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New mannose-derived ketones as organocatalysts for enantioselective dioxirane-mediated epoxidation of arylalkenes. Part 3: Chiral ketones from sugars☆

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ABSTRACT

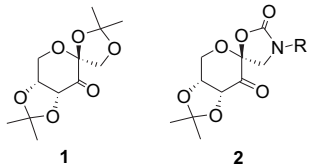
New D-*arabino*-hexopyranosid-3-uloses were synthesized by a simple method from mannopyranoside derivatives. The common skeleton possesses a tunable alkoxy group as steric sensor on carbon 2 of the sugar. The new ketones were employed in the dioxirane-mediated epoxidation of a range of *trans*- and trisubstituted arylalkenes giving enantiomeric excesses from low to good (30–90%). The effect of the size of the steric sensor on the enantioselectivity was also studied. The least bulky group (methoxy group) enhanced the stereoselectivity (up to 90% ee toward triphenylethylene).

1. Introduction

In the field of asymmetric transformations, the enantioselective epoxidation of alkenes is an important objective of many research groups for two reasons: optically active oxiranes are important synthetic intermediates widely employed in organic synthesis[1] and the epoxide functional group itself is an essential structural moiety of many natural products.[2] Among the methods for enantioselective epoxidation of olefins, the development of dioxirane-mediated epoxidations employing chiral ketones constitutes an attractive catalytic process since the first one was described by Curci co-woekers[3] A key issue to successfully obtain stereochemical control is the design of new and efficient chiral ketones. High catalytic activity, application on different structural types of alkenes, easy and high-yielding synthesis and high stereochemical differentiation are some criteria required for ketones. In order to obtain good stereofacial discrimination, ketone process design should take under consideration the two reacting sites of the dioxirane and possible competition between them. A usual approach is the preparation of chiral ketones that yield dioxiranes with one face blocked, so oxygen transfer occurs almost exclusively from the other face (efficient asymmetric environment is then maintained).[4]

In this sense many research groups have described different chiral ketones and high excess values have been reported for catalytic enantioselective alkene epoxidation, employing bile acids,[5] (+)-dihydrocarvone,[6] *N*-carbethoxytropinone,[7] D-(−)-quinic acid,[8] mannitol and (+) tartaric acid,[9] as chiral precursors for the synthesis of ketones.

In 1996 Shi and co-workers described a new fructose-derived ketone **1**, as a highly reactive and enantioselective epoxidation catalyst for *trans*- and trisubstituted olefins.[10] Their contributions in this area have extensively demonstrated that fructose- and glucose-derived ketones are exceptionally stereoselective tools and that they are applicable to a wide range of alkene substitution patterns [high enantioselectivities have been obtained with a variety of (*E*)- and trisubstituted olefins, a number of (*Z*)-olefins and certain terminal and tetrasubstituted olefins]. Their mechanistic studies have contributed to the development of efficient catalysts, (as example **2**)[11] (Fig. 1).



1 2

Fig. 1. Shi's fructose-derived ketones.

☆ For Part 2 see: Ref. 17.

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Shing and co-workers have described the synthesis of new glucose- **3**[12] and arabinose-derived uloses **4**,**5**,[1b,13] and have obtained high stereochemical communication between the ketone catalyst and the alkene [(*E*)-, trisubstituted and (*Z*)-alkenes] (Fig. 2).

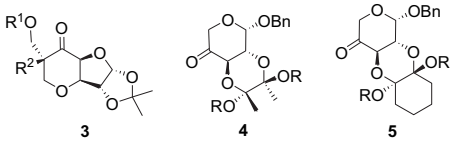


Fig. 2. Shing's glucose and arabinose-derived uloses.

Recently a systematically varied series of conformationally restricted ketones, readily prepared from *N*-acetyl-D-glucosamine, were tested against representative olefins as asymmetric epoxidation catalysts showing useful selectivities against terminal olefins and, in particular, typically difficult 2,2-disubstituted terminal olefins[14] (**6**, Fig. 3).

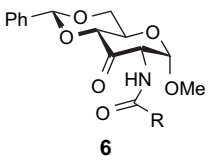


Fig. 3. *N*-acetyl-D-glucosamine-derived ketone.

These new ketones belong to a new class designed on the basis of the following considerations: (a) the reacting carbonyl placed close to the chiral control elements, (b) conformational rigidity due to the presence of fused ring (it has been noted that conformational flexibility in such epoxidising organocatalysts might have dramatically detrimental effects on stereoselectivity), (c) the approach of an olefin to the reacting dioxirane is directed by sterically blocking on one face, (d) the presence of electron-withdrawing substituents on C-α to activate the carbonyl group.[4a,b,11a,b,15]

One of our group's lines of research pursues the development of methods for the synthesis of enantiomerically pure epoxides,[16] the design of carbohydrate-derived ketones and their use to generate new chiral ketone–Oxone® systems.

We have recently described a new chiral carbohydrate-derived ketone **7**, with the reactive group located on a seven-membered ring fused to positions 2 and 3 of the sugar moiety.[17] Its general structure is a tri-cyclic system: the *trans* -decalin- like benzylidene-4,6-*O*-acetal, the dioxepane ring where the ketone function is located, and the sugar moiety. Choosing the adequate commercially available precursor (alkyl and aryl, α and β, D-*gluco* and D-*galacto* derivatives) and applying this synthetic methodology a number of ketones have been obtained with high chemical yields (**8**). We have employed them in dioxirane-mediated epoxidation of arylalkenes obtaining moderate-to-good excesses. Best ee's were obtained with compound **9**, α-methyl-D-galacto derivative[18] (Fig. 4).

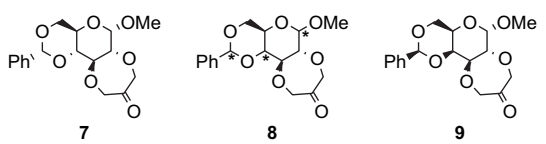


Fig. 4. General structure of Vega-Pérez's glucose and galactose-derived ketone.

Our general structure **8** had properties that made it an effective scaffold for organocatalyst in asymmetric epoxidation: easy and high-yielding synthesis, conformational rigidity, the presence of electron-withdrawing groups on C-α, appropriate control of the approach to alkene by sterically blocking on one face and the reactive group placed close to chiral elements. The conformational rigidity, the sugar chirality and sugar substituents provided satisfactory levels of stereofacial differentiation.

As a continuation of our work, we focused on the design of new backbone models for carbohydrate-derived ketones with points of structural modifications. We present here a new D-*arabino*-hexopyranoside-3-ulose skeleton **10** with a tunable alkoxy group on position 2 of the sugar moiety as the steric blocker (Fig. 5). The features of this general structure comply with the requisites mentioned above as crucial in the design of the ketone. We would like to point out two aspects: the reactive group is a sugar carbon is and no mannose derivatives have been previously reported as precursors in the field of the synthesis of new ketones from carbohydrates. However, different glucose, arabinose, and fructose derivatives have been employed, achieving large enantiomeric excesses. According to our catalyst's design shown in Fig. 5, the effect of the structure of the steric sensor on the enantioselectivity of the process is studied.

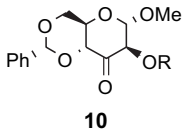
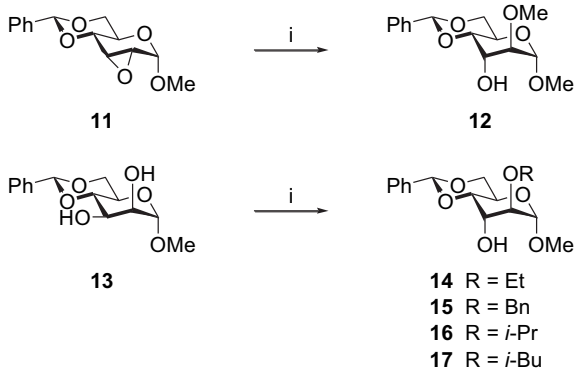


Fig. 5. General structure of mannose-derived ketone.

