



wwPDB X-ray Structure Validation Summary Report ⓘ

Mar 7, 2026 – 03:20 AM UTC

PDB ID : 8TDU / pdb_00008tdu
Title : STX-478, a Mutant-Selective, Allosteric Inhibitor bound to PI3Kalpha
Authors : Hilbert, B.J.; Brooijmans, N.; Buckbinder, L.; St.Jean Jr., D.J.
Deposited on : 2023-07-05
Resolution : 3.11 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 ⓘ symbol.

The types of validation reports are described at

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

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

MolProbity	:	4-5-2 with Phenix2.0
Mogul	:	2022.3.0, CSD as543be (2022)
Xtriage (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

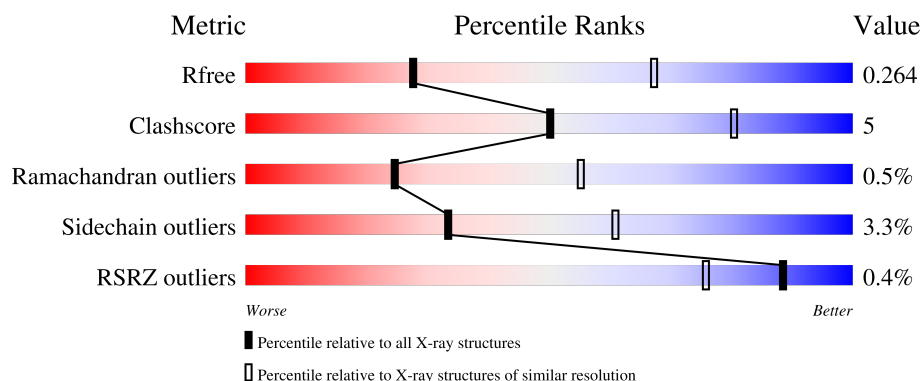
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION

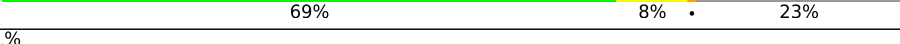
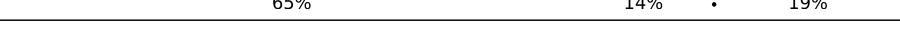
The reported resolution of this entry is 3.11 Å.

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	1816 (3.14-3.10)
Clashscore	190562	1906 (3.14-3.10)
Ramachandran outliers	187476	1802 (3.14-3.10)
Sidechain outliers	187428	1802 (3.14-3.10)
RSRZ outliers	180081	1816 (3.14-3.10)

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 ≥ 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	1068	 81% 14% . .
1	C	1068	 79% 14% 6%
2	B	293	 69% 8% . 23%
2	D	293	 65% 14% . 19%

2 Entry composition

There are 5 unique types of molecules in this entry. The entry contains 20704 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
1	A	1021	Total	C	N	O	S	0	1	0
			8367	5359	1428	1511	69			
1	C	1000	Total	C	N	O	S	0	1	0
			8212	5260	1397	1487	68			

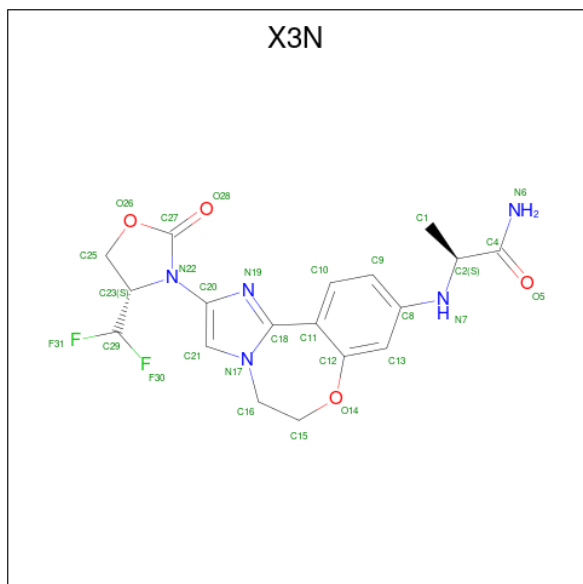
- Molecule 2 is a protein called Phosphatidylinositol 3-kinase regulatory subunit alpha.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
2	D	237	Total	C	N	O	S	0	0	0
			2018	1265	358	389	6			
2	B	227	Total	C	N	O	S	0	0	0
			1948	1221	344	378	5			

There are 14 discrepancies between the modelled and reference sequences:

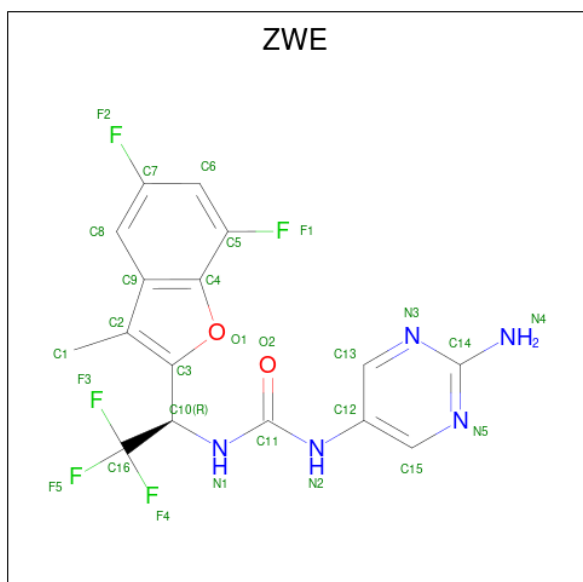
Chain	Residue	Modelled	Actual	Comment	Reference
D	301	MET	-	initiating methionine	UNP P27986
D	302	HIS	-	expression tag	UNP P27986
D	303	HIS	-	expression tag	UNP P27986
D	304	HIS	-	expression tag	UNP P27986
D	305	HIS	-	expression tag	UNP P27986
D	306	HIS	-	expression tag	UNP P27986
D	307	HIS	-	expression tag	UNP P27986
B	301	MET	-	initiating methionine	UNP P27986
B	302	HIS	-	expression tag	UNP P27986
B	303	HIS	-	expression tag	UNP P27986
B	304	HIS	-	expression tag	UNP P27986
B	305	HIS	-	expression tag	UNP P27986
B	306	HIS	-	expression tag	UNP P27986
B	307	HIS	-	expression tag	UNP P27986

