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Glycosyl hydroperoxides derived from 2-deoxysugars

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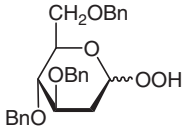
ABSTRACT

Oxidation of 3,4,6-tri-*O*-benzyl-2-deoxy-D-glucose and D-galactose or their *t*-butyl glycosides to the corresponding glycosyl hydroperoxides can be performed with hydrogen peroxide in the presence of an acid catalyst. Several reaction conditions and their influence on the effectiveness of the oxidation are discussed. Separation of the α - and β-anomers of the glycosyl hydroperoxides was achieved through mixed peroxide formation by reaction of the hydroperoxide group with 2-methoxypropene and subsequent deprotection.

1. Introduction

Recently, we have reported on the oxidation of 2-deoxysugars or their glycosides with 50% hydrogen peroxide, in the presence of molybdenum trioxide or in dioxane with sulfuric acid, to the corresponding glycosyl hydroperoxides.[1–3] Hydroperoxides **1–3** are relatively stable; they can be purified by silica gel chromatography and stored for months in the refrigerator without visible decomposition.



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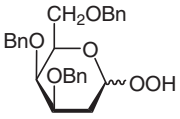

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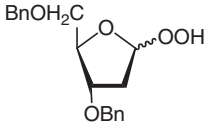

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Compounds **1–3** were used for enantioselective epoxidation of electrophilic olefins such as 2-methylnaphthoquinone, chalcone, (*E*)-1,2-dibenzoylethylene and (*E*)-iso-butyrylphenylethylene.[3] In the presence of sodium hydroxide the epoxidations showed exceptionally high asymmetric induction; the exchange of sodium by potassium ion resulted in a lower asymmetric induction. These results pointed to the crucial role of the counterion and strongly suggested the coordination of the alkali metal ion in the transition state of the epoxidation process by both reactants, the hydroperoxide and the olefin. DFT theoretical studies of the reaction mechanism were in good agreement with the experimental facts.[3]

2. Results and discussion

The attractiveness of glycosyl hydroperoxides as chiral epoxidising reagents prompted us to find an easier and more effective way of synthesising them. The use of pure α- or β-anomers would help clarify the reaction mechanism and the calculations. The readily available 3,4,6-tri-*O*-benzyl-D-glucal (**4**) and 3,4,6-tri-*O*-benzyl-D-galactal (**5**) were selected as starting materials.[4] Both glycals were transformed into the corresponding 2-deoxysugars[5] **6**, **7** or their *t*-butyl glycosides **8–11**[6] for use in the oxidation experiments. Compounds **8–11** have been obtained earlier by the other method, but their spectral and analytical data have been reported only partly.[7] Previously we found that the configuration of the anomeric centre in the starting sugar does not influence the ratio of α- and β-anomers of the resulting hydroperoxides and so inseparable mixtures of α,β-anomers of free sugars **6** and **7**, as well as *t*-butyl glycosides **8** and **9**, were used for the oxidation.

Three methods of oxidation were chosen for comparison. Previously we used a method proposed by Snatzke and co-workers[8] and Taylor and co-workers[9], that is, hydrogen peroxide in dioxane in the presence of concd sulfuric acid. For the synthesis of glycosyl peroxides directly from glycals or 2,3-unsaturated glycosides, the Taylor group[9] used a solution of hydrogen peroxide in diethyl ether (prepared by extracting 50% hydrogen peroxide with ether), with concd sulfuric acid. We turned our attention to a softer version of this method, preparing a solution of hydrogen peroxide in ether by extraction of 30% hydrogen peroxide. This solution, described by Mąkosza and Surowiec,[10] has been used by them for multi-gram reactions without any problems. Finally, we proposed a new method of oxidation—a solution of hydrogen peroxide in *tert*-butanol prepared according to Milas and Sussman,[11] using commercially available 50% hydrogen peroxide instead of 30%.

