

IUCrJ

Volume 8 (2021)

Supporting information for article:

Crystallographic models of SARS-CoV-2 3CLpro protease: in-depth assessment of structure quality and validation

Mariusz Jaskolski, Zbigniew Dauter, Ivan Shabalin, Mirosław Gilski, Dariusz Brzezinski, Marcin Kowiel, Bernhard Rupp and Alexander Wlodawer

Supplementary Table S1. External Table in sortable MS Excel Table format containing additional data items used in or useful for further analysis. Using Custom Sort from the sort and filter menu allows for example to sort by space group and then by resolution. The Table can also be exported in other machine-readable formats. The non-tabular items are explanatory or ancillary only, the charts show examples for some statistical analysis.

| | |
|---------------------------------------|--|
| PDB ID | 4-character PDB identifier |
| Resol (Å) | reported resolution in PDB file |
| a, b, c (Å), alpha, beta, gamma (deg) | unit cell constants from CRYST1 record |
| Space group | space group symbol from CRYST1 plus polymorph indicator [*] |
| Vol (Å ³) | unit cell volume, computed as in (Rupp, 2009) |
| N (asu) | number of molecules in asymmetric unit, from PDB file |
| Z | multiplicity of general position for given space group |
| Vm (Å ³ /Da) | Matthews coefficient (Matthews, 1968) calculated as in (Weichenberger & Rupp, 2014) |
| Vs (%) | solvent content in % , calculated as in (Weichenberger & Rupp, 2014) |
| Rfree original | reported R _{free} from PDB file |
| Rfree re-refined | R _{free} after re-refinement per protocol listed in methods section |
| Temp | data collection temperature, cryogenic or room temperature |
| Source | type of X-ray or neutron source; sync: Synchrotron, home: Laboratory X-ray source, N: Neutron spallation source, XFEL: X-ray free electron laser |
| Inhibitor | trade name of inhibitor; self: self-inhibition by protease C terminus; 0: unliganded |
| Link | type of linkage; linked protease residue Cys145 |
| LIG | 3-letter HET identifier from PDB (multiple for inhibitory peptide analogs) |
| Tag/Mut | tags and mutants indicated <i>via</i> sequence number and single letter identifier extracted from SEQADV |
| pH | crystallization pH parsed from REMARK 280 if available [**] |
| Precip | presumed primary precipitant, parsed from REMARK 280, encoded as %Molecular_weight of PEG [**] |
| DMSO | percentage of DMSO added, if reported [**] |
| Buffer | main buffer component extracted from REMARK 280; encoded as molarity and buffer type abbreviation (self-explanatory) [**] |
| Remarks and reference | self-explanatory |

[*] Polymorph indicator *_a, _b, _c* indicates a non-isomorphous polymorph of the same space group. (*/2*) indicates that, for consistency, the original */2* unit cell was transformed to polymorph *C2_a*.

[**] Crystallization condition reporting is not standardized in any machine-readable form; this table includes only a limited subjective subset.

