Available online at www.sciencedirect.com
SCIENCE DIRECT
Carbohydrate Research 341 (2006) 846–854
Carbohydrate RESEARCH

Synthesis of 2(*R*),3-dihydroxypropyl and 2(*R*),3(*R*)-dihydroxybutyl β-D-fructopyranosides and some derivatives

Fortunatus Sung'hwa,† Axel Strik, Henk Regeling,* Binne Zwanenburg and Gordon J. F. Chittenden

Department of Organic Chemistry, IMM Center, Radboud University Nijmegen, Toernooiveld 1, NL-6525 ED Nijmegen, The Netherlands

Received 9 September 2005; received in revised form 24 January 2006; accepted 9 February 2006
Available online 10 March 2006

Abstract—The synthesis of 2(*R*),3-dihydroxypropyl and 2(*R*),3(*R*)-dihydroxybutyl β-D-fructopyranosides, and some derivatives, employing Sharpless-type catalytic asymmetric dihydroxylation procedures is described. Some aspects of the reactions, including stereoselectivities and chemical evidence for the assigned stereochemistry of the main products are reported.

Keywords: Alkenyl fructosides; Dihydroxyalkyl fructosides; Asymmetric dihydroxylations; Fructosyl glycolipids

1. Introduction

Glycosides of glycerol are important basic units of glyceroglycolipids. These are widely distributed in nature, and have been isolated from many sources including plants, animal tissue, bacteria and marine organisms.[1–4] The glycerol hydroxyl groups are usually esterified or etherified by a variety of long-chain fatty acids or alkyl residues. They play important roles in cell surface recognition–interaction and the maintenance of membrane structure and fluidity.[2] There has been a recent resurgence of interest in these compounds, particularly those in which a sugar unit is β-linked to a primary position of glycerol, because of the newly discovered interesting biological properties including inter alia, anti-tumour and anti-inflammatory activities.[5–7]

No lipid structures containing D-fructose have been reported despite it being the second most abundant natural monosaccharide. The intermediate formation of glyceryl-fructosides during the enzymatic synthesis of some levans from sucrose has been implied, but never substantiated.[8] Treatment of D-fructose with glycerol in the presence of mesoporous catalysts yielded[9] complicated mixtures, which were not separated or investigated. The enzymatic synthesis of some D-fructosyl glycerols by reaction of sucrose with glycerol in the presence of levan sucrases from *Bacillus circulans* and *Bacillus subtilis* has been reported.[10] Concurrent hydrolysis of the products and levan synthesis by the enzymes gave low yield. There was only a slight preference of reaction on glycerol at either of the two primary hydroxyl groups over the secondary group. The authors refer consistently to their products as pyranose derivatives but present structures in the furanoid form. The physical data presented support the latter.

We now report the synthesis of 2(*R*),3-dihydroxypropyl β-D-fructopyranoside (1-*O*-fructopyranosyl-*sn*-glycerol, **1**) and some related compounds. Long-chain alkyl esters of compound **1** are also described.

2. Results and discussion

The synthesis of specifically defined fructosides is difficult.[11] Normal acid catalyzed glycosidation tends to lead

* Corresponding author at present address: MercaChem BV, PO Box 31070, 6503 CB Nijmegen, The Netherlands. Tel.: +31 (0)243 528832; fax: +31 (0)243 653881; e-mail: regeling@mercachem.com
† Present address: Department of Chemistry, University of Dar es Salaam, PO Box 35061, Dar es Salaam, Tanzania.

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.02.005

to complex anomeric mixtures of pyranosides and furanosides and dehydration–decomposition products arising from elimination. Koenigs–Knorr procedures using D-fructose are also difficult. The catalytic asymmetric dihydroxylation (AD)[12,13] of allyl β-D-fructopyranoside[14] (**2**) was investigated. There are few examples of the use of the Sharpless AD protocol for the synthesis of dihydroxyalkyl glycosides.[15–18] The synthesis of several glycosyl glycerols was described recently.[19] Acetylated allyl glycosides were converted into 1-*O*-(glycopyranosyl)-*rac*-glycerols by epoxidation with *m*-chloroperbenzoic acid, followed by opening of the resultant oxiranes with $BF_3{\cdot}Et_2O$. There was little or no diastereoselectivity indicated.

Benzylation of **2** gave the crystalline tetra-*O*-benzyl derivative **3**. This was used as the basic substrate for the various AD reactions. The benzyl group was chosen as a protecting function for its known stability and the eventual ease of removal by catalytic hydrogenolysis. This was an important factor for the projected synthesis of some long-chain acyl esters of the glyceryl fructosides to be anticipated from the oxidations. A recent report[18] also suggested that mutual π–π stacking of aromatic nuclei with some AD ligands can lead to enhanced facial diastereoselectivity. The use of *O*-acetyl protecting groups on some polyhydroxy substrates in AD reactions has not always resulted in good stereoselectivities.[15–17]

Compound **3** was initially subjected to catalytic osmylation using the phthalazine-based chiral ligands $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$ at 22 °C. These two ligands are components of the commercially available AD-mix α, and AD-mix β, respectively. The pyrimidine-based ligands $(DHQD)_2PYR$ and $(DHQ)_2Py$ were also included in this study. The yields of crystalline material, mixtures of diastereoisomers, obtained after column chromatography and the respective degrees of stereoselectivity as expressed by the de values are summarized in Table 1. The de values were determined by analysis (GLC) of per-O-acetylated samples obtained from the isolated reaction products by sequential de-O-benzylation (catalytic hydrogenolysis; H_2/Pd–C, 10%), followed by acetylation in the usual manner.

The use of pyrimidine-based ligands led to consistent, and relatively high de values. A previous observation suggests that the dihydroquinidine ligand $(DHQD)_2$-PYR was superior in most AD reactions of terminal olefins.[20] The importance of chiral ligand structures in AD reactions has been discussed.[16]

Table 1. Asymmetric dihydroxylation of compound **3** at 22 °C

Chiral ligand	Chemical yield (%)	de[a] (%)
$(DHQD)_2PHAL$	97.5	67
$(DHQ)_2PHAL$	70	27
$(DHQD)_2PYR$	82	56
$(DHQ)_2PYR$	88	76
$(DHQD)_2AQN$	97.5	63.5
$(DHQ)_2AQN$	90	27

[a] Determined by GLC—see Experimental section.

When the above reactions were conducted at 0 °C no improvements in yields or de values were noted. Previous studies on other AD-type reactions involving alkenyl glycosides conducted at 0 °C noted improved yields and higher selectivities.[15–18]

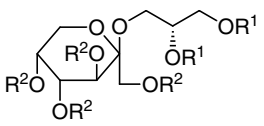
Recrystallization of the products obtained from the AD reactions of compound **3** appeared to give the same pure diastereomer **1**, mp 101–103 °C, $[\alpha]_D$ −59, in each case.

