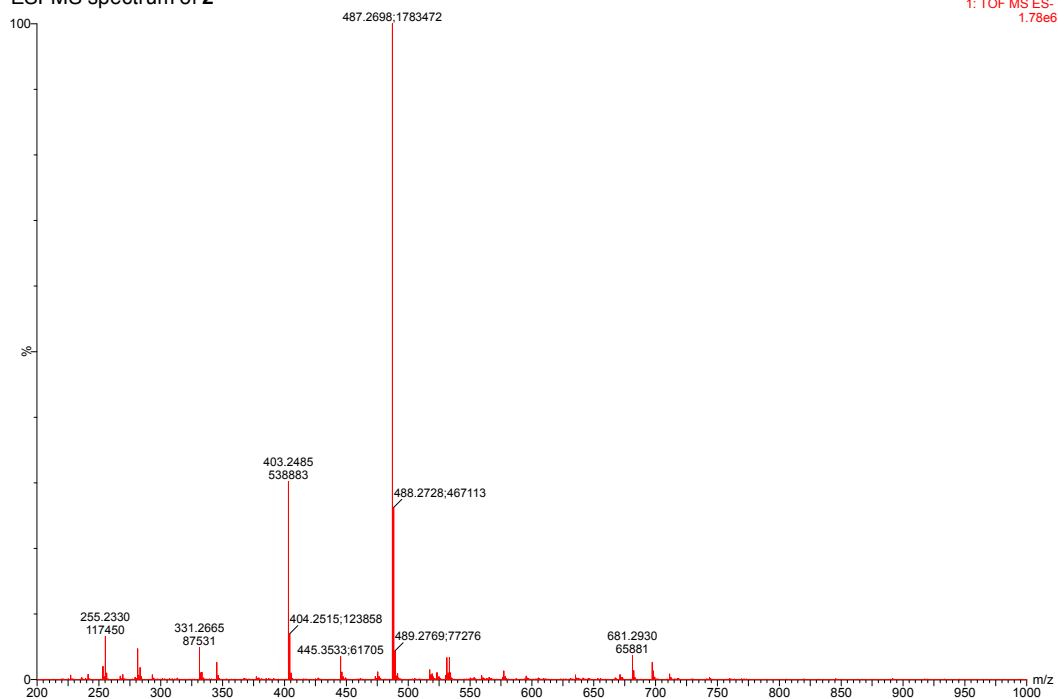


NOESY spectrum of **3** (500 MHz, CDCl₃, 0.0052 M)

