A Class of C_2 and Pseudo C_2 Symmetric Ketone Catalysts for Asymmetric Epoxidation. Conformational Effect on Catalysis

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A class of C_2 and pseudo C_2 symmetric ketones with one fused ring at each side of the carbonyl group have been prepared from quinic acid and found to be effective catalysts for the asymmetric epoxidation of a variety of olefins. Electron deficient olefins such as enones can be efficiently epoxidized. Encouragingly good enantioselectivity is also obtained for the epoxidation of styrenes. The studies show that the ketone conformation plays an important role in the reactivity and selectivity of the catalyst.

Dioxiranes generated *in situ* from Oxone and chiral ketones have been shown to be remarkably promising oxidation reagents for the asymmetric epoxidation of olefins.[1−4] A variety of chiral ketones have been investigated in a number of laboratories, and very good progress has been made.[3,4] One of our main efforts has been focusing on ketones having the general structural features of ketones **1** and **4** (Scheme 1). The stereogenic centers are placed in the vicinity of the reacting carbonyl group to optimize the stereochemical communication between olefin substrates and the catalyst during the epoxidation. Fused ring(s) or a quaternary carbon α to the carbonyl group are introduced with the intention of maintaining the chiral elements in the ketone by minimizing the potential epimerization. Among the ketones closely related to **1**, we recently found that fructose-derived ketone **3** displayed high enantioselectivity for a wide range of *trans*-disubstituted and trisubstituted olefins.[4] In addition to ketone **1**, we have also been actively studying ketone **4**, which contains a second fused ring to replace the quaternary center of **1**. Ketones **6a**−**p**, as close analogues to **4**, have been synthesized and investigated (Scheme 2).[5] These ketones differ mainly from one another in the substituents at the β-position of the carbonyl. These variations were introduced to test the conformational and electronic effects on ketone reactivity and selectivity. Herein we wish to report in detail the preparation and catalytic properties of these ketones.[6]

Results and Discussion

Ketones **6a**−**p** were prepared from readily available (−)-quinic acid by adapting the reported procedures.[7] The synthesis of C_2 symmetric ketone **6a** is outlined in Scheme 3. Hydroxy ketone **9** was prepared from (−)-quinic acid in three steps following the established transformations.[8,9] Reduction of **9** using $NaBH_4$ gave diol **10**, which was tosylated to give an inseparable mixture

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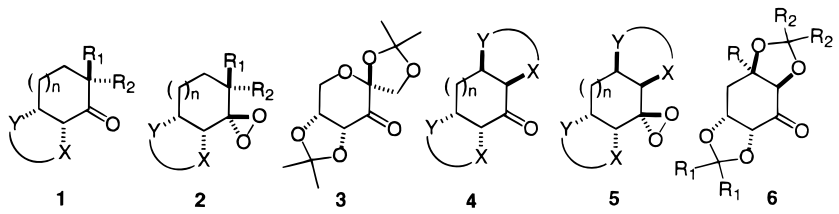
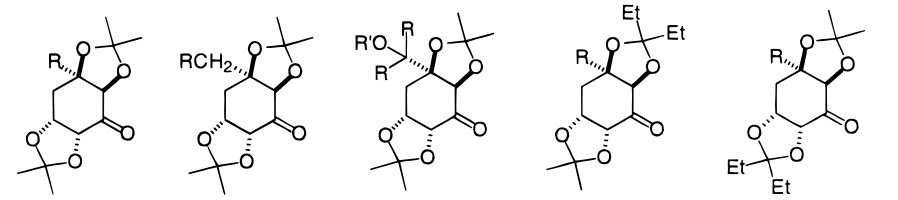
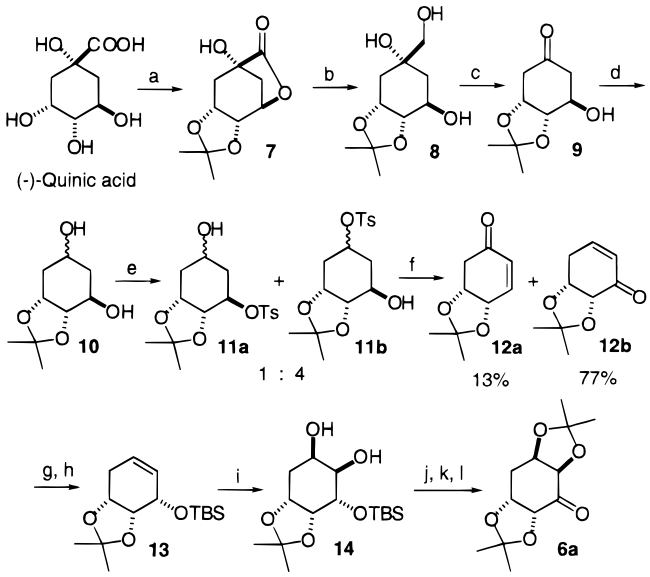
Scheme 1



Scheme 2



Scheme 3[a]



[a] Reaction conditions: (a) 2,2-dimethoxypropane, benzene, TsOH (cat.), reflux, 84%; (b) $NaBH_4$, EtOH, rt, 15 h, 98%; (c) $NaIO_4$–silica gel, CH_2Cl_2, rt, 100%; (d) $NaBH_4$, MeOH, 0 °C, 100%; (e) TsCl, pyridine, DMAP, CH_2Cl_2, 0 °C, 15 h, 60%; (f) PCC, 3A MS, pyridine, CH_2Cl_2, rt, 1.5 h, 13% for **12a**, 77% for **12b**; (g) $NaBH_4$–$CeCl_3 \cdot 7H_2O$, EtOH, rt, 0.5 h, 90%; (h) TBSCl, imidazole, DMAP, CH_2Cl_2, rt, 2 h, 81%; (i) OsO_4, NMO, *t*-BuOH, pyridine, H_2O, reflux, 3 h, 87%; (j) 2-methoxypropene, CSA (cat.), CH_2Cl_2, rt, 1 h; (k) TBAF, THF, rt, 0.5 h, 98% two steps; (l) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 95%.

of tosylates **11a** and **11b** in a ratio of 1:4 as determined by ^1H NMR analysis. PCC oxidation of the mixture led to easily separable enones **12a** and **12b** in 13% and 77% isolated yields, respectively. An attempt was made to convert enone **12b** into the desired ketone **6a** in two steps by dihydroxylation[10] and ketalization, but a complex mixture was obtained. Instead, enone **12b** was reduced and silylated to give TBS ether **13**, which was smoothly converted into ketone **6a** by dihydroxylation, ketalization, desilylation, and oxidation.

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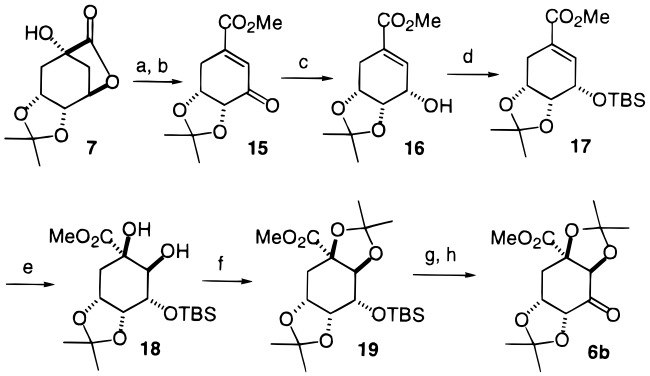
Scheme 4[a]



[a] Reaction conditions: (a) MeONa, MeOH, rt, 5 h, 82%; (b) PCC, 3A MS, pyridine, CH_2Cl_2, rt, 24 h, 60%; (c) $NaBH_4$, MeOH, 1 h, 98%; (d) TBSCl, imidazole, DMAP, CH_2Cl_2, rt, 3 h, 96%; (e) OsO_4, NMO, *t*-BuOH, pyridine, H_2O, reflux, 4 h, 95%; (f) 2-methoxypropene, CSA (cat.), CH_2Cl_2, rt, 2 h, 94%; (g) TBAF, rt, 1 h, 70%; (h) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 99%.

Ketone **6b** was synthesized on the basis of the reported procedures for similar compounds (Scheme 4).[11] Briefly, lactone **7** was converted to enone **15** in two steps by methanolysis and oxidation–dehydration.[11d,f,g] Initially an attempt was made to convert **15** into the desired ketone **6b** by dihydroxylation with $RuCl_3$–$NaIO_4$[10] and subsequent ketalization, but the resulting diol resisted ketalization, probably due to the electron-withdrawing effects of the existing carbonyl groups. Enone **15** was then reduced with $NaBH_4$ and protected as a TBS ether.[11e] The resulting TBS ether **17** was smoothly converted into ketone **6b** by dihydroxylation, ketalization, desilylation, and oxidation.

The synthesis of ketone **6c** is shown in Scheme 5. Triol **8** was selectively silylated at the primary alcohol using

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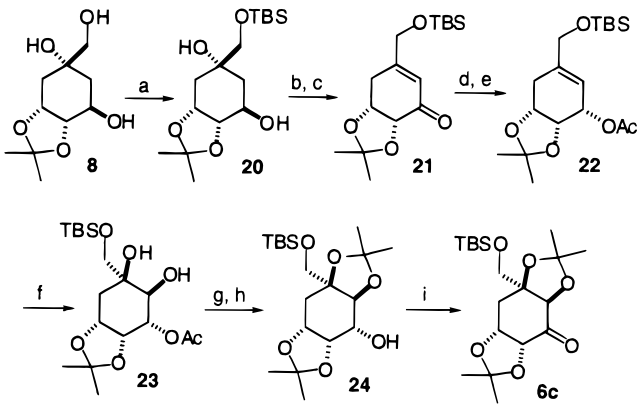
Scheme 5[a]



[a] Reaction conditions: (a) TBSCl, imidazole, DMAP, CH_2Cl_2, 0 °C; (b) PCC, 3A MS, CH_2Cl_2, rt, overnight; (c) $POCl_3$, pyridine, rt, 16 h, 54% from **8**; (d) $NaBH_4$, MeOH, rt, 2 h; (e) Ac_2O, pyridine, DMAP, CH_2Cl_2, rt, 10 h, 96%; (f) OsO_4, NMO, *t*-BuOH, pyridine, H_2O, reflux, 3 h, 72%; (g) 2-methoxypropene, CSA (cat.), CH_2Cl_2, rt, 2 h, 96%; (h) DIBAL-H (1 M in hexane), THF, −20 to 0 °C, 94%; (i) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 90%.

