Bicyclic CLIPS

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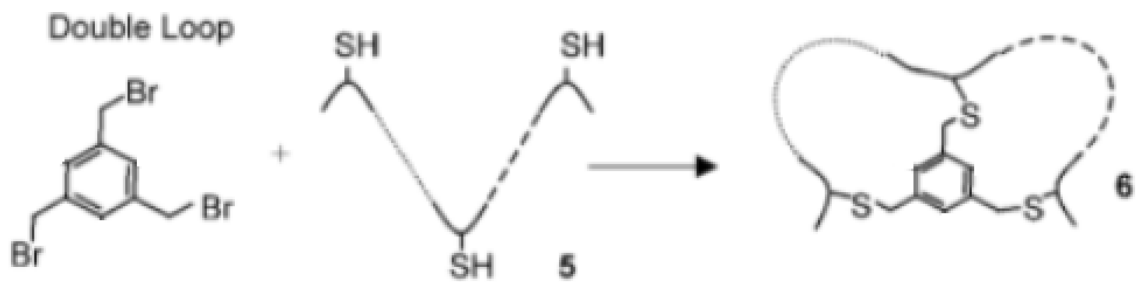


Steps in Project

1. Create library using IBM with benzylic tribromide + peptide chain + thiol. – Completed

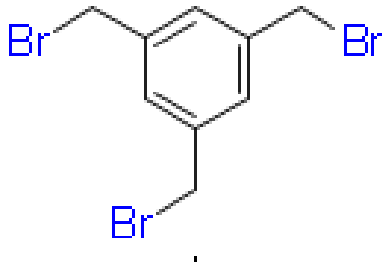
2. Use Monte Carlo Multiple Minimum for conformational sampling.

3. Modify format of MCMM output to match Protein Data Bank and overlay cyclic peptides with protein backbones. Find low RMSD values.

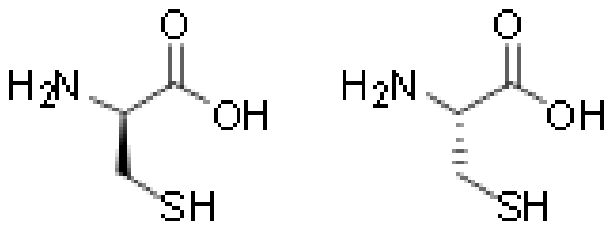
4. Align with Kirtzer hot loops to find possible mimics

