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D-Fructose- and L-sorbose-derived *endo*- and *exo*-hydroxyglycal esters and some of their chemistry☆

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Dedicated to Professor Karsten Krohn on the occasion of his 60th birthday

Abstract—Dehydrobrominations of benzoylated β-D-fructopyranosyl and α-L-sorbo-pyranosyl bromides have been examined to obtain suitable conditions for effecting the elimination toward the *exo*- as well as the *endo*-positions. In the fructose case, exposure to DBU in acetonitrile generates the *exo*-hydroxyfructal ester (81%) while refluxing in xylene gives the *endo* analog (53%). In the L-sorbose case, the regioselectivities are the inverse. Simple reactions of *exo*- and *endo*-products provide a series of highly versatile enantiopure six-carbon building blocks, together with a crystalline derivative of the fungal metabolite microthecin.

1. Introduction

2-Hydroxyglycal esters, first encountered by Maurer and Mahn in 1927,[2] have become exceedingly well accessible as the three steps required from a basic sugar—acylation, anomeric halogenation, and amine-promoted dehydrohalogenation—can be combined into a continuous one-pot operation allowing overall yields in the 70–80% range.[3,4] Their basic chemistry has already been reviewed 50 years ago,[5] yet the vast potential toward the generation of enantiomerically pure five- or six-carbon building blocks has only been exploited within the last 20 years.[1,6] These recent developments are illustrated in Scheme 1 with the ensuing reactions of the D-glucose-derived perbenzoyl-1-deoxy-D-*arabino*-hex-1-enitol **1**: BF_3-catalyzed peracid oxidation effectively elicits conversion into enol lactone **2**,[7] due to elimination of the allylic benzoyloxy group, the seizure of the pyranoid allyloxonium ion by the peracid at the anomeric carbon, and the fragmentation of the perester. Acid-induced addition of an alcohol smoothly affords 2,3-unsaturated glycosides, for example, **3**.[3b] Exposure to NBS/methanol efficiently elaborates the 2-ketohexosyl bromide **4**,[8] a most useful glycosyl donor for the indirect generation of β-D-mannosidic linkages, since its glycosidation exclusively yields β-D-glycosiduloses[8,9] while the subsequent hydride reduction can be performed in an essentially *manno*-specific manner.[9] This preparatively expedient sequence **1** → **4** → **5** constitutes as the essence of the 'ulosyl donor approach' to β-D-mannosides,[6c,10–13] which has been carried to the hexasaccharide level[14] and also applied to the acquisition of *C*-glycosides.[15] Treatment with hydroxylamine in pyridine exclusively cleaves the enol ester linkage to provide oxime **6**,[16] opening up, via deoximation, a simple access to 1,5-anhydro-D-fructose tribenzoate **7**, and, through acetate-induced β-elimination of benzoic acid, to dihydropyranone **8**[16]—a most useful enantiopure building block, as it has enabled straightforward syntheses of the marine natural products (*S*,*S*)-palythazin[17] and (*S*,*S*)-bissetone.[18] Of similar preparative versatility are the readily accessible six-carbon synthons **9**,[19] **10** (this paper), and **11**,[20] in which a useful functionality on one side of the pyranoid ring is paired with chirality on the other, so that addition reactions proceed with high stereoselectivity.[6b,21]

In view of the wealth of synthetic uses that have been found for D-glucose-based hydroxyglycal esters of type **1**, it is somewhat surprising that not more attention

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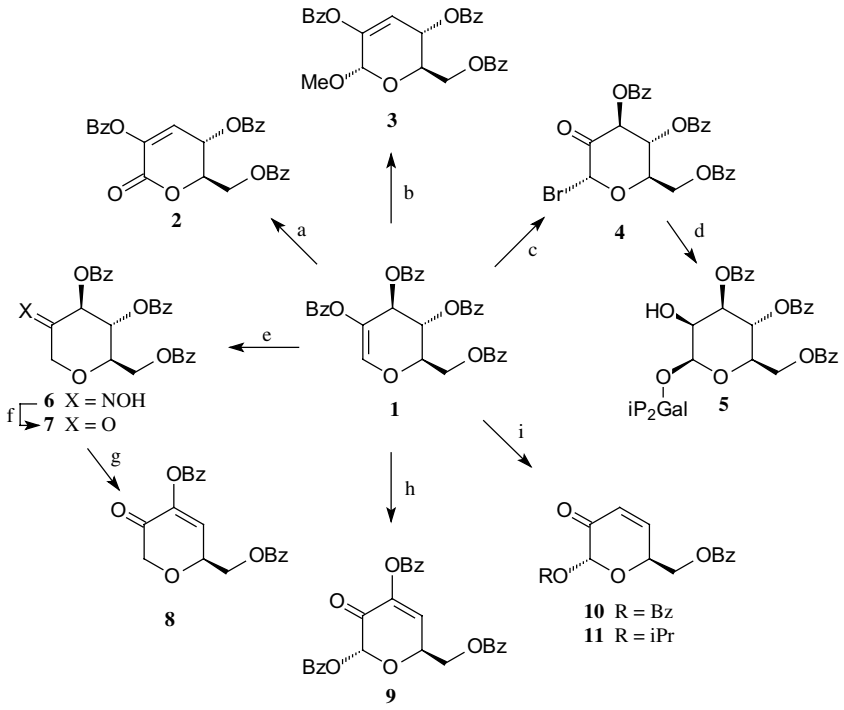


Scheme 1. Reagents and yields: (a) 3-$ClC_6H_4CO_3H$, BF_3, 91%;[7] (b) MeOH, BF_3, 72%;[3b] (c) NBS, MeOH, 89%;[8] (d) *i*P_2Gal, Ag_2CO_3, then L-selectride, 79%;[9] (e) NH_2OH, pyridine, 93%;[16] (f) CH_3CHO, HCl, 88%;[16] (g) NaOAc, acetone, 92%;[16] (h) Cl_2 in toluene, −30 °C, then aq $NaHCO_3$, 65%;[19] (i) **10**: $BF_3{\cdot}OEt_2$, CH_2Cl_2, 62% (see Experimental); **11**: *i*PrOH, $SnCl_4$, 42%.[20]

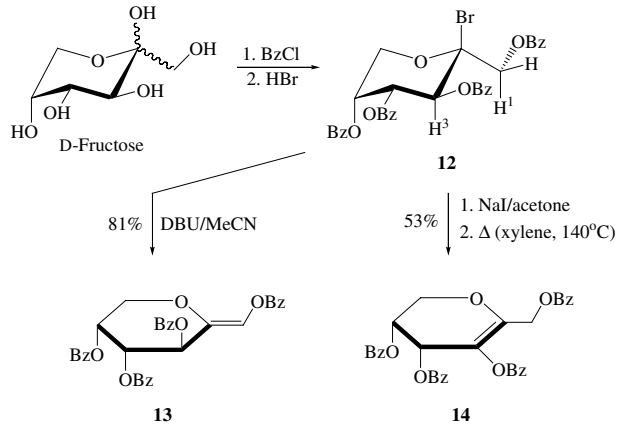
has been paid to the analogs derived from well-accessible ketoses such as D-fructose and L-sorbose. The reasons undoubtedly lie in their hitherto insufficient preparative accessibility. L-Sorbose-derived *endo*-3-hydroxyglycals have been encountered as side products in the synthesis of L-sorbosyl-nucleosides,[22–24] acetylated *exo*-analogs on thermolysis of D-fructose and L-sorbose peracetates in yields of 1–15%.[25] As a consequence, we herein report the development of viable procedures for the acquisition of D-fructose-derived *exo*- **13** and *endo*-hydroxyglycal esters **14**, their preparatively adequate generation and the first evaluation of their chemistry.