The stereochemistry at position C-2 of the generated dihydroxypropyl unit was established in the following manner. Samples of the products obtained using $(DHQD)_2PHAL$ and $(DHQ)_2PYR$, as representative ligands, were benzylated in the usual manner and these products were subjected to acid hydrolysis. Column chromatography of the resultant products gave the known[21] 2(*R*)-1,2-dibenzyloxypropan-1-ol (**6**) in each case. Further elution gave the tetra-*O*-benzyl-D-fructoses **5**, as anomeric mixtures, which were not investigated.

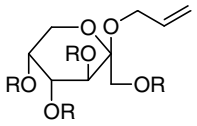
These results established the stereochemistry at C-2 as the same in each case. It may have been expected that the use of ligands based on dihydroquinidine and dihydroquinine could have given rise to different configurations of the hydroxyl group at C-2 in each case.

It seemed that the relatively large *O*-benzyl group attached to the C-1 position of the β-D-fructopyranosyl unit has a profound effect on the approach of the effective reagent complexes. Previous studies[15,16,18] have indicated that it is not always possible to achieve respectable diastereoselectivities during the dihydroxylation of alkenyl glycosides in the presence of chiral auxiliaries. A number of other factors play a significant role. These include the length of the alkenyl chain, the position of the unsaturation, the nature and size of the protecting functions, the anomeric configuration and the preferred conformation of the sugar ring. These intramolecular factors seem to outweigh other considerations, which can determine diastereofacial preferences in the chiral auxiliary catalyzed dihydroxylation processes.

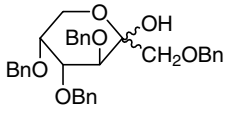
Next we studied the preparation of some long-chain di-*O*-acyl derivatives of the glycerol compound **1**. Treatment of **1** in pyridine–dichloromethane solution at 0 °C with dodecanoyl, tetradecanoyl and hexadecanoyl chloride (3 equiv) in the usual manner yielded the esters **7**–**9**, respectively. The products, which were colourless oils, required purification by column chromatography (75–91% yield). Subsequent removal of the *O*-benzyl protecting groups from these products by catalytic hydrogenolysis (H_2/Pd–C, 10%) gave the crystalline glyceryl derivatives **10**–**12**. The slightly modest yields (50–58%) of these compounds could be attributed to the



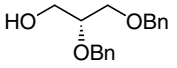
1 R^1 = H, R^2 = Bn
4 R^1 = R^2 = Bn
7 R^1 = $C_{11}H_{23}CO$; R^2= Bn
8 R^1 = $C_{13}H_{27}CO$; R^2= Bn
9 R^1 = $C_{15}H_{31}CO$; R^2= Bn
10 R^1 = $C_{11}H_{23}CO$; R^2= H
11 R^1 = $C_{13}H_{27}CO$; R^2= H
12 R^1 = $C_{15}H_{31}CO$; R^2= H



2 R = H
3 R = Bn



5

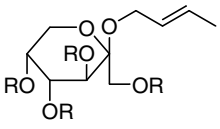


6

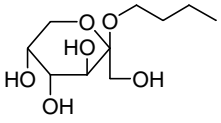
Scheme 1.

difficulties encountered in purifying the crude products (Scheme 1).

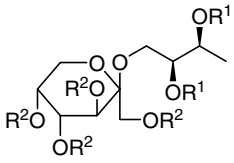
This study was extended to the preparation and dihydroxylation of the but-2-enyl derivative **13**. The necessary starting compound **14** had not been described previously. Treatment of D-fructose with but-2-en-1-ol (crotyl alcohol; cis/trans, 1:19) in the presence of a catalytic quantity of acetyl chloride at room temperature for 48 h gave crystalline **14**. The reaction mixture remained heterogeneous throughout the reaction period. Catalytic hydrogenation[14] of a portion of the product gave the known butyl[22] compound **15**. Benzylation of the fructoside **14** yielded the tetra-*O*-benzyl derivative **13** (88.5%), as an oil (Scheme 2).



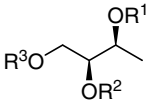
13 R = Bn
14 R = H



15

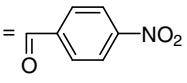


16 R^1 = H, R^2 = Bn
17 R^1 = R^2 = Bn



18 R^1 = R^2 = Bn, R^3 = H

19 R^1 = R^2 = R^3 =



Scheme 2.

Catalytic asymmetric dihydroxylation of **13** was carried out as described earlier, but using only two ligands, namely, $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$. The reactions were performed at room temperature, and in the presence of methanesulfonamide, which has been claimed[23–25] to enhance the rate of hydrolysis of intermediate osmate esters. In each case only one main product was obtained in 82% and 88% yield, respectively. Analysis (GLC) on samples subjected to a sequential hydrogenolysis/acetylation sequence (vide supra) showed high de values of 97% and 96%, respectively. The recrystallized products from each of the two reactions appeared to be the same compound **16**, and implying that the expected alteration of product stereochemistry using the AD-α and AD-β ligands was not observed. Intramolecular stereocontrol by the fructosyl unit appears to prevail over the molecular control by the chiral catalyst, despite the double bond being situated between two secondary carbon atoms in the middle of the aglycon. This situation could have imposed greater selectivity in the chiral auxiliary catalyzed reaction due to increased diastereofacial preference.

The absolute configuration of the 2,3-diol group in compound **16** was determined as described for compound **1**. Benzylation of **16** under basic conditions yielded the per-*O*-benzyl derivative **17**, which was hydrolyzed (TFA–H_2O, 9:1) to give the 1-deoxy-D-threitol compound **18**. Catalytic hydrogenolysis (Pd–C, 10%) of **18** followed by reaction of the resultant product with *p*-nitrobenzoyl chloride in pyridine gave the known[26–28] tris-*p*-nitrobenzoate **19**, which established the 2(*R*),3(*R*) configuration for the diol group at C-2 and C-3.

3. Experimental

General—Optical rotations were determined with a Perkin–Elmer automatic polarimeter, model 241 MC, at 20 °C, on 1% solutions in the solvents indicated. Column chromatography was performed using silica gel 60 (E. Merck) using the eluents indicated. Thin layer chromatography (TLC) on pre-coated plates of silica gel GF_{254} (E. Merck) was conducted in the solvent mixtures indicated. Compounds were detected by spraying with 3% H_2SO_4 in EtOH, followed by heating at 140 °C. Gas-liquid chromatography (GLC) was performed on a Hewlett–Packard 5890 gas chromatograph using a fused capillary column (25 m) coated with HP-1, cross-linked methyl silicone (gum phase) operating at 100 → 200 °C ($t = 0$ min, isothermal, $t = 5$ min, 5 °C min^{-1}) with nitrogen as carrier gas at 2 mL min^{-1}. ^1H NMR spectra were recorded on Bruker AC 100 (100 MHz, FT), AC 300 (300 MHz) or AC (400 MHz) spectrometers on solutions in $CDCl_3$ (internal standard Me_4Si) or D_2O (internal standard HDO). ^{13}C NMR

spectra were recorded on a Bruker AC 100 (100 MHz), AC 300 (300 MHz) or AM 400 spectrometers operating at 25.0, 75.0 and 100.6 MHz, respectively, in $CDCl_3$ (internal Me_4Si) or D_2O (external 1,4-dioxane, 76.8 ppm). Mass spectra were recorded using a double focussing VG 7070E spectrometer in the mode indicated. $(DHQD)_2PHAL$, $(DHQ)_2PHAL$, $(DHQD)_2PYR$, $(DHQ)_2PYR$, $(DHQD)_2AQN$ and $(DHQ)_2AQN$ were purchased from Sigma–Aldrich and were used as supplied.

