The Chan–Evans–Lam Coupling

**Significance:** In 1998, Chan and Lam as well as Evans (Tetrahedron Lett. 1998, 39, 2937) independently reported a copper(II)-promoted oxidative cross-coupling of aryl boronic acids and heteroatomic nucleophiles such as amines and alcohols to form C(sp²)–heteroatom bonds. The reaction proceeds with stoichiometric amounts of copper under oxidative conditions (air or O₂) at room temperature.

**Comment:** Over the past decades, the Chan–Evans–Lam coupling has been thoroughly investigated and reaction conditions were significantly enhanced to turn this reaction into a catalytic process. C(sp²)–S, C(sp²)–P and C(sp²)–halogen bond formations have been achieved. Studies for the elucidation of the mechanism have been recently described (J. C. Vantourout et al. J. Am. Chem. Soc. 2017, 139, 4769).

**CH₂Cl₂ (w/ or w/o 4 Å MS) \( \text{r.t.}, 24–72 \text{ h under air} \)**

\[ \text{E} = \text{O, NH} \]

\[ \text{Cu(OAc)}_2 \] (1.0–2.0 equiv)

\[ \text{Et}_3\text{N or py (2.0–3.0 equiv)} \]

\[ \text{Ar}^+ \] (2.0–3.0 equiv)

15 examples

4–96% yield

Selected examples:

**Chan et al. (1998)**

\[
\begin{align*}
\text{H} & \quad \text{N} & \quad \text{R} \\
\text{Me} & \quad \text{N} & \quad \text{t}-\text{Bu} \\
\text{t}-\text{Bu} & \quad \text{R} & \quad \text{H} \\
\end{align*}
\]

63% yield

45% yield

73% yield

13 examples

6–88% yield

**Lam et al. (1998)**

\[
\begin{align*}
\text{H} & \quad \text{N} & \quad \text{R} \\
\text{Me} & \quad \text{N} & \quad \text{Me} \\
\text{N} & \quad \text{N} & \quad \text{Ph} \\
\end{align*}
\]

67% yield

26% yield

**Proposed mechanism:**

\[ \text{[Cu(OAc)}_2\text{]xH}_2\text{O} \]

\[ \text{E} = \text{O, NH} \]

\[ \text{Cu(OAc)}_2 \]

\[ \text{Et}_3\text{N or py} \]

\[ \text{Ar}^+ \]

\[ \text{Solv} \]

\[ \text{AcO}^- \]

\[ \text{R–EH} \]

\[ \text{E} = \text{O, NH} \]

\[ \text{transmetalation} \]

\[ \text{disproportionation} \]

\[ \text{reductive elimination} \]

\[ \text{oxidative turnover} \]

\[ \text{denucleation} \]

\[ \text{[Cu}^2\text{](OAc)}_2 \]

\[ \text{[CuI(OAc)]}_2 \]

\[ \text{Ar}^+ \]

\[ \text{E} = \text{O, NH} \]

\[ \text{Ar}^+ \]

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