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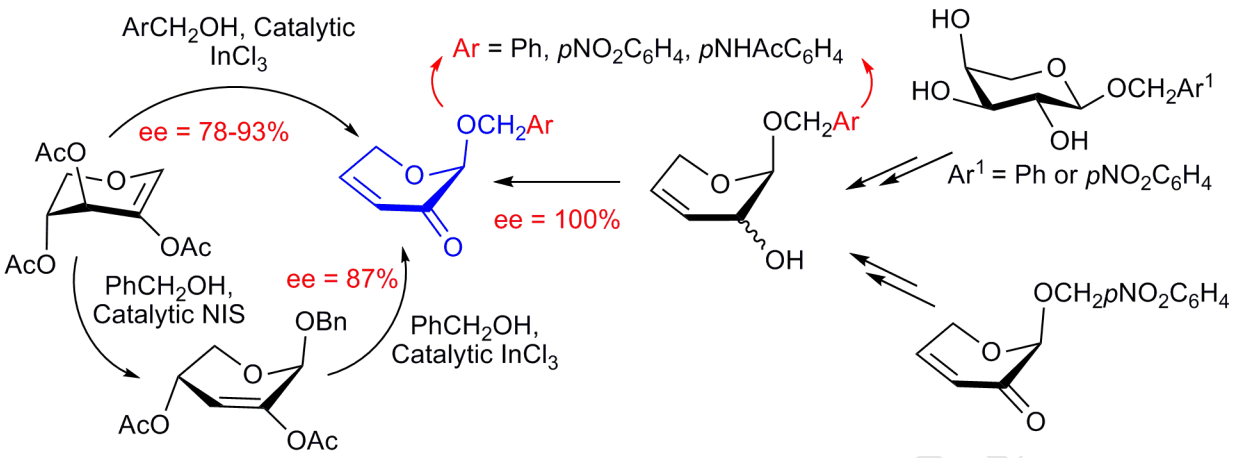

Synthesis of enantiomerically pure enones (2-benzyloxypyran-3-ones) derived from pentoses

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Highlights

- Efficient synthesis of enantiomerically enriched or pure enones from pentoses.
- Glycosylation of 2-acetoxyglycals with BnOH/$InCl_3$ gave enones with ee > 78%.
- Enantiomerically pure enones were synthesized from benzyl pentopyranosides.
- Reactions involving substituted benzyl groups gave lower yields than those unsubstituted.

Abstract

The useful synthons sugar enones (2-benzyloxypyran-3-ones) derived from pentoses have been prepared starting from 2-acetoxyglycals or benzyl pentopyranosides. The glycals were glycosylated with benzyl alcohol in the presence of a Lewis acid ($SnCl_4$ or $InCl_3$) to give enantioenriched enones (ee = 80-90%). Under catalysis with $InCl_3$, benzyl 2-enopyranosides gave also the enones (ee = 87%). On the other hand, enantiomerically pure enones were synthesized via an improved straightforward and high yielding sequence (70% overall) from benzyl pentopyranosides. However, the yields of both, the glycosylation of glycals as well as some specific reactions of the sequence from glycosides, were lowered when a *p*-nitro substituent was introduced into the benzyl group. These routes became impractical in the case of *p*-acetamidobenzyl derivatives, because of the large extent of decomposition. Therefore, alternative sequences have been developed for the synthesis of 2-(*p*-acetamidobenzyloxy)pyran-3-ones.

Keywords:

Pentopyranoside

Sugar enone

3-Enopyranose

2-Benzyloxy pyranone

Glycal rearrangement

Introduction

Common carbohydrates and derivatives are widely used as chiral precursors in enantiospecific synthesis. Particularly, sugar enones, which combine the versatile unsaturated carbonyl motif in addition with the intrinsic chirality of the carbohydrate, are useful synthons for the synthesis of a wide variety of natural and unnatural compounds [1-4]. The most popular sugar enone is levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose), which is considered to be a promising platform for both fine and commodity chemical industries [5] and even for the development of new therapeutics [6]. The varied applications of this chiral template for the synthesis of enantiomerically pure compounds, as well as its reactivity and chemical transformations to provide key intermediates, chiral auxiliaries, catalysts, and organocatalysts useful in asymmetric synthesis have been profusely reviewed [5, 7-10].

Levoglucosenone is usually obtained as one of the products of pyrolysis of cellulose [7-10], in contrast to these rather drastic reaction conditions we have described mild and efficient procedures (see below) for the preparation of analogous sugar enones (alkyl 3-enopyranosid-2-uloses or 2-alkoxypyran-3-ones). These compounds proved to be useful precursors in the synthesis of a varied type of molecules. Thus, they have been employed as dienophiles in Diels-Alder cycloadditions with butadienes and cyclic dienes [11-15], or dipolarophiles in 1,3-dipolar cycloadditions with azomethine ylides [16-18]. The enones also behave as Michael acceptors of thiols or 1-thioaldoses in the respective synthesis of 3-deoxy-4-thio-glycosides [19-22] or thiodisaccharides [23-27]. Furthermore, sugar 3,4-epoxides, prepared by epoxidation of pyranones, underwent nucleophilic substitution by 1-thioaldoses to give (1→3)- and (1→4)-linked thiodisaccharides [28]. Analogous opening of

thiiranes derived from enones led to branched thiooligosaccharides and disulfides [29]. Naturally occurring amino deoxy sugars, constituents of antibiotics, have been synthesized starting from pyranones [30,31].

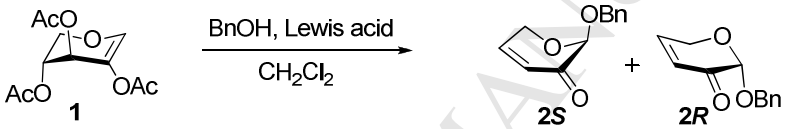
One of the most useful methods to prepared sugar-derived 2-alkoxypyran-3-ones is the Lewis acid-promoted glycosylation of 2-acetoxyglycal derivatives obtained from common pentoses [11] or hexoses [32,33]. This procedure applied to glycals derived from hexoses led to enantiomerically pure enones, while glycals derived from pentoses gave pyranones having enantiomeric excesses (ee) in the range 80-90% [11]. To prepare enantiomerically pure enones derived from pentopyranoses, we have developed a multistep sequence from common glycosides [34], or employed chiral alcohols for the glycosylation. Thus, the use of 2(*R*) or 2(*S*)-octanol led to practically enantiomerically pure enones (ee > 97%), after a rather difficult separation of the diastereoisomers by column chromatography [11]. When (−)-menthol was employed as chiral alcohol, the analogous pryranones were crystalline products, that were readily purified by recrystallization to obtain the enantiomerically pure product [16-18]. However, we have demonstrated that the stereocenters in the aglycon affected the stereochemical course of the reactions performed on the α,β-unsaturated carbonyl system [16-18]. Furthermore, the benzyloxy substituent at the anomeric center of the pentopyranoside unit of (1→4) thiodisaccharides inhibitors, obtained from 2-benzyloxy pyranones, play an important role in the interaction with the catalytic site of the enzyme [35]. Particularly, saturation transfer difference (STD) and transferred-NOESY experiments showed major transfer to the aromatic benzyl protons. We expected that the introduction in the benzyl aromatic ring of substituents with different electronic properties and able to participate in hydrogen bonding could affect the interaction with the enzyme, and hence the

inhibitory activity. To explore this hypothesis we needed, as precursor of the thiodisaccharides, pyran-3-ones carrying benzyloxy rings with substituents of diverse nature. Therefore, we have explored and we report here the approaches developed for the preparation of such enantiomerically pure 2-benzyloxypyranones.

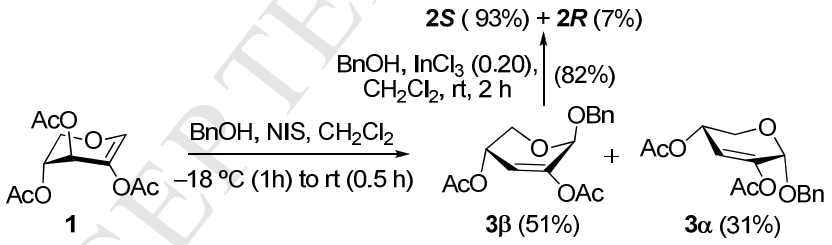
Results and discussion

The Lewis acid-promoted glycosylation of 2-acetoxylglycal derivatives of pyranoses proved to be a straightforward and high yielding procedure for the synthesis of sugar enones (alkyl 3-enopyranosid-2-uloses) [11,32,33]. During such glycosylation the Lewis acid promotes a double allylic (Ferrier) rearrangement to afford the pyran-3-one. The alcohol nucleophile is diastereoselectively introduced, as the axial orientation is preferred because of the anomeric effect. Thus, glycals from hexopyranoses gave the α-anomer of the enone as practically the only product. In contrast, the stereochemistry of the C-4 substituent in glycals of pentopyranoses induces the approach of the alcohol from the opposite face, and with assistance of the anomeric effect affords the corresponding α or β anomers [11]. When common alcohols (no chiral ones) are employed, the glycosylation leads to enantioenriched enones as the only stereocenter in the product is that generated during the reaction (C-1). For example, the reaction of D-xylal **1** with benzyl alcohol, promoted by $SnCl_4$ led to the enone **2*S*** having an enantiomeric excess (ee) of approximately 86% (Scheme 1) [11]. Now, we have explore this reaction using $InCl_3$ as an alternative to the hygroscopic and moisture sensitive $SnCl_4$. In view of the different properties of these two Lewis acids and their capacity to promote the conversion of glycals into enones, in the

present work we have focused on them. An advantage of using $InCl_3$ over $SnCl_4$ was that the concentration of the indium catalyst could be lowered to 20 mole% and the enone was obtained in an excellent yield (91%), and the ee (78%) was slightly lower compared with that of $SnCl_4$. The ee were estimated as optical purities, according to the ratio between the optical rotation of the product and that of the pure enone **2*S*** [34] ($[\alpha]_D$ = +248.4). Further lowering in the indium catalyst to 5 mole% led to a similar ee (80%), but the reaction required a longer time (as happened with the use of catalytic $SnCl_4$) and some degradation of the product took place, leading to a lower yield of the reaction (83%).



