



# Full wwPDB X-ray Structure Validation Report ⓘ

May 1, 2016 – 05:14 AM EDT

PDB ID : 5EI8  
Title : Rapid Discovery of Pyrido[3,4-d]pyrimidine Inhibitors of Monopolar Spindle kinase 1 (MPS1) Using a Structure-Based Hybridization Approach  
Authors : Innocenti, P.; Woodward, H.L.; Solanki, S.; Naud, N.; Westwood, I.M.; Cronin, N.; Hayes, A.; Roberts, J.; Henley, A.T.; Baker, R.; Faisal, A.; Mak, G.; Box, G.; Valenti, M.; De Haven Brandon, A.; O'Fee, L.; Saville, J.; Schmitt, J.; Burke, R.; van Montfort, R.L.M.; Raymaud, F.I.; Eccles, S.A.; Linardopoulos, S.; Blagg, J.; Hoelder, S.  
Deposited on : 2015-10-29  
Resolution : 2.17 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](mailto: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.

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

MolProbity : 4.02b-467  
Mogul : 1.7.1 (RC1), CSD as537be (2016)  
Xtriage (Phenix) : 1.9-1692  
EDS : rb-20027457  
Percentile statistics : 20151230.v01 (using entries in the PDB archive December 30th 2015)  
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) : rb-20027457

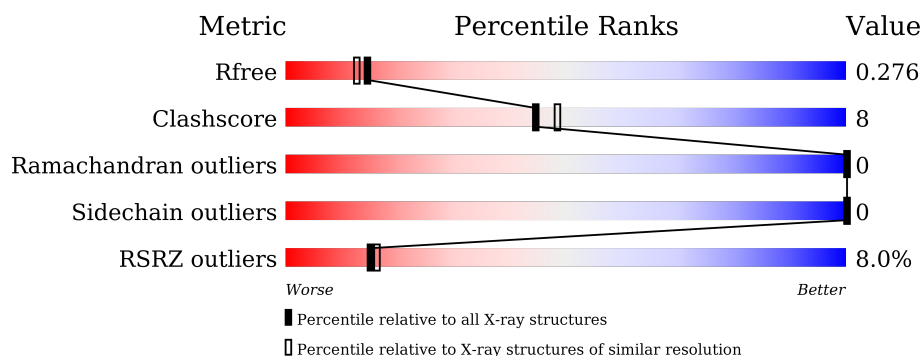
# 1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

*X-RAY DIFFRACTION*

The reported resolution of this entry is 2.17 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))
$R_{free}$	91344	5130 (2.20-2.16)
Clashscore	102246	5965 (2.20-2.16)
Ramachandran outliers	100387	5863 (2.20-2.16)
Sidechain outliers	100360	5864 (2.20-2.16)
RSRZ outliers	91569	5142 (2.20-2.16)

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  $\geq 3$ , 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	313	<div> <div>7%</div> <div>72%</div> <div>11%</div> <div>17%</div> </div>

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
3	DMS	A	902	-	-	-	X
3	DMS	A	903	-	-	-	X

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Mol	Type	Chain	Res	Chirality	Geometry	Clashes	Electron density
3	DMS	A	904	-	-	-	X

## 2 Entry composition

There are 4 unique types of molecules in this entry. The entry contains 2123 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 Dual specificity protein kinase TTK.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	261	Total	C	N	O	S	0	0	0
			2040	1317	333	377	13			

