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Catalytic asymmetric epoxidation of alkenes with arabinose-derived uloses

Tony K. M. Shing,* Yiu C. Leung and Kwan W. Yeung

Department of Chemistry, The Chinese University of Hong Kong, Shatin, Hong Kong, People's Republic of China

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Abstract—Four L-*erythro*-2-uloses were readily prepared from L-arabinose via a reaction sequence involving Fischer glycosidation, acetalization and oxidation. Bulky steric sensors at the anomeric center could enhance the stereoselectivity of the dioxirane epoxidation and one of the uloses performed with good enantioselectivity towards trans-stilbene (up to 90% ee). However, the catalysts decomposed during the epoxidation and the maximum chemical yield was only 13% under the basic conditions. Three L-*threo*-3-uloses could overcome the decomposition problem based on the electron withdrawing effect of the ester group(s) α to the ketone functionality. The best chemical yield was up to 93% using a ketone with two flanking ester groups. One of the improved uloses displayed moderate enantioselectivity towards trans-disubstituted and trisubstituted alkenes (40–68% ee).

1. Introduction

Catalytic asymmetric epoxidation of alkenes is a versatile synthetic method to introduce chirality into organic molecules. This protocol is useful in the synthesis of many natural products and bioactive compounds. Catalytic asymmetric epoxidation based on transition metal containing complexes is well developed and chiral epoxides could be obtained from allylic alcohols[1] and unfunctionalized *cis*-alkenes[2] with high enantioselectivity. In recent years, chiral dioxiranes[3–5] have become promising reagents for asymmetric epoxidation. The work reported by Shi and his co-workers are the most impressive.[5] Various types of alkenes have been epoxidized with good ee using chiral dioxiranes generated in situ from Oxone® and D-fructose-derived ketones.[5] However, L-fructose is not commercially available and its scarcity diminishes its attractiveness as the enantio-complement since a short and facile preparation of

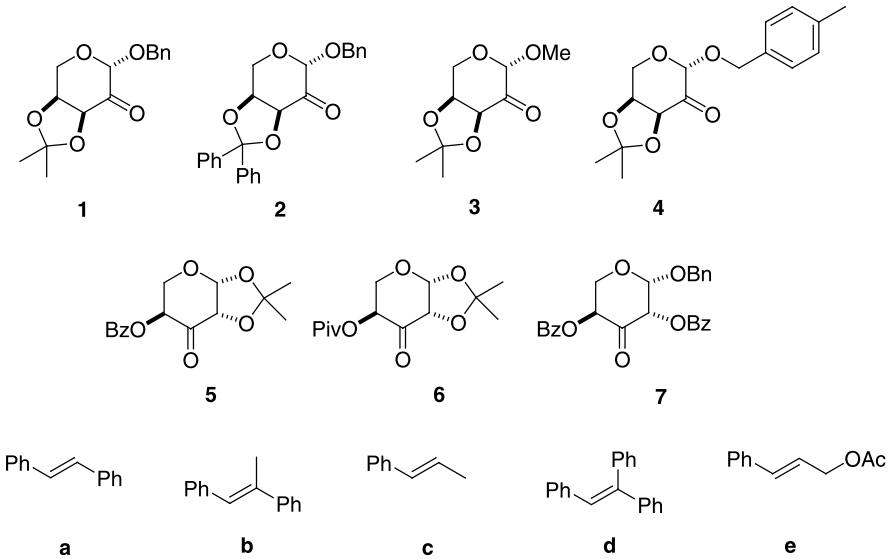

Figure 1. Catalysts and alkenes for asymmetric epoxidation.

Keywords: asymmetric epoxidation; ulose; arabinose.

* Corresponding author. Tel.: +852-2609-6344; fax: +852-2603-5057; e-mail: tonyshing@cuhk.edu.hk

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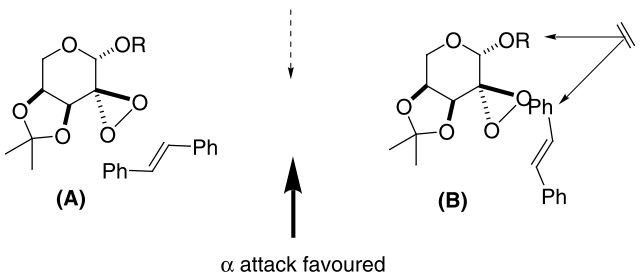


Figure 2. Design of catalyst based on steric effect and spiro transition state.

L-fructose is still a problem remaining to be solved.[5d] Other uloses derived from D-arabinose, D-mannose, D-glucose and L-sorbose were also reported by Shi,[5i] but they afforded poor chemical yields (0–57% yield) on epoxidation. The controlling factors and structural requirements for high enantioselectivity are not well understood[5p] and there is still ample room for the discovery of new ulose catalysts for asymmetric epoxidation. Our long-term interest in the application of carbohydrates in asymmetric synthesis has prompted us to search for efficient ulose catalysts to induce chirality with high ee in asymmetric epoxidation. The abundance of arabinose in the chiral pool and its commercial availability in large quantities for both enantiomers have made it the first choice for our studies. Over the years, we had described the use of arabinose-derived alcohols as chiral auxiliaries in asymmetric Diels–Alder reaction[6,7] and in asymmetric Hosomi–Sakurai reaction.[8] In this paper, we report our results on asymmetric epoxidation of unfunctionalized alkenes, using Oxone® as oxidant, catalyzed by L-*erythro*-2-uloses **1**–**4** and L-*threo*-3-uloses **5**–**7** (Fig. 1). The design of the catalyst is based on the established spiro transition states[4,5a,d,g] for the dioxirane epoxidation. The favoured transition state should result from the minimum steric intereaction between the dioxirane substituents and the substrate. Firstly, for uloses **1**–**4**, the approach of the alkenes substrate is controlled by the isopropylidene fused ring and therefore should be on the less hindered α-face. Following the same reasoning, the attack

Table 1. Study of ulose **1** in catalyzing in situ epoxidation of *trans*-stilbene

Entry	Conditions[a]	*p*H	mol%	Yield (%)[b]	ee (%)[c]
1	A	7	30	0	–
2	A	7	300	0	–
3	B	10	30	13	90
4	B	10	300	42	87

[a] Conditions A. Reactions were carried out at 0°C (bath temperature) with substrate (0.1 mmol), ketone, Oxone® (0.5 mmol) and $NaHCO_3$ (1.55 mmol) in CH_3CN: 4×10^{-4} M aqueous EDTA 2.5:1, v/v; Condition B. Reactions were carried out at 0°C (bath temperature) with substrate (0.1 mmol), ketone, Oxone® (0.14 mmol) and K_2CO_3 (0.58 mmol) in CH_3CN: 0.05 M $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous EDTA 2.5:1, v/v.

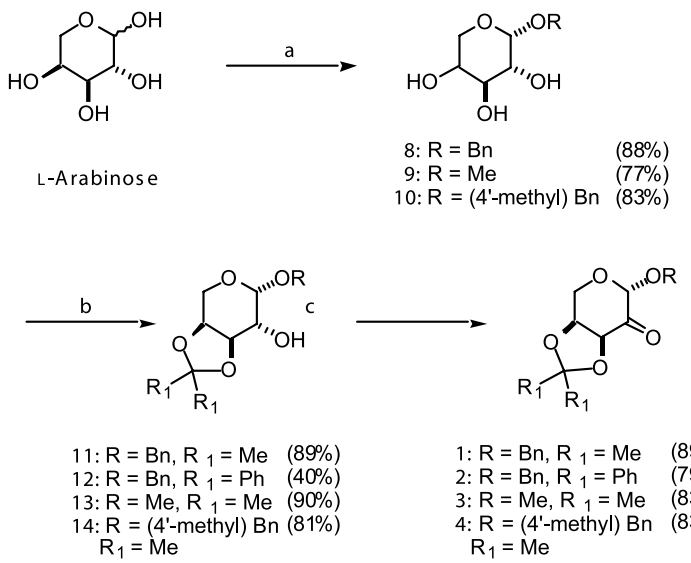
[b] Isolated yield.

[c] Enantioselectivity was determined by ^1H NMR analysis of the epoxide products directly with $Eu(hfc)_3$ shift reagent.

