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Synthesis of new carbohydrate-derived ketones as organocatalysts in the enantioselective epoxidation of arylalkenes. Part 2: Chiral ketones from sugars☆

José M. Vega-Pérez *, Margarita Vega-Holm, Ignacio Periñán, Carlos Palo-Nieto, Fernando Iglesias-Guerra *

Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad de Sevilla, E-41071 Sevilla, Spain

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ABSTRACT

A range of new, somewhat complex, stereochemically varied, and structurally related carbohydrate-derived ketones were synthesised by a simple method from the carbohydrate precursor (D-*gluco* and D-*galacto* derivatives). The common skeleton possesses the keto function sited on a seven-membered ring fused to positions 2 and 3 of the sugar moiety. Their chirality transfer capability in the dioxirane-mediated epoxidation of arylalkenes was evaluated.

1. Introduction

Due to the great importance of optically active epoxides as chiral synthons in organic synthesis, the development of efficient methods for asymmetric epoxidation of olefins provides a powerful approach to the synthesis of such epoxides and is the goal of many research groups. Our work in this field is focused on two intrinsically related aims: the access to chiral epoxides with high stereocontrol, and the use of carbohydrates as crucial tools responsible for the process of stereofacial differentiation (carbohydrates are a naturally occurring, inexpensive, renewable, readily available source of chirality which contain a high density of stereogenic centers and may provide advantageously rigid frameworks).[1]

We have previously described the diastereoselective epoxidation of olefin moieties by using carbohydrate derivatives as chiral auxiliaries. The olefinic chain was joined to different positions of the sugar molecule, via various functionalities (glycoside,[2] amide,[3] and acetals[4]), employing *m*-chloroperoxybenzoic acid as oxidant under mild conditions. This method has enabled us to synthesise a variety of compounds with potential biological interest.[4]

Enantioselective epoxidation of unfunctionalised alkenes is another important issue in this area – in particular, dioxirane-mediated epoxidation, which constitutes an attractive catalytic process. Indeed, many research groups are focused on designing new chiral ketones to successfully obtain stereochemical control.[5–7] Because of the important role of carbohydrate moieties in stereochemical differentiations, the possibility of employing them as precursors for chiral ketones – and subsequently as catalysts in epoxidation reactions – is an interesting goal for various research groups, and new chiral ketones from sugar derivatives have been described and employed, giving high enantiomeric excess.[8–10]

Recently, we have described a new backbone model of chiral carbohydrate-derived ketone and its use as an efficient chirality transfer agent in dioxirane-mediated epoxidation, giving moderate-to-good enantiomeric excesses in the epoxidation of a wide range of arylalkenes, compound **1**[11] (Fig. 1). Our model has features of structure, synthesis, and catalytic properties that make it an interesting catalyst motif. With regard to structure, its reactive group is located on a seven-membered ring fused to positions 2 and

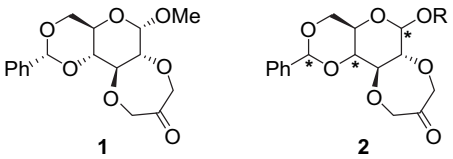

Fig. 1.

☆ For Part 1 see: Ref. 11.

* Corresponding authors. Tel./fax: +34 95 4556737; e-mail addresses: vega@us.es (J.M. Vega-Pérez), iglesias@us.es (F. Iglesias-Guerra).

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3 of the sugar moiety in a rigid system, with the sugar chirality in its structure and with electron-withdrawing groups on C_α.[5,6,12] With regard to its preparation, it is easily synthesised from the commercial carbohydrate precursor in good yields; and finally, it is recovered without loss of activity in high yields (70–75%).

Encouraged by these results, we decided to tackle the preparation of new chiral ketones derived from sugars with this general skeleton **2** (Fig. 1) by this efficient and simple method using commercial products, and study their chirality transfer capability. In order to obtain the range of new ketones, we made the following structural modifications in the proximity of the seven-membered ring fused to positions 2 and 3 of the sugar moiety possessing the reactive group: firstly, the modification of the substituent R at the anomeric position, and secondly, the modification of the configuration of the sugar stereocentres contiguous to carbons 2 and 3 of the sugar residue. We used as starting materials different *gluco*- and galactopyranoside derivatives (α and β configuration, alkyl and aryl substituents on carbon 1).

Subsequently, we studied their usefulness as dioxirane precursors for the epoxidation reaction of unfunctionalised *trans* and *cis* arylalkenes. Herein, we present our results in this area.

2. Results and discussion

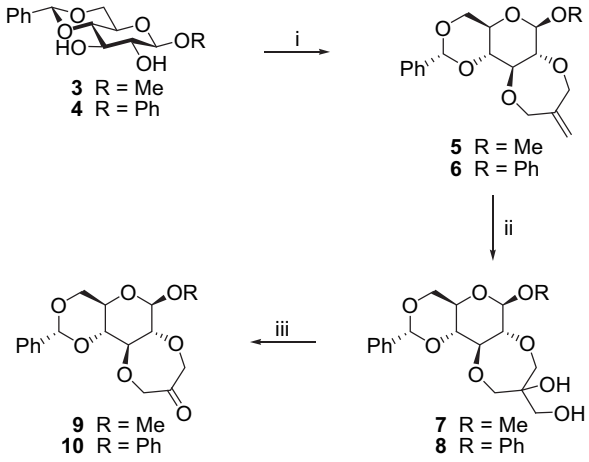
The method followed, which we have previously described, involves a simple sequence of three reactions starting from the corresponding benzylidene acetal derivatives. They take place with good chemical yields, and enabled us to obtain, using different carbohydrate precursors, a series of ketones of some complexity, very functionalised, stereochemically varied, and all structurally related.

Taking compound **1** as model, we first proceeded to change the anomeric configuration. The carbohydrates chosen as precursors for the synthesis of new ketones potentially useful as source of chiral dioxiranes were the compounds methyl 4,6-*O*-(*R*)-benzylidene-β-D-glucopyranoside **3** and phenyl 4,6-*O*-(*R*)-benzylidene-β-D-glucopyranoside **4**, both β anomers and with alkyl and aryl group, respectively, at the anomeric position.

The first step consisted of incorporating to the sugar residue the cycle fused to positions 2 and 3 of the carbohydrate, which will later possess the reactive group. This was incorporated to the monosaccharide residue from a simple substance, such as 3-chloro-2-chloromethylpropene by a double etherification reaction.

Dialkylation of the starting compounds **3** and **4** in tetrahydrofurane with 3-chloro-2-chloromethylpropene, in presence of solid potassium hydroxide and the 18-crown-6, leads – in 5–7 days at room temperature – to the cyclic compound methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-methylidene-1,3-propylene)-β-D-glucopyranoside **5** and phenyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-methylidene-1,3-propylene)-β-D-glucopyranoside **6**. In ^{1}H NMR spectra of both compounds, the signals for the hydrogens of the alkene function appear around δ 5.0 ppm, and the hydrogens of the OCH_2 groups, which act as spacer groups between the ketone and the stereocentres, in the range 4.5–4.2 ppm.

Next was the dihydroxylation of the double bond with osmium tetroxide, in catalytic amounts, and trimethylamine *N*-oxide, using dichloromethane as solvent. The reaction took place at room temperature, and yielded the corresponding glycols methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-hydroxy-2-hydroxymethyl-1,3-propylene)-β-D-glucopyranoside **7** and phenyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-hydroxy-2-hydroxymethyl-1,3-propylene)-β-D-glucopyranoside **8** as a mixture of stereoisomers in the same proportion (^{1}H NMR spectral study). These compounds were employed directly in the following step – the generation of the keto function. It was carried out through an oxidative cleavage, using an aqueous solution of sodium metaperiodate as oxidising agent. The compounds methyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-oxo-1,3-propylene)-β-D-glucopyranoside **9** and phenyl 4,6-(*R*)-*O*-benzylidene-2,3-*O*-(2-oxo-1,3-propylene)-β-D-glucopyranoside **10** were obtained in high yields as white solids (Scheme 1).

