

Roy et al.
Supplemental Materials

Tables S1-S2
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Supplemental Table 1: IC₅₀ of the selected compounds in AS, FP, and FRET assays

Compound Identification number (CID)	Vendor ID	IC ₅₀ AS SARS-CoV-2 (μM)	IC ₅₀ FP SARS-CoV-2 (μM)	IC ₅₀ AS MDO2 (μM)	IC ₅₀ AS MERS (μM)	IC ₅₀ FRET SARS-CoV-2 (μM)
ADP-ribose		1.5 ±0.05	9.74 ±0.75	0.42 ±0.05	1.25 ±0.23	N.D.
Compounds inhibit AS only						
652774	SEW06255 (4)	7.95 ± 0.8	>300	N.D.	N.D.	N.D.
146057618	F594-1030 (8)	139.85 ± 3.0	>300	>300	N.D.	N.D.
146057597	F594-0985 (9)	74.91 ± 4.5	>300	>300	N.D.	N.D.
73089208	NP-002118 (14)	36.67 ± 3.7	>300	93.0	N.D.	N.D.

(N.D.) not determined

Table S2: Compound docking scores

Compound #	docking score	glide emodel	Mac1 Structure
1	-7.857	-81.695	6WOJ
6	-4.563	-50.414	7RK0
7	-3.338	-34.249	7RK0
8	-4.064	-57.015	7RK0
9	-4.287	-61.816	7RK0
10	-4.806	-59.941	6WEY
11	-5.306	-58.757	6WEY

