Improved Peptide and Protein Torsional Energetics with the OPLS-AA Force Field

Supplementary Information

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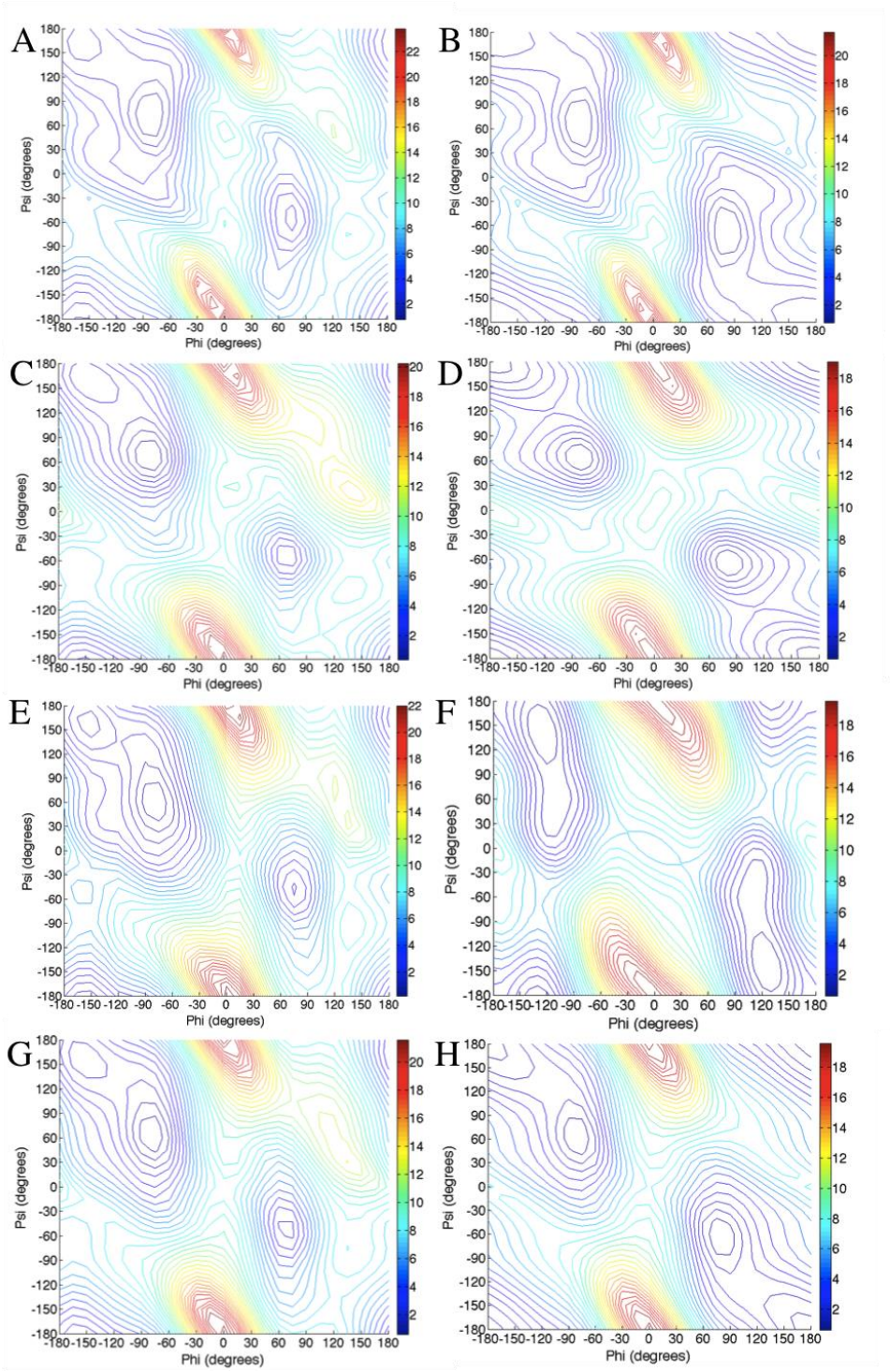

Figure S1. Two dimensional phi-psi potential energy surfaces calculated for A) alanine at the B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) level of theory, B) glycine at the B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) level of theory, C) alanine with the

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Table S1. Summary of the Force Field Parameters Developed and Tested in this Work for the Alanine and Glycine Peptide Backbone and their Boltzmann-Weighted Errors Compared to the B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) Relative Energies. Parameters Noted with a * are those Selected for the OPLS-AA/M Force Field.

		Parameters[a]				Boltzmann Weighted Error[a]			
		V1	V2	V3		500 K	1000 K	2000 K	Unweighted
OPLS-AA	φ	-2.365	0.912	-0.850	Alanine	0.1055	0.2779	0.5283	1.2606
	ψ	1.816	1.222	1.581	Glycine	0.2765	0.5689	0.8932	1.6028
	φ'	0.000	0.462	0.000					
	ψ'	1.173	0.189	-1.200					
OPLS-AA/L	φ	-0.596	0.279	-4.913	Alanine	0.1073	0.2646	0.5317	1.3811
	ψ	0.743	2.508	-0.805	Glycine	0.6807	1.1942	1.7343	3.0049
	φ'	0.519	0.877	5.223					
	ψ'	1.865	0.089	0.351					
Optimized Parameters									
500 K	φ	-2.196	0.286	-0.493	Alanine	0.0814	0.2074	0.4089	1.0437
	ψ	1.508	1.592	-0.44	Glycine	0.1503	0.3357	0.5548	1.0913
	φ'	-1.2	0.733	0.26					
	ψ'	1.19	0.508	-0.012					
1000 K	φ	-2.417	0.266	-0.383	Alanine	0.0866	0.1995	0.3761	0.9518
	ψ	1.55	1.96	-0.5	Glycine	0.1423	0.3023	0.3848	1.0007
	φ'	-0.73	0.318	0.439					
	ψ'	1.502	0.47	-0.023					
*2000 K	φ	-2.511	0.21	-0.2	Alanine	0.0934	0.2037	0.3719	0.9271
	ψ	1.81	2.155	-0.47	Glycine	0.1497	0.2975	0.4766	0.9558
	φ'	-0.682	0.13	0.338					
	ψ'	1.779	0.419	-0.11					
Unweighted	φ	-2.271	0.072	0.017	Alanine	0.1053	0.2169	0.3792	0.9128
	ψ	2.016	2.217	-0.517	Glycine	0.1658	0.3124	0.3870	0.9544
	φ'	-0.632	-0.053	0.055					
	ψ'	1.946	0.255	-0.146					

[a]Both the parameters and the RMSD values have units of kcal/mol

Table S2. Summary of the χ_1 Force Field Parameters Developed and Tested in this Work and their Boltzmann-Weighted Errors Compared to the B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) Relative Energies. Parameters Noted with a * are those Selected for the OPLS-AA/M Force Field.

