



wwPDB X-ray Structure Validation Summary Report ⓘ

Jun 11, 2024 – 04:32 PM EDT

PDB ID : 6MQ3
Title : Structure of Cysteine-free Human Insulin-Degrading Enzyme in complex with Substrate-selective Macrocyclic Inhibitor 63
Authors : Tan, G.A.; Seeliger, M.A.; Welsh, A.J.; Maianti, J.P.; Liu, D.R.
Deposited on : 2018-10-09
Resolution : 3.57 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 ⓘ 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 ⓘ](#)) 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	:	2.36.2
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)	:	2.36.2

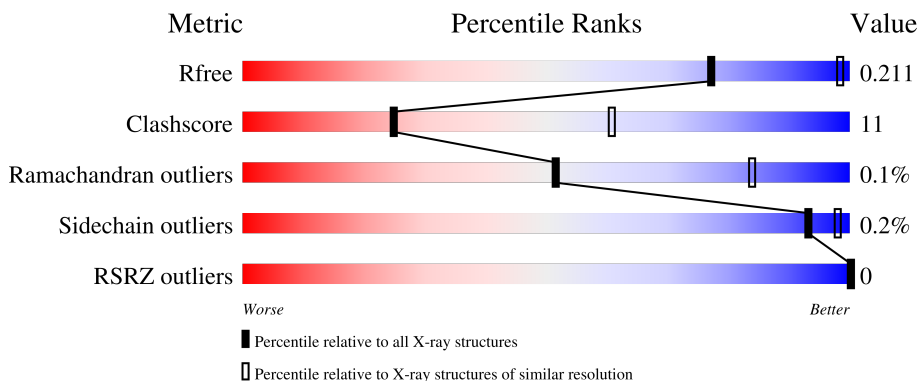
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 3.57 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	1020 (3.62-3.50)
Clashscore	141614	1100 (3.62-3.50)
Ramachandran outliers	138981	1065 (3.62-3.50)
Sidechain outliers	138945	1066 (3.62-3.50)
RSRZ outliers	127900	1009 (3.64-3.48)

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 $\leq 5\%$. 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	978	
1	B	978	

2 Entry composition

There are 3 unique types of molecules in this entry. The entry contains 15798 atoms, of which 102 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 Insulin-degrading enzyme.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	959	Total	C	N	O	S	0	0	0
			7798	5021	1310	1445	22			
1	B	959	Total	C	N	O	S	0	0	0
			7798	5021	1310	1445	22			

There are 28 discrepancies between the modelled and reference sequences:

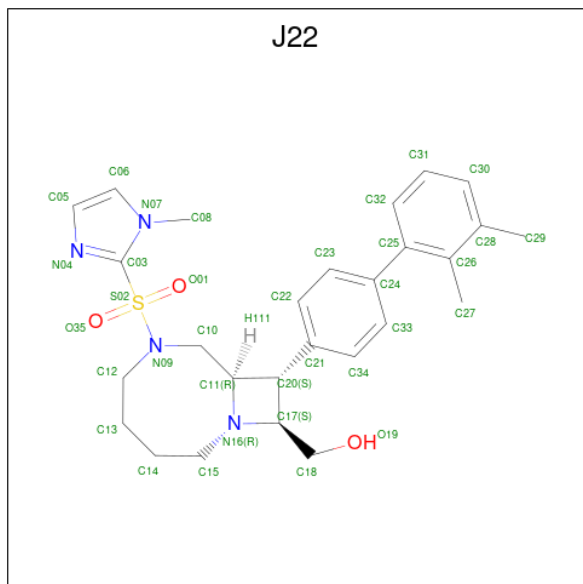
Chain	Residue	Modelled	Actual	Comment	Reference
A	110	LEU	CYS	engineered mutation	UNP P14735
A	111	GLN	GLU	engineered mutation	UNP P14735
A	171	SER	CYS	engineered mutation	UNP P14735
A	178	ALA	CYS	engineered mutation	UNP P14735
A	257	VAL	CYS	engineered mutation	UNP P14735
A	414	LEU	CYS	engineered mutation	UNP P14735
A	573	ASN	CYS	engineered mutation	UNP P14735
A	590	SER	CYS	engineered mutation	UNP P14735
A	789	SER	CYS	engineered mutation	UNP P14735
A	812	ALA	CYS	engineered mutation	UNP P14735
A	819	ALA	CYS	engineered mutation	UNP P14735
A	904	SER	CYS	engineered mutation	UNP P14735
A	966	ASN	CYS	engineered mutation	UNP P14735
A	974	ALA	CYS	engineered mutation	UNP P14735
B	110	LEU	CYS	engineered mutation	UNP P14735
B	111	GLN	GLU	engineered mutation	UNP P14735
B	171	SER	CYS	engineered mutation	UNP P14735
B	178	ALA	CYS	engineered mutation	UNP P14735
B	257	VAL	CYS	engineered mutation	UNP P14735
B	414	LEU	CYS	engineered mutation	UNP P14735
B	573	ASN	CYS	engineered mutation	UNP P14735
B	590	SER	CYS	engineered mutation	UNP P14735
B	789	SER	CYS	engineered mutation	UNP P14735
B	812	ALA	CYS	engineered mutation	UNP P14735
B	819	ALA	CYS	engineered mutation	UNP P14735

