wwPDB X-ray Structure Validation Summary Report (i)

Feb 11, 2024 – 12:11 PM EST

PDB ID	:	3CS9
Title	:	Human ABL kinase in complex with nilotinib
Authors	:	Cowan-Jacob, S.W.; Fendrich, G.; Manley, P.; Liebetanz, J.; Fabbro, D.
Deposited on	:	2008-04-09
Resolution	:	2.21 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 types of validation reports are described at
http://www.wwpdb.org/validation/2017/FAQs#types.

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

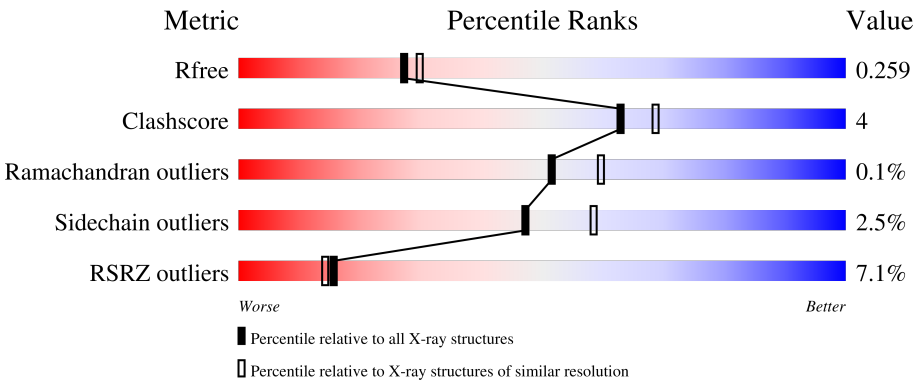
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	1.13
EDS	:	2.36
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Refmac	:	5.8.0158
CCP4	:	7.0.044 (Gargrove)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.36

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 2.21 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	5912 (2.24-2.20)
Clashscore	141614	6646 (2.24-2.20)
Ramachandran outliers	138981	6543 (2.24-2.20)
Sidechain outliers	138945	6544 (2.24-2.20)
RSRZ outliers	127900	5797 (2.24-2.20)

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	277	2%, 85%, 10%, 5%
1	B	277	3%, 78%, 10%, •, 11%
1	C	277	3%, 73%, 14%, •, 12%
1	D	277	18%, 81%, 14%, • 5%

2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 8696 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.

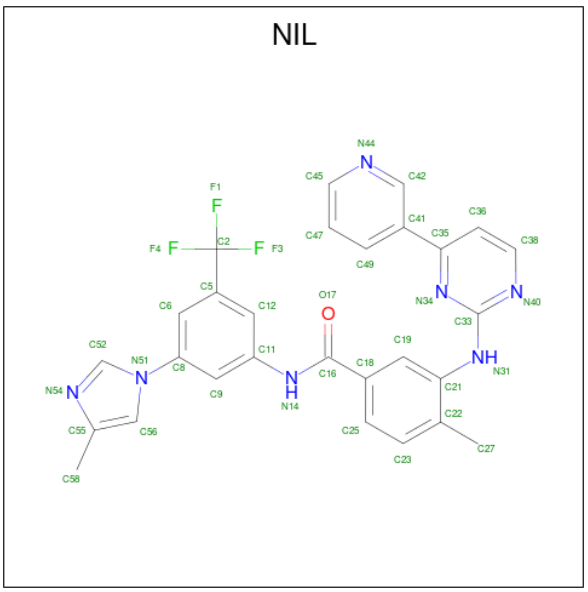
- Molecule 1 is a protein called Proto-oncogene tyrosine-protein kinase ABL1.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
			Total	C	N	O	S			
1	A	264	2142	1383	351	392	16	0	0	0
1	B	247	2033	1315	328	374	16	0	2	0
1	C	243	1984	1287	323	359	15	0	0	0
1	D	263	2115	1363	343	392	17	0	0	0

There are 20 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	224	GLY	-	expression tag	UNP P00519
A	225	ALA	-	expression tag	UNP P00519
A	226	MET	-	expression tag	UNP P00519
A	227	ASP	-	expression tag	UNP P00519
A	228	PRO	-	expression tag	UNP P00519
B	224	GLY	-	expression tag	UNP P00519
B	225	ALA	-	expression tag	UNP P00519
B	226	MET	-	expression tag	UNP P00519
B	227	ASP	-	expression tag	UNP P00519
B	228	PRO	-	expression tag	UNP P00519
C	224	GLY	-	expression tag	UNP P00519
C	225	ALA	-	expression tag	UNP P00519
C	226	MET	-	expression tag	UNP P00519
C	227	ASP	-	expression tag	UNP P00519
C	228	PRO	-	expression tag	UNP P00519
D	224	GLY	-	expression tag	UNP P00519
D	225	ALA	-	expression tag	UNP P00519
D	226	MET	-	expression tag	UNP P00519
D	227	ASP	-	expression tag	UNP P00519
D	228	PRO	-	expression tag	UNP P00519

- Molecule 2 is Nilotinib (three-letter code: NIL) (formula: $C_{28}H_{22}F_3N_7O$).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	F	N	O	0	0
			39	28	3	7	1		
2	B	1	Total	C	F	N	O	0	0
			39	28	3	7	1		
2	C	1	Total	C	F	N	O	0	0
			39	28	3	7	1		
2	D	1	Total	C	F	N	O	0	0
			39	28	3	7	1		

- Molecule 3 is water.

