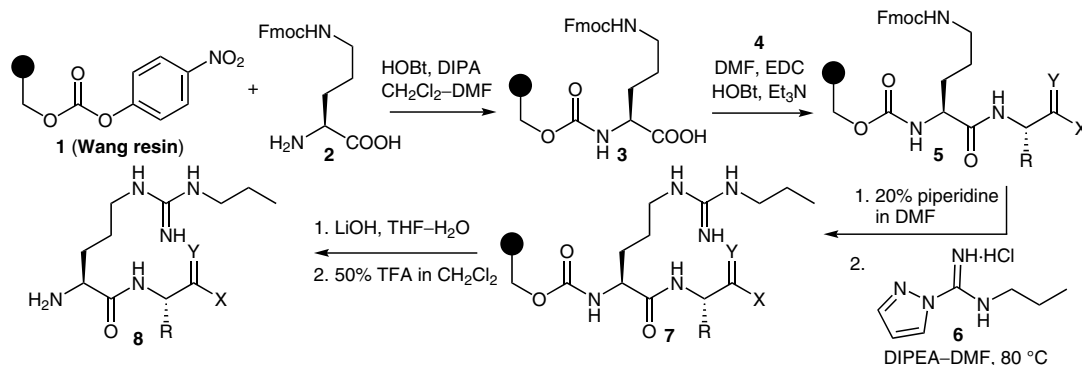


# $N$ -Propyl-1*H*-pyrazole-1-carboximidamide for the Synthesis of $N^{\omega}$ -Propylarginine-Containing Dipeptides

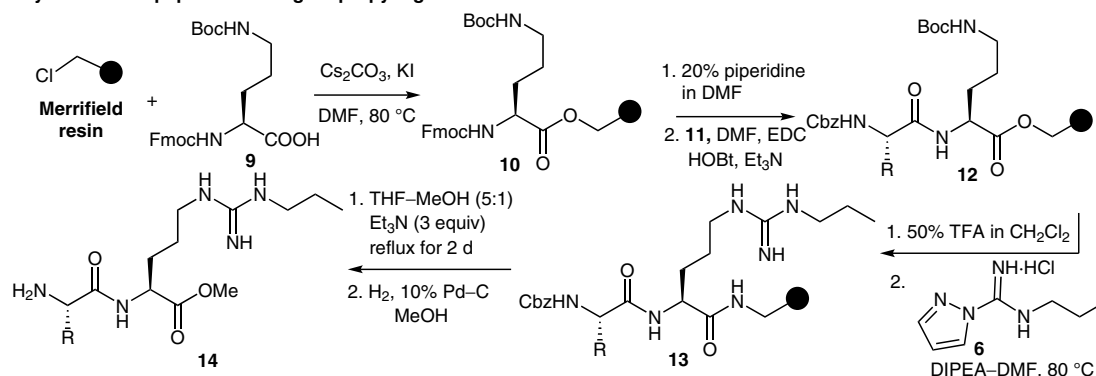
## Synthesis of dipeptides bearing $N^{\omega}$ -propylarginine at N-terminus:



### Selected examples:

Reactant 4	Product 8 <sup>a</sup>	Yield% of 8 <sup>b</sup>	Reactant 4	Product 8 <sup>a</sup>	Yield% 8 <sup>b</sup>
H <sub>2</sub> N-Gly-OCH <sub>3</sub>	H <sub>2</sub> N-L-Arg <sup>Pr</sup> -Gly-OH	46%	H <sub>2</sub> N-L-Orn-OCH <sub>3</sub>	H <sub>2</sub> N-L-Arg <sup>Pr</sup> -L-Orn-OCH <sub>3</sub>	40%
H <sub>2</sub> N-L-His-OCH <sub>3</sub>	H <sub>2</sub> N-L-Arg <sup>Pr</sup> -L-His-OCH <sub>3</sub>	36%	H <sub>2</sub> N-Gly-NH <sub>2</sub>	H <sub>2</sub> N-L-Arg <sup>Pr</sup> -Gly-OCH <sub>3</sub>	51%

## Synthesis of dipeptides bearing $N^{\omega}$ -propylarginine at C-terminus:



### Selected examples:

Reactant 11	Product 14 <sup>a</sup>	Yield% of 14 <sup>b</sup>	Reactant 11	Product 14 <sup>a</sup>	Yield% 14 <sup>b</sup>
Cbz-HN-L-Ala-OH	H <sub>2</sub> N-L-Ala-L-Arg <sup>Pr</sup> -OCH <sub>3</sub>	11%	Cbz-HN-L-Ser-OH	H <sub>2</sub> N-L-Ser-L-Arg <sup>Pr</sup> -OCH <sub>3</sub>	16%
Cbz-HN-L-Phe-OH	H <sub>2</sub> N-L-Phe-L-Arg <sup>Pr</sup> -OCH <sub>3</sub>	9%	Cbz-HN-L-Gln-OH	H <sub>2</sub> N-L-Gln-L-Arg <sup>Pr</sup> -OCH <sub>3</sub>	9%

<sup>a</sup> Arg<sup>Pr</sup> stands for  $N^{\omega}$ -propylarginine. <sup>b</sup> % 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:**  $N^{\omega}$ -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  $N^{\omega}$ -propylarginine-containing dipeptides.

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