wwPDB X-ray Structure Validation Summary Report (i)

Oct 11, 2021 – 07:40 AM EDT

PDB ID	:	3C1X
Title	:	Crystal structure of the tyrosine kinase domain of the hepatocyte growth factor receptor c-MET in complex with a Pyrrolotriazine based inhibitor
Authors	:	Sack, J.
Deposited on	:	2008-01-24
Resolution	:	2.17 Å(reported)

This is a wwPDB X-ray Structure Validation Summary 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 (i)) were used in the production of this report:

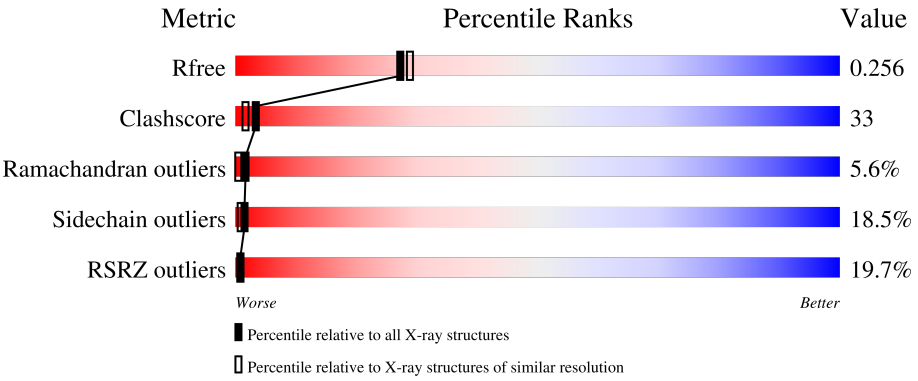
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.23.2
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.23.2

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 2.17 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}	130704	6864 (2.20-2.16)
Clashscore	141614	7689 (2.20-2.16)
Ramachandran outliers	138981	7564 (2.20-2.16)
Sidechain outliers	138945	7564 (2.20-2.16)
RSRZ outliers	127900	6738 (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 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	373	15% 41% 27% 8% · 22%

2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 2440 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 Hepatocyte growth factor receptor.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	290	2309	1493	394	408	14	0	0	0

There are 65 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	988	MET	-	expression tag	UNP P08581
A	989	SER	-	expression tag	UNP P08581
A	990	PRO	-	expression tag	UNP P08581
A	991	ILE	-	expression tag	UNP P08581
A	992	ASP	-	expression tag	UNP P08581
A	993	PRO	-	expression tag	UNP P08581
A	994	MET	-	expression tag	UNP P08581
A	995	GLY	-	expression tag	UNP P08581
A	996	HIS	-	expression tag	UNP P08581
A	997	HIS	-	expression tag	UNP P08581
A	998	HIS	-	expression tag	UNP P08581
A	999	HIS	-	expression tag	UNP P08581
A	1000	HIS	-	expression tag	UNP P08581
A	1001	HIS	-	expression tag	UNP P08581
A	1002	GLY	-	expression tag	UNP P08581
A	1003	ARG	-	expression tag	UNP P08581
A	1004	ARG	-	expression tag	UNP P08581
A	1005	ARG	-	expression tag	UNP P08581
A	1006	ALA	-	expression tag	UNP P08581
A	1007	SER	-	expression tag	UNP P08581
A	1008	VAL	-	expression tag	UNP P08581
A	1009	ALA	-	expression tag	UNP P08581
A	1010	ALA	-	expression tag	UNP P08581
A	1011	GLY	-	expression tag	UNP P08581
A	1012	ILE	-	expression tag	UNP P08581
A	1013	LEU	-	expression tag	UNP P08581
A	1014	VAL	-	expression tag	UNP P08581

