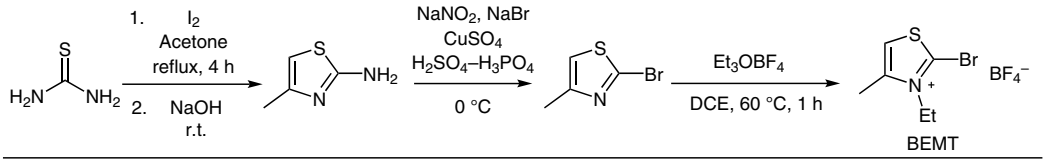
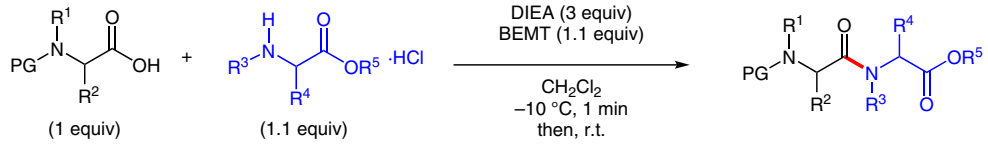
P. LI, J. C. XU* (SHANGHAI INSTITUTE OF ORGANIC CHEMISTRY, P. R. OF CHINA)

A Novel Thiazolium Type Peptide Coupling Reagent for Hindered Amino Acids
Tetrahedron Lett. **1999**, *40*, 8301–8304, DOI: 10.1016/S0040-4039(99)01763-3.

Design and Synthesis of a Thiazolium-Based Coupling Reagent for Peptide Synthesis

Synthesis of coupling reagent 2-bromo-3-ethyl-4-methyl thiazolium tetrafluoroborate (BEMT):





Substrate scope:

Entry	Peptide	Yield (%)
1	Cbz-MeVal–MeVal-OMe	88
2	Cbz-Aib–Aib-OMe	95
3	Fmoc-MeLeu–MeVal-O*t*-Bu	91
4	Fmoc-MeLeu–MeLeu-MeVal-O*t*-Bu	87
5	Fmoc-D-Ala–MeLeu-MeLeu-MeVal-O*t*-Bu	89
6	Fmoc-Nva-Sar–MeLeu-Val-MeLeu-Ala-OBzl	86
7	Fmoc-MeLeu–Nva-Sar-MeLeu-Val-MeLeu-Ala-OBzl	92

Significance: The development of efficient and novel coupling reagents for peptide-bond formation is the backbone of the peptide industry and has attracted extreme attention for the last three decades. In 1999, Xu and Li developed an efficient thiazolium-type peptide coupling agent for the synthesis of peptides containing *N*-allyl amino acid residues.

Comment: 2-Bromo-3-ethyl-4-methylthiazolium tetrafluoroborate (BEMT) is an efficient coupling agent for the synthesis of oligopeptides bearing *N*-alkyl or α-*C*-dialkyl amino acids. This coupling agent can produce a series of hindered peptides in high yields with negligible racemization. The mechanism of the coupling reaction was studied with the help of NMR, HPLC, and IR spectroscopy.

SYNFACTS Contributors: Hisashi Yamamoto, Isai Ramakrishna
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Category
Peptide Chemistry

Key words
bromoethylmethyl-thiazolium tetrafluoroborate
amino acids
coupling reagent