3.1. Allyl 1,3,4,5-tetra-*O*-benzyl β-D-fructopyranoside (3)

A cooled (0 °C), stirred mixture of allyl β-D-fructopyranoside (**2**)[14] (7.41 g, 33.7 mmol) in Me_2SO (30 mL) containing powdered KOH (7.54 g, 135 mmol) was treated with benzyl chloride (15.5 mL, 135 mmol), and set aside at room temperature for 12 h. The mixture was treated with ether (100 mL) and water (40 mL), the separated aqueous layers extracted with ether (50 mL), the combined organic layers washed with saturated aqueous NaCl, dried ($MgSO_4$) and concentrated in vacuo. Column chromatography (hexane–EtOAc, 3:1) of the crude material gave **3** (15.5 g, 79.5%) a pure colourless oil, $[\alpha]_D$ −49.6 ($CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ 7.40–7.19 (m, 20H, aromatic H), 5.93–5.84 (m, lH, H-2′), 5.23(dd, 1H, $J_{2'a,3'a}$ 15.8, $J_{3'a,3'b}$ 1.3 Hz, H-3′a), 5.00 (dd, 1H, $J_{2b'3'b}$, 1.1, $J_{3a',3b'}$1.3 Hz H-3′b), 4.93, 4.62 (2d, each 1H, J 11.2 Hz, benzylic H), 4.76, 4.71 (2d, each 1H, J 12.6 Hz, benzylic H), 4.68, 4.45 (2d, each 1H, J 11.9 Hz, benzylic H), 4.62–4.56 (m, each 1H, benzylic-H), 4.39 (d, 1H, H-3), 4.14–4.12 (m, 2H, H-1′a, H-1′b), 4.10 (m, 1H, H-5), 4.01 (dd, 1H, $J_{3,4} = J_{4,5}$ 3.1 Hz, H-4), 3.87 (dd, 1H, $J_{5,6eq}$ 1.4, $J_{6ax,6eq}$ −12.4 Hz, H-6eq), 3.84, 3.77 (2d, each 1H, J −10.1 Hz, H-1a, H-1b), 3.55 (dd, 1H, $J_{5,6ax}$ 1.4, $J_{6ax,6eq}$ −12.4 Hz, H-6ax) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.84, 138.62, 138.74, 137.99, 128.20, 128.07, 128.02, 127.67, 127.57, 127.37, 127.22 (aromatic C), 135.12 ($OCH_2CH–CH_2$), 115.88 ($OCH_2OH–CH_2$), 101.83 (C-2), 78.73 (C-3), 76.17 (C-4), 75.43 (benzylic-C), 73.62 (C-5), 73.43, 72.17, 71.09 (benzylic-C), 70.15 (C-1), 62.20 (C-1′) and 61.14 (C-6) ppm.

3.2. 2(*R*),3-Dihydroxypropyl 1′,3′,4′,5′tetra-*O*-benzyl-β-D-fructopyranoside (1)

By Sharpless-type asymmetric dihydroxylation (AD) of compound **2**—*General procedure*—A stirred solution of potassium(IV)osmate·dihydrate (12.22 mg), K_2CO_3 (3.66 g), $K_3Fe(CN)_6$ (8.65 g) and the appropriate chiral ligand (8.5×10^{-5} mol; see Table 1) in H_2O (25 mL) was added to a rapidly stirred solution of compound **2** (5.06 g, 8.75 mmol) in 2-methylpropan-2-ol (30 mL) and then set aside for ca. 12 h. The mixture was treated with Na_2SO_3 (15 g) stirred for 1 h and then treated with ether (100 mL) and water (30 mL). The aqueous layer was extracted with ether (2×30 mL) and the combined organic layers washed with saturated aqueous NaCl (40 mL), dried ($MgSO_4$) and concentrated in vacuo. Column chromatography (hexane–EtOAc, 1:3) of the resultant material gave white crystals (4.85 g, 90.5%) as mixtures of diastereoisomers. Pure compound **1** (2.71–3.25 g, 50–60%) was obtained by recrystallization of the material (isopropylether), mp 101–102 °C $[\alpha]_D$ −59.3 ($CHCl_3$); MS (CI-CH_4) m/z 615 $(M+H)^+$ 523 $(M+H-HOCH_2-CH(OH)CH_2OH)^+$. ^1H NMR ($CDCl_3$, 400 MHz): δ 7.39–7.17 (m 20H, aromatic H), 4.87, 4.61 (2d, each 1H, J 10.8 Hz, benzylic H), 4.73–4.69 (2d, each 1H, J 12.6 Hz, benzylic H) 4.64–4.62 (m, 2H, benzylic H), 4.58, 4.42 (2d, each 1H, J 11.9 Hz, benzylic H), 4.33 (d, 1H, J 10.0 Hz, H-3), 3.90 (dd, 1H, $J_{3,4}$–$J_{4,5}$ 3.0 Hz, H-4), 3.85 (dd, 1H, $J_{5,6eq}$ 1.8, $J_{6ax,6eq}$ −12.4 Hz, H-6_{eq}), 3.73 (d, 1H, J −10.2 Hz, H-1a), 3.72 (m, 1H, H-5), 3.55 (dd, 1H, $J_{5,6ax}$ 1.7, $J_{6ax,6eq}$ −12.4 Hz, H-6_{ax}), 3.52 (m, 1H, H-2′), 3.44–3.41 (m, 2H, H-1′a, 1′b), 3.42 (d, 1H, $J_{3'a,2}$ 6.1 Hz, H-3′a), 3.39 (d, 1H, $J_{3'b,2}$ 6.1 Hz, H-3′b), 2.97 (br s, 1H, OH), 2.26 (br s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.34, 138.27, 137.66, 128.21, 128.12, 128.03, 127.77, 127.63, 127.53, 127.43 (aromatic C), 101.04 (C-2), 78.58 (C-3), 76.49 (C-4), 75.60, 73.53 (benzylic-C), 73.24 (C-5), 71.94, 71.12 (benzylic-C), 70.09 (C-2′, C′3), 63.69 (C-1, C-1′), 61.03 (C-6) ppm. Anal. Calcd for $C_{37}H_{42}O_8$: C, 72.29; H, 6.89. Found: C, 72.45; H, 6.87.

3.3. Determination of degree of enantioselectivity (de) values

Samples (25–30 mg) of products arising from various AD reactions (Table 1) dissolved in methanol (25 mL) were hydrogenated (1 atm) in the presence of palladized charcoal (10%, 8 mg) for 18–20 h. The mixtures were filtered, the inorganic material washed with methanol (2×10 mL) and the combined filtrate and washings concentrated in vacuo. The resultant residues were treated with Ac_2O (1.5 mL) and pyridine (4 mL) in the usual manner and the products obtained after processing were dissolved in CH_2Cl_2 and used directly for analysis (GLC).

