

Supporting Information

Novel tricyclic indeno[2, 1-*d*]pyrimidines with dual antiangiogenic and cytotoxic activities as potent antitumor agents

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Elemental Analysis
High-Resolution Mass spectra (HRMS) (EI)
UPLC/UV/ELSD/MS method and data

Elemental analysis

#	Formula	Calcd (%)						Found %					
		C	H	N	F	Cl	Br	C	H	N	F	Cl	Br
5	C ₁₇ H ₁₃ FN ₄ ·0.4H ₂ O	68.17	4.64	18.71	6.34			68.36	4.47	18.42	6.40		
7	C ₁₇ H ₁₃ ClN ₄	66.13	4.24	18.15	11.48			66.15	4.26	18.07		11.56	
9	C ₁₇ H ₁₃ BrN ₄ ·0.6CH ₃ OH	56.76	4.17	15.04			21.45	56.95	3.93	15.16			21.21
10	C ₁₈ H ₁₃ F ₃ N ₄	63.16	3.83	16.37	16.65			62.78	3.81	16.21	16.51		
13	C ₁₇ H ₁₂ ClFN ₄	62.49	3.70	17.15	5.81	10.85		62.24	3.76	16.98	5.65	10.66	
16	C ₁₁ H ₉ N ₃ O·0.1H ₂ O	65.73	4.61	20.94				65.76	4.50	21.13			

High-Resolution mass spectra (HRMS) (EI)

#	Formula	Calcd mass	Found mass
1	C ₁₇ H ₁₄ N ₄	274.1218	274.1218
2	C ₂₀ H ₂₁ N ₄	317.1766	317.1751
3	C ₂₀ H ₂₀ N ₄	316.1688	316.1704
4	C ₁₇ H ₁₃ FN ₄	292.1124	292.1123
6	C ₁₇ H ₁₃ ClN ₄	308.0829	308.0838
8	C ₁₇ H ₁₄ BrN ₄	353.0402	353.0387
11	C ₁₈ H ₁₆ N ₄ O	304.1324	304.1390
12	C ₁₇ H ₁₂ ClFN ₄	326.0735	326.0744
17	C ₁₇ H ₁₃ N ₄ O ₅ S	385.0607	385.0584

UPLC/UV/ELSD/MS System. Optical LC-MS grade acetonitrile was purchased from Fisher (), and formic acid was obtained from Sigma-Aldrich (St. Louis, MO). Milli-Q water as an ultrapure laboratory grade water was used in aqueous mobile phase.

Chromatographic separation was performed on an Acquity UPLC BEH C18 1.7 μm , 2.1 x 50 mm column (Waters Corporation, Milford, MA) using an Acquity ultra performance liquid chromatography system. Data were acquired using Masslynx v. 4.1 and analyzed using the Openlynx software suite. This was coupled to an Acquity photodiode array detector, which acquired UV data from 210-400 nm. The flow was then split, with half directed to an evaporative light scattering detector (ELSD) and half to an SQ mass spectrometer. The total flow rate was 1.0 mL/min. The sample injection volume was 2 μL . The UPLC column was maintained at 55 $^{\circ}\text{C}$ and the gradient program started at 90% A (0.1% formic acid in MilliQ H₂O), changed to 70% A over 0.2 min, to 95 % B (0.1% formic acid in Acetonitrile) over 1.4 minutes, held for 0.35 minutes, then to 90% A over 0.05 minutes. The mass spectrometer was operated in positive-ion mode with electrospray ionization. The conditions were as follows: capillary voltage 3.4 kV, cone voltage 30 V, source temperature 130 $^{\circ}\text{C}$, desolvation temperature 350 $^{\circ}\text{C}$, desolvation gas 650 L/hr, cone gas 46 L/hr. A full scan range from $m/z = 100-1000$ in 0.2 s was used to acquire MS data. The ELSD-drift tube temperature was set at 50 $^{\circ}\text{C}$.

All compounds' average UV and ELSD purity is more than 95%.¹

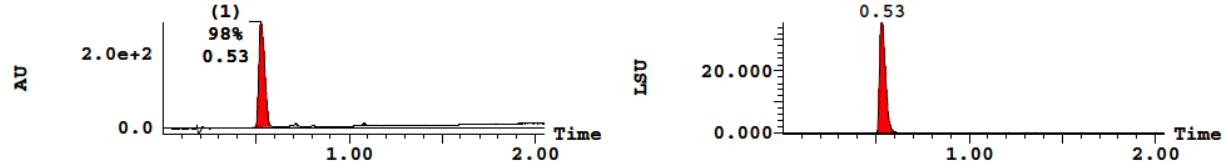
1. Lemoff, A.; Yan, B. Dual Detection Approach to a More Accurate Measure of Relative Purity in High-Throughput Characterization of Compound Collections. *J. Comb. Chem.* **2008**, *10*, 746-751.

