Copper-Catalyzed Asymmetric Cross-Aldol Reactions

**Double-aldol reaction:**

\[ \text{MesCu} (5-10 \text{ mol%}) \]
\[ (R)-\text{DTBM-SEGPHOS} (5-10 \text{ mol%}) \]
\[ 4\text{-MeOC}_{6}\text{H}_{4}\text{OH} (1 \text{ equiv}) \]
\[ \text{THF}, -60 ^\circ \text{C} \]
\[ \text{LiBH}_4 \]
\[ R^1 \]
\[ R^2 \]
\[ \text{OBpin} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ X = H \text{ or Bpin} \]
\[ \text{dr} = 96:1:3 \]
\[ >99\% \text{ ee} \]

**Triple-aldol reaction:**

\[ \text{MesCu} (10 \text{ mol%}) \]
\[ (R)-\text{DTBM-SEGPHOS} (10 \text{ mol%}) \]
\[ 4\text{-MeOC}_{6}\text{H}_{4}\text{OH} (1 \text{ equiv}) \]
\[ \text{Et}_3\text{N} (2 \text{ equiv}) \]
\[ \text{THF}, -60 ^\circ \text{C} \]
\[ \text{LiBH}_4 \]
\[ R^1 \]
\[ R^2 \]
\[ \text{OBpin} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{X} = \text{H or Bpin} \]
\[ \text{dr} = 96:1:3 \]
\[ >99\% \text{ ee} \]

**Quadruple-aldol reaction:**

\[ \text{MesCu} (10 \text{ mol%}) \]
\[ (R)-\text{DTBM-SEGPHOS} (10 \text{ mol%}) \]
\[ i\text{PrOH} (10 \text{ mol%}) \]
\[ \text{Me}_2\text{N}^+ \text{NMMe}_2^- (1.5 \text{ equiv}) \]
\[ \text{THF}, -60 ^\circ \text{C} \]
\[ \text{LiBH}_4 \]
\[ R^1 \]
\[ R^2 \]
\[ \text{OBpin} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{dr} = 91:9 \]
\[ >99\% \text{ ee} \]

**Significance:** The authors report copper-catalyzed asymmetric iterative and domino cross-aldol reactions. A variety of 1,3-polyols were obtained in high yields and high diastereo- and enantioselectivities.

**Comment:** In this reaction, the use of amine additives permits asymmetric triple and quadruple aldol reactions to be performed in a one-pot process. The method should be useful for the straightforward synthesis of enantiomerically and diastereomerically enriched 1,3-polyols.