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 \(C\).

**SYNFACTS Contributors:** Philip Kocienski

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