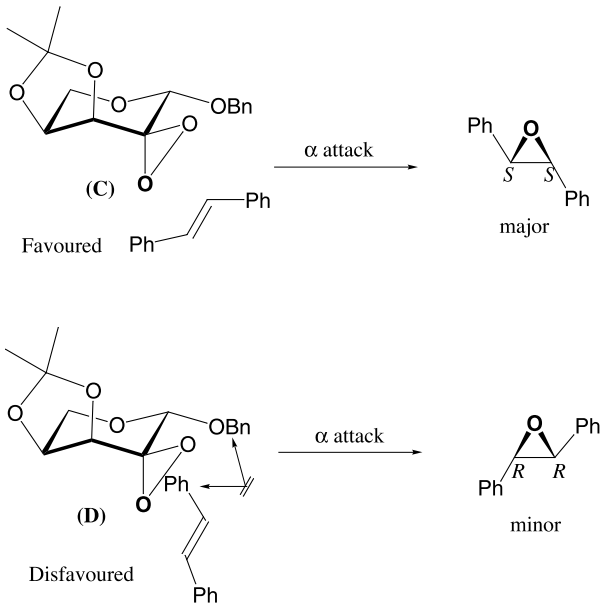
of the alkenes on the dioxiranes derived from uloses **5**–**7** should be on the less hindered β-face. Secondly, the favoured spatial orientation of the alkene should impose minimum steric interaction with the steric sensor, i.e. the aglycone in uloses **1**–**4** and the β-benzoate in uloses **5**–**7**. For an example, Figure 2 shows that the favoured transition state for the epoxidation should be (**A**) according to the reasoning presented above.

2. Results and discussion

Uloses **1**–**4** were readily prepared from L-arabinose via a standard reaction sequence involving Fischer glycosidation, acetalization, and oxidation (Scheme 1).[9] The glycosides **8**–**10**, prepared from their corresponding alcohols, were converted into their respective acetonides **11**, **13** and **14** on treatment with 2,2-dimethoxypropane (DMP) and acetone. Acetal **12** was prepared from the acetalization reaction with benzophenone using a Dean and Stark apparatus and the chemical yield was poor (up to 40% yield). The poor yield may be caused by the steric repulsion between the benzyl aglycone in glycoside **8** and benzophenone or by the lower



Scheme 1. Syntheses of uloses 1–4. Key: (a) ROH, AcCl (cat.), rt; (b) For **11**, **13** and **14**: H^+, DMP, acetone, rt; **12**: H^+, benzophenone, benzene, reflux; (c) PDC, AcOH (cat.), 4 Å MS, CH_2Cl_2, rt.



Scheme 2. Spiro transition states for the expoxidation catalyzed by ulose **1**.

reactivity of the carbonyl group in benzophenone. Oxidation of the free alcohol in acetals **11**–**14** with PDC gave uloses **1**–**4** in good yields. Uloses **1**–**4** had steric sensors of different sizes that may induce different degree of enantioselectivity in the epoxidation of alkenes.

With the catalysts in hand, we initiated our investigation using *trans*-stilbene as a test substrate and ulose **1** as the catalyst under different reaction conditions. The results are summarized in Table 1. In Table 1 (entries 1 and 2), no stilbene oxide was observed under neutral reaction conditions (conditions A). The starting material, stilbene, was recovered but the ulose catalyst **1** could not be isolated after column chromatography. Under the basic conditions, the chemical yield of stilbene oxide was 42% with 3 mole equiv. of ulose **1** (Table 1, entry 4). The yield was decreased to 13% with 30 mol% of **1** used (Table 1, entry 3) and the catalyst could not be recovered after work-up. This indicated that ulose **1** decomposed during the epoxidation but we could not isolate any decomposition products. Although ulose **1** did not afford good chemical yields, it did induce good enantioselectivity towards *trans*-stilbene and

Table 2. *p*H study of ulose **1** in catalyzing in situ epoxidation of *trans*-stilbene

Entry[a]	*p*H	Yield (%)[b]	ee (%)[c]	Config.[d]
1	7	No reaction	–	–
2	8	No reaction	–	–
3	9	12	90	(−)-(*S*,*S*)
4	10	13	89	(−)-(*S*,*S*)
5	11	No reaction	–	–
6	12	No reaction	–	–

[a] All reactions were carried out at 0°C (bath temperature) with substrate (1 mmol), ketone (0.3 mmol), Oxone® (2.5 mmol) in CH_3CN:buffer (2.5:1, v/v).
[b] Isolated yield.
[c] Enantioselectivity was determined by ^1H NMR analysis of the epoxide products directly with Eu(hfc)$_3$ shift reagent.
[d] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.[12]

Table 3. Study of uloses **1**–**4** in catalyzing in situ epoxidation of *trans*-stilbene

Entry[a]	Catalyst	Yield (%)[b]	ee (%)[c]	Config[d]
1	**1**	13	89	(−)-(*S*,*S*)
2	**2**	10	6	(−)-(*S*,*S*)
3	**3**	10	82	(−)-(*S*,*S*)
4	**4**	8	90	(−)-(*S*,*S*)

[a] All reactions were carried out at 0°C (bath temperature) with substrate (0.1 mmol), ketone (0.03 mmol), Oxone® (0.14 mmol) and K_2CO_3 (0.58 mmol) in CH_3CN: 0.05 M $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous EDTA 2.5:1, v/v.
[b] Isolated yield.
[c] Enantioselectivity was determined by ^1H NMR analysis of the epoxide products directly with Eu(hfc)$_3$ shift reagent.
[d] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.[12]

the ee of the stilbene oxide is up to 90% (Table 1, entry 3). The structure of **1** gives good stereochemical communication between the catalyst and the substrate. The preponderant formation of the (*S*,*S*)-enantiomer may be rationalized by the favoured transition state shown in Scheme 2. Firstly, the approach of the *trans*-stilbene should be on the α-face because the β-face is shielded by the acetonide fused ring. Secondly, the steric repulsion between the phenyl group and the benzyl aglycone in transition state (**D**) is absent in (**C**).

Experimental results (Table 1) show that *p*H is an important factor for the catalytic dioxirane epoxidation.[5d,f] Studies were carried out to investigate the optimum *p*H conditions for the epoxidation using ulose **1** as catalyst and the results are summarized in Table 2. The reaction was carried out at 0°C with 1 mmol of substrate and 30 mol% of ulose **1**. The epoxidation reactions essentially stopped after 2 h at each *p*H value studied. The *p*H was monitored by a *p*H meter and adjusted with a buffer solution. Epoxidation only occurred between *p*H 9 and 10 (Table 2, entries 3 and 4). The chemical yield of the epoxidation was still poor (13%). It is noteworthy that no catalyst could be recovered, hinting at decomposition of the catalyst during reaction.

According to our design of the catalyst shown in Figure 2, the change in the structure of the steric sensor, i.e. the aglycone moiety, may improve the enantioselectivity of the catalytic epoxidation. For this reason, studies were carried out to investigate the epoxidation catalyzed by uloses **2**–**4**. The reactions were carried out at 0°C with 0.1 mmol of substrate and 30 mol% of catalyst. The conditions were maintained at *p*H 9–10 in aqueous CH_3CN and the results are summarized in Table 3. The uloses **2**–**4** with steric sensors different from that in **1** did not improve the chemical yield of the catalytic epoxidation. The highest chemical yield was still only 13% (Table 3, entry 1), but the enantioselectivity was sensitive to the size of the steric sensor. Uloses **1** and **4** have steric sensors of similar size at the anomeric center (a benzyl group and a (4′-methyl)benzyl group). They both induced 90% ee towards *trans*-stilbene (Table 3, entries 1 and 4). When the benzyl sensor was replaced by a less bulky methyl group as in ulose **3**, the ee decreased to 82% (Table 3, entry 3). On the other hand, the size of the acetal group also can affect the enantioselectivity.

