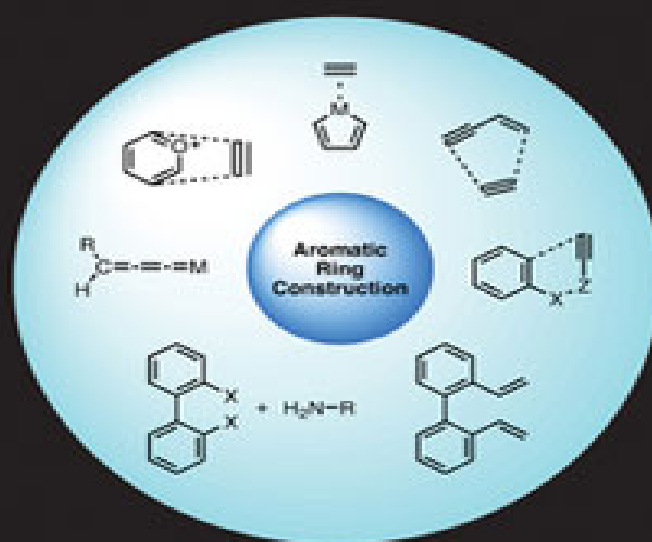


# Transition- Metal-Mediated Aromatic Ring Construction



Edited By  
**KEN TANAKA**

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# **TRANSITION-METAL-MEDIATED AROMATIC RING CONSTRUCTION**

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**Edited by**

**KEN TANAKA**

Tokyo University of Agriculture and Technology  
Tokyo, Japan

**WILEY**

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***Library of Congress Cataloging-in-Publication Data:***

Transition-metal-mediated aromatic ring construction / edited by Ken Tanaka, Tokyo University of Agriculture and Technology, Tokyo, Japan.

pages cm

Includes bibliographical references and index.

ISBN 978-1-118-14892-1 (hardback)

1. Aromatic compounds—Synthesis. 2. Transition metal catalysts. I. Tanaka, Ken, 1967–

QD331.T73 2013

547'.6—dc23

2012049882

# CONTRIBUTORS

**Naoki Asao**, WPI-Advanced Institute for Materials Research, Tohoku University, 2-1-1 Katahira, Sendai 980-8577, Japan; E-mail: asao@m.tohoku.ac.jp

**Catherine J. Ball**, Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Oxford, OX1 3TA, UK

**Shunsuke Chiba**, Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore; E-mail: SHUNSUKE@ntu.edu.sg

**Vincent Gandon**, ICMMO (UMR CNRS 8182), University of Paris-sud, 91405 Orsay cedex, France; E-mail: vincent.gandon@u-psud.fr

**Vladimir Gevorgyan**, Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061; E-mail: vlad@uic.edu

**Julien Grand**, Laboratoire de Chimie Moléculaire et Thio-organique, UMR CNRS 6507, INC3M, FR 3038, ENSICAEN and Université de Caen, 6 Boulevard du Maréchal Juin, 14050 Caen, France

**James Wallace Herndon, Jr.**, Department of Chemistry and Biochemistry, New Mexico State University, MSC 3C, Las Cruces, New Mexico 88003-8001; E-mail: jherndon@nmsu.edu

**Gerhard Hilt**, Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Str., 35043 Marburg, Germany; E-mail: hilt@chemie.uni-marburg.de

**Yoshifumi Ishikawa**, Department of Chemistry, Graduate School of Science, Tohoku University, 6-3 Aramaki aza aoba, Sendai 980-8578, Japan

**Tsugio Kitamura**, Department of Chemistry and Applied Chemistry, Graduate School of Science and Engineering, Saga University, 1 Honjo-machi, Saga 840-8502, Japan; E-mail: kitamura@cc.saga-u.ac.jp

**Puneet Kumar**, Department of Chemistry, Henry Eyring Building, University of Utah, 315 S. 1400 E, Salt Lake City, Utah 84112-0850

**Takuya Kurahashi**, Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyotodaigaku-Katsura, Nishikyo, Kyoto 615-8510, Japan; E-mail: tkuraha@orgrxn.mbox.media.kyoto-u.ac.jp

