Two New Aristolochic Acid Analogues from the Roots of *Aristolochia contorta* with Significant Cytotoxic Activity

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Supporting Information Content:

S1. The HR-ESI–MS spectrum of compound 9.

S2. The UV spectrum of compound 9 (methanol).

S3. The IR spectrum of compound 9.

S4. The ¹H NMR spectrum of compound **9** (DMSO- d_6 , 500 MHz).

S5. The 13 C NMR spectrum of compound 9 (DMSO- d_6 , 125 MHz).

S6. The HSQC spectrum of compound 9 (DMSO-*d*₆, 500 MHz).

S7. The HMBC spectrum of compound 9 (DMSO- d_6 , 500 MHz).

S8. A: tR of compound 9;

B: m/z of compound 9 at the same retention time;

C: TIC of the methanol extract from root of A.contorta by LC-Q-TOF/MS;

D: EIC of m/z 397.03 from the methanol extract from root of A.*contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions;

E: Compound **9** was identified from the methanol extract from root of A. *contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions. As indicated by symbols # and *.

S9.The HR-ESI–MS spectrum of compound 10.

S10.The UV spectrum of compound 10 (methanol).

S11.The ¹H NMR spectrum of compound **10** (DMSO- d_6 , 500 MHz).

S12.The ¹³C NMR spectrum of compound **10** (DMSO-*d*₆, 125 MHz).

S13.The HSQC spectrum of compound **10** (DMSO-*d*₆, 500 MHz).

S14. F: tR of compound 10;

G: m/z of compound 10 at the same retention time;

H: TIC of the methanol extract from root of A.contorta by LC-Q-TOF/MS;

I: EIC of m/z 413.035 from the methanol extract from root of A.*contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions;

J: Compound **10** was identified from the methanol extract from root of A. *contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions. As indicated by symbols & and δ .

S15.¹H NMR (DMSO- d_6 , 500 MHz) and ¹³C NMR (DMSO- d_6 , 125 MHz) spectral data for compounds **1**, **3**, **5**, **6**, and **7**.

S16.¹H NMR (DMSO- d_6 , 500 MHz) and ¹³C NMR (DMSO- d_6 , 125 MHz) spectral data for compounds **2**, **4**, **8**, **11**, and **12**.

S17.Structure of PDB code **4NOG**.

S18.4NOG generated with ligand by SWISS-MODEL software get 45.39% identity with OAT1.

S1. HR-ESI–MS spectrum of compound 9.

HR-ESI(+) -MS spectrum of compound 9.



HR-ESI(-) -MS spectrum of compound 9.







S3. IR spectrum of compound 9.





S4. ¹H NMR spectrum of compound 9 (DMSO-*d*₆, 500 MHz).

S5. ¹³C NMR spectrum of compound 9 (DMSO- d_6 , 125 MHz).



S6. HSQC spectrum of compound 9 (DMSO-*d*₆, 500 MHz).



S7. HMBC spectrum of compound 9 (DMSO- d_6 , 500 MHz).



S8. A: tR of compound 9;

B: m/z of compound 9 at the same retention time;

C: TIC of the methanol extract from root of A.*contorta* by LC-Q-TOF/MS;

D: EIC of m/z 397.03 from the methanol extract from root of A.*contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions;

E: Compound **9** was identified from the methanol extract from root of A. *contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions. As indicated by symbols # and *.





S9. HR-ESI–MS spectrum of compound 10.

HR-ESI(+)–MS







S10. UV spectrum of 10 (methanol).



S12. The ¹³C NMR spectrum of compound **10** (DMSO- d_6 , 125 MHz).



-57.1



S13. HSQC spectrum of compound 10 (DMSO-d₆, 500 MHz).



S14. F: tR of compound 10;

G: m/z of compound 10 at the same retention time;

H: TIC of the methanol extract from root of A. *contorta* by LC-Q-TOF/MS;

I: EIC of m/z 413.035 from the methanol extract from root of A.*contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions;

J: Compound **10** was identified from the methanol extract from root of A.*contorta* by LC-Q-TOF/MS under the same liquid chromatography and mass spectrometry conditions. As indicated by symbols & and δ .







S15. ¹H NMR (DMSO- d_6 , 500 MHz) and ¹³C NMR (DMSO- d_6 , 125 MHz) spectral data for compounds **1**, **3**, **5**, **6**, and **7** (δ in ppm, J in Hz).