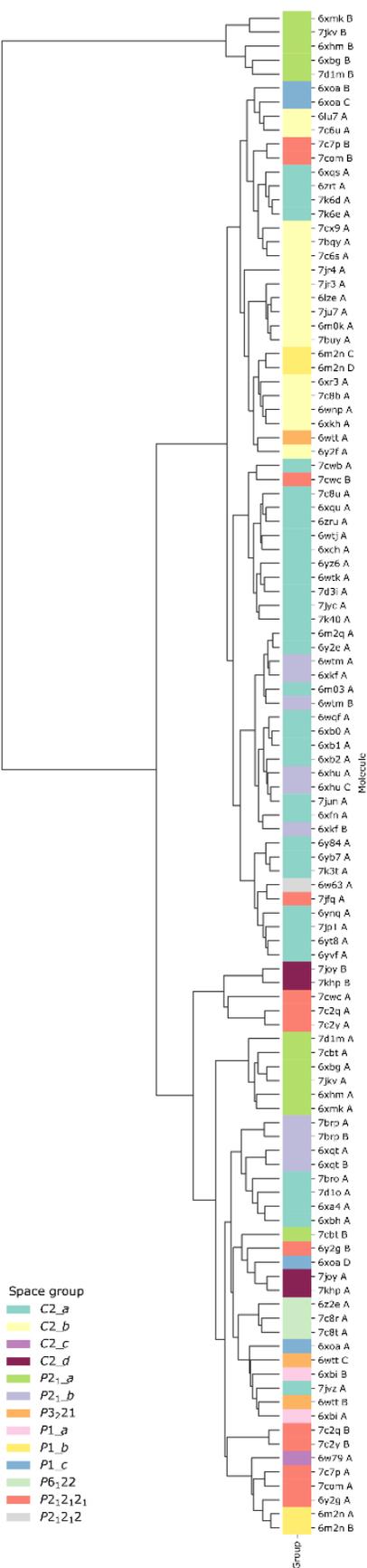
Supplementary Table S2. Selected geometrical parameters of 3CLpro models as originally deposited in the PDB. The values in each row are: torsion angle N-C α -C β -S γ of Cys145 [χ_1 (C145)], torsion angles C α -C β -C γ -N δ_1 of His41 [χ_2 (H41)] and His164 [χ_2 (H164)], distance between the N δ_1 atoms of His41 and His164 [δ (N δ_1)], distances from the “catalytic water” to atoms N of Cys145, N δ_1 of His41, N δ_1 of His164, and O $\delta_1/2$ of Asp187. For covalent complexes by with oligopeptidic inhibitors, H-bond lengths between the hemiacetal/hemiketal oxygen atom and the N atom of Cys145 or Ne2 atom of His41 are given. "dens" means that there is no catalytic water in the PDB model, but there is clear electron density in an appropriate place. Structures with unusual features, discussed in the main text, are marked with an asterisk.

