DEMYSTIFYING THE SOAI REACTION

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The extraordinary Soai reaction has profoundly impacted chemists' perspective of chiral symmetry breaking, absolute asymmetric synthesis and its role in the origin of biological homochirality [1]. Herein, we describe the unprecedented observation of asymmetry amplifying autocatalysis in the alkylation of 5-(trimethylsilylethynyl)pyridine-3-carbaldehyde using diisopropylzinc (Figure 1a). Kinetic studies with a "Trojan-horse" substrate and spectroscopic analysis of a series of zinc-alkoxides that incorporate specific structural mutations reveal a 'pyridine-assisted cube escape' (Figure 1c). The new cluster functions as a catalyst that activates the '*floor-to-floor*' bound aldehyde and poises a coordinated diisopropylzinc moiety for alkyl group transfer. Transition-state models leading to both the homochiral and heterochiral products were validated by density functional theory calculations (Figure 1b). Moreover, experimental and computational analysis of the heterochiral complex provides a definitive explanation for the non-linear behavior of this system. Our deconstruction of the Soai system contributes substantially to understanding the mechanism of this transformation that has stood as a longstanding challenge in chemistry.

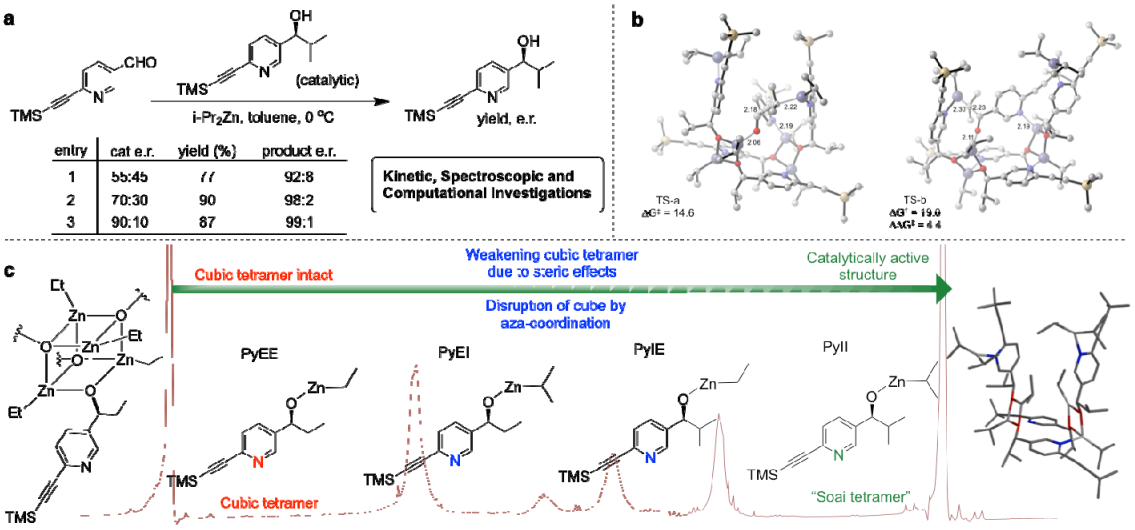

Figure 1: **a.** Amplifying autocatalysis with 5-(trimethylsilylethynyl)pyridine-3-carbaldehyde and diisopropylzinc.
b. Transition state models leading to the homochiral (TS-a) and heterochiral product (TS-b) **c.** Evolution of the Soai tetramer due to pyridine coordination assisted 'cube escape'.

[1] K. Soai, T. Kawasaki, A. Matsumoto, *Acc. Chem. Res.*, 47 (2014), 3643-3654.