

wwPDB X-ray Structure Validation Summary Report (i)

Feb 1, 2024 – 02:06 PM JST

PDB ID : 8WXY

Title: Crystal Structure of the first bromodomain of human BRD4 in complex with

the inhibitor 23

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Deposited on : 2023-10-30

Resolution : 2.87 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 (1)) were used in the production of this report:

MolProbity: 4.02b-467

Mogul : 1.8.5 (274361), CSD as541be (2020)

Xtriage (Phenix) : NOT EXECUTED

EDS : NOT EXECUTED

buster-report : 1.1.7 (2018)

Percentile statistics : 20191225.v01 (using entries in the PDB archive December 25th 2019)

Ideal geometry (proteins) : Engh & Huber (2001) Ideal geometry (DNA, RNA) : Parkinson et al. (1996)

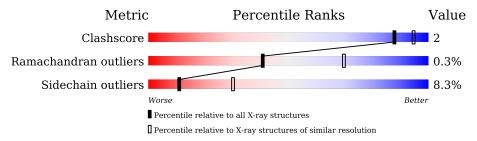
Validation Pipeline (wwPDB-VP) : 2.36

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 2.87 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	Similar resolution
Metric	$(\# ext{Entries})$	$(\# ext{Entries}, ext{ resolution range}(ext{Å}))$
Clashscore	141614	2947 (2.90-2.86)
Ramachandran outliers	138981	2868 (2.90-2.86)
Sidechain outliers	138945	2871 (2.90-2.86)

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%

Note EDS was not executed.

Mol	Chain	Length	Quality of chain					
1	A	141	65%	10%		24%		
1	В	141	68%	7%		24%		
1	С	141	65%	9%		24%		



2 Entry composition (i)

There are 4 unique types of molecules in this entry. The entry contains 2840 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 Bromodomain-containing protein 4.

Mol	Chain	Residues		At	oms			ZeroOcc	AltConf	Trace
1	A	107	Total	С	N	О	S	0	0	0
1	A	107	903	592	145	160	6	0	0	0
1	D	107	Total	С	N	О	S	0	0	0
1	Б	107	905	593	145	161	6	0	0	0
1	С	107	Total	С	N	О	S	0	0	0
1		107	903	592	145	160	6	0	0	U

There are 48 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	28	MET	-	initiating methionine	UNP O60885
A	29	LYS	-	expression tag	UNP O60885
A	30	LYS	-	expression tag	UNP O60885
A	31	GLY	-	expression tag	UNP O60885
A	32	HIS	-	expression tag	UNP O60885
A	33	HIS	-	expression tag	UNP O60885
A	34	HIS	-	expression tag	UNP O60885
A	35	HIS	-	expression tag	UNP O60885
A	36	HIS	-	expression tag	UNP O60885
A	37	HIS	-	expression tag	UNP O60885
A	38	LEU	-	expression tag	UNP O60885
A	39	VAL	-	expression tag	UNP O60885
A	40	PRO	-	expression tag	UNP O60885
A	41	ARG	-	expression tag	UNP O60885
A	42	GLY	-	expression tag	UNP O60885
A	43	SER	-	expression tag	UNP O60885
В	28	MET	-	initiating methionine	UNP O60885
В	29	LYS	-	expression tag	UNP O60885
В	30	LYS	-	expression tag	UNP O60885
В	31	GLY	-	expression tag	UNP O60885
В	32	HIS	-	expression tag	UNP O60885
В	33	HIS	-	expression tag	UNP O60885
В	34	HIS	-	expression tag	UNP O60885