| PDB mol. | χ_1 (C145) | χ_2 (H41) | χ_2 (H164) | d(N δ_1) | distance from catalytic water | | | | distance from aldo/keto O | |
|----------|-----------------|----------------|-----------------|------------------|-------------------------------|------|--------------|-----------------|---------------------------|----|
| | | | | | to | N145 | N δ_1 | N δ_1 64 | OD187 | to |
| 6yb7 A | -63.2 | 68.38 * | -120.35 | 4.18 | HOH644 | 3.05 | 3.10 | 2.87 | 2.75 | |
| 6m03 A | -56.2 | 71.61 * | 63.34 * | 4.07 | dens | 3.06 | 2.77 | 2.83 | 3.10 | |
| 6y2e A | -68.4 | -119.20 | -122.43 | 4.34 | HOH582 | 3.07 | 2.98 | 2.94 | 2.98 | |
| 6xb0 A | -59.2 * | -114.40 | -117.24 | 4.36 | HOH571 | 3.20 | 2.93 | 2.92 | 2.88 | |
| 6m2q A | -63.8 | -104.92 | -114.70 | 4.30 | HOH518 | 3.07 | 2.90 | 2.92 | 2.94 | |
| 6wqf A | -62.9 | -104.62 | -105.45 | 4.22 | HOH417 | 3.14 | 2.79 | 3.02 | 2.94 | |
| 7jp1 A | -60.1 | -137.12 | -118.27 | 4.27 | HOH477 | 3.00 | 3.13 | 2.99 | 2.78 | |
| 7bro A | -93.2 | 77.59 * | -109.97 | 4.43 | dens | 3.18 | 2.81 | 3.06 | 3.12 | |
| 7cwb A | -58.5 | -101.98 | -116.20 | 4.36 | HOH441 | 3.19 | 2.85 | 2.88 | 2.81 | |
| 7jun A | -48.2 | -92.18 | -116.79 | 4.47 | DOD409 | 3.15 | 2.64 | 3.10 | 2.78 | |
| 7jvz A | -60.9 | -107.70 | -110.71 | 4.37 | HOH429 | 3.29 | 3.19 | 2.94 | 3.03 | |
| 7k3t A | -62.4 | -120.20 | -123.02 | 4.31 | HOH601 | 3.09 | 3.07 | 2.86 | 2.75 | |
| 6y84 A | -63.0 | 71.49 * | -118.26 | 4.14 | HOH604 | 3.07 | 3.12 | 2.85 | 2.72 | |
| 7jr3 A | -68.4 | 60.21 * | -114.12 | 4.19 | HOH492 | 3.00 | 3.36 | 2.96 | 2.77 | |
| 7jr4 A | -65.9 | 66.03 * | -115.70 | 4.13 | HOH628 | 3.09 | 3.17 | 2.94 | 2.87 | |
| 6xkh A | -47.3 * | -126.82 | -123.18 | 4.06 | HOH602 | 2.95 | 3.17 | 3.00 | 2.84 | |
| 6xhu A | -59.5 | -103.08 | -119.76 | 4.40 | HOH429A | 3.15 | 2.93 | 2.88 | 2.76 | |
| 6xhu C | -60.5 | -103.08 | 41,67 * | 4.36 | HOH441C | 3.27 | 2.87 | 2.85 | 2.80 | |
| 6wtm A | -63.6 | 78.63 * | -115.41 | 4.28 | HOH460A | 3.15 | 3.09 | 2.95 | 2.79 | |
| 6wtm B | -62.2 | -115.41 | -115.64 | 4.27 | HOH455B | 3.16 | 2.97 | 2.83 | 2.97 | |
| 6xkf A | -59.6 | -104.73 | -117.20 | 4.33 | HOH557A | 3.06 | 2.94 | 2.93 | 2.97 | |
| 6xkf B | -65.0 | -114.75 | -114.81 | 4.30 | HOH536B | 3.17 | 2.92 | 2.90 | 2.97 | |
| 7cwc A | -60.8 | 74.17 * | -112.43 | 4.24 | HOH423A | 3.29 | 3.30 | 2.88 | 3.10 | |
| 7cwc B | -69.3 | 69.86 * | -110.10 | 4.36 | HOH421B | 3.29 | 3.06 | 3.01 | 3.17 | |
| 7c2y A | -72.2 | -116.34 | -121.68 | 4.31 | HOH346A | 3.03 | 3.04 | 2.93 | 2.76 | |
| 7c2y B | -74.4 | 67.76 * | -116.23 | 4.24 | HOH347B | 2.89 | 3.04 | 3.04 | 2.96 | |
| 7c2q A | -69.2 | 68.82 * | -128.52 | 4.35 | HOH334A | 3.02 | 3/05 | 2.92 | 2.76 | |
| 7c2q B | -79.9 | 63.79 * | -118.60 | 4.33 | HOH337B | 3.00 | 3.16 | 2.95 | 2.89 | |
| 7jfq A | -62.4 | -105.10 | -117.65 | 4.25 | HOH513B | 3.34 | 2.62 | 3.01 | 2.67 | |
| 6xoa A | -79.7 * | 80.77 * | 67.60 * | 4.14 | HOH512A | 2.93 | 3.09 | 3.16 | 3.17 | |
| 6xoa B | -66.4 * | 79.51 * | 69.73 * | 3.92 | dens | 3.19 | 3.00 | 3.04 | 2.98 | |
| 6xoa C | -77.3 * | 69.73 * | 65.45 * | 4.28 | HOH515C | 3.18 | 3.25 | 3.07 | 3.14 | |

