Helix-Coil Transition at a Glycine Following a Nascent α-Helix: A Synergetic Guidance Mechanism for Helix Growth

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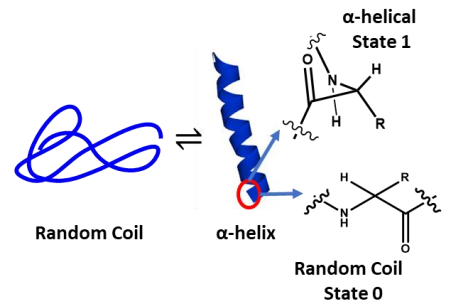
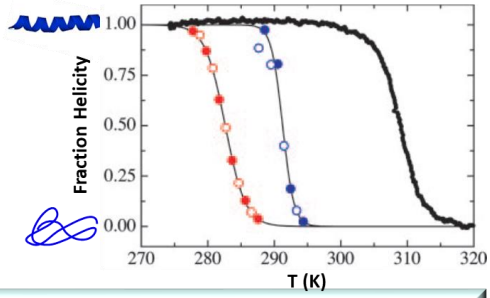
1. Two-state Helix-Coil Transition (HCT)

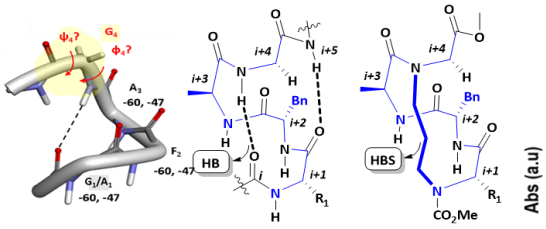
a) Theoretical Predicted Residue-Level HCT



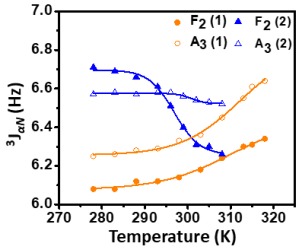
b) Experimentally Observed Bulk-State HCT



2. HBS model to slow down HCT at the i+4th residue

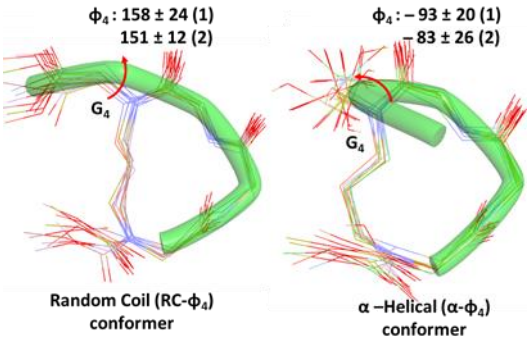


3. Sigmoidal Two-state Transition: Temperature-dependent ^{1}H-NMR

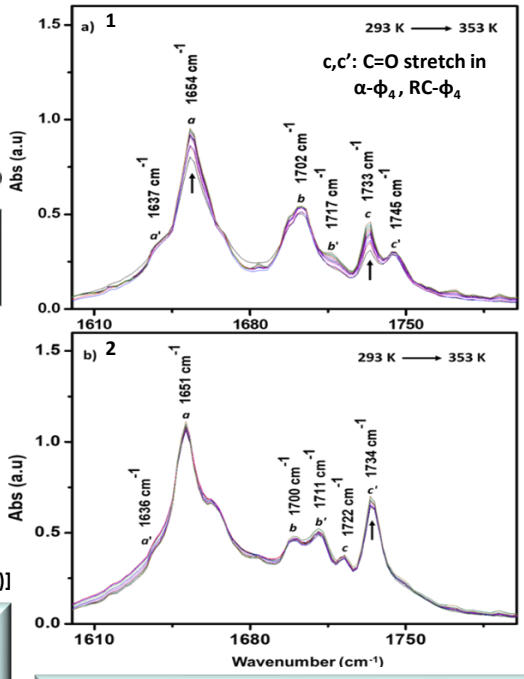


cpd.	(ϕ)	ΔH kcalmol^{-1}	ΔS calmol^{-1}K^{-1}	ΔG$^{\#}$ kcalmol^{-1}	T_m K	Δϕ deg.
1	F_2	23.37	75.5	1.10	309.9	1.49
	A_3	28.95	92.8	1.57	311.8	4.30
2	F_2	54.63	184.3	0.26	296.9	9.00
	A_3	78.57	261.2	1.52	300.8	0.96