TBSCl. The resulting diol was oxidized with PCC and dehydrated with $POCl_3$−pyridine[11b,e,h] to give enone **21**, which was then converted to acetate **22** by reduction and acetylation. Acetate **22** was transformed into ketone **6c** by dihydroxylation, ketalization, deacetylation, and oxidation.

Ketones **6d**−**g** were prepared as shown in Scheme 6. Intermediate **19** was reduced with DIBAL-H to give alcohol **25**, which was converted into ketones **6d**−**f** by acetylation, benzoylation, or tosylation, followed by desilylation and oxidation. The synthesis of ketone **6g** was achieved by triflation of alcohol **25**, followed by fluorination,[12] desilylation, and oxidation.

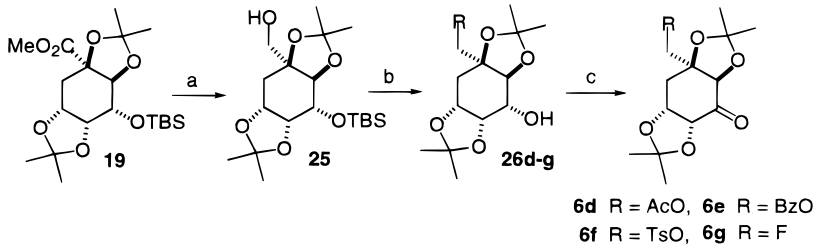
Ketones **6h**−**j** were also prepared from intermediate **19** (Scheme 7). Treatment of **19** with CH_3MgBr and PhMgBr gave tertiary alcohols **27h** and **27i**, respectively. Desilylation and subsequent oxidation of these two compounds gave ketones **6h** and **6i**. Ketone **6j** was prepared by methylation of **27h**, followed by desilylation and oxidation.

Ketones **6k**−**p** differ from ketones **6b**, **6d**, and **6h** in one of the ketal moieties. The synthesis of ketones **6k**−**m** is outlined in Scheme 8. Diol **18** was ketalized with 3-methoxy-2-pentene using CSA as catalyst to give compound **29**, which was desilylated and oxidized to give ketone **6k**. The synthesis of ketone **6l** was accomplished from **29** by reduction of the ester, acetylation, desilylation, and oxidation. Ketone **6m** was prepared from **29** by addition of CH_3MgBr, desilylation, and oxidation.

Ketones **6n**−**p** were prepared as shown in Scheme 9. Alcohol **16** was protected as the *tert*-butyldiphenylsilyl ether, followed by deketalization using aqueous acetic acid to give diol **31**,[13] which was then ketalized with 3-methoxy-2-pentene to give compound **32**. Dihydroxylation of **32** and subsequent ketalization with 2-methoxypropene gave compound **34**, which was converted to ketone **6n** by desilylation and oxidation. Ketones **6o** and **6p** were synthesized from **34** with a reaction sequence similar to that used for ketones **6l** and **6m**.

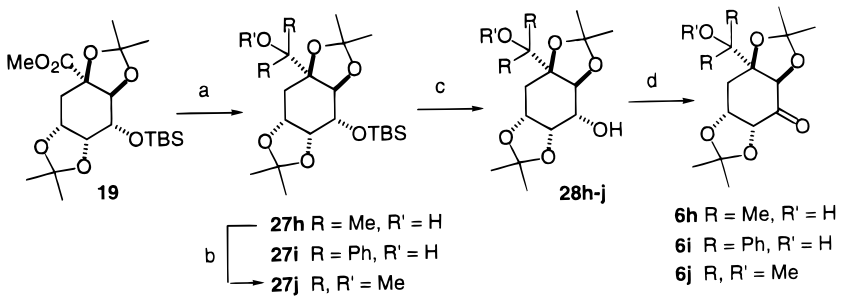
With these ketones in hand, we first briefly optimized the reaction conditions. The epoxidation of *trans*-*β*-methylstyrene using ketone **6d** as catalyst was initially carried out to determine the solvent and pH effects on the reaction. Among the solvents tested (Table 1), dimethoxyethane (DME) was found to be the solvent of choice for both reactivity and selectivity. We have previously shown that the pH has a dramatic effect on the asymmetric epoxidation catalyzed by fructose-derived ketone **3**. The conversion of *trans*-*β*-methylstyrene to its

Scheme 6[a]



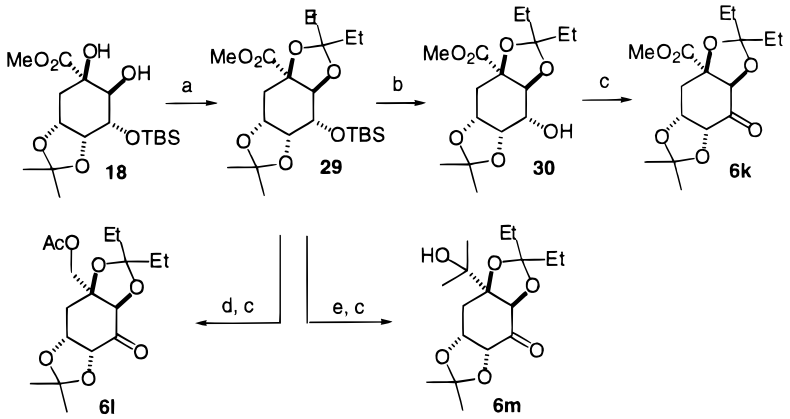
[a] Reaction conditions: (a) DIBAL-H (1 M in hexane), THF, −20 to 0 °C, 92%; (b) (1) for **6d**, Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, 2 h, then TBAF, rt, 2 h, 86% two steps; (2) for **6e**, BzCl, Et_3N, DMAP, CH_2Cl_2, rt, 2 h, then TBAF, rt, 1 h, 99% two steps; (3) for **6f**, TsCl, Et_3N, DMAP, CH_2Cl_2, rt, 30 h, then TBAF, rt, 1 h, 82% two steps; (4) for **6g**, Tf_2O, 2,6-lutidine, CH_2Cl_2, then TBAF, 96%; (c) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 95−100%.

Scheme 7[a]



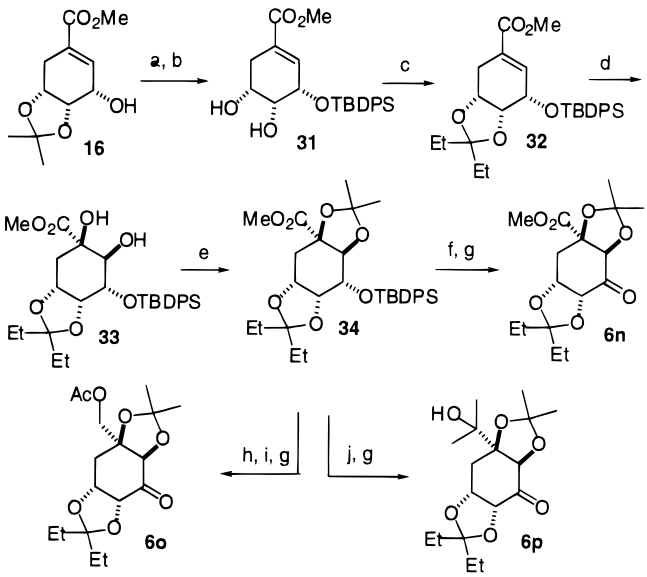
[a] Reaction conditions: (a) (1) for **27h**, CH_3MgBr, THF, 0 °C to rt, 5 h, 100%; (2) for **27i**, PhMgBr, THF, rt to reflux, 15 h; (b) NaH, MeI, THF, 30 °C, 15 h; (c) TBAF, THF, 92−99%; (d) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 95−97%.

Scheme 8[a]



[a] Reaction conditions: (a) 3-methoxy-2-pentene, CSA, CH_2Cl_2, rt, 2 h, 78%; (b) TBAF, THF, rt, 0.5 h, 99%; (c) DMSO, oxalyl chloride, Et_3N, CH_2Cl_2, −78 °C, 88−98%; (d) (1) DIBAL-H, THF; (2) Ac_2O, Et_3N, DMAP, rt, 2 h; (3) TBAF, THF, rt, 0.5 h, 93% from 29; (e) MeMgBr, THF, 0 °C to rt, 5.5 h, then TBAF, rt, 0.5 h, 94% two steps.

