COMPREHENSIVE ORGANIC TRANSFORMATIONS

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A Guide to Functional Group Preparations

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Library of Congress Cataloging-in-Publication Data

Larock, Richard C., 1944–
Comprehensive organic transformations: a guide to functional group preparations/by Richard Larock; foreword by H. C. Brown

p. cm.
Includes index.
ISBN 0-89573-710-8
1. Chemistry, Organic—Synthesis. I. Title.
QD262.L355 1989
547'.2—dc19 89-30333
CIP

British Library Cataloguing in Publication Data

Larock, Richard C.
Comprehensive organic transformations:
a guide to functional group preparations.
1. Organic compounds. Synthesis
I. Title
547'.2

ISBN 0-89573-710-8

Printed in the United States of America.
ISBN 0-89573-710-8 VCH Publishers
ISBN 3-527-26953-3 VCH Verlagsgesellschaft

Printing History:
10 9 8 7 6 5 4 3 2

Published jointly by:

VCH Publishers, Inc.
220 East 23rd Street
Suite 909
New York, New York 10010

VCH Verlagsgesellschaft mbH
P.O. Box 10 11 61
D-6940 Weinheim
Federal Republic of Germany

VCH Publishers (UK) Ltd.
8 Wellington Court
Cambridge CB1 1HW
United Kingdom

The text and chemical structures in this book were set by
Science Typographers, Inc., 15 Industrial Boulevard,
Medford, L.I., New York 11763

FOREWORD

At one time organic chemists looked askance at those who elected to devote their research effort to the development of new, selective methods for achieving chemical transformations of organic compounds. Early practitioners in this area received many critical comments—it was felt that the proper objective of organic chemists was the synthesis of natural products, and that one should only develop a new method when such a method was required to overcome a hurdle in the synthetic procedure. But we persisted. Now there appears to be a general acceptance of the value of such research.

Now a new problem has appeared. We have brought forth so many new, highly selective synthetic methods that it is difficult for the chemist to know all of them and to select the method that would be most effective for the synthesis in hand. One approach is to publish monographs that review specialized areas. For example, my own field of borane reagents was reviewed 15 years ago (*Organic Syntheses via Boranes*, by H. C. Brown, Wiley, 1975). A more recent book of this sort is *Borane Reagents*, by A. Pelter, K. Smith, and H. C. Brown, Academic Press, 1988.

But such specialized books solve only part of the problem. In the present work, Richard C. Larock has set himself the goal of organizing the entire panoply of synthetic methods. But there are now so many methods that even brief descriptions of each procedure would have produced a work as large as the new Oxford English Dictionary (16 volumes, Oxford University Press, 1986). Instead, he adopted the unique solution of indicating the reagent and transformation, with pertinent references. This provides a concise summary that should be of enormous assistance to those searching for a selective reaction to achieve a desired transformation in the presence of difficult substituents. This problem is frequently faced today by those who undertake the involved syntheses that are often an important objective of current research.

One must admire Richard Larock's courage in undertaking this monumental task.

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PREFACE

Organic synthesis is one of the most rapidly developing areas of chemistry. Every day useful new reagents and reactions are reported worldwide in the chemical literature. It is increasingly difficult for the organic chemist to keep up with the latest in synthetic organic methodology without spending an inordinate amount of time reading a wide variety of chemical journals, including those whose focus is not strictly synthetic organic chemistry.

In recent years a variety of books and reviews have appeared to aid the organic chemist interested in synthetic methodology, but even the best of these have now ballooned to inconvenient multivolume sets whose cost is prohibitive to those just entering the field. The intent of the present volume is to provide a comprehensive, highly condensed, systematic collection of useful synthetic methodology that both the beginning student and the long-time practitioner of organic synthesis will find useful.

This book began in 1973 as a series of course handouts designed to cover the key reactions of the major organic functional groups. Like the aforementioned publications, this reference work has grown rapidly over the years to a major treatise covering a vast amount of synthetic organic methodology. It was felt that the synthetic organic community might find this compilation useful, so a serious effort has been made in the last two years to thoroughly update and organize this material for publication.

