Full wwPDB X-ray Structure Validation Report (i)

May 26, 2020 – 01:54 pm BST

PDB ID	:	1XH6
Title	:	Crystal Structures of Protein Kinase B Selective Inhibitors in Complex with Protein Kinase A and Mutants
Authors	:	Breitenlechner, C.B.; Friebe, W.-G.; Brunet, E.; Werner, G.; Graul, K.; Thomas, U.; Kuenkele, K.-P.; Schaefer, W.; Gassel, M.; Bossemeyer, D.; Huber, R.; Engh, R.A.; Masjost, B.
Deposited on	:	2004-09-17
Resolution	:	1.90 Å(reported)

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

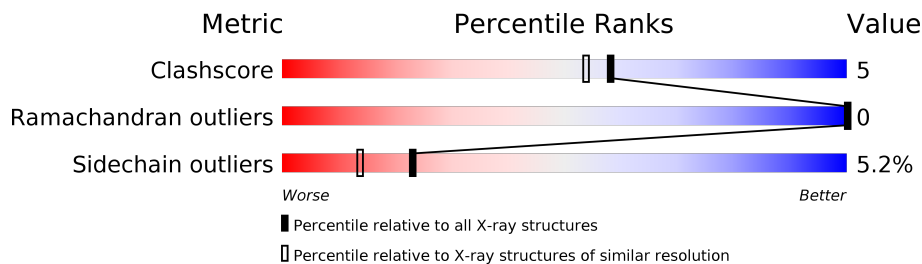|		
MolProbity	:	4.02b-467
Mogul	:	1.8.5 (274361), CSD as541be (2020)
Xtriage (Phenix)	:	NOT EXECUTED
EDS	:	NOT EXECUTED
buster-report	:	1.1.7 (2018)
Percentile statistics	:	20191225.v01 (using entries in the PDB archive December 25th 2019)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et al. (1996)
Validation Pipeline (wwPDB-VP)	:	2.11

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	Percentile Ranks	Value
Clashscore		5
Ramachandran outliers		0
Sidechain outliers		5.2%

Worse   *Better*

■ Percentile relative to all X-ray structures

▯ Percentile relative to X-ray structures of similar resolution

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)

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 on 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	350	79% 14% • 5%
2	B	20	85% 10% 5%

2 Entry composition (i)

There are 4 unique types of molecules in this entry. The entry contains 3221 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 cAMP-dependent protein kinase, alpha-catalytic subunit.

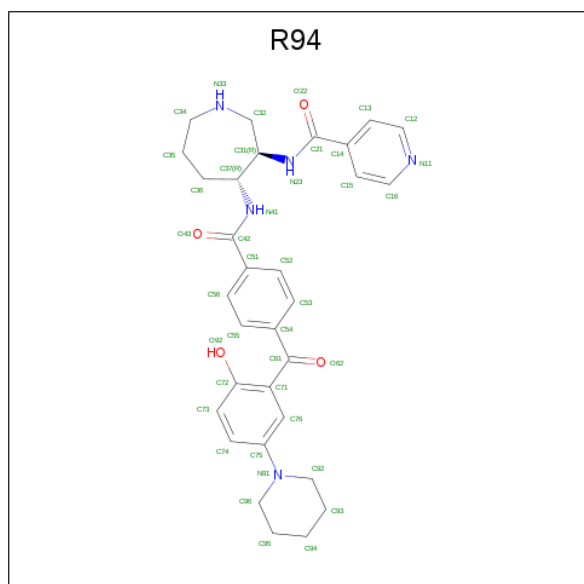| Mol	Chain	Residues	Atoms						ZeroOcc	AltConf	Trace
1	A	333	Total	C	N	O	P	S	0	0	0
			2747	1781	460	495	2	9			

There are 2 discrepancies between the modelled and reference sequences:

Chain	Residue	Modelled	Actual	Comment	Reference
A	197	TPO	THR	MODIFIED RESIDUE	UNP P00517
A	338	SEP	SER	MODIFIED RESIDUE	UNP P00517

- Molecule 2 is a protein called cAMP-dependent protein kinase inhibitor, alpha form.

