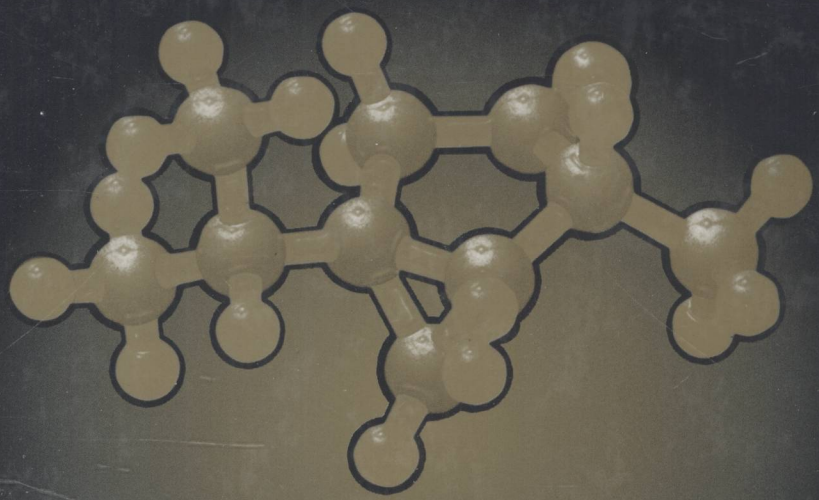
WILEY



Handbook of Reagents for Organic Synthesis

Fluorine-Containing Reagents

Edited by

Leo A. Paquette

Handbook of Reagents for Organic Synthesis

Fluorine-Containing Reagents

Edited by

Leo A. Paquette

The Ohio State University, Columbus, OH, USA

The Atrium, Southern Gate,
Chichester, West Sussex
PO19 8SQ, England

Telephone (+44) 1243 779777

Email (for orders and customer service enquiries): cs-books@wiley.co.uk
Visit our Home Page on www.wileyeurope.com or www.wiley.com

Other Wiley Editorial Offices

John Wiley & Sons Inc., 111 River Street,
Hoboken, NJ 07030,USA

Jossey-Bass, 989 Market Street,
San Francisco, CA 94103-1741,USA

Wiley-VCH Verlag GmbH, Boschstr. 12,
D-69469 Weinheim,Germany

John Wiley & Sons Australia Ltd, 42 McDougall Street,
Milton, Queensland 4064,Australia

John Wiley & Sons (Asia) Pte Ltd, 2 Clementi Loop #02-01,
Jin Xing Distripark, Singapore129809

John Wiley & Sons Canada Ltd, 6045 Freemont Boulevard,
Mississauga, Ontario, Canada L5R4J3

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Anniversary Logo Design: Richard J. Pacifico

Library of Congress Cataloging- in-Publication Data

Handbook of reagents for organic synthesis.
p.cm
Includes bibliographical references.
Contents: [1] Reagents, auxiliaries and catalysts for C–C bond formation / edited by Robert M. Coates and Scott E. Denmark [2] Oxidizing and reducing agents / edited by Steven D. Burke and Riek L. Danheiser [3] Acidic and basic reagents / edited by Hans J. Reich and James H. Rigby [4] Activating agents and protecting groups / edited by Anthony J. Pearson and William R. Roush [5] Chiral reagents for asymmetric synthesis / edited by Leo A. Paquette [6] Reagents for high-throughput solid-phase and solution-phase organic synthesis / edited by Peter Wipf [7] Reagents for glycoside, nucleotide and peptide synthesis / edited by David Crich [8] Reagents for direct functionalization of C–H bonds/edited by Philip L. Fuchs [9] Fluorine-Containing Reagents/edited by Leo A. Paquette

ISBN 0-471-97924-4 (v. 1)
ISBN 0 471 97925-2 (v. 3)
ISBN 0-470-85625-4 (v. 5)
ISBN 0-470-02304-X (v. 7)
ISBN 978-0-470-02177-4(v. 9)
ISBN 0-471-97926-0 (v. 2)
ISBN 0-471-97927-9 (v. 4)
ISBN 0-470-86298-X (v. 6)
ISBN 0-470-01022-3 (v. 8)