There are 78 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	496	MET	-	initiating methionine	UNP P33981
A	497	HIS	-	expression tag	UNP P33981
A	498	HIS	-	expression tag	UNP P33981
A	499	HIS	-	expression tag	UNP P33981
A	500	HIS	-	expression tag	UNP P33981
A	501	HIS	-	expression tag	UNP P33981
A	502	HIS	-	expression tag	UNP P33981
A	503	SER	-	expression tag	UNP P33981
A	504	SER	-	expression tag	UNP P33981
A	505	GLY	-	expression tag	UNP P33981
A	506	VAL	-	expression tag	UNP P33981
A	507	ASP	-	expression tag	UNP P33981
A	508	LEU	-	expression tag	UNP P33981
A	509	GLY	-	expression tag	UNP P33981
A	510	THR	-	expression tag	UNP P33981
A	511	GLU	-	expression tag	UNP P33981
A	512	ASN	-	expression tag	UNP P33981
A	513	LEU	-	expression tag	UNP P33981
A	514	TYR	-	expression tag	UNP P33981
A	515	PHE	-	expression tag	UNP P33981
A	516	GLN	-	expression tag	UNP P33981
A	517	SER	-	expression tag	UNP P33981
A	518	MET	-	expression tag	UNP P33981
A	754	ILE	-	expression tag	UNP P33981
A	755	GLU	-	expression tag	UNP P33981
A	756	PHE	-	expression tag	UNP P33981
A	757	PRO	-	expression tag	UNP P33981

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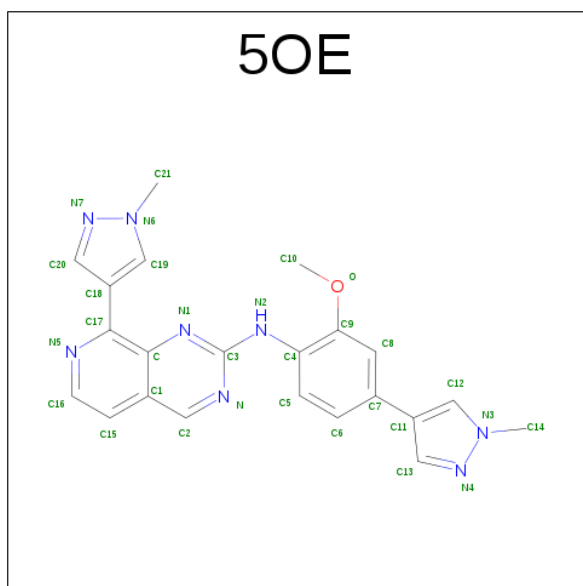
Chain	Residue	Modelled	Actual	Comment	Reference
A	758	ASP	-	expression tag	UNP P33981
A	759	ILE	-	expression tag	UNP P33981
A	760	PRO	-	expression tag	UNP P33981
A	761	GLU	-	expression tag	UNP P33981
A	762	LYS	-	expression tag	UNP P33981
A	763	ASP	-	expression tag	UNP P33981
A	764	LEU	-	expression tag	UNP P33981
A	765	GLN	-	expression tag	UNP P33981
A	766	ASP	-	expression tag	UNP P33981
A	767	VAL	-	expression tag	UNP P33981
A	768	LEU	-	expression tag	UNP P33981
A	769	LYS	-	expression tag	UNP P33981
A	770	CYS	-	expression tag	UNP P33981
A	771	CYS	-	expression tag	UNP P33981
A	772	LEU	-	expression tag	UNP P33981
A	773	LYS	-	expression tag	UNP P33981
A	774	ARG	-	expression tag	UNP P33981
A	775	ASP	-	expression tag	UNP P33981
A	776	PRO	-	expression tag	UNP P33981
A	777	LYS	-	expression tag	UNP P33981
A	778	GLN	-	expression tag	UNP P33981
A	779	ARG	-	expression tag	UNP P33981
A	780	ILE	-	expression tag	UNP P33981
A	781	SER	-	expression tag	UNP P33981
A	782	ILE	-	expression tag	UNP P33981
A	783	PRO	-	expression tag	UNP P33981
A	784	GLU	-	expression tag	UNP P33981
A	785	LEU	-	expression tag	UNP P33981
A	786	LEU	-	expression tag	UNP P33981
A	787	ALA	-	expression tag	UNP P33981
A	788	HIS	-	expression tag	UNP P33981
A	789	PRO	-	expression tag	UNP P33981
A	790	TYR	-	expression tag	UNP P33981
A	791	VAL	-	expression tag	UNP P33981
A	792	GLN	-	expression tag	UNP P33981
A	793	ILE	-	expression tag	UNP P33981
A	794	GLN	-	expression tag	UNP P33981
A	795	THR	-	expression tag	UNP P33981
A	796	HIS	-	expression tag	UNP P33981
A	797	PRO	-	expression tag	UNP P33981
A	798	VAL	-	expression tag	UNP P33981
A	799	ASN	-	expression tag	UNP P33981

