

SELECTION OF OXIDANTS IN SYNTHESIS

Oxidation at the Carbon Atom

LELAND J. CHINN

G. D. Searle & Co.
Chicago, Illinois

MARCEL DEKKER, INC., New York, 1971

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MARCEL DEKKER, INC.

95 Madison Avenue, New York, New York 10016

Library of Congress Catalog Card Number 71-134781

ISBN 0-8247-1098-3

Printed in the United States of America

SELECTION OF OXIDANTS IN SYNTHESIS

Oxidation at the Carbon Atom

OXIDATION IN ORGANIC CHEMISTRY

A Series of Monographs

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PREFACE

The present age has been characterized as one in which there is a deluge of information and a surfeit of publications. Consequently, any individual thinking of writing a book must ask whether his work will serve a useful purpose before he undertakes the beguiling task.

Certainly, the result must, at least, justify the inconveniences and demands imposed upon his family. It must also justify the help given him by his employer and colleagues.

Ideally, the book should provide the information that the reader wants, and it should make him feel that the time he spent reading it was not wasted.

Although a number of excellent works on oxidation and on specific oxidizing agents are available, the author feels there is a need, especially among those who are engaged in organic synthesis, for a monograph in which not only are the various reagents employed in oxidation categorized but that the conditions under which the reagents are best employed and the stereochemical course of the reaction are also presented.

The present monograph was conceived with this objective in mind. It was the author's hope that he would be able to achieve this objective. The ultimate goal was to place into the hands of the synthetic chemist a source of reference which would enable him to choose an oxidant that would accomplish selectively a specific transformation.

Unfortunately, however, it soon became apparent to the author that the state of the art is not sufficiently advanced as to allow the attainment of this attractive goal. Nevertheless, the need for a comprehensive, integrated monograph on oxidants that are applicable for synthetic purposes remains, and the author has attempted to compile such a volume.

In this monograph, the oxidants are classified in a manner that is most familiar to the synthetic organic chemist, namely, according to the particular chemical transformation. The monograph is divided into

three sections. Chapters 2 to 8 inclusive are devoted to those oxidative processes in which two electrons are transferred to the oxidant. Chapters 9, 10, and 11 cover those processes in which four electrons are removed by the oxidant, while the processes considered in the last two chapters are those in which six or more electrons are transferred to the oxidizing agent. Chapter 1, the introductory chapter, is concerned with the determination of the oxidation number of an atom and of the net change of electrons in a given oxidation.

The effects which steric, electronic, and stereoelectronic factors play in a particular reaction are discussed at length. Stereochemistry is also emphasized. Although kinetic data have been omitted, the results derived from such data have not been ignored.

The author hopes this volume will prove useful not only to research chemists who are engaged in organic synthesis but also to graduate students and advanced undergraduate students in chemistry who are interested in the rationale behind the selection of an oxidizing agent for a particular transformation.

The author is deeply grateful to his wife, Wilberta, for typing the manuscript and to his colleagues, Drs. George Lenz, William Sprenger, and Masateru Miyano, for reviewing it and for their suggestions and criticism.

The author is also pleased to record his appreciation of the encouragement which he had received from Dr. John W. Cusic and Dr. Byron Riegel, Research Advisor and Director of Chemical Research at G. D. Searle & Co., respectively.

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chapter 1

OXIDATION NUMBERS

Oxidation involves the removal of electrons. The atom that is oxidized is raised to a higher oxidation state, and this is reflected by the change in its oxidation number. For our purpose oxidation may be simply conceived as a process in which one or more oxygen atoms is added to a particular compound followed possibly by either addition or elimination of water (or its equivalent, e.g., ammonia). If we assume that the oxidizing agent is atomic oxygen, we find that its oxidation number undergoes a change from 0 to -2 in the process.

Tables 1-1 through 1-5 list the oxidation numbers of carbon, nitrogen, oxygen, sulfur, and the halogens in some of the different species or compounds derived from them. From these tables one can determine the net number of electrons involved in the transformation of one class of compounds to another. Thus the oxidation of a single molecule of methane to formic acid requires the removal of six electrons.

In these tables the substituents about carbon, nitrogen, oxygen, and halogens are hydrogen atoms. Hydrogen is more electropositive than the other atoms (1), so that in these compounds the oxidation number of hydrogen is assumed to be $+1$ (2). Replacement of one of the hydrogen atoms by a substituent that is also electropositive relative to the central atom does not affect the oxidation state of the latter. However, if the replacement is more electronegative than the central atom, then the oxidation number of the latter will be raised by 2. If the electronegativity of the replacement is the same as that of the central atom, the latter's oxidation number will be raised by 1.

