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Enantioselective Synthesis: Introduction

Although enantioselective synthesis is sometimes viewed as a subdiscipline of organic chemistry, in actuality this topical field transcends any parochial classification and pervades essentially all of chemistry. Naturally, enantioselective synthesis strongly impacts upon pharmaceutical and agricultural chemistry, where the efficacy of a chiral biological agent often depends upon the enantiomer administered. However, a variety of solid-state materials and inorganic compounds can also be chiral and frequently have unique and exploitable properties in optically pure form. In all cases, enantioselective syntheses have the positive environmental consequence that unneeded by products can be reduced by up to 50%.

Importantly, many of the physical techniques employed in synthesis are capable of enantioselection. Of course, virtually all of the biological techniques are. Regardless of the reagents, apparatus, enzymes, antibodies, or empirical recipes utilized, complex mechanistic questions abound. Further, a diverse armament of analytical methods is required to assay enantiomeric excesses, and robotics has recently been enlisted for process optimization. Thus, this dynamic discipline unites leading research themes from organic, inorganic, physical, biological, materials, and analytical chemistry. From this convergence is coming some of the most exciting science of our times——advances that are recognized and narrated in this special issue of *Chemical Reviews*.

Two of the sixteen reviews in this issue focus on special techniques for enantioselective synthesis. The treatise by Santaniello, Ferraboschi, Grisenti, and Manzocchi provides a detailed overview of biocatalytic approaches, whereas Inoue classifies and analyzes a variety of types of asymmetric photoreactions. Four articles cover enantioselective variants of classical organic reactions. For example, Kagan and Riant review the rapidly developing area of catalytic asymmetric Diels–Alder reactions, while Mikami and Shimizu report on useful and elegant asymmetric ene reactions. Rossiter and Swingle provide an exegesis of the literture on asymmetric conjugate additions, and asymmetric metal-catalyzed transfer hydrogenations are systematized by Zassinovich, Mestroni, and Gladiali.

Since the carbonyl group is a key fulcrum for organic synthesis, it is not surprising that several reviews deal with asymmetric additions to aldehydes. Duthaler and Hafner treat chiral titanium reagents, whereas Soai and Niwa cover chiral organozinc compounds. Asymmetric aldol condensations feature prominently in Ito and Sawamura's analysis of secondary interactions between chiral ligands and substrates in enantioselective processes. Another group of articles spotlights important chiral synthetic targets. For example, Schurig and Betschinger describe metal-mediated enantioselective routes to unfunctionalized aliphatic epoxides, whereas Williams and Hendrix detail asymmetric syntheses of arylglycines. Valuable methods for the conversion of enolates to enantiomerically enriched α-hydroxycarbonyl compounds are enumerated by Davis and Chen.

Finally, four reviews focus on classes of chiral auxiliaries. Blaser provides an insightful compilation of naturally occurring "chiral pool" molecules that see use as components of enantioselective catalysts. Whitesell documents the broad utility of cyclohexyl-based chiral auxiliaries, frequently in the context of reactions noted above. The rapidly growing number of organometallic complexes with chiral cyclopentadienyl ligands, and their promising applications, are reviewed by Halterman. Chan and Wang report on advances in the use of chiral organosilicon compounds in asymmetric synthesis.

In summary, the articles in this special issue on "Enantioselective Synthesis" amply illustrate and justify the intense excitement that presently characterizes the discipline. However, the field is young, and this protasis can only hint at the developments to come. Single copies of this issue may be purchased, as detailed on the masthead page.

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