2. Results and discussion

2.1. *exo*- and *endo*-3-Hydroxyfructal esters

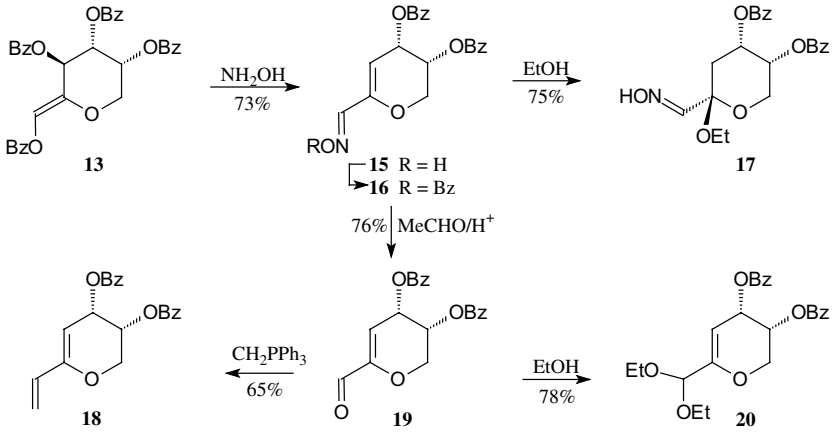
Dehydrohalogenation of benzobromofructose **12**, readily prepared from the parent ketose in a two-step one-pot procedure,[26] may proceed either toward the *exo*- or *endo*-product, depending on whether abstraction of an exocyclic or a pyranoid ring hydrogen is involved. Thus, conditions had to be found that steer the elimination exclusively or at least with high regioselectivity in one or the other direction.

Exposure of **12** to DBU in acetonitrile at ambient temperature smoothly effected the elaboration of a single product, isolable in 81% yield, which proved to be the *Z*-*exo*-hydroxyfructal ester **13**. The *Z*-configuration at its double bond followed from the comparatively high field signals for C-1 and C-2 (136.0 and 123.8 ppm), which correlate well with the data found for the respective acetylated analog previously obtained in low yield on thermolysis of fructopyranose pentaacetate, whilst corresponding signals for the *E*-isomer appeared at distinctly lower field.[25] Thus, the base-induced elimination of HBr in **12** exclusively occurs from a conformation in which *O*-1 and the ring oxygen are in a *gauche* disposition, utilizing the exocyclic hydrogen *anti* to the bromine rather than the neighboring, equally *anti*-disposed ring proton (Scheme 2).



Scheme 2. Preparation of *exo*- and *endo*-hydroxyfructal esters.

As the amine-induced dehydrobromination of **12** exclusively elaborated the *exo*-product, the generation of the *endo*-hydroxyfructal ester **14** required basically different conditions. Refluxing of **12** or the respective chloride[27] with mercuric cyanide in benzene[24] or xylene (140 °C)



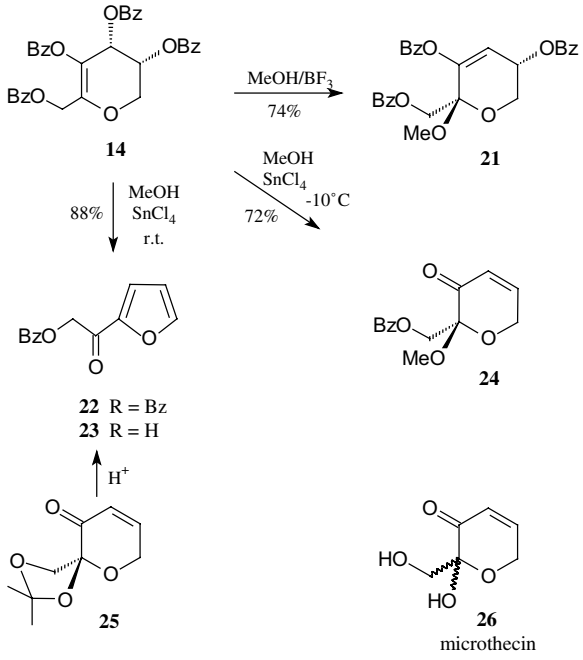
Scheme 3. Versatile enantiopure six-carbon building blocks from *exo*-hydroxyfructal ester **13**.

invariably resulted in 1:1 to 2:1 mixtures of *endo*- **14** and *exo*- **13** products (^{1}H NMR), from which the former could be isolated in yields of up to 35% only. After extensive experimentation, optimum conditions were found in refluxing the respective iodide, generated in situ from bromide **12**, for 4 h in xylene, that is, without $Hg(CN)_2$. The 5:1 *endo*/*exo* mixture (^{1}H NMR) thus obtained allowed the isolation of the *endo*-product, dihydropyran **14**, in 53% yield.

With the *exo*- and *endo*-hydroxyfructal esters **13** and **14** now in hand on a preparative scale—their obtention from D-fructose requires three large scale-adaptable steps feasible in 57% and 45% overall yield, respectively, their chemistry could be studied.

As enol ester cleavage in aldose-derived hydroxyglycal esters can selectively be effected by hydroxylaminolysis thus capturing the ketone liberated as its oxime,[16] the *exo*-hydroxyfructal ester **13** was expected to provide the respective aldoxime. The reaction, however, went further since the initially generated aldehyde, under the slightly basic conditions, eliminated benzoic acid prior to oximation to give the enal-oxime **15** (73%). The underlying enal could readily be liberated by trans-oximation with an acetaldehyde (**15** → **19**), and could be olefinated via a standard Wittig methodology (**19** → **20**). The enal-oxime **15** as well as the free enal readily underwent addition of alcohols, with traces of acid in chloroform already being sufficient enough to generate either a glycoside (**15** → **17**) or the acetal of 2-formyldihydropyran (**19** → **18**) (Scheme 3).

The basic ensuing reactions of *endo*-hydroxyfructal ester **14** are expectedly different. When exposed at ambient temperature to methanol in CH_2Cl_2 in the presence of BF_3-etherate, addition to the pro-anomeric carbon of the double bond occurs stereoselectively from the side opposite to the two chiral benzoyloxy substituents, elaborating through concomitant β-elimination, dihydropyran **21** (74%). Performing the addition with a stronger Lewis acid such as $SnCl_4$, the outcome depended on the conditions: at room temperature, a pyran → furan skeletal rearrangement was elicited to provide benzoyloxyacetyl-furan **22** (88%), whereas at −10 °C, the initial



Scheme 4. Products derived from benzoylated *endo*-hydroxyfructal.

formation of **21** was followed by another elimination of benzoic acid to give the well-crystallizing dihydropyranone **24**—not only a uniquely functionalized six–carbon building block, but de facto the first enantiopure, crystalline derivative of microthecin **26**, a fungal metabolite, which, due to its free anomeric center, is isolable from natural sources[28] in its racemic form only (Scheme 4).

