



Full wwPDB X-ray Structure Validation Report ⓘ

Feb 13, 2017 – 09:16 pm GMT

PDB ID : 3UUO
Title : The discovery of potent, selectivity, and orally bioavailable pyrozoloquinolines as PDE10 inhibitors for the treatment of Schizophrenia
Authors : Ho, G.D.; Yang, S.; Smotryski, J.; Bercovici, A.; Nechuta, T.; Smith, E.M.; McElroy, W.; Tan, Z.; Tulshian, D.; Mckittrick, B.; Greenlee, W.J.; Hruza, A.; Xiao, L.; Rindgen, D.; Guzzi, M.; Zhang, X.; Bleickardt, C.; Mullins, D.; Hodgson, R.
Deposited on : 2011-11-28
Resolution : 2.11 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	:	1.7.2 (RC1), CSD as538be (2017)
Xtriage (Phenix)	:	1.9-1692
EDS	:	trunk28620
Percentile statistics	:	20161228.v01 (using entries in the PDB archive December 28th 2016)
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)	:	recalc28949

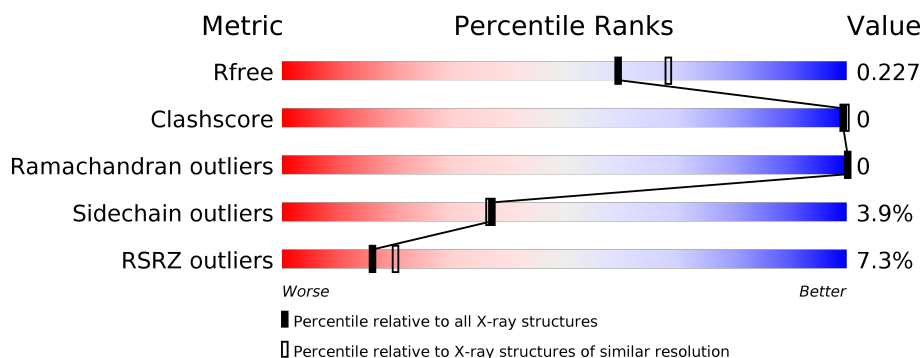
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.11 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}	100719	4988 (2.14-2.10)
Clashscore	112137	5557 (2.14-2.10)
Ramachandran outliers	110173	5504 (2.14-2.10)
Sidechain outliers	110143	5505 (2.14-2.10)
RSRZ outliers	101464	5021 (2.14-2.10)

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	337	<div> <div>4%</div> <div>88%</div> <div>9%</div> </div>
1	B	337	<div> <div>9%</div> <div>89%</div> <div>7%</div> </div>

2 Entry composition

There are 6 unique types of molecules in this entry. The entry contains 10218 atoms, of which 5019 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.

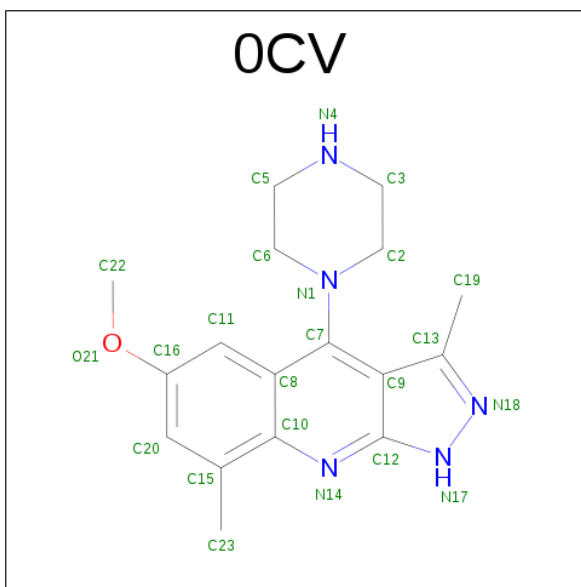
- Molecule 1 is a protein called cAMP and cAMP-inhibited cGMP 3',5'-cyclic phosphodiesterase 10A.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
1	A	305	Total	C	H	N	O	S	0	0	0
			4921	1580	2448	423	448	22			
1	B	315	Total	C	H	N	O	S	0	0	0
			5089	1638	2529	436	463	23			

There are 16 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	434	GLY	-	EXPRESSION TAG	UNP Q9Y233
A	435	SER	-	EXPRESSION TAG	UNP Q9Y233
A	436	HIS	-	EXPRESSION TAG	UNP Q9Y233
A	437	MET	-	EXPRESSION TAG	UNP Q9Y233
A	438	GLY	-	EXPRESSION TAG	UNP Q9Y233
A	446	SER	-	EXPRESSION TAG	UNP Q9Y233
A	447	HIS	-	EXPRESSION TAG	UNP Q9Y233
A	448	MET	-	EXPRESSION TAG	UNP Q9Y233
B	434	GLY	-	EXPRESSION TAG	UNP Q9Y233
B	435	SER	-	EXPRESSION TAG	UNP Q9Y233
B	436	HIS	-	EXPRESSION TAG	UNP Q9Y233
B	437	MET	-	EXPRESSION TAG	UNP Q9Y233
B	438	GLY	-	EXPRESSION TAG	UNP Q9Y233
B	446	SER	-	EXPRESSION TAG	UNP Q9Y233
B	447	HIS	-	EXPRESSION TAG	UNP Q9Y233
B	448	MET	-	EXPRESSION TAG	UNP Q9Y233

