

Advanced Organic Chemistry



Reaction Mechanisms

Reinhard Bruckner

A D V A N C E D O R G A N I C C H E M I S T R Y S E R I E S

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Foreword

We are at the start of a revolution in molecular science that will more profoundly change our lives, our culture, indeed, our world than did the Industrial Revolution a century ago. From the human genome project, the largest natural product characterization effort ever, to the search for the molecular signatures of life on other planets, this molecular revolution is creating an ever-expanding view of ourselves and our universe. At the core of this revolution is chemistry, the quintessential molecular science within which is organic chemistry, a discipline that will surely be the source of many of the major advances in chemistry, biology, medicine, materials science, and environmental science in the 21st century.

In his text on organic chemistry, the translation of which has been impressively led by Professors Harmata and Glaser, Professor Bruckner has masterfully addressed the core concepts of the discipline, providing a rich tapestry of information and insight. The student of contemporary organic chemistry will be well-served by the depth and quality of this treatment. The underlying philosophy of this text is that much of chemistry can be understood in terms of structure, which in turn influences reactivity, ultimately defining the higher order activities of synthesis. Whether one seeks to understand nature or to create the new materials and medicines of the future, a key starting point is thus understanding structure and mechanism.

Professor Bruckner addresses the interrelationship of structure and mechanism with the rich insight of one schooled at the interface of physical organic chemistry and synthesis. His treatment is impressively rigorous, integrated, and broad. He achieves breadth through the careful selection of representative and fundamental reactive intermediates and reactions. Rigor and integration derive from his disciplined adherence to structure, orbital theory, and mechanism. The result is a powerfully coherent treatment that enables the student to address the rich subject matter at hand and importantly by analogy the far-ranging aspects of the field that lie beyond the scope of the book. Extending from his treatment of radicals, nucleophiles, carbenium ions, and organometallic agents to concerted reactions and redox chemistry, Bruckner provides an analysis that effectively merges theory and mechanism with examples and applications. His selection of examples is superb and is further enhanced by the contemporary references to the literature. The text provides clarity that is essential for facilitating the educational process.

This is a wonderfully rich treatment of organic chemistry that will be a great value to students at any level. Education should enable and empower. This text does both, providing the student with the insights and tools needed to address the tremendous challenges and opportunities in the field. Congratulations to Professors Bruckner, Harmata, and Glaser for providing such a rich and clear path for those embarking on an understanding of the richly rewarding field of organic chemistry.

Paul A. Wender
Stanford University

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Preface to the English Edition

Writing a textbook at any level is always a challenge. In organic chemistry, exciting new discoveries are being made at an ever-increasing pace. However, students of the subject still arrive in the classroom knowing only what they have been taught, often less. The challenge is to present appropriate review material, present venerable, classic chemistry while dealing with the latest results, and, most importantly, provoke thought and discussion. At the time this book was written, there was a need for an advanced text that incorporated these aspects of our science.

The German version of the text was designed for second- and third-year chemistry majors: 60–70% of the contents of this book address students before the “Diplom-chemiker-Vorexamen,” while the remaining 30–40% address them thereafter. The German book is typically used one year after a standard introductory textbook such as that by Vollhardt and Schore, Streitwieser and Heathcock, or McMurry. Accordingly, in the United States this text can be used in a class for advanced undergraduates or beginning graduate students. Curricula of other English-speaking countries should allow the use of this text with optimum benefit at a similar point of progress. A good understanding of the fundamentals of organic and physical chemistry will suffice as a foundation for using this textbook to advantage.

The approach taken in this book conveys the message that the underlying theory of organic chemistry pervades the entire science. It is not necessary at this level to restrict the learning of reactions and mechanisms to any particular order. MO theory and formalisms such as electron pushing with arrows are powerful tools that can be applied not only to the classic chemistry that led to their development but also to the most recently developed reactions and methods, even those that use transition metals.

Theory, mechanism, synthesis, structure, and stereochemistry are discussed throughout the book in a qualitative to semiquantitative fashion. Fundamental principles such as the Hammond postulate that can be applied in the most varied contexts are reinforced throughout the book. Equations such as the Eyring equation or the rate laws of all kinds of reactions are introduced with the view that they have context and meaning and are not merely formulas into which numbers are plugged.

The present text, to the best of our knowledge, does not duplicate the approach of any other treatment at a comparable level. We are convinced that this book, which has already filled a niche in the educational systems of German- and the French-speaking countries (a French translation appeared in 1999), will do the same in the textbook market of English-speaking countries now that an English edition has become available.

We hope that you enjoy many fruitful hours of insight in the course of studying this book, and we welcome your constructive comments on its content and approach.

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April 16, 2001

Preface to the German Edition

To really understand organic chemistry requires three passes. First, one must familiarize oneself with the physical and chemical properties of organic chemical compounds. Then one needs to understand their reactivities and their options for reactions. Finally, one must develop the ability to design syntheses. A typical schedule of courses for chemistry students clearly incorporates these three components. Introductory courses focus on compounds, a course on reaction mechanisms follows, and a course on advanced organic chemistry provides more specialized knowledge and an introduction to retrosynthesis.

