This concept chapter provides an overview of strategies to produce chiral compounds in nonracemic form, using racemates or mixtures of diastereomers as starting materials, via desymmetrization, resolution, and deracemization. Special emphasis is given to dynamic systems, such as dynamic kinetic resolutions (DKR) and dynamic kinetic asymmetric transformations (DYKAT). Based on a discussion of the underlying kinetics, user-friendly online tools are introduced that allow analysis and optimization of these asymmetric catalytic transformations. Merits and limitations are highlighted by examples proven on the synthetic scale.

**Keywords:** desymmetrization • kinetic resolution • enantioconvergent • stereoconvergent • deracemization • de-epimerization • asymmetric transformation • dynamic kinetic asymmetric transformation • dynamic kinetic resolution • biocatalysis • organocatalysis • transition-metal catalysis • reaction kinetics
Organocatalytic Dynamic Kinetic Resolution
X. Wu, Y. Liu, and Z. Jin

There has long been interest in obtaining optically pure molecules from racemic or non-chiral starting materials through environmentally friendly chemical transformations with high yields and enantioselectivities. Organocatalytic reactions possess the inherent advantages of non-toxicity and good efficiency and are insensitive to air and moisture. Dynamic kinetic resolution (DKR) represents one class of the most efficient strategies for the preparation of chiral molecules from racemic mixtures with up to 100% yields. Therefore, DKR reactions promoted by various organic catalysts are attractive based on their efficiencies, selectivities, and low toxicities. In this review, we introduce some representative examples of the reported DKR reactions catalyzed by typical organic catalysts, including chiral amines, Brønsted acids, N-heterocyclic carbenes, phosphines, guanidines, and isothioureas. The aim is to provide readers with a general overview of the scope and efficiency of organocatalytic DKR transformations and to inspire groundbreaking ideas for the development and applications of organocatalytic DKR reactions in future research.

Keywords: dynamic kinetic resolution · organocatalysis · enantioselectivity · chirality · asymmetric transformation · functional molecules · organic synthesis
Dynamic kinetic asymmetric transformations (DYKAT) are an important way of converting simple organic molecules into complex small molecules as single diastereo- and enantiomers. Herein we describe selected examples that are catalyzed by small organic molecules, which utilize activation mechanisms similar to enzymes for accomplishing the high stereoselectivity. The research area of DYKAT is growing and remarkable examples for producing important organic molecules and pharmaceuticals are demonstrated. In this context, organocatalysis will play an important role.

**Keywords:** dynamic kinetic asymmetric transformation • organocatalysis • highly enantioselective • highly diastereoselective • dual catalysis • hydrogen-bond donation • small-molecule catalysis
5  Chemoenzymatic Dynamic Kinetic Resolution of Amines

K. Adriaensen and D. De Vos

Enantiopure amines are valuable intermediates in the fine-chemical industry but can be challenging to obtain. The combination of racemization techniques with enzymatic resolution into a chemoenzymatic dynamic kinetic resolution yields an invaluable and efficient method to achieve enantiopure amines. This chapter discusses the main differences between the recent dynamic kinetic resolution approaches, as well as their respective (dis)advantages, with a focus on the overall applicability to a wide substrate scope. Additionally, various industrially relevant examples cement the value of the chemoenzymatic dynamic kinetic resolution of amines.

Keywords: amines • chemoenzymatic • enzymes • dynamic kinetic resolution • kinetic resolution • racemization • acylation • lipase • ruthenium • palladium • thiyl

6  Chemoenzymatic Dynamic Kinetic Resolution of Alcohols

K. Kanomata and S. Akai

Chemoenzymatic dynamic kinetic resolution is one of the simplest and most reliable methods to obtain optically pure alcohol derivatives from racemates. For this purpose, hydrolases, especially lipases, have been widely used in the enantioselective esterification processes, and a variety of racemization catalysts with high catalytic efficiency and compatibility with lipases have been developed. This review introduces chemoenzymatic DKR of alcohols based on the category of racemization catalysts. DKR of axially chiral hydroxybiaryls and the use of engineered lipases to obtain opposite enantiomers, as well as the synthetic applications of the DKR products, are also discussed.
Applications of Chemoenzymatic Dynamic Kinetic Resolution for the Synthesis of Biologically Active Compounds and Natural Products

S. González-Granda and V. Gotor-Fernández

Dynamic kinetic resolutions of racemic compounds provide elegant synthetic possibilities for the preparation of valuable enantiopure organic molecules with a theoretical maximum 100% yield. This chapter describes the combination of stereoselective enzymatic methods with suitable conditions for the racemization of the slow-reacting enantiomer from racemates of various types of compounds, such as alcohols, amines, and amino acids, for the synthesis of biologically active compounds and natural products. This contribution has been divided into three main topics based on the enzyme that catalyzes the asymmetric transformation and the racemization conditions of choice. These are: (i) the use of hydrolases and metal species; (ii) the use of hydrolases without requiring a metal catalyst for the racemization step; (iii) the use of other enzyme classes. A selection of scalable experimental procedures is provided in each case to demonstrate the robustness of the methodology described.

