Supplementary Materials

Structure-Based Design of Potent Peptidomimetic Inhibitors Covalently Targeting SARS-CoV-2 Papain-Like Protease

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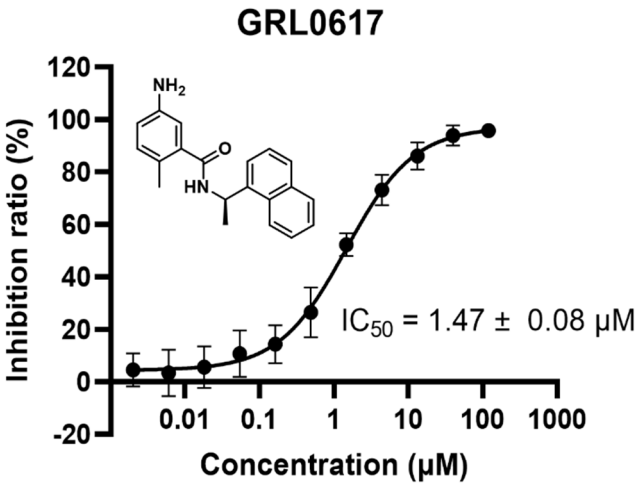


Figure S1. The chemical structure and inhibition profile for GRL0617 against SARS-CoV-2 PL^{pro} with RLRGG-AMC substrate.

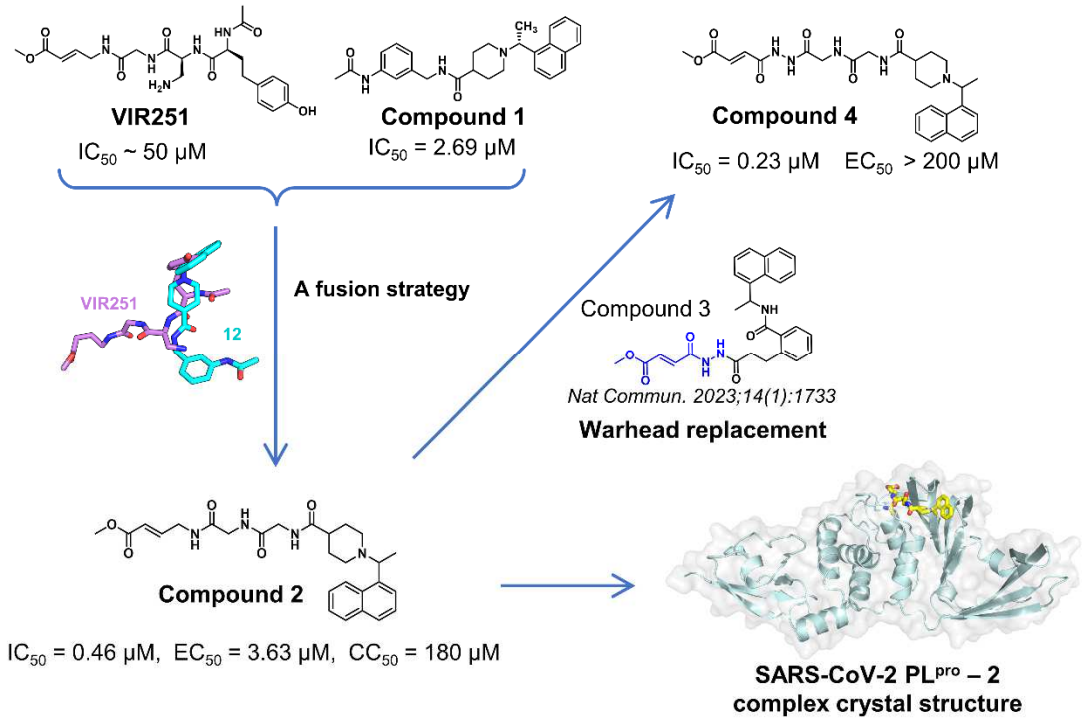


Figure S2. A diagram of workflow and conclusions.