| | | | | | | | | | | | | | | |
|------|---|----------|---------|---------|--------|---------|------|------|------|------|-----|-----------------|---------|-----------|
| 6xoa | D | -54.8 * | 65.45 * | 73.55 * | 3.66 | dens | 2.93 | 2.57 | 3.03 | 3.18 | | | | |
| 6zrt | A | -70.1 | -105.80 | -119.57 | 4.14 | HOH708 | 3.41 | 2.55 | 2.88 | 2.81 | S | keto | Nε2 41 | 2.59 |
| 6xqs | A | -70.0 | -96.31 | -120.48 | 4.02 | HOH524 | 3.36 | 2.64 | 2.94 | 2.87 | S | keto | Nε2 41 | 2.53 |
| 7k6e | A | -63.4 | -102.41 | -123.45 | 4.13 | HOH520 | 3.33 | 2.73 | 2.90 | 2.83 | S | keto | Nε2 41 | 2.47 |
| 7k6d | A | -64.7 | -97.71 | -121.36 | 4.15 | HOH519 | 3.36 | 2.72 | 2.96 | 2.77 | S | keto | Nε2 41 | 2.49 |
| 7c8u | A | -77.5 | -113.38 | -112.68 | 4.22 | HOH520 | 3.25 | 3.06 | 2.88 | 2.76 | S | aldo | N 145 | 3.28 |
| 6wtj | A | -78.9 | -95.88 | -114.50 | 4.29 | HOH528 | 3.12 | 2.88 | 2.93 | 2.92 | S | aldo | N 145 | 3.04 |
| 6wtk | A | -78.6 | -103.40 | -113.87 | 4.12 | HOH512 | 3.17 | 2.75 | 2.80 | 2.73 | S | aldo | N 145 | 3.10 |
| 6zru | A | -73.4 | -111.87 | -117.15 | 4.04 | HOH 10 | 3.32 | 2.73 | 2.94 | 2.85 | S | keto | Nε2 41 | 2.57 |
| 7k40 | A | -71.8 | -99.85 | -122.59 | 4.18 | HOH581 | 3.42 | 2.72 | 2.86 | 2.77 | S | keto | Nε2 41 | 2.51 |
| 6xqu | A | -78.5 | -98.28 | -114.60 | 4.18 | HOH516 | 3.45 | 2.68 | 2.91 | 2.87 | S | keto | Nε2 41 | 2.42 |
| 7d1o | A | -63.1 | -107.29 | -116.77 | 4.10 | HOH563 | 3.48 | 2.87 | 2.88 | 3.04 | S | keto | Nε2 41 | 2.55 |
| 7jyc | A | -70.1 | -102.60 | -121.18 | 4.02 | HOH572 | 3.42 | 2.71 | 2.87 | 2.73 | S | keto | Nε2 41 | 2.45 |
| 6xch | A | -73.9 | -103.68 | -114.32 | 4.31 | HOH426 | 3.31 | 2.68 | 3.02 | 3.09 | S | aldo | N 145 | 3.09 |
| 6yz6 | A | -64.6 | -104.09 | -116.57 | 4.34 | HOH667 | 2.45 | 2.85 | 2.98 | 2.88 | S/R | aldo | N145/41 | 2.83/2.56 |
| 6xfn | A | 34.4 * | -95.60 | -122.83 | 4.11 | HOH640 | 3.27 | 2.68 | 2.98 | 2.76 | R | keto | Nε2 41 | 2.41 * |
| 6xbh | A | -71.3 | 59.89 * | -121.31 | 4.13 | HOH698 | 3.04 | 3.31 | 2.96 | 2.82 | S | aldo | N 145 | 2.83 |
| 6xa4 | A | -73.3 | 67.71 * | -122.99 | 4.21 | HOH698 | 3.04 | 3.03 | 2.90 | 2.92 | S | aldo | N 145 | 2.89 |
| 6yt8 | A | -60.4 | -107.60 | -113.26 | 4.30 | HOH564 | 3.09 | 2.70 | 2.93 | 3.26 | | non-peptidic | | |
| 7d3i | A | -68.4 | -97.62 | -121.36 | 4.16 | HOH603 | 3.19 | 2.75 | 2.88 | 2.75 | S | aldo | N 145 | 2.89 |
