Supported Library-Based Screening of Peptide Catalysts

Significance: A resin-supported peptide 1 [Pro-D-Pro-AA¹-AA²-AA³-Leu-Leu-Aib]-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-Tyr-His-(Leu-Leu-Alb)²] and [Pro-D-Pro-Alb-Phe-His-(Leu-Leu-Alb)²]. The authors indicated that the histidine moiety plays a critical role for accelerating the reaction by capturing the substrate.