

# Formation of C-C Bonds

---

Jean Mathieu and Jean Weill-Raynal

Preface by D. H. R. Barton

Volume III

## Introduction of an $\alpha$ -Functional Carbon Chain



Georg Thieme Publishers Stuttgart

# Formation of C-C Bonds

Jean Mathieu and  
Jean Weill-Raynal

Preface by D.H.R. Barton

Volume III

# Introduction of an $\alpha$ -Functional Carbon Chain

1235 Formula Schemes  
and 300 Tables



Georg Thieme Publishers  
Stuttgart 1979

Pr. JEAN MATHIEU  
Directeur des Recherches Extérieures de Roussel Uclaf  
Professeur à l'Ecole Nationale Supérieure de Techniques Avancées  
Roussel Uclaf, Division Scientifique  
F-93 Romainville

Dr. JEAN WEILL-RAYNAL  
Assistant à la Direction des Recherches Extérieures de Roussel Uclaf  
Maître de Conférence à l'Ecole Supérieure de Techniques Avancées  
Roussel Uclaf, Division Scientifique  
F-93 Romainville

**CIP-Abbreviated title entry in catalog of Deutsche Bibliothek**

**Mathieu, Jean:**

Formation of C-C bonds / Jean Mathieu and Jean Weill-Raynal.  
Pref. by D.H.R. Barton. — Stuttgart : Thieme.

NE: Weill-Raynal, Jean:

Vol. 3. Introduction of an  $\alpha$ -functional carbon chain : 1235 formula  
schemes and 300 tables. — 1979. —

ISBN 3-13-496201-2

Some of the product names, patents and registered designs referred to are in fact registered trademarks or proprietary names even though specific reference to this fact is not always made in the text. Therefore, the appearance of a name without designation as proprietary is not to be construed as a representation by the publisher that it is in the public domain.

All rights, including the rights of publication, distribution and sales, as well as the right to translation, are reserved. No part of this work covered by the copyrights hereon may be reproduced or copied in any form or by any means — graphic, electronic or mechanical including photocopying, recording, taping, or information and retrieval systems — without permission of the publisher.

© 1979 Georg Thieme Verlag, Herdweg 63, Postfach 732, D 7000 Stuttgart 1, Printed in Germany by Tutte,  
D 8391 Salzweg-Passau. (Monophoto 400/31).

ISBN: 3 13 4962 01-2

J. Mathieu and J. Weill-Raynal  
**Formation of C-C Bonds**  
Volume III

Dedicated to the memory of  
JEAN-CLAUDE ROUSSEL  
for his confidence in the future of research

## Introduction

The third volume of this series is devoted to reactions by which a chain can be attached to another chain, aromatic or aliphatic ring, at carbon atoms  $\alpha$  to a heteroatom (halogen, oxygen, sulfur, nitrogen). Amongst these reactions, hydroxyalkylation and acylation are probably the most important.

This volume deals both with reactions which insert a chain substituted with a single  $\alpha$ -heteroatom (i.e. in the first oxidation state) namely:

- $\alpha$ -haloalkylation
- $\alpha$ -hydroxyalkylation and  $\alpha$ -alkoxyalkylation
- $\alpha$ -thioalkylation
- $\alpha$ -aminoalkylation and  $\alpha$ -amidoalkylation

and those involving a chain substituted on the  $\alpha$ -carbon atom either with 2 heteroatoms or a double-bonded heteroatom (i.e. in the second oxidation state) namely:

- *gem*- $\alpha$ -dihaloalkylation
- acylation, *gem*- $\alpha$ -dialkoxyalkylation,  $\alpha$ -alkoxyalkylidenation and related reactions
- thioacylation, *gem*- $\alpha$ -dithioalkylation and  $\alpha$ -thioalkylidenation
- iminoalkylation,  $\alpha$ -aminoalkylidenation and related reactions

In each chapter, reactions are classified with respect to the hybridization of the attacked carbon atom in the following order:

- activated carbon atoms
- aliphatic organometallics
- olefins undergoing addition reactions
- aromatic rings
- aromatic organometallics
- olefins undergoing substitution reactions
- vinylic organometallics
- 1-alkynes

In the same way as in the preceding volumes, we have used a general concept of organic chemistry with the nucleophilic molecule being considered as the substrate and the electrophilic one as the reagent.

We hope that these systematic classifications provide a useful guide to the easy retrieval of a specific reaction.

