DOI: 10.1002/ejoc.200900888

Synthesis of New Chiral Ketones from D-Glucose Derivatives and Their Use in the Enantioselective Epoxidation of Arylalkenes

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Keywords: Chiral ketones / Carbohydrates / Asymmetric catalysis / Chiral dioxiranes / Epoxidation / Asymmetric synthesis

A new backbone model for a chiral carbohydrate-derived ketone for asymmetric epoxidation is presented. The oxo function is sited in a seven-membered ring fused to the sugar moety. The synthesized compound is an effective chirality-transfer agent in dioxirane-mediated epoxidation, giving *ee*s of up to 74 %.

Introduction

Chiral epoxides are widely employed in organic synthesis because they are useful synthetic intermediates that can be easily transformed into a variety of target molecules.[1] The epoxide functional group itself is also an essential structural moiety of many natural products and biologically active compounds.[2]

The development of efficient methods to achieve access to chiral epoxides with high enantiomeric excesses is an important objective of many research groups. Among such methods, the asymmetric epoxidation of olefins is a powerful strategy, and is the most widely employed route. Epoxidation of olefins is typically performed either with an organic peracid (such as *m*-chloroperbenzoic acid) or with a combination of a transition metal catalyst and a co-oxidant. Several chiral catalyst systems based on transition metal complexes have been developed, and great success has been achieved in metal-catalysed epoxidation reactions of unfunctionalised alkenes.

In the last few years, however, non-metal-based "organocatalysis" has become an emergent area.[3] One attractive catalytic process in this field is dioxirane-mediated epoxidation. Dioxiranes can be generated in situ from ketones and potassium peroxomonosulfate (Oxone®), and when a chiral ketone is employed its reaction with Oxone® yields a chiral dioxirane, which may react selectively on one enantiotopic face of the substrate alkene. After oxygen atom transfer from dioxirane to alkene, the chiral ketone can be recovered in high yield without loss of activity, and can thus be employed in another epoxidation reaction. The reaction is rapid and mild, and several efficient protocols have been described by different research groups since the first one by Curci et al.[4] High catalytic activity, high stereochemical differentiation, usefulness on different structural types of alkene, and easy and high-yielding synthesis are some criteria required for ketones. The design of new chiral ketones to provide successful stereochemical control in dioxirane-mediated epoxidation reactions is an important issue in this area. Because a dioxirane has two reacting sites, restriction of possible competition between them is an important factor for stereochemical control and should be taken into consideration during the ketone design process. Research groups working in this area have reported very high enantiomeric excess values for different types of alkene, with two different approaches usually being applied. The first is to design C_2-symmetric ketones (different chiral backbones have been employed) so that the two faces of the generated dioxiranes have exactly the same chiral environment, and there should be no problems of competition.[5–9] The second option is the preparation of chiral ketones that yield dioxiranes with one face blocked, so that oxygen transfer occurs almost selectively from the other face. In this area, many research groups have achieved attractive and interesting results with different chiral ketone/Oxone® systems.[10–13]

Because of the important role of carbohydrate moieties in stereochemical differentiation (they are cheap, available, and offer various functional groups and stereogenic centres in one molecule unit), the possibility of employing them as precursors for chiral ketones – and subsequently as catalysts in epoxidation reactions – is an interesting goal. In this context, Shing and co-workers have developed new glucose-[14] and arabinose-derived[11b,15] uloses and have achieved high stereochemical communication between the ketone catalyst and the alkene [(*E*)-, trisubstituted and (*Z*)-alkenes]. Shi and co-workers have reported the synthesis of a variety of

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200900888.

new fructose- and glucose-derived ketones that have been shown to be effective and excellent catalysts for asymmetric epoxidation of olefins with a broad substrate scope [high enantioselectivities have been obtained with a wide variety of (*E*)- and trisubstituted olefins, a number of (*Z*)-olefins and certain terminal and tetrasubstituted olefins]. The same authors have also extensively investigated the reaction transition states and factors for stereochemical control in order to develop more efficient catalysts.[16]

Our research group has a long-term interest in the use of carbohydrates in asymmetric processes. We have employed carbohydrate derivatives as chiral templates for the stereoselective synthesis of different compounds: diamino sugars, chiral oxazolidines and compounds with potential anticancer activity.[17]

Part of our work with carbohydrates involves their use as auxiliaries in asymmetric transformations of olefins. Recently, we have described the use of new carbohydrate derivatives in the stereoselective synthesis of cyclopropanes.[18]

In the field of the development of epoxidation reactions of olefins with the most successful stereocontrol (diastereoselectivity), our group has described the stereoselective epoxidation of olefin moieties linked through various functionalities (glycoside,[19,20] amide[21] and acetals[22]) to different positions of carbohydrate residues with *m*-chloroperbenzoic acid as oxidant under mild conditions. The different types of chiral epoxide obtained (epoxyglycosides, epoxyamides and epoxyacetals) can be transformed into a variety of compounds.

Focusing on dioxirane-mediated epoxidations, we have prepared new chiral carbohydrate-derived ketones and have used them as catalysts. Here we present our initial effort in this area in the shape of the synthesis of two new chiral ketones: the first a chiral ketone with its carbonyl group on a ring fused to the sugar moiety of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside as precursor, and the second a C_2-symmetric ketone derived from 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose as starting material. We include our stereochemical results for the epoxidation of (*E*)- and trisubstituted alkenes with these ketones as chiral catalysts. These preliminary results have encouraged us to continue our studies in this area.

Results and Discussion

Syntheses of new carbohydrate-derived ketones are described in the literature. The reactive centre in such a compound is close to the stereogenic centres, and the sugar moiety is suitably functionalised in order to optimise the role as chiral catalyst. Compounds of this type function as efficient catalysts in dioxirane-mediated epoxidations and yield high enantiomeric excesses. Examples are Shi's fructose-derived ketone **1**[23] and Shing's arabinose-derived ketone **2**[15] (Figure 1).

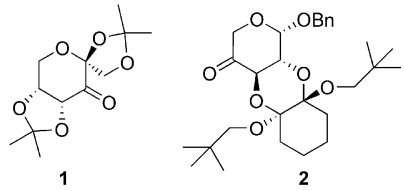


Figure 1. Compounds **1** and **2**.

Another reported approach for the design of chiral ketones (and that we wish to mention here) is through the incorporation of the ketone function on a cycle. In such cases, the chiral environment necessary for the stereochemical differentiation is given by the axial chirality of a biaryl moiety, linked to the ketone function through a spacer group. Examples are Yang's ketone **3**,[5] Song's ketone **4**[6] and Denmark's ketone **5**[8] (Figure 2).

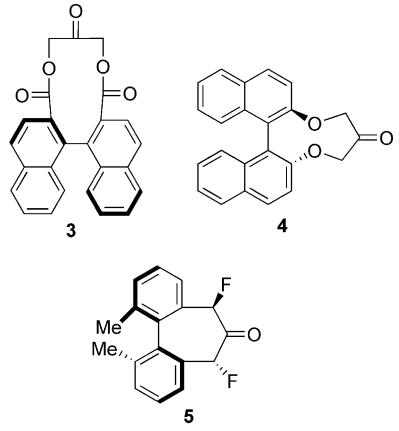
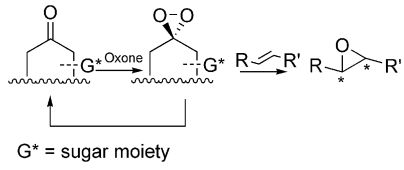


Figure 2. Compounds **3**, **4** and **5**.

Our aim was to design new chiral ketones derived from sugars, based on the two methods described below. For the first method we employed the carbohydrate moiety as chiral backbone in order to obtain an efficient asymmetric environment, and for the second approach we used the presence of the ketone function on a cycle fused to the sugar moiety (in this case through positions 2 and 3 as can be seen in compound **9**; Scheme 2, bottom). Our compound also features spacer groups between the ketone and the stereocentres (Scheme 1).

