211. *Reactions of β-Methylarabinoside. Part I. 3 : 4-Benzylidene and 3 : 4-Ethylidene β-Methylarabinopyranoside.*

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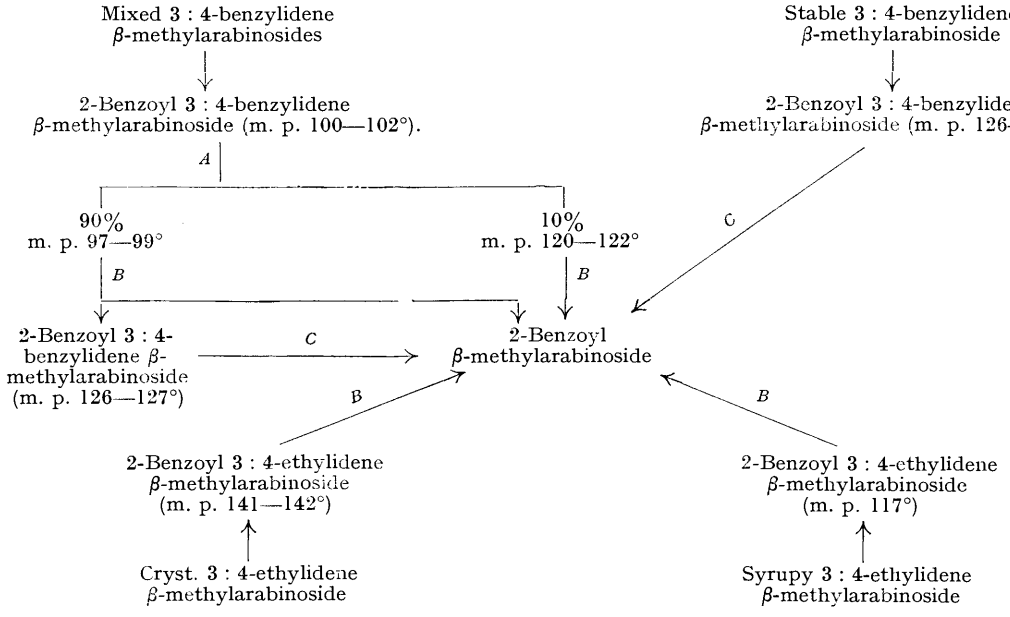
When benzaldehyde and β-methylarabinoside are heated together, a syrupy mixture of the two possible 3 : 4-*benzylidene β-methylarabinopyranosides* is obtained. The two forms are distinguished by the difference in the stability of the benzylidene group in the isomeric 2-*benzoyl* 3 : 4-*benzylidene β-methylarabinosides*. The preparation of 2-*methyl arabinose* is described. Paraldehyde and β-methylarabinoside give a syrupy mixture of the two 3 : 4-*ethylidene β-methylarabinopyranosides* from which one form can be separated in the crystalline state. No difference in the stability of the ethylidene groups in the isomeric 2-benzoyl 3 : 4-ethylidene β-methylarabinosides is apparent.

When benzaldehyde and β-methylarabinoside are heated together, syrupy benzylidene β-methylarabinoside is obtained. On standing, the compound partly decomposes to β-methylarabinoside and benzaldehyde. If the conditions used for the condensation are too drastic, dibenzylidene arabinose is also formed. Hydrolysis with 0·25% hydrochloric acid removes the benzylidene residue but not the methyl group, while under identical conditions methylarabinofuranosides are converted into arabinose. This stability of the methyl group (Haworth, *Ber.*, 1928, **61**, 50) shows that the compound is benzylidene β-methylarabinopyranoside. Methylation of the syrup by Purdie and Irvine's method followed by acid hydrolysis gives a methyl β-methylarabinoside which crystallises as a monohydrate. Removal of the glycosidic group leads to a methyl arabinose from which arabinosazone is obtained with loss of the methyl group. Thus the monomethyl arabinose is 2-*methyl arabinose* and the benzylidene compound 3 : 4-*benzylidene* β-*methylarabinopyranoside*. It is interesting to note that the benzylidene group of 3 : 4-*benzylidene* 2-*methyl* β-*methylarabinoside* is more stable than that of the parent substance. On condensation with acetone, 2-methyl arabinose forms a crystalline product in which C_1 must be unsubstituted as the compound is reducing and methylation followed by hydrolysis regenerates 2-methyl arabinose. The stability of the glycosidic group in the 2-methyl acetone methylarabinosides shows that the substance is pyranosidic and hence the acetone derivative is 2-*methyl* 3 : 4-*acetone arabinose*.



