

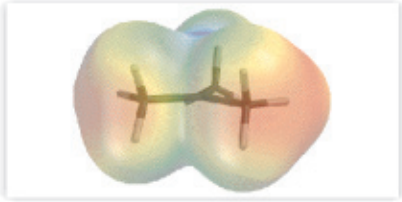
A GUIDE TO USING THIS TEXT

The following pages provide a walk-through of the key features of this text. Every element in this book has a purpose and serves the overall goal of leading students to a true understanding of the processes in organic chemistry.

INTEGRATED TEXT AND VISUALS

With All-new Figures

Because visualization is so important to understanding, illustrations work hand-in-hand with text to convey information. The author generated many of the figures himself as he wrote the text using Spartan software, so that images are fully coordinated with the text.



CHAPTER 4
ALCOHOLS AND ALKYL HALIDES

On the first page, a diagram established some fundamental principles concerning the structure of organic molecules. In this chapter we begin our discussion of organic chemical reactions by discussing reactions to alcohols and alkyl halides. These two reactions are the most useful classes of organic compounds because they often serve as starting materials for the preparation of numerous other families.

Two reactions that lead to alkyl halides will be described in this chapter. Both illustrate functional-group transformations. In the first, the hydroxyl group of an alcohol is replaced by halogen as treatment with a hydrogen halide.

$$\text{R-OH} + \text{H-X} \rightarrow \text{R-X} + \text{H}_2\text{O}$$

Alcohol Hydrogen halide Alkyl halide Water

In the second reaction with chlorine or bromine, one of the hydrogen substituents of an alkane is replaced by halogen.

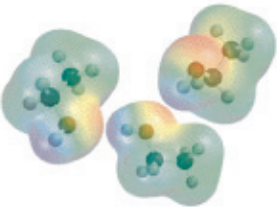
$$\text{R-H} + \text{X}_2 \rightarrow \text{R-X} + \text{H-X}$$

Alkane Halogen Alkyl halide Hydrogen halide

Both reactions are classified as *substitutions*, a term that describes the relationship between reactants and products—one functional group replaces another. In this chapter we go beyond the simple listing of reactions and products and consider the mechanism of each reaction. A *mechanism* attempts to show how starting materials are converted into products to bring a chemical reaction.

While developing these forms of reaction and mechanism, we will also use alcohols and alkyl halides as vehicles to extend the principles of IUPAC nomenclature, a

4.1 Physical Properties of Alcohols and Alkyl Halides Before Chemical Tests 111



PROBLEM 4.1 Hydrogen bonding in ethanol involves the oxygen of one molecule and the proton of an -OH group of another. Hydrogen bonding is much stronger than most other types of intermolecular attractions.

parties involved must be bonded to an electronegative element, usually oxygen or nitrogen. Because a C—H bond does not participate in hydrogen bonding, thus, because there, even though it is a polar bond and supports a dipole-dipole attraction, does not form hydrogen bonds and, therefore, has a lower boiling point than ethanol.

Hydrogen bonding can be expected in molecules that have —OH or —NH groups. Individual hydrogen bonds are about 20–25 times weaker than typical covalent bonds, but the effects of multiple hydrogen bonds are often dipole-dipole attractive forces, so molecules hydrogen bonds are strong enough to impose a relatively high degree of structural order on systems in which they are possible. As will be seen in Chapter 17, the three-dimensional structures adopted by polymers and nucleic acids, the organic molecules of life, are directed by patterns of hydrogen bonds.

PROBLEM 4.5 The constitutional isomer of ethanol, dimethyl ether (CH₃OCH₃), is a gas at room temperature. Suggest an explanation for this observation.

Table 4.1 lists the boiling points of some representative alkyl halides and alcohols. When comparing the boiling points of related compounds as a function of the alkyl group, we shall find the boiling point increases with the number of carbon atoms, as it does with alkanes.