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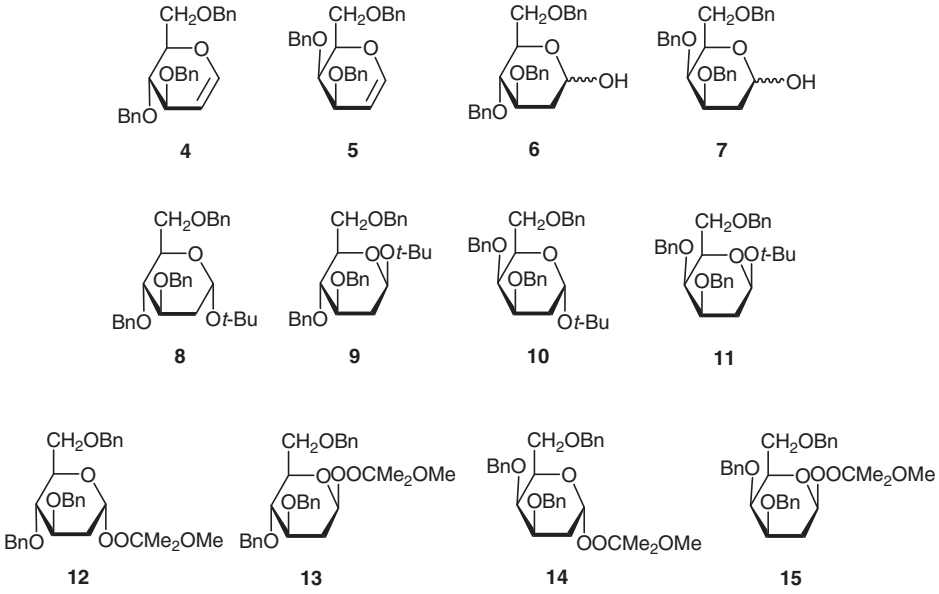

All three methods provided similar ratios of anomers **1α**,**1β** and **2α**,**2β** (Table 1). The highest yield (up to 95%) and the shortest reaction time (1 h) were obtained for the H_2O_2/Et_2O solution. Lowering the temperature of the oxidation experiment (procedure D) led to a higher yield of the β-anomer of **2**.

Since chromatographic separation of hydroperoxides **1α**,**1β** and **2α**,**2β** is not easy, we devised an efficient protection/deprotection methodology which enabled their separation. A mixture of the α,β-anomers of hydroperoxides **1** or **2** was treated with 2-methoxypropene in the presence of pyridinium *p*-toluenesulfonate[12] to yield α,β-anomer mixtures of the corresponding (1-methoxy-1-methyl)ethyl peroxides **12**, **13** and **14**, **15**. The mixtures were separated by chromatography and then each compound was deprotected with diluted sulfuric acid in acetone solution giving anomerically pure hydroperoxides. Also pyridine *p*-toluenesulfonate in acetone could be used for deprotection but the reaction was very slow.

Mixed (1-methoxy-1-methyl)ethyl peroxides are usually quite stable compounds, and we were surprised to notice that β-anomer **15** started spontaneously losing its protecting group and that product **2β** was accompanied by bisglycosyl peroxide **16**. Formation of **16** (α,α-anomeric configuration) is the result of a sequence of reactions involving formation of the hydroperoxide followed by its addition to the anomeric oxonium cation. Peroxide **16** was synthesised in our laboratory previously[13] but this time we were able to grow a suitable crystal for an X-ray measurement. The X-ray structure of compound **16** is shown in Figure 1.[14]

Similarly, crystal structure of compounds **1α** and **2β** is presented in Figures 2 and 3, respectively. Intramolecular hydrogen bonds between hydroperoxide protons and the corresponding ring oxygen atoms, postulated by us previously for both compounds in solution[3,15] was not observed in the solid state. Instead, a helical arrangement of molecules connected by intermolecular hydrogen bonds was the dominating structural pattern for both hydroperoxides.

