

The Art of Writing Reasonable Organic Reaction Mechanisms. By Robert B. Grossman. Springer, 1999, 331 pp, DM 79, ISBN: 0-387-98540-9.

For many, an attractive feature of organic chemistry is that the basic principles taught in initial exposure to the field serve well as scaffolds for understanding new concepts and more complex transformations. It is certainly true that the outcome of a large number of reactions can be rationalized by a handful of “mechanisms,” which are the organic chemists’ method of representing what is occurring at the molecular level in a particular transformation. To a large extent the emphasis in undergraduate instruction is centered on these mechanisms. Nevertheless, the advanced undergraduate or the beginning graduate student often has trouble applying the understanding of basic mechanisms to those systems where there is greater molecular complexity or where multiple reactions occur in a single synthetic transformation. For the organic chemist, whether in industry or academia, this skill of rationalizing the transformation from reactant to product is considered essential, and it is especially important to those organic students who are in the various qualification stages in pursuit of a Ph.D. Bob Grossman’s book is written to teach students to formulate reasonable mechanisms for reactions they have not previously seen.

The Art of Writing Reasonable Reaction Mechanisms is organized around reaction types. In this respect it resembles a closely related book, *Writing Organic Reaction Mechanisms in Organic Chemistry*, by Audrey Miller (New York: Academic Press, 1992). The reaction types covered in the Grossman book include polar reactions under basic conditions, polar reactions under acidic conditions, pericyclic reactions, free radical reactions and transition metal-catalyzed and metal-mediated reactions (the transition metal-catalyzed and -mediated reactions are not covered in the Miller book). The first chapter is an introductory one that briefly covers conventions for drawing structures, concepts of acidity and basicity, some basic guidance in drawing mechanisms and an overview of the classes of mechanisms dealt with in more detail in the subsequent chapters.

The second chapter covers polar reactions under basic conditions and includes S_N2 reactions, substitutions at aryl and alkenyl carbons, addition of nucleophiles to electrophilic π bonds, addition-elimination reactions, $S_{RN}1$ reactions, carbene reactions and base-promoted rearrangements. “Polar Reactions under Acidic Conditions” (Chapter 3) covers carbocation formation and typical rearrangements, electrophilic addition to nucleophilic carbon-carbon double bonds, and acid catalyzed reactions with electrophilic π bonds.

The coverage in the chapter on pericyclic reactions is quite typical: electrocyclic reactions, cycloadditions, sigmatropic rearrangements and ene reactions. The reaction types are discussed in terms of typical reactions for each class, and the regioselectivity and stereoselectivity of the

transformations. Sufficient discussion of MO’s is provided to rationalize regio- and stereochemical outcomes, and the illustrations in this chapter are particularly helpful in visualizing the transformations.

The following chapter on free-radical reactions includes free-radical substitution, addition and fragmentation reactions. Also covered in this chapter are reductions with metals and triplet carbene and nitrene reactions.

Chapter six covers transition metal-catalyzed and -mediated reactions and includes a brief introduction to the chemistry of transition metals. The coverage of metal-mediated reactions includes addition reactions (dihydroxylation of alkenes hydrozirconation, mercury-mediated additions to alkenes, organocuprate conjugate addition reactions, reductive coupling reactions and the Pauson-Khand reaction) and substitution and elimination reactions (the Ullmann reaction, the Tebbe reaction, chromium-mediated oxidation of alcohols and decarbonylation of aldehydes). The metal-catalyzed reactions covered include addition (hydrogenation, hydroformylation, alkene polymerization, nucleophilic addition to alkynes, oxidation of alkenes and sulfides, conjugate addition of Grignard reagents, and cyclopropanation), substitution (hydrogenolysis, carbonylation of alkyl halides, the Heck reaction, the Kumada, Stille, Suzuki and Sonogashiri couplings, allylic substitution), rearrangement (alkene isomerizations and olefin metathesis) and elimination reactions. The final chapter provides the opportunity to practice reactions that incorporate mixed mechanistic types.

The style of Grossman’s book might be described as “user friendly” and relatively informal. Grossman incorporates “Common Error Alerts”, which accurately reflect the common errors that students make in formulating plausible mechanisms. The book is well organized and could be readily utilized either as a textbook or as a self-help manual. The book has numerous examples of solved problems within the chapters and contains a multitude of problems at the end of each chapter. The problems are selected from the current literature, and solutions are available on the internet at no extra cost. I have taught a one-credit course with this book for three years, and, uniformly, the students have rated this book highly for its clarity and for the scope of the problems. Although there might be reason to quibble over minor points of coverage or choice of chapter for a particular topic (Grossman anticipates most of these in his introduction), the bottom line is that this book does an excellent job at its stated goal: “to teach students to come up with reasonable mechanisms for reactions they have never seen before.”

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The Organic Chemistry of Drug Synthesis, Volume 6. By Daniel Lednicer. Wiley: Chichester, 1999, 244 pp. £ 70. Hardback. ISBN 0-471-24510-0.

