wwPDB X-ray Structure Validation Summary Report (i)

Jun 26, 2024 – 02:24 AM EDT

PDB ID	:	6U3X
Title	:	PCSK9 in complex with compound 2
Authors	:	Lu, J.; Soisson, S.
Deposited on	:	2019-08-22
Resolution	:	2.64 Å(reported)

This is a wwPDB X-ray Structure Validation Summary Report for a publicly released PDB entry.

We welcome your comments at *validation@mail.wwpdb.org*
A user guide is available at
https://www.wwpdb.org/validation/2017/XrayValidationReportHelp
with specific help available everywhere you see the (i) symbol.

The types of validation reports are described at
http://www.wwpdb.org/validation/2017/FAQs#types.

The following versions of software and data (see references (i)) were used in the production of this report:

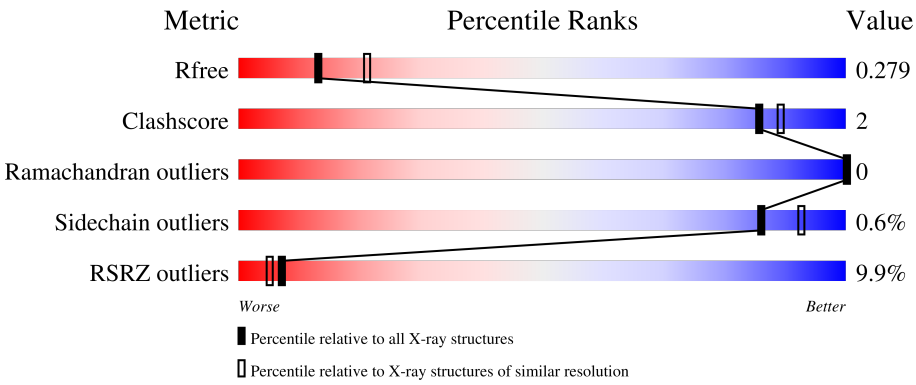
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.37.1
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.37.1

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
X-RAY DIFFRACTION

The reported resolution of this entry is 2.64 Å.

Percentile scores (ranging between 0-100) for global validation metrics of the entry are shown in the following graphic. The table shows the number of entries on which the scores are based.



Metric	Whole archive (#Entries)	Similar resolution (#Entries, resolution range(Å))
R_{free}	130704	1426 (2.66-2.62)
Clashscore	141614	1472 (2.66-2.62)
Ramachandran outliers	138981	1446 (2.66-2.62)
Sidechain outliers	138945	1446 (2.66-2.62)
RSRZ outliers	127900	1408 (2.66-2.62)

The table below summarises the geometric issues observed across the polymeric chains and their fit to the electron density. The red, orange, yellow and green segments of the lower bar indicate the fraction of residues that contain outliers for >=3, 2, 1 and 0 types of geometric quality criteria respectively. A grey segment represents the fraction of residues that are not modelled. The numeric value for each fraction is indicated below the corresponding segment, with a dot representing fractions <=5% The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density. The numeric value is given above the bar.

Mol	Chain	Length	Quality of chain
1	A	707	13% 87%
1	B	707	8% 63% 6% 31%

2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 4439 atoms, of which 0 are hydrogens and 0 are deuteriums.

In the tables below, the ZeroOcc column contains the number of atoms modelled with zero occupancy, the AltConf column contains the number of residues with at least one atom in alternate conformation and the Trace column contains the number of residues modelled with at most 2 atoms.

- Molecule 1 is a protein called Proprotein convertase subtilisin/kexin type 9.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	92	739	474	133	130	2	0	0	0
			Total	C	N	O	S			
1	B	486	3607	2224	666	685	32	0	0	0

