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Book review

The Collected Papers of H. S. Isbell, edited by H. S. EL KHADEM AND H. L. FRUSH, Carbohydrate Division of the American Chemical Society, Washington D.C., 1988, 3 Volumes, xv + vii + ix + 1762 pages + Table of Contents + Author and Subject Indexes, $50.00.

This collection is a compilation of the major contributions of Professor Horase S. Isbell in the area of carbohydrate chemistry. It is a historic, three-volume set that includes 188 research papers and review articles, and is a manifest of over sixty years of Dr. Isbell's distinguished career in carbohydrate chemistry.

The Editors (Prof. Hassan S. El Khadem and Dr. Harriet L. Frush) are to be congratulated on the success of the immense task of collecting and assembling of a vast and diverse material, including careful preparation of the text for direct photo-printing. Now a few words about the editor Dr. Frush. Almost every piece of work and research paper that originated from Dr. Isbell's laboratory received Harriet's professional touch. The Carbohydrate Division owes her long-overdue recognition of her devoted and unselfish, life-long sevice to carbohydrate chemistry since 1930.

Trained as an organic chemist, with a Ph.D. thesis on organic gold compounds under the famous Prof. M. H. Karasch, Dr. Isbell joined the carbohydrate group of the distinguished chemist Dr. Claude S. Hudson at the National Bureau of Standards. Soon, Dr. Isbell embraced a new field, and became a carbohydrate chemist for life. Being himself self-disciplined and dedicated, and a hard worker, Dr. Isbell set an example to his highly productive staff. A partial list of his co-workers and associates includes Drs. W. Ward Pigman, Harriet L. Frush, Joseph D. Moyer, R. Stuart Tipson, Robert Schaffer, Lornao T. Sniegoski, Clarence W. R. Wade, John V. Karabinos, Alexander J. Fatiadi, Hassan S. El Khadem, and Nancy B. Holt.

The largest in the set, Volume 1 (704 pages) is divided into five sections: (I) Optical Rotation and Ring Structure of Sugars and Glycosides; (II) Mutarotation and Preparation of Rare Sugars; (III) Glycosylamines; (IV) Transformation of Sugars in Alkaline Solutions; and (V) Conformational and Configurational Relationships of Carbohydrates. The volume opens with the Sir Norman Haworth Memorial Medal Address, delivered at Oxford, England and published in 1974. Here, Dr. Isbell discussed at length the famous Hudson–Haworth controversy, out of which grew our currently accepted concepts of carbohydrate ring-structure. The pioneer work by Dr. Isbell on bromine oxidation of D-glucose, D-mannose, D-galactose, D-arabinose, D-xylose, D-ribose, and other aldoses clearly demonstrated the presence of an oxygen-containing ring-structure and the actual conformation of

the sugars; this work preceded by some 20 years the n.m.r.-spectral evidence. The prestigious paper also discusses and explains the mechanism of the classical Walden inversion reaction as applied to carbohydrate chemistry; this topic is again covered at the beginning of the next volume. Volume 1 next comprises two important reviews on the mutarotation of sugars in solution (see also, Volume 3), and presents a classical paper on the new electronic approach to carbohydrate chemistry [*Annu. Rev. Biochem.*, 32 (1943) 205–232]. Here, the electronic concept of organic reactions was applied for the first time to carbohydrate reactions. A mechanism involving enolization and consecutive electron-displacement was rationalized for the formation of a series of benzene derivatives from inososes and, as shown later, from di- and tri-ketoinositols. The concept of consecutive electron-displacement was also successfully applied to a series of other carbohydrates; this included the formation of saccharinic acids by the action of alkali on sugars. Other mechanisms developed included alkaline degradation of cellulose, formation and cleavage of anhydro sugars, glycal isomerization, and many other reactions. The volume next examines an important topic, namely, advances in the field of branched-chain higher sugars by the alkaline aldol reaction. It was found that branched-chain aldoses containing 8 to 14 carbon atoms can be obtained in reasonably good yield by the aldol reaction of suitable sugar derivatives. This work opened up a new avenue in the synthesis of unique, branched sugars, including higher ketoses. The volume concludes with a review of ring conformation and neighboring-group effects, and some study of conformations of the pyranoid sugars by infrared spectroscopy; this is touched on again, in more detail, in the next volume.

