



Full wwPDB X-ray Structure Validation Report ⓘ

Jan 16, 2017 – 08:29 PM EST

PDB ID : 5TC0
Title : Structure-based optimization of 1H-imidazole-2-carboxamides as Axl kinase inhibitors utilizing a Mer mutant surrogate
Authors : Hoffman, I.D.; Lawson, J.D.
Deposited on : 2016-09-13
Resolution : 2.24 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

<http://wwpdb.org/validation/2016/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 : 1.7.1 (RC1), CSD as537be (2016)
Xtriage (Phenix) : 1.9-1692
EDS : rb-20028442
Percentile statistics : 20151230.v01 (using entries in the PDB archive December 30th 2015)
Refmac : 5.8.0135
CCP4 : 6.5.0
Ideal geometry (proteins) : Engh & Huber (2001)
Ideal geometry (DNA, RNA) : Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP) : rb-20028442

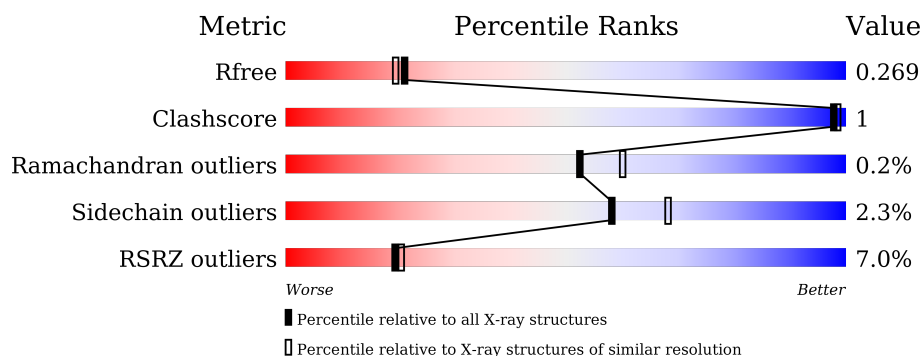
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.24 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}	91344	1611 (2.26-2.22)
Clashscore	102246	1764 (2.26-2.22)
Ramachandran outliers	100387	1724 (2.26-2.22)
Sidechain outliers	100360	1724 (2.26-2.22)
RSRZ outliers	91569	1616 (2.26-2.22)

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 on the lower bar indicate the fraction of residues that contain outliers for ≥ 3 , 2, 1 and 0 types of geometric quality criteria. 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	314	<div> <div>7%</div> <div> <div></div> <div>72%</div> <div>•</div> <div>24%</div> </div> </div>
1	B	314	<div> <div>4%</div> <div> <div></div> <div>75%</div> <div>5%</div> <div>20%</div> </div> </div>

2 Entry composition

There are 3 unique types of molecules in this entry. The entry contains 4002 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
1	A	238	Total	C	N	O	S	0	0	0
			1915	1229	318	348	20			
1	B	250	Total	C	N	O	S	0	0	0
			2024	1296	338	370	20			

There are 40 discrepancies between the modelled and reference sequences:

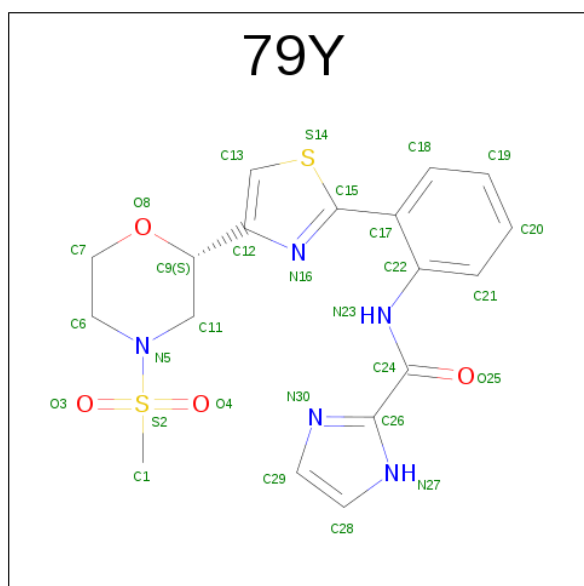
Chain	Residue	Modelled	Actual	Comment	Reference
A	551	MET	-	initiating methionine	UNP Q12866
A	552	GLY	-	expression tag	UNP Q12866
A	553	SER	-	expression tag	UNP Q12866
A	554	SER	-	expression tag	UNP Q12866
A	555	HIS	-	expression tag	UNP Q12866
A	556	HIS	-	expression tag	UNP Q12866
A	557	HIS	-	expression 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	SER	-	expression tag	UNP Q12866
A	562	SER	-	expression tag	UNP Q12866
A	563	GLY	-	expression tag	UNP Q12866
A	564	LEU	-	expression tag	UNP Q12866
A	565	VAL	-	expression tag	UNP Q12866
A	566	PRO	-	expression tag	UNP Q12866
A	567	ARG	-	expression tag	UNP Q12866
A	568	GLY	-	expression tag	UNP Q12866
A	569	SER	-	expression tag	UNP Q12866
A	650	MET	ILE	conflict	UNP Q12866
B	551	MET	-	initiating methionine	UNP Q12866
B	552	GLY	-	expression tag	UNP Q12866
B	553	SER	-	expression tag	UNP Q12866
B	554	SER	-	expression tag	UNP Q12866
B	555	HIS	-	expression tag	UNP Q12866

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Chain	Residue	Modelled	Actual	Comment	Reference
B	556	HIS	-	expression tag	UNP Q12866
B	557	HIS	-	expression tag	UNP Q12866
B	558	HIS	-	expression tag	UNP Q12866
B	559	HIS	-	expression tag	UNP Q12866
B	560	HIS	-	expression tag	UNP Q12866
B	561	SER	-	expression tag	UNP Q12866
B	562	SER	-	expression tag	UNP Q12866
B	563	GLY	-	expression tag	UNP Q12866
B	564	LEU	-	expression tag	UNP Q12866
B	565	VAL	-	expression tag	UNP Q12866
B	566	PRO	-	expression tag	UNP Q12866
B	567	ARG	-	expression tag	UNP Q12866
B	568	GLY	-	expression tag	UNP Q12866
B	569	SER	-	expression tag	UNP Q12866
B	650	MET	ILE	conflict	UNP Q12866

- Molecule 2 is N-(2-{4-[(2S)-4-(methylsulfonyl)morpholin-2-yl]-1,3-thiazol-2-yl}phenyl)-1H-imidazole-2-carboxamide (three-letter code: 79Y) (formula: C₁₈H₁₉N₅O₄S₂).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	N	O	S	0	0
			29	18	5	4	2		

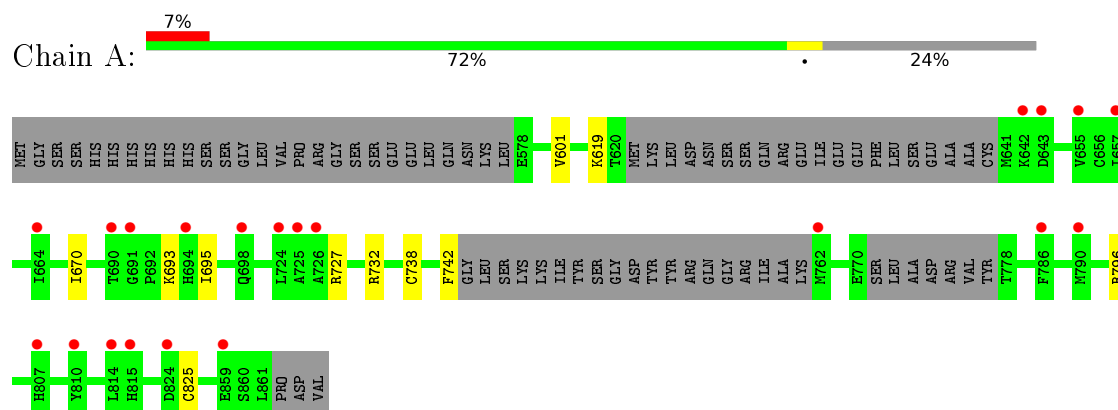
- Molecule 3 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	19	Total 19	O 19	0	0
3	B	15	Total 15	O 15	0	0

