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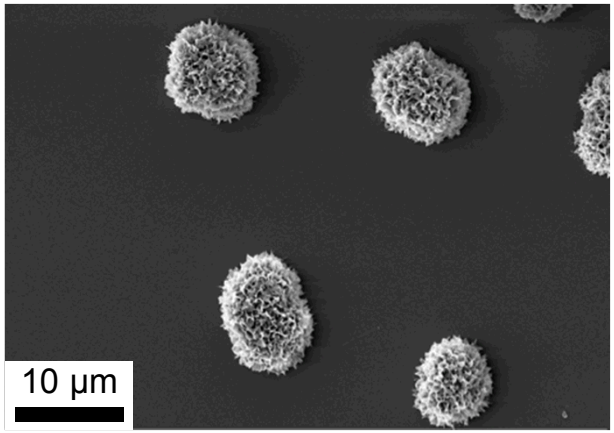

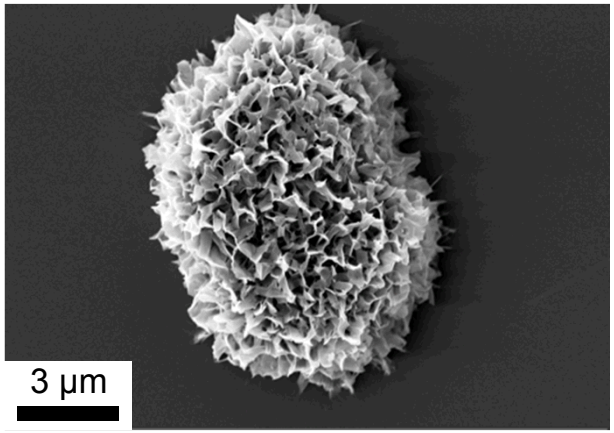

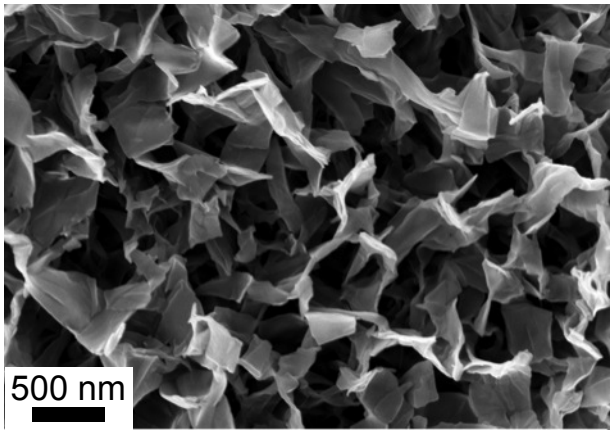

Self Assembly of Boronic Acid-Functionalized Peptides

Brad H. Jones, Alina M. Martinez, Jill S. Wheeler, Bonnie B. McKenzie, David R. Wheeler, and Erik D. Spoerke

October 6, 2014

U.S. DEPARTMENT OF ENERGY

NNSA National Nuclear Security Administration

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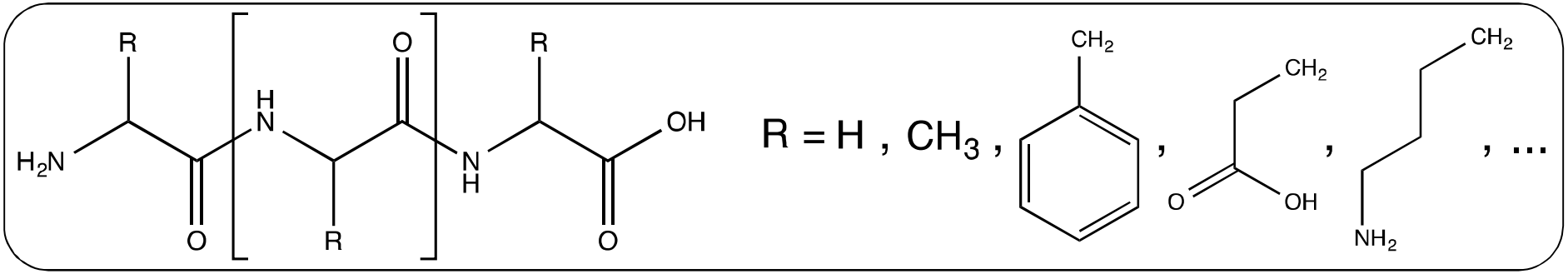
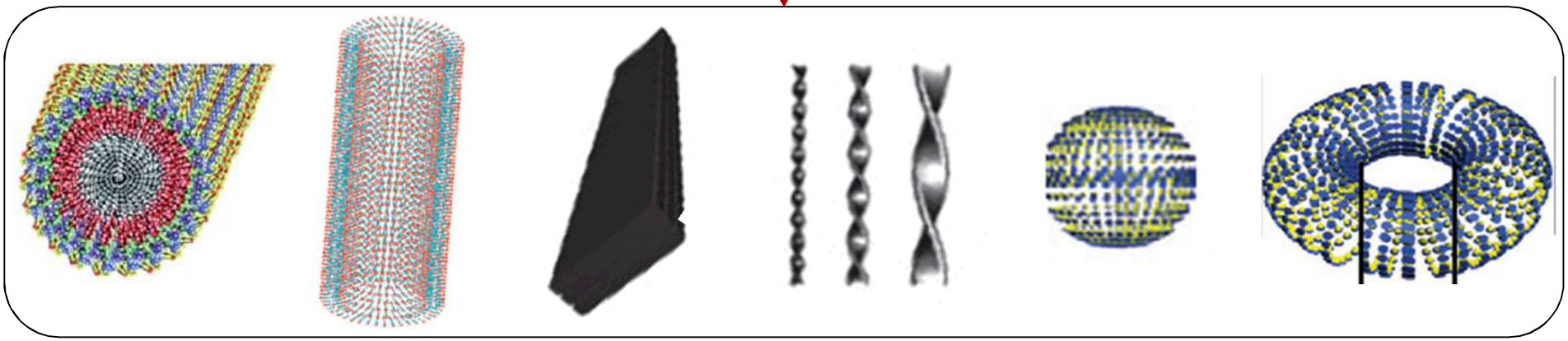
Introduction to Peptides

A complex balance of interactions drives spontaneous self-assembly



electrostatic interactions hydrogen bonding aromatic stacking hydrophobic interactions

chemical environment

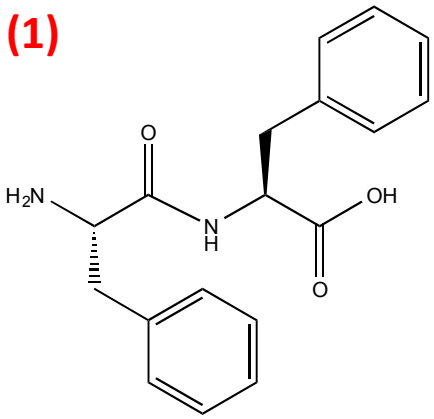


Hamley, I.W. *Soft Matter* **2011**, *7*, 4122-4138; Zhao, X.; *et al. Chem. Soc. Rev.* **2010**, *39*, 3480-3498.

