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N-Methylated Peptide Synthesis via Acyl N-Methylimidazolium Cation Generation Accelerated by a Brønsted Acid

Synthesis of Peptides with Acyl N-Methylimidazolium Cations

Significance: Peptide synthesis is a significant process in organic chemistry and medicinal chemistry due to the increasing application of peptide drugs. The authors have developed an efficient Brønsted acid-catalyzed amide-bond formation approach to the preparation of peptides via acyl N-methylimidazolium cations.

Comment: Various dipeptides were synthesized from common amino acids. The yields of the reactions were moderate to good, with broad functional-group tolerance. Moreover, severe racemization was avoided in the reaction.

Results:

94% yield (<0.1% epimer)
97% yield (0.12% epimer)
93% yield (<0.1% epimer)
97% yield (<0.1% epimer)
88% yield (<0.1% epimer)
90% yield (0.82% epimer)
67% yield (<0.1% epimer)
87% yield (<0.1% epimer)
90% yield (<0.1% epimer)