



wwPDB X-ray Structure Validation Summary Report ⓘ

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PDB ID : 6TMZ
Title : Rapid optimisation of fragments and hits to lead compounds from screening of crude reaction mixtures
Authors : Baker, L.M.; Aimon, A.; Murray, J.B.; Surgenor, A.E.; Matassova, N.; Roughley, S.D.; von Delft, F.; Hubbard, R.E.
Deposited on : 2019-12-05
Resolution : 2.71 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	:	4.02b-467
Mogul	:	2022.3.0, CSD as543be (2022)
Xtriage (Phenix)	:	1.20.1
EDS	:	2.37.1
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)	:	2.37.1

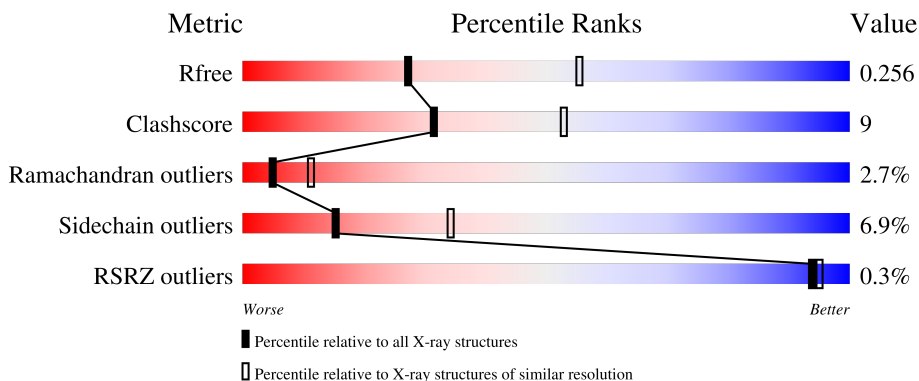
1 Overall quality at a glance

The following experimental techniques were used to determine the structure:

X-RAY DIFFRACTION


The reported resolution of this entry is 2.71 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	3359 (2.74-2.70)
Clashscore	141614	3686 (2.74-2.70)
Ramachandran outliers	138981	3622 (2.74-2.70)
Sidechain outliers	138945	3623 (2.74-2.70)
RSRZ outliers	127900	3276 (2.74-2.70)

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	AAA	394	

2 Entry composition [i](#)

There are 5 unique types of molecules in this entry. The entry contains 5548 atoms, of which 2751 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.

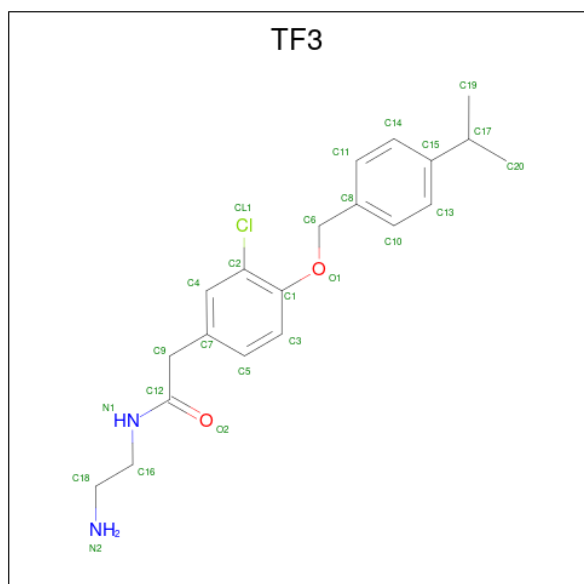
- Molecule 1 is a protein called [Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial.

Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
1	AAA	337	Total	C	H	N	O	S	141	1	0
			5414	1741	2704	445	507	17			

There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
AAA	6	GLY	ALA	conflict	UNP Q15119
AAA	7	SER	GLY	conflict	UNP Q15119

- Molecule 2 is N-(2-AMINOETHYL)-2-{3-CHLORO-4-[(4-ISOPROPYLBENZYL)OXY]PHENYL} ACETAMIDE (three-letter code: TF3) (formula: C₂₀H₂₅ClN₂O₂).