We express our grateful acknowledgements to Drs. H. Felkin and J. B. Taylor for their careful reading of the manuscript and valuable suggestions; to Miss H. Deforeit for her help in the literature data research and to Mrs. Cohen and Devine and Miss D. Salaün for the checking of literature data, manuscript and proofs.

This work has been done by courtesy of the Direction Générale de Roussel-Uclaf.

Jean Mathieu

Jean Weill-Raynal

**Used Abbreviations**

anh	anhydrous
aq	aqueous
at	technical atmosphere
conc.	concentrated
d	day
DABCO	1,4-diazobicyclo [2.2.2.] octane
DCC	dicyclohexylcarbodiimide
DMF	dimethylformamide
HMPT	hexamethylphosphoric triamide
hr	hour, hours
hydr	hydrolysis
<i>i</i>	iso
i. b. t.	ice bath temperature
i. s. m.	ice salt mixture
liq	liquid
min	minute

NMP	<i>N</i> -methylpyrrolidone
ovn	overnight
PE	petroleum ether
PPA	polyphosphoric acid
rfx	reflux
r. t.	room temperature
<i>s</i>	secondary
s. b.	steam bath
sec	second
soln	solution
sym.	symmetrical (ly)
<i>t</i>	tertiary
THF	tetrahydrofuran
Tos	tosyl (p-toluenesulfonyl)
TMEDA	<i>N,N,N',N'</i> -tetramethyl-ethylenediamine
TMU	<i>N,N,N',N'</i> -tetramethylurea
u. p.	under pressure

# Contents

Introduction . . . . .	VII
Used Abbreviations . . . . .	XII
<b>III A <math>\alpha</math>-Haloalkylation of Organic Compounds</b> . . . . .	2
III A a $\alpha$ -Haloalkylation of Aliphatic Compounds . . . . .	2
III A b $\alpha$ -Haloalkylation of Aromatic Rings . . . . .	4
<b>III B <math>\alpha</math>-Hydroxyalkylation and <math>\alpha</math>-Alkoxyalkylation of Organic Compounds</b> . . . . .	5
<i>III B<sub>1</sub> <math>\alpha</math>-Hydroxyalkylation</i> . . . . .	10
III B <sub>1</sub> a <sub>1</sub> $\alpha$ -Hydroxyalkylation of Activated Carbon Atoms . . . . .	10
III B <sub>1</sub> a <sub>2</sub> $\alpha$ -Hydroxyalkylation of Aliphatic Organometallics . . . . .	66
III B <sub>1</sub> a <sub>3</sub> $\beta$ -Hydro- $\alpha$ -hydroxyalkylation of Olefins . . . . .	116
III B <sub>1</sub> b <sub>1</sub> $\alpha$ -Hydroxyalkylation of Aromatic Rings . . . . .	118
III B <sub>1</sub> b <sub>2</sub> $\alpha$ -Hydroxyalkylation of Aromatic Organometallics . . . . .	130
III B <sub>1</sub> c <sub>1</sub> $\alpha$ -Hydroxyalkylation of Olefins . . . . .	148
III B <sub>1</sub> c <sub>2</sub> $\alpha$ -Hydroxyalkylation of Vinylic Organometallics . . . . .	150
III B <sub>1</sub> d $\alpha$ -Hydroxyalkylation of 1-Alkynes . . . . .	162
<i>III B<sub>2</sub> <math>\alpha</math>-Alkoxyalkylation</i> . . . . .	186
III B <sub>2</sub> a <sub>1</sub> $\alpha$ -Alkoxyalkylation of Activated Carbon Atoms . . . . .	186



