Iridoids from Carbohydrates via Pauson−Khand Reaction: Synthesis of Advanced Highly Oxygenated Cyclopentane-Annulated Pyranosides from D-Glucal Derivatives

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The Pauson−Khand reaction on suitable 4-oxa-hept-1-en-6-ynes (**1**, **17**) obtained from 3,4,6-tri-*O*-acetyl-D-glucal gives the cyclopentane-annulated pyranosides (**2**, **18**) that can be efficiently and stereoselectivelly transformed into chiral, advanced, highly oxygenated intermediates (**10**, **16**, **24**) for the synthesis of iridoid aglycones.

Introduction

Very recently we[1] and others[2] have shown that the Pauson−Khand[3] (PK) reaction of conveniently functionalized 1,6-enynes in carbohydrate templates is an excellent method for the rapid and highly stereoselective synthesis of cyclopentane-annulated sugars[4] (Scheme 1).

The iridoids are a large family of natural products which are characterized by a highly oxygenated, fused cyclopenta[*c*]pyran ring skeleton (*cis*-2-oxabicyclo[4.3.0]-nonane) (Figure 1). Most naturally occurring iridoids have a b nonreducing link to a sugar (D-glucose) at C-1 and a double bond at C-3/C-4. Certain iridoids possess interesting biological activities.[5] In Figures 2−4 we have shown some representative examples of this family of compounds.

A simple inspection on the skeleton of iridoids[5] reveals that the synthesis of the cyclopentane-annulated pyranoside framework present in these molecules could be achieved by PK-mediated strategies from conveniently functionalized carbohydrate derivatives. Our continued interest[6] in this class of natural products has moved us to undertake a large project aimed at designing new synthetic routes[7] for the synthesis of these compounds.

In previous communications[8a,b] we have reported our recent ventures in this subject, showing the synthetic possibilities of this strategy using as starting material L-arabinose. Although these results were promising and have paved the way for new developments in our project, the chemical yields of the cyclopentane-annulated adducts were low and not very encouraging. In addition, the key intermediate, 3,4-di-*O*-acetyl-L-arabinal, is not commercial and was prepared from L-arabinose, as described, but in poor to moderate overall yield.[9] Finally, as expected, the subsequent Ferrier reaction gave a mixture of the two anomers with poor diastereoselection.[10]

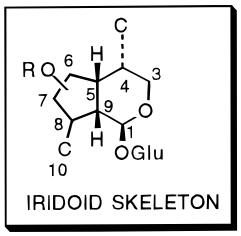

Figure 1.

Scheme 1

In this work we describe the results that we have obtained using D-glucal derivatives for the preparation of suitable intermediates for the synthesis of iridoid aglycones. In Scheme 2 we have shown the general steps that we have planned in order to achieve these goals. In fact, all the problems detailed above could be circumvented by using other glycals, such as 3,4,6-tri-*O*-acetyl-

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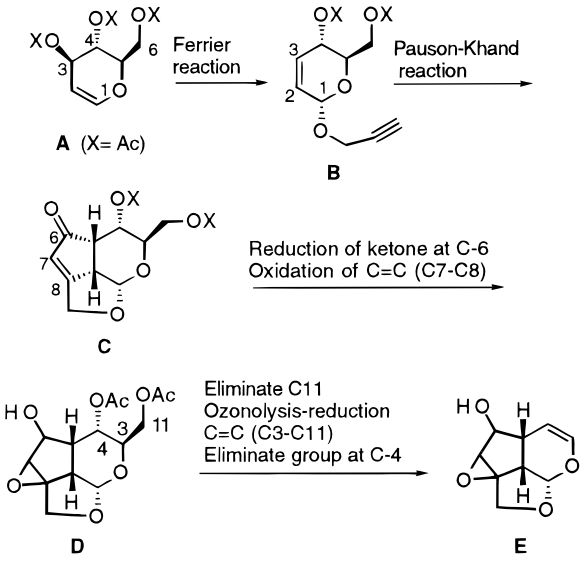
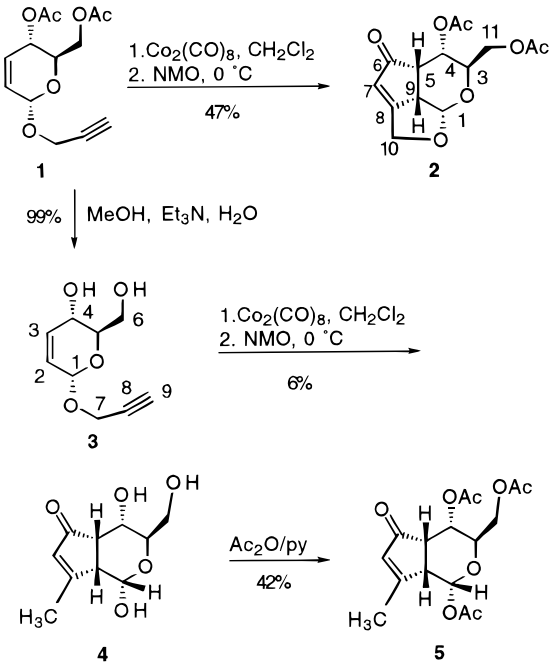
Scheme 2. General Strategy for Chiral Iridoid Aglycone Synthesis from D-Glucal Derivatives



Scheme 3



D-glucal [**A** (X = Ac), Scheme 2], which is cheap and commercially available. Ferrier reactions on this type of compounds have been reported to yield almost exclusively the α-anomers (**B**) (Scheme 2).[11] This is critical for the stereochemical outcome of the PK (**B** → **C**, Scheme 2) reaction in order to prepare the natural aglycones with the correct absolute configurations at the *cis*-fused rings. In this paper we report the results that we have obtained in the first step (reduction of ketone at C-6 and epoxidation of the double bond at C-7/C-8) (**C** → **D**, Scheme 2).[8c]

Results and Discussion

Starting with the known 2-(prop-2-ynyl)-4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1**) (Scheme 3),[11] obtained from "triacetylglucal" in 91% yield, according to Koreeda's version[12] of the Ferrier reaction, we tried the "one-pot reaction" protocol of the PK reaction, without isolation of the intermediate hexacarbonyldicobalt complex and using chemical activation[13] for decomposition of the intermediate adduct (see Experimental Section). In these conditions multigram quantities of compound **2** have been obtained (∼47%) that can be scaled up (we routinely perform the reaction using quantities of ∼4 mmol of compound **1**) without appreciable loss of chemical yield. This fact was of great importance in order to attack the desired transformations in a presumed long synthetic sequence. Compound **2** was described in our preliminary seminal communication[1a] on the Pauson−Khand reaction in carbohydrates, but the experimental protocol and physical and spectroscopic data were not provided. In the Experimental Section we present now full details of this important, key intermediate. Regarding the spectroscopic analysis of this product, it is interesting to note that the 2D COSY spectrum showed the connection between the signals at 5.63 ppm and at 3.54−3.49 ppm (H-1 and H-9); a cross-peak between these signals in the NOESY experiment established that the cyclopentane annulation has taken place, as expected, from the bottom side (α-face) of the molecule;[1] an additional cross-peak between the multiplets at H-5+H-9 and H-4, clearly confirmed this point and established the absolute configuration at the new formed stereocenters during the ring closure.

