REVIEWS OF REACTIVE
INTERMEDIATE CHEMISTRY

Edited by

MATTHEW S. PLATZ

ROBERT A. MOSS

MAITLAND JONES Jr.

REVIEWS OF REACTIVE INTERMEDIATE CHEMISTRY

Edited by

Matthew S. Platz
Department of Chemistry
Ohio State University
Columbus, OH

Robert A. Moss
Department of Chemistry
Rutgers University
New Brunswick, NJ

Maitland Jones, Jr.
Department of Chemistry
Princeton University
Princeton, NJ

REVIEWS OF REACTIVE INTERMEDIATE CHEMISTRY

THE WILEY BICENTENNIAL—KNOWLEDGE FOR GENERATIONS

*E*ach generation has its unique needs and aspirations. When Charles Wiley first opened his small printing shop in lower Manhattan in 1807, it was a generation of boundless potential searching for an identity. And we were there, helping to define a new American literary tradition. Over half a century later, in the midst of the Second Industrial Revolution, it was a generation focused on building the future. Once again, we were there, supplying the critical scientific, technical, and engineering knowledge that helped frame the world. Throughout the 20th Century, and into the new millennium, nations began to reach out beyond their own borders and a new international community was born. Wiley was there, expanding its operations around the world to enable a global exchange of ideas, opinions, and know-how.

For 200 years, Wiley has been an integral part of each generation's journey, enabling the flow of information and understanding necessary to meet their needs and fulfill their aspirations. Today, bold new technologies are changing the way we live and learn. Wiley will be there, providing you the must-have knowledge you need to imagine new worlds, new possibilities, and new opportunities.

Generations come and go, but you can always count on Wiley to provide you the knowledge you need, when and where you need it!

WILLIAM J. PESCE
PRESIDENT AND CHIEF EXECUTIVE OFFICER

PETER BOOTH WILEY
CHAIRMAN OF THE BOARD

■■■■ PREFACE

In 2004, Moss, Platz and Jones edited Reactive Intermediate Chemistry. This book contained chapters written by leading experts on the chemistry of the reactive intermediates commonly encountered in mechanistic organic chemistry; carbocations, radicals, carbanions, singlet and triplet carbenes, nitrenes and nitrenium ions. A three-dimensional approach was offered integrating venerable methods of chemical analysis of reaction products, direct observational studies of reactive intermediates (RI's) and high accuracy calculations of the geometries, potential energy surfaces and spectra of RI's. The book was aimed at beginning graduate students and newcomers to a particular field to provide him or her with an introductory chapter that would rapidly allow them to pursue advanced work.

Such is the richness and intellectual vibrancy of the field of RI chemistry that an additional book was needed to cover silicon, germanium and tin centered RI's, as well as tetrahedral intermediates and topics of increasing importance such as quantum mechanical tunelling, conical intersections, solid-state chemistry, and combustion chemistry. These topics are covered in this new book.

We hope *Reviews of Reactive Intermediate Chemistry* well captures the continuing evolution and breadth of Reactive Intermediate Chemistry, assists chemists to appreciate the state of the art and encourages new research in this area.

MATTHEW S. PLATZ
ROBERT A. MOSS
MAITLAND JONES, JR.

CONTRIBUTORS

M. J. Bearpark
Department of Chemistry
Imperial College London
South Kensington campus
London SW7 2AZ UK
email: m.bearpark@imperial.ac.uk

L. M. Campos
University of California, Los Angeles
Department of Chemistry and
    Biochemistry
607 Charles E. Young Drive East
Los Angeles, CA 90095-1569
email: lcampos@chem.ucla.edu

M. Garcia-Garibay
University of California, Los Angeles
Department of Chemistry and
    Biochemistry
607 Charles E. Young Drive East
Los Angeles, CA 90095-1569
email: mgg@chem.ucla.edu

K. S. Gates
Department of Chemistry
125 Chem Bldg.
University of Missouri
Columbia, MO 65211
email: GatesK@missouri.edu

J. P. Guthrie
The University of Western Ontario
Department of Chemistry
London, Ontario, Canada
N6A 5B8
email: peter.guthrie@uwo.ca

C. M. Hadad
Department of Chemistry
Ohio State University
100 West 18th Avenue
Columbus, OH 43210
email: hadad.1@osu.edu

W. M. Kwok
Department of Chemistry
The University of Hong Kong
Pokfulam Road
Hong Kong
email: kwokwm@hkucc.hku.hk

V. Ya. Lee
Department of Chemistry
Graduate School of Pure and Applied
    Sciences
University of Tsukuba
Tsukuba, Ibaraki 305-8571, Japan
email: leevya@chem.tsukuba.ac.jp

