



HETEROCYCLIC CHEMISTRY

A Two Day Short Course

presented by

Professor Albert Padwa, Emory University

and

Dr. William Pearson, Vice President for R&D, Berry & Associates
Adjunct Professor, University of Michigan

Learn the properties, synthesis, and uses of heterocyclic compounds.

Who Should Attend?

Chemists at all levels (B.S., M.S., Ph.D.) involved in any aspect of the design, synthesis, or manufacture of heterocyclic organic compounds will strengthen and update their background in heterocyclic chemistry. The course will also be valuable to those who have had little or no training in heterocyclic chemistry.

Why a Short Course in Heterocyclic Chemistry?

A majority of the compounds produced by nature have heterocyclic rings as part of their structures. Many heterocyclic rings are found as key components in biological systems. Significant numbers of compounds synthesized in the industrial sector each year are heterocyclic in nature. Thus, industrial organic chemists need to be aware of the major new developments in this area. However, undergraduate and graduate training experiences seldom include heterocyclic chemistry as a specific area of study. The chemist is often left to assimilate heterocyclic chemistry in a piecemeal fashion. We offer an intensive two day course on heterocyclic chemistry which is designed to benefit company chemists at all levels. Those who have not had formal training in heterocyclic chemistry will find the lectures and course materials useful in bringing their level of knowledge up to that necessary to operate effectively in the field. Those who have expertise in heterocyclic chemistry will be able to update and otherwise complement their existing knowledge, since much of the course will focus on current heterocyclic chemistry.

The course is aimed at providing chemists with practical, usable knowledge that will allow them to carry out research and development in heterocyclic chemistry. An emphasis on "how heterocyclic chemists think" is a guiding philosophy behind the course. Participants can expect to improve their ability to solve research problems, especially synthetic problems, in heterocyclic chemistry.

How Participants will Benefit

- *Will be able to make predictions about the reactivity and properties of unfamiliar heterocycles by examination of structure.
- *Knowledge of modern heterocyclic synthetic methods will be updated.
- *A manageable conceptual framework for the organization of heterocyclic synthetic methods will be acquired, based on broad chemical concepts.
- *Will be able to propose reasonable synthetic routes to unfamiliar heterocycles by applying basic disconnection approaches.
- *Will become familiar with the use of heterocyclic compounds as intermediates for organic synthesis.
- *The ability to effectively use the literature of heterocyclic chemistry will be gained.
- *An extensive set of notes and references on heterocyclic chemistry (900 pages) will be provided.
- *An extensive computer database (*ca* 100,000 references) covering heterocyclic chemistry is available for only \$500 for a site license at your location. The database is searchable on Apple Macintosh or IBM-compatible computers.

Course Materials

The participants will receive an extensive set of notes (750 pages) consisting of structural formulas and references for the lecture material as well as information not presented in the lectures. It is understood that these notes are for use within the company only.

A computer database containing 100,000 literature references in heterocyclic chemistry is available for only \$500 for a site license at your location. The database shall not be distributed outside the company.

Course Content

1. Structure, Properties, and Reactivity of Heterocycles

Using carbocyclic rings as a common point of reference, the effects of heteroatom substitution on the structure, properties, and reactivity of heterocycles will be discussed. Heterocyclic compounds will be grouped into three categories: (1) pi-Deficient heteroaromatic compounds; (2) pi-Excessive heteroaromatic compounds; (3) Nonaromatic heterocyclic compounds.

- Aim: To allow chemists to make predictions about the reactivity and properties of unfamiliar heterocycles based on structure.

2. General Aspects of Heterocyclic Ring Synthesis

Heterocyclic ring syntheses will be grouped into three broad categories: (1) Cyclization processes; (2) Concerted cycloaddition reactions; (3) Modification of existing rings. The first two categories will be emphasized to the greatest extent. General strategies for retrosynthetic analysis will be presented.

- Aim: To allow chemists to propose a reasonable synthetic approach to unfamiliar heterocycles based on general retrosynthetic concepts.

3. Specific Heterocyclic Ring Syntheses

An overview of some of the most useful modern methods for the synthesis of specific heterocycles will be presented. References to more classical methods will be provided.

- Aim: To provide the chemist with specific knowledge of heterocyclic synthetic approaches, and to reinforce the application of the general synthetic concepts learned in Section 2 above.

4. Heterocycles in Organic Synthesis

The use of heterocycles as intermediates for organic synthesis will be covered.