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Valine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.761	1.011	1.293	1.846
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.946	0.383	0.440	0.370	0.474	0.575	0.751
	χ_1'	-1.294	0.748	0.000				
2000 K Val	χ_1	2.804	0.081	0.511	0.139	0.221	0.315	0.496
	χ_1'	-1.823	0.797	0.000				
*2000 K Val/Ile	χ_1	2.994	0.252	0.300	0.169	0.260	0.360	0.553
	χ_1'	-1.422	1.068	0.000				
2000 K Val/Ile/Leu	χ_1	2.561	0.283	0.277	0.185	0.277	0.377	0.574
	χ_1'	-1.407	1.279	0.000				
Isoleucine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.660	1.003	1.363	2.022
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	2.647	0.954	0.522	0.264	0.473	0.703	1.145
	χ_1'	0.678	1.276	0.000				
2000 K Ile	χ_1	3.746	0.483	0.185	0.169	0.344	0.552	1.001
	χ_1'	-0.756	1.241	0.000				
*2000 K Val/Ile	χ_1	2.994	0.252	0.300	0.191	0.382	0.602	1.066
	χ_1'	-1.422	1.068	0.000				
2000 K Val/Ile/Leu	χ_1	2.561	0.283	0.277	0.197	0.388	0.609	1.085
	χ_1'	-1.407	1.279	0.000				
Leucine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.318	0.560	0.859	1.498
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.110	0.263	0.594	0.324	0.560	0.847	1.490
	χ_1'	-0.539	0.073	0.000				
*2000 K Leu	χ_1	1.572	0.159	0.200	0.263	0.457	0.695	1.238
	χ_1'	-1.751	1.606	0.000				
2000 K Val/Ile/Leu	χ_1	2.561	0.283	0.277	0.281	0.483	0.741	1.313
	χ_1'	-1.407	1.279	0.000				
Serine								
OPLS-AA	χ_1	6.280	-1.467	2.030	0.404	0.645	0.977	1.717
	χ_1'	-6.180	0.000	0.000				
OPLS-AA/L	χ_1	5.429	-0.879	1.058	0.418	0.643	0.935	1.577
	χ_1'	-5.654	-0.872	0.000				
2000 K Ser	χ_1	5.835	-0.607	0.705	0.309	0.475	0.692	1.169
	χ_1'	-5.006	0.809	0.000				
*2000 K Ser Empirical	χ_1	6.258	-1.037	1.367	0.359	0.556	0.815	1.388
	χ_1'	-5.793	0.405	0.000				

[a]Both the parameters and the error values have units of kcal/mol

Table S2 Continued

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Threonine								
OPLS-AA	χ_1^C	0.845	-0.962	0.713	0.598	0.981	1.486	2.582
	$\chi_1^{C,}$	-1.697	-0.456	0.585				
	χ_1^O	6.280	-1.467	2.030				
	$\chi_1^{O,}$	-6.180	0.000	0.000				
OPLS-AA/L	χ_1^C	0.845	-0.962	0.713	0.444	0.700	1.029	1.783
	$\chi_1^{C,}$	-1.697	-0.456	0.585				
	χ_1^O	5.429	-0.879	1.058				
	$\chi_1^{O,}$	-5.654	-0.872	0.000				
2000 K Val/Ile/Leu χ_1^C	χ_1^C	2.561	0.283	0.957	0.314	0.491	0.725	1.269
Ser χ_1^O	$\chi_1^{C,}$	-1.407	1.279	-0.680				
	χ_1^O	5.835	-0.607	0.705				
	$\chi_1^{O,}$	-5.006	0.809	0.000				
*2000 K Val/Ile χ_1^C	χ_1^C	2.994	0.252	0.300	0.346	0.554	0.827	1.455
Ser Empirical χ_1^O	$\chi_1^{C,}$	-1.422	1.068	0.000				
	χ_1^O	6.258	-1.037	1.367				
	$\chi_1^{O,}$	-5.793	0.405	0.000				
Aspartate								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.367	0.949	2.017	5.626
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	-9.457	-0.154	-0.253	0.201	0.446	0.914	2.757
	χ_1'	-4.774	3.031	0.000				
2000 K Asp/Asn	χ_1	-5.885	1.243	0.000	0.143	0.321	0.645	1.881
	χ_1'	0.897	2.069	0.433				
2000 K Asp	χ_1	-8.290	0.662	0.997	0.107	0.216	0.442	1.463
	χ_1'	1.543	3.096	0.000				
*2000 K Asp Empirical	χ_1	-7.890	0.662	0.997	0.191	0.354	0.638	1.807
	χ_1'	1.543	0.696	0.000				
Asparagine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.825	1.342	2.111	4.076
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	-3.467	-0.677	1.465	0.387	0.685	1.116	2.207
	χ_1'	1.045	-1.603	0.000				
2000 K Asp/Asn	χ_1	-5.885	1.243	0.000	0.280	0.442	0.671	1.246
	χ_1'	0.897	2.069	0.433				
*2000 K Asn	χ_1	-5.501	1.527	0.000	0.250	0.403	0.613	1.127
	χ_1'	0.598	1.558	0.255				
Glutamine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.259	0.461	0.722	1.368
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	1.167	-0.526	0.805	0.230	0.411	0.646	1.219
	χ_1'	-2.692	0.836	0.000				
2000 K Leu	χ_1	1.572	0.159	0.200	0.233	0.414	0.648	1.220
	χ_1'	-1.751	1.606	0.000				
2000 K Gln	χ_1	1.240	0.838	0.983	0.163	0.279	0.441	0.872
	χ_1'	-2.096	0.821	0.000				
*2000 K Gln/Lys	χ_1	0.884	0.897	0.880	0.162	0.283	0.454	0.910
	χ_1'	-2.358	0.911	0.000				