When subjected to $SnCl_4$ in $CHCl_2$ in the presence of methanol, or on brief heating in aqueous solution with a strongly acidic ion exchanger, **21** as well as **24** elaborated the benzoyloxymethyl-furyl-ketone **22**—as did the previously prepared,[29] albeit syrupy, microthecin derivative **25** on the attempt to remove the isopropylidene group by acid treatment (**25** → **23**).

Attempts to subject **14** to hydroxylaminolysis for liberation of the C-3 carbonyl as its oxime were not successful, as the enol ester linkage proved to be stable toward

standard conditions (NH_2OH/pyridine, rt), even after prolonged exposure (7 days), whereas at 50 °C, complex product mixtures were formed, seemingly due to enol ester cleavage and subsequent elimination of benzoic acid.

2.2. *endo*-3-Hydroxysorbal

With L-sorbose being the 5-epimer of D-fructose, it was anticipated that the conditions elaborated for the regioselective dehydrobromination of **12** toward the *exo*- or *endo*-hydroxyfructal esters could also be applied to the tetrabenzoyl-α-L-sorbopyranosyl bromide **27**. Surprisingly though, on in situ generation of the iodide by exposure to NaI in acetone and subsequent addition of DBU, the direction of the elimination was in favor of the *endo*-product **28**—obviously due to the fact that the equatorially disposed 5-OBz in **27** exerts no steric shielding on H-3 (as is the case in the fructose analog **12** with its axially oriented 5-OBz), thereby minimizing the difference in the ease of abstraction of H-1 and H-3 by base. Accordingly, mixtures of *endo*-**28** and *exo*-**29** isomers are obtained, which are not appreciably separable by chromatography due to nearly identical R_f values. Most favorable conditions found for acquiring a high proportion of the *endo*-hydroxysorbal ester **28** comprised in situ generation of the sorbosyl iodide followed by DBU-promoted dehydrohalogenation. The resulting 5:1 mixture of **28** and **29** (^{1}H NMR) was subjected to hydroxylaminolysis, which converted the *exo*-isomer into ene-oxime **32**, yet—in analogy to **14**—left the *endo*-isomer untouched. In this way, **28** was obtained in its pure form with a yield of 54% (based on **27**) (Scheme 5).

The reactions of **28** paralleled those of the fructal analog, for example, BF_3-promoted addition of methanol preferentially occurred from the side opposite to the 5-OBz group and was followed by the elimination of the allylic 4-OBz to provide the (2*R*,5*S*)-dihydropyran **30**, the enantiomer of fructose-derived **21**. Exposure to triethylsilane in the presence of BF_3-etherate—conditions that have successfully been used for the allylic deoxygenation of glycals[30]—resulted in a sterically analogous course involving hydride addition and subsequent elimination to deliver the dihydropyran-building block **31** in a crystalline form. When using stronger Lewis acids such as $SnCl_4$ in CH_2Cl_2 in the presence of an alcohol, or on brief heating with a strongly acidic ion exchanger, ring contraction to the 2-(benzoyloxyacetyl)furan **22** prevailed.

3. Conclusion

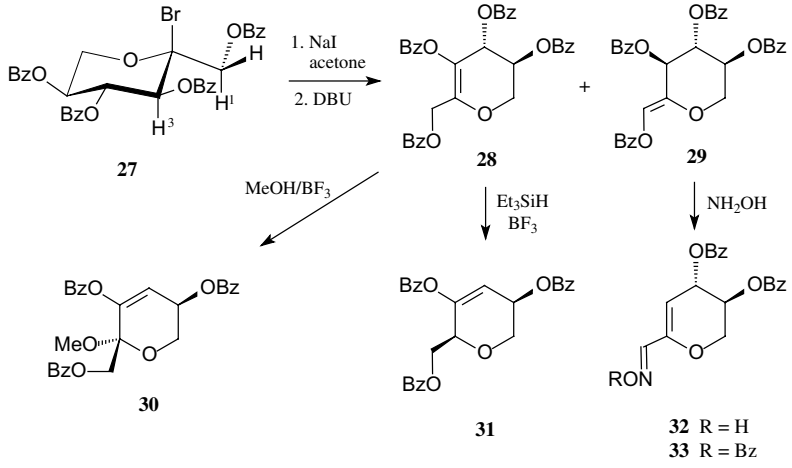
In summary, practical protocols have been developed for the dehydrohalogenation of perbenzoylated β-D-fructopyranosyl bromide **12**. A strong base (DBU in acetonitrile) caused a 1,2-elimination to give the *exo*-hydroxyfructal ester **13** (81%), while refluxing in xylene resulted in the preferential 3,2-excision toward the *endo*-product **14** (53%). The axially disposed 5-OBz in **12** was seen to impose a distinct control over the regioselectivity of the elimination by shielding H-3 from abstraction by base. With α-L-sorbosyl bromide **27**, bearing the 5-OBz in an equatorial orientation, base treatment preferentially utilizes the unshielded H-3 for halide elimination to give the *endo*-hydroxysorbal ester **28** (54%).

In analogy to the aldose-derived 2-hydroxyglycal esters, which have served as starting materials for a plethora of enantiopure building blocks (cf. Scheme 1),[5,6] the ketose-derived *endo*- and *exo*-hydroxyglycals described herein give a rich ensuing chemistry, as simple reactions providing a set of highly versatile enantiopure six-carbon synthons. One has already been utilized to prepare a crystalline derivative of the fungal metabolite microthecin.

4. Experimental

4.1. General methods

Melting points were determined with a Bock hot-stage microscope and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 °C



Scheme 5. L-Sorbose-derived *endo*-hydroxyglycal esters and ensuing products.

using a cell of 1 m path length; concentration (*c*) in g/100 mL and solvent are given in parentheses. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX-300 or a Bruker Avance 500 spectrometer in $CDCl_3$. Mass spectra were acquired on Varian MAT 311 and MAT 212 spectrometers. Microanalyses were determined on a Perkin–Elmer 240 elemental analyzer. Analytical thin layer chromatography (TLC) was performed on precoated Merck plastic sheets (0.2 mm silica gel 60 F_{254}) with detection by UV (254 nm) and/or spraying with H_2SO_4 (50%) and heating. Column and flash chromatography was carried out on Fluka silica gel 60 (70–230 mesh) using the specified eluants.

