WORLDWIDE wwPDB PROTEIN DATA BANK

Full wwPDB X-ray Structure Validation Report ⓘ

Oct 5, 2023 – 03:00 AM EDT

PDB ID : 6VEI
Title : Crystal Structure of Human Cytosolic Isocitrate Dehydrogenase (IDH1) R132H Mutant in Complex with NADPH and AG-881 (Vorasidenib) Inhibitor
Authors : Padyana, A.; Jin, L.
Deposited on : 2020-01-02
Resolution : 2.10 Å(reported)

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 2.10 Å.

There are no overall percentile quality scores available for this entry.

MolProbity and EDS failed to run properly - the sequence quality summary graphics cannot be shown.

2 Entry composition (i)

There are 10 unique types of molecules in this entry. The entry contains 7591 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 Isocitrate dehydrogenase [NADP] cytoplasmic.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	413	Total 3320	C 2119	N 555	O 628	S 18	0	11	0
1	B	417	Total 3362	C 2144	N 566	O 633	S 19	0	12	0

There are 24 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	132	HIS	ARG	engineered mutation	UNP O75874
A	415	SER	-	expression tag	UNP O75874
A	416	LEU	-	expression tag	UNP O75874
A	417	GLU	-	expression tag	UNP O75874
A	418	HIS	-	expression tag	UNP O75874
A	419	HIS	-	expression tag	UNP O75874
A	420	HIS	-	expression tag	UNP O75874
A	421	HIS	-	expression tag	UNP O75874
A	422	HIS	-	expression tag	UNP O75874
A	423	HIS	-	expression tag	UNP O75874
A	424	HIS	-	expression tag	UNP O75874
A	425	HIS	-	expression tag	UNP O75874
B	132	HIS	ARG	engineered mutation	UNP O75874
B	415	SER	-	expression tag	UNP O75874
B	416	LEU	-	expression tag	UNP O75874
B	417	GLU	-	expression tag	UNP O75874
B	418	HIS	-	expression tag	UNP O75874
B	419	HIS	-	expression tag	UNP O75874
B	420	HIS	-	expression tag	UNP O75874
B	421	HIS	-	expression tag	UNP O75874
B	422	HIS	-	expression tag	UNP O75874
B	423	HIS	-	expression tag	UNP O75874
B	424	HIS	-	expression tag	UNP O75874
B	425	HIS	-	expression tag	UNP O75874

- Molecule 2 is NADPH DIHYDRO-NICOTINAMIDE-ADENINE-DINUCLEOTIDE PHOSPHATE (three-letter code: NDP) (formula: $C_{21}H_{30}N_7O_{17}P_3$).
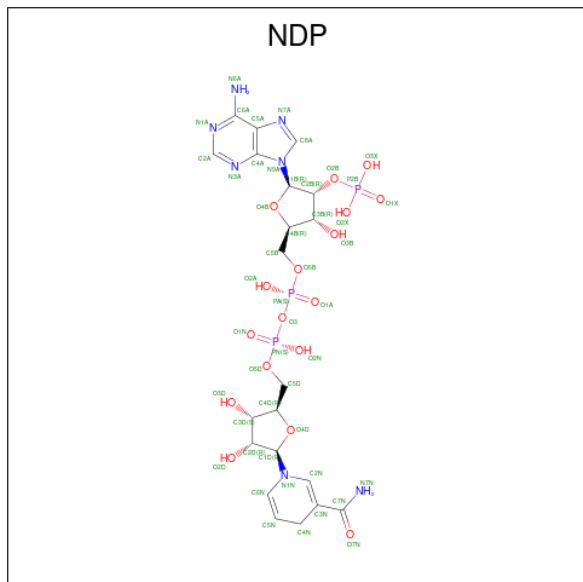
Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	N	O	P	0	1
			96	42	14	34	6		
2	B	1	Total	C	N	O	P	0	0
			48	21	7	17	3		

- Molecule 3 is SULFATE ION (three-letter code: SO4) (formula: O_4S).
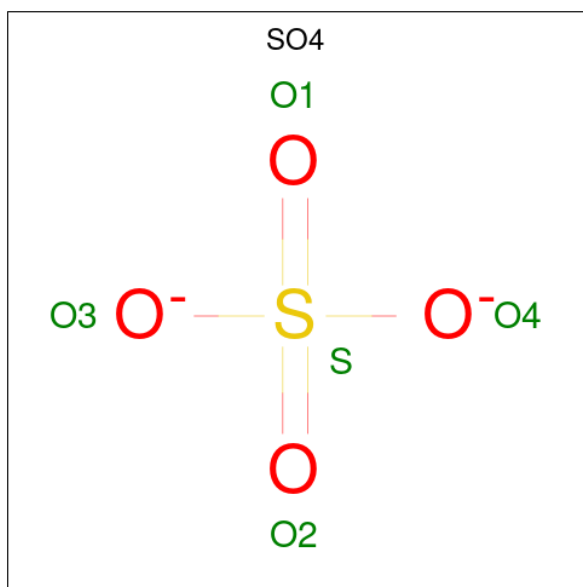
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
			Total	O	S		
3	A	1	5	4	1	0	0

- Molecule 4 is 3,6,9,12,15,18,21,24,27,30,33,36-dodecaoxaoctatriacontane-1,38-diol (three-letter code: 33O) (formula: $C_{26}H_{54}O_{14}$).