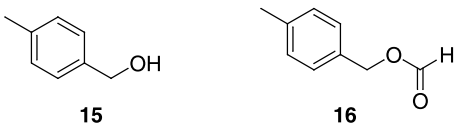


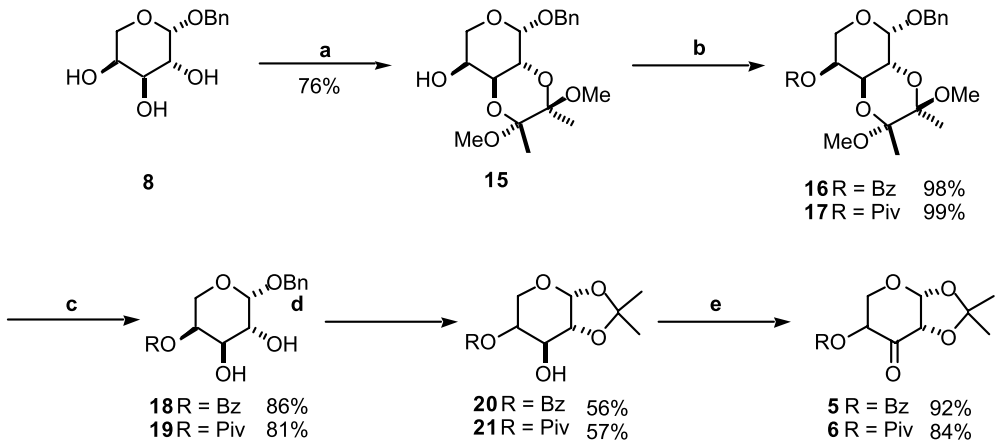
Figure 3. By-products from epoxidation catalyzed by ulose **4**.

The dramatic decrease of the ee (6%) for ulose catalyst **2** was the evidence (Table 3, entry 2).

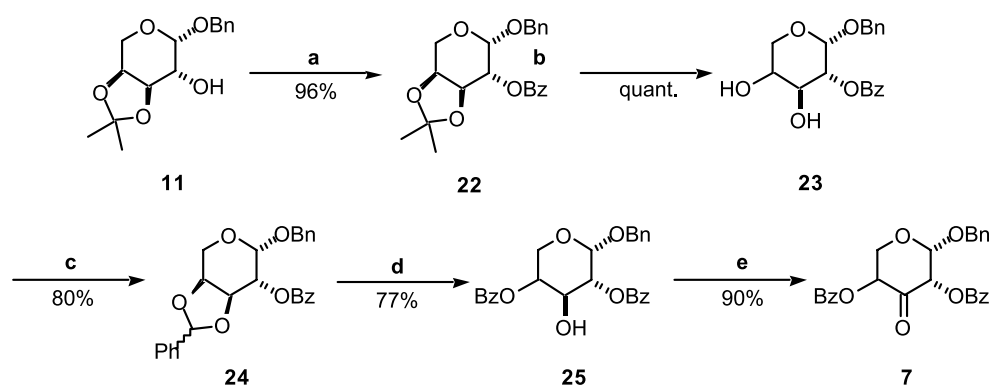
Compounds **15** and **16** (Fig. 3) were isolated from the epoxidation reaction of ulose **4** (Table 3, entry 4). It was evident that the poor chemical yield was caused by the decomposition of the catalyst but there was insufficient evidence that the Baeyer–Villiger reaction[10] was the major decomposition pathway for the L-*arabino*-2-ulose. Most research groups propose that Baeyer–Villiger reaction was the main decomposition pathway, but only in two cases were the lactone by-products successfully isolated.[3f,5j] They also gave evidence that the change of migratory aptitude of the α-carbon might inhibit the decomposition of the ketone catalyst.

The L-*erythro*-2-uloses **1**–**4** gave poor chemical yields for the catalytic dioxirane epoxidation. The reason was the decomposition of the catalyst during epoxidation. The stability of new ulose catalysts to overcome the decomposition was then considered. α-Benzoate and the more steric demanding α-pivalate uloses were synthesized as new catalysts. The ester group was chosen as the steric sensor because it could overcome the problem of decomposition. The electron withdrawing ester groups displayed poor migratory aptitude in Baeyer–Villiger reaction.[11] As a result, the decomposition problem of the ulose during epoxidation would be solved. L-*erythro*-3-uloses **5** and **6** were readily prepared from glycoside **8** as shown in Scheme 3 and dibenzoate ulose **7** was prepared from acetonide **11** as shown in Scheme 4. Uloses **5**–**7** were used as catalysts for the asymmetric epoxidation and the results are summarized in Table 4.

Ulose catalysts **5**–**7** afforded good chemical yields (76–93%) of the epoxides in catalytic asymmetric epoxidation (Table 4, entries 1–12). The C-4 ester steric sensor overcame the problem of decomposition and the catalyst could be recovered after epoxidation. The ees were poor for ulose **7** (up to 54% ee), especially for substrate **b** (16% ee, Table 4, entry 6). The keto group in ulose **7** is more electrophilic than that in **5** and in **6**. It should induce higher reactivity to form the dioxirane and hence better chemical yields resulted. The enantioselectivity of ulose **6** (entries 2, 5, 8, 10 and 12) was superior to that of ulose **5** (entries 1, 4, 7, 9 and 11). Changing the size of the steric sensor from the benzoate to the more bulky pivalate group enhanced the ee of the epoxides. The preponderant formation of the (*S*,*S*)-enantiomer may be rationalized by the favoured



Scheme 3. (a) Syntheses of uloses **5** and **6**. Key: (a) tetramethoxybutane, H^+, MeOH, reflux; (b) RCl, pyridine, DMAP(cat.); (c) 90% TFA, CH_2Cl_2; (d) i) H_2, Pd/C, EtOH–EtOAc; (ii) DMP, H^+, acetone; (e) PDC, AcOH (cat.), 4 Å MS, CH_2Cl_2, rt.



Scheme 4. Synthesis of ulose **7**. Key: (a) BzCl, pyridine, DMAP(cat.); (b) 90% TFA, CH_2Cl_2; (c) PhCHO, H^+, benzene, Dean–Stark trap; (d) NBS, AIBN(cat.), benzene–H_2O; (e) PDC, AcOH (cat.), 4 Å MS, CH_2Cl_2, rt.

Table 4. Study of uloses **5**–**7** in catalyzing in situ epoxidation of alkenes

Entry[a]	Catalyst	Substrate	Yield (%)[b]	ee (%)[c]	Config.[d]
1	**5**	**a**	78	54	(−)-(*S*,*S*)[12]
2	**6**	**a**	80	67	(−)-(*S*,*S*)[12]
3	**7**	**a**	87	54	(−)-(*S*,*S*)[12]
4	**5**	**b**	77	27	(−)-(*S*,*S*)[13]
5	**6**	**b**	82	43	(−)-(*S*,*S*)[13]
6	**7**	**b**	93	16	(−)-(*S*,*S*)[13]
7	**5**	**c**	82	24	(−)-(*S*,*S*)[14]
8	**6**	**c**	84	40	(−)-(*S*,*S*)[14]
9	**5**	**d**	76	67	(+)-(*S*)[13]
10	**6**	**d**	77	68	(+)-(*S*)[13]
11	**5**	**e**	93	48	(−)
12	**6**	**e**	89	59	(−)

[a] All reactions were carried out at room temperature with substrate (0.1 mmol), ketone (0.01 mmol), Oxone® (1 mmol) and $NaHCO_3$ (3.1 mmol) in CH_3CN:4×10^{-4} M aqueous EDTA (5:1, v/v) for 2.5 h.
[b] Isolated yield.
[c] Enantioselectivity was determined by ^{1}H NMR analysis of the epoxide products directly with Eu(hfc)$_3$ shift reagent.
[d] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.

transition state shown in Scheme 5. Firstly, the approach of the alkene should be from the top face (β-face) because the α-face is hindered by the acetonide fused ring. Secondly, the steric repulsion between the phenyl group and the C-4 ester group in transition state (**F**) is absent in (**E**). However, the stereochemical communication between the catalyst and substrate was still moderate (up to 68% ee for substrate **d**).