- Molecule 3 is N 2 -{(4S,11aP)-2-[(4S)-4-(difluoromethyl)-2-oxo-1,3-oxazolidin-3-yl]-5,6-dihydroimidazo[1,2-d][1,4]benzoxazepin-9-yl}-L-alaninamide (CCD ID: X3N) (formula: C₁₈H₁₉F₂N₅O₄) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
3	A	1	Total	C	F	N	O	0	0
			29	18	2	5	4		
3	C	1	Total	C	F	N	O	0	0
			29	18	2	5	4		

- Molecule 4 is N-(2-aminopyrimidin-5-yl)-N'-[(1R)-1-(5,7-difluoro-3-methyl-1-benzofuran-2-yl)-2,2,2-trifluoroethyl]urea (CCD ID: ZWE) (formula: C₁₆H₁₂F₅N₅O₂) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
4	A	1	Total	C	F	N	O	0	0
			28	16	5	5	2		
4	C	1	Total	C	F	N	O	0	0
			28	16	5	5	2		

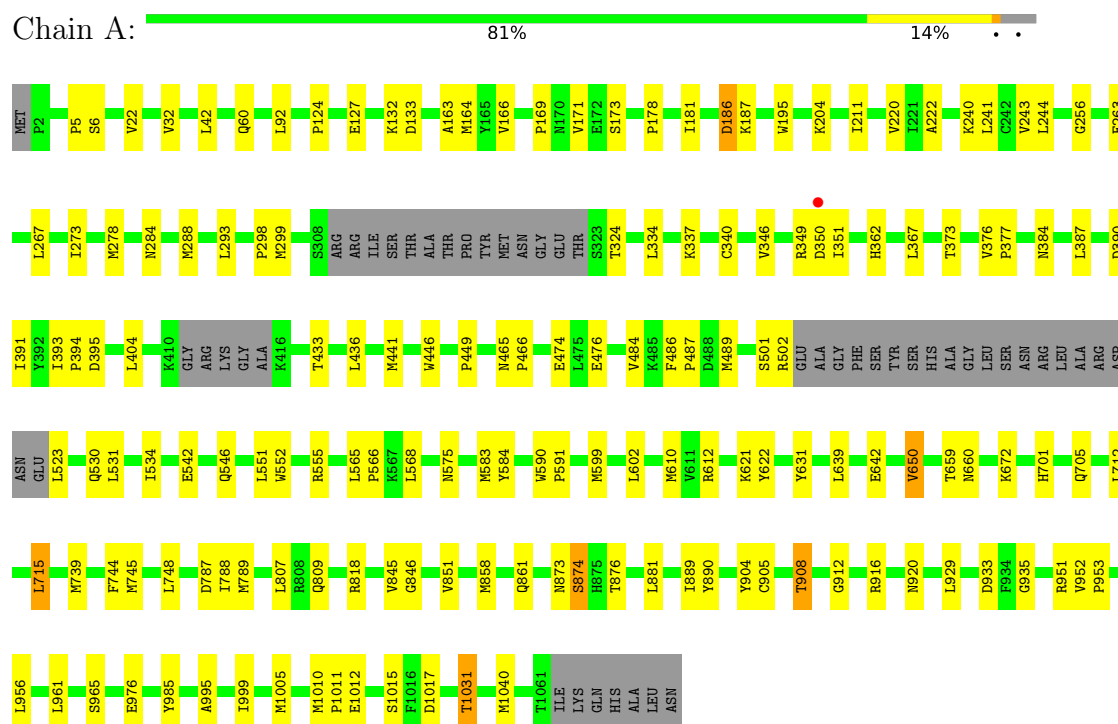
- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	A	35	Total	O	0	0
			35	35		
5	C	9	Total	O	0	0
			9	9		
5	B	1	Total	O	0	0
			1	1		

