Gold-Catalyzed Enantioselective Cyclizations of Enynes through Remote Enantioinduction

**Significance:** Various cyclizations were realized in an enantioselective fashion through the use of a modified JohnPhos ligand with a distal C₂-2,5-diar-rylpyrrolidine.

**Comment:** Hydrocyclization products were used successfully in the first enantioselective total syntheses of three natural products from the carexane family.

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**Synthesis of azabicyclo[4.1.0]hept-4-enes:**

\[
(R,R)-Au\text{-cat. (4 mol%)} \quad AgPF_6 \text{(4 mol%)} \\
\text{DCE, 24 °C, 12 h to 14 d} \\
17 \text{examples} \\
tp \text{99% yield} \\
\text{er up to 96:4}
\]

**Selected examples:**
- \( R_1 = \text{CO}_2\text{Me}, R_2 = \text{Me}, R_3 = \text{H}, 64\% \text{yield, er = 93:7} \)
- \( R_1 = \text{CH}_2\text{OMe}, R_2 = \text{Me}, R_3 = \text{OME}, 97\% \text{yield, er = 96:4} \)
- \( R_1 = \text{CH}_2\text{OMe}, R_2 = \text{Me}, R_3 = \text{t-Bu}, 99\% \text{yield, er = 91:9} \)

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**Synthesis of 1,2-dihydronaphthalenes:**

\[
(R,R)-Au\text{-cat. (1 mol%)} \quad AgSbF_6 \text{(1 mol%)} \\
\text{PhCF}_3, 24 °C, 12–18 h \\
12 \text{examples} \\
tp \text{75% yield} \\
\text{er up to 99:1}
\]

**Selected examples:**
- \( R_1 = \text{H}, R_2 = \text{Ph}, NuH = \text{BuOH}, 75\% \text{yield, er = 95:5} \)
- \( R_1 = \text{H}, R_2 = 4-\text{CF}_3\text{C}_6\text{H}_4, \text{NuH = H}_2\text{O}, 52\% \text{yield, er = 96:4} \)
- \( R_1 = 6-\text{CF}_3, R_2 = \text{Ph}, \text{NuH = H}_2\text{O}, 69\% \text{yield, er = 94:6} \)
- \( R_1 = 6-\text{OME}, R_2 = \text{Ph}, \text{NuH = H}_2\text{O}, 60\% \text{yield, er = 97:3} \)

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**Asymmetric total syntheses of carexanes I, O, and P:**

\[
\text{H}_2, \text{Pd/C, MeOH–EtOAc (1:1)} \\
24 °C, 24 h \\
62\% \text{yield over 2 steps}
\]

**Selected examples:**
- \( R_1 = \text{H}, R_2 = \text{Ph}, \text{NuH = BuOH}, 89\% \text{yield, er = 90:10} \)
- \( R_1 = \text{Ts}, R_2 = \text{H}, Ar = 4-\text{MeOC}_6\text{H}_4, 74\% \text{yield, er = 94:6} \)
- \( R_1 = \text{H}, R_2 = 4-\text{ClC}_6\text{H}_4, \text{NuH = MeOH}, 52\% \text{yield, er = 96:4} \)
- \( R_1 = 6-\text{CF}_3, R_2 = \text{Ph}, \text{NuH = H}_2\text{O}, 69\% \text{yield, er = 94:6} \)
- \( R_1 = 6-\text{OME}, R_2 = \text{Ph}, \text{NuH = H}_2\text{O}, 60\% \text{yield, er = 97:3} \)

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**Synfact of the Month**

**Category:** Metals in Synthesis

**Key words:** gold catalysis remote enantioinduction enynes carexanes