33O
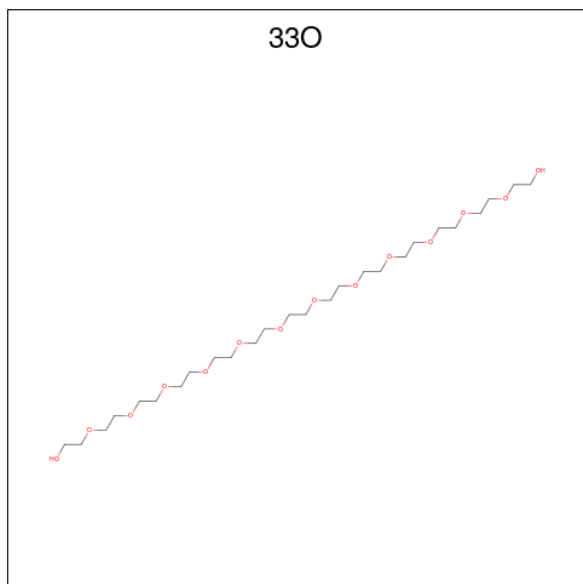
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
			Total	C	O		
4	A	1	40	26	14	0	0

- Molecule 5 is DI(HYDROXYETHYL)ETHER (three-letter code: PEG) (formula: $C_4H_{10}O_3$).

PEG
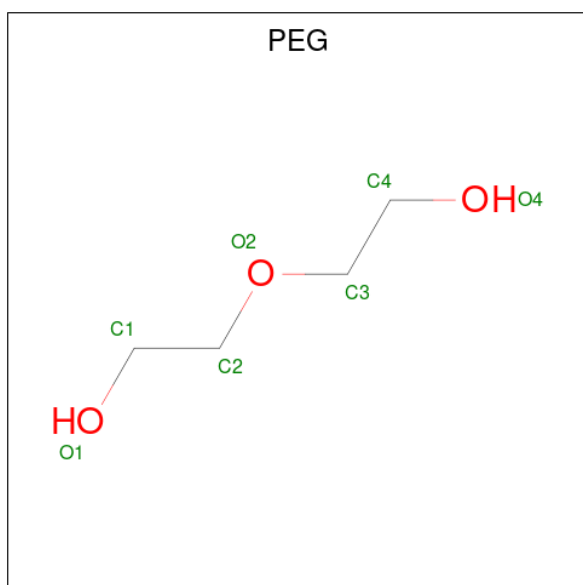
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
5	A	1	Total 7	C 4	O 3	0	0
5	A	1	Total 7	C 4	O 3	0	0
5	B	1	Total 14	C 8	O 6	0	1
5	B	1	Total 7	C 4	O 3	0	0

- Molecule 6 is ACETATE ION (three-letter code: ACT) (formula: $C_2H_3O_2$).
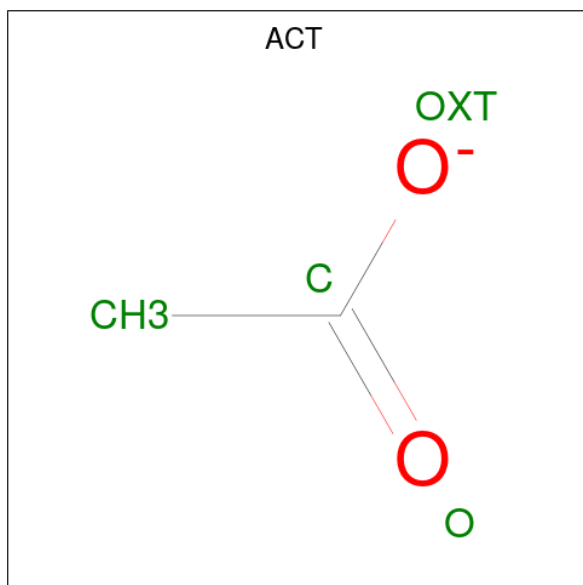
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
6	A	1	Total 4	C 2	O 2	0	0

