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Stereocontrolled Diels−Alder Cycloadditions of Sugar-Derived Dihydropyranones with Dienes

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2-Acetoxy-3,4-di-*O*-acetyl-D-arabinal (**6**), similar to its D-xylo analogue **4**, reacted with benzyl alcohol by the tin(IV) chloride-promoted glycosylation to produce optically active (*S*)-2-benzyloxy-2*H*-pyran-3(6*H*)-one (**8a**). The L-arabinal derivative (**5**) gave **9a**, the dihydropyranone enantiomer of **8a**. These results indicated that the configuration of the C-4 stereocenter in the starting glycal defines the configuration of the new chiral center in the resulting dihydropyranone. The influence of other catalysts (BF_3 or iodine) employed for the glycosylation on the optical purity of the dihydropyranone was studied. Enantiomerically pure dihydropyranones **8b** and **9c** were obtained using chiral alcohols ((*R*)- and (*S*)-2-octanol, respectively) as glycosylating agents. Compounds **8a**,**b** and **9a**,**c** proved to be reactive dienophiles in thermal and Lewis acid-promoted Diels−Alder reactions. The addition of 2,3-dimethylbutadiene, cyclopentadiene, and 1,3-cyclohexadiene to the *β*-pyranones **8a**,**b** led to the corresponding adducts **10a**,**b**, **12a**,**b**, and **16a**,**b** as major products. Enantiomeric cycloadducts were synthesized from the α-pyranones **9a**,**c**. The main products were formed by highly facial-diastereoselective addition of dienes to the pyranone ring, guided by the sterical hindrance of the alkoxy substituent of the C-2 stereocenter. As cycloadditions with cycloalkadienes were also highly endo diastereoselective, these reactions gave access to pure tetrahydrobenzopyranones that carry a multitude of stereogenic centers installed in a predictable way.

Introduction

Optically active dihydropyranones derived from common sugars are useful chiral templates for the synthesis of natural products and their analogues.[1] We have reported a practical and large-scale procedure for the synthesis of 6-acyloxymethyl dihydropyranones from 2-acyloxy-hex-1-enitol (glycal) derivatives.[2] Due to the highly stereoselective nature of addition reactions to such chiral enones, they have been employed as precursors of the diamino tetradeoxy sugars component of antibiotics[3] and for the preparation of modified glycosides.[4] We have also described recently a convenient synthesis of 2-alkoxy-2*H*-pyran-3(6*H*)-ones starting from D-xylose,[5] and proved their usefulness as dienophiles in Diels−Alder reactions with butadienes. In fact, [4+2] cycloadditions of a number of structurally related pyranones, such as 2-alkoxy-2*H*-pyran-5(6*H*)-ones,[6] 2-alkoxy-4-*O*-benzoyl-6-benzoyloxymethyl-2*H*-pyran-3(6*H*)-ones (enolones),[7] levoglucosenone,[8] and isolevoglucosenone,[9] have been conducted in order to obtain optically pure carbocyclic derivatives.

In contrast with cyclohexenone derivatives[10] and sugar enolones[7] that displayed low dienophilicity, the dihydropyranones derived from D-xylal were excellent dienophiles toward butadienes.[5] Furthermore the cycloadditions took place with high diastereofacial selectivity, with the stereocontrol exerted by the chiral center of the dihydropyranone. Therefore, as an extension of the previous work, we report here the synthesis of the enantiomeric (2*R*)- and (2*S*)-2-alkoxy-2*H*-pyran-3(6*H*)-ones, as a way to control the facial diastereoselection of the cycloaddition. For thermal and Lewis acid promoted reactions of dihydropyranone dienophiles with cycloalkadienes the endo/exo diastereoselectivity was also established, to determine the level of stereocontrol attainable.

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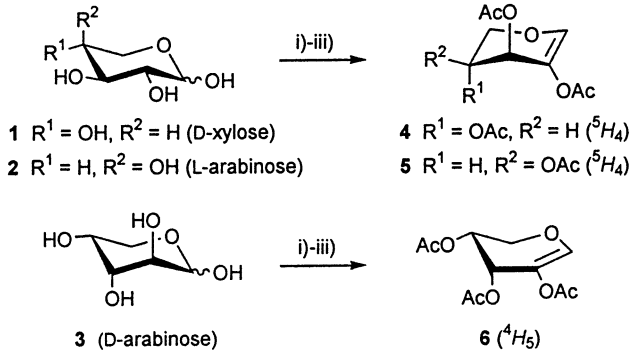
SCHEME 1[a]



[a] Reagents and conditions: (i) Ac_2O, C_5H_5N, 0 °C, 16 h; (ii) 32% HBr/AcOH, 0 °C, 1 h; (iii) DBU, −18 °C, 20 min.

Results and Discussion

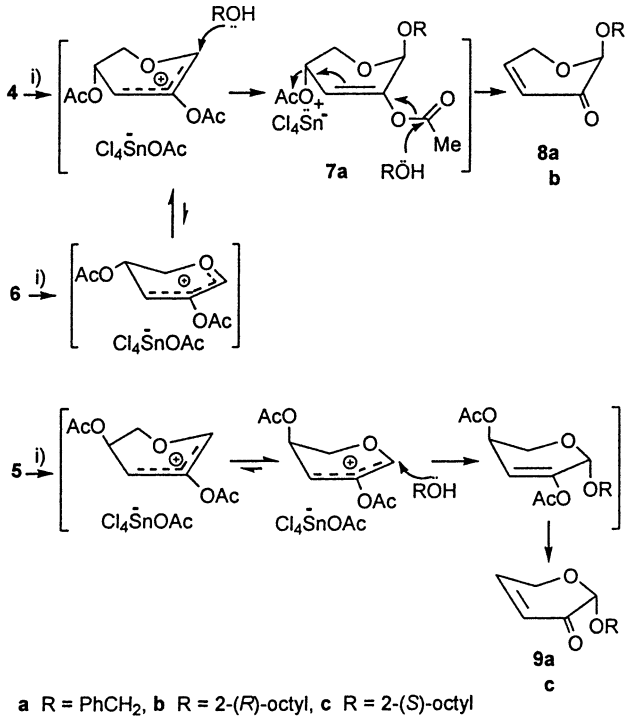
2-Acetoxy-3,4-di-*O*-acetylglycal derivatives **4**, **5**, and **6**, the key precursors of dihydropyranones, were readily prepared starting from the per-*O*-acetyl derivatives of pentopyranoses **1**, **2**, and **3**. Further conversion of the peracetates into the corresponding glycosyl bromides, followed by 1,8-diazabycyclo[5.4.0]undec-7-ene (DBU)-promoted elimination of hydrogen bromide, afforded the glycal derivatives **4**−**6** (Scheme 1). The conformational preference for the enantiomeric compounds **5** and **6** was deduced from their ^{1}H NMR spectra. The large value for the coupling constant between H-4 and H-5′ (10.2 Hz) indicated a quasidiaxial disposition for these protons, compatible with a $^5H_4$ conformation for **5** ($^4H_5$ for **6**). Similar conformations were found for the D-xylal derivative **4**,[5] and for the 2-unsubstituted analogues of **4** and **6**.[11] For the latter compounds an entropy contribution has been assessed to determine the equilibrium position between the two half-chair forms.[11] Also, stabilizing nonbonded interactions[12] ("allylic effect") have been invoked to account for the preference for one of the conformers.

