Supplementary Material

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Mechanism of the Activation Step of the Aminoacylation Reaction: A Significant difference between Class I and Class II Synthetases

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Section A. A brief summary of the interaction pattern observed between active site residues and substrates

In the following we mention common types of interactions between susbtrate and active site residues as present in different regions of the active sites of various aaRSs.

In the ATP binding region, the π electron cloud present in adenosine group of ATP can have favorable π-stacking interaction with the electron cloud of active site amino acids such as Phe. The presences of such residues are noted in different aaRSs. Interaction of the π electron cloud of active site Phe group with adenosine group is noted in AsnRS, SerRS, HisRS as well as in GlyRS. Hydrogen bonding between the nitrogen atoms of the adenosine base and active site residues such as His, Pro, Asp, Asn, Met and Gln are observed. Such hydrogen bonding interactions are present in IleRS with active site His and with Met in ValRS.

The α-phosphorous atom of ATP directly participates in the reaction and considered to be located in the intervening region. The reduction of the unfavorable electrostatic potential between the α- phosphorous atom of ATP and carboxylic acid group of substrate amino acid is a prerequisite to carry out the nucleophilic reaction. The positively charged amino acids (such as His, Lys, Arg); polar residues such as Thr or one/more divalent Mg^{2+} cation carry out the task of reduction of electrostatic potential. The presence of one or more such residue or ion is observed in the ATP binding site of different aaRSs. Interactions with His residues and triphosphate group of ATP are observed in ArgRS and CysRS. Similarly, interactions with triphosphate group of ATP and different positively charged amino acid residues and cation are noted in GlnRS with His and Lys, in GluRS with Arg, in IleRS with His, Lys, in TyrRS with Lys and in AsnRS with Arg and His residues as well as three Mg^{2+} ions. The triphosphate group of ATP in ProRS

interacts with active site Arg, His and Thr. Interactions between Arg residues and Mg^{2+} ions and the triphosphate group of ATP are noted in class II aaRSs such as GlyRS, HisRS, LysRS and SerRS. The triphosphate groups are also involved in hydrogen bonding interaction with polar active site groups in some aaRS. In few cases, triphosphate group is involved in hydrogen bonding with amide hydrogen of main chain of a peptide linkage located nearby in the active site.

The α-carboxylic acid group of the substrate amino acid in the intervening region can have favorable interaction with the positively charged active site amino acid residues such as Arg/Lys/His or active site amino acid containing polar side chain such as Asn or Gln. Various such active site residues bearing positive charge or with polar nature, present in proximity of α-carboxylic acid group of the substrate amino acid of different aaRS active site are noted. The examples are residues such as Asn, Gln and His in ArgRS, Arg and Lys in LysRS, Arg in HisRS, Gln in IleRS and His in LeuRS. Other than the polar groups (as mentioned before) and the amino group of a peptide linkage can form hydrogen bond with the carboxylic acid group. The positively charged α-amino group of the substrate amino acid, also considered to be located in the intervening region (based on its proximity with the reaction center) can have favorable interaction with negatively charged active side residues such as Asp or Glu. The negatively charged active site Asp residue interacts with positively charged α-amino group of the substrate amino acid in GlnRS and in LeuRS. Similarly, interaction between negatively charged active site Glu and α-amino group of the substrate amino acid is noted in GluRS, LysRS, SerRS and HisRS. Active site residues with polar side chains such as Asn, Ser, Gln, Tyr and Thr are also observed in the vicinity of the α-amino group of substrate amino acid which can form stabilizing hydrogen bond interaction. Presence of such hydrogen bond is noted between α-amino group of the substrate amino acid and Asn as well as Ser in ArgRS and with Thr in CysRS.

Unlike the invariant carboxylic acid and amino groups, the side chains are variable in the structure of amino acids (glycine have no side chain). The related active site residues are considered in the amino acid binding pocket of active site. For example, the side chains could be positively charged, negatively charged, polar, non-polar or may have sulfur containing group. When the side chain of the substrate amino acid is positively charged like those in Arg or Lys,

the vicinity of the active site close to the side chain is composed of negatively charged amino acids like Glu, Asp or polar amino acid such as Tyr. Presence of active site Glu, Asp and Tyr is noted in the proximity of positively charged side chain of the substrate Arg. Active site Tyr and Glu are present in LysRS. Similar interactions with Tyr and Glu are noted in HisRS where the side chain of the substrate amino acid can be in protonated state (ionic) or nonprotonated (polar) state. The binding pocket for the substrate amino acid bearing negatively charged side chain (such as Glu, Asp) may contain positively charged active site amino acid such as Arg or Lys, or amino acid which can form hydrogen bond (such as Gln, Tyr, Ser or Asn) with the carboxylic acid group of substrate amino acid side chain. The residues such as Arg, Tyr, Asn and Arg interact with the side chain in GluRS. In AspRS, interaction with the active site Arg, Lys, Gln, Asp and Ser are noted in the vicinity of negatively charged side chain of substrate amino acid.

When the side chain of the substrate amino acid is polar (for example, side chains of Gln, Asn, Ser, Cys), hydrogen bonding with polar active site residues such as Tyr, Thr or water molecule or interaction with charged active site residue such as Glu, Arg are observed. Such interactions with Tyr and water molecule are noted in GlnRS, interaction with Arg and Glu are noted in AsnRS, interaction with Thr and Glu are noted in SerRS. In the case of substrate amino acid with non-polar side chain, the corresponding active site pocket is composed of non-polar amino acids such as Pro, Trp, Phe and Ile which might have favorable van der Waals and hydrophobic interaction with the side chain of the substrate. Further, presence of the hydrophobic part of the side chain of amino acids such as Met, His and Tyr are observed near the non-polar side chain of the substrate. Examples of the nonpolar active site residue and the hydrophobic part of the side chain of charged or polar amino acids near the non-polar side chain of the substrate amino acid are as follows. Pro and Trp are present in active site of IleRS, Pro, Ile and Trp are present in ValRS, Trp and Gly are present in ProRS, Met, Phe, Tyr, His are present in LeuRS near the non-polar side chain of the substrate amino acid.

In cases of few amino acids such as Cys or Gly, customized interactions by the active site residues or ions to form favorable interaction with these amino acids are noted. The side chain binding pocket of Cys contains a Zn^{2+} ion which is involved in a coordination interaction. The Zn^{2+} ligates the Cys substrate via the side chain thiolate, while the remaining four coordination

site of Zn^{2+} ion are satisfied by the active site amino acids such as multiple Cys, His and Glu. Gly is the smallest amino acid and is achiral. Due to the absence of side chain, the specificity of GlyRS depends exclusively on the carboxylic acid and amino acid group. The negatively charged carboxylic acid group of two Glu residues interacts directly with the α-NH^{3+} group. Another Glu fills up the space in the binding pocket which could have been occupied by the side chain of substrate amino acids other than Gly and helps in retaining the fidelity exhibited by GlyRS. The pro-L α-hydrogen atom interacts with the carboxyl oxygen atom of a second Glu residue. The side chain oxygen atom of serine is involved with the hydrogen bonding with the α-ammonium group. This interaction specifies the orientation of substrate glycine moiety and prevents binding of amino acid with similar chemical structure such as alanine by creating steric block for methyl group of alanine.

Since the electrostatic nature of the groups of the substrate amino acid and ATP are limited to polar, nonpolar, positively or negatively charged or groups with π electron cloud, the pattern of interactions between these moieties and active site residues bear commonalities as mentioned above. Various aaRSs use different residues or set of residues, which are analogous in terms of their interaction and recognition of the substrate, positioning of them and in carrying out the related function (for example, reduction of the unfavorable potential or by catalytic action). In other words, although the active site walls of different aaRSs have diversification in composition, one or clusters of such residues have common roles in different aaRSs. For example, the reduction of unfavorable electrostatic potential between the amino acid and ATP is carried out by two Mg^{2+} ions and two Arg in HisRS; one Arg residues, one Lys and two Mg^{2+} in ThrRS; one Arg, one His and two Mg^{2+} ions in ProRS; one Arg and three Mg^{2+} ions in LysRS and PheRS; one His, one Lys and one Mg^{2+} ion in GlnRS etc. Such commonality can be noted in the case of other type of interactions played by different active site residues as mentioned before using crystallographic studies and recent computational analysis. The study indicates that the types or natures of interactions (electrostatic, hydrogen bonding, π-stacking and hydrophobic) between the active site residues and substrates are common in all aaRSs, although the particular residue/ion (or clusters of residues) participating in these interactions may differ. Presumably, the residues forming such common interaction patterns for an amino acid are conserved through evolution in different species.

We mentioned those residues which have favorable interactions with ATP and substrate amino acids in different aaRSs as observed from the available crystallographic data. The various species for which the information of the active site of different aaRS available are *Bacillus stearothermophilus* (*BS*)*, EC*, *Thermus thermophilus* (*TT*), *Staphylococcus Aureus*; (*SA*) and *Saccharomyces cerevisiae* (yeast).

