



## Full wwPDB X-ray Structure Validation Report

Mar 6, 2026 – 02:14 PM UTC

PDB ID : 8A2D / pdb\_00008a2d  
Title : EGFR kinase domain (L858R/V948R) in complex with 2-[4-(difluoromethyl)-6-[2-[4-[[4-(hydroxymethyl)-1-piperidyl]methyl]phenyl]ethynyl]-7-methyl-indazol-2-yl]-2-spiro[6,7-dihydropyrrolo[1,2-c]imidazole-5,1'-cyclopropane]-1-yl-N-tiazol-2-yl-acetamide  
Authors : Kuglstatter, A.; Ehler, A.  
Deposited on : 2022-06-03  
Resolution : 1.11 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

<https://www.wwpdb.org/validation/2017/XrayValidationReportHelp>

with specific help available everywhere you see the  symbol.

The types of validation reports are described at

<http://www.wwpdb.org/validation/2017/FAQs#types>.

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The following versions of software and data (see [references](#) ①) were used in the production of this report:

MolProbity : 4-5-2 with Phenix2.0  
Mogul : 2022.3.0, CSD as543be (2022)  
Xtrriage (Phenix) : 2.0  
EDS : 3.0  
Buster-report : wwPDB partial adaption of 1.1.7 (2018)  
Percentile statistics : 20250101.v01 (using entries in the PDB archive January 1st 2025)  
CCP4 : 9.0.010 (Gargrove)  
Density-Fitness : 1.0.12  
Ideal geometry (proteins) : Engh & Huber (2001)  
Ideal geometry (DNA, RNA) : Parkinson et al. (1996)  
Validation Pipeline (wwPDB-VP) : 2.49

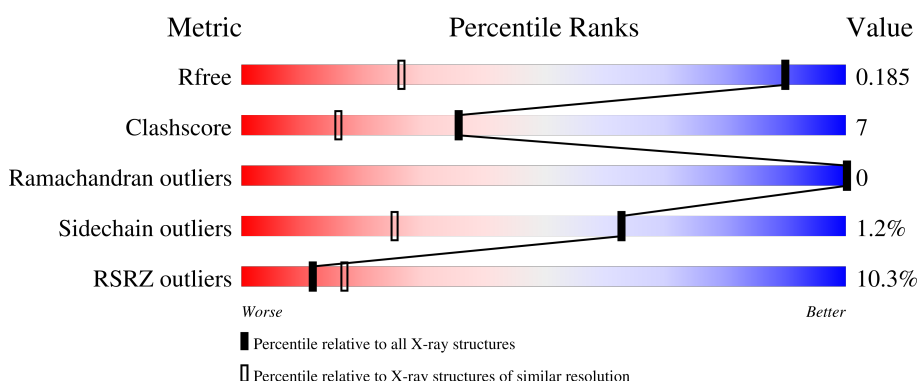
# 1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

*X-RAY DIFFRACTION*

The reported resolution of this entry is 1.11 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))
$R_{free}$	180053	1985 (1.14-1.10)
Clashscore	190562	2021 (1.14-1.10)
Ramachandran outliers	187476	1978 (1.14-1.10)
Sidechain outliers	187428	1974 (1.14-1.10)
RSRZ outliers	180081	1984 (1.14-1.10)

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  $\geq 3$ , 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	326	

## 2 Entry composition [i](#)

There are 5 unique types of molecules in this entry. The entry contains 2770 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.

