W O R L D W I D E

wwPDB

P R O T E I N   D A T A   B A N K

wwPDB X-ray Structure Validation Summary Report (i)

Sep 15, 2020 – 02:29 PM EDT

PDB ID	:	6P3D
Title	:	The co-crystal structure of BRAF(V600E) with ponatinib
Authors	:	Agianian, B.; Gavathiotis, E.
Deposited on	:	2019-05-23
Resolution	:	2.11 Å(reported)

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

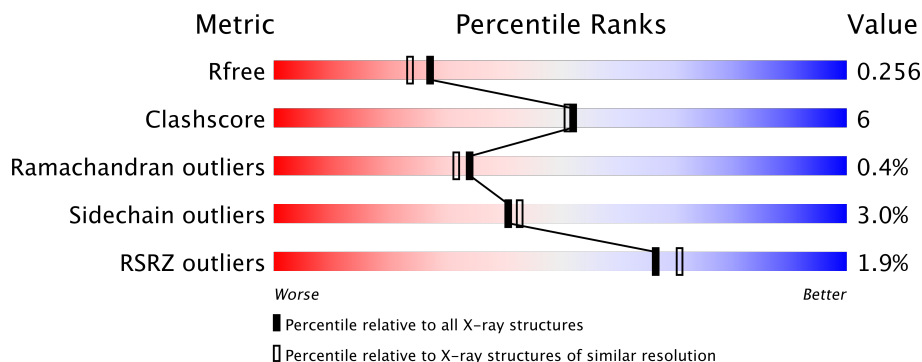|		
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.14.4
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.14.4

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	Percentile Ranks	Value
Rfree		0.256
Clashscore		6
Ramachandran outliers		0.4%
Sidechain outliers		3.0%
RSRZ outliers		1.9%

Worse   *Better*

■ Percentile relative to all X-ray structures
◻ Percentile relative to X-ray structures of similar resolution

Metric	Whole archive (#Entries)	Similar resolution (#Entries, resolution range(Å))
R$_{free}$	130704	6241 (2.14-2.10)
Clashscore	141614	6778 (2.14-2.10)
Ramachandran outliers	138981	6705 (2.14-2.10)
Sidechain outliers	138945	6706 (2.14-2.10)
RSRZ outliers	127900	6112 (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 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 <=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	297	2% 76% 11% · 11%

The following table lists non-polymeric compounds, carbohydrate monomers and non-standard residues in protein, DNA, RNA chains that are outliers for geometric or electron-density-fit criteria:

Mol	Type	Chain	Res	Chirality	Geometry	Clashes	Electron density
4	NH4	A	1010	-	-	X	-

2 Entry composition ⓘ

There are 6 unique types of molecules in this entry. The entry contains 2293 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 Serine/threonine-protein kinase B-raf.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	264	2108	1333	374	387	14	0	0	0

There are 38 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	427	MET	-	initiating methionine	UNP P15056
A	428	GLY	-	expression tag	UNP P15056
A	429	SER	-	expression tag	UNP P15056
A	430	SER	-	expression tag	UNP P15056
A	431	HIS	-	expression tag	UNP P15056
A	432	HIS	-	expression tag	UNP P15056
A	433	HIS	-	expression tag	UNP P15056
A	434	HIS	-	expression tag	UNP P15056
A	435	HIS	-	expression tag	UNP P15056
A	436	HIS	-	expression tag	UNP P15056
A	437	SER	-	expression tag	UNP P15056
A	438	SER	-	expression tag	UNP P15056
A	439	GLY	-	expression tag	UNP P15056
A	440	LEU	-	expression tag	UNP P15056
A	441	VAL	-	expression tag	UNP P15056
A	442	PRO	-	expression tag	UNP P15056
A	443	ARG	-	expression tag	UNP P15056
A	444	GLY	-	expression tag	UNP P15056
A	445	SER	-	expression tag	UNP P15056
A	446	LYS	-	expression tag	UNP P15056
A	447	MET	-	expression tag	UNP P15056
A	543	ALA	ILE	conflict	UNP P15056
A	544	SER	ILE	conflict	UNP P15056
A	551	LYS	ILE	conflict	UNP P15056
A	562	ARG	GLN	conflict	UNP P15056
A	588	ASN	LEU	conflict	UNP P15056
A	600	GLU	VAL	conflict	UNP P15056

