[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

Synthesis and Characterization of 2,3-Di-*O*-methyl-D-arabinose[1]

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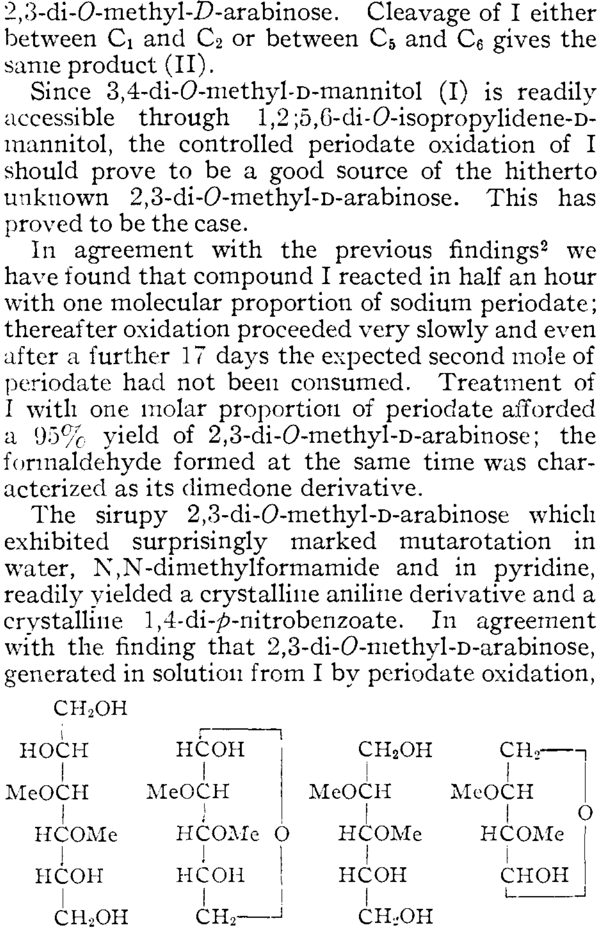
2,3-Di-*O*-methyl-D-arabinose (II) has been obtained from 3,4-di-*O*-methyl-D-mannitol by controlled periodate oxidation. The properties of II and some of its derivatives are described.

Treatment of 3,4-di-*O*-methyl-D-mannitol (I) with sodium periodate has been shown[2] to result in the rapid consumption of one molecular proportion of oxidant with the liberation of one molecular proportion of formaldehyde. Our investigations into cyclic acetal formation in periodate-oxidized carbohydrates[3-5] indicated that the consumption of one instead of two moles of periodate probably was due to the formation of the cyclic acetal II, namely, 2,3-di-*O*-methyl-*D*-arabinose. Cleavage of I either between C_1 and C_2 or between C_5 and C_6 gives the same product (II).

Since 3,4-di-*O*-methyl-D-mannitol (I) is readily accessible through 1,2;5,6-di-*O*-isopropylidene-D-mannitol, the controlled periodate oxidation of I should prove to be a good source of the hitherto unknown 2,3-di-*O*-methyl-D-arabinose. This has proved to be the case.

In agreement with the previous findings[2] we have found that compound I reacted in half an hour with one molecular proportion of sodium periodate; thereafter oxidation proceeded very slowly and even after a further 17 days the expected second mole of periodate had not been consumed. Treatment of I with one molar proportion of periodate afforded a 95% yield of 2,3-di-*O*-methyl-D-arabinose; the formaldehyde formed at the same time was characterized as its dimedone derivative.

The sirupy 2,3-di-*O*-methyl-D-arabinose which exhibited surprisingly marked mutarotation in water, N,N-dimethylformamide and in pyridine, readily yielded a crystalline aniline derivative and a crystalline 1,4-di-*p*-nitrobenzoate. In agreement with the finding that 2,3-di-*O*-methyl-D-arabinose, generated in solution from I by periodate oxidation, is stable to periodate presumably because of the presence of the pyranose ring, it was observed, as expected, that after isolation pure II was relatively stable to periodate. On the other hand, the open chain 2,3-di-*O*-methyl-D-arabitol (III), obtained from II by reduction with sodium borohydride, readily reacted with one molar proportion of periodate to give 2,3-di-*O*-methyl-D-threose (IV) the chemistry of which will form the subject of a later communication.



