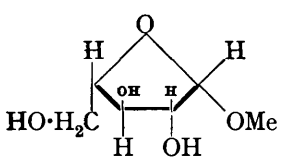
154. 2 : 3-*Dimethyl* l-*Arabinose and its Derivatives.*

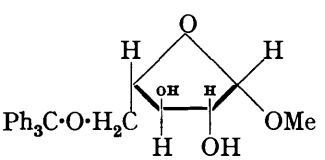
By F. Smith.

A preparation of 2 : 3-dimethyl *l*-arabinose has been effected by the following series of reactions : *l*-arabinose ⟶ methyl-*l*-arabofuranoside ⟶ 5-*trityl methyl*-l-*arabofuranoside* ⟶ 5-*trityl* 2 : 3-*dimethyl methyl*-l-*arabofuranoside* ⟶ 2 : 3-dimethyl methyl-*l*-arabinoside ⟶ 2 : 3-dimethyl *l*-arabinose. From the last the following crystalline derivatives have been prepared : 3-*methyl* l-*arabinose phenylosazone*, 2 : 3-*dimethyl* l-*arabinose anilide*, 2 : 3-dimethyl γ-*l*-arabonolactone, 2 : 3-dimethyl *l*-arabonamide, and α-*hydroxy*-βγ-*dimethoxy*-l-*araboglutaramide*.

Autohydrolysis of arabic acid furnishes among other products 3-*d*-galactosido-*l*-arabinose, which can be transformed into heptamethyl 3-*d*-galactopyranosido-*l*-arabopyranose and heptamethyl 3-*d*-galactopyranosido-*l*-arabofuranose according to the conditions of methylation adopted (preceding paper). These two methylated disaccharides furnish 2 : 4-dimethyl and 2 : 5-dimethyl *l*-arabinose respectively. 2 : 3-Dimethyl *l*-arabinose, recently obtained as one of the products of hydrolysis of a methylated araban (Hirst and Jones, J., 1938, 504), and its derivatives were required for comparison purposes and for reference compounds in the study of polysaccharide gums.



(I.)



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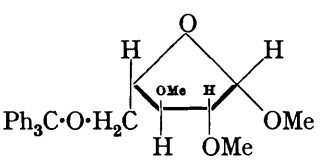

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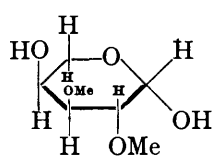
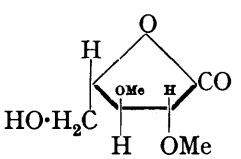


(IV.)



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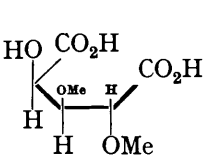

(VI.)

Methyl *l*-arabofuranoside (I) (Haworth and Baker, J., 1925, **127**, 365) was allowed to react with triphenylmethyl chloride in pyridine, 5-*trityl methylarabofuranoside* (II) being obtained. Methylation of the latter with Purdie's reagents gave 5-*trityl* 2 : 3-*dimethyl methylarabofuranoside* (III). The trityl residue was then removed by means of hydrogen chloride in chloroform and the methylarabofuranoside obtained was hydrolysed by heating with aqueous acid. The 2 : 3-dimethyl *l*-arabinose (IV), which formed a crystalline *anilide*, gave, after oxidation with bromine, a crystalline lactone (V). An aqueous solution of this exhibited the slow mutarotation characteristic of γ-lactones. When treated with ammonia, the lactone was smoothly transformed into 2 : 3-dimethyl *l*-arabonamide. This amide gave a negative Weerman test for α-hydroxy-amides (*Rec. Trav. chim.*, **1917**, **36**, 16), showing that the hydroxyl on C_2 must be protected by a methyl residue. This view was confirmed by the fact that when 2 : 3-dimethyl *l*-arabinose (IV) was treated with phenylhydrazine there was obtained 3-*methyl* l-*arabinose phenylosazone*, the methoxyl residue on C_2 being eliminated in the process. Finally, by oxidation with nitric acid, the compound (IV) yielded α-hydroxy-βγ-dimethoxy-*l*-araboglutaric acid (VI). Since the oxidation of the primary alcohol group occurs without loss of methoxyl, the second methyl group is not terminal. α-*Hydroxy*-βγ-*dimethoxy*-l-*araboglutaramide* was derived from the methyl ester of (VI) and gave a positive Weerman test, thus providing additional proof of the presence of a free hydroxyl group on C_4.

Experimental.

