Full wwPDB X-ray Structure Validation Report ⓘ

Oct 4, 2023 – 07:18 PM EDT

PDB ID	:	6PKC
Title	:	Inhibition of Human Menin by VTP-50469
Authors	:	McKeever, B.M.; Chen, G.; Van Orton, R.
Deposited on	:	2019-06-29
Resolution	:	1.90 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*
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:

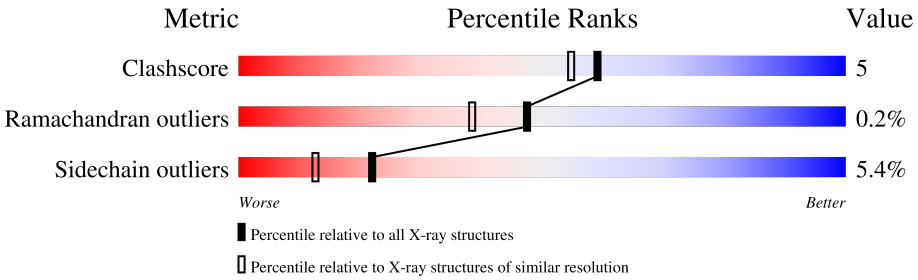
MolProbity	:	4.02b-467
Xtriage (Phenix)	:	1.13
EDS	:	FAILED
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.35.1

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 1.90 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))
Clashscore	141614	6847 (1.90-1.90)
Ramachandran outliers	138981	6760 (1.90-1.90)
Sidechain outliers	138945	6760 (1.90-1.90)

2 Entry composition (i)

There are 3 unique types of molecules in this entry. The entry contains 8097 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.

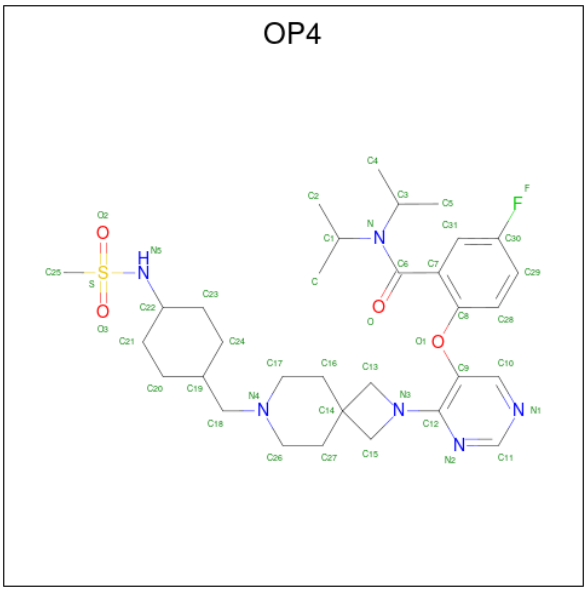
- Molecule 1 is a protein called Menin,Menin.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	462	Total	C	N	O	S	0	7	0
			3708	2371	634	687	16			
1	B	461	Total	C	N	O	S	0	10	0
			3729	2381	640	692	16			

There are 6 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	0	GLY	-	expression tag	UNP O00255
A	1	SER	-	expression tag	UNP O00255
A	5	THR	ALA	engineered mutation	UNP O00255
B	0	GLY	-	expression tag	UNP O00255
B	1	SER	-	expression tag	UNP O00255
B	5	THR	ALA	engineered mutation	UNP O00255

- Molecule 2 is 5-fluoro-2-({4-[7-({trans-4-[(methylsulfonyl)amino]cyclohexyl}methyl)-2,7-diazaspiro[3.5]nonan-2-yl]pyrimidin-5-yl}oxy)-N,N-di(propan-2-yl)benzamide (three-letter code: OP4) (formula: $C_{32}H_{47}FN_6O_4S$) (labeled as "Ligand of Interest" by depositor).



Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
2	A	1	Total C F N O S 44 32 1 6 4 1	0	0
2	B	1	Total C F N O S 44 32 1 6 4 1	0	0

- Molecule 3 is water.

Mol	Chain	Residues	Atoms	ZeroOcc	AltConf
3	A	289	Total O 289 289	0	0
3	B	283	Total O 283 283	0	0

SEQUENCE-PLOTS INFOmissingINFO

3 Data and refinement statistics (i)

EDS failed to run properly - this section is therefore incomplete.