III B <sub>2</sub> a <sub>2</sub> α-Alkoxyalkylation of Aliphatic Organometallics	$\begin{array}{c}   \\ -\text{C}-\text{X} \end{array} \left( \begin{array}{c}   \\ -\text{C}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{OR (Ar)} \end{array}$	190
III B <sub>2</sub> a <sub>3</sub> α-Alkoxyalkylation of Enol Ethers and Related Compounds	$\text{RO}-\text{C}=\text{C} \begin{array}{c} / \\ \text{R}'\text{O} \\ \backslash \\ \text{R}'\text{O} \end{array} + \begin{array}{c} \text{R}'\text{O} \\   \\ \text{C} \\   \\ \text{R}'\text{O} \end{array} \longrightarrow \begin{array}{c} \text{RO} \quad \text{R}'\text{O} \\   \quad   \\ \text{C}-\text{C}-\text{C}- \\   \quad   \quad   \\ \text{R}'\text{O} \quad \text{OR}' \end{array}$	196
III B <sub>2</sub> a <sub>4</sub> β-Halo-α-alkoxyalkylation of Olefins	$\text{C}=\text{C} \begin{array}{c} / \\ \text{X} \\ \backslash \\ \text{RO} \end{array} + \begin{array}{c} \text{X} \\   \\ \text{C} \\   \\ \text{RO} \end{array} \longrightarrow \text{X}-\begin{array}{c}   \quad   \\ \text{C}-\text{C}-\text{C}-\text{OR} \\   \quad   \end{array}$	202
III B <sub>2</sub> b <sub>1</sub> α-Alkoxyalkylation of Aromatic Rings	$\text{Ar}-\text{H} \longrightarrow \begin{array}{c}   \\ \text{Ar}-\text{C}- \\   \\ \text{OR} \end{array}$	203
III B <sub>2</sub> b <sub>2</sub> α-Alkoxyalkylation of Aromatic Organometallics	$\text{Ar}-\text{X} \left( \begin{array}{c}   \\ \text{Ar}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \\ \text{Ar}-\text{C}- \\   \\ \text{OR} \end{array}$	204
III B <sub>2</sub> c α-Alkoxyalkylation of Vinylic Organometallics	$\text{C}=\text{C}-\text{X} \left( \begin{array}{c}   \\ \text{C}=\text{C}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \\ \text{C}=\text{C}-\text{C}- \\   \quad   \\ \text{OR} \end{array}$	205
III B <sub>2</sub> d α-Alkoxyalkylation of 1-Alkynes	$-\text{C}\equiv\text{C}-\text{H} \longrightarrow \begin{array}{c}   \\ -\text{C}\equiv\text{C}-\text{C}- \\   \\ \text{OR} \end{array}$	206
<b>III C α-Thioalkylation of Organic Compounds</b>		210
III Ca <sub>1</sub> α-Alkylthioalkylation of Activated Carbon Atoms	$\begin{array}{c}   \\ -\text{C}-\text{H} \end{array} \longrightarrow \begin{array}{c}   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{SR} \end{array}$	211
III Ca <sub>2</sub> α-Thioalkylation of Aliphatic Organometallics	$\begin{array}{c}   \\ -\text{C}-\text{X} \end{array} \left( \begin{array}{c}   \\ -\text{C}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{SR} \end{array}$	212
III Ca <sub>3</sub> α-Alkylthioalkylation of Enol Ethers and Ketenes	$\text{Z}-\text{C}=\text{C} \begin{array}{c} / \\ \text{RS} \\ \backslash \\ \text{RS} \end{array} + \begin{array}{c} \text{RS} \\   \\ \text{C} \\   \\ \text{RS} \end{array} \longrightarrow \begin{array}{c} \text{Z} \quad \text{RS} \quad \text{RS} \\   \quad   \quad   \\ \text{C}-\text{C}-\text{C}- \\   \quad   \quad   \\ \text{SR} \quad \text{SR} \end{array}$	212
III Cb <sub>1</sub> α-Alkyl and Arylthioalkylation of Aromatic Rings	$\text{ArH} \longrightarrow \begin{array}{c}   \\ \text{Ar}-\text{C}- \\   \\ \text{S-R (Ar)} \end{array}$	213
III Cb <sub>2</sub> α-Alkylthioalkylation of Aromatic Organometallics	$\text{Ar}-\text{X} \left( \begin{array}{c}   \\ \text{Ar}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \\ \text{Ar}-\text{C}- \\   \\ \text{SR} \end{array}$	216
<b>III D α-Aminoalkylation and α-Amidoalkylation of Organic Compounds</b>		217
<b>III D<sub>1</sub> α-Aminoalkylation</b>		217
III D <sub>1</sub> a <sub>1</sub> α-Aminoalkylation of Activated Carbon Atoms	$\begin{array}{c}   \\ -\text{C}-\text{H} \end{array} \longrightarrow \begin{array}{c}   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{N} \end{array}$	219
III D <sub>1</sub> a <sub>2</sub> α-Aminoalkylation of Aliphatic Organometallics	$\begin{array}{c}   \\ -\text{C}-\text{X} \end{array} \left( \begin{array}{c}   \\ -\text{C}-\text{M} \end{array} \right) \longrightarrow \begin{array}{c}   \quad   \\ -\text{C}-\text{C}- \\   \quad   \\ \text{N} \end{array}$	230