1. Chemical tests and reagents. 2. Organic compounds-Synthesis.
QD77.H37 1999
547′.2 dc 21
98-53088
CIP

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN 10: 0-470 02177-2 (Hb)
ISBN 13:978-0-470-02177-4

Typeset in 9½/11½ pt Times Roman by Thomson Press (India) Ltd., New Delhi.
Printed and bound in Great Britain by Antony Rowe, Chippenham, Wiltshire
This book is printed on acid-free paper responsibly manufactured from sustainable forestry in which at least two trees are planted for each one used for paper production.

General Abbreviations

Ac	acetyl
acac	acetylacetonate
AIBN	2,2′-azobisisobutyronitrile
Ar	aryl
BBN	borabicyclo[3.3.1]nonane
BCME	dis(chloromethyl)ether
BHT	butylated hydroxytoluene (2,6-di-*t*-butyl-*p*-cresol)
BINAL-H	2,2′-dihydroxy-1,1′-binaphthyl-lithium aluminum hydride
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BINOL	1,1′-bi-2,2′-naphthol
bipy	2,2′-bipyridyl
BMS	borane–dimethyl sulfide
Bn	benzyl
Boc	*t*-butoxycarbonyl
BOM	benzyloxymethyl
bp	boiling point
Bs	brosyl (4-bromobenzenesulfonyl)
BSA	*N,O*-bis(trimethylsilyl)acetamide
Bu	*n*-butyl
Bz	benzoyl
CAN	cerium(IV) ammonium nitrate
Cbz	benzyloxycarbonyl
CDI	*N,N′*-carbonyldiimidazole
CHIRAPHOS	2,3-bis(diphenylphosphino)butane
Chx	= Cy
cod	cyclooctadiene
cot	cyclooctatetraene
Cp	cyclopentadienyl
CRA	complex reducing agent
CSA	10-camphorsulfonic acid
CSI	chlorosulfonyl isocyanate
Cy	cyclohexyl
d	density
DABCO	1,4-diazabicyclo[2.2.2]octane
DAST	*N,N′*-diethylaminosulfur trifluoride
dba	dibenzylideneacetone
DBAD	di-*t*-butyl azodicarboxylate
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N,N′*-dicyclohexylcarbodiimide
DCME	dichloromethyl methyl ether
DDO	dimethyldioxirane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
de	diastereomeric excess
DEAD	diethyl azodicarboxylate
DET	diethyl tartrate
DIBAL	diisobutylaluminum hydride
DIEA	= DIPEA
DIOP	2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane
DIPEA	diisopropylethylamine
diphos	=dppe
DIPT	diisopropyl tartrate
DMA	dimethylacetamide
DMAD	dimethyl acetylenedicarboxylate
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
dmg	dimethylglyoximato
DMPU	*N,N′*-dimethylpropyleneurea
DMS	dimethyl sulfide
DMSO	dimethyl sulfoxide
DMTSF	dimethyl(methylthio) sulfonium tetrafluoroborate
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
DTBP	di-*t*-butyl peroxide
EDA	ethyl diazoacetate
EDC	1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide
EDCI	= EDC
ee	enantiomeric excess
EE	1-ethoxyethyl
Et	ethyl
ETSA	ethyl trimethylsilylacetate
EWG	electron withdrawing group
Fc	ferrocenyl
Fmoc	9-fluorenylmethoxycarbonyl
fp	flash point
Hex	*n*-hexyl
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoric triamide
HOBt	1-hydroxybenzotriazole
HOBT	=HOBt
HOSu	*N*-hydroxysuccinimide
Im	imidazole (imidazolyl)
Ipc	isopinocampheyl
IR	infrared
KHDMS	potassium hexamethyldisilazide
LAH	lithium aluminum hydride
LD_{50}	dose that is lethal to 50% of test subjects