Section B. Details of the models of reactant and product (adenylate) state of aaRSs used for computation

The reactant states of class I aaRSs studied are GluRS (2CV1.PDB), GlnRS (1QRU.PDB; 1ZJW.PDB), TyrRS (1H3E.PDB) and TrpRS (1MAU.PDB). Reactant states of class II aaRSs considered are HisRS (1KMN.PDB), LysRS (1E24.PDB), ProRS (1H4Q.PDB). The adenylate state of class I aaRS such as CysRS (3C8Z.PDB), GluRS (1N78.PDB), GlnRS (1QTQ.PDB), LeuRS (1OBC.PDB), IleRS (1JZQ.PDB), MetRS (2CT8.PDB), TyrRS (3TS1.PDB) and ValRS (1GAX.PDB) are also studied. Adenylate states of class II aaRSs studied are AlaRS (3HXY.PDB), AspRS (1COA.PDB), AsnRS (2XGT.PDB), GlyRS (1GGM.PDB), HisRS (1KMM.PDB), PheRS (1B7Y.PDB), ThrRS (1KOG.PDB)) (Sekine et al, 2003; Rath et al, 1998 ; Gruic-Sovulj et al, 2005; Yaremchuk et al, 2002; Brick, 1989; Retailleau et al, 2003; Arnez et al, 1997; Yaremchuk et al, 2001; Desogus et al, 2000; Lincecum et al, 2003; Fukai et al, 2000; Nakama et al, 2001; Eiler et al, 1999; Crepin et al, 2011; Guo et al, 2009; Arnez et al, 1999; Reshetnikova et al, 1999; Torres-Larios et al, 2002; Weinreb et al, 2011). While the aaRS structures contain both AA and ATP in the reacting conformation in few crystalline states, are unavailable in some cases. The crystal structure of the reactant state of LysRS contains both substrate amino acid (AA) and ATP. The crystal structures of the reactant state of GluRS, TyrRS, HisRS and ProRS contains the corresponding alcohol (glutaminol, tyrosinol, histidnol and prolinol, respectively) instead of the respective substrate AA. The hydroxy-methyl group (–CH_2OH) of the glutaminol, tyrosinol, histidinol and prolinol, are replaced by the carboxylate anion (-COO^- group) for GluRS, TyrRS, HisRS and ProRS, respectively. The crystal structure of the reactant state of TrpRS is complexed with ATP and tryptophanamide. The amide group (–$CONH_2$) of tryptophanamide is replaced by the –COO^- group for TrpRS. The two crystal structures of the reactant state of GlnRS are individually complexed with ATP, and AMP, amino acid. The position of the ATP is mapped from the 1QRU.PDB to 1ZJW.PDB. The negative

charge over the two oxygen atoms of the carboxylic acid group is delocalized and the separation between the carbon atom and two oxygen atoms should be same. Consequently the C=O bond lengths of the carboxylate group of substrate AA is set at an average separation of 1.25Å for all aaRSs.

Table 1

The separation between the pair of oxygen atoms of carboxylic acid group of substrate AA and αP atom of ATP, designated as ΔR (Å) as calculated from the crystal structure of reactant state of class I and class II aaRSs. The corresponding dihedral angle between the nitrogen atom of α-amino group, the chiral carbon atom, the carbonyl carbon atom and the oxygen atom of carboxylic group (designated as ψ (C^{α}-$C^{/}$)) are listed. Corresponding conformation based on the crystal structure of various class I and class II aaRSs are also mentioned.

Class I								Class II						
aaRS	ψ (C^{α}-$C^{/}$)(°)	Conformation	ΔR(Å)	ψ (C^{α}-$C^{/}$) (°)	Conformation	ΔR (Å)		aaRS	ψ (C^{α}-$C^{/}$)(°)	Conformation	ΔR (Å)	ψ (C^{α}-$C^{/}$) (°)	Conformation	ΔR(Å)
GluRS	-25.40	*syn*	2.93	154.61	*anti*	3.49		HisRS	153.89	*anti*	2.29	-26.11	*syn*	4.01
GlnRS	67.42	*syn*	2.96	-112.66	*anti*	3.30		LysRS	171.70	*anti*	3.10	-7.74	*syn*	4.13
TyrRS	-61.97	*syn*	3.52	118.03	*anti*	3.86		ProRS	-99.20	*anti*	3.08	80.80	*syn*	4.99
TrpRS	-180.00	*anti*	3.20	0.00	*syn*	4.12								

Table 2

The dihedral angle between the nitrogen atom of α-amino group, the chiral carbon atom, the carbonyl carbon atom and the oxygen atom of carboxylic group covalently linked with αP in the adenylate state (designated as ψ (C^{α}-$C^{/}$)) as well as conformation of the corresponding oxygen atom for various class I and class II aaRSs based on the available crystal structure.

Class I						Class II				
aaRS	PDB Code	Notation of the Adenylate	ψ (C^{α}-$C^{/}$) (°)	Conformation		aaRS	PDB Code	Notation of the Adenylate	ψ (C^{α}-$C^{/}$) (°)	Conformation
GlnRS	1QTQ	QSI 998	-0.79	*syn*		HisRS	1KMM	HAM D 450	164.07	*anti*
GluRS	1N78	GOM 600	39.09	*syn*		AspRS	1COA	AMO 831	167.18	*anti*
LeuRS	1OBC	LEU A1814	-3.96	*syn*		AsnRS	2XGT	NSS B1550	145.75	*anti*
ValRS	1GAX	VAA A 990	14.98	*syn*		AlaRS	3HXY	5AL A 442	143.86	*anti*
IleRS	1JZQ	ILA 1301	-1.90	*syn*		GlyRS	1GGM	GAP B2550	-169.39	*anti*
TyrRS	3TS1	TYA A 420	-51.01	*syn*		PheRS	1B7Y	FYA A1002	-125.58	*anti*
CysRS	3C8Z	5CA B 416	-27.09	*syn*		ThrRS	1KOG	TSB H9002	161.02	*anti*
MetRS	2CT8	MSP A 501	-15.37	*syn*		ProRS	1H4S	PSD B1478	-166.37	*anti*
TrpRS	3KT3	TYM D 800	157.86	*anti*						

Table 3.A

The Cartesian coordinates of the atoms of the optimized reactant state, transition state and product state of GlnRS using two level ONIOM (HF/6-31G*:PM3) method.

Reactant State				Transition State				Product State			
Atom	X	Y	Z	Atom	X	Y	Z	Atom	X	Y	Z
C	-7.38385	2.102883	4.755644	C	6.04641	0.661544	2.467432	C	-6.64504	-1.451901	3.179012
C	-6.233832	1.876886	3.81266	C	5.311897	1.638081	1.590805	C	-5.732033	-1.95066	2.0934
O	-6.371074	1.700142	2.607347	O	5.161044	1.484592	0.380079	O	-5.567231	-1.362147	1.023925
N	-4.918996	1.965377	4.359936	N	4.69285	2.750768	2.225882	N	-4.958749	-3.109796	2.358172
C	-3.767261	1.373137	3.654373	C	4.30142	3.94467	1.451029	C	-4.296028	-3.851982	1.267125
C	-3.319212	0.027775	4.212045	C	5.312522	5.079499	1.537606	C	-5.101053	-5.04423	0.771176
O	-3.72282	-0.446777	5.264234	O	6.311198	5.053099	2.245379	O	-6.156693	-5.412814	1.269405
N	-2.261624	-0.628361	3.525875	N	5.02184	6.273059	0.837464	N	-4.538015	-5.827622	-0.26172
C	-1.607912	6.544724	-2.364726	C	3.505303	-4.564363	4.808185	C	1.285908	0.2585	6.452133
C	-1.30013	5.277638	-1.702529	C	2.708896	-3.699952	3.938557	C	0.430723	0.390419	5.274862
N	-2.260942	4.316868	-1.432508	N	3.164159	-3.241131	2.710908	N	-0.823801	0.998037	5.314553
C	-0.137365	4.786385	-1.237397	C	1.471045	-3.196054	4.093456	C	0.616184	0.001246	4.002043
C	-1.69313	3.29281	-0.831311	C	2.236567	-2.488833	2.159355	C	-1.354403	0.965978	4.112218
N	-0.411301	3.553277	-0.697527	N	1.206936	-2.448739	2.972707	N	-0.514992	0.376247	3.307636
C	-5.947929	5.236482	-2.872689	C	7.023735	-4.169056	1.718031	C	-4.816941	2.642625	5.232893
C	-5.878032	4.028312	-1.969924	C	6.346195	-3.103812	0.891297	C	-4.888569	2.225861	3.7834
O	-4.810966	3.747048	-1.313649	O	5.191174	-2.644523	1.213129	O	-3.861392	1.783463	3.161413
O	-6.83521	3.240984	-1.802279	O	6.853703	-2.603946	-0.137565	O	-5.94796	2.288103	3.112887
C	-0.186883	1.995193	4.367538	C	0.543185	4.46109	2.017902	C	-0.514729	-4.079485	2.009644
N	0.656364	1.206263	3.411282	N	0.044221	3.68686	0.838127	N	0.165709	-3.217579	1.031165
C	-3.213633	-4.621651	1.791319	C	2.767011	3.822184	-2.26658	C	-3.052237	-3.088734	-4.420029
O	-2.744579	-4.581682	3.13457	O	2.685433	4.935539	-1.378494	O	-3.461365	-4.261673	-3.732816
C	-2.017043	-4.484662	0.821962	C	1.605227	3.901865	-3.280273	C	-1.509317	-3.079222	-4.489108
O	-2.076823	-3.373531	-0.01742	O	0.859666	2.739448	-3.476396	O	-0.946636	-1.807287	-4.465884

