

# **Name Reactions and Reagents in Organic Synthesis**

**Bradford P. Mundy**

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# Preface

New Year's Day, 1988, and the book is finished. This has been an enjoyable and interesting project—we have both learned a lot. As I (B.P.M.) sit at the word processor and reflect on the last two years of effort, I know what I would do differently, and how the task could be made more simple. But this did not start as a planned project.

A number of years ago, one of us (B.P.M.) was involved in teaching a course about how to carry out simple one-step transformations, as a starting point for a second course in design of complex syntheses. It was clear that many students did not have a useful vocabulary of reactions, reagents, and knowledge of the “key players” of organic chemistry. I started by preparing a number of reaction and reagent cards. Each class period there would be 3–5 new cards added to the growing list, and each class period I would shuffle the cards and give a random quiz.

As this developed, I needed to add more examples, mechanisms, and so on. The cards developed into full sheets of paper and students were now putting these into ring binders. The format was simple to follow, however; I really didn't take a lot of time to prepare them. A senior chemistry major (M.G.E.) was in my course one year, and after the quarter was over I happened to have the opportunity to see his class notes—they were beautiful! I copied the notes for my own use.

During this developmental period, a number of visiting seminar speakers would see these notes and reaction formats as we discussed educational aspects of the graduate program—and a number of these well-known chemists encouraged me to provide them with copies. During the National Organic Symposium held in Bozeman, Dr. Ted Hoffman, of Wiley-Interscience, encouraged me to organize the handouts into a book. I agreed, and immediately asked Mike Ellerd to participate in the project. This book is the result of this collaboration.

I must give special thanks to Mike as a coauthor—he did all of the artwork and was a tireless library worker. He could find references to reactions and reagents in a spectacular way. This is more difficult these days when the indexing schemes do not list reactions and reagents as commonly as they used to.

This book is written for the students of organic chemistry—be they young or old. We have not included every reaction and reagent—this would be impossible for one text. The Fieser's *Reagents* series is an indispensable compilation for practicing organic chemists, and we must give credit to this work for many of the leads we have incorporated into the Reagent portion of this book. The reactions and reagents picked for inclusion express our own natural prejudices, but we have tried to include those materials usually listed in the most common graduate texts.

Many thanks are required. A number of classes of students have used various levels of handouts and have given useful insight to teaching effectiveness. Dr. Andrew G. Williams and Mr. Scott R. Harring read the entire manuscript and gave

valuable suggestions for us and found a number of “typos” and minor errors in artwork. Kathy Deter, of Kwik-Kopy Printing, spent countless hours making copies of all the drawings, one page at a time. We have tried to check each yield, reaction condition, and reference for proper citation (it is absolutely amazing how many citation errors exist in the literature and other monographs). However, there will be errors in this text also—and for these we apologize to those whose work we have incorrectly represented. We would appreciate receiving comments from users of this book. Are there reactions or reagents that should be included in a next edition? Are there better examples? We encourage anyone to send in a two-page format (the same as in this text) for future inclusion. The authors will be properly cited for the effort.

Bradford P. Mundy  
Michael G. Ellerd

*Bozeman, Montana*  
*January 1988*

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In the following section are a number of common named reactions for organic chemistry. The format for each reaction is the same: The left-facing page has a general scheme for the reaction, a mechanism, some notes and references. The right-facing page will have a number of examples.

=====

**Left-facing page:**

=====

**REACTION:** REACTION NAME

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**March's Advanced Organic Chemistry :** References to March's text.

=====

**GENERAL SCHEME:**

A general reaction scheme

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**MECHANISM:**

A possible mechanism

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**NOTES:**

Where applicable, notes are keyed by .

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**REFERENCES:**

References to the reaction examples.