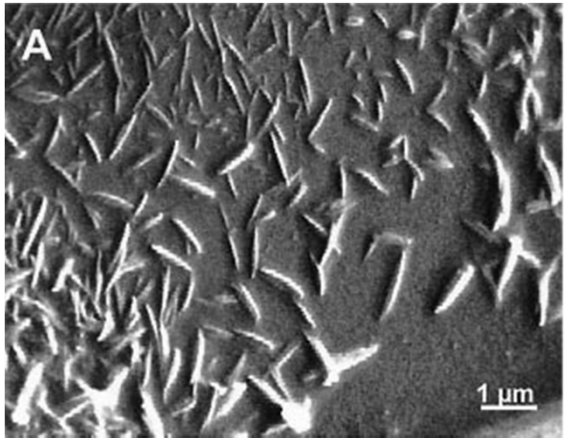
Peptide Nanotubes from Di(phenylalanine)

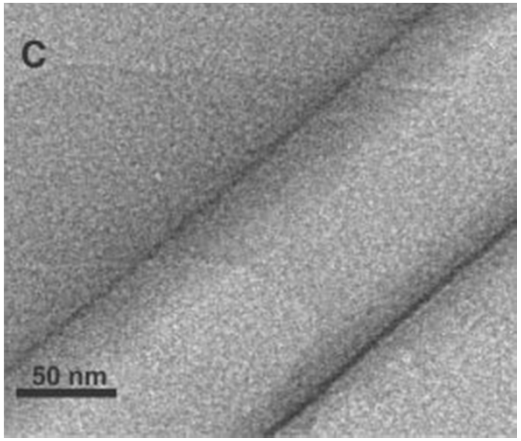
The dipeptide of phenylalanine forms crystalline nanotubes in H_2O

(1)

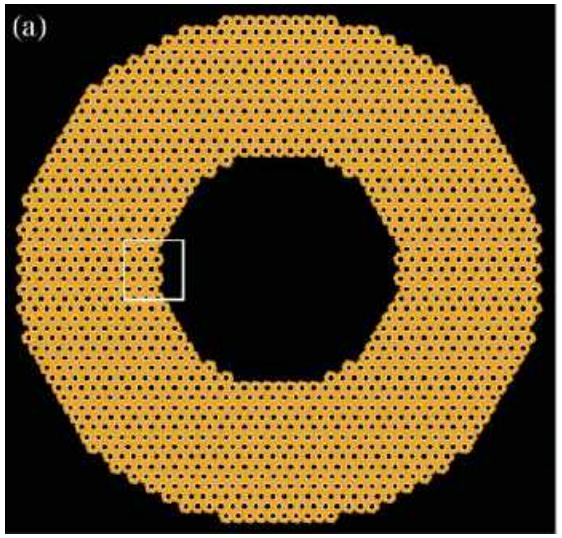


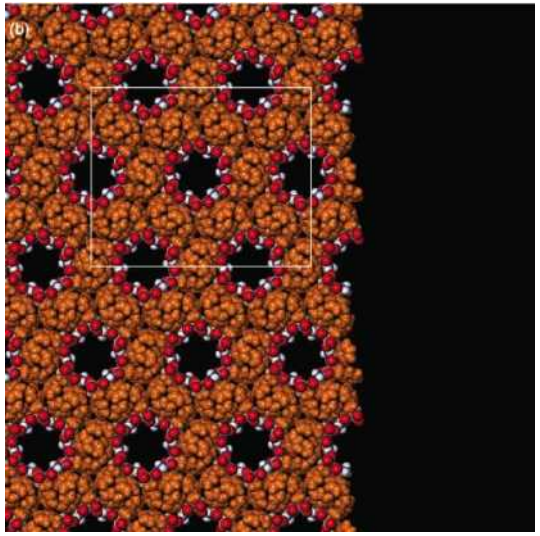
H_2O

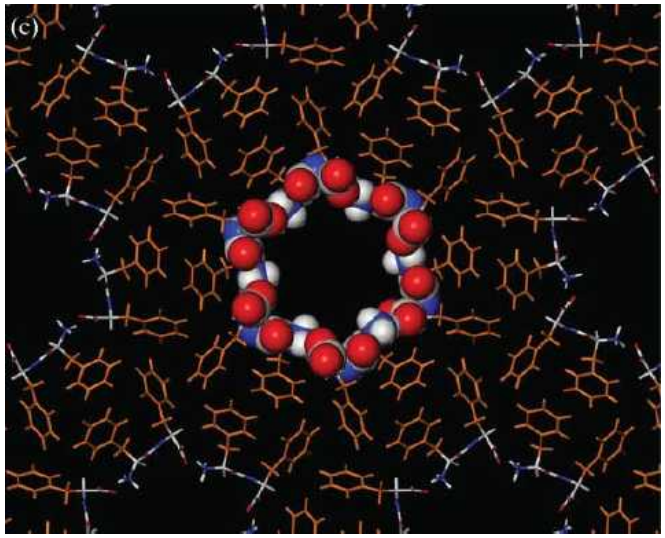




(2)



