# THE PREPARATION OF SOME DERIVATIVES OF D-RIBONO-1-4-LACTONE AND D-RIBITOL<sup>1</sup>

L. HOUGH,<sup>2</sup> J. K. N. JONES, AND D. L. MITCHELL<sup>2</sup>

ABSTRACT

Reaction of D-ribono- $1 \rightarrow 4$ -lactone with acetone gave the 2,3-O-isopropylidene derivative from which 5-O-methyl-D-ribitol, 5-deoxy-D-ribitol, and 2,3-O-isopropylidene-D-ribitol were prepared.

# INTRODUCTION

5-Deoxy and 5-O-substituted derivatives of p-ribitol were required and consequently attempts were made to prepare from D-ribono-1 $\rightarrow$ 4-lactone (I) the 2,3-O-isopropylidene intermediate (II) for specific substitution of the primary alcohol group (e.g. methylation, tosylation), followed by reduction of the lactone function and finally hydrolysis of the ketal. D-Ribono-1 $\rightarrow$ 4-lactone (I) readily condensed with acetone, the reaction being catalyzed by concentrated and dilute mineral acid or anhydrous copper sulphate, although it also underwent condensation with acetone, without any added catalyst, because of the favored *cis*-configuration of the hydroxyls at carbons 2 and 3. The formation of the O-isopropylidene derivative was accompanied by a significant change in optical rotation which fell from an initial value of  $[\alpha]_{\rm D}$  43° to an approximate value of  $[\alpha]_{\rm D}$  -80°. The rate and extent of the condensation reaction was dependent upon the catalyst selected and in particular on the concentration of the mineral acid. Hydrolysis of the lactone derivative (II) in water proceeded slowly in a manner typical of a  $1\rightarrow 4$  lactone, but the presence of an O-isopropylidene ring superimposed on the lactone ring may make this evidence unreliable. The position of the ketal ring was located by reaction of the sodium O-isopropylidene-D-ribonate (III), obtained by mild alkaline hydrolysis of the lactone derivative (II), with sodium metaperiodate which resulted in the consumption of 1.03 moles of oxidant and the formation of 1.02 moles of formaldehyde. The O-isopropylidene group must therefore be situated at carbons 2 and 3. This was confirmed by methylation of the 2,3-O-isopropylidene-D-ribonolactone (II), followed by mild acid hydrolysis of the mono-O-methyl derivative (IV) to produce in good yield 5-O-methyl-D-ribono-1 $\rightarrow$ 4lactone (V); this compound was identical with the lactone obtained by the alkalinebromine oxidation of 5-O-methyl-D-ribose (1). The methylation evidence is thus compatible with the presence of a  $1 \rightarrow 4$  lactone ring in the O-isopropylidene derivative (II). The possibility that the change in optical rotation prior to or during ketal formation was due to a ring shift from a  $1\rightarrow 5$ - to the  $1\rightarrow 4$ -lactone was considered. However, the original D-ribonolactone slowly hydrolyzed in water at room temperature  $[[\alpha]_{\rm D}$  17.8° (initial)  $\rightarrow [\alpha]_{\rm p} 8^{\circ}$  (13 days)], a property characteristic of 1 $\rightarrow$ 4-lactones (2) and the magnitude of the values recorded by Rehorst for L-ribono- $1 \rightarrow 4$ -lactone is similar (3). 2,3-O-Isopropylidene-D-ribono- $1 \rightarrow 4$ -lactone and D-ribonolactone possessed an infrared absorption maximum at  $1790 \text{ cm}^{-1}$  and  $1793 \text{ cm}^{-1}$  respectively, which is consistent with the  $1 \rightarrow 4$ -lactone structure (cf. reference 3 (a)). The stabilizing effect of the exocyclic double bond, thus making carbon 1 trigonal, must be a considerable influence in this case because the *cis*-hydroxyls at carbons 2 and 3 would be expected to create steric pressure as a result of the close proximity of these groups on a five-membered ring.

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Contribution from the Department of Chemistry, Queen's University, Kingston, Ontario, and the Department of Organic Chemistry, The University, Bristol 8, England. <sup>2</sup>Present address: Department of Organic Chemistry, The University, Bristol 8, England.

