Kinetic Insight into Specific Features of the Autocatalytic Soai Reaction

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Abstract The addition of diisopropylzinc to prochiral pyrimidine carbaldehydes (Soai reaction) is the only known example of spontaneous asymmetric synthesis in organic chemistry. It serves as a model system for the spontaneous occurrence of chiral asymmetry from achiral initial conditions. This review describes the possible kinetic origin of specific experimental features of this reaction. It is shown that generic kinetic models, including enantioselective autocatalysis and mutual inhibition between the enantiomers,
are adequate to describe a variety of the astonishing properties of the Soai reaction. Namely, these are the unprecedented strong chiral amplification, extreme sensitivity to the presence of very small amounts of chiral initiator, mirror-symmetry breaking when starting from achiral conditions, and the reversal of enantioselectivity of chiral catalysts by addition of achiral additives. The described kinetic approach allows a closer insight into the nonlinear dynamics of the Soai reaction. It also reveals that a number of open questions concerning the detailed reaction mechanism are still to be solved and that further experimental studies are required.

1 Introduction

Spontaneous asymmetric synthesis has been envisaged by theoretical models for more than 50 years [1–7]. This process features the generation and amplification of optical activity during the course of a chemical reaction. It stands in contrast to asymmetric procedures, such as stoichiometric resolution, conglomerate crystallization, or chiral chromatography, in which the optical activity can be increased but no additional chiral product is formed [8]. It is also different from classical asymmetric synthesis, in which new chiral product is obtained but the resulting enantiomeric excess ($ee$) is usually less than or, at most, equal to that of the chiral initiator or catalyst\(^1\).

The first experimental invention of spontaneous asymmetric synthesis was achieved only a little more than a decade ago in an organic reaction system by Soai and coworkers [9–15]. The Soai reaction (Scheme 1) comprises the addition of diisopropylzinc to prochiral pyrimidine carbaldehydes yielding isopropylzinc alkoxides that, after hydrolysis, are usually converted into stable chiral pyrimidyl alkanols.

\[ \text{ArCHO} + \text{Zn} \rightarrow \text{ArOZn} \stackrel{\text{hydrolysis}}{\longrightarrow} \text{ArOH} \]

\begin{center}
\text{prochiral diisopropylzinc isopropylzinc alkoxide optically active alcohol}
\end{center}

\textbf{Scheme 1} The Soai reaction; \text{Ar} = 3-pyridyl, 3-quinolyl, 5-pyrimidinyl, ferrocenyl, 2-alkyl-5-pyrimidinyl (see Table 1)

At first glance, the Soai reaction appears to be one of the prominent examples of catalytic asymmetric organozinc additions to carbonyl com-

\(^1\) On some occasions an exception from this case can be observed by so-called nonlinear effects in asymmetric synthesis, in which the relation between the enantiomeric excess of the chiral catalyst or initiator and that of the product deviates from linearity (see Sect. 3.3)