Allenone-Mediated Formations of Peptide Bonds

Significance: The development of an efficient method for amide bond formation is important in peptide drug discovery. The authors have developed an allenone-mediated peptide synthesis.

Comment: This allenone-mediated amidation reaction affords peptides containing a variety of amino acid residues in high yields without any epimerization.

Selected examples:

1. PG-NH-peptide1-CO2H (2 equiv) in DCE, r.t. 10–96 h
   NH2-peptide2-O-t-Bu (1.1 equiv) in DMF, r.t. 20–120 min
   PG-NH-peptide1-CONH-peptide2-O-t-Bu

   94% yield in 2 steps, de > 99%

2. PG-NH-peptide1-CO2H in DCE, r.t. 10–96 h
   NH2-peptide2-O-t-Bu (1.1 equiv) in DMF, r.t. 20–120 min
   PG-NH-peptide1-CONH-peptide2-O-t-Bu

   82% yield in 2 steps, de > 99%

3. PG-NH-peptide1-CO2H in DCE, r.t. 10–96 h
   NH2-peptide2-O-t-Bu (1.1 equiv) in DMF, r.t. 20–120 min
   PG-NH-peptide1-CONH-peptide2-O-t-Bu

   90% yield in 2 steps, de > 99%

4. PG-NH-peptide1-CO2H in DCE, r.t. 10–96 h
   NH2-peptide2-O-t-Bu (1.1 equiv) in DMF, r.t. 20–120 min
   PG-NH-peptide1-CONH-peptide2-O-t-Bu

   86% yield in 2 steps, de > 99%

Key words:
- allenones
- α-carbonyl vinyl esters
- peptide-bond formation

Category: Peptide Chemistry