DEHYDRATION OF 2-(D-*arabino*-TETRAHYDROXYBUTYL)FURANS
PART II[1]. THE STERIC COURSE AND MECHANISM OF THE REACTION*

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ABSTRACT

Acid-catalyzed dehydration of methyl and ethyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoate (**4a, b**) takes place preferentially with inversion of configuration at C-1′, yielding the corresponding 5-(1,4-anhydro-D-*ribo*-tetrahydroxybutyl)-2-methyl-3-furoate (**6a, b**), and, to a much smaller extent, with retention of configuration giving the isomeric D-*arabino* anhydro-derivative (**5a, b**). The reaction is reversible, the equilibrium being set up when there is a high concentration of the thermodynamically more-stable D-*ribo* anhydro-derivative in the presence of the D-*arabino* isomer, the starting (D-*arabino*-tetrahydroxybutyl)furan (**4a, b**), and a compound thought to be methyl (or ethyl) 2-methyl-5-(D-*ribo*-tetrahydroxybutyl)-3-furoate (**13**). A mechanism is proposed for this reaction which involves the C-1′ carbonium ion **15** as the key intermediate. The anhydro derivatives of the D-*ribo* and D-*arabino* configurations can be distinguished by their optical rotations, the chemical shifts of H-1′, and the $J_{1',2'}$ coupling constants.

INTRODUCTION

2-(D-*arabino*-Tetrahydroxybutyl)furans (**1**), the condensation products of D-glucose with β-dicarbonyl compounds[2], have the property[3] of losing a molecule of water when treated with acids, yielding 2-(1,4-anhydrotetrahydroxybutyl)furans (**2**). A similar reaction is given by other compounds having a polyhydroxyalkyl chain linked to a heterocycle (pyrrole[4], benzimidazole[5], 2-phenyl-1,2,3-triazole[6]) and by the sugar osazones[7]. We have demonstrated previously[1] that the products so far isolated in the dehydration of 2-(D-*arabino*-tetrahydroxybutyl)furans (**1**) have the D-*ribo* configuration (**3**), thus indicating that the reaction takes place with inversion of configuration at C-1′. In order to obtain a more-detailed knowledge of the steric course and mechanism of this reaction, we have carried out a study of the dehydration reactions of methyl and ethyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoate (**4a, b**).

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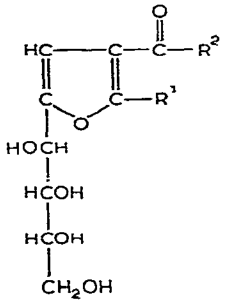
*Dedicated to Professor M. Stacey, C.B.E., F.R.S., in honour of his 65th birthday.



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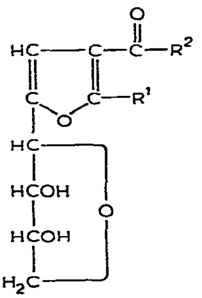

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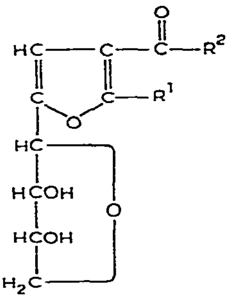

