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Arabinose-Derived Ketones as Catalysts for Asymmetric Epoxidation of Alkenes

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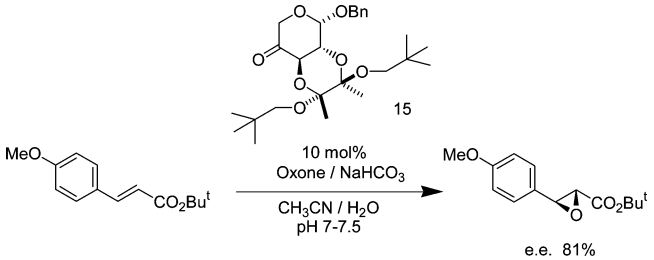

Readily available arabinose-derived ketones, containing a tunable butane-2,3-diacetal as the steric blocker, displayed increasing enantioselectivity (up to 90% ee) with the size of the acetal alkyl group in catalytic asymmetric epoxidation of trans-disubstituted and trisubstituted alkenes. The stereochemical communication between our ketone catalysts and the alkene substrates is mainly due to steric effect, and electronic effect involving $\pi-\pi$ interaction between phenyl groups of substrate and of catalyst did not appear to be operative in our system.

Introduction

Catalytic asymmetric epoxidation of alkenes is a versatile synthetic method to induce chirality into organic molecules, and many natural products contain epoxide units for their biological activities.[1] Catalytic enantioselective epoxidation based on transition metal-containing complexes is well developed, and chiral epoxides could be obtained from allylic alcohols[2] and unfunctionalized cis-alkenes[3] with high enantioselectivity. In recent years, chiral dioxiranes, generated in situ from Oxone and chiral ketones, have become promising reagents for asymmetric epoxidation of unfunctionalized alkenes.[4] The pioneering asymmetric epoxidation using chiral ketone catalysts was reported by Curci et al. in 1984.[5] Subsequently, elegant 11-membered C_2 symmetry biaryl ketones developed by the Yang group[6] afforded impressive enantioselectivity results that then have encouraged worldwide investigation on the subject. Now, many research groups,[7] including Adam,[8] Armstrong,[9] Denmark,[10] Shi,[11] and Solladié-Cavallo,[12] have achieved attractive results using different chiral ketone/oxone systems. A notable application of this epoxidation protocol has been described recently, using Yang's 11-membered C_2 symmetry binaphthyl ketone[6] as

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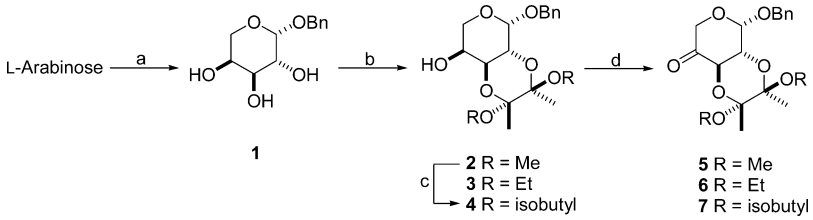
SCHEME 1. [19] Syntheses of Chiral Ketones from L-Arabinose[a]



[a] Reagents and conditions: (a) BnOH, AcCl (0.6 equiv), room temperature (rt), 5 d, 87%; (b) 2,2,3,3-tetramethoxybutane (1.2 equiv), $CH(OMe)_3$ (4 equiv), (±)-CSA (0.1 equiv), reflux, 12 h, 76% for **2**; 2,2,3,3-tetraethoxybutane (1.2 equiv), $CH(OEt)_3$ (4 equiv), (±)-CSA (0.1 equiv), reflux, 12 h, 50% for **3**; (c) 2-methyl-1-propanol (4 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 85%; (d) PDC (1.5 equiv), 3 Å MS, CH_2Cl_2, rt, 12 h, 90% for **5**, 85% for **6**, 95% for **7**.

the catalyst, in a practical synthesis methyl (2*R*,3*S*)-3-(4-methoxyphenyl)glycidate, a key intermediate for calcium antagonist diltiazem hydrochloride.[13] Our long-term interest in the application of carbohydrates in asymmetric synthesis has prompted us to search for a readily prepared ketone catalyst 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[14] and in asymmetric Hosomi−Sakurai reaction.[15] Our efforts toward enantioselective epoxidation of alkenes have furnished chiral ketone catalysts derived from D-glucose[16] as well as 2-uloses and 3-uloses derived from L-arabinose.[17] Recently, we reported in a communication that readily available arabinose-derived 4-uloses **5**−**7**, containing a tunable butane-2,3-diacetal[18] as the steric blocker and using Oxone as oxidant, displayed increasing enantioselectivity with the size of the acetal alkoxy group in catalytic asymmetric epoxidation of trans-disubstituted and trisubstituted alkenes.[19] These sugar ketones **5**−**7** were readily prepared from L-arabinose in three (for **5** and **6**) or four steps (for **7**), involving Fischer glycosidation, transacetalization, and oxidation reactions (Scheme 1).[19] According to this protocol, the methoxy substituents in bis-acetal **2** have now been exchanged to different alkoxy groups by transacetalization[20] under acidic conditions, and ketones with various acetals, such as an isopropyl group, an isopentyl, a neopentyl, a benzyl group, and a cyclohexylmethyl group, have been synthesized. The enantioselectivities displayed by these ketones **7**[21] and **13**−**17** in catalytic asymmetric epoxidation of olefins are reported in this article.

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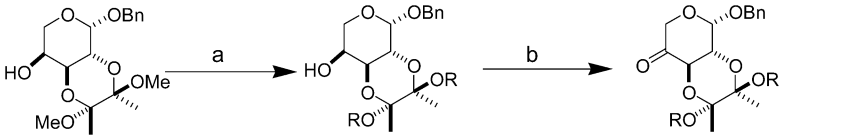
SCHEME 2. Preparation of Chiral Ketones via Transacetalization[a]



2

8 R = isopropyl
9 R = isopentyl
10 R = neopentyl
11 R = benzyl
12 R = cyclohexylmethyl

13 R = isopropyl
14 R = isopentyl
15 R = neopentyl
16 R = benzyl
17 R = cyclohexylmethyl

[a] Reagents and conditions: (a) 2-propanol (4 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 70% for **8**; 3-methyl-1-butanol (4 equiv) *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 80% for **9**; neopentyl alcohol (7 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 87% for **10**; benzyl alcohol (3.5 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 80% for **11**; cyclohexylmethyl alcohol (4 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 76% for **12**; (b) PDC (1.5 equiv), 4 Å MS, CH_2Cl_2, rt, 12 h, 87% for **13**, 89% for **14**, 96% for **15**, 84% for **16**, 92% for **17**.

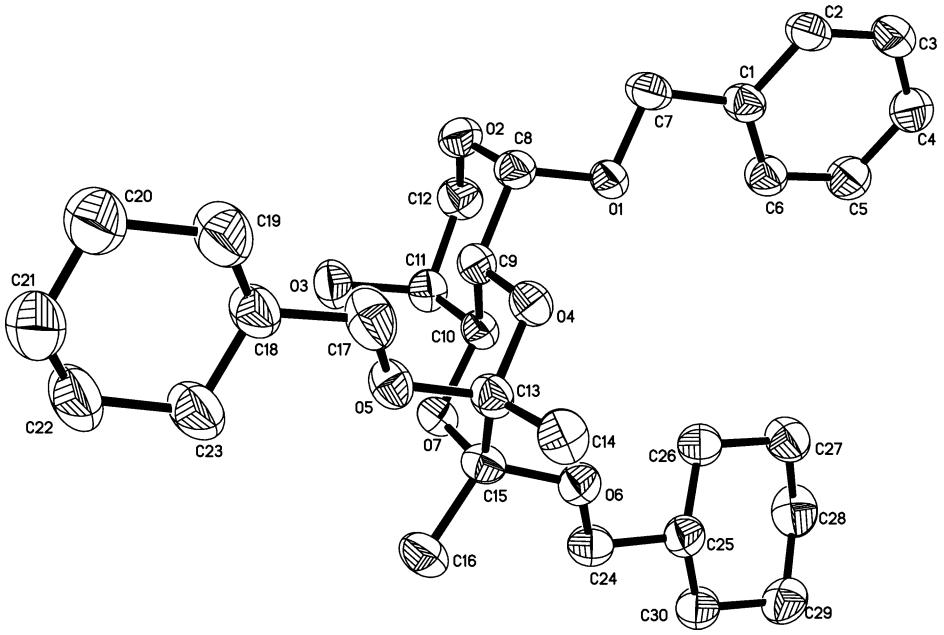


FIGURE 1. X-ray structure of alcohol **12** (ORTEP view).