LDA	lithium diisopropylamide
LDMAN	lithium 1-(dimethylamino)naphthalenide
LHMDS	= LiHMDS
LICA	lithium isopropylcyclohexylamide
LiHMDS	lithium hexamethyldisilazide
LiTMP	lithium 2,2,6,6-tetramethylpiperidide
LTMP	= LiTMP
LTA	lead tetraacetate
lut	lutidine
m-CPBA	*m*-chloroperbenzoic acid
MA	maleic anhydride
MAD	methylaluminum bis(2,6-di-*t*-butyl-4-methylphenoxide)
MAT	methylaluminum bis(2,4,6-tri-*t*-butylphenoxide)
Me	methyl
MEK	methyl ethyl ketone
MEM	(2-methoxyethoxy)methyl
MIC	methyl isocyanate
MMPP	magnesium monoperoxyphthalate
MOM	methoxymethyl
MoOPH	oxodiperoxomolybdenum(pyridine)-(hexamethylphosphoric triamide)
mp	melting point
MPM	= PMB
Ms	mesyl (methanesulfonyl)
MS	mass spectrometry; molecular sieves
MTBE	methyl *t*-butyl ether
MTM	methylthiomethyl
MVK	methyl vinyl ketone
n	refractive index
NaHDMS	sodium hexamethyldisilazide
Naph	naphthyl
NBA	*N*-bromoacetamide
nbd	norbornadiene (bicyclo[2.2.1]hepta-2,5-diene)
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NIS	*N*-iodosuccinimide
NMO	*N*-methylmorpholine *N*-oxide
NMP	*N*-methyl-2-pyrrolidinone
NMR	nuclear magnetic resonance
NORPHOS	bis(diphenylphosphino)bicyclo[2.2.1]-hept-5-ene
Np	= Naph
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Pent	*n*-pentyl
Ph	phenyl
phen	1,10-phenanthroline
Phth	phthaloyl
Piv	pivaloyl
PMB	*p*-methoxybenzyl
PMDTA	*N,N,N′,N″,N″*-pentamethyldiethylene-triamine
PPA	polyphosphoric acid
PPE	polyphosphate ester
PPTS	pyridinium *p*-toluenesulfonate
Pr	*n*-propyl
PTC	phase transfer catalyst/catalysis
PTSA	*p*-toluenesulfonic acid
py	pyridine
RAMP	(R)-1-amino-2-(methoxymethyl)pyrrolidine
rt	room temperature
salen	bis(salicylidene)ethylenediamine
SAMP	(*S*)-1-amino-2-(methoxymethyl)pyrrolidine
SET	single electron transfer
Sia	siamyl (3-methyl-2-butyl)
TASF	tris(diethylamino)sulfonium difluorotrimethylsilicate
TBAB	tetrabutylammonium bromide
TBAF	tetrabutylammonium fluoride
TBAD	= DBAD
TBAI	tetrabutylammonium iodide
TBAP	tetrabutylammonium perruthenate
TBDMS	*t*-butyldimethylsilyl
TBDPS	*t*-butyldiphenylsilyl
TBHP	*t*-butyl hydroperoxide
TBS	= TBDMS
TCNE	tetracyanoethylene
TCNQ	7,7,8,8-tetracyanoquinodimethane
TEA	triethylamine
TEBA	triethylbenzylammonium chloride
TEBAC	= TEBA
TEMPO	2,2,6,6-tetramethylpiperidinoxyl
TES	triethylsilyl
Tf	triflyl (trifluoromethanesulfonyl)
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
THP	tetrahydropyran; tetrahydropyranyl
Thx	thexyl (2,3-dimethyl-2-butyl)
TIPS	triisopropylsilyl
TMANO	trimethylamine *N*-oxide
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TMG	1,1,3,3-tetramethylguanidine
TMS	trimethylsilyl
Tol	*p*-tolyl
TPAP	tetrapropylammonium perruthenate
TBHP	*t*-butyl hydroperoxide
TPP	tetraphenylporphyrin
Tr	trityl (triphenylmethyl)
Ts	tosyl (*p*-toluenesulfonyl)
TTN	thallium(III) nitrate
UHP	urea–hydrogen peroxide complex
Z	= Cbz