Step 1: Building Library – Completed

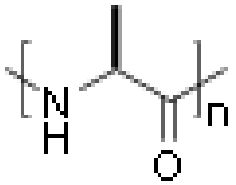
Pool 1: Tribromide benzylic



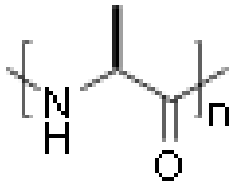
Pool 2: Thiols



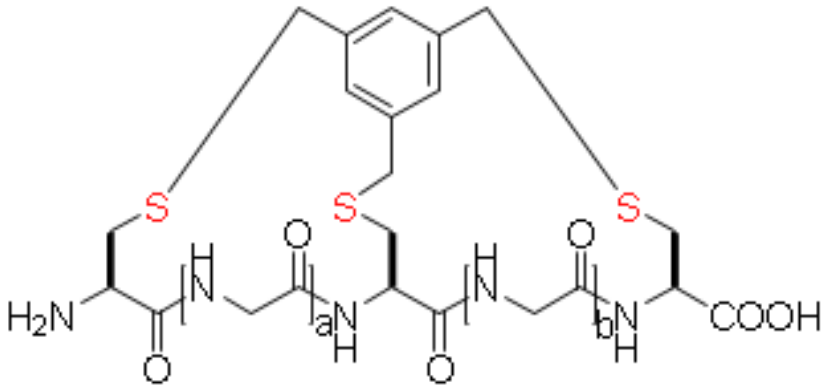
Pool 3: Linear Peptides



N = 1 - 10



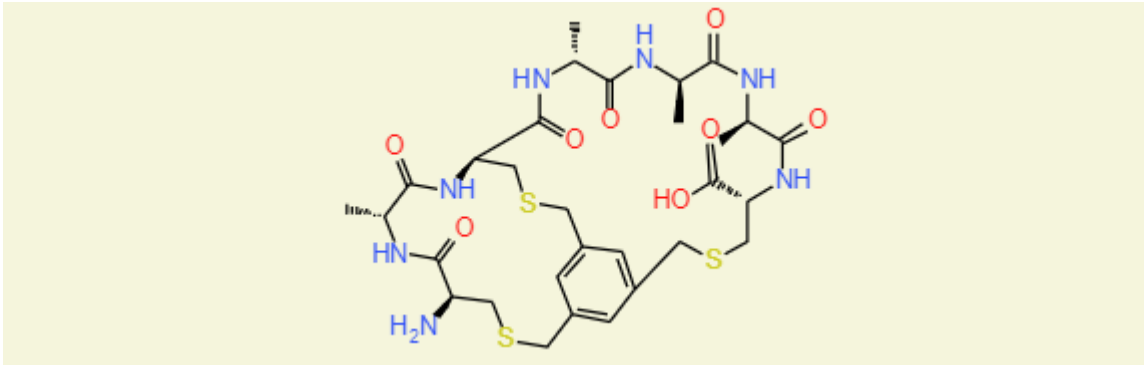
N = 3 - 10

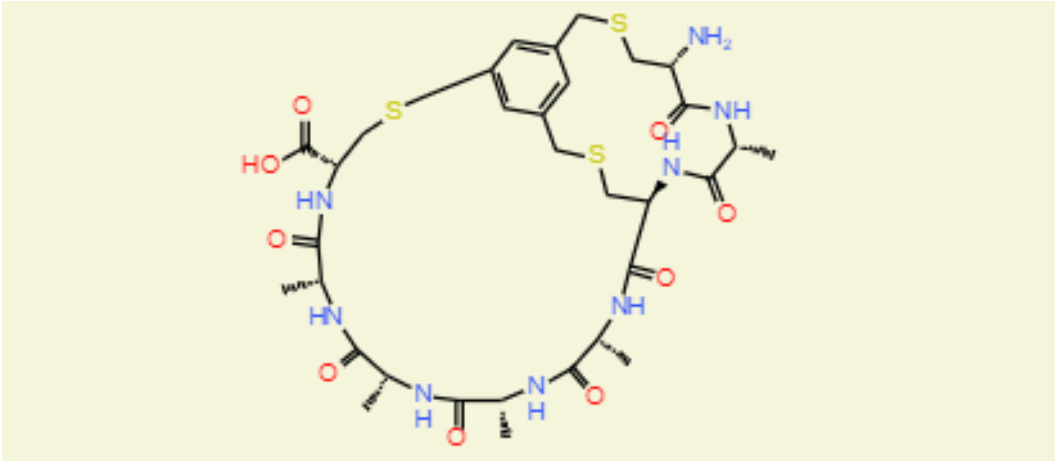


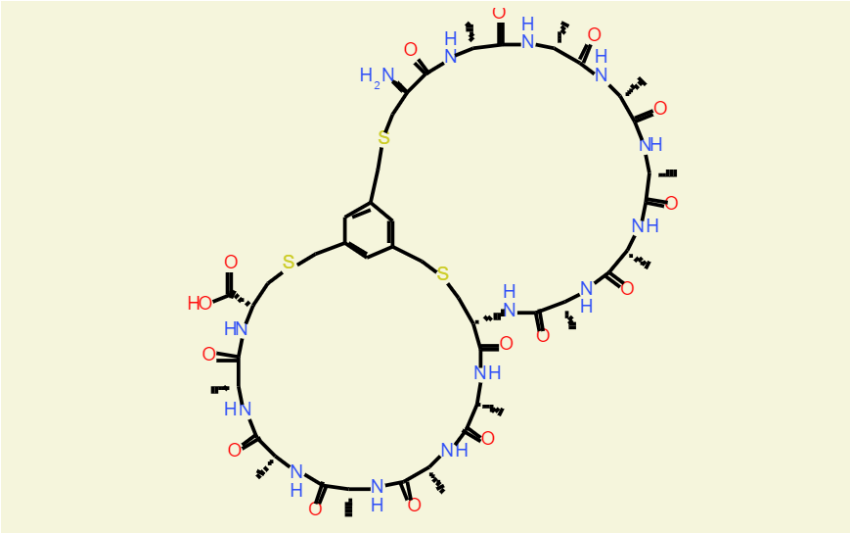
bicyclic peptide

640 bicyclic peptides in library

Examples of Completed Bicyclic Peptides in Library



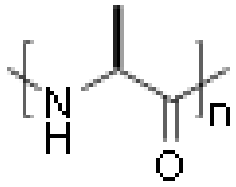


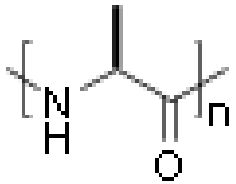


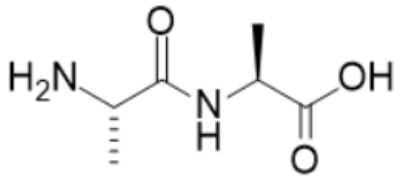
Reaction From SMARTS Used To Build Library

- SMARTS is a language used to modify SMILES format

rxnAddAla = AllChem.ReactionFromSmarts('[O:1]([C:2])>>[N:1]([C:2])[C@H:3]([C:4])[C:5](=[O:6])[O:7]')







Used to add thiol group to peptide chain
rxnThiol = AllChem.ReactionFromSmarts('[O:2]([C:3](=[O:4])).[N:1] >> [N:1][C:3]=[O:4] ‘)

Used to add bromide to sulfur
rxnBromo = AllChem.ReactionFromSmarts('[Br:0].[S:2]([C:3]) >> [S:0]([C:3])')

Goals for next week

- Use MCMM with exported library for conformational sampling.