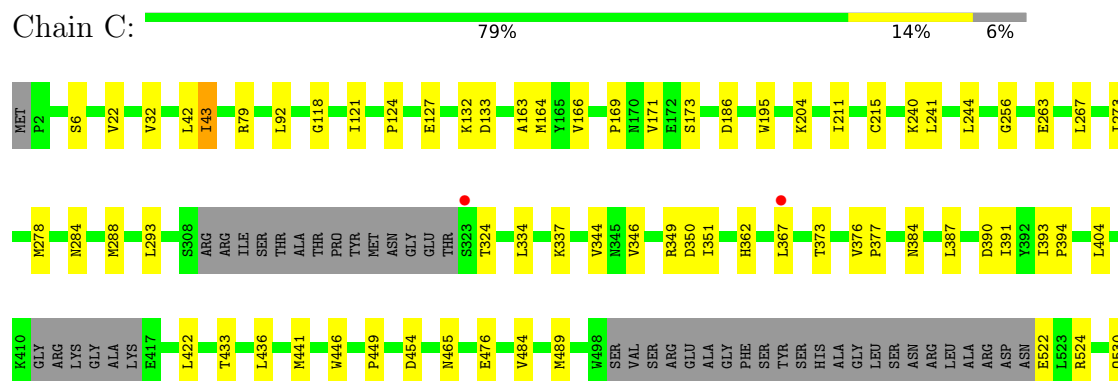
3 Residue-property plots

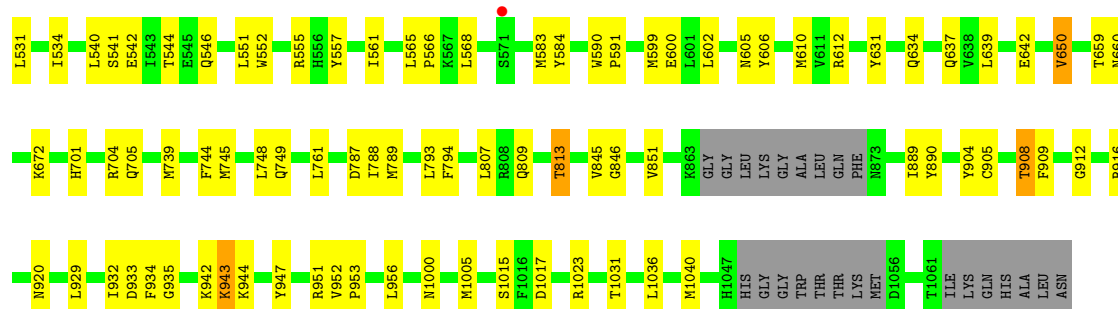
These plots are drawn for all protein, RNA, DNA and oligosaccharide chains in the entry. The first graphic for a chain summarises the proportions of the various outlier classes displayed in the second graphic. The second graphic shows the sequence view annotated by issues in geometry and electron density. 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: Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform

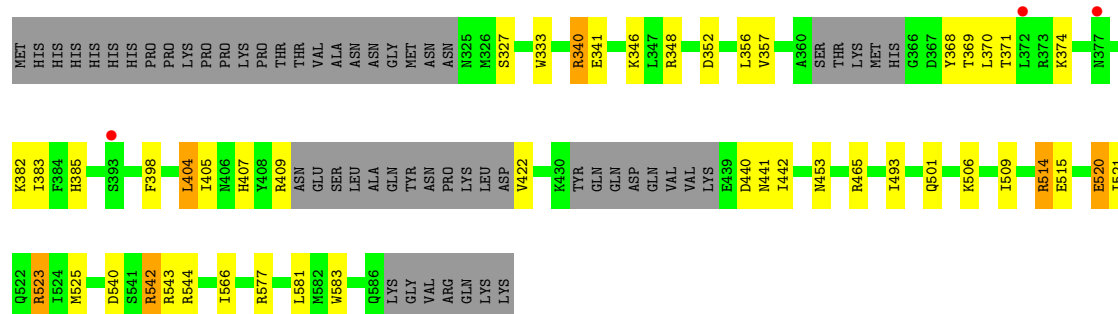


- Molecule 1: Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform

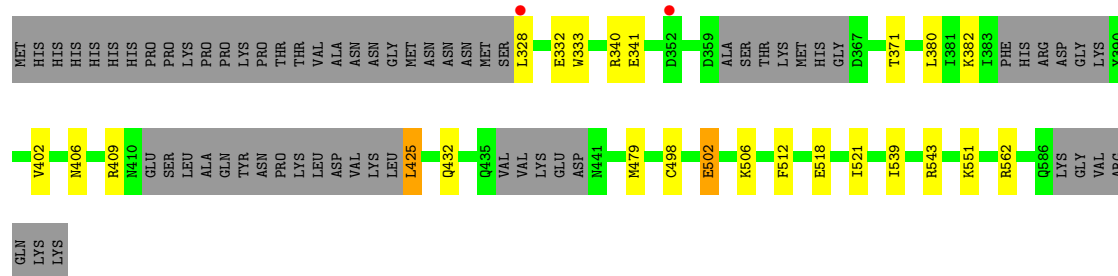




• Molecule 2: Phosphatidylinositol 3-kinase regulatory subunit alpha



• Molecule 2: Phosphatidylinositol 3-kinase regulatory subunit alpha



4 Data and refinement statistics

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants a, b, c, α , β , γ	86.34Å 124.72Å 165.84Å 90.00° 92.80° 90.00°	Depositor
Resolution (Å)	48.77 – 3.11 48.77 – 3.11	Depositor EDS
% Data completeness (in resolution range)	100.0 (48.77-3.11) 99.9 (48.77-3.11)	Depositor EDS
R_{merge}	0.09	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	3.23 (at 3.12Å)	Xtriage
Refinement program	REFMAC 5.8.0405	Depositor
R, R_{free}	0.208 , 0.267 0.210 , 0.264	Depositor DCC
R_{free} test set	3067 reflections (4.85%)	wwPDB-VP
Wilson B-factor (Å ²)	90.0	Xtriage
Anisotropy	0.250	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.29 , 47.3	EDS
L-test for twinning ²	$\langle L \rangle = 0.50$, $\langle L^2 \rangle = 0.34$	Xtriage
Estimated twinning fraction	0.011 for h,-k,-l	Xtriage
F_o, F_c correlation	0.95	EDS
Total number of atoms	20704	wwPDB-VP
Average B, all atoms (Å ²)	107.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.90% 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: ZWE, X3N

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	0.44	0/8559	0.87	0/11567
1	C	0.43	0/8398	0.86	0/11350
2	B	0.41	0/1977	0.92	0/2644
2	D	0.41	0/2049	0.89	0/2739
All	All	0.43	0/20983	0.87	0/28300

Chiral center outliers are detected by calculating the chiral volume of a chiral center and verifying if the center is modelled as a planar moiety or with the opposite hand. A planarity outlier is detected by checking planarity of atoms in a peptide group, atoms in a mainchain group or atoms of a sidechain that are expected to be planar.

