

Supporting Information for

Azidothymidine (AZT) “clicked” into 1,2,3-Triazoles: First Report on Carbonic Anhydrase-Telomerase Dual Hybrid Inhibitors

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Table S1. Summary of Data Collection and Atomic Model Refinement Statistics

	HCAII + 1b	HCAII + 3b
PDB ID	6YPW	6WKA
Wavelength (Å)	1.00000	1.00000
Space Group	P2 ₁	P2 ₁
Unit cell (a, b, c, α , β , γ) (Å, °)	42.387, 41.358, 72.075, 90.000, 104.385, 90.000	42.2, 41.5, 72.0, 90.0, 104.4, 90.0
Limiting resolution (Å)	41.36-1.10 (1.11-1.10)	41.5-1.34 (1.36-1.34)
Unique reflections	88794 (2400)	49061
Rmerge (%)	4.8 (43.7)	7.8 (47.2)
Rmeas (%)	5.5 (45.9)	-
Rpim (%)	3.1 (31.5)	3.1 (20.8)
Redundancy	6.3 (4.6)	7.1 (5.7)
Completeness overall (%)	90.7 (49.3)	95.0 (74.6)
$\langle I/\sigma(I) \rangle$	19.5 (3.1)	14.3 (2.9)
CC (1/2)	0.999 (0.831)	0.999 (0.848)
Refinement statistics		
Resolution range (Å)	41.092-1.1	39.9-1.34
Unique reflections, working/free	84333/81550	1660/1270
Rfactor (%)	11.43	15.77
Rfree(%)	13.20	18.32
r.m.s.d. bonds(Å)	0.0123	0.010
r.m.s.d. angles (°)	1.8022	1.636
Ramachandran statistics (%)		
Most favored	97.7	96.9
additionally allowed	2.3	3.1
outlier regions	0.0	0.0
Average B factor (Å²)		
All atoms	12.279	11.0
inhibitors	15.837	21.8
solvent	25.095	25.4

HPLC-DAD method for purity analysis

The employed chromatographic parameters to check the purity of studied compounds were reported as follows:

- column, Luna PFP length = 50 mm, internal diameter= 2 mm; particle size = 3 μm purchased from Phenomenex (Bologna, Italy);
- the eluents used were 5 mM ammonium formate in water solution (solvent A) and 10 mM ammonium formate in methanol (solvent B);
- flow rate and the injection volume were 0.35 mL min⁻¹ and 5 μL , respectively.

The elution gradient is shown in **Table S2**.

Table S2: Elution gradient of mobile phase used for LC-DAD analysis

Time (min)	A (%)
0.00	90
8.00	10
14.00	10
14.01	90
20.00	90

HPLC traces

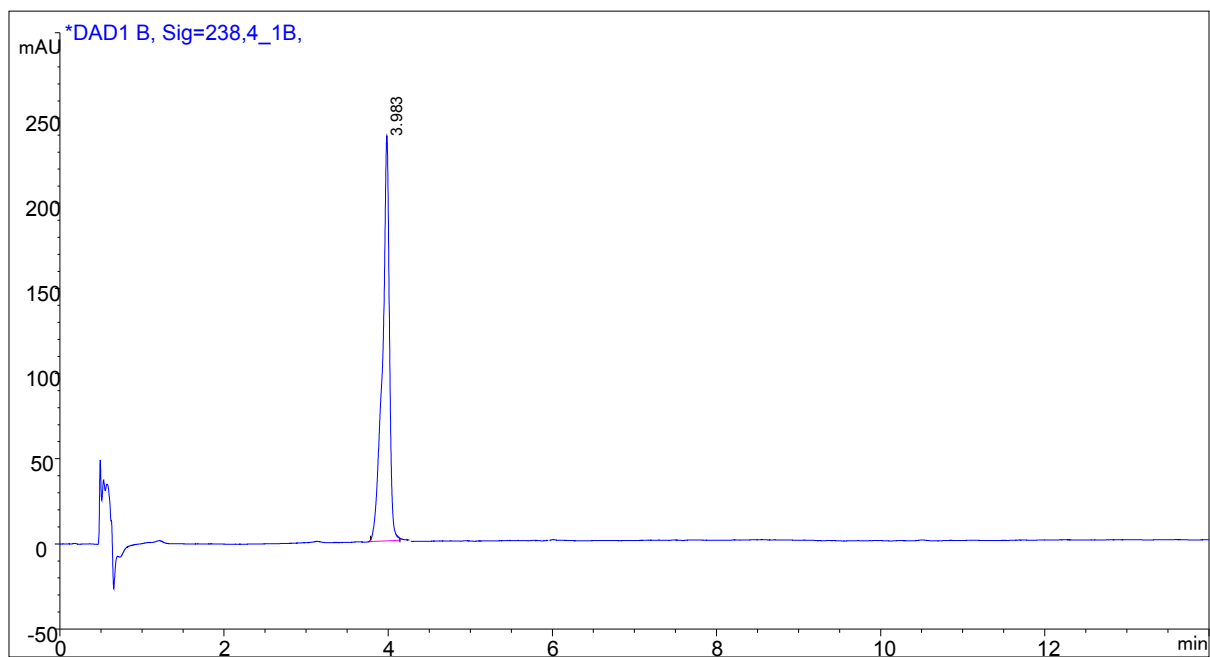


Figure S1. Chromatographic profile of **1b** monitored at $\lambda=238$ nm.

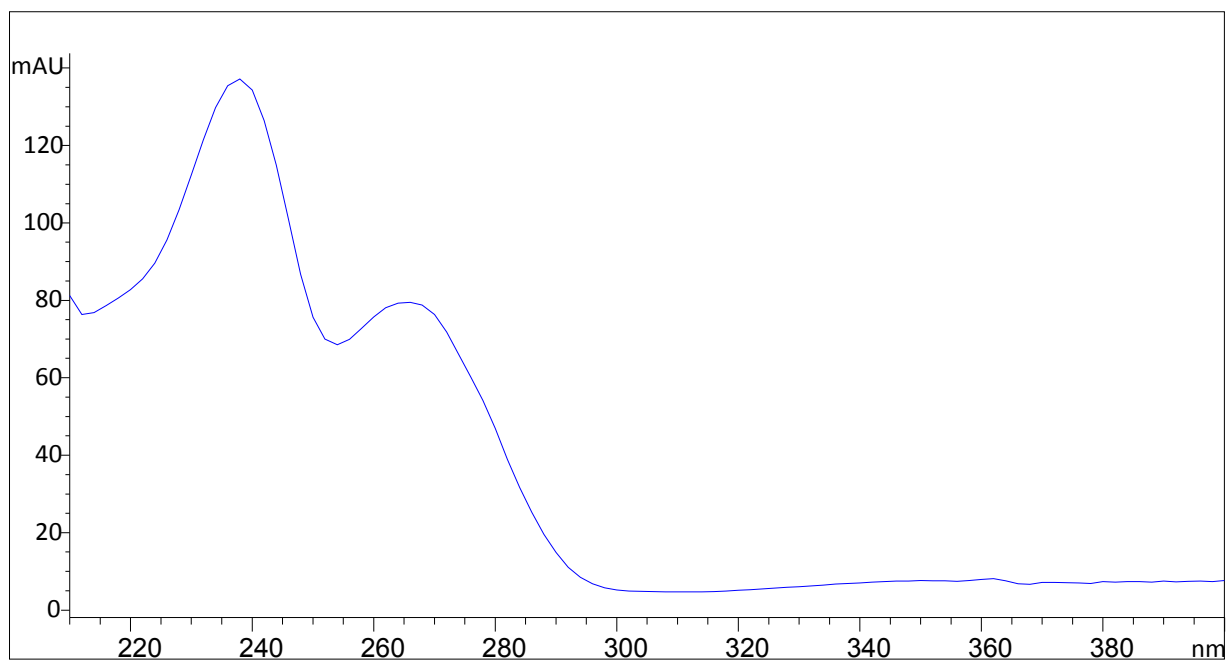


Figure S2. UV spectrum of the compound **1b**.

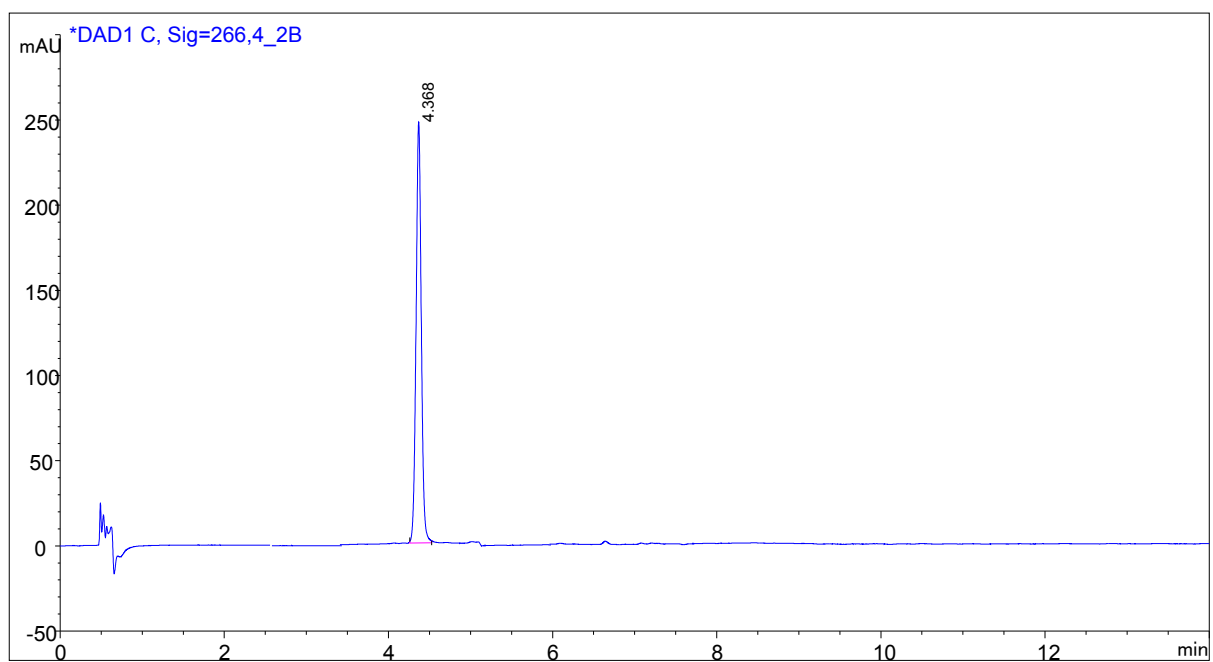


Figure S3. Chromatographic profile of **2b** monitored at $\lambda=266$ nm.

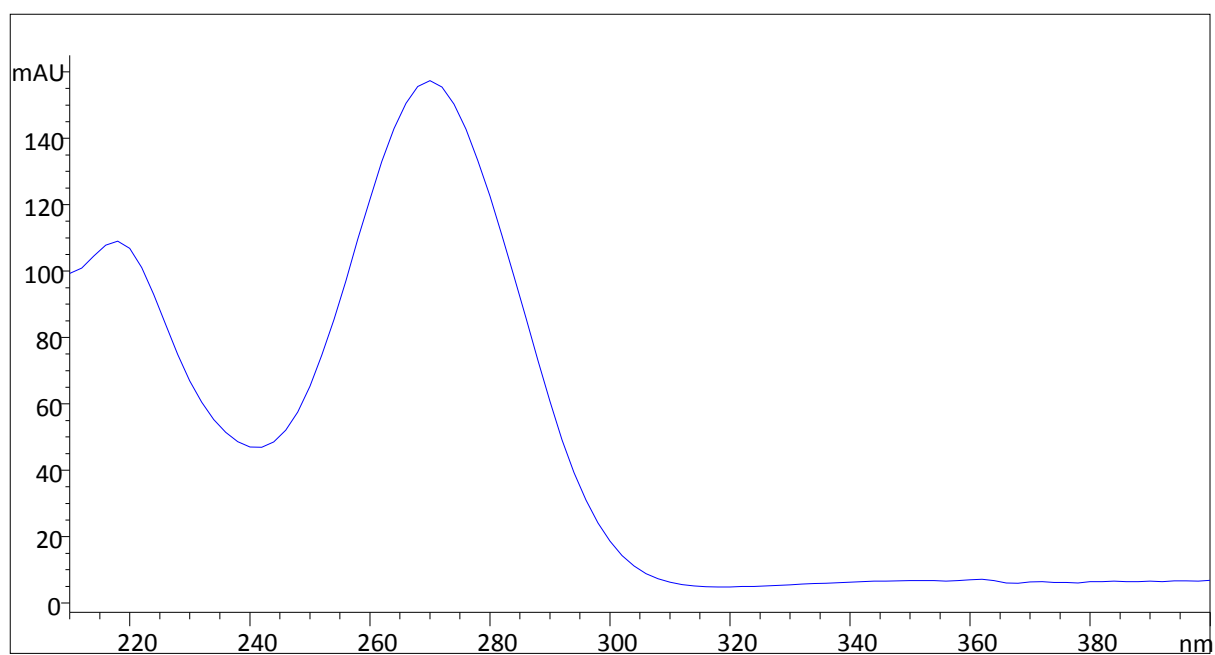


Figure S4. UV spectrum of the compound **2b**.

