## ORGANIC HEMISTRY with Biological Topics

FIFTH EDITION

Mc Graw Hill Education Janice Gorzynski Smith Heidi R. Vollmer-Snarr

	-		n N	4	2	9	~	9	2
8A	Helium 4.0026	Neon 20.1797	Argon 39.948	Krypton 83.80	54 Xenon 131.29	Badon (222)	118 — (294)	Lutetium 174.967	103 Lr Lawrencium (260)
	ΤA	9 Fluorine 18.9984	Chlorine 35.4527	Bromine 79.904	53 Iodine 126.9045	B5 Atatine (210)	117 — (294)	Ytterbium 173.04	Nobelium (259)
	6A	Oxygen 15.9994	16 Sulfur 32.066	Selenium 78.96	Tellunium 127.60	Polonium (209)	116 LV Livermorium (293)	E9 Thulium 168.9342	Mendelevium (258)
	5A	Nitrogen 14.0067	Phosphorus 30.9738	Arsenic 74.9216	S1 SD Antimony 121.760	<sup>83</sup> Bismuth 208.9804	115  - (288)	68 Erbium 167.26	Fermium (257)
	4A	Carbon Carbon 12.011	Silicon 28.0855	Germanium 72.64	<b>SO</b> Tin 118.710	<b>PD</b> <sup>Lead</sup> <sup>2072</sup>	Flerovium (289)	67 Holmium 164.9303	Einsteinium (252)
	ЗА	5 Boron 10.811	Aluminum 26.9815	<b>Gallium</b> 69.723	49 Indium 114.82	Thallium 204.3833	113 	Dysprosium 162.50	Californium (251)
			2B	30 Zinc 65.41	Cadmium 112.411	Mercury 200.59	Copernicium (285)	E5 Terbium 158.9253	Berkelium (247)
			1B	Copper 63.546	Ag Silver 107.8682	AU Gold 196.9665	Roentgenium (280)	Gadolinium 157.25	Be Curium (247)
		tht	8B	28 Nickel 58.693	Palladium 106.42	Platinum 195.08	Darmstactium (281)	Europium 151.964	95 Americium (243)
	ymbol	tomic weig	8B	Cobalt 58.9332	Hodium 102.9055	77 Iridium 192.22	Meitnerium (276)	Samarium 150.36	Plutonium (244)
		lmium 9303 A	8B	E55.845	Ruthenium 101.07	Osmium 190.2	Hassium (270)	Promethium (145)	Neptunium (237)
		ame 162 An e	7B	Manganese 54.9380	$\stackrel{43}{\Gamma_{echnetium}^{43}}$	Rhenium 186.207	Bohrium (272)	Neodymium 144.24	92 Uranium 238.0289
	tomic num	Z	6B	Chromium 51.9961	Molybdenum 95.94	Tungsten 183.84	Seaborgium (271)	59 Praseodymium 140.9076	Protactinium 231.0359
	4		5B	Vanadium 50.9415	Niobium 92.9064	Tantalum 180.9479	Dubnium (268)	Cerium Cerium 140.115	Thorium 232.0381
			4B	Titanium 47.88	$Z_{1224}^{40}$	Hafnium 178.49	Rutherfordium (267)	anides 6	tinides 7
			3B	Scandium 44.9559	39 Vttrium 88.9059	57 Lanthanum 138.9055	Actinium (227)	Lanth	Ac
	2A	Beryllium 9.0122	Magnesium 24.3050	Calcium Calcium 40.078	Strontium 87.62	Barium 137.327	Radium (226)		
↓ 1A	Hydrogen 1.0079	3 Lithium 6.941	22:9898	Potassium 39.0983	B5.4678	Cesium 132.9054	Francium (223)		
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**Periodic Table of the Elements** 