| 6xb2 | A | -67.7 | -124.63 | -115.67 | 4.52 | HOH532 | 3.13 | 3.09 | 2.90 | 2.91 | | non-peptidic | | |
| 6xb1 | A | -63.2 * | -120.03 | -118.34 | 4.32 | HOH570 | 3.20 | 3.02 | 2.87 | 2.84 | | non-peptidic | | |
| 6ynq | A | -76.3 | 53.96 | -108.66 | 4.31 | HOH666 | 3.02 | 3.20 | 2.95 | 3.13 | | non-peptidic | | |
| 6yvf | A | -66.4 | -121.02 | -114.88 | 4.20 | HOH647 | 3.07 | 3.07 | 2.94 | 2.82 | | non-covalent | | |
| 7c6u | A | -69.6 | -96.69 | -103.07 | 4.15 | HOH583 | 3.21 | 2.84 | 2.93 | 3.12 | S | aldo | N 145 | 2.72 |
| 7c6s | A | -67.5 | -103.29 | -117.52 | 4.12 | HOH609 | 3.31 | 2.76 | 2.89 | 2.86 | S | keto | Nε2 41 | 2.54 |
| 6wnp | A | -67.7 | -107.17 | -124.73 | 4.17 | HOH604 | 3.18 | 2.79 | 2.97 | 2.85 | S | keto | Nε2 41 | 2.60 |
| 7c8b | A | -70.2 | -125.41 | -117.60 | 4.20 | HOH589 | 3.24 | 2.89 | 2.95 | 2.77 | | non-peptidic | | |
| 7bqy | A | -71.0 | -110.78 | -115.12 | 4.14 | HOH570 | 3.27 | 2.84 | 2.83 | 2.80 | | non-peptidic | | |
| 6lu7 | A | -81.0 | -106.83 | -109.11 | 4.13 | HOH445 | 3.32 | 2.80 | 3.08 | 2.90 | | covalent adduct | | |
| 7buy | A | -63.8 * | 66.95 * | -119.63 | 4.10 | HOH571 | 3.00 | 3.25 | 2.92 | 2.77 | | thioester | | |
| 7ju7 | A | -67.2 | -117.81 | -118.17 | 4.27 | HOH595 | 3.02 | 3.05 | 2.95 | 2.83 | | non-covalent | | |
| 6xr3 | A | -70.8 | 93.57 * | -120.92 | 2.91 * | dens | 2.65 | 1.93 | 3.04 | 2.69 | S | aldo | N 145 | 2.91 |
| 6lze | A | -72.3 | 64.56 * | -119.88 | 4.09 | HOH584 | 2.97 | 3.26 | 2.93 | 2.79 | S | aldo | N 145 | 2.88 |
| 6m0k | A | -69.5 | 70.70 * | -115.22 | 4.09 | HOH592 | 2.93 | 3.08 | 2.99 | 2.87 | S | aldo | N 145 | 2.83 |
| 6y2f | A | -72.6 | -113.11 | -116.68 | 3.94 | HOH654 | 3.27 | 2.76 | 2.86 | 2.83 | S | keto | Nε2 41 | 2.68 |
| 7cx9 | A | -154.8 * | -110.33 | -117.56 | 7.12 * | HOH619 | 3.03 | 5.13 | 2.94 | 2.78 | | thioester | | |
| 6w79 | A | -53.7 | 68.94 * | -120.78 | 4.08 | HOH623 | 3.03 | 3.10 | 2.97 | 2.75 | | non-covalent | | |
| 7joy | A | ALA | -100.30 | -113.48 | 4.19 | HOH417A | 3.27 | 2.79 | 3.03 | 2.64 | | no Cys | | |
| 7joy | B | ALA | -100.32 | -113.42 | 4.16 | HOH421B | 3.32 | 2.86 | 2.90 | 2.65 | | no Cys | | |
| 7khp | A | -62.1 | -114.30 | -116.37 | 4.22 | HOH503A | 3.26 | 3.29 | 3.07 | 2.43 | | no complex | | |
| 7khp | B | -65.2 * | -116.37 | -113.04 | 4.18 | HOH537B | 2.99 | 2.83 | 3.08 | 2.88 | | thioester | | |
| 7d1m | A | -73.9 | -103.02 | -115.72 | 4.17 | HOH626A | 3.22 | 2.85 | 3.09 | 2.80 | S/R | aldo | N145/41 | 2.88/2.85 |