- Aim: To demonstrate the role of heterocyclic compounds in the broader realm of organic synthesis. This section will also further illustrate the reactivity patterns of heterocyclic compounds.

5. Asymmetric Synthesis

The growing importance of chiral, nonracemic heterocycles in medical and agricultural applications necessitates an overview of methods for the assembly of enantiomerically pure heterocycles. Heterocyclizations that introduce asymmetry will be covered.

- Aim: To provide an overview of the asymmetric synthetic methods most useful to heterocyclic chemists.

6. Retrieval of Heterocyclic Chemical Information

In addition to the extensive information on specific aspects of heterocyclic chemistry that will be provided in the notes throughout the course, a brief tour of the important sources of information in heterocyclic chemistry will also be supplied. An easy-to-use Heterocyclic Chemistry Database is available for a slight supplement which will allow rapid retrieval of leading references to all aspects of heterocyclic chemistry. The database runs on common desktop PC's, and contains over 100,000 references

- Aim: To provide the chemist with practical information on finding heterocyclic chemical information in an efficient manner.

7. Nomenclature of Heterocyclic Compounds

Brief coverage of the basics of Trivial, Hantzsch-Widman, and Replacement methods of nomenclature will be covered in handout form.

Heterocyclic Computer Database

Over 100,000 References Available

Operates using Either a Macintosh or IBM-PC Compatible Computer

Are you having difficulty locating a particular reference in the area of heterocyclic chemistry and spending valuable time in the library? Let us help you. Keyword searching using the heterocyclic database -- CHEMKEY -- will save you both time and money. Over 100,000 references dealing with the heterocyclic literature have been collected over a thirty year period from journals that organic chemists traditionally use. Particular attention has been devoted to synthetic methods, reactive intermediates, organometallic chemistry, photochemistry, stereochemistry, theory, asymmetric synthesis of heterocycles and much more. It is possible to add your own references to the search routine for more personalized searches.

Check out: <http://euch6f.chem.emory.edu/index.html>

Keyword searching offers many advantages over graphics programs such as Reaccs or Synlib. Searches simply involve typing a combination of keywords and/or authors. Unlike CAS on-line searching, the results are immediately available on your personal computer with no additional charges. You will save an enormous amount of time in locating key references in the literature of heterocyclic chemistry.

"The availability of the "key word driven" ChemKey data base has been a truly valuable source of the organic literature, particularly in reactions and synthetic methods, as well as authors. After some 10 years we have utilized the data base virtually every day to search out answers to questions dealing with literature on a functional group, properties of classes of compounds, and synthetic routes. The rich reference source (over 100,000 references) are added automatically in a timely sequence so the data base increases steadily. There is just enough information given with each hit to assess the contents of each reference in a particular search. The ability to print out an entire list of the references makes one's subsequent library visit much easier. The system is very easy to use and can be taught to students in a matter of minutes. They will then be in a position to access thousands of references dealing with virtually every question that arises in organic synthetic research. One must not confuse this facile data base with a totally complete version (Crossfire, Scifinder, etc) but the ready entry into the chemical literature cannot be overstated. The efforts by the Padwa group in assembling this data base must be gratefully acknowledged. It is hard to see how anyone would not benefit from this very affordable "poor man's version" of Scifinder or Crossfire." -- A. I. Meyers, Professor of Chemistry, Colorado State University

Features

*Ease of operation. No manual is necessary. You will be an expert in minutes.

*Data is displayed on screen and may be printed or stored on disk.

About the Instructors

Albert Padwa was born in New York City on October 3, 1937. His undergraduate years were spent at Columbia University where he earned a BA (1959). Graduate studies were continued at Columbia University and led to the award of his Ph. D. (November, 1962). Since graduation from Columbia, he was a National Science Foundation Postdoctoral Fellow at the University of Wisconsin (1962-1963). On September 1, 1963, he was appointed Assistant Professor in the Department of Chemistry at Ohio State University. In 1966 he moved to SUNY Buffalo as an Associate Professor and advanced to the rank of Professor in 1969. He moved to Emory University in August 1979 as the William P. Timmie Professor of Chemistry.

He has authored over 600 publications in such diverse areas as heterocyclic chemistry, reactive intermediates, photochemistry, small ring chemistry, radical reactions, molecular rearrangements, reaction mechanisms, molecular orbital theory and the synthesis of biochemically active drugs for treatment of diseases.

