[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 247]

The Action of Hydrogen Peroxide in *t*-Butanol upon D-Arabinal, D-Galactal and their Acetates in the Presence of Osmium Tetroxide

BY ROBERT C. HOCKETT AND SARAH R. MILLMAN[1]

In a previous paper,[2] it was reported that both triacetyl-D-glucal and D-glucal are acted upon by hydrogen peroxide in *t*-butanol with osmium tetroxide as a catalyst, to produce mainly glucose or a glucose derivative. This production of glucose from glucal, which by the action of benzoperacid gives mostly mannose, provides a practicable method for passing from mannose to glucose which supplements the procedure of Bergmann.[3] The main objectives in investigating D-arabinal and D-galactal were to learn whether hydroxylation could be effected by the present method, and whether the products would be mainly arabinose and galactose or the epimers of these, namely, ribose and talose. The same observations were to be made with respect to the acetates of these glycals.

Each substance was treated with a double molecular proportion of the peroxide in *t*-butanol at room temperature for six or eight days. The progress of reaction could be followed polarimetrically in the case of the glycal acetates and the mixtures were worked up when a cessation of optical changes was noted. The solutions containing free glycals were usually too colored to read for several days, but faded sufficiently for an optical observation of the end-point.

In each case, after removal of excess peroxide, catalyst, butanol and acetyl groups if they were present, the products were made up to a definite volume. Aliquots were titrated to determine the non-volatile acids and the sugars were isolated as suitable derivatives.

Arabinose was isolated as such in the crystalline form. Mother liquors from which D-arabinose separated were treated with benzylphenylhydrazine and a further recovery of the sugar as benzylphenylhydrazone was achieved. After removal of excess benzylphenylhydrazine by a treatment with benzaldehyde, D-ribose was sought as the *p*-bromophenylhydrazone.

Galactose was isolated both as the characteristic methylphenylhydrazone and as mucic acid. Talose was sought as salts of talomucic acid.

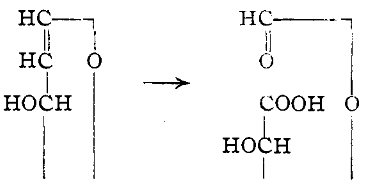
Table I summarizes the results which were obtained with the four substances investigated.

TABLE I

In each case 2 moles of peroxide was used for each mole of sample, 1 cc. of 0.5% OsO_4 was used and the volume of the solution was 25 cc.

Substance	Sample, g.	Mole	Products found	Equiv. of non-volatile acid per mole of substance taken
Diacetyl-D-arabinal	2.243	0.0112	30% D-arabinose; no ribose	Trace
D-Arabinal	3.0086	.015	17.3% D-arabinose; no ribose	0.33, D-erythronic acid identified
Triacetyl-D-galactal	2.0478	.0075	42.4% D-galactose; no talose	0.053
D-Galactal	1.3246	.0087	52.9% D-galactose; no talose	.35

It is notable that acid production is much greater from the non-acetylated glycals than from their acetyl derivatives, which seems to indicate an easier fission of the double bond. Such fission would be expected to yield D-erythronic acid from D-arabinal and D-lyxonic acid from D-galactal along with an equivalent of formic acid from each. The latter would be lost during removal of solvents.



If non-volatile acid is indeed produced from glycals in a 1:1 molecular ratio, the quantities found indicate that oxidative fission has occurred in about one-third of the sample submitted to the treatment with peroxide. From arabinal, D-erythronic acid was identified among the products, both as a calcium salt and as the phenylhydrazide. Lyxonic acid was not positively identified.

It appears from these results that the stereochemical aspect of the hydroxylation of these

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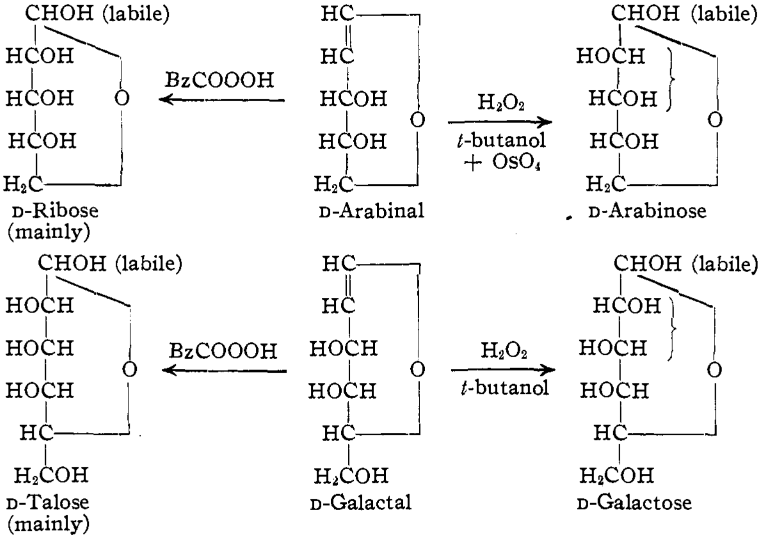
[1] This paper is taken from a thesis submitted by Sarah R. Millman in partial fulfilment of the requirements for the degree of Doctor of Philosophy in June, 1940. A paper including this material was read at the Boston Meeting of the American Chemical Society in September, 1939. Miss Millman was Ellen H. Richards Fellow in Chemistry from 1935 to 1938.

