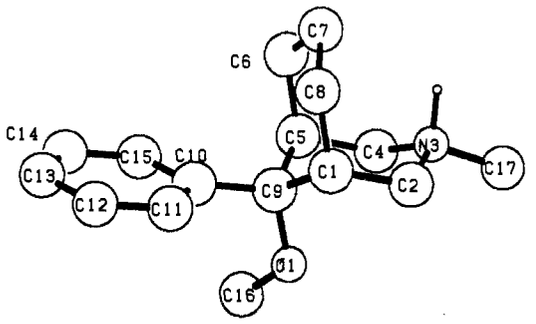

Figure 6. The more morphine-like of the two mirror image conformers that are possible for β-azabicyclane.[7]

morphine-like conformer of (+)-phenylmorphan, may contribute to the agonism of the (−)-antipode. However, by putting methyl groups in the 4- or 9-positions, the resultant compounds become conformationally homogeneous (unpublished results). Especially interesting would be the not yet synthesized β-4-methyl compounds since calculation predicts that they have the same conformational preferences as the parent compounds.

One would also like to compare the phenylmorphans to the structurally related β-azabicyclane[7] (Figure 6), a phenyl-equatorial opiate whose phenolic derivative has 6 times the affinity of morphine for opiate receptors. There appear to be some significant conformational differences between the two. β-Azabicyclane is a very sterically hindered molecule with a very high barrier (16 kcal/mol) to rotation of the phenyl ring. Of the two mirror image orientations of the phenyl ring that are possible, the more morphine-like one has a phenyl ring that differs some 60° from that of morphine though it would still be in the same quadrant. In addition, it would require some 9 kcal/mol for this molecule to achieve a morphine-like phenyl orientation. In contrast, the barrier for phenyl rotation in phenylmorphan is only 4 kcal/mol. Also, while the most morphine-like conformer differs by about 40° from the morphine-like orientation, only about 1 kcal/mol would be required to achieve that conformation (Figure 3).

In summary, there appear to be two distinct phenyl orientations that are associated with different pharmacological profiles for opiates. Compounds in which the preferred phenyl orientation is in the same quadrant as morphine, such as the (+)-antipode of phenylmorphan, appear to be typical morphine-like opiates. In contrast, compounds like β-prodine and (−)-phenylmorphan in which the preferred phenyl orientation is in the opposite quadrant have been identified as being atypical and probably interact with either different receptors as has been suggested for (−)-phenylmorphan or bind to a different portion of the μ-receptor as has been suggested for α-3-allylprodine.

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Registry No. (+)-Phenylmorphan, 91190-14-6; (−)-phenylmorphan, 91190-15-7.

Book Reviews

Serono Symposia Publications from Raven Press. Volume 5. Functional Radionuclide Imaging of the Brain. Edited by Philippe L. Magistretti. Raven Press, New York, 1983. 384 pp. 16 × 24 cm. ISBN 0-89004-962-9 $59.00.

Traditional brain imaging was based on visualization of brain areas associated with breakdown of the blood–brain barrier and presented a static image. The advent of single photon and positron tomography in the last few years, new instrumentation, and new radiolabeled agents introduced valuable techniques for looking at brain function by following the kinetics of radiopharmaceuticals that penetrate the undamaged BBB in relationship to blood flow or agents that are designed to reflect changes in the metabolic feature of brain tissue.

The editors of this book assembled reviews on the new instrumentation and discussions of the old and new techniques used today in brain research in nuclear medicine. As such the editors provide a book that is mostly directed toward an audience of physicians, scientists that require more basic scientific or background information. The book also bridges the information between scientists and physicians who are interested in new methods applied in brain investigations. The book is combined of review reports of authors that contributed to the different areas of investigation. The papers are summaries of the authors' experience in brain imaging.

