Exp.3 Synthesis of Dipeptide

Introduction:

Peptides are short polymers of amino acid monomers linked by *peptide* bonds (*amide* bonds), structurally like those of proteins, but smaller, typically containing fewer than 50 monomer units. The shortest peptides are **di**peptides, consisting of **two** amino acids joined by a single peptide bond. The *number* of amino-acid residues present is indicated by a prefix: an **octa**peptide, eight; an **oligo**peptide, a few; a **poly**peptide, many. Peptides can be obtained by hydrolysis of proteins or be synthesized.

Liquid-phase peptide synthesis (**LPPS**) is a classical approach, requiring carefully purified after each step to prevent unwanted cross-reactions. It needs more labor, time, skill, but it retains usefulness in large-scale production of peptides for industrial purposes. Solid-phase peptide synthesis (**SPPS**) is more popular in most labs, particularly in longer sequences. It was developed by Bruce Merrifield, using a polymer (small solid beads supports, insoluble but **porous resin**) with reactive sites ('linkers') covalently bound to the developing peptide chain. It is high yield and could be automated synthesizers for repetitious steps.

Chemical peptide synthesis starts at the *C-terminal end* of the peptide and ends at the N-terminal.There are four main steps for LPPS: ***protection, activation, coupling*** and ***de-protection.*** Repeat the cycles to build the desired peptide.

Amino acids have reactive moieties at the N- and C-terminal, side chain functional groups, which can interact with each others during synthesis and negatively influence yield and purity. Specific ***protecting*** groups have been developed to bind and block, or protect, the functional group from side reactions. For ***coupling*** the peptides the *carboxyl* group is usually ***activated***, and then the amino group of others can form the peptide bond by nucleophilic attack.

Once the desired peptide bond is created, the protective group can be **removed** with appropriate selectivity. Because multiple protecting groups are normally used, these groups must be compatible to allow de-protection of distinct protecting groups while not affecting other protecting groups.

For example, Fmoc is cleaved under mild basic conditions, (e.g. piperidine), and the t-Boc is removed by acid (e.g. cold trifluoroacetic acid).

Reagents:

1. Boc-Glycine
2. Ala-OMe
3. HONB
4. EDAC
5. 95% Ethanol
6. 6M HCl
7. Ninhydrin reagent

Procedure:

Add 0.5mL of Boc-Glycine into a test tube, and then 0.5mL of HONB, 0.5mL of EDAC. After vortex mixer~1min , add 0.5mL of Ala-OMe, mixing. The coupling is carried out in a 75℃ water bath for ~20 minutes. If there is white precipitate produced, filter and collect the solution in another tube.

Remove the Boc group by adding 0.5mL of 6M HCl and heating in 75℃ water bath for ~20 minutes. Check by Ninhydrin test.

Results：

1. Record your results.

Discussions：