DEGRADATIVE STUDIES ON STREPTOMYCIN

Sir:

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

Anal. Calcd. for $C_{45}H_{65}N_7O_{24}$: 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 portion[2] 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-streptobiosaminide[4] ($A' + B = -65,900$ 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 ($\pm 25,000 \pm 5,000$) 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°, $[\alpha]_D$ $-45°$.

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 neces sarily 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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(1) All rotations are recorded in chloroform solution at 25 ± 5° with $c < 5$ and $\lambda = 5892.5$Å.

(2) H. E. Carter, Y. H. Lee and P. S. Skell, *J. Biol. Chem.*, **168**, 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).

(8) M. L. Wolfrom and Alva Thompson, *ibid.*, in press.

(9) Bristol Laboratories Research Fellow.

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