Scheme 9[a]



[a] Reaction conditions: (a) TBDPSCl, imidazole, DMAP, DMF, rt, 5 h; (b) 80% aqueous acetic acid, 50 °C, 2 h, 92% from **16**; (c) 3-methoxy-2-pentene, CSA, rt, 0.5 h, 96%; (d) OsO_4, NMO, pyridine, *t*-BuOH, 93%; (e) 2-methoxypropene, CSA, CH_2Cl_2, rt, 2 h, 96%; (f) TBAF, THF, rt, 1 h, 41%; (g) DMSO, oxalyl chloride, CH_2Cl_2, −78 °C, 94−97%; (h) DIBAL-H, THF, 0 °C, 1 h; (i) Ac_2O, DMAP, Et_3N, rt, 2 h, then TBAF, THF, rt, 0.5 h, 73% from **34**; (j) MeMgBr, THF, 0 °C to rt, 4.5 h, then TBAF, THF, rt, 0.5 h, 93%.

epoxide increased more than 10-fold from a lower pH (7−8) to a higher pH (>10), and the enantioselectivity remained high.[4b,4c] The pH study with ketone **6d** also showed enhanced conversion at high pH (Table 2). Among the buffer systems tested, a system of aqueous AcOH/K_2CO_3 was found to be the best for both reactivity and selectivity.[14]

To test whether substituents at the β-position have any effect on the epoxidation, three types of olefins, *trans*, *cis*, and terminal, were employed as substrates. The results presented in Table 3 show that the ketone catalysts epoxidize the three classes of olefins with varying degrees of efficiency and selectivity. It is very interesting to note that the unsubstituted C_2-symmetric ketone **6a** is the least reactive ketone along with ketone **6i**, while the rest of the ketones display excellent reactivity and good enantioselectivity. Ketones **6h** and **6j** provide the highest conversion and enantiomeric excess for *trans* and terminal olefins but the lowest for the *cis* olefin. Ketone **6i**, which has the biggest β substituent, gives the highest ee for the *cis* olefin (88% ee) albeit with low conversion.

Table 1. The Solvent Effect on Asymmetric Epoxidation of β-Methylstyrene with Ketone 6d[a]

entry	solvent	*T* (°C)	*t* (h)	convn (%)	% ee
1	CH_3CN	0	4	58	63
2	DME[b]	0	4	100	70
3	DME	−10	4	95	73
4	DMM[b]	0	4	43	66
5	dioxane	0	4	99	67
6	DMM/CH_3CN (2/1)	0	4	91	67
7	DMF	0	3	99	64

[a] All reactions were carried out with *trans*-β-methylstyrene (0.4 mmol), ketone **6d** (0.02 mmol), Oxone (0.55 mmol), and K_2CO_3 (2.31 mmol) in organic solvent (6 mL) and buffer (0.05 M $Na_2B_4O_7 \cdot 10H_2O$ in 4×10^{-4} M aqueous EDTA) (4 mL). The conversion was determined by GC (HP-17 column), and the enantioselectivity was determined by Chiral GC (Chiraldex G-TA column). [b] DME = dimethoxyethane, DMM = dimethoxymethane.

Table 2. The pH Effect on Asymmetric Epoxidation Catalyzed by Ketone 6d[a]

entry	pH[c]	convn (%)[d]	ee (%)[e]
1	8.5	15	64
2	9.5	32	67
3	10.5	44	67
4[b]	11.7−12.3	50	66

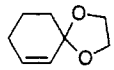
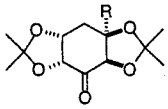
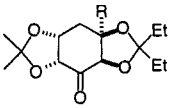
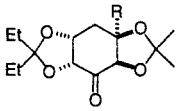
[a] All reactions were carried out at 0 °C with *trans*-β-methylstyrene (1 mmol), ketone **6d** (0.02 mmol), Oxone (1.38 mmol) in DME (12 mL), and buffer (0.05 M $Na_2B_4O_7 \cdot 10H_2O$ in 4×10^{-4} M aqueous EDTA, the pH was adjusted with 1.0 M aqueous KH_2PO_4 for pH 8.5−10.5, and used directly for pH 11.7−12.3) (8 mL). Oxone was added over 4 h, and the conversion and ee values were checked by GC every hour. [b] The pH was adjusted by adding aqueous K_2CO_3 (5.8 mmol). [c] The pH was monitored with a Corning 320 pH meter with a 3-in-1 pH combination electrode and was maintained within ±0.1 by adding aqueous K_2CO_3 except for entry 4. [d] The conversion was determined by GC (HP-17 column) after 2 h. [e] The enantioselectivity was determined by Chiral GC (Chiraldex G-TA column) after 2 h.

(12) Chi, D. Y.; Kilbourn, M. R.; Katzenellenbogen, J. A.; Welch, M. J. *J. Org. Chem.* **1987**, *52*, 658.

(13) Deketalization of TBS ether **17** was attempted, but desilylation also occurred under the reaction conditions.

(14) The buffer is prepared by mixing 1 L of 0.1 M aqueous K_2CO_3 with 5 mL of AcOH. The buffer pH is initially around 9.3, and the pH changes to 11.3 upon addition of DME (buffer:DME 1:1.5 v/v).

Table 3. Asymmetric Epoxidation of Four Representative Olefins by Ketone 6[a]

								
ketone	cat (%)	conv.(ee)[b] (%)	cat (%)	yield (ee)[c] (%)	cat (%)	conv.(ee)[b] (%)	cat (%)	conv.(ee)[b] (%)
								
6a R = H	5	29 (73)	10	11 (93)	10[d]	13 (67)	10	9 (66)
6b R = CO_2Me	5	61 (75)	10	66 (95)	10	90 (67)	10	56 (66)
6c R = CH_2OTBS	5	77 (73)	10	77 (90)	10	100 (66)	10	70 (73)
6d R = CH_2OAc	5	95 (75)	10	95 (90)	5	96 (65)	10	82 (68)
6e R = CH_2OBz	5	76 (72)	10	91 (90)	5	99 (65)	10	67 (71)
6f R = CH_2OTs	5	60 (72)	10	74 (90)	5	70 (67)	10	62 (71)
6g R = CH_2F	5	78 (73)	10	71 (89)	5	76 (67)	10	66 (71)
6h R = CMe_2OH	5	97 (80)	10	91 (96)	5	79 (69)	10	55 (45)
6i R = CPh_2OH	5	7 (50)	--	--	10	7 (59)	10	7 (88)
6j R = CMe_2OMe	5	95 (80)	10	94 (96)	5	100 (70)	10	47 (40)
								
6k R = CO_2Me	5	43 (74)	10	65 (94)	5	94 (60)	10	41 (65)
6l R = CH_2OAc	5	60 (75)	10	77 (92)	5	66 (67)	10	73 (62)
6m R = CMe_2OH	5	35 (76)	10	57 (95)	5	31 (65)	10	47 (44)
								
6n R = CO_2Me	5	78 (77)	10	58 (93)	5	77 (65)	10	59 (61)
6o R = CH_2OAc	5	100 (72)	10	75 (92)	5	100 (62)	10	75 (63)
6p R = CMe_2OH	5	100 (79)	10	57 (94)	5	80 (65)	10	61 (42)

[a] For *trans*-β-methylstyrene, the reactions were carried out with olefin (0.4 mmol), ketone (0.02 mmol), Oxone (0.55 mmol), and K_2CO_3 (2.31 mmol) in DME (5 mL) and aqueous AcOH−K_2CO_3 (prepared by mixing 100 mL of 0.1 M aqueous K_2CO_3 with 0.5 mL of AcOH) (3.2 mL) at −15 °C; the reactions were stopped after 4 h except for ketone **6i** (1 h). For *trans*-stilbene, the reactions were carried out with olefin (0.2 mmol), ketone (0.02 mmol), Oxone (0.276 mmol), and K_2CO_3 (1.16 mmol) in DME−DMM (3 mL, 2/1, v/v) and aqueous AcOH−K_2CO_3 (prepared by mixing 100 mL of 0.1 M aqueous K_2CO_3 with 0.5 mL of AcOH) (2 mL) at −10 °C; the reactions were stopped after 6 h. For styrene, the reactions were carried out in the same way to *trans*-β-methylstyrene except for ketone **6b**−**6f**; in these cases, the reactions were carried out at −10 °C. For 3,3-ethylenedioxycyclohexene, the reactions were carried out in the same way as for *trans*-stilbene except that 3 mL of DME was used instead of 3 mL of DME−DMM. The reaction was stopped after 6 h except for ketone **6i** (1 h). [b] The conversions were determined by GC (HP-17). Enantioselectivities were determined by chiral GC (Chiraldex G-TA column). The epoxides have the *R* configurations. [c] Isolated yields. Enantioselectivities were determined by chiral HPLC (Chiralcel OD column). The epoxide has the *R* configuration. [d] The reaction was stopped after 6 h.

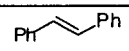
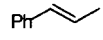
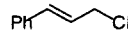
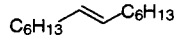
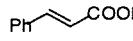
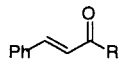
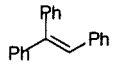
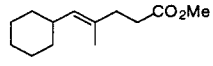
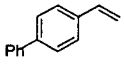
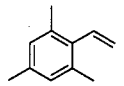
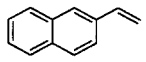
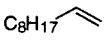
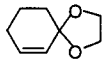
To further reveal the catalytic features of these ketones, two of the most reactive ketones, **6d** and **6h**, were chosen as representatives to explore the epoxidation of a variety of olefins. The results are shown in Table 4. A few noticeable features of these ketones are the following: (a) Both **6d** and **6h** are highly enantioselective for *trans*-disubstituted and trisubstituted olefins with phenyl substituents. (b) Electron deficient olefins can be epoxidized by **6d** and **6h** (Table 4, entries 5−8), indicating that the dioxirane derived from this type of ketone is very electrophilic.[15] The high enantioselectivity obtained with enones (Table 4, entries 6−8) suggests that the catalyst can effectively compete with the ketones present in the substrates and epoxide products.[16] (c) The enantiomeric excess for the epoxidation of styrenes is encouragingly high (Table 4, entries 14−17).[17]

(15) For leading references on nucleophilic asymmetric epoxidation, see: (a) Enders, D.; Zhu, J.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1725. (b) Elston, C. L.; Jackson, R. F. W.; MacDonald, S. J. F.; Murray, P. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 410. (c) Bougauchi, M.; Watanabe, S.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 2329. (d) Bentley, P. A.; Bergeron, S.; Cappi, M. W.; Hibbs, D. E.; Hursthouse, M. B.; Nugent, T. C.; Pulido, R.; Roberts, S. M.; Wu, L. E. *J. Chem. Soc., Chem. Commun.* **1997**, 739.