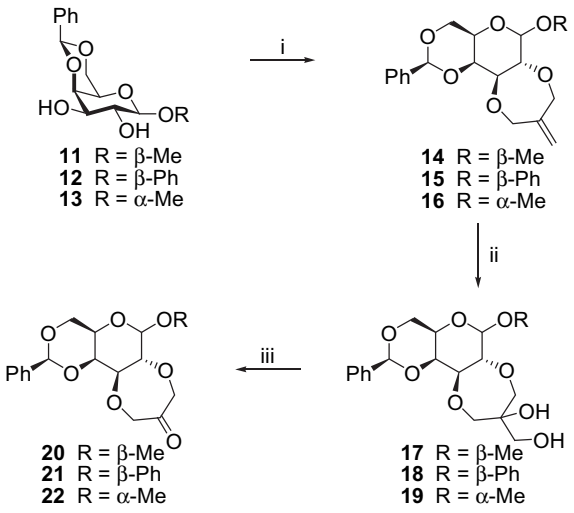


Scheme 1. (i) $(ClCH_2)_2C{=}CH_2$, KOH, 18-crown-6, THF, 95%; (ii) OsO_4 (*t*-BuOH), Me_3NO, CH_2Cl_2, 60–80%; (iii) $NaIO_4$ (H_2O), EtOH–H_2O, 75–85%.

Secondly, and with the aim of obtaining new structurally related ketones derived from carbohydrates, we proceeded to the configurational variation at other positions of the sugar. We chose D-galactose as precursor. We had strong reasons for that choice. On one hand, using this residue as carbohydrate precursor fulfills the aforementioned aims of structural modification on the general skeleton of chiral ketone (Fig. 1, compound **2**). On the other, our group has recently reported the great efficiency of the D-galactose residue as chiral inducer in synthetically important reactions. Specifically, we have carried out reactions of cyclopropanation and epoxidation of a wide range of allyl alcohols joined to the chiral auxiliary via a glycosidic bond (alkenyl β-D-galactopyranoside derivatives were the precursors for these reactions) and which take place with high diastereoselectivity.[2c] In the present context, obtaining this skeleton of ketone fused to a D-galactose residue was therefore an interesting goal. Lastly, because in the field of the synthesis of new chiral ketones (and thus of new catalysts for epoxidation reactions) from carbohydrates, the use has been described of different glucose, arabinose, and fructose derivatives as precursors, achieving large enantiomeric excesses[6–10] but the use of galactose-derived compounds has not been reported.

The synthetic procedure was carried out in the same way as for compounds **9** and **10**. In this case, we used as starting compounds the corresponding benzylidene acetals readily synthesised from commercially available alkyl or aryl D-galactopyranoside derivatives. Thus, the compounds methyl 4,6-*O*-(*S*)-benzylidene-β-D-galactopyranoside **11**, phenyl 4,6-*O*-(*S*)-benzylidene-β-D-galactopyranoside **12**, and methyl 4,6-*O*-(*S*)-benzylidene-α-D-galactopyranoside **13** were subjected to double etherification reaction to generate the fused cycle and introduce the double bond precursor of the keto function. The compounds **14**–**16** were obtained with high chemical yields (95%) (Scheme 2). Characteristic ^{1}H NMR spectral data for these compounds are the signals for alkene protons that appear at about δ 4.9 ppm, and the signal for the protons of both OCH_2 groups in the range 4.5–4.3 ppm.

Hydroxylation of the double bond led to the corresponding glycols **17**–**19**. As the reaction generates a new stereocentre in the molecule and the substrates are derived from another sugar (D-galactose), we studied the stereochemical course of the reaction, in the same way as we have done for the corresponding analogue

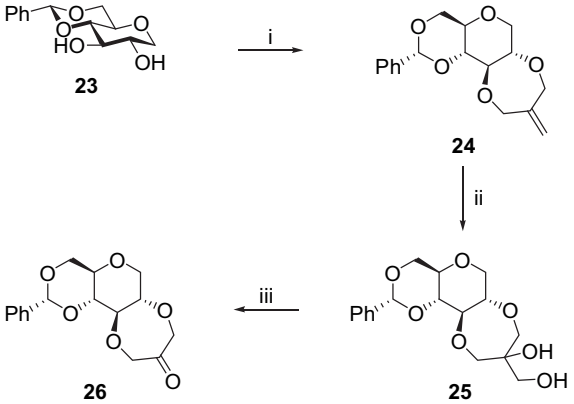


Scheme 2. (i) $(ClCH_2)_2C{=}CH_2$, KOH, 18-crown-6, THF, 96%; (ii) OsO_4 (*t*-BuOH), Me_3NO, CH_2Cl_2, 60–90%; (iii) $NaIO_4$ (H_2O), EtOH–H_2O, 85–95%.

gluco derivatives (compound **1**,[11] compounds **9**–**10**, although in these cases the two stereoisomers were formed in equal amounts). The ^{1}H NMR spectral study shows the signal for hydrogen acetalic PhC*H* as two singlets at δ 5.59 and 5.58 ppm (for compound **17**), at δ 5.76 and 5.75 ppm (for compound **18**), and at δ 5.54 and 5.53 ppm (for compound **19**); and that for H-1 of the sugar as two doublets at δ 4.40 and 4.33 ppm ($J_{1,2}$ 7.5 Hz) (for compound **17**), at δ 4.97 and 4.96 ppm ($J_{1,2}$ 7.9 Hz) (for compound **18**), and at δ 4.97 and 4.93 ppm ($J_{1,2}$ 3.5 Hz) (for compound **19**). The relative integral of the two signals for the same hydrogen in each of the stereoisomers showed that they were formed in equal amounts. Most of the ^{13}C NMR signals of these compounds were also split.

The diol oxidative rupture reaction (with sodium metaperiodate as oxidising agent) of compounds **17**–**19** provided the new galactopyranoside-derived ketones **20**–**22** in high yields.

Thirdly, we used as precursor the compound 1,5-anhydro-4,6-*O*-(*R*)-benzylidene-D-glucitol **23**, which we transformed into the ketone **26** following a sequence of reactions similar to that described (Scheme 3). We were interested in obtaining this compound in order to be able to study its chirality transfer capability. It is a compound analogous to the ketones **1**, **9**, and **10** (*gluco* derivative), but with the anomeric position defunctionalised, and thus lacking stereocentre and substituent.

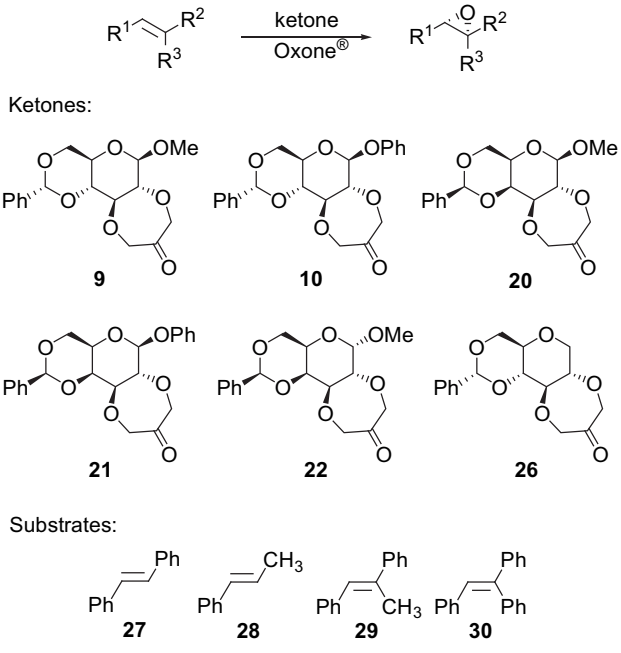


Scheme 3. (i) $(ClCH_2)_2C{=}CH_2$, KOH, 18-crown-6, THF, 97%; (ii) OsO_4 (*t*-BuOH), Me_3NO, CH_2Cl_2, 80%; (iii) $NaIO_4$ (H_2O), EtOH–H_2O, 60%.

The structure of the new ketone sugar derivatives **9**, **10**, **20**–**22**, and **26** was confirmed by analysis of their NMR spectra. Noteworthy features for the ^{1}H NMR spectra are the signals for the hydrogen atoms vicinal to the carbonyl group, which appear at around δ 4.4–4.3 ppm in all these ketones; those for the ^{13}C NMR spectra were the signal for the carbonyl carbon at δ 210 ppm and that for C-1 at δ 99 ppm (δ 72 ppm for compound **26**).

