247. *Synthesis of Some Derivatives of* D- *and* L-*Arabinose.*

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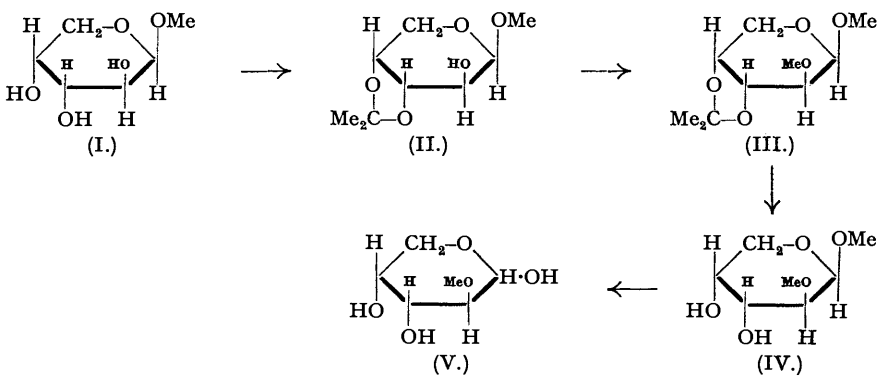
D-Arabinose has been converted into 2-*methyl* D-*arabinose via* 3 : 4-*monoacetone* β-*methyl*-D-*arabopyranoside* and its 2-methyl derivative. Crystalline 2-p-*toluenesulphonyl* 3 : 4-*monoacetone* β-*methyl*-D-*arabopyranoside* has also been isolated together with the crystalline p-*toluenesulphonylhydrazone* of 2-*methyl* D-*arabinose*. Analogous compounds, as well as the crystalline anilide of 2-*methyl monoacetone* L-*arabinose*, have been obtained from L-arabinose.

The identification of D-arabofuranose as a constituent sugar of the polysaccharides of *M. tuberculosis* (Haworth, Stacey, and Kent, *Abs. Amer. Chem. Soc.*, Chicago Meeting, 1946, 5 R.) is of considerable interest. Although the L-isomer has been found extensively in natural polysaccharides such as the plant gums, reports of the occurrence of D-arabinose in natural compounds are comparatively rare. Its presence in barbaloin has been claimed by Leger (*Bull. Soc. chim.*, 1910, **7**, 800) and it has been found in some animal secretions (Neuberg and Wohlgemuth, *Z. physiol. Chem.*, 1902, **35**, 31).

The wide occurrence of L-arabinose has led to the formation and study of many of its derivatives whereas the reactions and compounds of D-arabinose are incompletely known. With a view to obtaining reference compounds and to the chemical synthesis of biologically important pentose-related substances, *e.g.*, 2-deoxyribose compounds, a number of derivatives of D-arabinose were synthesised. The present paper describes these and also some derivatives of L-arabinose required for similar purposes.

D-Arabinose obtained from calcium gluconate by essentially the method of Hockett and Hudson (*J. Amer. Chem. Soc.*, 1934, **56**, 1562) was converted into crystalline β-methyl-D-arabopyranoside (I). When this compound was treated with acetone in the presence of a suitable dehydrating agent, it gave a syrupy monoacetone derivative which was shown to be 3 : 4-monoacetone β-methyl-D-arabopyranoside (II) as follows. On its being methylated with



methyl iodide and silver oxide there was formed a crystalline monomethyl monoacetone β-methyl-D-arabopyranoside (III) (m. p. 45°) which, on hydrolysis with methanolic hydrogen

chloride, afforded the 2-methyl β-methyl-D-arabopyranoside (IV) of von Schmidt and Simon (*J. pr. Chem.*, 1939, **152**, 190). This compound underwent further hydrolysis with aqueous acid giving 2-methyl D-arabinose (V) which was converted into a crystalline *p*-toluenesulphonylhydrazone having properties identical with those of the β-methyl-D-arabinose *p*-toluenesulphonylhydrazone obtained by von Schmidt and Simon (*loc. cit.*) by the degradation of 3-methyl D-glucose.

