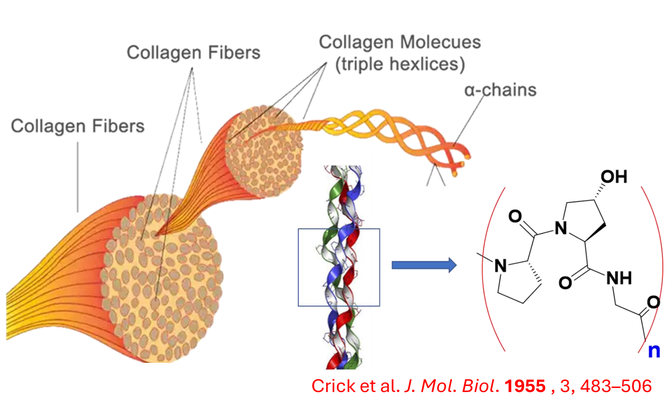
Twist in the Tail: Capping Turns Modulates Collagen Thermal Stability

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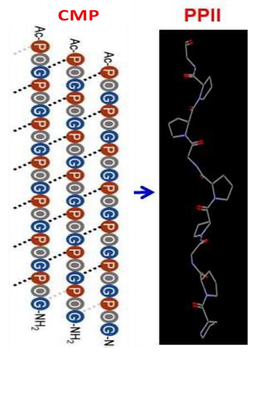
EPS-2026

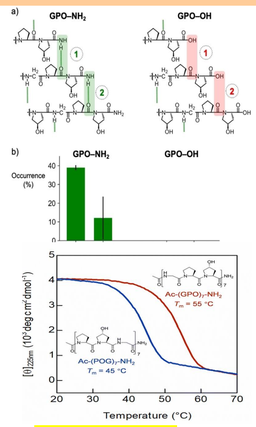
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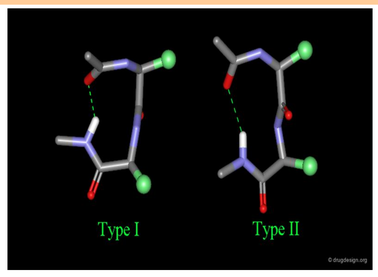
Frame-dependent differences in collagen triple-helix stability are well recognized, yet their structural basis remains unclear. Here, we investigate the role of a C-terminal β-turn as a potential competing structural motif governing this dependence. In collagen mimetic peptides adopting the POG frame, a C-terminal amide can promote intramolecular hydrogen bonding that may sequester the Pro carbonyl and interfere with interstrand hydrogen bonds required for triple-helix assembly. By contrast, in the GPO frame, such competition is reduced, allowing the terminal amide to participate in stabilizing interstrand interactions.



Crick et al. *J. Mol. Biol.* **1955** , 3, 483–506

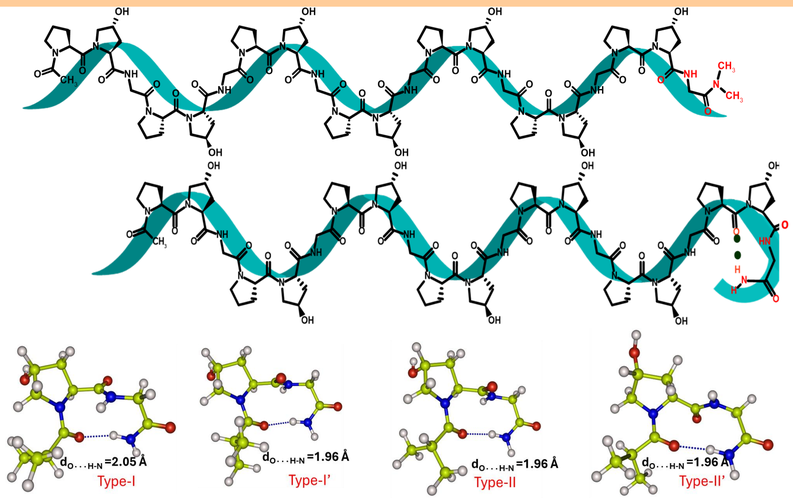






Does Proline(Hyp) and Glycine diad facilitate the formation of any competing intra strand interaction ?

Can we have a terminal cap at C terminal which is neutral to any inter or intra-strand interaction ?



