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Figure S2. Thermal stability of recombinant Nps5 (protein concentration: 3.4 μ M) in Tris buffer (20 mM Tris, 140mM NaCl, pH 8) before (wild type Mpro) and after the labelling reaction (red Mpro). The experiment was carried out using nano-DSF with Tycho NT.6 instrument.

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Figure S8. MST binding curve of urolithin D (**11**) against the main protease Nsp5. The curve is obtained plotting the initial fluorescence change (Raw Fluorescence) vs ligand concentration (M).

Table S1.

Protein Sample	T_i (°C)
Nsp5 (wild type Mpro)	60.1 ± 0.1
Nsp5 (wild type Mpro) – after 48 h	60.3 ± 0.1
NT650-Nps5 (red Mpro)	60.3 ± 0.1

Table S2.

Compound	GScore (kcal/mol) Replica #1	GScore (kcal/mol) Replica #2	GScore (kcal/mol) Replica #3	GScore (kcal/mol) Replica #4	GScore (kcal/mol) Replica #5	GScore (kcal/mol) Replica #6	Mean \pm st. dev.
Myricetin (2)	-7.073	-7.073	-7.073	-7.073	-7.073	-7.073	-7.073 \pm 0.000
Ellagic Acid (7)	-6.085	-6.085	-6.085	-6.085	-6.085	-6.085	-6.085 \pm 0.000
Urolithin A (8)	-6.343	-6.462	-6.462	-6.462	-6.462	-6.462	-6.44217 \pm 0.04858
Urolithin B (9)	-5.739	-5.739	-5.739	-5.739	-5.739	-5.739	-5.739 \pm 0.000
Urolithin C (10)	-6.082	-6.081	-6.081	-6.081	-6.081	-6.081	-6.08117 \pm 0.00041
Urolithin D (11)	-6.520	-6.518	-6.518	-6.518	-6.518	-6.518	-6.51833 \pm 0.00082

Figure S1.