There are 94 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	474	ILE	VAL	engineered mutation	UNP Q8NBP7
A	670	GLU	GLY	engineered mutation	UNP Q8NBP7
A	693	LYS	-	expression tag	UNP Q8NBP7
A	694	GLY	-	expression tag	UNP Q8NBP7
A	695	ASN	-	expression tag	UNP Q8NBP7
A	696	SER	-	expression tag	UNP Q8NBP7
A	697	ALA	-	expression tag	UNP Q8NBP7
A	698	ASP	-	expression tag	UNP Q8NBP7
A	699	ILE	-	expression tag	UNP Q8NBP7
A	700	GLN	-	expression tag	UNP Q8NBP7
A	701	HIS	-	expression tag	UNP Q8NBP7
A	702	SER	-	expression tag	UNP Q8NBP7
A	703	GLY	-	expression tag	UNP Q8NBP7
A	704	GLY	-	expression tag	UNP Q8NBP7
A	705	ARG	-	expression tag	UNP Q8NBP7
A	706	SER	-	expression tag	UNP Q8NBP7
A	707	SER	-	expression tag	UNP Q8NBP7
A	708	LEU	-	expression tag	UNP Q8NBP7
A	709	GLU	-	expression tag	UNP Q8NBP7
A	710	GLY	-	expression tag	UNP Q8NBP7
A	711	PRO	-	expression tag	UNP Q8NBP7
A	712	ARG	-	expression tag	UNP Q8NBP7
A	713	PHE	-	expression tag	UNP Q8NBP7
A	714	GLU	-	expression tag	UNP Q8NBP7
A	715	GLY	-	expression tag	UNP Q8NBP7

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Chain	Residue	Modelled	Actual	Comment	Reference
A	716	LYS	-	expression tag	UNP Q8NBP7
A	717	PRO	-	expression tag	UNP Q8NBP7
A	718	ILE	-	expression tag	UNP Q8NBP7
A	719	PRO	-	expression tag	UNP Q8NBP7
A	720	ASN	-	expression tag	UNP Q8NBP7
A	721	PRO	-	expression tag	UNP Q8NBP7
A	722	LEU	-	expression tag	UNP Q8NBP7
A	723	LEU	-	expression tag	UNP Q8NBP7
A	724	GLY	-	expression tag	UNP Q8NBP7
A	725	LEU	-	expression tag	UNP Q8NBP7
A	726	ASP	-	expression tag	UNP Q8NBP7
A	727	SER	-	expression tag	UNP Q8NBP7
A	728	THR	-	expression tag	UNP Q8NBP7
A	729	ARG	-	expression tag	UNP Q8NBP7
A	730	THR	-	expression tag	UNP Q8NBP7
A	731	GLY	-	expression tag	UNP Q8NBP7
A	732	HIS	-	expression tag	UNP Q8NBP7
A	733	HIS	-	expression tag	UNP Q8NBP7
A	734	HIS	-	expression tag	UNP Q8NBP7
A	735	HIS	-	expression tag	UNP Q8NBP7
A	736	HIS	-	expression tag	UNP Q8NBP7
A	737	HIS	-	expression tag	UNP Q8NBP7
B	474	ILE	VAL	engineered mutation	UNP Q8NBP7
B	670	GLU	GLY	engineered mutation	UNP Q8NBP7
B	693	LYS	-	expression tag	UNP Q8NBP7
B	694	GLY	-	expression tag	UNP Q8NBP7
B	695	ASN	-	expression tag	UNP Q8NBP7
B	696	SER	-	expression tag	UNP Q8NBP7
B	697	ALA	-	expression tag	UNP Q8NBP7
B	698	ASP	-	expression tag	UNP Q8NBP7
B	699	ILE	-	expression tag	UNP Q8NBP7
B	700	GLN	-	expression tag	UNP Q8NBP7
B	701	HIS	-	expression tag	UNP Q8NBP7
B	702	SER	-	expression tag	UNP Q8NBP7
B	703	GLY	-	expression tag	UNP Q8NBP7
B	704	GLY	-	expression tag	UNP Q8NBP7
B	705	ARG	-	expression tag	UNP Q8NBP7
B	706	SER	-	expression tag	UNP Q8NBP7
B	707	SER	-	expression tag	UNP Q8NBP7
B	708	LEU	-	expression tag	UNP Q8NBP7
B	709	GLU	-	expression tag	UNP Q8NBP7
B	710	GLY	-	expression tag	UNP Q8NBP7