Having synthesised the ketones **9**, **10**, **20**–**22**, and **26**, our next objective was to test their effectiveness as chiral catalysts in dioxirane-mediated epoxidation reactions. First, we chose the substrates for the epoxidation reaction – a variety of unfunctionalised *trans* and trisubstituted alkenes. We chose the arylalkenes (**27**–**30**) because they had shown the largest enantiomeric excesses (57–74%) and highest chemical yields (66–73%) on being subjected to epoxidation with the ketone **1**.[11] Our aim was to compare the stereofacial differentiation capacity of these new ketones with that reported, and thereby the effect of the structural modifications on the stereochemical result of the process, with the idea of obtaining a more efficient chiral catalyst.

Our preliminary essays employed sub-stoichiometric quantities (0.5 equiv) of ketone, however, not only the reaction time was high (1–2 days), but also the reaction was not completed (recovering alkene without epoxidation). The use of different quantities of ketone did not give different stereochemical results (enantiomeric excess and major oxirane configuration). After screening various reaction conditions with a view to improving the efficiency of the epoxidation reaction (in terms of chemical and enantiomeric yields as well as reaction times), an epoxidation reaction with these ketones was carried out at 0 °C with substrate (0.2 mmol), ketone (0.2 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) (Scheme 4). In all cases, the absolute configuration of the major enantiomers obtained was assigned by comparing the signal shifts in presence of (+)-Eu(hfc)$_3$ with those reported in the literature, and also by comparing the sign of optical rotation with the reported ones.



Scheme 4. Epoxidation conditions (see text).

Table 1 gathers the results of the epoxidation of the alkenes **27**–**30** with the ketones whose sugar residue is a derivative of *gluco* configuration, ketones **9** and **10** (methyl and phenyl β-D-glucopyranoside derivatives, respectively) and ketone **26** with position 1

Table 1
Catalytic asymmetric epoxidation of alkenes **27**–**30** in the presence of D-glucose derived ketones **9**, **10**, and **26**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**9**	**27**	68	49	(−)-(1*S*,2*S*)
2	**9**	**28**	70	46	(−)-(1*S*,2*S*)
3	**9**	**29**	74	49	(−)-(1*S*,2*S*)
4	**9**	**30**	80	50	(+)-(2*S*)
5	**10**	**27**	71	47	(−)-(1*S*,2*S*)
6	**10**	**29**	72	38	(−)-(1*S*,2*S*)
7	**10**	**30**	76	59	(+)-(2*S*)
8	**26**	**27**	55	48	(−)-(1*S*,2*S*)
9	**26**	**28**	57	47	(−)-(1*S*,2*S*)
10	**26**	**29**	78	60	(−)-(1*S*,2*S*)
11	**26**	**30**	52	39	(+)-(2*S*)
12	**1**[e]	**27**	73	68	(−)-(1*S*,2*S*)
13	**1**[e]	**28**	68	57	(−)-(1*S*,2*S*)
14	**1**[e]	**29**	72	67	(−)-(1*S*,2*S*)
15	**1**[e]	**30**	66	74	(+)-(2*S*)

[a] Conditions: substrate (1 equiv), ketone (1 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 ^1H NMR spectroscopy of the epoxide products directly with shift reagent (+)-Eu(hfc)$_3$.
[d] The absolute configuration of the major enantiomer was assigned by comparing the signal shifts with those reported in the literature and also by comparing the sign of optical rotation with the reported one in each case.
[e] Previously reported for us, see Ref. 11.

defunctionalised (1,5-anhydroglucitol derivative). The epoxides were isolated in satisfactory chemical yields (70–80%, entries 1–7) – slightly lower when using the ketone **26** (52–78%, entries 8–11). The epoxidation reaction was completed in a few hours. The enantiomeric excesses obtained were low-to-moderate (38–60%, entries 1–11), and somewhat lower than those obtained with the ketone **1**, the previously described methyl α-D-glucopyranoside derivative (57–74%, entries 12–15). The absolute configuration of the major enantiomer obtained was in all cases the same for each alkene.

Comparison of the results obtained with the new D-*gluco*-derived ketones showed that better enantiomeric excesses are obtained with the derivative of α methyl anomeric configuration **1**, than with the derivatives of β anomeric configuration **9** and **10**, or with the D-glucitol derivative **26**. Moreover, the ees obtained with both alkyl and aryl β-glucopyranoside ketones are of the same order (Me entries 1–4 vs Ph entries 5–7), around 50%, and similar to those obtained with **26**, defunctionalised on 1 (entries 8–11).

The results of the epoxidation of the alkenes **27**–**30** with the ketones of D-*galacto* configuration **20**–**22** are gathered in Table 2. In all cases the chemical yields were good (60–75%, entries 1–10). The ketone **20**, methyl β-D-galactopyranoside derivative, gave enantiomeric excesses very similar to those obtained with the ketone **1**, methyl α-D-glucopyranoside derivative (entries 1–4 vs 11–14). However, the excesses obtained when using the ketone **21**, phenyl β-D-galactopyranoside derivative, were somewhat smaller than with the ketone **1** (entries 6 and 7 vs 13–14). The ketone **22** gave the largest enantiomeric excesses (81–100%, entries 8–10), exceeding those obtained with the ketone **1** (57–74%, entries 11–14). The absolute configuration of the major enantiomer obtained is also the same for each alkene in all cases.

We can also see that in contrast to the β-*gluco*, the ketones of β-*galacto* configuration yield results stereochemically different from one another, the enantiomeric excesses being larger with the β-methyl derivative **20** than with the β-phenyl **21** (entries 1–4 vs entries 5–7).

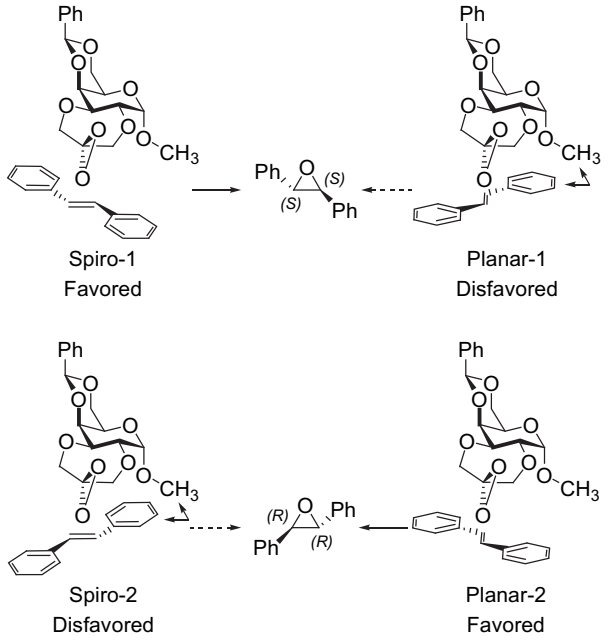
In all cases, ketones were recovered in high yields – 75–80% for glucopyranoside derivatives (**9**, **10**, and **26**) and slightly lower for galactopyranoside derivatives, 65–70% (**20**–**22**) – without loss of activity. This shows their stability under the reaction conditions, and thus the possibility of their being recycled and employed in various catalytic cycles.

Table 2
Catalytic asymmetric epoxidation of alkenes **27**–**30** in the presence of D-galactose derived ketones **20**–**22**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**20**	**27**	60	72	(−)-(1*S*,2*S*)
2	**20**	**28**	67	60	(−)-(1*S*,2*S*)
3	**20**	**29**	67	73	(−)-(1*S*,2*S*)
4	**20**	**30**	70	77	(+)-(2*S*)
5	**21**	**27**	75	69	(−)-(1*S*,2*S*)
6	**21**	**29**	69	53	(−)-(1*S*,2*S*)
7	**21**	**30**	70	58	(+)-(2*S*)
8	**22**	**27**	62	100	(−)-(1*S*,2*S*)
9	**22**	**29**	74	81	(−)-(1*S*,2*S*)
10	**22**	**30**	58	88	(+)-(2*S*)
11	**1**[e]	**27**	73	68	(−)-(1*S*,2*S*)
12	**1**[e]	**28**	68	57	(−)-(1*S*,2*S*)
13	**1**[e]	**29**	72	67	(−)-(1*S*,2*S*)
14	**1**[e]	**30**	66	74	(+)-(2*S*)

[a] Conditions: substrate (1 equiv), ketone (1 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 ^1H NMR spectroscopy of the epoxide products directly with shift reagent (+)-Eu(hfc)$_3$.
[d] The absolute configuration of the major enantiomer was assigned by comparing the signal shifts with those reported in the literature and also by comparing the sign of optical rotation with the reported one in each case.
[e] Previously reported for us, see Ref. 11.

