Molecular Dynamics-Based Models Explain the Unexpected Diastereoselectivity of the Sharpless Asymmetric Dihydroxylation of Allyl D-Xylosides

Nicolas Moitessier,[a] Bernard Maigret,[b] Françoise Chrétien,[a] and Yves Chapleur*[a]

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The catalytic asymmetric dihydroxylation of several allyl 2-*O*-benzyl-α-D-xylosides with AD-mix β and PYR(DHQD)$_2$ shows almost no diastereofacial selectivity if the 3- and 4-OH groups are unprotected or acetylated. Acetal, benzyl ethers and benzoyl esters enhance the diastereoselectivity, in the opposite sense to that predicted by the "AD mnemonic", which is completely lost using AD-mix α. In an attempt to understand this behaviour, computational studies of the asymmetric dihydroxylation (AD) of olefins using Sharpless' and Corey's catalysts have been carried out using molecular dynamics. A three-step algorithm was developed taking advantage of the enzyme-like behaviour of catalyst-olefin systems and applied using an ESFF force field. To validate our approach, the first sampling step procedure was then refined and performed using a modified CVFF force field. This led to a U-shaped model in good agreement with that proposed by Corey for the AD of allyl 4-methoxybenzoates, which brings to the fore a role for the methoxy group. This model also accounts for the observed enantioselectivity of styrene dihydroxylation. When applied to the AD of allyl xylosides using AD-mix β, our model accounts well for the observed diastereoselectivity. Both synthetic and modelling results confirmed that aromatic groups on the olefin could be involved in π-π stacking interactions with the aromatic rings of the catalyst and should be important, if not a prerequisite, to achieve high enantio- and diastereoselectivity.

Introduction

In connection with a synthetic programme aimed at the synthesis of *myo*-inositol-1,4,5-trisphosphate mimics we required a number of [(2*S*)-2-hydroxypropyl]-D-xylosides.[1] These compounds are, in principle, available by glycosylation of a suitable xylose donor and a suitably protected chiral glycerol. This route had some disadvantages, such as the preparation of a suitably protected xylosyl donor and also the enantiospecific preparation of the glycerol acceptor. For these reasons we chose to prepare these compounds from readily available allyl α-D-xyloside[1b] and we turned to the diastereoselective dihydroxylation of the allyl ether. Although allyl glycosides **1a** are highly asymmetric, the chiral centres of the xylose moiety are too distant from the reacting double bond to significantly influence the diastereofacial selectivity on the terminal olefin. Thus we expected that the asymmetric dihydroxylation (AD) of the allyl ether moiety would provide a straightforward solution to this problem.

Several methods are available to achieve the dihydroxylation of olefins and these rely on osmium tetroxide oxidation. The enantioselective catalytic version developed by Sharpless has become a powerful method for the enantioselective synthesis of diols from prochiral olefins. A considerable body of results has been accumulated in recent years and this area has been the subject of a comprehensive review by Sharpless' group.[2] The introduction of chiral nitrogen-containing ligands has greatly improved the efficacy of osmium tetroxide dihydroxylation. Several groups have proposed different catalysts based on diamino compounds[3] but the development of quinine-derived ligands led to considerable improvements.[3f,4] The cinchona alkaloids are now mainly used in the last generation of AD catalysts. The main characteristics of these catalysts is the presence of two copies of a chiral alkaloid, linked by aromatic bridges consisting of a *para* substituted heterocycle varying from phthalazine to pyridazine and including more substituted aromatic systems. Accordingly, the Sharpless procedure has found wide-ranging applications for the enantioselective AD of prochiral olefins including allyl ethers[5] and esters[6] but the AD of chiral allyl ethers is less documented. Only a few examples of substituted olefins where the sugar is linked by carbon–carbon bonds have been reported.[7]

We report in this paper our results on the AD of D-xylose-derived allyl ethers, which show that poor to good diastereofacial selectivity can be obtained depending on the protecting groups used on the sugar moiety. The most striking result came, however, from the sense of the observed diastereoselectivity, which we found to be opposite to that expected. Such a reversal has not been extensively reported in the literature and led us to study in more detail the course of the AD by computational methods. Molecular

[a] Groupe SUCRES, Unité Mixte 7565 CNRS, Université Henri Poincaré-Nancy 1, I.N.C.M,
B. P. 239, F-54506 Nancy-Vandoeuvre, France
Fax: (internat.) + 33-3/83912479
E-mail: yves.chapleur@meseb.u-nancy.fr
[b] Groupe de Biochimie Théorique, Unité Mixte 7565 CNRS, Université Henri Poincaré-Nancy 1, I.N.C.M,
B. P. 239, F-54506 Nancy-Vandoeuvre, France

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dynamics calculations provided theoretical models of the AD, which were found to be in good agreement with the CPK model proposed by Corey.[8] These models can also explain the enantioselective AD of styrene and the allyl 4-methoxybenzoates and allow a good rationalisation of our results.

Results and Discussion

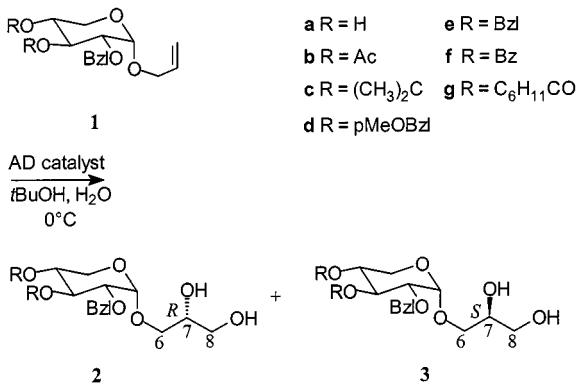
Syntheses

The target structures of our synthetic plan needed to be protected at position 2 of the sugar ring and should be of (*S*) configuration at the central position of the glycerol aglycon. We started with the 2-*O*-benzyl ether **1a**, which was treated according to the procedure of Sharpless using AD-mix β and was supposed to give the required (*S*) configuration according to the "AD mnemonic".[9] Dihydroxylation proceeded well but, to our disappointment, almost equal amounts of both diastereomers [diastereoisomeric ratio (*dr*) 1.2:1] were obtained as seen from ^{13}C-NMR spectroscopy, which proved to be a reliable method for this analysis. Catalytic AD is a two phase reaction and we suspected that compound **1a**, which was slightly water soluble, could react in the aqueous phase with the osmium(VIII) species. This reaction, which occurs in the absence of the chiral ligand, clearly led to a complete lack of selectivity as observed in the reaction of osmium tetroxide with *N*-methyl morpholine *N*-oxide as the cooxidant (Table 1, Entry 1). To lower its solubility in the aqueous phase, compound **1a** was acetylated under standard conditions to give olefin **1b**. This compound was treated as above with AD-mix β to yield a *dr* of 1.4:1.

Table 1. Asymmetric dihydroxylation of allyl α-D-xylosides **1**

Entry	Substrate	Reagent	Products	*dr* ratio[a]
1	**1a**	OsO_4 cat., NMO	**2a**, **3a**	1:1
2	**1a**	AD-mix β≅[b]	**2a**, **3a**	1.2:1
3	**1b**	AD-mix β[b]	**2b**, **3b**	1.4:1
4	**1c**	AD-mix β[b]	**2c**, **3c**	2.1:1
5	**1d**	AD-mix β[b]	**2d**, **3d**	2.3:1
6	**1e**	AD-mix β[b]	**2e**, **3e**	4.5:1
7	**1f**	AD-mix β[b]	**2f**, **3f**	4.3:1
8	**1g**	AD-mix β[b]	**2g**, **3g**	5.6:1
9	**1e**	$(DHQD)_2PYR$, 1 mol-%[c]	**2e**, **3e**	2.7:1
10	**1e**	$(DHQD)_2PYR$, 4 mol-%[c]	**2e**, **3e**	5.2:1
11	**1e**	AD-mix β−$(DHQD)_2PYR$[d]	**2e**, **3e**	4.8:1
12	**1f**	AD-mix β−$(DHQD)_2PYR$[d]	**2f**, **3f**	8.1:1
13	**1f**	AD-mix α[b]	**2f**, **3f**	1.1:1

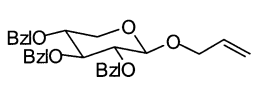
[a] Ratio (major/minor diastereoisomers) determined by ^{1}H- and ^{13}C-NMR spectroscopy by averaging the integrals values of H-1, C-1, and C-8 signals respectively. – [b] Commercial reagents (Aldrich) were used according to Sharpless' recommended procedure (ref.[2]). – [c] AD mix has been prepared using the catalyst percentage indicated according to Sharpless' procedure (ref.[2]). – [d] 1 mol-% of each catalyst was used.



Alternatively, compound **1a** was treated with dimethoxypropane in acidic acetone to provide the acetal **1c**. Slightly improved results were obtained (Table 1, Entry 4, *dr* 2.1:1) and these can be attributed to an enhancement of the lipophilicity of the substrate or to the introduction of a conformational bias in this substrate by formation of a *trans*-fused ring system. To shed light on this point, we prepared nonbiased derivatives such as benzyl ethers **1d** and **1e**. The *dr* was in the same range for compound **1d** protected with *p*-methoxybenzyl ethers (Table 1, Entry 5 *dr* 2.3:1) and, gratifyingly, this *dr* increased to 4.5:1 with benzyl ethers as protecting groups (compound **1e**, Table 1, Entry 6). Finally, the more synthetically useful compound **1f** was prepared and gave identical results (Table 1, Entry 7) with a *dr* ratio of 4.3:1. This *dr* enhancement in the AD of compounds **1d**–**1f** should be attributed to stacking interactions between the aromatic rings of the protecting groups and those of the catalyst, which should contribute to the correct orientation of the substrate in the catalytic centre. However, this hypothesis seemed inconsistent with the results obtained with compound **1g** (Table 1, Entry 8), in which the aromatic rings were replaced by cyclohexyl rings. Thus the observed improvements should be the result of favourable hydrophobic interactions[10] between the protecting groups and the catalyst and/or steric hindrance between these bulky groups, which tend to favour one orientation of the substrate in the catalytic centre.