Results and Discussion

Design of Ketones for Better Chiral Induction Capabilities in Asymmetric Epoxidation. Initially, we prepared ketones **5**−**7** to test our design of catalysts.[19] On the basis of the established spiro transition states[6i,11h] for chiral dioxirane epoxidation and of our previous studies,[16,17] we reasoned that the enantioselectivity should be sensitive to the size of the acetal steric blocker. Indeed, ketone **7** with a more bulky isobutyl acetal group consistently displayed better chiral induction than methyl acetal **5** (e.g., the ee with *trans*-stilbene could be improved from 42 to 65%).[19] Encouraged by these results, we therefore synthesized ketones with various acetals and investigated their chiral induction capabilities. Ketones **13**−**17** were readily accessible from dimethyl acetal **2** via a reaction sequence involving transacetalization and oxidation in good overall yields (Scheme 2). Thus, the methoxy groups in dimethyl acetal **2** were exchanged with 2-propanol, isopentanol, neopentanol, benzyl alcohol, and cyclohexylmethyl alcohol under acidic conditions to give diisopropyl acetal **8**, diisopentyl acetal **9**, dineopentyl acetal **10**, dibenzyl acetal **11**, and dicyclohexylmethyl acetal **12** in 70, 80, 87, 80, and 76%, respectively. The stereochemistry of bis-acetals **8**−**12** resulted from the thermodynamically controlled formation of a stable trans-decalin structure.[18] The constitution of alcohol **12** was confirmed by X-ray crystallography (Figure 1). Oxidation of the free alcohol in bis-acetals **8**−**12** with pyridinium dichromate (PDC) gave the respective ketones **13**−**17** in good yields. The relative stereochemistry of ketone **16** was also confirmed by X-ray crystallography (Figure 2). Ketones **13**−**17** had steric blockers, that is, the acetal alkoxy groups, of different sizes that might induce different degrees of enantioselectivity in catalytic epoxidation of alkenes.

With the new catalysts in hand, we began to study the effect of chain length of the branching carbon in the acetal on enantioselectivity of the catalytic epoxidation. Ketones **13** (isopropyl acetal, branching α to oxygen), **7** (isobutyl acetal, branching β to oxygen), and **14** (isopentyl acetal, branching γ to oxygen) had steric blockers with the same bulkiness at the termini but with different carbon chain length. The results are summarized in Table 1. As the carbon chain of the steric blockers became longer (from isopropyl group to isobutyl to isopentyl), enantioselectivity first increased and then decreased.

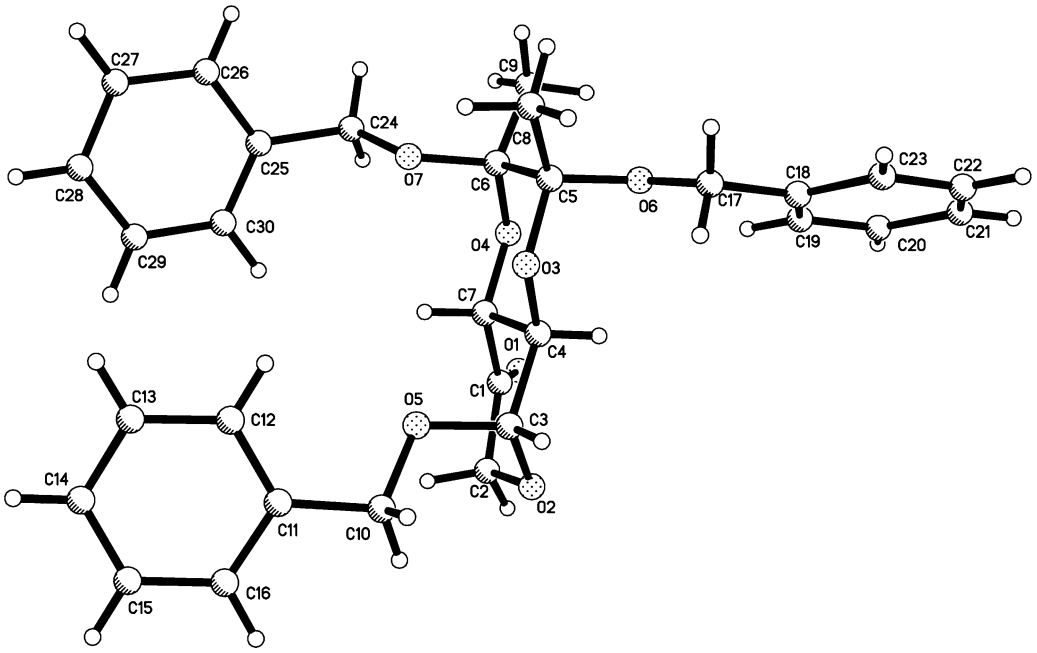


FIGURE 2. X-ray structure of ketone **16** (ORTEP view).

This means that steric blockers of appropriate carbon chain length could induce higher enantioselectivity. Ketone **7** performed better selectivity than ketones **13** and **14** (Table 1, entries 2, 5, 8, 11, and 14). Ketone **7** gave the highest 85% ee in the reaction with triphenylethylene (Table 1, entry 14). However, the enantioselectivities toward trans-disubstituted alkenes are still poor (Table 1, entries 2, 5, and 8).

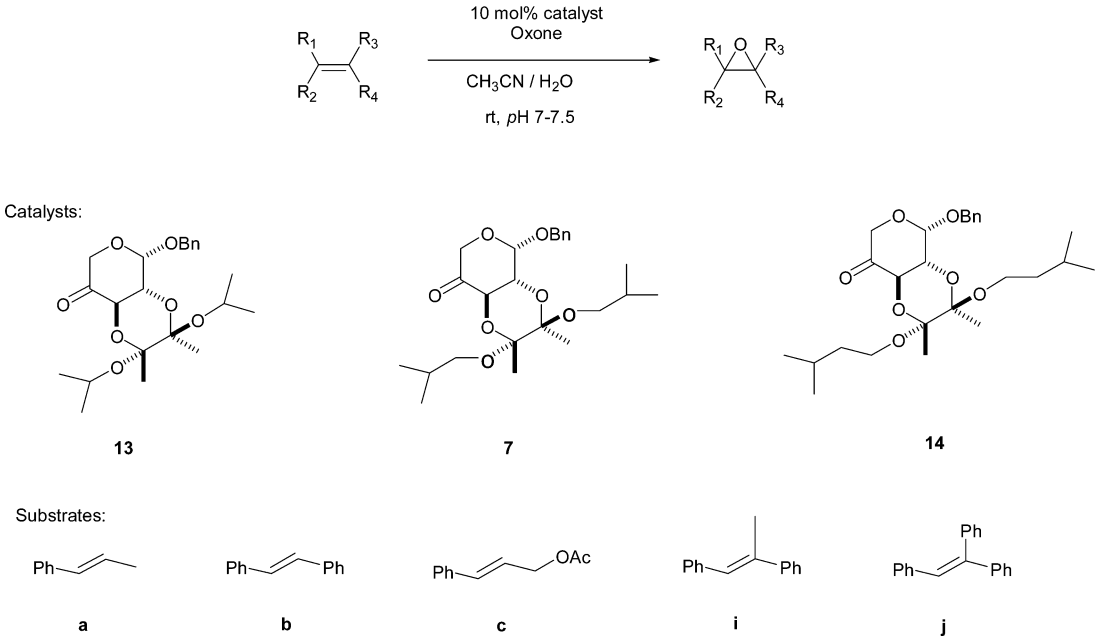
The above findings led us to prepare ketones **15**−**17**, all with acetal branching β to oxygen of the alkoxy group. The epoxidation reactions were carried out at 0 °C with 0.1 mmol of alkene and 10 mol % of catalyst in aqueous CH_3CN at almost neutral conditions (pH 7−7.5). The catalytic and chiral induction properties of **7**[21] and **15**−**17** with trans-disubstituted and trisubstituted alkenes were studied, and the results are summarized in Table 2. In all cases, the epoxides were isolated in high chemical yields (81−99% yield), indicating that all the ketones are efficient catalysts. In the enantioselective epoxidation of trans-disubstituted alkenes (Table 2, entries 5−32), ketone **15** with a more bulky neopentyl acetal group consistently displayed the best chiral induction (62−86% ee) among the ketones except for entries 1−4. The neopentyl group was thus demonstrated to be a good steric blocker to induce high degree of enantioselectivity in asymmetric epoxidation. A high ee of 86% was obtained with (*E*)-*tert*-butyl cinnamate (Table 2, entry 18). A high ee of 81% was also observed for (*E*)-*tert*-butyl 4-methoxycinnamate (Table 2, entry 26), which was better than Seki's result[13] (77% ee, using Yang's 11-membered C_2 symmetry binaphthyl ketone[6] as the catalyst). However, the ee for the asymmetric epoxidation of methyl *p*-methoxycinnamate (MPC) (Table 2, entry 30) was a moderate 62%. The resultant chiral epoxide, methyl (2*R*,3*S*)-3-(4-methoxyphenyl)glycidate, was a key intermediate for synthesizing diltiazem hydrochloride, a drug for the treatment of angina and hypertension.[13] Our results showed that the bulkiness of the ester moiety could affect the enantioselectivity in asymmetric epoxidation of cinnamates, a conclusion different from Seki's[13] findings which employed Yang's catalyst, and demonstrated that the more bulky *tert*-butyl esters gave higher ee than the corresponding methyl esters (Table 2, entries 25−32).