3.4. 2(*R*)3-Dibenzyloxypropyl 1′3′4′5′-tetra-*O*-benzyl-β-D-fructopyranoside (4)

A stirred, cooled (0 °C) solution of compound **1** (1.603 g, 2.6 mmol) in Me_2SO (10 mL) was treated sequentially with powdered KOH (437 mg, 7.8 mmol, 3 equiv) and benzyl chloride (0.8 mL, 7.8 mmol, 3 equiv) and set aside at room temperature for 18 h. The mixture was treated with water (20 mL) and ether (70 mL), the separated aqueous layer was extracted with ether (2×15 mL) and the combined organic layers washed with water, dried (Na_2SO_4) and concentrated in vacuo.

Column chromatography (3:1; *n*-hexane–EtOAc) gave compound **4** (1.83 g, 77%) as an oil $[\alpha]_D$ −57.4 ($CHCl_3$). ^1H NMR ($CDCl_3$, 100 MHz): δ 7.44–7.21 (m, 30H, aromatic H), 4.98–4.61 (d, 1H, *J* 11.4 Hz, benzylic H), 4.77, 4.71 (2d, each 1H, *J* 12.8 Hz, benzylic H), 4.68–4.57 (m, 8H, benzylic H), 4.44 (d, 1H, *J* 11.9 Hz, benzylic H), 4.36 (d, 1H, $J_{3,4}$ 10.1 Hz, H-3), 3.93 (dd, 1H, $J_{4,5}$ 3.2 Hz, H-4), 3.85–3.54 (m, 9H, H-1a, H-1b, H′1a, H′1b, H-2′, H-3′, H-5, H-6_{ax}, H-6_{eq}) 1.17 (d, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 Hz): δ 138.50, 138.35, 138.34, 137.71, 128.29, 128.17, 127.85, 127.86, 127.79, 127.68, 127.65, 127.57, 127.53 (aromatic C), 100.95 (C-2), 78.73 (C-3), 76.65 (C-4), 75.52, 73.66 (benzylic C), 70.24 C-1, 68.50 (C-3′) 64.85 (C-1), 61.24 (C-6) ppm.

3.5. 2(*R*),3-Dibenzyloxypropan-1-ol (6)

A stirred solution of compound **4** (1.75 g, 2.21 mmol) in dioxane (41 mL) was treated with 2 M aqueous HCl (2.48 mL), stirred for 8 days at 50 °C and treated with a saturated aqueous sodium hydrogen carbonate solution (50 mL). The mixture was extracted with ether (3 × 50 mL), and the combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and concentrated in vacuo. Column chromatography (dichloromethane–methanol, 200:1) of the resultant material gave compound **5** (511 mg, 61%); $[\alpha]_D$ −32 ($CHCl_3$) (anomeric mixture) as a colourless oil. ^1H NMR ($CDCl_3$ 300 MHz): δ 7.41–7.10 (m, aromatic H), 4.96–4.92 (d, *J* 11.2 Hz), 4.80–4.76 (m), 4.73–4.67 (m), 4.63 (s), 4.59–4.35 (m), 4.06–3.95 (m), 3.93–3.64 (m), 3.53 (d, 1H, *J* 9.9 Hz), 3.50 (d, 1H, *J* 9.9 H), 3.37 (d, 1H, *J* 9.7 Hz) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.35, 138.08, 137.72, 137.63, 128.48, 128.38, 128.36, 128.33, 128.30, 128.14, 128.09, 127.99, 127.93, 127.85, 127.77, 127.70, 127.66, 127.58 (aromatic C), 98.06 (C-2, β-anomer), 97.38 (C-2, α-anomer), 78.87, 75.73, 75.43, 74.41, 74.32, 73.98, 73.78, 73.72, 73.41, 73.16, 72.03, 71.97, 71.62, 71.41, 71.18, 60.08, 57.28 ppm. Further elution gave compound **6** (339 mg, 57%) as a colourless oil. $[\alpha]_D$ +17.9 ($CHCl_3$); lit.[20] $[\alpha]_D$ +15.7 ($CHCl_3$); lit.[29] $[\alpha]_D$ (*S*-enantiomer) −17.2 ($CHCl_3$). ^1H NMR ($CDCl_3$, 100 MHz): δ 7.36–7.24 (m, 10H, aromatic H), 4.66, 4.53 (2s, 4H, benzylic-H), 3.87–3.54 (m, 5H, aliphatic H), 2.26 (br s, 1H, O*H*) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.61, 128.47, 127.94, 127.70, 127.69, 127.64, 127.55, 127.52 (aromatic-C), 72.35, 70.20 (benzylic-C), 65.13, 63.69, 62.65 (C-1, C-2, C-3 glycerol).

3.6. 2(*R*),3-Dihydroxypropyl 1′3′4′-5′-tetra-*O*-benzyl-β-D-fructopyranoside 2,3-di-dodecanoate [2(*R*),3-didodecanoyloxypropyl 1′3′4′5′-tetra-*O*-benzyl-β-D-fructopyranoside] (7)

A stirred, cooled (0 °C), solution of **1** (345 mg, 0.56 mmol) in dry pyridine (5 mL) was treated gradually with a solution of dodecanoyl chloride (0.38 mL, 1.68 mmol, 3 equiv) in dichloroethane (10 mL) and then maintained at room temperature for a further 2 h.

The mixture was treated with ice-water (15 mL), diluted with more CH_2Cl_2 (20 mL) and the separated organic layer washed successively with 2 M aqueous hydrochloric acid (20 mL), saturated aqueous sodium hydrogencarbonate (20 mL), water (20 mL), dried (Na_2SO_4) and concentrated in vacuo. Column chromatography (hexane–ethyl acetate, 9:1) of the residue gave **7** (501 mg, 91%) as a pure colourless oil, $[\alpha]_D$ −35 ($CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40–7.19 (m, 20H, aromatic H), 5.21 (m, 1H, H-2′), 4.92, 4.62 (2d, each 1H, *J* 11.4 Hz, benzylic-H), 4.77, 4.71 (2d, each 1H, *J* 12.7 Hz, benzylic-H), 4.64, 4.43 (2d, each 1H, *J* 11.9 Hz, benzylic-H), 4.60, 4.58 (2d, each 1H, *J* 11.6 Hz, benzylic-H), 4.32 (d, 1H, *J* 10.0 Hz, H-3), 4.10 (d, 1H, *J* 6.2 Hz, H-1a′), 4.0 (d, 1H, *J* 6.2 Hz, H-1b′), 3.95 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.1 Hz, H-4), 3.88 (dd, 1H, $J_{5,6eq}$ 1.6 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6eq), 3.84 (dd, 1H, $J_{5,6ax}$ 1.5 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6ax), 3.77 (m, 1H, H-5), 3.75 (d, 1H, *J* −10.2 Hz, H-1a), 3.64 (dd, 1H, $J_{3'a,2'}$ 6.5 Hz, H-3′a), 3.62 (d, 1H, *J* −10.2 Hz, H-1b), 3.58 (d, 1H, $J_{3'b,2'}$ 6.5, H-3′b), 2.3–2.2 (m, 4H, COCH_2), 1.60–1.54 (m, 4H, $CH_2CH_2CH_3$), 1.25 (m, 32H, aliphatic H) and 0.87 (2 × t, 6H, *J* 6.8 Hz 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.30, 172.93 (*C*=O), 139.02, 138.52, 138.43, 137.86, 128.22, 128.03, 127.67, 127.51, 127.41, 127.11 (aromatic-C), 101.65 (C-2), 78.44 (C-3) 76.99 (C-4), 74.96, 73.68 (benzylic-C), 73.54 (C-5), 72.28, 71.23 (benzylic-C), 70.00 (C-1), 69.92 (C-2′), 62.44 (C-1′), 61.31 (C-6), 59.86 (C-3′), 34.21 (CO*C*H_2), 34.06 (CO*C*H_2), 31.86–22.64 (aliphatic C) and 14.08 (*C*H_3) ppm.