Experience shows that the *second* pass, the presentation of the material organized according to reaction mechanisms, is of central significance to students of organic chemistry. This systematic presentation reassures students not only that they can master the subject but also that they might enjoy studying organic chemistry.

I taught the reaction mechanisms course at the University of Göttingen in the winter semester of 1994, and by the end of the semester the students had acquired a competence in organic chemistry that was gratifying to all concerned. Later, I taught the same course again—I still liked its outline—and I began to wonder whether I should write a textbook based on this course. A text *of this kind* was not then available, so I presented the idea to Björn Gondesen, the editor of *Spektrum*. Björn Gondesen enthusiastically welcomed the book proposal and asked me to write the “little booklet” as soon as possible. I gave up my private life and wrote for just about two years. I am grateful to my wife that we are still married; thank you, Jutta!

To this day, it remains unclear whether Björn Gondesen used the term “little booklet” in earnest or merely to indicate that he expected *one* book rather than a series of volumes. In any case, I am grateful to him for having endured patiently the mutations of the “little booklet” first to a “book” and then to a “mature textbook.” In fact, the editor demonstrated an indestructible enthusiasm, and he remained supportive when I presented him repeatedly with increases in the manuscript of yet another 50 pages. The reader has Björn Gondesen to thank for the two-color production of this book. All “curved arrows” that indicate electron shifts are shown in red so that the student can easily grasp the reaction. Definitions and important statements also are graphically highlighted.

In comparison to the preceding generation, students of today study chemistry with a big handicap: an explosive growth of knowledge in all the sciences has been accompanied in particular by the need for students of organic chemistry to learn a greater number of reactions than was required previously. The omission of older knowledge is possible only if that knowledge has become less relevant and, for this reason, the following reactions were omitted: Darzens glycidic ester synthesis, Cope elimination, S_Ni reaction, iodoform reaction, Reimer–Tiemann reaction, Stobbe condensation, Perkin synthesis, benzoin condensation, Favorskii rearrangement, benzil–benzilic acid rearrangement, Hofmann and Lossen degradation, Meerwein–Ponndorf reduction, and Cannizzaro re-

action. A few other reactions were omitted because they did not fit into the current presentation (nitrile and alkyne chemistry, cyanohydrin formation, reductive amination, Mannich reaction, enol and enamine reactions).

This book is a highly modern text. All the mechanisms described concern reactions that are used today. The mechanisms are not just *l'art pour l'art*. Rather, they present a conceptual tool to facilitate the learning of reactions that one needs to know in any case. Among the modern reactions included in the present text are the following: Barton–McCombie reaction, Mitsunobu reaction, Mukaiyama redox condensations, asymmetric hydroboration, halolactonizations, Sharpless epoxidation, Julia–Lythgoe and Peterson olefination, *ortho*-lithiation, *in situ* activation of carboxylic acids, preparations and reactions of Gilman, Normant, and Knochel cuprates, alkylation of chiral enolates (with the methods by Evans, Helmchen, and Enders), diastereoselective aldol additions (Heathcock method, Zimmerman–Traxler model), Claisen–Ireland rearrangements, transition metal-mediated C,C-coupling reactions, Swern and Dess–Martin oxidations, reductive lithiations, enantioselective carbonyl reductions (Noyori, Brown, and Corey–Itsuno methods), and asymmetrical olefin hydrogenations.

The presentations of many reactions integrate discussions of stereochemical aspects. Syntheses of mixtures of stereoisomers of the target molecule no longer are viewed as valuable—indeed such mixtures are considered to be worthless—and the control of the stereoselectivity of organic chemical reactions is of paramount significance. Hence, suitable examples were chosen to present aspects of modern stereochemistry, and these include the following: control of stereoselectivity by the substrate, the reagent, or an ancillary reagent; double stereodifferentiation; induced and simple diastereoselectivity; Cram, Cram chelate, and Felkin–Anh selectivity; asymmetric synthesis; kinetic resolution; and mutual kinetic resolution.

You might ask how then, for heaven's sake, is one to remember all of this extensive material? Well, the present text contains only about 70% of the knowledge that I would expect from a *really well-trained* undergraduate student; the remaining 30% presents material for graduate students. To ensure the best orientation of the reader, the sections that are most relevant for optimal undergraduate studies are marked in the margin with a B on a gray background, and sections relevant primarily to graduate students are marked with an A on a red background. I have worked most diligently to show the reactions in reaction diagrams that include every intermediate—and in which the flow of the valence electrons is highlighted in color—and, whenever necessary, to further discuss the reactions in the text. It has been my aim to describe all reactions so well, that in hindsight—because the course of every reaction will seem so plausible—the readers feel that they might even have *predicted* their outcome. I tried especially hard to realize this aim in the presentation of the chemistry of carbonyl compounds. These mechanisms are presented in four chapters (Chapters 7–11), while other authors usually cover all these reactions in one chapter. I hope this pedagogical approach will render organic chemistry more comprehensible to the reader.