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Chain	Residue	Modelled	Actual	Comment	Reference
A	630	SER	LYS	conflict	UNP P15056
A	667	GLU	PHE	conflict	UNP P15056
A	673	SER	TYR	conflict	UNP P15056
A	688	ARG	ALA	conflict	UNP P15056
A	706	SER	LEU	conflict	UNP P15056
A	709	ARG	GLN	conflict	UNP P15056
A	713	GLU	SER	conflict	UNP P15056
A	716	GLU	LEU	conflict	UNP P15056
A	720	GLU	SER	conflict	UNP P15056
A	722	SER	-	expression tag	UNP P15056
A	723	GLY	-	expression tag	UNP P15056

- Molecule 2 is 3-(imidazo[1,2-b]pyridazin-3-ylethynyl)-4-methyl-N-{4-[(4-methylpiperaz in-1-yl)methyl]-3-(trifluoromethyl)phenyl}benzam ide (three-letter code: 0LI) (formula: $C_{29}H_{27}F_3N_6O$) (labeled as "Ligand of Interest" by author).
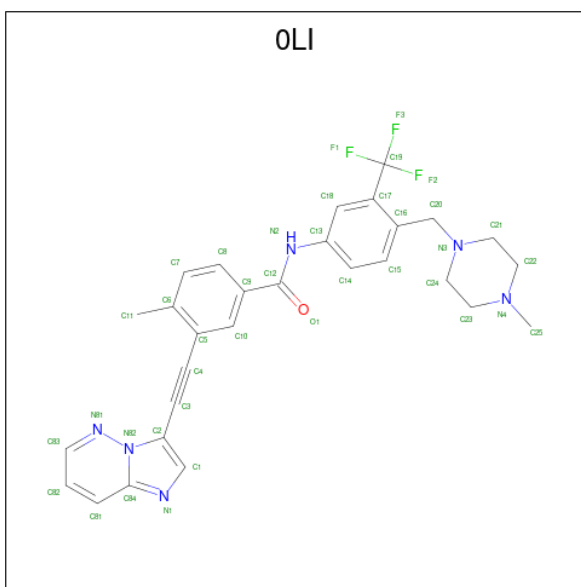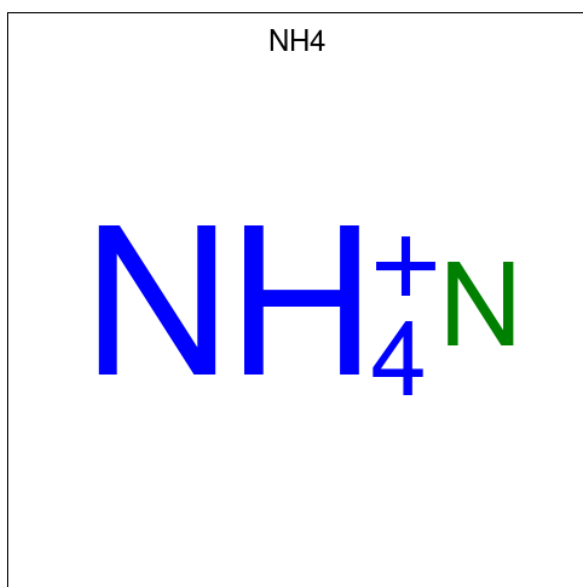

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	F	N	O		
2	A	1	39	29	3	6	1	0	0

- Molecule 3 is SULFATE ION (three-letter code: SO4) (formula: O_4S).

Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0
3	A	1	Total 5	O 4	S 1	0	0

- Molecule 4 is AMMONIUM ION (three-letter code: NH4) (formula: H_4N).

NH4

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	1	Total 1	N 1	0	0

- Molecule 5 is 1,2-ETHANEDIOL (three-letter code: EDO) (formula: $C_2H_6O_2$).

EDO

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

- Molecule 6 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
6	A	97	Total 97	O 97	0	0