Figure 1: Compound 1 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 6 Vial 2:H,4 ID File YZHAO_070711_04 Date 07-Jul-2011 Time 14:07:31 Description

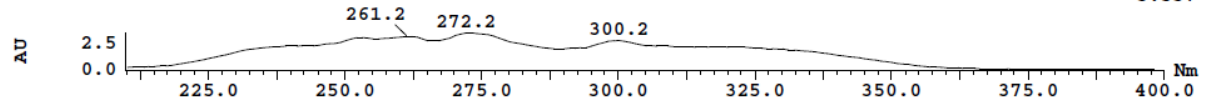
2: UV Detector: TIC (1) ELSD Signal (1) 35.510
 Range: 2.954e+2 100% Range: 35.547



Peak ID	Compound	Time	Mass Found
1		0.53	

1:(Time: 0.53) Combine (573)

2:UV Detector
3.537 AU



Peak ID	Compound	Time	Mass Found
1		0.53	

1:MS ES+
8.8e+007

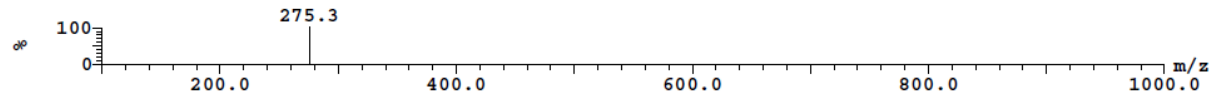
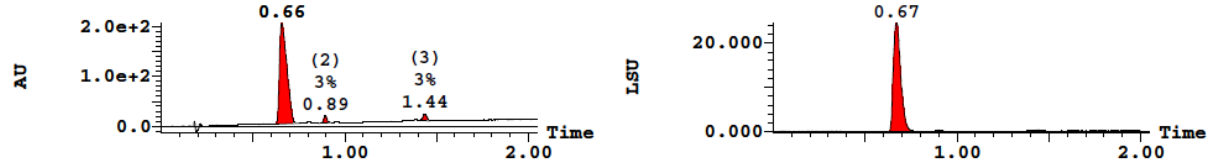


Figure 2: Compound 2 HPLC/MS/ELSD analysis data

Sample Report:

Sample 3 Vial 2:H,1 ID File YZHAO_070711_01_2 Date 07-Jul-2011 Time 14:27:06 Description

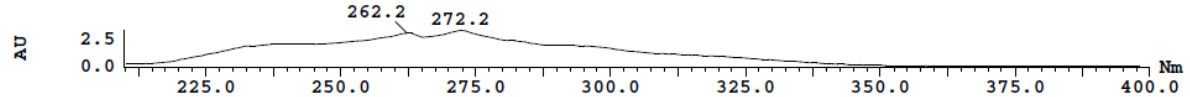
2: UV Detector: TIC (1) ELSD Signal (1) 24.538
 Range: 2.177e+2 100% Range: 24.599



Peak ID	Compound	Time	Mass Found
1		0.66	

1:(Time: 0.66) Combine (730)

2:UV Detector
3.361 AU



Peak ID	Compound	Time	Mass Found
1		0.66	

1:MS ES+
1.1e+008

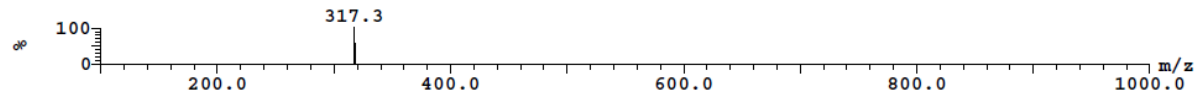


Figure 3: Compound 3 HPLC/MS/ELSD analysis data

Sample 4 Vial 2:H,2 ID File YZHAO_070711_02 Date 07-Jul-2011 Time 14:01:58 Description