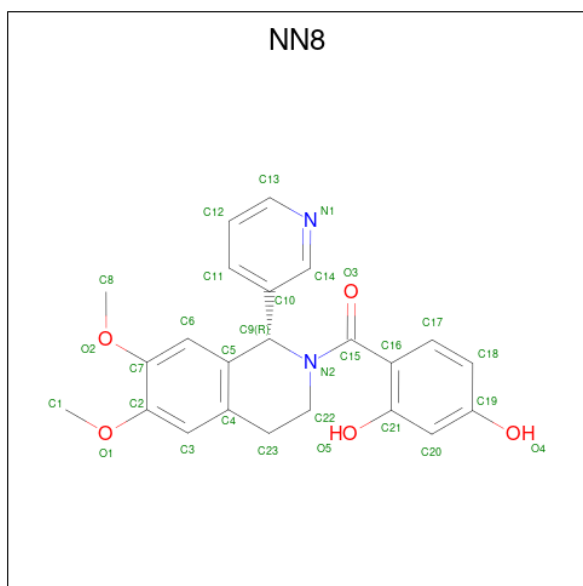


Mol	Chain	Residues	Atoms						ZeroOcc	AltConf
2	AAA	1	Total	C	Cl	H	N	O	0	0
			50	20	1	25	2	2		

- Molecule 3 is MAGNESIUM ION (three-letter code: MG) (formula: Mg).

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	AAA	1	Total	Mg	0	0
			1	1		

- Molecule 4 is [2,4-bis(oxidanyl)phenyl]-[(1 {R})-6,7-dimethoxy-1-pyridin-3-yl-3,4-dihydro-1 {H}-isoquinolin-2-yl]methanone (three-letter code: NN8) (formula: C₂₃H₂₂N₂O₅) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
4	AAA	1	Total	C	H	N	O	2	0
			52	23	22	2	5		

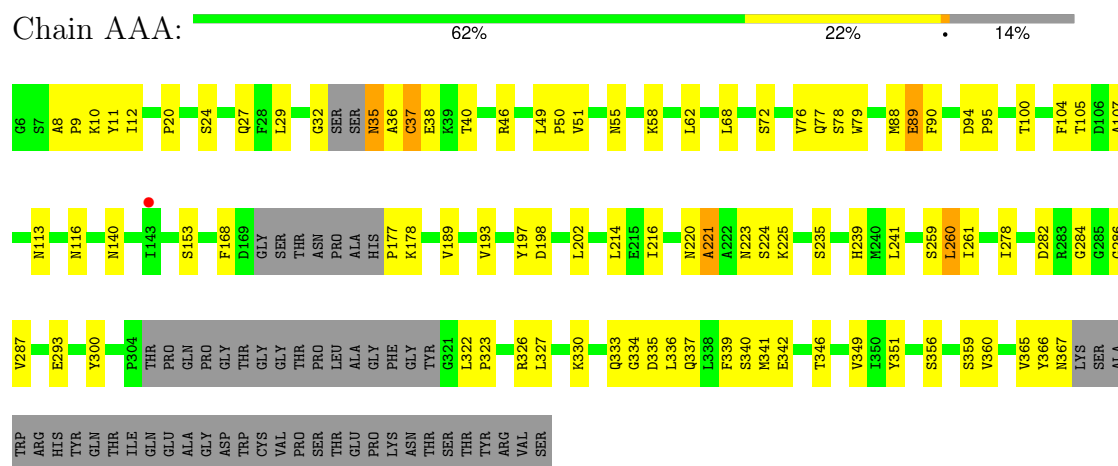
- Molecule 5 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
5	AAA	31	Total	O	0	0
			31	31		

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: [Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial



4 Data and refinement statistics

Property	Value	Source
Space group	P 64	Depositor
Cell constants a, b, c, α , β , γ	110.38Å 110.38Å 83.68Å 90.00° 90.00° 120.00°	Depositor
Resolution (Å)	55.19 – 2.71 95.59 – 2.66	Depositor EDS
% Data completeness (in resolution range)	63.7 (55.19-2.71) 67.4 (95.59-2.66)	Depositor EDS
R_{merge}	0.10	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	0.00 (at 2.65Å)	Xtriage
Refinement program	REFMAC 5.8.0258	Depositor
R, R_{free}	0.194 , 0.262 0.199 , 0.256	Depositor DCC
R_{free} test set	862 reflections (5.14%)	wwPDB-VP
Wilson B-factor (Å ²)	69.0	Xtriage
Anisotropy	0.031	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.35 , 34.4	EDS
L-test for twinning ²	$\langle L \rangle = 0.49$, $\langle L^2 \rangle = 0.32$	Xtriage
Estimated twinning fraction	0.051 for h,-h-k,-l	Xtriage
F_o, F_c correlation	0.93	EDS
Total number of atoms	5548	wwPDB-VP
Average B, all atoms (Å ²)	71.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 3.64% 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

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: NN8, TF3, MG

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	AAA	0.69	0/2775	0.90	0/3756

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	AAA	2710	2704	2685	48	1
2	AAA	25	25	25	0	0
3	AAA	1	0	0	0	0
4	AAA	30	22	0	6	0
5	AAA	31	0	0	2	0
All	All	2797	2751	2710	49	1

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 9.

The worst 5 of 49 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:AAA:35:ASN:HD22	1:AAA:37:CYS:HA	1.39	0.86
1:AAA:20:PRO:HD2	1:AAA:365:VAL:HG23	1.68	0.75
1:AAA:24:SER:OG	1:AAA:27:GLN:HG3	1.87	0.74
1:AAA:287:VAL:HG22	4:AAA:403:NN8:C5	2.24	0.67
1:AAA:58:LYS:HG2	1:AAA:366:TYR:CE1	2.31	0.66

All (1) symmetry-related close contacts are listed below. The label for Atom-2 includes the symmetry operator and encoded unit-cell translations to be applied.

Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:AAA:10:LYS:HZ2	1:AAA:260:LEU:O[2_544]	1.46	0.14

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	AAA	330/394 (84%)	282 (86%)	39 (12%)	9 (3%)	5 11

5 of 9 Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	AAA	95	PRO
1	AAA	37	CYS
1	AAA	89	GLU
1	AAA	221	ALA
1	AAA	224	SER

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	AAA	306/353 (87%)	285 (93%)	21 (7%)	15	34

5 of 21 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	AAA	260	LEU
1	AAA	326	ARG
1	AAA	367	ASN
1	AAA	339	PHE
1	AAA	293	GLU

Sometimes 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 monosaccharides in this entry.

5.6 Ligand geometry [i](#)

Of 3 ligands modelled in this entry, 1 is monoatomic - leaving 2 for Mogul analysis.

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	NN8	AAA	403	-	33,33,33	0.39	0	44,47,47	0.43	0
2	TF3	AAA	401	-	26,26,26	0.38	0	33,34,34	0.94	2 (6%)

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	NN8	AAA	403	-	-	2/16/29/29	0/4/4/4
2	TF3	AAA	401	-	-	6/17/17/17	0/2/2/2

There are no bond length outliers.

All (2) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	AAA	401	TF3	C1-C2-CL1	-2.75	116.30	119.44
2	AAA	401	TF3	O1-C1-C3	2.22	128.79	123.95

There are no chirality outliers.

5 of 8 torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	AAA	401	TF3	N1-C16-C18-N2
2	AAA	401	TF3	C4-C7-C9-C12
2	AAA	401	TF3	C5-C7-C9-C12
2	AAA	401	TF3	C2-C1-O1-C6
4	AAA	403	NN8	N2-C15-C16-C21

