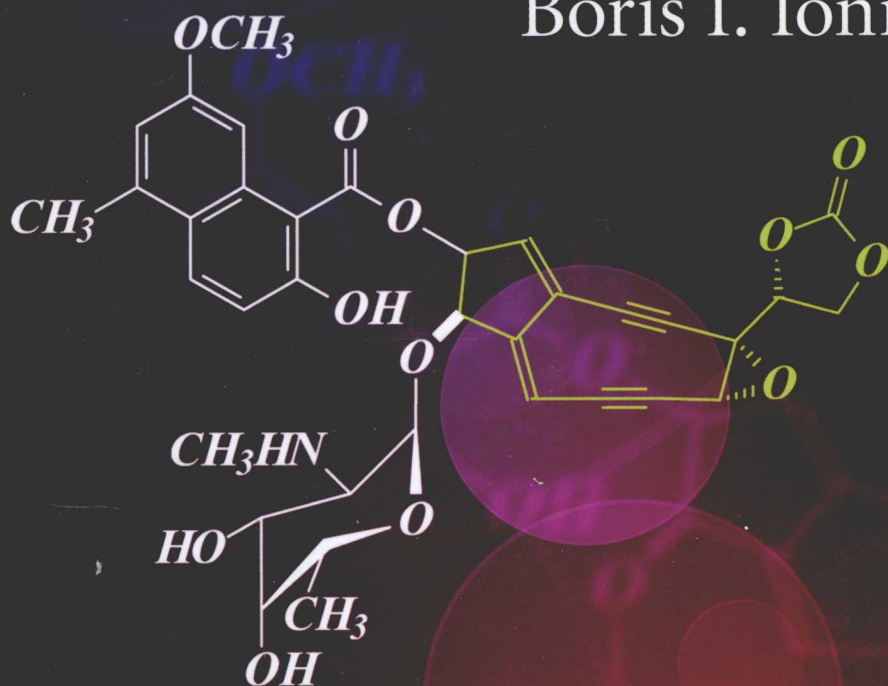


# Alkynes in Cycloadditions

Irina A. Maretina  
Boris I. Ionin



Consulting Editor John C. Tebby

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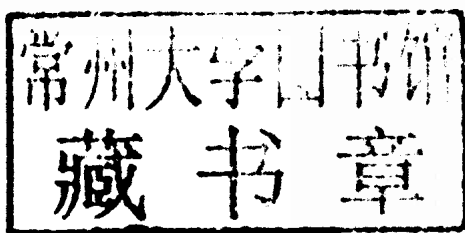
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This edition first published 2014  
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John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, United Kingdom

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*Library of Congress Cataloging-in-Publication Data*

Alexandrovna, Maretina I.

Alkynes in cycloadditions / author, Maretina I. Alexandrovna ; translated from the Russian by Boris I. Ionin ; consulting editor, John C. Tebby.

pages cm

Includes index.

ISBN 978-1-118-61532-4 (cloth)

1. Alkynes. 2. Ring formation (Chemistry) I. Tebby, John C., 1933- II. Title.

QD305.H8M23 2014

547'.413-dc23

2013019891

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

ISBN: 9781118615324

Typeset in 10.5/13pt Sabon by Aptara Inc., New Delhi, India

Printed and bound in Malaysia by Vivar Printing Sdn Bhd

*On the 100th anniversary of Anatoly Petrov*

# Preface

The monograph presents a modern methodology of regioselective synthesis of aromatic and nonaromatic carbocyclic and heterocyclic ring systems based mainly on [2+2+2] and [4+2] cycloaddition, and other reactions of acetylenic units, including enediynes and enyne-allenes. The features of the construction of polyaromatic structures, including heterostructures, based on cycloaddition reactions is used in the synthesis of advanced materials including nanomaterials.

New strategies are described for the formation of aromatic and polynuclear hydrocarbons, reflecting a modern approach to organic synthesis based on (*Z*)-hex-3-en-1,5-diyne and (*Z*)-hepta-1,2,4-triene-6-yne blocks. One-step synthesis of benzene derivatives,  $\beta$ -substituted naphthalenes, and acenes by the cycloaromatization of enediynes and enyne-allenes by Bergman, Myers-Saito and Schmittel is discussed. Included are the mechanisms of cycloaromatization resulting in the formation of fulvene and indene systems. The reactions of cascade cyclizations are considered. Heterocyclization involving enyne-carbodiimides are also covered. The practical value of the above mentioned syntheses includes the formation of nanostructures, naturally occurring compounds, and chemosensory materials for nonlinear optics and the design of electronic and photonic devices.

We also consider new achievements in some classical cycloaddition reactions such as the Diels-Alder condensation with acetylenic dienophiles, [2+2] cycloadditions with acetylene component leading to creation of cyclobutene ring, and new results in cyclobutene syntheses by [2+2] acyclization of phosphorus containing 1,3-butadiene derivatives synthesized starting with propargyl-type alcohols.

