



Full wwPDB X-ray Structure Validation Report ⓘ

Feb 22, 2021 – 11:17 AM GMT

PDB ID : 7AW4
Title : MerTK kinase domain with type 3 inhibitor from a DNA-encoded library
Authors : Pflug, A.; Nissink, J.W.M.; Blackett, C.; Goldberg, K.; Hennessy, E.J.; Hardaker, E.; McCoull, W.; McMurray, L.; Collingwood, O.; Overman, R.; Preston, M.; Rawlins, P.; Rivers, E.; Schimpl, M.; Smith, P.; Underwood, E.; Truman, C.; Warwicker, J.; Winter, J.; Woodcock, S.
Deposited on : 2020-11-06
Resolution : 1.98 Å(reported)

This is a Full wwPDB X-ray Structure Validation 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 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 : 2.17.1.dev1
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) : 2.17.1.dev1

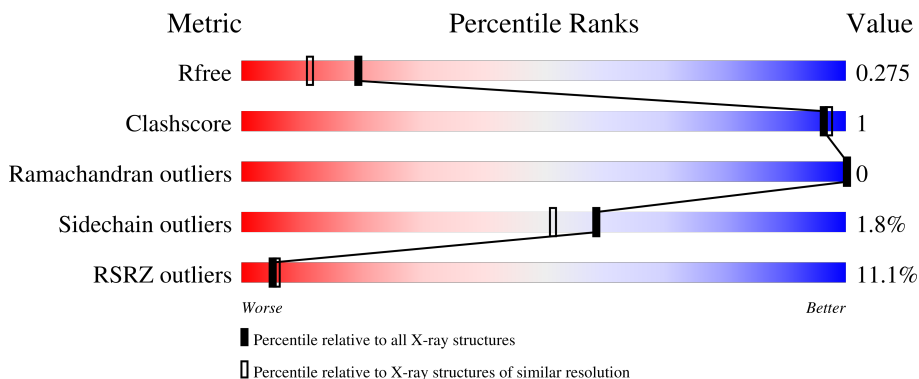
1 Overall quality at a glance i

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 1.98 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	11647 (2.00-1.96)
Clashscore	141614	1014 (1.98-1.98)
Ramachandran outliers	138981	1006 (1.98-1.98)
Sidechain outliers	138945	1006 (1.98-1.98)
RSRZ outliers	127900	11410 (2.00-1.96)

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	313	
1	B	313	

2 Entry composition i

There are 5 unique types of molecules in this entry. The entry contains 4524 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 Tyrosine-protein kinase Mer.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	264	2110	1352	349	389	20	0	2	0
1	B	257	2020	1297	335	369	19	0	0	0

There are 36 discrepancies between the modelled and reference sequences:

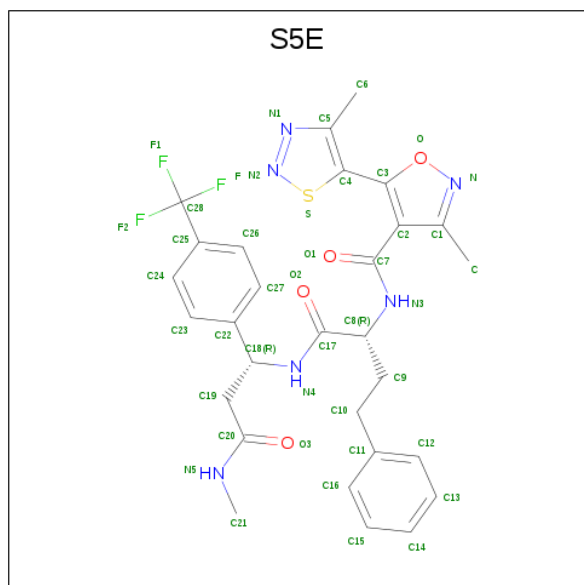
Chain	Residue	Modelled	Actual	Comment	Reference
A	552	MET	-	initiating methionine	UNP Q12866
A	553	GLY	-	expression tag	UNP Q12866
A	554	SER	-	expression tag	UNP Q12866
A	555	SER	-	expression tag	UNP Q12866
A	556	HIS	-	expression tag	UNP Q12866
A	557	HIS	-	expression tag	UNP Q12866
A	558	HIS	-	expression tag	UNP Q12866
A	559	HIS	-	expression tag	UNP Q12866
A	560	HIS	-	expression tag	UNP Q12866
A	561	HIS	-	expression tag	UNP Q12866
A	562	SER	-	expression tag	UNP Q12866
A	563	SER	-	expression tag	UNP Q12866
A	564	GLY	-	expression tag	UNP Q12866
A	565	LEU	-	expression tag	UNP Q12866
A	566	VAL	-	expression tag	UNP Q12866
A	567	PRO	-	expression tag	UNP Q12866
A	568	ARG	-	expression tag	UNP Q12866
A	569	GLY	-	expression tag	UNP Q12866
B	552	MET	-	initiating methionine	UNP Q12866
B	553	GLY	-	expression tag	UNP Q12866
B	554	SER	-	expression tag	UNP Q12866
B	555	SER	-	expression tag	UNP Q12866
B	556	HIS	-	expression tag	UNP Q12866
B	557	HIS	-	expression tag	UNP Q12866
B	558	HIS	-	expression tag	UNP Q12866

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Chain	Residue	Modelled	Actual	Comment	Reference
B	559	HIS	-	expression tag	UNP Q12866
B	560	HIS	-	expression tag	UNP Q12866
B	561	HIS	-	expression tag	UNP Q12866
B	562	SER	-	expression tag	UNP Q12866
B	563	SER	-	expression tag	UNP Q12866
B	564	GLY	-	expression tag	UNP Q12866
B	565	LEU	-	expression tag	UNP Q12866
B	566	VAL	-	expression tag	UNP Q12866
B	567	PRO	-	expression tag	UNP Q12866
B	568	ARG	-	expression tag	UNP Q12866
B	569	GLY	-	expression tag	UNP Q12866

- Molecule 2 is 3-methyl-5-(4-methyl-1,2,3-thiadiazol-5-yl)-N-((R)-1-(((R)-3-(methylamino)-3-oxo-1-(4-(trifluoromethyl)phenyl)propyl)amino)-1-oxo-4-phenylbutan-2-yl)isoxazole-4-carboxamide (three-letter code: S5E) (formula: C₂₉H₂₉F₃N₆O₄S) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	
			Total	C	F	N	O			S
2	A	1	Total	C	F	N	O	S	0	0
			43	29	3	6	4	1		
2	B	1	Total	C	F	N	O	S	0	0
			43	29	3	6	4	1		

- Molecule 3 is CHLORIDE ION (three-letter code: CL) (formula: Cl).

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
3	A	2	Total Cl 2 2	0	0
3	B	1	Total Cl 1 1	0	0

- Molecule 4 is 1,2-ETHANEDIOL (three-letter code: EDO) (formula: C₂H₆O₂).



Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
4	A	1	Total C O 4 2 2	0	0
4	A	1	Total C O 4 2 2	0	0
4	A	1	Total C O 4 2 2	0	0
4	A	1	Total C O 4 2 2	0	0
4	B	1	Total C O 4 2 2	0	0
4	B	1	Total C O 4 2 2	0	0