The importance of the ligand structure has already been pointed out.[2] We checked this point by submitting compound **1e** to AD using the $(DHQD)_2$/PYR-based reagent developed for terminal olefins.[5b] The diastereomeric ratio decreased to 2.7:1 on using 1 mol-% of the catalyst but some improvements (5.2:1) were observed using 4 mol-% of the catalyst. This showed that the nature of the ligand did not greatly influence the diastereomeric ratio but, not unexpectedly, the amount of catalyst seems to be important. A mixture of catalysts [$(DHQD)_2PYR$ and $(DHQD)_2PHAL$, 1 mol-% of each] can be successfully used to improve the *dr* to 4.8:1 for compound **1e** and 8.1:1 for compound **1f** (Table 1, Entries 11 and 12).

We next attempted to reverse the diastereoselectivity using AD-mix α, which is supposed to give the opposite facial selectivity as compared to AD-mix β. Surprisingly, the *dr* dropped to 1.1:1 with *the major diastereoisomer being the*



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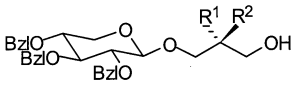


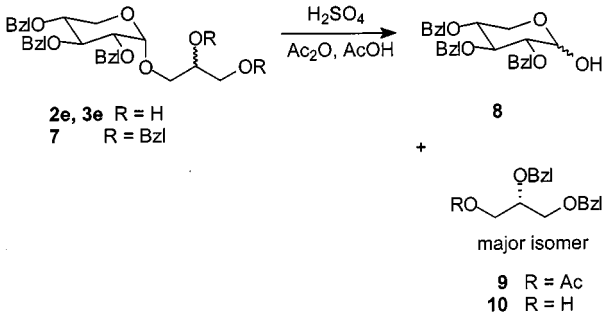
5 R^1 = OH, R^2 =H
6 R^1 = H, R^2 = OH

one formed using AD-mix . Thus it was concluded that compounds **1e–1g** and AD-mix β formed matched pairs. Assuming that the stereochemistry at the anomeric centre plays an important role, we investigated the AD of compound **4** using AD-mix β and AD-mix α. In both experiments a modest diastereomeric induction was observed accompanied by a reversal of diastereoselectivity on going from AD-mix α to AD-mix β (see Table 2, Entries 14, 15). This clearly indicates that none of these pairs were matched and that compound **4** was a poor substrate for AD.

Table 2. Asymmetric dihydroxylation of allyl β-D-xyloside **4**

Entry	Compound	Reagent	*dr* ratio[a]
14	**4**	AD-mix β	**5/6** 1.2:1
15	**4**	AD-mix α	**6/5** 1.3:1

[a] No attempts were made to determine the absolute configuration at C-7 of **5** and **6**.



2e, 3e R = H
7 R = Bzl

8

major isomer

9 R = Ac
10 R = H

The rather low selectivities in the AD of matched pairs **1e–1g** and AD-mix β was intriguing, thus we investigated thoroughly the absolute configuration of the dihydroxylation products **2e** and **3e**. For that purpose, the mixture was benzylated under standard conditions to give the benzyl ether **7**. This compound was submitted to acid hydrolysis to liberate the aglycon, which was isolated as its acetate **9**. Removal of the acetyl group gave the known di-*O*-benzyl *sn* glycerol **10**. Its optical rotation {$[\alpha]_D$ –11.2 (*c* = 1, $CHCl_3$), compared with literature data $[\alpha]_D$ –17.2 (*c* = 1, $CHCl_3$)}[11] indicated that this compound was an 82:18 mixture of (*S*/*R*) compound. Thus we concluded that asymmetric dihydroxylation of compounds **1** gave mainly the (7*R*) derivative, instead of the (7*S*) derivative predicted by the AD mnemonic.

Molecular Dynamics Calculations

Principles

The results described above concerning the combination of unusually low diastereoselection in an unexpected sense warranted further investigation. Only a few reports on the AD of olefins have dealt with an "abnormal" sense of asymmetric induction.[12,13] We decided to use molecular modelling to investigate the approximate stereochemical course of the AD. Some theoretical investigations into the AD mechanism, which is not completely elucidated, have been reported. Two mechanisms accounting for the reaction of the olefin with osmium tetroxide have been suggested. A stepwise mechanism including a [2 + 2] cycloaddition was proposed by Sharpless on the basis of kinetic measurements and kinetic isotope effects.[14] According to Corey, a [3 + 2] cycloaddition mechanism is supported by kinetic measurements[15] and by calculations[15b,16] showing that the energetically favoured process should be the [3 + 2] cycloaddition. These two mechanisms led to different arrangements of the olefin-catalyst systems.

On the other hand, models have been proposed to explain the stereochemical course of the AD reaction. Sharpless developed a model to account for the reaction of styrene with $(DHQD)_2$-PHAL in which the PHAL ring constitutes a floor and one methoxy-quinoxaline is a wall. This L-shaped model accommodates the styrene ring in such a way that the aromatic ring of styrene is parallel to the catalyst floor. This last model can be used with a number of substrates and accounts well for the observed enantioselectivity. Moreover, on the basis of experimental results, Sharpless suggested the AD mnemonic, which can predict the sense of the AD and whether AD-mix α or β should be used to prepare the desired enantiomer.[9]

Corey proposed a model that accounts well for the excellent enantioselectivity observed in the AD reaction of allyl 4-methoxybenzoates.[6a,8,17] In this model the olefinic "substrate" is accommodated in a U-shaped binding pocket composed of the two methoxyquinoline units of the catalyst.[18] Stacking of aromatic rings would be responsible for the stability of the complex in which the carbon atoms of the double bond are very close to the oxygen atoms of osmium tetroxide complexed on the alkaloid nitrogen. Only a small motion is thus needed to achieve the [3 + 2] cycloaddition.

Although investigations using molecular mechanics studies have been performed (MM2),[14d] to the best of our knowledge molecular dynamics calculations have not yet been used in this context and we felt that our results may afford a good starting point for this type of investigation. For the sake of comparison, the same calculations were performed on three different systems, the AD of allyl 4-methoxybenzoate with the $(DHQD)_2$-PYDZ catalyst, the AD of styrene with the $(DHQD)_2$-PHAL catalyst and the AD of allyl xyloside **1a** with AD-mix-β.

We first chose a mechanistic model. The [3 + 2] mechanism,[14c,15b,16b,16c,19,20] which now seems the most likely, has been assumed in all our calculations. Secondly, wishing to carry out more of a qualitative than a quantitative study, we adopted a simple and fast procedure to estimate the free energy of the process.[21] However, the approximations used above would be validated by fitting with two well-known systems. The main simplification is the absence of the solv-

ent. In fact, the complexity of the medium would be an obstacle to fast calculations (mixture of solvent and presence of salts). Moreover, we assumed that such hydrophobic systems are more governed by intramolecular forces than by the polar and protic surrounding environment.[22] Nevertheless, this first assumption will be approved *a posteriori* by evaluating the accessible surface area of the lipophilic solvent on each of the conformers obtained.[21c] The second approximation is intrinsic to molecular mechanics. Contrary to the hybrid method employed by Ujaque et al.,[19] molecular mechanics accounts for neither the reaction itself nor the polarisation of the reacting centres.[23] However, the aim of the study is firstly to account for the asymmetry of the reaction controlled very early in the process and to perform an exhaustive conformational search, which is limited by the chemist's view in the hybrid method approach or in transition state studies.[24,16a] The last hypothesis was the omission of the entropy change during the process. In fact, the loss of translational and rotational entropy, the additional conformational entropy cost and the desolvation gain were assumed to follow a similar profile for all conformers. As a result, the measure of the free energy of the process was limited to the internal energy added to the intramolecular interactions of a rigid model.

Given the binding-pocket-like behaviour of such a system, the procedure can be defined using the docking procedure that has been extensively studied in enzyme or receptor/ligand systems.[25] However, existing procedures allow only a limited flexibility of the binding site. To explore the conformational flexibility of both the catalyst and the olefin, we chose the simulated annealing as a search algorithm.[26] Thus the bimolecular systems were subjected to a conformational search procedure exploiting both concepts of docking and simulated annealing using the fairly new empirical rules-based ESFF forcefield.[27] The partners were annealed and successively taken apart, scrambled by high temperature MD, then stepwise-docked and cooled down. The directed docking was limited to conformers that could lead to the expected reaction (i.e. olefin facing the osmium tetroxide) by means of a distance constraint between the olefin and the osmium tetroxide.

As a first validation, the inherent errors of the force field as well as the strength of the algorithm were tested by employing the well-established CVFF force field[28] and a refined procedure (more steps of MD and slower cooling). As reported by Martins,[29] the CVFF force field provided similar results to ESFF, thus validating the fast conformation search used previously. From these calculations a set of 200 assemblies was thus obtained and the ten lower energy assemblies were selected and divided into different families by visual inspection.