[a]Both the parameters and the error values have units of kcal/mol

Table S2 Continued

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Lysine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.320	0.500	0.741	1.347
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.639	-0.214	0.399	0.296	0.461	0.684	1.310
	χ_1'	-2.235	-0.536	0.00				
2000 K Leu	χ_1	1.572	0.159	0.200	0.239	0.410	0.648	1.283
	χ_1'	-1.751	1.606	0.000				
2000 K Lys	χ_1	0.357	0.932	0.750	0.147	0.272	0.465	1.014
	χ_1'	-2.745	1.015	0.000				
*2000 K Gln/Lys	χ_1	0.884	0.897	0.880	0.155	0.286	0.482	1.024
	χ_1'	-2.358	0.911	0.000				
Glutamate								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.387	0.650	1.052	2.691
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	4.952	-0.257	-0.235	0.369	0.585	0.987	2.629
	χ_1'	-1.618	-0.571	0.000				
2000 K Leu	χ_1	1.572	0.159	0.200	0.328	0.558	0.917	2.444
	χ_1'	-1.751	1.606	0.000				
2000 K Glu	χ_1	3.287	0.457	0.820	0.213	0.341	0.621	1.970
	χ_1'	-1.764	1.100	0.000				
*2000 K Glu Empirical	χ_1	1.987	0.457	0.820	0.280	0.440	0.734	2.132
	χ_1'	-1.764	0.700	0.000				
Cysteine								
OPLS-AA	χ_1	1.428	0.086	0.029	0.534	0.852	1.199	1.845
	χ_1'	-4.344	-1.714	0.000				
OPLS-AA/L	χ_1	1.428	0.086	0.029	0.544	0.872	1.225	1.876
	χ_1'	-4.344	-1.714	0.000				
2000 K Cys	χ_1	2.355	0.529	0.544	0.199	0.375	0.572	0.940
	χ_1'	-3.323	1.469	0.000				
*2000 K Cys Empirical	χ_1	2.055	0.529	0.544	0.246	0.435	0.652	1.062
	χ_1'	-3.323	0.529	0.000				
Methionine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.354	0.547	0.764	1.185
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	1.493	0.199	-0.098	0.377	0.554	0.728	1.045
	χ_1'	0.384	-0.762	0.000				
2000 K Leu	χ_1	1.572	0.159	0.200	0.293	0.476	0.677	1.084
	χ_1'	-1.751	1.606	0.000				
*2000 K Met	χ_1	0.214	0.541	0.392	0.185	0.276	0.369	0.553
	χ_1'	-0.911	0.699	0.000				
Arginine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.298	0.464	0.639	0.975
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	1.821	0.951	1.168	0.298	0.506	0.728	1.166
	χ_1'	-0.678	1.653	0.000				
2000 K Leu	χ_1	1.572	0.159	0.200	0.223	0.385	0.565	0.941
	χ_1'	-1.751	1.606	0.000				
*2000 K Arg	χ_1	0.103	0.653	0.563	0.146	0.245	0.365	0.662
	χ_1'	-1.971	0.770	0.000				
Phenylalanine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.412	0.682	0.996	1.641
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.845	-0.962	0.713	0.394	0.673	0.994	1.645
	χ_1'	-1.697	-0.456	0.585				
*2000 K Phe	χ_1	1.712	0.725	0.366	0.201	0.377	0.577	0.990
	χ_1'	-1.406	1.777	0.000				

[a]Both the parameters and the error values have units of kcal/mol

Table S2 Continued

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Tyrosine								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.405	0.686	1.007	1.663
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.845	-0.962	0.713	0.390	0.682	1.014	1.676
	χ_1'	-1.697	-0.456	0.585				
2000 K Tyr	χ_1	1.611	0.653	0.535	0.200	0.379	0.584	1.011
	χ_1'	-1.491	1.792	0.000				
*2000 K Phe	χ_1	1.712	0.725	0.366	0.202	0.382	0.587	1.014
	χ_1'	-1.406	1.777	0.000				
Tryptophan								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.410	0.683	0.980	1.548
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	-1.294	0.562	0.094	0.369	0.618	0.911	1.541
	χ_1'	-1.058	-0.625	0.000				
2000 K Phe	χ_1	1.712	0.725	0.366	0.226	0.446	0.723	1.330
	χ_1'	-1.406	1.777	0.000				
2000 K Trp	χ_1	0.068	1.020	0.665	0.221	0.361	0.529	0.893
	χ_1'	-0.506	1.375	0.000				
*2000 K Trp Empirical	χ_1	-0.588	1.020	0.665	0.260	0.413	0.593	0.970
	χ_1'	-0.506	0.975	0.000				
Histidine-ε								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.323	0.651	1.053	1.883
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	-0.713	0.502	0.289	0.304	0.584	0.921	1.633
	χ_1'	-1.607	0.046	0.000				
2000 K Hie	χ_1	-0.437	0.538	0.000	0.255	0.419	0.631	1.105
	χ_1'	-1.416	2.050	-0.082				
*2000 K Hie/Hid	χ_1	-0.542	0.435	0.000	0.251	0.421	0.637	1.113
	χ_1'	-1.282	1.645	-0.017				
Histidine-δ								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.428	0.724	1.084	1.809
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	-0.713	0.502	0.289	0.333	0.560	0.827	1.364
	χ_1'	-1.607	0.046	0.000				
2000 K Hid	χ_1	-0.614	0.455	0.013	0.247	0.439	0.670	1.155
	χ_1'	-1.055	1.204	0.000				
*2000 K Hie/Hid	χ_1	-0.542	0.435	0.000	0.250	0.445	0.679	1.177
	χ_1'	-1.282	1.645	-0.017				
Protonated His								
OPLS-AA	χ_1	0.845	-0.962	0.713	0.514	0.806	1.233	2.654
	χ_1'	-1.697	-0.456	0.585				
OPLS-AA/L	χ_1	0.347	-0.350	1.468	0.514	0.799	1.171	2.253
	χ_1'	1.679	0.082	0.000				
2000 K Hid/Hie	χ_1	-0.542	0.435	0.000	0.310	0.538	0.898	2.047
	χ_1'	-1.282	1.645	-0.017				
*2000 K Hip	χ_1	-3.038	0.419	0.000	0.243	0.449	0.761	1.747
	χ_1'	-1.708	1.516	-0.502				

[a]Both the parameters and the error values have units of kcal/mol

Table S3. Summary of the χ_2 Force Field Parameters Developed and Tested in this Work and their Boltzmann-Weighted Errors Compared to the ωB97X-D/6-311++G(d,p) and, where Applicable, B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) Relative Energies. Parameters Noted with a * are those Selected for the OPLS-AA/M Force Field.

