Supplementary Material for

Evolution of amide stacking in larger γ-peptides: Triamide H-bonded cycles

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Table of Contents

Table S1. Relative energies and calculated amide NH stretch frequencies for the assigned conformers of Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe at the B3LYP/6-31+G(d) level of theory.

Conformer	H-bond Family	Structure	ΔE (kJ/mol)	Calc. Amide NH Stretches (cm^{-1})[a]
		Ac-γ^2-hPhe-γ^2-hAla-NHMe		
A	C9/C9	C9/C9(a)	0.34	3337 3349 3475
B	C9/C9	C9/C9(g-)	0.00	3329 3341 3476
C	C7/C7/C14	C7/C7/C14(g-)	14.06	3414 3426 3442
D	C9/C9	C9/C9(g+)	22.84	3331 3343 3486
		Ac-γ^2-hAla-γ^2-hPhe-NHMe		
A	C9/C9	C9/C9(a)	0.00	3331 3339 3474
B	C9/C14	C9/C14(a)	4.71	3386 3429 3470
C	C7/C7/C14	C7/C7/C14(g-)	12.07	3373 3429 3438

[a]Scaled 0.96 B3LYP/6-31+G(d)

Table S2. Relative energies, relative free energies, single-point TDDFT excitation energies, and calculated amide NH stretch frequencies for the assigned conformers of Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe at the M05-2X/6-311++G(d,p) level of theory.

Conformer	H-bond Family	Structure	ΔE (kJ/mol)	ΔG^{493} (kJ/mol)	TDDFT S_0-S_1 (cm^{-1})[a]	Calc. Amide NH Stretches (cm^{-1})[b]
		Ac-γ^2-hPhe-γ^2-hAla-NHMe				
A	C9/C9	C9/C9(a)	0.83	0.09	37535	3351 3360 3486
B	C9/C9	C9/C9(g-)	0.00	0.00	37422	3330 3353 3483
C	C7/C7/C14	C7/C7/C14(g-)	2.91	1.58	37436	3390 3422 3432
D	C9/C9	C9/C9(g+)	11.65	2.35	37235	3345 3354 3499
		Ac-γ^2-hAla-γ^2-hPhe-NHMe				
A	C9/C9	C9/C9(a)	0.00	0.00	38068	3343 3352 3486
B	C9/C14	C9/C14(a)	7.85	1.31	37473	3406 3423 3479
C	C7/C7/C14	C7/C7/C14(g-)	0.90	10.17	37367	3378 3422 3429

[a]Scaled 0.8337 for Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe single point TDDFT M05-2X/6-311++G(d,p)

[b]Scaled 0.9417 M05-2X/6-311++G(d,p)

Table S3. Relative energies, relative free energies, single-point TDDFT excitation energies, and calculated amide NH stretch frequencies for the assigned conformers of Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe at the M06-2X/6-311++G(d,p) level of theory.

Conformer	H-bond Family	Structure	ΔE (kJ/mol)	ΔG^{493} (kJ/mol)	TDDFT S_0-S_1 (cm^{-1})[a]	Calc. Amide NH Stretches (cm^{-1})[b]		
			Ac-γ^2-hPhe-γ^2-hAla-NHMe					
A	C9/C9	C9/C9(a)	3.82	0.63	37535	3353	3361	3485
B	C9/C9	C9/C9(g-)	3.11	0.00	37434	3334	3357	3482
C	C7/C7/C14	C7/C7/C14(g-)	2.63	1.88	37452	3391	3428	3432
D	C9/C9	C9/C9(g+)	9.99	2.23	37233	3351	3360	3499
			Ac-γ^2-hAla-γ^2-hPhe-NHMe					
A	C9/C9	C9/C9(a)	2.45	0.00	37406	3344	3355	3484
B	C9/C14	C9/C14(a)	9.76	1.92	37485	3408	3420	3477
C	C7/C7/C14	C7/C7/C14(g-)	0.00	5.53	37365	3378	3425	3435

[a]Scaled 0.8491 for Ac-γ^2-hPhe-γ^2-hAla-NHMe and Ac-γ^2-hAla-γ^2-hPhe-NHMe single point TDDFT M06-2X/6-311++G(d,p)

[b]Scaled 0.9489 M06-2X/6-311++G(d,p)

