



wwPDB X-ray Structure Validation Summary Report i

Mar 1, 2014 – 12:14 AM GMT

PDB ID : 4M6P
Title : Identification of Amides Derived From 1H-Pyrazolo[3,4-b]pyridine-5-carboxylic Acid as Potent Inhibitors of Human Nicotinamide Phosphoribosyltransferase (NAMPT)
Authors : Giannetti, A.M.; Zheng, X.; Skelton, N.; Wang, W.; Bravo, B.; Feng, Y.; Gunzner-Toste, J.; Ho, Y.; Hua, R.; Wang, C.; Zhao, Q.; Liederer, B.M.; Liu, Y.; O'Brien, T.; Oeh, J.; Sampath, D.; Shen, Y.; Wang, L.; Wu, H.; Xiao, Y.; Yuen, P.; Zak, M.; Zhao, G.; Dragovich, P.S.
Deposited on : 2013-08-10
Resolution : 1.75 Å (reported)

This is a wwPDB validation summary report for a publicly released PDB entry.

We welcome your comments at validation@mail.wwpdb.org

A user guide is available at <http://wwpdb.org/ValidationPDFNotes.html>

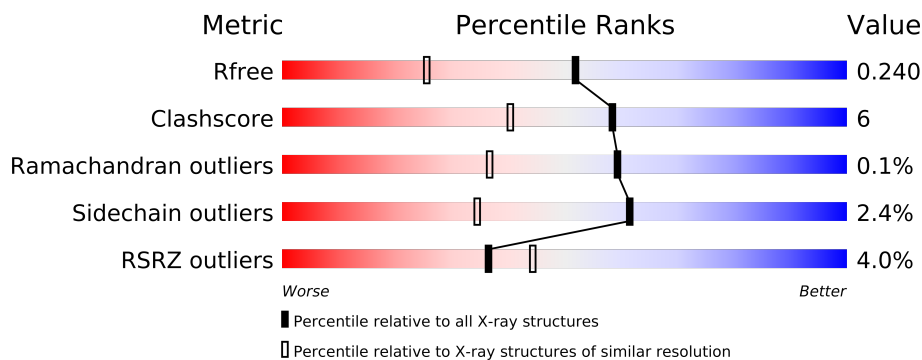
The following versions of software and data (see [references](#)) were used in the production of this report:

MolProbity	:	4.02b-467
Mogul	:	1.15 2013
Xtriage (Phenix)	:	dev-1323
EDS	:	stable22639
Percentile statistics	:	21963
Refmac	:	5.8.0049
CCP4	:	6.3.0 (Settle)
Ideal geometry (proteins)	:	Engh & Huber (2001)
Ideal geometry (DNA, RNA)	:	Parkinson et. al. (1996)
Validation Pipeline (wwPDB-VP)	:	stable22683

1 Overall quality at a glance

The reported resolution of this entry is 1.75 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}	66092	1134 (1.76-1.76)
Clashscore	79885	1304 (1.76-1.76)
Ramachandran outliers	78287	1288 (1.76-1.76)
Sidechain outliers	78261	1288 (1.76-1.76)
RSRZ outliers	66119	1135 (1.76-1.76)

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. The upper red bar (where present) indicates the fraction of residues that have poor fit to the electron density.

Mol	Chain	Length	Quality of chain
1	A	501	
1	B	501	

2 Entry composition

There are 4 unique types of molecules in this entry. The entry contains 8808 atoms, of which 0 are hydrogen and 0 are deuterium.

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.

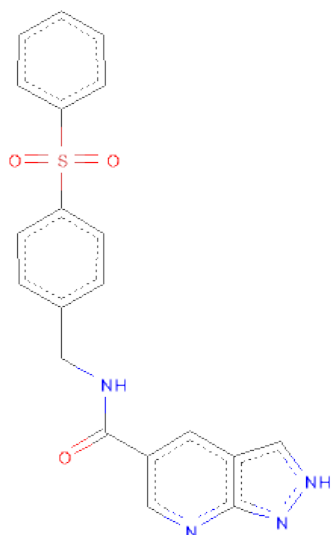
- Molecule 1 is a protein called Nicotinamide phosphoribosyltransferase.