Mol	Chain	Residues	Atoms				ZeroOcc	AltConf	Trace
2	B	20	Total	C	N	O	0	0	0
			157	94	32	31			

- Molecule 3 is N-(4-{[4-(2-HYDROXY-5-PIPERIDIN-1-YLBENZOYL)BENZOYL]AMINO} AZEPAN-3-YL)ISONICOTINAMIDE (three-letter code: R94) (formula: $C_{31}H_{35}N_5O_4$).

Mol	Chain	Residues	Atoms				ZeroOcc	AltConf
3	A	1	Total 40	C 31	N 5	O 4	0	0

- Molecule 4 is water.

Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	249	Total 249	O 249	0	0
4	B	28	Total 28	O 28	0	0

3 Residue-property plots (i)

These plots are drawn for all protein, RNA and DNA 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 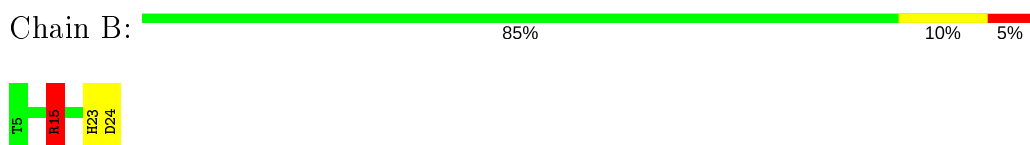the sequence view annotated by issues in geometry. Residues are color-coded according to the number of geometric quality criteria for which they contain at least one outlier: green = 0, yellow = 1, orange = 2 and red = 3 or more. Stretches of 2 or more consecutive residues without any outlier are shown 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: cAMP-dependent protein kinase, alpha-catalytic subunit

Chain A:

79%   14%   5%

GLY ASN ALA ALA ALA ALA LYS LYS GLY SER GLU GLN GLU SER VAL LYS GLU F18 E24 D25 D41 S53 F54 G55 R56 V57 M58 L59 Y69 D75 Q84 T88 L95 E107 M120 E121 R144 F145 Y146 H158 S159 L160 D161 D166 I180

F187 A188 K189 R190 T195 W196 T197 L198 E203 K217 D220 F239 A240 D241 I246 K249 P258 S259 H260 L268 L269 R270 V275 D276 G282 N283 L284 K285 K295 K309 K317 F318 K319 G322 D323 D328 D329 R336 F350
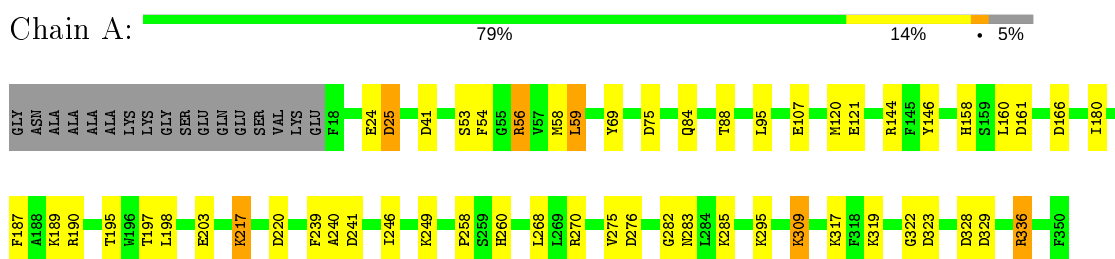
• Molecule 2: cAMP-dependent protein kinase inhibitor, alpha form

Chain B:

85%   10%   5%

T5 H15 H23 D24

4 Data and refinement statistics (i)

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

Property	Value	Source
Space group	P 21 21 21	Depositor
Cell constants a, b, c, α, β, γ	61.37Å　　76.98Å　　78.70Å 90.00°　　90.00°　　90.00°	Depositor
Resolution (Å)	25.00　–　1.90	Depositor
% Data completeness (in resolution range)	98.3 (25.00-1.90)	Depositor
R_{merge}	(Not available)	Depositor
R_{sym}	(Not available)	Depositor
Refinement program	REFMAC 5.1.24	Depositor
R, R_{free}	0.189　, 　0.249	Depositor
Estimated twinning fraction	No twinning to report.	Xtriage
Total number of atoms	3221	wwPDB-VP
Average B, all atoms (Å²)	26.0	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: TPO, R94, SEP

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	0.74	1/2797 (0.0%)	0.93	19/3771 (0.5%)
2	B	0.75	0/159	1.31	3/212 (1.4%)
All	All	0.74	1/2956 (0.0%)	0.96	22/3983 (0.6%)

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	58	MET	SD-CE	-6.41	1.42	1.77

All (22) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	144	ARG	NE-CZ-NH2	-10.62	114.99	120.30
2	B	15	ARG	NE-CZ-NH2	-10.41	115.10	120.30
1	A	144	ARG	NE-CZ-NH1	9.86	125.23	120.30
2	B	15	ARG	NE-CZ-NH1	9.23	124.91	120.30
1	A	270	ARG	NE-CZ-NH1	8.87	124.74	120.30
1	A	270	ARG	NE-CZ-NH2	-7.82	116.39	120.30
1	A	56	ARG	NE-CZ-NH1	7.73	124.17	120.30
1	A	56	ARG	NE-CZ-NH2	-7.72	116.44	120.30
1	A	190	ARG	NE-CZ-NH2	-6.95	116.83	120.30
1	A	328	ASP	CB-CG-OD2	6.89	124.50	118.30
1	A	161	ASP	CB-CG-OD2	5.96	123.67	118.30
2	B	24	ASP	CB-CG-OD2	5.89	123.60	118.30
1	A	41	ASP	CB-CG-OD2	5.84	123.55	118.30
1	A	329	ASP	CB-CG-OD2	5.69	123.42	118.30
1	A	323	ASP	CB-CG-OD2	5.63	123.36	118.30
1	A	190	ARG	NE-CZ-NH1	5.51	123.05	120.30
1	A	120	MET	CB-CA-C	-5.50	99.39	110.40
1	A	336	ARG	NE-CZ-NH2	-5.50	117.55	120.30

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Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
1	A	166	ASP	CB-CG-OD2	5.50	123.25	118.30
1	A	25	ASP	CB-CG-OD2	5.48	123.23	118.30
1	A	75	ASP	CB-CG-OD2	5.12	122.91	118.30
1	A	241	ASP	CB-CG-OD2	5.09	122.88	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	2747	0	2711	25	0
2	B	157	0	146	10	0
3	A	40	0	35	4	0
4	A	249	0	0	3	0
4	B	28	0	0	1	0
All	All	3221	0	2892	28	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 5.

All (28) 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:A:84:GLN:HE22	2:B:23:HIS:CD2	1.59	1.21
1:A:84:GLN:NE2	2:B:23:HIS:CD2	2.23	1.06
1:A:203:GLU:OE2	2:B:15:ARG:HD3	1.73	0.89
1:A:295:LYS:HE3	4:A:463:HOH:O	1.84	0.75
1:A:25:ASP:HB2	4:A:499:HOH:O	1.88	0.72
3:A:351:R94:H931	2:B:23:HIS:HB2	1.79	0.65
1:A:84:GLN:NE2	2:B:23:HIS:HD2	1.94	0.64
1:A:203:GLU:OE2	2:B:15:ARG:CD	2.46	0.63
1:A:187:PHE:HZ	3:A:351:R94:H932	1.65	0.62
1:A:246:ILE:HD11	2:B:15:ARG:HD2	1.84	0.59
1:A:84:GLN:HG3	3:A:351:R94:H921	1.86	0.57