III D <sub>1</sub> b <sub>1</sub> $\alpha$ -Aminoalkylation of Aromatic Rings	$\text{Ar-H} \longrightarrow \text{Ar}-\underset{\text{N}}{\underset{ }{\text{C}}}-$	239
III D <sub>1</sub> b <sub>2</sub> $\alpha$ -Aminoalkylation of Aromatic Organometallics	$\text{Ar-X} \left( \longrightarrow \text{Ar-M} \right) \longrightarrow \text{Ar}-\underset{\text{N}}{\underset{ }{\text{C}}}-$	242
III D <sub>1</sub> c $\alpha$ -Aminoalkylation of Vinylic Organometallics	$\text{>C=C-X} \left( \longrightarrow \text{>C=C-M} \right) \longrightarrow \text{>C=C}-\underset{\text{N}}{\underset{ }{\text{C}}}-$	246
III D <sub>1</sub> d $\alpha$ -Aminoalkylation of 1-Alkynes	$-\text{C}\equiv\text{C-H} \longrightarrow -\text{C}\equiv\text{C}-\underset{\text{N}}{\underset{ }{\text{C}}}-$	247
III D <sub>2</sub> $\alpha$ -Amidoalkylation		248
III D <sub>2</sub> a <sub>1</sub> $\alpha$ -Amidoalkylation of Activated Carbon Atoms	$-\underset{ }{\text{C}}-\text{H} \longrightarrow -\underset{\text{N}-\text{CO}-}{\underset{ }{\text{C}}}-$	248
III D <sub>2</sub> a <sub>2</sub> $\alpha$ -Amidoalkylation of Aliphatic Organometallics	$-\underset{ }{\text{C}}-\text{X} \left( \longrightarrow -\underset{ }{\text{C}}-\text{M} \right) \longrightarrow -\underset{\text{N}-\text{CO}-}{\underset{ }{\text{C}}}-$	252
III D <sub>2</sub> b <sub>1</sub> $\alpha$ -Amidoalkylation of Aromatic Rings	$\text{Ar-H} \longrightarrow \text{Ar}-\underset{\text{N}-\text{CO}-}{\underset{ }{\text{C}}}-$	252
III D <sub>2</sub> b <sub>2</sub> $\alpha$ -Amidoalkylation of Aromatic Organometallics	$\text{Ar-X} \left( \longrightarrow \text{Ar-M} \right) \longrightarrow \text{Ar}-\underset{\text{N}-\text{CO}-}{\underset{ }{\text{C}}}-$	253
III D <sub>2</sub> c $\alpha$ -Amidoalkylation of Vinylic Organometallics	$\text{>C=C-X} \left( \longrightarrow \text{>C=C-M} \right) \longrightarrow \text{>C=C}-\underset{\text{N}-\text{CO}-}{\underset{ }{\text{C}}}-$	253
III E <i>gem</i> - $\alpha$ -Dihaloalkylation of Organic Compounds		254
III Ea <i>gem</i> - $\alpha$ -Dihaloalkylation of Olefins	$\text{>C=C} + \text{X}'-\underset{\text{X}}{\underset{ }{\text{C}}}-\text{X} \longrightarrow \text{X}'-\underset{\text{X}}{\underset{ }{\text{C}}}-\underset{\text{X}}{\underset{ }{\text{C}}}-$	254
III Eb <i>gem</i> - $\alpha$ -Dihaloalkylation of Aromatic Rings	$\text{Ar-H} + \text{X}_3\text{C-} \longrightarrow \text{Ar}-\underset{\text{X}}{\underset{\text{X}}{\underset{ }{\text{C}}}}-$	258
III F Acylation, <i>gem</i> - $\alpha$ -Dialkoxyalkylation, $\alpha$ -Alkoxyalkylidenation and $\alpha$ -Acyloxyalkylidenation of Organic Compounds		259
III F <sub>1</sub> Acylation		264
III F <sub>1</sub> a <sub>1</sub> Acylation of Activated Carbon Atoms	$-\underset{ }{\text{C}}-\text{H} + \text{Z-CO-} \longrightarrow -\underset{ }{\text{C}}-\text{CO-}$	264

