Polymer-Supported Helical Peptide Catalyst for Enantioselective Nitro-Michael Addition

Significance: An N-terminal guanidinylated helical peptide supported on PS-PEG resin 1 catalyzed the enantioselective nitro-Michael addition of acetylacetones or β-keto esters to nitroalkenes to afford the corresponding nitro-Michael adducts in up to 99% yield and 99% ee.

Comment: In the enantioselective nitro-Michael addition of acetylacetone to β-nitrostyrene, the catalyst was recovered and reused four times without loss of its catalytic performance. The authors have previously reported the synthesis of PS-PEG-supported peptide catalysts and their application in a cyanosilylation of aldehydes (Tetrahedron Lett. 2012, 53, 5981) and an enantioselective Michael addition (J. Org. Chem. 2016, 81, 6343).

Results:

- \( R = \text{H}; 95\% \text{ yield}, 96\% \text{ ee} \)
- \( R = 2-\text{Me}; 93\%, 97\% \text{ ee} \)
- \( R = 3-\text{Me}; 77\% \text{ yield}, 96\% \text{ ee} \)
- \( R = 4-\text{Me}; 89\% \text{ yield}, 96\% \text{ ee} \)
- \( R = 4-\text{OMe}; 89\% \text{ yield}, 96\% \text{ ee} \)
- \( R = \text{NO}_2; 87\% \text{ yield}, 96\% \text{ ee} \)
- \( R = 4-\text{Br}; 73\% \text{ yield}, 99\% \text{ ee} \)

- \( R = \text{n-Pr}; 97\% \text{ yield}, 91\% \text{ ee} \)
- \( R = \text{i-Pr}; 84\% \text{ yield}, 92\% \text{ ee} \)
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85% yield, \( \text{dr} = 95:5 \)
90% yield, \( \text{ee} = 94, 67\% \)
85% yield, \( \text{dr} = 90:10 \)
87% yield, \( \text{ee} = 92\% \)
86% yield, \( \text{ee} = 94\% \) (1; 20 mol%, 0 °C)