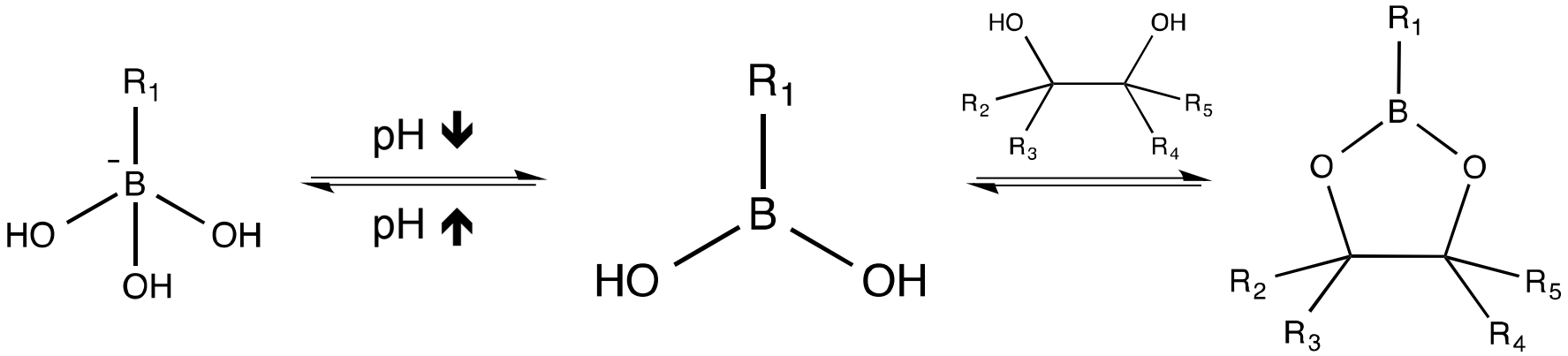


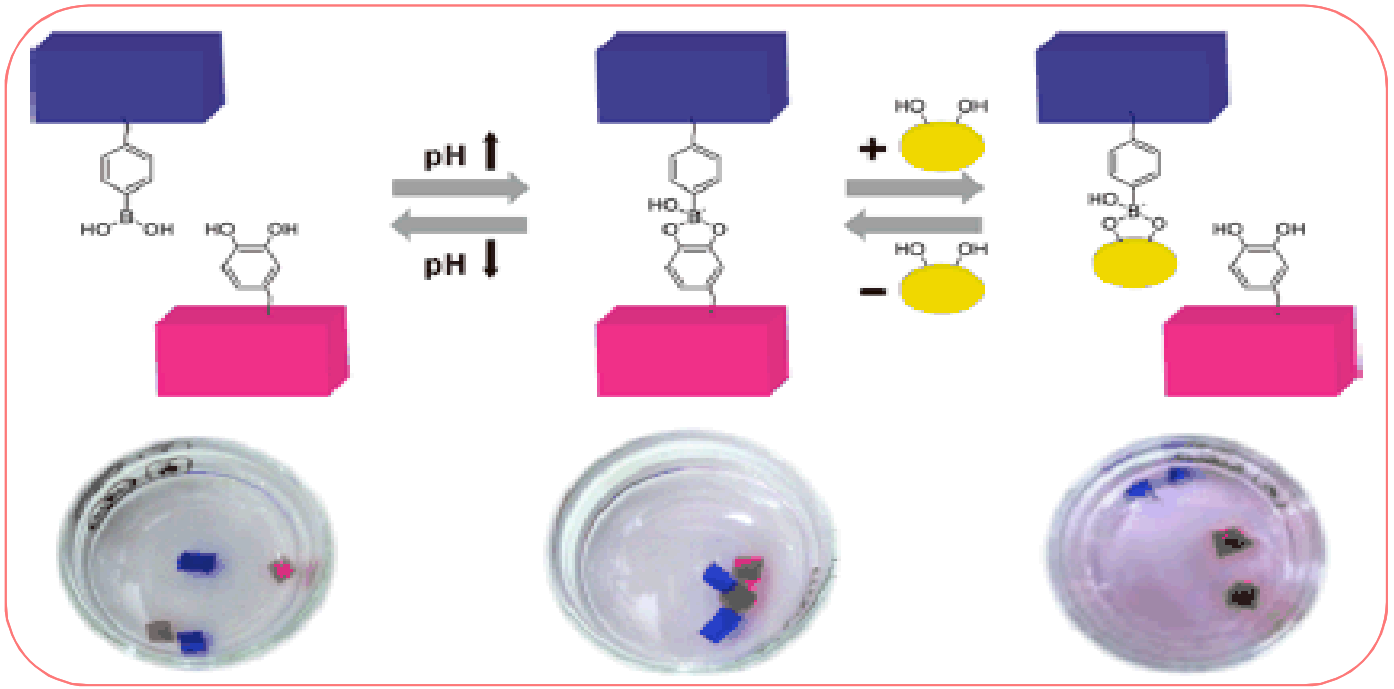


(1) Reches, M.; Gazit, E. *Science* **2003**, *300*, 625-627. **(2)** Gorbitz, C.H. *Chem. Comm.* **2006**, 2332-2334.

Boronic Acids

Boronic acids are pH- and sugar-responsive chemical functionalities

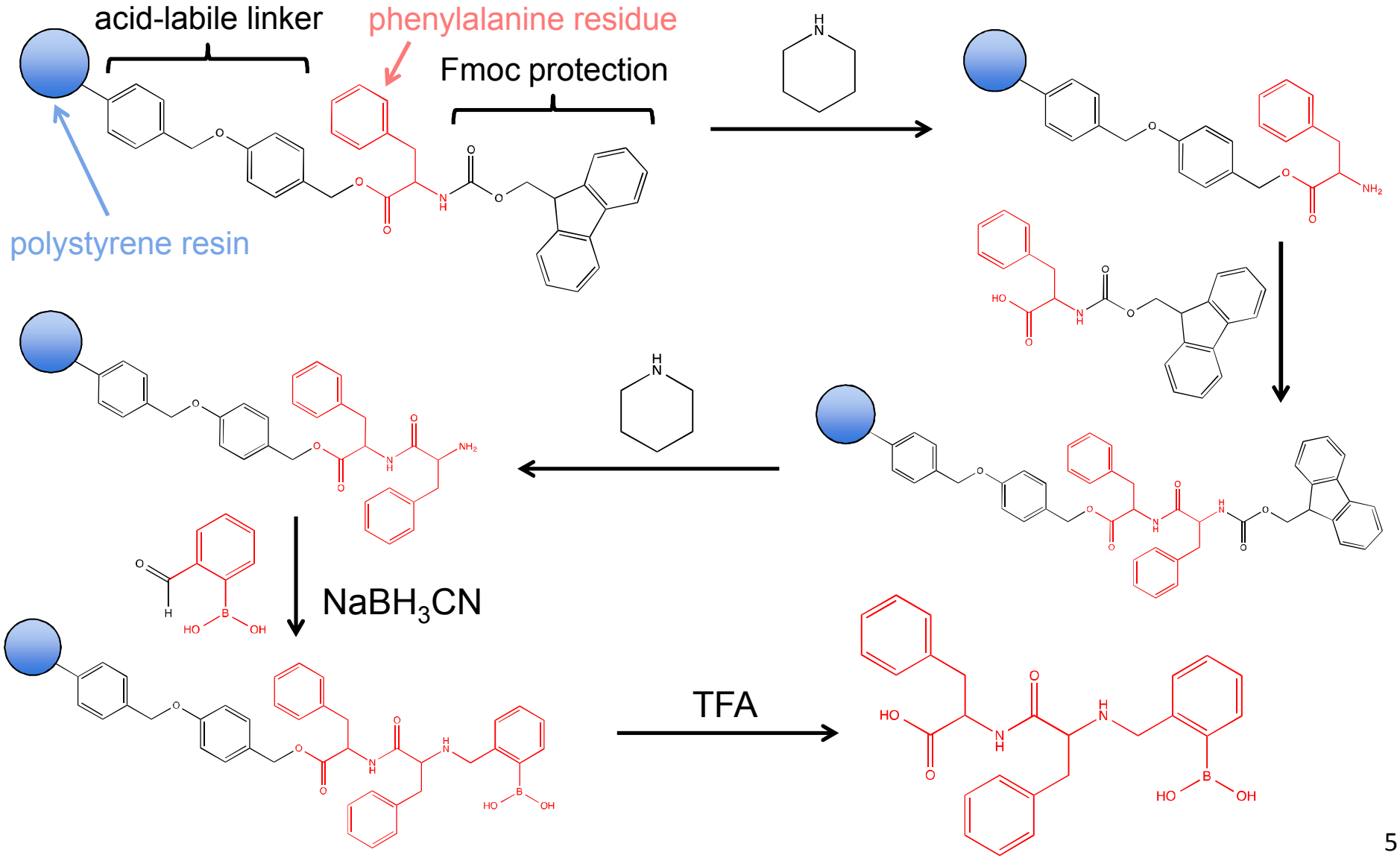




Nakahata, M.; *et al. ACS Macro Lett.* **2014**, *3*, 337-340.

