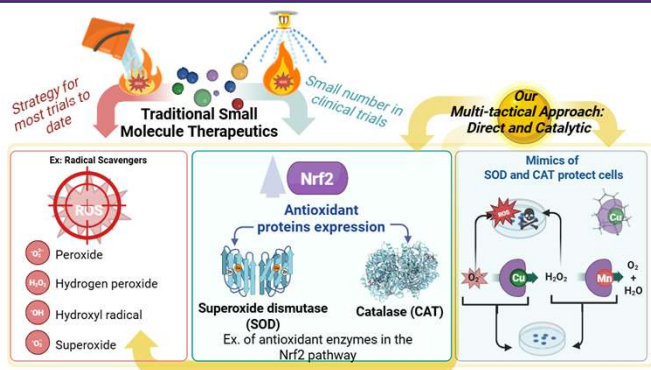


INTRODUCTION



- Chronic exposure to reactive oxygen species (ROS) leads to neurological diseases.
- Ex: Alzheimer's Disease
- Macrocycles have shown promise in targeting ROS.

Problem to be addressed: Increasing BBB permeability of antioxidant molecules.

WORKFLOW

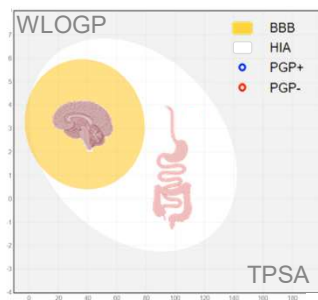
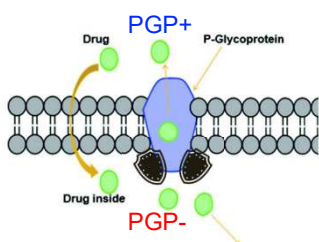


BOILED-EGG MODEL

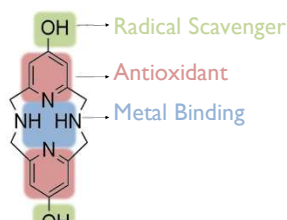
What is this BOILED-egg?

A model that predicts BBB permeability and GI absorption based on lipophilicity and polarity

Y-axis: fat solubility
X-axis: polar surface area

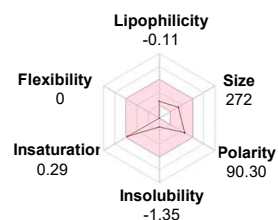


RESULTS

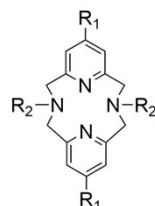
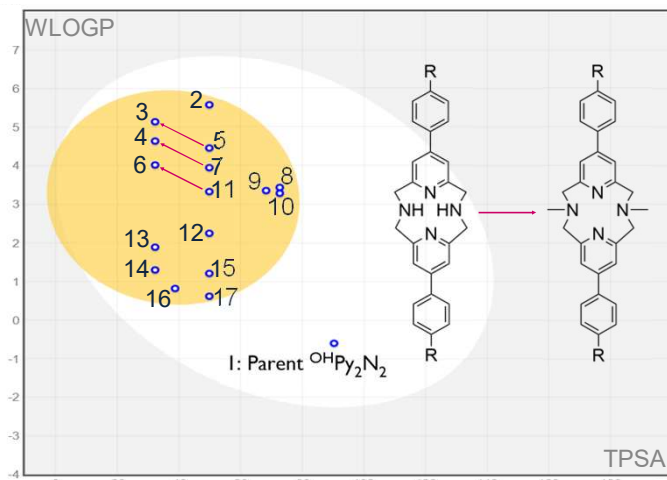


Target Values

Lipophilicity: 5
Size (g/mol): 150
Polarity ($\text{\AA}^2$): 20
Insolubility (mol/L): 0
Flexibility: 0



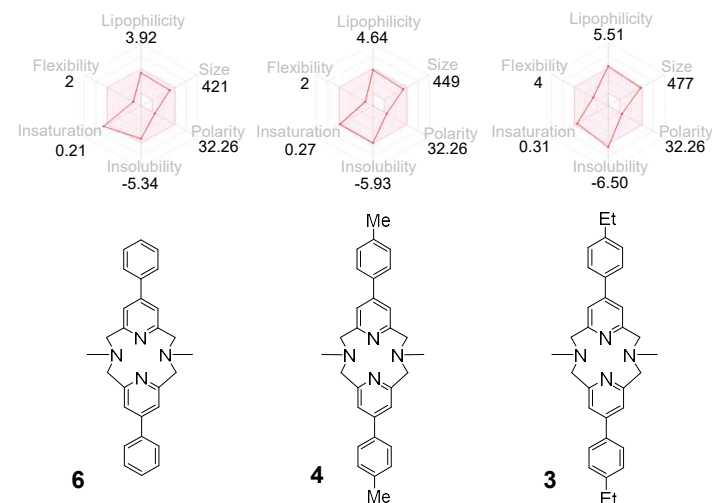
Design Strategy:
 $OH\text{Py}_2\text{N}_2$ properties must be improved to obtain BBB permeability



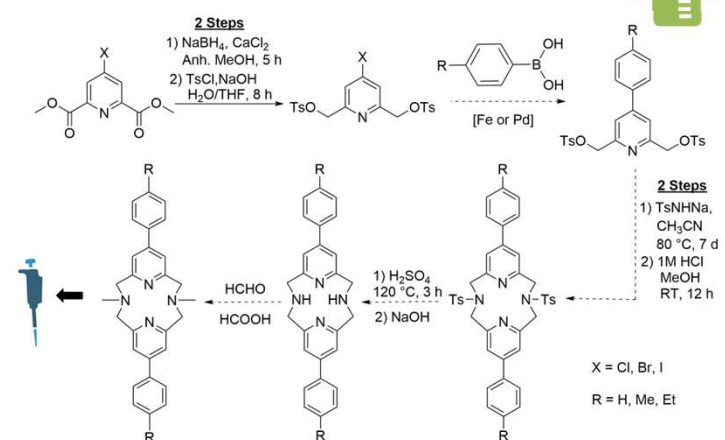
- $R_1=OH, R_2=H$
- $R_1=i\text{-PrPh}, R_2=H$
- $R_1=PhEt, R_2=Me$
- $R_1=PhMe, R_2=Me$
- $R_1=PhEt, R_2=H$
- $R_1=Ph, R_2=Me$
- $R_1=PhMe, R_2=H$
- $R_1=PhOH, R_2=Me$

- $R_1=MeO\text{Ph}, R_2=H$
- $R_1=CH_2\text{PhOH}, R_2=Me$
- $R_1=Ph, R_2=H$
- $R_1=i\text{-Pr}, R_2=H$
- $R_1=Me, R_2=Me$
- $R_1=I, R_2=H$
- $R_1=N,N\text{-DMA}, R_2=Me$
- $R_1=Me, R_2=H$

TARGET MOLECULES



FUTURE DIRECTIONS



ACKNOWLEDGMENTS