Lewis acid (mol equiv)	Reaction conditions	Yield (%)	Ratio (%) 2*S*	2*R*
$SnCl_4$ (1.20)	–18 ºC (0.5 h)	85	93	7
$InCl_3$ (0.20)	0 ºC (1h) to rt (2 h)	91	89	11
$InCl_3$ (0.05)	rt (12 h)	83	90	10



Scheme 1. Lewis acid-promoted glycosylation and rearrangement of 2-acetoxyglycals.

In order to obtain enantiomerically pure enones the double allylic rearrangement was conducted in two steps. This is, the intermediate enopyranosides **3α** and **3β**, formed by Ferrier rearrangement upon glycosylation of **1**, were isolated and the major isomer (**3β**) was converted into the enone **2*S***, via a second allylic rearrangement promoted by a Lewis acid.

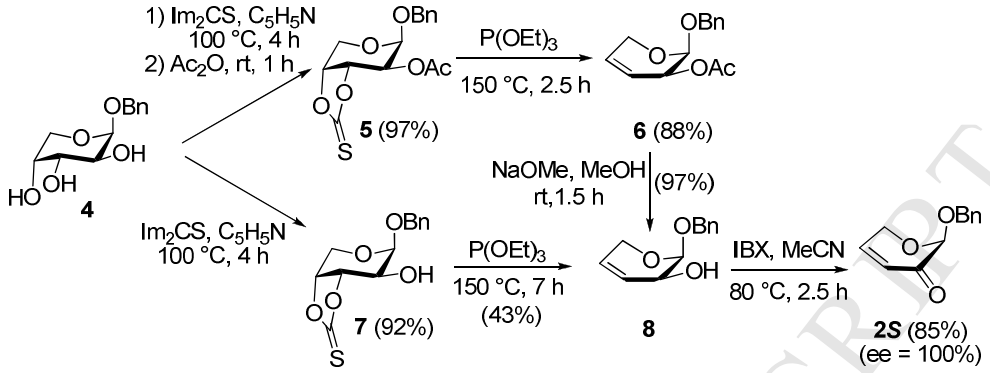
As *N*-iodosuccinimide (NIS) is a convenient reagent for the conversion of 2-acetoxyglycals into enopyranosides [36], the glycosylation of **1** with benzyl alcohol was conducted using catalytic NIS (20 mole%) to successfully produce the enopyranosides **3α,β**. This diastereomeric mixture was separated by column chromatography. The anomeric configuration of each product was stablished by conversion of the major isomer (**3β**) into the known enone (see below) and also on the basis of the ^{1}H NMR spectra. Interestingly, the coupling constant pattern for **3β** showed a high preference of this compound for the $^{5}H_{O}$ conformation as deduced from the values for the vinylic ($^{3}J_{3,4}$ = 6.9 Hz) and allylic ($^{4}J_{1,3}$ ~ 0 Hz) coupling constants in agreement with the magnitude estimated from dihedral angle (Θ) formed between those protons (Garbisch equation [37]). In addition, such a conformation is also supported by the W-coupling between H-3 and H-5eq ($^{4}J_{3,5eq}$ = 1.1 Hz) and the small values for the $J_{4,5ax}$ (2.8 Hz) and $J_{4,5eq}$ (0.9 Hz).

The $^{5}H_{O}$ conformation of **3β** is stabilized by the anomeric and allylic effects [38-40], as both the anomeric benzyloxy and the allylic acetate are axially disposed. In contrast, the isomer **3α** cannot satisfied both stereoelectronic effects, and hence its conformation may be described as an equilibrium $^{5}H_{O} \rightleftharpoons {}^{O}H_{5}$ since $J_{3,4}$, $J_{4,5}$ and $J_{4,5'}$ showed values characteristic of the $^{5}H_{O}$ form ($J_{1,3}$ = 0.6, $J_{1,5}$ = 0.7 and $J_{3,5'}$ = 0.5 Hz), while the small $J_{3,4}$ (2.8 Hz) and large $J_{4,5'}$ (8.0 Hz) magnitudes are indicative of the presence of the $^{O}H_{5}$ conformer. In addition, the long-range homoallylic coupling constant $^{5}J_{1,4}$ = 1.2 Hz, observed only for **3α** is in agreement with the *cis* axial-equatorial disposition of H-1 and H-4 in both conformers [41], while in **3β** these protons are unfavorably disposed (*trans*-diequatorial) and the homoallylic coupling is not detected.

As next step, the enopyranoside **3β** was converted into the pyranone **2*S*** upon treatment with benzyl alcohol and $InCl_3$ (20 mole%). In contrast to our expectations,

compound **2*S*** showed an optical rotation that was in absolute value ($[\alpha]_D = -216$) smaller than that of the enantiomerically pure enone. This result indicated that **3β** underwent partial isomerization of the anomeric center, under the acidic conditions employed for the rearrangement, to give an ee ≈ 87%. To confirm that the product obtained was enantioenriched, NMR experiments were performed using a chiral lanthanide shift reagent for racemic resolution. Thus, addition of increasing amounts of europium (III) tris[3-heptafluoropropylhydroxymethylene-(+)-camphorate] showed gradual splitting of some signal (See Supporting Information). In particular, the anomeric proton signal, which appeared in a clean region of the spectrum, split into two broad singlets. From the integral of these signals (er = 93:7) the enantiomeric composition was estimated as ee ≈ 86%, in agreement with the value determined from the optical rotation.

In view of the difficulties encountered to prepare the enantiomerically pure enone from the glycal **1**, we turned back to the enantioespecific synthesis of **2*S*** or **2*R*** from benzyl pentopyranosides that we have already described [34]. Following, the original synthetic scheme, an improvement was now achieved by modifying the reagents and reaction conditions employed in some steps (Scheme 2). Thus, the starting benzyl β-D-arabinopyranoside (**4**) was treated with 1,1'-thiocarbonylimidazole followed by acetylation to give the 2-*O*-acetyl-3,4-thionocarbonate derivative **5** in 97% yield. The increment in the yield compared with the previous synthesis (75%) was reached by using higher temperature (100 °C against 80 °C) and shorter time (4 h against 40 h) in the formation of the thionocarbonate. In addition, a slight excess of the reagent (1.3 equiv) was added at the beginning of the reaction and no successive additions were required, that led to a larger amount (2.7 equiv) of the reagent in the reported synthesis.



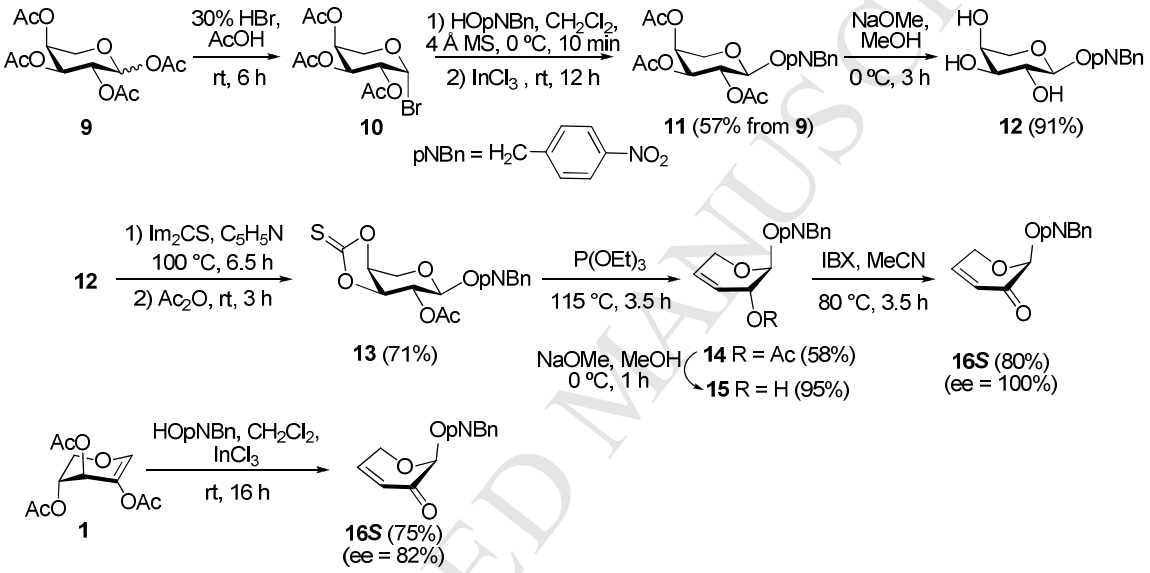
Scheme 2. Enantiospecific synthesis of 2(*S*)-benzyloxy-2*H*-pyran-3(6*H*)-one (**2*S***).

For the Corey-Winter olefination of the thionocarbonate **5** the originally employed trimethyl phosphite, which needed distillation prior to use, was replaced by triethyl phosphite that was used as commercially provided. The yield in both cases was similar (~ 90%) using the same reaction temperature but a shorter time for triethyl phosphite (2.5 h instead of 10 h). Furthermore, it was confirmed that the acetylation step prior to the olefination is needed, as although the alcohol derivative **8** was also obtained in good yield (92%), it partially decomposed during the elimination to afford **7** in 43% yield.

The oxidation of the hydroxyl group of **8** was conducted with 2-iodoxybenzoic acid (IBX), thus avoiding the use of the chromium (VI) oxidizing agent PDC previously employed. The expected enone **2*S*** was obtained after a rapid purification by column chromatography in a yield (85%) somewhat higher than in the PDC oxidation (80%). The optical rotation value of **8** ($[\alpha]_D$ −248.3) was coincident with that determined for the enantiomerically pure enone [34] ($[\alpha]_D$ −248.4).

As next step, we have employed the optimized sequence described above to prepare enone analogues of **2S** with a substituent on the benzyl aromatic ring. As explained in the

introduction section, the resulting enone will be employed as starting material in the synthesis of thiodisaccharides, in order to study how such a substitution modifies the interaction with the *E. coli* β-galactosidase. In first instance, we explore the preparation of the enantiomerically pure enone **16*S*** having an electron withdrawing (nitro) group on the benzyl substituent (Scheme 3).