The second step of these calculations involved refinement of a typical assembly extracted from each family as obtained above. For that purpose, the lowest energy assembly of each family was selected and submitted to a stepwise relaxation procedure leading to an unconstrained conformer. The energy barrier between the unconstrained system and the strained system, in which the olefin–OsO_4 distance is set to 2.5 Å, can reflect the ease of approach of the oxidant to the olefin after entering the catalytic site. In the following discussion this energy barrier will be referred to as the "approaching energy". In no way is this energy barrier that of the reaction, but it may reflect the torsions needed for the olefin to approach the reagent OsO_4.

In the third step we performed calculations aimed at the evaluation of a possible energy barrier for entering the olefin into the catalyst, although such a barrier was not detected in the preceding MDs carried out at high temperature. For that purpose both partners from the low-energy assembly obtained in step 2 were slowly taken away until the total energy remained roughly constant (see Figure 1). This energy difference is subsequently referred to as the "interaction energy" in this paper. Finally, both previously defined energies were compared (see for example Figure 2) and led to a more energetically favourable assembly that can be used as a model.

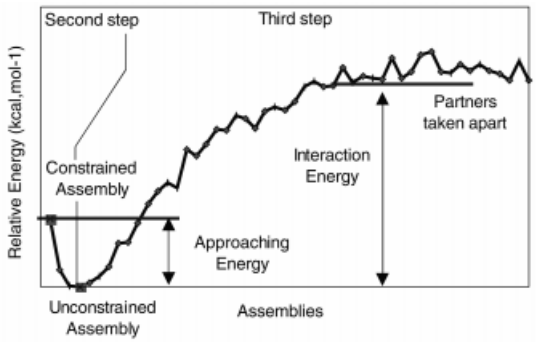


Figure 1. Definition of both energies determined for each assembly during the second and the third calculation steps; example of assembly **A1** in $(DHQD)_2$-PYDZ – allyl 4-methoxybenzoate modelling

Results

The three-step calculation procedure described above was first applied to the AD of allyl 4-methoxybenzoate with the $(DHQD)_2$-PYDZ catalyst. The sampling procedure of these calculations allowed the construction of four main assemblies (**F1**–**F4**), which were submitted to two last steps. In the final assembly a stacking of the aromatic rings of the catalyst and the benzoate ring was observed and this should explain the gain in energy. Moreover, in these assemblies the olefinic bond was placed in such a way that the (*S*) isomer would be formed as expected.

It can be seen in assembly **A1** that the distances between oxygens and olefinic atoms were almost the same in the constrained system and in the lowest-in-energy assembly without the distance constraint obtained from the above calculations.

For the modelling of the AD of allyl 4-methoxybenzoate with $(DHQD)_2$-PYDZ, step 3 of our calculations was applied to one representative of each family and showed that no energy barrier exists for the entry of the olefin into the catalyst. The difference between the approaching and the interaction energies can be calculated for each representative of the different families. These differences are shown in

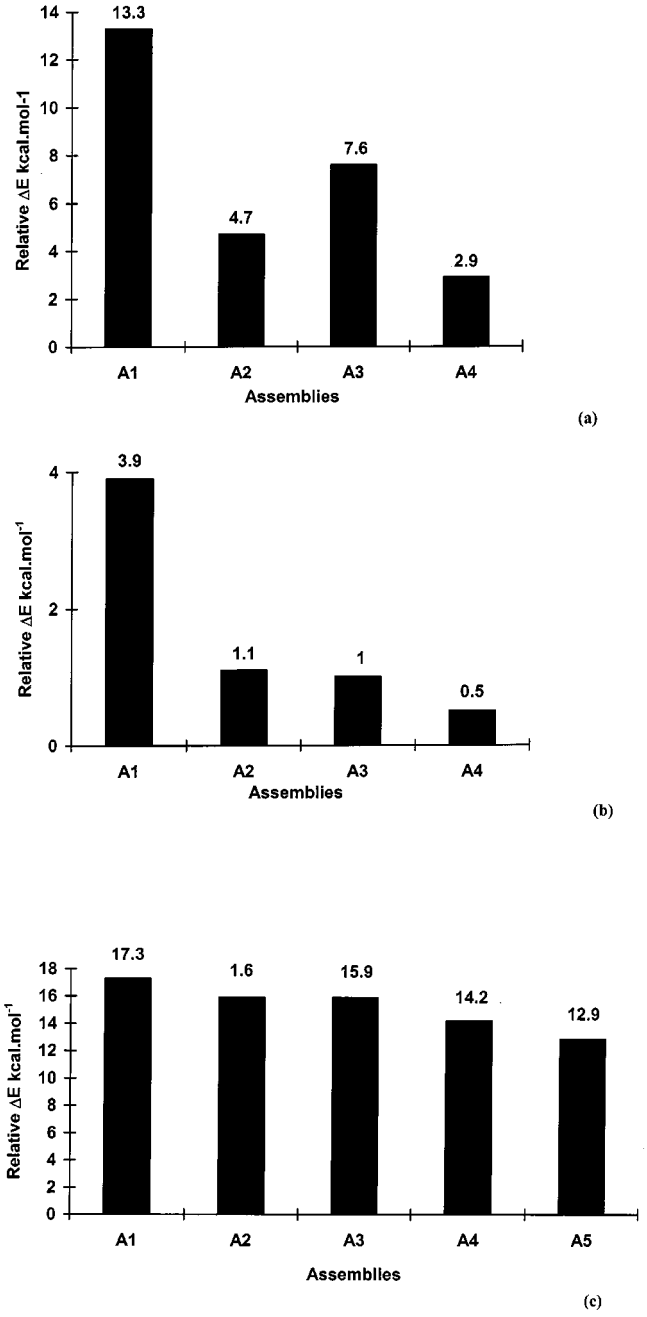


Figure 2. Graphs showing the difference between the approaching and interaction energies for one representative of the each families of assemblies of the three systems **a**: $(DHQD)_2$-PYDZ – allyl 4-methoxybenzoate; **b**: $(DHQD)_2$-PHAL – styrene; **c**: $(DHQD)_2$-PHAL – allyl 2,3,4-tri-*O*-benzyl-α-D-xyloside **1e**

Figure 2a for the four representatives. Assembly **A1**, which is representative of the most important family **F1**, has the highest difference between approaching energy and interaction energy as compared to **A2** (which led to the minor isomer), **A3** and **A4**. Thus this assembly should represent a good picture of the olefin-catalyst.

The set of assemblies obtained in step 3 of the calculations can be used to simulate the approach of the olefin into the catalytic site, which was closed in at the start in order to increase π-π interactions between the two quinoline rings of the catalyst. The aromatic part of the olefin approaches the catalyst so that the methoxy group sinks into the catalyst, but the presence of the pyridazine ring then forces the aromatic ring to rotate, maximising the π-π interactions and presenting the olefin in the proper way to interact with OsO_4. The unexpected role of the 4-MeO group found here should explain the extremely high enantioselectivity reported in the AD of allyl 4-methoxybenzoates.[6a]

It is worthy of note that the model (Figure 3) obtained from our calculations fits well with that proposed by Corey on an intuitive basis using CPK models and on the basis of molecular mechanics.[6a,8,17] Both approaches thus give self-consistent results. Moreover, the *s-cis* conformation of the allyl ester already proposed by Corey on the basis of MM2 calculations is also found in our model.[6a] Given the high convergence between our approach and the previous one, our modelling procedure could be applied to other systems with some confidence.

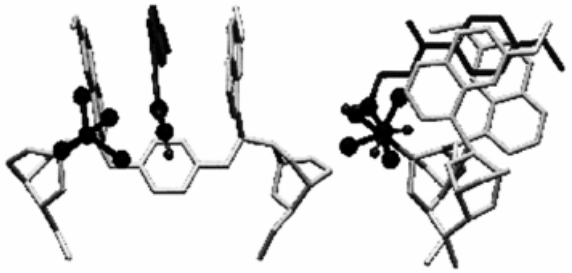


Figure 3. $(DHQD)_2$-PYDZ – allyl 4-methoxybenzoate model; the double bond and OsO_4 are depicted in black, the catalyst is depicted in light grey, and the 4-methoxybenzoate moiety is depicted in dark grey; two orthogonal views are shown

To prove the validity of in vacuo calculations it seemed appropriate to evaluate the solvation contribution. Evaluation of surface areas accessible to lipophilic solvent, which can be used to describe solvation free energy changes, was carried out. Thus it appeared that in the first system [$(DHQD)_2$-PYDZ–(allyl 4-MeO-benzoate)] the most energetically favoured assembly had the smallest lipophilic solvent-accessible areas. These results are again in favour of the first assembly increasing the energy difference between this specific conformation and the others. Thus, the distance-dependent dielectric constant appeared as an adequate and sufficient representation of the polar solvent in such a process controlled by hydrophobic effects.

Our calculation procedure was next applied to the AD of styrene using Sharpless' catalyst, $(DHQD)_2$-PHAL. A U-shaped form has been proposed by Corey for this catalyst in its interaction with olefins.[30] Evidence supporting such a model came recently from calculations using a mixed method and based on the [3 + 2] mechanism.[19] However, using a [2 + 2] mechanism, Sharpless has pictured a different model in which the aromatic ring of styrene interacts with the phthalazine ring of the catalyst "floor".[14d]

In the styrene case our calculations led to four families of assemblies. The energies of interactions and the approaching energies were evaluated and compared (Fig-

ure 2b). This resulted in the selection of an assembly as a likely model of the styrene-catalyst interaction. As shown in Figure 4 the styrene ring is placed parallel to *one* quinoline ring of the catalyst. This constitutes the main difference with the preceding model, in which both quinoline rings interacted with the 4-methoxyphenyl ring. This might be explained by the longer distance between the olefin and the aromatic ring in allyl 4-methoxybenzoate as compared to styrene, the shorter distance in the latter disfavouring interactions with the quinoline ring on the OsO_4 side of the catalyst. As above, the solvent-accessible area calculated for the most favourable assembly obtained for the $(DHQD)_2$-PHAL-styrene system was the lowest while maintaining the accessibility of the polar moieties. The model stemming from our calculations is in agreement with that recently proposed by Maseras et al. for styrene and $(DHQD)_2$-PYDZ catalyst using a hybrid method.[19,31] This may constitute a further validation of our modelling approach.

