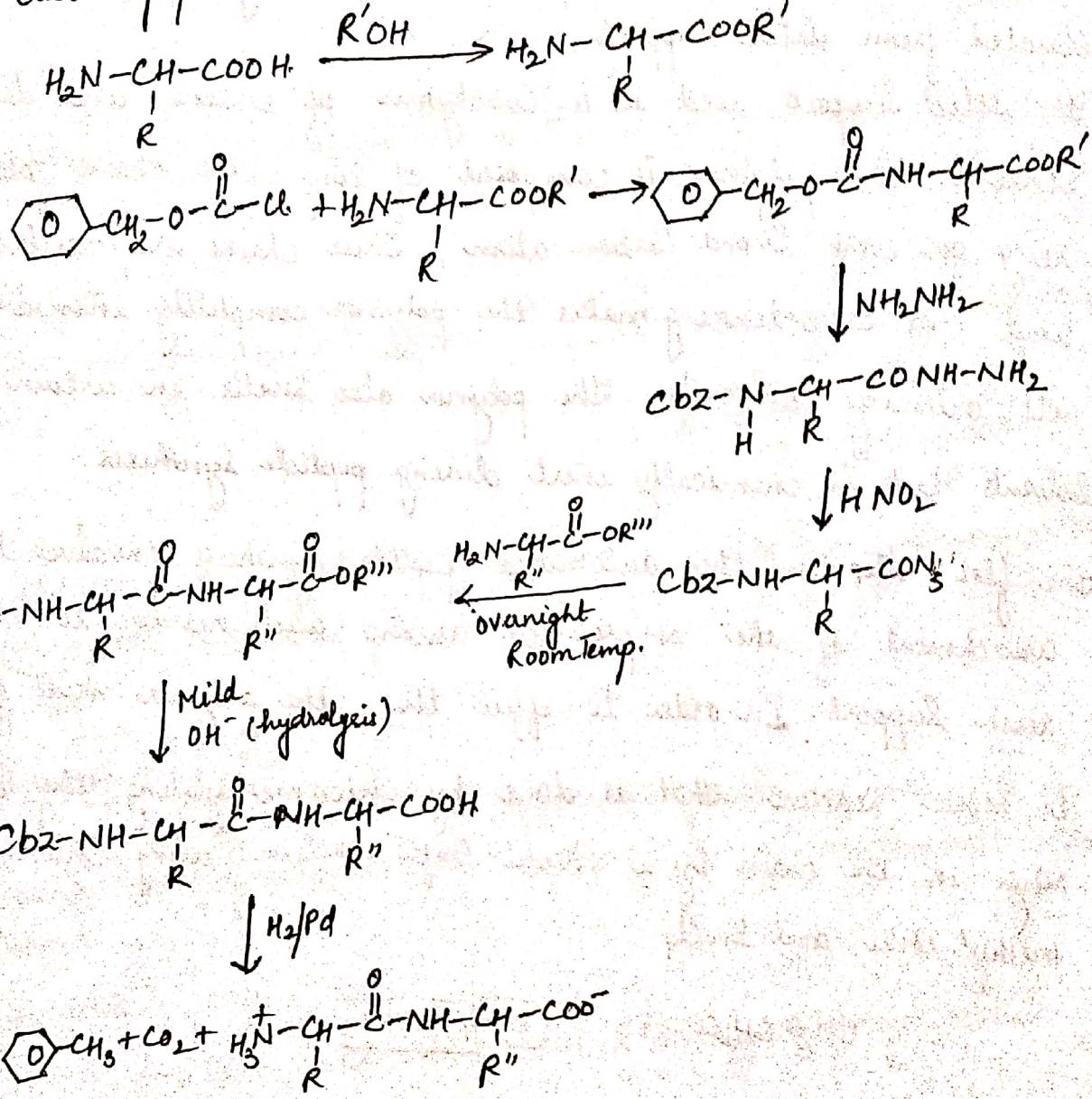
Curtius Azide Method

In this method - N- protected amino acid is converted to its hydrazide which gives the corresponding azide by reaction with HNO_2. N-protected amino acid azide is then reacted with amino acid ester to give the desired peptide.



* This synthesis is accomplished without of racemisation. However some disadvantages are there

1. Number of steps involved are more.
2. The acyl azide may undergo the citrus rearrangement to give the formation of isocyanate.

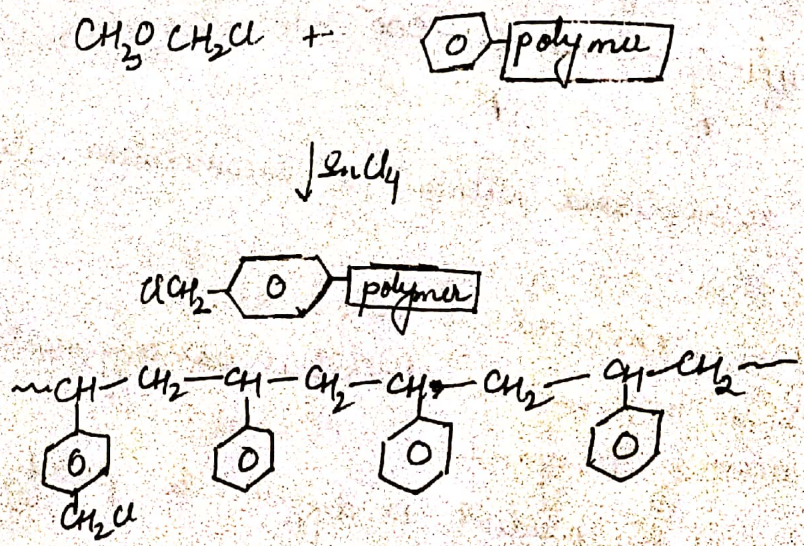
Therefore, the desired the product is difficult to purify.