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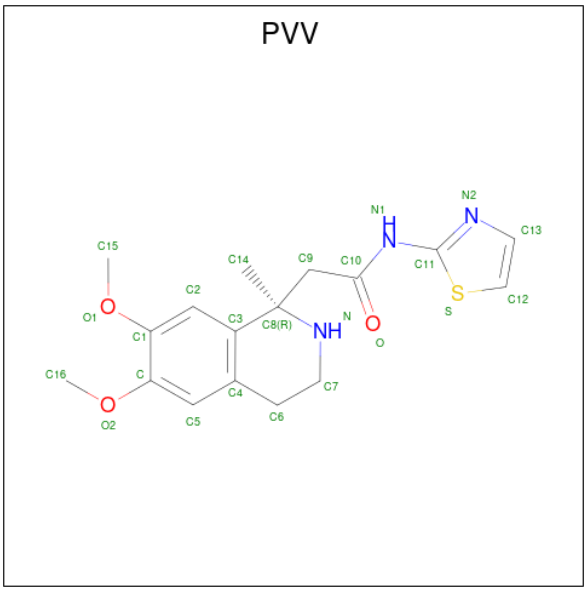
Chain	Residue	Modelled	Actual	Comment	Reference
B	711	PRO	-	expression tag	UNP Q8NBP7
B	712	ARG	-	expression tag	UNP Q8NBP7
B	713	PHE	-	expression tag	UNP Q8NBP7
B	714	GLU	-	expression tag	UNP Q8NBP7
B	715	GLY	-	expression tag	UNP Q8NBP7
B	716	LYS	-	expression tag	UNP Q8NBP7
B	717	PRO	-	expression tag	UNP Q8NBP7
B	718	ILE	-	expression tag	UNP Q8NBP7
B	719	PRO	-	expression tag	UNP Q8NBP7
B	720	ASN	-	expression tag	UNP Q8NBP7
B	721	PRO	-	expression tag	UNP Q8NBP7
B	722	LEU	-	expression tag	UNP Q8NBP7
B	723	LEU	-	expression tag	UNP Q8NBP7
B	724	GLY	-	expression tag	UNP Q8NBP7
B	725	LEU	-	expression tag	UNP Q8NBP7
B	726	ASP	-	expression tag	UNP Q8NBP7
B	727	SER	-	expression tag	UNP Q8NBP7
B	728	THR	-	expression tag	UNP Q8NBP7
B	729	ARG	-	expression tag	UNP Q8NBP7
B	730	THR	-	expression tag	UNP Q8NBP7
B	731	GLY	-	expression tag	UNP Q8NBP7
B	732	HIS	-	expression tag	UNP Q8NBP7
B	733	HIS	-	expression tag	UNP Q8NBP7
B	734	HIS	-	expression tag	UNP Q8NBP7
B	735	HIS	-	expression tag	UNP Q8NBP7
B	736	HIS	-	expression tag	UNP Q8NBP7
B	737	HIS	-	expression tag	UNP Q8NBP7

- Molecule 2 is 2-[(1R)-6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl]-N-(1,3-thiazol-2-yl)acetamide (three-letter code: PVV) (formula: $C_{17}H_{21}N_3O_3S$) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	N	O	S		
2	B	1	24	17	3	3	1	0	0

- Molecule 3 is water.