# Organic Chemistry with Biological Topics

Fifth Edition

## Janice Gorzynski Smith

University of Hawai'i at Mānoa

## Heidi R. Vollmer–Snarr

Stanford University



#### ORGANIC CHEMISTRY WITH BIOLOGICAL TOPICS, FIFTH EDITION

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For Megan Sarah Smith and Charles J. Vollmer

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### Preface

Since the publication of *Organic Chemistry* in 2005, chemistry has witnessed a rapid growth in its understanding of the biological world. The molecular basis of many complex biological processes is now known with certainty, and can be explained by applying the basic principles of organic chemistry. Because of the close relationship between chemistry and many biological phenomena, *Organic Chemistry with Biological Topics* presents an approach to traditional organic chemistry that incorporates the discussion of biological applications that are understood using the fundamentals of organic chemistry.

#### **The Basic Features**

*Organic Chemistry with Biological Topics* continues the successful student-oriented approach used in *Organic Chemistry* by Janice Gorzynski Smith. This text uses less prose and more diagrams and bulleted summaries for today's students, who rely more heavily on visual imagery to learn than ever before. Each topic is broken down into small chunks of information that are more manageable and easily learned. Sample Problems illustrate stepwise problem solving, and relevant examples from everyday life are used to illustrate topics. New concepts are introduced one at a time so that the basic themes are kept in focus.

The organization of *Organic Chemistry with Biological Topics* provides the student with a logical and accessible approach to an intense and fascinating subject. The text begins with a healthy dose of review material in Chapters 1 and 2 to ensure that students have a firm grasp of the fundamentals. Stereochemistry, the three-dimensional structure of molecules, is introduced early (Chapter 5) and reinforced often. Certain reaction types with unique characteristics and terminology are grouped together. These include acid–base reactions (Chapter 2), oxidation and reduction (Chapters 12 and 20), radical reactions (Chapter 15), and reactions of organometallic reagents (Chapter 20). Each chapter ends with Key Concepts, end-of-chapter summaries that succinctly organize the main concepts and reactions.

#### New to Organic Chemistry with Biological Topics

While there is no shortage of biological applications that can be added to an organic chemistry text, we have chosen to concentrate on the following areas.

- **Chapter 3** on functional groups now includes an expanded section on four types of biomolecules—amino acids and proteins, monosaccharides and carbohydrates, nucleotides and nucleic acids, and lipids. This material augments the discussions of vitamins and the cell membrane, topics already part of *Organic Chemistry* in past editions. Phosphorus-containing compounds such as ATP (adenosine triphosphate), the key intermediate used in energy transfer in cells, are also introduced in this chapter.
- **Chapter 6** now uses biological examples to illustrate the basic types of organic reactions, and the energetics of coupled reactions in metabolism is presented. The discussion of enzymes as biological catalysts is expanded, and a specific example of an enzyme's active site is shown.
- **Chapter 17** now applies the discussion of aromatic heterocycles to the bases in DNA, the high molecular weight molecule that holds the encrypted genetic instructions for our development and cellular processes. In addition, new material has been added on the synthesis of female sex hormones with the aromatase enzyme, which has resulted in the development of drugs used to treat estrogen-dependent breast cancers.

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- **Chapter 19** contains a section on the Henderson–Hasselbalch equation, a mathematical expression that allows us to tell whether a compound exists as an uncharged compound or ion at the cellular pH of 7.4. A section on phosphoric acid esters has been added, and the ionization of amino acids is now explained using the Henderson–Hasselbalch equation.
- **Chapter 22** contains additional material on two common carboxylic acid derivatives—acyl phosphates and thioesters. The role of these functional groups in the biosynthesis of amino acids and the metabolism of fatty acids is discussed.
- **Chapter 24** contains a new section on biological carbonyl condensation reactions. Topics include the biological aldol reaction in the citric acid cycle, the retro-aldol reaction in the metabolism of glucose, and the biological Claisen reaction in the biosynthesis of fatty acids.