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**Right-facing page:**

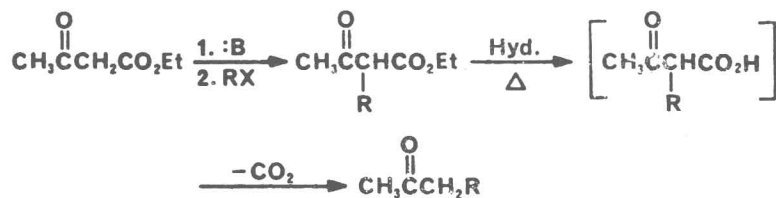
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**EXAMPLES:**

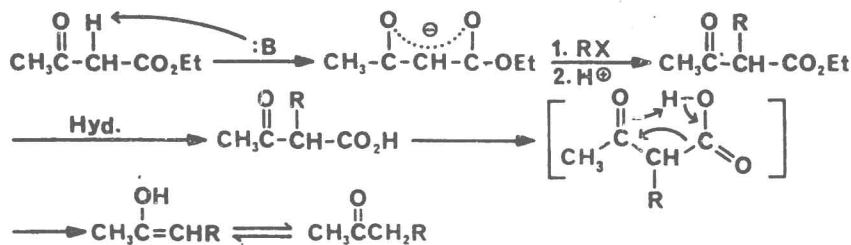
## REACTION: ACETOACETIC ESTER SYNTHESIS

March's Advanced Organic Chemistry : 413

### GENERAL SCHEME:



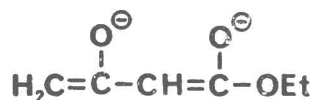
### MECHANISM:



### NOTES:

1. The acidic proton is readily removed by base.
2. By using very strong bases, such as LDA and t-BuLi, a dianion can be formed that will preferentially alkylate at the methyl group.

Via:



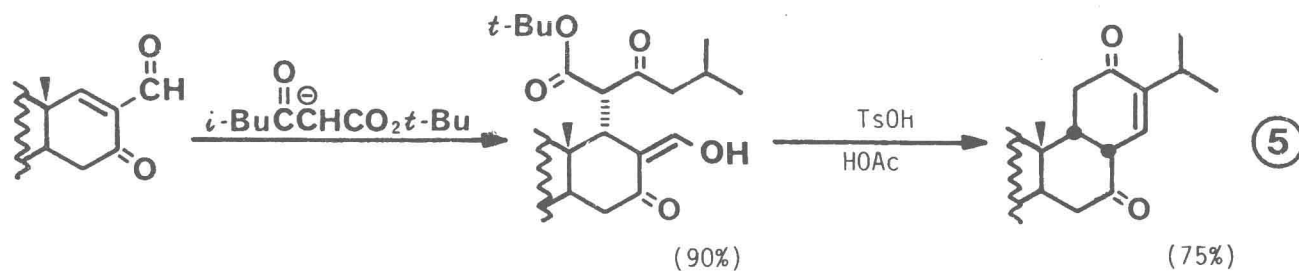
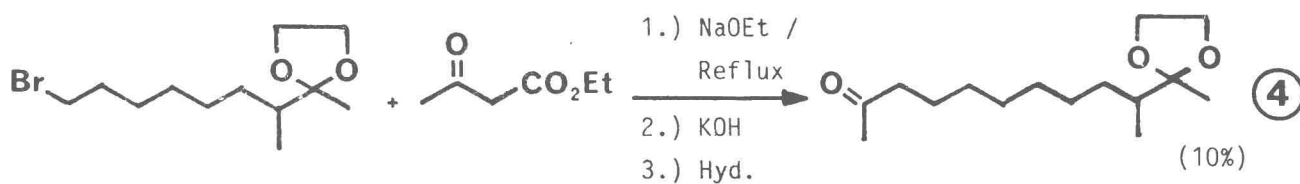
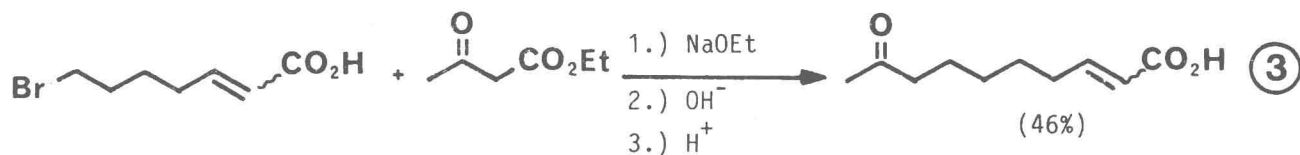
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1. S.N. Harkin and L. Weiler, *J. Am. Chem. Soc.*, (1974), 96, 1082.
2. K. Mori, *Tetrahedron*, (1974), 30, 4223.
3. J. Kennedy, N.J. McCorkindale and R.A. Raphael, *J. Chem. Soc.*, (1961), 3813.
4. R. Nishida, T. Sato, Y. Kuwahara, H. Fukami and S. Ishii, *Agric. Biol. Chem.*, (1976), 40, 1407.
5. W.L. Meyer, M.J. Brannon, C. da G. Burgos, T.E. Goodwin and R.W. Howard, *J. Org. Chem.*, (1985), 50, 438.