In hydrogen peroxide the oxidation number of each of the two hydrogen atoms is $+1$. If the two oxygen atoms have the same electronegativity, which implies that the pair of electrons that form the $O-O$

TABLE I
OXIDATION NUMBER OF CARBON

Species	Oxidation Number
$\text{CH}_4, \text{CH}_3^-$	-4
$\text{CH}_3\text{OH}, \text{CH}_3^+, \text{H}_2\text{C:}$	-2
$\begin{array}{ccccccc} \text{OH} & & \text{O} & & \text{O} & & \text{OH} \\ & & & & & & \\ \text{H}_2\text{C}-\text{OH}, & \text{H}_2\text{C:}, & \text{HOCH}_2^+, & \text{HC:}^-, & \text{HC:} & & \\ & & & & & & \\ \text{OH} & & \text{O} & & \text{O} & & \text{O} \\ & & & & & & \\ \text{HC}-\text{OH}, & \text{HCOH}, & \text{HC}^+, & \text{HOC:}^-, & \text{C:} & & \\ & & & & & & \\ \text{OH} & & & & & & \end{array}$	0
$\begin{array}{ccccccc} \text{OH} & & \text{O} & & \text{O} & & \text{O} \\ & & & & & & \\ \text{HO}-\text{C}-\text{OH}, & \text{HOCOH}, & \text{C}, & \text{HOC}^+ & & & \\ & & & & & & \\ \text{OH} & & \text{O} & & & & \end{array}$	+2
$\begin{array}{ccccccc} \text{OH} & & \text{O} & & \text{O} & & \text{O} \\ & & & & & & \\ \text{HO}-\text{C}-\text{OH}, & \text{HOCOH}, & \text{C}, & \text{HOC}^+ & & & \\ & & & & & & \\ \text{OH} & & \text{O} & & & & \end{array}$	+4
$\text{H}_2\text{C}=\text{CH}_2$	-2 ^a
$\text{HC}\equiv\text{CH}$	-1 ^a

^aOxidation number of each carbon atom.

valance bond are equally shared by the two atoms, then the oxidation number of each of the two oxygen atoms will be -1, in contrast to the oxidation number of oxygen in water which is -2. If, however, the two oxygen atoms have different electronegativity, then the pair of electrons that form the O—O bond must be closer to one of the oxygen atoms than to the other. As a result, the oxidation number of one of the oxygen atoms will be -2 and that of the other will be 0.

In many complex organic molecules, the oxidation state of a particular atom cannot be readily determined. Fortunately, however, the synthetic organic chemist is not as interested in the oxidation state of an atom as he is in the overall change in the oxidation state of the molecule in going from one compound to another. For the purpose of determining the overall change in the oxidation state in a given transformation, the chemist needs only to assume that the oxidation number for a particular substituent is the same in both the reactant and the product. For example, the oxidation of ethane to acetic acid is analogous to the oxidation of methane to formic acid and should therefore involve the removal of the same number of electrons. In methane the oxidation number of the carbon atom is -4, while in ethane the oxidation number of each of the carbon atoms is -3 if we assume that the

TABLE 1-2
OXIDATION NUMBER OF NITROGEN

Species	Oxidation Number
$\text{H}_3\text{N:}, \text{H}_2\text{N:}^-$	-3
$\text{H}_2\text{N}-\text{OH}, \text{H}_2\text{N}^+, \text{H}\ddot{\text{N}}^- - \text{OH}, \text{HN:},$ $\text{H}_3\text{N}^+ - \text{O}^-, \text{H}_2\text{N}-\text{O}^-$	-1
$\begin{array}{ccccc} \text{OH} & \text{OH} & \text{OH} & \text{OH} & \text{H} \\ & & & & \\ \text{HN}-\text{OH}, & \text{HN}^+, & \text{HON:}^-, & \text{N:}, & \text{HN}^+ - \text{OH} \\ & & & & \\ & & & & \text{O}^- \end{array}$	+1
$\begin{array}{ccccc} \text{OH} & & \text{OH} & & \text{OH} \\ & & & & \\ \text{HO}-\text{N}-\text{OH}, & \text{HO}-\text{N}^+, & \text{HO}-\text{N}=\text{N}^+, & \text{HN}^+ - \text{OH}, \\ & & & \\ & & & \text{O}^- \end{array}$	+3
$\begin{array}{ccccc} \text{O} & & \text{OH} & & \text{O}^- & \text{O} \\ & & & & & \\ \text{H}-\text{N}^+ - \text{O}^- & & \text{HO}-\text{N}^+ - \text{OH}, & \text{HO}-\text{N}^+, & \text{HO}-\text{N}^+, & \text{N}^+ \\ & & & & & \\ \text{O}^- & & \text{O} & & \text{O} & \text{O} \end{array}$	+5
$\text{H}_2\ddot{\text{N}}-\ddot{\text{N}}\text{H}_2$	-2 ^a
$\text{HN}=\ddot{\text{N}}\text{H}$	-1 ^a
$\begin{array}{c} \text{O}^- \\ \\ \text{HN}^+ = \ddot{\text{N}}\text{H} \end{array}$	+1 ^b , -1 ^c

^aOxidation number of each nitrogen atom.

^bOxidation number of oxygen-bearing nitrogen.

^cOxidation number of second nitrogen atom.

TABLE 1-3
OXIDATION NUMBER OF OXYGEN

Species	Oxidation Number
$\text{H}\ddot{\text{O}}\text{H}, \text{H}\ddot{\text{O}}:^-$	-2
$\text{H}\ddot{\text{O}}-\ddot{\text{O}}\text{H}, \text{H}\ddot{\text{O}}-\ddot{\text{O}}:^-, \text{H}\ddot{\text{O}}\cdot$	-1 ^a
$\text{H}\ddot{\text{O}}^+$	0

^aOxidation number of each oxygen atom.