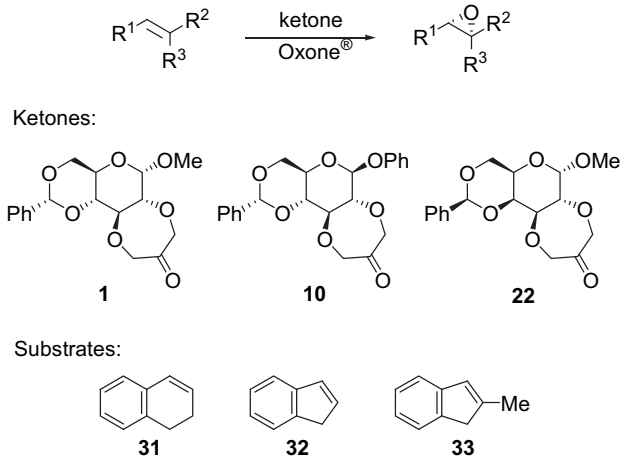
It is of interest to understand the possible geometry of the transition state in dioxirane epoxidations. Two mechanistic extremes (spiro and planar) are presented in Scheme 5 for the *trans*-stilbene epoxidation catalyzed by ketone **22**. A spiro transition state was proposed by Baumstark,[13] based on the observation that *cis*-olefins were more reactive that the corresponding *trans*-olefins for epoxidation using dimethyldioxirane. In our study, if the reaction proceeds via a spiro mode, (*S*,*S*)-stilbene oxide is expected to be favored (spiro-1 vs spiro-2). In contrast, (*R*,*R*)-enantiomer will be favored if the reaction proceeds via a planar mode (planar-2 vs planar-1). In the present study, it is found that (*S*,*S*)-stilbene oxide is produced predominately, which supports the spiro transition state. Beside, the attack on the other oxygen of the dioxirane yields also the (*S*,*S*)-enantiomer. In addition, computational studies showed that the spiro transition state is favored for the epoxidation of



Scheme 5. The spiro and planar transition states for *trans*-stilbene epoxidation catalyzed by ketone **22**.

ethylene with dimethyldioxirane, presumably due to the stabilizing interaction of an oxygen lone pair with the π^* orbital of the alkene in the spiro transition state.[14]

A complementary part of our work was to begin preliminary trials to evaluate the efficiency of this type of ketone as chiral inducer in the epoxidation of *cis*-olefins, because while dioxiranes generated in situ from chiral ketones are efficient for asymmetric epoxidation of *trans*-olefins and trisubstituted olefins,[5a,b] *cis*-alkenes remain challenging substrates for epoxidation with high stereoselectivity. We chose the compounds **1**, **10**, and **22** as ketone precursors of the reactive dioxiranes, and used the reaction conditions described. The substrates employed for these preliminary studies were the alkenes **31**–**33**. We chose these cyclic olefins in order to restrict reacting approach for the olefin substrate, hoping thereby to obtain a greater enantiomeric excess (Scheme 6).



Scheme 6. Epoxidation conditions (see text).

The reaction took place with good chemical yields in all cases (55–73% for the *gluco* ketone derivatives, 70–80% for those of *galacto* configuration), and the chiral catalysts had satisfactory percentages of recovery (though somewhat higher for the *gluco* (65–70%) than for the *galacto* (40%)). However, in no case did we achieve enantioselectivity. These results are in agreement with the transition state proposed (Scheme 5), because in the epoxidation of *cis*-alkenes spiro-1 and spiro-2 are favored.

In summary, our group has recently described a new backbone model for a chiral carbohydrate-derived ketone **1**, and tested its efficiency as catalyst in the asymmetric epoxidation of alkenes.[11] As a continuation of that work, and as part of our line of research on the synthesis of new sugar-derived ketones, this work had two general aims.

On one hand, the synthesis of different ketones structurally related to that previously described, having the same type of general skeleton – the tri-cyclic system comprising the *trans*- or *cis*-decalin-like benzylidene-4,6-*O*-acetal, the dioxepane ring where the ketone function is sited, and the sugar moiety – but varying stereochemically. For this, in the structural and stereochemical modification, we began with the anomeric position and position 4 of the sugar residue when choosing the carbohydrate precursor.

In the first part of the work we have applied our synthetic method to obtain the new ketones **9**, **10**, and **20**–**22** from the appropriate commercially available carbohydrate precursor: alkyl and aryl, α and β, D-*gluco* and D-*galacto* derivatives. A new ketone **26**, D-glucitol-derived, was also synthesised using this method. All these new ketones were synthesised with good chemical yields and were duly characterised.

The second part was focused on their use in the epoxidation reaction of different arylalkenes, and the comparison of the chemical and stereochemical yields both with those obtained with the ketone **1** and among them.

3. Conclusions

With regard to chemical yield, the results obtained were satisfactory in all cases (70–80%), and similar to those obtained with the ketone **1**. The ketone **26** (D-glucitol-derived) gave smaller chemical yields (52–78%). The percentages of recovery without loss of activity of the new ketones were good, enabling their use in various catalytic cycles.

With regard to stereochemical yield, firstly we observed that the new ketones possess the same alkene stereofacial differentiation pattern as the ketone **1** (they provide the same major enantiomer). Secondly, to study the effect of the structural modifications (α or β configuration, alkyl or aryl substituent at the anomeric position, and configuration at carbon 4 of the sugar residue, D-*gluco* or D-*galacto* derivative) on the stereochemical result of the process (and thereby the possible obtaining of a more efficient chiral catalyst), we compared the ees both with that of the ketone **1** and among them.

Modifying the configuration at the anomeric position enables us to deduce that the α-configuration ketones give greater enantiomeric excesses than their β configuration analogues.

The use of two types of sugar residue, D-*gluco* or D-*galacto*, enables the deduction that when the ketones are D-*galacto* derivatives, the enantiomeric excesses are greater than for their D-*gluco* analogues.

The alkyl (Me) or aryl (Ph) nature of the substituent at the anomeric position does not affect the chiral induction capacity of the β-*gluco* ketones, similar ees being obtained. However, this structural modification does affect the stereoselectivity obtained on using β-D-*galacto* derivatives, with the Ph group causing a decrease in the enantiomeric excess obtained.

The use of the ketone with structure derived from 1,5-anhydro-D-glucitol **26**, enables the conclusion that the defunctionalisation of the anomeric position generates a reduction in the efficacy as catalyst in comparison with the ketone **1**, generating ees similar to those of the β-D-derivatives.

In summary, for the epoxidation of *trans*-olefins and trisubstituted olefins, the presence of a sugar residue of α-D-*galacto* configuration and an alkyl (methyl) group are structural characteristics that potentiate the eficacia as chiral catalyst of this type of general structure of ketones, and will be taken into account for the design of new ketones, and in tackling modifications to the 4,6-*O*-acetal system.

Lastly, we began the study of the epoxidation of *cis*-olefins, using the ketones **1**, **10**, and **22** as source of chiral dioxiranes. We chose these three ketones because one of them **1** had been our starting compound when proposing this type of general skeleton of chiral ketones; another **22** has given in this work the best degree of enantioselectivity in the epoxidation of *trans*-olefins; and **10** has given the lowest ees. The aim was to evaluate their capacity of chiral induction with these substrates, and to be able to reach structural conclusions. Unfortunately, in no case was stereoselectivity achieved.

