Enantioselective Synthesis and Stereoselective Rearrangements of Enol Ester Epoxides

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Enol esters can be epoxidized with high enantioselectivities using the fructose-derived chiral ketone **1** as catalyst and Oxone as oxidant. A detailed study of enantiomerically enriched enol ester epoxides has revealed that the acid-catalyzed rearrangement can proceed through two distinct pathways, one with retention of configuration and the other with inversion. The competition between the two pathways is highly dependent upon the nature of the acid catalyst. A strong acid favors retention of configuration and a weak acid favors inversion of configuration. Under thermal conditions, these epoxides rearrange highly stereoselectively with inversion of configuration. Either enantiomer of an α-acyloxy ketone can be formed from one enantiomer of an enol ester epoxide by judicious choice of reaction conditions.

Enol ester epoxides are synthetically useful intermediates. Among many synthetic transformations, these epoxides can readily rearrange to α-acyloxy ketones or aldehydes under thermal or acidic conditions.[1,2] When enol ester epoxides are chiral, enantiomerically enriched α-acyloxy carbonyl intermediates could be derived. Asymmetric oxidation of prochiral enol derivatives has been well studied, and a variety of chiral α-hydroxy carbonyl compounds can effectively be obtained.[3] However, the formation of chiral enol ester epoxides by asymmetric epoxidation of enol esters has been elusive, presumably due to their instability under many reaction conditions. We have found that chiral enol ester epoxides can be efficiently prepared by asymmetric epoxidation of enol esters using the fructose-derived ketone **1** as catalyst and Oxone as oxidant. Furthermore these chiral epoxides can undergo stereospecific rearrangements under both acidic and thermal conditions to give enantiomerically enriched α-acyloxy ketones (Scheme 1). Herein we report the detailed study of both the synthesis and rearrangement of chiral enol ester epoxides.[4]

Asymmetric Epoxidation of Enol Esters. Our epoxidation studies started with the enol acetate and enol benzoate of cyclohexanone (Table 1, entries 1 and 2). Subjecting these enol esters to the in situ epoxidation conditions[5] led to a smooth formation of product.[6] In both cases the epoxides were found to be relatively stable under the reaction conditions and could be isolated through a Et_3N-buffered silica gel column. A 93% ee was obtained for the epoxide of the enol benzoate (Table 1, entry 2) while the enol acetate gave a lower ee (Table 1, entry 1). Altering the electronics of the benzoate did not lead to a large effect on the ee of the epoxide (Table 1, entries 2−6). Enol pivaloate gave a similar ee to the benzoate (Table 1, entry 7).

Encouraged by these results, a number of cyclic and acyclic enol esters were subsequently prepared and epoxidized to further test the generality of the process (Table 1, entries 8−14). In all cases the reactions were relatively clean, the epoxides were isolated in good yields,

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Scheme 1

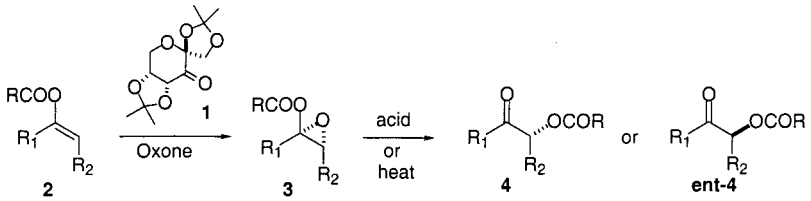


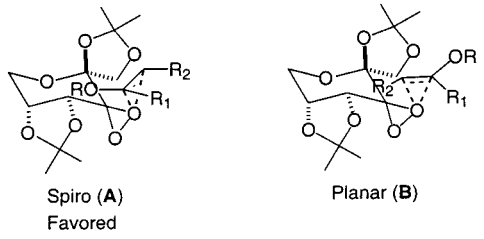
Table 1. Asymmetric Epoxidation of Enol Esters by Ketone 1[a]

entry	substrate	t (h)	yield (%)[b]	ee (%)	config.
1	R = CH_3	2.0	59	75[c]	(R,R)[g]
2	R = Ph	1.5	82	93[d]	(R,R)[g]
3	R = *p*-CH_3-Ph	1.5	84	90[d]	(R,R)[g]
4	R = *p*-CH_3O-Ph	1.5	71	90[d]	(R,R)[g]
5	R = *p*-Cl-Ph	1.5	84	90[e]	(R,R)[g]
6	R = *p*-NO_2-Ph	1.5	61	90[c]	(R,R)[g]
7	R = $(CH_3)_3C$	2.0	68	91[c]	(R,R)[g]
8		1.5	73	95[f]	(R,R)[g]
9		1.5	79	80[d]	(R,R)[g]
10		1.5	87	91[d]	(R,R)[h]
11		1.5	82	95[d]	(R,R)[g]
12		1.5	92	88[d]	(R,R)[h]
13		2.0	66	91[c]	(S,R)[h]
14		3.0	46	90[c]	(S,R)[h]

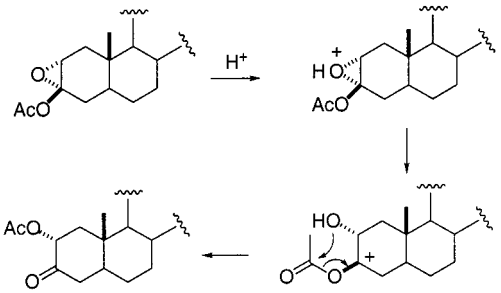
[a] All reactions were carried out at 0 °C (bath temperature) with substrate (1 equiv), ketone (0.3 equiv), Oxone (1.38 equiv) and K_2CO_3 (5.8 equiv) in organic solvent (15 mL) and aqueous buffer solution (10 mL). The organic solvent used was either CH_3CN (entries 9, 11, and 13) or CH_3CN−DMM (1/2, v/v) (entries 1−8, 10, 12, and 14). For entries 2, 9, 11, 12, and 13, 0.05 M $Na_2B_4O_7 \cdot 10H_2O$ of EDTA (4×10^{-4} M) was used as buffer; for others, AcOH−0.1 M K_2CO_3 (1/250, v/v) was used as buffer. [b] The epoxides were purified on silica gel column (silica gel was pretreated with Et_3N) by flash chromatography and gave satisfactory spectroscopic characterization. [c] Enantioselectivity was determined by ^1H NMR shift analysis of epoxide products directly with Eu(hfc)$_3$. [d] Enantioselectivity was determined by chiral HPLC (Chiracel OD). [e] Enantioselectivity was determined by chiral HPLC (Chiracel OJ). [f] Enantioselectivity was determined by chiral HPLC (Chiralpak AD). [g] The absolute configuration was tentatively assumed by analogy based on the spiro reaction mode. [h] The epoxides were hydrolyzed under basic conditions to α-hydroxy ketones, and the absolute configurations were determined by comparing the measured optical rotations of the α-hydroxy ketones with the reported ones (for entry 10, see ref 13; for entry 12 see ref 14; for entries 13 and 14 see refs 3b and 3d, respectively).

and the enantioselectivities were high in most cases. Among the cyclic substrates, it was found that six-, seven-, and eight-membered rings gave the highest ee's

Scheme 2



Scheme 3



(Table 1, entries 2−8, 10, and 11), while the five-membered ring gave lower ee (Table 1, entry 9).

The absolute configurations of some of the epoxides (Table 1, entries 10, 12−14) were determined by hydrolyzing the epoxides to α-hydroxy ketones and comparing the measured optical rotations of the resulting α-hydroxy ketones with reported ones (for details see Table 1). The results in all these cases were consistent with the spiro reaction mode (Scheme 2).[5]

Acid-Catalyzed Rearrangement of Chiral Enol Ester Epoxides. Enol ester epoxides can rearrange to α-acyloxy ketones or aldehydes under acidic or thermal conditions.[1,2] Investigations of these rearrangements have largely been carried out on conformationally rigid steroids,[2a,b,d,g,h,k,l,n] and the mechanistic conclusions have been based on the analysis of the diastereomeric products. Most of the reported acid-catalyzed rearrangements occur with retention of configuration (Scheme 3).[2b,h,k,l] While the proposed mechanisms have provided reasonable explanations for the observed stereochemistry in these cases, some uncertainty remains.[7] The availability of enantiomerically enriched enol ester epoxides provided us an opportunity to further study the factors involved in the rearrangements of these epoxides under acidic conditions with the aim of developing a route to enantiomerically enriched α-acyloxy ketones.[3]

(7) For example, it was observed that treating an enol ester epoxide of epiandrosterone acetate with silicic acid at 50 °C for 17 h led to the formation of a mixture α and β epimeric 16-acetoxy ketones with a ratio of 1.8:1 in a 16.7% isolated yield (see ref 2d). The α isomer resulted from a rearrangement with retention of configuration, and the β isomer resulted from a rearrangement with inversion. On the basis of the observation that the α and β isomers did not undergo isomerization under the reaction conditions, it was suggested that these two isomers came from two competing reactions. However, it is not clear whether these two reactions were induced by acid alone or both acid and heat since the reaction was carried out at 50 °C.