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RESULTS AND DISCUSSION

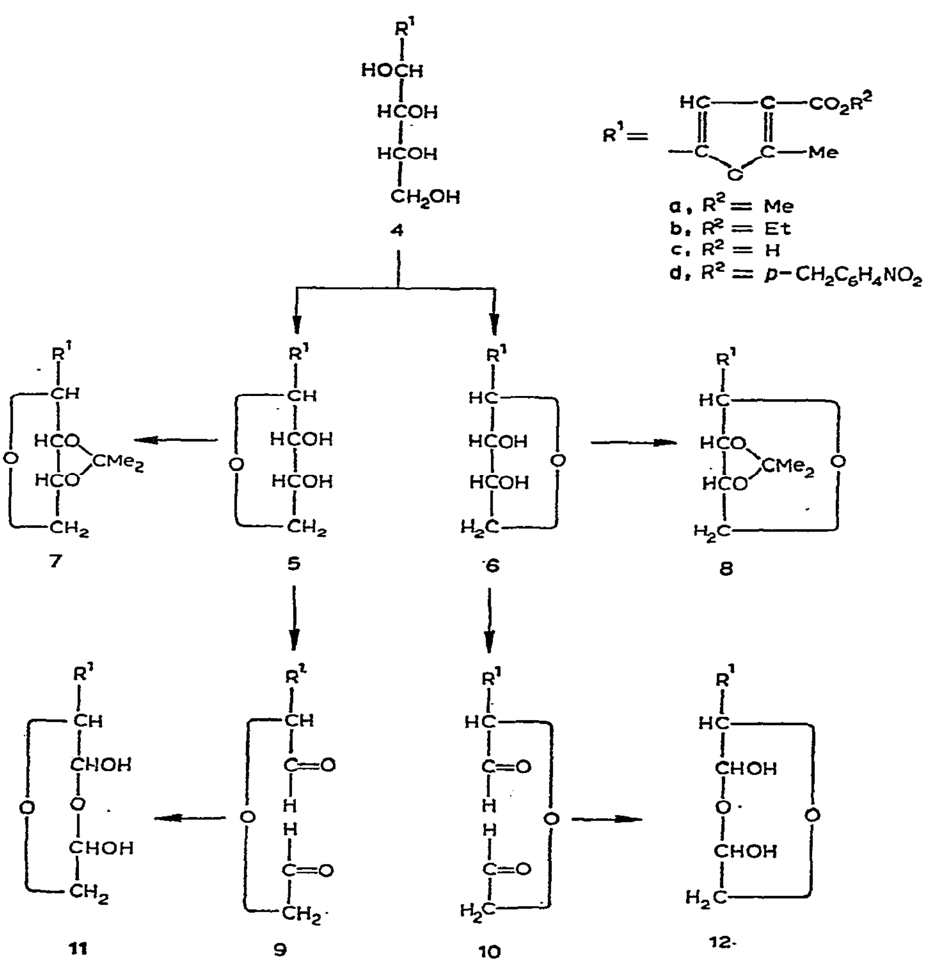
Dehydration of methyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoate[8] (**4a**) was carried out with conc. hydrochloric acid at 0° as described[9] for the ethyl ester **4b**. From the resulting mixture of anhydro derivatives **5a** and **6a**, methyl 5-(1,4-anhydro-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**5a**) was crystallised and shown to be identical with the compound synthesized[1] from 3,6-anhydro-D-glucose and methyl acetoacetate. Yields of the readily crystallisable **5a** were consistently low (*ca.* 6%), and it seemed that compound **5a** was a minor product of the reaction.

When the crude, syrupy product of the dehydration of **4a** was treated with acetone and anhydrous copper sulphate, two isopropylidene derivatives were formed (t.l.c.), of which the minor product was chromatographically identical to methyl 5-(1,4-anhydro-2,3-*O*-isopropylidene-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**7a**), previously obtained[1] by acetonation of **5a**. From the mixture of isopropylidene derivatives, *ca.* 50% of compound **8a** was crystallised. The i.r. and p.m.r. spectra of **8a** were consistent with the proposed structure, and its stereochemistry was deduced from its conversion into the known[10] *p*-nitrobenzyl ester **8d** which has the D-*ribo* configuration. Compound **8a** had been previously obtained[11] (though incorrectly formulated) by acetonation and subsequent methylation of 5-(1,4-anhydro-D-*ribo*-tetrahydroxybutyl)-2-methyl-3-furoic acid[1,2] (**6c**).

From the mother liquors of **8a**, a low yield of the syrupy isopropylidene derivative **7a** was obtained by chromatography on silica gel and transformed into the known[1,10], crystalline *p*-nitrobenzyl ester **7d**.