(16) The slightly lower enantioselectivity of *trans*-4-phenyl-3-buten-2-one oxide (Table 4, entry 7) was due to the fact that the formed epoxide was also a good catalyst for epoxidation. A better enantioselectivity (88% ee) was obtained with a short reaction time (0.5 h).

(17) For leading references on asymmetric epoxidation of styrenes, see: (a) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791. (b) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (c) Halterman, R. L.; Jan, S.-T. *J. Org. Chem.* **1991**, *56*, 5253. (d) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991**, *113*, 6865. (e) Collman, J. P.; Lee, V. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1993**, *115*, 3834. (f) Collman, J. P.; Lee, V. J.; Kellen-Yuen, C. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1995**, *117*, 692−703. (g) Palucki, M.; McCormick, G. J.; Jacobsen, E. N. *Tetrahedron Lett.* **1995**, *36*, 5457. (h) Gross, Z.; Ini, S. *J. Org. Chem.* **1997**, *62*, 5514. (i) Collman, J. P.; Wang, Z.; Straumanis, A.; Quelquejeu, M.; Rose, E. *J. Am. Chem. Soc.* **1999**, *121*, 460.

Table 4. Asymmetric Epoxidation of Representative Olefins by Ketones 6d and 6h[a]

entry	substrate	cat (mol%)	T (°C)	t (h)	yield (%)[c]	ee (%)	configuration[i]
1[b]		**6h**(10)	-10	6	91	96[e]	(+)-(R,R)[4c,22]
2		**6h**(5)	-15	4	94	80[f]	(+)-(R,R)[4c,23]
3		**6h**(10)	0	6	95	82[f]	(+)-(2S,3R)[4c]
		6h(10)	-10	6	95	84[f]	(+)-(2S,3R)
4		**6d**(10)	-10	4	51	42[g]	(+)-(R,R)[4c]
5		**6d**(10)	0	8	34	86[f]	(+)-(2S,3R)[24]
		6h(10)	0	8	35	89[f]	(+)-(2S,3R)
6							
	R = Ph	**6d**(10)	0	6	80	94[e]	(+)-(2S,3R)[15c]
		6h(10)	0	6	85	96[e]	(+)-(2S,3R)
7	R = Me	**6h**(10)	0	8	75	82[f]	(+)-(2S,3R)[15c]
8	R = ^{i}Pr	**6h**(10)	0	8	70	89[f]	(+)-(2S,3R)[15c]
9[b]		**6d**(10)	0	5	86	87[e]	(+)-(R,R)[4c,25]
		6h(10)	0	6	95	92[e]	(+)-(R,R)
10		**6d**(5)	-10	4	96	43[h]	(+)-(R,R)[4c]
11	 R = Ph	**6d**(5)	-10	4	95	68[f]	(+)-(R,R)[4c,26]
		6h(5)	-10	4	94	85[f]	(+)-(R,R)
12	R = Me	**6h**(5)	-15	4	100[d]	12[f]	(-)-(1R,2S)[4c,27]
13	R = Bu	**6h**(5)	-15	4	96	13[h]	(-)-(1R,2S)[4c]
14		**6h**(5)	-15	4	79	69[f]	(-)-(R)[4c,28]
15		**6d**(5)	-10	4	54	65[e]	(-)[29]
16		**6d**(5)	-10	4	83	66[h]	(-)[29]
17		**6d**(5)	-10	4	89	54[h]	(-)-(R)[30]
18		**6d**(5)	-10	4	85	15[h]	(+)-(R)[4c,31]
19		**6d**(5)	-10	3	92	52[e]	(+)-(R)[4c,32]
20		**6d**(10)	-10	6	78	68[f]	(+)-(R,R)[4c]
21		**6d**(5)	-10	4	93	21[h]	(+)-(1R,2S)[4c,33]

[a] All reactions were carried out with substrate (1 equiv), ketone (0.05 or 0.1 equiv), Oxone (1.38 equiv), and K_2CO_3 (5.8 equiv) in DME−aqueous AcOH−K_2CO_3 (1.5:1, v/v) except for entries 1 and 9. [b] The reactions were carried out in DME−DMM−aqueous AcOH−K_2CO_3 (2:1:2, v/v). [c] The epoxides were purified by flash chromatography and gave satisfactory spectroscopic characterization. [d] This value was the conversion as determined by GC (HP-17 column). [e] Enantioselectivity was determined by chiral HPLC (Chiralcel OD column). [f] Enantioselectivity was determined by chiral GC (Chiraldex G-TA column). [g] The epoxide was opened (NaOMe−MeOH), and the resulting alcohol was converted to its acetate; enantioselectivity was then determined by ^{1}H NMR shift analysis of the resulting acetate with $Eu(hfc)_3$. [h] Enantioselectivity was determined by ^{1}H NMR shift analysis of the epoxide product directly with $Eu(hfc)_3$. [i] The absolute configurations were determined by comparing the measured optical rotations with reported ones.

Most of ketones **6a**−**p** exist partially in hydrate forms, suggesting that the carbonyl groups are quite electrophilic. The reactivity and selectivity differences displayed by these ketones seems to be more consistent with

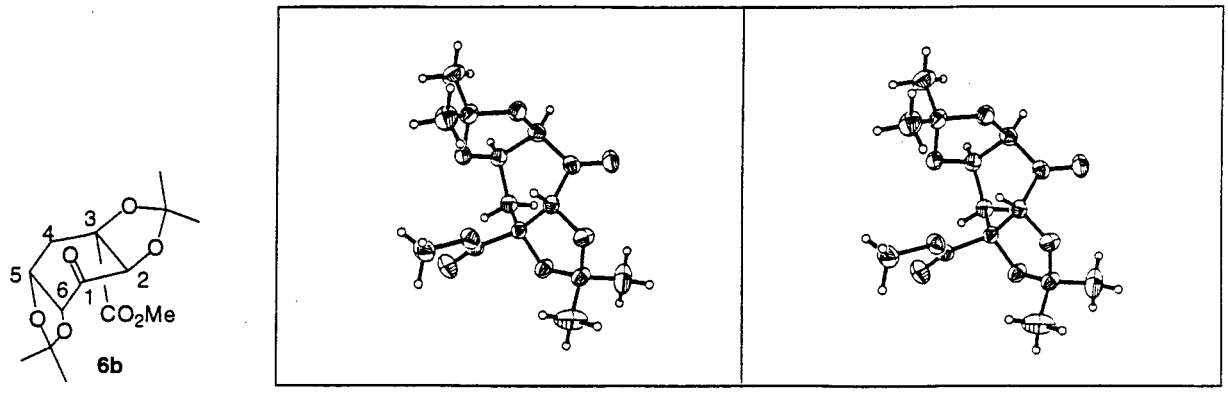


Figure 1. The X-ray structure of ketone **6b** (stereoview).

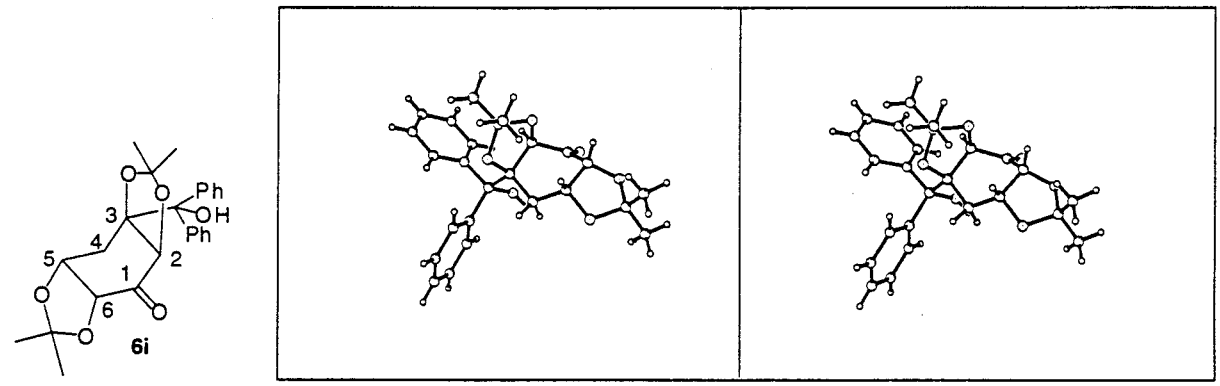
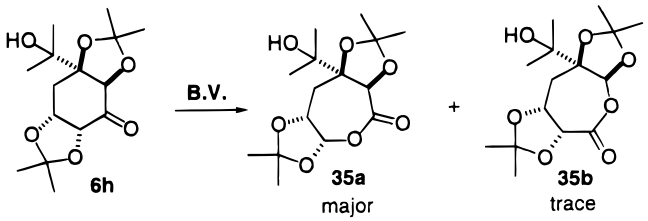


Figure 2. The X-ray structure of ketone **6i** (stereoview).

conformational effects rather than electronic effects. Among these ketones, we were able to obtain the crystal structures for ketones **6b** and **6i** (Figures 1 and 2). Both ketones exist in boat conformations. For ketone **6b**, the β-ester group and 5,6-*O*-isopropylidene group are in axial positions and the 2,3-*O*-isopropylidene group is in an equatorial position. In contrast, for ketone **6i**, the large β-group and 5,6-*O*-isopropylidene group are in equatorial positions and the 2,3-*O*-isopropylidene group is in an axial position. It follows that ketones with different substituents would have significantly different ring conformations, consequently displaying different catalytic properties.

