Synthesis of Sterically Hindered Tripeptides Using a Modified Ugi Reaction

Significance: Peptides constructed with \( \alpha,\alpha \)-disubstituted amino acids are found in various natural products and are biologically active molecules. Furthermore, they play an inherent role in chemical biology in understanding the metabolic pathways of enzymes and hormones. In 1998, the authors developed a modified three-component Ugi reaction for the synthesis of tripeptides containing \( \alpha,\alpha \)-diphenylglycine.

Comment: The modified Ugi reaction of \( N \)-benzyl- 

\[ \text{acyclononyl} \] 

amino acids, diphenylmethanimine, and isocyanides derived from amino acids is proceeded smoothly and produced a series of sterically hindered tripeptides in moderate to good yields. This method is useful for the synthesis of crowded peptides that contain \( \alpha,\alpha \)-diphenyl glycine along with very bulky \( \alpha,\alpha \)-disubstituted glycines.