2 H, H-16), 250–2.62 (m, 2 H, H-17), 2.62–2.76 (m, 1 H, H-7α?, 2.90–3.31 (m, 1 H, H-7β?), 3.25 (s, 1 H, H-9), 3.94 (s, 3 H, OCH_3), 4.73 (s, 1 H, H-5β), 5.04 (d, 1 H, H-10β, collapsed to a singlet after treatment with D_2O), 5.13 (s, 1 H, 14β-OH exchangeable with D_2O), 6.90 (m, 2 H, H-1, H-2); MS, *m/e* 371.2 (M^+) (calcd mass 371.4). Anal. C, H. N.

Oxidation of 5 and 8 with CrO_3–DMP. The CrO_3–DMP complex was prepared from 7.4 mg (0.077 mmol) of DMP, 7.6 mg (0.076 mmol) of CrO_3, and 1.0 mL of CH_2Cl_2.[7] After 20 min 10 mg (0.030 mmol) of **5** was added. Fifteen minutes later, the mixture was worked up as described above to give 7 mg of **6**, mp 236–239 °C, identical in all respects with an authentic sample.

Similarly oxidation of 10 mg of **8** gave 9.2 mg of **9**, mp 108–110 °C after crystallization from hexane.

10-Ketooxymorphone (10). A solution of 0.84 mL (8.78 mmol) of BBr_3 in 10 mL of dry $CHCl_3$ was added in one portion to a stirred solution of 240 mg (0.73 mmol) of **6** in 40 mL of dry $CHCl_3$ at room temperature. After 43 h a solution of 15 mL of concentrated NH_4OH in 15 mL of H_2O was added and stirring was continued for 45 min. The $CHCl_3$ layer was separated and washed with 20 mL of the diluted NH_4OH and then with H_2O. Evaporation of the $CHCl_3$ gave 57 mg (24%) of crude starting material, which was purified with the aid of preparative TLC (silica gel and $CHCl_3$ as the eluant).

The combined NH_4OH solutions were cooled to −5 °C (ice–salt bath) and carefully neutralized with HCl. The pH was adjusted to 7 with $NaHCO_3$ solution and the mixture was extracted several times with $CHCl_3$. Evaporation of the combined extracts left 117 mg (51%) of **10**, mp 250–253 °C dec. After crystallization from benzene, there was obtained 85 mg (37%) of the analytically pure sample: mp 246–248 °C dec; IR 3650–3000 (3-OH and 14β-OH), 1720 (C=O at C-6), 1670 cm^{-1} (C=O at C-10); NMR δ 1.50–1.73 (t, 2 H, H-15), 1.75–2.00 (m, 2 H, H-8), 2.00–3.20 (m, 4 H, H-16, H-7), 2.50 (s, 3 H, NCH_3), 3.02 (s, 1 H, H-9), 3.50–4.60 (br s, 2 H, 3-OH, 14β-OH, exchangeable with D_2O), 4.80 (s, 1 H, H-5β), 6.90 (d, 1 H, *J* = 9 Hz, H-2), 7.44 (d, 1 H, *J* = 9 Hz, H-1); MS, *m/e* 315 (M^+) (calcd mass 315.3). Anal. C, H. N.

10-Ketonaltrexone (11). The reagents used were 0.75 mL (7.8 mmol) of BBr_3 in 50 mL of dry $CHCl_3$ and 240 mg (0.65 mmol) of **9**. After 43 h the mixture was worked up as described directly above. The $CHCl_3$ layers gave 81 mg (34%) of unreacted **9** and the NH_4OH layers furnished 113 mg (49%) of almost pure 10-ketonaltrexone, which after crystallization from benzene afforded 88 mg (38%) of pure 10-ketonaltrexone, which decomposed over the range 135–180 °C: IR 3640–3000 (3-OH, 14β-OH), 1720 (C=O at C-6) 1669 cm^{-1} (C=O at C-10); NMR δ 0.04–0.22, 0.28–0.42, 0.44–0.60, 0.80–1.08 (4 m, 5 H, c-C_3H_5), 1.50–1.84 (m, 2 H, H-15), 1.88–2.24 (m, 2 H, H-8), 2.24–2.45 (m, 2 H, H-16 or H-17), 2.50–2.80 (m, 2 H, H-16 or H-17), 2.80–3.24 (m, 2 H, H-7), 3.36 (s, 1 H, H-9), 4.84 (s, 1 H, H-5β), 6.94 (d, 1 H, H-2), 7.42 (d, 1 H, H-1); MS, *m/e* 355 (M^+) (calcd M 355.4). Anal. C, H. N.

