339. *Deoxy-sugars. Part XIX. The Conversion of* D-*Arabinose into* 3-*Deoxy*-D-*xylose Derivatives.*

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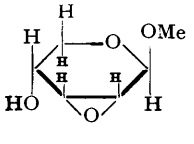
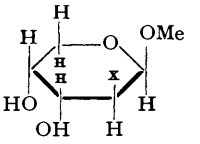
Cleavage of the anhydro-ring in β-methyl-2 : 3-anhydro-D-riboside with hydrochloric acid results in the formation predominantly of β-methyl-3-chloro-3-deoxy-D-xyloside. Scission of the anhydro-ring with lithium aluminium hydride gives mainly β-methyl-3-deoxy-D-xyloside. Fresh evidence is forwarded to support the structures already assigned to the methylglycosides of 2-deoxy-D-ribose (cf. Stacey *et al.*, *J.*, 1949, 2836).

In attempts to prepare 2-deoxyribose in improved yield, Kent, Stacey, and Wiggins (*J.*, 1949, 1232) showed that β-methyl-2 : 3-anhydro-D-riboside (I) when treated with hydrobromic acid yielded mainly β-methyl-3-bromo-3-deoxy-D-xyloside. This work has now been extended and the methylanhydroriboside has been treated with hydrochloric acid to determine whether the halogeno-derivative of arabinose (II; X = Cl) could be obtained in larger amount. The results were simliar to those obtained when using hydrobromic acid, the predominant product being β-methyl-3-chloro-3-deoxy-D-xyloside (III; X = Cl).

β-Methyl-2 : 3-anhydro-D-riboside (I) (cf. Honeyman, *J.*, 1946, 990) was prepared by the method described by Kent *et al.* (*loc. cit.*) and was characterized as its crystalline 4-acetyl-,

4-toluene-*p*-sulphonyl-, 4-benzoyl-, and 4-*p*-nitrobenzoyl derivatives. Treatment of the anhydroriboside with hydrochloric acid in acetone afforded a syrupy mixture of β-methyl-2-chloro-2-deoxy-D-arabinoside (II; X = Cl) and β-methyl-3-chloro-3-deoxy-D-xyloside (III; X = Cl). When this mixture reacted with lead tetra-acetate under Hockett and McClenahan's conditions (*J. Amer. Chem Soc.*, 1939, **61**, 1667) the uptake of the oxidant indicated the presence


(I.)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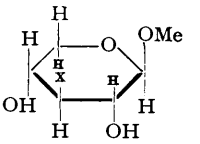
(III.)

of 18·4% of (II; X = Cl) in the mixture but, in view of the subsequent difficulties encountered in separation, this figure is considered to be high owing to some over-oxidation. The crude syrupy mixture of chloro-derivatives was hydrolysed with N-hydrochloric acid and the product examined by the chromatographic technique (see Experimental section). The chromatogram indicated that the product was predominantly derived from (III; X = Cl) and only faint indications of a derivative of (II; X = Cl) were obtained. Separation by means of the *iso*propylidene derivatives (cf. Kent *et al.*, *loc. cit.*, for separation of the corresponding bromo-derivatives) was unsuccessfully attempted but β-methyl-3-chloro-3-deoxy-D-xyloside was obtained pure.

