PREFACE TO VOLUME 75

The publication of Volume 75, the Diamond Anniversary, in the Organic Reactions series was a much-anticipated event. Thus, to celebrate this milestone, the Board of Editors chose to feature chapters authored by present and former members from its own ranks. The logic was impeccable; how better to guarantee the appearance of such an important volume containing chapters of the highest quality in a timely fashion. Alas, although the former objective was most certainly achieved, the latter was unfortunately not, the responsibility for which rests solely with the present author. That caveat notwithstanding, the four chapters in this volume represent the state of the art in organometallic chemistry, asymmetric catalysis, and complex molecule synthesis.

The first chapter by T. V. RajanBabu (Board of Editors, 1997–2007) describes the asymmetric hydrocyanation of alkenes and alkynes. The controlled hydrofunctionalization of carbon-carbon multiple bonds (i.e. addition of H–C and H–X where X = B, O, N, S, Si, P, Sn) is a powerful method for construction of stereodefined tetrahedral and trigonal carbon centers in organic synthesis. These transformations are highly atom economical and can provide rapid access to important building blocks for fine chemicals and pharmaceutical agents. Hydrocyanation (along with hydroformylation and hydrovinylation) represents one of the very few methods for the direct formation of carbon-carbon bonds by addition to alkenes. For this process to be successful, the catalyst must be exquisitely designed to control the regio- and stereoselectivity of the addition. In this chapter the author describes the development of glucose-derived phosphinite ligands which in conjunction with nickel(0) sources provide selective construction of branched nitriles with high enantioselectivity. The ligands are highly modular and allow for tuning of electronic and steric effects. Careful mechanistic investigations reveal the basis for the effects of ligands and the origin of enantioselectivity.

The second chapter by Huw M. L. Davies (Board of Editors, 2004–2010) and Phillip M. Pelphrey covers one of the most exciting areas of research in synthetic organic chemistry today, namely the functionalization of C–H bonds. These authors have pioneered the use of chiral rhodium complexes for the generation of metallocarbenoids from diazocarbonyl compounds for the enantioselective formation of carbon-carbon bonds by intermolecular insertion into carbon-hydrogen bonds of activated substrates (i.e. benzylic, allylic, and bearing heteroatomic groups). Although a variety of carbenoid types have been investigated, these transformations are particularly successful with captodative carbenoid precursors, i.e. those bearing both donor and acceptor groups. The chiral rhodium carbenoid complexes are prepared from readily available derivatives of L-proline or other amino acids. Of particular note is an imaginative extension of this process that involves insertion of carbenoids derived from vinylidiaoacetates into allylic C–H bonds. The resulting 1,5-diene can undergo a spontaneous Cope rearrangement to shift a double bond into conjugation with the ester and generate two new stereogenic centers. Overall, the insertion of carbenoids into C–H
bonds results in products that represent some of the most classical constructions in organic synthesis (e.g. alkylations, aldol additions, Mannich reactions, and Michael additions).

The third chapter by Wen-Tau T. Chang, Russell C. Smith, Christopher S. Regens, Aaron D. Bailey, Nathan S. Werner, and the present Editor-in-Chief (Board of Editors, 1994–2003, 2008-present) represents the first comprehensive overview of the use of organosilicon reagents in cross-coupling reactions. The importance of palladium-catalyzed cross-coupling reactions cannot be overstated as evidenced by the awarding of the 2010 Nobel Prize in Chemistry to Richard F. Heck, Ei-Ichi Negishi, and Akira Suzuki for the introduction and development of these processes. The use of organosilicon compounds for cross-coupling, pioneered by Tamejiro Hiyama, represents an important subset of these general carbon-carbon bond forming reactions. Unlike their better-known cousin, the Stille coupling of organotin compounds, which was the subject of the Golden Anniversary Volume 50 (authored by Vittorio Farina, Ventkat Krishnamurthy, and William J. Scott), the organosilicon variant is notable for the enormous variety of silicon-based moieties that can participate as donors in the reaction. This chapter details the characteristics of each organofunctional silicon grouping for the transfer of aryl, heteroaryl, alkenyl, alkynyl, and alkyl building blocks. One of the defining advantages of the silicon-based cross-coupling process is the myriad of practical methods for the introduction of organosilicon moieties, which often can be telescoped into one-pot processes for programmed carbon-carbon bond formation. Moreover, and again in contrast to the (primarily) thermally activated Stille couplings, silicon-based cross-coupling reactions generally require activators such as fluorides, alkoxides, or other Brønsted bases. These reaction parameters, along with choice of palladium sources and ligands, are evaluated in the context of preparative generality and functional group compatibility. To complement the description of the many individual organosilicon moieties, the tabular survey is organized according to starting material structure. This organization allows the reader to directly compare all of the available silicon components for a given combination of subunit structures.