**Shi Li**, State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, CAS, 345 Lingling Lu, Shanghai 200032; E-mail: lishi006@sioc.ac.cn

**Janis Louie**, Department of Chemistry, Henry Eyring Building, University of Utah, 315 S. 1400 E, Salt Lake City, Utah 84112-0850; E-mail: louie@chem.utah.edu

**Seihiro Matsubara**, Department of Material Chemistry, Graduate School of Engineering, Kyoto University,

Kyotodaigaku-Katsura, Nishikyo, Kyoto 615-8510, Japan; E-mail: matsubar@orgrxn.mbox.media.kyoto-u.ac.jp

**Takanori Matsuda**, Department of Applied Chemistry, Faculty of Science, Tokyo University of Science, 1-3 Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan; E-mail: mtd@rs.tus.ac.jp

**Masahiro Miura**, Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan; E-mail: miura@chem.eng.osaka-u.ac.jp

**Itaru Nakamura**, Research and Analytical Center for Giant Molecules, Graduate School of Science, Tohoku University, 6-3 Aramaki Aza Aoba, Aoba-ku, Sendai 980-8578, Japan; E-mail: itaru-n@m.tohoku.ac.jp

**Koji Nakano**, Department of Organic and Polymer Materials Chemistry, Tokyo University of Agriculture and Technology, 2-24-16 Naka-Cho, Koganei, Tokyo 184-8588, Japan; E-mail: k\_nakano@cc.tuat.ac.jp

**Yoshiaki Nishibayashi**, Institute of Engineering Innovation, School of Engineering, The University of Tokyo, Yayoi, Bunkyo-ku, Tokyo, 113-8656, Japan; E-mail: ynishiba@sogo.t.u-tokyo.ac.jp

**Hiroaki Ohno**, Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan; E-mail: hohno@pharm.kyoto-u.ac.jp

**Tetsuya Satoh**, Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita,

Osaka 565-0871, Japan; E-mail: [satoh@chem.eng.osaka-u.ac.jp](mailto:satoh@chem.eng.osaka-u.ac.jp)

**Takanori Shibata**, Department of Chemistry and Biochemistry, Advanced Science and Engineering, Waseda University, 3-4-1, Okubo, Shinjuku, Tokyo, 169-8555, Japan; E-mail: [tshibata@waseda.jp](mailto:tshibata@waseda.jp)

**Yu Shibata**, Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Naka-Cho, Koganei, Tokyo 184-8588, Japan

**Masaki Shimizu**, Department of Biomolecular Engineering, Graduate School of Science and Technology, Kyoto Institute of Technology, Hashigami-cho 1, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan; E-mail: [mshimizu@kit.ac.jp](mailto:mshimizu@kit.ac.jp)

**Tamotsu Takahashi**, Catalysis Research Center and Graduate School of Life Science, Hokkaido University, Kita-ku, Sapporo 001-0021, Japan; E-mail: [tamotsu@cat.hokudai.ac.jp](mailto:tamotsu@cat.hokudai.ac.jp)

**Ryo Takeuchi**, Department of Chemistry and Biological Science, Aoyama Gakuin University, 5-10-1 Fuchinobe, Chuo, Sagami-hara, Kanagawa 252-5258, Japan; E-mail: [takeuchi@chem.aoyama.ac.jp](mailto:takeuchi@chem.aoyama.ac.jp)

**Ken Tanaka**, Department of Applied Chemistry, Graduate School of Engineering, Tokyo University of Agriculture and Technology, 2-24-16 Naka-Cho, Koganei, Tokyo 184-8588, Japan; E-mail: [tanaka-k@cc.tuat.ac.jp](mailto:tanaka-k@cc.tuat.ac.jp)

**Yi-Feng Wang**, Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

**Michael C. Willis**, Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Oxford, OX1 3TA, UK; E-mail: michael .willis@chem.ox.ac.uk

**Bernhard Witulski**, Laboratoire de Chimie Moléculaire et Thio-organique, UMR CNRS 6507, INC3M, FR 3038, ENSICAEN and Université de Caen, 6 Boulevard du Maréchal Juin, 14050 Caen, France; E-mail: bernhard.witulski@ensicaen.fr

