Full wwPDB X-ray Structure Validation Report (i)

May 16, 2020 – 12:08 am BST

PDB ID	:	1XH5
Title	:	Crystal Structures of Protein Kinase B Selective Inhibitors in Complex with Protein Kinase A and Mutants
Authors	:	Breitenlechner, C.B.; Friebe, W.-G.; Brunet, E.; Werner, G.; Graul, K.; Thomas, U.; Kuenkele, K.-P.; Schaefer, W.; Gassel, M.; Bossemeyer, D.; Huber, R.; Engh, R.A.; Masjost, B.
Deposited on	:	2004-09-17
Resolution	:	2.05 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 following versions of software and data (see references (1)) were used in the production of this report:

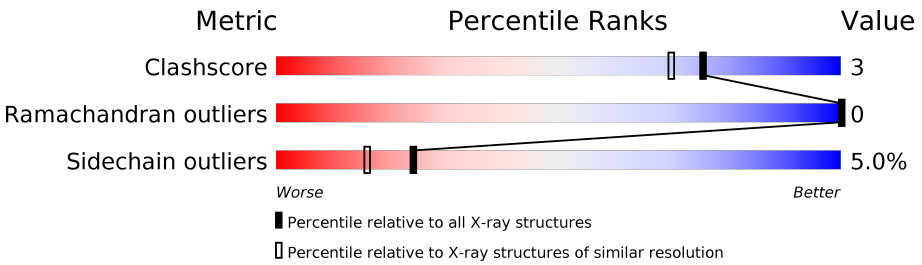
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	NOT EXECUTED
EDS	:	NOT EXECUTED
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, 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 2.05 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))
Clashscore	141614	1773 (2.04-2.04)
Ramachandran outliers	138981	1752 (2.04-2.04)
Sidechain outliers	138945	1752 (2.04-2.04)

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%

Note EDS was not executed.

Mol	Chain	Length	Quality of chain
1	A	350	86% 9% • •
2	B	20	80% 15% 5%

2 Entry composition (i)

There are 5 unique types of molecules in this entry. The entry contains 3176 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 cAMP-dependent protein kinase, alpha-catalytic subunit.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
			Total	C	N	O	P	S			
1	A	337	2746	1777	459	499	2	9	0	0	0

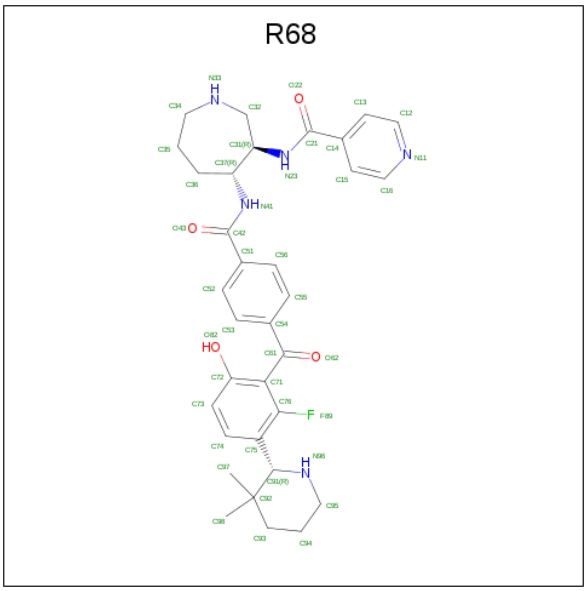
There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	197	TPO	THR	MODIFIED RESIDUE	UNP P00517
A	338	SEP	SER	MODIFIED RESIDUE	UNP P00517

- Molecule 2 is a protein called cAMP-dependent protein kinase inhibitor, alpha form.