Methyl 5-(1,4-anhydro-D-*ribo*-tetrahydroxybutyl)-2-methyl-3-furoate (**6a**) was obtained by hydrolysis of its isopropylidene derivative **8a** using Amberlite IR-120 (H^+) resin. The hydrolysis was limited in order to minimise the contact of **6a** with acid which might have caused partial isomerization into **5a**. Re-acetonation of **6a** gave **8a**. Saponification of **6a** gave the known[1,2] furoic acid **6c** having the D-*ribo* configuration, and the *p*-nitrobenzyl ester **6d** of **6c** was identical with the substance previously described[12].

Oxidation of **6a** with periodic acid gave the dialdehyde **10a** as a monohydrate, to which is assigned the hemialdal structure **12a** on the basis of its i.r. spectrum and



by analogy with similar substances[13]. Compound **12a** was enantiomeric with the product **11a** obtained[1] by periodate oxidation of methyl 5-(1,4-anhydro-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**5a**).

Dehydration of ethyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoate[2] (**4b**) with conc. hydrochloric acid at 0° also gave a mixture of the two isomeric anhydro-derivatives **5b** and **6b**. The minor component of this mixture (**5b**, the D-*arabino* isomer) was isolated (*ca.* 3%) crystalline. Acetonation of the mixture of **5b** and **6b** afforded the known isopropylidene derivatives **7b** and **8b** (major product); **8b** was isolated crystalline (60%), and the syrupy D-*arabino* isomer **7b** was further characterized as its crystalline *p*-nitrobenzyl ester[1,10] **7d**. The transformations of **8b** into the furoic acid **8c** and into *p*-nitrobenzyl ester **8d** have been previously reported[10].

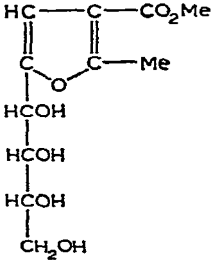
Syrupy ethyl 5-(1,4-anhydro-D-*ribo*-tetrahydroxybutyl)-2-methyl-3-furoate (**6b**), obtained by hydrolysis of its isopropylidene derivative **8b**, consumed one mol. of periodic acid to afford the dialdehyde **10b**, isolated as the hemialdal **12b**. The enantiomer (**11b**) of hemialdal **12b** was obtained by periodate oxidation of the anhydro ethyl ester **5b** having the D-*arabino* configuration.

Both anhydro-derivatives **5** and **6** were also formed when the dehydration reaction was carried out with dilute (0.1M) acid at 40° (see Experimental).

According to previous data[2,14], the dehydration of 2-(D-*arabino*-tetrahydroxybutyl)furans (**1**) is a reversible, acid-catalyzed process. Therefore, a 2-(1,4-anhydrotetrahydroxybutyl)furan (**2**) of a given configuration, when dissolved in acid, could revert to 2-(tetrahydroxybutyl)furan(s), which in turn could give rise to an anhydro derivative of configuration other than that of the starting substance. At equilibrium, the thermodynamically more-stable anhydro-derivative would be preponderant. In order to verify this view, a solution of methyl 5-(1,4-anhydro-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**5a**) (i.e., the isomer expected to be thermodynamically less-stable) in 0.1M hydrochloric acid was stored at room temperature until the optical rotation became constant. T.l.c. then showed a major component and two trace products (possibly **4a** and **13**). Acetonation of the mixture yielded both isopropylidene derivatives **7a** and **8a**. The major product (**8a**, D-*ribo* configuration) was isolated crystalline in a yield of 58%.

Thus, the conversion of the D-*arabino* compound **5a** into its D-*ribo* isomer **6a** was extensive. The reverse transformation was observed on prolonged treatment of the D-*ribo* isopropylidene derivative **8a** with Amberlite IR-120 (H^+) resin.

