ORGANIC CHEMISTRY

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Second Edition

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This book is dedicated to Courtney—
a loving daughter and burgeoning research chemist,
who perceives the beauty of organic chemistry as
readily as she sees the splendors of the Carolina coast
and the majesty of the Rocky Mountains.

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PREFACE

The manner of teaching organic chemistry has changed somewhat since my days as a student in the early 1970s. Most notably, organic chemistry textbooks offer more and better descriptions of topics in related fields, such as biochemistry and materials science; the internet allows one to search for information about specific topics; and computer software is readily available for modeling chemical structures and reactions. The overall level of sophistication has also risen for the presentation of traditional themes such as stereochemistry, bonding, reaction mechanisms, spectroscopy, and synthesis.

In spite of these changes, however, the mastery of organic chemistry as a course of study still requires a sound knowledge of the principles of molecular structure and chemical reactivity, which are topics introduced in most general chemistry courses. With such a background, a student studying organic chemistry begins to focus on a more limited set of atomic building blocks, particularly of carbon and its elemental neighbors. And while the study of a smaller portion of the periodic table might be expected to be easily manageable, understanding organic chemistry can still seem overwhelming because of the diverse ways that this handful of elements can combine and interact. To learn organic chemistry, one must grasp the recurring patterns that correlate the presented facts.

Toward that end, this textbook organizes and discusses the patterns of chemical reactivity, which constitutes the majority of the subject matter, by combining information about the structures of functional groups (the reactive portions of a molecule) with the reaction mechanisms (pathways of chemical reactions) that these functional groups undergo. This approach differs from the one presented in many other texts, which describe *every* type of reaction that can occur for a given functional group; each approach has its advantages and disadvantages. The one I have utilized here evolved from my objective to integrate discussions about biochemical processes with the types of reactions that are carried out in chemistry laboratories. With the use of two points of reference—structures *and* mechanisms—the similarities that associate biochemical and synthetic reactions can be appreciated more easily.

ORGANIZATION OF THE TEXT

A sound knowledge of structures, bonding, and stereochemistry—the three-dimensional arrangements and shapes of molecules—is required in order to understand the patterns of chemical reactivity. For that reason, this book begins in Chapters 1–4 with a detailed treatment of molecular structures. After Chapter 5, which describes some general aspects of chemical reactions, specific transformations are presented in the next several chapters.

Spectroscopic methods are then covered in Chapters 13 and 14 (and used in subsequent chapters), with the emphasis in the first of these two chapters on nuclear magnetic resonance (NMR) spectroscopy. Chapter 14 introduces other analytical methods and integrates a number of techniques for the elucidation of molecular structures.

The topic of chemical synthesis constitutes a sizable portion of Chapters 15 and 16, with the latter focusing on enantioselective reactions. As with the spectroscopic methods presented in the previous two chapters, synthetic methods are used throughout the remainder of the text.

Chapter 17 summarizes the structures and reactions of aromatic compounds, and then the next several chapters present information about the reactions associated with the carbon–oxygen double bond, a structural feature of organic molecules that is pervasive in biochemical systems. Chapters 18–24 pay particular attention to chemical reactions that occur in nature.

The final four chapters cover specific topics that make use of the basic structures and reactions that have already been presented. The closing two chapters describe the chemistry of amino and nucleic acids, which establish the background for subsequent studies in biology, biochemistry, and molecular biology.

EXERCISES

Rodger Griffin, Jr., who taught me organic chemistry, was fond of saying that organic chemistry was best learned by solving problems and not by reading chapter-by-chapter as one would do for a history or philosophy course. This text has many exercises incorporated within the text as well as at the end of each chapter. Furthermore, this second edition has included many more examples (solved exercises) within the chapters so that students can see successful approaches to problem solving. The accompanying *Solutions to Exercises* book has the answer to every exercise; in many instances, the approach needed to work toward the answer is included along with the factual solution.

TO THE STUDENT

"Organic Chemistry" at most colleges and universities carries the unfortunate status of being among the more difficult and demanding courses offered. With its position in the curriculum as the prerequisite for many upper level chemistry, biology, and pharmacy courses, its negative repute is unrivaled. No wonder many students refer to this two-semester sequence as the "premed weed-out courses!"