I II III IV

Experimental

Unless stated otherwise evaporations were conducted *in vacuo* at 35–40° (bath temp.).

Oxidation of 3,4-Di-*O*-methyl-D-mannitol with Sodium Periodate.—To a solution of 3,4-di-*O*-methyl-D-mannitol[9] (0.84 g., m.p. 152°, $[\alpha]^{21}\text{D}$ +40° in water (c 1)) in water (35 ml.), was added 0.163 *N* sodium metaperiodate (50 ml.) and the volume was adjusted to 100 ml. The reaction mixture, which was kept in the dark at 22°, showed this series of changes in specific optical rotation based on the weight of the 3,4-di-*O*-methyl-D-mannitol: $[\alpha]^{22}\text{D}$ −76° (after 3 min.), −84.5° (5 min.), −90.5° (10 min.), −92° (15 min.), −93° (25 min.), −94° (30 min.). At this time the consumption of periodate[6] was 1.0 mole per mole of 3,4-di-*O*-methyl-D-mannitol.

The mixture was treated first with dilute aqueous barium chloride until no more precipitate was produced and then with barium carbonate (0.2 g.), filtered and the residue washed with water. The combined filtrate and washings were concentrated and the distillate *A* collected for characterization of the formaldehyde formed during the oxidation. The residue was extracted with ethanol, the extract was filtered, evaporated and the sirupy product purified by extraction with acetone. Filtration and concentration gave 2,3-di-*O*-methyl-D-arabinose as a clear, pale yellow sirup which appeared from paper chromatography to be pure since it consisted of only one component, *Rf* 0.81 (solvent: pyridine–ethyl acetate–water (1:2.5:3.5),[7] 0.49 (solvent: butanone–water azeotrope,[8] characteristic trailing exhibited) using ammoniacal silver nitrate as the spray reagent.[9]

Treatment of a portion of the distillate *A* obtained above with dimedone reagent in the usual way gave the characteristic formaldehyde derivative, m.p. and mixed m.p. 195° (after recrystallization from 50% aqueous ethanol).

Distillation of the crude 2,3-di-*O*-methyl-D-arabinose obtained above gave the pure material as a clear, colorless liquid, 0.674 g., b.p. (bath temp.) 140-145° (1 mm.), $n^{24}\text{D}$ 1.4707, $[\alpha]^{20}\text{D}$ −61° after 5 min, in water (c 1.1) changing in 16 hr. to −110°: $[\alpha]^{19}\text{D}$ −31° after 3 min. in N,N-dimethylformamide (c 1) changing in 6 days to +4°; $[\alpha]^{24}\text{D}$ −37° after 5 min. in pyridine (c 1.7) changing in 3 days to −17°. *Anal.* Calcd. for $C_7H_{14}O_5$: OCH_3, 34.8. Found: OCH_3 35.3.

A solution of 2,3-di-*O*-methyl-D-arabinose (28 mg.) in dry pyridine (0.7 ml) was treated with *p*-nitrobenzoyl chloride (75 mg.) for 1 day at room temperature. The reaction mixture was poured into a saturated sodium bicarbonate solution, and the crystalline solid so formed was filtered and washed with water. Recrystallization either from chloroform–light petroleum ether, or better still from methanol, of the crude product, m.p. 148°, which appears to consist of anomeric forms, gave 2,3-di-*O*-methyl-D-arabinose 1,4-di-*p*-nitrobenzoate, m.p. 184°, $[\alpha]^{23}\text{D}$ +15° in chloroform (c 0.9). *Anal.* Calcd. for $C_{21}H_{20}O_{11}N_2$: C, 53.13; H, 4.22; N, 5.86. Found: C, 53.02; H, 4.24; N, 6.12.

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(1) This Paper No. 3974 Scientific Journal Series, Minnesota Agricultural Experiment Station, will form part of a thesis to be submitted by H. S. D. to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Ph.D.