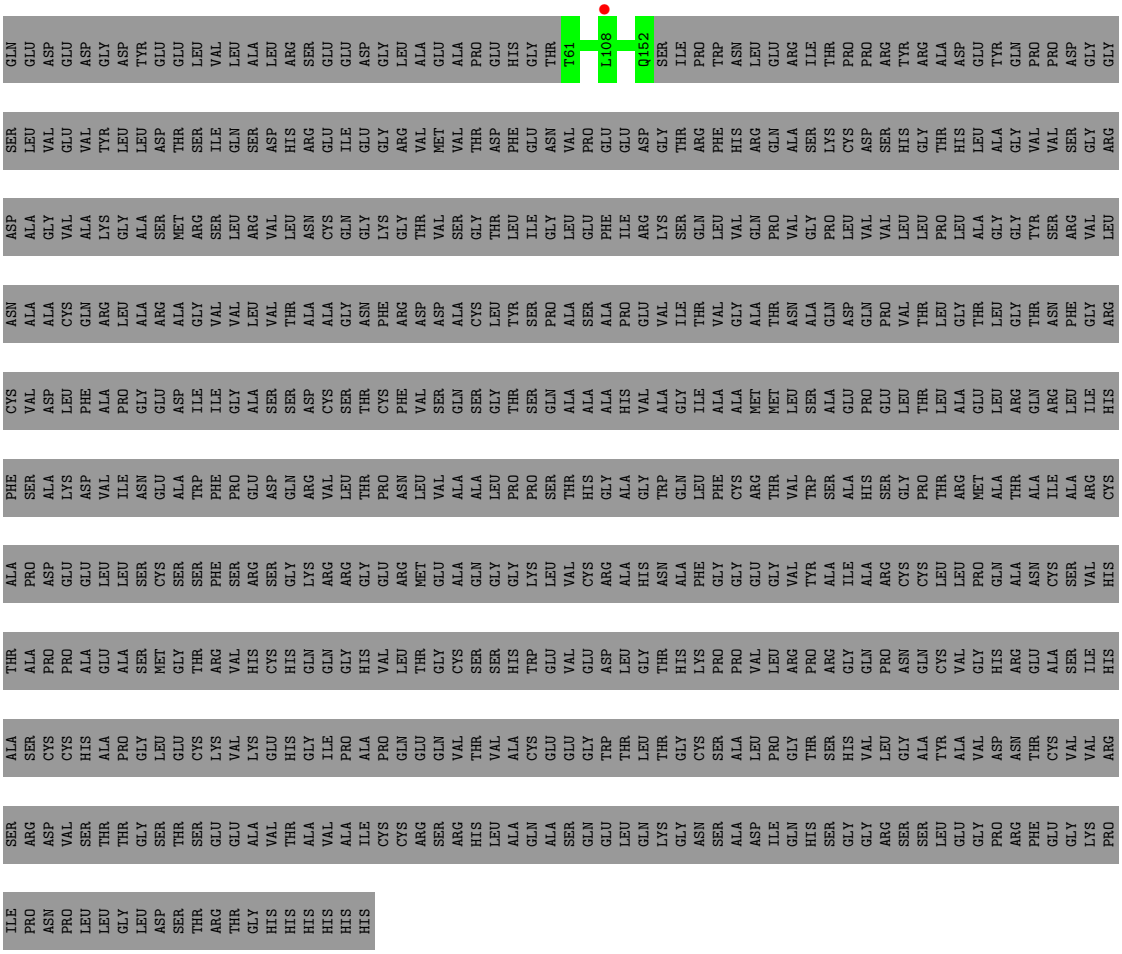
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
			Total	O		
3	A	22	22	22	0	0
			Total	O		
3	B	47	47	47	0	0

3 Residue-property plots (i)

These plots are drawn for all protein, RNA, DNA and oligosaccharide chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. A red dot above a residue indicates a poor fit to the electron density (RSRZ > 2). Stretches of 2 or more consecutive residues without any outlier are shown as a green connector. Residues present in the sample, but not in the model, are shown in grey.

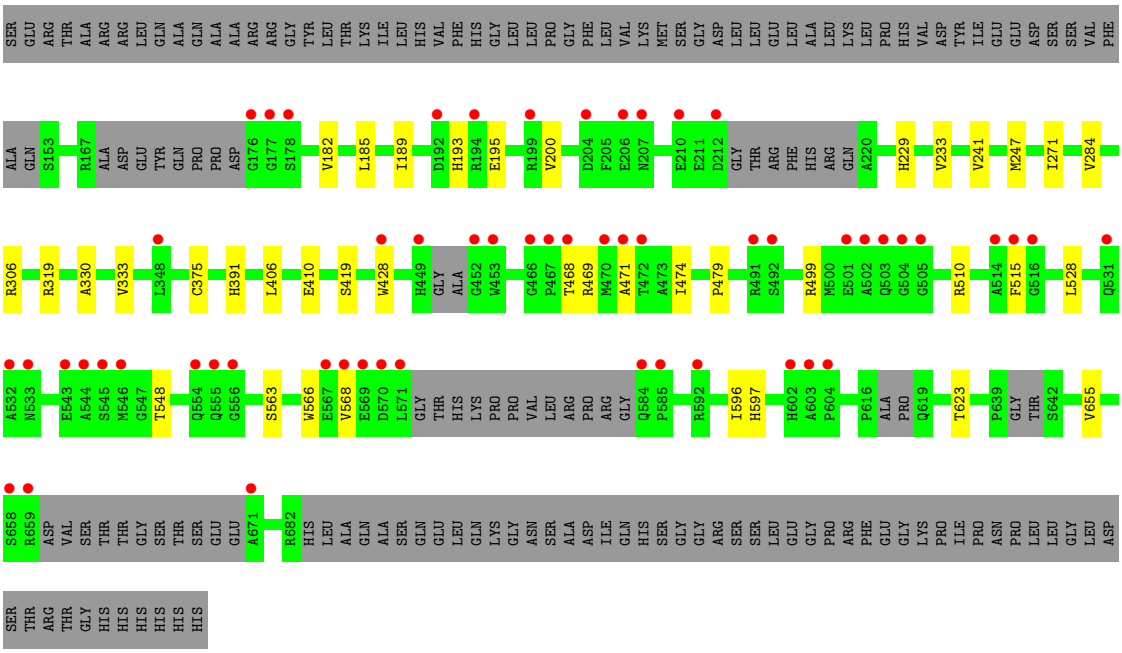
- Molecule 1: Proprotein convertase subtilisin/kexin type 9