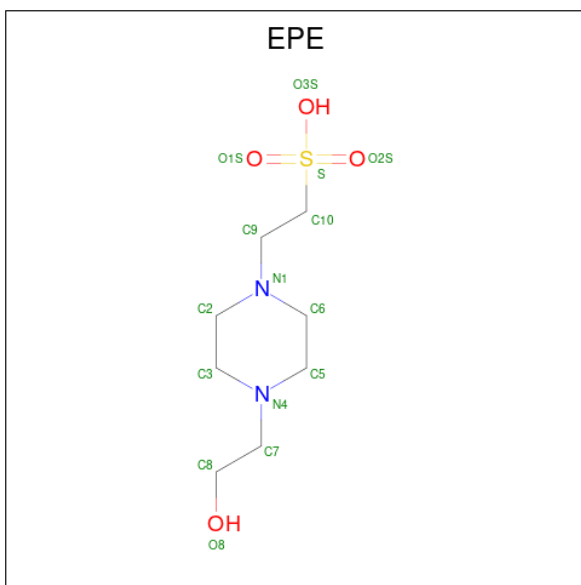
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Chain	Residue	Modelled	Actual	Comment	Reference
B	904	SER	CYS	engineered mutation	UNP P14735
B	966	ASN	CYS	engineered mutation	UNP P14735
B	974	ALA	CYS	engineered mutation	UNP P14735

- Molecule 2 is {(8R,9S,10S)-9-(2',3'-dimethyl[1,1'-biphenyl]-4-yl)-6-[(1-methyl-1H-imidazol-2-yl)sulfonyl]-1,6-diazabicyclo[6.2.0]decan-10-yl}methanol (three-letter code: J22) (formula: C₂₇H₃₄N₄O₃S).