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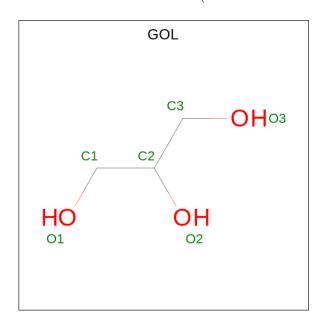
Chain	Residue	Modelled	Actual	Comment	Reference
В	35	HIS	-	expression tag	UNP O60885
В	36	HIS	-	expression tag	UNP O60885
В	37	HIS	-	expression tag	UNP O60885
В	38	LEU	-	expression tag	UNP O60885
В	39	VAL	-	expression tag	UNP O60885
В	40	PRO	-	expression tag	UNP O60885
В	41	ARG	-	expression tag	UNP O60885
В	42	GLY	-	expression tag	UNP O60885
В	43	SER	-	expression tag	UNP O60885
С	28	MET	-	initiating methionine	UNP O60885
С	29	LYS	-	expression tag	UNP O60885
С	30	LYS	-	expression tag	UNP O60885
С	31	GLY	-	expression tag	UNP O60885
С	32	HIS	-	expression tag	UNP O60885
С	33	HIS	-	expression tag	UNP O60885
С	34	HIS	-	expression tag	UNP O60885
С	35	HIS	-	expression tag	UNP O60885
С	36	HIS	-	expression tag	UNP O60885
С	37	HIS	-	expression tag	UNP O60885
С	38	LEU	-	expression tag	UNP O60885
С	39	VAL	-	expression tag	UNP O60885
С	40	PRO	-	expression tag	UNP O60885
С	41	ARG	-	expression tag	UNP O60885
С	42	GLY	-	expression tag	UNP O60885
С	43	SER	-	expression tag	UNP O60885

• Molecule 2 is 5-[2-(4-fluoranyl-2,6-dimethyl-phenoxy)-5-(2-oxidanylpropan-2-yl)phenyl]-1-methyl-4-[(2-morpholin-4-yl-2-oxidanylidene-ethyl)amino]pyridin-2-one (three-letter code: XGN) (formula: $C_{29}H_{34}FN_3O_5$) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms				ZeroOcc	AltConf	
2	Δ	1	Total	С	F	N	О	0	0
2	Λ	1	38	29	1	3	5	U	U
2	B	1	Total	С	F	N	О	0	0
2	Ъ	1	38	29	1	3	5	0	0
2	С	1	Total	С	F	N	О	0	0
		1	38	29	1	3	5		0

 \bullet Molecule 3 is GLYCEROL (three-letter code: GOL) (formula: $\mathrm{C_3H_8O_3}).$



Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
3	A	1	Total C O 6 3 3	0	0



• Molecule 4 is water.

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
4	A	4	Total O 4 4	0	0
4	В	3	Total O 3 3	0	0
4	С	2	Total O 2 2	0	0

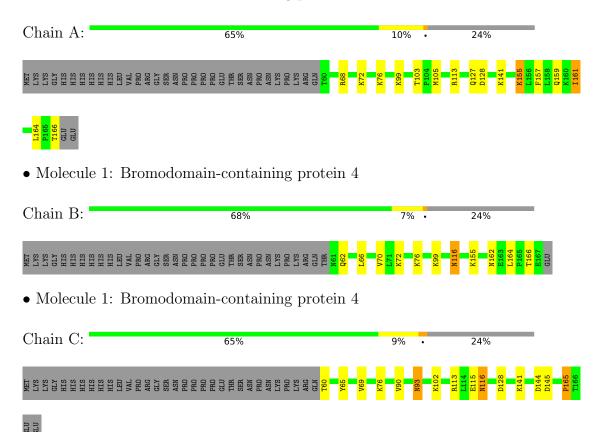


3 Residue-property plots (i)

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. 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. 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.

Note EDS was not executed.

• Molecule 1: Bromodomain-containing protein 4





4 Data and refinement statistics (i)

Xtriage (Phenix) and EDS were not executed - this section is therefore incomplete.