- Molecule 7 is MALONIC ACID (three-letter code: MLA) (formula: $C_3H_4O_4$).
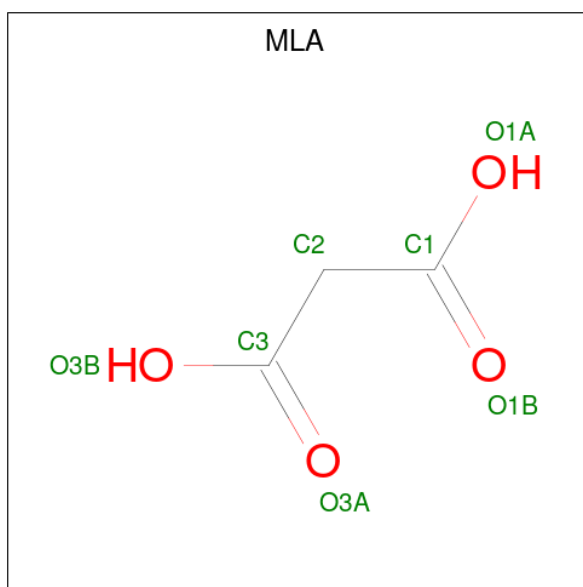
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
7	A	1	Total 7	C 3	O 4	0	0

- Molecule 8 is 6-(6-chloropyridin-2-yl)-N2,N4-bis[(2R)-1,1,1-trifluoropropan-2-yl]-1,3,5-tria zine-2,4-diamine (three-letter code: 9UO) (formula: $C_{14}H_{13}ClF_6N_6$) (labeled as "Ligand of Interest" by depositor).
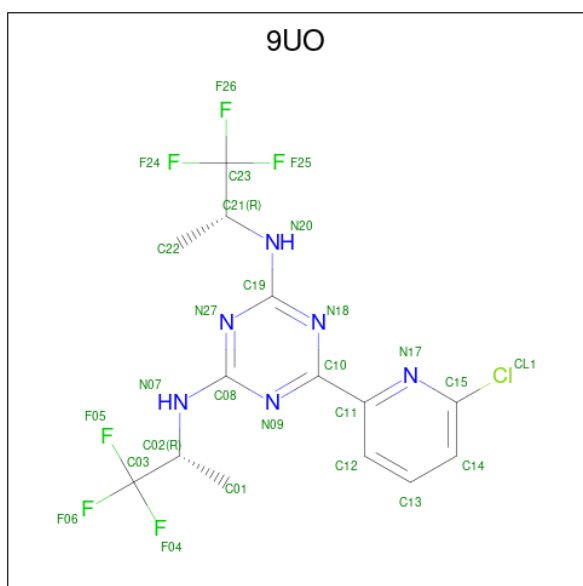
Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
8	B	1	Total 27	C 14	Cl 1	F 6	N 6	0	0

- Molecule 9 is D-MALATE (three-letter code: MLT) (formula: $C_4H_6O_5$).

MLT
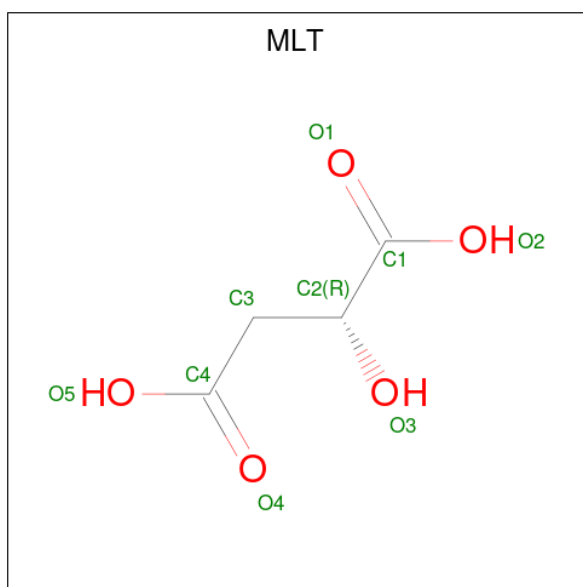
Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
9	B	1	Total 9	C 4	O 5	0	0

- Molecule 10 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
10	A	292	Total 292	O 292	0	0
10	B	346	Total 346	O 346	0	0

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

3 Data and refinement statistics (i)

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

Property	Value	Source
Space group	P 21 21 2	Depositor
Cell constants a, b, c, α, β, γ	117.21Å 85.10Å 96.66Å 90.00° 90.00° 90.00°	Depositor
Resolution (Å)	35.51 – 2.10	Depositor
% Data completeness (in resolution range)	99.8 (35.51-2.10)	Depositor
R_{merge}	0.10	Depositor
R_{sym}	(Not available)	Depositor
$<I/\sigma(I)>$ [1]	25.84 (at 2.10Å)	Xtriage
Refinement program	PHENIX 1.17.1_3660	Depositor
R, R_{free}	0.158 , 0.195	Depositor
Wilson B-factor (Å^2)	27.1	Xtriage
Anisotropy	0.025	Xtriage
L-test for twinning[2]	$<\lvert L \rvert> = 0.48$, $<L^2> = 0.31$	Xtriage
Estimated twinning fraction	No twinning to report.	Xtriage
Total number of atoms	7591	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 4.26% of the height of the origin peak. No significant pseudotranslation is detected.*