[2] Hockett, Sapp and Millman, THIS JOURNAL, **63**, 2051 (1941).

[3] Bergmann and Schotte, *Ber.*, **54**, 440, 1564 (1921).

substances by the present reagents is analogous to that observed[2] with glucal and its triacetate. The configuration assumed by the groups around carbon two on restoration of asymmetry to this carbon is mainly opposite that of the groups around carbon three. On the contrary, the Bergmann reagent gives mainly talose from galactal and galactose derivatives from substituted galactals.[4] The study will be extended to L-rhamnal and its acetate.



Experimental

Materials.—Diacetyl-D-arabinal was prepared as described by Gehrke and Aichner[5] and obtained as a sirup which after redistillation rotated[6] +265.3° (*C*, 4.00; $CHCl_3$). D-Arabinal was obtained by deacetylation of weighed samples of the corresponding acetate by barium hydroxide under quantitative conditions.[5] Triacetyl-D-galactal made according to the procedure of Levene and Tipson[4] and redistilled in high vacuum, rotated[6] −11.6° (*C*, 1.00; $CHCl_3$, 22°). On deacetylating as these authors describe, crystalline D-galactal melting 98–100° was obtained. Other materials were the same as those described in the previous communication.[2]

Procedure.—Solutions were made up with the concentrations and compositions indicated in Table I and were kept in a constant temperature room at 20° until optical changes ceased. Solvent, excess peroxide and catalyst were removed by evaporation under reduced pressure. The residues from arabinal and galactal were then made up to 25.0 cc. with water. In the cases of the glycal acetates, the residues were first dissolved in methanol and deacetylated by the overnight action of barium methylate (5 cc. of approx. 0.1 *N* barium methylate to the sample in 20 cc. of methanol). After quantitative removal of barium ion with sulfuric acid and evaporation of methanol under reduced pressure, the samples were made up to 25.0 cc. with water. These solutions were then examined as to optical rotation and an aliquot part of each was titrated with standard sodium hydroxide solution.

Products from Diacetyl-D-arabinal.—The aqueous solution rotated −5.25° in a 1-dm. tube. If only D-arabinose were present, this reading would correspond to a 74.3% yield. The pentose, isolated crystalline by evaporation and treatment with alcohol and ether, weighed 0.1934 g., rotated −98.8° (*C*, 1.06; H_2O)[6] and melted 148–150°. It was converted to its benzylphenylhydrazone[7] which melted from 172–173°. The mother liquors yielded 0.4093 g. more benzylphenylhydrazone of the same melting point. Since experiments with pure D-arabinose yielded only 73% of the calculated amount of benzylphenylhydrazone, the quantity isolated from the reaction products was estimated to be equivalent to 0.3114 g. of the sugar. After treatment of the mother liquors with benzaldehyde to regenerate all remaining sugars from their hydrazones, a search for D-ribose was made with *p*-bromophenylhydrazine.[8] No ribose *p*-bromophenylhydrazone was obtained although control experiments under similar conditions yielded it readily.

Products from D-Arabinal.—The analysis was conducted in the same manner with the results indicated in Table I. When a considerable amount of acid was indicated by titration, an aliquot part of the solution was neutralized with calcium carbonate and evaporated dry. Methyl cellosolve extraction removed non-salt material leaving a salt which when washed and dried was analyzed.

Anal. Calcd. for $(C_4H_4O_2)_2Ca$: Ca, 30.97; C, 12.95. Found: Ca, 31.70; C, 12.93. Since the analysis was close to that of calcium D-erythronate, a sample was freed from calcium by means of sulfuric acid and treated with phenylhydrazine in an ethyl acetate solution. The recrystallized phenylhydrazide melted from 125–127° (recorded value, 128°).

Products from Triacetyl-D-galactal.—The aqueous solution rotated +3.12° in a 1-dm. tube. This would indicate a 71.5% yield of galactose if no other substance contributed to the rotation. D-Galactose methylphenylhydrazone melting 178–181° and melting at the same point when mixed with an authentic specimen, was obtained in a yield of 0.3000 g. Mother liquors, after treatment with benzaldehyde to regenerate sugars from hydrazones and complete extraction of aromatic substances with chloroform, were oxidized by nitric acid (sp. gr. 1.10).[7] A total of 0.1943 g. of mucic acid was obtained, melting 214–215° without depression when mixed with authentic acid, and showing characteristic properties under the polar-

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(4) Levene and Tipson, *J. Biol. Chem.*, **93**, 631 (1931).