Scheme 3. Synthesis of 2(*S*)-(4-nitrobenzyloxy)-2*H*-pyran-3(6*H*)-one (**16*S***).

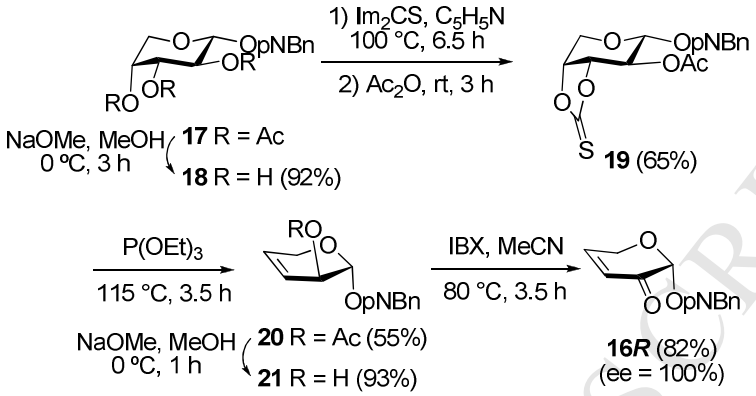
The sequence involves treatment of tetra-*O*-acetyl-α,β-L-arabinopyranose (**9**) with 30% HBr in AcOH to produce the glycosyl bromide **10** [42], which was employed crude for the next step. The glycosylation of **10** with 4-nitrobenzyl alcohol in the presence of $InCl_3$ [43], led after purification by column chromatography the α-L-arabinopyranoside derivative **11**. The ^{1}H NMR spectrum of **11** was in agreement with that previously reported [44]. The anomeric configuration was confirmed based on the coupling constant values for $J_{1,2}$ (7.6 Hz), $J_{2,3}$ (9.3 Hz) and small ones for $J_{3,4}$, $J_{4,5ax}$ and $J_{4,5eq}$ (3.5, 3.6 and 1.9 Hz

respectively). Removal of the acetyl groups of **11** with NaOMe/MeOH gave the crystalline, unprotected glycoside **12**. Compound **12** possesses the convenient *cis* equatorial-axial orientation of OH-3 and OH-4 for the formation of the thionocarbonate ring, which was obtained upon treatment with 1,1'-thiocarbonyldiimidazole to give **13** after acetylation. This compound was sensitive to the temperature employed for the elimination with triethyl phosphite. At 150 °C high decomposition was observed, so the temperature was lowered to 115 °C. After 3.5 h of heating about 50% of conversion of **13** into the enopyranoside **14** was observed, and then the decomposition increased rapidly. Therefore, the mixture was concentrated and fractioned by column chromatography to give enopyranoside **14** and remaining starting **13** was also recovered. A second elimination process applied to the remaining **13** afforded some additional **14** (58% overall yield). The 2-*O*-acetyl group of enopyranoside **14** was quantitatively hydrolyzed with NaOMe/MeOH to the corresponding HO function, which was oxidized with IBX in acetonitrile (80 °C, 3.5 h). The target enone **16S** was thus obtained, although in an overall yield (~32% from **12**) smaller than that of the preparation from **4** (70% overall).

Alternatively, the enone **16*S*** was prepared by the $InCl_3$-promoted glycosylation of glycal **1** with *p*-nitrobenzyl alcohol. The target molecule **16*S*** was obtained in 75% yield, but the optical rotation ($[\alpha]_D = -136.8$) smaller in absolute value to that of **16*S*** obtained from **12**, indicated partial isomerization of the stereocenter (ee ≈ 82%).

In order to obtain the enone **16*R***, enantiomer of **16*S***, the elimination/oxidation route was applied to 4-nitrobenzyl 2,3,4-tri-*O*-acetyl-α-D-arabinopyranoside (**17**) (Scheme 4). Compound **17** was prepared from the enantiomer of **9** as previously described, and it was

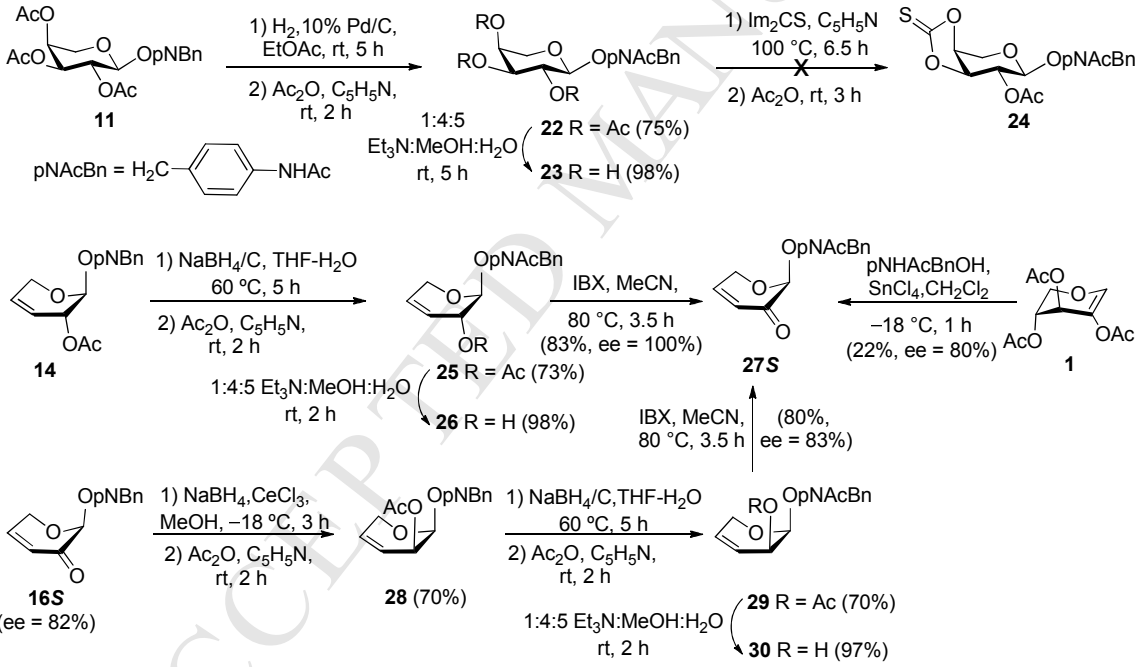
O-deacetylated to give **18**. The 4-nitrobenzyl glycoside **18** was converted into the thionocarbonate **19**, which via the enopyranoside **21** led to **16*R*** (27% overall yield).



Scheme 4. Enantiospecific synthesis of 2(*R*)-(4-nitrobenzyloxy)-2*H*-pyran-3(6*H*)-one (**16*R***).

As described above, the introduction of a nitro substituent on the benzyl group led to a lower yield in the formation of the thionocarbonate **13** from the 4-nitrobenzyl glycoside **12**, with respect to that of and **5** from the benzyl glycoside **4**. The yield was even more severely lowered in the Corey-Winter olefination of thionocarbonate **13** (4-nitrobenzyl) to the enopyranoside **14** compared with the analogous reaction of **5** (benzyl) to **6**. Therefore, the substituent of the benzyl group plays a relevant role in these two reactions. In order to obtain the 2(*S*)-(4-acetamidobenzyloxy)-2*H*-pyran-3(6*H*)-one (**27S**) through a similar route, the 4-acetamidobenzyl α-L-arabinopyranoside (**23**) was required. The attempted preparation of **23** from **9**, according to the route applied for the synthesis of glycoside **12**, was unsuccessful when *p*-acetamidobenzyl alcohol was employed. However, **23** was satisfactorily prepared via **22**, by catalytic hydrogenation of the nitro group of **11** followed by acetylation (Scheme 5). Treatment of **22** with 1:4:5 Et_3N:MeOH:H_2O resulted in the removal of the *O*-protecting groups to afford **23**. The next step of the sequence, the formation of the thionocarbonate **24**, was unsuccessful and led to decomposition under the

varied reaction conditions assayed. Again, the replacement of the benzyl group (in **5**) by 4-acetamidobenzyl (in **23**) led to an unexpected instability of the compounds involved in the thionocarbonation reaction. To overcome this difficulty, an alternative route was designed starting from the enopyranoside **14**. Thus, the nitro group of **14** was successfully reduced under mild conditions with $NaBH_4$/charcoal [45] to give, upon acetylation, the 4-acetamidobenzyl glycoside **25**. Removal of the *O*-acetyl group, followed by IBX-oxidation of the resulting OH group in **26** led to the target enantiomerically pure 2-(4-acetamidobenzyloxy)-pyranone **27*S*** (59% overall yield from **14**).



Scheme 5. Synthesis of 2(*S*)-(4- acetamidobenzyloxy)-2*H*-pyran-3(6*H*)-one (**27*S***).

The enone **27*S*** (having an ee = 80%) was alternatively prepared by the $SnCl_4$-promoted glycosylation of 2-acetoxyglycal **1** with *p*-acetamidobenzyl alcohol, but the yield obtained was low (22%). This reaction failed when the catalyst employed was $InCl_3$. As the

first step in the catalytic process is the coordination of the metal (Lewis acid) with the allylic acetoxy group [4,11], which leads to the allylic rearrangement, probably the acetamido group (a stronger Lewis base) could compete with the acetoxy group for chelation of the metal, diminishing the effective concentration of the catalyst. In this context, In(III), a softer acid than Sn(IV), is expected to exhibit lower reactivity against hard basic centers. These considerations are in agreement with the fact that the analogous reaction with benzyl or *p*-nitrobenzyl alcohols took place with good yields. The enone **16*S*** (ee = 82%), which is the product of the last mentioned reaction, was employed as starting material for the synthesis of **27*S***. Thus, the carbonyl function of **16*S*** was reduced with $NaBH_4$ in the presence of $CeCl_3$ to give, after acetylation, the enol ester **28**. The nitro substituent of the benzyl group of **28** was reduced with $NaBH_4$/charcoal to afford the corresponding amine, which was acetylated to give **29**. The *O*-acetyl group of **29** was hydrolyzed under smooth basic conditions (1:4:5 Et_3N:MeOH:H_2O) to produce the allylic alcohol **30**, which was oxidized with IBX to the target pyranone **27*S*** (26% overall yield from **16*S***). From the optical rotation value of **27*S*** ($[\alpha]_D$ = −137.1) was estimated the ee (83%), which was in agreement with that of the starting enone **16*S***.