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[1]Intensities estimated from amplitudes.
[2]Theoretical values of $<\lvert L \rvert>$, $<L^2>$ 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 ⓘ

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

4.2 Too-close contacts ⓘ

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

4.3 Torsion angles ⓘ

4.3.1 Protein backbone ⓘ

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

4.3.2 Protein sidechains ⓘ

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

4.3.3 RNA ⓘ

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

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

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

4.5 Carbohydrates ⓘ

There are no monosaccharides in this entry.

4.6 Ligand geometry ⓘ

14 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	NDP	A	501[B]	-	45,52,52	0.51	0	53,80,80	0.51	1 (1%)
3	SO4	A	502	-	4,4,4	0.13	0	6,6,6	0.09	0
8	9UO	B	502	-	28,28,28	2.45	3 (10%)	32,42,42	3.13	10 (31%)
5	PEG	B	503[B]	-	6,6,6	0.48	0	5,5,5	0.28	0
5	PEG	A	504	-	6,6,6	0.48	0	5,5,5	0.28	0
7	MLA	A	507	-	6,6,6	1.35	0	7,7,7	1.21	0
4	33O	A	503	-	39,39,39	0.55	0	38,38,38	0.37	0
2	NDP	B	501	-	45,52,52	0.49	0	53,80,80	0.55	1 (1%)
2	NDP	A	501[A]	-	45,52,52	0.51	0	53,80,80	0.52	1 (1%)
5	PEG	A	505	-	6,6,6	0.49	0	5,5,5	0.28	0
9	MLT	B	505	-	8,8,8	1.05	0	10,10,10	1.60	1 (10%)
6	ACT	A	506	-	3,3,3	1.26	0	3,3,3	1.53	0
5	PEG	B	504	-	6,6,6	0.49	0	5,5,5	0.28	0
5	PEG	B	503[A]	-	6,6,6	0.48	0	5,5,5	0.26	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	NDP	A	501[B]	-	-	11/30/77/77	0/5/5/5
5	PEG	B	503[B]	-	-	1/4/4/4	-
5	PEG	A	504	-	-	0/4/4/4	-
7	MLA	A	507	-	-	2/4/4/4	-
4	33O	A	503	-	-	18/37/37/37	-
2	NDP	B	501	-	-	9/30/77/77	0/5/5/5
2	NDP	A	501[A]	-	-	6/30/77/77	0/5/5/5
5	PEG	A	505	-	-	1/4/4/4	-
9	MLT	B	505	-	-	2/8/8/8	-
8	9UO	B	502	-	-	0/24/24/24	0/2/2/2
5	PEG	B	504	-	-	2/4/4/4	-
5	PEG	B	503[A]	-	-	1/4/4/4	-

All (3) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
8	B	502	9UO	C08-N07	8.53	1.45	1.34
8	B	502	9UO	C19-N20	8.24	1.45	1.34
8	B	502	9UO	C15-CL1	2.03	1.78	1.74

All (14) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
8	B	502	9UO	C08-N09-C10	8.23	119.85	114.60
8	B	502	9UO	C19-N18-C10	7.90	119.64	114.60
8	B	502	9UO	C19-N20-C21	-7.72	118.19	124.53
8	B	502	9UO	C08-N07-C02	-5.01	120.42	124.53
8	B	502	9UO	N27-C08-N09	-4.06	119.80	126.23
8	B	502	9UO	N27-C19-N18	-3.77	120.26	126.23
8	B	502	9UO	C19-N27-C08	3.64	120.06	113.89
9	B	505	MLT	O2-C1-C2	3.41	120.21	112.72
8	B	502	9UO	N18-C10-N09	-3.00	120.38	125.23
2	A	501[B]	NDP	C5A-C6A-N6A	2.34	123.92	120.35
2	A	501[A]	NDP	C5A-C6A-N6A	2.32	123.88	120.35
2	B	501	NDP	C5A-C6A-N6A	2.30	123.85	120.35
8	B	502	9UO	C14-C15-N17	-2.21	121.43	125.50
8	B	502	9UO	N07-C08-N09	2.10	120.33	117.18

There are no chirality outliers.