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(3) J. E. Cadotte, G. G. S. Dutton, I. J. Goldstein, B. A. Lewis, F. Smith and J. W. Van Cleve, *ibid.*, **79**, 691 (1957).

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(6) L. Malaprade, *Bull. soc. chim.*, **43**, 683 (1928).

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(8) L. Boggs, L. S. Cuendet, I. Ehrenthal, R. Koch and F. Smith, *Nature*, **166**, 520 (1950).

(9) W. E. Trevelyan, D. P. Proctor and J. S. Harrison, *ibid.*, **166**, 444 (1950).

Examination of the mother liquid provided the second anomer, m.p. 158°[10] (after recrystallization from chloroform–light petroleum ether), $[\alpha]^{23}$D −12° in chloroform (*c* 0.3).

The *N*-phenyl-2,3-di-*O*-methyl-D-arabinosylamine prepared in the usual way by treatment with ethanolic aniline had m.p. 138°, $[\alpha]^{24}$D −143° after 10 min. in chloroform (*c* 0.4) changing in 4 hr. to −44° (constant value) (after recrystallization from chloroform–petroleum ether); lit.[11] m.p. 139° for L-isomer.

Prolonged Treatment of 3,4-Di-*O*-methyl-D-mannitol with Sodium Periodate.—When the periodate oxidation of 3,4-di-*O*-methyl-D-mannitol was allowed to proceed longer than 0.5 hr., the molar periodate consumption was: 1.0 mole (after 0.5 hr.), 1.06 (1.5 hr.), 1.35 (12 hr.), 1.47 (24 hr.), 1.52 (37 hr.), 1.60 (49 hr.), 1.66 (61 hr.), 1.71 (88 hr.), oxidation incomplete.

Oxidation of 2,3-Di-*o*-methyl-D-arabinose with Sodium Periodate.—When 2,3-di-*O*-methyl-D-arabinose (50 mg.) was allowed to react with 0.03 *N* sodium periodate (25 ml.) these reading changes in specific optical rotation and periodate consumption per mole of 2,3-di-*O*-methyl-D-arabinose, respectively, were observed: $[\alpha]$D −110° (after 3 min.); −110°, 0.03 mole (1 hr.); −110°, 0.103 mole (4 hr.); −105° 0.25 mole (18 hr.); −105°, 0.35 mole (30 hr.); −100°, 0.43 mole (42 hr.); −85°, 0.54 mole (56 hr.); −80°, 0.68 mole (5 days); −75°, 0.83 mole (9 days); −70°, 0.91 mole (17 days).

Reduction of 2,3-Di-*O*-methyl-D-arabinose with Sodium Borohydride.—To a solution of sodium borohydride (65 mg.) in methanol (2 ml.) was added a solution of 2,3-di-*O*-methyl-D-arabinose (298 mg.) in methanol (10 ml.). After 3 hr. the reaction mixture was treated with an additional portion (25 mg.) of sodium borohydride. Since this addition produced no change in rotation (observed for 2 hr.), the reaction mixture was neutralized with dilute acetic acid (tested with universal *p*H indicator paper) and evaporated to dryness. The residue was boiled for 4 hr. with acetic anhydride (10 ml.) in the presence of anhydrous sodium acetate (0.5 g.) to facilitate[12] the isolation of the product. The reaction mixture was poured with stirring into water and the product extracted with chloroform. After washing with dilute sodium bicarbonate and with water, the chloroform extract was dried ($MgSO_4$) and evaporated. The 2,3-di-*O*-methyl-D-arabitol triacetate (400 mg.) thus obtained showed $[\alpha]^{23}$D +21° in ethanol (*c*, 4).

The sirupy 2,3-di-*O*-methyl-D-arabitol triacetate was heated for 0.5 hr. with *N* ethanolic potassium hydroxide (6 ml.). After standing overnight the solution was treated with water (10 ml.), deionized by passing successively through a cation (Amberlite IR-120) and an anion (Duolite A4) exchange resin. Evaporation of the solution yielded 2,3-di-*O*-methyl-D-arabitol as a clear, light-yellow liquid (208 mg.), $[\alpha]^{19}$D +5° in ethanol (*c*, 4), *R* 0.31 (solvent, butanone–water azeotrope; spray reagent, ammoniacal silver nitrate).