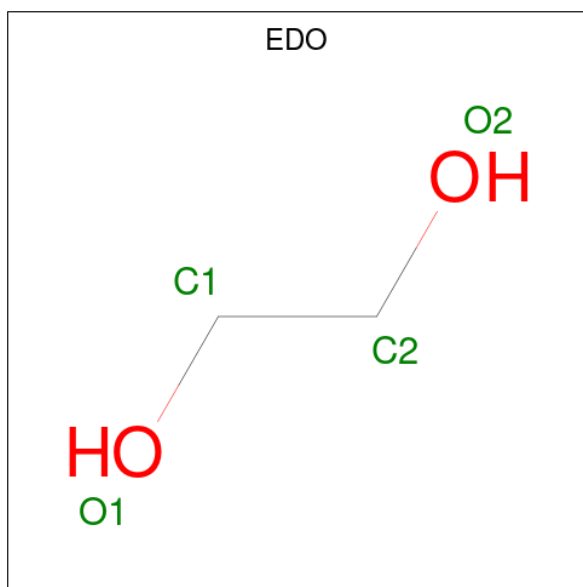
- Molecule 1 is a protein called Epidermal growth factor receptor.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	281	2318	1495	392	413	18	0	9	0

There are 5 discrepancies between the modelled and reference sequences:

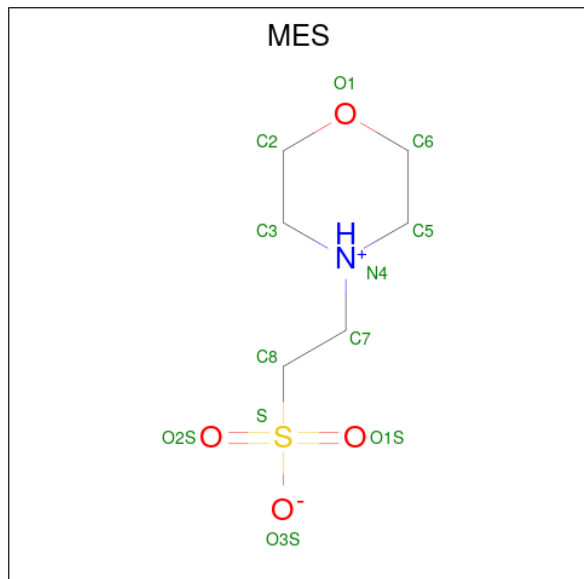
Chain	Residue	Modelled	Actual	Comment	Reference
A	697	GLY	-	expression tag	UNP P00533
A	698	SER	-	expression tag	UNP P00533
A	699	MET	-	expression tag	UNP P00533
A	858	ARG	LEU	engineered mutation	UNP P00533
A	948	ARG	VAL	engineered mutation	UNP P00533

- Molecule 2 is 1,2-ETHANEDIOL (CCD ID: EDO) (formula: C<sub>2</sub>H<sub>6</sub>O<sub>2</sub>).



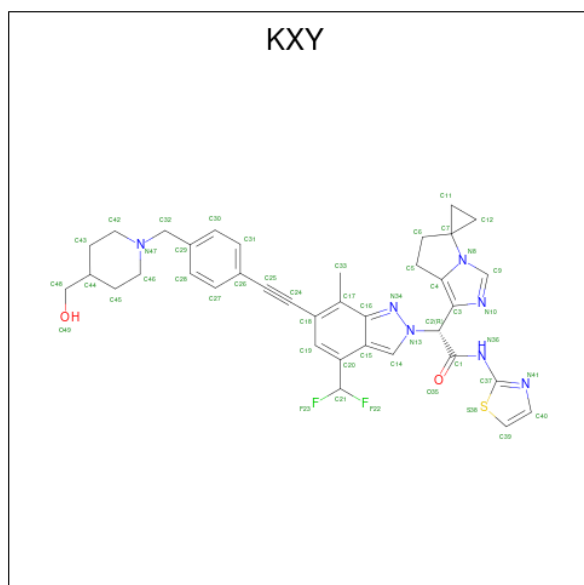
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
			Total	C	O		
2	A	1	4	2	2	0	0

- Molecule 3 is 2-(N-MORPHOLINO)-ETHANESULFONIC ACID (CCD ID: MES) (formula:  $C_6H_{13}NO_4S$ ).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
			Total	C	N	O	S		
3	A	1	12	6	1	4	1	0	0