Finally, it is my pleasure to thank—in addition to my untiring editor—everybody who contributed to the preparation of this book. I thank my wife, Jutta, for typing “version 1.0” of most of the chapters, a task that was difficult because she is not a chemist and that at times became downright “hair raising” because of the inadequacy of my dicta-

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Indicates relevance for
undergraduate students

A

Indicates relevance for
graduate students

tion. I thank my co-workers Matthias Eckhardt (University of Göttingen, Dr. Eckhardt by now) and Kathrin Brüscke (chemistry student at the University of Leipzig) for their careful reviews of the much later “version .10” of the chapters. Their comments and corrections resulted in “version .11” of the manuscript, which was then edited professionally by Dr. Barbara Elvers (Oslo). In particular, Dr. Elvers polished the language of sections that had remained unclear, and I am very grateful for her editing. Dr. Wolfgang Zettelmeier (Laaber-Waldetzenberg) prepared the drawings for the resulting “version .12,” demonstrating great sensitivity to my aesthetic wishes. The typesetting was accomplished essentially error-free by Konrad Triltsch (Würzburg), and my final review of the galley pages led to the publication of “version .13” in book form. The production department was turned upside-down by all the “last minute” changes—thank you very much, Mrs. Notacker! Readers who note any errors, awkward formulations, or inconsistencies are heartily encouraged to contact me. One of these days, there will be a “version .14.”

It is my hope that your reading of this text will be enjoyable and useful, and that it might convince many of you to specialize in organic chemistry.

Reinhard Brückner

Göttingen, August 8, 1996

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Acknowledgments

My part in this endeavor is over. Now, it is entirely up to the staff at Harcourt/Academic Press to take charge of the final countdown that will launch *Advanced Organic Chemistry: Reaction Mechanisms* onto the English-speaking market. After three years of intense trans-Atlantic cooperation, it is my sincere desire to thank those individuals in the United States who made this enterprise possible. I am extremely obliged to Professor Michael Harmata from the University of Missouri at Columbia for the great determination he exhibited at *all* phases of the project. It was he who doggedly did the legwork at the 1997 ACS meeting in San Francisco, that is, cruised from one science publisher's stand to the next, dropped complimentary copies of the German edition on various desks, and talked fervently to the responsables. David Phanco from Academic Press was immediately intrigued and quickly set up an agreement with the German publisher. David Phanco was farsighted enough to include Mike Harmata on board as a "language polisher" (of the translation) before he passed on the torch to Jeremy Hayhurst in what then was to become Harcourt/Academic Press. The latter's sympathetic understanding and constant support in the year to follow were absolutely essential to the final success of the project: Mike Harmata, at that time a Humboldt Fellow at the University of Göttingen, and I needed to develop a very Prussian sense of discipline when doing our best to match the first part of the translation to the quality of the original. I am very much indebted to Professor Rainer Glaser, who reinforced the Missouri team and, being bilingual, finished the second half of the translation skillfully and with amazing speed. He also contributed very valuably to improving the galley proofs, as did Joanna Dinsmore, Production Manager at Harcourt/Academic Press. It is she who deserves a great deal of gratitude for her diligence in countless hours of proofreading, and for her patience with an author who even at the page proof stage felt that it was never too late to make all sorts of small amendments for the future reader's sake. It is my sincere hope, Ms. Dinsmore, that in the end you, too, feel that this immense effort was worth the trials and tribulations that accompanied it.

Reinhard Bruckner

Freiburg, April 25, 2001

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Radical Substitution Reactions at the Saturated C Atom

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In a substitution reaction a part X of a molecule R—X is replaced by a group Y (Figure 1.1). The subject of this chapter is substitution reactions in which a part X that is bound to an sp^3 -hybridized C atom is replaced by a group Y via radical intermediates. Radicals are valence-unsaturated and therefore usually short-lived atoms or molecules. They contain one or more unpaired (“lone”) electrons. From inorganic chemistry you are familiar with at least two radicals, which by the way are quite stable: NO and O₂. NO contains one lone electron; it is therefore a monoradical or simply a “radical.” O₂ contains two lone electrons and is therefore a biradical.

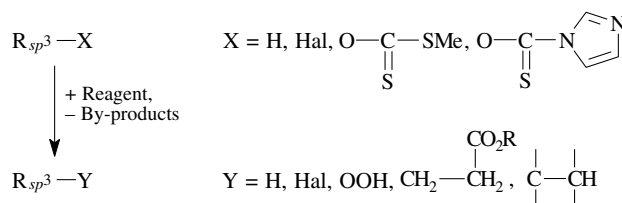


Fig. 1.1. Some substrates and products of radical substitution reactions.