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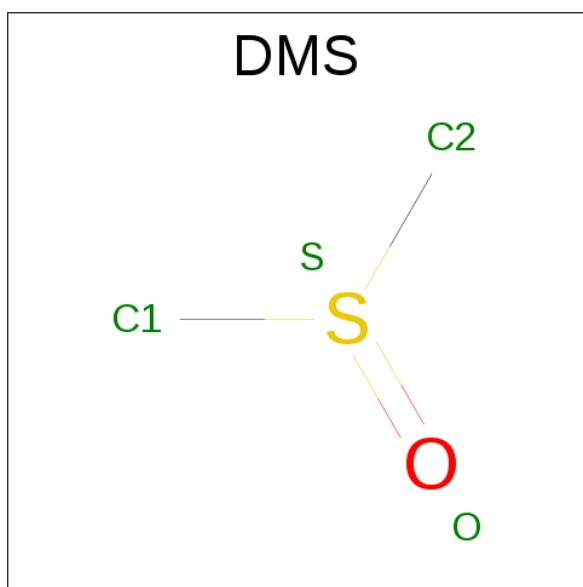
Chain	Residue	Modelled	Actual	Comment	Reference
A	800	GLN	-	expression tag	UNP P33981
A	801	MET	-	expression tag	UNP P33981
A	802	ALA	-	expression tag	UNP P33981
A	803	LYS	-	expression tag	UNP P33981
A	804	GLY	-	expression tag	UNP P33981
A	805	THR	-	expression tag	UNP P33981
A	806	THR	-	expression tag	UNP P33981
A	807	GLU	-	expression tag	UNP P33981
A	808	GLU	-	expression tag	UNP P33981

- Molecule 2 is {N}-[2-methoxy-4-(1-methylpyrazol-4-yl)phenyl]-8-(1-methylpyrazol-4-yl)pyrido[3,4-d]pyrimidin-2-amine (three-letter code: 5OE) (formula: C<sub>22</sub>H<sub>20</sub>N<sub>8</sub>O).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
2	A	1	Total	C	N	O	0	0
			31	22	8	1		

- Molecule 3 is DIMETHYL SULFOXIDE (three-letter code: DMS) (formula: C<sub>2</sub>H<sub>6</sub>OS).



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

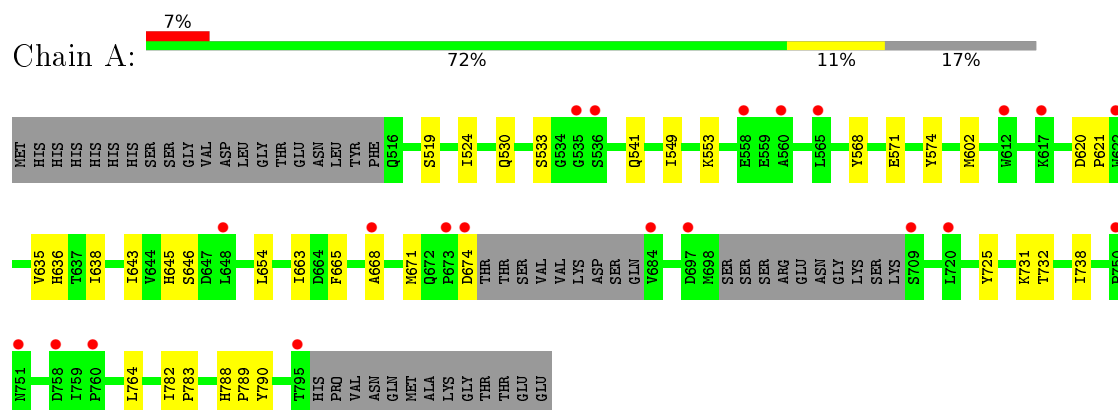
- Molecule 4 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	40	Total	O	0	0
			40	40		