C	-0.768519	-4.5092	1.787625	C	0.682217	5.044552	-2.696022	C	-1.079234	-4.063499	-3.328064
O	0.331693	-3.72372	1.456313	O	-0.411351	4.586159	-1.937178	O	-0.418366	-3.509312	-2.231655
C	-1.38354	-4.187347	3.16583	C	1.650939	5.821118	-1.787108	C	-2.4014	-4.755998	-2.929264
N	-5.681857	1.584101	-0.133428	N	4.856261	-1.034143	-0.812392	N	-5.047268	1.375532	0.861204
C	-5.329232	0.136778	-0.368917	C	3.974288	-1.207519	-2.024946	C	-4.831676	2.013581	-0.497849
C	-3.918183	-0.19168	0.280546	C	2.581651	-0.506893	-1.790349	C	-3.662187	1.346658	-1.262543
O	-3.839724	-1.287818	0.823931	O	2.224775	0.266984	-2.661185	O	-3.595183	1.356296	-2.441632
C	-5.300152	-0.182419	-1.864756	C	3.785233	-2.69483	-2.335243	C	-4.554509	3.516812	-0.334553
C	-5.327936	-1.998828	-3.579734	C	2.856816	-4.365771	-3.933771	C	-4.489728	5.745652	-1.454941
C	-5.325717	-1.687165	-2.09717	C	3.089243	-2.89035	-3.674021	C	-4.867847	4.284611	-1.610205
N	-4.073945	-2.008307	-4.261548	N	3.912967	-5.130901	-4.481618	N	-5.514571	6.716303	-1.48994
O	-6.316734	-2.314237	-4.220179	O	1.830172	-4.960141	-3.628372	O	-3.35008	6.135929	-1.22895
H	-7.475892	1.267384	5.463704	H	7.085977	0.991374	2.606177	H	-7.653568	-1.866473	3.039203
H	-3.976993	1.290373	2.564267	H	4.113199	3.667986	0.389719	H	-4.063418	-3.16757	0.423676
H	-2.287759	-0.492569	2.534571	H	4.504378	6.142965	-0.002127	H	-3.945128	-5.325048	-0.892397
H	-0.935672	6.713189	-3.21753	H	3.529108	-4.170975	5.834096	H	2.222591	-0.255761	6.195694
H	-1.476571	7.38853	-1.672206	H	4.546956	-4.665153	4.466514	H	0.798217	-0.325272	7.246451
H	0.845497	5.198655	-1.242825	H	0.769129	-3.300644	4.89002	H	1.424746	-0.508036	3.518532
H	-3.272538	4.364913	-1.62952	H	4.096201	-3.375751	2.296875	H	-1.258882	1.394182	6.119146
H	0.245644	2.914377	-0.261435	H	0.400697	-1.899228	2.740541	H	-0.665902	0.210424	2.31816
H	-2.207623	2.40903	-0.512733	H	2.30647	-1.993203	1.216109	H	-2.351855	1.363601	3.835026
H	-4.97587	5.73975	-2.968228	H	6.412809	-4.476392	2.577897	H	-3.861033	2.364803	5.696192
H	-6.282813	4.955543	-3.878856	H	7.22497	-5.061056	1.111696	H	-4.928261	3.730682	5.321965
H	-1.197433	2.176047	3.949896	H	0.435265	3.876351	2.943649	H	-1.593577	-4.23609	1.813885
H	-0.318315	1.46299	5.322377	H	1.619086	4.699033	1.899788	H	-0.032277	-5.065204	2.03577
H	1.536373	0.93423	3.832076	H	-0.14726	4.264958	0.01654	H	1.926994	-2.272725	1.662541
H	0.863875	1.697458	2.509473	H	-0.789831	3.090714	1.012086	H	-0.319992	-2.339239	0.938108
H	0.208693	0.343844	3.068096	H	0.69363	2.94414	0.520775	H	0.141892	-3.656191	0.125032

H	-4.393329	0.264307	-2.323971	H	3.191633	-3.177105	-1.530548	H	-3.494361	3.680414	-0.045341
H	-6.165431	0.283351	-2.38332	H	4.767145	-3.213947	-2.343527	H	-5.159466	3.935757	0.498036
H	-4.458456	-2.171631	-1.598511	H	2.113532	-2.357017	-3.678983	H	-4.300699	3.864518	-2.467167
H	-6.225567	-2.131609	-1.62452	H	3.681996	-2.432654	-4.492008	H	-5.939137	4.164577	-1.8736
H	-3.396772	-1.397023	-3.847692	H	4.538747	-4.62393	-5.064147	H	-6.308415	6.475007	-2.037271
H	-4.131455	-1.903866	-5.25049	H	3.662239	-6.020978	-4.849696	H	-5.220746	7.65971	-1.6087
H	-6.114322	-0.496087	0.120813	H	4.485297	-0.719476	-2.895728	H	-5.772117	1.876522	-1.094482
H	-5.865544	1.711793	0.851549	H	4.942716	-0.050948	-0.578256	H	-5.288443	0.396067	0.747798
H	-6.498488	1.879843	-0.690052	H	5.791946	-1.441772	-0.969557	H	-5.793379	1.851856	1.395913
H	-4.909514	2.204122	-0.420691	H	4.468265	-1.538407	-0.00151	H	-4.201447	1.448744	1.454563
H	-1.331169	-3.1072	3.41711	H	1.204215	6.194918	-0.850376	H	-2.6795	-4.587477	-1.867567
H	-0.323394	-5.530749	1.784132	H	0.259396	5.688627	-3.498094	H	-0.324861	-4.797858	-3.703989
H	-0.001157	-2.845339	1.307627	H	-0.519475	3.701841	-2.270724	H	-0.887367	-2.706484	-2.015995
H	-1.958773	-5.332456	0.103447	H	1.966984	4.201224	-4.289783	H	-1.144447	-3.479004	-5.461578
H	-2.654707	-2.72424	0.389543	H	1.333496	2.006517	-3.074408	H	-1.282508	-1.384194	-3.679873
H	-3.960903	-3.812917	1.674151	H	2.73998	2.920953	-1.622721	H	-3.463223	-2.208686	-3.890184
C	0.233674	-0.151298	-4.32902	C	-1.030977	-2.791937	-3.667489	C	-0.3747	4.634893	-1.8948
C	0.963364	-1.4458	-3.909246	C	-2.328559	-2.695908	-2.835333	C	1.090891	4.543935	-1.421376
C	-0.036544	-2.146345	-2.941533	C	-2.763535	-1.200507	-2.960765	C	1.595804	3.208824	-2.061983
C	-1.037405	-1.032219	-2.562886	C	-1.491274	-0.503649	-3.507365	C	0.46295	2.784806	-3.036529
C	-0.7808	-0.479938	-1.143697	C	-0.66463	0.246249	-2.439893	C	-0.180337	1.425225	-2.674878
O	0.609612	-0.662159	1.380632	O	0.875931	1.458387	-0.243141	O	-1.492707	-0.936743	-1.803406
O	5.007242	0.074798	-1.078365	O	-3.896443	0.178987	0.163784	O	3.633475	-0.399399	0.008708
O	6.791869	1.908149	2.615084	O	-4.015924	-1.694983	4.267367	O	7.453698	0.397711	2.278202
O	1.31868	-2.276692	-4.983651	O	-3.31438	-3.63232	-3.179268	O	1.891709	5.646915	-1.761554
O	1.17392	1.718854	0.793745	O	0.174415	-0.678388	1.153408	O	-0.825108	-0.257292	0.569477
O	4.466026	-2.013651	0.592984	O	-3.993526	2.454235	1.52085	O	4.369382	-2.93559	0.372452
O	5.240934	0.093682	4.007684	O	-3.207633	0.773313	5.203816	O	7.214554	-2.169804	3.269797

O	-0.572634	-3.262267	-3.627265	O	-3.894803	-0.998025	-3.772152	O	2.854805	3.287903	-2.687183
O	2.654115	-0.16706	-0.055021	O	-1.625664	1.434599	0.662576	O	2.574509	-1.664555	2.01833
O	4.860697	0.146839	1.60662	O	-3.185457	0.511924	2.761108	O	5.282138	-1.353449	1.959669
O	6.901592	-0.792018	2.363908	O	-5.288862	0.68915	3.842478	O	7.293393	-1.873642	0.806841
O	-0.975877	-0.039085	-3.589583	O	-0.732978	-1.50471	-4.189172	O	-0.49463	3.842363	-3.067559
O	0.474362	0.151002	-1.064186	O	-0.629753	-0.449934	-1.215083	O	-0.492252	1.357992	-1.309287
P	1.190416	0.270685	0.380949	P	0.198174	0.182609	-0.016307	P	-1.332198	0.091286	-0.762116
P	4.314473	-0.462449	0.149706	P	-3.115229	1.10148	1.177993	P	3.936209	-1.520535	1.019732
P	6.174365	0.561242	2.917743	P	-3.982885	-0.177368	4.322507	P	7.175709	-1.083791	2.234219
H	-0.064371	-0.133897	-5.391356	H	-1.107855	-3.451335	-4.549407	H	-0.707193	5.642262	-2.19951
H	0.458543	-2.592735	-2.052043	H	-3.105051	-0.780922	-1.986742	H	1.786171	2.434854	-1.28482
H	-2.105764	-1.370312	-2.614652	H	-1.714778	0.219071	-4.326308	H	0.807226	2.732409	-4.095582
H	-0.833343	-1.331559	-0.434326	H	-1.132278	1.237179	-2.271329	H	0.554599	0.619455	-2.912105
H	-1.589395	0.244017	-0.846565	H	0.396409	0.397979	-2.794667	H	-1.085646	1.255172	-3.291053
H	-1.500516	-3.111652	-3.768101	H	-3.654713	-1.209369	-4.666906	H	2.820244	3.982679	-3.335869
H	0.270154	2.971757	4.584373	H	-0.005165	5.404677	2.147191	H	-0.42052	-3.629269	3.006552
H	0.833648	0.75049	-4.122538	H	-0.166397	-3.126781	-3.066202	H	-1.076749	4.261818	-1.126371
H	-2.641253	6.585374	-2.743147	H	3.073187	-5.574426	4.855487	H	1.553899	1.238697	6.872737
H	-0.940582	-4.753473	3.999518	H	2.112376	6.675653	-2.312444	H	-2.389634	-5.843985	-3.105146
O	-3.055899	0.691733	0.168377	O	1.998116	-0.840043	-0.732199	O	-2.793137	0.805965	-0.420675
H	-2.147973	-1.598099	3.759765	H	5.785066	6.904484	0.735988	H	-5.164976	-6.450085	-0.720164
H	-7.252678	3.024637	5.339012	H	5.593271	0.56378	3.463279	H	-6.306978	-1.734618	4.185308
H	-8.338018	2.185433	4.217449	H	6.078183	-0.343264	2.017888	H	-6.733825	-0.354837	3.15722
H	-6.66569	5.966924	-2.478748	H	7.986231	-3.807865	2.10131	H	-5.622283	2.180293	5.816988
Mg	5.245727	-1.559691	2.214544	Mg	-4.128547	2.004474	3.308213	Mg	5.944078	-2.980057	1.357373
H	-3.734303	-5.587991	1.696114	H	3.755926	3.873905	-2.751673	H	-3.538471	-3.157209	-5.405684
H	0.554523	-2.83365	-5.140156	H	-3.491419	-3.549595	-4.108519	H	1.563863	6.013819	-2.574136
H	1.936077	-1.217371	-3.423506	H	-2.142013	-2.953643	-1.769457	H	1.178895	4.521384	-0.314394