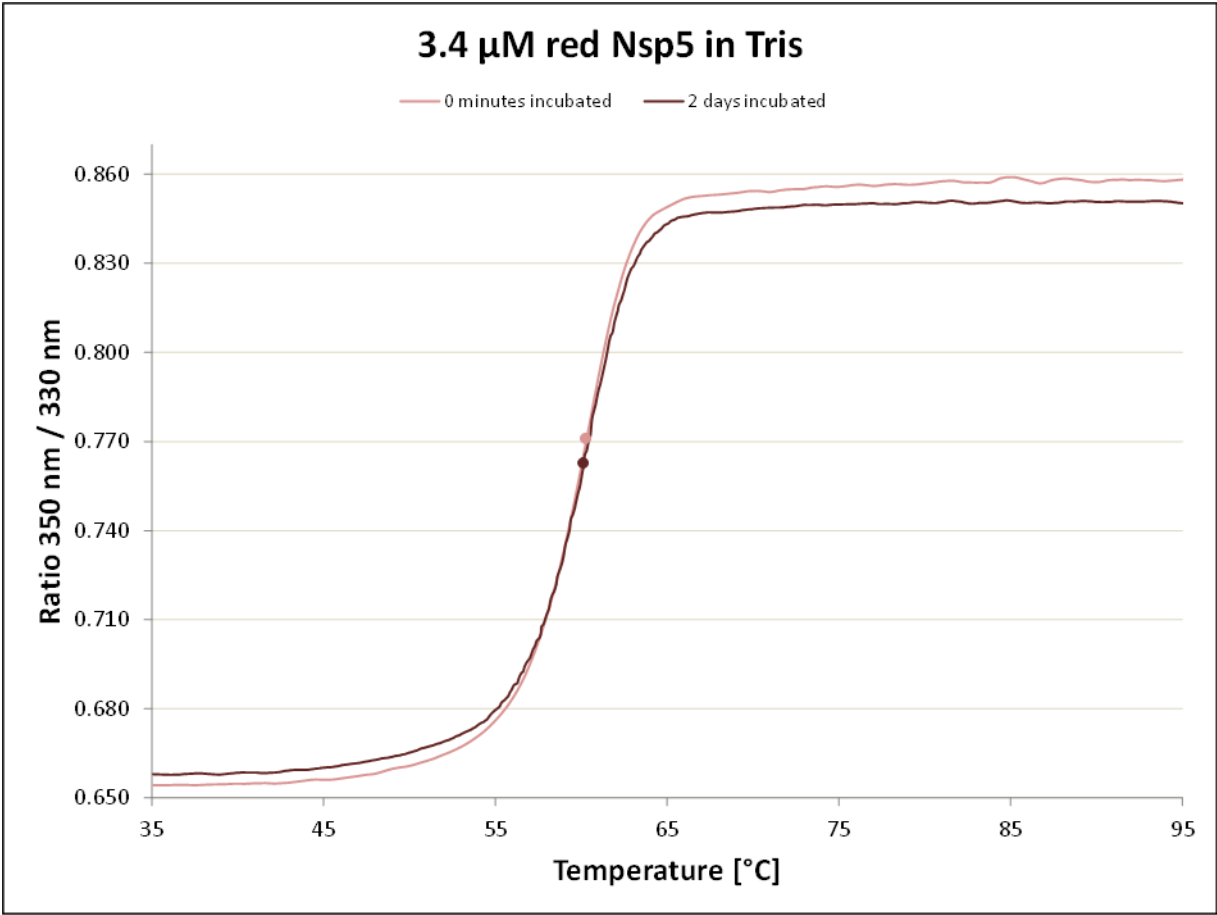


Figure S2.