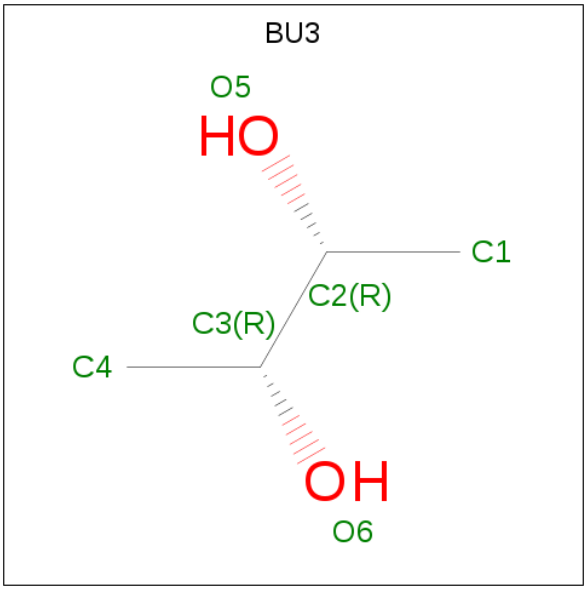
Mol	Chain	Residues	Atoms				ZeroOcc	AltConf	Trace
			Total	C	N	O			
2	B	20	157	94	32	31	0	0	0

- Molecule 3 is N-{4-[(4-{3-[(2R)-3,3-DIMETHYLPIPERIDIN-2-YL]-2-FLUORO-6-HYDROXYBENZOYL}BENZOYL)AMINO]AZEPAN-3-YL}ISONICOTINAMIDE (three-letter code: R68) (formula: $C_{33}H_{38}FN_5O_4$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	F	N	O		
3	A	1	43	33	1	5	4	0	0

- Molecule 4 is (R,R)-2,3-BUTANEDIOL (three-letter code: BU3) (formula: $C_4H_{10}O_2$).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
			Total	C	O			
4	A	1	6	4	2		0	0
			Total	C	O			
4	A	1	6	4	2		0	0
			Total	C	O			
4	B	1	6	4	2		0	0

- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
			Total	O		
5	A	194	194	194	0	0
			Total	O		
5	B	18	18	18	0	0

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 the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry. 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. 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.

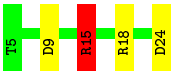
Note EDS was not executed.

- Molecule 1: cAMP-dependent protein kinase, alpha-catalytic subunit

Chain A:

- Molecule 2: cAMP-dependent protein kinase inhibitor, alpha form

Chain B:



4 Data and refinement statistics (i)

Xtriage (Phenix) and EDS were not executed - this section is therefore incomplete.

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	74.09Å 76.81Å 79.53Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	18.63 – 2.05	Depositor
% Data completeness (in resolution range)	99.9 (18.63-2.05)	Depositor
R_{merge}	(Not available)	Depositor
R_{sym}	(Not available)	Depositor
Refinement program	REFMAC 5.1.24	Depositor
R, R_{free}	0.182 , 0.236	Depositor
Estimated twinning fraction	No twinning to report.	Xtriage
Total number of atoms	3176	wwPDB-VP
Average B, all atoms ($Å^2$)	33.0	wwPDB-VP

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: TPO, BU3, R68, SEP

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	0.74	0/2795	0.88	12/3772 (0.3%)
2	B	0.84	0/159	1.36	3/212 (1.4%)
All	All	0.75	0/2954	0.91	15/3984 (0.4%)

There are no bond length outliers.

All (15) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	B	15	ARG	NE-CZ-NH2	-11.12	114.74	120.30
1	A	56	ARG	NE-CZ-NH1	10.05	125.32	120.30
1	A	56	ARG	NE-CZ-NH2	-9.64	115.48	120.30
1	A	112	ASP	CB-CG-OD2	7.32	124.89	118.30
1	A	328	ASP	CB-CG-OD2	7.00	124.60	118.30
1	A	41	ASP	CB-CG-OD2	6.79	124.42	118.30
2	B	9	ASP	CB-CG-OD2	6.39	124.05	118.30
2	B	15	ARG	NE-CZ-NH1	5.92	123.26	120.30
1	A	184	ASP	CB-CG-OD2	5.90	123.61	118.30
1	A	45	ARG	NE-CZ-NH2	-5.86	117.37	120.30
1	A	75	ASP	CB-CG-OD2	5.79	123.51	118.30
1	A	191	VAL	CB-CA-C	-5.41	101.11	111.40
1	A	161	ASP	CB-CG-OD2	5.33	123.10	118.30
1	A	308	ARG	NE-CZ-NH2	-5.28	117.66	120.30
1	A	144	ARG	NE-CZ-NH2	-5.21	117.69	120.30

