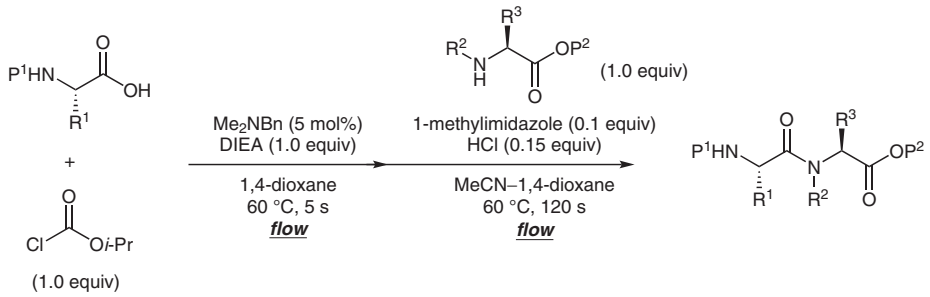
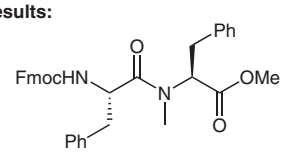
Y. OTAKE, Y. SHIBATA, Y. HAYASHI, S. KAWAUCHI, H. NAKAMURA, S. FUSE* (NAGOYA UNIVERSITY, JAPAN)

N-Methylated Peptide Synthesis via Acyl N-Methylimidazolium Cation Generation Accelerated by a Brønsted Acid
Angew. Chem. Int. Ed. **2020**, DOI: 10.1002/anie.202002106.

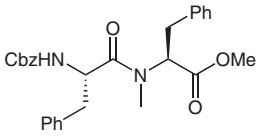
Synthesis of Peptides with Acyl *N*-Methylimidazolium Cations



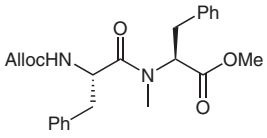
Results:



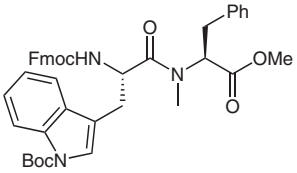
94% yield
(<0.1% epimer)



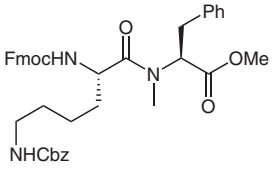
97% yield
(0.12% epimer)



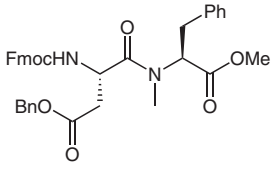
93% yield
(<0.1% epimer)



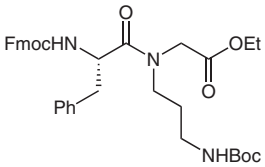
97% yield
(<0.1% epimer)



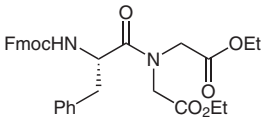
88% yield
(<0.1% epimer)



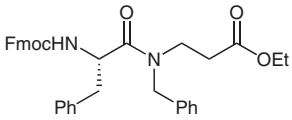
90% yield
(0.82% epimer)



67% yield
(<0.1% epimer)



87% yield
(<0.1% epimer)



90% yield
(<0.1% epimer)

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.

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Category
Peptide Chemistry

Key words
Brønsted acid catalysis
methylimidazole
peptide coupling
amidation

Synfact of the Month