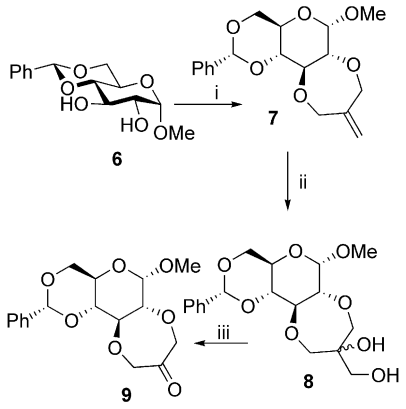


Scheme 1.

Given that to synthesise compound **9** we had to fuse a cycle containing a ketone function to the sugar ring, we decided to conduct its synthesis by using a double bond as

precursor. This could be incorporated through the use of a simple substance such as 3-chloro-2-(chloromethyl)propene by means of a double etherification reaction with a monosaccharide residue – in our case, the commercial product methyl 4,6-*O*-(*R*)-benzylidene-α-D-glucopyranoside (**6**). The aim, beyond the preparation of the designed compound **9**, was to establish a simple sequence of reactions that could be used to obtain a series of precursor substances of some complexity, highly functionalised and stereochemically relevant, and endowed with diverse but constitutionally similar chemical features.

Dialkylation of the starting compound **6** (Scheme 2) in tetrahydrofuran with 3-chloro-2-(chloromethyl)propene in the presence of solid potassium hydroxide and 18-crown-6 leads (at room temperature in 5 d) to the cyclic compound methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-methylidene-1,3-propanediyl)-α-D-glucopyranoside (**7**), one of the key intermediates.

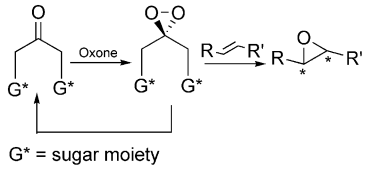


Scheme 2. Reagents and conditions: (i) $(ClCH_2)_2CH_2$/KOH/18-crown-6/THF, 63%; (ii) OsO_4 (*t*BuOH)/Me_3NO/CH_2Cl_2, 81%; (iii) $NaIO_4$ (H_2O)/EtOH/H_2O, 85%.

Next was the dihydroxylation of the double bond with osmium tetroxide (in catalytic amounts) and trimethylamine *N*-oxide, in dichloromethane as solvent. The reaction took place at room temperature, yielding the glycol methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-[2-hydroxy-2-(hydroxymethyl)-1,3-propanediyl]-α-D-glucopyranoside (**8**) as a white solid. The dihydroxylation reaction generates a new stereocentre in the molecule. In our case, ^{1}H NMR spectral study shows the signal for the acetal PhC*H* hydrogen atom as two singlets at δ = 5.51 and 5.49 ppm, that for 1-H of the sugar as two doublets at δ = 4.82 and 4.78 ppm ($J_{1,2}$ = 3.6 Hz), and that for the methyl group as two singlets at δ = 3.43 and 3.42 ppm. The relative integrals for the two signals for the same hydrogen atom in each of the stereoisomers show that they were formed in equal amounts.

The second step was an oxidative cleavage carried out with an aqueous solution of sodium metaperiodate as oxidising agent. An ethanol/water mixture was used as solvent to dissolve compound **8** (insoluble in water) and the ionic reagent (not very soluble in ethanol). The reaction was complete at room temperature overnight and yielded, as a white solid, the compound methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-oxo-1,3-propanediyl)-α-D-glucopyranoside (**9**), the spectroscopic data for which are consistent with the proposed structure (Scheme 2).

On the other hand, the C_2-symmetric ketones reported in the literature to act as efficient chiral catalysts in epoxidation reactions are rigid systems.[5–9] In this context, our second aim was to design a ketone possessing the structure of acetone substituted on C-1 and C-3 by two identical, appropriately functionalised molecules of D-glucose, thus representing a ketone with C_2 symmetry but with conformational flexibility. Our goal was to assess whether this new molecule would afford good stereofacial discrimination in the epoxidation reaction (Scheme 3).

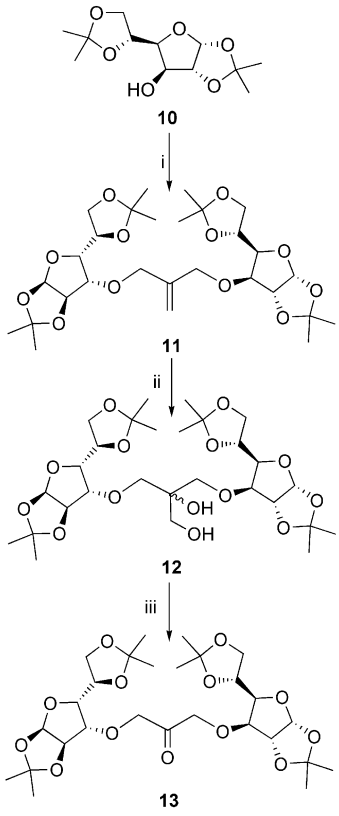


Scheme 3.

For this we used 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**10**, Scheme 4) as starting material. Treatment of 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose with 3-chloro-2-(chloromethyl)propene (2 equiv.) in tetrahydrofuran, in the presence of potassium hydroxide and 18-crown-6, led to the compound 3-[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]-2-{[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]methyl}propene (**11**) as a syrup, in excellent yield.

The C_2 symmetry presented by the molecule of compound **11** is confirmed by the simplicity of its ^{1}H and ^{13}C NMR spectra – there are single sets of signals for the two D-glucose fragments. The ^{1}H NMR spectrum presents a single signal at δ = 5.12 ppm (singlet) for the two equivalent protons of the double bond, whereas two doublets with the same coupling constant (3.7 Hz) are observed at δ = 5.76 and 4.46 ppm, corresponding to the 1-H and 2-H atoms of the two sugar molecules. The 2-H doublet indicates that it is coupled only with 1-H and not with 3-H, which is typical of α-D-furanose rings blocked at the 1-OH and 2-OH groups and in which there is a relative *trans* arrangement between hydrogen atoms 2-H and 3-H, which have a coupling constant between them that is practically zero. The ^{13}C NMR spectrum shows the typical signals for the double bond at δ = 141.6 and 115.6 ppm and for C-1 at δ = 105.0 ppm. The rest of the signals in the two spectra were assigned with the help of two-dimensional experiments.

The transformation of **11** into the corresponding ketone followed a sequence of reactions similar to that described for the synthesis of compound **9**. Dihydroxylation with osmium tetroxide and trimethylamine oxide gave the glycol 3-[(1,2:5,6-di-*O*-isopropylidene-α-D-glucopyranos-3-yl)oxy]-2-{[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]-methyl}-1,2-propanediol (**12**) as a syrup in high yield.



Scheme 4. Reagents and conditions: (i) $(ClCH_2)_2CH_2$/KOH/18-crown-6/THF, 96%; (ii) OsO_4 (*t*BuOH)/Me_3NO/CH_2Cl_2, 88%; (iii) $NaIO_4$ (H_2O)/EtOH/H_2O, 72%.

It should be noted that compound **12** has lost the C_2 symmetry of its precursor. The quaternary carbon atom bearing the hydroxy group is a prochiral carbon atom, so that the two equal substituents on this carbon atom are two diastereotopic groups. This is demonstrated by the NMR spectra of compound **12**, which present different signals for all of the hydrogen and carbon atoms of the two D-glucose fragments that form part of the two diastereotopic groups of the molecule. The ^{1}H NMR spectrum shows two doublets (with coupling constants of 3.7 Hz) at δ = 5.88 and 5.84 ppm for the two 1-H atoms, together with two doublets (with the same coupling constant) at δ = 4.55 and 4.52 ppm for the two 2-H atoms, as well as two double doublets at δ = 3.61 and 3.48 ppm, assigned to the diastereotopic methylene hydrogen atoms of the CH_2OH group. The ^{13}C NMR spectrum shows signals at δ = 105.7 and 105.6 ppm for the two C-1 atoms, and signals at δ = 74.7 and 64.0 ppm for the two carbon atoms bearing the hydroxy groups.