From the monoacetone glycoside (II) there were obtained the crystalline 2-*p*-toluenesulphonyl and 2-methanesulphonyl derivatives (m. p. 134° and 135° respectively), which could not be converted directly into the 2-iodo-compound.

In the presence of acetone and excess of concentrated sulphuric acid, β-methyl-D-arabopyranoside and monoacetone β-methyl-D-arabopyranoside, lost their glycosidic groups and were converted into diacetone D-arabinose which had properties analogous to those of the diacetone L-arabinose synthesised by Svanberg and Bergman (*Chem. Zentr.*, 1924, i, 1021).

It has been reported (Ohle and Berend, *Ber.*, 1927, **60**, 810) that treatment of L-arabinose with acetone in the presence of anhydrous cupric sulphate gave a monoacetone derivative which reduced Fehling's solution. An analogous *monoacetone* derivative has now been prepared from D-arabinose, and although the structure of this has not been fully investigated it is likely that the *iso*propylidene group engages the 3 : 4-positions. Thus on further treatment with acetone containing 2% sulphuric acid the monoacetone compound was converted into a non-reducing diacetone D-arabinose. This was identical with a diacetone D-arabinose prepared by the action of acetone containing 3% sulphuric acid upon either β-methyl-D-arabinoside or monoacetone β-methyl-D-arabopyranoside in which it is known that the acetone group engaged the 3 : 4-positions.

In the L-series, β-methyl-L-arabopyranoside was converted into 3 : 4-*monoacetone* β-*methyl*-L-*arabopyranoside*, from which a crystalline 2-*toluenesulphonyl* derivative (m. p. 134°) was obtained. Methylation of the monoacetone glycoside afforded 2-*methyl* 3 : 4-*monoacetone* β-*methyl*-L-*arabopyranoside*. In this compound scission of the acetone group was effected by treatment with acetic acid, and the product, 2-*methyl* β-*methyl*-L-*arabopyranoside*, was hydrolysed with dilute sulphuric acid giving 2-*methyl* L-*arabinose* from which a crystalline *phenylhydrazone* was isolated.

Treatment of 2-methyl L-arabinose with acetone in the presence of a dehydrating agent yielded a crystalline 2-*methyl monoacetone* L-*arabinose* which was reducing to Fehling's solution and, on being boiled with ethanolic aniline, gave a readily crystallised *anilide*.

Experimental.

D-*Arabinose from Calcium* D-*Gluconate*.—The method employed was a modification of that described by Hockett and Hudson (*J. Amer. Chem. Soc.*, 1934, **56**, 1632). A solution of ferric acetate, prepared by addition of 21 g. of ferric sulphate in 60 c.c. of water to 10·5 g. of barium acetate in 60 c.c. of water, was mixed with calcium D-gluconate (200 g. in 2 l. of water), and the resulting solution heated to boiling. After filtration, the solution was warmed to 60° and 120 c.c. of 30% hydrogen peroxide in 1 l. of water were slowly added. After 2 hours, a further 120 c.c. of 30% hydrogen peroxide was added to the dark solution (at 60°). After 2 hours the solution was filtered and evaporated to 200 c.c. under diminished pressure. To the resulting syrup methanol (1600 c.c.) and ether (800 c.c.) were added. The precipitate formed was separated and the filtrate concentrated further to a thick syrup, which readily crystallised on standing at 0°. Yield of recrystallised D-arabinose, 51 g.; m. p. 155°; $[\alpha]_D^{18°}$ − 105° (*c*, 1·5 in water).

D-Arabinose (2 g.) was shaken with dry acetone (1 l.), anhydrous cupric sulphate (80 g.), and barium carbonate (10 g.) for 8 days at room temperature. The filtered solution was evaporated to dryness and the resulting syrup recrystallised from ether (0·2 g.); m. p. 78°; $[\alpha]_D^{19°}$ − 111° (*c*, 1·1 in water, no mutarotation) (cf. monoacetone L-arabinose, Ohle and Berend, *loc. cit.*; m. p. 76—77°; $[\alpha]_D$ + 128°). Treatment of this product with acetone and concentrated sulphuric acid yielded diacetone D-arabinose; m. p. 40—41° $[\alpha]_D^{19°}$ −4° (*c*, 1·1 in water).

