Carbonless Amino Acids and a Carbonless GHK Peptide

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Supplementary Information

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Definitions of canonical dihedral (torsional) angles

Each dihedral angle (ψ, ω, φ) was defined along the two internal peptide links Gly→His and His→Lys using four consecutive backbone atoms. In the case of the carbonless GHK$^+$ (cGHK$^+$) analogue, the atom B replacing the C$_\alpha$ carbon is denoted as B$_\alpha$, and the nitrogen atom replacing the carbonyl carbon C' is denoted as N'. All dihedral angles were expressed in degrees within the conventional range (−180, 180] and treated as circular variables in all subsequent statistical analyses.

Canonical dihedral angles $\sphericalangle$ in GHK$^+$ are defined as:

ψ(Gly) = $\sphericalangle$(N(Gly), C$_\alpha$(Gly), C'(Gly), N(His))

ω(Gly–His) = $\sphericalangle$(C$_\alpha$(Gly), C'(Gly), N(His), C$_\alpha$(His))

φ(His) = $\sphericalangle$(C'(Gly), N(His), C$_\alpha$(His), C'(His))

ψ(His) = $\sphericalangle$(N(His), C$_\alpha$(His), C'(His), N(Lys))

ω(His–Lys) = $\sphericalangle$(C$_\alpha$(His), C'(His), N(Lys), C$_\alpha$(Lys))

φ(Lys) = $\sphericalangle$(C'(His), N(Lys), C$_\alpha$(Lys), C'(Lys))

Canonical dihedral angles $\sphericalangle$ in cGHK$^+$ are defined as:

ψ(cGly) = $\sphericalangle$(N(cGly), B$_\alpha$(cGly), N'(cGly), N(cHis))

ω(cGly–cHis) = $\sphericalangle$(B$_\alpha$(cGly), N'(cGly), N(cHis), B$_\alpha$(cHis))

φ(cHis) = $\sphericalangle$(N'(cGly), N(cHis), B$_\alpha$(cHis), N'(cHis))

ψ(cHis) = $\sphericalangle$(N(cHis), B$_\alpha$(cHis), N'(cHis), N(cLys))

ω(cHis–cLys) = $\sphericalangle$(B$_\alpha$(cHis), N'(cHis), N(cLys), B$_\alpha$(cLys))

φ(cLys) = $\sphericalangle$(N'(cHis), N(cLys), B$_\alpha$(cLys), N'(cLys))

Table S1. Canonical dihedral angles (ψ, ω, φ) in degrees for the four lowest-energy conformers within each family (GHK$^+$ and cGHK$^+$), together with their Boltzmann populations (relative statistical weights p_i).

GHK$^+$	p_i	ψ(Gly)	ω(Gly-His)	φ(His)	ψ(His)	ω(His-Lys)	φ(Lys)
GHK(**1**)	0.9383966	-142.4	167.6	-67.0	-18.0	161.5	-125.2
GHK(**2**)	0.0458703	-142.4	171.1	-70.7	-12.8	147.2	-127.3
GHK(**3**)	0.0101308	-137.8	166.7	-60.4	-26.7	167.3	-132.0
GHK(**4**)	0.0018142	-141.4	171.9	-58.1	-36.0	154.2	-110.3
cGHK$^+$	p_i	ψ(cGly)	ω(cGly-cHis)	φ(cHis)	ψ(cHis)	ω(cHis-cLys)	φ(cLys)
cGHK(**1**)	0.8531919	-166.0	-167.6	-92.2	-4.9	-162.4	174.5
cGHK(**2**)	0.0695581	-152.3	-178.5	-70.9	-19.0	154.6	-127.4
cGHK(**3**)	0.0621059	166.4	178.2	-120.8	35.7	-175.4	-178.3
cGHK(**4**)	0.0140846	-150.2	-176.0	-64.6	-26.0	154.5	-134.6

Circular mean $\langle\theta\rangle$ and circular standard deviation s

For each torsion within each peptide family, the circular mean $\langle\theta\rangle$ and circular standard deviation s (both in degrees) were obtained according to

$$C = \sum_i w_i \cos\theta_i \ , \qquad S = \sum_i w_i \sin\theta_i \ , \qquad R = \frac{\sqrt{C^2 + S^2}}{\sum_i w_i}$$

$$\langle\theta\rangle = atan2(S,C) \quad , \qquad s = \sqrt{-2\ln R}\frac{180}{\pi}$$

Table S2. Circular mean $\langle\theta\rangle$ (in degrees) and circular standard deviation s (in degrees) for torsion angles in GHK$^+$ and cGHK$^+$ (reported to one decimal place, consistent with the precision of the input torsional data)

System	torsion	$\langle\theta\rangle$	s
GHK$^+$	ψ(Gly)	-142.4	0.5
	ω(Gly-His)	167.8	0.8
	φ(His)	-67.1	1.1
	ψ(His)	-17.9	1.6
	ω(His-Lys)	160.9	3.1
	φ(Lys)	-125.3	1.0
cGHK$^+$	ψ(cGly)	-166.5	7.9
	ω(cGly-cHis)	-169.4	4.3
	φ(cHis)	-92.1	9.6
	ψ(cHis)	-3.8	10.9
	ω(cHis-cLys)	-166.6	11.9
	φ(cLys)	179.1	15.4

All ensemble-averaged values were computed using Boltzmann-normalized weights w_i.