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Atom-1	Atom-2	Interatomic distance (Å)	Clash overlap (Å)
1:A:158:HIS:HE1	1:A:220:ASP:OD2	1.90	0.54
1:A:146:TYR:HB3	1:A:180:ILE:HD11	1.90	0.54
1:A:121:GLU:CD	4:A:422:HOH:O	2.46	0.53
1:A:217:LYS:NZ	1:A:282:GLY:O	2.45	0.50
1:A:197:TPO:CG2	2:B:23:HIS:HE1	2.25	0.49
1:A:69:TYR:CE1	1:A:107:GLU:HG3	2.48	0.49
1:A:217:LYS:NZ	1:A:283:ASN:HA	2.28	0.48
1:A:258:PRO:HB2	1:A:260:HIS:CD2	2.50	0.47
1:A:240:ALA:O	2:B:15:ARG:HG3	2.15	0.46
1:A:239:PHE:O	1:A:249:LYS:NZ	2.42	0.46
1:A:84:GLN:O	1:A:88:THR:HG23	2.16	0.45
2:B:15:ARG:NH2	4:B:52:HOH:O	2.50	0.45
1:A:275:VAL:HG13	1:A:276:ASP:N	2.32	0.44
3:A:351:R94:H74	3:A:351:R94:H922	1.83	0.43
1:A:59:LEU:HD11	1:A:322:GLY:HA2	2.01	0.42
1:A:189:LYS:HE2	1:A:195:THR:OG1	2.21	0.41
1:A:309:LYS:HE2	1:A:309:LYS:HB2	1.93	0.40

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	329/350 (94%)	318 (97%)	11 (3%)	0	100	100
2	B	18/20 (90%)	18 (100%)	0	0	100	100
All	All	347/370 (94%)	336 (97%)	11 (3%)	0	100	100

There are no Ramachandran outliers to report.

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	290/303 (96%)	275 (95%)	15 (5%)	23	14
2	B	15/15 (100%)	14 (93%)	1 (7%)	16	7
All	All	305/318 (96%)	289 (95%)	16 (5%)	23	14

All (16) residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	24	GLU
1	A	53	SER
1	A	54	PHE
1	A	56	ARG
1	A	59	LEU
1	A	95	LEU
1	A	160	LEU
1	A	198	LEU
1	A	217	LYS
1	A	268	LEU
1	A	285	LYS
1	A	309	LYS
1	A	317	LYS
1	A	319	LYS
1	A	336	ARG
2	B	15	ARG

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (5) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	42	GLN
1	A	84	GLN
1	A	113	ASN
1	A	158	HIS
2	B	23	HIS

5.3.3　RNA (i)

There are no RNA molecules in this entry.

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

2 non-standard protein/DNA/RNA residues 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	$\#|Z| > 2$
1	SEP	A	338	1	8,9,10	1.40	1 (12%)	8,12,14	1.78	1 (12%)
1	TPO	A	197	1	8,10,11	0.79	0	10,14,16	1.26	1 (10%)

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
1	SEP	A	338	1	-	3/5/8/10	-
1	TPO	A	197	1	-	0/9/11/13	-

All (1) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	338	SEP	P-O1P	3.05	1.60	1.50

All (2) bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	338	SEP	OG-CB-CA	4.38	112.41	108.14
1	A	197	TPO	P-OG1-CB	-2.14	116.75	123.21

There are no chirality outliers.

All (3) torsion outliers are listed below:

Mol	Chain	Res	Type	Atoms
1	A	338	SEP	N-CA-CB-OG
1	A	338	SEP	CA-CB-OG-P
1	A	338	SEP	CB-OG-P-O2P

There are no ring outliers.

1 monomer is involved in 1 short contact:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
1	A	197	TPO	1	0

5.5 Carbohydrates (i)

There are no carbohydrates in this entry.