In the asymmetric epoxidation of trisubstituted alkenes (Table 2, entries 33−48), the enantioselectivity remained high for ketones **7** and **15**. Interestingly, ketone **7** performed even better in two cases (entries 37 and 41, with triphenylethylene, its ee was 90%, the highest ee reported for this series of arabinose-derived ketones).

Ketones **16** and **17** were prepared to study the electronic effect of our asymmetric epoxidation. It was interesting to find that, in our ketone-catalyzed epoxidation system, no significant $\pi-\pi$ interaction was observed between the phenyl group of the alkene and the benzyl moiety in ketone **16** for both trans-disubstituted and trisubstituted alkenes. In some cases (Table 2, entries 7, 8; 11, 12; 35, 36; and 43, 44), ketone **16** containing a benzyl acetal group afforded higher ee than ketone **17** with a cyclohexylmethyl group, whereas in other cases (entries 15, 16; 19, 20; 27, 28; and 39, 40), ketone **16** gave lower ee values. Our results are in contrast to Shi's findings[11c] that the attractive interaction between the phenyl group of the alkene and the oxazolidinone of the catalyst is important for ketone-catalyzed epoxidation. It is noteworthy that our ketones could be recovered in no less than 95% yield after workup and the recovered catalyst did not undergo epimerization.

With the best catalyst **15** for disubstituted alkenes in hand, we studied the effect of alcohol protecting group on enantioselectivity in the asymmetric epoxidation of (*E*)-hex-3-en-1-ol, and the results are summarized in Table 3. The enantioselectivity enhanced with the size of the protecting group, and hence the alkene bearing the most sterically demanding trityl group furnished the highest ee of 55% (Table 3, entry 4). It was surprising that the ee observed from using a TBS protecting group (Table 3, entry 3) was lower than that from using a benzyl

TABLE 1. Effect of Acetal Alkoxy Chain Length on Asymmetric Epoxidation of Alkenes Catalyzed by Ketones 7, 13, and 14



entry[a]	catalysts	substrates	yield (%)[b]	ee (%)[c]	configuration[d]
1	**13**	a	91	56	(−)-(*S*,*S*)[23]
2	**7**	a	92	68	(−)-(*S*,*S*)[23]
3	**14**	a	87	56	(−)-(*S*,*S*)[23]
4	**13**	b	92	51	(−)-(*S*,*S*)[22]
5	**7**	b	93	65	(−)-(*S*,*S*)[22]
6	**14**	b	94	54	(−)-(*S*,*S*)[22]
7	**13**	c	90	59	(−)-(*S*,*S*)
8	**7**	c	90	67	(−)-(*S*,*S*)
9	**14**	c	94	57	(−)-(*S*,*S*)
10	**13**	i	95	82	(−)-(*S*,*S*)[24]
11	**7**	i	95	83	(−)-(*S*,*S*)[24]
12	**14**	i	93	68	(−)-(*S*,*S*)[24]
13	**13**	j	87	69	(+)-(*S*)[24]
14	**7**	j	96	85	(+)-(*S*)[24]
15	**14**	j	95	80	(+)-(*S*)[24]

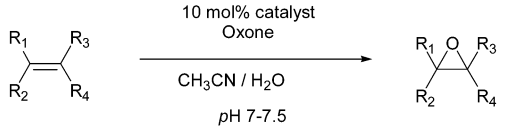
[a] All epoxidations were carried out at room temperature with substrate (0.1 mmol), ketone (0.01 mmol), Oxone (1 mmol), and $NaHCO_3$ (3.1 mmol) in CH_3CN/4 × 10^{-4} M aqueous EDTA (5:1, v/v) for 12 h. [b] Isolated yield. [c] Enantioselectivity was determined by ^1H NMR analysis of the epoxide products directly with shift reagent Eu(hfc)$_3$. [d] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.

protecting group (Table 3, entry 2) since the silyl group should be more bulky. Nevertheless, the ee of the asymmetric epoxidation of (*E*)-hex-3-en-1-ol could be improved from 16 to 55% by means of a trityl protecting group.

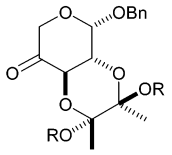
On the other hand, we found that when the double bond was closest to the protecting group, the ee would be the highest. We investigated the effect of the double bond position in the alkene substrate on enantioselectivity of (*E*)-hexenyl benzyl ethers, and the results are shown in Table 4. As the double bond was positioned gradually away from the protecting group, as shown in the benzyl ethers of (*E*)-hex-2-en-1-ol, (*E*)-hex-3-en-1-ol, and (*E*)-hex-4-en-1-ol, the ee of the asymmetric epoxidation would gradually decrease from 67 to 34%. On the basis of our results, the stereochemical communication between our ketone catalysts and the alkenes substrates is mainly due to steric effect.

To further investigate the possibility of $\pi-\pi$ interaction in our system, ketone **20**, which has a nonaromatic methoxy group at the anomeric center, was synthesized (Scheme 3). trans-Diol protection of methyl β-L-arabinopyranoside[17] gave dimethyl acetal **18**. The methoxy groups in dimethyl acetal **18** were exchanged with isobutanol to give diisobutyl acetal **19**, which was oxidized to ketone **20**. The catalytic and chiral induction properties of methyl glycoside **20** with trans-disubstituted and trisubstituted alkenes were studied and compared with those of benzyl glycoside **7**.[21] The results are summarized in Table 5. Like the catalysts described earlier, methyl glycoside **20** also afforded good chemical yields of epoxides (87−97% yield). However, the change of the blocking group at the anomeric center from benzyl to methyl caused no appreciable change in enantioselectivity (Table 5). This indicated that the blocking group at the anomeric carbon of our system is not a controlling factor for enantioselectivity in asymmetric epoxidation. Thus the argument of a possible $\pi-\pi$ interaction between the OBn group of ketone catalyst and the phenyl groups of alkene substrates was not substantiated.

TABLE 2. Asymmetric Epoxidation of Alkenes Using Ketones 7, 15, 16, and 17 as Catalysts at 0 °C

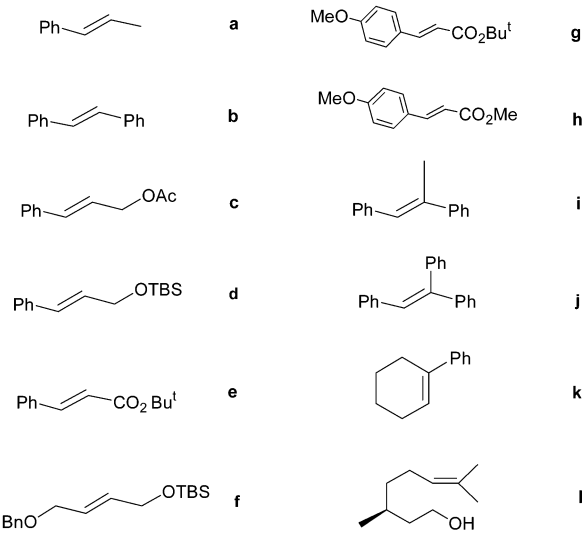


Catalysts:



7 R = isobutyl
15 R = neopentyl
16 R = benzyl
17 R = cyclohexylmethyl

Substrates:

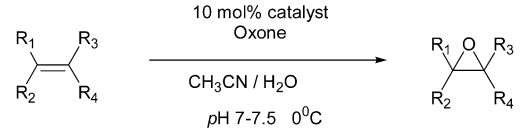


entry[a]	catalysts	substrates	yield (%)[b]	ee (%)	configuration[g]	entry[a]	catalysts	substrates	yield (%)[b]	ee (%)	configuration[g]
1	**7**	a	83	69[c]	(−)-(*S*,*S*)[23]	25	**7**	g	96	80[c]	(−)-(2*R*,3*S*)[13]
2	**15**	a	90	69[c]	(−)-(*S*,*S*)[23]	26	**15**	g	92	81[c]	(−)-(2*R*,3*S*)[13]
3	**16**	a	90	72[c]	(−)-(*S*,*S*)[23]	27	**16**	g	89	63[c]	(−)-(2*R*,3*S*)[13]
4	**17**	a	80	72[c]	(−)-(*S*,*S*)[23]	28	**17**	g	93	72[c]	(−)-(2*R*,3*S*)[13]
5	**7**	b	97	76[d]	(−)-(*S*,*S*)[22]	29	**7**	h	91	61[d]	(−)-(2*R*,3*S*)[13]
6	**15**	b	91	83[d]	(−)-(*S*,*S*)[22]	30	**15**	h	93	62[d]	(−)-(2*R*,3*S*)[13]
7	**16**	b	97	77[d]	(−)-(*S*,*S*)[22]	31	**16**	h	88	42[d]	(−)-(2*R*,3*S*)[13]
8	**17**	b	84	67[d]	(−)-(*S*,*S*)[22]	32	**17**	h	91	59[d]	(−)-(2*R*,3*S*)[13]
9	**7**	c	93	77[c]	(−)-(*S*,*S*)	33	**7**	i	93	87[d]	(−)-(*S*,*S*)[24]
10	**15**	c	94	82[c]	(−)-(*S*,*S*)	34	**15**	i	84	88[d]	(−)-(*S*,*S*)[24]
11	**16**	c	94	77[c]	(−)-(*S*,*S*)	35	**16**	i	97	83[d]	(−)-(*S*,*S*)[24]
12	**17**	c	86	62[c]	(−)-(*S*,*S*)	36	**17**	i	81	80[d]	(−)-(*S*,*S*)[24]
13	**7**	d	85	75[f]	(−)-(*S*,*S*)[11r,11s]	37	**7**	j	99	90[d]	(+)-(*S*)[24]
14	**15**	d	85	81[f]	(−)-(*S*,*S*)[11r,11s]	38	**15**	j	96	88[d]	(+)-(*S*)[24]
15	**16**	d	93	68[f]	(−)-(*S*,*S*)[11r,11s]	39	**16**	j	98	82[d]	(+)-(*S*)[24]
16	**17**	d	92	79[f]	(−)-(*S*,*S*)[11r,11s]	40	**17**	j	89	85[d]	(+)-(*S*)[24]
17	**7**	e	88	81[e]	(−)	41	**7**	k	92	85[c]	(−)-(*S*,*S*)[25,26]
18	**15**	e	90	86[e]	(−)	42	**15**	k	80	77[c]	(−)-(*S*,*S*)[25,26]
19	**16**	e	92	66[e]	(−)	43	**16**	k	94	79[c]	(−)-(*S*,*S*)[25,26]
20	**17**	e	84	77[e]	(−)	44	**17**	k	81	60[c]	(−)-(*S*,*S*)[25,26]
21	**7**	f	78	68[e]	(−)	45	**7**	l	85	56[h]	(−)
22	**15**	f	87	77[e]	(−)	46	**15**	l	88	58[h]	(−)
23	**16**	f	81	47[e]	(−)	47	**16**	l	93	48[h]	(−)
24	**17**	f	82	56[e]	(−)	48	**17**	l	85	48[h]	(−)

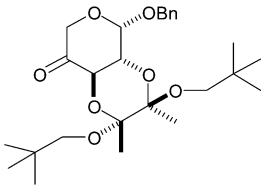
[a] All epoxidations were carried out with substrate (0.1 mmol), ketone (0.01 mmol), Oxone (1 mmol), and $NaHCO_3$ (3.1 mmol) in CH_3CN/4 × 10^{-4} M aqueous EDTA (5:1, v/v) for 12 h. [b] Isolated yield. [c] ee was determined by ^1H NMR analysis of the epoxide products directly with shift reagent Eu(hfc)$_3$. [d] ee was determined by HPLC using Chiralcel OD-H column. [e] ee was determined by ^1H NMR analysis of the derived acetate with Eu(hfc)$_3$. [f] ee was determined by HPLC using Chiralcel OD-H column after desilylation with TBAF. [g] The absolute configurations were determined by comparing the measured optical rotations with the reported ones. [h] ee was determined by ^1H NMR analysis of the derived acetate with Eu(hfc)$_3$.

Transition States in Asymmetric Epoxidation. The preponderant formation of the (*S*,*S*)-enantiomer may be rationalized by the spiro[6g,i,11h,o] transition state resulted from a minimum steric interaction between the steric blocker and the alkene substrate, using (*E*)-1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene as an example. First, equatorial attack of the alkene on the equatorial oxygen in dioxirane should be preferred because the axial approach of the alkene would be significantly more hindered by the axial proton of the pyran ring (Figure 3). Second, Figure 4 shows that the steric repulsion between the phenyl group and the acetal alkyl group in transition state (**spiro-2**) is absent in (**spiro-1**). On the basis of steric ground, transition state (**spiro-4**) is the

TABLE 3. Blocking Group Effect in Asymmetric Epoxidation of (*E*)-Hex-3-en-1-ol

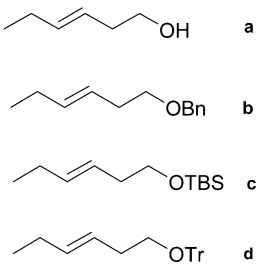


Catalyst:



15

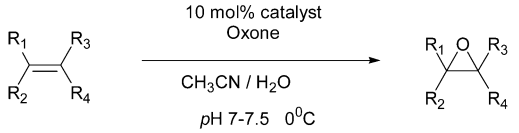
Substrates:



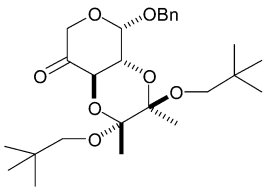
entry[a]	substrates	yield (%)[b]	ee (%)[c]	configuration[e]
1	a	88	16	(−)-(*S*,*S*)[11s]
2	b	88	45[d]	(−)-(*S*,*S*)[27]
3	c	87	36	(−)-(*S*,*S*)[11s]
4	d	95	55	(−)-(*S*,*S*)[f]

[a] All epoxidations were carried out 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 12 h. [b] Isolated yield. [c] Enantioselectivity was determined by ^1H NMR analysis of the derived acetate with Eu(hfc)$_3$. [d] Enantioselectivity was determined by ^1H NMR analysis of the corresponding benzoate with Eu(hfc)$_3$. [e] The absolute configurations were determined by comparing the measured optical rotations with the reported ones. [f] The absolute configuration was tentatively assigned by analogy based on the spiro reaction mode.

TABLE 4. Effect of Double Bond Position in Asymmetric Epoxidation of (*E*)-Hexenyl Benzyl Ether

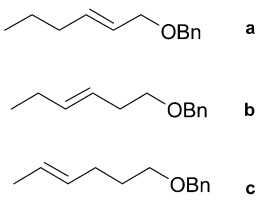


Catalyst:



15

Substrates:



entry[a]	substrates	yield (%)[b]	ee (%)[c]	configuration[e]
1	a	89	67	(−)-(*S*,*S*)[27]
2	b	88	45[d]	(−)-(*S*,*S*)[27]
3	c	82	34	(−)-(*S*,*S*)[f]

[a] All epoxidations were carried out 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 12 h. [b] Isolated yield. [c] Enantioselectivity was determined by HPLC using Chiralcel OD-H column. [d] Enantioselectivity was determined by ^1H NMR analysis of the corresponding benzoate with Eu(hfc)$_3$. [e] The absolute configurations were determined by comparing the measured optical rotations with the reported ones. [f] The absolute configuration was tentatively assigned by analogy based on the spiro reaction mode.

least favored and transition state (**spiro-3**) is less favored than (**spiro-1**) because the TBS group is sterically more demanding than the phenyl group. We have also readily prepared the enantiomer of **15** from D-arabinose, and ent-**15** displayed almost identical conversion yields and ee values for the (*R*,*R*)-enantiomer.

Conclusion

In summary, ketones **7**, **13**−**17**, and **20**, easily prepared from L-arabinose in four steps, afforded excellent chemical yields (78−99%) of epoxides in catalytic asymmetric epoxidation of alkenes. Steric blockers **7** and **15**−**17** with branching β to the acetal oxygen exhibited good stereochemical communication toward trans-disubstituted and trisubstituted alkenes, and the enantioselectivity increased with the size of the blocker (up to 90% ee). For trans-disubstituted alkenes, ketone catalyst **15**, bearing the neopentyl blocking group, was shown to display the best chiral induction power. A high ee of 81% was observed for the formation of *tert*-butyl (2*R*,3*S*)-3-(4-methoxyphenyl)glycidate, amenable for a chiral synthesis of calcium antagonist diltiazem hydrochloride. The excellent catalytic property of **15** was demonstrated by the epoxidation/recovery cycle without loss of activity. In asymmetric epoxidation of trisubstituted alkenes, both ketones **7** and **15** induce good enantioselectivity and complement each other.