Scheme 4

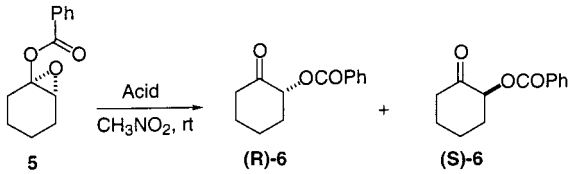


Table 2. Effects of Different Acid Catalysts on the Rearrangement of 1-Benzoyloxy-1,2-epoxycyclohexane (5)[a]

entry	acid	*t* (min)	ee % (**5**)[b]	ee % (**6**)[b]	yield (%)[c]
1	*p*-TsOH	10	93	90 (*R*)	89
2	H_2SO_4	3	93	87 (*R*)	57
3	$Sn(OTf)_2$	10	93	85 (*R*)	84
4	TMSOTf	10	93	82 (*R*)	90
5	$Sc(OTf)_3$	10	93	80 (*R*)	74
6	$FeCl_3$	10	93	71 (*R*)	63
7	TiF_4	5	93	69 (*R*)	44
8	$BF_3{\cdot}Et_2O$	1500	93	67 (*R*)	52
9	$AlCl_3$	1	92	26 (*R*)	74
10	$La(OTf)_3$	40	93	15 (*R*)	88
11	$Yb(OTf)_3$	5	92	66 (*R*)	67
12	$YbCl_3$	90	93	82 (*S*)	76
13	$ZnBr_2$	10	93	12 (*S*)	48
14	$VCl_3(THF)_3$	300	93	15 (*S*)	58
15	$ErCl_3$	90	90	80 (*S*)	73
16	$AlMe_3$	5	91	87 (*S*)	85
17	$AlEt_2Cl$	17	91	67 (*S*)	54
18	$AlEtCl_2$	10	91	30 (*S*)	41
19	silica gel	720	92	91 (*S*)	83

[a] All reactions were carried out in nitromethane under anhydrous conditions at room temperature using 10 mol % acid catalysts except entry 19 where 5−10 times (by weight) silica gel (Davisil 35−60 mesh, pH 7.0) was used. Epoxide **5** was freshly made and stored at −20 °C to avoid decomposition. [b] The enantiomeric excess was determined by HPLC (Chiracel OD). The absolute configuration of **6** was determined by comparing HPLC chromatograms with the authentic sample prepared from commercially available (*R*,*R*)-1,2-*trans*-cyclohexanediol. [c] Isolated yield.

Our studies started with (*R*,*R*)-1-benzoyloxy-1,2-epoxycyclohexane (**5**) as a test substrate (Scheme 4). Treating epoxide **5** with a protic acid such as *p*-TsOH led to a facile rearrangement with retention of configuration (Table 2, entry 1). The reaction was complete within 10 min as monitored by TLC, and the product showed only a 3% decrease in ee compared to the starting epoxide.[8] In addition to protic acids, Lewis acids were also investigated as catalysts for this rearrangement. It was found that the enantiomeric excess of the product varied dramatically with the Lewis acids. For example, 85% and 80% ee were obtained, respectively, for the product when $Sn(OTf)_2$ and $Sc(OTf)_3$ were used (Table 2, entries 3 and 5), but only 26% and 15% ee were obtained when $AlCl_3$ and $La(OTf)_3$ were used (Table 2, entries 9 and 10). The low ee obtained with $AlCl_3$ and $La(OTf)_3$ was initially thought to be due to the racemization of the rearranged benzoyloxy ketone via enolization under the acidic reaction conditions. However, in a control experiment, only a 3% decrease of the ee was observed upon stirring benzoyloxy ketone (*R*)-**6** (91% ee) in nitromethane with $La(OTf)_3$ for 0.5 h. The results suggested that in the acid-catalyzed rearrangement there was a competing pathway which gave rise to the *S* isomer via inversion of configuration, thereby reducing the ee. To investigate the existence of the competing pathway, more Lewis acids were tested.[9] *Strikingly, it was found that the S isomer (inverted product) actually became the major product when certain Lewis acids were utlized* (Table 2, entries 12−19). Good enantioselectivities (80−91% ee) were obtained with $YbCl_3$, $ErCl_3$, $AlMe_3$, and silica gel[10] (Table 2, entries 12, 15, 16, and 19).

The results presented in Table 2 clearly indicate that there are two distinct pathways involved in the acid-catalyzed rearrangement of enol ester epoxides, leading to two different enantiomers. Although a full understanding of the factors controlling this competition has not been attained, the acidity of the catalyst seems to play an important role. For example, when $Yb(OTf)_3$ was used as the catalyst, the *R* enantiomer of the rearranged product was obtained in 66% ee (Table 2, entry 11). On the other hand, when a notably weaker Lewis acid $YbCl_3$ was used, the *S* enantiomer was obtained in 82% ee (Table 2, entry 12). Pathways a and b outlined in Scheme 5 provide plausible mechanisms for the results. In pathway a, the complexation of a strong acid to the epoxide oxygen of **3** leads to cleavage of C_1−O bond to form carbocation intermediate **8**. Subsequent acyloxy migration with retention of configuration gives acyloxy ketone **4**. In pathway b, the complexation of a weak acid to **3** weakens both epoxide bonds, facilitating acyloxy migration with inversion of configuration (**9**) to give acyloxy ketone *ent*-**4**.[11,12]

Among other possible pathways, it was also conceivable that enol ester epoxide **5** could rearrange to (*S*)-**6** with a net inversion of configuration via a hydride shift mechanism (pathway c) (Scheme 6). To further differentiate between pathways b and c, 1-benzoyloxy-1,2-epoxy-4,4-dimethylcyclohexane (**10**) was then investigated (Scheme 7). As indicated in Scheme 7, two different structural isomers **11** and **12** would arise from the two pathways. Enol ester epoxide **10** was then treated with $YbCl_3$, $AlMe_3$, and silica gel. In all these cases, compound **11** was formed predominately as judged by the NMR analysis, suggesting that pathway c is not the major operating pathway at least for enol ester epoxide **10**.

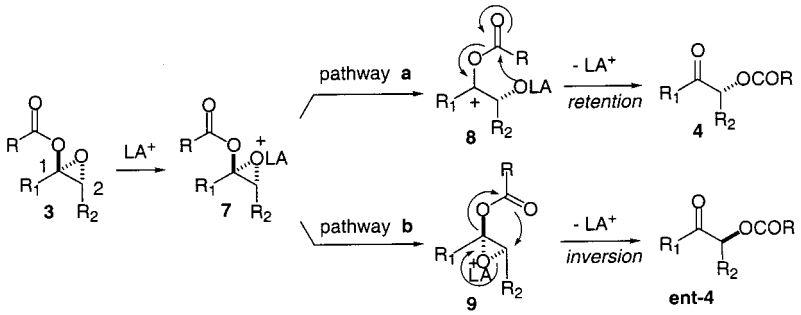
The discovery of the two different rearrangement pathways prompted us to investigate more substrates to test the generality. Of particular interest was the possibility of generating either enantiomer of an acyloxy ketone in high ee from a single enantiomerically enriched enol ester epoxide under mild conditions. As shown in Table 3, *p*-TsOH proved to be an effective catalyst for rearrangement via pathway a for a variety of epoxides, giving products with retention of configuration in high stereospecificity. In most cases, the resulting α-acyloxy ketones were crystalline, and the enantiomeric excess could be further enhanced by recrystallization. To test the generality of the rearrangement via pathway b, silica gel, $YbCl_3$, and $AlMe_3$ were used (Table 3). In most cases the isomer with inverted configuration was the major product, however, in two cases (Table 3, entries 7 and 8) the rearrangement proceeded with retention of configuration. The preference for pathway a with these benzylic

(8) Studies showed that the enantiomeric excess of the rearranged product **6** was somewhat solvent dependent. Among a few solvents tested, nitromethane was shown to be the best. The other solvents tested include $CHCl_3$ (83% ee), CH_2Cl_2 (83% ee), CH_3CN (80% ee), Et_2O (80% ee), C_6H_6 (79% ee), DMF (no reaction).

