Supporting Information

An Overview of Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) 3CL Protease Inhibitors: Peptidomimetics and Small Molecule Chemotherapy

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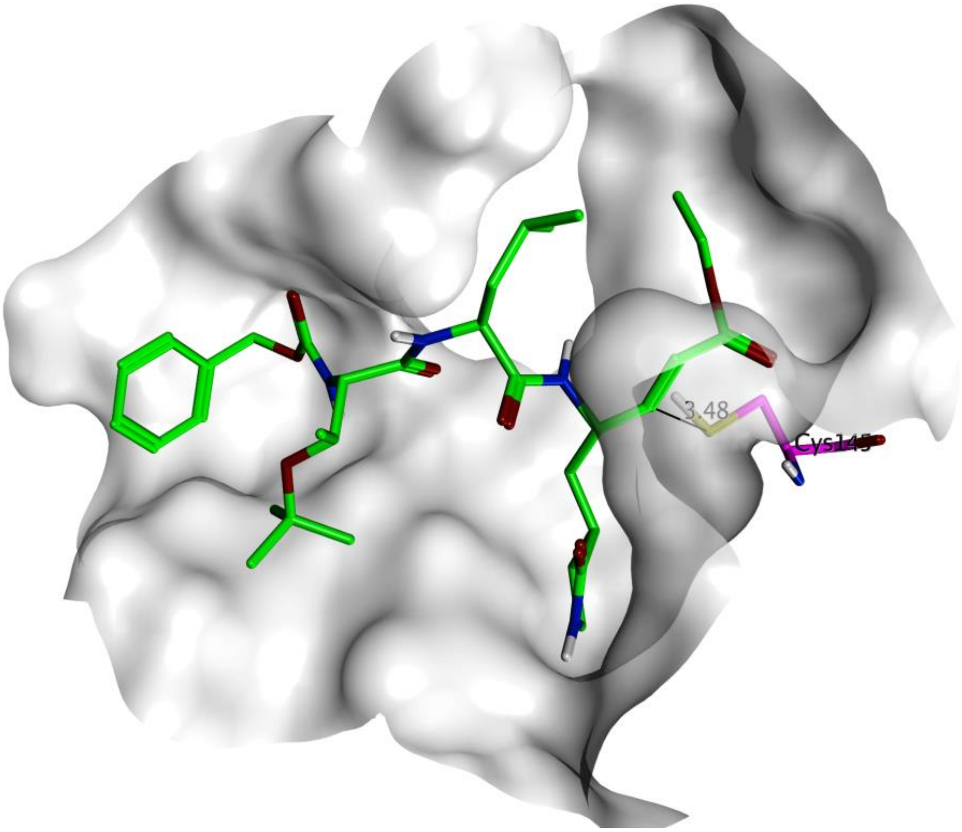

Figure S1: The docked pose of compound **18** (green) into the binding pocket of SARS 3CL^{pro} (PDB ID: 2GX4).[1] The key interacting amino acid Cys145 is highlighted in magenta and binding pocket in grey.