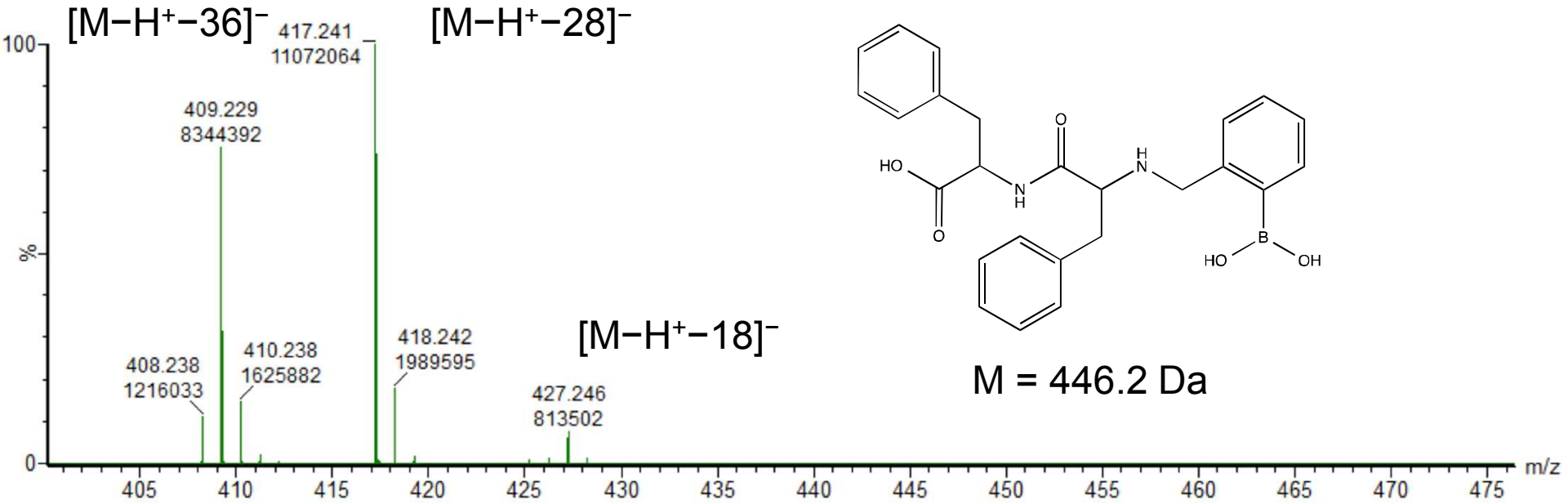
Synthesis of a Boronic Acid Dipeptide

Solid phase chemistry is a simple route to BA-functionalized di(phenylalanine)

