

SESSION I: SPEAKER ABSTRACTS

Demystifying the Soai Reaction

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The autocatalytic, asymmetry-amplifying alkylation of pyrimidine-5-carbaldehydes with diisopropylzinc, crowned as the ‘Soai reaction’, occupies a venerable position in organic chemistry. Enantiopure products are obtained in three reaction cycles even with calculated autocatalyst e.e. as low as $5 \times 10^{-5} \%$. In the absence of added catalyst, symmetry breaking can yield non-racemic products, thus categorizing the transformation as an example of absolute asymmetric synthesis. A large variety of chiral additives, circularly polarized light and even isotopic chirality can influence the outcome of the reaction by biasing an initial imbalance toward one of the enantiomers. Soai’s seminal discoveries have received widespread attention in diverse chemical fields and have revived discussions regarding absolute asymmetric synthesis, chiral symmetry breaking, and the origin of biological homochirality.

We describe the unprecedented observation of asymmetry amplifying autocatalysis in the alkylation of the related 5-(trimethylsilylethynyl)pyridine-3-carbaldehyde using diisopropylzinc (fig. 1a). Kinetic studies with a “Trojan-horse” substrate and detailed spectroscopic analysis of a series of zinc-alkoxides incorporating specific structural mutations reveal a ‘pyridine-assisted cube escape’ to access a tetrameric product aggregate (fig. 1c). The new cluster functions as a catalyst that activates the aldehyde and poises a bound diisopropylzinc moiety for alkyl group transfer. Transition-state models leading to both the homochiral and heterochiral products were validated by density functional theory calculations (fig. 1b). This study provides the first definitive experimental rationalization to understand the fundamental basis of the structural requirements of the Soai reaction and reveal the alkyl-transfer transition state, thus contributing substantially to understanding the mechanism of this transformation that has stood as a longstanding challenge in chemistry.

