3,5,3′,5′-tetrasubstituted compound has resulted in enhanced activity.[8] Since 3,5,3′-trimethyl-L-thyronine (L-Me_3) could therefore be expected to be more active than L-Me_4, this trisubstituted analog was prepared by the general method described previously,[7] and L-Me_4 and L-Me_3 were tested in the rat for thyroxine-like activity.

N-Acetyl-3,5-dinitro-4-(4-methoxy-3-methylphenoxy)-L-phenylalanine ethyl ester [mp 122–123°; $[\alpha]^{23}D$ −52.5° (*c* 2.0, dioxane); *Anal.* ($C_{21}H_{23}N_3O_9$) C, H] was converted to the 3,5-diiodo derivative [mp 121–122°; $[\alpha]^{24}D$ +49.2° (*c* 1.8, dioxane); *Anal.* ($C_{21}H_{23}I_2NO_5$) C, H] which was then allowed to react with $Cu_2(CN)_2$ to form the 3,5-dicyano compound [mp 162–163°; $[\alpha]^{23}D$ +57.6° (*c* 2.0, $CHCl_3$); *Anal.* ($C_{23}H_{23}N_3O_5$) N]. Catalytic hydrogenation at 175° in *p*-cymene produced the protected 3,5,3′-trimethyl derivative [mp 139–140°; $[\alpha]^{23}D$ +19.0° (*c* 2.0, EtOH); *Anal.* ($C_{23}H_{29}NO_5$) C, H] which was hydrolyzed by HI in AcOH to yield 3,5,3′-trimethyl-L-thyronine [mp 210–212°; $[\alpha]^{24}D$ +11.6° (*c* 1.9, 0.1 *N* HCl in 50% EtOH); *Anal.* ($C_{18}H_{21}NO_4$) C, H; chemical ionization mass spectrum $[M-H]^+$ 316; glc,[9] single peak; tlc (*i*-PrOH–concentrated NH_4OH, 4:1) single ninhydrin-positive spot, R_f 0.31].

Since iodine-containing intermediates were used in the synthesis, sensitive analytical methods were applied to ensure the absence of trace amounts of iodinated impurities in the test compounds. Unit resolution chemical ionization mass spectroscopy of L-Me_4, of L-Me_3, and of the intermediate *N*-acetyl-3,5-dimethyl-4-(4-methoxy-3-methylphenoxy)-L-phenylalanine ethyl ester showed no 3-iodo or 3,5-diiodo compounds to be present, under conditions which would have detected less than 0.1%. High-resolution chemical ionization mass spectra of the minor peaks of mass greater than those of the L-Me_3 and L-Me_4 molecular ions showed that none of these could contain iodine.

In the rat antigoiter assay,[10] L-Me_3 produced complete reversal of thiouracil-induced goiter. Its activity was estimated at 2% that of L-thyroxine (L-T_4). In the same assay system at a molar dose ratio of L-Me_4/L-T_4 equals 100/1, L-Me_4 showed no thyroxine-like activity. This antigoitrogenic activity of L-Me_3 represents the first published report of thyroid hormone activity for a compound which contains no halogen.†

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†At the Sept 21, 1972, Meeting of the American Thyroid Association, Chicago, Ill., J. A. Pittman, R. J. Beschi, Paul Block, Jr., and R. H. Lindsay reported that L-Me_4 showed approximately 1–5% T_4-like activity in O_2 consumption and heart-rate assays on thyroidectomized rats.

Book Reviews

Magnetic Resonances in Biological Research. Edited by Cafiero Franconi, with 94 other contributors. Gordon and Breach, New York, N. Y. 1971. xii + 408 p. 15.5 × 23.5 cm. $24.50.

The book is a compilation of 38 papers given at the Third International Conference on Magnetic Resonances in Biological Research, held at S. Margherita of Cagliari, Italy, in 1969. A diverse range of techniques is dealt with, including high-resolution proton magnetic resonance and magnetic resonance studies with ^2H, ^{13}C, ^{17}O, ^{25}Mg, and ^{59}Co, epr, endor, hfs–zero-field magnetic resonance, and Mössbauer spectroscopy. A partial list of the topics covered includes curve-fitting procedures for the study of binding of small molecules to multi-subunit protein, epr and Mössbauer spectroscopy on several iron-containing proteins, epr studies on copper-containing proteins, vitamin B_{12}, and a variety of organic radicals, endor studies on flavoproteins, and nmr studies on proteins and small biological molecules. For the researcher interested in recent advances in a variety of fields, this volume should prove useful.