Mol	Chain	Residues	Atoms					ZeroOcc	AltConf	Trace
1	A	472	Total	C	N	O	S	0	1	0
			3769	2424	622	716	7			
1	B	471	Total	C	N	O	S	0	1	0
			3773	2427	622	717	7			

There are 20 discrepancies between the modelled and reference sequences:

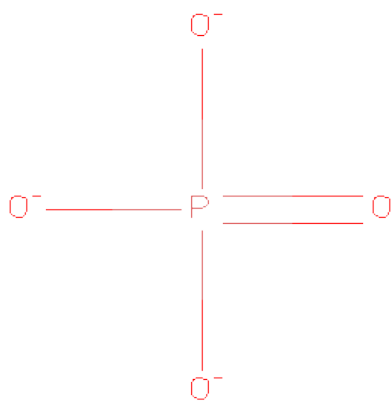
Chain	Residue	Modelled	Actual	Comment	Reference
A	492	LEU	-	EXPRESSION TAG	UNP P43490
A	493	GLU	-	EXPRESSION TAG	UNP P43490
A	494	HIS	-	EXPRESSION TAG	UNP P43490
A	495	HIS	-	EXPRESSION TAG	UNP P43490
A	496	HIS	-	EXPRESSION TAG	UNP P43490
A	497	HIS	-	EXPRESSION TAG	UNP P43490
A	498	HIS	-	EXPRESSION TAG	UNP P43490
A	499	HIS	-	EXPRESSION TAG	UNP P43490
A	500	HIS	-	EXPRESSION TAG	UNP P43490
A	501	HIS	-	EXPRESSION TAG	UNP P43490
B	492	LEU	-	EXPRESSION TAG	UNP P43490
B	493	GLU	-	EXPRESSION TAG	UNP P43490
B	494	HIS	-	EXPRESSION TAG	UNP P43490
B	495	HIS	-	EXPRESSION TAG	UNP P43490
B	496	HIS	-	EXPRESSION TAG	UNP P43490
B	497	HIS	-	EXPRESSION TAG	UNP P43490
B	498	HIS	-	EXPRESSION TAG	UNP P43490
B	499	HIS	-	EXPRESSION TAG	UNP P43490
B	500	HIS	-	EXPRESSION TAG	UNP P43490
B	501	HIS	-	EXPRESSION TAG	UNP P43490

- Molecule 2 is N-[4-(PHENYLSULFONYL)BENZYL]-2H-PYRAZOLO[3,4-B]PYRIDINE-5-CARBOXAMIDE (three-letter code: 20R) (formula: C₂₀H₁₆N₄O₃S).



Mol	Chain	Residues	Atoms					ZeroOcc	AltConf
2	A	1	Total	C	N	O	S	0	0
			28	20	4	3	1		
2	B	1	Total	C	N	O	S	0	0
			28	20	4	3	1		

- Molecule 3 is PHOSPHATE ION (three-letter code: PO4) (formula: O_4P).



Mol	Chain	Residues	Atoms			ZeroOcc	AltConf
3	A	1	Total	O	P	0	0
			5	4	1		
3	B	1	Total	O	P	0	0
			5	4	1		

- Molecule 4 is water.