H	-2.920425	2.09341	3.756129	H	3.319433	4.289189	1.858163	H	-3.310905	-4.198546	1.665725
H	-4.893666	1.810453	5.346505	H	5.099602	2.977008	3.109929	H	-5.356545	-3.707462	3.052443
C	8.618113	3.628883	-1.628409	C	-4.985566	-4.776281	0.575558	C	5.936447	4.135367	-0.547306
N	7.664444	2.696569	-2.082721	N	-4.704818	-3.593207	-0.135048	N	4.934543	3.18217	-0.807024
C	8.570684	3.590484	-0.244615	C	-4.913648	-4.449279	1.919567	C	6.815859	3.549467	0.349809
C	7.044	2.098367	-1.010504	C	-4.460607	-2.563505	0.743853	C	5.185024	2.036497	-0.087995
N	7.599974	2.645257	0.115289	N	-4.590411	-3.087711	2.001944	N	6.338894	2.26088	0.618318
C	0.772152	-5.785002	-1.333369	C	-7.959603	3.998885	-2.183784	C	2.208635	-4.048906	-4.690005
N	1.864072	-5.338745	-2.218763	N	-7.392476	2.638069	-2.196577	N	2.313403	-2.639651	-4.265204
C	2.759408	-4.337624	-1.798046	C	-6.19206	2.372729	-1.477934	C	2.826024	-2.321413	-2.987104
N	3.020667	-4.139688	-0.478015	N	-5.751133	3.221904	-0.488492	N	3.684321	-3.178081	-2.340432
N	3.595296	-3.761301	-2.764973	N	-5.440339	1.27752	-1.786659	N	2.688368	-1.03356	-2.520553
H	9.155721	4.162008	0.48142	H	-5.069	-5.086293	2.793928	H	7.723486	3.963322	0.797289
H	7.473924	2.5006	-3.032335	H	-4.651185	-3.523511	-1.121927	H	4.155379	3.316611	-1.431996
H	7.342521	2.384609	1.083831	H	-4.444443	-2.556002	2.880166	H	6.789495	1.575294	1.244444
H	6.21868	1.285151	-1.050355	H	-4.195185	-1.456267	0.480944	H	4.546947	1.075993	-0.075845
H	0.497667	-6.807365	-1.626795	H	-9.01084	3.92867	-2.494396	H	2.245158	-4.068434	-5.78766
H	1.0818	-5.803224	-0.273738	H	-7.931588	4.425963	-1.167821	H	3.045319	-4.656665	-4.309857
H	1.600292	-5.295025	-3.181019	H	-7.435651	2.206988	-3.096111	H	1.527246	-2.08959	-4.550251
H	2.399906	-4.564078	0.177707	H	-6.391801	3.934773	-0.21694	H	3.726362	-4.109897	-2.688909
H	3.611721	-3.371769	-0.143683	H	-5.086722	2.899815	0.232884	H	3.958556	-3.031173	-1.364778
H	3.218655	-3.687264	-3.684279	H	-5.754572	0.676679	-2.510603	H	1.932692	-0.481575	-2.874374
H	4.122351	-2.967685	-2.477862	H	-4.758073	0.885255	-1.112185	H	3.027367	-0.785358	-1.585545
H	-0.123652	-5.144827	-1.412236	H	-7.44182	4.693001	-2.862412	H	1.261119	-4.522095	-4.365207
C	9.469134	4.447426	-2.50933	C	-5.288232	-6.072849	-0.054794	C	5.979891	5.478066	-1.152175
H	10.136119	3.821651	-3.119182	H	-6.244053	-6.040552	-0.596578	H	6.359509	5.43319	-2.182916
H	8.869378	5.06636	-3.191358	H	-4.506552	-6.369697	-0.768269	H	4.987366	5.950029	-1.178665
H	10.098817	5.121873	-1.913951	H	-5.363651	-6.860406	0.706365	H	6.649173	6.134627	-0.580754

Table 3.B

The Cartesian coordinates of the atoms of the optimized reactant state, transition state and product state of HisRS using two level ONIOM (HF/6-31G*:PM3) method.

Reactant State				Transition State				Product State			
Atom	X	Y	Z	Atom	X	Y	Z	Atom	X	Y	Z
C	-6.910746	1.233728	2.485701	C	-3.454614	-5.35146	1.288382	C	-6.491334	0.436231	2.972077
C	-5.842883	0.829183	1.495542	C	-3.596402	-3.864166	1.066815	C	-5.547006	0.049958	1.867309
O	-5.648341	-0.40603	1.217385	O	-3.930426	-3.396665	-0.073228	O	-4.543128	-0.723051	2.035069
O	-5.111822	1.657472	0.904166	O	-3.403206	-3.014491	1.975275	O	-5.651575	0.446094	0.677206
C	-3.636305	3.476195	-0.850424	C	-2.869846	-1.871265	4.60567	C	1.4273	5.419875	-1.913068
N	-2.208067	3.47975	-0.481153	N	-1.518902	-1.278093	4.621277	N	1.351305	5.431881	-0.438017
C	-1.763907	2.927827	0.729271	C	-0.724041	-1.240711	3.460021	C	0.976266	4.242571	0.244359
N	-2.620588	2.617153	1.685173	N	-0.862746	-2.185501	2.554879	N	0.209519	3.366879	-0.367136
N	-0.454018	2.972624	0.961338	N	0.277771	-0.368736	3.422633	N	1.321021	4.113316	1.505963
H	-1.603843	3.304001	-1.257335	H	-1.466707	-0.460369	5.193468	H	2.145111	5.893786	-0.039869
C	3.111997	1.264665	-1.917543	C	-0.029662	4.415687	3.3759	C	6.563497	4.904804	0.750226
C	1.653065	1.55401	-1.690664	C	-0.742823	3.091992	3.378066	C	5.388051	4.014026	0.460235
O	1.23392	2.630851	-1.259015	O	-0.486149	2.17493	4.160642	O	4.215279	4.392494	0.485766
N	0.705907	0.588556	-2.068342	N	-1.831249	2.908561	2.503142	N	5.627672	2.693335	0.045717
C	-6.374491	-2.205605	3.930582	C	-3.0481	-5.718207	-2.468461	C	-5.085426	-2.0458	5.560847
N	-5.14333	-2.174658	4.743542	N	-1.686989	-5.302405	-2.859382	N	-3.869665	-1.457935	6.157687
C	-3.874222	-1.955633	4.141855	C	-1.263009	-3.958284	-2.689883	C	-2.72376	-1.266479	5.348737
N	-3.79698	-1.423517	2.956154	N	-1.898998	-3.167321	-1.872075	N	-2.855386	-1.021532	4.070259
N	-2.804497	-2.278356	4.859762	N	-0.182474	-3.572492	-3.358372	N	-1.533772	-1.290473	5.932425
H	-5.136172	-2.906145	5.424787	H	-1.417519	-5.697909	-3.736876	H	-3.675871	-1.835702	7.065693
N	-4.373321	-0.925673	-1.143788	N	-4.670434	-0.750324	0.224953	N	-3.710186	-0.773325	-0.612165
C	-3.053527	-1.561715	-0.785045	C	-3.759385	0.134457	-0.596512	C	-2.34481	-1.397298	-0.430847
C	-2.10187	-0.439454	-0.162815	C	-2.29512	0.111797	-0.001257	C	-1.325891	-0.334014	0.048811
O	-1.847417	0.5028	-0.921443	O	-2.148227	0.539192	1.125012	O	-1.089892	0.628951	-0.609397
H	-4.800977	-0.550561	-0.283908	H	-4.390244	-1.733083	0.110781	H	-4.166208	-0.509977	0.311958
C	-2.360695	-2.210135	-1.980708	C	-4.27898	1.572269	-0.657531	C	-1.838889	-2.036846	-1.73032

C	2.145538	-2.600254	-0.740671	C	-1.47395	4.30384	-0.868531	C	4.947343	-3.213188	1.97845
C	3.525638	-2.144572	-0.209712	C	-0.154711	4.996841	-0.469085	C	5.463633	-2.083559	1.056376
C	3.316772	-1.975603	1.328709	C	0.940597	4.167714	-1.20769	C	4.650143	-0.823399	1.491918
C	1.774926	-2.082776	1.503192	C	0.152363	3.296923	-2.226309	C	3.625651	-1.374243	2.523648
C	1.089916	-0.698852	1.634789	C	0.538547	1.799069	-2.243751	C	2.203728	-1.53413	1.927791
O	-0.380012	-0.95005	4.312758	O	0.615786	-1.141875	-2.043618	O	-0.03487	-0.385644	3.522869
O	1.44684	1.242659	7.532179	O	5.032884	-0.300396	-2.513572	O	-2.915928	-2.534767	11.009352
O	5.150236	3.325694	7.305853	O	7.554293	-1.74013	0.574752	O	-0.184005	-0.344139	12.890836
O	4.543925	-3.083384	-0.453184	O	-0.094694	6.337462	-0.897629	O	6.840644	-1.827052	1.203687
O	-0.423275	1.496575	3.538819	O	0.819911	-0.778492	0.55497	O	0.115681	1.618356	1.903643
O	1.773777	3.442553	5.734589	O	4.241951	-2.610105	-1.026327	O	-2.411498	0.26063	10.603397
O	4.875343	2.853279	4.90795	O	5.450479	-1.652627	1.850187	O	0.883105	0.036659	10.882809
O	4.013508	-2.8832	2.134441	O	1.966907	4.912035	-1.797811	O	5.414612	0.233406	2.005181
O	1.363903	0.680483	5.168932	O	3.05297	-0.04323	-1.07175	O	-2.080256	-1.855087	8.805589
O	3.467158	1.478906	6.431923	O	5.478702	-0.309112	-0.240482	O	-0.68801	-1.855799	10.930096
O	6.048314	0.881801	6.525197	O	6.990291	0.699535	1.66043	O	1.558145	-2.442254	12.166961
O	1.264142	-2.769672	0.355535	O	-1.247873	3.458627	-1.980888	O	4.105462	-2.644692	2.968126
O	1.480602	-0.055848	2.821367	O	0.599047	1.243307	-0.951062	O	1.670021	-0.277606	1.59742
P	0.322121	0.278169	3.911673	P	0.67964	-0.341253	-0.825344	P	0.253511	0.18836	2.205036
P	1.826264	1.959187	6.153232	P	4.270181	-1.061067	-1.291547	P	-2.226643	-1.248895	10.266095
P	5.274437	2.154391	6.321172	P	6.617204	-0.696814	1.210531	P	0.736579	-1.210025	11.892723
H	-6.623299	2.124791	3.056418	H	-2.623659	-5.585213	1.964865	H	-6.355684	1.491303	3.240487
H	-7.12691	0.422541	3.199977	H	-3.288491	-5.890083	0.341217	H	-6.329401	-0.167234	3.879606
H	-3.755298	3.232951	-1.918139	H	-3.6534	-1.095453	4.65271	H	2.32479	4.914276	-2.299874
H	-4.265456	2.762204	-0.265468	H	-3.082092	-2.504353	3.705929	H	0.541632	4.934388	-2.35455
H	-3.59177	2.428707	1.446381	H	-1.727541	-2.722046	2.509961	H	-0.048591	3.489799	-1.326209
H	-2.225108	2.147169	2.482315	H	-0.359831	-2.0338	1.696101	H	-0.075014	2.523213	0.109868
H	-0.144086	2.497878	1.793503	H	0.741131	-0.287284	2.530783	H	1.037392	3.272153	1.987104
H	0.176042	2.9429	0.17033	H	0.195612	0.496763	3.940238	H	1.976737	4.729838	1.936856
H	3.424894	0.343681	-1.393867	H	0.185002	4.76346	2.349319	H	7.130701	4.539156	1.617133
H	3.323263	1.130506	-2.986985	H	-0.641592	5.183747	3.868499	H	7.25152	4.94669	-0.105455
H	1.052758	-0.349539	-2.049037	H	-1.805628	3.495136	1.691744	H	6.494704	2.30854	0.343429
H	-0.230405	0.678188	-1.688962	H	-2.069093	1.95597	2.267405	H	4.864281	2.056992	0.117078