Ketones **6a**−**p** are generally more stable than the fructose-derived ketone **3**, but they were also found to decompose under the reaction conditions. Although the Baeyer−Villiger reaction has been anticipated to be the main decomposition pathway, we had not been able to previously isolate any of the lactone products, since they most likely hydrolyzed under the reaction conditions. However, in the case of ketone **6h**, the resulting lactone can be isolated in 86% yield. It is very interesting to note that both ^{1}H and ^{13}C NMR showed the isolated lactone was **35a**, while **35b** was barely detectable (Scheme 10), indicating that the Baeyer−Villiger reaction was highly regioselective. To further address the regioselectivity, the Baeyer−Villiger reactions of some of ketones **6** were investigated. To avoid the lactone hydrolysis, the reactions were run under anhydrous conditions using *m*-CPBA as oxidant.[18] As shown in Table 5, the ratios of the two lactone isomers are highly dependent upon the

Scheme 10



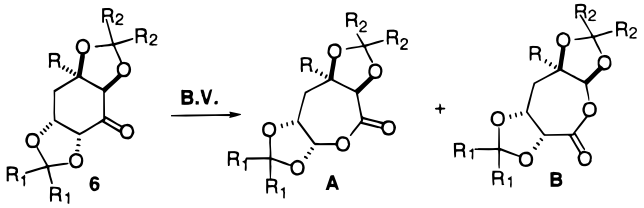
β-substituents. The change of migratory aptitude of the α-carbons could be attributed to the conformational effects imposed by these substituents.[19] The low conversion seen with ketone **6i** might be partially due to its instability since it was found to decompose quickly under the reaction conditions. The instability of ketone **6i** could be attributed to the fact that the conformation adopted by this ketone is particularly prone to the Baeyer−Villiger reaction. These results suggest that the Baeyer−Villiger decomposition of the ketones be minimized by using the proper substituents to lock the ketones into certain favorable conformations, consequently leading to more efficient and robust ketone catalysts. Such studies are currently underway.

It has been shown that the epoxidation by dioxirane proceeds mainly via a spiro transition state (Figure 3).[4a,c,3f,m,20] The expected spiro transition states of two ketones with different boat conformations are shown in Figures 4 and 5, respectively.[21] Since either oxygen atom of the dioxirane can potentially be transferred to the olefin during the epoxidation, there exist four possible

(18) Mehta, G.; Mohal, N. *J. Chem. Soc., Perkin Trans. 1* **1998**, 505.

(19) For a recent review of the Baeyer−Villiger oxidation, see: Krow, G. R. *Org. React.* **1993**, *43*, 251.

Table 5. The Baeyer–Villiger Reactions of Ketone 6 with *m*-CPBA[a]



entry	ketone	A/B[b]
1	**6b**, $R_1 = R_2 = Me$, $R = CO_2Me$	2.8
2	**6c**, $R_1 = R_2 = Me$, $R = CH_2OTBS$	1.5
3	**6d**, $R_1 = R_2 = Me$, $R = CH_2OAc$	3.4
4	**6g**, $R_1 = R_2 = Me$, $R = CH_2F$	2.9
5	**6h**, $R_1 = R_2 = Me$, $R = CMe_2OH$	103
6	**6i**, $R_1 = R_2 = Me$, $R = CPh_2OH$	57
7	**6j**, $R_1 = R_2 = Me$, $R = CMe_2OMe$	27
8	**6k**, $R_1 = Me$, $R_2 = Et$, $R = CO_2Me$	2.8
9	**6m**, $R_1 = Me$, $R_2 = Et$, $R = CMe_2OH$	103
10	**6n**, $R_1 = Et$, $R_2 = Me$, $R = CO_2Me$	3.7
11	**6p**, $R_1 = Et$, $R_2 = Me$, $R = CMe_2OH$	73

[a] All reactions were carried out with ketone (0.1 mmol), $NaHCO_3$ (0.01 g, 0.11 mmol), and *m*-CPBA (0.05 g, 0.2 mmol) in CH_2Cl_2 (3 mL) at 0 °C for 40 min. Both ^1H and ^{13}C NMR analysis of crude reaction mixture showed that all ketones were completely converted into lactones. [b] The ratios were determined by ^1H NMR analysis.

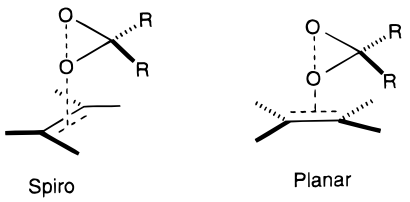


Figure 3. The spiro and planar transition states for the dioxirane epoxidation of olefins.

spiro transition states in each case. In transition states **A** and **B** (or **a** and **b**), the olefin approaches the dioxirane from the top; in transition states **C** and **D** (or **c** and **d**), the olefin approaches the dioxirane from the bottom. Among these transition states, transition states **A** and **C** (or **a** and **c**) are sterically favored and transition states **B** and **D** (or **b** and **d**) are sterically disfavored. The determined configurations of epoxides derived from *trans*-substituted and trisubstituted olefins in Table 4 are consistent with the transition states **A** and **C** (or **a** and **c**). For *cis* and terminal olefins, it is difficult to determine which transition states are favored. Among the two competing transition states **B** and **D** (or **b** and **d**), transition state **B** (or **d**) is probably the major one, since in this transition state the cyclic ketal moiety is in an equatorial position and it is a less efficient control element. The enantioselectivity of the epoxidation is therefore highly dependent on the interaction between this ketal moiety and the R group of the olefin. When the R group is large, the interaction between the ketal moiety and the R group will be strong, and as a result high enantioselectivities can be obtained (for example, Table 4, entries 1, 6, and 9). When the R group is small or flexible, the interaction between the ketal moiety and the R group will be weak, and as a result low enantioselectivities are obtained (for example, Table 4, entries 4, 10, 12, and 13). Further improvement of enantioselectivity with this type of ketone catalyst would be expected if transition state **B** (or **d**) is suppressed. Such efforts will be pursued in the future.

In summary, a ketone with a fused ring at each side of the carbonyl group has been shown to be an effective catalyst for asymmetric epoxidation. It has also been found that ring conformation in this class of pseudo C_2 symmetric ketone catalysts has a large effect on the reactivity and selectivity during asymmetric epoxidation. In addition, the stability of the ketone catalyst to Baeyer–Villiger oxidative decomposition could be affected by substituents β to the carbonyl. These results provide intriguing insights in designing new ketone catalysts. Future effort will be devoted to the further elucidation of the structural requirements for a ketone

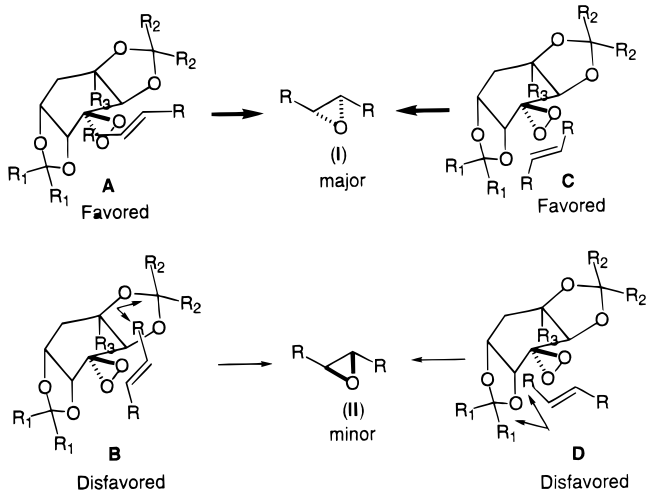


Figure 4. The spiro transition states of ketones with the conformations similar to that of **6b**.

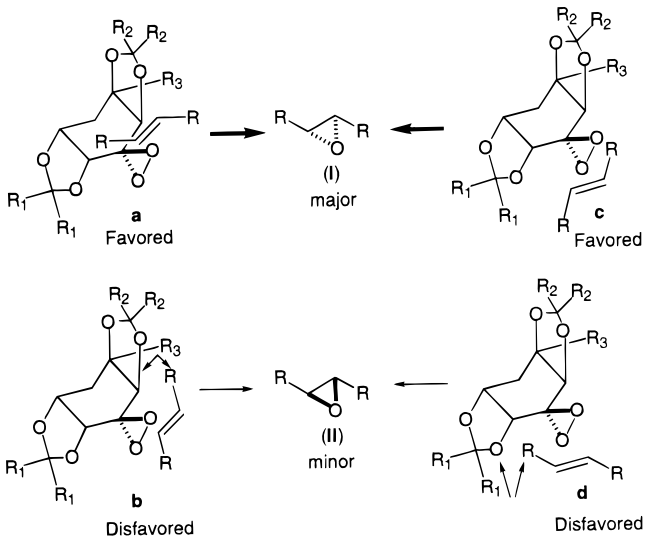


Figure 5. The spiro transition states of ketones with the conformations similar to that of **6i**.

(20) (a) Baumstark, A. L.; McCloskey, C. J. *Tetrahedron Lett.* **1987**, *28*, 3311. (b) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1988**, *53*, 3437. (c) Bach, R. D.; Andres, J. L.; Owensby, A. L.; Schlegel, H. B.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1992**, *114*, 7207. (d) Houk, K. N.; Liu, J.; DeMello, N. C.; Condroski, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10147. (e) Jenson, C.; Liu, J.; Houk, K. N.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1997**, *119*, 12982.

