Design and Exploration of Tubular Assemblies of Hybrid Cyclic Peptides

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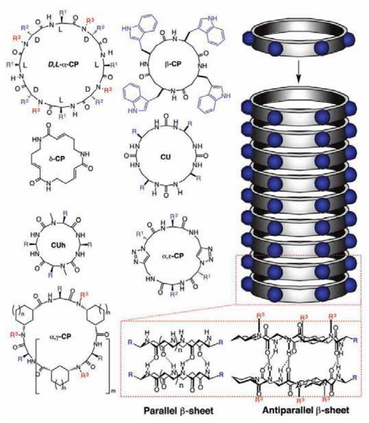
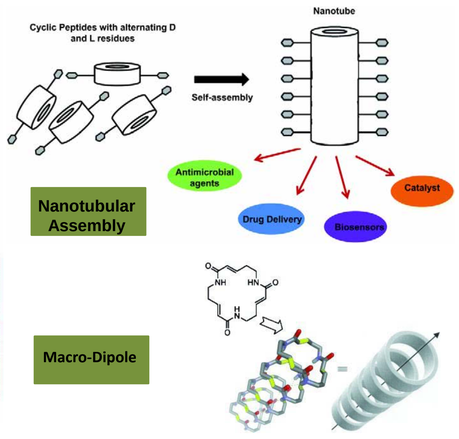
Abstract

Self-assembling cyclic peptides are important building blocks to construct synthetic nanotubes. They can be primarily classified into cyclic α-alt(D,L)-peptides, cyclic β-peptides, cyclic α,γ-peptides, and cyclic peptides incorporating δ- or ε-amino acids based on their composition.[1] Our research focuses on design of novel cyclic peptides derived from β(O)-δ^5 -amino acid residues, consisting of a hybrid structure of crown ether and peptide macrocycles. These peptides exhibit unique self-assembly, forming hollow sub-nanotubular structures with unidirectional hydrogen bonds. These cyclic dipeptides, adopting non-centrosymmetric space groups, display significant anisotropy, suggesting potential macroscopic dipole extensions.[2] Furthermore, their inherent macrodipole orientation inspires investigation into their piezoelectric properties, opening new avenues for diverse applications. Additionally, we have synthesized size-variant macrocycles featuring β(O)-δ^5 amino acid residues which also fold into self-assembled nanotubes in solution and gas phase. This apparent supramolecular size-variant nanotube acts as an anion-selective transporter. The ion channel activity and selective transport of these structures are examples of the great potential that cyclic peptide nanotubes show for the construction of functional artificial transmembrane transporters.[3]

Background

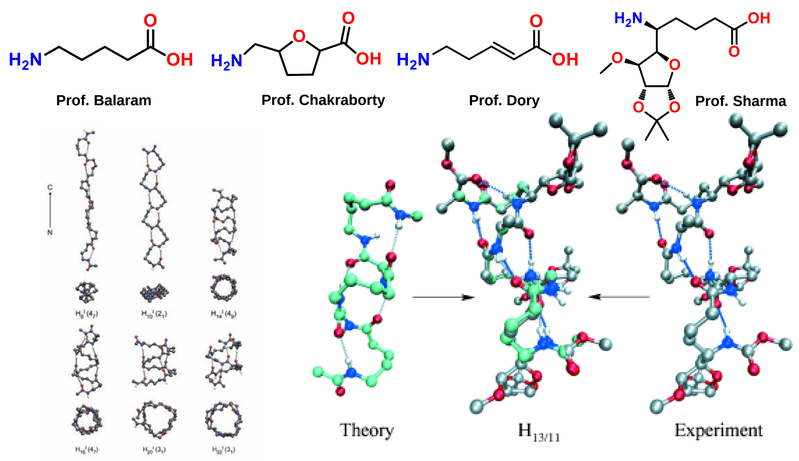


Chemical Reviews **2021**, *121*, 13936–13995.



Angew. Chem. Int. Ed. **2001**, *113*, 24.

