



Full wwPDB X-ray Structure Validation Report ⓘ

May 21, 2020 – 12:47 pm BST

PDB ID : 5UKJ
Title : The co-structure of N,N-dimethyl-4-[(6R)-6-methyl-5-(1H-pyrrolo[2,3- b]pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5- a]pyrazin-3-yl]benzenesulfonamide and a rationally designed PI3K-alpha mutant that mimics ATR
Authors : Knapp, M.S.; Elling, R.A.; Mamo, M.
Deposited on : 2017-01-23
Resolution : 2.80 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 ⓘ symbol.

The following versions of software and data (see [references ⓘ](#)) 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 : 2.11
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) : 2.11

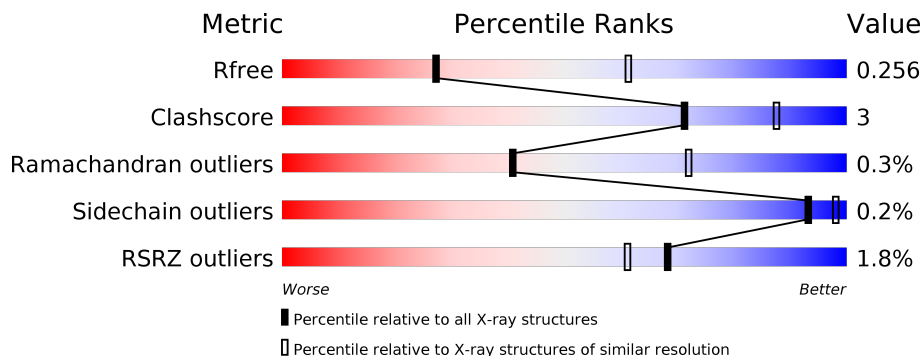
1 Overall quality at a glance i

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

The reported resolution of this entry is 2.80 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	3140 (2.80-2.80)
Clashscore	141614	3569 (2.80-2.80)
Ramachandran outliers	138981	3498 (2.80-2.80)
Sidechain outliers	138945	3500 (2.80-2.80)
RSRZ outliers	127900	3078 (2.80-2.80)

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 $\leq 5\%$. 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	1074	<div style="display: flex; align-items: center;"> <div style="margin-right: 5px;">2%</div> <div style="flex-grow: 1; position: relative;"> <div style="position: absolute; top: -10px; left: 0; width: 20px; height: 10px; background-color: red;"></div> <div style="position: absolute; top: 0; left: 20px; width: 80%; height: 10px; background-color: green;"></div> <div style="position: absolute; top: 0; left: 80%; width: 10%; height: 10px; background-color: yellow;"></div> <div style="position: absolute; top: 0; left: 90%; width: 10%; height: 10px; background-color: grey;"></div> </div> <div style="margin-left: 5px; text-align: center;">84%</div> <div style="margin-left: 10px; text-align: center;">10%</div> <div style="margin-left: 10px; text-align: center;">6%</div> </div>
2	B	293	<div style="display: flex; align-items: center;"> <div style="flex-grow: 1; position: relative;"> <div style="position: absolute; top: 0; left: 0; width: 80%; height: 10px; background-color: green;"></div> <div style="position: absolute; top: 0; left: 80%; width: 10%; height: 10px; background-color: yellow;"></div> <div style="position: absolute; top: 0; left: 90%; width: 10%; height: 10px; background-color: grey;"></div> </div> <div style="margin-left: 5px; text-align: center;">83%</div> <div style="margin-left: 10px; text-align: center;">•</div> <div style="margin-left: 10px; text-align: center;">12%</div> </div>

2 Entry composition [i](#)

There are 4 unique types of molecules in this entry. The entry contains 10424 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 Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	1009	8079	5165	1377	1471	66	0	0	0