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	2746	0	2675	18	0
2	B	157	0	146	3	0
3	A	43	0	37	1	0
4	A	12	0	20	4	0
4	B	6	0	10	0	0
5	A	194	0	0	2	0
5	B	18	0	0	0	0
All	All	3176	0	2888	18	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 (18) 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:203:GLU:OE2	2:B:15:ARG:HD3	1.82	0.79
1:A:56:ARG:HD2	4:A:901:BU3:O5	1.86	0.75
1:A:91:GLU:OE2	5:A:1021:HOH:O	2.12	0.67
1:A:158:HIS:HE1	1:A:220:ASP:OD2	1.83	0.61
1:A:39:HIS:H	1:A:42:GLN:HE21	1.48	0.60
1:A:40:LEU:HD22	5:A:1194:HOH:O	2.02	0.59
1:A:246:ILE:HD11	2:B:15:ARG:HD2	1.86	0.57
1:A:203:GLU:OE2	2:B:15:ARG:CD	2.52	0.56
1:A:295:LYS:HE3	1:A:295:LYS:H	1.69	0.56
1:A:189:LYS:HG2	1:A:191:VAL:HG22	1.90	0.53
1:A:69:TYR:CE1	1:A:107:GLU:HG3	2.45	0.51
1:A:142:HIS:CD2	1:A:146:TYR:CE2	3.02	0.47
1:A:144:ARG:CD	4:A:903:BU3:O6	2.66	0.44
1:A:138:PHE:HB3	1:A:142:HIS:HB3	2.00	0.43
1:A:39:HIS:CE1	1:A:41:ASP:OD1	2.73	0.42
1:A:144:ARG:HD3	4:A:903:BU3:O6	2.21	0.41
1:A:144:ARG:HD2	4:A:903:BU3:C2	2.51	0.41
1:A:57:VAL:HG23	3:A:1001:R68:C42	2.52	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	333/350 (95%)	322 (97%)	11 (3%)	0	100	100
2	B	18/20 (90%)	18 (100%)	0	0	100	100
All	All	351/370 (95%)	340 (97%)	11 (3%)	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	285/303 (94%)	273 (96%)	12 (4%)	30	22
2	B	15/15 (100%)	12 (80%)	3 (20%)	1	0
All	All	300/318 (94%)	285 (95%)	15 (5%)	24	16

All (15) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	14	SER
1	A	40	LEU
1	A	41	ASP
1	A	53	SER
1	A	59	LEU
1	A	160	LEU
1	A	213	LYS
1	A	252	SER

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Mol	Chain	Res	Type
1	A	268	LEU
1	A	295	LYS
1	A	325	SER
1	A	349	GLU
2	B	15	ARG
2	B	18	ARG
2	B	24	ASP

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (5) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	42	GLN
1	A	113	ASN
1	A	158	HIS
1	A	181	GLN
1	A	289	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)

2 non-standard protein/DNA/RNA residues 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	$\#\|Z\| > 2$
1	TPO	A	197	1	8,10,11	0.80	0	10,14,16	0.80	0
1	SEP	A	338	1	8,9,10	1.32	1 (12%)	8,12,14	1.65	1 (12%)

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
1	TPO	A	197	1	-	1/9/11/13	-
1	SEP	A	338	1	-	3/5/8/10	-

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	338	SEP	P-O1P	2.98	1.60	1.50

All (1) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	A	338	SEP	OG-CB-CA	3.69	111.74	108.14

There are no chirality outliers.

All (4) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
1	A	338	SEP	N-CA-CB-OG
1	A	338	SEP	CA-CB-OG-P
1	A	338	SEP	CB-OG-P-O2P
1	A	197	TPO	O-C-CA-CB

There are no ring outliers.

No monomer is involved in short contacts.