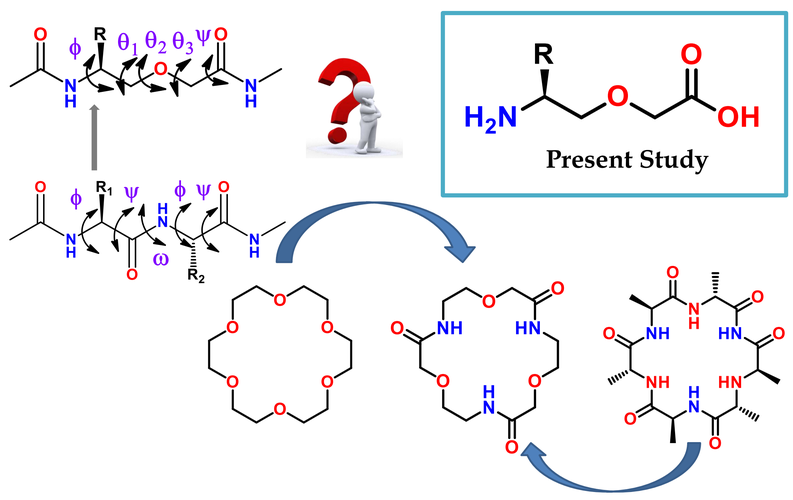
δ-amino Acid Foldamers



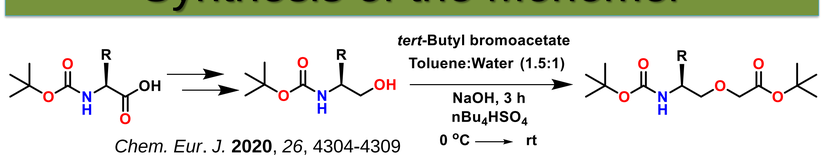
J. Org. Chem. **2004**, *19*, 6214.

Chem. Eur. J. **2009**, *15*, 5552.