OGP Frame

Ac-(OGP)9-NH2
Ac-(OGP)9-NH2
Ac-(OGP)9-NH2

T_m = 42.3 °C

POG Frame

Ac-(POG)9-NH2
Ac-(POG)9-NH2
Ac-(POG)9-NH2

T_m = 43.7 °C

GPO Frame

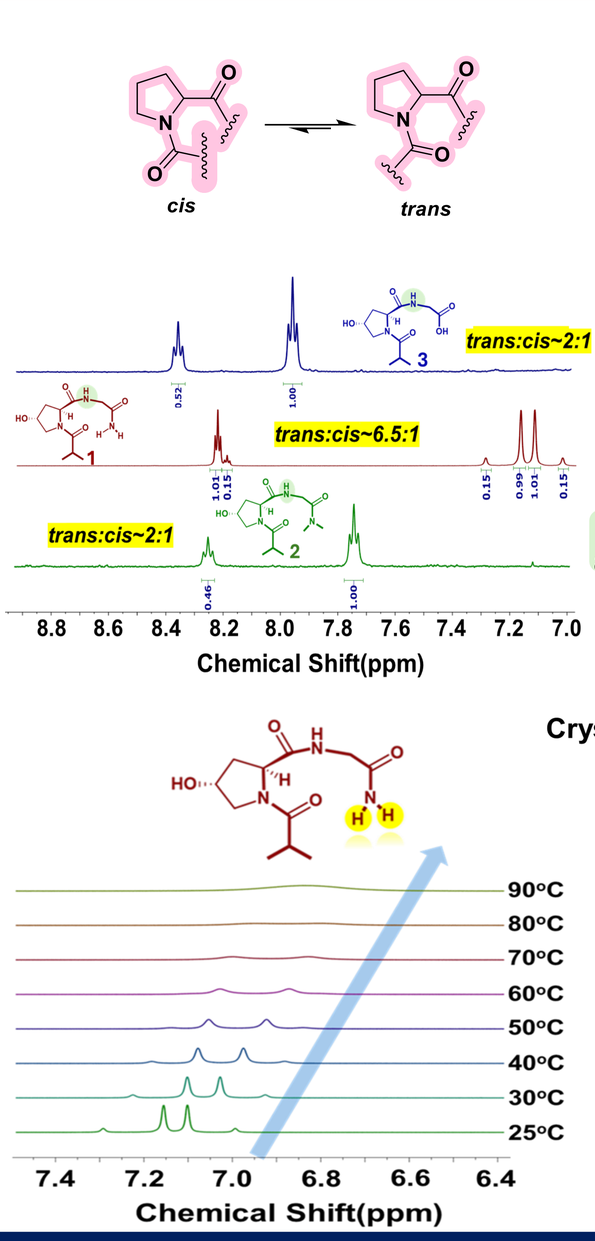
Ac-(GPO)9-NH2
Ac-(GPO)9-NH2
Ac-(GPO)9-NH2

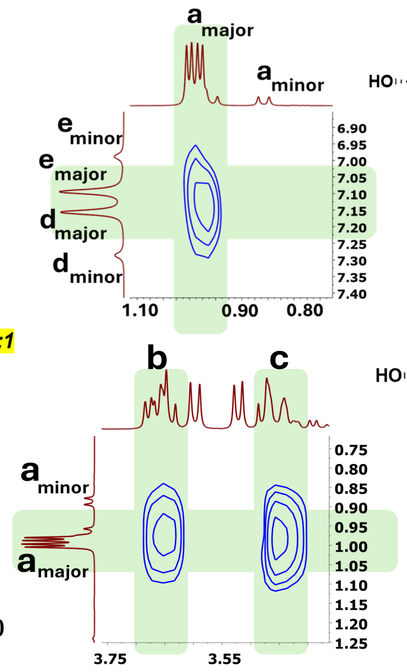
T_m = 53.2 °C

^{t}BU-Hyp-Gly-NH$_2$(1)	Type-I	Type-I'	Type-II	Type-II'	PPII
Δ(ΔE+ZPE) [kcal/mol]	3.03	0.17	0.00	-0.05	3.53

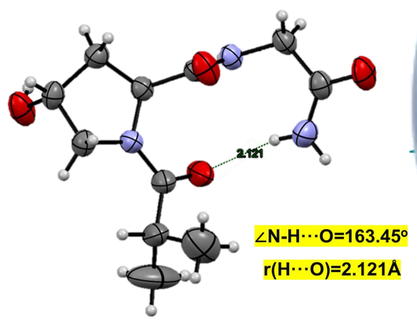
Formation of β Turns : Systematic Studies on Small Molecules and Collagen Mimetic Peptides

