

Syntheses and Conformational Studies of Cyclo-propane Amino Acids

Dongyeol Lim

Outline

- 1. Background**
- 2. Syntheses of 2,3-Methanoamino Acids**
- 3. Syntheses and Conformational Analyses
of RGD Derivatives**
- 4. Conclusion**

Representative Secondary Structures of Peptides and Proteins

1. Reverse Turns

- a) β I Turn
- b) β I' Turn
- c) β II Turn
- d) β II' Turn
- e) γ Turn

2. β Sheets

- a) Parallel
- b) Antiparallel

3. Helices

- a) α Helices
- b) 310 Helices
- c) π Helices

Molecular Recognition of Peptides and Proteins

1. Reverse Turns (β or γ Turn)

- a) Ligand-receptor interactions
- b) Antigen-antibody recognition

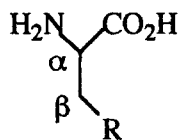
2. β -Sheets

- a) Enzyme inhibitors
- b) Immune recognition

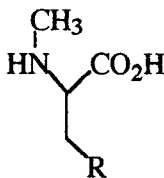
3. Helices

- a) Cytokine-receptor interactions
- b) Protein-DNA interactions

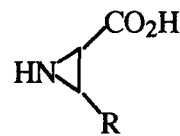
Representative Unnatural Amino Acids



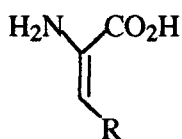
natural amino acid



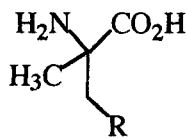
N-methyl amino acid



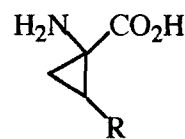
aziridine carboxylic acid



dehydro amino acid



α -methyl amino acid

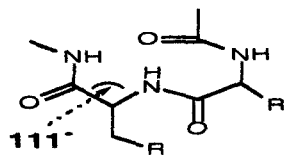


2,3-methano amino acid

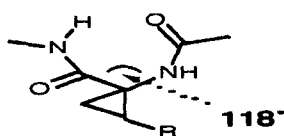
Why Unnatural Amino Acids?

1. Poor bioavailability
2. Rapid proteolytic degradation
3. Flexible conformation

Comparison of N-C α -C Angle

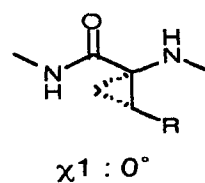
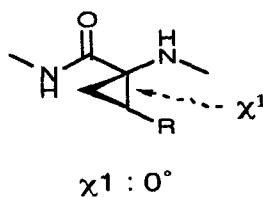


natural amino acids

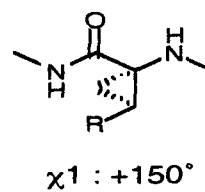
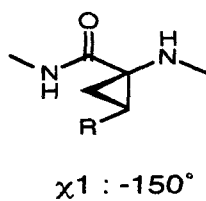
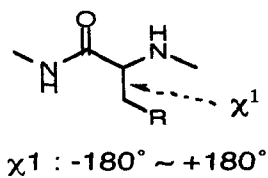


methanologs

Comparison of Side Chain Dihedrals

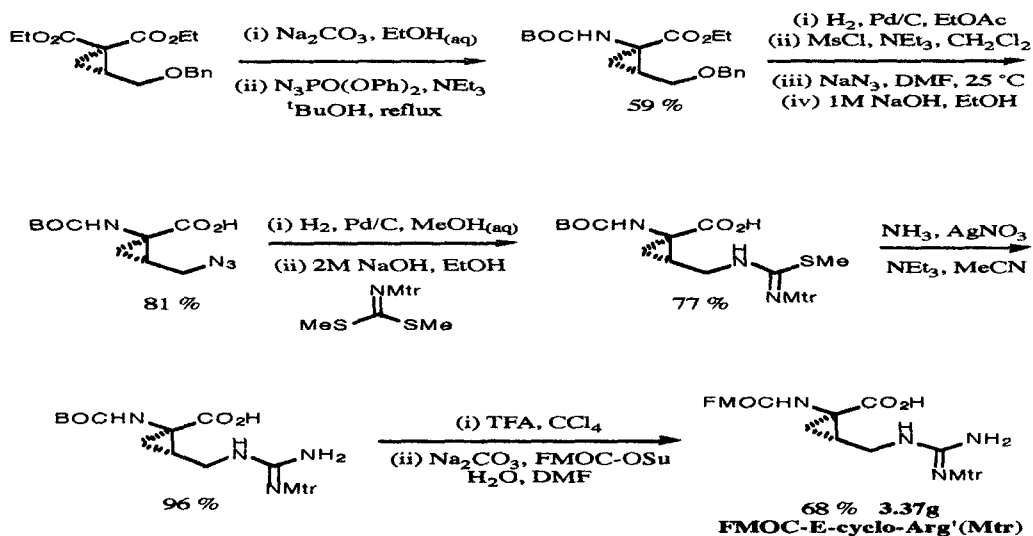


cis-methanologs

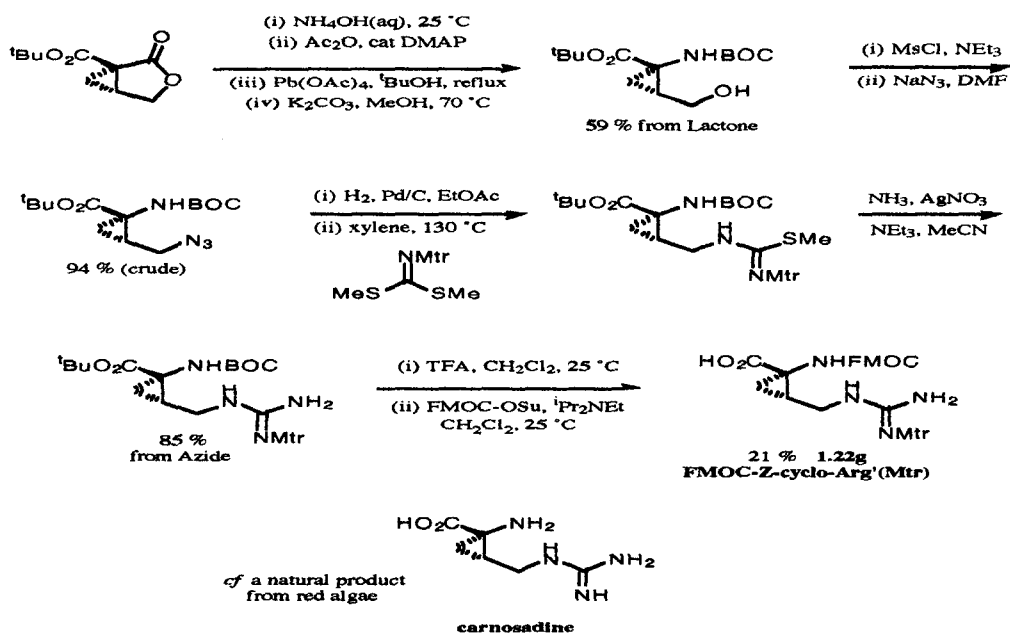


trans-methanologs

Synthesis of FMOC-E-cyclo-Arg'(Mtr)



Synthesis of FMOC-Z-cyclo-Arg'(Mtr)



RGD Peptides: Background

- key motif for the binding to cell surface receptors (integrins)
- signal transduction
- fibrinogen and vitronectin binding
- snake venom proteins (echistatin and kistrin)
- leech proteins (decorsin and ornatins)

Syntheses and Conformational Studies of RGD Derivatives