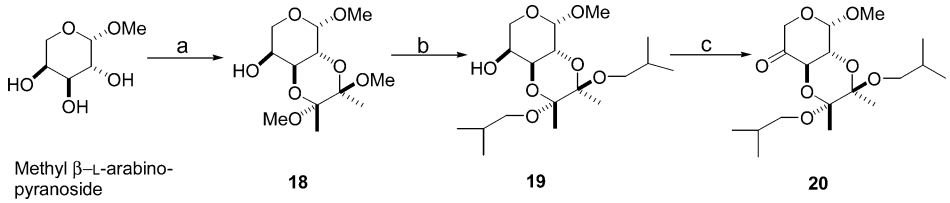
Since the enantioselectivities displayed by benzyl acetal ketone **16** and cyclohexylmethyl acetal ketone **17** were similar, electronic effect involving $\pi-\pi$ interaction between phenyl groups of alkene substrates and the benzyl group in ketone catalyst **16** did not appear to be operative in our system. The change of the blocking group at the anomeric center from benzyl (**7**) to methyl (**20**) caused no appreciable change in enantioselectivity, indicating that the anomeric aglycone of our system is not a controlling factor for enantioselectivity. The possibility of $\pi-\pi$ interaction between the anomeric OBn group of ketone catalysts and the phenyl groups of alkene substrates was not substantiated. The stereochemical communication of our ketone catalysts with alkene substrates was attributed to steric effect, and the most sterically demanding trityl protecting group afforded the highest ee of 55% in the epoxidation of protected (*E*)-hex-3-en-1-ols. When the double bond in the alkene substrate was positioned closest to the protecting group, the steric effect was most significant.

It is noteworthy that the benzyl aglycone in ketone **15** is amenable for elaboration into a polymer support and hence opens an avenue for the development of solid-phase catalysis. Research in this direction is also under active investigation.

Experimental Section[17]

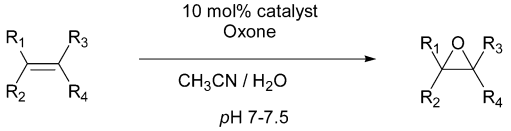
General in Situ Epoxidation Procedure at 0 °C. To a stirred solution of *trans*-stilbene (0.1 mmol), ketone (10 mol %), and *n*-Bu_4NHSO_4 (0.5 mg) in CH_3CN (10 mL) was added an aqueous a buffer (5 mL, 4 × 10^{-4} M aqueous EDTA). The resulting solution was cooled to 0 °C (bath temperature). A solution of Oxone (307 mg, 0.5 mmol) in aqueous EDTA (5 mL, 4 × 10^{-4} M) and a solution of $NaHCO_3$ (260 mg, 3.1 mmol) in

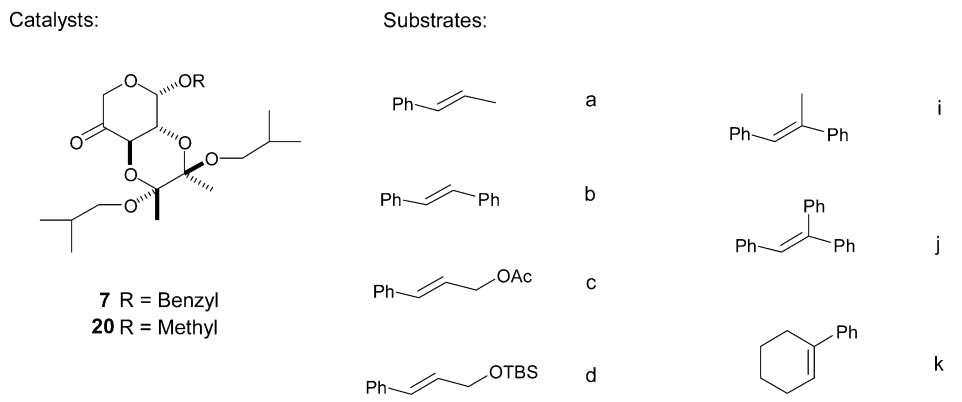
SCHEME 3. Preparation of Chiral Ketones from Methyl β-L-Arabinopyranoside[a]



[a] Reagents and conditions: (a) 2,2,3,3-tetramethoxybutane (1.5 equiv), $CH(OMe)_3$ (4 equiv), (±)-CSA (0.1 equiv), reflux, 12 h, 69%; (b) 2-methyl-1-propanol (4 equiv), *p*-TsOH, PhH, Dean−Stark trap, reflux, 12 h, 87%; (c) PDC (1.5 equiv), 3 Å MS, CH_2Cl_2, rt, 12 h, 94%.

TABLE 5. Effect of Blocking Group at Anomeric Center on Asymmetric Epoxidation of Alkenes Catalyzed by Ketones 7 and 20





entry[a]	catalysts	substrates	yield (%)[b]	ee (%)[c]	configuration[d]
1	**7**	a	83	69	(−)-(*S*,*S*)[23]
2	**20**	a	95	70	(−)-(*S*,*S*)[23]
3	**7**	b	97	76	(−)-(*S*,*S*)[22]
4	**20**	b	97	82	(−)-(*S*,*S*)[22]
5	**7**	c	93	77	(−)-(*S*,*S*)
6	**20**	c	94	80	(−)-(*S*,*S*)
7	**7**	d	85	75	(−)-(*S*,*S*)[11r,11s]
8	**20**	d	87	74	(−)-(*S*,*S*)[11r,11s]
9	**7**	i	93	87	(−)-(*S*,*S*)[24]
10	**20**	i	96	89	(−)-(*S*,*S*)[24]
11	**7**	j	99	90	(+)-(*S*)[24]
12	**20**	j	97	89	(+)-(*S*)[24]
13	**7**	k	92	85	(−)-(*S*,*S*)[25,26]
14	**20**	k	89	87	(−)-(*S*,*S*)[25,26]

[a] All epoxidations were carried out at 0 °C 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 12 h. [b] Isolated yield. [c] Enantioselectivity was determined by ^1H NMR analysis of the epoxide products directly with shift reagent Eu(hfc)$_3$. [d] The absolute configurations were determined by comparing the measured optical rotations with the reported ones.

H_2O (5 mL) were added dropwise concomitantly via two dropping funnels. The pH of the mixture was maintained at about 7−7.5 over a period of 12 h. The reaction mixture was then poured into water (10 mL), extracted with Et_2O (3×), dried with anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a residue that was purified by flash column chromatography to give the epoxide.

Diisobutyl Acetal 4. A solution of dimethyl acetal **2** (228 mg, 0.64 mmol) in benzene (20 mL) containing 2-methyl-1-propanol (190 mg, 2.56 mmol) and *p*-TsOH (5 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisobutyl acetal **4** as a syrup (240 mg, 85%): R_f 0.22 (hexanes−Et_2O, 2.5:1); $[\alpha]^{23}_D$ +13.6 (*c* 1.2, $CHCl_3$); IR (thin film) 3449 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40−7.26 (5H, m), 4.99 (1H, d, *J* = 3 Hz), 4.79 (1H, d, *J* = 12.3 Hz), 4.64 (1H, d, *J* = 12.3 Hz), 4.24 (2H, m), 3.90 (1H, d, *J* = 1.5 Hz), 3.81 (1H, dd, *J* = 11.7, 1.2 Hz), 3.74 (1H, dd, *J* = 12.6, 1.5 Hz), 3.25−3.15 (4H,m), 2.29 (1H, brs), 1.87−1.82 (2H, m), 1.33 (3H, s), 1.32 (3H, s), 0.95−0.92 (12H, m); ^{13}C NMR ($CDCl_3$) δ 138.0, 128.1, 127.2, 127.0, 100.3, 100.2, 98.0, 69.5, 68.6, 66.1, 65.9, 65.6, 63.5, 29.0, 20.1, 19.9, 18.9; MS (EI) *m/z* (relative intensity)

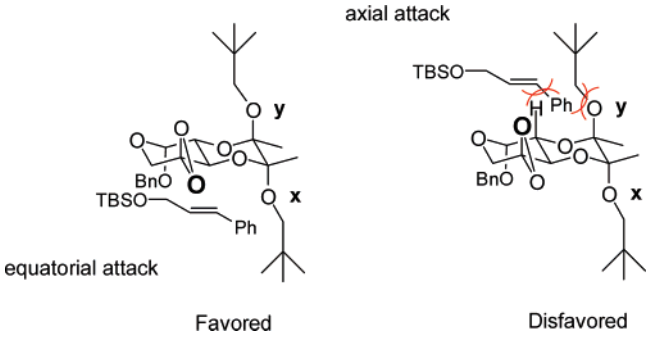


FIGURE 3. Approach of alkene substrates based on steric effect.