III F <sub>1a2</sub> Acylation of Aliphatic Organometallics . . . . .	$\text{>C-X} \left( \rightarrow \text{>C-M} \right) + \text{Z-CO-} \rightarrow \text{>C-CO-}$ . . . . .	346
III F <sub>1a3</sub> Acylation of Diazoalkanes by means of Aldehydes . . . . .	$\text{>C=N}_2 + \text{OHC-} \rightarrow \text{H-C-CO-}$ . . . . .	370
III F <sub>1a4</sub> Hydroacylation of Olefins . . . . .	$\text{>C=C<} + \text{OHC-} \rightarrow \text{H-C-C-CO-}$ . . . . .	374
III F <sub>1a5</sub> $\beta$ -Haloacylation of Olefins . . . . .	$\text{>C=C<} + \text{Cl-CO-} \rightarrow \text{Cl-C-C-CO-}$ . . . . .	380
III F <sub>1b1</sub> Acylation of Aromatic Rings . . . . .	$\text{Ar-H} + \text{Z-CO-} \rightarrow \text{Ar-CO-}$ . . . . .	384
III F <sub>1b2</sub> Acylation of Aromatic Organometallics . . . . .	$\text{Ar-X} \left( \rightarrow \text{Ar-M} \right) \rightarrow \text{Ar-CO-}$ . . . . .	454
III F <sub>1c1</sub> Acylation of Olefins . . . . .	$\text{>C=C-H} \rightarrow \text{>C=C-CO-}$ . . . . .	470
III F <sub>1c2</sub> Acylation of Vinylic Organometallics . . . . .	$\text{>C=C-M} \rightarrow \text{>C=C-CO-}$ . . . . .	476
III F <sub>1c3</sub> Acylation of Enol Ethers, Enamines and Keteneacetals . . . . .	$\text{Z-C=C-H} \rightarrow \text{Z-C=C-CO-}$ . . . . .	480
III F <sub>1c4</sub> $\beta$ -Haloacylation of 1-Alkynes . . . . .	$\text{-C}\equiv\text{CH} + \text{Cl-CO-} \rightarrow \text{Cl-C=CH-CO-}$ . . . . .	490
III F <sub>1d</sub> Acylation of 1-Alkynes . . . . .	$\text{-C}\equiv\text{CH} \rightarrow \text{-C}\equiv\text{C-CO-}$ . . . . .	494
III F <sub>2</sub> <i>gem</i> - $\alpha$ -Dialkoxyalkylation, $\alpha$ -Alkoxyalkylidenation, $\alpha$ -Acyloxyalkylidenation and $\alpha$ -Acyloxyvinylation . . . . . 500		
III F <sub>2a1</sub> $\alpha$ -Alkoxyalkylidenation of Active Methylene Groups . . . . .	$\text{-CH}_2 + (\text{RO})_3\text{C-} \rightarrow \text{>C=C-OR}$ . . . . .	500
III F <sub>2a2</sub> $\alpha$ -Acyloxyalkylidenation of Active Methylene Groups . . . . .	$\text{-CH}_2 \rightarrow \text{>C=C-O-CO-}$ . . . . .	502
III F <sub>2a3</sub> <i>gem</i> - $\alpha$ -Dialkoxyalkylation, $\alpha$ -Alkoxyalkylidenation and $\alpha$ -Acyloxyalkylidenation of Aliphatic Organometallics . . . . .	$\text{-CH-X} \left( \rightarrow \text{-CH-M} \right) \rightarrow \text{>C=C-OR} \text{ or } \text{-CH-C(OR)}_2$ . . . . .	506
III F <sub>2a4</sub> $\alpha$ -Alkoxyalkylidenation and $\alpha$ -Acyloxyalkylidenation of Alkylidene-Phosphoranes and Phosphonates . . . . .	$\text{>C=P-} + \text{O=C-O-} \rightarrow \text{>C=C-O-CO-}$ . . . . .	508
III F <sub>2b</sub> $\alpha$ -Acyloxyvinylation of Aromatic Rings . . . . .	$\text{Ar-H} + \text{O=C-CH-O-CO-} \rightarrow \text{Ar-C=C-O-CO-}$ . . . . .	510
III F <sub>2c</sub> <i>gem</i> - $\alpha$ -Dialkoxyalkylation and $\alpha$ -Alkoxyalkylidenation of 1-Alkynes . . . . .	$\text{-C}\equiv\text{CH} + (\text{RO})_3\text{C-} \rightarrow \text{-C}\equiv\text{C-C(OR)}_2$ . . . . .	510

