Solid-State Synthesis of a β-Turn Mimetic

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

Boc-Phe-OH

N-methylmorpholine (1.1 equiv)

isobutyrylchlorofomate (1 equiv)

THF, 0 °C, 15 min

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Sythesis

piperidine

DMF, 30 min

hydrocinnamaldehyde (5 equiv)

2,6-dimethylphenyl isocyanide (5 equiv)

(R)-(−)-2-bromopropionic acid (5 equiv)

CHCl_3–MeOH (4:1), 2 h × 2

TFA

CH_2Cl_2, 1 h

DIPEA

CH_2Cl_2, r.t., 18 h

1 (5 equiv)

TFA

DMF, 6 h

CH_2Cl_2, 1 h

i-PrOH, 50 °C, 18 h

2 M AcOH

total: 22% yield

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 mimetic 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 mimetic in high yield.