

Photochemical Deracemization of Activated Amino Acid Equivalents by Reversible Hydrogen Atom Transfer

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Amino acids, natural or unnatural, are uniquely important building blocks for example in medicinal chemistry. Herein, we report the first deracemization of activated amino acid derivatives that are suited as reagents for peptide coupling. *N*-carboxyanhydrides (NCAs) can be accessed by a simple one step synthesis from their parent amino acids and are often used as precursors for a wide range of valuable amino acid derivatives.^[1]

Our method uses two-point hydrogen bonding between a substrate and a chiral benzophenone photocatalyst for the selective racemization of only one enantiomer presumably by hydrogen atom abstraction followed by hydrogen atom back transfer and keto-enol tautomerization.^[2] We found that a wide range of different NCAs can be deracemized and that only the stereogenic center in α -position is affected while other stereogenic centers remain untouched. We demonstrated the applicability of this method by a myriad of derivatization reactions including the synthesis of dipeptides with unprotected *N*-termini and the abbreviated synthesis of a JAK3 inhibitor (Figure 1).

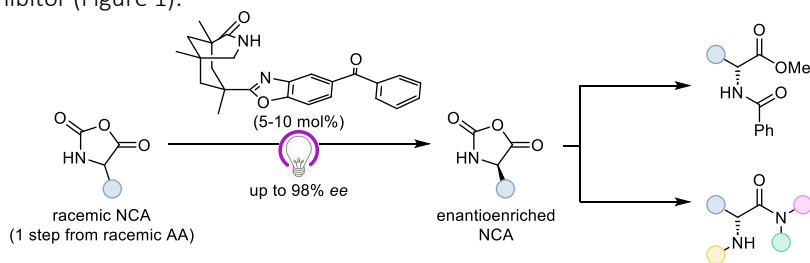


Figure 1: Photochemical deracemization of *N*-Carboxyanhydrides (NCAs) by reversible hydrogen atom transfer and subsequent derivatizations to methyl esters and different amides.

[1] Kricheldorf, H. R. *R-Amino acid-N-Carboxyanhydrides and Related Materials*; Springer-Verlag: New York, 1987.

[2] Kutta, R.J. *et al.* *J. Am. Chem. Soc.*, 2023, *145*, 4, 2354–2363.