**Hiroto Yoshida**, Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University, Higashi-Hiroshima 739-8527, Japan; E-mail: yhiroto@hiroshima-u.ac.jp

**Kazuhiro Yoshida**, Department of Chemistry, Graduate School of Science, Chiba University, 1-33 Yayoi-Cho, Inage-Ku, Chiba 263-8522, Japan; E-mail: kyoshida@faculty.chiba-u.jp

**Yoshihiko Yamamoto**, Department of Basic Medicinal Sciences, Graduate School of Pharmaceutical Sciences, Nagoya University, Chikusa, Nagoya 464-8601, Japan; E-mail: yamamoto-yoshi@ps.nagoya-u.ac.jp

**Olga V. Zatolochnaya**, Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061

# PREFACE

Because complex aromatic compounds have been utilized in various functional organic materials (e.g., liquid crystals, organic light-emitting devices), functional reagents (e.g., ligands, catalysts), and biologically active compounds (e.g., medicines, pesticides), the development of new reactions for the synthesis of aromatic compounds is a hot research field in modern organic synthesis. A conventional synthetic route to aromatic compounds is that of substitution reactions of aromatic nucleus, but this approach is not satisfactory in some cases. Recent significant advances in the area of transition-metal-mediated aromatization reactions enable the efficient construction of substituted aromatic rings in practical as well as convenient ways. These aromatic ring construction reactions would open promising new routes to complex aromatic compounds. Consequently, these reactions have been the subject of intense research in recent years, as evidenced by the number of research papers and reviews that have appeared.

Although transition-metal-mediated substitution reactions of aromatic nucleus have been well described in a number of books, a book that focuses on the transition-metal-mediated construction of aromatic rings has not appeared to date. A book explaining the use of transition-metal-mediated aromatic ring construction reactions for the complex aromatic compounds targeted would, therefore be useful for both academic and industrial chemists. For these reasons, in this book we demonstrate comprehensively how to use transition-metal-mediated aromatic ring construction reactions for the synthesis of complex aromatic compounds.

I would like to thank the authors of the individual chapters, each of whom is as a world expert in their area of research

into aromatic ring construction reactions, for their willingness to contribute. I would also like to thank the team at Wiley, especially Jonathan Rose, for his valuable assistance and encouragement during this project. Finally, I deeply appreciate students in my research group for their valuable assistances.