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	58.97Å 86.08Å 202.04Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	48.65 – 1.90	Depositor
% Data completeness (in resolution range)	99.9 (48.65-1.90)	Depositor
R_{merge}	0.05	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	5.93 (at 1.90Å)	Xtriage
Refinement program	REFMAC 5.8.0135	Depositor
R, R_{free}	0.168 , 0.206	Depositor
Wilson B-factor (Å^2)	23.9	Xtriage
Anisotropy	0.030	Xtriage
L-test for twinning[2]	$< \|L\| > = 0.46$, $< L^2 > = 0.29$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
Total number of atoms	8097	wwPDB-VP
Average B, all atoms (Å^2)	29.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 4.77% 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.

4 Model quality

4.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: OP4

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	1.01	3/3791 (0.1%)	1.10	21/5141 (0.4%)
1	B	1.00	2/3812 (0.1%)	1.10	25/5168 (0.5%)
All	All	1.01	5/7603 (0.1%)	1.10	46/10309 (0.4%)

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	2

All (5) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	386	GLY	C-N	7.77	1.51	1.34
1	B	207	ARG	CD-NE	-6.14	1.36	1.46
1	A	573	SER	CB-OG	-5.53	1.35	1.42
1	A	415	ARG	CD-NE	-5.41	1.37	1.46
1	B	285	ASP	CB-CG	5.09	1.62	1.51

All (46) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	B	207	ARG	NE-CZ-NH2	-19.50	110.55	120.30
1	A	207	ARG	NE-CZ-NH2	-19.48	110.56	120.30
1	B	207	ARG	NE-CZ-NH1	17.68	129.14	120.30
1	A	207	ARG	NE-CZ-NH1	16.75	128.68	120.30
1	A	415	ARG	NE-CZ-NH1	-15.99	112.31	120.30
1	A	218	ARG	NE-CZ-NH1	14.31	127.46	120.30

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Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	A	218	ARG	NE-CZ-NH2	-13.61	113.49	120.30
1	B	218	ARG	NE-CZ-NH2	-13.08	113.76	120.30
1	B	218	ARG	NE-CZ-NH1	12.47	126.54	120.30
1	B	137	ARG	NE-CZ-NH2	-12.41	114.09	120.30
1	B	137	ARG	NE-CZ-NH1	12.10	126.35	120.30
1	B	386	GLY	O-C-N	11.24	140.69	122.70
1	A	415	ARG	CD-NE-CZ	10.69	138.56	123.60
1	B	386	GLY	C-N-CA	-10.53	95.38	121.70
1	A	137	ARG	NE-CZ-NH2	-9.65	115.47	120.30
1	A	137	ARG	NE-CZ-NH1	9.40	125.00	120.30
1	B	386	GLY	CA-C-N	-8.96	97.50	117.20
1	A	415	ARG	CG-CD-NE	7.07	126.64	111.80
1	A	418	ASP	CB-CG-OD1	6.87	124.48	118.30
1	B	315	ASP	CB-CG-OD1	6.83	124.45	118.30
1	A	358	GLU	CA-CB-CG	6.74	128.23	113.40
1	A	29	ARG	NE-CZ-NH1	6.70	123.65	120.30
1	B	231	ASP	CB-CG-OD1	6.27	123.94	118.30
1	B	29	ARG	NE-CZ-NH1	6.08	123.34	120.30
1	A	92	ARG	NE-CZ-NH1	5.74	123.17	120.30
1	A	285	ASP	CB-CG-OD1	5.73	123.46	118.30
1	A	115	ARG	NE-CZ-NH2	-5.70	117.45	120.30
1	B	229	ARG	CG-CD-NE	-5.69	99.86	111.80
1	A	115	ARG	NE-CZ-NH1	5.66	123.13	120.30
1	B	67	PRO	CA-N-CD	-5.60	103.67	111.50
1	A	177	LEU	CB-CG-CD2	-5.58	101.52	111.00
1	A	231	ASP	CB-CG-OD1	5.56	123.30	118.30
1	B	561	MET	CG-SD-CE	-5.52	91.36	100.20
1	B	285	ASP	CB-CG-OD1	5.44	123.19	118.30
1	B	218	ARG	CG-CD-NE	-5.40	100.47	111.80
1	B	177	LEU	CB-CG-CD2	-5.35	101.91	111.00
1	A	207	ARG	CD-NE-CZ	5.23	130.93	123.60
1	B	218	ARG	CD-NE-CZ	5.22	130.91	123.60
1	B	207	ARG	CD-NE-CZ	5.16	130.82	123.60
1	A	218	ARG	CG-CD-NE	-5.14	101.00	111.80
1	B	249	LEU	CA-CB-CG	5.12	127.07	115.30
1	B	232	ARG	NE-CZ-NH1	5.08	122.84	120.30
1	B	131	ARG	NE-CZ-NH1	5.07	122.84	120.30
1	B	92	ARG	NE-CZ-NH1	5.04	122.82	120.30
1	B	131	ARG	NE-CZ-NH2	-5.02	117.79	120.30
1	A	249	LEU	CA-CB-CG	5.01	126.82	115.30