In conclusion, we succeeded in the preparation of the target enones derived from pentoses, which have a benzyloxy group or a benzyloxy derivative attached to the anomeric center. The substituent of the benzyloxy group affect the stability of the compounds, and hence the yield of most of the reactions. Thus, the Lewis acid-promoted glycosylation of 2-acetoxyglycals derived from pentoses took place satisfactorily for benzyl or *p*-nitrobenzyl alcohols, but failed for the *p*-acetamidobenzyl alcohol. The pyranones obtained by these

procedures were enantioenriched products, with one of the enantiomers strongly prevailing over the other (high enantiomeric excesses).

A straightforward and high yielding route for the enantioselective synthesis of this type of enones was optimized. Thus, starting from benzyl arabinopyranoside, the corresponding 2-benzyloxy-pyran-3-one was obtained in 70% overall yield and in enantiomerically pure form. However, the nitro substitution on the benzyloxy group of the starting glycoside resulted in a lower yield of two steps of such route: the formation of a thionocarbonate, which involved OH-3 and OH-4 of the pentopyranoside, and the following olefination to the corresponding enopyranoside. The thionocarbonation led only to decomposition in the case of the 4-acetamidobenzyl glycoside. This result, prompted the development of alternative sequences to the enantiomerically pure or enantioenriched 2-(4-acetamidobenzyloxy)pyran-3-one, starting respectively from a 4-nitrobenzyl enopyranoside or enone compounds, that have been prepared as part of previous synthesis within the present work.

3. Experimental section

3.1. General experimental procedures

NMR spectra were recorded (25 °C) at 500 MHz (^{1}H) or 125.7 MHz (^{13}C). Chemical shifts (δ, in ppm) are referred to internal standard (Me_4Si in $CDCl_3$ (δ 0.0) for ^{1}H and $CDCl_3$ (δ 77.0) for ^{13}C) or to a residual solvent peak. Data multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); coupling constants (*J*) given in Hertz (Hz). Assignments of ^{1}H and ^{13}C NMR spectra were assisted by 2D ^{1}H-COSY or NOESY, and 2D ^{1}H-^{13}C HSQC or HMBC experiments. The NMR

spectra for compounds **2*S*** [11], and **4** to **8** [34] were in good agreement with those previously published. High-resolution mass spectra (HRMS) were obtained using the electrospray ionization (ESI) technique and Q-TOF detection. Analytical thin-layer chromatography (TLC) was carried out on silica gel 60 F254 aluminum-supported plates (layer thickness 0.2 mm). The spots were visualized by exposure to UV light and by charring with 5% v/v sulfuric acid in EtOH, containing 0.5% *p*-anisaldehyde. Column chromatography was carried out with silica gel 60 (230–400 mesh) and using a stepwise solvent polarity gradient correlated with TLC mobility, unless otherwise stated. Optical rotations were measured at the sodium D line at room temperature in a 1 dm cell, in the solvent indicated. Unless otherwise noted, all commercially available compounds were used as obtained from suppliers without further purification.

3.2. Synthesis of enantioenriched 2(S)-Benzyloxy-2H-pyran-3(6H)-one **2*S*** *from 2-acetoxyglycal* **1**

3.2.1. Catalysis with $InCl_3$

To a solution of **1** [11] (1.00 g, 3.87 mmol) and benzyl alcohol (0.45 mL, 4.33 mmol) in dry CH_2Cl_2 (30 mL) was added $InCl_3$ (42 mg, 0.19 mmol). The solution was stirred overnight (12 h) at rt. When TLC (CH_2Cl_2/EtOAc 30:1) showed formation of a less polar product (R_f 0.83) and complete disappearance of the starting glycal (R_f 0.28). The organic solution was diluted with CH_2Cl_2 (30 mL) and washed with sat aq $NaHCO_3$, water and brine. After drying ($MgSO_4$), solvent evaporation afforded a residue that was purified by column chromatography (hexane/EtOAc, 9:1) to afford **2*S*** (0,66 g, 83%); and $[\alpha]_D$ −198.0 (*c* 1.13, $CHCl_3$); ee = 80%.

3.2.2. Via the enopyranoside **3β**

3.2.2.1. Benzyl 2,4-di-O-acetyl-3-deoxy-β-D-glycero-pent-2-enopyranoside **3β** *and its α-anomer* **3α**

A solution of benzyl alcohol (0.24 mL, 2.3 mmol) and NIS (90 mg, 0.39 mmol) in dry CH_2Cl_2 (2.0 mL) was stirred at room temperature. When the pale-yellow solution turned to a light red color, the mixture was cooled to −18 °C and 2,3,4-tri-*O*-acetyl-1,5-anhydro-D-*threo*-pent-1-enitol (2-acetoxy-3,4-di-*O*-acetyl-D-xylal **1**, 500 mg, 1.92 mmol) was added. The temperature was kept for 1 h and then the solution was allowed to reach room temperature and it was stirred for 30 min. At this point TLC (CH_2Cl_2/EtOAc 20:1) revealed the conversion of the starting **1** (R_f 0.40) into two main products (R_f 0.69 and 0.62), which were separated by column chromatography (19:1→9:1 hexane/EtOAc). The first compound that eluted from the column was identified as **3α** (180 mg, 31%); $[\alpha]_D$ +69.2 (*c* 1.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40–7.29 (m, 5H, OBn), 5.79 (dt, 1H, $J_{1,3} \approx J_{3,5'}$ = 0.6, $J_{3,4}$ = 2.8 Hz, H-3), 5.50 (dddd, 1H, $J_{1,4}$ = 1.2, $J_{3,4}$ = 2.8, $J_{4,5}$ = 5.6, $J_{4,5'}$ = 8.0 Hz, H-4), 5.14 (m, 1H, $J_{1,3} \approx J_{1,5} \approx$ 0.6, $J_{1,4}$ = 1.2 Hz, H-1), 4.84, 4.62 (2 d, 2H, *J* = 12.0 Hz, OC*H*$_2$Ar), 3.95 (ddd, 1H, $J_{1,5}$ = 0.7, $J_{4,5}$ = 5.6, $J_{5,5'}$ = 11.2 Hz, H-5), 3.90 (ddd, 1H, $J_{3,5'}$ = 0.5, $J_{4,5'}$ = 8.0, $J_{5,5'}$ = 11.2 Hz, H-5'), 2,14, 2.09 (2 s, 3H each, C*H*$_3$CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.4, 168.2 (CH_3*C*O), 147.4 (C-2), 137.3, 128.4, 127.9, 127.8 (*C*-aromatic), 115.3 (C-3), 92.9 (C-1), 70.3 (O*C*H$_2$Ar), 65.5 (C-4), 60.2 (C-5), 20.9, 20.8 (*C*H$_3$CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{18}NaO_6$ 329.0996, found 329.1004; $[M+K]^+$ calcd for $C_{16}H_{18}KO_6$ 345.0735, found 345.0727.

From further fractions from the column compound was isolated **3β** (160 mg, 51%); $[\alpha]_D$ +52.7 (*c* 0.53, $CHCl_3$); ee = 100%; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40–7.29 (m, 5H, OBn), 5.90 (dd, 1H, $J_{3,4}$ = 6.9, $J_{3,5eq}$ = 1.1 Hz, H-3), 5.18 (ddd, 1H, $J_{3,4}$ = 6.9, $J_{4,5ax}$ = 2.8,

$J_{4,5eq}$ = 0.9 Hz, H-4), 5.09 (s, 1H, H-1), 4.78, 4.59 (2 d, 2H, J = 12.2 Hz, OCH_2Ar), 4.19 (dd, 1H, $J_{4,5ax}$ = 2.8, $J_{5ax,5eq}$ = 13.0 Hz, H-5ax), 3.84 (dt, 1H, $J_{3,5eq} \approx J_{4,5eq}$ = 1.0, $J_{5ax,5eq}$ = 13.0 Hz, H-5eq), 2,12, 2.08 (2 s, 3H each, CH_3CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.6, 167.9 (CH_3CO), 149.2 (C-2), 137.3, 128.4, 128.0, 127.9 (C-aromatic), 111.7 (C-3), 92.0 (C-1), 70.1 (OCH$_2$Ar), 64.9 (C-4), 61.2 (C-5), 21.0, 20.9 (CH$_3$CO). Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74%; H, 5.92%. Found: C, 62.79%; H, 5.97%. HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{18}NaO_6$ 329.0996, found 329.0997; $[M+K]^+$ calcd for $C_{16}H_{18}KO_6$ 345.0735, found 345.0722.

3.2.2.2. Conversion of the β-enopyranoside **3β** *into 2(S)-benzyloxy-2H-pyran-3(6H)-one* **2*S***.

A solution of **3β** (155 mg, 0.51 mmol) and benzyl alcohol (0.1 mL, 1.0 mmol) in anhydrous CH_2Cl_2 (1 mL) was stirred at room temperature and $InCl_3$ (24 mg, 0.10 mmol) was added. The reaction was kept for 2 h, when monitoring by TLC (CH_2Cl_2/EtOAc 20:1) revealed complete conversion of the starting material (R_f 0.69) into a less polar product (R_f 0.72). The mixture was diluted with CH_2Cl_2 and extracted with 10% aq $NaHCO_3$ and brine. The organic extract was dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography as above led to enone **2*S*** (85 mg, 82%); $[\alpha]_D$ −216 (*c* 1.40, $CHCl_3$); ee = 88% (from optical purity).