All (53) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
2	A	501[A]	NDP	C5B-O5B-PA-O1A
2	A	501[A]	NDP	C5D-O5D-PN-O2N
2	A	501[B]	NDP	C5B-O5B-PA-O1A
2	A	501[B]	NDP	C5D-O5D-PN-O2N
2	B	501	NDP	C5B-O5B-PA-O1A
2	B	501	NDP	C5D-O5D-PN-O1N
2	B	501	NDP	C5D-O5D-PN-O2N
4	A	503	33O	O21-C43-C44-O22
4	A	503	33O	O22-C45-C46-O23
4	A	503	33O	O27-C55-C56-O28
4	A	503	33O	O25-C51-C52-O26
5	A	505	PEG	O1-C1-C2-O2
4	A	503	33O	O19-C39-C40-O20
4	A	503	33O	C61-C62-O31-C63
4	A	503	33O	O20-C41-C42-O21
2	A	501[B]	NDP	C2D-C1D-N1N-C2N

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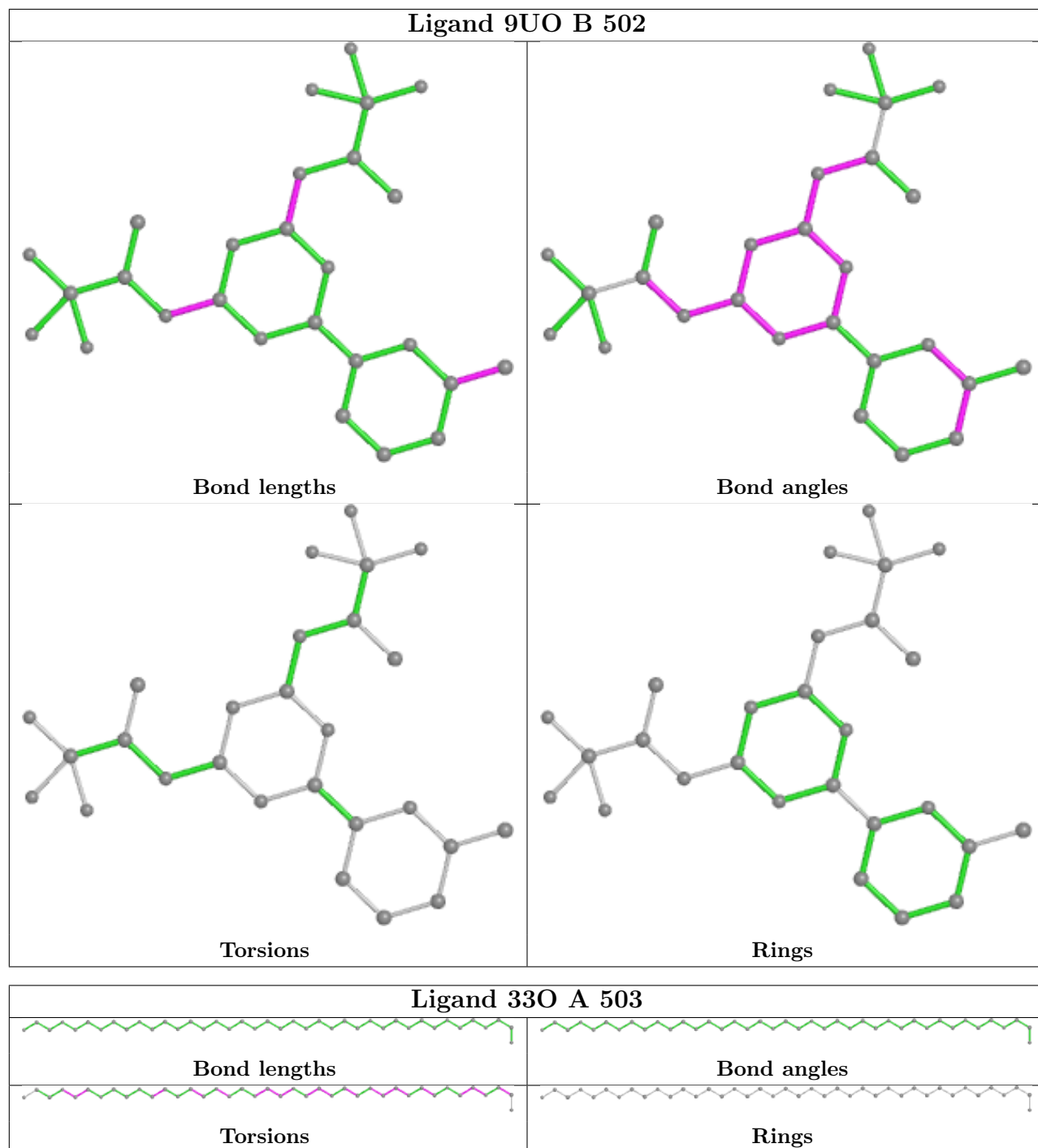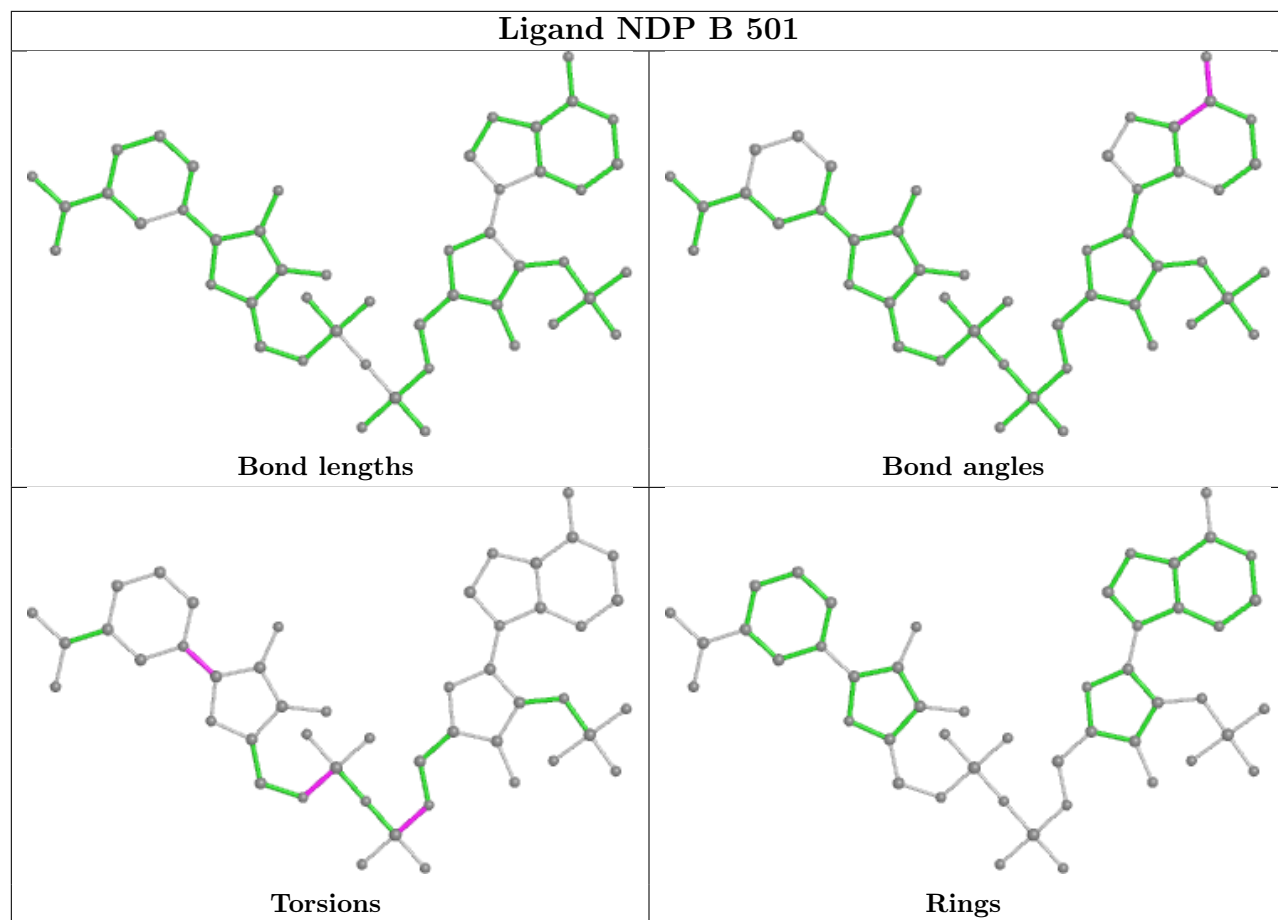| Mol	Chain	Res	Type	Atoms
4	A	503	33O	O28-C57-C58-O29
7	A	507	MLA	O1A-C1-C2-C3
2	A	501[B]	NDP	C2D-C1D-N1N-C6N
4	A	503	33O	O24-C49-C50-O25
7	A	507	MLA	O1B-C1-C2-C3
5	B	504	PEG	C1-C2-O2-C3
4	A	503	33O	C45-C46-O23-C47
