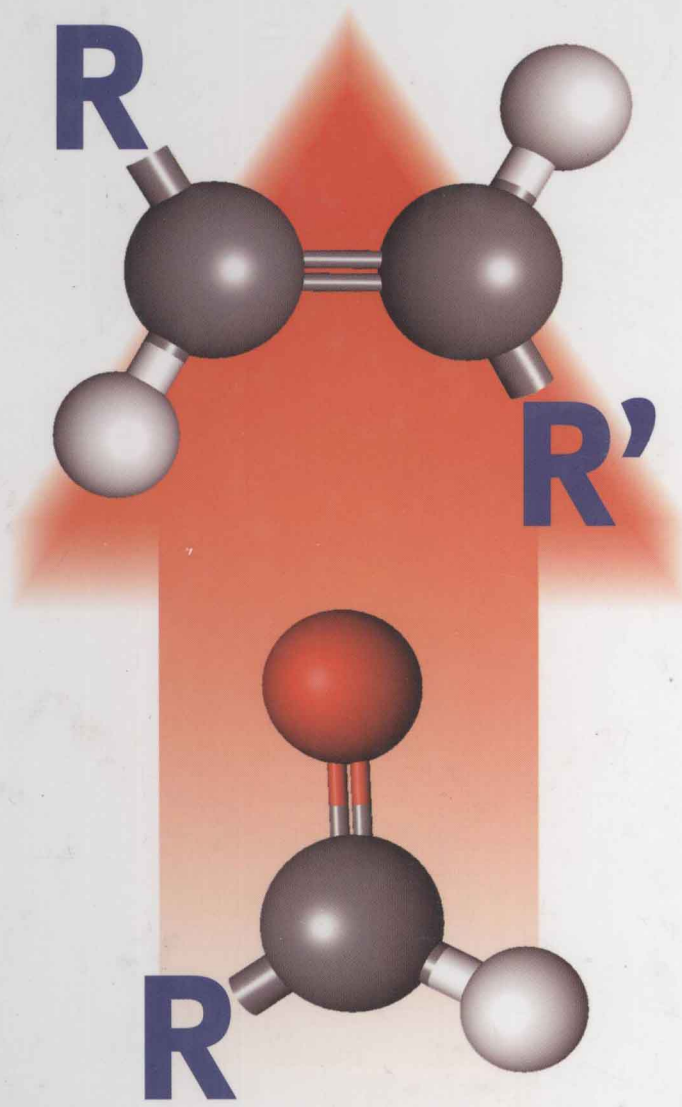


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# Modern Carbonyl Olefination

Methods and Applications



*Takeshi Takeda (Ed.)*

## **Modern Carbonyl Olefination**



WILEY-VCH Verlag GmbH & Co. KGaA

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**Library of Congress Card No.: applied for**

A catalogue record for this book is available from the British Library.

Bibliographic information published by Die Deutsche Bibliothek

Die Deutsche Bibliothek lists this publication in the Deutsche

Nationalbibliografie; detailed bibliographic data is available in the Internet at <http://dnb.ddb.de>

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Printed in the Federal Republic of Germany.

Printed on acid-free paper.

**Typesetting** Asco Typesetters, Hong Kong

**Printing** Strauss Offsetdruck GmbH, Mörlenbach

**Bookbinding** J. Schäffer GmbH & Co. KG, Grünstadt

**ISBN** 3-527-30634-X

*Takeshi Takeda (Ed.)*

**Modern Carbonyl  
Olefination**

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## Preface

This book summarizes the recent progress in the major methodologies of carbonyl olefination, which is one of the most fundamental transformations in organic synthesis. Carbonyl olefination has been extensively studied since Professor Georg Wittig discovered in 1953 the reaction of phosphonium ylides with carbonyl compounds, which has become known as the Wittig reaction. Since then, a variety of reagents have been developed for this transformation by a number of chemists. These reagents enable us to transform various carbonyl functions into carbon-carbon double bonds with different chemo- and stereoselectivities and are utilized in a variety of organic syntheses.

The mechanisms of these reactions bear marked similarities, in spite of the differences in their reactivities and selectivities. Thus, in certain cases, a four-membered intermediate similar to the 1,2-oxaphosphetane intermediate in the Wittig reaction appears in the Peterson reaction as a pentacoordinate 1,2-oxasiletanide. Reactions of transition metal carbene complexes with carbonyl compounds also proceed through the formation of a four-membered oxametallacycle, which was recently found to be an intermediate of some McMurry reactions. Carbonyl olefination utilizing dimetallic species of zinc or chromium is somewhat similar to the Julia reaction in that they both involve the process of  $\beta$ -elimination.

In this book, an effort has been made to provide comprehensive yet concise commentaries on the mechanisms of each reaction, as well as on their synthetic applications. These provide an accurate prescription for their use and should be useful for the development of a broader perspective on carbonyl olefination. The final chapter is concerned with asymmetric carbonyl olefination, which is one of the frontiers of organic synthesis. As this subject exemplifies, the established methodologies are not necessarily perfect and there still remain many problems to be solved in the field of carbonyl olefination. It is hoped that this book will be of wide use to all chemists engaged in organic synthesis, both in industrial laboratories and in academic institutions.