Table 1
Results of the oxidation experiments

Compound	Reaction conditions[a]	Yield (%)	α:β ratio from HPLC[b]
6	A	78.2	68.6:31.4
6	B	89.3	61.5:38.5
6	C	89.8	65.1:34.9
8/9	A	82.2	62.1:37.9
8/9	B	85.6	58.0:42.0
8/9	C	94.9	63.3:36.7
8/9	D	84.9	58.8:41.2
7	A	74.4	80.4:19.6
7	B	79.1	84.7:15.3
7	C	83.7	88.7:11.3
10	A	91.3	86.5:13.5
10	B	87.8	77.0:23.0
10	C	95.0	89.5:10.4

[a] (A) 0.25 mmol substrate, Milas solution (H_2O_2 in *t*-BuOH, ca. 3.2 M, 15 mL) concd H_2SO_4 (225 μL), rt; (B) 0.25 mmol substrate, 50% H_2O_2 (3 mL), dioxane (3–4 mL), concd H_2SO_4, (75 μL) rt; C.0.25 mmol substrate in toluene (1 mL), H_2O_2 solution in ether (ca. 2 M, 2 mL), concd H_2SO_4 (75 μL), rt; (D) conditions C, 0 to 5 °C.
[b] LichroCART® 250-4, eluent: hexane–isopropanol 99.5:0.5, 1 mL/min (**1α**,**1β**); 95:5, 1 mL/min. (**2α**,**2β**).

3. Experimental

3.1. General methods

^1H and ^{13}C NMR spectra were recorded on a Brucker DRX 500 Avance Spectrometer, using deuteriated solvents and TMS as an internal standard. Chemical shifts are reported as δ values in ppm and coupling constants are in Hertz. Infrared spectra were recorded on a FT-IR-1600 Perkin–Elmer spectrophotometer. The optical rotations were measured with a JASCO J-2000 digital polarimeter. High-resolution mass spectra were recorded on an ESI-TOF Mariner Spectrometer (Perspective Biosystem). Thin layer chromatography was performed on aluminium sheet Silica Gel 60 F254 ($20 \times 20 \times 0.2$) from Merck. Column chromatography was carried out using Merck silica gel (230–400 mesh). X-Ray experiment was performed on Bruker X8APEX diffractometer equipped with APEXII CCD detector. ^1H and ^{13}C NMR spectral data matched those reported before[2] were not provided.

3.2. Synthesis of *tert*-butyl glycosides

3.2.1. *tert*-Butyl 3,4,6-tri-*O*-benzyl-α- and β-D-*arabino*-hexopyranoside (8) and (9)

tert-Butanol (0.67 g, 9 mmol) and triphenylphosphine hydrobromide (TPHB, 51.6 mg, 0.15 mmol) were added to a solution of 3,4,6-tri-*O*-benzyl-D-glucal (**1**) (1.29 g, 3 mmol) in dry dichloromethane (15 mL) and the reaction mixture was stirred at rt for 5 h. Then it was diluted with ethyl acetate (100 mL) and washed

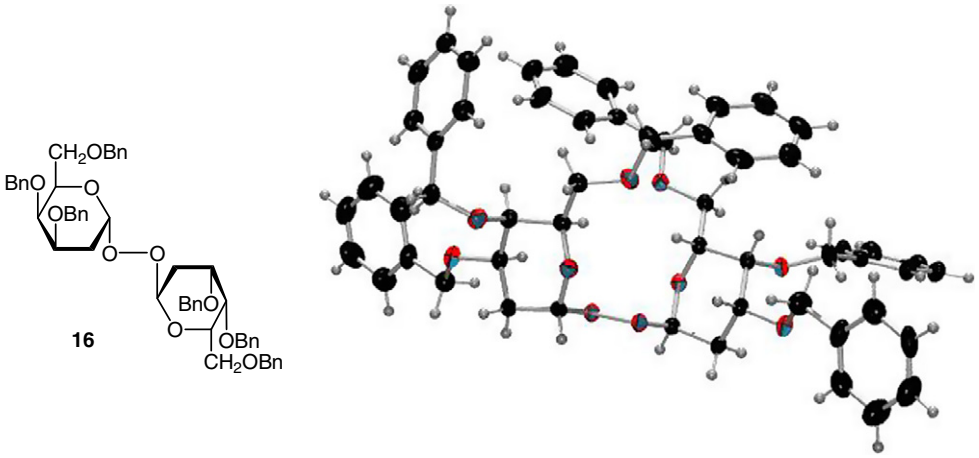

Figure 1. Crystal structure of compound **16**. Thermal ellipsoids shown at 30% probability level.

