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Carbohydrate Research 307 (1998) 263–270

CARBOHYDRATE RESEARCH

Preparation of modified glycosyl glycerol derivatives by glycal rearrangement

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Received 29 September 1997; accepted 26 January 1998

Abstract

By Lewis acid catalysed allylic rearrangement reactions of various glycals with glycerol derivatives 2,3-unsaturated mono- and disaccharide glycosyl glycerol derivatives were obtained in good yields. A triglycosyl glycerol was successfully synthesized in a straightforward three step way from 3,4,6- tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol. © 1998 Elsevier Science Ltd. All rights reserved

Keywords: Ferrier reaction; Glycerol derivatives; Deoxy sugars

1. Introduction

Glycosyl diacylglycerol derivatives are known as major components of membrane lipids in a wide variety of plants and microorganisms [1–3]. These lipids consist of a polar carbohydrate ''headgroup'', which is attached to di-*O*-acyl-glycerol derivatives via an α- or β-linkage. The simple lipids with one to three sugar units in the ''headgroup'' and a glycerol part which is acylated with long chain saturated or unsaturated aliphatic acids are major structural components of cell membranes. Other lipids, with more sugar units, are involved in cell surface recognition events. Therefore, the preparation and investigation of modified structures of this class of compounds is of interest.

The concept for the synthesis of unsaturated glycosyl glycerols has not yet been investigated. By employment of the Ferrier reaction [4–6] with 1,2- or 1,3-protected glycerol derivatives as nucleophiles the formation of these modified compounds is possible in high yields. Thus, under allylic rearrangement glycals can be converted into the corresponding 2,3-unsaturated glycosides by treatment with nucleophiles in the presence of Lewis acids as catalyst. In the present context, we have studied this reaction with a variety of aglycons [7,8] as a way of gaining easy access to modified glycoconjugates. Here, we wish to report on the synthesis of modified glycosyl glycerols under Ferrier conditions.

2. Results and discussion

First, the commercially available (*R*,*S*)-1,2-*O*-isopropylidene glycerol was used as nucleophile to test a Ferrier reaction with boron trifluoride etherate as catalyst. However, an excess of catalyst can lead to opening of the acid labile isopropylidene

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PII S0008-6215(98)00038-X

ring and reduce the yield. Therefore, the reaction was performed at low temperature in the presence of only a catalytic amount of boron trifluoride etherate. As expected, 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (3,4,6-tri-*O*-acetyl-D-glucal, **1**) reacted under typical Ferrier conditions with 1.5 equivalents of 1,2-*O*-isopropylidene glycerol to give the α-glycoside **2** as a mixtures of diastereomers, which was purified after flash chromatography in 85% yield (Scheme 1). No β-anomer was detected and this result was consistent with previous findings [4–8].

It proved to be advantageous to select 1,3-di-*O*-benzylglycerol [9] because the benzyl groups are easy to remove by hydrogenation and showed suitable stability under acidic conditions. In a series of experiments, this was reacted with various glycals (Scheme 2).

The first attempt was with glucal **1** under boron trifluoride etherate catalysis at −25 °C. After 30 min at −10 °C a new compound was detected by TLC, which was isolated after work-up on silica gel in 90% yield and characterised by NMR spectroscopy as the desired α-glycoside **8**.

By the corresponding reaction with tri-*O*-benzyl-D-glucal (**3**) the desired α-glycoside **9a** and benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**9b**) were obtained in 66 and 18% yield, respectively. All attempts to avoid the formation of the undesired compounds **9b** by variation of reaction time, temperature and amount of catalyst were unsuccessful, however, the compounds could be separated easily by flash chromatography.

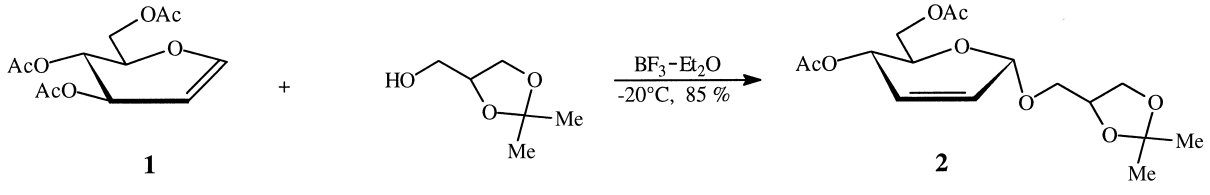
The analogous reaction of 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*threo*-pent-1-enitol (3,4-di-*O*-acetyl-D-xylal, **4**) with 1,3-di-*O*-benzylglycerol at −45 °C afforded a separable anomeric mixture **10a** and **10b** in overall yield of 81%. Compound **10a** proved to be the α-anomer and compound **10b** the β-anomer, which could be established by ^{1}H NMR spectroscopy. In case of **10a**, the chemical shift of H-4 (5.29 ppm) and the coupling constants $J_{4,5ax}$, $J_{4,5eq}$ and $J_{5ax,5eq}$ indicate a favourable $^{\circ}H_5$(D) conformation. In the ^{1}H NMR spectrum of **10b** the signal of H-4 was shifted to higher field (4.95 ppm) and the coupling constants $J_{4,5ax}$, $J_{4,5eq}$ and $J_{5ax,5eq}$ are in accord with a preferential ^5H_o(D) conformation [10] and an axially oriented glycerol aglycon.

Similar to monosaccharide glycals, the disaccharide glycals reacted smoothly with 1,3-di-*O*-benzylglycerol under Ferrier conditions to give the corresponding 2,3-dideoxy-hex-2-enopyranosides. In both reactions of 1,3-di-*O*-benzylglycerol with 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl- and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl-(1→4)-3,6-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (hexaacetyl lactal, **5** and hexaacetyl maltal, **6**), exclusively the desired α-glycosides **11** and **12** were obtained in good yields.