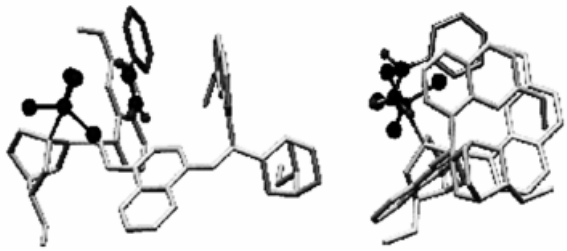


Figure 4. $(DHQD)_2$-PHAL – styrene model; two orthogonal views are shown

We next turned to the modelling of the AD of our substrate **1e** with $(DHQD)_2$-PHAL. The same procedure was applied. In contrast with the preceding models the U-shaped form of the catalyst is no longer retained. It appeared clear that the most likely assembly gave the (*R*) isomer **3e**, as is observed experimentally. However, an assembly leading to the (*S*) isomer **2e** was only less favourable by 1 kcal in terms of approaching interactions and only by less than 2 kcal in terms of interaction energy (Figure 2c). Finally, evaluation of the solvent-accessible surface was also in favour of these two assemblies

The results shown here may explain the poor diastereoselectivity observed in the AD of **1e**. Finally, as shown from the most likely assembly (Figure 5) the main stabilising interactions would be the π-π stacking of the aromatic rings of the benzyl protecting groups at C-3 and C-4 of the sugar and the methoxyquinoline residues of the catalyst. This

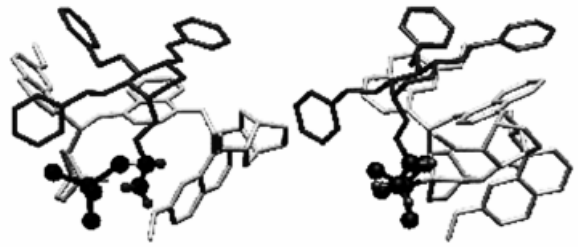


Figure 5. $(DHQD)_2$-PHAL – allyl tri-*O*-benzyl-α-D-xylopyranoside model; two orthogonal views are shown

should explain the role of aromatic protecting groups for a good diastereoselectivity in the AD of **1e** and **1f**. However, the efficiency of cyclohexanoyl protecting groups in the AD of compound **1g** seems in contrast with favourable stacking interactions and more in favour of simple hydrophobic interactions.

Conclusion

In conclusion, the asymmetric dihydroxylation of chiral allyl ethers strongly depends on the nature of the chiral substituent and, in our case, on the protecting groups of the xylose moiety. Large hydrophobic protecting groups favour the diastereoselectivity, although this still remains poor, but *the observed selectivity is opposed to that expected from the AD mnemonic*. The selectivity is completely lost by simply changing the configuration of the asymmetric centre near the allylic reacting centre (going from the α-anomer to the β-anomer).

The computational studies of the AD reaction of a few olefins led us to propose a fast calculation protocol, which gave rise to suitable models to explain the high enantioselectivity in the AD of olefins. For allyl 4-methoxybenzoate, the model found is in complete agreement with that proposed by Corey to explain his results. On the basis of the now well accepted [3 + 2] mechanism, the model proposed here accounts well for the AD of styrene studied by Sharpless. Finally, this model is able to explain our own results and shows that care should be taken with the prediction of the sense of AD of large chiral olefinic molecules. It also points out an essential role for aromatic or, more generally, lipophilic substituents capable of stacking interactions with the catalyst to achieve high enantioselectivity. In other words AD catalysts would really present a U-shaped "catalytic site" that can accommodate only a few aromatic substrates.[18,30]

Experimental Section

General: All reactions were performed under a nitrogen atmosphere. – Melting points are uncorrected and were recorded with a Büchi capillary tube melting point apparatus. – Optical rotations were measured on a Perkin–Elmer 141 polarimeter in a 1 dm cell at 20 °C. – FTIR spectra were recorded on a Perkin–Elmer Spectrum 1000 using NaCl windows or KBr pellets. – ^{1}H-NMR (250 MHz) and ^{13}C-NMR (62.5 MHz) spectra were recorded on a Bruker AC 250 spectrometer. Chemical shifts are reported in ppm using the residual chloroform as the internal standard (δ = 7.27 and 77.0, respectively). In the NMR data of all compounds the aglycon chain is numbered 6–8. Assignments of ^{13}C signals are based on the *J*-modulated spin-echo sequence. – AD-mix α and β were commercial products purchased from Aldrich and used as received. – Analytical thin layer chromatography was performed on Merck 60 F_{254} pre-coated silica gel plates. – Preparative chromatography was performed on silica gel 60 (230–40 mesh ASTM) using ethyl acetate (E) and hexane (H) mixtures.

Computational Details: Computational simulations were performed with the InsightII 95.0/Discover3 package using the ESFF force

field and the InsightII 95.0/Discover package using the CVFF force field on Silicon Graphics® Indy and Indigo2 workstations. The osmium set of CVFF parameters have been derived from the corresponding MM2 parameters successfully employed by Houk et al.[16a] and Sharpless et al.[14a] Thus, we closely reproduced the energetical rotational profile and geometry for the osmium complex by implementing parameters given in the supporting information. Moreover, the poor reliability of the derived osmium parameters has been circumvented by constraining the complex in the starting conformation. Molecular dynamics simulations were carried out using a time step of 1 fs. Optimisations were performed by conjugate gradients energy minimisation with a convergence criterion of 0.001 kcal/mol^{-1}. Solvent conditions were represented implicitly using a distance-dependent dielectric constant $\varepsilon = r$. Atom partial charges were generated using the MOPAC semiempirical method for the determination of the Mulliken electronic population. The distance constraints were imposed using a harmonic potential function with a force constant of 100 kcal/mol^{-1} Å^{-1}.

The first step calculations used the following procedure. After optimising the olefin and the catalyst taken individually, a starting assembly was built manually by placing the two partners at a distance of about 17 Å. This starting structure was the entry point of an annealing loop procedure as described below. Each loop of the annealing began with molecular dynamics (MD) performed at 1100 K during 2000 fs, a distance constraint being set between the olefin and the catalyst, starting at 17 Å. The temperature was then decreased in 200 K steps and the distance constraint was also decreased stepwise (2 Å at each step), with this process being repeated until the temperature was below 800 K and the distance was 13 Å. At this stage, in order to select only conformations that could lead to reactions, an additional distance constraint was then set between the oxygen atoms of OsO_4 and the olefinic carbons. Starting at 8.5 Å this distance was decreased in steps of 2 Å, and the temperature decreased by steps of 200 K until the temperature reached 400 K. MD (2000 fs) were performed at each step of the cycle. When the second distance constraint between oxygen and olefinic atoms reached 2.5 Å, the first distance constraint was released and again an MD of 4000 fs was processed at 300 K. Each assembly obtained in this way was energy-minimised and stored. This procedure was automatically repeated 100 times as before. In order to explore all possibilities, the whole process was performed twice: one time with the axial oxygen of OsO_4 linked to the terminal olefinic atom and the second time with the axial oxygen linked to the nonterminal olefinic atom. The second procedure was applied to the conformers extracted from the first step. The distance constraint between olefin and the oxide was increased by steps of 0.25 Å until 6 Å was reached. In each step the assembly was scrambled by MD at 300 K during 300 fs and energy minimised. The lowest in energy was kept and energy minimised without any constraint. For the third step the constraint between the catalyst and the olefin was set again and increased in 0.5 Å steps. In each case an MD at 300 K during 500 fs was achieved and after energy minimisation the assembly was stored. The protocol was reiterated until the energy was roughly constant.

Details of the algorithms and all Cartesian coordinates are given in the Supporting information and are available on request from the authors. Graphical displays were printed out from the InsightII® molecular modelling system.

Allyl 3,4-Di-*O*-acetyl-2-*O*-benzyl-α-D-xylopyranoside (1b): To a solution of 850 mg ($3.03\cdot10^{-3}$ mol) of diol **1a** in 20 mL of pyridine was added 1 mL of acetic anhydride. The mixture was stirred overnight. The mixture was concentrated in vacuo and the residue was taken up in dichloromethane (150 mL). The organic layer was washed with a 1 N solution of hydrochloric acid, water, 1 N sodium hydroxide solution and water until neutral. Purification on a silica gel column (H/E, 4:1) gave 980 mg of **1b** (88%) as a gum. *Rf* = 0.88 (H/E, 1:1). $[\alpha]_D^{20} = +87$ (c = 1.6, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 1749 cm^{-1} (CO). – ^{1}H NMR ($CDCl_3$): δ = 2.01 (s, 6 H, OAc), 3.50 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10 Hz, *H*-2), 3.63 (dd, 1 H, J_{4-5} 10, $J_{5-5'}$ 10 Hz, *H*-5), 3.70 (dd, 1 H, $J_{4-5'}$ 6.5 Hz, *H*-5′), 3.97 (dd, 1 H, $J_{6-6'}$ 13, J_{6-7} 6.5 Hz, *H*-6), 4.18 (dd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 4.60 (s, 2 H, CH_2Ph), 4.80 (d, 1 H, *H*-1), 4.88 (ddd, 1 H, J_{3-4} 10 Hz, *H*-4), 5.22 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.33 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.46 (dd, 1 H, *H*-3), 5.92 (dddd, 1 H, H-7), 7.30 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 20.6, 20.7 (2 C, OAc), 58.2 (1 C, *C*-5), 68.3 (1 C, *C*-6), 69.3 (1 C, *C*-4), 70.9 (1 C, *C*-3), 72.5 (1 C, CH_2Ph), 76.7 (1 C, *C*-2), 95.1 (1 C, *C*-1), 117.7 (1 C, *C*-8), 127.5, 127.6, 128.4 (5 C, aromatic *C*), 133.2 (1 C, *C*-7), 137.5 (1 C, aromatic *C*), 168.2 (1 C, *C*=O), 174.5 (1 C, *C*=O). – MS (70 eV): *m*/*z* (%): 365.0 [M$^{\circ+}$ + 1], 321.1 [M$^+$ – Ac], 307.1 [M$^+$ – OAll], 91.0 (100) [Bn], 42.9 [Ac]. – $C_{19}H_{24}O_7$ (364.3) calcd. C 62.62, H 6.63; found C 62.81, H 6.51.