H	-7.200518	-2.540498	4.572046	H	-3.200253	-6.752281	-2.805773	H	-5.79448	-2.270898	6.368405
H	-6.320239	-2.878038	3.061322	H	-3.846257	-5.095325	-2.899368	H	-4.899759	-2.97267	4.998374
H	-4.613981	-1.162094	2.398763	H	-2.720604	-3.446859	-1.332408	H	-3.743136	-0.984544	3.569568
H	-2.900694	-1.229095	2.522323	H	-1.544437	-2.235472	-1.701942	H	-2.011017	-0.824895	3.564623
H	-2.912158	-2.558467	5.811898	H	0.365822	-4.232341	-3.868264	H	-1.492971	-1.400028	6.939967
H	-1.901818	-1.88193	4.61176	H	0.260711	-2.708148	-3.078954	H	-0.738375	-0.982809	5.402793
H	-1.320652	-2.458809	-1.683773	H	-3.576232	2.181894	-1.26317	H	-0.830205	-2.459396	-1.544316
H	-2.266932	-1.487787	-2.821333	H	-4.276419	2.030746	0.356417	H	-1.706618	-1.271156	-2.523386
H	-3.24807	-2.349223	-0.012611	H	-3.738587	-0.277176	-1.639499	H	-2.452628	-2.204179	0.346888
H	-4.218378	-0.175053	-1.815042	H	-4.615039	-0.484404	1.20602	H	-3.633223	0.047286	-1.184022
H	-4.986724	-1.608333	-1.550279	H	-5.627056	-0.606628	-0.10878	H	-4.302654	-1.435512	-1.078884
O	-1.748623	-0.646534	0.993466	O	-1.456136	-0.376601	-0.798295	O	-0.814012	-0.664988	1.208584
H	2.156095	-3.574945	-1.256222	H	-2.271474	4.997451	-1.186828	H	5.735004	-3.736667	2.545736
H	3.709895	-1.001671	1.694377	H	1.509441	3.542633	-0.482999	H	4.148517	-0.336095	0.62665
H	1.484307	-2.745145	2.34829	H	0.278795	3.680033	-3.267942	H	3.592949	-0.769288	3.45692
H	-0.026339	-0.79483	1.542892	H	1.536274	1.704007	-2.715641	H	1.555838	-2.085065	2.637608
H	1.433769	-0.034509	0.81546	H	-0.193768	1.23879	-2.85874	H	2.244179	-2.116016	0.9866
H	3.840216	-3.759045	1.811016	H	1.579984	5.551419	-2.384415	H	5.96177	-0.110376	2.701359
H	3.811445	-1.159771	-0.665277	H	0.001967	4.965148	0.642202	H	5.260899	-2.321725	-0.013553
H	4.64288	-3.132374	-1.394398	H	-0.787907	6.798409	-0.44507	H	7.286405	-2.644274	1.024545
H	-7.843235	1.465635	1.955782	H	-4.371737	-5.751096	1.739677	H	-7.53501	0.305003	2.661216
H	-6.625951	-1.188534	3.570232	H	-3.155492	-5.710385	-1.366139	H	-5.574374	-1.321249	4.883114
H	-4.033876	4.488001	-0.691661	H	-2.968422	-2.503006	5.498288	H	1.444462	6.464111	-2.252684
H	3.749308	2.082642	-1.556386	H	0.925261	4.362608	3.915398	H	6.249063	5.9334	0.97146
Mg	2.675534	-0.06465	7.119381	Mg	5.179821	1.136038	-1.377985	Mg	-1.447846	-3.499259	10.488196
Mg	3.561216	3.82924	5.697145	Mg	5.434169	-2.686843	0.354246	Mg	-0.79811	0.579649	11.421703
O	4.288853	-0.815434	7.668657	O	6.445317	2.20995	-0.521112	O	-0.170728	-4.44075	11.477668
H	4.438451	-1.748179	7.548472	H	6.232508	3.122715	-0.353714	H	0.237652	-5.206568	11.086038
H	5.088207	-0.308381	7.351101	H	6.791874	1.793906	0.318885	H	0.538152	-3.850032	11.85328
O	-3.821277	0.935244	-3.183994	O	-4.868072	0.339174	2.796893	O	-5.901886	0.130344	-2.435728
H	-2.874816	0.832333	-3.259429	H	-4.259244	1.072875	2.829997	H	-6.168857	0.801521	-3.053816
H	-3.994176	1.834445	-2.904337	H	-4.640571	-0.267039	3.50214	H	-6.382129	0.274569	-1.623867
H	1.700414	-1.853261	-1.430928	H	-1.878488	3.677476	-0.047134	H	4.366842	-3.966993	1.417713

C	-4.688023	-4.791972	-3.104307	C	-7.754666	1.046555	-1.636438	C	-3.90933	-5.0038	-2.191901
C	-3.024223	-3.443449	-2.46571	C	-5.642696	1.666683	-1.232421	C	-2.729717	-3.110635	-2.228625
H	-3.372507	-6.368282	-3.653776	H	-8.186609	2.796333	-2.75871	H	-4.418054	-4.877791	-4.25514
N	-4.412389	-3.570927	-2.603719	N	-6.612533	0.672759	-1.02284	N	-3.169468	-4.174706	-1.431937
N	-3.480798	-5.456388	-3.291764	N	-7.526471	2.276964	-2.23979	N	-3.944239	-4.48313	-3.484278
C	-2.428799	-4.621448	-2.891114	C	-6.203728	2.67567	-1.996891	C	-3.209788	-3.292874	-3.518587
H	-1.375714	-4.900038	-2.930068	H	-5.765033	3.603128	-2.366487	H	-3.074703	-2.680119	-4.410292
H	-5.689741	-5.173033	-3.322392	H	-8.685721	0.471593	-1.643564	H	-4.389906	-5.921882	-1.841802

Table 4
Comparison of the ρ_b values (in a.u.) for the reactant state and transition state of GlnRS and HisRS at the bond critical points.

Different parts of the substrate	GlnRS (reactant state)			GlnRS (transition state)			HisRS (reactant state)			HisRS (transition state)		
	ρ_b	Active site residue	Substrate	ρ_b	Active site residue	Substrate	ρ_b	Active site residue	Substrate	ρ_b (au)	Active site residue	Substrate
γP	0.0613	Lys270	ATP	0.0694	Mg	ATP	0.0476	Mg1	ATP	0.0725	Mg1	ATP
	0.0197	Mg	ATP	0.0436	His40	ATP	0.0464	Arg121	ATP			
							0.0314	Arg121	ATP			
Bridging oxygen atom of γP and βP	0.0367	Mg	ATP	0.0646	Mg	ATP	0.0116	Mg2	ATP	0.0601	Mg2	ATP
βP	0.0313	Mg	ATP	0.0653	Mg	ATP	0.0231	Mg1	ATP	0.0684	Mg2	ATP
	0.0112	Lys270	ATP	0.0454	His40	ATP	0.0554	Arg113	ATP	0.0682	Mg1	ATP
	0.0076	His43	ATP	0.0448	Arg260	ATP	0.0002	Gly260	ATP			
	0.0003	His40	ATP	0.0397	Arg260	ATP						
	0.0016	Arg260	ATP									
αP	0.0120	Lys270	ATP	0.0457	Lys270	ATP	0.0491	Arg259	ATP	0.0250	Arg259	ATP
	0.0060	His43	ATP	0.0205	His43	ATP	0.0537	Arg113	ATP	0.0089	Arg259	ATP
	0.0097	Glu34	ATP	0.0012	A76	ATP	0.0011	Leu261	ATP	0.0197	Arg113	ATP
	0.0079	Glu34	ATP							0.0193	Arg113	ATP
	0.0064	Pro33	ATP									
α-Carboxylic acid group	0.1563	A76	Gln	0.0204	A76	Gln	0.0144	Gln127	His	0.0311	Gln127	His
							0.0058	Glu83	His	0.0188	Arg259	His
							0.0006	Leu261	His	0.0054	Arg113	His
α-Amino group	0.0045	Pro32	Gln	0.0329	Pro32	Gln	0.0159	Glu83	His	0.043	Glu83	His
	0.0016	Asp66	Gln	0.0402	Asp66	Gln	0.0051	Glu83	His			

Figure Legends for supporting information

Fig. S1. Schematic representations of the *syn* and *anti* conformations of the oxygen atoms of the carboxylic acid group of substrate amino acid relative to the amino group is shown in (a). The dihedral angle with one oxygen of carboxylic acid group is ψ (C^{α}-$C^{/}$) and that of the other is ψ (C^{α}-$C^{/}$). The planes showing the dihedral angle are shown in (b).