Oxidative cleavage of the glycol **12** with sodium metaperiodate under the conditions described above led to 1,3-bis[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)-oxy]acetone (**13**) as a syrup that was purified by column chromatography. Its structure was confirmed by analysis of its NMR spectra, which featured single sets of signals for the two groups joined to the carbonyl group. Noteworthy features of the ^{1}H NMR spectrum are the doublets for the 1-H and 2-H atoms at δ = 5.92 and 4.66 ppm, together with a broad singlet for the four hydrogen atoms vicinal to the carbonyl group, whereas those of the ^{13}C NMR spectrum are the signal for the carbonyl carbon atom at δ = 204.9 ppm and that for C-1 at δ = 105.2 ppm.

Catalytic Asymmetric Epoxidation

Having synthesised the ketones **9** and **13**, we were able to test their efficiencies as chiral catalysts in dioxirane-mediated epoxidation reactions. As test substrates we first chose (*E*)-stilbene and phenylcyclohexene, representing (*E*)- and trisubstituted alkenes, respectively, and screened various sets of reaction conditions with a view to improving the efficiency of the epoxidation (in terms of chemical and enantiomeric yields). Our preliminary essays employed substoichiometric quantities (0.5 equiv.) of ketone; not only were the reaction times long (1–2 d), however, but in addition the reactions did not go to completion (recovery of alkene without epoxidation). The use of different quantities of ketone did not give different stereochemical results (enantiomeric excesses or major oxirane configuration). That is why, finally, all epoxidations were carried out at 0 °C with substrate (0.2 mmol), ketone (0.3 mmol), Oxone® (0.4 mmol) and $NaHCO_3$ (1.2 mmol) in DME/4×10^{-4} M aqueous EDTA (1.2:1, v/v). The pH of the mixture was maintained at about 8.0 for the period of time necessary to complete the reaction (3–7 h, TLC analysis).

Whereas the epoxidation reactions of (*E*)-stilbene and phenylcyclohexene with ketone **9** and Oxone® gave 68% and 74% enantiomeric excesses, respectively (Table 1), no enantioselectivity was achieved with the use of ketone **13** as chiral dioxirane source. We think that despite its being a molecule with C_2 symmetry, its conformational flexibility (a structural feature conspicuously absent in the C_2-symmetric ketones described in the literature, which are characterised by their rigidities) is responsible for the absence of stereodiscrimination in the dioxirane formed in its interaction with the alkene. We believe that as a result of this conformational flexibility in ketone **13** the two reactive centres of the generated dioxirane never attain the same chiral environment.

Encouraged by the preliminary results with ketone **9**, we went on to investigate its chiral induction capability in the asymmetric epoxidation of a variety of unfunctionalised (*E*)- and trisubstituted olefins (**a**–**g**) in order to explore the substrate scope of this catalyst (Scheme 5).

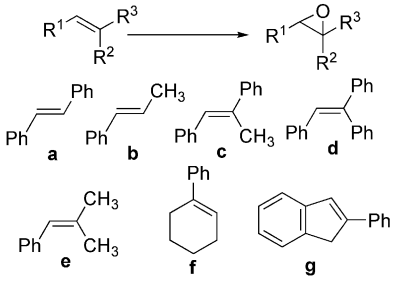
Moderate to good enantiomeric excesses were obtained (57–74%, Entries 1–4, 6). Triphenyloxirane and phenylcyclohexene oxide were obtained with highest excess (74%, Entries 4 and 6). However, both 2,2-dimethyl-3-phenyloxirane (Entry 5) and 2-phenylindene oxide (Entry 7) were obtained with poor stereoselectivity (6% and 25%).

The absolute configurations of the major enantiomers obtained were assigned by comparison of the signal shifts in the presence of (+)-Eu(hfc)$_3$ with those reported in the literature, and also by comparison of the signs of optical rotation with the reported ones. In one case (Entry 7) a ten-

Table 1. Catalytic asymmetric epoxidation of alkenes in the presence of ketone **9**.[a]

Entry	Alkene	Yield[b] (%)	*ee*[c] (%)	Configuration[d]
1	**a**	73	68	(–)-(1*S*,2*S*)
2	**b**	68	57	(–)-(1*S*,2*S*)
3	**c**	72	67	(–)-(1*S*,2*S*)
4	**d**	66	74	(+)-(2*S*)
5	**e**	54	6	(–)-(2*S*)
6	**f**	61	74	(–)-(1*S*,2*S*)
7	**g**	35[e]	25	(–)-(1*S*,2*S*)[f]

[a] Epoxidation conditions: substrate (1 equiv.), ketone (1.5 equiv.), Oxone® (2 equiv.), $NaHCO_3$ (6 equiv.), DME/aqueous EDTA [4×10^{-4} M (1.2:1)], 0 °C. [b] Yields after column chromatography. [c] Enantiomeric excesses were determined by direct ^{1}H NMR examination of the epoxide products with shift reagent (+)-Eu(hfc)$_3$. [d] The absolute configuration of the major enantiomer was assigned by comparison of the signal shifts with those reported in the literature and also by comparison of the sign of optical rotation with the reported one in each case. [e] Unreacted alkene was recovered after column chromatography. [f] Tentatively assigned (see text).



Scheme 5. Epoxidation conditions (see Table 1).

tative assignment was made. For this it was important to analyse the chemical shifts of the oxirane protons for the epoxides, shown in Figure 3 (Table 2). For epoxides of (*E*)-stilbene and phenylcyclohexene, the signal for the major enantiomer appears in each case at a higher chemical shift than that for the minor enantiomer (Entries 1 and 2), and the profile is the same as for phenylindene oxide, so we tentatively assigned the same configuration for its major epoxide (Entry 3).

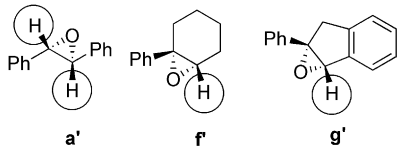


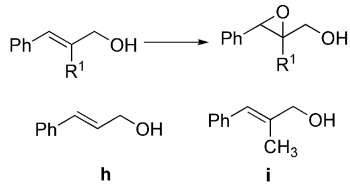
Figure 3. Oxirane protons used for stereochemical assignments.

Focusing on testing the oxidant capacity of ketone **9** and studying its potential for employment for the epoxidation of a variety of alkenyl substrates (unfunctionalised and differently functionalised olefins) – in other words, the generality of this system – we carried out epoxidations of two allylic alcohols as another kind of test substrate (Scheme 6, Table 3).

Table 2. Comparative ^{1}H NMR chemical shifts of epoxide proton signals.[a]

Entry	Epoxide	Signal profiles[b]	Configuration[c]
1	**a′**	4.15 (M)/4.13 (m)	(–)-(1*S*,2*S*)
2	**f′**	3.70 (M)/3.58 (m)	(–)-(1*S*,2*S*)
3	**g′**	4.62 (M)/4.60 (m)	(–)-(1*S*,2*S*)[d]

[a] ^{1}H NMR spectroscopic data for epoxide in the presence of the shift reagent (+)-Eu(hfc)$_3$. [b] (M) for the major enantiomer, (m) for the minor enantiomer. [c] Absolute configuration assigned according to literature data. [d] Tentatively assigned.



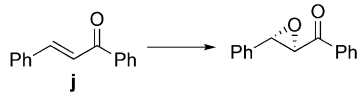
Scheme 6. Epoxidation conditions (see Table 3).

