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Highly Enantioselective Addition of Enals to Isatin-Derived Ketimines Catalyzed by N-Heterocyclic Carbenes:
Synthesis of Spirocyclic \( \gamma \)-Lactams

**NHC-Catalyzed Annulation of Isatin \( N \)-Boc Ketimines and Enals**

\[
\begin{align*}
\text{R}^1 = & \text{H, Me, OMe, Cl} \quad \text{R}^2 = \text{H, Me, Bn, Ac} \\
\text{R}^3 = & \text{Ar, Alk}
\end{align*}
\]

**Significance:** Chi and co-workers report an N-heterocyclic carbene (NHC)-catalyzed annulation of isatin \( N \)-Boc imines with enals, which affords spirocyclic oxindole-\( \gamma \)-lactams bearing one quaternary chiral center in good diastereo- and excellent stereoselectivities (dr up to >20:1 and er > 99.5:0.5). Ketimines and \( \gamma \)-aryl enals with electron-donating substituents lead to better yield and selectivity compared to electron-withdrawing substituents. The presence of a trace of water is beneficial for the conversion of the reaction. The resulting products can be easily deprotected to free \( \gamma \)-lactams in high yield.

**Comment:** \( \gamma \)-Lactams are privileged scaffolds found in naturally occurring and synthetic biologically active compounds. Herein, the authors have developed a novel NHC-catalyzed annulation methodology, which allows for a rapid construction of spirocyclic oxindole-\( \gamma \)-lactams with high diastereoselectivity and enantioselectivity. More efficient catalysts and the application to more challenging substrates are expected.

**Selected examples:**

- 83% yield dr > 20:1 er = 99.5:0.5
- 64% yield dr = 17:1 dr er = 99.5:0.5
- 80% yield dr > 20:1 er = 99.5:0.5
- 64% yield dr = 4:1 er = 97:3

**Removal of the Boc protecting group:**

\[
\begin{align*}
\text{BocN} & \quad \text{BocN} \\
\text{Me} & \quad \text{Me} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

83% yield dr > 20:1 er = 99.5:0.5

- 64% yield dr = 17:1 dr er = 99.5:0.5
- 80% yield dr > 20:1 er = 99.5:0.5
- 64% yield dr = 4:1 er = 97:3

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