Asymmetric Synthesis of (S)-Ketoprofen

**Significance:** A synthesis of the non-steroidal anti-inflammatory drug (S)-ketoprofen exemplifies a new general tandem catalysis approach to the enantioselective organocatalytic \( \alpha \)-arylation of aldehydes. The scope of the reaction is illustrated by 22 examples (67–95% yield, 91–94% ee) involving ten different aldehydes and 13 different diaryliodonium salts. A five-step synthesis of catalyst C (17% overall) from L-phenylglycine \( N \)-methylamide is provided.

**Comment:** A mechanism is proposed involving reaction of the aryl copper(III) species G (derived from oxidative addition of CuBr to the diaryliodonium salt A) with the enamine H (derived from condensation of the organocatalyst C with propanal) to give the \( \eta^1 \)-iminium copper(III) species I. Reductive elimination with retention of configuration then gives the \( \alpha \)-aryl iminium salt J, which hydrolyzes to the product with regeneration of the organocatalyst C.

**Proposed mechanism for the aldehyde \( \alpha \)-arylation:**

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\text{BrCu}^{(III)}\text{OTf} + \text{Me}_2\text{N}\text{C}=\text{O} \rightarrow \text{Me}_2\text{N}\text{C}^{+}\text{Cu}^{(III)}\text{Ph}^{-}\text{OTf}^{-} \rightarrow \text{Me}_2\text{N}\text{C}^{+}\text{Cu}^{(III)}\text{Ph}^{-} \rightarrow \text{Me}_2\text{N}\text{C}=\text{O} + \text{CuBr}
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