The glycal derivatives **4**−**6**, as well as glycals derived from hexoses,[2] underwent a highly facial-diastereoselective tin(IV) chloride-promoted glycosylation, which is accompanied by a double allylic rearrangement. This way, glycal **4** reacted with benzyl alcohol to give the optically active dihydropyranone **8a**, having the β anomeric configuration.[5] To obtain the enantiomeric α-dihydropyranone, and to assess the influence of the C-3 and C-4 configuration of the starting glycal on the stereochemical course of the reaction, the glycosylation of glycals **5** and **6** was conducted. As shown in Table 1, the configuration of C-3 does not influence the stereochemistry at C-1, since the derivatives of D-xylal (**4**) and D-arabinal (**6**), which have opposite configurations at C-3, afforded the same dihydropyranone **8a** with identical optical purity. However, the pyranone **9a** (enantiomer of **8a**) could be readily obtained, as expected, from glycal **5** (enantiomer of **6**). Therefore, the stereocenter at C-4 seems to direct the addition of the alcohol to C-1. This result may be justified by assuming the formation of a carbocation during the acid-promoted elimination of the 3-acetoxy group (Scheme 2). Such a carbocation, probably stabilized by participation of the oxygen ring lone pair, could shift its conformation to locate the allylic acetoxy group at C-4 in the preferred axial orientation[11,12] ("allylic effect"). Hence, the nucleophilic addition of the alcohol should be induced to occur preferentially from the opposite face, accounting for the stereochemistry at C-1 of the intermediate enopyranoside (**7a**, when starting from **4**). Such an intermediate could be isolated in some cases, as explained later. The enopyranoside **7a** (or its enantiomer when starting from **5**) underwent a second allylic rearrangement, which does not involve C-1, to give the final product **8a** (or **9a**). The enantiomeric composition of **8a** and **9a** was established, as previously described,[5] by means of NMR experiments conducted with chiral lanthanide shift reagents. Thus, the enantiomeric excesses determined for **8a** and **9a** were higher than 86% (ee >86%).

TABLE 1. Preparation of Dihydropyranones 8a and 9a

starting glycal	catalyst (mol equiv)	temp (°C)	time (min)	yield (%)	$[\alpha]_D$	ee (%)
4	$SnCl_4$ (1.3)	−18	30	85	−200.6	>86
5	$SnCl_4$ (1.3)	−18	30	81	+200.3	>86
6	$SnCl_4$ (1.3)	−18	30	83	−200.4	>86
4	$Et_2O{\cdot}BF_3$ (2.0)	5	30	82	−210.8	>91
6	$Et_2O{\cdot}BF_3$ (2.0)	5	30	81	−211.2	>91
4	I_2 (1.0)	25	45	75	−167.9	>72

SCHEME 2[a]



[a] Reagents and conditions: (i) $SnCl_4$, −18 °C, 30 min.

On the basis of the mechanism proposed we assumed that isolating the enopyranoside (**7a**), postulated as an intermediate, could increase the optical purity of the dihydropyranones. The stereocenter at C-4 of the enopyranoside is maintained during the addition of the alcohol to C-1, hence affording a mixture of anomers that may be separated by standard procedures. However, **7a** could

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not be isolated when tin(IV) chloride was employed as catalyst under the usual reaction conditions, and the dihydropyranone **8a** was always the lone product obtained.

Boron trifluoride etherate promoted also the reaction of **4** or **6** with benzyl alcohol to give **8a**. This catalyst was less effective than tin(IV) chloride; therefore, higher concentrations of BF_3 and higher temperatures were required for completion of the reaction.

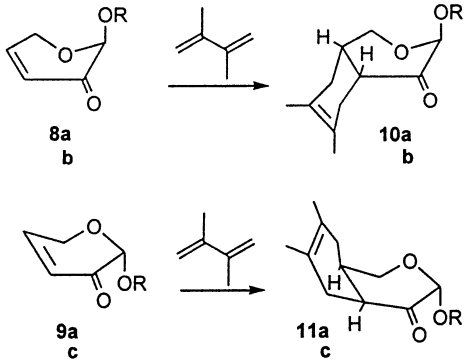
We observed that the structure of the starting glycal has incidence in the reactivity; thus, under the same Lewis acid-catalyzed conditions, glycal **4** reacted more rapidly than glycals **5** and **6**. This behavior may be attributed to the 4-acetoxy group in **4**, which being disposed anti to the C-3−O linkage, facilitates the rupture of this bond by anchimeric participation. Similarly, it has been reported that glycals derived from hexoses having a trans arrangement for the substituents at C-3 and C-4 take part in allylic rearrangements much more readily than do those with a cis disposition of such groups.[13]

On the other hand, iodine and electrophilic iodine releasing agents have been widely used for the anomeric activation of glycals.[14] We have found that an alkyl 2-enopyranoside was the major product in the *N*-iodosuccinimide-mediated glycosylation of glycals derived from hexoses.[15] Therefore, the iodine-promoted glycosylation of **4**−**6** was attempted. The reaction led to somewhat lower yields and poorer optical purity of **8a** and **9a** than those obtained under catalysis by Lewis acids. Furthermore, it was observed that the reaction proceeded more rapidly when conducted in the presence of higher concentrations of iodine or in polar solvents (acetonitrile > dichloromethane > toluene). In particular, when the reaction of **4** in acetonitrile was conducted in the presence of 0.07 equiv of iodine (instead of 1 equiv) the elusive enopyranoside **7a** was detected by TCL. However, the attempted chromatographic purification by column chromatography was not practical as **7a** and its α anomer had similar chromatographic mobility in a number of solvents. Thus, compound **7a** could be isolated in low yield (∼20%) as an 8:1 mixture of β and α anomers, as indicated by the NMR spectra. Interestingly, the anomeric composition of the mixture was in agreement with the enantiomeric ratio determined for the dihydropyranone **8a**, which is produced from **7a**.

In view of the results discussed above, and taking into account that the enantiomerically pure dihydropyranone **8b** had been successfully prepared with (*R*)-2-octanol as glycosylating agent under Lewis acid catalysis,[5] the synthesis of **9c**, the enantiomer of **8b**, was attempted. For this purpose (*S*)-2-octanol was employed for the tin(IV) chloride-promoted glycosylation of **5**. After purification by column chromatography, compound **9c** exhibited identical spectral properties as **8b** and a diastereomeric excess higher than 97% (de >97%).

Dihydropyranones **8a**,**b** proved to be useful as dienophiles for Diels−Alder cycloadditions with butadienes,

SCHEME 3



a R = $PhCH_2$, **b** R = 2-(*R*)-octyl, **c** R = 2-(*S*)-octyl,

under thermal and Lewis acid-catalyzed conditions.[5] Their reactivity, compared with that of common cyclohexenones, was probably enhanced by the presence of an oxygen atom in the six-membered ring.[6a,7] Furthermore, cycloadditions were highly diastereoselective, as a result of the steric hindrance exerted by the axially oriented alkoxy substituent (in the preferred E_0 conformation[5] of **8a**,**b**) on one of the faces of the double bond. Thus, the C-2 configuration of **8a**,**b** controls the configuration of the stereocenters (C-4a and C-8a) generated in the cycloaddition of butadienes. This way, as **8a** and **9a** have opposite configuration at C-2, the addition of a diene should lead to enantiomeric cycloadducts. As expected, boron trifluoride diethyl etherate-catalyzed addition of 2,3-dimethylbutadiene to **9a**, under the optimized conditions established for **8a**,[5] led to the cycloadduct **11a**, the enantiomer of **10a** (Scheme 3). The coincidence in the absolute value of the optical rotation of both products indicated that they possess the same optical purity (ee >86%). To synthesize the enantiomerically pure cycloadduct **11c**, the dihydropyranone **9c** (enantiomer of **8b**) was employed as the dienophile. The resulting tetrahydrobenzopyranone **11c** was the enantiomer of **10b**.