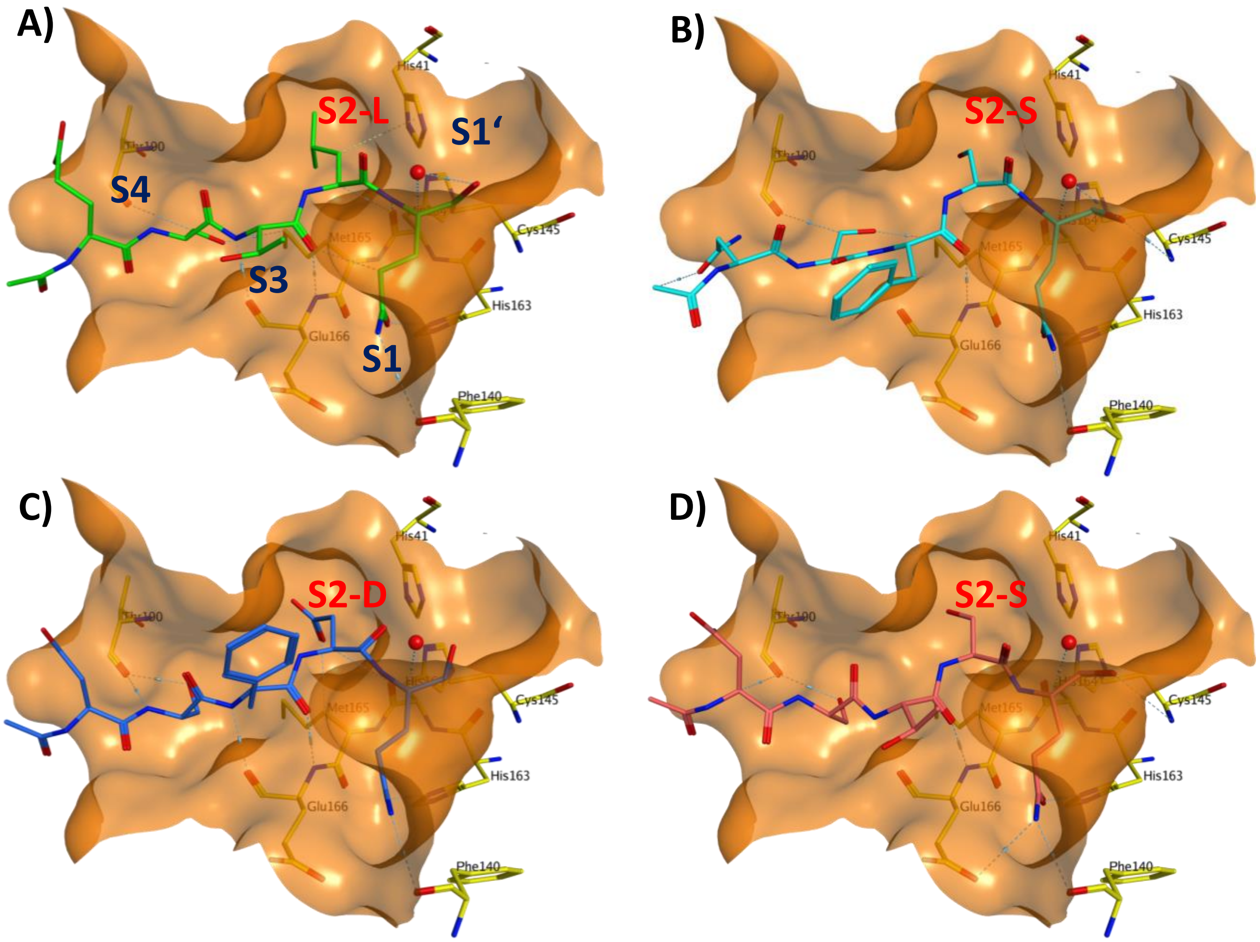

Figure S2: The crystal structure of compounds **40-43** complexed with SARS $3CL^{pro}$. The compounds A) 41 (green, PDB ID:3SNE) B) 42 (cyan, PDB ID:3SNA) C) 43 (blue, PDB ID:3SNB) and D) 44 (brown, PDB ID:3SNC) shown in stick model and highlighted with their respective amino acids in the S2 pocket.[2]

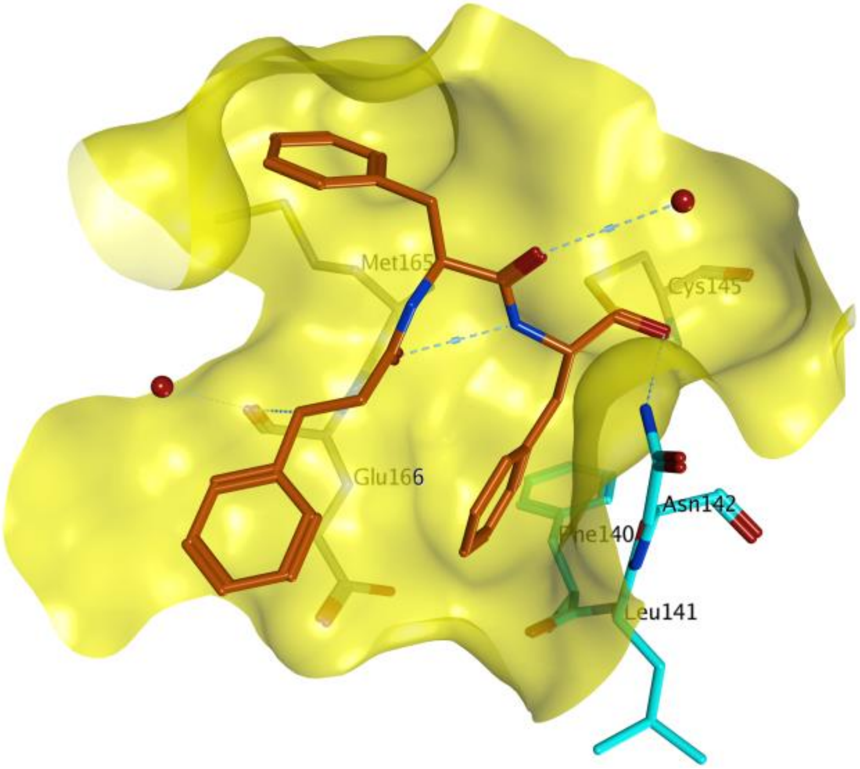

Figure S3: The crystal structure of compound **44**(brown) bound with SARS 3CL^{pro}. The amino acids in the binding pocket (grey) with the important amino acids (cyan) are highlighted.[2]