364 ($M^+ - C_4H_{10}O$, 23), 291 (10); Anal. Calcd for $C_{24}H_{38}O_7$: C, 65.73; H, 8.73. Found: C, 65.68; H, 9.20.

Diisobutyl Ketone 7. To a solution of alcohol **4** (170 mg, 0.39 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (177 mg, 0.47 mmol) and powdered 3 Å molecular sieves (170 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisobutyl ketone **7** as a syrup (161 mg, 95%). R_f 0.35 (Et_2O−hexane, 3:7); $[\alpha]^{23}_D$ +12.2 (*c* 1.4, $CHCl_3$); IR (thin film) 1743, 1736 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43−7.26 (5H, m), 5.11 (1H, d, J = 3 Hz), 5.02 (1H, d, J = 10.8 Hz), 4.85 (1H, d, J = 12.3 Hz), 4.77 (1H, d, J = 12.3 Hz), 4.17 (1H, d, J = 15.6 Hz), 4.11 (1H, dd, J = 7.8, 3.0 Hz), 3.92 (1H, d, J = 15.0 Hz), 3.27−3.16 (4H, m), 1.86−1.80 (2H, m), 1.40 (3H, s), 1.36 (3H, s), 0.93−0.89 (12H, m); ^{13}C NMR ($CDCl_3$) δ 200.9, 137.3, 128.7, 128.07, 127.7, 100.5, 99.9, 97.6, 71.3, 70.6, 70.3, 67.6, 67.5, 67.3, 29.0, 20.1, 19.9, 19.8, 18.8, 18.7; MS (EI) *m/z* (relative intensity) 362 ($M^+ - C_4H_{10}O$, 100), 288 (8). Anal. Calcd for $C_{24}H_{36}O_7$: C, 66.03; H, 8.31. Found: C, 66.19; H, 8.38.

Diisopropyl Acetal 8. A solution of dimethyl acetal **2** (50 mg, 0.14 mmol) in benzene (20 mL) containing 2-propanol (33.6 mg, 0.56 mmol) and *p*-TsOH (5 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisopropyl acetal **8** as a syrup (40 mg, 70%): R_f 0.35 (hexanes−EtOAc, 2:1); $[\alpha]^{23}_D$ +27 (*c* 1.0, $CHCl_3$); IR (thin film) 3476 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.28 (5H, m), 4.94 (1H, d, J = 1.5 Hz), 4.79 (1H, d, J = 12.3 Hz), 4.67 (1H, d, J = 12.3 Hz), 4.41 (2H, m), 4.11 (2H, m), 3.88 (1H, d, J = 1.2 Hz), 3.76 (1H, dd, J = 12.6, 1.2 Hz), 3.72 (1H, dd, J = 12.6, 1.2 Hz), 2.26 (1H, brs), 1.37 (3H, s), 1.34 (3H, s), 1.25 (3H, 6 Hz), 1.21 (3H, 6 Hz), 1.19 (3H, 6 Hz), 1.16 (3H, 6 Hz); ^{13}C NMR ($CDCl_3$) δ 138.5, 128.6, 127.7, 127.6, 101.3, 101.1, 97.8, 69.3, 68.6, 66.2, 65.7, 64.4, 64.3, 63.5, 24.8, 24.4, 24.3, 20.1, 20.0; MS (EI) *m/z* (relative intensity) 350 ($M^+ - i$-PrOH, 25), 91 (100); Anal. Calcd for $C_{22}H_{34}O_7$: C, 64.37; H, 8.35. Found: C, 64.00; H, 8.21.

Diisopentyl Acetal 9. A solution of dimethyl acetal **2** (100 mg, 0.28 mmol) in benzene (30 mL) containing 3-methyl-1-butanol (98 mg, 1.12 mmol) and *p*-TsOH (5 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisopentyl acetal **9** as a syrup (104.3 mg, 80%): R_f 0.47 (hexanes−Et_2O, 3:1); $[\alpha]^{23}_D$ +5.4 (*c* 1.2, $CHCl_3$); IR (thin film) 3455 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.28 (5H, m), 4.98 (1H, s), 4.77 (1H, d, J = 12.3 Hz), 4.64 (1H, d, J = 12.3 Hz), 4.22−4.21 (2H, m), 3.90 (1H, s), 3.81 (1H, dd, J = 12.9, 1.5 Hz), 3.72 (1H, dd, J = 12.9, 1.8 Hz), 3.49−3.43 (4H, m), 2.17 (1H, brs), 1.78−1.68 (2H, m), 1.49−1.45 (4H, m) 1.36 (3H, s), 1.32 (3H, s), 0.92−0.86 (12H, m); ^{13}C NMR ($CDCl_3$) δ 138.5, 128.6, 127.7, 127.6, 100.4, 101.1, 98.0, 69.6, 68.6, 66.0, 65.6, 63.4, 59.1, 58.9, 39.2, 39.1, 25.7, 25.4, 23.2, 23.1, 22.9, 18.9; MS (EI) *m/z* (relative intensity) 378 (100); Anal. Calcd for $C_{26}H_{42}O_7$: C, 66.93; H, 9.07. Found: C, 66.82; H, 9.19.

Dineopentyl Acetal 10. A solution of dimethyl acetal **2** (125 mg, 0.35 mmol) in benzene (20 mL) containing neopentyl alcohol (239 mg, 2.7 mmol) and *p*-TsOH (5 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dineopentyl acetal **10** as a white solid (141 mg, 87%): R_f 0.28 (hexanes−Et_2O, 4:1); mp 112−113 °C; $[\alpha]^{20}_D$ −0.58 (*c* 1.44, $CHCl_3$); IR (thin film) 3454 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38−7.25 (5H, m), 4.99 (1H, d, J = 2.4 Hz), 4.79 (1H, d, J = 12.3 Hz), 4.61 (1H, d, J = 12.3 Hz), 4.27 (2H, m), 3.90 (1H, brs), 3.83 (1H, d, J = 12.6 Hz), 3.79 (1H, dd, J = 12.6, 1.5 Hz), 3.13−3.04 (4H, m), 1.90 (1H, brs), 1.34 (3H, s), 1.33 (3H, s), 0.95 (9H, s), 0.94 (9H, s); ^{13}C NMR ($CDCl_3$) δ 138.5, 128.5, 127.6, 127.3, 100.3, 100.1, 98.2, 70.7, 69.5, 68.6, 65.9, 63.5, 32.1, 27.4, 18.8; MS (FAB) *m/z* (relative intensity) 489 ($[M + Na]^+$, 18), 379 (34), 91 (100), 71 (76); HRMS (FAB) calcd for $C_{26}H_{42}O_7$ $[M + Na]^+$ 489.2823, found 489.2846.

Dibenzyl Acetal 11. A solution of dimethyl acetal **2** (100 mg, 0.28 mmol) in benzene (20 mL) containing benzyl alcohol (121 mg, 1.12 mmol) and *p*-TsOH (10 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dibenzyl acetal **11** as a syrup (115 mg, 80%): R_f 0.35 (hexanes−Et_2O, 1:1); $[\alpha]^{23}_D$ +17.0 (*c* 1.4, $CHCl_3$); IR (thin film) 3462 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.22 (15H, m), 5.04 (1H, d, J = 3.0 Hz), 4.81 (1H, d, J = 12.3 Hz), 4.70−4.58 (5H, m), 4.41 (1H, dd, J = 10.5, 3.0 Hz), 4.35 (1H, dd, J = 10.5, 3.0 Hz) 3.91 (1H, s), 3.90 (1H, dd, J = 12.6, 1.2 Hz), 3.77 (1H, dd, J = 12.6, 1.5 Hz), 2.11 (1H, brs), 1.51 (3H, s), 1.50 (3H, s); ^{13}C NMR ($CDCl_3$) δ 139.0, 128.8, 128.7, 127.6, 127.3, 126.8, 100.8, 97.9, 69.8, 68.5, 66.4, 65.9, 63.5, 62.9, 62.4, 19.5; MS (EI) *m/z* (relative intensity) 398 ($M^+ - C_7H_8O$, 15), 91 (100); Anal. Calcd for $C_{30}H_{34}O_7$: C, 71.13; H, 6.76. Found: C, 71.17; H, 6.86.