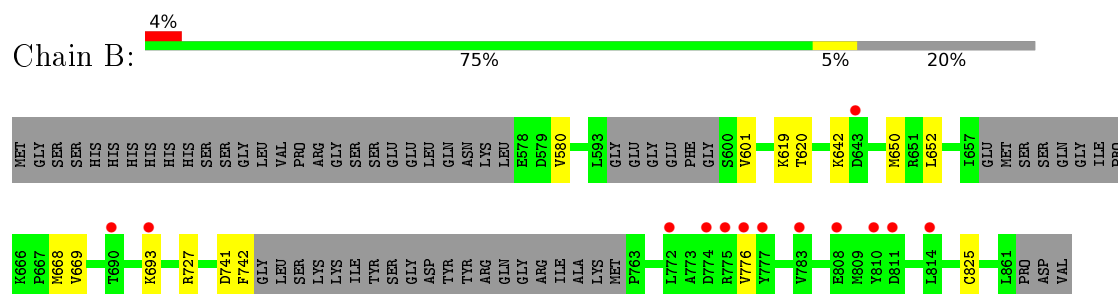
3 Residue-property plots [i](#)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors 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 ($\text{RSRZ} > 2$). 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	50.41Å 91.50Å 69.54Å 90.00° 99.47° 90.00°	Depositor
Resolution (Å)	30.00 – 2.24 29.10 – 2.24	Depositor EDS
% Data completeness (in resolution range)	83.8 (30.00-2.24) 83.9 (29.10-2.24)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	3.54 (at 2.24Å)	Xtriage
Refinement program	REFMAC	Depositor
R, R_{free}	0.228 , 0.262 0.239 , 0.269	Depositor DCC
R_{free} test set	1237 reflections (5.17%)	DCC
Wilson B-factor (Å ²)	40.3	Xtriage
Anisotropy	0.164	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.33 , 35.3	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o, F_c correlation	0.93	EDS
Total number of atoms	4002	wwPDB-VP
Average B, all atoms (Å ²)	56.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 7.29% 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: 79Y

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	0.43	0/1955	0.71	0/2639
1	B	0.42	0/2064	0.69	1/2786 (0.0%)
All	All	0.42	0/4019	0.70	1/5425 (0.0%)

There are no bond length outliers.

All (1) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	B	727	ARG	NE-CZ-NH1	5.81	123.20	120.30

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	1915	0	1925	4	0
1	B	2024	0	2038	4	0
2	A	29	0	0	1	0
3	A	19	0	0	2	0
3	B	15	0	0	0	0
All	All	4002	0	3963	9	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 (9) 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:580:VAL:HG23	1:B:642:LYS:HD3	1.92	0.52
1:A:732:ARG:NE	3:A:1201:HOH:O	2.43	0.51
1:A:738:CYS:HB3	3:A:1201:HOH:O	2.11	0.51
1:B:652:LEU:CD1	1:B:669:VAL:HG13	2.41	0.50
1:A:601:VAL:HG22	1:A:619:LYS:HG2	1.97	0.46
1:A:695:ILE:O	1:A:796:ARG:NH2	2.49	0.45
1:B:601:VAL:HG22	1:B:619:LYS:HG2	1.98	0.45
2:A:1100:79Y:N23	2:A:1100:79Y:N16	2.65	0.42
1:B:620:THR:HG22	1:B:668:MET:HG2	2.03	0.41

There are no symmetry-related clashes.

