

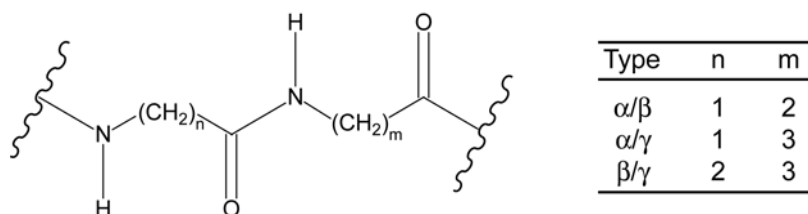
## Secondary Structure Formation and Folding in $\alpha/\beta$ -, $\alpha/\gamma$ -, and $\beta/\gamma$ - Oligopeptides (Hybridpeptides)

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The design of peptides with novel properties is a great challenge for biochemists and chemists. The use of non-canonical amino acids has a great tradition both for the exchange of single residues in sequences of  $\alpha$ -amino acids and for the design of peptides completely built from unusual amino acids. These compounds are able to form characteristic secondary structures and belong to the group of foldamers. A great influence on foldamer research came from investigations on the homologous  $\beta$ - and  $\gamma$ -peptides. A further extension of this concept are sequences composed alternately of  $\alpha$ - and  $\beta$ -,  $\alpha$ - and  $\gamma$ - and  $\beta$ - and  $\gamma$ -amino acids, respectively. The insertion of such elements in  $\alpha$ -peptide sequences has a considerable potential for secondary structure design. Thus the combination of a  $\beta$ - and a  $\gamma$ -amino acid residue can substitute three  $\alpha$ -amino acid residues.<sup>1</sup> Recently, co-oligomers of  $\alpha$ - and  $\beta$ -amino acid building blocks have been studied.<sup>2,3</sup> Several types of secondary structure have been suggested, e.g. helices with H-bonds in backward and in forward direction.



Here, we present the results of a systematic theoretical study on three types of co-oligomers with  $\alpha$ - and  $\beta$ -,  $\alpha$ - and  $\gamma$ -, and  $\beta$ - and  $\gamma$ -amino acids, respectively. For all three types, we found secondary structures with the H-bonds only in backward and in forward direction, but also structures with H-bonding patterns of mixed or  $\beta$ -helices. In all three cases, the most stable secondary structures were the mixed helices with alternating  $i \rightarrow (i+3)$  and  $i \leftarrow (i+5)$  amino acid interactions at the HF/6-31G\* level of ab initio MO theory.

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