With compound **2** in hands we attacked the projected synthetic sequence aimed at the preparation of advanced oxygenated cyclopentane-fused compounds for the total synthesis of iridoids (Scheme 2). For our purposes we needed the deprotected compound derived from **2**. Unfortunately, the basic hydrolysis of this product, under mild, usual conditions (MeOH, Et_3N, H_2O), did not give the expected molecule; only decomposition was observed. In view of this, we hydrolyzed pyranoside **1** to give product **3** in quantitative yield (Scheme 3) that under the PK conditions gave a complex reaction mixture from where we could only isolate adduct **4** in very poor yield. This compound proved to be unstable and was transformed into the peracetylated derivative **5** (Scheme 3); only the α-anomer was detected and isolated, albeit in moderate yield. The structure of this compound was easily established by the analytical and spectroscopic data (see Supporting Information). Support to these assignments was found in the literature data for the α-anomer of dihydrocatalpogenin (Figure 2).[14a] The formation of product **4** means that hydrogenolysis of the $CH_2$10−OC1 bond has taken place leaving a methyl group at C-8 and a free hydroxyl at C-1. In our studies in the PK reaction on sugar derivatives,[1,8] we have never detected the formation of hydrogenolysis products of the type shown in compound **4**, but similar processes have been described before in more simple substrates.[15]

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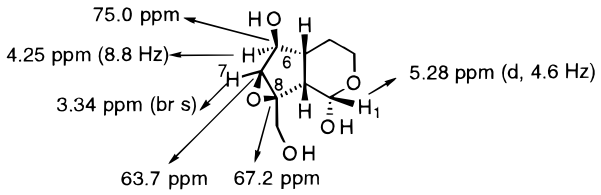
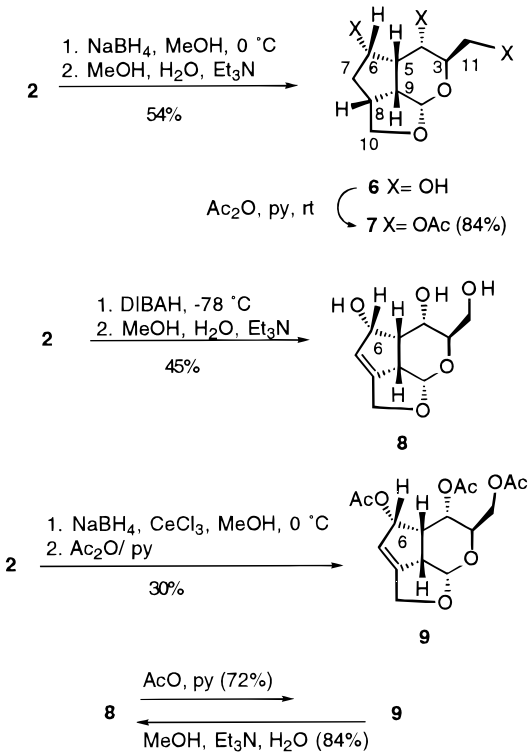


Figure 2. Selected spectroscopic data of dihydrocatalpogenin.[14a]

Scheme 4. Reduction of the Ketone (C-6) in Compound 2



The unsuccessful reactions shown in Scheme 3 were probably due to the highly reactive β-acetyloxy or β-hydroxy ketone moiety present in compound **2**. On the basis of this, in the following experiments we directed our efforts to reduce the keto group at C-6 in enone **2**, preventing in this way possible, undesired secondary reactions. We anticipated new problems, such as 1,2- versus 1,4-hydride reduction; in addition, in the reduction of the ketone at C-6, two diastereomers are possible, but only one diastereoisomer was desired for simplicity and efficiency; in this case, a simple Mitsunobu inversion would provide the other epimer.

Hydride Reduction of Compound 2. According to this, several reducing agents were tested: (a) **Sodium Borohydride**. The reduction of compound **2** in methanol, at 0 °C, gave a complex mixture, the major product being the fully reduced plus deacetylated compound **6** (Scheme 4) accompanied with other reduced, partially acetylated compounds; the hydrolysis (MeOH, H_2O, Et_3N) of the whole crude mixture gave pure product **6** in 54% overall yield from **2**. Acetylation of **6** gave product **7** (84%). Alternatively, the acetylation of the whole crude mixture, after reduction, provided the peracetylated derivative **7** (46% overall yield from adduct **2**). The 1,2-reduction at C-6 and the 1,4-reduction at β-C(7)=C(8) occurred with complete diastereoselection, as only one isomer was detected and isolated. The ^{1}H and ^{13}C NMR spectra of compound **6** clearly established that the keto group at C-6 and the olefinic protons or carbons were absent (see Experimental Section). Thus, we concluded that not only the ketone has been reduced, but hydride 1,4-conjugate addition has also taken place. The absolute configurations at C-6 and C-8, the newly stereocenters formed in the reduction, have been established as shown in Scheme 4 by a strong and selective NOE between the signals at 3.06 (H-8) and 2.90 (H-9) ppm, and between 4.65 (H-6) and 2.64 (H-5) ppm. The coupling constant for H-3 and H-4 (10.2 Hz) is a typical value for an axial−axial disposition of protons, suggesting that the cyclohexane B ring is in a chairlike conformation with substituents at C-3 and C-4 in pseudoequatorial positions. Analysis of the peracetylated material **7** showed similar spectroscopic trends and confirmed the structural determination. In addition, support to these assignments were found in the literature data for catalpin[14b] (Figure 3). The striking differences in the coupling constants with our products (**6**, **7**) suggest that in our case the absolute configuration at H-6 is the opposite.

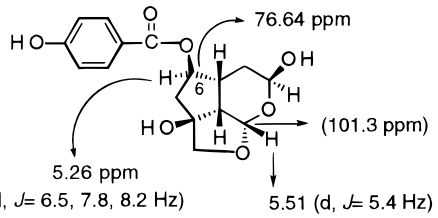


Figure 3. Selected spectroscopic data of catalpin.[14b]

The high stereochemical control observed in this reduction is noteworthy, and highlights that the hydride attack to the ketone at C-6 and the 1,4-conjugate addition at C-8 takes place exclusively from the top, less hindered, face of the molecule. Anyway, and for our proposed synthetic sequence, the reduction at the double bond at C-7/C-8 is an undesired reaction and efforts were directed to obtain the unsaturated alcohol **8** (Scheme 4).

For this purpose we used sodium borohydride/cerium trichloride, the reagent of choice.[16] Using hexahydrated cerium trichloride in methanol as solvent, followed by the usual basic hydrolysis (Scheme 4), to our great surprise a compound was isolated in 37% overall yield that by direct TLC, analysis of the spectroscopic data and comparison with an authentic sample was the reduced, fully saturated compound **6**. Using anhydrous cerium trichloride, at low temperature (−78 °C), followed by the usual basic hydrolysis (Scheme 4), compound **2** afforded a mixture of compounds **6** and **8** in a 3.4 to 1 ratio, respectively, as determined by ^{1}H NMR. Apparently, the effect of the temperature and the type of cerium trichloride used was critical, because in the same conditions, but at 0 °C, followed by acetylation, product **9** was obtained in modest yield (30%) (only traces of product **7** were detected). Compound **9**, after basic, mild hydrolysis gave compound **8** in 84% yield. Alternatively, triol **8** on acetylation afforded derivative **9** in good yield (72%) (Scheme 4). The structure of products **8** and **9** has been established by analytical and spectroscopic data. Very interestingly, the 2D COSY spectrum and selective NOE experiments in the ^{1}H NMR spectrum allowed us to determine that the absolute configuration at C-6 is *S* (a strong NOE between H-5 and H-6, and between H-1 and

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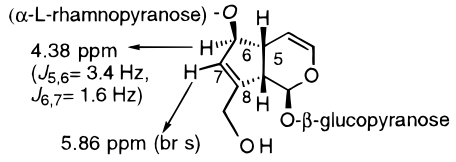


Figure 4. Selected spectroscopic data of sinuatol.[14c]

H-9, were observed). The exclusive formation of the *S* isomer during the reduction of ketone **2** with sodium borohydride/cerium trichloride is also in agreement with the reduction of compound **2** with sodium borohydride to give only compound **6**, with the same stereochemistry at C-6. The hydride attack on the ketone at C-6 proceeds again from the top, less-hindered face, giving only one isomer. Note also the impressive effect of the temperature on the regioselectivity of the reduction using cerium trichloride as additive: at 0 °C product **9** (along with traces of derivative **7**) was isolated, albeit in modest yield. The structure of compound **9** follows also from its full analysis (see Experimental Section). Revision of the literature has shown that the allylic alcohol fragment at carbons C-6/C-7/C-8 is present in several natural products in the iridoid family. In Figure 4 we show the structure of sinuatol (6-*O*-α-L-rhamnopyranosylaucubin).[14c] Note that in this compound the configuration at C-6 is the opposite to the one found in our synthetic samples (**8** or **9**); very interestingly, the reported chemical shift for H-6(a), in CD_3OD, is 4.38 ppm with vicinal coupling constants: $J_{5,6} = 3.4$ Hz, $J_{6,7} = 1.6$ Hz, while in product **8** these significant data are very different: H-6(b) (in the same solvent) appears at 5.67−5.63 ppm ($J_{5,6} = 7.7$ Hz).