### III G Thioacylation, *gem*- $\alpha$ -Dithioalkylation and $\alpha$ -Thioalkylidenation of Organic Compounds . . . . . 511



### III H Iminoalkylation, $\alpha$ -Aminoalkylidenation and Related Reactions . . . . . 515

#### III H<sub>1</sub> Iminoalkylation . . . . . 518



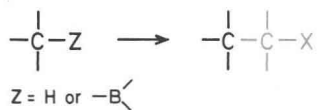
#### III H<sub>2</sub> $\alpha$ -Aminoalkylidenation . . . . . 556



# Introduction of an $\alpha$ -Functional Carbon Chain

### III A $\alpha$ -Haloalkylation of Organic Compounds

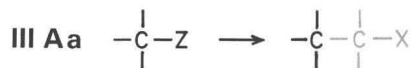
$\alpha$ -Haloalkylation of organic compounds has been developed to a much smaller extent than halomethylation.



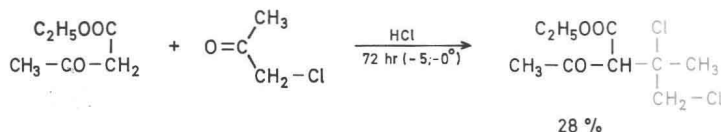
There are a few examples of haloalkylation of activated carbon atoms by means of aldehydes and ketones in the presence of hydrogen halides.

Boranes are haloalkylated by dihalocarbanions (see III A a).

Reactive aromatic compounds are haloalkylated by aldehydes in the presence of hydrogen halides or by  $\alpha$ -halo ethers (see III A b).



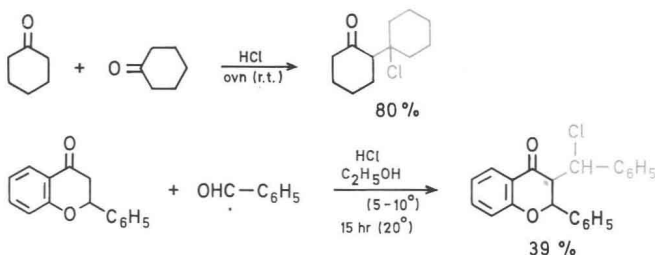
#### $\alpha$ -Haloalkylation of Aliphatic Compounds



1 Apart from the halomethylation of activated carbon atoms (see I A<sub>1</sub> a), there are a few examples of  $\alpha$ -haloalkylation of aliphatic compounds.

The active methylene group of ethyl acetoacetate reacts with chloroacetone to give ethyl 2-acetyl-3,4-dichloro-3-methylbutanoate in low yield<sup>1</sup>.

An analogous reaction occurs with propiophenone which is chlorobenzylated by benzaldehyde in the presence of hydrochloric acid<sup>2</sup>.



3 On the other hand, the aldolization of cyclohexanone can be effected in acidic medium to give 2-(1-chloro-cyclohexyl)-cyclohexanone in good yield<sup>3,4</sup>. In the mixed condensation of benzaldehyde with 2-phenyl-chromanone, chloroalkylation occurs only in fair

yield, with concomitant dehydrochlorination<sup>5</sup>.

5

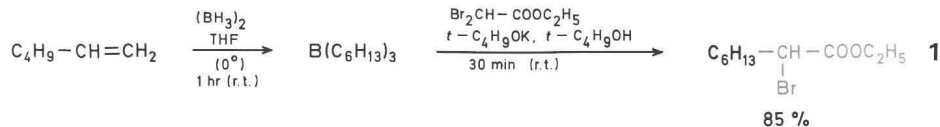
<sup>1</sup>E. R. Alexander, S. Baldwin, J. Am. Chem. Soc. **73**, 356 (1951).

<sup>2</sup>R. D. Abell, J. Chem. Soc. **1953**, 2834.

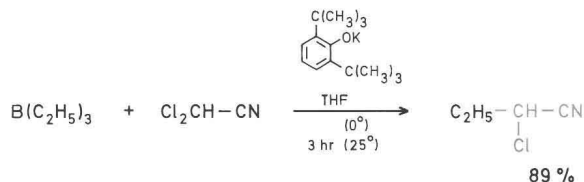
<sup>3</sup>J. Plešek, Chem. Listy **49**, 1844 (1955); C.A. **50**, 9306 (1956).