Table 3. Catalytic asymmetric epoxidation of allylic alcohols in the presence of ketone **9**.[a]

Entry	Substrate	Yield (%)[b]	*ee* (%)[c]	Configuration[d]
1	**h**	43[e]	56	(–)-(2*S*,3*S*)
2	**i**	41[e]	9	(–)-(2*S*,3*S*)

[a] Epoxidation conditions: substrate (1 equiv.), ketone (1.5 equiv.), Oxone® (2 equiv.), $NaHCO_3$ (6 equiv.), DME/aqueous EDTA [4×10^{-4} M (1.2:1)], 0 °C. [b] Yields after column chromatography. [c] Enantiomeric excesses were determined by direct ^{1}H NMR examination of the epoxide products in the presence of the shift reagent (+)-Eu(hfc)$_3$. [d] The absolute configuration of the major enantiomer was assigned in each case by comparison of the signal chemical shifts with those reported in the literature and also by comparison of the sign of optical rotation with that reported. [e] Attributed to isolation problems.

The development of efficient methods for the asymmetric epoxidation of α,β-enones is another important goal in organic synthesis. Although a variety of valuable systems have been proposed for this reaction, the development of mild and convenient methods of epoxidation with use of recyclable catalysts remains an emergent area. In this context, we carried out the epoxidation reaction of (*E*)-chalcone in the presence of ketone **9** (Scheme 7, Table 4) and Oxone®.



Scheme 7. Epoxidation conditions (see Table 4).

In almost all cases the epoxides were isolated in satisfactory chemical yields (60–73%), and the epoxidation reactions were complete after a few hours, indicating that ketone **9** is an efficient catalyst (in terms of reactivity) for generation of the active dioxirane. In the cases of phenylindene (Table 1, Entry 7) and (*E*)-chalcone (Table 4), however, the reactions were not complete even after 24 h, and significant amounts of the starting materials were reco-

Table 4. Catalytic asymmetric epoxidation of (*E*)-chalcone in the presence of ketone **9**.[a]

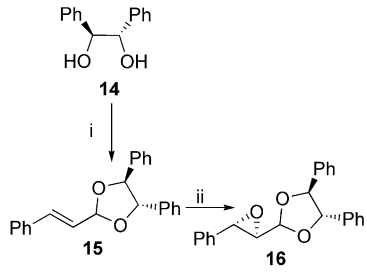
Yield (%)[b]	*ee* (%)[c]	Configuration[d]
52	38	(–)-(2*R*,3*S*)

[a] Epoxidation conditions: substrate (1 equiv.), ketone (1.5 equiv.), Oxone® (2 equiv.), $NaHCO_3$ (6 equiv.), DME/aqueous EDTA [4×10^{-4} M (1.2:1)], 0 °C. [b] Unreacted substrate was recovered after column chromatography. [c] Enantiomeric excess was determined by chiral HPLC analysis on a Chiralcel OD column. [d] The absolute configuration of the major enantiomer was assigned by comparison of the sign of optical rotation with the reported one and of the HPLC retention times with the literature.

vered. We observed that for most reactions the *ee*s were about 57–74%, except in two cases in which they were dramatically decreased (Table 1, Entry 5; Table 3, Entry 2) to 6% and 9%, respectively, indicating that ketone **9** could not induce enough stereofacial discrimination to afford high *ee*s. In each of these cases, one of the carbon atoms in the double bond of the precursor is a quaternary centre without aromatic substituents (two methyl groups in one case, and a methyl and a hydroxymethyl group in the other), in contrast with the cases of the other trisubstituted alkenes used, each of which possesses a quaternary centre but with aromatic substituents (Table 1, Entries 3 and 4); in these cases the enantioselectivities are considerably higher and similar to those obtained with the (*E*)-olefins employed (Table 1, Entries 1, 2 and 6; Table 3 Entry 1). It should be mentioned that at least one of the carbon atoms in the double bond possesses a phenyl group as substituent in all the substrates employed. We suggest that not only steric interactions but also electronic ones are factors controlling the approach between groups with π-systems both in the alkene substrate and in the ketone. Further studies in this area are in progress to determine what influence the aromatic or aliphatic natures of the blocking groups at the two positions in the ketone – acetal and anomeric carbon atoms – and the use of substrates lacking aromatic substituents on the carbon atoms of the double bond have on the enantioselectivities of the reactions.

In all cases, ketone **9** was recovered in high yields (70–75%) without loss of activity. This shows its stability under the reaction conditions, and thus the possibility of its being recycled.

In the synthesis of natural products, an important goal is to obtain epoxides highly diastereoselectively. Our group has described stereoselective epoxidations of olefin moieties linked through various functionalities to different positions of carbohydrate residues[19–22] in the presence of *m*-chloroperoxybenzoic acid as oxidant under mild conditions. A logical consequence was that in this work we would study the capacity of ketone **9** to induce diastereoselectivity – in other words, double asymmetric induction. For this, we chose as substrate the simple alkenylidene acetal **15** (Scheme 8), derived from (*S*,*S*)-hydrobenzoin (**14**), that we had synthesised previously in good yield (81%). Its epoxidation with ketone **9** under the conditions described gave the corresponding oxirane **16** with a 79% diastereoisomeric excess and in good chemical yield (72%; Scheme 8, Table 5). However, in order to be able to determine to what extent that excess could be attributed to the chirality of ketone **9** and what was the effect of the chirality of the substrate (the pre-existing stereocentres are the carbon atoms derived from hydrobenzoin – C-4 and C-5 of the dioxolane ring, rather distant from the double bond) we also carried out the epoxidation of compound **14** in the presence of two different oxidative systems: *m*-chloroperoxybenzoic acid and CF_3COCH_3/Oxone®. Neither reaction resulted in diastereoselection, so all of the chirality obtained is attributed to good stereochemical communication between the alkenyl acetal **15** and the dioxirane derived from ketone **9**.



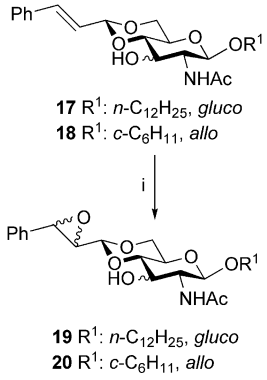
Scheme 8. Reagents and conditions: (i) PhCH=CHCH$(OCH_3)_2$/camphorsulfonic acid/ACN, 81%; (ii) ketone **9** (1.5 equiv.), Oxone® (2 equiv.), $NaHCO_3$ (6 equiv.), DME/aqueous EDTA [4×10^{-4} M (1.2:1)], 0 °C, 72%.

Table 5. Catalytic asymmetric epoxidation of compound **15** in the presence of ketone **9**.[a]

Yield (%)[b]	*de* (%)[c]	Configuration[d]
72	79	(–)-(2*R*,3*S*)

[a] Epoxidation conditions: substrate (1 equiv.), ketone (1.5 equiv.), Oxone® (2 equiv.), $NaHCO_3$ (6 equiv.), DME/aqueous EDTA [4×10^{-4} M (1.2:1)], 0 °C. [b] Yield after column chromatography. [c] Diastereoisomeric excess was determined by ^{1}H NMR spectroscopy of the epoxide by signal integration. [d] For oxirane stereocentres, tentatively assigned.

We chose this alkenylidene acetal because it is a simple substrate in which the alkenyl portion is similar to those in other acetals that we have described previously[22] and with which we have carried out epoxidation reactions diastereoselectively with metachloroperbenzoic acid. In these cases the stereochemical courses of the reactions depend on the sugars chosen as chiral auxiliaries to which the alkenyl residues are attached through acetal functions, and afford the major oxirane of (2*R*,3*S*) configuration when the sugar used is of *gluco* configuration {compound **17**, dodecyl 2-acetamido-2-deoxy-4,6-*O*-[(*R*,*E*)-3-phenyl-2-propenylidene]-β-D-glucopyranoside; Scheme 9}, or that of (2*S*,3*R*) configuration when the sugar residue has the *allo* configuration {compound **18**, cyclohexyl 2-acetamido-2-deoxy-4,6-*O*-[(*R*,*E*)-3-phenyl-2-propenylidene]-β-D-allopyranoside}. In this way we had previously synthesized both diastereoisomeric oxiranes and so could compare them (NMR spectroscopic data) with compound **16** to determine the configuration of its major oxirane.