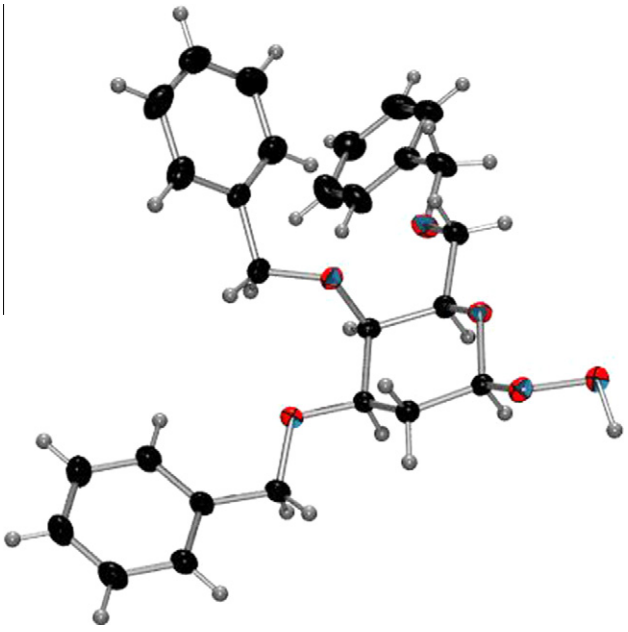

Figure 2. X-ray structure of **1α**. Thermal ellipsoids shown at 30% probability level.

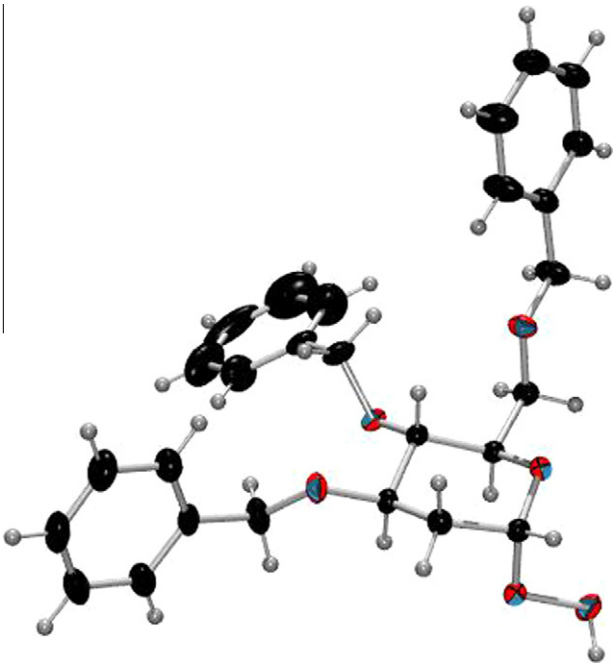

Figure 3. X-ray structure of **2β**. Thermal ellipsoids shown at 30% probability level.

with satd $NaHCO_3$ solution (10 mL) and water (3 × 15 mL). After drying (Na_2SO_4), solvents were removed and the residue was flash-chromatographed (hexanes–ethyl acetate 9:1) affording an inseparable mixture (ca. 85:15) of **8** and **9** (R_f 0.18, 1.34 g, 88.6%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.21 and 7.19–7.16 (m, 15H, aromatic); 5.27 (br d, 1H, *J* 2.6 Hz, H-1); 4.69–4.62 (m, 3H), 4.87, 4.51 and 4.47 (3d, 3H, *CH*$_2$Ph); 4.04 (ddd, 1H, *J* 9.8, 8.9, 3.4 Hz, H-3); 3.94 (ddd, 1H, *J* 9.9, 3.4, 2.1 Hz, H-5); 3.80 (dd, 1H, *J* 10.4, 3.7 Hz, H-6a); 3.64–3.60 (m, 2H, H-6b, H-4); 2.11 (ddd, 1H, *J* 12.5, 4.9, 1.3 Hz, H-2e); 1.72 (dt, 1H, *J* 12.7, *J* 3.7 Hz, H-2a), 1.21 (s, 9H, *t*-Bu).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.7, 138.3, 128.39, 128.33, 128.29, 128.26, 127.96, 127.82, 127.65, 127.59, 127.52, 127.49, 127.43, 92.0, 78.6, 77.9, 75.0, 74.5, 73.4, 71.7, 70.3, 69.1, 37.0, 28.6.