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Book Reviews

Clinical Pharmacy Education and Patient Education: Proceedings of the 12th European Symposium on Clinical Pharmacy, Barcelona, 1983. Progress in Clinical Pharmacy. (Volume I). Edited by Joaquin Bonal and J. W. Poston. Cambridge University Press, Cambridge. 1984. xiv + 322 pp. 16 × 23.5 cm. ISBN 0-521-26610-6. $49.50.

This volume presents selected papers from the 12th European Symposium on Clinical Pharmacy conducted in Barcelona, Spain, in October 1983. The meeting was held together with the XXVIII Congress of the Spanish Society of Hospital Pharmacists. It is not suprising, therefore, that the topics predominately represent current issues in hospital pharmacy practice in Europe.

The major themes of the meeting are reflected in the title of the proceedings. About one-third of the textbook is devoted to papers dealing with patient education programs or undergraduate and postgraduate educational programs in clinical pharmacy in Europe and the United States. For American pharmacy educators, these papers can provide an interesting comparison of the sequencing and implementing of educational programs in the various countries. A few of these papers address efforts toward integrating clinical pharmacy services in community practice.

The balance of the volume presents numerous papers of original research on a wide range of topics in clinical pharmacy. These papers are brief, averaging four pages double-spaced, and are referenced. They vary considerably in rigor of study design and patient population size. Due to these shortcomings, many papers can only be considered preliminary reports. Topics in the administrative area include drug utilization studies, technician training programs, unit dose, and computerization of routine pharmacy functions. These papers offer few, if any, new ideas for American hospital pharmacy practitioners. Several articles report intravenous admixture stability studies especially for chemotherapeutic agents and total parenteral nutrition. Case reports and studies appear on adverse drug reactions associated with total parenteral nutrition, narcotics, and diuretics. A substantial number of papers present clinical pharmacokinetic studies of antibiotics, anticonvulsants, and chemotherapeutic agents in the presence of disease states. Some of this material presents new knowledge in the field, especially for drugs which are not commercially available in the United States (for example, the antibiotic ceftazidime) or are dosed in a manner not commonly employed (for example, epidural or intrathecal administration of morphine).

This symposium proceedings can provide American pharmacy educators–practitioners with an interesting comparison of state-of-the-art practice and education in Europe and the United States. The noticeable omission of a subject or author index impedes the reader from quickly accessing information. For practitioners specializing in oncology, neurology, or infectious diseases, the research reports can provide a brief overview of clinical trials and pharmacokinetic studies conducted by their international pharmacy colleagues.

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Phosphorus-31 NMR. PRINCIPLES AND APPLICATIONS. Edited by David G. Gorenstein. Academic Press, Orlando, FL. 1984. xiv + 604 pp. 16 × 23.5 cm. ISBN 0-12-291750-2. $79.00.

This book is a superbly edited collection of 18 chapters from experts on ^{31}P NMR. Five of the chapters were written by the editor, David G. Gorenstein. Gorenstein contributed the first two chapters, which provide a well-balanced discussion of ^{31}P chemical shifts and coupling constants in relation to theoretical treatments, and the final chapter, which is an appendix of shift and coupling data for selected compounds. All of the other chapters, with the

exception of an introduction to two-dimensional ^{31}P NMR, deal with biochemical or biological aspects of the subject. Each chapter has a brief introduction, which places the subject in a historical or theoretical context and which cross-references other chapters in this collection. Most chapters include a further introduction to the principles of a particular technique of ^{31}P NMR spectroscopy. The text is liberally illustrated with spectra, graphs, and structures. Literature coverage is through 1982.

Essentially all of the important NMR techniques and types of information are included: solid-state NMR (powder and oriented sample spectra, not magic-angle spinning spectra), two-dimensional NMR, line-shape studies of exchange processes, relaxation times, ^{18}O isotope shifts, ^{17}O quadrupolar effects, and, of course, chemical shifts and coupling constants. However, this book should not be considered a book about technique, as it is especially rich in biochemical information gleaned from the NMR applications. The NMR applications include the study of enzymes through observation of ^{31}P-containing substrates; the direct observation of phosphoproteins; the use of chiral thiophosphates and phosphates for exploring phosphoryl transfer; the study of structure and dynamics of nucleic acids and phospholipid-based ordered systems; and the identification of diseased states of mammalian tissues.

