Thiourea-Catalyzed Asymmetric Cyanation of N-Boc Ketimines

**Significance:** The first catalytic asymmetric cyanation of isatin-derived N-Boc ketimines has been reported by Zhou and co-worker. Wide substrate scope and excellent enantioselectivities were obtained. A tandem aza-Wittig–Strecker reaction has also been reported, which was applied to the total synthesis of spirohydantoin I.

**Comment:** An aza-Wittig–Strecker reaction sequence has been reported, which offers a good methodology to develop a catalytic asymmetric reaction of N-Boc ketimines, generated in situ from the achiral ketones. The strategy has potential applications in other types of reactions, in which N-Boc imines are involved.

**Application to the total synthesis of spirohydantoin I:**

\[
\begin{align*}
\text{NBoc} & \quad + \quad \text{TMSCN} \\
\text{catalyst (5 mol\%)} & \quad \text{HFIP (1.0 equiv)} \\
\text{Cl} & \quad \text{CH}_2\text{Cl}_2, -70 \degree \text{C} \\
\end{align*}
\]

19 examples
65–95% yield
er from 95:5 to >99.5:0.5

\[
\begin{align*}
\text{NBoc} & \quad \text{Cl} \\
\text{Cl} & \quad \text{BocHN} \\
\end{align*}
\]

82% yield
er = 97:3

3 steps

\[
\begin{align*}
\text{NBoc} & \quad \text{Cl} \\
\text{Cl} & \quad \text{spirohydantoin I} \\
\end{align*}
\]

34% yield
er = 89.5:10.5
(er = 99.5:0.5 after one recrystallization)

\[
\begin{align*}
\text{NBoc} & \quad \text{Cl} \\
\text{Cl} & \quad \text{spirohydantoin I} \\
\end{align*}
\]

84% yield
er = 97:3

3 steps

\[
\begin{align*}
\text{NBoc} & \quad \text{Cl} \\
\text{Cl} & \quad \text{spirohydantoin I} \\
\end{align*}
\]

82% yield
er = 97:3

(sp = 3.5-(CF\textsubscript{3})\textsubscript{2}C\textsubscript{6}H\textsubscript{3} catalyst)

**Key words**
- thioureas
- cyanation
- ketimines