Property	Value	Source	
Space group	P 61 2 2	Depositor	
Cell constants	140.32Å 140.32Å 135.23Å	Depositor	
a, b, c, α , β , γ	90.00° 90.00° 120.00°	Depositor	
Resolution (Å)	121.52 - 2.87	Depositor	
% Data completeness	96.0 (121.52-2.87)	Depositor	
(in resolution range)	30.0 (121.02 2.01)		
R_{merge}	0.26	Depositor	
R_{sym}	(Not available)	Depositor	
Refinement program	REFMAC 5.8.0189	Depositor	
R, R_{free}	0.188 , 0.249	Depositor	
Estimated twinning fraction	No twinning to report.	Xtriage	
Total number of atoms	2840	wwPDB-VP	
Average B, all atoms (Å ²)	73.0	wwPDB-VP	



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: GOL, XGN

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	Boı	nd lengths	Bond angles		
IVIOI	Chain	RMSZ	# Z > 5	RMSZ	# Z > 5	
1	A	0.78	0/927	0.89	$2/1259 \ (0.2\%)$	
1	В	0.76	1/929 (0.1%)	0.86	0/1261	
1	С	0.70	1/927 (0.1%)	0.85	2/1259 (0.2%)	
All	All	0.75	$2/2783 \ (0.1\%)$	0.87	4/3779 (0.1%)	

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 maintain group or atoms of a sidechain that are expected to be planar.

Mol	Chain	#Chirality outliers	#Planarity outliers
1	С	0	1

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	\mathbf{Z}	$\operatorname{Observed}(\text{\AA})$	Ideal(A)
1	В	116	ASN	CG-ND2	5.49	1.46	1.32
1	С	116	ASN	CG-ND2	5.38	1.46	1.32

All (4) bond angle outliers are listed below:

Mol	Chain	Res	Type	oe Atoms		$Observed(^o)$	$\operatorname{Ideal}({}^{o})$
1	A	164	LEU	CA-CB-CG	5.54	128.04	115.30
1	С	128	ASP	CB-CG-OD1	5.24	123.01	118.30
1	A	68	ARG	NE-CZ-NH1	5.17	122.89	120.30
1	С	113	ARG	NE-CZ-NH1	5.13	122.87	120.30

There are no chirality outliers.

All (1) planarity outliers are listed below:



Mol	Chain	Res	Type	Group
1	С	165	PRO	Peptide

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	903	0	905	4	0
1	В	905	0	904	5	0
1	С	903	0	905	5	0
2	A	38	0	0	0	0
2	В	38	0	0	0	0
2	С	38	0	0	0	0
3	A	6	0	8	0	0
4	A	4	0	0	0	0
4	В	3	0	0	0	0
4	С	2	0	0	0	0
All	All	2840	0	2722	11	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 2.

The worst 5 of 11 close contacts within the same asymmetric unit are listed below, sorted by their clash magnitude.

Atom-1	Atom-2	$\begin{array}{c} {\rm Interatomic} \\ {\rm distance} \ ({\rm \AA}) \end{array}$	$\begin{array}{c} \text{Clash} \\ \text{overlap } (\text{\AA}) \end{array}$
1:C:65:TYR:CZ	1:C:69:VAL:HG11	2.30	0.67
1:B:116:ASN:ND2	1:C:116:ASN:HD21	2.06	0.54
1:B:116:ASN:ND2	1:C:116:ASN:ND2	2.63	0.47
1:B:62:GLN:HE21	1:B:164:LEU:HG	1.82	0.45
1:A:113:ARG:NH1	1:A:128:ASP:OD2	2.50	0.45

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	105/141 (74%)	100 (95%)	5 (5%)	0	100	100	
1	В	105/141 (74%)	102 (97%)	3 (3%)	0	100	100	
1	С	105/141 (74%)	94 (90%)	10 (10%)	1 (1%)	15	42	
All	All	315/423 (74%)	296 (94%)	18 (6%)	1 (0%)	41	70	

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	С	93	ASN

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	tameric Outliers			Percentiles		
1	A	100/132~(76%)	90 (90%)	10 (10%)		7	21		
1	В	100/132 (76%)	94 (94%)	6 (6%)		19	46		
1	С	100/132 (76%)	91 (91%)	9 (9%)		9	26		
All	All	300/396 (76%)	275 (92%)	25 (8%)		11	30		

5 of 25 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	В	162	ASN
1	С	76	LYS