Some 3 : 4-benzylidene β-methylarabinoside, prepared six months previously, after being freed from β-methylarabinoside which had formed, gave on benzoylation 2-*benzoyl* 3 : 4-*benzylidene* β-*methylarabinoside*, m. p. 126—127°. The benzylidene group of this product is stable to 0·05N-hydrochloric acid. Freshly prepared 3 : 4-benzylidene β-methylarabinoside on benzoylation yields 2-*benzoyl* 3 : 4-*benzylidene* β-*methylarabinoside*, m. p. 100—102°. When this is hydrolysed with 0·05N-hydrochloric acid until no further change in optical rotation takes place, the product is 2-*benzoyl* β-*methylarabinoside* together with the 2-benzoyl 3 : 4-benzylidene β-methylarabinoside, m. p. 126—127°, previously obtained. It is apparent, therefore, that the 2-benzoyl 3 : 4-benzylidene β-methylarabinoside, m. p. 126—127°, is stable under the conditions of hydrolysis used, while the form, m. p. 100—102°, is a mixture of isomers of which one is benzoyl benzylidene β-methylarabinoside, m. p. 126—127°, and the other is more readily hydrolysed to 2-benzoyl β-methylarabinoside. By repeated extraction with small amounts of light petroleum the mixture (m. p. 100—102°) can be separated into two fractions, (*a*) m. p. 97—99° (90%), and (*b*) m. p. 120—122° (10%). Hydrolysis of (*a*) with 0·05N-hydrochloric acid leads to crystals, m. p. 116—118°, which can be separated by fractional solution into equal parts of 2-benzoyl 3 : 4-benzylidene β-methylarabinoside, m. p. 126—127°, and 2-benzoyl β-methylarabinoside. Thus (*a*) is a mixture of approximately equal parts of benzoyl benzylidene β-methylarabinoside, m. p. 126—127°, and the less stable isomer. When (*b*) is hydrolysed with 0·05N-hydrochloric acid, a quantitative yield of 2-benzoyl β-methylarabinoside is obtained, showing (*b*) to be the more easily hydrolysed form of 2-benzoyl 3 : 4-benzylidene β-methylarabinoside. If the concentration of hydrochloric acid used for hydrolysis is increased to 0·1N, then the more stable form of 2-benzoyl 3 : 4-benzylidene β-methylarabinoside also gives a quantitative yield of 2-benzoyl β-methylarabinoside. The difference in the products obtained by benzoylating freshly prepared and stored specimens of 3 : 4-benzylidene β-methylarabinoside is due to the fact that

the freshly prepared syrup is a mixture of two isomeric forms—produced because of the asymmetry of the benzylidene group—while in the stored specimen all the more readily hydrolysed form has decomposed, leaving, after purification, only the more stable isomer. The reactions are summarised in the scheme on p. 987.

Paraldehyde and β-methylarabinoside, when shaken with anhydrous copper sulphate and sulphuric acid, yield crystals of ethylidene β-methylarabinoside together with a smaller amount of a syrup of the same analysis. Both compounds give only β-methylarabinoside when hydrolysed with 0·25% hydrochloric acid, and hence both are arabinopyranosides. When the crystals are benzoylated, a *benzoyl ethylidene β-methylarabinoside* (m. p. 141—142°) is obtained, while the syrup gives an *isomer*, m. p. 117°. On acid hydrolysis with 0·05N-hydrochloric acid, both the isomers lead to excellent yields of 2-benzoyl β-methylarabinoside. Thus the crystals and syrup are isomeric forms of 3 : 4-*ethylidene β-methylarabinopyranoside*, the isomerism depending on the new asymmetric centre introduced with the ethylidene group.