Mol	Chain	#Chirality outliers	#Planarity outliers
1	A	0	1
2	D	0	1
All	All	0	2

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

All (2) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	A	818	ARG	Sidechain
2	D	340	ARG	Sidechain

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	8367	0	8387	91	0
1	C	8212	0	8221	94	0
2	B	1948	0	1912	13	0
2	D	2018	0	1990	32	0
3	A	29	0	0	0	0
3	C	29	0	0	0	0
4	A	28	0	0	0	0
4	C	28	0	0	0	0
5	A	35	0	0	1	0
5	B	1	0	0	0	0
5	C	9	0	0	0	0
All	All	20704	0	20510	216	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 5.

The worst 5 of 216 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:C:809:GLN:O	1:C:813:THR:HG22	1.67	0.95
1:A:873:ASN:O	1:A:874:SER:HB3	1.85	0.76
1:A:602:LEU:O	1:A:612:ARG:NH2	2.22	0.73
1:C:164:MET:HE1	1:C:263:GLU:HB2	1.71	0.72
1:A:164:MET:HE1	1:A:263:GLU:HB2	1.71	0.72

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	1014/1068 (95%)	940 (93%)	69 (7%)	5 (0%)	24	55
1	C	989/1068 (93%)	922 (93%)	62 (6%)	5 (0%)	24	55
2	B	217/293 (74%)	203 (94%)	13 (6%)	1 (0%)	24	55
2	D	229/293 (78%)	213 (93%)	14 (6%)	2 (1%)	14	42
All	All	2449/2722 (90%)	2278 (93%)	158 (6%)	13 (0%)	24	55

5 of 13 Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	449	PRO
1	C	449	PRO
1	C	943	LYS
2	D	442	ILE
2	B	432	GLN

5.3.2 Protein sidechains ⓘ

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	939/974 (96%)	913 (97%)	26 (3%)	38	64
1	C	924/974 (95%)	898 (97%)	26 (3%)	38	64
2	B	213/272 (78%)	203 (95%)	10 (5%)	23	52
2	D	220/272 (81%)	206 (94%)	14 (6%)	16	42
All	All	2296/2492 (92%)	2220 (97%)	76 (3%)	33	61

5 of 76 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
2	D	465	ARG
2	B	502	GLU
2	D	506	LYS

Continued on next page...

Continued from previous page...

Mol	Chain	Res	Type
2	D	583	TRP
2	B	562	ARG

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 55 such sidechains are listed below:

Mol	Chain	Res	Type
1	C	284	ASN
1	C	661	GLN
2	B	586	GLN
2	B	344	ASN
1	C	345	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 oligosaccharides 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	$\# Z > 2$
3	X3N	A	1101	-	30,32,32	1.29	2 (6%)	36,47,47	2.54	10 (27%)

Mol	Type	Chain	Res	Link	Bond lengths			Bond angles		
					Counts	RMSZ	# Z > 2	Counts	RMSZ	# Z > 2
3	X3N	C	1101	-	30,32,32	1.03	1 (3%)	36,47,47	2.80	13 (36%)
4	ZWE	C	1102	-	29,30,30	1.63	7 (24%)	36,45,45	2.37	16 (44%)
4	ZWE	A	1102	-	29,30,30	1.71	8 (27%)	36,45,45	2.26	12 (33%)

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	X3N	A	1101	-	-	1/13/39/39	0/4/4/4
3	X3N	C	1101	-	-	7/13/39/39	0/4/4/4
4	ZWE	C	1102	-	-	2/15/18/18	0/3/3/3
4	ZWE	A	1102	-	-	2/15/18/18	0/3/3/3

The worst 5 of 18 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
4	A	1102	ZWE	O1-C3	-4.68	1.33	1.38
4	C	1102	ZWE	O1-C3	-4.17	1.34	1.38
3	A	1101	X3N	C27-N22	-3.57	1.33	1.39
4	C	1102	ZWE	F3-C16	3.52	1.42	1.33
4	A	1102	ZWE	F4-C16	3.41	1.41	1.33

The worst 5 of 51 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
3	C	1101	X3N	C21-C20-N19	-9.85	106.32	112.77
3	A	1101	X3N	C21-C20-N19	-8.09	107.47	112.77
3	A	1101	X3N	O26-C27-N22	6.64	114.24	108.78
4	A	1102	ZWE	C12-C15-N5	-6.42	118.76	124.07
4	C	1102	ZWE	C12-C13-N3	-5.96	119.14	124.07

There are no chirality outliers.

5 of 12 torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
3	C	1101	X3N	N7-C2-C4-O5
3	C	1101	X3N	N7-C2-C4-N6
3	C	1101	X3N	N22-C23-C29-F30

Continued on next page...