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Mol	Chain	Res	Type
1	С	165	PRO
1	С	60	THR
1	С	90	VAL

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. 5 of 11 such sidechains are listed below:

Mol	Chain	Res	Type
1	С	62	GLN
1	С	93	ASN
1	С	162	ASN
1	С	116	ASN
1	В	116	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 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 R	Res	Link	Bo	ond leng	$ ag{ths}$	В	ond ang	gles		
		Chain	Chain nes		Counts	RMSZ	# Z > 2	Counts	RMSZ	# Z > 2	
	2	XGN	A	201	-	41,41,41	3.20	8 (19%)	54,60,60	1.87	10 (18%)



Mol	Tuno	Chain	Res	Link	Bo	ond leng	$ ag{ths}$	В	ond ang	gles
IVIOI	Type	Chain	nes	Lilik	Counts	RMSZ	# Z > 2	Counts	RMSZ	# Z >2
2	XGN	В	201	-	41,41,41	3.21	8 (19%)	54,60,60	1.70	10 (18%)
2	XGN	С	201	-	41,41,41	3.02	9 (21%)	54,60,60	1.75	8 (14%)
3	GOL	A	202	-	5,5,5	0.59	0	5,5,5	0.43	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
2	XGN	A	201	-	-	0/23/31/31	0/4/4/4
2	XGN	В	201	_	-	0/23/31/31	0/4/4/4
2	XGN	С	201	-	-	6/23/31/31	0/4/4/4
3	GOL	A	202	_	-	2/4/4/4	-

The worst 5 of 25 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	\mathbf{Z}	$\operatorname{Observed}(\text{\AA})$	$Ideal(\AA)$
2	В	201		CAH-CAE		1.42	1.53
2	A	201	XGN	CAH-CAE	-16.01	1.42	1.53
2	С	201	XGN	CAH-CAE	-14.71	1.43	1.53
2	В	201	XGN	CAR-CAM	-6.27	1.38	1.51
2	С	201	XGN	CAA-CAU	-5.73	1.41	1.49

The worst 5 of 28 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	\mathbf{Z}	$\mathbf{Observed}(^o)$	$\operatorname{Ideal}({}^o)$
2	С	201	XGN	CAA-CAU-CAV	7.61	127.34	120.00
2	A	201	XGN	CAA-CAU-CAV	6.24	126.02	120.00
2	В	201	XGN	CBM-NBF-CBI	6.16	124.48	112.62
2	A	201	XGN	CBM-NBF-CBI	5.13	122.50	112.62
2	В	201	XGN	CAA-CAU-CAV	5.05	124.87	120.00

There are no chirality outliers.

5 of 8 torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
3	A	202	GOL	C1-C2-C3-O3
2	С	201	XGN	CAW-CAV-N-CA
3	A	202	GOL	O2-C2-C3-O3
2	С	201	XGN	CAU-CAV-N-CA

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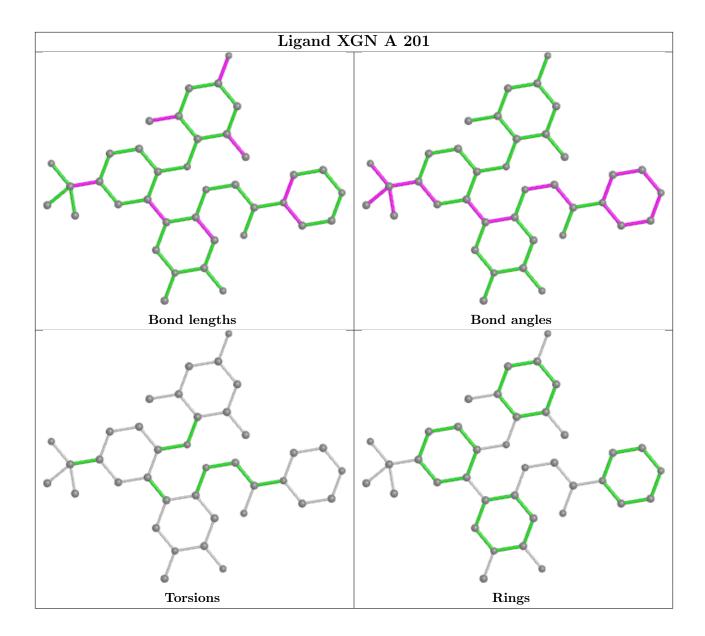
Mol	Chain	Res	Type	Atoms
2	С	201	XGN	NBF-C-CA-N

There are no ring outliers.