TABLE 4.1 Boiling Points of Some Alkyl Halides and Alcohols


Name of alkyl group	Formula	Functional group X and boiling point, °C (1 atm)					
		Cl	F	Br	I	OH	SH
Methyl	CH ₃ X	-78	-24	5	42	65	—
Ethyl	CH ₃ CH ₂ X	-25	12	38	72	50	—
Propyl	CH ₃ CH ₂ CH ₂ X	-3	47	31	102	58	—
Isopropyl	(CH ₃) ₂ CHCH ₂ X	65	106	129	159	124	—
Butyl	CH ₃ (CH ₂) ₃ X	90	134	155	185	137	—

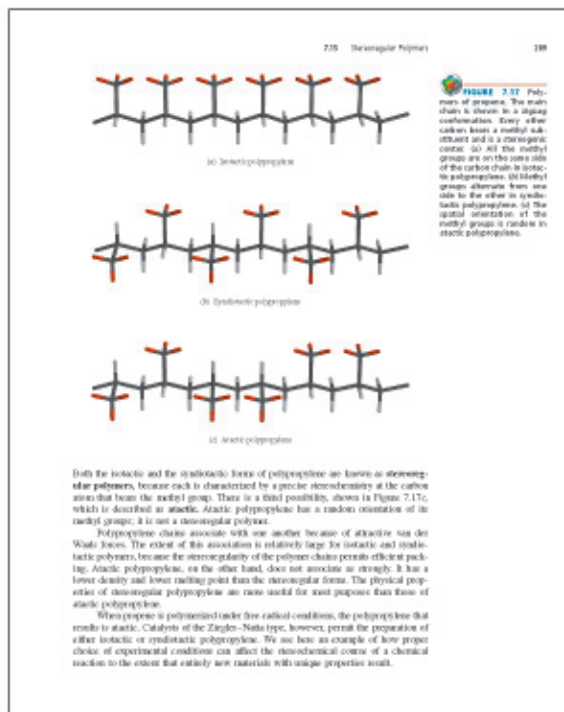
EFFECTIVE ORGANIZATION OF FUNCTIONAL GROUPS

Reaction mechanisms are stressed early and often, but within a functional framework. For example, Chapter 4 is the first chapter to cover a functional group (alcohols and alkyl halides) but it introduces *mechanism* simultaneously.

LEARNING BY MODELING

A Full Correlation

Not only can students view molecular models while using the book, but with the free CD-ROM that accompanies the text, they have access to the software that was used to create the images. With the SpartanView and SpartanBuild software, students can view models from the text and also make their own. The SpartanView icon  identifies molecules and animations that can be seen on the CD. Appendix 3 provides a complete tutorial guide to the CD.



16.2 STRUCTURE AND BONDING IN ETHERS AND EPOXIDES

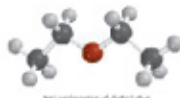
Bonding in ethers is readily understood by comparing ethers with water and alcohols. Van der Waals steric repulsion involving alkyl groups causes the bond angle at oxygen to be larger in ethers than alcohols, and larger in alcohols than in water. An extreme example is di-*tert*-butyl ether, where steric hindrance between the *tert*-butyl groups is responsible for a dramatic increase in the C—O—C bond angle.



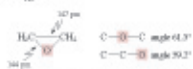
Typical carbon—oxygen bond distances in ethers are similar to those of alcohols (142 pm) and are shorter than carbon—carbon bond distances in alkanes (153 pm).

As ether oxygen affects the conformation of a molecule in much the same way that a CH₃ unit does. The most stable conformation of diethyl ether is the all-staggered and conformation. Simultaneously it is most stable in the chair conformation—a fact that has an important bearing on the structure of many carbohydrates.

 Click Learning by Modeling to explore models of many molecules, including water, methanol, dimethyl ether, and di-*tert*-butyl ether. Examine their geometries and compare what happens to the C—O—C bond angle. Compare the C—O bond distances in diethyl ether and di-*tert*-butyl ether.



Incorporating an oxygen atom into a three-membered ring requires its bond angle to be seriously distorted from the normal tetrahedral value. In ethylene oxide, for example, the bond angle at oxygen is 61.5°.




This epoxide, like cyclopropane, is strained. They tend to undergo reactions that open the three-membered ring by cleaving one of the carbon—oxygen bonds.

PROBLEM 16.2 The heats of combustion of 1,2-epoxybutane (2-ethyloxirane) and tetrahydrofuran have been measured: 2051.2 kJ/mol (491.6 kcal/mol); the other is 2548.8 kJ/mol (609.1 kcal/mol). Match the heats of combustion with the respective compounds.