Dicyclohexylmethyl Acetal 12. A solution of dimethyl acetal **2** (100 mg, 0.28 mmol) in benzene (30 mL) containing cyclohexylmethyl alcohol (128 mg, 1.12 mmol) and *p*-TsOH (10 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dicyclohexylmethyl acetal **12** as white crystals (110.3 mg, 76%): R_f 0.58 (hexanes−Et_2O, 1:1) mp 119−120 °C; $[\alpha]^{23}_D$ +8.4 (*c* 1.1, $CHCl_3$); IR (thin film) 3429 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40−7.26 (5H, m), 4.99 (1H, d, J = 1.8 Hz), 4.78 (1H, d, J = 12.3 Hz), 4.62 (1H, d, J = 12.3 Hz), 4.22 (2H, s), 3.90 (1H, s), 3.83 (1H, d, J = 12.6 Hz), 3.74 (1H, dd, J = 12.6, 1.2 Hz), 3.26−3.20 (4H, m), 2.17 (1H, brs), 1.81−1.65 (12H, m), 1.26 (3H, s), 1.23 (3H, s), 0.98−0.93 (10H, m); ^{13}C NMR ($CDCl_3$) δ 138.5, 128.6, 127.6, 127.4, 100.3, 100.1, 98.1, 69.6, 68.6, 66.1, 65.9, 65.6, 63.5, 38.5, 38.4, 30.8, 30.6, 27.0, 26.3, 18.9; MS (EI) *m/z* (relative intensity) 404 (M^+ −

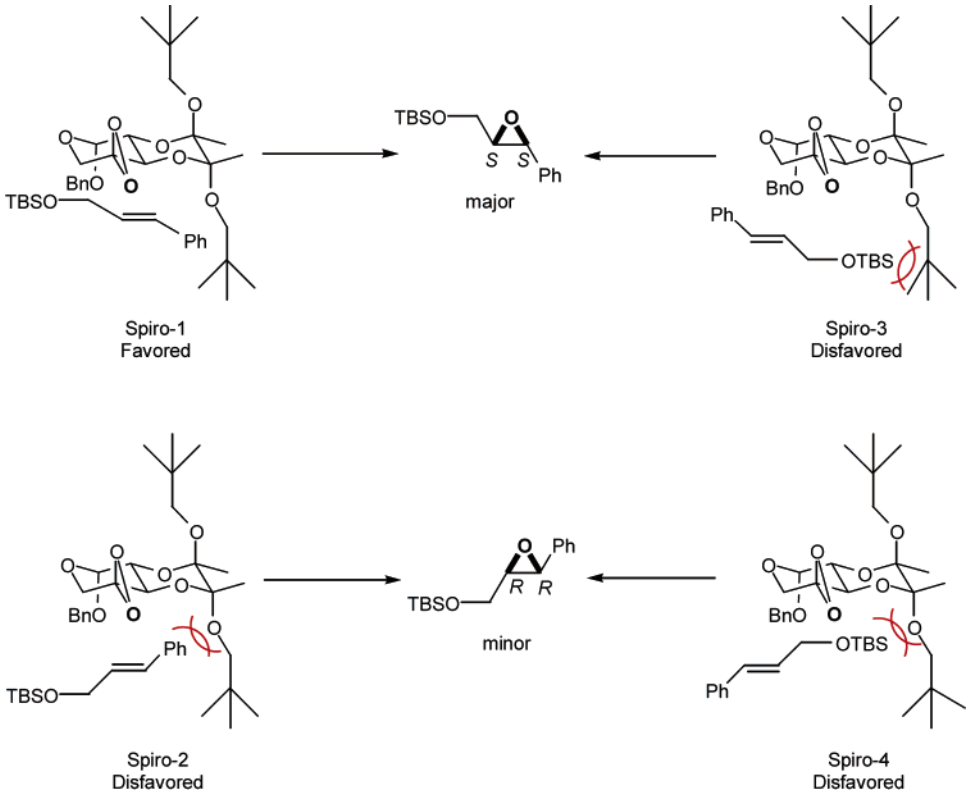


FIGURE 4. Four spiro transition states for 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene epoxidation catalyzed by ketone **15**.

$C_7H_{14}O$, 79), 290 (30); Anal. Calcd for $C_{30}H_{46}O_7$: C, 69.47; H, 8.94. Found: C, 69.54; H, 9.08.

Diisopropyl Ketone 13. To a solution of alcohol **8** (70 mg, 0.17 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (77 mg, 0.20 mmol) and powdered 4 Å molecular sieves (170 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisopropyl ketone **13** as a syrup (60 mg, 87%). R_f 0.45 (hexanes−Et_2O, 1:1); $[\alpha]^{23}_D$ +23 (*c* 1.2, $CHCl_3$); IR (thin film) 1750 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43−7.26 (5H, m), 5.17 (1H, d, J = 10.8 Hz), 5.07 (1H, d, J = 3 Hz), 4.83 (1H, d, J = 12.6 Hz), 4.78 (1H, d, J = 12.6 Hz), 4.34 (1H, dd, J = 10.8, 3.0 Hz), 4.19−4.03 (3H, m), 3.87 (1H, d, J = 15 Hz), 1.39 (3H, s), 1.37 (3H, s), 1.28−1.13 (12H, m); ^{13}C NMR ($CDCl_3$) δ 200.9, 137.3, 128.7, 128.07, 127.7, 101.5, 100.7, 97.6, 71.3, 70.6, 70.3, 67.6, 64.9, 64.7, 24.7, 24.4, 24.3, 19.7, 19.6; MS (EI) *m/z* (relative intensity) 408 (M^+, 10), 366 (100). Anal. Calcd for $C_{22}H_{32}O_7$: C, 64.69; H, 7.90. Found: C, 64.45; H, 7.78.

Diisopentyl Ketone 14. To a solution of alcohol **9** (140 mg, 0.3 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (135 mg, 0.36 mmol) and powdered 4 Å molecular sieves (130 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisopentyl ketone **14** as a syrup (124 mg, 89%). R_f 0.45 (hexanes−Et_2O, 1:1); $[\alpha]^{23}_D$ +15.2 (*c* 2.2, $CHCl_3$); IR (thin film) 1743, 1729 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43−7.26 (5H, m), 5.11 (1H, d, J = 3 Hz), 4.97 (1H, d, J = 11.1 Hz), 4.83 (1H, d, J = 12.3 Hz), 4.77 (1H, d, J = 12.3 Hz), 4.14 (1H, d, J = 14.4 Hz), 4.10 (1H, dd, J = 11.3, 3 Hz), 3.90 (1H, d, J = 14.4 Hz), 3.52−3.41 (4H, m), 1.75−1.68 (2H, m), 1.52−1.41 (4H, m), 1.39 (3H, s), 1.36 (3H, s), 0.91−0.84 (12H, m); ^{13}C NMR ($CDCl_3$) δ 200.8, 137.7, 128.7, 128.1, 127.7, 100.6, 100.0, 97.6, 71.4, 70.6, 70.3, 67.6, 59.3, 39.1, 38.9, 25.4, 23.2, 23.1, 22.8, 22.7, 18.8, 18.7; MS (EI) *m/z* (relative intensity) 376 (M^+ − $C_5H_{12}O$, 100). Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.18; H, 8.60.

Dineopentyl Acetal 15. To a solution of alcohol **10** (56 mg, 0.12 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (55 mg, 0.15 mmol) and powdered 4 Å molecular sieves (60 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dineopentyl ketone **15** as a syrup (53 mg, 96%): R_f 0.28 (hexanes−Et_2O, 1:1); $[\alpha]^{20}_D$ −5.7 (*c* 2.83, $CHCl_3$); IR (thin film) 1743 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.26 (5H, m), 5.12 (1H, d, J = 3.0 Hz), 5.05 (1H, d, J = 10.8 Hz), 4.84 (1H, d, J = 12.3 Hz), 4.75 (1H, d, J = 12.3 Hz), 4.16 (1H, d, J = 15.6 Hz), 4.07 (1H, dd, J = 8.1, 3.3 Hz), 3.92 (1H, d, J = 15.0 Hz), 3.14−3.02 (4H,m), 1.40 (3H, s), 1.36 (3H, s), 0.92 (9H, s), 0.91 (9H, s); ^{13}C NMR ($CDCl_3$) δ 201.0, 137.7, 128.7, 128.0, 127.6, 100.5, 99.9, 97.7, 71.3, 71.0, 70.8, 70.6, 70.4, 67.6, 32.1, 27.3, 27.2, 18.7, 18.6; MS (FAB) *m/z* (relative intensity) 487 ($[M + Na]^+$, 2), 377 (14), 91 (100), 71 (80); HRMS (FAB) calcd for $C_{26}H_{40}O_7$ $[M + Na]^+$ 487.2666, found 487.2680; Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.22; H, 8.68. Found: C, 67.31; H, 8.31.