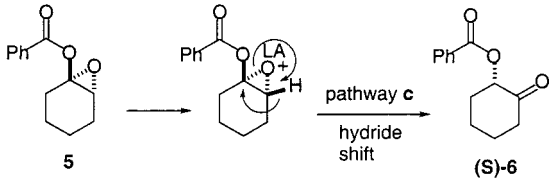
(9) No rearrangement occurred with Lewis acids such as $MgBr_2$, $Ti(O^iPr)_4$, $Zr(OEt)_4$, $Pd(OAc)_2$, $Cu(OAc)_2$, $LaCl_3$, $PrCl_3$.

(10) For examples of silica gel catalyzed rearrangements, see refs 2a, b, and d. Both inversion and retention of configuration were reported.

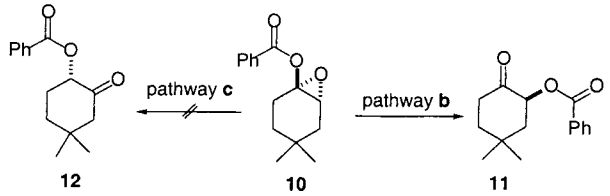
Scheme 5



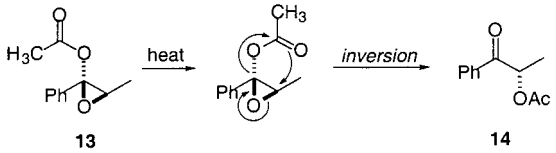
Scheme 6



Scheme 7



Scheme 8



epoxides is probably due to a stabilized carbocation intermediate **8**.

Thermal Rearrangement of Chiral Enol Ester Epoxides. As shown above, in many cases the acid-catalyzed rearrangement of chiral enol ester epoxides could lead to the formation of α-acyloxy ketones with either retention or inversion of configurations. In the case of retention of configuration, all the examples presented in Table 3 worked well. However, in the case of inversion of configuration, the results were somewhat substrate dependent. For example, with benzylic epoxides (Table 3, entries 7 and 8), the rearrangement with inversion of configuration could not become the major pathway with any of the acids tested.

It has been shown that rearrangements of steroid enol ester epoxides under thermal conditions proceed diastereoselectively via intramolecular migration of the acyloxy group with inversion of configuration at the carbon to which the acyloxy group migrates.[2a,g,n] The stereoselectivity of thermal rearrangement demonstrated on these systems prompted us to investigate the thermal rearrangement of chiral enol ester epoxides with the aim of achieving the rearrangement with inversion of configuration for a wider range of substrates.

Our studies started with (1*S*,2*R*)-1-acetoxy-1-phenyl-1,2-epoxypropane (**13**) (94% ee) as a test substrate (Scheme 8). The thermal rearrangement was initially performed in a sealed tube at 120 °C. Heating the epoxide at this temperature for 2.0 h gave the rearranged product with 11% isolated yield. It was found that the rearrangement could be dramatically facilitated by raising the temperature. For example, heating epoxide **13** at 153 °C in a sealed tube for 2.0 h, the rearranged product was obtained in 59% isolated yield with 86% ee. When the reaction temperature was further raised to 195 °C, the rearrangement was complete after 0.5 h and gave a quantitative yield of the product (Table 4, entry 12). More importantly, the product ee was determined to be 90%, showing only a 4% decrease in ee compared with the starting epoxide. It seems that shorter reaction time as a result of higher reaction temperature is important to obtain the high product ee. Further studies showed that the rearranged product had the *S* configuration. As anticipated, the rearrangement proceeded with inversion of configuration. Upon demonstrating that thermal rearrangement of epoxide **13** proceeded with inversion of configuration with high stereoselectivity, the process was then extended to a wide range of epoxides (Table 4). For those epoxides that can readily rearrange, the reaction can be performed in a vial under N_2 (Table 4, entries 1−3). However, for many other epoxides, the rearrangement needs to be carried out at higher temperature and in a sealed tube to obtain high stereoselectivity (Table 4, entry 5 vs 6). As shown in Table 4, all the epoxides including benzylic epoxides (Table 4, entries 12−14) underwent the rearrangement with a clean inversion of configuration. Good yields and high ee's were obtained by careful control of the reaction temperature and time.[15] This thermal rearrangement in combination with the

(11) While the acidity of the catalyst is an important factor affecting the competition of the two pathways, the size and the coordination number of the Lewis acid could also be important. Full elucidation of these factors is difficult at present.

(12) To test whether the rearrangements proceed intermolecularly or intramolecularly, crossover experiments were carried out using a mixture of 1-acetoxy-1,2-epoxycyclohexane and 1-benzoyloxy-1,2-epoxycycloheptane as substrates under acidic conditions (*p*-TsOH, $YbCl_3$, $AlMe_3$, silica gel) (Scheme 5). In the case of *p*-TsOH, small amounts of crossover products were detected by GC and ^1H NMR. The amounts of these products were found to be concentration dependent (ca 6.8% at substrate concentration of 0.64 M and ca. 1.7% at substrate concentration of 0.018 M). In the cases of $YbCl_3$, $AlMe_3$, and silica gel, the crossover products were found to be minimal (less than 0.5% at substrate concentration of 0.64 M and less than 0.2% at substrate concentration of 0.018 M). All of these results suggest that the acid-catalyzed rearrangements proceed predominantly in an intramolecular fashion, particularly for pathway b. Further experiments with enantiomerically enriched enol ester epoxides showed that the enantioselectivities of the rearranged products were not affected by the substrate concentrations.

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(15) It was found that the product ee was also affected by the purity of the starting epoxide.

Table 3. Examples of Acid-Catalyzed Rearrangements of Enol Ester Epoxides[a]

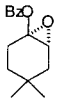
entry	epoxide	acid	time (h)	epoxide ee (%)	product ee (%)[d]	yield (%)[i]
1		*p*-TsOH	0.2	93	90 (99) (R)[e]	89
		Silica gel	12	92	91 (S)	83
		$YbCl_3$	0.5	92	88 (S)	73
		$AlMe_3$	0.1	91	87 (S)	85
2		*p*-TsOH	0.1	93	93 (99) (R)[e]	70
		Silica gel	19	93	88 (S)	87
		$AlMe_3$	0.1	91	85 (S)	85
3		*p*-TsOH	0.3	92	87 (99) (R)[e]	72
		Silica gel	12	92	90 (S)	95
		$YbCl_3$	0.5	92	94 (S)	79
		$AlMe_3$	0.2	92	89 (S)	90
4		*p*-TsOH	0.4	95	79 (R)[g]	92
		Silica gel	16	95	94 (S)	91
		$YbCl_3$	0.5	95	95 (S)	97
		$AlMe_3$	0.3	95	83 (S)	94
5		*p*-TsOH	0.3	97	97 (R)[f]	77
		Silica gel	48	97	97 (S)	70
		$YbCl_3$	0.3	97	96 (S)	84
		$AlMe_3$	0.2	97	69 (S)	91
6[k]		*p*-TsOH	2	94	90 (99) (R)[g]	68
		$YbCl_3$	3	94	77 (S)	87
		$AlMe_3$[b]	0.1	94	69 (S)	79
7[k]		*p*-TsOH	0.3	94	94 (R)[h]	72
		$AlMe_3$[c]	5	94	90 (R)	71
8		*p*-TsOH	0.05	99	99 (R)[f]	79
		Silica gel	48	99	38 (R)	45[j]
		$YbCl_3$	2.5	99	57 (R)	87
		$AlMe_3$	0.1	99	93 (R)	81

[a] All reactions were carried out at room temperature with 10 mol % *p*-TsOH (dried by azeotropic removal of its hydrate) in dry CH_3NO_2, or 5−10 times (by weight) silica gel (Davisil 35−60 mesh, pH 7.0) in CH_3NO_2, or 10 mol % $YbCl_3$ in CH_2Cl_2, or 10 mol % $AlMe_3$ in CH_3NO_2 unless otherwise noted. [b] 100 mol % acid catalyst was used. [c] 20 mol % acid catalyst was used. [d] Enantioselectivity was determined by chiral HPLC (Chiralcel OD) except entries 3 and 4 where enantioselectivity was determined by ^1H NMR shift analysis with $Eu(hfc)_3$ or by chiral HPLC (Chiralpak AD), respectively. The values in parentheses are the ee's after recrystallization. [e] The absolute configurations were determined by comparing HPLC chromatograms (entries 1 and 2) or ^1H NMR shift analysis using $Eu(hfc)_3$ (entry 3) with the authentic sample prepared from commercially available (*R,R*)-1,2-*trans*-cyclohexanediol. [f] The α-acyloxy ketones were hydrolyzed to α-hydroxy ketones, and the absolute configurations were determined by comparing the measured optical rotations of the α-hydroxy ketones with the literature (for entry 5 see ref 13; for entry 8 see ref 14). [g] The absolute configuration was tentatively assigned by analogy. [h] The absolute configuration was determined by comparing the measured optical rotation with the literature (see ref 3a). [i] Isolated yield. [j] Conversion determined by the ^1H NMR of the crude reaction mixture. [k] No reaction was found with silica gel.

acid-catalyzed rearrangements allows the formation of either enantiomer of α-acyloxy ketone from one enantiomer of an enol ester epoxide (Scheme 9).