There are 14 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	232	LYS	MET	engineered mutation	UNP P42336
A	233	LYS	LEU	engineered mutation	UNP P42336
A	770	GLU	ARG	engineered mutation	UNP P42336
A	780	LYS	TRP	engineered mutation	UNP P42336
A	798	ILE	GLU	engineered mutation	UNP P42336
A	800	MET	ILE	engineered mutation	UNP P42336
A	850	TRP	VAL	engineered mutation	UNP P42336
A	930	VAL	PHE	engineered mutation	UNP P42336
A	1069	HIS	-	expression tag	UNP P42336
A	1070	HIS	-	expression tag	UNP P42336
A	1071	HIS	-	expression tag	UNP P42336
A	1072	HIS	-	expression tag	UNP P42336
A	1073	HIS	-	expression tag	UNP P42336
A	1074	HIS	-	expression tag	UNP P42336

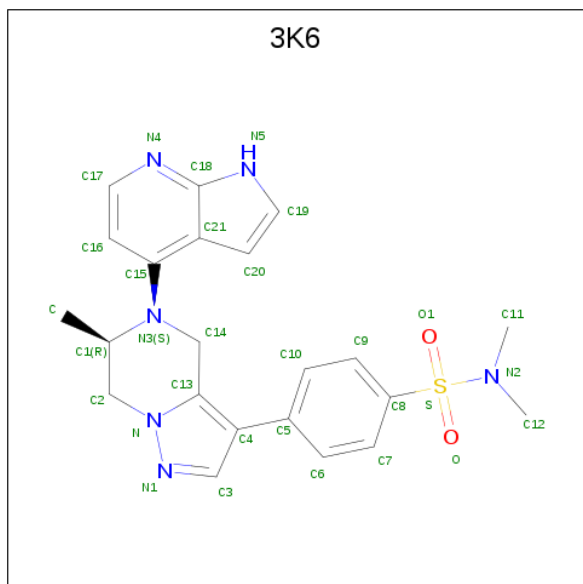
- Molecule 2 is a protein called Phosphatidylinositol 3-kinase regulatory subunit alpha.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
2	B	257	2102	1312	369	416	5	0	0	0

There is a discrepancy between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
B	306	TYR	THR	engineered mutation	UNP P27986

- Molecule 3 is N,N-dimethyl-4-[(6R)-6-methyl-5-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4,5,6,7-tetrahydropyrazolo[1,5-a]pyrazin-3-yl]benzenesulfonamide (three-letter code: 3K6) (formula: $C_{22}H_{24}N_6O_2S$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	N	O	S		
3	A	1	31	22	6	2	1	0	0

- Molecule 4 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
			Total	O		
4	A	171	171	171	0	0
4	B	41	41	41	0	0

4 Data and refinement statistics

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α , β , γ	100.19Å 109.43Å 136.15Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	47.01 – 2.80 47.01 – 2.80	Depositor EDS
% Data completeness (in resolution range)	93.8 (47.01-2.80) 93.8 (47.01-2.80)	Depositor EDS
R_{merge}	0.09	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.77 (at 2.81Å)	Xtrriage
Refinement program	BUSTER-TNT 2.11.6	Depositor
R, R_{free}	0.187 , 0.252 0.192 , 0.256	Depositor DCC
R_{free} test set	1712 reflections (4.86%)	wwPDB-VP
Wilson B-factor (Å ²)	57.8	Xtrriage
Anisotropy	0.277	Xtrriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.29 , 53.4	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.33$	Xtrriage
Estimated twinning fraction	No twinning to report.	Xtrriage
F_o, F_c correlation	0.94	EDS
Total number of atoms	10424	wwPDB-VP
Average B, all atoms (Å ²)	63.0	wwPDB-VP

Xtrriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.18% 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 [i](#)

5.1 Standard geometry [i](#)

Bond lengths and bond angles in the following residue types are not validated in this section: 3K6

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	0.48	0/8264	0.69	0/11205
2	B	0.48	0/2133	0.68	0/2868
All	All	0.48	0/10397	0.69	0/14073

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	8079	0	7888	64	0
2	B	2102	0	1985	8	0
3	A	31	0	24	1	0
4	A	171	0	0	2	0
4	B	41	0	0	0	0
All	All	10424	0	9897	70	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 3.