| | | | | | | | | | | | | | | |
|------|---|---------|-----------|---------|--------|----------|------|------|------|------|-----|------|---------|------------------------|
| 7d1m | B | -72.3 | -115.72 | -117.91 | 4.24 | HOH631B | 3.21 | 2.90 | 2.87 | 2.78 | S/R | aldo | N145/41 | 2.87/2.83 |
| 7cbt | A | -73.2 | 62.16 * | -116.04 | 4.16 | dens | 3.19 | 2.85 | 2.90 | 3.02 | S | aldo | N 145 | 3.16 |
| 7cbt | B | -72.9 | 72.38 * | -121.52 | 4.32 | HOH549B | 3.03 | 3.05 | 3.03 | 2.92 | S | aldo | N 145 | 3.04 |
| 6xbg | A | -76.4 | -91.30 | -118.23 | 3.96 | HOH450A | 3.33 | 2.73 | 2.95 | 2.78 | S | keto | Nε2 41 | 2.59 |
| 6xbg | B | -75.9 | -118.23 | -118.75 | 4.03 | HOH663B | 3.34 | 2.84 | 2.89 | 2.70 | S | keto | Nε2 41 | 2.64 |
| 7jkv | A | -75.4 | 90.41 * | -115.90 | 2.82 * | ----- | | | | | S | aldo | N 145 | 2.89 |
| 7jkv | B | -73.4 | 88.92 * | -115.67 | 2.83 * | dens | 3.30 | 1.92 | 3.25 | 2.87 | S | aldo | N 145 | 2.94 |
| 6xhm | A | -73.9 | 87.09 * | -120.15 | 3.98 | HOH9150A | 3.33 | 2.81 | 2.91 | 2.74 | R | keto | Nε2 41 | 2.95 |
| 6xhm | B | -73.8 | -120.15 | -121.50 | 4.09 | HOH9133B | 3.34 | 2.80 | 2.90 | 2.86 | R | keto | Nε2 41 | 2.95 |
| 6xmk | A | -73.4 | -114.16 | -114.86 | 4.19 | HOH586A | 3.06 | 2.95 | 2.99 | 2.98 | S | aldo | N 145 | 2.95 |
| 6xmk | B | -74.5 | -106.78 | -120.98 | 4.24 | HOH591B | 3.14 | 2.94 | 2.92 | 2.81 | S | aldo | N 145 | 2.87 |
| 7brp | A | -70.5 | -102.00 | -112.55 | 4.05 | HOH559A | 3.41 | 2.72 | 2.96 | 2.99 | S | keto | Nε2 41 | 2.65 |
| 7brp | B | -68.3 | -112.55 | -112.99 | 4.12 | HOH575B | 3.50 | 2.75 | 2.96 | 2.92 | S | keto | Nε2 41 | 2.58 |
| 6xqt | A | -70.4 | -103.72 | 70.32 * | 4.05 | HOH503A | 3.49 | 2.45 | 3.09 | 3.08 | S | keto | Nε2 41 | 2.78 |
| 6xqt | B | -73.2 | -93.87 | 72.64 * | 3.98 | HOH504B | 3.41 | 2.47 | 3.13 | 2.89 | S | keto | Nε2 41 | 2.66 |
| 6xbi | A | -75.1 | -91.17 | -119.24 | 3.91 | HOH625A | 3.16 | 2.61 | 2.93 | 2.88 | S | keto | Nε2 41 | 2.69 |
| 6xbi | B | -73.2 | -99.08 | -116.19 | 3.96 | HOH651B | 3.37 | 2.71 | 2.81 | 2.77 | S | keto | Nε2 41 | 2.74 |
| 6m2n | A | -83.0 | 67.59 * | -108.90 | 4.29 | dens | 2.95 | 2.98 | 3.06 | 3.35 | | | | non-covalent |
| 6m2n | B | -89.7 | 60.28 * | -109.76 | 4.35 | HOH501B | 3.05 | 3.11 | 3.13 | 2.31 | | | | non-covalent |
| 6m2n | C | -83.5 | 60.35 * | 50.25 * | 4.29 | dens | 2.98 | 2.84 | 3.30 | 2.99 | | | | non-covalent |