The first two papers in the volume do not deal with any type of magnetic resonance but instead treat the problems of the interaction of proteins with small molecules, conformational changes, and the forces involved in determining stable conformations. Since many of the properties being probed by the magnetic resonance techniques involve conformational changes of proteins and ligand–protein interactions, these papers should be a useful aid in the interpretation of magnetic resonance data.

Most researchers in biologically related areas are probably not aware of the variety of magnetic resonance techniques that can be used to approach biological problems. This volume presents a wide spectrum to choose from and should be helpful in the development of new techniques.

Although the range of techniques and applications is large, some important areas have been omitted. For example, the use of nitroxide spin labels as probes of membrane structure has not been included nor has the method for the determination of atomic scale distances using the distance dependence of the effect of paramagnetic species in relaxing nuclei.

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Seven-Membered Heterocyclic Compounds Containing Oxygen and Sulfur. Edited by Andre Rosowsky. Heterocyclic Compounds. Vol. 26. Wiley-Interscience, New York, N. Y. 1972. xxvii + 949 pp. 23 × 16 cm. $75.00.

This volume represents the twenty-sixth in the Chemistry of Heterocyclic Compounds monograph series and appears to be the definitive work in its field. The book is very well organized into a format which facilitates its easy use as a reference text, yet is gen-

erally quite well written and easily understood, making it a pleasure to read. The liberal use of illustrations and reaction schemes certainly contributes to its overall quality.

Subjects which are covered include the detailed chemistry of the monocyclic and polycyclic oxepins and reduced oxepins, as well as the condensed oxepins (benzoxepins). A separate chapter is devoted exclusively to the dioxepins and trioxepins. Extensive coverage is also afforded the naturally occurring oxepinoid systems, as evidenced by separate chapters dealing with terpenes (mainly ϵ-lactones and ϵ-lactols), steroids (further divided into sections according to rings A, B, and C oxepins), carbohydrates (1,6-anhydrohexoses and 2,7-anhydroheptuloses), and alkaloids (mainly the Strychnine and Cularine groups). The less common seven-membered sulfur heterocycles are treated in two chapters, the first concerning the monocyclic compounds containing one, two, three, and four or more sulfur atoms and the second chapter considering the condensed thiepins and bridged systems containing sulfur.

Each major topic is treated clearly and systematically, beginning with a review of the nomenclature and physical properties of each class of compounds, followed by a treatment of the methods employed in the literature for the synthesis of the parent compound and derivatives. The reported reactions and transformations of each compound are then discussed in detail. Concluding each chapter are comprehensive summary tables containing published physical constants and literature references to the compounds discussed. The literature is surveyed in detail, generally through 1969, with some references included from 1970.

This work covers its chosen field extremely well and in great detail and might alternatively have been titled "Everything You Always Wanted to Know About Oxepins and Thiepins but Didn't Know Whom to Ask." It has broad appeal to both organic and medicinal chemists and, to a lesser degree, even theoretical chemists. While writing primarily from an organic chemical point of view, the editor and coauthors have made every effort to include references to the interesting medicinal effects of many of the compounds. They also have not hesitated to consider interesting theoretical aspects where appropriate, such as valence tautomerism in the oxepin system. These facts, in addition to the book's applicability to the field of natural products mentioned above, clearly justify its existence as a reference text, despite the rather high price.

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Biochemical Applications of Mass Spectrometry. Edited by George R. Waller, with more than 65 contributions. Wiley-Interscience, New York, N. Y. 1972. xiv + 872 pp. $49.95.

During the past 15 years the use of mass spectrometry in biochemistry and other biomedical areas has emerged as a most powerful technique in the identification and structure elucidation of biologically active compounds. With this growth has come the need for a comprehensive source which will enable the interested scientist to acquaint himself with the advantages as well as the limitations of this technique in solving biological problems. This book should answer that need.