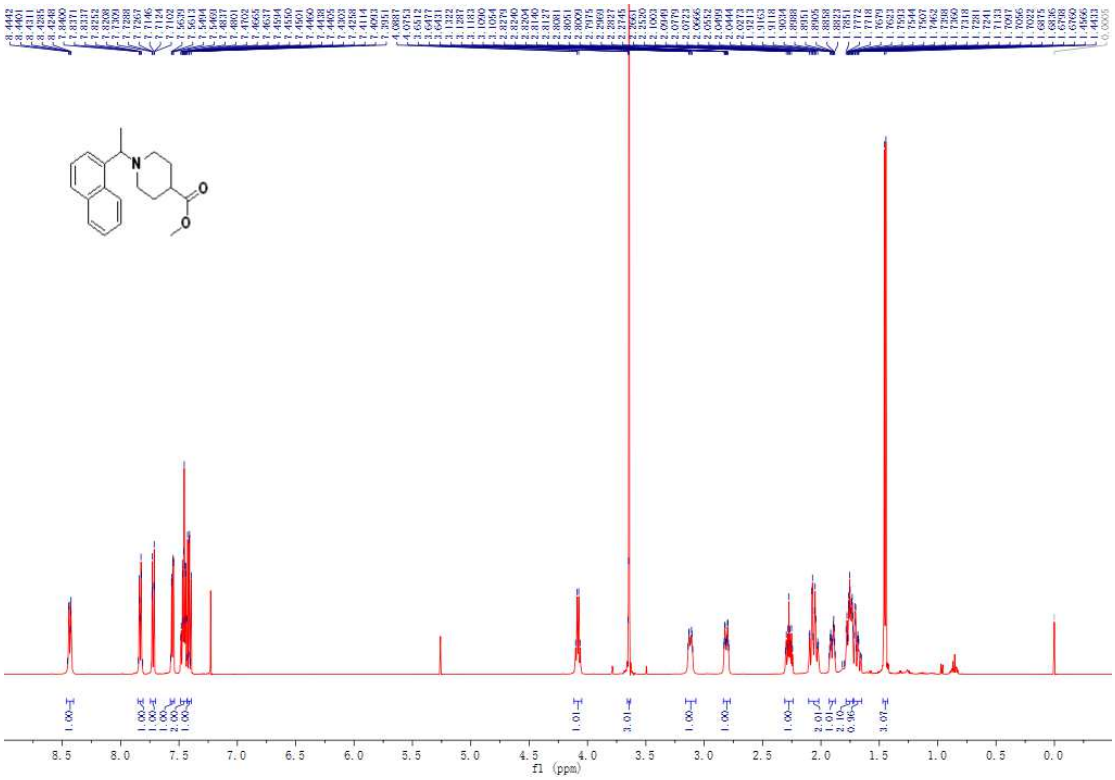


Figure S3. ^{1}H NMR Spectra for compound **2b**.