(5) Gehrke and Aichner, *Ber.*, **60**, 918 (1927).

(6) All rotations cited refer to specific rotations of the D line of sodium at 20°.

(7) Van der Haar, "Anleitung zum Nachweis und Bestimmung der Monosaccharide," Berlin, 1920, p. 167.

(8) Karrer, *Helv. Chim. Acta*, **18**, 1445 (1935).

izing microscope. Talomucic acid could not be found.

Products from D-Galactal.—These products were similarly examined (Table I). Attempts to isolate a crystalline derivative of the non-volatile acid found were not successful. The presence of D-lyxonic acid is surmised.

Summary

1. Four unsaturated sugar derivatives, diacetyl-D-arabinal, D-arabinal, triacetyl-D-galactal and D-galactal were treated with hydrogen peroxide in *t*-butanol with osmium tetroxide as a catalyst.

2. D-Arabinose was identified as a reaction product from both arabinal and its diacetate and the yield was determined roughly. D-Ribose was not found.

3. D-Galactose was identified and roughly estimated as a product from galactal and its triacetate. D-Talose was not found.

4. D-Arabinal and D-galactal were partially oxidized by the reagent producing, respectively, D-erythronic acid and (probably) D-lyxonic acid.

5. The stereochemical aspects of the reaction are discussed.

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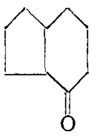
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

A New Synthesis of 4-Ketohexahydroindan

BY W. E. BACHMANN AND W. S. STRUVE[1]

4-Ketohexahydroindan (I), which has been prepared previously from indan[2] and from δ-ketosebacic acid,[3] has now been synthesized from 2-carboethoxycyclopentanone. The potassium derivative of the latter compound reacted with ethyl γ-bromobutyrate to give ethyl γ-(1-carboethoxy-2-ketocyclopentyl)-butyrate (II) in good yield. By hydrolysis of the ester followed by decarboxylation of the dicarboxylic acid, γ-(2-ketocyclopentyl)-butyric acid (III) was obtained. The methyl ester of this keto acid was converted to the cyanohydrin, methyl γ-(2-hydroxy-2-cyanocyclopentyl)-butyrate (IV). When the cyanohydrin was dehydrated with thionyl chloride and pyridine according to the procedure used by Cook and Linstead on an analogous compound,[4] and the unsaturated cyanide was hydrolyzed with concentrated hydrochloric acid, a crystalline unsaturated acid was obtained which is probably γ-(2-carboxycyclopenten-1-yl)-butyric acid (V), but the results were not reproducible. By dehydrating the cyanohydrin by means of thionyl chloride and pyridine entirely in the cold and hydrolyzing the resultant unsaturated cyanide with dilute alkali, a different unsaturated acid was obtained which is probably γ-(2-carboxycyclopenten-2-yl)-butyric acid (VI). Both unsaturated acids gave the same reduced acid γ-(2-carboxycyclopentyl)-butyric acid (VII) on hydrogenation with Adams platinum catalyst. It is not known whether this saturated acid is the *cis* or *trans* form.



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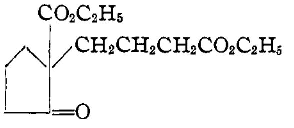

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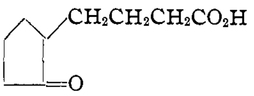

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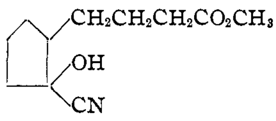

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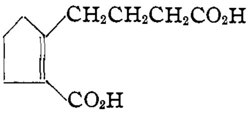

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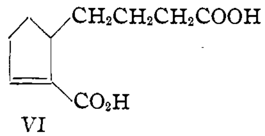

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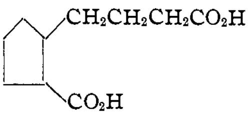

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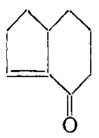

VIII

γ-(2-Carboxycyclopenten-2-yl)-butyric acid (VI) was cyclized by means of acetic anhydride to what is probably 4-ketohexahydroindene-3 (VIII). This is an isomer of the compound obtained by Hückel and Schlüter[3] by treating δ-ketosebacic acid with acetic anhydride and believed by them to be 4-ketohexahydroindene-8, although the position of the double bond was not definitely

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[1] Du Pont Post-doctoral Fellow.

[2] Hückel and Goth, *Ber.*, **67**, 2104 (1934).

[3] Hückel and Schlüter, *ibid.*, **67**, 2107 (1934).

[4] Cook and Linstead, *J. Chem. Soc.*, 946 (1934).