3.7. 2(*R*),3-Dihydroxypropyl 1′3′4′5′-tetra-*O*-benzyl-β-D-fructopyranoside 2,3-ditetradecanoate [2(*R*),3-(di-tetradecanoyloxy)propyl 1′3′4′5′-tetra-*O*-benzyl-β-D-fructopyranoside] (8)

Compound **1** (205 mg, 0.33 mmol) was treated with tetradecanoyl chloride (0.22 mL, 0.999 mmol, 3 equiv) as described above to yield **8** (257 mg, 75%), $[\alpha]_D$ −28 ($CHCl_3$) as a colourless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.53–7.19 (m, 20H, aromatic H), 5.21 (m, 1H, H-2′), 4.91, 4.61 (2d, each 1H, *J* 11.5 Hz, benzylic-H), 4.76, 4.73 (2d, each 1H, *J* 12.7 Hz, benzylic-H), 4.64, 4.43 (2d, each 1H, *J* 11.9 Hz, benzylic-H), 4.60, 4.58 (2d, each 1H, *J* 11.6 Hz, benzylic-H), 4.30 (d, 1H, *J* 10.0 Hz, H-3), 4.10 (d, 1H, *J* 6.2 Hz, 1a′), 4.00 (d, 1H, *J* 6.2 Hz, H-1b′), 3.94 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.1 Hz, H-4), 3.88 (dd, 1H, $J_{5,6eq}$ 1.7 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6eq), 3.84 (dd, 1H, $J_{5,6ax}$ 1.6 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6ax), 3.77 (m, 1H, H-5), 3.75 (d, 1H, *J* −10.2 Hz, H-1a), 3.62 (d, 1H, *J* −10.2 Hz, H-1b), 3.64 (d, 1H, $J_{3'a,2'}$ 6.5 Hz, H-3′a), 3.58 (d, 1H, $J_{3'b,2'}$ 6.5 Hz,

H-3′b), 2.3–2.2 (m, 4H, $COCH_2$), 1.62–1.53 (m, 4H, $CH_2CH_2CH_3$), 1.25 (m, 40H, aliphatic H) and 0.87 (2 × t, 6H, *J* 6.8 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.35, 172.96 (*C*=O), 139.07, 138.57, 138.49, 137.91, 128.26, 128.07, 127.74, 127.69, 127.55, 127.50, 127.45, 127.15 (aromatic-C), 101.69 (C-2), 78.49 (C-3), 76.58 (C-4), 74.99, 73.77 (benzylic-C), 73.59 (C-5), 72.33, 71.29 (benzylic-C), 70.13 (C-1), 69.97 (C-2′), 62.49 (C-1′), 61.37 (C-6), 59.92 (C-3′), 34.25, 34.10 ($COCH_2$), 31.89–22.70 (aliphatic C) and 14.10 (CH_3) ppm.

3.8. 2(*R*),3-Dihydroxypropyl 1′,3′,4′,5′-tetra-*O*-benzyl-β-D-fructopyranoside, 2,3-dihexadecanoate [2(*R*),3-dihexadecanoyloxypropyl 1′,3′,4′,5′-tetra-*O*-benzyl-β-D-fructopyranoside] (9)

Treatment of compound **1** (182 mg, 0.296 mmol) with hexadecanoylchloride (0.20 mL, 0.888 mmol, 3 equiv) as described above yielded compound **9** (255 mg, 79%), $[\alpha]_D$ −33.2 ($CHCl_3$) as a pure colourless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40–7.21 (m, 20H, aromatic H), 5.28 (m, 1H, H-2′), 4.91, 4.61 (2d, each 1H, *J* 11.5 Hz, benzylic-H), 4.76, 4.73 (2d, each 1H, *J* 12.7 Hz, benzylic-H), 4.64, 4.43 (2d, each 1H, *J* 11.9 Hz, benzylic H), 4.60, 4.58 (2d, each 1H, *J* 11.6 Hz, benzylic-H), 4.31 (d, 1H, *J* 10.0 Hz, H-3), 4.10 (d, 1H, *J* 6.2 Hz, H-1a′), 4.00 (d, 1H, 6.2 Hz, H-1b′), 3.94 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.1 Hz, H-4), 3.87 (dd, 1H, $J_{5,6eq}$ 1.7 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6eq), 3.83 (dd, 1H, $J_{5,6ax}$ 1.6 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6ax), 3.77 (m, 1H, H-5), 3.75 (d, 1H, *J* −10.2 Hz, H-1a), 3.64 (d, 1H, $J_{3'a,2'}$ 6.5 Hz, H-3′a), 3.62 (d, 1H, *J* −10.2 Hz, H-1b), 3.58 (d, 1H, $J_{3'b,2'}$ 6.5 Hz, H-3′b), 2.3–2.2 (m, 4H, $COCH_2$), 1.60–1.53 (m, 4H, $CH_2CH_2CH_3$), 1.25 (m, 48H, aliphatic H) and 0.87 (2 × t, 6H, *J* 6.8 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.32, 172.95 (*C*=O), 139.07, 138.57, 138.48, 137.90, 128.25, 128.06, 127.73, 127.69, 127.54, 127.49, 127.44, 127.14 (aromatic-C), 101.69 (C-2), 78.48 (C-3), 76.57 (C-4), 74.98, 73.77 (benzylic-C), 73.58 (C-5), 72.32, 71.29 (benzylic-C), 70.12 (C-1), 69.96 (C-2′), 62.48 (C-1′), 61.37 (C-6), 59.91 (C-3′), 34.24, 34.10 ($COCH_2$), 31.90–22.68 (aliphatic C) and 14.10 (CH_3) ppm.

