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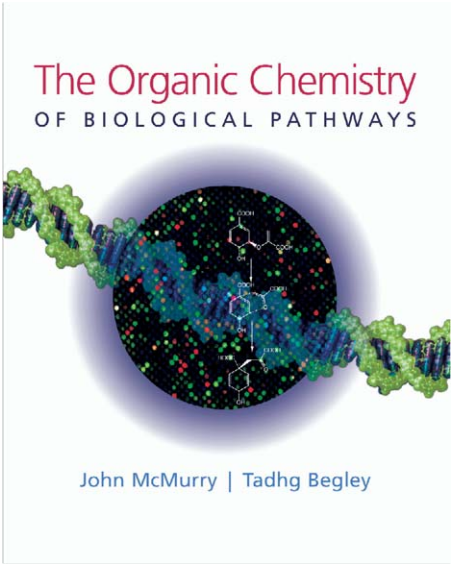
Book Review

The Chemistry of Metabolic and Biosynthetic Pathways

The Organic Chemistry of Biological Pathways
By John McMurry and Tadhg Begley
Englewood, CO: Roberts and Company Publishers (2005). 512 pp. $92.00



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The blossoming field of chemical biology is unique among the disciplines in that a thorough understanding of both chemical and biochemical concepts is necessary to advance the field. Most often, a combination of synthetic organic chemistry, enzymology, and molecular biology drives intellectual pursuits within the field. Unfortunately, new initiates into this fascinating area oftentimes lack the proper background or understanding of the interdisciplinary nature of chemistry and biology. This is partially due to the lack of an appropriate undergraduate/graduate-level textbook that lays the foundation and serves as a springboard for discussion. Elegantly filling the void is a new book authored by John McMurry and Tadhg Begley, prominent scholars in the fields of organic chemistry and mechanistic enzymology, respectively, elegantly fills this void. They have assembled a text that demystifies the world of enzymatic reactions by deconstructing them from an organic, mechanistic perspective. The information is presented in a very readable manner that should appeal to both chemists and biologists interested in learning more about the complementary nature of chemistry and biology.

This book contains eight chapters grouped into four main sections: (1) Common Organic Reactions in Biological Systems, (2) Metabolic Pathways for the Major Classes of Biomolecules such as Lipids, Carbohydrates, Amino Acids, and Nucleotides, (3) Biosynthesis of Natural Product Classes Represented by Nonribosomal Polypeptides, Alkaloids, Fatty Acids, and Polyketides, and (4) Summary of Biological Transformations. Additionally, the book includes an appendix with instructional information regarding the use of the free computer-based visualization program, the Swiss PDB Viewer (www.spdbv.niehs.nih.gov). A second appendix describes how to use KEGG (Kyoto Encyclopedia of Genes and Genomes, www.genome.ad.jp/kegg) and BRENDA (The Comprehensive Enzyme Information System, www.brenda.uni-koeln.de). These databases provide useful information related to the biosynthetic pathways of various primary and secondary metabolites as well as information on specific enzymes, respectively. The main strength of this book, which becomes immediately apparent as soon as one begins to read the text, is its meticulous attention to detail regarding the various enzyme-catalyzed chemical transformations. The mechanism for each reaction is carefully illustrated to depict accurately the structure of each intermediate along the reaction coordinate as well as the flow of electrons during the reaction. The use of color to highlight the functional groups involved as well as the electron flow allows one to follow the chemistry that is taking place. Moreover, many figures are accompanied by a step-by-step commentary that provides such useful information as the reaction class and nomenclature for reactive intermediates.

The first section provides a review of fundamental organic principles such as functional group nomenclature, acids and bases, and electrophiles and nucleophiles. This review is followed by a discussion of some of the common mechanisms encountered in biological systems: (1) Electrophilic Addition Reactions, (2) Nucleophilic Substitution Reactions, (3) Nucleophilic Carbonyl Addition Reactions including alcohol, imine (Schiff base), and acetal formation, and conjugate (1,4) additions, (4) Nucleophilic Acyl Substitution Reactions, (5) Carbonyl Condensation Reactions, (6) Elimination Reactions, and (7) Oxidation and Reduction Reactions. Each reaction class is discussed in sufficient detail so that novices to the field will readily acquire an appreciation of how these transformations occur.

The main portion of this book, comprising five chapters, focuses on the chemistry underlying the metabolic pathways involved in the formation and modification of lipids, carbohydrates, amino acids, and nucleotides. The first of these chapters serves as an introduction to each class of biomolecule, providing relevant examples of each while defining their important structural characteristics. Moreover, the chapter also provides the reader with a brief review of important chemical concepts as they relate to biological systems such as chirality, coupled reactions, and protein structure. This nicely introduces the next four chapters, each with a

more in-depth analysis of the chemistry of these important biological macromolecules. Not only do the authors provide many classic examples, but they also incorporate pathways that are of current intense interest in the scientific community. A nice facet of these chapters is that the involvement of coenzymes in enzymatic reactions is illustrated in the same detailed, yet clear and concise, mechanistic perspective as the rest of the text and not merely glossed over as in other textbooks.

The next portion of this book is dedicated to the biosynthesis of various natural products, also a forefront of research under intense scrutiny. The examples used, (1) Penicillins and Cephalosporins, (2) Morphine, (3) Prostaglandins and Eicosanoids, (4) Erythromycin, and (5) Coenzyme B_{12}, effectively illustrate the structural complexity of secondary metabolites while also demonstrating the myriad enzymatic reactions that were presented in previous chapters. Furthermore, traditionally difficult enzymatic reactions to comprehend, such as those catalyzed by iron-oxo enzymes, are explained in a manner that allows the reader to grasp fully the mechanistic subtleties and implications. This chapter also nicely illustrates how combinatorial biosynthetic methods can be used to alter the native metabolic pathway to produce structurally diverse compounds that may find use as novel chemotherapeutic agents. The final section in this book is a summary of biological transformations grouped by reaction type and a review of the different chemical reactions seen throughout the text.

While various textbooks are available that discuss enzyme-catalyzed reactions, they do so mainly from a biochemical perspective. The chemical perspective applied by McMurry and Begley to what is traditionally considered a biological domain is refreshing. They provide an exceptional contemporary overview of the field of mechanistic enzymology while elegantly integrating basic organic and biochemical theories and their application toward more complex systems. This book bridges the gap between traditional organic chemistry and biochemistry courses for junior/senior-level undergraduates or beginning graduate students. It fills a void in bioorganic chemistry and will appeal to students on both sides of the chemical biology divide.

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