Scheme 9. Reagents and conditions: (i) *m*-CPBA/$CHCl_3$/–15 °C.

In order to assign the configuration on the stereogenic centres in the oxirane ring in compound **16** formed in the epoxidation reaction, it is important to analyse the NMR chemical shifts of the proton and carbon signals corresponding to the oxidised acetal system and to compare them with the spectroscopic data for the cinnamaldehyde acetals previously described by us (Figure 4, Table 6). For oxiranes derived from (*E*)-cinnamaldehyde, the signal corresponding to 3′-H is easily identifiable in the ^{1}H NMR spectra at $\delta \approx 4$ ppm as a doublet, with the signal for C-3′ in the ^{13}C NMR spectra at $\delta \approx 55$ ppm. In a previous paper[22a] we assigned the (2*R*,3*S*) configuration to the major isomer of compound **19** (*gluco* configuration), and it can be seen that the doublet corresponding to 3′-H of the major isomer appeared at a lower chemical shift than that of the minor isomer, and that the signal for C-3′ of the major isomer appeared at a higher chemical shift than that of the minor isomer. In another previous paper[22b] we assigned the (2*S*,3*R*) configuration to the major isomer of compound **20**

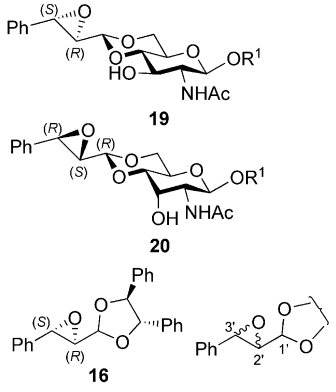


Figure 4. Oxirane protons used for stereochemical assignments.

(*allo* configuration). This showed a different profile in the 3′-H and C-3′ signals, so a different configuration was assigned to its major isomer. Compound **16** showed the same profile as compound **19** for 3′-H and C-3′, and a different profile in these signals, as well as in the C-2′ signal, from that of compound **20**. From these profiles we assigned a (2*R*,3*S*) configuration for the major isomer of compound **16**.

Conclusions

We present a new chiral carbohydrate-derived ketone – compound **9** – easily prepared in four steps from the commercially available methyl 4,6-*O*-(*R*)-benzylidene-α-D-glucopyranoside. We have carried out epoxidation reactions of different (*E*)- and trisubstituted alkenes with this ketone, which afforded satisfactory chemical yields (60–73%). The excellent catalytic properties were demonstrated by the recovery of the ketone without loss of activity, in high yields (70–75%).

Ketone **9** has features of structure, synthesis and as chirality transfer agent that make it an interesting catalyst motif. Firstly, its reactive group is located on a seven-membered ring fused to positions 2 and 3 of the sugar moiety and not close to stereocentres (there are no problems of epimerisation). Secondly, although not a C_2-symmetric system, it is rigid, with the sugar chirality in its structure and with electron-withdrawing groups on C-α (it is known that this increases the reactivity of the carbonyl group to generate the active dioxirane).[5,8,16] Thirdly, the substituents on the acetal and anomeric positions are points of structural modification, and fourthly, it is easily synthesized from the commercially available carbohydrate precursor in a simple process that can also be applied with other precursors. Finally, the moderate-to-good excesses obtained (57–74%) indicate the efficient chirality transfer capability of this ketone, and thus its usefulness as a dioxirane precursor for the epoxidation reaction.

On the basis of the results presented here, we are encouraged to continue our research in this area, focusing on two general aims. The first is to carry out epoxidations of other kinds of olefins [(*Z*)- and terminal alkenes and electron-deficient olefins] in the presence of ketone **9**, and to study the presence of both steric and electronic effects in the chirality transfer process. The second is the preparation of new chiral ketones by this efficient and easy synthetic methodology and their use in epoxidation reactions of different alkenes.

Table 6. NMR spectroscopic data (δ [ppm]) for the acetal group in oxiranes derived from (*E*)-cinnamaldehyde.[a]

Entry	Compound	2′-H	3′-H	C-2′	C-3′	Configuration[b]
1	**16**	3.44(M)/3.40(m)	4.10(m)/4.08(M)	62.1(m)/61.9(M)	55.8(M)/55.1(m)	(2*R*,3*S*)[c]
2	**19**	–	3.99(m)/3.98(M)	60.1	54.7(M)/54.5(m)	(2*R*,3*S*)
3	**20**	3.18	3.93(M)/3.91(m)	60.7(M)/60.5(m)	56.3(m)/55.4(M)	(2*S*,3*R*)

[a] (M) for the major, (m) for the minor enantiomer. [b] Absolute configuration of the stereogenic centres in the oxirane ring. [c] Tentatively assigned.

Experimental Section

General: Melting points were obtained with a Stuart SMP 10 melting point apparatus and are uncorrected. Optical rotations were obtained with a Perkin–Elmer Model 341 polarimeter at 25 °C. Mass spectra were recorded with a Micromass AUTOSPECQ mass spectrometer: EI at 70 eV and CI at 150 eV, HR mass measurements with resolutions of 10000. FAB mass spectra were recorded by use of a thioglycerol matrix. NMR spectra were recorded at 25 °C with a Bruker AMX 500 spectrometer and a Bruker AV 500 spectrometer at 500 MHz for ^{1}H and 125 MHz for ^{13}C. The chemical shifts are reported in ppm on the δ scale relative to TMS. COSY, DEPT, HSQC and NOESY experiments were performed to assign the signals in the NMR spectra. Silica gel 60 (230–400 ASTM) was used for flash column chromatography. All solvents were reagent or analysis grade. Evaporations were conducted under reduced pressure. Reactions were monitored by thin-layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F254 silica gel. Compounds were visualised with the aid of UVA irradiation at a wavelength of 254 nm or stained by exposure to an ethanolic solution of phosphomolybdic acid and subsequent heating. Enantiomeric excesses were determined by proton nuclear magnetic resonance spectroscopy in the presence of europium(III) tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] as the chiral shift reagent, or by chiral HPLC with a Chiralcel OD column. Absolute configurations were assigned by comparison with the signal shifts reported in the literature in the cases of epoxides **a**–**i**[5a,23–25] and by chiral HPLC retention times and comparison with the literature in that of epoxide **j**.[27] Absolute configurations were also determined by comparison of the signs of optical rotation with the reported ones.[5a,23–27]

