# Studies in Natural Products Chemistry

# Volume 14

## Stereoselective Synthesis (Part I)

Edited by

Atta-ur-Rahman
*H.E.J. Research Institute of Chemistry,*
*University of Karachi, Karachi 75270, Pakistan*

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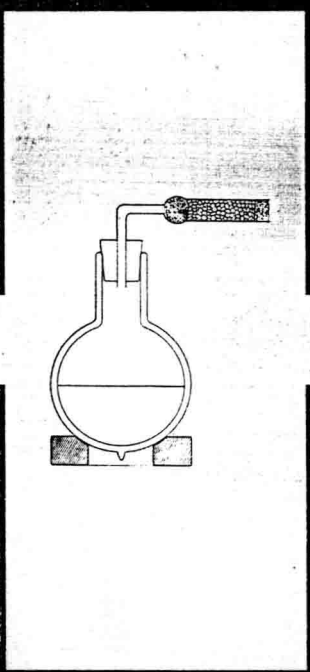
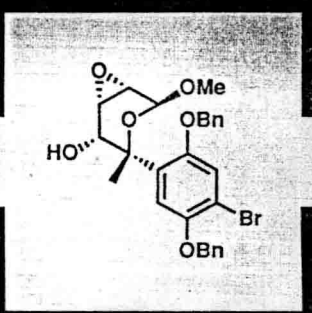
Atta-ur-Rahman/Editor



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Vol. 1 Stereoselective Synthesis (Part A)
Vol. 2 Structure Elucidation (Part A)
Vol. 3 Stereoselective Synthesis (Part B)
Vol. 4 Stereoselective Synthesis (Part C)
Vol. 5 Structure Elucidation (Part B)
Vol. 6 Stereoselective Synthesis (Part D)
Vol. 7 Structure and Chemistry (Part A)
Vol. 8 Stereoselective Synthesis (Part E)
Vol. 9 Structure and Chemistry (Part B)
Vol.10 Stereoselective Synthesis (Part F)
Vol.11 Stereoselective Synthesis (Part G)
Vol.12 Stereoselective Synthesis (Part H)
Vol.13 Bioactive Natural Products (Part A)
Vol.14 Stereoselective Synthesis (Part I)

# FOREWORD

Natural products play an important role in contemporary chemical research. The diversity of the structures of compounds found in the plant and animal kingdom, their pharmacological activity, and the fact that they often occur only in minute amounts provide a major challenge to organic chemists. Nowadays, as in the past, structure elucidation, biosynthetic pathways and total synthesis are areas of active research, greatly aided by modern separation and spectroscopic techniques. The key role of stereo-directed synthesis in natural product chemistry is clearly evident in this book and can be considered a *signum temporis*. Indeed, the last decade has witnessed enormous progress in asymmetric synthesis. Optically pure compounds are becoming of increasing importance as drugs and new materials. However, recent achievements, although impressive, must be seen in the perspective of Nature performing multistep syntheses under very mild conditions in aqueous solutions in very high yields. Clearly, there is much work to be done by organic chemists to improve current methodologies before our synthetic procedures can be considered to be competitive.

The present volume of the well established series edited by Professor Atta-ur-Rahman covers a broad range of natural products focusing on the synthesis of the following groups of compounds: antibiotics and anticancer agents - anthracyclines, tetramic acid, taxodione, vinblastine and vincristine. The anthracyclines are among the compounds with the largest share of the anticancer drug market, while vinblastine and vincristine are potent for the treatment of Hodgkin's disease and acute leukemia in children.

The stereocontrolled synthesis of polysaccharides, which is an important problem in carbohydrate chemistry, is addressed in a chapter covering the latest developments in this fascinating area. The synthesis of bioactive carbohydrates 3- and 4-deoxy-hexoses is presented in another article involving this field. Current methodology of asymmetric synthesis taking advantage of chiral synthons, templates and auxiliaries is reflected throughout the book and particularly in the applications of levoglucosenone, unsaturated nitro compounds, chiral pyrrolidines and piperidines, sulfoxides and acetals.