The author takes full responsibility (and credit?) for the choice of reactions and references. Obviously not every reaction or reference could be included. In choosing material for this text the author has observed the following guidelines. All reactions to be included should be general in scope or else so unique that the methodology will find real synthetic utility. Yields should generally be at least 50%. Reagents should be readily available or easily prepared and handled in the laboratory. As much as possible, similar transformations should appear together in as concise a format as possible. Significant limitations in methodology shall be noted. No effort has been made to cover the use of protecting groups since excellent reviews on this subject are already available. Likewise, heterocyclic chemistry has consciously been omitted, except where heterocycles have been employed to effect simple functional group manipulations. Multiple group transformations have been covered, although they present certain organizational problems. To those chemists whose contributions to synthetic organic chemistry may have been slighted or altogether ignored, I apologize. It would be appreciated if major errors or omissions be brought to the author's attention so that future printings or subsequent editions may be corrected.

All reactions have been systematically organized according to the functional group being synthesized, with no attempt to cover the less important functional groups. Within each section the methodology is subdivided into major processes, such as oxidation, reduction,

alkylation, etc. It is hoped that the reader will easily find the desired transformations by skimming the detailed Table of Contents, although an extensive Transformation Index is available in time of need.

Literature coverage is complete through 1987. Some 160 or more primary chemical journals and a number of books and reviews have been abstracted. Obscure journals not readily available to most synthetic organic chemists have been avoided. The names of authors have been omitted to save space. Original publications have not always been cited if they do not necessarily describe the best reaction conditions for running the reaction or purvey little of the scope of the reaction. References containing full experimental procedures, though they may be buried in an experimental section, have been favored over communications lacking such details. An attempt has been made to highlight reviews and significant publications. One immediately encounters problems in deciding where to draw the line on references. Initial reports of a useful new reaction have received complete coverage. However, the time soon comes when a truly significant reaction, such as the use of ester enolates in synthesis, appears routinely in publication after publication and no reviews have appeared. In such situations, the author has tended to include all new material and may not have had the time to omit the more inconsequential earlier references.

It is hoped that the reader finds this effort worthwhile and will not hesitate to make suggestions on ways this material may be improved.

Richard C. Larock
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May, 1988

ACKNOWLEDGMENTS

The preparation of a book of this magnitude requires the assistance of a number of people. The author is indebted to Iowa State University for providing the time and assistance necessary for the preparation of much of this book. The Department of Chemistry at the University of Hawaii at Manoa is gratefully acknowledged for having provided a visiting professorship which allowed the author to push this manuscript through to publication.

To those around me who have had to "endure" this book, your patience and perseverance are appreciated. To my students who have sometimes had to take a back seat to this project, I thank them for waiting. To those who volunteered to help in proofing the final text, I extend my gratitude.

I must also acknowledge a core of dedicated secretaries over the years who have continually updated this material for classroom use. Most important of these secretaries is Mrs. Nancy Qvale, who is responsible for the preparation of a major portion of this work and bore the burden of putting this manuscript in final form. Without her outstanding technical assistance and dedication, this book might never have materialized.

