Enzymatic Zinc Hydrides Expand New-to-Nature Toolbox

**Significance:** Hartwig and co-workers report an asymmetric reduction of ketones catalyzed by zinc-containing carbonic anhydrases in the presence of silanes. The authors provide strong evidence that the reaction proceeds via a protein-bound mononuclear zinc hydride, produced by a metathesis reaction between zinc hydroxide in the native active site and the added silicon hydride. The asymmetric reductions are efficient and induce excellent levels of enantioselectivity, are catalyzed by an Earth-abundant metal without a cofactor, and can be performed on a gram scale in whole cells.

**Comment:** Several research groups have leveraged the evolvability and adaptability of enzymes to discover new-to-nature chemical transformations, e.g., carbene and nitrene transfer processes. Here, the authors introduce a new reactivity paradigm in abiotic enzyme catalysis by demonstrating the intermediacy of a mononuclear zinc hydride, a catalytic intermediate unknown in nature. Given the prevalence of metal hydrides in small-molecule catalysis, this work holds enormous promise to unlock new enzymatic reactivity and to provide sustainable solutions to longstanding synthetic challenges.