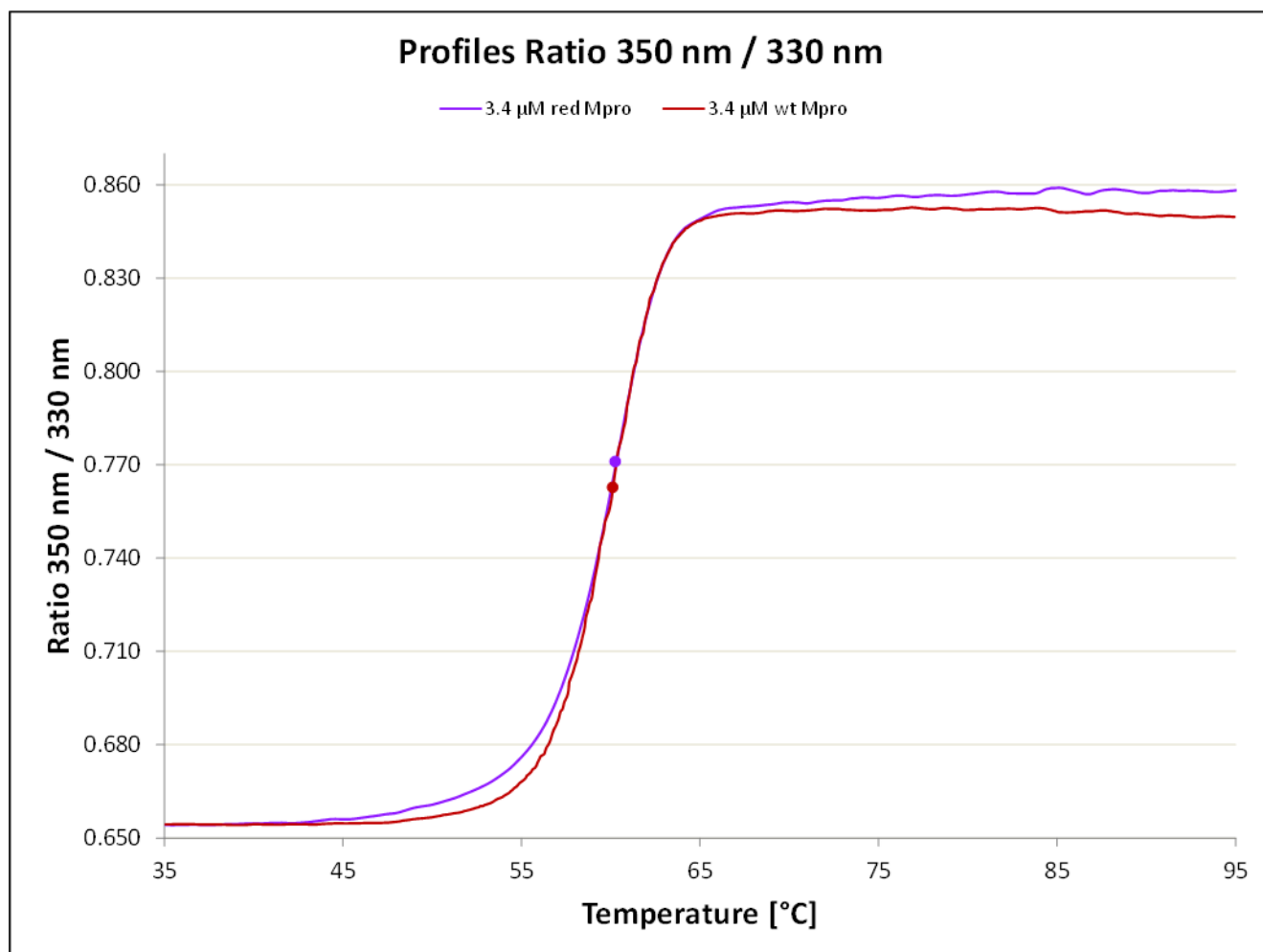


Figure S3.

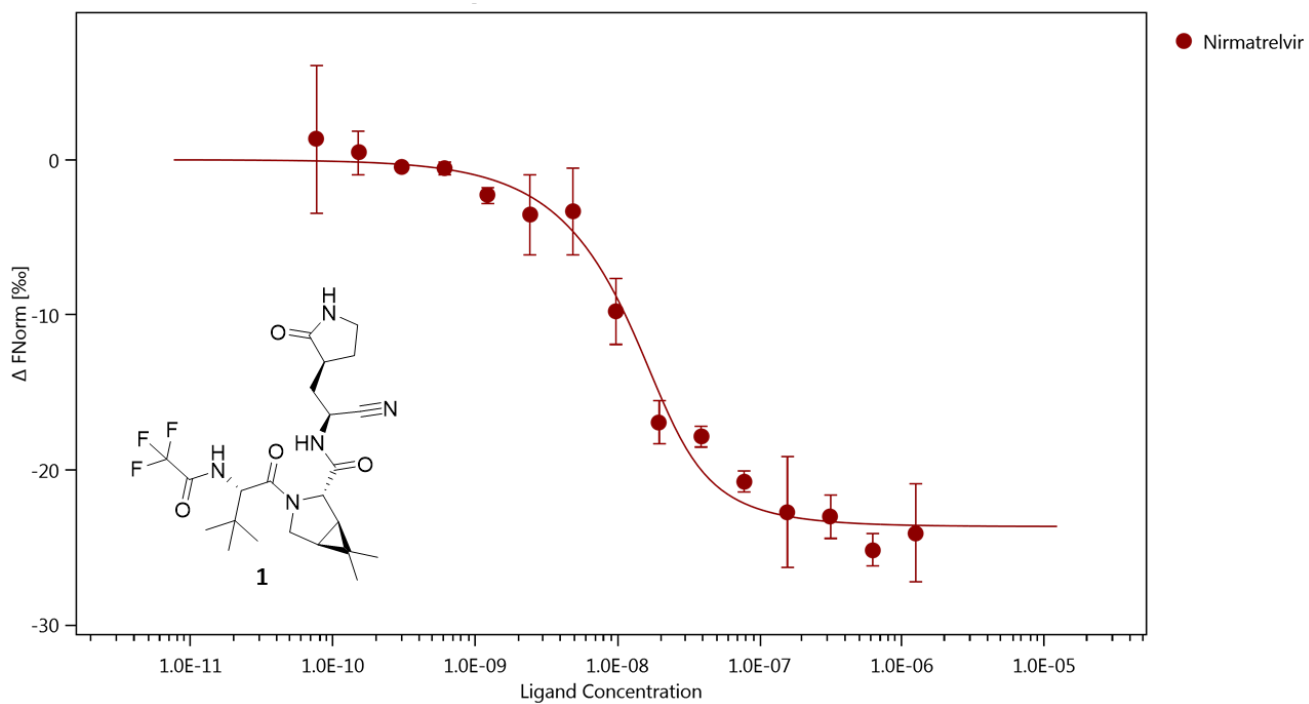


Figure S4.