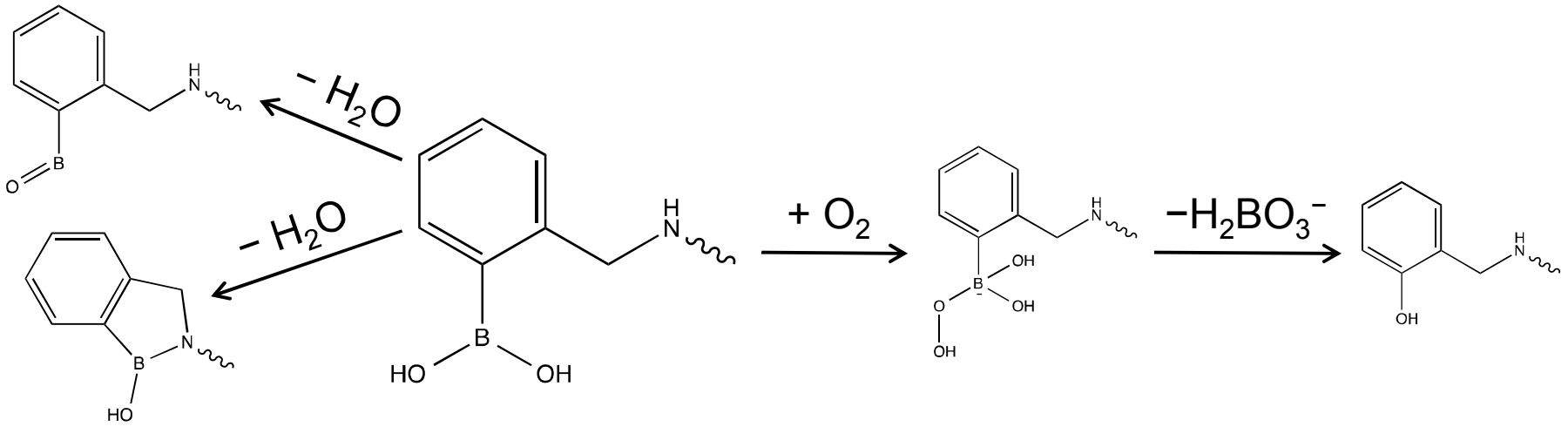


Mass Spectrometry of Boronic Acids

MS analysis is consistent with successful BA-functionalization



M = 446.2 Da



Aqueous Assembly Behavior

Our functionalized peptide self-assembles into flower-like particles in H_2O

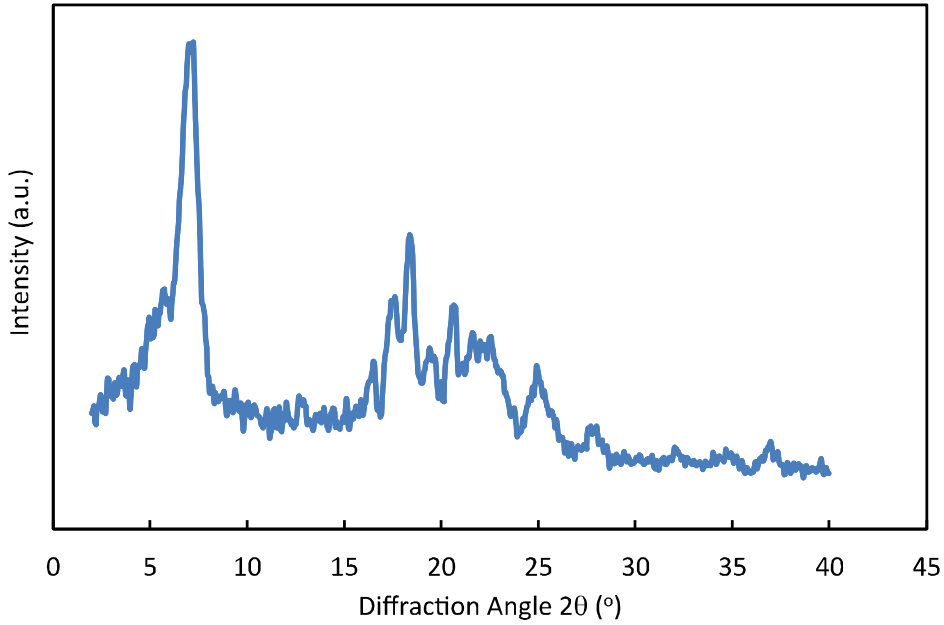
lyophilized peptide

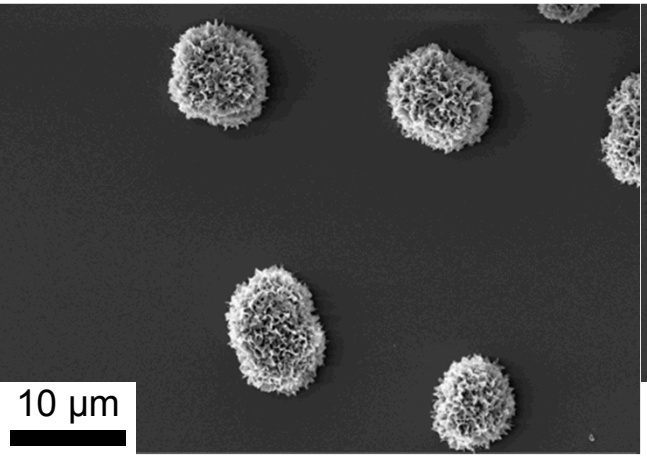
↓

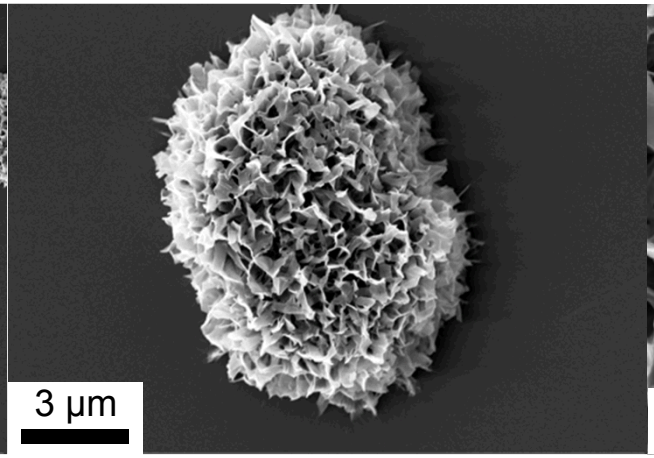
concentrate at 10 wt % in hexafluoroisopropanol (HFIP)

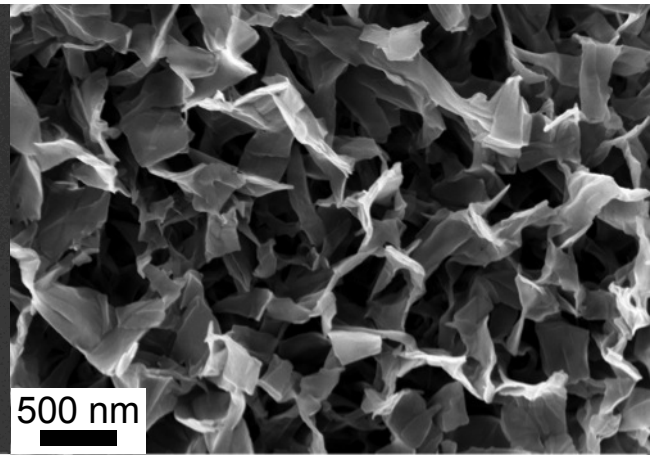
↓

dilute to 0.2-1% with H_2O





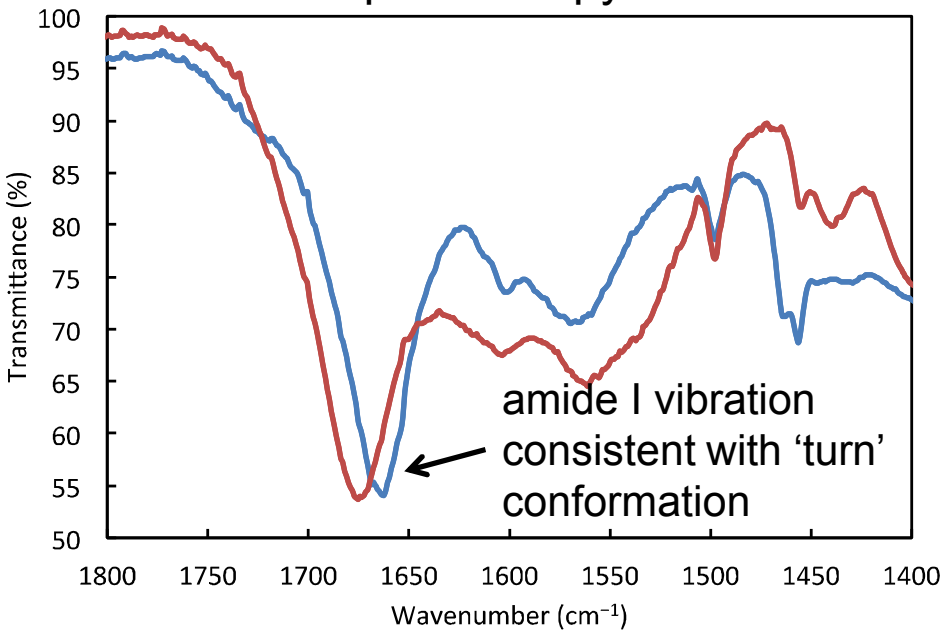




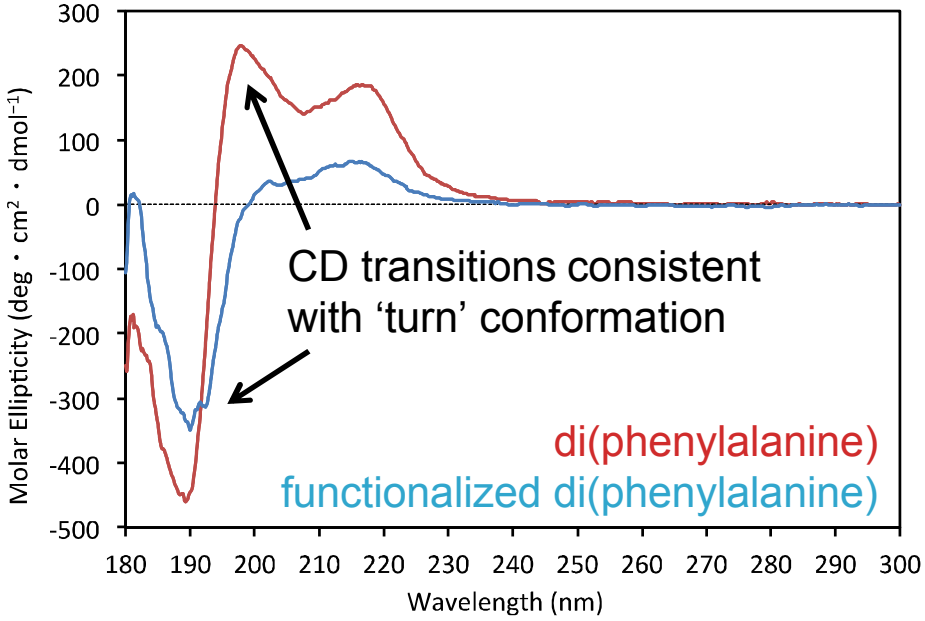
Spectroscopic Characterization

Spectroscopy shows change in peptide conformation after BA-functionalization

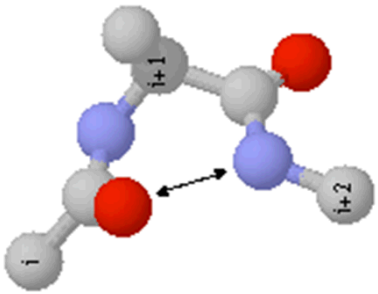
Fourier transform infrared (FTIR) spectroscopy