The book is divided into four sections, starting with an independent and relevant brief preface discussion by Oldendorf on the BBB phenomenom. The first section reviews mainly traditional brain imaging with polar agents, mostly $^{99m}TcO_4^-$, and the discussions summarize brain imaging in cerebrovascular disorders, changes in cerebral blood flow, and changes in the BBB permeability of brain tumors. The second section is combined from reviews on the use of Xe-133 as an indicator of cerebral blood flow. The discussions review the limitations and accuracy of the techniques of the clearance measurements. Selected studies using these methods in patient care are described in ischemia, stroke, and head injury. The use of the technique for the evaluation of CBF in dementia and neuropsychiatry are also reported. Section three is a summary of the state-of-the-art SPECT techniques used for performing noninvasive in vivo measurements of CBF using different radiopharmaceuticals. A special emphasis is being put on the use of iodoamphetamine and HIPDM as lipophilic agents that penetrate the brain in relation to blood flow and have the advantage of being retained in the brain or have a slow washout from brain, therefore allowing collection of high-quality images representing flow. A preliminary study with this agent in epilepsy is reported.

Section four is a contribution from centers that have positron tomography instrumentation. The special strength of the technique in elucidating physiological parameters on a regional basis are demonstrated in the many investigations of CBF and metabolism using simple labels such as O-15-labeled CO, CO_2, H_2O, and O_2 or more complex metabolic substrates such as F-18-labeled fluordeoxyglucose or C-11-labeled methionine. The examples reviewed are cases in stroke, degenerative diseases, epilepsy, ischemia, pathologic aging, dementia, and brain tumors. A preliminary study using ligand–receptor interaction as a concept for investigating brain disorders associated with dopaminergic activity is reported.

The book concludes with a chapter by DeLand reviewing the new progress in cysternography and their clinical significance.

The book appears to fulfill the editors' goal reviewing the current status of functional brain imaging with radionuclides by

combining works from groups that use these techniques in their investigations. In general, the book also envisions some aspects of future direction in brain research by including work that is mostly in an investigative phase.

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Protein Synthesis. Translational and Post-Translational Events. Edited by Abraham K. Abraham, Thor S. Eikhom, and Ian F. Pryme. The Humana Press, Clifton, 1984. xvii + 477 pp. 15.5 × 23.5 cm. ISBN 0-89603-060-1. $59.50.

This book is a collection of presentations made at the 13th Linderstrøm-Lang Conference held at Godøysund, Norway, June 14–18, 1983. From this volume the reader gains a perspective of the state-of-the-art with respect to protein biosynthesis and related topics, as well as an indication of the current directions of many of the prominent research groups in this field. The articles are organized into six sections: Initiation of Protein Synthesis, Protein Synthesis on Endoplasmic Reticulum, Translational Fidelity, Intracellular Protein Transport, Protein Glycosylation, and Protein Phosphorylation. The individual articles provide an introductory background to the topic, a clear description of experimental details, and sufficient references. A concise summary is presented at the end of each section.

There are many fascinating aspects to protein biosynthesis. The article by Dobberstein, Lipp, Lauer, and Singer, for example, documents the "Biosynthesis and Intracellular Transport of Ia Antigens". In the case of this histocompatibility antigen, three different gene products, the variant α and β chains and the invariant Ii chain, are synthesized on the ribosome. During biosynthesis they are inserted through the membrane of the endoplasmic reticulum via a mechanism involving the signal recognition particle and the docking protein. Interestingly, the Ii chain is in the opposite orientation to the α and β chains, which protrude into the lumen with their amino termini. The ternary complex is transported to the Golgi apparatus where the carbohydrate side chains are modified. The Ii chain then dissociates from the complex and is rapidly degraded, while the remaining dimer becomes expressed on the cell surface.

It should be noted that this volume is not a textbook on protein biosynthesis. There is some overlap between certain articles, and there are many relevant topics that are not covered. However, the articles are well-written, and only a modest knowledge of protein biochemistry is required to fully understand the contents. In summary, this book provides a basic education on key aspects of protein biosynthesis, while it preserves the excitement of recent research results from leading laboratories.

