Media Reviews

Organic Chemistry. By J. P. Clayden, N. Greeves, S. Warren, and P. D. Wothers; Oxford University Press, 2001, ISBN 0 19 850346 6, 53 Chapters, 1508 pages. Cost is £31.99 and the solutions manual is £18.99.

This text opens with a sequence of eight chapters which covers the ery basic skills that students require for understanding organic chemistry. Thus, a useful early chapter shows students how to draw organic molecules using the structural shorthand of chemistry; an essential skill ignored in many texts. A chapter on the methods that are used to determine structure follows, and the text then moves on to consider structure in more detail. Some of this material is mathematical in concept, but is well presented, and allows the nonmathematical student to get the important information; a fact facilitated by excellent in-chapter summaries. Atomic orbitals, molecular orbitals, bond formation, and hybridization are introduced, which prepare the reader for a section on reactivity. Electron flow and orbital overlap form the background to this section, and great emphasis is placed on the use (and incorrect use) of curly arrows. Nucleophilic addition to the carbonyl group is selected as the first reaction to be detailed, and, given the central role of carbonyl compounds within organic chemistry, this choice makes a refreshing change from the usual alkane, alkene, alkyl halide type of approach. This approach is logical because the addition of a nucleophile to a carbonyl is easier to understand than S_N1, S_N2, etc., which many texts introduce very early on. Chapters on conjugation and delocalization, and on acidity, basicity, and pK_a complete the introductory eight chapters on structure and reactivity.

The next fifteen chapters consider the most important classes of organic reaction in more detail. Carbonyls are well covered, with chapters on carbon–carbon bond formation from carbonyl plus organometallic, on conjugate additions to enones, on the addition of nucleophiles to carboxylic acid derivatives, and on nucleophilic substitution at carbonyl with loss of the carbonyl oxygen. Also included are chapters dealing with the following reaction types: nucleophilic addition at a saturated center (S_N1 and S_N2, but also the Mitsunobu and Staudinger reactions); elimination reactions (E1, E2 and E1cB); electrophilic additions to alkenes; the formation and reactions of enols and enolates, including stable enolate equivalents and enol ethers; electrophilic aromatic substitution; electrophilic alkenes (which looks at Michael acceptors and nucleophilic epoxidation); nucleophilic aromatic substitution (the addition–elimination mechanism, the S_N1 mechanism for nucleophilic aromatic substitution, the benzyne mechanism) and, finally, allylic systems (including a look at S_N2'). Chapters on aspects of NMR (^1H, ^{19}F, ^{31}P, heteronuclear couplings, etc.), together with chapters on kinetics and thermodynamics, chirality, and conformational analysis (alkanes and cycloalkanes, including student-friendly drawing tips) make up the remaining part of these fifteen chapters. These chapters are well written, cover all the crucial points, and form the core of any undergraduate course in organic chemistry. The reader is provided with lots of engaging instances of chemistry in context. Examples include explorations of cassava and cyanohydrin chemistry, a consideration of cimetidine and pK_a, lithiation and the synthesis of the antitumor antibiotic fredericamycin, termite self-defense, and the synthesis of a spider toxin by reductive amination.

With the basic foundations of the subject now laid, the text moves onto a further 28 chapters (over 900 pages) of in-depth discussion on many of the more advanced aspects of undergraduate level organic chemistry, often in important subject areas not covered in other general organic texts. There is a focus on synthesis and mechanism, and on why chemists select each step of a given synthetic sequence. The whole is illustrated throughout by up-to-date examples of synthesis, with many important reactions and reagents receiving coverage.

Appropriately enough, therefore, Chapter 24 deals with issues of chemoselectivity, and uses the familiar ground of carbonyl chemistry to deal with many important concepts, such as selectivity in oxidation and reduction, and introduces reactions such as Dess–Martin and Swern. A useful list of protecting groups is developed within this chapter. The next chapter provides some all-important, well-selected examples of synthesis that will enable the student to begin to understand how and why a sequence is planned. The examples used include the hormone thyroxine, and, by way of illustrating carbonyl chemistry and protecting group chemistry, peptide synthesis. A four-chapter, 100-page section covers the alkylation of enolates, the reactions of enolates with aldehydes and ketones, acylation at carbon, and conjugate additions of enolates.