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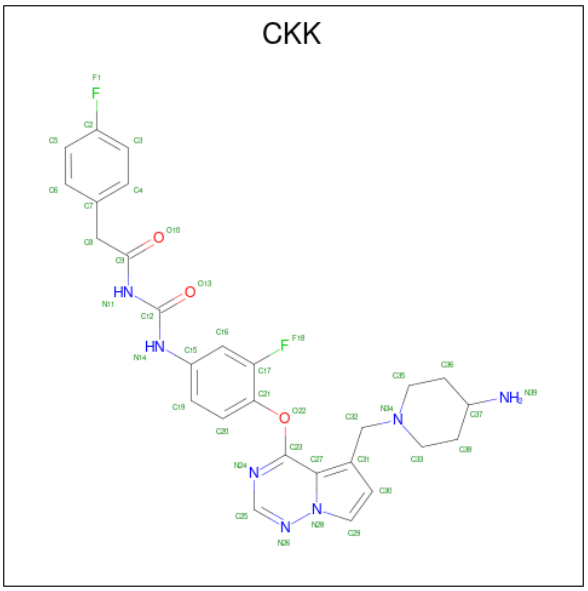
Chain	Residue	Modelled	Actual	Comment	Reference
A	1015	PRO	-	expression tag	UNP P08581
A	1016	ARG	-	expression tag	UNP P08581
A	1017	GLY	-	expression tag	UNP P08581
A	1018	SER	-	expression tag	UNP P08581
A	1019	PRO	-	expression tag	UNP P08581
A	1020	GLY	-	expression tag	UNP P08581
A	1021	LEU	-	expression tag	UNP P08581
A	1022	ASP	-	expression tag	UNP P08581
A	1023	GLY	-	expression tag	UNP P08581
A	1024	ILE	-	expression tag	UNP P08581
A	1025	CYS	-	expression tag	UNP P08581
A	1026	SER	-	expression tag	UNP P08581
A	1027	ILE	-	expression tag	UNP P08581
A	1028	GLU	-	expression tag	UNP P08581
A	1029	GLU	-	expression tag	UNP P08581
A	1030	LEU	-	expression tag	UNP P08581
A	1031	SER	-	expression tag	UNP P08581
A	1032	THR	-	expression tag	UNP P08581
A	1033	SER	-	expression tag	UNP P08581
A	1034	LEU	-	expression tag	UNP P08581
A	1035	TYR	-	expression tag	UNP P08581
A	1036	LYS	-	expression tag	UNP P08581
A	1037	LYS	-	expression tag	UNP P08581
A	1038	ALA	-	expression tag	UNP P08581
A	1039	GLY	-	expression tag	UNP P08581
A	1040	SER	-	expression tag	UNP P08581
A	1041	GLU	-	expression tag	UNP P08581
A	1042	ASN	-	expression tag	UNP P08581
A	1043	LEU	-	expression tag	UNP P08581
A	1044	TYR	-	expression tag	UNP P08581
A	1045	PHE	-	expression tag	UNP P08581
A	1046	GLN	-	expression tag	UNP P08581
A	1047	GLY	-	expression tag	UNP P08581
A	1048	ALA	-	expression tag	UNP P08581
A	1194	PHE	TYR	engineered mutation	UNP P08581
A	1234	PHE	TYR	engineered mutation	UNP P08581
A	1235	ASP	TYR	engineered mutation	UNP P08581
A	1272	LEU	VAL	engineered mutation	UNP P08581

- Molecule 2 is N-{[4-({5-[(4-aminopiperidin-1-yl)methyl]pyrrolo[2,1-f][1,2,4]triazin-4-yl}oxy)-3-fluorophenyl]carbamoyl}-2-(4-fluorophenyl)acetamide (three-letter code: CKK) (formula: $C_{27}H_{27}F_2N_7O_3$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	F	N	O	0	0
			39	27	2	7	3		

- Molecule 3 is water.