- Molecule 2 is 6-METHOXY-3,8-DIMETHYL-4-(PIPERAZIN-1-YL)-1H-PYRAZOLO[3,4-B]QUINOLINE (three-letter code: 0CV) (formula: C₁₇H₂₁N₅O).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	H	N	O	0	0
			44	17	21	5	1		
2	B	1	Total	C	H	N	O	0	0
			44	17	21	5	1		

- 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 PHOSPHATE ION (three-letter code: PO4) (formula: O₄P).



Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
5	A	1	Total	O	P	0	0
			5	4	1		
5	B	1	Total	O	P	0	0
			5	4	1		

- Molecule 6 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
6	A	55	Total	O	0	0
			55	55		
6	B	51	Total	O	0	0
			51	51		

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



4 Data and refinement statistics

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α , β , γ	50.57Å 82.23Å 161.34Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	29.79 – 2.11 29.67 – 2.11	Depositor EDS
% Data completeness (in resolution range)	94.2 (29.79-2.11) 94.3 (29.67-2.11)	Depositor EDS
R_{merge}	0.08	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.73 (at 2.12Å)	Xtriage
Refinement program	BUSTER 2.11.2	Depositor
R, R_{free}	0.195 , 0.227 0.198 , 0.227	Depositor DCC
R_{free} test set	1874 reflections (5.29%)	DCC
Wilson B-factor (Å ²)	32.9	Xtriage
Anisotropy	0.730	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.42 , 49.3	EDS
L-test for twinning ²	$\langle L \rangle = 0.48$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o, F_c correlation	0.96	EDS
Total number of atoms	10218	wwPDB-VP
Average B, all atoms (Å ²)	52.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.94% 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

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: PO4, MG, OCV, ZN

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	0/2534	0.57	0/3430
1	B	0.47	0/2624	0.58	0/3553
All	All	0.46	0/5158	0.57	0/6983

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

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	2473	2448	2446	0	0
1	B	2560	2529	2527	1	0
2	A	23	21	21	0	0
2	B	23	21	21	0	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	5	0	0	0	0
5	B	5	0	0	0	0
6	A	55	0	0	0	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
6	B	51	0	0	0	0
All	All	5199	5019	5015	1	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 0.

All (1) 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:483:GLU:HA	1:B:486:TRP:CE2	2.51	0.44

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	303/337 (90%)	299 (99%)	4 (1%)	0	100	100
1	B	313/337 (93%)	308 (98%)	5 (2%)	0	100	100
All	All	616/674 (91%)	607 (98%)	9 (2%)	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	275/304 (90%)	265 (96%)	10 (4%)	40	40
1	B	284/304 (93%)	272 (96%)	12 (4%)	34	33
All	All	559/608 (92%)	537 (96%)	22 (4%)	37	36

All (22) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	467	ARG
1	A	551	LEU
1	A	635	LEU
1	A	642	ARG
1	A	656	LEU
1	A	686	LYS
1	A	711	ILE
1	A	713	MET
1	A	727	LEU
1	A	760	SER
1	B	467	ARG
1	B	484	ASN
1	B	517	LYS
1	B	582	LEU
1	B	585	LEU
1	B	615	SER
1	B	617	SER
1	B	620	GLU
1	B	656	LEU
1	B	686	LYS
1	B	714	MET
1	B	727	LEU

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 molecules 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 [i](#)

There are no carbohydrates in this entry.

5.6 Ligand geometry [i](#)

Of 8 ligands modelled in this entry, 4 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	OCV	A	1	-	22,26,26	1.79	6 (27%)	26,38,38	3.62	11 (42%)
5	PO4	A	773	3,4	4,4,4	3.00	3 (75%)	6,6,6	0.69	0
2	OCV	B	1	-	22,26,26	1.70	5 (22%)	26,38,38	3.15	7 (26%)
5	PO4	B	773	3,4	4,4,4	3.04	2 (50%)	6,6,6	0.46	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
2	OCV	A	1	-	-	0/6/14/14	0/4/4/4
5	PO4	A	773	3,4	-	0/0/0/0	0/0/0/0
2	OCV	B	1	-	-	0/6/14/14	0/4/4/4
5	PO4	B	773	3,4	-	0/0/0/0	0/0/0/0

All (16) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1	OCV	C19-C13	-3.91	1.48	1.50
2	B	1	OCV	C6-N1	-3.85	1.40	1.46
2	A	1	OCV	C7-C9	-2.77	1.38	1.44
2	B	1	OCV	C7-C9	-2.68	1.38	1.44
2	A	1	OCV	C12-N14	-2.37	1.32	1.34
2	B	1	OCV	C12-N14	-2.21	1.32	1.34