### 3 Residue-property plots [i](#)

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors 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: Dual specificity protein kinase TTK



## 4 Data and refinement statistics

Property	Value	Source
Space group	I 2 2 2	Depositor
Cell constants a, b, c, $\alpha$ , $\beta$ , $\gamma$	70.00Å 101.98Å 110.87Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	37.53 – 2.17 37.53 – 2.18	Depositor EDS
% Data completeness (in resolution range)	99.2 (37.53-2.17) 99.2 (37.53-2.18)	Depositor EDS
$R_{merge}$	(Not available)	Depositor
$R_{sym}$	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ <sup>1</sup>	1.19 (at 2.18Å)	Xtriage
Refinement program	BUSTER 2.10.2	Depositor
R, $R_{free}$	0.214 , 0.244 0.245 , 0.276	Depositor DCC
$R_{free}$ test set	1092 reflections (5.23%)	DCC
Wilson B-factor (Å <sup>2</sup> )	40.0	Xtriage
Anisotropy	0.403	Xtriage
Bulk solvent $k_{sol}$ (e/Å <sup>3</sup> ), $B_{sol}$ (Å <sup>2</sup> )	0.35 , 62.1	EDS
L-test for twinning <sup>2</sup>	$\langle  L  \rangle = 0.49$ , $\langle L^2 \rangle = 0.33$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
$F_o, F_c$ correlation	0.95	EDS
Total number of atoms	2123	wwPDB-VP
Average B, all atoms (Å <sup>2</sup> )	64.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 8.24% of the height of the origin peak. No significant pseudotranslation is detected.*

<sup>1</sup>Intensities estimated from amplitudes.

<sup>2</sup>Theoretical values of  $\langle |L| \rangle$ ,  $\langle L^2 \rangle$  for acentric reflections are 0.5, 0.375 respectively for untwinned datasets, and 0.333, 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: DMS, 5OE

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	0.45	0/2086	0.61	0/2835

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	2040	0	1952	31	0
2	A	31	0	0	1	0
3	A	12	0	18	0	0
4	A	40	0	0	1	0
All	All	2123	0	1970	32	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 8.

All (32) 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:574:TYR:CD1	1:A:643:ILE:HD11	2.00	0.96
1:A:788:HIS:ND1	1:A:789:PRO:HD2	1.87	0.90
1:A:738:ILE:H	1:A:738:ILE:HD12	1.41	0.84
1:A:788:HIS:CE1	1:A:789:PRO:HD2	2.18	0.78
1:A:530:GLN:NE2	1:A:674:ASP:OD2	2.15	0.78
1:A:645:HIS:O	1:A:646:SER:OG	2.03	0.76
1:A:620:ASP:OD1	1:A:621:PRO:HD2	1.87	0.74
1:A:738:ILE:HD12	1:A:738:ILE:N	2.02	0.74
1:A:574:TYR:CE1	1:A:643:ILE:HD11	2.25	0.70
1:A:533:SER:C	1:A:671:MET:HE3	2.14	0.68
1:A:788:HIS:CG	1:A:789:PRO:HD2	2.31	0.65
1:A:738:ILE:CD1	1:A:738:ILE:H	2.12	0.61
1:A:635:VAL:O	1:A:638:ILE:HG12	2.03	0.59
1:A:654:LEU:HB2	1:A:663:ILE:HD11	1.86	0.58
1:A:788:HIS:ND1	1:A:789:PRO:CD	2.65	0.55
1:A:620:ASP:OD1	1:A:621:PRO:CD	2.57	0.53
1:A:788:HIS:CG	1:A:789:PRO:CD	2.92	0.51
1:A:782:ILE:HB	1:A:783:PRO:HD3	1.94	0.49
1:A:568:TYR:CE1	1:A:668:ALA:HB1	2.48	0.48
1:A:533:SER:CA	1:A:671:MET:CE	2.93	0.46
1:A:764:LEU:HD13	1:A:790:TYR:CZ	2.50	0.46
1:A:571:GLU:HG2	1:A:665:PHE:HD1	1.81	0.45
1:A:636:HIS:HB2	1:A:782:ILE:HG21	1.98	0.45
1:A:541:GLN:NE2	1:A:549:ILE:HD11	2.32	0.45
1:A:519:SER:HB2	1:A:524:ILE:HD13	2.00	0.44
1:A:645:HIS:CD2	1:A:665:PHE:HA	2.53	0.43
1:A:553:LYS:HB2	1:A:602:MET:CE	2.49	0.42
1:A:725:TYR:HD1	1:A:731:LYS:O	2.02	0.41
1:A:782:ILE:N	1:A:783:PRO:CD	2.82	0.41
1:A:533:SER:CA	1:A:671:MET:HE3	2.52	0.40
2:A:901:5OE:C19	2:A:901:5OE:N1	2.84	0.40
1:A:732:THR:HB	4:A:1010:HOH:O	2.20	0.40