KEN TANAKA

*November 2012*



# PART I

## [2 + 2 + 2] AND RELATED CYCLOADDITION REACTIONS

# 1

## COBALT-MEDIATED [2 + 2 + 2] CYCLOADDITION

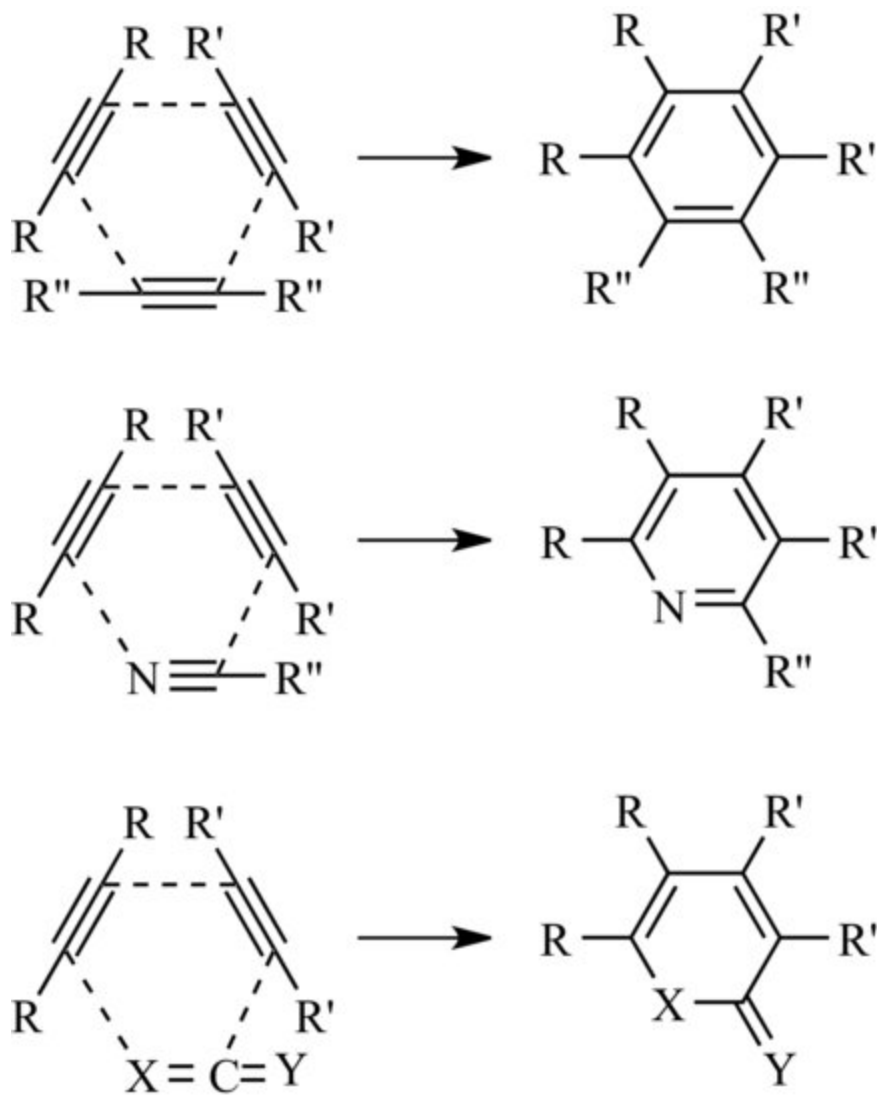
VINCENT GANDON

### 1.1 INTRODUCTION

An expedient way to envisage the synthesis of conjugated six-membered rings such as benzenes, pyridines, pyridones, and related heterocycles is by a [2 + 2 + 2] cycloaddition retrosynthetic approach. These conjugated systems can indeed be viewed as cycloadducts of three readily available unsaturated partners, such as alkynes, nitriles, isothiocyanates, carbon disulfide, isocyanates, and carbodiimides ([Scheme 1.1](#), X = N, S; Y = N, O, S). Although the thermal version of this reaction is usually hardly feasible [1], it becomes straightforward in the presence of the appropriate catalyst. The first example of transition-metal-catalyzed [2 + 2 + 2] cycloaddition was reported by Reppe and Schweckendiek in 1948 [2]. A nickel complex was used as a precatalyst to cyclotrimerize alkynes into benzenes. Until the early 1970s, it was shown that many other metals could be employed, notably cobalt. Afterward, led by Vollhardt, who reported a considerable number of applications, this chemistry clearly proved to be priceless in organic synthesis. Since the topic has already been thoroughly reviewed [3], in this chapter we emphasize the

latest development of the cobalt-catalyzed [2 + 2 + 2] cycloaddition reaction over the past 10 years.

[Scheme 1.1](#)



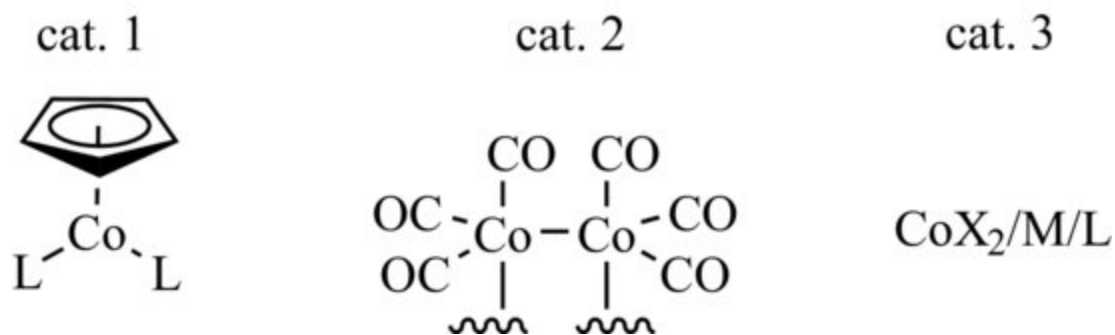
## 1.2 SYNTHESIS OF BENZENES

### 1.2.1 New Catalytic Systems

The typical cobalt complexes used to form benzenes by [2 + 2 + 2] cycloadditions can be classified into three categories ([Figure 1.1](#)). The first concerns those containing