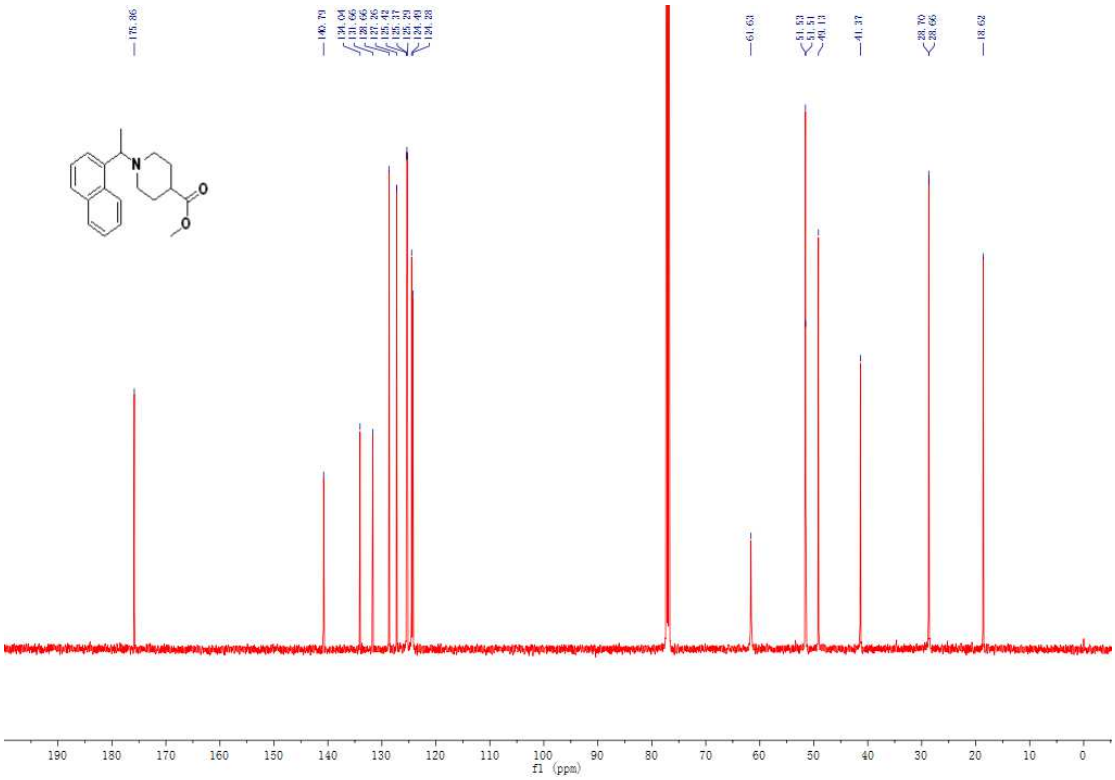


Figure S4. ^{13}C NMR Spectra for compound **2b.**

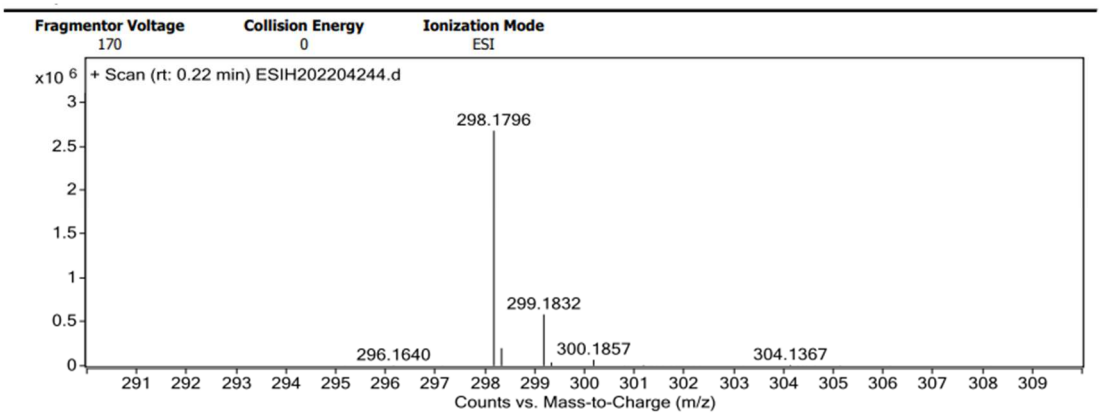


Figure S5. HRMS-ESI for compound **2b.**

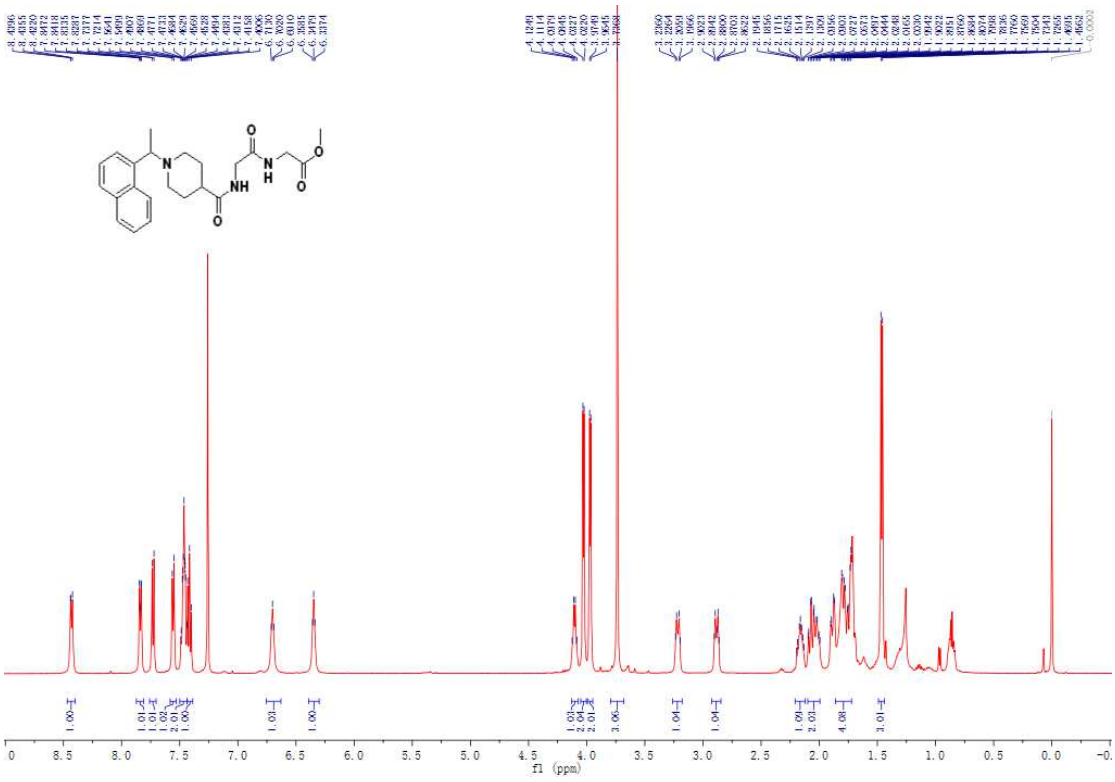


Figure S6. ^{1}H NMR Spectra for compound **2d.**

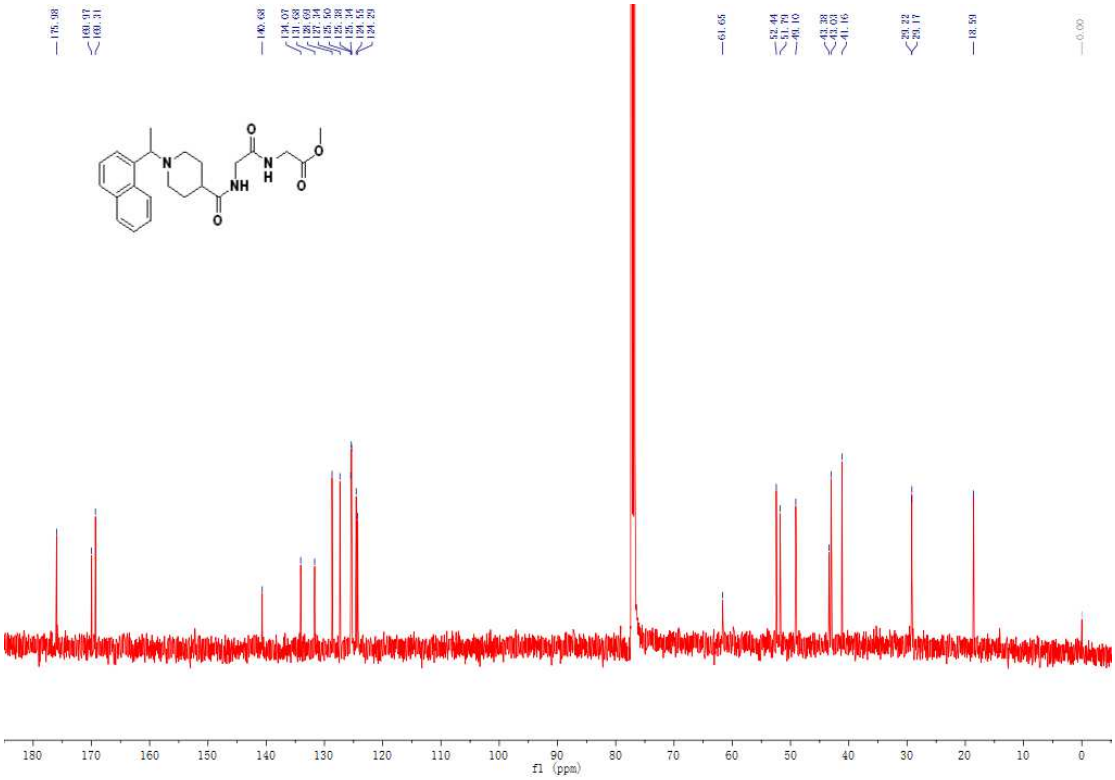