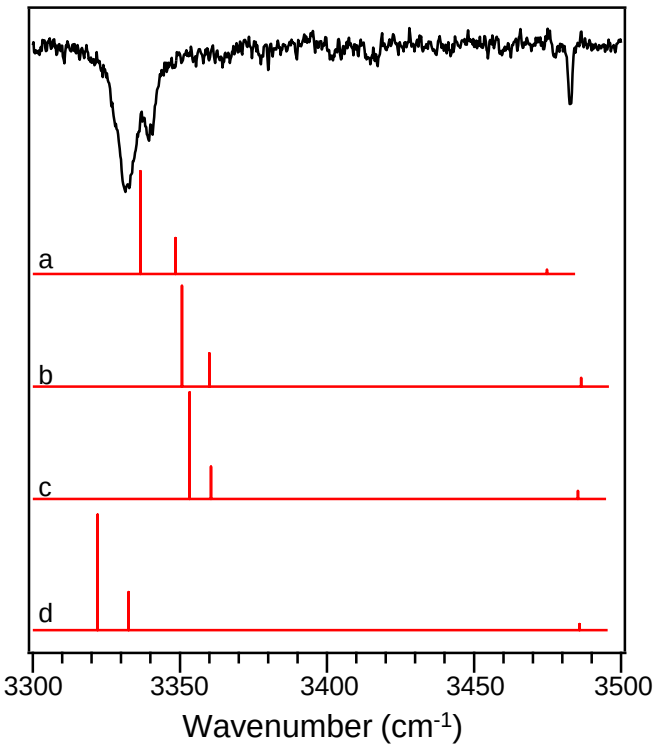

Figure S1: Experimental RIDIR spectrum of conformer A of Ac-γ^2-hPhe-γ^2-hAla-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

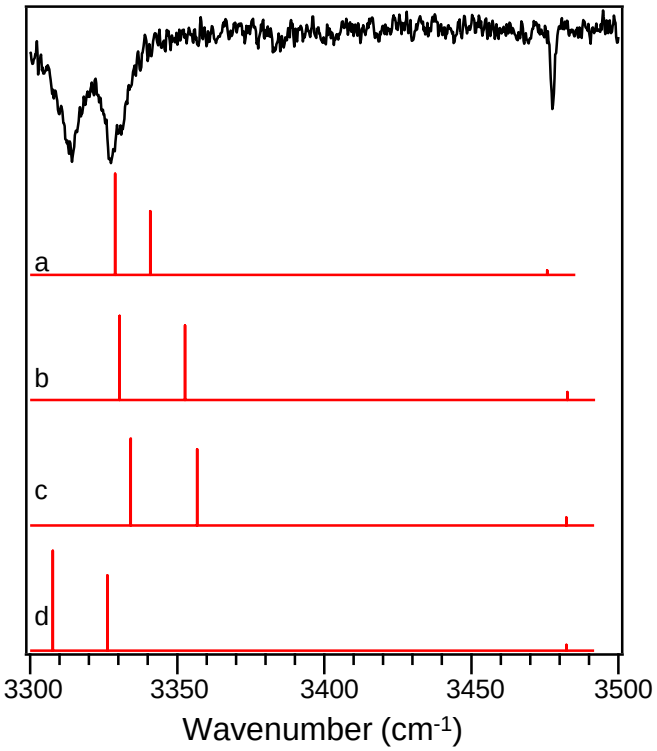

Figure S2: Experimental RIDIR spectrum of conformer B of Ac-γ^2-hPhe-γ^2-hAla-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

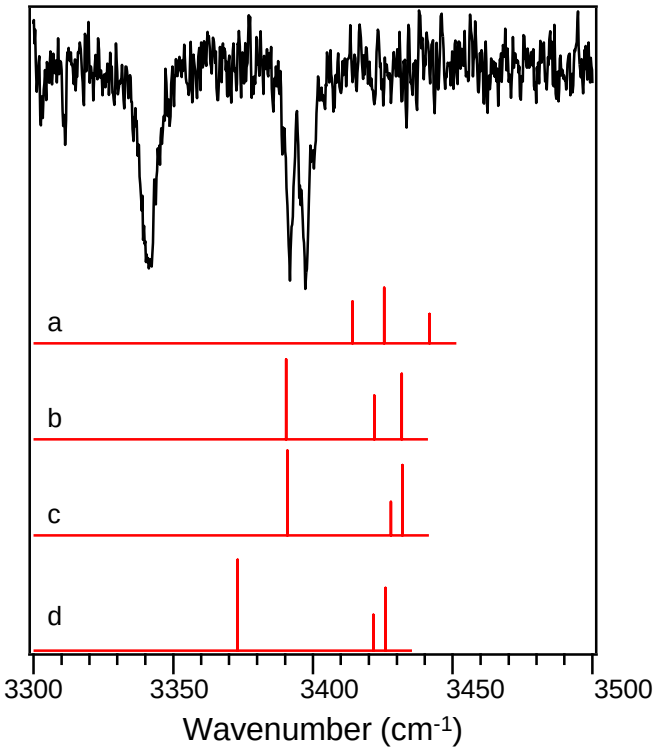

Figure S3: Experimental RIDIR spectrum of conformer C of Ac-γ^2-hPhe-γ^2-hAla-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