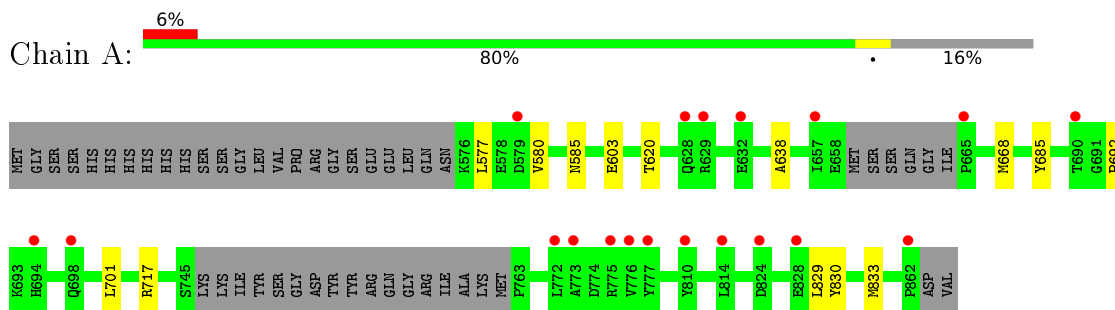
- Molecule 5 is water.

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
5	A	149	Total O 149 149	0	0
5	B	132	Total O 132 132	0	0

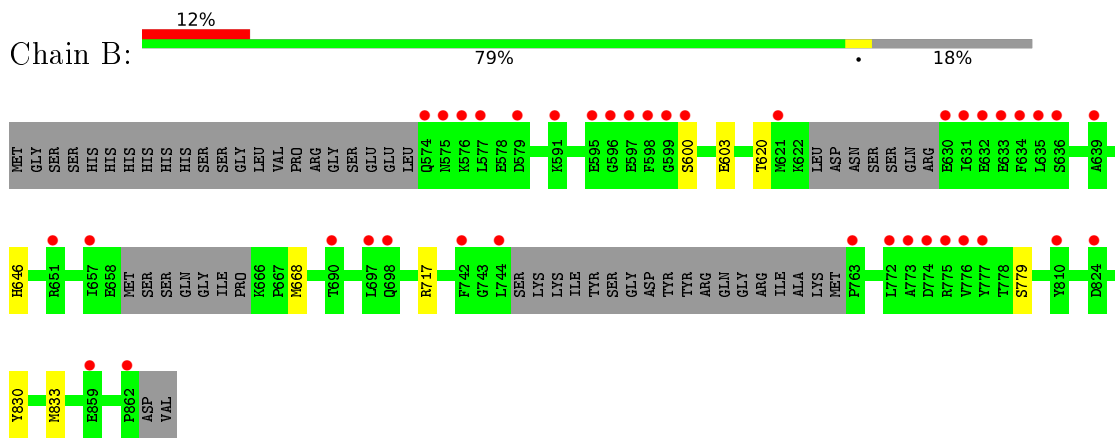
3 Residue-property plots [i](#)

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: Tyrosine-protein kinase Mer



- Molecule 1: Tyrosine-protein kinase Mer



4 Data and refinement statistics

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants a, b, c, α , β , γ	50.57Å 90.49Å 69.42Å 90.00° 99.37° 90.00°	Depositor
Resolution (Å)	39.48 – 1.98 39.48 – 1.98	Depositor EDS
% Data completeness (in resolution range)	95.5 (39.48-1.98) 95.5 (39.48-1.98)	Depositor EDS
R_{merge}	0.15	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	1.74 (at 1.98Å)	Xtrriage
Refinement program	BUSTER 2.11.7	Depositor
R, R_{free}	0.214 , 0.246 0.240 , 0.275	Depositor DCC
R_{free} test set	2053 reflections (4.99%)	wwPDB-VP
Wilson B-factor (Å ²)	21.7	Xtrriage
Anisotropy	0.656	Xtrriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.35 , 56.0	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtrriage
Estimated twinning fraction	No twinning to report.	Xtrriage
F_o, F_c correlation	0.93	EDS
Total number of atoms	4524	wwPDB-VP
Average B, all atoms (Å ²)	36.0	wwPDB-VP

Xtrriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 14.74% of the height of the origin peak. No significant pseudotranslation is detected.*

¹ Intensities estimated from amplitudes.