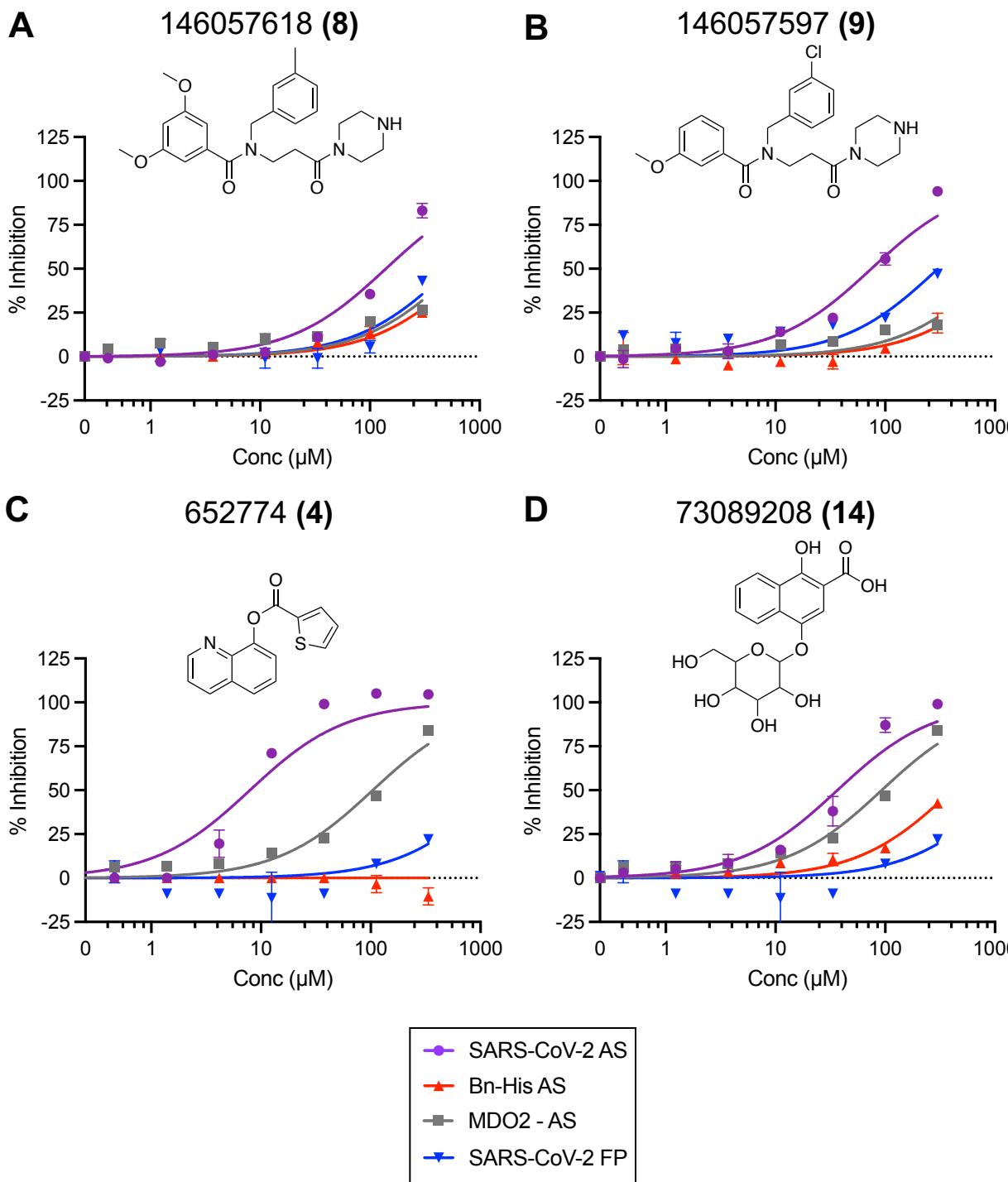


Fig. S1. Identification of chemical compounds that inhibit SARS-CoV-2 Mac1 ADP-ribose binding. Dose-response curves representing hit compounds identified in the HTS that only inhibited the AS assay, including compounds 8 (A), 9 (B), 4 (C), and 14 (D). Data was analyzed as described in Methods. Data represent the means \pm SD of at least 2 independent experiments for each compound. Structures were created using ChemDraw.