All (70) 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:158:SER:HB2	1:A:159:PRO:HD2	1.62	0.81
1:A:158:SER:CB	1:A:159:PRO:CD	2.61	0.78
1:A:772:MET:HB2	1:A:778:PRO:HD2	1.73	0.70
1:A:158:SER:HB3	1:A:159:PRO:HD3	1.76	0.68
1:A:311:ILE:HD12	1:A:313:THR:H	1.59	0.67
1:A:158:SER:HB2	1:A:159:PRO:CD	2.21	0.67
1:A:158:SER:HB3	1:A:159:PRO:CD	2.27	0.64
1:A:198:VAL:HG22	1:A:200:PRO:HD2	1.79	0.63
1:A:744:PHE:CZ	1:A:748:LEU:HD22	2.35	0.60
1:A:883:ASP:HA	1:A:886:LYS:HE2	1.84	0.58
1:A:79:ARG:HG3	2:B:493:ILE:HD11	1.87	0.57
2:B:494:PHE:HB3	2:B:535:ILE:HG12	1.87	0.56
1:A:937:PHE:HD1	1:A:938:LEU:HG	1.70	0.56
1:A:809:GLN:HG3	4:A:1243:HOH:O	2.05	0.55
1:A:612:ARG:O	1:A:616:VAL:HG23	2.06	0.55
1:A:269:GLN:HA	1:A:274:ARG:HH21	1.72	0.55
1:A:830:ASP:OD1	1:A:832:ARG:HD3	2.07	0.54
1:A:339:LEU:HB2	1:A:474:GLU:HB2	1.90	0.54
1:A:738:GLN:HB3	1:A:741:ARG:HH21	1.72	0.54
1:A:800:MET:CE	1:A:848:ILE:HD12	2.38	0.53
1:A:162:ARG:HB3	1:A:297:LEU:HD23	1.90	0.53
1:A:27:PRO:HD2	1:A:62:LEU:HD22	1.90	0.53
1:A:572:VAL:HG21	1:A:583:MET:HG2	1.89	0.52
1:A:744:PHE:CE1	1:A:748:LEU:HD22	2.45	0.52
1:A:552:TRP:HZ3	1:A:583:MET:HE2	1.74	0.52
1:A:1027:ALA:HB1	1:A:1030:LYS:HD2	1.92	0.51
1:A:46:LYS:HE3	1:A:65:GLU:HG2	1.92	0.50
1:A:427:ILE:HD11	1:A:443:LEU:HD22	1.91	0.50
1:A:916:ARG:HB3	1:A:921:ILE:HD11	1.93	0.50
1:A:832:ARG:HH21	1:A:896:LEU:HD13	1.76	0.50
1:A:534:ILE:HG21	1:A:551:LEU:HD11	1.95	0.49
1:A:363:GLY:N	1:A:607:PRO:HG3	2.28	0.49
1:A:559:VAL:HG13	1:A:591:PRO:HD3	1.94	0.49
2:B:339:SER:HB3	2:B:342:GLU:HG3	1.95	0.48
1:A:711:LYS:HB2	1:A:748:LEU:HD11	1.95	0.48
1:A:267:LEU:HG	1:A:273:ILE:HG13	1.95	0.47
1:A:538:ASP:HA	1:A:996:ASN:OD1	2.14	0.47
1:A:943:LYS:HB2	4:A:1224:HOH:O	2.14	0.47
1:A:341:ALA:HB3	1:A:381:PRO:HB2	1.97	0.46
1:A:147:CYS:HB3	1:A:694:ALA:HB2	1.97	0.46
1:A:159:PRO:HB2	1:A:294:TYR:CD2	2.50	0.46
1:A:193:VAL:HG22	1:A:208:THR:HG23	1.97	0.46