In addition, the later chapters of the text are now reorganized to emphasize the connection of biomolecules to prior sections. The chapter on Amino Acids and Proteins (Chapter 26) now directly follows the chapter on Amines (Chapter 25), followed by the remaining chapters on biomolecules, Carbohydrates (Chapter 27) and Lipids (Chapter 28).

## **Tools to Make Learning Organic Chemistry Easier**

#### Illustrations

*Organic Chemistry with Biological Topics* is supported by a well-developed illustration program. Besides traditional skeletal (line) structures and condensed formulas, there are numerous ball-and-stick molecular models and electrostatic potential maps to help students grasp the three-dimensional structure of molecules (including stereochemistry) and to better understand the distribution of electronic charge.



#### **Micro-to-Macro Illustrations**

Unique to *Organic Chemistry with Biological Topics* are microto-macro illustrations, where line art and photos combine with chemical structures to reveal the underlying molecular structures giving rise to macroscopic properties of common phenomena. Examples include starch and cellulose (Chapter 5), adrenaline (Chapter 7), partial hydrogenation of vegetable oil (Chapter 12), and dopamine (Chapter 25).



#### **Spectra**

Over 100 spectra created specifically for *Organic Chemistry with Biological Topics* are presented throughout the text. The spectra are color-coded by type and generously labeled. Mass spectra are green; infrared spectra are red; and proton and carbon nuclear magnetic resonance spectra are blue.



H<sub>2</sub>Ö:

H<sub>2</sub>SO<sub>4</sub>

nism 9.2 Dehydration of a 1° ROH—An E2 Mechanis

HSO4

Protonation of the oxygen atom converts the poor leaving group (\*OH) into a good leaving group (H<sub>2</sub>O). Two bonds are broken and two bonds are formed. The base (HSO<sub>4</sub><sup>-</sup> or H<sub>2</sub>O) removes a proton from the β carbon; the electron pair in the  $\beta$  C+H bond froms the new x bond and the leaving group (H<sub>2</sub>O) departs.

#### **Mechanisms**

Curved arrow notation is used extensively to help students follow the movement of electrons in reactions.

#### **Problem Solving**

#### **Sample Problems**

Sample Problems show students how to solve organic chemistry problems in a logical, stepwise manner. More than 800 follow-up problems are located throughout the chapters to test whether students understand concepts covered in the Sample Problems.



#### How To's

*How To*'s provide students with detailed instructions on how to work through key processes.



cycloł

xylic acid

Answer: tert-butyl cyclohexanecarboxylat

cvcloh

derived from acetic acid

Answer: ethyl acetate

#### **Applications and Summaries**

#### **Key Concept Summaries**

Succinct summary tables reinforcing important principles and concepts are provided at the end of each chapter.

#### **Margin Notes**

Margin notes are placed carefully throughout the chapters, providing interesting information relating to topics covered in the text. Some margin notes are illustrated with photos to make the chemistry more relevant.



All soaps are saits of fatty acids. The main difference between soaps is the addition of other ingredients that do not alter their cleaning properties: dyes for color, scents for a pleasing odor, and oils for lubrication. Soaps that float are aerated, so that they are less dense than water.







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CH 05 States of Consciousness START: 12/12 - DUE: 12/23 - PSYCHOLOGY 101-	SECTION 1A HOMEWORK
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- **Tables** Every table that appears in the text has been saved in electronic form for use in classroom presentations and/or quizzes.
- Animations Full-color animations illustrating important processes are also provided. Harness the visual impact of concepts in motion by importing these files into classroom presentations or online course materials.

#### Student Study Guide/Solutions Manual

Written by Janice Gorzynski Smith and Erin R. Smith, the Student Study Guide/Solutions Manual provides step-by-step solutions to all in-chapter and end-of-chapter problems. Each chapter begins with an overview of key concepts and includes a short-answer practice test on the fundamental principles and new reactions.