4. Experimental

4.1. General

All solvents were reagent or analysis grade. Evaporations were conducted under reduced pressure. Reactions were monitored using thin-layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F_{254} silica gel. Compounds were

visualised by UVA radiation at a wavelength of 254 nm or stained by exposure to an ethanolic solution of phosphomolybdic acid and subsequent heating. Silica gel 60 (230–400 ASTM) was used for all flash column chromatography. Melting points were obtained on a Stuart Melting Point Apparatus SMP 10 and are uncorrected. Optical rotations were obtained on a Perkin–Elmer Polarimeter Model 341 at 25 °C. Mass spectra were recorded on a Micromass AUTOSPECQ mass spectrometer: EI at 70 eV and CI at 150 eV, HR mass measurements with resolutions of 10,000. FAB mass spectra were recorded using a thioglycerol matrix. NMR spectra were recorded at 25 °C on a Bruker AMX500 spectrometer and on a Bruker AV500 spectrometer at 500 MHz for ^{1}H and 125 MHz for ^{13}C. The chemical shifts are reported in parts per million on the δ scale relative to TMS. COSY, DEPT, HSQC, and NOESY experiments were performed to assign the signals in the NMR spectra. 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. Absolute configuration was assigned by comparison with the signal shifts reported in the literature for epoxides of alkenes **27**–**33**.[12a,c,15–18] The absolute configuration was also determined by comparing the sign of optical rotations with the reported ones.[12a,c,15–18]

4.2. Synthesis of 2,3-*O*-(2-methylidene-1,3-propylene)-D-hexopyranoside derivatives (5, 6, 14–16, 24)

To a cooled solution (5 °C) of the corresponding 4,6-*O*-(*R*)-benzylidene-D-hexopyranoside derivative (obtained using the procedure describe by our group[2c]) (35.4 mmol) in dry THF (70 mL) were added, successively, freshly powdered potassium hydroxide (7.0 g, 125 mmol), 18-crown-6 (0.38 g, 1.4 mmol), and 3-chloro-2-chloromethylpropene (4.1 mL, 35.4 mmol). 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 (5–7 days, approximately), then diluted with dichloromethane (60 mL) and washed successively with water and aqueous saturated solution of sodium bicarbonate, dried ($MgSO_4$), filtered, and the filtrate was evaporated to dryness.

*4.2.1. Methyl 4,6-O-(R)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-β-D-glucopyranoside (**5**).* The solid obtained was purified by flash chromatography on silica gel (7:1 hexane–ethyl acetate) to give compound **5** (11.3 g, 95%) as a white solid; [Found: C, 64.74; H, 6.94. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%]; mp 130–132 °C; $[\alpha]_D^{25}$ −19.9 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.6–7.3 (5H, m, Ph), 5.51 (1H, s, PhC*H*), 5.04, 5.02 (2H, 2s, C=CH_2), 4.48 [1H, d, J_{gem} 14.1 Hz, (OCH_AH$_B$)C(CH$_D$H$_E$O)], 4.44 [1H, d, J_{gem} 14.1 Hz, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.36 (1H, d, $J_{1,2}$ 7.7 Hz, H-1), 4.33 (1H, dd, $J_{5,6e}$ 4.9 Hz, $J_{6e,6a}$ 10.5 Hz, H-6$_e$), 4.28 [1H, d, J_{gem} 14.1 Hz, (OCH$_A$*H*$_B$)C(CH$_D$H$_E$O)], 4.26 [1H, d, J_{gem} 14.1 Hz, (OCH$_A$H$_B$)C(CH$_D$*H*$_E$O)], 3.75 (1H, t, $J_{5,6e}$=$J_{6e,6a}$ 10.2 Hz, H-6$_a$), 3.58–3.51 (5H, m, H-3, H-4, OCH_3), 3.44–3.36 (1H, m, H-5), 3.29–3.25 (1H, m, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.6 (*C*=CH_2), 137.0–126.4 (Ph), 114.3 (C=*C*H$_2$), 102.8 (PhCH), 101.8 (C-1), 86.7 (C-2), 82.6 (C-3), 78.9 (C-4), 73.2, 72.9 [(OCH$_2$)C(*C*H$_2$O)], 68.7 (C-6), 66.4 (C-5), 57.4 (OCH_3); MS (CI): *m*/*z* 335 (80%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 335.1495. $C_{18}H_{23}O_6$ requires 335.1495.

*4.2.2. Phenyl 4,6-O-(R)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-β-D-glucopyranoside (**6**).* The solid obtained was purified by flash chromatography on silica gel (3:1 hexane–ethyl acetate) to give compound **6** (13.5 g, 96%) as a white solid; [Found: C, 69.62; H, 6.29. $C_{23}H_{24}O_6$ requires C, 69.68; H, 6.10%]; mp 96–97 °C; $[\alpha]_D$ −3.8 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.0 (10H, m, 2Ph), 5.54 (1H, s, PhC*H*), 5.07, 5.01 (2H, 2s, C=CH_2), 5.04 (1H, d, $J_{1,2}$ 7.7 Hz, H-1), 4.52 [1H, d, J_{gem} 14.1 Hz, (OCH_AH$_B$)C(CH$_D$H$_E$O)], 4.46 [1H, d, J_{gem} 13.6 Hz, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.38–4.33 [2H, m, H-6$_e$, (OCH$_A$*H*$_B$)C(CH$_D$H$_E$O)], 4.28 [1H, d, J_{gem} 13.6 Hz, (OCH$_A$H$_B$)C(CH$_D$*H*$_E$O)], 3.78 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.4 Hz, H-6$_a$), 3.69–3.66 (2H, m, H-3, H-4), 3.56–3.51 (2H, m, H-2, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.8 (*C*=CH_2), 137.6–126.0 (Ph), 114.5 (C=*C*H$_2$), 101.9 (PhCH), 100.1 (C-1), 83.5 (C-2), 82.7 (C-3), 78.8 (C-4), 73.4, 73.0 [(OCH$_2$)C(*C*H$_2$O)], 68.7 (C-6), 66.6 (C-5); MS (CI): *m*/*z* 397 (90%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 397.1648. $C_{23}H_{25}O_6$ requires 397.1651.

*4.2.3. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-β-D-galactopyranoside (**14**).* The solid obtained was purified by flash chromatography on silica gel (1:1 hexane–ethyl acetate) to give compound **14** (11.4 g, 97%) as a white solid; [Found: C, 64.76; H, 6.60. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%]; mp 161–162 °C; $[\alpha]_D$ +67.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.3 (5H, m, Ph), 5.54 (1H, s, PhC*H*), 4.97–4.94 (2H, m, C=CH_2), 4.56 [1H, d, J_{gem} 14.6 Hz, (OCH_AH$_B$)C(CH$_D$H$_E$O)], 4.51 [1H, d, J_{gem} 14.6 Hz, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.37–4.27 [5H, m, H-1, H-4, H-6$_e$, (OCH$_A$*H*$_B$)C(CH$_D$*H*$_E$O)], 4.07 (1H, dd, $J_{5,6a}$ 1.3 Hz, $J_{6e,6a}$ 12.5 Hz, H-6$_a$), 3.74 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 9.3 Hz, H-2), 3.58 (3H, s, OCH_3), 3.43 (1H, dd, $J_{2,3}$ 9.8 Hz, $J_{3,4}$ 3.4 Hz, H-3), 3.41 (1H, m, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3 (*C*=CH_2), 137.6–126.7 (Ph), 111.9 (C=*C*H$_2$), 102.4 (C-1), 101.6 (PhCH), 83.2 (C-2), 80.2 (C-3), 75.8 (C-4), 73.8, 73.3 [(OCH$_2$)C(*C*H$_2$O)], 69.1 (C-6), 66.6 (C-5), 56.9 (OCH_3); MS (EI): *m*/*z* 334 (40%, $[M]^{+\bullet}$); HRMS (EI): $[M]^{+\cdot}$, found 334.1417. $C_{18}H_{22}O_6$ requires 334.1416.

