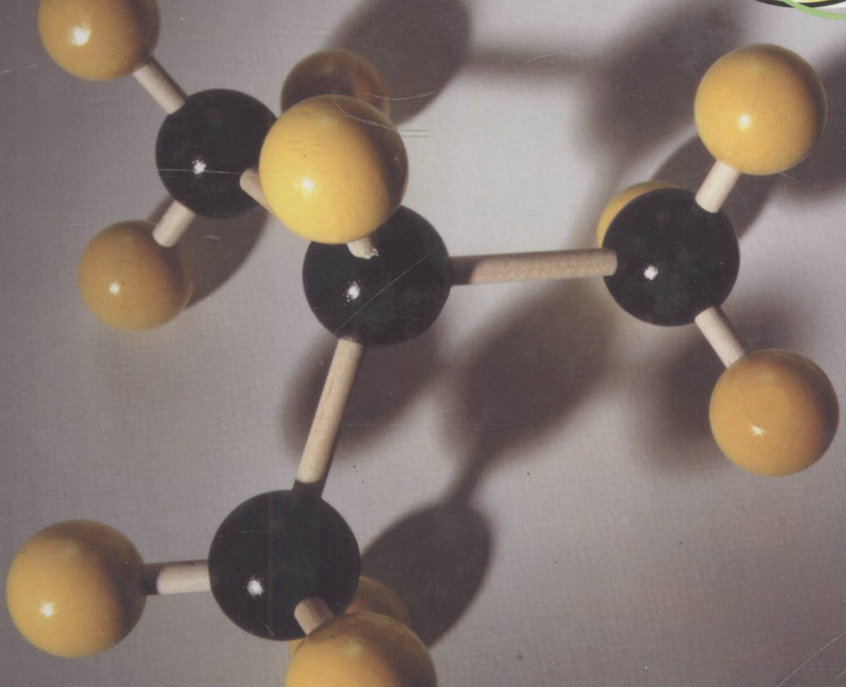
MARCH'S

Advanced Organic Chemistry

Reactions, Mechanisms, and Structure

5th edition



Michael B. Smith and Jerry March

MARCH'S ADVANCED ORGANIC CHEMISTRY

REACTIONS, MECHANISMS, AND STRUCTURE

FIFTH EDITION

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MARCH'S ADVANCED ORGANIC CHEMISTRY

This book is dedicated to the memory of Professor Jerry March, who introduced the first edition of this book more than 40 years ago. Jerry faithfully researched and compiled four editions of Advanced Organic Chemistry, the last in 1994. This book has had a profound influence on the education of thousands of organic chemists all over the world, including me. Although he passed away before the fifth edition could be completed, Jerry worked with editor Ted Hoffman, now retired from Wiley, to make certain this work would continue. Jerry will be missed by the organic community. It is my great honor to bring Jerry's work to the next generation of organic chemists, with the hope that this fifth edition and succeeding editions will be as valuable to them as the previous editions were to me.

Thank you Jerry.

Michael B. Smith

PREFACE

Knowledge of organic chemistry continues to move ahead on many fronts. New journals continue to appear and older ones increase in frequency of publication and/or in number of papers published. This Fifth Edition of *Advanced Organic Chemistry* has been thoroughly revised to reflect this growth. Every topic retained from the fourth edition has been brought up to date. Changes, ranging from minor to extensive, have been made on virtually every page of the Fifth Edition. More than 2800 new references have been added. Several older references were deleted and in cases where a series of papers by the same principal author were cited, all but the most recent were deleted. The older citations should be found in the more recent one or ones. A few changes were made in the organization, but the structure of the Fifth Edition is essentially the same as that of all previous ones. A total of 41 new sections were added, and 54 old ones were deleted. In most cases, the information from the deleted sections was combined with others or moved to another section. The new sections reflect new aspects of organic chemistry. Representative examples include **10–20** (hydroxylation of silanes), **15–36** (radical cyclization), **15–47** (dihydroxylation of aromatic rings), and **19–15** (oxidation of methylene to OH, O_2CR, or OR). In some cases, old sections were split to reflect modern applications. Representative examples are the Diels–Alder reaction (split into the normal reaction and heteroatom Diels–Alder reactions; **15–58** and **15–59**); the aldol and the Mukaiyama aldol reaction (**16–38** and **16–39**); and the reaction of organometallic reagents with alkyl halides (**10–94** for Group I and II metals, **10–95** for organocuprates, and **10–96** for other metal reagents). Like the first four editions, this edition is intended to be a textbook for a course in advanced organic chemistry taken by students who have had the standard undergraduate organic and physical chemistry courses.