This article reports the stereochemical results obtained when we employed these new ketones as chiral precursors of dioxiranes for the epoxidation reaction of a variety of unfunctionalised *trans*- and trisubstituted arylalkenes.

2. Results and discussion

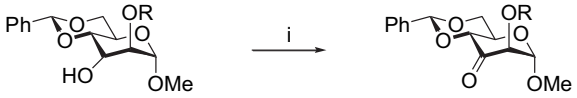
In order to prepare a systematically varied series of conformationally restricted ketones with general structure **10**, we first designed the synthetic sequence starting with the anhydro allopyranoside derivative **11** through a nucleophilic opening reaction of oxiranes with different sodium alkoxides (methoxide, ethoxide, isopropoxide). The reaction with sodium methoxide yielded compound **12**, methyl 4,6-*O*-(*R*)-benzylidene-2-*O*-methyL-α-D-altropyranoside,[19] (90%). However for the rest of the other 2-*O*-alkyl-derivatives designed, since the opening reaction did not take place, we had to design a different synthetic strategy. To do this we changed both the carbohydrate precursor, methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[20] **13**, and the reaction introducing structural variation, in this case a selective 2-O-alkylation with different alkyl halides. Compounds methyl 2-*O*-alkyl-4,6-*O*-(*R*)-benzylidene-α-D-mannopyranoside (**14**–**17**) were obtained with yields between 50 and 60% after flash column chromatography. 3-*O*-Alkyl mannopyranoside derivatives as well as starting diols were also recovered in small amount[21] (Scheme 1).



Scheme 1. (i) NaMeO, MeOH, reflux, 95%; (ii) NaOH, R–I, CH_2Cl_2, 45 °C, 50–60%.

^{1}H NMR spectral study shows characteristic signal of H-1 of the sugar as a doublet around δ 4.70 ppm and a coupling constant $J_{1,2}$ 1.0–1.4 Hz, the signals for those hydrogen atoms vicinal to the oxygen in the 2-*O*-alkyl groups at around δ 3.4–3.7 ppm in all cases, except compound **15**, whose benzylic hydrogens appear at δ 4.70 and 4.76 ppm. A doublet with almost the same coupling constant (J 8.9 Hz) is observed in ^{1}H NMR spectrum of these compounds at δ 2.3 ppm in all cases, corresponding to the hydroxyl group on carbon 3 of the sugar, whose hydrogen is coupled with H-3 atom of the sugar moiety.

The next step was the oxidation of the hydroxyl in position 3 of the sugar without epimerisation occurring, in order to provide the keto function on this carbon preserving the stereochemistry of carbon 2.[22] When the altropyranoside **12**, and the mannopyranosides **14**–**17** were treated with pyridinium chlorochromate in dichloromethane, the corresponding methyl 2-*O*-alquil-4,6-*O*-(*R*)-benzylidene-α-D-*arabino*-hexopiranoside-3-uloses (**18**–**22**) was isolated in 70–84% yield. (Scheme 2).



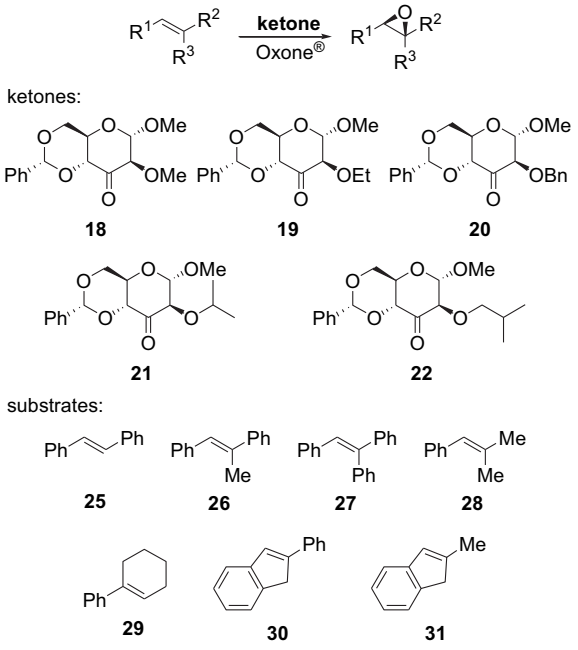
12 R = Me, *altro* — **18** R = Me
14 R = Et, *manno* — **19** R = Et
15 R = Bn, *manno* — **20** R = Bn
16 R = *i*-Pr, *manno* — **21** R = *i*-Pr
17 R = *i*-Bu, *manno* — **22** R = *i*-Bu

Scheme 2. (i) PCC, CH_2Cl_2, molecular sieves 3 Å, rt, 70–85%.

A noteworthy feature for the ^{1}H NMR spectra of these compounds is the signal for H-1 atom of the sugar moiety as a doublet (coupling constant $J_{1,2}$ 1.0–1.2 Hz in all these ketones) at δ 4.99 ppm, δ 5.57 ppm for compound **19**, δ 4.91 ppm for compound **21**; and for the ^{13}C NMR spectra was the signal for the carbonyl carbon at δ 198 ppm in all cases. The rest of the signals in the two spectra were assigned with the help of two-dimensional experiments and confirmed the structure of these sugar derived ketones.

After obtaining these ketone organocatalysts, we investigated suitable conditions for the epoxidation reaction. Our preliminary essays chose *trans*-stilbene as a testing model olefin, and ketone **18** as catalyst, indicating similar reactivity to our previously described ketones.[17,18] When we employed sub-stoichiometric quantities (0.5 equiv) of ketone, the reaction time was high (1–2 days) and conversion was low under these conditions (recovering alkene without epoxidation). Increasing the amount of ketone allowed us to improve the efficiency of the epoxidaton reaction (yields and reaction times) but without changing stereochemical results (ee and major oxirane configuration). After screening various reaction conditions the epoxidation 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 h, TLC analysis) (Scheme 3).

We chose as substrates for the epoxidation reaction a variety of unfunctionalised *trans*- and trisubstituted olefins (**25**–**31**) in order to explore the substrate scope of these catalysts. Our aim was to study the stereofacial differentiation capacity of these new ketones and the effect of the structural differences on the stereochemical result of the process, in order to obtain a more efficient chiral catalyst. In all cases, the absolute configuration of the major enantiomers obtained was assigned by comparing both the signal shifts in presence of (+)-Eu(hfc)$_3$ and the sign of optical rotation with those reported in the literature.



Scheme 3. Epoxidation conditions: see text.

The epoxides were isolated in satisfactory chemical yields (60–80%) and were recovered in high percentages without loss of activity (around 70%) showing their stability under the reaction conditions and enabling their use in various catalytic cycles.

The relationship between the size of the alkoxy group and the enantioselectivity of the epoxidation is summarized in Table 1.