A chapter on the control of double bond geometry looks at Julia, Peterson, Wittig, and alkyne-based methodologies. A highly readable chapter on retrosynthetic analysis brings together many of the reactions and principles discussed in earlier parts of the book, and allows the student to see that they are now able to plan synthetic sequences. The determination of stereochemistry by spectroscopic means gets a chapter, and includes a useful introduction to the NOE. Stereoselective reactions of cyclic compounds (focusing on six-membered rings) and diastereoselectivity (looking at reactions of alkenes, carbonyls, and the aldol reaction) are presented in two further chapters.

Pericyclic reactions are split into two chapters, one of which details cycloaddition reactions ([2 + 2], 1,3-dipolar, Diels–Alder), whilst the other deals with sigmatropic and electrocyclic reactions. Both chapters are nicely illustrated with examples of pericyclic reactions in natural product synthesis. A chapter on the common rearrangements (Payne, Baeyer–Villiger, Beckmann, etc.), and their use in synthesis, is followed by a chapter on fragmentation, which is illustrated with total syntheses of longifolene and nootkatone. Chapter 39 is dedicated to free radical chemistry, although some of the material in this chapter could, perhaps, have been put into an earlier introductory chapter on free radicals. A chapter on carbenes considers the generation and use of carbenes, focusing on synthetically useful processes such as cyclopropanation and Grubbs' olefin metathesis.

Saturated heterocycles, and the synthesis, structure and chemistry of the aromatic heterocycles are dealt with in three separate chapters. These deal with issues such as rate of formation of saturated rings, the Thorpe–Ingold effect,

Baldwin's rules, and the synthesis, properties and chemistry of pyridines, pyridones, pyridine-*N*-oxides, pyrroles, furans, thiophenes, indoles, quinolines, and isoquinolines. Also covered, albeit in less detail, are less common heterocycles such as imidazoles, triazoles, benzotriazoles, purines, pyrazines, oxazoles, thiazoles, and porphins. A look at the synthesis of compounds such as Viagra and the dihydropyridine antihypertensives serves to illustrate the important role of heterocyclic synthesis in medicine. A chapter on asymmetric synthesis starts with chiral-pool synthesis, and contains some well-chosen examples from the amino acid and sugar chiral pools. Asymmetric synthesis itself occupies the rest of this excellent chapter, with particular focus on chiral auxiliaries and catalytic asymmetric synthesis, with, for example, information on Evans' oxazolidinone auxiliaries, the CBS reagent, Sharpless' asymmetric epoxidation, and asymmetric dihydroxylation.

The organic chemistry of sulfur gets a chapter almost to itself (there is a short section on selenium), and this serves as an excellent introduction to the subject, covering subjects such as sulfonium ylides, the synthesis and chemistry of sulfoxides, and the Swern oxidation. These are well illustrated by the synthesis of the natural product nuciferal, and a by tour of the chemistry of the *Alliums*. A chapter on boron, silicon, and tin follows. Boron is dealt with well enough, and hydroboration receives good coverage. The relatively lengthy silicon section covers some very important material, but does so in a style that seems to lack the usual focus and context; indeed, this is one of the very few examples where a jarring change of style makes itself apparent (the free radical chapter is another). A short section on organotin compounds usefully deals with tin–lithium exchange. An organometallic chapter focuses on palladium, but does look briefly at other metals (iron, iridium, and cobalt). The Heck reaction, Stille coupling, Suzuki coupling, Sonagashira coupling, and π-allyl complexes are discussed, and the section is illustrated superbly by Hegedus' synthesis of the ergot alkaloid clavicipitic acid, which utilizes four palladium steps.