# Acknowledgments

I express my gratitude to all those who took part in the creation of this monograph.

As a child I lived in Leningrad during the period of the siege. Great respect is due to the people who saved our lives.

I wish to thank my parents, who were chemists and students of the academician AE Poray-Kosice.

I would like to thank my mentor Anatoly Petrov. As a student of the Leningrad University of Technology in 1953, I heard his brilliant lectures on organic chemistry, and worked for 50 years (1954–2004) at the academic department that he established. I started my work as an analyst and finished as a professor, having gained a keen interest in the chemistry of highly unsaturated conjugated systems.

My interests include the chemistry of alkynes, the synthesis and reactivity of unsaturated heteroatomic compounds, as well as nitrogen-containing heterocyclic compounds.

I led projects in the area of diacetylene and its derivatives—functionalization reaction and heterocyclization oriented toward industry—with Professor Petrov's continued support.

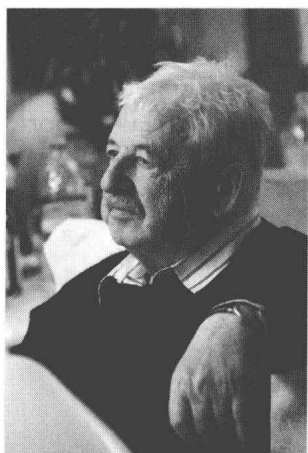
I wish to give my special thanks to RAS academician BA Trofimov for suggesting the topic of the book. He supported us with publications on AA Petrov's work and the topic of diacetylenes.

I am indebted to my colleague, Professor BI Ionin, who was a protégé of Anatoly Petrov. He translated the book into English and did a lot of work to edit the Russian and English versions, and fully wrote Chapter 4.

My sincere thanks go to Professor John Tebby for his cooperation, valuable comments and for his support to the project.

Maretina I. Alexandrovna  
Department of Organic Chemistry  
St Petersburg, Russia

# Biography



Professor Dr. Boris  
Iosifovich Ionin,  
1935–2013.

Professor Ionin dedicated his professional life to the study of chemistry and exploring its applications and uses. He died on April 4, 2013, just before this book was published. This publication is a reflection of Professor Ionin's long-standing commitment to making Russian science available to the rest of the world. After graduating from the Leningrad Lensoviet Institute of Technology in 1956, he defended his doctoral PhD dissertation in 1962, and his professorship dissertation in 1972. The entirety of Professor Ionin's professional life was connected with the St Petersburg State Institute of Technology.

Professor Ionin published numerous papers in the field of organophosphorus chemistry, and was a regular and highly respected participant at symposia and international conferences. His research included electrophilic addition reactions of phosphorus pentachloride to double and triple bonds and photo-initiated free-radical halogenophosphonylation. His studies of the Arbuzov reaction involving halogeno acetylation led to his pioneering studies of this reaction using dichloroacetylene. This work opened many new ways for the synthesis of a variety of organophosphorus compounds that included the preparation and characterisation of new stable carbanions.

Professor Ionin's keen interest in physical–organic chemistry included the development of new computer programs and the exploitation and development of heteronuclear NMR spectroscopy. His monograph

*Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* was published and translated for marketing in the United States. He was on the editorial board of *Zhurnal Obshchei Khimii* and was widely acknowledged for his English translation of Russian chemistry literature. He was a member of the Academic Council of the Institute of Organic Chemistry at the Academy of Sciences in Riga, and of the Presidium of the St Petersburg office of the Mendeleyev Russian Chemical Society. In 2007, he received the award of Honoured Science Worker of the Russian Federation.

Boris was greatly respected and liked by his colleagues, students, and collaborators. His ability to make trusted friends led to a considerable amount of national and international collaboration. The latter included Nippon Chemicals, Union Carbide, and major projects, such as the European-Commission-funded INTAS project involving teams of chemists from the United Kingdom and across Russia. He was also a key contributor to a substantial pharmaceutical project with university and hospital scientists in the United Kingdom that, with commercial support, led to clinical trials and potential medical applications.



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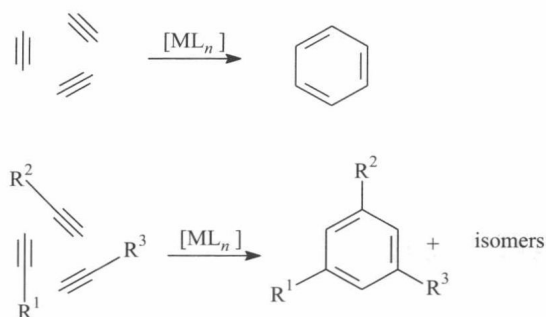
# 1

## Introduction

Polysubstituted benzenes are widely used both in industry and in research laboratories. Regioselective construction of polysubstituted benzenes is usually achieved through the gradual introduction of substituents in the aromatic ring by Friedel–Crafts reaction or similar reactions of electrophilic substitution or through organometallic synthesis. In 1948, Reppe reported the [2+2+2] trimerization of substituted acetylenes in the presence of transition metals to form polysubstituted benzenes (Scheme 1.1) [1].