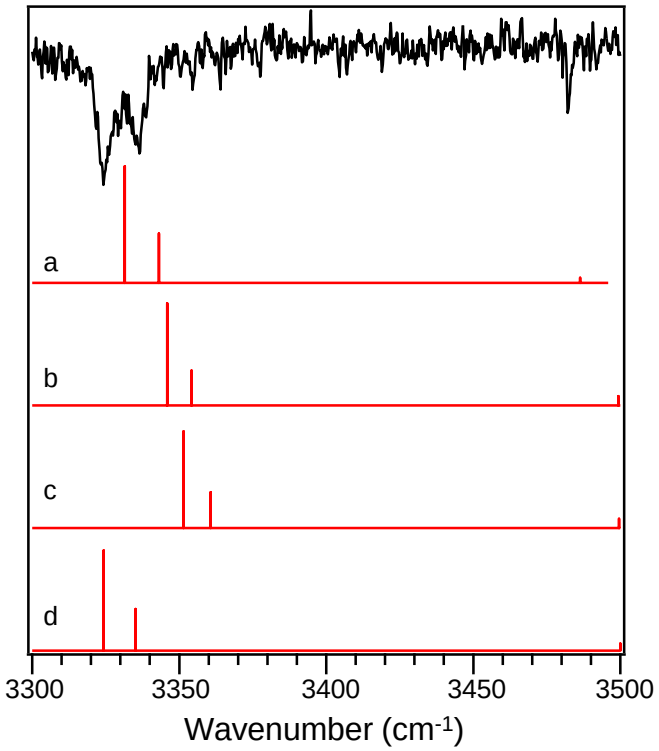

Figure S4: Experimental RIDIR spectrum of conformer D of Ac-γ^2-hPhe-γ^2-hAla-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

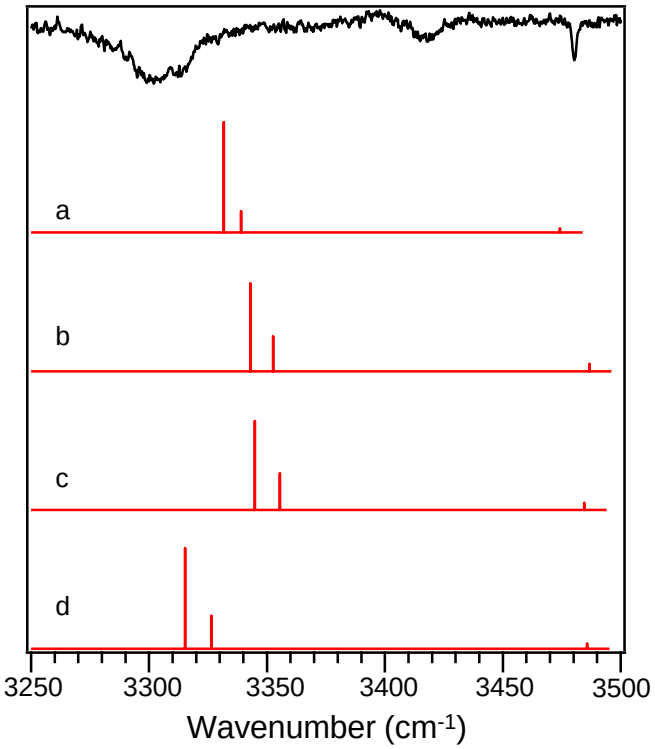

Figure S5: Experimental RIDIR spectrum of conformer A of Ac-γ^2-hAla-γ^2-hPhe-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

