Asymmetric Friedel–Crafts Reaction Using a Chiral-at-Metal Iridium Catalyst

**Significance:** The widespread use of asymmetric catalysis in academia and industry can be directly attributed to the vast array of synthetically and commercially available chiral ligands. However, the utilization of chiral-at-metal complexes in asymmetric catalysis is relatively underdeveloped. Here, the authors report the efficient synthesis of a chiral-at-iridium catalyst and its application to an asymmetric Friedel–Crafts reaction.

**Comment:** The authors present the asymmetric Friedel–Crafts reaction of indoles and acyl imidazole derivatives using a chiral-at-iridium complex as catalyst. The reaction proceeds with excellent yields and selectivities by employing a low loading (1–2 mol%) of this interesting catalyst. The authors suggest that once coordinated, the achiral ligands block the re face of the indole, resulting in a highly selective si-face attack.

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**Overall transformation:**

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\text{NiCl}_3 \cdot 3\text{H}_2\text{O} \quad (2.1 \text{ equiv}) \quad \text{Et}_3\text{N} \quad \text{EtOH} \quad 50 \ ^\circ\text{C}, 4 \text{ h} \quad 99% \text{ yield, } >99% \text{ ee}
\]

**Selected examples:**

- 97% yield 96% ee (1 mol% \(\Lambda-1\))
- 99% yield 94% ee (1 mol% \(\Delta-1\))
- 97% yield 90% ee (2% \(\Lambda-1\))
- 97% yield 98% ee (1% \(\Delta-1\))

**Synthesis of chiral-at-metal iridium complexes (\(\Lambda-1\) and \(\Delta-1\)):**

1. Reflux in THF, r.t., 18–60 h (0.3 mmol scale)

2. Chromatographic resolution

\[
\text{NH}_4\text{PF}_6 \quad \text{MeCN} \quad 50 \ ^\circ\text{C}, 4 \text{ h} \quad (95% \text{ yield, } >99% \text{ ee})
\]