Figure S7. ^{13}C NMR Spectra for compound **2d.**

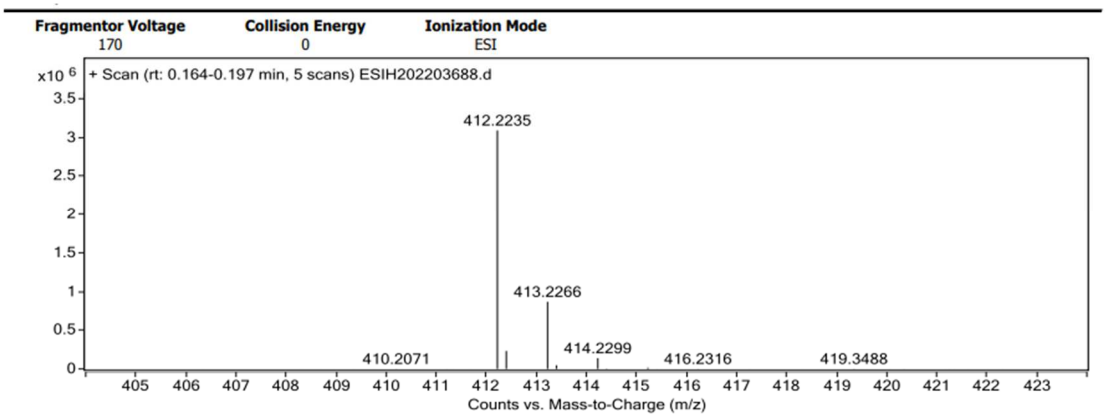


Figure S8. HRMS-ESI for compound **2d.**

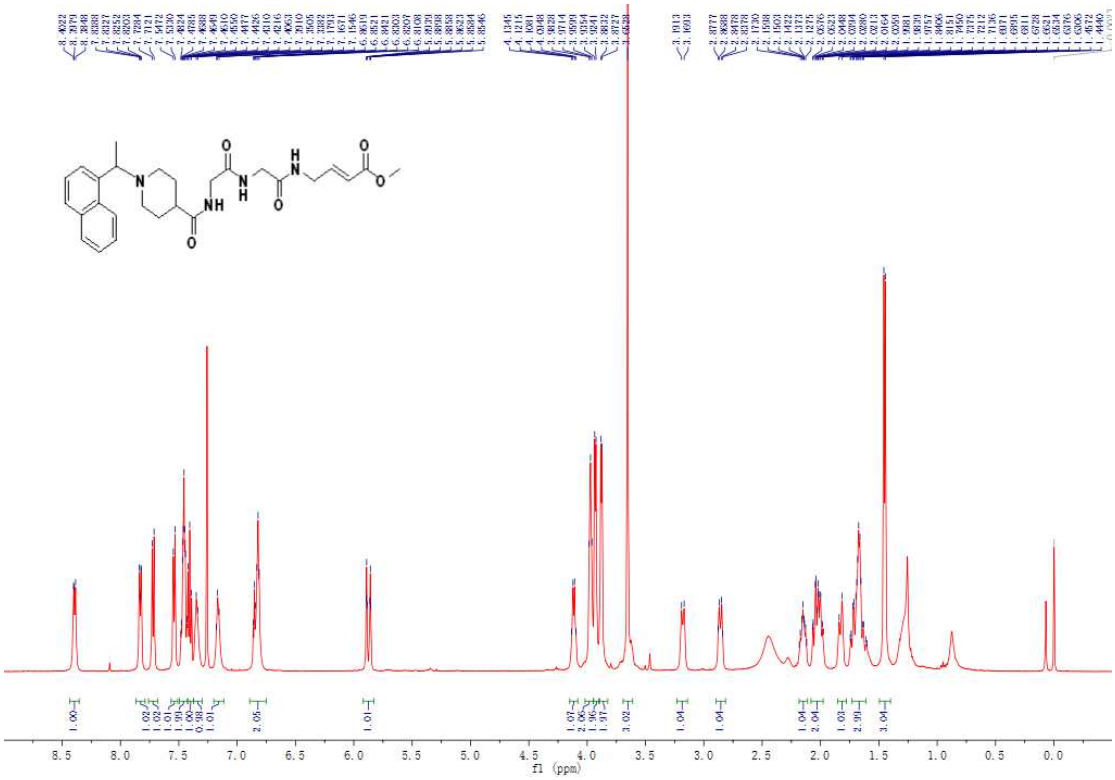


Figure S9. ^{1}H NMR Spectra for compound **2.**

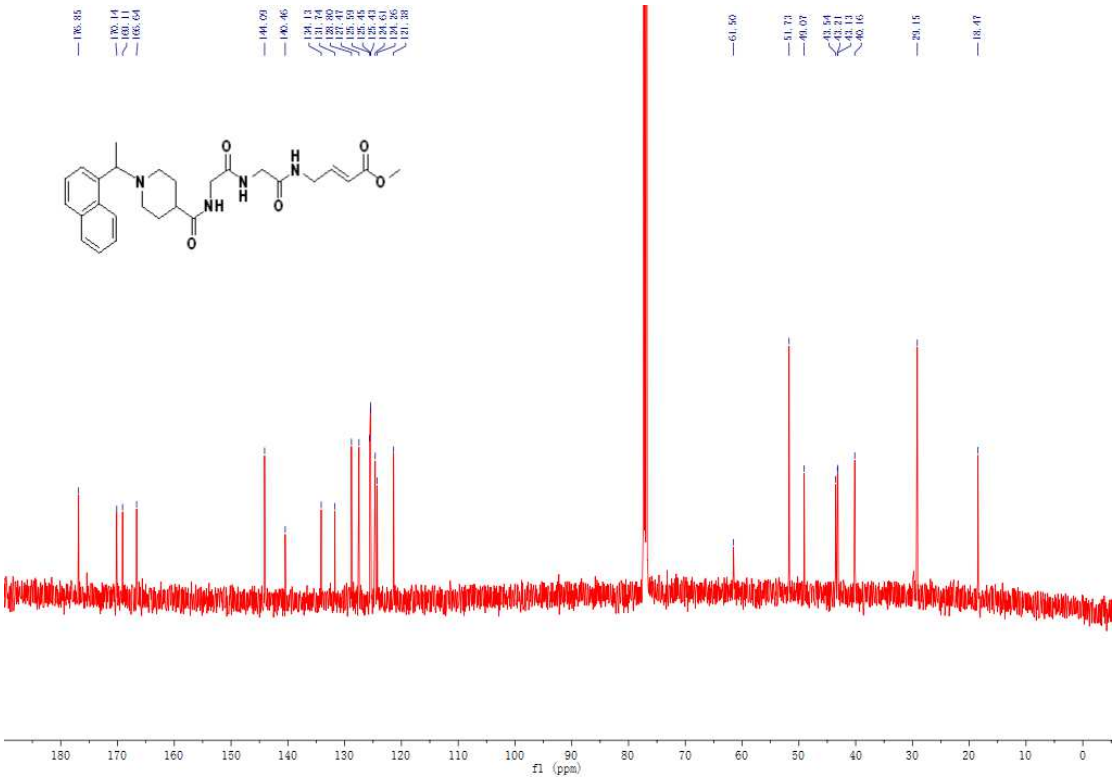


Figure S10. ^{13}C NMR Spectra for compound **2.**

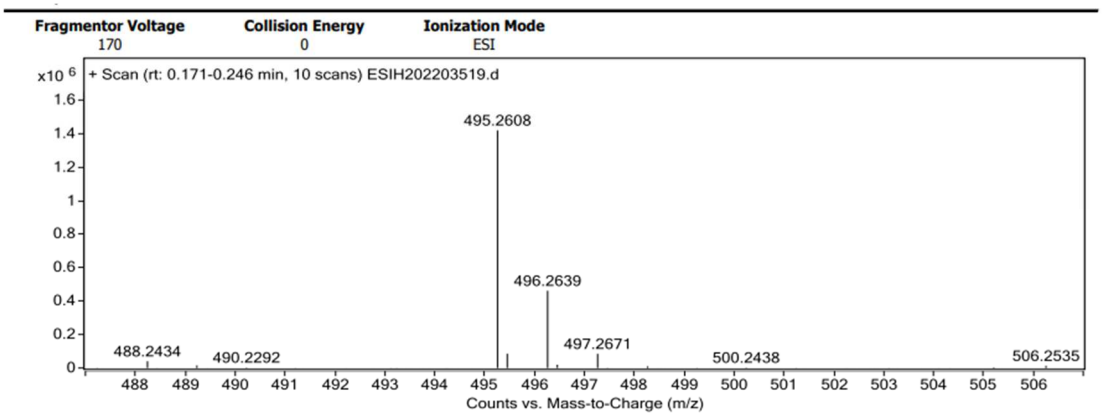