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:151:VAL:HG21	1:A:302:PHE:HB2	1.99	0.45
1:A:197:ILE:HG22	1:A:202:ASN:HA	1.99	0.45
1:A:339:LEU:HD12	1:A:474:GLU:HB3	1.98	0.45
2:B:338:ILE:HG23	2:B:358:ARG:HD3	2.00	0.44
1:A:336:ILE:HD13	1:A:402:LEU:HD22	1.99	0.44
1:A:440:LYS:HA	1:A:475:LEU:O	2.17	0.44
1:A:896:LEU:HD23	1:A:926:ASP:HB3	2.00	0.44
1:A:147:CYS:O	1:A:151:VAL:HG23	2.18	0.43
1:A:121:ILE:HG12	1:A:688:LEU:HB3	2.01	0.43
2:B:562:ARG:O	2:B:566:ILE:HG12	2.18	0.43
1:A:916:ARG:HD2	1:A:931:HIS:ND1	2.34	0.43
1:A:157:ASN:HB3	1:A:161:SER:HB3	2.01	0.43
1:A:10:LEU:HB2	1:A:13:ILE:HB	2.00	0.42
1:A:250:TYR:HA	1:A:289:ALA:HA	2.02	0.42
1:A:807:LEU:HD12	1:A:846:GLY:HA3	2.01	0.42
1:A:676:HIS:CG	1:A:843:ASP:HB2	2.54	0.42
2:B:343:VAL:HG21	2:B:358:ARG:HE	1.84	0.42
1:A:932:ILE:HD13	3:A:1101:3K6:H11	2.01	0.42
1:A:337:LYS:HB3	1:A:476:GLU:HB3	2.01	0.42
1:A:616:VAL:O	1:A:620:GLU:HG3	2.19	0.41
1:A:739:MET:HB3	1:A:766:LEU:HD21	2.01	0.41
2:B:567:LYS:O	2:B:571:ILE:HG12	2.21	0.41
1:A:599:MET:HB2	1:A:599:MET:HE2	1.98	0.41
1:A:735:LEU:HD11	1:A:779:LEU:HD21	2.02	0.41
1:A:2:PRO:HG2	2:B:482:THR:HG23	2.03	0.41
1:A:749:GLN:HG2	1:A:764:LEU:H	1.85	0.41
1:A:587:VAL:HA	1:A:590:TRP:HB2	2.02	0.40
1:A:354:ILE:HD11	1:A:381:PRO:HB3	2.03	0.40

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	999/1074 (93%)	953 (95%)	42 (4%)	4 (0%)	34	66
2	B	249/293 (85%)	242 (97%)	7 (3%)	0	100	100
All	All	1248/1367 (91%)	1195 (96%)	49 (4%)	4 (0%)	41	72

All (4) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	158	SER
1	A	776	LYS
1	A	524	ARG
1	A	264	LYS

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	880/980 (90%)	878 (100%)	2 (0%)	93	98
2	B	220/272 (81%)	220 (100%)	0	100	100
All	All	1100/1252 (88%)	1098 (100%)	2 (0%)	93	98

All (2) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	777	ARG
1	A	872	PHE

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (1) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	920	ASN

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 carbohydrates in this entry.

5.6 Ligand geometry [i](#)

1 ligand is 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
3	3K6	A	1101	-	30,35,35	0.55	0	36,53,53	0.79	1 (2%)

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
3	3K6	A	1101	-	-	2/20/32/32	0/4/5/5

There are no bond length outliers.

All (1) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
3	A	1101	3K6	C4-C13-N	-3.76	106.27	110.18

There are no chirality outliers.