<sup>4</sup>E. Wenkert, S. K. Bhattacharya, E. M. Wilson, J. Chem. Soc. **1964**, 5617.

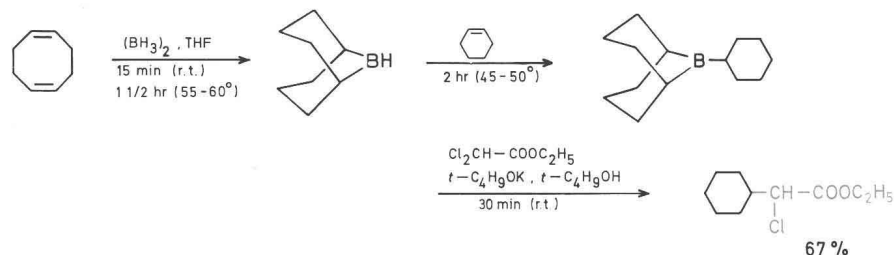
<sup>5</sup>L. Reichel, H. Grytzka, Justus Liebigs Ann. Chem. **720**, 154 (1968).



Organoboranes formed by the addition of diborane to olefins are haloalkylated by condensation with the carbanion formed from ethyl dibromoacetate in the presence of potassium *t*-butoxide; an intramolecular substitution of one of the halogen atoms by an alkyl group transferred from the boron atom gives rise to  $\alpha$ -bromo esters **1** (see II A<sub>4</sub> a).

**3**

An improvement has been obtained by using potassium 2,6-di-*t*-butylphenoxide instead of potassium *t*-butoxide<sup>2</sup> especially when dichloroacetonitrile is employed as the haloalkylating reagent<sup>3</sup>.

**4**

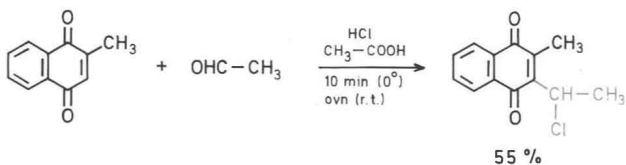
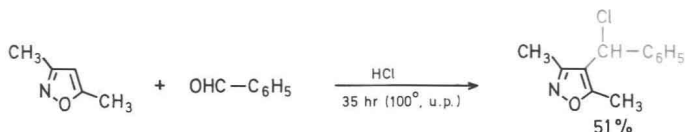
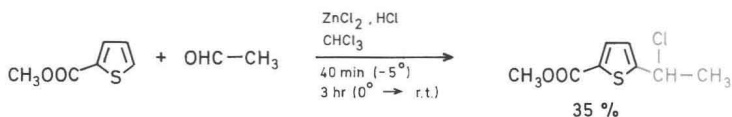
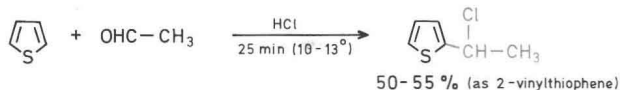
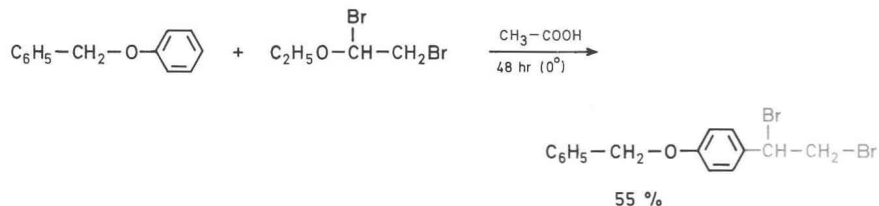
As only one of the three alkyl groups is transferred from the boron atom, the use of mixed alkylboranes formed from 9-bora[2.2.2]bicyclononane (9-BBN) and an olefin allows a selective transfer. This procedure has been applied to  $\alpha$ -haloalkylations by ethyl dichloroacetate<sup>4</sup> and by dichloroacetonitrile<sup>3</sup>.

<sup>1</sup>H. C. Brown, M. M. Rogic, M. W. Rathke, G. W. Kabalka, J. Am. Chem. Soc. **90**, 1911 (1968).

<sup>2</sup>H. C. Brown, H. Nambu, M. M. Rogic, J. Am. Chem. Soc. **91**, 6855 (1969).