(21) Planar transition states could also be involved to some extent (see ref 4c). For the simplicity of discussion, these transition states are not shown.

to be an effective catalyst for asymmetric epoxidation, particularly for terminal olefins.

Experimental Section

General Methods. THF and ethyl ether were distilled from sodium−benzophenone. Dichloromethane was distilled from calcium hydride. (−)-Quinic acid and Oxone were purchased from Aldrich and used without further purification (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 may catalyze the decomposition of Oxone. Melting points were obtained using chromatographically purified material unless otherwise stated and are uncorrected. High-resolution mass spectra were performed at the mass spectrometry facility of Colorado State University. Elemental analyses were performed by M-H-W Laboratories (Phoenix, AZ). X-ray crystallographic analyses of ketone **6b** and **6i** were performed at the X-ray Crystallographic Laboratory of Colorado State University. Silica gel 60 (230−400 mesh) from E. Merck Co. was employed for all flash chromatography.

Preparation of Triol 8.[8] To a suspension of (−)-quinic acid (46 g, 0.239 mol) in 2,2-dimethoxypropane (60 mL) and benzene (180 mL) was added *p*-TsOH (0.1 g, 0.52 mmol). Upon refluxing for 15 h, the reaction mixture was cooled to room temperature, quenched with triethylamine (0.5 mL, 3.5 mmol), and concentrated to give a residue which was treated with ethyl acetate (100 mL). After filtration, the filtrate was concentrated and recrystallized in hexane−ethyl acetate to yield lactone **7** as white needles (43 g, 84%): mp 139−142 °C; $[\alpha]^{25}_D = -30.0$ (*c* 1.27, $CHCl_3$) [lit.[8a] mp 143−144 °C, $[\alpha]^{25}_D = -34.46°$ (*c* 1.625, $CHCl_3$)].

Lactone **7** (6.2 g, 29.0 mmol) was dissolved in EtOH (120 mL), and $NaBH_4$ (4 g, 105.7 mmol) was added.[8d] After being stirred at room temperature for 15 h, saturated aqueous NaCl (50 mL) was added. After stirring for another 15 h, the reaction mixture was concentrated to remove EtOH and water, and the resulting solid was extracted with CH_2Cl_2−MeOH (2:1, v/v). The extracts were concentrated, and the residue was recrystallized from EtOH to give triol **8** as white crystals (6.2 g, 98%): mp 115−117 °C; $[\alpha]^{25}_D = -55.9$ (*c* 1.27, CH_3OH) [lit.[8a] mp 117−117.5 °C, $[\alpha]^{25}_D = -56.07$ (*c* 1.437, CH_3OH)].

Preparation of Enone 12. The oxidative cleavage of triol **8** was performed using silica gel-supported $NaIO_4$ following Shing's procedure.[9] To a vigorously stirred solution of triol **8** (6.5 g, 30 mmol) in CH_2Cl_2 (200 mL) and methanol (10 mL) was added portionwise $NaIO_4$−silca gel [freshly prepared by adding silica gel (45 g) to a solution of $NaIO_4$ (9.63 g, 45 mmol) in hot water (21 mL) with vigorous shaking]. After being stirred at room temperature for 30 min, the reaction mixture was filtered and washed with ether. The filtrate was evaporated to give hydroxy ketone **9**[8b,e] (5.6 g, 100%) as a slightly yellow solid, which was used without further purification.

To an ice cold solution of hydroxy ketone **9** (7.5 g, 40 mmol) in MeOH (50 mL) was added $NaBH_4$ (1.52 g, 40 mmol) portionwise over 20 min. Upon stirring at this temperature for an additional 30 min, the reaction was quenched with saturated aqueous NH_4Cl and concentrated. The resulting residue was dissolved in CH_2Cl_2 (100 mL), filtered through a Celite pad, and washed with CH_2Cl_2. Upon evaporation, 100 mL of benzene was added. The solution was evaporated to remove possible water, and diol **10** was obtained as a white solid (7.51 g, 100%) which was used directly for the next step: IR (NaCl) 3391 cm^{-1}; ^1H NMR δ 4.38 (m, 1H), 4.16 (ddd, J = 11.0, 6.6, 4.5 Hz, 1H), 4.12 (m, 1H), 3.90 (dd, J = 6.6, 5.1 Hz, 1H), 2.51 (d, J = 7.8 Hz, 1H, OH), 2.42 (br d, J = 3.3 Hz, 1H, OH), 2.20 (dm, J = 15.5 Hz, 1H), 2.09 (dtd, J = 13.5, 4.5, 1.8 Hz, 1H), 1.93 (dt, J = 15.5, 4.5 Hz, 1H), 1.52 (m, 1H), 1.52 (s, 3H), 1.35 (s, 3H); ^{13}C NMR δ 109.1, 80.51, 74.46, 68.08, 65.97, 37.43, 33.48, 28.74, 26.15.

To an ice cold solution of diol **10** (1.2 g, 6.5 mmol) and DMAP (cat.) in pyridine (5 mL) was added *p*-TsCl (1.27 g, 6.5 mmol). Upon stirring at 0 °C for 15 h, the reaction was quenched with ice−water, extracted with CH_2Cl_2, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ethyl acetate, 1:1 v/v) to give a colorless syrup (1.4 g, 60%). ^1H NMR showed it was a mixture of two isomers **11a** and **11b** (1:4).

A mixture of the above tosylates (0.85 g, 2.48 mmol), PCC (1.34 g, 6.2 mmol), powdered 3 Å molecular sieves (1 g), and pyridine (1 mL, 12.3 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 1.5 h. Upon dilution with ether (20 mL), the mixture was filtered through a Celite pad and washed with ether. The filtrate was concentrated and purified by flash chromatography (hexane−ethyl acetate, 2:1 v/v) to give enone **12a**[8b,e] as a colorless oil (0.06 g, 13%) and enone **12b** as white crystals (0.36 g, 77%). For **12b**, mp 72−74 °C; $[\alpha]^{25}_D = -119.2$ (*c* 0.87, $CHCl_3$); IR (NaCl) 1668, 1622 cm^{-1}; ^1H NMR δ 6.85 (dddd, J = 10.2, 4.8, 3.0, 1.6 Hz, 1H), 6.14 (ddd, J = 10.2, 2.5, 1.5 Hz, 1H), 4.64 (m, 1H), 4.27 (d, J = 4.8 Hz, 1H), 2.88 (ddt, J = 20.4, 4.8, 1.6 Hz, 1H), 2.78 (ddt, J = 20.4, 4.8, 2.7 Hz, 1H), 1.38 (s, 3H), 1.32 (s, 3H); ^{13}C NMR δ 196.5, 146.5, 128.3, 109.3, 75.62, 73.03, 27.9, 27.57, 26.12. Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.11; H, 7.27.

Preparation of Ketone 6a. To an ice cold mixture of enone **12b** (0.3 g, 1.79 mmol) and $CeCl_3 \cdot 7H_2O$ (0.615 g, 1.65 mmol) in EtOH (10 mL) was added portionwise $NaBH_4$ (0.062 g, 1.63 mmol) over 10 min. Upon stirring at room temperature for 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 × 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated to give the alcohol as white crystals (0.27 g, 90%) which were used without further purification: IR (NaCl) 3228, 1636 cm^{-1}; ^1H NMR δ 5.85−5.73 (m, 2H), 4.54 (dddd, J = 7.5, 4.5, 2.4, 0.9 Hz, 1H), 4.48 (ddd, J = 7.5, 4.2, 1.2 Hz, 1H), 4.05 (m, 1H), 2.64 (m, 1H), 2.40 (ddd, J = 16.5, 6.0, 2.4 Hz, 1H), 2.0 (ddq, J = 16.5, 4.5, 2.4 Hz, 1H), 1.39 (s, 3H), 1.34 (s, 3H); ^{13}C NMR δ 131.9, 125.6, 108.8, 76.52, 72.58, 66.81, 27.61, 26.09, 24.67.

To a solution of the above alcohol (0.27 g, 1.6 mmol) in CH_2Cl_2 (5 mL) were added imidazole (0.18 g, 2.5 mmol), *tert*-butyldimethylsilyl chloride (0.3 g, 2.0 mmol), and DMAP (cat.). Upon stirring at room temperature for 2 h, the reaction mixture was diluted with ether, washed with saturated aqueous NH_4Cl, water, and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 1:1 v/v) to give TBS ether **13** as a colorless oil (0.38 g, 81%): $[\alpha]^{25}_D = -7.3$ (*c* 2.14, $CHCl_3$); ^1H NMR δ 5.84−5.70 (m, 2H), 4.46 (dddd, J = 7.3, 5.1, 2.1, 0.9 Hz, 1H), 4.39 (ddd, J = 7.3, 3.6, 1.5 Hz, 1H), 4.16 (dq, J = 3.6, 2.4 Hz, 1H), 2.35 (ddd, J = 16.5, 6.3, 2.1 Hz, 1H), 1.94 (ddq, J = 16.5, 5.1, 2.4 Hz, 1H), 1.40 (s, 3H), 1.32 (s, 3H), 0.93 (s, 9H), 0.13 (s, 6H); ^{13}C NMR δ 132.9, 124.8, 108.7, 78.25, 73.23, 69.38, 28.58, 26.28 (4C), 24.67, 18.79, −4.282, −4.306.