In the ^{1}H NMR spectrum only a few signals for compound **9** were clearly separated: 3.74 (dd, 1H, *J* 10.7, 1.8 Hz, H-6); 2.21 (ddd, 1H, *J* 12.5, 5.0, 1.9 Hz, H-2); 1.27 (s, *t*-Bu).

IR ($CHCl_3$) 2978, 1454, 1366, 1092, 995, 699 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_5Na$ (M+Na$^+$) 513.26115. Found: 513.26199.

3.2.2. *tert*-Butyl 3,4,6-tri-*O*-benzyl-α-D-*lyxo*-hexopyranoside (10) and *tert*-butyl 3,4,6-tri-*O*-benzyl-β-D-*lyxo*-hexopyranoside (11)

3,4,6-Tri-*O*-benzyl-D-galactal (**5**) (2.08 g, 5 mmol) in dry dichloromethane (25 mL) was reacted with *tert*-butanol (1.11 g, 15 mmol) and triphenylphosphine hydrobromide (TPHB, 86 mg, 0.25 mmol). After 3 h the reaction mixture was worked-up as in the preceding experiment. The crude product was flash-chromatographed; elution with 5% ethyl acetate in hexanes afforded as a first fraction product **10** (R_f 0.21, 1.52 g, 62.4% yield), which was crystallised from hexanes, mp 62.5–64 °C, $[\alpha]_D$ +57.4 (*c* 1, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.20 (m, 15 H, aromatic); 5.28 (br d, 1H, *J* 3.0 Hz, H-1); 4.92, 4.48, 4.42 (3d, 3H, *CH*$_2$Ph) and 4.63–4.57 (m, 3H, *CH*$_2$Ph); 4.08 (br t, 1H, *J* 6.9 Hz, H-5); 3.99 (ddd, 1H, *J* 12.0, 4.2, 2.4 Hz, H-3); 3.63 (dd, 1H, *J* 9.2, 7.7 Hz, H-6a); 3.50 (dd, 1H, *J* 9.2, 5.7 Hz, H-6b); 2.33 (dt, 1H, *J* 12.1, 3.9 Hz, H-2a); 1.82 (ddt, 1H, *J* 12.1, 4.3, 1.4 Hz, H-2e); 1.21 (s, 9H, *t*-Bu).

^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 138.7, 138.3, 128.3, 128.11, 128.09, 127.7, 127.6, 127.4, 127.3, 92.4, 75.1, 74.3, 74.2, 73.4, 73.3, 70.4, 69.5, 69.3, 32.8, 28.6.

IR ($CHCl_3$) 2978, 1454, 1367, 1091, 699 cm^{-1}.

Calcd for $C_{31}H_{38}O_5$: C, 75.89; H, 7.81. Found: C, 75.88; H, 7.92.

Further elution of the column gave β-anomer **11** (R_f 0.17, 0.37 g, 15.1%) as an oil. $[\alpha]_D$ −28.0 (*c* 1.8, $CHCl_3$).

^{1}H NMR (500 MHz, C_6D_6) δ 7.37–7.06 (m, 15H, aromatic); 5.05, 4.61 (2d, 21H) and 4.36–4.27 (m, 4H, CH_2Ph); 4.52 (dd, 1H, *J* 9.6, 2.0 Hz, H-1); 3.81 (dd, 1H, *J* 9.0, 7.3 Hz, H-6a); 3.75 (br s, 1H, H-4); 3.66 (dd, 1H, *J* 9.0, 5.6 Hz, H-6b); 3.38 (br t, 1H, H-5); 3.31 (ddd, 1H, *J* 12.2, 4.2, 2.7 Hz, H-3); 2.47 (dt, 1H, *J* 12.2, 9.7 Hz, H-2a); 1.96 (dm, 1H, H-2e); 1.24 (s, 9H, *t*-Bu).