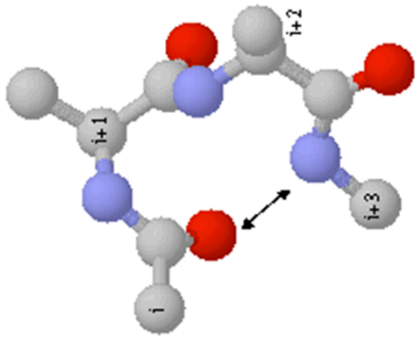


circular dichroism (CD) spectroscopy



γ-turn



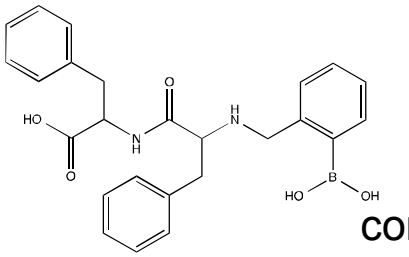


type I β-turn

Berndt, K.D. "Turns." http://www.cryst.bbk.ac.uk/PPS2/course/section8/ss-960531_16.html

Assembly in Organic Solvents

Self-assembly varies dramatically in different chemical environments

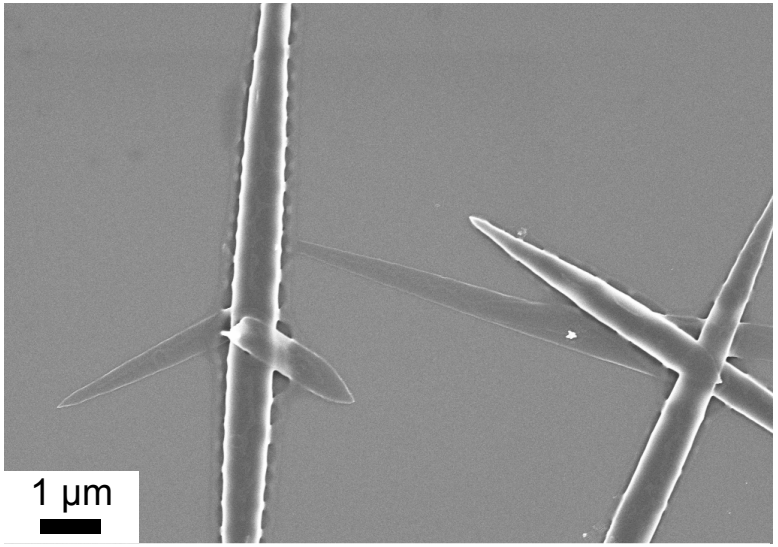


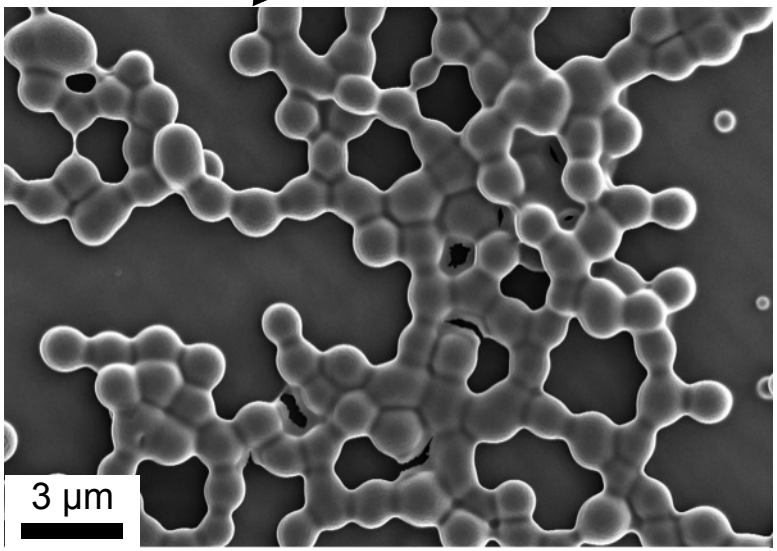
concentrated HFIP solution

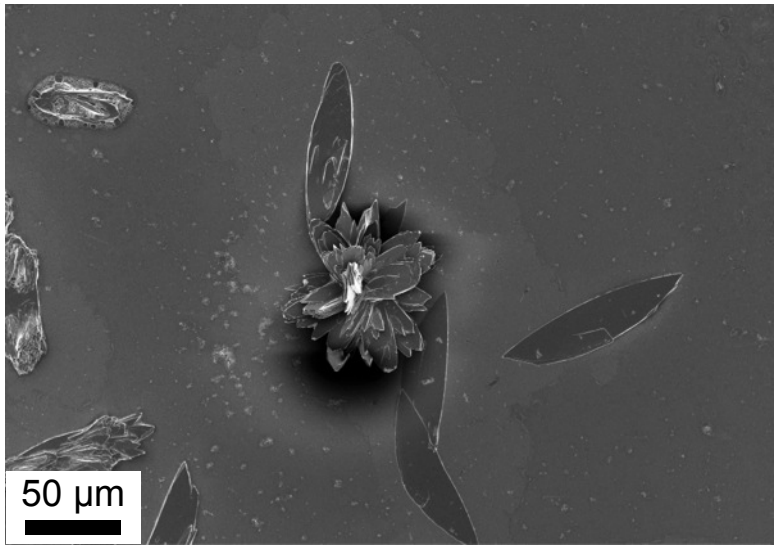
dilution in THF

dilution in $CHCl_3$

dilution in EtOH