LITERATURE ABBREVIATIONS

Acct Chem Res	*Accounts of Chemical Research*
Acta Chem Scand	*Acta Chemica Scandinavica*
Acta Chem Scand B	*Acta Chemica Scandinavica. Series B: Organic Chemistry and Biochemistry*
Adv Alicyclic Chem	*Advances in Alicyclic Chemistry*
Adv Carbohydr Chem	*Advances in Carbohydrate Chemistry*
Adv Catalysis	*Advances in Catalysis*
Adv Chem Ser	*Advances in Chemistry Series*
Adv Heterocyclic Chem	*Advances in Heterocyclic Chemistry*
Adv Org Chem	*Advances in Organic Chemistry: Methods and Results*
Adv Organometal Chem	*Advances in Organometallic Chemistry*
Adv Photochem	*Advances in Photochemistry*
Adv Phys Org Chem	*Advances in Physical Organic Chemistry*
Agric Biol Chem	*Agricultural and Biological Chemistry*
Anal Chem	*Analytical Chemistry*
Anal de Quim	*Anales de Quimica*
Angew	*Angewandte Chemie*
Angew Int	*Angewandte Chemie, International Edition in English*
Ann	*Justus Liebig's Annalen der Chemie*
Ann Chim	*Annales de Chimie*
Ann NY Acad Sci	*Annals of the New York Academy of Sciences*
Ann Rep Med Chem	*Annual Reports in Medicinal Chemistry*
Appl Microbiol	*Applied Microbiology*
Appl Microbiol Biotechnol	*Applied Microbiology and Biotechnology*
Arch Pharm	*Archiv der Pharmazie*
Arkiv Kemi	*Arkiv for Kemi*
Austral J Chem	*Australian Journal of Chemistry*
BCSJ	*Bulletin of the Chemical Society of Japan*
Ber	*Berichte der Deutschen Chemischen Gesellschaft*
Biochem	*Biochemistry*
Biochem Biophy Res Commun	*Biochemical and Biophysical Research Communications*
Biochem J	*Biochemical Journal*
Biochim Biophys Acta	*Biochimica et Biophysica Acta*
Bioorg Chem	*Bioorganic Chemistry*
BSCF	*Bulletin de la Societe Chimique de France*
Bull Acad Polon Sci, Ser Sci Chem	*Bulletin de l'Academie Polonaise des Sciences, Serie des Sciences Chimiques*
Bull Acad Sci USSR, Div Chem Sci	*Bulletin of the Academy of Sciences of the USSR. Division of Chemical Science*
Bull Korean Chem Soc	*Bulletin of the Korean Chemical Society*
Bull Soc Chim Belg	*Bulletin des Societes Chimiques Belges*
CA	*Chemical Abstracts*
Can J Chem	*Canadian Journal of Chemistry*
Cancer Lett	*Cancer Letters*

Carbohydr Res	*Carbohydrate Research*
Catal Rev	*Catalysis Reviews*
CC	*Journal of the Chemical Society: Chemical Communications*
Chem Eng News	*Chemical and Engineering News*
Chem in Britain	*Chemistry in Britain*
Chem Ind	*Chemistry and Industry*
Chem Listy	*Chemicke Listy*
Chem Pharm Bull	*Chemical and Pharmaceutical Bulletin*
Chem Phys Lipids	*Chemistry and Physics of Lipids*
Chem Rev	*Chemical Reviews*
Chem Scripta	*Chemica Scripta*
Chem Soc Rev	*Chemical Society Reviews*
Chem Weekb	*Chemisch Weekblad*
Chem Zeitung	*Chemiker Zeitung*
Chem Zentr	*Chemisches Zentralblatt*
CL	*Chemistry Letters*
Coll Czech Chem Commun	*Collection of Czechoslovak Chemical Communications*
Compt Rend	*Comptes Rendus Hebdomadaires des Seances de l'Academie des Sciences*
Compt Rend C	*Comptes Rendus Hebdomadaires des Seances de l'Academie des Sciences. Serie C: Sciences Chimiques*
Curr Sci	*Current Science*
Discuss Faraday Soc	*Discussions of the Faraday Society*
Fortschr Chem Forsch	*Fortschritte der Chemischen Forschung*
Fund Res Homogeneous Catal	*Fundamental Research in Homogeneous Catalysis*
Gazz Chim Ital	*Gazzetta Chimica Italiana*
Helv	*Helvetica Chimica Acta*
Ind Eng Chem	*Industrial and Engineering Chemistry*
Ind J Chem	*Indian Journal of Chemistry*
Ind J Chem B	*Indian Journal of Chemistry. Section B: Organic Chemistry and Medicinal Chemistry*
Inorg	*Inorganic Chemistry*
Int J Sulfur Chem	*International Journal of Sulfur Chemistry*
Intra-Science Chem Reports	*Intra-Science Chemistry Reports*
Israel J Chem	*Israel Journal of Chemistry*
Izv Akad Nauk SSSR, Ser Khim	*Izvestiia Akademii Nauk SSSR. Seriia Khimicheskaia*
J Am Oil Chem Soc	*Journal of the American Oil Chemists' Society*
J Antibiotics	*Journal of Antibiotics*
J Biol Chem	*Journal of Biological Chemistry*
J Catalysis	*Journal of Catalysis*
J Chem Ed	*Journal of Chemical Education*
J Chem Eng Data	*Journal of Chemical and Engineering Data*
J Chem Res (S)	*Journal of Chemical Research. Synopses*
J Fluorine Chem	*Journal of Fluorine Chemistry*
J Gen Chem USSR	*Journal of General Chemistry of the USSR*
J Heterocyclic Chem	*Journal of Heterocyclic Chemistry*
J Ind Chem Soc	*Journal of the Ind... Chemical Society*