To a solution of **13** (0.30 g, 1.07 mmol), *N*-methylmorpholine *N*-oxide (0.23 g, 1.5 mmol), pyridine (0.5 mL, 6.1 mmol), and water (0.1 mL, 5.6 mmol) in *t*-BuOH (3.5 mL) was added OsO_4 (cat.) at room temperature under N_2. Upon refluxing under N_2 for 3 h, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $Na_2S_2O_3$ (1 mL), concentrated, and purified by flash chromatography (hexane−ethyl acetate, 1:1 v/v) to afford diol **14** as white crystals (0.29 g, 87%): mp 58−59 °C; $[\alpha]^{25}_D = -39.0$ (*c* 0.48, $CHCl_3$); IR (NaCl) 3445 cm^{-1}; ^1H NMR δ 4.40 (ddd, J = 9.0, 6.3, 4.8 Hz, 1H), 4.32 (dd, J = 4.8, 3.9 Hz, 1H), 4,12 (m, 1H), 4.11 (dd, J = 9.3, 3.9 Hz, 1H), 3.88 (dd, J = 9.3, 2.7 Hz, 1H), 2.40 (br s, 1H, OH), 2.28 (br s, 1H, OH), 2.16 (ddd, J = 14.2, 6.3, 4.2 Hz, 1H), 1.68 (ddd, J = 14.2, 9.0, 3.9 Hz, 1H), 1.52 (s, 3H), 1.34 (s, 3H), 0.95 (s, 9H), 0.171 (s, 3H), 0.166 (s, 3H); ^{13}C NMR δ 109.5, 77.34, 73.19, 71.63, 70.67, 68.89, 33.49, 28.69, 26.11, 26.09, 18.48, −4.01, −4.22.

To a solution of diol **14** (0.28 g, 0.88 mmol) and 2-methoxypropene (0.15 mL, 1.6 mmol) in dry CH_2Cl_2 (3 mL) was added camphorsulfonic acid (cat.) under N_2 at room temperature. Upon stirring at room temperature for 1 h, the reaction mixture was quenched with several drops of triethylamine, concentrated, and purified by flash chromatography (hexane−ether, 10:1 v/v) to afford a colorless oil (0.31 g), which was then

dissolved in TBAF (1.0 M in THF, 2 mL, 2 mmol). After being stirred at room temperature for 30 min, the reaction mixture was diluted with ether (20 mL), washed with saturated aqueous NH_4Cl, water, and brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether, 2:1 to 1:1 v/v) to give the alcohol as colorless oil (0.21 g, 98%): IR (NaCl) 3455 cm^{-1}; ^1H NMR δ 4.56−4.44 (m, 2H), 4.37 (dd, J = 7.8, 3.3 Hz, 1H), 4.30 (dd, J = 7.5, 6.0 Hz, 1H), 3.83 (ddd, J = 6.0, 3.9, 3.3 Hz, 1H), 2.46 (m, 1H), 2.25 (ddd, J = 14.1, 6.0, 4.5 Hz, 1H), 1.92 (dddd, J = 14.1, 6.9, 4.5, 1.2 Hz, 1H), 1.48 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C NMR δ 108.4, 108.3, 75.39, 74.15, 71.72, 71.59, 70.17, 29.93, 26.92, 27.33, 23.96, 23.7.

To a solution of DMSO (0.156 g, 2 mmol) in dry CH_2Cl_2 (0.5 mL) was added dropwise oxalyl chloride (0.087 mL, 1 mmol) under N_2 at −78 °C. The mixture was stirred at −78 °C for 10 min and then removed from the coolant and stirred for 3 min. Upon recooling to −78 °C, a solution of the above alcohol (0.2 g, 0.82 mmol) in dry CH_2Cl_2 (1.5 mL) was added. The resulting reaction mixture was stirred at −78 °C for 1 h, and then triethylamine (0.4 mL, 2.8 mmol) was added dropwise. After being stirred at −78 °C for an additional 10 min, the reaction mixture was warmed to room temperature, quenched with saturated aqueous NH_4Cl (5 mL), extracted with CH_2Cl_2 (3 × 10 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 10:1 to 2:1, v/v) to give ketone **6a** as a colorless syrup (0.19 g, 95%): $[\alpha]^{25}_D$ = −20.2 (*c* 1.32, $CHCl_3$); IR (NaCl) 3469 (hydrate), 1748 cm^{-1}. **Ketone**: ^1H NMR δ 4.83 (dt, J = 8.0, 5.3 Hz, 2H), 4.72 (d, J = 8.0 Hz, 2H), 1.96 (t, J = 5.3 Hz, 2H), 1.54 (s, 6H), 1.35 (s, 6H); ^{13}C NMR δ 204.4, 111.0, 77.55, 75.01, 32.36, 26.51, 24.19. **Hydrate**: ^1H NMR δ 4.54 (dt, J = 7.7, 5.7 Hz, 2H), 4.25 (d, J = 7.7 Hz, 2H), 3.5 (br s, 2H, OH), 2.13 (t, J = 5.7, 2H), 1.49 (s, 6H), 1.36 (s, 6H); ^{13}C NMR δ 108.8, 93.39, 76.7, 72.29, 29.85, 26.56, 23.74. Anal. Calcd for $C_{12}H_{18}O_5 \cdot 0.8H_2O$: C, 56.15; H, 7.69. Found: C, 56.17; H, 7.71.

Preparation of Ketone 6b. To a solution of **7** (14.8 g, 69 mmol) in MeOH (75 mL) was added MeONa (4.9 g, 90 mmol). After stirring at room temperature for 5 h, the reaction mixture was quenched by a slow addition of AcOH (5.15 mL, 90 mmol) and concentrated under reduced pressure. The resultant syrup was dissolved in ethyl acetate (100 mL), filtered through a thin silica gel pad, and washed with ether and ethyl acetate. The filtrate was concentrated and purified by flash chromatography (hexane−ethyl acetate, 2:1 to 1:2 v/v) to afford the ester as a slightly yellow syrup (13.8 g, 82%) along with recovered lactone **7** (1.1 g, 7.5%): $[\alpha]^{25}_D$ = −44.4 (*c* 0.48, $CHCl_3$); IR (NaCl) 3437, 1736 cm^{-1}; ^1H NMR δ 4.43 (m, 1H), 4.1 (m, 1H), 3.95 (m, 1H), 3.77 (s, 3H), 2.22 (m, 2H), 2.03 (m, 1H), 1.81 (m, 1H), 1.51 (s, 3H), 1.33 (s, 3H); ^{13}C NMR δ 175.7, 109.3, 80.19, 74.06, 73.53, 68.18, 53.16, 39.16, 34.91, 28.31, 25.81.

To a solution of the above ester (10.0 g, 40.6 mmol) and pyridine (10 mL, 123 mmol) in dry CH_2Cl_2 (100 mL) were added PCC (25.0 g, 116 mmol) and grounded 3 Å molecular sieves (17.0 g). After stirring at room temperature for 24 h, the reaction mixture was diluted with ether (300 mL), filtered through Celite, and washed carefully with ether. The filtrate was concentrated and purified by flash chromatography (hexane−ethyl acetate, 3:1 v/v) followed by recrystallization with hexane to afford enone **15**[11b] as white needles (5.5 g, 60%): mp 84−85 °C; $[\alpha]^{25}_D$ = −51.7 (*c* 0.5, $CHCl_3$); IR (NaCl) 1725, 1688, 1631 cm^{-1}; ^1H NMR δ 6.85 (dd, J = 2.8, 0.9 Hz, 1H), 4.70 (ddd, J = 5.1, 5.1, 1.8 Hz, 1H), 4.31 (d, J = 5.1 Hz, 1H), 3.86 (s, 3H), 3.22 (ddd, J = 20.4, 1.8, 0.9 Hz, 1H), 2.88 (ddd, J = 20.4, 5.1, 2.8 Hz, 1H), 1.41 (s, 3H), 1.32 (s, 3H); ^{13}C NMR δ 197.6, 166.4, 144.4, 131.5, 109.8, 75.31, 72.73, 53.06, 27.57, 26.86, 26.05. Anal. Calcd for $C_{11}H_{14}O_5 \cdot 0.1H_2O$: C, 57.94; H, 6.23. Found: C, 57.74; H, 6.10.

To a solution of enone **15** (5 g, 22.1 mmol) in MeOH (30 mL) at 0 °C was added $NaBH_4$ (1.0 g, 26 mmol) portionwise. After being stirred at room temperature for 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl (15 mL). Upon the removal of MeOH under reduced pressure, the resulting aqueous solution was extracted with CH_2Cl_2 (4 x 15 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give alcohol **16** as a white solid (5 g, 98%) which was used without further purification.

To a solution of **16** (3.2 g, 14 mmol), imidazole (1.7 g, 25 mmol), and DMAP (cat.) in dry CH_2Cl_2 (50 mL) was added *tert*-butyldimethylsilyl chloride (3.0 g, 20 mmol). After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 30 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 5:1, v/v) to give TBS ether **17** as a colorless syrup (4.6 g, 96%): $[\alpha]^{25}_D$ = +17.9 (*c* 0.9, $CHCl_3$); IR (NaCl) 1719, 1644 cm^{-1}; ^1H NMR δ 6.91 (m, 1H), 4.55 (ddd, J = 7.2, 4.5, 1.8 Hz, 1H), 4.44 (ddd, J = 7.2, 3.7, 1.5 Hz, 1H), 4.16 (dt, J = 3.7, 1.9 Hz, 1H), 3.76 (s, 3H), 2.98 (dd, J = 16.3, 1.8 Hz, 1H), 1.89 (dddd, J = 16.3, 4.5, 2.4, 2.1 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 0.94 (s, 9H), 0.144 (s, 6H); ^{13}C NMR δ 166.3, 143.9, 128.2, 109.0, 78.07, 73.21, 70.63, 52.03, 27.67, 26.19, 25.86, 24.49, 18.68, −4.326, −4.349.

