Y. YANG, T. J. L. MUSTARD, P. H.-Y. CHEONG,* S. L. BUCHWALD* (MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE AND OREGON STATE UNIVERSITY, CORVALLIS, USA)

Palladium-Catalyzed Completely Linear-Selective Negishi Cross-Coupling of Allylzinc Halides with Aryl and Vinyl Electrophiles


Palladium-Catalyzed Linear-Selective Negishi Cross-Coupling of Allylzinc Halides

**Significance:** Cheong, Buchwald, and co-workers report the first completely linear-selective palladium-catalyzed Negishi cross-coupling of various 3,3-disubstituted allylzinc reagents with (hetero)aryl and vinyl (pseudo)halides, leading to prenylated (hetero)aryl and alkenyl compounds in high yield and with excellent regioselectivity.

**Comment:** Apart from (hetero)aryl and vinyl bromides and chlorides, nonaflates and triflates were successfully used in this protocol. Computational studies reveal that an \( \eta^1-\alpha \) reductive elimination is preferred due to energetic reasons, leading exclusively to the prenylated products. Thus, the choice of catalyst and transmetalation reagent is crucial.

\[
\text{R}^1 \ X \ \text{LiCl} \ \cdot \ Y \ Zn \ (1.5 \ \text{equiv}) \\
\text{THF, 25 °C, 2 h} \\
\text{R}^1 \ \text{X} \ \text{LiCl} \ Y \ Zn \ (1.3 \ \text{equiv}) \\
\text{THF, 25 °C} \\
\text{up to 97% yield} \\
\text{α/γ up to >99:1} \\
\text{X = Br, Cl, ONf, OTf} \\
\text{Y = Br, OP(O)(OEt)}_2 \\
\text{R}^1 \ = \text{various substituted aryl and heteroaryl,} \\
\text{different mono-, di-, and trisubstituted alkenyls} \\
\text{R}^2 \ = \text{Me} \\
\text{R}^3 \ = \text{Me, Ph, t-Bu, Cy} \\
\text{CPhos precat.} \\
\text{L} = \text{CPhos} \\
\text{L = CPhos} \\
\text{X = Br, Y = Br} \\
\text{N} \text{N} \\
\text{BocN} \\
93% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = ONf, Y = Br} \\
\text{92% yield} \\
\text{X = ONf, Y = Br} \\
90% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = OTf, Y = Br} \\
75% \text{ yield} \\
\text{E/Z > 99:1} \\
\text{X = OTf, Y = OP(O)(OEt)}_2 \\
\text{92% yield} \\
\text{α/γ > 99:1} \\
\text{EZ = 84:16} \\
\text{X = Br, Y = Br} \\
78% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
95% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
94% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
\text{92% yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
\text{93% yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
\text{95% yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
94% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
90% \text{ yield} \\
\text{α/γ > 99:1} \\
\text{X = OTf, Y = Br} \\
75% \text{ yield} \\
\text{E/Z > 99:1} \\
\text{X = OTf, Y = OP(O)(OEt)}_2 \\
\text{94% yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \\
\text{92% yield} \\
\text{α/γ > 99:1} \\
\text{X = Br, Y = Br} \"]