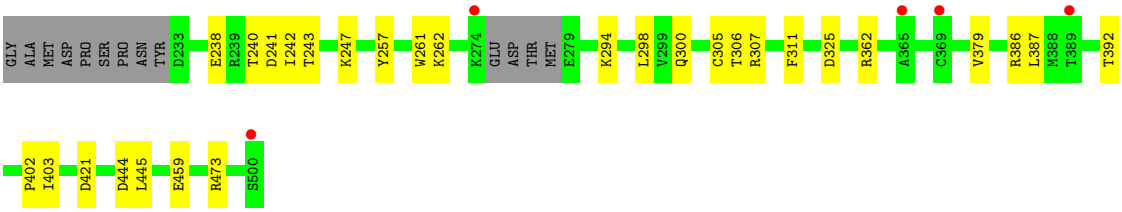
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
3	A	99	Total	O	0	0
			99	99		
3	B	79	Total	O	0	0
			79	79		
3	C	63	Total	O	0	0
			63	63		
3	D	25	Total	O	0	0
			25	25		

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.

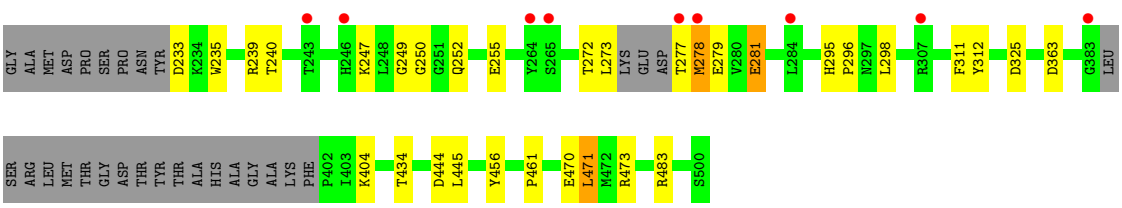
• Molecule 1: Proto-oncogene tyrosine-protein kinase ABL1

Chain A:



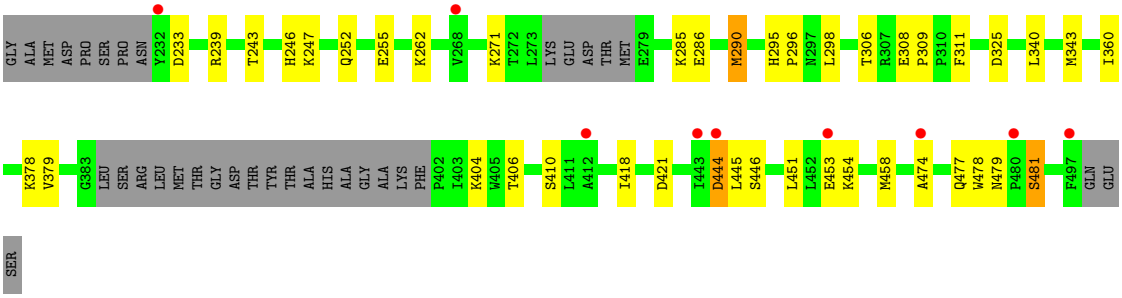
• Molecule 1: Proto-oncogene tyrosine-protein kinase ABL1

Chain B:



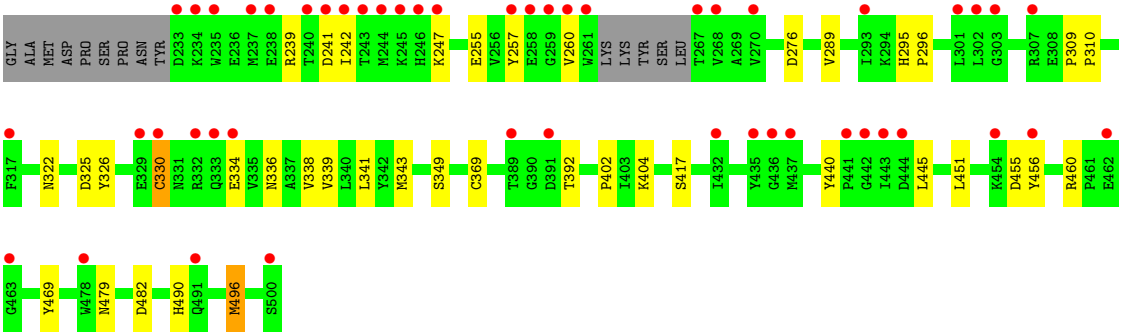
• Molecule 1: Proto-oncogene tyrosine-protein kinase ABL1

Chain C:



• Molecule 1: Proto-oncogene tyrosine-protein kinase ABL1

Chain D:


GLY ALA MET ASP PRO SER PRO ASN TYR D233 K234 W235 E236 M237 E238 R239 T240 D241 I242 T243 M244 K245 H246 K247 E255 V256 Y257 E258 G259 V260 W261 LYS LYS TYR SER LEU T267 V268 A269 V270 D276 V289 I293 K294 H295 P296 L301 L302 G303 R307 E308 P309 P310
F317 N322 D325 Y326 E329 C330 N331 R332 Q333 E334 V335 N336 A337 V338 V339 L340 L341 Y342 M343 S349 C369 T389 G390 D391 T392 P402 I403 K404 S417 I432 Y435 G436 M437 Y440 P441 G442 I443 D444 L445 L451 K454 D455 Y456 R460 P461 E462
G463 Y469 W478 N479 D482 H490 Q491 M496 S500

4 Data and refinement statistics (i)

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	93.93Å 118.09Å 123.68Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	40.00 – 2.21 37.40 – 2.21	Depositor EDS
% Data completeness (in resolution range)	98.6 (40.00-2.21) 98.6 (37.40-2.21)	Depositor EDS
R_{merge}	0.06	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	3.58 (at 2.20Å)	Xtriage
Refinement program	REFMAC 5.1.9999	Depositor
R, R_{free}	0.197 , 0.242 0.217 , 0.259	Depositor DCC
R_{free} test set	3477 reflections (5.05%)	wwPDB-VP
Wilson B-factor (Å^2)	39.6	Xtriage
Anisotropy	0.083	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.37 , 49.4	EDS
L-test for twinning[2]	$< \|L\| > = 0.49$, $< L^2 > = 0.33$	Xtriage
Estimated twinning fraction	0.013 for -h,l,k	Xtriage
F_o,F_c correlation	0.94	EDS
Total number of atoms	8696	wwPDB-VP
Average B, all atoms (Å^2)	49.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 4.54% 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 (i)

5.1 Standard geometry (i)

Bond lengths and bond angles in the following residue types are not validated in this section: NIL

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	0.94	0/2197	0.91	6/2971 (0.2%)
1	B	0.91	1/2093 (0.0%)	0.91	7/2828 (0.2%)
1	C	0.87	1/2036 (0.0%)	0.85	2/2755 (0.1%)
1	D	0.67	0/2169	0.77	2/2938 (0.1%)
All	All	0.85	2/8495 (0.0%)	0.86	17/11492 (0.1%)

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	C	290	MET	SD-CE	-5.72	1.45	1.77
1	B	456	TYR	CD1-CE1	5.55	1.47	1.39

The worst 5 of 17 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	B	473	ARG	NE-CZ-NH2	-11.26	114.67	120.30
1	A	473	ARG	NE-CZ-NH2	-9.28	115.66	120.30
1	A	421	ASP	CB-CG-OD1	7.01	124.61	118.30
1	B	471	LEU	CA-CB-CG	6.67	130.63	115.30
1	D	455	ASP	CB-CG-OD2	6.59	124.23	118.30

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	2142	0	2099	13	0
1	B	2033	0	1986	16	0
1	C	1984	0	1943	22	0
1	D	2115	0	2043	20	0
2	A	39	0	22	0	0
2	B	39	0	22	1	0
2	C	39	0	22	1	0
2	D	39	0	22	1	0
3	A	99	0	0	3	0
3	B	79	0	0	3	0
3	C	63	0	0	5	0
3	D	25	0	0	2	0
All	All	8696	0	8159	72	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 4.

The worst 5 of 72 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:454:LYS:HB2	3:C:651:HOH:O	1.85	0.76
1:C:246:HIS:HE1	3:C:656:HOH:O	1.72	0.73
1:B:404:LYS:HE3	1:B:445:LEU:HD23	1.74	0.69
1:C:243:THR:OG1	1:C:262:LYS:HD2	1.95	0.66
1:C:444:ASP:HA	3:C:622:HOH:O	1.95	0.66

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	260/277 (94%)	247 (95%)	13 (5%)	0	100	100
1	B	243/277 (88%)	232 (96%)	11 (4%)	0	100	100
1	C	237/277 (86%)	226 (95%)	11 (5%)	0	100	100
1	D	259/277 (94%)	247 (95%)	11 (4%)	1 (0%)	34	37
All	All	999/1108 (90%)	952 (95%)	46 (5%)	1 (0%)	51	60

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	D	255	GLU

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	227/241 (94%)	223 (98%)	4 (2%)	59	71
1	B	219/241 (91%)	212 (97%)	7 (3%)	39	49
1	C	211/241 (88%)	205 (97%)	6 (3%)	43	54
1	D	222/241 (92%)	217 (98%)	5 (2%)	50	62
All	All	879/964 (91%)	857 (98%)	22 (2%)	47	58

5 of 22 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	C	446	SER
1	D	241	ASP
1	C	481	SER
1	D	330	CYS
1	B	277	THR

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	C	358	ASN
1	D	252	GLN
1	D	490	HIS
1	A	490	HIS
1	A	300	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)

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	$\#\|Z\| > 2$
2	NIL	A	600	-	38,43,43	1.18	5 (13%)	48,62,62	1.38	6 (12%)
2	NIL	C	600	-	38,43,43	1.30	3 (7%)	48,62,62	1.74	13 (27%)
2	NIL	B	600	-	38,43,43	1.39	7 (18%)	48,62,62	1.77	9 (18%)
2	NIL	D	600	-	38,43,43	1.47	4 (10%)	48,62,62	1.98	11 (22%)