## Acknowledgments

*Organic Chemistry with Biological Topics* is an outgrowth of many fruitful discussions with McGraw-Hill personnel about how best to meld biological applications with basic organic chemistry. Special thanks go to Brand Manager Andrea Pellerito, an organic chemist with extensive teaching experience, who understood the need to maintain the integrity and rigor of organic chemistry in this approach, and devised a method to bring this plan to reality.

Special thanks are also due to Senior Product Developer Mary Hurley, who skillfully navigated the logistics involved with integrating a new project within the framework of an existing text. Much appreciation also goes to Production Manager Sherry Kane, who managed an aggressive but workable production schedule. In truth, this new text is the result of an entire team of publishing professionals, beginning with manuscript preparation and culminating with publication of the completed text that is brought to the chemistry community through the dedicated work of the marketing and sales team. Our sincere appreciation goes out to all of them.

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HVS: I am honored to be working with Jan Smith and have already learned so much from her. Thanks to my colleagues Steve Wood, Megan Brennan, Charlie Cox, Jen Schwartz Poehlmann, Chris Chidsey, Dan Stack, and Justin Du Bois for many great conversations about using biological examples to teach the fundamental concepts of organic chemistry. Work on this book would not have been possible without the support of my husband Trent and our three energetic children, Zach, Grady, and Elli. I am also grateful for the encouragement of my mother and brother, Jeanette and Devin Vollmer. This book is dedicated to my father, Chuck Vollmer, who could not have been prouder of my work on this book, but passed away before it was published.

Among the many others that go unnamed but who have profoundly affected this work are the thousands of students we have been lucky to teach over many years. We have learned so much from our daily interactions with them, and we hope that the wider chemistry community can benefit from this experience.

This edition has evolved based on the helpful feedback of many people who reviewed the fourth edition text and digital products, class-tested the book, and attended focus groups or symposiums. These many individuals have collectively provided constructive improvements to the project.

Listed below are the reviewers of the *Organic Chemistry*, fourth edition text:

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Although every effort has been made to make this text and its accompanying Student Study Guide/Solutions Manual as error-free as possible, some errors undoubtedly remain. Please feel free to email one of the authors about any inaccuracies, so that subsequent editions may be further improved.

With much aloha,

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## List of How To's

*How To* boxes provide detailed instructions for key procedures that students need to master. Below is a list of each *How To* and where it is presented in the text.

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## List of Mechanisms

Mechanisms are the key to understanding the reactions of organic chemistry. For this reason, great care has been given to present mechanisms in a detailed, step-by-step fashion. The list below indicates when each mechanism in the text is presented for the first time.

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## **List of Selected Applications**

Applications make any subject seem more relevant and interesting—for nonmajors and majors alike. The following is a list of the biological, medicinal, and environmental applications that have been integrated throughout *Organic Chemistry with Biological Topics*. Each chapter opener showcases an interesting and current application relating to the chapter's topic. (Code: G = general; M = medicinal; B = biological; E = environmental)

#### Prologue

- G Methane, the main component of natural gas
- G Ethanol, the alcohol in beverages
- E Trichlorofluoromethane, a CFC responsible for destroying the stratospheric ozone layer
- M Amoxicillin, a widely used antibiotic
- M Fluoxetine, the antidepressant Prozac
- M AZT, a drug used to treat HIV
- M Capsaicin, a compound found in topical pain relief creams
- E DDT, a nonspecific pesticide that persists in the environment
- M The antimalarial drugs quinine, chloroquine, and artemisinin

#### Chapter 1 Structure and Bonding

- M L-Dopa, a drug used to treat Parkinson's disease (Chapter opener and Section 1.14)
- M Alendronic acid (Fosamax), a drug used to prevent osteoporosis (Section 1.5)
- B Enanthotoxin, a poisonous compound isolated from hemlock water dropwort (Section 1.7)
- G Vanillin, the principal component in the extract of the vanilla bean (Section 1.8B)
- M Structures of active ingredients in common sunscreens (Section 1.8B)
- G Ethane, a component of natural gas (Section 1.10A)
- G Ethylene, a hydrocarbon used to make the plastic polyethylene (Section 1.10B)
- G Acetylene, a gas used in welding torches (Section 1.10C)
- G Cucumber aldehyde, the compound responsible for the odor of freshly cut cucumbers (Section 1.10C)
- M Sinemet, a drug used to treat Parkinson's disease that combines L-dopa and carbidopa (Section 1.14)
- B Vitamin  $B_6$  (Section 1.14)