1.1 Bonding and Preferred Geometries in C Radicals, Carbenium Ions and Carbanions

At the so-called radical center an organic radical R· has an electron septet, which is an electron deficiency in comparison to the electron octet of valence-saturated compounds. Carbon atoms are the most frequently found radical centers and most often have three neighbors (see below). Carbon-centered radicals with their electron septet occupy an intermediate position between the carbenium ions, which have one electron less (electron sextet at the valence-unsaturated C atom), and the carbanions, which have one electron more (electron octet at the valence-unsaturated C atom). Since there is an electron deficiency present both in C radicals and in carbenium ions, the latter are more closely related to each other than C radicals are related to carbanions. Because of this, C radicals and carbenium ions are also stabilized or destabilized by the same substituents.

Nitrogen-centered radicals ($(R_{sp^3})_2\text{N}\cdot$ or oxygen-centered radicals ($(R_{sp^3})\text{O}\cdot$) are less stable than C-centered radicals ($(R_{sp^3})_3\text{C}\cdot$). They are higher in energy because of the higher electronegativity of these elements relative to carbon. Nitrogen- or oxygen-centered radicals of the cited substitution pattern consequently have only a limited chance to exist.

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Which geometries are preferred at the valence-unsaturated C atom of C radicals, and how do they differ from those of carbenium ions or carbanions? And what types of bonding are found at the valence-unsaturated C atoms of these three species? It is simplest to clarify the preferred geometries first (Section 1.1.1). As soon as these geometries are known, molecular orbital (MO) theory will be used to provide a description of the bonding (Section 1.1.2).

We will discuss the preferred geometries and the MO descriptions of C radicals and the corresponding carbenium ions or carbanions in two parts. In the first part we will examine C radicals, carbenium ions, and carbanions with a trivalent central C atom. The second part treats the analogous species with a divalent central C atom. A third part (species with a monovalent central C atom) can be dispensed with because the only species of this type that is important in organic chemistry is the alkynyl anion, which, however, is of no interest here.

1.1.1 Preferred Geometries

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The preferred geometries of carbenium ions and carbanions are correctly predicted by the valence shell electron pair repulsion (VSEPR) theory. The VSEPR theory, which comes from inorganic chemistry, explains the stereostructure of covalent compounds of the nonmetals and the main group metals. It makes no difference whether these compounds are charged or not.

The VSEPR theory analyzes the stereostructure of these compounds in the environment of the central atom. This stereostructure depends mainly on (a) the number n of atoms or atom groups (in inorganic chemical terminology, referred to as ligands) linked to the central atom and (b) the number m of nonbonding valence electron pairs localized at the central atom. If the central atom under consideration is a C atom, $n + m \leq 4$. In this case, the VSEPR theory holds in the following shorthand version, which makes it possible to determine the preferred geometries: the compound considered has the stereostructure in which the repulsion between the n bonding partners and the m nonbonding valence electron pairs on the C atom is as small as possible. This is the case when the orbitals that accommodate the bonding and the nonbonding electron pairs are as far apart from each other as possible.

For carbenium ions this means that the n substituents of the valence-unsaturated central atom should be at the greatest possible distance from each other:

- In alkyl cations R_3C^+ , $n = 3$ and $m = 0$. The substituents of the trivalent central atom lie in the same plane as the central atom and form bond angles of 120° with each other (trigonal planar arrangement). This arrangement was confirmed experimentally by means of a crystal structural analysis of the *tert*-butyl cation.
- In alkenyl cations $=C^+-R$, $n = 2$ and $m = 0$. The substituents of the divalent central atom lie on a common axis with the central atom and form a bond angle of 180° . Alkenyl cations have not been isolated yet because of their low stability (Section 1.2). However, calculations support the preference for the linear structure.

According to the VSEPR theory, in carbanions the n substituents at the carbanionic C atom and the nonbonding electron pair must move as far away from each other as possible:

- In alkyl anions R_3C^- , $n = 3$ and $m = 1$. The substituents lie in one plane, and the central atom lies outside it. The carbanion center has a trigonal pyramidal geometry. The bond angles are similar to the tetrahedral angle ($109^\circ 28'$). This stereostructure may be called pseudotetrahedral when the carbanionic electron pair is counted as a pseudosubstituent.
- In alkenyl anions $=\text{C}^-\text{—R}$, $n = 2$ and $m = 1$. The substituents and the divalent central atom prefer a bent structure. The bond angle in alkenyl anions is approximately 120° . When the nonbonding valence electron pair is considered as a pseudosubstituent of the carbanion center, this preferred geometry may also be called pseudotrigonal planar.

The most stable structures of alkyl and alkenyl anions predicted with the VSEPR theory are supported by reliable calculations. There are no known experimental structural data. In fact, up to recently, one would have cited the many known geometries of the lithium derivatives of these carbanions as evidence for the structure. One would simply have “dropped” the C—Li bond(s) from these geometries. However, it is now known that the considerable covalent character of most C—Li bonds makes organolithium compounds unsuitable models for carbanions.