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	NIL	A	600	-	-	2/18/26/26	0/5/5/5
2	NIL	C	600	-	-	2/18/26/26	0/5/5/5
2	NIL	B	600	-	-	1/18/26/26	0/5/5/5
2	NIL	D	600	-	-	2/18/26/26	0/5/5/5

The worst 5 of 19 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	D	600	NIL	C9-C8	4.51	1.43	1.40
2	C	600	NIL	C36-C35	-3.73	1.35	1.41
2	A	600	NIL	C36-C35	-3.67	1.35	1.41
2	D	600	NIL	C36-C35	-3.54	1.35	1.41
2	B	600	NIL	C36-C35	-3.40	1.36	1.41

The worst 5 of 39 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
2	D	600	NIL	N40-C33-N34	-6.13	120.60	126.52
2	B	600	NIL	N40-C33-N34	-5.67	121.04	126.52
2	D	600	NIL	C21-N31-C33	-5.67	112.51	129.60
2	D	600	NIL	N31-C33-N40	4.88	131.42	116.28
2	C	600	NIL	N31-C33-N40	4.40	129.95	116.28

There are no chirality outliers.

5 of 7 torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	B	600	NIL	C22-C21-N31-C33
2	C	600	NIL	C22-C21-N31-C33
2	A	600	NIL	C22-C21-N31-C33
2	A	600	NIL	C19-C21-N31-C33
2	C	600	NIL	C19-C21-N31-C33

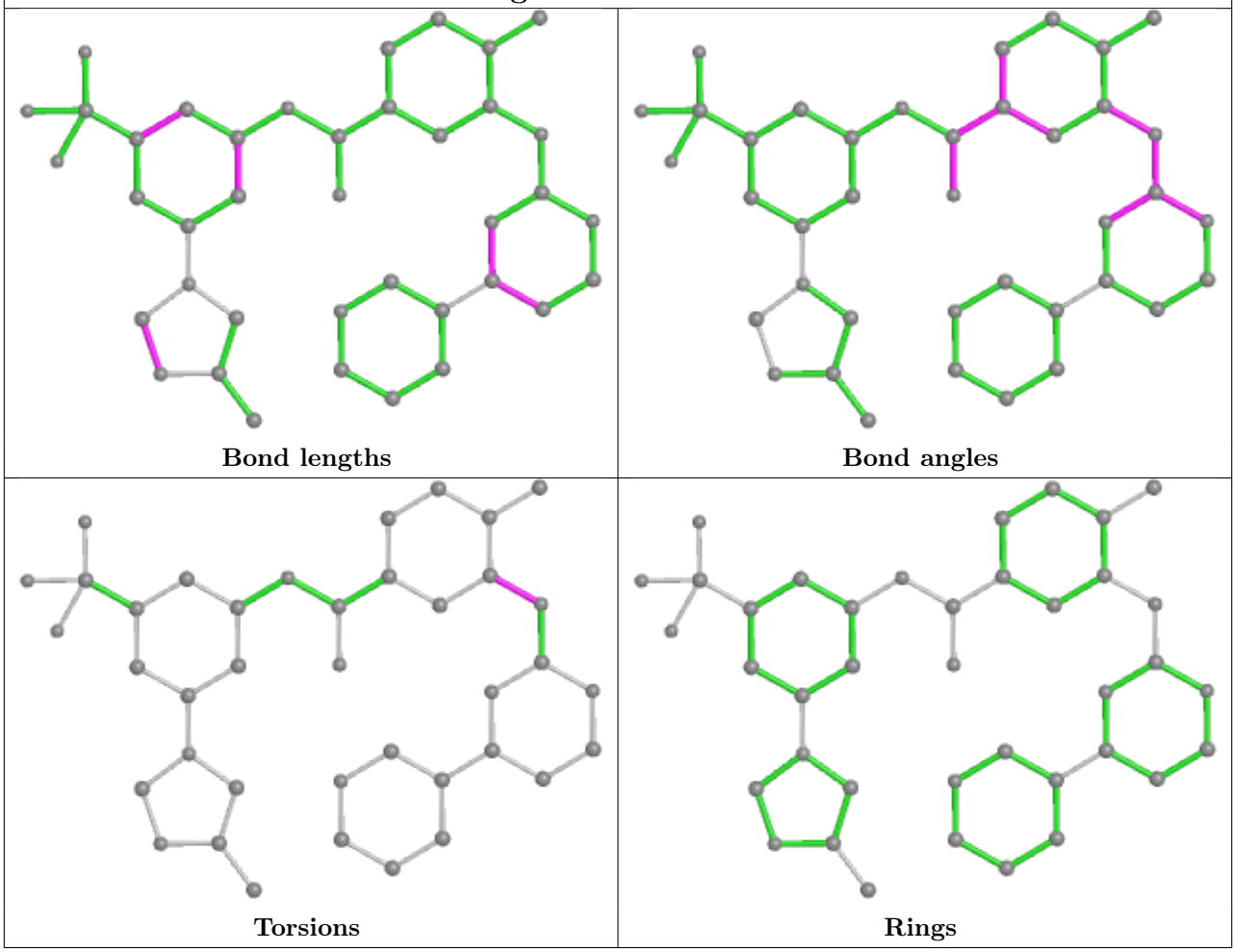
There are no ring outliers.