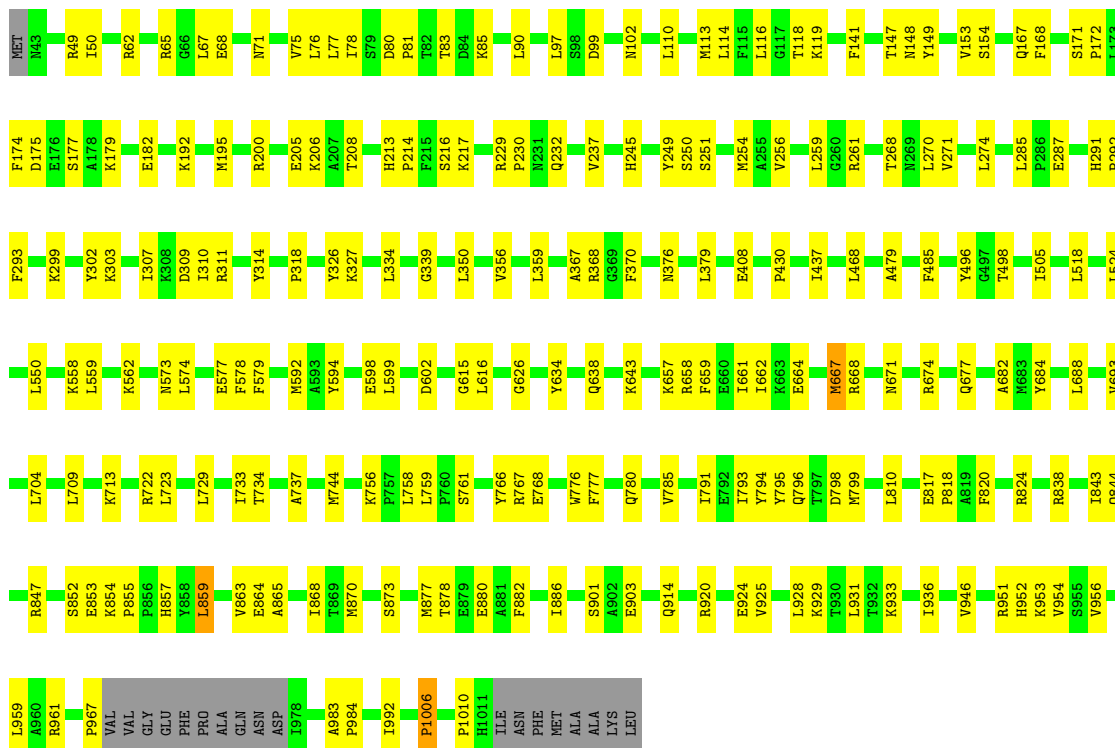
Mol	Chain	Residues	Atoms						ZeroOcc	AltConf
			Total	C	H	N	O	S		
3	A	1	32	8	17	2	4	1	0	0
3	B	1	32	8	17	2	4	1	0	0

3 Residue-property plots

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: Insulin-degrading enzyme

Chain A:  76% 22%



- Molecule 1: Insulin-degrading enzyme

Chain B:  72% 26%



V954	E413	P587	L719	S852	P967
L959	D416	L588	R722	E853	VAL
A960	L417	L594	L723	K854	VAL
R961	V420	E598	L729	P855	GLY
	R423	L599	I733	P856	PHE
	F424	L600	A737	H857	PRO
	K425	L616	M744	L858	ALA
	E428	Q638	L758	L859	GLN
	Y433	K643	Y766	V863	ASN
	I437	K648	W776	I868	ASP
	E457	F652	F777	T889	I978
	F458	K657	Q780	M870	
	F459	R658	V785	S873	P984
	I464	F659	H786	I874	
	L468	I661	M787	1874	1992
	M475	I662	E792	M877	M995
	F485	E664	I793	E880	P1006
	T498	M667	Y794	F881	
	L518	R668	Q796	F882	
	I531	M671	T797	R892	
	L540	R674	D798	R893	
	P548	A675	M799	L894	
	A549	E676	N805	S901	
	L550	Q677	L810	A902	
	I551	H679	Q813	E903	
	K552	M683	I814	A926	
	K558	L688	E817	Y927	
	L559	V693	P818	L928	
	K562	E699	A819	L931	
	Q563	L700	F820	T932	
	D564	L704	L823	K933	
	D565	V707	R824	I936	
	K566	L709	I832	E942	
	N573	K713	V833	V946	
	L574	A714	R838	P949	
	E577	F715	I843	R950	
	F578	S580	Q844	R951	
	F579	P581	G845	H952	
			L846	K953	
			R847		

4 Data and refinement statistics

Property	Value	Source
Space group	P 65	Depositor
Cell constants a, b, c, α , β , γ	263.25Å 263.25Å 91.23Å 90.00° 90.00° 120.00°	Depositor
Resolution (Å)	65.81 – 3.57 84.70 – 3.57	Depositor EDS
% Data completeness (in resolution range)	99.9 (65.81-3.57) 93.4 (84.70-3.57)	Depositor EDS
R_{merge}	0.11	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.22 (at 3.58Å)	Xtriage
Refinement program	PHENIX 1.11.1_2575	Depositor
R, R_{free}	0.162 , 0.211 0.162 , 0.211	Depositor DCC
R_{free} test set	2066 reflections (4.78%)	wwPDB-VP
Wilson B-factor (Å ²)	69.5	Xtriage
Anisotropy	0.124	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.34 , 47.7	EDS
L-test for twinning ²	$\langle L \rangle = 0.46$, $\langle L^2 \rangle = 0.29$	Xtriage
Estimated twinning fraction	0.038 for h,-h-k,-l	Xtriage
F_o, F_c correlation	0.93	EDS
Total number of atoms	15798	wwPDB-VP
Average B, all atoms (Å ²)	71.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 1.78% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

