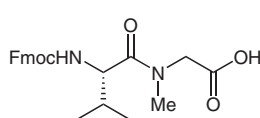
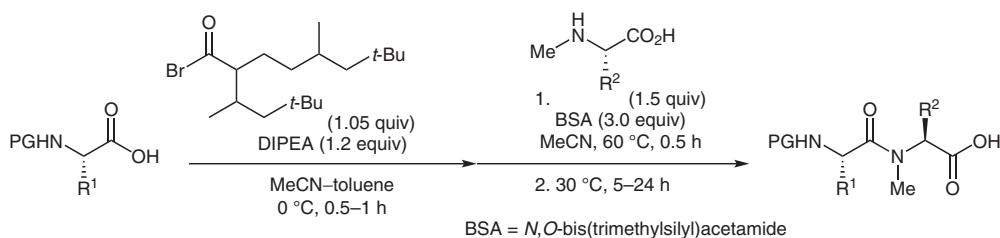
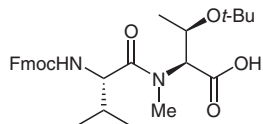


H. KURASAKI* A. NAGAYA, Y. KOBAYASHI, A. MATSUDA, M. MATSUMOTO, K. MORIMOTO, T. TAGURI, H. TAKEUCHI, M. HANDA, D. R. CARY, N. NISHIZAWA*, K. MASUYA* (PEPTIDREAM, INC., KAWASAKI AND NISSAN CHEMICAL CORPORATION, FUNABASHI, JAPAN)
 Isostearyl Mixed Anhydrides for the Preparation of N-Methylated Peptides Using C-Terminally Unprotected N-Methylamino Acids
Org. Lett. **2020**, *22*, 8039–8043, DOI: 10.1021/acs.orglett.0c02984.

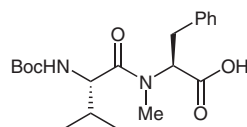
Anhydride-Mediated Peptide Synthesis with C-Terminal Unprotected N-Methylamino Acids



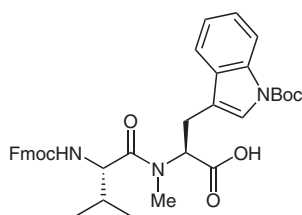
94% yield, > 99.9% ee



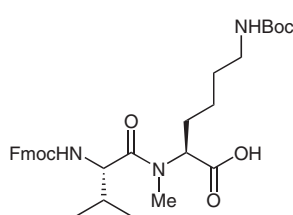
86% yield, dr > 99.5:0.5



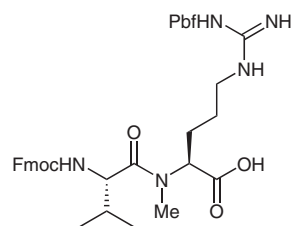
96% yield, dr > 99.5:0.5



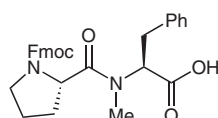
97% yield, dr > 99.5:0.5



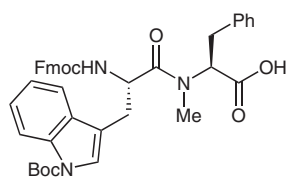
76% yield, dr > 99.5:0.5



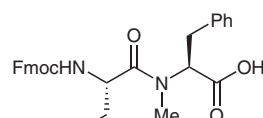
96% yield, dr > 99.5:0.5



77% yield, dr^a > 99.5:0.5



91% yield, dr > 99.5:0.5



93% yield, dr^a = 98.6:1.4

^a Coupling reaction was conducted at 60 °C.

Significance: The synthesis of N-methylated peptides is an important field in organic chemistry and medicinal chemistry. The authors used isostearyl acid bromide to generate mixed anhydrides to react with C-terminal-unprotected N-methylamino acids to prepare N-methylated peptides with the assistance of a silylation reagent.

Comment: Various N-methylated peptides were prepared through the mixed anhydrides intermediate. The reaction proceeds under mild conditions, and the yields of the desired products are good to excellent.

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Peptide Chemistry

Key words

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silylation reagent

N-methylamino acids

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