



wwPDB X-ray Structure Validation Summary Report

Aug 22, 2014 – 01:59 AM EDT

PDB ID : 4C1I
Title : Selective Inhibitors of PDE2, PDE9, and PDE10: Modulators of Activity of the Central Nervous System
Authors : Jorgensen, M.; Kehler, J.; Langgard, M.; Svenstrup, N.; Tagmose, L.
Deposited on : 2013-08-12
Resolution : 2.40 Å(reported)

This is a wwPDB validation summary 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>

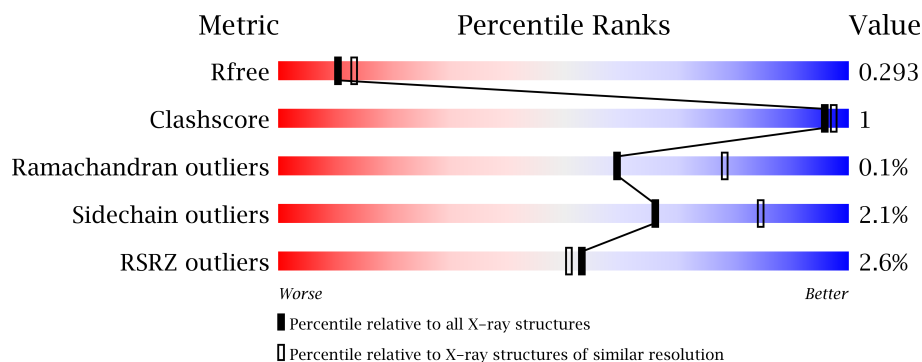
The following versions of software and data (see [references](#)) were used in the production of this report:

MolProbity : 4.02b-467
Mogul : 1.16 November 2013
Xtriage (Phenix) : dev-1439
EDS : stable23489
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) : stable23489

1 Overall quality at a glance

The reported resolution of this entry is 2.40 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	2207 (2.40-2.40)
Clashscore	79885	2789 (2.40-2.40)
Ramachandran outliers	78287	2736 (2.40-2.40)
Sidechain outliers	78261	2737 (2.40-2.40)
RSRZ outliers	66119	2210 (2.40-2.40)

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	353	
1	B	353	
1	C	353	
1	D	353	

2 Entry composition

There are 5 unique types of molecules in this entry. The entry contains 10670 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 CGMP-DEPENDENT 3', 5'-CYCLIC PHOSPHODIESTERASE.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	325	Total	C	N	O	S	0	0	0
			2625	1673	451	476	25			
1	B	320	Total	C	N	O	S	0	0	0
			2581	1646	437	473	25			
1	C	319	Total	C	N	O	S	0	0	0
			2577	1641	440	472	24			
1	D	319	Total	C	N	O	S	0	0	0
			2551	1626	434	466	25			

There are 36 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	576	MET	-	EXPRESSION TAG	UNP O00408
A	577	GLY	-	EXPRESSION TAG	UNP O00408
A	922	ARG	-	EXPRESSION TAG	UNP O00408
A	923	HIS	-	EXPRESSION TAG	UNP O00408
A	924	HIS	-	EXPRESSION TAG	UNP O00408
A	925	HIS	-	EXPRESSION TAG	UNP O00408
A	926	HIS	-	EXPRESSION TAG	UNP O00408
A	927	HIS	-	EXPRESSION TAG	UNP O00408
A	928	HIS	-	EXPRESSION TAG	UNP O00408
B	576	MET	-	EXPRESSION TAG	UNP O00408
B	577	GLY	-	EXPRESSION TAG	UNP O00408
B	922	ARG	-	EXPRESSION TAG	UNP O00408
B	923	HIS	-	EXPRESSION TAG	UNP O00408
B	924	HIS	-	EXPRESSION TAG	UNP O00408
B	925	HIS	-	EXPRESSION TAG	UNP O00408
B	926	HIS	-	EXPRESSION TAG	UNP O00408
B	927	HIS	-	EXPRESSION TAG	UNP O00408
B	928	HIS	-	EXPRESSION TAG	UNP O00408
C	576	MET	-	EXPRESSION TAG	UNP O00408
C	577	GLY	-	EXPRESSION TAG	UNP O00408
C	922	ARG	-	EXPRESSION TAG	UNP O00408

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Chain	Residue	Modelled	Actual	Comment	Reference
C	923	HIS	-	EXPRESSION TAG	UNP O00408
C	924	HIS	-	EXPRESSION TAG	UNP O00408
C	925	HIS	-	EXPRESSION TAG	UNP O00408
C	926	HIS	-	EXPRESSION TAG	UNP O00408
C	927	HIS	-	EXPRESSION TAG	UNP O00408
C	928	HIS	-	EXPRESSION TAG	UNP O00408
D	576	MET	-	EXPRESSION TAG	UNP O00408
D	577	GLY	-	EXPRESSION TAG	UNP O00408
D	922	ARG	-	EXPRESSION TAG	UNP O00408
D	923	HIS	-	EXPRESSION TAG	UNP O00408
D	924	HIS	-	EXPRESSION TAG	UNP O00408
D	925	HIS	-	EXPRESSION TAG	UNP O00408
D	926	HIS	-	EXPRESSION TAG	UNP O00408
D	927	HIS	-	EXPRESSION TAG	UNP O00408
D	928	HIS	-	EXPRESSION TAG	UNP O00408