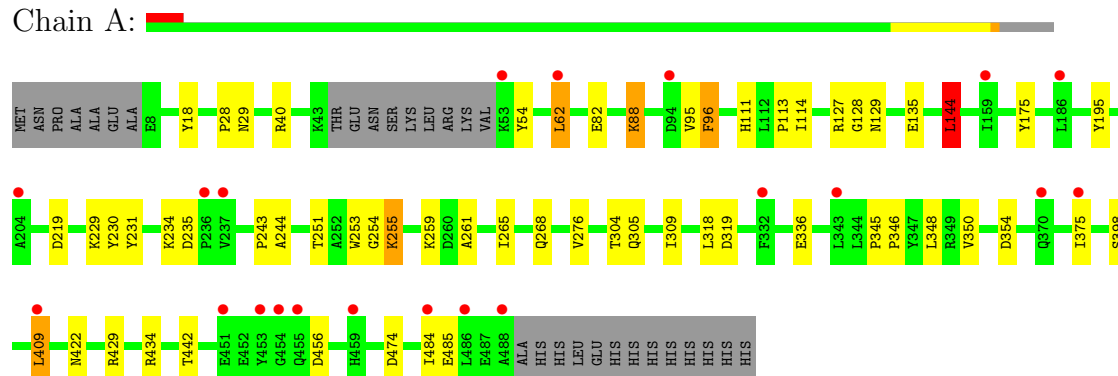
Mol	Chain	Residues	Atoms		ZeroOcc	AltConf
4	A	601	Total 601	O 601	0	0
4	B	599	Total 599	O 599	0	0

3 Residue-property plots

These plots are drawn for all protein, RNA and DNA chains in the entry. The first graphic for a chain summarises the proportions of errors 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.

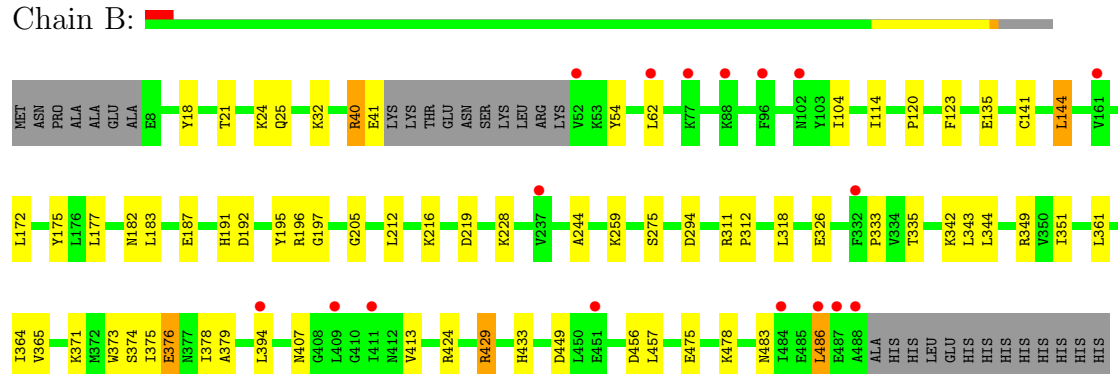
- Molecule 1: Nicotinamide phosphoribosyltransferase

Chain A:



- Molecule 1: Nicotinamide phosphoribosyltransferase

Chain B:



4 Data and refinement statistics

Property	Value	Source
Space group	P 1 21 1	Depositor
Cell constants a, b, c, α , β , γ	60.63Å 106.36Å 83.11Å 90.00° 96.43° 90.00°	Depositor
Resolution (Å)	46.35 – 1.75 46.35 – 1.75	Depositor EDS
% Data completeness (in resolution range)	99.7 (46.35-1.75) 99.8 (46.35-1.75)	Depositor EDS
R_{merge}	(Not available)	Depositor
R_{sym}	(Not available)	Depositor
$\langle I/\sigma(I) \rangle$ ¹	2.54 (at 1.75Å)	Xtriage
Refinement program	PHENIX (phenix.refine: 1.8.2_1309)	Depositor
R, R_{free}	0.192 , 0.241 0.192 , 0.240	Depositor DCC
R_{free} test set	5261 reflections (4.99%)	DCC
Wilson B-factor (Å ²)	15.4	Xtriage
Anisotropy	0.495	Xtriage
Bulk solvent k_{sol} (e/Å ³), B_{sol} (Å ²)	0.35 , 35.2	EDS
Estimated twinning fraction	No twinning to report.	Xtriage
L-test for twinning	$\langle L \rangle = 0.50$, $\langle L^2 \rangle = 0.33$	Xtriage
Outliers	0 of 105479 reflections	Xtriage
F_o, F_c correlation	0.94	EDS
Total number of atoms	8808	wwPDB-VP
Average B, all atoms (Å ²)	18.0	wwPDB-VP

Xtriage's analysis on translational NCS is as follows: *The largest off-origin peak in the Patterson function is 15.35% of the height of the origin peak. No significant pseudotranslation is detected.*

¹Intensities estimated from amplitudes.