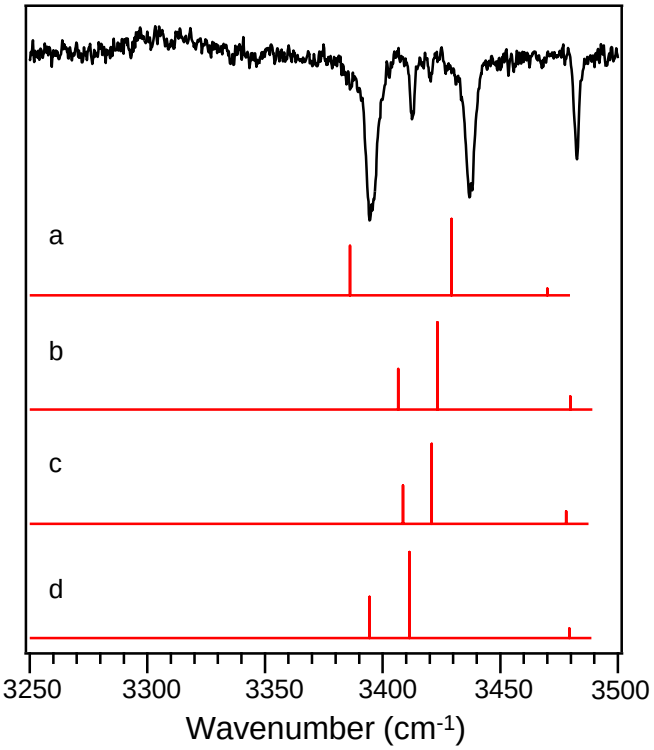

Figure S6: Experimental RIDIR spectrum of conformer B of Ac-γ^2-hAla-γ^2-hPhe-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

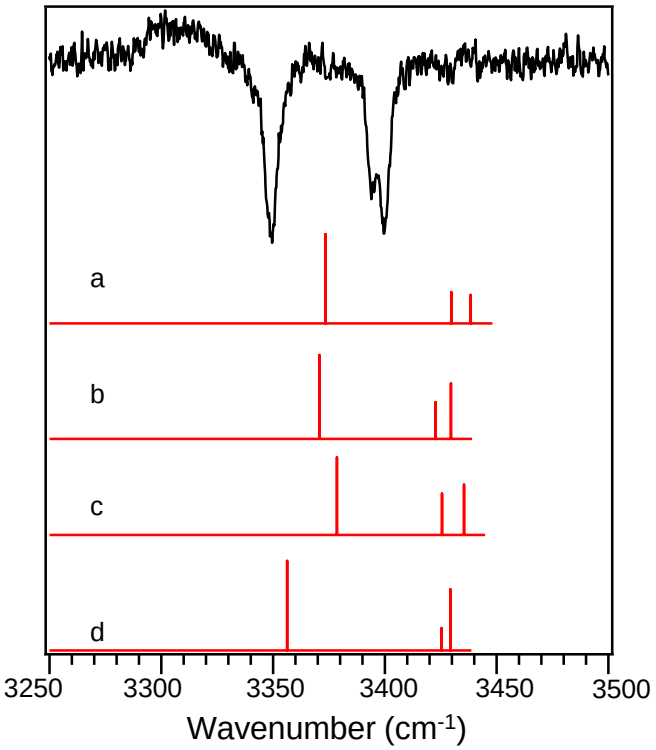

Figure S7: Experimental RIDIR spectrum of conformer C of Ac-γ^2-hAla-γ^2-hPhe-NHMe (black trace) and calculated IR spectra at the a) B3LYP/6-31+G(d) (scaled 0.96), b) M05-2X/6-311++G(d,p) (scaled 0.9417), c) M06-2X/6-311++G(d,p) (scaled 0.9489), and d) ωB97X-D/6-311++G(d,p) (scaled 0.9466) levels of theory.

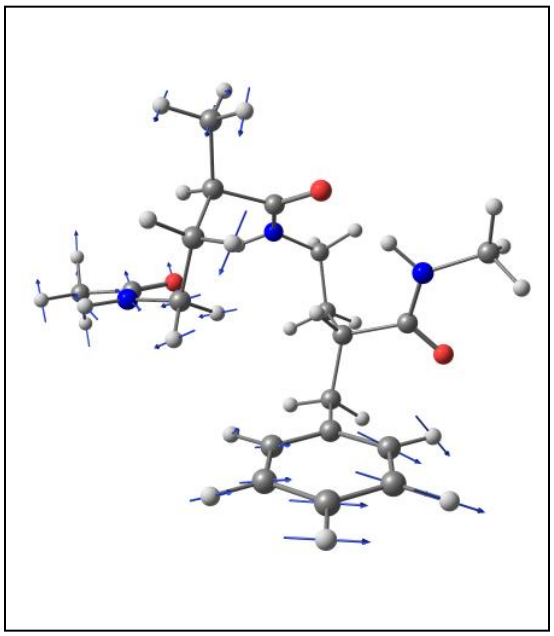

Figure S8: Lowest vibrational mode of the C9/C9(*a*) structure of conformer A of Ac-γ^2-hAla-γ^2-hPhe-NHMe. The frequency of the mode, ~14 cm^{-1}, is similar to the 9 cm^{-1} progression observed experimentally.