<sup>3</sup>H. Nambu, H. C. Brown, J. Am. Chem. Soc. **92**, 5790 (1970).

<sup>4</sup>H. C. Brown, M. M. Rogic, J. Am. Chem. Soc. **91**, 2146 (1969).



<sup>1</sup>G.A. Olah, W.S. Tolgyesi in G.A. Olah, *Friedel-Crafts and Related Reactions*, Vol. II, Part. 2, p. 659, J. Wiley & Sons, New York, 1964.

<sup>2</sup>P. Bapsères, R. Quelet, *Bull. Soc. Chim. France* **1953**, C. 50.

## $\alpha$ -Haloalkylation of Aromatic Rings

$\alpha$ -Haloalkylations of aromatic rings are less frequently carried out than halomethylations<sup>1</sup> (see I A b<sub>1</sub>).

2 The condensation of benzyl phenyl ether with 1,2-dibromoethyl ether should be mentioned<sup>2</sup>.

3 The  $\alpha$ -chloroethylation of thiophene is used for the preparation of the precursor of 2-vinylthiophene<sup>3</sup>.

4 The less sensitive methyl 2-thiophenecarboxylate reacts in the presence of zinc chloride<sup>4</sup>.

5 3,5-Dimethylisoxazole has been condensed with benzaldehyde in the presence of hydrogen chloride in a sealed vessel<sup>5</sup>.

6 Quinones which have some aromatic character have been haloalkylated under analogous conditions<sup>6</sup>.

<sup>3</sup>W.S. Emerson, T.M. Patrick, *Org. Synth. Coll. Vol.* **4**, 980 (1963).

<sup>4</sup>M. Janda, F. Dvorak, O. Exner, *Collect. Czech. Chem. Commun.* **27**, 1191 (1962).

<sup>5</sup>N.K. Kochetkov, S.D. Sokolov, V.E. Zhvirblis, *Zh. Obshch. Khim.* **30**, 3675 (1960); *C.A.* **55**, 18707 (1961).

<sup>6</sup>R.H. Thomson, *J. Chem. Soc.* **1953**, 1196.



### III B $\alpha$ -Hydroxyalkylation and $\alpha$ -Alkoxyalkylation of Organic Compounds

The introduction of a chain bearing on the  $\alpha$ -carbon atom an oxygen-containing function of the first oxidation state includes the following two processes:  $\alpha$ -hydroxyalkylation, i.e. introduction of a chain with a hydroxyl group, and  $\alpha$ -alkoxyalkylation, i.e. introduction of a chain with an alkoxy group, or, in some cases, an aryloxy group.

These processes can be effected either on an aliphatic chain or on an aromatic ring.

In almost all cases, they involve reaction of a nucleophilic substrate with an electrophilic reagent.

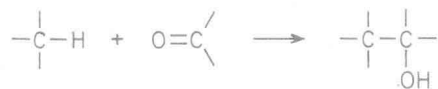
Aldehydes and ketones are used as electrophilic reagents in  $\alpha$ -hydroxyalkylations, whereas acetals,  $\begin{array}{c} \text{OR} \\ \diagup \text{C} \diagdown \\ \text{OR} \end{array}$ ,  $\alpha$ -halo ethers,  $\begin{array}{c} \text{OR} \\ \diagup \text{C} \diagdown \\ \text{X} \end{array}$ , or, in a few cases, aminals,  $\begin{array}{c} \text{OR} \\ \diagup \text{C} \diagdown \\ \text{N} \end{array}$  are employed in  $\alpha$ -alkoxyalkylations.

The nucleophilic substrates include:

- Enolate anions formed from substrates containing carbon atoms activated by one or two electron-withdrawing groups such as ester, cyano, or keto groups.
- Carbanions formed in the  $\alpha$ -position to aromatic rings or to double and triple carbon-carbon bonds.
- Organometallics prepared from alkyl, aryl, or vinyl halides.
- Metallic derivatives of 1-alkynes.
- Aromatic rings.
- Some reactive olefins and enol ethers which react by addition.

#### III B<sub>1</sub> $\alpha$ -Hydroxyalkylation

Aldehydes and ketones have been reacted with various nucleophilic substrates:



Carbon atoms activated by one or two electron-withdrawing heteroatoms or groups generally react by a nucleophilic mechanism involving formation of an anion which adds to the carbonyl group of aldehydes and ketones (see III B<sub>1</sub> a<sub>1</sub>).