Supported Library-Based Screening of Peptide Catalysts

**Significance:** A resin-supported peptide [Pro-D-Pro-Alb-Tyr-His-(Leu-Leu-Alb)]<sub>2</sub>-TentaGel was identified as an efficient peptide catalyst for the Michael addition of malonates to α,β-unsaturated aldehydes via a combinatorial approach using a resin-supported peptide library. Thus, the reaction of para-nitrocinnamaldehyde with the dye-anchored malonate was carried out with a resin-supported peptide library (100 members) during which a CHO group of the resulting Michael adduct condensed with the terminal prolyl unit of the library in situ. Through this screening protocol, a resin bead bearing a more catalytically active peptide was stained more strongly.

**Comment:** A resin-supported peptide 1 catalyzed the Michael reaction of dialkyl malonates and an α,β-unsaturated aldehydes to afford the corresponding products in up to 89% yield with up to 98% ee. The catalytic activity of 1 in which a histidine moiety was equipped at the fifth position was superior to that of [Pro-D-Pro-Alb-His-Phe-(Leu-Leu-Alb)]<sub>2</sub> and [Pro-D-Pro-Alb-Phe-His-(Leu-Leu-Alb)]<sub>2</sub>. The authors indicated that the histidine moiety plays a critical role for accelerating the reaction by capturing the substrate.

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