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	$\#\|Z\| > 2$
4	BU3	A	903	-	4,5,5	0.87	0	6,6,6	0.41	0
3	R68	A	1001	-	42,47,47	1.12	1 (2%)	53,67,67	1.25	7 (13%)
4	BU3	B	902	-	4,5,5	0.94	0	6,6,6	1.01	0
4	BU3	A	901	-	4,5,5	0.61	0	6,6,6	0.86	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
4	BU3	A	903	-	-	0/4/4/4	-
3	R68	A	1001	-	-	2/28/54/54	0/5/5/5
4	BU3	B	902	-	-	0/4/4/4	-
4	BU3	A	901	-	-	0/4/4/4	-

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	1001	R68	C21-N23	2.30	1.39	1.34

All (7) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
3	A	1001	R68	O82-C72-C71	-3.54	114.52	121.14
3	A	1001	R68	F89-C76-C71	-3.17	115.82	119.95
3	A	1001	R68	O22-C21-N23	-2.71	117.46	122.45
3	A	1001	R68	C32-C31-N23	-2.63	104.66	109.61
3	A	1001	R68	C73-C72-C71	2.29	123.11	120.17
3	A	1001	R68	O43-C42-N41	-2.16	118.48	122.45
3	A	1001	R68	C51-C42-N41	2.10	121.09	117.06

There are no chirality outliers.

All (2) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
3	A	1001	R68	C76-C75-C91-N96
3	A	1001	R68	C74-C75-C91-N96

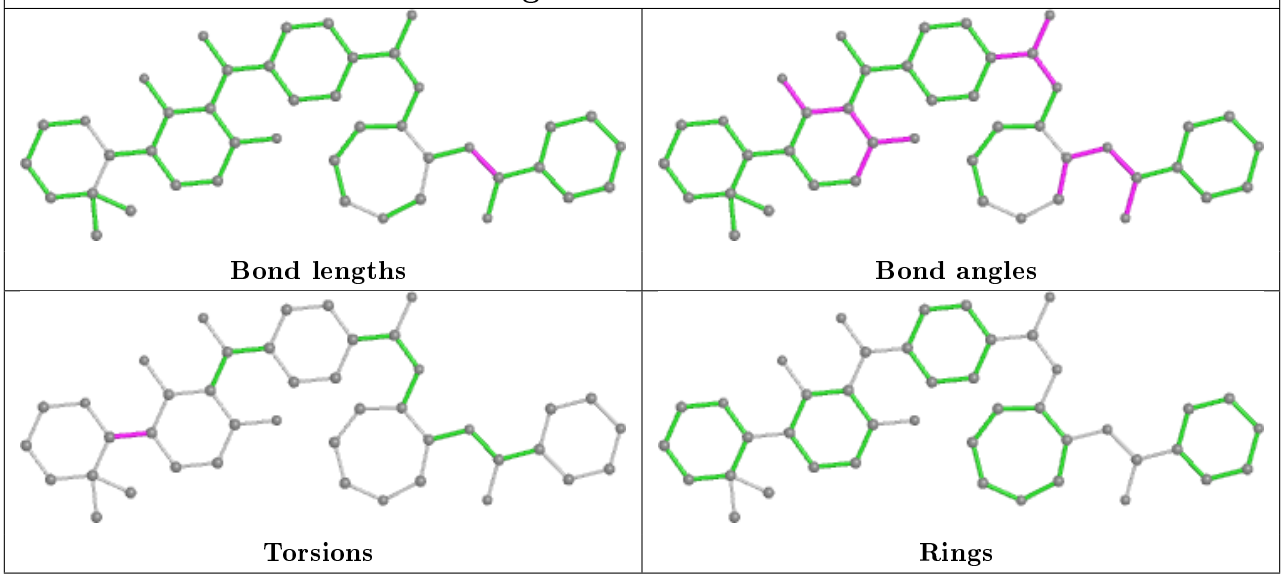
There are no ring outliers.

3 monomers are involved in 5 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
4	A	903	BU3	3	0
3	A	1001	R68	1	0
4	A	901	BU3	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 R68 A 1001



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)

EDS was not executed - this section is therefore empty.

6.2 Non-standard residues in protein, DNA, RNA chains (i)

EDS was not executed - this section is therefore empty.

6.3 Carbohydrates (i)

EDS was not executed - this section is therefore empty.

6.4 Ligands (i)

EDS was not executed - this section is therefore empty.

6.5 Other polymers (i)

EDS was not executed - this section is therefore empty.