Since the VSEPR theory describes the mutual repulsion of valence electron *pairs*, it can hardly be used to make statements about the preferred geometries of C radicals. It is intuitively expected that C radicals assume a middle position between their carbenium ion and carbanion analogs. In agreement with this, alkyl radicals are either planar (methyl radical) or slightly pyramidal but able to swing rapidly through the planar form (inversion) to another near-planar structure (*tert*-butyl radical). In addition, some carbon-centered radicals are considerably pyramidalized (e.g., those whose carbon center is substituted with several heteroatoms). Alkenyl radicals are bent, but they can undergo *cis/trans* isomerization through the linear form very rapidly. Because they are constrained in a ring, aryl radicals are necessarily bent.

1.1.2 Bonding

The type of bonding at the valence-unsaturated C atom of carbenium ions, carbanions, and C-centered radicals follows from the geometries described in Section 1.1.1. From the bond angles at the central C atom, it is possible to derive its hybridization. Bond angles of $109^\circ 28'$ correspond to sp^3 , bond angles of 120° correspond to sp^2 , and bond angles of 180° correspond to sp hybridization. From this hybridization it follows which atomic orbitals (AOs) of the valence-unsaturated C atom are used to form the molecular orbitals (MOs). The latter can, on the one hand, be used as bonding MOs. Each one of them then contains a valence electron pair and represents the bond to a substituent of the central atom. On the other hand, one AO of the central atom represents a nonbonding MO, which is empty in the carbenium ion, contains an electron

in the radical, and contains the nonbonding electron pair in the carbanion. How the valence electrons are distributed over the respective MO set follows from the *Aufbau* principle: they are placed, one after the other, in the MOs, in the order of increasing energy. The Pauli principle is also observed: any MO can take up only two electrons and only on the condition that they have opposite spins.

The bonding at the valence-unsaturated C atom of carbenium ions R_3C^+ is therefore described by the MO diagram in Figure 1.2 (left), and the bonding of the valence-unsaturated C atom of carbenium ions of type $=C^+-R$ is described by the MO diagram in Figure 1.3 (left). The MO description of R_3C^- carbanions is shown in Figure 1.2 (right), and the MO description of carbanions of type $=C^--R$ is shown in Figure 1.3 (right). The MO description of the radicals $R\cdot$ or $=C\cdot$ employs the MO picture for the analogous carbenium ions or carbanions, depending on which of these species the geometry of the radical is similar to. In each case only seven instead of six or eight valence electrons must be accommodated (Figures 1.2 and 1.3, left).

Fig. 1.2. Energy levels and occupancies (red) of the MOs at the trivalent C atom of planar carbenium ions R_3C^+ (left) and pyramidal carbanions R_3C^- (right).

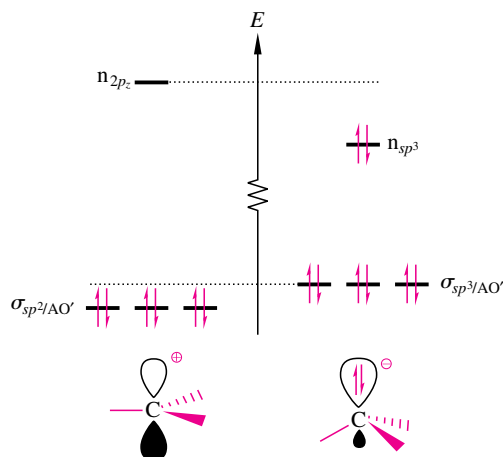
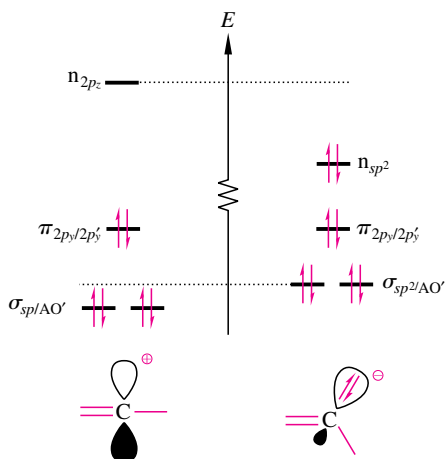


Fig. 1.3. Energy levels and occupancies (red) of the MOs at the divalent C atom of linear carbenium ions $=C^+-R$ (left) and bent carbanions $=C^--R$ (right).



1.2 Stability of Radicals

Stability in chemistry is not an absolute but a relative concept. It always refers to a stability difference with respect to a reference compound. Let us consider the standard heats of reaction ΔH^0 of the dissociation reaction $\text{R}-\text{H} \rightarrow \text{R}\cdot + \text{H}\cdot$, that is, the dissociation enthalpy (DE) of the broken C—H bond. It reflects, on the one hand, the strength of this C—H bond and, on the other hand, the stability of the radical $\text{R}\cdot$ produced. As you see immediately, the dissociation enthalpy of the R—H bond depends in many ways on the structure of R. But it is not possible to tell clearly whether this is due to an effect on the bond energy of the broken R—H bond and/or an effect on the stability of the radical $\text{R}\cdot$ that is formed.