$$\text{CH}_3\text{C}(=\text{O})\text{CH}_2\text{CO}_2\text{Et} + \text{CH}_2=\text{CHCH}_2\text{Br} \xrightarrow[\text{THF, 30 min}]{\text{NaH, n-BiLi}} \begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2\text{CCH}_2\text{CO}_2\text{Et} \\ | \\ \text{CH}_2\text{CH}=\text{CH}_2 \end{array} \quad \textcircled{1} \quad \textcircled{2}$$

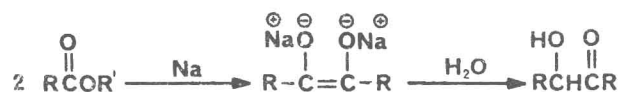
(83%)



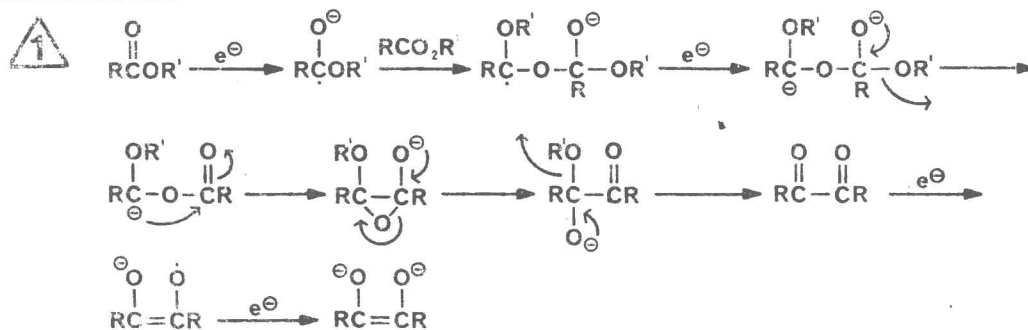
## REACTION: ACYLOIN CONDENSATION

March's Advanced Organic Chemistry : 1113-1116

### GENERAL SCHEME:



### MECHANISM:



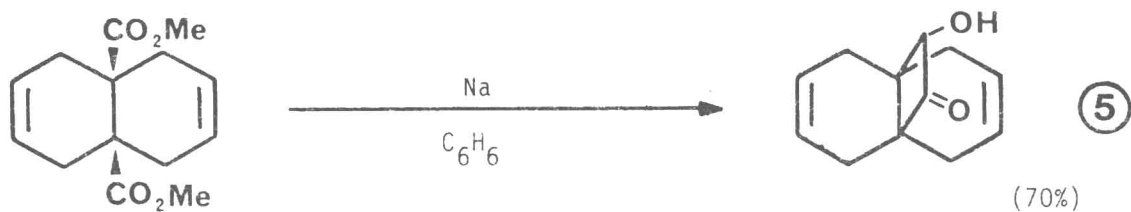