Your experience does not have to be that way, however. Below are listed several suggestions I make at the beginning of each semester aimed at maximizing my students' success in this subject.

- *Go to class and participate.*

  I have written as clearly about organic chemistry as I can, but let's be honest—if you could learn this stuff on your own by reading the book and working exercises, then you're a whiz kid and going to class probably won't matter. If you're a typical student, however, verbal explanations *will* help, and that's one thing that class is about. It's also about seeing how problems are solved and how others look at them. Students who genuinely participate usually learn a lot. They also impress their professors, which can't hurt.

- *Be prepared.*

  Read the sections in the book that will be covered in class on a given day and think about how the material fits with what you know or have covered recently. Much of the material that you will learn in your organic chemistry courses is conceptually new—organic chemistry is *not* a repeat of general chemistry. If you have an idea beforehand about the key points of the topics being discussed, you will learn the material faster. On the other hand, don't spend hours and hours reading and taking notes—organic chemistry is not an English or history course.

- *Study (even a little) every day.*

  Easier said than done: I had many teachers tell me this when I was a student, and I myself have said the same thing to countless students. Does anyone listen? Maybe for about a week at the beginning of the semester. Then the pressures of life and your other courses get in the way, and you're back to cramming the night before an exam. I learned this lesson by experience: If you want to do well, studying one hour each day of a week is at least twice as good as studying seven hours once each week.

- *Work the assigned exercises.*

  Understanding organic chemistry is about seeing and learning the recurring *patterns* that correlate the many facts being presented. Those who see and learn these patterns—among structures, chemical reactions, molecular properties—usually do well. Those who don't (or can't) learn these patterns will struggle. Your brain may be wired in ways that make it difficult for you to see the underlying design of organic chemistry. There's not much that can be done about this, but it doesn't mean you will fail—it just means that you may have to work harder than others in order to succeed. The best way to learn these patterns is to work problems. And then work more problems. And then work even more problems.

  The answers to many of the study exercises may not be obvious when you first read the problem. Do not give up quickly and do not consult the *Solutions to Exercises* book without making a *determined* effort to solve the exercise on your own. Many people can read an answer and understand it. Don't be fooled into thinking that you can solve problems because you understand the answers when you see them. Write the solution to each exercise on paper. Even if the answer seems obvious, writing it will help you remember and learn. Also, do several problems before you look at their answers. If you look up the solution as you do each exercise, you may catch a glimpse of the answer to the next problem. The result is that you are not really working the next one.

- *Make flash cards.*

  In addition to doing the study exercises, some students find it useful to make "flash cards," especially to learn the many chemical reactions that you will have to commit to memory. A set of cards with important information makes it easy to review the course material while you're waiting for a movie to begin, sitting between classes, riding the bus, or any time during the day when you may have five or ten minutes to study. Organic chemistry is a cumulative subject. At the end of the semester, you will need to know material presented on the first day of the course just as much as you will need to know it for the first exam. A set of cards will be invaluable for review. NOTE WELL: Using flash cards prepared by someone else has limited benefit. Much of their advantage comes from having to think about structures and chemical reactions enough to prepare the cards.

- *Before an exam, get a good night of sleep.*

  Many of you will be expected to solve problems on exams that you have not seen before. If you have studied regularly, then being alert and relaxed is more important than last minute cramming. If you haven't studied regularly, you're probably in trouble whether you're rested or not. So you might as well be rested.

- *Get help early.*

  The sooner you realize that you're in trouble, the better. Go talk to your professor, a teaching assistant, or a tutor. Or form a study group. Some students find that other students can help them sort out confusing facts as well as anyone, and an added benefit is a measure of accountability to your peers.

I am always interested to hear from students about what works and what doesn't. If you find factual errors or discussions that are confusing, please send me an email to let me know (sorrell@unc.edu). Such comments are important to keep this text evolving so that it is as useful as possible to its readers—you, the students. Sometimes the most innocent remark can make me understand where a student has lost the thread of thought that winds through the presentation of a particular topic, and it is that type of input that teaches me and helps me to teach others better.

