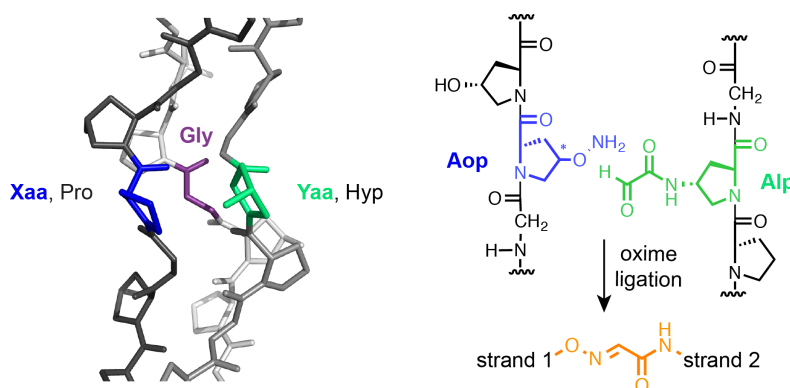


Cross-Linked Collagen Triple Helices by Oxime Ligation

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Collagen is the most abundant protein in mammals and the main component of their extracellular matrix.^{1,2} The chemical synthesis of collagen is attractive for medical and nanotechnological applications³ since it can provide access to structurally defined and functionalizable materials.^{4,5} However, the bottom-up design of materials mimicking the fibrous structures of natural collagen is hampered by the entropically unfavorable assembly of short single strands into triple helices.^{1,2} To lay the foundation for higher-ordered assemblies of collagen model peptides (CMPs), we covalently connected CMPs by oxime linkages between aminooxyproline (Aop)⁶ and 2-oxoacetamidoproline (Alp) derivatives placed in neighboring strands. The cross-linked strands folded into collagen triple helices with remarkably high thermal stabilities ($T_m \sim 80^\circ\text{C}$). The design of the cross-links was guided by an analysis of the conformational properties of Aop, studies on the stability and functionalization of Aop-containing collagen triple helices, and molecular dynamics calculations. Our findings open new opportunities for the design of functional collagen-based materials forming by the sticky-ended assembly of structurally well-defined triple helices.



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