Construction of Peptide Macrocycles via Radical-Mediated Intramolecular C–H Alkylation

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Catalytic Intramolecular C–H Alkylation for the Synthesis of Peptide Macrocycles

**Significance:** Peptide macrocycles provide an important platform for drug discovery. The authors have developed intramolecular C–H alkylations under blue LED irradiation for the macrocyclization of peptides.

**Comment:** Copper- or iridium-catalyzed intramolecular C–H alkylations were successfully promoted by blue LED irradiation. The desired peptide macrocycles were obtained in moderate yields.

**Selected examples:**

**Catalyst 1:**

\[
\text{[Cu(Xantphos)(DMP)]PF}_6 \quad (10 \text{ mol\%})
\]

- HFIP, argon
- r.t., 12 h
- blue LED (24 W)

- 43% yield, dr > 20:1
- 67% yield, dr > 20:1
- 52% yield, dr = 10:1
- 34% yield, dr > 20:1

**Catalyst 2:**

\[
\text{[Ir(dF(CF3)ppy)2(dtbp)]PF}_6 \quad (2 \text{ mol\%})
\]

- BINOL phosphoric acid (1.5 equiv)
- CH$_2$Cl$_2$, argon
- r.t., 24–40 h
- blue LED (34 W)

- 55% yield
- 50% yield
- 58% yield

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