Supplementary information

Conformational preferences of the 2-methylproline residue and its role in stabilizing β-turn and polyproline II structures of peptides

Young Kee Kang*[a] and Hae Sook Park[b]

[a] *Department of Chemistry and BK21 PLUS Research Team, Chungbuk National University, Cheongju, Chungbuk 361-763, Republic of Korea. E-mail: ykkang@chungbuk.ac.kr; Fax: +82-43-273-2991; Tel: +82-43-261-2285*

[b] *Department of Nursing, Cheju Halla University, Cheju 690-708, Republic of Korea.*

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Table S1 Torsion angles, puckering parameters, and thermodynamic properties of local minima and transition states for Ac-Ala-Pro-NHMe at the M06-2X/cc-pVTZ//SMD M06-2X/6-31+G(d) level of theory in water[a]

	Turn	Backbone torsion angles[b]						Endocyclic torsion angles[b]					Therm. properties					
Conf.	type	ϕ_1	ψ_1	ω_1	ϕ_2	ψ_2	ω_2	χ^0	χ^1	χ^2	χ^3	χ^4	ΔE_e[c]	$\Delta\Delta G_s$[d]	$\Delta E_{e,w}$[e]	ΔH_w[f]	ΔG_w[g]	p^h
FtFu		-60.2	150.2	167.3	-51.2	147.1	175.8	3.7	-26.2	38.8	-35.9	20.3	7.43	-6.95	0.48	0.72	0.00	29.1
EtAd		-159.8	153.9	174.8	-71.1	-18.6	-179.9	-10.5	29.6	-38.0	31.1	-13.0	4.85	-2.86	2.00	1.87	0.28	18.3
EtFu		-159.6	157.5	169.9	-53.0	146.2	178.1	2.5	-25.6	38.7	-36.5	21.5	4.47	-3.03	1.44	1.53	0.28	18.1
FcAd	VIa1	-54.6	144.9	5.1	-88.5	11.0	174.4	-20.4	37.0	-40.4	27.9	-4.6	0.00	0.00	0.00	0.00	0.43	14.0
AtFu		-56.7	-39.4	-179.5	-56.3	145.0	175.3	5.6	-28.0	39.9	-35.9	19.1	14.39	-12.87	1.52	1.72	0.97	5.7
EcFd	VIb	-159.3	155.0	-11.7	-68.1	163.8	176.9	-20.1	35.3	-38.1	25.8	-3.5	5.07	-2.83	2.24	2.35	1.43	2.6
EtAu		-162.0	166.3	175.2	-67.1	-21.1	-178.1	-3.9	-20.7	36.9	-38.6	26.9	5.31	-2.83	2.48	1.73	1.44	2.5
FtAu		-61.4	153.1	170.9	-60.6	-27.6	-177.2	0.4	-23.1	36.8	-35.9	22.4	9.71	-7.93	1.78	2.08	1.58	2.0
EcFu	VIb	-161.4	153.9	-17.1	-55.3	162.9	176.8	-0.8	-22.7	37.1	-36.8	23.8	6.18	-3.29	2.89	2.85	1.74	1.5
AtAu	I	-52.7	-35.9	178.7	-64.8	-18.7	-177.7	-0.1	-23.4	37.7	-37.2	23.5	5.34	-4.56	0.79	1.01	1.83	1.3
EcAd	VIa2	-159.4	148.8	-3.1	-78.3	-10.5	-179.4	-18.3	34.3	-38.2	26.9	-5.3	4.07	-1.34	2.74	2.63	1.90	1.2
A*tFd		47.5	50.8	177.7	-60.7	145.4	175.7	-5.8	27.1	-38.1	33.9	-17.8	9.96	-7.68	2.28	2.41	1.96	1.1
AtAd	I	-49.7	-42.0	-176.2	-86.3	3.0	179.7	-24.4	36.5	-35.8	21.2	2.2	5.30	-3.28	2.02	1.97	2.13	0.8
AtFd		-54.9	-53.6	-179.5	-65.3	148.4	176.9	-8.3	28.7	-38.3	32.7	-15.3	14.72	-11.38	3.34	3.63	2.50	0.4
FcAu	VIa1	-54.5	146.8	1.7	-73.5	-7.7	175.5	0.8	-24.1	38.0	-37.0	22.8	2.22	-0.32	1.90	2.10	2.68	0.3
DcAd		-129.0	59.3	3.5	-93.4	-10.2	-178.8	-21.7	36.0	-37.7	24.5	-1.6	4.65	-2.18	2.48	2.45	2.79	0.3
EtCd		-160.7	153.3	-178.5	-85.0	59.5	179.4	-16.7	34.8	-40.6	29.9	-8.3	0.05	3.21	3.27	3.37	2.95	0.2
DtAd		-125.9	62.5	-179.6	-67.4	-22.4	-179.3	-9.7	29.8	-38.9	32.4	-14.3	7.05	-3.71	3.34	3.43	3.06	0.2
A*cAd		53.8	54.0	7.6	-98.0	-12.1	-175.3	-20.7	36.0	-38.5	25.9	-3.1	4.25	-2.49	1.76	1.89	3.15	0.1
EcAu	VIa2	-158.4	149.6	-8.9	-67.1	-19.5	-176.6	-4.4	-19.8	35.9	-37.8	26.7	5.49	-1.42	4.07	4.07	3.20	0.1
A*cFd		52.2	55.9	4.0	-92.9	161.5	173.2	-22.8	36.8	-37.8	24.0	-0.5	12.05	-10.48	1.56	1.15	3.52	0.1
F*cAd		77.8	150.6	-5.6	-84.4	-3.1	-178.6	-22.8	36.6	-37.5	23.7	-0.4	12.91	-6.74	6.17	6.32	4.42	0.0
F*tAu	II'	70.0	176.0	177.5	-66.0	-21.7	-178.3	0.5	-24.2	38.4	-37.4	23.3	13.32	-8.09	5.23	5.32	4.63	0.0
AtCd		-56.7	-43.0	-171.1	-89.2	62.4	-177.3	-22.2	35.9	-37.1	23.4	-0.7	5.73	-1.22	4.51	4.68	4.63	0.0