Volume 2 is divided into six sections: (VI) Walden Inversion, Orthoacetates and Opposite-Face Mechanisms; (VII) Compounds with Inorganic Constituents; (VIII) Oxidation and Reduction-Reactions, Aldonic Acids, Lactones, and Salts, (IX) Uronic Acids and Keto Acids; (X) Cyclic Polyhydroxy Ketones and Phenylhydrazine Derivatives; and (XI) Infrared Spectra. The interaction of aldoses with inorganic salts constituted an important field of study. Addition of calcium chloride to aqueous D-gulose causes a rapid change in the optical rotation; this was explained as due to a shift in the equilibrium existing between the various modifications of the aldose in solution. Similar behavior was observed with the cadmium and mercury salts examined. Several stable adducts were isolated, particularly calcium chloride adducts of methyl α- and β-D-gulosides. It would be of interest to supplement these findings by n.m.r.-spectral or by X-ray analysis of the adducts, to characterize any preference by the particular inorganic ions. This project was continued by an examination of several sugars and sugar alcohols in the presence of tetraborate ions (formation of the classical Böeseken type of complexes). The volume also comprises comprehensive studies on the oxidation of aldoses to aldonic acids by bromine water, the chlorite ion, and iodine under alkaline conditions, or electrolytically. These efforts led to the industrial preparation of calcium D-gluconate from D-glucose and the commercial preparation of calcium lactobionate or lactobionic 1,5-lactone. A similar process has been used for the synthesis of

vitamin C from beet pulp and other pectic compounds that are abundant in the required D-galacturonic acid. As a general interest on cyclic polyhydroxy ketones, the volume reported new work on oxidation products from *myo*-inositol. The isolation for the first time of the enolic ketoinositol and then of triketoinositol proved the existence of the "missing link"-intermediates necessary to explain the chemical aromatization of inositols. Here again, a consecutive electron-displacement mechanism was found useful in order to clarify the formation of polyhydroxybenzenes. Furthermore, the synthesized 2-oxo-1,3-bis(phenylhydrazono) derivative of triketoinositol was readily converted (*via* catalytic reduction), for the first time, into the important antibiotic streptomycin (see *NBS Highlights*, 1965). The volume concludes with a multi-page report on the infrared absorption spectra of a series of fully acetylated pyranoses. Although this technique is useful in structural characterization of sugars (or ester groups), the anomeric identification of sugars is less reliable. Consequently, the infrared studies reported are of historical importance and of little practical value in regard to conformational assignments as compared to n.m.r. spectroscopy.

Volume 3 is divided into seven sections: (XII) Carbon-14- and Tritium-Labeled Carbohydrates; (XIII) Reaction of Carbohydrates with Hydroxyperoxides; (XIV) Miscellaneous Reactions and Procedures; (XV) Patents; (XVI) Non-Carbohydrate Papers; (XVII) Index of Original Publications; and (XVIII) Author and Subject Indexes. As a significant milestone in Dr. Isbell's professional life may be regarded his pioneer work in development and implementation of radioisotope-labeled carbohydrates. Recognition by chemists, biochemists, bacteriologists, and biologists that radioactive carbohydrates provide a tool for attacking many previously unsolved problems led to a demand for sugars position-labeled with carbon-14 or tritium. Of the many new and powerful tools with which modern organic chemists find themselves equipped, carbon-14 and tritium are among the most versatile. ^{14}C-Labeled aldoses (C-1, -2, or -6), ^{14}C-labeled disaccharides (lactose, maltose, β-gentiobiose), or tritium-labeled alditols are a few examples from a list of radioactive sugars synthesized and commercialized by N.B.S. The scientific community is grateful for these well-executed efforts. Tritium-labeled carbohydrates, especially alditols, have been found particularly suitable for the study of isotope effects and reaction mechanisms. Similarly, an application of carbon-14 tracer techniques has been particularly valuable in the study of complex biological mixtures, as well as in enzyme chemistry, metabolism, and photosynthesis. A part of the volume is devoted to a long-standing interest in the mechanism of degradation of sugars by peroxides. It was estalished that, under suitable conditions, alkaline peroxides oxidatively degrade aldoses, ketoses, alditols, alduronic acids, and keto acids, as well as hexodiuloses, by nucleophilic addition of a hydroperoxide anion to the carbonyl function, to give an adduct; this then decomposes into cleavage products. Similar results were observed with 2-deoxyaldoses, disaccharides, and L-ascorbic acid; also, with triketoinositol, cyclic ketones, and oxocarbons. The action of the Fenton reagent ($Fe^{2+} + H_2O_2$) on sugars was also studied; here,

the decomposition of the peroxide adduct may take place by a free-radical process as well as by an ionic mechanism.

Dr. Isbell's work leaves a remarkable imprint on the profession of the carbohydrate chemist, and the three-volume set now belongs to the innovative annals of classical carbohydrate chemistry. The set, in addition to reporting pioneer work on pyranose conformations, is a useful reference source; it also contains an abundance of carbohydrate reaction-mechanisms.

Fortunately, because of its low price, the three-volume set is highly recommended to every carbohydrate chemist and every chemical library.

I conclude with a citation from a special book announcement by the Division of Carbohydrate Chemistry. "This set chronicles the advancement of carbohydrate chemistry from the early days of Claude Hudson to the present. In addition to their historical value, many of the articles are still of current interest, a testament to Professor Isbell's vision for the future of the field".

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