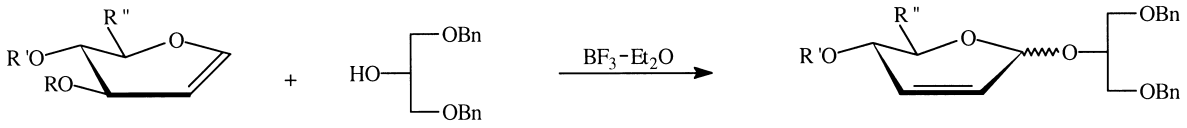
Finally, methyl 3,4-di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol-uronate (methyl-3,4-di-*O*-acetyl-D-glucuronal, **7**) [11] was treated correspondingly to afford within 30 min the glycoside **13**. By ^{1}H NMR, this proved to be the α-anomer in the energetically favoured $^{\circ}H_5$(D) conformation as confirmed by coupling constants $J_{1,2}$ and $J_{4,5}$, with values corresponding to literature data [12,13] for components of similar structure.

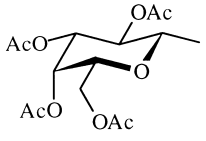
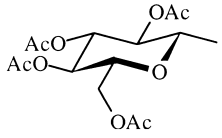
Compound **13** was deacetylated with sodium carbonate in methanol to give **14** in almost quantitative yield. By reaction of this as aglycone with the glucuronal **7** in the presence of stannic chloride in dichloromethane at −45 °C within 1 h, the unsaturated disaccharide **15** was obtained in poor yield (28%, Scheme 3). We did not succeed, however, in finding more suitable conditions to increase the yield because always compound **13** formed as by-product, apparently due to acetyl migration (Scheme 3). In the ^{1}H NMR spectrum of **15**, the large coupling between H-4′ and H-5′ of 9.7 Hz and a small coupling constant of $J_{1',2'}$ (1.5 Hz) are in accord with an α-anomer also in the non-reducing ring.

Another proof for the supposed α configuration of glycoside **8** was obtained by hydrogenolysis with Pd/C in methanol which simultaneously removed the benzyl groups and the double bond to give the



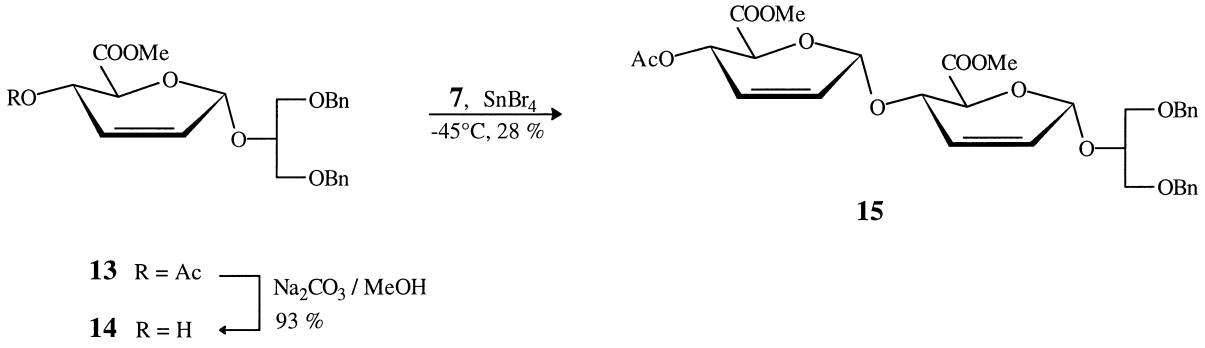
Scheme 1.



glycal	R	R'	R''	temp.[°C]	product	anomer	yield [%]
1	Ac	Ac	CH_2OAc	–25	**8**	α	90
3	Bn	Bn	CH_2OBn	–35	**9a** [a]	α	66
4	Ac	Ac	H	–45	**10a** **10b**	α β	14 67
5	Ac		CH_2OAc	–20	**11**	α	86
6	Ac		CH_2OAc	–20	**12**	α	75
7	Ac	Ac	COOMe	–40	**13**	α	80

[a] side-product: benzyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**9b**), 18 % yield

Scheme 2.



Scheme 3.

saturated glycoside **16**. The ^1H NMR spectrum of **16** showed an equatorial/axial and diequatorial proton arrangement with typical small coupling constants of $J_{1,2ax} = 2.5$ and $J_{1,2eq} \approx 0$ Hz.

Further deacetylation of **16** with sodium carbonate gave the completely unprotected glycoside **17** in 91% yield. Alternatively, hydrogenolysis of all benzyl groups and hydrogenation of the double

bond in **9a** directly led to the same compound **17** in 80% yield. The structure of **17** was established by ^{1}H NMR and ^{13}C DEPT spectroscopy. In the ^{1}H NMR spectrum, the $J_{1,2ax}$ and $J_{1,2eq}$ coupling constants of approximately 1.0–2.5 Hz proved the desired α-configuration. In the ^{13}C DEPT spectrum signals of the CH_2-groups, C-6 and C-1′ or C-3′ of the glycerol residue were found at 62.15, 62.06, and 61.43 ppm, respectively.