Ethers, like water and alcohols, are polar. Diethyl ether, for example, has a dipole moment of 1.2 D. Cyclic ethers have larger dipole moments; ethylene oxide and tetrahydrofuran have dipole moments in the 1.7- to 1.8-D range—about the same as that of water.

LEARNING BY MODELING

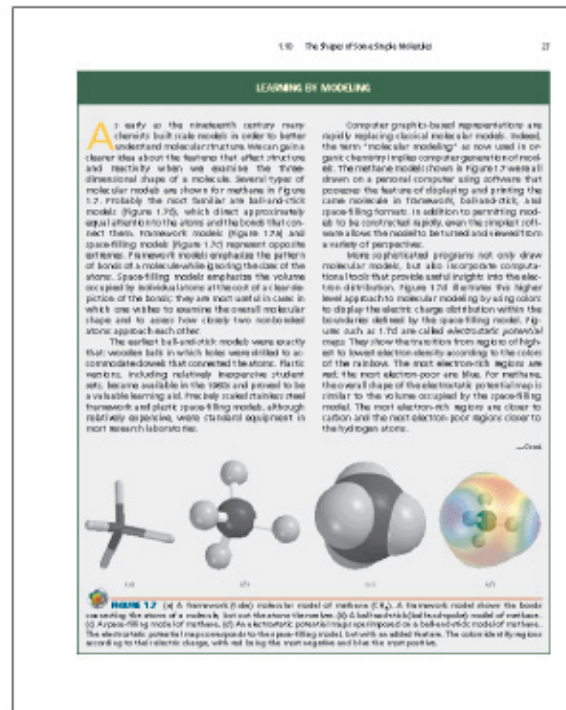
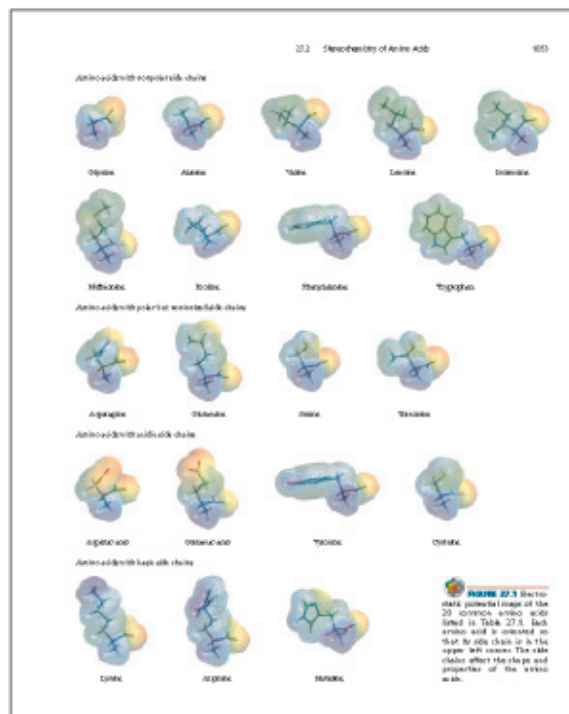
An Active Process

Many of the problems in this edition of the text have been expressly written to involve use of the SpartanBuild software on the *Learning By Modeling* CD-ROM. Students discover the connection between structure and properties by actually building molecules on their own. The SpartanBuild icon  directs them when to use this tool.

LEARNING BY MODELING

From Spartan to the Page

New in this edition's figures are molecular models that the author generated using the Spartan modeling application. Electrostatic potential maps give a vivid look at the charge distribution in a molecule, showing the forces that govern structure and properties in organic chemistry.



LEARNING BY MODELING

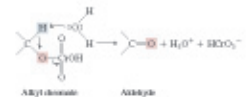
Build Biomolecules

In the biological-specific chapters, learning is once again enhanced by the access to Spartan model building. Carbohydrates, lipids, amino acids, peptides, proteins, and nucleic acid benefit from Spartan, and many for this edition were generated from imported crystallographic data. And students can view models of the 20 common amino acids on *Learning By Modeling*, and rotate them in three dimensions, or view them as ball-and-spoke, tube, or space-filling models.

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CHAPTER 15 Alcohols, Aldehydes, and Ketones

This allylic chromate then undergoes an elimination reaction to form the carbon–oxygen double bond.




Allylic chromate **Alpha,beta-unsaturated carbonyl**

In the elimination step, chromium is reduced from Cr(VI) to Cr(IV). Since the eventual product is Cr(III), further electron-transfer steps are also involved.

