Self-Assembly of Helical Pores from Nonpolar Dendritic Dipeptides

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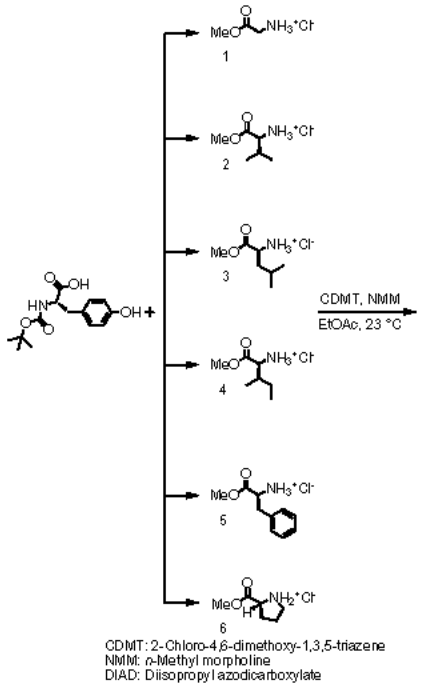
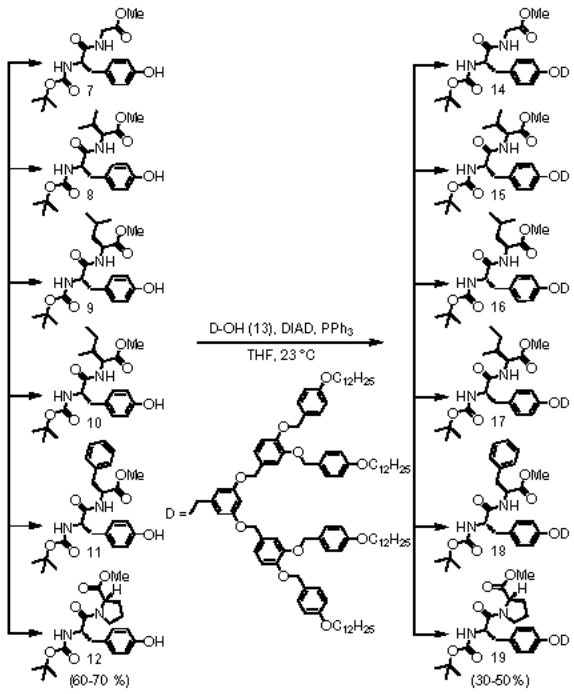
Natural porous proteins function as viral helical coats,[1] transmembrane channels responsible for ion regulation and transport, molecular recognition and response, and energy transduction,[2] antibiotics,[3] antimicrobials,[4] and toxins.[5] Remodeled porous proteins are used for reversible encapsulation of molecules[6] and in stochastic sensing.[7] Integral membrane proteins, including those functioning as transmembrane channels, exist in very low natural abundance, and since they form 3-dimensional functional structures only in the membrane environment, their crystallization had limited success. Therefore, the molecular details of their structure and function are not well understood.[2,3] Simple synthetic assemblies that mimic the structure and function of transmembrane channels are expected to contribute to the understanding of the structure and function of the more complex natural proteins. Strategies for the synthesis and assembly of porous or tubular supramolecular structures have been elaborated.[8] Natural porous proteins are stable in the fluid membrane environment and in solid state. However, with few exceptions,[9] porous protein mimics do not assemble into periodically ordered structures that are stable in solution and in solid state. This behavior limits their structural analysis by combinations of solution and solid-state complementary techniques. Recently, our laboratory elaborated a new strategy to helical porous protein mimics that is based on the self-assembly of amphiphilic dendritic dipeptides.[10] The internal structure and stability of the porous structure self-assembled from dendritic dipeptides is programmed by the stereochemistry[11a] and protective groups[11b] of the dipeptide, by the number of methylenic units from the alkyl groups of the dendron,[11c] and by the primary structure of the dendron attached to the dipeptide.[11d,e]

These experiments provided some of the molecular principles required to program the self-assembly of helical pores from dendritic dipeptides. This cooperative self-assembly process involves allosteric regulation.[11,12] In all previous studies the dendritic dipeptide was constructed from Boc-Tyr-Ala-OMe dipeptide containing various combinations of Tyr and Ala stereochemistry,[10,11a] different protective groups,[11b] and dendron architectures.[11c-e] In order to assess the scope, limitations, and generality of this self-assembly strategy, the synthesis, self-assembly, structural and retrostructural analysis of the dendritic dipeptides (4-3,4-3,5)12G2-CH_2-Boc-L-Tyr-X-OMe, in which X are all nonpolar α-amino acids Gly, L-Val, L-Leu, L-Ile, L-Phe, and L-Pro, were investigated. The scheme below outlines the synthesis of the dendritic dipeptides to be discussed. The results of this study will be discussed in this lecture and compared with that of the dendritic dipeptide with X=L-Ala which was studied previously[10,11] and was reinvestigated.





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