Can. J. Chem. Vol. 36 (1958)

# HOUGH ET AL.: PREPARATION OF SOME DERIVATIVES

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# CANADIAN JOURNAL OF CHEMISTRY, VOL. 36, 1958

Recent studies on the periodate oxidation of monosaccharides at pH 3.6 have revealed that they are oxidized almost completely in their ring forms with the formation of esters (formyl, glycollyl, and glycyylyl) of glyceraldehyde and glycollaldehyde, further oxidation being dependent upon the rate of hydrolysis of the ester intermediates (4, 5). Similar oxidations of  $1 \rightarrow 4$ - and  $1 \rightarrow 5$ -pentonolactones would be expected to give rise to glyoxylic acid esters of glyceraldehyde (XI) and glycollaldehyde respectively. However, the former ester should be distinguished by a fairly rapid overoxidation reaction because the electrophilic hydroxyl group (from carbon 5) neighboring the ester linkage would facilitate its hydrolysis. In accord with this theory D-ribono-1→4-lactone and its 5-O-methyl derivative each consumed approximately one mole of periodate rapidly, which was followed by a slower but extensive oxidation, typical of 2-O-esters of glyceraldehyde to the approximate theoretical values (Fig. 1). Lactobiono-1-5-lactone behaved similarly after the initial rapid reaction with 3 moles of periodate (Fig. 1). The similarity between the oxidation curves of D-ribonolactone and 5-O-methyl-D-ribono-1 $\rightarrow$ 4-lactone would suggest that the former compound was indeed oxidized as a  $1 \rightarrow 4$ -lactone and it therefore seems likely that the change in optical rotation during acetonation cannot be ascribed to a ring shift (1 $\rightarrow$ 5- to 1 $\rightarrow$ 4-lactone), but must actually be related to the formation of the ketal ring.

 $1 \rightarrow 4$ -Lactones are believed to be planar or nearly planar, but some degree of ring buckling might arise in the pentono- and hexono-lactones if the molecule possesses a bulky group at carbon 5 and substituents at carbons 2 and 3 in the true *cis*-configuration (XII) (cf. reference 5 (a)). Deviations from planarity have been observed in the D-ribofuranosyl ring system of crystalline adenosine (6) by X-ray analysis, but  $1 \rightarrow 4$ -lactol and  $1 \rightarrow 4$ -lactone ring systems are not precisely comparable. A shift in molecular rotation which should measure approximately the extent of ring buckling has been observed for 2,3-di-Omethyl-D-ribono-1 $\rightarrow$ 4-lactone and 2,3,5-tri-O-methyl-D-ribono-1 $\rightarrow$ 4-lactone (Table I). Such an effect is probably responsible for the large molecular rotational shift in the formation of 2,3-O-isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone, although buckling of the lactone ring will result in a distortion of the O-isopropylidene ring which will then be asymmetric (cf. D-galactose and its 1,2-3,4-di-O-isopropylidene derivative). Asymmetrical O-isopropylidene rings have been suggested as being one of the factors responsible for molecular rotational shifts between methyl O-isopropylidene pyranosides and the corresponding methyl pyranosides (7). The substitution of a methoxyl group for the hydroxyl group at carbon 5 of various D-ribono-1 $\rightarrow$ 4-lactone derivatives results in a molecular rotational shift (in the positive direction) of approximately the same magnitude for each pair (Table I).

Tosylation of 2,3-O-isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (II) at a low temperature (ca.  $-20^{\circ}$  C; 10 hours) produced the 5-O-tosyl derivative (VII) in quantitative yield.

TABLE I

	Rotations	OF	DERIVATIVES	OF	d-ribono- $1 \rightarrow 4$	-LACTONE	IN	WATER	
-		_		_					 

	$[\alpha]_{\mathrm{D}}$	$M_{ m D}$	Difference	Reference
D-Ribono-1→4-lactone 5-O-Methyl-lactone 2,3-Di-O-methyl-lactone 2,3-5-Tri-O-methyl-lactone 2,3-O-Isopropylidene-lactone 2,3-O-Isopropylidene-5-O-methyl-lactone	$     \begin{array}{r}       17.8 \\       27.4 \\       -31.5 \\       -19 \\       -57.5 \\       -44.1 \\     \end{array} $	$\begin{array}{c} 2636 \\ 4445 \\ -5538 \\ -3784 \\ -10820 \\ -8920 \\ \end{array}$	+1809 +1754 +1900	$(*) \\ (1) \\ (8) \\ (9) \\ (*) $

\*Present paper.