*4.2.4. Phenyl 4,6-O-(S)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-β-D-galactopyranoside (**15**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **15** (13.5 g, 95%) as a white solid; [Found C, 69.57; H, 6.34. $C_{23}H_{24}O_6$ requires C, 69.68; H, 6.10%]; mp 85–87 °C; $[\alpha]_D$ −3.0 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.1 (10H, m, 2Ph), 5.52 (1H, s, PhC*H*), 5.00 (1H, d, $J_{1,2}$ 7.8 Hz, H-1), 4.97 (2H, m, C=CH_2), 4.53 [1H, d, J_{gem} 14.1 Hz, (OCH_AH$_B$)C(CH$_D$H$_E$O)], 4.51 [1H, d, J_{gem} 14.1 Hz, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.37–4.29 [5H, m, H-1, H-4, H-6$_e$, (OCH$_A$*H*$_B$)C(CH$_D$*H*$_E$O)], 4.07 (1H, dd, $J_{5,6a}$ 1.8 Hz, $J_{6e,6a}$ 12.4 Hz, H-6$_a$), 3.95 (1H, dd, $J_{1,2}$ 7.7 Hz, $J_{2,3}$ 9.3 Hz, H-2), 3.52 (1H, m, H-5), 3.51 (1H, dd, $J_{2,3}$ 9.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3 (*C*=CH_2), 137.6–117.9 (Ph), 112.1 (C=*C*H$_2$), 101.6 (C-1), 100.2 (PhCH), 83.3 (C-2), 79.8 (C-3), 75.5 (C-4), 73.9, 73.3 [(OCH$_2$)C(*C*H$_2$O)], 69.1 (C-6), 66.8 (C-5); MS (EI): *m*/*z* 396 (20%, $[M]^{+\cdot}$); HRMS (EI): $[M]^{+\cdot}$, found 396.1543. $C_{23}H_{24}O_6$ requires 335.1573.

*4.2.5. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-α-D-galactopyranoside (**16**).* The solid obtained was purified by flash chromatography on silica gel (1:1 hexane–ethyl acetate) to give compound **16** (11.6 g, 98%) as a white solid; [Found: C, 64.56; H, 6.61. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%]; mp 54–55 °C; $[\alpha]_D$ +280.0 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.3 (5H, m, Ph), 5.53 (1H, s, PhC*H*), 4.97 (1H, d, $J_{1,2}$ 3.6 Hz, H-1), 4.89–4.87 (2H, m, C=CH_2), 4.52 [1H, d, J_{gem} 14.7 Hz, (OCH_AH$_B$)C(CH$_D$H$_E$O)], 4.50 [1H, d, J_{gem} 14.4 Hz, (OCH$_A$H$_B$)C(CH_DH$_E$O)], 4.34–4.29 [3H, m, H-4, (OCH$_A$*H*$_B$)C(CH$_D$*H*$_E$O)], 4.25 (1H, dd, $J_{5,6e}$ 1.6 Hz, $J_{6e,6a}$ 12.5 Hz, H-6$_e$), 4.07 (1H, dd, $J_{5,6a}$ 1.7 Hz, $J_{6e,6a}$ 12.5 Hz, H-6$_a$), 3.96 (1H, dd, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.8 Hz, H-2), 3.84 (1H, dd, $J_{2,3}$ 9.8 Hz, $J_{3,4}$ 3.4 Hz, H-3), 3.66 (1H, m, H-5), 3.44 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.7 (*C*=CH_2), 137.8–126.6 (Ph), 110.6 (C=*C*H$_2$), 101.3 (C-1), 99.8 (PhCH), 79.3 (C-2, C-3), 76.2 (C-4), 73.9 [(OCH$_2$)C(*C*H$_2$O)], 69.3 (C-6), 62.8 (C-5), 55.6 (OCH_3); MS (CI): *m*/*z* 335 (70%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 335.1479. $C_{18}H_{23}O_6$ requires 335.1495.

*4.2.6. 1,5-Anhydro-4,6-O-(R)-benzylidene-2,3-O-(2-methylidene-1,3-propylene)-D-glucitol (**24**).* The solid obtained was purified by flash chromatography on silica gel (2:1 hexane–ethyl acetate) to give

compound **24** (10.4 g, 97%) as a white solid; [Found: C, 67.11; H, 6.40. $C_{17}H_{20}O_5$ requires C, 67.09; H, 6.62%]; mp 79–81 °C; $[\alpha]_D$ +9.5 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.2 (5H, m, Ph), 5.51 (1H, s, PhC*H*), 5.04 (2H, m, C=CH_2), 4.50–4.24 [6H, m, H-1_e, H-6_e, (OCH_2)C(CH_2O)], 4.03–3.97 (1H, m, H-1_a), 3.68–3.45 (3H, m, H-3, H-4, H-6_a), 3.40–3.31 (1H, m, H-5), 3.28–3.21 (1H, m, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.0 (*C*=CH_2), 137.2–126.4 (Ph), 112.1 (C=CH_2), 101.9 (Ph*C*H), 83.9 (C-2), 79.9 (C-3), 79.3 (C-4), 73.1, 72.9 [(OCH_2)C(CH_2O)], 71.4 (C-1), 68.8 (C-6), 62.7 (C-5); MS (EI): *m*/*z* 304 (80%, $[M]^{+\cdot}$); HRMS (EI): $[M]^{+\cdot}$, found 304.1316. $C_{17}H_{20}O_5$ requires 304.1311.

4.3. Dihydroxylation reaction

To a solution of compounds **5**, **6**, **14**–**16**, **24** (4.0 mmol) in dichloromethane (300 mL) were added trimethylamine *N*-oxide (0.58 g, 5.2 mmol) and a solution of osmium tetroxide in 2-propanol (2.5% w/v) in catalytic amount (0.5 mL, 0.04 mmol). The mixture was stirred for 24 h at room temperature. The solution was washed successively with dilute aqueous solution of sodium bisulphite and water, dried ($MgSO_4$), and evaporated to dryness. The solid obtained was purified by flash chromatography on silica gel, yielding a pale yellow solid, as a diastereoisomeric mixture (1:1).

*4.3.1. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-hydroxy-2-hydroxymethyl-1,3-propylene)-β-D-galactopyranoside (**17**).* Two stereoisomers were obtained in 1:1 ratio. The pure diastereomeric mixture was obtained by flash chromatography on silica gel (1:1 hexane–ethyl acetate) to give compound **17** (0.9 g, 60%) as a pale yellow solid; [Found: C, 58.42; 6.70.$C_{18}H_{24}O_8$ requires C, 58.69; H, 6.57%]; mp 161–162 °C; $[\alpha]_D$ +8.4 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.3 (5H, m, Ph), 5.59, 5.58 (1H, 2s, PhC*H*), 4.40, 4.33 (1H, 2d, $J_{1,2}$ 7.5 Hz, H-1), 4.37, 4.36 [1H, 2d, J_{gem} 12.5 Hz, (OCH_AH_B)C(CH_DH_EO)], 4.32, 4.31 (1H, 2dd, $J_{5,6e}$ 1.0 Hz, $J_{6e,6a}$ 12.8 Hz, H-6_e), 4.12, 4.10 (1H, 2dd, $J_{5,6a}$ 1.9 Hz, $J_{6e,6a}$ 12.6 Hz, H-6_a), 4.08–4.02 [3H, m, (OCH_AH_B)C(CH_DH_EO)], 3.96–3.68 [5H, m, H-2, H-3, H-4, CH_2(OH)], 3.62, 3.61 (3H, 2s, OCH_3), 3.55–3.42 (3H, m, H-5, 2OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6–126.4 (Ph), 102.3, 102.1 (PhCH), 101.2, 101.1 (C-1), 82.3, 81.6 (C-2), 79.7, 79.2 (C-3), 76.9, 76.5 [C(OH)], 76.4, 76.3 (C-4), 73.7, 73.6 [(OCH_2)C(CH_2O)], 69.1 (C-6), 66.5, 66.4 (CH_2OH), 64.6, 64.2 (C-5), 56.8, 56.7 (OCH_3); MS (CI): *m*/*z* 369 (25%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 369.1556. $C_{18}H_{25}O_8$ requires 369.1549.

