Solid-State Synthesis of a β-Turn Mimetic

**Significance:** The β-turn is one of the most interesting structural peptides and has attracted significant attention not only from biologists, but also from organic chemists. In 2000, the authors have demonstrated the construction of a β-turn mimic by solid-supported synthesis.

**Comment:** Solid-supported synthesis is an effective method for forming peptide bonds. The Ugi reaction was used in the cyclization step to afford the β-turn mimic in high yield.

**Preparation of the isobutylcarboxylic acid mixed anhydride of Boc-Phe-OH (1)**

1. Boc-Phe-OH + N-methylmorpholine (1.1 equiv) + isobutylchloroformate (1 equiv) → THF, 0 °C, 15 min
2. piperidine, DMF, 30 min
3. hydrocinnamaldehyde (5 equiv) + 2,6-dimethylphenyl isocyanide (5 equiv) + (R)-(+)−2-bromopropionic acid (5 equiv) → CHCl₃−MeOH (4:1), 2 h × 2
4. TFA in CH₂Cl₂, 1 h
5. DIPEA in CH₂Cl₂, r.t., 18 h

**Synthesis**

1. (5 equiv) + TFA in CH₂Cl₂, 1 h
2. 2 M AcOH in i-PrOH, 50 °C, 18 h

**Total:** 22% yield