Probing formation of β turns through NMR & SC-XRD



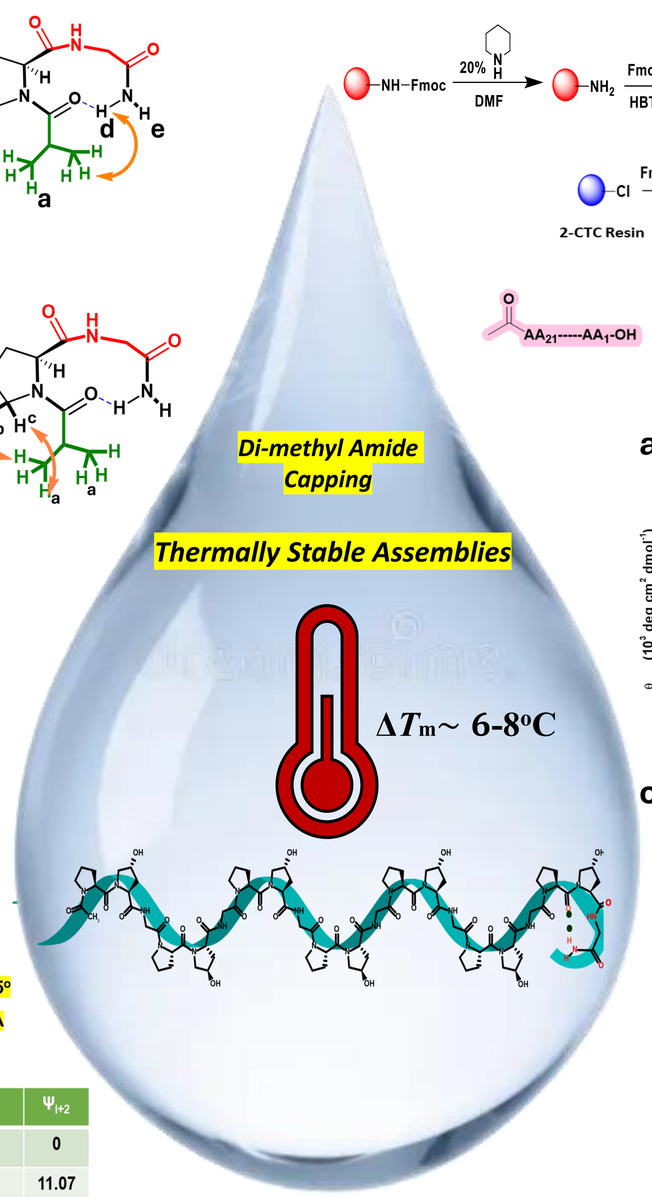


Crystal Structure of Compound 1

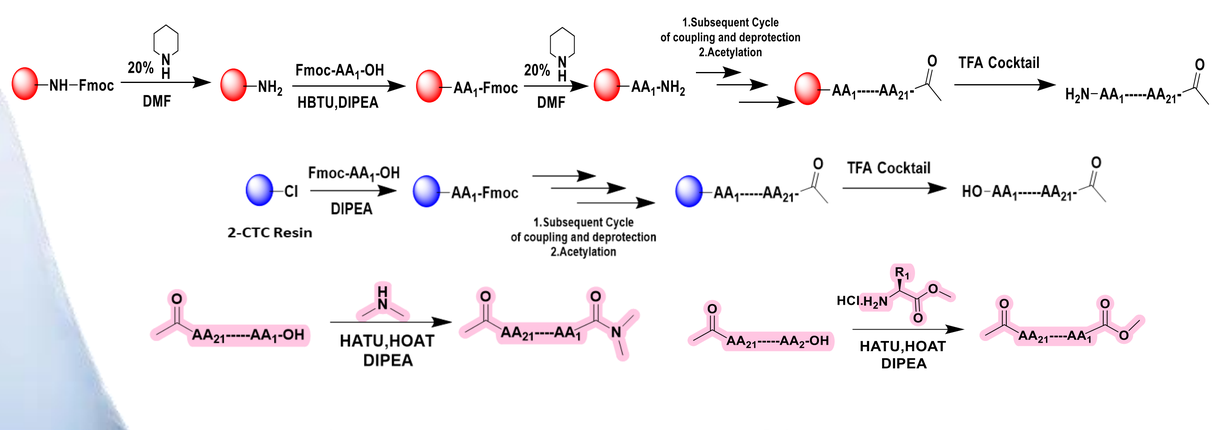