C. Ma
Department of Chemistry
The University of Hong Kong
Pokfulam Road
Hong Kong
email: macs@hkucc.hku.hk

J. K. Merle
National Institute of Standards
    and Technology
100 Bureau Drive, Stop 8380
Gaithersburg, MD 20899-8380
email: john.merle@nist.gov

D. L. Phillips
Department of Chemistry
The University of Hong Kong
Pokfulam Road
Hong Kong
email: phillips@hkucc.hku.hk

M. A. Robb
Department of Chemistry
Imperial College London
South Kensington campus
London SW7 2AZ UK
email: mike.robb@imperial.ac.uk

A. Sekiguchi
Department of Chemistry
Graduate School of Pure and Applied
    Sciences

University of Tsukuba
Tsukuba, Ibaraki 305-8571, Japan
email: sekiguch@chem.tsukuba.ac.jp

R. S. Sheridan
Department of Chemistry/216
University of Nevada, Reno
Reno, NV 89557
email: rss@chem.unr.edu

J. P. Toscano
Department of Chemistry
Johns Hopkins University
3400 N. Charles Street
Baltimore, MD 21218
email: jtoscano@jhu.edu

P. G. Wenthold
Department of Chemistry
Purdue University
560 Oval Drive
West Lafayette, Indiana, 47907-2084
email: pgw@purdue.edu

■■■ CONTENTS

REACTIVE INTERMEDIATES

Tetrahedral Intermediates Derived from Carbonyl Compounds, Pentacoordinate Intermediates Derived from Phosphoryl and Sulfonyl Compounds, and Concerted Paths Which Avoid Them

J. PETER GUTHRIE

Department of Chemistry, University of Western Ontario, London, Ontario, Canada N6A 5B7

1.1. TETRAHEDRAL INTERMEDIATES

This chapter will deal mainly with tetrahedral intermediates from carbonyl deriva-
tives, with some discussion on the much less-studied analogs for phosphorus and
sulfur. It will also address the issue of concerted mechanisms which can sometimes
bypass these intermediates.

Carbonyl reactions are extremely important in chemistry and biochemistry, yet they
are often given short shrift in textbooks on physical organic chemistry, partly because
the subject was historically developed by the study of nucleophilic substitution at satu-
rated carbon, and partly because carbonyl reactions are often more difficult to study.
They are generally reversible under usual conditions and involve complicated multistep
mechanisms and general acid/base catalysis. In thinking about carbonyl reactions, I
find it helpful to consider the carbonyl group as a (very) stabilized carbenium ion, with
an O^- substituent. Then one can immediately draw on everything one has learned about
carbenium ion reactivity and see that the reactivity order for carbonyl compounds:

$$CH_2=O > CH_3CH=O > PhCH=O > (CH_3)_2C=O > CH_3COPh$$
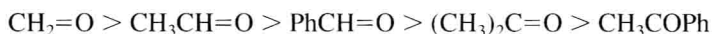
corresponds almost perfectly to the order for carbenium ions (see Table 1.1).

$$CH_3CH_2^+ > (CH_3)_2CH^+ > Ph(CH_3)CH^+ \sim (CH_3)_3C^+ > (CH_3)_2(Ph)C^+$$
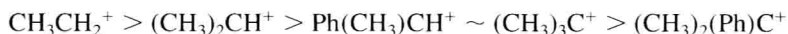
The difference between carbonyl chemistry and (simple) carbocation chemistry is
a result of much greater stability of the carbonyl group relative to a simple carbenium

TABLE 1.1. Reactivity of carbonyl compounds and carbenium ions.[a]

	$CH_3CH_2^+$	$(CH_3)_2CH^+$	$Ph(CH_3)CH^+$	$(CH_3)_3C^+$	$(CH_3)_2(Ph)C^+$
pK_R^+	-29.6[b]	-22.7[b]	-16.2[c]	-16.4[d]	-13.1[e]
	$CH_2=O$	$CH_3CH=O$	$PhCH=O$	$(CH_3)_2C=O$	CH_3COPh
$\log K_{H_2O}$[f]	1.61	-1.72	-3.82	-4.60	-6.92

[a]All in aqueous solution at 25°C; standard states are 1M ideal aqueous solution with an infinitely dilute
reference state, and for water the pure liquid.
[b]Reference 1.
[c]Reference 2.
[d]Reference 3.
[e]Reference 4.
[f]Reference 5.