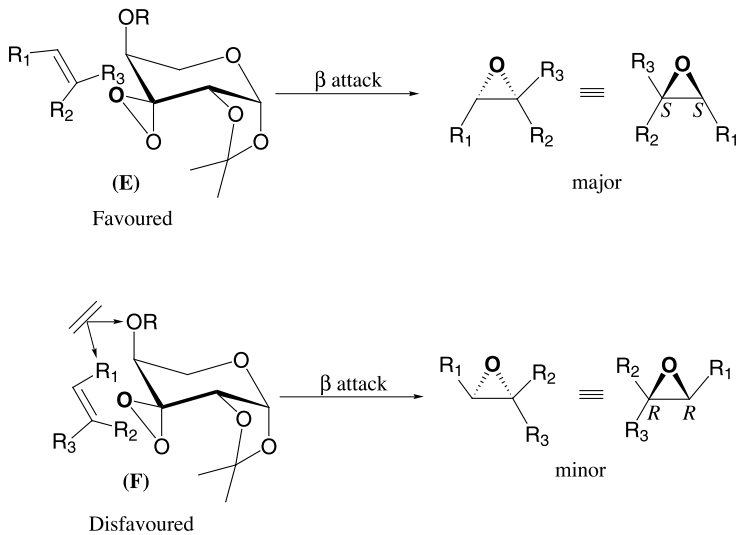
In summary, L-*erythro*-2-uloses **1**–**4** were easily prepared from L-arabinose. The anomeric aglycone steric sensors of suitable size (e.g. uloses **1** and **4**) exhibited good stereochemical communication towards *trans*-stilbene (up to 90% ee). The chemical yields of the epoxides catalyzed by uloses **1**–**4** were poor (up to 13% yield) because of the decomposition of the ulose catalysts during the reaction. L-*threo*-3-Uloses **5**–**7** were also readily prepared as catalysts and they could overcome decomposition based on the electron withdrawing effect of the ester group(s) at the α-position. The chemical yields were good (up to 93% for ulose **7**), but moderate results were obtained for enantioselectivity (up to 68% ee for ulose **6**). Thus, new L-*arabino*-ulose catalysts had to be explored in order to enhance the chemical yield and ee of the asymmetric dioxirane epoxidation. Research in this direction is in progress.

3. Experimental

Melting points were measured in degrees Celsius and uncorrected. IR spectra were recorded on a FT-IR spectrophotometer as neat films on KBr plates. Optical rotations were obtained at 589 nm. ^{1}H NMR spectra were measured at either 250 MHz or 500 MHz. ^{13}C NMR spectra were obtained at 62.9 MHz. 2D NMR spectra were measured at 500 MHz. Elemental analyses were performed at either the Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, China, or MEDAC Ltd, Department of Chemistry, Brunel University, UK. Mass spectra were obtained using EI or FAB technique. All reactions were monitored by analytical TLC being performed on Merck aluminum precoated plates of silica gel 60 F_{254} with detection by spraying with 5% w/v dodecamolybdophosphoric acid in ethanol and subsequent heating. All columns were packed wet using E. Merck silica gel 60 (230–400 mesh) as the stationary phase and eluted using the flash chromatographic technique. THF was distilled from sodium benzophenone ketyl under a nitrogen atmosphere.

3.1. General in situ epoxidation procedure under neutral conditions

To a stirred solution of alkene (0.1 mmol), ketone (0.01 mmol) and *n*-Bu_4NHSO_4 (0.5 mg) in CH_3CN (5 mL) containing a buffer (1 mL, 4×10^{-4} M aqueous EDTA) was added dropwise, concomitantly, a solution of Oxone® (1 mmol) in aqueous EDTA (3 mL, 4×10^{-4} M) and a solution of $NaHCO_3$ (3.1 mmol) in H_2O (3 mL) via two dropping funnels. The *p*H of the mixture was maintained at about 7–7.5 over a period of 2.5 h. The reaction mixture was then poured into water (10 mL), extracted with $CHCl_3$ (3×10 mL). The combined extracts were dried with



Scheme 5. Spiro transition states for the epoxidation catalyzed by ulose **5** or **6**.

anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to give a residue that was fractionated by flash column chromatography to give the epoxide.

3.2. General in situ epoxidation procedure under basic conditions

A stirred solution of alkene (0.1 mmol), ketone (0.03 mmol) and *n*-Bu_4NHSO_4 (0.5 mg) in CH_3CN (5 mL) containing a buffer (2 mL, 0.05 M $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous EDTA) was cooled to 0°C. A solution of Oxone® (0.14 mmol in 1 mL 4×10^{-4} M aqueous EDTA) and a solution of K_2CO_3 (0.58 mmol in 1 mL H_2O) were added dropwise over a period of 1.5 h. The reaction mixture was then poured into water (10 mL), extracted with $CHCl_3$ (3×10 mL). The combined extracts were dried with anhydrous $MgSO_4$, and filtered. After removal of solvent from the filtrate under reduced pressure, the residue was fractionated by flash column chromatography to give the epoxide.

3.3. Experimental procedure for epoxidation at different *p*H

A stirred solution of alkene (1 mmol), ketone (0.3 mmol) and *n*-Bu_4NHSO_4 (1 mg) in CH_3CN (25 mL) containing a buffer [(i) *p*H 7, 10 mL 4×10^{-4} M aqueous EDTA adjusted with 1.0 M $NaHCO_3$; (ii) *p*H 7.5–8.5, 10 mL 4×10^{-4} M aqueous EDTA adjusted with 1.0 M KOH; (iii) *p*H 8.5–10.5, 10 mL 0.05 M $Na_2B_4O_7{\cdot}10H_2O$ in 4×10^{-4} M aqueous EDTA adjusted with 1.0 M KH_2PO_4; (iv) *p*H 11–12, 10 mL 0.05 M K_2HPO_4/0.1 M NaOH, (2:1, v/v)] was cooled to 0°C. Oxone® (0.14 mmol in 10 mL 4×10^{-4} M aqueous EDTA) and a solution of K_2CO_3 (0.58 mmol in 10 mL H_2O) were added dropwise over a period of 1.5 h. The reaction mixture was then poured into water (10 mL), extracted with $CHCl_3$ (3×20 mL). The combined extracts were dried with anhydrous $MgSO_4$, and filtered. After removal of solvent from the filtrate under reduced pressure, the residue was fractionated by flash column chromatography to give the epoxide.

3.3.1. Benzyl β-L-arabinopyranoside (8). Acetyl chloride (7.5 mL, 109.5 mmol) was added dropwise to BnOH (130 mL, 1.3 mol) which was cooled in an ice-water bath with stirring. L-Arabinose (25 g, 166.5 mmol) was added and the reaction temperature was raised to rt. The resulting mixture was vigorously stirred at rt for 5 d. Et_2O (500 mL) was then added to precipitate the benzyl glycoside that was filtered and the crude white solid washed with Et_2O (100 mL). Recrystallization from EtOH gave the glycoside **8** (35.0 g, 88%) as white crystals: mp 177–178°C; R_f 0.66 ($MeOH-CHCl_3$, 5:1); $[\alpha]_D^{20}=+210.5$ (*c* 1.2, DMF) {lit.,[9] mp 172–173°C; $[\alpha]_D^{20}=+209$ (*c* 0.4, H_2O)}; IR (MeOH) 3280 (OH) cm^{-1}; ^1H NMR (CD_3OD) δ 7.61–7.48 (5H, m), 5.07 (1H, d, *J*=2.3 Hz), 4.92–4.72 (2H, d, *J*=12.0 Hz), 4.08–3.98 (4H, m), 3.78 (1H, dd, *J*=12.5, 2.5 Hz); ^{13}C NMR (d_6-DMSO) δ 138.1, 128.0, 127.3, 127.2, 98.9, 69.1, 68.7, 68.4, 68.2, 63.2; MS (EI) *m/z* 163 (M^+-77, 13.9), 131 (15.1), 92 (100).

3.3.2. Methyl β-L-arabinopyranoside (9). Acetyl chloride (2 mL, 29.4 mmol) was added dropwise to methanol (40 mL, 0.56 mol) at 0°C. After the addition, L-arabinose (5 g, 33.3 mmol) was added slowly in portions and the solution was maintained at 0–5°C for 1 h. Then, the resulting mixture was heated under reflux for 7 h and cooled at 0°C overnight. The crude white solid was filtered and was recrystallized from EtOH to give the glycoside **9** (4.2 g, 77%) as white crystals: mp 170–171°C; $[\alpha]_D^{22}=+240.7$ (*c* 0.7, DMF) {lit.,[9] mp 169–170°C; $[\alpha]_D^{20}=+244$ (*c* 1.7, H_2O)}; ^{13}C NMR (CD_3OD) δ 102.0, 70.8, 70.7, 70.3, 63.9, 55.8.