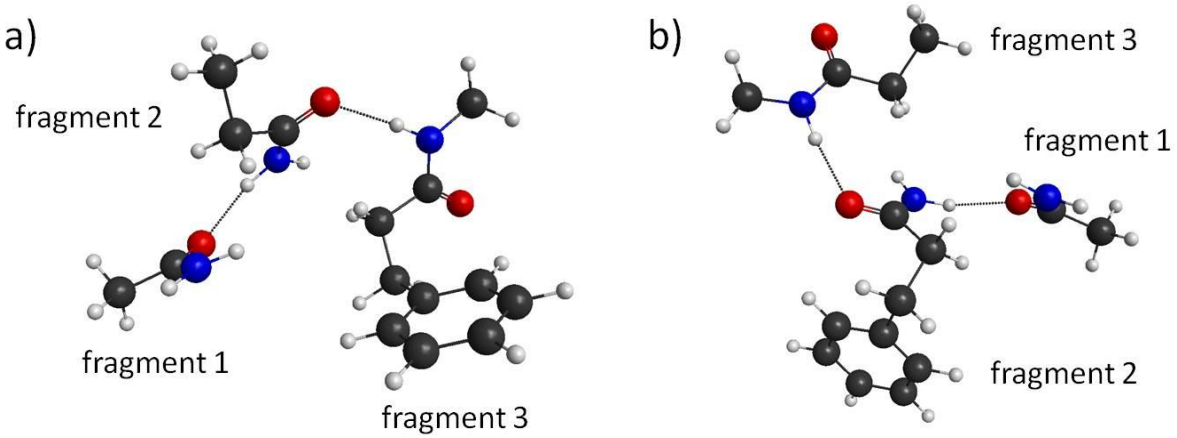

Fig. S9. Fragmentation of a) Ac-γ^2-hAla-γ^2-hPhe-NHMe and b) Ac-γ^2-hPhe-γ^2-hAla-NHMe employed in FMO-PIEDA for calculating non-bonded interactions.

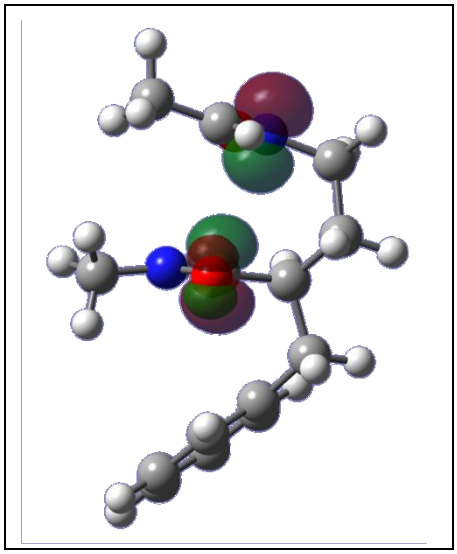

Figure S10: Orbitals calculated to interact using Natural Bond Orbital analysis for the amide stacked conformer of Ac-γ^2-hPhe-NHMe.

Table S4. Cartesian coordinates for conformer C (C7/C7/C14(g-)) of Ac-γ^2-hPhe-γ^2-hAla-NHMe at the ωB97X-D/6-311++G(d,p) level of theory.