Experimental.

Except where otherwise stated, solvents were removed under reduced pressure at $\not>45°$ and benzene and chloroform solutions were dried over anhydrous sodium sulphate. The light petroleum used had b. p. 60—80°.

β-Methyl-l-arabinopyranoside (I).—This method is a modification of that of Hudson (*J. Amer. Chem. Soc.*, 1925, **47**, 267). Finely powdered *l*-arabinose (50 g.) was refluxed for 7 hours with dry methanol (400 ml.) containing hydrogen chloride (1%). The crystals which appeared on cooling were filtered off and washed with dry methanol (3 × 50 ml.). The combined filtrates were refluxed for 2 hours and the solution was concentrated to 150 ml. The crystals obtained were washed with methanol (3 × 30 ml.). The combined crops on recrystallisation from absolute alcohol gave pure (I) (40 g., 73%), m. p. 169—170°, $[\alpha]_D^{18°}$ +244·8° (*c* = 1·353 in water). Hudson (*loc. cit.*) gives m. p. 169°, $[\alpha]_D^{20°}$ +245·5°.

Benzylidene β-Methylarabinoside.—(i) Under the conditions described by Freudenberg (*Ber.*, 1928, **61**, 1758) for preparing 4 : 6-benzylidene α-methylglucoside no condensation took place, unchanged (I) being recovered. (ii) The method used by Irvine and Scott (*J.*, 1913, **103**, 581) for the glucoside proved to be too drastic, leading to a low yield of impure dibenzylidene arabinose. (iii) Benzaldehyde (50 ml.) and (I) (10 g.) were heated at 140° for 4 hours while a slow stream of carbon dioxide was bubbled through the liquid. Excess of benzaldehyde was removed under reduced pressure and the syrupy product poured into benzene. Unchanged (I) (2 g.) separated (identified by m. p. and mixed m. p.) and was filtered off. After the solution had been washed with 2% sodium hydroxide and dried, the benzene was removed, leaving a pale yellow syrup (10 g.), which was divided into three portions : (*a*) Distillation (160°/0·1 mm.) led to decomposition, crystalline (I) being regenerated. (*b*) After 3 days' exposure to the atmosphere crystals appeared in the syrup, but these were shown to be (I) formed by decomposition. (*c*) Solution of the syrup in hot alcohol followed by careful precipitation with light petroleum yielded a small crop (0·6 g.) of crystals. These were dried, washed with dilute sodium hydroxide and with water, and recrystallised from methanol; m. p. 154° (Found : C, 69·1; H, 5·5; OMe, nil. Dibenzylidene arabinose, $C_{19}H_{18}O_5$, requires C, 69·9; H, 5·5%). [van Ekenstein and Blanksma (*Rec. Trav. chim.*, 1906, **25**, 183) give m. p. 154°.] The residual syrup, freed from solvent, was benzylidene β-methylarabinoside (II), $[\alpha]_D^{16°}$ +112·3° (*c* = 4·9 in chloroform) (Found : C, 61·7; H, 6·3; OMe, 12·1. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4; OMe, 12·3%). (iv) A purer product was obtained by carrying out the condensation at 135° for 3½ hours with the pressure reduced to 18 ins. of mercury. In this way (I) (10 g.) gave (II) (9·5—10 g.) free from dibenzylidene arabinose, together with unchanged (I) (2·4 g.).

Benzylidene Methyl β-Methylarabinoside.—Two methylations of (II) (9·5 g.) by Purdie and Irvine's method gave a syrup which was dissolved in benzene and extracted with water to remove partially methylated arabinosides which did not contain the benzylidene group. Removal of benzene followed by distillation gave *benzylidene methyl β-methylarabinoside* (III) as a middle fraction (9·5 g., 95%) (Found : C, 63·0; H, 6·7; OMe, 23·0. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·7; OMe, 23·3%).