2	A	501[B]	NDP	O4D-C1D-N1N-C2N
2	A	501[A]	NDP	C5B-O5B-PA-O3
2	A	501[A]	NDP	C5D-O5D-PN-O3
2	A	501[B]	NDP	C5B-O5B-PA-O3
2	A	501[B]	NDP	C5D-O5D-PN-O3
2	B	501	NDP	C5B-O5B-PA-O3
2	B	501	NDP	C5D-O5D-PN-O3
4	A	503	33O	C52-C51-O25-C50
5	B	503[A]	PEG	C4-C3-O2-C2
2	A	501[A]	NDP	O4D-C1D-N1N-C6N
2	A	501[A]	NDP	C5D-O5D-PN-O1N
2	A	501[B]	NDP	C5D-O5D-PN-O1N
2	A	501[B]	NDP	C2N-C3N-C7N-N7N
4	A	503	33O	O23-C47-C48-O24
2	A	501[B]	NDP	C2N-C3N-C7N-O7N
4	A	503	33O	C46-C45-O22-C44
4	A	503	33O	C53-C54-O27-C55
2	A	501[B]	NDP	O4D-C1D-N1N-C6N
2	B	501	NDP	O4D-C1D-N1N-C2N
2	B	501	NDP	C2D-C1D-N1N-C2N
4	A	503	33O	C42-C41-O20-C40
4	A	503	33O	C50-C49-O24-C48
5	B	504	PEG	C4-C3-O2-C2
2	B	501	NDP	O4D-C1D-N1N-C6N
2	B	501	NDP	C2D-C1D-N1N-C6N
5	B	503[B]	PEG	C4-C3-O2-C2
4	A	503	33O	O30-C61-C62-O31
9	B	505	MLT	O1-C1-C2-C3
9	B	505	MLT	O2-C1-C2-C3
4	A	503	33O	C51-C52-O26-C53