Terpenes are represented by chapters on the chemistry of thujone, eudesmenols, hydroazulene sesquiterpenes and the above-mentioned taxodione. Oxidation of the related azulenic hydrocarbons is also discussed. The chapter on thujone reveals interesting possibilities for the utilization of waste foliage from "Western red cedar". The foliage, a rich source of thujone, is an environmental pollutant at present.

Biomimetic and synthetic studies on benzo[C]-phenantridine, lupine and

indole alkaloids are described. The Norrish Type II photocyclization is applied as a versatile tool for the synthesis of heterocycles. Cationic cyclopent-annelation is shown to be a convenient method for rapid assembly of substituted alkylidene cyclopentenediones. Finally, recent progress in the synthesis of branched oligoribonucleotides is presented.

The diverse natural product chemistry presented in this volume will no doubt be of interest to the synthetic organic community. For myself, it is a personal pleasure to see borane reagents utilized in the majority of chapters. Fortunately, the results of my research on boron hydrides, which started as a war project in the early forties, turned out to be exceptionally fruitful in applications for the synthesis of pharmaceuticals, natural products and the development of environmentally safe processes.

Herbert C. Brown
Purdue University

# PREFACE

The synthesis of natural products continues to offer new challenges for fertile minds. The same molecule may be mentally dissected in a number of quite different and highly personalized ways by different synthetic chemists, leading to a variety of different synthetic approaches to it. It is this difference of planning and approach that stamps each synthesis with the characteristic ingenuity of the mind of its propounder.

The present volume, the 14th in this series, should offer much to satisfy many organic chemists. It contains discourses on the stereoselective synthesis of the anticancer anthracycline antibiotics, tetramic acid antibiotics, 3-and 4-deoxyhexoses, polysaccharides, levoglucosenone as precursor to natural products, synthesis of oligoribonucleotides, oxidation of guaiazulene, synthesis of hydroazulene sesquiterpenes and thujone as the starting point for the synthesis of natural products. The synthesis of eudesmenols, asymmetric synthesis using chiral acetals and chiral sulfoxide auxiliary and the asymmetric construction of versatile chiral precursors is presented. Chapters on cyclopentannelation reactions, chiral construction of quaternary carbons, organic synthesis involving hydrogen abstraction reactions, synthesis of taxodione, indole alkaloids, lupine and nitraria alkaloids, and benzo [c] phenanthridine alkaloids should also prove to be of much interest to the readers. The last chapter describes the major synthetic achievements during the last three decades in the synthesis of the binary anti-tumor alkaloids, vinblastine and vincristine. It is hoped that the present volume will be received with the same warmth and appreciation as the previous ones of this series.

I wish to express my thanks to Miss Anis Fatima, Miss Farzana Akhtar and Mr. Ejaz Ahmed Soofi for their assistance in index preparation, Mr. Waseem Ahmed for the typing work and Mr. Mahmood Alam for secretarial help.

August 1993

**Atta-ur-Rahman,** *Editor*

## CONTRIBUTORS


| | |
|---|---|
| Atta-ur-Rahman | H.E.J. Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan. |
| Ajoy Kumar Banerjee | Ministerio de Sanidad y Asistencia Social, Instituto Venezolano de Investigaciones Cientificas (I.V.I.C), Apartado 21827, Caracas 1020A-Venezuela. |
| Maria Celia Carrasco | Ministerio de Sanidad y Asistencia Social, Instituto Venezolano de Investigaciones Cientificas (I.V.I.C), Apartado 21827, Caracas 1020 A-Venezuela. |
| Daniela Fattori | Section de Chimie de l'Universite de Lausanne, 2, rue de la Barre, CH 1005 Lausanne, Switzerland. |
| Kaoru Fuji | Institute for Chemical Research Kyoto University, UJI, Kyoto-Fu 611, Japan. |
| Hiromichi Fujioka | Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita Osaka 565, Japan. |
| Ae. De Groot | Department of Organic Chemistry, Wageningen Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands. |
| Miyoji Hanaoka | Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-Machi, Kanazawa 920, Japan. |
| Yoshiro Hirai | Faculty of Science, Toyama University, 3190-Gofuku, Toyama 930, Japan. |
| Takeshi Imanishi | Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita Osaka, Japan. |
| Zahida Iqbal | H.E.J. Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan. |
| Chuzo Iwata | Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita Osaka, Japan. |