This is the latest volume in a series dealing with practical synthetic approaches to medicinally important drug candidates. The book covers both patent and open literature for the period 1994-1998. This has ensured continuity within the series since publication of the last volume (Volume 5) in 1995. This latest volume covers only drug candidates which are based on an understanding of the disease process. This is reflected in the large coverage of new disease areas in which receptors and enzymes are the targets. Drug candidates in these areas are exemplified by leukotriene receptor antagonists, HIV protease and fibrinogen inhibitors.

There are a total of 10 chapters in this volume which are followed by a well presented cross index of drugs, a cumulative index for volumes 1-6 and a subject index. The 10 chapters are as follows: open chain compounds (Chapter 1), monocyclic aromatics (Chapter 2), carbocyclic compounds (Chapter 3), five-membered heterocycles (Chapter 4), six- and seven-membered heterocycles (Chapter 5), five-membered heterocycles fused to one benzene ring (Chapter 6), six-membered heterocycles fused to one benzene ring (Chapter 7), β lactam antibiotics (Chapter 8), bicyclic fused heterocycles (Chapter 9), polycyclic fused heterocycles (Chapter 10).

As can be seen, material in the chapters is arranged and discussed in terms of chemical structure. This is in marked contrast to most medicinal chemistry books that tend to be arranged according to pharmacological categories. Coupled with the fact that synthetic organic chemists, in the opinion of this reviewer, are excited by chemical structures, presentation of the material in such a unified way should make the book user friendly and attractive to synthetic chemists. Although only thumbnail descriptions of the therapeutic action of the drugs is given, the biology is described in sufficient detail to permit understanding by at least an organic chemist in graduate school.

This reviewer, however, was disappointed in the following: (a) incorrect abbreviations and molecular formulae representation in some cases. For example on pages 24-25, 48-49, 63 the **benzyl** protecting group is incorrectly abbreviated as Bz. The correct abbreviation is **Bn**. **Bz** is the abbreviation for the **benzoyl** group; the molecular formulae for **thionyl chloride** through out the book is incorrectly given as SO_2Cl (pages 24, 95-96, 143, 147, 157, 180, 193 and 203) instead of SOCl_2 ; (b) incorrectly spelt named reactions: the **Mitsunobu** (pages 29, 95, 164, 208) and **Knoevenagel** (pages 36, 173) reactions are incorrectly spelt as Mitsonobu and Knoevnagel reactions respectively. It is important to get the named reaction correctly spelt to avoid "inventing" other named (albeit honorary!) reactions; (c) misuse of the word **stereospecificity** in the aldol condensation between the boron enolate **103** and ac-

rolein on pages 184-185. Strictly speaking this aldol reaction with the oxazolidinone (not "oxazolinone" as indicated in the book) chiral auxiliary (the Evans asymmetric aldol reaction) does not proceed stereospecifically per se as seems to be implied by the author. This reaction is in fact highly **diastereoselective** (highly **stereoselective**) exclusively in favor of the 2,3-*syn* aldol product with no trace of the 2,3-*anti* aldol product. Stereospecificity maybe used in the context of the geometry of the boron enolate determining a specific stereochemical outcome (such as the 2,3-*syn* stereochemical relationship in aldol product **104** on page 185). In general *Z* boron enolates expected from the chiral oxazolidinone auxiliary give rise to 2,3-*syn* aldol products while *E* enolates generally lead to 2,3-*anti* aldol products. Of course recent developments involving the use of Lewis acids in the Evans asymmetric aldol reactions using oxazolidinone-derived *Z* boron enolates lead to the "unexpected" 2,3-*anti* aldol products. In the absence of Lewis acids reactions between *Z* boron enolates based on the oxazolidinone chiral auxiliary and aldehydes proceed via the Zimmerman-Traxler pericyclic transition state (4 transition state models are possible) while in the presence of Lewis acids, the same reaction proceeds via an open transition state in spite of the same *Z* enolate geometry. In summary, stereospecific reactions are those reactions whose mechanism demands a specific stereochemical outcome (the mechanism offers no alternative pathways) while stereoselective reactions are those whose mechanism offers alternative, chemically equivalent pathways so that the reaction may select the most favorable pathway (kinetic control) or the most stable product (thermodynamic control). Stereoselective reactions (as with the reaction in question on page 184-185) commonly involve setting up one chiral centre in the presence of others. To be fair to the author perhaps more clarity as to the nature of the stereospecificity would have been good enough, needless to mention that stereospecificity and stereoselectivity are two widely misused terms amongst organic chemists.

In summary, this is an excellent, well-written, user friendly and informative book containing the organic chemistry of 250-odd compounds and 284 references mainly from the open and current literature. It contains some unusual reactions that should be a source of continued education to the synthetic organic chemist. It is highly recommended by this reviewer not only to graduate students, practising synthetic organic and medicinal chemists but also to teachers of courses in medicinal chemistry at undergraduate level and to science libraries.

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