The editor has carefully organized the writings of an international body of more than 65 contributors into 31 chapters under three major headings–*Instrumentation, Interpretation of Mass Spectra,* and *Applications.* With the increasing use of computers in acquiring and processing mass spectral data, descriptions of 17 of the most successful mass spectrometer–computer installations featured in the *Instrumentation* section should be very useful to the investigator considering automation.

In section II (*Interpretation of Mass Spectra*) chapters on *Origins of Mass Spectra* and *Metastable Ions* provide a very readable and succinct survey of the basic physics of mass spectrometry useful for more detailed studies of spectra. Two additional chapters in section II discuss the use of computers in compound identification from the mass spectrum by matching the sample spectrum with reference spectra and by automated scientific inference.

The major portion of this book and probably the most important to the biomedical investigator, section III (*Applications*), includes applications of mass spectrometry in the major classes of biological compounds such as antibiotics, amino acids and peptides, nucleic acids, carbohydrates, lipids, hormones, steroids, alkaloids, pesticides, drug metabolism, and clinical uses to name a few. A chapter on the use of stable isotopes is particularly timely with the increased use of such stable isotopes as carbon-13. Chapters on field ionization, chemical ionization, and negative ions round out this section on applications and techniques.

This book should be a useful addition to the library of any investigator using mass spectrometry in biochemical research. The work is well organized and the chapters are very readable. The literature is cited only through early 1970 making some of the discussions out of date; however, for basic references in a given subject area this limitation should not be too great a problem. The greatest fault of the book is the price. While this book would be ideal for graduate students in chemistry, biochemistry, and biomedical field, the $50.00 price tag will definitely be out of their range. In fact, at this price it will probably be only libraries and well-established investigators who will be able to afford it. This is unfortunate, because the book should be in the hands of the students, post-doctoral fellows, and beginning researchers as well.

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Annual Reports in Medicinal Chemistry. Vol. 7. Edited by R. V. Heinzelman. Academic Press, New York and London. 1972. ix + 315 pp. 17.5 × 25 cm. $9.00.

This edition contains 28 chapters, dealing with topics grouped under sections on CNS Agents, Pharmacodynamic Agents, Chemotherapeutic Agents, Metabolic Diseases and Endocrine Function, Topics in Biology, and Topics in Chemistry. The choice of chapter topics reveals continuing concern by the editors for timeliness and is, in general, successful. Annual Reports has not settled into a traditional, stodgy, predictable catalog of "subjects to be covered;" however, it was gratifying to note the reappearance of what are to this reviewer annual high points: chapters on "Reactions of Interest in Medicinal Chemistry" and on "Biopharmaceutics-Pharmacokinetics." This latter chapter represents a much neglected and poorly appreciated but extremely pertinent area for the medicinal chemist.

Chapters unique to this edition which seem especially noteworthy are: "Transition State Analogs as Enzyme Inhibitors;" "Intramolecular Catalysis in Medicinal Chemistry;" and the several chapters in the Biology Section which emphasize various aspects of the immunological process. All of these chapters seem ripe with ideas for exploitation by the medicinal chemist.

Of less value to this reviewer was the chapter on "Preparation of Radioisotope-Labeled Drugs." The chapter is too brief and its format too incohesive to be of use to the novice, and it seemed too elementary in scope and outlook to be of value to the active worker in the field. Literature citations frequently were 3–10 years old. This reviewer feels that reviews of this type are inapropos to Annual Reports in Medicinal Chemistry.

Also included in this edition is what appears to be an abbreviated version of the 1972 Medicinal Chemistry Award Address by Dr. George H. Hitchings. This brief printed account did not generate in this reader the sense of excitement and awe at a magnificent research effort which Dr. Hitchings' oral presentation of the work at the 1972 Medicinal Chemistry Symposium did.

The new chief editor, in his introduction to the volume, has correctly analyzed portions of the book as being less drug-oriented and more provocative; this is one great strength of the volume. The change in chief editorship seems to have been a placid one, maintaining overall quality and demonstrating continuing improvement in the quality of Annual Reports.

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