

Peptide Bond Formation

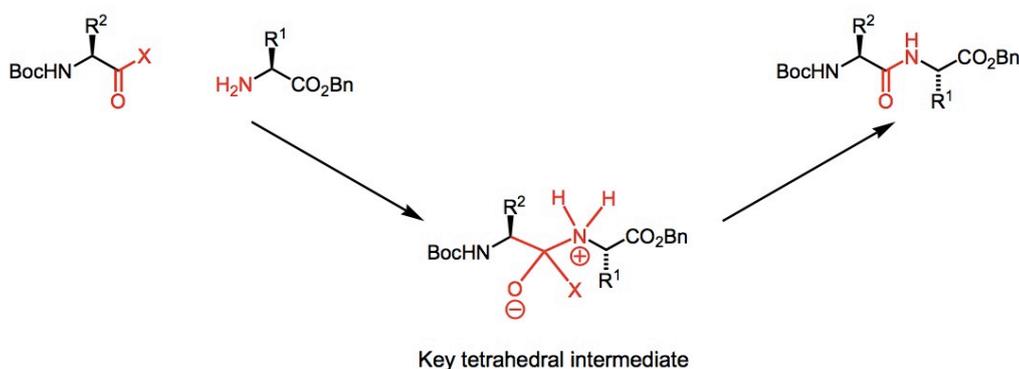
For the peptide bond to form, the carboxylic needs to be converted into a good leaving group because OH is a terrible leaving group. The reaction between the C-terminus and N-terminus. as they are, is not spontaneous because they are not electronically favourable.

Because the conditions to make an acid chloride are too harsh and the Boc group is not orthogonal (it is acid labile), replacing the OH with Cl will not work.

Coupling reagents can be used, such as:

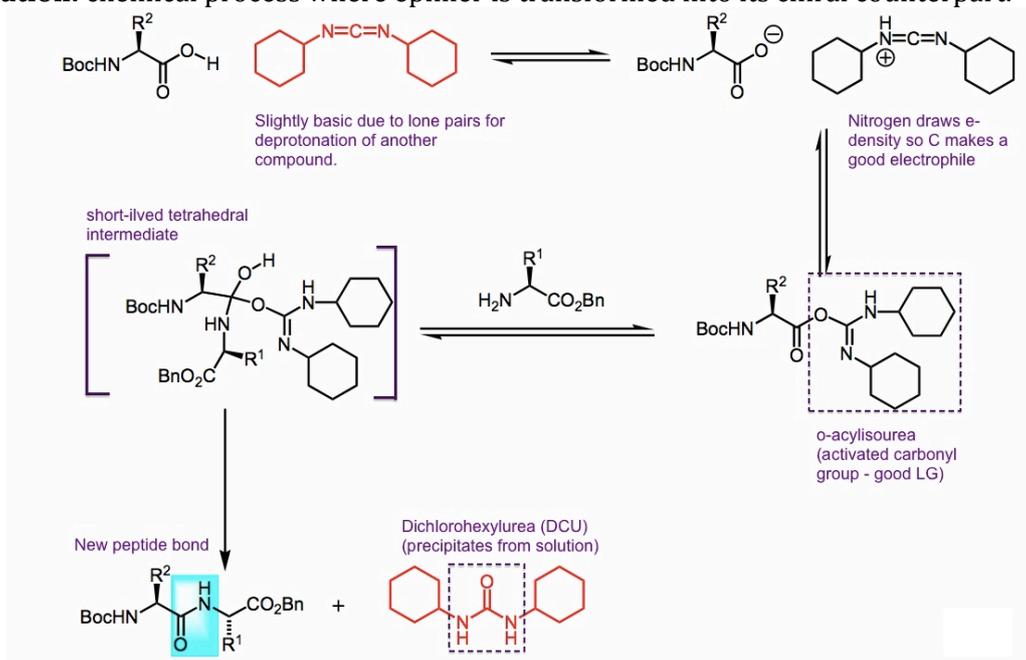
- **Carbodiimides**
 - Dicyclohexylcarbodiimide (DCC)
- **Active esters:**
 - Pentafluorophenyl ester
 - *N*-hydroxysuccinimide ester
- **Phosphonium reagents**
 - PyBOP
- **Uronium reagents**
 - HBTU
 - HATU

Mechanism of peptide formation where X = leaving group (LG):