5 Model quality

5.1 Standard geometry

Bond lengths and bond angles in the following residue types are not validated in this section: PO4, 20R

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	0.88	1/3857 (0.0%)	0.85	6/5229 (0.1%)
1	B	0.84	1/3861 (0.0%)	0.84	4/5232 (0.1%)
All	All	0.86	2/7718 (0.0%)	0.85	10/10461 (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 mainchain group or atoms of a sidechain that are expected to be planar.

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

All (2) bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
1	A	127	ARG	CG-CD	-5.45	1.38	1.51
1	B	376	GLU	CB-CG	-5.39	1.42	1.52

The worst 5 of 10 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
1	A	456	ASP	CB-CG-OD2	7.48	125.03	118.30
1	A	409	LEU	CA-CB-CG	7.42	132.37	115.30
1	B	429	ARG	NE-CZ-NH2	-6.87	116.87	120.30
1	A	127	ARG	CA-CB-CG	-6.75	98.55	113.40
1	A	62	LEU	CB-CG-CD2	6.04	121.28	111.00

There are no chirality outliers.

All (1) planarity outliers are listed below:

Mol	Chain	Res	Type	Group
1	B	40	ARG	Peptide

5.2 Close contacts ⓘ

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 hydrogens added by MolProbity. The Clashes column lists the number of clashes within the asymmetric unit, and the number in parentheses is this value normalized per 1000 atoms of the molecule in the chain. The Symm-Clashes column gives symmetry related clashes, in the same way as for the Clashes column.

Mol	Chain	Non-H	H(model)	H(added)	Clashes	Symm-Clashes
1	A	3769	0	3730	43	0
1	B	3773	0	3745	51	0
2	A	28	0	16	0	0
2	B	28	0	16	1	0
3	A	5	0	0	1	0
3	B	5	0	0	1	0
4	A	601	0	0	25	3
4	B	599	0	0	26	3
All	All	8808	0	7507	94	3

Clashscore is defined as the number of clashes calculated for the entry per 1000 atoms (including hydrogens) of the entry. The overall clashscore for this entry is 6.

The worst 5 of 94 close contacts within the same asymmetric unit are listed below.

Atom-1	Atom-2	Distance(Å)	Clash(Å)
1:B:343:LEU:HB3	4:B:1162:HOH:O	1.65	0.97
1:B:40:ARG:NH2	4:B:864:HOH:O	2.05	0.88
1:A:40:ARG:HD3	1:A:422:ASN:O	1.75	0.86
1:A:276:VAL:N	4:A:1263:HOH:O	2.11	0.83
1:B:343:LEU:HD13	1:B:376:GLU:HG3	1.59	0.81

All (3) 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	Distance(Å)	Clash(Å)
4:A:1198:HOH:O	4:B:1229:HOH:O[1_554]	2.11	0.09
4:A:1274:HOH:O	4:B:1262:HOH:O[2_645]	2.12	0.08
4:A:1252:HOH:O	4:B:1273:HOH:O[2_646]	2.17	0.03

5.3 Torsion angles

5.3.1 Protein backbone ⓘ

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	469/501 (94%)	459 (98%)	9 (2%)	1 (0%)	56	34
1	B	468/501 (93%)	455 (97%)	13 (3%)	0	100	100
All	All	937/1002 (94%)	914 (98%)	22 (2%)	1 (0%)	59	37

All (1) Ramachandran outliers are listed below:

Mol	Chain	Res	Type
1	A	96	PHE

5.3.2 Protein sidechains ⓘ

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	412/440 (94%)	401 (97%)	11 (3%)	57	30
1	B	414/440 (94%)	405 (98%)	9 (2%)	64	38
All	All	826/880 (94%)	806 (98%)	20 (2%)	61	34

5 of 20 residues with a non-rotameric sidechain are listed below:

Mol	Chain	Res	Type
1	A	409	LEU
1	A	434	ARG
1	B	212	LEU
1	A	259	LYS
1	A	318	LEU

Some sidechains can be flipped to improve hydrogen bonding and reduce clashes. All (2) such sidechains are listed below:

Mol	Chain	Res	Type
1	A	483	ASN
1	B	483	ASN

5.3.3 RNA ⓘ

There are no RNA chains in this entry.

