been reported.[3] Recently another physiologically active component of the resin has been isolated and shown to be l-Δ^8-tetrahydrocannabinol (IX)[4] and a total synthesis of the racemic modification of this material has also been reported.[5] These syntheses require a separation of isomers either by vapor phase chromatography[5] or repeated column chromatography.[3] This communication describes a convenient total synthesis and isolation of the racemic modification of these two active compounds.

Thus, the von Pechmann condensation of olivetol (I) and diethyl α-acetoglutarate (II) in the presence of phosphorus oxychloride gave the coumarin III, mp 123–124°,[6,7] in 74% yield. Cyclization of III with sodium hydride in dimethyl sulfoxide at 15–20° gave a 60% yield of IV, mp 205.5–207.5°. The latter compound was converted (94%) to the ketal V isolated as two polymorphs, mp 114.5–116° and 145–148°. Treatment of V with methylmagnesium iodide followed by acid hydrolysis gave VI, mp 198–199°, in 66% yield. Reduction of VI with lithium in liquid ammonia at Dry Ice temperature afforded a 59% yield of the *trans* ketone VII, also isolated as two polymorphs, mp 148–150° and 163–165°.[8] Conversion of VII to its tetrahydropyranyl ether followed by treatment with methylmagnesium iodide and subsequent removal of the protecting group gave a 37% yield of the carbinol VIII, mp 162–163°.[9] Dehydration of VIII with a catalytic amount of p-toluenesulfonic acid in refluxing benzene gave a 90% yield of dl-Δ^8-tetrahydrocannabinol (IX) as a viscous oil. This material was a single isomer as shown by glpc, and its nmr spectrum[11] (olefinic H-8 proton signal in $CDCl_3$ at 5.40 and in CCl_4 at 5.33) was identical with that reported[5] for IX.

Treatment of an acetic acid solution of the alcohol VIII with Lucas reagent afforded a 60% yield of X, mp 87–90°.[12] Dehydrochlorination of X with sodium hydride in refluxing tetrahydrofuran gave in quantitative yield a mixture containing 74% of XI and 26% of IX as shown by glpc.[13] This mixture was treated with m-nitrobenzenesulfonyl chloride to give the m-nitrobenzenesulfonate of XI, mp 105.5–107.5°, in 23% yield. Mild basic hydrolysis of the latter compound then gave an 84% yield of dl-Δ^9-tetrahydrocannabinol (XI), mp (vac) 64.5–65.5°[14] (no detectable impurities by glpc), with spectra (nmr olefinic H-10 proton signal in $CDCl_3$ and in CCl_4 at 6.30) identical with those of natural l-Δ^9-tetrahydrocannabinol.[15]

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(3) R. Mechoulam and Y. Gaoni, *J. Am. Chem. Soc.*, **87**, 3273 (1965).

(4) R. Hively, F. Hoffmann, and W. A. Mosher; see footnote 4 in ref 5.

(5) E. C. Taylor, K. Lenard, and Y. Shvo, *J. Am. Chem. Soc.*, **88**, 367 (1966).

(6) All compounds prepared in the course of this work have satisfactory elemental analytical data, and have infrared, ultraviolet, and nmr spectra compatible with the assigned structures.

(7) The structure proof of III, which precludes the other possible coumarin or the two possible chromones, will be given in the full paper.

(8) The proof of *trans* ring fusion in VII will be given in the full paper.

(9) The axial configuration of the hydroxyl group in VIII is supported by the facile acidic dehydration to give IX. An equatorial hydroxyl group would be expected[10] to give the exocyclic olefin. We have prepared the exocyclic olefin by another method and have shown that it does not isomerize under the dehydration conditions.

(10) C. E. Cook, R. C. Corley, and M. E. Wall, *Tetrahedron Letters*, 891 (1965).

(11) Determined on a Varian A-60 spectrometer; values given in ppm relative to TMS as internal standard.

(12) The over-all yield of X from VII could be raised to 60% by allowing the Lucas reagent to react directly with the crude product of the reaction of VII with the Grignard reagent.

(13) Column, 0.5% NPGS and 0.5% PEG4000MS on Anakrom ABS 60/70 mesh; gas, nitrogen 100 ml/min; column temperature, 220°; retention time of XI, 20 min; retention time of IX, 18 min.

(14) Previously obtained as an oil.[3]

(15) We are indebted to Dr. Nathan B. Eddy of the Department of Health, Education and Welfare for a sample of l-Δ^9-tetrahydrocannabinol of natural origin.