Methyl β-Methylarabinoside.—(III) (7 g.) was dissolved in acetone (105 ml.) and water (140 ml.), and N/10-hydrochloric acid (105 ml.) was added. After 2 hours' refluxing, the liberated benzaldehyde was extracted with chloroform and the aqueous solution neutralised with barium carbonate. The residue obtained on evaporation to dryness was extracted with chloroform; the resultant solution yielded on concentration a stiff syrup (4 g., 80%) which crystallised immediately. Recrystallisation from ether gave white needles (3·5 g., 68%), m. p. 46—47°, $[\alpha]_D^{18°}$ +208° (*c* = 2·5 in methyl alcohol). After vacuum drying the crystal form altered and m. p. changed to 63—65°. The change is due to dehydration of *methyl β-methylarabinoside monohydrate* (Found : C, 42·9; H, 8·2; OMe, 31·9. $C_7H_{16}O_6$ requires C, 42·8; H, 8·2; OMe, 31·6%).

Methyl Arabinose.—Hydrolysis of monomethyl β-methylarabinoside with hydrochloric acid gave poor yields owing to the production of furfural derivatives. However, after 3 hours' boiling with 20 parts of sulphuric acid (5%) followed by neutralisation with barium carbonate, filtration, evaporation, and extraction with alcohol, a glass, methyl arabinose (yield 90%), was obtained; $[\alpha]_D^{18°}$ +96·0° (*c* = 5·0 in water) (Found : OMe, 18·8. $C_6H_{12}O_5$ requires OMe, 18·9%). The product, on treatment with phenylhydrazine, gave arabinosazone (m. p. 149—152°) which did not depress the m. p. of authentic arabinosazone (m. p. 151—153°) (Found : OMe, nil). Thus the compound is 2-*methyl arabinose*.

Condensation of 2-Methyl Arabinose with Acetone.—Monomethyl arabinose (3 g.) was dissolved in acetone (100 ml.) containing hydrogen chloride (0·5%), and after 2 hours the solution was poured into dilute aqueous potassium bicarbonate. Extraction with chloroform gave, on evaporation, a syrup (2·6 g., 68%) which rapidly crystallised. Recrystallisation from aqueous alcohol gave methyl monoacetone arabinose (IV), m. p. 116—118°, $[\alpha]_D^{18°}$ +91·5° in chloroform, +117·5° in acetone, +124·5° in methanol (Found : OMe, 15·6. $C_9H_{16}O_5$ requires OMe, 15·2%).

Examination of (IV).—(i) The crystals reduced Fehling's solution. (ii) Methylation gave a non-reducing syrup, $[\alpha]_D^{18}$ +124·6° (Found : OMe, 28·0. Methyl acetone methylarabinoside requires OMe, 28·8%). The acetone residue was hydrolysed from this arabinoside with sulphuric acid (0·1%) to give a non-reducing syrupy mixture of methyl methylarabinosides. Thus the acetone condensation product is 2-*methyl* 3 : 4-*monoacetone arabinose*.

Acid Hydrolysis of (II).—The substance (2 g.) was refluxed with hydrochloric acid (50 ml., 0·25%) for 6 hours. The solid, isolated after neutralisation with barium carbonate and removal of the water, was recrystallised from alcohol and identified (m. p., mixed m. p. and $[\alpha]_D$) as β-methylarabinopyranoside (1·4 g., 80%). No arabinose was detected (Fehling's solution) at any stage of the reaction.

Acid Hydrolysis of Methylarabinofuranosides.—The mixed α- and β-methylarabinofuranosides (Baker and Haworth, *J.*, 1925, **127**, 365) when treated as (II) gave arabinose (m. p., mixed m. p.) as the sole product. Thus (II) is 3 : 4-*benzylidene β-methylarabinopyranoside*.