3.2.2.3. Enantiomeric resolution of 2(S)-benzyloxy-2H-pyran-3(6H)-one **2*S***.

The enantiomeric excess (ee) for enone **2*S*** obtained from the enopyranoside **3β**, as described in item 3.2.2.2, was determined by ^{1}H NMR using europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] as a chiral resolving reagent. To a solution of **2*S*** (0.05 mmol) in carbon tetrachloride containing 1% benzene-d_6 (0.6 mL) was

added increasing amounts of the europium reagent. When 0.3 molar equiv were added, the ^{1}H NMR spectrum showed a splitting of the H-1 signal into two broad singlets (enantiomeric shift difference $\Delta\Delta\delta$ = 0.12). From the integral of these signals (**2*S***:**2*R*** 0.93:0.07), the enantiomeric composition (ee ≈ 86%) was established for **2*S***.

3.3. Synthesis of enantiomerically pure 2(S)-Benzyloxy-2H-pyran-3(6H)-one **2*S*** from benzyl glycoside **4**

3.3.1. Benzyl 2-O-acetyl-β-D-arabinopyranoside 3,4-thionocarbonate **5**

Benzyl β-D-arabinopyranoside **4** (719 mg, 3.00 mmol) was dissolved in pyridine (6.8 mL) in a thick-wall tube, and 1,1′-thiocarbonyldiimidazole (719 mg, 4.03 mmol) was added. The tube was sealed and heated to 100 °C for 4 h under an inert Ar atmosphere. TLC analysis (hexane/EtOAc 1:1) showed complete conversion of **4** (R_f 0) into **7** (R_f 0.79). The mixture was left to reach temperature and acetic anhydride (2.8 mL) was added. After stirring for 1 h, the solution was diluted with MeOH and concentrated. The residue was purified by column chromatography (hexane/EtOAc 9:1→8:2) to afford **5** (938 mg, 97%); $[\alpha]_D$ −235.1 (*c* 0.8, $CHCl_3$, lit. [34] $[\alpha]_D$ −234.7).

3.3.2. Benzyl 2-O-acetyl-3,4-dideoxy-α-L-glycero-pent-3-enopyranoside **6**

The thionocarbonate **5** (516 mg, 1.59 mmol) was dissolved in commercial triethyl phosphite (3.8 mL). The tube was sealed under N_2 atmosphere and heated at 150 °C for 2.5 h when TLC (hexane/EtOAc 2:1) showed complete conversion into a single spot of R_f 0.64. Triethyl phosphite was distilled under vacuum and the resulting syrup was subjected to column chromatography (hexane/EtOAc 2:1) to afford the enopyranoside **6** (348 mg, 88%); $[\alpha]_D$ −128.9 (*c* 0.9, $CHCl_3$, lit. [34] $[\alpha]_D$ −131.4).

3.3.3. Benzyl β-D-arabinopyranoside 3,4-thionocarbonate **7**

Compound **7** was synthetized under the conditions described for **5**. The glycoside **4** (419 mg, 1.74 mmol) was allowed to react with 1,1′-thiocarbonyldiimidazole in pyridine at 100 °C for 4 h. The solvent was distilled under vacuum with toluene and the residue was purified by column chromatography (hexane/EtOAc 9:1→8:2) to afford **7** (455 mg, 92%); $[\alpha]_D$ −170.9 (*c* 0.70, $CHCl_3$, lit. [34] $[\alpha]_D$ +172.1 for the enantiomer).

3.3.4. Benzyl 3,4-dideoxy-α-L-glycero-pent-3-enopyranoside **8**

*3.3.4.1. Starting from the enopyranoside **6***

The 2-*O*-acetyl derivative **6** (348 mg, 1.40 mmol) was treated with NaOMe/MeOH 0.1 M, 15 mL) at room temperature for 1.5 h. TLC (hexane/EtOAc 2:1) showed complete conversion into a lower moving compound (R_f 0.49). The reaction mixture was diluted with MeOH and neutralized with Dowex 50W (H^+) resin, filtered and concentrated up to dryness, to afford **8** (280 mg, 97%); $[\alpha]_D$ −131.9 (*c* 1.1, $CHCl_3$, lit. [34] $[\alpha]_D$ −132.3).

3.3.4.2. Starting from thionocarbonate **7**

Compound **7** (419 mg, 1.48 mmol) was heated in a sealed tube under N_2 atmosphere with commercial triethyl phosphite (4 mL) at 150 °C for 7 h. TLC (hexane/EtOAc 2:1) showed complete consumption of **7** (R_f 0.37) and formation of a higher moving compound (R_f 0.49) as main product. The same work-up as above and purification by column chromatography (hexane/EtOAc 9:1→8:2) afforded **8** (133 mg, 43%); $[\alpha]_D$ −131.5 (*c* 0.9, $CHCl_3$, lit. [34] $[\alpha]_D$ −132.3).

3.3.5. Oxidation of enopyranoside **8** *to 2(S)-benzyloxy-2H-pyran-3(6H)-one* **2*S***.

To a solution of **8** (120 mg, 0.58 mmol) in anhydrous MeCN (3.5 mL) was added 2-iodoxybenzoic acid (IBX, 354 mg, 1.26 mmol) and stirred at 80 °C for 2.5 h. The reaction mixture was diluted with CH_2Cl_2 and filtered through a celite bed. Concentration of the filtrate and further purification by column chromatography (hexane/EtOAc, 9:1) led to **2*S*** (101 mg, 85%); $[\alpha]_D$ −248.3 (*c* 1.03, $CHCl_3$, lit. [34] $[\alpha]_D$ −248.4).

3.4. Synthesis of enantiomerically pure 2(S)-(4-Nitrobenzyloxy)-2H-pyran-3(6H)-one **16*S*** *from 4-nitrobenzyl glycoside* **12**

3.4.1. 4-Nitrobenzyl 2,3,4-tri-O-acetyl-α-L-arabinopyranoside **11**

Per-*O*-acetyl-α,β-L-arabinopyranose **9** (700 mg, 2.20 mmol) was stirred in the dark with a solution of 30% HBr in glacial acetic acid (2.2 mL) at 0 °C for 1 h and then at room temperature for 5 h, when monitoring by TLC (hexane/EtOAc 1:1) showed complete conversion of the starting material (R_f 0.64) into a less polar product (R_f 0.79). The reaction mixture was diluted with CH_2Cl_2 and extracted twice with cold sat aq $NaHCO_3$. The organic extract was dried, filtered and concentrated in vacuo at 20 °C in a dark brown round-bottom flask, to avoid exposure to light. The crude glycosyl bromide **10** [42] was dissolved in dry CH_2Cl_2 (20 mL) and 4-nitrobenzyl alcohol (370 mg, 2.42 mmol) and recently dried 4Å molecular sieves (500 mg) were added. The mixture was stirred for 10 min at 0 °C and upon addition of $InCl_3$ (240 mg, 1.08 mmol) the stirring was continued at room temperature overnight (14 h). Monitoring by TLC (hexane/EtOAc 1:1) showed a main spot (R_f 0.60) and disappearance of the starting bromide. The reaction was diluted with CH_2Cl_2 and filtered through a celite bed. Purification by column chromatography (hexane/EtOAc 4:1→3:2) led to **11** (516 mg, 57%) as a pale-yellow syrup; $[\alpha]_D$ −19.0 (*c* 0.8, $CHCl_3$, lit. [44] $[\alpha]_D$ −11); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.21, 7.48 (d, 2H, *J* = 8.8 Hz,

H-aromatic), 5.30 (dd, 1H, $J_{1,2}$ = 6.6, $J_{2,3}$ = 9.3 Hz, H-2), 5.29 (m, 1H, overlapped with H-2, H-4), 5.08 (dd, 1H, $J_{2,3}$ = 9.3, $J_{3,4}$ = 3.5 Hz, H-3), 4.99, 4.70 (2d, 2H, J = 13.3 Hz, -OC*H*$_2$Ar), 4.55 (d, 1H, $J_{1,2}$ = 6.6 Hz, H-1), 4.06 (dd, 1H, $J_{4,5ax}$ = 3.6, $J_{5ax,5eq}$ = 13.0 Hz, H-5ax), 3.66 (dd, 1H, $J_{4,5eq}$ = 1.9, $J_{5ax,5eq}$ = 12.9 Hz, H-5eq); 2.14, 2.07, 2.03 (s, 3H each, C*H*$_3$CO-); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.4, 170.2, 169.6 (CH$_3$*C*O), 147.6, 144.8, 127.6, 123.8 (C-aromatic), 100.2 (C-1), 70.0 (C-3), 69.2 (C-4,O*C*H$_2$Ar), 67.5 (C-2), 63.2 (C-5), 21.1, 20.9, 20.8 (*C*H$_3$CO). HRMS (ESI) m/z [M+Na]$^+$ calcd for $C_{18}H_{21}NNaO_{10}$ 434.1058, found 434.1077.

3.4.2. 4-Nitrobenzyl α-L-arabinopyranoside **12**

Glycoside **11** (339 mg, 0.82 mmol) was treated with 0.4 M NaOMe/MeOH (12 mL) at 0 °C for 3 h. The reaction mixture was diluted with MeOH, neutralized with Dowex-H$^+$ resin and filtered. Solvent evaporation and recrystallization from EtOH afforded **12** (210 mg, 91%) as white solid product; mp 88-89 °C; $[\alpha]_D$ −17.1 (*c* 0.9, MeOH); ^{1}H NMR (pyridine-d_5 with D_2O, 500 MHz) δ 8.09, 7.64 (d, 2H, J = 8.3 Hz, H-aromatic), 5.15, 4.90 (2d, 2H, J = 13.6 Hz, OC*H*$_2$Ar), 4.81 (d, 1H, $J_{1,2}$ = 8.3 Hz, H-1), 4.56 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 8.3 Hz, *H*-2), 4.37 (m, 2H, H-4, H-5eq), 4.22 (dd, 1H, $J_{2,3}$ = 8.8, $J_{3,4}$ = 3.2 Hz, H-3), 3.81 (dd, 1H, $J_{4,5ax}$ = 2.4, $J_{5ax,5eq}$ = 12.9 Hz, H-5ax); ^{13}C NMR (pyridine-d_5 with D_2O, 125.7 MHz) δ 136.2, 128.7, 124.2, 124.0 (C-aromatic), 105.1 (C-1), 74.9 (C-3), 72.8 (C-2), 69.8 (O*C*H$_2$Ar), 69.7 (C-4), 67.6 (C-5). HRMS (ESI) m/z; [M+Na]$^+$ calcd for $C_{12}H_{15}NNaO_7$ 308.0741, found 308.0749.