- Molecule 4 is (2R)-2-[4-[bis(fluoranyl)methyl]-6-[2-[4-[[4-(hydroxymethyl)piperidin-1-yl]methyl]phenyl]ethynyl]-7-methyl-indazol-2-yl]-2-spiro[6,7-dihydropyrrolo[1,2-c]imidazole-5,1'-cyclopropane]-1-yl-N-(1,3-thiazol-2-yl)ethanamide (CCD ID: KXY) (formula:  $C_{37}H_{37}F_2N_7O_2S$ ) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	
			Total	C	F	N	O			S
4	A	1	49	37	2	7	2	1	0	0

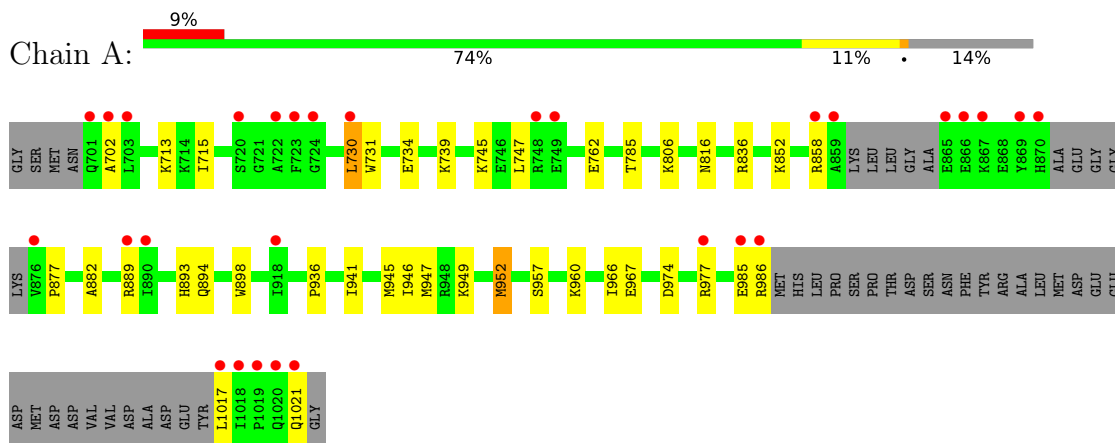
- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	A	387	Total	O	0	0
			387	387		

### 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: Epidermal growth factor receptor



## 4 Data and refinement statistics

Property	Value	Source
Space group	C 1 2 1	Depositor
Cell constants a, b, c, $\alpha$ , $\beta$ , $\gamma$	119.62Å 34.95Å 83.93Å 90.00° 128.81° 90.00°	Depositor
Resolution (Å)	65.40 – 1.11 65.40 – 1.11	Depositor EDS
% Data completeness (in resolution range)	89.7 (65.40-1.11) 89.7 (65.40-1.11)	Depositor EDS
$R_{merge}$	(Not available)	Depositor
$R_{sym}$	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ <sup>1</sup>	1.50 (at 1.11Å)	Xtrriage
Refinement program	REFMAC 5.8.0267	Depositor
R, $R_{free}$	0.163 , 0.179 0.170 , 0.185	Depositor DCC
$R_{free}$ test set	4722 reflections (4.46%)	wwPDB-VP
Wilson B-factor (Å <sup>2</sup> )	11.8	Xtrriage
Anisotropy	0.170	Xtrriage
Bulk solvent $k_{sol}$ (e/Å <sup>3</sup> ), $B_{sol}$ (Å <sup>2</sup> )	0.36 , 34.2	EDS
L-test for twinning <sup>2</sup>	$\langle  L  \rangle = 0.50$ , $\langle L^2 \rangle = 0.34$	Xtrriage
Estimated twinning fraction	No twinning to report.	Xtrriage
$F_o, F_c$ correlation	0.97	EDS
Total number of atoms	2770	wwPDB-VP
Average B, all atoms (Å <sup>2</sup> )	17.0	wwPDB-VP

Xtrriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 10.19% 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, 0.333 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: KXY, EDO, MES

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	1.27	5/2393 (0.2%)	1.23	6/3231 (0.2%)

All (5) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	893	HIS	ND1-CE1	7.58	1.40	1.32
1	A	747	LEU	C-O	-6.79	1.14	1.23
1	A	966	ILE	C-O	5.54	1.30	1.24
1	A	936	PRO	CA-C	5.47	1.54	1.51
1	A	702	ALA	C-O	5.01	1.30	1.23

All (6) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	947	MET	CG-SD-CE	-14.44	69.13	100.90
1	A	836	ARG	NE-CZ-NH2	6.73	125.26	119.20
1	A	952	MET	CG-SD-CE	-6.02	87.66	100.90
1	A	952	MET	CB-CG-SD	5.96	130.57	112.70
1	A	894	GLN	OE1-CD-NE2	-5.48	117.12	122.60
1	A	877	PRO	N-CA-CB	-5.27	98.61	102.35

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	2318	0	2392	34	0
2	A	4	0	6	0	0
3	A	12	0	13	0	0
4	A	49	0	0	1	0
5	A	387	0	0	13	0
All	All	2770	0	2411	35	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 7.

All (35) 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:816[B]:ASN:HD22	1:A:1017:LEU:HD22	1.02	1.06
1:A:816[B]:ASN:HD22	1:A:1017:LEU:CD2	1.74	0.99
1:A:816[B]:ASN:ND2	1:A:1017:LEU:HD22	1.86	0.89
1:A:986:ARG:CZ	5:A:1206:HOH:O	2.22	0.87
1:A:730:LEU:HD11	1:A:739:LYS:HB3	1.63	0.80
1:A:713:LYS:HE3	1:A:715:ILE:HD11	1.70	0.72
1:A:974:ASP:HB2	1:A:1021:GLN:HE21	1.54	0.70
1:A:952:MET:HE3	1:A:957[B]:SER:OG	1.93	0.69
1:A:785[A]:THR:HG21	5:A:1263:HOH:O	1.93	0.68
1:A:941:ILE:O	1:A:945[B]:MET:HG2	1.95	0.67
1:A:762[A]:GLU:OE1	1:A:858:ARG:NE	2.31	0.64
1:A:730:LEU:HD11	1:A:739:LYS:CB	2.30	0.61
1:A:949:LYS:HE2	5:A:1201:HOH:O	2.01	0.59
1:A:889:ARG:NH2	5:A:1205:HOH:O	2.36	0.59
1:A:949:LYS:CE	5:A:1201:HOH:O	2.51	0.59
1:A:816[B]:ASN:ND2	1:A:1017:LEU:CD2	2.57	0.58
1:A:986:ARG:NE	5:A:1206:HOH:O	2.37	0.56
1:A:745:LYS:CE	5:A:1207:HOH:O	2.55	0.55
1:A:762[A]:GLU:OE1	1:A:858:ARG:NH1	2.40	0.54
1:A:852:LYS:NZ	5:A:1209:HOH:O	2.40	0.54
1:A:762[A]:GLU:CD	1:A:858:ARG:HE	2.16	0.53
4:A:1103:KXY:S38	4:A:1103:KXY:O35	2.70	0.49
1:A:730:LEU:HD13	1:A:731:TRP:N	2.28	0.48
1:A:974:ASP:HB2	1:A:1021:GLN:NE2	2.25	0.48
1:A:946:ILE:CD1	1:A:967:GLU:HG2	2.44	0.47
1:A:985:GLU:OE2	1:A:985:GLU:HA	2.15	0.47
1:A:945[B]:MET:HG3	5:A:1348:HOH:O	2.15	0.47