1722

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### HOUGH ET AL.: PREPARATION OF SOME DERIVATIVES

When higher reaction temperatures and longer reaction periods were employed, lower yields and tarry products were often obtained. A simultaneous reduction of the lactone function to the primary alcohol and reductive cleavage of the tosyloxy group was effected in good yield by lithium aluminum hydride in tetrahydrofuran to give 2,3-O-isopropyl-idene-5-deoxy-D-ribitol (VIII). Hydrolysis of the product with cation exchange resin (H form) afforded 5-deoxy-D-ribitol (IX). Similarly, 5-O-methyl-D-ribono-1 $\rightarrow$ 4-lactone (V) and 2,3-O-isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (II) were reduced with lithium aluminum hydride to syrupy 5-O-methyl-D-ribitol (VI) and syrupy 2,3-O-isopropylidene-D-ribitol (X) respectively. The structures were verified by periodate oxidation experiments (Table III).

2,3-O-Isopropylidene-D-ribitol compounds are of interest because D-erythro hydroxyls are involved in the formation of a five-membered ketal ring of the  $\alpha$ C-type (10, 11, 12) with bulky substituents in the *cis*-configuration at carbons 2 and 3. This unfavorable conformation (VIII' and X') would be expected to cause the ketal ring to be labile to acid, since deformation from the preferred zigzag conformation is considerable.





#### EXPERIMENTAL

Solutions were concentrated under reduced pressure (ca. 15 mm). Melting points were uncorrected and optical rotations were determined in water unless otherwise stated. Paper chromatography was carried out by the descending method (13) on Whatman No. 1 filter paper using the following solvent systems (v:v): (a) ethyl acetate – acetic acid – water (9:2:2); (b) ethyl acetate – acetic acid – formic acid – water (18:3:1:4); (c) butan-1-ol-ethanol-water (40:11:19); and (d) butan-1-ol-pyridine-water (10:3:3). Non-reducing compounds were detected on paper chromatograms with an alkaline

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silver nitrate spray reagent (14). The rate of movement of the compound on paper chromatograms is quoted relative to that of the solvent front ( $R_f$  value). Wave numbers of infrared data are given to within  $\pm 10$  cm<sup>-1</sup>.

# 2,3-O-Isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone

(Assisted by R. J. Stoodley.) A solution of D-ribono-1 $\rightarrow$ 4-lactone (15 g) in acetone (600 ml) containing concentrated hydrochloric acid (6 ml) was shaken continuously for 18 hours at 25° C. The initial positive rotation decreased rapidly to reach a constant negative value (Table II). A control solution of D-ribono-1 $\rightarrow$ 4-lactone in dioxane and concentrated hydrochloric acid (2 drops) showed a relatively small change in optical rotation (Table II).

The solution was neutralized (silver or lead carbonate) and the inorganic salts were separated by filtration through a pad of cellulose. The combined filtrate and washings deposited crystals when concentrated. After trituration with cold acetone – light petroleum (b.p. 60–80° C), the crystals (14.0 g; 73.5%) were collected on a suction filter. They had a melting point of 138–139° C,  $[\alpha]_{D}^{25\circ} -57.5^{\circ}$  (initial value; c, 2.3)  $\rightarrow -16.1^{\circ}$  (20 days) and  $[\alpha]_{D}^{24\circ} -65.7^{\circ}$  (c, 2.13, pyridine; unchanged after 80 hours).  $\nu_{max}$  1790 cm<sup>-1</sup> (chloroform; C = 0 for 1 $\rightarrow$ 4-lactone (15, 16)). D-Ribono-1 $\rightarrow$ 4-lactone gave an adsorption peak at 1793 cm<sup>-1</sup> (nujol). Recrystallization from acetone–cyclohexane did not affect these constants. Anal. Calc. for C<sub>8</sub>H<sub>12</sub>O<sub>5</sub>: C, 51.1; H, 6.4. Found: C, 51.4; H, 6.4.