² Theoretical 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: CL, S5E, EDO

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	0.42	0/2154	0.58	0/2914
1	B	0.42	0/2061	0.58	0/2792
All	All	0.42	0/4215	0.58	0/5706

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	2110	0	2092	5	0
1	B	2020	0	1992	3	0
2	A	43	0	0	0	0
2	B	43	0	0	0	0
3	A	2	0	0	0	0
3	B	1	0	0	0	0
4	A	16	0	24	0	0
4	B	8	0	12	1	0
5	A	149	0	0	0	0
5	B	132	0	0	0	0
All	All	4524	0	4120	8	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 1.

All (8) 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:A:620:THR:HG22	1:A:668:MET:HG2	1.70	0.72
1:B:620:THR:HG22	1:B:668:MET:HG2	1.77	0.67
1:A:580:VAL:HG21	1:A:638:ALA:HB1	1.96	0.48
1:B:646:HIS:HA	4:B:903:EDO:H12	1.99	0.45
1:A:701:LEU:HD21	1:A:829:LEU:HD13	2.02	0.42
1:B:830:TYR:HA	1:B:833:MET:HG2	2.03	0.41
1:A:830:TYR:HA	1:A:833:MET:HG2	2.03	0.40
1:A:685:TYR:HB3	1:A:692:PRO:HD2	2.04	0.40

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	260/313 (83%)	258 (99%)	2 (1%)	0	100	100
1	B	249/313 (80%)	247 (99%)	2 (1%)	0	100	100
All	All	509/626 (81%)	505 (99%)	4 (1%)	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	233/280 (83%)	229 (98%)	4 (2%)	60	53
1	B	219/280 (78%)	215 (98%)	4 (2%)	59	51
All	All	452/560 (81%)	444 (98%)	8 (2%)	59	51

All (8) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	577	LEU
1	A	585	ASN
1	A	603	GLU
1	A	717	ARG
1	B	600	SER
1	B	603	GLU
1	B	717	ARG
1	B	779	SER

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. There are no such sidechains identified.

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](#)

Of 11 ligands modelled in this entry, 3 are monoatomic - leaving 8 for Mogul analysis.

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
4	EDO	A	905	-	3,3,3	0.60	0	2,2,2	0.28	0
4	EDO	B	903	-	3,3,3	0.62	0	2,2,2	0.27	0
4	EDO	A	906	-	3,3,3	0.50	0	2,2,2	0.41	0
2	S5E	B	901	-	37,46,46	0.56	1 (2%)	46,65,65	0.26	0
2	S5E	A	901	-	37,46,46	0.56	1 (2%)	46,65,65	0.31	0
4	EDO	A	904	-	3,3,3	0.64	0	2,2,2	0.37	0
4	EDO	B	904	-	3,3,3	0.57	0	2,2,2	0.32	0
4	EDO	A	907	-	3,3,3	0.55	0	2,2,2	0.41	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
4	EDO	A	905	-	-	0/1/1/1	-
4	EDO	B	903	-	-	0/1/1/1	-
4	EDO	A	906	-	-	0/1/1/1	-
2	S5E	B	901	-	-	2/33/41/41	0/4/4/4
2	S5E	A	901	-	-	0/33/41/41	0/4/4/4
4	EDO	A	904	-	-	0/1/1/1	-
4	EDO	B	904	-	-	0/1/1/1	-
4	EDO	A	907	-	-	0/1/1/1	-

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	901	S5E	C5-N1	2.31	1.37	1.34
2	B	901	S5E	C5-N1	2.30	1.37	1.34

There are no bond angle outliers.

There are no chirality outliers.