There are no ring outliers.
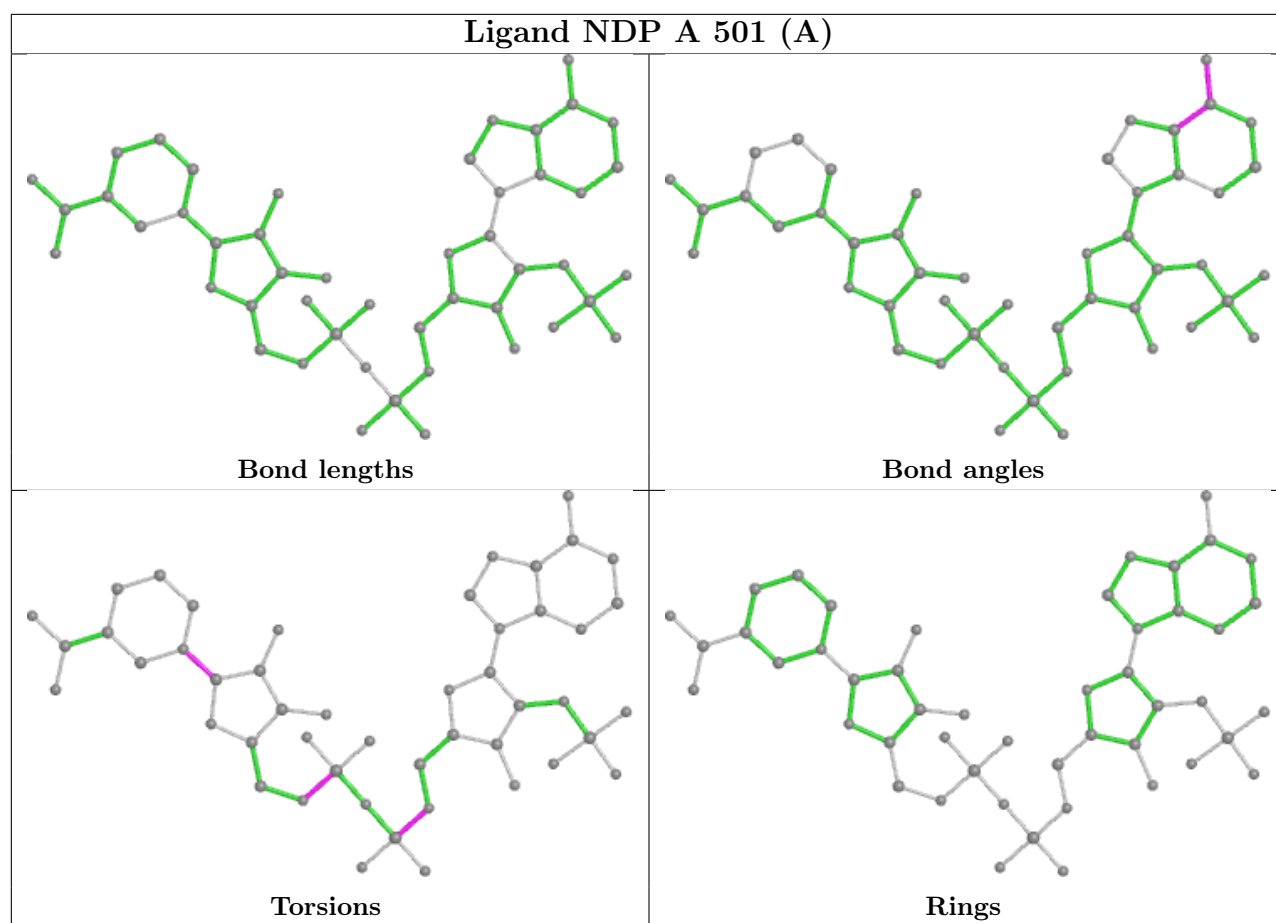
No monomer is involved in short contacts.

