Full wwPDB X-ray Structure Validation Report (i)

Sep 6, 2023 – 02:04 PM EDT

PDB ID	:	4H1E
Title	:	Structure of BACE-1 Bound to (7aR)-6-benzoyl-7a-(4-(3-cyanophenyl)thiophen-2-yl)-3-methyl-4-oxohexahydro-1H-pyrrolo[3,4-d]pyrimidin-2(3H)-iminium
Authors	:	Orth, P.
Deposited on	:	2012-09-10
Resolution	:	1.90 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
https://www.wwpdb.org/validation/2017/XrayValidationReportHelp
with specific help available everywhere you see the (i) symbol.

The types of validation reports are described at
http://www.wwpdb.org/validation/2017/FAQs#types.

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

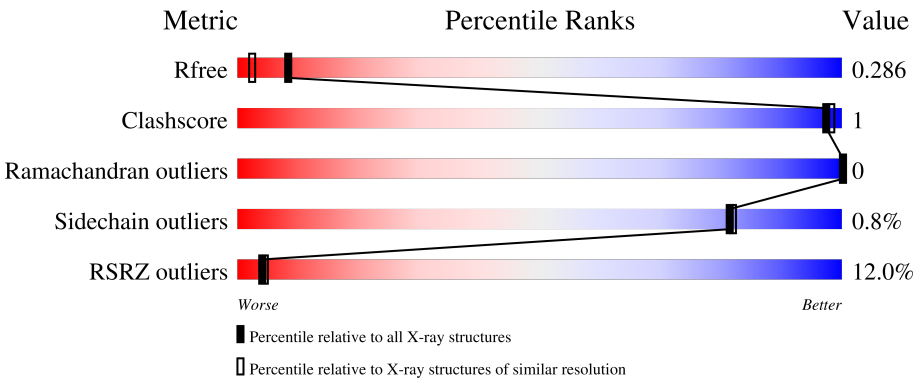
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.35
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.35

1 Overall quality at a glance (i)

The following experimental techniques were used to determine the structure:
X-RAY DIFFRACTION

The reported resolution of this entry is 1.90 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}	130704	6207 (1.90-1.90)
Clashscore	141614	6847 (1.90-1.90)
Ramachandran outliers	138981	6760 (1.90-1.90)
Sidechain outliers	138945	6760 (1.90-1.90)
RSRZ outliers	127900	6082 (1.90-1.90)

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 of 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	414	14% 91% • 7%
1	B	414	9% 91% • 7%

2 Entry composition (i)

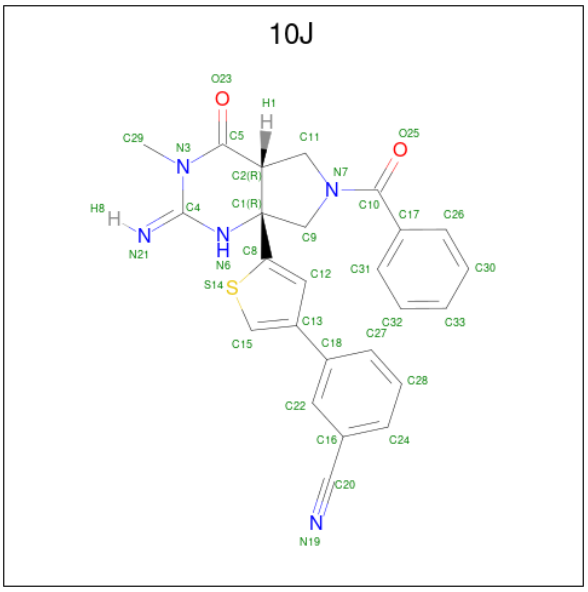
There are 3 unique types of molecules in this entry. The entry contains 6608 atoms, of which 0 are hydrogens and 0 are deuteriums.