²Theoretical values of $\langle |L| \rangle$, $\langle L^2 \rangle$ 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: EPE, J22

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	0.25	0/7994	0.40	0/10824
1	B	0.24	0/7994	0.40	0/10824
All	All	0.24	0/15988	0.40	0/21648

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	7798	0	7684	163	2
1	B	7798	0	7684	180	1
2	A	35	34	0	1	0
2	B	35	34	0	0	0
3	A	15	17	17	0	0
3	B	15	17	17	0	0
All	All	15696	102	15402	337	2

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 11.

The worst 5 of 337 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:118:THR:HG21	1:B:167:GLN:HB3	1.21	1.19
1:B:777:PHE:HB3	1:B:992:ILE:HD11	1.34	1.08
1:A:118:THR:HG21	1:A:167:GLN:HB3	1.22	1.08
1:A:880:GLU:HG3	1:B:457:GLU:HG3	1.10	1.06
1:A:777:PHE:HB3	1:A:992:ILE:HD11	1.33	1.03

All (2) symmetry-related close contacts are listed below. The label for Atom-2 includes the symmetry operator and encoded unit-cell translations to be applied.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:408:GLU:OE2	1:A:734:THR:OG1[3_655]	2.12	0.08
1:A:761:SER:OG	1:B:699:GLU:OE2[5_555]	2.18	0.02

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	955/978 (98%)	914 (96%)	40 (4%)	1 (0%)	51	84
1	B	955/978 (98%)	913 (96%)	41 (4%)	1 (0%)	51	84
All	All	1910/1956 (98%)	1827 (96%)	81 (4%)	2 (0%)	51	84

All (2) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	1006	PRO
1	B	1006	PRO

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	842/870 (97%)	839 (100%)	3 (0%)	91	97
1	B	842/870 (97%)	841 (100%)	1 (0%)	93	98
All	All	1684/1740 (97%)	1680 (100%)	4 (0%)	93	98

All (4) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	667	MET
1	A	759	LEU
1	A	859	LEU
1	B	82	THR

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (1) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	134	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

4 ligands are 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	J22	A	1101	-	33,39,39	1.69	9 (27%)	39,58,58	2.30	6 (15%)
3	EPE	A	1102	-	15,15,15	0.75	1 (6%)	18,20,20	1.81	5 (27%)
2	J22	B	1101	-	33,39,39	1.81	8 (24%)	39,58,58	2.26	4 (10%)
3	EPE	B	1102	-	15,15,15	0.78	1 (6%)	18,20,20	1.94	6 (33%)

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	J22	A	1101	-	-	5/16/49/49	0/4/5/5
3	EPE	A	1102	-	-	7/9/19/19	0/1/1/1
2	J22	B	1101	-	-	10/16/49/49	0/4/5/5
3	EPE	B	1102	-	-	5/9/19/19	0/1/1/1

The worst 5 of 19 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	1101	J22	C10-N09	4.23	1.53	1.48
2	A	1101	J22	C13-C12	2.84	1.58	1.52
2	B	1101	J22	S02-N09	2.80	1.67	1.63
2	B	1101	J22	C18-C17	2.73	1.56	1.52
2	A	1101	J22	O01-S02	2.64	1.46	1.43

The worst 5 of 21 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	1101	J22	O35-S02-O01	-9.63	103.91	119.52

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Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	B	1101	J22	O35-S02-O01	-9.59	103.98	119.52
2	B	1101	J22	O35-S02-N09	6.82	112.91	106.69
2	A	1101	J22	O35-S02-N09	6.62	112.72	106.69
2	A	1101	J22	O01-S02-N09	5.38	111.60	106.69

There are no chirality outliers.