Cycloadditions of cyclopentadiene and 1,3-cyclohexadiene with 2-alkoxy-2*H*-pyran-3(6*H*)-ones were conducted to extend their use as dienophiles in the construction of more complex chiral carbocycles. The resulting cycloadducts will carry in their structures four new stereocenters. The dihydropyranone **8a** was used as a model dienophile and the Diels−Alder additions were performed under thermal conditions and boron trifluoride catalysis. Reaction conditions which led to good yields of adducts are shown in Table 2. Cycloadditions of **8a** with cyclic dienes, as with butadienes, were highly diastereofacial selective, with a remarkable preference for the addition of the cyclic diene (guided by the C-2 anomeric substituent) from the α face of the dihydropyranone. Addition of cyclopentadiene to **8a** gave the α-endo adduct **12a** as the main product, and the isomers **13a** (α-exo) and **14a** (β-endo) were isolated in low yields (Scheme 4). Starting from **9a** (enantiomer of **8a**) the cycloadduct **15a** (enantiomer of **12a**) was obtained as the major product. Cyclohexadiene was less reactive than cyclopentadiene toward dihydropyranones as cycloadditions, under thermal conditions or Lewis acid catalysis, required higher temperatures and longer reaction times. Thermal Diels−Alder reaction of **8a** with 1,3-cyclohexadiene afforded

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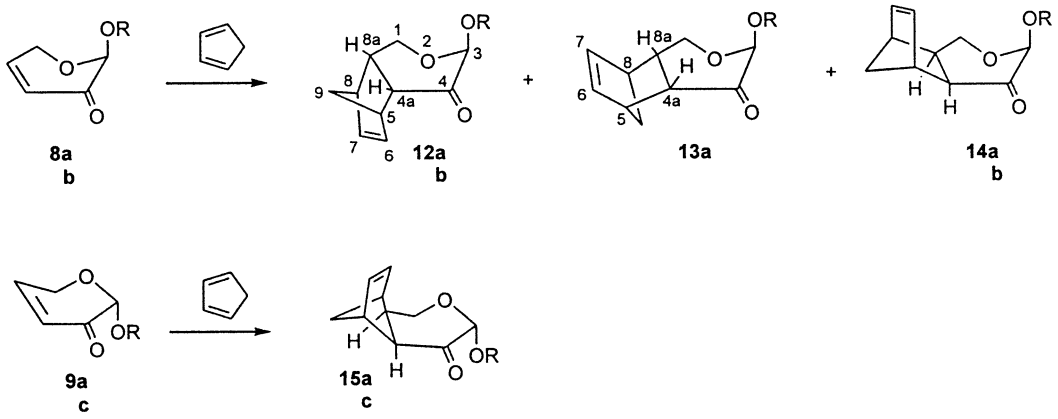
TABLE 2. Diels–Alder Reactions of Dihydropyranone 8a with Cyclic Dienes under Thermal and $Et_2O{\cdot}BF_3$ Catalyzed Conditions

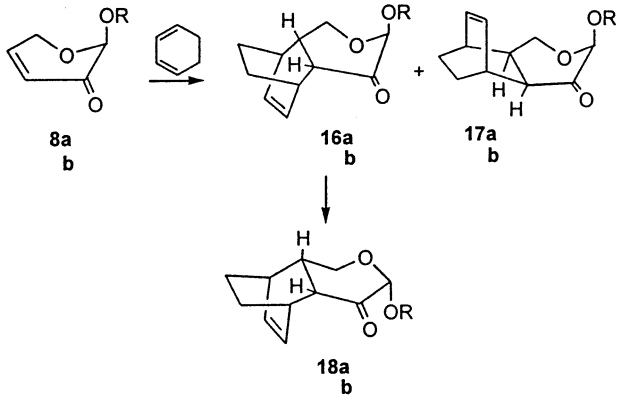
diene (mol equiv)	mol equiv of $Et_2O{\cdot}BF_3$	temp (°C)	time (h)	dr[a] α/β endo	dr[a] endo/exo	yield of adducts[b]
cyclopentadiene (3.4)		90	96	21.4:1	10.1:1	79
1,3-cyclohexadiene (11.2)		130	110	10.9:1	>30:1	70
cyclopentadiene (2.0)	1.0	−18	0.25	18.7:1	13.4:1	64
1,3-cyclohexadiene (12.7)	1.0	0	0.75	3.3:1[c]	>30:1	68

[a] The diastereomeric ratio (dr) was calculated from the ^{1}H NMR spectrum of the crude reaction mixture. [b] Yield of adducts after isolation by flash chromatography. [c] Includes also the isomerization product **18a** (see text).

SCHEME 4



SCHEME 5



mainly the α-endo adduct **16a**, the analogue of **12a**, together with the β-endo diastereomer (**17a**) (Scheme 5). The observed proportion of the latter compound (**17a**) was remarkably increased in the boron trifluoride-promoted reaction, indicating an apparently poor stereoselection for the addition of the diene to **8a**. However, in this case, compound **17a** exhibited an optical rotation value opposite in sign to that of the same product obtained under thermal conditions. The unexpected change in its optical rotation could be justified if we assume that, under the Lewis acid catalysis, the acetal carbon (C-3) of the α-endo adduct **16a** undergoes isomerization to produce **18a**, the enantiomer of **17a**. This way, the partial conversion of **16a** into **18a** would result in an apparent increment of **17a** and in a modification of its optical rotation. To confirm the proposed isomerization, compound **16a** was treated with boron trifluoride, under the conditions employed for the cycloaddition. Monitoring of the mixture by TLC showed the gradual conversion of **16a** into a more polar product having the same mobility as **17a**. Moreover, the spectra of the reaction mixture evidenced the presence of both **16a** and the isomerization product **18a**, which is spectroscopically identical with **17a**. The Lewis acid seems to promote the isomerization of **16a** to **18a** under the higher temperature and longer times required for the BF_3-catalyzed cycloaddition of **8a** with 1,3-cyclohexadiene (compared with those employed for cyclopentadiene). The isomerization of the α-endo adduct was further proved, as explained later, by addition of 1,3-cyclohexadiene to pyranone **8b**. This reaction led to the diastereomeric adducts **17b** and **18b** (the respective analogues of **17a** and **18a**) which could be isolated and characterized.

Cycloadditions of cyclopentadiene and 1,3-cyclohexadiene to **8a** were also highly endo diastereoselective, as predicted by the Alder endo rule.[16] For example, in the reaction of **8a** with 1,3-cyclohexadiene the formation of exo adducts was negligible. The endo stereoselectivity has been rationalized satisfactorily in terms of interplay of stabilizing secondary interactions and steric effects between diene and dienophile in the endo transition state.[17]

The structure of cycloadducts **12a**–**17a** was determined on the basis of their NMR spectra as well as by 2D NMR experiments. As reported for related systems,[7] the α or β facial annulation of the carbocyclic portion onto the pyranone ring was clearly revealed by the coupling constants of H-1 and H-1′ to the vicinal H-8a. In two of the isomers (**12a** and **13a**) the relatively small *J* values

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indicated that the C−H-8a bond bisects the angle of the H-1−C−H-1′ group, an arrangement characteristic of α-adducts. In contrast, the isomer **14a** showed a large *J* value between H-8a and H-1′, consistent with a diaxial orientation of such protons, as expected for a *β*-adduct.

The endo/exo assignments were aided greatly by NMR data reported for adducts of cycloalkadienes with 2-cyclohexenones[18,19] and enolones.[7] The *δ* values of the olefinic protons (H-6 and H-7) were diagnostic of the stereochemistry of the cycloadducts. Two of the isomers (**12a** and **14a**) showed larger shift differences for H-6 and H-7, compared with that of **13a**. The magnetic similarity for the vinylic protons in **13a** is consistent with the absence of any shielding effects exerted by the pyranoid ring or its substituents, as expected for an exo adduct. In contrast, the olefinic protons in the endo adducts **12a** and **14a** are relatively closer to the pyranoid ring, and its anisotropy induces larger chemical shift differences between H-6 and H-7. Furthermore, the chemical shift of the protons of the fused rings (H-4a and H-8a) is stereochemistry dependent. Such protons appeared strongly shielded in the exo compound (as they are facing the double bond that exerts its shielding effect) and deshielded in the endo products (because of the removal of the anisotropy of the olefinic bond). Similar anisotropic effects on H-1ax and H-3 in **12a**−**14a** supported the assignment of the α or *β* and endo/exo orientation of the carbocycle. Thus H-1ax, which is facing the *π* bond in the *β*-endo isomer **14a**, resonates upfield (∼1 ppm) compared to H-1ax in **12a** and **13a**, where such a proton is located far away from the double bond. The pattern of signals in the endo and exo adducts of levoglucosenone with cyclopentadiene was similar to those of **12a** and **13a**, respectively.[8]

