

DEGRADATIVE STUDIES ON STREPTOMYCIN

Sir:

An amorphous and chromatographically purified dodecaacetyldihydrostreptomycin, $[\alpha]_D -67^\circ$,¹ has been prepared through crystalline streptomycin helianthate.

Anal. Calcd. for $C_{48}H_{75}N_7O_{24}$: C, 49.68; H, 6.03; N, 9.01; mol. wt., 1088. Found: C, 49.81; H, 6.06; N, 8.84; mol. wt. (Rast), 1000.

If the meso streptidine portion² in the dodecaacetyldihydrostreptomycin does not substantially affect the contributions to rotation, the molecular rotation may be expressed as $[M] = A_s + B = -72,900$, following the isorotation rules of Hudson.³ The known anomeric forms of methyl pentaacetyldihydro-L-streptobiosaminide⁴ ($A' + B = -65,900$ and $-A' + B = -19,100$) allow B ($-42,500$) to be evaluated, from which $A_s = -30,400$. Tetraacetyldidesoxydihydro-L-streptobiosamine^{5,6} shows $[M'] = A_g + B' + x = -40,900$; where A_g is the rotatory contribution of the lactol carbon, B' that of the remainder of the N-methyl-L-glucosamine portion and x that of the optically active didesoxydihydrostreptose moiety. The value of x is not known but is assumed to approximate that of didesoxydihydrostreptose (4,200).⁷ The term B' ($-24,150$) is evaluated from the rotations ($A'' + B' = -41,600$ and

$-A'' + B' = -6,700$) of the known anomeric forms of pentaacetyl-N-methyl-L-glucosamine,⁸ whence $A_g = -20,950$. The numerical sign of the values for A_g and A_s , together with our knowledge that the sugars belong to the L-series, would indicate that both glycosidic linkages in streptomycin are α -L. The magnitude of these values is of the order ($\approx 25,000 \pm 5,000$) expected for contributions to rotation by the lactol carbon of sugar alkyl glycosides.

We report the isolation of a new anomeric form of methyl tetraacetyl-L-streptobiosaminide dimethyl acetal; m. p. 118.5–119.5°, $[\alpha]_D -45^\circ$.

The periodate oxidation of methyl N-acetyldihydro- α -L-streptobiosaminide (I) and of methyl N-acetyl- α -L-streptobiosaminide dimethyl acetal (II) was found to differ in the rapid consumption by I of one mole of periodate with the concomitant formation of formaldehyde. This oxidation necessarily took place at an α -glycol in the streptose portion of I, which must have been formed on the conversion of streptomycin to dihydrostreptomycin. This, together with the known structure of didesoxydihydrostreptose,⁷ offers proof for the point of attachment of N-methyl-L-glucosamine (C2) to the L-streptose and presents confirmatory evidence for the presence of the tertiary hydroxyl group in streptose. When the trihydrochlorides of streptomycin and dihydrostreptomycin were oxidized with 1.5 moles of periodate, formaldehyde (0.4 mole, by dimedone reagent) was formed from the latter only, showing that the 1,4-furanose ring demonstrated for streptobiosamine, is likewise present in streptomycin.

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- (8) M. L. Wolfrom and Alva Thompson, *ibid.*, in press.
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- (1) All rotations are recorded in chloroform solution at $25 \pm 5^\circ$ with $c < 5$ and $\lambda = 5892.5\text{\AA}$.
(2) H. E. Carter, Y. H. Lee and P. S. Skell, *J. Biol. Chem.*, **166**, 401 (1947); F. A. Kuehl, Jr., R. L. Peck, C. E. Hoffhine, Jr., Elizabeth W. Peel and K. Folkers, *THIS JOURNAL*, **69**, 1234 (1947).
(3) C. S. Hudson, *ibid.*, **31**, 66 (1909).
(4) N. G. Brink, F. A. Kuehl, Jr., E. H. Flynn and K. Folkers, *ibid.*, **68**, 2557 (1946).
(5) F. A. Kuehl, Jr., E. H. Flynn, N. G. Brink and K. Folkers, *ibid.*, **68**, 2096 (1946).
(6) I. R. Hooper, L. H. Klemm, W. J. Polglase and M. L. Wolfrom, *ibid.*, **68**, 2120 (1946).
(7) N. G. Brink, F. A. Kuehl, Jr., E. H. Flynn and K. Folkers, *ibid.*, **68**, 2405 (1946).

NEW BOOKS

Chemistry and Methods of Enzymes. By JAMES B. SUMNER, Professor of Biochemistry, Cornell University, and G. FRED SOMERS, Plant Physiologist, U. S. Plant, Soil and Nutrition Laboratory, Ithaca, N. Y. Second edition, Revised and Enlarged. Academic Press, Inc., 125 East 23rd Street, New York, N. Y., 1947. 415 pp. 15.5 × 23.5 cm. Price, \$6.50.