C—C bond is unpolarized. Thus the oxidation number of each of the two methyl groups that comprise the ethane molecule is 0. In acetic acid it is assumed that the oxidation number of the methyl group is also 0. Since the oxidation numbers of the hydroxyl group and the carbonyl

TABLE 1-4
OXIDATION NUMBER OF SULFUR

Species	Oxidation Number
$\text{H}\ddot{\text{S}}\text{H}, \text{H}\ddot{\text{S}}:^-$	-2
$\text{H}\ddot{\text{S}}-\text{OH}, \text{H}\ddot{\text{S}}^+, \text{HO}-\ddot{\text{S}}:^-, \text{H}\overset{\text{O}}{\parallel}\text{SH}, \text{HS}^-$	0
$\text{HO}-\overset{\text{O}}{\parallel}\text{S}-\text{OH}, \text{HO}-\ddot{\text{S}}^+, \text{H}\overset{\text{O}}{\parallel}\text{S}-\text{OH}, \text{H}\overset{\text{O}}{\parallel}\text{S}^+, \text{HO}-\overset{\text{O}}{\parallel}\text{S}^-,$ $\text{H}\overset{\text{O}}{\parallel}\text{SH}, \text{HS}^-$	+2
$\text{HO}-\overset{\text{O}}{\parallel}\text{S}-\text{OH}, \text{HO}-\ddot{\text{S}}^+, \text{H}\overset{\text{O}}{\parallel}\text{SOH}, \text{HS}^+, \text{HOS}^-$	+4
$\text{HO}-\overset{\text{O}}{\parallel}\text{S}-\text{OH}, \text{HO}-\overset{\text{O}}{\parallel}\text{S}^+$	+6
$\text{H}\ddot{\text{S}}-\ddot{\text{S}}\text{H}$	-1 ^a

^aOxidation number of each sulfur atom.

TABLE 1-5
OXIDATION NUMBER OF HALOGEN

Species	Oxidation Number
$\text{H}\ddot{\text{X}}:, :\ddot{\text{X}}:^-$	-1
$\text{HO}-\ddot{\text{X}}:, \ddot{\text{X}}^+, \text{H}\overset{\text{O}}{\parallel}\text{X}:, \text{X}\overset{\text{O}^-}{\parallel}$	+1
$\text{HO}-\overset{\text{O}}{\parallel}\text{X}:, \text{X}^+$	+3
$\text{HO}-\overset{\text{O}}{\parallel}\text{X}^+-\text{O}^-, \text{X}^+=\text{O}$	+5
$\text{HO}-\overset{\text{O}}{\parallel}\text{X}^+=\text{O}, \text{X}^+=\text{O}$	+7

oxygen are -1 and -2 , respectively, the algebraic sum of the oxidation numbers of all the groups attached to the carboxyl carbon is -3 . In order that the net charge on the acetic acid molecule be 0 , the oxidation number of the carboxyl carbon must be $+3$. Hence the oxidation of ethane to acetic acid results in the removal of six electrons just as in the oxidation of methane to formic acid, for the oxidation number of the carbon atom oxidized in the transformation of ethane to acetic acid increases from -3 to $+3$.

Alternatively, the number of electrons removed can be determined by balancing the equation



Here the formal assumption is made that water is the source of oxygen in the product. Since there are two oxygen atoms in acetic acid, two molecules of water are required. The excess hydrogen atoms on the left-hand side of the equation are offset by introducing six protons on the right-hand side. The six positive charges resulting from the introduction of the protons are then balanced by adding six electrons to the equation, so that the stoichiometric equation for the conversion of ethane to acetic acid is



The six electrons used to balance the equation represent the number of electrons that must be removed from ethane by the oxidizing agent in order that one molecule of ethane be transformed into one molecule of acetic acid.

REFERENCES

1. L. Pauling, *The Nature of the Chemical Bond*, Cornell Univ. Press, Ithaca, New York, 1960, p. 88.
2. C. K. Jørgenson, *Oxidation Numbers and Oxidation States*, Springer, New York, 1969, p. 11.

In the approach adopted by Jørgenson, the carbon and hydrogen atoms of methane are assigned the oxidation numbers of $+4$ and -1 , respectively. Accordingly, the oxidation of methane to methyl alcohol is considered to involve a change in the oxidation number of one of the hydrogen atoms from -1 to $+1$, the oxidation number of the carbon atom remaining the same. In our approach the carbon and hydrogen atoms of methane are assumed to have the oxidation numbers of -4 and $+1$, respectively. The oxidation of methane to methyl alcohol is regarded as involving a change in the oxidation number of carbon from -4 to -2 .

Only meager evidence was presented by Jørgenson in support of his assignment. In view of the difficulties associated with the assignment of a -1 oxidation number to the hydrogen atom in a hydrocarbon, difficulties that Jørgenson enumerated, we find it more desirable to base the oxidation numbers on the electronegativity scale of the elements (1).