A chapter entitled "The Chemistry of Life" looks at nucleic acids, proteins, sugars, and lipids, but, with the exception of the sugar section, does so in far less detail than that required by many university courses in organic chemistry. Two additional chapters cover mechanisms in biological chemistry and natural products and their biosynthesis, and these are very well detailed and explained, providing the student with an excellent opportunity for revision of previous material. A look at amino acid biosynthesis, racemization, and decarboxylation starts these chapters. A consideration of Nature's enols links the glycolysis process to the citric acid cycle and the role and biosynthesis of acetyl CoA, and includes a detailed look at the functions of thiamine pyrophosphate. The shikimic acid pathway is covered in detail in a chapter that also contains some chemistry pertaining to amino acid ammonia lyases, biotin, hemoglobin and oxygen transfer, and $FAD/FADH_2$ (hydroxylation). The biosynthesis of the pyrrolidine and isoquinoline alkaloids, the fatty acids, polyketides, terpenes, and steroids all receive good coverage.

The penultimate chapter concerns polymerization. A look at several familiar polymers is followed by consideration of the main polymerization mechanisms, including consideration of co-polymerization and cross-linking. This section is illustrated by familiar polymers such as Bakelite, Araldite, elastomer, PVC, polystyrene, Teflon, and the acrylics and finishes by describing the Ziegler–Natta polymerization of alkenes. Time is given to study the reactions of polymers (vulcanization, for example), and this allows a discussion of polymer bound synthesis and polymer bound reagents to develop. This looks at polymer-supported Wittig reactions and solid phase peptide synthesis. The final chapter has the title "Organic Chemistry Today", and the main theme is a well-explained synthesis of the HIV protease inhibitor Crixivan, with great emphasis placed upon fundamental research in organic synthesis, and the multidisciplinary nature of the research that led to the development of this drug.

In summary, this text contains everything that is relevant to the study of university-level organic chemistry. The first twenty-three chapters lay down a solid foundation of the key concepts and reactions, which are central to understanding organic chemistry. These chapters are presented in a style that facilitates an understanding of the subject—they have a friendly approach and take time to build upon those all-important areas of familiarity. The tradition of using alkane, alkene, alkyne, and alkyl halide as the focus for the opening reactions is abandoned in favor of a carbonyl opening; this approach works well.

Chapters that will make the text stand out from the many other similar sized texts entitled "organic synthesis" are those which provide in-depth coverage of important subjects that often get little space in many general organic chemistry texts. These chapters cover retrosynthesis, synthesis in action, chemoselectivity, controlling double bond geometry, carbenes, saturated and aromatic heterocycles, rearrangements and fragmentations, asymmetric synthesis, organo–main-group and organometallic chemistry, mechanisms in biological chemistry, natural products and biosynthesis, advanced carbonyl chemistry, and the later chapters relating to stereochemistry and spectroscopy. These chapters present important and up-to-date reactions, which are often backed up by well-chosen synthetic sequences, and which enable the student to see how an understanding of organic chemistry links in to the real and natural worlds.

A potential disadvantage of this text is the surprising number of errors. The first error in a chemical structure occurs on the first page with the first structure. The book contains several other errors in chemical structures (for example, grandisol on page 649, aspartic acid on page 654, aspartame on page 655, and Tagamet on page 1147), whilst on page 1349 (—ATT—) pairs "reliably with (—TTA—)." There are errors with the cross-referencing, for example on pages 969 (sigmatropic rearrangements) and 649 (nitrile reaction "on p. 528"). There are also annoying production errors (for example, the truncated diagrams on pages 27, 193, and 319; and symbol-font or typographic errors on pages 86, 176, 319, and 1300).

In its current edition, I can certainly recommend the text as an excellent tool and resource for the tutor, teacher or instructor of organic chemistry. As a text for students to purchase and use, I would certainly put the text on a reading list. I would, however, have some minor reservations about its use as "the text to buy" for organic chemistry, given the current level of errors. This is a shame, because if this book had been thoroughly proofread and corrected, then I would have no hesitation in recommending its adoption as *the* text for

purchase and use by students undertaking a university course in organic chemistry.

Karl Hemming
Department of Chemistry and Biological Sciences,
University of Huddersfield

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