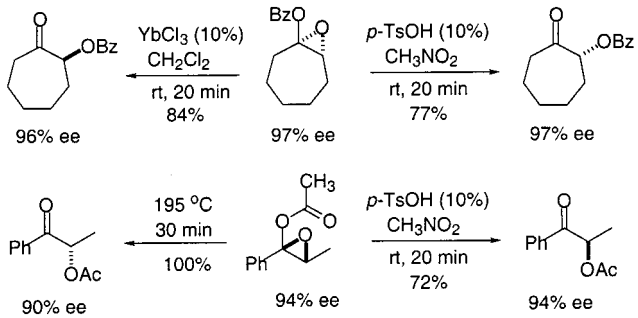
In summary, we have shown that enol esters can be epoxidized with high ee's using the fructose-derived chiral ketone **1** as catalyst and Oxone as oxidant. The availability of the enantiomerically enriched enol ester epoxides provided us the opportunities to study their rearrangement under acidic and thermal conditions. Our studies have shown that the acid-catalyzed rearrangement of these epoxides operates through two distinct pathways, one with retention of configuration and the other with inversion. Acidity of the catalyst is one important factor, with strong acids favoring retention of configuration and weak acids favoring inversion. Under thermal conditions, these epoxides rearrange highly stereoselectively with inversion of configuration. In addition to the mechanistic significance, the current study

Table 4. Examples of Thermal Rearrangements of Enol Ester Epoxides

entry	epoxide	temp. (°C)	time (min)	epoxide ee (%)	product ee (%)	yield (%)[j]
						
1	R = Ph	120[a]	30	90	90[c] (S)[f]	92
2	R = *p*-CH_3-Ph	120[a]	30	90	90[c] (S)[f]	95
3	R = *p*-CH_3O-Ph	120[a]	30	90	90[c] (S)[f]	84
4	R = *p*-Cl-Ph	165[b]	5	88	88[d] (S)[f]	89
5	R = *p*-NO_2-Ph	120[a]	30	90	69[c] (S)[f]	89
6	R = *p*-NO_2-Ph	165[b]	5	90	90[c] (S)[f]	95
7	R = $(CH_3)_3C$	190[b]	2	92	90[e] (S)[f]	95
8	R = CH_3	190[b]	2	75	75[e] (S)[f]	99
9		165[b]	5	95	94[d] (S)[h]	97
10		160[b]	5	>99	>99[c] (S)[g]	99
11		160[b]	5	96	93[c] (S)[h]	95
12		195[b]	30	94	90[c] (S)[i]	100
13		185[b]	15	90	87[c] (S)[g]	97
14		165[b]	4	99	88[c] (S)[g]	89

[a] Rearrangements were performed neat under N_2. [b] Rearrangements were performed neat under N_2 in a sealed tube. [c] Enantioselectivity was determined by chiral HPLC (Chiralcel OD). [d] Enantioselectivity was determined by chiral HPLC (Chiralpak AD). [e] Enantioselectivity was determined by ^{1}H NMR shift analysis with Eu(hfc)$_3$. [f] The absolute configurations were determined by comparing HPLC chromatograms (entries 1−6) or ^{1}H NMR shift analysis using Eu(hfc)$_3$ (entries 7 and 8) with the authentic samples prepared from commercially available (*R,R*)-1,2-*trans*-cyclohexanediol. [g] The α-acyloxy ketones were hydrolyzed to α-hydroxy ketones, and the absolute configurations were determined by comparing the measured optical rotations of the α-hydroxy ketones with the literature (for entry 10, see ref 13; for entry 13, see refs 3b and 3d; for entry 14, see ref 14). [h] The absolute configuration was tentatively assigned by analogy. [i] The absolute configuration was determined by comparing the measured optical rotation with the literature (see ref 3a). [j] Isolated yield.

Scheme 9



also provides the flexibility to synthesize either enantiomer of α-acyloxy ketone from one enantiomer of an enol ester epoxide by judicious choice of reaction conditions.

Experimental Section

General Methods. Oxone was purchased from Aldrich (it has been found that the oxidation activity of the purchased Oxone occasionally varies with different batches). All glassware used for the epoxidation was carefully washed to be free of any trace metals which catalyze the decomposition of Oxone. Elemental analyses were performed by M−H−W Laboratories, Phoenix, AZ.

Preparation of Enol Esters.

Method A.[16] To a mixture of cyclohexanone (9.82 g, 100 mmol) and benzoic anhydride (90%, 28.9 g, 115 mmol) in hexane (200 mL) was added $HClO_4$ (0.2 mL). Upon stirring at room temperature for 2 h, the mixture was filtered to remove the formed solids. The filtrate was washed with 1 N NaOH solution (100 mL), saturated $NaHCO_3$ solution (2 × 100 mL), and brine (2 × 100 mL), dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexanes−ether, 50:1, v/v) to afford 1-benzoyloxy-1-cyclohexene[6b,17] as a colorless liquid (11.9 g, 59%). IR (NaCl) 1730, 1690 cm^{-1}; ^{1}H NMR δ 8.07 (m, 2H), 7.58 (m, 1H), 7.45 (m, 2H), 5.50 (m, 1H), 2.27 (m, 2H), 2.17 (m, 2H), 1.80 (m, 2H), 1.66 (m, 2H); ^{13}C NMR δ

(16) Whitlock, H. W., Jr.; Overman, L. E. *J. Org. Chem.* **1969**, *34*, 1962.

(17) Goldblum, A.; Mechoulam, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1889.

165.3, 148.8, 133.3, 130.3, 130.1, 128.6, 114.5, 27.2, 23.9, 22.9, 22.0.

Method B.[18] To a stirred suspension of KH (washed with pentane) (2.4 g, 60.0 mmol) in DME (25 mL) under N_2 at −5 °C was added a solution of cyclohexanone (4.9 g, 50 mmol) in dry DME (5 mL). The resulting enolate solution was then added by syringe to a mixture of *p*-toluoyl chloride (11.5 g, 75.0 mmol) and DMAP (0.30 g, 2.5 mmol) in DME (15 mL) over a period of 10 min at room temperature. Upon stirring for another 20 min at r.t., the mixture was poured into ice−water, extracted with hexane, washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (silica gel column was pretreated with Et_3N, 2−4% EtOAc in hexane was used as eluent) to afford 1-(*p*-methylbenzoyloxy)cyclohexene as a colorless semi-solid (5.72 g, 53%). IR (NaCl) 1729, 1677 cm^{-1}; ^1H NMR δ 7.96 (d, J = 6.3 Hz, 2H), 7.24 (d, J = 6.3 Hz, 2H), 5.48 (m, 1H), 2.42 (s, 3H), 2.25 (m, 2H), 2.17 (m, 2H), 1.79 (m, 2H), 1.66 (m, 2H); ^{13}C NMR δ 165.3, 148.7, 143.9, 130.0, 129.2, 127.5, 114.3, 27.2, 24.0, 23.0, 22.0, 21.9.

A Representative Epoxidation Procedure. To an ice-cold mixture of 1-benzoyloxy-1-cyclohexene (0.134 g, 0.67 mmol), 10 mL of CH_3CN−DMM (v/v, 1/2), 6.7 mL of buffer (0.05 M $Na_2B_4O_7$ in 4×10^{-4} M aqueous Na_2EDTA), Bu_4NHSO_4 (0.009 g, 0.027 mmol), and ketone **1** (0.0516 g, 0.20 mmol) were added a solution of Oxone (0.567 g, 0.92 mmol) in 4.3 mL of aqueous Na_2EDTA (4×10^{-4} M) and a solution of K_2CO_3 (0.567 g, 3.87 mmol) in 4.3 mL of water simultaneously through two syringes via syringe pump over a period of 1.5 h. The reaction was quenched with hexane and brine. The mixture was extracted with hexane, washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (silica gel was buffered with Et_3N, using 5% ether in hexane as eluent) to afford 1-benzoyloxy-1,2-epoxycyclohexane[6a,b,19] as a colorless oil (0.12 g, 82% yield, 93% ee) (Table 1, entry 2). $[\alpha]^{25}_D$ = −39.2 (*c* 0.53, $CHCl_3$); IR (NaCl) 1728, 1267 cm^{-1}; ^1H NMR δ 8.00 (d, J = 7.8 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.40 (t, J = 7.8 Hz, 2H), 3.39 (m, 1H), 2.32 (dt, J = 14.3, 6.9 Hz, 1H), 2.20 (dt, J = 14.3, 6.2 Hz, 1H), 2.10−1.86 (m, 2H), 1.58−1.36 (m, 4H); ^{13}C NMR δ 165.4, 133.6, 129.9, 129.6, 128.6, 83.7, 59.5, 28.3, 24.8, 20.5, 19.0. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.82; H, 6.31.

