

Studies in Natural Products Chemistry

Volume 14

Stereoselective Synthesis (Part I)

Edited by

Atta-ur-Rahman

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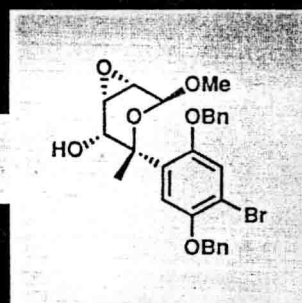
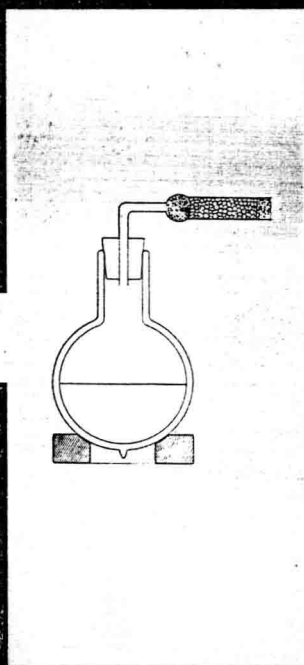
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Atta-ur-Rahman/Editor



Volume 14

Stereoselective Synthesis (Part I)

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**Volume 14
Stereoselective Synthesis (Part I)**

Studies in Natural Products Chemistry
edited by Atta-ur-Rahman

- Vol. 1 Stereoselective Synthesis (Part A)
- Vol. 2 Structure Elucidation (Part A)
- Vol. 3 Stereoselective Synthesis (Part B)
- Vol. 4 Stereoselective Synthesis (Part C)
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- 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 Attar-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-annulation 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 cyclopentannulation 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

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Stereoselective Synthesis