The above results demonstrate that the dehydration of 2-(D-*arabino*-tetrahydroxybutyl)furans (**1**) is a reversible process which proceeds preferentialy with inversion of the configuration at C-1′, yielding the thermodynamically more-stable compound **3** having the D-*ribo* configuration. A possible mechanism for the reaction is shown in Scheme 1. The key intermediate is the resonance-stabilized carbonium ion **15** which can undergo intramolecular nucleophilic attack to yield the conjugate acids (**18** and **19**) of the anhydro compounds having the D-*arabino* and D-*ribo* configurations. This mechanism is compatible with the kinetics[14] of the reaction. The reversible character of the reaction and its high velocity in concentrated acid media[14] would explain the preferential formation of the more-stable isomer **3** having the D-*ribo* configuration. The greater stability of **3** can be accounted for by the *trans*



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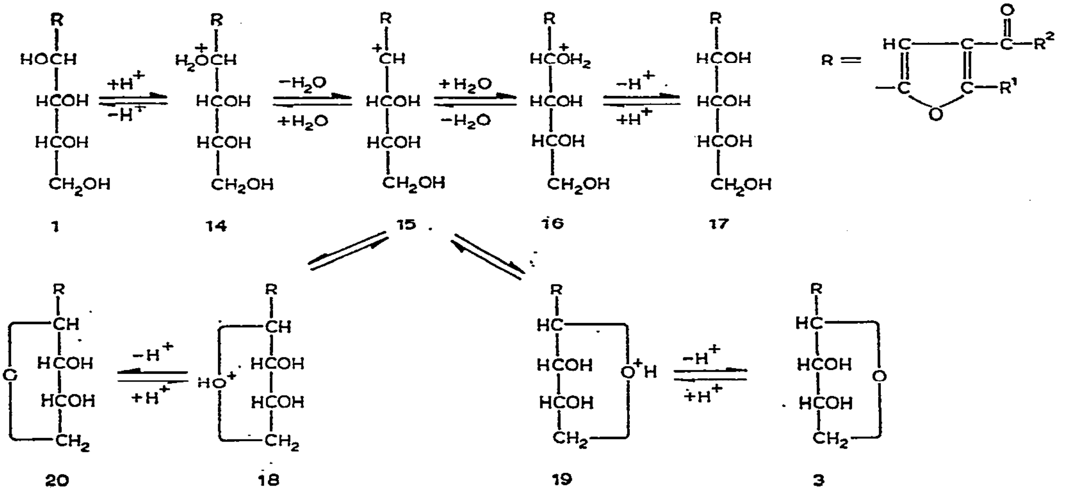
arrangement of the bulky 2-furyl substituent of the tetrahydrofuran ring and the hydroxyl groups, as compared with the *cis*-arrangement in the D-*arabino* compound.



SCHEME 1

Anhydro derivatives having the D-*arabino* and D-*ribo* configurations can be distinguished by the values of their optical rotations, the chemical shifts of H-1', and the values of $J_{1',2'}$ (Table I). The D-*ribo* isomers (which can be considered as *C*-nucleosides having the β-D-anomeric configuration) are more strongly levorotatory than the D-*arabino* isomers **20** (similar to α-D *C*-nucleosides). Also H-1' of the D-*ribo* isomers appears at higher field and has a larger $J_{1',2'}$ than the same proton of the D-*arabino* isomers.

TABLE I

CHARACTERISTIC PHYSICAL PROPERTIES OF ANHYDRO-DERIVATIVES **2** HAVING THE D-*ribo* AND D-*arabino* CONFIGURATIONS

Substance	*Configuration*	$[\alpha]_{5461}$[a] *(degrees)*	δ_{H-1}[b]	$J_{1',2'}$ *(Hz)*	*Reference*
5a	D-*arabino*	−20.1	4.79	4.5	
6a	D-*ribo*	−95.65	4.55	6.1	
5b	D-*arabino*	−18.8	4.80	4.5	
6b	D-*ribo*	−90.2			
5c	D-*arabino*	−35.7[c]	4.82	4.4	1
6c	D-*ribo*	−120.0[c,d]	4.56	6.7	1, 2
5d	D-*arabino*	−8.4[e]			1
6d	D-*ribo*	−73.0[e]			
8a	D-*ribo*	−98.2			
8b	D-*ribo*	−95.6			10