3 : 4-*Monoacetone* β-*Methyl*-D-*arabinoside*.—D-Arabinose (25 g.) was converted into the glycoside by being refluxed with methanolic hydrogen chloride (1%; 500 c.c.) for 10 hours. The β-form readily crystallised from a small amount of methanol; m. p. 168°. Yield, 12 g.

β-Methyl D-arabinose (2 g.) was shaken at room temperature with dry acetone (100 c.c.) and concentrated sulphuric acid (1·0 c.c.) for 72 hours. The acid was neutralised (litmus) by addition of anhydrous sodium carbonate. The filtered solution was evaporated to dryness, and the remaining syrup distilled in a high vacuum; b. p. 90° (vap. temp.)/0·3 mm.; $n_D^{19°}$ 1·4600 (Found: OMe, 9·2. Calc. for $C_9H_{16}O_5$: OMe, 8·9%).

β-Methyl-D-arabinoside (10 g.) or 3 : 4-monoacetone β-methyl-D-arabinoside (10 g.) was shaken for 24 hours with dry acetone (300 c.c.) and concentrated sulphuric acid (5 c.c.) at room temperature. After neutralisation with sodium carbonate the filtered solution was evaporated to dryness and distilled in a high vacuum. The distillate rapidly crystallised from ligroin; m. p. 41°; OMe content, nil (m. p. 41·5—43° for diacetone L-arabinose; Svanberg and Bergman, *loc. cit.*).

2-p-*Toluenesulphonyl* 3 : 4-*Monoacetone* β-*Methyl*-D-*arabinoside*.—3 : 4-Monoacetone β-methyl-D-arabinoside (0·2 g.) was dissolved in dry pyridine (7 c.c.) to which was added *p*-toluenesulphonyl chloride (0·8 g.). After 24 hours at room temperature the mixture was poured into water (200 c.c.), and the crude *product* which separated was recrystallised from alcohol (0·2 g.); m. p. 134° (Found: C, 53·3; H, 6·1; S, 9·3; OMe, 9·2. $C_{16}H_{22}O_7S$ requires C, 53·5; H, 6·15; S, 8·95; OMe, 8·65%).

2-*Methanesulphonyl* 3 : 4-*Monoacetone* β-*Methyl*-D-*arabinoside*.—3 : 4-Monoacetone β-methyl-D-arabinoside (0·3 g.) was dissolved in dry pyridine (10 c.c.) and treated with methanesulphonyl chloride (0·5 g.). After 48 hours the solution was poured into water (250 c.c.). No solid separated, and the aqueous solution was extracted several times with chloroform. The chloroform solution was washed with dilute hydrochloric acid and then with water and finally dried (Na_2CO_3). Evaporation of the resulting solution afforded a syrup which readily crystallised (0·2 g.) from alcohol; the *compound* had m. p. 135° (Found: OMe, 10·9. $C_{10}H_{18}O_7S$ requires OMe, 11·0%).

Attempted Formation of 2-*Iodo* 3 : 4-*Monoacetone* β-*Methyl*-D-*arabinoside*.—(i) 2-*p*-Toluenesulphonyl 3 : 4-monoacetone β-methyl-D-arabinoside (0·2 g.) was dissolved in dry acetone (20 c.c.) to which was added dry sodium iodide (2 g.). The mixture was heated at 110° for 12 hours in a sealed tube. The starting material (0·16 g.) was recovered unchanged.

(ii) 2-Methanesulphonyl 3 : 4-monoacetone β-methyl-D-arabinoside (0·5 g.) was heated with dry acetone (25 c.c.) and sodium iodide (2 g.) in a sealed tube at 110° or 130° for 48 hours. The starting material was recovered unchanged.