Handbook of Reagents
for Organic Synthesis

Fluorine-Containing Reagents

OTHER TITLES IN THIS COLLECTION

Reagents for Direct Functionalization of C–H Bonds
Edited by Philip L. Fuchs
ISBN 0 470 01022 3

Reagents for Glycoside, Nucleotide, and Peptide Synthesis
Edited by David Crich
ISBN 0 470 02304 X

Reagents for High-Throughput Solid-Phase and Solution-Phase Organic Synthesis
Edited by Peter Wipf
ISBN 0 470 86298 X

Chiral Reagents for Asymmetric Synthesis
Edited by Leo A. Paquette
ISBN 0 470 85625 4

Oxidizing and Reducing Agents
Edited by Steven D. Burke and Rick L. Danheiser
ISBN 0 471 97926 0

Acidic and Basic Reagents
Edited by Hans J. Reich and James H. Rigby
ISBN 0 471 97925 2

Activating Agents and Protecting Groups
Edited by Anthony J. Pearson and William R. Roush
ISBN 0 471 97927 9

Reagents, Auxiliaries, and Catalysts for C–C Bond Formation
Edited by Robert M. Coates and Scott E. Denmark
ISBN 0 471 97924 4

This volume is dedicated to the memory of my former colleague, Professor Albert L. Henne (1925–1967), whose lifelong commitment to pioneering research in organofluorine chemistry at The Ohio State University was inspirational to the international community at large.

e-EROS Editorial Board

Preface

As stated in its Preface, the major motivation for our undertaking publication of the *Encyclopedia of Reagents for Organic Synthesis* was "to incorporate into a single work a genuinely authoritative and systematic description of the utility of all reagents used in organic chemistry." By all accounts, this reference compendium succeeded admirably in approaching this objective. Experts from around the globe contributed many relevant facts that define the various uses characteristic of each reagent. The choice of a masthead format for providing relevant information about each entry, the highlighting of key transformations with illustrative equations, and the incorporation of detailed indexes serve in tandem to facilitate the retrieval of desired information.

Notwithstanding these accomplishments, the editors came to recognize that the large size of this eight-volume work and its cost of purchase often deterred the placement of copies of the *Encyclopedia* in or near laboratories where the need for this type of information is most critical. In an effort to meet this demand in a cost-effective manner, the decision was made to cull from the major work that information having the highest probability for repeated consultation and to incorporate the same into a set of handbooks. The latter would also be purchasable on a single unit basis.

The ultimate result of these deliberations was the publication of the *Handbook of Reagents for Organic Synthesis*, the first four volumes of which were published in 1999:

Oxidizing and Reducing Agents
Edited by Steven D. Burke and Rick L. Danheiser

Acidic and Basic Reagents
Edited by Hans J. Reich and James H. Rigby

Activating Agents and Protecting Groups
Edited by Anthony J. Pearson and William R. Roush

Reagents, Auxiliaries, and Catalysts for C–C Bond Formation
Edited by Robert M. Coates and Scott E. Denmark

Since then, the fifth, sixth, seventh, and eighth members of this series listed below have made their appearance:

Chiral Reagents for Asymmetric Synthesis
Edited by Leo A. Paquette

Reagents for High-Throughput Solid-Phase and Solution-Phase Organic Synthesis
Edited by Peter Wipf

Reagents for Glycoside, Nucleotide, and Peptide Synthesis
Edited by David Crich

Reagents for Direct Functionalization of C–H Bonds
Edited by Philip L. Fuchs

Each of the volumes contain a selected compilation of those entries from the original *Encyclopedia* that bear on the specific topic. The coverage of the last four handbooks also extends to the electronic sequel *e-EROS*. Ample listings can be found to functionally related reagents contained in the original work. For the sake of current awareness, references to recent reviews and monographs have been included, as have relevant new procedures from *Organic Syntheses*.