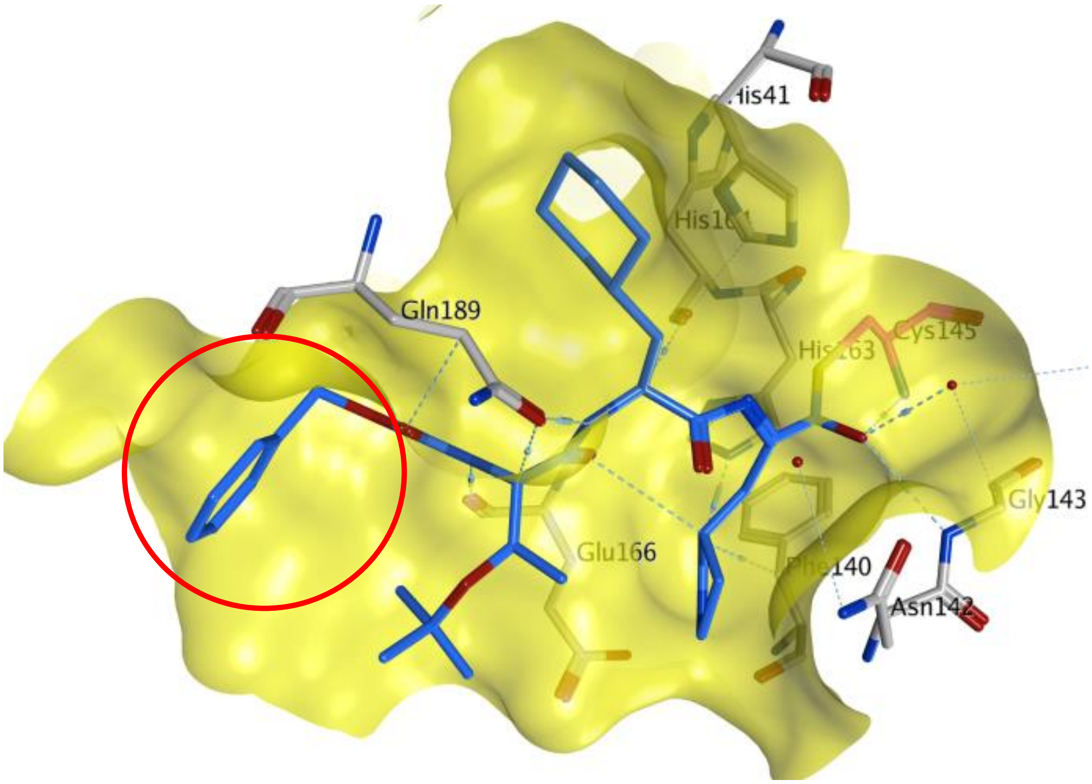

Figure S4: The crystal structure complex of compound **45**(blue) and SARS 3CL^{pro}. The unique conformation of benzyloxy is shown in red circle, the amino acids in the binding pocket (grey) and covalent bonding of **45** with Cys145 (magenta) is highlighted.[1]