This book should be a standard reference in the field of ^{31}P NMR, serving both as a fundamental resource and a stimulus for further work.

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Isotopes in Organic Chemistry. Volume 6. Isotope Effects: Recent Developments in Theory and Experiment. Edited by E. Buncel and C. C. Lee. Elsevier, New York. 1984. xii + 266 pp. 17 × 25 cm. ISBN 0-444-42368-0. $88.50

This series treats the application of isotope methods (kinetic and spectral) to determination of reaction mechanisms, biosynthetic pathways, and structural assignments. Volume 6, however, deals specifically with isotopic effects on ^{13}C NMR and with current applications of the kinetic isotope effect.

The lead chapter, "Isotope Effects on ^{13}C NMR Shifts and Coupling Constants", by D. A. Forsyth begins with a conclusion reached by earlier reviewers of this subject: "isotope effects (on ^{13}C NMR spectra) are unlikely to provide detailed information about a particular structural parameter". Nevertheless, this author then proceeds to document numerous situations in which both the so-called α-effect and the more remote two- or three-bond isotope effects do provide useful structural information and support reaction mechanism studies.

The diminution of a ^{13}C signal by deuteration exchange of its attached proton, the pronounced upfield shift of the ^{13}C residual resonance (up to ca. 0.5 ppm), and the modest upfield shift of ^{13}C signals β or γ to the site of deuteration often have value in structure assignment, especially if the locus of deuteration is known. Furthermore, since separate measurements can be made of deuterated and undeuterated carbon, this α-isotope effect can be used to quantitatively monitor site-specific deuteration reactions.

Forsyth also discusses shifts and coupling changes induced by ^{18}O, ^{15}N, ^{34}S, and ^{37}Cl. Not only has he well documented the literature (>140 references) but he has also provided useful tables of such shifts and inserted critical/speculative comments about the utility of the literature data to structural, mechanistic, and spectroscopic chemists. He does note that the small magnitudes of such isotopic shifts place the measured values perilously close to the experimental limits inherent in the earlier NMR instrumentation and implies that more useful correlations of shifts with structure may be forthcoming from improved instrumentation.

Physical chemists have long used the K_H/K_D kinetic isotope effect with its expected maximum of ca. 8 at 25 °C as a useful criterion for the extent of bond making/bond breaking in the transition state. Chapter 2 in this volume, "The Effect of Pressure on Kinetic Isotope Effects" by Neil S. Isaacs, offers possible explanations for those experimental cases in which K_H/K_D ratios over 8 are observed; a frequent explanation has been quantum mechanical tunnelling. From kinetic studies of eight very different organic hydrogen-transfer reactions performed under pressure, Isaacs finds a correlation between anomalous kinetic isotope effects and the changes in volumes of activation between a protonated and a deuterated substrate undergoing the same reaction. He suggests that if quantum mechanical tunnelling is correct, then a pressure effect may serve as one further criterion that such nonclassical behavior is taking place.

Nicholas J. Turro and Bernhard Kraeutler in Chapter 3, "Magnetic Isotope Effects", present a persuasive argument for broadening the accepted view of the origin of the isotope effect. Traditional opinion is that isotope effects arise exclusively from differences in the isotopic masses of the nuclei involved. Turro and Kraeutler supply examples in which reaction rates, in molecules differing by a key isotopic substitution, are influenced by nuclear spins and magnetic fields. Such reactions as photolysis of dibenzyl ketones, thermolysis of endoperoxides, autooxidation of aryl alkyl hydrocarbons, and other reaction mechanisms involving diradicals often show rate and/or product distributions which vary with external magnetic fields, making a strong case for the inclusion of an isotope effect due to the nuclear magnetic moment. This concept constitutes a new viewpoint to most physical organic chemists.

The most extensive topical treatment in this volume is "Bond Order Methods for Calculating Isotope Effects in Organic Reactions" by Leslie B. Sims and David E. Lewis. In this unit, Chapter 4 in the book, there is an excellent introduction to a mathematical modeling method for the calculation of isotope effects. The particular scheme is a modification of H. S. Johnston's approach to calculating the rates of hydrogen-transfer reactions. As presented by Sims and Lewis, this Bond Order calculation can be readily learned by chemists with no prior experience in performing calculations. The reader is clearly led, step-by-step, through the method. Illustrative applications to calculating kinetic isotope effects on S_N1 and S_N2 reactions, on base-catalyzed elimination reactions, and on rearrangement reactions give a practical demonstration of the utility of the method.