There are no chirality outliers.

All (2) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	A	386	GLY	Mainchain
1	A	415	ARG	Sidechain

4.2 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	3708	0	3671	26	1
1	B	3729	0	3684	45	1
2	A	44	0	0	0	0
2	B	44	0	0	0	0
3	A	289	0	0	3	0
3	B	283	0	0	4	0
All	All	8097	0	7355	70	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 5.

All (70) 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:B:429:THR:HG22	1:B:430:PRO:HD2	1.24	1.16
1:B:429:THR:CG2	1:B:430:PRO:HD2	1.90	1.01
1:B:335:ARG:HG2	1:B:409[C]:CYS:SG	2.08	0.93
1:B:384:GLU:O	1:B:387:GLU:HG2	1.69	0.93
1:B:353:TYR:O	1:B:428:PRO:HD2	1.74	0.86
1:B:385:ALA:C	1:B:387:GLU:H	1.79	0.85
1:B:384:GLU:O	1:B:387:GLU:CG	2.29	0.81
1:A:338:LEU:HD12	1:A:409[B]:CYS:SG	2.23	0.79
1:B:66:SER:N	1:B:67:PRO:HD3	1.99	0.76
1:A:338:LEU:CD1	1:A:409[B]:CYS:SG	2.74	0.76
1:B:429:THR:HG22	1:B:430:PRO:CD	2.12	0.75
1:B:338:LEU:HD12	1:B:409[B]:CYS:SG	2.29	0.72
1:B:385:ALA:C	1:B:387:GLU:N	2.44	0.69
1:B:66:SER:N	1:B:67:PRO:CD	2.56	0.67