5 of 27 torsion outliers are listed below:

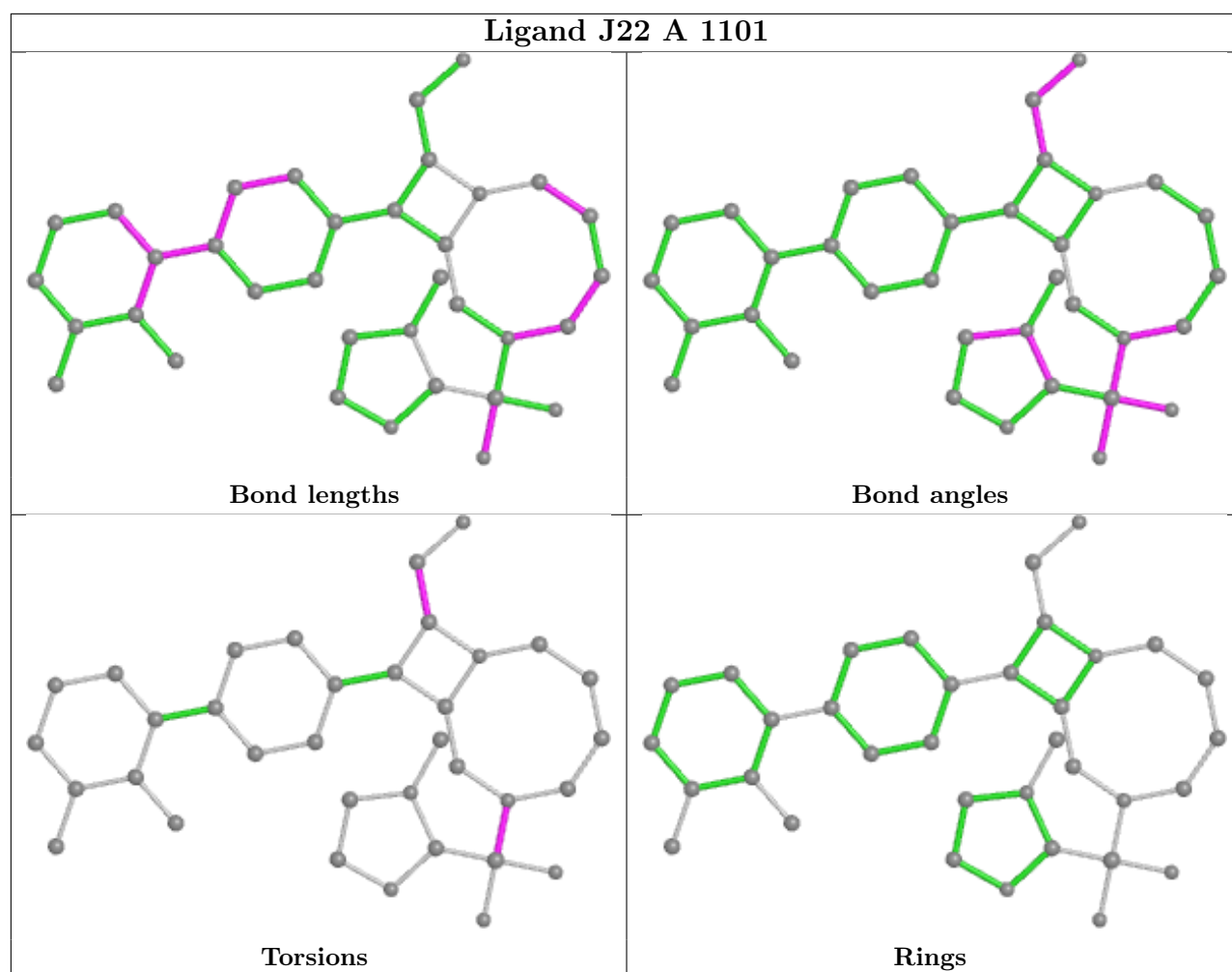
Mol	Chain	Res	Type	Atoms
2	A	1101	J22	N16-C17-C18-O19
2	A	1101	J22	C12-N09-S02-O35
2	B	1101	J22	C20-C17-C18-O19
2	B	1101	J22	N16-C17-C18-O19
2	B	1101	J22	C10-N09-S02-O35