Chain A:



- Molecule 1: Proprotein convertase subtilisin/kexin type 9

Chain B:


SER GLU ARG THR ALA ARG ARG LEU GLN ALA GLN ALA ALA ARG ARG GLY TYR LEU THR LYS ILE LEU HIS VAL PHE HIS GLY LEU LEU PRO GLY PHE LEU VAL LYS MET SER GLY ASP LEU LEU GLU LEU ALA LEU LYS LEU PRO HIS VAL ASP TYR ILE GLU GLU ASP SER SER VAL PHE
ALA GLN S153 R167 ALA ASP GLU TYR GLN PRO PRO ASP G176 G177 S178 V182 L185 I189 D192 H193 R194 E195 R199 V200 D204 F205 E206 N207 E210 E211 D212 GLY THR ARG PHE HIS ARG GLN A220 H229 V233 V241 M247 I271 V284
R306 R319 A330 V333 L348 C375 H391 L406 E410 S419 W428 H449 GLY ALA G452 W453 G466 P467 T468 R469 M470 A471 T472 A473 I474 P479 R491 S492 R499 M500 E501 A502 Q503 G504 G505 R510 A514 F515 G516 L528 Q531
A532 N533 E543 A544 S545 M546 G547 T548 Q554 Q555 G556 S563 W566 E567 V568 E569 D570 L571 GLY THR HIS LYS PRO PRO VAL LEU ARG PRO ARG GLY Q584 P585 R592 I596 H597 H602 A603 P604 P616 ALA PRO Q619 T623 P639 GLY THR S642 V655
S658 R659 ASP VAL SER THR THR GLY SER THR SER GLU GLU A671 R682 HIS LEU ALA GLN ALA SER GLN GLU LEU GLN LYS GLY ASN SER ALA ASP ILE GLN HIS SER GLY GLY ARG SER SER LEU GLU GLY PRO ARG PHE GLU GLY LYS PRO ILE PRO ASN PRO LEU LEU GLY LEU ASP
SER THR ARG THR GLY HIS HIS HIS HIS HIS

4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	62.31Å 70.42Å 148.20Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	40.44 – 2.64 40.44 – 2.64	Depositor EDS
% Data completeness (in resolution range)	94.3 (40.44-2.64) 94.3 (40.44-2.64)	Depositor EDS
R_{merge}	0.11	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	2.23 (at 2.65Å)	Xtriage
Refinement program	BUSTER 2.11.7	Depositor
R, R_{free}	0.248 , 0.284 0.254 , 0.279	Depositor DCC
R_{free} test set	958 reflections (5.12%)	wwPDB-VP
Wilson B-factor (Å^2)	42.2	Xtriage
Anisotropy	0.721	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.34 , 41.5	EDS
L-test for twinning[2]	$< \|L\| > = 0.49$, $< L^2 > = 0.33$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o,F_c correlation	0.90	EDS
Total number of atoms	4439	wwPDB-VP
Average B, all atoms (Å^2)	47.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 6.61% of the height of the origin peak. No significant pseudotranslation is detected.*

[1]Intensities estimated from amplitudes.

[2]Theoretical values of $< |L| >$, $< L^2 >$ for acentric reflections are 0.5, 0.333 respectively for untwinned datasets, and 0.375, 0.2 for perfectly twinned datasets.

5 Model quality (i)

5.1 Standard geometry (i)

Bond lengths and bond angles in the following residue types are not validated in this section: PVV

The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 5$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Chain	Bond lengths		Bond angles	
		RMSZ	$\#\|Z\| >5$	RMSZ	$\#\|Z\| >5$
1	A	0.36	0/756	0.61	0/1023
1	B	0.37	0/3671	0.61	0/4981
All	All	0.37	0/4427	0.61	0/6004

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

There are no planarity outliers.