cyclopentadienyl ligands ( $\text{CpCoL}_2$ ,  $\text{Cp}^*\text{CoL}_2$ , or other modified  $\text{Cp}'\text{CoL}_2$ ). The most common ones are  $\text{CpCo}(\text{CO})_2$ ,  $\text{CpCo}(\text{C}_2\text{H}_4)_2$ , and  $\text{CpCo}(\text{COD})$ , sometimes associated with a phosphine.  $\text{CpCoL}_2$  catalysts can be used in a variety of organic solvents, as well as supercritical  $\text{CO}_2$  or  $\text{H}_2\text{O}$  [3m]. The functionalization of the Cp (cyclopentadienyl) ring with a polar side chain allows the reaction to take place in aqueous solution [4]. As shown below, new complexes of type  $\text{CpCo}(\text{alkene})(\text{L})$  have recently been used as catalysts. The second category deals with such cobalt carbonyls as  $\text{Co}_2(\text{CO})_8$ ,  $\text{Co}_3(\text{H})(\text{CO})(\text{PMe}_3)_6$ , and  $\text{Co}_4(\text{CO})_{12}$ . A new versatile complex has also been developed. The third category contains cobalt halides of type  $\text{CoX}(\text{PR}_3)_3$  or  $\text{CoX}(\text{PR}_3)(\text{CO})_2$  ( $\text{X} = \text{Cl}, \text{Br}$ ;  $\text{R} = \text{Ph}, \text{Me}$ ), as well as  $\text{CoX}_2/\text{M}/\text{L}$  catalytic systems ( $\text{X} = \text{Cl}, \text{Br}, \text{I}$ ;  $\text{M} = \text{Mn}, \text{Zn}, \text{NaBH}_4$ , etc.;  $\text{L} = \text{phosphines}, \text{imines}, \text{etc.}$ ). These systems, based on  $\text{Co}(\text{II})$  sources, have aroused great enthusiasm in the past 10 years.

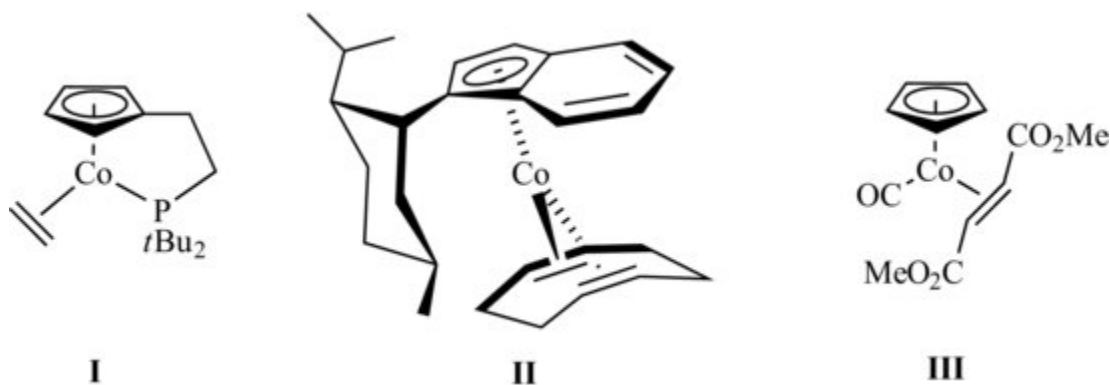
[Figure 1.1](#)