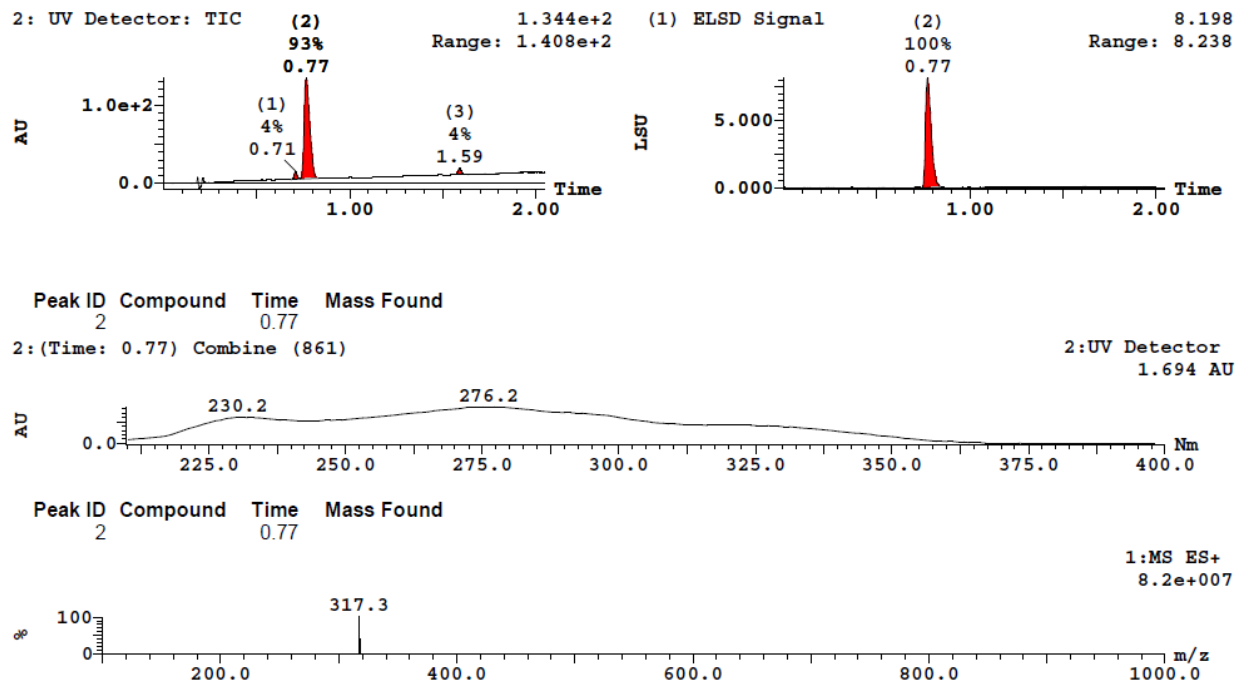


Figure 4: Compound 4 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 10 Vial 2:H,12 ID File YZHAO_070711_08_1 Date 07-Jul-2011 Time 14:44:44 Description

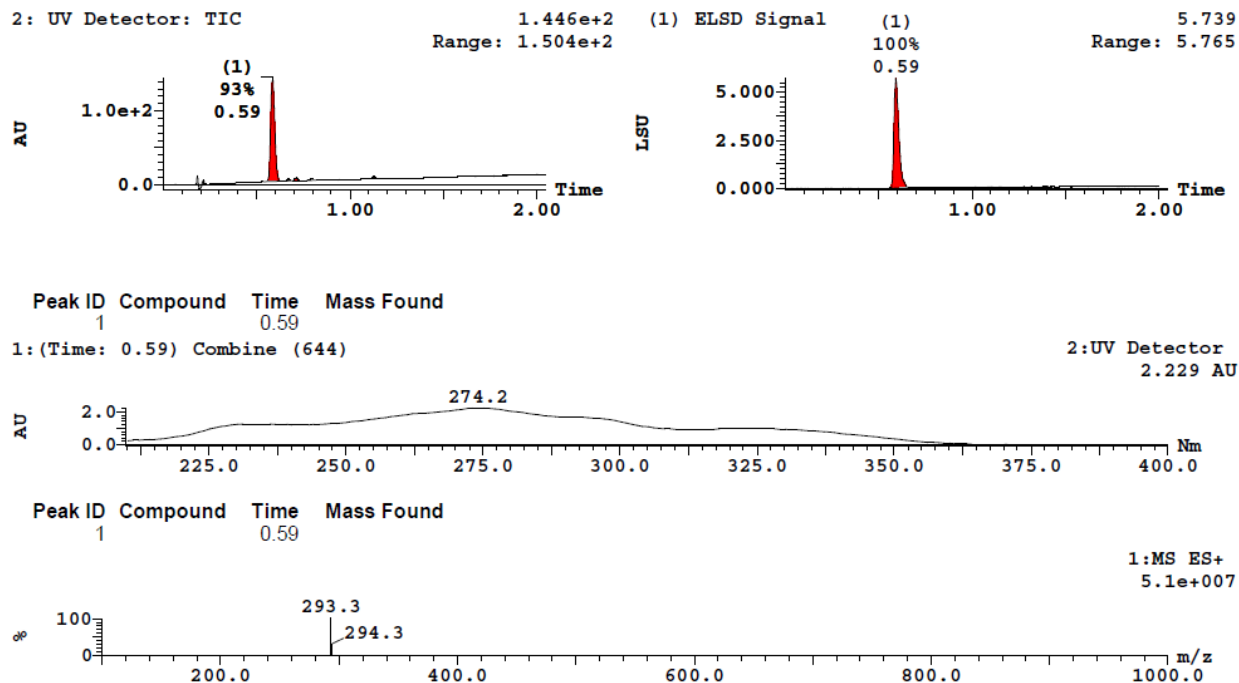
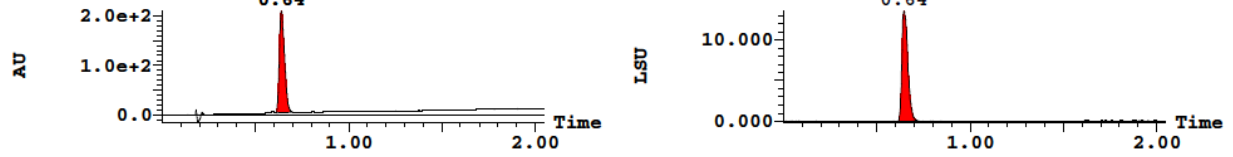