4.2. (2*R*,6*S*)-2-Benzoyloxy-6-(benzoyloxymethyl)-2*H*-pyran-3(6*H*)-one 10

BF_3-etherate (0.24 mL, 1.9 mmol) was added dropwise to a stirred solution of tetra-*O*-benzoyl-D-*arabino*-hex-1-enitol **1**[3] in CH_2Cl_2 (1.00 g, 1.72 mmol in 50 mL), and stirring at ambient temperature was continued for a total of 3 days with another $BF_3{\cdot}Et_2O$ portion (0.24 mL) having been added after 24 h. The brownish mixture was then poured into 50 mL of satd $NaHCO_3$ solution, followed, after stirring for 1 h, by separation of the organic layer, and repeated extraction of the aqueous phase with CH_2Cl_2. Washing of the combined CH_2Cl_2 extracts with HCl and water (2 × 25 mL each), drying over Na_2SO_4, and removal of the solvent in vacuo left a syrup, which was purified by elution from a silica gel column (2.5 × 30 cm) with 20:1 toluene/EtOAc. The major fraction contained **10** (R_f 0.33, toluene/EtOAc, 10:1), which was isolated by evaporation to dryness, the solid residue crystallizing on trituration with ether: 0.37 g (62%); mp 96–97 °C; $[\alpha]_D^{20} = -168.8$ (*c* 1, $CHCl_3$).[31] ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.51 and 4.67 (two 1H-dd, CH_2), 5.04 (oct, 1H, H-6), 6.41 (ddd, 1H, H-4), 6.48 (s, 1H, H-2), 7.23 (dd, 1H, H-5), 7.4–8.1 (m, 10H, 2C$_6H_5$); $J_{2,4} = 0.5$, $J_{4,5} = 10.7$, $J_{4,6} = 2.5$, $J_{5,6} = 1.7$, $J_{6,CH_2} = 4.8$, $J_{CH_2} = 11.7$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 64.7 (*C*H$_2$), 68.5 (C-6), 90.0 (C-2), 126.7 (C-4), 128.5–133.9 (C$_6$H$_5$), 147.5 (C-5), 164.6 and 166.1 (Bz*C*O), 186.7 (C-3); MS (FI) *m*/*z* 352 (M^+). Anal. Calcd for $C_{20}H_{16}O_6$ (352.34): C, 68.18; H, 4.58. Found: C, 68.10; H, 4.53.

4.3. 1,3,4,5-Tetra-*O*-benzoyl-2,6-anhydro-D-*arabino*-hex-1-(*Z*)-enitol 13

To a stirred solution of 10.0 g (15.2 mmol) of 1,3,4,5-tetra-*O*-benzoyl-β-D-fructopyranosyl bromide **12**[26] and freshly desiccated molecular sieves (4 Å) in anhydrous acetonitrile (100 mL), DBU (3.4 mL, 22.7 mmol) was added dropwise and with care over the course of 30 min, and stirring then continued for 1.5 h. Concentration in vacuo of the resulting brown solution to about one-third and subsequent dilution with $CHCl_3$ (50 mL) were followed by washing with water, 2 M HCl, satd $NaHCO_3$ solution, and water (2 × 50 mL each). Drying over $MgSO_4$ and removal of the solvent in vacuo left a yellowish syrup, which was purified by quick elution from a silica gel column (3 × 30 cm) with 10:1 toluene/EtOAc. Evaporation of the eluate to dryness yielded 7.15 g (81%) of **13** as a colorless foam; $[\alpha]_D^{20} = -48.6$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.36 (dd, 1H, H-6a), 4.40 (dd, 1H, H-6b), 5.84 (dd, 1H, H-4), 5.94 (ddd, 1H, H-5), 6.14 (dd, 1H, H-3), 7.34 (d, 1H, H-1), 7.24–8.12 (m, 20H, 4C$_6H_5$); $J_{1,3} = 0.7$, $J_{3,4} = 6.7$, $J_{4,5} = 3.1$, $J_{5,6} = 4.2$ and 6.2, $J_{6,6} = 11.5$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 67.0 (C-6), 67.3 (C-3), 67.4 (C-5), 69.7 (C-4), 123.8 (C-1), 128.5–133.7 (C$_6$H$_5$), 136.0 (C-2), 162.9, 164.9, 165.2, 165.4 (4Bz*C*O). MS (FD) *m*/*z* 578 (M^+-Bz). Anal. Calcd for $C_{34}H_{26}O_9$ (578.6): C, 70.58; H, 4.53. Found: C, 70.48; H, 4.50.

Essential for the success is the use of an acetic acid-free bromide **12**, prepared by treatment of tetra-*O*-benzoyl-β-D-fructopyranose with HBr in CH_2Cl_2.[26] When generating **12** by exposure to HBr in acetic acid, it contains 0.25–0.3 mol equiv of acetic acid.[32]

4.4. (3*R*,4*R*)-3,4,5-Tri(benzoyloxy)-6-benzoyloxymethyl-3,4-dihydro-2*H*-pyran 14

To a stirred solution of fructosyl bromide **12**[26] (2.0 g, 3.0 mmol) and freshly desiccated molecular sieves (4 Å) in anhydrous acetone (50 mL), sodium iodide (0.7 g, 4.7 mmol) was added and the mixture kept at ambient temperature for 10 h. The resulting suspension was filtered through a layer of silica gel, followed by the removal of the solvent in vacuo at a bath temperature not exceeding 25 °C. The syrup thus obtained was taken up in boiling xylene (50 mL) and the solution stirred at 140 °C for 1.5 h. The mixture was then allowed to return to room temperature, whereafter water (20 mL) was added (to hydrolyze residual fructosyl iodide), followed by filtration of the brown solution through a layer of silica gel, and removal of the solvent in vacuo. The resulting residue was dissolved in $CHCl_3$ (50 mL) and the solution successively washed with water, $NaHCO_3$ solution, and again with water (25 mL each). Drying over $MgSO_4$, and concentration in vacuo gave a syrup consisting of **13** (R_f 0.28, TLC in 10:1 toluene/EtOAc), **14** (major, R_f 0.20), and fructose tetrabenzoate (**12**, OH instead of Br; R_f 0.12). Separation was effected on a silica gel column (4 × 40 cm) by elution with 10:1 toluene/EtOAc. Removal of the solvents from the fraction eluted first afforded 183 mg (11%) of *exo*-olefin **13** as a uniform foam.

Evaporation of the next major fraction eluted (R_f 0.20), yielded 0.93 g (53%) of *endo*-hydroxyfructal ester **14** as an amorphous powder; $[\alpha]_D^{20} = +7.1$ (*c* 2.7, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.35 (dd, 1H, H-2a), 4.43 (dd, 1H, H-2b), 4.96, 5.00 (two 1Hd, CH_2OBz), 5.80 (ddd, 1H, H-3), 6.33 (dd, 1H, H-4), 7.25–8.05 (m, 20H, 4C$_6H_5$); $J_{2,2} = 10.8$, $J_{2,3} = 3.8$ and 9.1, $J_{2,4} = 1.0$, $J_{3,4} = 4.2$, $J_{CH_2} = 13.3$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 59.0 (*C*H$_2$OBz), 63.8 (C-2), 65.2 (C-4), 66.0 (C-3), 125.4 (C-5), 146.6 (C-6), 128.3–133.7 (C$_6$H$_5$), 165.1, 165.8, 166.0 (4Bz*C*O). MS (FD) *m*/*z* 578 (M^+-1), 457 (M^+-HOBz). Anal. Calcd for $C_{34}H_{26}O_9$ (578.6): C, 70.58; H, 4.53. Found: C, 70.39; H, 4.64.