The first edition of this book appeared four years ago. In the interval, some half dozen or more enzymes have been crystallized, others have had prosthetic groups identified, and the senior author has received the Nobel Prize for his contributions to the field.

The present edition follows the pattern of treatment employed in the first edition. Some fifty additional pages have been added and the price increased by \$1.50. The

introductory chapter on general properties of enzymes has been enlarged and revised. The phosphatases have received more attention in the chapter headed, "Esterases." The chapter formerly headed, "Enzymes of Carbohydrate Metabolism," has now been entitled, "Phosphorylases, Transphosphorylases, Phospho-isomerases and Phosphomutases," reflecting the activity and interest which has centered around these enzymes in recent years.

The errors of the first edition have been corrected, and the more important recent advances in the field have been incorporated. This book remains one of the best available for those who desire a handy, brief reference to the whole field of enzymes.

ERIC G. BALL

Analytica Chimica Acta. International Journal dealing with Every Branch of Analytical Chemistry. Editor, PAUL-E. WENGER (Geneva). Vol. 1, No. 1, 1947. Elsevier Publishing Company, Inc., 118 Spuistraat, Amsterdam-C, Holland (New York). 72 pp. Illustrated. 17 × 25 cm. Price, \$9.50 per annum.

The need for the establishment of a new journal in this field has been acute since the suspension of the publication of certain European journals in 1944. The new Journal is stated to have the aims of filling the void thus created and of publishing reliable and up-to-date information in the field of analytical chemistry. All investigators in this field will welcome an additional reliable outlet for publication.

Papers are published either in French, German or English, with summaries both in French and in English.

The Assistant Editors are: G. Charlot and C. Duval, Paris; F. Feigl, Rio de Janeiro; R. Flatt, Lausanne; J. Gillis, Gand; C. J. Van Nieuwenburg, Delft; and N. Strafford, Manchester.

The first number contains eight papers of which two are of a review nature: Quantitative Spectrochemical Analysis, by J. Gillis, and The Utility of the Brönsted Definition of Acids and Bases in Chemical Analysis, by G. Charlot. The other papers deal with a variety of subjects as follows: The Acidimetric Estimation of Aluminum Ion, by S. Lacroix; A Colorimetric Method For the Determination of Borax, by D. Monnier, Y. Rusconi and P. Wenger; A New Method of Measurement in Electrotitration, by P. Delahay; The Semi-micro Gravimetric and Volumetric Estimation of Silica, by C. Duval; Compounds of Cadmium Iodide with Heterocyclic Nitrogen Bases, II Alkaloids, by P. Duquéniois; The Detection of Scandium, Rare Earths, Zirconium and Thorium with Murexide, by G. Beck.

N. H. FURMAN

The Alkaline-Earth and Heavy-Metal Soaps. By STANLEY B. ELLIOTT, Assistant to the President, The Ferro Chemical Corporation, Subsidiary of Ferry Enamel Corp., Cleveland, Ohio (A. C. S. Monograph Series.) Reinhold Publishing Corporation, 330 West 42nd Street, New York, N. Y., 1946 × 342 pp. Illustrated. 15.5 × 23.5 cm. Price, \$7.50.

The metallic soaps find innumerable uses in industry, but there has been no comprehensive treatment of these academically neglected substances in the English language. Here at last is an authoritative reference book that gives a review of these important materials. Only one field is purposely neglected, presumably because of the 873-page monograph by Klemgard, published in 1937, on lubricating greases. Incidentally, no attempt has been made to bring this subject up to date, in spite of the active developments of the war years.

Elliott's monograph begins with a discussion of raw materials and manufacture, described in helpful detail. The author points out that much of the interest in metallic soaps is due to the fact that they are almost the only common compounds containing considerable metal and yet soluble in organic solvents. He describes useful soaps derived from 28 different heavy metals. They are placed in three groups: those whose uses are based on the nature of the metal, those whose uses are based on physical characteristics of the soaps, and those whose usefulness is the ability to influence the characteristics of liquids. Likewise, he mentions the various addition agents which increase solubility, stability and resistance to oxidation, discoloration or skinning. This portion of the book occupies the first half of the text.

Next follows a systematic description of the applications of metallic soaps: first as catalysts, fungicides, glazes and in pharmacy; next, in regulating the appearance and hardness of paints and leather materials; in lubrication, in water proofing and sealing. The third group concerns the influence upon liquids; in wetting, dispersing, preventing sludge or separation of polymers,

affording lathering and detergency, producing emulsions, in soap greases and extreme pressure lubricants, in thickening, or imparting conductivity.