The goal, as in previous editions, is to give equal weight to the three fundamental aspects of the study of organic chemistry: reactions, mechanisms, and structure. A student who has completed a course based on this book should be able to approach the literature directly, with a sound knowledge of modern basic organic chemistry. Major special areas of organic chemistry (terpenes, carbohydrates, proteins, many organometallic reagents, combinatorial chemistry, polymerization and electrochemical reactions, steroids, etc.) have been treated lightly or ignored completely. I share Professor March's opinion that these topics are best approached after the first year of graduate study, when the fundamentals have been mastered, either in advanced courses, or directly, by consulting the many excellent books and review articles available on these subjects. In addition, many of these topics are so vast, they are beyond the scope of this book.

The organization is based on reaction types, so the student can be shown that despite the large number of organic reactions, a relatively few principles suffice to explain nearly all of them. Accordingly, the reactions–mechanisms section of this book (Part 2) is divided into 10 chapters (**10–19**), each concerned with a different type of reaction. In the first part of each chapter, the appropriate basic mechanisms are discussed along with considerations of reactivity and orientation, while the second part consists of numbered sections devoted to individual reactions, where the scope and the mechanism of each reaction are discussed. Numbered sections are used for the reactions. For a further discussion of the arrangement of Part 2, see page 382. Since the methods for the preparation of individual classes of compounds (e.g., ketones and nitriles) are not treated all in one place, an index has been provided (Appendix B) by use of which all methods for the preparation of a given type of compound will be found. For each reaction, a list of *Organic Syntheses* references is given when that is possible. Thus for most reactions the student can consult actual examples in *Organic Syntheses*. It is important to note that the numbers for each reaction *differ* from one edition to the other, and many of the sections in the Fifth Edition do not correlate with the Fourth. Hydroboration was found in Section **15–12** in the Fourth Edition, for example, but it appears in Section **15–16** in the Fifth.

The structure of organic compounds is discussed in the first five chapters of Part 1. This section provides a necessary background for understanding mechanisms and is also important in its own right. The discussion begins with chemical bonding and ends with a chapter on stereochemistry. There follow two chapters on reaction mechanisms in general, one for ordinary reactions and the other for photochemical reactions. Part 1 concludes with two more chapters that give further background to the study of mechanisms.

In addition to reactions, mechanisms, and structure, the student should have some familiarity with the literature of organic chemistry. A chapter devoted to this topic has been placed in Appendix A, though many teachers may wish to cover this material at the beginning of the course.

The IUPAC names for organic transformations, first introduced in the Third Edition, is included. Since then the rules have been broadened to cover additional cases; hence more such names are given in this edition. Furthermore, IUPAC has now published a new system for designating reaction mechanisms (see p. 384), and some of the simpler designations are included.

In treating a subject as broad as the basic structures, reactions, and mechanisms of organic chemistry, it is obviously not possible to cover each topic in great depth. Nor would this be desirable even if possible. Nevertheless, students will often wish to pursue individual topics further. An effort has therefore been made to guide the reader to pertinent review articles and books published since about 1965. In this respect, this book is intended to be a guide to the secondary literature (since about 1965) of the areas it covers. Furthermore, in a graduate course, students should be encouraged to consult primary sources. To this end, more than 12,000 references to original papers have been included.

Although basically designed for a one-year course on the graduate level, this book can also be used in advanced undergraduate courses but a one-year course in organic chemistry prior to this is essential, and a one-year course in physical chemistry is strongly recommended. It can also be adapted, by the omission of a large part of its contents, to a one-semester course. Indeed, even for a one-year course, more is included than can be conveniently covered. Many individual sections can be easily omitted without disturbing continuity.