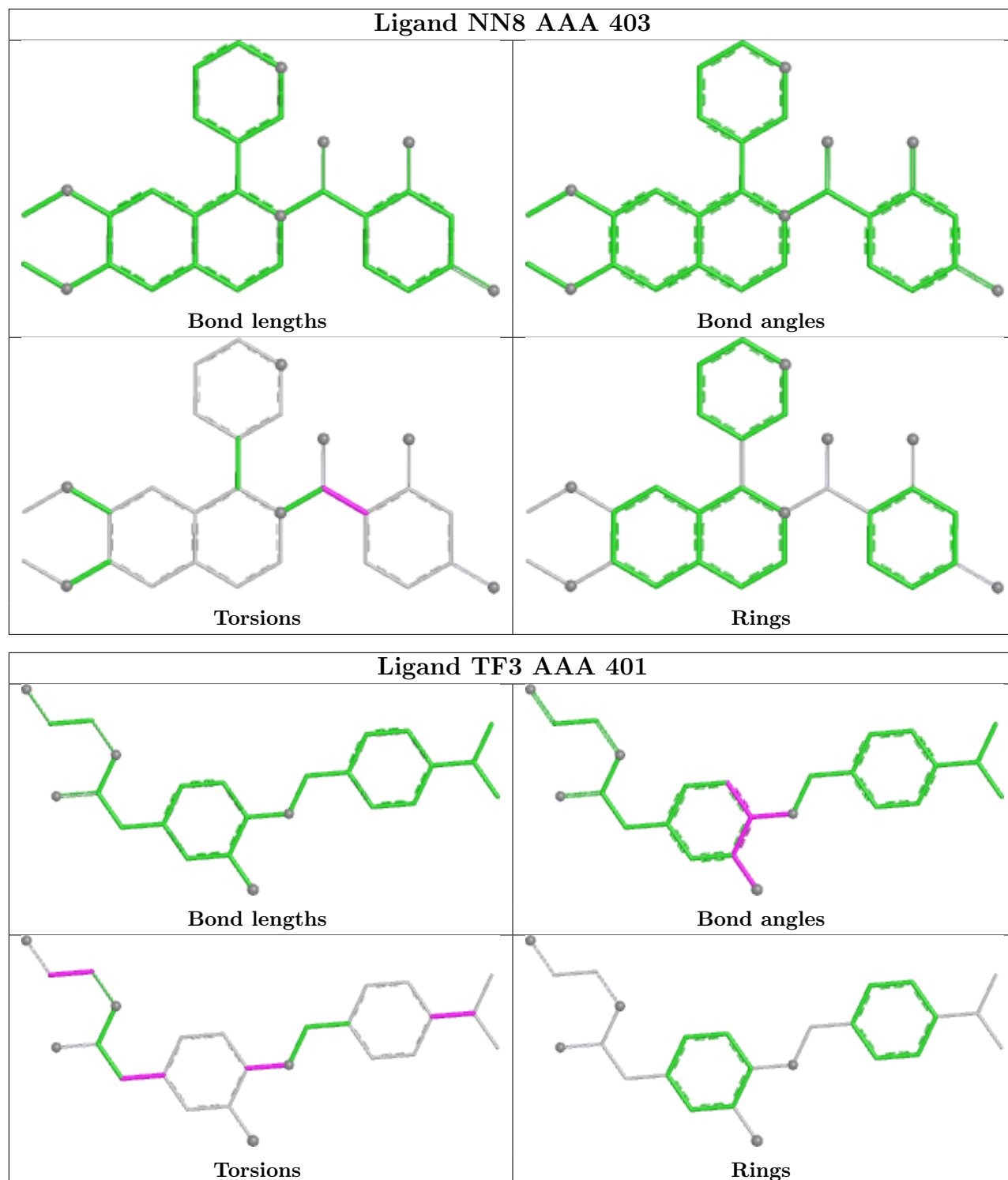
There are no ring outliers.

1 monomer is involved in 6 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
4	AAA	403	NN8	6	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 [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	AAA	337/394 (85%)	-0.09	1 (0%) 94 95	30, 68, 107, 129	1 (0%)

All (1) RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	AAA	143	ILE	2.2

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 monosaccharides 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.