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	$\text{HC}\equiv\text{C}_{sp}-\text{H}$	 $\text{C}_{sp^2}-\text{H}$	$\text{H}_2\text{C}=\overset{\text{H}}{\text{C}_{sp^2}}-\text{H}$	$\text{H}_3\text{C}-\overset{\text{H}_2}{\text{C}_{sp^3}}-\text{H}$
$\frac{DE}{\text{kcal/mol}}$	131	111	110	98

To what must one ascribe, for example, the fact that the dissociation enthalpy of a $\text{C}_{sp^n}-\text{H}$ bond depends essentially on n alone and increases in the order $n = 3, 2$, and 1 ?

To help answer this question it is worthwhile considering the following: the dissociation enthalpies of bonds such as $\text{C}_{sp^n}-\text{C}$, $\text{C}_{sp^n}-\text{O}$, $\text{C}_{sp^n}-\text{Cl}$, and $\text{C}_{sp^n}-\text{Br}$ also depend heavily on n and increase in the same order, $n = 3, 2$, and 1 . The extent of the n -dependence of the dissociation energies depends on the element which is cleaved off. This is only possible if the n -dependence reflects, at least in part, an n -dependence of the respective C_{sp^n} -element bond. (Bond enthalpy tables in all textbooks ignore this and assign a bond enthalpy to each C_{sp^n} -element bond that is dependent on the element but not on the value of n !) Hence, the bond enthalpy of every C_{sp^n} -element bond increases in the order $n = 3, 2$, and 1 . This is so because all C_{sp^n} -element bonds become shorter in the same order. This in turn is due to the s character of the C_{sp^n} -element bond, which increases in the same direction.

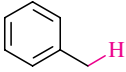
An immediate consequence of the different ease with which C_{sp^n} -element bonds dissociate is that in radical substitution reactions, alkyl radicals are preferentially formed. Only in exceptional cases are vinyl or aryl radicals formed. Alkynyl radicals do not appear at all in radical substitution reactions. In the following we therefore limit ourselves to a discussion of substitution reactions that take place via radicals of the general structure $\text{R}^1\text{R}^2\text{R}^3\text{C}\cdot$.

1.2.1 Reactive Radicals

If radicals $\text{R}^1\text{R}^2\text{R}^3\text{C}\cdot$ are produced by breaking the C—H bond in molecules of the type $\text{R}^1\text{R}^2\text{R}^3\text{C}-\text{H}$, one finds that the dissociation enthalpies of such C—H bonds differ with molecular structure. Experience shows that these differences can be explained completely by the effects of the substituents R^1 , R^2 , and R^3 on the stability of the radicals $\text{R}^1\text{R}^2\text{R}^3\text{C}\cdot$ formed.

Table 1.1 shows one substituent effect, which influences the stability of radicals. The dissociation enthalpies of reactions that lead to $\text{R}-\text{CH}_2\cdot$ radicals are listed. The substituent R varies from C_2H_5 through $\text{H}_2\text{C}=\text{CH}-$ (vinyl substituent, vin) to C_6H_5- (phenyl substituent, Ph). The dissociation enthalpy is greatest for $\text{R} = \text{H}$. This shows that a radical center is stabilized by 9 kcal/mol by the neighboring $\text{C}=\text{C}$ double bond of an alkenyl or aryl substituent.

Table 1.1. Stabilization of Radicals by Unsaturated Substituents

	$\frac{DE}{\text{kcal/mol}}$	VB formulation of the radical $\text{R}\cdot$
	98	
	89	$\left\{ \text{CH}_2=\text{CH}\cdot \longleftrightarrow \cdot\text{CH}_2\text{CH}=\text{CH}_2 \right\}$
	89	$\left\{ \text{C}_6\text{H}_5\cdot \longleftrightarrow \text{C}_6\text{H}_5\text{CH}=\text{CH}_2 \longleftrightarrow \text{C}_6\text{H}_5\text{CH}=\text{CH}\cdot \longleftrightarrow \text{C}_6\text{H}_5\text{CH}=\text{CH}\cdot \right\}$

In the valence-bond (VB) model this effect results from the fact that radicals of this type can be described by superpositioning several resonance forms (Table 1.1, right). In the MO model, the stabilization of radical centers of this type is due to the overlap of the π system of the unsaturated substituent with the $2p_z$ AO at the radical center (Figure 1.4). This overlap is called conjugation.

Fig. 1.4. Stabilization by overlap of a singly occupied $2p_z$ AO with adjacent parallel $\pi_{\text{C}=\text{C}}$ or $\pi^*_{\text{C}=\text{C}}$ MOs.