*4.3.2. Phenyl 4,6-O-(S)-benzylidene-2,3-O-(2-hydroxy-2-hydroxymethyl-1,3-propylene)-β-D-galactopyranoside (**18**).* Two stereoisomers were obtained in 1:1 ratio. The pure diastereomeric mixture was obtained by flash chromatography on silica gel (1:1 hexane–ethyl acetate) to give compound **18** (1.5 g, 88%) as a pale yellow solid; [Found: C, 64.03; 6.12. $C_{23}H_{26}O_8$ requires C, 64.18; H, 6.09%]; mp 175–176 °C; $[\alpha]_D$ +52.9 (*c* 0.9, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.8–7.1 (10H, m, 2Ph), 5.76, 5.75 (1H, 2s, PhC*H*), 4.97, 4.96 (1H, 2d, $J_{1,2}$ 7.9 Hz, H-1), 4.38–4.05 [6H, m, H-6_e, H-6_a, (OCH_2)C(CH_2O)], 3.93–3.67 [5H, m, H-2, H-3, H-4, CH_2(OH)], 3.56–3.38 (3H, m, H-5, 2OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.4–116.4 (Ph), 101.9, 101.8 (PhCH), 98.9, 98.7 (C-1), 82.9, 82.7 (C-2), 79.7, 79.2 (C-3), 76.9, 76.5 [C(OH)], 75.7, 75.6 (C-4), 73.7, 73.6 [(OCH_2)C (CH_2O)], 69.1 (C-6), 66.5, 66.4 (CH_2OH), 64.6, 64.2 (C-5); MS (CI): *m*/*z* 431 (30%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 431.1721. $C_{23}H_{27}O_8$ requires 431.1706.

*4.3.3. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-hydroxy-2-hydroxymethyl-1,3-propylene)-α-D-galactopyranoside (**19**).* Two stereoisomers were obtained in 1:1 ratio. The pure diastereomeric mixture was obtained by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **19** (1.4 g, 95%) as a pale yellow solid; [Found: C, 58.55; 6.53.$C_{18}H_{24}O_8$ requires C, 58.69; H, 6.57%]; mp 80–82 °C; $[\alpha]_D$ +140.1 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.3 (m, 5H, Ph), 5.54, 5.53 (2s, 1H, PhC*H*), 4.97, 4.93 (2d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 4.34, 4.32 [2d, 1H, J_{gem} 11.4 Hz, (OCH_AH_B)C(CH_DH_EO)], 4.25, 4.24 [2d, 1H, J_{gem} 12.5 Hz, (OCH_AH_B)C(CH_DH_EO)], 4.17–3.86 [m, 5H, H-4, H-6_e, H-6_a, (OCH_AH_B)C(CH_DH_EO)], 3.80–3.56 [m, 4H, H-2, H-3, CH_2(OH)], 3.43, 3.42 (2s, 3H, OCH_3), 3.40–3.37 (m, 2H, H-5, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7–126.2 (Ph), 101.1, 100.9 (PhCH), 100.1, 100.0 (C-1), 84.5, 83.5 (C-2), 79.9, 79.7 (C-3), 77.2, 76.7 [C(OH)], 76.2, 76.1 (C-4), 73.3, 73.1, 72.5, 72.84 [(OCH_2)C (*C*H_2O)], 69.4, 69.2 (C-6), 64.4, 64.3 (CH_2OH), 63.1, 62.9 (C-5), 55.7, 55.6 (OCH_3); MS (CI): *m*/*z* 369 (20%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 369.1538. $C_{18}H_{25}O_8$ requires 369.1549.

4.4. Diol oxidative rupture reaction

To a solution of compounds **7**, **8**, **17**–**19**, **25** (1.8 mmol) in ethanol–water (1:2) (120 mL), a solution of sodium periodate (0.77 g) in water (9 mL) was added, and the reaction mixture was stirred overnight at room temperature. The solvent was evaporated to a small volume (40–50 mL), and the solution was extracted with dichloromethane (5×40 mL), dried ($MgSO_4$), and evaporated to dryness. The solid obtained was purified by flash chromatography on silica gel.

*4.4.1. Methyl 4,6-O-(R)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-β-D-glucopyranoside (**9**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **9** (0.4 g, 73%) as a white solid; [Found: C, 60.82; H, 6.01. $C_{17}H_{20}O_7$ requires C, 60.71; H, 5.99%]; mp 163–164 °C; $[\alpha]_D$ +34.8 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.6–7.3 (5H, m, Ph), 5.53 (1H, s, PhC*H*), 4.43 (1H, d, $J_{1,2}$ 7.8 Hz, H-1), 4.41–4.22 [5H, m, H-6_e, (OCH_2)C(CH_2O)], 3.79 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.1 Hz, H-6_a), 3.73–3.66 (2H, m, H-3, H-4), 3.55 (3H, s, OCH_3), 3.46 (1H, dt, $J_{5,6e}$ 5.0 Hz, $J_{4,5}$=$J_{5,6a}$ 9.9 Hz, H-5), 3.71 (1H, t, $J_{1,2}$=$J_{2,3}$ 8.0 Hz, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.0 (C=O), 129.8–119.3 (Ph), 95.4 (PhCH), 94.8 (C-1), 87.0 (C-2), 86.0 (C-3), 78.4 (C-4), 78.0, 77.7 [(OCH_2)C (CH_2O)], 68.6 (C-6), 66.7 (C-5), 57.5 (OCH_3); MS (CI): *m*/*z* 337 (40%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 337.1292. $C_{17}H_{21}O_7$ requires 337.1287.

*4.4.2. Phenyl 4,6-O-(R)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-β-D-glucopyranoside (**10**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **10** (0.6 g, 88%) as a white solid; [Found: C, 66.14; H, 5.62. $C_{22}H_{22}O_7$ requires C, 66.32; H, 5.57%]; mp 148–150 °C; $[\alpha]_D$ +13.4 (*c* 0.9, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.5–7.1 (10H, m, 2Ph), 5.55 (1H, s, PhC*H*), 5.12 (1H, d, $J_{1,2}$ 7.7 Hz, H-1), 4.44–4.26 [5H, m, H-6_e, (OCH_2)C(CH_2O)], 3.84–3.73 (3H, m, H-3, H-4, H-6_a), 3.64 (1H, t, $J_{1,2}$=$J_{2,3}$ 8.0 Hz, H-2) 3.59 (1H, dt, $J_{5,6e}$ 5.0 Hz, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.8 (C=O), 136.7–117.4 (Ph), 101.9 (PhCH), 99.6 (C-1), 86.6 (C-2), 86.0 (C-3), 78.2 (C-4), 78.0, 77.8 [(OCH_2) C(*C*H_2O)], 68.6 (C-6), 66.9 (C-5); MS (CI): *m*/*z* 399 (35%, $[M+H]^+$); HRMS (EI): $[M]^{+\cdot}$, found 398.1359. $C_{22}H_{22}O_7$ requires 398.1366.

*4.4.3. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-β-D-galactopyranoside (**20**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **20** (0.5 g, 90%) as a white solid; [Found: C, 60.41; H, 6.01. $C_{17}H_{20}O_7$ requires C, 60.71; H, 5.99%]; mp 90–91 °C; $[\alpha]_D$ +38.8 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.3 (5H, m, Ph), 5.54 (1H, s, PhC*H*), 4.40 (1H, d, $J_{1,2}$ 7.6 Hz, H-1), 4.38–4.33 [4H, m, H-4, (OCH_2)C(CH_AH_BO)], 4.31 (1H, dd, $J_{5,6e}$ 1.5 Hz, $J_{6e,6a}$ 11.9 Hz, H-6_e), 4.25 [1H, d, J_{gem}=16.2 Hz, (OCH_2)C(CH_AH_BO)], 4.09 (1H, dd, $J_{5,6a}$ 1.8 Hz, $J_{6a,6e}$ 12.2 Hz, H-6_a), 3.90 (1H, dd, $J_{1,2}$ 7.5 Hz, $J_{2,3}$ 9.5 Hz, H-2),

3.60–3.57 (4H, m, H-3, OCH_3), 3.47 (1H, m, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.9 (C=O), 137.4–126.6 (Ph), 101.9 (PhCH), 101.6 (C-1), 85.4 (C-2), 82.6 (C-3), 77.8, 77.4 [(OCH_2)C(CH_2O)], 75.6 (C-4), 69.1 (C-6), 66.6 (C-5), 57.0 (OCH_3); MS (CI): *m/z* 337 (20%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 337.1279. $C_{17}H_{21}O_7$ requires 337.1287.