Treatment of 2,3-di-*O*-methyl-D-arabitol (25 mg.) with *p*-nitrobenzoyl chloride (67 mg.) in pyridine (1 ml.) in the usual way, gave the corresponding 1,4,5-tri-*p*-nitrobenzoate, m.p. 131.5°, $[\alpha]^{21}$D +43° in chloroform (*c* 0.8) (after recrystallization from acetone–ethanol). *Anal.* Calcd. for $C_{23}H_{25}O_{14}N_3$: C, 53.59; H, 4.02; N, 6.70; OCH_3, 9.88. Found: C, 53.99; H, 4.09; N, 6.61; OCH_3, 9.4.

Oxidation of 2,3-Di-*O*-methyl-D-arabitol with Sodium Periodate.—A solution of 2,3-di-*O*-methyl-D-arabitol in 0.044 *M* sodium periodate was allowed to stand at room temperature. After keeping overnight, 0.91 mole of periodate was consumed per mole of 2,3-di-*O*-methyl-D-arabitol. Addition of barium chloride to remove iodate and periodate, filtration and evaporation gave a distillate which was shown to contain formaldehyde since it yielded the crystalline dimedone derivative, m.p. and mixed m.p. 190°. The other product of this reaction, namely, 2,3-di-*O*-methyl-D-threose, is being examined and will form the subject of a later communication.

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(10) *Cf.* H. C. Srivastava and F. Smith, THIS JOURNAL, **79**, 982 (1957).

(11) F. Smith, *J. Chem. Soc.*, 753 (1939).

(12) H. Klosterman and F. Smith, THIS JOURNAL, **74**, 5336 (1952).

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[CONTRIBUTION FROM THE NAVAL STORES STATION[1]]

The Decomposition of Pinane Hydroperoxide. II[2]

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Further studies of the decomposition of pinane hydroperoxide have revealed that the yield of pinan-2-ols can be increased to nearly 50% by carrying out the reduction in the presence of both pinane and a base. Evidence also was obtained for attack at the secondary carbon atoms of pinane during the oxidation and for isomerization of pinane to monocyclic hydrocarbons during the decomposition.

The previous paper of this series[4] reported the identification of 2,2-dimethyl-3-ethylacetylcyclobutane as one of the major decomposition products of pinane hydroperoxide. It was observed that in the absence of pinane up to half of the pinane hydroperoxide decomposed was converted to high boiling tars during decomposition and distillation. Little or no monomeric bicyclic products were obtained under these conditions. However, when pinane was used as a diluent, the yield of tars was reduced to about 28%, the yield of the ketone was increased to about 20% and some isopinan-2-ol[5] was isolated.

In view of the well known instability of the bicyclic terpenes toward acids it seemed reasonable that acids formed during the preparation and decomposition of the pinane hydroperoxide contributed to the destruction of the expected bicyclic products and the formation of tars. This was supported by the fact that the use of a diluent which lowered the concentration of acids decreased the production of tars during decomposition and increased the yield of isopinan-2-ol.

In the present investigation, the formation of acids during the peroxidation was minimized by operating at a relatively low temperature and terminating the oxidation before peroxide decomposition became excessive. Decomposition was

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(1) One of the laboratories of the Southern Utilization Research & Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

(2) Presented before the 6th Southeastern Regional American Chemical Society Meeting, Birmingham, Ala., October 21–23, 1954.

(3) General Electric Co., Waterford, N. Y.

(4) G. A. Schmidt and G. S. Fisher, THIS JOURNAL, **76**, 5426 (1954).

(5) The term "iso" has been widely used to designate *p*-menthane derivatives, such as isomenthol, in which the methyl and isopropyl groups are *cis*, as well as to denote a *cis* relation of the methyl group to the isopropylidene bridge in the 3- and 4-hydroxypinanes. The authors feel that use of the same convention in naming the two pinan-2-ols is preferable to the use of trivial names such as methyl nopinol or the prefixes *cis* and *trans*.