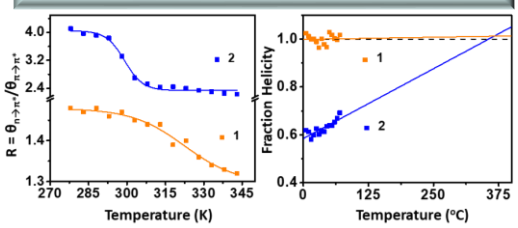
4. Conformers from GROMACS Molecular Dynamics Simulations



5. Temperature-dependent FT-IR indicates dynamic equilibrium

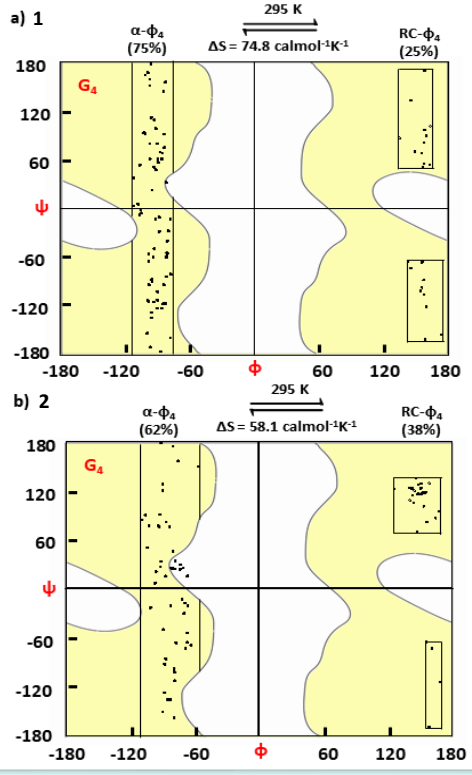


6. CD analysis: concentration of α-ϕ4 increases with T

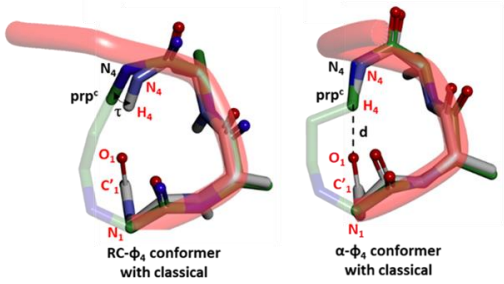


cpd.	ΔH kcalmol^{-1}	ΔS calmol^{-1}K^{-1}	ΔG$^{\#}$ kcalmol^{-1}	T_m K
1	24.43	74.8	2.36	324.9
2	17.40	58.1	0.26	299.3

7. Population of α-ϕ4 is entropically favored to increase with T.



8. Synergetic Guidance Mechanism for Helix Growth



Summary

(1) α-Helical turn guides ϕ_{i+4} into predominantly populated α-ϕ4 or scarcely populated RC-ϕ4.
(2) α-ϕ4 favors the stability of preceding α-helical turn, while RC-ϕ4 disrupts it.
(3) Entropy-driven synergetic guidance mechanism for helix growth following helix-nucleation.

References

(1) Zimm, B. H.; Bragg, J. *J. Chem. Phys.* **1959**, *31*, 526.
(2) Lifson, S.; Roig, A. *J. Chem. Phys.* **1961**, *34*, 1963.
(3) Prabhakaran et al. *ACS Omega* **2020**, *5*, 13902.
(4) Prabhakaran et al. *J. Phys. Chem. A* **2020**, *124*, 7478.