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:785[A]:THR:HG23	5:A:1273:HOH:O	2.15	0.47
1:A:960:LYS:HE2	5:A:1462:HOH:O	2.16	0.45
1:A:945[A]:MET:HB3	1:A:945[A]:MET:HE3	1.67	0.45
1:A:945[B]:MET:HE2	1:A:945[B]:MET:HB3	1.79	0.45
1:A:882:ALA:HA	1:A:898:TRP:CD2	2.51	0.45
1:A:806:LYS:HE3	5:A:1283:HOH:O	2.18	0.43
1:A:762[A]:GLU:OE1	1:A:858:ARG:CZ	2.68	0.41
1:A:960:LYS:CE	5:A:1462:HOH:O	2.68	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	282/326 (86%)	277 (98%)	5 (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	260/287 (91%)	257 (99%)	3 (1%)	63 25

All (3) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	730	LEU
1	A	734	GLU
1	A	977	ARG

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (4) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	756	ASN
1	A	787	GLN
1	A	849	GLN
1	A	1021	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 oligosaccharides in this entry.

## 5.6 Ligand geometry [i](#)

3 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	KXY	A	1103	-	51,56,56	1.60	11 (21%)	58,83,83	1.58	11 (18%)
3	MES	A	1102	-	12,12,12	1.15	1 (8%)	15,16,16	1.18	1 (6%)
2	EDO	A	1101	-	3,3,3	0.38	0	2,2,2	0.44	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	KXY	A	1103	-	-	4/27/57/57	0/8/8/8
3	MES	A	1102	-	-	0/6/14/14	0/1/1/1
2	EDO	A	1101	-	-	0/1/1/1	-

All (12) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
4	A	1103	KXY	C2-C1	-4.66	1.49	1.55
4	A	1103	KXY	C17-C16	-3.54	1.37	1.43
4	A	1103	KXY	C7-N8	-3.22	1.41	1.48
4	A	1103	KXY	C18-C17	-3.20	1.38	1.41
4	A	1103	KXY	C28-C27	3.03	1.43	1.38
4	A	1103	KXY	C4-C3	-2.82	1.33	1.37
4	A	1103	KXY	C9-N8	-2.79	1.34	1.37
3	A	1102	MES	C8-S	2.43	1.81	1.77
4	A	1103	KXY	C12-C11	2.30	1.55	1.50
4	A	1103	KXY	C12-C7	2.19	1.53	1.50
4	A	1103	KXY	C11-C7	2.08	1.53	1.50
4	A	1103	KXY	C5-C4	2.01	1.54	1.50

All (12) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
4	A	1103	KXY	C30-C29-C28	4.03	124.22	118.23
3	A	1102	MES	O2S-S-C8	-3.49	101.45	106.73
4	A	1103	KXY	C46-N47-C42	3.37	116.10	108.84
4	A	1103	KXY	C29-C32-N47	-3.20	106.60	113.15
4	A	1103	KXY	C33-C17-C18	3.19	124.41	120.60
4	A	1103	KXY	C31-C26-C27	2.69	123.60	118.96
4	A	1103	KXY	C19-C20-C15	-2.65	115.53	118.36
4	A	1103	KXY	C31-C30-C29	-2.50	117.71	121.00
4	A	1103	KXY	C27-C28-C29	-2.43	117.80	121.00
4	A	1103	KXY	C27-C26-C25	-2.26	116.78	120.78
4	A	1103	KXY	C32-C29-C28	-2.19	116.71	120.75
4	A	1103	KXY	C7-N8-C9	2.15	139.23	129.99

There are no chirality outliers.