AcFu	-72.2	-9.5	-9.5	-47.5	157.4	-172.6	9.7	-30.7	40.1	-33.8	15.1	9.21	-5.23	3.98	4.15	4.77	0.0
ts1	-59.9	153.5	117.5	-126.0	1.0	178.1	-10.3	32.1	-41.3	35.5	-15.7	20.88	0.74	21.61	20.38	20.20	

[a] At the SMD M06-2X/6-31+G*(d) level of theory in water, all optimized structures and their solvation free energies as well as enthalpic and entropic terms are taken from ref. 41. Only the conformers with $\Delta G_w < 5$ kcal/mol are listed. [b] Units in degrees. [c] Relative single-point electronic energies (kcal/mol) at the M06-2X/cc-pVTZ level of theory, which are newly calculated in this work. [d] Relative solvation free energies (kcal/mol) in water. [e] Relative electronic energies (kcal/mol) obtained by the sum of ΔE_e and $\Delta\Delta G_s$ in water. [f] Relative enthalpies (kcal/mol) at 25 °C in water. [g] Relative Gibbs free energies (kcal/mol) at 25 °C in water. [h] Population (%) for each local minimum calculated by its ΔG_w in water.

Optimized Cartesian coordinates of P_{II} structures of Ac-$(Pro)_2$-(2-MePro)-$(Pro)_2$-NMe_2 and Ac-(Hyp-Gly-2-MePro)-(Hyp-Gly-Pro)-NMe_2 at the SMD M06-2X/6-31+G(d) level of theory in water:

Ac-$(Pro)_2$-(2-MePro)-$(Pro)_2$-NMe_2

E = -1950.1703308 Hartrees

H	-9.378615	0.080592	2.031993
H	-9.520865	0.911491	0.455774
H	-8.387425	1.514156	1.674544
C	-8.832229	0.607390	1.249018
O	-7.405449	-1.332361	1.314726
C	-7.743238	-0.287802	0.722595
N	-7.139762	0.082786	-0.419619
C	-7.317375	1.373939	-1.108169
C	-6.007155	-0.678739	-0.928950
H	-6.295553	-1.720782	-1.089017
C	-5.662765	0.046701	-2.244055
C	-4.835492	-0.612672	0.050244
O	-4.707880	0.329959	0.850004
H	-4.611636	-0.070978	-2.521082
H	-6.283490	-0.364275	-3.046437
C	-6.047719	1.500073	-1.951020
H	-5.259177	1.988280	-1.369661
H	-6.218480	2.082258	-2.859072
H	-7.422896	2.183617	-0.382525
H	-8.215708	1.341468	-1.734548
N	-3.935822	-1.604378	-0.015949
C	-3.884168	-2.679400	-1.025041
C	-2.715568	-1.515947	0.780742
H	-2.971354	-1.476657	1.841810
C	-1.953453	-2.801576	0.403502
C	-1.917405	-0.270760	0.385427
O	-1.986021	0.187775	-0.766226
H	-0.870450	-2.682260	0.495570
H	-2.272024	-3.610922	1.067856
C	-2.407502	-3.072120	-1.034499
H	-1.856831	-2.431943	-1.730744
H	-2.263949	-4.112847	-1.332774
H	-4.227449	-2.320685	-1.997178
H	-4.520906	-3.513370	-0.709636
N	-1.133996	0.264309	1.333496
C	-0.830731	-0.372531	2.632643
C	-0.242825	1.398797	1.027661
C	0.399328	1.663442	2.409538
C	0.850039	0.880505	0.061682
O	0.998900	-0.340738	-0.112302
H	1.368753	2.161560	2.332781
H	-0.279490	2.311222	2.977156
C	0.483190	0.281685	3.050709
H	1.331530	-0.276236	2.641101
H	0.588708	0.324454	4.136731
H	-0.739564	-1.455565	2.524281
H	-1.630887	-0.154426	3.348541
N	1.669874	1.751197	-0.558138
C	1.813899	3.208488	-0.355768
C	2.788627	1.192537	-1.319141
H	2.411321	0.543382	-2.112458
C	3.511160	2.434735	-1.866348
C	3.707112	0.394764	-0.392744
O	3.789663	0.652681	0.820068
H	4.573924	2.249598	-2.045107
H	3.044536	2.730117	-2.811359
C	3.254514	3.484835	-0.784617
H	3.933961	3.331249	0.059698
H	3.378609	4.507034	-1.148538
H	1.636178	3.485636	0.683407
H	1.102923	3.743761	-0.992907
N	4.438052	-0.573153	-0.962210
C	4.529724	-0.866980	-2.405807
C	5.440811	-1.282104	-0.177413
H	4.969491	-1.702020	0.712937
C	5.940432	-2.361972	-1.153765
C	6.573449	-0.326679	0.221144
O	6.725414	0.751850	-0.376869
H	6.956168	-2.695616	-0.927421
H	5.270462	-3.225961	-1.098576
C	5.825465	-1.671834	-2.516121
H	6.672733	-0.994855	-2.666415
H	5.795776	-2.378816	-3.347745
H	4.561357	0.054325	-2.992010
H	3.660265	-1.455416	-2.718519
N	7.393045	-0.705436	1.220233
C	7.451608	-2.055288	1.773439
C	8.568190	0.119097	1.487546
H	9.335013	-0.033280	0.719131
H	8.293737	1.173829	1.512340
H	8.974874	-0.167809	2.458387
H	7.624909	-1.986462	2.849995
H	6.524232	-2.600383	1.611612
H	8.276775	-2.615271	1.318698
C	-1.025650	2.614253	0.505458
H	-0.555936	3.544582	0.831795
H	-1.109599	2.626146	-0.582733
H	-2.036330	2.588450	0.923079