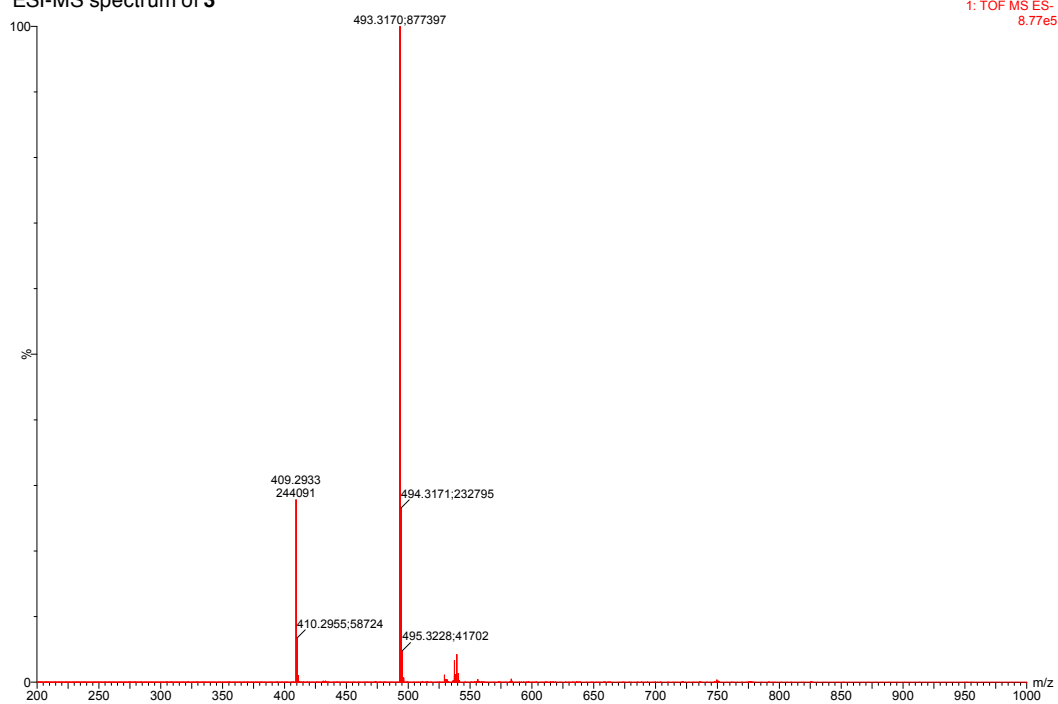


III. MS spectra of **2** and **3**

ESI-MS spectrum of **2**

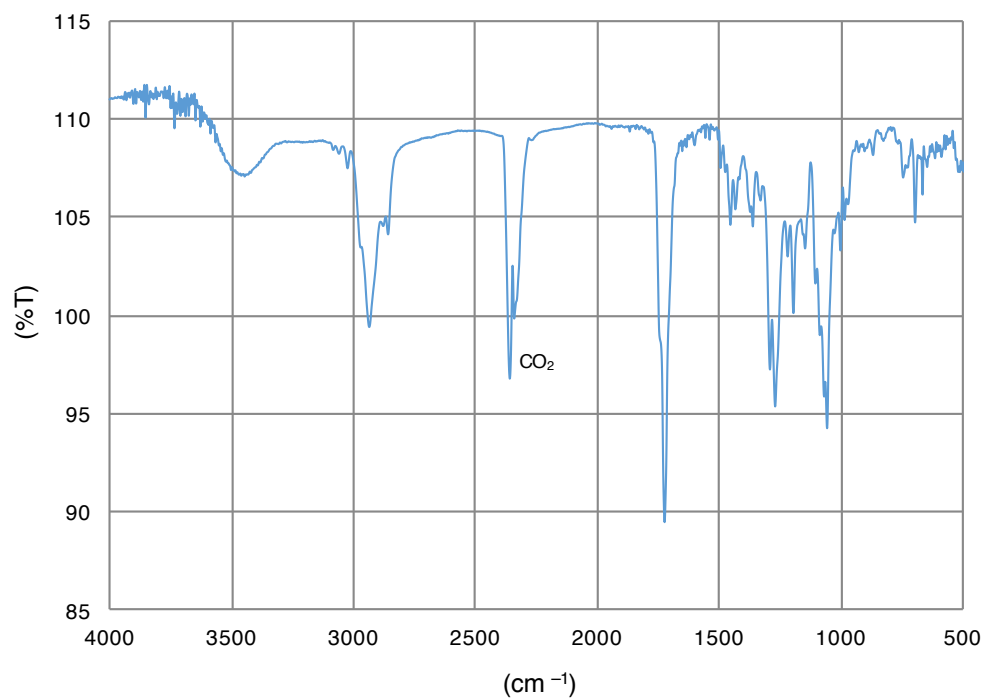


ESI-MS spectrum of **3**

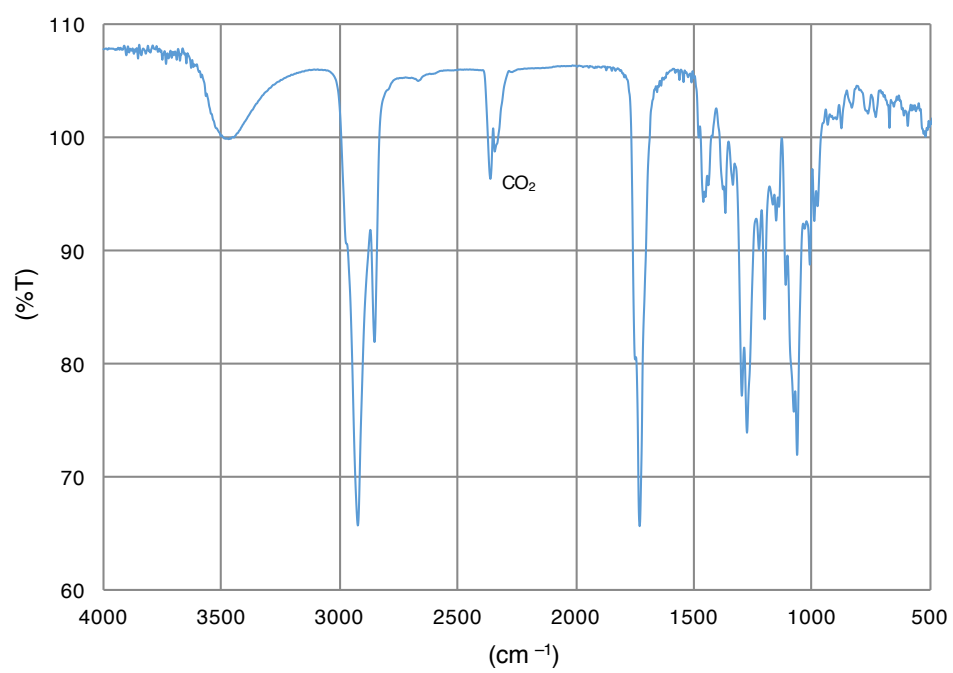


IV. IR spectra of **2** and **3**

IR spectrum of **2**



IR spectrum of **3**



V. Growth inhibitory activities of **2** and **3** towards 39 human cancer cell lines

cancer cell lines		log GI ₅₀ (M)		
		1 ^a	2	3
Breast	HBC-4	−7.48	−7.76	−7.20
	BSY-1	−4.91	−4.88	−4.99
	HBC-5	−4.82	−4.83	−4.90
	MCF-7	−4.84	−4.99	−5.29
	MDA-MB-231	−6.90	−5.63	−5.68
CNS	U251	−4.79	−4.76	−4.80
	SF-268	−4.83	−4.78	−4.86
	SF-295	−4.98	−4.90	−5.20
	SF-539	−4.88	−4.90	−4.91
	SNB-75	−4.92	−4.91	−4.89
	SNB-78	−6.05	−4.81	−4.79
Colon	HCC2998	−6.47	−6.21	−6.08
	KM-12	−4.82	−4.87	−4.99
	HT-29	−4.81	−4.95	−5.05
	HCT-15	−4.87	−4.78	−4.76
	HCT-116	−4.89	−5.02	−5.07