TO THE INSTRUCTOR

As noted in the Preface to the first edition of this book, I became dissatisfied with many organic chemistry texts when I started teaching biochemistry. The same students who had done well in organic chemistry could not seem to remember even simple reactions related to the ones being covered in the biochemistry course. Yet I remembered, for example, covering the structures and reactions of carbohydrates, amino acids, and nucleic acids in the previous courses. I concluded that the text we were using had failed to *associate* the material shared by the two disciplines because the topics related to biochemistry were segregated within their own chapters and students had compartmentalized the material they had learned, mentally labeling the information as "organic chemistry" or "biochemistry."

In writing this textbook, and especially this second edition, my goal has been to integrate the information about many of the fundamental biochemical reactions with the corresponding transformations that are carried out in organic chemistry laboratories. Many who teach the biochemistry courses will give scant attention to the details of the chemical reactions that constitute metabolic processes, which I think is useful information to be learned by the students who hope to pursue a career in the health professions and who constitute the majority of those taking organic chemistry. The organic chemistry courses provide the best (and perhaps only) forum to make students aware of such details. I believe that this awareness can be facilitated by illustrating the parallels between biochemical processes and the simpler chemical reactions that are being discussed. Even if students cannot remember specific facts later, they will likely recall that such associations exist; and they will be more likely later to dig out their organic chemistry texts to review these topics when they want to understand a particular biochemical process at the molecular level. As most organic chemistry instructors know, the key for understanding chemical reactions resides in comprehending their mechanisms. Therefore, reaction mechanisms comprise the major organizational theme of this text, and their details are presented in order to illustrate and underscore the similarities between synthetic and biochemical processes.

To develop these connections about chemical reactions, however, one cannot gloss over the facts about molecular structures, stereochemistry, and thermodynamics. Therefore, these topics are developed in the first five chapters of this book, and I trust they are presented with sufficient depth that students who intend to become organic chemists will not be shortchanged. Toward that same end of serving the future chemists in the organic chemistry classes, I have also included presentations of synthetic reactions that appear frequently in the current literature (e.g., the Misunobu, Swern, and Suzuki reactions) as well as topics such an enantioselective synthesis and molecular recognition.

NEW TO THIS EDITION

Based on the feedback given to me by hundreds of students as well as from the critiques of the dedicated reviewers listed in the Acknowledgments, several of whom taught their courses using the first edition of this text, I have made changes that are meant to make the material better organized and easier to understand. I estimate that one-quarter to one-third of the text has been completely rewritten. A substantial change in the content comprises the inclusion of more examples (solved exercises).

As is often true of second editions, a number of the more specialized topics (and chemical reactions) that appeared in the first edition have been left out. Most notably absent is the first chapter of the previous edition, which provided a historical perspective of organic chemistry. The current first chapter—on basic structures and nomenclature—still stands as the organizational pillar of structural chemistry for the book, but it has been modified by incorporating the strategies for naming compounds (which was Appendix A in the first edition) and eliminating the discussions of some types of groups that are better saved until later in the book (esters, in particular).

The first chapter that concerns a specific type of chemical reaction (nucleophilic substitution) has been expanded and divided into two chapters in this edition (Chapters 6 and 7). In this way, alkyl halides and alcohol substitution reactions are treated separately, and some sulfur-containing molecules are now included in the chapter on alcohols.

The oxidation reactions of alcohols have been removed from the chapter on elimination reactions (first edition), and a separate chapter on reduction and oxidation reactions has been created here (Chapter 11). The information in this chapter also includes discussions about the reduction and oxidation reactions of alkenes, which were covered previously in a chapter about alkene addition reactions. Also, the chemistry of dienes, including the Diels–Alder reaction, have been collected in a chapter separate from the one devoted to the addition reactions of simple alkenes.

The order of topics in the chapters that present spectroscopic methods has been reversed from that in the previous edition, so nuclear magnetic resonance spectroscopy is now covered first. The subsequent spectroscopy chapter integrates the use of several techniques, including elemental analysis, for the elucidation of molecular structures.