Allyl 2-*O*-Benzyl-3,4-*O*-isopropylidene-α-D-xylopyranoside (1c): A solution of diol **1a** (1 g, $(3.57\cdot10^{-3}$ mol) in 20 mL of anhydrous acetone and 15 mL of dimethoxypropane and a catalytic amount of *para*-toluenesulfonic acid was stirred for 24 h at room temperature. 200 mg of sodium carbonate was then added and the mixture stirred until neutral. The solid was removed and the solvent was evaporated in vacuo. The crude residue was taken up in dichloromethane (150 mL). The organic phase was washed with water, dried with magnesium sulfate and concentrated in vacuo. Chromatographic separation (H/E, 4:1) gave 766 mg of **1c** (67%), oil, *Rf* = 0.42 (H/E, 4:1). $[\alpha]_D^{20} = +42.0$ (c = 1.0, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 1.45 [s, 6 H, C(CH_3)$_2$], 3.38 (m, 1 H, *H*-4), 3.64 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-2), 3.72 (dd, 1 H, J_{4-5} 10.5, $J_{5-5'}$ 10.5 Hz, *H*-5), 3.84 (dd, $J_{4-5'}$ 5 Hz, *H*-5′), 3.92 (dd, 1 H, J_{3-4} 10 Hz, *H*-3), 3.96 (dd, 1 H, $J_{6-6'}$ 13, J_{6-7} 6.5 Hz, *H*-6), 4.18 (dd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 4.62 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.82 (d, 1 H, CH_2Ph), 4.86 (d, 1 H, *H*-1), 5.21 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.32 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.91 (dddd, 1 H, H-7), 7.33 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 26.5, 26.9 [2 C, C(*C*H$_3$)$_2$], 61.2 (1 C, *C*-5), 68.6 (1 C, *C*-6), 71.9 (1 C, *C*H$_2$Ph), 74.3, 78.1 (3 C, *C*-2, *C*-3, *C*-4), 96.4 (1 C, *C*-1), 110.6 [1 C, *C*(CH$_3$)$_2$], 117.8 (1 C, *C*-8), 127.7, 127.9, 128.3 (aromatic *C*H), 133.9 (1 C, *C*-7), 138.2 (1 C, aromatic *C*). – MS (70 eV): *m*/*z* (%): 321.1 (15) [M$^{\circ+}$ + 1], 263.0 (10) [M$^+$ – C_3H_5O], 131.0 (15), 91.0 (100) [Bn]. – $C_{18}H_{24}O_5$ (320.3): calcd. C 67.48, H 7.55; found C 67.72, H 7.38.

Allyl 2-*O*-Benzyl-3,4-di-*O*-*p*-methoxybenzyl-α-D-xylopyranoside (1d): To a suspension of 180 mg of sodium hydride (60%, 4 equiv) in 20 mL of dry DMF was added, at 0 °C, 320 mg ($1.15\cdot10^{-3}$ mol) of diol **1a** in 5 mL of DMF. The mixture was stirred for 15 min and 0.5 mL of *p*-methoxybenzyl bromide was added. The stirring was continued for 12 h and 5 mL of methanol was added. The solvents were removed and the residue was taken up in 100 mL of dichloromethane. The organic layer was washed with water (2·10 mL) and dried with magnesium sulfate and concentrated. Column chromatography (H/E, 9:1) gave 480 mg of **1d** (80%), gum, *Rf* = 0.57 (H/E, 4:1). $[\alpha]_D^{20} = +48.1$ (c = 0.4, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 3.43 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-2), 3.54 (m, 3 H, *H*-4, *H*-5, *H*-5′), 3.80 (s, 3 H, CH_3O), 3.81 (s, 3 H, CH_3O), 3.89 (dd, 1 H, J_{3-4} 10 Hz, *H*-3), 3.97 (dd, 1 H, $J_{6-6'}$ 13, J_{6-7} 6.5 Hz, *H*-6), 4.16 (dd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 4.54 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.64 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.69 (d, 1 H, CH_2Ph), 4.71 (d, 1 H, *H*-1), 4.78 (d, 1 H, CH_2Ph), 4.79 (d, 1 H, J_{gem} 11.5 Hz,

CH_2Ph), 4.86 (d, 1 H, CH_2Ph), 5.21 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.32 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.92 (dddd, 1 H, *H*-7), 6.88 (2d, 4 H, *J* 10 Hz, aromatic *p*-MeOBzl), 7.33 (m, 9 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 55.2 (2 C, CH_3O), 63.8 (1 C, *C*-5), 70.2 (1 C, *C*-6), 72.8, 73.1, 73.6 (3 C, CH_2Ph), 76.5, 79.1, 79.5 (3 C, *C*-2, *C*-3, *C*-4), 97.5 (1 C, *C*-1), 113.9, 114.3 (4 C, aromatic *C*H), 119.2 (1 C, *C*-8), 127.9, 128.1, 128.3, 129.3, 129.7 (9 C, aromatic *C*H), 130.5, 131.4, 136.8 (3 C, aromatic *C*), 134.5 (1 C, *C*-7), 161.8, 162.1 (2 C, aromatic *C*). – $C_{31}H_{36}O_7$ (520.6) calcd C 71.52, H 6.96; found C 71.87, H 7.03.

Allyl 2,3,4-Tri-*O*-benzyl-α-D-xylopyranoside (1e): To a suspension of 1.8 g (1.5 equiv./OH) of freshly washed sodium hydride in DMF was added, at 0 °C, 1.9 g (0.01 mol) of allyl α-D-xylopyranoside. After 20 min was added 3.9 mL (1.1 equiv./OH) of benzyl bromide. The mixture was stirred at room temperature overnight and then treated as described for compound **1d** to give 3.78 g (82%) of **1e**, amorphous solid, *Rf* = 0.67 (H/E, 4:1). $[\alpha]_D^{20}$ = +36.1 (*c* = 0.4, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 3.47 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, *H*-2), 3.58 (m, 3 H, *H*-3, *H*-4, H-5), 3.94 (dd, 1 H, $J_{6-6'}$ 13, J_{6-7} 5 Hz, *H*-6), 3.99 (dd, 1 H, $J_{4-5'}$ 7, $J_{5-5'}$ 12 Hz, *H*-5′), 4.17 (dd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 4.63 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.65 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.88 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.73 (d, 1 H, *H*-1), 4.75 (d, 1 H, CH_2Ph), 4.78 (d, 1 H, CH_2Ph), 4.95 (d, 1 H, CH_2Ph), 5.22 (dd, 1 H, J_{7-8} 11, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.33 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.94 (dddd, 1 H, H-7), 7.31 (m, 15 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 59.9 (1 C, *C*-5), 67.9 (1 C, *C*-6), 73.1, 73.3, 75.6 (3 C, CH_2Ph), 77.9 (1 C, *C*-4), 79.4 (1 C, *C*-2), 81.2 (1 C, *C*-3), 95.5 (1 C, *C*-1), 117.9 (1 C, *C*-8), 127.4, 127.6, 127.8, 128.2 (15 C, aromatic *C*), 133.6 (1 C, *C*-7), 138.0, 138.1, 138.7 (3 C, aromatic *C*). – MS (70 eV): *m*/*z* (%): 458.9 (3) [$M^{\circ+}$ – 2], 416.9 (7), 402.8 (5) [M^+ – C_3H_5O], 253.2 (20), 181.2 (35), 105 (50), 91.0 (100) [Bn]. – $C_{29}H_{32}O_5$ (460.57): calcd. C 75.62, H 7.00; found C 75.94, H 6.75.