Atom	x	y	z
C	-3.397633	2.804709	-0.159669
C	-2.328865	2.137389	-0.996233
N	-1.07044	2.258021	-0.535797
C	0.094141	1.736991	-1.235318
C	1.281386	1.53347	-0.296808
C	1.197145	0.305623	0.614639
C	-0.003806	0.373415	1.551864
N	-0.655308	-0.793795	1.724896
C	-1.939894	-0.872127	2.39784
C	-3.102481	-0.504988	1.471265
C	-3.470015	-1.546047	0.396695
C	-2.260681	-1.98039	-0.430913
N	-1.988217	-1.296023	-1.556588
C	-0.866524	-1.664532	-2.394289
O	-2.605173	1.547065	-2.039121
O	-0.327699	1.413962	2.116847
O	-1.553602	-2.917655	-0.06204
C	2.475342	0.139443	1.466925
C	5.942251	-0.550006	-0.999434
C	4.993808	-1.552244	-0.821762
C	3.886524	-1.327407	-0.014629
C	3.704897	-0.101226	0.627403
C	4.663242	0.893527	0.444219
C	5.774805	0.673105	-0.362607
C	-4.648778	-1.054243	-0.445951
H	6.808487	-0.724327	-1.627558
H	5.120208	-2.512669	-1.30912
H	3.153439	-2.117147	0.124192
H	4.53747	1.851711	0.938922
H	6.511209	1.458592	-0.491805
H	-2.483327	-0.441088	-1.784128
H	-0.404444	-1.587046	1.150942
H	-0.92896	2.588954	0.408884
H	-3.080277	2.986147	0.869067
H	-3.648097	3.761927	-0.623945
H	-4.294846	2.185785	-0.164608
H	-0.179869	0.798771	-1.721158
H	0.37504	2.434775	-2.030994
H	2.177615	1.430998	-0.914089
H	1.427073	2.428738	0.31828
H	-2.056797	-1.887701	2.782771
H	-1.91593	-0.183474	3.243157
H	-3.995056	-0.337377	2.083843
H	-2.867367	0.45158	0.997225
H	-0.842834	-0.993355	-3.252643
H	0.082884	-1.591499	-1.853916
H	-0.968686	-2.694399	-2.742535
H	2.602595	1.03487	2.082294
H	2.331184	-0.701158	2.153016
H	-4.931594	-1.790584	-1.201667
H	-5.516603	-0.877943	0.195363
H	-4.422558	-0.115414	-0.960265
H	-3.763935	-2.464015	0.915283
H	1.094341	-0.584826	-0.017298

Table S5. Cartesian coordinates for conformer C (C7/C7/C14(g-)) of Ac-γ^2-hAla-γ^2-hPhe-NHMe at the ωB97X-D/6-311++G(d,p) level of theory.

Atom	x	y	z
C	-0.493307	2.776392	0.15109
C	0.590885	2.130444	0.983797
N	1.848927	2.351612	0.553801
C	3.029036	1.774458	1.171905
C	3.391142	0.37076	0.678781
C	3.71046	0.224372	-0.821306
C	2.459789	0.495032	-1.656844
N	1.564288	-0.510196	-1.721227
C	0.225914	-0.336662	-2.258079
C	-0.773976	-1.266802	-1.578119
C	-0.826579	-1.134151	-0.055132
C	0.304432	-1.894759	0.636823
N	0.619292	-1.442382	1.868405
C	1.611997	-2.113444	2.681212
O	0.327489	1.483691	1.997041
O	2.25694	1.590774	-2.172645
O	0.853681	-2.870761	0.135455
C	4.332474	-1.14877	-1.094412
C	-2.173483	-1.644706	0.513646
C	-5.354098	1.131018	-0.351961
C	-5.27482	-0.068243	-1.047823
C	-4.258262	-0.974964	-0.763045
C	-3.308211	-0.697282	0.217032
C	-3.401038	0.509638	0.91418
C	-4.413566	1.417021	0.633211
H	5.30722	-1.218756	-0.605274
H	0.32852	-0.50465	2.126983
H	1.78529	-1.407468	-1.312218
H	1.960919	2.702257	-0.387627
H	-0.146529	3.062594	-0.843338
H	-1.341413	2.09703	0.060712
H	-0.841833	3.670407	0.674482
H	3.860335	2.461279	0.988794
H	2.855462	1.740287	2.248937
H	4.270275	0.043976	1.245514
H	2.578975	-0.312351	0.93576
H	-0.054788	0.708526	-2.103122
H	0.220945	-0.509436	-3.339511
H	-1.759341	-1.03479	-1.9914
H	-0.555269	-2.309732	-1.827792
H	2.568387	-2.201821	2.156631
H	1.75744	-1.538784	3.595608
H	1.28046	-3.121262	2.940536
H	3.715077	-1.962014	-0.698308
H	4.477334	-1.318306	-2.163796
H	-2.381749	-2.636203	0.099869
H	-2.079715	-1.762371	1.596685
H	-0.73483	-0.081207	0.226337
H	4.419643	1.003526	-1.116294
H	-6.146337	1.83788	-0.571323
H	-6.006169	-0.30168	-1.813752
H	-4.204138	-1.912483	-1.308058
H	-2.66726	0.73877	1.682701
H	-4.472065	2.347804	1.186873