3.3.3. 4′-Methylbenzyl β-L-arabinopyranoside (10). Acetyl chloride (2 mL, 29.4 mmol) was added dropwise to 4′-methylbenzyl alcohol (30 g, 245.9 mmol) at 0°C. After the addition, L-arabinose (5 g, 33.3 mmol) was added slowly and the solution was maintained at 0–5°C for 1 h. The resulting mixture was vigorously stirred at 65°C for 5 days. Et_2O (100 mL) was then added to the cooled solution. The precipitate was filtered and was washed by Et_2O (20 mL). Recrystallization from EtOH gave the glycoside **10** (7.0 g, 83%) as white crystals: mp 178–180°C; R_f 0.74 ($MeOH-CHCl_3$, 1:3); $[\alpha]_D^{20}=+223$ (*c* 1.0, DMF) {lit.,[7] mp 178–180°C; $[\alpha]_D^{20}=+221.2$ (*c* 1.2, DMF)}; IR (MeOH) 3210 (OH) cm^{-1}; ^1H NMR (CD_3OD) δ 7.20 (4H, m), 4.89 (1H, d, *J*=2.5 Hz), 4.68 (1H, d, *J*=11.7 Hz), 4.49 (1H, d, *J*=11.7 Hz), 3.89–3.57 (5H, m), 2.33 (3H, s); ^{13}C NMR (d_6-DMSO) δ 135.0, 128.6, 127.5, 98.7, 69.1, 68.7, 68.3, 68.2, 63.2, 20.6; MS (EI) *m/z* 149 (M^+-105, 6.5), 106 (100), 105 (82).

3.3.4. Benzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (11). To a solution of glycoside **8** (2.8 g, 11.6 mmol) in acetone (30 mL) were added 2,2-dimethoxypropane (1.5 mL, 12.2 mmol) and *p*-TsOH (5 mg). The resulting suspension was stirred at rt for 12 h and all the suspension had dissolved. The reaction was quenched with NEt_3 and then concentrated in vacuo to give a crude yellow syrupy residue. Flash column chromatography (EtOAc–hexane, 1:1) of the residue gave a white solid which was recrystallized from EtOAc–hexane to give the acetonide **11** (2.9 g, 89%) as white crystals: mp 56–57°C; R_f 0.50 (EtOAc–hexane, 1:1); $[\alpha]_D^{20}=+217.8$ (*c* 1.2, $CHCl_3$) {lit.,[9] mp 54–56°C; $[\alpha]_D^{20}=+220$ (*c* 1, $CHCl_3$)}; IR ($CHCl_3$) 3440 (OH) cm^{-1}; ^{13}C NMR δ 137.1, 128.5, 127.9, 109.2, 96.9, 75.9, 72.9, 69.9, 69.8, 60.1, 27.8, 25.9; MS (EI) *m/z* 265 (M^+-15, 5.2), 189 (10.6), 91 (100).

3.3.5. Benzyl 3,4-*O*-diphenylmethylidene-β-L-arabinopyranoside (12). To a solution of **8** (1.0 g, 4.2 mmol) in benzene (50 mL) was added benzophenone (2.2 g, 12.3 mmol) and *p*-TsOH (5 mg). The resulting solution was heated under reflux with a Dean–Stark trap for 5 d. The solvent was then evaporated under reduced pressure, and the residue was flash column chromatographed (hexane–Et_2O, 3:1) to give a colorless syrup, **12** (0.2 g, 12%): R_f 0.58 (hexane–EtOAc, 1:1); $[\alpha]_D^{20}=+78.8$ (*c* 0.7, $CHCl_3$); IR (EtOAc) 3442 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.27 (15H, m), 4.93 (1H, d, *J*=3.0 Hz), 4.79 (1H, d, *J*=11.7 Hz), 4.55 (1H, d, *J*=11.7 Hz), 4.35 (1H, t, *J*=6.3 Hz), 4.18–4.15 (1H, m,), 2.35 (1H, brs); ^{13}C NMR ($CDCl_3$) δ 143.5, 137.6, 129.2, 128.8, 128.8, 128.7, 127.7, 126.8, 126.7, 97.3, 77.0, 74.0, 70.4, 70.0, 66.0, 60.4; MS (FAB) *m/z* 405 ($M+H^+$,81),

327 (50), 219 (6), 183 (100), 154 (6). Anal. Calcd for $C_{25}H_{24}O_5$: C, 74.24; H, 5.98. Found: C, 73.79; H, 5.90.

3.3.6. Methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (13). Acetonation of glycoside **9** (3.3 g, 20 mmol) in a similar manner as in the preparation of the acetonide **11** gave the acetonide **13** (3.7 g, 90%) as a syrup: R_f 0.4 (hexane–EtOAc, 1:1); $[\alpha]_D^{20}$=+218.8 (*c* 1.2, $CHCl_3$) {lit.,[9] $[\alpha]_D^{20}$=+220 (*c* 1, $CHCl_3$)}; MS (FAB) *m/z* 205 ($M+H^+$, 42), 173 (65), 154 (100), 137 (67).

3.3.7. 4′-Methylbenzyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside (14). Acetonation of glycoside **10** (3.2 g, 12.6 mmol) in a similar manner as in the preparation of acetonide **11** gave acetonide **14** (3.0 g, 81%) as white crystals: R_f 0.50 (hexane–EtOAc, 1:1): mp 179–180°C; $[\alpha]_D^{22}$=+119 (*c* 1.0, $CHCl_3$) {lit.,[7] mp 178–180°C; $[\alpha]_D^{22}$=+117.8 (*c* 1.2, $CHCl_3$)}; IR ($CHCl_3$) 3530 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20 (4H, m), 4.92 (1H, d, *J*=3.7 Hz), 4.75 (1H, d, *J*=11.7 Hz), 4.51 (1H, d, *J*=11.7 Hz), 4.25–4.16 (2H, m), 4.02 (1H, dd, *J*=13.1, 2.4 Hz), 3.93 (1H, dd, *J*=13.1, 1.2 Hz), 3.83–3.75 (1H, m), 2.36 (3H, s), 2.20 (1H, d, *J*=7.8 Hz), 1.54 (3H, s), 1.37 (3H, s); ^{13}C NMR ($CDCl_3$) δ 137.8, 134.0, 129.2, 128.1, 109.1, 96.8, 75.9, 72.9, 69.9, 69.6, 60, 27.8, 25.8, 21.1; MS (EI) *m/z* 279 (M^+-15, 1.0), 189 (3.1), 105 (100).

3.3.8. Benzyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosid-2-ulose (1). Acetonide **11** (1.8 g, 6.4 mmol) was dissolved in dry CH_2Cl_2 (15 mL). PDC (2.6 g, 7 mmol), powdered 4 Å molecular sieve (2 g) and glacial acetic acid (0.1 mL) were added slowly. The mixture was stirred at rt for 4 h and was suction filtered through a bed of silica gel. The filtrate was concentrated under reduced pressure to give a crude colorless syrup. Flash column chromatography (Et_2O–hexane, 3:7) gave ulose **1** (1.6 g, 89%) as a colorless syrup: R_f 0.50 (EtOAc–hexane, 1:1); $[\alpha]_D^{22}$=+236.7 (*c* 0.7, $CHCl_3$) {lit.,[9] $[\alpha]_D^{20}$=+239.6 (*c* 0.01, $CHCl_3$)}; MS (FAB) *m/z* 301 ($M+Na^+$, 54), 279 ($M+H^+$, 85), 263 (78), 171 (99), 101 (100).

3.3.9. Benzyl 3,4-*O*-diphenylmethylidene-β-L-*erythro*-pentopyranosid-2-ulose (2). Oxidation of acetonide **12** (3.8 g, 9.4 mmol) in a similar manner as in the preparation of ulose **1** gave ulose **2** (3.0 g, 79%) as a yellowish syrup: R_f 0.60 (EtOAc–hexane, 3:7); $[\alpha]_D^{20}$=+60.5 (*c* 0.3, $CHCl_3$); IR ($CHCl_3$) 1636 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.25 (15H, m), 4.93 (1H, s), 4.79 (1H, d, *J*=3 Hz), 4.76 (1H, d, *J*=2.4 Hz), 4.40 (1H, d, *J*=11.7 Hz), 4.45–4.47 (1H, m), 4.24–4.25 (2H, m); ^{13}C NMR ($CDCl_3$) δ 197.8, 129.3, 129.2, 129.0, 128.9, 128.8, 128.6, 127.2, 127.1, 127.0, 99.2, 78.2, 77.1, 70.7, 59.4; MS (FAB) *m/z* 403 ($M+H^+$, 38), 325 (31), 207 (40), 183 (100). Anal. Calcd for $C_{25}H_{22}O_5$: C, 74.61; H, 5.51. Found: C, 74.09; H, 5.63.