1-Acetoxy-1,2-epoxycyclohexane (Table 1, entry 1).[19]

Enol Ester. The enol ester was prepared by the method described in ref 19. IR (NaCl) 1751, 1686 cm^{-1}; ^1H NMR δ 5.36 (m, 1H), 2.11 (s, 3H), 2.20−2.05 (m, 4H), 1.74 (m, 2H), 1.59 (m, 2H); ^{13}C NMR δ 169.7, 148.6, 114.2, 27.0, 23.8, 22.8, 21.9, 21.3.

Epoxide. $[\alpha]^{25}_D$ = −51.9 (*c* 1.12, $CHCl_3$) (75% ee); IR (NaCl) 1747, 1231 cm^{-1}; ^1H NMR δ 3.30 (ddd, J = 2.7, 1.8, 0.9 Hz, 1H), 2.24 (dtd, J = 14.5, 6.6, 0.9 Hz, 1H), 2.09 (dt, J = 14.5, 6.3 Hz, 1H), 2.06 (s, 3H), 1.92 (m, 2H), 1.51−1.32 (m, 4H); ^{13}C NMR δ 169.7, 83.0, 59.4, 28.1, 24.8, 21.3, 20.4, 18.9. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.72; H, 8.11.

1-(*p*-Methylbenzoyloxy)-1,2-epoxycyclohexane (Table 1, entry 3). $[\alpha]^{25}_D$ = −30.6 (*c* 0.51, $CHCl_3$) (90% ee). IR (NaCl) 1725, 1611, 1269 cm^{-1}; ^1H NMR δ 7.91 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 3.41 (m, 1H), 2.40 (s, 3H), 2.34 (dt, J = 14.1, 6.9 Hz, 1H), 2.22 (dt, J = 14.1, 6.6 Hz, 1H), 2.07−1.89 (m, 2H), 1.61−1.49 (m, 2H), 1.49−1.38 (m, 2H); ^{13}C NMR δ 165.5, 144.3, 130.0, 129.3, 126.8, 83.5, 59.5, 28.4, 24.9, 21.8, 20.5, 19.0. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.23; H, 7.19.

1-(*p*-Methoxybenzoyloxy)-1,2-epoxycyclohexane (Table 1, entry 4).

Enol Ester (Method B)**.** IR (NaCl) 1723, 1685 cm^{-1}; ^1H NMR δ 8.00 (dt, J = 9.0, 2.4 Hz, 2H), 6.93 (dt, J = 9.0, 2.4 Hz, 2H), 5.45 (tt, J = 3.9, 1.5 Hz, 1H), 3.83 (s, 3H), 2.23 (m, 2H), 2.14 (m, 2H), 1.76 (m, 2H), 1.63 (m, 2H); ^{13}C NMR δ 165.0, 163.7, 148.8, 132.1, 122.7, 114.3, 113.8, 55.6, 27.2, 23.9, 22.9, 22.0.

Epoxide. $[\alpha]^{25}_D$ = −23.6 (*c* 0.49, $CHCl_3$) (90% ee). IR (NaCl) 1720, 1606, 1257 cm^{-1}; ^1H NMR δ 7.98 (m, 2H), 6.91 (m, 2H), 3.86 (s, 3H), 3.41 (m, 1H), 2.33 (dt, J = 14.4, 6.9 Hz, 1H), 2.22 (dt, J = 14.4, 6.3 Hz, 1H), 2.06−1.90 (m, 2H), 1.58−1.38 (m, 4H); ^{13}C NMR δ 165.2, 163.9, 132.1, 121.9, 113.9, 83.5, 59.6, 55.6, 28.4, 24.9, 20.5, 19.0. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.49. Found: C, 67.73; H, 6.34.

1-(*p*-Chlorobenzoyloxy)-1,2-epoxycyclohexane (Table 1, entry 5).

Enol Ester (Method B). IR (NaCl) 1731, 1684, 1590, 1272 cm^{-1}; ^1H NMR δ 8.00 (m, 2H), 7.43 (m, 2H), 5.50 (m, 1H), 2.24 (m, 2H), 2.17 (m, 2H), 1.80 (m, 2H), 1.66 (m, 2H); ^{13}C NMR δ 164.3, 148.6, 139.7, 131.4, 128.9, 128.7, 114.6, 27.1, 23.9, 22.9, 21.9.

Epoxide. $[\alpha]^{25}_D$ = −26.4 (*c* 1.1, $CHCl_3$) (90% ee); IR (NaCl) 1728, 1594 cm^{-1}; ^1H NMR δ 7.92 (m, 2H), 7.37 (m, 2H), 3.38 (m, 1H), 2.32 (dt, J = 14.1, 6.9 Hz, 1H), 2.17 (dt, J = 14.1, 6.1 Hz, 1H), 2.03−1.87 (m, 2H), 1.51−1.37 (m, 4H); ^{13}C NMR δ 164.5, 140.1, 131.3, 129.0, 128.1, 83.9, 59.5, 28.3, 24.8, 20.5, 19.0. Anal. Calcd for $C_{13}H_{13}ClO_3$: C, 61.79; H, 5.19. Found: C, 61.81; H, 5.47.

1-(*p*-Nitrobenzoyloxy)-1,2-epoxycyclohexane (Table 1, entry 6).

Enol Ester[17] (Method B). IR (NaCl) 1737, 1690, 1527 cm^{-1}; ^1H NMR δ 8.30 (m, 2H), 8.24 (m, 2H), 5.54 (m, 1H), 2.27 (m, 2H), 2.19 (m, 2H), 1.82 (m, 2H), 1.68 (m, 2H); ^{13}C NMR δ 163.3, 150.7, 148.6, 135.7, 131.1, 123.7, 115.0, 26.9, 23.8, 22.8, 21.8.

Epoxide. $[\alpha]^{25}_D$ = −30.6 (*c* 0.33, $CHCl_3$) (90% ee); IR (NaCl) 1714, 1527 cm^{-1}; ^1H NMR δ 8.30 (dt, J = 8.8, 1.8 Hz, 2H), 8.20 (dt, 8.8, 1.8 Hz, 2H), 3.45 (m, 1H), 2.40 (dt, J = 14.2, 6.6 Hz, 1H), 2.22 (dt, J = 14.2, 6.3 Hz, 1H), 2.00 (m, 2H), 1.61−1.40 (m, 4H); ^{13}C NMR δ 163.3, 150.8, 134.8, 130.9, 123.6, 84.3, 59.3, 28.1, 24.7, 20.4, 18.9. Anal. Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.09; H, 5.18; N, 5.26.

1-Pivaloyloxy-1,2-epoxycyclohexane (Table 1, entry 7).

Enol Ester (Method A). IR (NaCl) 1746, 1690 cm^{-1}; ^1H NMR δ 5.29 (m, 1H), 2.07 (m, 4H), 1.70 (m, 2H), 1.57 (m, 2H), 1.20 (s, 9H); ^{13}C NMR δ 177.3, 148.7, 113.8, 38.9, 27.3, 26.8, 23.8, 22.8, 21.9.

Epoxide.[19] $[\alpha]^{25}_D$ = −40.5 (*c* 0.60, $CHCl_3$) (91% ee); IR (NaCl) 1740, 1142 cm^{-1}; ^1H NMR δ 3.25 (m, 1H), 2.22 (dt, J = 14.1, 6.8 Hz, 1H), 2.03 (dt, J = 14.1, 6.3 Hz, 1H), 1.92 (m, 2H), 1.62−1.32 (m, 4H), 1.19 (s, 9H); ^{13}C NMR δ 177.6, 83.1, 59.5, 38.8, 28.2, 27.0, 24.8, 20.4, 18.9. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.67; H, 9.50.

1-Benzoyloxy-1,2-epoxy-4,4-dimethylcyclohexane (Table 1, entry 8).

Enol Ester (Method A). IR (NaCl) 1724, 1685 cm^{-1}; ^1H NMR δ 8.08 (m, 2H), 7.58 (m, 1H), 7.45 (m, 2H), 5.40 (m, 1H), 2.27 (m, 2H), 1.95 (m, 2H), 1.55 (t, J = 6.6 Hz, 2H), 1.02 (s, 6H); ^{13}C NMR δ 165.3, 147.8, 133.2, 130.2, 130.0, 128.5, 113.3, 37.9, 35.7, 29.0, 28.2, 24.9.