All (2) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	B	901	S5E	N4-C18-C22-C23

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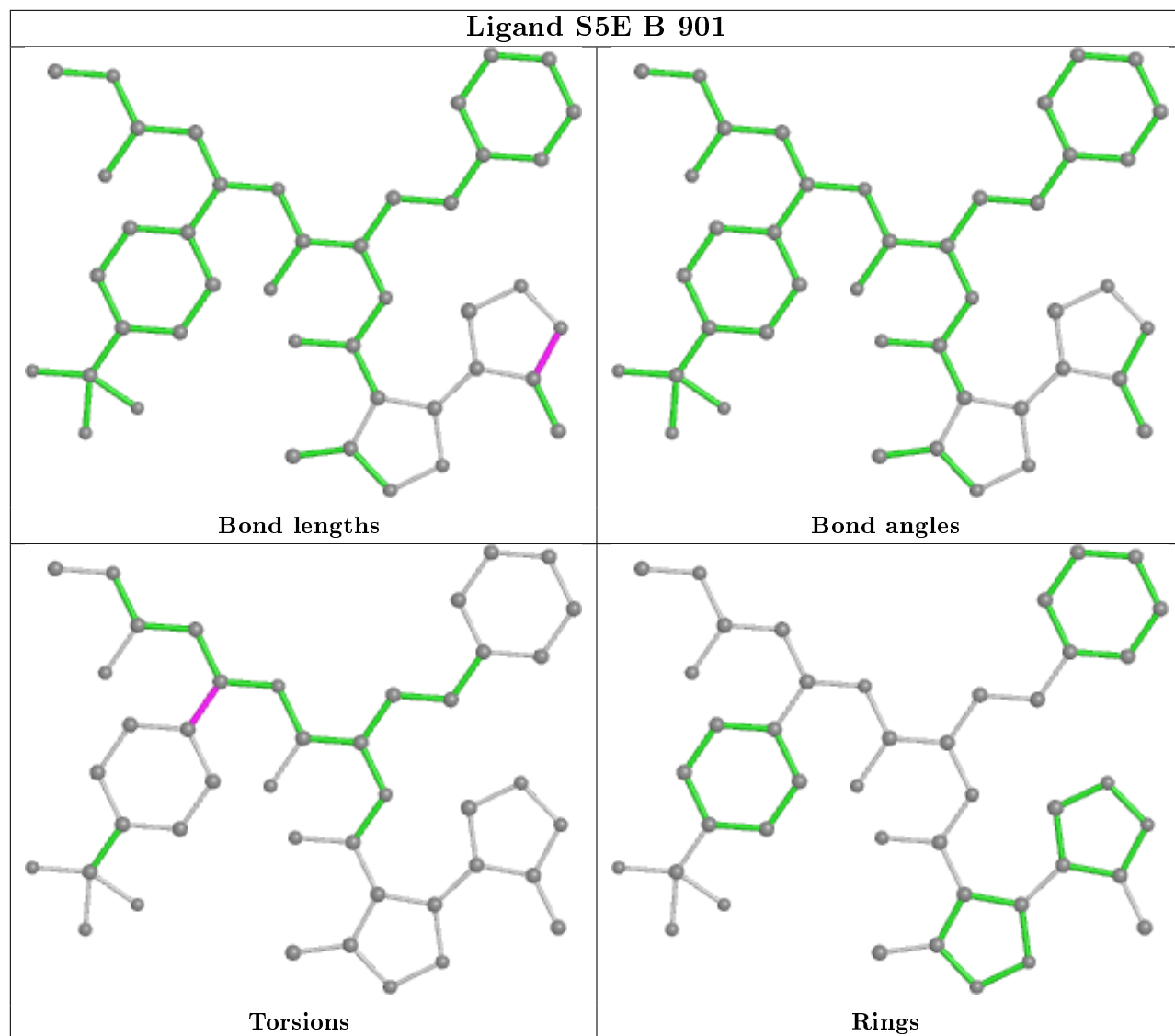
Mol	Chain	Res	Type	Atoms
2	B	901	S5E	N4-C18-C22-C27

