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Efficient Asymmetric α-Oxyamination of Aldehydes by Resin-Supported Peptide Catalyst in Aqueous Media

Supported Peptide for Asymmetric α-Oxyamination of Aldehydes

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\begin{align*}
R\text{-CHO} + &\quad \text{(4 equiv)} \\
\text{Peptide catalyst 1:} \\
\text{Pro-D-Pro-Aib-Trp-Trp} &\quad \text{(Leu)_{20-4}} \\
\text{catalytically active site} &\quad \text{hydrophobic chain} \\
\text{amphiphilic resin} &
\end{align*}
\]

\[\text{NaBH}_4\]

\[
\text{up to 87% yield up to 93% ee}
\]

\[
R\text{-OH}
\]

\[
\text{75% yield, 93% ee}
\]

\[
\text{73% yield, 87% ee}
\]

\[
\text{87% yield, 90% ee}
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\[
\text{84% yield, 88% ee}
\]

\[
\text{76% yield, 87% ee}
\]

**Significance:** A polystyrene-poly(ethylene glycol) resin supported peptide catalyst bearing terminal five-residue Pro-D-Pro-Aib-Trp-Trp combined with polyleucine was prepared. The polymeric peptide was successfully applied to the asymmetric α-oxyamination of aldehydes with TEMPO in the presence of a catalytic amount of FeCl₂ and NaN₂O₂ to give the corresponding products under aqueous aerobic conditions with up to 87% yield and 93% ee (5 examples).

**Comment:** The Kudo group has previously reported asymmetric hydrogenation (K. Akagawa et al. Tetrahedron: Asymmetry 2009, 20, 461; K. Akagawa et al. Org. Lett. 2008, 10, 2035) and asymmetric Friedel–Crafts alkylation (K. Akagawa et al. Tetrahedron Lett. 2009, 50, 5602) in aqueous media with this catalyst. The polyleucine moiety between the tryptophan and the resin support not only provides a hydrophobic environment, but also effects the stereoselectivity of the reaction.