The final chapter by Larry E. Overman (Board of Editors, 1981–1992, 2000–2007), Philip G. Humphreys, and Gregory S. Welmaker chronicles the development and application of a highly engineered cascade process that has transformed the synthesis of alkaloids, namely the tandem aza-Cope-Mannich reaction. In this reaction, a rapid, but thermodynamically unfavorable sigmatropic rearrangement is coupled with an exothermic capture of an iminium ion to form, with exquisite stereoselectivity, a 3-acylpyrrolidine. Through imaginative extension that involves the elaboration of the 1-amino-3-buten-2-ols, complex molecular architectures can be rapidly assembled in a predictable and stereoselective fashion. This high level of stereoselectivity is brought about by the cationic [3,3]-sigmatropic rearrangement which occurs preferentially by chair topography and the Mannich cyclization, which occurs more rapidly than stereomutation of the enol and iminium ion groups. The authors detail various methods for
construction of the key precursors (1-amino-3-buten-2-ols), the scope of substitution on the double bond, methods for generation of the initial iminium ion, and modes of stereoinduction. The prevalent occurrence of pyrrolidine rings in both alkaloids and pharmaceutical agents has led to the development and use of the aza-Cope–Mannich reaction in several complex natural product syntheses, including the first asymmetric total synthesis of (−)-strychnine. This crowning achievement serves to illustrate the power of this strategy in the most challenging of molecular settings.

It is appropriate here to acknowledge the expert assistance of the entire editorial board, and in particular Scott Rychnovsky (RajanBabu), Vittorio Farina (Davies and Denmark), and Peter Wipf (Overman), who shepherded the four chapters in this volume. The contributions of the authors, editors, and the publisher were expertly coordinated by the responsible secretary, Robert Bittman. In addition, the Organic Reactions enterprise could not maintain the quality of production without the dedicated efforts of its editorial staff, Dr. Linda S. Press and Dr. Danielle Soenen. Insofar as the essence of Organic Reactions chapters resides in the massive tables of examples, the authors’ and editorial coordinators’ painstaking efforts are highly prized.

The year 2010 witnessed the publication of no new volumes of Organic Reactions. But as in music, art, and literature, a period of tranquility is often followed by a burst of activity, and so it will be for Organic Reactions with the release of Volumes 76 and 77 already on the horizon.

SCOTT E. DENMARK
Urbana, Illinois
SPECIAL PREFACE TO VOLUME 75: ARE DIAMONDS FOREVER?

In the annals of scientific publications, the celebration of a diamond anniversary represents more than achieving the respectability of age, it is a testimony to the vitality and enduring relevance of the medium. Although the Organic Reactions series is not yet three-quarters of a century old, the appearance of the 75th volume confirms that it possesses wisdom beyond its years!

The release of Volume 75 of Organic Reactions provides an important milestone from which to evaluate the historical evolution of the series, the status of the organization that produces it, and the prospects for its future. Organic Reactions celebrated similar milestones with the publication of its 25th and 50th volumes in 1977 and 1997, respectively, but the world of scientific publication in those years was not very different from that in 1942 when the series began. How this publication will continue to be relevant in the rapidly changing landscape of the electronic age will be addressed in a later section, but for now, we indulge in a bit of nostalgic reminiscence.