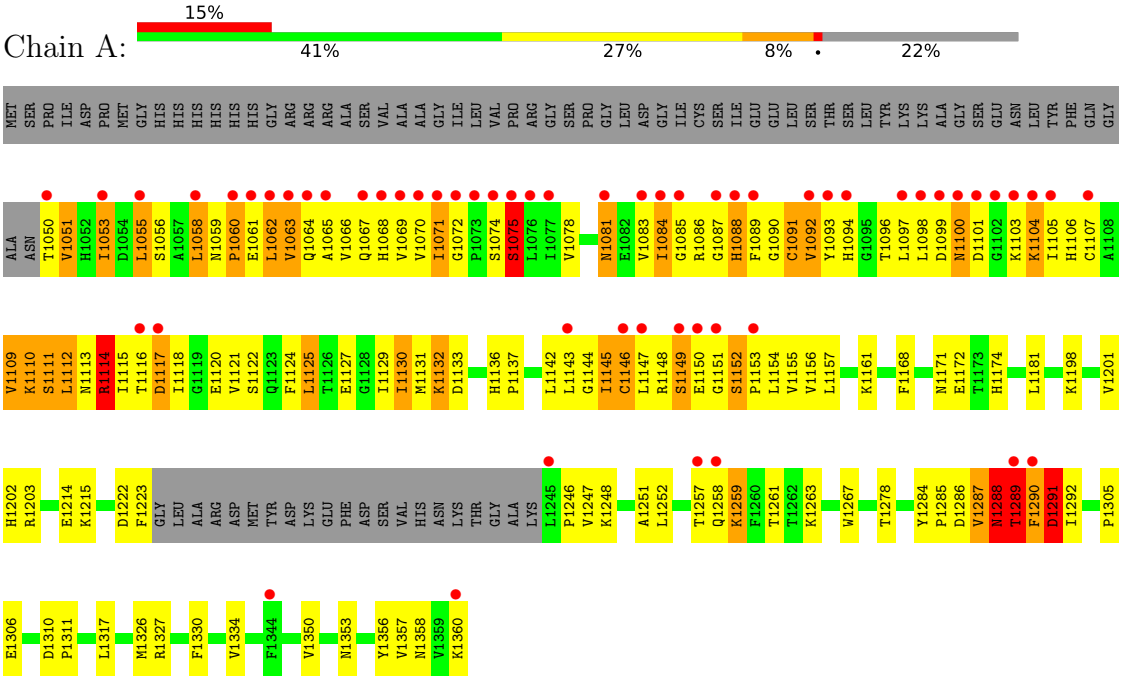
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	92	Total	O	0	0
			92	92		

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: Hepatocyte growth factor receptor

Chain A:



4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	42.78Å 46.15Å 151.02Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	37.76 – 2.17 37.76 – 2.18	Depositor EDS
% Data completeness (in resolution range)	80.5 (37.76-2.17) 80.7 (37.76-2.18)	Depositor EDS
R_{merge}	0.11	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	2.67 (at 2.18Å)	Xtriage
Refinement program	BUSTER-TNT 2.1.1	Depositor
R, R_{free}	0.205 , 0.262 0.210 , 0.256	Depositor DCC
R_{free} test set	791 reflections (5.97%)	wwPDB-VP
Wilson B-factor (Å^2)	38.4	Xtriage
Anisotropy	0.160	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.36 , 66.0	EDS
L-test for twinning[2]	$< \|L\| > = 0.50$, $< L^2 > = 0.34$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
F_o,F_c correlation	0.94	EDS
Total number of atoms	2440	wwPDB-VP
Average B, all atoms (Å^2)	54.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 7.65% of the height of the origin peak. No significant pseudotranslation is detected.*

[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: CKK

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	0.36	0/2367	0.55	0/3209

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	2309	0	2332	152	0
2	A	39	0	27	4	0
3	A	92	0	0	6	0
All	All	2440	0	2359	154	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 33.

The worst 5 of 154 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:1288:ASN:ND2	1:A:1288:ASN:H	1.49	1.06

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:1288:ASN:HD22	1:A:1288:ASN:N	1.55	0.98
1:A:1248:LYS:HE3	1:A:1289:THR:HB	1.53	0.88
1:A:1053:ILE:HD11	1:A:1118:ILE:HB	1.54	0.88
1:A:1083:VAL:HG12	1:A:1093:TYR:CE1	2.09	0.88

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	286/373 (77%)	252 (88%)	18 (6%)	16 (6%)	2 0

5 of 16 Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	1058	LEU
1	A	1060	PRO
1	A	1113	ASN
1	A	1258	GLN
1	A	1289	THR

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.

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Mol	Chain	Analysed	Rotameric	Outliers	Percentiles

Mol	Chain	Analysed	Rotameric	Outliers	Percentiles
1	A	259/325 (80%)	211 (82%)	48 (18%)	1 1

5 of 48 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	1132	LYS
1	A	1154	LEU
1	A	1133	ASP
1	A	1147	LEU
1	A	1172	GLU

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 6 such sidechains are listed below:

Mol	Chain	Res	Type
1	A	1167	ASN
1	A	1174	HIS
1	A	1288	ASN
1	A	1068	HIS
1	A	1064	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)

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	$\#\|Z\| > 2$
2	CKK	A	1500	-	38,43,43	1.32	5 (13%)	49,60,60	1.86	15 (30%)

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	CKK	A	1500	-	-	1/19/30/30	0/5/5/5