#### Chapter 2 Acids and Bases

- M Aspirin, a common analgesic and antipyretic (Chapter opener and Section 2.7)
- M The acid–base chemistry of morphine (Section 2.1)
- M The nasal decongestant pseudoephedrine (Section 2.5, Problem 2.17)
- M Glycolic acid, an α-hydroxy acid used in skin care products (Section 2.5, Problem 2.20)
- E Sulfuric acid, a major contributor to acid rain (Section 2.6)
- M Salicin, an analgesic found in willow bark (Section 2.7)

#### Chapter 3 Introduction to Organic Molecules and Functional Groups

- B Vitamin C, a water-soluble vitamin that is important in the formation of collagen (Chapter opener and Section 3.5B)
- E Hemibrevetoxin B, a neurotoxin produced by algal blooms ("red tides") (Section 3.2B)
- M Diethyl ether, the first common general anesthetic (Section 3.2B)
- B Sucrose and the antibiotic amoxicillin (Section 3.2B, Problem 3.3)
- M Dexamethasone, a synthetic steroid (Section 3.2B, Problem 3.5)
- B Spermine, isolated from semen, and meperidine, the narcotic Demerol (Section 3.2B, Problem 3.6)
- M The anticancer agent doxorubicin (Adriamycin) (Section 3.2B, Problem 3.7)
- M Thyrotropin-releasing hormone (Section 3.2C, Problem 3.8)
- M Tamiflu, an antiviral drug used to treat influenza (Section 3.2C, Problem 3.9)
- B Pyruvic acid, lipoic acid, and folic acid as examples of biological molecules with multiple functional groups (Section 3.2C, Problem 3.10)
- B Biological phosphorus compounds (Section 3.2D)
- G How geckos use van der Waals forces to stick to walls (Section 3.3B)
- B Ionic, water-soluble biological compounds: isopentenyl diphosphate and acetylcholine (Section 3.4C)
- G MTBE, a high-octane additive in unleaded gasoline, and 4,4'-dichlorobiphenyl, a PCB (Section 3.4C)
- B Phenylalanine and 11-cis-retinal (Section 3.4C, Sample Problem 3.4)

- B Adrenaline and estrone (Section 3.4C, Problem 3.17)
- B Progesterone and testosterone (Section 3.4C, Sample Problem 3.5)
- B Norethindrone, an oral contraceptive, and arachidonic acid, a fatty acid (Section 3.4C, Problem 3.18)
- B Vitamin A (retinol), a fat-soluble vitamin found in the vision receptors of the eyes (Section 3.5A)
- B  $\beta$ -Carotene, a precursor to vitamin A (Section 3.5A)
- B Vitamin B<sub>3</sub> and vitamin K<sub>1</sub> (Section 3.5B, Problem 3.19)
- B Avocados as a source of pantothenic acid, vitamin  $B_5$  (Section 3.5B, Problem 3.20)
- M Morphine and heroin (Section 3.7A, Problem 3.23)
- M The antibiotics nonactin and valinomycin (Section 3.7B)
- B The reactive features of isopentenyl diphosphate and pyruvic acid (Section 3.8)
- B The nucleophilic thiol of coenzyme A (Section 3.8)
- B Methionine, ATP, and S-adenosylmethionine (Section 3.8, Problem 3.28)
- B Amino acids and proteins (Section 3.9A)
- B Monosaccharides and carbohydrates (Section 3.9B)
- B Nucleotides and nucleic acids (Section 3.9C)
- B Lipids (Section 3.9D)
- M, B End-of-chapter problems: 3.33–3.35, 3.37, 3.38, 3.40, 3.48–3.57, 3.60, 3.61, 3.63–3.65, and 3.67

