A thorough study of this reaction and its scope is continuing.

GEORGE HERBERT JONES LABORATORY
UNIVERSITY OF CHICAGO W. H. URRY
CHICAGO 37, ILLINOIS J. W. WILT

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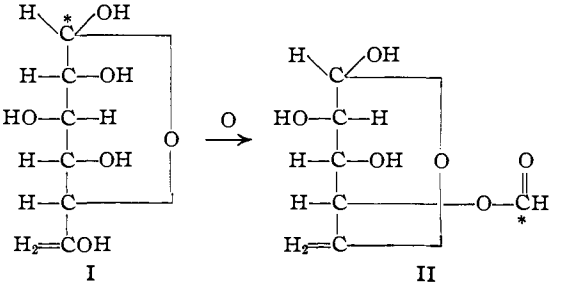
SHORTENING THE CARBON CHAIN OF SUGARS[1]

Sir:

Several methods have been described for preparing sugars with fewer carbons than the starting compound by degradation of the appropriate higher-numbered family member. A critical evaluation of the various methods has been presented by Pigman and Goepp.[2] The author has now found that a reasonably selective degradation also may be achieved by direct oxidation of reducing sugars with lead tetraacetate or sodium bismuthate. The reaction appears to be controlled partly by the relative ease with which the oxidant cleaves hemiacetal-glycol groups,[3,4] *i.e.*, the diol of carbons 1 and 2 in the cyclic form of the reducing sugar (I), and also by the consequent formation of a stable formyl ester (II) which prevents attack of the lower portion of the molecule. Thus D-arabinose is easily prepared in at least 35% yield by oxidation of D-mannose in acetic acid with 1.5 moles of lead tetraacetate. The glycol cleavage is not, however, confined exclusively to carbons 1 and 2 for still lower members, such as D-erythrose, are also produced and indeed become the major products when a larger proportion of oxidant is used. The reaction has also been used to prepare D-arabinose from D-glucose, and D-lyxose from D-galactose, and appears to be applicable to reducing sugars generally.



I II

In addition to its use as a preparative method the reaction is well suited to the stepwise degradation of sugars containing radioactive carbon. For example, the possibility of radioactive-carbon transfer during an experiment with a sugar labeled in carbon atom 1 may be examined conveniently on the micro scale. Thus 0.5 mg. of glucose-1-C^{14} (I) (diluted with 1.5 mg. of glucose) was oxidized in 97% acetic acid with lead tetraacetate equivalent to 1–1.5 moles per mole and, after precipitation of lead, the formyl esters were gently hydrolyzed. The products were separated on the paper chromatogram and radioactive areas were located by radioautography and by scanning with an end-window counter. The oxidation products, arabinose and erythrose, were non-radioactive while the unoxidized glucose retained its activity. It was evident, therefore, that the radioactivity resided entirely in carbon atom 1 of the glucose, in agreement with the expected result. A chromatogram of the oxidation products prior to hydrolysis contained radioactive spots, one of which gave the characteristic pentose color. These compounds were undoubtedly the expected intermediate formates esterified with the radioactive formic acid derived from carbon atom 1 (*e.g.*, II) since after hydrolysis they were replaced on the chromatogram by the free, non-radioactive, pentose and tetrose.

It is seen also that the radioactivity of carbons 1 and 2, and possibly of other carbon atoms, in samples of glucose of unknown labeling may be assayed by difference, by determining the specific activities of the individual sugars in the oxidation mixture after elution from the chromatogram.

The work will be described in detail elsewhere.

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DIVISION OF APPLIED BIOLOGY
NATIONAL RESEARCH LABORATORIES A. S. PERLIN
OTTAWA, CANADA

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THE SYNTHESIS OF β-HYDROXY-β-METHYLGLUTARIC ACID IN RAT LIVER HOMOGENATES[1]

Sir:

β,β-Dimethylacrylic acid has been postulated as a precursor of the isoprene-like unit which is thought to polymerize to rubber[2] in plants and to cholesterol in animal tissues.[3] It has been found recently that the rat liver homogenate preparation of Bucher[4] could synthesize β-DMA from acetic acid.[5] Thus incubation with $C^{14}H_3COOH$ gave β-DMA labeled chiefly in carbons 2, 4 and 4′ and little or no labeling in carbons 1 and 3. These results show that β-DMA, a branched chain fatty acid, is synthesized in animal tissues from small units and suggest that this compound may be a precursor of cholesterol since the pattern of labeling is similar to that postulated for the isoprenoid precursors of cholesterol by Würsch, *et al.*[3]

The fact that carboxyl labeled acetoacetate appears to be incorporated into cholesterol[6] without prior cleavage into C_2 units, seems to rule out the

(1) Issued as N. R. C. No. 3277.

(2) W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, Inc., New York, N. Y., 1948.

(3) R. Criegee, *Ber.*, **65**, 1770 (1932).

(4) R. C. Hockett and W. S. McClenahan, THIS JOURNAL, **61**, 1667 (1939).

(1) The following abbreviations are used: β-DMA = β,β-dimethylacrylic acid; β-HMG = β-hydroxy-β-methylglutaric acid; ATP = adenosine triphosphate; DPN = diphosphopyridine nucleotide; s.a. = specific activity; CoA = Coenzyme A. This investigation was supported by research grants from the Life Insurance Medical Research Fund and the Elisabeth Severance Prentiss Fund of Western Reserve University.

(2) B. Arreguin, J. Bonner and B. F. Wood, *Arch. Biochem.*, **21**, 104 (1949).

(3) J. Würsch, R. L. Huang and K. Bloch, *J. Biol. Chem.*, **195**, 439 (1952).

(4) N. L. R. Bucher, THIS JOURNAL, **75**, 498 (1953).

(5) H. Rudney, *Fed. Proc.*, **13**, 286 (1954).

(6) R. O. Brady and S. Gurin, *J. Biol. Chem.*, **189**, 371 (1951).