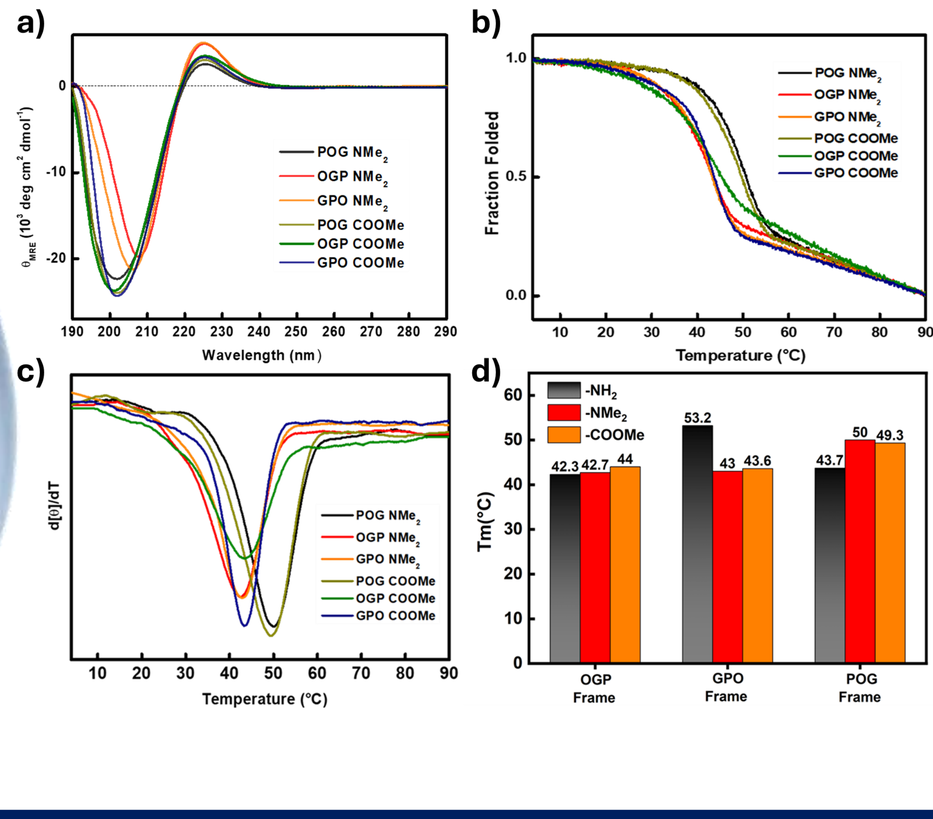
∠N-H···O=163.45°
r(H···O)=2.121Å

Type	φ_{i+1}	Ψ_{i+1}	φ_{i+2}	Ψ_{i+2}
Type-II β turn	-60	120	80	0
^{t}Bu-OG-NH$_2$(1)	-61.17	122.72	74.18	11.07