Table 1
Catalytic asymmetric epoxidation of alkenes (**25**–**31**) in the presence of ketones **18**–**22**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**18**	**25**	68	80	(+)-(1*R*,2*R*)
2	**18**	**26**	70	70	(+)-(1*R*,2*R*)
3	**18**	**27**	74	90	(−)-(*R*)
4	**18**	**28**	76	28	(+)-(*R*)
5	**18**	**29**	80	60	(+)-(1*R*,2*R*)
6	**18**	**30**	71	52	(+)-(1*R*,2*R*)[e]
7	**18**	**31**	55	31	(−)-(1*R*,2*S*)
8	**19**	**25**	78	70	(+)-(1*R*,2*R*)
9	**19**	**26**	71	58	(+)-(1*R*,2*R*)
10	**19**	**27**	67	78	(−)-(*R*)
11	**19**	**30**	62	39	(+)-(1*R*,2*R*)[e]
12	**20**	**25**	78	65	(+)-(1*R*,2*R*)
13	**20**	**26**	52	59	(+)-(1*R*,2*R*)
14	**20**	**27**	73	71	(−)-(*R*)
15	**20**	**29**	68	63	(+)-(1*R*,2*R*)
16	**20**	**30**	72	33	(+)-(1*R*,2*R*)[e]
17	**21**	**25**	76	68	(+)-(1*R*,2*R*)
18	**21**	**26**	79	58	(+)-(1*R*,2*R*)
19	**21**	**27**	65	73	(−)-(*R*)
20	**21**	**29**	77	62	(+)-(1*R*,2*R*)
21	**21**	**30**	61	38	(+)-(1*R*,2*R*)[e]
22	**22**	**25**	67	47	(+)-(1*R*,2*R*)
23	**22**	**26**	59	44	(+)-(1*R*,2*R*)
24	**22**	**27**	75	64	(−)-(*R*)
25	**22**	**30**	64	28	(+)-(1*R*,2*R*)[e]

[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 ^{1}H 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 and the sign of optical rotation with those reported in the literature.
[e] Previously reported by us, see Ref. 16.

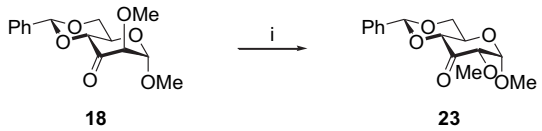
For *trans*- and trisubstituted 1,2-diarylalkenes (**25**–**27** and **30**) we have found a relationship between the enantioselectivity and the size of the alkoxy group on carbon 2. Ketone catalyst **18** with the least bulky alkoxy group (OMe) displayed the best enantioselectivity (entries 1–3 and 6, highest ee 90% for alkene **27**). Lower enantioselectivities and similar values of ee's were obtained with ketones **19** (OEt group, entries 8–11, highest ee 78% for alkene **27**), **20** (OBn group, entries 12–14 and 16, highest ee 71% for alkene **27**), and **21** (O*i*-Pr, entries 17–19 and 21, highest ee 73% for alkene **27**). Ketone **22** with an *O*-isobutyl group (branching β to oxygen) induced low degree of enantioselectivity (entries 22–24, highest ee 64% for alkene **27**). The absolute configuration of the major enantiomer is the same for each alkene in all cases.

Shing and co-workers[13c,d] have reported the epoxidation reaction of *trans*- and -trisubstituted alkenes with new arabinose-derived 4-uloses containing tunable cyclohexane-1,2-diacetal and butane-1,2-diacetal as steric blockers. Their results showed that the enantioselectivity was sensitive and increased with the size of the acetal alkoxy group. Steric blockers branched β to the acetal oxygen also exhibited good stereochemical communication toward this type of alkenes.

In all cases we have obtained the opposite major enantiomer than Shing's epoxides, and based on our results we concluded that the enantioselectivity was also sensitive decreasing with the size of the alkoxy group (best ee's were obtained when an OMe group is present, ketone **18**) as well as steric blockers with branching β to oxygen exhibited poor stereofacial discrimination (ketone **22** with an *O*-isobutyl group).

However, the epoxidation reaction of the phenylcyclohexene (1-arylalkene) afforded similar ee's with ketones **18** (*O*-methyl group), **20** (*O*-benzyl group), and **21** (*O*-isopropyl group) as catalysts (60–62%, entries 5, 15, and 20).

In order to determine the influence of the C-2 configuration in the enantiofacial discrimination, we have synthesized the C-2 epimeric *ribo*-hexopyranoside-3-ulose, **23**[23] (Scheme 4).



18 23

Scheme 4. (i) EtOH 96%, Et_3N, reflux, 61%.

The signal for H-1 atom, appears at δ 5.2 ppm (coupling constant $J_{1,2}$ 4.3 Hz), and the signal for H-2 atom, at δ 4.0 ppm as a double doublet (coupling constants $J_{1,2}$ 4.3 Hz, $^4J_{2,4}$ 1.5 Hz).

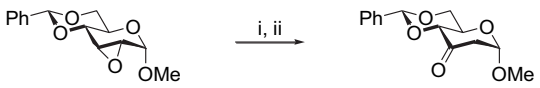
We performed the epoxidation reaction of alkenes **25**–**27** with ketone **23** as catalyst in similar reaction conditions. We obtained the major enantiomer in all cases but with lower stereochemical yields. (Table 2).

Table 2
Catalytic asymmetric epoxidation of alkenes (**25**–**27**) in the presence of ketones **18** and **23**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**23**	**25**	55	—	—
2	**18**	**25**	68	80	(+)-(1*R*,2*R*)
3	**23**	**26**	57	14	(+)-(1*R*,2*R*)
4	**18**	**26**	70	70	(+)-(1*R*,2*R*)
5	**23**	**27**	72	23	(−)-(*R*)
6	**18**	**27**	74	90	(−)-(*R*)

[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 ^{1}H 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 and the sign of optical rotation with those reported in the literature.

Finally, the next objective was to prepare the 2-deoxy derivative methyl 4,6-*O*-(*R*)-benzylidene-2-deoxy-α-D-*erythro*-3-ulose **24** by reaction of compound **11** with $LiAlH_4$ and following oxidation to generate the keto function on carbon 3 of the sugar residue (Scheme 5).



11 24

Scheme 5. (i) $LiAlH_4$, THF, reflux, 66%; (ii) PCC, CH_2Cl_2, molecular sieves 3 Å, rt, 71%.

^{1}H NMR spectrum of compound **24** shows the signal for H-1 at 5.18 ppm ($J_{1,2a}$ 4.7 Hz). In the ^{13}C NMR spectrum the carbonyl group signal appears at 198 ppm.

We carried out the epoxidation of alkenes **25**–**27** with this ketone under the same reaction conditions. The stereochemical yields compared with those obtained with ketone **18**, are presented in Table 3. The same major enantiomer configuration was found, but with lower ee's.

Table 3
Catalytic asymmetric epoxidation of alkenes (**25**–**27**) in the presence of ketones **18** and **24**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration[d]
1	**24**	**25**	67	33	(+)-(1*R*,2*R*)
2	**18**	**25**	68	80	(+)-(1*R*,2*R*)
3	**24**	**26**	65	6	(+)-(1*R*,2*R*)
4	**18**	**26**	70	70	(+)-(1*R*,2*R*)
5	**24**	**27**	58	39	(−)-(*R*)
6	**18**	**27**	74	90	(−)-(*R*)

[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 ^{1}H 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 and the sign of optical rotation with those reported in the literature.