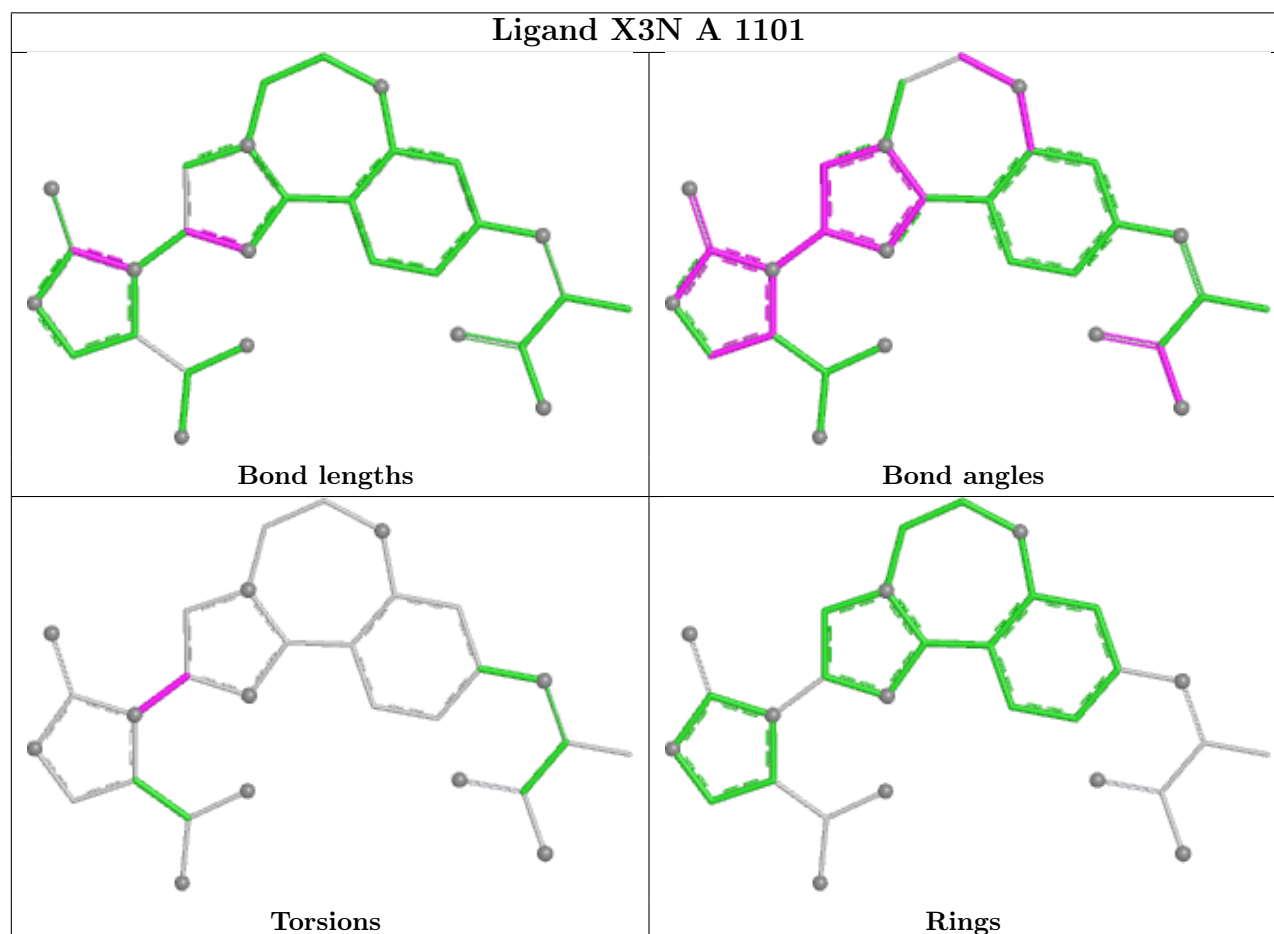
Continued from previous page...