5.2 Too-close contacts (i)

In the following table, the Non-H and H(model) columns list the number of non-hydrogen atoms and hydrogen atoms in the chain respectively. The H(added) column lists the number of hydrogen atoms added and optimized by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, whereas Symm-Clashes lists symmetry-related clashes.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	739	0	750	0	0
1	B	3607	0	3517	19	0
2	B	24	0	0	0	0
3	A	22	0	0	0	0
3	B	47	0	0	0	0
All	All	4439	0	4267	19	0

The all-atom clashscore is defined as the number of clashes found per 1000 atoms (including hydrogen atoms). The all-atom clashscore for this structure is 2.

The worst 5 of 19 close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:B:185:LEU:HD11	1:B:271:ILE:HD11	1.52	0.90
1:B:306:ARG:HH12	1:B:479:PRO:HG2	1.57	0.70
1:B:469:ARG:HE	1:B:515:PHE:HD1	1.44	0.66
1:B:200:VAL:HG22	1:B:247:MET:HB2	1.86	0.58
1:B:319:ARG:HG3	1:B:428:TRP:CH2	2.39	0.56

There are no symmetry-related clashes.

5.3 Torsion angles (i)

5.3.1 Protein backbone (i)

In the following table, the Percentiles column shows the percent Ramachandran outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the backbone conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles	
1	A	90/707 (13%)	85 (94%)	5 (6%)	0	100	100
1	B	470/707 (66%)	457 (97%)	13 (3%)	0	100	100
All	All	560/1414 (40%)	542 (97%)	18 (3%)	0	100	100

There are no Ramachandran outliers to report.

5.3.2 Protein sidechains (i)

In the following table, the Percentiles column shows the percent sidechain outliers of the chain as a percentile score with respect to all X-ray entries followed by that with respect to entries of similar resolution.

The Analysed column shows the number of residues for which the sidechain conformation was analysed, and the total number of residues.

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles	
1	A	79/571 (14%)	79 (100%)	0	100	100
1	B	388/571 (68%)	385 (99%)	3 (1%)	81	89
All	All	467/1142 (41%)	464 (99%)	3 (1%)	86	93

All (3) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	B	189	ILE
1	B	375	CYS
1	B	419	SER

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (3) such sidechains are listed below:

Mol	Chain	Res	Type
1	B	193	HIS
1	B	344	GLN
1	B	464	HIS

5.3.3 RNA (i)

There are no RNA molecules in this entry.

5.4 Non-standard residues in protein, DNA, RNA chains (i)

There are no non-standard protein/DNA/RNA residues in this entry.

5.5 Carbohydrates (i)

There are no monosaccharides in this entry.

5.6 Ligand geometry (i)

1 ligand is modelled in this entry.

In the following table, the Counts columns list the number of bonds (or angles) for which Mogul statistics could be retrieved, the number of bonds (or angles) that are observed in the model and the number of bonds (or angles) that are defined in the Chemical Component Dictionary. The Link column lists molecule types, if any, to which the group is linked. The Z score for a bond length (or angle) is the number of standard deviations the observed value is removed from the expected value. A bond length (or angle) with $|Z| > 2$ is considered an outlier worth inspection. RMSZ is the root-mean-square of all Z scores of the bond lengths (or angles).

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	$\#\|Z\| > 2$	Counts	RMSZ	$\#\|Z\| > 2$
2	PVV	B	801	-	23,26,26	0.87	2 (8%)	20,37,37	0.58	0

In the following table, the Chirals column lists the number of chiral outliers, the number of chiral centers analysed, the number of these observed in the model and the number defined in the Chemical Component Dictionary. Similar counts are reported in the Torsion and Rings columns. '-' means no outliers of that kind were identified.

Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
2	PVV	B	801	-	-	1/11/26/26	0/3/3/3

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	801	PVV	C14-C8	2.65	1.55	1.53
2	B	801	PVV	C7-N	2.54	1.50	1.47

There are no bond angle outliers.

There are no chirality outliers.