As in the examples earlier investigated the predominant isomer was the xylose derivative, so that this method was of no value for the preparation of intermediates suitable for conversion into 2-deoxyribose derivatives. Consequently the method recently reported by Prins (*J. Amer. Chem. Soc.*, 1948, **70**, 3955) whereby 2 : 3-anhydro-rings were cleaved by lithium aluminium hydride was examined. By this method β-methyl-2 : 3-anhydro-D-riboside (I) gave a syrup which gave a positive Dische diphenylamine test (*Mikrochemie*, 1930, **8**, 4), indicating the probable presence of a derivative of 2-deoxy-D-ribose. On treatment with lead tetra-acetate, the uptake of oxidant indicated the presence of 14% of β-methyl-2-deoxy-D-riboside (II; X = H) (cf. Todd and Mukherjee, *J.*, 1947, 969), the other compound in the product being β-methyl-3-deoxy-D-xyloside (III; X = H). Attempts to separate these components as crystalline derivatives yielded only compounds derived from 3-deoxy-D-xylose, *e.g.*, 2 : 4-ditoluene-*p*-sulphonyl β-methyl-3-deoxy-D-xyloside and, after acidic hydrolysis, etc., 3-deoxy-D-xylose anilide and 3-deoxy-D-xylitol tetrabenzoate (Kent *et al.*, *loc. cit.*).

The syrupy reaction product from the ring scission was hydrolysed with N-hydrochloric acid at 100° and also at room temperature and then examined on a paper chromatogram together with authentic 2-deoxy-D-ribose and 3-deoxy-D-xylose as reference compounds. After being sprayed with aniline hydrogen phthalate and heated at 80—100° for 5 minutes, the chromatogram indicated the presence of only 3-deoxy-D-xylose. However no anomaly existed between this result and that obtained from the lead tetra-acetate oxidation since control experiments showed that the treatment required to hydrolyse β-methyl-3-deoxy-D-xyloside (III; X = H) resulted in the decomposition of the corresponding labile methylglycoside of 2-deoxy-D-ribose (II; X = H) (Deriaz, Overend, Stacey, and Wiggins, *J.*, 1949, 2836).

During this work several new derivatives of 2-deoxy-D-ribose were synthesised for comparison purposes, *e.g.*, 3 : 4-ditoluene-*p*-sulphonyl β-methyl-2-deoxy-D-ribopyranoside and 3 : 5-ditoluene-*p*-sulphonyl αβ-methyl-2-deoxy-D-ribofuranoside. The former derivative underwent no reaction when heated under anhydrous conditions with sodium iodide in acetone whereas under the same conditions the latter afforded one mol. of sodium toluene-*p*-sulphonate, thereby indicating the presence of one toluene-*p*-sulphonyloxy-group formed by esterification of a primary hydroxyl group. β-Methyl-2-deoxy-D-ribopyranoside formed a mono*iso*propylidene derivative whereas no reaction occurred with αβ-methyl-2-deoxy-D-ribofuranoside. These experiments extend and confirm the evidence put forward for the assignment of the structures to the methylglycosides of 2-deoxy-D-ribose (Deriaz *et al.*, *loc. cit.*) 2-Deoxy-D-ribose was shown to form a crystalline triacetate, tribenzoate, and *p*-nitrophenylhydrazone.

Experimental.

3 : 4-*Di*-p-*nitrobenzoyl* 2-*Toluene*-p-*sulphonyl* β-*Methyl*-D-*arabinoside*.—This was prepared by the standard method from 2-toluene-*p*-sulphonyl β-methyl-D-arabinoside and had m. p. 145—148° and $[\alpha]_D^{20}$ −207° (*c*, 0·21 in chloroform) (Found: C, 52·7; H, 3·8; N, 4·5. $C_{27}H_{24}O_{13}N_2S$ requires C, 52·6; H, 3·9; N, 4·5%).