Methylation of 3 : 4-*Monoacetone* β-*Methyl*-D-*arabopyranoside*.—The monoacetone glycoside (0·7 g.) was heated for 6 hours with methyl iodide (5 c.c.) and silver oxide (1 g.). After 3 such methylations, the syrupy product was distilled; b. p. 136—137° (bath temp.)/2 mm. The distillate ($n_D^{18°}$ 1·4520) readily crystallised on standing, and after recrystallisation from acetone–ligroin the *compound* had m. p. 43°; $[\alpha]_D^{19°}$ − 145° (*c*, 1·8, in water) (Found: C, 55·1; H, 8·2; OMe, 28·2. $C_{10}H_{18}O_5$ requires C, 54·9; H, 8·3; OMe, 28·4%). Yield, 0·5 g.

Formation of 2-*Methyl* β-*Methyl*-D-*arabopyranoside*.—2-Methyl 3 : 4-monoacetone β-methyl-D-arabopyranoside (0·3 g.) was heated for 3 hours with methanolic hydrogen chloride (20 c.c.; 5%); $[\alpha]_D^{20°}$ − 130° → − 35°. The resulting solution was neutralised (litmus) with silver carbonate and the filtrate evaporated, giving a syrup, $n_D^{14°}$ 1·4602, which crystallised on standing (0·2 g.). After recrystallisation from methanol–ether the *compound* had m. p. 48° (Found: OMe, 31·6. $C_7H_{14}O_5,H_2O$ requires OMe, 31·6%).

2-*Methyl* D-*Arabinose*.—2-Methyl β-methyl-D-arabopyranoside (0·2 g.) was heated at 100° for 6 hours with sulphuric acid (N; 10 c.c.); $[\alpha]_D^{18°}$ − 96° → − 56°. The solution reduced Fehling's solution and was neutralised (phenolphthalein) with sodium hydroxide and evaporated, and the residue extracted with chloroform. On evaporation of the chloroform extract to dryness, 2-*methyl* D-*arabinose* was obtained as a reducing syrup (0·1 g.); $n_D^{17°}$ 1·4710 (Found: OMe, 18·6. $C_6H_{12}O_5$ requires OMe, 18·9%).

Treatment of this syrup with phenylhydrazine (3 drops), glacial acetic acid (4 drops), and water (2 c.c.) at room temperature for several hours afforded a crystalline *phenylhydrazone* which, after recrystallisation from aqueous ethanol, had m. p. 113° (Found: OMe, 12·2. $C_{12}H_{18}O_4N_2$ requires OMe, 12·2%).

Formation of 2-*Methyl* D-*Arabinose* p-*Toluenesulphonylhydrazone*.—2-Methyl D-arabinose (0·1 g.) was dissolved in absolute alcohol (8 c.c.), treated with *p*-toluenesulphonylhydrazine (Freudenberg and Blümmel, *Annalen*, 1924, **440**, 51) (0·1 g.), and the mixture heated under reflux for 1 hour. On removal of the solvent, the p-*toluenesulphonylhydrazone* separated, and after recrystallisation from aqueous alcohol had m. p. 143° (decomp.); $[\alpha]_D^{16°}$ − 17·0° (*c*, 0·8 in water) (initial value) (Found: OMe, 9·1. $C_{13}H_{20}O_6N_2S$ requires OMe, 9·4%).

3 : 4-*Monoacetone* β-*Methyl*-L-*arabinoside*.—(*a*) β-Methyl-L-arabopyranoside (2 g.) was shaken with acetone (250 c.c.) and anhydrous copper sulphate (10 g.) for 7 days. The solution was then filtered and the filtrate concentrated under diminished pressure to a syrup (2 g.), $n_D^{22°}$ 1·4642.

(*b*) (Cf. Robertson and Speedie, *J.*, 1934, 824.) The arabinoside (2 g.) was shaken with acetone (20 c.c.) containing hydrogen chloride (2 g.) for 48 hours. The clear solution was then poured into excess of dilute sodium hydroxide solution and the product extracted thrice with chloroform. The chloroform solution was then dried (Na_2CO_3), filtered, and concentrated under reduced pressure to a syrup (1·8 g.) which was distilled; the *compound* had b. p. 105° (bath temp.)/0·01 mm.; $n_D^{22°}$ 1·4628 (Found: C, 52·9; H, 8·1. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9%)