When the condensation was catalyzed by 2 N hydrochloric acid (1% v:v), the rotation decreased less rapidly and reached a final rotation of  $[\alpha]_{\mathbf{p}}^{25\circ} - 62.5^{\circ}$  (30 hours).

A 5% solution of D-ribono-1 $\rightarrow$ 4-lactone in acetone revealed a polarimetric behavior similar to the acid-catalyzed reaction (Table II). After the optical rotation had reached a constant value, crystals of 2,3-O-isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone were deposited, when the solution was concentrated.

			TABLE II						
Optical	ROTATION	OF	D-RIBONO-1	IN	VARIOUS	SOLVENTS	AT	$25^{\circ}$	С

		_						
Acidified acetone, $c =$	2.48 Hours:	0	0.33	0.5	2.8	3.8	15.8	18.3
	$[\alpha]_{\mathrm{D}}$ :	$42.3^\circ$	$-25^{\circ}$	$-44.4^{\circ}$	$-77.4^{\circ}$	$-79^{\circ}$	$-82.3^{\circ}$	$-82.3^{\circ}$
Acidified dioxane, $c =$	2.5 Hours:	0	0.1	<b>2</b> . $0$	3.5	6.3	<b>24.0</b>	30.7
	$[\alpha]_{\rm D}$ :	$52^{\circ}$	$49.5^{\circ}$	$48.5^{\circ}$	48°	46.8°	$45^{\circ}$	$43.6^{\circ}$
Water, $c = 2.3$	Hours:	0.25	<b>23.0</b>	42.5	66.2	90.5	138.5	322.8
	$[\alpha]_{\mathrm{D}}$ :	17.8°	17.4°	16.1°	14.8°	13.9°	$11.7^{\circ}$	8.0°
Acetone, $c = 5.0$	Hours:	0.3	7	19	27	48	115	213
	$[\alpha]_{\rm D}$ at 26° C:	39.8°	$29.3^\circ$	7.4°	$-3.9^{\circ}$	$-24.2^{\circ}$	$-48.7^{\circ}$	$-65.2^{\circ}$

A solution of D-ribono-1 $\rightarrow$ 4-lactone (25 g) in acetone (500 ml) was heated under reflux in anhydrous conditions (calcium chloride tube). The optical rotation of the reaction mixture fell slowly, reaching a value of  $[\alpha]_{D}^{25\circ} - 8^{\circ}$  after 92 hours. Anhydrous copper sulphate (5 g) was then added to the solution and the optical rotation fell to  $[\alpha]_{D}^{25\circ} - 77^{\circ}$ (192.5 hours). The filtered solution was concentrated to a crystalline mass which was recrystallized from acetone – light petroleum (b.p. 60–80° C) to yield the *O*-isopropylidene derivative (21.5 g; 67%).

# 2,3-O-Isopropylidene-5-O-methyl-D-ribono-1 $\rightarrow$ 4-lactone

2,3-O-Isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (5.28 g) was treated three times with methyl iodide and active silver oxide (in the presence of anhydrous calcium sulphate), to aid solution chloroform was added to the first methylation. After filtration, the silver salts were thoroughly digested with chloroform. Concentration of the combined filtrates

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### HOUGH ET AL.: PREPARATION OF SOME DERIVATIVES

yielded a pale yellow syrup (6.0 g) which was distilled at 90–100° C (bath temp.) and 10<sup>-5</sup> mm to give the 5-O-methyl derivative [4.76 g; 84% with  $n_{\rm D}^{23\circ}$  1.4490 at 90° C,  $n_{\rm D}^{23\circ}$  1.4500 at 100° C,  $[\alpha]_{\rm D}^{27\circ}$  -56.8° (c, 3.0 ethanol), and  $[\alpha]_{\rm D}^{26\circ}$  -44.1° (c, 2.5)]. Anal. Calc. for C<sub>9</sub>H<sub>14</sub>O<sub>5</sub>: C, 53.45; H, 7.0; OMe, 15.35. Found: C, 53.4; H, 7.5; OMe, 17.2.