	1		3		5		6		7	
С	$\delta_{\rm H}$	$\delta_{\rm C}$	$\delta_{\rm H}$	$\delta_{\rm C}$	δН	δC	δΗ	$\delta_{\rm C}$	$\delta_{\rm H}$	δ_{C}
1 2		128.		124.		124.		120.		121.
		5		3		1		4		5
2	7.0	111.	7.0	112.		110.		112.		111.
2	/.8, s	8	/.8, s	2	/./, s	8	/./4, s	4	/./5, s	7
2		146		146		145.		145.		145.
3		146		146		8		8		4
		146.		146.		146.		146.		145.
4		4		7		3		2		8
4.		117.		116.		117.		117.		117.
4a		2		8		8		1		3
4b		128.		129.		132.		132.		132.

		8		9		7		1		4
5	9.10, d	126.	8.65,	118.	9 70 4(0.05)	121.	۹ <u>۵</u> ۵ -	103.	0 40 J ())	111.
3	(8.4)	5	d(8.5)	4	8.70, d(9.03)	9	8.09, 8	1	8.48, d (2.2)	1
6	7.83,	130.	7.85,	131.	7.50 1(0.05)	122.	10.86, br,s(-	161.		159.
0	t(7.3)	4	t(8.2)	6	7.30, d(9.03)	8	OH)	7		8
7	7.92,	128.	7.37,	108.	10.44, br,s(-	148.	6.04	104.	7.29, dd (8.7,	116.
/	t(7.6)	7	d(8.1)	9	OH)	4	0.84, \$	2	2.2)	6
Q	8.27,	130.		156.		148.		158.	9 00 1(9 7)	130.
0	d(7.9)	4		3		9		5	8.09, d(8.7)	9
Q _		129.		118.		122.		112.		121.
8a		6		8		8		6		5
0	050 -	125.	050 -	119.	8 40 (111 a)	121.	9.46 -	120.	Q 4Q -	126.
9	8.38, S	8	8.38, S	4	8.40, (1H, S)	5	8.40, S	5	8.48, S	3
10		146		146		142.		143.		143.
10		140		140		9		2		5
10		116.		117.		115.		118.		118.
10a		6		3		5		2		7
-OCH			4.07	5()	2.00	(0.0	4.01	566		
3			4.07, s	56.5	3.98, s	60.9	4.01, s	36.6		
-CH2	(51)	102.	(50	102.		102.	C AC	100.	C 40	102.
О-	0.31, S	9	6.30, s	9	0.43, s	6	0.40, s	2	0.49, s	7

S16.¹H NMR (DMSO- d_6 , 500 MHz) and ¹³C NMR (DMSO- d_6 , 125 MHz) spectral data for compounds **2**, **4**, **8**, **11**, and **12** (δ in ppm, J in Hz).

	•				` ••		,					
	2		4		8		11		12			
С	$\delta_{\rm H}$	δ_{C}	$\delta_{\rm H}$	$\delta_{\rm C}$								
1		119.		122.		124.		118.		117.		
1		3		2		1		1		3		
2	7.66,s	105.	7 63 5	113.	7778	106.	7.72,s	106	774 s	105.		
2		8	7.05,8	4	7.77,8	5		100	7.74,5	6		
2		148.		152.		149.		148.		148.		
3		9		3		4		8		7		
4		147.		148.		148.		147.		147.		
4		2	10.77,8	8		1 8	8		5			
49		110	120.		111		111.			111.		
та		110		3	111			2	3			