β-Methyl-2 : 3-anhydro-D-riboside.—The anhydro-derivative was prepared both from 2-toluene-*p*-sulphonyl and from 2-methanesulphonyl β-methyl-D-arabinoside by the method described by Kent, Stacey, and Wiggins (*J.*, 1949, 1232). It was obtained as colourless needles, m. p. 52—53°, $[\alpha]_D^{18}$ −49·2°, −48·4° (*c*, 1·38, 0·43 in chloroform) (Found: OMe, 21·3. Calc. for $C_6H_{10}O_4$: OMe, 21·2%). Kent, Stacey, and Wiggins (*loc. cit.*) give m. p. 46° and $[\alpha]_D^{22}$ −35·8° in chloroform. This compound readily afforded 4-*acetyl* {m. p. 73°, $[\alpha]_D^{23}$ +22·4° (*c*, 0·45 in chloroform) (Found: C, 51·0; H, 6·5. $C_8H_{12}O_5$ requires C, 51·0; H, 6·4%)}, 4-*toluene*-p-*sulphonyl* {m. p. 89°, $[\alpha]_D^{20}$ −25·5° (*c*, 0·48 in chloroform) (Found: C, 51·9; H, 5·2. $C_{13}H_{16}O_6S$ requires C, 52·0; H, 5·3%)}, 4-*benzoyl* {m. p. 106—106·5°, $[\alpha]_D^{18}$ +25·4° (*c*, 0·47 in chloroform) (Found: C, 62·4; H, 5·4. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6%)}, and 4-p-*nitrobenzoyl* {m. p. 159—160°, $[\alpha]_D^{24}$ +24·6° (*c*, 0·33 in chloroform) (Found: C, 53·0; H, 4·3. $C_{13}H_{13}O_7N$ requires C, 52·9; H, 4·4%)} derivatives.

Treatment of β-Methyl-2 : 3-anhydro-D-riboside with Hydrochloric Acid.—β-Methyl-2 : 3-anhydro-D-riboside (1·02 g.) was boiled under reflux for 4 hours with acetone (150 c.c.) containing 5N-hydrochloric acid (5 c.c.). The solution was neutralised with lead carbonate, then filtered, and the residue washed with acetone. Evaporation of the combined filtrate and washings to remove the acetone gave a residue to which water was added. The aqueous solution was extracted with ether (4 × 20 c.c.), and the extract evaporated to yield only a small amount of residue (0·14 g.). The aqueous solution was concentrated at 40° to dryness and the solid residue was extracted with hot ethyl acetate. Evaporation of this extract to dryness yielded a pale yellow syrup (1·059 g.) which was a mixture (A) (Found: C, 39·0; H, 5·5. Calc. for $C_6H_{11}O_4Cl$: C, 39·5; H, 6·0%) of β-methyl-2-chloro-2-deoxy-D-arabinoside and β-methyl-3-chloro-3-deoxy-D-xyloside.

This mixture of chloro-derivatives (0·099 g.) was dissolved in AnalaR acetic acid (49 c.c.), and 0·0751N-lead tetra-acetate solution (in AnalaR acetic acid) (50 c.c.) was added. The solution was made up to 100 c.c. and oxidation was allowed to proceed at room temperature. At intervals aliquots (10 c.c.) were withdrawn and the extent of oxidation was determined in the usual manner. Results obtained were as follows:

Time (hours)	0·5	1·0	2·0	6·0	19·0
Uptake of $Pb(OAc)_4$ (mols.)	0·092	0·111	0·129	0·184	0·184

Attempt to prepare iso*Propylidene Derivatives from the Chloro-derivatives.*—The syrupy mixture (0·763 g.) was shaken with acetone (50 c.c.) containing 0·5% of sulphuric acid. After 12 hours the solution was neutralised with potassium carbonate, then filtered, and the filtrate evaporated to dryness at 35—40°. The syrupy residue (0·7 g.) was placed in solution in ethanol–benzene (1 : 1), on an activated alumina column (12 × 1 cm.). Elution with the same solvent mixture gave only a single fraction, as an extremely viscous pale yellow syrup (0·25 g.), b. p. 135—140° (bath-temp.)/0·008 mm., n^{18} 1·4950, $[\alpha]_D^{18}$ −24·3° (*c*, 0·74 in chloroform). It was *β-methyl-3-chloro-3-deoxy-D-xyloside* (Found: C, 39·4; H, 6·2. $C_6H_{11}O_4Cl$ requires C, 39·5; H, 6·0%). When this compound (0·065 g.) in solution in methanol (30 c.c.) was shaken at room temperature for either 5 or 7 hours in an atmosphere of hydrogen with Raney nickel and diethylamine (2 c.c.), no reaction occurred.