All (1) torsion outliers are listed below:

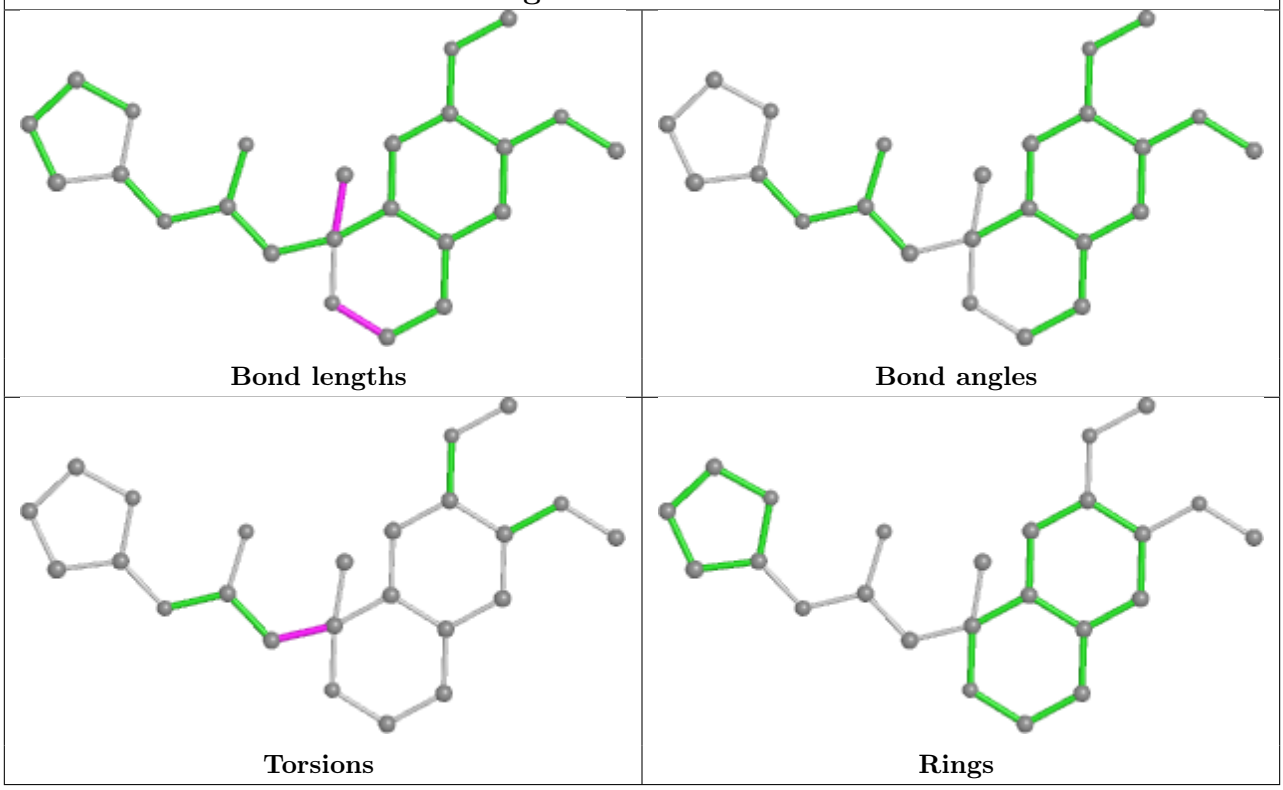
Mol	Chain	Res	Type	Atoms
2	B	801	PVV	N-C8-C9-C10

There are no ring outliers.

No monomer is involved in short contacts.

The following is a two-dimensional graphical depiction of Mogul quality analysis of bond lengths, bond angles, torsion angles, and ring geometry for all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the validation Tables will also be included. For torsion angles, if less then 5% of the Mogul distribution of torsion angles is within 10 degrees of the torsion angle in question, then that torsion angle is considered an outlier. Any bond that is central to one or more torsion angles identified as an outlier by Mogul will be highlighted in the graph. For rings, the root-mean-square deviation (RMSD) between the ring in question and similar rings identified by Mogul is calculated over all ring torsion angles. If the average RMSD is greater than 60 degrees and the minimal RMSD between the ring in question and any Mogul-identified rings is also greater than 60 degrees, then that ring is considered an outlier. The outliers are highlighted in purple. The color gray indicates Mogul did not find sufficient equivalents in the CSD to analyse the geometry.

Ligand PVV B 801



5.7 Other polymers (i)

There are no such residues in this entry.

5.8 Polymer linkage issues (i)

There are no chain breaks in this entry.

