

## PREFACE TO VOLUME 86

The chapters in this volume concern two of the more reactive functional groups in organic chemistry, namely, epoxides and aldehydes. The high electronegativity of oxygen combined with the strain energy of oxiranes or the unsaturation and steric accessibility of aldehydes provide low-energy pathways for myriad chemical transformations. Indeed, controlling the reactivity of these functions represents a significant challenge for selective chemical synthesis. Fortunately, thanks to decades of accumulated experience and knowledge, many such selective transformations are now available, two of which are elaborated in detail in this volume.

The first chapter authored by John W. Kramer, John M. Rowley, and Geoffrey W. Coates describes the catalyzed insertion of carbon monoxide into oxiranes to produce a wide variety of ring-expanded heterocyclic compounds. The most common illustration of this reaction is the simple insertion of one molecule of carbon monoxide to generate four-membered-ring lactones ( $\beta$ -lactones). These strained heterocycles are extremely useful building blocks in the synthesis of natural products, unnatural amino acids, as well as in the generation of biodegradable polyesters. These insertion reactions are highly stereospecific (proceeding with clean inversion of configuration at the site of insertion) which, combined with the wide availability of enantiomerically enriched epoxides, allows for efficient access to enantiomerically enriched lactones. Higher lactones are also accessible from this process if epoxides bearing hydroxyl groups are employed. Moreover, multiple insertions of carbon monoxide are also possible to form succinic anhydrides. Even multicomponent reactions can be engineered by the addition of isocyanates to a carbonylation mixture to afford 1,3-oxazinane-2,4-diones or by the addition of sulfur to afford 1,3-oxathiolan-2-ones. The key to successful implementation of these reactions is the choice of transition-metal catalyst. Two classes of catalyst are available, one of which has been pioneered and extensively developed by Professor Coates and his research group, namely, the hybrid cationic Lewis acid-tetracarbonylcobaltate salts. These salts (based on aluminum or chromium) act as bifunctional catalysts in which the cationic Lewis acid activates the epoxide by coordination to the oxygen electron pairs, thus enabling attack by the cobaltate anion on one of the carbon atoms. An interesting sequence of insertion, capture, and reductive elimination leads to the lactone product and regenerates the catalyst. Other catalysts, based on iron, rhodium, or palladium that do not require Lewis acid activation and are specific for conjugated epoxides. Thanks to the superb expertise and clear descriptions from the Coates laboratories, these reactions are now operationally straightforward, functional group tolerant, and provide access to a diverse array of useful building blocks for small molecule and polymer synthesis.

The second chapter authored by Ari M. P. Koskinen and Antti O. Kataja details the controlled dimerization and trimerization of aldehydes known as the Tishchenko Reaction. Known for over 100 years, the “classical” Tishchenko reaction involves the

catalyzed redox dimerization of aldehydes to form esters. This variant is mechanistically related to the Cannizzaro Reaction (*Org. React.* **1944**, 2, 94) and Oppenauer Oxidation (*Org. React.* **1951**, 6, 207) in that a hydride transfer takes place from a tetrahedral adduct of one aldehyde molecule (formed from the metal alkoxide catalyst) to another aldehyde molecule, thus increasing the oxidation state of the first while lowering the oxidation state of the second. The newly generated alkoxide then reenters the catalytic cycle thereby creating a symmetrical redox dimer. Many different classes of alkoxide catalysts have been employed over the years and their advantages and disadvantages are clearly outlined in this chapter. In recent years a more modern variant of the process has been developed which involves a tandem, aldol-Tishchenko sequence. In this variant, three molecules of an aldehyde are engaged, the first two combine in an aldol addition reaction to create a  $\beta$ -hydroxy aldehyde. The third aldehyde molecule is then captured by the hydroxyl group to form the selfsame tetrahedral intermediate involved in the "classical" Tishchenko reaction which then effects a hydride transfer to the aldehyde carbonyl group in the same molecule. By this process, a selectively protected, 1,3-diol monoester is generated. Because of the different roles of the aldehydes, this variant is better suited for creation of crossed-Tishchenko products in which different aldehyde components are incorporated. The recognition that an intramolecular redox process is occurring in the aldol-Tishchenko reaction has led to a third variant introduced by Prof. David A. Evans (Harvard University) which is thus called the Evans-Tishchenko reaction. The implementation of this variant begins at the advanced vantage point of an existing, stereo-defined, aldol product (an assembly intimately associated with Prof. Evans) and involves the use of a sacrificial aldehyde under catalysis by a samarium iodide. The geometrical restrictions of an intramolecular hydride transfer lead to the highly selective formation of *anti*-1,3-diol monoesters. This process has found extensive application in the synthesis of polyketide and other natural products that contain such functional arrays. Professor Koskinen and Dr. Kataja have expertly delineated the opportunities for all three of these variants and the catalysts preferred for specific combinations, including chiral catalysts. Their thorough and lucid presentation of chemistry that spans over a century will certainly facilitate the application of this process ... perhaps even inspire the invention of still newer variants!

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