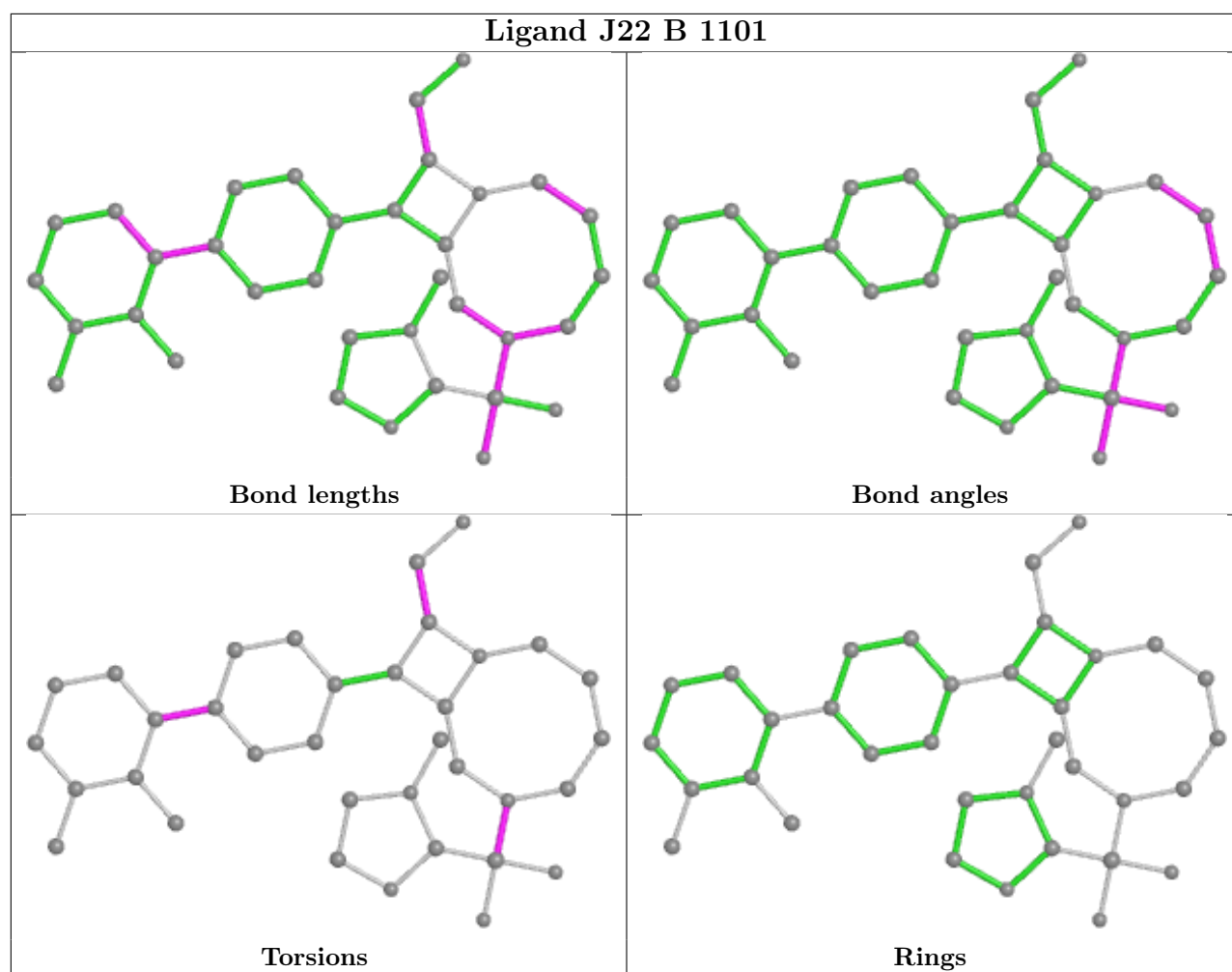
There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	1101	J22	1	0

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 than 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.