ion. This means that for many carbonyl group/nucleophile combinations the carbonyl compound is more stable than the adduct, which is not the case for what are traditionally considered carbenium ions until one gets to stabilized triaryl cations (e.g., crystal violet) or to very non-nucleophilic solvents such as magic acid.[6]
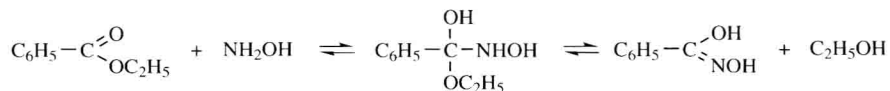
Thus carbonyl chemistry can be considered as analogous to S_N1 chemistry and is in fact inherently faster than S_N2 chemistry (not that S_N2 reactions cannot be fast, but this requires a strong thermodynamic driving force: for a comparable driving force the carbonyl reaction is faster).

The big difference is that for simple carbenium ions the cation is a transient intermediate and the covalent adduct is the normally encountered form, while for carbonyl compounds the "carbenium ion" is the stable form (with a few exceptions) and the covalent adduct is the transient intermediate. In fact, in many cases, the tetrahedral intermediate is too unstable to be detected (at least with current techniques) and yet the rate of overall reaction is strongly influenced by the height of this thermodynamic barrier. By Hammond's Postulate, a reaction leading to a high energy intermediate will have a transition state resembling this intermediate in structure and energy. If we can estimate the energy of the intermediate, then we have taken the first step toward estimating the rate of reaction.

For many carbonyl reactions, attempts have been made to prepare catalytic antibodies which accelerate the reaction. Such antibodies are normally obtained by challenging the immune system of a suitable animal with a compound resembling the tetrahedral intermediate in the reaction of interest. The idea is that if the antibody binds to and thus stabilizes the tetrahedral intermediate it will facilitate the reaction.[7,8] If the intermediate is a tetrahedral intermediate based on carbon then the analog is often a phosphate or phosphonate derivative, which is a stable tetrahedral species with a geometry and surface charge distribution resembling those of the intermediate in the reaction to be catalyzed.[9] A complimentary idea is that anything which resembles the transition state for an enzyme-catalyzed reaction, but is unreactive, will be a very strong inhibitor of that reaction.[10,11] Thus mimics of the tetrahedral intermediate can be strong inhibitors of enzymes catalyzing reactions which proceed by way of reactive tetrahedral intermediates.

1.1.1. Evidence for Tetrahedral Species as Reactive Intermediates

As early as 1899, Stieglitz[12] proposed a tetrahedral intermediate for the hydrolysis of an imino ether to an amide. Thus it was clear quite early that a complicated overall transformation, imino ether to amide, would make more sense as the result of a series of simple steps. The detailed mechanism proposed, although reasonable in terms of what was known and believed at the time, would no longer be accepted, but the idea of tetrahedral intermediates was clearly in the air. Stieglitz stated of the aminolysis of an ester that "it is now commonly supposed that the reaction takes place with the formation of an intermediate product as follows:" referring to work of Lossen.[13] (Note that the favored tautomer of a hydroxamic acid was as yet unknown.)

$$C_6H_5-C\underset{OC_2H_5}{\overset{O}{\diagdown}} \;+\; NH_2OH \;\rightleftharpoons\; C_6H_5-\overset{\overset{\textstyle OH}{|}}{\underset{\underset{\textstyle OC_2H_5}{|}}{C}}-NHOH \;\rightleftharpoons\; C_6H_5-C\underset{NOH}{\overset{OH}{\diagdown}} \;+\; C_2H_5OH$$

For many reactions of aldehydes or ketones with nucleophiles, the tetrahedral adduct is more or less readily detectable. Formaldehyde is overwhelmingly converted to methylenediol in water,[14] acetaldehyde is about 50% hydrated in water,[15] and acetone is only slightly converted to the hydrate, although the hydrate is readily detected by modern NMR instruments (the signal for the hydrate CH_3 is somewhat smaller than that for the ^{13}C satellite for the CH_3 of the keto form).[16] Thus, it is reasonable to assume that all carbonyl compounds can undergo nucleophilic addition, even when it is not directly detectable. For functional groups such as esters, the adduct with water or alcohol or even alkoxide is, for normal esters, at such low concentrations as to be undetectable. However, electron-withdrawing groups favor the addition of nucleophiles, so that CF_3COOMe will add MeO^-[17,18] and the equilibrium constant in methanol can be determined by ^{19}F NMR titration; at high concentrations of methoxide the conversion is essentially complete.[19]