The foregoing assignments agreed with chemical shift data obtained from the ^{13}C NMR spectra of the adducts. Thus, the carbon signal of the 5,8-methano bridge (C-9) is much more shielded (∼4 ppm) in the exo adduct (**13a**) than in the endo products (**12a** and **14a**). Also, the C-1 signal is shifted upfield (∼2 ppm) in **12a** compared with **13a**, as described for endo isomers and their exo counterparts.[19]

A similar spectroscopic analysis was performed for the structural assignment of the cycloadducts derived from **8a** and 1,3-cyclohexadiene. The configuration of the C-4a and C-8a of the two isomers, which resulted from the addition of the diene to the α-face (**16a**) or from the *β*-face (**17a**) of the pyranone, was readily deduced, as for the cyclopentadiene products, on the basis of the magnitude of the coupling constants between H-1 and H-1′ with H-8a. The endo stereochemistry for **16a** and **17a** was assigned taking into account characteristic chemical shifts of certain signals (H-6, H-7, H-4a, H-8a, etc). Finally, the structural assignments of the adducts **12a**−**14a** and **16a**,**17a** were confirmed by NOESY experiments.[20] The observed cross-peaks in the NOESY spectra of **12a**−**14a** were fully consistent with the structures previously proposed. The stereochemistry of **16a** and **17a** was also firmly established by diagnostic cross-peaks in their spectra. For example, cross-peaks between the interacting 1,3-disposed protons H-4a with H-1′ax and H-10, and H-8a with H-9 clearly defined the α-endo configuration of **16a**; whereas the cross-peaks between H-1eq and H-8, H-8a with H-9, and H-4a with H-10 were indicative of a *β*-endo structure for **17a**.

The optically active cycloadducts **12a**−**14a** and **16a** exhibited the same enantiomeric purity (>86%) as their precursor pyranone **8a**. To obtain enantiomerically pure Diels−Alder products, thermal and $Et_2O{\cdot}BF_3$-promoted reactions were conducted starting from the optically pure dihydropyranones **8b** and **9c** and cyclopentadiene. Thus, optically pure cycloadducts **12b** and **14b** were synthesized from **8b**, whereas the endo cycloadduct **15c** (enantiomer of **12b**) was obtained from **9c** (enantiomer of **8b**). As for reactions with 2,3-dimethylbutadiene, the C-2 stereocenter of the starting dihydropyranone (**8b** or **9c**) efficiently controlled the facial addition of the diene, and together with the high endo selectivity afforded good yields of the corresponding major adducts (**12b** and **15c**) having opposite configuration for all the stereocenters. The structure of the enantiomerically pure compounds **12b** and **15c** was established from their NMR spectra that greatly resemble to those of the analogous 3-benzyloxy-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one **12a** and **15a**.

Similar to the reaction with cyclopentadiene, the addition of 1,3-cyclohexadiene to **8b** under thermal conditions afforded the α-endo adduct (**16b**) as the main product. However, the same reaction promoted by a Lewis acid brought additional evidence of the isomerization of the C-3 acetal stereocenter of **16b**, similar to that observed for **16a**. Thus, isomerization of the α-endo adduct **16b** afforded **18b**, which has the opposite configuration for all the chiral centers compared to **17b**, except for that of the alkoxy substituent which is *R* in both compounds. Therefore, in contrast with **17a** and **18a** (its enantiomeric isomerization product), the diastereomeric adducts **17b** and **18b** could be separated by column chromatography. Although their ^{1}H NMR spectra were very similar, the ^{13}C NMR spectrum of **17b** showed distinctive signals for C-3 and for the carbons located near the stereocenter in the alkoxy chain of **18b**, whereas the signals for the carbocycle backbone remained unchanged. Finally, as described for **16a**, compound **16b** gradually converted into **18b** when exposed to a solution of the Lewis acid.

In summary, in this work we reported the synthesis, starting from readily accessible glycal derivatives, of both optically active (2*R*)- and (2*S*)-benzyloxydihydropyranones. The enantiomerically pure analogues were obtained using chiral alcohols as glycosylating agents of the glycals. The dihydropyranones were employed as reactive dienophiles in Diels−Alder reactions with 2,3-dimethylbutadiene, cyclopentadiene, and 1,3-cyclohexadiene, under thermal and Lewis acid-promoted conditions. The cycloadditions were highly facial and endo diastereoselective, providing a straightforward access to both enantiomers of carbocycles that possess a number of stereocenters, which can be generated with remarkable stereocontrol.

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Experimental Section

General Methods. Melting points are uncorrected. Optical rotations were measured at 25 °C. Column chromatographic separations were performed with silica gel 60, 240−400 mesh. Analytical TLC was conducted on silica gel 60 F_{254} precoated plates (0.2 mm). Visualization of the spots was effected by exposure to UV light and charring with a solution of 5% sulfuric acid in EtOH, containing 0.5% *p*-anisaldehyde. Solvents were reagent grade and, in most cases, were dried and distilled prior to use according to standard procedures.

2,3,4-Tri-*O*-acetyl-1,5-anhydro-L-*erythro*-pent-1-enitol (2-Acetoxy-3,4-di-*O*-acetyl-L-arabinal, 5). L-Arabinose (**2**, 4.50 g, 29.97 mmol) was dissolved in boiling anhydrous pyridine (20 mL) with vigorous stirring. The mixture was rapidly cooled to 0 °C and acetic anhydride (35 mL) was added dropwise. After standing overnight at 0 °C, the solution was poured into ice−water and the mixture extracted several times with CH_2Cl_2. The organic layer was washed with ice-saturated (satd) aqueous (aq) $NaHCO_3$, then with ice−water, dried ($MgSO_4$), and concentrated. Pyridine was removed by successive evaporations at room temperature with toluene. The resulting product was dissolved in 32% HBr in glacial acetic acid (34 mL) keeping the temperature to 0 °C, and then acetic anhydride (0.34 mL) was added dropwise in the dark. After 1 h, TLC showed a main spot ($R_f = 0.53$, hexane/EtOAc 2:1) and no starting material ($R_f = 0.34$) remaining. The solution was concentrated in a vacuum and successively dissolved and evaporated with toluene and ethyl ether to afford a partly crystalline product, which was rapidly washed with anhydrous ethyl ether. The residue was dissolved in anhydrous CH_2Cl_2 (20 mL), and to the resulting solution, cooled to −18 °C, was added 1,8-diazabycyclo[5.4.0]undec-7-ene (DBU, 5 mL) dropwise in the dark. After stirring for 20 min TLC showed a main spot having $R_f = 0.39$; and the mixture was diluted with CH_2Cl_2, washed with 10% aq HCl, satd aq $NaHCO_3$, and satd aq NaCl. The organic extract was dried ($MgSO_4$), concentrated, and purified by flash chromatography (hexane/EtOAc 7:1) to afford crystalline **5** (3.33 g, 43% from **2**); mp 61−62 °C; $[\alpha]_D$ −207.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.67 (br s, 1, H-1), 5.72 (dd, 1, $J_{3,4} = 4.4$ Hz, $J_{3,5} = 1.2$ Hz, H-3), 5.29 (ddd, 1, $J_{4,5} = 4.0$ Hz, $J_{4,5'} = 10.2$ Hz, H-4), 4.03 (ddd, 1, $J_{5,5'} = 10.6$ Hz, H-5), 3.92 (dd, 1, H-5′), 2.11, 2.08, 2.05 (3 s, 9, CH_3CO); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.4, 169.6, 169.4 (CH_3CO), 141.2 (C-1), 127.1 (C-2), 65.4, 64.4 (C-3,4), 62.7 (C-5), 20.8, 20.6, 20.5 (CH_3CO). Anal. Calcd for $C_{11}H_{14}O_7$: C, 51.17; H, 5.46. Found: C, 51.33; H, 5.64.