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 Beta-secretase 1.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	386	3002	1923	496	569	14	0	0	0
1	B	387	3021	1934	502	571	14	0	0	0

- Molecule 2 is 3-{5-[(2E,4aR,7aR)-6-benzoyl-2-imino-3-methyl-4-oxooctahydro-7aH-pyrrolo[3,4-d]pyrimidin-7a-yl]thiophen-3-yl}benzonitrile (three-letter code: 10J) (formula: $C_{25}H_{21}N_5O_2S$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	N	O	S		
2	A	1	33	25	5	2	1	0	0
2	B	1	33	25	5	2	1	0	0

- Molecule 3 is water.

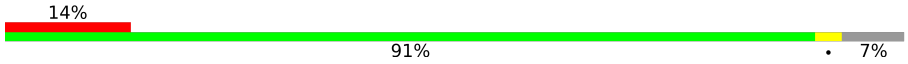
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
			Total	O		
3	A	255	255	255	0	0
			Total	O		
3	B	264	264	264	0	0

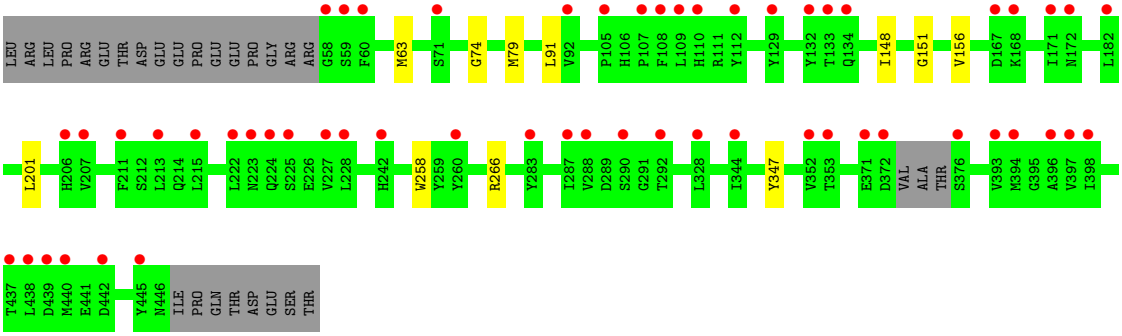
3 Residue-property plots (i)

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: Beta-secretase 1

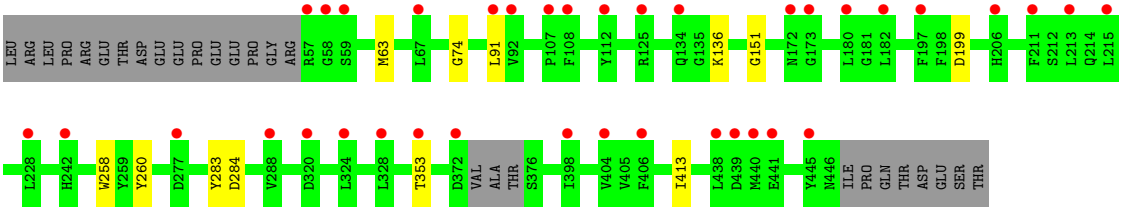
Chain A:





- Molecule 1: Beta-secretase 1

Chain B:



4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	86.21Å 89.94Å 131.32Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	31.37 – 1.90 31.37 – 1.90	Depositor EDS
% Data completeness (in resolution range)	99.0 (31.37-1.90) 98.8 (31.37-1.90)	Depositor EDS
R_{merge}	0.11	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	1.39 (at 1.89Å)	Xtriage
Refinement program	BUSTER-TNT BUSTER 2.11.1, BUSTER 2.11.1	Depositor
R, R_{free}	0.260 , 0.297 0.251 , 0.286	Depositor DCC
R_{free} test set	3255 reflections (4.05%)	wwPDB-VP
Wilson B-factor (Å^2)	29.8	Xtriage
Anisotropy	0.612	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.34 , 44.1	EDS
L-test for twinning[2]	$< \|L\| > = 0.51$, $< L^2 > = 0.35$	Xtriage
Estimated twinning fraction	0.000 for k,h,-l	Xtriage
F_o,F_c correlation	0.95	EDS
Total number of atoms	6608	wwPDB-VP
Average B, all atoms (Å^2)	36.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The analyses of the Patterson function reveals a significant off-origin peak that is 55.37 % of the origin peak, indicating pseudo-translational symmetry. The chance of finding a peak of this or larger height randomly in a structure without pseudo-translational symmetry is equal to 3.1953e-05. The detected translational NCS is most likely also responsible for the elevated intensity ratio.*