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The High Nitrogen Compounds. By Frederic R. Benson. Wiley, New York, 1984. viii + 679 pp. 16.5 × 24 cm. ISBN 0-471-02652-2. $125.00.

The content of this book is unfortunately not immediately clear from the title. The work concerns acyclic and cyclic compounds with three or more contiguous nitrogen atoms. The term "high nitrogen compound" was encountered by the author during research on such substances at the Picatinny Arsenal during World War II: it will be appreciated that a good number of the compounds described are thermally unstable or explosive in nature.

The text lays a considerable emphasis on the structure, physical properties, and uses of the compounds discussed: only the last third of the book deals with the synthesis and reactions of the polynitrogen systems.

The first major chapter, occupying one third of the book, concerns existence, structure, and thermal stability, commencing with compounds containing three sequential nitrogens linked either in an acyclic chain, or all within a ring, or in an acyclic-cyclic manner, and continues up to examples with an acyclic-cyclic 10-nitrogen sequence. This style of classification overrides the conventional style in the sense that, for example, all 1,2,3-triazoles are not discussed together, *N*-amino-1,2,3-triazoles appearing under the section on acyclic-cyclic four-nitrogen chains with one exocyclic nitrogen.

A chapter concerning the physical and physical-chemical properties of the polynitrogen compounds provides representative data under sections covering molecular dimensions, thermochemical properties, dipole moments, spectra including nitrogen NMR, acid–base properties, and explosive properties.

An interesting chapter on the nonbiological uses of the compounds is followed by one on the biological properties. This discusses toxicity studies and the relatively limited pharmaceutical applications of compounds containing three or more linked nitrogens: for example, several modified cephalosporin antibiotics have a tetrazole-containing side chain, and the triazenoimidazole, dacarbazine, is used as an antineoplastic agent.

The chapter on reactions deals only with those of the nitrogen chain and not reactions at other sites in the molecule. First considered are the responses of the chains to alkylation, arylation, and acylation. This section is 59 pages in length with no subheadings, which makes for some difficulty in locating information sought. Although shorter, the same is the case for further sections concerning reactions with electrophiles other than those forming a C–N bond, with nucleophiles, and oxidation and reduction processes. The final chapter concerns the formation of nitrogen–nitrogen bonds and cyclizations with intact nitrogen chains.

The work is well produced with very few errors and is well referenced although with no author index. It is a commendable achievement to have brought together discussion of such a wide range of compounds into one text.

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Isopentenoids in Plants—Biochemistry and Function. Edited by W. D. Nes, G. Fuller, and L.-S. Tsai. Marcel Dekker, New York and Basel, 1984. xiii + 596 pp. 16 × 23.5 cm. ISBN 0-8247-1909-3. $99.75.

The isopentenoids of plants have been the subject of research ever since the beginning of natural products chemistry. This book, which embodies the Proceedings of a Symposium on the Biochemistry and Function of Isopentenoids in Plants held at the USDA Western Regional Research Center in 1982, is broadly indicative of the current interest in the biological function and natural roles of isopentenoids.

Modern separation techniques have enabled investigators to analyze more quickly and precisely than ever before the complex mixtures of related isopentenoids occurring in many plants. Instrumental advances have speeded up the determination of structures, and a good understanding is being developed of biosynthesis, especially among some chemical families. This book touches upon the function of isopentenoids as plant hormones, as insect juvenile hormones, as chemotaxonomic markers and as mammalian teratogens, and there is pervasive evidence throughout the chapters of the fact that these compounds all have a physiological or ecological role to play in the life of the organisms that give rise to them.

The monoterpenoids, sesquiterpenoids, (especially lactones), diterpenoids (especially gibberellins), triterpenoids, and phytosterols are the main compounds of interest, and there are notable chapters on steroidal alkaloids. This book will serve as an admirable point of departure for students beginning work on any aspect of the chemistry, biochemistry, or function of these compounds, as well as being useful to experienced investigators in the field.

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