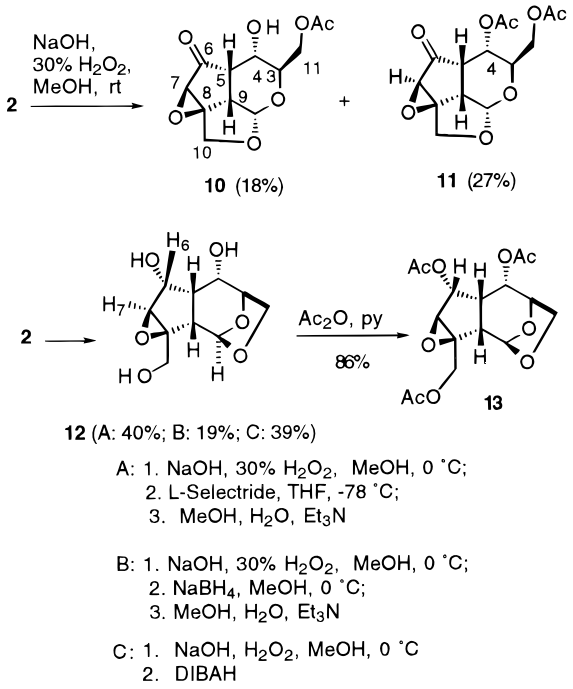
In view of these results, other reductive agents were tested: (b) **DIBALH**. The reduction of compound **2** using 3 equiv of the reagent, at −78 °C, followed by our standard hydrolysis protocol gave product **8** in a reasonable yield (45%) (Scheme 4). (c) **LAH**. The reduction of compound **2** with LAH, at room temperature (the basic hydrolysis was not necessary), afforded a mixture of products **6** and **8**, in 1.5/1 ratio, respectively, as determined by ^{1}H NMR, but in poor overall yield (∼13%). (d) **L-Selectride**. Proceeding as in the reduction with DIBALH, only product **6** was isolated in 45% yield. The structure of the products isolated in these experiments were found identical, by comparison of the NMR data and TLC behavior on different solvents, to the corresponding molecules previously synthesized.

In summary, the reduction of compound **2** has afforded pure or mixtures of product **6** (the 1,2- plus 1,4-conjugate addition) or compound **8** (the 1,2-addition product), depending of the reagents, from poor to moderate yield, but with complete diastereoselection: only one diastereoisomer was detected in all the cases studied.

Before continuing with the analysis of the epoxidation of compounds **8** and **9**, according to our synthetic project (Scheme 2), we decided to analyze the direct epoxidation plus reduction protocol of product **2**.

Epoxidation + Hydride Reduction of Intermediate 2. Using standard conditions for α,β-unsaturated ketone epoxidation (H_2O_2, NaOH, MeOH, 0 °C), a mixture of epoxides **10** (18%) and **11** (27%) (Scheme 5) were easily isolated and characterized. Monoacetate **10** is the result of the epoxidation followed by partial hydrolysis at the less sterically hindered primary carbon C-11 followed by acetyl migration from *O*-C-4 to *O*-C-11. This is supported

Scheme 5. Epoxidation (H_2O_2) and Reduction in Compound 2



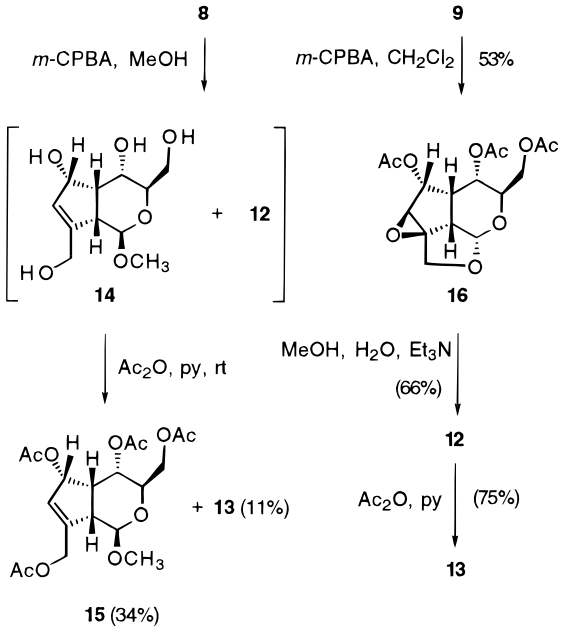
by the detailed comparison of the spectroscopic data of compounds **10** and **11** (see Supporting Information). The configuration at the newly formed stereocenters, C-7 and C-8, has been tentatively assigned as shown in Scheme 5. Basic hydrolysis in mild conditions (MeOH, H_2O, Et_3N) of the mixture **10**/**11** gave a complex reaction mixture that was not further elaborated; this is not surprising in view of the similar result observed in identical treatment of compound **2**.

As a consequence, we considered most appropriate this three-step sequence: epoxidation + reduction + basic hydrolysis. Using sodium borohydride as reducing agent (conditions B; see Scheme 5), the epoxy alcohol **12** (Scheme 5) was obtained in 19% yield. With L-Selectride (conditions A; see Scheme 5), the overall yield was 40%; finally, with DIBALH (conditions C; see Scheme 5) as reducing agent, no additional basic hydrolysis was needed, and compound **12** was isolated in 39% yield. In all these cases, only one and the same isomer was detected. Acetylation under standard conditions gave the peracetylated material **13** (86% yield; Scheme 5).

The structure we propose for compounds **12** and **13** implies that after basic hydrolysis the primary hydroxyl at C-11 attacks at C-1 giving a rearranged 1,11-anhydro sugar. This behavior was totally unexpected and was fully understood when we prepared compound **16** (Scheme 6), a peracetylated isomer of compound **13**, using a synthetic scheme (see below) that prevented the rearrangement leading to the 1,11-anhydro sugar formation.

The structure of compound **12** is in agreement with the elemental analysis and spectroscopic data (see Experimental Section). The DEPT, HMQC, 2D COSY experiments allowed us to assign without a doubt the chemical shifts for protons and carbons and the coupling constants. Selective NOE experiments clearly established also that H-6, H-5, H-9, H-4, and H-1 are all *cis* positioned, in the same plane of the molecule. As no n.O.e effect was observed between H-7 and H-5 or H-9, we concluded that the epoxide has the β-C7−O−C8 orienta-

Scheme 6. Epoxidation (*m*-CPBA) and Reduction in Compound 2

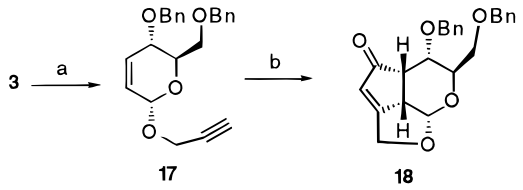


tion. With these results the absolute configuration at these stereocenters could be assigned as shown in Scheme 5. Compared to compound **10** (Scheme 5), where H-4 shows a vicinal coupling constant with H-3 equal to 9.4 Hz, corresponding to an axial−axial arrangement, in compound **12** this value is equal to 0 Hz. As expected, inspection of molecular models shows that in a 1,11-anhydrosugar the dihedral angle between H-3 and H-4 is 90°, explaining the observed vicinal coupling and confirming the rearranged structure found in compound **12**. This spectroscopic value has resulted in great diagnostic value in all the structural assignments that we have proposed for the other related, resulting structures obtained in this study (see below).

As suggested by the molecular models, we hypothesize that in the intermediate having the OH−C-11 free alcohol leading to product **12**, conformational flexibility is possible, giving a presumed reactive species with a *trans* diaxial disposition between OH−C-11 and O−C-1 that clearly favors the attack at C-1 leading to the observed molecule. In addition, the presence of the epoxide at C-8/C-7 is mandatory for these facts to take place, because in compound **9**, with a double bond at C-7/C-8 (Scheme 4), during the basic hydrolysis, no rearranged product was detected.

The above results moved us to study the *m*-chloroperbenzoic acid (*m*-CPBA) epoxidation of compounds **8** and **9**, the allylic alcohol and acetate, respectively, derived from product **2** (Scheme 4). Compound **8** was insoluble in methylene chloride, and methanol was used as solvent. In these conditions, the reaction gave a mixture of compounds **14** and **12** (Scheme 6) that was not separated, but submitted to acetylation to give, after flash chromatography, a product identical to compound **13** (Scheme 5), isolated in 11% yield, and a new molecule, **15** (in 34% yield). These results suggest that the epoxidation has partially failed in the case of product **15** and, in addition, acid-catalyzed (due to the *m*-MCPA) methanolysis at C-1 resulted in the formation of the *β*-methyl glycoside present in compound **15**. This assignment follows from the 1,2-vicinal coupling constant of H-1 and H-9 (8.4 Hz),

Scheme 7[a]



[a] Reagents: (a) $BrCH_2C_6H_5$, NaH (90%); (b) i: $Co_2(CO)_8$, CH_2Cl_2; ii: NMO, H_2O (50%).

