

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

Category

Peptide Chemistry

Key words

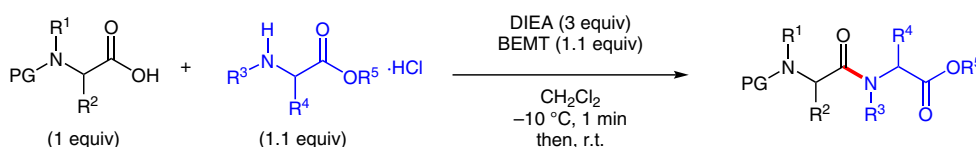
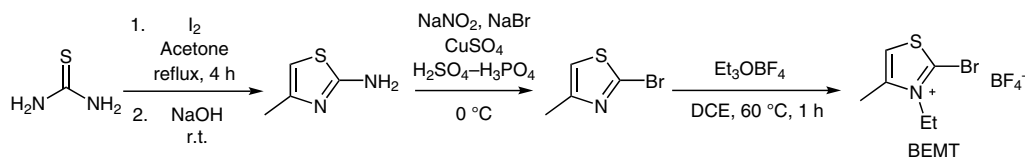
bromoethylmethyl-  
thiazolium  
tetrafluoroborate

amino acids

coupling reagent



## 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 <sup>t</sup> Bu             | 91        |
| 4     | Fmoc-MeLeu-MeLeu-MeVal-O <sup>t</sup> Bu       | 87        |
| 5     | Fmoc-D-Ala-MeLeu-MeLeu-MeVal-O <sup>t</sup> 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  $\alpha$ -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.