Fig. S2. Crystal structures of aminoacyl adenylate of various class I aaRSs such as (a) GlnRS, (b) GluRS, (c) LeuRS, (d) ValRS, (e) IleRS, (f) TyrRS, (g) CysRS, (h) MetRS (i) TrpRS.

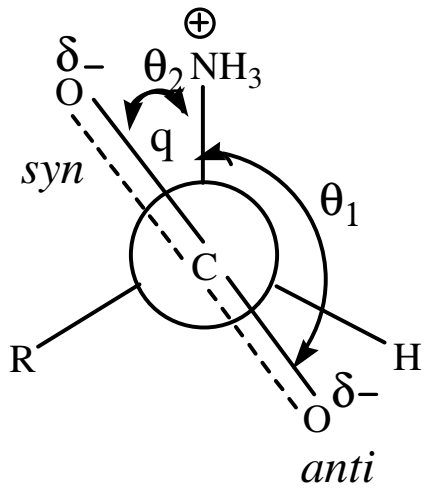
Fig. S3. Crystal structures of aminoacyl adenylate of various class II aaRSs such as (a) HisRS, (b) AspRS, (c) AsnRS, (d) AlaRS, (e) GlyRS, (f) ProRS, (g) PheRS and (h) ThrRS.

Fig. S4. The variation of ρ_b (a.u.) between a pair of oxygen atoms of substrate AA and αP atom of ATP with the conformation of the respective oxygen atom in the adenylate state for various class I aaRSs such as (a) GlnRS, (b) GluRS, (c) CysRS, (d) MetRS, (e) LeuRS, (f) IleRS, (g) ValRS, (h) TyrRS (i) TrpRS using HF/6-31G** level of theory.

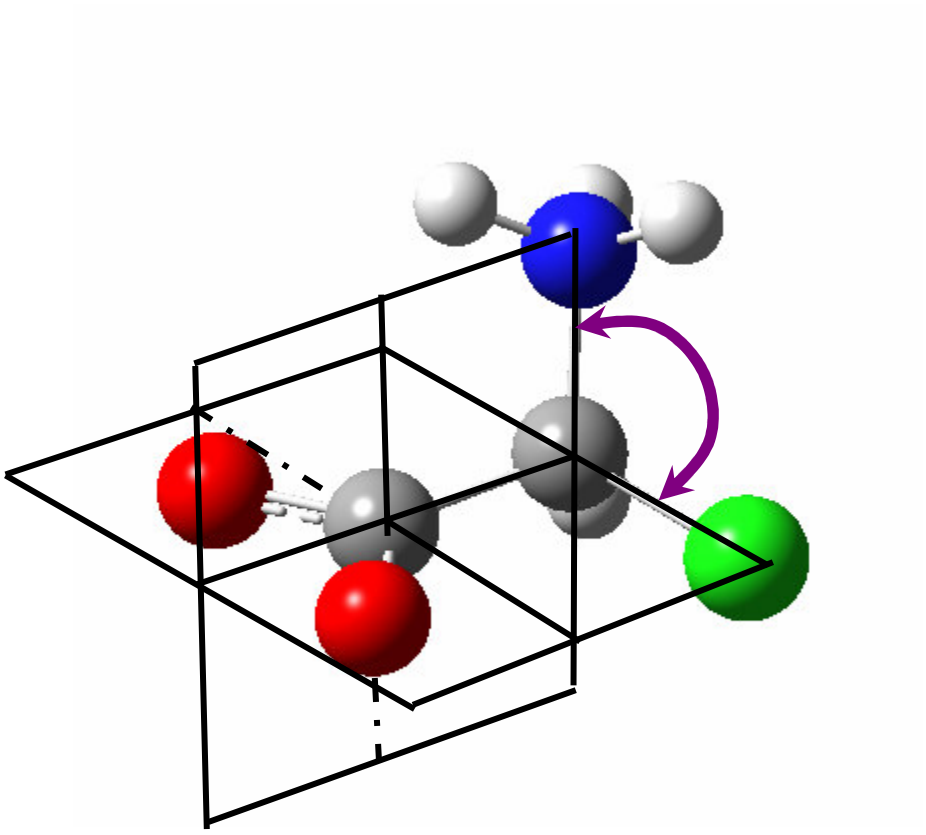
Fig. S5. the variation of ρ_b (a.u.) between a pair of oxygen atoms of substrate AA and αP atom of ATP with the conformation of the respective oxygen atom in the adenylate state for various class II aaRSs such as (a) HisRS, (b) AspRS, (c) AsnRS, (d) GlyRS, (e) PheRS, (f) ThrRS, (g) AlaRS using HF/6-31G** level of theory.

Fig. S6. The variation of interaction energy (kcal. mol^{-1}) as a function of separation (Å) between a pair of oxygen atoms of the carboxylic acid group of substrate AA and αP atom of ATP (referred as ΔR) in the reactant state for (a) GluRS, (b) GlnRS, (c) TyrRS, (d) TrpRS.

Fig. S7. The variation of interaction energy as a function of separation (Å) between a pair of oxygen atoms of the carboxylic acid group of substrate AA and αP atom of ATP (referred as ΔR) in the reactant state for (a) GluRS, (b) GlnRS, (c) TyrRS, (d) TrpRS, (e) HisRS, (f) LysRS and (g) ProRS.



(a)



(b)

Fig. S1

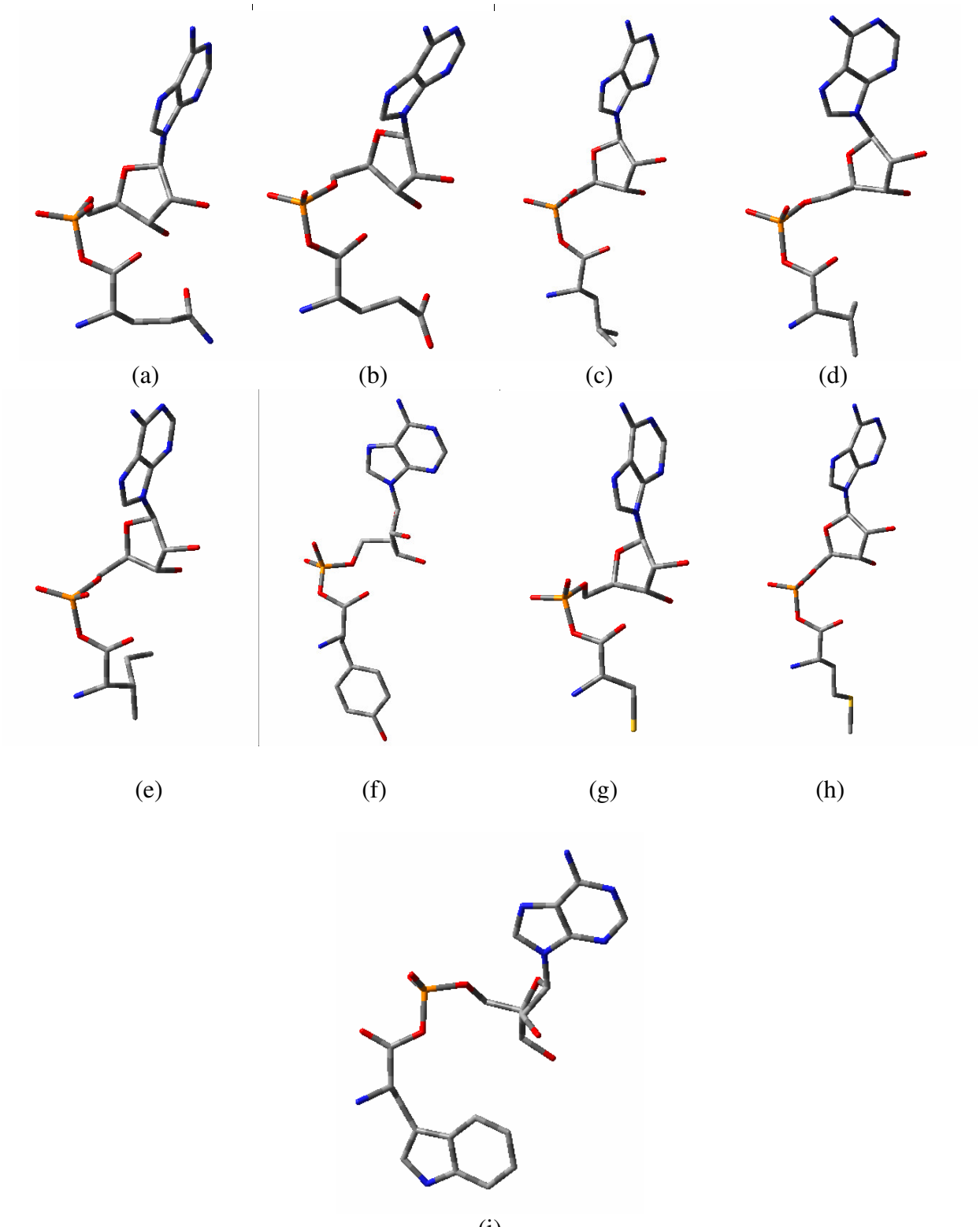


Fig. S2

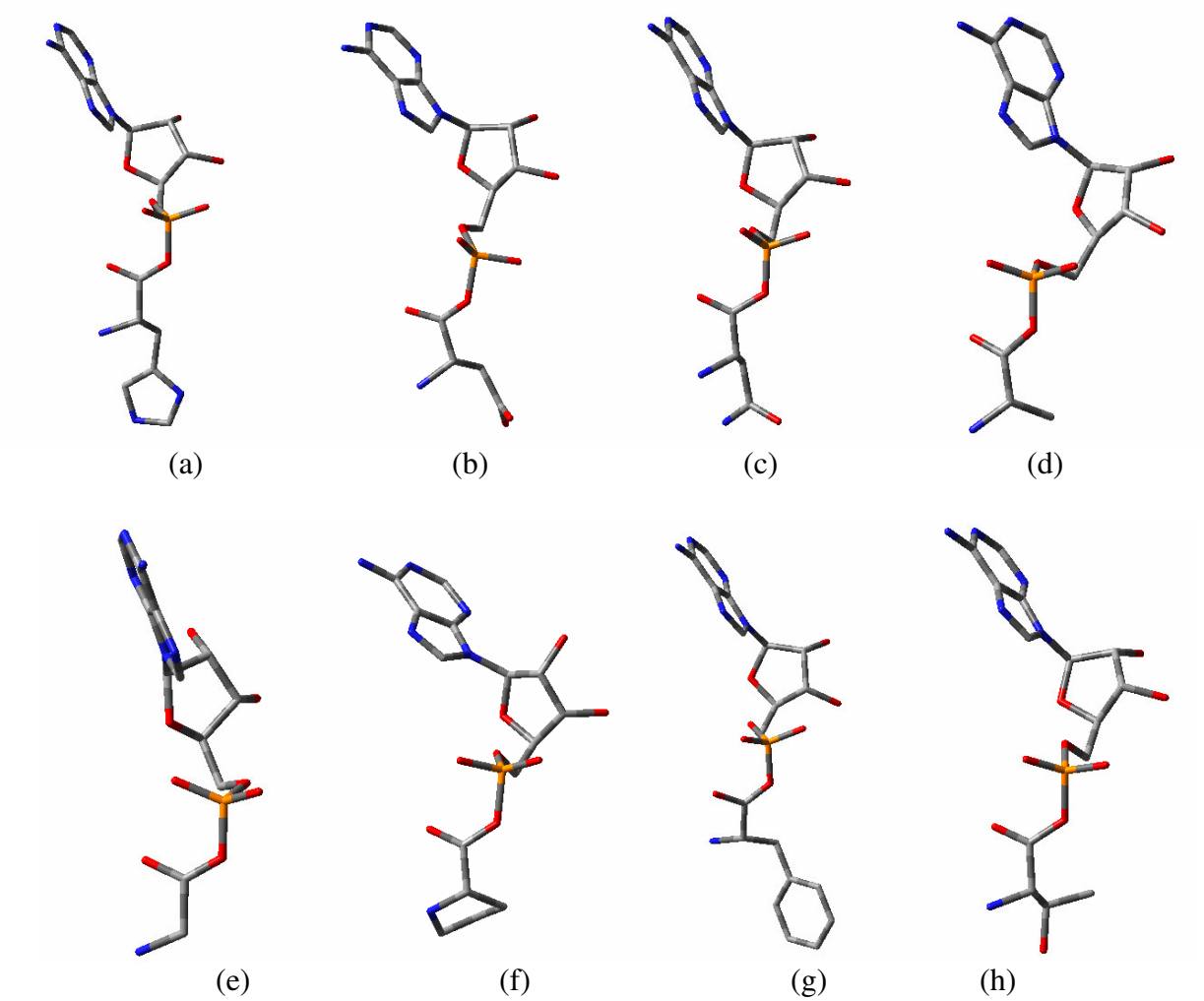
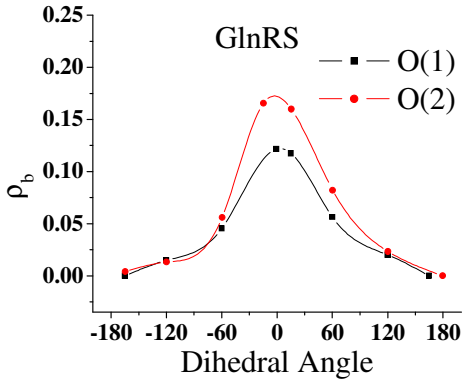
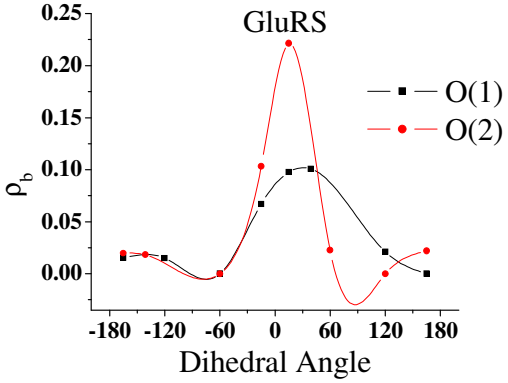


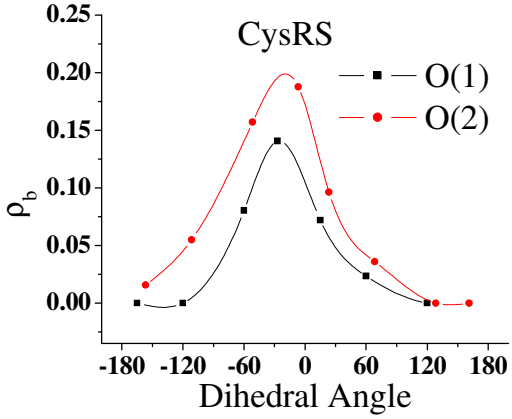
Fig. S3


GlnRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

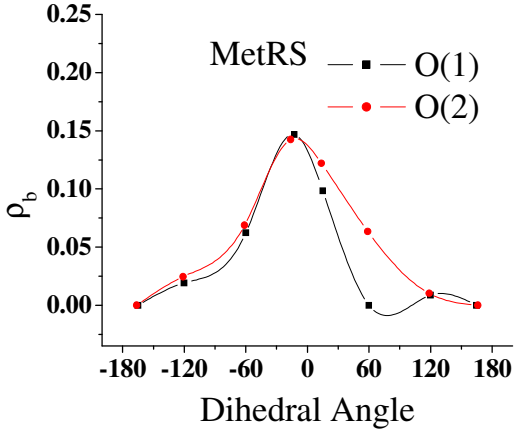
(a)


GluRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

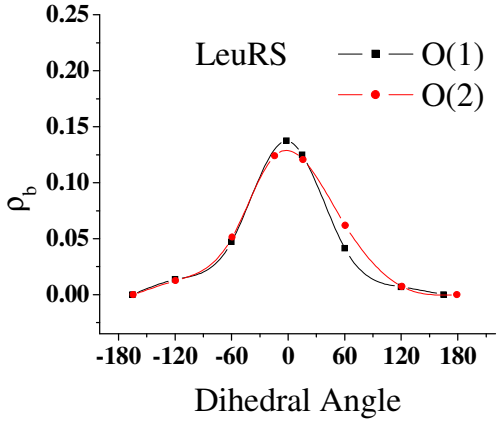
(b)


CysRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

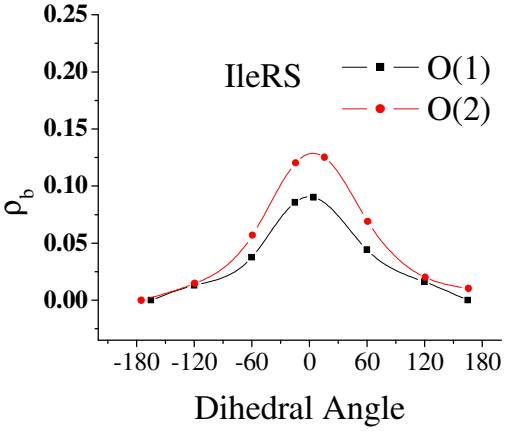
(c)


MetRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

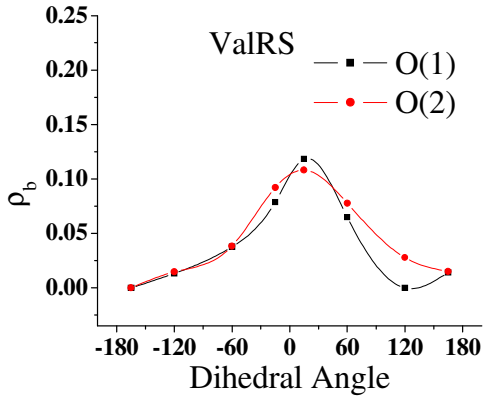
(d)


LeuRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

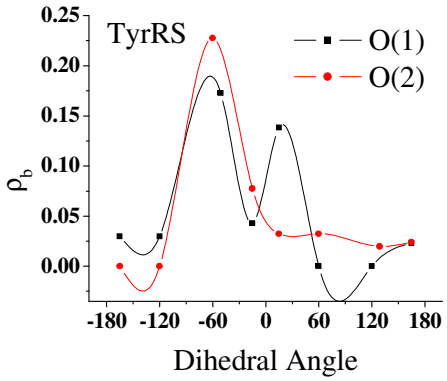
(e)


IleRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

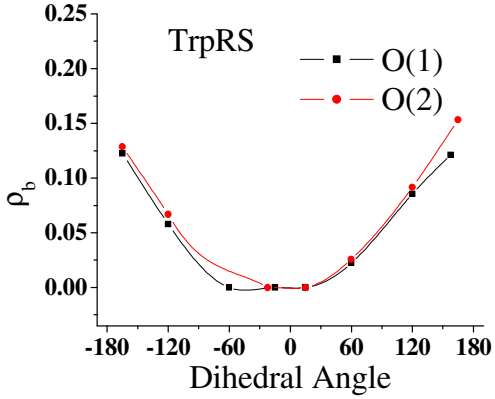
(f)


ValRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(g)

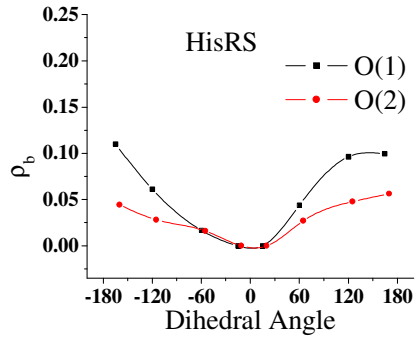

TyrRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(h)