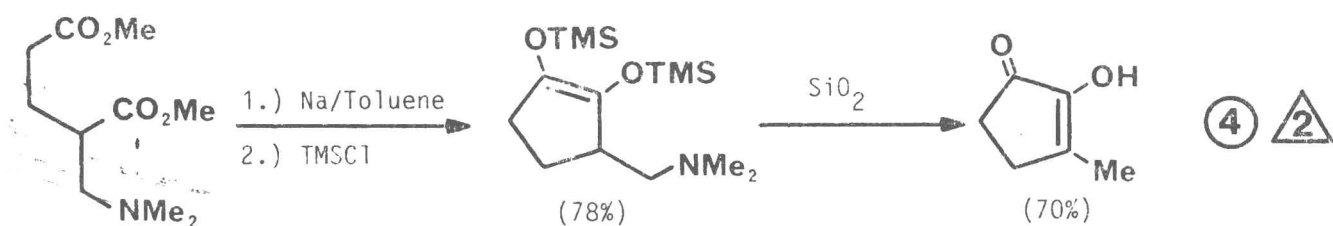
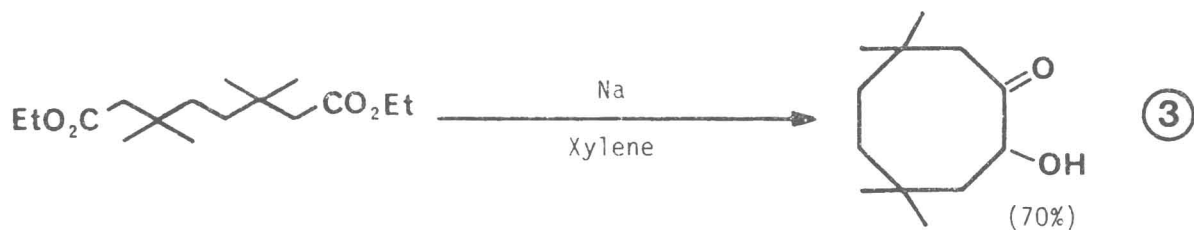
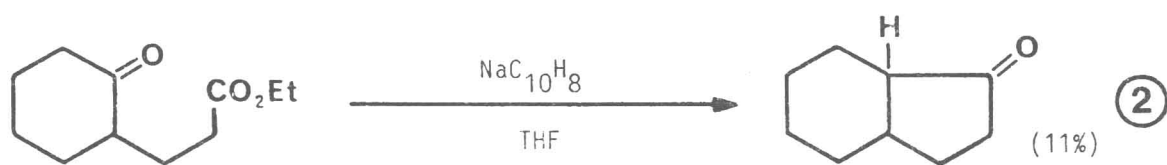
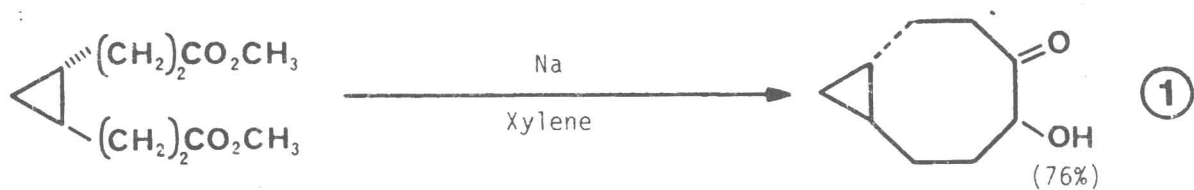
### NOTES:

1. J.J. Bloomfield and D.C. Owsley, *J. Org. Chem.*, (1975), **40**, 393. For a complete explanation of mechanism, see also, NOTE 2.
2. **TMSCl** = Trimethylchlorosilane,  $\text{Me}_3\text{SiCl}$ . It is very important to use freshly distilled TMSCl in this reaction. The TMSCl should be distilled from  $\text{CaH}_2$  under nitrogen to remove any other silane impurities. See: *Organic Reactions*, **23**, 306, (1976).