3 Residue-property plots ⓘ

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: Serine/threonine-protein kinase B-raf
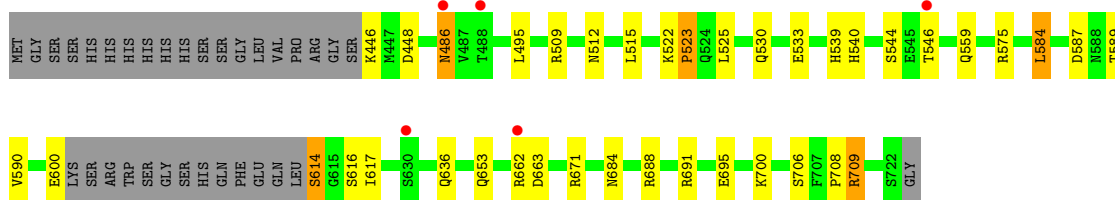
4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 43 2 2	Depositor
Cell constants a, b, c, α, β, γ	118.84Å 118.84Å 51.53Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	84.03 – 2.11 84.03 – 2.11	Depositor EDS
% Data completeness (in resolution range)	99.4 (84.03-2.11) 99.4 (84.03-2.11)	Depositor EDS
R_{merge}	(Not available)	Depositor
R_{sym}	0.10	Depositor
$< I/\sigma(I) >$ [1]	4.42 (at 2.10Å)	Xtriage
Refinement program	REFMAC 5.8.0158	Depositor
R, R_{free}	0.185 , 0.245 0.195 , 0.256	Depositor DCC
R_{free} test set	1117 reflections (5.11%)	wwPDB-VP
Wilson B-factor (Å^2)	27.0	Xtriage
Anisotropy	0.024	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.37 , 46.0	EDS
L-test for twinning[2]	$< |L| > = 0.46, < L^2 > = 0.28$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o,F_c correlation	0.94	EDS
Total number of atoms	2293	wwPDB-VP
Average B, all atoms (Å^2)	33.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 7.61% of the height of the origin peak. No significant pseudotranslation is detected.*

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[1]Intensities estimated from amplitudes.
[2]Theoretical values of $< |L| >$, $< L^2 >$ 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: NH4, SO4, 0LI, 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	0.91	1/2150 (0.0%)	0.96	6/2895 (0.2%)

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	533	GLU	CB-CG	5.26	1.62	1.52

The worst 5 of 6 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	709	ARG	NE-CZ-NH2	-7.37	116.61	120.30
1	A	575	ARG	NE-CZ-NH1	6.70	123.65	120.30
1	A	509	ARG	NE-CZ-NH2	-5.80	117.40	120.30
1	A	663	ASP	CB-CG-OD1	5.75	123.47	118.30
1	A	575	ARG	NE-CZ-NH2	-5.32	117.64	120.30

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	2108	0	2123	23	0
2	A	39	0	27	0	0

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Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
3	A	40	0	0	2	0
4	A	1	0	0	2	0
5	A	8	0	12	1	0
6	A	97	0	0	4	0
All	All	2293	0	2162	24	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 6.

The worst 5 of 24 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:515:LEU:H	1:A:530:GLN:HE21	1.35	0.73
1:A:495:LEU:HD23	1:A:525:LEU:HD21	1.77	0.67
1:A:512:ASN:HD21	1:A:559:GLN:HE21	1.45	0.64
3:A:1008:SO4:O1	6:A:1101:HOH:O	2.14	0.62
1:A:544:SER:HB3	1:A:546:THR:HG22	1.85	0.58

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	260/297 (88%)	252 (97%)	7 (3%)	1 (0%)	34	32

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	523	PRO

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	232/260 (89%)	225 (97%)	7 (3%)	41	43

5 of 7 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	584	LEU
1	A	691	ARG
1	A	614	SER
1	A	448	ASP
1	A	671	ARG

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (2) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	530	GLN
1	A	559	GLN

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 ⓘ

There are no monosaccharides in this entry.

5.6 Ligand geometry ⓘ

Of 12 ligands modelled in this entry, 1 is modelled with single atom - leaving 11 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	$\#|Z| > 2$
3	SO4	A	1003	-	4,4,4	0.48	0	6,6,6	0.29	0
3	SO4	A	1008	-	4,4,4	0.63	0	6,6,6	0.61	0
3	SO4	A	1007	-	4,4,4	0.46	0	6,6,6	0.40	0
5	EDO	A	1012	-	3,3,3	0.41	0	2,2,2	0.57	0
3	SO4	A	1006	-	4,4,4	0.37	0	6,6,6	0.39	0
2	0LI	A	1001	-	40,43,43	2.03	6 (15%)	51,62,62	1.77	11 (21%)
3	SO4	A	1005	-	4,4,4	0.40	0	6,6,6	0.52	0
3	SO4	A	1002	-	4,4,4	0.20	0	6,6,6	0.69	0
3	SO4	A	1009	-	4,4,4	0.26	0	6,6,6	0.40	0
5	EDO	A	1011	-	3,3,3	0.71	0	2,2,2	0.22	0
3	SO4	A	1004	-	4,4,4	0.58	0	6,6,6	0.45	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	0LI	A	1001	-	-	2/20/33/33	0/5/5/5
5	EDO	A	1011	-	-	0/1/1/1	-
5	EDO	A	1012	-	-	1/1/1/1	-