The present volume entitled *Fluorine-Containing Reagents* constitutes the ninth entry into a continuing series of utilitarian reference works. As with its predecessors, this handbook is intended to be an affordable, enlightening compilation that will hopefully find its way into the laboratories of all practicing synthetic chemists. Every attempt has been made to be of the broadest possible relevance and the expectation is that our many colleagues will share in this opinion.

Leo A. Paquette
Department of Chemistry
The Ohio State University
Columbus, OH, USA

Introduction

With increasing recognition of the desirable and often unique properties intrinsic to fluorine-containing substances has come a dramatically heightened interest in the chemical and biological features of this family of compounds. The resulting demands placed on synthetic, mechanistic, and medicinal chemists emerge in many forms, not the least of which bear on understanding reactivity, controlling the regio- and stereoselectivity associated with introduction of the fluorine atoms, and establishing bioactivity relationships. This flurry of activity has been spurred on by the ever-present need to gain ready access to proper building blocks and to develop an enhanced appreciation of the associated changes in electronic character, Lewis acidity, and bioavailability to name a few. Given the evolution of these many developments, the present time was considered to be appropriate for incorporating into a single volume a compilation that lists a great many of the more important organofluorine reagents, as well as the key fluorine-containing catalysts presently in vogue.

The reagents featured in this volume have been culled from three sources. A minority of the entries appeared initially in the *Encyclopedia of Reagents for Organic Synthesis (EROS)* which issued in 1995. Since that time, a significant number of the entries for these classical reagents have been updated (*eEROS*), and this important add-on information is also found herein in the form of extensions to the original articles. The third pool of reagents is constituted of entirely new entries that detail the chemical and physical properties of an added subset of fluorinated compounds. In some instances, sets of isomeric agents appear in close proximity in order to facilitate comparative analysis. Subsets consisting of 2-, 3-, and 4-(trifluoromethyl)pyridine and of *o*-, *m*-, and *p*-trifluoromethylacetophenone are exemplary.

The reader may find it beneficial to examine the opening segments of this volume. The first consists of a listing of recent monographs and overviews dealing with different aspects of organofluorine chemistry. Following that, there is a section that illustrates those procedures relevant to the field that have appeared in Volumes 68–82 of *Organic Syntheses*. The body of the reagent compilation is presented in alphabetical order in the anticipation that benefits may be derived from scanning the content of adjoining pages.

Finally, it is hoped that this handbook will prove to be a valued adjunct to researchers experienced in fluorine chemistry, and a particularly useful compilation for others seeking to gain a foothold in the field as expediently as possible. These goals will have been realized if advances materialize from exposure to its contents.

Leo A. Paquette
Department of Chemistry
The Ohio State University
Columbus, OH, USA

Contents

Recent Monographs and Overview Articles

Monographs

Kirsch, P. *Modern Fluoroorganic Chemistry*; Wiley-VCH: Weinheim, 2004.

Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell Publishing: Oxford, CRC Press: Boca Raton, FL, 2004.

Gladysz, J. A.; Curran, D. P.; Horvath, J. T., Eds. *Handbook of Fluorous Chemistry*; Wiley-VCH: Weinheim, 2004.

Hiyama, T. *Organofluorine Compounds: Chemistry and Applications*; Springer Verlag: Berlin, 2000.

Banks, R. E., Ed. *Fluorine Chemistry at the Milennium - Fascinated by Fluorine*; Elsevier: Amseterdam, 2000.

Baasner, B.; Hagemann, H.; Tatlow, J. C., Eds. *Organo-Fluorine Chemistry*; Thieme: New York, 2000.