### REFERENCES:

1. P.G. Gassman, J. Seter and F.J. Williams, *J. Am. Chem. Soc.*, (1971), **93**, 1673.
2. G.D. Gutsche, I.Y.C. Tao, and J. Kozma, *J. Org. Chem.*, (1967), **32**, 1782.
3. A. Krebs, *Tetrahedron Lett.*, (1968), 4511.
4. R.C. Cookson and S.A. Smith, *J. Chem. Soc., Perkin I*, (1979), 2447.
5. J.J. Bloomfield and J.R.S. Irelan, *J. Org. Chem.*, (1966), **31**, 2017.

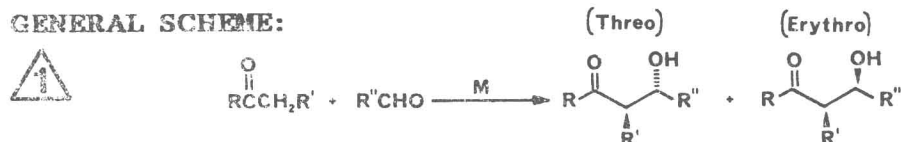
**EXAMPLES:**



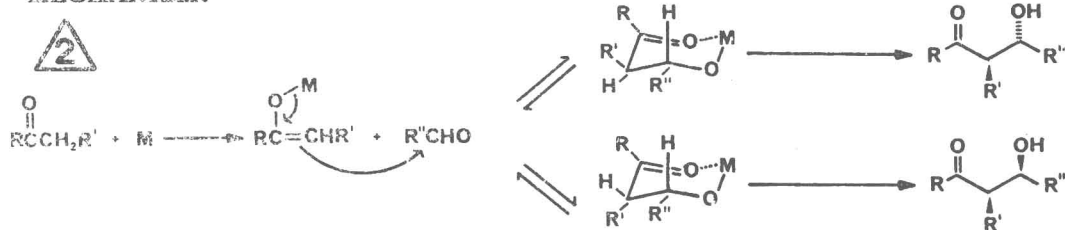
## REACTION: ALDOL CONDENSATION (DIRECTED)

March's Advanced Organic Chemistry : 8298- 34, 844.

### GENERAL SCHEME:



### MECHANISM:



### NOTES:

1. M = Metal = B, Si, Al, Zn, Mg, or Li



Base	Z / E ratio
i-Pr <sub>2</sub> NLi	61:39
Me <sub>3</sub> Si) <sub>2</sub> NLi	85:15
Me <sub>2</sub> ArSi) <sub>2</sub> NLi	99:1
Et <sub>3</sub> Si) <sub>2</sub> NLi	94:6

S. Masamune and W. Choy, Aldrichimica, (1982), 15, 47.

It has been well established that (Z)-enolates give rise to erythro aldol products and that (E)- enolates provide threo aldols. Dialkylboryltriflates have been shown to be effective in the stereoselective formation of (Z)-enolates.

2. C.H. Heathcock, in Current Trends in Organic Synthesis, Proceedings of the Fourth International Conference on Organic Synthesis, Pergamon Press, New York, 1983.