The fraction eluted last contained 1,3,4,5-tetra-*O*-benzoyl-β-D-fructopyranose (350 mg, 19%), formed by the hydrolysis of the unreacted in situ-generated fructosyl iodide.

4.5. (3*S*,4*S*)-Bis(benzoyloxy)-6-formyl-3,4-dihydro-2*H*-pyran oxime 15

Hydroxylamine hydrochloride (7.2 g, 0.1 mol) was added to a solution of 7.5 g (13 mmol) of *exo*-hydroxyfructal ester **13** in anhydrous pyridine (75 mL) and the mixture was stirred at 60 °C for 24 h, whereafter TLC (toluene/EtOAc, 10:1) indicated complete conversion. This was followed by concentration in vacuo to about one-third, dilution with water (250 mL), extraction with Et_2O (3 × 150 mL), and successive washing of the combined ether extracts with water, 2 M HCl, satd $NaHCO_3$ solution (2 × 50 mL each), and again with water (50 mL). Drying over Na_2SO_4 and removal of the solvent in vacuo provided a syrup, which was purified by quick elution from a short silica gel column with toluene/EtOAc (20:1): 3.5 g (73%) of **15** as a colorless syrup; $[\alpha]_D^{20} = +205.3$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.41 (m, 2H, 2C*H*$_2$), 5.37 (d, 1H, H-5), 5.62 (m, 1H, H-3), 5.94 (dd, 1H, H-4), 7.32–8.00 (m, 10H, 2C$_6$*H*$_5$), 7.60 (s, 1H, C*H*N), 9.54 (br S, 1H, NO*H*); $J_{2,4} = 0.4$, $J_{3,4} = 4.2$, $J_{4,5} = 4.8$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 64.0 (C-4), 64.1 (C-2), 65.9 (C-3), 103.5 (C-5), 128.4–133.4 (*C*$_6$H$_5$), 144.6 (*C*HN), 150.2 (C-6), 165.4, 165.9 (2Bz*C*O). MS (FD) *m*/*z* 367 (M^+). Anal. Calcd for $C_{20}H_{17}NO_6$ (367.4): C, 65.39; H, 4.66; N, 3.81. Found: C, 63.37; H, 4.68; N, 3.75.

4.6. (3*R*,4*S*)-3,4-Bis(benzoyloxy)-6-formyl-3,4-dihydro-2*H*-pyran *O*-benzoyloxime 16

Benzoylchloride (0.4 mL, 3.4 mmol) was added dropwise to a vigorously stirred solution of 500 mg (1.4 mmol) of oxime **15** in anhydrous pyridine (20 mL). After 24 h at ambient temperature, the reaction mixture was quenched with water (1 mL). The residue obtained after concentration in vacuo was diluted with CH_2Cl_2 (25 mL), followed by filtration, and washing with 2 M HCl (3 × 25 mL), $NaHCO_3$ solution, and water (2 × 15 mL). The organic layer was dried over $MgSO_4$ and evaporated to a slightly yellowish syrup, which crystallized on trituration with Et_2O: 510 mg (79%) **16** as colorless needles; mp 162–165 °C, $[\alpha]_D^{20} = +205.5$ (*c* 1.3, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.48 (ddd, 1H, H-2a), 4.51 (dd, 1H, H-2b), 5.65 (d, 1H, H-5), 5.67 (ddd, 1H, H-3), 5.99 (dd, 1H, H-4), 7.35–8.12 (m, 15H, 3C$_6$*H*$_5$), 8.02 (s, 1H, CHN); $J_{2,2} = 10.7$, $J_{2,3} = 4.6$ and 5.2, $J_{2b,4} = 0.5$, $J_{3,4} = 3.9$, $J_{4,5} = 4.5$ Hz; MS (FD) *m*/*z* 471 (M^+). Anal. Calcd for $C_{27}H_{21}NO_7$ (471.5): C, 68.78; H, 4.49; N, 2.96. Found: C, 68.75; H, 4.47; N, 2.97.

4.7. (2*S*,4*S*,5*R*)-4,5-Bis(benzoyloxy)-2-ethoxy-2-formyl-tetrahydropyran oxime 17

Oxime **15** (500 mg, 1.4 mmol) was solved in a stirred mixture of anhydrous $CHCl_3$ (4 mL) and absolute EtOH (4 mL). Stirring at ambient temperature was continued for 3 days, whereafter TLC indicated absence of educt. Concentration of the solution in vacuo left a syrup, which was purified by elution from a silica gel column (3 × 13 cm) with 10:1 toluene/EtOAc to furnish, upon evaporation of the eluant in vacuo, **17** (421 mg, 75%) as a colorless foam; $[\alpha]_D^{20} = -152.8$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (t, 3H, EtC*H*$_3$), 2.35 (m, 2H, 3H$_2$), 3.58 (two 1H-q, EtC*H*$_2$), 4.07 (dd, 1H, H-6a), 4.13 (dd, 1H, H-6b), 5.60 (m, 1H, H-5), 5.70 (m, 1H, H-4), 7.3–8.1 (m, 10H, 2C$_6$*H*$_5$), 7.47 (s, 1H, CHN), 8.59 (s, 1H, NOH); $J_{5,6} = 1.2$ and 1.8, $J_{6,6} = 13.0$ Hz. MS (FD) *m*/*z* 413 (M^+). Anal. Calcd for $C_{22}H_{23}NO_7$ (413.4): C, 63.91; H, 5.61; N, 3.39. Found: C, 63.71; H, 5.46; N, 3.22.

4.8. (3*R*,4*S*)-3,4-Bis(benzoyloxy)-6-vinyl-3,4-dihydro-2*H*-pyran 18

Methyl triphenylphosphonium bromide (734 mg, 2.1 mmol) was suspended in anhydrous THF (50 mL), and after thorough flushing with dry nitrogen (15 min), 1.4 mL (2.2 mmol) of a 1.6 M solution of *n*-butyl lithium in *n*-hexane was added dropwise at ambient temperature. After 30 min, the reaction mixture was cooled to −10 °C, a solution of enal **19** (320 mg, 0.9 mmol) in anhydrous THF (5 mL) was added dropwise. Stirring at −10 °C under N_2 was continued for 24 h, whereafter TLC indicated complete conversion (**19**: R_f 0.59 in 20:1 CH_2Cl_2/EtOAc). The mixture was hydrolyzed with water (40 mL) followed by extraction with CH_2Cl_2 (3 × 25 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo, followed by further purification of the residue by quick elution from a silica gel column (3 × 15 cm) with CH_2Cl_2/EtOAc (19:1), and concentration of the fractions containing **18** gave a colorless syrup, which crystallized from 10:1 *i*PrOH/Et_2O: 174 mg (55%); mp 133–134 °C; $[\alpha]_D^{20} = +322.6$ (*c* 1.0, acetone). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.34 (m, 2H, 2H$_2$), 5.11 (d, 1H, H-5), 5.26 (dd, 1H, H-8*Z*), 5.55 (m, 1H, H-3), 5.70 (dd, 1H, H-8*E*), 5.89 (dd, 1H, H-4), 6.13 (dd, 1H, H-7), 7.3–8.0 (m, 10H, 2C$_6$*H*$_5$); $J_{3,4} = 4.8$, $J_{4,5} = 5.2$, $J_{7,(Z)} = 10.9$, $J_{7,8(E)} = 17.2$, $J_{8,8} = 1.4$ Hz. MS (FD) *m*/*z* 350 (M^+). Anal. Calcd for $C_{21}H_{18}O_5$ (350.37): C, 71.99; H, 5.18. Found: C, 72.07; H, 5.19.