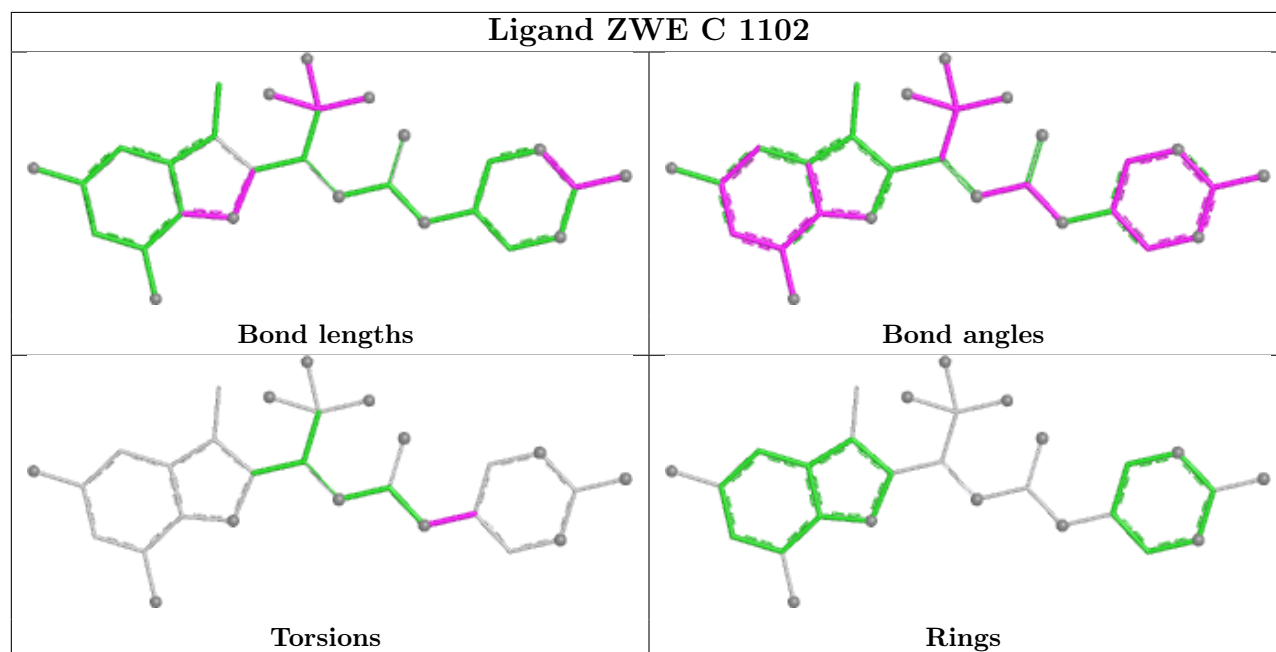
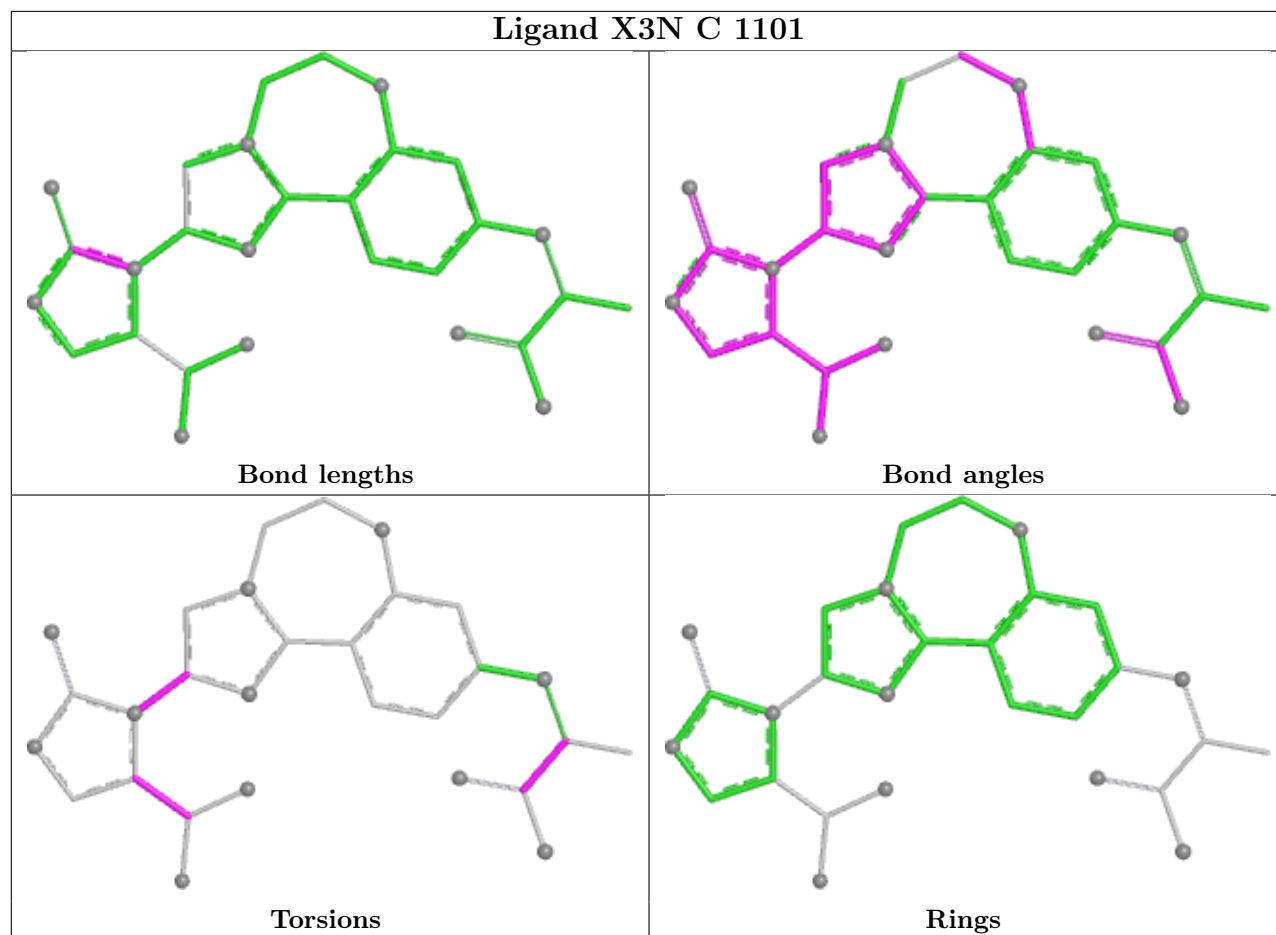
Mol	Chain	Res	Type	Atoms
3	C	1101	X3N	N22-C23-C29-F31
3	C	1101	X3N	C25-C23-C29-F30

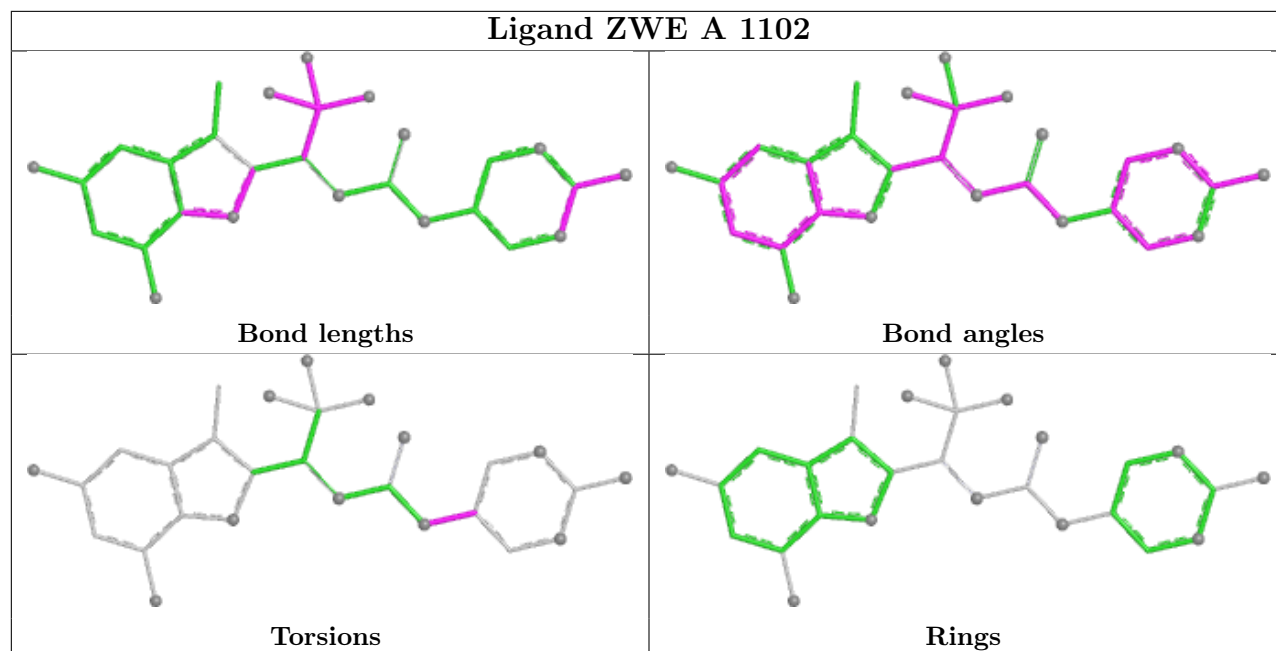
There are no ring outliers.