[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 (i)

5.1 Standard geometry (i)

Bond lengths and bond angles in the following residue types are not validated in this section: 10J

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	0.51	0/3078	0.68	0/4188
1	B	0.50	0/3097	0.67	0/4211
All	All	0.51	0/6175	0.68	0/8399

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 (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	3002	0	2881	5	0
1	B	3021	0	2911	4	0
2	A	33	0	20	0	0
2	B	33	0	20	1	0
3	A	255	0	0	0	0
3	B	264	0	0	1	0
All	All	6608	0	5832	10	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 (10) 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:63:MET:HG2	1:A:151:GLY:HA2	1.82	0.62
1:A:156:VAL:HG11	1:A:201:LEU:HA	1.90	0.54
1:A:79:MET:HG2	1:A:148:ILE:HG12	1.94	0.50
1:B:260:TYR:HB3	1:B:413:ILE:HD11	1.96	0.47
1:B:63:MET:HG2	1:B:151:GLY:HA2	1.98	0.45
1:A:74:GLY:HA3	1:A:91:LEU:HD11	1.99	0.44
1:B:74:GLY:HA3	1:B:91:LEU:HD11	2.00	0.43
1:B:283:TYR:HA	1:B:284:ASP:HA	1.90	0.42
2:B:501:10J:H13	3:B:755:HOH:O	2.21	0.41
1:A:266:ARG:HB3	1:A:347:TYR:HB2	2.02	0.41

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	382/414 (92%)	375 (98%)	7 (2%)	0	100	100
1	B	383/414 (92%)	375 (98%)	8 (2%)	0	100	100
All	All	765/828 (92%)	750 (98%)	15 (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	321/355 (90%)	320 (100%)	1 (0%)	92	93
1	B	324/355 (91%)	320 (99%)	4 (1%)	71	70
All	All	645/710 (91%)	640 (99%)	5 (1%)	81	82

All (5) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	258	TRP
1	B	136	LYS
1	B	199	ASP
1	B	258	TRP
1	B	353	THR

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

Mol	Chain	Res	Type
1	B	172	ASN
1	B	272	GLN

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 monosaccharides in this entry.

5.6 Ligand geometry (i)

2 ligands are 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	10J	B	501	-	31,37,37	1.82	7 (22%)	34,55,55	1.33	4 (11%)
2	10J	A	501	-	31,37,37	1.87	8 (25%)	34,55,55	1.28	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	10J	B	501	-	-	2/14/52/52	0/5/5/5
2	10J	A	501	-	-	2/14/52/52	0/5/5/5

All (15) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	501	10J	C31-C17	3.75	1.45	1.39
2	B	501	10J	C4-N3	3.68	1.41	1.38
2	A	501	10J	C4-N3	3.55	1.41	1.38
2	A	501	10J	C5-N3	3.45	1.43	1.38
2	A	501	10J	C15-C13	3.45	1.39	1.37
2	B	501	10J	C15-C13	3.45	1.39	1.37
2	B	501	10J	C5-N3	3.37	1.43	1.38
2	B	501	10J	C33-C30	3.35	1.46	1.38
2	B	501	10J	C26-C17	3.22	1.44	1.39
2	A	501	10J	C33-C32	2.72	1.45	1.38
2	A	501	10J	C26-C17	2.65	1.43	1.39
2	B	501	10J	C31-C17	2.48	1.43	1.39
2	A	501	10J	C27-C18	2.24	1.44	1.39
2	B	501	10J	C10-N7	2.19	1.39	1.34
2	A	501	10J	C33-C30	2.02	1.43	1.38

All (9) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	A	501	10J	O23-C5-N3	3.23	126.66	121.13
2	B	501	10J	C30-C26-C17	-3.12	116.66	120.34
2	A	501	10J	C15-C13-C18	-2.90	123.62	127.58

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Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	B	501	10J	C13-C15-S14	-2.86	110.45	112.29
2	B	501	10J	C15-C13-C18	-2.78	123.78	127.58
2	B	501	10J	C31-C17-C26	2.42	122.04	118.59
2	A	501	10J	C31-C17-C26	2.40	122.01	118.59
2	A	501	10J	O23-C5-C2	-2.31	115.89	121.32
2	A	501	10J	C31-C17-C10	-2.17	114.79	120.29

There are no chirality outliers.