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 NDP A 501 (B)

Bond lengths

Bond angles

Torsions

Rings

Ligand 9UO B 502

Bond lengths

Bond angles

Torsions

Rings

Ligand 33O A 503

Bond lengths

Bond angles

Torsions

Rings

Ligand NDP B 501

Bond lengths

Bond angles

Torsions

Rings

Ligand NDP A 501 (A)
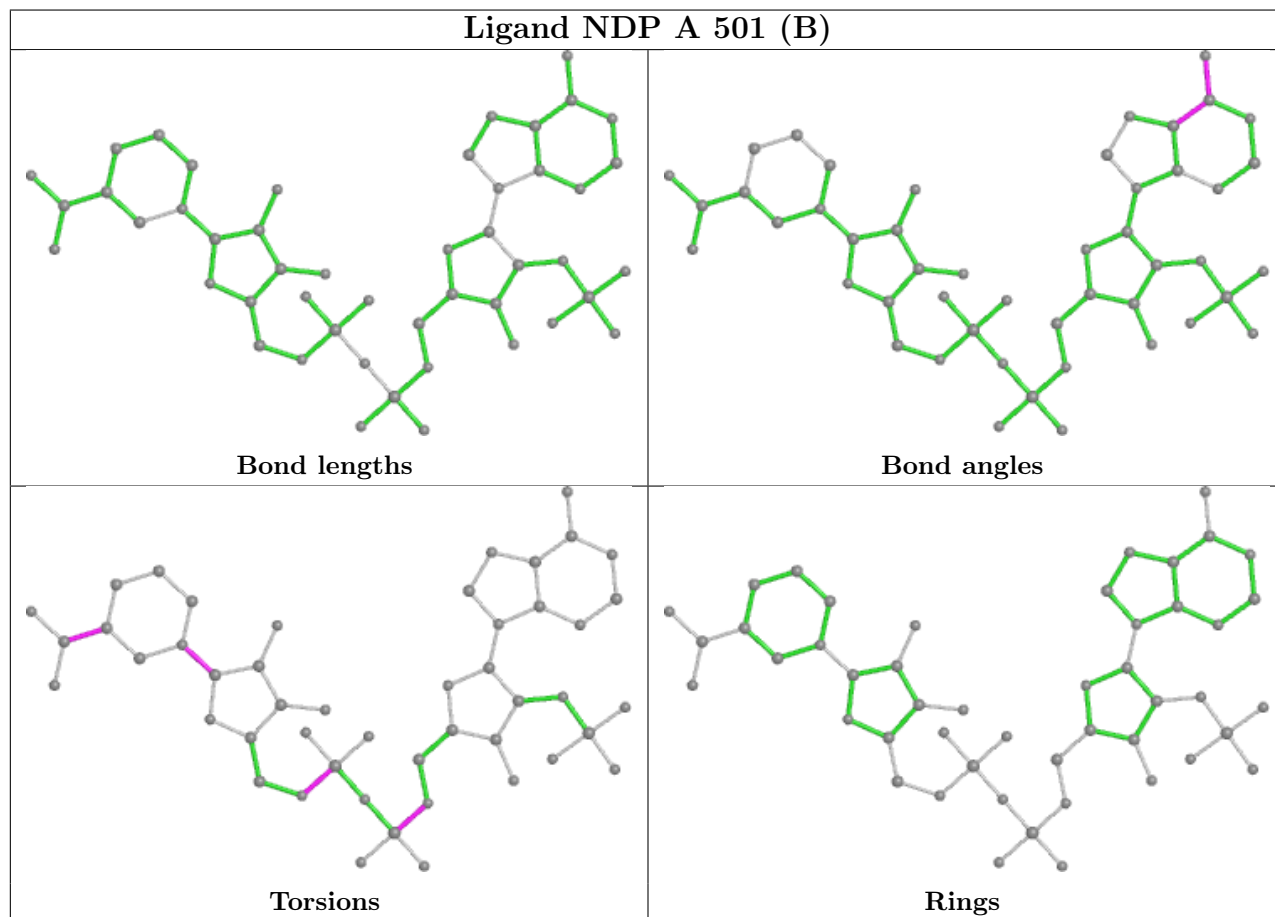
4.7 Other polymers ⓘ

There are no such residues in this entry.

4.8 Polymer linkage issues ⓘ

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.