15.11 BIOLOGICAL OXIDATION OF ALCOHOLS

Many biological processes involve oxidation of alcohols to carbonyl compounds or the reverse process, reduction of carbonyl compounds to alcohols. Ethanol, for example, is metabolized in the liver to acetaldehyde. Such processes are catalyzed by enzymes; the enzyme that catalyzes the oxidation of ethanol is called alcohol dehydrogenase.



Ethanol **Acetaldehyde**

In addition to enzymes, biological oxidations require substances known as coenzymes. Coenzymes are organic molecules that, in concert with an enzyme, act on a substrate to bring about chemical change. Most of the substances that we call vitamins are coenzymes. The coenzyme contains a functional group that is complementary to a functional group of the substrate; the enzyme catalyzes the interaction of these mutually complementary functional groups. If ethanol is oxidized, some other substance must be reduced. This other substance is the oxidized form of the coenzyme nicotinamide adenine dinucleotide (NAD). Chemists and biochemists abbreviate the oxidized form of this

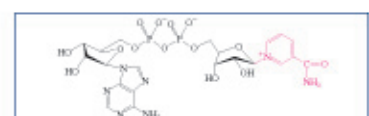


FIGURE 15.2 Structure of NAD⁺, the oxidized form of the coenzyme nicotinamide adenine dinucleotide.

BIOLOGICAL APPLICATIONS THROUGHOUT

While biological topics receive greatest emphasis in Chapters 25–27, they are also introduced throughout the book, reflecting their growing role in the study of organic chemistry. Examples include:

- Biological oxidation of alcohols (p. 600)
- Epoxides in biological processes (p. 637)
- “Methane and the Biosphere” (boxed essay, p. 58)
- A biological dehydrogenation (new, p. 181)
- Figure 19.5, showing a realistic representation of a micelle (p. 744)
- “Chiral drugs” (boxed essay, p. 273)

SPECTROSCOPY

Spectroscopy coverage is up-to-date and thorough in this edition. Chapter 13, “Spectroscopy,” features NMR spectra that were newly recorded on a high-field instrument, and all the text figures were produced directly from electronic files. In addition, spectroscopy is integrated into all the functional group chapters that follow 13: Chapters 15, 16, 17, 19, 20, 22, and 24, which contain spectroscopy sections and examples and problems based on displayed spectra.

13.9 Splitting Patterns: Pairs of Doublets

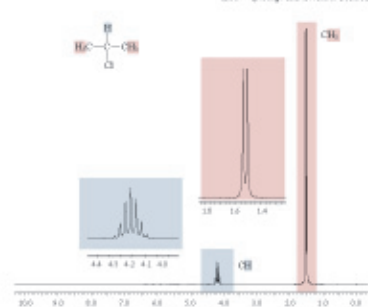
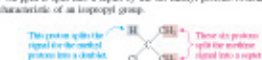


FIGURE 13.9 The 200-MHz ¹H NMR spectrum of isopropyl chloride, showing the doublet-split pattern of an isopropyl group.

13.9 SPLITTING PATTERNS: THE ISOPROPYL GROUP

The NMR spectrum of isopropyl chloride (Figure 13.9) illustrates the appearance of an isopropyl group. The signal for the six equivalent methyl protons at 1.5 ppm is split into a doublet by the proton of the H—C—Cl unit. In turn, the H—C—Cl proton signal at 4.2 ppm is split into a septet by the six methyl protons. A doublet–septet pattern is characteristic of an isopropyl group.



13.10 SPLITTING PATTERNS: PAIRS OF DOUBLETS

We often see splitting patterns in which the intensities of the individual peaks do not match those given in Table 13.2, but are disturbed in that the signals for coupled protons “lean” toward each other. This leaning is a general phenomenon, but is most easily illustrated for the case of two nonequivalent vicinal protons as shown in Figure 13.10.

$$H_1 - C - C - H_2$$

The appearance of the splitting pattern of protons 1 and 2 depends on their coupling constant *J* and the chemical shift difference $\Delta\delta$ between them. When the ratio $\Delta\delta/J$ is large, two symmetrical 1:1 doublets are observed. We refer to this as the “AA’” case, using two

74 CHAPTER TWENTY Carboxylic Acid Derivatives: Substituted Acyl Substitution

In acidic solution, water gives a new resonance form, which loses a molecule of alcohol in step 3. Along with the alcohol, the protonated form of the carboxylic acid starts the dissociation of the tetrahedral intermediate. Its deprotonation in step 6 completes the process.