Our Design

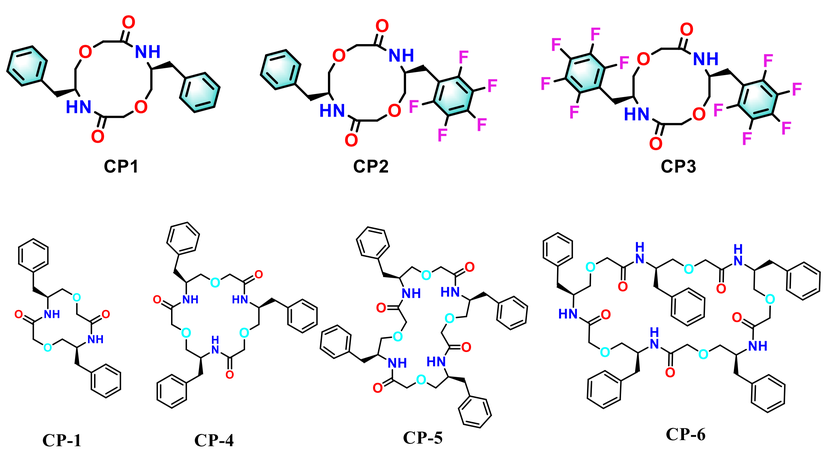


Synthesis of the Monomer

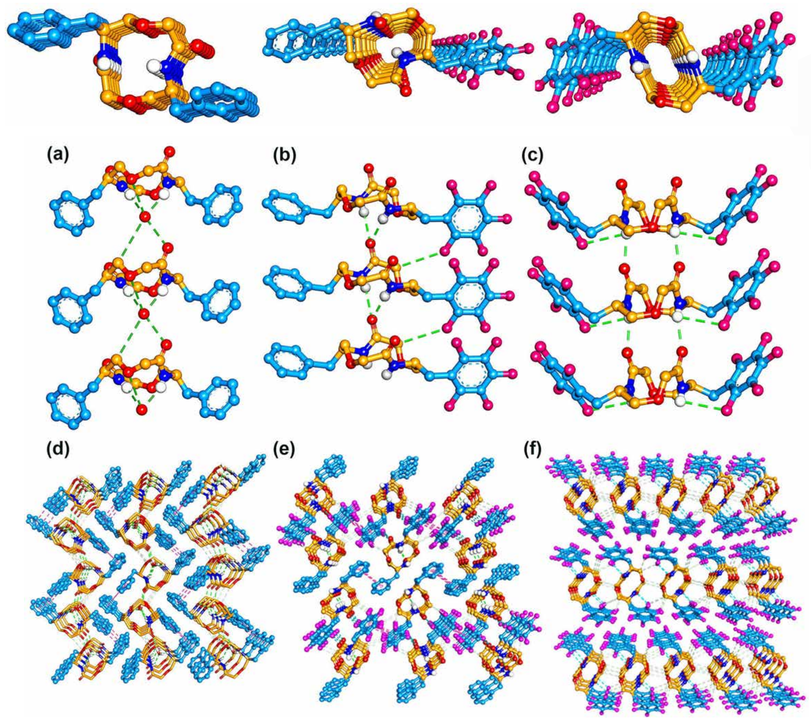


Chem. Eur. J. **2020**, *26*, 4304-4309

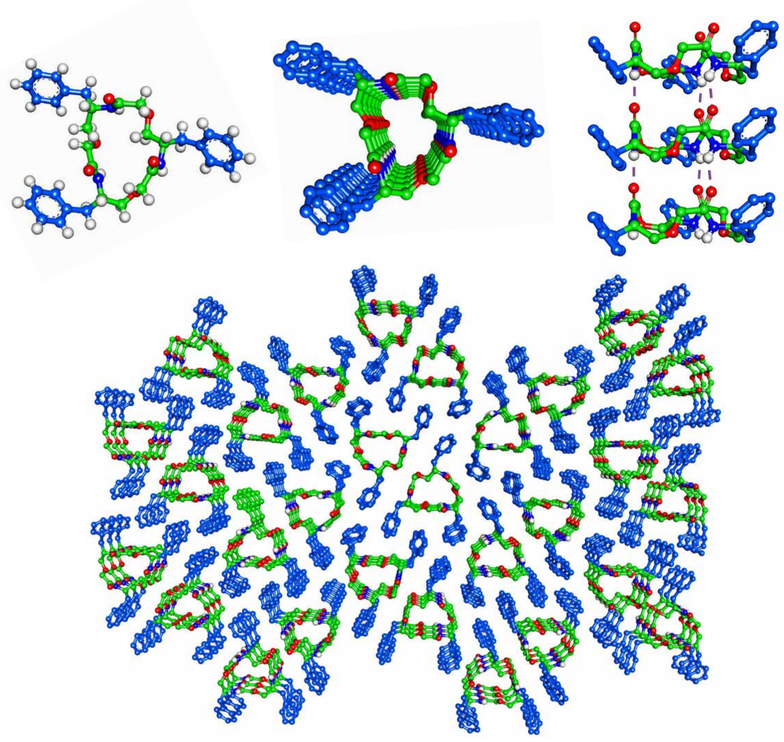
CPs Library Synthesis



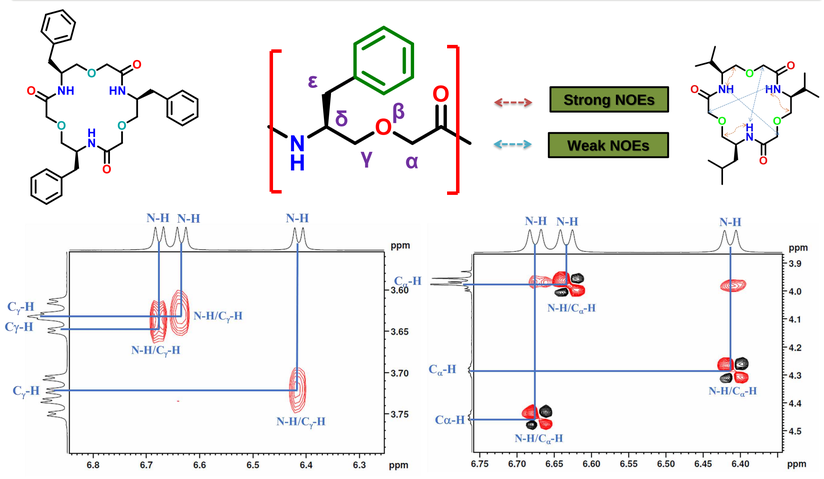
Crystal Analysis of Cyclic Dipeptides

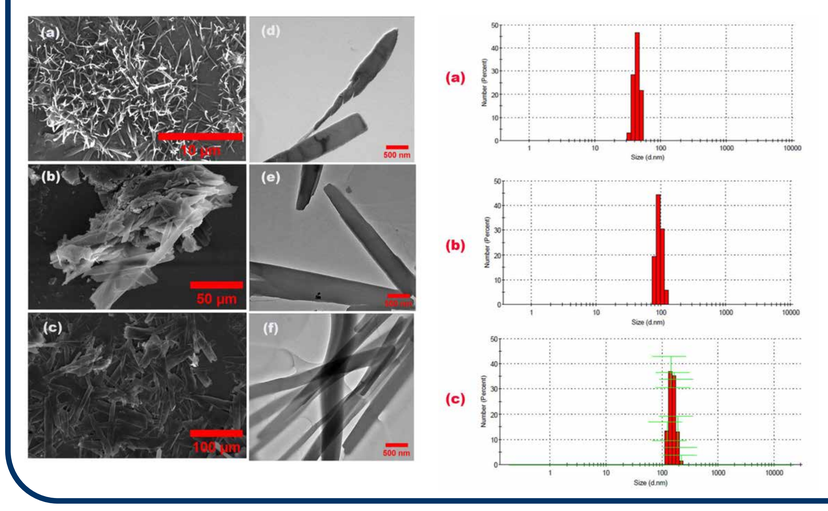


Crystal Analysis of Cyclic Tripeptide

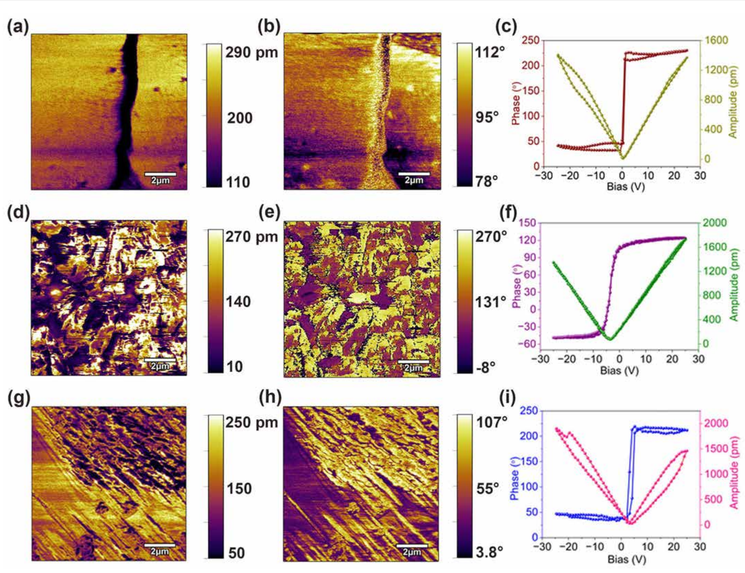


Solution Structure Analysis

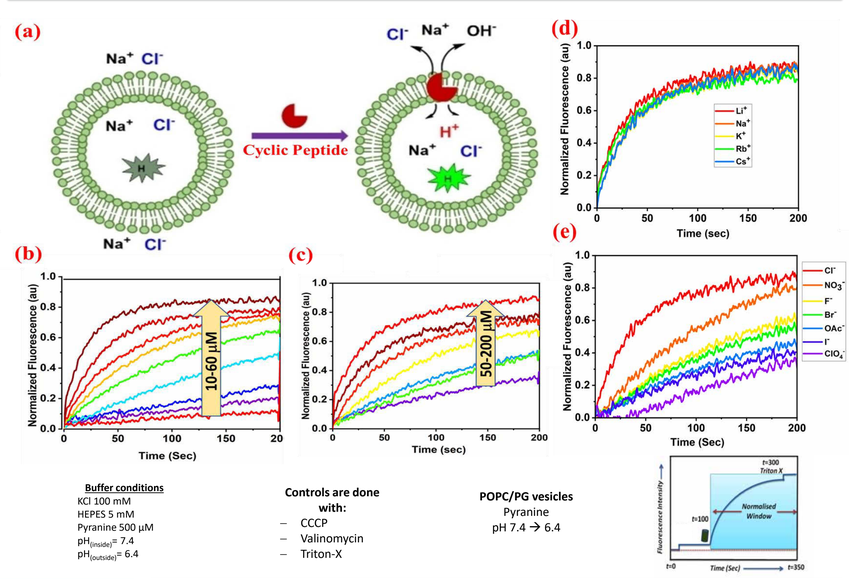