No monomer is involved in short contacts.

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 [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, 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	1021/1068 (95%)	-0.37	1 (0%) 92 86	45, 82, 139, 193	1 (0%)
1	C	1000/1068 (93%)	-0.16	3 (0%) 90 80	58, 105, 159, 203	1 (0%)
2	B	227/293 (77%)	-0.22	2 (0%) 81 63	65, 125, 175, 214	0
2	D	237/293 (80%)	-0.04	3 (1%) 75 56	96, 166, 212, 239	0
All	All	2485/2722 (91%)	-0.24	9 (0%) 88 76	45, 100, 176, 239	2 (0%)

The worst 5 of 9 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
2	B	352	ASP	3.0
1	C	571	SER	2.9
1	C	367	LEU	2.6
1	C	323	SER	2.5
2	D	377	ASN	2.5

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](#)

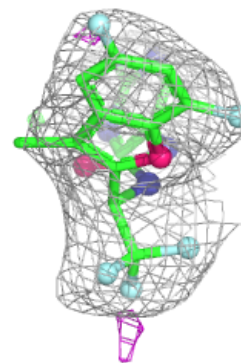
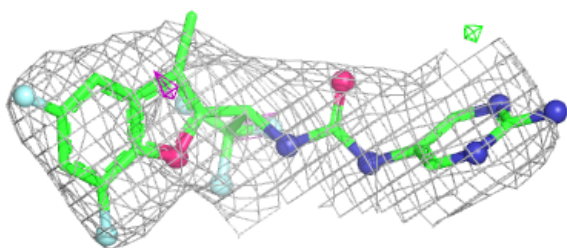
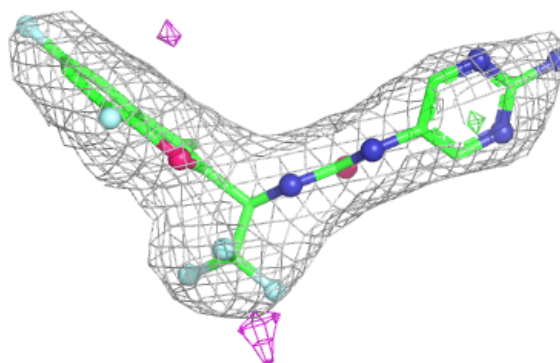
In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled ‘Q< 0.9’ lists the number of atoms with occupancy less than 0.9.

Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors($\text{\AA}^2$)	Q<0.9
4	ZWE	C	1102	28/28	0.93	0.09	79,93,114,118	0
3	X3N	A	1101	29/29	0.96	0.07	50,60,71,78	0
4	ZWE	A	1102	28/28	0.97	0.06	51,61,75,84	0
3	X3N	C	1101	29/29	0.97	0.07	78,84,88,101	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.

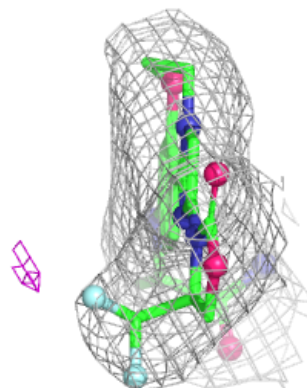
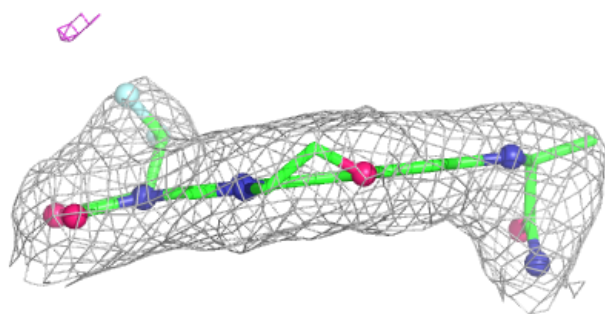
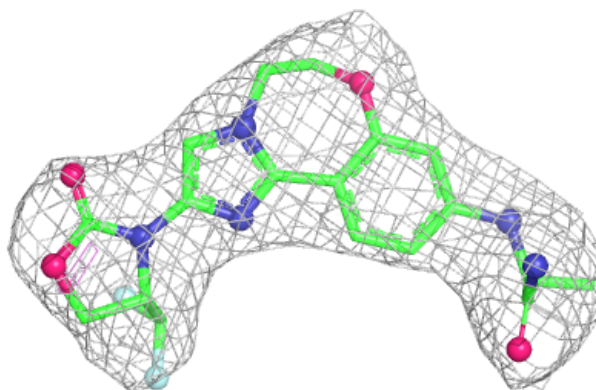
Electron density around ZWE C 1102:

2mF_o-DF_c (at 0.7 rmsd) in gray
mF_o-DF_c (at 3 rmsd) in purple (negative)
and green (positive)