[a] In chloroform, unless otherwise indicated. [b] In chloroform-*d*–methyl sulfoxide-d_6–deuterium oxide. [c] In water. [d] $[\alpha]_D$. [e] In pyridine.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were dried with $MgSO_4$ and were evaporated under diminished pressure below 40°. Light petroleum refers to the fraction of b.p. 50–70°. Identification of products was based on mixed melting points, and comparison of i.r. spectra and chromatographic mobilities. Thin-layer chromatography (t.l.c.) was performed on Silica gel HF_{254} (Merck), and detection was effected by irradiating the chromatoplates with u.v. light of 254 nm. Column chromatography was performed with silica gel (Merck) of particle size 0.05–0.2 mm. Optical rotations at 5461 Å were determined with a Bendix–Ericsson Type 143C polarimeter. The i.r. spectra were obtained for KBr discs, unless otherwise indicated, on a Perkin–Elmer 621 spectrophotometer. The p.m.r. spectra were measured on a Varian HA-100 spectrometer, with tetramethylsilane as the internal standard.

Dehydration of methyl 2-methyl-5-(D-arabino-*tetrahydroxybutyl*)*-3-furoate* (**4a**). — A solution of compound **4a** (5.0 g) in ice-cooled conc. hydrochloric acid (20 ml) was allowed to stand for 5 min at 0°. The reaction mixture was diluted with ice-cooled water (40 ml), neutralized with solid sodium hydrogen carbonate, and extracted with chloroform (5 × 20 ml). The combined extracts were successively washed with saturated, aqueous sodium chloride (30 ml) and water (20 ml), and dried. T.l.c. (ether) showed the presence of a product(s) of R_F 0.35. Evaporation of the solvent afforded a syrupy mixture of compounds **5a** and **6a** (4.25 g, 91%). Crystallisation from water (4.5 ml) gave methyl 5-(1,4-anhydro-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**5a**) (0.3 g, 6%), m.p. 131–132°, R_F 0.35 (ether), identical with an authentic sample[1].

The mother liquor was extracted with chloroform (3 × 6 ml), and the combined extracts were dried and evaporated. The residual syrup (3.2 g), dissolved in warm water (4 ml), afforded a second crop of **5a** (80 mg).

*Methyl 5-(1,4-anhydro-2,3-*O*-isopropylidene-*D-arabino-*tetrahydroxybutyl)-2-methyl-3-furoate* (**7a**) *and methyl 5-(1,4-anhydro-2,3-*O*-isopropylidene-*D-ribo-*tetrahydroxybutyl)-2-methyl-3-furoate* (**8a**). — A solution of the crude, syrupy dehydration product (**5a**+**6a**) (25.0 g) in dry acetone (1 litre) was shaken with anhydrous copper sulphate (250 g) for 4 days. T.l.c. (ether–light petroleum, 1:1) showed the formation of two products, R_F 0.51 and 0.72 (major product). The copper sulphate was filtered off and washed thoroughly with acetone, and the combined filtrate and washings were evaporated. The resulting, partly syrupy solid was extracted with boiling, light petroleum (500 ml), leaving an insoluble residue that was discarded. Cooling of the extract afforded crystalline compound **8a**, R_F 0.72 (ether–light petroleum, 1:1), containing trace amounts of the slower-moving substance. Two additional recrystallizations from the same solvent afforded chromatographically homogeneous **8a** (15.4 g, 49%), m.p. 99–100°, $[\alpha]^{29}_{5461}$ −98.23° (*c* 0.5, chloroform); lit.[11], m.p. 99°, $[\alpha]_D$ −89°; ν_{max} 3113s (furan CH), 1715s (CO_2Me), 1617s and 1588s cm^{-1} (furan ring); p.m.r. data (chloroform-*d*): δ 6.48 (1-proton singlet, furan CH), 5.00–4.86 (3-proton multiplet) and 4.10–3.90 (2-proton multiplet) (H-1,′ H-2′, H-3′, and 2H-4′), 3.80 (3-proton singlet, CO_2Me), 2.54 (3-proton singlet, =C–Me), 1.55 (3-proton singlet) and 1.36 (3-proton singlet) (CMe_2).

