Category
Peptide Chemistry

Key words
phosphonopeptides
solid-phase synthesis
aldehyde dimethylphosphite

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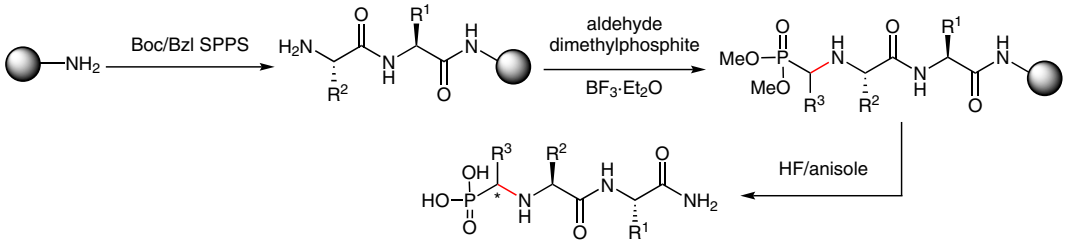
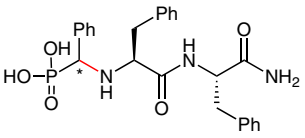
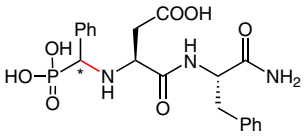
An Expedient Method for the Solid-Phase Synthesis of α-Aminoalkyl Phosphonopeptides
Tetrahedron Lett. **2002**, *43*, 4103–4106, DOI: 10.1016/S0040-4039(02)00695-0.

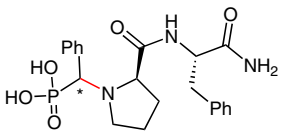
Solid-Phase Synthesis of α-Amino Alkyl or Aryl Phosphonopeptide Derivatives

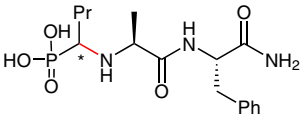


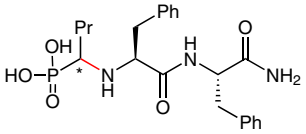
Selected examples:

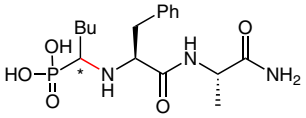

85% yield, dr = 4:1

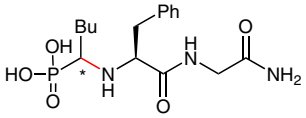

79% yield, dr = 2:3

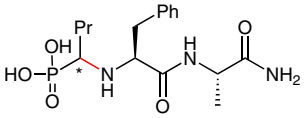

82% yield, dr = 9:1


88% yield, dr = 4:1

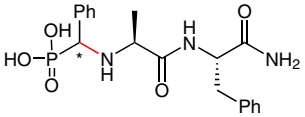

92% yield, dr n.d.


71% yield, dr n.d.


88% yield, dr = 5:3


65% yield, dr n.d.

n.d. = not determined


83% yield, dr = 1:2

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 $BF_3{\cdot}Et_2O$.

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.

SYNFACTS Contributors: Hisashi Yamamoto, Isai Ramakrishna
Synfacts 2022, 18(04), 0454 Published online: 18.03.2022
DOI: 10.1055/s-0041-1737549; **Reg-No.:** H01022SF