Solid phase Polypeptide Synthesis (Merrifield Method)

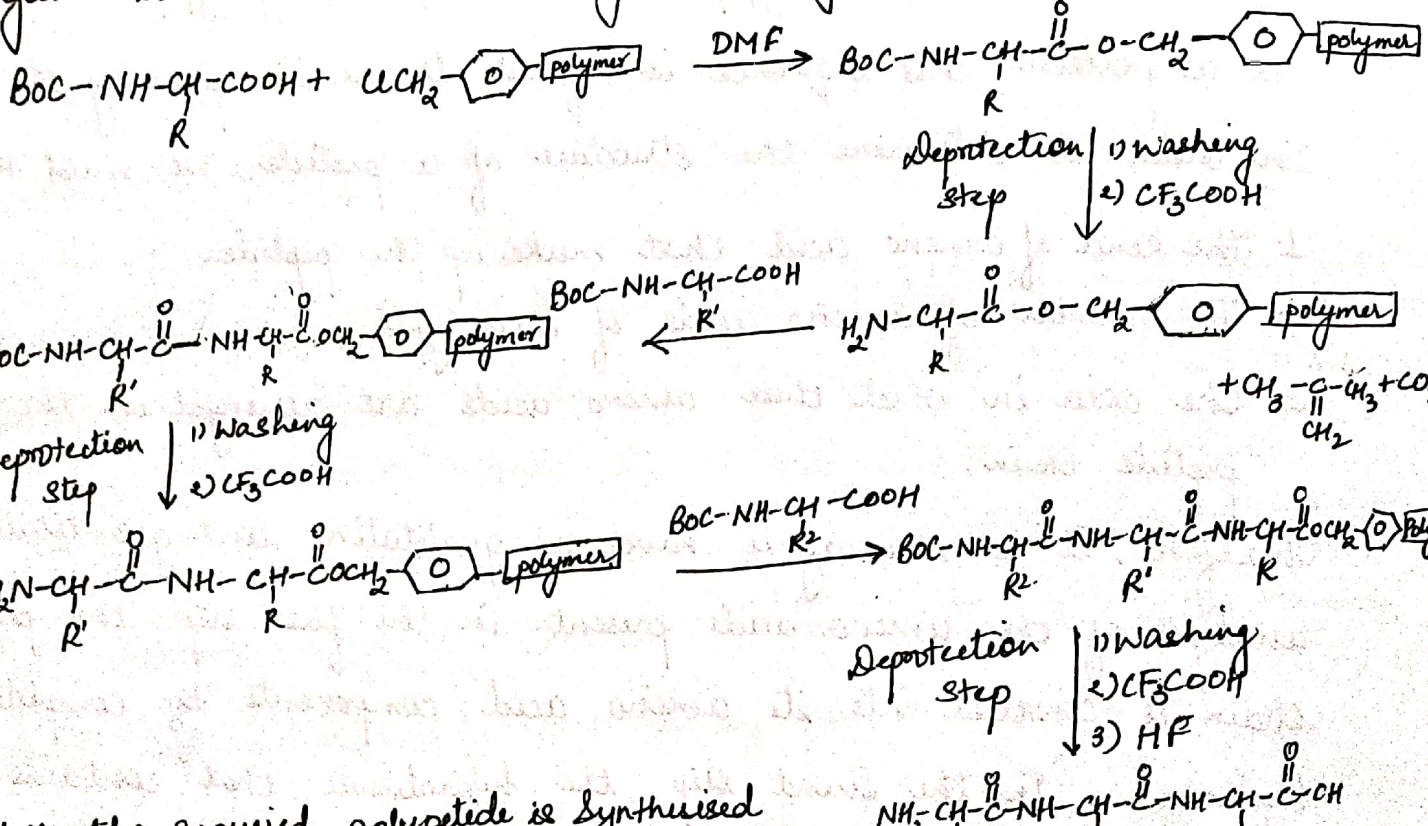
Merrifield has introduced the "Solid phase" method in which an amino-acid or a peptide bound to insoluble Synthetic resin and chain is built up, one amino acid at a time. The method has been automated. When desired peptide has been Synthesized it is liberated from Solid Support.

The Solid Support used is a Copolymer of styrene and divinyl benzene. The polymer is composed of long alkyl chains bearing ring on every Second Carbon atom. These chains are crosslinked and this cross-linking makes the polymer completely insoluble in all ordinary solvents. The polymer also Swells in certain organic Solvents but is chemically inert during peptide Synthesis.

The first step in the automated peptide Synthesis involves the attachment of the N-protected amino acid residue to the resin Support. In order to effect this, the polymer must first be made reactive. That is done by chloromethylating the benzene rings in the chain by a Friedel-Crafts reaction using Chloromethyl methyl ether and $SnCl_4$



The C-terminal amino acid desired peptide is now bound to the polymer by shaking a solution of N-protected amino acid in an organic solvent with chloromethylated polymer.



Once the required polypeptide is synthesised the polypeptide is released from co-polymer by reaction with HF.

Advantages of solid phase method:-

1.) Because of used of insoluble solid support, purification of product is not necessary. Excess of reagents being removed by thorough washing with suitable solvent.

2) High Yields

3) The time has been considerably shortened for synthesising peptides.