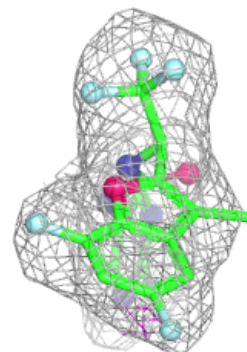
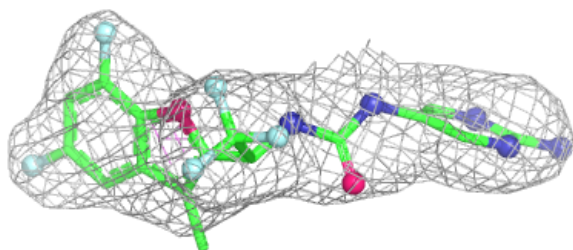
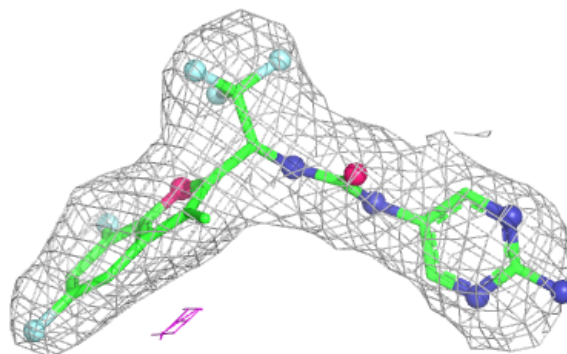


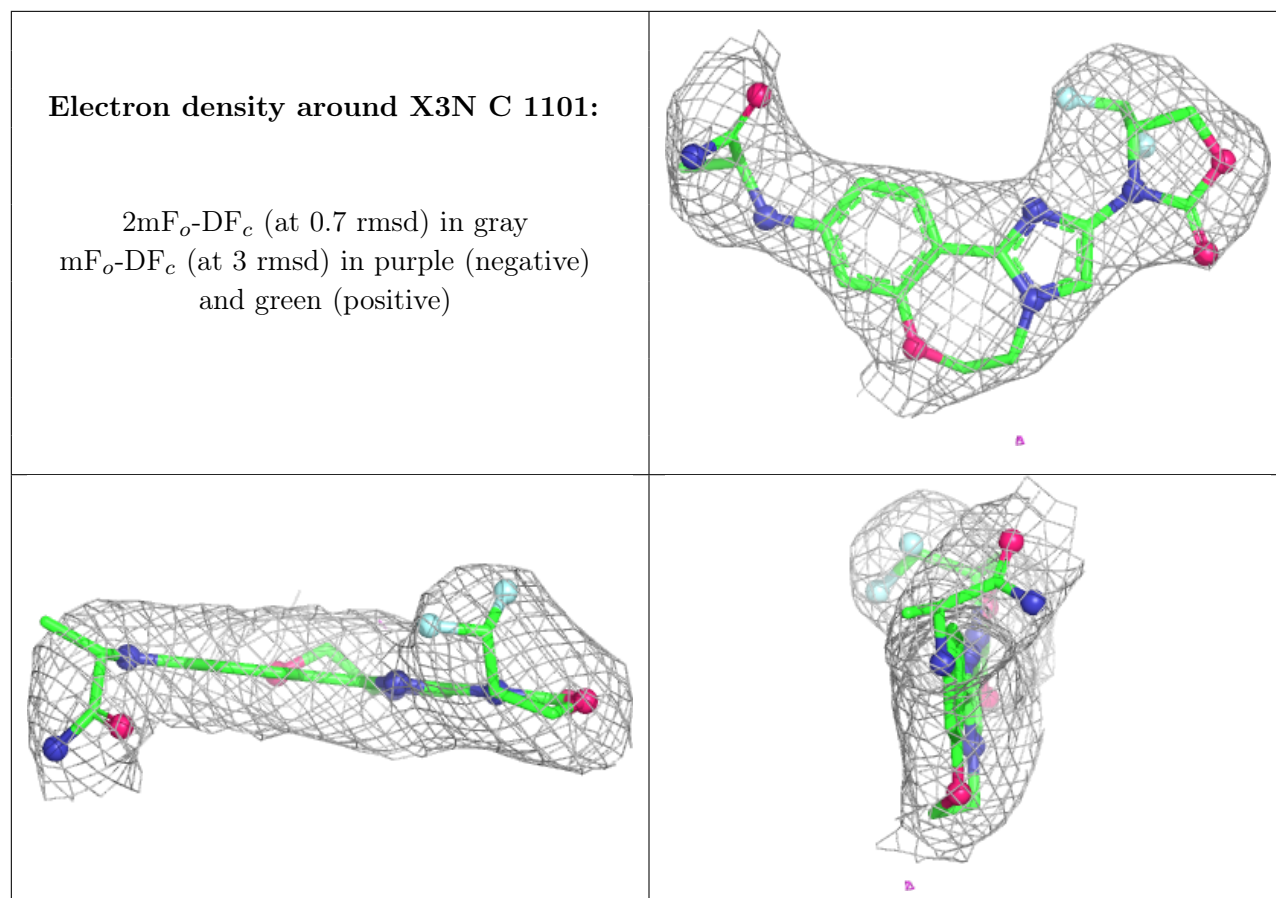
Electron density around X3N A 1101:

$2mF_o-DF_c$ (at 0.7 rmsd) in gray
 mF_o-DF_c (at 3 rmsd) in purple (negative)
and green (positive)

**Electron density around ZWE A 1102:**

$2mF_o-DF_c$ (at 0.7 rmsd) in gray
 mF_o-DF_c (at 3 rmsd) in purple (negative)
and green (positive)





6.5 Other polymers ⓘ

There are no such residues in this entry.