



Full wwPDB X-ray Structure Validation Report

Feb 26, 2014 – 04:29 PM GMT

PDB ID : 3UI7
Title : Discovery of orally active pyrazoloquinoline as a potent PDE10 inhibitor for the management of schizophrenia
Authors : Yang, S.; Smotryski, J.; Mcelroy, W.; Ho, G.; Tulshian, D.; Greenlee, W.J.; Hodgson, R.; Xiao, L.; Hruza, A.
Deposited on : 2011-11-04
Resolution : 2.28 Å(reported)

This is a full wwPDB 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/ValidationPDFNotes.html>

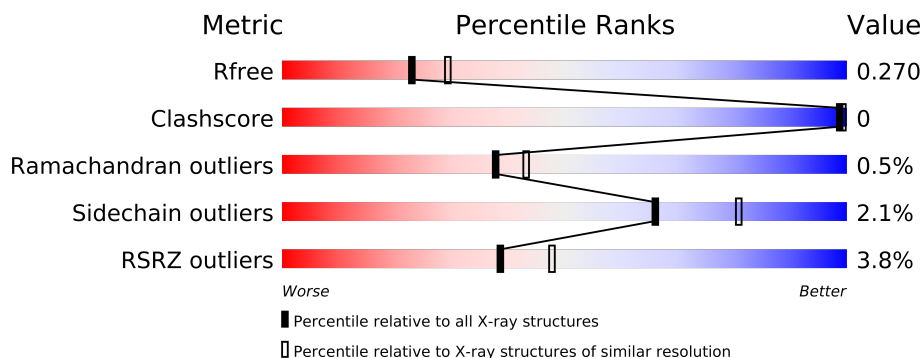
The following versions of software and data (see [references](#)) were used in the production of this report:

MolProbity : 4.02b-467
Mogul : 1.15 2013
Xtriage (Phenix) : dev-1323
EDS : stable22639
Percentile statistics : 21963
Refmac : 5.8.0049
CCP4 : 6.3.0 (Settle)
Ideal geometry (proteins) : Engh & Huber (2001)
Ideal geometry (DNA, RNA) : Parkinson et. al. (1996)
Validation Pipeline (wwPDB-VP) : stable22683

1 Overall quality at a glance



The reported resolution of this entry is 2.28 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}	66092	3861 (2.30-2.26)
Clashscore	79885	4801 (2.30-2.26)
Ramachandran outliers	78287	4729 (2.30-2.26)
Sidechain outliers	78261	4728 (2.30-2.26)
RSRZ outliers	66119	3864 (2.30-2.26)

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. The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density.

Mol	Chain	Length	Quality of chain
1	A	333	
1	B	333	

2 Entry composition

There are 5 unique types of molecules in this entry. The entry contains 5275 atoms, of which 0 are hydrogen and 0 are deuterium.

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.

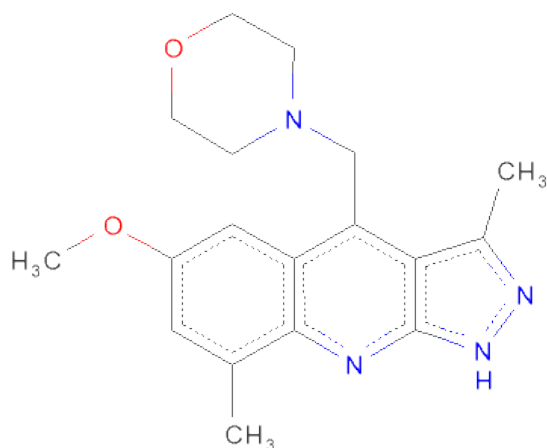
- Molecule 1 is a protein called cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	315	Total	C	N	O	S	0	0	0
			2560	1638	436	463	23			
1	B	315	Total	C	N	O	S	0	0	0
			2560	1638	436	463	23			

There are 8 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	438	GLY	-	EXPRESSION TAG	UNP Q9Y233
A	446	SER	-	INSERTION	UNP Q9Y233
A	447	HIS	-	INSERTION	UNP Q9Y233
A	448	MET	-	INSERTION	UNP Q9Y233
B	438	GLY	-	EXPRESSION TAG	UNP Q9Y233
B	446	SER	-	INSERTION	UNP Q9Y233
B	447	HIS	-	INSERTION	UNP Q9Y233
B	448	MET	-	INSERTION	UNP Q9Y233

- Molecule 2 is 6-METHOXY-3,8-DIMETHYL-4-(MORPHOLIN-4-YLMETHYL)-1H-PYRAZOLO[3,4-B]QUINOLINE (three-letter code: C1L) (formula: C₁₈H₂₂N₄O₂).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	A	1	Total	C	N	O	0	0
			24	18	4	2		
2	B	1	Total	C	N	O	0	0
			24	18	4	2		

- Molecule 3 is MAGNESIUM ION (three-letter code: MG) (formula: Mg).