With its >420 references covering the literature through 1983 and its comprehensive index (>350 headings), this volume provides the chemical kineticist and the NMR spectrocopist with a valuable reference volume for the latest material on ^{13}C and kinetic isotope effects.

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Peptide and Protein Reviews. Volume 4. Edited by Milton T. W. Hearn. Marcel Dekker, Inc., New York. 1984. 16 × 23.5 cm. vii + 255 pp. ISBN 0-8247-7292-X. $52.50/U.S. and Canada; $63.00/all other countries.

Presenting the latest work of 12 leading, international scientists, Volume 4 deals with the structure–function relationships of a variety of biologically important enzymes. These relationships have been revealed by X-ray and neutron diffraction studies and associated protein crystallographic investigations.

Staff

Graduate Research: A Guide for Students in the Sciences. By Robert V. Smith. ISI Press, Philadelphia, 1984. 15 × 23 cm. xi + 182 pp. ISBN 0-89495-038-X. $14.95/U.S., Canada, Mexico (soft cover), $17.95/all other countries (soft cover); $21.95/U.S., Canada, Mexico (hard cover), $24.95/all other countries (hard cover).

This book is a source of practical information about the actual process of doing research at the graduate level. Chronologically developed, the book opens with an orientation to graduate research departments. This is followed by chapters on commitments and creativity, making choices (e.g., research problems and an advisor), and managing time. These are followed by chapters on the principles of scientific research and ethics in science. Subsequent chapters are devoted to library research, writing skills, preparing theses and dissertations, and presenting and publishing papers.

The book continues with chapters on research with human subjects, animals, and biohazards, and writing and applying for grants.

Short, concise, and crisply written, this book promises to be one of the most frequently referred to books in the new student's library. It will continue to be a source of tips and hints as the student's graduate research work progresses. And it will also be useful to faculty advisors and department chairs who need to provide their graduate students a framework within which to pursue their research interests.

Staff

Organic Syntheses. Volume 62. An Annual Publication of Satisfactory Methods for the Preparation of Organic Chemicals. Edited by Martin F. Semmelhack, et al. Wiley, Somerset, NJ. 1984. 16 × 23.5 cm. xvi + 269 pp. ISBN 0-471-81764-4. $26.50.

With Volume 62, the Editors of "Organic Syntheses" began a new presentation and distribution policy to shorten the time between submission and appearance of an accepted procedure and to make the annual volumes more easily available to users. The soft cover edition of this column is produced by a rapid and inexpensive process and is sent at no charge to members of the Organic Division of the American Chemical Society. The soft cover edition is intended as the personal copy of the owner and is not for library use. A hard cover edition is published by John Wiley and Sons Inc. in the traditional format and differs in content primarily in the inclusion of an index. The hard cover edition is intended primarily for library collections and is available for purchase through the publisher. Annual Volumes 60–64 will be included in a new 5-year version of the collective volumes of "Organic Syntheses" which will appear as "Collective Volume Seven" in the traditional hard cover format, after the appearance of annual Volume 64. It will be available for purchase from the publishers.

Staff

Advances in Chromatography. Volume 24. Edited by J. Calvin Giddings, Eli Grushka, Jack Cazes, and Phyllis R. Brown. Marcel Dekker, Inc., New York. 1984. 16 × 23.5 cm. xvii + 335 pp. ISBN 0-8247-7253-9. $65.00/U.S. and Canada; $78.00/all other countries.

This volume in this series presents discussions of statistical methods for chromatographic data, multifactor optimization of HPLC conditions, statistical and graphic methods of isocratic solvent selection for optimal separation in liquid chromatography, electrochemical detectors for liquid chromatography, reversed-flow gas chromatography as applied to physicochemical measurement, development of high-speed countercurrent chromatography, determination of the solubility of gases in liquids by gas–liquid chromatography, and multiple selection in gas chromatography.

Staff

Analytical and Preparative Isotachophoresis. Proceedings of the Third International Symposium on Isotachophoresis. Goslar, Germany, 1-4 June 1982. Edited by C. J. Holloway. Walter de Gruyter, Berlin. 1984. 17 × 24 cm. xiii + 404 pp. ISBN 3-11-010178-5. 170DM.

This book contains a comprehensive and up-to-date collection of papers on isotachophoresis which is a little-known, but potentially powerful new analytical tool. In particular, this volume complements more general treatises on the electrophoretic techniques.

Staff