The worst 5 of 6 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1001	0LI	C5-C4	-7.45	1.30	1.43
2	A	1001	0LI	C16-C17	5.28	1.47	1.40
2	A	1001	0LI	C84-N1	4.63	1.37	1.33
2	A	1001	0LI	C5-C6	3.80	1.47	1.40
2	A	1001	0LI	C13-N2	-3.42	1.34	1.41

The worst 5 of 11 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	A	1001	0LI	C9-C10-C5	4.67	124.68	120.61
2	A	1001	0LI	C24-C23-N4	-4.33	105.92	110.80
2	A	1001	0LI	O1-C12-C9	-3.83	114.11	120.94
2	A	1001	0LI	C9-C12-N2	3.56	123.75	115.92
2	A	1001	0LI	C22-C21-N3	-3.45	103.56	110.64

There are no chirality outliers.

All (3) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	A	1001	0LI	C3-C4-C5-C6
2	A	1001	0LI	C3-C4-C5-C10
5	A	1012	EDO	O1-C1-C2-O2

There are no ring outliers.

3 monomers are involved in 3 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
3	A	1008	SO4	1	0
3	A	1007	SO4	1	0
5	A	1011	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 then 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.

Ligand 0LI A 1001

Bond lengths

Bond angles

Torsions

Rings
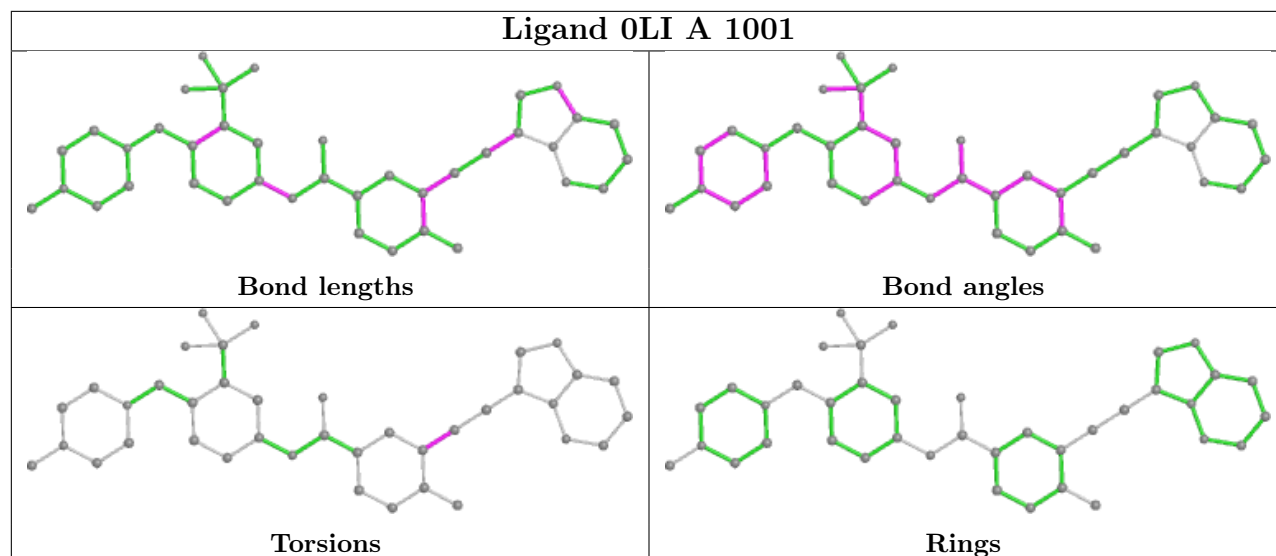
5.7 Other polymers ⓘ

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	264/297 (88%)	-0.16	5 (1%)	66	71	17, 29, 68, 83	0

All (5) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	630	SER	3.7
1	A	488	THR	2.8
1	A	486	ASN	2.7
1	A	546	THR	2.6
1	A	662	ARG	2.4