#### Chapter 4 Alkanes

- E Oil slicks that result from crude petroleum being spilled into the ocean from oil tankers or oil wells (Chapter opener)
- B The cockroach pheromone undecane (Section 4.1)
- B Cyclohexane, one component of mangoes (Section 4.1)
- B Allicin, a compound responsible for the odor of garlic (Section 4.3)
- M Systematic names, generic names, and trade names in over-the-counter drugs like Motrin (Section 4.3)
- G Fossil fuels such as natural gas and petroleum (Section 4.7)
- E The combustion of alkanes and how it contributes to climate change (Section 4.14B)
- B Lipids such as fat-soluble vitamins, phospholipids, waxes, prostaglandins, and steroids (Section 4.15)
- B Pristane, a high molecular weight alkane found in shark liver oil (Section 4.15, Problem 4.33)
- B End-of-chapter problems: 4.66 and 4.69

#### Chapter 5 Stereochemistry

- M, B Paclitaxel (Taxol), a drug used to treat ovarian, breast, and other cancers (Chapter opener)
  - B How differences in the three-dimensional structure of starch and cellulose affect their shape and function (Section 5.1)
- M, B Identifying stereogenic centers in Darvon (an analgesic), ephedrine (a decongestant), and fructose (a simple sugar) (Section 5.4A)
  - M The three-dimensional structure of thalidomide, an anti-nausea drug that caused catastrophic birth defects (Section 5.5)
- M, B Identifying stereogenic centers in paclitaxel (anticancer agent) and sucrose (Section 5.5)
  - M Identifying stereogenic centers in gabapentin (a drug used to treat seizures and chronic pain), gabapentin enacarbil, cholesterol, and Zocor (cholesterol-lowering drug) (Section 5.5, Problems 5.9 and 5.10)
  - M Assigning *R* and *S* configurations in the drugs Plavix and Zestril (Section 5.6, Problems 5.14 and 5.15)
  - B The sweetener sorbitol (Section 5.9, Problem 5.24)
  - B The specific rotation of MSG, a common flavor enhancer (Section 5.12D, Problem 5.32)
  - M Chiral drugs and how mirror image isomers can have drastically different properties—the analgesic ibuprofen, the antidepressant fluoxetine, and the anti-inflammatory agent naproxen (Section 5.13A)
  - B The sense of smell and how mirror image isomers (e.g., carvone and celery ketone) can smell different (Section 5.13B and Problem 5.35)
- M, B End-of-chapter problems: 5.36, 5.43, 5.49, 5.50, 5.53, 5.55, 5.60, and 5.65–5.71

#### Chapter 6 Understanding Organic Reactions

- B Entropy changes in the metabolism of glucose (Chapter opener and Section 6.4)
- B A biological substitution reaction: the hydrolysis of a triacylglycerol to glycerol + fatty acids (Section 6.2A)
- B A biological elimination reaction in the citric acid cycle (Section 6.2B)
- B A biological addition reaction with a thioester, a key step in fatty acid metabolism (Section 6.2C)
- B Four enzyme-catalyzed steps in the citric acid cycle (Section 6.2C, Problem 6.2)
- B The air oxidation of vegetable oils (Section 6.3C, Sample Problem 6.1)
- B Examples of exothermic reactions: the hydrolysis of ATP and the oxidation of glucose (Section 6.4)
- B Coupled reactions in metabolism (Section 6.5C)
- G The reaction of gasoline with  $O_2$  (Section 6.9A)
- G Refrigeration and spoilage (Section 6.9A)
- B Enzymes, biological catalysts (Section 6.11)
- B End-of-chapter problems: 6.27, 6.28, 6.32, 6.39, 6.41, 6.52, and 6.56