Keywords: acylation • alcohols • amines • asymmetric synthesis • dynamic kinetic resolution • DKR • enzymes • natural products • organic synthesis

Chemoenzymatic Dynamic Kinetic Asymmetric Transformation

O. Pàmies

The combination of enzymes and metal complexes can be used to achieve the de-epimerization of diastereoisomeric mixtures. Thus, by means of this chemoenzymatic dynamic kinetic asymmetric transformation (DYKAT), a wide range of racemic diols and, to a lesser extent, amino alcohols and diamines, have been transformed into a single diastereomer in excellent yields, and diastereo- and enantioselectivities.

Keywords: dynamic kinetic asymmetric transformation • DYKAT • enzymes • metal complexes • diols • amino alcohols • diamines • chirality
Dynamic kinetic asymmetric transformations (DYKAT) are an extensively utilized class of reactions to construct carbon–carbon and carbon–heteroatom bonds from racemic starting materials. Much like DYKAT, stereoablative transformations grant access to enantioenriched building blocks from racemic substrates. In contrast to DYKAT, stereoablative transformations function via irreversible destruction of the stereocenter rather than a catalyst-promoted epimerization. While this review is not exhaustive, it focuses on transition-metal-catalyzed processes and outlines the current state-of-the-art of this field.

**DYKAT**

\[
\begin{align*}
\text{racemic} & \xrightarrow{\text{chiral catalyst}} \left[ \begin{array}{c} \text{ML}^+ \\text{catalyst-mediated racemization} \\
R^1 \text{R}^2 \end{array} \right] \\
& \xrightarrow{E^-} \text{E} \text{R}^1 \text{R}^2
\end{align*}
\]

**stereoablative transformations**

\[
\begin{align*}
\text{racemic} & \xrightarrow{\text{chiral catalyst}} \left[ \begin{array}{c} \text{XML}^+ \\
R^1 \text{R}^2 \end{array} \right] \\
& \xrightarrow{E^-} \text{E} \text{R}^1 \text{R}^2
\end{align*}
\]

**Keywords:** transition-metal catalysis • asymmetric transformations • DYKAT • stereoablative transformations • enantioselective catalysis • chiral building blocks

The stereocontrolled synthesis of complex molecules is a key technology for the pharmaceutical, agrochemical, and fine-chemical industries, a well-established field of organic chemistry, and the ultimate proving ground for the value of newly developed synthetic methods. This chapter illustrates how metal-catalyzed dynamic kinetic resolutions (DKR) and dynamic kinetic asymmetric transformations (DYKAT) have been used in the synthesis of complex molecules such as natural products, pharmaceuticals, and chiral ligands. This approach has unique strategic advantages over other methods as it allows the use of racemic starting materials, where asymmetry is introduced at a later stage in a synthetic sequence and can even be used to set multiple stereogenic centers in a single step.
Keywords: asymmetric catalysis • dynamic kinetic resolution • dynamic kinetic asymmetric transformation • DKR • DYKAT • natural products • pharmaceuticals • total synthesis • transition metals • isomerization • resolution • racemic starting materials • hydrogenation • reduction • cross coupling • stereochemical arrays • allylic substitution

Dynamic Kinetic Resolution in Asymmetric Hydrogenation and Transfer Hydrogenation
J.-H. Xie and Q.-L. Zhou

Catalytic asymmetric hydrogenation and transfer hydrogenation via dynamic kinetic resolution are atom-economical and powerful tools for the conversion of racemic compounds into optically pure enantiomers. Over the past three decades, considerable efforts have been made in this field and remarkable advances have been achieved. This chapter provides an overview of effective asymmetric hydrogenation and transfer hydrogenation of racemic compounds, such as α-substituted ketones and β-keto esters, via dynamic kinetic resolution to form enantioenriched chiral products, such as chiral alcohols and amines.

Keywords: asymmetric hydrogenation • asymmetric transfer hydrogenation • dynamic kinetic resolution • DKR • catalysis • transition metals • isomerization • resolution • racemic starting materials • hydrogenation • reduction • cross coupling • stereochemical arrays • allylic substitution
Stereoenriched atropisomeric compounds find important applications in various areas of chemistry and their synthesis is therefore a critical research target. This chapter presents a selection of the best methods available to date for the asymmetric preparation of atropisomeric compounds using dynamic stereoselective techniques. For the more common (hetero)biaryls, the selected reactions are classified according to the conformational stability of the substrates, i.e. whether they are freely rotating or are configurationally stable and require a chemically induced, temporary lowering of their rotation barrier before an asymmetric transformation can lock the axial chirality again. Strategies towards the stereoselective synthesis of non-biaryl atropisomers using dynamic resolution techniques are also covered.

**Keywords:** asymmetric synthesis, asymmetric catalysis, enantioselectivity, diastereoselectivity, conformation, atropisomers, dynamic kinetic resolution, dynamic kinetic asymmetric transformation, DKR, DYKAT, dynamic thermodynamic resolution, chiral auxiliaries, palladium, organocatalysis, biaryls, nitrogen heterocycles, amides