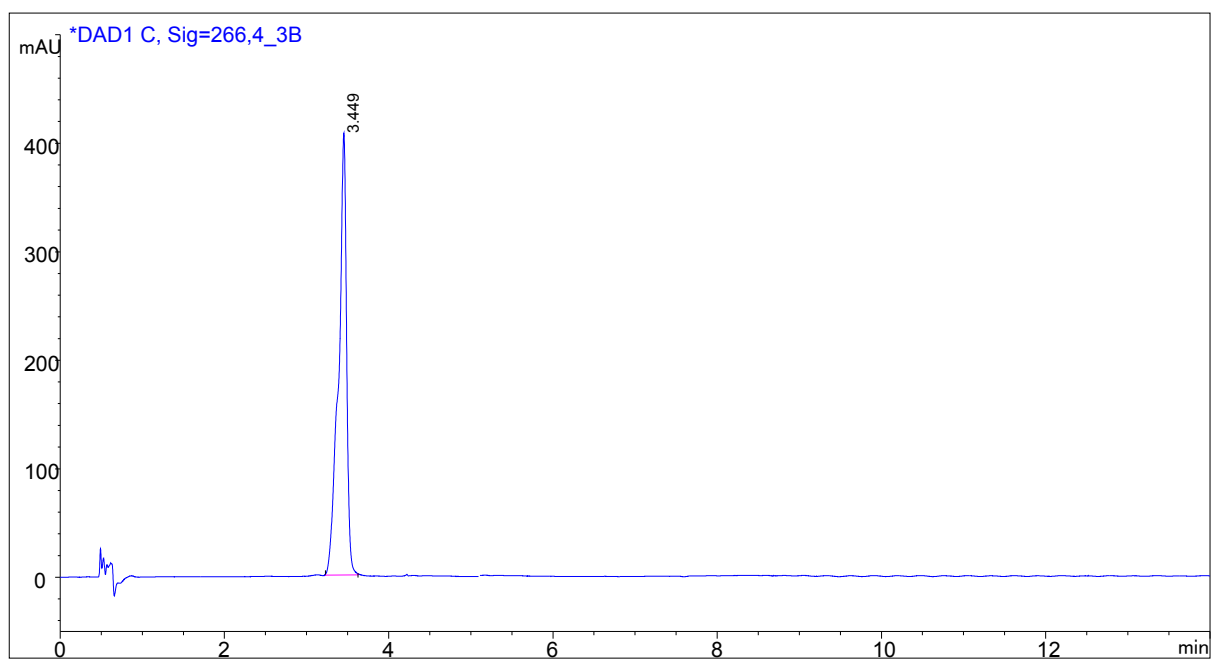


Figure S5. Chromatographic profile of **3b** monitored at $\lambda=266$ nm.

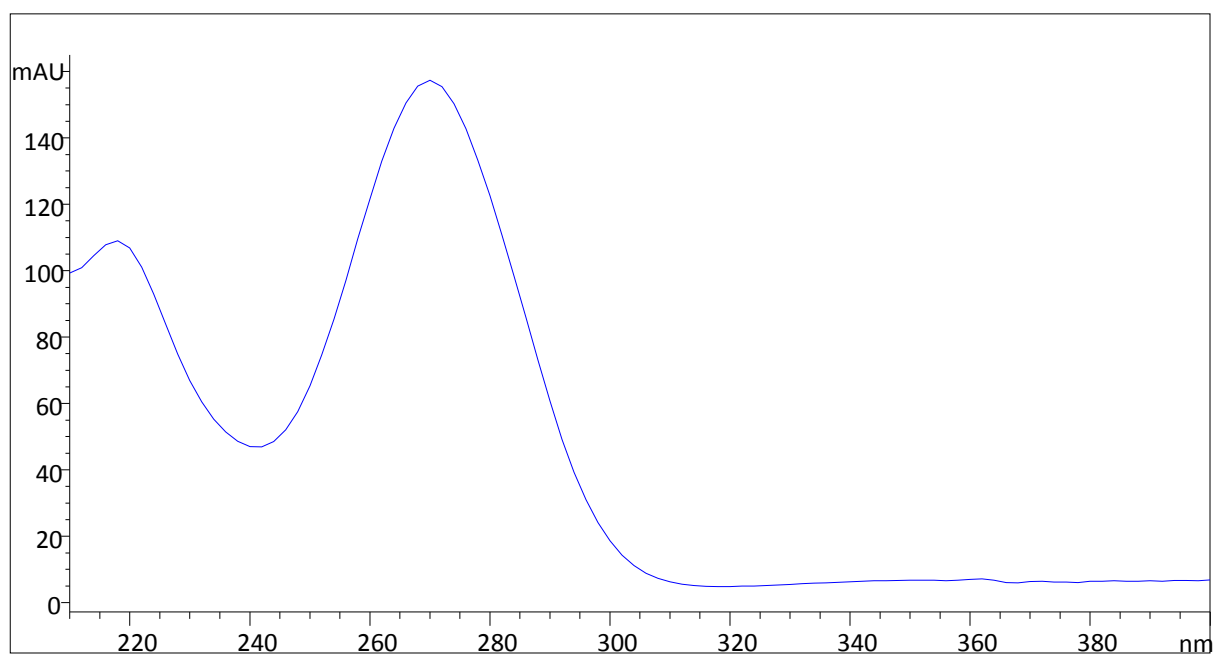


Figure S6. UV spectrum of the compound **3b**.

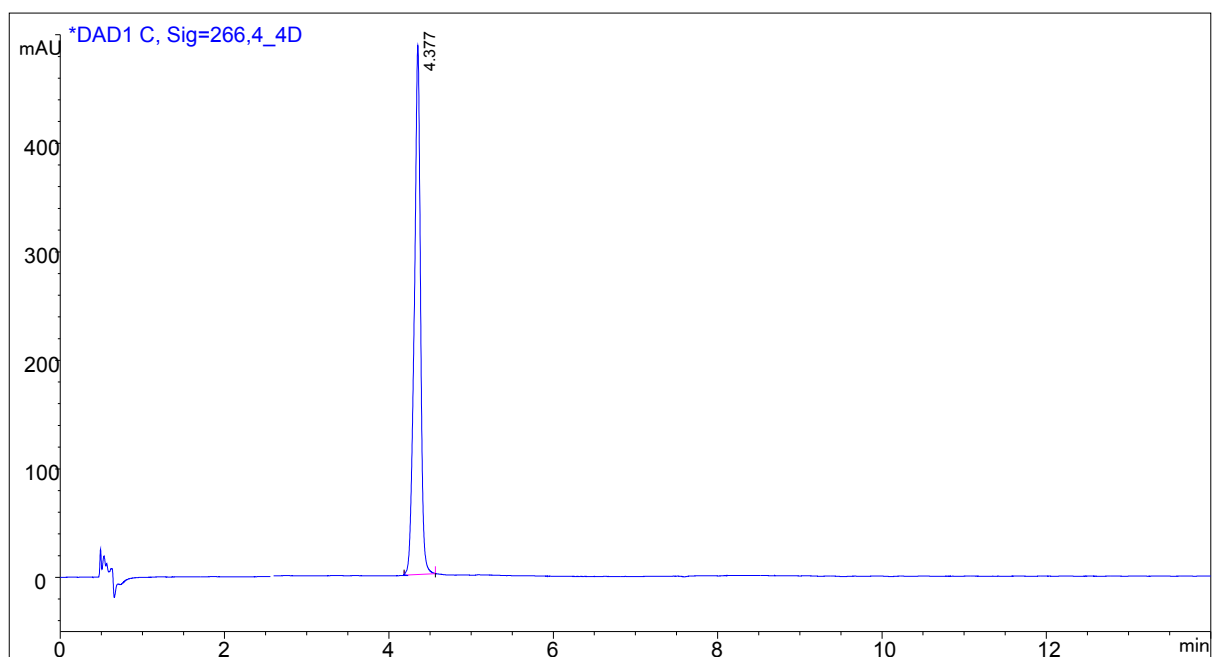


Figure S7. Chromatographic profile of **4d** monitored at $\lambda=266$ nm.

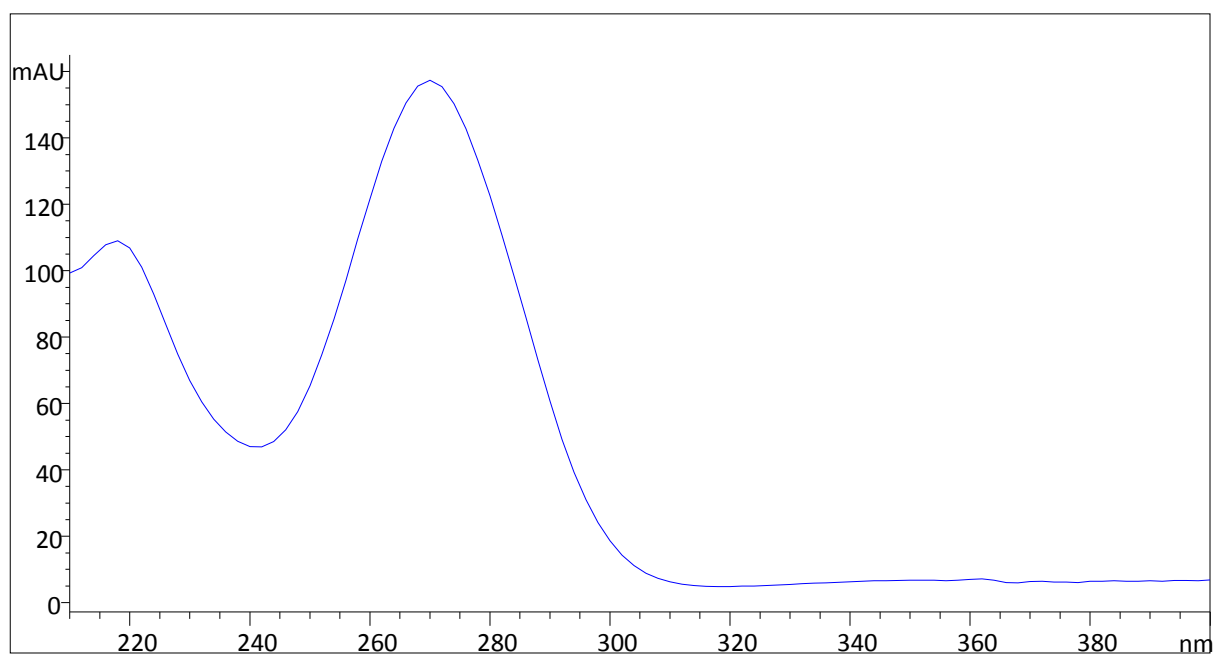


Figure S8. UV spectrum of the compound **4d**.

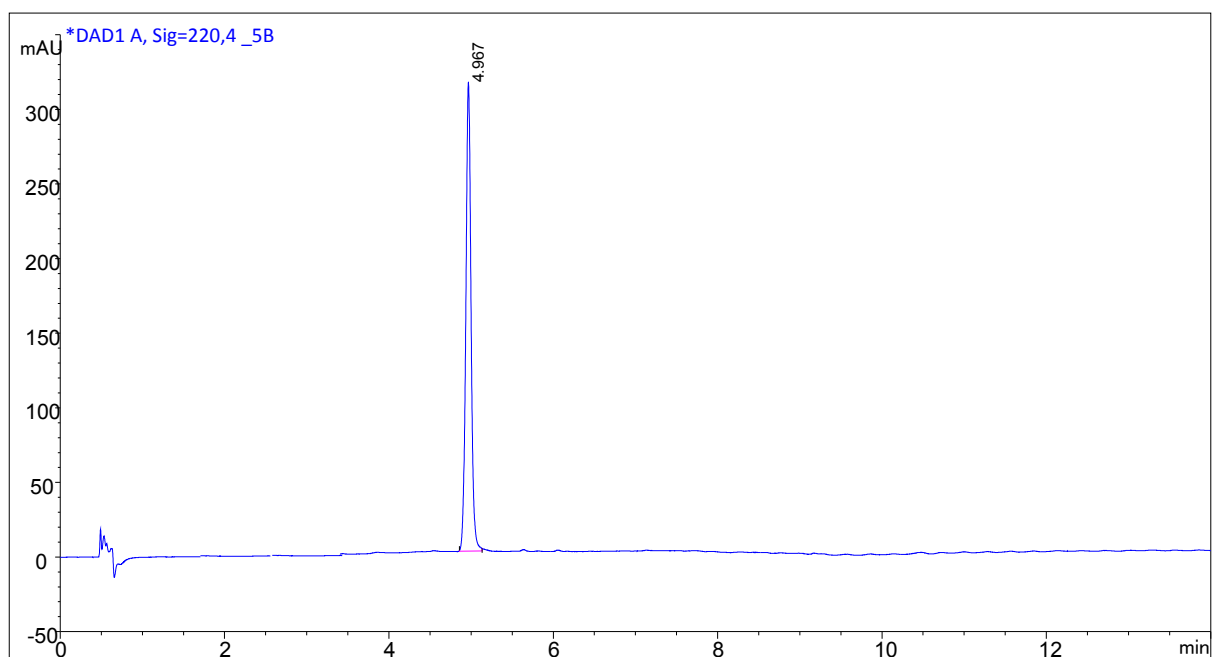


Figure S9. Chromatographic profile of **5b** monitored at $\lambda=220$ nm.