All (4) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	A	501	10J	O25-C10-N7-C9
2	B	501	10J	O25-C10-N7-C9
2	B	501	10J	C17-C10-N7-C9
2	A	501	10J	C17-C10-N7-C9

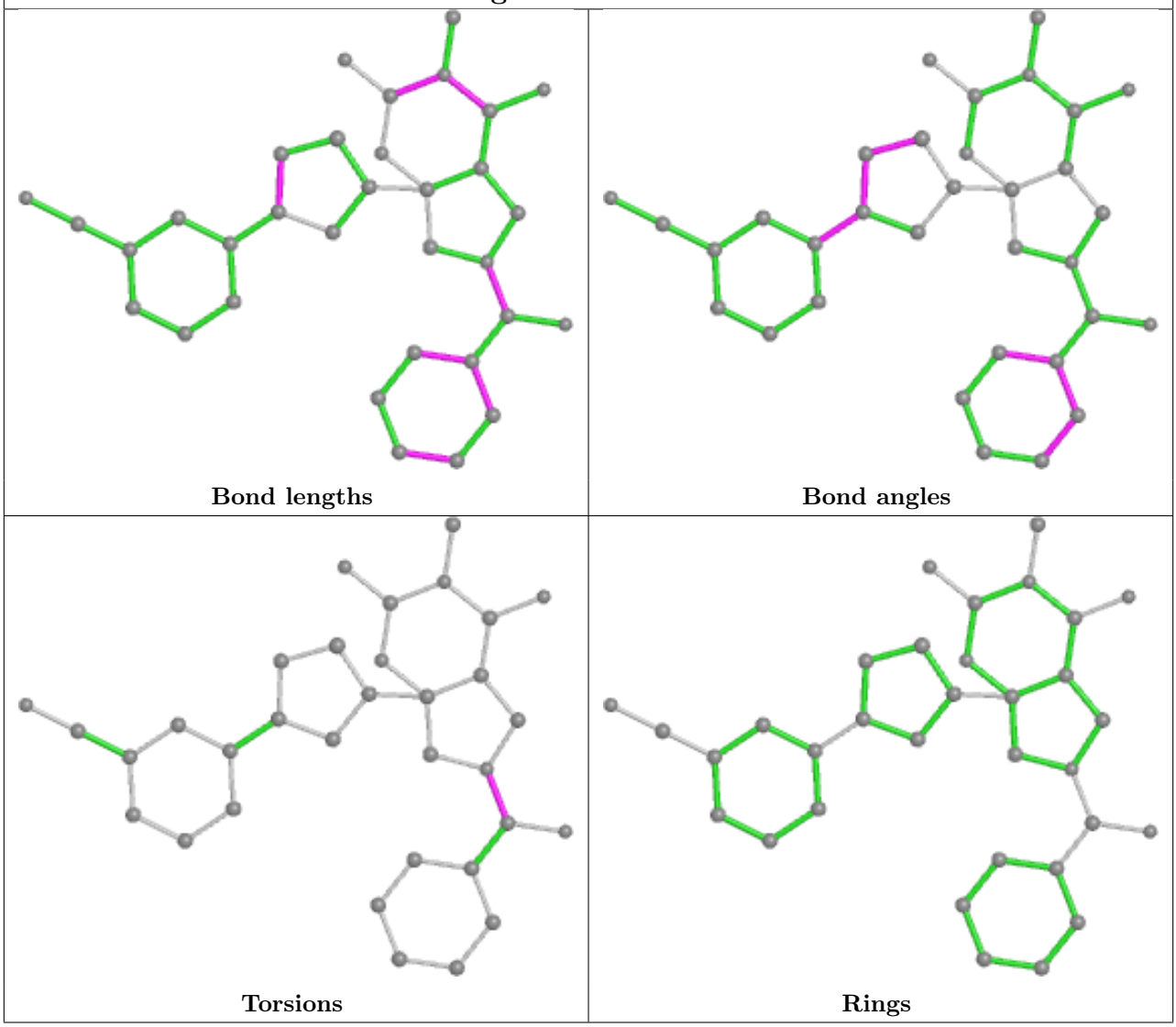
There are no ring outliers.

