Oxidation of Primary Alcohols to Carboxylic Acids

BASIC REACTIONS IN ORGANIC SYNTHESIS

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Oxidation of Alcohols to Aldehydes and Ketones:
A Guide to Current Common Practice, by Gabriel Tojo and Marcos Fernández

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This book is dedicated to the thousands of scientists cited in the references who constructed our present knowledge on the oxidation of primary alcohols to carboxylic acids. Thanks to their collective effort, the preparation of medicines, pesticides, colorants, and a variety of chemicals that make life more enjoyable, is greatly facilitated.

Preface to the Series

There is natural selection in the synthetic organic laboratory. Successful reagents find their way into specialized journals and tend to populate researchers' benches. Sometimes, old species—like active manganese dioxide in the oxidation of unsaturated alcohols—are so well adapted to a certain reaction niche that they remain unchallenged for a long time. On other occasions, a successful new species—like Dess Martin periodinane—enjoys a population explosion and very quickly inhabits a great number of laboratories. On the other hand, the literature is filled with promising new reagents that fell into oblivion because nobody was able to replicate the initial results on more challenging substrates.

This series, which consists of a collection of monographs on basic reactions in organic synthesis, is not primarily aimed at specialized researchers interested in the development of new reagents. Rather, it is written with the objective of being a practical guide for any kind of scientist, be it a chemist of whatever sort, a pharmacologist, a biochemist, or whoever has the practical need to perform a certain basic synthetic operation in the quickest and most reliable way. Therefore, great emphasis is given to those reagents that are employed most often in laboratories, because their ubiquity proves that they possess a greater reliability. Reagents appearing in only a few publications, regardless of promising potential, are only briefly mentioned. We prefer to err on the side of ignoring some good reagents, rather than including bad reagents that would lead researchers to lose precious time.

The books from this series are meant to be placed near working benches in laboratories, rather than on the shelves of libraries. That is why full experimental details for important reactions are provided. Although many of references from the literature are facilitated, this series is written with the aim of avoiding as much as possible the need to consult original research articles. Many researchers do not have scientific libraries possessing numerous chemical journals readily available, and, many times, although such libraries might be on hand, it is inconvenient to leave the laboratory in order to consult some reference.

Our aim is to facilitate practical help for anybody preparing new organic compounds.

Preface

There is a common view among organic chemists that simple functional group transformations are a mature technology away from the forefront in the Art of Organic Synthesis. This is undoubtedly not the case in the conversion of primary alcohols into carboxylic acids. An ideal reagent for such transformation should be (1) reliable and efficient with regard to all molecules, including complex structures possessing oxidation-sensitive functional groups, (2) cheap, and (3) environmentally friendly. There is no such reagent, even if we limit ourselves to the more mundane need of anything able to provide a certain much-needed carboxylic acid, regardless of price and ecology. This state of affairs is highlighted by the fact that in forty percent of cases the oxidation of primary alcohols to acids is performed using a two-step procedure via the corresponding aldehydes; something that proves that the oxidation of alcohols to aldehydes is a much more mature technology than the oxidation of alcohols to carboxylic acids.

This monograph is a laboratory guide for the transformation of primary alcohols into carboxylic acids. It displays a panorama of the state of the art for this functional group transformation, highlighting the weaponry currently available for scientists and areas where further progress is needed. In conformity with the rest of the series, a selection is made to include those procedures that have proved more reliable in many laboratories around the globe.

Abbreviations

Ac	acetyl
Alloc	allyloxycarbonyl
BAIB	bis(acetoxy)iodobenzene
Bn	benzyl
Boc	*t*-butoxycarbonyl
b.p.	boiling point
Bu	*n*-butyl
t-Bu	*tert*-butyl
Bz	benzoyl
ca.	circa
CA	*Chemical Abstracts*
cat.	catalytic
Cbz	benzyloxycarbonyl
DCAA	dichloroacetic acid
DCC	*N*,*N*′-dicyclohexyl carbodiimide
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMSO	dimethyl sulfoxide
ee	enantiomeric excess
EE	1-ethoxyethyl
eq.	equivalent
Et	ethyl
Fmoc	9-fluorenyl methoxycarbonyl
g	gram
h	hour
i-Pr	isopropyl
L	liter
m	multiplet
M	mol/L
MCPBA	*m*-chloroperoxybenzoic acid
Me	methyl
MEM	(2-methoxyethoxy)methyl
min.	minute
MOM	methoxymethyl
MS	molecular sieves
MTBE	methyl *t*-butyl ether
MW	molecular weight
NCS	*N*-chlorosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
NMR	nuclear magnetic resonance
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl
PhF	9-phenylfluorenyl
Pht	phthaloyl
PMB	*p*-methoxybenzyl
ppm	parts per million
Pr	propyl
Py	pyridine
ref.	reflux
r.t.	room temperature
sat.	saturated
T	temperature
TBDPS	*t*-butyldiphenylsilyl
TBS	*t*-butyldimethylsilyl
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy free radical
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride

THF	tetrahydrofuran	TPAP	tetrapropylammonium perruthenate
THP	tetrahydropyran-2-yl	v	volume
T_i	internal temperature	w	weight
TIPS	triisopropylsilyl	Z	benzyloxycarbonyl
TMS	trimethylsilyl		

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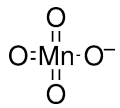
Permanganate



1.1. Introduction

Potassium permanganate is a very strong oxidant that was recurrently employed at the end of the 19th century and the beginning of the 20th century for the determination of organic structures by oxidative degradation. During these degradation studies it became clear that potassium permanganate was able to oxidize primary alcohols to carboxylic acids, and, in 1907[1] and 1909,[2] Fournier proposed the use of aqueous potassium permanganate under strongly alkaline conditions for the oxidation of alcohols to acids. Obviously, these conditions are appropriate for oxidation of alcohols with a certain solubility in water and possessing resistance to degradation by aqueous alkali. In order to broaden the scope of the permanganate oxidation, a number of modifications were later introduced, including:

- Using diverse pH from highly alkaline, as proposed by Fournier, to strongly acidic.[3]
- Adding an organic cosolvent[4] to facilitate the mixing of the alcohol with permanganate.
- Running the reaction in a solvent[5] possessing high solubilizing capacity for both potassium permanganate and alcohols.
- Performing the reaction in a biphasic system with an added phase-transfer catalyst.[6]
- Adding a crown ether[7] that forms a complex with potassium permanganate and facilitates the dissolution of permanganate in organic solvents.
- Employing a tetraalkylammonium permanganate[8] that is soluble in organic solvents thanks to the lipophilic properties of the tetraalkylammonium cation.

The available data are consistent, for most alcohols, with the following mechanism for the oxidation of alcohols to acids using permanganate.

A hydride is transferred—from an alcohol or from the corresponding alkoxide—to either a permanganate anion (MnO_4^-) or to permanganic acid