2,3,4-Tri-*O*-acetyl-1,5-anhydro-D-*erythro*-pent-1-enitol (2-Acetoxy-3,4-di-*O*-acetyl-D-arabinal, 6). Compound **6** was prepared as described for **5**, starting from D-arabinose (**3**, 4.24 g, 28.24 mmol). The glycal **6** (3.21 g, 44% from **3**) gave $[\alpha]_D$ +207.6 (*c* 1.0, $CHCl_3$) (lit.[21] $[\alpha]_D$ +202) and ^{1}H and ^{13}C NMR spectra identical with those of **5**.

2-Benzyloxy-2*H*-pyran-3(6*H*)-ones (8a and 9a). The procedure described for the $SnCl_4$-promoted glycosylation of glycal derivatives was essentially followed.[5] A solution of glycal **4**, **5**, or **6** (0.10 g, 0.39 mmol) and benzyl alcohol (50 μL, 0.49 mmol) in anhydrous CH_2Cl_2 (6.5 mL) was cooled to the temperature indicated in Table 1, and the corresponding Lewis acid was added. The mixture was stirred for 30 min and then diluted with CH_2Cl_2. After the usual workup, the residue was purified by flash chromatography (hexane/EtOAc 14:1).

For the iodine-promoted glycosylation, a solution of **4** (135 mg, 0.52 mmol) and benzyl alcohol (108 μL, 1.05 mmol) in anhydrous acetonitrile (2 mL) was treated, in the dark, with iodine (132 mg, 0.52 mmol) at room temperature for 45 min. Upon dilution with CH_2Cl_2, the solution was washed with a 5:1 (v/v) mixture of satd aq $Na_2S_2O_3$ and satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated and the resulting residue purified by flash chromatography as above.

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The dihydropyranones **8a** and **9a** were isolated as colorless oils; their yields and specific rotations are reported in Table 1. Compound **9a** exhibited ^{1}H and ^{13}C NMR spectra identical with those of the enantiomeric **8a**.[5]

Isolation of Benzyl 2,4-Di-*O*-acetyl-3-deoxy-β-D-*glycero*-hex-2-enopyranoside (7a). The iodine-promoted glycosylation of **4** (442 mg, 1.71 mmol) was performed with benzyl alcohol (187 μL, 1.82 mmol) in the presence of iodine (29.1 mg, 0.11 mmol). The reaction was conducted in dry acetonitrile (6 mL) for 20 min, according to the procedure described above. After the usual workup, the reaction mixture was chromatographed with hexane/EtOAc 14:1 to afford **7a** (106 mg, 20% yield) as a 8:1 mixture of β and α anomers, determined from the ^{1}H NMR spectrum (200 MHz, $CDCl_3$); for the β anomer δ 7.32 (br s, 5, H-aromatic), 5.89 (d, 1, $J_{3,4} = 5.8$ Hz, H-3), 5.16 (dd, 1, $J_{4,5} = 2.7$ Hz, H-4), 5.08 (br s, 1, H-1), 4.78, 4.58 (2 d, 2, $J = 12.2$ Hz, PhCH_2O), 4.18 (dd, 1, $J_{5,5'} = 13.2$ Hz, H-5ax), 3.83 (d, 1, $J_{4,5'} < 1$ Hz, H-5′eq), 2.11, 2.07 (2 s, 6, CH_3CO); for the α anomer (distinctive signals) δ 5.75 (d, $J_{3,4} = 2.9$ Hz, H-3), 5.10 (br s, 1, H-1); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.5, 167.9 (CH_3CO), 149.2 (C-2), 137.4, 128.5, 128.0, 127.9 (C-aromatic), 111.7 (C-3), 92.1 (C-1), 70.1 (PhCH_2O), 65.0 (C-4), 61.2 (C-5), 21.0, 20.9 (CH_3CO); for the α anomer (partial spectrum) δ 115.3 (C-3), 92.9 (C-1), 70.3 (PhCH_2O), 65.3 (C-4), 60.2 (C-5).

(2*S*)-[(*R*)-2′-Octyloxy]-2*H*-pyran-3(6*H*)-one (8b) and (2*R*)-[(*S*)-2′-Octyloxy]-2*H*-pyran-3(6*H*)-one (9c). Compound **8b** was prepared by the tin(IV) chloride-promoted glycosylation of **4** with (*R*)-2-octanol, as previously reported.[5] The same procedure was employed for the synthesis of **8b** from **6**, and for the preparation of **9c** from **5** and (*S*)-2-octanol.

Compound **9c** (de > 97%) gave $[\alpha]_D$ +183.5 (*c* 1.0, $CHCl_3$) (lit.[5] $[\alpha]_D$ −183.6 for the enantiomer **8b** (de > 97%)). Dihydropyranones **8b** and **9c** showed identical ^{1}H and ^{13}C NMR spectra.

Adducts of Dihydropyranones 9a,c with 2,3-Dimethylbutadiene: (3*R*,4a*S*,8a*R*)-3-Benzyloxy-6,7-dimethyl-4a,5,8,8a-tetrahydro-1*H*-2-benzopyran-4(3*H*)-one (11a) and (3*R*,4a*S*,8a*R*)-6,7-Dimethyl-3-[(*S*)-2′-octyloxy]-4a,5,8,8a-tetrahydro-1*H*-2-benzopyran-4(3*H*)-one (11c). The boron trifluoride-promoted cycloaddition of 2,3-dimethylbutadiene to **9a** (51.3 mg, 0.25 mmol, ee > 86%) and to **9c** (54.6 mg, 0.24 mmol, de > 97%) afforded respectively **11a** (59.1 mg, 82% yield) and **11c** (60.3 mg, 81% yield). Adduct **11a** gave $[\alpha]_D$ +49.8 (*c* 1.0, $CHCl_3$) (lit.[5] $[\alpha]_D$ −49.7 for the enantiomer **10a** (ee > 86%)); **11c** gave $[\alpha]_D$ +39.9 (*c* 1.0, $CHCl_3$) (lit.[5] $[\alpha]_D$ −39.7 for the enantiomer **10b**). The ^{1}H and ^{13}C NMR spectra of **11a** and **11c** were identical with those of **10a** and **10b**, respectively.[5]

Adducts of Dihydropyranone 8a with Cyclopentadiene and 1,3-Cyclohexadiene: 3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-ones (12a−14a) and 3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-ones (16a, 17a). Thermal Cycloaddition General Procedure. A solution of the dihydropyranone **8a** (204 mg, 1 mmol) and hydroquinone (10 mg) in dry toluene (0.2 mL) was placed in a thick-walled glass tube and the freshly distilled diene (see Table 2) was added. The glass tube was flushed with dry argon, sealed, and heated at the temperature and for the time indicated in Table 2. The solution was then concentrated and purified by flash chromatography (1−2% EtOAc in hexane) to afford adducts **12a**−**14a** and **16a**,**17a**. This procedure led to the following isolated yields of cycloadducts for the reaction of **8a** (75.0 mg, 0.37 mmol) with cyclopentadiene: **12a** (70.2 mg, 70.7%), **13a** (5.8 mg, 5.8%), and **14a** (3.0 mg, 3.0%). Whereas, thermal cycloaddition of **8a** (263 mg, 1.29 mmol) with 1,3-cyclohexadiene afforded **16a** (238 mg, 65.0%) and **17a** (17.4 mg, 4.8%).