Anal. Calc. for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.36; H, 6.70.

A sample (100 mg) of compound **8a** was refluxed with 10% ethanolic potassium hydroxide (1 ml) for 1 h. The pH of the cooled reaction mixture was brought to 8 with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with water, and the combined filtrate and washings were evaporated. A solution of the residue (78.5 mg) in ethanol–water (2:1, 1.5 ml) was heated under reflux with *p*-nitrobenzyl bromide (47 mg) for 1 h. Refrigeration of the reaction mixture gave a crystalline solid which, upon recrystallization from ethanol–water (2:1), afforded *p*-nitrobenzyl ester **8d** (55 mg), m.p. 74–75°, identical with the compound previously described[1,10].

The combined mother liquors of **8a** were evaporated, and the syrupy residue (2.2 g) was chromatographed on silica gel (45 g), using ether–light petroleum as eluant. A group of fractions containing only a compound of R_F 0.51 were combined and evaporated to give compound **7a** (200 mg) as a syrup that was chromatographically identical with the compound previously described[1].

A sample (120 mg) of **7a** was transformed into *p*-nitrobenzyl ester **7d**, as described above for compound **8a**. The product (130 mg), m.p. 94–95°, was identical with an authentic sample[1,10].

*Methyl 5-(1,4-anhydro-*D-ribo*-tetrahydroxybutyl)-2-methyl-3-furoate* (**6a**). — A solution of compound **8a** (0.3 g) in methanol–water (2:1, 45 ml) was shaken with Amberlite IR-120 (H^+) resin (2.5 ml) for 50 h at room temperature. T.l.c. of the reaction mixture then indicated that hydrolysis was almost complete. The resin was filtered off and washed thoroughly with methanol. The combined filtrate and washings were evaporated to 6 ml and extracted with chloroform (3 × 5 ml). The extract, which contained **6a** (R_F 0.35, ether) and a small amount of compound **8a**, was dried and evaporated. Elution of the syrupy residue (242 mg) from silica gel (10 g) with ether gave **6a** (132 mg) as a colourless syrup, $[\alpha]_{5461}^{24}$ −95.65° (*c* 1.4, chloroform); ν_{max} (film) 3400b-m (OH), 3120w (furan CH), 1717s (CO_2Me), 1618m and 1585m cm^{-1} (furan ring); p.m.r. data (chloroform-*d*–methyl sulfoxide-d_6–deuterium oxide): δ 6.59 (1-proton singlet, furan CH), 4.55 (1-proton doublet, $J_{1',2'}$ 6.1 Hz, H-1′), 3.65–4.30 (4-proton multiplet, H-2′, H-3′, and 2H-4′), 3.69 (3-proton singlet, CO_2Me), 2.54 (3-proton singlet, =C–Me).

Anal. Calc. for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83. Found: C, 54.62; H, 5.83.

Re-acetonation of this substance yielded **8a**, R_F 0.75 (ether–light petroleum, 1:1), as the only product detectable by t.l.c.

When the hydrolysis of **8a** was allowed to proceed to completion, the product **6a** was contaminated with **5a**, as was shown by re-acetonation of the mixture which gave **8a** containing traces of **7a**.

*5-(1,4-Anhydro-*D-ribo*-tetrahydroxybutyl)-2-methyl-3-furoic acid* (**6c**). — Methyl ester **6a** (1.9 g) was refluxed with 10% sodium hydroxide (12 ml) for 1 h. The pH of the cooled reaction mixture was brought to 8 with Amberlite IR-120 (H^+) resin, and the resin was filtered off and washed with water. The combined filtrate and washings were evaporated, and the residue was dissolved in water (2 ml). Acidification of this solution with phosphoric acid afforded the title compound. After recrystallization from water, the product (1.1 g, 61%) had m.p. 140–141°, and was identical with an authentic sample[1,2]. P.m.r. data (chloroform-*d*–methyl sulfoxide-d_6–deuterium oxide): δ 6.58 (1-proton singlet, furan CH), 4.82 (1-proton doublet, $J_{1',2'}$ 6.7 Hz, H-1'), 3.6–4.5 (4-proton multiplet, H-2', H-3', and 2H-4'), 2.52 (3-proton singlet, =C–Me).

