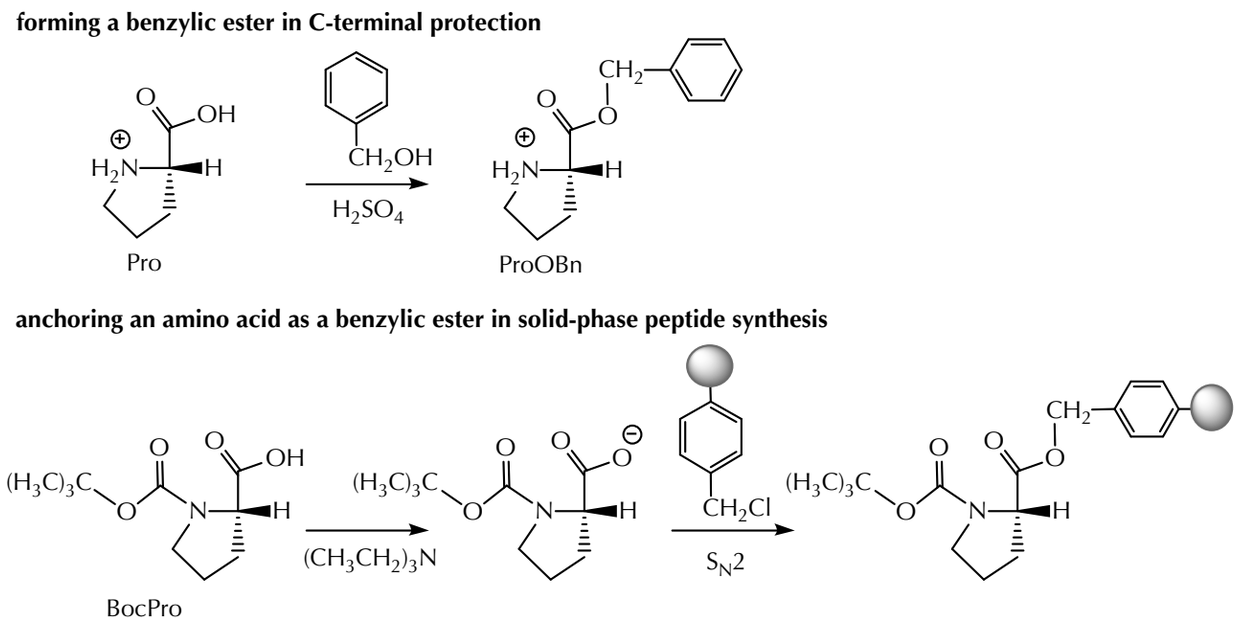
These chemically modified polystyrene beads are commercially available, so no one needs to worry about carrying out these reactions if they are interested in using them for peptide synthesis. Seen from another perspective, the rings with the chloromethyl groups on them look like benzyl chlorides with a huge polymer molecule attached at the *para*-position. The drawing shown in the figure, with a nondescript circular object attached to the ring, is commonly used to represent one of the benzyl groups protruding from the polymer bead.

These benzyl groups are going to be used in place of forming a simple ester for the C-terminal end of a synthetic peptide (Figure 1741).

Figure 1741

Insoluble polystyrene beads provide a solid anchor at the C-terminal end of a synthetic peptide: attaching the first amino acid.



Except for the fact that the chemistry is going to be carried out on the surface of these beads, the chemical steps are all typical organic reactions.

In the solution chemistry synthesis of the pentapeptide in Section 17.4C (Ala-Asn-Leu-Pro-Pro), a benzyl ester of the C-terminal proline was used in the first step. In the solid-phase synthesis, an S_N2 reaction, using the conjugate base of an N-protected proline, binds the first amino acid onto the solid support by forming an ester. The N-protected proline is used so that the amine group does not compete in the substitution reaction.

From a practical perspective, the number of chloromethyl groups is the limiting reagent, and a large excess of the N-protected amino acid can be used. The main objective is a 100% yield for attaching a proline to every one of the chloromethyl groups and leaving none of them unreacted, which will avoid side reactions later. After an appropriate amount of time, any excess proline can be separated from the beads by filtration, and the beads can be washed of any residue. In principle, every chloromethyl group is now a proline ester, and the amine group can be restored by the standard trifluoracetic acid deprotection conditions.

Each polymer bead now has a trillion deprotected proline amines bonded to it. At this point, except for the bead, the proline looks exactly like the one in Figure 1737, before the first peptide bond was formed.