Hydrolysis of the Crude Mixture of Chloro-derivatives.—The syrupy mixture of chloroglycosides (A) (0·201 g.) was heated at 100° with N-hydrochloric acid (20 c.c.). The reaction was followed polarimetrically and the following values for change in optical rotation were observed:

Time (hours)	1	2	3	9	10	11	12
$[\alpha]_D^{21}$	−17·9°	−1·9°	0°	+27·9°	+27·9°	+29·8°	+29·8°

After 12 hours the solution was neutralised with silver carbonate and filtered through a charcoal pad, and the filtrate evaporated to dryness. The residue was extracted with ethanol, and the extract when concentrated gave a clear syrup (0·131 g., 58·7%) which reduced Fehling's solution. A 1% aqueous solution of this syrup was prepared and one drop was run on filter paper (Whatman No. 1) and eluted with butanol–ammonia–water in an atmosphere of butanol–water. (The solvents were prepared from butanol 40%, ethanol 10%, water 49%, and ammonia 1% by separation of the butanol phase, which was used for elution, and the aqueous phase, which was used to saturate the paper.) The chromatogram was developed in the usual way. The result indicated that the original mixture consisted predominantly of β-methyl-3-chloro-3-deoxy-D-xyloside with very faint indications of the presence of the other isomer expected.

Treatment of β-Methyl-2 : 3-anhydro-D-riboside with Lithium Aluminium Hydride.—β-Methyl-2 : 3-anhydro-D-riboside (0·303 g.) was dissolved in absolute ether (40 c.c.) and lithium aluminium hydride (0·6 g.) in absolute ether (20 c.c.) was added. The mixture was heated under reflux in anhydrous conditions for 3 hours and then a further amount of lithium aluminium hydride (0·6 g.) in absolute ether (20 c.c.) was added. Heating was continued for another hour, and then water (40 c.c.) and 5N-sulphuric acid were added cautiously to the well-stirred mixture, which was subsequently filtered. The ethereal layer was separated, the aqueous phase extracted with ether (3 × 40 c.c.), and the extract added to the ethereal layer. Evaporation of the ethereal solution, after being dried ($MgSO_4$), gave a minute amount of residue which gave a negative test with the Dische diphenylamine reagent. The aqueous solution was neutralised with ammonium carbonate and the copious precipitate filtered off and washed with a small amount of water. The filtrate and washings were combined and evaporated to dryness at 40°. The residue was extracted with hot chloroform (6 × 40 c.c.), and evaporation of the extract gave a syrupy residue (0·218 g., 71%) which gave a positive reaction with the Dische diphenylamine reagent. This residue was heated at 100° for 4 hours with N-hydrochloric acid (10 c.c.), and then the solution was neutralised (Ag_2CO_3) and stirred with charcoal. After filtration the solution was concentrated to dryness and the solid residue extracted with ethanol. Evaporation of the extract gave a clear syrup (B) (0·104

g., 60%) which readily reduced Fehling's solution. A 1% aqueous solution of this syrup was run on a paper chromatogram as described above. 1% Aqueous solutions of 2-deoxy-D-ribose and of 3-deoxy-D-xylose were also placed on the same chromatogram and run as standard materials for comparison. The chromatogram was eluted with butanol–water–ammonia, dried, sprayed with aniline hydrogen phthalate and developed by heating at 80—100° for 5 minutes. The developed chromatogram showed the presence of only 3-deoxy-D-xylose in the product from the ring scission of the anhydro-compound (cf. 3-deoxy-D-xylose, R_F 0·498, 2-deoxy-D-ribose, R_F 0·435). This product (0·1036 g.) was then subjected to a milder hydrolysis by treatment with N-hydrochloric acid at room temperature. The following changes in the optical rotation of the solution were observed:

Time (hours)	0	1	3	4	4·5	5·8	7	8	8·75	21	22·5
$[\alpha]_D^{21}$	−92·7°	−92·7°	−90·7°	−89·8°	−88·9°	−83°	−81°	−79·3°	−77·3°	−75·3°	−73·9°

After 23 hours the solution was neutralised with silver carbonate and sodium carbonate, filtered through a charcoal pad, and concentrated to dryness. The residue was extracted with hot ethanol (2 × 25 c.c.), the extract decolorised, and the clear solution concentrated to dryness leaving a syrupy residue (0·0727 g.). A 1% aqueous solution of this syrup (1 drop) was run on a paper chromatogram which was developed with aniline hydrogen phthalate in the usual manner. It showed one spot only, identical with 3-deoxy-D-xylose.

Attempts to use even milder methods for the hydrolysis of the product (0·035 g.) from the ring scission of the anhydro-compound by treatment with 0·01N-acetic acid (5 c.c.) at 100° for 2 hours, followed by evaporation to dryness at room temperature in a vacuum-desiccator over phosphoric oxide and potassium hydroxide, were unsuccessful. When the product from this treatment was run on a paper chromatogram according to the usual procedure, no spots were discernible.

Oxidation by Lead Tetra-acetate.—The syrupy deoxyglycoside mixture (0·1056 g.) was dissolved in AnalaR acetic acid (49 c.c.), and 0·074N-lead tetra-acetate in acetic acid solution (30 c.c.) was added. The solution was made up to 100 c.c. and oxidation allowed to proceed at room temperature. At suitable intervals aliquots (10 c.c.) were withdrawn and titrated iodometrically:

Time (hours)	1	3	4	6	9	23
$Pb(OAc)_4$ absorbed (mols.)	0·084	0·098	0·112	0·126	0·126	0·14

2 : 4-*Ditoluene*-p-*sulphonyl* β-*Methyl*-3-*deoxy*-D-*xyloside.*—The syrupy deoxyglycoside mixture (0·169 g.) in pyridine solution (0·5 c.c.) readily reacted with toluene-*p*-sulphonyl chloride (0·48 g.). The product was purified by passage down an alumina column (20 × 1·5 cm.) and gave crystalline 2 : 4-*ditoluene*-p-*sulphonyl* β-*methyl*-3-*deoxy*-D-*xyloside*, m. p. 89°, $[\alpha]_D^{21}$ −61° (*c*, 0·39 in chloroform) (Found: C, 52·2; H, 5·3. $C_{20}H_{24}O_8S_2$ requires C, 52·6; H, 5·3%) (cf. m. p. 99° for 3 : 4-ditoluene-*p*-sulphonyl β-methyl-2-deoxy-D-riboside).

3-*Deoxy*-D-*xylitol* 1 : 2 : 4 : 5-*Tetrabenzoate.*—The clear syrup (B) (0·347 g.) in solution in water (300 c.c.) was shaken for 18 hours at 100° in an atmosphere of hydrogen (25 atmospheres' pressure) with Raney nickel. After filtration the solution was evaporated to dryness and afforded a syrup (0·258 g.) ($[\alpha]_D^{18}$ ±0° in methanol). This (0·224 g.) was dissolved in absolute pyridine (1 c.c.), and the solution cooled to 0°. Benzoyl chloride (4·4 mols., 1·025 c.c.) was added and the mixture kept at room temperature for 12 hours. Ice-water (50 c.c.) was then added. The syrup which was precipitated was extracted with chloroform, and the extract was washed successively with dilute hydrochloric acid, sodium hydrogen carbonate solution, and water and then dried ($MgSO_4$). Evaporation of the extract gave a syrup which crystallised on nucleation with 3-deoxy-D-xylitol tetrabenzoate, m. p. 104° alone or on admixture with an authentic sample, $[\alpha]_D^{14}$ ±0° in methanol (cf. Kent *et al.*, *loc. cit.*).