Soloshonok, V. A., Ed., *Enantiocontrolled Synthesis of Fluoro-Organic Comounds*; Wiley: Chichester, 1999.

Kitazume, T.; Yamazaki, T. *Experimental Methods in Organic Fluorine Chemistry*; Kodonsha, Gordon, and Breach: Tokyo, 1998.

Ojima, I.; McCarthy, J. F.; Welch, J. T., Eds. *Biomedical Frontiers of Fluorine Chemistry*; ACS Symposium Series 639, American Chemical Society: Washington, 1996.

Hudlicky, M.; Pavlath, A. E., Eds. *Chemistry of Organic Fluorine Compounds II: A Critical Review*; ACS Monograph 187, American Chemical Society: Washington, 1995.

Banks, R. E.; Smart, B. E.; Tatlow, J. C., Eds. *Organofluorine Chemistry - Principles and Commercial Applications*; Plenum Press: New York, 1994.

Mukhar, V. P.; Soloshonok, V. A., Eds. *Fluorine-Containing Amino Acids: Synthesis and Properties*; Wiley: Chichester, 1994.

Filler, R.; Kobayashi, Y.; Yagupolski, L. M., Eds. *Biomedicinal Aspects of Fluorine Chemistry*; Elsevier: Amsterdam, 1993.

Olah, G. A.; Chambers, R. D.; Surya Prakash, G. K., Eds. *Synthetic Fluorine Chemistry*; Wiley: New York, 1992.

Huclicky, M., Ed. *Chemistry of Organic Fluorine Compounds; 2nd Edition*, Ellis Horwood: New York, 1992.

Welch, J. T., Ed. *Selective Fluorination in Organic and Bioorganic Chemistry*; ACS Symposium Series 456: Washington, 1991.

Liebman, J. F.; Greenberg, A.; Dolbier, W. R., Eds. *Fluorine-Containing Molecules: Structure, Reactivity, Synthesis, and Applications*; VCH: New York, 1988.

Overview Articles

Thayer, A. M. Fabulous fluorine. *C&EN* **2006**, *84*(23), 15.

Thayer, A. M. Constructing life sciences compounds, *C&EN* **2006**, *84*(23), 27.

Dolbier, W. R., Jr. Fluorine chemistry at the milennium. *J. Fluorine Chem.* **2005**, *126*, 157.

Hiyama, T.; Shimizu, M. Modern synthetic methods for fluorine substituted target molecules. *Angew. Chem. Int. Ed.* **2005**, *44*, 214.

Smart, B. E., Fluorine substituent effects (on bioreactivity). *J. Fluorine Chem.* **2001**, *109*, 3.

Fluorine chemistry. *Chem. Rev.* **1996**, *96*, 1555.

Rozen, S. Elemental fluorine: Not only for fluoroorganic chemistry! *Acc. Chem. Res.* **1996**, *29*, 243.

Fluoroorganic Chemistry: Synthetic challenges and biomedical rewards, tetrahedron symposium-in-print, No. 58. *Tetrahedron*, **1996**, *52*, 1.

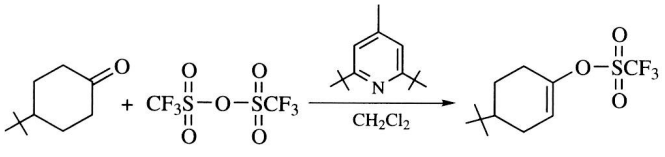
Enantiocontrolled synthesis of fluoro-organic compounds. *Tetrahedron: Asymmetry*, Special Issue **1994**, *5*(6), 955.