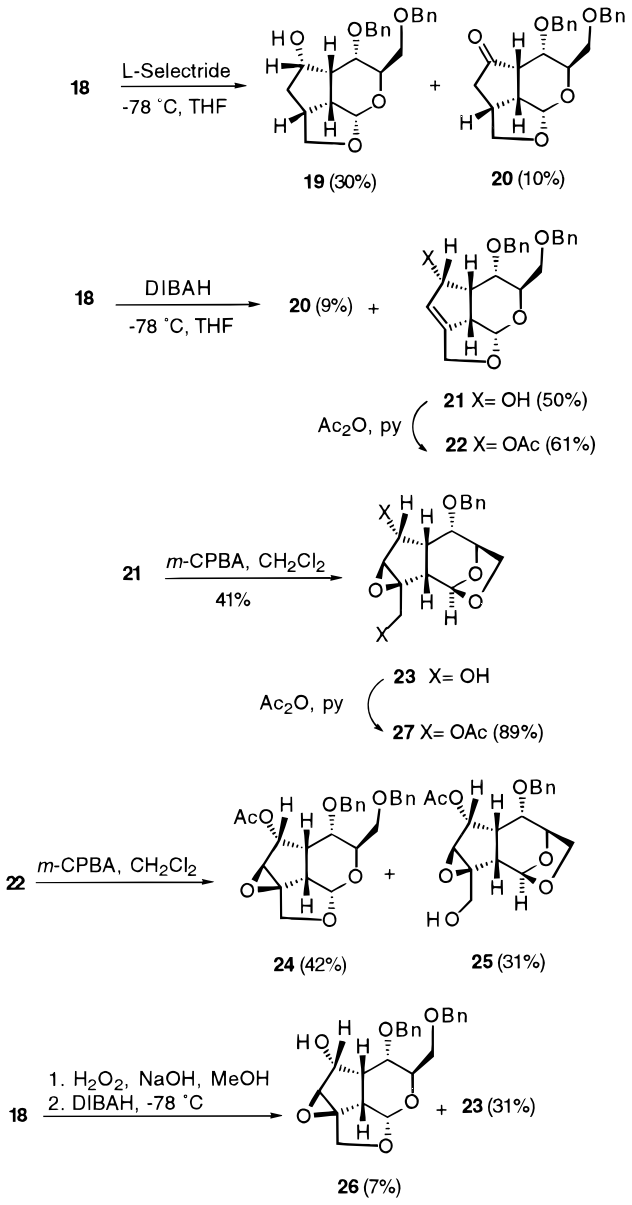
a typical value for a *trans* 1,2-diaxial arrangement of protons. In summary, in the methanol/peracid-promoted epoxidation of compound **8**, partial *intermolecular* methanolysis from the *β*-side, without epoxidation, leading to **14**, and exclusive epoxidation from the *β*-side at the C-7/C-8 followed by *intramolecular* 1,11 anhydro sugar formation, leading to product **12**, was observed. After acetylation, derivatives **13** and **15** were isolated and characterized.

These results prompted us to test the same protocol in compound **9**, where the acetylated nature of the substituents could prevent first, the methanolysis, as this product is soluble in methylene chloride, and second, the 1,11-anhydro sugar formation. Fortunately, this was the case and, after epoxidation, compound **16** (Scheme 6) was isolated in 53% yield. The analytical and spectroscopic data of this product clearly supported the structure of epoxy-4,6,11-tri-*O*-acetate isomer of product **13** (Scheme 5). Despite this, and not surprisingly, after mild basic hydrolysis, compound **16** afforded product **12** in 66% yield, showing that once the epoxy ring has been installed at C-7/C-8 with *β*-orientation, after deblocking the hydroxy gruoup at C-11, the scenario was set up for the formation of the 1,11-anhydro sugar. The structure of the hydrolyzed derivative (**12**) obtained from compound **16** has been definitively confirmed by acetylation to give the expected compound **13** in 75% yield.

The above-described results were interesting and helped us to know more about the reactivity of our intermediates. But for the sake of efficiency and simplicity we decided to use more stable protecting groups located at C-11 in new PK adducts. In view of this, we selected the benzyl group and, as a result, we prepared the enyne precursor **17** (Scheme 7), readily obtained by di-*O*-benzylation of diol **3** (Scheme 3). The PK reaction of this molecule (**17**) proved specially efficient, giving the expected product **18** in 50% yield. The spectroscopic and analytical data of this compound were in good agreement with this structure and correlated well with those of the adduct **2** (Scheme 3).

With compound **18** and derivatives (Scheme 8) we analyzed similar reduction/epoxidation protocols as we have already tested in compound **2** (see Supporting Information). As shown in Scheme 8, the reaction with L-Selectride gave a mixture of the 1,4/1,2 and 1,4 reduction products (**19** and **20**), in a 3 to 1 ratio, respectively, in moderate overall yield (40%). Fortunately, the reaction with DIBALH was more promising, as only traces of compound **20**, accompanied by the 1,2-reduction derivative **21** (50% yield), was isolated. Under standard acetylation this product afforded compound **22** in 61% yield. The stereochemistry at the newly formed stereocenters in compounds **19**−**22** has been established by detailed analysis of the spectroscopic data and selective NOE experiments.

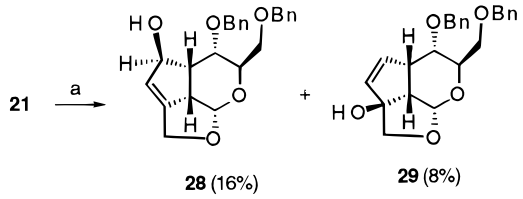
Scheme 8. Transformations of Compounds 18, 21, and 22



The epoxidation of product **21**, using methylene chloride as solvent, gave compound **23** as only one β-epoxy isomer at C-7/C-8 with the rearranged structure (only one aromatic group was present in the ^{1}H NMR spectrum) of 1,11-anhydro sugar, as it could be deduced from the spectroscopic pattern observed for the protons at C-4/C-3/C-11. Unfortunately, the epoxidation of acetate **22** was not very encouraging, as a mixture of the "normal" (**24**) and the rearranged (**25**) derivatives were obtained in 42% and 31% yield, respectively.

The total (in compound **21**) or partial (in product **22**) hydrogenolysis of the C11O−CH_2Ph bond, under reaction with *m*-CPBA, was surprising and totally unexpected, and we have not found an easy explanation for this reactivity. In addition, the reaction of ketone **18** with hydrogen peroxide in basic conditions, followed by DIBALH reduction, gave minor amounts of the reduced, "normal" product accompanied with the major hydrogenolysis and "rearranged" product **23** (31% yield), whose acetylation afforded the acetate **27**. The stereochemistry at C-7 and C-8 in compounds **23**−**27** has been established

Scgene 9[a]



[a] (a) i. *p*-$NO_2C_6H_4CO_2H$, DEAD, Ph_3P; ii: NaOMe, MeOH.

by the usual spectroscpic experiments showing that the epoxide is β-oriented, confirming that the epoxidation takes place from the less-hindered β face of the molecules. The comparison of the chemical shifts for H-7 and C-7 [($CDCl_3$) **23**: H-7, 3.84 ppm, s; C-7, 85.4 ppm; **24**: H-7, 3.51 ppm, s; C-7, 65.3 ppm; **25**: H-7, 4.06 ppm, s; C-7, 81.8 ppm; **27**: H-7, 4.48 ppm, s; C-7, 79.5 ppm] with the data in the literature for dihydrocatalpogenin[14a] (Figure 2) showed also good accordance.