4b		124.		126.		124.		100		125.				
4b		9		7		8		126		2				
5	<u>8 1 d(6 2)</u>	118.	0.11 d(7.7)	126	9 21 d(9 05)	118.	8014(25)	110	<u> 00 <i>d</i>(0 1)</u>	117.				
3	8.1,d(0.2)	8	9.11,d(7.7)	120	8.21,d(8.05)	2	8.01,d,(2.3)	118	8.08, <i>a</i> (8.1)	6				
6	7.52,	125	7.52-7.58,	125.	7.60,t(8.05,8.0	126.		156.	7.43,t(7.9,7.	126.				
0	t(6.6)	125	m	2	5)	9		2	8)	4				
7	7.21,d(6.	108.	7.52-7.58,	127.	7 26 d(8 05)	111.	7.13,dd(2.5,6.	118.	7.12 d(7.8)	112.				
,	6)	4	m	2	7.20,0(0.05)	6	1)	2	7.12, u(7.0)	5				
8		155.	7.93,d(8.5	128.		155.	7 87 d(8 7)	130.		154				
0		3	5)	9		9	7.07, u (0.7)	9		154				
89		124		134.		119.		126.		122.				
ou		121		8		2		9		8				
9	7 36 s	s 97.9	97 9	97.9	979	979	7 09 s	103.	7.66 s	109.	7.35.s	107.	7.64.s	101.
	7.36,s	,,,,	7.09,5	8	7.00,5	1	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	9	7.01,5	1				
10		132.		135.		134.		131.		132.				
10		8		3		1		9		7				
10a		125.		121.		125.		125.		124.				
100		8		7		4		1		5				
CONR	10 77 s	168.		168.		166.		166.		166.				
cont	10.77,3	2		4		6		5		2				
-OCH2	6 48 s	103.			651 s	103.	6 52 s	103.	6 50 s	103.				
О-	0.40,5	3			0.51,5	9	0.52,5	7	0.50,5	3				
-OCH3	4.00,s	55.9	4.02,s	59.4 3	4.02,s	56.5								
1"					5.35,d(9.3)	82.8	5.34,d(9.5)	82.3	5.35,d(9.3)	81.8				
2"						70.9		70.6		69.9				
3"						77.9		78		77.5				
4"						72.8		70.3		70.4				
5"						80.6		80.6		80.2				
6"						61.8		61.8		61.3				

S17. Structure of PDB code **4NOG**.



S18. **4NOG** generated with ligand by SWISS-MODEL software get 45.39% identity with OAT1.

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• 🗆 •	5eav.1.8	8 Ornithine aminotransferase, mitochondrial, putative Uniganded structure of the omithine aminotransferase from Totoplasma gondil		0.77	0.78	48.71	X-ray, 1.8Å	homo-dimer 🗸	None						
* ¥ /	fnog.17	A Putative ornithine aminotransferase, mitochondrial Crystal structure of a putative ornithine aminotransferase from Toxoplasma gondil ME49 h complex with pyrodoxal-S-phosphate		0.74	0.75	45.39	X-ray, 1.2Å	homo-dimer 🗸	2 x PLP ⁽⁰ , 1 x BTB ⁽⁰						
¥ 🗆	őeav.1.8	8 Ornithine aminotransferase, mitochondrial, putative Uniganded structure of the omithine aminotransferase from Toxoplasma gondi		0.72	0.76	50.37	X-ray, 1.6Å	homo-dimer 🗸	None						
¥ 🗆	4nog.1J	Putative ornithine aminotransferase, mitochondrial Crystal studene of a putative ornithine aminotransferase from Toxoplasma gondil ME49 in complex with pyrodoxal-8-phosphate		0.72	0.74	50.37	X-ray, 1.2Å	homo-dimer 🗸	2 x PLP ^{ID} , 1 x BTB ^{ID}	(000	2		
× 🗆	2can 1.	A ORNITHINE AMINOTRANSFERASE HUMAN ORNITHINE AMINOTRANSFERASE COMPLEXED WITH L-CANALINE		0.72	0.70	52.94	X-ray, 2.3Å	homo-dimer 🗸	2 x CAN-PLP			(G	2	
¥ 🗆	2byl.1.4	ORNITHINE AMINOTRANSFERASE Structure of omithine aminotransferase triple mutant Y851 Y55A G320P		0.73	0.87	52.57	X-ray, 2.1Å	homo-dimer 🗸	2 x PLP ²				45	9	
• 🗆	20/j.1.A	A ORNITHINE AMINOTRANSFERASE Ombine antinotransferase nutant Y85I		0.73	0.66	49.82	X-ray, 3.0Å	homo-dimer 🖌	2 x PLP ²	0	7	23	4	2	
× 🗆	1z7d.1.J	A omithine aminotransferase Omithine aminotransferase PY00104 from Plasmodium Yoelli		0.68	0.70	46.38	X-ray, 2.1Å	homo-dimer 🗸	None		T	Sa	-		
• D	6bx7.1.J	A Omithine aminotransferase, mitochondrial Crystal structure of human R180T variant of ORNITHINE AMINOTRANSPERASE at 1.8 Angelosm		0.72	0.67	49.45	X-ray, 1.8Å	homo-dimer ✓	2 x PLP ⁽⁾		X	Ser Contraction	R	2	
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