Formation of α-Chiral Centers by Asymmetric β-C(sp³)–H Arylation, Alkenylation, and Alkynylation

**Palladium-Catalyzed Asymmetric C–H Functionalizations of Isobutanamides**

\[
\text{OE} + \text{Ar}_F \overset{\text{Pd(MeCN)}_2\text{Cl}_2 (10 \text{ mol} \%) \text{ ligand (20 mol})%}{\xrightarrow{\text{Ag}_2\text{CO}_3 (2 \text{ equiv}) \text{ NaTFA (2 equiv)}} \text{PhMe, 60 °C, 72 h}} \text{OE}\]

Selected examples:

\[
\begin{align*}
\text{68% yield, er = 98:2} \\
\text{70% yield, er = 98:2} \\
\text{70% yield, er = 96:4} \\
\text{73% yield, er = 97:3} \\
\text{62% yield, er = 95:5} \\
\text{50% yield, er = 98:2} \\
\text{52% yield, er = 97:3} \\
\text{60% yield, er = 98:2}
\end{align*}
\]

Selected examples:

\[
\begin{align*}
\text{60% yield, er = 94:6} \\
\text{57% yield, er = 94:6} \\
\text{42% yield, er = 95:5} \\
\text{61% yield, er = 94:6} \\
\text{50% yield, er = 95:5} \\
\text{60% yield, er = 95:5} \\
\text{43% yield, er = 94:6}
\end{align*}
\]

**Significance:** Desymmetrization of isopropyl moieties has remained an unanswered challenge. The authors have developed new ligands for the formation of a chiral center at the α-position of isobutyric acid derivatives through β-C(sp³)–H functionalization.

**Comment:** This palladium-catalyzed protocol promotes an asymmetric β-C(sp³)–H arylation, alkenylation, or alkynylation to form a chiral center at the α-position of a range of isobutyric acid derivatives with moderate yields and excellent enantioselectivities.