COLLEGE OF ENGINEERING

RETICULAR SYNTHESIS OF HOMOCHIRAL METAL-ORGANIC FRAMEWORKS FOR ENHANCED ENANTIOSELECTIVE SEPARATION OF RACEMIC DRUGS

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INTRODUCTION

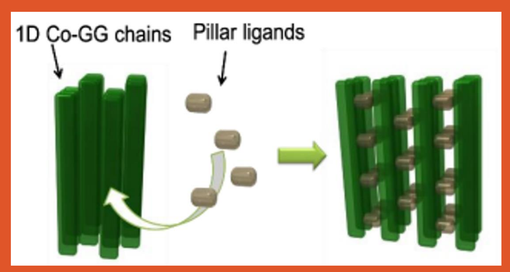
In pharmaceutics, over half of all drugs exhibit chirality or "handedness." Among those, the majority are marketed as a racemic 50:50 mixture of their enantiomers. In some cases, one chiral configuration is pharmacologically less active or toxic to the human body. D-Penicillamine, for example, is an antiarthritic used to treat Wilson's Disease whereas L-Penicillamine inhibits vitamin B_6 in the body.

Metal-organic frameworks (MOFs) are effective chiral adsorbents as their frameworks can be designed with chiral recognition sites and their porosity can be controlled through reticular synthesis, enhancing separation

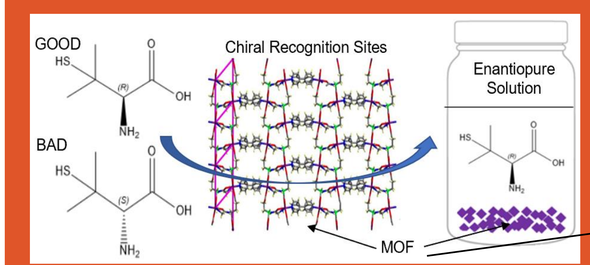
OBJECTIVES

- Synthesize rigid homochiral frameworks
- Enantioselectively separate racemic DL-Penicillamine (Pen)
- Investigate the effects of reticular synthesis on enantioselectivity

METHODS



Racemates diffuse through porous channels and interact with chiral recognition sites



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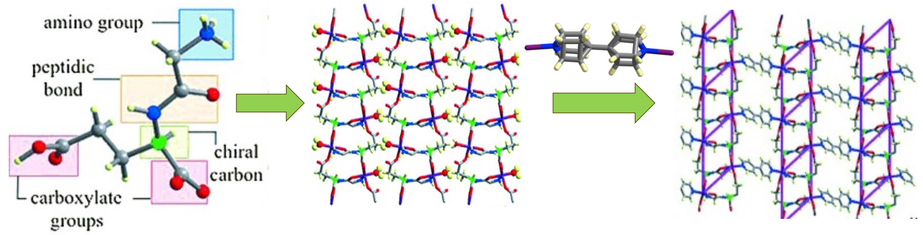
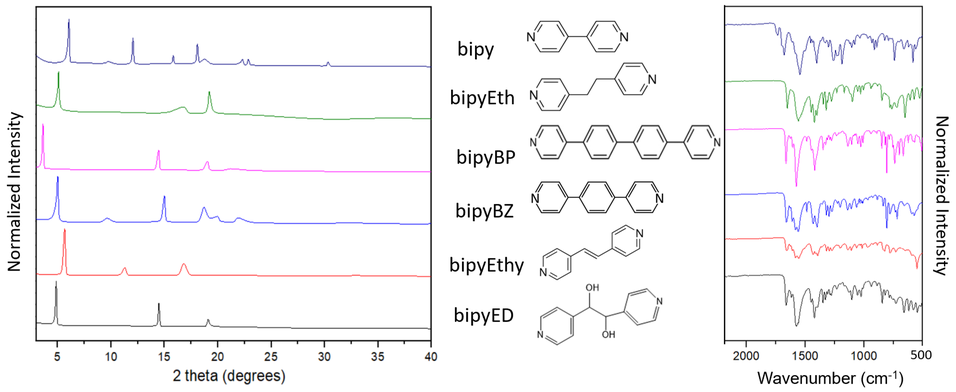
SYNTHESIS OF FRAMEWORKS