### 1.2.1.1 [CpCo] Complexes

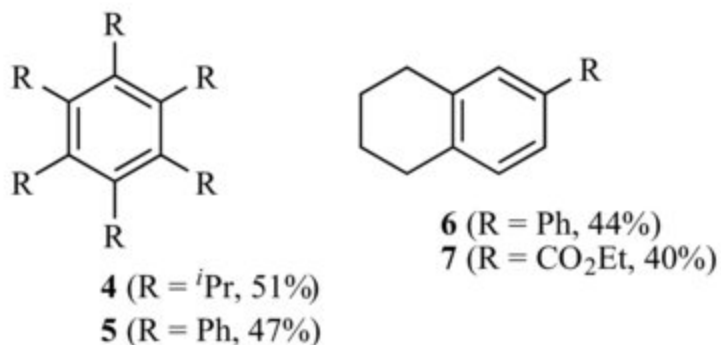
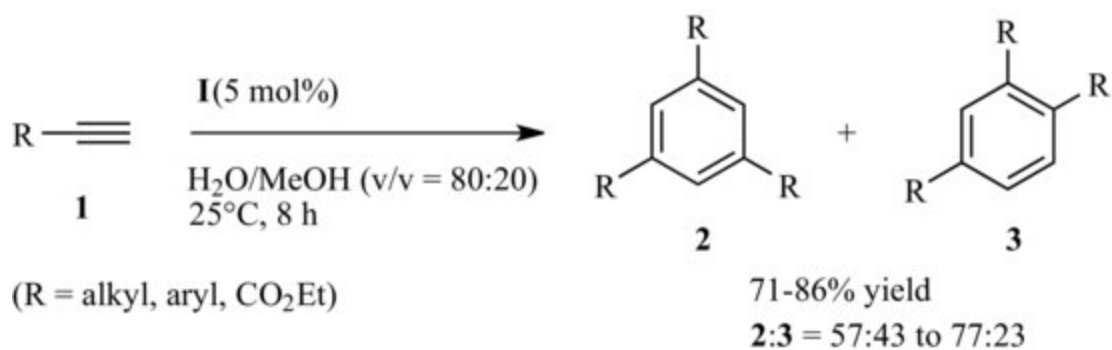
Various problems associated with the synthesis of benzenes have been circumvented recently by using precatalysts **I** to **III**, displayed in [Figure 1.2](#).

[Figure 1.2](#)



Yong and Butenschön succeeded in achieving alkyne cyclotrimerizations in an aqueous medium at room temperature using **I** [5]. While standard catalysts such as CpCo(COD) allow the formation of pyridines at room temperature in water [6], this feature has so far not been possible for benzenes, for which an elevated temperature is required [4]. Complex **I** was tested toward the cyclotrimerization of mono-substituted alkynes **1** and gave the expected regioisomeric mixture **2/3** in good yields and often good selectivities compared to reactions carried out in organic solvents ([Scheme 1.2](#)). The cyclotrimerization of the disubstituted alkynes 2,5-dimethyl-3-hexyne and diphenylacetylene to give **4** and **5**, respectively, was also reported, as well as bimolecular reactions between 1,7-octadiyne and phenylacetylene or ethyl propiolate to give **6** and **7**, respectively. Catalyst **I** could also be used to assemble pyridines (see Section 1.3.1.1).

[Scheme 1.2](#)



The [2 + 2 + 2] cycloaddition reaction can give rise to chiral compounds, especially biaryls [3q]. Control of the enantioselectivity in such transformations is of prime importance, notably because biaryls can be used as ligands in asymmetric catalysis. This topic is covered in detail in Chapter 9. Nowadays, cobalt still looks like a poor relation in this field, which is largely dominated by rhodium. Nevertheless, a report from Heller et al. shows for the first time that phosphorus-bearing axially chiral biaryls **9** can be formed by enantioselective benzene formation using the neomenthyl-indenyl cobalt complex **II** as a catalyst ([Scheme 1.3](#)) [7]. Good yields and ee values were obtained after the cycloaddition of 2 equiv of acetylene with alkynyl phosphine oxides **8**.

### [Scheme 1.3](#)