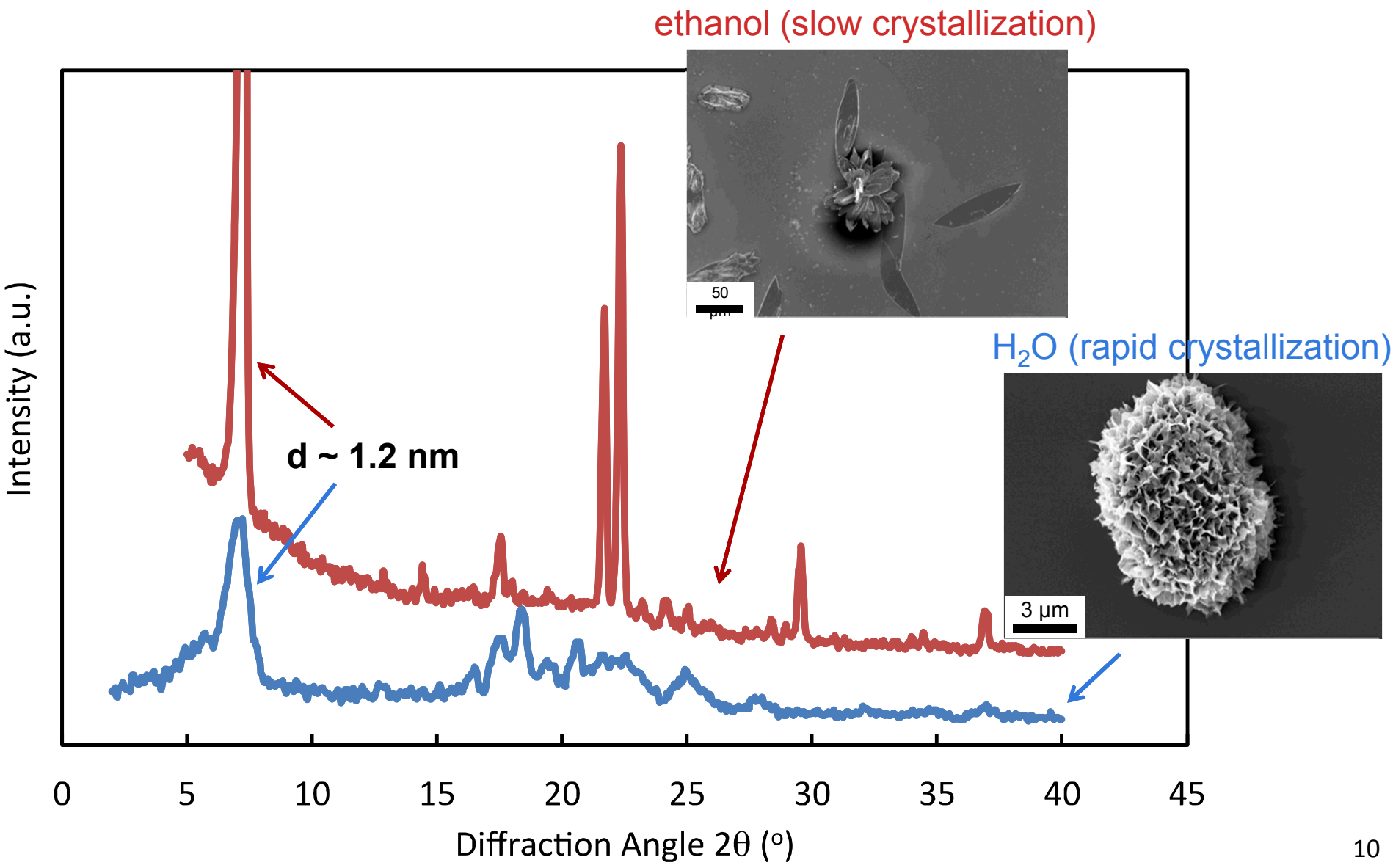






Comparing Assembly in H_2O to EtOH

XRD suggests a similar crystalline structure between H_2O and EtOH



A Closer Look at Crystals from Ethanol

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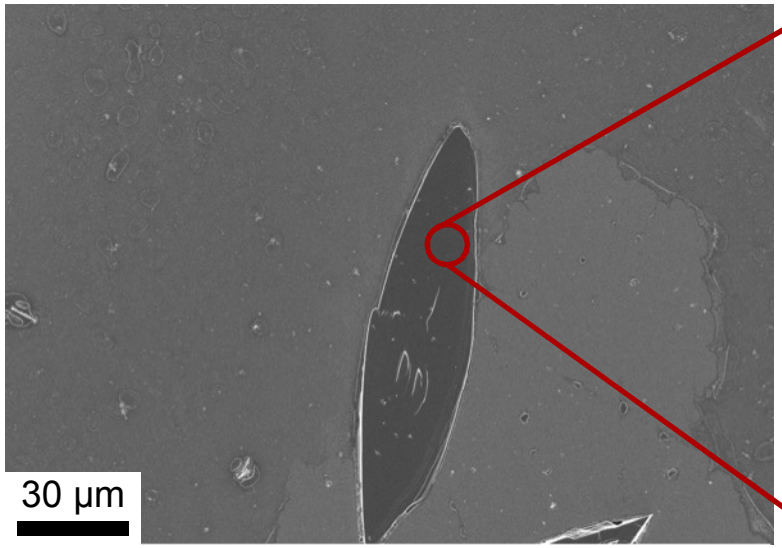
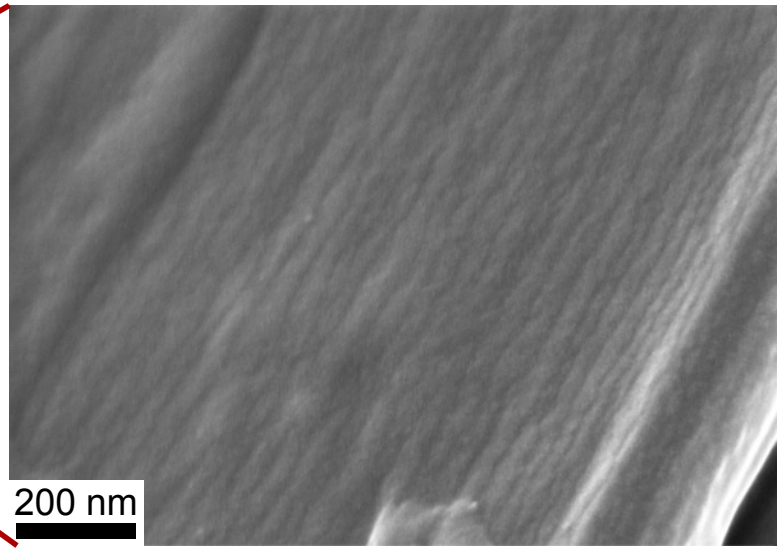
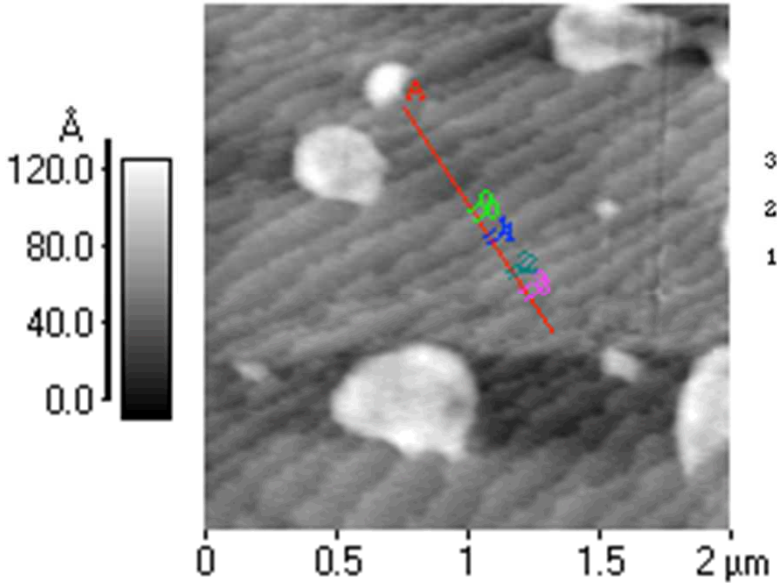
Our functionalized peptide crystallizes into ~ 1-2 nm thick lamellae

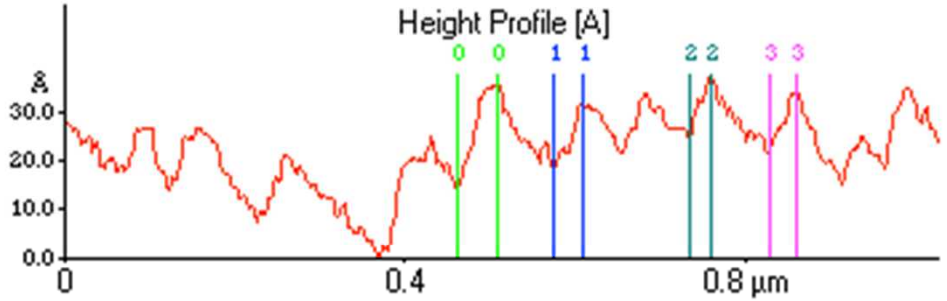
SEM





AFM





Height	Distance
0: 21.4 Å	0: 456 Å
1: 12.8 Å	1: 337 Å
2: 13.9 Å	2: 228 Å
3: 13.0 Å	3: 337 Å