All (4) torsion outliers are listed below:

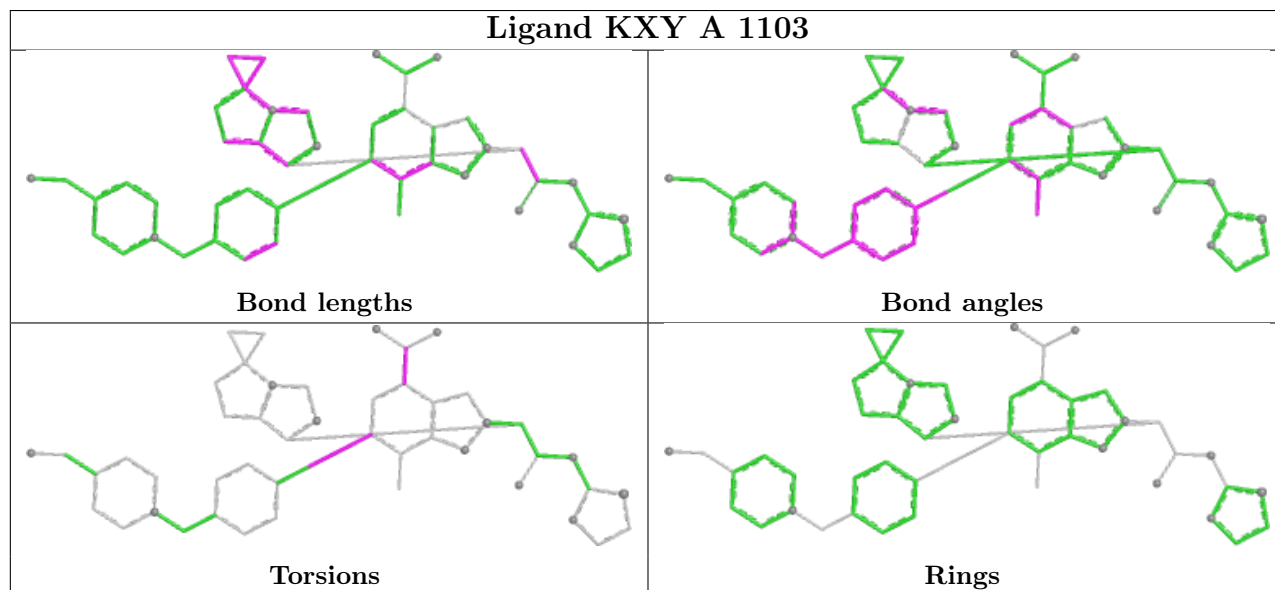
Mol	Chain	Res	Type	Atoms
4	A	1103	KXY	C17-C18-C24-C25
4	A	1103	KXY	C19-C18-C24-C25
4	A	1103	KXY	C19-C20-C21-F22
4	A	1103	KXY	C18-C24-C25-C26

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
4	A	1103	KXY	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

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<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	281/326 (86%)	0.56	29 (10%) <b>12</b> <b>17</b>	6, 12, 32, 64	9 (3%)

All (29) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	A	1018	ILE	7.3
1	A	859	ALA	7.0
1	A	869	TYR	6.6
1	A	1019	PRO	5.5
1	A	1017	LEU	5.1
1	A	723	PHE	4.4
1	A	865	GLU	4.2
1	A	870	HIS	3.9
1	A	1021	GLN	3.7
1	A	889	ARG	3.2
1	A	722	ALA	3.2
1	A	867	LYS	3.1
1	A	876	VAL	3.1
1	A	866	GLU	3.0
1	A	724	GLY	3.0
1	A	701	GLN	2.8
1	A	977	ARG	2.7
1	A	1020	GLN	2.7
1	A	748	ARG	2.5
1	A	730	LEU	2.5
1	A	986	ARG	2.5
1	A	749	GLU	2.4
1	A	720	SER	2.4
1	A	858	ARG	2.3
1	A	702	ALA	2.3
1	A	703	LEU	2.3
1	A	985	GLU	2.2

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Mol	Chain	Res	Type	RSRZ
1	A	918	ILE	2.2
1	A	890	ILE	2.1