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- The chemical structure shows a pyrazoloquinoline core. The quinoline ring is fused to a pyrazole ring. At position 4 of the quinoline ring, there is an amino group (NH₂). At position 7 of the pyrazole ring, there is a side chain consisting of a chiral center (C20(R)) bonded to a hydroxyl group (OH, O38) and a 4-oxopentyl group (C21-C26-C28-C30-C31-C34). The side chain is drawn with a dashed bond to the chiral center, indicating its stereochemistry.

Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	A	1	Total 20	C 14	N 5	O 1	0	0
2	B	1	Total 20	C 14	N 5	O 1	0	0
2	C	1	Total 20	C 14	N 5	O 1	0	0

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Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	D	1	Total	C	N	O	0	0
			20	14	5	1		

- Molecule 3 is ZINC ION (three-letter code: ZN) (formula: Zn).

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	B	1	Total	Zn	0	0
			1	1		
3	A	1	Total	Zn	0	0
			1	1		
3	D	1	Total	Zn	0	0
			1	1		
3	C	1	Total	Zn	0	0
			1	1		

- Molecule 4 is MAGNESIUM ION (three-letter code: MG) (formula: Mg).

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	B	1	Total	Mg	0	0
			1	1		
4	A	1	Total	Mg	0	0
			1	1		
4	D	1	Total	Mg	0	0
			1	1		
4	C	1	Total	Mg	0	0
			1	1		

- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	A	68	Total	O	0	0
			68	68		
5	B	59	Total	O	0	0
			59	59		
5	C	74	Total	O	0	0
			74	74		
5	D	47	Total	O	0	0
			47	47		

4 Data and refinement statistics

Property	Value	Source
Space group	P 1	Depositor
Cell constants a, b, c, α , β , γ	47.05Å 81.81Å 93.34Å 110.16° 95.66° 93.21°	Depositor
Resolution (Å)	18.47 – 2.40 18.41 – 2.40	Depositor EDS
% Data completeness (in resolution range)	94.0 (18.47-2.40) 94.2 (18.41-2.40)	Depositor EDS
R_{merge}	0.10	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.21 (at 2.40Å)	Xtriage
Refinement program	REFMAC 5.7.0032	Depositor
R, R_{free}	0.225 , 0.287 0.232 , 0.293	Depositor DCC
R_{free} test set	2434 reflections (5.39%)	DCC
Wilson B-factor (Å ²)	29.0	Xtriage
Anisotropy	0.123	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.37 , 18.0	EDS
Estimated twinning fraction	No twinning to report.	Xtriage
L-test for twinning	$\langle L \rangle = 0.47$, $\langle L^2 \rangle = 0.30$	Xtriage
Outliers	0 of 47580 reflections	Xtriage
F_o, F_c correlation	0.90	EDS
Total number of atoms	10670	wwPDB-VP
Average B, all atoms (Å ²)	30.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 5.37% 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, EH9

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	0.31	0/2689	0.48	0/3636
1	B	0.31	0/2644	0.50	0/3577
1	C	0.31	0/2640	0.48	0/3573
1	D	0.30	0/2613	0.47	0/3538
All	All	0.31	0/10586	0.48	0/14324

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	2625	0	2531	4	0
1	B	2581	0	2481	8	0
1	C	2577	0	2472	3	0
1	D	2551	0	2437	5	0
2	A	20	0	23	0	0
2	B	20	0	23	2	0
2	C	20	0	23	2	0
2	D	20	0	23	0	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
3	A	1	0	0	0	0
3	B	1	0	0	0	0
3	C	1	0	0	0	0
3	D	1	0	0	0	0
4	A	1	0	0	0	0
4	B	1	0	0	0	0
4	C	1	0	0	0	0
4	D	1	0	0	0	0
5	A	68	0	0	0	0
5	B	59	0	0	0	0
5	C	74	0	0	0	0
5	D	47	0	0	0	0
All	All	10670	0	10013	24	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 1.

The worst 5 of 24 close contacts within the same asymmetric unit are listed below.

