



Technical Support Information Bulletin 1197

Click Cyclization on Resin

Click chemistry is the term often applied to the copper catalyzed cycloaddition of azide with an alkyne. Click reactions are convenient for introducing cyclizations into peptides. The reaction proceeds in high yield, no byproducts are formed, and the residues to be cyclized do not require deprotection.

Click Chemistry on Resin¹

1. Swell the peptide-resin in DCM (10 mL/g resin) for 10 minutes.
2. Bubble nitrogen through DMSO (12 mL/g resin) for at least 10 minutes.
3. Dissolve CuBr (1 eq. Based on resin loading) completely in the DMSO.
4. Remove the DCM from the resin and add the CuBr solution to the resin.
5. Add 1 eq of 0.1 M aqueous ascorbic acid solution.
6. Add 10 eq of 2,6-lutidine and 10 eq of DIEA.
7. Purge the reaction flask with nitrogen for 5 minutes.
8. Seal the flask and gently shake at room temperature for 16-18 hours.
9. Filter the resin.
10. Wash the resin 3 times with Isopropanol/DMSO 5:3 v/v, 3 times with DMF, and 3 times with DCM.
11. Dry the resin *in vacuo* before cleavage.

¹ Procedure based on procedures reported in S. Ingale, P.E. Dawson, *Org. Lett.*, **2011**, *13*, 2822-5.