PROBLEM 20.10 On the basis of the general mechanism for acid-catalyzed ester hydrolysis shown in Figure 20.4, write an analogous sequence of steps for the specific case of ethyl benzoate hydrolysis.

The most important species in the mechanism for ester hydrolysis is the tetrahedral intermediate. Evidence in support of the existence of the tetrahedral intermediate was developed by Professor Myron Bender as the basis of isotopic labeling experiments he carried out at the University of Chicago. Bender prepared ethyl benzoate, labeled with the mass-18 isotope of oxygen at the carbonyl oxygen, then subjected it to acid-catalyzed hydrolysis in ordinary (unlabeled) water. He found that ethyl benzoate, recovered from the reaction before hydrolysis was complete, had lost a portion of its isotopic label. This observation is consistent only with the reversible formation of a tetrahedral intermediate under the reaction conditions.

The two C—O groups in the tetrahedral intermediate are equivalent, and so either the labeled or the unlabeled one can be lost when the tetrahedral intermediate reverts to ethyl benzoate. Both are retained when the tetrahedral intermediate goes on to form benzoic acid.

PROBLEM 20.11 In a similar experiment, unlabeled 4-butanone was allowed to stand in an acidic solution in which the water had been labeled with ^{18}O . When the ketone was extracted from the solution after 4 days, it was found to contain ^{18}O . Which oxygen of the lactone do you think became isotopically labeled?

20.10 ESTER HYDROLYSIS IN BASE: SAPONIFICATION

Unlike its acid-catalyzed counterpart, ester hydrolysis in aqueous base is irreversible.

This is because carboxylic acids are converted to their corresponding carboxylate anions under these conditions, and these anions are incapable of acyl transfer to alcohols.

... AND MORE PROBLEMS

Every chapter ends with a comprehensive bank of problems that give students liberal opportunity to master skills by working problems. And now many of the problems are written expressly for use with the software on the *Learning By Modeling* CD-ROM. Both within the chapters and at the end, these problems are flagged with the Spartan-Build icon.

PROBLEM SOLVING—BY EXAMPLE

Problem-solving strategies and skills are emphasized throughout. Understanding of topics is continually reinforced by problems that appear within topic sections. For many problems, sample solutions are given.

66 CHAPTER SIXTEEN Ethers, Epoxides, and Sulfides

may be used to synthesize 2-methyl-1,3-dioxepane. Using the space proffers in this way, name each of the following compounds:

16.21 The name of the parent six-membered cyclic ether-containing heterocycle is dioxane. It is numbered beginning at sulfur. Multiple incorporation of sulfur in the ring is indicated by the prefixes di-, tri-, and so on.

16.22 How many methyl-substituted dioxanes are there? Which ones are chiral?

16.23 Write structural formulas for 1,3-dioxane and 1,3-dithiane.

16.24 Which dithiane isomer is a diastereol?

16.25 Draw the two most stable conformations of the molecule derived from 8.16c.

16.26 The most stable conformation of 1,3-dioxan-5-ol is the chair form that has its hydroxyl group in an axial orientation. Suggest a reasonable explanation for this fact. Building a molecular model is helpful.

16.27 Outline the steps in the preparation of each of the constitutionally isomeric ethers of molecular formula $\text{C}_4\text{H}_{10}\text{O}$ starting with the appropriate alcohols. Use the Williamson ether synthesis as your key reaction.

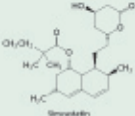
16.28 Predict the principal organic product of each of the following reactions. Specify stereochemistry where appropriate.

108 CHAPTER TWENTY-ONE Lipids

GOOD CHOLESTEROL? BAD CHOLESTEROL? WHAT'S THE DIFFERENCE?