Figure 5: Compound 6 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 9 Vial 2:H,7 ID File YZHAO_070711_07 Date 07-Jul-2011 Time 14:15:49 Description

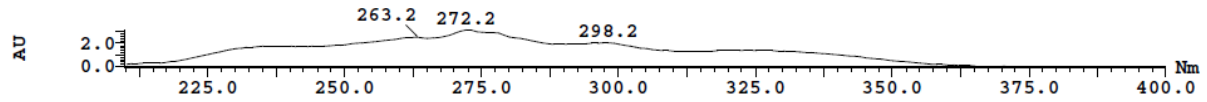
2: UV Detector: TIC (1) 2.096e+2 (1) ELSD Signal (1) 13.585
 Range: 2.224e+2 Range: 13.615



Peak ID	Compound	Time	Mass Found
1		0.64	

1: (Time: 0.64) Combine (708)

2:UV Detector
3.152 AU



Peak ID	Compound	Time	Mass Found
1		0.64	

1:MS ES+
6.9e+007

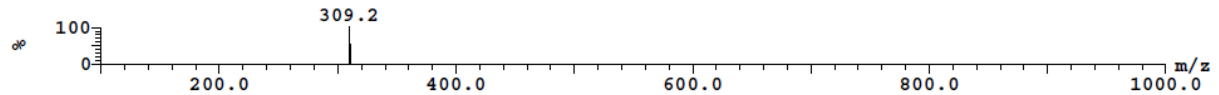
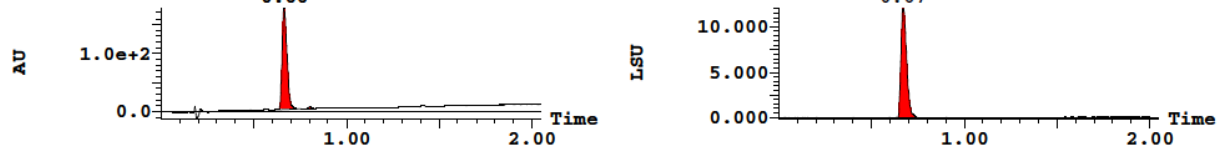


Figure 6: Compound 8 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 5 Vial 2:H,3 ID File YZHAO_070711_03 Date 07-Jul-2011 Time 14:04:45 Description

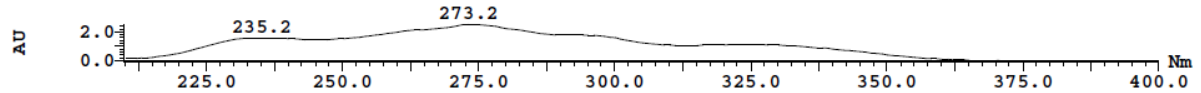
2: UV Detector: TIC (1) 1.777e+2 (1) ELSD Signal (1) 12.052
 Range: 1.884e+2 Range: 12.089



Peak ID	Compound	Time	Mass Found
1		0.66	

1: (Time: 0.66) Combine (737)

2:UV Detector
2.532 AU



Peak ID	Compound	Time	Mass Found
1		0.66	

1:MS ES+
5.2e+007

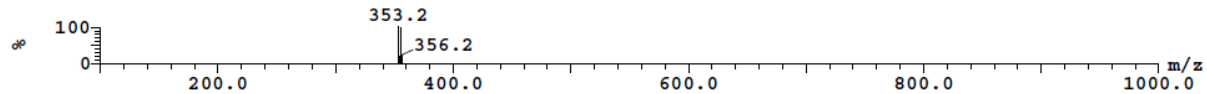
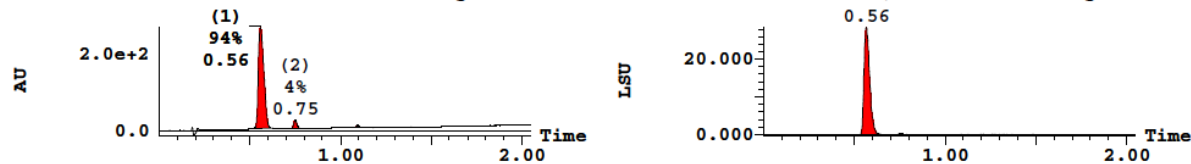


Figure 7: Compound 11 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 7 Vial 2:H,5 ID File YZHAO_070711_05 Date 07-Jul-2011 Time 14:10:17 Description

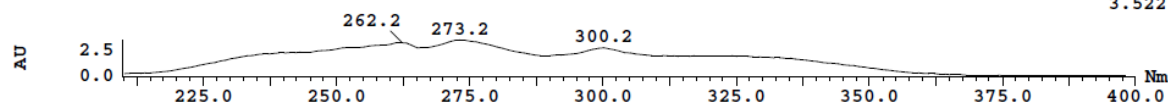
2: UV Detector: TIC (1) 2.711e+2 (1) ELSD Signal (1) 28.437
 Range: 2.825e+2 Range: 28.473



Peak ID	Compound	Time	Mass Found
1		0.56	

1: (Time: 0.56) Combine (612)

2: UV Detector
3.522 AU



Peak ID	Compound	Time	Mass Found
1		0.56	

1: MS ES+
8.6e+007

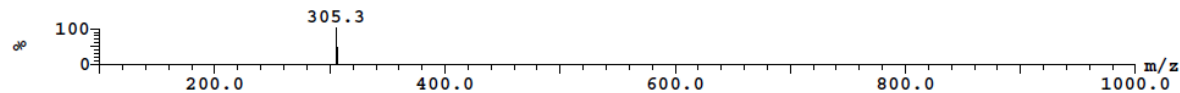
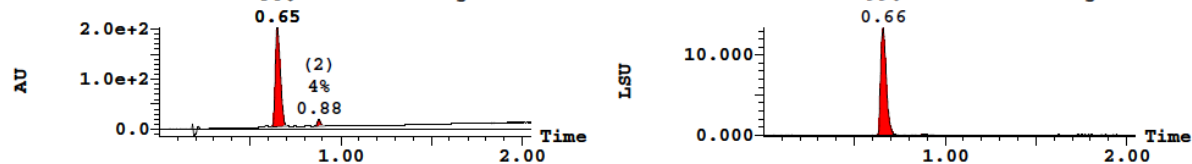


Figure 8: Compound 12 HPLC/MS/ELSD analysis data

Sample Report (continued):

Sample 8 Vial 2:H,6 ID File YZHAO_070711_06 Date 07-Jul-2011 Time 14:13:02 Description

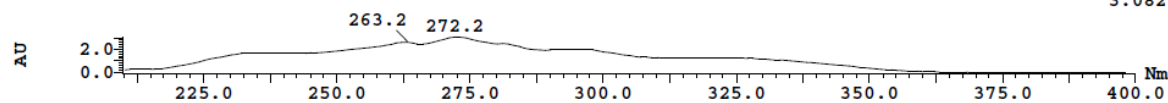
2: UV Detector: TIC (1) 2.026e+2 (1) ELSD Signal (1) 13.438
 Range: 2.152e+2 Range: 13.482



Peak ID	Compound	Time	Mass Found
1		0.65	

1: (Time: 0.65) Combine (721)

2: UV Detector
3.082 AU



Peak ID	Compound	Time	Mass Found
1		0.65	

1: MS ES+
7.2e+007