Utilizing the Boronic Acid Functionality

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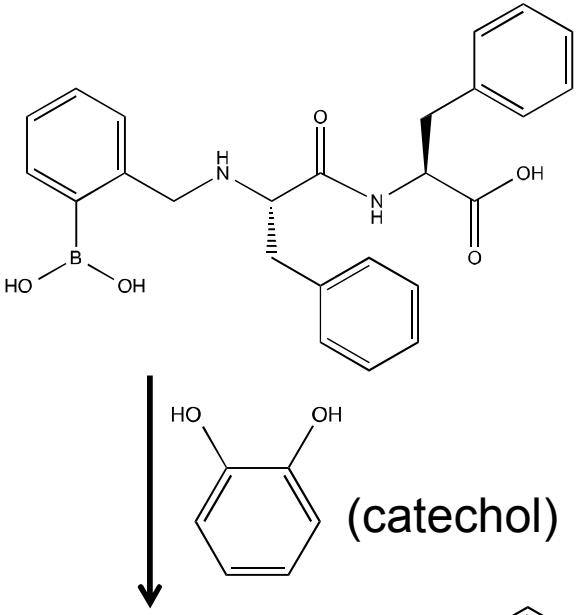
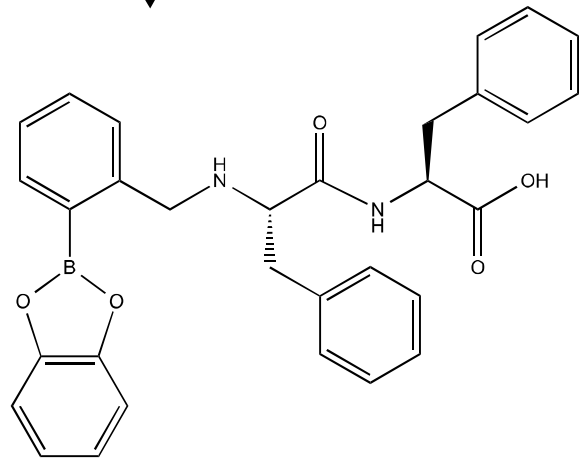
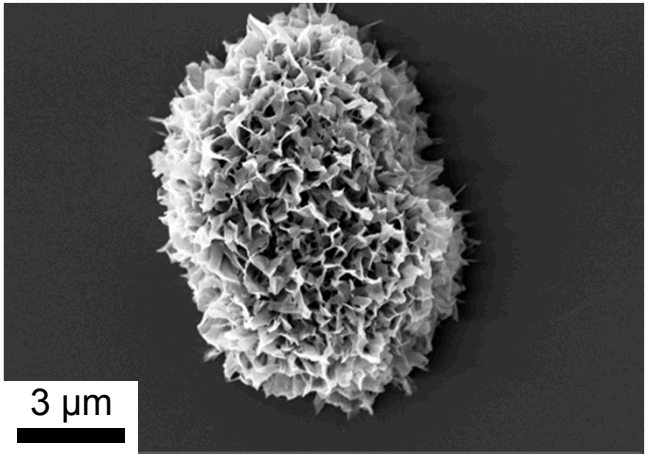
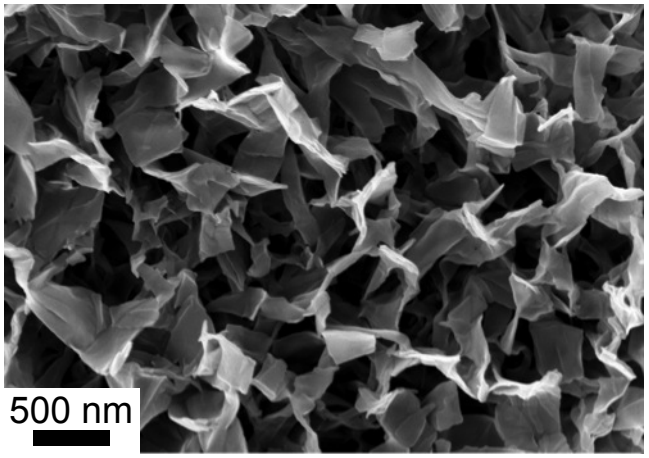
Microscopy suggests self-assembly responds to presence of diols

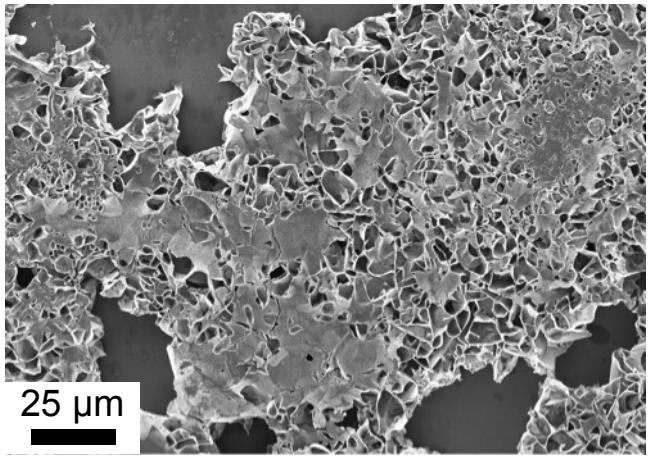


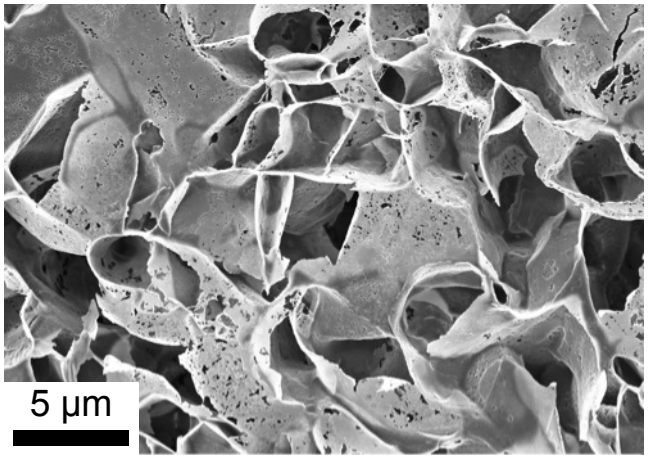
(catechol)











Conclusions

- **Modification of the N-terminus of di(phenylalanine) with an aryl boronic acid functionality fundamentally alters its self-assembly behavior**
  - di(phenylalanine) → nanotubes in H_2O
  - functionalized di(phenylalanine) → lamellar structures in H_2O
- **Functionalized di(phenylalanine) produces a diverse range of morphologies when assembled in varying solvents, including:**
  - flower-like particles
  - flakes
  - needles
- **Preliminary data suggest the assembly behavior of functionalized di(phenylalanine) is responsive to the presence of hydroxylated compounds**

Acknowledgements

- **Lance Miller and Dr. James Hochrein** – mass spectrometry
- **James Greigo and Dr. Mark Rodriguez** – x-ray diffraction
- **This research was supported by the U.S. Department of Energy, Office of Basic Energy Sciences, Division of Materials Sciences and Engineering, Project KC0203010**