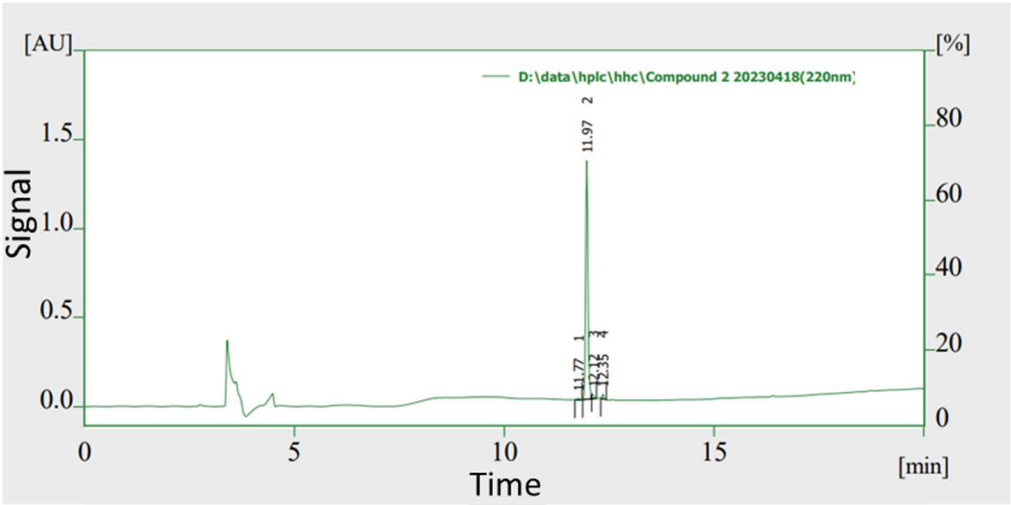
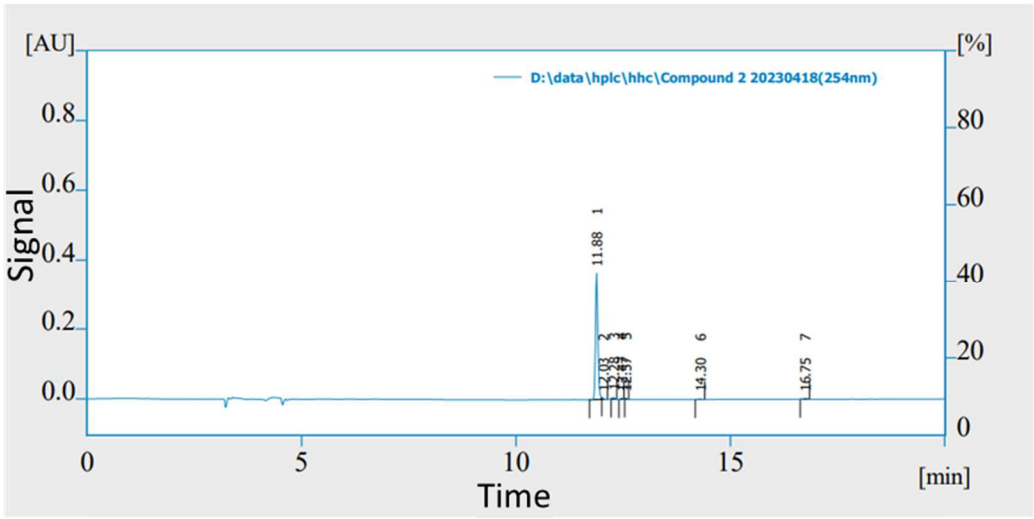


Figure S11. HRMS-ESI for compound **2**



Results Table:

	Retention Time [min]	Peak Area [mAU.s]	Area [%]	Peak Height [mAU]
1	11.767	32.990	0.6	9.545
2	11.967	5101.261	95.7	1339.993
3	12.117	110.727	2.1	22.794
4	12.350	83.274	1.6	25.261
	Total	5328.252	100.0	1397.593



Results Table:

	Retention Time [min]	Peak Area [mAU.s]	Area [%]	Peak Height [mAU]
1	11.883	1417.414	96.0	364.688
2	12.033	15.761	1.1	3.068
3	12.283	14.680	1.0	4.216
4	12.467	8.598	0.6	2.792
5	12.567	7.218	0.5	2.303
6	14.300	5.333	0.4	1.188
7	16.750	8.094	0.5	1.656
	Total	1477.098	100.0	379.910

