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Solid-Phase Syntheses of N^{ω}-Propylarginine-Containing Dipeptides, Dipeptide Esters, and Dipeptide Amides
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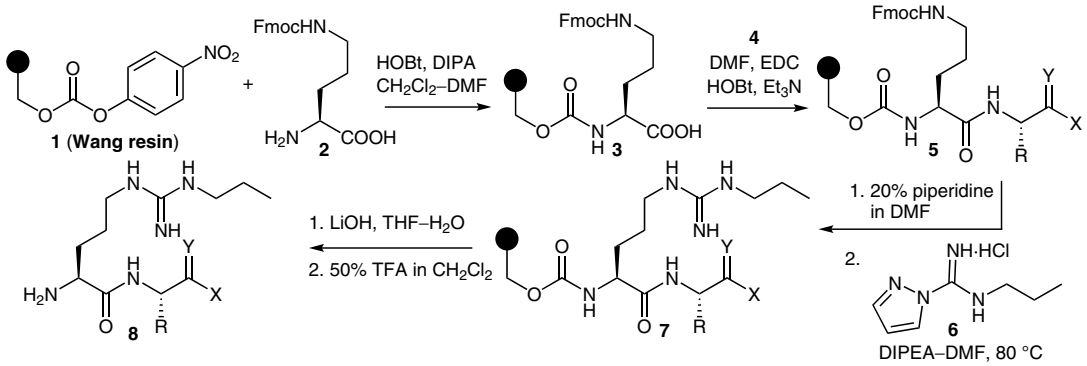
N-Propyl-1*H*-pyrazole-1-carboximidamide for the Synthesis of N^{ω}-Propylarginine-Containing Dipeptides

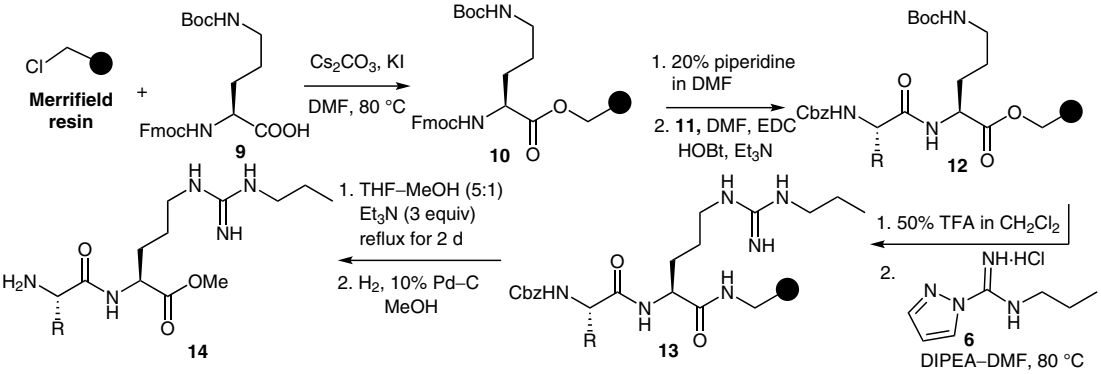
Synthesis of dipeptides bearing N^{ω}-propylarginine at N-terminus:



Selected examples:

Reactant **4**	Product **8**[a]	Yield% of **8**[b]	Reactant **4**	Product **8**[a]	Yield% **8**[b]
H_2N-Gly-OCH_3	H_2N-L-Arg^{pr}-Gly-OH	46%	H_2N-L-Orn-OCH_3	H_2N-L-Arg^{pr}-L-Orn-OCH_3	40%
H_2N-L-His-OCH_3	H_2N-L-Arg^{pr}-L-His-OCH_3	36%	H_2N-Gly-NH_2	H_2N-L-Arg^{pr}-Gly-OCH_3	51%

Synthesis of dipeptides bearing N^{ω}-propylarginine at C-terminus:



Selected examples:

Reactant **11**	Product **14**[a]	Yield% of **14**[b]	Reactant **11**	Product **14**[a]	Yield% **14**[b]
Cbz-HN-L-Ala-OH	H_2N-L-Ala-L-Arg^{pr}-OCH_3	11%	Cbz-HN-L-Ser-OH	H_2N-L-Ser-L-Arg^{pr}-OCH_3	16%
Cbz-HN-L-Phe-OH	H_2N-L-Phe-L-Arg^{pr}-OCH_3	9%	Cbz-HN-L-Gln-OH	H_2N-L-Gln-L-Arg^{pr}-OCH_3	9%

[a] Arg^{pr} stands for N^{ω}-propylarginine. [b] % yields were determined by weight of the product relative to the loading level of the purchased resin (0.83 mmol/g for Wang resin and **1** mmol/g for Merrifield resin).

Significance: N^{ω}-Substituted arginine-containing peptides have a significant role in the endogenous synthesis of nitric oxide (NO). In 1999, Lee and Silverman developed an efficient method for the solid-phase synthesis of N^{ω}-propylarginine-containing dipeptides.

Comment: *N*-Propyl-1*H*-pyrazole-1-carboxamidine is an efficient guanylating agent for the synthesis of N^{ω}-propylarginine-containing dipeptides in moderate yields. The method can be used for the synthesis of peptides having an N^{ω}-propylarginine at either the N- or the C-terminus.

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Peptide Chemistry

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