He has been a research fellow of the Alfred P. Sloan Foundation (1968-1970), a National Institute of Health Special Senior Postdoctoral Fellow (1972-1973), a NATO Senior Research Fellow (1973), a John Simon Guggenheim Memorial Fellow (1982), an Alexander von Humboldt Senior Scientist (1983), a JSPS Research Fellow (1984), and a Fulbright Hays Fellowship. He was a member of the executive committee of the Interamerican Photochemical Society and a Medalist of the Southeast American Chemical Society Section and was Chairman of the Organic Division of the American Chemical Society in 1985-1986.

He has also been a member of the Medicinal Chemistry A Study Section of the NIH, the Chairman of the Gordon Research Conference on Heterocycles, the NSF Workshop on Reactive Intermediates and a member of the Advisory Board of the Petroleum Research Fund. He has served as editor for the Marcel Dekker Organic Photochemistry series as well as for the John Wiley Dipolar Cycloaddition series. He has been a visiting Professor at the University of Lyons (France), University of Wurzburg (Germany), University of California at Berkeley, the Imperial College of Science (England) and was recently appointed the Wilmore Fellow at Melbourne University in Australia. He has been awarded the Southern Chemist prize, the Senior Award in Heterocyclic Chemistry from the International Society of Heterocyclic Chemists, and an Arthur C. Cope Scholar Award from the ACS. He has served as the President of the International Society of Heterocyclic Chemistry, a Volume Editor for Science of Synthesis (SOS), Editor for a Monograph on 1,3-Dipolar Cycloadditions-Chemistry of Heterocyclic Compounds, Volume Editor for Comprehensive Heterocyclic Chemistry III, a Member of the Editorial Board of Topics in Heterocyclic Chemistry, and is currently an Associate Editor of the Journal of Organic Chemistry.

William Pearson was born in Raleigh, North Carolina, on September 8, 1956. His undergraduate work was carried out at the University of North Carolina at Chapel Hill, where he received his B. S. degree in 1978. After obtaining his Ph. D. degree from the University of Wisconsin at Madison in 1982, he was a National Institutes of Health Fellow at Yale University from 1982-1984. He then joined the faculty at the University of Michigan as an Assistant Professor in 1984 and advanced to the rank of Professor in 1996. In 2003, he moved to Berry & Associates, a company that specializes in the synthesis of chemicals that are useful in the nucleic acids and nucleoside fields. He is currently Vice President for Research and Development, and retains a position at the University of Michigan as Adjunct Professor.

He has authored approximately 120 publications in the area of synthetic heterocyclic chemistry, and has presented invited lectures at over 110 universities, companies, and symposia. In particular, his research

group has demonstrated that 2-azaallyllithiums are excellent cycloaddition partners for the synthesis of pyrrolidine-containing target molecules. In related work, novel methods for the generation of azomethine ylides have also been developed for use in cycloaddition reactions. Another long-standing theme has been the use of azide chemistry to install nitrogen into organic molecules by cycloaddition and rearrangement reactions. At Berry & Associates, Dr. Pearson is leading a research effort in the area of nucleic acid synthesis and purification.

He was awarded a Camille and Henry Dreyfus Award for Newly Appointed Faculty in Chemistry (1984-1989), and was an Eli Lilly Grantee (1988-1989). His interest in teaching at the graduate and undergraduate levels led to an Excellence in Education Award and a Faculty Achievement Award at the University of Michigan. Most recently, he received the Katritzky Award in Heterocyclic Chemistry from the International Society of Heterocyclic Chemistry and an A. C. Cope Scholar Award from the American Chemical Society.

He has been a consultant in pharmaceutical and agricultural industries in both the research and process areas, and has served as an expert witness in the field of heterocyclic chemistry. He has been a member of the Advisory Committee for Personnel at the American Cancer Society, was Series Editor of "Advances in Heterocyclic Natural Products Synthesis," JAI Press, and has organized or co-organized several symposia and scientific meetings. He was Visiting Professor at Emory University and spent a sabbatical at Parke-Davis.

Interested?

Please contact either instructor for further information, or to arrange a short course at your company.