I would like to thank the authors of the individual chapters for their excellent contributions. This volume was only possible with the cooperation of the authors, who are experts in each field. Finally, I express my sincere gratitude to my wife, Yukiko, whose continuous encouragement was essential to the editing of this book.

**Takeshi Takeda**  
*Tokyo, 2003*

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## 1

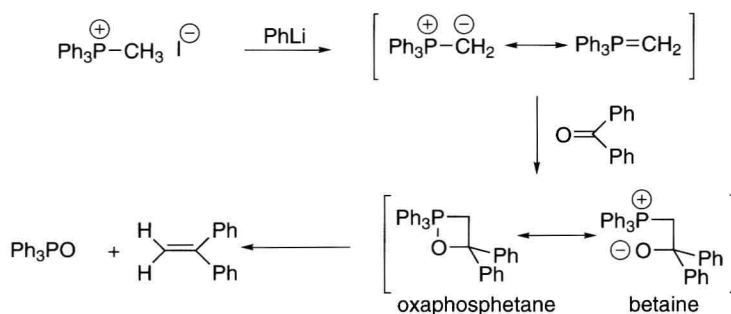
## The Wittig Reaction

Michael Edmonds and Andrew Abell

## 1.1

## Introduction

The reaction of a phosphorus ylide with an aldehyde or ketone, as first described in 1953 by Wittig and Geissler [1] (see Scheme 1.1), is probably the most widely recognized method for carbonyl olefination.



**Scheme 1.1.** The Wittig reaction.

This so-called Wittig reaction has a number of advantages over other olefination methods; in particular, it occurs with total positional selectivity (that is, an alkene always directly replaces a carbonyl group). By comparison, a number of other carbonyl olefination reactions often occur with double-bond rearrangement. In addition, the factors that influence *E*- and *Z*-stereoselectivity are well understood and can be readily controlled through careful selection of the phosphorus reagent and reaction conditions. A wide variety of phosphorus reagents are known to participate in Wittig reactions and the exact nature of these species is commonly used to divide the Wittig reaction into three main groups, namely the “classic” Wittig reaction of phosphonium ylides, the Horner–Wadsworth–Emmons reaction of phosphonate anions, and the Horner–Wittig reaction of phosphine oxide anions. Each of these reaction types has its own distinct advantages and limitations, and



these must be taken into account when selecting the appropriate method for a desired synthesis.

## 1.2

### The “Classic” Wittig Reaction [1–4]

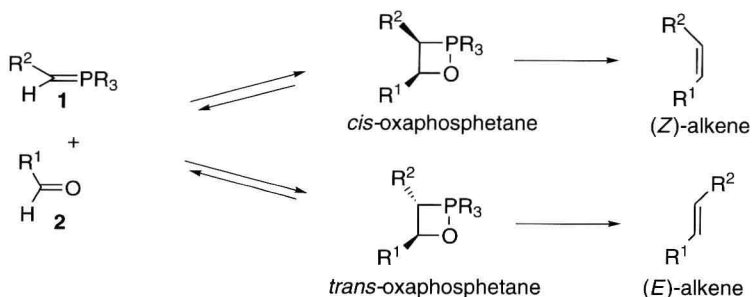
The original work of Wittig and Geissler [1], as depicted in Scheme 1.1, provides a good example of a classic Wittig reaction in which a phosphonium ylide reacts with an aldehyde or ketone to afford the corresponding alkene and phosphine oxide. This reaction is very general and provides a convenient method for the preparation of a range of alkenes with good stereocontrol. The starting phosphonium ylides are themselves readily generated by the addition of a suitable base to the corresponding phosphonium salt (refer to Section 1.2.3).

#### 1.2.1

##### Mechanism and Stereoselectivity

The mechanism of the Wittig reaction has long been considered to involve two intermediate species, a diionic betaine and an oxaphosphetane, as shown in Scheme 1.1. However, there has been much debate as to which of these two species plays the most important mechanistic role and also as to how each influences the stereochemical outcome under different reaction conditions. For many years, it was generally accepted that the betaine is the more important intermediate [5, 6]; however, recent low temperature  $^{31}\text{P}$  NMR studies suggest that this may not be the case [7, 8]. This supposition is further supported by recent calculations that reveal that oxaphosphetanes are of lower energy than the corresponding betaines [9]. As such, the currently accepted mechanism for the Wittig reaction is as shown in Scheme 1.2 [4]. For a more detailed account of the evolution of the Wittig mechanism, the reader is referred to the excellent reviews by Vedejs and co-workers [4, 10].

The stereoselectivity of the Wittig reaction is directly linked to this mechanism. In particular, the reaction of a carbonyl compound with an ylide produces both the



**Scheme 1.2.** The mechanism of the Wittig reaction.