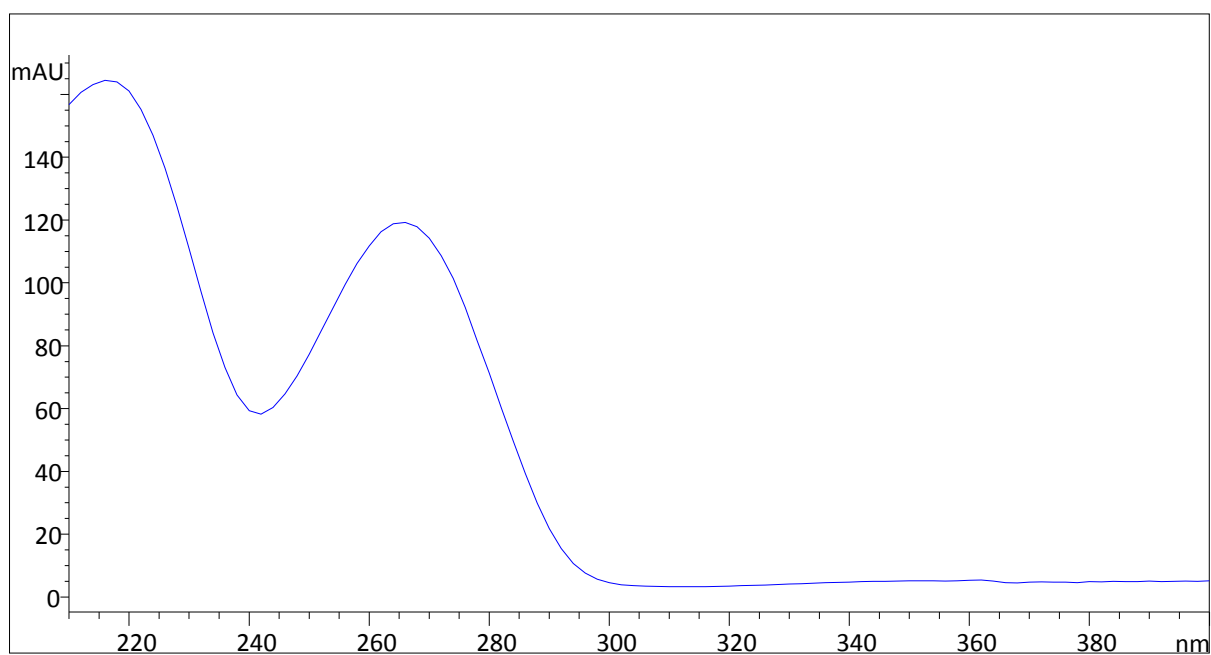


Figure S10. UV spectrum of the compound **5b**.

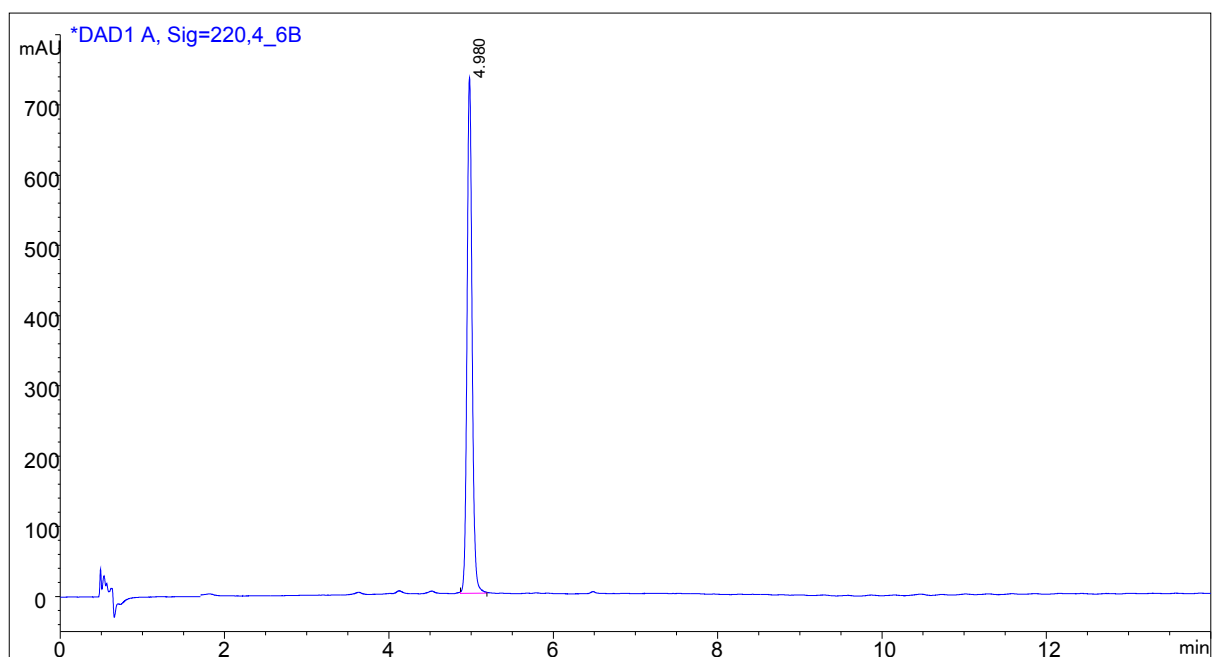


Figure S11. Chromatographic profile of **6b** monitored at $\lambda=220$ nm.

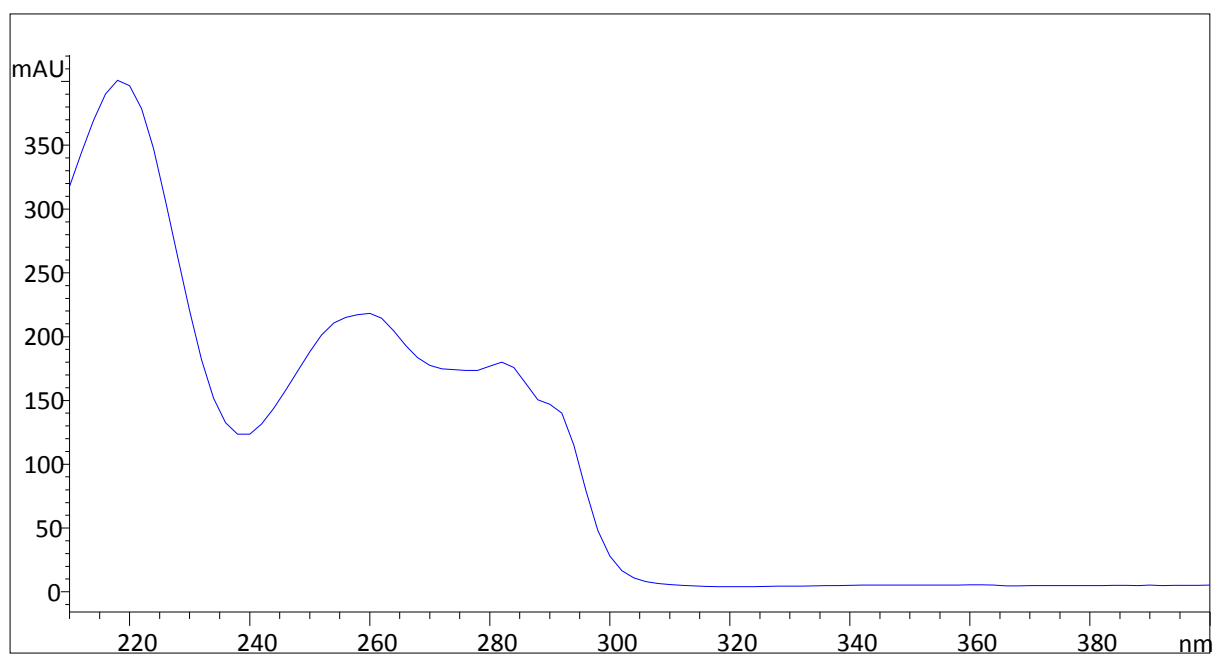


Figure S12. UV spectrum of the compound **6b**.

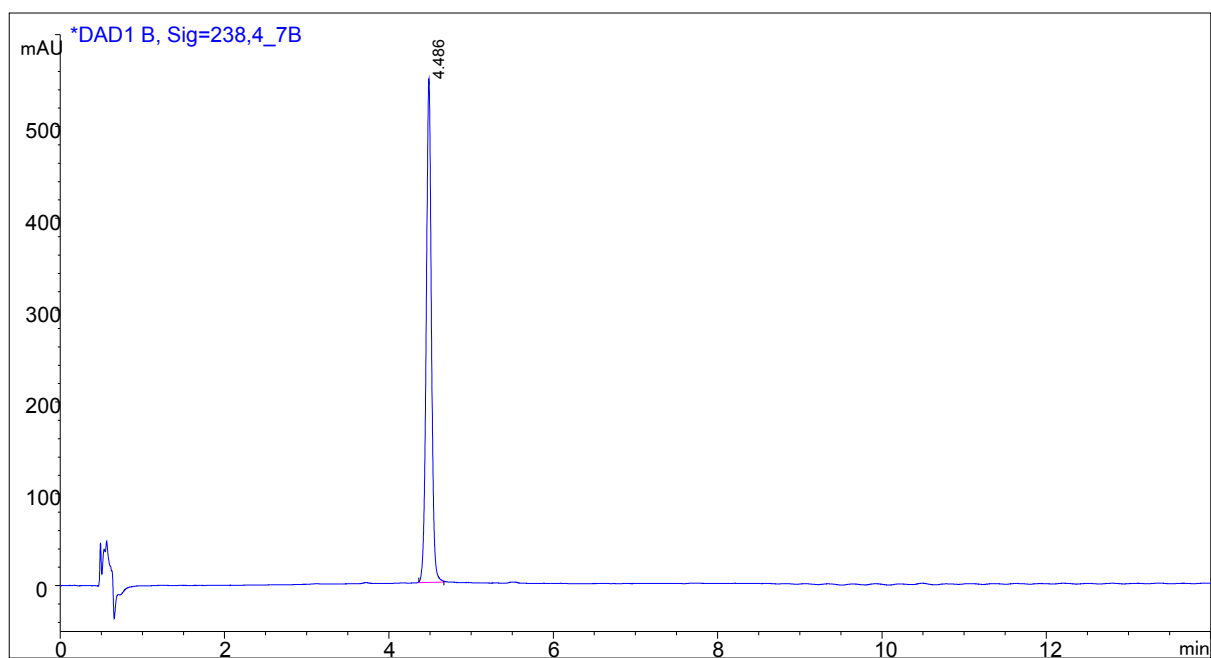


Figure S13. Chromatographic profile of **7b** monitored at $\lambda=238$ nm.

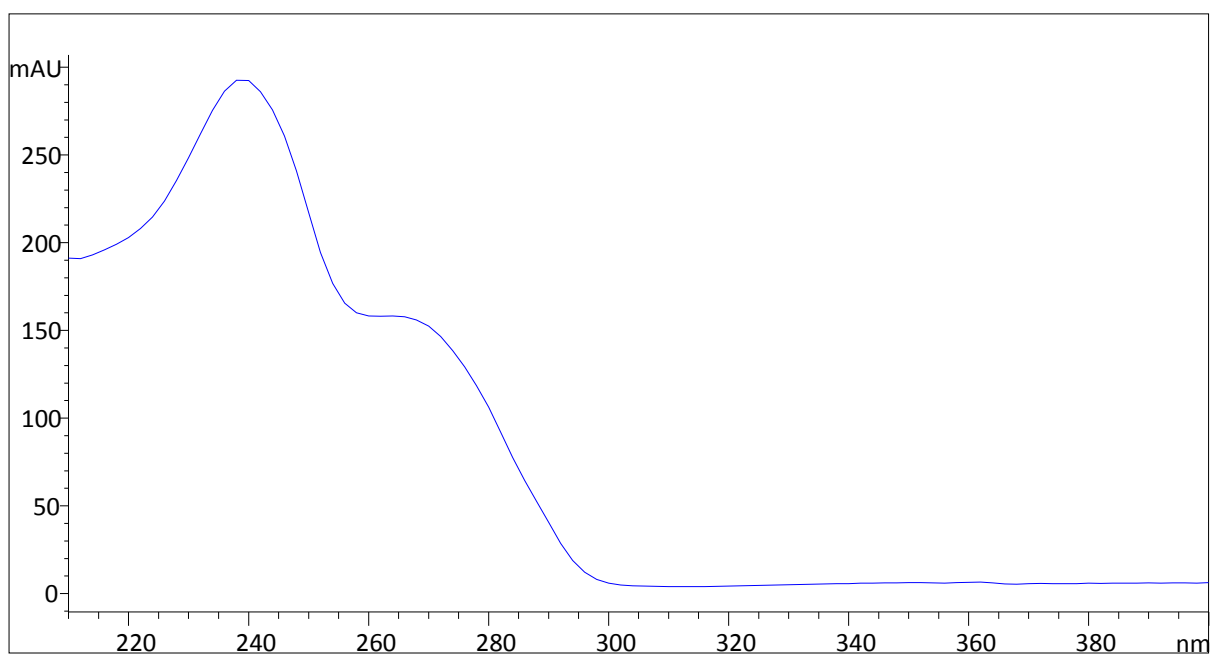


Figure S14. UV spectrum of the compound **7b**.