| 6m2n | D | -81.7 | 54.11 * | -118.61 | 4.23 | dens | 2.90 | 3.05 | 3.13 | 2.99 | | | | non-covalent |
| 7c7p | A | -64.5 | -105.55 | -128.89 | 4.09 | HOH535A | 3.23 | 2.90 | 2.96 | 2.62 | S | keto | Nε2 41 | 2.44 |
| 7c7p | B | -63.7 | -128.89 | -115.64 | 4.01 | HOH567B | 3.23 | 3.05 | 2.95 | 2.74 | S | keto | Nε2 41 | 2.55 |
| 7com | A | -70.8 | -103.07 | -118.26 | 4.15 | HOH566A | 3.24 | 2.76 | 2.95 | 2.79 | S | keto | Nε2 41 | 2.46 |
| 7com | B | -63.8 | -118.26 | -116.03 | 4.15 | HOH566A | 3.21 | 2.76 | 2.95 | 2.79 | S | keto | Nε2 41 | 2.44 |
| 6y2g | A | -73.2 | -106.66 | -118.95 | 4.03 | HOH535B | 3.24 | 2.78 | 2.98 | 2.72 | S | keto | Nε2 41 | 2.81 |
| 6y2g | B | -79.1 | -100.84 | -113.78 | 3.79 | HOH560A | 3.22 | 2.82 | 2.94 | 2.94 | S | keto | Nε2 41 | 2.92 |
| 6w63 | A | -48.6 | 62.85 * | -116.18 | 4.12 | HOH576 | 3.10 | 3.33 | 2.88 | 2.73 | | | | non-covalent |
| 6wtt | A | -69.5 | -104.24 | -105.93 | 4.08 | HOH557A | 3.16 | 2.94 | 2.82 | 3.03 | S | aldo | N 145 | 2.93 |
| 6wtt | B | -65.2 | 83.07 * | 57.48 * | 4.67 | HOH519B | 3.11 | 3.60 | 3.12 | 2.61 | S | aldo | N 145 | 2.82 |
| 6wtt | C | -74.2 | -111.99 | -117.44 | 4.42 | HOH517C | 3.37 | 2.91 | 3.19 | 2.69 | R | aldo | N 145 | 2.91 * |
| 6z2e | A | -71.9 | -106.60 * | -118.99 | 4.25 | HOH571 | 3.42 | 2.72 | 2.92 | 2.73 | | | | covalent, not peptidic |
| 7c8r | A | -71.9 | 55.55 * | 73.78 * | 7.25 * | HOH546 | 3.14 | 5.53 | 3.13 | 2.89 | | | | covalent, not peptidic |
| 7c8t | A | -70.0 * | 59.35 * | -128.06 | 4.46 | HOH572 | 3.01 | 3.39 | 3.08 | 2.87 | | | | thioester |

Supplementary Figure S1. Detailed view of the clustering presented in Figure 8 of the main text. The dendrogram presents the hierarchical clustering of all 3CLpro structures using Ward's method (Ward, 1963). Colors at the leaves represent structural polymorphs. The lengths of the dendrogram branches are proportional to the difference between clusters.



References

Matthews, B. W. (1968). *J. Mol. Biol.* **33**, 491-497.

Rupp, B. (2009). *Biomolecular Crystallography Principles, Practice, and Application to Structural Biology*, 1st ed.
New York: Garland Science Titles.

Ward, J. H. (1963). *J. Amer. Stat. Assoc.* **58**, 236-244.

Weichenberger, C. X. & Rupp, B. (2014). *Acta Cryst.* **D70**, 1579-1588.