4.9. (3*R*,4*S*)-3,4-Bis(benzoyloxy)-6-formyl-3,4-dihydro-2*H*-pyran 19

A solution of oxime **15** (5.8 g, 15.8 mmol) in acetonitrile (100 mL) and HCl (50 mL) was stirred for 20 min at room temp whereafter 70 mL of acetaldehyde were added dropwise. After 3 days at ambient temperature, the reaction mixture was diluted with 1 L of water, followed by continuous extraction with EtOAc (1 L), and dried over $MgSO_4$. Removal of the solvent in vacuo left a syrup, which contained **19** as the main product (R_f 0.45 in 4:1 toluene/acetone) apart from small amounts of a second compound (R_f 0.23). Purification by elution from a silica gel column (4.5 × 45 cm) with 10:1 toluene/EtOAc, removal of the solvent from the eluate, and several coevaporations with toluene (≈100 mL) afforded 4.2 g (76%) of enal **19** as a solid foam; $[\alpha]_D^{20} = +148.2$

(*c* 1.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.42 (ddd, 1H, H-2a), 4.49 (dd, 1H, H-2b), 5.69 (ddd, 1H, H-3), 6.00 (dd, 1H, H-5), 6.07 (ddd, 1H, H-4), 7.20–7.99 (m, 10H, $2C_6H_5$), 9.30 (s, 1H, C*H*O); $J_{2,2} = 11.8$, $J_{2,3} = 3.0$ and 6.5, $J_{2b,4} = 1.2$, $J_{3,4} = 4.0$, $J_{3,5} = 0.5$, $J_{4,5} = 3.8$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 63.9 (C-4), 65.0 (C-3), 65.1 (C-2), 114.8 (C-5), 128.2–133.5 (C_6H_5), 153.2 (C-6), 165.3, 165.5 (2Bz*C*O), 185.9 (*C*HO). MS (FD) *m/z* 352 (M^+). Anal. Calcd for $C_{20}H_{16}O_6$ (352.3): C, 57.39; H, 4.58. Found: C, 57.42; H, 4.65.

4.10. (3*R*,4*S*)-3,4-Bis(benzoyloxy)-6-(diethoxy)methyl-3,4-dihydro-2*H*-pyran 20

Enal **19** (700 mg, 2 mmol) was dissolved in dry $CHCl_3$ (5 mL) and anhydrous EtOH (5 mL) and the mixture stirred for 4 d at room temp. After completion of the addition (monitoring by TLC in 20:1 toluene/EtOAc), the solvents were removed in vacuo, and the residue purified by elution from a silica gel column with 20:1 toluene/EtOAc. Concentration of the appropriate eluate furnished 660 mg (78%) of **20** as a colorless syrup; $[\alpha]_D^{20} = +145.3$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 1.25, 1.26 (two 3H-t, 2EtCH_3), 3.63 (m, 4H, 2EtCH_2), 4.32 (m, 2H, $2H_2$), 4.90 (s, 1H, C*H*$(OEt)_2$), 5.40 (d, 1H, H-5), 5.56 (m, 1H, H-3), 5.88 (dd, 1H, H-4, 7.30–8.00 (m, 10H, $2C_6H_5$); $J_{3,4} = 4.4$, $J_{4,5} = 4.8$ Hz; MS (FD) *m/z* 426 (M^+). Anal. Calcd for $C_{24}H_{26}O_7$ (426.4): C, 67.59; H, 6.14. Found: C, 67.46; H, 6.04.

4.11. (2*R*,5*S*)-3,5-Bis(benzoyloxy)-2-(benzoyloxymethyl)-2-methoxy-5,6-dihydro-2*H*-pyran 21

To a solution of *endo*-hydroxyfructal ester **14** (520 mg, 0.9 mmol) in CH_2Cl_2 (20 mL) was added dry methanol (0.18 mL, 4.4 mmol) and freshly desiccated molecular sieves (4 Å), and the mixture cooled to 0 °C. BF_3-etherate (0.46 mL, 3.9 mmol) was then added dropwise in several portions. The mixture was then stirred at ambient temperature for 2 days, after which TLC (10:1 toluene/EtOAc), indicated the absence of educt. Quenching by pouring into satd $NaHCO_3$ solution (50 mL), followed by extraction with CH_2Cl_2 (3×30 mL), and subjection of the combined organic extracts to washing with 2 M HCl and water (2×20 mL each), gave after drying over Na_2SO_4 and concentration in vacuo, approximately a 5:1 mixture (^1H NMR) of **16** and its 2-epimer (α-anomer). Separation was effected on a silica gel column (3.0×25 cm) by elution with toluene/EtOAc (35:1). The main eluate (R_f 0.30, TLC in 10:1 toluene/EtOAc) afforded upon removal of the solvents in vacuo 320 mg (74%) of syrupy **21**; $[\alpha]_D^{20} = -60.6$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 3.48 (s, 3H, OCH_3), 4.17 (ddd, 1H, H-6a), 4.37 (dd, 1H, H-6b), 4.63, 4.79 (two 1H-d, CH_2OBz), 5.57 (ddd, 1H, H-5), 6.36 (dd, 1H, H-4), 7.14–8.06 (m, 15H, $3C_6H_5$); $J_{4,5} = 6.1$, $J_{4,6b} = 0.6$, $J_{5,6} = 1.2$ and 2.6, $J_{6,6} = 12.9$, $J_{CH_2} = 11.2$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 50.4 (OCH_3), 62.8 (C-6), 63.5 (*C*H_2OBz), 65.7 (C-5), 96.3 (C-2), 113.6 (C-4), 128.3–133.8 (C_6H_5), 148.8 (C-3), 163.3, 165.9, 166.1 (3Bz*C*O). MS (FD) *m/z* 488 (M^+). Anal. Calcd for $C_{28}H_{24}O_8$ (488.5): C, 68.85; H, 4.95. Found: C, 69.09; H, 5.02.

