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PHOTO-OXYGENATION OF GLYCOSYLFURANS. REARRANGEMENT OF *C*-GLYCOSYL INTO *O*-GLYCOSYL DERIVATIVES

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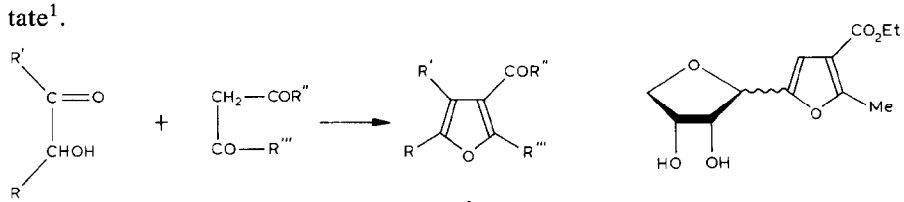
ABSTRACT

Photo-oxygenation of 3-ethoxycarbonyl-5-(2,3-*O*-isopropylidene-β-D-erythrofuranosyl)-2-methylfuran and 3-hydroxymethyl-5-(2,3-*O*-isopropylidene-β-D-erythrofuranosyl)-2-methylfuran yields the corresponding *endo*-peroxides which rearrange at room temperature into the *O*-glycosyl derivatives ethyl 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 2-acetylfumarate and 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 3-acetyl-3-hydroxymethylacrylate, respectively. The *endo*-peroxides can be reduced without rearrangement, yielding *C*-glycosyl derivatives. Alcoholysis of the *O*-glycosyl derivatives yields 2,3-*O*-isopropylidene-D-erythrose, dialkyl 2-acetyl-3-alkoxysuccinates, 4-ethoxycarbonyl-5-methoxy-5-methyl-2-oxo-2,5-dihydrofuran and 4-hydroxymethyl-5-methoxy-5-methyl-2-oxo-2,5-dihydrofuran.

INTRODUCTION

α-Hydroxyaldehydes and α-hydroxyketones (including aldoses and ketoses) react with β-dicarbonyl compounds to give furan derivatives (**1**) as the main products. Thus, aldohexoses yield derivatives of 2-tetrahydroxybutylfuran which, under acid catalysis, are easily cyclised to give such *C*-glycosyl derivatives (2-glycofuranosylfurans) as **2**, which can be obtained from D-glucose and ethyl acetoacetate[1].



Oxidation of such compounds as **2** with singlet oxygen[2] cleaves the furan ring and yields *C*-glycosyl derivatives that are functionalised at the anomeric carbon atom and have potential for the synthesis of other heterocyclic *C*-glycosyl derivatives. This singlet oxygen reaction generally involves a 4 + 2 addition, yielding

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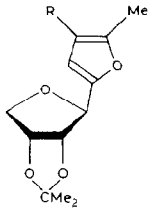
endo-peroxides with ozonide-like structures (*e.g.*, **4**) which are moderately stable although they can rearrange into non-peroxide structures (diketoepoxides or acetaldiepoxides)[3]. We now report on the photo-oxygenation of some glycosylfurans and the rearrangement of *C*- into *O*-glycosyl derivatives.

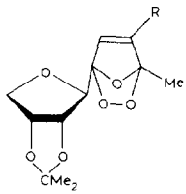
RESULTS AND DISCUSSION

Ethyl 5-D-erythrofuranosyl-2-methyl-3-furoate (**2**) is formed as a mixture of α and β anomers when ethyl 5-(D-*arabino*-tetrahydroxybutyl)-2-methyl-3-furoate is cyclised[1]. These products could be isolated[4] as the diacetates and then saponified to give α-**2** and β-**2**. The minor component α-**2** has been prepared by another method[5].

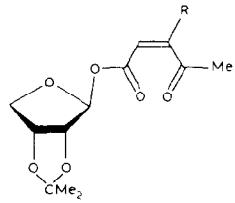
The 2′,3′-*O*-isopropylidene derivative (**3**) of β-**2** was prepared by the



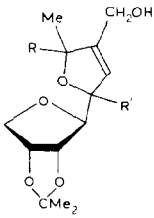
3 R = CO_2Et
6 R = CH_2OH



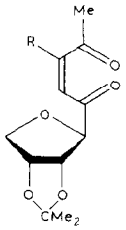
4 R = CO_2Et
7 R = CH_2OH



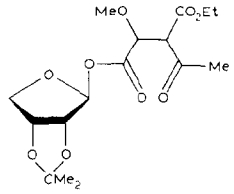
5 R = CO_2Et
14 R = CH_2OH



8 R = OOH, R′ = OMe
9 R = OMe, R′ = OOH
11 R = OH, R′ = OMe
12 R = OMe, R′ = OH
24 R = R′ = OH



10 R = CH_2OH
20 R = CO_2Et



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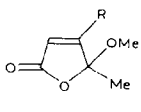
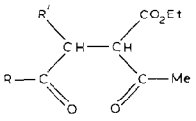
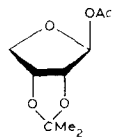


15 R = CO_2Et
16 R = CH_2OH



17 R = MeO, R′ = MeO
18 R = EtO, R′ = EtO
19 R = EtO, R′ = MeO



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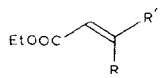


22 R = COMe, R′ = CO_2Et
23 R = CO_2Et, R′ = COMe

acetonation of α,β-**2** followed by chromatography[6]. Photo-oxygenation of **3** at 0° in acetone yielded the *endo*-peroxide **4**, which was identified on the basis of ^{1}H-n.m.r. data. The signal of the furan Me-5 was shifted from δ 2.52 in **3** to δ 1.95 in **4**, reflecting the 3-methyl-1,2,4-trioxolane structure. Likewise, the signal for furan H-4 was shifted from δ 6.46 to δ 7.10, reflecting its vinylic character and the *cis*-CO_2Et group. The *endo*-peroxide **4**, which could be quantitatively reduced with dimethyl sulfide, was unstable at room temperature and rearranged into the *O*-glycosyl derivative **5**. This process appeared to be stereospecific since the β-D-erythrofuranosyl derivative was isolated in high yield. The configuration at the anomeric carbon atom was preserved during *C*→*O*-glycosyl transformation.

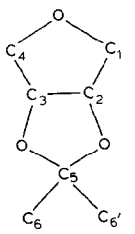
The small number of precedents for the occurrence of this type of *endo*-peroxide rearrangement[7] during photo-oxygenation of furans prompted an investigation of the influence of the CO_2Et group on the rearrangement. This group in **3** was reduced with $LiAlH_4$, and the resulting alcohol (**6**) was photo-oxidised in methanol. The expected *endo*-peroxide **7** could not be detected by ^{1}H-n.m.r. spectroscopy, which reflected its easy reaction with the solvent to yield a hydroperoxide **8** or **9** (n.m.r. signals for OOH, acetal Me, and OMe at δ 9.45, 1.43, and 3.21, respectively). No attempt was made to identify the isomer (**8** or **9**) formed, but it oxidised dimethyl sulfide to give dimethyl sulfoxide, and the resulting diketone **10** added methanol to yield **11** or **12**; the steric interaction between the *cis* C=O groups is relieved by this addition.

The easy nucleophilic addition of methanol to the double bond in **5** (storage of the methanolic solution at room temperature) is probably due to the three carbonyl groups attached to that bond. The ^{1}H- and ^{13}C-n.m.r. spectra of the product (**13**) revealed the formation of only two of the four possible diastereomers. The ^{1}H-n.m.r. spectrum showed, *inter alia*, two signals for MeCO (δ 2.27 and 2.32), MeO (δ 3.44 and 3.47), CH_3CH_2 (δ 1.27 and 1.30), and anomeric CH (δ 6.17 and 6.18). In the ^{13}C-n.m.r. spectrum, there were double signals for the carbons near the two new chiral centres (see Table II). The diastereomers could not be isolated, probably because of racemisation at the new chiral centres due to the enolisable character (β-ketoester) of one and facile elimination–addition of alcohol at the other.

TABLE I

^{13}C-N M.R. DATA FOR CARBOHYDRATE MOIETIES OF **3**, **13**, **14**, **21**, AND 2,3-*O*-ISOPROPYLIDENE-D-ERYTHROSE

	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-6'*	*-COO*	*CH_3COO*
3[a]	83.7	81.3	79.7	72.8	113.0	26.6	25.1		
14[a]	102.4	84.7	79.5	74.1	113.1	26.3	25.1		
13	102.8	84.0							
	103.0	84.7	79.5	74.2	113.1	26.3	25.0		
21	101.4	84.6	79.4	73.6	112.7	26.1	24.8	169.3	20.8
A[b]	101.2	84.9	79.6	71.3	111.9	25.8	24.3		



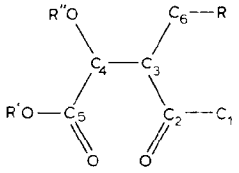
[a]Signal assignments confirmed by off-resonance experiments. [b]*A* = 2,3-*O*-Isopropylidene-D-erythrose.

TABLE II

^{13}C-N M R. DATA FOR **13**, **14**, **17–19**, **22**, AND **23**

	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*R*, OCH_2-CH_3		*R'*, OCH_2-CH_3		*R''*
							CH_2	CH_3	CH_2	CH_3	CH_3
13	30.5 29.6	200.0	61.8	78.4 78.7	165.5 166.6	168.5 168.7	61.1	13.9			59.4 59.5
14[a]	30.2	204.6	160.8	115.2	163.7	62.7					
17	30.9 29.7	200.2	62.2	77.0	170.6	171.0	61.9 61.5	14.0			59.7 59.5
18[a,b]	31.1 29.7	200.6	62.5	77.2	170.4 170.3	166.7	61.2 61.4	14.1	61.7	14.1	
19	30.8 29.7	200.3 200.2	67.6	78.4 77.4	170.0	166.7	61.5 61.2	14.1	62.8 61.8	14.0	59.7 59.4
22, 23	30.2 26.8	199.5 193.9	147.3 144.7	128.7 128.2	162.8 164.1	164.2 165.2	62.4	14.0	61.8	14.0	

[a]Signal assignments confirmed by off-resonance experiments. [b]Signal assignments confirmed by INEPT subprogramme.



The photo-oxygenation of 3-hydroxymethyl-5-(2,3-*O*-isopropylidene-β-D-erythrofuranosyl)-2-methylfuran (**6**) at 0° in acetone gave an *endo*-peroxide which rearranged into **14** as described for **4**. Compound **14** has only two carbonyl groups and addition of methanol to its double bond did not occur.

Thus, the ethoxycarbonyl group is not an important factor in inducing the rearrangement **3**→**5**. The presence of the oxygen atom in the vicinity of the anomeric carbon atom could be an important factor since this feature has been observed in similar rearrangements[7].

The structures of **5** and **14** were elucidated by treatment of these compounds with aqueous sodium hydroxide, which gave 2,3-*O*-isopropylidene-D-erythrose, and with methanolic sodium methoxide, which also gave this isopropylidene derivative and the lactones **15** and **16**, respectively. In the solvolysis of **5**, the ester **17** was also isolated. As expected, the lactone **16** showed optical activity, reflecting the chirality of the starting product.

When ethyl 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 2-acetyl-3-methoxysuccinate (**13**, mixture of diastereomers) was solvolysed in ethanolic sodium ethoxide, 2,3-*O*-isopropylidene-D-erythrose was formed together with diethyl 2-acetyl-3-ethoxysuccinate (**18**, mixture of diastereomers). Signals for four EtO groups were observed in the ^{1}H-n.m.r. spectrum together with two for Ac

groups. The results of decoupling experiments on the multiplet at δ 3.25–3.90 reflected the mixture of diastereoisomers and the diastereotopic character of the CH_2 protons in the EtO group (see Experimental). During the solvolysis, the chirality at C-3 was partially preserved, because the succinic derivative **18** showed some optical activity which gradually disappeared in methanolic solution due to racemisation at C-2 and C-3 in **19**, as noted above for **13**. The product was an almost equimolar mixture of enantiomers, as shown by ^{1}H-n.m.r. spectroscopy. The optical activity of **18** indicated that solvolysis of the acetalic ester group in **5** was faster than the exchange of the alkoxyl group.

The structure of **18** was confirmed by synthesis *via* the Knoevenagel reaction between the ethyl hemiacetal of ethyl glyoxylate and ethyl acetoacetate to yield a mixture of diethyl 2-acetylfumarate and diethyl 2-acetylmaleate. This mixture adds ethanol to yield **18**; addition of methanol gives **19**.

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hotplate microscope, and are uncorrected. Solutions were dried over Na_2SO_4 or $MgSO_4$ before concentration under diminished pressure. I.r. spectra were recorded with a Pye Unicam SP 1000 instrument. N.m.r. spectra (^{1}H, 80 MHz; ^{13}C, 20 MHz) were obtained with a Bruker WP-80-SY spectrometer. Optical rotations were measured at 20° with a Perkin–Elmer 141 polarimeter. Elemental analysis were performed with a Carlo Erba Elemental Analyzer 1106. T.l.c. was performed on Silica Gel G (Merck), using ether–hexane mixtures, with detection by charring with sulfuric acid. Column chromatography was performed on silica gel (Merck, 7734).

Photo-oxygenations were performed at 0° by illumination with a Tunsgram Halogen 60000 T8 R7-s-15 lamp of solutions of the substrate also containing 0.01% of Methylene Blue. The reactions were monitored by measuring the volume of oxygen consumed. After the reaction was completed, the solution was filtered through a short column of silica gel (Merck, 7734) to remove the Methylene Blue.

*3-Ethoxycarbonyl-5-(2,3-*O*-isopropylidene-β-*D*-erythrofuranosyl)-2-methylfuran*[5,6] (**3**). — A mixture of ethyl 5-D-erythrofuranosyl-2-methyl-3-furoate (**2**; 7 g, 0.027 mol), $CuSO_4$ (6 g), and anhydrous acetone (400 mL) was shaken at room temperature for 40 h, filtered, and concentrated to give **3** and its α anomer. Column chromatography (hexane–ether, 5:1) afforded **3**, m.p. 70–71°, $[\alpha]_D$ −10° (*c* 0.6, ethanol), R_F 0.88 (hexane–ether, 1:1); ν_{max}^{Nujol} 3160, 1710, 1609, 1580, 1078, 1045, 996, 927, 877, 871, and 856 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H, δ 1.30 (t, 3 H, *J* 7.2 Hz, CH_3CH_2), 1.33, 1.51 (2 s, 6 H, CMe_2), 2.52 (s, 3 H, Me), 3.77–4.09 (m, 2 H, H-4′), 4.24 (q, 2 H, *J* 7.2 Hz, CH_3CH_2), 4.85–4.98 (m, 3 H, H-1′,2′,3′), and 6.46 (s, H-4); ^{13}C (see Table I), δ 13.9 (Me), 14.4 (CH_3CH_2), 60.3 (CH_3CH_2), 108.8 (C-4), 114.2, (C-3), 149.6 (C-5), 159.6 (C-2), and 163.8 (COO).

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.78; H, 7.16.

Photo-oxygenation of (**3**). — (*a*) *In dichloromethane.* Photo-oxygenation of **3** (1 g, 3.37 mmol) in CH_2Cl_2 (30 mL) was carried out under the general conditions. The reaction, which was monitored by t.l.c., was complete in 7 h. Concentration of the solution afforded ethyl 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 3-acetylfumarate (**5**; 1 g, 96%) as a yellow, viscous liquid, $[\alpha]_D$ −90° (*c* 4, chloroform); ν_{max}^{film} 1740 (COO), 1635 (C=C), and 1375 (CMe_2) cm^{-1}; $\lambda_{max}^{CHCl_3}$ 230 nm (ε 7100). ^{1}H-N.m.r. data (CCl_4): δ 1.26 (t, 3 H, *J* 7 Hz), 1.26 (s, 3 H), 1.42 (s, 3 H), 2.35 (s, 3 H), 3.38–4.00 (m, 2 H), 4.23 (q, 2 H, *J* 7 Hz), 4.49–4.85 (m, 2 H), 6.06 (s, 1 H), and 6.56 (s, 1 H).

Anal. Calc. for $C_{15}H_{20}O_8$: C, 54.87; H, 6.14. Found: C, 54.54; H, 6.39.

(*b*) *In acetone.* Photo-oxygenation of **3** (1.8 g, 6 mmol) in acetone (50 mL) was carried out for 1 h. Concentration *in vacuo* of an aliquot of the solution at room temperature gave the *endo*-peroxide **4**. ^{1}H-N.m.r. data (CCl_4): δ 7.1 (s, 1 H, vinylic H) and 1.95 (s, 3 H, Me-C$\begin{smallmatrix}OO\\O\end{smallmatrix}$). The rearrangement **4**→**5** was readily observed by the appearance of signals at δ 6.56 (s, 1 H, =CH) and 2.35 (s, 3 H, MeCO), and the disappearance of the singlets noted above.

Another aliquot (2 mL) of the solution was treated with Me_2S. The ^{1}H-n.m.r. spectrum of the product was a mixture of methyl sulphoxide (δ 2.52, s, 6 H) and the diketone **20** [δ 7.20 (s, 1 H, =CH) and 2.37 (s, 3 H, Me-CO)].

The remainder of the solution was kept at room temperature and the ester **5** was formed as in (*a*).

(*c*) *In methanol.* Photo-oxygenation of **3** (4 g, 13.48 mmol) in methanol (50 mL) for 24 h, under the general conditions, gave ethyl 2,3-*O*-isopropylidene-β-D-erythrofuranosyl 2-acetyl-3-methoxysuccinate (**13**; 4.67 g, 96%) as the main product after purification by column chromatography (hexane–ether, 2:1). It was a viscous liquid which gave a positive enol test and had $[\alpha]_D$ −33° (*c* 2.25, methanol); ν_{max}^{film} 1740 (COO), 1725 (COO), and 1375 (CMe_2) cm^{-1}; λ_{max}^{MeOH} 243 nm (ε 540). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.27, 1.30 (2 t, 3 H, *J* 7 Hz), 1.33, 1.47 (2 s, 6 H), 2.27, 2.32 (2 s, 3 H), 3.44, 3.47 (2 s, 3 H), 3.88–4.37 (m, 6 H), 4.67 (d, 1 H, *J* 6 Hz), 4.88 (dd, 1 H, *J* 6 and 3 Hz), 6.17 and 6.18 (2 s, 1 H).

Anal. Calc. for $C_{16}H_{20}O_9$: C, 53.33; H, 6.66. Found: C, 53.14; H, 6.61.

Saponification of ethyl 2,3-O-isopropylidene-β-D-erythrofuranosyl 2-acetylfumarate (**5**). — A solution of **5** (2 g, 5.6 mmol) in 2.75M NaOH (5 mL) was boiled under reflux for 1 h, cooled, and extracted with ethyl acetate (5 × 6 mL). The combined extracts were washed with water and concentrated. The residue was purified by column chromatography (hexane–ether, 3:1) and identified as 2,3-*O*-isopropylidene-D-erythrose[9] (550 mg, 60%), m.p. 27°, $[\alpha]_D$ −72° (*c* 1.64, methanol); ν_{max}^{KBr} 3410 (OH), 1375 (CMe_2), and 1165 (dioxolane ring) cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 1.26 (s, 3 H), 1.38 (s, 3 H), 3.62–3.84 (bs, 1 H), 3.90 (d, 1 H, *J* 2 Hz), 4.43 (d, 1 H, *J* 6 Hz), 4.70 (dt, 1 H, *J* 6 and 2 Hz), and 5.25 (s, 1 H).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.50; H, 7.50. Found: C, 52.35; H, 7.25.

Acetylation of 2,3-*O*-isopropylidene-D-erythrose with acetic anhydride–

pyridine gave the β-acetate **21** (84%), m.p. 61–63° (from ethanol–water), $[\alpha]_D$ −104.5° (*c* 1, methanol); ν_{max}^{KBr} 1750, 1385, 1240–1220, and 1100 cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.17 (s, 1 H), 4.88 (dd, 1 H, *J* 6 and 3 Hz), 4.66 (d, 1 H, *J* 6 Hz), 4.15 (d, 1 H, *J* 10 Hz), 3.96 (dd, 1 H, *J* 10 and 3 Hz), 2.05 (s, 3 H), 1.47 (s, 3 H), and 1.32 (s, 3 H).

Anal. Calc. for $C_9H_{14}O_5$: C, 53.45; H, 6.97. Found: C, 53.65; H, 7.02.

Methanolysis of ethyl 2,3-O-isopropylidene-β-D-erythrofuranosyl 2-acetylfumarate (**5**). — A solution of **5** (1.8 g, 5.5 mmol) in methanol (25 mL) containing sodium methoxide (from 2 mg of sodium) was kept at room temperature for 48 h, neutralised with glacial acetic acid, and concentrated. The residue was subjected to column chromatography (hexane–ether, 3:1) to yield, first, a syrup (300 mg) that was rechromatographed to yield 4-ethoxycarbonyl-5-methoxy-5-methyl-2-oxo-2,5-dihydrofuran (**15**; 100 mg, 9%) as a colourless oil; ν_{max}^{film} 1780 (lactone CO), 1730 (COO), and 1650 (C=C) cm^{-1}. ^{1}H-N.m.r. data (CCl_4): δ 6.46 (s, 1 H), 4.19 (q, 2 H, *J* 7 Hz), 3.08 (s, 3 H), 1.70 (s, 3 H), and 1.30 (t, 3 H, *J* 7 Hz). Eluted second was ethyl methyl 2-acetyl-3-methoxysuccinate (two pairs of enantiomers) (**17**; 600 mg, 47%) as a colourless liquid; ν_{max}^{film} 1740 (COO) cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H, δ 1.27, 1.30 (2 t, 3 H, *J* 7 Hz), 2.30, 2.32 (2 s, 3 H), 3.47, 3.51 (2 s, 3 H), 3.78, 3.80 (2 s, 3 H), and 3.92–4.50 (m, 4 H); ^{13}C (see Table II), δ 52.3 (CH_3OCO); $\lambda_{max}^{CCl_4}$ 243 nm (ε 550).

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.72; H, 6.90. Found: C, 51.42; H, 6.59.

Eluted third was 2,3-*O*-isopropylidene-D-erythrose (750 mg, 85%).

Ethanolysis of ethyl 2,3-O-isopropylidene-β-D-erythrofuranosyl 2-acetyl-3-methoxysuccinate (**13**). — A solution of **13** (1.95 g, 5.42 mmol) in ethanol (25 mL) containing a catalytic amount of sodium ethoxide (from 5 mg of sodium) was kept at room temperature for 90 h, and then neutralised with glacial acetic acid and concentrated. The residue was subjected to column chromatography (hexane–ethyl acetate, 4:1) to give, first, diethyl 2-acetyl-3-ethoxysuccinate (mixture of diastereomers) (**18**; 420 mg, 30%) as a colourless oil, $[\alpha]_D$ +4° (*c* 0.76, methanol); λ_{max}^{MeOH} 248 nm (ε 3900); ν_{max}^{film} 1750, 1730, 1370, 1250, and 1090 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H, δ 1.16, 1.30, 1.31, and 1.27 (4 t, 9 H, *J* 7 Hz), 2.28, 2.32 (2 s, 3 H), 3.30–3.95 (m, 2 H), 4.03 (dd, 1 H, *J* 9 and 1.2 Hz), 4.10–4.40 (m, 4 H), and 4.46 (d, 1 H, *J* 9 Hz); ^{13}C (see Table II), δ 67.7 and 67.6 (t, $-OCH_2CH_3$ ether) and 15.1 (q, $-OCH_2CH_3$ ether).

Anal. Calc. for $C_{12}H_{20}O_6$: C, 55.38; H, 7.69. Found: C, 54.78; H, 7.47.

Eluted second was 2,3-*O*-isopropylidene-D-erythrose (860 mg, 98%).

Diethyl 2-acetyl-3-methoxysuccinate (**19**). — A solution of **18** (150 mg, 0.58 mmol) in methanol (25 mL) was kept at room temperature for 5 days; the $[\alpha]_D$ value was then 0°. Removal of the solvent left **19** as a colourless syrup; ν_{max}^{film} 1745, 1725, 1360, and 1080 cm^{-1}; λ_{max}^{MeOH} 247 nm (ε 3900). ^{1}H-N.m.r. data ($CDCl_3$): δ 1.26, 1.29 (2 t, 6 H, *J* 7 Hz), 2.28, 2.31 (2 s, 3 H), 3.45, 3.48 (2 s, 3 H), 4.00 (dd, 1 H, *J* 8.8 and 2.3 Hz), 4.35 (d, 1 H, *J* 8.8 Hz), and 4.06–4.40 (m, 4 H).

Anal. Calc. for $C_{11}H_{18}O_6$: C, 53.66; H, 7.31. Found: C, 53.72; H, 7.55.

Diethyl 2-acetylfumarate (**22**) *and diethyl 2-acetylmaleate* (**23**). — The ethyl alcoholate of ethyl glyoxylate was prepared by periodate oxidation of diethyl tartrate (30.6 g) in aqueous solution. Ethanol was added, the precipitated $NaIO_3$ was removed, and the filtrate was concentrated *in vacuo*. Addition of ethanol, filtration, and concentration was repeated until no more $NaIO_3$ precipitated. Distillation then gave the product, b.p. 121–122° (16 g, 50%).

To a mixture of this product (5.02 g) and ethyl acetoacetate (4.4 g) was added piperidine (0.3 mL). Heat was developed. Distillation then yielded a mixture (6.1 g, 85%) of **22** and **23** as a pale-yellow liquid, b.p. 106–108°/1 mmHg (lit.[8] b.p. 150–152°/20 mmHg); ν_{max}^{film} 1750–1720, 1640, 1255, and 1020 cm^{-1}. ^{1}H-N.m.r. ($CDCl_3$) data: δ 6.74, 6.68 (2 s, 1 H), 4.37, 4.29, 4.23 (4 q, 4 H, *J* 7.1 Hz), 2.45, 2.39 (2 s, 3 H), 1.35, 1.32, 1.31, and 1.30 (4 t, 6 H, *J* 7.1 Hz).

A solution of the mixture of **22** and **23** in $CDCl_3$ containing just more than 1 equiv. of methanol or ethanol was stored at room temperature. The addition to the double bond was monitored by ^{1}H-n.m.r. spectroscopy. After the completion of this reaction (no vinyl proton signal), the solvent was removed, yielding **18** and **19**, respectively. The products were identifical with those prepared as above.

*3-Hydroxymethyl-5-(2,3-*O*-isopropylidene-β-*D*-erythrofuranosyl)-2-methylfuran* (**6**). — The furoic ester **3** (9.5 g, 32 mmol) was reduced in anhydrous ether (100 mL) by its gradual addition to a suspension of $LiAlH_4$ (2 g, 53 mmol) in the same solvent (50 mL). The reaction was monitored by t.l.c. and was complete in 3 h. The excess of $LiAlH_4$ was decomposed by the gradual addition of water (50 mL), the aqueous layer was removed and extracted with ether (3 × 35 mL), and the combined extracts were concentrated, to yield **6** (7.3 g, 89%) as a colourless syrup, $[\alpha]_D$ −71° (*c* 1, chloroform); ν_{max}^{film} 3540 (OH), 1650 (furan ring), and 1390 (CMe_2) cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.05 (s, 1 H), 4.75 (bs, 3 H), 3.77 (s, 2 H), 2.90 (s, 1 H, OH), 3.12 (s, 3 H), 1.45 (s, 3 H), and 1.26 (s, 3 H). This crude product was used for the next photo-oxygenation without further purification.

Photo-oxygenation of **6**. — (*a*) *In methanol.* A solution of crude **6** (50 mg, 0.2 mmol) was photo-oxygenated for 0.5 h in methanol (10 mL) under the general conditions. The product appeared to be a hydroperoxide (**8** or **9**) according to the ^{1}H-n.m.r. signals at δ 9.45 (bs, 1 H, OOH), 3.20 (s, 3 H), and 1.45 (s, 3 H). On addition of Me_2S, the signal at δ 9.45 disappeared and the formation of methyl sulphoxide was shown by the appearance of a signal at δ 2.5 (s, 6 H). In this reduction to give **11** or **12**, the ^{1}H-n.m.r. spectrum remained practically unchanged, but the OMe signal was shifted to δ 3.22.

When water was evaporated several times from **11** (**12**), the methanol was displaced, to yield the hydrate (**24**) of **10**, and the signal at δ 3.22 disappeared.

(*b*) *In acetone.* The photo-oxygenation of **6** (1.53 g, 6 mmol) in acetone (40 mL) was performed as described above for 2 h, to yield **14** (0.95 g, 55%), m.p. 100–101° (after purification by column chromatography with hexane–ether, 2:1), $[\alpha]_D$ −100° (*c* 1, chloroform); ν_{max}^{KBr} 3480 (OH), 1735 (COO), 1700 (C=O), 1650 (C=C), and 1385 (CMe_2) cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.13 (s, H-1′), 5.86 (t, 1 H, *J*

1.9 Hz, vinylic H), 4.88–4.78 (dd, 1 H, *J* 5.7 and 3.3 Hz, H-3′), 4.62 (d, 1 H, *J* 5.7 Hz, H-2′), 4.34–4.27 (dd, 2 H, *J* 5.4 and 1.8 Hz, CH_2OH), 4.17–4.05 (d, 1 H, *J* 10.5 Hz, H-4′), 3.99–3.86 (dd, 1 H, *J* 10.5 and 3.3 Hz, H-4′), 2.60 (t, 1 H, *J* 5.4 Hz, OH), 2.35 (s, 3 H, Me-CO), 1.43 and 1.28 (2 s, 6 H, Me_2C).

Anal. Calc. for $C_{13}H_{18}O_7$: C, 54.54; H, 6.34. Found: C, 54.49; H, 6.38.

Methanolysis of 2,3-O-isopropylidene-β-D-erythrofuranosyl (Z)-3-acetyl-3-hydroxymethylacrylate (**14**). — A solution of **14** (0.72 g, 2.5 mmol) in methanol (25 mL) containing a catalytic amount of sodium methoxide (from 2.5 mg of sodium) was heated under reflux for 1 h and then kept at room temperature for 12 h. The reaction was monitored by t.l.c. After neutralisation with acetic acid, the solution was concentrated and the residue was subjected to column chromatography (ether–hexane, 2:1), to yield, first, 2,3-*O*-isopropylidene-D-erythrose (360 mg, 90%) as a colourless syrup, and then 4-hydroxymethyl-5-methoxy-5-methyl-2-oxo-2,5-dihydrofuran (**16**; 230 mg, 53.7%) also as a colourless oil, $[\alpha]_D$ −2° (*c* 10, chloroform); ν_{max}^{film} 3450 (OH), 1760 (CO lactone), and 1665 (C=C) cm^{-1}. ^{1}H-N.m.r. data ($CDCl_3$): δ 6.00 (t, 3 H, *J* 3 Hz), 4.00 (bs, 1 H), 3.08 (s, 3 H), and 1.55 (s, 3 H).

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