All (2) torsion outliers are listed below:

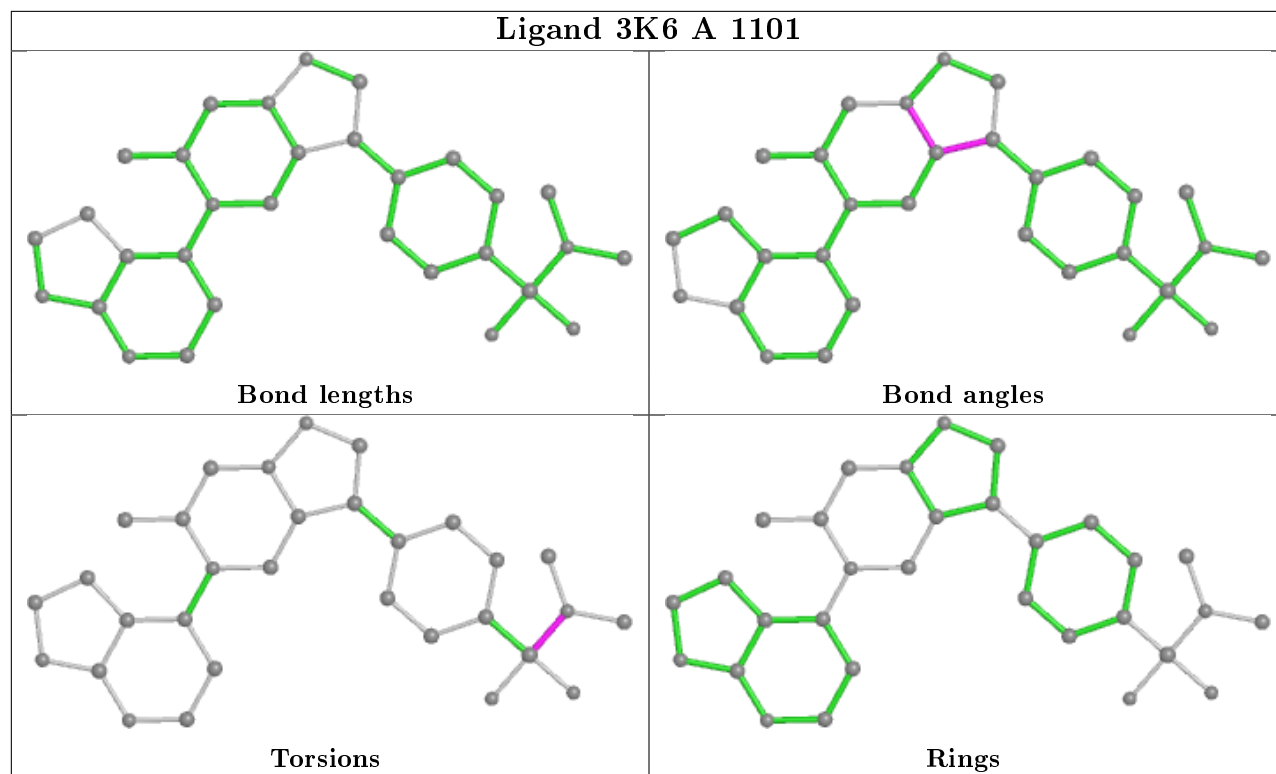
Mol	Chain	Res	Type	Atoms
3	A	1101	3K6	C11-N2-S-O
3	A	1101	3K6	C11-N2-S-C8

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
3	A	1101	3K6	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 than 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.



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	1009/1074 (93%)	-0.23	23 (2%) 60 51	32, 59, 96, 151	0
2	B	257/293 (87%)	-0.33	0 100 100	37, 64, 101, 121	0
All	All	1266/1367 (92%)	-0.25	23 (1%) 68 61	32, 60, 98, 151	0

All (23) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	247	GLN	4.4
1	A	243	VAL	3.4
1	A	287	LEU	3.0
1	A	242	CYS	2.9
1	A	294	TYR	2.8
1	A	523	LEU	2.7
1	A	190	ILE	2.6
1	A	525	GLU	2.6
1	A	188	GLY	2.6
1	A	218	GLU	2.6
1	A	246	TYR	2.5
1	A	217	PRO	2.4
1	A	189	GLN	2.4
1	A	789	MET	2.4
1	A	411	GLY	2.3
1	A	199	SER	2.2
1	A	250	TYR	2.2
1	A	888	GLU	2.2
1	A	194	ILE	2.1
1	A	414	GLY	2.1
1	A	207	TYR	2.1
1	A	293	LEU	2.0
1	A	215	CYS	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](#)