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

- Molecule 4 is ZINC ION (three-letter code: ZN) (formula: Zn).

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	B	1	Total	Zn	0	0
			1	1		
4	A	1	Total	Zn	0	0
			1	1		

- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	A	56	Total	O	0	0
			56	56		

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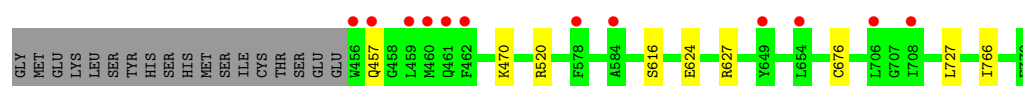
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	B	47	Total	O	0	0
			47	47		

3 Residue-property plots

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 ($RSRZ > 2$). 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.

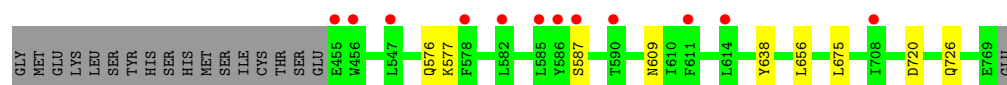
- Molecule 1: cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A

Chain A: 



- Molecule 1: cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A

Chain B: 



4 Data and refinement statistics

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α , β , γ	49.54Å 81.61Å 158.58Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	79.29 – 2.28 79.29 – 2.28	Depositor EDS
% Data completeness (in resolution range)	98.8 (79.29-2.28) 98.8 (79.29-2.28)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	0.07	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.43 (at 2.27Å)	Xtriage
Refinement program	BUSTER 2.11.2	Depositor
R, R_{free}	0.195 , 0.240 0.218 , 0.270	Depositor DCC
R_{free} test set	1527 reflections (5.13%)	DCC
Wilson B-factor (Å ²)	42.4	Xtriage
Anisotropy	0.526	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.32 , 60.7	EDS
Estimated twinning fraction	No twinning to report.	Xtriage
L-test for twinning	$\langle L \rangle = 0.40$, $\langle L^2 \rangle = 0.23$	Xtriage
Outliers	0 of 29801 reflections	Xtriage
F_o, F_c correlation	0.95	EDS
Total number of atoms	5275	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 4.37% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

5 Model quality

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: ZN, MG, C1L

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	0.46	0/2624	0.63	0/3553
1	B	0.46	0/2624	0.64	0/3553
All	All	0.46	0/5248	0.63	0/7106

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

There are no planarity outliers.

5.2 Close contacts

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 hydrogens added by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, and the number in parentheses is this value normalized per 1000 atoms of the molecule in the chain. The Symm-Clashes column gives symmetry related clashes, in the same way as for the Clashes column.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	2560	0	0	1	0
1	B	2560	0	0	1	0
2	A	24	0	22	0	0
2	B	24	0	22	1	0
3	A	1	0	0	0	0
3	B	1	0	0	0	0
4	A	1	0	0	0	0
4	B	1	0	0	0	0
5	A	56	0	0	0	0
5	B	47	0	0	0	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
All	All	5275	0	44	2	0

Clashscore is defined as the number of clashes calculated for the entry per 1000 atoms (including hydrogens) of the entry. The overall clashscore for this entry is 0.

All (2) close contacts within the same asymmetric unit are listed below.

Atom-1	Atom-2	Distance(Å)	Clash(Å)
1:B:726:GLN:NE2	2:B:1:C1L:H17	2.32	0.45
1:A:624:GLU:OE2	1:A:627:ARG:NH2	2.53	0.42

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	313/333 (94%)	299 (96%)	13 (4%)	1 (0%)	50	59
1	B	313/333 (94%)	300 (96%)	11 (4%)	2 (1%)	33	38
All	All	626/666 (94%)	599 (96%)	24 (4%)	3 (0%)	38	43

All (3) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	B	587	SER
1	A	676	CYS
1	B	609	ASN

5.3.2 Protein sidechains ⓘ

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	284/301 (94%)	278 (98%)	6 (2%)	66	81
1	B	284/301 (94%)	278 (98%)	6 (2%)	66	81
All	All	568/602 (94%)	556 (98%)	12 (2%)	66	81

All (12) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	457	GLN
1	A	470	LYS
1	A	520	ARG
1	A	616	SER
1	A	727	LEU
1	A	766	ILE
1	B	576	GLN
1	B	577	LYS
1	B	638	TYR
1	B	656	LEU
1	B	675	LEU
1	B	720	ASP

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

5.3.3 RNA ⓘ

There are no RNA chains in this entry.