^{13}C NMR (125 MHz, $CDCl_3$) δ 139.8, 139.2, 139.0, 128.6, 128.5, 128.4, 128.3, 128.2, 128.11, 128.06, 128.0, 127.9, 127.7, 127.6, 127.4, 95.4, 78.4, 74.73, 74.70, 74.0, 73.5, 72.9, 70.1, 70.0, 34.5, 29.0.

IR ($CHCl_3$) 2870, 1454, 1366, 1099, 1069, 698 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_5Na$ (M+Na$^+$) 513.26115. Found: 513.25892.

3.3. Oxidation

Method A. According to Taylor and co-workers.[9] To a solution of substrate (0.25 mmol) in dioxane (3–4 mL). 50% H_2O_2 (3 mL) was added followed by concd sulfuric acid (75 μL). When tlc showed the disappearance of the starting material, the reaction mixture was diluted with dichloromethane (50 mL) and washed with water (5 × 20 mL). After drying (Na_2SO_4) and removal of solvents the residue was flash-chromatographed.

Method B. Substrate (0.25 mmol, *t*-butyl glycoside or free sugar) was dissolved in Milas solution (15 mL) and to this solution concentrated H_2SO_4 (75 μL) was added. The reaction mixture was stirred at room temperature and monitored by tlc. After 1–2 days the reaction mixture was worked-up as in the preceding experiment.

Method C. To a solution of substrate (0.25 mmol) in toluene (2 mL) was added a solution of H_2O_2 in diethyl ether (2 mL) and concd sulfuric acid (75 μL). After 1 h tlc showed the reaction was complete. It was diluted with diethyl ether (50 mL) and washed with water until neutral. After drying (Na_2SO_4) and evaporation of solvents the residue was flash-chromatographed affording pure product.

3.3.1. 3,4,6-Tri-*O*-benzyl-α- (12) and β-D-*arabino*-hexopyranosyl (1-methoxy-1-methyl)ethyl peroxide (13)

To a solution of hydroperoxide **1** (775 mg, 1.72 mmol) in dichloromethane (20 mL), 2-methoxypropene (144 mg, 2 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 30 mg, 0.12 mmol) were added and the reaction mixture was stirred at rt. After 3 h the reaction mixture was diluted with ether (100 mL) and washed with satd $NaHCO_3$ (10 mL) and water (5 × 10 mL). After drying (Na_2SO_4) the solvents were removed and the residue was flash-chromatographed. Eluting with 10% acetone in hexanes gave α -anomer **12** (R_f 0.16, 450 mg, 43.7%), $[\alpha]_D$ +108.0 (*c* 1.1, CH_2Cl_2).

^{1}H NMR (500 MHz, C_6D_6) δ 7.33–7.06 (m, 15H, aromatic); 5.48 (br d, 1H, *J* 3.9 Hz, H-1); 5.06, 4.70, 4.51 and 4.41 (4 × d, 4H, CH_2Ph); 4.34–4.31 (m, 2H, H-3, H-4); 4.28 (dm, 1H, *J* 9.7 Hz, H-5); 3.97–3.85 (m, 3H, H-6a, CH_2Ph); 3.78 (dd, 1H, *J* 10.8, 1.6 Hz, H-6b); 3.21 (s, 3H, OCH_3), 2.16 (ddd, 1H, *J* 13.4, 4.9, 1.0 Hz, H-2e); 1.62 (ddd, 1H, *J* 13.4, 11.6, 4.6 Hz, H-2a); 1.33 and 1.32 (2 × s, 6H, 2 × CH_3).

^{13}C NMR(125 MHz, C_6D_6) δ 139.6, 139.4, 139.3, 128.5, 128.44, 128.40, 128.3, 128.1, 127,9, 127.8, 127.7, 127.55, 127.52, 127.50, 105.1, 100.3, 78.6, 77.7, 75.0, 73.5, 72.5, 71.6, 69.6, 49.1, 33.5, 23.2, 22.9.

IR (CCl_4) 3032, 2942, 1454, 1368, 1210, 1100 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_7Na$ (M+Na$^+$) 545.25096. Found: 545.25172.