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Isoleucine								
*OPLS-AA	χ_2	1.300	-0.200	0.200	0.196	0.295	0.407	0.661
2000 K Ile	χ_2	0.595	-0.240	0.295	0.157	0.253	0.366	0.629
Leucine								
*OPLS-AA	χ_2	1.300	-0.200	0.200	0.166	0.283	0.424	0.733
2000 K Ile	χ_2	0.295	-0.005	0.300	0.160	0.265	0.387	0.640
Serine								
*OPLS-AA	χ_2	-0.356	-0.174	0.492	0.355	0.530	0.687	0.929
OPLS-AA/L	χ_2	-0.991	-0.869	0.739	0.359	0.534	0.685	0.912
2000 K Ser	χ_2	-0.366	-0.849	0.542	0.315	0.486	0.639	0.875
Cysteine								
*OPLS-AA	χ_2	-0.759	-0.282	0.680	0.249	0.426	0.581	0.813
2000 K Cys	χ_2	-0.754	-1.502	0.745	0.231	0.368	0.485	0.659
Methionine								
OPLS-AA	χ_2	2.619	-0.620	0.258	0.318	0.481	1.166	2.665
*2000 K Met	χ_2	-1.565	-0.009	-0.450	0.160	0.285	0.463	1.196
Asparagine								
OPLS-AA	χ_2 N	2.844	-0.361	-0.325	0.226	0.465	0.838	1.737
	χ_2'O	0.406	1.304	0.139				
OPLS-AA/L	χ_2 N	-0.546	-2.127	-0.832	0.354	0.537	0.779	1.333
	χ_2'O	0.000	1.166	0.000				
*2000 K Asn	χ_2 N	1.494	-0.511	0.125	0.159	0.263	0.413	0.759
	χ_2'O	1.656	1.304	0.439				
Aspartate								
OPLS-AA	χ_2	0.000	0.546	0.000	0.239	0.382	0.547	0.878
*2000 K Asp	χ_2	0.000	1.000	1.350	0.187	0.298	0.433	0.710
Glutamine								
OPLS-AA	χ_2	-1.567	-0.979	0.636	0.181	0.362	0.615	1.476
2000 K Gln	χ_2	-0.867	-0.829	0.036	0.143	0.279	0.484	1.295
*2000 K Gln Emp.	χ_2	-1.267	0.479	-0.486	0.172	0.349	0.489	1.384
Glutamate								
OPLS-AA	χ_2	-3.185	-0.825	0.493	0.195	0.445	0.888	2.506
2000 K Glu	χ_2	-6.745	-0.759	-0.647	0.143	0.346	0.766	2.493
*2000 K Glu Emp.	χ_2	-0.885	1.025	-1.293	0.281	0.554	1.062	2.819
Phenylalanine								
*OPLS-AA	χ_2	0.000	0.000	0.000	0.128	0.243	0.373	0.616
2000 K Phe	χ_2	-2.955	0.095	1.015	0.126	0.232	0.354	0.584
Tyrosine								
*OPLS-AA	χ_2	0.000	0.000	0.000	0.157	0.270	0.405	0.662
2000 K Tyr	χ_2	-3.040	0.150	0.125	0.158	0.261	0.386	0.630
Tryptophan								
*OPLS-AA	χ_2	-0.714	0.000	0.000	0.274	0.455	0.684	1.295
2000 K Trp	χ_2	-1.714	-0.800	-0.900	0.260	0.417	0.608	1.104
Histidine-ε								
OPLS-AA	χ_2	2.366	-0.262	0.505	0.363	0.538	0.729	1.109
OPLS-AA/L	χ_2	-0.543	0.014	0.700	0.235	0.354	0.491	0.778
2000 K Hie	χ_2	-0.790	-0.335	0.140	0.164	0.244	0.344	0.576
*2000 K Hie/Hid	χ_2	-0.560	-0.740	0.349	0.181	0.265	0.364	0.581

[a]Both the parameters and the Error values have units of kcal/mol

Table S3 Continued

		Parameters[a]			Average Boltzmann Weighted Error Per Scan[a]			
		V1	V2	V3	500 K	1000 K	2000 K	Unweighted
Histidine-δ								
OPLS-AA	χ_2	2.366	-0.262	0.505	0.187	0.390	0.646	1.152
OPLS-AA/L	χ_2	-0.543	0.014	0.700	0.202	0.353	0.526	0.850
2000 K Hid	χ_2	-0.585	-1.100	0.375	0.125	0.211	0.314	0.522
*2000 K Hie/Hid	χ_2	-0.560	-0.740	0.349	0.132	0.222	0.326	0.531
Protonated His								
OPLS-AA	χ_2	2.366	-0.262	0.505	0.610	1.030	1.792	3.976
OPLS-AA/L	χ_2	-0.543	0.014	0.700	0.392	0.693	1.227	2.740
*2000 K Hip	χ_2	-3.990	1.680	0.290	0.265	0.444	0.713	1.395
2000 K Hie/Hid	χ_2	-0.560	-0.740	0.349	0.431	0.750	1.310	2.887

[a]Both the parameters and the Error values have units of kcal/mol

Table S4. Summary of the Results of the Molecular Dynamics Simulations of Blocked Dipeptides Performed in this Work with all Force Fields.

Valine	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000K Val/Ile/Leu	2000K Val/Ile
$^3J(H_NH_\alpha)$ (Hz)	7.30		8.15 ± 0.02	8.01 ± 0.01	7.40 ± 0.01	7.39 ± 0.01
%m	8.1 ± 2.5	9.3	74.0 ± 5.2	62.2 ± 3.0	6.0 ± 0.6	8.1 ± 1.2
%p	39.2 ± 5.7	33.3	13.1 ± 2.9	9.9 ± 1.9	18.4 ± 2.6	13.6 ± 0.9
%t	52.8 ± 6.8	57.4	13.0 ± 2.4	27.9 ± 1.2	75.6 ± 2.6	78.3 ± 0.3
Isoleucine	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000K Val/Ile/Leu	2000K Val/Ile
$^3J(H_NH_\alpha)$ (Hz)	7.33		8.19 ± 0.06	7.81 ± 0.00	7.42 ± 0.00	7.40 ± 2.3
%m	63.1 ± 6.7	61.2	3.7 ± 1.8	71.3 ± 1.6	57.8 ± 7.2	55.6 ± 6.3
%p	28.3 ± 6.0	26.7	85.0 ± 12.9	23.0 ± 0.1	24.2 ± 3.5	19.2 ± 10.2
%t	8.6 ± 4.4	12.1	11.3 ± 11.3	5.7 ± 1.6	18.1 ± 2.0	25.2 ± 4.1
Leucine	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000K Val/Ile/Leu	2000 K Leu
$^3J(H_NH_\alpha)$ (Hz)	6.88		8.04 ± 0.01	7.72 ± 0.02	7.28 ± 0.00	7.40 ± 0.01
%m	73.6 ± 6.0	73.1	55.9 ± 4.7	81.3 ± 1.0	36.7 ± 1.4	66.1 ± 1.7
%p	7.0 ± 6.8	1.8	10.1 ± 6.3	5.3 ± 1.2	0.8 ± 0.1	1.6 ± 0.1
%t	19.6 ± 4.6	25.1	34.0 ± 2.3	13.4 ± 0.7	62.5 ± 1.5	32.3 ± 1.8
Serine	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Ser	2000 K Ser Reweighted
$^3J(H_NH_\alpha)$ (Hz)	7.02		7.87 ± 0.00	7.87 ± 0.04	7.10 ± 0.01	7.21 ± 0.01
%m	33.1 ± 0.7	29.4	13.9 ± 2.9	10.3 ± 0.4	66.8 ± 2.3	40.0 ± 2.9
%p	29.4 ± 0.3	53.4	63.0 ± 6.5	75.6 ± 1.1	17.7 ± 1.9	28.6 ± 4.4
%t	37.5 ± 1.0	17.2	23.1 ± 3.6	14.1 ± 0.9	15.5 ± 0.9	31.4 ± 3.7
Threonine	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Ser	2000 K Ser Reweighted
$^3J(H_NH_\alpha)$ (Hz)	7.35		8.01 ± 0.01	8.02 ± 0.08	7.13 ± 0.03	7.22 ± 0.04
%m	39.3 ± 7.3	27.3	6.1 ± 4.6	1.1 ± 0.1	64.2 ± 8.2	46.9 ± 11.6
%p	46.6 ± 5.1	63.7	92.3 ± 6.6	54.5 ± 33.3	34.2 ± 8.4	51.1 ± 11.6
%t	14.1 ± 7.1	9.0	1.7 ± 2.4	44.3 ± 33.9	1.6 ± 0.6	2.0 ± 0.4