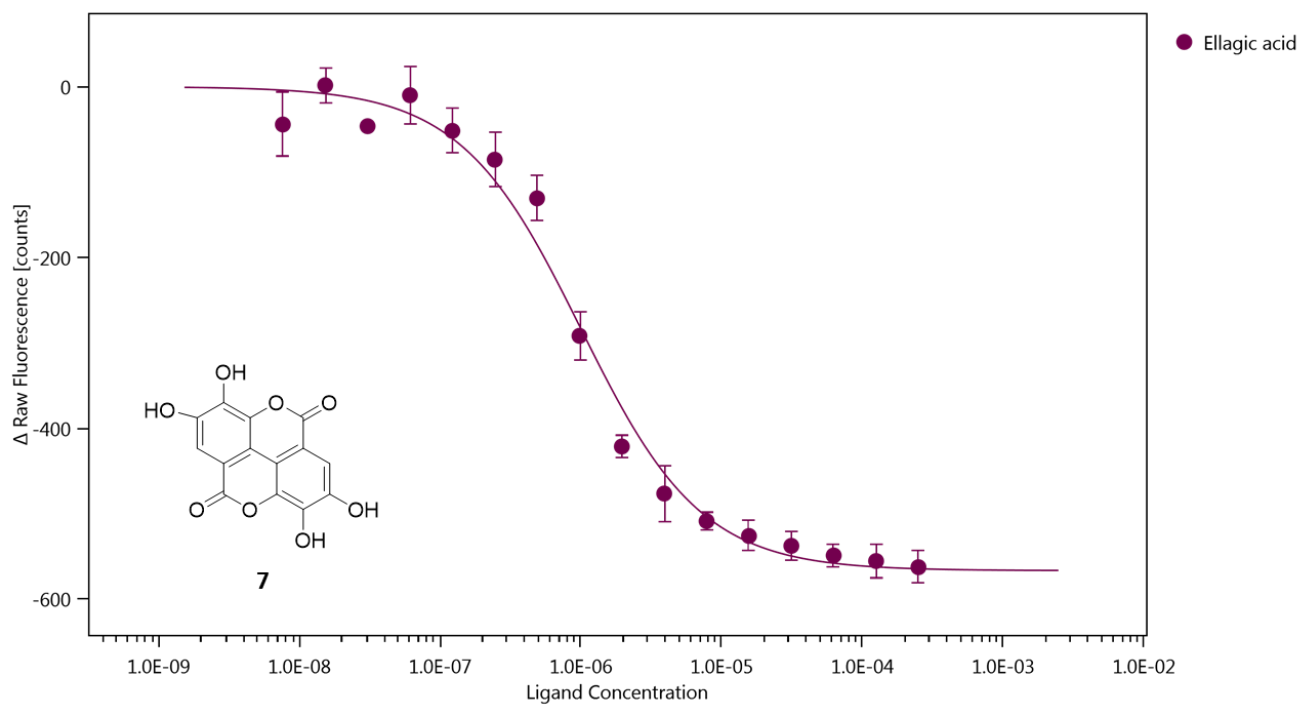


Figure S5.

