## Supplementary Information

# The convenient aqueous synthesis and biological evaluation of ortho-(3,4,5-trimethoxybenzoyl)acetanilides as novel anti-cancer agents

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Table of Contents	
1. Stability test of compound 13 and Combretastatin A-4	S2
2. The results of stability test of compound 13	S2
3. The results of stability test of Combretastatin A-4	• S4
4. Copies of NMR spectra	S7
5. HPLC chromatograms of compounds 1-11, 13-17	-S23

**S**1

#### Stability test of compound 13 and Combretastatin A-4 (CA-4)

As the cis double bond of CA-4 could isomerizes to the more stable trans-form during storage, which result a decrease of antitumor activity. The stability assays of compound 13 and CA-4 were performed. Compound 13 and CA-4 were dissolved in CH<sub>3</sub>CN to a concentration of 3mg/ml. The solution was positioned at room temperature and the purity was tested at different time. The purity of the samples was determined by HPLC, conducted on a Shimadzu LC-20AT series system, TC-C18 column ( $4.6 \times 250$  mm, 5 µm), eluted with CH<sub>3</sub>CN/ water system, at a flow rate of 1 mL/min. The results showed that the purity of compound 13 did not change up to 5 days, which suggested compound 13 exhibited good stability. However, the results of CA-4 indicated that three impurities appeared in 24h, which are presumed as CA-4 decompose or isomerize products.

#### The results of stability test of compound 13.

T=0h, CH<sub>3</sub>CN/water = 50:50,  $t_{maior}$  =6.665.



T=24h, CH<sub>3</sub>CN/water = 50:50,  $t_{major}$  =6.670



T=120h, CH<sub>3</sub>CN/water = 50:50,  $t_{major}$  =6.656



The results of stability test of Combretastatin A-4.





min



T=5h, CH<sub>3</sub>CN/water = 60:40, t<sub>major</sub> =6.898



T=10h, CH<sub>3</sub>CN/water = 60:40, t<sub>major</sub> = 6.884



T=10h, CH<sub>3</sub>CN/water = 60:40, t<sub>major</sub> = 6.885



1	5.281	BB	0.1085	16.72594	2.31046	0.5757
2	6.885	BV	0.1165	2710.57178	357.31735	93.3013
3	7.129	VB	0.1207	137.56677	16.95029	4.7352
4	12.611	BB	0.2224	40.31554	2.82668	1.3877

Copies of NMR spectra.

n ann a dha a bha China Ann Ann an Ann Ann an A

170 160

210 200 190 180



S7

90 80 70 60 50 40 30 20 10 0 -10

150 140 130 120 110 100 f1 (ppm) -0

-50



**S**8







S11





S12

-0

--100





S14



S15



S16



S17













### HPLC chromatograms of compounds 1-11, 13-17.





2





0.2469 2624.88452



2

10.060 BB



157.15117

98.1550

# .	[min]		[min]	[mAU*s]	[mAU]	8
 1	4 231	BR	0 1217	8 89093	1 06116	0 2288
2	5.133	BB	0.1220	3856.43652	478.66516	99.2555
3	5.648	BB	0.1559	20.03383	1.85603	0.5156

 $CH_3CN/water = 60:40, t_{major} = 11.184.$ 



5



6

 $CH_3CN/water = 60:40, t_{major} = 7.073.$ 



 $CH_3CN/water = 60:40, t_{major} = 6.926.$ 



8



 $CH_3CN/water = 60:40, t_{major} = 6.136.$ 





 $CH_3CN/water = 60:40, t_{major} = 10.089.$ 



#	[min]			[min]	[mAU*s]	[mAU]	ક
1	8.035	MM	Т	0.7497	9.06673	2.01556e-1	0.3627
2	10.089	BB		0.2303	2490.43848	164.81633	99.6373

11



0.2363 1.44076e4

13

3

 $CH_3CN/water = 50:50, t_{major} = 6.384.$ 

9.962 BB

932.24786

99.0498



1	3.719	BB	0.2259	147.76073	9.17457	2.1780
2	6.384	BB	0.3050	6636.34961	298.88147	97.8220



 $CH_3CN/water = 60:40, t_{major} = 6.909.$ 







 $CH_3CN/water = 60:40, t_{major} = 6.355.$ 





 $CH_3CN$ /water = 60:40,  $t_{major}$  =10.059.