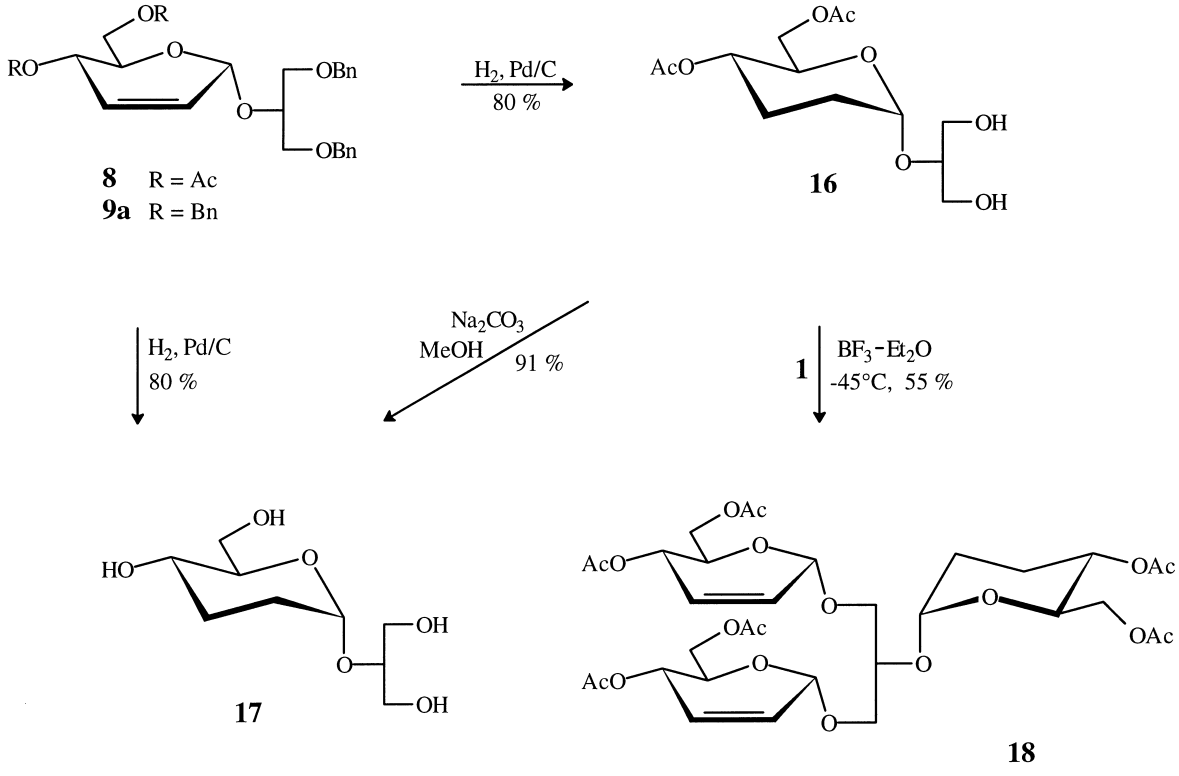
It is known that structurally important glycoglycerol lipids are acylated at the glycerol moiety with higher aliphatic acids. The synthesis of such compounds, starting from glycosyl glycerol derivatives with a free hydroxyl function at glycerol, was already successfully achieved and reported [2,3]. However, a further functionalisation of these hydroxy groups, for example, with carbohydrates has not yet been described. It was an additional purpose of these studies to synthesize such a triglycosyl glycerol employing the Ferrier reaction.

Thus, compound **16** was treated with 2 equivalents of glycal **1** in the presence of boron trifluoride etherate to give the corresponding triglycosyl glycerol **18** in acceptable 55% yield. At the beginning of this reaction at −40 °C the formation of two products was detected by TLC. The polar product disappeared however promptly at elevated temperature, and as a single product, compound **18** could be isolated by flash chromatography (Scheme 4).

Whereas in the ^{1}H NMR spectrum of **18** the signals of H-4 and H-1 from both unsaturated rings coincide at 5.09 and 5.35 ppm, respectively, the corresponding signals of H-2 and H-3 were observed separatly. In comparison with compound **16**, the signal of H-1 from the saturated ring was shifted to lower field (5.05 ppm). The coupling constants between H-1 and H-2 of the unsaturated rings were identical ($J_{1,2} = J_{1',2'} = 1.5$ Hz) and indicate α-linkages in both cases. After hydrogenation and deacetylation, the triglycosyl glycerol **18** could be further functionalised, for example with higher aliphatic acids to obtain sugar spacered glycerol derivatives.

3. Experimental

General methods.—All reactions were carried out using dried solvents and were monitored by TLC (E. Merck, Silica Gel plates GF_{245}). The products were purified by flash chromatography (E. Merck, Silica Gel 60, 230–400 mesh) with distilled solvents. Optical rotations were measured on a Perkin–Elmer



Scheme 4.

243 polarimeter (sodium D line: 589 nm) in a 10 cm polarimeter cuvette at 20 °C. NMR spectra were recorded on Bruker AMX-400 spectrometer (400 MHz for ^{1}H and 100.67 MHz for ^{13}C) in $CDCl_3$ with TMS as internal standard.

General procedure for Ferrier reaction (GM 1).— To a soln of glycal (1 equiv) and aglycon (1.1–1.5 equiv) in anhyd CH_2Cl_2 the catalyst (0.2 equiv) was introduced in one portion at the given temperature (−20 to −45 °C). The mixture was stirred until the reaction was complete according to TLC. Then, the reaction mixture was neutralized with saturated $NaHCO_3$ soln, washed with water, and the organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure and the crude product was purified on silica gel.

General procedure for deacetylation (GM 2).— The compound was dissolved in dry MeOH and one equivalent of Na_2CO_3 added. After complete reaction (ca. 3 h) monitored by TLC, the mixture was filtered and the solvent evaporated under reduced pressure at 40 °C. If required, the residue was purified by column chromatography on silica gel. Water-soluble compounds were dissolved in distilled water and then lyophilised.

General procedure for hydrogenation (GM 3).— The compound was dissolved in dry MeOH and 10% Pd/C added. The mixture was hydrogenated overnight under normal pressure. After complete reaction, the catalyst was filtered over celite and the soln was concentrated in vacuo.