A more difficult challenge is to establish that a tetrahedral intermediate is on the reaction path for the transformation of a carbonyl containing functional group. Isotopic exchange occurring with rates and a rate law very similar to hydrolysis provides strong evidence that the tetrahedral intermediate is on the reaction path and is partitioning between proceeding on to product or reverting to starting material with the loss of isotope.[20] This simple interpretation assumes that proton transfers involving the tetrahedral intermediate are fast relative to breakdown, which need not always be true.[21]
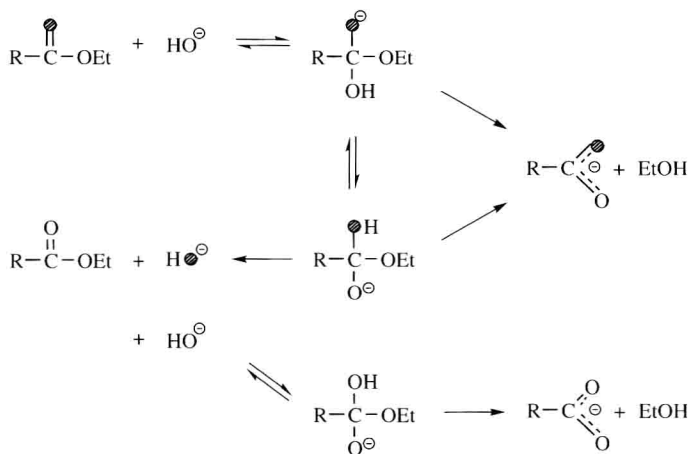
In other ester reactions, there may be concern that the reaction might be concerted, bypassing the tetrahedral intermediate. We will return to this question later. If the properties of Nu: or Lv: can be varied so that the relative leaving group

abilities within the tetrahedral intermediate change from "Lv:" being poorer than "Nu:" to "Lv:" being better than "Nu:" (allowing where necessary for any other factors which influence relative leaving group ability), then there will be a change in rate determining step if the mechanism is stepwise by way of a tetrahedral intermediate. This will show up as a break in a linear free energy relation (whether Hammett, or Taft, or Brønsted plot) for the stepwise mechanism, but as a simple linear relationship for the concerted mechanism[22] (see below). This test requires that the two competing steps of the stepwise reaction (breakdown of the intermediate to starting material or to product) have sufficiently different slopes for the linear free energy relation to give a clear break. This need not be the case if both are fast; that is, if the intermediate is of relatively high energy, so that by Hammond's Postulate the two transition states are close to the structure of the intermediate (and necessarily also to each other) and thus respond similarly to changes in reactant structure.
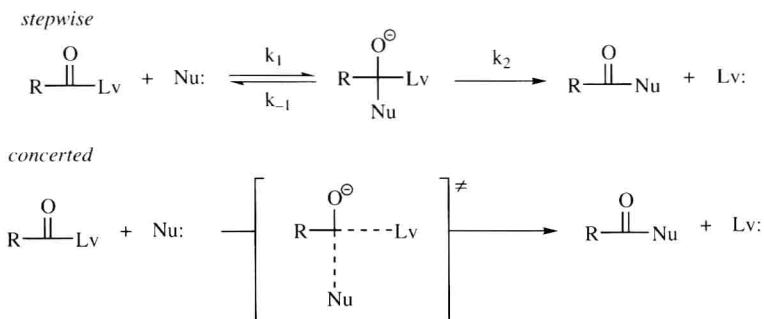
If the formation and breakdown steps of a mechanism involving a tetrahedral intermediate respond differently to changes in pH or catalyst concentration, then one can find evidence from plots of rate versus pH or rate versus catalyst concentration for a change in rate determining step and thus for a multistep mechanism. An example would be the maximum seen in the pH rate profile for the formation of an imine from a weakly basic amine (such as hydroxylamine).[23] On the alkaline side of the maximum, the rate determining step is the acid-catalyzed dehydration of the preformed carbinolamine; on the acid side of the maximum, the rate determining step is the uncatalyzed addition of the amine to form the carbinolamine. The rate decreases on the acid side of the maximum because more and more of the amine is protonated and unable to react.

If some change in reaction conditions leads to a change in the products of a reaction, without changing the observed rate, then there must be an intermediate which partitions in ways which respond to these changed reaction conditions, and formation of the intermediate must be rate determining. For instance, the products from the hydrolysis of the iminolactone shown below change with changing pH over a range where there is no change in the observed rate law.[24]