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 monosaccharides 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. 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.
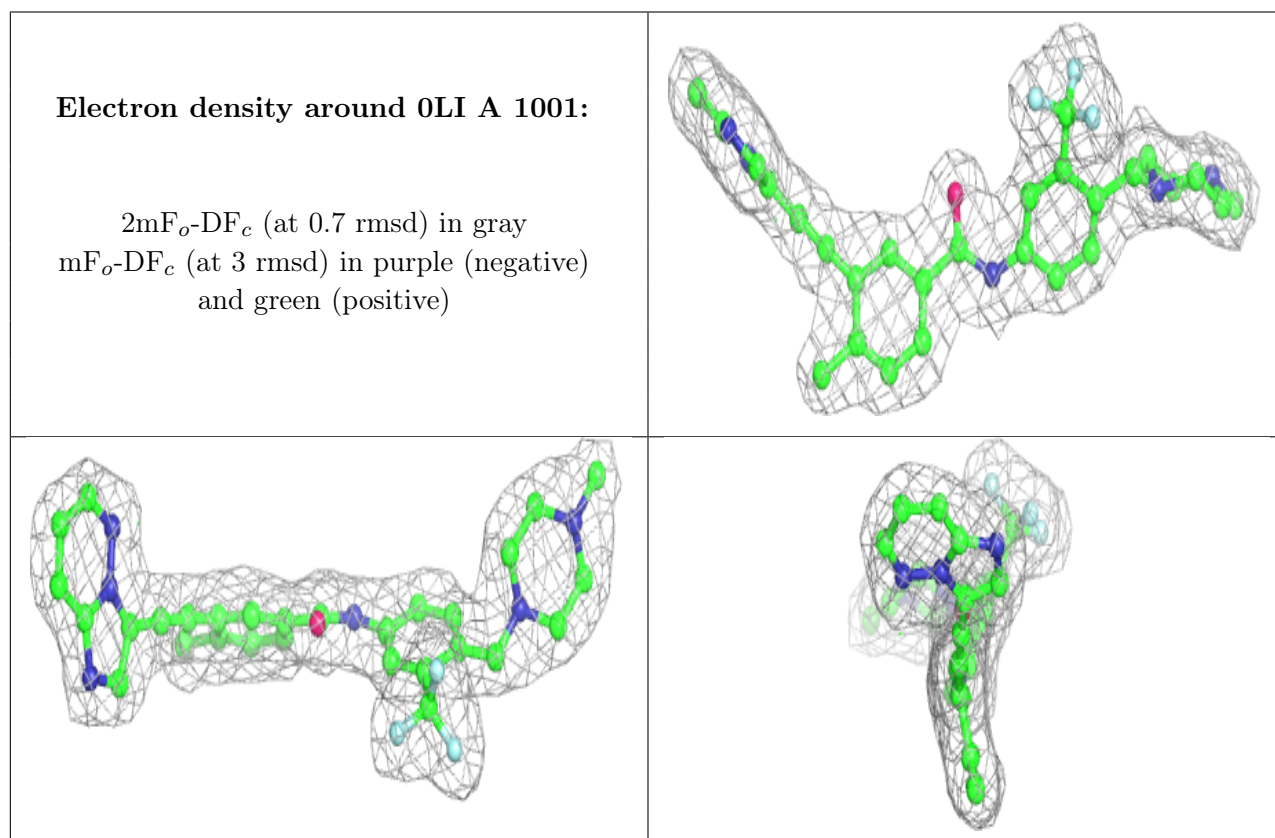
Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å^2)	Q<0.9
5	EDO	A	1011	4/4	0.91	0.14	42,44,45,51	0
4	NH4	A	1010	1/1	0.92	0.11	24,24,24,24	0

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Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å^2)	Q<0.9
3	SO4	A	1004	5/5	0.92	0.26	70,71,83,90	0
3	SO4	A	1006	5/5	0.93	0.14	70,72,84,85	0
3	SO4	A	1007	5/5	0.93	0.21	75,82,83,89	0
5	EDO	A	1012	4/4	0.94	0.20	32,34,38,39	0
3	SO4	A	1008	5/5	0.95	0.15	28,31,33,33	5
3	SO4	A	1005	5/5	0.96	0.21	74,75,78,78	0
3	SO4	A	1003	5/5	0.97	0.09	47,50,53,56	0
2	0LI	A	1001	39/39	0.97	0.10	17,20,23,24	0
3	SO4	A	1009	5/5	0.98	0.12	36,38,42,44	5
3	SO4	A	1002	5/5	0.98	0.15	39,39,49,54	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 0LI A 1001:

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

6.5   Other polymers ⓘ

There are no such residues in this entry.