5.3 Torsion angles ⓘ

5.3.1 Protein backbone ⓘ

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	230/314 (73%)	225 (98%)	5 (2%)	0	100	100
1	B	242/314 (77%)	237 (98%)	4 (2%)	1 (0%)	39	42
All	All	472/628 (75%)	462 (98%)	9 (2%)	1 (0%)	52	60

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	B	776	VAL

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	215/281 (76%)	210 (98%)	5 (2%)	58	68
1	B	228/281 (81%)	223 (98%)	5 (2%)	60	70
All	All	443/562 (79%)	433 (98%)	10 (2%)	58	68

All (10) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	670	ILE
1	A	693	LYS
1	A	727	ARG
1	A	742	PHE
1	A	825	CYS
1	B	650	MET
1	B	693	LYS
1	B	741	ASP
1	B	742	PHE
1	B	825	CYS

Some 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 carbohydrates in this entry.

5.6 Ligand geometry

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	79Y	A	1100	-	26,32,32	2.46	3 (11%)	29,46,46	3.48	9 (31%)

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	79Y	A	1100	-	-	0/12/32/32	0/4/4/4

All (3) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1100	79Y	C26-C24	-10.85	1.46	1.53
2	A	1100	79Y	S2-N5	2.51	1.66	1.63
2	A	1100	79Y	C13-S14	4.25	1.77	1.70

All (9) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	1100	79Y	C1-S2-N5	-7.12	100.98	107.44
2	A	1100	79Y	O25-C24-C26	-2.72	117.70	120.93
2	A	1100	79Y	C22-C17-C15	-2.39	119.81	122.91
2	A	1100	79Y	C28-N27-C26	2.03	108.96	103.97
2	A	1100	79Y	C17-C15-N16	2.33	127.52	123.50
2	A	1100	79Y	C18-C17-C22	2.58	120.62	117.98
2	A	1100	79Y	C6-N5-S2	3.28	119.20	116.13
2	A	1100	79Y	C7-C6-N5	8.20	113.69	108.17
2	A	1100	79Y	C6-N5-C11	13.17	122.79	112.54

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	1100	79Y	1	0

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	238/314 (75%)	0.64	21 (8%) 12 13	32, 53, 87, 100	0
1	B	250/314 (79%)	0.44	13 (5%) 31 32	33, 54, 81, 103	0
All	All	488/628 (77%)	0.54	34 (6%) 19 20	32, 54, 84, 103	0

All (34) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	762	MET	7.9
1	A	664	ILE	4.2
1	B	810	TYR	4.2
1	A	642	LYS	4.0
1	A	810	TYR	4.0
1	B	775	ARG	4.0
1	A	643	ASP	3.8
1	A	814	LEU	3.7
1	A	698	GLN	3.6
1	A	691	GLY	3.4
1	A	725	ALA	3.3
1	B	811	ASP	3.1
1	B	693	LYS	3.0
1	B	776	VAL	3.0
1	A	690	THR	3.0
1	A	655	VAL	2.8
1	A	657	ILE	2.8
1	B	643	ASP	2.7
1	A	859	GLU	2.7
1	A	824	ASP	2.7
1	A	815	HIS	2.7
1	B	777	TYR	2.6
1	B	808	GLU	2.5
1	B	690	THR	2.5

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Mol	Chain	Res	Type	RSRZ
1	A	694	HIS	2.4
1	B	814	LEU	2.4
1	A	726	ALA	2.3
1	A	790	MET	2.1
1	B	774	ASP	2.1
1	B	783	VAL	2.1
1	B	772	LEU	2.1
1	A	807	HIS	2.0
1	A	724	LEU	2.0
1	A	786	PHE	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 carbohydrates 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. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. 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	LLDF	B-factors(\AA^2)	Q<0.9
2	79Y	A	1100	29/29	0.95	0.13	-0.24	41,47,58,62	0

6.5 Other polymers [i](#)

There are no such residues in this entry.