3.3.10. Methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosid-2-ulose (3). Oxidation of acetonide **13** (1.5 g, 7.3 mmol) in a similar manner as in the preparation of ulose **1** gave ulose **3** (1.2 g, 83%) as a yellowish syrup: R_f 0.40 (EtOAc–hexane, 1:1); $[\alpha]_D^{20}$=+136.5 (*c* 1.2, $CHCl_3$) {lit.,[9] $[\alpha]_D^{20}$=+138.3 (*c* 0.08, $CHCl_3$)}; MS (FAB) *m/z* 255 ($M+Na^+$, 19), 203 ($M+H^+$), 187 (27), 171 (50), 154 (37).

3.3.11. 4′-Methylbenzyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosid-2-ulose (4). Oxidation of acetonide **14** (1.7 g, 5.8 mmol) in a similar manner as in the preparation of ulose **1** gave ulose **4** (1.4 g, 83%) as a yellowish syrup: R_f 0.5 (EtOAc–hexane, 1:1); $[\alpha]_D^{20}$=+119.5 (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 1634 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20 (4H, m), 4.89 (1H, s), 4.76 (1H, d, *J*=11.4 Hz), 4.69 (1H, d, *J*=5.7 Hz), 4.56 (1H, d, *J*=11.4 Hz), 4.52 (1H, dd, *J*=5.7 and 2.1 Hz), 4.30 (1H, dd, *J*=13.5 and 2.1 Hz), 4.10 (1H, d, *J*=13.5 Hz), 2.36 (3H, s), 1.46 (3H, s), 1.39 (3H, s); ^{13}C NMR ($CDCl_3$) δ 199.3, 138.7, 133.4, 129.8, 129.7, 128.9, 128.8, 110.9, 99.4, 78.1, 75.9, 70.4, 59.1, 27.7, 26.6, 21.7; MS (FAB) *m/z* 315 ($M+Na^+$, 9), 293 ($M+H^+$, 0.4), 289 (7), 154 (72), 105 (100). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 66.21; H, 7.33.

3.3.12. Acetal 15. A suspension of **8** (0.5 g, 2.1 mmol) in methanol (15 mL) containing 2,2,3,3-tetramethoxybutane[15] (0.45 g, 2.5 mmol), trimethyl orthoformate (0.9 mL) and camphorsulfonic acid (5 mg) was heated under reflux for 12 h. The cooled reaction mixture was then treated with powdered $NaHCO_3$ (ca. 0.5 g), filtered and the filtrate concentrated under reduced pressure. The crude residue was flash chromatographed (hexane–EtOAc, 2:1) to afford acetal **15** as a white solid (0.56 g, 76%). Recrystallization from hexane–EtOAc gave white prisms: mp 140–141°C; $[\alpha]_D^{23}$=+5 (*c* 1.5, $CHCl_3$); R_f 0.45 (hexane–EtOAc, 1:1); IR ($CHCl_3$) 3469 (OH) cm^{-1}; ^1H NMR δ 7.42–7.26 (5H, m), 4.95 (1H, d, *J*=3.0 Hz), 4.75 (1H, d, *J*=12.3 Hz), 4.67 (1H, d, *J*=12.3 Hz), 4.19 (1H, dd, *J*=10.5, 3.0 Hz), 4.14 (1H, dd, *J*=10.5, 2.7 Hz), 3.93 (1H, m), 3.82 (1H, dd, *J*=12.6, 1.0 Hz), 3.70 (1H, dd, *J*=12.6, 1.5 Hz), 3.26 (3H, s), 3.22 (3H, s), 1.85 (1H, brs), 1.33 (3H, s), 1.31 (3H, s); ^{13}C NMR δ 137.6, 128.2, 127.9, 127.5, 100.2, 100.1, 96.8, 69.3, 68.0, 65.7, 65.1, 62.9, 47.9, 47.8, 17.7; MS (EI) *m/z* 322 (M^+-MeOH, 5), 291 (3), 91 (100). Anal. Calcd for $C_{18}H_{26}O_7$: C, 61.00; H, 7.39. Found: C, 60.87; H, 7.43.

3.3.13. Benzoate 16. To a solution of alcohol **15** (1.5 g, 4.24 mmol) in dry CH_2Cl_2 (20 mL) containing pyridine (0.67 mL, 8.48 mmol) and a catalytic amount of DMAP was added benzoyl chloride (0.6 mL, 5.09 mmol). The reaction mixture was stirred for 24 h at rt and was then poured into saturated NH_4Cl (2 mL). The aqueous phase was extracted with CH_2Cl_2 (3×10 mL) and the combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash column chromatography (hexane–Et_2O, 5:1) provided **18** (1.88 g, 97%) as a syrup: $[\alpha]_D^{23}$=+5.3 (*c* 1.2, $CHCl_3$); R_f 0.65 (hexane–Et_2O. 1:1); IR ($CHCl_3$) 1690 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07–7.29 (10H, m), 5.30 (1H, d, *J*=1.5 Hz), 5.02 (1H, d, *J*=3 Hz), 4.77 (1H, d, *J*=12.6 Hz), 4.71 (1H, d, *J*=12.6 Hz), 4.36 (1H, dd, *J*=10.5, 3 Hz), 4.31 (1H, dd, *J*=10.5, 3 Hz), 3.93 (1H, d, *J*=13 Hz), 3.81 (1H, dd, *J*=13, 1.5 Hz), 3.29 (3H, s), 3.27 (3H, s), 1.34 (3H, s), 1.22 (3H, s); ^{13}C NMR δ 166.2, 137.3, 132.8, 130.3, 129.7, 128.2, 127.9, 127.5, 99.8, 96.7, 70.4, 69.5, 65.6, 64.0, 61.6, 47.8, 47.7, 17.5; MS (EI) *m/z* 458 (M^+, 2), 444 (100). Anal. Calcd for $C_{25}H_{30}O_8$: C, 65.49; H, 6.59. Found: C, 65.38; H, 6.59.

3.3.14. Pivalate 17. To a solution of alcohol **15** (1.5 g,

4.24 mmol) in dry CH_2Cl_2 (20 mL) containing pyridine (0.67 mL, 8.48 mmol) and a catalytic amount (10 mg) of DMAP was added pivaloyl chloride (PivCl) (0.6 mL, 4.6 mmol). The reaction mixture was stirred for 24 h at rt and was then poured into saturated NH_4Cl (2 mL). The aqueous phase was extracted with CH_2Cl_2 (3×10 mL) and the combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash column chromatography (hexane–Et_2O, 9:1) provided ester **17** (1.83 g, 99%) as white crystals: mp 117–118°C; $[\alpha]_D^{23}$=+12 (*c* 0.3, $CHCl_3$); R_f 0.75 (hexane–Et_2O, 1:1); IR ($CHCl_3$) 1729 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.28 (5H, m), 5.15 (1H, m), 4.96 (1H, d, *J*=2.7 Hz), 4.74 (1H, d, *J*=12.6 Hz), 4.69 (1H, d, *J*=12.6 Hz), 4.19 (1H, dd, *J*=10.8, 3 Hz), 4.15 (1H, dd, *J*=10.8, 3 Hz), 3.85 (1H, d, *J*=12.3 Hz), 3.58 (1H, dd, *J*=12.9, 1.8 Hz), 3.24 (3H, s), 3.20 (3H, s), 1.30 (3H, s), 1.23 (9H, s), 1.19 (3H, s); ^{13}C NMR δ 177.8, 137.4, 128.2, 127.9, 127.5, 99.8, 99.6, 96.8, 69.5, 68.8, 65.5, 64.1, 61.8, 47.9, 47.5, 38.9, 27.0, 17.6, 17.5; MS (EI) *m/z* 406 (M^+–MeOH, 100), 348 (13). Anal. Calcd for $C_{23}H_{34}O_8$: C, 63.00; H, 7.81. Found: C, 63.21; H, 7.85.

3.3.15. Benzyl 4-*O*-benzoyl-β-L-arabinopyranoside (18). To a solution of benzoate **16** (720 mg, 1.57 mmol) in CH_2Cl_2 (10 mL) was added 90% aqueous TFA (0.5 mL) at rt. The mixture was stirred for 24 h at rt, and was then poured into saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and filtered. Concentration of the filtrate followed by flash chromatography (hexane–EtOAc, 1:1) gave the diol **18** (464 mg, 86%) as a syrup: $[\alpha]_D^{23}$=+222 (*c* 0.5, $CHCl_3$); R_f 0.3 (hexane–EtOAc, 1:1); IR ($CHCl_3$) 3395 (OH), 1723 (C=O) cm^{-1}; ^1H NMR δ 8.07–7.33 (10H, m), 5.42 (1H, s), 5.10 (1H, d, *J*=3.6 Hz), 4.79 (1H, d, *J*=11.7 Hz), 4.57 (1H, d, *J*=11.7 Hz), 4.09 (1H, dd, *J*=9.6, 3.3 Hz), 4.01–3.96 (2H, m), 3.88 (1H, dd, *J*=12.9, 1.8 Hz), 1.94 (2H, brs); ^{13}C NMR δ 166.5, 136.7, 133.3, 129.7, 129.5, 128.5, 128.4, 128.1, 97.7, 72.0, 69.9, 69.8, 68.9, 60.9; MS (EI) *m/z* 344 (M^+, 1), 253 (3), 91 (100). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.42; H, 5.99.

3.3.16. Benzyl 4-*O*-pivaloyl-β-L-arabinopyranoside (19). To a solution of pivalate **17** (60 mg, 0.13 mmol) in CH_2Cl_2 (10 mL) was added 90% aqueous TFA (0.5 mL) at rt. The mixture was stirred for 24 h, and was then poured into saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and filtered. Concentration of filtrate followed by flash chromatography (hexane–EtOAc, 2:1) gave the diol **19** (34 mg, 81%) as an oil: $[\alpha]_D^{23}$=+170 (*c* 1.3, $CHCl_3$); R_f 0.44 (hexane–EtOAc, 1:1); IR ($CHCl_3$) 3415 (OH), 1729 (C=O) cm^{-1}; ^1H NMR δ 7.34–7.29 (5H, m), 5.07 (1H, m), 4.97 (1H, d, *J*=3.6 Hz), 4.71 (1H, d, *J*=11.7 Hz), 4.50 (1H, d, *J*=11.7 Hz), 3.97 (1H, dd, *J*=9.9, 3.3 Hz), 3.81 (2H, m), 3.65 (1H, dd, *J*=12.9, 1.8 Hz), 2.47 (2H, brs); ^{13}C NMR δ 178.4, 136.9, 128.4, 127.9, 97.9, 71.1, 69.7, 69.6, 68.7, 60.9, 39.0, 27.0; MS (EI) *m/z* 324 (M^+, 4), 233 (23), 217 (100). Anal. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.47. Found: C, 62.76; H, 7.51.

3.3.17. 4-*O*-Benzoyl-1,2-*O*-isopropylidene-β-L-arabinopyranose (20). To a suspension of palladium-on-charcoal (10 mg) in ethanol (5 mL) was stirred at rt for 1 h under H_2 atmosphere (ballon). A solution of the diol **18** (340 mg, 1 mmol) in EtOAc (8 mL) was added and the resulting mixture was stirred for 24 h under H_2 atmosphere. The mixture was then filtered through celite and the filtrate was concentrated to give the triol that was used for next step without purification. The triol was dissolved in acetone (30 mL), 2,2-dimethoxypropane (0.15 mL, 1.2 mmol) and *p*-TsOH (10 mg) was added. The resulting suspension was stirred at rt for 12 h. The reaction was quenched with NEt_3 and then concentrated in vacuo to give a crude yellow syrup. Flash column chromatography (Et_2O–hexane, 1:1) gave acetonide **20** (164 mg, 56%) as a white solid: mp 138–139°C; $[\alpha]_D^{23}$=+20 (*c* 4.5, $CHCl_3$); R_f 0.37 (hexane–Et_2O, 1:1); IR ($CHCl_3$) 3489 (OH), 1716 (C=O) cm^{-1}; ^1H NMR δ 8.03–7.41 (5H, m), 5.43 (1H, d, *J*=3.3 Hz), 5.38–5.33 (1H, m), 4.44 (1H, t, *J*=3.6 Hz), 4.20 (1H, t, *J*=3.6 Hz), 4.02 (1H, dd, *J*=12, 4.8 Hz), 3.88 (1H, dd, *J*=12, 7.2 Hz), 2.41 (1H, brs), 1.58 (3H, s), 1.39 (3H, s); ^{13}C NMR δ 165.6, 133.5, 129.7, 129.3, 128.4, 111.1, 96.4, 77.8, 68.9, 67.2, 60.5, 27.7, 26.0; MS (EI) *m/z* 295 (M^++1, 8), 279 (46), 237 (100). Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.15; H, 6.12.

3.3.18. 1,2-*O*-Isopropylidene-4-*O*-pivaloyl-β-L-arabinopyranose (21). To a suspension of palladium-on-charcoal (10 mg) in ethanol (5 mL) was stirred at rt for 1 h under H_2 atmosphere. A solution of diol **19** (240 mg, 0.74 mmol) in EtOAc (8 mL) was added and the resulting mixture was stirred for 24 h under H_2 atmosphere. The mixture was then filtered through celite and the filtrate was concentrated to give the triol that was used for next step without purification. The triol was dissolved in acetone (30 mL), 2,2-dimethoxypropane (0.13 mL, 1 mmol) and *p*-TsOH (10 mg) was added. The resulting suspension was stirred at rt for 12 h. The reaction was quenched with NEt_3 and then concentrated in vacuo to give a crude yellow syrup. Flash column chromatography (Et_2O–hexane, 1:1) gave the acetonide **21** (116 mg, 57%) as a white solid: mp 52–53°C; $[\alpha]_D^{23}$=+0.1 (*c* 6.1, $CHCl_3$); R_f 0.32 (hexane–Et_2O, 1:1); IR ($CHCl_3$) 3496 (OH), 1723 (C=O) cm^{-1}; ^1H NMR δ 5.37 (1H, d, *J*=3 Hz), 5.09 (1H, m), 4.29 (1H, t, *J*=3.6 Hz), 4.14 (1H, t, *J*=3.6 Hz), 3.92 (1H, dd, *J*=11.7, 5.1 Hz), 3.70 (1H, dd, *J*=12, 6.9 Hz), 2.21 (1H, brs), 1.55 (3H, s), 1.34 (3H, s), 1.22 (9H, s); ^{13}C NMR δ 177.5, 111.0, 96.5, 77.8, 68.1, 67.3, 60.7, 38.9, 27.6, 27.0, 26.0; MS (EI) *m/z* 274 (M^+, 7), 259 (32), 217 (100). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.76; H, 8.44.

3.3.19. 4-*O*-Benzoyl-1,2-*O*-isopropylidene-β-L-*threo*-pentopyranos-3-ulose (5). To a solution of the alcohol **20** (104 mg, 0.37 mmol) was dissolved in dry CH_2Cl_2 (10 mL) were added PDC (167 mg, 0.44 mmol) and powdered 4 Å molecular sieve (170 mg). The mixture was stirred at rt for 4 h and was then suction filtered through a pad of silica gel. The filtrate was concentrated under reduced pressure to give a crude syrup that was flash column chromatographed (Et_2O–hexane, 1:2) to give ulose **5** (94 mg, 92%) as a white solid: mp 100–101°C; $[\alpha]_D^{23}$=+18 (*c* 0.4, $CHCl_3$); R_f 0.4 (hexane–Et_2O, 1:1); IR ($CHCl_3$) 1730 (C=O) cm^{-1}; ^1H NMR δ 8.11–7.44 (5H, m), 5.88 (1H, dd, *J*=6.3, 3.3 Hz),

5.71 (1H, d, J=4.2 Hz), 4.81 (1H, dd, J=13.2, 6.3 Hz), 4.45 (1H, d, J=4.2 Hz), 3.96 (1H, dd, J=13.2, 3.3 Hz), 1.74 (3H, s), 1.41 (3H, s); ^{13}C NMR δ 197.6, 165.4, 133.6, 130.0, 128.9, 128.5, 113.4, 101.4, 78.6, 73.2, 64.5, 26.0, 25.5; MS (EI) m/z 292 (M^+, 59), 234 (43), 105 (100). Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.66; H, 5.52.

3.3.20. 1,2-*O*-Isopropylidene-4-*O*-pivaloyl-β-L-*threo*-pentopyranos-3-ulose (6). Oxidation of the acetonide **21** (100 mg, 0.36 mmol) in a similar manner as in the preparation of ulose **5** gave ulose **6** (82 mg, 84%) as a white solid: mp 61–63°C; $[\alpha]_D^{23}$=−14 (c 0.8, $CHCl_3$); R_f 0.34 (hexane–Et_2O, 1:1); IR ($CHCl_3$) 1729 (C=O) cm^{-1}; ^{1}H NMR δ 5.69 (1H, d, J=4.2 Hz), 5.59 (1H, dd, J=6.3, 3.3 Hz), 4.67 (1H, dd, J=12.9, 6.3 Hz), 4.37 (1H, d, J=4.2 Hz), 3.79 (1H, dd, J=12.9, 3.3 Hz), 1.69 (3H, s), 1.38 (3H, s), 1.26 (9H, s); ^{13}C NMR δ 197.6, 177.3, 113.2, 101.3, 78.5, 72.3, 64.3, 38.7, 27.1, 26.0, 25.7; MS (EI) m/z 272 (M^+, 100), 256 (78). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.34; H, 7.40.