Torsion Fingerprint Deviation (TFD) metric

TFD values quantify the mean normalized torsional differences between ensembles, taking into account the circular nature of dihedral angles (ψ, ω, φ). A value of zero corresponds to identical torsional geometries, while higher values indicate increasing conformational disparity.

For two conformers A and B characterized by K common torsions $\{\theta_k\}$, the pairwise deviation is

$$\Delta\theta_k = \pi - \left|\pi - \left|\theta_k^{(A)} - \theta_k^{(B)}\right|\right| , \quad \delta_k = \frac{\Delta\theta_k}{\pi} ,$$

$$TFD(A,B) = \frac{1}{K}\sum_{k=1}^{K}\delta_k ,$$

which yields 0 for identical torsions and 1 for completely different angular sets.

Ensemble-averaged deviations were then computed as

$$\langle TFD\rangle_{A,B} = \sum_{i \in A}\sum_{j \in B} w_i^{(A)} w_j^{(B)} TFD(i,j)$$

calculated (i) within GHK$^+$, (ii) within cGHK$^+$, and (iii) between GHK$^+$ and cGHK$^+$.

Table S3. Ensemble-averaged Torsion Fingerprint Deviations (⟨TFD⟩) computed for the four lowest-energy conformers of GHK$^+$ and cGHK$^+$.

Comparison	Description	⟨TFD⟩
GHK$^+$ (intra)	Within the four lowest conformers of GHK$^+$	0.0031
cGHK$^+$ (intra)	Within the four lowest conformers of cGHK$^+$	0.0366
GHK$^+$ ↔ cGHK$^+$ (inter)	Between the GHK$^+$ and cGHK$^+$ ensembles	0.1622

All ensemble-averaged values were computed using Boltzmann-normalized weights w_i.

Table S4. Canonical dihedral angles (ψ, ω, φ) in degrees for the three lowest-energy conformers within each family (Cu–GHK and Cu–cGHK), together with their Boltzmann populations (relative statistical weights p_i).

Cu–GHK	p_i	ψ (Gly)	ω (Gly-His)	φ (His)	ψ (His)	ω (His-Lys)	φ (Lys)
Cu–GHK(**1**)	0.6827383	-13.7	-179.6	-117.7	15.1	-154.2	101.3
Cu–GHK(**2**)	0.1550833	-13.3	-179.6	-122.7	30.4	-154.1	74.1
Cu–GHK(**3**)	0.1504080	-15.5	-179.7	-113.1	-1.6	-154.0	151.1
Cu–cGHK	p_i	ψ (cGly)	ω (cGly-cHis)	φ (cHis)	ψ (cHis)	ω (cHis-cLys)	φ (cLys)
Cu–cGHK(**1**)	0.7323459	3.2	-172.6	-80.9	50.4	-177.2	172.9
Cu–cGHK(**2**)	0.1932494	8.8	-176.1	-80.3	64.2	-169.9	-86.4
Cu–cGHK(**3**)	0.0688910	6.3	-172.6	-78.8	48.0	-166.2	-150.8

Table S5. Circular mean $\langle\theta\rangle$ (in degrees) and circular standard deviation s (in degrees) for torsion angles (reported to one decimal place, consistent with the precision of the input torsional data)

System	torsion	$\langle\theta\rangle$	s
Cu–GHK	ψ(Gly)	-13.9	0.7
	ω(Gly-His)	-179.6	0.0
	φ(His)	-117.8	2.7
	ψ(His)	15.0	8.9
	ω(His-Lys)	-154.2	0.1
	φ(Lys)	104.1	21.9
Cu–cGHK	ψ(cGly)	4.5	2.3
	ω(cGly-cHis)	-173.3	1.4
	φ(cHis)	-80.6	0.5
	ψ(cHis)	52.9	5.6
	ω(cHis-cLys)	-175.0	3.7
	φ(cLys)	-170.0	39.2

All ensemble-averaged values were computed using Boltzmann-normalized weights w_i.

Table S6. Ensemble-averaged Torsion Fingerprint Deviations (⟨TFD⟩) computed for the three lowest-energy conformers of Cu–GHK and Cu–cGHK.

Comparison	Description	⟨TFD⟩
Cu–GHK (intra)	Within the three lowest conformers of Cu–GHK	0.0292
Cu–cGHK (intra)	Within the three lowest conformers of Cu–cGHK	0.0423
Cu–GHK ↔ Cu–cGHK (inter)	Between the Cu–GHK and Cu–cGHK ensembles	0.1943

All ensemble-averaged values were computed using Boltzmann-normalized weights w_i.