3 monomers are involved in 3 short contacts:

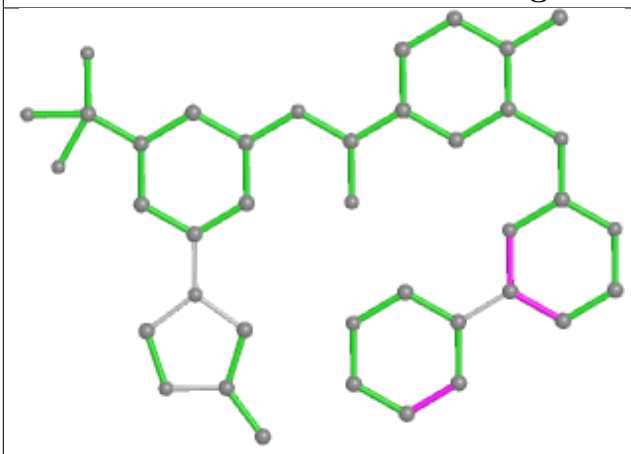
Mol	Chain	Res	Type	Clashes	Symm-Clashes
2	C	600	NIL	1	0
2	B	600	NIL	1	0
2	D	600	NIL	1	0

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.

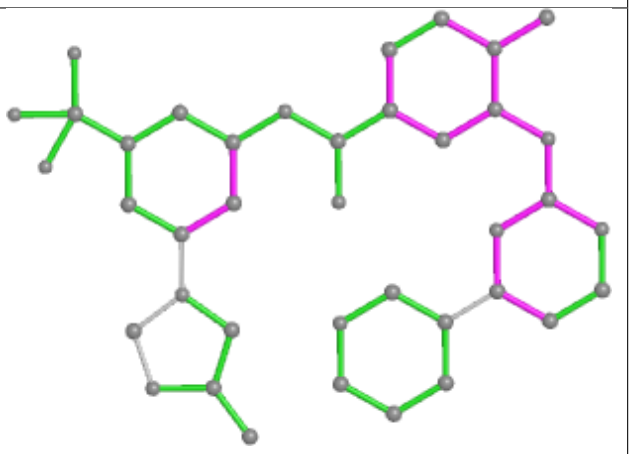
Ligand NIL A 600



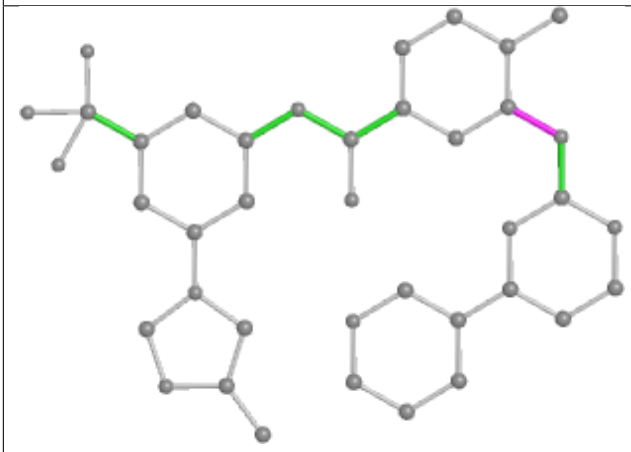
Ligand NIL C 600



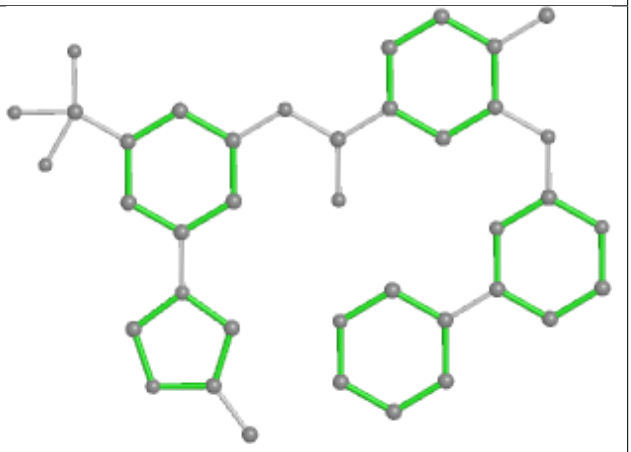
Bond lengths



Bond angles

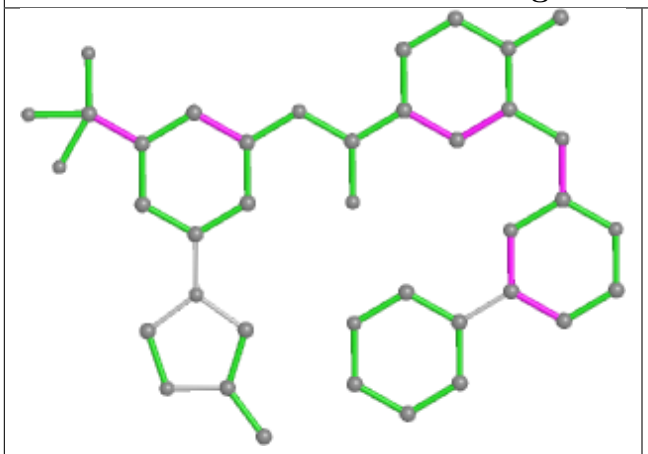


Torsions

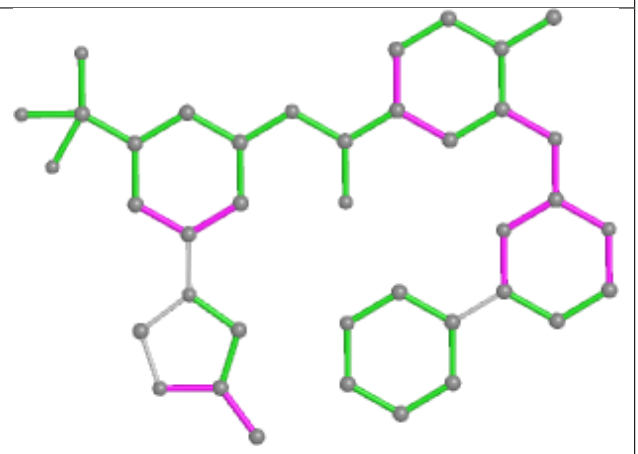


Rings

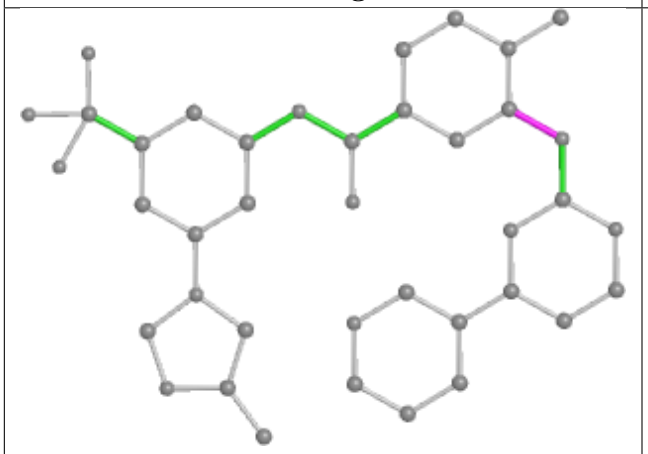
Ligand NIL B 600



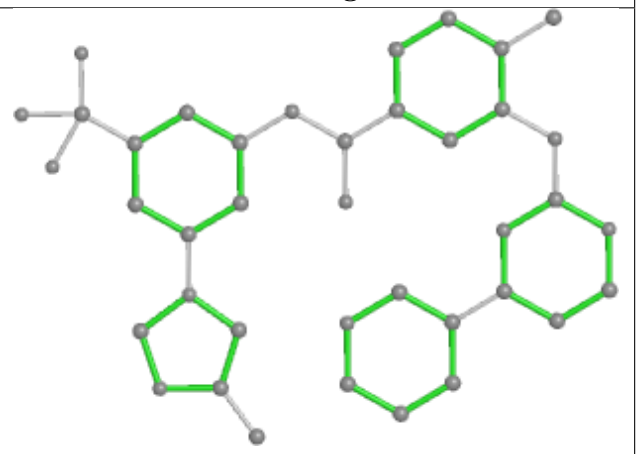