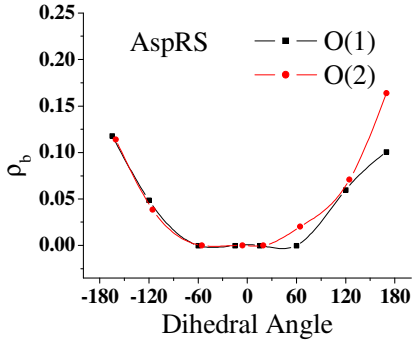

TrpRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(i)

Fig. S4


HisRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(a)


AspRS
O(1)
O(2)
ρ_b
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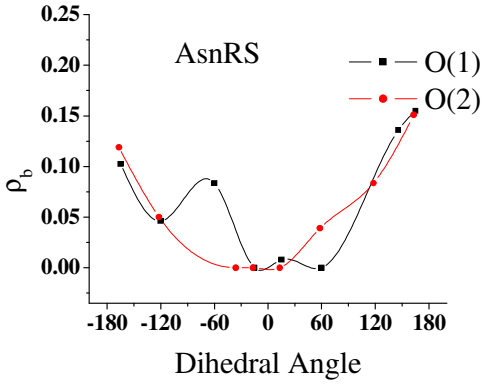
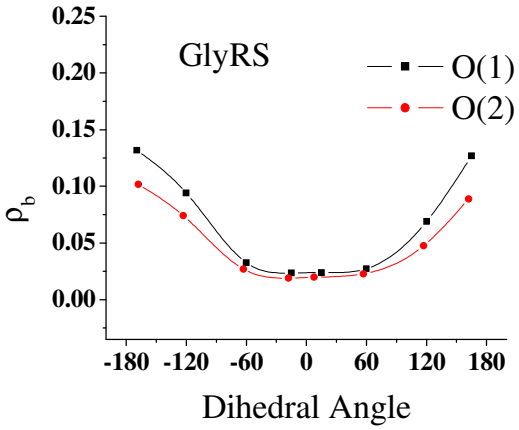
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

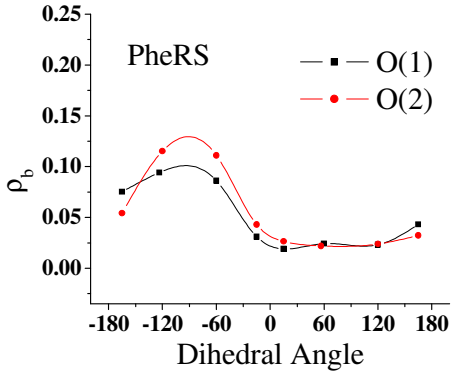
(b)


AsnRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

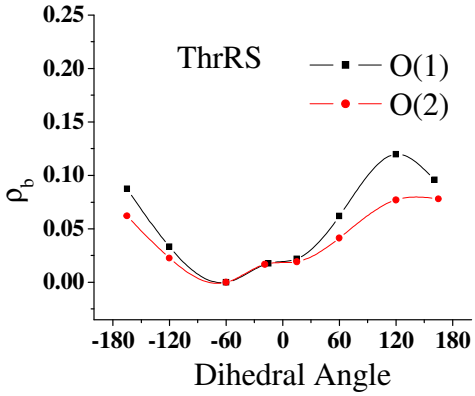
(c)


GlyRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(d)


PheRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(e)


ThrRS
O(1)
O(2)
ρ_b
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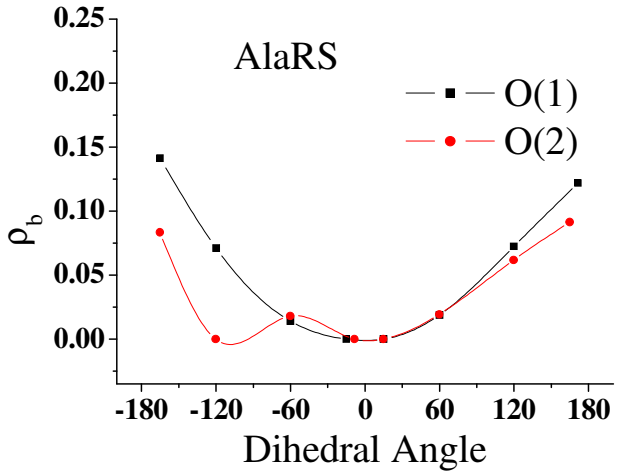
0.20
0.15
0.10
0.05
0.00
-180 -120 -60 0 60 120 180
Dihedral Angle

(f)


AlaRS
O(1)
O(2)
ρ_b
0.25
0.20
0.15
0.10
0.05
0.00
-180
-120
-60
0
60
120
180
Dihedral Angle

(g)

Fig. S5

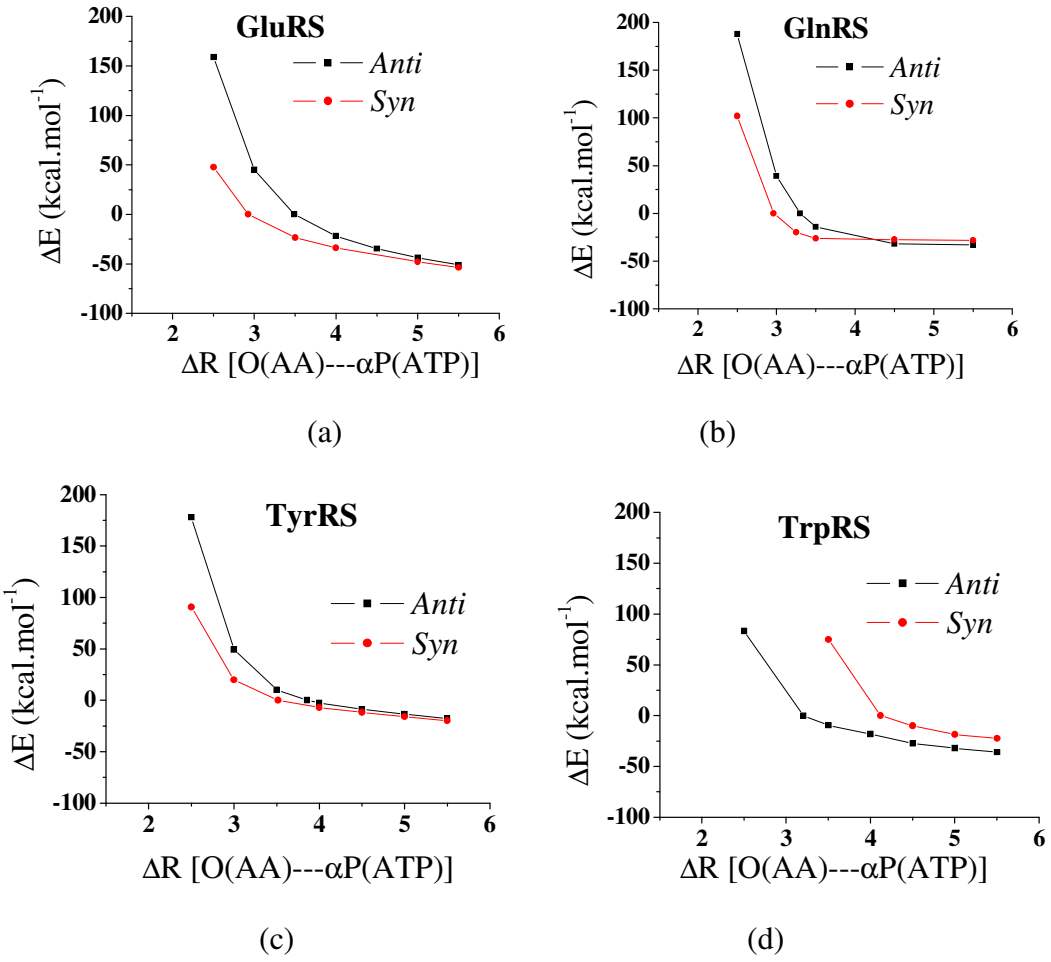
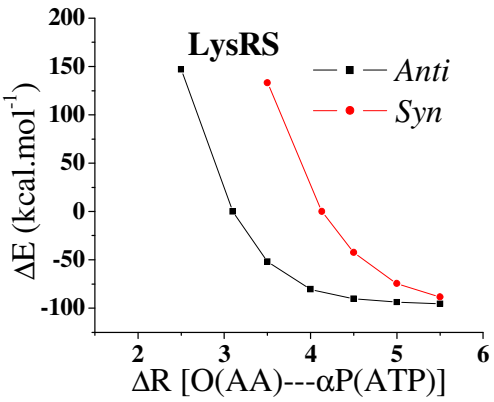
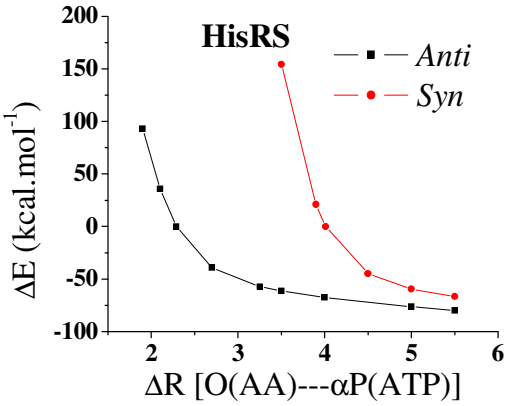

GluRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]
(a)
GlnRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]
(b)
TyrRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]
(c)
TrpRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]
(d)

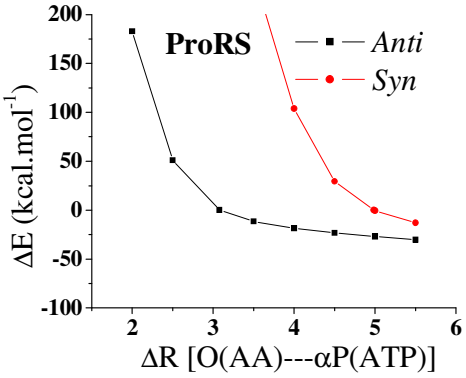
Fig. S6


LysRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]

(a)


HisRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]

(b)


ProRS
Anti
Syn
ΔE (kcal.mol-1)
ΔR [O(AA)---αP(ATP)]

(c)

Fig. S7