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

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

5.5 Carbohydrates ⓘ

There are no carbohydrates in this entry.

5.6 Ligand geometry ⓘ

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	20R	A	601	-	31,31,31	1.51	2 (6%)	42,44,44	2.14	11 (26%)
3	PO4	A	602	-	4,4,4	0.25	0	6,6,6	0.35	0
2	20R	B	601	-	31,31,31	1.56	5 (16%)	42,44,44	2.45	13 (30%)
3	PO4	B	602	-	4,4,4	0.18	0	6,6,6	0.32	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	20R	A	601	-	-	0/21/21/21	0/2/4/4

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Mol	Type	Chain	Res	Link	Chirals	Torsions	Rings
3	PO4	A	602	-	-	0/0/0/0	0/0/0/0
2	20R	B	601	-	-	0/21/21/21	0/2/4/4
3	PO4	B	602	-	-	0/0/0/0	0/0/0/0

The worst 5 of 7 bond length outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(Å)	Ideal(Å)
2	B	601	20R	C23-N24	-6.18	1.30	1.33
2	A	601	20R	C23-N24	-6.11	1.30	1.33
2	A	601	20R	C27-N28	-3.35	1.31	1.37
2	B	601	20R	C27-N28	-3.10	1.32	1.37
2	B	601	20R	O9-S7	-2.49	1.40	1.44

The worst 5 of 24 bond angle outliers are listed below:

Mol	Chain	Res	Type	Atoms	Z	Observed(°)	Ideal(°)
2	B	601	20R	C20-C29-N28	-7.92	119.79	125.31
2	B	601	20R	O8-S7-C4	-6.20	101.85	107.95
2	A	601	20R	C20-C29-N28	-6.02	121.11	125.31
2	A	601	20R	O9-S7-C10	5.51	113.38	107.95
2	B	601	20R	C29-N28-C27	4.95	122.41	116.85

There are no chirality outliers.

There are no torsion outliers.

There are no ring outliers.

5.7 Other polymers ⓘ

There are no such residues in this entry.

5.8 Polymer linkage issues

There are no chain breaks in this entry.

6 Fit of model and data ⓘ

6.1 Protein, DNA and RNA chains ⓘ

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	472/501 (94%)	0.68	21 (4%)	33 40	6, 15, 29, 51	0
1	B	471/501 (94%)	0.65	17 (3%)	41 48	6, 14, 29, 66	0
All	All	943/1002 (94%)	0.67	38 (4%)	36 44	6, 14, 29, 66	0

The worst 5 of 38 RSRZ outliers are listed below:

Mol	Chain	Res	Type	RSRZ
1	B	52	VAL	7.0
1	B	486	LEU	4.6
1	A	53	LYS	4.4
1	A	486	LEU	4.4
1	B	409	LEU	3.5

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

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

6.3 Carbohydrates ⓘ

There are no carbohydrates in this entry.

6.4 Ligands ⓘ

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. LLDF column lists the quality of electron density of the group with respect to its neighbouring residues in protein, DNA or RNA chains. 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	RSR	LLDF	B-factors(\AA^2)	Q<0.9
3	PO4	A	602	5/5	0.17	1.66	32,33,43,44	0
3	PO4	B	602	5/5	0.15	1.16	26,34,36,42	0
2	20R	A	601	28/28	0.13	0.33	6,16,21,25	0
2	20R	B	601	28/28	0.12	-0.13	7,14,27,29	0

6.5 Other polymers ⓘ

There are no such residues in this entry.