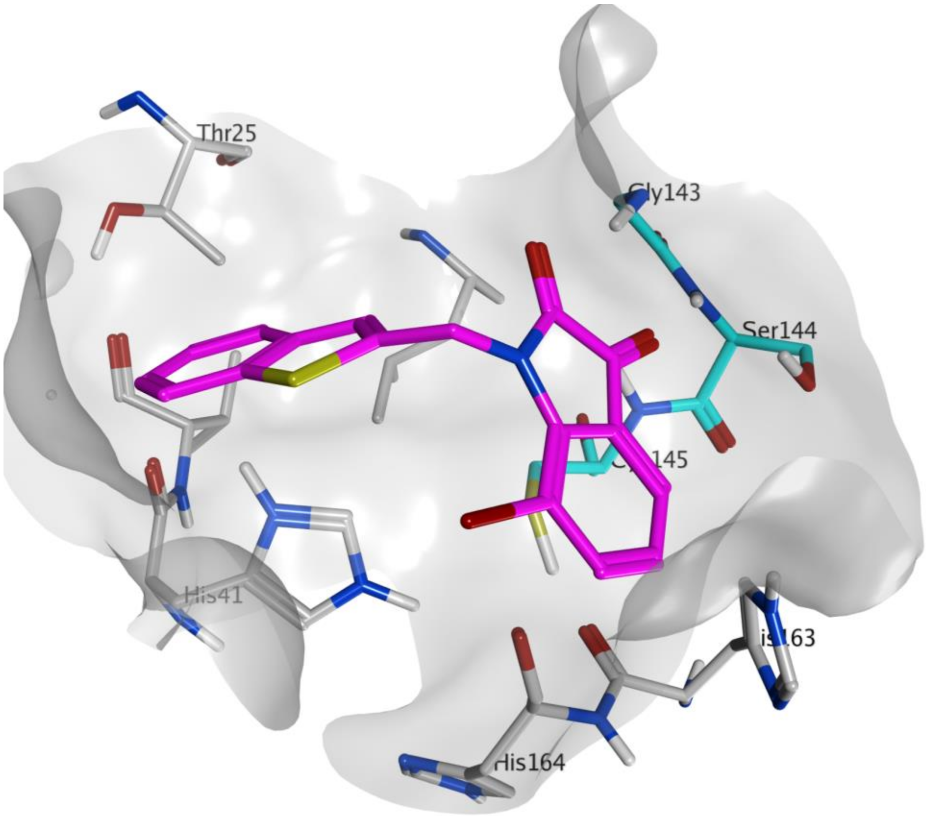

Figure S5: The docked pose of compound **78**(magenta) into the binding pocket of SARS 3CL^{pro} (PDBID: 1UK4).[3]The key interacting amino acids (cyan) are highlighted with the amino acids in the binding pocket (grey).

