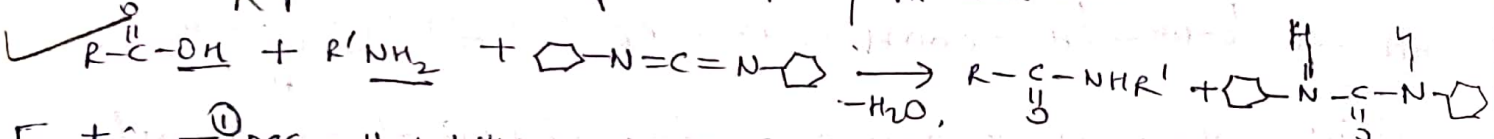
DCC reacts with a free carboxyl end of 1 A.A. or peptide that is to be coupled, forming an activated ester intermediate. The intermediate then reacts in situ with AA or peptide to form a new peptide.

DCC is an effective catalyst for condensn. of carboxylic acids & amines.

③ **DCC method** — Dicyclohexylcarbodiimide is a coupling agent used in the rxn of an amine with an acid to form an amide (peptide bond) at room T in (coupling) presence of inert solvents — THF, CH_2Cl_2. By-pdt is Dicyclohexyl urea which has Low solubility and which is separated as a solid by filtration at the end.

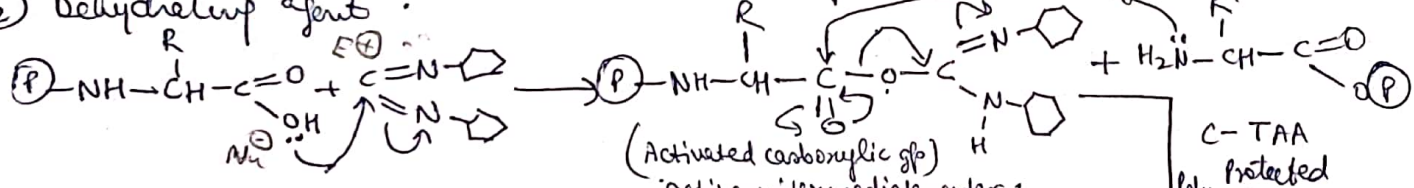
① ADV

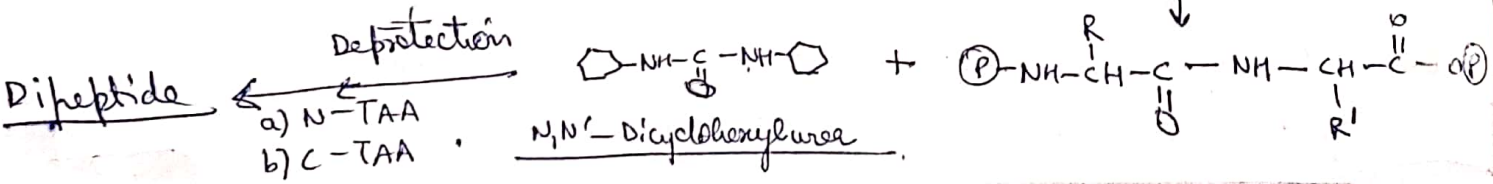
DCC is used as a coupling agent b/w −COOH & $-NH_2$ gps. So the −COOH of $-NH_2$ gps which do not have to participate in peptide bond formation are protected I before coupling rxn with DCC.



Function — ① DCC activated the carboxylic C so that Nu ic attack of the free $-NH_2$ gp. of another AA. (−COOH protected AA) (of NH_2 Protected AA) occurs readily at the carboxylic C.

② Dehydrating agent.





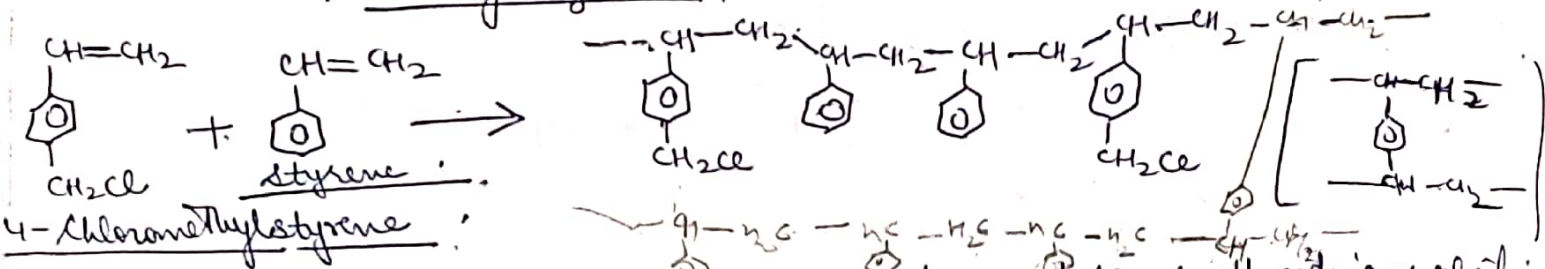
Solid Phase Polypeptide Synthesis

Merrifield Solid Phase PP synthesis

This
① Method of peptide synthesis is carried out in the following steps :—

(1) An Amino Acid is bound chemically to an insoluble synthetic resin

The Merrifield method involves the use of a solid support which consists of beads of a copolymer. The polymer used as resin / solid support is Polystyrene which is synthesised from rn. of styrene with 4-(chloromethyl) styrene. i.e. - some of the rings are linked to $-CH_2Cl$ gp. Polymer is cross linked with about 2% divinylbenzene :



4-Chloromethylstyrene styrene

Cross Linking makes the polymer completely insoluble in all ordinary solvents. Polymeric chains are cross linked at every 50th carbon by p-disubstituted residues derived from divinyl benzene.

The polymer swells in certain organic solvents but is chemically inert during peptide synthesis. The resin is used in the form of fine beads with 20-70 micron in diameter.

I step in automated peptide Merrifield solid phase synthesis is the attachment of N-protected A.A residue to the resin support. In order to effect this the polymer must first be made reactive. This is done by chloromethylating the benzene rings in the chain by a Friedel Crafts rn. using chloromethyl methyl ether & stannic chloride.

$$CH_3OCH_2Cl + \text{Polymer} \xrightarrow{SnCl_4} ClCH_2\text{-Polymer}$$

Solid Phase Synthesis of Peptide

Starts from C-T-AA & proceeds towards N-T-AA
This is opposite to solution phase peptide synthesis in which synthesis is from N-T-AA to C-T-AA.

ADVANTAGES.

1) High Yields are obtained.
2) Solid Support is insoluble, therefore, purification of products is not necessary.
3) Excess of reagent is removed by thorough washing with suitable solvents.
4) Time for peptide synthesis is reduced.
5) Since the process of peptide synthesis involves repetition of a small number of simple & similar peptides, this solid phase peptide synthesis is carried out by an automatically programmed machine. So, each addition of amino acid is done automatically at a predetermined rate.
6) Less impurities / side products are obtained.

Basic steps Involved in Merrifield's Solid Phase Synthesis

1) C-T-AA is bound to polymer support
2) N-T-AA is protected at its free $-NH_2$ N-Terminal end
3) NH_2 protected N-T-AA is coupled with polymer bound C-T-AA in presence of DCC as a coupling agent.
4) One peptide is synthesised
5) Steps are Repeated
6) Deprotect BOC make NH_2 of N-T-AA free.
7) Remove Polymer Support.

SOLID PHASE SYNTHESIS OF Gly·Val·Val

OR MERRIFIELD'S SOLID PHASE SYNTHESIS OF Gly → Val → Val