J Label Compds	*Journal of Labelled Compounds*
J Lipid Res	*Journal of Lipid Research*
J Med Chem	*Journal of Medicinal Chemistry*
J Mol Catal	*Journal of Molecular Catalysis*
J Nat Prod	*Journal of Natural Products*
J Pharm Sci	*Journal of Pharmaceutical Sciences*
J Photochem	*Journal of Photochemistry*
J Polym Sci, Polym Chem Ed	*Journal of Polymer Science: Polymer Chemistry Edition*
J Prakt Chem	*Journal für Praktische Chemie*
J Russ Phys Chem Soc	*Journal of the Russian Physical Chemical Society*
J Sci Ind Res B	*Journal of Scientific and Industrial Research. Part B: Physical Sciences*
J Vitaminol (Osaka)	*Journal of Vitaminology*
JACS	*Journal of the American Chemical Society*
JCS	*Journal of the Chemical Society*
JCS A	*Journal of the Chemical Society. Section A: Inorganic, Physical and Theoretical*
JCS B	*Journal of the Chemical Society. Section B: Physical Organic*
JCS C	*Journal of the Chemical Society. Section C: Organic*
JCS D	*Journal of the Chemical Society. Section D: Chemical Communications*
JCS Dalton	*Journal of the Chemical Society: Dalton Transactions*
JCS Japan	*Journal of the Chemical Society of Japan*
JCS Perkin I	*Journal of the Chemical Society: Perkin Transactions I*
JCS Perkin II	*Journal of the Chemical Society: Perkin Transactions II*
JOC	*Journal of Organic Chemistry*
JOC USSR	*Journal of Organic Chemistry of the USSR*
JOMC	*Journal of Organometallic Chemistry*
Methods Carbohydr Chem	*Methods in Carbohydrate Chemistry*
Monatsh	*Monatshefte für Chemie*
Natl Prod Repts	*Natural Product Reports*
Naturwiss	*Naturwissenschaften*
Newer Methods Prep Org Chem	*Newer Methods of Preparative Organic Chemistry*
Nouv J Chim	*Nouveau Journal de Chimie*
Org Mag Res	*Organic Magnetic Resonance*
Org Photochem	*Organic Photochemistry*
Org Prep Proc Int	*Organic Preparations and Procedures International*
Org Rxs	*Organic Reactions*
Org Syn	*Organic Syntheses*
Org Syn Coll Vol	*Organic Syntheses. Collective Volume*
Organomet	*Organometallics*
Organomet Chem Rev A	*Organometallic Chemistry Reviews. Section A: Subject Reviews*
Organomet Chem Syn	*Organometallics in Chemical Synthesis*
Phosphorus	*Phosphorus and the Heavier Group Va Elements*
Phosphorus and Sulfur	*Phosphorus and Sulfur and the Related Elements*
Photochem Photobiol	*Photochemistry and Photobiology*
Pol J Chem	*Polish Journal of Chemistry*
Polym J	*Polymer Journal*