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	959/978 (98%)	-0.17	0 100 100	42, 65, 88, 133	0
1	B	959/978 (98%)	-0.11	0 100 100	49, 73, 96, 135	0
All	All	1918/1956 (98%)	-0.14	0 100 100	42, 69, 92, 135	0

There are no RSRZ outliers to report.

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.

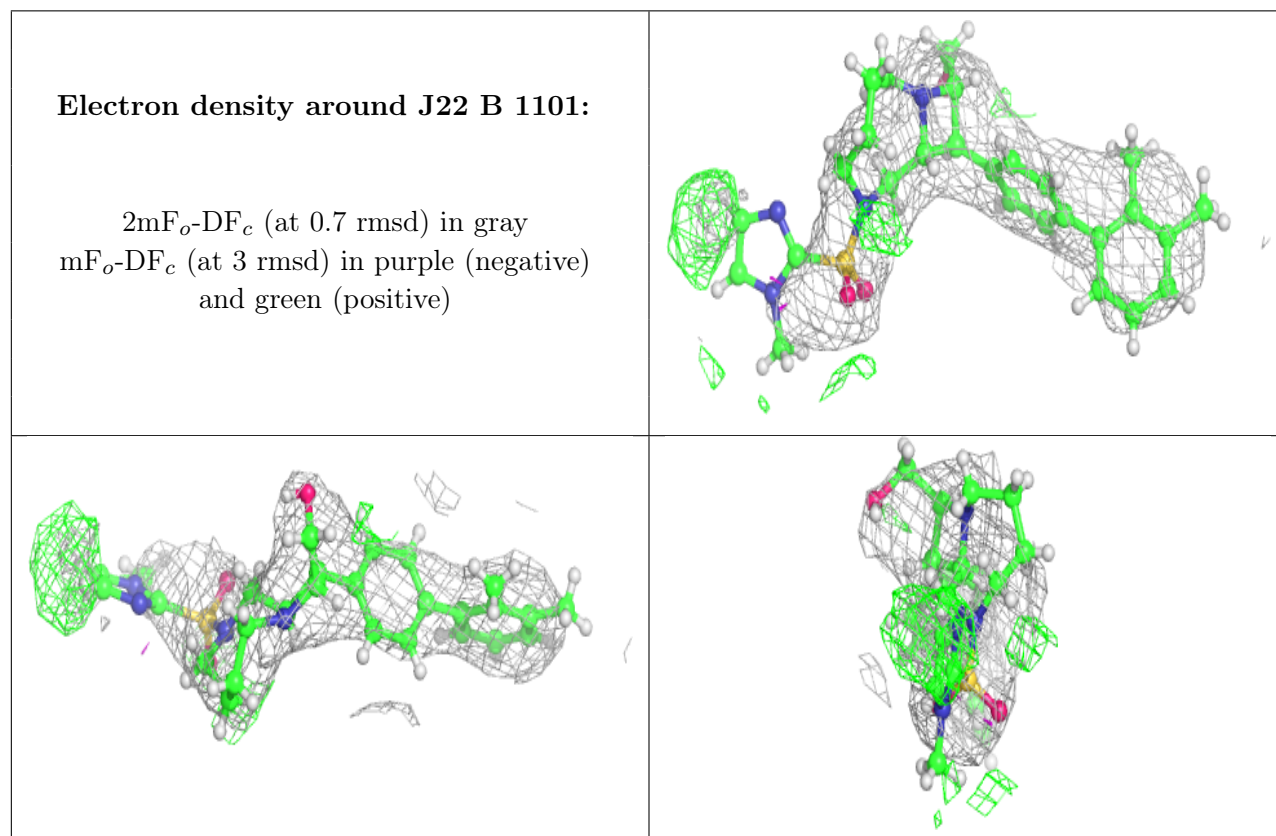
6.4 Ligands [i](#)

