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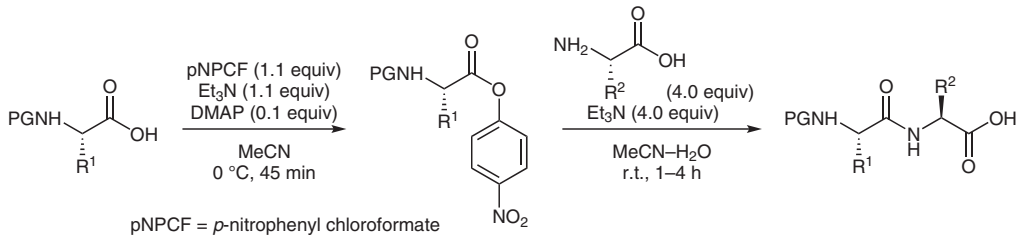
Peptide Coupling of Unprotected Amino Acids through in situ *p*-Nitrophenyl Ester Formation
Tetrahedron Lett. **2002**, *43*, 7717–7719, DOI: 10.1016/S0040-4039(02)01840-3.

Peptide Bond Formation by Using *p*-Nitrophenyl Esters



pNPCF = *p*-nitrophenyl chloroformate

Product	Isolated yield / %	Product	Isolated yield / %
Cbz-Phe-Cys-OH	98[a]	Cbz-Phe-Phe-Val-OH	66[a,b]
Cbz-Phe-His-OH	88[a]	Boc-Gln-Gly-OH	35[c]
Cbz-Phe-Ser-OH	67[a]	Cbz-Gln-Gly-OH	65[c]
Fmoc-Phe-Phe-OH	82[a]	Cbz-Gln-Ser-OH	31[c]
Cbz-Gln-Ala-OH	66[a]	Cbz-Gln-Gly-Gly-OH	30[b,c]
Cbz-Gln-Leu-OH	70[a]	Cbz-Gly-Gln-Gly-OH	15[b,c]
Cbz-Gln-Phe-OH	79[a]	Cbz-Gln-Leu-OH	71[c]
Cbz-Gln-Val-OH	44[a]	Cbz-Gly-Leu-Gly-OH	43[b,c]

[a] Purified by precipitation. [b] Overall yield for two coupling steps. [c] Purified by chromatography.

Significance: Reactive amino acid phenyl esters have been used in peptide synthesis. In 2002, Keillor and co-workers reported a method for peptide bond formation between *p*-nitrophenyl esters and unprotected amino acids in aqueous solution.

Comment: By using *p*-nitrophenyl esters formed in situ, various dipeptides or tripeptides were synthesized without classical peptide-coupling reagents. The yields of the target peptides were moderate to excellent.

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