

## AgNO<sub>3</sub>/TiO<sub>2</sub>-photocatalyzed N-Methylation of Amino Acids with Methanol

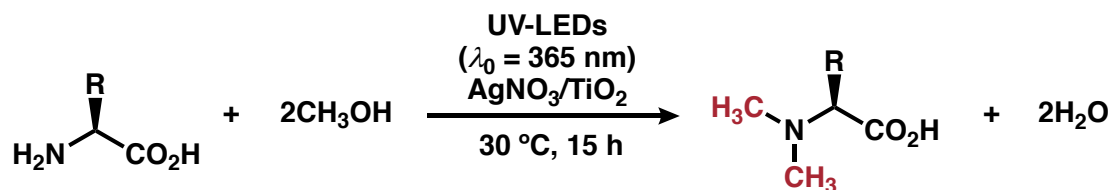
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N-Methylated amino acids are important structural features in peptides. *N,N*-Dimethyl amino acids derived from valine, leucine, and phenylalanine are commonly found in pharmaceuticals, dyes, detergents, synthetic intermediates, and bioactive natural products. Representative examples include cobamide A<sup>1</sup> and dolastatin 10<sup>2</sup>, both of which are natural products with potent antitumor activity. Direct N-methylation of primary or secondary amino acids is a very powerful method for producing N-methylated amino acids. Conventional methods include the direct N-methylation of amino acids with alkyl halides<sup>3</sup> and the reductive amination of formaldehyde using stoichiometric amounts of reducing agents<sup>4</sup>. We previously demonstrated that L-proline can be N-methylated with methanol using a silver-loaded titanium dioxide (Ag/TiO<sub>2</sub>) photocatalyst under irradiation with near UV-light.<sup>5</sup> This photocatalytic method is advantageous over conventional methods because the Ag/TiO<sub>2</sub> system does not require any hazardous reducing reagents. However, the scope on other amino acids remained unclear.

Herein, we developed a method for the direct N-methylation of various amino acids with methanol at ambient temperature using a silver(I)-loaded TiO<sub>2</sub> photocatalyst. The methylating reagent methanol is cheap and abundant. This method does not require any hazardous stoichiometric reducing reagents, water being the only byproduct. Various N-methylated amino acids were obtained after mixing amino acids with 10.0 mg of the photocatalyst in 10 mL dehydrated methanol, and exposing the stirring reaction mixture for 15 h under the UV-light irradiation.



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