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Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
5	A	773	PO4	P-O2	2.16	1.62	1.54
5	A	773	PO4	P-O3	2.21	1.62	1.54
5	B	773	PO4	P-O3	2.28	1.62	1.54
2	A	1	0CV	C20-C15	2.50	1.41	1.37
2	B	1	0CV	C20-C15	2.92	1.42	1.37
2	A	1	0CV	C7-C8	3.02	1.44	1.40
2	A	1	0CV	C9-C12	3.28	1.51	1.43
2	B	1	0CV	C7-C8	3.75	1.45	1.40
5	A	773	PO4	P-O1	4.91	1.61	1.50
5	B	773	PO4	P-O1	5.15	1.61	1.50

All (18) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	B	1	0CV	C8-C10-N14	-4.72	117.53	123.38
2	A	1	0CV	C8-C10-N14	-4.01	118.41	123.38
2	A	1	0CV	C8-C7-C9	-3.55	115.40	122.05
2	B	1	0CV	C8-C7-C9	-3.30	115.87	122.05
2	A	1	0CV	C11-C8-C7	-2.91	119.09	123.32
2	A	1	0CV	C11-C16-C20	-2.22	118.56	121.30
2	A	1	0CV	C23-C15-C20	-2.20	117.56	120.77
2	B	1	0CV	C23-C15-C10	2.63	122.83	120.08
2	A	1	0CV	C15-C10-N14	2.65	122.06	118.30
2	A	1	0CV	C16-C11-C8	2.67	123.82	120.05
2	A	1	0CV	C10-N14-C12	2.72	120.64	116.57
2	B	1	0CV	C16-C11-C8	2.78	123.99	120.05
2	A	1	0CV	C23-C15-C10	2.98	123.19	120.08
2	B	1	0CV	C2-N1-C6	3.92	119.88	111.57
2	B	1	0CV	C10-N14-C12	4.29	122.98	116.57
2	A	1	0CV	C2-N1-C6	5.58	123.39	111.57
2	B	1	0CV	C7-C8-C10	12.28	122.27	116.30
2	A	1	0CV	C7-C8-C10	14.82	123.50	116.30

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

No monomer is involved in short contacts.

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	305/337 (90%)	0.16	15 (4%) 30 36	28, 46, 84, 107	0
1	B	315/337 (93%)	0.45	30 (9%) 9 11	30, 48, 96, 132	0
All	All	620/674 (91%)	0.31	45 (7%) 16 20	28, 47, 88, 132	0

All (45) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	457	GLN	6.3
1	A	585	LEU	5.1
1	A	467	ARG	4.9
1	B	533	VAL	4.2
1	A	584	ALA	4.1
1	B	551	LEU	3.8
1	A	502	CYS	3.8
1	B	458	GLY	3.5
1	B	560	CYS	3.5
1	A	501	SER	3.4
1	A	533	VAL	3.4
1	B	536	CYS	3.3
1	B	613	THR	3.3
1	A	466	VAL	3.0
1	B	461	GLN	3.0
1	B	534	ALA	2.9
1	B	585	LEU	2.9
1	B	456	TRP	2.9
1	B	606	GLU	2.9
1	B	616	SER	2.9
1	A	647	GLU	2.9
1	B	673	CYS	2.7
1	B	532	THR	2.7
1	B	537	MET	2.7

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Mol	Chain	Res	Type	RSRZ
1	B	559	ALA	2.7
1	B	670	MET	2.6
1	A	673	CYS	2.6
1	A	768	GLY	2.6
1	A	505	LEU	2.6
1	B	619	TYR	2.5
1	B	531	VAL	2.5
1	A	536	CYS	2.5
1	B	563	HIS	2.4
1	A	766	ILE	2.4
1	B	581	PRO	2.4
1	B	557	LEU	2.4
1	A	532	THR	2.4
1	B	501	SER	2.3
1	B	578	PHE	2.2
1	B	676	CYS	2.1
1	B	506	GLU	2.1
1	B	675	LEU	2.0
1	B	671	THR	2.0
1	B	618	GLU	2.0
1	A	674	ASP	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(Å ²)	Q<0.9
3	MG	A	771	1/1	0.98	0.19	0.61	29,29,29,29	0

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Mol	Type	Chain	Res	Atoms	RSCC	RSR	LLDF	B-factors(\AA^2)	Q<0.9
3	MG	B	771	1/1	0.99	0.20	0.59	37,37,37,37	0
2	OCV	A	1	23/23	0.94	0.13	-0.02	39,44,48,50	0
5	PO4	B	773	5/5	0.97	0.15	-0.03	43,45,45,46	0
5	PO4	A	773	5/5	0.99	0.16	-0.14	32,35,38,40	0
2	OCV	B	1	23/23	0.96	0.12	-0.24	35,40,42,42	0
4	ZN	A	772	1/1	1.00	0.15	-0.78	35,35,35,35	0
4	ZN	B	772	1/1	1.00	0.12	-1.17	37,37,37,37	0

6.5 Other polymers [i](#)

There are no such residues in this entry.