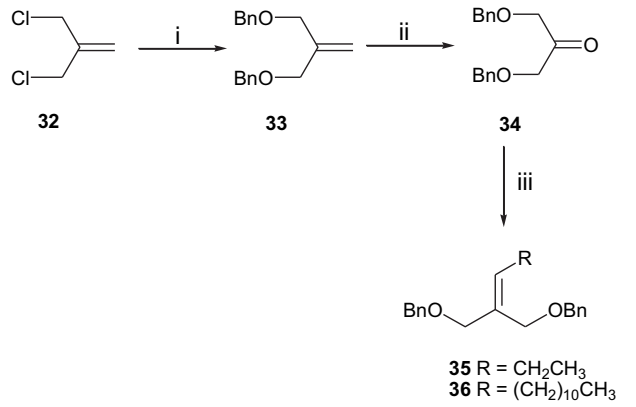
A complementary part of our work involved preliminary trials to evaluate the efficiency of this type of ketone as chiral inductor in the epoxidation of *cis*-olefins. It has been extremely challenging for chiral dioxiranes to epoxidize *cis*-olefins and terminal olefins with high enantioselectivity.[24]

We chose ketone **18** (that gave best ee's) and used the reaction conditions described above. The substrates employed for these preliminary studies were styrene (terminal olefin) and dihydronaphthalene (*cis*-alkene).

Although the reaction took place with good chemical yields (72 and 57%, respectively) the ee was low for terminal alkene (20%) and no ee was found for cis one.

Finally, we wanted to study the oxidation reaction of alkylalkenes using this model of ketone as catalyst. We chose appropriate alkenes in order to obtain optically active oxyranes that could act as precursors for interesting compounds, particularly new enantiomerically pure glycerol analogues. To prepare these alkenes we synthesized ketone **34**[25] following a simple sequence, and it reacted with different alkyl triphenylphosphonium bromides to give alkenes **35** and **36** (Scheme 6).

Their epoxidation reaction with ketone **18** gave **37** and **38** (Fig. 6). Chemical yields and enantioselectivities obtained are summarized in Table 4.



Scheme 6. (i) KOH (8.3 mmol), 18-crown-6 (20 mg), BnBr (4.1 mol), THF, 3 h, 90%; (ii) OsO_4 (*t*-BuOH)/Me_3NO/CH_2Cl_2, 90%; (iii) $NaIO_4$ (H_2O)/EtOH/H_2O, 95%; (iv) RCH_2PPh_3Br (2 mmol), BuLi (2 mmol), THF, −78 °C, 55%.

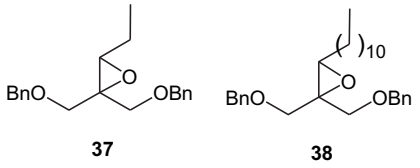


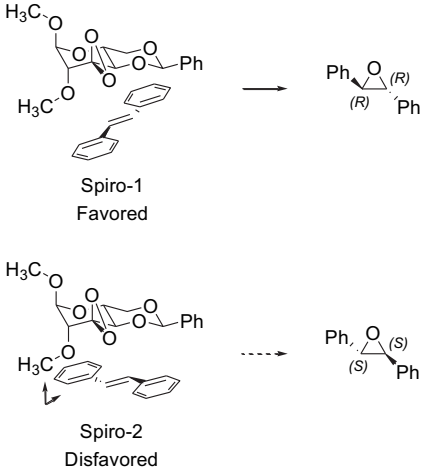
Fig. 6. New chiral dialkyl epoxide.

Table 4
Catalytic asymmetric epoxidation of alkenes (**33**, **34**) in the presence of ketone **18**[a]

Entry	Ketone	Alkene	Yield[b] (%)	ee[c] (%)	Configuration
1	**18**	**35**	61	53	(−)[d]
2	**18**	**36**	53	17	(−)[d]

[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 ^{1}H NMR spectroscopy of the epoxide products directly with shift reagent (+)-Eu(hfc)$_3$.
[d] The absolute configuration was not determined.

It is of interest to understand the possible geometry of the transition state in dioxirane epoxidations. A spiro transition state was proposed by Baumstark,[26] based on the observation that *cis*-olefins were more reactive than the corresponding *trans*-olefins for epoxidation using dimethyldioxirane. In addition, computational studies showed that the spiro transition state is favored versus the planar transition state for the epoxidation of 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.[27] In our study, the proposed mechanism is presented in Scheme 7 for the *trans*-stilbene epoxidation catalyzed by ketone **18**. The corresponding dioxirane of ketone **18** has two diastereomeric oxygens, and the equatorial oxygen is likely to be sterically more accessible for olefin approach.[4c] If the reaction proceeds via a spiro mode, (*R*,*R*)-stilbene oxide is expected to be favored (spiro-1 vs spiro-2). In the present study, it is found that (*R*,*R*)-stilbene oxide is produced predominantly, which supports the spiro transition state proposed.



Scheme 7. The spiro transition states for *trans*-stilbene epoxidation catalyzed by ketone **18**.

3. Conclusions

In this article we have reported a new backbone model for chiral ketones from sugar easily prepared from commercially available methyl α-D-mannopyranoside in four steps with high chemical yields. These are the first mannose-derived ketones to be described. The general structure of our ketones, methyl 2-*O*-alkyl-4,6-*O*-(*R*)-benzylidene-α-D-*arabino*-hexopyranoside-3-ulose, contains as a point of structural modification the tunable alkoxy group on position 2 of the sugar moiety, being the steric blocker.

The epoxidation reaction of *trans*- and trisubstituted olefins with these ketones were performed with satisfactory chemical yields (60–80%) and the percentages of recovery without loss of activity of ketones were good (70%), enabling their use in various catalytic cycles.

With regard to stereochemical yield, firstly we observed that these new ketones possess the same alkene sterofacial differentiation, which is opposite to the other sugar ketones previously described by us,[17,18] displaying enantioselectivity from low to good (30–90% ee). Secondly, we studied the effect of the size of the steric blocker on the stereochemical results of the process and we found that enantioselectivity was sensitive and decreased with the size of the steric blocker. Ketone **18** with the least bulky alkoxy group (OMe) displayed the best enantioselectivity (up to 90% ee).

The C-2 epimeric ketone, methyl 4,6-*O*-(*R*)-benzylidene-2-*O*-methyl-α-D-*ribo*-hexopyranoside-3-ulose, **23**, as well as the 2-deoxy-derivative **24**, as catalysts did not improve the ee's.

In summary the choice of the ketone with an alkoxy steric sensor of suitable size (OMe) and with the appropriate sugar configuration (*arabino*) would provide high values of stereoselectivity in the epoxidation of *trans*- and trisubstituted 1,2-diarylalkenes. Preliminary assays of epoxidation reaction of dialkyl olefins with this ketone gave moderate values of ee's.

4. Experimental

4.1. General

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. Silica gel 60 (230–400 ASTM) was used for all flash column chromatography. All solvents were reagent or analysis grade. Evaporations were conducted under reduced pressure. Reactions were monitored using thin-layer chromatography (TLC) on

aluminum-backed plates coated with Merck Kieselgel 60 F_{254} silica gel. Compounds were visualized by UVA radiation 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. Absolute configuration was assigned by comparison with the signal shifts reported in the literature for epoxides (**25**–**31**).[4b,9,23–28] The absolute configuration was also determined by comparing the sign of optical rotations with the reported ones.[4b,10,28–30]

4.2. Methyl 4,6-*O*-(*R*)-benzylidene-2-*O*-methyl-α-D-altropyranoside 12[19]

To a sodium methoxide (9.0 mmol) in methanol (15 mL) solution methyl 2,3-anhydro-4,5-*O*-(*R*)-benzylidene-α-D-allopyranoside **11** was added (3.0 mmol). The mixture was heated at reflux overnight. The reaction mixture was cooled at room temperature, poured into water (50 mL), and extracted with dichloromethane (3×20 mL). The organic extracts were dried ($MgSO_4$), filtered, and evaporated to dryness. Yield: 0.8 g (90%). The organic compound isolated was employed without purification in the oxidation reaction (see Section 4.4).