| | |
|---|---|
| Louis Henri Dieudonne Jenniskens | Department of Organic Chemistry, Wageningen Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands. |
| Ronald Peter Wilhelmus Kesselmans | Department of Organic Chemistry, Wageningen Agricultural University, Dreijenplein 8, 6703 HB Wageningen, The Netherlands. |
| Yasuyuki Kita | Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita Osaka 565, Japan. |
| Nikolay K. Kochetkov | N.D. Zelinsky Institute of Organic Chemistry, Academy of Sciences of the U.S.S.R., Moscow B 334, Leninsky prospect 47, U.S.S.R. |
| Gerrit-Jan Koomen | Department of Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands. |
| George A. Kraus | Department of Chemistry, Iowa State University, Gilman Hall, Ames, Iowa 50011-3111, U.S.A. |
| James P. Kutney | Department of Chemistry, The University of British Columbia, 2036 Main Mall, Vancouver, B.C. Canada V6T 1Z1. |
| Mauri Lounasmaa | Laboratory for Organic and Bioorganic Chemistry, Technical University of Helsinki, SF-02150 Espoo, Finland. |
| Yoshiharu Matsubara | Department of Chemistry, Faculty of Science, Okayama University, Tsushima, Okayama 700, Japan. |
| Fuyuhiko Matsuda | Department of Chemistry, Faculty of Science, Hokkaido University Sapporo 060, Japan. |
| Takefumi Momose | Faculty of Science, Toyama University, 3190 Gofuku, Toyama 930, Japan. |
| Chisato Mukai | Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-Machi, Kanazawa 920, Japan. |
| Habib Nasir | H.E.J. Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan. |

| | |
|---|---|
| Tetsuo Nozoe | Department of Chemistry, Faculty of Science, Okayama University, Tsushima, Okayama 700, Japan. |
| Mark D. Schwinden | Department of Chemistry, Iowa State University, Gilman Hall, Ames, Iowa 50011-3111, U.S.A. |
| Mitsuo Sekine | Department of Life Science, Tokyo Institute of Technology Nagatsuta, Midoriku, Yokohama 227, Japan. |
| Stephen J. Shimshock | Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742, U.S.A. |
| Philip De Shong | Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742, U.S.A. |
| Shiro Terashima | Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060, Japan. |
| Marcus A. Tius | Department of Chemistry, University of Hawaii at Manoa 2545, The Mall. Honolulu, Hawaii 96822. |
| Pierre Vogel | Section de Chimie de 1' Universite de Lausanne, 2, rue de la Barre, CH 1005 Lausanne, Switzerland. |
| Martin J. Wanner | Department of Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands. |
| Desmond M.S. Wheeler | Department of Chemistry, University of Nebraska-Lincoln, Hamilton Hall, Lincoln, NE 68588-0304, U.S.A. |
| Margaret Mary Wheeler | Department of Chemistry, University of Nebraska Lincoln, Hamilton Hall, Lincoln, NE 68588-0304, U.S.A. |
| Joannes Bernardus Pieter Antonius Wijnberg | Department of Organic Chemistry, Wageningen Agricultural University, Dreijenplein 8, 6703 HB, Wageningen, The Netherlands. |
| Zbigniew J. Witczak | School of Pharmacy, Box U-92, Room R-103, University of Connecticut 372 Fairfield Road Storrs, CT 06268, U.S.A. |

Hiroshi Yamamoto — Department of Chemistry, Faculty of Science, Okayama University Tsushima, Okayama 700, Japan.

## CONTENTS

# Stereoselective Synthesis