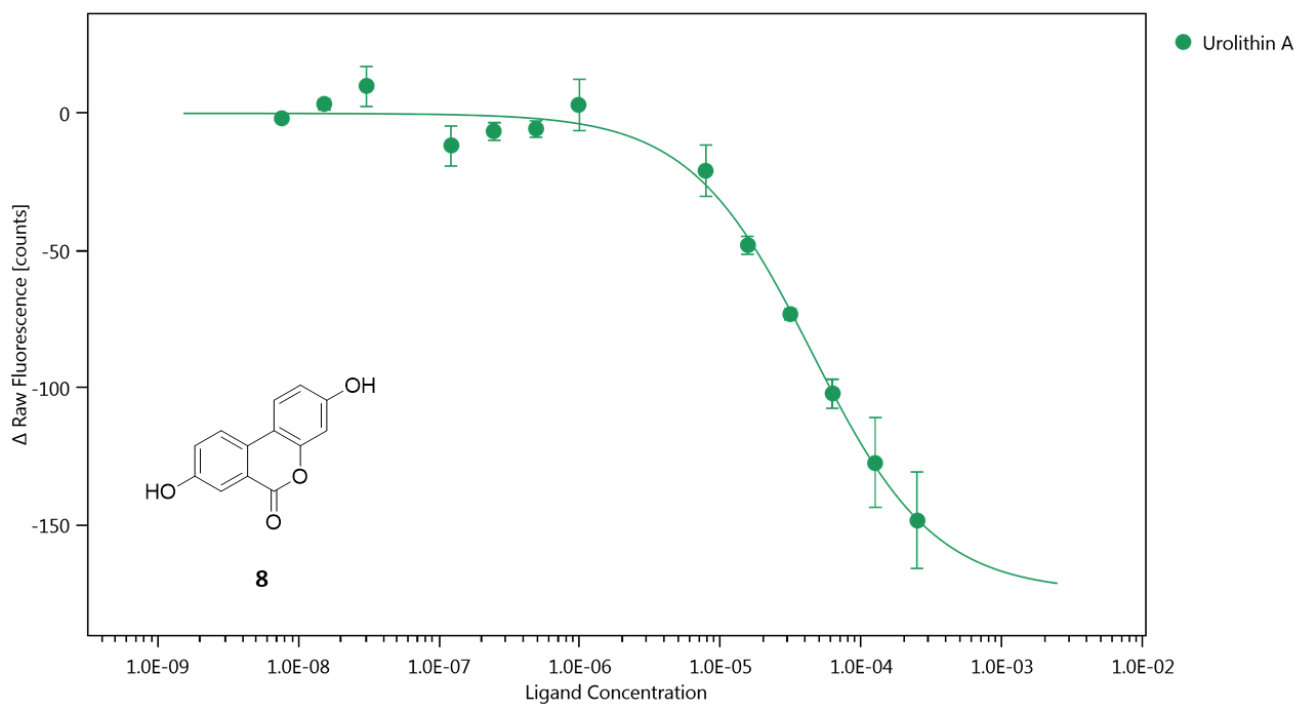


Figure S6.

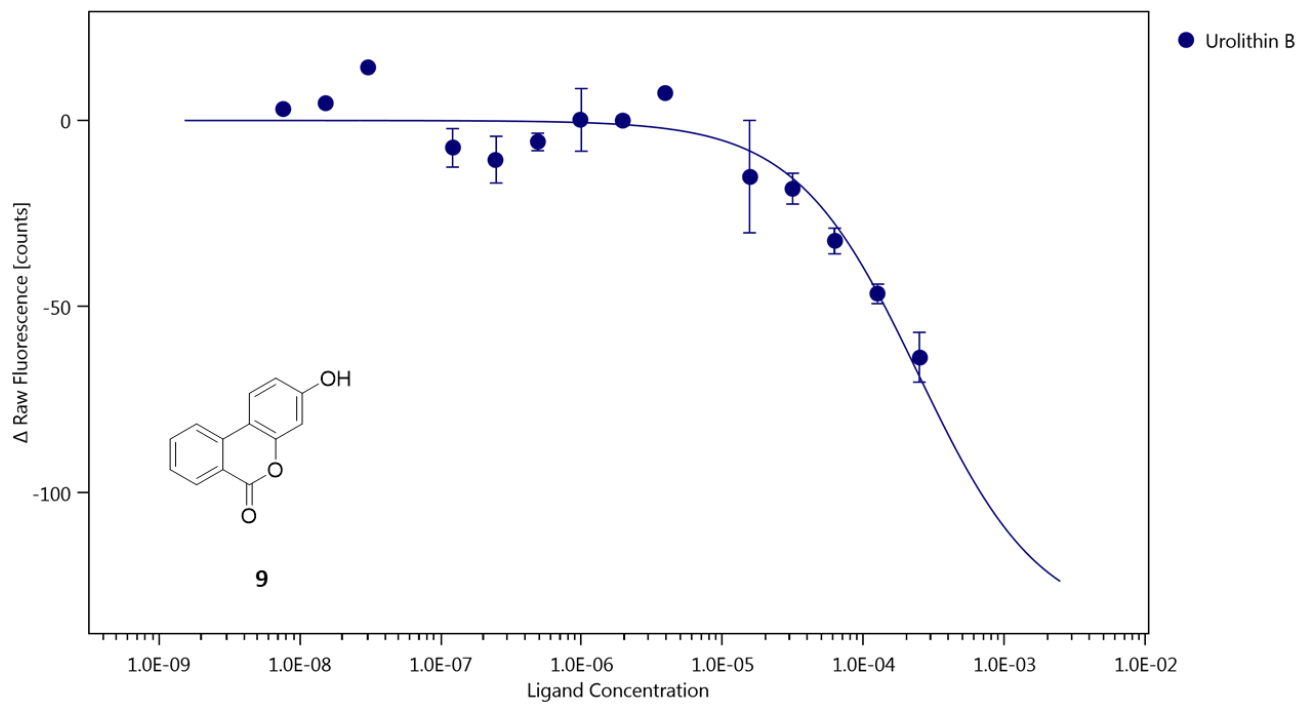


Figure S7.

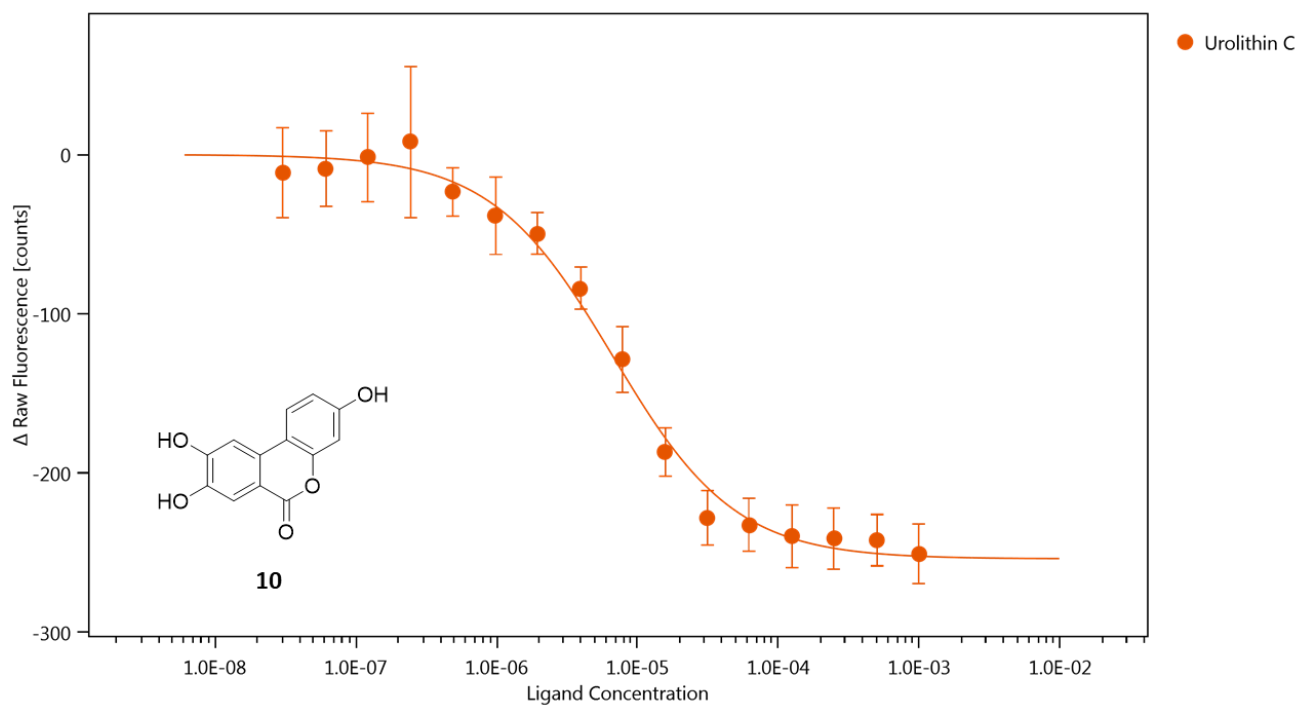


Figure S8.