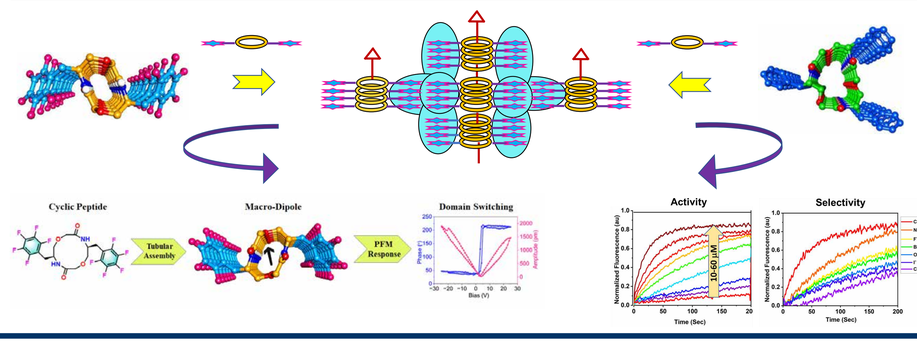
PFM Analysis of CPs



Vesicle Leakage Assay



Conclusion



References

[1] D. Gauthier, Y. L. Dory, *Angew. Chem. Int. Ed.* **2001**, *113*, 24.
[2] S. Panda Mahapatra, S.Pahan. A.Chatterjee, S.Roy, D. R. Puneeth Kumar, H. N. Gopi, *Angew. Chem. Int. Ed.* **2024,** e202409969.
[3] T. D. Clark, L. K. Buehler, M. R. Ghadiri, *J. Am. Chem. Soc.* **1998**, *120*, 651-656.

Acknowledgements

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