4.3. Synthesis of methyl 2-*O*-alkyl-4,6-*O*-(*R*)-benzylidene-α-D-mannopyranosides 14–17[21]

To a solution of methyl 4,6-*O*-(*R*)-benzylidene-α-D-mannopyranoside **13** (1.0 mmol) in dry CH_2Cl_2 (10 mL) were added tetrabutylammonium hydrogen sulfate catalytic (20–25 mg), sodium hydroxide (1.5 mmol), and the appropriate alkyl iodide (1.5 mmol). The reaction mixture was stirred and heated at 45 °C for 3 h. Then diluted with dichloromethane (20 mL), washed with water, dried ($MgSO_4$), filtered, and the filtrate evaporated to dryness.

*4.3.1. Methyl 4,6-O-(R)-benzylidene-2-O-ethyl-α-D-mannopyranoside (**14**)*[31]. The syrup obtained was purified by flash chromatography on silica gel (2:1 hexane–ethyl acetate) to give compound **14** (0.15 g, 50%) as a pale yellow syrup; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36–7.33 (5H, m, Ph), 5.57 (1H, s, PhC*H*), 4.77 (1H, d, $J_{1,2}$ 1.0 Hz, H-1), 4.26 (1H, dd, $J_{5,6e}$ 4.7 Hz, $J_{6e,6a}$ 10.1 Hz, H-6$_e$), 4.03 (1H, dt, $J_{2,3}$ 4.0 Hz, $J_{3,4}$=$J_{3,OH}$ 9.4 Hz, H-3), 3.80 (4H, m, H-4, H-5, H-6$_a$, OCH_AH$_B$CH$_3$), 3.66 (1H, dd, $J_{1,2}$ 1.3 Hz, $J_{2,3}$ 4.0 Hz, H-2), 3.61 (1H, m, OCH$_A$*H*$_B$CH$_3$), 3.39 (3H, s, OC*H*$_3$), 2.39 (1H, d, $J_{3,OH}$ 8.9 Hz, OH), 1.26 (1H, t, *J* 7.0 Hz, OCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.3–126.3 (Ph), 102.1 (Ph*C*H), 99.2 (C-1), 79.5 (C-4), 79.8 (C-2), 68.7 (C-6), 68.3 (C-3), 67.2 (O*C*H$_2$CH$_3$), 63.2 (C-5), 54.4 (OCH$_3$), 15.2 (OCH$_2$*C*H$_3$); MS (CI): *m*/*z* 311 (90%, [M+H]$^+$); HRMS (CI): [M+H]$^+$, found 311.1495. $C_{16}H_{23}O_6$ requires 311.1495.

*4.3.2. Methyl 2-O-benzyl-4,6-O-(R)-benzylidene-α-D-mannopyranoside (**15**)*[31]. The solid was purified by flash chromatography on silica gel (6:1 hexane–ethyl acetate) to give compound **15** (0.17 g, 45%) as a white solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.26 (10H, m, 2Ph), 5.57 (1H, s, PhC*H*), 4.76 (1H, d, J_{gem} 11.6 Hz, OCH_AH$_B$Ph), 4.75 (1H, d, $J_{1,2}$ 1.4 Hz, H-1), 4.70 (1H, d, J_{gem} 11.6 Hz, OCH$_A$*H*$_B$Ph), 4.26 (1H, dd, $J_{5,6e}$ 4.4 Hz, $J_{6e,6a}$ 9.8 Hz, H-6$_e$), 4.08 (1H, m, H-3), 3.91 (1H, t, $J_{5,6e}$=$J_{6e,6a}$ 9.8 Hz, H-6$_a$), 3.81 (3H, m, H-2, H-4, H-5), 3.36 (3H, s, OC*H*$_3$), 2.36 (1H, d, $J_{3,OH}$ 8.5 Hz, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7–126.3 (2Ph), 102.1 (Ph*C*H), 99.4 (C-1), 79.5 (C-2), 78.5 (C-4), 73.7 (O*C*H$_2$Ph), 68.8 (C-6), 68.7 (C-3), 63.3 (C-5), 54.9 (O*C*H$_3$); MS (CI): *m*/*z* 373 (60%, [M+H]$^+$); HRMS (CI): [M+H]$^+$, found 373.1639. $C_{21}H_{25}O_6$ requires 373.1651.

*4.3.3. Methyl 4,6-O-(R)-benzylidene-2-O-isopropyl-α-D-mannopyranoside (**16**).* The solid was purified by flash chromatography on silica gel with (4:1 hexane–ethyl acetate) to give compound **16** (0.17 g, 50%) as a white solid; [Found: C, 62.62; H, 7.45. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.46%]; mp 87–88 °C; $[\alpha]_D^{25}$ +47.1 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51–7.32 (5H, m, Ph), 5.57 (1H, s, PhC*H*), 4.69 (1H, d, $J_{1,2}$ 1.1 Hz, H-1), 4.24 (1H, dd, $J_{5,6e}$ 4.7 Hz, $J_{6e,6a}$ 10.2 Hz, H-6$_e$), 4.00 (3H, m, H-3, H-4, H-6$_a$), 3.63 (1H, dd, $J_{1,2}$ 1.2 Hz, $J_{2,3}$ 4 Hz, H-2), 4.00 (1H, dt, $J_{3,4}$=$J_{3,OH}$ 9.5 Hz, $J_{2,3}$ 4.0 Hz, H-3), 3.79 [4H, m, H-4, H-5, H-6$_a$, OC*H*(CH$_3$)$_2$], 3.73 (1H, dd, $J_{1,2}$ 1.2 Hz, $J_{2,3}$ 4.0 Hz, H-2), 3.38 (3H, s, OC*H*$_3$), 2.28 (1H, d, $J_{3,OH}$ 8.9 Hz, OH), 1.22 [6H, m, OCH(C*H*$_3$)$_2$]; ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.4–126.3 (Ph), 102.1 (Ph*C*H), 100.5 (C-1), 79.6 (C-2), 77.2 [O*C*H(CH$_3$)$_2$], 73.0 (C-3), 68.8 (C-3), 68.2 (C-6), 63.2 (C-5), 54.8 (OCH$_3$), 22.9–22.1 [OCH(*C*H$_3$)$_2$]; MS (CI): *m*/*z* 325 (80%, [M+H]$^+$); HRMS (CI): [M+H]$^+$, found 325.1657. $C_{17}H_{25}O_6$ requires 325.11651.

*4.3.4. Methyl 4,6-O-(R)-benzylidene-2-O-isobuyl-α-D-mannopyranoside (**17**).* The syrup was purified by flash chromatography on silica gel with (5:1 hexane–ethyl acetate) to give compound **17** (0.2 g, 60%) as a pale yellow syrup; $[\alpha]_D^{25}$ −3.6 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36–7.26 (5H, m, Ph), 5.58 (1H, s, PhC*H*), 4.77 (1H, d, $J_{1,2}$ 1.2 Hz, H-1), 4.25 (1H, dd, $J_{5,6e}$ 5.3 Hz, $J_{6e,6a}$ 9.9 Hz, H-6$_e$), 4.06 (1H, dt, $J_{2,3}$ 3.9 Hz, $J_{3,4}$=$J_{3,OH}$ 9.4 Hz, H-3), 3.78 (3H, m, H-4, H-5, H-6$_a$), 3.63 (1H, dd, $J_{1,2}$ 1.2 Hz, $J_{2,3}$ 4.0 Hz, H-2), 3.43 [1H, m, OCH_AH$_B$CH(CH$_3$)$_2$], 3.39 (3H, s, OC*H*$_3$), 3.31 [1H, m, OCH$_A$*H*$_B$CH(CH$_3$)$_2$], 2.38 (1H, d, $J_{3,OH}$ 9.7 Hz, OH), 1.92 [1H, m, OCH$_2$C*H*(CH$_3$)$_2$], 0.94 [6H, m, OCH$_2$CH(C*H*$_3$)$_2$]; ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.3–126.3 (Ph), 102.1 (Ph*C*H), 98.9 (C-1), 79.6 (C-4), 79.1 (C-2), 78.4 [OCH$_2$CH(CH$_3$)$_2$], 68.8 (C-6), 68.5 (C-3), 63.2 (C-5), 54.9 (OCH$_3$), 28.7 [OCH$_2$*C*H(CH$_3$)$_2$], 19.2 [OCH$_2$CH(*C*H$_3$)$_2$]; MS (CI): *m*/*z* 339 (50%, [M+H]$^+$); HRMS (CI): [M+H]$^+$, found 339.1808. $C_{18}H_{27}O_6$ requires 339.1807.