Further elution of the column gave β-anomer **13** (R_f 0.13, 240 mg, 23.3%), $[\alpha]_D$ − 46.8 (*c* 1, CH_2Cl_2).

^{1}H NMR (500 MHz, C_6D_6) δ 7.33–7.07 (m, 15H, aromatic); 4.97 (dd, 1H, *J* 10.4, 2.0 Hz, H-1); 4.91, 4.60, 4.51, 4.44, 4.37 and 4.28 (6d, 6H, CH_2Ph); 3.78–3.73 (m, 2H, H-3, H-4); 3.64 (t, 1H, *J* 9.0 Hz, H-6a); 3.44 (m, 2H, H-6b, H-5); 3.32 (s, 3H, OCH_3); 2.14 (ddd, 1H, *J* 12.2, 5.1, 2.0 Hz, H-2e); 1.64 (q, 1H, *J* ≈ 11.4 Hz, H-2a); 1.46 and 1.36 (2s, 6H, 2 × CH_3).

^{13}C NMR (125 MHz, C_6D_6) δ 139.4, 139.2, 139.1, 128.52, 128.49, 128.40, 128.3, 128.2, 128.1, 127.91, 127.87, 127.70, 127.67, 127.6, 105.3, 101.5, 96.4, 79.8, 78.2, 75.8, 74.9, 73.6, 71.2, 69.7, 49.1, 33.7, 23.4, 23.0.

IR (CCl_4) 3032, 2868, 1454, 1364, 1211, 1088 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_7Na$ (M+Na$^+$) 545.25098. Found: 545.25063.

3.3.2. 3,4,6-tri-*O*-Benzyl-α- (14) and β-D-*lyxo*-hexopyranosyl (1-methoxy-1-methyl)ethyl peroxide (15)

To a solution of 3,4,6-tri-*O*-benzyl-D-*lyxo*-hexopyranosyl hydroperoxide (**2**, 842 mg, 1.87 mmol) in dry dichloromethane (20 mL) 2-methoxypropene (150 mg, 2.08 mmol) and PPTS (31.2 mg, 0.12 mmol) were added. After 3 h the reaction mixture was diluted with ether (50 mL) and washed with satd $NaHCO_3$ (10 mL) solution and finally with water (3 × 10 mL). After drying (Na_2SO_4) and evaporation of solvents the residue was flash-chromatographed. Elution with 20% of ethyl acetate in hexanes gave a first fraction α-anomer **14** (R_f 0.34, 668 mg, 68.9%), $[\alpha]_D$ + 82.7 (*c* 1.1, CH_2Cl_2).

^{1}H NMR (500 MHz, C_6D_6) δ 7.39–7.05 (m, 15H, aromatic); 5.55 (br d, 1H, *J* 4.3 Hz, H-1); 5.01, 4.61, 4.35. 4.29, 4.20 and 4.15 (6d, 6H, CH_2Ph); 4.41 (dd, 1H, *J* 7.9, 5.5 Hz, H-5); 3.99 (br s, 1H, H-4); 3.96 (t, 1H, *J* 8.6 Hz, H-6a); 3.79–3.74 (m, 2H, H-6b, H-3); 3.21 (s, 3H, OCH_3); 2.40 (dt, 1H, *J* 12.7, 4.6 Hz, H-2e); 1.97 (br dd, 1H, *J* 13.0, 4.6 Hz, H-2a); 1.33 and 1.30 (2s, 6H, 2CH_3).

^{13}C NMR (125 MHz, C_6D_6) δ 139.8, 139.1, 139.0, 128.50, 128.49, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 127.58, 127.52, 105.1, 100.8, 74.93, 74.88, 73.7, 73.5, 71.1, 70.4, 69.5, 49.1, 29.2, 23.1, 23.0.

IR (CCl_4) 3067, 2944, 1454. 1368, 1210, 1115, 1097, 1068 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_7Na$ (M+Na$^+$) 545.25098. Found: 545.25079.

Further elution of the column gave β-anomer **15** (R_f 0.23, 84 mg, 8.6% yield), $[\alpha]_D$ −56.6 (*c* 1.3, CH_2Cl_2).