3.4.3. 4-Nitrobenzyl 2-O-acetyl-α-L-arabinopyranoside 3,4-thionocarbonate **13**

A solution of glycoside **12** (150 mg, 0.52 mmol) and 1,1'-thiocarbonyldiimidazole (120 mg, 0.67 mmol) in pyridine (1.2 mL) was stirred at 100 °C for 6.5 h. Monitoring by

TLC (hexane/EtOAc 1:1.5) showed a faster moving spot (R_f 0.28). Acetic anhydride (1 mL) was added to the mixture and the stirring was continued at room temperature for 3 h, when analysis by TLC (hexane/EtOAc 1:1.5) revealed a main spot (R_f 0.50). The mixture was diluted with methanol and concentrated. The residue was purified by column chromatography (hexane/EtOAc 4:1→3:2) to afford **13** (138 mg, 71%) as main product; $[\alpha]_D$ −151.5 (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.20, 7.50 (d, 2H, *J* = 8.6 Hz, H-aromatic), 5.18 (t, 1H, $J_{1,2} \approx J_{2,3} \approx 3.8$ Hz, H-2), 5.06 (dt, 1H, $J_{4,5} \approx J_{4,5'} \approx 4.1$, $J_{3,4} = 8.2$ Hz, H-4), 4.96 (dd, 1H, $J_{3,4} = 8.1$, $J_{3,4} = 3.8$ Hz, H-3), 4.92, 4.68 (2d, 2H, *J* = 13.4 Hz, -OC*H*$_2$Ar), 4.81 (d, 1H, $J_{1,2} = 3.6$ Hz, H-1), 4.19 (dd, 1H, $J_{5,5'} = 13.5$, $J_{4,5} = 4.2$ Hz, H-5), 3.98 (dd, 1H, $J_{5,5'} = 13.5$, $J_{4,5'} = 4.0$ Hz, H-5); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 190.1 (C=S), 169.0 (CH_3*C*O-), 147.7, 144.0, 128.0, 123.8 (C-aromatic), 97.3 (C-1), 77.8 (C-3), 76.2 (C-2), 69.0 (O*C*H$_2$Ar), 68.0 (C-2), 60.0 (C-5), 20.8 (*C*H$_3$CO-). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{15}H_{15}NNaO_8S$ 392.0411, found 392.0424.

3.4.4. 4-Nitrobenzyl 2-O-acetyl-3,4-dideoxy-β-D-glycero-pent-3-enopyranoside **14**

The thionocarbonate **13** (130 mg, 0.35 mmol) was dissolved in triethyl phosphite (3 mL) and heated in a sealed tube under N_2. After stirring at 115 °C for 3.5 h, TLC (hexane/EtOAc 1:1) showed the formation of a main product (R_f 0.67) and some stating material (R_f 0.22) remaining. Column chromatography (hexane/EtOAc 4:1→3:2) led to **14** (46 mg, 45%) and then the remaining **13** (36 mg, 0.10 mmol) was recovered. The unreacted **13** was treated with triethyl phosphite as described above. Column chromatography afforded some additional **14** (14 mg, 58% overall yield); $[\alpha]_D$ −243.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.22, 7.52 (d, 2H, *J* = 8.6 Hz, H-aromatic), 6.11 (dt, 1H, $J_{3,4} = 10.5$, $J_{4,5} \approx J_{4,5'} \approx 2.6$ Hz, H-4), 5.88 (ddd, 1H, $J_{2,3} = 4.2$, $J_{4,5} = 10.5$, $J_{3,5'} = 2.3$ Hz, H-3),

5.08 (br d, 1H, $J_{2,3}$ = 4.2 Hz, H-2), 4.91 (d, 1H, $J_{1,2}$ < 1.0 Hz, H-1), 4.90, 4.73 (2d, 2H, *J* = 13.4 Hz, OC*H*$_2$Ar), 4.21 (t, 2H, *H*-5, *H*-5'), 2.10 (s, 3H, C*H*3CO-); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.5 (CH_3*C*O-), 147.7, 145.1, 127.9, 123.9 (C-aromatic), 131.3 (C-4), 120.3 (C-3), 97.4 (C-1), 68.6 (O*C*H$_2$Ar), 65.9 (C-2), 59.9 (C-5), 21.2 (*C*H$_3$CO-). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{15}NNaO_6$ 316.0792, found 316.0798.

3.4.5. 4-Nitrobenzyl 3,4-dideoxy-β-D-glycero-pent-3-enopyranoside **15**

Compound **14** (112 mg, 0.38 mmol) was treated with NaOMe/MeOH (0.2 M, 6 mL) at 0 °C for 1 h. TLC (hexane/EtOAc 1:1.5) showed complete conversion of **14** (R_f 0.74) into a lower moving compound (R_f 0.44). The reaction mixture was diluted with MeOH and neutralized with Dowex 50W (H^+) resin, filtered and concentrated up to dryness, to afford **15** (91 mg, 95%); $[\alpha]_D$ −184.0 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.21, 7.52 (d, 2H, *J* = 8.5 Hz, H-aromatic), 5.95 (dt, 1H, $J_{3,4}$ = 10.4, $J_{4,5} \approx J_{4,5'} \approx$ 2.1 Hz, H-4), 5.91 (ddd, 1H, $J_{2,3}$ = 2.0, $J_{3,4}$ = 10.4, $J_{3,5'}$ = 3.7 Hz, H-3), 4.92, 4.72 (2d, 2H, *J* = 13.3 Hz, -OC*H*$_2$Ar), 4.81 (d, 1H, $J_{1,2}$ = 2.7 Hz, H-1), 4.22 (ddd, 1H, $J_{4,5}$ = 2.0, $J_{3,5}$ = 3.7, $J_{5,5'}$ = 17.0 Hz, H-5), 4.15 (dq, 1H, $J_{3,5'} \approx J_{4,5'} \approx$ 2.1 Hz, H-5'), 3.97 (m, 1H, H-2), 1.93 (d, 1H, $J_{2,OH}$ = 8.3 Hz, O*H*); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 147.6, 145.2, 128.0, 123.8 (C-aromatic), 129.0 (C-4), 124.6 (C-3), 100.53 (C-1), 68.9 (O*C*H$_2$Ar), 64.9 (C-2), 61.1 (C-5). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{12}H_{13}NNaO_5$ 274.0686, found 274.0679.

3.4.6. 2(S)-(4-Nitrobenzyloxy)-2H-pyran-3(6H)-one **16*S***

To a solution of **15** (90 mg, 0.36 mmol) in dry MeCN (3 mL) was added IBX (235 mg, 0.84 mmol) and stirred at 80 °C for 3.5 h. The reaction mixture was diluted with CH_2Cl_2 and filtered through a celite bed. Concentration of the filtrate and further purification by column chromatography (hexane/EtOAc 4:1) led to **16*S*** (72 mg, 80%).

$[\alpha]_D$ −166.6 (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 8.21, 7.52 (d, 2H, *J* = 8.0 Hz, H-aromatic), 7.09 (dt, 1H, $J_{4,3}$ = 10.6, $J_{5,6}$ = 1.8, $J_{5,6'}$ = 1.8 Hz, H-5), 6.17 (dddd, 1H, $J_{2,4}$ < 1.0, $J_{3,4}$ = 10.6, $J_{4,6}$ = 2.5, $J_{4,6'}$ = 1.8 Hz, H-4), 4.93 (br d, 1H, $J_{2,3}$ < 1.0 Hz, H-2), 4.93, 4.81 (2d, 2H, *J* = 13.2 Hz, OCH_2Ar), 4.54 (ddd, 1H, $J_{4,6}$ = 2.4, $J_{5,6}$ = 2.1, $J_{6,6'}$ = 19.1 Hz, H-6), 4.33 (ddd, 1H, $J_{4,6'}$ = 1.9, $J_{5,6'}$ = 3.9, $J_{6,6'}$ = 19.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 188.1 (C-3), 148.1 (C-5), 147.7, 144.4, 128.0, 123.9 (C-aromatic), 124.9 (C-4), 97.5 (C-2), 69.4 (OCH_2Ar), 60.0 (C-6). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{15}NNaO_6$ 272.0529, found 272.0519.

3.5. Synthesis of enantioenriched 2(S)-(4-nitrobenzyloxy)-2H-pyran-3(6H)-one **16*S*** *starting from 2-acetoxyglycal* **1**

To a solution of compound **1** (502 mg, 1.94 mmol) and 4-nitrobenzyl alcohol (300 mg, 1.96 mmol) in anhydrous CH_2Cl_2 (10 mL) was added $InCl_3$ (22 mg, 0.10 mmol), and the solution was stirred overnight (16 h) at rt. Analysis by TLC (CH_2Cl_2/EtOAc 30:1) showed formation of a less polar product (R_f 0.76) and complete disappearance of the starting glycal (R_f 0.28). The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with sat aq $NaHCO_3$, water and brine. After drying ($MgSO_4$), solvent evaporation afforded a residue that was purified by column chromatography (hexane/EtOAc, 9:1→4:1) to afford **16*S*** (364 mg, 75%); and $[\alpha]_D$ −136.8 (*c* 0.8, $CHCl_3$). The optical rotation indicated an ee ~ 82%.

3.6. Synthesis of enantiomerically pure 2(R)-(4-Nitrobenzyloxy)-2H-pyran-3(6H)-one **16*R*** *from 4-nitrobenzyl glycoside* **18**

The NMR spectra of compounds **17-21** and **16*R*** were in good agreement with those of the respective enantiomers of section 3.4.

3.6.1. 4-Nitrobenzyl 2,3,4-tri-O-acetyl-α-D-arabinopyranoside **17**

The procedure for the glycosylation of **9** applied to per-*O*-acetyl-α,β-D-arabinopyranose (480 mg, 1.50 mmol) afforded **17** (328 mg, 53%); $[\alpha]_D$ +21.3 (*c* 1.1, $CHCl_3$).