All (5) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	A	1500	CKK	C8-C7	-3.62	1.45	1.51
2	A	1500	CKK	C12-N11	-3.27	1.32	1.39
2	A	1500	CKK	C27-N28	-2.89	1.36	1.40
2	A	1500	CKK	C25-N26	-2.17	1.30	1.33
2	A	1500	CKK	C19-C15	2.03	1.42	1.39

The worst 5 of 15 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	A	1500	CKK	C9-N11-C12	-4.58	123.06	129.02
2	A	1500	CKK	C21-O22-C23	-4.16	111.73	117.82
2	A	1500	CKK	C15-C16-C17	3.75	121.82	118.76
2	A	1500	CKK	O22-C23-N24	3.55	124.25	119.58
2	A	1500	CKK	O13-C12-N14	2.98	128.66	123.62

There are no chirality outliers.

All (1) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	A	1500	CKK	C27-C23-O22-C21

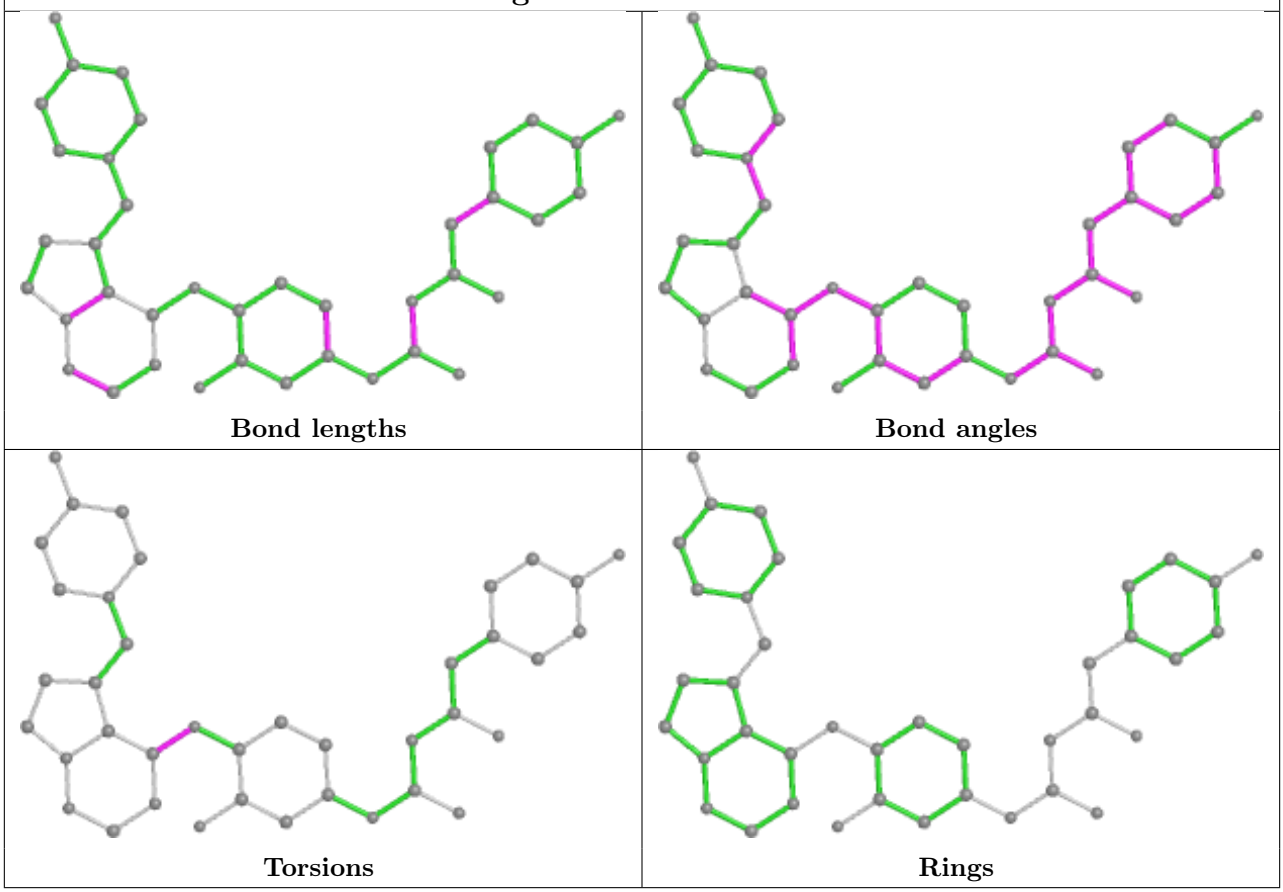
There are no ring outliers.