Benzoylation of (II).—A sample of (II prepared six months previously was freed from (I) by shaking its benzene solution with water. Reaction of the purified material (3·8 g.) with benzoyl chloride (2·2 ml.) in pyridine (4 ml.) at room

temperature led, after the usual purification, to a brown syrup (3·8 g.) which on stirring with light petroleum yielded crystals. Recrystallisation from alcohol–light petroleum gave white needles. The syrup obtained by evaporation of the mother liquors yielded, after further treatment with benzoyl chloride, a further crop of crystals. The crops (3·5 g., 67%) which were identical (m. p. and mixed m. p.) were combined and recrystallised from light petroleum to give *2-benzoyl* 3 : 4-*benzylidene β-methylarabinoside*, m. p. 126—127° (V), $[\alpha]_D^{18°}$ +174·0° (*c* = 3·2 in chloroform) (Found : C, 67·1; H, 5·6; OMe, 8·6. $C_{20}H_{20}O_6$ requires C, 67·4; H, 5·6; OMe, 8·7%). The experiment was repeated on a larger scale using freshly prepared (II) (27 g.). The alcohol–light petroleum extract of the crude product (34·5 g.) yielded crystals (28·6 g., 75%) which were recrystallised from light petroleum to give *2-benzoyl* 3 : 4-*benzylidene β-methylarabinoside*, m. p. 100—102° (VI), $[\alpha]_D^{18°}$ +214·9° (in chloroform) (Found : C, 67·2; H, 5·6; OMe, 8·6%). The residual syrup (6·9 g.) after retreatment with benzoyl chloride gave crystals (1 g.) identical with (VI) and a second crop (0·2 g.) identical with (V). The non-crystalline residue was impure tribenzoyl β-methylarabinoside (Found : OMe, 6·2. Calc. for $C_{29}H_{24}O_8$: OMe, 6·5%) produced owing to the loss of the benzylidene group during benzoylation.

Examination of (V) *and* (VI).—Hydrochloric acid (1 ml., N/2) was added to a solution of (V) (0·35 g.) in acetone (9 ml.) and the solution boiled for 1 hour. No change in the optical rotation occurred and the product obtained after neutralisation and removal of the solvent proved to be unchanged (V) (m. p. and mixed m. p.).

Under the same conditions (VI) (5 g.) gave a syrup which on rubbing with ether crystallised (2·25 g., 60%); m. p. 137—140°. Recrystallisation from alcohol gave prisms of pure *2-benzoyl β-methylarabinoside* (VII), m. p. 146—147°, $[\alpha]_D^{18°}$ +257° (in acetone) (Found : C, 58·2; H, 6·0; OMe, 11·9. $C_{13}H_{16}O_6$ requires C, 58·2; H, 6·0; OMe, 11·6%). The alcoholic mother liquors on evaporation yielded (V) (0·2 g.). The ethereal liquors deposited crystals (1 g.) of unchanged (VI) (m. p. and mixed m. p.) and on further concentration a small crop (0·2 g.) of (V) (m. p. and mixed m. p.).

By repeated extraction with small amounts of light petroleum (VI) was separated into three fractions : (*a*) m. p. 97—99°; (*b*) the most soluble, crystallising as agglomerates of prisms, m. p. 120—122°, mixed m. p. with (IV) 94°; and (*c*) intermediate fractions, m. p. 100—102°.

Examination of (VI*a*).—(VI*a*) (10 g.) was hydrolysed under the same conditions as before. After 30 minutes' boiling the acidic reaction mixture was neutralised with barium carbonate and evaporated to dryness. The residue, after extraction with ether, was boiled with acetone. The ether solution gave crystals (3·6 g.) contaminated with benzaldehyde. After being washed with cold light petroleum, the crystals were fractionally extracted with boiling light petroleum to give two fractions (1·5 g.), m. p. 118—121°, and a third, m. p. 115—120°. Recrystallisation of the main fractions from aqueous alcohol gave crystals, m. p. 126—127°, shown to be identical with (V) (m. p. and mixed m. p.) (Found : OMe, 8·9%).