4.4. Synthesis of methyl 2-*O*-alkyl-4,6-*O*-(*R*)-benzylidene-α-D-*arabino*-hexopyranoside-3-uloses 18–22

To a solution of the appropriate methyl 2-*O*-alkyl-4,6-*O*-(*R*)-benzylidene-α-D-hexopyranoside **12**, **14**–**17** (1.0 mmol) in dry dichloromethane (20 mL) were added pyridinium chlorochromate (2.0 mmol) and molecular sieves 3 Å (5 g). The reaction mixture was stirred overnight at room temperature. After TLC showed that the reaction was finished, the mixture was diluted with diethylether (20 mL) and filtered through a column with silica–$CaSO_4$ (10%).

*4.4.1. Methyl 4,6-O-(R)-benzylidene-2-O-methyl-α-D-arabino-hexopyranoside-3-ulose (**18**)*[22]. The filtrate was evaporated to dryness to give compound **18** (0.25 g, 84%) as a pale yellow syrup; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.36 (5H, m, Ph), 5.60 (1H, s, PhC*H*), 4.99 (1H, d, $J_{1,2}$ 1.0 Hz, H-1), 4.80 (1H, d, $J_{4,5}$ 9.7 Hz, H-4), 4.38 (1H, dd, $J_{5,6e}$ 4.7 Hz, $J_{6e,6a}$ 10.1 Hz, H-6$_e$), 4.10 (1H, dt, $J_{5,6e}$ 4.7 Hz, $J_{4,5}$=$J_{5,6a}$ 9.8 Hz, H-5), 4.00 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.2 Hz, H-6$_a$), 3.66 (1H, d, $J_{1,2}$ 1.0 Hz, H-2), 3.42 (3H, s, OC*H*$_3$), 3.40 (3H, s, OC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.1 (C=O), 136.5–126.3 (Ph), 103.1 (C-1), 102.2 (Ph*C*H), 85.2 (C-2), 80.9 (C-4), 69.3 (C-6), 66.3 (C-5), 58.0 (OCH$_3$), 55.1 (OC*H*$_3$); MS (CI): *m*/*z* 295 (50%, [M+H]$^+$). HRMS (CI): [M+H]$^+$, found 295.1183. $C_{15}H_{19}O_6$ requires 295.1182.

*4.4.2. Methyl 4,6-O-(R)-benzylidene-2-O-ethyl-α-D-arabino-hexopyranoside-3-ulose (**19**).* The filtrate was evaporated to dryness to give compound **19** (0.2 g, 65%) as a pale yellow syrup; $[\alpha]_D^{25}$ +71.4 (*c* 1.0, CH_2Cl_2); ^{1}H NMR(500 MHz, $CDCl_3$): δ 7.52–7.35 (5H, m, Ph), 5.61 (1H, s, PhC*H*), 4.98 (1H, d, $J_{1,2}$ 1.0 Hz, H-1), 4.83 (1H, d, $J_{4,5}$ 9.7 Hz, H-4), 4.38 (1H, dd, $J_{5,6e}$ 4.6 Hz, $J_{6e,6a}$ 10.2 Hz, H-6$_e$), 4.08 (1H, dt, $J_{5,6e}$ 4.6 Hz, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-5), 4.00 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.2 Hz, H-6$_a$), 3.77 (1H, d, $J_{1,2}$ 1.0 Hz, H-2), 3.57 (2H, m, OCH_2CH$_3$), 3.40 (3H, s, OCH_3), 1.24 (3H, t, *J* 7.0 Hz, OCH$_2$CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.5 (C=O), 136.1–126.3 (Ph), 103.3 (C-1), 102.1 (Ph*C*H), 83.6

(C-2), 80.9 (C-4), 69.3 (OCH_2CH_3), 66.3 (C-6), 66.2 (C-5), 55.1 (CH_3O), 15.1 (OCH_2CH_3); MS (CI): *m/z* 309 (100%, $[M+H]^+$). HRMS (CI): $[M+H]^+$, found 309.1338. $C_{16}H_{21}O_6$ requires 309.1336.

*4.4.3. Methyl 2-O-benzyl-4,6-O-(R)-benzylidene-α-D-arabino-hexopyranoside-3-ulose (**20**).* The filtrate was evaporated to dryness to give compound **20** (0.3 g, 80%) as a white solid; [Found: C, 68.02; H, 6.22. $C_{21}H_{23}O_6$ requires C, 68.10; H, 5.99%]; mp 105–106 °C; $[\alpha]_D^{25}$ +48.1 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71–7.66 (10H, m, 2Ph), 5.60 (1H, s, PhC*H*), 4.99 (1H, d, $J_{1,2}$ 1.1 Hz, H-1), 4.87 (1H, d, $J_{4,5}$ 9.6 Hz, H-4), 4.67 (1H, d, J_{gem} 11.8 Hz, OCH_AH_BPh), 4.50 (1H, d, J_{gem} 11.8 Hz, OCH_AH_BPh), 4.38 (1H, dd, $J_{5,6e}$ 4.7 Hz, $J_{6e,6a}$ 10.2 Hz, H-6_e), 4.10 (1H, dt, $J_{5,6e}$ 4.6 Hz, $J_{4,5}$=$J_{5,6a}$ 9.8 Hz, H-5), 3.99 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 9.9 Hz, H-6_a), 3.87 (1H, d, $J_{1,2}$=1.3 Hz, H-2), 3.38 (3H, s, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0 (C=O), 136.5–126.3 (2Ph), 103.1 (C-1), 102.1 (PhCH), 82.6 (C-2), 81.0 (C-4), 72.2 (OCH_2Ph), 69.3 (C-6), 66.3 (C-5), 55.0 (OCH_3); MS (CI): *m/z* 371 (30%, $[M+H]^+$); HRMS (CI): $[M+H]^+$, found 371.1486. $C_{21}H_{22}O_6$ requires 371.1495.

*4.4.4. Methyl 4,6-O-(R)-benzylidene-2-O-isopropyl-α-D-arabino-hexopyranoside-3-ulose (**21**).* The filtrate was evaporated to dryness to give compound **21** (0.25 g, 77%) as a pale yellow syrup; $[\alpha]_D^{25}$ +53.4 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.26 (5H, m, Ph), 5.61 (1H, s, PhC*H*), 4.91 (1H, d, $J_{1,2}$ 1.0 Hz, H-1), 4.85 (1H, d, $J_{4,5}$ 9.6 Hz, H-4), 4.37 (1H, dd, $J_{6e,6a}$ 10.2 Hz, $J_{5,6e}$ 4.4 Hz, H-6_e), 4.08 (1H, dt, $J_{5,6e}$ 4.4 Hz, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-5), 4.00 (1H, t, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-6_a), 3.86 (1H, d, $J_{1,2}$ 1.4 Hz, H-2), 3.37 [1H, m, *J* 6.2 Hz, C*H*$(CH_3)_2$], 3.39 (3H, s, OCH_3), 1.19 [6H, m, $OCH(CH_3)_2$]; ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.8 (C=O), 139.6–126.4 (Ph), 103.8 (C-1), 102.1 (PhCH), 81.5 (C-2), 80.9 (C-4), 76.7 [O*C*H$(CH_3)_2$], 69.3 (C-6), 66.3(C-5), 55.0 (OCH_3), 22.8, 21.5 [OCH($CH_3)_2$]; MS (CI): *m/z* 323 (60%, $[M+H]^+$). HRMS (CI): $[M+H]^+$, found 323.1486. $C_{17}H_{23}O_6$ requires 323.1495.