Finally, and as most of the natural products in the iridoid familly have free or functionalized hydroxyl groups at C-6 in β-orientation, and in our substrates we have only obtained reduced derivatives at C-6 with hydroxyl groups in α-orientation, we have analyzed the Mitsunobu inversion reaction[17] in our readily available intermediate compound **21** (Scheme 8). We anticipated that the allylic structure of this material could be a problem, as inverted and/or 1,3-rearranged allylic derivatives are possible.[18] With these ideas in mind we submitted compound **21** to the standard Mitsunobu protocol, with *p*-nitrobenzoic acid. After basic hydrolysis of the crude reaction product, a complex reaction mixture resulted from where, after flash chromatography, products **28** and **29** in 16% and 8% chemical yields, respectively (Scheme 9), were isolated (see Supporting Material). The full analysis of these products showed that these compounds were isomers with two aromatic groups in the molecule, showing that at least in these conditions the hydrogenolysis of the C11O−CH_2Ph bond does not occur. The detailed inspection of the ^{1}H and ^{13}C NMR spectra of compound **28** showed that this product is the inverted reaction derivative at C-6. The absolute configuration at C-8 in product **29** has been tentatively assigned as shown based on mechanistic grounds, assuming that this product comes from the intermediate species by S_N2' rearrangement from the opposite less-hindered β face.

Conclusions

In summary, we have described an extensive analysis of the reactivity of ring A in key intermediates **2** and **18**, readily available by PK reaction of conveniently functionalized carbohydrate derivatives. We have found that the reduction of the ketone at C-6 in these compounds or the epoxidation of the double bond C-7/C-8 plus reduction of the ketone occur with complete stereochemical control and moderate yield. In all the cases studied and with all the reagents used, the attack on these functions proceeds from the less-hindered β face. We have also found a very interesting, totally unexpected reactivity of the C-11(OH) when an epoxide is located at C-7/C-8: during the hydrolysis/hydrogenolysis of the precur-

(17) Mitsunobu, O. *Synthesis* **1981**, 1.
(18) Mizuno, M.; Shioiri, T. *Chem. Commun.* **1997**, 2165.

sor leading to the free C-11(OH) group a rearrangement takes place giving 1,11-anhydro sugar derivatives. As a result, we have obtained a series of highly oxygenated cyclopentane-annulated pyranosides that can be considered advanced intermediates for the total synthesis of iridoids with the correct absolute configurations at the *cis*-fused rings. Work is now in progress to analyze the C-11 elimination in the normal or rearranged products to give products with the adequate skeleton present in the natural products.[8c]

Experimental Section

General Methods. See ref 1b.

General Procedure for the PK Reaction. To a solution on the precursor (0.18 M) in dry methylene chloride, under argon and at room temperature, $Co_2(CO)_8$ (1.1 equiv) was added, and the mixture was stirred until no precursor remained (TLC control) (∼30 min). The reaction was cooled at 0 °C and all the NMO (6 equiv) was added in one portion. After stirring for 3 h at room temperature, the crude was filtered over Celite 545, the cake was washed with methylene chloride, and the solvent was evaporated. The residue was submitted to chromatography, eluting with hexane/ethyl acetate mixtures.

General Procedure for Basic Hydrolysis. The compound to be hydrolyzed was dissolved in a mixture of methanol, water, and triethylamine (5/4/1, volume ratio) and stirred at room temperature until no starting material remained. The solvent was evaporated, and the residue was submitted to flash chromatography to give the product.

General Procedure for Acetylations. The product was treated with a mixture of acetic anhydride/pyridine (1:1, in volume) at room temperature for 24 h. The solvent was evaporated, codistilling with toluene. The residue was submitted to flash chromatography to give the product.

General Procedure for Reductions. (A) Using Sodium Borohydride. The compound to be reduced was dissolved in MeOH (0.4 M), in a methanolic solution of $CeCl_3 \cdot 6H_2O$ (1 equiv, 0.4 M), or in a methanolic solution of anhydrous $CeCl_3$ (1 equiv, 0.4 M), was cooled at the stated temperature in each case, and was treated with sodium borohydride (1 equiv). After 90 min, the reaction was complete, and an aqueous saturated solution of ammonium chloride was added. The solvent was eliminated, and the crude was processed following the appropriate general procedure. **(B) Using Diisobutyl Aluminum Hydride (DIBALH).** The compound to be reduced was dissolved in dry THF (0.09 M) and cooled at − 78 °C under argon, DIBALH (3 equiv, 1.0 M in toluene) was added dropwise. After 6 h, MeOH was added, and the mixture was warmed at room temperature. The suspension was filtered over Celite 545, washing with MeOH. The solvent was evaporated, and the crude was processed following the appropriate general procedure. **(C) Using L-Selectride**. The compound to be reduced was dissolved in dry THF (0.14 M) and cooled at − 78 °C under argon, and L-Selectride (3.2 equiv, 1.0 M in THF) was added. After 6 h, an aqueous saturated solution of ammonium chloride was added, and the mixture was stirred at room temperature. The solvent was evaporated, the residue dissolved in ethyl acetate and washed with brine. The combined organic layer was dried and evaporated, and the residue was processed following the appropriate general procedure.

General Procedure for Epoxidations. (A) Using H_2O_2, NaOH, and MeOH. The compound to be epoxidized was dissolved in MeOH (0.16 M), and 30% H_2O_2 (3 equiv) was added. The mixture was cooled at 0 °C, and a solution of NaOH (0.5 equiv, 6 N) was added dropwise. After 45 min, the mixture was warmed at room temperature, diluted with ethyl acetate, and washed with brine. The combined organic layer was dried and evaporated, and the residue was processed following the appropriate general procedure. **(B) Using *m*-CPBA**. The compound to be epoxidized was dissolved in MeOH (0.12 M) or methylene chloride (0.05 M) and cooled at 0 °C, and *m*-CPBA (2 equiv, commercial grade 85% pure) was added. After 5 h at room temperature, the solvent (MeOH) was evaporated and the residue dissolved in CH_2Cl_2 and washed successively with a 10% aqueous solution of sodium thiosulfate, a 5% aqueous sodium bicarbonate solution, and brine. The solvent was evaporated, and the residue was submitted to chromatography or, in the event the combined organic layer was dried, evaporated, and the residue was processed following the appropriate general procedure.

[4a*S*-(4aα,5*β*,6α,7aα,7bα)]-5-(Acetyloxy)-6-[(acetyloxy)-methyl]-5,6,7a,7b-tetrahydro-2*H*-1,7-dioxacyclopent[*cd*]-inden-4(4a*H*)-one (2).[1a] Following General Procedure for the PK Reaction, starting from pyranoside **1** (863 mg, 3.22 mmol), after flash chromatography (hexane:ethyl acetate 4:6), product **2** was isolated (447 mg, 47% yield): oil; $[\alpha]^{25}_D$ +77 (*c* 0.22, $CHCl_3$); IR (film) ν 1725, 1695, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.25 (br s, 1 H, H-7), 5.62 (d, $J_{1,9} = 5.9$ Hz, 1 H, H-1), 5.00 (dd, $J_{4,5} = 8.8$ Hz, $J_{3,4} = 10.1$ Hz, 1 H, H-4), 4.88 (d, $J_{10,10'} = 15.3$ Hz, 1 H, H-10), 4.67 (d, 1 H, H-10′), 4.22−4.12 (m, 2 H, 2 H-11), 3.82 (ddd, $J_{3,11} = 2.6$ Hz, $J_{3,11'} = 4.2$ Hz, 1 H, H-3), 3.54−3.49 (m, 2 H, H-5, H-9), 2.08, 2.06 (s, s, 3 H, 3 H, 2 × $OCOCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 205.1 (CO), 180.6 (C-8), 170.7 and 169.9 (2 × $OCOCH_3$), 126.4 (C-7), 96.8 (C-1), 66.8 (C-3), 66.0 (2 C, C-4, C-10), 63.3 (C-11), 48.1 (C-5), 46.5 (C-9), 21.2 (2 × $OCOCH_3$); MS (70 eV) *m*/*z* 223 (14), 43 (100). Anal. Calcd for $C_{14}H_{16}O_7$: C, 56.76; H, 5.44. Found: C, 56.75; H, 5.47.