# $5-O-Methyl-D-ribono-1 \rightarrow 4-lactone$

A mixture of a solution of 2,3-*O*-isopropylidene-5-*O*-methyl-D-ribono-1 $\rightarrow$ 4-lactone (4.5 g) in 40% aqueous acetone (100 ml) together with Amberlite resin IR-120 (H) (3 ml) was treated under reflux at 50° C. The initial specific rotation,  $[\alpha]_D^{270} - 42.7^\circ$ , rose to  $[\alpha]_D^{270}$  9.5° (constant value; 60 hours). After it had been cooled, the solution was decanted from the resin, concentrated to a crystalline mass, and recrystallized from ethyl acetate to give 5-*O*-methyl-D-ribono-1 $\rightarrow$ 4-lactone (2.3 g; 63.5%) with m.p. 110–111° C, mixed m.p. 108.5–110° C,  $[\alpha]_D^{250}$  26° (0.08 hours)  $\rightarrow$  19° (168 hours) (c, 0.94).  $R_f$  0.71 (solvent b) and  $R_f$  0.67 (solvent d).  $\nu_{max}$  1765 cm<sup>-1</sup> (nujol) [lit. m.p. 109–110° C,  $[\alpha]_D^{180}$  27.4°  $\rightarrow$  15.3° (7 hours; c, 9.0) (1)]. Anal.Calc. for C<sub>6</sub>H<sub>16</sub>O<sub>5</sub>: C, 44.4; H, 6.2; OMe, 19.1. Found: C, 44.8; H, 6.2; OMe, 19.9.

# 5-O-Methyl-D-ribitol

A solution of 5-O-methyl-D-ribono-1 $\rightarrow$ 4-lactone (1.0 g) in anhydrous tetrahydrofuran (25 ml) was added dropwise to a suspension of lithium aluminum hydride (0.57 g) in tetrahydrofuran (25 ml). After the mixture had been heated under reflux for 4 hours, then cooled, ethyl acetate (2 ml) was added, followed by 70% aqueous alcohol (100 ml). The precipitate was separated by centrifugation and was washed twice with ethanol. The combined supernatants were percolated through Amberlite IR-120 (H) resin prior to concentration to a colorless syrup (0.78 g; 76%). Paper chromatographic examination of the compound revealed only a single spot with  $R_f$  0.40 (solvent b),  $R_f$  0.42 (solvent d),  $[\alpha]_{\rm D}^{250}$  10° (c, 1.0), and  $n_{\rm D}^{200}$  1.4802. Anal. Calc. for C<sub>6</sub>H<sub>14</sub>O<sub>5</sub>: C, 43.4; H, 8.5; OMe, 18.7. Found: C, 43.5; H, 7.8; OMe, 20.6.

# 2,3-O-Isopropylidene-5-O-toluene-p-sulphonyl-p-ribono-1 $\rightarrow$ 4-lactone

2,3-O-Isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (1.13 g) was dissolved in cold (-20° C), anhydrous pyridine and toluene-*p*-sulphonyl chloride (2.38 g; 100% excess) was added in one portion. After the mixture had been kept for 10 hours at -20° C, with intermittent shaking, water (0.5 ml) was added and the solution was poured slowly into ice water (600 ml) with vigorous stirring. The crystals were collected by filtration and dried under reduced pressure at room temperature (2.07 g; 100%). Recrystallization from methanol gave prisms melting at 117.5–118° C and with  $[\alpha]_{\rm D}^{24\circ}$  -15.8° (*c*, 2.4 acetone).  $\nu_{\rm max}$  1810 cm<sup>-1</sup> (chloroform). Anal. Calc. for C<sub>15</sub>H<sub>18</sub>O<sub>7</sub>S: C, 52.6; H, 5.3; S, 9.4. Found: C, 52.7; H, 5.3; S, 9.7.