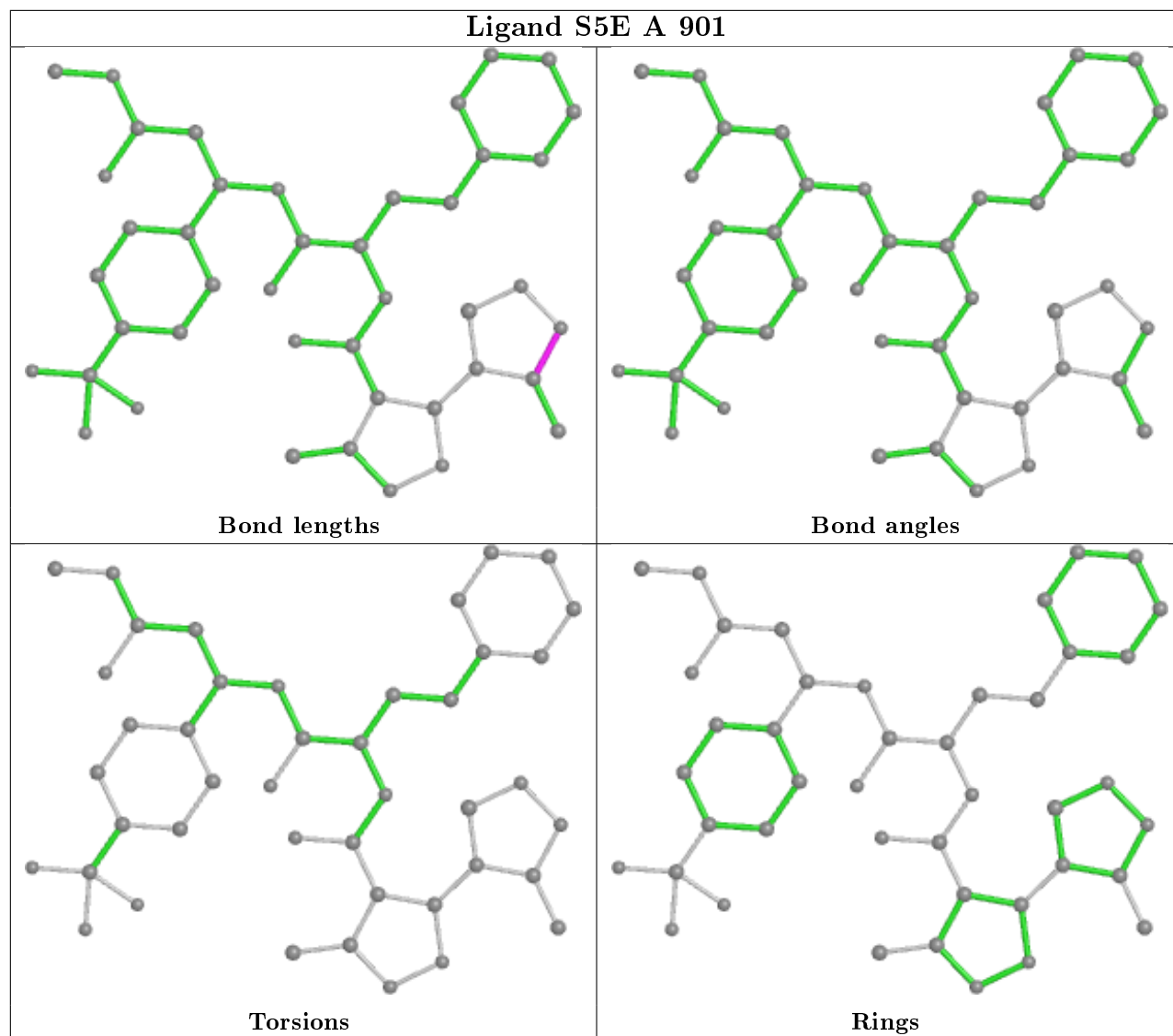
There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
4	B	903	EDO	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

