

## Nucleic- & Amino acids as Biopolymers

Exam part 1 Monday 8 April 2013

9:00 lecture hall 3

Available time: 3 uur

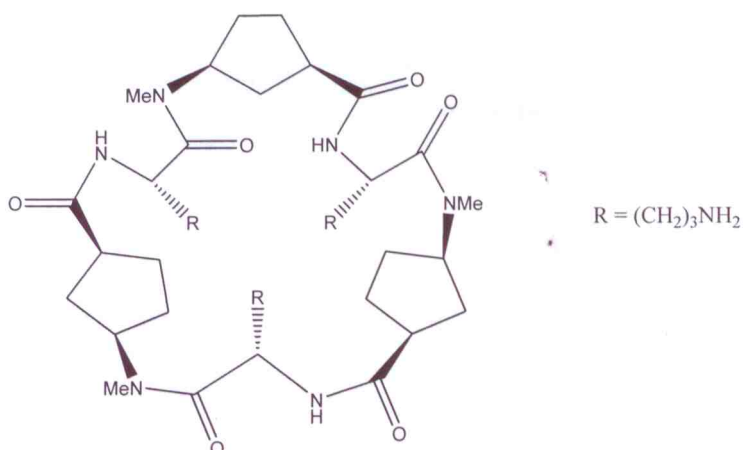
Books, lecture notes or other material may **not** be used.

Please, print your name in capital letters.

### Problem I

Provide a synthetic scheme towards the hereunder cyclic peptide by addressing the following:

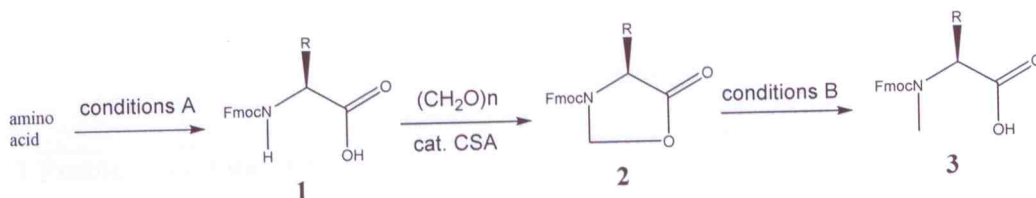
- Are there potentially difficult coupling reaction towards the assembly of the linear sequence.
- Is there a residue in the sequence that upon activation as the entire linear fragment cannot readily epimerize.
- Show the attachment of the first residue to the resin and provide all the details (that is, protective group strategy, coupling reagent/additive, structure of the resin, deprotection conditions and cyclization conditions, and such).



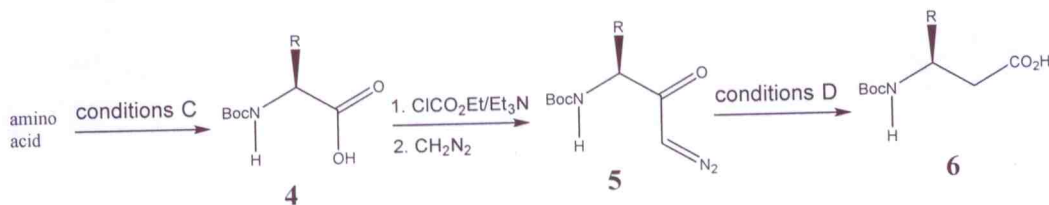
### Problem II

(a) What is a depsipeptide?

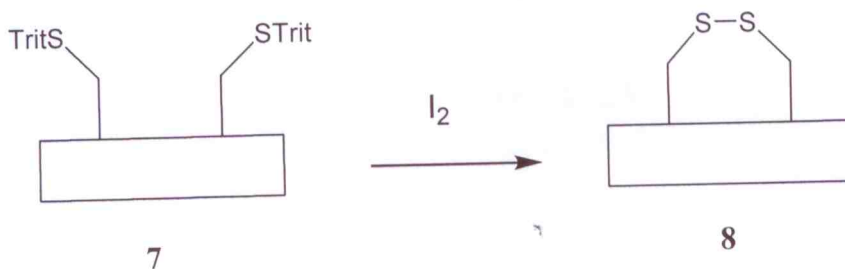
(b) Provide the mechanism of the conversion of amino acid **1** into compound **2** and provide the reaction **conditions A** and **B**. Suggest what kind of side-chains **R** are compatible with the applied conditions.



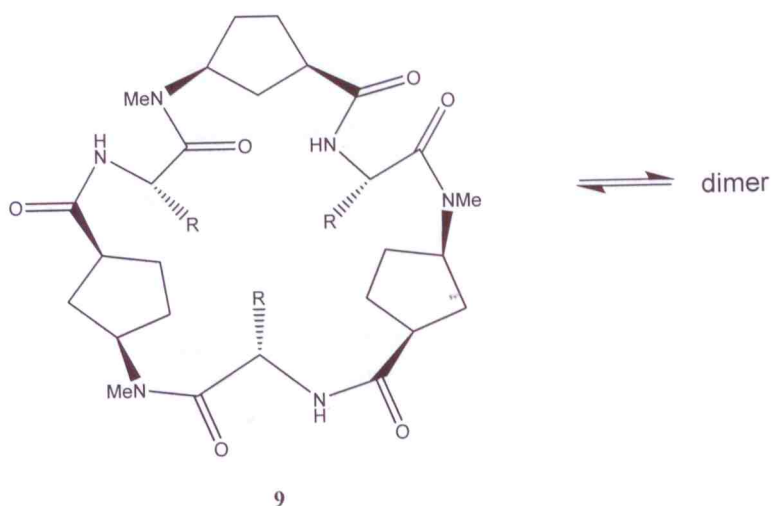
(c) Provide the mechanism of the conversion of the amino acid **4** into the derivative **5** and provide the reaction **conditions C** and **D**. Suggest what kind of side-chains R are compatible with the applied conditions:



(d) Provide the mechanism of the oxidation reaction hereunder:

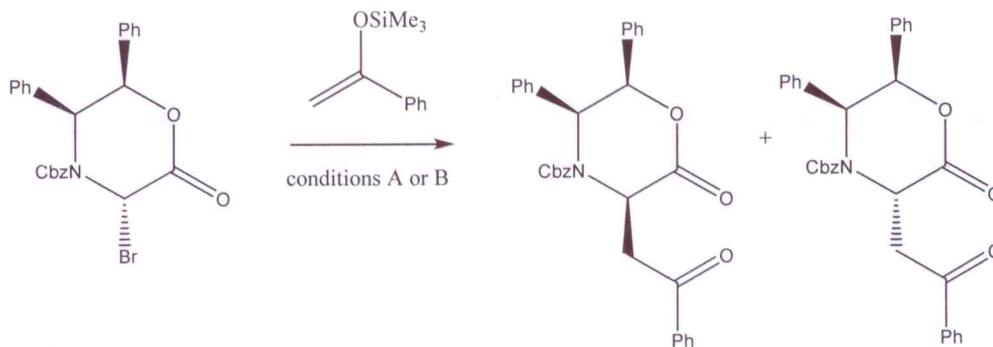


(e) How many hydrogen bonding interactions are formed in the dimeric structure of cyclic peptide **9**?



8 **Problem III (total pnt):**

(a) Explain the following observed product ratio's:



conditions A: 1 : 25  
AgOTf/THF

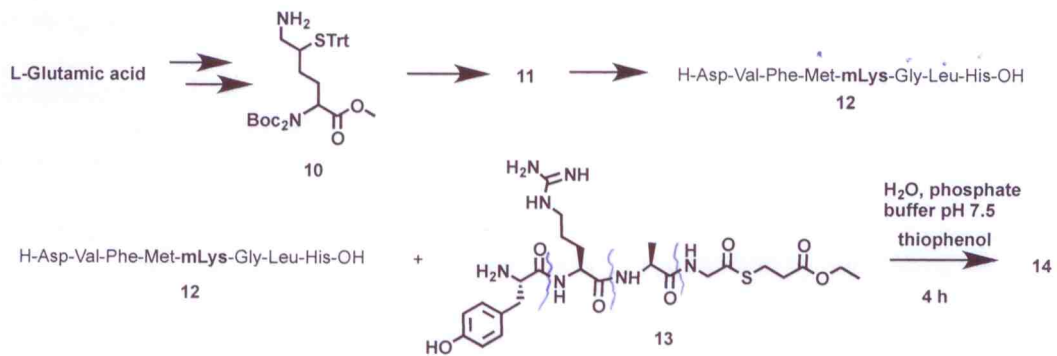
conditions B: 34 : 1  
ZnCl<sub>2</sub>/CH<sub>2</sub>Cl<sub>2</sub>

**Problem IV**

A non-natural amino acid  $\delta$ -mercaptolysin is prepared from L-Glutamic acid in a partially protected form **10** and used subsequently in a number of synthetic transformations.

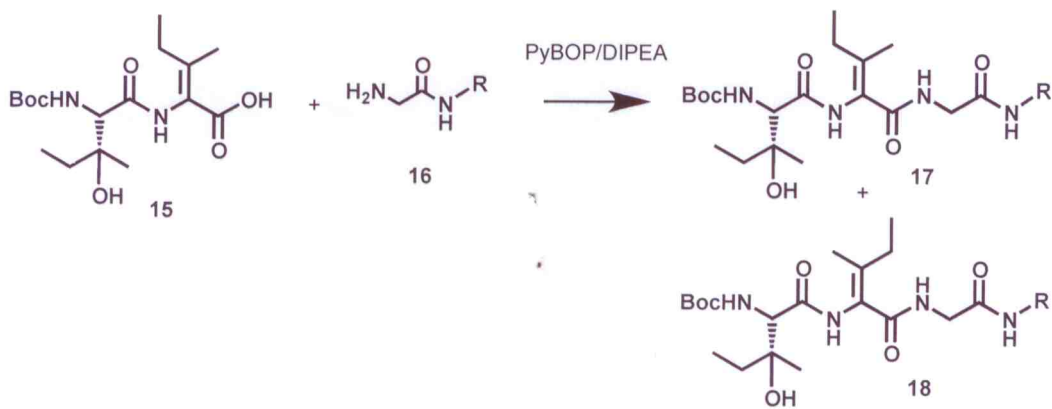
Work the following problems:

1. Draw the structure of L-Glutamic acid.
2. Show the stereochemistry of  $\alpha$ -carbon in **10**.
3. Give the reagents and conditions of all synthetic steps necessary to prepare mercaptolysin building block **11** useful in a solid phase synthesis of peptide **12** (the mercaptolysin residue is abbreviated as m-Lys).
4. Draw structure of all other amino acids building blocks necessary to prepare **12** via a solid phase approach. Give the structure of a suitable linker and all reagents necessary to synthesize **12**.
5. Peptide **12** was mixed with peptide thioester under native chemical ligation conditions. Show the structure of the product **14**.
6. Write the sequence of **13** using the three-letter code.



### Problem V

Explain the following observation.



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