# 2,3-O-Isopropylidene-5-deoxy-D-ribitol

To a suspension of lithium aluminum hydride (5.5 g) in anhydrous tetrahydrofuran (50 ml), a solution of 2,3-O-isopropylidene-5-O-toluene-*p*-sulphonyl-D-ribono-1 $\rightarrow$ 4-lactone (5.38 g) in tetrahydrofuran (50 ml) was added dropwise. The reaction mixture was heated under reflux for 5 hours, then ethyl acetate (20 ml) was slowly added dropwise, followed by 10% aqueous ethanol until the inorganic salts were precipitated. After filtration, the organic solvents were evaporated by repeated dilution with water and the product, obtained by continuous extraction with chloroform, was a syrup (2.38 g; 84%) with  $n_{\rm D}^{20^{\circ}}$  1.4510 and  $[\alpha]_{\rm D}^{27^{\circ}}$  -15.5° (*c*, 2.7, ethanol). Anal. Calc. for C<sub>8</sub>H<sub>16</sub>O<sub>4</sub>: C, 54.5; H, 9.15. Found: C, 52.9; H, 9.2.

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TABLE III

1726

RESULTS OF PERIODATE OXIDATION EXPERIMENTS

					ł		Time	(hours			
Compound	Determination	μd	0.08	0.15	0.25	0.50	0.66	1.0	3.5	4.0	
p-Ribitol	Uptake*	7.5	4.0		4.0						(4.0-1.7 hr)
2,3-0-1sopropynaene-D-ribono-1-74- lactone Sodiiym 2.3-0-isooropylidene-D-ribonate	Uptake* Uptake*	10 C	0.08	0.92	$0.08 \\ 0.99$	1.03	0.08	$0.08 \\ 1.03$	1.03		
Sodium 5-0-methyl-D-ribonate	Formaldehyde* Uptake*	10	$0.94 \\ 2.3$		0.95 2.65	2.84		$1.02 \\ 2.94$	$\frac{1.02}{2.97}$	2.99	
5-0-Methyl-D-ribono-l→4-lactone	Formaldehyde* Uptake*	$\frac{10}{3.7}$	1.38	1.34					2.52		(Nil-24 hr) (3.0-9.0 hr)
5-0-Methyl-D-ribitol	Formaldehyde* Uptake*	3.7		2.23		2.38		2.48		2.50	(3.05-21 hr) (Nil-13 hr) (1.5 80 5 1-)
2,3-0-Isopropylidene-5-deoxy-D-ribitol	Acia Formaldehyde* Uptake*	ממ		0.02	$0.88 \\ 0.08$	$0.88 \\ 0.04$		$0.89 \\ 0.04$		1.4	(1.3-20.3 hr)
5-Deoxy-D-ribitol	Uptake* Uptake*	7.5 U	$2.24 \\ 2.99$			$3.01 \\ 2.96$			3.14	3.16	(2.96-2.0  hr)
	Acid*	Ŋ	1.78			1.85					(2.96-22 hr) (1.78-2.5 hr)
2,3-0-Isopropylidene-D-ribitol	Formaldehyde* Uptake* Formaldehyde*	מממ		0.93	1.02 1.05	$\begin{array}{c} 1.09\\ 0.89\\ 1.0\end{array}$		06.0		1.03 1.0	$\begin{pmatrix} 1.74-25 \text{ hr} \\ 0.99-16.5 \text{ hr} \\ (0.92-18 \text{ hr} ) \\ (0.95-16 \text{ hr} ) \end{pmatrix}$
U = Unbuffered. *In moles of periodate per mole substrat	) )     		,				)				

CANADIAN JOURNAL OF CHEMISTRY, VOL. 36, 1958

### 5-Deoxy-D-ribitol

The above O-isopropylidene compound (2.09 g) was hydrolyzed with Amberlite IR-120 (H) resin under the conditions previously described for the preparation of 5-O-methyl-pribono-1 $\rightarrow$ 4-lactone. The product (1.51 g; 93%) crystallized spontaneously when the solution was concentrated to dryness. Recrystallization from ethyl acetate – methanol (5:1 v:v) gave 5-deoxy-p-ribitol with m.p. 77–80° C. The product contained solvent of crystallization which could be removed under reduced pressure to give a product melting at 65–69° C and  $[\alpha]_{D}^{25\circ}$  –10.6° (c, 1.7). Anal. Calc. for C<sub>5</sub>H<sub>12</sub>O<sub>4</sub>: C, 44.1; H, 8.9. Found: C, 44.1; H, 8.6.