Lung	NCI-H23	−4.87	−4.75	−4.74
	NCI-H226	−6.15	−4.94	−5.02
	NCI-H522	−4.86	−4.88	−4.98
	NCI-H460	−7.07	−7.09	−6.85
	A549	−6.01	−6.12	−5.78
	DMS273	−4.88	−4.93	−5.32
	DMS114	−5.05	−4.91	−4.87
Melanoma	LOX-IMVI	−6.21	−4.76	−4.84
Ovarian	OVCAR-3	−4.88	−4.79	−4.95
	OVCAR-4	−4.77	−4.78	−4.84
	OVCAR-5	−4.92	−4.88	−4.97
	OVCAR-8	−4.75	−4.80	−4.82
	SK-OV-3	−4.88	−4.76	−4.81
Renal	RXF-631L	−4.84	−4.75	−4.84
	ACHN	−4.94	−4.90	−4.97
Stomach	St-4	−6.24	−5.93	−5.89
	MKN1	−4.87	−4.85	−4.91
	MKN-B	−4.80	−4.92	−5.29
	MKN-A	−4.82	−4.93	−4.95
	MKN45	−4.97	−6.51	−6.13
	MKN74	−4.68	−4.85	−4.85
Prostate	DU-145	−4.82	−4.84	−4.85
	PC-3	−4.94	−4.97	−4.95
MG-MID ^b		−5.24	−5.15	−5.18

^a Kikumori, M.; Yanagita, R. C.; Tokuda, H.; Suzuki, N.; Nagai, H.; Suenaga, K.; Irie, K. *J. Med. Chem.* **2012**, 55, 5614-5626.

^b MG-MID: average of the log GI₅₀ values of each 39 human cancer cell line.