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

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

5.5 Carbohydrates ⓘ

There are no carbohydrates in this entry.

5.6 Ligand geometry ⓘ

Of 6 ligands modelled in this entry, 4 are monoatomic - leaving 2 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$
2	C1L	A	1	-	27,27,27	1.33	4 (14%)	34,39,39	1.34	6 (17%)
2	C1L	B	1	-	27,27,27	1.46	3 (11%)	34,39,39	1.39	5 (14%)

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	C1L	A	1	-	-	0/6/14/14	0/1/4/4
2	C1L	B	1	-	-	0/6/14/14	0/1/4/4

All (7) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	1	C1L	C14-C9	3.57	1.43	1.37
2	A	1	C1L	C14-C9	3.56	1.43	1.37
2	B	1	C1L	C13-C7	-3.01	1.48	1.50
2	B	1	C1L	N11-N12	-2.84	1.32	1.37
2	A	1	C1L	N11-N12	-2.27	1.33	1.37
2	A	1	C1L	C14-C10	2.17	1.43	1.38
2	A	1	C1L	C18-N19	2.07	1.51	1.47

All (11) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	B	1	C1L	C18-N19-C20	3.47	117.09	111.07
2	A	1	C1L	C18-N19-C24	2.85	116.01	111.07
2	A	1	C1L	C2-C1-C3	-2.74	116.42	119.82
2	B	1	C1L	C24-N19-C20	2.44	114.92	108.86
2	B	1	C1L	C18-C1-C3	2.41	124.59	120.96
2	A	1	C1L	C5-C10-C14	-2.40	118.11	121.40
2	B	1	C1L	C23-O22-C21	2.34	117.88	109.90
2	A	1	C1L	C1-C18-N19	-2.30	109.70	113.39

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Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	1	C1L	C10-C14-C9	2.27	122.96	120.57
2	A	1	C1L	C18-N19-C20	2.05	114.63	111.07
2	B	1	C1L	C5-C10-C14	-2.04	118.61	121.40

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

5.7 Other polymers ⓘ

There are no such residues in this entry.

5.8 Polymer linkage issues

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	315/333 (94%)	0.09	12 (3%)	38 48	34, 64, 119, 241	0
1	B	315/333 (94%)	0.10	12 (3%)	38 48	40, 64, 118, 155	0
All	All	630/666 (94%)	0.10	24 (3%)	38 48	34, 64, 119, 241	0

All (24) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	456	TRP	7.0
1	B	708	ILE	4.2
1	B	614	LEU	4.1
1	A	706	LEU	3.9
1	A	457	GLN	3.7
1	A	459	LEU	3.6
1	B	578	PHE	3.5
1	B	587	SER	3.1
1	A	708	ILE	3.0
1	B	582	LEU	2.9
1	B	455	GLU	2.8
1	A	584	ALA	2.8
1	B	590	THR	2.7
1	B	611	PHE	2.7
1	B	547	LEU	2.6
1	A	578	PHE	2.4
1	B	585	LEU	2.3
1	A	461	GLN	2.2
1	A	654	LEU	2.1
1	A	649	TYR	2.1
1	A	462	PHE	2.1
1	B	586	TYR	2.1
1	A	460	MET	2.0
1	B	456	TRP	2.0

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

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

6.3 Carbohydrates ⓘ

There are no carbohydrates in this entry.

6.4 Ligands ⓘ

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	RSR	LLDF	B-factors(Å ²)	Q<0.9
2	C1L	A	1	24/24	0.15	0.88	40,44,50,52	0
4	ZN	B	772	1/1	0.11	-0.45	47,47,47,47	0
2	C1L	B	1	24/24	0.10	-0.56	35,39,47,51	0
4	ZN	A	772	1/1	0.09	-0.81	39,39,39,39	0
3	MG	A	771	1/1	0.07	-2.68	38,38,38,38	0
3	MG	B	771	1/1	0.07	-2.73	28,28,28,28	0

6.5 Other polymers ⓘ

There are no such residues in this entry.