Transition metal catalyzed cycloaddition reactions enables facile design of blocks of highly functionalized molecules in a single step. Reactions of [2+2+2] cycloaddition of alkynes are an effective method for the formation of substituted arenes and nonaromatic rings, as described in a monograph [2] and reviews [3–9]. However, high regioselectivity and good yield can be achieved using the right choice of reagents and synthetic routes. Another promising methodology consists in the construction of the benzene ring in a [4+2] reaction of conjugated enyne with alkyne in the presence of a Lewis acid [10, 11] or by the transition metal catalyst [2, 12, 13]. More recently, it was shown that the construction of the benzene ring may proceed using dienyynes, triynes, and tetraynes [3, 14, 15]. Similar approaches can be used for the creation of naphthalene and other condensed aromatic systems, for example, acenes.

Many articles have been published on the formation of substituted arenes by this type of reaction in the presence of transition metals. The current development of the field of organic synthesis focuses on the design of intermolecular substituted arenes, which makes it possible to control the construction of a precursor in the synthesis of the product

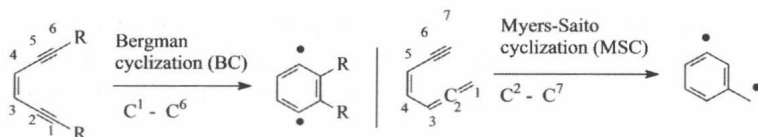


Scheme 1.1

[3, 5–9]. There is a problem of stereoselectivity in the synthesis of arenes by intramolecular [2+2+2] cycloaddition.

The thermal reaction of benzannulation of enediynes, the Bergman cycloaromatization, that occupies a special place, has been intensively studied [16]. These methods include also the less studied Myers–Saito [17] and Schmittle [18] cycloaromatization. Cycloaromatization of enediyne and enyne-allene blocks is described in books [19–23] and reviews (Scheme 1.2) [24–30].

During the study of systems containing (Z)-hex-3-en-1,5-diyne and (Z)-hepta-1,2,4-triene-6-yne blocks, a new methodology of organic synthesis was created, which involved one-pot synthesis of aromatic structures. These comprised  $\beta$ -substituted naphthalenes, linearly fused acenes, fulvene, and indene systems, as well as helical structures, spherical polycyclic aromatic hydrocarbons, the building blocks for the construction of fullerenes, and finally, condensed heterocycles containing O, N, and S atoms [26–32]. Polycyclic aromatic hydrocarbons and related compounds containing one or more heteroatoms are important to many areas of chemistry and material science as a basis for new materials [23, 27]. A specific role of diacetylene systems involves fundamentally new approaches to obtaining nanostructures based on cascade reactions.



**Scheme 1.2** Intermediate biradicals in the Bergman and Myers–Saito cyclization reactions.

Such syntheses are difficult by classical methods [30–32]. Chemical modifications of triple carbon–carbon bonds in reactions such as nucleophilic addition and cycloaddition lead to a wide range of new heterocycles, that cannot be synthesized by other routes [33–37]. This area of chemistry of acetylene compounds is extremely promising since it complements earlier methods. New methodology for the formation of cyclic systems based on cycloaddition reactions of acetylene units has been described in the recent literature; works published in the years 2000–2012 are considered in detail in Chapter 2.

Many of these reactions have attracted the attention of researchers due to the fact that these processes occur in the body during the application of anticancer drugs containing an enediyne block. Chapter 3 is devoted mainly to the analysis of papers related to the study of the cyclization mechanism. Chapter 4 includes additional material on cycloaddition with acetylenic units or those sourced from acetylenic compounds, leading to the formation of carbo- and heterocycles of different structures. The concluding Chapter 5 includes some recent results.





# 2

## Regioselective Syntheses of Polysubstituted Benzenes Catalyzed by Transition Metal Complexes

### 2.1 [2+2+2] CYCLOADDITION REACTIONS OF ACETYLENES

#### 2.1.1 Reactions of Alkynes with Metallocyclopentadiene as an Intermediate

The cyclotrimerization of alkynes catalyzed by transition metals is a general method for building substituted benzenes from aliphatic precursors. Multiple bonds are formed in these reactions in a single operation. Although the reaction of thermal trimerization relates to allowed electrocyclic processes, it is catalyzed by several transition metals, such as Co, Ni, Rh, Pd, Rh, and Ru [38]. Most recent publications show promise for the participation of transition metal complexes in [2+2+2] cycloaddition reactions based on zirconium, titanium, and indium [9]. This reaction has synthetic potential for using metallocyclopentadienes as intermediates in the cyclotrimerization of alkynes. The reaction mechanism is shown in Scheme 2.1 [3, 38]. Two alkyne molecules coordinated to the metal, that is, complex **2.1**, couple to form cyclopentadiene **2.2**. Next there is either addition of the alkyne to the metallocycle **2.3** to form the metallocycle