[a]J couplings for dipeptides given in reference 48. Rotamer populations and errors given are the averages and standard deviations over all residues in denatured ubiquitin and protein G from reference reference 42 [b]Coil library data from reference 43

Table S4 Continued

Cysteine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Cys	2000 K Cys Reweighted	
$^3J(H_NH_\alpha)$ (Hz)	7.31		7.89 ± 0.01	8.01 ± 0.03	7.23 ± 0.00	7.25 ± 0.01	
%m		45.8	3.7 ± 0.3	2.9 ± 0.4	78.2 ± 1.6	57.8 ± 0.9	
%p		29.2	63.3 ± 4.9	74.3 ± 2.6	6.7 ± 0.7	13.8 ± 1.6	
%t		25.0	33.0 ± 4.5	22.9 ± 2.3	15.1 ± 2.1	28.4 ± 0.0	
Methionine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Met		
$^3J(H_NH_\alpha)$ (Hz)	7.02		7.97 ± 0.01	7.66 ± 0.01	7.45 ± 0.02		
%m		61.3	21.1 ± 1.4	21.2 ± 0.4	52.9 ± 0.9		
%p		13.9	33.7 ± 7.2	8.6 ± 1.4	8.2 ± 0.2		
%t		24.8	45.2 ± 5.86	70.2 ± 1.3	38.9 ± 1.0		
Asparagine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Asn		
$^3J(H_NH_\alpha)$ (Hz)	7.45		7.88 ± 0.00	7.84 ± 0.17	7.39 ± 0.00		
%m	46.1 ± 3.2	55.1	0.0 ± 0.0	5.0 ± 2.8	60.9 ± 2.9		
%p	27.1 ± 3.4	18.9	0.0 ± 0.0	53.9 ±- 25.5	9.1 ± 1.8		
%t	26.5 ± 4.4	26.0	100.0 ± 0.0	41.0 ± 22.7	30.0 ± 1.4		
Aspartate	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Asp	2000K Asp/Asn	2000 K Asp Reweighted
$^3J(H_NH_\alpha)$ (Hz)	6.93		7.75 ± 0.01	7.80 ± 0.00	6.85 ± 0.01	7.05 ± 0.00	6.99 ± 0.02
%m	44.9 ± 5.5	48.2	0.0 ± 0.0	0.2 ± 0.0	97.0 ± 1.3	23.9 ± 1.7	55.8 ± 5.2
%p	30.3 ± 5.9	22.8	0.0 ± 0.0	97.5 ± 0.2	2.2 ± 1.1	4.6 ± 0.4	25.4 ± 4.6
%t	24.8 ± 4.3	28.9	100.0 ± 0.0	2.3 ± 0.2	0.8 ± 0.9	71.4 ± 1.6	18.8 ± 2.7
Glutamine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000K Gln/Lys		
$^3J(H_NH_\alpha)$ (Hz)	7.14		8.27 ± 0.06	7.85 ± 0.02	7.37 ± 0.02		
%m	61.4 ± 3.5	64.0	80.1 ± 6.4	63.6 ± 3.2	52.3 ± 3.5		
%p	15.7 ± 2.0	11.4	7.5 ± 5.1	14.5 ± 2.8	5.4 ± 0.8		
%t	22.9 ± 3.5	24.6	12.3 ± 2.0	21.9 ± 2.1	42.3 ± 3.9		
Glutamate	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Glu	2000 K Glu Reweighted	
$^3J(H_NH_\alpha)$ (Hz)	6.63		7.58 ± 0.03	7.22 ± 0.10	7.08 ± 0.03	6.97 ± 0.04	
%m	60.8 ± 3.1	60.1	84.1 ± 4.2	88.3 ± 5.4	42.3 ± 9.9	70.4 ± 5.5	
%p	16.4 ± 2.3	13.9	8.9 ± 2.1	6.8 ± 2.2	0.00 ± 0.00	4.7 ± 3.6	
%t	22.7 ± 2.6	26.0	6.9 ± 2.2	4.9 ± 3.2	57.2 ± 10.0	24.9 ± 4.6	
Lysine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000K Gln/Lys		
$^3J(H_NH_\alpha)$ (Hz)	6.83		8.12 ± 0.01	7.90 ± 0.02	7.37 ± 0.02		
%m	60.7 ± 3.2	64.9	61.8 ± 3.9	26.0 ± 1.5	43.2 ± 2.7		
%p	15.3 ± 2.1	10.6	24.7 ± 6.1	49.9 ± 2.1	10.5 ± 1.9		
%t	24.0 ± 3.1	24.6	13.4 ± 2.2	24.1 ± 0.1	46.3 ± 4.3		
Arginine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Arg		
$^3J(H_NH_\alpha)$ (Hz)	6.85		8.18 ± 0.02	7.82 ± 0.11	7.53 ± 0.02		
%m	59.5 ± 1.9	60.6	52.4 ± 6.0	74.3 ± 0.9	56.4 ± 4.0		
%p	16.1 ± 3.0	16.6	23.7 ± 9.6	1.8 ± 0.2	15.7 ± 0.7		
%t	24.4 ± 2.1	22.8	23.9 ± 3.6	23.9 ± 1.0	27.9 ± 3.7		

[a]J couplings for dipeptides given in reference 48. Rotamer populations and errors given are the averages and standard deviations over all residues in denatured ubiquitin and protein G from reference reference 42 [b]Coil library data from reference 43

Table S4 Continued

Phenylalanine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Phe	
$^3J(H_NH_\alpha)$ (Hz)	7.18		8.18 ± 0.01	8.01 ± 6.4	7.41 ± 0.02	
%m	60.7 ± 5.3	51.6	36.5 ± 6.0	26.7 ± 8.2	51.3 1.3	
%p	12.2 ± 5.0	19.0	33.1 ± 9.0	51.9 ± 14.1	2.0 0.6	
%t	27.2 ± 3.6	29.5	30.4 ± 3.1	21.4 ± 6.0	46.7 1.1	
Tyrosine	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Tyr	
$^3J(H_NH_\alpha)$ (Hz)	7.13		8.21 ± 0.02	8.05 ± 0.05	7.46 ± 0.05	
%m	59.4 ± 7.8	48.4	38.8 ± 3.5	31.3 ± 5.3	49.7 ± 4.4	
%p	14.1 ± 2.0	18.8	26.6 ± 9.9	42.6 ± 10.5	2.1 ± 0.3	
%t	26.5 ± 6.2	32.8	34.7 ± 6.7	26.0 ± 5.2	48.2 ± 4.2	
Tryptophan	Experiment (NMR) [a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Trp	2000 K Trp Reweighted
$^3J(H_NH_\alpha)$ (Hz)	6.91		8.01 ± 0.03	7.91 ± 0.05	7.46 ± 0.04	7.55 ± 2.8
%m	52.0	44.7	6.0 ± 2.3	11.9 ± 0.3	44.7 ± 6.0	56.2 ± 2.7
%p	14.3	23.3	36.8 ± 0.6	47.6 ± 4.9	3.5 ±1.0	9.2 ± 0.8
%t	33.6	32.0	57.2 ± 4.3	40.5 ± 5.1	51.8 ± 5.0	34.6 ± 1.9
Histidine-δ	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Hid	
$^3J(H_NH_\alpha)$ (Hz)			7.94 ± 0.01	7.70 ± 0.06	7.40 ± 0.02	
%m		55.6	31.7 ± 0.4	22.7 ± 1.0	67.8 ± 3.7	
%p		18.9	9.7 ± 7.2	26.6 ± 6.1	9.0 ± 0.7	
%t		25.5	58.7 ± 7.6	50.7 ± 5.2	23.1 ± 3.5	
Histidine-ε	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Hie	
$^3J(H_NH_\alpha)$ (Hz)			7.88 ± 0.3	7.60 ± 0.05	7.17 ± 0.01	
%m		55.6	25.5 ± 6.9	21.4 ± 2.1	71.0 ± 1.9	
%p		18.9	31.8 ± 8.8	40.8 ± 3.4	10.7 ± 1.1	
%t		25.5	42.7 ± 1.9	37.7 ± 1.4	18.4 ± 1.0	
Histidine Protonated	Experiment (NMR)[a]	Coil Library[b]	OPLS-AA	OPLS-AA/L	2000 K Hip	
$^3J(H_NH_\alpha)$ (Hz)	7.76		7.97 0.01	8.05 0.02	7.54 0.02	
%m	60.1	55.6	9.3 0.9	71.4 8.8	73.0 2.4	
%p	14.0	18.9	13.2 2.9	13.2 10.5	16.2 1.7	
%t	25.9	25.5	77.5 3.8	15.3 3.5	10.8 0.7	

[a]J couplings for dipeptides given in reference 48. Rotamer populations and errors given are the averages and standard deviations over all residues in denatured ubiquitin and protein G from reference reference 42 [b]Coil library data from reference 43

Table S5. Relative Conformer Energies (in kcal/mol) for the Blocked Alanine Dipeptide Calculated with Various *Ab Initio* Methods and Molecular Mechanics Force Fields

	CCSD(T)/ CBS[a]	DF-LCCSD(T0)[b]	OPLS-AA	OPLS-AA/L	500K	1000K	2000K	Unweighted
C7-eq	0	0	0.00	0.00	0.00	0.00	0.00	0.00
C5	1.43	1.24	1.37	0.98	1.54	1.43	1.21	0.81
C7-ax	2.45	2.42	2.52	2.48	2.04	2.15	2.16	2.11
B2[c]	3.31	3	5.39	3.33	3.85	3.65	3.55	3.28
Alpha L[c]	4.95		8.26	7.26	6.29	6.01	5.85	5.81
Alpha Prime	6.56		6.56	6.19	6.64	6.90	7.04	6.95
RMSD Minima			0.05	0.29	0.21	0.23	0.30	0.40
RMSD All		0.18	1.60	0.97	0.61	0.49	0.45	0.48

[a]Reference 16 [b]Reference 15 [c]Not true minima with the force fields, phi and psi were fixed at their values from the ωB97X-D/6-311++G(d,p) calculations

Table S6. Relative Conformer Energies (in kcal/mol) for the Blocked Alanine Tetrapeptide Calculated with Various *ab initio* and DFT Methods

Conformer Number		ωB97X-D/6-311++g(p,d) Optimized Geometry			M06-2X/6-31+g(d) Optimized Geometry		
	RI-MP2(CBS)//HF/6-31G** Energy[a]	ωB97X-D/6-311++g(p,d) Energy	ωB97X-D/aug-cc-pVTZ Energy	ωB97X-D/jun-cc-pVQZ Energy	M06-2X/6-31+g(d) Energy	M06-2X/aug-cc-pVTZ Energy	M06-2X/jun-cc-pVQZ Energy
1	4.13	6.18	5.05	4.72	6.94	5.31	4.95
2	4.19	5.93	4.99	4.71	6.64	5.28	4.96
3	0.57	0.71	0.62	0.57	2.52	2.09	1.96
4	5.73	7.43	6.44	6.14	8.37	6.93	6.62
5	5.26	6.97	6.05	5.79	7.96	6.53	6.26
6	2.90	3.29	3.11	3.08	3.23	2.71	2.65
7	6.67	7.40	7.01	6.95	8.24	7.24	7.25
8	4.64	5.89	5.69	5.62	5.61	5.31	5.31
9	7.92	8.38	7.95	7.79	10.23	9.45	9.22
10	7.79	8.57	8.80	8.80	8.93	8.70	8.54
11	0	0.43	0.45	0.46	0.80	0.45	0.56
12	0.29	0.00	0.00	0.00	0.00	0.00	0.00
13	3.66	5.09	4.27	4.02	5.74	4.61	4.34
14	4.68	5.61	4.97	4.78	6.31	5.56	5.36
15	2.19	2.84	2.85	2.84	2.33	2.33	2.33
16	3.55	4.09	3.87	3.79	4.93	4.67	4.59
17	3.42	3.17	3.15	3.15	4.21	3.94	3.98
18	1.91	3.29	2.61	2.42	3.75	2.92	2.70
19	3.82	4.71	4.16	3.97	5.66	4.95	4.73
20	1.76	3.13	2.64	2.46	3.62	3.24	3.06
22	2.92	6.85	0.89	6.84	7.54	4.38	7.31
25	2.50	4.09	3.58	3.43	4.40	3.84	3.76
26	0.67	2.35	1.99	1.89	2.39	2.10	2.10

[a]Reference 30

Table S7. Values of φ and ψ for the Alanine Tetrapeptides Calculated at the ωB97X-D/6-311++g(p,d) Level of Theory

Conformer Number	ωB97X-D/6-311++g(p,d) Optimized Geometry					
	Ala1 φ	Ala1 ψ	Ala2 φ	Ala2 ψ	Ala3 φ	Ala3 ψ
1	201.8	167.4	203.2	169.4	204.1	165.2
2	200.9	164.9	201.8	163.8	277.3	78.5
3	280.4	88.6	74.4	303.4	284.2	82.8
4	201.1	162.5	276.9	83.6	201.2	154.6
5	202.3	170.8	280.0	348.6	205.3	166.5
6	272.4	62.6	56.0	23.2	181.7	148.5
7	53.9	204.9	270.8	65.4	194.7	299.3
8	71.0	288.9	304.8	132.6	61.8	23.6
9	74.2	303.3	74.7	304.1	74.3	302.2
10	68.4	12.9	48.3	40.3	71.2	288.9
11	63.6	255.8	300.1	326.1	278.5	76.5
12	62.8	242.7	296.1	339.7	254.1	23.0
13	201.2	158.1	276.6	69.6	273.5	71.6
14	199.3	162.1	293.1	339.7	251.4	16.2
15	292.9	116.1	54.7	37.9	85.9	345.7
16	291.7	113.9	74.5	311.9	269.1	357.6
17	274.2	69.5	67.2	291.7	286.2	121.5
18	276.2	70.9	274.7	65.9	274.4	71.6
19	276.9	70.6	274.7	71.6	71.6	303.7
20	277.5	73.6	290.3	339.5	261.2	10.5
21	272.2	67.0	110.0	294.8	294.8	111.7
22	63.4	31.5	72.1	304.6	240.5	11.1
23						
24	289.2	336.0	275.9	67.5	63.0	32.8
25	286.8	350.4	286.0	344.7	276.0	70.3
26	291.7	338.8	294.4	346.0	262.2	6.4
27	292.4	334.6	240.6	35.4	69.5	283.8

Table S8. Values of φ and ψ for the Alanine Tetrapeptides Calculated at the M06-2X/6-31+g(d) Level of Theory

Conformer Number	M06-2X/6-31+g(d) Optimized Geometry					
	Ala1 φ	Ala1 ψ	Ala2 φ	Ala2 ψ	Ala3 φ	Ala3 ψ
1	197.8	168.3	199.0	167.6	198.0	166.5
2	198.4	166.5	198.6	160.9	277.0	73.0
3	279.2	86.9	75.7	303.3	285.0	84.5
4	198.3	160.1	276.0	76.5	196.9	156.9
5	198.6	168.1	280.2	349.1	200.7	168.7
6	272.7	64.0	53.2	26.9	180.4	148.9
7	51.4	204.3	271.8	65.0	196.5	301.8
8	70.7	284.6	308.9	137.9	60.7	22.7
9	75.6	304.1	76.0	306.3	75.1	308.5
10	64.5	22.7	54.5	31.5	73.2	303.2
11	60.1	245.9	305.1	326.3	281.4	78.3
12	61.5	240.0	297.3	337.8	255.9	22.4
13	197.4	159.1	276.3	68.4	274.1	67.9
14	197.0	162.2	293.2	339.7	264.4	9.0
15	294.7	118.2	53.6	39.8	84.8	347.4
16	292.9	109.3	75.0	313.0	273.3	355.1
17	276.4	69.7	65.3	282.7	295.3	127.6
18	276.5	71.9	274.7	66.3	274.6	68.4
19	276.7	71.1	274.4	71.4	73.3	304.7
20	277.1	73.8	291.6	338.3	265.4	8.4
21	217.6	40.6	71.3	285.9	308.2	138.4
22	63.2	31.5	73.5	307.2	221.2	23.4
23	61.8	32.4	73.6	302.8	200.2	358.0
24	290.2	337.5	277.0	110.2	61.8	32.9
25	289.4	346.1	285.8	348.6	276.5	68.1
26	292.8	337.4	295.1	345.3	272.9	359.3
27	291.8	338.2	263.7	9.3	74.9	301.6

Table S9. Relative Conformer Energies (in kcal/mol) for the Blocked Proline Dipeptide Calculated with Various *ab initio* Methods and Molecular Mechanics Force Fields

	CCSD(T)/CBS[a]	OPLS-AA	OPLS-AA/L	2000 K
tCd	0.00	0.00	0.00	0.00
tCu	1.44	3.81	3.84	1.70
cAd	3.27	3.03	1.61	2.90
cAu	4.29	4.82	4.52	4.29
tAu	4.95			
cFd	6.00	3.35	3.21	6.40
cFu	6.50	4.85	5.10	6.31
RMSD		1.58	1.67	0.26

[a]Reference 16

Table S10. Summary of the Force Field Parameters Developed and Tested in this Work for Proline and their Average per Scan Boltzmann-Weighted Errors Compared to the B2PLYP-D3BJ/aug-cc-pVTZ//ωB97X-D/6-311++G(d,p) Energies for the Two Proline ψ Scans. Parameters Noted with a * are those Selected for the OPLS-AA/M Force Field.

		Parameters[a]			Atoms	Boltzmann Weighted Error[a]			
		V1	V2	V3		500 K	1000 K	2000 K	Unweighted
OPLS-AA	ψ	1.816	1.222	1.581	N-Cα-C-N	0.266	0.653	1.287	3.331
	ψ'	1.173	0.189	-1.200	N-C-Cα-Cβ				
	χ_1	0.845	-0.962	0.713	N-Cα-Cβ-Cγ				
	χ_1'	-1.697	-0.456	0.585	C-Cα-Cβ-Cγ				
	φ'''	-1.737	1.251	-3.501	Cδ-N-Cα-C				
	χ_5	4.753	-0.734	0.00	Cδ-N-Cα-Cβ				
	χ_4	2.859	2.058	-11.266	Cγ-Cδ-N-Cα				
OPLS-AA/L	ψ	0.743	2.508	-0.805	N-Cα-C-N	0.199	0.498	0.964	2.550
	ψ'	1.865	0.089	0.351	N-C-Cα-Cβ				
	χ_1	0.845	-0.962	0.713	N-Cα-Cβ-Cγ				
	χ_1'	-1.697	-0.456	0.585	C-Cα-Cβ-Cγ				
	φ'''	-1.737	1.251	-3.501	Cδ-N-Cα-C				
	χ_5	4.753	-0.734	0.00	Cδ-N-Cα-Cβ				
	χ_4	2.859	2.058	-11.266	Cγ-Cδ-N-Cα				
*2000 K Pro	ψ	-0.940	2.755	-2.670	N-Cα-C-N	0.170	0.331	0.568	1.116
	ψ'	5.029	0.719	2.240	N-C-Cα-Cβ				
	χ_1	1.572	0.159	0.200	N-Cα-Cβ-Cγ				
	χ_1'	-1.751	1.606	0.000	C-Cα-Cβ-Cγ				
	φ'''	-1.737	1.251	-3.501	Cδ-N-Cα-C				
	χ_5	4.753	-0.734	0.00	Cδ-N-Cα-Cβ				
	χ_4	2.859	2.058	-11.266	Cγ-Cδ-N-Cα				