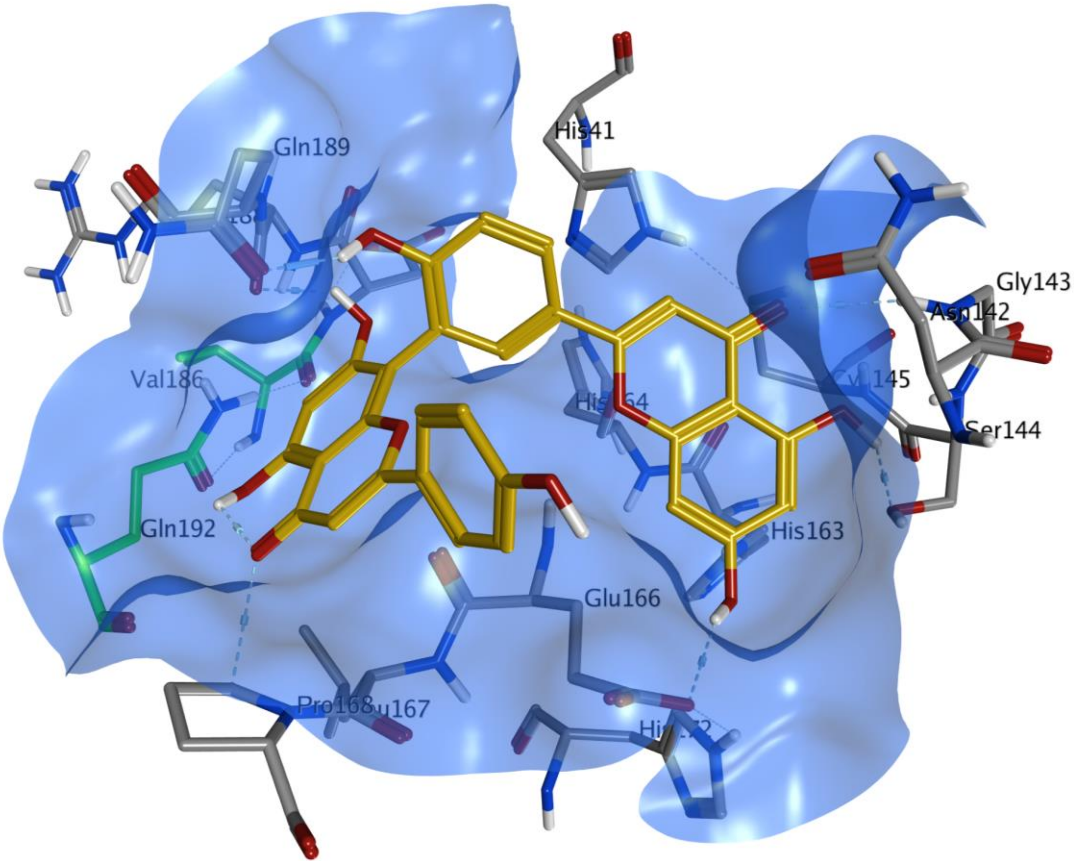

Figure S6: The docked pose of compound **86**(golden yellow) in the binding pocket of SARS 3CL^{pro} (PDBID: 2Z3E).[4] The key interacting amino acids Gln192 and Val186 (green) are highlighted with the amino acids in the binding pocket (grey).

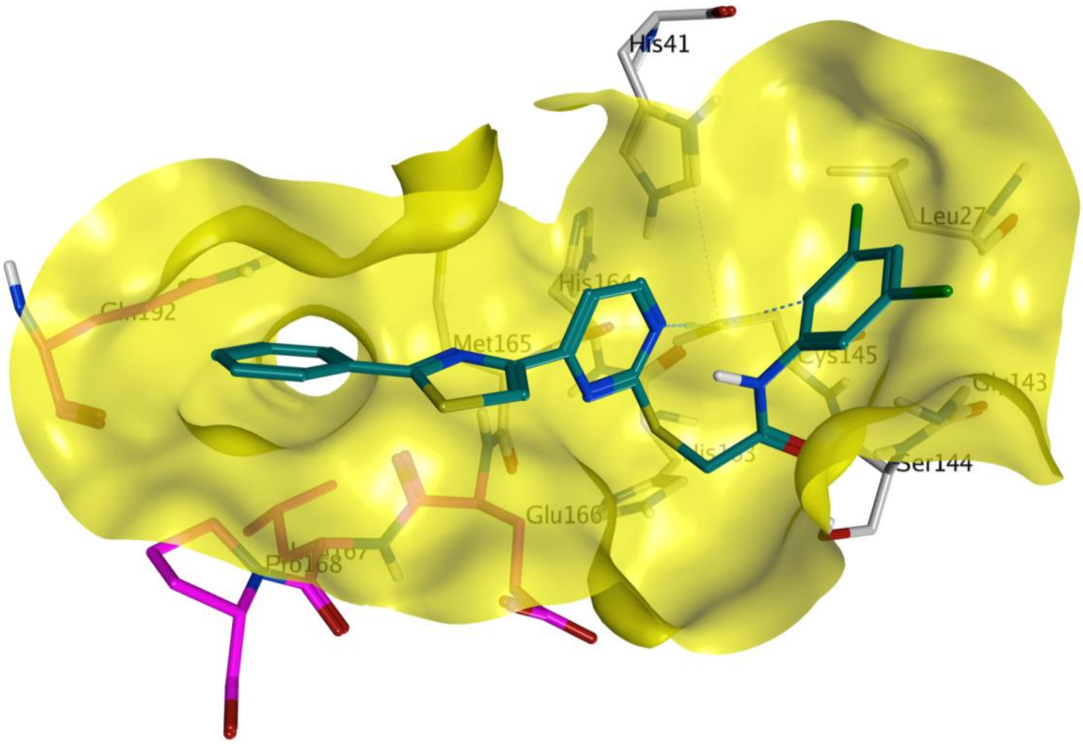

Figure S7: The docked pose of compound **105**(blue) in the binding pocket of SARS 3CL^{pro} (PDBID: 1UK4).[3] The key interacting amino acids Glu166, Pro168, and Gln192 (magenta) are highlighted with the amino acids in the binding pocket (grey).