3.3.21. Benzyl 2-*O*-benzoyl-3,4-*O*-isopropylidene-β-L-arabinopyranoside (22). To a solution of acetonide **11** (1.9 g, 6.78 mmol) in dry CH_2Cl_2 (20 mL) containing pyridine (1 mL), and a catalytic amount (10 mg) of DMAP was added benzoyl chloride (0.9 mL, 8.0 mmol). The reaction mixture was stirred for 24 h at rt and was then poured into saturated NH_4Cl (2 mL). The aqueous phase was extracted with CH_2Cl_2 (3×10 mL) and the combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash column chromatography (hexane–Et_2O, 3:1) provided benzoate **22** (2.52 g, 97%) as a syrup: $[\alpha]_D^{23}$=+171 (c 1.1, $CHCl_3$); R_f 0.31 (hexane–Et_2O, 3:1); IR ($CHCl_3$) 1716 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.11–7.18 (10H, m), 5.18 (1H, dd, J=8.1, 3.3 Hz), 5.12 (1H, d, J=3.6 Hz), 4.75 (1H, d, J=12.3 Hz), 4.57 (1H, dd, J=8.1, 5.7 Hz), 4.51 (1H, d, J=12.3 Hz), 4.33 (1H, dt, J=5.7, 1.5 Hz), 4.09 (2H, d, J=1.8 Hz), 1.59 (3H, s), 1.38 (3H, s); ^{13}C NMR δ 165.9, 137.1, 133.1, 129.9, 129.7, 128.3, 128.2, 127.7, 127.4, 109.4, 95.4, 73.6, 73.0, 72.6, 69.5, 58.8, 28.0, 26.3; MS (EI) m/z 277 ($M^+-C_7H_7O$, 100). Anal. Calcd for $C_{22}H_{24}O_6$: C, 68.74; H, 6.29. Found: C, 69.07; H, 6.28.

3.3.22. Benzyl 2-*O*-benzoyl-β-L-arabinopyranoside (23). To a solution of benzoate **22** (1.30 g, 3.38 mmol) in CH_2Cl_2 (10 mL) was added 90% aqueous TFA (0.5 mL) at rt. The mixture was stirred for 24 h rt and was then poured into saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and filtered. Concentration of the filtrate followed by flash chromatography (hexane–EtOAc, 2:1) gave the diol **23** (1.16 g, quant. yield) as white crystals: mp 120–122°C; $[\alpha]_D^{23}$=+186 (c 0.3, $CHCl_3$); R_f 0.27 (hexane–EtOAc, 1:1); IR ($CHCl_3$) 3435 (OH), 1629 (C=O) cm^{-1}; ^{1}H NMR δ 8.07–7.23 (10H, m), 5.25 (1H, dd, J=9.9, 3.6 Hz), 5.18 (1H, d, J=3.6 Hz), 4.77 (1H, d, J=12.3 Hz), 4.55 (1H, d, J=12.3 Hz), 4.28 (1H, dd, J=9.9, 3.6 Hz), 4.09 (1H, m), 4.01 (1H, dd, J=12.9, 1.2 Hz), 3.84 (1H, dd, J=12.6, 1.8 Hz), 2.18 (2H, brs); ^{13}C NMR δ 166.8, 137.2, 133.2, 129.8, 129.5, 128.2, 127.6, 127.4, 96.0, 72.1, 69.5, 69.4, 67.8, 62.4; MS (EI) m/z 345 (M^++1, 100), 288 (80). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.29; H, 5.86.

3.3.23. Benzyl 2-*O*-benzoyl-3,4-*O*-benzylidene-β-L-arabinopyranoside (24). To a solution of the diol **23** (2.0 g, 5.8 mmol) in benzene (50 mL) was added benzylaldehyde (0.7 g, 6.6 mmol) and p-TsOH (10 mg). The resulting solution was heated under reflux with a Dean–Stark trap for 12 h and was then poured into saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified through flash column chromatography (hexane–Et_2O, 10:1) to give the major benzylidene isomer **24** (2.0 g, 80%) as a colorless syrup (1.3 g,): R_f 0.33 (hexane–Et_2O, 3:1); $[\alpha]_D^{23}$=+142 (c 0.7, $CHCl_3$); IR ($CHCl_3$) 1629 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.12–7.22 (15H, m), 6.27 (1H, s), 5.33 (1H, dd, J=8.4, 3.6 Hz), 5.22 (1H, d, J=3.6 Hz), 4.87 (1H, dd, J=8.1, 5.1 Hz), 4.77 (1H, d, J=12.3 Hz), 4.55 (1H, d, J=12.3 Hz), 4.33 (1H, dd, J=5.1, 1.8 Hz), 4.43 (1H, d, J=13.2 Hz), 4.07 (1H, dd, J=13.2, 2.4 Hz); ^{13}C NMR (CDCl3) δ 166.0, 138.7, 136.9, 133.7, 133.2, 130.1, 129.9, 129.5, 129.1, 128.3, 127.8, 127.5, 126.1, 102.8, 95.3, 74.3, 73.5, 69.9, 69.6, 58.8; MS (EI) m/z 433 (M+H+, 100), 432 (59), 325 (15). Anal. Calcd for C26H24O6: C, 72.21; H, 5.59. Found: C, 72.04; H, 5.67.

3.3.24. Benzyl 3,4-di-*O*-benzoyl-β-L-*threo*-pentopyranosid-3-ulose (7). A solution of the benzylidene **24** (1.4 g, 3.2 mmol) in benzene (50 mL) containing barium carbonate (5.0 g), NBS (0.95 g, 5.3 mmol), water (0.25 g, 13.9 mmol), and AIBN (10 mg) was heated under reflux for 1 h. The cooled mixture was then poured into saturated $NaHCO_3$ (5 mL). The aqueous layer was extracted with Et_2O (2×10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to give the crude dibenzoate **25** that was used for next step without purification. To a solution of the dibenzoate **25** (1.1 g, 2.45 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (1.1 g, 2.94 mmol) and powdered 4 Å molecular sieve (1 g). The mixture was stirred at rt for 4 h and was then suction filtered through a pad of silica gel. The filtrate was concentrated under reduced pressure to give a crude syrup. Flash column chromatography (Et_2O–hexane, 1:4) gave ulose **7** (0.98 g, 69% from **24**) as a syrup: $[\alpha]_D^{23}$=+181 (c 0.5, $CHCl_3$); R_f 0.51 (Et_2O–hexane, 1:1); IR ($CHCl_3$) 1729, 1709 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.08–7.24 (15H, m), 6.05 (1H, d, J=4 Hz), 5.48 (1H, d, J=4 Hz), 5.41 (1H, d, J=1.2 Hz), 4.80 (1H, d, J=12.3 Hz), 4.61 (1H, d, J=12.3 Hz), 4.30 (1H, dd, J=13.2, 1.2 Hz), 4.22 (1H, dd, J=13.2, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 193.4, 165.0, 136.2, 133.7, 133.5, 129.9, 129.8, 128.7, 128.6, 128.5, 128.4, 128.0, 127.6, 99.1, 76.8, 74.7, 69.5, 63.4; MS (EI) m/z 339 ($M^+-C_7H_7O$, 20), 338 (100). Anal. Calcd for $C_{26}H_{22}O_7$: C, 69.95; H, 4.97. Found: C, 69.89; H, 5.23.

3.3.25. Cinnamyl acetate epoxide.[16] ^{1}H NMR δ 7.27–7.16 (5H, m), 4.39 (1H, dd, J=12.3, 3.3 Hz), 4.00 (1H, dd, J=12.3, 5.7 Hz), 3.71 (1H, d, J=1.8 Hz), 3.19–3.15 (1H, m), 2.02 (3H, s); ^{13}C NMR δ 170.3, 136.0, 128.2, 128.1, 125.4,

63.9, 58.9, 56.0, 20.4; MS (FAB) *m/z* 193 (M^++1, 62), 133 (100).

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