General $Et_2O{\cdot}BF_3$-Promoted Cycloaddition. A solution of **8a** (204.2 mg, 1 mmol) in dry toluene (4 mL) was cooled to −18 °C and $Et_2O{\cdot}BF_3$ (125 μL, 1 mmol) was added under argon. The vial was sealed and the mixture was stirred at −18 °C for 15 min, then the diene dissolved in toluene (1 mL) was slowly injected into the solution. When the addition was

finished, the mixture was stirred at the temperature and for the time indicated in Table 2. The reaction mixture was diluted with ethyl ether, washed with satd aq $NaHCO_3$, dried ($MgSO_4$), and concentrated. Addition of hexane to the residue produced the precipitation of polymeric material. The hexane solution was subjected to flash chromatography with 1−2% EtOAc in hexane affording the corresponding cycloadducts. Thus, starting from **8a** (137 mg, 0.67 mmol) and cyclopentadiene, **12a** (103.3 mg, 57.0%), **13a** (7.0 mg, 3.9%), and **14a** (5.3 mg, 2.9%) were obtained. Similarly, reaction of **8a** (416 mg, 2.04 mmol) with 1,3-cyclohexadiene gave **16a** (314 mg, 54.2%) and **17a** (together with **18a**, total 80 mg, 13.8%).

The starting dihydropyranone **8a**, employed for all these reactions, had an ee >86%; therefore, the respective cycloadducts **12a**−**14a** and **16a** exhibited the same optical purity. The enantiomeric composition for the major products was determined by ^{1}H NMR experiments with ytterbium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] and it is indicated in any individual case. Compounds **12a**−**14a** and **16a**−**18a** showed the following properties (the reported R_f values were determined using hexane/EtOAc, 5:2).

(3*S*,4a*R*,5*S*,8*R*,8a*S*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (α-Endo-Adduct, 12a). The major product **12a** (ee > 86%, R_f = 0.56) gave $[\alpha]_D$ −123.4 (*c* 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (br s, 5, H-aromatic), 6.20 (dd, 1, $J_{6,7}$ = 5.6 Hz, $J_{7,8}$ = 3.0 Hz, H-7), 6.07 (dd, 1, $J_{5,6}$ = 2.9 Hz, H-6), 4.71, 4.55 (2 d, 2, J = 11.7 Hz, PhCH_2O), 4.38 (br s, 1, H-3), 4.21 (dd, 1, $J_{1,8a}$ = 6.0 Hz, $J_{1,1'}$ = 12.2 Hz, H-1ax), 3.49 (dd, 1, $J_{1',8a}$ = 3.3 Hz, H-1′eq), 3.35 (m, 1, H-5), 3.05 (dd, 1, $J_{4a,5}$ = 4.3 Hz, $J_{4a,8a}$ = 9.3 Hz, H-4a), 2.95 (br s, 1, H-8), 2.67 (dddd, 1, $J_{8,8a}$ = 3.0 Hz, H-8a), 1.43 (dt, 1, $J_{5,9} \sim J_{8,9} \sim$ 1.8 Hz, $J_{9,9'}$ = 8.4 Hz, H-9), 1.32 (br d, 1, $J_{5,9'} \sim J_{8,9'} <$ 1 Hz, H-9′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 204.8 (C-4), 136.9, 128.5, 128.1, 128.0 (C-aromatic), 136.0, 135.1 (C-6,7), 96.9 (C-3), 69.9 (Ph*C*H_2O), 61.0 (C-1), 49.3 (C-9), 48.3, 47.5, 47.4 (C-4a,5,8), 37.5 (C-8a). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.29; H, 6.76.

(3*S*,4a*R*,5*R*,8*S*,8a*S*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (α-Exo-Adduct, 13a). For the less polar adduct **13a** (ee > 86%, R_f = 0.62); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (br s, 5, H-aromatic), 6.27, 6.19 (2 dd, 2, $J_{5,6}$ = $J_{7,8}$ = 2.9 Hz, $J_{6,7}$ = 5.5 Hz, H-6,7), 4.77, 4.61 (2 d, 2, J = 11.7 Hz, PhCH_2O), 4.68 (br s, 1, H-3), 4.35 (dd, 1, $J_{1,8a}$ = 5.5 Hz, $J_{1,1'}$ = 12.4 Hz, H-1ax), 3.70 (dd, 1, $J_{1',8a}$ = 3.1 Hz, H-1′eq), 3.24 (br s, 1, H-5), 2.76 (br s, 1, H-8), 2.35 (br d, 1, $J_{4a,8a}$ = 8.8 Hz, H-4a), 1.89 (dddd, 1, $J_{8,8a}$ = 1.8 Hz, H-8a), 1.59 (d, 1, $J_{5,9} \sim J_{8,9} <$ 1.0 Hz, $J_{9,9'}$ = 9.1 Hz, H-9), 1.28 (ddd, 1, $J_{5,9'}$ = $J_{8,9'}$ = 1.8 Hz, H-9′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 205.9 (C-4), 139.0, 136.4 (C-6,7), 136.8, 128.5, 128.2, 128.0 (C-aromatic), 96.9 (C-3), 70.1 (PhCH_2O), 63.1 (C-1), 48.6, 48.1, 46.9 (C-4a,5,8), 44.9 (C-9), 36.9 (C-8a).

(3*S*,4a*S*,5*R*,8*S*,8a*R*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (β-Endo-Adduct, 14a). The more polar product **14a** (ee > 86%, R_f = 0.46) gave mp 59−60 °C; $[\alpha]_D$ +29.2 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (m, 5, H-aromatic), 6.27 (dd, 1, $J_{5,6}$ = 2.8 Hz, $J_{6,7}$ = 5.7 Hz, H-6), 5.95 (dd, 1, $J_{7,8}$ = 3.0 Hz, H-7), 4.73, 4.60 (2 d, 2, J = 12.4 Hz, PhCH_2O), 4.67 (br s, 1, H-3), 3.91 (dd, 1, $J_{1,1'}$ = 11.5 Hz, $J_{1,8a}$ = 6.6 Hz, H-1eq), 3.32 (br s, 1, H-5), 3.17 (dd, 1, $J_{1',8a}$ = 12.0 Hz, H-1′ax), 3.06 (dddd, 1, $J_{4a,8a}$ = 9.9 Hz, $J_{8,8a}$ = 3.3 Hz, H-8a), 2.86 (br s, 1, H-8), 2.83 (dd, 1, $J_{4a,5}$ = 3.9 Hz, H-4a), 1.58 (ddd, 1, $J_{5,9}$ = $J_{8,9}$ = 1.8 Hz, $J_{9,9'}$ = 8.5 Hz, H-9), 1.38 (br d, 1, $J_{5,9'} \sim J_{8,9'} <$ 1 Hz, H-9′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 207.9 (C-4), 138.3, 134.0 (C-6,7), 137.0, 128.4, 128.1, 127.8 (C-aromatic), 95.8 (C-3), 69.2 (PhCH_2O), 64.5 (C-1), 49.2 (C-4a), 48.7 (C-9), 44.1, 43.4, 41.6 (C-5,8,8a). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.18; H, 6.68.

(3*S*,4a*R*,5*S*,8*R*,8a*S*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (α-Endo-Adduct, 16a). The major product of the thermal cycloaddition of **8a** with 1,3-cyclohexadiene was **16a** (ee > 86%, R_f = 0.68); $[\alpha]_D$ −114.3 (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (br s, 5, H-aromatic), 6.25 (br t, 1, $J_{6,7}$ = 7.6 Hz, $J_{7,8}$ = 6.5 Hz, $J_{5,7}$ < 1 Hz, H-7), 6.18 (ddd, 1, $J_{5,6}$ = 6.5 Hz, $J_{6,8}$ = 1.1 Hz, H-6), 4.75, 4.59 (2 d, 2, J = 11.9 Hz, PhCH_2O), 4.51 (br s, 1, H-3), 4.06 (dd, 1, $J_{1,8a}$ = 5.1 Hz, $J_{1,1'}$ = 12.1 Hz, H-1), 3.33 (dd, 1, $J_{1',8a}$ = 6.3 Hz, H-1′), 3.07 (m, 1, H-5), 2.86 (dd, 1, $J_{4a,5}$ = 3.0 Hz, $J_{4a,8a}$ = 10.0 Hz, H-4a), 2.53 (dddd, 1, $J_{8a,8}$ = 1.5 Hz, H-8a), 2.50 (m, 1, H-8), 1.62 (m, 1, H-9), 1.55 (m, 1, H-10), 1.32 (m, 1, H-10′), 1.27 (m, 1, H-9′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 206.2 (C-4), 137.0, 128.5, 128.1, 127.9 (C-aromatic), 134.1, 132.7 (C-6,7), 97.9 (C-3), 70.1 (PhCH_2O), 64.6 (C-1), 49.4 (C-4a), 39.3 (C-8a), 34.1, 32.6 (C-5,8), 26.1, 23.3 (C-9,10). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.77; H, 7.33.