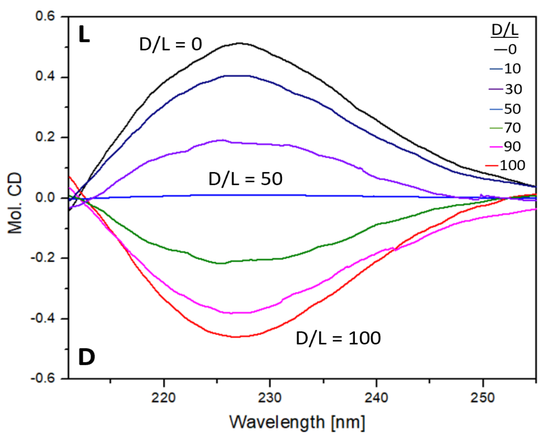
- Cobalt and glycyl-L-glutamic acid (L-GG) form Co-L-GG 1D ladders
- Pillar ligands space ladders apart, affording porosity

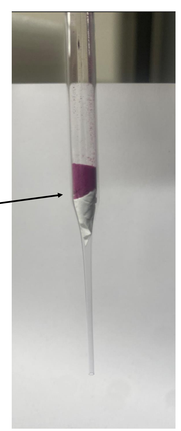


6 novel isoreticular 3D porous Co-L-GG(R) MOFs were synthesized

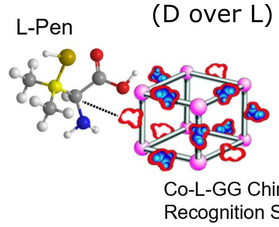
CHIRAL MOFS EXPERIMENTS

- Circular dichroism used for qualitative measures of plane-polarized light rotation in DL-Pen
- Absorbances taken are taken at λ_{max} = 227 nm for mixed DL-Pen enantiomer ratios





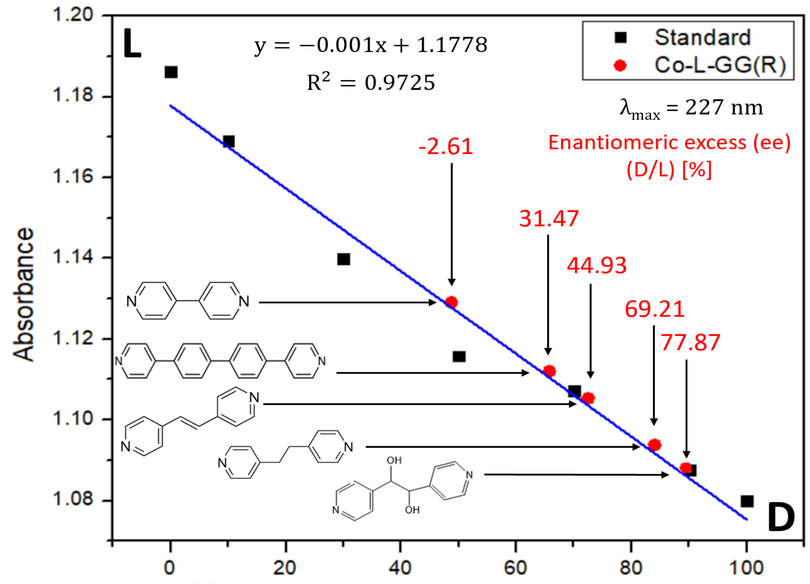
- Resolved solutions after MOF immersion are collected to determine enantiomeric excess (ee) (D over L) from calibration curve



$$\%ee = \frac{|D - L|}{D + L} \times 100$$

SEPARATION RESULTS

Overnight suspension



Using packed MOF bed

Co-L-GG(R)	ee (D/L) [%]
bipyEth	46.34
bipyED	84.22

Enhanced ee for bipyED suggests that the hydroxyl groups are influential for molecular affinity to the substrate

CONCLUSION

- Co-L-GG(R) is selective for adsorbing L-Pen, allowing for D-pen to resolve in solution
- Chiral adsorption is dependent on proximal interactions with the pore surface area; larger linkers decrease the interaction of chiral molecules to chiral recognition sites within the channels
- The influence of the chemical environment and pore size on enantioselectivity can be tuned using reticular synthesis
- Future works will investigate other functional ligands and be conducted on separating larger, aromatic drugs such as RS-Ibuprofen and DL-Dopa

ACKNOWLEDGEMENTS

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REFERENCE

[1] Engineering Homochiral Metal-Organic Frameworks by Spatially Separating 1D Chiral Metal-Peptide Ladders: Tuning the Pore Size for Enantioselective Adsorption