3.9. 2(*R*),3-Di-dodecanoyloxypropyl β-D-fructopyranoside (10)

A solution of compound **7** (253 mg, 0.258 mmol) in methanol (30 mL) was treated with palladized charcoal (10%, 60 mg) and then hydrogenated (1 atm) at room temperature for 2 h. The mixture was filtered through a layer of Celite, the inorganic material washed with methanol (10 mL) and the combined filtrate and washings concentrated in vacuo. The crystalline material was recrystallized (ether–EtOH) to give **10** (836 mg, 50%), mp 110–112 °C. $[\alpha]_D$ −48 (DMF). MS (FAB-Na^+) *m*/*z* 641 $(M+Na)^+$, 458 $(M+Na-COC_{11}H_{23})^+$, 257 $(M+Na-2\times COC_{11}H_{23}, -H_2O)^+$. ^1H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 5.20 (m, 1H, H-2′), 4.40 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.6 Hz, H-4), 4.18 (d, 1H, *J* 6.6 Hz, H-1a′), 4.16 (d, 1H, *J* 6.6 Hz, H-1b′), 3.90 (d, 1H, *J* 9.8 Hz, H-3), 3.80–3.68 (m, 7H, H-1, H-3′, H-5, H-6), 2.3–2.2 (m, 4H, $COCH_2$), 1.58 (m, 4H, $CH_2CH_2CH_3$), 1.26 (m, 32H, aliphatic H) and 0.87 (2 × t, 6H, *J* 6.8 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$+CD_3OD, 75 MHz): δ 173.79, 173.25 (*C*=O), 100.12 (C-2), 70.20 (C-3), 70.03 (C-4), 69.95 (C-5), 69.11 (C-2′), 63.64 (C-1), 62.43 (C-6), 62.29 (C-1′), 59.54 (C-3′), 34.12, 33.96 (–$COCH_2$), 31.73–22.49 (aliphatic C) and 13.87 (CH_3) ppm. Anal. Calcd for $C_{33}H_{62}O_{10}$: C, 64.05; H, 10.10. Found: C, 64.40; H, 9.83.

3.10. 2(*R*),3-Di-tetradecanoyloxypropyl β-D-fructopyranoside (11)

Hydrogenolysis of **8** (836 mg, 0.81 mmol) as described above gave compound **11** (316 mg, 58%), mp 116 °C (ether–EtOH), $[\alpha]_D$ −45.4 (DMF). MS (FAB-Na^+) *m*/*z* 697 $(M+Na)^+$, 514 $(M+Na-C_{13}H_{27})^+$, 285 $(M+Na-C_{13}H_{27}, -COC_{13}H_{27}, -H_2O)^+$. ^1H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 5.22 (m, 1H, H-2′), 4.41 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.6 Hz, H-4), 4.20 (d, 1H, *J* 6.6 Hz, H-1a′), 4.18 (d, 1H, *J* 6.6 Hz, H-1b′), 3.92 (d, 1H, *J* 9.8 Hz, H-3), 3.80–3.68 (m, 7H, H-1, H-3′, H-5, H-6), 2.3–2.2 (m, 4H, $COCH_2$), 1.58 (m, 4H, $CH_2CH_2CH_3$), 1.26 (m, 40H, aliphatic H) and 0.87 (2 × t, 6H, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$+CD_3OD, 75 MHz): δ 173.69, 173.15 (*C*=O), 100.11 (C-2), 70.19 (C-3), 70.13 (C-4), 69.98 (C-5), 69.11 (C-2′), 63.62 (C-1), 62.39 (C-6), 62.25 (C-1′), 59.52 (C-3′), 34.12, 33.90 (–$COCH_2$), 31.73–22.49 (aliphatic C) and 13.87 (CH_3) ppm. Anal. Calcd for $C_{37}H_{70}O_{10}$: C, 65.84; H, 10.45. Found: C, 65.87; H, 10.57.

3.11. 2(*R*),3-Di-hexadecanoyloxypropyl β-D-fructopyranoside (12)

Treatment of compound **9** (200 mg, 0.183 mmol) in the same above manner yielded **12** (63 mg, 54%), mp 120 °C (ether–EtOH), $[\alpha]_D$ +44.4 (DMF). MS (FAB-Na^+) *m*/*z* 752 $(M+Na)^+$, 330 $(M+Na-2\times C_{15}H_{31})^+$, 312 $(M+Na-2\times C_{15}H_{31}-H_2O)^+$. ^1H NMR ($CDCl_3$+CD_3OD, 400 MHz): δ 5.23 (m, 1H, H-2′), 4.42 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.6 Hz, H-4), 4.22 (d, 1H, *J* 6.6 Hz, H-1a′), 4.19 (d, 1H, *J* 6.6 Hz, H-1b′), 3.94 (d, 1H, *J* 9.8 Hz, H-3), 3.80–3.68 (m, 7H, H-1, H-3′, H-5, H-6), 2.3–2.2 (m, 4H, $COCH_2$), 1.58 (m, 4H, $CH_2CH_2CH_3$), 1.26 (m, 48H, aliphatic H), 0.87 (2 × t, 6H, *J* 6.8 Hz, 2 × CH_3) ppm. ^{13}C NMR ($CDCl_3$+CD_3OD, 75 MHz): δ 173.76, 173.34 (*C*=O), 100.13 (C-2), 70.18 (C-3),

70.12 (C-4), 69.97 (C-5), 69.11 (C-2′), 63.63 (C-1), 62.38 (C-6), 62.24 (C-1′), 59.53 (C-3′), 34.12, 33.90 (–CO*C*H$_2$), 31.73–22.49 (aliphatic C) and 13.87 (*C*H$_3$) ppm. Anal. Calcd for $C_{39}H_{74}O_{10}$: C, 65.86; H, 10.44. Found: C, 65.89; H, 10.54.

3.12. But-2-enyl β-D-fructopyranoside (14)

D-Fructose (10.0 g, 55.55 mmol) was added to a stirred mixture of crotyl alcohol (cis/trans, 1:19; 50 mL) and acetyl chloride (1.5 mL) and then set aside at room temperature for 48 h. The crystalline material was collected by filtration, washed with ethanol (20 mL) and ether (20 mL) and recrystallized from ethanol containing a few drops of concd aqueous ammonia solution (25%) to give **14** (8.56 g, 66%), mp 179–180 °C, $[\alpha]_D$ −148 (MeOH), MS (FAB-Na$^+$) *m*/*z* 257 (M+Na)$^+$. ^{1}H NMR (D$_2$O, 300 MHz): δ 4.0–3.90 (m, 3H, H-2′, H-3′, H-3), 3.89–3.84 (m, 2H, H-4, H-5), 3.79–3.65 (m, 6H, H-1, H-1′, H-6), 1.62 (d, 3H, $J_{3',4'}$ 6.4 Hz, CH$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ 131.72 (–OCH$_2$*C*H=CH$_2$CH$_3$), 127.83 (–OCH$_2$CH=*C*H$_2$CH$_3$), 102.06 (C-2), 70.85 (C-3), 70.37 (C-4), 69.4 (C-5), 65.17 (C-1), 63.00 (C-1′), 62.57 (C-6) and 18.28 (*C*H$_3$) ppm. Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.27; H, 7.75. Found: C, 50.95; H, 7.68.

3.13. *n*-Butyl β-D-fructopyranoside (15)

A solution of compound **14** (500 mg, 2.14 mmol) in water (30 mL) containing one drop of Et$_3$N was treated with palladized charcoal (5%, 80 mg) and hydrogenated (1 atm) at rt for 6 h. The inorganic material was removed by filtration through a thin layer of Celite, washed with water (20 mL) and the combined filtrate and washings were concentrated in vacuo to give **15** (450 mg, 89%), mp 156–158 °C (ethanol), $[\alpha]_D$ −146 (MeOH); lit.[21] mp 156–158 °C, $[\alpha]_D$ −145 (MeOH).