Bond lengths



Bond angles

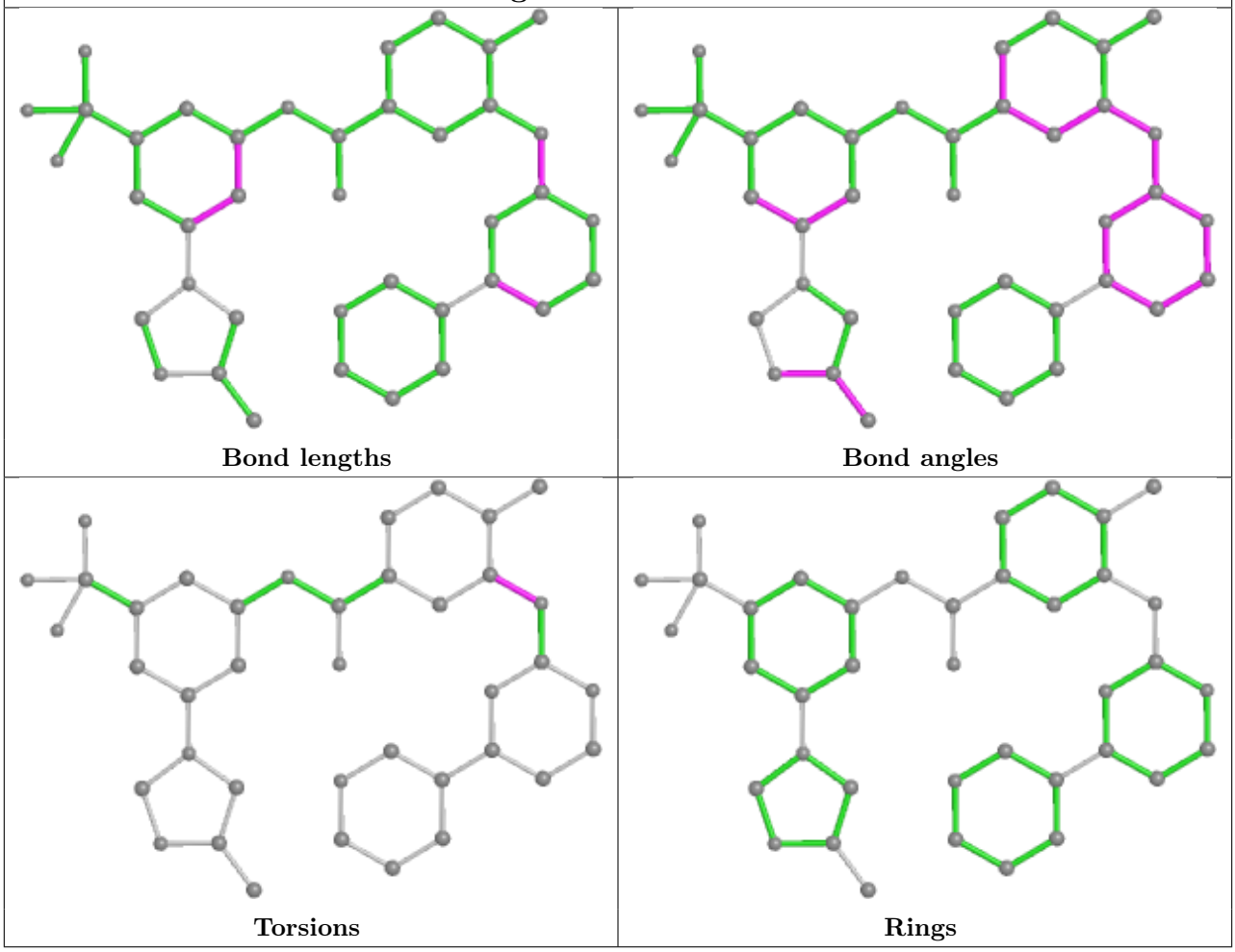


Torsions



Rings

Ligand NIL D 600



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	264/277 (95%)	0.01	5 (1%)	66	65	27, 36, 60, 65	0
1	B	247/277 (89%)	0.12	9 (3%)	42	40	28, 43, 71, 77	0
1	C	243/277 (87%)	0.17	9 (3%)	41	39	33, 46, 61, 70	0
1	D	263/277 (94%)	0.89	49 (18%)	1	1	50, 63, 83, 92	0
All	All	1017/1108 (91%)	0.30	72 (7%)	16	14	27, 48, 73, 92	0

The worst 5 of 72 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	D	259	GLY	5.7
1	D	333	GLN	5.6
1	D	442	GLY	5.1
1	D	242	ILE	5.1
1	D	240	THR	4.9

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)