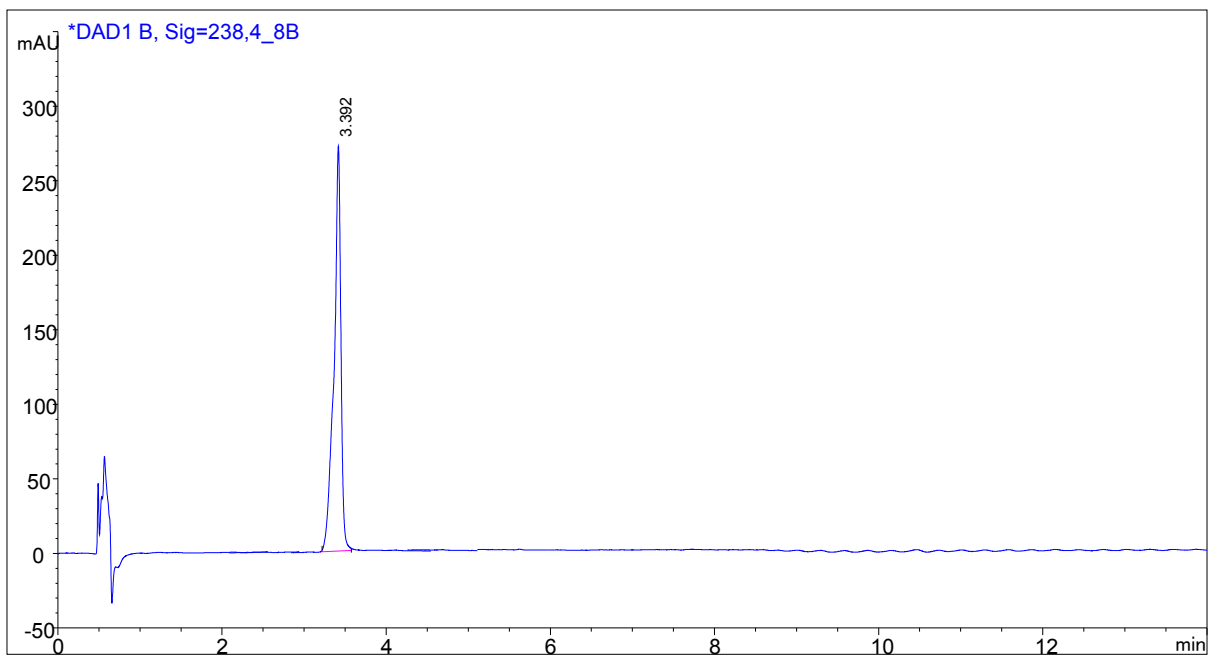


Figure S15. Chromatographic profile of **8b** monitored at $\lambda=238$ nm.

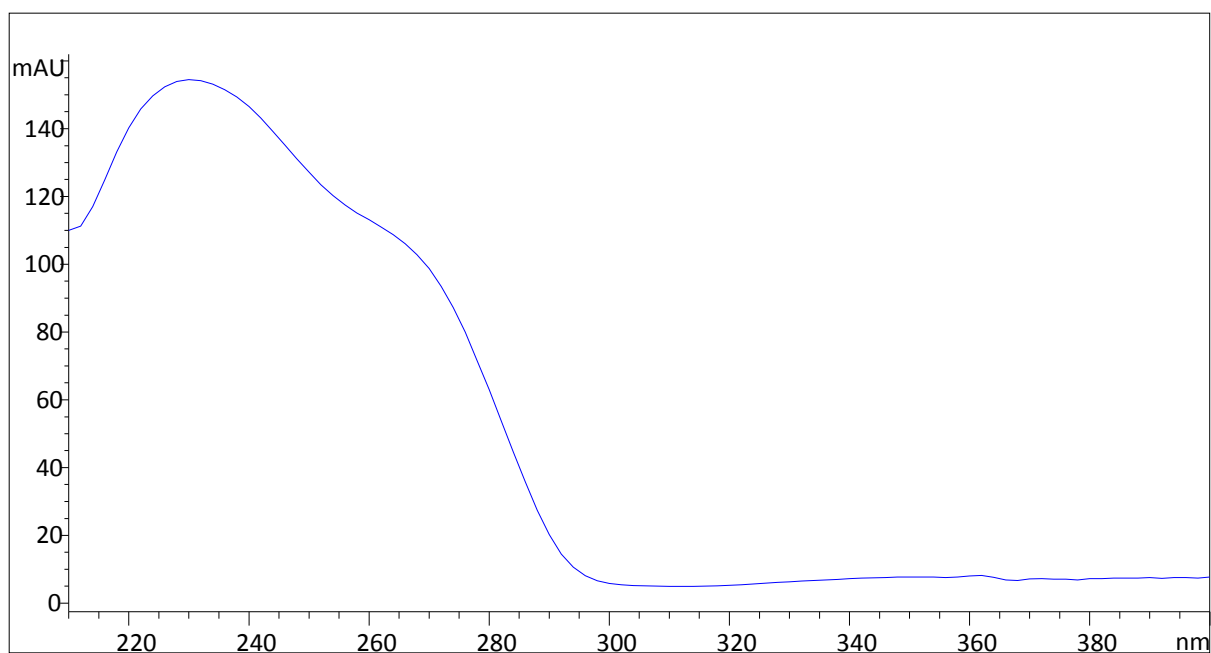


Figure S16. UV spectrum of the compound **8b**.

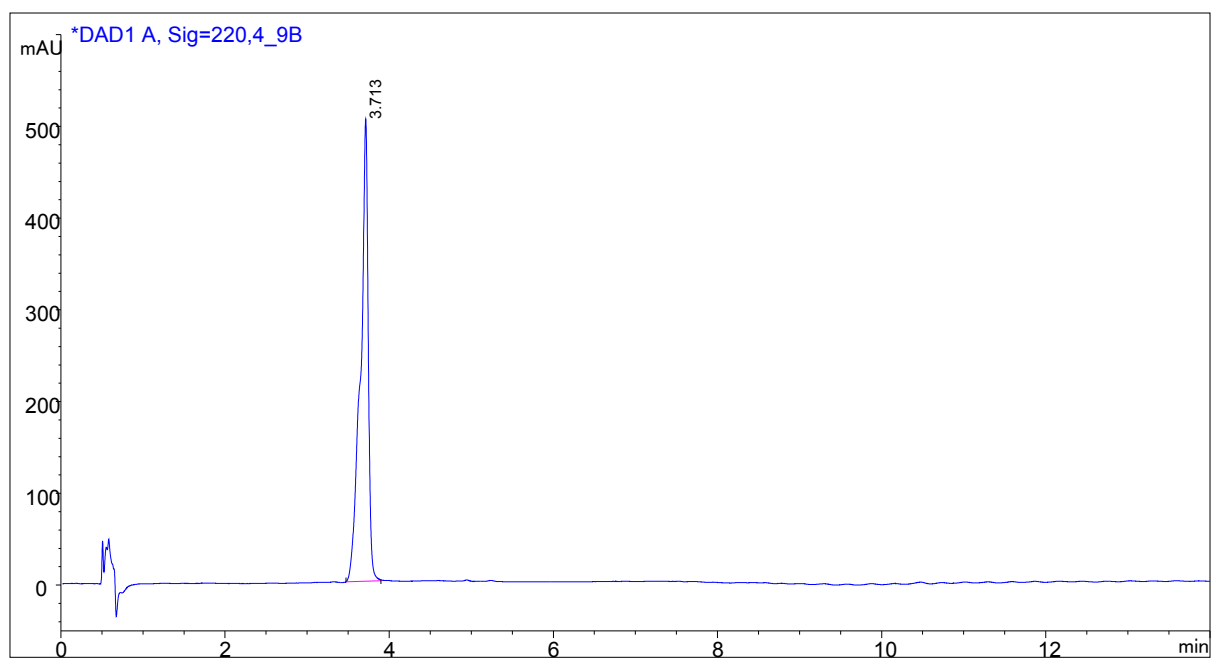


Figure S17. Chromatographic profile of **9b** monitored at $\lambda=220$ nm.

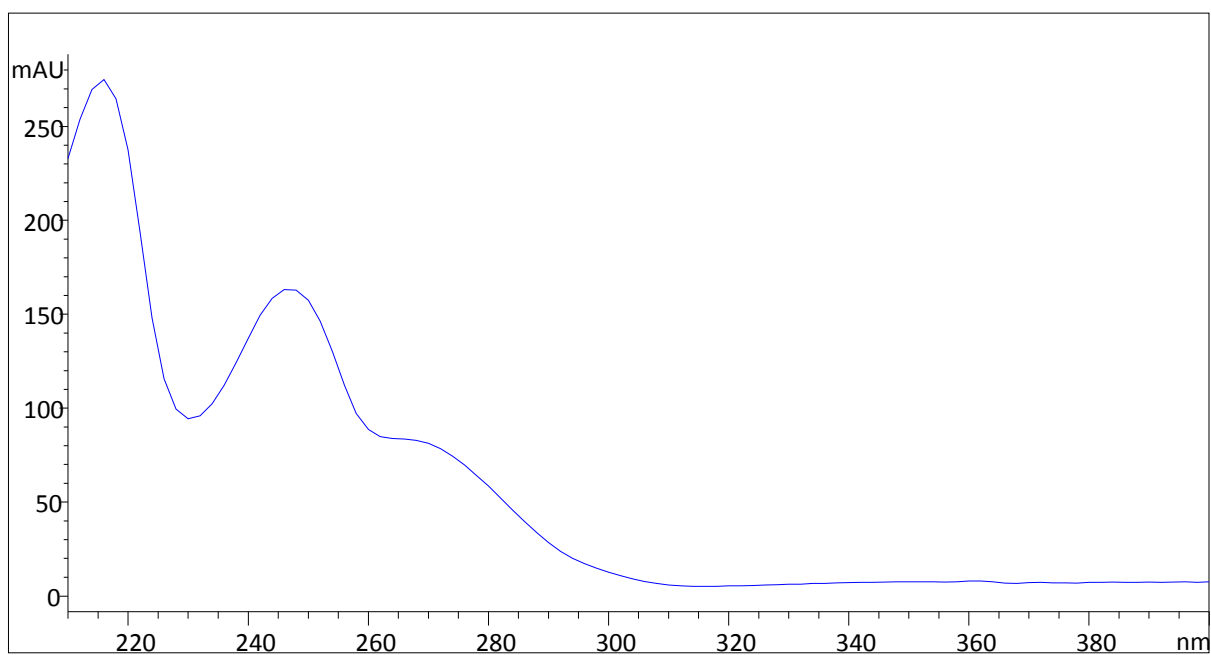


Figure S18. UV spectrum of the compound **9b**.

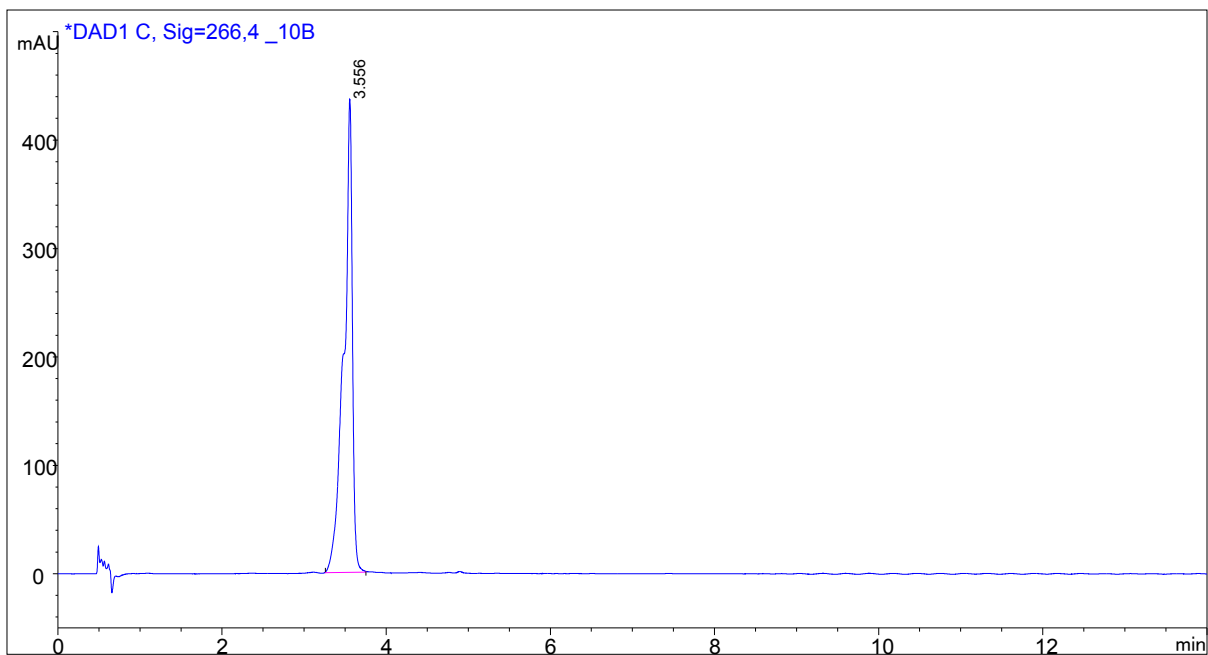


Figure S19. Chromatographic profile of **10b** monitored at $\lambda=266$ nm.

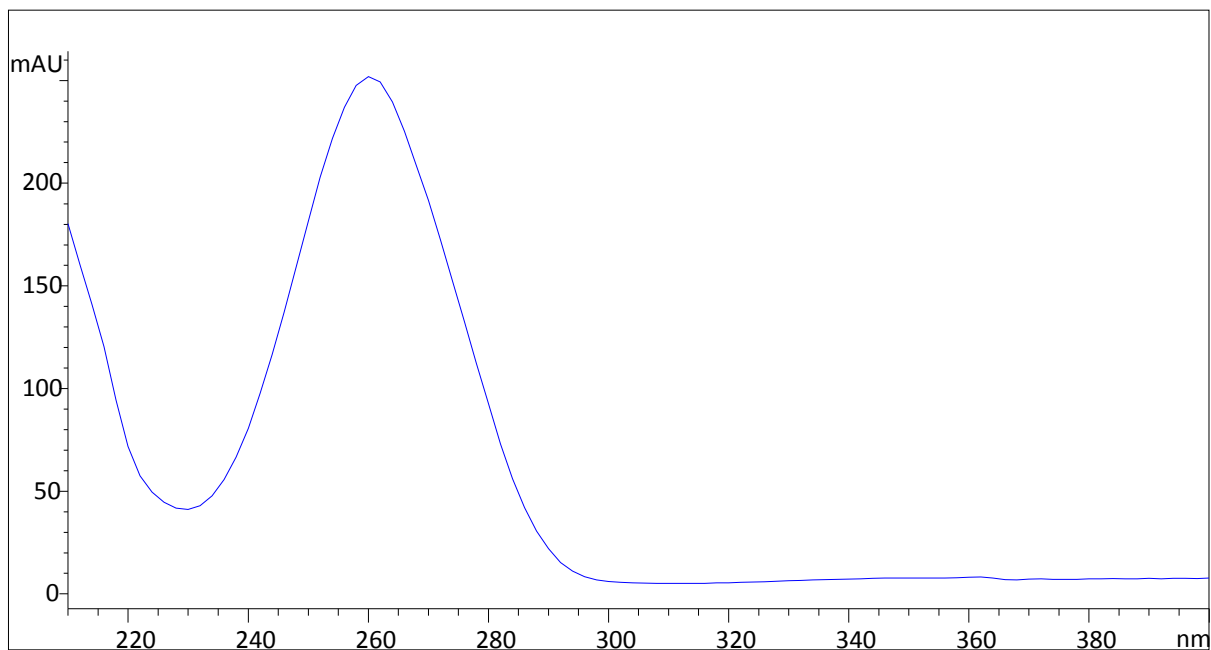


Figure S20. UV spectrum of the compound **10b**.

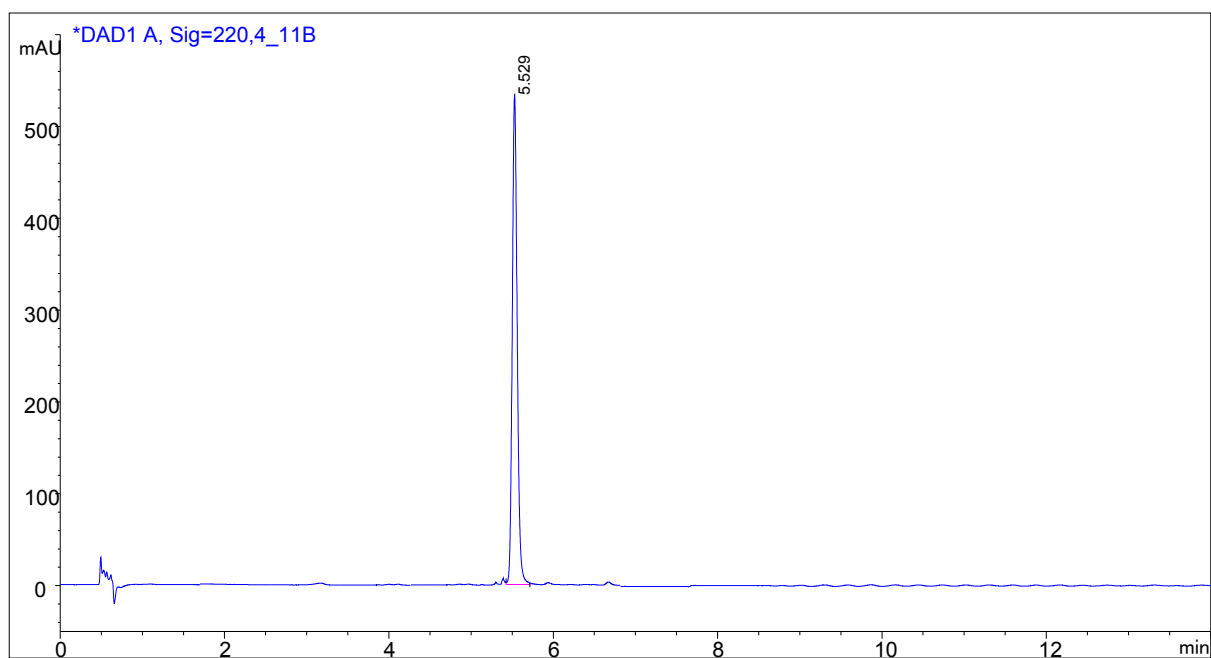


Figure S21. Chromatographic profile of **11b** monitored at $\lambda=220$ nm.

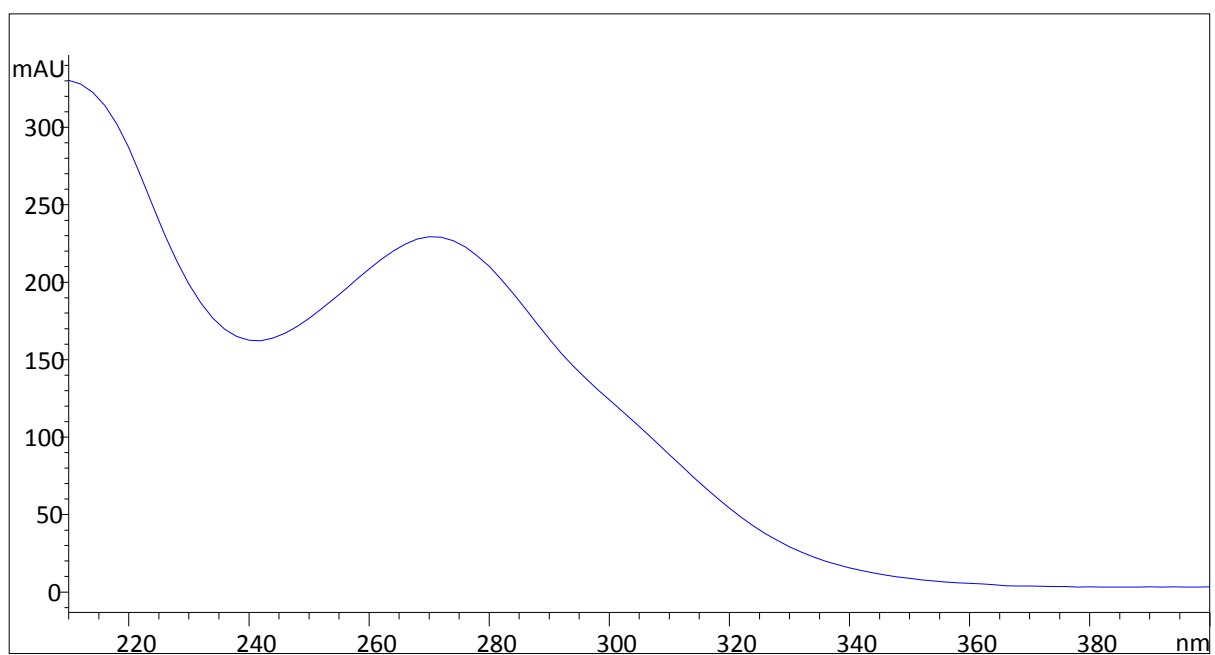


Figure S22. UV spectrum of the compound **11b**.

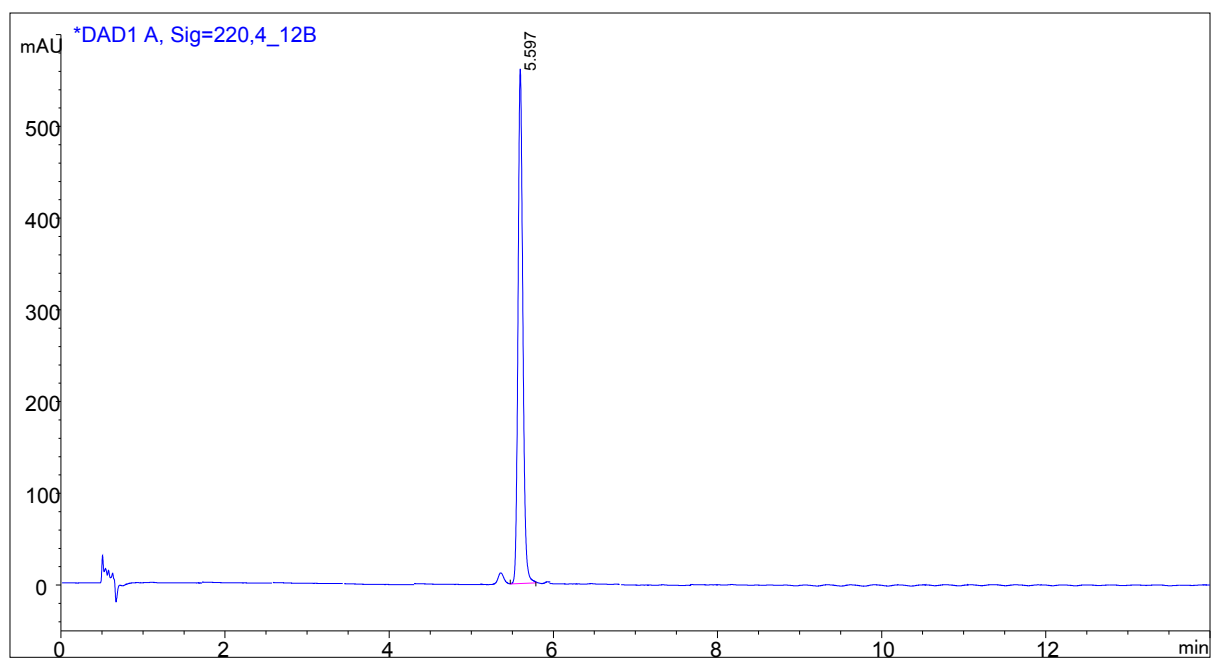


Figure S23. Chromatographic profile of **12b** monitored at $\lambda=220$ nm.

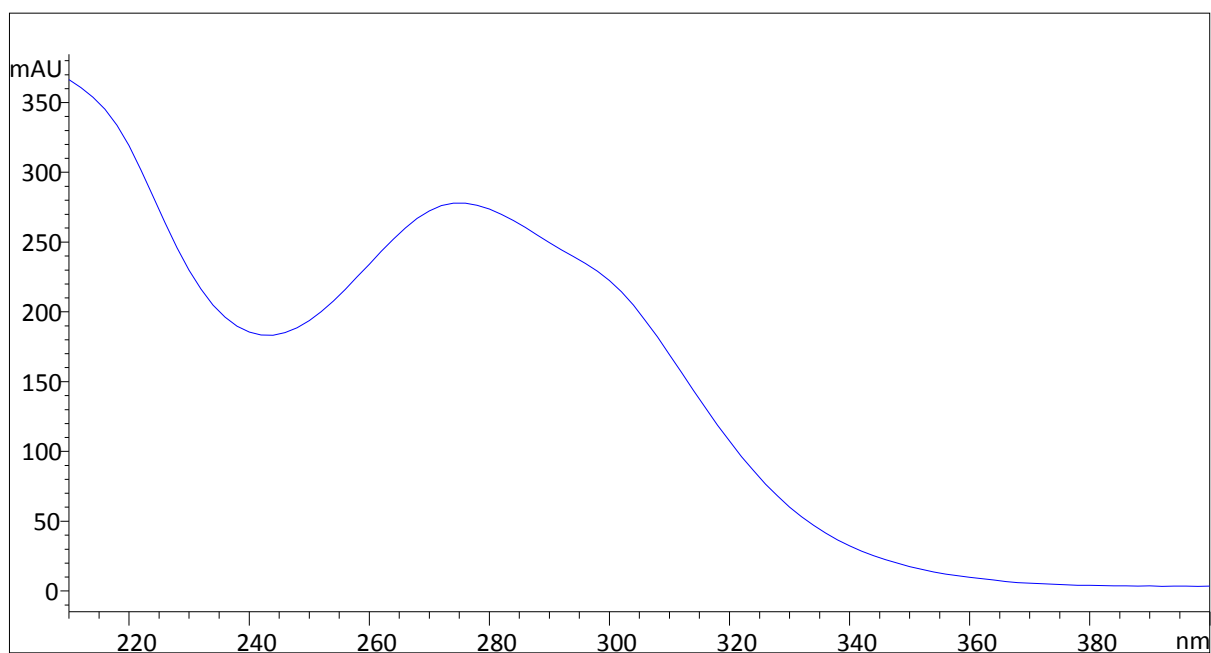


Figure S24. UV spectrum of the compound **12b**.

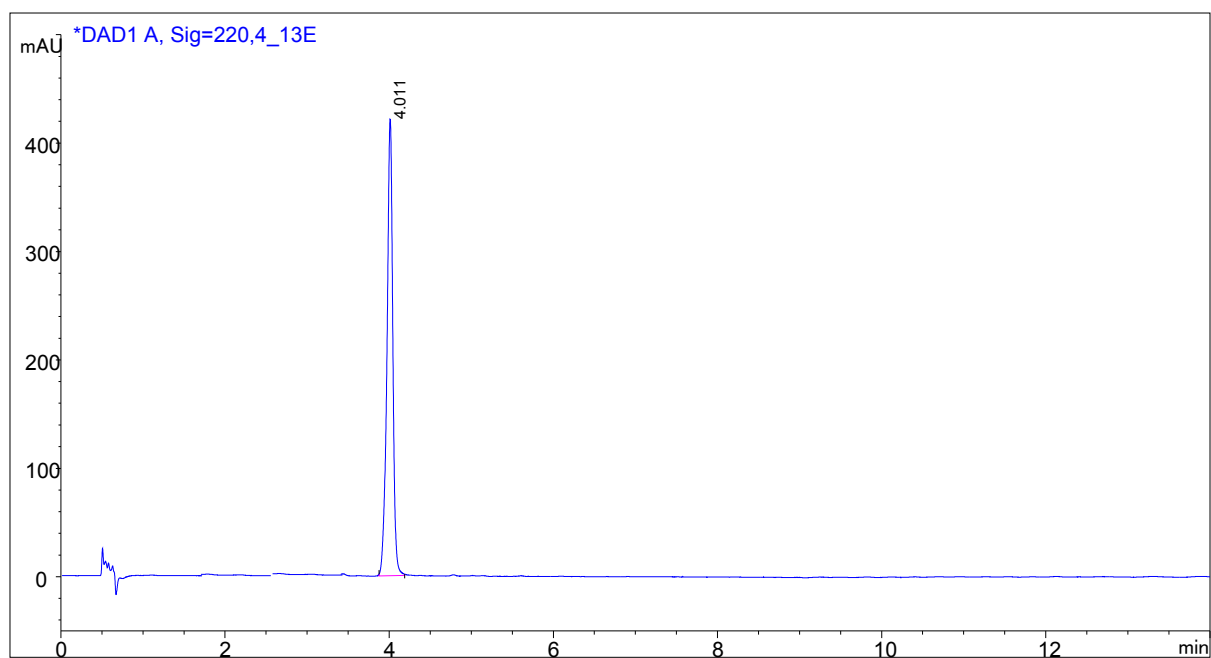


Figure S25. Chromatographic profile of **13e** monitored at $\lambda=220$ nm.

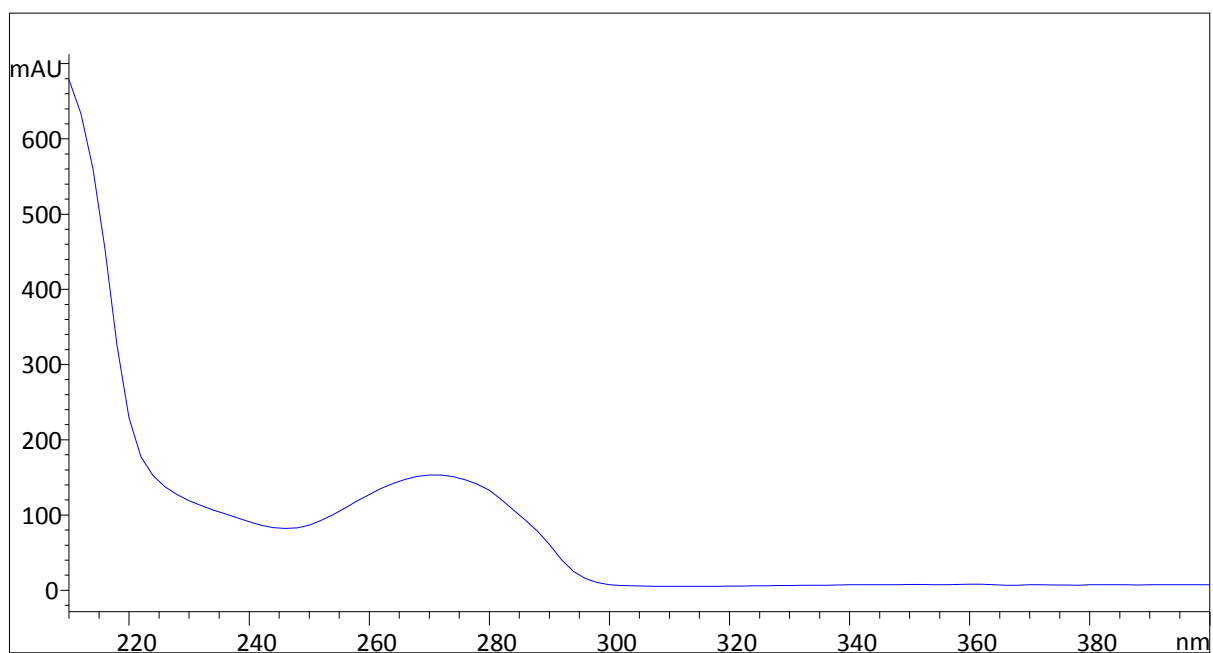


Figure S26. UV spectrum of the compound **13e**.

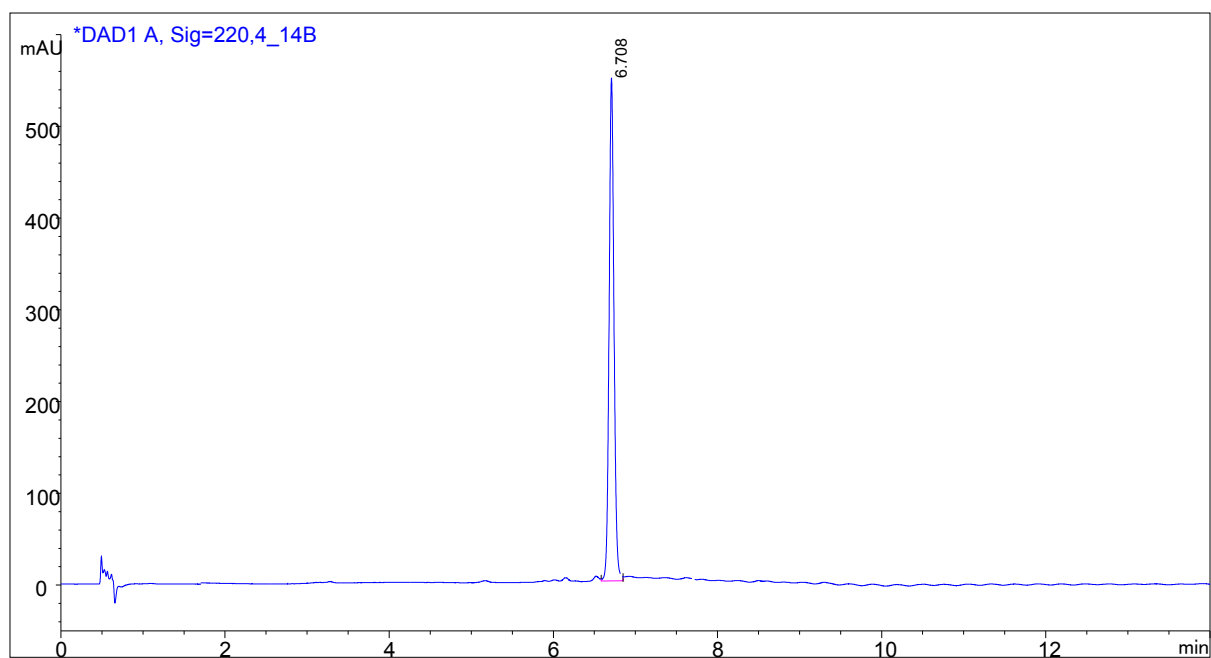


Figure S27. Chromatographic profile of **14b** monitored at $\lambda=220$ nm.

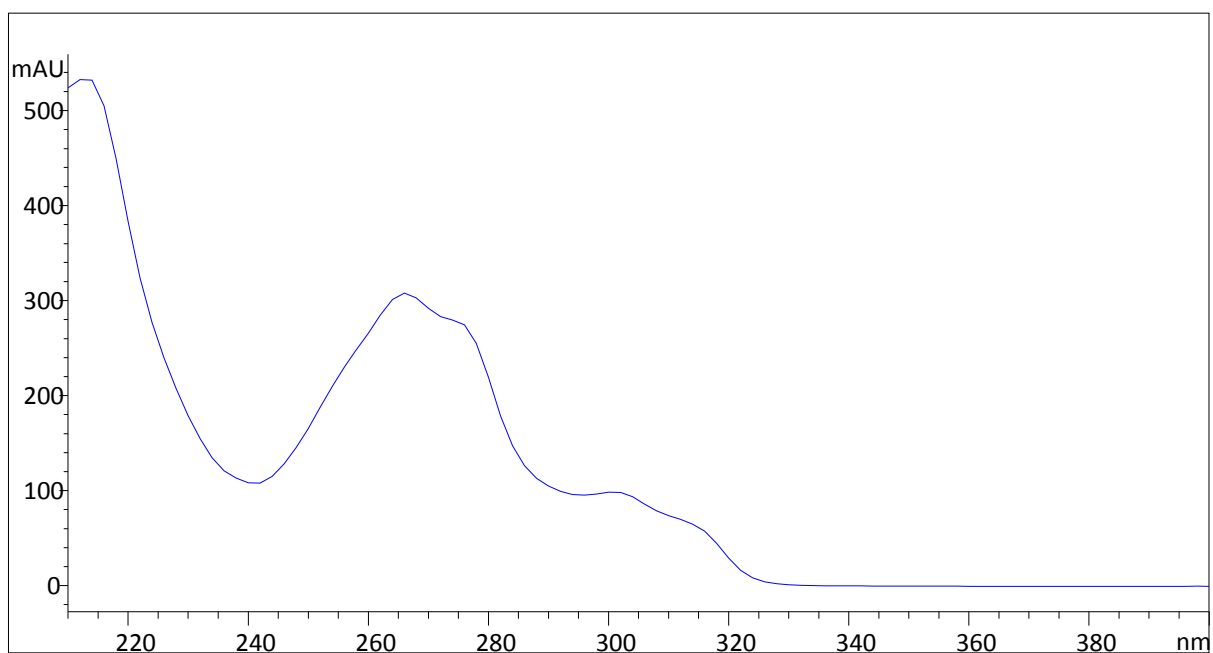


Figure S28. UV spectrum of the compound **14b**.

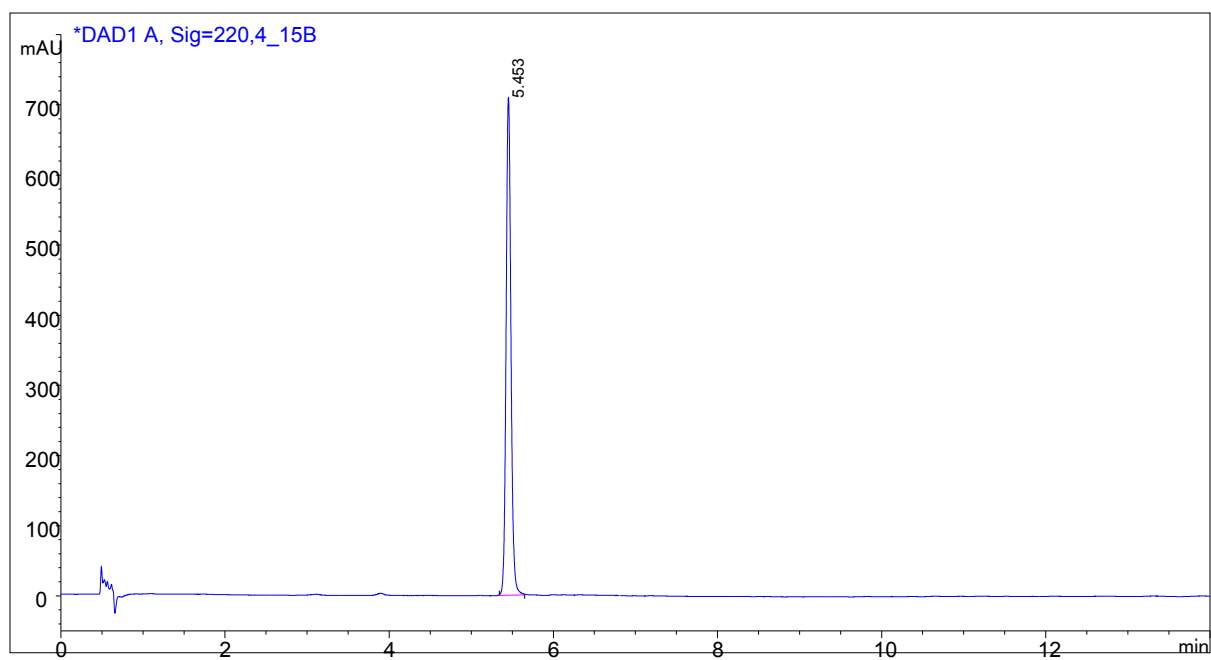


Figure S29. Chromatographic profile of **15b** monitored at $\lambda=220$ nm.

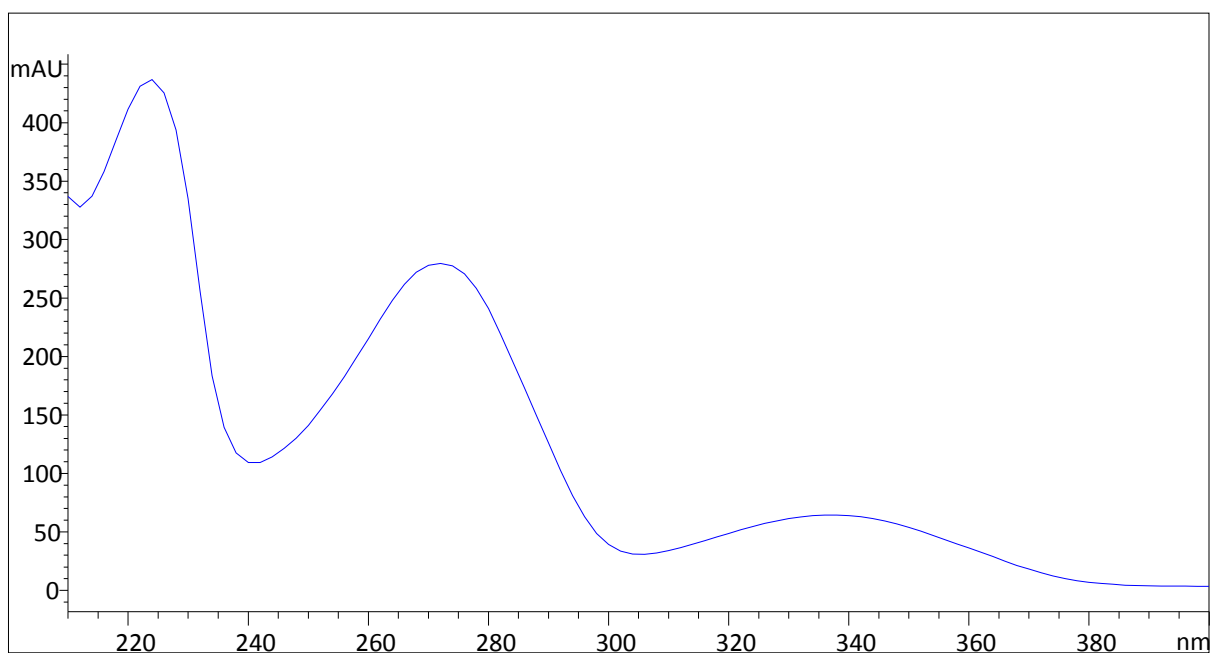


Figure S30. UV spectrum of the compound **15b**.

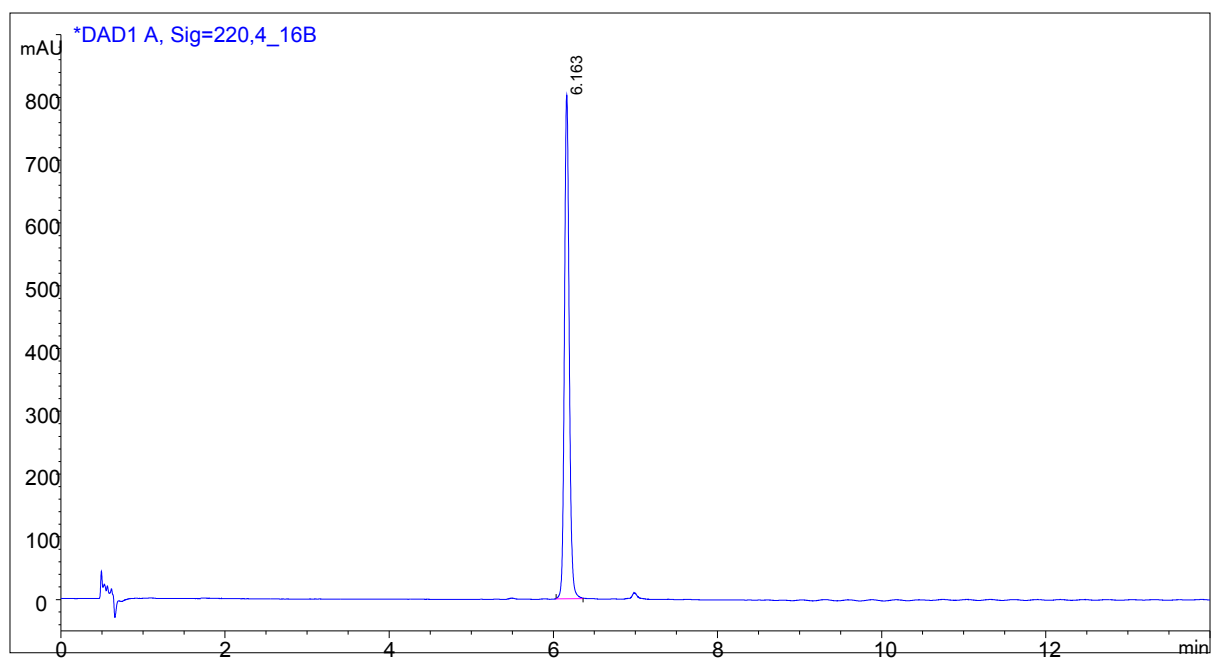


Figure S31. Chromatographic profile of **16b** monitored at $\lambda=220$ nm.

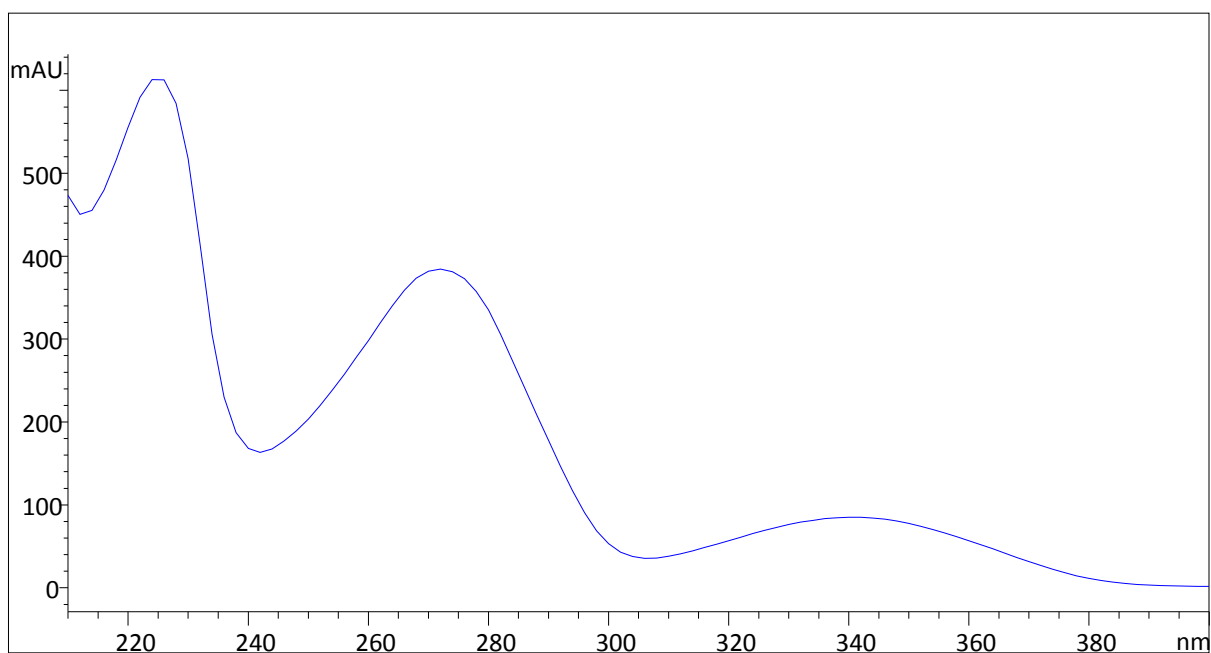


Figure S32. UV spectrum of the compound **16b**.

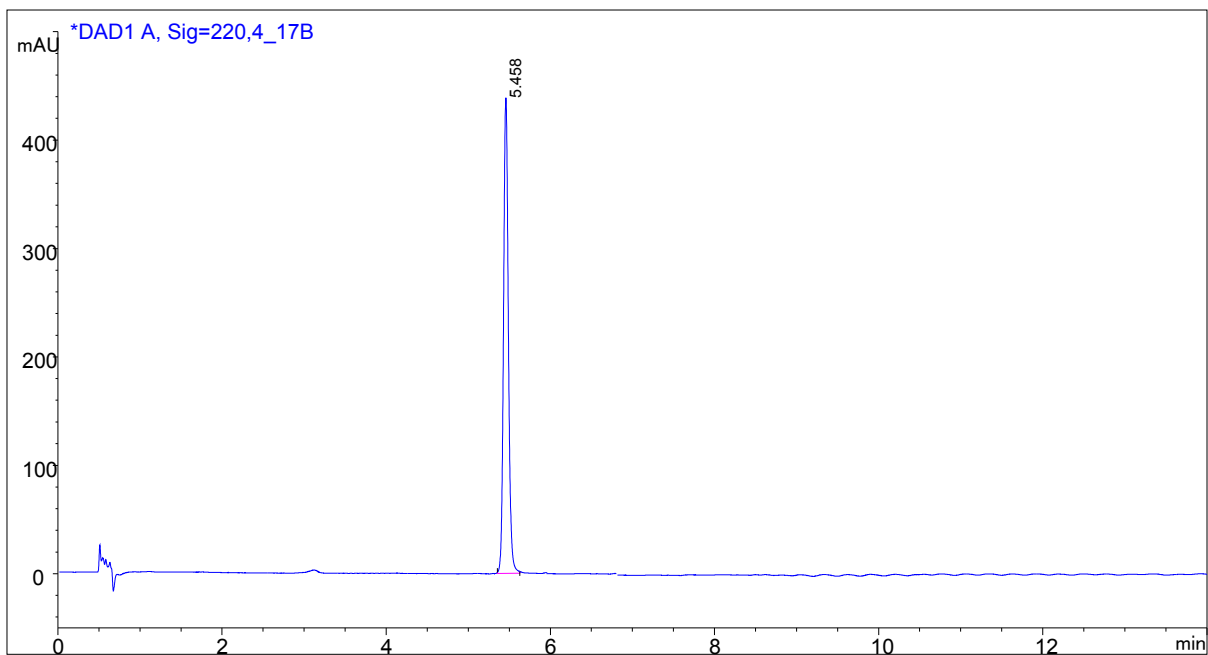


Figure S33. Chromatographic profile of **17b** monitored at $\lambda=220$ nm.

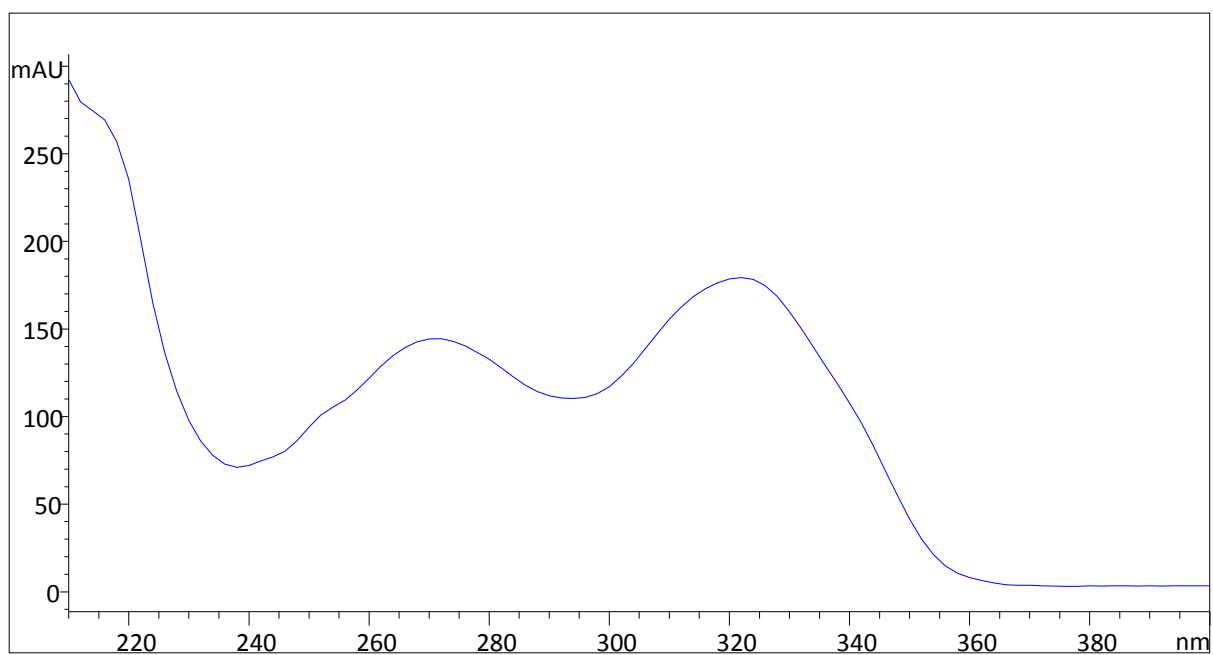


Figure S34. UV spectrum of the compound **17b**.

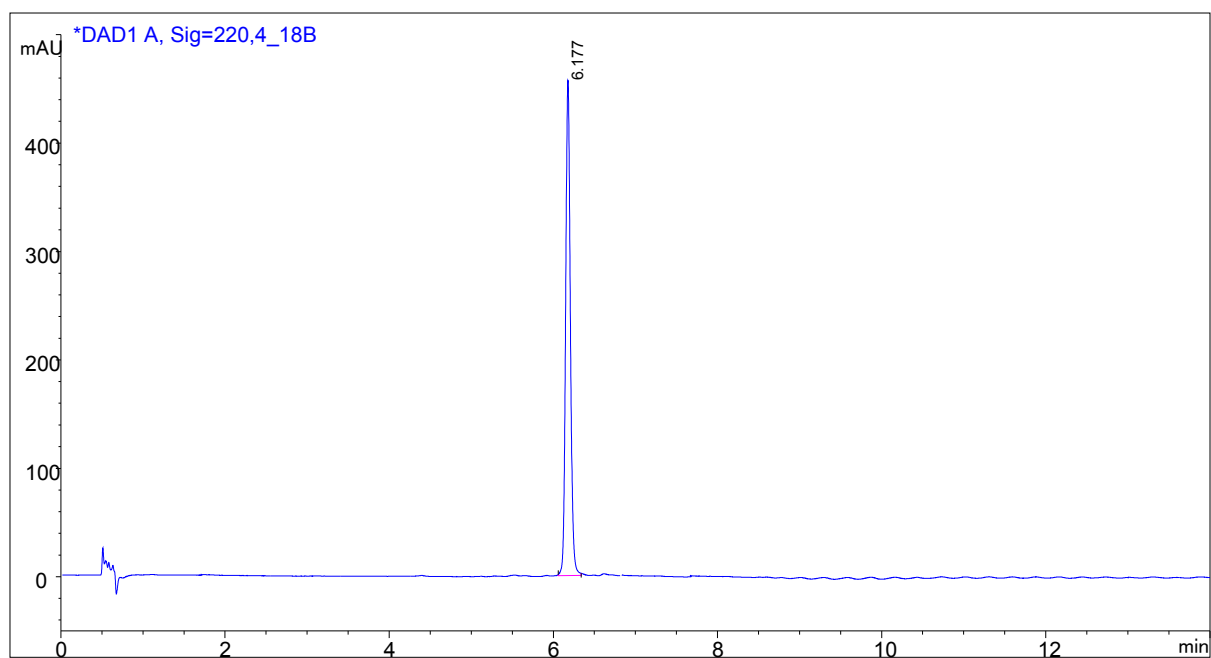


Figure S35. Chromatographic profile of **18b** monitored at $\lambda=220$ nm.