Allyl 3,4-Di-*O*-benzoyl-2-*O*-benzyl-α-D-xylopyranoside (1f): To a solution of 322 mg ($1.15 \cdot 10^{-3}$ mol) of diol **1a** in 20 mL of pyridine was added 1 g of benzoyl chloride. The mixture was stirred for 16 h, concentrated in vacuo and the residue was taken up in dichloromethane (150 mL). The organic layer was washed with a 1 N solution of hydrochloric acid, water, 1 N sodium hydroxide solution and water until neutral. Purification on a silica gel column (eluent H/E, 9:1 then 4:1) gave 480 mg (81%) of **1f**, *Rf* = 0.61 (H/E, 4:1). $[\alpha]_D^{20}$ = +52.1 (*c* = 0.5, $CHCl_3$). – IR (neat) $\tilde{\nu}$ = 1730 cm^{-1} (CO). – ^{1}H NMR ($CDCl_3$): δ = 3.72 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-2), 3.78 (dd, 1 H, J_{4-5} 10, $J_{5-5'}$ 10 Hz, *H*-5), 3.96 (dd, 1 H, $J_{4-5'}$ 6 Hz, *H*-5′), 4.05 (ddd, 1 H, $J_{6-6'}$ 13, J_{6-7} 6, J_{6-8} 1 Hz, *H*-6), 4.26 (ddd, 1 H, $J_{6'-7}$ 5, J_{6-8} 1 Hz, *H*-6′), 4.61 (s, 2 H, CH_2Ph), 4.93 (d, 1 H, *H*-1), 5.21 (ddd, 1 H, J_{3-4} 10 Hz, *H*-4), 5.26 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.39 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.97 (dd, 1 H, *H*-3), 5.98 (dddd, 1 H, H-7), 7.20 (m, 4 H, aromatic *H*), 7.33 (m, 5 H, aromatic *H*), 7.51 (m, 2 H, aromatic *H*), 7.96 (dd, 4 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 58.5 (1 C, *C*-5), 68.4 (1 C, *C*-6), 70.3 (1 C, *C*-4), 71.3 (1 C, *C*-2), 72.5 (1 C, CH_2Ph), 76.7 (1 C, *C*-3), 95.4 (1 C, *C*-1), 117.9 (1 C, *C*-8), 127.7, 128.2, 128.3 (5 C, aromatic *C*H), 128.9, 129.2 (2 C, aromatic C), 129.5, 129.6, 129.9, 132.8, 133.1, 133.5 (10 C, aromatic *C*H), 133.4 (1 C, *C*-7), 137.4 (1 C, aromatic *C*), 165.5, 165.6 (2 C, *C*=O). – $C_{29}H_{28}O_7$ (488.5): calcd. C 71.30, H 5.77; found C 71.42, H 5.84.

Allyl 2-*O*-Benzyl-3,4-di-*O*-*cyclo*-hexanecarbonyl-β-D-xylopyranoside (1g): To a solution of 270 mg ($0.96 \cdot 10^{-3}$ mol) of diol **1a** in 15 mL of pyridine was added 0.37 mL of *cyclo*-hexanecarbonyl chloride. The mixture was stirred for 16 h and then concentrated. The residue was taken up in 100 mL of dichloromethane. The organic layer was washed with a 1 N solution of hydrochloric acid, water, 1 N sodium hydroxide solution and water until neutral. Column chromatography (H/E, 9:1 then 4:1) gave 307 mg of **1g**, (64%), gum. *Rf* = 0.61 (H/E, 4:1). $[\alpha]_D^{20}$ = +36.3 (*c* = 1.9, $CHCl_3$). – IR (neat) $\tilde{\nu}$ = 1749 cm^{-1} (CO). – ^{1}H NMR ($CDCl_3$): δ = 1.28 (m, 10 H, C_6H_{11}), 1.72 (m, 10 H, C_6H_{11}), 2.23 (m, 2 H, C_6H_{11}), 3.52 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-2), 3.48 (dd, 1 H, J_{4-5} 10.5, $J_{5-5'}$ 10.5 Hz, *H*-5), 3.67 (dd, 1 H, $J_{4-5'}$ 6.5 Hz, *H*-5′), 3.95 (ddd, 1 H, $J_{6-6'}$ 13, J_{6-7} 6.5 Hz, *H*-6), 4.18 (ddd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 4.54 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.63 (d, 1 H, CH_2Ph), 4.76 (d, 1 H, *H*-1), 4.90 (ddd, 1 H, J_{3-4} 10 Hz, *H*-4), 5.21 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.34 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.50 (dd, 1 H, *H*-3), 5.92 (dddd, 1 H, H-7), 7.33 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 25.2, 25.3, 25.4, 25.6, 25.7, 26.5, 28.8, 28.9, 29.0, 29.1 (10 C, C_6H_{11}), 42.9, 43.0 (2 C, C_6H_{11}), 58.7 (1 C, *C*-5), 68.4 (1 C, *C*-6), 69.1, 70.5 (2 C, *C*-3, *C*-4), 72.9 (1 C, CH_2Ph), 77.1 (*C*-2), 95.6 (1 C, *C*-1), 118.0 (1 C, C8), 127.9, 127.94, 128.4 (5 C, aromatic *C*H), 133.6 (1 C, *C*-7), 137.8 (1 C, aromatic *C*), 175.0, 175.2 (2 C, *C*=O). – MS (70 eV): *m*/*z* (%): 443.5 (25) [M^+ – C_3H_5O], 389.3 (7), 187.0 (30), 111 (50), 91.0 (100) [Bn]. – $C_{29}H_{40}O_7$ (500.6): calcd. C 69.57, H 8.05; found C 69.85, H 7.86.

Allyl 2,3,4-Tri-*O*-benzyl-β-D-xylopyranoside (4): To a suspension of 3.1 g (1.5 equiv./OH) of freshly washed sodium hydride in DMF was added, at 0 °C, 3.25 g (16 mmol) of allyl β-D-xylopyranoside. After 20 min was added 6.2 mL (1.1 equiv./OH) of benzyl bromide. The mixture was stirred at room tempearture overnight and then treated as described for compound **1d** to give 6.2 g (83%) of **4** as white crystals, *Rf* = 0.70 (H/E, 4:1), m.p. 64–66 °C. $[\alpha]_D^{20}$= +8.0 (*c* = 0.2, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 3.21 (dd, 1 H, J_{4-5} 11, $J_{5-5'}$ 11 Hz, *H*-5), 3.40 (dd, 1 H, J_{1-2} 8.5, J_{2-3} 8.5 Hz, *H*-2), 3.60 (m, 2 H, *H*-3, *H*-4), 3.93 (dd, 1 H, $J_{4-5'}$ 4.5 Hz, *H*-5′), 4.13 (dd, 1 H, $J_{6-6'}$ 13, J_{6-7} 4.5 Hz, *H*-6), 4.38 (dd, 1 H, $J_{6'-7}$ 14 Hz, *H*-6′), 4.78 (m, 7 H, *H*-1, CH_2Ph), 5.22 (dd, 1 H, J_{7-8} 10, $J_{8-8'}$ 1.5 Hz, *H*-8), 5.34 (dd, 1 H, $J_{7-8'}$ 17 Hz, *H*-8′), 5.96 (dddd, 1 H, H-7), 7.33 (m, 15 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 63.7 (1 C, *C*-5), 70.0 (1 C, *C*-6), 73.1, 74.8, 75.4 (3 C, CH_2Ph), 77.7 (1 C, *C*-4), 81.7 (1 C, *C*-2), 83.6 (1 C, *C*-3), 103.1 (1 C, *C*-1), 117.1 (1 C, *C*-8), 127.3, 127.4, 127.5, 127.6, 127.7, 127.9, 128.1, 128.2, 128.2 (15 C, aromatic *C*H), 133.8 (1 C, *C*-7), 138.0, 138.3, 138.5 (3 C, aromatic *C*). – $C_{29}H_{32}O_5$ (460.57): calcd. C 75.62, H 7.00; found C 75.44, H 6.84.

General Procedure for Asymmetric Dihydroxylation with AD-mix-β and α: To a solution of 1.4 g of AD-mix in 10 mL of *tert*-butyl alcohol/water (1:1) at 0 °C was added the desired olefin ($1 \cdot 10^{-3}$ mol) in solution or suspension in 2 mL of *tert*-butyl alcohol/water mixture. The mixture was stirred at 0 °C until the reaction was complete (tlc monitoring). 1.5 g of sodium sulfite was added and the mixture was stirred for 30 min. The products were extracted with dichloromethane (2 × 100 mL) and the organic layer was dried with magnesium sulfate and concentrated under reduced pressure. The crude product was pure enough for diastereomeric ratio determination by ^{13}C-NMR spectroscopy. The same procedure was used for other trials with $(DHQD)_2$-PYR (Table 1, Entries 9, 10) and mixtures of the latter with AD-mix (Entries 11, 12).

(2,3-Dihydroxypropyl) 2-*O*-Benzyl-α-D-xylopyranoside (2a, 3a): The reaction, performed on 280 mg ($1 \cdot 10^{-3}$ mol) of **1a**, gave 299 mg (89%) of the mixture of **2a** and **3a**. *Rf* = 0.20 (CH_2Cl_2/MeOH, 9:1). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH). – ^{1}H NMR (D_2O): δ = 3.24 (m, 1.45 H, *H*-2, *H*-6b), 3.31 (dd, 0.55 H, $J_{6-6'}$ 11.5, J_{6-7} 6.5 Hz, *H*-6a), 3.41 (m, 2 H, *H*-8, *H*-8′), 3.50 (m, 3 H, *H*-4, *H*-5, *H*-6′), 3.65 (m, 3 H, *H*-3, *H*-5′, *H*-7), 4.57 (d, 0.45 H, J_{gem} 12 Hz, CH_2Ph), 4.58 (d, 0.55 H, J_{gem} 12 Hz, CH_2Ph), 4.65 (d, 0.55 H, J_{1-2} 3.5 Hz, *H*-1a), 4.66 (d, 0.45 H, J_{1-2} 3.5 Hz, *H*-1b), 4.69 (d, 1 H, CH_2Ph),

7.31 (m, 5 H, aromatic *H*). – ^{13}C NMR (CD_3OD): δ = 63.7 (1 C, *C*-5), 65.1 (1 C, *C*-6), 70.8 (0.55 C, CH_2Ph), 71.2 (0.45 C, CH_2Ph), 72.3, 75.1 (2 C, *C*-2, *C*-4), 72.7 (0.55 C, *C*-7a), 72.9 (0.45 C, *C*-7b), 81.7 (1 C, *C*-3), 99.2 (0.55 C, *C*-1a), 99.5 (0.45 C, *C*-1b), 129.8, 130.1, 130.3 (5 C, aromatic *C*H), 140.2 (1 C, aromatic *C*).