6.1 Protein, DNA and RNA chains

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	264/313 (84%)	0.74	19 (7%) 15 17	20, 33, 54, 90	0
1	B	257/313 (82%)	1.14	39 (15%) 2 2	20, 36, 69, 102	0
All	All	521/626 (83%)	0.93	58 (11%) 5 6	20, 34, 60, 102	0

All (58) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	862	PRO	8.1
1	B	631	ILE	6.0
1	B	775	ARG	5.9
1	B	632	GLU	5.9
1	B	824	ASP	5.5
1	B	598	PHE	5.5
1	A	775	ARG	5.3
1	B	596	GLY	5.1
1	B	773	ALA	5.1
1	B	621	MET	5.1
1	B	810	TYR	4.6
1	A	824	ASP	4.6
1	B	639	ALA	4.5
1	B	744	LEU	4.0
1	B	597	GLU	4.0
1	B	635	LEU	4.0
1	B	776	VAL	4.0
1	B	577	LEU	3.9
1	A	776	VAL	3.9
1	B	575	ASN	3.8
1	A	810	TYR	3.8
1	B	630	GLU	3.8
1	B	657	ILE	3.7
1	A	773	ALA	3.7

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Mol	Chain	Res	Type	RSRZ
1	B	633	GLU	3.6
1	A	862	PRO	3.5
1	A	698	GLN	3.5
1	A	632	GLU	3.5
1	B	576	LYS	3.5
1	B	574	GLN	3.5
1	B	772	LEU	3.4
1	A	690	THR	3.3
1	A	657	ILE	3.2
1	A	665	PRO	3.0
1	B	636	SER	3.0
1	B	774	ASP	3.0
1	B	595	GLU	2.9
1	B	579	ASP	2.9
1	B	651	ARG	2.9
1	A	629	ARG	2.8
1	B	634	PHE	2.8
1	A	579	ASP	2.7
1	B	742	PHE	2.7
1	A	777	TYR	2.6
1	B	698	GLN	2.6
1	B	777	TYR	2.5
1	B	697	LEU	2.5
1	B	763	PRO	2.4
1	B	690	THR	2.4
1	A	828	GLU	2.4
1	B	599	GLY	2.4
1	A	694	HIS	2.3
1	A	814	LEU	2.3
1	B	859	GLU	2.2
1	A	772	LEU	2.1
1	A	628	GLN	2.1
1	B	591	LYS	2.1
1	B	600	SER	2.0

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](#)

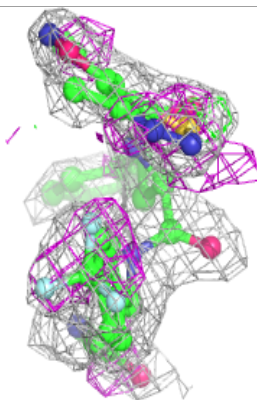
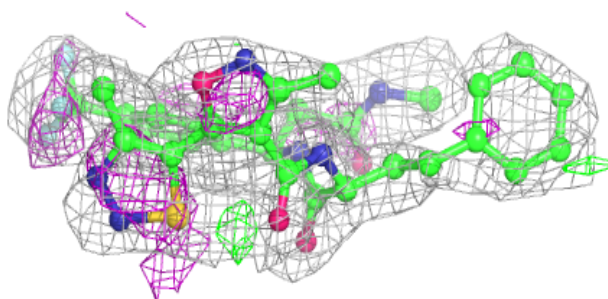
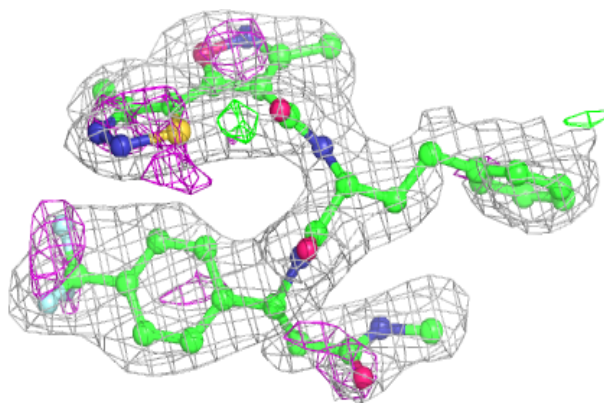
In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists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

Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å ²)	Q<0.9
4	EDO	A	906	4/4	0.66	0.22	48,50,52,53	0
4	EDO	A	904	4/4	0.70	0.19	42,43,44,44	0
4	EDO	A	907	4/4	0.72	0.27	73,73,73,73	0
4	EDO	B	904	4/4	0.74	0.28	53,53,53,53	0
4	EDO	A	905	4/4	0.77	0.21	44,45,46,47	0
4	EDO	B	903	4/4	0.79	0.19	40,41,42,42	0
2	S5E	B	901	43/43	0.79	0.23	31,41,55,55	0
2	S5E	A	901	43/43	0.88	0.17	21,29,40,40	0
3	CL	A	903	1/1	0.96	0.07	16,16,16,16	0
3	CL	A	902	1/1	0.97	0.09	24,24,24,24	0
3	CL	B	902	1/1	0.97	0.07	18,18,18,18	0

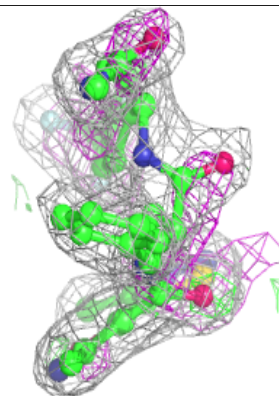
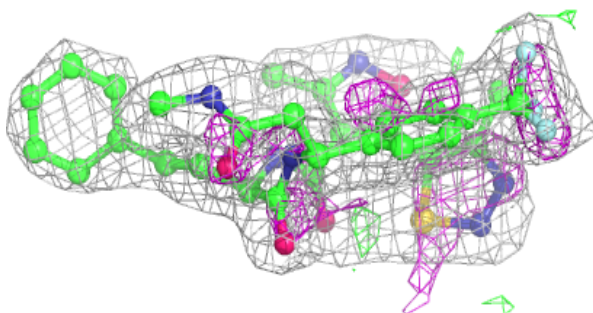
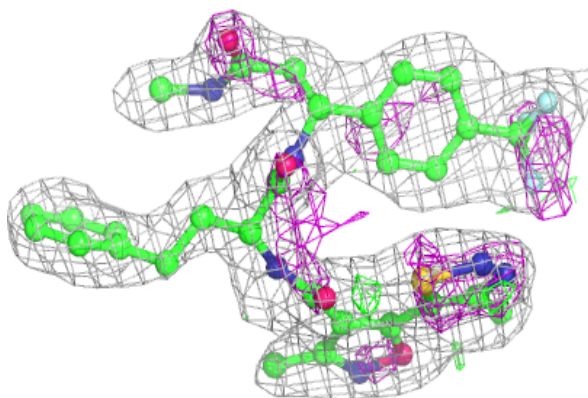
The following is a graphical depiction of the model fit to experimental electron density of all instances of the Ligand of Interest. In addition, ligands with molecular weight > 250 and outliers as shown on the geometry validation Tables will also be included. Each fit is shown from different orientation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

Electron density around S5E B 901:

$2mF_o-DF_c$ (at 0.7 rmsd) in gray
 mF_o-DF_c (at 3 rmsd) in purple (negative)
and green (positive)

**Electron density around S5E A 901:**

$2mF_o-DF_c$ (at 0.7 rmsd) in gray
 mF_o-DF_c (at 3 rmsd) in purple (negative)
and green (positive)



6.5 Other polymers

There are no such residues in this entry.