Epoxide. $[\alpha]^{25}_D$ = −15.1 (*c* 0.45, $CHCl_3$) (95% ee); IR (NaCl) 1724 cm^{-1}; ^1H NMR δ 8.04 (m, 2H), 7.58 (m, 1H), 7.44 (m, 2H), 3.41 (d, J = 5.1 Hz, 1H), 2.33 (m, 2H), 1.86 (ddd, J = 15.9, 5.1, 2.1 Hz, 1H), 1.62 (d, J = 15.9 Hz, 1H), 1.42 (ddd, J = 13.5, 11.4, 5.7 Hz, 1H), 1.29 (m, 1H), 1.16 (s, 3H), 0.93 (s, 3H); ^{13}C NMR δ 165.2, 133.6, 129.9, 129.5, 128.6, 83.7, 58.9, 38.4, 33.2, 31.2, 28.4, 26.9, 24.2. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.13; H, 7.37. Found: C, 73.16; H, 7.18.

1-Benzoyloxy-1,2-epoxycyclopentane (Table 1, entry 9).

Enol Ester[17] (Method A). IR (NaCl) 1736, 1665, 1267 cm^{-1}; ^1H NMR δ 8.08 (m, 2H), 7.59 (tt, J = 7.2, 1.5 Hz, 1H), 7.46 (m, 2H), 5.56 (dt, J = 4.2, 2.1 Hz, 1H), 2.58 (m, 2H), 2.44 (m, 2H), 2.02 (m, 2H); ^{13}C NMR δ 164.4, 151.3, 133.4, 130.1, 129.9, 128.6, 113.5, 31.2, 28.9, 21.3.

Epoxide. $[\alpha]^{25}_D$ = −26.8 (*c* 0.41, $CHCl_3$) (80% ee); IR (NaCl) 1722, 1272 cm^{-1}; ^1H NMR δ 8.02 (m, 2H), 7.57 (m, 1H), 7.43 (m, 2H), 3.78 (s, 1H), 2.43 (dd, J = 13.2, 8.4 Hz, 1H), 2.11 (ddd, J = 13.2, 9.9, 9.0 Hz, 1H), 1.93 (m, 2H), 1.73 (m, 1H), 1.54 (m, 1H); ^{13}C NMR δ 165.2, 133.8, 130.1, 129.3, 128.7, 90.0, 62.8, 28.4, 26.3, 20.2. Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.35; H, 6.00.

(18) Riehl, J. J.; Ladjama, D. *Synthesis* **1979**, 504.

(19) Amos, R. A.; Katzenellenbogen, J. A. *J. Org. Chem*. **1977**, *42*, 2537.

1-Benzoyloxy-1,2-epoxycycloheptane (Table 1, entry 10).

Enol Ester[17] (Method A)**.** IR (NaCl) 1725, 1691, 1269 cm^{-1}; ^1H NMR δ 8.06 (m, 2H), 7.57 (tt, J = 7.3, 1.7 Hz, 1H), 7.45 (m, 2H), 5.60 (t, J = 6.4 Hz, 1H), 2.46 (m, 2H), 2.16 (m, 2H), 1.61−1.80 (m, 6H); ^{13}C NMR δ 165.6, 153.5, 133.2, 130.3, 130.0, 128.5, 118.4, 33.4, 31.2, 27.2, 25.5, 25.4.

Epoxide. $[\alpha]^{25}_D = -29.9$ (c 0.70, $CHCl_3$) (91% ee); IR (NaCl) 1720, 1275 cm^{-1}; ^1H NMR δ 8.01 (m, 2H), 7.57 (tt, J = 7.4, 1.6 Hz, 1H), 7.43 (m, 2H), 3.38 (d, J = 5.4 Hz, 1H), 2.48 (ddd, J = 15.2, 11.9, 3.2 Hz, 1H), 2.38 (m, 1H), 2.22 (m, 1H), 2.02 (dddd, J = 15.2, 11.9, 3.0, 1.2 Hz, 1H), 1.85−1.59 (m, 3H), 1.49−1.22 (m, 2H), 1.09 (m, 1H); ^{13}C NMR δ 165.6, 133.5, 130.0, 129.9, 128.6, 87.9, 63.4, 31.8, 30.0, 27.5, 24.1. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.28; H, 6.89.

1-Benzoyloxy-1,2-epoxycyclooctane (Table 1, entry 11).

Enol Ester (Method A). IR (NaCl) 1729, 1687, 1273 cm^{-1}; ^1H NMR δ 8.08 (m, 2H), 7.57 (tt, J = 7.7, 1.8 Hz, 1H), 7.45 (m, 2H), 5.42 (t, J = 8.4 Hz, 1H), 2.44 (m, 2H), 2.20 (m, 2H), 1.64 (m, 8H); ^{13}C NMR δ 165.8, 150.7, 133.3, 130.4, 130.1, 128.6, 116.7, 29.8, 29.5, 28.1, 26.5, 26.0, 25.1.

Epoxide. $[\alpha]^{25}_D = +7.2$ (c 0.62, $CHCl_3$) (95% ee); IR (NaCl) 1731, 1275 cm^{-1}; ^1H NMR δ 8.01 (m, 2H), 7.57 (tt, J = 7.4, 1.6 Hz, 1H), 7.43 (m, 2H), 3.20 (ddd, J = 10.0, 4.6, 0.8 Hz, 1H), 2.88 (m, 1H), 2.27 (ddd, J = 13.8, 7.8, 4.5 Hz, 1H), 1.92−1.20 (m, 10H); ^{13}C NMR δ 165.2, 133.5, 130.1, 129.9, 128.6, 86.0, 60.5, 28.1, 28.0, 26.2, 25.2, 24.9. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.38; H, 7.27.

1-Benzoyloxy-1,2-epoxytetrahydronaphthalene (Table 1, entry 12).

Enol Ester[17] (Method A). IR (NaCl) 1738, 1658, 1264 cm^{-1}; ^1H NMR δ 8.21 (m, 2H), 7.62 (tt, J = 7.5, 1.8 Hz, 1H), 7.51 (m, 2H), 7.15 (m, 4H), 5.84 (t, J = 4.5 Hz, 1H), 2.93 (t, J = 8.1 Hz, 2H), 2.52 (td, J = 8.1, 4.5 Hz, 2H); ^{13}C NMR δ 165.1, 146.0, 136.6, 133.7, 130.7, 130.3, 129.7, 128.8, 128.1, 127.8, 126.6, 121.0, 115.9, 27.7, 22.3.

Epoxide.[17] $[\alpha]^{25}_D = -204.1$ (c 0.44, $CHCl_3$) (88% ee); IR (NaCl) 1735, 1271 cm^{-1}; ^1H NMR δ 8.18 (m, 2H), 7.64 (m, 1H), 7.51 (t, J = 8.1 Hz, 2H), 7.44 (d, J = 7.5 Hz, 1H), 7.32−7.15 (m, 3H), 3.98 (d, J = 2.7 Hz, 1H), 2.81 (m, 1H), 2.68 (dd, J = 15.3, 5.7 Hz, 1H), 2.46 (m, 1H), 2.11 (ddd, J = 13.8, 13.5, 5.7 Hz, 1H); ^{13}C NMR δ 165.0, 136.3, 134.0, 131.3, 130.3, 129.2, 129.0, 128.8, 128.7, 126.6, 125.6, 80.7, 62.4, 25.3, 21.9. Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found: C, 76.69; H, 5.47.

1-Acetoxy-1-phenyl-1,2-epoxypropane (Table 1, entry 13).

Enol Ester. The enol ester was prepared by a method similar to that described in ref 20. A mixture of propiophenone (6.70 g, 50 mmol), acetic anhydride (10.2 g, 100 mmol), and *p*-toluenesulfonic acid monohydrate (0.060 g, 0.31 mmol) was heated in an oil bath (160−170 °C) for 7 h, and acetic acid formed during the reaction was distilled off (ca. 3 mL). Upon cooling, the reaction mixture was poured into cold saturated $NaHCO_3$, extracted with hexane, dried (K_2CO_3), filtered, concentrated, and purified by flash chromatography (hexane) to afford *Z*-1-acetoxy-1-phenylpropene as a colorless liquid (5.89 g, 61%). IR (NaCl) 1757, 1670, 1207 cm^{-1}; ^1H NMR δ 7.41−7.21 (m, 5H), 5.89 (q, J = 7.2 Hz, 1H), 2.29 (s, 3H), 1.70 (d, J = 7.2 Hz, 3H); ^{13}C NMR δ 168.8, 147.1, 135.2, 128.7, 128.2, 124.4, 112.8, 20.8, 11.8.