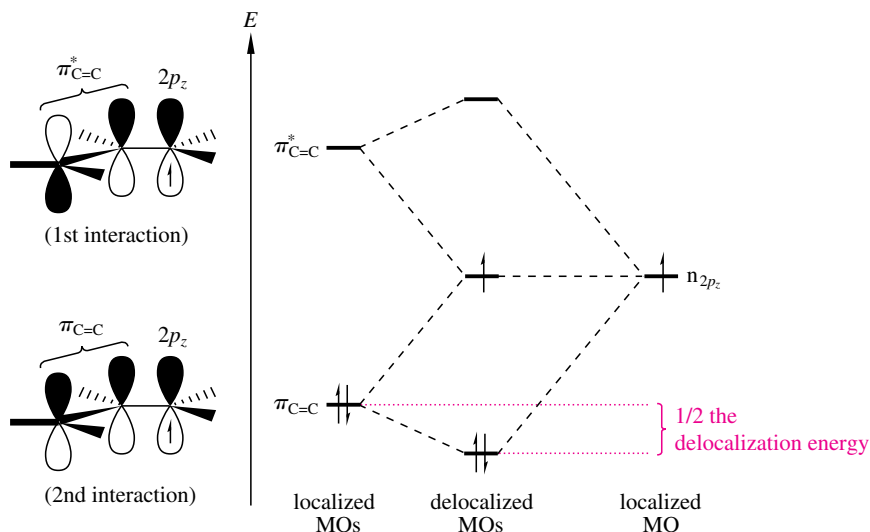


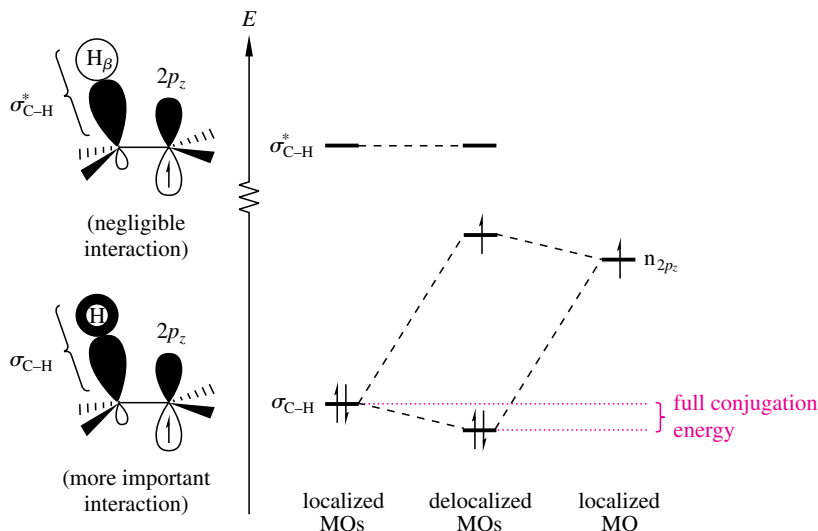
Table 1.2 illustrates an additional substituent effect on radical stability. Here the dissociation enthalpies of reactions that lead to polyalkylated radicals $(\text{Alk})_{3-n}\text{H}_n\text{C}\cdot$ are listed (“Alk” stands for alkyl group). From these dissociation enthalpies it can be seen that alkyl substituents stabilize radicals. A primary radical is 6 kcal/mol more stable, a secondary radical is 9 kcal/mol more stable, and a tertiary radical is 12 kcal/mol more stable than the methyl radical.

Table 1.2. Stabilization of Radicals by Alkyl Substituents

	$\frac{DE}{\text{kcal/mol}}$	VB formulation of the radical $\text{R}\cdot$
$\text{H}_3\text{C}-\text{H}$	104	
$\text{H}_3\text{C}-\text{H}_2\text{C}-\text{H}$	98	
$(\text{H}_3\text{C})_2\text{HC}-\text{H}$	95	
$(\text{H}_3\text{C})_3\text{C}-\text{H}$	92	

In the VB model, this effect is explained by the fact that radicals of this type, too, can be described by the superpositioning of several resonance forms. These are the somewhat exotic no-bond resonance forms (Table 1.2, right). From the point of view of the MO model, radical centers with alkyl substituents have the opportunity to interact with these substituents. This interaction involves the C—H bonds that are in the position α to the radical center and lie in the same plane as the $2p_z$ AO at the radical center. Specifically, $\sigma_{\text{C}-\text{H}}$ MOs of these C—H bonds are able to overlap with the radical $2p_z$ orbital (Figure 1.5). This overlap represents the rare case of lateral overlap between a σ bond and a p orbital. It is referred to as hyperconjugation to distinguish it from lateral overlap between π bonds and p orbitals, which is referred to as conjugation. When the $\sigma_{\text{C}-\text{H}}$ bond and the $2p_z$ AO enclose a dihedral angle χ that is different from that required for optimum overlap (0°), the stabilization of the radical center by hyperconjugation decreases. In fact, it decreases by the square of the cosine of the dihedral angle χ .