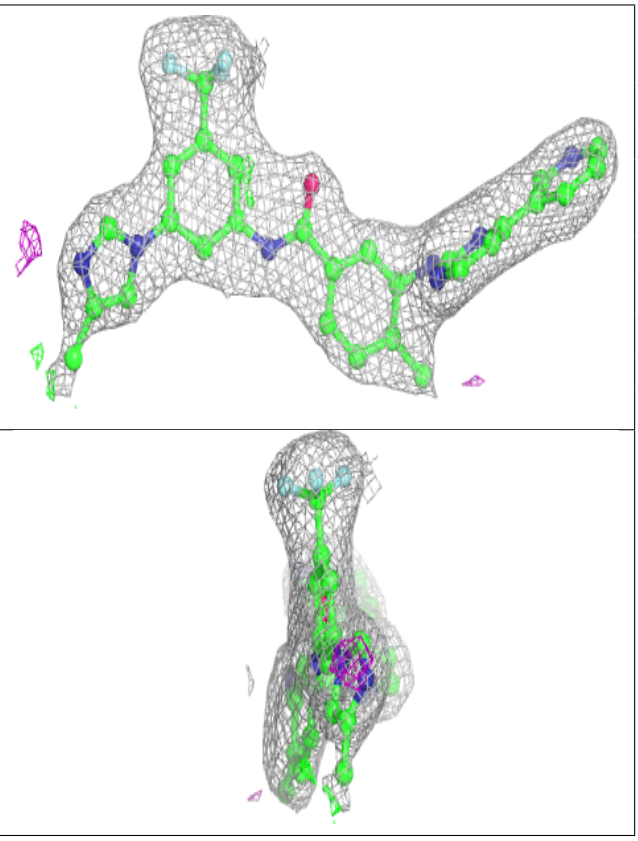
In the following table, the Atoms column lists the number of modelled atoms in the group and the number defined in the chemical component dictionary. The B-factors column lists the minimum, median, 95th percentile and maximum values of B factors of atoms in the group. The column labelled 'Q< 0.9' lists 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	NIL	D	600	39/39	0.92	0.14	51,60,63,64	0
2	NIL	C	600	39/39	0.94	0.16	33,37,48,51	0
2	NIL	B	600	39/39	0.95	0.14	38,44,55,55	0
2	NIL	A	600	39/39	0.96	0.16	27,34,45,46	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.