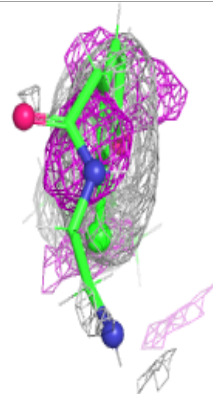
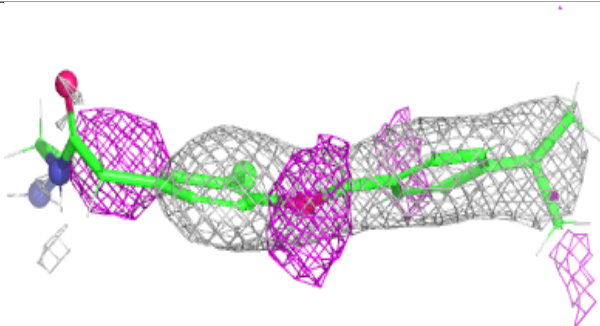
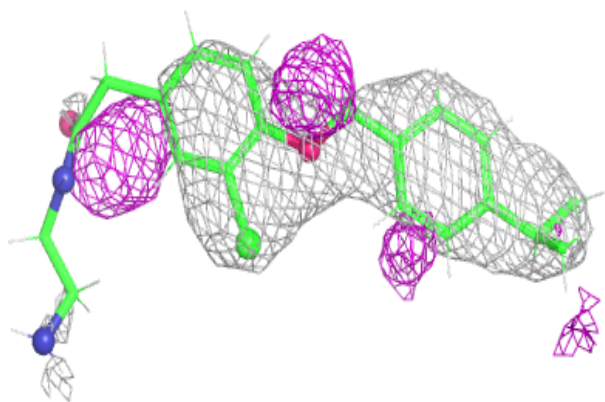
Mol	Type	Chain	Res	Atoms	RSCC	RSR	B-factors(Å ²)	Q<0.9
2	TF3	AAA	401	25/25	0.89	0.42	55,75,122,126	0
4	NN8	AAA	403	30/30	0.96	0.17	31,37,55,58	2
3	MG	AAA	402	1/1	0.98	0.22	33,33,33,33	0

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.

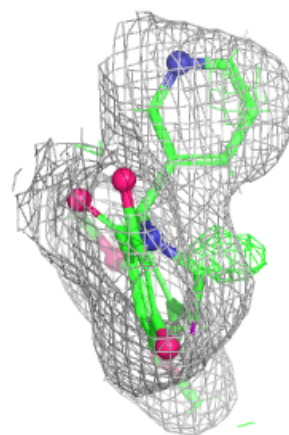
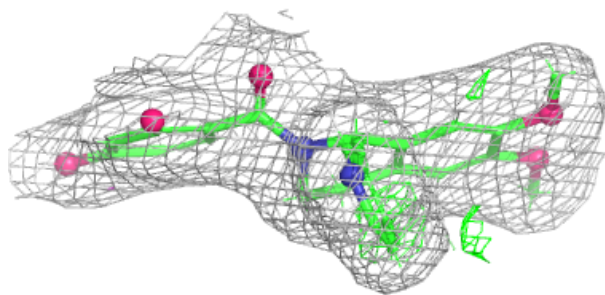
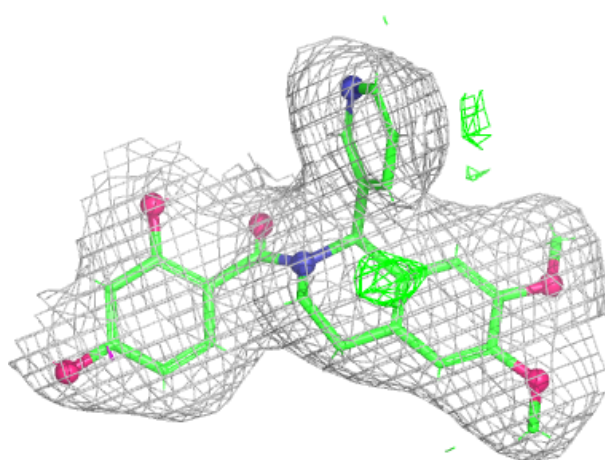
Electron density around TF3 AAA 401:

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



Electron density around NN8 AAA 403:

$2mF_o-DF_c$ (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.