Dibenzyl Ketone 16. To a solution of alcohol **11** (310 mg, 0.61 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (275 mg, 0.73 mmol) and powdered 4 Å molecular sieves (270 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dibenzyl ketone **16** as white crystals (258 mg, 84%): R_f 0.37 (hexanes−Et_2O, 1:1); mp 174−176 °C; $[\alpha]^{23}_D$ +20 (*c* 3.4, $CHCl_3$); IR (thin film) 1743, 1729 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41−7.24 (15H, m), 5.15 (1H, d, J = 2.7 Hz), 5.12 (1H, d, J = 10.8 Hz), 4.87 (1H, d, J = 12.3 Hz), 4.79 (1H, d, J = 12.3 Hz), 4.70−4.66 (2H, m), 4.63−4.59 (2H, m), 4.25 (1H, dd, J = 10.8, 3.0 Hz), 4.15 (1H, d, J = 15.0 Hz), 3.87 (1H, d, J = 15.0 Hz), 1.57 (3H, s), 1.55 (3H, s); ^{13}C NMR ($CDCl_3$) δ 200.1, 138.7, 138.6, 137.5, 128.8, 128.7, 128.6, 128.2,128.1, 127.7, 127.6,

127.3, 127.0, 126.6, 100.9, 100.4, 97.3, 71.4, 70.6, 70.4, 67.4, 62.9, 62.6, 19.3, 19.1; MS (EI) *m/z* (relative intensity) 504 (M^+, 2), 414 (100); Anal. Calcd for $C_{30}H_{32}O_7$: C, 71.41; H, 6.39. Found: C, 71.16; H, 6.50.

Dicyclohexylmethyl Ketone 17. To a solution of alcohol **12** (335 mg, 0.65 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PDC (293 mg, 0.78 mmol) and powdered 4 Å molecular sieves (290 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dicyclohexylmethyl ketone **17** as a syrup (308 mg, 92%): R_f 0.41 (hexanes−Et_2O, 1:1); $[\alpha]^{23}_D$ +4.4 (*c* 1.0, $CHCl_3$); IR (thin film) 1743, 1729 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42−7.26 (5H, m), 5.11 (1H, d, J = 3.0 Hz), 4.99 (1H, d, J = 11.1 Hz), 4.85 (1H, d, J = 12.3 Hz), 4.77 (1H, d, J = 12.3 Hz), 4.17 (1H, d, J = 15.9 Hz), 4.11 (1H, dd, J = 10.8, 3.0 Hz), 3.92 (1H, d, J = 15.9 Hz), 3.28−3.20 (4H, m), 1.79−1.53 (12H, m), 1.38 (3H, s), 1.25 (3H, s), 1.00−0.90 (10H, m); ^{13}C NMR ($CDCl_3$) δ 201.3, 138.1, 129.1, 128.4, 127.9, 100.9, 100.2, 98.4, 71.6, 70.6, 77.3, 67.8, 66.9, 66.7, 38.7, 38.6, 31.0, 30.9, 30.7, 27.3, 26.7, 26.6, 25.5, 19.1, 19.0; MS (EI) *m/z* (relative intensity) 516 (M^+, 1), 402 (9), 91 (100); Anal. Calcd for $C_{30}H_{44}O_7$: C, 69.74; H, 8.58. Found: C, 69.32; H, 8.63.

Dimethyl Acetal 18. A suspension of methyl β-L-arabinopyranoside (1.51 g, 9.2 mmol) in methanol (20 mL) containing 2,2,3,3-tetramethoxybutane (3.27 g, 18.4 mmol), trimethyl orthoformate (3.2 mL, 36.8 mmol), and 10-camphorsulfonic acid (213 mg, 10 mol %) was heated under reflux for 12 h. The cooled reaction mixture was then treated with powdered $NaHCO_3$ (0.5 g) and filtered, and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc, and the solution was washed with saturated aqueous $NaHCO_3$ solution. The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford dimethyl acetal **18** as a colorless syrup (1.78 g, 69%): R_f 0.17 (hexanes−EtOAc, 1:1); IR (thin film) 3424 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.78 (1H, d, J = 3.3 Hz), 4.21 (1H, dd, J = 10.5, 3.3 Hz), 4.11 (1H, dd, J = 10.5, 3.3 Hz), 3.94 (1H, t, J = 1.5 Hz), 3.83 (1H, dd, J = 12.6, 1.2 Hz), 3.76 (1H, dd, J = 12.8, 1.5 Hz), 3.42 (3H, s), 3.26 (3H, s), 3.24 (3H, s), 1.90 (1H, brs), 1.30 (3H, s), 1.28 (3H, s); ^{13}C NMR ($CDCl_3$) δ 100.6, 98.9, 68.4, 66.1, 65.5, 62.9, 55.6, 48.3, 18.2, 18.1; MS (EI) *m/z* (relative intensity) 247 (100), 263 ($[M - CH_3]^+$, 20); HRMS (EI) calcd for $C_{12}H_{22}O_7$ $[M - CH_3]^+$ 263.1125, found 263.1118.

Diisobutyl Acetal 19. A solution of dimethyl acetal **18** (70 mg, 0.25 mmol) in benzene (15 mL) containing 2-methyl-1-propanol (75 mg, 1.01 mmol) and *p*-TsOH (2 mg) was heated under reflux with a Dean−Stark trap for 12 h. The cooled reaction mixture was then treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisobutyl acetal **19** as a syrup (79 mg, 87%): R_f 0.34 (hexanes−Et_2O, 2:1); $[\alpha]^{20}_D$ −10.7 (*c* 0.6, $CHCl_3$); IR (thin film) 3434 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.74 (1H, d, J = 3.3 Hz), 4.20 (1H, dd, J = 10.5, 3.3 Hz), 4.11 (1H, dd, J = 10.5, 3.0 Hz), 3.90 (1H, d, J = 1.5 Hz), 3.79 (1H, d, J = 12.6 Hz), 3.73 (1H, dd, J = 12.6, 1.5 Hz), 3.39 (3H, s), 3.23−3.14 (4H, m), 2.53 (1H, brs), 1.92−1.79 (2H, m), 1.35 (3H, s), 1.30 (3H, s), 0.93−0.87 (12H, m); ^{13}C NMR ($CDCl_3$) δ 100.4, 100.2, 99.0, 68.4, 67.4, 67.1, 65.9, 65.5, 62.8, 55.6, 28.9, 28.9, 20.1, 20.0, 19.9, 19.0, 18.9; MS (FAB) *m/z* (relative intensity) 385 ($[M + Na]^+$, 12), 289 (32), 100 (53), 87 (60), 57 (100); HRMS (FAB) calcd for $C_{18}H_{34}O_7$ $[M + Na]^+$ 385.2195, found 385.2200.

Diisobutyl Ketone 20. To a solution of alcohol **19** (193 mg, 0.53 mmol) in dry CH_2Cl_2 (10 mL) were added slowly PCC (171 mg, 0.80 mmol) and powdered 3 Å molecular sieve (200 mg). The mixture was stirred at room temperature for 12 h. The mixture was suction filtered through a pad of silica gel, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford diisobutyl ketone **20** as a syrup (180 mg, 94%): R_f 0.38 (Et_2O−hexane, 2:1); IR (thin film) 1745 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.88 (1H, d, J = 10.8 Hz), 4.86 (1H, d, J = 3.3 Hz), 4.19 (1H, d, J = 14.7 Hz), 4.11 (1H, dd, J = 10.8, 3.3 Hz), 3.94 (1H, d, J = 14.7 Hz), 3.50 (3H, s), 3.27−3.17 (4H, m), 1.87−1.80 (2H, m), 1.35 (3H, s), 1.32 (3H, s), 0.95−0.89 (12H, m); ^{13}C NMR ($CDCl_3$) δ 200.7, 100.6, 100.0, 98.6, 71.2, 70.3, 67.6, 67.5, 67.0, 56.4, 28.9, 20.0, 19.9, 19.8, 19.7, 18.8, 18.7; MS (CI) *m/z* (relative intensity) 360 (M^-, 17), 198 (31), 153 (30), 143 (100); HRMS (CI) calcd for $C_{18}H_{32}O_7$ M^- 360.2154, found 360.2146.

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Supporting Information Available: ^1H NMR spectral and HPLC data for the determination of the enantiomeric excess of the epoxides. ^1H and ^{13}C NMR spectral characterization data for compounds **4**, **7**, and **8**−**20**. X-ray data of compounds **12** and **16**. This material is available free of charge via the Internet at http://pubs.acs.org.

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