6 Fit of model and data (i)

6.1 Protein, DNA and RNA chains (i)

In the following table, the column labelled '#RSRZ> 2' contains the number (and percentage) of RSRZ outliers, followed by percent RSRZ outliers for the chain as percentile scores relative to all X-ray entries and entries of similar resolution. The OWAB column contains the minimum, median, 95th percentile and maximum values of the occupancy-weighted average B-factor per residue. The column labelled 'Q< 0.9' lists the number of (and percentage) of residues with an average occupancy less than 0.9.

Mol	Chain	Analysed	<RSRZ>	#RSRZ>2	OWAB(Å^2)	Q<0.9
1	A	92/707 (13%)	-0.08	1 (1%) 80 78	28, 39, 51, 55	1 (1%)
1	B	486/707 (68%)	0.59	56 (11%) 4 3	27, 46, 74, 83	1 (0%)
All	All	578/1414 (40%)	0.48	57 (9%) 7 5	27, 45, 73, 83	2 (0%)

The worst 5 of 57 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	470	MET	5.5
1	B	452	GLY	5.1
1	B	568	VAL	5.1
1	B	531	GLN	5.0
1	B	515	PHE	5.0

6.2 Non-standard residues in protein, DNA, RNA chains (i)

There are no non-standard protein/DNA/RNA residues in this entry.

6.3 Carbohydrates (i)

There are no monosaccharides in this entry.

6.4 Ligands (i)

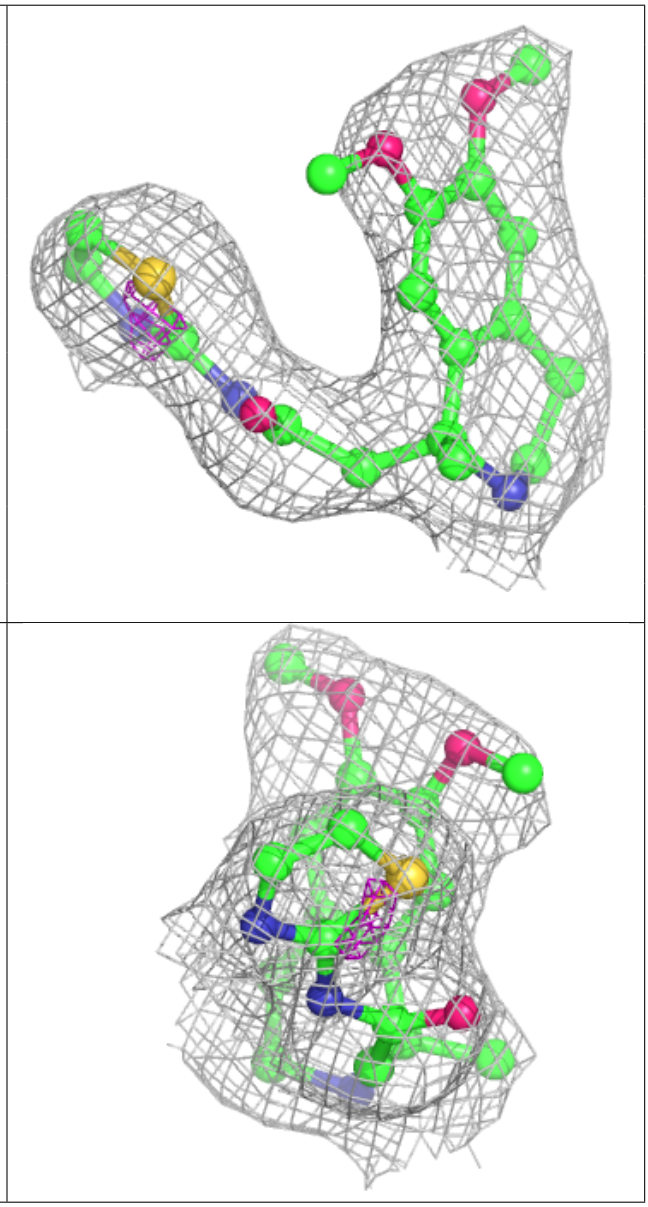
In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å^2)	Q<0.9
2	PVV	B	801	24/24	0.85	0.21	49,53,62,62	0

The following is a graphical depiction of the model fit to experimental electron density of all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the geometry validation Tables will also be included. Each fit is shown from different orientation to approximate a three-dimensional view.

Electron density around PVV B 801:

2mF$_o$-DF$_c$ (at 0.7 rmsd) in gray
mF$_o$-DF$_c$ (at 3 rmsd) in purple (negative) and green (positive)



6.5 Other polymers (i)

There are no such residues in this entry.