^{1}H NMR (500 MHz, C_6D_6) δ 7.34–7.05 (m, 15H, aromatic); 4.98, 4.59, 4.29, 4.24, 4.21 and 4.16 (6d, 6H, CH_2Ph); 4.95 (dd, 1H, *J* 10.4, 2.1 Hz, H-1); 3.85 (dd, 1H, *J* 8.9, *J* 7.8 Hz, H-5); 3.75 (br s, 1H, H-4); 3.69 (dd, 1H, *J* 9.0, 5.3 Hz, H-6a); 3.29 (s, 3H, OCH_3); 3.19 (dd, 1H, *J* 12.0, 4.3, 2.6 Hz, H-3); 3.27 (q, 1H, *J* ≈ 11.4 Hz. H-2a); 1.95 (dm, 1H, *J* 11.7 Hz, H-2e); 1.41 and 1.35 (2 × s, 6H, 2 × CH_3).

^{13}C NMR (125 MHz, C_6D_6) δ 139.7, 139.0, 138.9, 128.6, 128.5, 128.4, 128.3, 128.1, 127.9, 127.75, 127.70, 127.5, 127.4, 105.2, 102.3, 78.3, 74.8, 74.3, 73.6, 72.7, 70.3, 69.4, 49.1, 29.9, 23.3, 23.1.

IR (CCl_4) 3032, 2867, 1363, 1098, 1063 cm^{-1}.

HRMS Calcd for $C_{31}H_{38}O_7Na$ (M+Na$^+$) 545.25098. Found: 545.25333.

3.3.3. 2,4,6-Tri-*O*-benzyl-α-D-*arabino*-hexopyranosyl hydroperoxide (1α)

Diluted sulfuric acid (20% w/w, 0.5 mL) was added to a solution of peroxide **12** (450 mg, 0.86 mmol) in acetone (20 mL) and the reaction mixture was stirred at rt for 1 h when tlc showed the disappearance of starting material. Most of the acetone was evaporated at rt and the residue was dissolved in dichloromethane (50 mL) and washed with water until neutral. Drying (Na_2SO_4) and removing the solvent gave a crude product. Flash-chromatography in hexanes–ethyl acetate 7:3 afforded pure **1α** which was crystallised from ethyl acetate–hexanes. Mp 100.5–102 °C, $[\alpha]_D$ +90 (*c* 0.5, $CHCl_3$), R_f 0.23.

Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.99; H, 6.66.

3.3.4. 2,4,6-Tri-*O*-benzyl-β-D-*lyxo*-hexopyranosyl hydroperoxide (2β)

To a solution of peroxide **15** (84 mg, 0.18 mmol) in acetone (5 mL) PPTS (5 mg, 0.02 mmol) was added. After 30 min the acetone was evaporated at rt and the residue was diluted with dichloromethane (30 mL), washed with water (5 × 10 mL) and dried (Na_2SO_4). After removing the solvents the crude product was flash-chromatographed in hexanes–ethyl acetate (7:3) to afford peroxide **16** (R_f 0.5, 8 mg) and hydroperoxide **2β** (R_f 0.25, 54 mg, 74.5% yield) which was crystallised from ethyl acetate–hexanes. Mp 118.5–120 °C, $[\alpha]_D$ −25.1 (*c* 0.5, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (br s, 1H, OOH); 7.36–7.25 (m, 15H, aromatic), 4.98 (dd, 1H, *J* 8.3, 3.9 Hz, H-1); 4.88, 4.61, 4.60, 4.57, 4.49 and 4.45 (6d, 6H, CH_2Ph); 3.83 (br s, 1H, H-4); 3.80 (dd, 1H, *J* 8.4, 5.6 Hz, H-6a); 3.68–3.60 (m, 3H, H-6b, H-3, H-5); 2.08–1.99 (m, 2H, H-2a, H-2b).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.0, 137.8, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 102.8, 76.3, 73.9, 73.6, 73.5, 72.1, 70.6, 69.1, 29.2.

IR (KBr) 3291, 2921, 2868, 1454, 1119, 1039, 729 cm^{-1}.

Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 71.93; H, 6.64.

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