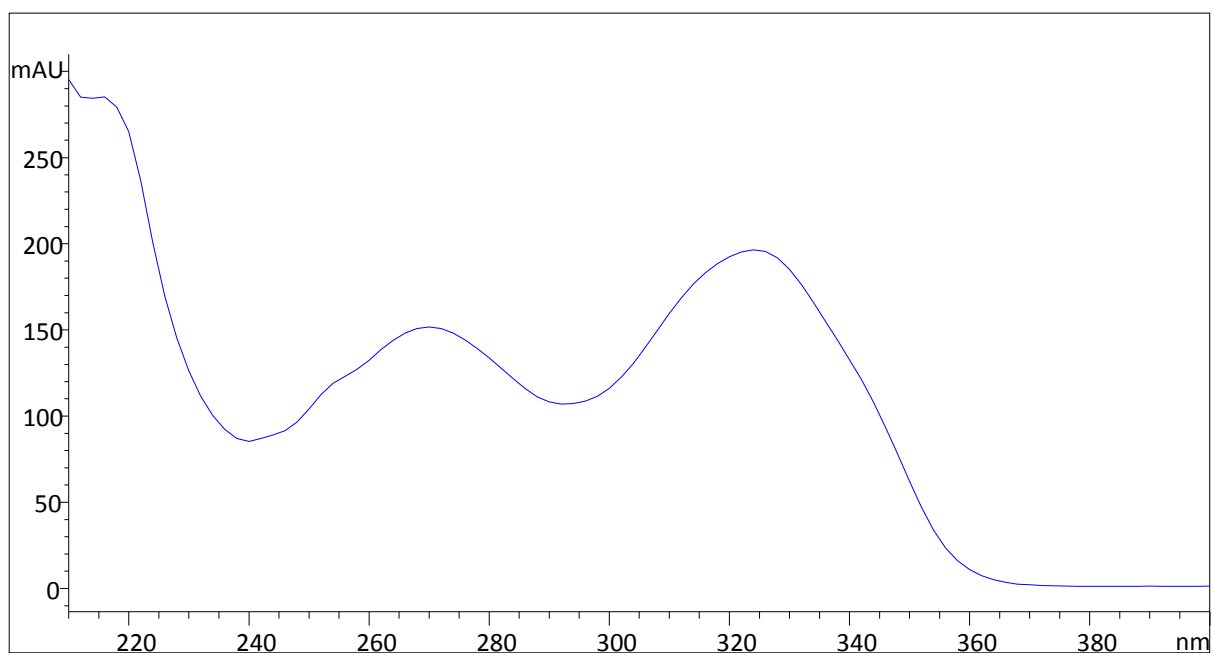


Figure S36. UV spectrum of the compound **18b**.

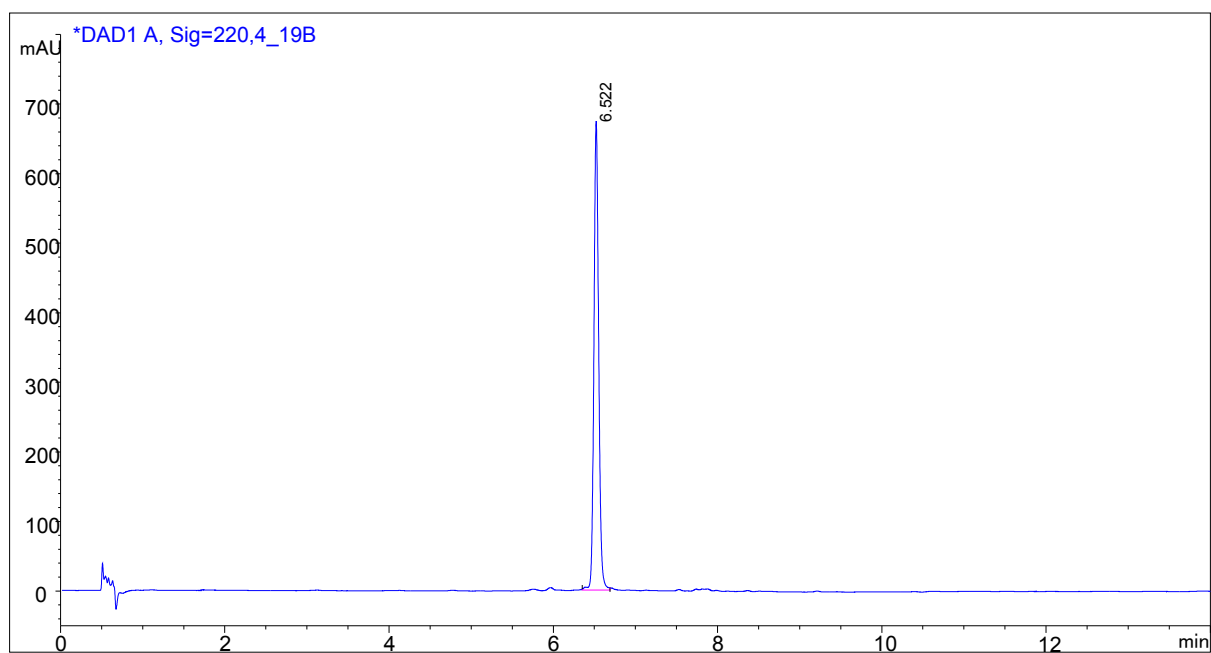


Figure S37. Chromatographic profile of **19b** monitored at $\lambda=220$ nm.

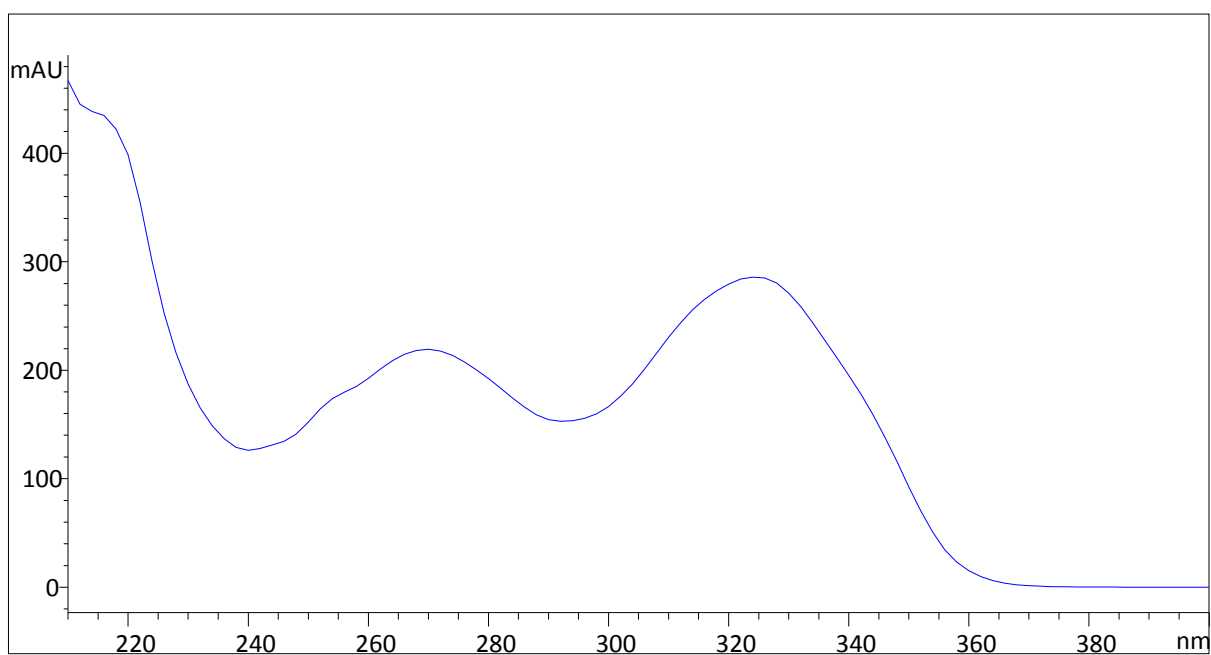


Figure S38. UV spectrum of the compound **19b**.

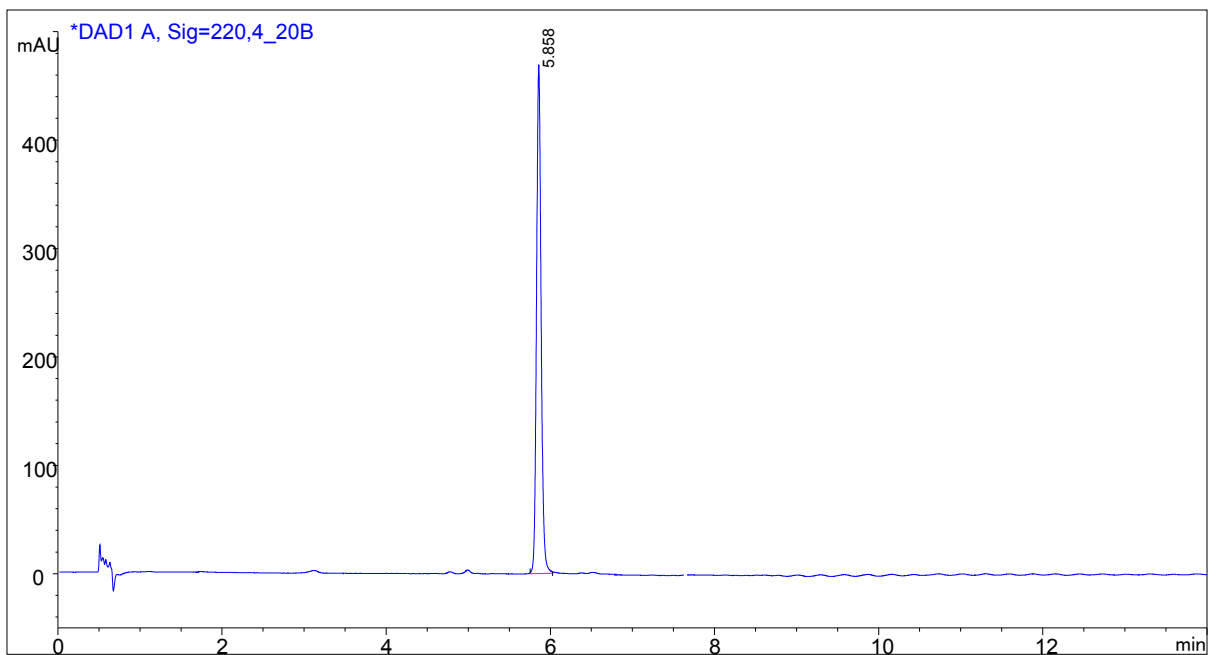


Figure S39. Chromatographic profile of **20b** monitored at $\lambda=220$ nm.

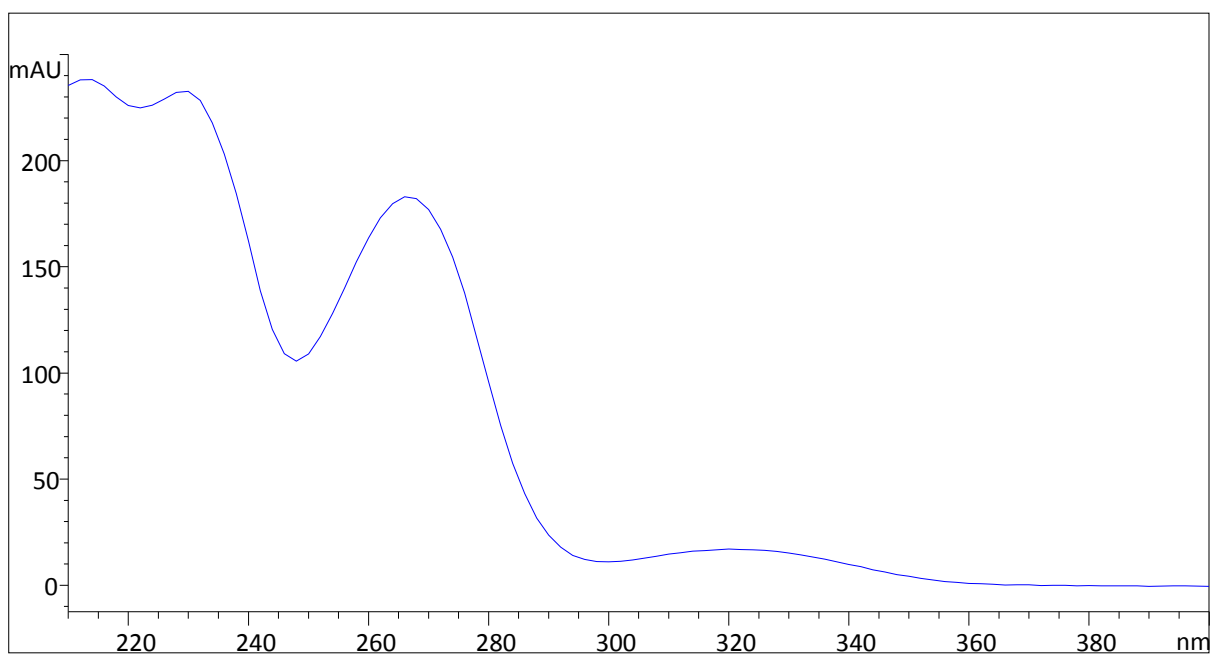


Figure S40. UV spectrum of the compound **20b**.