The reader will observe that this text contains much material that is included in first-year organic and physical chemistry courses, though in most cases it goes more deeply into each subject and, of course, provides references, which first-year texts do not. It has been my experience that students who have completed the first-year courses often have a hazy recollection of the material and greatly profit from a representation of the material if it is organized in a different way. It is hoped that the organization of the material on reactions and mechanisms will greatly aid the memory and the understanding. In any given course, the teacher may want to omit some chapters because his students already have an adequate knowledge of the material, or because there are other graduate courses that cover the areas more thoroughly. Chapters 1, 4, and 7 especially may fall into one of these categories.

Although this is a textbook, it has been designed to have reference value also. Students preparing for qualifying examinations and practicing organic chemists will find that Part 2 contains a survey of what is known about the mechanism and scope of about 580 reactions, arranged in an orderly manner based on reaction type and on which bonds are broken and formed. Also valuable for reference purposes are the previously mentioned lists of reactions classified by type of compound prepared (Appendix B) and of all of the *Organic Syntheses* references to each reaction.

Anyone who writes a book such as this, where international rules mandate one system, but published papers use another is faced with the question of which units to use. Two instances are the units used for energies and for bond distances. For energies, IUPAC mandates joules, and many journals do use this unit exclusively. However, organic chemists who publish in United States journals overwhelmingly use calories, and this situation shows no signs of changing in the near future. Since previous editions of this book have been used extensively both in this country and abroad, I have now adopted the practice of giving virtually all energy values in both calories and joules. The question of units for bond distances is easier to answer. Although IUPAC does not recommend angstrom units, nearly all bond distances published in the literature anywhere in the world, whether in organic or in crystallographic journals, are in these units, though a few papers do use picometers. Therefore, I continue to use only angstrom units.

I acknowledge the contributions of those chemists cited and thanked by Professor March in the previous four editions.

Special thanks are due to the STM division of John Wiley & Sons, Dr. Darla Henderson, Shirley Thomas, and Jeannette Stiefel and the other editors at Wiley for their fine work in turning the manuscript into the finished book. I gratefully acknowledge the contribution of Ted Hoffman, the editor who worked with Professor March to make sure there was a Fifth Edition. I am also grateful to those readers who wrote to tell Professor March about errors they discovered in the preceding editions or to make other comments. Such letters are always welcome.

I encourage those who read and use the Fifth Edition to contact me directly with comments, errors, and with publications that might be appropriate for future editions. I hope that this new edition will carry on the tradition that Professor March began with the first edition.

My Email address is smith@nucleus.chem.uconn.edu and my homepage is http://orgchem.chem.uconn.edu/home/mbs-home.html

Finally, I want to thank my wife Sarah and my son Steven for their patience and understanding during the preparation of this manuscript. Without their support, this work would not have been possible.

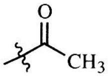
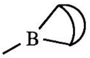
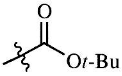
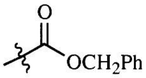
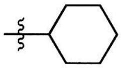
MICHAEL B. SMITH
Storrs, Connecticut

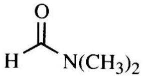
BIBLIOGRAPHICAL NOTE

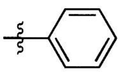
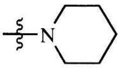
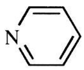
In this book, the practices in citing references are slightly different from those prevailing elsewhere. The reader should note:

1. For review articles, only the first page number is given. If reference is made to only a portion of the article, these page numbers are also given.
2. When a journal is available both in Russian and in English, the page numbers of each article are, of course, different. The language of the journal title indicates whether the page number cited is to be found in the Russian or in the English version.