Professor Albert Padwa
Department of Chemistry
Emory University
1515 Dickey Drive
Atlanta, Georgia 30322

Phone: 404-727-0283
Fax: 404-727-6629
E-mail: chemap@emory.edu

Dr. William H. Pearson
Vice President for Research and Development
Berry & Associates, Inc.
2434 Bishop Circle East
Dexter, Michigan 48130

Phone: 734-426-3787
Fax: 734-426-9077
E-mail: wpearson@berryassoc.com

Heterocyclic Chemistry Short Course

Professor Albert Padwa and Dr. Will Pearson

Typical Course Outline (May be tailored to your company's needs)

Day I

- 8-8:15 a.m. Registration and Coffee
8:15-8:30 a.m. Introductory Comments and Computer Database (Padwa)
8:30-10 a.m. Session IA (Chemistry of Heteroaromatics)
10-10:15 a.m. Break
10:15-11:45 a.m. Session IB (Synthesis of Non-Aromatic Heterocycles Part 1)
11:45-1 p.m. Lunch
1-2:30 p.m. Session IIA (Heterocycles as Vehicles for Organic Synthesis)
2:30-2:45 p.m. Break
2:45-4:15 p.m. Session IIB (Synthesis of Non-Aromatic Heterocycles Part 2)

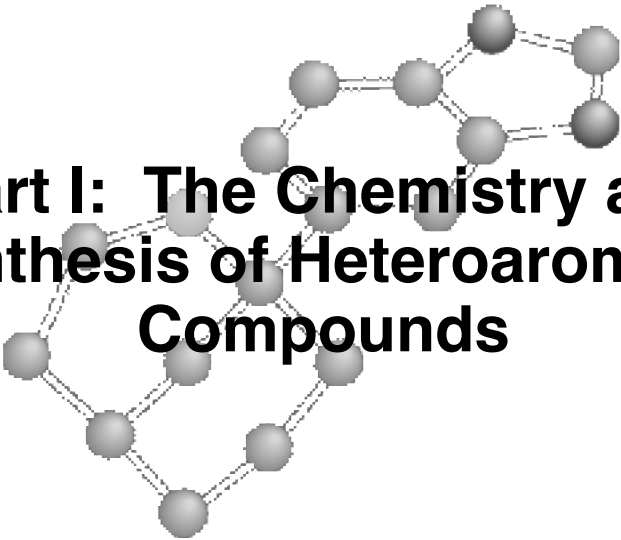
Day II

- 8-8:30 a.m. Registration and Coffee
8:30-10 a.m. Session IIIA (Cycloaddition and Cyclization Processes)
10-10:15 a.m. Break
10:15-11:45 a.m. Session IIIB (Synthesis of Non-Aromatic Heterocycles: Part 3)
11:45-1 p.m. Lunch
1-2:30 p.m. Session IVA (Reactive Intermediates in Heterocyclic Chemistry)
2:30-2:45 p.m. Break
2:45-4:15 p.m. Session IVB (Synthesis of Non-Aromatic Heterocycles: Part 3)

PART ONE OF TWO

HETEROCYCLIC CHEMISTRY

A Short Course



Part I: The Chemistry and Synthesis of Heteroaromatic Compounds

Albert Padwa

*Professor of Chemistry
Emory University
Atlanta, Georgia*

Heterocyclic Chemistry Short Course - Part 1

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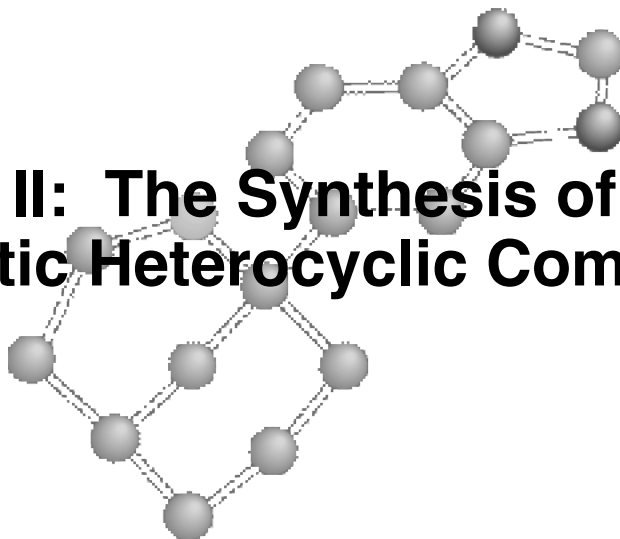
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PART TWO OF TWO

HETEROCYCLIC CHEMISTRY

A Short Course

Part II: The Synthesis of Non-Aromatic Heterocyclic Compounds



William H. Pearson

*Adjunct Professor
University of Michigan
&*

Vice President for R&D, Berry & Associates, Inc.

wpearson@berryassoc.com

Heterocyclic Chemistry Short Course - Part 2

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