Proc Acad Sci USSR, Chem Sec	*Proceedings of the Academy of Sciences of the USSR. Chemistry Section*
Proc Chem Soc	*Proceedings of the Chemical Society (London)*
Proc Ind Acad Sci A	*Proceedings — Indian Academy of Sciences. Section A, Part 1: Chemical Sciences*
Proc Natl Acad Sci USA	*Proceedings of the National Academy of Sciences of the United States of America*
Pure Appl Chem	*Pure and Applied Chemistry*
Quart Rev	*Quarterly Reviews — Chemical Society, London*
Rec Chem Prog	*Record of Chemical Progress*
Rec Trav Chim	*Recueil des Travaux Chimiques des Pays-Bas*
Recl J R Neth Chem Soc	*Recueil: Journal of the Royal Netherlands Chemical Society*
Rev Chem Intermed	*Reviews of Chemical Intermediates*
Rev Pure Appl Chem	*Reviews of Pure and Applied Chemistry*
Rocz	*Roczniki Chemii*
Russ Chem Rev	*Russian Chemical Reviews*
Soc Chem Ind	*Society of Chemical Industry, London Chemical Engineering Group, Proceedings*
Syn	*Synthesis*
Syn Commun	*Synthetic Communications*
Tetr	*Tetrahedron*
TL	*Tetrahedron Letters*
Topics Curr Chem	*Topics in Current Chemistry*
Topics Stereochem	*Topics in Stereochemistry*
Trans Faraday Soc	*Transactions of the Faraday Society*
Transition Met Chem	*Transition Metal Chemistry (New York)*
Z Chem	*Zeitschrift für Chemie*
Z Naturforsch B	*Zeitschrift für Naturforschung. Tiel B: Anorganische Chemie, Organische Chemie, Biochemie, Biophysik, Biologie*
Zh Obshch Khim	*Zhurnal Obshchei Khimii*

CHEMICAL ABBREVIATIONS

Ac	Acetyl
acac	acetylacetonate [$CH_3COCHCOCH_3$]
acaen	*N*,*N*′-bis(1-methyl-3-oxobutylidene)ethylenediamine
AIBN	2,2′-azobisisobutyronitrile [$Me_2C(CN)N{=}NC(CN)Me_2$]
Am	amyl
aq	aqueous
Ar	aryl
	9-borabicyclo[3.3.1]nonyl
9-BBN	9-borabicyclo[3.3.1]nonane []
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
bipy	2,2′-bipyridyl
Bu	butyl
c	cyclo
cat	catalytic
COD	**cis,cis**-1,5-cyclooctadiene
Cp	Cyclopentadienyl
Cy	cyclohexyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DBA	dibenzylideneacetone [*Ph*CH=CHCOCH=*CH*Ph]
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
diop	(2,3)-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
dppe	1,2-bis(diphenylphosphino)ethane [$Ph_2PCH_2CH_2PPh_2$]
E^+	electrophile
EDA	ethylenediamine [$H_2NCH_2CH_2NH_2$]
EDTA	ethylenediaminetetraacetate
Et	ethyl
fod	6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato [$CF_3CF_2CF_2COCHCOC(CH_3)_3$]
Fp	dicarbonyl(η^5-cyclopentadienyl)iron(*I*) [$Fe(CO)_2$(cyclopentadienyl)]
Het	heterocycle
HMPA = HMPT	hexamethylphosphoramide

i	iso
L	ligand
LDA	lithium diisopropylamide [$LiN(i\text{-}C_3H_7)_2$]
m	meta
Me	methyl
Mes	mesityl
mesal	*N*-methylsalicylaldimine
Ms	methanesulfonyl
n	normal
NBA	*N*-bromoacetamide
NBD	norbornadiene
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NIS	*N*-iodosuccinimide
Nuc	nucleophile
o	ortho
p	para
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
PEG-400	poly(ethylene glycol)-400
Ph	phenyl
phen	1,10-phenanthroline
PPA	polyphosphoric acid
Pr	propyl
py	pyridine
R	an organic group
R_f	perfluoroalkyl
Salen	*N*,*N*′-ethylenebis(salicylideneiminato)
salophen	*o*-phenylenebis(salicylideneiminato)
sec	secondary
Sia	1,2-dimethylpropyl [$(CH_3)_2CHCHCH_3$]
S,S-chiraphos	(S,S)-2,3-bis(diphenylphosphino)butane [$(S,S)\text{-}Ph_2PCH(CH_3)CH(CH_3)PPh_2$]
t	tertiary
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
THP	2-tetrahydropyranyl
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylenediamine [$Me_2NCH_2CH_2NMe_2$]
Tol	tolyl
tolbinap	2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthyl
Ts	*p*-toluenesulfonyl

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