5-*Trityl Methyl*-l-*arabofuranoside* (II).—Methyl-*l*-arabofuranoside (1 part) was dissolved in pyridine (2 parts) and allowed to react with trityl chloride (0·95 mol.) at 20° for 5 days. The solution was then poured into water, and the insoluble syrup washed several times by decantation with dilute acetic acid (3%). The syrup, dissolved in chloroform, was washed with dilute acetic acid, to remove the last traces of pyridine, and then with water, and finally dried over anhydrous magnesium sulphate. Evaporation of the solvent gave a glassy residue of 5-*trityl methyl*-l-*arabofuranoside* in almost quantitative yield. It had $[\alpha]_D^{20°}$ — 17° in chloroform (*c*, 1·4) (Found : OMe, 8·6. $C_{25}H_{26}O_5$ requires OMe, 7·6%).

5-*Trityl* 2 : 3-*Dimethyl Methyl*-l-*arabofuranoside* (III).—5-Trityl methyl-*l*-arabofuranoside was methylated with methyl iodide and silver oxide in the usual way, the material being isolated by means of acetone. After three such treatments the product was isolated as a glass, which had $[\alpha]_D^{20°}$ — 12·3° in chloroform (*c*, 1·6) (Found : OMe, 19·5. $C_{27}H_{30}O_5$ requires OMe, 21·4%).

2 : 3-*Dimethyl Methyl*-l-*arabinoside*.—A solution of 5-trityl 2 : 3-dimethyl methyl-*l*-arabofuranoside (20 g.) in chloroform (500 c.c.) at 0° was saturated with hydrogen chloride, kept for 1 hour each at 0° and 20°, and then exhaustively extracted with water. The combined aqueous extracts were neutralised with silver carbonate, filtered, and evaporated to dryness under diminished pressure, giving a syrup, which was boiled with methyl-alcoholic hydrogen chloride (200 c.c. of 1%) for 8 hours to effect glycoside formation. Removal of the solvent yielded 2 : 3-dimethyl methyl-*l*-arabinoside as an oil (6·0 g.), b. p. 86° (bath temp.)/0·04 mm.; n_D^{19} 1·4505 (Found : OMe, 46·7. Calc. for $C_8H_{16}O_5$: OMe, 48·4%).

2 : 3-*Dimethyl* l-*Arabinose* (IV).—A solution of 2 : 3-dimethyl methylarabinoside (5·5 g.) in dilute sulphuric acid (100 c.c. of 3%) was heated on a boiling water-bath until the rotation became constant; it was then neutralised with barium carbonate, filtered, and evaporated to dryness. The syrupy 2 : 3-dimethyl *l*-arabinose obtained (5·0 g.) had $[\alpha]_D^{18°}$ + 86·4° (initial value in water, *c*, 1·0), changing in 2½ hours to + 107° (equilibrium value) (Found : OMe, 34·0. Calc. for $C_7H_{14}O_5$: OMe, 34·8%).

When 2 : 3-dimethyl *l*-arabinose (0·1 g.) was heated with aniline (0·05 g.; 1 mol.) in absolute alcoholic solution (3 c.c.) for 4 hours, 2 : 3-*dimethyl* l-*arabinose anilide* was produced. After removal of the excess of solvent the solid residue was triturated with ether–light petroleum, and recrystallised from acetone–light petroleum; m. p. 139° (Found : C, 61·5; H, 7·6; OMe, 24·3; N, 5·6. $C_{13}H_{19}O_4N$ requires C, 61·65; H, 7·6; OMe, 24·5; N, 5·5%).

3-*Methyl* l-*Arabinose Phenylosazone*.—The syrupy 2 : 3-dimethyl *l*-arabinose (1 mol.) was heated with phenylhydrazine (4 mols.) in dilute acetic acid (5 c.c.) for 5 hours at 80°. The *phenylosazone* obtained contained only one methoxyl residue and separated from aqueous alcohol in yellow needles, m. p. 163° (Found : OMe, 8·4; N, 16·3. $C_{18}H_{22}O_3N_4$ requires OMe, 9·1; N, 16·4%).