Ac-(Hyp-Gly-2-MePro)-(Hyp-Gly-Pro)-NMe_2

E = -2191.8392673 Hartrees

C	-10.224310	-1.341423	0.601447
H	-10.952470	-1.339279	-0.216843
C	-8.837221	-1.546977	0.056289
O	-8.187837	-2.589168	0.268848
N	-8.316586	-0.555530	-0.685680
C	-8.974282	0.710063	-1.036219
C	-6.963769	-0.653480	-1.224299
H	-6.915468	-1.445145	-1.980751
C	-6.730995	0.736959	-1.844776
C	-5.942796	-0.926301	-0.128959
O	-6.039595	-0.421026	0.995977
H	-6.308786	1.416141	-1.095598
H	-6.061769	0.700194	-2.707466
C	-8.139773	1.205855	-2.206632
O	-8.621586	0.548786	-3.377390
H	-8.205232	2.291448	-2.324230
H	-8.929014	1.417890	-0.201114
H	-10.016827	0.548763	-1.319128
H	-8.040694	0.782405	-4.120053
N	-4.906444	-1.702194	-0.484059
H	-4.836751	-2.020504	-1.443769
C	-3.765749	-1.838942	0.387340
H	-4.080156	-2.247558	1.352537
H	-3.068970	-2.549698	-0.065460
C	-3.046413	-0.506222	0.597643
O	-3.268637	0.470892	-0.131629
N	-2.177335	-0.471033	1.619011
C	-1.701575	-1.666818	2.346868
C	-1.345168	0.718720	1.864549
C	-0.555537	0.286300	3.121140
C	-0.342890	0.828502	0.686976
O	-0.222285	-0.113145	-0.112387
H	0.383082	0.835806	3.228152
H	-1.179137	0.496643	3.997890
C	-0.368659	-1.218074	2.945518
H	0.448736	-1.423726	2.247224
H	-0.154761	-1.728854	3.886701
H	-1.585965	-2.514306	1.667160
H	-2.421140	-1.936224	3.127574
H	-10.302636	-0.382493	1.122682
H	-10.460001	-2.154476	1.288588
N	0.474327	1.897118	0.587802
C	0.497034	3.140632	1.380504
C	1.609578	1.821077	-0.338546
C	1.483102	4.019906	0.626185
H	0.845864	2.952087	2.401605
H	-0.481822	3.615104	1.408586
H	1.263062	1.898328	-1.374566
C	2.484471	3.020435	0.061430
C	2.406918	0.536409	-0.158457
O	0.756958	4.674610	-0.412460
H	1.948187	4.757461	1.286901
H	3.179825	2.724301	0.854823
H	3.053516	3.418521	-0.781900
O	2.619309	0.046577	0.957074
N	2.924738	0.022487	-1.285064
H	1.386402	5.183770	-0.948850
H	2.789736	0.522215	-2.156597
C	3.907867	-1.029742	-1.232193
H	3.517361	-1.879191	-0.663695
H	4.102300	-1.374281	-2.251687
C	5.222736	-0.557844	-0.617124
O	5.466597	0.644404	-0.428440
N	6.095334	-1.522987	-0.298300
C	5.957588	-2.954987	-0.626987
C	7.433928	-1.174178	0.164199
C	7.390343	-3.478341	-0.514958
H	5.544027	-3.085060	-1.629982
H	5.291695	-3.437376	0.096656
H	7.359088	-0.512880	1.029583
C	8.036321	-2.546619	0.514058
C	8.210738	-0.475743	-0.963262
H	7.898158	-3.382477	-1.479781
H	7.418044	-4.526934	-0.212025
H	9.127774	-2.551330	0.470913
H	7.727145	-2.817980	1.528442
O	7.841452	-0.599424	-2.143592
N	9.300902	0.227677	-0.609906
C	9.700422	0.458073	0.777205
C	10.029889	1.006992	-1.602823
H	9.173401	1.318614	1.204320
H	9.524765	-0.420673	1.397386
H	10.772365	0.665251	0.787578
H	11.101428	0.819811	-1.495018
H	9.713519	0.723727	-2.604507
H	9.841371	2.075681	-1.450510
C	-2.204661	1.961950	2.136095
H	-1.705311	2.624443	2.846660
H	-2.443500	2.522031	1.230291
H	-3.142825	1.633906	2.593389