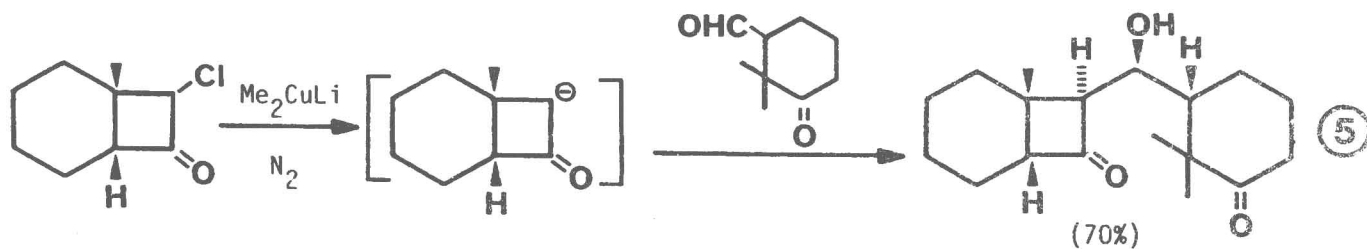
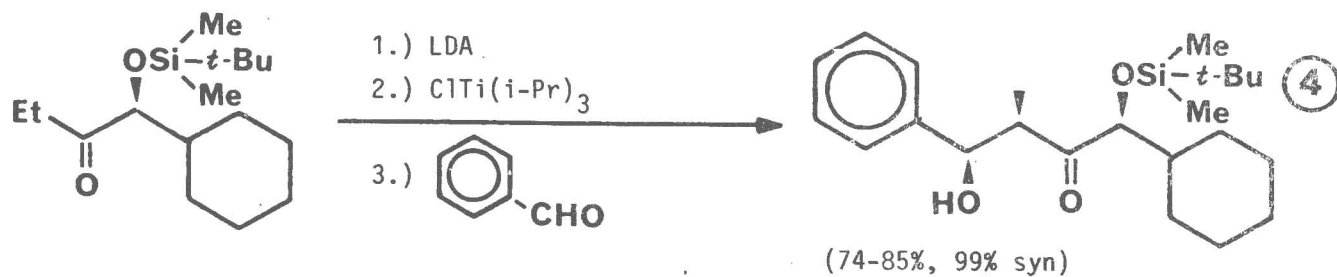
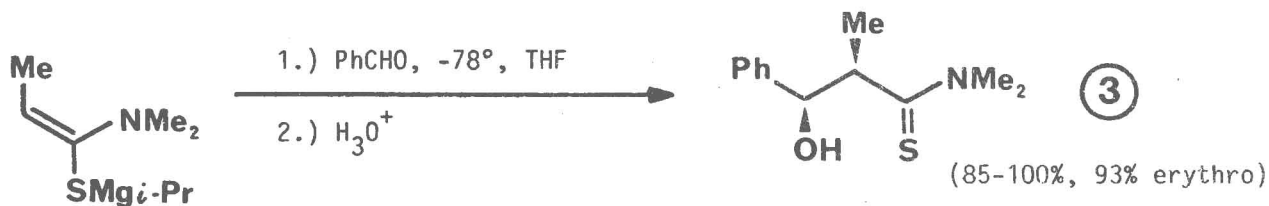
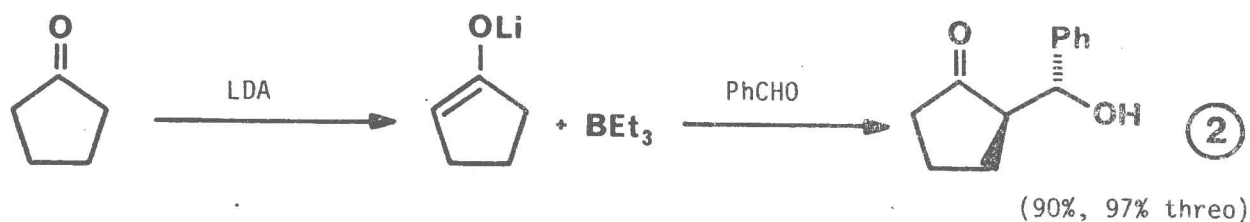
### REFERENCES:

1. D.A. Evans and L.R. McGee, Tetrahedron Lett., (1980), 3975.
2. Y. Yamamoto, H. Yatagai and K. Maruyama, Tetrahedron Lett., (1982), 2387.
3. Y. Tamura, T. Harada, S. Nishi, M. Mizutani, T. Hioki and Z. Yoshida, J. Am. Chem. Soc., (1980), 102, 7806.