1 monomer is involved in 1 short contact:

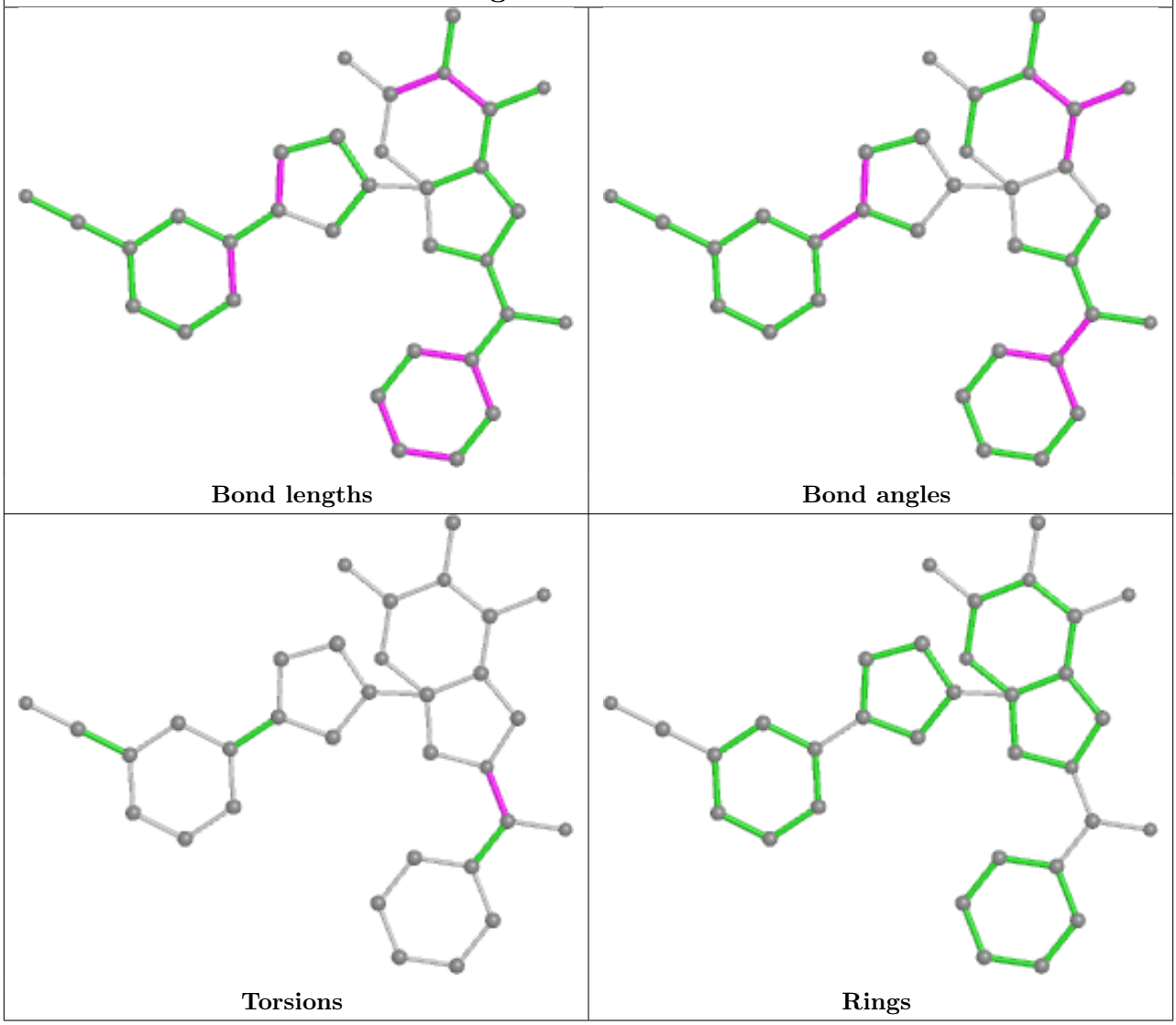
Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	B	501	10J	1	0