The origins of the series have been described in detail by Harold Blatt in his preface, Recollections, that served to mark the silver anniversary issue of Volume 25. Similarly, Bob Joyce composed an expanded and updated version in his preface to Volume 50 entitled A Golden Anniversary. This memoir will continue that tradition by chronicling the events of the past 14 years. The astute reader will immediately recognize that it took 36 years to produce the first 25 volumes, 20 years to produce the next 25, and only 14 to produce the third score and five.

The goals of Organic Reactions have remained the same since it was founded in 1939 as a non-profit educational, research, and philanthropic organization. Those goals were clearly laid out by Roger Adams in the Preface to the Series published in every volume since 1942, and are reproduced here on page v. In view of the aforementioned changes brought about by the advent of electronic databases and search engines, I felt that a reaffirmation of these goals was warranted; therefore, on assuming the role of Editor-in-Chief, I wrote an updated Introduction to the Series (see page vi).

The Organic Reactions Family

The Elders. Whereas the goals of Organic Reactions have remained the same, the individuals entrusted with preserving the institution and its mission have changed. Professor Leo A. Paquette stepped down as Editor-in-Chief and President in 2000 and was succeeded by Professor Larry E. Overman, who passed on the honor to me in 2008. The composition of the Board of Directors has changed little since 1997. Prof. William G. Dauben stepped down in 1996 as did Prof. Paquette in 2007. Currently the Board of Directors includes Professors Robert Bittman, Scott Denmark, Andrew Kende, Larry Overman, William Roush, Amos Smith, Peter Wipf, and Dr. Jeffery Press.
MEMBERS OF THE BOARD OF DIRECTORS

ROBERT BITTMAN
SCOTT E. DENMARK
ANDREW S. KENDE
LARRY E. OVERMAN
JEFFERY B. PRESS
WILLIAM R. ROUSH
The bulk of the editing of chapters and communications with authors falls to the members of the Board of Editors. As chapters have significantly increased in length over the past 14 years, this task has required a greater investment of time to assure that the manuscripts adhere to the strict style and format that characterizes *Organic Reactions*. Those individuals who have edited chapters appearing in Volumes 1–75 appear below; the names listed in bold are current members of the Editorial Board. Those listed with an asterisk have passed away.

Roger Adams*   Jacquelyn Gervay-Hague   Heinz W. Gschwend
Homer Adkins*   Stephen Hanessian
Werner E. Bachmann*   Richard F. Heck
John E. Baldwin   Louis Hegedus
Peter Beak   Ralph F. Hirschmann*
Robert Bittman   Herbert O. House
A. H. Blatt*   Jeffrey S. Johnson
Virgil Boekelheide*   John R. Johnson*
George A. Boswell, Jr.   Robert M. Joyce*
Dale L. Boger   Robert C. Kelly
Theodore L. Cairns*   Andrew S. Kende
André B. Charette   Laura Kiessling
Engelbert Ciganek   Willy Leimgruber*
Arthur C. Cope*   Steven V. Ley
Donald J. Cram*   James A. Marshall
Dennis P. Curran   Michael J. Martinelli
David Y. Curtin   Stuart W. McCombie
Anthony W. Czarnik   Frank C. McGrew*
Samuel J. Danishefsky   Blaine C. McKusick*
William G. Dauben*   Jerrold Meinwald
Huw M. L. Davies   Scott J. Miller
Scott E. Denmark   John Montgomery
Vittorio Farina   Carl Niemann*
Louis F. Fieser*   Larry E. Overman
John Fried   Leo A. Paquette
Peter Beak
Robert Bittman   Andrew J. Phillips
A. H. Blatt*   Nicola Pohl
Virgil Boekelheide*   Gary H. Posner
George A. Boswell, Jr.   Jeffery B. Press
Dale L. Boger   Linda S. Press
Theodore L. Cairns*   T. V. RajanBabu
André B. Charette   Hans J. Reich
Engelbert Ciganek   James H. Rigby
Arthur C. Cope*   William R. Roush
Donald J. Cram*   Tomislav Rovis
Dennis P. Curran   Scott D. Rychnovsky
David Y. Curtin   Martin F. Semmelhack
Anthony W. Czarnik   Charles Sih
Samuel J. Danishefsky   Amos B. Smith, III
William G. Dauben*   Harold R. Snyder*
Huw M. L. Davies   Danielle Soenen
Scott E. Denmark   Barry M. Trost
Vittorio Farina   Milán Uskokovic
Louis F. Fieser*   Steven M. Weinreb
John Fried   Boris Weinstein*
Peter Beak
PETER WIPF
EDITORIAL BOARD MEMBERS FOR VOLUMES 51-75