p-*Nitrobenzyl 5-(1,4-anhydro-*D-ribo-*tetrahydroxybutyl)-2-methyl-3-furoate* (**6d**). — Compound **6a** was converted into **6d**, as described above for compound **8a**. The product (43%) had m.p. 145–146°, $[\alpha]^{22}_{5461}$ −73.0° (*c* 2, pyridine), and was identical with an authentic sample[12].

(2R)-*3,5-Dihydroxy-2-(3-methoxycarbonyl-2-methyl-5-furyl)-1,4-dioxane* (**12a**). — To a cooled (0°) solution of compound **6a** (414 mg, 1.75 mmoles) in water (2 ml) periodic acid (570 mg, 2.5 mmoles) was added portionwise with stirring. The reaction mixture was kept at 0° for 30 min. The thick, crystalline mass formed was filtered off and washed thoroughly with water. Recrystallization from water afforded **12a** (320 mg, 73%), p.m. 112–113°, $[\alpha]^{20}_{5461}$ −34.1° (equilib., *c* 0.5, acetone); ν_{max} 3460s-sh and 3410s-b (OH), 3160 (furan CH), 1721s (CO_2Me), 1618s and 1577s cm^{-1} (furan ring).

Anal. Calc. for $C_{11}H_{14}O_7$: C, 51.16; H, 5.46. Found: C, 50.81; H, 5.43.

*Dehydration of methyl 2-methyl-5-(*D-arabino-*tetrahydroxybutyl)-3-furoate* (**4a**) *with dilute acid.* — A 1% solution (500 ml) of **4a** in 0.1M hydrochloric acid was kept at 40° until the optical rotation became constant ($[\alpha]_D$ −44→−80°, 28 days). T.l.c. of the neutralized, reaction mixture showed the formation of a product(s) having R_F 0.35 (ether). The solution was evaporated to 90 ml and extracted with chloroform (3 × 50 ml). Evaporation of the dried extract gave a syrupy residue (3.4 g, 70%) which was acetonated, as indicated above, to give a semi-crystalline mixture of the two isopropylidene derivatives **7a** and **8a** [R_F 0.51 and 0.72 (ether–light petroleum, 1:1), respectively]. Two recrystallizations from light petroleum yielded **8a** (2.3 g, 58%), m.p. 98–99°, identical with the compound described above.

Conversion of compound **5a** *into compound* **6a**. — A 1% solution (10 ml) of D-*arabino* anhydro-derivative **5a** in 0.1M hydrochloric acid was kept at room temperature until a constant $[\alpha]_D$ value (−24→−100°, 10 days) was obtained. T.l.c. (ethyl acetate) of the neutralized solution showed the presence of a product(s) having the same mobility (R_F 0.60) as that of the starting substance, in addition to trace amounts of products of R_F 0.25 and 0.15. The substance of R_F 0.25 was chromatograpically identical to methyl 2-methyl-5-(D-*arabino*-tetrahydroxybutyl)-3-furoate (**4a**). The solution was evaporated and the residue extracted with chloroform (6 × 5 ml). Evaporation of the extract gave a syrup (95 mg) that was acetonated as described above. T.l.c. (ether–light petroleum, 1:1) showed the presence of **8a** (R_F 0.72) and **7a** (R_F 0.51), Several recrystallizations of the crude acetonation product from light petroleum afforded **8a** (67 mg, 58%), m.p. 98–99°, identical with the sample described above.