2-(Prop-2-ynyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (3). Following General Procedure for Basic Hydrolysis, compound **1** (297 mg, 1.21 mmol), after flash chromatography (hexane/ethyl acetate: 1/1), gave product **3** (205 mg, 99%): mp 75−77 °C; $[\alpha]^{25}_D$ +133 (*c* 0.39, $CHCl_3$); IR (KBr) ν 3260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.01 (dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 8.2$ Hz, 1 H, H-3), 5.77 (dt, $J_{1,2} = J_{2,4} = 2.5$ Hz, 1 H, H-2), 5.20 (br s, 1 H, H-1), 4.31 (d, $J_{7,9} = 2.4$ Hz, 2 H, 2 H-7), 4.25 (ddd, $J_{4,5} = 9.3$ Hz, 1 H, H-4), 3.88 (d, $J_{6,5} = 4.2$ Hz, 2 H, 2 H-6), 3.72 (dt, 1 H, H-5), 2.46 (t, $J_{7,9} = 2.4$ Hz, 1 H, H-9), 2.21−2.13 (m, 2 H, 2 OH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 133.8 (C-3), 125.8 (C-2), 92.8 (C-1), 79.4 (C-9), 74.7 (C-8), 71.7 (C-5), 64.3 (C-4), 62.7 (C-6), 55.1 (C-7); MS (70 eV) *m*/*z* 129 (36), 85 (100). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.74; H, 6.48.

[2a*R*-(4*β*,4aα,5*β*,6α,7aα,7bα)]-2a,3,4,4a,5,6,7a,7b-Octahydro-4,5-(dihydroxy)-6-[(hydroxy)methyl]-2*H*-1,7-dioxacyclopent[*cd*]indene (6). Following General Procedure for Reductions ($NaBH_4$) and Basic Hydrolysis, compound **2** (85 mg, 0.32 mmol) was transformed into **6** (36.5 mg, 54%), isolated by flash chromatography (methylene chloride/methanol: 95/5). Following General Procedure for Reductions ($NaBH_4/CeCl_3 \cdot 6H_2O$) and Basic Hydrolysis, compound **2** (79 mg, 0.27 mmol) was transformed into product **6** (21 mg, 37%). Following General Procedure for Reductions (L-Selectride) compound **2** (83 mg, 0.28 mmol) was transformed into derivative **6** (27 mg, 45%): mp 45−48 °C; $[\alpha]^{25}_D$ +135 (*c* 0.27, MeOH); IR (KBr) ν 3400 cm^{-1}; ^1H NMR (CD_3OD, 300 MHz) δ 5.43 (d, $J_{1,9} = 5.7$ Hz, 1 H, H-1), 4.65 (t, $J_{6,7b} = J_{5,6} = 4.6$ Hz, 1 H, H-6), 4.43 (ddd, $J_{3,4} = 10.2$ Hz, $J_{3,11} = 5.1$ Hz, $J_{3,11'} = 2.8$ Hz, 1 H, H-3), 4.12 (dd, $J_{4,5} = 3.8$ Hz, 1 H, H-4), 4.07 (d, $J_{10,10'} = 8.7$ Hz, 1 H, H-10), 4.02 (d, $J_{10,10'} = 8.7$ Hz, 1 H, H-10′), 3.99 (dd, $J_{11,11'} = 11.8$ Hz, 1 H, H-11′), 3.87 (dd, 1 H, H-11), 3.06 (m, 1 H, H-8), 2.90 (ddd, $J_{5,9} = 10.5$ Hz, $J_{8,9} = 8.8$ Hz, 1 H, H-9), 2.64 (ddd, 1 H, H-5), 2.18 (ddd, $J_{7a,7b} = 14.1$ Hz, $J_{7b,8} = 7.9$ Hz, 1 H, H-7b), 2.04 (d, $J_{7a,7b'} = 14.1$ Hz, 1 H, H-7a); ^{13}C NMR (CD_3OD, 50 MHz) δ 102.5 (C-1), 76.4 (C-6), 72.7 (C-3), 72.6 (C-10), 66.3 (C-4), 63.2 (C-11), 46.4 (C-5), 44.6 (C-9), 43.8 (C-3), 42.5 (C-7); MS (70 eV) *m*/*z* 185 (27), 81 (100). Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.75; H, 7.47.

[2a*R*-(4*β*,4aα,5b,6a,7aα,7bα)]-4,5-(Diacetyloxy)-6-[(acetyloxy)methyl]-2a,3,4,4a,5,6,7a,7b-octahydro-2*H*-1,7-dioxacyclopent[*cd*]indene (7). Following General Procedure for Acetylation, compound **6** (9 mg, 0.042 mmol) gave product **7** (12 mg, 84%) by flash chromatography (hexane/ethyl acetate 1/1): mp 48−50 °C; $[\alpha]^{25}_D$ −56 (*c* 0.03, $CHCl_3$); IR (KBr) ν 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.41 (t, $J_{5,6} = J_{6,7b} = 4.5$

Hz, 1 H, H-6), 5.35 (d, $J_{1,9}$ = 5.3 Hz, 1 H, H-1), 5.00 (dd, $J_{3,4}$ = 10.6 Hz, $J_{4,5}$ = 7.2 Hz, 1 H, H-4), 4.64 (ddd, $J_{3,11}$ = 4.8 Hz, $J_{3,11'}$ = 2.3 Hz, 1 H, H-3), 4.28 (dd, $J_{11,11'}$ = 12.1 Hz, 1 H, H-11′), 4.16 (dd, 1 H, H-11), 3.93 (t, $J_{10,10'} = J_{8,10'}$ = 8.9 Hz, 1 H, H-10′), 3.86 (dd, $J_{8,10}$ = 3.5 Hz, 1 H, H-10), 2.95−2.74 (m, 3 H, H-5, H-8, H-9), 2.08, 2.07, 2.01 (s, s, s, 9 H, 3 × $OCOCH_3$), 2.01 (ddd, $J_{7a,7b}$ = 14.8 Hz, $J_{7b,8}$ = 7.5 Hz, 1 H, H-7b), 1.91 (d, 1 H, H-7a); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.9, 170.3, 170.1 (3 × $OCOCH_3$), 101.3 (C-1), 75.6 (C-6), 71.8 (C-10), 66.4 (C-4), 65.8 (C-3), 63.0 (C-11), 43.1 (C-9), 42.3 (C-8), 41.1 (C-5), 39.8 (C-7), 21.5, 20.8, 20.7 (3 × $OCOCH_3$); MS (70 eV) *m*/*z* 222 (19), 43 (100). Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.14; H, 6.48. Found: C, 56.35; H, 6.47.

[4*S*-(4aα,5*β*,6α,7aα,7bα)]-4,4a,5,6,7a,7b-Hexahydro-4,5-(dihydroxy)-6-[(hydroxy)methyl]-2*H*-1,7-dioxacyclopent-[*cd*]indene (8). Following General Procedure for Reductions ($NaBH_4$/$CeCl_3$) and Basic Hydrolysis, compound **2** (85 mg, 0.9 mmol) was transformed into mixture of **8** + **6** (44 mg, in a 3.4/1 ratio, respectively, that we were unable to separate by flash chromatography (methylene chloride/methanol 98/2). Following General Procedure for Reductions (DIBAH) and Basic Hydrolysis, compound **2** (109 mg, 0.37 mmol) was transformed into pure **8** (36 mg, 45%). **8**: oil; $[\alpha]^{25}_D$ −50 (*c* 0.19, MeOH); IR (film) ν 3500−3100 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 5.87−5.85 (m, 1 H, H-7), 5.67−5.63 (m, 1 H, H-6), 5.56 (d, $J_{1,9}$ = 5.0 Hz, 1 H, H-1), 4.72 (dt, $J_{10,10'}$ = 12.9 Hz, $J_{6,10'} = J_{7,10'}$ = 1.7 Hz, 1 H, H-10′), 4.42 (ddd, $J_{6,10}$ = 1.9 Hz, $J_{7,10}$ = 3.7 Hz, 1 H, H-10), 4.17 (dt, $J_{3,4}$ = 6.7 Hz, $J_{3,11} = J_{3,11'}$ = 5.0 Hz, 1 H, H-3), 4.05 (t, $J_{4,5}$ = 6.7 Hz, 1 H, H-4), 3.86 (d, $J_{3,11}$ = 5.0 Hz, 2 H, 2 H-11), 3.37−3.32 (m, 1 H, H-9), 2.64 (dt, $J_{5,9} = J_{5,6}$ = 7.7 Hz, 1 H, H-5); ^{13}C NMR (CD_3OD, 50 MHz) δ 147.4 (C-8), 127.1 (C-7), 96.9 (C-1), 86.9 (C-6), 77.6 (C-3), 68.6 (C-4), 65.4 (C-10), 62.6 (C-11), 52.6 (C-9), 43.6 (C-5); MS (70 eV) *m*/*z* 165 (31), 79 (100). Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.75; H, 6.47.