Figure S12. HPLC traces for compound **2**

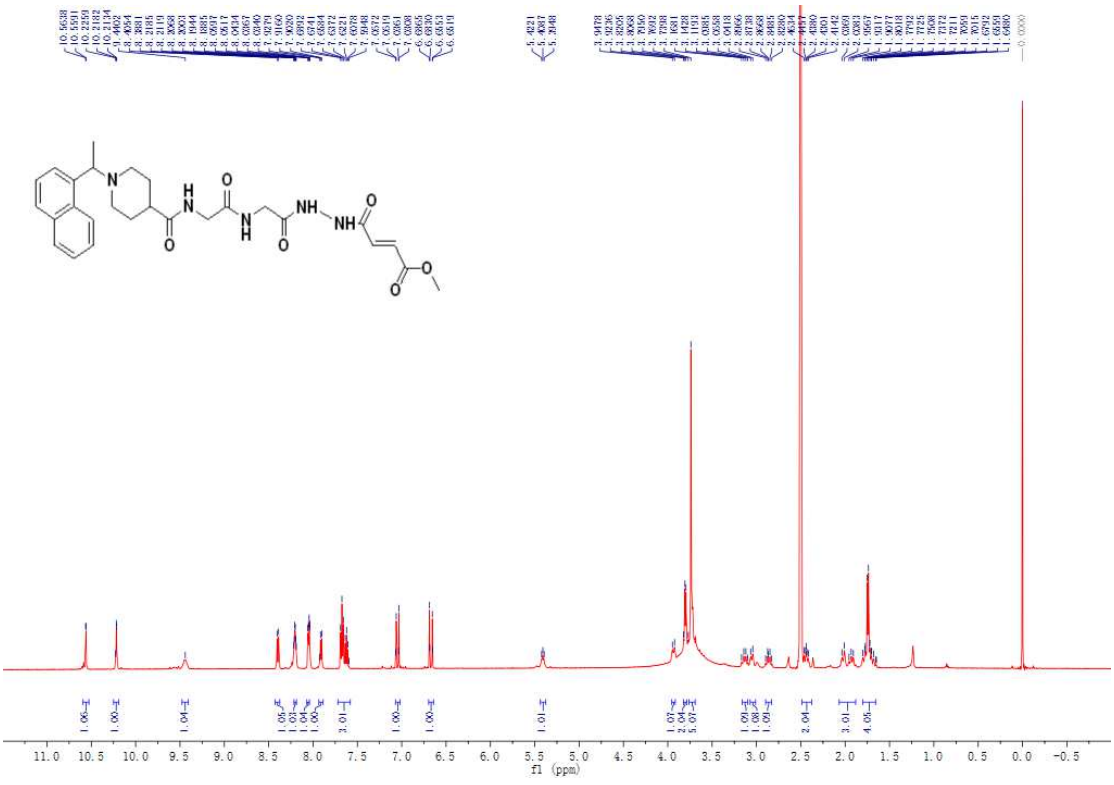


Figure S13. [1]H NMR Spectra for compound **4.**

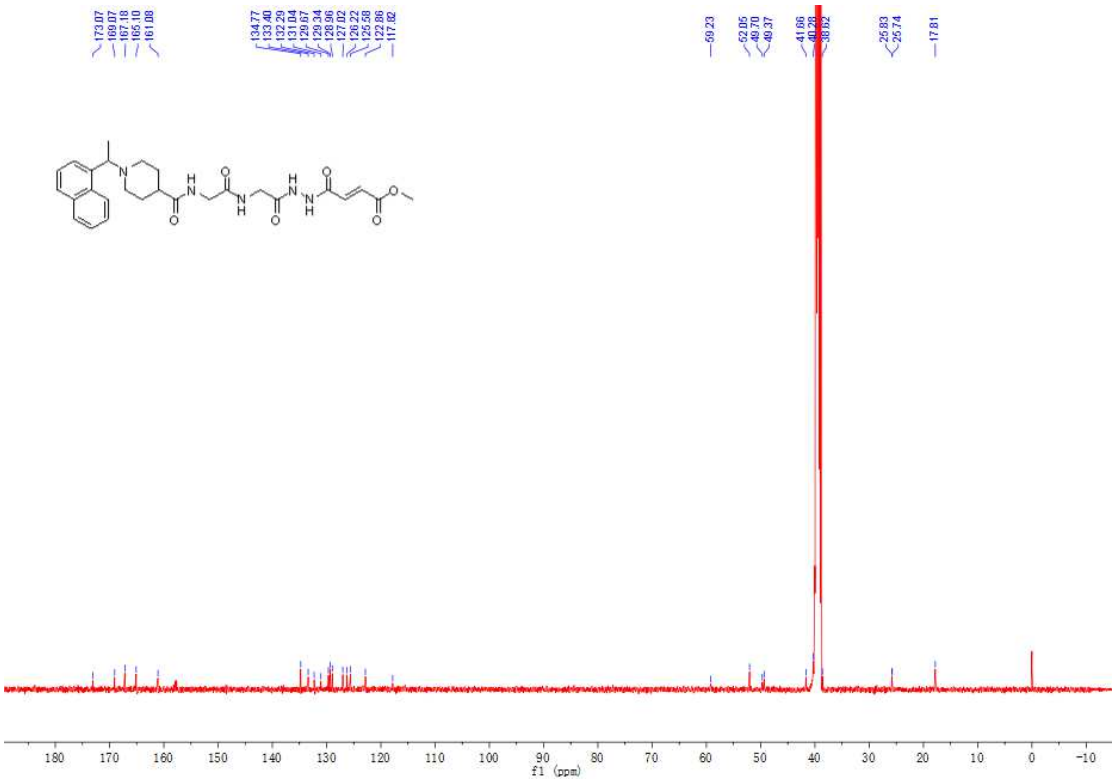


Figure S14. [13]C NMR Spectra for compound **4.**

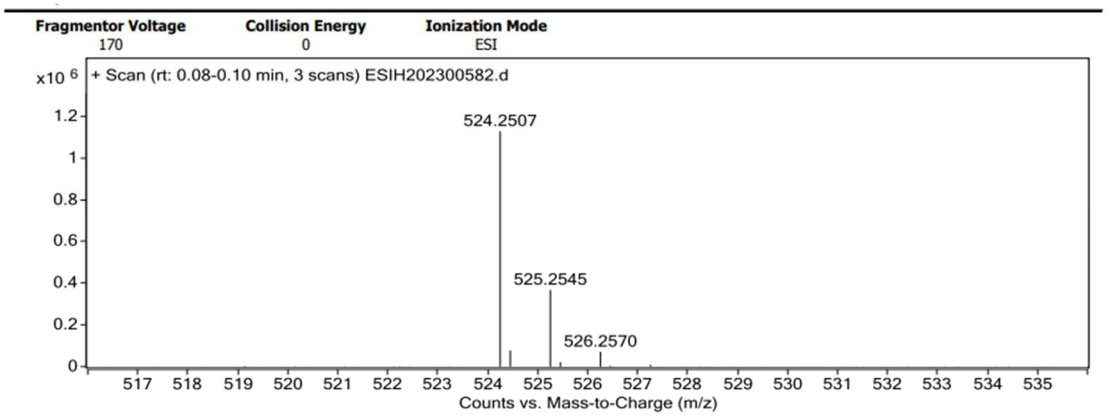
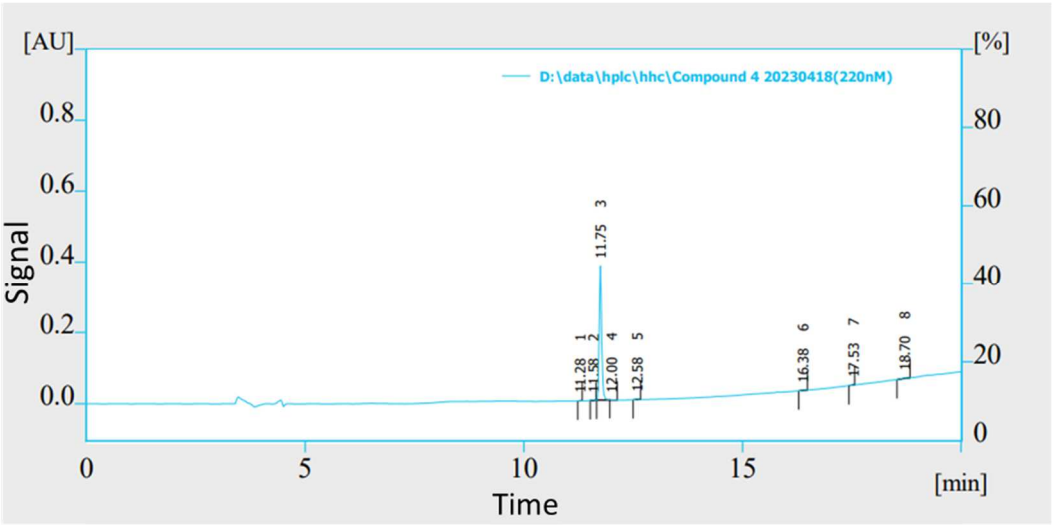
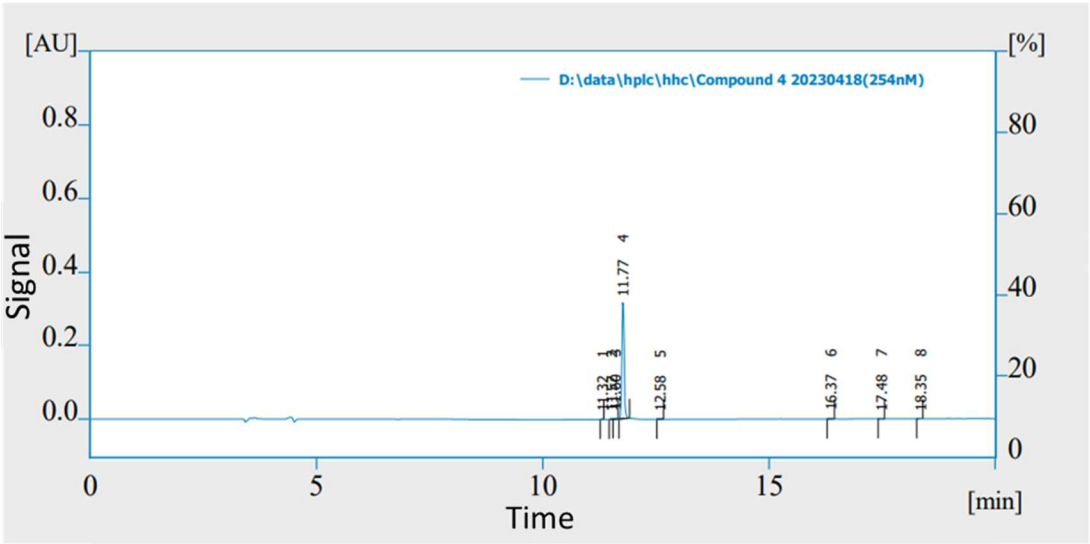


Figure S15. HRMS-ESI for compound **4.**



Results Table

	Retention Time [min]	Peak Area [mAU.s]	Area [%]	Peak Height [mAU]
1	11.283	2.238	0.1	0.774
2	11.583	6.362	0.4	1.836
3	11.750	1469.927	97.0	379.153
4	12.000	9.065	0.6	1.373
5	12.583	8.370	0.6	2.110
6	16.383	4.572	0.3	1.188
7	17.533	1.472	0.1	0.327
8	18.700	13.916	0.9	2.267
	Total	1515.922	100.0	389.029



Results Table:

	Retention Time [min]	Peak Area [mAU.s]	Area [%]	Peak Height [mAU]
1	11.317	1.568	0.1	0.619
2	11.517	4.117	0.3	1.471
3	11.600	12.635	1.1	3.119
4	11.767	1158.280	96.8	314.900
5	12.583	3.176	0.3	0.803
6	16.367	9.186	0.8	2.185
7	17.483	4.656	0.4	1.221
8	18.350	3.324	0.3	0.952
	Total	1196.942	100.0	325.270

Figure S16. HPLC traces for compound **4**