1-O-*(4,6-Di*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl)-2,3*-O-*isopropylidene-glycerol* (**2**).—Triacetylglucal **1** (500 mg, 1.84 mmol) and 2,3-*O*-isopropylidenglycerol (340 μl, 2.76 mmol) were treated at −20 °C in the presence of BF_3–Et_2O according to GM 1. The reaction was stopped after 1 h at −5 °C and the crude product was purified by flash chromatography (3:1 petroleum ether-EtOAc) to give **2** (537 mg, 85%) as a colourless syrup; $[\alpha]_D^{20}$ +88° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ (dd∼d, 1H, H-2), 5.79 (dt, 1H, H-3), 5.24 (ddd, 1H, H-4), 5.00 (bs,1H, H-1), 4.23 (ddd, 1H, H-5), 4.15 (dd, 1H, H-6a), 4.11 (dd, 1H, H-6b), 4.04–3.48 (m, 5H, 2 CH_2-glycerol, CH-glycerol), 2.04, 2.01 (each s, 3H, OAc), 1.36, 1.29 (each s, each 3H, isopropylidene-CH_3); $J_{1,2}$ 1.0, $J_{1,3}$ 1.5, $J_{2,3}$ 11.2, $J_{2,4}$ 1.5, $J_{3,4}$ 2.1, $J_{4,5}$ 9.7, $J_{5,6a}$ 5.6, $J_{5,6b}$ 2.6, $J_{6a,6b}$ 12.2 Hz; ^{13}C NMR ($CDCl_3$) δ 169.79, 167.53 (2 C=O), 128.89, 127.05 (C-2, C-3),109.65 ($OCMe_2$), 94.09 (C-1), 74.13 (C-2′-glycerol), 69.23, 66.56, 66.60, 64.85, 62.53 (C-6, C-1′, C-3′-glycerol), (C-4, C-5), 26.39, 24.98 (2 isopropylidene-CH_3), 20.50, 20.31 (2 OAc). Anal. Calcd for $C_{16}H_{24}O_8$ (344.4): C, 55.81; H 7.02. Found: C, 55.23; H 7.09.

2-O-*(4,6-Di*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl)-1,3-di*-O-*benzyl-glycerol* (**8**).— Triacetylglucal **1** (1.0 g, 3.67 mmol) and 1,3-di-*O*-benzylglycerol (1.1 g, 4.04 mmol) were treated at −25 °C in the presence of BF_3–Et_2O according to GM 1. The reaction was stopped at −10 °C and the crude product was purified by flash chromatography (3:1 petroleum ether–EtOAc) to give **8** (1.61 g, 90%) as a syrup; $[\alpha]_D^{20}$ +41.7° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.35–7.26 (m, 10H, H-Ph), 5.87 (dd∼d, 1H, H-2), 5.83 (dt, 1H, H-3), 5.31 (dd, 1H, H-4), 5.28 (d, 1H, H-1), 4.56–4.53 (m, 4H, CH_2-Ph), 4.17–4.09 (m, 2H, H-6a, H-6b), 4.01 (m, 1H, CH-glycerol), 3.62–3.50 (m, 5H, H-5, 2 CH_2-glycerol), 2.08, 2.04 (each s, 3H, OAc); $J_{1,2}$ 1.2, $J_{1,3}$ 1.6, $J_{2,3}$ 10.8, $J_{3,4}$ 2.5, $J_{4,5}$ 9.6 Hz. Anal. Calcd for $C_{27}H_{32}O_8$ (484.6): C, 66.93; H 6.66. Found: C, 66.84; H 6.52.

2-O-*(4,6-Di*-O-*benzyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl)-1,3-di*-O-*benzyl-glycerol* (**9a**) *and Benzyl 4,6-Di*-O-*benzyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranoside* (**9b**).—Tribenzylglucal **3** (1.5 g, 3.6 mmol) and 1,3-di-*O*-benzylglycerol (1.5 g, 5.4 mmol) were treated at −35 °C in the presence of BF_3–Et_2O according to GM 1. The reaction was stopped at −20 °C and both products were separated by flash chromatography (8:1 petroleum ether–EtOAc). Product **9a** was isolated as a colourless syrup in 65% (1.36 g) yield and product **9b** as yellow syrup in 18% (270 mg) yield; **9a**: $[\alpha]_D^{20}$ +19.7° (*c* 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.38–7.18 (m, 20H, H-Ph), 6.05 (dd∼d, 1H, H-2), 5.78 (dt, 1H, H-3), 5.26 (d∼bs, 1H, H-1), 4.71–4.40 (m, 8H, CH_2-Ph), 4.19–4.11 (m, 2H, H-4, CH-glycerol), 3.99 (ddd, 1H, H-5), 3.67 (dd, 1H, H-6a) 3.64–3.55 (m, 4H, 2 CH_2-glycerol), 3.53 (dd, 1H, H-6b); $J_{1,2}$ 2.0, $J_{1,3}$ 1.5, $J_{2,3}$ 10.2, $J_{3,4}$ 3.0, $J_{4,5}$ 9.7, $J_{5,6a}$ 4.1, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 10.2 Hz; ^{13}C NMR ($CDCl_3$): δ 138.32–126.63 (C-2, C-3, Ph-C), 94.56 (C-1), 75.57 (C-2′-glycerol), 73.33, 73.25, 73.22, 70.93, 70.64, 70.39 (C-1′, C-3′-glycerol, 4 CH_2 -Bn), 70.31, 69.06 (C-4, C-5), 68.72 (C-6). Anal. Calcd for $C_{37}H_{40}O_6$ (580.7): C, 76.53; H 6.94. Found: C, 76.49; H 6.98. **9b**: $[\alpha]_D^{20}$ +24.5° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.38–7.19 (m, 15H, H-Ph), 6.08 (dd∼d, 1H, H-2), 5.79 (dt, 1H, H-3), 5.12 (d∼bs, 1H, H-1), 4.83–4.43 (m, 8H, CH_2-Ph), 4.19 (dd, 1H, H-4), 4.00 (ddd, 1H, H-5), 3.72 (dd, 1H,