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:455[A]:VAL:CG1	1:A:457:ILE:HD12	2.26	0.66
1:B:338:LEU:CD1	1:B:409[B]:CYS:SG	2.84	0.65
1:A:321:TYR:HB2	1:A:344:THR:HG22	1.81	0.62
1:A:438[B]:THR:HG21	1:B:358:GLU:OE1	2.00	0.61
1:A:455[A]:VAL:HG11	1:A:457:ILE:HD12	1.82	0.61
1:A:335:ARG:HG2	1:A:409[C]:CYS:SG	2.42	0.60
1:B:384:GLU:O	1:B:387:GLU:CB	2.50	0.59
1:B:268:TYR:OH	1:B:304:LYS:HE3	2.03	0.58
1:A:455[A]:VAL:CG1	1:A:457:ILE:CD1	2.80	0.58
1:B:429:THR:CG2	1:B:430:PRO:CD	2.76	0.57
1:B:385:ALA:O	1:B:387:GLU:N	2.38	0.56
1:A:377:LYS:HE2	3:B:769:HOH:O	2.04	0.56
1:A:229:ARG:NH1	3:A:703:HOH:O	2.38	0.55
1:B:282:ASN:HB2	3:B:719:HOH:O	2.06	0.55
1:A:366[A]:GLU:OE2	1:A:370:ASP:OD2	2.24	0.54
1:A:4:LYS:HE3	1:A:6:ALA:HB3	1.90	0.53
1:B:422:LYS:HE3	3:B:937:HOH:O	2.09	0.53
1:B:217:GLU:OE1	1:B:356:GLU:OE1	2.27	0.52
1:B:4:LYS:HE3	1:B:6:ALA:HB3	1.91	0.52
1:B:71:PRO:HG2	1:B:75:LEU:HG	1.91	0.51
1:B:300:THR:O	1:B:304:LYS:HG3	2.10	0.51
1:B:115:ARG:HG2	1:B:119:LYS:HD2	1.93	0.51
1:B:106:TYR:O	1:B:108:ARG:N	2.46	0.49
1:A:51:ASN:O	1:A:51:ASN:ND2	2.45	0.49
1:A:455[A]:VAL:HG13	1:A:457:ILE:CD1	2.43	0.48
1:B:332:ARG:NH2	3:B:704:HOH:O	2.44	0.48
1:B:384:GLU:O	1:B:387:GLU:N	2.48	0.47
1:B:284:ALA:HB3	1:B:302:TYR:CE1	2.50	0.47
1:A:364:PHE:CD1	1:A:420[A]:ILE:HD11	2.50	0.47
1:A:384:GLU:O	1:A:387:GLU:HG3	2.15	0.46
1:A:4:LYS:CE	1:A:6:ALA:HB3	2.45	0.46
1:B:4:LYS:CE	1:B:6:ALA:HB3	2.45	0.46
1:B:561:MET:HB3	1:B:578[A]:GLN:HG2	1.96	0.46
1:B:185:VAL:HG12	1:B:193:THR:HG22	1.97	0.46
1:B:384:GLU:O	1:B:387:GLU:HB3	2.16	0.45
1:B:364:PHE:CD1	1:B:420[A]:ILE:HD11	2.52	0.44
1:B:366:GLU:OE2	1:B:370:ASP:OD2	2.36	0.43
1:A:338:LEU:HD13	1:A:409[B]:CYS:SG	2.57	0.43
1:A:248:ASP:OD2	1:A:251:THR:HG23	2.19	0.43
1:B:427:SER:HB3	1:B:428:PRO:HD2	2.01	0.43
1:B:248:ASP:OD2	1:B:251:THR:HG23	2.19	0.43

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:B:29:ARG:O	1:B:233:LYS:NZ	2.53	0.42
1:A:29:ARG:O	1:A:233:LYS:NZ	2.53	0.42
1:B:301:LEU:HD23	1:B:304:LYS:HD2	2.02	0.41
1:B:300:THR:HG22	1:B:304:LYS:HE2	2.02	0.41
1:B:333:ASN:HB3	1:B:336:GLU:OE2	2.20	0.41
1:A:119:LYS:CE	3:A:835:HOH:O	2.67	0.41
1:B:181:HIS:HB2	1:B:221:LEU:HD11	2.02	0.41
1:A:185:VAL:HG12	1:A:193:THR:HG22	2.01	0.41
1:B:335:ARG:HG2	1:B:409[C]:CYS:HG	1.82	0.41
1:B:429:THR:HG23	1:B:430:PRO:HD2	1.94	0.40
1:A:180:ASP:HB2	1:A:220:TRP:CH2	2.56	0.40
1:A:181:HIS:HB2	1:A:221:LEU:HD11	2.03	0.40
1:A:196:VAL:O	1:A:207:ARG:HD2	2.20	0.40
1:B:4:LYS:HG2	1:B:5:THR:N	2.36	0.40
1:A:116:GLU:HB2	3:A:800:HOH:O	2.21	0.40

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:A:109:GLU:OE1	1:B:111:GLY:N[1_445]	1.83	0.37

4.3 Torsion angles (i)

4.3.1 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	463/490 (94%)	455 (98%)	8 (2%)	0	100 100
1	B	465/490 (95%)	454 (98%)	9 (2%)	2 (0%)	34 24
All	All	928/980 (95%)	909 (98%)	17 (2%)	2 (0%)	47 38

All (2) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	B	107	PRO
1	B	386	GLY

4.3.2 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	395/413 (96%)	371 (94%)	24 (6%)	18 9
1	B	397/413 (96%)	376 (95%)	21 (5%)	22 13
All	All	792/826 (96%)	747 (94%)	45 (6%)	22 11

All (45) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	4	LYS
1	A	50	VAL
1	A	51	ASN
1	A	112	VAL
1	A	119	LYS
1	A	191	GLU
1	A	201	LYS
1	A	204	GLU
1	A	205	ASP
1	A	218	ARG
1	A	249	LEU
1	A	250	HIS
1	A	251	THR
1	A	254[A]	LEU
1	A	254[B]	LEU
1	A	276	TYR
1	A	282	ASN
1	A	289	LEU
1	A	339	GLN
1	A	378	GLU
1	A	415	ARG
1	A	429	THR