*4.4.5. Methyl 4,6-O-(R)-benzylidene-2-O-isobutyl-α-D-arabino-hexopyranoside-3-ulose (**22**).* The filtrate was evaporated to dryness to give compound **22** (0.28 g, 83%) as a pale yellow syrup; $[\alpha]_D^{25}$ +70.9 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.36 (5H, m, Ph), 5.6 (1H, s, PhC*H*), 4.99 (1H, d, $J_{1,2}$ 1.2 Hz, H-1), 4.78 (1H, d, $J_{4,5}$ 9.6 Hz, H-4), 4.37 (1H, dd, $J_{5,6e}$ 4.6 Hz, $J_{6e,6a}$ 10.0 Hz, H-6_e), 4.08 (1H, dt, $J_{5,6e}$ 4.6 Hz, $J_{4,5}$=$J_{5,6a}$ 9.6 Hz, H-5), 4.08 (1H, t, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-6_a), 3.74 (1H, d, $J_{1,2}$ 1.2 Hz, H-2), 3.40 (3H, s, OCH_3), 3.26 [2H, m, $OCH_2CH(CH_3)_2$], 1.89 [1H, m, $OCH_2CH(CH_3)_2$], 0.92 [6H, m, $OCH_2CH(CH_3)_2$]; ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.3 (C=O), 136.5–126.3 (Ph), 103.2 (C-1), 102.2 (PhCH), 83.9 (C-2), 81.0 (C-4), 77.2 [$OCH_2CH(CH_3)_2$], 69.4 (C-6), 66.3 (C-5), 55.0 (OCH_3), 28.3 [$OCH_2CH(CH_3)_2$], 19.1 [$OCH_2CH(CH_3)_2$]; MS (CI): *m/z* 337 (10%, $[M+H]^+$). HRMS (EI): $[M]^{+\cdot}$, found 336.1574. $C_{18}H_{24}O_6$ requires 336.1573.

4.5. Synthesis of methyl 4,6-O-(R)-benzylidene-2-O-methyl-α-D-*ribo*-hexopyranoside-3-ulose 23[23]

To a solution of methyl 4,6-*O*-(*R*)-benzylidene-2-*O*-methyl-α-D-*arabino*-hexopyranoside-3-ulose **18**, (1.0 mmol) in ethanol (60 mL) was added triethylamine (3.0 mmol). The reaction mixture was heated at reflux for 5 h. Then, the solution was poured into water (150 mL) and extracted with dichloromethane (3×20 mL). The organic layer was dried ($MgSO_4$) and evaporated to dryness to give compound **23** (0.28 g, 70%) as a white solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.33 (5H, m, Ph), 5.53 (1H, s, PhC*H*), 5.19 (1H, dd, $J_{1,2}$ 4.3 Hz, ^4J 0.3 Hz, H-1), 4.39 (1H, dd, $J_{5,6e}$ 4.7 Hz, $J_{6e,6a}$ 10.3 Hz, H-6_e), 4.24 (1H, dd, $J_{4,5}$ 9.8 Hz, $^4J_{2,4}$ 1.4 Hz, H-4), 4.06 (1H, dt, $J_{5,6e}$ 4.7 Hz, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-5), 4.02 (1H, dd, $J_{1,2}$ 4.2 Hz, $^4J_{2,4}$ 1.4 Hz, H-2), 3.90 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.3 Hz, H-6_a), 3.54 (3H, s, OCH_3), 3.44 (3H, s, OCH_3); MS (CI): *m/z* 295 (60%, $[M+H]^+$).

4.6. Synthesis of methyl 4,6-O-(R)-benzylidene-2-deoxy-α-D-*erythro*-hexopyranoside-3-ulose 24[32]

To a solution of methyl 2,3-anhydro-4,6-*O*-(*R*)-benzylidene α-D-allopyranoside **11** (1.0 mmol) in THF (20 mL) was added $LiAlH_4$ (3.0 mmol). The mixture was heated at reflux for 8 h and cooled to room temperature. A saturated solution of sodium sulfate was added (3×0.3 mL), filtered and the filtrate was evaporated to dryness yielding compound **24** (0.25 g, 70%) as a white solid, that was used in the epoxidation reaction (see Section 4.4) without purification; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49–7.33 (5H, m, Ph), 5.56 (1H, s, PhC*H*), 5.11 (1H, dd, $J_{1,2a}$ 4.7 Hz, H-1), 4.35 (1H, dd, $J_{5,6e}$ 4.8 Hz, $J_{6e,6a}$ 10.3 Hz, H-6_e), 4.35 (1H, dd, $J_{4,5}$ 9.9 Hz, $^4J_{2a,4}$ 1.1 Hz, H-4), 4.12 (1H, dt, $J_{5,6e}$ 4.8 Hz, $J_{4,5}$=$J_{5,6a}$ 10.0 Hz, H-5), 3.89 (1H, t, $J_{5,6a}$=$J_{6e,6a}$ 10.5 Hz, H-6_a), 3.36 (3H, s, OCH_3), 2.81 (1H, ddd, $J_{1,2a}$ 4.7 Hz, $^4J_{2a,4}$ 1.1 Hz, J_{gem} 14.5 Hz, H-2_{ax}), 2.65 (1H, d, $J_{1,2e}$ 0.6, J_{gem} 14.5 Hz, H-2_e); MS (EI): *m/z* 264 (60%, $[M]^{+\cdot}$).

4.7. Reaction with alkyl triphenylphosphonium bromide

To a stirred solution of the appropriate alkyl triphenylphosphonium bromide (2 mmol) in THF (10 mL) under argon at −78 °C, was added butyllithium (2 mmol) dropwise and stirred for 1 h at −40 °C. Then a solution of ketone **31** (1 mmol) in THF (5 mL) was added and kept with stirring at −40 °C for 2 h. After, the reaction mixture was diluted with ethyl acetate (20 mL) and quenched with saturated ammonium chloride solution (15 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated to dryness.

*4.7.1. 1-Benzyloxy-2-benzyloxymethyl-pent-2-ene (**35**).* A syrup was obtained after flash chromatography using a mixture of hexane–ethyl acetate (15:1) as eluent. (0.16 g, 55%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37–7.29 (10H, m, 2Ph), 5.74 (1H, t, *J* 7.4 Hz, EtCH), 4.53, 4.52 (4H, 2br s, $2CH_2OPh$), 4.14, 4.09 (4H, 2br s, $2OCH_2C$), 2.17 (2H, q, *J* 7.4 Hz, CH_2), 1.04 (3H, t, *J* 7.4 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6–127.5 (2Ph), 138.63 ($2OCH_2C$), 132.4 (EtCH), 72.2, 72.1 ($2OCH_2Ph$), 72.9, 65.4 ($2OCH_2C$), 20.9 (CH_2), 14.3 (CH_3); MS (CI): *m/z* 297 (20%, $[M+H]^+$). HRMS (CI): $[M+H]^+$, found 297.1863. $C_{20}H_{25}O_2$ requires 297.1555.