Methyl 4,6-*O*-(*R*)-Benzylidene-2,3-*O*-(2-methylidene-1,3-propanediyl)-α-D-glucopyranoside (7): Freshly powdered potassium hydroxide (7.0 g, 125 mmol), 18-crown-6 (0.38 g, 1.4 mmol) and 3-chloro-2-(chloromethyl)propene (4.1 mL, 35.4 mmol) were added successively to a cooled solution (5 °C) of methyl 4,6-*O*-(*R*)-benzylidene-α-D-glucopyranoside (**1**; 10.0 g, 35.4 mmol) in dry THF (70 mL). The reaction mixture was stirred at this temperature for 3 h and left at room temperature until all the starting material had been consumed, as monitored by TLC (5 d, approximately). It was then diluted with dichloromethane (60 mL), washed successively with water and aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and filtered, and the filtrate was concentrated to dryness. The solid obtained was purified by flash chromatography on silica gel with dichloromethane/hexane (10:1) as eluent, yielding a white solid (7.5 g, 63%). M.p. 114–115 °C. $[\alpha]_D^{25}$ = +118.2 (c = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.5–7.3 (m, 5 H, Ph), 5.51 (s, 1 H, PhC*H*), 4.98, 4.96 (2 s, 2 H, C=CH_2), 4.80 (d, $J_{1,2}$ = 4.8 Hz, 1 H, 1-H), 4.54 [d, $^2J_{A,B}$ = 14.4 Hz, 1 H, (OCH_AH$_B$)C(CH_DH$_E$O)], 4.44 [d, $^2J_{D,E}$ = 14.3 Hz, 1 H, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.31–4.25 [m, 3 H, 6e-H, (OCH$_A$$H_B$)C(CH$_D$$H_E$O)], 3.87 (t, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.83 (dt, $J_{5,6e}$ = 4.8, $J_{4,5}$ = $J_{5,6a}$ = 10.0 Hz, 1 H, 5-H), 3.71 (t, $J_{5,6e}$ = $J_{6e,6a}$ = 10.2 Hz, 1 H, 6a-H), 3.55 (t, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 3.45–3.41 (m, 4 H, 2-H, OCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.2 (*C*=CH$_2$), 137.2, 129.1, 128.2, 126.4 (Ph), 112.2 (C=*C*H$_2$), 102.0 (Ph*C*H), 99.5 (C-1), 83.1 (C-2), 80.3 (C-3), 79.7 (C-4), 73.8, 73.1 [(O*C*H$_2$)C(*C*H$_2$O)], 69.0 (C-6), 62.3 (C-5), 55.3 (OCH_3) ppm. MS (FA): m/z (%) = 357 (50) [M + Na]$^+$. HRMS (FAB): calcd. for $C_{18}H_{22}O_6Na$ (357.13) [M + Na]$^+$ 357.131408; found 357.132039. $C_{18}H_{22}O_6$ (334.14): calcd. C 64.66, H 6.63; found C 64.51, H 6.58.

Methyl 4,6-*O*-(*R*)-Benzylidene-2,3-*O*-[2-hydroxy-2-(hydroxymethyl)-1,3-propanediyl]-α-D-glucopyranoside (8): Trimethylamine *N*-oxide (0.58 g, 5.2 mmol) and a solution of osmium tetroxide in propan-2-ol (2.5% w/v) in catalytic amount (0.5 mL, 0.04 mmol) were added to a solution of **7** (1.3 g, 4.0 mmol) in dichloromethane (300 mL). The mixture was stirred at room temperature for 24 h. The solution was washed successively with dilute aqueous sodium bisulfite and water and dried ($MgSO_4$), and the solvents were evaporated to dryness. The solid obtained was purified by flash chromatography on silica gel, with dichloromethane/hexane (80:1) as eluent, yielding a pale yellow solid (1.2 g, 81%) as a diastereoisomeric mixture (1:1). M.p. 48–50 °C. $[\alpha]_D^{25}$ = +74.2 (c = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.6–7.2 (m, 5 H, Ph), 5.51, 5.49 (2 s, 1 H, PhC*H*), 4.82, 4.78 (2 d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.26 (m, 1 H, 6e-H), 3.43, 3.42 (2 s, OCH_3), 3.05, 2.10 (2 s, 2 H, 2 OH) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.1, 137.0, 129.2, 129.1, 128.3, 128.2, 126.4 (Ph), 102.0, 101.9 (Ph*C*H), 99.8, 99.5 (C-1), 83.1, 82.2 (C-2), 80.4, 79.7 (C-3), 79.6, 79.5 (C-4), 77.1 [C(OH)], 75.8, 75.5, 75.3, 74.8 [(O*C*H$_2$)C (*C*H$_2$O)], 69.0, 68.9 (C-6), 64.9, 64.5 (CH$_2$OH), 62.9, 62.8 (C-5), 55.5, 55.4 (OCH_3) ppm. MS (EI): m/z (%) = 368 (45) [M]$^{+\cdot}$. HRMS (EI): calcd. for $C_{18}H_{24}O_8$ (368.15) [M]$^{+\cdot}$ 368.147118; found 368.146992. $C_{18}H_{24}O_8$ (368.15): calcd. C 58.69, H 6.57; found C 58.57, H 6.67.

Methyl 4,6-*O*-(*R*)-Benzylidene-2,3-*O*-(2-oxo-1,3-propanediyl)-α-D-glucopyranoside (9): A solution of sodium periodate (0.77 g) in water (9 mL) was added to a solution of **8** (0.67 g, 1.8 mmol) in ethanol/water (1:2, 120 mL), and the reaction mixture was stirred at room temperature overnight. The mixture was concentrated to a small volume (40–50 mL), the solution was extracted with dichloromethane (5 × 40 mL) and dried ($MgSO_4$), and the solvents were evaporated to dryness. The solid obtained was purified by flash chromatography on silica gel with dichloromethane/hexane (10:1) as eluent, yielding a white solid (0.5 g, 85%). M.p. 124–125 °C. $[\alpha]_D^{25}$ = +208.8 (c = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.6–7.3 (m, 5 H, Ph), 5.53 (s, 1 H, PhC*H*), 4.88 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.4–4.2 [m, 5 H, 6e-H, (OCH$_2$)C(CH$_2$O)], 4.04 (t, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.88 (dt, $J_{5,6e}$ = 4.7, $J_{4,5}$ = $J_{5,6a}$ = 10.0 Hz, 1 H, 5-H), 3.75 (t, $J_{5,6e}$ = $J_{6e,6a}$ = 10.3 Hz, 1 H, 6a-H), 3.63 (t, $J_{3,4}$ = $J_{4,5}$ = 9.4 Hz, 1 H, 4-H), 3.59 (dd, $J_{1,2}$ = 3.7, $J_{2,3}$ = 9.0 Hz, 1 H, 2-H), 3.47 (s, 3 H, OCH_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.7 (C=O), 137.1, 129.3, 128.3, 126.4 (Ph), 102.0 (Ph*C*H), 99.1 (C-1), 85.2 (C-2), 82.8 (C-3), 79.2 (C-4), 77.9, 77.3 [(O*C*H$_2$)C(*C*H$_2$O)], 68.9 (C-6), 62.7 (C-5), 55.5 (OCH_3) ppm. MS (EI): m/z (%) = 336 (100) [M]$^{+\cdot}$. HRMS (EI): calcd. for $C_{17}H_{20}O_7$ (336.12) [M]$^+$ 336.120903; found 336.120591. $C_{17}H_{20}O_7$ (336.12): calcd. C 60.71, H 5.99; found C 60.55, H 6.12.

3-[(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]-2-{[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]methyl}propene (11): Freshly powdered potassium hydroxide (6.0 g, 107 mmol), 18-crown-6 (0.33 g, 1.2 mmol) and 3-chloro-2-(chloromethyl)propene (1.8 mL, 15.1 mmol) were added successively to a cooled solution (5 °C) of 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**10**; 7.8 g, 30.0 mmol) in dry THF (40 mL). The reaction mixture was stirred at this temperature for 3 h and left at room temperature until all the starting material had been consumed, as monitored by TLC (7 d, approximately). It was then diluted with dichloromethane (100 mL), washed successively with water and aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and filtered, and the filtrate was concentrated to dryness. The syrup obtained was purified by flash chromatography on silica gel, with hexane/ethyl acetate (6:1) as eluent, to yield a colourless oil (8.2 g, 96%). $[\alpha]_D^{25}$ = –24.0 (c = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.76 (d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 1-H), 5.12 (s, 2 H, C=CH_2), 4.46 (d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 2-H), 4.20 (m, 2 H, 2 5-H), 4.12 [d, $^2J_{A,B}$ = 12.3 Hz, 2 H, (OCH_AH$_B$)-C(CH_AH$_B$O)], 4.00–3.95, 3.90–3.85 [2 m, 10 H, 2 3-H, 2 4-H, 2 6$_A$-

H, 2 6_B-H, (OCH_AH_B)C(CH_AH_BO)], 1.38, 1.32, 1.26, 1.21 [4 s, 24 H, 4 C(CH_3)$_2$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.6 (*C*=CH_2), 115.6 (C=*C*H_2), 111.5, 108.8 [4 *C*(CH_3)$_2$], 105.0 (2 C-1), 82.1 (2 C-2), 81.3, 81.0 (2 C-3, 2 C-4), 72.1 (2 C-5), 70.3 [(O*C*H_2)-C(*C*H_2O)], 67.2 (2 C-6), 26.6, 26.1, 25.2 [4 C(*C*H_3)$_2$] ppm. MS (EI): *m*/*z* (%) = 572 (2) $[M]^{+\cdot}$. HRMS (EI): calcd. for $C_{28}H_{44}O_{12}$ (572.28) $[M]^{+\cdot}$ 572.283277; found 572.282660.