ABBREVIATIONS

Ac	Acetyl	
acac	Acetylacetonate	
AIBN	*azo-bis*-Isobutyronitrile	
aq.	Aqueous	
	9-Borabicyclo[3.3.1]nonylboryl	
9-BBN	9-Borabicyclo[3.3.1]nonane	
BER	Borohydride exchange resin	
BINAP	*2R,3S,2,2′-bis*-(diphenylphosphino)-1,1′-binapthyl	
Bn	Benzyl	
Bz	Benzoyl	
BOC	*t*-Butoxycarbonyl	
bpy (Bipy)	2,2′-Bipyridyl	
Bu	*n*-Butyl	$-CH_2CH_2CH_2CH_3$
CAM	Carboxamidomethyl	
CAN	Ceric ammonium nitrate	$(NH_4)_2Ce(NO_3)_6$
c-	Cyclo-	
cat.	Catalytic	
Cbz	Carbobenzyloxy	
Chirald	2*S*,3*R*-(+)-4-dimethylamino-1,2-diphenyl-3-methylbutan-2-ol	
COD	1,5-Cyclooctadienyl	
COT	1,3,5-Cyclooctatrienyl	
Cp	Cyclopentadienyl	
CSA	Camphorsulfonic acid	
CTAB	Cetyltrimethylammonium bromide	$C_{16}H_{33}NMe_3^+Br^-$
Cy (c-C_6H_{11})	Cyclohexyl	
°C	Temperature in degrees Centigrade	
DABCO	1,4-Diazabicylco[2.2.2]octane	
dba	Dibenzylidene acetone	
DBE	1,2-Dibromoethane	$BrCH_2CH_2Br$

DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene	
DBN	1,5-Diazabicyclo[4.3.0}non-5-ene	
DCC	1,3-Dicyclohexylcarbodiimide	$c\text{-}C_6H_{11}\text{—}N{=}C{=}N\text{—}C_6H_{11}$
DCE	1,2-Dichloroethane	$ClCH_2CH_2Cl$
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone	
% de	% Diasteromeric excess	
DEA	Diethylamine	$HN(CH_2CH_3)_2$
DEAD	Diethylazodicarboxylate	$EtO_2C\text{—}N{=}NCO_2Et$
Dibal-H	Diisobutylaluminum hydride $(Me_2CHCH_2)_2AlH$	
Diphos (dppe)	1,2-*bis*-(Diphenylphosphino)ethane	$Ph_2PCH_2CH_2PPh_2$
Diphos-4 (dppb)	1,4-*bis*-(Diphenylphosphino)butane	$Ph_2P(CH_2)_4PPh_2$
DMAP	4-Dimethylaminopyridine	
DMA	Dimethylacetamide	
DME	Dimethoxyethane	$MeOCH_2CH_2OMe$
DMF	*N,N′*-Dimethylformamide	
dmp	*bis*-[1,3-Di(*p*-methoxyphenyl)-1,3-propanedionato]	
DMSO	Dimethylsulfoxide	
dpm	Dipivaloylmethanato	
dppb	1,4-*bis*-(Diphenylphosphino)butane $Ph_2P(CH_2)_4PPh_2$	
dppe	1,2-*bis*-(Diphenylphosphino)ethane $Ph_2PCH_2CH_2CH_2PPh_2$	
dppf	*bis*-(Diphenylphosphino)ferrocene	
dppp	1,3-*bis*-(Diphenylphosphino)propane $Ph_2P(CH_2)_3PPh_2$	
dvb	Divinylbenzene	
e^-	Electrolysis	
% ee	% Enantiomeric excess	
EE	1-Ethoxyethoxy EtO(Me)CH—	
Et	Ethyl	$-CH_2CH_3$
EDA	Ethylenediamine	$H_2NCH_2CH_2NH_2$
EDTA	Ethylenediaminetetraacetic acid	
FMN	Flavin mononucleotide	
fod	*tris*-(6,6,7,7,8,8,8)-Heptafluoro-2,2-dimethyl-3,5-octanedionate	
Fp	Cyclopentadienyl-*bis*-carbonyl iron	
FVP	Flash Vacuum Pyrolysis	
h	Hour (hours)	
hν	Irradiation with light	
1,5-HD	1,5-Hexadienyl	
HMPA	Hexamethylphosphoramide	$(Me_2N)_3P{=}O$
HMPT	Hexamethylphorous triamide	$(Me_2N)_3P$