Dehydration of ethyl 2-methyl-5-(D-arabino-*tetrahydroxybutyl*)*-3-furoate* (**4b**). — Compound **4b** (5.0 g) was treated with conc. hydrochloric acid as described above for methyl ester **4a**. T.l.c. (ether) of the crude, syrupy product (3.6 g) showed a single spot of the same mobility (R_F 0.37) as compound **5b**. This material was dissolved in hot water (1 ml). Refrigeration of the solution afforded ethyl 5-(1,4-anhydro-D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate (**5b**) (0.12 g, 3%), m.p. 105–107°, identical with the compound previously described[1].

*Ethyl 5-(1,4-anhydro 2,3-*O*-isopropylidene-*D-arabino-*tetrahydroxybutyl*)*-2-methyl-3-furoate* (**7b**) *and ethyl 5-(1,4-anhydro-2,3-*O*-isopropylidene-*D-ribo-*tetrahydroxybutyl*)*-2-methyl-3-furoate* (**8b**). — The crude syrup (16.0 g) resulting from the dehydration of **4b** was acetonated, as indicated above for the mixture of compounds **5a** and **6a**. T.l.c. (ether–light petroleum, 1:1) of the semi-crystalline product (24.3 g) showed the presence of two substances of R_F 0.53 and 0.88 (major product). This material was extracted with boiling, light petroleum (100 ml), and the insoluble residue (3.4 g) was discarded. Cooling of the extract gave crystalline **8b** (7.6 g), R_F 0.88, containing a trace of the slower-moving substance. Several recrystallizations from light petroleum yielded **8b** (5.7 g), m.p. 70–71°, $[\alpha]_{5461}^{21}$ −95.6° (*c* 0.7, chloroform), identical with the substance previously described[10].

The mother liquors of **8b** were evaporated, and the partly crystalline residue (9.0 g) was chromatographed on silica gel (170 g). Elution with ether–light petroleum afforded **8b** (2.8 g, total yield 45%) and syrupy **7b** (1.1 g), R_F 0.53.

A sample (200 mg) of **7b** was converted into *p*-nitrobenzyl ester **7d**, as indicated above for the methyl ester **7a**. The product (147 mg) had m.p. 94–96° and was identical with the substance previously described[1,10].

*Ethyl 5-(1,4-anhydro-*D-ribo-*tetrahydroxybutyl*)*-2-methyl-3-furoate* (**6b**). — Isopropylidene derivative **8b** (2.4 g) was hydrolyzed as described above for methyl ester **8a**. Evaporation of the hydrolysate to half volume gave 0.6 g of **8b**. After filtration, the solution was extracted with chloroform (7 × 25 ml), and the dried extract was evaporated to yield a syrup (1.35 g). Chromatography of this material on silica gel (35 g) afforded compound **6b** (1.1 g, 71% on reacted **8b**) as a colourless syrup, $[\alpha]_{5461}^{29}$ −90.2° (*c* 4.3, chloroform); ν_{max} (film) 3420b-s (OH), 3122w (furan CH), 1718s (CO_2Et), 1622m and 1590m cm^{-1} (furan ring).

Anal. Calc. for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 55.80; H, 6.13.

(2R)-*3,5-Dihydroxy-2-(3-ethoxycarbonyl-2-methyl-5-furyl)-1,4-dioxane* (**12b**). — Compound **6b** was oxidized with periodic acid, as indicated above for methyl ester **6a**. The product (46%) had m.p. 105–112° (from water), $[\alpha]_{5461}^{27}$ $+17.5 \rightarrow -37.5°$ (24 h, *c* 3, acetone); ν_{max} 3440b-s (OH), 3168w (furan CH), 1715s (CO_2Et), 1625s and 1580s cm^{-1} (furan ring).

Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 52.75; H, 5.90.

(2S)-*3,5-Dihydroxy-2-(3-ethoxycarbonyl-2-methyl-5-furyl)-1,4-dioxane* (**11b**). — Oxidation of compound **5b** with periodic acid, performed as described above for **6a**, gave the title compound (92%), m.p. 105–112° (from water), $[\alpha]_{5461}^{27}$ $-17.6 \rightarrow +37.5°$

(24 h, *c* 3, acetone). The i.r. spectrum of this substance was identical to that of compound **12b**.

Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 53.16; H, 5.98.

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