3-[(1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]-2-{[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]methyl}propane-1,2-diol (12): Trimethylamine *N*-oxide (1.16 g, 10.4 mmol) and a solution of osmium tetroxide in propan-2-ol (2.5% w/v) in catalytic amount (1.0 mL, 0.08 mmol) were added to a solution of **11** (4.3 g, 8.0 mmol) in dichloromethane (300 mL). The mixture was stirred at room temperature for 24 h. The solution was washed successively with dilute aqueous sodium bisulfite and water and dried ($MgSO_4$), and the solvents were evaporated to dryness. The syrup obtained was purified by flash chromatography on silica gel with dichloromethane/methanol (100:1) as eluent, yielding a pale yellow oil (4.3 g, 88%) as a diastereoisomeric mixture (1:1). $[\alpha]_D$ = –41.5 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.88, 5.84 (2 d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 1-H), 4.55, 4.52 (2 d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 2-H), 4.28, 4.23 (2 m, 2 H, 2 5-H), 4.15–4.05 (m, 4 H, 2 4-H, 2 6_A-H), 4.00–3.95 (m, 4 H, 2 4-H, 2 6_B-H), 3.79, 3.75 [2 dd, ^2J = 10.2, 9.7 Hz, 2 H, (OCH_AH_B)C(CH_AH_BO)], 3.72 (s, 1 H, COH), 3.61 (dd, $J_{HA,OH}$ = 5.8, $^2J_{A,B}$ = 11.6 Hz, 1 H, CH_AH_BOH), 3.48 (dd, $J_{HB,OH}$ = 8.3, $^2J_{A,B}$ = 11.6 Hz, 1 H, CH_AH_BOH), 3.37, 3.35 [2 dd, $^2J_{A,B}$ = 9.6, 10.2 Hz, 2 H, (OCH_AH_B)C(CH_AH_BO)], 2.76 (dd, $J_{HA,OH}$ = 5.8, $J_{HB,OH}$ = 8.3 Hz, 1 H, CH_AH_BOH), 1.47, 1.46, 1.41, 1.40, 1.35, 1.33, 1.30, 1.29 [8 s, 24 H, 4 C(CH_3)$_2$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 112.0, 109.5, 109.4 [4 *C*(CH_3)$_2$], 105.7, 105.6 (2 C-1), 84.5, 84.0 (2 C-3), 82.3 (2 C-2), 81.4, 81.3 (2 C-4), 74.7 (COH), 73.0, 72.8 (2 C-5), 71.7, 71.1 [(O*C*H_2)C(*C*H_2O)], 67.9, 67.8 (2 C-6), 64.0 (CH_2OH), 26.9, 26.8, 26.7, 26.3, 26.2, 25.1 [4 C(*C*H_3)$_2$] ppm. MS (CI): *m*/*z* (%) = 607 (10) $[M + H]^+$. HRMS (CI): calcd. for $C_{28}H_{47}O_{14}$ (607.30) $[M + H]^+$ 607.296582; found 607.294492.

1,3-Bis[(1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)oxy]acetone (13): A solution of sodium periodate (0.86 g, 4.0 mmol) in water (5 mL) was added to a solution of **12** (1.20 g, 2.0 mmol) in ethanol/water (1:2, 120 mL), and the reaction mixture was stirred at room temperature overnight. The mixture was concentrated to a small volume (40–50 mL), the solution was extracted with dichloromethane (5 × 40 mL) and dried ($MgSO_4$), and the solvents were evaporated to dryness. The syrup obtained was purified by flash chromatography on silica gel, with hexane/ethyl acetate (2:1) as eluent, yielding a colourless oil (0.85 g, 72%). $[\alpha]_D^{25}$ = –9.3 (*c* = 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.92 (d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 1-H), 4.66 (d, $J_{1,2}$ = 3.7 Hz, 2 H, 2 2-H), 4.45 [br. s, 4 H, (OCH_2)C(CH_2O)], 4.33 (m, 2 H, 2 5-H), 4.14 (dd, $J_{5,6A}$ = 6.2, $J_{6A,6B}$ = 8.7 Hz, 2 H, 2 6_A-H), 4.11 (dd, $J_{3,4}$ = 3.0, $J_{4,5}$ = 8.3 Hz, 2 H, 2 4-H), 4.03 (dd, $J_{5,6B}$ = 5.3, $J_{6A,6B}$ = 8.7 Hz, 2 H, 2 6_B-H), 3.92 (d, $J_{3,4}$ = 3.0 Hz, 2 H, 2 3-H), 1.52, 1.45, 1.38, 1.34 [4 s, 24 H, 4 C(CH_3)$_2$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 204.9 (C=O), 112.0, 109.2 [4 *C*(CH_3)$_2$], 105.2 (2 C-1), 83.8 (2 C-3), 82.8 (2 C-2), 81.1 (2 C-4), 74.6, 72.4 [(O*C*H_2)C(*C*H_2O)], 67.5 (2 C-6), 62.7 (2 C-5), 26.9, 26.8, 26.2, 25.4 [4 C(*C*H_3)$_2$] ppm. MS (CI): *m*/*z* (%) = 575 (100) $[M + H]^+$. HRMS (CI): calcd. for $C_{27}H_{43}O_{13}$ (575.27) $[M + H]^+$ 575.270367; found 575.267985.

(4*S*,5*S*)-4,5-Diphenyl-2-styryl-1,3-dioxolane (15): Cinnamaldehyde dimethyl acetal (2 equiv., 0.8 g), and camphorsulfonic acid (catalytic) were added to a solution of (–)-(*S*,*S*)-hydrobenzoin (**14**; 0.43 g, 2.0 mmol) in acetonitrile (15 mL). The reaction mixture was stirred at room temperature for 6 d. Triethylamine was added to neutralise the medium. The solvent was evaporated to dryness. The syrup obtained was purified by flash chromatography on silica gel, with hexane/ethyl acetate (50:1) as eluent, yielding a colourless oil (0.53 g, 81%). $[\alpha]_D^{25}$ = –71.8 (*c* = 0.6, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.5–7.3 (m, 15 H, 5 Ph), 6.90 (d, $J_{(E)}$ = 16.0 Hz, 1 H, PHC*H*=CH), 6.43 (dd, *J* = 6.0, $J_{(E)}$ = 16.0 Hz, 1 H, PHCH=C*H*), 5.99 (dd, *J* = 6.0, *J* = 0.8 Hz, 1 H, CH), 4.84 (m, 2 H, 2 OC*H*Ph) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.9–126.4 (Ph), 128.1, 125.5 (Ph*C*H=*C*H), 104.7 (CH), 86.6, 84.8 (2O*C*HPh) ppm. MS (CI): *m*/*z* (%) = 328 (70) $[M + H]^+$.