3.6.2. 4-Nitrobenzyl α-D-arabinopyranoside **18**

Deacetylation of **17** (280 mg, 0.68 mmol) gave **18** (178 mg, 92%); Mp 89 °C; $[\alpha]_D$ +17.3 (*c* 0.9, MeOH).

3.6.3. 4-Nitrobenzyl 2-O-acetyl-α-D-arabinopyranoside 3,4-thionocarbonate **19**

The synthesis of **13** from **12** was applied to **18** (130 mg, 0.45 mmol) to afford **19** (108 mg, 65%); $[\alpha]_D$ +153.1 (*c* 0.5, $CHCl_3$).

3.6.4. 4-Nitrobenzyl 2-O-acetyl-3,4-dideoxy-β-L-glycero-pent-3-enopyranoside **20**

Heating compound **19** (98 mg, 0.26 mmol) under the conditions stated for **13** led to **20** (42 mg, 55% overall yield); $[\alpha]_D$ +247.3 (*c* 0.5, $CHCl_3$).

3.6.5. 4-Nitrobenzyl 3,4-dideoxy-β-L-glycero-pent-3-enopyranoside **21**

Removal of the *O*-acetyl group from **20** (40 mg, 0.14 mmol) afforded **21** (33 mg, 93%); **[**$\alpha]_D$ +180.3 (*c* 0.7, $CHCl_3$).

3.6.6. 2(R)-(4-Nitrobenzyloxy)-2H-pyran-3(6H)-one **16*R***

Oxidation of **21** (32 mg, 0.13 mmol) with IBX, as described for **16*S***, gave **16*R*** (27 mg, 82%); **[**α]$_D$ +165.8 (*c* 0.8, $CHCl_3$).

3.7. Synthesis of enantiomerically pure 2(S)-(4-acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S*** *from glycoside* **11**

3.7.1. 4-Acetamidobenzyl 2,3,4-tri-O-acetyl-α-L-arabinopyranoside **22**

The glycoside **11** (424 mg, 1.03 mmol) was dissolved in EtOAc (20 mL) and treated with H_2 in the presence of 10% Pd/C (63 mg) at rt for 5 h. Monitoring by TLC (hexane/EtOAc 1:1.5) showed conversion of **11** (R_f 0.60) into a lower moving spot (R_f 0.43). The reaction mixture was diluted with CH_2Cl_2, filtered through a celite bed and concentrated. The crude product was acetylated with acetic anhydride (0.9 mL) in pyridine (1,5 mL) at rt for 2 h, when TLC (EtOAc) showed a main product of R_f 0.62. The solution was diluted with MeOH and concentrated. The residue was purified by column chromatography (hexane/EtOAc 3:2→2:3) to afford **22** (327 mg, 75%); [α]$_D$ –25.0 (c 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50, 7.22 (d, 2H, *J* = 8.1 Hz, H-aromatic), 7.43 (br s, 1H, N*H*), 5.31 (m, 1H, overlapped with H-2, H-4), 5.21(dd, 1H, $J_{1,2}$ = 6.8, $J_{2,3}$ = 9.3 Hz, H-2), 5.01 (dd, 1H, $J_{2,3}$ = 9.2, $J_{3,4}$ = 3.5 Hz, H-3), 4.85, 4.55 (2d, 2H, *J* = 12.2 Hz, -OC*H*$_2$Ar), 4.47 (d, 1H, $J_{1,2}$ = 6.8 Hz, H-1), 4.05 (dd, 1H, $J_{4,5a}$ = 3.5, $J_{5a,5b}$ = 13.0 Hz, H-5a), 3.62 (dd, 1H, $J_{4,5b}$ = 1.6, $J_{5a,5b}$ = 13.0 Hz, H-5eq); 2.16, 2.12, 2.02, 2.00 (s, 3H each, C*H*$_3$CO-); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.5, 170.3, 169.6, 168.5 (CH_3*C*O), 137.8, 132.9, 128.6, 119.9 (C-aromatic), 99.5 (C-1), 70.2 (C-3), 70.1 (O*C*H$_2$Ar), 69.3 (C-2), 67.7 (C-4), 63.1 (C-5), 24.7, 21.0, 20.9, 20.8 (*C*H$_3$CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{20}H_{25}NNaO_9$ 446.1422, found 446.1420.

3.7.2. 4-Acetamidobenzyl α-L-arabinopyranoside **23**

Glycoside **22** (300 mg, 0.71 mmol) was treated with 1:4:5 Et_3N:MeOH:H_2O (2.5 mL) and stirred at rt for 5 h, when TLC (EtOAc) showed complete conversion of **22** (R_f 0.62) into a main spot (R_f 0). Reaction mixture was concentrated to dryness to afford **23** (207 mg, 98%); $[\alpha]_D$ −18.3 (c 1.0, MeOH); ^{1}H NMR (pyridine-d_5, 500 MHz) δ 7.98, 7.53 (d, 2H, J = 8.5 Hz, H-aromatic), 5.11, 4.79 (2d, 2H, J = 11.7 Hz, OCH_2Ar), 4.81 (d, 1H, $J_{1,2}$ = 7.0 Hz, H-1), 4.50 (t, 1H, $J_{1,2}$ = 7.1, $J_{2,3}$ = 8.7 Hz, *H*-2), 4.36 (m, 2H, H-4, H-5eq), 4.19 (dd, 1H, $J_{2,3}$ = 8.7, $J_{3,4}$ = 3.0 Hz, H-3), 3.78 (dd, 1H, $J_{4,5ax}$ = 2.7, $J_{5ax,5eq}$ = 13.3 Hz, H-5ax); ^{13}C NMR (pyridine-d_5, 125.7 MHz) δ 169.3 (CH_3CO), 140.4, 134.1 129.6, 120.3 (C-aromatic), 104.7 (C-1), 75.0 (C-3), 72.9 (C-2), 69.8 (OCH_2Ar), 69.9 (C-4), 67.4 (C-5), 24.7 (CH_3CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{20}H_{25}NNaO_9$ 446.1422, found 446.1420.

3.7.3. 4-Acetamidobenzyl 2-O-acetyl-α-L-arabinopyranoside 3,4-thionocarbonate **24**

All the attempts to prepare **24** from glycoside **23** at temperatures ranging from 50 to 100 °C were unsuccessful, as highly polar decomposition products were formed in all cases.

3.8. Synthesis of enantiomerically pure 2(S)-(4-acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S*** *from enopyranoside* **14**

3.8.1. 4-Acetamidobenzyl 2-O-acetyl-3,4-dideoxy-β-D-glycero-pent-3-enopyranoside **25**

To a solution of **14** (135 mg, 0.46 mmol) in a mixture of THF (6 mL) and H_2O (3 mL), was added activated charcoal (160 mg) and $NaBH_4$ (104 mg, 2.7 mmol). After 3 hours of stirring at 60 °C an additional amount of $NaBH_4$ (153 mg, 4.0 mmol) was added and the stirring was maintained for 2 h. TLC (hexane/EtOAc 1:1) showed complete conversion of

14 (R_f 0.66) into a more polar product (R_f 0.20). The mixture was diluted with MeOH, filtered through a celite bed and concentrated. The crude product was acetylated with acetic anhydride (1 mL) in pyridine (1 mL) at rt for 2 h and concentrated. The residue was purified by column chromatography (hexane/EtOAc 4:1→3:2) to afford **25** (102 mg, 73%). $[\alpha]_D$ −199.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.51–7.28 (2 d, 4H, *J* = 8.3 Hz, H-aromatic), 7.20 (br s, 1H, -N*H*), 6.08 (dt, 1H, $J_{4,5} \approx J_{4,5'} \approx 2.3$, $J_{3,4}$ = 10.4 Hz, H-4), 5.85 (m, 1H, H-3), 4.99 (br d, $J_{2,3}$ = 4.0 Hz, H-2), 4.87 (br s, 1H, H-1), 4.75, 4.58 (2 d, 2H, *J* = 12.0 Hz, OC*H*$_2$Ar), 4.24 (ddd, 1H, $J_{3,5}$ = 2.1, $J_{4,5}$ = 4.2, $J_{5,5'}$ = 7.1 Hz, H-5), 4.16 (dt, 1H, $J_{3,5'} \approx J_{4,5'} \approx 2.3$, $J_{5,5'}$ = 7.1 Hz, H-5'), 2.17, 2.07 (2 s, 3H each, C*H*$_3$CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.4, 168.4 (CH_3*C*O), 137.7, 133.3, 128.9, 120.0 (*C*-aromatic), 131.4 (C-4), 122.3 (C-3), 96.6 (C-1), 69.5 (O*C*H$_2$Ar), 66.1 (C-2), 59.7 (C-5), 24.8, 21.2 (*C*H$_3$CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{19}NNaO_5$ 328.1155, found 328.1165.

3.8.2. 4-Acetamidobenzyl 3,4-dideoxy-β-D-glycero-pent-3-enopyranoside **26**

Compound **25** (100 mg, 0.33 mmol) was dissolved in 1:4:5 Et_3N:MeOH:H_2O (2.5 mL) and stirred at rt for 2 h. Monitoring by TLC (hexane/EtOAc 1:3) showed conversion of **25** (R_f 0.58) into a more polar product (R_f 0.25). The reaction mixture was concentrated to dryness to afford **26** (85 mg, 98%); $[\alpha]_D$ −195.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50–7.28 (2 d, 4H, *J* = 8.2 Hz, H-aromatic), 7.40 (br s, 1H, N*H*), 5.92 (br d, 1H, $J_{3,4}$ = 10.6 Hz, H-4), 5.87 (br d, 1H, $J_{3,4}$ = 10.6 Hz, H-3), 4.77 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 4.77, 4.56 (2 d, 2H, *J* = 11.8 Hz, OC*H*$_2$Ar), 4.24 (m, 1H, $J_{5,5'}$ = 16.9 Hz, H-5), 4.13 (m, 1H, $J_{5,5'}$ = 16.9 Hz, H-5'), 3.91 (m, 1H, $J_{1,2}$ = 1.5 Hz, H-2), 2.16 (1 s, 3H, C*H*$_3$CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 168.5 (CH_3*C*O), 137.7, 133.4, 129.0, 120.0 (C-aromatic), 129.1 (C-

4), 124.7 (C-3), 99.8 (C-1), 69.7 (O*C*H_2Ar), 65.1 (C-2), 61.1 (C-5), 24.7 (*C*H_3CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{15}NNaO_6$ 286.1050, found 286.1057.