Compound **16a**, obtained by the $Et_2O{\cdot}BF_3$-catalyzed cycloaddition, showed the same properties as those described above.

(3*S*,4a*S*,5*R*,8*S*,8a*R*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (β-Endo-Adduct, 17a) and (3*R*,4a*R*,5*S*,8*R*,8a*S*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (18a, C-3 Isomerization Product of 16a). The byproduct (**17a**) of the thermal cycloaddition of **8a** with 1,3-cyclohexadiene was isolated by flash chromatography (R_f = 0.60). Compound **17a** gave $[\alpha]_D$ +10.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (m, 5, H-aromatic), 6.32 (ddd, 1, $J_{6,7}$ = 7.2 Hz, $J_{5,6}$ = 6.4 Hz, $J_{6,8}$ = 1.1 Hz, H-6), 6.05 (t, 1, $J_{7,8}$ = 6.7 Hz, $J_{5,7}$ < 1 Hz, H-7), 4.74, 4.60 (2 d, 2, J = 12.2 Hz, PhCH_2O), 4.73 (br s, 1, H-3), 3.73 (dd, 1, $J_{1,8a}$ = 6.4 Hz, $J_{1,1'}$ = 11.7 Hz, H-1eq), 3.30 (dd, 1, $J_{1',8a}$ = 12.1 Hz, H-1′ax), 3.17 (br m, 1, H-5), 2.80 (dddd, 1, $J_{4a,8a}$ = 10.5 Hz, $J_{8,8a}$ = 1.3 Hz, H-8a), 2.59 (dd, 1, $J_{4a,5}$ = 2.7 Hz, H-4a), 2.38 (br s, 1, H-8), 1.59 (m, 1, H-9), 1.53 (m, 1, H-10), 1.33 (m, 2, H-9′,10′); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 206.4 (C-4), 137.1, 128.3, 128.0, 127.7 (C-aromatic), 135.0, 132.0 (C-6,7), 96.7 (C-3), 69.1 (PhCH_2O), 64.5 (C-1), 49.7 (C-4a), 41.5 (C-8a), 31.0, 30.1 (C-5,8), 25.5, 23.4 (C-9,10). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.70; H, 7.28.

The analogous $Et_2O{\cdot}BF_3$-promoted reaction afforded a minor product having $[\alpha]_D$ −6.7 (*c* 1.0, $CHCl_3$) and ^{1}H and ^{13}C NMR spectra identical with those of **17a**, described above. In fact, the product proved to be (see next) a partially racemic mixture of **18a** and **17a** (4:1 ratio).

Conversion of the α-Endo Adduct 16a into 18a. A solution of **16a** (52 mg, 0.18 mmol) in dry toluene (1 mL) was cooled to −18 °C and $Et_2O{\cdot}BF_3$ (22.6 μL, 0.18 mmol) was added under argon. The mixture was stirred at 0 °C, and TLC showed gradual conversion of the starting **16a** (R_f = 0.68) into a slower migrating product (R_f = 0.60) that had the same mobility of **17a**. After 25 min the mixture was subjected to the usual workup, and the resulting crude product was flash chromatographed to afford **18a**; $[\alpha]_D$ −11.2 (*c* 0.9, $CHCl_3$) and ^{1}H and ^{13}C NMR spectra identical with those of its enantiomer **17a**.

Adducts of Dihydropyranone 8b with Cyclopentadiene: (3*S*,4a*R*,5*S*,8*R*,8a*S*)-3-[(*R*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (12b) and (3*S*,4a*S*,5*R*,8*S*,8a*R*)-3-[(*R*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (14b). The general $Et_2O{\cdot}BF_3$-promoted cycloaddition procedure was followed starting from **8b** (72 mg, 0.32 mmol) and freshly distilled cyclopentadiene (57 mg, 0.86 mmol). The usual workup of the reaction mixture and flash chromatography purification afforded first the less polar α-endo-adduct **12b** (54 mg, 58%); $[\alpha]_D$ −100.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.20 (dd, 1, $J_{6,7}$ = 5.6 Hz, $J_{7,8}$ = 3.1 Hz, H-7), 6.10 (dd, 1, $J_{5,6}$ = 2.8 Hz, H-6), 4.38 (br s, 1, H-3), 4.22 (dd, 1, $J_{1,1'}$ = 12.3 Hz, $J_{1,8a}$ = 6.1 Hz, H-1), 3.74 (m, 1, J = 6.1 Hz, *H*CO octyl), 3.44 (dd, 1, $J_{1',8a}$ = 3.4 Hz, H-1′), 3.37 (br s, 1, H-5), 3.07 (dd, 1, $J_{4a,5}$ = 4.3 Hz, $J_{4a,8a}$ = 9.5 Hz, H-4a), 2.96 (br s, 1, H-8), 2.67 (dddd, 1, $J_{8,8a}$ = 3.2 Hz, H-8a), 1.44 (dt, 1, $J_{5,9} \sim J_{8,9} \sim$ 1.8 Hz, $J_{9,9'}$ = 8.5 Hz, H-9), 1.34 (br d, 1, H-9′), 1.62−1.27 (m, 10, CH_2 octyl), 1.14 (d, 3, J = 6.1 Hz, CH_3-1 octyl), 0.90 (t, 3, J = 6.1 Hz, CH_3-8 octyl); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5 (C-4), 136.1, 134.9 (C-6,7), 95.6 (C-3), 73.9 (C-2 octyl), 61.0 (C-

1), 49.3 (C-9), 48.2, 47.4, 47.2 (C-4a,5,8), 37.6 (C-8a), 37.1, 31.8, 29.3, 25.7, 22.6 (CH_2 octyl), 19.2, 14.1 (CH_3 octyl). Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 73.78; H, 9.84.

Concentration of the next fractions from the column afforded the minor β-endo-adduct **14b** (5 mg, 5%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (dd, 1, $J_{5,6}$ = 2.8 Hz, $J_{6,7}$ = 5.7 Hz, H-6), 5.95 (dd, 1, $J_{7,8}$ = 2.9 Hz, H-7), 4.69 (br s, 1, H-3), 3.86 (dd, 1, $J_{1,1'}$ = 11.2 Hz, $J_{1,8a}$ = 6.6 Hz, H-1), 3.72 (m, 1, J = 6.1 Hz, *H*CO octyl), 3.33 (br s, 1, H-5), 3.17 (t, 1, $J_{1',8a}$ = 12.0 Hz, H-1′), 3.05 (dddd, 1, $J_{4a,8a}$ = 10.0 Hz, $J_{8,8a}$ = 3.4 Hz, H-8a), 2.86 (br s, 1, H-8), 2.83 (dd, 1, $J_{4a,5}$ = 3.9 Hz, H-4a), 1.57 (ddd, 1, $J_{5,9} \sim J_{8,9} \sim$ 1.8 Hz, $J_{9,9'}$ = 8.6 Hz, H-9), 1.39 (br d, 1, H-9′), 1.60−1.24 (m, 10, CH_2 octyl), 1.14 (d, 3, J = 6.1 Hz, CH_3-1 octyl), 0.88 (t, 3, J = 7.0 Hz, CH_3-8 octyl); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 208.4 (C-4), 138.2, 134.0 (C-6,7), 94.9 (C-3), 72.8 (C-2 octyl), 64.0 (C-1), 49.2 (C-4a), 48.7 (C-9), 44.3, 43.5, 41.5 (C-5,8,8a), 37.0, 31.8, 29.2, 25.7, 22.6 (CH_2 octyl), 19.1, 14.1 (CH_3 octyl).