#### 2,3-O-Isopropylidene-D-ribitol

2,3-*O*-Isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (1.50 g) was treated with lithium aluminum hydride by the method described for the preparation of 5-*O*-methyl-D-ribitol, except the reaction period was extended to 8 hours and the ion exchange resin, Amberlite IR-120, was used in the ammonium form. The syrupy product (1.6 g) moved on paper chromatograms as a single spot ( $R_f$  0.39; solvent b) and had  $[\alpha]_D^{260} - 4.3^\circ$  (c, 2.8, ethanol),  $n_D^{200}$  1.4730. Anal. Calc. for C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>: C, 50.0; H, 8.4. Found: C, 49.2; H, 8.0.

### D-Ribitol (Adonitol)

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2,3-O-Isopropylidene-D-ribono-1 $\rightarrow$ 4-lactone (130 mg) was dissolved in ethanol (5 ml) and sodium borohydride (93 mg) was added in one portion. The solution was heated at 50° C for 5 hours and then kept at room temperature overnight. After acidification with acetic acid, the solution was passed down a column of Amberlite resin IR-120 (H) and the effluent was evaporated to dryness. After removal of acetic and boric acids by repeated co-distillations with methanol, the syrupy product was hydrolyzed with 0.01 N sulphuric acid (10 ml, 3 hours, 95° C). The cooled solution was neutralized (barium carbonate), then filtered, and the filtrate concentrated to a syrup. Examination of the product in solvent systems (a) and (c) revealed a single component which had a rate of movement identical with that of an authentic specimen of adonitol. The syrup readily crystallized on seeding with adonitol (ribitol).

When the reduction was carried out using water as the solvent under the conditions described above, the major product was an acid (paper chromatography) and only a small amount of adonitol was detected.

# Periodate Oxidation Experiments

All reactions were carried out in the dark and at room temperature ( $ca. 18^\circ$ ).

#### (i) Determination of the Reacted Periodate

The lactone or pentitol derivative (10-15 mg; accurately weighed) was dissolved in water or the required buffer solution containing 0.3 *M* sodium metaperiodate solution (1 or 2 ml). The total volume was made up to 10 ml with additional buffer solution. A blank was run concurrently. Aliquot portions (2 ml) were withdrawn at intervals and pipetted into phosphate buffer (pH 7.0; 25 ml) containing 20% potassium iodide solution (1-3 ml), and the liberated iodine was titrated with 0.01 *N* sodium thiosulphate solution using starch solution as indicator (17).

In some cases the lactone was hydrolyzed to the aldonic acid (sodium salt) with a slight excess of 0.01 N sodium hydroxide solution prior to the addition of the sodium metaperiodate solution and sufficient water to bring the total volume to 20 ml. (Buffer solutions: pH 7.5, 0.05 M sodium bicarbonate solution; pH 3.7, 0.05 M acetic acid – sodium acetate solution.)

### CANADIAN JOURNAL OF CHEMISTRY, VOL. 36, 1958

### (ii) Estimation of the Formic Acid Produced

1728

Solutions containing ca. 5 mg of compound per milliliter of solution were oxidized with sodium metaperiodate solution under unbuffered conditions. At various intervals of time, ethylene glycol (1 ml) was added to aliquot portions (5 ml) and the acidic solution was titrated with 0.01 N sodium hydroxide solution using methyl red, screened with methylene blue as the indicator. A blank was run concurrently.

# (iii) Determination of the Formaldehyde Liberated

Samples (2-4 mg; accurately weighed) were dissolved in water or buffer solution containing 0.3 M sodium metaperiodate solution (1 ml) and made up to 25 ml. At intervals. aliquot samples (1 ml) were withdrawn and the formaldehyde was estimated by the chromotropic acid method (18). A known weight of erythritol (periodate oxidized) was used as the source of formaldehyde for the preparation of the standard curve.

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