[4*S*-(4aα,5*β*,6α,7aα,7bα)]-4,5-(Diacetyloxy)-6-[(acetyloxy)-methyl]-4,4a,5,6,7a,7b-hexahydro-2*H*-1,7-dioxacyclopent-[*cd*]indene (9). Following General Procedure for Reduction ($NaBH_4$/$CeCl_3$, MeOH, 0 °C) and Acetylation, compound **2** (80 mg, 0.27 mmol) gave recovered **2** (10 mg), **9** (13 mg, 14%), and a mixture of **9** and **7** (14 mg in a 2.2/1 ratio, determined by ^{1}H NMR) after flash chromatography (hexane/ethyl acetate 8/2). **9**: oil; $[\alpha]^{25}_D$ −80 (*c* 0.13, $CHCl_3$); IR (film) ν 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.19−6.16 (m, 1 H, H-6), 5.65 (br s, 1 H, H-7), 5.44 (d, 1 H, $J_{1,9}$ = 4.7 Hz, 1 H, H-1), 5.07 (t, $J_{4,5} = J_{3,4}$ = 6.2 Hz, 1 H, H-4), 4.60 (dq, $J_{10,10'}$ = 12.9 Hz, *J* = 1.7 Hz, 1 H, H-10′), 4.29 (ddt, $J_{6,10}$ = 2.2 Hz, $J_{7,10}$ = 3.6 Hz, 1 H, H-10), 4.25−4.07 (m, 3 H, H-3, 2 H-11), 3.40 (dt, $J_{5,6}$ = 6.2 Hz, $J_{5,9}$ = 8.1 Hz, 1 H, H-5), 3.24−3.20 (m, 1 H, H-9), 2.07, 2.04, 2.02 (s, s, s, 9 H, 3 × $OCOCH_3$); ^{13}C NMR (CD_3OD, 50 MHz) δ 170.6, 170.4, 169.9 (3 × $OCOCH_3$), 146.7 (C-8), 122.6 (C-7), 94.9 (C-1), 83.8 (C-6), 72.0 (C-3), 65.2 (C-4), 64.5 (C-10), 62.7 (C-11), 51.9 (C-9), 40.5 (C-5), 21.1, 21.0, 20.2 (3 × $OCOCH_3$), MS (70 eV) *m*/*z* 160 (16), 43 (100). Anal. Calcd for $C_{16}H_{20}O_8$: C, 56.47; H, 5.92. Found: C, 56.69; H, 5.73.

[1*R*-(1α,3α,4*β*,4aα,5*β*,6α,7aα)]-1,3-(Epoxymethane)-3,4,-4a,5,6,7a-hexahydro-4,5-(dihydroxy)-7*β*-[(hydroxy)methyl]-6,7-oxireno-cyclopenta[*c*]pyran (12). Following General Procedure for Epoxidation (A) + Reduction with Sodium Borohydride and Basic Hydrolysis, compound **2** (107 mg, 0.36 mmol) gave product **12** (16.2 mg, 19%) after flash chromatography (methylene chloride/methanol 96/4). Following General Procedure for Epoxidation (A) + Reduction with L-Selectride and Basic Hydrolysis or General Procedure for Epoxidation (A) + Reduction with DIBALH, compound **12** was obtained in 40% and 39% yield, respectively. **12**: oil; $[\alpha]^{25}_D$ −5 (*c* 0.38, MeOH); IR (film) ν 3350−3100 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 5.81 (d, $J_{1,9}$ = 7.8 Hz, 1 H, H-1), 4.79 (d, $J_{5,6}$ = 1.8 Hz, 1 H, H-6), 4.65 (d, $J_{10,10'}$ = 9.2 Hz, 1 H, H-10′), 4.58 (br s, 1 H, H-4), 4.25 (t, $J_{3,11} = J_{3,11'}$ = 4.8 Hz, 1 H, H-3), 3.95 (s, 1 H, H-7), 3.80 (d, 1 H, H-10), 3.75 (d, 2 H, 2 H-11), 2.70 (ddd, $J_{5,9}$ = 5.3 Hz, $J_{4,9}$ = 1.8 Hz, 1 H, H-9), 2.54 (ddd, $J_{5,4}$ = 2.5 Hz, 1 H, H-5); ^{13}C NMR (CD_3OD, 50 MHz) δ 100.9 (C-1), 86.2 (C-8), 85.1 (C-7), 79.7 (C-6), 75.8 (C-10), 74.9 (C-4), 73.3 (C-3), 64.8 (C-11), 48.8 (C-9), 40.5 (C-5); MS (70 eV) *m*/*z* 212 (46), 85 (100). Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 53.85; H, 6.47.

[1*R*-(1α,3α,4*β*,4aα,5*β*,6α,7aα)]-4,5-(Diacetoxy)-7b-[(acetoxy)methyl]-1,3-(epoxymethane)-3,4,4a,5,6,7a-hexahydro-6,7-oxireno-cyclopenta[*c*]pyran (13). Following General Procedure for Acetylation, compound **12** (15 mg, 0.065 mmol) gave product **13** (20 mg, 87%) after flash chromatography (hexane/ethyl acetate: 7/3). **13**: mp 99−102 °C; $[\alpha]^{25}_D$ +7 (*c* 0.23, $CHCl_3$); IR (KBr) ν 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.71 (d, $J_{1,9}$ = 7.8 Hz, 1 H, H-1), 5.22 (d, $J_{5,6}$ = 2.2 Hz, 1 H, H-6), 4.79 (d, $J_{10,10'}$ = 10.6 Hz, 1 H, H-10′), 4.49 (s, 1 H, H-7), 4.39 (t, $J_{3,11} = J_{3,11'}$ = 4.7 Hz, 1 H, H-3), 4.25 (br s, 1 H, H-4), 4.15 (d, 2 H, 2 H-11), 3.86 (d, 1 H, H-10), 2.95 (ddd, $J_{5,9}$ = 5.2 Hz, $J_{4,9}$ = 1.7 Hz, 1 H, H-9), 2.61 (ddd, $J_{5,4}$ = 2.5 Hz, 1 H, H-5), 2.10, 2.08, 2.02 (s, s, s, 9 H, 3 × $OCOCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.7, 170.2, 169.6 (3 × $OCOCH_3$), 98.2 (C-1), 89.5 (C-8), 79.6, 78.6 (C-6, C-7), 74.0 (C-4), 72.4 (C-10), 68.5 (C-3), 65.3 (C-11), 44.7 (C-9), 37.5 (C-5), 21.0, 20.9, 20.8 (3 × $OCOCH_3$); MS (70 eV) *m*/*z* 296 (47), 43 (100). Anal. Calcd for $C_{16}H_{20}O_9$: C, 53.93; H, 5.66. Found: C, 53.88; H, 5.70.

[1*R*-(1α,3α,4*β*,4aα,5*β*,7aα)]-4,5-(Diacetoxy)-3,7-[(diacetoxy)methyl]-3,4,4a,5,7a-pentahydro-1-methoxy-cyclopenta[*c*]pyran (15). Following General Procedure for Epoxidation (B, MeOH) and Acetylation, compound **8** (mg, mmol) gave compound **13** (10 mg, 11%) and **15** (35 mg, 34%) after flash chromatography (hexane/ethyl acetate 85/15). **15**: oil; $[\alpha]^{25}_D$ +51(*c* 0.47, $CHCl_3$); IR (film) ν 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.84 (br d, $J_{6,7}$ = 2.8 Hz, 1 H, H-7), 5.75 (dd, $J_{5,6}$ = 6.4 Hz, 1 H, H-6), 4.99 (dd, $J_{4,5}$ = 7.9 Hz, $J_{3,4}$ = 10.3 Hz, 1 H, H-4), 4.80 (dd, $J_{10,10'}$ = 15.6 Hz, $J_{7,10'}$ = 1.4 Hz, 1 H, H-10′), 4.64 (d, 1 H, H-10), 4.42 (d, $J_{1,9}$ = 8.4 Hz, 1 H, H-1), 4.21 (d, $J_{3,11}$ = 4.1 Hz, 2 H, 2 H-11), 4.04 (dt, 1H, H-3), 3.52 (s, 3 H, OCH_3), 3.08 (ddd, $J_{5,9}$ = 7.4 Hz 1 H, H-5), 2.70 (dd, 1 H, H-9), 2.10, 2.09, 2.07, 2.03 (s, s, s, s, 12 H, 4 × $OCOCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.9, 170.4, 170.3, 169.8 (4 × $OCOCH_3$), 148.1 (C-8), 125.8 (C-7), 106.1 (C-1), 75.8 (C-6), 72.9 (C-3), 67.4 (C-4), 63.2, 62.0 (C-10, C-11), 56.7 (OCH_3), 49.3 (C-9), 41.2 (C-5), 21.5, 20.8, 20.7 (4 × $OCOCH_3$); MS (70 eV) *m*/*z* 192 (62), 43 (100). Anal. Calcd for $C_{19}H_{26}O_{10}$: C, 55.07; H, 6.32. Found: C, 55.20; H, 6.44.