Thermal cycloaddition of **8b** with cyclopentadiene afforded **12b** and **14b**, which exhibited the same properties as those of the same products synthesized under Lewis acid catalysis.

Adducts of Dihydropyranones 9a and 9c with Cyclopentadiene: (3*R*,4a*S*,5*R*,8*S*,8a*R*)-3-Benzyloxy-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (15a). The general $Et_2O{\cdot}BF_3$-catalyzed procedure was followed for the cycloaddition of **9a** (122 mg, 0.60 mmol) with cyclopentadiene (81 mg, 1.22 mmol) to give **15a** (91 mg, 56% yield, ee > 86%); $[\alpha]_D$ +122.9 (*c* 1.0, $CHCl_3$); having spectral data identical with those of **12a**.

(3*R*,4a*S*,5*R*,8*S*,8a*R*)-3-[(*S*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-methano-1*H*-2-benzopyran-4(3*H*)-one (15c). The $Et_2O{\cdot}BF_3$-promoted cycloaddition of cyclopentadiene (91 mg, 1.38 mmol) with **9c** (156 mg, 0.69 mmol) afforded the major endo adduct **15c** (115 mg, 57% yield), which showed $[\alpha]_D$ +100.4 (*c* 1.1, $CHCl_3$) and NMR spectra identical with those of **12b**.

Adducts of the dihydropyranone 8b with 1,3-Cyclohexadiene: (3*S*,4a*R*,5*S*,8*R*,8a*S*)-3-[(*R*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (16b), (3*S*,4a*S*,5*R*,8*S*,8a*R*)-3-[(*R*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (17b), and (3*R*,4a*R*,5*S*,8*R*,8a*S*)-3-[(*R*)-2′-Octyloxy]-4a,5,8,8a-tetrahydro-5,8-ethano-1*H*-2-benzopyran-4(3*H*)-one (18b). The general procedure for the cycloaddition promoted by $Et_2O{\cdot}BF_3$ was followed starting from **8b** (407 mg, 1.80 mmol) and 1,3-cyclohexadiene (1.75 g, 21.8 mmol). The reaction was conducted at 0 °C for 45 min. After the usual workup, flash chromatography afforded three products. The faster migrating was **16b** (71 mg, 13% yield); $[\alpha]_D$ −95.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.26 (br t, 1, $J_{6,7} \sim J_{7,8}$ = 7.0 Hz, H-7), 6.21 (dt, 1, $J_{5,6} \sim$ 7.0 Hz, $J_{6,8}$ = 1.3 Hz, H-6), 4.51 (br s, 1, H-3), 4.03 (dd, 1, $J_{1,8a}$ = 5.2 Hz, $J_{1,1'}$ = 12.0 Hz, H-1eq), 3.76 (sextet, 1, J = 6.2 Hz, *H*CO octyl), 3.28 (dd, 1, $J_{1',8a}$ = 6,6 Hz, H-1′ax), 3.08 (m, 1, H-5), 2.87 (dd, 1, $J_{4a,5}$ = 3.0 Hz, $J_{4a,8a}$ = 10.0 Hz, H-4a), 2.55 (dddd, 1, $J_{8a,8}$ = 1.6 Hz, H-8a), 2.49 (m, 1, H-8), 1.65−1.27 (m, 14, H-9,9′, H-10,10′, CH_2 octyl), 1.14 (d, J = 6.2 Hz, CH_3-1 octyl), 0.90 (t, J = 6.2 Hz, CH_3-8 octyl)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7 (C-2), 133.9, 132.8 (C-6,7), 96.8 (C-3), 74.2 (H*C*O octyl), 64.5 (C-1), 49.2 (C-4a), 39.4 (C-8a), 37.1, 34.0, 29.2, 26.1, 25.6, 23.3, 22.6 (C-9, 10, *C*H$_2$ octyl), 32.3, 31.8 (C-5,8), 19.4 (*C*H$_3$-1 octyl), 14.1 (*C*H$_3$-8 octyl). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.26; H, 9.79.

The second compound eluted from the column was **18b** (206 mg, 37% yield); $[\alpha]_D$ −1.0 (*c* 1.1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.33 (dd, $J_{6,7}$ = 7.7 Hz, $J_{5,6}$ = 6.5 Hz, H-6), 6.05 (dd, $J_{7,8}$ = 7.3 Hz, H-7), 4.77 (br s, 1, H-3), 3.70 (m, 2, $J_{1,8a}$ = 6.2 Hz, $J_{1,1'}$ = 12.1 Hz, H-1eq, *H*CO octyl), 3.30 (t, 1, $J_{1',8a}$ = 12.1 Hz, H-1′ax), 3.18 (br s, 1, H-5), 2.79 (ddd, 1, $J_{4a,8a}$ = 10.5 Hz, H-8a), 2.60 (dd, 1, $J_{4a,5}$ = 2.7 Hz, H-4a), 2.39 (br s, 1, H-8), 1.59 (m, 2, H-9,10), 1.40−1.28 (m, 12, H-9′,10′,CH_2 octyl), 1.17 (d, 3, J = 6.1 Hz, CH_3-1 octyl), 0.88 (t, 3, J = 6.1 Hz, CH_3-8 octyl); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 207.0 (C-4), 135.1, 132.0 (C-6,7), 97.7 (C-3), 75.1 (H*C*O octyl), 64.1 (C-1), 49.7 (C-4a), 41.6 (C-8a), 36.4, 31.8, 29.4, 25.6, 25.4, 23.5, 22.6 (C-9,10,*C*H$_2$ octyl), 31.0, 30.2 (C-5,8), 21.3 (*C*H$_3$-1 octyl), 14.1 (*C*H$_3$-8 octyl). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.09; H, 9.84.

The lower migrating product was the β-endo adduct **17b** (11.3 mg, 2.1% yield); $[\alpha]_D$ −39.9 (*c* 1.1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.32 (dd, $J_{6,7}$ = 7.7 Hz, $J_{5,6}$ = 6.5 Hz, H-6), 6.05 (dd, $J_{7,8}$ = 7.3 Hz, H-7), 4.76 (br s, 1, H-3), 3.70 (m, 2, $J_{1,8a}$ = 6.3 Hz, $J_{1,1'}$ = 12.1 Hz, H-1eq, *H*CO octyl), 3.30 (t, 1, $J_{1',8a}$ = 12.1 Hz, H-1′ax), 3.18 (br s, 1, H-5), 2.79 (ddd, 1, $J_{4a,8a}$ = 10.2 Hz, H-8a), 2.60 (dd, 1, $J_{4a,5}$ = 2.6 Hz, H-4a), 2.39 (br s, 1, H-8), 1.60 (m, 2, H-9,10), 1.40−1.26 (m, 12, H-9′,10′,CH_2 octyl), 1.14 (d, 3, J = 6.2 Hz, CH_3-1 octyl), 0.88 (t, 3, J = 6.2 Hz, CH_3-8 octyl); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 207.3 (C-4), 135.1, 132.0 (C-6,7), 95.9 (C-3), 72.9 (H*C*O octyl), 64.1 (C-1), 49.7 (C-4a), 41.5 (C-8a), 37.0, 31.9, 29.2, 25.7, 25.5, 23.6, 22.6 (C-9,10,*C*H$_2$ octyl), 31.0, 30.4 (C-5,8), 19.2 (*C*H$_3$-1 octyl), 14.1 (*C*H$_3$-8 octyl). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.18; H, 9.82.

The thermal cycloaddition of 1,3-cyclohexadiene (718 mg, 8.96 mmol) with **8b** (180 mg, 0.80 mmol) afforded as major adduct **16b** (123 mg, 50%) with a negligible amount of **17b**. The adduct **16b** showed the same physical and spectral properties as those previously described.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **12a**−**14a**; ^{13}C NMR spectra for **17b** and **18b**; DEPT and 2D COSY NMR spectra for **12a** and **14a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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