iPr	Isopropyl	$—CH(CH_3)_2$
LICA (LIPCA)	Lithium cyclohexylisopropylamide	
LDA	Lithium diisopropylamide	$LiN(iPr)_2$
LHMDS	Lithium hexamethyl disilazide	$LiN(SiMe_3)_2$
LTMP	Lithium 2,2,6,6-tetramethylpiperidide	
MABR	Methylaluminum *bis*-(4-bromo-2,6-di-*tert*-butylphenoxide)	
MAD	*bis*-(2,6-di-*t*-butyl-4-methylphenoxy)methyl aluminum	
mCPBA	*meta*-Chloroperoxybenzoic acid	
Me	Methyl	$—CH_3$
MEM	β-Methoxyethoxymethyl	$MeOCH_2CH_2OCH_2—$
Mes	Mesityl	$2,4,6\text{-tri-Me-}C_6H_2$
MOM	Methoxymethyl	$MeOCH_2—$
Ms	Methanesulfonyl	$CH_3SO_2—$
MS	Molecular Sieves (3Å or 4Å)	
MTM	Methylthiomethyl	$CH_3SCH_2—$
NAD	Nicotinamide adenine dinucleotide	
NADP	Sodium triphosphopyridine nucleotide	
Napth	Napthyl ($C_{10}H_8$)	
NBD	Norbornadiene	
NBS	*N*-Bromosuccinimide	
NCS	*N*-Chlorosuccinimide	
NIS	*N*-Iodosuccinimide	
Ni(R)	Raney nickel	
NMP	N-Methyl-2-pyrrolidinone	
Oxone	$2\ KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$	
Ⓟ	Polymeric backbone	
PCC	Pyridinium chlorochromate	
PDC	Pyridinium dichromate	
PEG	Polyethylene glycol	
Ph	Phenyl	
PhH	Benzene	
PhMe	Toluene	
Phth	Phthaloyl	
pic	2-Pyridinecarboxylate	
Pip	Piperidino	
PMP	4-Methoxyphenyl	
Pr	*n*-Propyl	$—CH_2CH_2CH_3$
Py	Pyridine	
quant.	Quantitative yield	
Red-Al	$[(MeOCH_2CH_2O)_2AlH_2]Na$	
sBu	*sec*-Butyl	$CH_3CH_2CH(CH_3)$

sBuLi	*sec*-Butyllithium	$CH_3CH_2CH(Li)CH_3$
Siamyl	Diisoamyl or *sec-iso*-amyl	$(CH_3)_2CHCH(CH_3)$-
TADDOL	$\alpha,\alpha,\alpha',\alpha'$-tetraaryl-4,5-dimethoxy-1,3-dioxolane	
TASF	*tris*-(Diethylamino)sulfonium difluorotrimethyl silicate	
TBAF	Tetrabutylammonium fluoride	$n\text{-}Bu_4N^+F^-$
TBDMS	*t*-Butyldimethylsilyl	$t\text{-}BuMe_2Si$
TBHP (*t*-BuOOH)	*t*-Butylhydroperoxide	Me_3COOH
t-Bu	*tert*-Butyl	$-C(CH_3)_3$
TEBA	Triethylbenzylammonium	$Bn(Et)_3N^+$
TEMPO	Tetramethylpiperdinyloxy free radical	
TFA	Trifluoroacetic acid	CF_3COOH
TFAA	Trifluoroacetic anhydride	$(CF_3CO)_2O$
Tf (OTf)	Triflate	$-SO_2CF_3$ $(-OSO_2CF_3)$
THF	Tetrahydrofuran	
THP	Tetrahydropyran	
TMEDA	Tetramethylethylenediamine	$Me_2NCH_2CH_2NMe_2$
TMG	1,1,3,3-Tetramethylguanidine	
TMS	Trimethylsilyl	$-Si(CH_3)_3$
TMP	2,2,6,6-Tetramethylpiperidine	
TPAP	tetra-*n*-Propylammonium perruthenate	
Tol	Tolyl	$4\text{-}C_6H_4CH_3$
Tr	Trityl	$-CPh_3$
TRIS	Triisopropylphenylsulfonyl	
Ts(Tos)	Tosyl = *p*-Toluenesulfonyl	$4\text{-}MeC_6H_4SO_2$
X_c	Chiral auxiliary	

MARCH'S ADVANCED ORGANIC CHEMISTRY

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PART 1

PART 2

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