3.8.3. 2(S)-(4-Acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S***

Compound **26** (80 mg, 0.30 mmol) was oxidized with IBX under the same conditions applied for the oxidation of **15** to **16*S***. TLC (hexane/EtOAc 1:3) showed conversion of **26** (R_f 0.25) into a faster moving spot (R_f 0.40). Purification by column chromatography (hexane/EtOAC 3:2) led to **27*S*** (65 mg, 83%); $[\alpha]_D$ −165.8 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.49, 7.31 (d, 4H, *J* = 8.6 Hz, H-aromatic), 7.04 (ddd, 1H, $J_{4,3}$ = 10.6, $J_{5,6}$ = 1.9, $J_{5,6'}$ = 4.0 Hz, H-5), 6.12 (br d, 1H, $J_{4,5}$ = 10.5, $J_{4,6}$ = 2.2, $J_{3,6'}$ = 2.0 Hz, H-4), 4.92 (br d, 1H, H-2), 4.77, 4.67 (2d, 2H, *J* = 11.7 Hz, OC*H*$_2$Ar), 4.51 (dt, 1H, $J_{4,6}$ = 2.2, $J_{5,6}$ = 2.2, $J_{6,6'}$ = 19.2 Hz, H-6), 4.30 (ddd, 1H, $J_{4,6'}$ = 1.9, $J_{5,6'}$ = 3.7, $J_{6,6'}$ = 19.2 Hz, H-6'); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 188.8 (C-3), 168.4 (NH*C*OCH$_3$), 148.1 (C-5), 137.9, 132.7, 129.1, 120.0 (C-aromatic), 124.9 (C-4), 97.0 (C-2), 70.5 (O*C*H_2Ar), 59.9 (C-6). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{15}NNaO_4$ 284.0893, found 284.0900.

3.9. Synthesis of enantioenriched 2(S)-(4-acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S*** *by glycosylation of 2-acetoxyglycal* **1**

A solution of **1** (100 mg, 0.39 mmol) and 4-acetamidobenzyl alcohol (97 mg, 0.58 mmol) in anhydrous CH_2Cl_2 (4 mL) was cooled at −18 °C. Upon addition of $SnCl_4$ (0.06 mL, 0.51 mmol), the reaction mixture was stirred at −18 °C for 1 h and then was diluted with CH_2Cl_2 and washed with sat aq $NaHCO_3$, water and brine. After drying ($MgSO_4$) and concentration, the residue was purified by column chromatography (hexane/EtOAc, 7:3→1:1) to afford **27*S*** (22 mg, 22%); $[\alpha]_D$ −132.8 (*c* 0.8, $CHCl_3$); ee = 80%.

3.10. Synthesis of enantioenriched 2(S)-(4-acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S*** *from enone* **16*S*** *(ee = 82%)*

3.10.1. 4- Nitrobenzyl 2-O-acetyl-3,4-dideoxy-α-L-glycero-pent-3-enopyranoside **28**

Compound **16*S*** (103 mg, 0.41 mmol) was dissolved in MeOH (3.3 mL) and $CeCl_3 \cdot 7H_2O$ (163 mg, 0.44 mmol) and $NaBH_4$ (60 mg, 1.54 mmol) were added. The reaction mixture was stirred at −18 °C for 3 h, when TLC (hexane/EtOAc 1:1) analysis showed complete conversion of **16*S*** (R_f 0.60) into a lower moving spot (R_f 0.48). The mixture was dissolved in CH_2Cl_2 (20 mL) and extracted with water twice (10 mL), dried ($MgSO_4$) and concentrated. The residue was treated with acetic anhydride (1 mL) in pyridine (1 mL) at rt for 2 h. Monitoring by TLC (hexane/EtOAc 1:1) showed conversion into a less polar product (R_f 0.68). The reaction mixture was diluted with MeOH, concentrated and purified by column chromatography (hexane→ hexane/EtOAc 9:1) to afford **28** (85 mg, 70%). $[\alpha]_D$ –93.4 (*c* 0.5, $CHCl_3$); ee = 82%; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.21–7.51 (2 d, 4H, J = 8.6 Hz, H-aromatic), 5.99 (dq, 1H, $J_{2,4} \approx J_{4,5} \approx J_{4,5'} \approx$ 2. 3, $J_{3,4}$ = 10.5 Hz, H-4), 5.72 (dq, 1H, $J_{2,3} \approx J_{3,5} \approx J_{3,5'} \approx$ 2.3, $J_{3,4}$ = 10.5 Hz, H-3), 5.34 (m, 1H, $J_{1,2}$ = 3.7, $J_{2,3} \approx J_{2,4} \approx J_{2,5} \approx J_{2,5'} \approx$ 2.3 Hz, H-2), 5.10 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.95–4.70 (2 d, 2H, J = 13.4 Hz, O*C*H_2Ar), 4.25 (dq, 1H, $J_{2,5} \approx J_{3,5} \approx J_{4,5} \approx$ 2.3, $J_{5,5'}$ = 17.0 Hz, H-5), 4.12 (dq, 1H, $J_{2,5'} \approx J_{3,5'} \approx J_{4,5'} \approx$ 2.3, $J_{5,5'}$ = 17.0 Hz, H-5'); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.7 (CH_3*C*O), 147.6, 145.3, 128.0, 123.8 (C-aromatic), 129.4 (C-4), 121.9 (C-3), 94.9 (C-1), 68.8 (O*C*H_2Ar), 66.2 (C-2), 61.0 (C-5), 21.2 (*C*H_3CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{15}NNaO_6$ 316.0792 found 316.0797.

3.10.2. 4-Acetamidobenzyl 2-O-acetyl-3,4-dideoxy-α-L-glycero-pent-3-enopyranoside **29**

The nitroarene group of **28** (80 mg, 0.27 mmol) was reduced under the conditions applied to the reduction and acetylation of **14**. Examination by TLC (hexane/EtOAc 1:1) showed complete conversion of **28** (R_f 0.68) into a more polar compound (R_f 0.26) which was purified by column chromatography (hexane/EtOAc 4:1→3:2) to afford **29** (58 mg, 70%). $[\alpha]_D$ –64.4 (*c* 0.7, $CHCl_3$); ee = 82%; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47–7.29 (2 d, 4H, *J* = 8.1 Hz, H-Aromatics), 7.22 (br s, 1H, -N*H*), 5.95 (dq, 1H, $J_{2,4} \approx J_{4,5} \approx J_{4,5'} \approx 2.5$, $J_{3,4}$ = 10.4 Hz, H-4), 5.68 (br d, 1H, $J_{2,3} \approx J_{3,5} \approx J_{3,5'} \approx 2.5$, $J_{3,4}$ = 10.4 Hz, H-3), 5.28 (m, 1H, H-2), 5.04 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.78, 4.59 (2 d, 2H, *J* = 12.2 Hz, OCH_2Ar), 4.25 (dq, 1H, $J_{2,5} \approx J_{3,5} \approx J_{4,5} \approx 2.3$, $J_{5,5'}$ = 16.9 Hz, H-5), 4.08 (dq, 1H, $J_{2,5'} \approx J_{3,5'} \approx J_{4,5'} \approx 2.5$, $J_{5,5'}$ = 16.9 Hz, H-5'), 2.17, 2.08 (2 s, 3H each, CH_3CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 170.7, 168.5 (CH_3CO), 137.7, 133.4, 129.5, 119.9 (C-aromatic), 133.4 (C-4), 122.0 (C-3), 93.8 (C-1), 69.5 (OCH_2Ar), 66.4 (C-2), 60.7 (C-5), 24.8, 21.2 (CH_3CO). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{16}H_{19}NNaO_5$ 328.1155, found 328.1154.

3.10.3 4-Acetamidobenzyl 3,4-dideoxy-α-L-glycero-pent-3-enopyranoside **30**

Compound **29** (58 mg, 0.19 mmol) was deacetylated as described for **25**. Monitoring by TLC (hexane/EtOAc 1:2) showed conversion of **29** (R_f 0.30) into a more polar spot (R_f 0.15). Reaction mixture was concentrated up to dryness to afford **30** (48 mg, 97%). $[\alpha]_D$ –61.1 (*c* 1.0, $CHCl_3$); ee = 82%; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48–7.29 (2 d, 4H, *J* = 8.1 Hz, H-aromatic), 7.41 (br s, 1H, N*H*), 5.81 (br d, 1H, $J_{3,4}$ = 10.6 Hz, H-4), 5.73 (br d, 1H, $J_{3,4}$ = 10.6 Hz, H-3), 4.93 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.80, 4.59 (2 d, 2H, *J* = 11.9 Hz, OCH_2Ar), 4.19–4.14 (m, 2H, H-2 overlapped with H-5), 4.04 (m, 1H, $J_{5,5'}$ = 17.1 Hz, H-5'), 2,29 (br s, 1H, O*H*), 2.16 (1 s, 3H, CH_3CO); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 168.5 (CH_3CO), 137.8, 133.3, 129.0, 120.1 (C-aromatic), 127.2 (C-4), 126.2 (C-3), 95.9 (C-1),

69.7 (O*C*H$_2$Ar), 64.3 (C-2), 60.5 (C-5), 24.7 (*C*H$_3$CO). HRMS (ESI) m/z [M+Na]$^+$ calcd for $C_{14}H_{17}NNaO_4$ 286.1050, found 286.1057.

3.10.4. 2(S)-(4-acetamidobenzyloxy)-2H-pyran-3(6H)-one **27*S***

Oxidation of **30** (48 mg, 0.18 mmol) with IBX, under the conditions applied for the oxidation of **15**, led to **27*S*** (38 mg, 80%); $[\alpha]_D$ –137.1 (*c* 0.6, $CHCl_3$); ee = 83%.

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