H-6a) 3.63 (dd, 1H, H-6b); $J_{1,2}$ 2.5, $J_{1,3}$ 2.0, $J_{2,3}$ 10.2, $J_{3,4}$ 2.0, $J_{4,5}$ 9.7, $J_{5,6a}$ 4.5, $J_{5,6b}$ 2.0, $J_{6a,6b}$ 10.7 Hz; ^{13}C NMR ($CDCl_3$): δ 138.23–126.56 (C-2, C-3, Ph-C), 93.99 (C-1), 73.41, 71.08, 70.06 (3 CH_2-Bn), 70.42, 69.36 (C-4, C-5), 68.81 (C-6).

2-O-*(4*-O-*Acetyl-2,3-dideoxy*-α-D-glycero-*pent-2-enopyranosyl)-1,3-di*-O-*benzyl-glycerol* (**10a**) *and 2*-O-*(4*-O-*acetyl-2,3-dideoxy*-β-D-glycero-*pent-2-enopyranosyl)-1,3-di*-O-*benzylglycerol* (**10b**).—Di-*O*-acetyl-D-xylal **4** (400 mg, 2.0 mmol) and 1,3-di-*O*-benzyl-glycerol (600 mg, 2.2 mmol) dissolved in CH_2Cl_2 (20 mL) were treated in the presence of BF_3–Et_2O at −45 °C according to the GM 1. The reaction was stopped at −5 °C and the anomers (α:β = 1:5) were separated by flash chromatography (6:1 petroleum ether–EtOAc). Products **10a** and **10b** were isolated as a colourless syrups in 14% (115 mg) and 67% yield (555 mg); **10a**: $[\alpha]_D^{20}$ +16.7° (*c* 0.3, $CHCl_3$); **10b**: $[\alpha]_D^{20}$ +44.5° (*c* 0.6, $CHCl_3$); **10a**: ^{1}H NMR ($CDCl_3$): δ 7.38–7.23 (m, 10H, H-Ph), 5.91 (dd, 1H, H-2), 5.87 (dt, 1H, H-3), 5.29 (m_c, 1H, H-4), 5.20 (bs, 1H, H-1), 4.54 (m∼s, 4H, CH_2-Ph), 4.10 (m, 1H, CH-glycerol), 3.81 (dd, 1H, H-5a), 3.77 (dd, 1H, H-5e), 3.70–3,54 (m, 4H, 2 CH_2-glycerol), 2.04 (s, 3H, OAc); $J_{1,2}$ 1.0, $J_{1,3}$ 1.5, $J_{2,3}$ 10.2, $J_{3,4}$ 2.0, $J_{4,5a}$ 8.1, $J_{4,5e}$ 5.6, $J_{5a,5e}$ 11.2 Hz. ^{13}C NMR ($CDCl_3$): δ 170.52 (C=O), 138.25–127.53 (C-2, C-3, Ph-C), 93.99 (C-1), 75.79 (C-2′-glycerol), 73.39, 73.29, 70.83, 70.37 (C-1′, C-3′-glycerol, 2 CH_2-Bn) 65.15 (C-4), 59.64 (C-5), 21.01 (2 OAc). **10b**: ^{1}H NMR ($CDCl_3$): δ 7.38–7.25 (m, 10H, H-Ph), 6.10 (dd, 1H, H-2), 6.06 (dd, 1H, H-3), 5.30 (d, 1H, H-1), 4.95 (m, 1H, H-4), 4.59-4.56 (m, 4H, CH_2-Ph), 4.22 (dd, 1H, H-5a), 4.15 (m, 1H, CH-glycerol), 3.78 (dd, 1H, H-5e), 3.70-5.53 (m, 4H, 2 CH_2-glycerol), 2.11 (s, 3H, OAc); $J_{1,2}$ 1.5, $J_{2,3}$ 10.2, $J_{3,4}$ 3.5, $J_{4,5a}$ 3.1, $J_{4,5e}$ 1.0, $J_{5a,5e}$ 13.2 Hz; ^{13}C NMR ($CDCl_3$): δ 170.67 (C=O), 138.22–124.84 (C-2, C-3, Ph-C), 92.87 (C-1), 75.37 (C-2′-glycerol), 73.29, 71.33, 70.75, 69.65 (C-1′, C-3′-glycerol, 2 CH_2 -Bn) 63.45 (C-4), 61.21 (C-5), 21.15 (2 OAc). Anal.Calcd for $C_{24}H_{28}O_6$ (412.5): C, 69.89; H, 6.84. Found: **10a**: C, 69.76; H, 6.77; **10b**: C, 69.79; H, 6.78.