Cholesterol is biosynthesized in the liver, transported throughout the body to be used in a variety of ways, and returned to the liver where it serves as the biosynthetic precursor to other steroids. But cholesterol is a lipid and isn't soluble in water. How can it move through the blood if it doesn't dissolve in it? The answer is that it doesn't dissolve, but it is instead carried through the blood and tissues as part of a lipoprotein (lipid + protein = lipoprotein). The proteins that carry cholesterol from the liver are called low-density lipoproteins, or LDLs; those that return it to the liver are the high-density lipoproteins, or HDLs. If too much cholesterol is being transported by LDL, or too little by HDL, the extra cholesterol builds up on the walls of the arteries causing atherosclerosis. A thorough physical examination nowadays measures not only total cholesterol concentration but also the distribution between LDL and HDL cholesterol. An elevated level of LDL cholesterol is a risk factor for heart disease. LDL cholesterol is "bad" cholesterol. HDL, on the other hand, removes excess cholesterol and also protects HDL cholesterol is "good" cholesterol.

The distribution between LDL and HDL cholesterol depends mainly on genetic factors, but can be altered. Regular exercise increases HDL and reduces LDL cholesterol, as does limiting the amount of saturated fat in the diet. Much progress has been made in developing new drugs to lower cholesterol. The statin class, beginning with lovastatin in 1988 followed by simvastatin in 1991 have proven especially effective.



The statins lower cholesterol by inhibiting the enzyme 3-hydroxy-3-methylglutaryl coenzyme A reductase, which is required for the biosynthesis of mevalonic acid (see Section 26.15). Mevalonic acid is an obligatory precursor to cholesterol, so less mevalonic acid translates into less cholesterol.

INSTRUCTIVE BOXED ESSAYS


The essays in the book aren't just for decoration; they help students think and learn by relating concepts to biological, environmental, and other real-world applications. Examples include:

- "Methane and the Biosphere"
- "An Enzyme-Catalyzed Nucleophilic Substitution of an Alkyl Halide"
- "Good Cholesterol? Bad Cholesterol? What's the Difference?"

THE SUMMARY

Summaries ending each chapter are crafted to allow students to check their knowledge and revisit chapter content in a study-friendly format. Learning is reinforced through concise narrative and through Summary Tables that students find valuable.

3.16 Summary 117



Lipids acid groups have required by a variety of different organisms. Lactonic acid contains the side of lactonic acid.

Many heterocyclic systems contain double bonds and are related to alicyclic. The most important representatives of this class are described in Sections 11.20 and 11.22.


3.16 SUMMARY

In this chapter we explored the three-dimensional shapes of alkanes and cycloalkanes. The most important point to be taken from the chapter is that a molecule adopts the shape that minimizes its total strain. The sources of strain in alkanes and cycloalkanes are:

1. Bond length distortion: destabilization of a molecule that results when one or more of its bond distances are different from the normal value.
2. Angle strain: destabilization that results from distortion of bond angles from their normal values.
3. Torsional strain: destabilization that results from the eclipsing of bonds on adjacent atoms.
4. Van der Waals strain: destabilization that results when atoms or groups on non-adjacent atoms are too close to one another.

The various spatial arrangements available to a molecule by rotation about single bonds are called **conformations**, and **conformational analysis** is the study of the differences in stability and properties of the individual conformations. Rotation around carbon-carbon single bonds is normally very fast, occurring hundreds of thousands of times per second at room temperature. Molecules are rarely frozen into a single conformation but engage in rapid equilibration among the conformations that are energetically accessible.

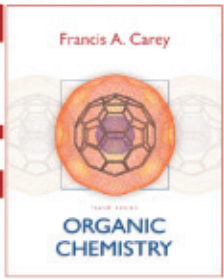
Section 3.5 The most stable conformation of ethane is the **staggered conformation**. It is approximately 12 kJ/mol (3 kcal/mol) more stable than the **eclipsed**, which is the least stable conformation.



Staggered conformation of ethane (lowest energy conformation) Eclipsed conformation of ethane (high energy conformation)

Organic Chemistry, 4/e

by Francis A. Carey



Francis A. Carey

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The exclusive Carey Online Learning Center, at www.mhhe.com/carey, is a rich resource that provides additional support for the fourth edition of *Organic Chemistry*, offering tutorials, practice problems, and assessment exercises for every chapter in the text.

The tutorial materials provide a short overview of the chapter content, drawing attention to key concepts. The Learning Center also provides access to review materials for these concepts, using multimedia images, movies, etc.—including Chime images—to enhance and facilitate learning. Practice problems and assessment exercises provide instant feedback, to pinpoint the topics on which a student needs to spend more time.