4. C. Siegel and E.R. Thornton, *Tetrahedron Lett.*, (1986), 457.

5. G.R. Clark, J. Lin and M. Nikaido, *Tetrahedron Lett.*, (1984), 2645.

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**EXAMPLES:**



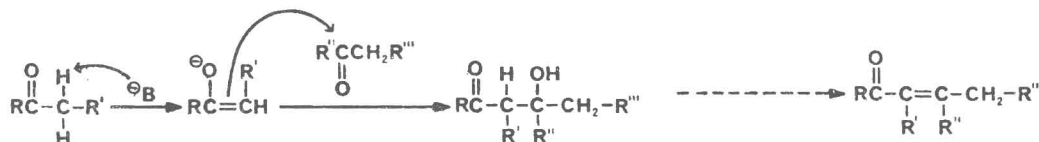
## REACTION: ALDOL CONDENSATION (GENERAL)

March's Advanced Organic Chemistry : 829-34, 844

### GENERAL SCHEME:



### MECHANISM:



### NOTES:

1. Although both the acid (via the enol) and the base (via the enolate) conditions can be used for the **aldol condensation**, base-catalyzed reactions are more frequently used.

2. This is an example of a "**mixed aldol**" condensation. In order for this to be a useful reaction, the second carbonyl should not have acidic hydrogens next to the carbonyl. Both formaldehyde and benzaldehyde are useful for this condensation.

3. This is an example of an "**intramolecular aldol condensation**".

4. The reaction of a nitroalkane with an aldehyde in the presence of base is called the **Henry Reaction**.



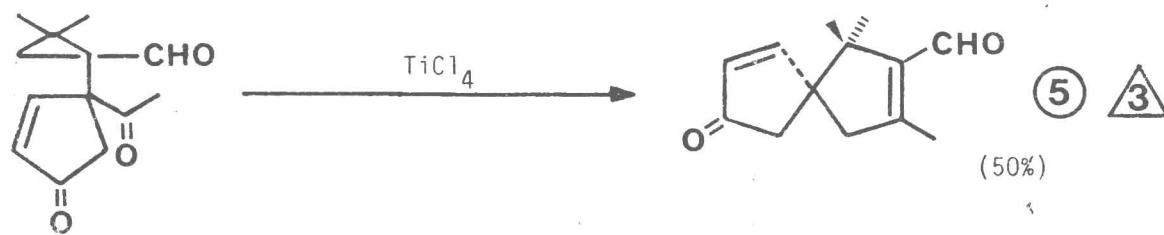
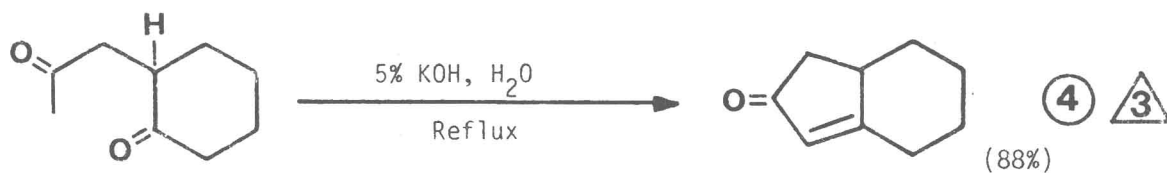
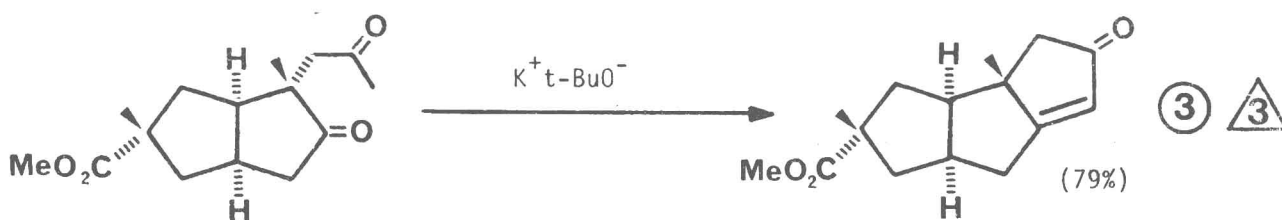
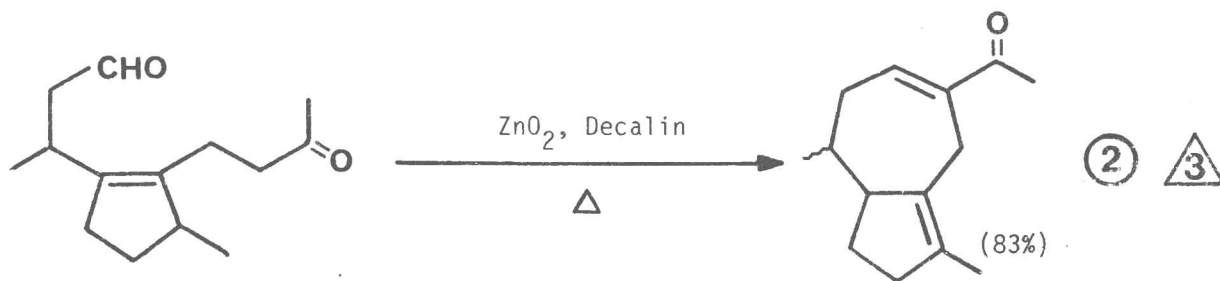
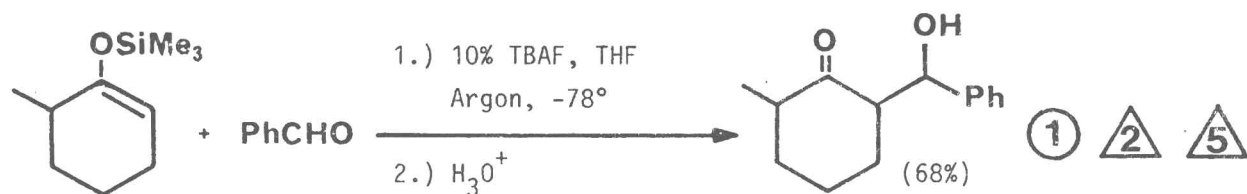
5. The preformed enol-silyl ether is a disguised enolate that is released with fluoride ion.