Typical Epoxidation Procedure: Chiral ketone **9** or **13** (0.3 mmol) and nBu$_4$NHSO$_4$ (5 mg) were added to a solution of an alkene (**a**–**j**; 0.2 mmol) in 1,2-dimethoxyethane (5 mL). The reaction mixture was cooled to 0 °C in an ice/water bath. Oxone® (0.4 mmol) was dissolved in a solution of Na_2EDTA (4×10^{-4} M, 2 mL), and separately, $NaHCO_3$ (1.2 mmol) was dissolved in a solution of Na_2EDTA (4×10^{-4} M, 2 mL). The two solutions were added separately to the reaction mixture (first the Oxone® solution, and then the $NaHCO_3$ solution) dropwise over a period of 1 h. The pH of the mixture was maintained at about 8.0. The reaction mixture was stirred until TLC showed that the epoxidation reaction was finished (3–7 h), and was then diluted with water (10 mL). The solution was extracted with dichloromethane (3 × 10 mL) and dried ($MgSO_4$), and the solvents were evaporated to dryness. The obtained crude reaction mixture was purified by flash chromatography, with hexane/ethyl acetate mixture as eluent, to afford the alkene epoxide. The eluent was changed to a mixture of dichloromethane/methanol (50:1), and the chiral ketone was recovered in a 70–75% yield.

Experimental Data for the (*E*)-Stilbene Epoxidation Reaction with Ketone 9: Column chromatography with elution with hexane/ethyl acetate (100:1) afforded (*E*)-stilbene oxide as white crystals (0.028 g, 73%), 68% *ee*, (–)-(2*S*,3*S*). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 10 H, 2 Ph), 3.88 [s, 2 H, 2 CH(O)] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.8, 128.5, 128.1, 125.6, 62.7 ppm. Ketone, methyl 4,6-*O*-(*R*)-benzylidene-2,3-*O*-(2-oxo-1,3-propanediyl)-α-D-glucopyranoside, recovered (0.072, 71%).

^{1}H NMR Spectroscopic Data for Epoxides

(–)-(1*S*,2*S*)-(*E*)-Stilbene Oxide:[5a,23] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 10 H, 2 Ph), 3.88 [s, 2 H, 2 CH(O)] ppm.

(–)-(1*S*,2*S*)-β-Methylstyrene Oxide:[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 10 H, 2 Ph), 3.59 [d, $J_{(E)}$ = 2.0 Hz, 1 H, CH(O)], 3.02 [dq, *J* = 5.1, $J_{(E)}$ = 2.0 Hz, 1 H, CH(O)], 1.44 (d, *J* = 5.1 Hz, 3 H, CH_3) ppm.

(–)-(1*S*,2*S*)-(*E*)-β-Methylstilbene Oxide:[23,24] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 10 H, 2 Ph), 3.96 [s, 1 H, CH(O)], 1.46 (s, 3 H, CH_3) ppm.

(+)-(2*S*)-Triphenylethylene Oxide:[5a,23,24] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.1 (m, 15 H, 3 Ph), 4.32 [s, 1 H, CH(O)] ppm.

(–)-(2*S*)-1,1-Dimethyl-2-phenylethylene Oxide:[25] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 5 H, Ph), 3.85 [s, 1 H, CH(O)], 1.47 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3) ppm.

(–)-(1*S*,2*S*)-1-Phenylcyclohexene Oxide:[5a,23,24] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 5 H, Ph), 3.5 [m, 1 H, CH(O)], 2.3–2.2 (m, 1 H, CH_AH_B), 2.2–2.0 (m, 1 H, CH_AH_B), 2.0–1.9 (m, 2 H, CH_2), 1.6–1.5 (m, 2 H, CH_2), 1.5–1.4 (m, 1 H, CH_AH_B), 1.3–1.2 (m, 1 H, CH_AH_B) ppm.

(–)-(1*S*,2*S*)-2-Phenylindane Oxide: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.5–7.2 (m, 9 H, 2 Ph), 4.33 [dd, *J* = 0.45, *J* = 1.3 Hz, 1 H, CH(O)], 3.57 (d, J_{gem} = 17.7 Hz, 1 H, 1 H, CH_AH_B), 3.41 (d, J_{gem} = 17.7 Hz, 1 H, 1 H, CH_AH_B) ppm. ^{13}C NMR (125 MHz, $CDCl_3$):

δ = 144.2–125.0 (Ph), 67.9, 67.7 [CH(O), *C*Ph(O)], 37.0 (CH_2) ppm.

(–)-(2*S*,3*S*)-2-(Hydroxymethyl)-3-phenyloxirane:[23,24] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 5 H, Ph), 3.91 [d, $J_{(E)}$ = 2.1 Hz, 1 H, PhCH (O)], 3.8 (m, 2 H, CH_2), 3.2 [m, 1 H, CH(O)] ppm.

(–)-(2*S*,3*S*)-2-(Hydroxymethyl)-2-methyl-3-phenyloxirane:[26] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.3 (m, 5 H, Ph), 4.19 [s, 1 H, PhC*H*(O)], 3.8 (m, 2 H, CH_2), 3.2 [m, 1 H, CH(O)], 1.07 (s, 3 H, CH_3) ppm.

(–)-(2*R*,3*S*)-(*E*)-Chalcone Oxide:[27] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.0–7.3 (m, 10 H, 2 Ph), 4.27 [d, $J_{(E)}$ = 1.9 Hz, 1 H, PhC*H*(O)], 4.07 [d, $J_{(E)}$ = 1.9 Hz, 1 H, PhC*H*(O)] ppm.

(–)-(4*S*,5*S*)-4,5-Diphenyl-2-[(2*R*,3*S*)-3-phenyloxiran-2-yl]-1,3-dioxolane (16): Two stereoisomers were obtained as a syrup in a diastereoisomeric excess of 79%. The pure diastereoisomeric mixture was obtained by flash chromatography on silica gel, with hexane/ethyl acetate (70:1) as eluent, yielding a white solid (0.05 g, 72%). $[\alpha]_D^{25}$ = –26.6 (*c* = 01.8, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.4–7.2 (m, 15 H, 5 Ph), 5.64 (d, *J* = 3.1 Hz, CH_{major}), 5.62 (d, *J* = 3.1 Hz, CH_{minor}), 4.89 (d, *J* = 8.3 Hz, OCH_APh_{major}), 4.87 (d, *J* = 8.0 Hz, OCH_APh_{minor}), 4.79 (d, *J* = 8.0 Hz, OCH_BPh_{minor}), 4.77 (d, *J* = 8.3 Hz, OCH_BPh_{major}), 4.10 [d, $J_{(E)}$ = 2.0 Hz, CH(O)C*H*Ph$_{minor}$], 4.08 [d, $J_{(E)}$ = 2.0 Hz, CH(O)C*H*Ph$_{major}$], 3.44 [dd, $J_{(E)}$ = 2.0, *J* = 3.1 Hz, C*H*(O)CHPh$_{major}$], 3.40 [dd, $J_{(E)}$ = 2.0, *J* = 3.1 Hz, C*H*(O)CHPh$_{minor}$] ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 136.7–125.5 (Ph), 102.9 (CH_{major}), 102.8 (CH_{minor}), 86.7 (OCH_APh_{minor}), 86.5 (OCH_APh_{major}), 85.7 (OCH_BPh_{major}), 85.3 (OCH_BPh_{minor}), 62.1 [*C*H(O)CHPh$_{minor}$], 61.9 [*C*H(O)CHPh$_{major}$], 55.8 [CH(O)*C*HPh$_{major}$], 55.1 [CH(O)*C*HPh$_{minor}$] ppm. MS (CI): *m*/*z* (%) = 344 (65) $[M + H]^+$.

Supporting Information (see footnote on the first page of this article): Synthesis and characterization of the chiral ketones (**9** and **13**), their precursors (**7**, **8**, **11** and **12**), hydrobenzoin acetal **15** and its epoxide **16**, experimental procedure and characterization of all epoxides from the employed alkenes (**a**–**j**), and data for the determination of the enantiomeric excesses obtained with ketone **9**.

Acknowledgments

We are grateful to the Junta de Andalucía and the Ministerio de Educación y Ciencia (Spain) and to the FEDER programme for financial support (P06-FQM-01885 and CTQ2007-61 185). The help of Dr. M. Angulo in recording ^{1}H NMR spectra is gratefully acknowledged.

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Received: August 4, 2009
Published Online: October 7, 2009