1,3-Di-O-*benzyl-2*-O-*[4*-O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl)-6*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl]-glycerol* (**11**).—Hexaacetyllactal **5** (1.0 g, 1.78 mmol) and 1,3-di-*O*-benzylglycerol (0.73 g, 2.67 mmol) were treated at −20 °C in the presence of BF_3–Et_2O according to GM 1. The reaction was stopped at 10 °C and the crude product was purified by flash chromatography (2:1 petroleum ether–EtOAc) to give **11** (1.19 g, 86%) as a colourless syrup; $[\alpha]_D^{20}$ +104.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.28–7.15 (m, 10H, H-Ph), 6.03 (dd∼d, 1H, H-2), 5.68 (dt, 1H, H-3), 5.31 (dd, 1H, H-4′), 5.17 (dd∼d, 1H, H-1), 5.14 (dd, 1H, H-2′), 4.93 (dd, 1H, H-3′), 4.51–4.42 (m, 4H, 2 CH_2-Ph), 4.46 (d, 1H, H-1′), 4.13–3.94 (m, 7H, H-4, H-5, H-6a, H-6b, H-6a′, H-6b′, CH-glycerol), 3.83 (ddd, 1H, H-5′), 3.62–3.45 (m, 4H, 2 CH_2-glycerol), 2.11, 2.01, 2.00, 1.98, 1.92 (each s, 3H, OAc); $J_{1,2}$ 2.0, $J_{1,3}$ 2.5, $J_{2,3}$ 10.2, $J_{3,4}$ 2.5, $J1',2'$ 8.1, $J_{2',3'}$ 10.7, $J_{3',4'}$ 3.6, $J_{4',5'}$ 1.0, $J_{5',6a'}$ 6.6, $J_{5',6b'}$ 7.1 Hz; ^{13}C NMR ($CDCl_3$): δ 170.30, 169.98, 169.79, 169.63, 168.93 (5 C=O), 137.97–126.60 (C-2, C-3, C-aryl), 102.10 (C-1′), 93.85 (C-1), 75.32 (C-2″-glycerol), 73.14, 70.48, 69.92, 68.42, 66.87, 66.45 (C-4, C-5, C-2′, C-3′, C-4′, C-5′), 72.93, 70.35, 70.29, 62.58, 60.81, 59.93 (C-6, C-6′, C-1″, C-3″-glycerol, 2 CH_2-Ph), 20.61, 20.58, 20.36, 20.19, 20.09 (5 OAc). Anal.Calcd for $C_{39}H_{48}O_{16}$ (772.8): C, 60.61; H, 6.26. Found: C, 60.58; H, 6.24.

1,3-Di-O-*benzyl-2*-O-*[4*-O-*(2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl)-6*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl]-glycerol* (**12**).—In analogy to the preparation of **11**, hexaacetylmaltal **6** (1.0 g, 1.78 mmol) and 1,3-di-*O*-benzylglycerol (0.73 g, 2.67 mmol) were converted into **12** (1.03 g, 75%); colourless syrup; $[\alpha]_D^{20}$ +93° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.38–7.14 (m, 10H, H-Ph), 5.75 (s, 2H, H-2, H-3), 5.36 (t, 1H, H-4′), 5.23 (d, 1H, H-1′), 5.17 (bs, 1H, H-1), 5.01 (dd, 1H, H-3′), 4.77 (dd, H-2′), 4.47 (d, 4H, 2 CH_2-Ph), 4.19 (dd, 1H, H-6a′), 4.16 (d, 1H, H-4), 4.10–3.99 (m, 4H, H-5, H-6a, H-6b, CH-glycerol), 3.97 (dd, 1H, H-6b′), 3.92 (ddd, 1H, H-5′), 3.62–3.47 (m, 4H, 2 CH_2-glycerol), 2.03, 2.01, 2.00, 1.98, 1.95 (each s, 3H, OAc); $J_{4,5}$ 9.7, $J_{1',2'}$ 4.1, $J_{2',3'}$ 10.2, $J_{3',4'}$ 9.7, $J_{4',5'}$ 10.2, $J_{5',6a'}$ 3.6, $J_{5',6b'}$ 2.5, $J_{6a',6b'}$ 12.2 Hz; ^{13}C NMR ($CDCl_3$): δ = 170.19, 170.17, 169.79, 169.54, 169.11 (5 C=O), 137.84–127.05 (C-2, C-3, C-aryl), 93.71, 93.47 (C-1, C-1′), 75.33 (C-2″-glycerol), 73.01, 72.94, 69.84, 69.38, 62.75, 61.45 (C-6, C-6′, C-1″, C-3″-glycerol, 2 CH_2-Ph), 70.33, 69.17, 68.91, 68.43, 67.74, 66.69 (C-4, C-5, C-2′, C-3′, C-4′, C-5′), 20.59, 20.48, 20.33, 20.22, 20.16 (5 OAc). Anal.Calcd for $C_{39}H_{48}O_{16}$ (772.8): C, 60.61; H, 6.26. Found: C, 59.97; H, 6.38.

1-O-*(1,3-Di*-O-*benzyl-glyceryl)-4*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranuronic acid methylester* (**13**).—Methyl 3,4-diacetyl-D-glucuronal **7** (100 mg, 0.77 mmol) and 1,3-di-*O*-benzyl-glycerol (225 mg, 0.94 mmol) were treated at −40 °C in the presence of BF_3–Et_2O according to

GM 1. The reaction was stopped at −20 °C and the crude product was purified by flash chromatography (3:1 toluene–EtOAc) to give **13** (229 mg, 80%) as a colourless syrup; $[\alpha]_D$ +56.8° (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.39–7.25 (m, 10H, H-Ph), 5.88 (dd, 1H, H-3), 5.84 (dd∼d, 1H, H-2), 5.56 (dd, 1H, H-4), 5.37 (bs, 1H, H-1), 4.54 (d, 1H, H-5), 4.52 (s, 4H, CH_2-Ph), 4.16 (m, 1H, CH-glycerol), 3.67 (s, 3H, OMe), 3.66–3.50 (m, 4H, 2 CH_2-glycerol), 2.08 (s, 3H, OAc); $J_{1,2}$ 1.5, $J_{1,3}$ 1.5, $J_{2,3}$ 10.2, $J_{3,4}$ 2.5, $J_{4,5}$ 9.7 Hz; ^{13}C NMR ($CDCl_3$): δ 170.24, 169.55 (2 C=O), 138.29–127.59 (C-2, C-3, Ph-C), 94.28 (C-1), 76.17 (C-2′-glycerol), 73.47, 73.34, 70.54, 70.23 (C-1′, C-3′-glycerol, 2 CH_2 -Bn), 68.19, 66.02 (C-4, C-5), 52.59 (OMe), 20.97 (OAc). Anal.Calcd for $C_{26}H_{30}O_8$ (470.5): C, 66.37; H, 6.43. Found: C, 66.35; H, 6.40.