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	255/313 (82%)	249 (98%)	6 (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	213/288 (74%)	213 (100%)	0	100	100

There are no protein residues with a non-rotameric sidechain to report.

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. There are no such sidechains identified.

### 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](#)

4 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	5OE	A	901	-	30,35,35	0.88	1 (3%)	38,50,50	0.97	4 (10%)
3	DMS	A	902	-	3,3,3	0.32	0	3,3,3	0.30	0
3	DMS	A	903	-	3,3,3	0.26	0	3,3,3	0.20	0
3	DMS	A	904	-	3,3,3	0.30	0	3,3,3	0.22	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	5OE	A	901	-	-	0/10/14/14	0/5/5/5
3	DMS	A	902	-	-	0/0/0/0	0/0/0/0
3	DMS	A	903	-	-	0/0/0/0	0/0/0/0
3	DMS	A	904	-	-	0/0/0/0	0/0/0/0

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	901	5OE	C18-C17	-3.99	1.44	1.49

All (4) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	A	901	5OE	C11-C12-N3	-2.16	106.79	109.84
2	A	901	5OE	C18-C19-N6	-2.14	106.82	109.84
2	A	901	5OE	C15-C1-C2	2.10	126.82	122.57
2	A	901	5OE	C16-N5-C17	2.31	119.58	117.94

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	901	5OE	1	0

## 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, 95<sup>th</sup> 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 <sup>2</sup> )	Q<0.9
1	A	261/313 (83%)	0.48	21 (8%) 15 16	40, 62, 97, 120	0

All (21) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	622	TRP	4.6
1	A	751	ASN	4.3
1	A	560	ALA	4.3
1	A	674	ASP	3.8
1	A	536	SER	3.6
1	A	617	LYS	3.4
1	A	750	PRO	3.3
1	A	648	LEU	3.2
1	A	795	THR	3.2
1	A	673	PRO	2.9
1	A	760	PRO	2.8
1	A	684	VAL	2.7
1	A	535	GLY	2.7
1	A	668	ALA	2.7
1	A	558	GLU	2.6
1	A	709	SER	2.6
1	A	612	TRP	2.5
1	A	720	LEU	2.4
1	A	697	ASP	2.2
1	A	758	ASP	2.2
1	A	565	LEU	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, 95<sup>th</sup> 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( $\text{\AA}^2$ )	Q<0.9
3	DMS	A	903	4/4	0.79	0.28	10.79	110,110,110,110	0
3	DMS	A	904	4/4	0.90	0.34	10.27	113,113,113,113	0
3	DMS	A	902	4/4	0.87	0.29	5.34	105,106,106,107	0
2	5OE	A	901	31/31	0.93	0.12	-0.16	36,43,57,59	0

### 6.5 Other polymers [i](#)

There are no such residues in this entry.