PETER BEAK
ROBERT BITTMAN
DALE L. BOGER
ANDRÉ B. CHARETTE
ENGELBERT CIGANEK
DENNIS P. CURRAN
SPECIAL PREFACE TO VOLUME 75: ARE DIAMONDS FOREVER? xv

ANTHONY W. CZARNIK

HUW M. L. DAVIES

SCOTT E. DENMARK

VITTORIO FARINA

JACQUELYN GERVAY-HAGUE

LOUIS HEGEDUS
SPECIAL PREFACE TO VOLUME 75: ARE DIAMONDS FOREVER?

SCOTT J. MILLER

JOHN MONTGOMERY

LARRY E. OVERMAN

LEO A. PAQUETTE

ANDREW J. PHILLIPS

NICOLA POHL
SPECIAL PREFACE TO VOLUME 75: ARE DIAMONDS FOREVER?

JEFFERY B. PRESS

LINDA S. PRESS

T. V. RAJANBABU

JAMES H. RIGBY

WILLIAM R. ROUSH

TOMISLAV ROVIS
Organic Reactions is especially proud that Richard F. Heck, who served on the Editorial Board for 12 years and who wrote a chapter in Volume 27 (published in 1982, our most highly cited chapter) entitled “Palladium-Catalyzed Vinylation of Organic Halides,” was a recipient of the 2010 Nobel Prize in Chemistry.
Bob Bittman and Jeffery Press joined Organic Reactions in 1968 and 1983, respectively, and continue to serve as responsible secretaries shepherding alternate volumes, while Jeff provides stability and continuity (through various administrations) as Secretary-Treasurer.

Bob Joyce continued in his capacity as Editorial Coordinator, despite debilitating arthritis in his hands. In view of the increased workload associated with producing “camera ready” for larger and larger tables, Leo Paquette conscripted Dr. Linda S. Press to serve as Bob’s apprentice in 1998. Sadly, Bob passed away in 2002 (one of the few remaining Ph.D. students of Roger Adams) and Linda succeeded Bob as Editorial Coordinator. To help offset the continually increasing workload, Dr. Danielle Soenen joined as Editorial Assistant in 2005.

The Recruits. Despite all of the advances in database searching, word processing, and graphics composition, the task of writing an Organic Reactions chapter has become a greater and greater challenge. The exponential growth of the chemical literature requires the authors to abstract hundreds if not thousands of papers and distill all of that information critically into concise, preparatively useful overviews. The compilation of the tables represents the greatest investment of effort as the requirement for comprehensive coverage of the subject has not changed. Happily, a newer protocol has been introduced by our publisher, John Wiley and Sons, that will greatly facilitate the composition of the tables to avoid the tedious assembly from hundreds of ChemDraw pages. It is, therefore, to our authors who painstakingly endure rounds of critical editing, “not for the strut and trade of charms on the ivory stages,” that we owe greatest debt of gratitude for without them, we would cease to exist.

The table below reveals several interesting trends. First, the number of chapters per volume continues to decrease, although less dramatically than in the previous 25 volumes. Most notably, the demographics of our authors have changed such that the majority is now from outside the USA. This trend clearly reflects the growth in the chemical sciences around the world, and particularly in Asia.

<table>
<thead>
<tr>
<th>Volumes</th>
<th>Chapters</th>
<th>Authors</th>
<th>USA</th>
<th>Foreign</th>
<th>Academic</th>
<th>Industrial</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–25</td>
<td>135</td>
<td>203</td>
<td>181</td>
<td>22</td>
<td>136</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td>26–50</td>
<td>59</td>
<td>109</td>
<td>70</td>
<td>39</td>
<td>90</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>51–75</td>
<td>55</td>
<td>121</td>
<td>62</td>
<td>59</td>
<td>97</td>
<td>23</td>
<td>1</td>
</tr>
</tbody>
</table>

