Zinc-Catalyzed Peptide Synthesis by Using a Nicotinate-Directed Protocol

Significance: Development of new systems for peptide-bond formation is an ongoing challenge to organic chemists. The authors report a new strategy using tert-butylnicotinate amino amides, formed from amino acids and tert-butylicloronicotinate with palladium catalysis, as excellent nucleophiles for the synthesis of dipeptides.

Comment: Various tert-butyl nicotinate amino amides were smoothly generated in high yields and high enantioselectivities. The products and amino acid ester HCl salts were easily converted into the corresponding dipeptides by using zinc catalysis. Furthermore, this protocol can also be applied in the synthesis of tripeptides.

Selected examples:

- Boc-L-Phe-L-Phe-OMe: 95% yield
- Boc-L-Ala-L-Leu-OAll: 99% yield
- Boc-L-Pro-L-Leu-OMe: 95% yield
- Boc-L-Met-L-Trp-OBn: 80% yield

Application:

Zn(OAc)₂ (20 mol%), NaOAc (1.1 equiv) in THF, 70 °C, 24 h

74% yield