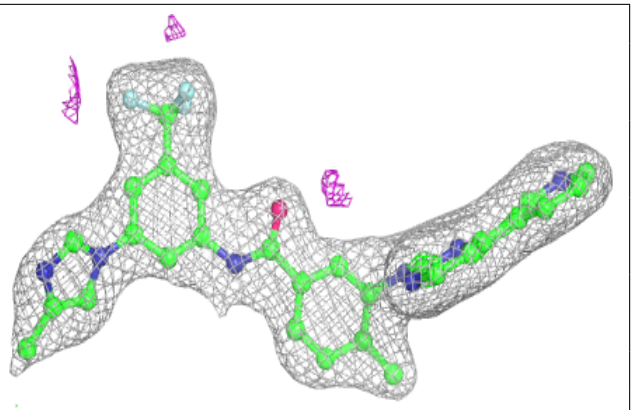
Electron density around NIL D 600:

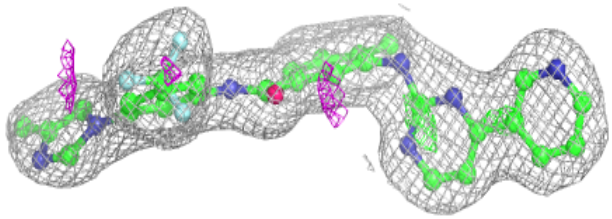
2mF$_o$-DF$_c$ (at 0.7 rmsd) in gray
mF$_o$-DF$_c$ (at 3 rmsd) in purple (negative) and green (positive)

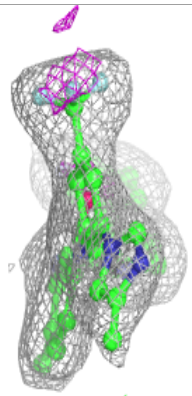


Electron density around NIL C 600:

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

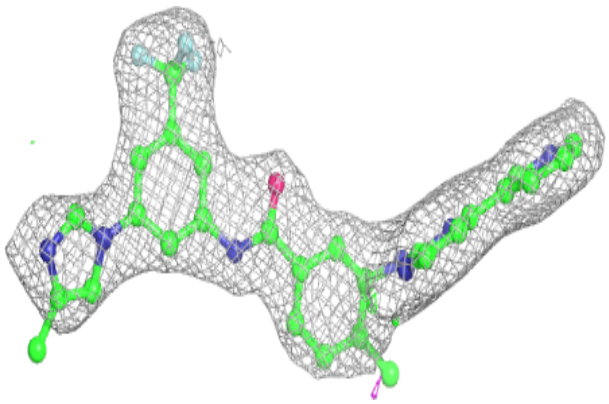


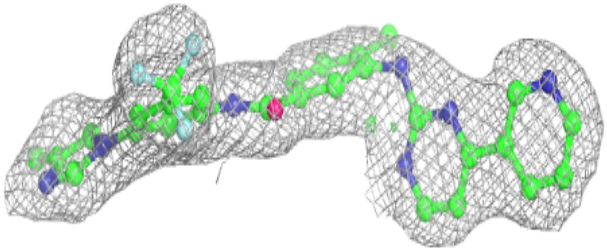


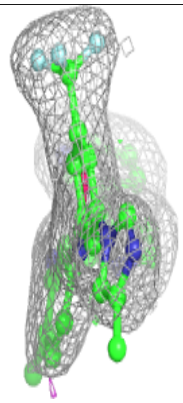


Electron density around NIL B 600:

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

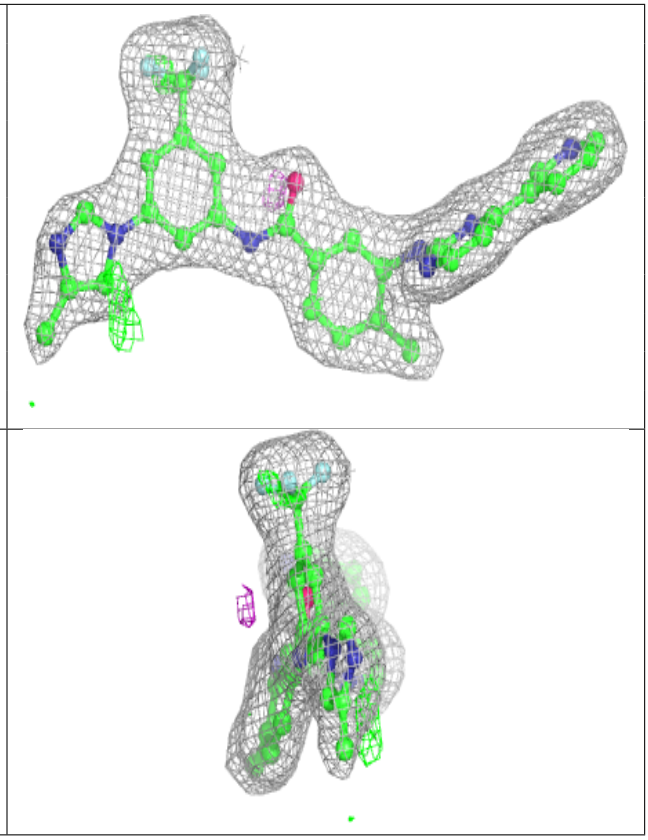






Electron density around NIL A 600:

$2mF_o$-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.