Fig. 1.5. Stabilization by overlap of a singly occupied $2p_z$ AO with vicinal nonorthogonal σ_{C-H} MOs.

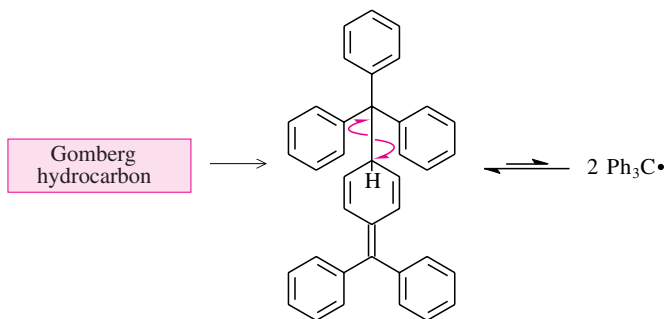


1.2.2 Unreactive Radicals

B

Just as several alkyl substituents increasingly stabilize a radical center (Table 1.2), two phenyl substituents stabilize a radical center more than one does. The diphenylmethyl radical (“benzhydryl radical”) is therefore more stable than the benzyl radical. The triphenylmethyl radical (“trityl radical”) is even more stable because of the three phenyl substituents. They actually stabilize the trityl radical to such an extent that it forms by homolysis from the so-called Gomberg hydrocarbon even at room temperature (Figure 1.6). Although this reaction is reversible, the trityl radical is present in equilibrium quantities of about 2 mol%.

Fig. 1.6. Reversible formation reaction of the triphenylmethyl radical. The equilibrium lies on the side of the Gomberg hydrocarbon.



A

Starting from the structure of the trityl radical, radicals were designed that can be obtained even *in pure form* as “stable radicals” (Figure 1.7). There are two reasons why these radicals are so stable. For one thing, they are exceptionally well resonance-stabilized. In addition, their dimerization to valence-saturated species has a considerably reduced driving force. In the case of the trityl radical, for example, dimerization

leads to the Gomberg hydrocarbon in which an aromatic sextet is lost. The trityl radical can not dimerize giving hexaphenylethane, because too severe van der Waals repulsions between the substituents would occur. There are also stable N- or O-centered radicals. The driving force for their dimerization is weak because relatively weak N—N or O—O bonds would be formed.

By the way, the destabilization of the dimerization product of a radical is often more important for the existence of stable radicals than optimum resonance stabilization. This is shown by comparison of the trityl radical derivatives **A** and **B** (Figure 1.7). In radical **A** the inclusion of the radical center in the polycycle makes optimum resonance stabilization possible because the dihedral angle χ between the $2p_z$ AO at the central atom and the neighboring π orbitals of the three surrounding benzene rings is exactly 0° . And yet radical **A** dimerizes! In contrast, the trityl radical derivative **B** is distorted like a propeller, to minimize the interaction between the methoxy substituents on the adjacent rings. The $2p_z$ AO at the central atom of radical **B** and the π orbitals of the surrounding benzene rings therefore form a dihedral angle χ of a little more than 45° . The resonance stabilization of radical **B** is therefore only one half as great— $\cos^2 45^\circ = 0.50$ —as that of radical **A**. In spite of this, radical **B** does not dimerize at all.

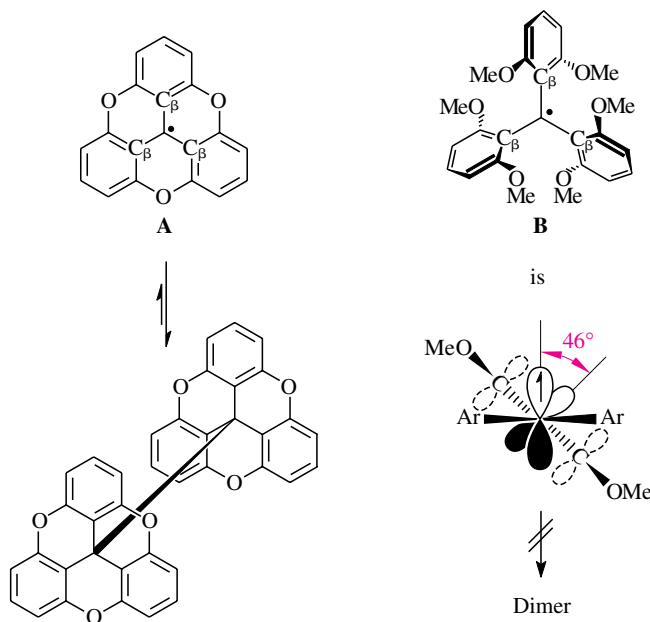


Fig. 1.7. Comparison of the trityl radical derivatives **A** and **B**; **A** dimerizes, **B** does not.

1.3 Relative Rates of Analogous Radical Reactions

In Section 1.2.1 we discussed the stabilities of reactive radicals. It is interesting that they make an evaluation of the relative rates of formation of these radicals possible.