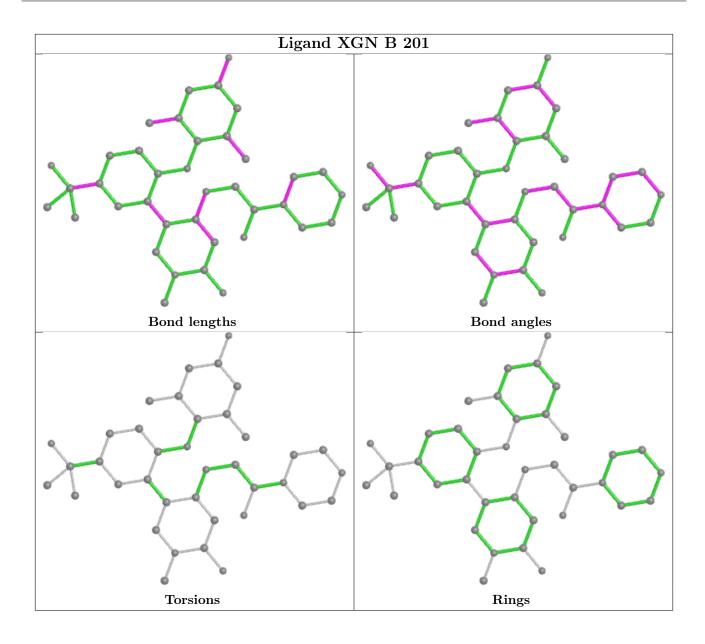
No monomer is involved in short contacts.

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 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.

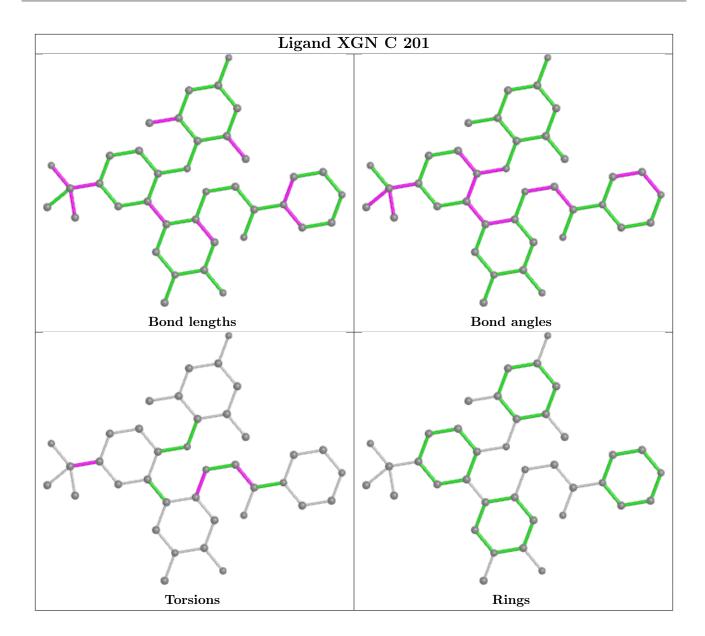












5.7 Other polymers (i)

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)

EDS was not executed - this section is therefore empty.

6.2 Non-standard residues in protein, DNA, RNA chains (i)

EDS was not executed - this section is therefore empty.

6.3 Carbohydrates (i)

EDS was not executed - this section is therefore empty.

6.4 Ligands (i)

EDS was not executed - this section is therefore empty.

6.5 Other polymers (i)

EDS was not executed - this section is therefore empty.