## 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](#)

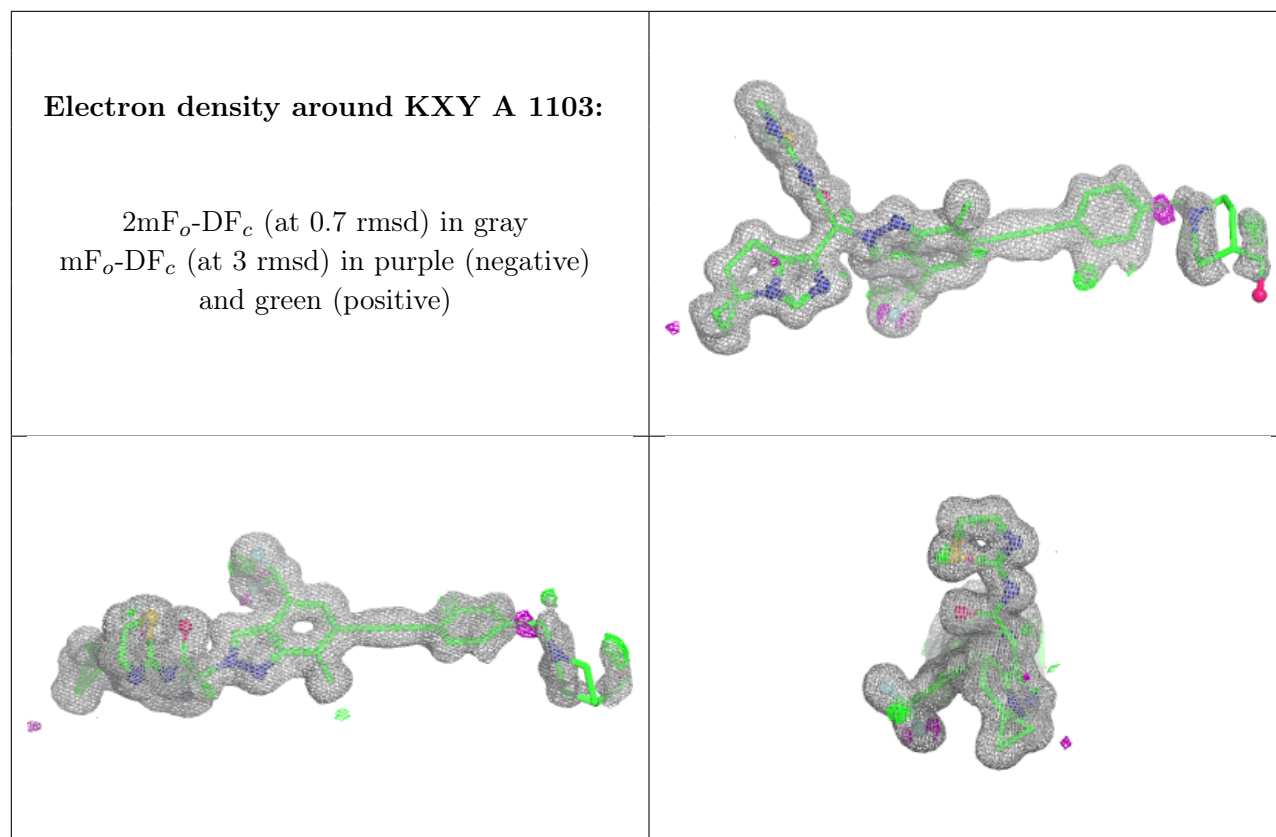
There are no oligosaccharides in this entry.

## 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, 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	B-factors( $\text{\AA}^2$ )	Q<0.9
3	MES	A	1102	12/12	0.88	0.16	17,26,36,40	0
2	EDO	A	1101	4/4	0.92	0.09	18,19,19,24	0
4	KXY	A	1103	49/49	0.98	0.08	8,10,45,59	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.