Epoxide. $[\alpha]^{25}_D = +11.4$ (c 0.65, $CHCl_3$) (91% ee). IR (NaCl) 1763, 1211 cm^{-1}; ^1H NMR δ 7.39−7.34 (m, 5H), 3.21 (q, J = 5.4 Hz, 1H), 2.17 (s, 3H), 1.49 (d, J = 5.4 Hz, 3H); ^{13}C NMR δ 169.3, 136.3, 129.0, 128.7, 125.8, 85.1, 61.6, 21.2, 14.0. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.76; H, 6.37.

1-Acetoxy-1,2-diphenyl-1,2-epoxyethane (Table 1, entry 14).

Enol ester[6b] (Method A)**.** IR (NaCl) 1757, 1645, 1198 cm^{-1}; ^1H NMR δ 7.52 (m, 4H), 7.39−7.22 (m, 6H), 6.70 (s, 1H), 2.30 (s, 3H); ^{13}C NMR δ 168.7, 146.8, 135.7, 134.5, 128.8, 127.8, 124.9, 117.0, 116.9, 21.3.

Epoxide.[6b] $[\alpha]^{25}_D = +85.0$ (c 0.70, $CHCl_3$) (90% ee); IR (NaCl) 1767 cm^{-1}; ^1H NMR δ 7.50−7.34 (m, 10H), 4.17 (s, 1H), 1.92 (s, 3H); ^{13}C NMR δ 169.0, 135.6, 133.3, 129.3, 128.8, 128.7, 128.3, 127.1, 125.9, 85.8, 65.8, 20.9. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.95; H, 5.92.

Representative Procedures for Acid-Catalyzed Rearrangement of Enol Ester Epoxides.

***p*-TsOH as Catalyst.** To a solution of (1*R*,2*R*)-2-benzoyloxy-1,2-epoxycyclohexane (0.030 g, 93% ee) in anhydrous nitromethane (0.4 mL) was added *p*-TsOH (0.0024 g, 0.0137 mmol). Upon stirring at room temperature for 10 min, the reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with ether, dried (Na_2SO_4), filtered, concentrated, and purified by flash column chromatography (silica gel buffered with 0.5−1% Et_3N)[EtOAc−CH_2Cl_2−hexane (3:7:40)] to afford (*R*)-2-benzoyloxycyclohexanone (0.0267 g, 89% yield, 90% ee) (Table 3, entry 1).

$YbCl_3$ as Catalyst. To a solution of (1*R*,2*R*)-2-benzoyloxy-1,2-epoxycyclohexane (0.030 g, 93% ee) in anhydrous CH_2Cl_2 (0.4 mL) was added $YbCl_3$ (0.0038 g, 0.0137 mmol). Upon stirring at room temperature for 30 min, the reaction mixture was quenched with saturated $NaHCO_3$ solution, extracted with ether, dried (Na_2SO_4), filtered, concentrated, and purified by flash column chromatography (silica gel buffered with 0.5−1% Et_3N)[EtOAc−CH_2Cl_2−hexane (3:7:40)] to afford (*S*)-2-benzoyloxycyclohexanone (0.022 g, 73% yield, 88% ee) (Table 3, entry 1).[21]

Representative Procedure for Thermal Rearrangement of Enol Ester Epoxides.

In a Vial. A 4 mL vial containing 1-benzoyloxy-1,2-epoxycyclohexane (0.10 g) was flushed with N_2 and then placed into an oil-bath (120 °C) for 30 min. The vial was then taken out and cooled to room temperature by air flow. The reaction mixture was directly purified by flash chromatography to afford (*S*)-2-benzoyloxycyclohexanone (0.092 g, 92% yield, 90% ee) (Table 4, entry 1).

In a Sealed Tube. A 1 mL ampule containing freshly prepared 1-phenyl-1-acetoxy-1,2-epoxypropane (0.040 g) was sealed under vacuum. After being immersed in a hot oil-bath (195 °C) for 30 min, the ampule was taken out and cooled to room temperature by air flow. Upon opening the ampule, the reaction mixture was directly purified by flash chromatography to afford 2-acetoxy propiophenone (0.040 g, 100% yield, 90% ee) (Table 4, entry 12).

Synthesis of (*R*)-2-Acyloxy Cyclohexanones from (1*R*,2*R*)-*trans*-1,2-Cyclohexanediol for the Determination of the Absolute Configurations of α-Acyloxy Cyclohexanones.

(*R*)-2-Benzoyloxycyclohexanone.[17,22] To an ice-cold solution of (1*R*,2*R*)-*trans*-1,2-cyclohexanediol (0.077 g, 0.667 mmol) and pyridine (0.158 g, 2.0 mmol) in CH_2Cl_2 (7.0 mL) was added dropwise a solution of benzoyl chloride (0.103 g, 0.735 mmol) in CH_2Cl_2 (2.0 mL) over a period of 2 h. The ice bath was removed, and the reaction mixture was stirred until the reaction was completed as monitored by TLC. The reaction mixture was washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (EtOAc−CH_2Cl_2-hexane 3:1:7 v/v) to afford (*R*,*R*)-2-benzoyloxy-1-cyclohexanol[23] (0.066 g, 45%). $[\alpha]^{25}_D = -55.5$ (c 1.56, $CHCl_3$); IR (NaCl) 3532, 1693, 1278 cm^{-1}; ^1H NMR δ 8.06 (m, 2H), 7.57 (tt, J = 7.5, 1.7 Hz, 1H), 7.44 (m, 2H), 4.85 (ddd, J = 10.3, 8.5, 4.7 Hz, 1H), 3.74 (ddd, J = 10.3, 8.3, 4.5 Hz, 1H), 2.14 (m, 3H), 1.77 (m, 2H), 1.52−1.25 (m, 4H); ^{13}C NMR: 166.9, 133.2, 130.5, 129.8, 128.5, 78.9, 73.0, 33.2, 30.2, 24.1, 23.9.

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(21) It was observed that small amounts of 2-chlorocyclohexanone was also formed in this reaction. The amount of this byproduct increased if the rearrangement was run at higher substrate concentration and/or if the reaction conditions were not completely dry.

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To a solution of (*R*,*R*)-2-benzoyloxy-1-cyclohexanol (0.036 g, 0.16 mmol) in CH_2Cl_2 (3.0 mL) was added pulverized dry molecular sieves (0.37 g, 4 Å) and pyridinium chlorochromate (0.185 g, 0.86 mmol) at room temperature. After the reaction was completed as monitored by TLC, the reaction mixture was diluted with hexane (2.0 mL) and directly loaded onto a silica gel column. The column was eluted with EtOAc−hexane (2:3, v/v) to afford (*R*)-2-benzoyloxycyclohexanone (0.035 g, 98%) (99% ee). $[\alpha]^{25}_D = +19.9$ (*c* 0.87, $CHCl_3$); IR (NaCl) 1732, 1712, 1272 cm^{-1}; ^1H NMR δ 8.09 (m, 2H), 7.57 (tt, *J* = 7.3, 1.7 Hz, 1H), 7.44 (m, 2H), 5.41 (dd, *J* = 11.1, 6.3 Hz, 1H), 2.62−2.39 (m, 3H), 2.18−1.60 (m, 5H); ^{13}C NMR δ 204.6, 165.8, 133.4, 130.1, 129.9, 128.6, 77.3, 41.0, 33.5, 27.5, 24.0. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.66; H, 6.52.

(*R*)-2-(*p*-Methylbenzoyloxy)cyclohexanone. $[\alpha]^{25}_D = +9.3$ (*c* 1.07, $CHCl_3$) (99% ee); IR (NaCl) 1732, 1718, 1271 cm^{-1}; ^1H NMR δ 7.98 (m, 2H), 7.24 (m, 2H), 5.40 (ddd, *J* = 10.8, 6.3, 1.2 Hz, 1H), 2.62−2.39 (m, 3H), 2.41 (s, 3H), 1.62−2.18 (m, 5H); ^{13}C NMR δ 204.7, 165.8, 144.0, 130.1, 129.2, 127.1, 77.0, 41.0, 33.4, 27.4, 24.0, 21.9. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.30; H, 6.69.