*4.7.2. 1-Benzyloxy-2-benzyloxymethyl-tetradec-2-ene (**36**).* A syrup was obtained after flash chromatography using a mixture of hexane–ethyl acetate (40:1) as eluent. (0.23 g, 55%). δ 7.39–7.29 (10H, m, 2Ph), 5.74 (1H, t, *J* 7.4 Hz, $CH_3(CH_2)_{10}CH$), 4.45 (4H, br s, $2CH_2OPh$), 4.14, 4.09 (4H, 2br s, $2OCH_2C$), 2.12 (2H, c, *J* 7.4 Hz, CH_2), 1.42–1.29 [m, 18H, $(CH_2)_9$], 0.92 (3H, t, *J* 7.1 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6–127.5 (2Ph), 138.63 ($2OCH_2C$),132.8 [$CH_3(CH_2)_{10}CH$], 72.2, 71.9 ($2OCH_2Ph$), 72.9, 65.4 ($2OCH_2C$), 31.9–27.6 [$(CH_2)_9$], 20.9 (CH_2CH), 14.1 (CH_3); MS (EI): *m/z* 422 (30%, $[M]^{+\bullet}$). HRMS (EI): $[M]^{+\bullet}$, found 422.3183. $C_{29}H_{42}O_2$ requires 422.3185.

4.8. General procedure for the enantioselective epoxidation

To a solution of the alkene (**25**–**33**) (0.2 mmol) in 1,2-dimethoxyethane (5 mL) were added chiral ketones **18**–**24** (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 (2–3 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 methylindene), to afford the pure alkene epoxide. The eluent was changed to a mixture of hexane–ethyl acetate (2.5:1 for ketones **18** and **19**, 4.5:1 for **20**, 4:1 for **21** and **22**, 1:3.5 for **23**, 1.5:1 for **24**) and the chiral ketone was recovered in 70–75%.

4.8.1. (+)-(1R,2R)-trans-Stilbene oxide[10,28]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (10H, m, 2Ph), 3.88 [2H, s, 2CH(O)].

4.8.2. (+)-(1R,2R)-trans-α-Methylstilbene oxide[10,29]. ^{1}H 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).

4.8.3. (−)-(R)-Triphenylethylene oxide[10,28,29]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.1 (15H, m, 3Ph), 4.32 [1H, s, CH(O)].

4.8.4. (+)-(R)-1,1-Dimethyl-2-phenylethylene oxide[4b,17]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (5H, m, Ph), 3.85 [1H, s, CH(O)], 1.47 (3H, s, CH_3), 1.06 (3H, s, CH_3).

4.8.5. (+)-(1R,2R)-1-Phenylcyclohexene oxide[9,28,29]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (5H, m, Ph), 3.5 [1H, m, CH(O)], 2.3–2.2 (1H, m, CH_AH_B), 2.2–2.0 (1H, m, CH_AH_B), 2.0–1.9 (2H, m, CH_2), 1.5–1.4 (1H, m, CH_AH_B), 1.3–1.2 (1H, m, CH_AH_B).

4.8.6. (+)-(1R,2R)-2-Phenylindene oxide[17]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5–7.2 (9H, m, 2Ph), 4.33 [1H, dd, J 0.45, 1.3 Hz, CH(O)], 3.57 (1H, d, J_{gem} 17.7 Hz, CH_AH_B), 3.41 (1H, d, J_{gem} 17.7 Hz, CH_AH_B).

4.8.7. (+)-(1R,2R)-2-Methylindene oxide[24,30]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.2 (4H, m, Ar), 4.04 [1H, s, $CH(O)C(CH_3)CH_2$], 3.17 (1H, d, J 17.5 Hz), 2.92 (1H, d, J 17.5 Hz), 1.71 (3H, s, CH_3).

4.8.8. Dihydronaphtalene oxide[28,30]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.2 (4H, m, Ar), 3.85 [1H, d, J 4.5 Hz, $CH(O)CHCH_2$], 3.73 [1H, dd, J 4.3, 3.0 Hz, $CH(O)CHCH_2$], 2.80 (1H, m), 2.55 (1H, dd, J 6.0, 15.5 Hz), 2.43 (1H, m), 1.78 (1H, m).

4.8.9. (−)-(R)-Styrene oxide[4b,24,33]. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.4–7.3 (5H, m, Ph), 3.83 [1H, dd, J_{cis} 4.1 Hz, J_{trans} 2.5 Hz, $PhCH(O)CH_AH_B$], 3.12 [1H, dd, J 5.8 Hz, J_{cis} 4.1 Hz, $PhCH(O)CH_AH_B$], 2.77 [1H, dd, J 5.8 Hz, J_{trans} 2.5 Hz, $PhCH(O)CH_AH_B$].

4.8.10. (−)-1-Benzyloxy-2-benzyloxymethyl-pent-2-ene oxide ***37***. $[\alpha]_D$ −1.3 (c 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26–7.35 (10H, m, 2Ph), 4.59, 4.57, 4.54, 4.49 (4d, 4H, J_{gem} 12.0 Hz, $2OCH_2Ph$), 3.72, 3.71, 3.64, 3.60 [4d, 4H, J_{gem} 10.7 Hz, $2OCH_2C(O)$], 2.93 [1H, t, J 6.6 Hz, $EtC(O)H$], 1.56 (2H, m, CH_2), 1.05 (3H, t, J 7.5 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2–127.6 (2Ph), 138.1 [$2OCH_2C(O)$], 73.5, 73.4 ($2OCH_2Ph$), 71.0, 68.4 [$2OCH_2C(O)$], 61.6 [$EtCH(O)$], 21.3 (CH_2), 10.7 (CH_3); MS (CI): m/z 313 (15%, $[M+H]^+$). HRMS (CI): $[M+H]^+$, found 313.1802. $C_{20}H_{25}O_3$ requires 313.1804.

4.8.11. (−)-1-Benzyloxy-2-benzyloxymethyl-tetradec-2-ene oxide ***38***. $[\alpha]_D$ −1.7 (c 0.5, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29–7.39 (10H, m, 2Ph), 4.64–4.51, (m, 4H, $2OCH_2Ph$), 3.74, 3.73, 3.67, 3.63 [4d, 4H, J_{gem} 10.7 Hz, $2OCH_2C(O)$], 2.93 [1H, t, J 6.6 Hz, $CH_2C(O)H$], 2.49 [2H, m, $CH_2C(O)H$], 1.48–1.29 [m, 18H, $(CH_2)_9$], 0.97 (3H, t, J 6.7 Hz, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6–127.7 (2Ph), 138.63 ($2OCH_2C$), 73.5, 71.1 ($2OCH_2Ph$), 72.9, 68.2 ($2OCH_2C$), 61.2 [$CH_3(CH_2)_{10}C(O)$], 31.9–26.7 [$(CH_2)_9$], 22.7 (CH_2CH), 14.2 (CH_3); MS (EI): m/z 438 (20%, $[M]^{+\bullet}$). HRMS (EI): $[M]^{+\bullet}$, found 431.3130. $C_{29}H_{42}O_3$ requires 438.3134.

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Supplementary data

These data include ^{1}H and ^{13}C spectra of the precursors (**14**–**17**), the chiral ketones (**18**–**24**), the new alkyl olefins (**35** and **36**) and their epoxides (**37** and **38**). ^{1}H NMR spectra used for the determination of enantiomeric excesses in the epoxidation reactions of alkenes are also included. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.07.014. These data include MOL files and InChIKeys of the most important compounds described in this article.

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