Derivatives of 2-*Deoxy*-D-*ribose.*—Acetylation of 2-deoxy-D-ribose (0·296 g.) in pyridine solution (1·65 c.c.) with freshly distilled acetic anhydride (1·08 c.c.) readily gave the 1 : 3 : 4-*triacetyl* derivative as small colourless needles (from methanol), m. p. 98°, $[\alpha]_D^{23}$ −171·8° (*c*, 0·56 in chloroform) (Found: C, 50·8; H, 6·3. Calc. for $C_{11}H_{16}O_7$: C, 50·8; H, 6·2%). Davoll and Lythgoe (*J.*, 1949, 2529) report this compound as a syrup, b. p. 180° (bath-temp.)/0·1 mm., $[\alpha]_D^{17}$ −52·5° (*c*, 2·5 in chloroform).

Similarly 2-deoxy-D-ribose (0·102 g.) affords a 1 : 3 : 4-*tribenzoyl* derivative as small white nodules (from ethanol), m. p. 127°, $[\alpha]_D^{23}$ −65° (*c*, 1·02 in chloroform) (Found: C, 69·9; H, 5·4. $C_{26}H_{22}O_7$ requires C, 69·9; H, 5·0%).

2-*Deoxy*-D-*ribose* p-*nitrophenylhydrazone*, prepared by the usual procedure, had m. p. 160°, $[\alpha]_D^{14}$ −11·1° (*c*, 0·09 in ethanol) (Found: C, 49·1; H, 5·6. $C_{11}H_{15}O_5N_3$ requires C, 49·1; H, 5·6%).

3 : 4-*Ditoluene*-p-*sulphonyl* β-*Methyl*-2-*deoxy*-D-*ribopyranoside.*—Toluene-*p*-sulphonylation of β-methyl-2-deoxy-D-ribopyranoside (0·045 g.) readily yielded the 3 : 4-*ditoluene*-p-*sulphonate* as silky needles (from aqueous ethanol), m. p. 104—107°, $[\alpha]_D^{20}$ −115·5° (*c*, 6·7 in chloroform) (Found: OMe, 6·0. $C_{20}H_{24}O_8S_2$ requires OMe, 6·7%). When this compound (0·034 g.) was heated at 105—110° for 3 hours with dry sodium iodide (0·028 g.) in anhydrous acetone (8 c.c.), no visible reaction occurred and no sodium toluene-*p*-sulphonate separated.

3 : 5-*Ditoluene*-p-*sulphonyl* αβ-*Methyl*-2-*deoxy*-D-*ribofuranoside.*—Prepared by the normal procedure the *ditoluene*-p-*sulphonate* was obtained in syrupy form, $[\alpha]_D$ −121° (*c*, 0·4 in chloroform) (Found: OMe, 7·0. $C_{20}H_{24}O_8S_2$ requires OMe, 6·7%). When this was heated in dry acetone (8 c.c.) with sodium iodide (1·1 mols., 0·085 g.) at 105—110° for 3 hours, rapid precipitation of sodium toluene-*p*-sulphonate occurred. This was collected by filtration in a sintered glass crucible, washed with dry acetone, dried at 120° for 1 hour, and weighed (0·095 g. ≡1 mol.).

3 : 4-iso*Propylidene β-Methyl-2-deoxy*-D-*ribopyranoside.*—β-Methyl-2-deoxy-D-ribopyranoside (0·1 g.) yielded the **3 : 4-iso*propylidene*** derivative (30 mg.) as a colourless oil, b. p. 110—115°/12 mm., n^{20} 1·4456, $[\alpha]_D^{20}$ −47·8° (*c*, 1·04 in water), which gave a positive iodoform test (Found : OMe, 16·0. $C_9H_{16}O_4$ requires OMe, 16·4%).

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