Atom-1	Atom-2	Distance(Å)	Clash(Å)
1:D:744:ASN:ND2	1:D:747:ASP:OD1	2.35	0.60
1:A:875:GLN:HE21	1:A:882:ALA:HA	1.74	0.53
2:B:1900:EH9:H402	2:B:1900:EH9:C14	2.40	0.51
1:B:582:TYR:CE1	1:B:641:ARG:HG3	2.46	0.50
2:C:1900:EH9:H402	2:C:1900:EH9:C14	2.42	0.49

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	323/353 (92%)	316 (98%)	7 (2%)	0	100	100
1	B	318/353 (90%)	311 (98%)	6 (2%)	1 (0%)	50	68

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Mol	Chain	Analysed	Favoured	Allowed	Outliers	Percentiles	
1	C	317/353 (90%)	313 (99%)	4 (1%)	0	100	100
1	D	317/353 (90%)	310 (98%)	7 (2%)	0	100	100
All	All	1275/1412 (90%)	1250 (98%)	24 (2%)	1 (0%)	59	78

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	B	747	ASP

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	282/319 (88%)	271 (96%)	11 (4%)	43	64
1	B	278/319 (87%)	274 (99%)	4 (1%)	78	92
1	C	277/319 (87%)	271 (98%)	6 (2%)	64	83
1	D	272/319 (85%)	270 (99%)	2 (1%)	91	97
All	All	1109/1276 (87%)	1086 (98%)	23 (2%)	66	84

5 of 23 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	901	LYS
1	B	617	MET
1	D	847	MET
1	B	584	LYS
1	B	683	ASP

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 11 such sidechains are listed below:

Mol	Chain	Res	Type
1	A	894	HIS
1	B	599	ASN
1	C	772	HIS

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Mol	Chain	Res	Type
1	A	875	GLN
1	C	666	HIS

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 12 ligands modelled in this entry, 8 are monoatomic - leaving 4 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	EH9	A	1906	-	21,21,21	1.43	2 (9%)	28,28,28	2.51	5 (17%)
2	EH9	B	1900	-	21,21,21	1.13	2 (9%)	28,28,28	2.54	7 (25%)
2	EH9	C	1900	-	21,21,21	1.30	2 (9%)	28,28,28	2.44	5 (17%)
2	EH9	D	1900	-	21,21,21	1.26	3 (14%)	28,28,28	2.40	5 (17%)

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	EH9	A	1906	-	1/1/2/2	0/11/14/14	0/2/2/2
2	EH9	B	1900	-	1/1/2/2	0/11/14/14	0/2/2/2
2	EH9	C	1900	-	1/1/2/2	0/11/14/14	0/2/2/2
2	EH9	D	1900	-	1/1/2/2	0/11/14/14	0/2/2/2

The worst 5 of 9 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1906	EH9	C36-C20	4.58	1.56	1.52
2	C	1900	EH9	C36-C20	3.70	1.56	1.52
2	D	1900	EH9	C3-N13	-3.56	1.32	1.37
2	B	1900	EH9	C3-N13	-3.40	1.32	1.37
2	C	1900	EH9	C3-N13	-3.35	1.32	1.37

The worst 5 of 22 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	1906	EH9	N4-C5-N6	-8.43	121.47	128.89
2	C	1900	EH9	N4-C5-N6	-8.27	121.62	128.89
2	D	1900	EH9	N4-C5-N6	-8.22	121.66	128.89
2	B	1900	EH9	N4-C5-N6	-8.13	121.74	128.89
2	A	1906	EH9	C2-C3-N4	-6.59	119.55	125.98

All (4) chirality outliers are listed below:

Mol	Chain	Res	Type	Atom
2	A	1906	EH9	C36
2	D	1900	EH9	C36
2	B	1900	EH9	C36
2	C	1900	EH9	C36

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	325/353 (92%)	0.03	6 (1%) 65 63	14, 26, 42, 79	0
1	B	320/353 (90%)	0.10	5 (1%) 68 67	16, 28, 45, 60	0
1	C	319/353 (90%)	0.10	7 (2%) 59 57	16, 28, 46, 64	0
1	D	319/353 (90%)	0.36	15 (4%) 30 28	19, 34, 57, 81	0
All	All	1283/1412 (90%)	0.15	33 (2%) 53 51	14, 29, 50, 81	0

The worst 5 of 33 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	582	TYR	4.8
1	A	587	HIS	4.8
1	D	583	THR	4.6
1	D	582	TYR	3.6
1	D	899	SER	3.5

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(\AA^2)	Q<0.9
2	EH9	B	1900	20/20	0.14	0.43	25,26,26,27	0
2	EH9	A	1906	20/20	0.15	0.25	23,24,26,26	0
2	EH9	C	1900	20/20	0.14	0.09	30,32,34,34	0
2	EH9	D	1900	20/20	0.15	-0.06	28,29,30,31	0
4	MG	A	1908	1/1	0.09	-1.94	16,16,16,16	0
4	MG	B	1902	1/1	0.07	-3.74	16,16,16,16	0
4	MG	D	1902	1/1	0.06	-4.38	19,19,19,19	0
4	MG	C	1902	1/1	0.05	-4.43	20,20,20,20	0
3	ZN	C	1901	1/1	0.03	-5.22	21,21,21,21	0
3	ZN	A	1907	1/1	0.02	-6.67	18,18,18,18	0
3	ZN	B	1901	1/1	0.05	-8.64	20,20,20,20	0
3	ZN	D	1901	1/1	0.04	-9.44	26,26,26,26	0

6.5 Other polymers ⓘ

There are no such residues in this entry.