4.12. 2-(2-Benzoyloxyacetyl)furan 22

To a cooled (−5 °C) solution of *endo*-hydroxyfructal ester **14** (400 mg, 0.7 mmol) in CH_2Cl_2 (20 mL) was added with stirring 0.15 mL (3.5 mmol) of dry methanol followed by 0.1 mL (0.85 mmol) of $SnCl_4$. The mixture was then allowed to warm to room temperature. Conversion of the educt was in favor of **17** (R_f 0.33, TLC in 10:1 toluene/EtOAc) being reached within 1 h. Dilution with CH_2Cl_2 (30 mL), thorough washing with $NaHCO_3$ solution (2×50 mL) and brine (50 mL), drying over Na_2SO_4 of the organic phase, and evaporation to dryness gave a residue, which was purified by elution from a silica gel column (3×15 cm) with 10:1 toluene/EtOAc. Evaporation of the eluate to dryness and crystallization of the residue from diethyl ether furnished 139 mg (88%) of **22** as colorless needles; mp 76–77 °C. ^1H NMR (300 MHz, $CDCl_3$): δ 5.41 (s, 2H, BzOCH_2), 6.58 (dd, 1H, H-4), 7.31 (dd, 1H, H-3), 7.44–8.15 (m, 5H, C_6H_5), 7.63 (dd, 1H, H-5); $J_{3,4} = 3.6$, $J_{3,5} = 0.6$, $J_{4,5} = 1.7$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 65.8 (BzO*C*), 112.5 (C-4), 117.9 (C-3), 128.5–133.4 (C_6H_5), 146.8 (C-5), 150.6 (C-2), 166.0 (BzCO), 181.6 (*C*O). MS (FI) *m/z* 230 (M^+). Anal. Calcd for $C_{13}H_{10}O_4$ (230.2): C, 67.82; H, 4.38. Found: C, 67.63; H, 4.37.

4.13. 2-(2-Hydroxyacetyl)furan 23

An aqueous solution of spirocyclic dihydropyranon **25**[29] (555 mg, 3 mmol, in 20 mL) was refluxed in the presence of 1 mL of amberlite 120 (H^+-form) for 1 h, followed by filtration, evaporation to dryness in vacuo, and purification of the brownish residue by elution from a silica gel column (2×30 cm) with 25:1 $CHCl_3$/MeOH). Removal of the solvents left **23** (355 mg, 93%), as colorless crystals of mp 78 °C. Lit.:[28] mp 78 °C.

4.14. (2*R*)-2-(Benzoyloxymethyl)-2-methoxy-2*H*-pyran-3(6*H*)-one 24

Molecular sieves (4 Å) and methanol (0.2 mL) were added to a CH_2Cl_2 solution of *endo*-hydroxyfructal ester **14** (390 mg in 30 mL), and after cooling to −10 °C, $SnCl_4$ (0.20 mL, 2.5 molar equiv) was added in several portions with stirring, which was continued for 1.5 h at −10 °C. The mixture was then poured into satd $NaHCO_3$ solution and processed as described for **16**. The eluate with R_f 0.24 (TLC, 10:1 toluene/EtOAc) was evaporated to dryness in vacuo. Trituration of the residue with diethyl ether resulted in crystallization of **24** (127 mg, 72%) as colorless platelets of mp 106–108 °C; $[\alpha]_D^{20} = -74.3$ (*c* 1.1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 3.50 (s, 3H, OCH_3), 4.42 and 4.57 (two 1H-ddd, $6H_2$), 4.66, 4.75 (two 1H-d, CH_2OBz), 6.18 (ddd, 1H, H-4), 7.07 (ddd, 1H, H-5), 7.4–8.0 (m, 5H, C_6H_5); $J_{4,5} = 10.5$, $J_{4,6} = 1.8$ and 2.5, $J_{5,6} = 1.9$ and 3.8, $J_{6,6} = 19.0$, $J_{CH_2} = 11.4$ Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 51.3 (OCH_3), 60.7 (C-6), 62.4 (*C*H_2OBz), 97.5 (C-2), 124.7 (C-4), 128.3–133.1 (C_6H_5), 147.7 (C-5), 165.9 (Bz*C*O),

188.7 (C-3); MS (FI) *m/z* 262 (M^+). Anal. Calcd for $C_{14}H_{14}O_5$ (262.3): C, 64.12; H, 5.38. Found: C, 64.14; H, 5.36.

4.15. (3*S*,4*R*)-3,4,5-Tri(benzoyloxy)-6-benzoyloxymethyl-3,4-dehydro-2*H*-pyran 28

Sodium iodide (3.4 g, 22.7 mmol) on freshly desiccated molecular sieves (4 Å) was added to a solution of 10.0 g (15.2 mmol) 1,3,4,6-tetra-*O*-benzoyl-α-L-sorbopyranosyl bromide **27**[26] in dry acetone (100 mL). After stirring for 15 h, the suspension was cooled to −10 °C and DBU (3.4 mL, 23 mmol) added dropwise, followed by stirring overnight at 10 °C and for 24 h at ambient temperature (TLC monitoring with 10:1 toluene/EtOAc). The mixture was then taken to dryness in vacuo, suspended in $CHCl_3$ (200 mL), filtered, and the filtrate washed successively with water, 2 M HCl, satd $NaHCO_3$ solution, and again with water. Drying over Na_2SO_4 and removal of the solvent in vacuo left a syrup, which was purified by fast elution from silica gel (3 × 25 cm column) with 35:1 toluene/Et_2O. Concentration of the eluate gave 6.75 g (77%) of a solid foam, which had an R_f of 0.59 in 20:1 toluene/Et_2O, yet proved (^{1}H NMR) to be a 5:1 mixture of *endo*-**28** and *exo*-**29** products.

As appreciable separation by chromatography could not be effected due to nearly identical R_f values, thus the *exo*-isomer **29** was removed by a reaction with hydroxylamine.

Hydroxylamine hydrochloride (1.4 g, 20 mmol) was added to a solution of 5.20 g (9 mmol) of the 5:1 mixture of hydroxysorbal esters **28/29**, as obtained above, in pyridine (60 mL). After stirring for 2 d at ambient temperature, the mixture was poured into water (500 mL), followed by five extractions with 100 mL portions of $CHCl_3$, and washing of the combined organic phases with water (2 × 100 mL), 2 M HCl (2 × 100 mL), $NaHCO_3$ solution, and again water (2 × 100 mL each). Drying over Na_2SO_4 and evaporation to dryness in vacuo left a residue comprising of an approximate 5:1 mixture of **28** (R_f = 0.60 in 20:1 toluene/EtOAc) and ene-oxime **32** (R_f 0.21). Separation was readily effected by elution from a silica gel column (3 × 20 cm) with 5:1 toluene/EtOAc. The first fraction contained the *endo*-product **28**, which was isolated as a colorless foam on removal of the solvents (2.84 g, 54% based on bromide **27**, 86% based on the mixture **28/29**); $[\alpha]_D^{20} = +173.1$ (*c* 1, $CHCl_3$).[33] ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.34 (dd, 1H, H-2a), 4.59 (ddd, 1H, H-2b), 4.93 and 5.05 (two 1H-d, C*H*$_2$OBz), 5.46 (m, 1H, H-3), 5.96 (m, 1H, H-4), 7.3–8.2 (m, 20H, 4C_6H_5), $J_{2,2}$ = 12.3, $J_{2,3}$ = 1.3 and 2.5, $J_{2,4}$ = 1.4, J_{CH_2} = 12.8. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 59.3 (*C*H$_2$OBz), 64.4 (C-2), 65.7 (C-4), 68.0 (C-3), 125.7 (C-5), 147.1 (C-6), 128.4–133.7 (C_6H_5), 165.3, 165.3, 166.1 (Bz*C*O). MS (FD) *m/z* 578 (M^+). Anal. Calcd for $C_{34}H_{26}O_9$ (578.6): C, 70.58; H, 4.53. Found: C, 70.47; H, 4.50.