The Organic Reactions Product. From a raw statistical perspective the composition of the Organic Reactions product has changed considerably over the years and this trend has continued in Volumes 51–75. The data in the table below clearly show that chapters continue to grow in size with the attendant decrease in the number of chapters per volume. The growth is most noticeable in the length of the tables, which now average nearly 200 pages per chapter.
Indeed, three of the past 25 volumes comprise single chapters: Volume 55 (*Synthesis of Nucleosides* by H. Vorbrüggen and C. Ruh-Polenz); Volume 71 (*Ionic and Organometallic-Catalyzed Organosilane Reductions* by G. R. Larson and J. L. Fry); and Volume 73 (*Allylboration of Carbonyl Compounds* by H. Lachance and D. G. Hall). These authors deserve a special acknowledgment for undertaking such mammoth tasks. Because all three represent such important chemical transformations, the chapters have been reprinted in paperback form (with updated references to the tables) to make them available to practitioners at a considerably lower price. In addition, a paperback edition of the two chapters on *Dioxirane Oxidations* by W. Adams et al. from Volumes 61 and 69 have been combined to create the first definitive work on this important class of oxidizing reagents.

In addition to the increasing size of the chapters, the breadth of chemical transformations now covered has also considerably increased. More and more chapters focus on advances in the use of organometallic reagents and catalysts as well as the growing development of asymmetric synthetic reactions. Recent chapters have covered the implementation of biochemical processes and synthetic reactions of carbohydrates and nucleosides. Remarkably, venerable reactions such as oxidation and reduction still occupy a major research activity in modern synthetic chemistry.

Although the detailed protocol by which chapters are processed has changed, the fundamental roles of the various contributors (authors, responsible editor, reviewing editors, editorial coordinator, and responsible secretary) have not. Advances in electronic media and data transfer have facilitated the distribution of manuscripts, but writing and editing are still the rate-limiting steps. However, beginning with Volume 75, a new procedure for the compilation of the tables has been introduced by our publisher. Instead of creating “camera ready” pages of tables using individual ChemDraw files, the authors can now provide single entries, coded with their location in a given table. Wiley then compiles the tables from these entries (and tags the structures to enable electronic searching), thus obviating the tedious process of compiling and reordering that invariably plagued the earlier process. Nevertheless, both Linda Press and Danielle Soenen still examine each table entry to assure that its layout, location, and content are correct.

**Organic Reactions, Inc**

Organic Reactions, Inc. was set up as a not-for-profit, private operating foundation whose mission is “the furtherance of scientific research in organic chemistry.”
This mission has been fulfilled through a number of different philanthropic activities.

**Roger Adams Award.** In recognition of his many years of service to organic chemistry, the ACS established the Roger Adams Award to recognize and encourage outstanding contributions to research in organic chemistry defined in its broadest sense. The award consists of a medallion and a replica, a certificate, and $25,000. The recipient will deliver a lecture at the Biennial National Organic Chemistry Symposium. Since 1959, this award has been co-sponsored by Organic Syntheses, Inc., Organic Reactions, Inc., and the ACS Division of Organic Chemistry.

The list of awardees is a veritable “who’s who” of organic chemistry that includes 11 Chemistry Nobel Prize winners (in bold).

```
```

**Organic Reactions Lectureship.** Since 1988, Organic Reactions, Inc. has sponsored a biennial lecture series that brings an outstanding young scientist (under 40) from overseas to visit the United States for 2–3 weeks. The Lectureship carries a stipend to cover expenses and provides an honorarium; the lecturer is invited to visit as many of the Board of Editors’ institutions as possible. As is evident from the list below, many of these visitors have become influential leaders in the field.

```
1988 Hisashi Yamamoto  Nagoya University
1990 Manfred Reetz  University of Marburg
1992 Ian Paterson  University of Cambridge
1994 Philip Kocienski  University of Southampton
1996 Paul Knochel  University of Marburg
1999 Alois Fürstner  Max Planck Institute, Mülheim
2001 Shu Kobayashi  University of Tokyo
2003 Mark Rizzacassa  University of Melbourne
2009 Benjamin List  Max Planck Institute, Mülheim
2011 Matthew Gaunt  University of Cambridge
```

**Organic Reactions Graduate Fellowship.** The Division of Organic Chemistry annually awards fellowships to outstanding third- and fourth-year graduate students in organic chemistry. The program has awarded over 300 fellowships
since 1981. The fellowship stipend is $26,000, and the Fellows travel to the National Organic Symposium to present a poster on their work. Awardees are selected on the basis of research accomplishments. The applicants submit a short original essay as part of the competition. Organic Reactions, Inc. and John Wiley have sponsored a Graduate Fellowship since 1994.