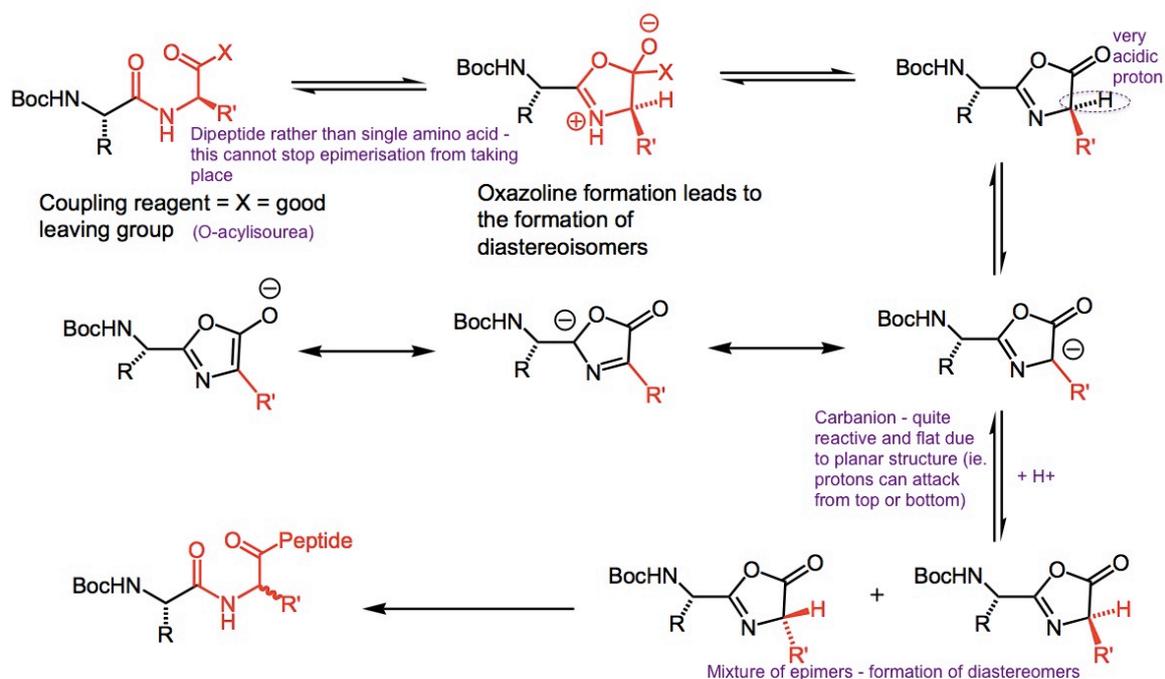


Dicyclohexylcarbodiimide (DCC)

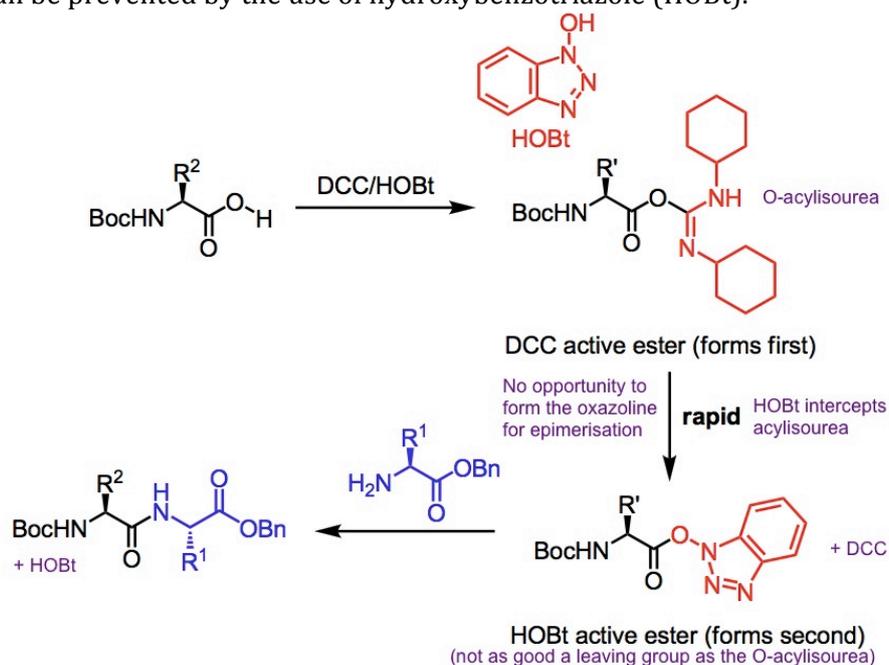
Epimerisation: chemical process where epimer is transformed into its chiral counterpart.



Because amino acids contain stereogenic centres, DCC can cause epimerisation.



Racemisation can be prevented by the use of hydroxybenzotriazole (HOBt).



The addition of HOBt to prevent racemisation is not necessary when using phosphonim and uranium reagents because they already contain a HOBt portion.