[2a*S*-(3α,4*β*,4aα,5*β*,6a,7aα,7bα)]-4,5-(Diacetyloxy)-6-[(acetyloxy)methyl]-3,4,4a,5,6,7a,7b-heptahydro-2a,3-oxireno-2*H*-1,7-dioxacyclopent[*cd*]indene (16). Following General Procedure for Epoxidation (B, CH_2Cl_2), compound **9** (81 mg, 0.24 mmol) gave compound **16** (45 mg, 53%) after flash chromatography (methylene chloride/methanol 99/1). **16**: oil; $[\alpha]^{25}_D$ − 4.2 (*c* 0.13, $CHCl_3$); IR (film) ν 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.50 (d, $J_{1,9}$ = 4.5 Hz, 1 H, H-1), 5.48 (d, $J_{5,6}$ = 6.2 Hz, 1 H, H-6), 5.03 (dd, $J_{4,5}$ = 7.8 Hz, $J_{3,4}$ = 5.8 Hz, 1 H, H-4), 4.35 (m, 1 H, H-3), 4.21 (dd, $J_{11,11'}$ = 12.1 Hz, $J_{3,11'}$ = 6.0 Hz, 1 H, H-11′), 4.17 (d, $J_{10,10'}$ = 9.7 Hz, 1 H, H-10′), 4.05 (d, 1 H, H-10), 4.04 (dd, $J_{3,11}$ = 3.0 Hz, 1 H, H-11), 3.61 (s, 1 H, H-7), 3.13 (ddd, $J_{5,9}$ = 8.7 Hz, 1 H, H-5), 2.76 (dd, 1 H, H-9), 2.11, 2.08, 2.01 (s, s, s, 9 H, 3 × $OCOCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.6, 169.7, 169.6 (3 × $OCOCH_3$), 96.9 (C-1), 76.4 (C-8), 73.7 (C-6), 73.0 (C-3), 66.0 (C-4), 64.9 (C-7), 63.2, 63.1 (C-10, C-11), 45.6 (C-9), 41.6 (C-5), 21.0, 20.8 (3 × $OCOCH_3$); MS (70 eV) *m*/*z* 181 (18), 43 (100). Anal. Calcd for $C_{16}H_{20}O_9$: C, 53.93; H, 5.66. Found: C, 53.77; H, 5.89. Following General Procedure for Basic Hydrolysis, compound **16** (35 mg, 0.098 mmol) gave product **12** (15 mg, 66%) (flash chromatography: methylene chloride/methanol 95/5). Following General Procedure for Acetylation, compound **12** (15 mg, 0.065 mmol) gave product **13** (20 mg, 87%) (flash chromatography: hexane/ethyl acetate 7/3).

2-(Prop-2-ynyl)-4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (17). Compound **3** (1.41 g, 7.64 mmol) was dissolved in dry THF (5 mL, 0.14 M), cooled at 0 °C, and under argon, sodium hydride (458 mg, 19.1 mmol, 2.5 equiv) was added. Tetrabutylammonium iodide (cat.) and benzyl bromide (1.83 mL, 15.3 mmol, 2.01 equiv) were added. The mixture was stirred at room temperature for 24 h. The reaction was cooled in an ice-bath, AcOH (10 mL) was slowly added, the mixture was filtered over Celite-545, the cake was washed

with methylene chloride, the solvent was evaporated, and the residue was submitted to flash chromatography (hexane/ethyl acetate 96/4) to give product **17** (2.52 g, 90%): oil; $[\alpha]^{25}_D$ +158 (*c* 2.7, $CHCl_3$); IR (film) ν 3250 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38−7.24 (m, 10 H, 2 x $OCH_2C_6H_5$), 6.12 (dd, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 1.5 Hz, 1 H, H-3), 5.79 (ddd, $J_{1,2}$ = 2.7 Hz, $J_{2,4}$ = 1.8 Hz, $J_{2,3}$ = 10.3 Hz, 1 H, H-2), 5.25−5.23 (m, 1 H, H-1), 4.67 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.62 (d, *J* = 11.5 Hz, 1 H, $OCH_2C_6H_5$), 4.52 (d, *J* = 12.1 Hz, 1 H, $OCH_2C_6H_5$), 4.46 (d, *J* = 11.5 Hz, 1 H, $OCH_2C_6H_5$), 4.33 (d, $J_{7,9}$ = 2.4 Hz, 2 H, H-7), 4.21 (ddd, $J_{4,5}$ = 9.4 Hz, $J_{3,4}$ = 1.5 Hz, 1 H, H-4), 3.96 (dt, $J_{5,6}$ = $J_{5,6'}$ = 1.5 Hz, 1 H, H-5), 3.75 (dd, $J_{6,6'}$ = 10.7 Hz, 1 H, H-6), 3.72 (dd, 1 H, H-6′), 2.43 (t, 1 H, H-9); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 138.0−127.6 (2 × $OCH_2C_6H_5$), 131.2 (C-3), 125.9 (C-2), 92.9 (C-1), 79.5 (C-9), 74.4 (C-8), 73.3, 71.0 (2 × $OCH_2C_6H_5$), 70.1 (C-4), 69.4 (C-5), 68.6 (C-6), 54.8 (C-7); MS (70 eV) *m*/*z* 214 (25), 91 (100). Anal. Calcd for $C_{23}H_{24}O_4$: C, 75.80; H, 6.64. Found: C, 75.66; H, 6.58.

[4a*S*-(4aα,5*β*,6α,7aα,7bα)]-5-(Benzyloxy)-6-[(benzyloxy)-methyl]-5,6,7a,7b-tetrahydro-2*H*-1,7-dioxacyclopent[*cd*]-inden-4(4a*H*)-one (18). Following General Procedure for the PK Reaction, starting from pyranoside **17** (256 mg, 0.70 mmol), after flash chromatography (hexane/ethyl acetate 7/3) product **18** was isolated (136 mg, 50% yield): oil; $[\alpha]^{25}_D$ −16 (*c* 1.12, $CHCl_3$); IR (film) ν 1725, 1690 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34−7.26 (m, 10 H, 2 × $OCH_2C_6H_5$), 6.22 (s, 1 H, H-7), 5.61 (d, $J_{1,9}$ = 6.0 Hz, 1 H, H-1), 4.98 (d, *J* = 10.6 Hz, 1 H, C4−$OCH_2C_6H_5$), 4.85 (dt, $J_{10,10'}$ = 15.3 Hz, J' = 1.2 Hz, 1 H, H-10), 4.64 (dt, *J* = 2.0, 1 H, H-10′), 4.56 (d, *J* = 12.1 Hz, 1 H, C11−$OCH_2C_6H_5$), 4.50 (d, 1 H, C11−$OCH_2C_6H_5$), 4.44 (d, 1 H, C4−$OCH_2C_6H_5$), 4.02 (t, $J_{4,5}$ = $J_{3,4}$ = 8.7 Hz, 1 H, H-4), 3.70 (dt, $J_{3,11}$ = $J_{3,11'}$ = 2.8 Hz, 1 H, H-3), 3.63 (d, 2 H, 2 H-11), 3.48 (dd, $J_{5,9}$ = 6.7 Hz, 1 H, H-5), 3.44−3.39 (m, 1 H, H-9); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 206.3 (CO), 179.6 (C-8), 138.0−127.6 (2 × $OCH_2C_6H_5$), 126.1 (C-7), 96.5 (C-1), 73.6, 72.4 (2 × $OCH_2C_6H_5$), 71.6 (C-4), 69.7 (C-3), 69.2 (C-11), 65.9 (C-10), 48.3 (C-5), 47.8 (C-9); MS (70 eV) *m*/*z* 91 (100). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.66; H, 6.01.

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Supporting Information Available: Experimental details and full characterization for compounds **5**, **10**, **11**, **19**−**29**. This material is available free of charge via Internet at http://pubs.acs.org.

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