The chapter that introduces synthetic methods has been largely preserved from the first edition, but it is followed directly by the chapter on enantioselective synthesis (previously, these two chapters were separated by the spectroscopy chapters). The discussion of enantioselective reactions has been completely rewritten, and its emphasis has been changed to encourage students to think about designing enantioselective syntheses without having to memorize a lot of details about specific reagents and conditions.

The topic of aromatic compounds (benzene and its derivatives) has been moved (from Chapter 12 in the first edition to Chapter 17 in the second) with the material on polycyclic arenes combined with an abbreviated discussion of heterocycles in Chapter 24. The presentations about diazonium compounds and nucleophilic aromatic substitution reactions, which were in the chapter on nitrogen-containing compounds (Chapter 23, first edition), have been incorporated into Chapter 17 (second edition).

The chapters describing carbonyl compounds have been kept largely intact. The most significant change is the division of Chapter 17 (first edition) about aldehydes, ketones, and carbohydrates into two chapters in the current edition. The division has been made according to the reaction mechanisms involved (nucleophilic addition versus nucleophilic addition—substitution), not according to the functional groups that are undergoing the reactions.

The chapter on nitrogen-containing compounds (Chapter 23 in the first edition) has been parceled in this edition among several chapters, as appropriate. In contrast, the discussions of polymer chemistry, which were interspersed throughout the book in the first edition, have been collected to form Chapter 26 in this edition. Some basic presentations of polymerization processes have been left in the earlier chapters to show the mechanistic similarities to other fundamental reactions, but many of the details are developed in this later chapter.

The final two chapters on amino and nucleic acids, including the topic of molecular recognition, are similar in style and content to those in the first edition.

ACKNOWLEDGMENTS

For its creation, a good textbook requires participation by many people besides the author, and I am profoundly grateful to the following individuals for the work they did to make this second edition a reality.

With their comments and questions while using the first edition of this text, the students that I have taught during the past several years contributed invaluably to the development and writing of this second edition.

My daughter Courtney, who is now a graduate student in chemistry at Georgia Tech, was especially helpful during the early and middle stages of the writing process as she helped with the typing, both of the text and *Solutions to Exercises*. Her work at Synthematix (a local startup company that has since been acquired by Symyx Technologies, Inc.), gave her the experience to offer suggestions that helped organize several topics better.

My professional peers offered much in the way of their technical comments, corrections, and support. At the University of North Carolina at Chapel Hill, my colleagues Maurice Brookhart, Joseph DeSimone, Richard Hiskey, Paul Kropp, and Gary Pielak shared their valuable expertise on specific topics that appeared in both editions. Paul Kropp suggested some especially constructive changes for this edition as a result of using the book in the Honors courses at UNC. At other institutions, the following persons read all or parts of the manuscripts and provided detailed critiques and suggestions that helped make the text more readable, more accurate, and more pedagogical.

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David Bergbreiter	*Texas A&M University*	Neil Marsh	*University of Michigan*
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During and after the writing process, a large amount of work is required to produce a finished book from hundreds of files containing the text and figures. As a publisher, Bruce Armbruster is among the best at orchestrating this transformation,

and along with Kathy Armbruster and Jane Ellis, this team at University Science Books did their usual excellent job. Mary Castellion, herself an author, was an especially effective collaborator during the writing of this edition in helping me to edit the previous text and to present more succinctly and accurately some of the difficult concepts. Jeannette Stiefel did a masterful job with the copy edit, while Ann Knight coordinated the production.

The accompanying *Solutions to Exercises* was originally fashioned with significant help from Julius Beau Lucks, a former undergraduate student who was a Churchill Scholar after graduation and is currently a graduate student in chemistry at Harvard University. Beau worked every exercise in the first edition and checked their solutions. Subsequent groups of students have found and corrected some errors in those solutions; the second edition of the *Solutions to Exercises* text was copyedited and checked by Christine Cleveland, a student in my 2002–03 course who will be attending the UNC–CH School of Medicine beginning in the 2005 fall semester.

I sincerely thank all of you for the efforts and support you have contributed to this creative process.

Thomas Sorrell

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