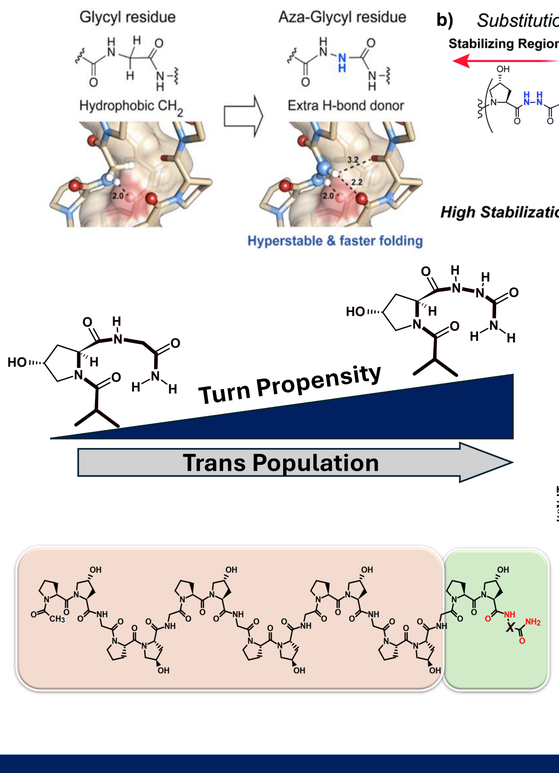
CD studies of CMPs





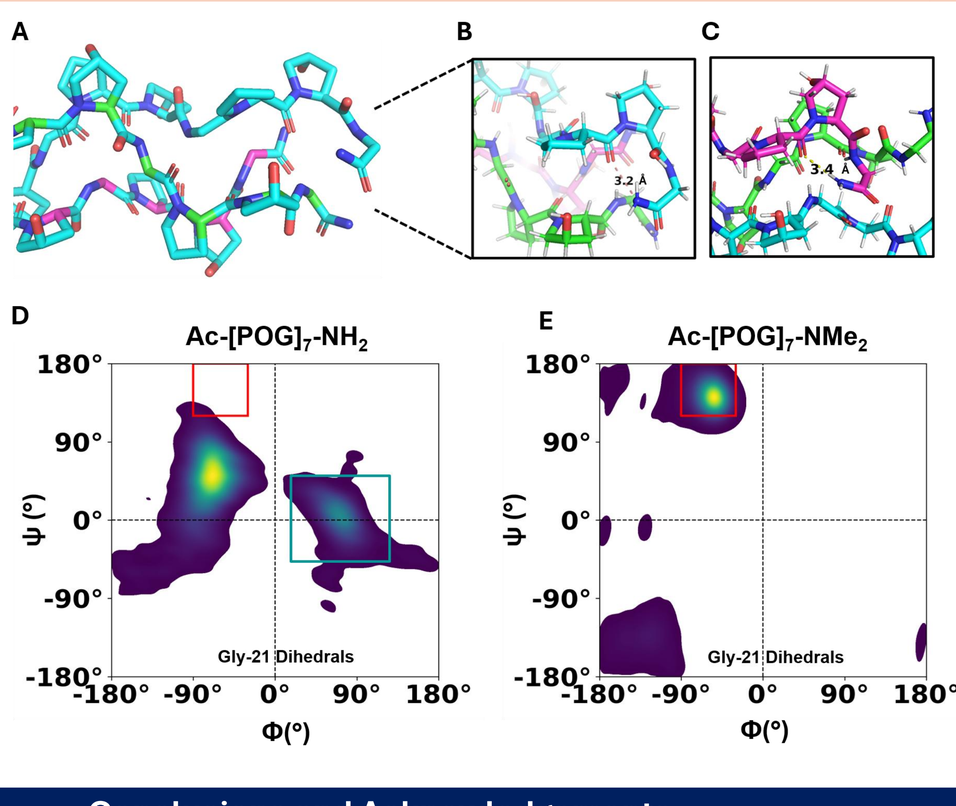
Effect of Competitive β Turns : From Cap to Core

Azaglycine incorporation in CMPs

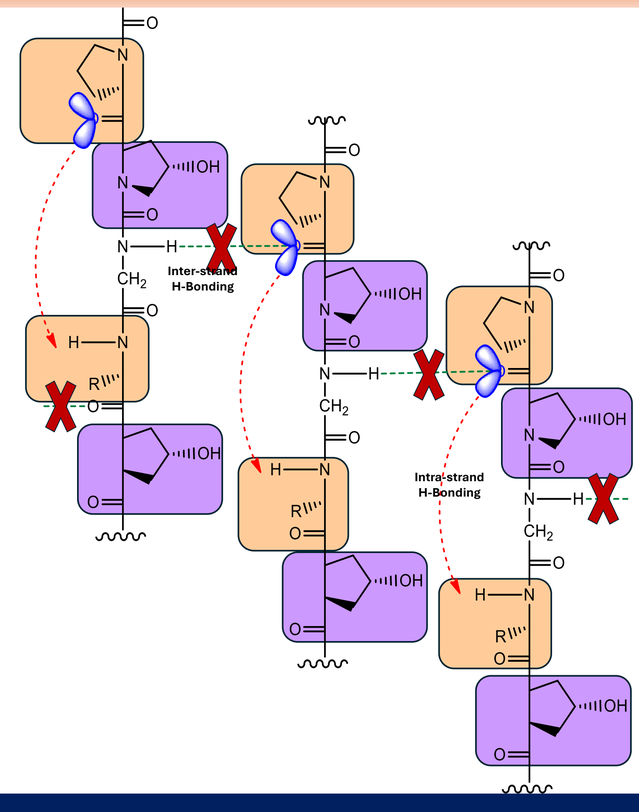


Chenoweth et al. *J. Am. Chem. Soc.* **2015**, 137, 12422−12425

MD simulations



Effect on core substitution



Conclusions and Acknowledgements

This study reveals that β-turn formation at Pro/Hyp–Gly diads competitively disrupts collagen triple-helix stability, with C-terminal caps modulating this effect through their hydrogen-bonding capacity. Frame-dependent analyses of GPO, POG, and OGP systems uncover distinct terminal interactions, establishing design rules for tuning collagen mimetic peptide stability. https://doi.org/10.17952/38EPS.2026.P470

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