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Mol	Chain	Res	Type
1	A	450	GLN
1	A	582	GLN
1	B	4	LYS
1	B	51	ASN
1	B	109	GLU
1	B	112	VAL
1	B	191	GLU
1	B	201	LYS
1	B	204	GLU
1	B	218	ARG
1	B	249	LEU
1	B	250	HIS
1	B	251	THR
1	B	254[A]	LEU
1	B	254[B]	LEU
1	B	276	TYR
1	B	282	ASN
1	B	289	LEU
1	B	378	GLU
1	B	415[A]	ARG
1	B	415[B]	ARG
1	B	450	GLN
1	B	582	GLN

Sometimes sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (3) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	51	ASN
1	A	282	ASN
1	B	203	ASN

4.3.3 RNA (i)

There are no RNA molecules in this entry.

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

There are no non-standard protein/DNA/RNA residues in this entry.

4.5 Carbohydrates (i)

There are no monosaccharides in this entry.

4.6 Ligand geometry (i)

2 ligands are modelled in this entry.

There are no bond length outliers.

There are no bond angle outliers.

There are no chirality outliers.

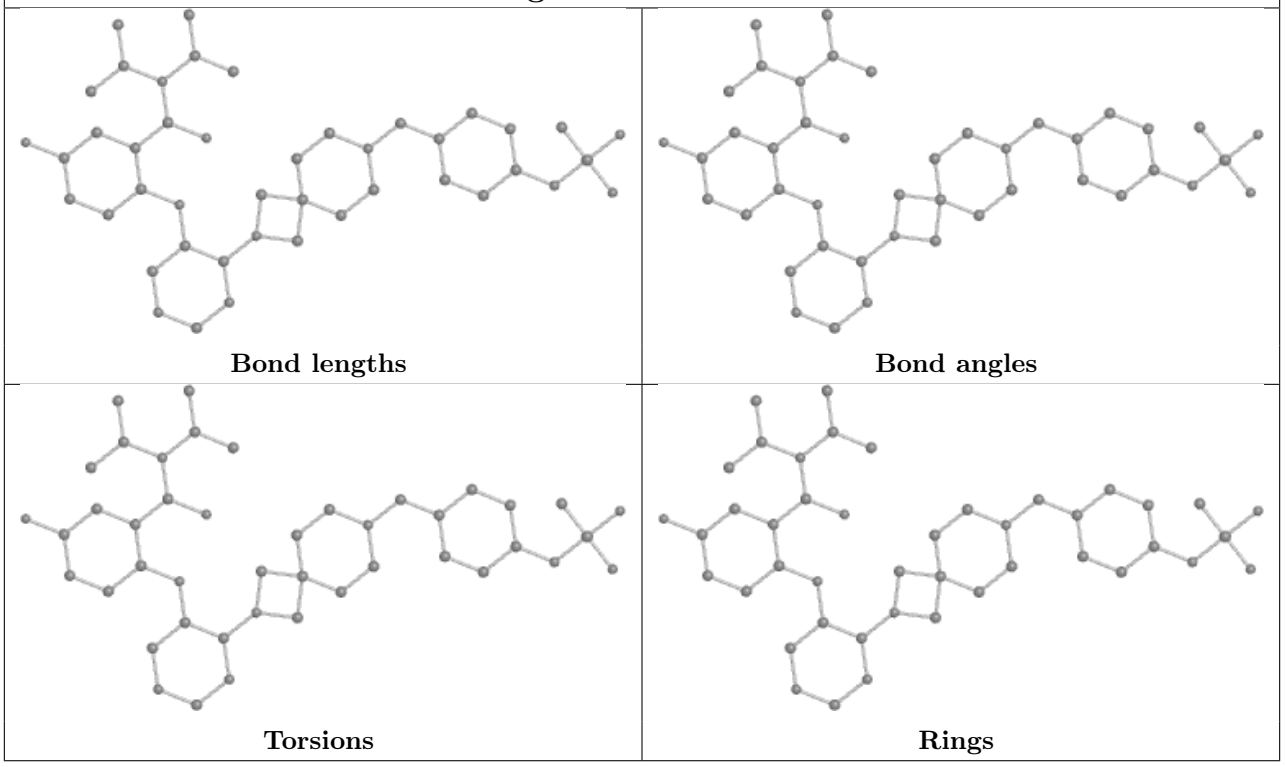
There are no torsion outliers.