*4.4.4. Phenyl 4,6-O-(S)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-β-D-galactopyranoside (**21**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **21** (0.6 g, 84%) as a white solid; [Found: C, 66.26; H, 5.82. $C_{22}H_{22}O_7$ requires C, 66.32; H, 5.57%]; mp 104–106 °C; $[\alpha]_D$ +15.6 (*c* 1.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 7.8–7.2 (10H, m, 2Ph), 5.55 (1H, s, PhC*H*), 5.12 (1H, d, $J_{1,2}$ 7.7 Hz, H-1), 4.44–4.26 [4H, m, H-4, H-6_e, (OCH_2)C(CH_2O)], 3.84–3.73 [3H, m, H-6_a, (OCH_2)C(CH_2O)], 3.64 (1H, t, $J_{1,2}$=$J_{2,3}$ 7.7 Hz, H-2), 3.61–3.53 (2H, m, H-3, H-5); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.9 (C=O), 136.8–116.7 (Ph), 102.0 (PhCH), 99.6 (C-1), 89.7 (C-2), 86.0 (C-3), 78.3, 78.0 [(OCH_2)C(CH_2O)], 75.6 (C-4), 68.6 (C-6), 66.9 (C-5), 57.0 (OCH_3); MS (CI): *m/z* 399 (20%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 399.1440. $C_{22}H_{23}O_7$ requires 399.1444.

*4.4.5. Methyl 4,6-O-(S)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-α-D-galactopyranoside (**22**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **22** (0.6 g, 94%) as a white solid; [Found: C, 60.44; H, 5.98. $C_{17}H_{20}O_7$ requires C, 60.71; H, 5.99%]; mp 99–101 °C; $[\alpha]_D$ +19.0 (*c* 0.5, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 7.5–7.3 (5H, m, Ph), 5.55 (1H, s, PhC*H*), 5.03 (1H, d, $J_{1,2}$ 3.6 Hz, H-1), 4.40 (1H, m, H-4), 4.32–4.29 [4H, m, (OCH_2)C(CH_2O)], 4.27 (1H, dd, $J_{5,6e}$ 1.4 Hz, $J_{6e,6a}$ 12.5 Hz, H-6_e), 4.13 (1H, dd, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.8 Hz, H-2), 4.09 (1H, dd, $J_{5,6a}$ 1.5 Hz, $J_{6e,6a}$ 12.5 Hz, H-6_a), 4.02 (1H, dd, $J_{2,3}$ 9.7 Hz, $J_{3,4}$ 3.4 Hz, H-3), 3.70 (1H, m, H-5), 3.47 (3H, s, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.9 (C=O), 137.4–126.5 (Ph), 101.4 (PhCH), 99.3 (C-1), 80.8 (C-2), 80.7 (C-3), 77.5, 77.4 [(OCH_2)C(CH_2O)], 75.8 (C-4), 69.2 (C-6), 62.8 (C-5), 55.7 (OCH_3); MS (CI): *m/z* 337 (30%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 337.1278. $C_{17}H_{21}O_7$ requires 337.1287.

*4.4.6. 1,5-Anhydro-4,6-O-(R)-benzylidene-2,3-O-(2-oxo-1,3-propylene)-D-glucitol (**26**).* The solid obtained was purified by flash chromatography on silica gel (4:1 hexane–ethyl acetate) to give compound **26** (0.3 g, 60%) as a white solid; [Found: C, 62.57; H, 6.15. $C_{16}H_{18}O_6$ requires C, 62.74; H, 5.92%]; mp 138–139 °C; $[\alpha]_D$ +14.7 (*c* 1.0, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): δ 7.8–7.2 (10H, m, 2Ph), 5.51 (1H, s, PhC*H*), 4.39–4.21 [6H, m, H-1_e, H-6_e, (OCH_2)C(CH_2O)], 4.09–4.03 (1H, m, H-1_a), 3.69 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.3 Hz, H-6_a), 3.64–3.58 (2H, m, H-3, H-4), 3.44–3.35 (1H, m, H-5), 3.32–3.29 (1H, m, H-2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 210.0 (C=O), 137.0–126.4 (Ph), 101.9 (PhCH), 87.4 (C-2), 83.3 (C-3), 78.9 (C-4), 77.8, 77.6 [(OCH_2)C(CH_2O)], 71.8 (C-1), 68.8 (C-6), 62.6 (C-5); MS (EI): *m/z* 306 (100%, $[M]^{+\cdot}$); HRMS (EI): $[M]^{+\cdot}$, found 306.11073. $C_{16}H_{18}O_6$ requires 306.1103.

4.5. General procedure for the enantioselective epoxidation

To a solution of the alkene (**27**–**33**) (0.2 mmol) in 1,2-dimethoxyethane (5 mL) were added chiral ketones **9**, **10**, **20**–**22**, and **26** (0.2 mmol) and *n*-Bu_4NHSO_4 (5 mg). The reaction mixture was cooled to 0 °C into an ice-water bath. Oxone® (0.4 mmol) was dissolved in a solution of Na_2EDTA 4×10^{-4} M (2 mL), and $NaHCO_3$ (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 then diluted with water (10 mL). The solution was extracted with dichloromethane (3×10 mL), dried ($MgSO_4$), and evaporated to dryness. The crude reaction mixture obtained was purified by flash chromatography, using a mixture of hexane–ethyl acetate (80:1) as eluent (50:1) for indene and methylindene, to afford the alkene epoxide. The eluent was changed to a mixture of hexane–ethyl acetate (2:1), and the chiral ketone was recovered in a 75–80% (for glucopyranoside derivatives) and 60–65% (for galactopyranoside derivatives).

4.5.1. (−)-(1S,2S)-trans-Stilbene oxide[12a,15]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (10H, m, 2Ph), 3.88 [2H, s, 2CH(O)].

4.5.2. (−)-(1S,2S)-β-Methylstyrene oxide[15]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (5H, m, Ph), 3.59 [1H, d, J_{trans} 2.0 Hz, PhC*H*(O)CHCH$_3$], 3.02 [1H, dq, *J* 5.1 Hz, J_{trans} 2.0 Hz, PhCH(O)C*H*CH$_3$], 1.44 (3H, d, *J*=5.1 Hz, CH_3).

4.5.3. (−)-(1S,2S)-trans-α-Methylstilbene oxide[15,16]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (10H, m, 2Ph), 3.96 [1H, s, CH(O)], 1.46 (3H, s, CH_3).

4.5.4. (+)-(2S)-Triphenylethylene oxide[12a,15,16]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.1 (15H, m, 3Ph), 4.32 [1H, s, CH(O)].

4.5.5. Dihydronaphtalene oxide[16,17]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.2 (4H, m, Ar), 3.85 [1H, d, *J* 4.5 Hz, C*H*(O)CHCH$_2$], 3.73 [1H, dd, *J* 4.3 Hz, *J* 3.0 Hz, CH(O)C*H*CH$_2$], 2.80 (1H, m), 2.55 (1H, dd, *J* 6.0 Hz, *J* 15.5 Hz), 2.43 (1H, m), 1.78 (1H, m).

4.5.6. Indene oxide[12c,18]. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.2 (4H, m, Ar), 3.48 [1H, dd, *J* 3.0 Hz, *J* 0.5 Hz, C*H*(O)CHCH$_2$], 4.15 [1H, t, *J* 3.0 Hz, CH(O)C*H*CH$_2$], 3.23 (1H, dd, *J* 0.5 Hz, *J* 18.0 Hz), 3.00 (1H, dd, *J* 3.0 Hz, *J* 18.0 Hz).

4.5.7. Methylindene oxide. ^1H NMR (500 MHz, $CDCl_3$): δ 7.4–7.2 (4H, m, Ar), 4.04 [1H, s, C*H*(O)C(CH$_3$)CH$_2$], 3.17 (1H, d, *J* 17.5 Hz), 2.92 (1H, d, *J* 17.5 Hz), 1.71 (3H, s, CH_3).

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Supplementary data

These data include ^1H and ^{13}C NMR spectra of chiral ketones described in this article, and ^1H NMR used in the determination of enantiomeric excesses in the epoxidation reactions of arylalkenes. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.11.033. These data include MOL files and InChIKeys of the most important compounds described in this article.

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