Organic Syntheses Procedures Featuring the Preparation of Organofluorine End-Products and of Fluorinated Reagents as Promoters, Volumes 68–82

Synthesis of Organofluorine Compounds

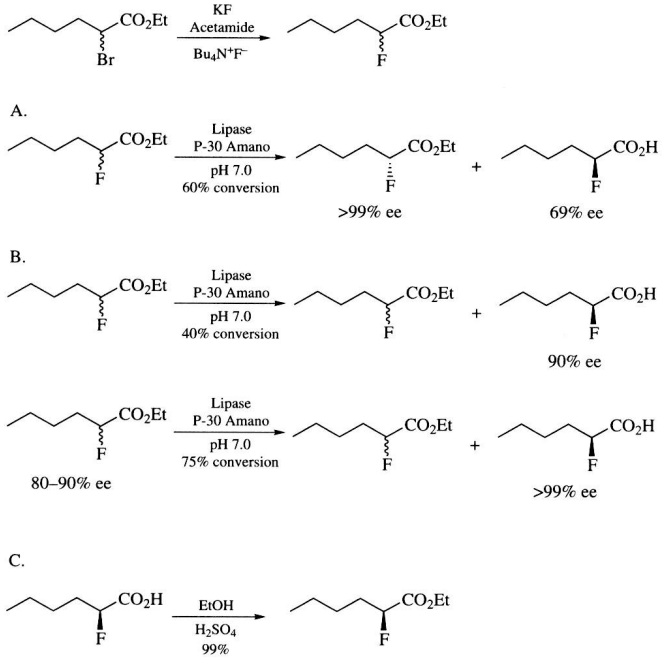
4-*tert*-Butylcyclohexen-1-yl Trifluoromethene-sulfonate

William J. Scott, G. T. Crisp, and J. K. Stille; *Org. Synth.* **1990**, *68*, 116.



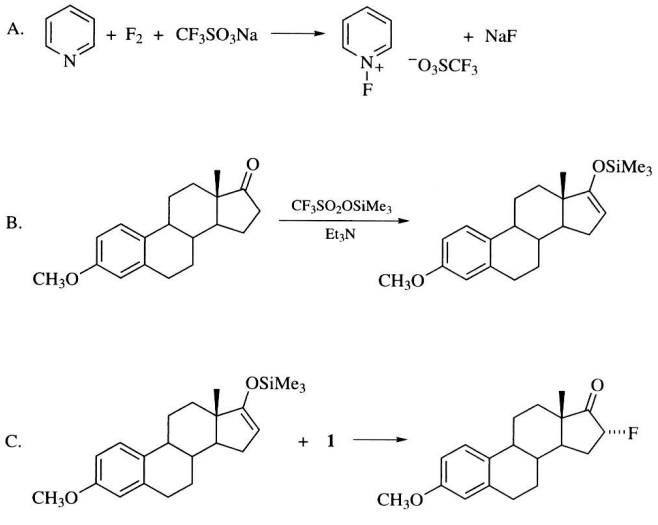
Ethyl (*R*)- and (*S*)- 2-fluorohexanoate

P. Kararitis and R. W. Regenye; *Org. Synth.* **1990**, *68*, 10.



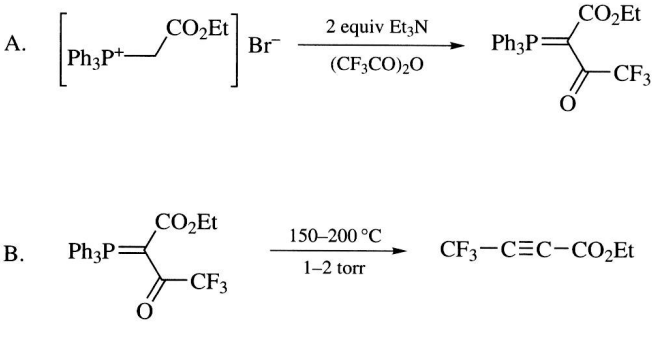
16α-Fluoro-3-methoxy-1,3,5(10)-estatrien-17-one

Teruo Umemoto, Kyoichi Tomita, and Kosuke Kawada; *Org. Synth.* **1990**, *69*, 129.



Ethyl 4,4,4-Trifluorotetrolate

B. C. Hamper; *Org. Synth.* **1992**, *70*, 246.



Avoid Skin Contact with All Reagents