2 : 3-*Dimethyl* γ-l-*Arabonolactone* (V).—2 : 3-Dimethyl *l*-arabinose (3 g.) was dissolved in water (30 c.c.) and allowed to react with bromine (3 mols.) at 25° for 3 days; the solution then

no longer reduced Fehling's solution. The excess of bromine was removed by aeration, and hydrobromic acid with silver oxide. The neutral solution was filtered, treated with hydrogen sulphide to remove silver, again filtered, and then evaporated under diminished pressure. The syrupy lactone thus produced distilled as a colourless oil (2·5 g.), b. p. 120° (bath temp.)/0·03 mm., $n_D^{18°}$ 1·4600; $[\alpha]_D^{18°}$ − 36° (initial value in water; *c*, 1·3), changing in 11 days to − 27° (equilibrium value) (Found: OMe, 35·1%). When the lactone was treated with methyl-alcoholic ammonia at − 5° for 12 hours, the corresponding amide was produced. Evaporation of the solvent under reduced pressure left a residue of 2 : 3-dimethyl *l*-arabonamide. After recrystallisation from alcohol–acetone–ether the product had m. p. 162°; $[\alpha]_D^{21°}$ + 17·4° in water (*c*, 1·2). This amide gave no sodium *iso*cyanate when treated with sodium hypochlorite, for on addition of semicarbazide, no hydrazodicarbonamide was produced (Found: C, 43·6; H, 7·8; OMe, 32·1; N, 7·4. Calc. for $C_7H_{15}O_5N$: C, 43·5; H, 7·8; OMe, 32·1; N, 7·25%).

Regeneration of the lactone from the amide (1·2 g.) was effected by heating the latter with a saturated solution of barium hydroxide (30 c.c.) at 75° in a current of nitrogen until evolution of ammonia ceased. The solution was neutralised with carbon dioxide, filtered, and treated with a slight deficiency of 0·1N-sulphuric acid (50 c.c.). The barium sulphate was filtered off, and the solution evaporated to dryness. The lactone thus produced distilled as a colourless oil (0·9 g.), b. p. (bath temp.) 120°/0·01 mm., $n_D^{19°}$ 1·4602. The material was only faintly acid to litmus and did not reduce Fehling's solution. The lactone crystallised on keeping at 0° and after recrystallisation from ether–light petroleum it had m. p. 35°; $[\alpha]_D^{18°}$ − 38° (initial value in water; *c*, 1·2); − 31·3° (6 days); − 25·4° (12 days, constant value). The free acid liberated from the sodium salt had $[\alpha]_D^{18°}$ + 8·2° (initial value in aqueous sulphuric acid solution; *c*, 1·0); + 4·0° (3 hours); ∓ 0·0° (6 hours); − 2° (8 hours); − 9° (15 hours); − 16° (25 hours); − 22° (40 hours); − 24·4° (55 hours); − 25·4° (74 hours, constant value) (Found: C, 47·6; H, 6·8; OMe, 35·5. Calc. for $C_7H_{12}O_5$: C, 47·7; H, 6·9; OMe, 35·2%).

α-Hydroxy-βγ-dimethoxy-l-araboglutaramide.—A solution of the crystalline 2 : 3-dimethyl *γ-l*-arabonolactone (1 g.) in nitric acid (10 c.c., *d* 1·42) was heated for 6 hours at 80°, diluted with water, and freed from solvent and nitric acid by distillation under diminished pressure, the last traces of acid being removed by addition of methyl alcohol. The dry syrup was boiled with methyl-alcoholic hydrogen chloride (50 c.c. of 2%) for 8 hours, and the solution cooled, neutralised with silver carbonate, filtered, and evaporated to dryness. The *methyl* ester (0·6 g.), b. p. 140° (bath temp.)/0·02 mm., $n_D^{20°}$ 1·4465, $[\alpha]_D^{20°}$ + 6° in water (*c*, 0·8) (Found: OMe, 48·0. $C_9H_{16}O_7$ requires OMe, 52·4%), was treated with methyl-alcoholic ammonia for 2 days at − 5°, and the excess of the solvent then removed. *α-Hydroxy-βγ-dimethoxy-l-araboglutaramide*, recrystallised from aqueous ethyl alcohol, had m. p. 195°, $[\alpha]_D^{21°}$ + 26·8° in water (*c*, 0·8) (Found: C, 40·8; H, 7·0; OMe, 30·2; N, 13·7. $C_7H_{14}O_5N_2$ requires C, 40·8; H, 6·9; OMe, 30·1; N, 13·6%).

A solution of the amide (20 mg.) in water (0·5 c.c.) was allowed to react with a slight excess of 1·5N-sodium hypochlorite solution for 30 minutes at 0°, the excess of hypochlorite destroyed with a few drops of sodium thiosulphate solution, and solid sodium acetate added, followed by three drops of a saturated solution of semicarbazide hydrochloride; after a few minutes hydrazodicarbonamide separated, m. p. and mixed m. p. 258°.

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