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Book Reviews

Histones and Other Nuclear Proteins. By Harris Busch, Department of Pharmacology, Baylor University College of Medicine, Houston, Texas. Academic Press Inc., 111 Fifth Ave., New York, N. Y. 1965. 266 pp. 16 × 23.5 cm. $9.50.

The introductory chapter contains a number of rather poorly integrated topics including a classification of nuclear proteins, the role of proteins in control of the genome, history of the nuclear proteins, composition of spermatazoa, and material on protamines, histones, and acidic proteins and enzymes of the nucleus. From the standpoint of the reviewer, the historical presentation is not very comprehensive.

Chapter I on the protamines contains historical material, material on protamine isolation, something on analysis and structure of protamines, and finally a section on function of the protamines which, however, contains very little material pertaining directly to protamine function. This chapter seems weak in respect to factual material.

Chapters II through VII constitute the major part of the material on the histones and the best part of the book. Here the work appears to have been painstakingly and thoroughly done, and the reader can obtain an excellent picture of modern work on the histones, both from the standpoint of experimentation and the development of general ideas as to the role of the histones. The work on the nucleohistones edited by Bonner and Ts'o (Holden Day Inc., San Francisco, 1964) should, however, be consulted for certain more recent material not included in the book of Busch. The topics covered in Chapters II through VII include the following topics concerning the histones: composition and number, isolation, fractionation, the role in chromosomal structure, function, sequential amino acid analysis, and metabolism. Something on the isolation of cell nuclei is also included to serve as a basis for material on the isolation of histones, although this section is somewhat incomplete.

Chapter VIII, entitled the "Acidic Nuclear Proteins," contains a wealth of material which, however, is not very critically evaluated. An example of a rather uncritical statement is the following (p 201): "... the ribonucleoproteins that are transported across the nuclear membrane include elements of both the ribosomes and the larger polysomic mass which contains both ribosomes and linear RNA filaments with a coding function...." No evidence is presented to substantiate the transfer of polysomes across the nuclear membrane, and it is not made clear what is meant by the elements of the ribosomes and polysomes. Some of the material included in this chapter, such as that concerning the NH_2-terminal amino acids of the acidic nuclear proteins, may be open to question because of failure to take into account the possibility of proteolytic autolysis. Nothing has been included concerning the relationship of the acidic nuclear proteins to the formation of gels by isolated nuclei, a topic which in the opinion of the reviewer ought to merit some attention. Finally, a number of statements seem to be presented as factual which are really inferences, and the chapter seems to be somewhat more didactic than is warranted, considering the difficulty of arriving at firm conclusions in the field being considered.

The last chapter (IX) on nuclear enzymes, on the other hand, appears to the reviewer not to be written in a sufficiently positive manner. References to the fairly recent literature are given, but the discussion seems weak, and, in spite of difficulties in interpreting the results of work on nuclear enzymes, the reviewer feels that a somewhat less vague picture could have been presented.

To recapitulate, the reviewer feels that the best part of the book is the part devoted directly to the histones, although the other sections are also valuable if the above-mentioned reservations are kept in mind. It seems likely that the book should be considered as a necessary addition to the bookshelves of those working on cell nuclei and histones, and that it would be of considerable value to anyone interested in these subjects. The style is good, there seem to be very few if any typographical errors, and the book is easy to read.

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Introduction to Mass Spectrometry and Its Applications. By Robert W. Kiser, Associate Professor, Department of Chemistry, Kansas State University. Prentice-Hall, Inc., Englewood Cliffs, N. J. 1965. xii + 356 pp. 16 × 23.5 cm. $14.00.

The timing of Professor Kiser's book is well-nigh perfect. Mass spectrometry is currently enjoying a period of great popularity, and chemists and physicists in growing numbers are looking into potential applications of this technique in their varied areas of interest. For newcomers to the field, whatever their special interests, this book does a nice job of introducing and surveying the principles and applications of mass spectrometry relatively clearly and painlessly.