**Organic Reactions e-MRW.** In 2006, Organic Reactions, Inc. and John Wiley and Sons launched the electronic version of the series in both Major Reference Work (e-MRW) and full database formats. The e-MRW version provides the chapters in Volumes 25-current in both HTML and PDF format with text-searching capabilities and PDF versions of the tables, whereas the database version provides full substructure-searching capability throughout the chapter. In 2010, Wiley announced that it will begin the process of converting the chapters in Volumes 1–24 to be electronically accessible as well.

To facilitate awareness and use of the e-MRW product, Organic Reactions, Inc. and John Wiley and Sons, in conjunction with the ACS Division of Organic Chemistry, provided free access to members of the Organic Division for three months in Fall 2009, including 10 free downloads of any *Organic Reactions* chapters. In addition to providing free access to the home institutions of the Board of Editors, Organic Reactions, Inc. and John Wiley and Sons also donate one year of free access to selected, top-tier institutions that have a significant presence in organic chemistry.

**Organicreactions.org.** As part of the commitment of Organic Reactions, Inc. to enhance research activities in organic chemistry and increase awareness of the series to a more and more electronically literate clientele, we have launched a dedicated website at [http://organicreactions.org](http://organicreactions.org). The website includes a Table of Contents of all of the chapters in the series organized by volume and alphabetically, complete with links to the chapters available on the Wiley website. In addition, in a joint project with Michael Evans, University of Illinois, we have created Wiki-style pages that contain condensed presentations of the content of the online *Organic Reactions* chapters. These pages are freely available to the public, but our hope, of course, is that the readers will want to access the full chapters for their characteristic in-depth and comprehensive coverage.

**Organic Reactions in the 21st Century**

Electronic search engines were already in existence long before the advent of the Internet. Although these tools provided researchers with the ability to locate
primary and secondary references, hard copy was still the only medium in which the information was available. At the end of the 20th century, scientific periodicals made the leap to the electronic medium and the marriage of searching and finding through the World Wide Web revolutionized the dissemination and capture of information in ways that are still evolving. Unfortunately, secondary reference sources (including Organic Reactions) were much slower to embrace the electronic revolution and have consequently been lost to a generation of scientists. This situation is very unfortunate because the modern students or researchers intent on informing themselves by a few keystrokes will be unaware of authoritative, critical, and comprehensive treatments of their subject matter. Instead, they are inundated by an avalanche of information and faced with the challenge of distilling that information into useful knowledge.

The Introduction to the Series (2008) clearly articulated why the need for such distilled and preparatively focused compilations of synthetically useful transformations is now even greater than in the pre-internet years. The question is not whether the content of the Organic Reactions series is needed, but rather how to inform new generations of scientists of its existence and how to make it so “user friendly” and available that it will rise above the cacophony of information overload that characterizes modern science. As described above, we have begun to take action to improve the “discoverability” of the content of Organic Reactions by mechanisms that are now the state of the art for information retrieval. We will continue to explore new and effective means of making practitioners of organic synthesis aware of this long-standing resource.

Roger Adams clearly understood that as long as organic chemists are charged with the preparation of complex target molecules for whatever end objective they may have in mind, a resource such as Organic Reactions will be invaluable to the success of their endeavors. The fact that many in the organic chemistry community continue to donate their time, effort, and intellect to this series as authors and editors is a humbling testimony to Adams’ vision. Because of their efforts and belief in the enduring value of this series, I am confident that we will celebrate Volume 100 of Organic Reactions in the not-too-distant future.

SCOTT E. DENMARK
Urbana, Illinois