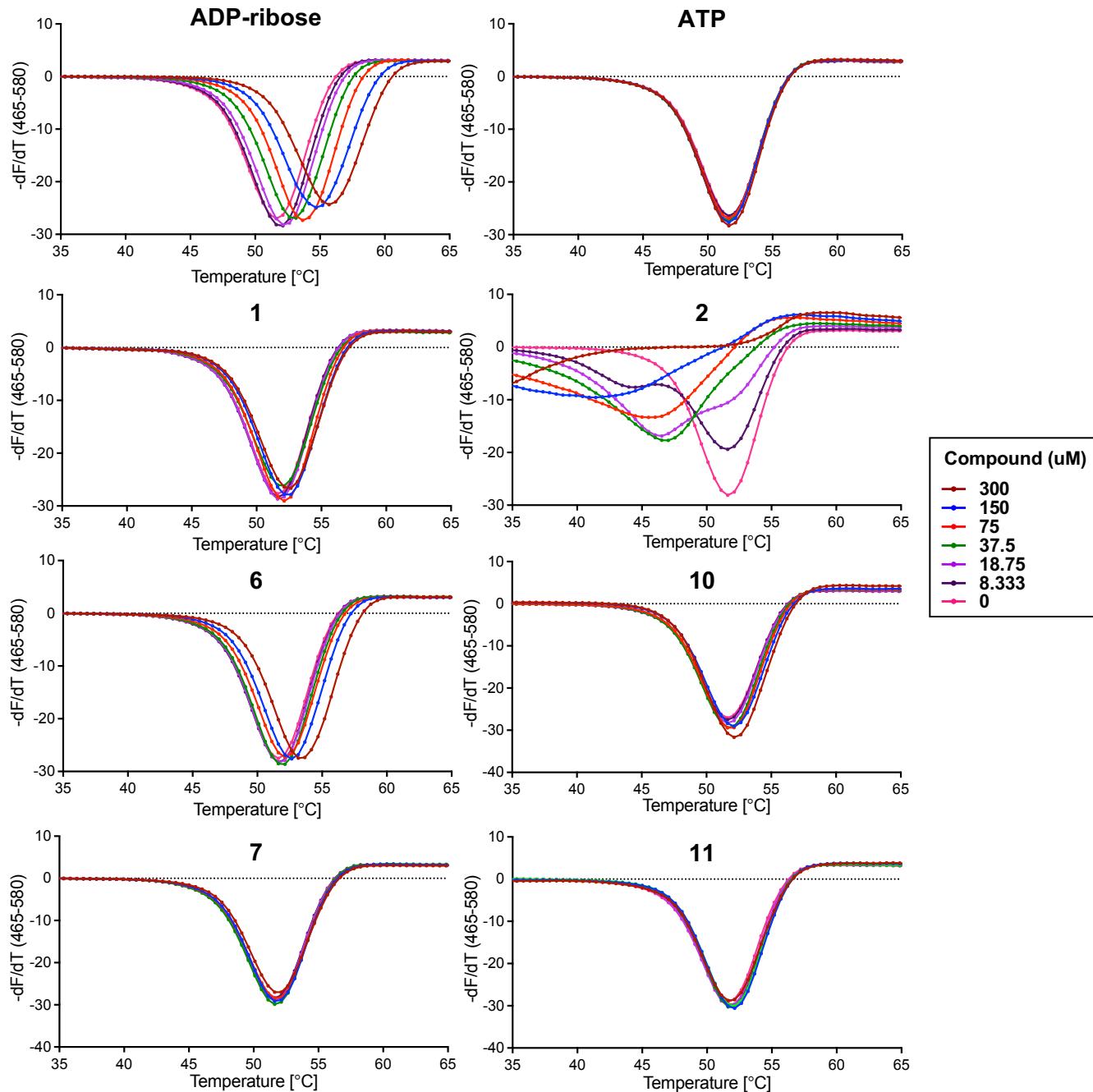


Fig. S2. Thermal stability of SARS-CoV-2 Mac1 after incubation with hit compounds. The top 6 hit compounds were tested for their ability to increase the thermal stability of SARS-CoV-2 Mac1 in a differential scanning fluorimetry assay (DSF). Thermal profiles are shown for each compound at different concentrations.

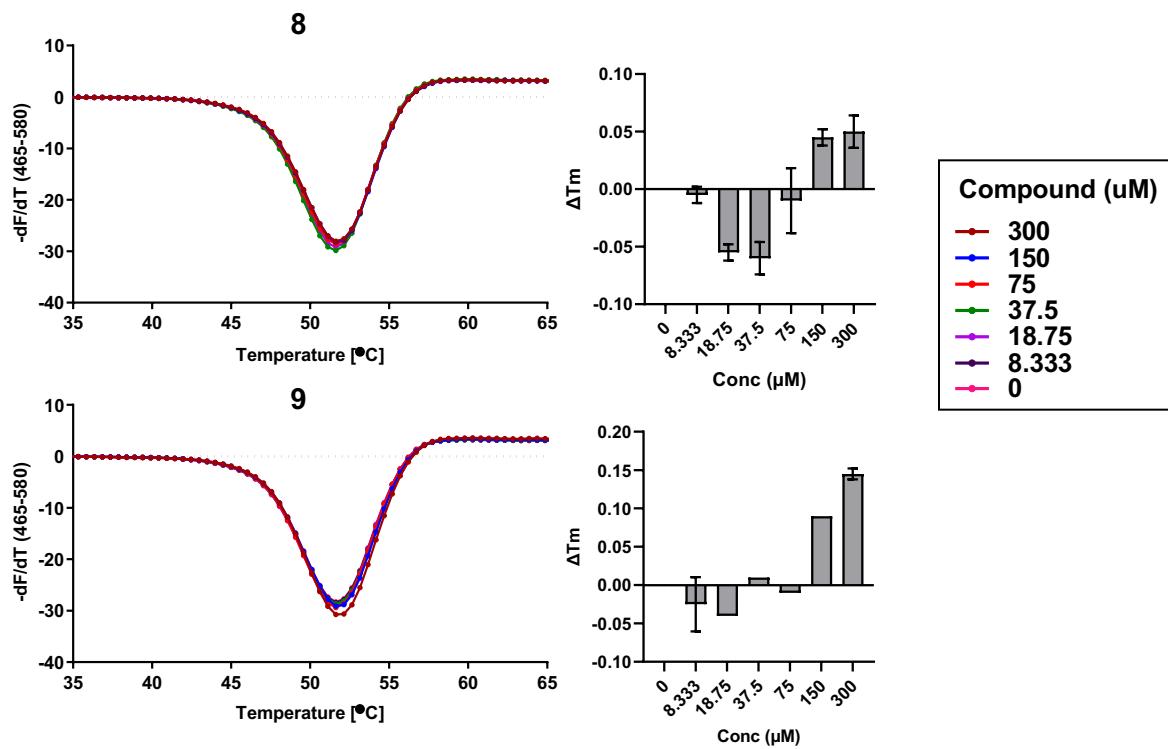


Fig. S3. Thermal stability of SARS-CoV-2 Mac1 after incubation with compound **6** analogs. Two analogs of **6**, **8** & **9**, are shown here for their ability to increase the thermal stability of SARS-CoV-2 Mac1 in a differential scanning fluorimetry assay (DSF). Thermal profiles and change in T_m are plotted for each compound at different concentrations.