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An Expedient Method for the Solid-Phase Synthesis of α-Aminoalkyl Phosphonopeptides


Solid-Phase Synthesis of α-Amino Alkyl or Aryl Phosphonopeptide Derivatives

Significance: Amino phosphonopeptides are highly significant molecules in biological systems as potent antimicrobial agents and as inhibitors of various enzymes. In 2002, Houghten and co-workers developed a solid-phase synthesis of α-aminoalkyl phosphonopeptides by using an aldehyde dimethylphosphite in the presence of the Lewis acid BF₃·Et₂O.

Comment: The developed method is one of the simplest and practically most viable methods for the generation of series of α-aminoalkyl or aryl phosphonopeptide derivatives in high yields with moderate stereoselectivity. The method can be used for the synthesis of libraries of peptide or non-peptide phosphonates.

Selected examples:

- 85% yield, dr = 4:1
- 79% yield, dr = 2:3
- 82% yield, dr = 9:1
- 88% yield, dr = 4:1
- 92% yield, dr n.d.
- 71% yield, dr n.d.
- 88% yield, dr = 5:3
- 65% yield, dr n.d.
- n.d. = not determined

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