3.14. But-2-enyl 1,3,4,5-tetra-*O*-benzyl-β-D-fructopyranoside (13)

A cooled (0 °C), stirred mixture of compound **14** (5.0 g, 21.4 mmol) and finely powdered potassium hydroxide (5.98 g, 107 mmol, 5 equiv) in Me$_2$SO (25 mL) was treated with benzyl chloride (12.2 mL, 107 mmol, 5 equiv) and the mixture set aside at room temperature for ca. 24 h. The mixture was treated with ether (100 mL) and water (40 mL). The aqueous layer was extracted with ether (50 mL) and the organic layers washed with satd aqueous sodium chloride solution (3 × 20 mL), dried (Na$_2$SO$_4$) and concentrated in vacuo. Column chromatography (hexane–ethyl acetate, 3:1) of the resultant material gave compound **13** (11.2 g, 88.5%) as a colourless oil, $[\alpha]_D$ −50.5 (CHCl$_3$). ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.42–7.21 (m, 20H, aromatic H), 5.68–5.47 (m, 2H, H-2′, H-3′), 4.93, 4.62 (2d, each 1H, *J* 11.3 Hz, benzylic-H), 4.77, 4.74 (2d, each 1H, *J* 12.6 Hz, benzylic-H), 4.68, 4.40 (2d, each 1H, *J* 11.9 Hz, benzylic-H), 4.63–4.60 (m, 2H, benzylic-H), 4.36 (d, 1H, H-3), 4.00–3.93 (m, 3H, H-1′a, H-1′b, H-4), 3.87 (dd, 1H, $J_{5,6eq}$ 1.8 Hz, $J_{6ax,6eq}$ −11.9 Hz, H-6eq), 3.83 (m, 1H, H-5), 3.77 (d, 1H, *J* −10.1 Hz, H-1a), 3.62 (d, 1H, *J* −10.1 Hz, H-1b), 3.55 (dd, 1H, $J_{5,6ax}$ 1.4 Hz, $J_{6ax,6eq}$ −11.9 Hz, 6ax), 1.65 (d, 3H, $J_{3',4'}$ 6.4 Hz, CH$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ 138.91, 138.72, 138.55, 138.01, 128.20, 128.14, 128.00, 127.95, 127.68, 127.67, 127.57, 127.35, 127.21 (aromatic-C), 131.82 (OCH$_2$*C*H=CH$_2$CH$_3$), 127.88 (OCH$_2$CH=*C*H$_2$CH$_3$), 101.79 (C-2), 78.87 (C-3), 76.25 (C-4), 75.49 (benzylic-C), 73.66 (C-5), 73.43, 72.19, 71.07 (benzylic-C), 70.23 (C-1), 62.00 (C-1′), 61.05 (C-6), and 17.68 (*C*H$_3$) ppm.

3.15. 2(*R*),3(*R*)-Dihydroxybutyl 1′,3′,4′,5′-tetra-*O*-benzyl-β-D-fructopyranoside (16)

A mixture of potassium osmate dihydrate (14.49 mg), K$_2$CO$_3$ (4.04 g), K$_3$Fe(CN)$_6$ (9.75 g), methanesulfonamide (941.3 mg) and (DHQD)$_2$PHAL (77 mg) in water (50 mL) was added gradually to a stirred solution of compound **13** (5.9 g, 9.9 mmol) in 2-methyl-propan-2-ol (50 mL). The mixture was stirred vigorously at room temperature for 4 h, quenched by the addition of Na$_2$SO$_3$ (15 g), stirred for a further 1 h and then treated with ether (100 mL) and water (60 mL). The separated aqueous phase was extracted with ether (2 × 50 mL) and the combined organic layers were washed sequentially with saturated aqueous sodium chloride, aqueous 2 M KOH solution, dried (MgSO$_4$) and concentrated in vacuo. Recrystallization (isopropylether) of the crystalline residue gave compound **16** (5.1 g, 82%), mp 134–135 °C, $[\alpha]_D$ −52.5 (CHCl$_3$). ^{1}H NMR (CDCl$_3$, 300 MHz): δ 7.40–7.20 (m, 20H, aromatic H), 4.90, 4.60 (2d, each 1H, *J* 11.0 Hz, benzylic-H), 4.73, 4.65 (2d, each 1H, *J* 12.6 Hz, benzylic-H), 4.62, 4.44 (2d, each 1H, *J* 11.9 Hz, benzylic-H), 4.30 (d, 1H, *J* 9.9 Hz, H-3), 4.04–3.97 (m, 2H, benzylic-H), 3.89 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.2 Hz, H-4), 3.88 (dd, 1H, $J_{5,6eq}$ 1.8 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6eq), 3.85 (dd, 1H, $J_{5,6ax}$ 1.6 Hz, $J_{6ax,6eq}$ −12.3 Hz, H-6ax), 3.80 (m, 1H, H-2′), 3.78 (m, 1H, H-5) 3.76 (d, 1H, *J* −10.2 Hz, H-1a), 3.65 (d, 1H, *J* −10.2 Hz, H-1b), 3.62–3.37 (m, 3H, H-1′a, H-1′b, H-3′), 2.97, 1.82 (2 × br s, 2H, OH), 1.17 (d, 3H, $J_{3',4'}$ 6.4 Hz, C*H*$_3$) ppm. ^{13}C NMR (CDCl$_3$, 75 MHz): δ 138.51, 138.37, 138.33, 137.70, 128.31, 128.19, 127.87, 127.85, 127.76, 127.67, 127.64, 127.55, 127.53, 127.46 (aromatic-C), 100.97 (C-2), 78.75 (C-3), 76.66 (C-4), 75.50, 73.64 (benzylic-C), 73.30 (C-5), 73.13 (C-2′), 72.19, 71.24 (benzylic-C), 70.26 (C-1′), 68.51 (C-3′), 64.87 (C-1), 61.21 (C-6), 19.58 (*C*H$_3$) ppm. Anal. Calcd

for $C_{38}H_{44}O_8$: C, 72.59; H, 7.05. Found: C, 72.47; H, 7.06.

In another experiment compound **13** (2.95 g, 4.95 mmol) was treated as above but in the presence of $(DHQ)_2PHAL$ (38.5 mg) to yield compound **16** (2.74 g, 88%) with the same physical and spectral constants as reported above.

