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Chemoselective Peptide Bond Formation Using Formyl-Substituted Nitrophenylthio Ester *Tetrahedron Lett.* **2003**, *44*, 3187–3190, DOI: 10.1016/s0040-4039(03)00471-4.

Dipeptide Synthesis from S-2-Formyl-4-Nitrophenyl Thioesters and Amino Acid Salts

product	isolated yield (%)	product	isolated yield (%)
Fmoc-Val-Val-O <i>t</i> -Bu	100	Fmoc-Val-Gly-O <i>t</i> -Bu	91
Fmoc-D-Val-Val-O <i>t</i> -Bu	91	Fmoc-Val-Thr(O <i>t</i> -Bu)-O <i>t</i> -Bu	95
Fmoc-Val-Lys(Cbz)-Ot-Bu	97	Fmoc-Val-Ser(OH)-OMe	82
Fmoc-Val-Pro-Ot-Bu	100	Fmoc-Val-Tyr(OH)-O <i>t</i> -Bu	98
ACHN NH 20% piperidine–I		r.t., 2.5 h	Achn NH Ot-E

Proposed mechanism:

Significance: Amide bond formation is very significant in peptide chemistry, and many approaches have been developed to form the peptide bonds. The authors used formyl-substituted *S*-4-nitrophenyl thioesters to synthesize dipeptides. The reaction could be conducted in the presence of water.

Comment: A broad variety of dipeptides can be synthesized from S-2-formyl-4-nitrophenyl thioesters and amino acid salts. *N*-Methylmaleimide is used to trap the resulting thiophenol to improve the final yield. The yields of the reactions are good to excellent.

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Key words dipeptides

formyl nitrophenyl thio esters methylmaleimide 1,4-addition chemoselectivity