The remainder of the text, Chapters X-XVIII, consists of a systematic review of the individual soaps of the eight groups of the periodic system, but confined to practical information and the more important applications of each.

Throughout the text there are brief indications of the physical chemistry of such systems which should serve to stimulate the development of an adequate theory of these non-aqueous systems by University men.

The usefulness of the book is enhanced by six appendices, the first of which lists the patents pertaining to the use of the various soaps. The next sets forth government and service specifications. Appendix 3 gives 43 pages of systematic, quantitative, tabular data. The last three contain useful tables, a list of the commonest available soaps, and tables of inorganic properties of the materials from which metallic soaps may be made.

It is clear that this volume of the A. C. S. Monograph Series will be indispensable to chemists in paint, lacquer and many other industries. Physical and colloid chemists will find in it important material that calls for theoretical study and explanation.

JAMES W. MCBAIN

Fundamentals of Semi-Micro Qualitative Analysis. By CARL ENGELDER. vii + 385 pages. John Wiley and Sons, Inc., 440 Fourth Ave., New York, N. Y., 1947. Price, \$3.50.

Analysis of the contents of this volume reveals that it contains approximately 175 pages devoted to topics in elementary inorganic chemistry. Much of this material is adequately covered in the standard college course in general chemistry, and should be superfluous for the student of average background. However, its inclusion should aid in smoothing out any inequalities in the students' previous training. Furthermore, even as review material, it may be valuable because of its analytical orientation and because of the generally persuasive reasoning, which begins with fundamental concepts and is developed through simple, transparently logical steps. The more important topics are illustrated with many carefully selected problems worked in complete detail, and there are numerous problems at the end of each section, most of them with subjoined answers.

Particularly thorough consideration is given to the topics of ionic equilibria and oxidation-reduction processes. The techniques of balancing "redox" equations are well discussed, and throughout the volume the essential nature of the more complex "redox" processes is demonstrated by deriving them from their component half-reactions. The treatment of electrode potentials appears to be somewhat sketchy for a book this size, and is not entirely convincing.

A second category of the contents, comprising some 105 pages, presents short but pithy accounts of the descriptive chemistry of the common elements, particularly emphasizing those properties which are of analytical significance. Possible quantitative methods are often indicated, and several alternative qualitative tests are sketched.

In a third category are found 70 pages devoted to analytical procedures. This includes "Preliminary Experiments" which follow the presentation of the chemistry of each element and which are well designed to exhibit the basic analytical chemistry of the ions. In most cases several qualitative tests are described in these exercises, and they also propose numerous questions artfully designed to encourage the student to draw reasoned conclusions from his experimental observations.

While the finally adopted analytical scheme appears generally sound, certain of the procedures did not impress this reader as completely satisfactory. The separation of the aluminum and nickel groups by what is essentially a basic acetate procedure may occasionally be troublesome; and the use of flame tests to confirm calcium and

strontium after a preliminary separation which is admittedly incomplete appears to be of dubious value.

The analytical system described by this text presents many instances in which, within a group or sub-group, the tests are conducted in parallel, with portions of the test material, rather than consecutively with the whole of it. While this may be advantageous in an analytical sense, in that an error in one operation need not affect a subsequent procedure, it appears that in a pedagogic sense basic analytical chemistry is better expounded through methods which provide a consecutive separation of the components present, as in quantitative analysis, rather than methods which employ special (organic) reagents or procedures to obviate the necessity of making separations.

For the purposes of this review the theoretical, the descriptive and the procedural sections have been considered separately. It should be emphasized, however, that as actually arranged in this text these subjects are excellently integrated, so that each chapter contains some items of procedure together with relevant theoretical and factual material. The presentation begins with the analysis of the alkali and alkaline earth metals, permitting parallel development of the simple theories involved in the analysis of these groups. The more advanced concepts involved in the other cation and anion groups are elaborated subsequently.

The strikingly successful integration of theory, fact and practise should greatly lighten the tasks of the teacher or student using this text. In general the organization and presentation is excellent and the scope is broad. There are a very few instances in which the wording is inaccurate, but the writing is generally clear, informative and precise. This book is well-bound, and has been clearly and carefully printed. It contains only a minimal number of misprints. It appears to be a very worthy addition to the literature of elementary inorganic analysis.

LEONARD K. NASH

Biochimica et Biophysica Acta. Editorial Board: W. T. ASTBURY, A. BRAUNSTEIN, C. F. CORI, CL. FROMAGOT, K. LINDERSTRÖM-LANG, H. G. K. WESTENBRINK and R. W. G. WYCKOFF. Vol. I, No. 1, 1947. Elsevier Publishing Company, Inc., 215 Fourth Ave., New York 3, N. Y. 100 pp. 17 × 24.5 cm. Price, \$9.00 per annum.