The second fraction eluted contained the minor product, ene-oxime **32**. Isolation and characterization cf. below.

4.16. (2*S*,5*R*)-3,5-Bis(benzoyloxy)-2-benzoyloxymethyl-2-methoxy-5,6-dihydro-2*H*-pyran 30

To a CH_2Cl_2 solution of **28** (580 mg, 1 mmol, in 20 mL) was added methanol (0.2 mL), molecular sieves (4 Å). After cooling to 0 °C, BF_3-etherate (0.5 mL) and the mixture were stirred at room temperature for 2 days. Processing as described for **14** → **21** (vide supra) afforded 335 mg (69%) of syrupy **30**; $[\alpha]_D^{20} = +63.1$ (*c* 1.1, $CHCl_3$). Spectroscopic data corresponded to those of its enantiomer **21**.

4.17. (2*S*,5*R*)-3,5-Bis(benzoyloxy)-2-benzoyloxymethyl-5,6-dihydro-2*H*-pyran 31

Triethylsilane (0.13 mL, 0.82 mmol) and BF_3-etherate (0.17 mL, 1.35 mmol) were added to a cooled (10 °C) solution of **28** in CH_2Cl_2 (400 mg, 0.69 mmol in 20 mL) containing 1.5 g of molecular sieves (4 Å). After stirring for 6 h, the mixture was poured into satd $NaHCO_3$ solution, followed by separation of the organic layer, and two extractions of the aqueous phase with CH_2Cl_2 (25 mL each). The combined organic phases were successively washed with 2 M HCl and water, dried over Na_2SO_4, and taken to dryness in vacuo. The residue was purified by elution from silica gel (3 × 15 cm column) with 35:1 toluene/ether. Removal of the solvents and trituration of the solid residue with Et_2O gave 205 mg (65%) of **31** in the form of colorless needles; mp 131–132 °C; $[\alpha]_D^{20} = +6.2$ (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98 (dd, 1H, H-6a), 4.22 (d, 1H, H-6b), 4.54 and 4.60 (two 1H-dd, C*H*$_2$OBz), 4.70 (m, 1H, H-2), 5.49 (m, 1H, H-5), 6.13 (d, 1H, H-4), 7.1–8.0 (m, 15H, 3C_6H_5), J_{2,CH_2} = 2.9 and 4.1, $J_{4,5}$ = 5.9, $J_{5,6a}$ = 2.4, $J_{6,6}$ = 12.0 Hz. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 63.4 (*C*H$_2$OBz), 66.5 (C-5), 67.4 (C-6), 72.5 (C-2), 112.8 (C-4), 128.4–134.1 (C_6H_5), 151.2 (C-3), 164.1, 166.3, and 166.3 (*C*OC_6H_5); MS (FD) *m/z* 458 (M^+), 353 (M^+−Bz). Anal. Calcd for $C_{27}H_{22}O_7$ (458.47): C, 70.73; H, 4.84. Found: C, 70.68; H, 4.82.

4.18. (3*S*,4*S*)-3,4-Bis(benzoyloxy)-6-formyl-3,4-dihydro-2*H*-pyran oxime 32

The second fraction obtained on column separation of the 5:1 mixture of **28** and **32** (cf. above) contained the product with R_f 0.21 (20:1 toluene/EtOAc), which was isolated by removal of the solvents as a colorless solid (425 mg, 11% based on sorbosyl bromide **27**); $[\alpha]_D^{20} = +243.5$ (*c* 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.35 (dd, 1H, H-2a), 4.59 (ddd, 1H, H-2b), 5.43 (m, 1H, H-4), 5.49 (dd, 1H, H-5), 5.54 (m, 1H, H-3), 7.4–8.1 (10H-m, 2C_6H_5), 7.59 (s, 1H, C*H*N), 8.40 (s, 1H, NO*H*), $J_{2,2}$ = 12.3, $J_{2,3}$ = 1.7 and 3.0, $J_{2b,4}$ = 1.6, $J_{3,5}$ = 1.4, $J_{4,5}$ = 5.1 Hz. MS (FD) *m/z* 367 (M^+). Anal. Calcd for $C_{20}H_{17}NO_4$ (357.36): C, 65.39; H, 4.66; N, 3.81. Found: C, 65.28; H, 4.70; N, 3.69.

4.19. (3*S*,4*S*)-3,4-Bis(benzoyloxy)-6-formyl-3,4-dihydro-2*H*-pyran *O*-benzoyloxime 33

To a cooled solution (0 °C) of oxime **32** (200 mg, 0.56 mmol) in CH_2Cl_2 (10 mL) and pyridine (10 mL)

was added benzoyl chloride (0.2 mL, 0.17 mmol) with stirring. The mixture was then allowed to stand at room temperature for 24 h, followed by processing as described for the fructose-derived analog (**15** → **16**): 223 mg (84%) of **33** as colorless needles; mp 176–177 °C; $[\alpha]_D^{20} = +183.7$ (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.39 (dd, 1H, H-2a), 4.68 (ddd, 1H, H-2b), 5.47 (m, 1H, H-3), 5.58 (ddd, 1H, H-4), 5.77 (dd, 1H, H-5), 8.00 (s, 1H, C*H*N), 7.4–8.1 (m, 15H, $3C_6H_5$); $J_{2,2} = 12.4$, $J_{2,3} = 1.6$ and 2.9, $J_{2b,4} = 1.8$, $J_{3,5} = 1.2$, $J_{4,5} = 5.1$ Hz. Anal. Calcd for $C_{27}H_{21}NO_7$ (471.47): C, 68.78; H, 4.49; N, 2.97. Found: C, 68.65; H, 4.50; N, 3.00.

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31. The high negative rotation of (2*R*,6*S*)-dihydropyranone **10** (−168.8 in $CHCl_3$) contrasts with the considerably smaller value for its isopropyl analog **11** (−7[20]) and the equally small positive rotation of enolone ester **9** (+3.6[19]). Compound **10** nevertheless has a (2*R*,6*S*)- or α-D-configuration followed from the small allylic $J_{5,6}$ couplings of 1.7–1.8 Hz uniformly observed for **9**–**11**, whilst the β-D-anomers invariably have $J_{5,6}$ values in the 3–3.5 Hz range.[19] Moreover, the acetylated analog of **10** had an $[\alpha]_D$ of −87.6 and $J_{5,6}$ of 1.6 Hz, the 2-epimeric β-D-analog −116.4 and 3.0 Hz. Köll, P.; Klenke, K.; Eisermann, D. *J. Carbohydr. Chem.* **1984**, *3*, 403–415; Obviously, in peracylated dihydropyranones of type **10** unlike those carrying 2-alkoxy substituents—the usual ^0E-conformation (cf. Lichtenthaler, F. W.; Rönninger, S.; Lindner, H. J.; Immel, S. *Carbohydr. Res.* **1993**, *249*, 305–324, is substantially distorted toward the $^0H_2$ halfchair).
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33. For a side product obtained on $HgCl_2$-promoted adenylation of **27**, believed to be **28**, a substantially lower rotation {$[\alpha]_D^{20} = +121$ in $CHCl_3$} was reported;[23] obviously the product was impure, containing substantial amounts of the *exo*-isomer **30**.