In accord with his objective of teaching mass spectrometry to those who know little or nothing about it, the author has gone out of his way to minimize the use of mathematics, jargon, and specialized terminology, although the results are not uniformly successful. The calculations required in quantitative analysis are couched largely in the language of matrix algebra; for the reader not at home in this branch of mathematics, such treatment can serve only to obscure the basic simplicity of the concepts and operations. At the other extreme, algebraic calculations at the high school freshman level are presented in full detail. Only very few examples of jargon survive, such as "coda compounds" (p 272) for cycloolefins, dienes, and acetylenes. Necessary specialized terms are carefully defined, although one might be inclined to take issue with some of the definitions. The author offers some of his preferred terminology as constituting "more basic definitions and distinctions" than the "somewhat confusing" more common usages; such a claim is at least challengeable and is certainly not convincingly demonstrated. A full chapter is devoted to classifying ions into numerous types, the descriptions of which serve a useful purpose. However, the seeming obsession with such classification leads to unnecessary complications and tends to obscure the common aspects of mass spectra with other chemical systems.

The definition of the "base peak" (p 128) as the most intense peak in a spectrum coincides with current practice of some workers but is far less useful than the older and broader sense of a peak arbitrarily selected by the spectrometrist, in accord with his convenience in the context of the problem at hand, to define the scale of relative intensities. The difficulty with Kiser's limited definition is well illustrated by his presentation of the partial spectra of isotopic benzaldehydes (p 271). Here the scale of relative intensities is, to say the least, of little help in bringing out significant relationships. To facilitate meaningful comparison of spectra of different isotopic species of a compound, the base peak should have as nearly as possible the same functional significance in the various spectra. The parent peak is often convenient for this purpose and, in this instance, was so used in the original paper. The strongest peak in the spectrum, assigned a relative intensity of 100 by Kiser, corresponds to the total $C_6H_5^+$ yield in the spectrum of unlabeled benzaldehyde, but to only part of the $C_6H_5^+$ yield in those of the labeled species.

A full chapter is devoted to an unquestionably useful survey of commercial instruments. Inevitably, such a survey is, in part, already out of date by the time the book is published; this limitation is explicitly recognized by the author. A second limitation, not so recognized, follows from the extent to which the author relied for his information on manufacturers' brochures and advertisements. He describes in impressive detail double-focusing mass spectrometers that have never been built except for prototype instruments in the manufacturers' plants. In view of the rapidity with which this field has been progressing, possible commercial production of such instruments will have to be preceded by extensive revision of specifications.

The book is an outgrowth of a series of lectures, the vestigial remains of which are evident in the chapter organization and in treatment of specific topics. In particular, the breakdown of the material on instruments incurs a great deal of repetition, sometimes to an extent slightly reminiscent of the Dick and Jane stories. A tighter organization would surely have been in order.

Perhaps the derivation of the book from lecture notes, with the attendant oversimplifications, can also account in part for some imprecise and misleading statements. One might cite, for example, the description of rearrangement ions (p 128) as "formed by rearrangements ... at the moment of the unimolecular decomposition of the parent ion." The events comprising rearrangement and decomposition of polyatomic molecules are, in general, rate processes, and I know of no *a priori* reason why rearrangement must be concerted with a decomposition step. The statement, "It is not uncommon that the production of rearrangement ions requires considerably more energy than for most of the fragmentation processes" (p 128), tends to perpetuate a common misconception. A similar statement, but with "more" replaced by "less," could be made with at least equal justification. The conventional explanation offered here—going back to vertical *vs.* adiabatic processes—for the discrepancies often found between values of ionization potentials measured by electron impact and by other means (p 166) is by no means firmly established and ought to be taken with a large grain of salt. To the statement that "The relative total ionization should be independent of the particular mass spectrometer employed" (p 132), one is tempted to ask how such a relationship can be expected in view of the assorted spectrum-distorting effects generally lumped as mass discrimination. The discussion of total ionization and its relationship to elemental composition and molecular structure would be much improved by replacing a few "indicates" with "suggests," and by clear recognition that the postulated relationship, although useful in some situations, is by no means rigorous and should be looked on as giving only a rough approximation. The loosely worded statement appearing here (p 199) of "Stevenson's rule" can only help to perpetuate erroneous thermochemical arguments that have been justified by reference to misstated versions of the rule.

The easy, semiconversational style lapses at times into simply poor grammar. The use of the word "impact" as a verb with the sense of "impinge," although not serious, is not correct and should have been caught by the author or a copyreader. The auxiliary verb "shall" seems to have a special attraction for the author, but nearly every time he uses it, he gets into trouble, swinging back and forth between "shall" and "will" for the first person, and following with "shall" for the third person. Such idiosyncrasies will not cause any confusion in the reader's mind, but they are annoying and they are surely uncalled for.

Now, having played the role of the devil's advocate, I want to return to my original thesis. The book covers a great deal of ter-