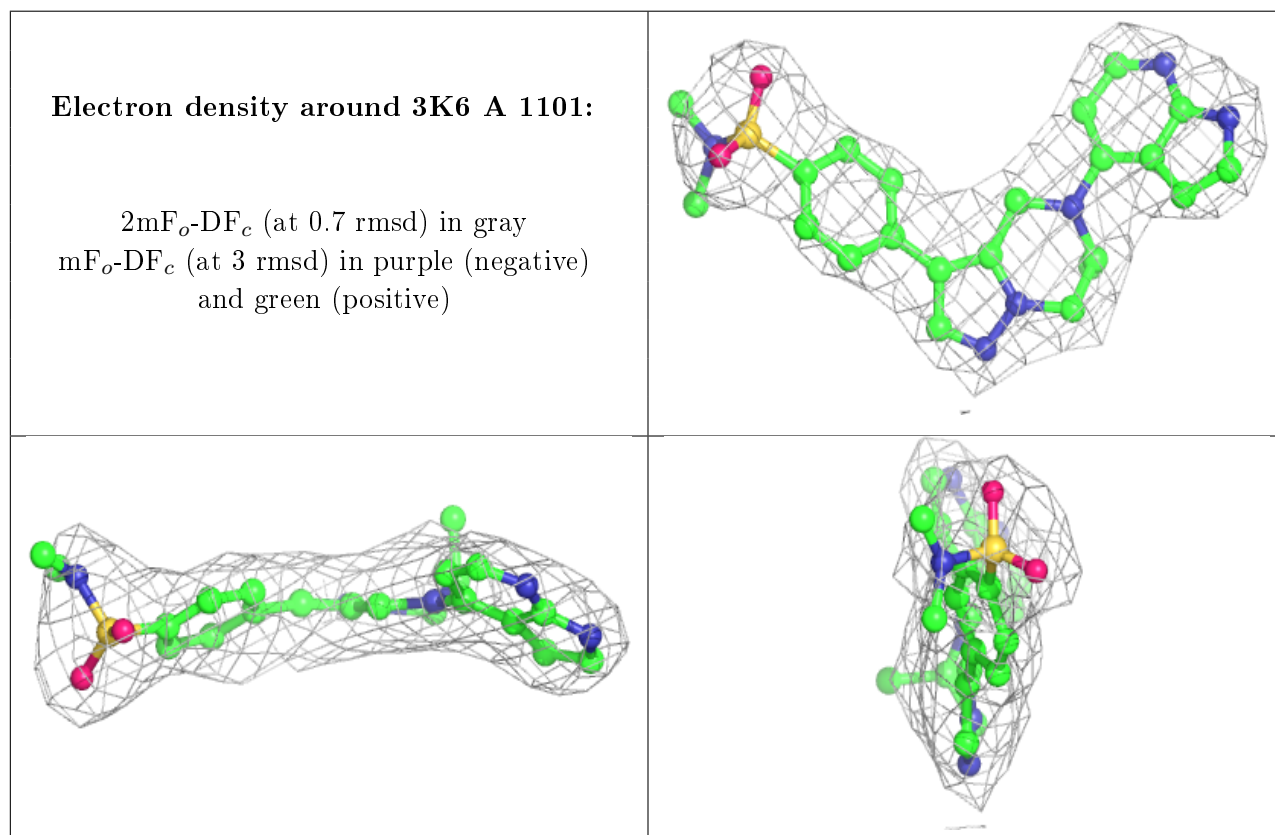
There are no carbohydrates in this entry.

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. 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(\AA^2)	Q<0.9
3	3K6	A	1101	31/31	0.96	0.16	50,55,77,78	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.



6.5 Other polymers [i](#)

There are no such residues in this entry.