5.6 Ligand geometry (i)

1 ligand is 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	#$|Z| > 2$
3	R94	A	351	-	41,44,44	1.29	4 (9%)	52,60,60	1.45	6 (11%)

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
3	R94	A	351	-	-	0/28/48/48	0/5/5/5

All (4) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	351	R94	C32-N33	4.39	1.51	1.47

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Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
3	A	351	R94	C42-N41	2.40	1.39	1.34
3	A	351	R94	C21-N23	2.34	1.39	1.34
3	A	351	R94	C37-N41	2.18	1.50	1.46

All (6) bond angle outliers are listed below:

| Mol	Chain	Res	Type	Atoms	Z	Observed(^{o})	Ideal(^{o})
3	A	351	R94	C72-C71-C61	5.52	124.58	119.96
3	A	351	R94	C71-C61-C54	4.48	126.92	119.53
3	A	351	R94	O62-C61-C54	-3.52	114.51	120.12
3	A	351	R94	O22-C21-N23	-2.37	118.09	122.45
3	A	351	R94	C14-C21-N23	2.30	121.47	117.06
3	A	351	R94	C96-N91-C92	2.26	116.51	111.52

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

1 monomer is involved in 4 short contacts:

Mol	Chain	Res	Type	Clashes	Symm-Clashes
3	A	351	R94	4	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 R94 A 351

Bond lengths

Bond angles

Torsions

Rings
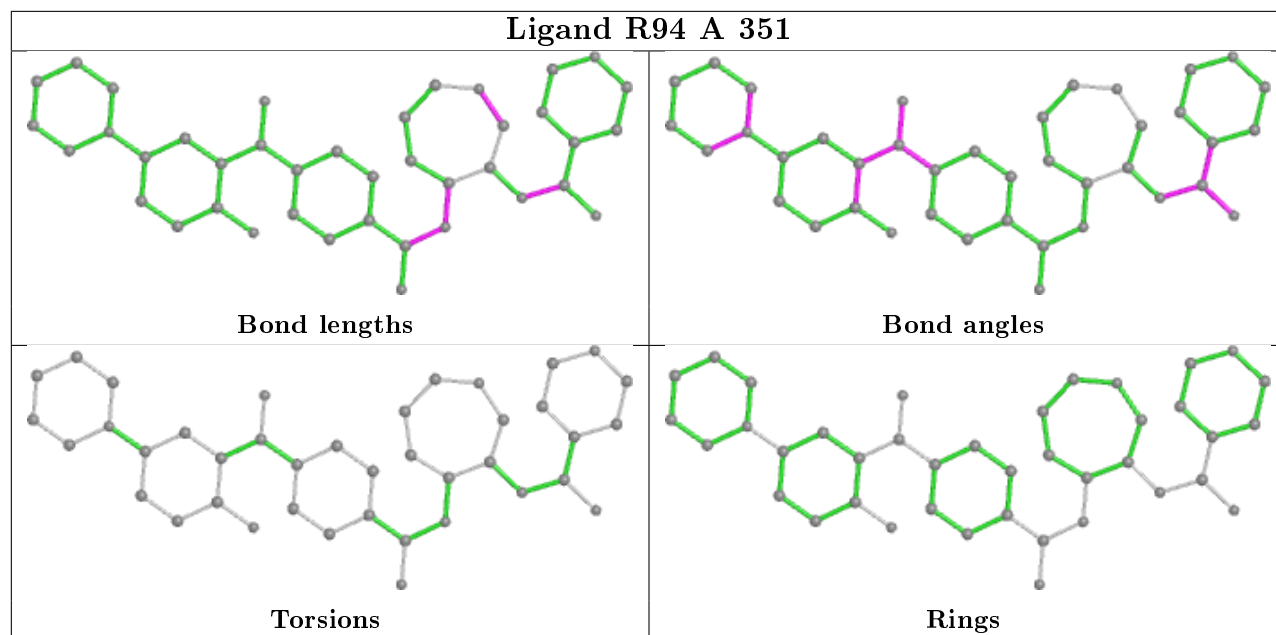
5.7 Other polymers (i)

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.