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 10J B 501



Ligand 10J A 501



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 (i)

6.1 Protein, DNA and RNA chains (i)

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	386/414 (93%)	0.80	56 (14%)	2	2	21, 33, 56, 86	0
1	B	387/414 (93%)	0.70	37 (9%)	8	9	22, 34, 53, 78	0
All	All	773/828 (93%)	0.75	93 (12%)	4	4	21, 33, 55, 86	0

All (93) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	171	ILE	5.5
1	B	57	ARG	5.2
1	A	133	THR	5.0
1	B	58	GLY	4.9
1	B	438	LEU	4.9
1	A	129	TYR	4.8
1	B	59	SER	4.5
1	A	353	THR	4.5
1	A	372	ASP	4.0
1	B	213	LEU	3.9
1	A	228	LEU	3.8
1	A	168	LYS	3.8
1	B	228	LEU	3.7
1	A	108	PHE	3.7
1	B	107	PRO	3.5
1	A	71	SER	3.5
1	A	215	LEU	3.5
1	A	105	PRO	3.5
1	A	134	GLN	3.4
1	B	353	THR	3.4
1	B	398	ILE	3.3
1	A	439	ASP	3.2
1	A	438	LEU	3.2
1	A	107	PRO	3.2

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Mol	Chain	Res	Type	RSRZ
1	A	112	TYR	3.1
1	B	441	GLU	3.1
1	B	206	HIS	3.0
1	A	223	ASN	3.0
1	B	92	VAL	2.9
1	B	215	LEU	2.9
1	A	445	TYR	2.9
1	B	328	LEU	2.9
1	B	242	HIS	2.8
1	A	206	HIS	2.8
1	B	439	ASP	2.8
1	B	324	LEU	2.8
1	A	110	HIS	2.8
1	A	442	ASP	2.8
1	A	182	LEU	2.7
1	A	288	VAL	2.7
1	B	182	LEU	2.7
1	B	197	PHE	2.7
1	B	372	ASP	2.7
1	A	290	SER	2.7
1	A	92	VAL	2.7
1	A	328	LEU	2.7
1	A	352	VAL	2.6
1	A	398	ILE	2.6
1	A	394	MET	2.6
1	B	134	GLN	2.6
1	B	112	TYR	2.6
1	B	108	PHE	2.5
1	A	376	SER	2.5
1	A	292	THR	2.5
1	A	58	GLY	2.5
1	A	393	VAL	2.5
1	A	371	GLU	2.5
1	A	283	TYR	2.5
1	B	67	LEU	2.5
1	B	445	TYR	2.5
1	A	172	ASN	2.4
1	B	125	ARG	2.4
1	B	180	LEU	2.4
1	A	242	HIS	2.4
1	A	213	LEU	2.4
1	A	222	LEU	2.4

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Mol	Chain	Res	Type	RSRZ
1	A	224	GLN	2.4
1	B	173	GLY	2.3
1	A	207	VAL	2.3
1	A	437	THR	2.3
1	A	167	ASP	2.3
1	B	91	LEU	2.3
1	A	344	ILE	2.3
1	A	109	LEU	2.3
1	A	260	TYR	2.2
1	A	60	PHE	2.2
1	B	440	MET	2.2
1	A	225	SER	2.2
1	B	288	VAL	2.2
1	A	440	MET	2.2
1	B	211	PHE	2.2
1	A	211	PHE	2.1
1	B	404	VAL	2.1
1	A	59	SER	2.1
1	B	406	PHE	2.1
1	B	172	ASN	2.1
1	A	397	VAL	2.1
1	A	132	TYR	2.1
1	A	227	VAL	2.1
1	A	287	ILE	2.1
1	A	396	ALA	2.0
1	B	277	ASP	2.0
1	B	320	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 monosaccharides 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. The B-factors column lists the minimum,