3.16. 2(*R*),3(*R*)-Dibenzyloxybutyl 1′,3′,4′,5′-tetra-*O*-benzyl-β-D-fructopyranoside (17)

A stirred mixture of compound **16** (1.0 g, 1.59 mmol) and finely powdered KOH (178 mg, 3.18 mmol, 2 equiv) in Me_2SO (10 mL) was treated with benzyl chloride (0.35 mL, 3.18 mmol, 2 equiv) as described above to give compound **17** (1.1 g, 87%) as a colourless oil, $[\alpha]_D$ −58.4 ($CHCl_3$), after column chromatography (hexane–ethyl acetate, 3:1). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43–7.20 (m, 30H, aromatic H), 4.98 (d, 1H, J 11.4 Hz, benzylic-H), 4.77, 4.72 (2d, 2H, J 12.8 Hz, benzylic-H), 4.68–4.56 (m, 8H, benzylic-H), 4.45 (1d, 1H, J 11.9 Hz, benzylic-H), 4.35 (d, 1H, J 10.1 Hz, H-3), 3.96 (dd, 1H, $J_{3,4}$, $J_{4,5}$ 3.2 Hz, H-4), 3.85–3.53 (m, 9H, H-1a, H-1b, H-1′a, H-1′b, H-2′, H-3′, H-5, H-6eq, H-6ax), 1.18 (d, 3H, $J_{3',4'}$ 6.4 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.51, 138.37, 138.33, 137.70, 128.31, 128.19, 127.87, 127.85, 127.76, 127.67, 127.64, 127.55, 127.53, 127.46 (aromatic-C), 100.97 (C-2), 78.75 (C-3), 76.66 (C-4), 75.50, 73.64 (benzylic-C), 73.30 (C-5), 73.13 (C-2′), 72.6, 72.9, 72.19, 71.24 (benzylic-C), 70.26 (C-1′), 68.51 (C-3′), 64.87 (C-1), 61.21 (C-6), 19.58 (CH_3) ppm.

3.17. 1-Deoxy-D-threitol 2,3,4 tris-*p*-nitrobenzoate (19)

A stirred solution of compound **17** (1.0 g, 1.24 mmol) in aqueous trifluoroacetic acid (90%, 5 mL) was maintained at rt for 10 min. and then concentrated in vacuo. Column chromatography (hexane–ethyl acetate, 9:2) of the resultant material gave compound **18** (259 mg, 73%), which was not characterized but dissolved in MeOH (40 mL), treated with palladized charcoal (10%, 60 mg) and hydrogenated at rt for 3 h. The inorganic material was removed by filtration through Celite, washed with MeOH (2 × 20 mL) and the combined filtrate and washings concentrated in vacuo. A stirred, cooled (0 °C) solution of the residue (89 mg) in pyridine (5 mL) was treated with *p*-nitrobenzoyl chloride (662.5 mg, 3.35 mmol) and then set aside at rt for 3 days. The mixture was concentrated in vacuo and the material obtained crystallized from $CHCl_3$–MeOH to give **19** (236 mg, 52%) as pale yellow crystals, mp 130–131 °C, $[\alpha]_D$ −9.0 ($CHCl_3$); lit.[26,27] mp 129–131 °C, $[\alpha]_D$ −9.05 ($CHCl_3$). {cf. lit.[28] (*erythro* isomer) mp 159–160 °C, $[\alpha]_D$ +8.1 ($CHCl_3$)}. Anal. Calcd for $C_{25}H_{19}O_{12}N_3$: C, 54.26; H, 3.46; N, 7.59. Found: C, 54.33; H, 3.29; N, 7.54.

References

1. van Hummel, H. C. *Fortsch. Org. Naturst.* **1975**, *32*, 267–295.
2. Ishizuka, I.; Yamakawa, T. In *New Comprehensive Biochemistry*; Neuberger, A., van Deenen, L. L. M., Weigandt, H., Eds.; Elsevier: Amsterdam, 1985; Vol. 10, pp 101–198.
3. Curafalo, W. *Biochem. Biophys. Acta* **1987**, *906*, 111–160.
4. Koynova, R. D.; Tenchov, B. G.; Kuttenreich, H.; Hinz, H. J. *Biochemistry* **1993**, *32*, 12437–12445, and references cited therein.
5. Sakata, K.; Ina, K. *Agric. Biol. Chem.* **1990**, *47*, 2957–2960.
6. Shirahashi, H.; Murakami, N.; Watanabe, M.; Nagatsu, A.; Sakakibara, J.; Tokuda, H.; Nishino, H.; Iwashima, A. *Chem. Pharm. Bull.* **1993**, *41*, 1664–1666.
7. Nagatsu, A.; Watanabe, M.; Ikemoto, K.; Hashimoto, M.; Murakami, N.; Sakakibara, J.; Tokuda, H.; Nishino, H.; Iwashima, A.; Yazawa, K. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1619–1622.
8. Erbert, K. H.; Stricker, H. Z. *Z. Naturforsch.* **1994**, *196*, 211–221.
9. van der Heijden, A. M.; van Rantwijk, F.; van Bekkum, H. *J. Carbohydr. Chem.* **1999**, *18*, 131–147.
10. Gonzalez-Muñoz, F.; Pérez-Oseguera, A.; Cassani, J.; Jiménez-Estrada, M.; Vazquez-Duhalt, R.; Lopéz-Munguia, A. *J. Carbohydr. Chem.* **1999**, *18*, 275–283.
11. Verstraeten, L. J. M. *Adv. Carbohydr. Chem. Biochem.* **1967**, *22*, 229–305.
12. Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; pp 227–272.
13. Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547, and references cited therein.
14. Raaijmakers, H. W. C.; Arnouts, E. G.; Zwanenburg, B.; Chittenden, G. J. F. *Carbohydr. Res.* **1994**, *257*, 293–297.
15. Gurjar, M. K.; Mainkar, A. S. *Tetrahedron: Asymmetry* **1992**, *3*, 21–24.
16. Peci, L. M.; Stick, R. V.; Tilbrook, D. M. G.; Winslade, M. L. *Aust. J. Chem.* **1997**, *50*, 1105–1107.
17. Fairweather, J. K.; Stick, R. V.; Tilbrook, D. W. G. *Aust. J. Chem.* **1998**, *51*, 471–478.
18. Moitessier, N.; Maigret, B.; Chrétien, F.; Chapleur, Y. *Eur. J. Org. Chem.* **2000**, 995–1006.
19. Suhr, R.; Scheel, O.; Thiem, J. J. *Carbohydr. Chem.* **1998**, *17*, 937–968.
20. Crispino, G. A.; Jeong, K.-S.; Kolb, H. C.; Wang, Z.-M.; Xu, D.; Sharpless, K. B. *J. Org. Chem.* **1993**, *58*, 3785–3786.
21. Cardillo, G.; Orena, M.; Romero, M.; Sandri, S. *Tetrahedron* **1989**, *45*, 1501–1508.
22. Raaijmakers, H. W. C.; Eveleens, S. M.; Arnouts, E. G.; Zwanenburg, B.; Chittenden, G. J. F. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 511–514.
23. Gobel, T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329–1331.
24. Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H. L.;

Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768–2771.
25. Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568–7570.
26. Charby, R.; Szabo, L. *Tetrahedron* **1971**, *27*, 3197–3205.
27. Saegebarth, K. A. *J. Org. Chem.* **1959**, *24*, 1212–1214.
28. Bebault, G. M.; Dutton, G. G. S. *Can. J. Chem.* **1972**, *50*, 3373–3374.
29. van Boeckel, C. A. A.; Visser, G. M.; van Boom, J. H. *Tetrahedron* **1985**, *41*, 4557–4565.