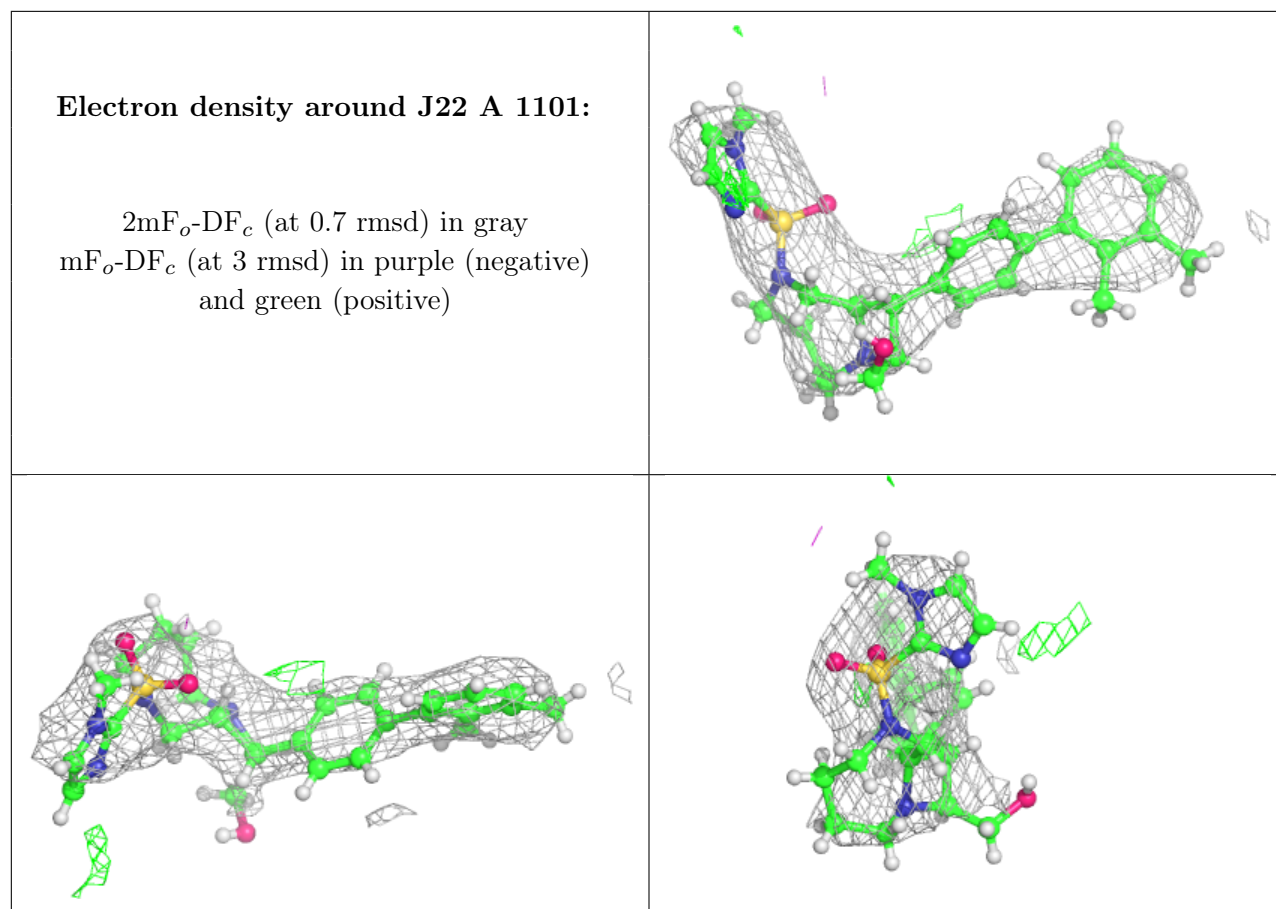
In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled ‘Q< 0.9’ lists 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	J22	B	1101	35/35	0.87	0.38	68,110,154,169	0
3	EPE	B	1102	15/15	0.91	0.35	57,75,96,101	32
3	EPE	A	1102	15/15	0.93	0.32	60,81,101,106	32
2	J22	A	1101	35/35	0.93	0.43	55,91,116,132	69

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.





6.5 Other polymers ⓘ

There are no such residues in this entry.