1-O-*(1,3-Di*-O-*benzyl-glyceryl)-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranuronic acid methylester* (**14**).—Compound **13** (200 mg, 0.43 mmol) was deprotected according to GM 2 to yield after chromatographic purification (3:1 toluene–EtOAc) the colourless syrup **14** (170 mg, 93%); $[\alpha]_D^{20}$ +2° (*c* 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.39–7.23 (m, 10H, H-Ph), 5.95 (dd∼d, 1H, H-2), 5.79 (dt, 1H, H-3), 5.33 (d, 1H, H-1), 4.55 (s, 2H, CH_2-Ph), 4.53 (d, 1H, H-5), 4.36 (s, 2H, CH_2-Ph), 4.18 (m, 1H, CH-glycerol), 3.72 (s, 3H, OMe), 3.69–3.47 (m, 5H, H-4, 2 CH_2-glycerol), 2.90 (d, 1H, 4-OH); $J_{1,2}$ 1.5, $J_{1,3}$ 2.0, $J_{2,3}$ 10.2, $J_{3,4}$ 1.5, $J_{4,OH}$ 3.1, $J_{4,5}$ 8.2 Hz; ^{13}C NMR ($CDCl_3$): δ 169.52 (C=O), 138.33–126.33 (C-2, C-3, Ph-C), 94.58 (C-1), 76.17 (C-2′-glycerol), 73.46, 73.36, 70.68, 70.49 (C-1′, C-3′-glycerol, 2 CH_2-Bn), 65.28, 57.62 (C-4, C-5), 52.59 (OMe). Anal.Calcd for $C_{24}H_{28}O_7$ (428.5): C, 67.28; H, 6.59. Found: C, 67.38; H, 6.56.

1-O-*(1,3-Di*-O-*benzyl-glyceryl)-4*-O-*(methyl-4*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl-uronate)-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranuronic acid methylester* (**15**).—Compounds **7** (40 mg, 0.15 mmol) and **14** (77 mg, 0.18 mmol) were treated at −45 °C in the presence of a catalytic amount of $SnBr_4$ according to GM 1. The reaction was stopped after 1 h at −25 °C and the crude product was purified by flash chromatography (5:1 toluene–EtOAc) to give **15** (27 mg, 28%) as a syrup; $[\alpha]_D^{20}$ +25.2° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.39–7.23 (m, 10H, H-Ph), 6.38 (s, 2H, H-2′, H-3′), 5.92 (dd∼d, 1H, H-2), 5.86 (dt, 1H, H-3), 5.57 (dd, 1H, H-4′), 5.29 (bs, 1H, H-1), 5.24 (bs, 1H, H-1), 4.60 (d, 1H, H-5), 4.58–4.50 (m, 5H, H-5′, 2 CH_2-Ph), 4.03 (m, 1H, CH-glycerol), 3.81 (dd∼d, 1H, H-4), 3.77, 3.76 (each s, 3H, 2 OMe), 3.60–3.50 (m, 4H, 2 CH_2-glycerol), 2.05 (s, 3H, OAc); $J_{1,2}$ 1.5, $J_{1,3}$ 1.5, $J_{2,3}$ 10.2, $J_{3,4}$ 2.0, $J_{4,5}$ 8.7, $J_{1',2'}$ .5, $J_{3',4'}$ 1.5, $J_{4',5'}$ 9.7 Hz; ^{13}C NMR ($CDCl_3$): δ 171.47, 170.57, 169.16 (3 C=O), 137.97–126.52 (C-2, C-3, C-2′, C-3′, Ph-C), 110.61 (C-1′), 93.66 (C-1), 76.51 (C-2″-glycerol), 73.47, 73.39, 71.31, 71.26 (C-1″, C-3″-glycerol, 2 CH_2-Bn), 72.36, 69.63, 68.40, 65.64 (C-4, C-5, C-4′, C-5′), 52.69, 52.60 (2 OMe), 20.83 (OAc).

2-O-*(4,6-Di*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hexopyranosyl)-glycerol* (**16**).—Compound **8** (1.0 g, 2.06 mmol) was hydrogenated according to GM 3. After purification by flash chromatography (3:1 EtOAc–petroleum ether), the colourless syrup **16** (505 mg, 80%) was obtained; $[\alpha]_D^{20}$ +10° (*c* 0., $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 4.98 (bs, 1H, H-1), 4.65 (m, 1H, H-4), 4.14–4.03 (m, 3H, H-6a, H-6b, CH-glycerol), 3.74–3.56 (m, 5H, H-5, 2 CH_2-glycerol), 2.04, 2.01 (each s, 3H, OAc), 2.00–1.74 (m, 4H, H-2a, H-2e, H-3a, H-3e); $J_{1,2a}$ 2.5, $J_{5,6a}$ 5.1, $J_{5,6b}$ 2.5, $J_{6a,6b}$ 12.2 Hz; ^{13}C NMR ($CDCl_3$): δ 170.40, 169.55 (2 C=O), 96.21 (C-1), 80.37 (C-2′-glycerol), 69.13, 67.52 (C-4, C-5), 63.09, 62.97, 61.94 (C-6, C-1′, C-3′-glycerol), 28.51, 23.33, (C-2, C-3), 20.57, 20.24 (2 OAc). Anal. Calcd for $C_{13}H_{22}O_8$ (306.3): C, 50.98; H 7.24. Found: C, 50.58; H 7.09.