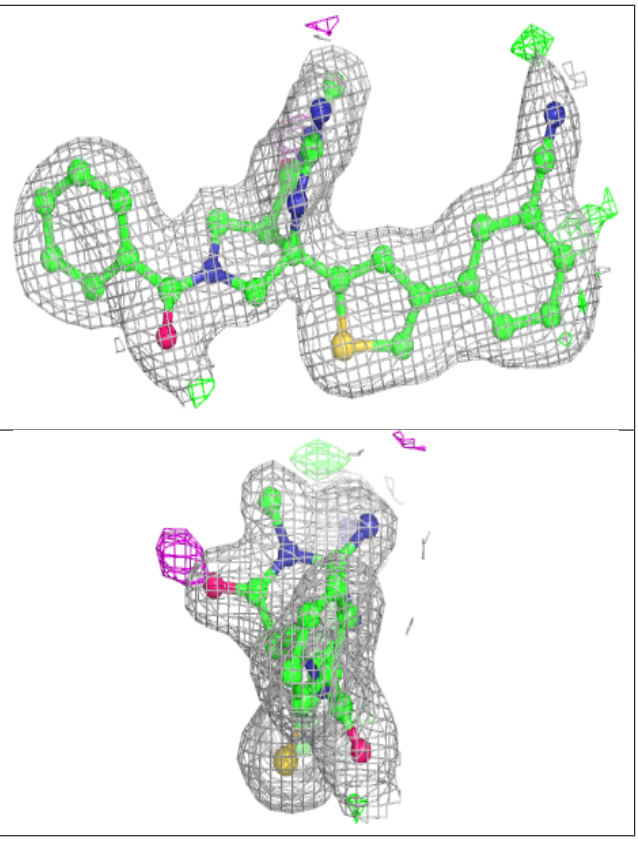
median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å^2)	Q<0.9
2	10J	A	501	33/33	0.92	0.13	25,31,35,35	0
2	10J	B	501	33/33	0.93	0.12	24,33,36,38	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.

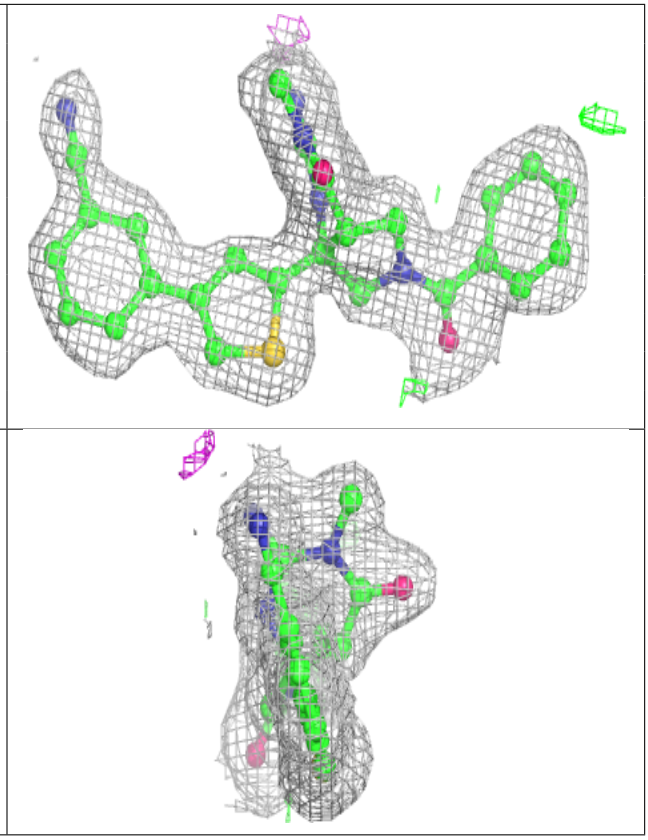
Electron density around 10J A 501:

2mF$_o$-DF$_c$ (at 0.7 rmsd) in gray
mF$_o$-DF$_c$ (at 3 rmsd) in purple (negative) and green (positive)



Electron density around 10J B 501:

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



6.5 Other polymers (i)

There are no such residues in this entry.