(*R*)-2-(*p*-Methoxybenzoyloxy)cyclohexanone. $[\alpha]^{25}_D = -21.4$ (*c* 0.66, C_6H_6) (99% ee); IR (NaCl) 1731, 1713, 1257 cm^{-1}; ^1H NMR δ 8.00 (m, 2H), 6.86 (m, 2H), 5.33 (ddd, *J* = 10.9, 6.1, 0.9 Hz, 1H), 3.81 (s, 3H), 2.55−2.32 (m, 3H), 2.12−1.57 (m, 5H); ^{13}C NMR δ 204.8, 165.5, 163.7, 132.1, 122.3, 113.7, 77.0, 55.6, 41.0, 33.5, 27.4, 24.0. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.72; H, 6.49. Found: C, 67.53; H, 6.56.

(*R*)-2-(*p*-Chlorobenzoyloxy)cyclohexanone. $[\alpha]^{25}_D = +14.1$ (*c* 0.45, $CHCl_3$) (99% ee); IR (NaCl) 1717, 1593, 1271 cm^{-1}; ^1H NMR δ 8.03 (m, 2H), 7.42 (m, 2H), 5.40 (dd, *J* = 11.8, 6.3 Hz, 1H), 2.62−2.39 (m, 3H), 2.21−1.61 (m, 5H); ^{13}C NMR δ 204.3, 164.9, 139.8, 131.4, 128.9, 128.3, 77.4, 40.9, 33.3, 27.4, 24.0. Anal. Calcd for $C_{13}H_{13}ClO_3$: C, 61.79; H, 5.19. Found: C, 61.42; H, 5.58.

(*R*)-2-(*p*-Nitrobenzoyloxy)cyclohexanone. $[\alpha]^{25}_D = +24.8$ (*c* 0.84, $CHCl_3$) (99% ee); IR (NaCl) 1732, 1712, 1273 cm^{-1}; ^1H NMR δ 8.32−8.23 (m, 4H), 5.43 (dd, *J* = 11.8, 6.4 Hz, 1H), 2.64−2.42 (m, 3H), 2.21−1.63 (m, 5H); ^{13}C NMR δ 203.8, 163.9, 150.8, 135.3, 131.2, 123.7, 78.0, 40.9, 33.2, 27.3, 24.0; HRMS Calcd for $C_{13}H_{14}NO_5$ ($M^+ + 1$) 264.0872. Found 264.0877.

(R)-2-Pivaloyloxycyclohexanone.[24] $[\alpha]^{25}_D = +50.7$ (*c* 0.56, $CHCl_3$) (99% ee); IR (NaCl) 1739, 1726, 1157 cm^{-1}; ^1H NMR δ 5.12 (ddd, *J* = 11.5, 6.4, 0.75 Hz, 1H), 2.54−2.23 (m, 3H), 2.13−1.91 (m, 2H), 1.85−1.55 (m, 3H), 1.25 (s, 9H); ^{13}C NMR δ 204.7, 177.8, 76.4, 40.9, 38.9, 33.1, 27.4, 23.9. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.80; H, 8.95.

2-Acetoxycyclohexanone.[22] $[\alpha]^{25}_D = -61.7$ (*c* 1.37, $CHCl_3$) (75% ee, Table 4, entry 8); IR (NaCl) 1732, 1721 cm^{-1}; ^1H NMR δ 5.17 (m, 1H), 2.52 (m, 1H), 2.41 (ddd, *J* = 13.2, 6.0, 0.6 Hz, 1H), 2.31 (m, 1H), 2.16 (s, 3H), 2.14−1.92 (m, 2H), 1.85−1.54 (m, 3H); ^{13}C NMR δ 204.7, 170.2, 76.7, 40.9, 33.2, 27.3, 23.9, 20.9.

2-Benzoyloxy-4,4-dimethylcyclohexanone. $[\alpha]^{25}_D = -18.5$ (*c* 0.34, $CHCl_3$) (94% ee, Table 4, entry 9); IR (NaCl) 1734, 1709 cm^{-1}; ^1H NMR δ 8.08 (m, 2H), 7.57 (m, 1H), 7.44 (m, 2H), 5.56 (ddd, *J* = 13.2, 6.3, 0.9 Hz, 1H), 2.65 (m, 1H), 2.44 (ddd, *J* = 14.4, 4.5, 2.6 Hz, 1H), 2.12 (ddd, *J* = 12.9, 6.3, 3.3 Hz, 1H), 1.91 (t, *J* = 12.9 Hz, 1H), 1.79 (m, 1H), 1.72 (td, *J* = 13.5, 4.2 Hz, 1H), 1.34 (s, 3H), 1.12 (s, 3H); ^{13}C NMR δ 204.9, 165.7, 133.2, 129.9, 129.8, 128.4, 74.3, 45.4, 39.8, 37.2, 32.2, 31.6, 24.9. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.13; H, 7.37. Found: C, 73.13; H, 7.15.

2-Benzoyloxycycloheptanone.[17,22] $[\alpha]^{25}_D = +44.5$ (*c* 1.36, $CHCl_3$) (99% ee, Table 4, entry 10); IR (NaCl) 1730, 1708 cm^{-1}; ^1H NMR δ 8.08 (m, 2H), 7.57 (tt, *J* = 7.5, 1.6 Hz, 1H), 7.44 (m, 2H), 5.46 (dd, *J* = 9.3, 3.3 Hz, 1H), 2.71 (m, 1H), 2.50 (m, 1H), 2.13 (m, 1H), 1.99−1.66 (m, 6H), 1.44 (m, 1H); ^{13}C NMR δ 207.5, 165.9, 133.4, 130.0, 129.8, 128.5, 79.2, 40.9, 30.6, 28.6, 26.6, 23.2.

2-Benzoyloxycyclooctanone.[22] $[\alpha]^{25}_D = +32.8$ (*c* 2.0, $CHCl_3$) (93% ee, Table 4, entry 11); IR (NaCl) 1714 cm^{-1}; ^1H NMR δ 8.07 (m, 2H), 7.57 (tt, *J* = 7.2, 1.8 Hz, 1H), 7.44 (m, 2H), 5.42 (dd, *J* = 8.7, 3.9 Hz, 1H), 2.75 (ddd, *J* = 14.1, 9.3, 3.6 Hz, 1H), 2.43 (ddd, *J* = 14.1, 9.0, 3.6 Hz, 1H), 2.34 (m, 1H), 2.13−1.82 (m, 4H), 1.74−1.48 (m, 4H), 1.28 (m, 1H); ^{13}C NMR δ 211.8, 166.2, 133.4, 130.0, 129.8, 128.6, 77.5, 40.7, 31.5, 27.7, 24.8, 24.7, 22.0. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 72.92; H, 7.33.

2-Acetoxypropiophenone.[3a,25] $[\alpha]^{25}_D = -29.7$ (*c* 1.06, C_6H_6) (90% ee, Table 4, entry 12); IR (NaCl) 1742, 1698, 1231 cm^{-1}; ^1H NMR δ 7.91 (m, 2H), 7.57 (tt, *J* = 7.4, 1.7 Hz, 1H), 7.46 (m, 2H), 5.95 (q, *J* = 7.2 Hz, 1H), 2.13 (s, 3H), 1.51 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 197.1, 170.6, 134.6, 133.8, 129.0, 128.7, 71.6, 21.0, 17.4.

2-Acetoxy-2-phenylacetophenone.[3a] $[\alpha]^{25}_D = +172$ (*c* 0.81, $CHCl_3$) (87% ee, Table 4, entry 13); IR (NaCl) 1739, 1696, 1229 cm^{-1}; ^1H NMR δ 7.93 (m, 2H), 7.54−7.33 (m, 8H), 6.86 (s, 1H), 2.20 (s, 3H); ^{13}C NMR δ 193.9, 170.7, 134.8, 133.8, 133.7, 129.5, 129.4, 129.0, 128.9, 128.8, 77.8, 21.0.

2-Benzoyloxy-1-tetralone.[17] $[\alpha]^{25}_D = -29.4$ (*c*1.90, $CHCl_3$) (88% ee, Table 4, entry 14); IR (NaCl) 1725, 1698, 1267 cm^{-1}; ^1H NMR: 8.15 (m, 2H), 8.06 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.58 (tt, *J* = 7.4, 1.9 Hz, 1H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.46 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 5.79 (dd, *J* = 12.8, 5.2 Hz, 1H), 3.30 (ddd, *J* = 17.2, 12.8, 4.8 Hz, 1H), 3.13 (ddd, *J* = 17.2, 4.8, 3.3 Hz, 1H), 2.53 (m, 1H), 2.43 (m, 1H); ^{13}C NMR δ 193.1, 166.0, 143.3, 134.2, 133.4, 131.9, 130.2, 130.0, 128.9, 128.6, 128.1, 127.2, 75.2, 29.5, 28.2.

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Supporting Information Available: The NMR spectral and HPLC data for the determination of the enantiomeric excess of the enol ester epoxides and α-acyloxyketones.

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