(2,3-Dihydroxypropyl) 3,4-Di-*O*-acetyl-2-*O*-benzyl-α-D-xylopyranoside (2b, 3b): The reaction, performed on 340 mg ($0.93\cdot10^{-3}$ mol) of **1b**, gave 370 mg (90%) of the mixture of **2b** and **3b**. *Rf* = 0.18 (H/E, 3:7). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH), 1749 (CO). – ^{1}H NMR ($CDCl_3$): δ = 1.90 (s, 1 H, O*H*), 2.01 (s, 6 H, OAc), 2.53 (s, 1 H, O*H*), 3.36 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 8 Hz, *H*-6), 3.50 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 10 Hz, *H*-2), 3.58 (m, 1 H, *H*-5), 3.70 (m, 2 H, *H*-8, *H*-8′), 3.80 (dd, 1 H, $J_{6'-7}$ 5 Hz, *H*-6′), 3.88 (m, 1 H, *H*-7), 4.58 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.63 (d, 1 H, CH_2Ph), 4.72 (d, 0.58 H, *H*-1a), 4.76 (d, 0.42 H, *H*-1b), 4.88 (ddd, 1 H, J_{3-4} 10, $J_{4-5'}$ 4.5 Hz, *H*-4), 5.45 (dd, 0.42 H, *H*-3b), 5.46 (dd, 0.58 H, *H*-3a), 7.31 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 20.3, 20.5 (2 C, OAc), 58.1 (1 C, *C*-5), 63.1 (0.58 C, *C*-8a), 63.2 (0.42 C, *C*-8b), 69.3 (0.42 C, *C*-6b), 69.9 (0.58 C, *C*-6a), 70.20 (0.42 C, *C*-7b), 70.22 (0.58 C, *C*-7a), 72.7 (1 C, CH_2Ph), 69.0, 70.9, 76.7 (3 C, *C*-2, *C*-3, *C*-4), 96.5 (0.42 C, *C*-1b), 96.8 (0.58 C, *C*-1a), 127.6, 127.8, 128.2 (5 C, aromatic *C*H C), 137.0 (0.58 C, aromatic *C*a), 137.0 (0.42 C, aromatic *C*b), 169.9, 170.0 (2 C, *C*=O).

(2,3-Dihydroxypropyl) 2-*O*-Benzyl-3,4-*O*-isopropylidene-α-D-xylopyranoside (2c, 3c): The reaction, performed on 320 mg ($1\cdot10^{-3}$ mol) of **1c**, gave 305 mg (86%) of the mixture of **2c** and **3c**. *Rf* = 0.22 (H/E, 3:7). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 1.44 [s, 6 H, C(CH_3)$_2$], 1.83 (s, 1 H, O*H*), 2.40 (s, 0.32 H, O*H*), 2.53 (m, 0.68 H, O*H*), 3.40 (m, 2 H, *H*-2, *H*-5), 3.70 (m, 8 H, *H*-3, *H*-4, *H*-5′, *H*-6, *H*-6′, *H*-7, *H*-8, *H*-8′), 4.62 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.83 (d, 0.32 H, *H*-1b), 4.86 (d, 0.68 H, *H*-1a), 4.88 (d, 1 H, CH_2Ph), 7.33 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 26.5, 26.8 [2 C, C(CH_3)$_2$], 61.2 (1 C, *C*-5), 63.5 (0.68 C, *C*-8a), 63.6 (0.32 C, *C*-8b), 70.0 (0.32 C, *C*-6b), 70.3 (0.32 C, *C*-7b), 70.6 (0.68 C, *C*-7a), 70.8 (0.68 C, *C*-6a), 72.1 (1 C, CH_2Ph), 74.0, 78.1 (3 C, *C*-2, *C*-3, *C*-4), 97.8 (0.32 C, *C*-1b), 98.3 (0.68 C, *C*-1a), 110.7 [1 C, $C(CH_3)_2$], 127.7, 127.9, 128.1, 128.3, 128.4 (5 C, aromatic *C*H), 137.5 (0.68 C, aromatic *C*a), 137.6 (0.32 C, aromatic *C*b).

(2,3-Dihydroxypropyl) 2-*O*-Benzyl-3,4-di-*O*-*p*-methoxybenzyl-α-D-xylopyranoside (2d, 3d): The reaction, performed on 260 mg ($0.5\cdot10^{-3}$ mol) of **1d**, gave 275 mg (95%) of the mixture of **2d** and **3d**. *Rf* = 0.34 (H/E, 3:7). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 2.00 (s, 1 H, O*H*), 2.58 (s, 1 H, O*H*) 3.40 (dd, 0.30 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-6b), 3.43 (dd, 0.70 H, J_{1-2} 3.5, J_{2-3} 10.5 Hz, *H*-6a), 3.60 (m, 8 H, *H*-2, *H*-4, *H*-5, *H*-5′, *H*-6′, *H*-7, *H*-8, H-8′), 3.80 (s, 3 H, CH_3O), 3.81 (s, 3 H, CH_3O), 3.87 (dd, 1 H, J_{3-4} 10 Hz, *H*-3), 4.54 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.63 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.64 (d, 0.70 H, *H*-1a), 4.65 (d, 0.30 H, *H*-1b), 4.67 (d, 1 H, CH_2Ph), 4.81 (d, 1 H, CH_2Ph), 4.86 (s, 2 H, CH_2Ph), 6.86 (2d, 4 H, *J* 10 Hz, aromatic *H p*-MeOBzl), 7.28 (2t, 4 H, *J* 10, *J* 10 Hz, aromatic *H p*-MeOBzl), 7.33 (m, 5 H, aromatic *H* Bzl). – ^{13}C NMR ($CDCl_3$): δ = 55.2 (2 C, CH_3O), 60.2 (0.70 C, *C*-8a), 60.3 (0.30 C, *C*-8b), 63.7 (1 C, *C*-5), 70.2 (0.30 C, *C*-7b), 70.4 (0.70 C, *C*-7a), 71.1 (1 C, *C*-6), 73.1, 73.7, 75.3 (3 C, CH_2Ph), 77.7, 79.47, 79.55, 81.0 (1 + 0.30 + 0.70 + 1 C, *C*-2, *C*-3, *C*-4), 98.0 (0.30 C, *C*-1b), 98.5 (0.70 C, *C*-1a), 113.7, 113.8 (4 C, aromatic *C*H), 127.9, 128.0, 128.4, 129.3, 129.5 (9 C, aromatic *C*H), 130.3, 130.9, 137.9 (3 C, aromatic *C*), 160.7, 161.0 (2 C, aromatic *C*).

(2,3-Dihydroxypropyl) 2,3,4-Tri-*O*-benzyl-α-D-xylopyranoside (2e, 3e): The reaction, performed on 459 mg ($1\cdot10^{-3}$ mol) of **1e**, gave 490 mg (95%) of the mixture of **2e** and **3e**. *Rf* = 0.40 (H/E, 3:7). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 2.02 (s, 1 H, O*H*), 2.68 (s, 1 H, O*H*), 3.38 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 6.5 Hz, *H*-6), 3.47 (dd, 1 H, J_{1-2} 3.5, J_{2-3} 9.5 Hz, *H*-2), 3.60 (m, 5 H, *H*-4, *H*-5, *H*-7, *H*-8, *H*-8′), 3.72 (dd, 1 H, $J_{4-5'}$ 4.5, $J_{5-5'}$ 11 Hz, *H*-5′), 3.86 (m, 2 H, *H*-6′, *H*-3), 4.62 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.64 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.65 (d, 1 H, *H*-1), 4.73 (d, 1 H, CH_2Ph), 4.81 (d, 1 H, CH_2Ph), 4.89 (s, 2 H, CH_2Ph), 7.33 (m, 15 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 59.6 (1 C, *C*-5), 63.1 (0.82 C, *C*-8a), 63.3 (0.18 C, *C*-8b), 69.4 (0.18 C, *C*-6b), 70.0 (0.82 C, *C*-6a), 70.1 (0.18 C, *C*-7b), 70.3 (0.82 C, *C*-7a), 73.0, 73.2, 75.3 (3 C, CH_2Ph), 77.8, 79.3, 80.9 (3 C, *C*-2, *C*-3, *C*-4), 97.2 (0.18 C, *C*-1b), 97.4 (0.82 C, *C*-1a), 127.2, 127.5, 127.6, 127.7, 127.8, 127.8, 128.1 (15 C, aromatic *C*H), 137.4, 137.5, 137.8, 138.5 (0.82 + 0.18 + 2 C, aromatic *C*).