The acetone solution gave crystals (5·6 g.) which on recrystallisation from alcohol deposited a main crop (3·4 g.), m. p. 116—117°, and a small second crop, m. p. 108°. A further recrystallisation of the main crop did not alter the m. p., yet analysis (Found : OMe, 10·1%) showed that complete removal of the benzylidene group had not been achieved. The crystals (2·4 g.) were extracted twice with small amounts of alcohol to give two fractions, of which the first (m. p. 116—120°) was further extracted with boiling light petroleum to give a soluble fraction (1 g.), m. p. 125—126°, shown (m. p. and mixed m. p.) to be (V), and an insoluble fraction (0·1 g.) identical with the crop obtained from the second alcohol extraction. These crystals were combined and recrystallised from ether–alcohol to give colourless prisms, m. p. 146—147°, shown to be (VII) (m. p., mixed m. p., and $[\alpha]_D$). Thus (VI*a*) is a mixture of approximately equal quantities of (IV) and a more readily hydrolysed isomer which gives (VII) on hydrolysis.

Examination of (VI*b*).—(VI*b*) (2·1 g.) was hydrolysed as for (VI) to give crystals (yield 98%), m. p. 143—146°. Recrystallisation gave pure (VII) (m. p. and mixed m. p.). No other product was isolated. Thus, (VI*b*) is a pure isomer of (V), and (VI) is a mixture of (VI*b*) and (V).

Hydrolysis of (V).—(V) (1 g.) was refluxed in a solution of acetone (17 ml.) containing hydrochloric acid (3 ml., 0·67N) for 2 hours. No hydrolysed material was detected and pure (VII) (m. p. and mixed m. p.) was isolated.

Ethylidene β-Methylarabinoside.—Anhydrous copper sulphate (5 g.) and (I) (5 g.) were shaken for 1 day at room temperature with dry, neutralised paraldehyde (50 ml.) containing concentrated sulphuric acid (0·5 ml.). The filtered solution was neutralised with potassium carbonate and a syrupy product (4·5 g.) isolated after filtration and evaporation. The bulk of the syrup dissolved in boiling light petroleum, but a small amount (0·7 g.) of unchanged (I) remained undissolved. The solution, on cooling, deposited sticky crystals. After tiling and recrystallising from light petroleum, ethylidene β-methylarabinoside (VIII) (3·5 g., 58%) was obtained, m. p. 76°, $[\alpha]_D^{18°}$ +204·6° (*c* = 3·6 in chloroform) (Found : C, 50·5; H, 7·5; OMe, 16·2. $C_8H_{14}O_5$ requires C, 50·5; H, 7·4; OMe, 16·3%). After exposure to the laboratory atmosphere for 14 days some decomposition to (I) and acetaldehyde had taken place, but when the material was stored in a sealed tube it was indefinitely stable. Extraction of the tile with boiling light petroleum gave a colourless syrup (IX) (1·2 g., 20%) (Found : OMe, 16·2%). Its stability is identical with that of (VIII).

Examination of (VIII) *and* (IX).—(i) *Acid hydrolysis.* Under the conditions described for (II) the sole product in each case was (I) uncontaminated by any reducing component.

(ii) *Benzoylation.* Treatment with benzoyl chloride (25% excess) in pyridine at room temperature gave almost quantitative yields of the monobenzoyl derivatives which were recrystallised from aqueous alcohol. (VIII) gave benzoyl ethylidene β-methylarabinoside, m. p. 141—142° (X), $[\alpha]_D^{20°}$ +125° (*c* = 2·6 in chloroform) (Found : C, 54·2; H, 5·4; OMe, 10·5. $C_{15}H_{18}O_6$ requires C, 54·3; H, 5·5; OMe, 10·5%). (IX) gave benzoyl ethylidene β-methylarabinoside, m. p. 117° (XI), $[\alpha]_D^{20°}$ +109° (*c* = 3·1 in chloroform) (Found : C, 54·3; H, 5·4; OMe, 10·5%).

Acid Hydrolysis of (X) *and* (XI).—Each substance was hydrolysed separately under the conditions described for (VI*b*). The products, which were identical, proved to be (VII) (m. p. and mixed m. p.).

Thus, (VIII) and (IX) are isomeric forms of 3 : 4-*ethylidene β-methylarabinopyranoside* and (X) and (XI) the corresponding *2-benzoyl* derivatives.

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