1 monomer is involved in 4 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	A	1500	CKK	4	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 CKK A 1500



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, 95^{th} 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	290/373 (77%)	0.95	57 (19%) 1 1	22, 42, 104, 118	1 (0%)

The worst 5 of 57 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	1068	HIS	6.7
1	A	1062	LEU	6.5
1	A	1050	THR	6.4
1	A	1076	LEU	6.4
1	A	1088	HIS	6.2

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, 95^{th} 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.

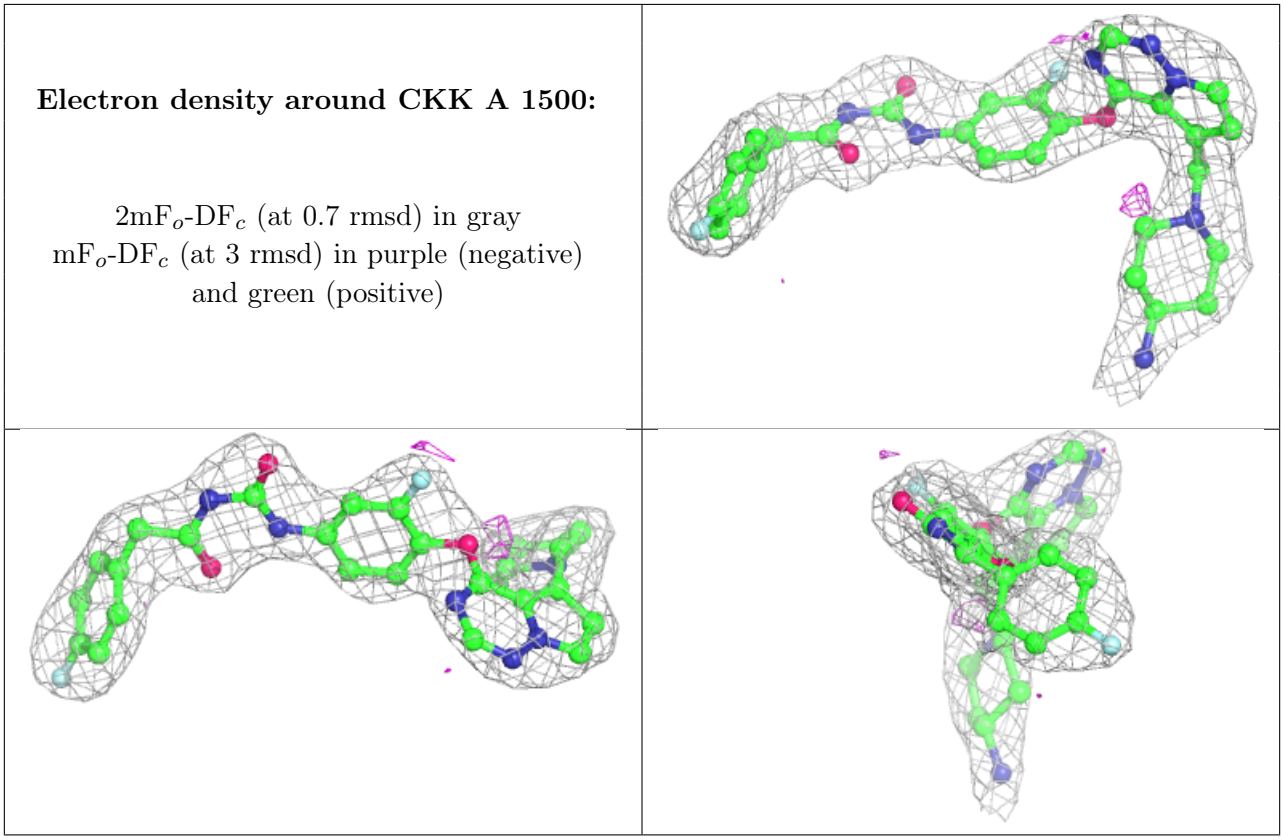
Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å^2)	Q<0.9
2	CKK	A	1500	39/39	0.92	0.13	41,49,57,58	0

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 CKK A 1500:

$2mF_o$-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.