The corresponding 2-p-*toluenesulphonyl* derivative was prepared by reaction of 3 : 4-monoacetone β-methyl-L-arabinoside (4·0 g.) with *p*-toluenesulphonyl chloride (4·5 g.; 1·1 ml.) in dry pyridine (25 c.c.) at 40°. The warm solution was diluted with water and cooled, and the product filtered off and dried. Yield, 4·5 g.; m. p. 134° (Found: C, 53·8; H, 5·6; OMe, 8·6. $C_{16}H_{22}O_7S$ requires C, 53·6; H, 6·2; OMe, 8·7%). Hydrolysis of this product with boiling 50% acetic acid gave 2-*p*-toluenesulphonyl β-methyl-L-arabinoside in low yield as deliquescent crystals of low melting point. The product was not further examined.

2-*Methyl* 3 : 4-*Monoacetone* β-*Methyl*-L-*arabopyranoside*.—3 : 4-Monoacetone β-methyl-L-arabopyranoside (2 g.) was methylated with silver oxide and methyl iodide and the product distilled under reduced pressure. The corresponding 2-*methyl ether* distilled at 100° (bath temp.)/0·01 mm.; $n_D^{20°}$ 1·4481 (Found: C, 54·9; H, 8·3; OMe, 28·4. $C_{10}H_{18}O_5$ requires C, 55·1; H, 8·2; OMe, 28·4%).

2-*Methyl* β-*Methyl*-L-*arabopyranoside*.—2-Methyl 3 : 4-monacetone β-methyl-L-arabopyranoside (1·86 g.) was boiled with water (20 c.c.) containing glacial acetic acid (5 c.c.) for 2 hours ($[\alpha]_D^{20°}$ +202° initial value, → + 186°). The solution was concentrated under reduced pressure to a syrup which was distilled in a vacuum; b. p. 130° (bath temp.)/0·01 mm.; $n_D^{21°}$ 1·4768. This *product* crystallised shortly after distillation; m. p. 59° (Found: C, 47·0; H, 8·2; OMe, 34·2. $C_7H_{14}O_5$ requires C, 47·2; H, 7·9; OMe, 34·8%). On recrystallisation from acetone–ether the arabinoside separated as the *monohydrate*, m. p. 47° (Found: C, 42·9; H, 7·7; OMe, 31·4. $C_7H_{14}O_5,H_2O$ requires C, 42·9; H, 8·2; OMe, 31·6%).

2-*Methyl* L-*Arabinose*.—β-Methyl 2-methyl-L-arabinoside (1·06 g.) was hydrolysed with boiling N-sulphuric acid (25 c.c.) for 4 hours; $[\alpha]_D^{20°}$ + 234° (initial value) → + 99° (constant value). The

cooled solution was neutralised with barium carbonate and filtered, and the filtrate evaporated under reduced pressure to a syrup which did not crystallise. With alcoholic phenylhydrazine crystalline 2-*methyl* L-*arabinose phenylhydrazone* was obtained, m. p. 116° after recrystallisation from alcohol–ether–light petroleum (Found : C, 56·8; H, 7·8; N, 10·9; OMe, 12·4. $C_{12}H_{18}O_4N_2$ requires C, 56·7; H, 7·1; N, 11·0; OMe, 12·2%). No crystalline anilide could be isolated.

On shaking an acetone solution with anhydrous copper sulphate 2-methyl L-arabinose gave 2-*methyl monoacetone* L-*arabinose* which, on evaporation of the filtered solution, was isolated as a crystalline reducing solid, m. p. 117°. It was purified by recrystallisation from acetone and sublimed in a vacuum (Found : C, 52·8; H, 7·8; OMe, 15·1. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8; OMe, 15·2%).

On being heated with alcoholic aniline this product gave crystalline 2-*methyl monoacetone* L-*arabinose anilide*, m. p. 143° after recrystallisation from ethyl alcohol (Found : C, 64·4; H, 7·4; N, 4·8; OMe, 11·0. $C_{15}H_{21}O_4N$ requires C, 64·6; H, 7·4; N, 5·0; OMe, 11·1%).

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