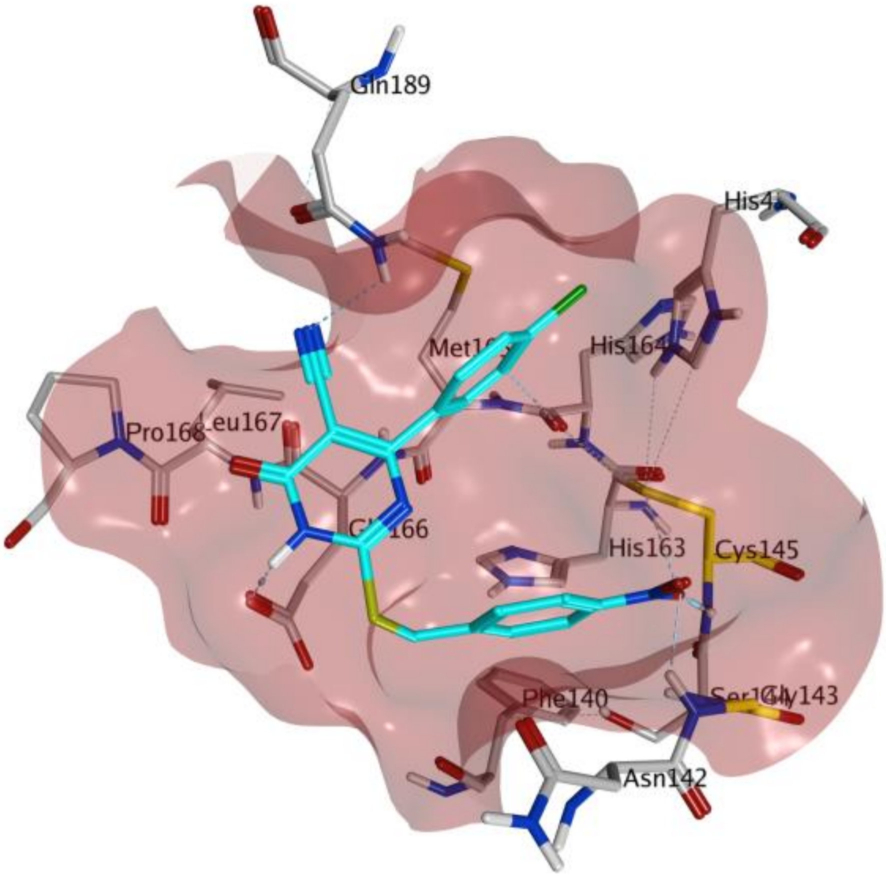

Figure S8: The docked pose of compound **140** (cyan) in the binding pocket of SARS 3CL^{pro} (PDBID: 1UK4).[3]Nitro group formed a hydrogen bond with side chains of Gly-143 and Cys145, and the 4-*c*hloro phenyl ring was predicted to fit into the S2 pocket.

Table 1. Sequence comparison analysis of 3CL^{pro} of Coronaviruses to the SARS-CoV 3CL^{pro} Tor2 strain.[12]

Coronaviruses	**Sequence identity to SARS-** 3CL^{pro} (%)	**Sequence similarity to** 3CL^{pro} (%)
HCoV-HKU1	48	62
HCoV NL63	43	60
HCoV-OC43	49	64
HCoV-229E	40	65
SARS-Civet	100	100
Bat-CoV	52	70
TGEV	44	67
PEDV	44	69
MHV	50	73
BCV	49	71
Giraffe-CoV	48	64
IBV	44	64
FIPV	43	60

Table 2. A List of X-ray crystal structures of ligand with proteases

E.No	PDB ID	Protein Name	Ligand Name	Resolution (Å)	Reference
1	**1CQQ**	Type 2 Rhinovirus 3C^{pro}	peptidomimetic **2** (or AG7088**)**	1,85	5
2	**1P9U**	Transmissible gastroenteritis coronavirus (TGEV) 3CL^{pro}	peptidomimetic **1** (or CMK inhibitor)	2,37	5
3	**1UK2**	SARS- Coronavirus 3CL^{pro}	Small molecule, **178**	2,20	6
4	**1UK4**	SARS- Coronavirus 3CL^{pro}	Small molecule, **178**	2,50	6
5	**1Z1I**	SARS- Coronavirus 3CL^{pro}	Phenyl mercuric acetate, **168**	2,80	7
6	**2GX4**	SARS- Coronavirus 3CL^{pro}	peptidomimetic **45 (or TG-0205221**	1,93	1
7	**2Z3C**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **19**	1,79	8
8	**2Z3D**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **19**	2,10	8
9	**2Z3E**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **19**	2,32	8
10	**3SN8**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **44**	1,99	2
11	**3SNA**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **41**	3,05	2
12	**3SNB**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **42**	2,40	2
13	**3SNC**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **43**	2,58	2
14	**3SNE**	SARS- Coronavirus 3CL^{pro}	Peptidomimetic, **40**	2,60	2
15	**3V3M**	SARS- Coronavirus 3CL^{pro}	Small molecule, **146**	1,96	9
16	**4MDS**	SARS- Coronavirus 3CL^{pro}	Small molecule, **157**	1,60	10
17	**4TWW**	SARS- Coronavirus 3CL^{pro}	Small molecule, **143**	2,42	11

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