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1. R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura and S. Shimizu, **J. Am. Chem. Soc.**, (1977), 99, 1265.
2. W. Hoffmann and H. Siegel, **Tetrahedron Lett.**, (1975), 533.
3. B.M. Trost, C.D. Shuey, F. Dininno, Jr., and S.S. McElvain, **J. Am. Chem. Soc.**, (1979), 101, 1234.
4. S.C. Welch, J.-M. Assercq and J.-P. Loh, **Tetrahedron Lett.**, (1986), 1115.
5. S.D. Burke, C.W. Murtiashaw, J.O. Saunders and M.S. Dike, **J. Am. Chem. Soc.**, (1982), 104, 872.



EXAMPLES:



**REACTION: ARBUZOV REACTION ( MICHAELIS - ARBUZOV )**

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**March's Advanced Organic Chemistry : 848**

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**GENERAL SCHEME:**

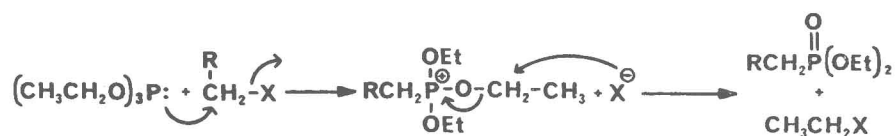
1

2



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**MECHANISM:**



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**NOTES:**

1. The reaction can also be carried out with trimethoxyphosphine
2. When the reaction is carried out with an alpha-bromo ketone it is called the **Perkow Reaction**.

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**REFERENCES:**

1. D.J. Burton and R.M. Flynn, **Synthesis**, (1979), 615.
2. A. Bhattacharya and G. Thyagarajan, **Chem. Rev.**, (1981), 81, 415.
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5. L.M. Harwood and M. Julia, **Synthesis**, (1980), 456.

EXAMPLES:

