Carbohydrate Research, 191 (1989) 209–221
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

PHOTO-OXYGENATION OF POLYHYDROXYALKYL- AND GLYCOSYL-FURANS: 1,3-DIPOLAR CYCLOADDITION REACTIONS OF THE PRODUCTS

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(Received August 2nd, 1988; accepted for publication, April 6th, 1989)

ABSTRACT

3-Acetyl-2-methyl-5-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-yl)furan (**1a**), 5-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-yl)-3-ethoxycarbonyl-2-phenylfuran (**1b**), 3-ethoxycarbonyl-5-(2,3-*O*-isopropylidene-β-D- and -α-D-erythrofuranosyl)-2-phenylfuran (**1c** and **1d**), 3-acetyl-5-(2,3-di-*O*-acetyl-β-D-erythrofuranosyl)-2-methylfuran (**1e**), 3-acetyl-5-(2,3-di-*O*-acetyl-α-D- and -β-D-threofuranosyl)-2-methylfuran (**1f** and **1g**) have been transformed, through the corresponding endoperoxides, into 3-*C*-acetyl-6,7,8,9-tetra-*O*-acetyl-1,3,4-trideoxy-D-*arabino*-non-3-eno-2,5-diulose (**3a**), ethyl (*E*)-2-*C*-benzoyl-2,3,4-trideoxy-5,6:7,8-di-*O*-isopropylidene-D-*arabino*-oct-2-en-4-ulosonate (**3b**), ethyl (*E*)-5,8-anhydro-2-*C*-benzoyl-2,3,4-trideoxy-6,7-*O*-isopropylidene-D-*ribo*- (**3c**) and -D-*arabino*-oct-2-en-4-ulosonate (**3d**), 2,3-di-*O*-acetyl-β-D-erythro- (**4e**) and -α-D-threo-furanosyl 3-*C*-acetyl-4-oxopent-2-enoate (**4f**), and 3-*C*-acetyl-7,8-di-*O*-acetyl-6,9-anhydro-1,3,4-trideoxy-D-*xylo*-non-3-eno-2,5-diulose (**3g**).

The above γ-diketones and γ-ketoesters reacted with methyl diazoacetate to yield 5,5-diacetyl-3-methoxycarbonyl-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-ylcarbonyl)-Δ^2-pyrazoline (**11a**), 5-benzoyl-4-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-ylcarbonyl)-5-ethoxycarbonyl-3-methoxycarbonyl-Δ^2-pyrazoline (**11b**), 4-(2,5-anhydro-3,4-*O*-isopropylidene-D-ribonyl- and -D-arabinonyl)-5-benzoyl-5-ethoxycarbonyl-3-methoxycarbonyl-Δ^2-pyrazoline (**11c** and **11d**), 2,3-di-*O*-acetyl-β-D-erythrofuranosyl and -α-D-threofuranosyl 5,5-diacetyl-3-methoxycarbonyl-Δ^2-pyrazoline-4-carboxylate (**11e** and **11f**), and 5,5-diacetyl-4-(3,4-di-*O*-acetyl-2,5-anhydro-D-xylonyl)-3-methoxycarbonyl-Δ^2-pyrazoline (**11g**) as pairs of diastereomers.

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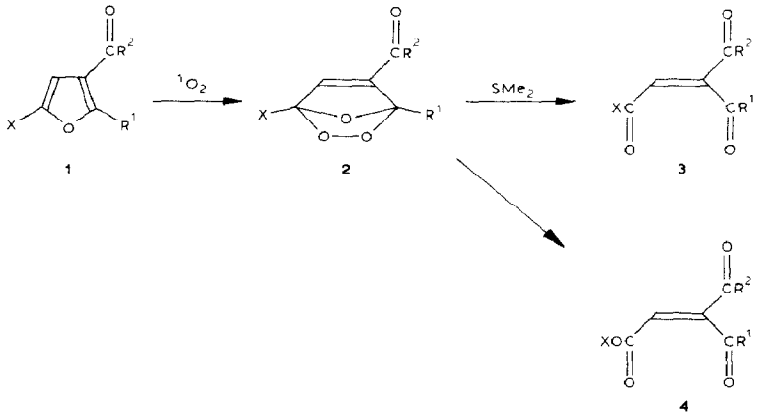
0008-6215/89/$ 03.50



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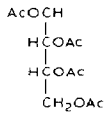
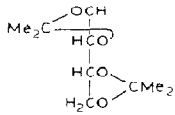
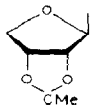
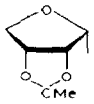
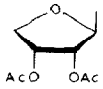
a	Me	Me	
b	Ph	OEt	
c	Ph	OEt	
d	Ph	OEt	
e	Me	Me	
f	Me	Me	
g	Me	Me	

INTRODUCTION

We have reported[1] on the reaction of furan derivatives with singlet oxygen and the rearrangement or reduction of the resulting endoperoxides, as applied to 2,3,5-trisubstituted furans with a polyhydroxyalkyl or glycosyl substituent at position 5 and an electron-withdrawing group at position 3 of the ring (type **1** compounds).

The sequence of reactions **1**→**2**→**3** (or **1**→**2**→**4**) gives high yields of polyhydroxyalkyl or glycosyl olefins of types **3** or **4**, which were used for the synthesis of polyhydroxyalkyl- or glycosyl-pyrimidines[1b].

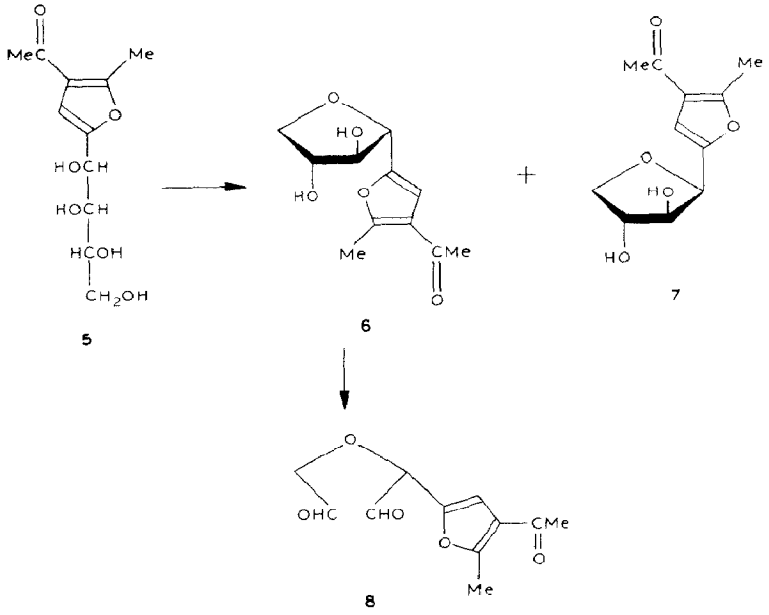
The three electron-withdrawing groups attached to the double bond in **3** and **4** result in marked electrophilic character[1a,2]. The polarity of the carbonyl groups conjugated with such double bonds promotes 1,3-dipolar cycloadditions, as with alkyl diazoacetate, to give pyrazolines[3,4]. The reaction sequence has now been applied to α,β-unsaturated-γ-ketoesters or γ-diketones to prepare polyhydroxyalkyl- or glycosyl-pyrazoline derivatives.

RESULTS AND DISCUSSION

The γ-diketones (**3a–f**) and γ-ketoesters (**4a–f**) were synthesised as shown. The olefins **3a–c** have been reported[1c,1d] and their structures established. The photo-oxygenation of **1d**[1c] was monitored on the basis of the volume of oxygen consumption (see Experimental). The endoperoxide **2d** was not isolated, but reduced immediately to give **3d**. The structures of **3d** and all new compounds described below were established on the basis of n.m.r. and i.r. spectroscopic data recorded in the Experimental.

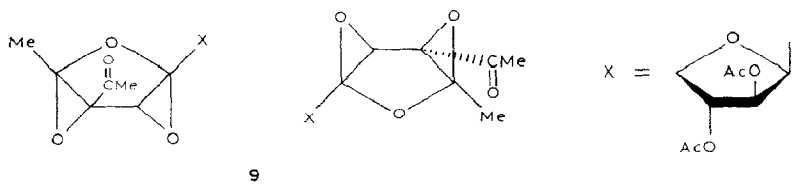
When 1 mol of oxygen had been consumed on photo-oxygenation of **1e**[5], the solution was kept at room temperature for 24 h to allow the endoperoxide **2e** to rearrange, by a process similar to Baeyer–Villiger rearrangement[1], to give **4e**. For the preparation of **3f** and **3g**, D-galactose and 2,4-pentanedione were reacted in the presence[6] of $ZnCl_2$ to give 3-acetyl-2-methyl-5-(D-*lyxo*-tetritol-1-yl)furan (**5**), which was not isolated, but dehydrated to give the threofuranosyl derivatives **6** and **7**. The diacetates (**1f** and **1g**) of **6** and **7** were separated by fractional crystallization. The absolute configurations at the anomeric centres of **1f** and **1g** were established by *O*-deacetylation of **1f** followed by periodate oxidation of **6** to yield the dialdehyde **8**, which had $[\alpha]_D$ +18° (water). Since the corresponding product prepared[7] from 3-acetyl-5-β-D-erythrofuranosyl-2-methylfuran had $[\alpha]_D$ −19° (water), **1f** and **6** are α and, consequently, **1g** and **7** are β.

Photo-oxygenation of **1f** and **1g** yielded the corresponding endoperoxides **2f** and **2g**, each comprising a pair of diastereomers[1e] as indicated by the ^{1}H-n.m.r. data. Thus, the spectrum of **2f** contained signals for OAc groups at δ 2.08, 2.07, 2.06, and 2.05. The reduction of **2f** and **2g** with dimethyl sulphide gave only one diketone (**3f**) as indicated by ^{1}H-n.m.r. spectroscopy, but the product could not be

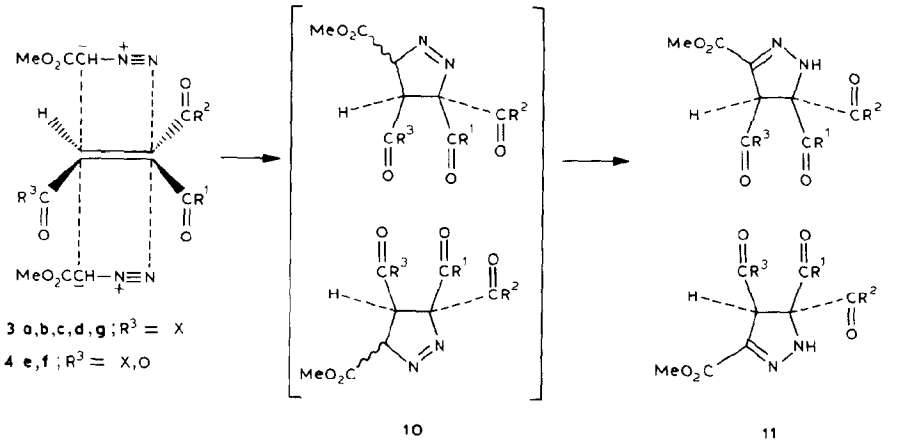


isolated. On dissolution in acetone for 10 h, the diastereomers of **2f** rearranged into **4f**.

In contrast, the pair of endoperoxides **2g** were more stable and one (**2g1**) was isolated by fractional crystallisation. In the solid state, **2g1** isomerised into the diepoxide **9**. In solution in acetone, **2g1** gave a mixture of products; the ^{1}H-n.m.r. spectrum revealed the presence of **9** and the rearranged product **4g**. The reduction of **2g** yielded the corresponding γ-diketone **3g**.



1,3-Dipolar cycloaddition is a general method for the synthesis of 5-membered heterocycles[8]. The reaction of **3** or **4** with methyl diazoacetate each gave, presumably, a mixture of diastereomeric Δ^1-pyrazolines **10** that were transformed immediately into the diastereomeric Δ^2-pyrazolines[9] **11**. In each reaction, the -CH- group of the diazo compound added to the less positive carbon atom of the C=C bond. The yields in the cycloaddition reactions were good. Attack at both faces of the double bond occurred but not to the same extent. There was a small degree of asymmetric induction, reaching a value of 67% diastereomeric excess for **11e**.



Each of the Δ^2-pyrazolines was isolated as a mixture of diastereomers; only for **11a** could a pure diastereomer be isolated by column chromatography.

EXPERIMENTAL

General methods. — Melting points were determined with a Reichter hotplate microscope and are uncorrected. Solutions were dried over Na_2SO_4 before concentration under diminished pressure. I.r. spectra were recorded with a Perkin–Elmer 983-G spectrometer. N.m.r. spectra (internal Me_4Si) (^1H, 300 and 80 MHz; ^{13}C, 75 and 20 MHz) were recorded with Bruker A-300 and WP-80-SY spectrometers. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. Elemental analyses were performed in a Carlo Erba Elemental Analyzer 1106. Satisfactory analyses could not be obtained for non-crystalline compounds, the homogeneity of which was established by chromatography. T.l.c. was performed on Silica Gel G (Merck), with detection by charring with sulfuric acid, and 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. Reactions were monitored by measuring the volume of oxygen consumed.

*3-Acetyl-5-(2,3-di-*O*-acetyl-β-*D*-erythrofuranosyl)-2-methylfuran* (**1e**). — A solution of 3-acetyl-2-methyl-5-(D-*arabino*-tetritol-1-yl)furan[5] (10 g) in the minimum amount of conc. hydrochloric acid was kept for 15 min at room temperature, water was added (50 mL), and the solution was neutralised with sodium hydrogencarbonate and extracted with ethyl acetate (4 × 30 mL). The combined extracts were dried and concentrated to give a syrup that was treated conventionally with acetic anhydride–pyridine to yield **1e** (11.0 g, 81%), isolated as a syrup, $[\alpha]_D$ −95° (*c* 1, methanol); ν_{max}^{film} 3110, 2940, 1745, 1675, 1600, 1565, 1230, 1055, and 950

TABLE I

^{1}H-N.M.R.[a] DATA (δ SCALE) FOR **6, 7, 1f, 1g,** AND **1e**

Atoms	**6**	**7**	**1f**	**1g**	**1e**
H-4	6.70	6.58	6.62	6.52	6.50
H-1′	4.57 (d, 5 Hz)	4.97 (d, 3 Hz)	4.76 (d, 5 Hz)	5.07 (d, 4 Hz)	5.70–3.30 (m, 5 H)
H-2′	4.98–3.50 (m, 6 H)	4.40–4.03 (m, 6 H)	5.45 (dd, 5 and 2 Hz)	5.42–5.20 (m, 2 H)	
H-3′	4.98–3.50 (m, 6 H)	4.40–4.03 (m, 6 H)	5.29–5.15 (m, 1 H)		
H-4′β	4.98–3.50 (m, 6 H)	4.40–4.03 (m, 6 H)	4.32–3.92 (m, 2 H)	4.40 (dd, 11 and 5 Hz)	
H-4′α	4.98–3.50 (m, 6 H)	4.40–4.03 (m, 6 H)	4.32–3.92 (m, 2 H)	3.65 (dd, 11 and 5 Hz)	
2 OH	4.98–3.50 (m, 6 H)	4.40–4.03 (m, 6 H)	4.32–3.92 (m, 2 H)		
Me	2.53	2.48	2.60	2.52	2.60
MeCO	2.33	2.31	2.40	2.33	2.40
MeCOO			2.10 (6 H)	2.09	2.12
				1.94	1.98

[a]80 MHz.

TABLE II

^{13}C-N.M.R. DATA (P.P.M.) FOR **6**, **7**, **1f**, **1g**, AND **1e**

Atom	**6**	**7**	**1f**	**1g**	**1e**
CH_3CO	194.3	195.0	193.7	193.6	193.5
C-2	158.2	158.6	158.9	158.5	159.0
C-5	152.2	148.7	148.5	147.1	148.3
C-3	122.8	122.1	122.1	122.0	121.9
C-4	109.1	109.6	109.4	109.0	109.8
C-1'[a]	82.0	77.9	79.4	77.1	74.6
C-2'[a]	80.8	77.1	78.3	76.4	73.4
C-3'[a]	78.6	76.6	78.0	75.4	71.0
C-4'	74.0	73.5	72.0	71.3	70.5
CH_3CO	29.0	29.0	29.0	29.0	28.8
CH_3	14.2	14.2	14.4	14.2	14.2
CH_3COO			170.4	169.1	169.7
			169.6		169.5
CH_3COO			20.7	20.7	20.4
				20.5	20.3

[a]These signals can be interchanged.

cm^{-1}. For the ^{1}H- and ^{13}C-n.m.r. data ($CDCl_3$), see Tables I and II, respectively.

Reactions of D-*galactose with pentane-2,4-dione*. — A mixture of D-galactose (15 g, 83.3 mmol), pentane-2,4-dione (15 mL), zinc chloride (7.5 g), water (15 mL), and ethanol (15 mL) was stirred and boiled under reflux for 48 h. The remaining pentane-2,4-dione was extracted with hexane (2 × 30 mL). The mixture was extracted with ethyl acetate (8 × 30 mL), and the combined extracts were dried and concentrated *in vacuo*. Column chromatography (AcOEt–hexane, 2:1) of the residue gave 3-acetyl-2-methyl-5-(α,β-D-threofuranosyl)furan (**6** + **7**; 18 g, 95%), isolated as a syrup. ^{1}H-N.m.r. data (80 MHz, $CDCl_3$): δ 6.70, 6.78 (2 s, 1 H, H-4), 4.97, 4.57 (2 d, 1 H, *J* 3 and 5 Hz, H-1'), 4.40–3.50 (m, 6 H, H-2',3',4'α,4'β and 2 OH), 2.53, 2.48 (2 s, 3 H, Me-2), 2.36 and 2.31 (2 s, 3 H, Ac-3).

The mixture (5 g, 22 mmol) of **6** + **7** was treated conventionally with acetic anhydride–pyridine. Column chromatography (AcOEt–hexane, 1:1) of the product gave a syrup (4.60 g) that crystallised from ether at −20° to give 3-acetyl-5-(2,3-di-*O*-acetyl-β-D-threofuranosyl)-2-methylfuran (**1g**; 1.18 g, 18.6%), m.p. 144°, $[\alpha]_D$ −6° (*c* 1, methanol); ν_{max}^{KBr} 3120, 2994, 1740, 1668, 1605, 1563, 1467, 1408, 1371, 1322, 1221, 1138, 1088, 1040, 961, 855, 783, and 640 cm^{-1}. For the ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Anal. Calc. for $C_{15}H_{18}O_7$: C, 58.05; H, 5.80. Found: C, 58.19; H, 5.81.

The mother liquor was concentrated *in vacuo* to yield 3-acetyl-5-(2,3-di-*O*-acetyl-α-D-threofuranosyl)-2-methylfuran (**1f**; 3.40 g, 41%), $[\alpha]_D$ +6° (*c* 1, methanol); ν_{max}^{film} 2993, 1744, 1677, 1564, 1360, 1228, 1045, and 949 cm^{-1}. For the ^{1}H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

*3-Acetyl-2-methyl-5-(α-*D-*threofuranosyl)furan* (**6**). — To a solution of **1f** (1

g, 3.2 mmol) in methanol (25 mL) was added methanolic sodium methoxide (1 mL of a solution prepared from 0.1 g of sodium and 35 mL of methanol). The mixture was stored at room temperature for 3 h, then neutralized with acetic acid, deionised, and concentrated. Column chromatography (AcOEt–hexane, 2:1) of the product gave **6**, isolated as a syrup (650 mg, 82%), $[\alpha]_D$ +10° (*c* 1, methanol); ν_{max}^{film} 3404, 2928, 1662, 1561, 1413, 1366, 1231, 1061, 952, and 814 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

3-Acetyl-2-methyl-5-(β-D-threofuranosyl)furan (**7**). — To a solution of **1g** (420 mg, 1.35 mmol) in methanol (25 mL) was added methanolic sodium methoxide (1 mL, as above). Column chromatography (AcOEt–hexane, 2:1) of the product gave **7** (240 mg, 73%), isolated as a syrup, $[\alpha]_D$ −10° (*c* 1, methanol); ν_{max}^{film} 3204, 2934, 1666, 1609, 1564, 1415, 1235, 1190, 1172, 1038, 960, and 800 cm^{-1}. For the ^1H- and ^{13}C-n.m.r. data, see Tables I and II, respectively.

Periodate oxidation of **6**. — To a solution of **6** (600 mg, 2.5 mmol) in acetone–water (50%, 50 mL), cooled in an ice–water bath, was added sodium periodate (600 mg, 2.8 mmol), and the mixture was kept at room temperature for 4 h. The acetone was evaporated *in vacuo*, the aqueous solution was extracted with ethyl acetate (4 × 25 mL), and the combined extracts were dried and concentrated under diminished pressure. Column chromatography of the residue gave the dialdehyde **8** (485 mg, 75%), m.p. 100°, $[\alpha]_D$ +18° (*c* 1, water); lit.[5,7] for the enantiomer, $[\alpha]_D$ −19° (water).

Photo-oxygenation of **1d**. — A solution of **1d** (1 g, 2.79 mmol) in acetone (35 mL) was photo-oxygenated for 20 min. Dimethyl sulphide (2 mL) was added, and the mixture was kept at room temperature for 30 min, then concentrated *in vacuo*. Short-column chromatography (ether–hexane, 5:1) of the residue gave (*E*)-5,8-anhydro-2-*C*-benzoyl-2,3,4-trideoxy-6,7-*O*-isopropylidene-D-*arabino*-oct-2-en-4-ulosonate (**3d**; 670 mg, 67%), $[\alpha]_D$ −95.2° (*c* 1, chloroform); ν_{max}^{film} 2939, 1713, 1687, 1619, 1583, 1450, 1371, 1249, 1160, 1090, 1016, 736, and 704 cm^{-1}. N.m.r. data ($CDCl_3$): ^1H (80 MHz), δ 7.70 (s, 1 H, HC=), 7.95–7.32 (m, 5 H, Ph), 5.00–4.00 (m, 6 H, CH_2CH_3, H-1′,2′,3′,4′α), 3.57 (dd, 1 H, *J* 11 and 3.5 Hz, H-4′β), 1.48, 1.30 (2 s, 6 H, CMe_2), and 1.20 (t, 3 H, *J* 7 Hz, CH_3CH_2); ^{13}C (20 MHz), δ 194.8, 193.2 (2 CO), 153.5 (C-1), 142.8 (C-2), 133.4, 135.4, 132.4, 129.6 (C-3 and aromatic C), 112.9 (CMe_2), 86.3, 82.2, 80.5 (C-1′,2′,3′), 73.2 (C-4′), 62.2 (CH_2CH_3), 25.7, 24.2 (CMe_2), and 13.7 (CH_2CH_3).

Sensitized photo-oxygenation of **1e**. — A solution of **1e** (1.55 g, 5 mmol) in acetone (35 mL) was photo-oxygenated for 40 min. The solution was kept at room temperature for 24 h, then concentrated *in vacuo*. Column chromatography (hexane–acetone, 5:1) of the residue gave 2,3-di-*O*-acetyl-β-D-erythrofuranosyl 3-*C*-acetyl-4-oxopent-2-enoate (**4e**; 800 mg, 47%), $[\alpha]_D$ −69° (*c* 1, chloroform); ν_{max}^{film} 3003, 1743, 1678, 1632, 1426, 1371, 1241, 1167, 980, and 740 cm^{-1}. N.m.r. data ($CDCl_3$): ^1H (300 MHz), δ 6.50 (s, 1 H, H-2), 6.21 (d, 1 H, *J* 1.5 Hz, H-1′), 5.57–5.30 (m, 2 H, H-2′,3′), 4.22–4.42 (dd, 1 H, *J* 10.2 and 5.25 Hz, H-4′α), 3.92–4.10 (dd, 1 H, *J* 10.2 and 4.15 Hz, H-4′β), 2.42, 2.41 (2 s, 6 H, 2 Ac), 2.15 and 2.10 (2

s, 6 H, 2 AcO); ^{13}C (75 MHz), δ 201.2, 195.8 (2 CH_3CO), 169.9, 169.3 (2 CH_3COO), 163.1 (C-1), 154.3 (C-2), 125.3 (C-3), 100.3 (C-1'), 74.7, 70.5 (C-2',3'), 71.1 (C-4'), 30.7, 26.8 (2 CH_3CO), and 20.3 (2 CH_3COO).

Photo-oxygenation of **1f**. — A solution of **1f** (700 mg, 2.2 mmol) in acetone (35 mL) was photo-oxygenated for 25 min, then concentrated *in vacuo*, ether (20 mL) was added to the residue, and the solution was filtered and concentrated to yield 3-acetyl-5-(2,3-di-*O*-acetyl-α-D-threofuranosyl)-2,5-epidioxy-2-methyl-2,5-dihydrofuran (**2f**) as a pair of diastereomers. ^1H-N.m.r. data ($CDCl_3$): δ 7.09 (s, 1 H, HC=), 5.48–5.43 (m, 1 H, H-2'), 5.28–5.12 (m, 1 H, H-3'), 4.45–4.37 (dd, 1 H, *J* 12 and 4.3 Hz, H-4'β), 4.28–4.02 (m, 2 H, H-4'α), 2.29 (s, 3 H, Ac), 2.08, 2.07, 2.06, 2.05 (4 s, 6 H, 2 AcO), and 1.96 (s, 3 H, Me–C$\lessdot^{O-O}_{O}$).

Rearrangement of **2f**. — A solution of **2f** (620 mg, 2 mmol) in dry acetone (20 mL) was kept at room temperature for 10 h, then concentrated under diminished pressure. Column chromatography (AcOEt–hexane, 2:1) of the residue gave 2,3-di-*O*-acetyl-α-D-threofuranosyl 3-*C*-acetyl-4-oxopent-2-enoate (**4f**; 530 mg, 78%), $[\alpha]_D$ +30° (*c* 1, methanol); ν_{max}^{film} 2993, 1739, 1678, 1426, 1371, 1225, 1115, 1066, 958, and 882 cm^{-1}. N.m.r. data ($CDCl_3$): ^1H (300 MHz), δ 6.52 (d, 1 H, H-2), 6.18 (s, 1 H, H-1'), 5.20–5.05 (m, 2 H, H-2',3'), 4.56–3.75 (m, 2 H, H-4'α,4'β), 2.43, 2.41 (2 s, 6 H, 2 Ac), and 2.17, 2.15 (2 s, 6 H, 2 AcO); ^{13}C (75 MHz), δ 201.2, 195.7 (2 CH_3CO), 170.2, 169.5 (2 CH_3COO), 163.1 (C-1), 154.1 (C-3), 125.4 (C-2), 100.7 (C-1'), 80.2, 75.6 (C-2',3'), 75.4 (C-4'), 30.9, 27.0 (2 CH_3CO), and 20.7, 20.6 (2 CH_3COO).

Reduction of **2f**. — A solution of **1f** (100 mg, 0.3 mmol) in acetone (30 mL) was photo-oxygenated. When the reaction was finished, the solvent was removed *in vacuo*, and to a solution of the residue in $CDCl_3$ were added 2 drops of dimethyl sulphide. The ^1H-n.m.r. (300 MHz) spectrum showed the signals corresponding to dimethyl sulphoxide [δ 2.55 (s, 6 H)] and 3-*C*-acetyl-7,8-di-*O*-acetyl-6,9-anhydro-1,3,4-trideoxy-D-*lyxo*-non-3-eno-2,5-diulose (**3f**): δ 7.14 (s, 1 H, HC=), 5.23 (s, 1 H, H-2'), 5.09–5.02 (m, 1 H, H-3'), 4.45 (s, 1 H, H-1'), 4.14 (dd, 1 H, *J* 10 and 4.3 Hz, H-4'β), 4.02 (d, 1 H, *J* 10 Hz, H-4'α), 2.25 (s, 6 H, 2 Ac), 1.99 and 1.91 (2 s, 6 H, 2 AcO).

Photo-oxygenation of **1g**. — A solution of **1g** (900 mg, 2.9 mmol) in acetone (35 mL) was photo-oxygenated for 30 min, then concentrated *in vacuo*. A solution of the residue in dry ether (15 mL) was filtered, light petroleum (5 mL) was added, and the solution was kept at −20° for 48 h to yield 3-acetyl-5-(2,3-di-*O*-acetyl-β-D-threofuranosyl)-2,5-epidoxy-2-methyl-2,5-dihydrofuran (**2g1**; 460 mg, 49%), m.p. 145–150° (dec.), $[\alpha]_D$ −82° (*c* 1, chloroform); ν_{max}^{KBr} 3010, 2936, 2920, 1761, 1688, 1598, 1407, 1396, 1266, 1236, 1212, 1154, 1043, 1048, 940, 899, 856, and 740 cm^{-1}. N.m.r. data ($CDCl_3$): ^1H (80 MHz), δ 7.10 (HC=), 5.75 (dd, 1 H, *J* 4 and 2 Hz, H-2'), 5.26–5.12 (m, 1 H, H-3'), 4.61 (d, 1 H, *J* 4 Hz, H-1'), 4.43 (dd, *J* 11 and 5 Hz, H-4'β), 3.78 (dd, 1 H, *J* 11 and 2 Hz, H-4'α), 2.32 (s, 3 H, Ac), and 2.10, 2.00 (2 s, 9 H, Me-C$\lessdot^{O-O}_{O}$ and Ac); ^{13}C (20 MHz), δ 193.4 (CH_3CO), 170.0, 169.0 (2 CH_3COO), 142.7 (C-3), 138.9 (C-4), 113.4, 111.3 (C-2,5), 76.9, 76.0, 75.9 (C-1',2',3'), 75.0 (C-4'), 27.6 (CH_3CO), 21.0 (CH_3COO), and 13.4 (Me, C-2).

Anal. Calc. for $C_{15}H_{18}O_9$: C, 52.63; H, 5.29. Found: C, 52.84; H, 5.18.

The ^{1}H-n.m.r. spectrum of an aliquot of the remaining solution showed the signals corresponding to **2g1** and its diastereomeric endoperoxide **2g2** (δ 7.12 for HC=).

Rearrangement of **2g1**. — (*a*) *In the solid state.* Solid **2g1** (326 mg, 1 mmol) was kept at room temperature for 4 days to give 1-acetyl-4-(2,3-di-*O*-acetyl-β-D-threofuranosyl)-6-methyl-3,5,7-trioxatricyclo[4.1.0.0^{2,4}]heptane (**9**), m.p. 138° (dec.), $[\alpha]_D$ −80° (*c* 1, chloroform); ν_{max}^{KBr} 2972, 1744, 1708, 1371, 1242, 1225, 1149, 1081, 1049, 1043, 990, 941, 861, and 753 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H (300 MHz), δ 5.49 (dd, 1 H, *J* 1.5 and 3.87 Hz, H-2′), 5.19–5.16 (m, 1 H, H-3′), 4.47 (d, 1 H, *J* 3.87 Hz, H-1′), 4.29 (dd, 1 H, *J* 4.89 and 10.66 Hz, H-4′β), 4.28 (s, 1 H, H-2), 3.82 (dd, 1 H, *J* 1.96 and 10.66 Hz, H-4′α), 2.18 (s, 3 H, Ac), 2.10, 2.09 (2 s, 6 H, 2 AcO); ^{13}C (75 MHz), δ 201.8 (CH_3CO), 169.8, 169.4 (CH_3COO), 100.5 (C-4), 95.9 (C-6), 76.9, 75.5, 74.5 (C-1′,2′,3′), 72.6 (CH_2, C-4′), 54.4 (CH, C-2), 26.8 (CH_3CO), 20.8, 20.7 (CH_3COO), and 15.6 (CH_3-2).

Anal. Calc. for $C_{15}H_{18}O_9$: C, 52.63; H, 5.29. Found: C, 52.76; H, 5.23.

(*b*) *In solution in acetone.* A solution of **2g1** (50 mg, 0.15 mmol) in dry acetone (25 mL) was kept at room temperature for 50 h, then concentrated *in vacuo*. The ^{1}H-n.m.r. spectrum ($CDCl_3$) of the residue contained signals for **9** and β-D-threofuranosyl 3-*C*-acetyl-4-oxopent-2-enoate (**4g**) [δ 6.48 (s, 1 H, H-2), 2.40 and 2.34 (2 s, 2 Ac)] in the ratio 1:5, together with signals of unidentified products.

Preparation of **3g**. — A solution of **1g** (1 g, 3 mmol) in dry acetone (35 mL) was photo-oxygenated. When the reaction was complete, dimethyl sulphide was added (2 mL), and the mixture was kept at 3° for 2 h, then concentrated under diminished pressure. Short-column chromatography (ether) of the residue gave 3-*C*-acetyl-7,8-di-*O*-acetyl-6,9-anhydro-1,3,4-trideoxy-D-*xylo*-non-3-eno-2,5-diulose (**3g**), isolated as a pale-yellow syrup, $[\alpha]_D$ −4.5° (*c* 1, chloroform); ν_{max}^{film} 2924, 2403, 2262, 1745, 1677, 1610, 1422, 1371, 1234, 1075, 1044, 940, and 731 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H (80 MHz), δ 7.07 (s, 1 H, HC=), 5.57 (d, 1 H, *J* 4.3 Hz, H-7), 5.15–5.13 (dd, 1 H, *J* 4.3 and 1.5 Hz, H-8), 4.70 (d, 1 H, *J* 4.3 Hz, H-6), 4.38 (dd, 1 H, *J* 10.7 and 4.3 Hz, H-9β), 3.97 (dd, 1 H, *J* 10.7 and 1.5 Hz, H-9α), 2.38, 2.34 (2 s, 6 H, 2 Ac), and 2.09, 2.01 (2 s, 6 H, 2 AcO); ^{13}C (20 MHz), δ 202.4 (C-5), 197.0, 196.2 (2 CH_3CO), 169.6, 169.0 (2 CH_3COO), 151.7 (C-3), 127.7 (HC=), 84.4 (C-6), 76.9, 76.7 (C-7,8), 73.2 (C-9), 30.5, 27.2 (2 CH_3CO), and 20.9, 20.5 (CH_3COO).

1,3-Dipolar cycloadditions. — (*a*) *Of* **3a**. To a solution of **3a** (1.28 g, 3 mmol) in dry tetrahydrofuran (5 mL) was added ethyl diazoacetate (500 mg, 5 mmol). The mixture was kept at room temperature for 5 days, then concentrated *in vacuo*. Column chromatography (ether–hexane, 2:1) of the residue yielded 5,5-diacetyl-3-methoxycarbonyl-4-(1,2,3,4-tetra-*O*-acetyl-D-*arabino*-tetritol-1-ylcarbonyl)-Δ^2-pyrazoline (**11a**; 520 mg, 33%; one diastereomer), m.p. 49° (from ether), $[\alpha]_D$ −131° (*c* 1, chloroform); ν_{max}^{KBr} 3331, 2960, 1750, 1567, 1371, 1213, 1030, 962, and 715 cm^{-1}. N.m.r. data ($CDCl_3$): ^{1}H (80 MHz), δ 7.72 (bs, 1 H, NH), 6.11 (dd, 1 H,

J 8 and 2 Hz, H-3'), 5.91 (d, 1 H, *J* 2 Hz, H-2'), 5.50–5.20 (m, 1 H, H-4'), 5.51 (s, 1 H, H-4), 4.60–4.30 (m, 2 H, H-5',5'), 3.88 (s, 3 H, OMe), 2.30, 2.28, 2.23, 2.17, 2.15, 2.10 (6 s, 18 H, 2 Ac and 4 AcO); ^{13}C (20 MHz), δ 202.1 and 201.8 (2 CH_3CO), 195.5 (CO-4), 170.8, 170.2, 169.9, and 169.7 (4 CH_3COO), 161.9 (COOMe), 137.9 (C-3), 91.9 (C-5), 75.3, 68.5, and 67.1 (C-2',3',4'), 61.9 (C-5'), 58.4 (OMe), 52.9 (C-4), 28.7 and 24.3 (2 CH_3CO), 20.8, 20.7, and 20.2 (CH_3COO).

Anal. Calc. for $C_{22}H_{28}N_2O_{13}$: C, 50.00; H, 5.30; N, 5.30. Found: C, 49.80; H, 5.13; N, 5.10.

(*b*) *Of* **3b**. To a solution of **3b** (200 mg, 0.48 mmol) in dry tetrahydrofuran (1 mL) was added ethyl diazoacetate (80 mg, 0.80 mmol). The mixture was kept at room temperature for 5 days, then concentrated. Column chromatography (ether–hexane, 3:2) of the residue gave 5-benzoyl-4-(1,2:3,4-di-*O*-isopropylidene-D-*arabino*-tetritol-1-ylcarbonyl)-5-ethoxycarbonyl-3-methoxycarbonyl-Δ^2-pyrazoline (**11b**; 200 mg, 80%) as a pair of diastereomers. ^{1}H-N.m.r. data (80 MHz, $CDCl_3$): δ 7.87–7.30 (m, 6 H, Ph and pyrazoline H-1), 5.90, 5.80 (2 s, 1 H, H-4), 4.34–3.85 (m, 7 H, H-2',3',4',5',5' and CH_2CH_3), 3.80 (s, 3 H, COOMe), 1.45, 1.42, 1.34, 1.30 (4 s, 12 H, 2 CMe_2), and 1.20 (t, 3 H, *J* 7 Hz, CH_2CH_3).

(*c*) *Of* **3**. To a solution of **3c** (374 mg, 1 mmol) in dry tetrahydrofuran (1 mL) was added ethyl diazoacetate (550 mg, 5.5 mmol). The solution was kept at room temperature for 3 days, then concentrated. The ^{1}H-n.m.r. spectrum ($CDCl_3$) of the residue contained signals corresponding to 4-(2,5-anhydro-3,4-*O*-isopropylidene-D-ribonyl)-5-benzoyl-5-ethoxycarbonyl-3-methoxycarbonyl-Δ^2-pyrazoline (**11c**; pair of diastereomers in a 4:3 ratio): δ 8.19–7.22 (m, 6 H, Ph and H-1), 5.70, 5.59 (2 s, 1 H, H-4), 5.28–4.50 (m, 2 H, H-3',4'), 4.40–3.50 (m, 5 H, H-2',5'α,5'β, and CH_2CH_3), 3.82, 3.70 (2 s, 3 H, COOMe), 1.52, 1.48, 1.42, and 1.36 (4 s, 6 H, CMe_2), 1.20 and 1.15 (2 t, *J* 7 Hz, CH_2CH_3), and the signals corresponding to the excess of ethyl diazoacetate [δ 5.75 (CH) and 3.70 (COOMe)]. Flash chromatography (hexane–acetone, 6:1) of the crude product gave the mixture of diastereomers (92%) [δ 8.0 (bs, 1 H, NH), 7.82–7.10 (m, 5 H, Ph), 5.59 (s, 1 H, H-4), 5.20–4.50 (m, 2 H, H-3',4'), 4.40–3.50 (m, 5 H, H-2',5'α,5'β and CH_2CH_3), 3.70 (s, 3 H, COOMe), 1.52, 1.36 (2 s, CMe_2), and 1.20 (t, 3 H, *J* 7 Hz, CH_2CH_3).

(*d*) *Of* **3d**. To a solution of **3d** (200 mg, 0.53 mmol) in dry tetrahydrofuran (1 mL) was added ethyl diazoacetate (80 mg, 0.8 mmol). The mixture was kept at room temperature for 5 days, then concentrated. Column chromatography (hexane–acetone, 5:1) of the residue gave 4-(2,5-anhydro-3,4-*O*-isopropylidene-D-arabinonyl)-5-benzoyl-5-ethoxycarbonyl-3-methoxycarbonyl-Δ^2-pyrazoline (**11d**; 90 mg, 36%; pair of diastereomers). ^{1}H-N.m.r. data (80 MHz, $CDCl_3$): δ 8.26–7.37 (m, 6 H, Ph and NH), 5.70–4.70 (m, 4 H, H-4,2',3',4'), 4.37–3.35 (m, 4 H, 2 CH_2), 3.87, 3.83 (2 s, 3 H, COOMe), and 1.41–1.05 (m, 9 H, CMe_2 and CH_2CH_3).

(*e*) *Of* **4e**. A mixture of **4e** (580 mg, 1.6 mmol) and ethyl diazoacetate (200 mg, 2 mmol) was kept at room temperature for 24 h. The ^{1}H-n.m.r. spectrum of the crude product contained signals corresponding to ethyl diazoacetate and 2,3-di-*O*-acetyl-β-D-erythrofuranosyl 5,5-diacetyl-3-methoxycarbonyl-Δ^2-pyrazoline-4-

carboxylate (**11e**, pair of diastereomers). Short-column chromatography (ether–hexane, 2:1) of the product gave **11e** as a pair of diastereomers (540 mg, 71%). N.m.r. data ($CDCl_3$): ^1H (300 MHz), δ 7.61, 7.52 (2 bs, 1 H, NH, H-1), 6.56, 6.62 (2 d, 1 H, J 2 and 2 Hz, H-1'), 5.49–5.39 (m, 1 H, H-2'), 5.35–5.31 (m, 1 H, H-3'), 4.94, 4.66 (2 s, 1 H, H-4), 4.41–4.22 (m, 1 H, H-4'β), 4.03–3.85 (m, 1 H, H-4'α), 3.88, 3.82 (2 s, 3 H, COOMe), 2.28, 2.20, 2.10, 2.04 (4 s, 12 H, 2 Ac and 2AcO); ^{13}C (75 MHz), δ 201.06, 200.97, 200.50, 200.40, (CH_3CO), 170.10, 169.44, 166.68, 166.35, 160.94 (R*C*OO), 139.92 (C-3), 100.87, 100.80, (C-1'), 91.17, 90.99 (C-5), 74.81, 70.63 (C-2',3'), 71.32 (C-4'), 55.21, 53.30, 52.78 (C-4 and COO*Me*), and 27.52, 24.94, 24.82, 22.28, 20.53, 20.44 (CH_3CO). The ^1H-n.m.r. data indicated a 67% diastereomeric excess.

(*f*) *Of* **4f**. A mixture of **4f** (240 mg, 1 mmol) and ethyl diazoacetate (107 mg, 1.1 mmol) was kept at room temperature for 24 h. The ^1H-n.m.r. spectrum of the crude product contained signals corresponding to ethyl diazoacetate and 2,3-di-*O*-acetyl-α-D-threofuranosyl 5,5-diacetyl-3-methoxycarbonyl-Δ^2-pyrazoline-4-carboxylate (**11f**, pair of diastereomers). Short-column chromatography (hexane–ether, 2:1) of the product gave **11f** as a pair of diastereomers (200 mg, 70%). N.m.r. data ($CDCl_3$): ^1H (300 MHz), δ 7.55, 7.53 (2 bs, 1 H, NH, H-1), 6.14, 6.10 (2 s, 1 H, H-1'), 5.13–5.08 (m, 2 H, H-2',3'), 4.72, 4.70 (2 s, 1 H, H-4), 4.45 (dd, 1 H, J 12 and 4 Hz, H-4'β), 3.98–3.88 (m, 1 H, H-4'α), 3.83, 3.82 (2 s, 3 H, MeOOC), 2.28, 2.27, 2.20, 2.19, 2.13, 2.11, 2.10, and 1.99 (8 s, 12 H, 2 Ac and 2AcO); ^{13}C (75 MHz), δ 200.85, 200.73, 200.36, 200.25, (2 CO), 170.39, 169.38, 166.11, 165.93, 160.80 (5 COO), 140.29 (C-3), 100.47, 100.33 (C-1'), 91.01, 90.81 (C-5), 79.76, 79.62, 75.24, 75.15 (C-2',3'), 73.61 (C-4'), 55.24, 52.68 (*Me*OOC), 27.22, 25.09, 25.01, and 20.24 (Me). The ^1H-n.m.r. data indicated a 16% diastereomeric excess.

(*g*) *Of* **3g**. A mixture of **3g** (300 mg, 0.8 mmol) and ethyl diazoacetate (98 mg, 0.9 mmol) was kept at room temperature for 24 h. The ^1H-n.m.r. spectrum of the crude product contained signals corresponding to ethyl diazoacetate and 5,5-diacetyl-4-(3,4-di-*O*-acetyl-2,5-anhydro-D-xylonyl)-3-methoxycarbonyl-Δ^2-pyrazoline (**11g**, pair of diastereomers). ^1H-N.m.r. data (80 MHz, $CDCl_3$): δ 7.55 (bs, 1 H, NH, H-1), 5.75 (dd, J 4 and 1 Hz, H-3'), 5.62 (d, J 4 Hz, H-2'), 5.37 and 5.22 (2 s, 1 H, H-4), 5.25–5.10 (m, 1 H, H-4'), 5.02 (d, J 4 Hz) and 4.93 (d, J 4 Hz, H-3'), 4.60–3.75 (m, 2 H, H-5'α,5'β), 3.82, 3.72 (2 s, 3 H, MeOOC), 2.37, 2.35, 2.25 (3 s, 3 H, Ac), 2.13, 2.12, 2.10, and 2.07 (4 s, 6 H, 2 AcO). The methyl diazoacetate was removed by column chromatography (hexane–ether, 2:1) to leave **11g** as a pair of diastereomers.

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