2-O-*(2,3-Dideoxy*-α-D-erythro-*hexopyranosyl)-glycerol* (**17**).—Method A: Compound **16** (260 mg, 0.63 mmol) was deacetylated according to GM 2. After purification of the crude product on silica gel (6:1 CH_2Cl_2-MeOH), **17** (172 mg, 91%) was obtained as a yellow syrup; method B: compound **9a** (300 mg, 0.52 mmol) was hydrogenated according to GM 3 to give **17** (92 mg, 80%); $[\alpha]_D^{20}$ +80.7° (*c* 0.3, $CHCl_3$); ^{1}H NMR (MeOD): δ 5.16 (dd∼d, 1H, H-1), 3.99–3.56 (m, 9H, H-4, H-5, H-6a, H-6b, CH-glycerol, 2 CH_2-glycerol), 2.07–1.39 (m, 4H, H-2ae, H-3ae); $J_{1,2a}$ 2.5, $J_{1,2e}$ 1.0 Hz; ^{13}C NMR (MeOD): δ 96.08 (C-1), 78.57 (C-2′-glycerol), 74.52, 66.24 (C-4, C-5), 62.15, 62.06, 61.43 (C-6, C-1′, C-3′-glycerol), 29.45, 27.06 (C-2, C-3). Anal.Calcd for $C_9H_{18}O_6$ (222.2): C, 48.64; H, 8.16. Found: C, 48.06; H, 8.24.

1,3-Di-O-*(4,6-di*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hex-2-enopyranosyl)-2*-O-*(4,6-di*-O-*acetyl-2,3-dideoxy*-α-D-erythro-*hexopyranosyl)-glycerol* (**18**).—Triacetylglucal **1** (90 mg, 0.33 mmol) and compound **16** (50 mg, 0.16 mmol) were treated at −45 °C under BF_3–etherate catalysis according to GM 1. The reaction was stopped after 1 h at −20 °C and the major product was isolated by column chromatography on silica gel (2:1 petroleum ether–EtOAc) to afford **17** (65 mg, 55%) as a

colourless syrup; $[\alpha]_D^{20}$ +154° (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.92 (dd∼d, 1H, H-2), 5.91 (dd∼d, 1H, H-2′), 5.84 (dt, 1H, H-3), 5.81 (dt, 1H, H-3′), 5.35 (m, 2H, H-4, H-4′), 5.09 (bs, 2H, H-1, H-1′), 5.05 (d, 1H, H-1″), 4.77 (m, 1H, H-4″), 4.33–4.03 (m, 10H, CH-glycerol, H-5, H-5′, H-5″, H-6a, H-6b, H-6a′, H-6b′, H-6a″, H-6b″), 3.97–3.90 (m, 2H, 2 CH_2-glycerol), 3.70–3.58 (m, 2H, 2 CH_2-glycerol), 2.11–2.05 (6s, 18H, 6 OAc), 2.04–1.82 (m, 4H, H-2ae″, H-3ae″); $J_{1,2}$ 1.5, $J_{1,3}$ 2.0, $J_{2,3}$ 10.2, $J_{3,4}$ 2.5, $J_{1',2'}$ 1.5, $J_{1',3'}$ 2.0, $J_{2',3'}$ 10.2, $J_{3',4'}$ 2.5, $J_{1'',2a''}$ 2.0 Hz; ^{13}C NMR ($CDCl_3$) : δ = 170.24–169.43 (6 C=O), 128.95, 128.94, 126.95, 126.93 (C-2, C-3, C-2′, C-3′), 95.27, 94.31, 94.28 (C-1, C-1′, C-1″), 73.74 (C-2*-glycerol), 68.34, 68.33 (C-1*, C-3*-glycerol), 67.80, 67.21, 66.84, 66.59, 66.58, 64.78 (C-4, C-5, C-4′, C-5′, C-4″, C-5″), 62.60, 62.45, 62.38 (C-6, C-6′, C-6″), 28.45, 23.37, (C-2″, C-3″), 20.60–20.34 (6 OAc). Anal.Calcd for $C_{33}H_{46}O_{18}$ (730.7): C, 54.24; H, 6.35. Found: C, 53.72; H, 6.35.

Acknowledgements

Support of this work by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

References

[1] H.P. Wehrli and Y. Pomeranz, *Chem. Phys. Lipids*, 3 (1969) 357–370.
[2] D.A. Mannock, R.N.A.H. Lewis, and R.N. McElhaney, *Chem. Phys. Lipids*, 55 (1990) 309–321.
[3] D.A. Mannock, R.N.A.H. Lewis, and R.N. McElhaney, *Chem. Phys. Lipids*, 43 (1987) 113–127.
[4] R.J. Ferrier and N. Prasad, *J. Chem. Soc.*, C (1969) 570–574.
[5] R.J. Ferrier, *Adv. Carbohydr. Chem.*, 20 (1965) 67–137.
[6] R.J. Ferrier, *Adv. Carbohydr. Chem. Biochem.*, 24 (1969) 199–266.
[7] E. Wieczorek and J. Thiem, *Synlett*, in press.
[8] E. Wieczorek and J. Thiem, *J. Carbohydr. Chem.*, in press.
[9] A. Fairbourne, G.P. Gibson, and D.-W. Stephens, *J. Chem. Soc.*, 133 (1931) 445–448.
[10] B. Doboszewski, N. Blaton, and P. Herdewijn, *J. Org. Chem.*, 60 (1995) 7909–7919.
[11] H.-W. Fehlhaber, G. Snatzke, and I. Vlahov, *Liebigs Ann. Chem.*, 1987, 637–638.
[12] R.R. Schmidt and R. Angerbauer, *Carbohydr. Res.*, 89 (1981) 159–162.
[13] R.R. Schmidt and R. Angerbauer, *Carbohydr. Res.*, 89 (1981) 193–201.