One of the aftermaths of the war has been the appearance of new scientific journals in many different fields. *Biochimica et Biophysica Acta*, published in Amsterdam and New York under the supervision of a broadly international and highly distinguished Editorial Board with the assistance of an equally distinguished Advisory Board, is designed to provide an outlet for research papers in these allied biological fields and so to assist in reestablishing international scientific coöperation. Especial emphasis is to be placed upon biophysics in the hope that the *Acta* may become a unifying influence in a field that has hitherto been somewhat of a stepchild.

The new journal contemplates the publication of original research papers, reviews and short communications in English, French or German with summaries in all three languages. The quality of the papers in the first number is excellent: they range in scope through enzymes, proteins, amino acids, vitamins and purines. Of the eleven papers, three are in English, six in French and two in German. There is a wealth of tabular data and a liberal number of line-cut illustrations. From the point of view of this reviewer, the most interesting is a confirmation by Desnuelle and Antonin in Marseille of Van Slyke's observations on the presence of hydroxylysine in gelatin together with a new method to determine this recent addition to the

roster of the protein amino acids. American biochemists will wish the *Acta* every success.

H. B. VICKERY

BOOKS RECEIVED

May 10, 1947-June 10, 1947

W. J. DANN and G. HOWARD SATTERFIELD, Editors. "Estimation of the Vitamins." Vol. XII in the Series entitled "Biological Symposia," edited by Jaques Cattell. The Ronald Press Company, 15 E. 26th St., New York 10, N. Y. 531 pp. \$6.50.

TAYLOR H. EVANS and HAROLD HIBBERT. "Bacterial Polysaccharides." Scientific Report Series, No. 6. Sugar Research Foundation, Inc., 52 Wall St., New York 5, N. Y. 32 pp.

MORRIS GOLDBERG. "English-Spanish Chemical and Medical Dictionary." Third Edition. McGraw-Hill Book Co., Inc., 330 W. 42nd St., New York 18, N. Y. 692 pp. \$10.00.

ALVIN GUTTAG. "Patents on the Reactions of Sugars." Technological Report Series, No. 1. Sugar Research Foundation, Inc., 52 Wall St., New York 5, N. Y. 108 pp.

MARTIN D. KAMEN. "Radioactive Tracers in Biology." Academic Press, Inc., 125 E. 23rd St., New York 10, N. Y. 281 pp. \$5.80.

MAX A. LAUFFER. "Viruses." From the Twentieth Annual Priestley Lectures. The Pennsylvania State College, State College, Pa. 62 pp.

Y. R. NAVES and G. MAZUYER. "Natural Perfume Materials." Translated from the First French Edition by Edward Sagarin. Reinhold Publishing Corporation, 330 W. 42nd St., New York 18, N. Y. 338 pp. \$3.75.

HANS STÄGER. "Allgemeine Werkstoffkunde." Verlag Birkhäuser, Elisabethenstrasse 15, Basel, Switzerland. 424 pp. Paper covers, 42.50; bound, 46.50 Fr.

PERCY D. STRAUSBAUGH and BERNAL R. WEDMER. "General Biology." Second Edition. John Wiley and Sons, Inc., 440 Fourth Ave., New York 16, N. Y. 718 pp. \$4.75.

JAMES B. SUMNER and G. FRED SOMERS. "Chemistry and Methods of Enzymes." Second Edition, Revised and Enlarged. Academic Press, Inc., 125 E. 23rd St., New York 10, N. Y. 415 pp. \$6.50.

A. SZENT-GYÖRGYI. "Chemistry of Muscular Contraction." Academic Press, Inc., 125 E. 23rd St., New York 10, N. Y. 150 pp. \$4.50.

ABRAHAM WALD. "Sequential Analysis." (Wiley Mathematical Statistics Series, edited by Walter A. Shewhart). John Wiley and Sons, Inc., 440 Fourth Ave., New York 16, N. Y. 212 pp. \$4.00.

FREDERICK Y. WISELOGLE. "A Survey of Antimalarial Drugs, 1941-1945." In Two Volumes. Vol. I, 536 pp. Vol. II (in Two Parts), 1921 pp. J. W. Edwards, Ann Arbor, Michigan. \$30.00.

Association of Vitamin Chemists, Inc. "Methods of Vitamin Assay." Interscience Publishers, Inc., 215 Fourth Ave., New York 3, N. Y. 189 pp. \$3.50.

"*Excerpta Medica*." Fifteen Journals Containing Abstracts of the World's Literature in the Fields of Clinical and Theoretical Medicine. Excerpta Medica Ltd., III, Kalverstraat, Amsterdam C., The Netherlands. 16 pp.