(2,3-Dihydroxypropyl) 3,4-*O*-Benzoyl-2-*O*-benzyl-α-D-xylopyranoside (2f, 3f): The reaction, performed on 244 mg (1 mmol) of **1f**, gave 260 mg (90%) of the mixture of **2f** and **3f**. *Rf* = 0. 44 (H/E, 1:4). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH), 1730 (CO). – ^{1}H NMR ($CDCl_3$): δ = 1.75 (br. s, 1 H, O*H*), 1.94 (br. s, 1 H, O*H*), 3.46 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 7 Hz, *H*-6), 3.63 (dd, 1 H, J_{7-8} 6, $J_{8-8'}$ 13 Hz, *H*-8), 3.76–3.85 (broad multiplet, 4 H, *H*-2, *H*-5, *H*-5′, *H*-8′), 3.93 (dd, 1 H, $J_{6'-7}$ 4.5 Hz, *H*-6′), 3.97 (m, 1 H, *H*-7), 4.60 (s, 2 H, CH_2Ph), 4.87 (d, 0.89 H, *H*-1a), 4.92 (d, 0.11 H, *H*-1b), 5.23 (ddd, 1 H, J_{3-4} 10, J_{4-5} 10, $J_{4-5'}$ 6 Hz, *H*-4), 5.92 (dd, 1 H, J_{2-3} 10 Hz, H-3), 7.20 (s, 4 H, aromatic *H*), 7.33 (m, 5 H, aromatic *H*), 7.51 (m, 2 H, aromatic *H*), 7.96 (m, 4 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 58.5 (1 C, *C*-5), 63.3 (0.89 C, *C*-8a), 63.5 (0.11 C, *C*-8b), 69.9 (0.11 C, *C*-6b), 70.0, 70.4, 71.3, 76.8 (4 C, *C*-2, *C*-3, *C*-4, *C*-7), 70.5 (0.89 C, *C*-6a), 72.7 (1 C, CH_2Ph), 97.0 (0.11 C, *C*-1b), 97.3 (0.89 C, *C*-1a), 127.8, 128.1, 128.2, 129.4, 132.9, 133.1 (13 C, aromatic *C*H), 128.8, 129.4 (2 C, aromatic *C*), 136.8 (1 C, aromatic *C*), 165.4, 165.6 (2 C, aromatic *C*).

(2,3-Dihydroxypropyl) 2-*O*-Benzyl-3,4-*O*-cyclohexanecarbonyl-α-D-xylopyranoside (2g, 3g): The reaction, performed on 160 mg ($0.32\cdot10^{-3}$ mol) of **1g**, gave 161 mg (95%) of the mixture of **2g** and **3g**. *Rf* = 0.36 (H/E, 1:4). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH), 1740 cm^{-1} (CO). – ^{1}H NMR ($CDCl_3$): δ = 1.21 (m, 10 H, C_6H_{11}), 1.73 (m, 10 H, C_6H_{11}), 2.20 (m, 2 H, C_6H_{11}), 2.79 (br. s, 2 H, O*H*), 3.33 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 7 Hz, *H*-6), 3.5–3.70 (broad multiplet, 5 H, *H*-2, *H*-5, *H*-5′, *H*-8, *H*-8′), 3.78 (m, 1 H, *H*-6′), 3.87 (m, 1 H, *H*-7), 4.53 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.62 (d, 1 H, CH_2Ph), 4.70 (d, 0.85 H, *H*-1a), 4.72 (d, 0.15 H, *H*-1b), 4.88 (ddd, 1 H, J_{3-4} 10, J_{4-5} 10, $J_{4-5'}$ 6 Hz, *H*-4), 5.42 (dd, 1 H, J_{2-3} 10 Hz, *H*-3), 7.30 (m, 5 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 25.0, 25.3, 25.6, 25.7, 28.7, 28.8, 28.9, 29.0 (10 C, C_6H_{11}), 42.9, 43.2 (2 C, C_6H_{11}), 58.6 (1 C, *C*-5), 63.4 (0.85 C, *C*-8a), 63.6 (0.15 C, *C*-8b), 68.8 (1 C, *C*-3), 69.8 (0.15 C, *C*-6b), 70.5, 70.6 (2 C, *C*-4, *C*-7), 70.6 (0.85 C, *C*-6a), 73.2 (1 C, CH_2Ph), 77.3 (1 C, *C*-2), 97.2 (0.15 C, *C*-1b), 97.5 (0.85 C, *C*-1a), 128.0, 128.1, 128.5 (5 C, aromatic *C*H), 137.2 (1 C, aromatic *C*), 175.0 (2 C, *C*=O).

(2,3-Dihydroxypropyl) 2,3,4-Tri-*O*-benzyl-β-D-xylopyranoside (5, 6): The reaction, performed on 230 mg ($0.5\cdot10^{-3}$ mol) of **4**, gave 245 mg (99%) of the mixture of **5** and **6**. *Rf* = 0.42 (H/E, 3:7). – IR (neat): $\tilde{\nu}$ = 3600 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 2.32 (br. s, 1 H, OH), 3.01 (br. s, 1 H, OH), 3.38 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 6.5 Hz, *H*-6), 3.70 (m, 6 H, *H*-2, *H*-4, *H*-5, *H*-7, *H*-8, *H*-8′), 3.80 (m, 2 H, *H*-3, *H*-5′), 3.96 (m, 1 H, *H*-6′), 4.35 (d, 0.55 H, J_{1-2} 7 Hz, *H*-1a), 4.39 (d, 0.45 H, J_{1-2} 7 Hz, *H*-1b), 4.62 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.72 (d, 1 H, CH_2Ph), 4.74 (d, 1 H, J_{gem} 11.5 Hz, CH_2Ph), 4.83 (d, 1 H, CH_2Ph), 4.89 (s, 2 H, CH_2Ph), 7.33 (m, 15 H, *H* aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 62.9, 62.98 (0.45 C + 0.55

C, *C*-8), 63.4 (1 C, *C*-5), 70.4 (0.45 C, *C*-7b), 70.5 (0.55 C, *C*-7a), 71.0 (0.45 C, *C*-6b), 71.4 (0.55 C, *C*-6a), 72.9, 74.6, 75.2 (3 C, CH_2Ph), 77.4, 81.3, 83.2, 83.3 (1 + 1 + 0.45 + 0.55 C, *C*-2, *C*-3, *C*-4), 104.0 (0.55 C, *C*-1a), 104.1 (0.45 C, *C*-1b), 127.2, 127.3, 127.4, 127.5, 127.7, 127.9, 127.9, 128.0 (15 C, aromatic *C*H), 137.7, 137.9, 137.95, 138.2 (1 + 0.55 + 0.45 + 1 C, aromatic *C*).

Absolute Configuration Determination

(2,3-Dibenzyloxypropyl) 2,3,4-Tri-*O*-benzyl-α-D-xylopyranoside (7): 2 g ($4.0 \cdot 10^{-3}$ mol) of diols **2e/3e** were benzylated using 487 mg (1.5 equiv./OH) of sodium hydride and 1.05 mL (1.1 equiv./OH) of benzyl bromide according to the procedure described for compound **1e** to give 2.09 g (77%) of **7** as a gum. *Rf* = 0.77 (H/E, 4:1). – ^{1}H NMR ($CDCl_3$): δ = 3.48 (dd, 1 H, $J_{6-6'}$ 10, J_{6-7} 4 Hz, *H*-6), 3.61 (m, 6 H, *H*-2, *H*-4, *H*-5, *H*-7, *H*-8, *H*-8′), 3.88 (m, 3 H, *H*-3, *H*-5′, *H*-6′), 4.56 (s, 2 H, CH_2Ph), 4.63 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.66 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.73 (m, 3 H, *H*-1, CH_2Ph), 4.76 (d, 1 H, CH_2Ph), 4.78 (d, 1 H, CH_2Ph), 4.88 (d, 1 H, J_{gem} 12 Hz, CH_2Ph), 4.94 (d, 1 H, CH_2Ph), 7.32 (m, 25 H, aromatic *H*). – ^{13}C NMR ($CDCl_3$): δ = 60.6 (1 C, *C*-5), 68.3 (0.18 C, *C*-8b), 68.8 (0.82 C, *C*-8a), 70.6 (1 C, *C*-6), 72.6 (0.18 C, CH_2Ph), 72.9 (0.82 C, CH_2Ph), 73.8, 74.0, 76.1 (4 C, CH_2Ph), 77.4 (0.82 C, C-7a), 77.8 (0.18 C, C-7b), 78.7, 80.5, 81.8 (3 C, *C*-2, *C*-3, *C*-4), 97.9 (0.18 C, *C*-1b), 98.0 (0.82 C, *C*-1a), 128.1, 128.2, 128.4, 128.5, 128.8, 128.9 (25 C, aromatic *C*H), 138.9, 139.0, 139.2, 139.3, 139.6 (5 C, aromatic *C*).

A solution of 2.05 g ($3.0 \cdot 10^{-3}$ mol) of the pentabenzyl derivatives **7** in 50 mL of glacial acetic acid was heated at 60 °C. 10 mL of a boiling 2 N solution of sulfuric acid was added to avoid product precipitation. The mixture was refluxed for 5 h. The resulting mixture was concentrated in vacuo and the residue was taken up in 150 mL of dichloromethane and washed with water until neutral. Column chromatography gave 1.2 g (93%) of the known compound **8**[32] and 860 mg (89%) of the protected glycerol **9** as an oil.

1,2-Dibenzylpropanetriol (10): To a solution of 860 mg ($2.74 \cdot 10^{-3}$ mol) of compound **9** in 50 mL of methanol was added 5 mg of sodium. After 1 h the mixture was neutralised with Dowex H^+ resin. Filtration and evaporation gave 740 mg of the 82:18 diastereomeric mixture of **10**. $[\alpha]_D$ = –11.2 (*c* = 1.1, $CHCl_3$). ref.[11]: $[\alpha]_D$ = –17.2 (*c* = 1.0, $CHCl_3$). *Rf* = 0.5 (toluene/acetone, 5:1). – ^{1}H NMR ($CDCl_3$): δ = 2.7 (s, 1 H, O*H*), 2.45 (m, 5 H, *H*-1, *H*-1′, *H*-2, *H*-3, *H*-3′), 4.48 (s, 2 H, CH_2Ph), 4.61 (s, 2 H, CH_2Ph), 7.33 (m, 10 H, aromatic *H*).

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