There are no ring outliers.

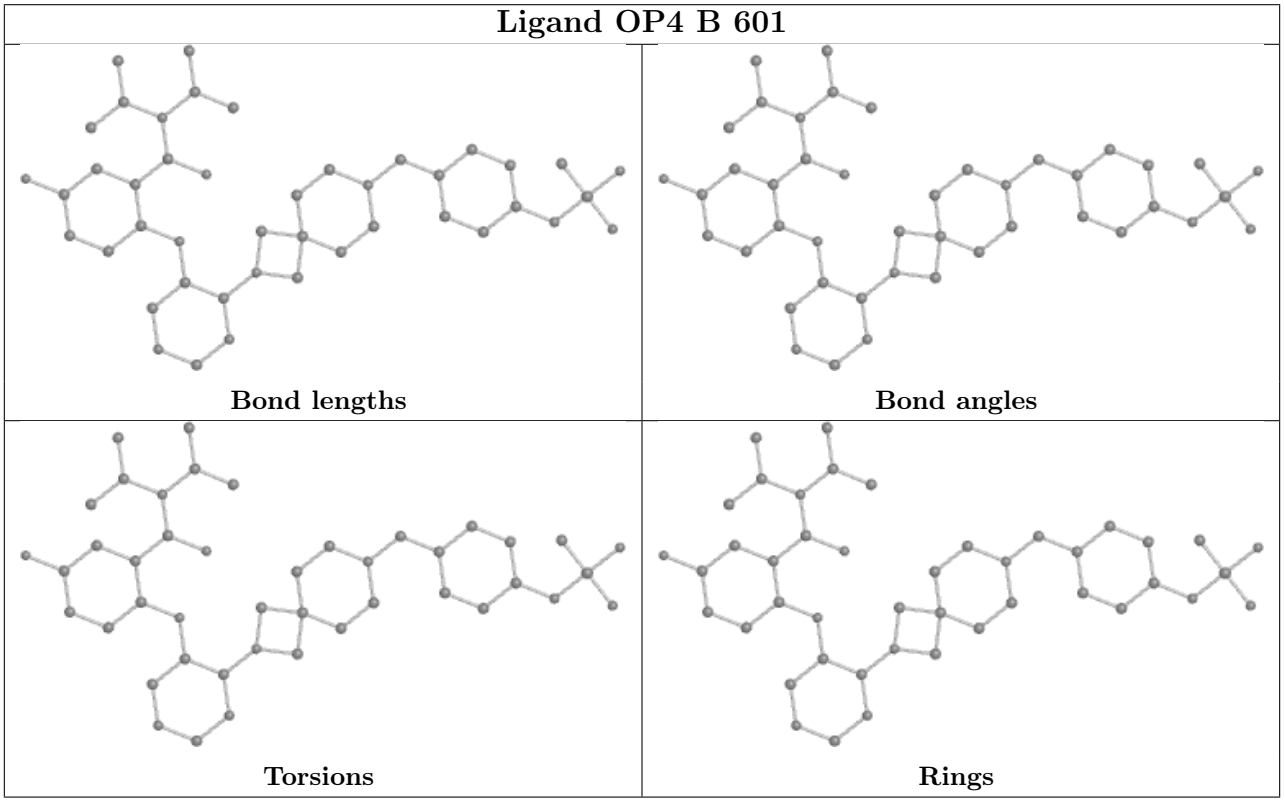
No monomer is involved in short contacts.

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.

Ligand OP4 A 601



Ligand OP4 B 601



4.7 Other polymers (i)

There are no such residues in this entry.

4.8 Polymer linkage issues (i)

There are no chain breaks in this entry.

5 Fit of model and data

5.1 Protein, DNA and RNA chains

EDS failed to run properly - this section is therefore empty.

5.2 Non-standard residues in protein, DNA, RNA chains

EDS failed to run properly - this section is therefore empty.

5.3 Carbohydrates

EDS failed to run properly - this section is therefore empty.

5.4 Ligands

EDS failed to run properly - this section is therefore empty.

5.5 Other polymers

EDS failed to run properly - this section is therefore empty.