[a]Both the parameters and the RMSD values have units of kcal/mol

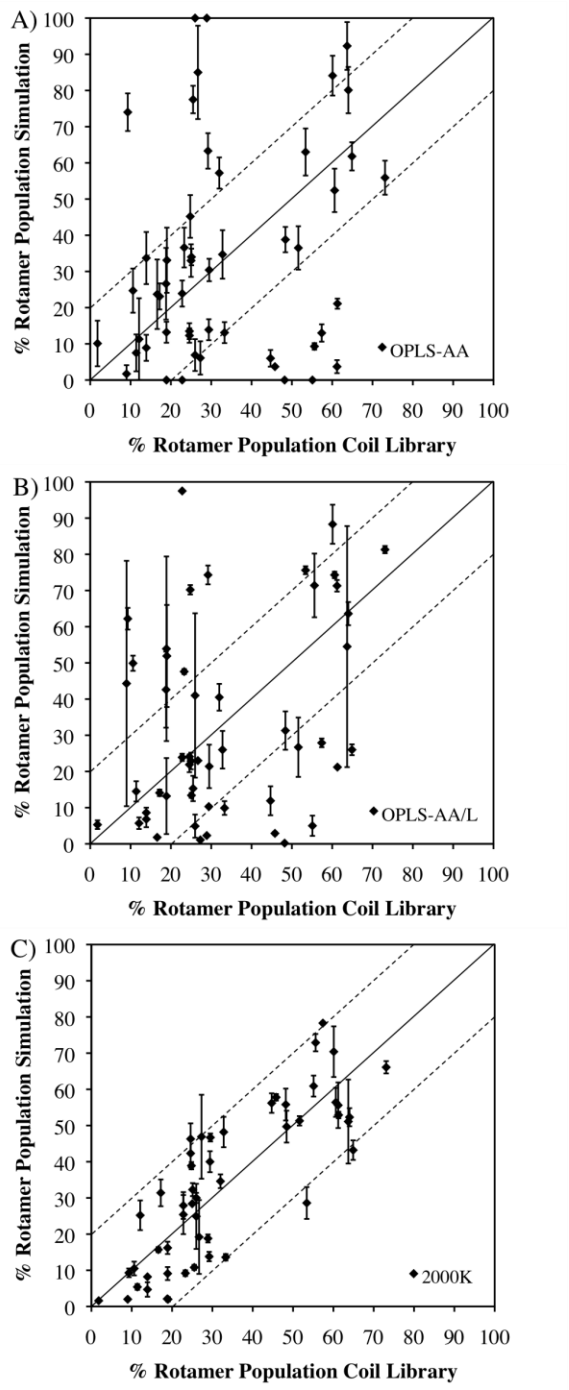

Figure SI2. The populations of each rotamer as a percentage from molecular dynamics simulations of blocked dipeptides versus the average populations from a coil library. Results are given for the OPLS-AA (A), OPLS-AA/L (B), and OPLS-AA/M (C). Dashed lines delineate the

region of populations that fall within +/- 20% of the experimental result. Error bars from simulation represent the standard deviation in the populations from triplicate 200 ns simulations.

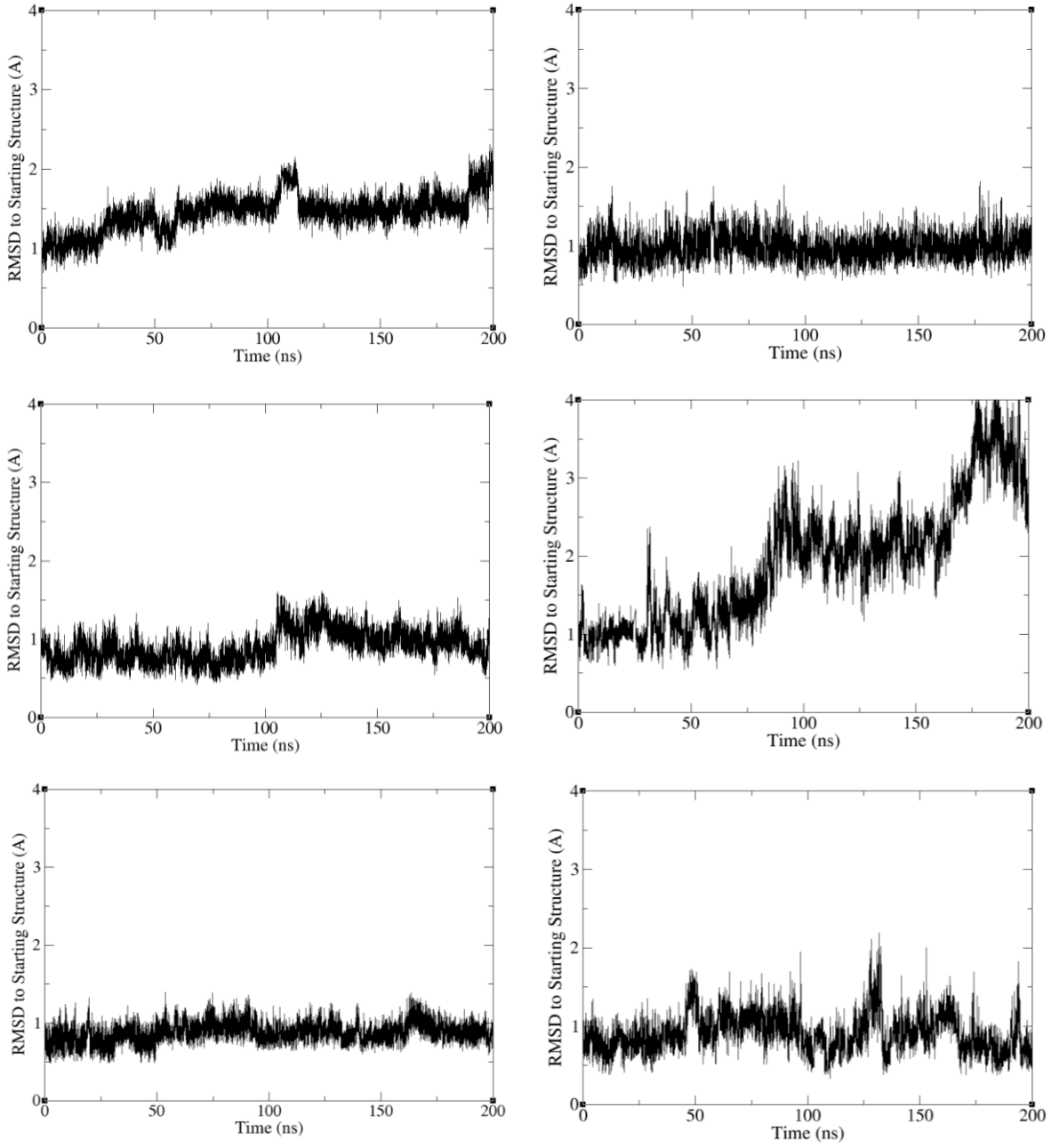

Figure SI3. The RMSD between the coordinates of the backbone atoms in the MD simulations compared to the starting experimental structure over the course of the trajectory for the first run.

The first, second, and third rows correspond to trajectories with OPLS-AA, OPLS-AA/L, and OPLS-AA/M, while the first and second columns correspond to ubiquitin residues 1-72 and GB3 respectively.