To a solution of **17** (4.6 g, 13.5 mmol), *N*-methylmorpholine *N*-oxide (2.8 g, 24 mmol), pyridine (7 mL, 85 mmol), and water (1.4 mL, 78 mmol) in *t*-BuOH (45 mL) at room temperature under N_2 was added OsO_4 (0.010 g, 0.04 mmol). Upon refluxing under N_2 for 3 h, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $Na_2S_2O_3$ (15 mL), concentrated, and purified by flash chromatography (hexane−ether, 1:1, v/v) to afford diol **18** as a colorless syrup (4.8 g, 95%): IR (NaCl) 3475, 1740 cm^{-1}; ^1H NMR δ 4.33 (m, 2H), 4.18−4.04 (m, 2H), 3.81 (s, 3H), 3.37 (br s, 1H, OH), 2.25 (br s, 1H, OH), 2.0 (m, 2H), 1.54 (s, 3H), 1.34 (s, 3H), 0.93 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR δ 174.4, 109.8, 77.39, 76.95, 72.93, 72.63, 71.36, 53.34, 36.38, 28.82, 26.22, 26.02, 18.42, −4.237, −4.266.

To a solution of diol **18** (4.8 g, 12.8 mmol) and 2-methoxypropene (8 mL, 83 mmol) in dry CH_2Cl_2 (80 mL) was added camphorsulfonic acid (cat.) under N_2 at room temperature. After being stirred for 2 h, the reaction mixture was quenched with triethylamine (0.5 mL), concentrated, and purified by flash chromatography (hexane−ether, 10:1 to 5:1, v/v) (the silica gel was buffered with 1% triethylamine in hexane) to afford TBS ether **19** as a colorless syrup (5.0 g, 94%): $[\alpha]^{25}_D$ = −15.0 (*c* 0.66, $CHCl_3$); IR (NaCl) 1741 cm^{-1}; ^1H NMR δ 4.76 (d, J = 3.6 Hz, 1H), 4.40 (dt, J = 7.8, 7.5 Hz, 1H), 4.31−4.24 (m, 2H), 3.78 (s, 3H), 2.35 (m, 2H), 1.48 (s, 3H), 1.44 (s, 3H), 1.34 (s, 3H), 1.29 (s, 3H), 0.91 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 173.6, 110.2, 108.3, 82.6, 78.26, 72.81, 70.43, 68.9, 52.83, 34.03, 28.86, 26.21, 26.03, 24.83, 24.14, 18.3, −4.334, −4.94.

TBS ether **19** (1.6 g, 3.9 mmol) was dissolved in a solution of TBAF in THF (1 M, 15 mL). After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 2:1 to 1:1, v/v) to give the alcohol as white crystals (0.82 g, 70%): $[\alpha]^{25}_D$ = −20.5 (*c* 0.22, $CHCl_3$); IR (NaCl) 3488, 1740 cm^{-1}; ^1H NMR δ 4.93 (d, J = 4.8 Hz, 1H), 4.45 (ddd, J = 7.8, 7.8, 5.1 Hz, 1H), 4.37 (dd, J = 7.8, 3.6 Hz, 1H), 4.14 (m, 1H), 3.81 (s, 3H), 2.56 (d, J = 2.4 Hz, 1H, OH), 2.40 (dd, J = 13.8, 7.8 Hz, 1H), 2.24 (dd, J = 13.8, 5.1 Hz, 1H), 1.48 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H); ^{13}C NMR δ 173.4, 110.3, 108.7, 82.07, 76.88, 72.94, 70.62, 68.57, 53.07, 33.88, 27.24, 26.07, 24.98, 23.96.

Swern oxidation of the above alcohol (0.67 g, 2.2 mmol) gave ketone **6b** as a white solid (0.66 g, 99%) after flash chromatography (hexane−ether, 1:1 to 1:2, v/v): mp 71.5−73 °C (hexane); $[\alpha]^{23}_D$ = −2.1 (*c* 0.9, $CHCl_3$); IR (NaCl) 3481(hydrate), 1749 cm^{-1}. **Ketone**: ^1H NMR δ 4.92 (s, 1H), 4.90 (dd, J = 8.4, 0.7 Hz, 1H), 4.85 (ddd, J = 8.5, 8.4, 3.9 Hz, 1H), 3.81 (s, 3H), 2.25 (ddd, J = 14.4, 3.9, 0.7 Hz, 1H), 2.0 (dd, J = 14.4, 8.5 Hz, 1H), 1.56 (s, 3H), 1.49 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H); ^{13}C NMR δ 202.4, 171.4, 113.6, 110.9, 85.1, 79.9, 77.29, 73.42, 53.34, 36.12, 26.71, 26.33, 24.97, 24.35. **Hydrate**: ^1H NMR δ 4.81 (s, 1H), 4.50 (ddd, J = 8.8, 7.8, 5.1 Hz, 1H), 4.35 (d, J = 7.8 Hz, 1H), 3.80 (s, 3H), 2.31 (dd, J = 13.8, 5.1 Hz, 1H), 2.18

(dd, J = 13.8, 8.8 Hz, 1H), 1.483 (s, 3H), 1.481 (s, 3H), 1.36 (s, 3H), 1.33 (s, 3H); ^{13}C NMR δ 172.7, 110.5, 109.6, 93.73, 82.5, 79.51, 76.01, 71.64, 53.14, 33.94, 26.86, 26.33, 24.69, 24.26. Anal. Calcd for $C_{14}H_{20}O_7 \cdot 0.2H_2O$: C, 55.33; H, 6.77. Found: C, 55.35; H 6.64.

Preparation of Ketone 6c. To a solution of triol **8** (4.1 g, 18.8 mmol), imidazole (1.9 g, 33 mmol), and DMAP (cat.) in dry CH_2Cl_2 (50 mL) at 0 °C was added portionwise *tert*-butyldimethylsilyl chloride (3.5 g, 23 mmol). After being stirred at 0 °C for 2 h, the reaction mixture was diluted with ether (100 mL), filtered through a thin pad of silica gel, and washed with ether (200 mL). The filtrate was concentrated to give TBS ether **20** as a colorless oil (5.5 g), which was used directly for the next step: $[\alpha]^{25}_D = -38.0$ (c 0.5, $CHCl_3$); ^{1}H NMR δ 4.50 (m, 1H), 4.03−3.94 (m, 2H), 3.42 (d, J = 9.3 Hz, 1H), 3.36 (d, J = 9.3 Hz, 1H), 3.01 (br s, 2H, OH), 2.07 (dd, J = 15.6, 3.6 Hz, 1H), 2.03−1.94 (m, 2H), 1.75 (m, 1H), 1.52 (s, 3H), 1.35 (s, 3H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR δ 108.8, 78.9, 73.96, 71.77, 70.66, 68.28, 38.55, 33.47, 27.94, 26.05, 25.23, 18.47, −5.34.

To a solution of TBS ether **20** (5.5 g) in CH_2Cl_2 (100 mL) were added powdered 3 Å MS (7 g), PCC (9 g, 41.7 mmol), and pyridine (5 mL, 61 mmol). After being stirred at room temperature overnight, the reaction mixture was diluted with ether (300 mL), filtered through a thin pad of silica gel, and washed with ether. The filtrate was concentrated to give a colorless syrup which was dissolved in pyridine (20 mL), followed by the addition of $POCl_3$ (2 mL, 21.5 mmol). After being stirred at room temperature for 16 h, the reaction mixture was quenched with saturated aqueous NH_4Cl and ether, extracted with ether (3 × 50 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ethyl acetate, 4:1, v/v) to afford enone **21** as a colorless syrup (3.1 g, 54% yield from **8**): $[\alpha]^{25}_D = -40.9$ (c 1.5, $CHCl_3$); IR (NaCl) 1680, 1650 cm^{-1}; ^{1}H NMR δ 6.25 (m, 1H), 4.64 (m, 1H), 4.28 (d, J = 5.1 Hz, 1H), 4.23 (br s, 2H), 2.67 (m, 2H), 1.40 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.078 (s, 6H); ^{13}C NMR δ 196.2, 160.4, 121.8, 109.6, 75.7, 72.83, 65.21, 27.97, 27.62, 26.22, 25.96, 18.46, −5.287, −5.319.

To a solution of enone **21** (1.1 g, 3.4 mmol) in EtOH (10 mL) was added $NaBH_4$ (0.3 g, 7.6 mmol). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL), extracted with CH_2Cl_2 (5 × 20 mL), washed with water and brine, dried (Na_2SO_4), and concentrated to give a crude alcohol.

To a solution of the above crude alcohol in dry CH_2Cl_2 (10 mL) were added pyridine (0.7 mL, 8.61 mmol), acetic anhydride (0.7 mL, 7.4 mmol), and DMAP (cat.). After being stirred at room temperature for 10 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 x 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 3:1, v/v) to give acetate **22** as a colorless syrup (1.2 g, 96%).

To a solution of acetate **22** (1.2 g, 3.5 mmol), *N*-methylmorpholine *N*-oxide (0.65 g, 5.5 mmol), pyridine (1.75 mL, 21.5 mmol), and water (0.35 mL, 19.4 mmol) in *t*-BuOH (10 mL) at room temperature under N_2 was added OsO_4 (0.010 g, 0.04 mmol). After being refluxed under N_2 for 3 h, the reaction mixture was cooled to room temperature, quenched with saturated aqueous $Na_2S_2O_3$ (5 mL), concentrated, and purified by flash chromatography (hexane−ether, 1:1, v/v) to afford diol **23** as white crystals (1.0 g, 72%): mp 118−119.5 °C (hexane); $[\alpha]^{25}_D = -31.6$ (c 0.67, $CHCl_3$); IR (NaCl) 3432, 3380, 1739, 1253, 1080 cm^{-1}; ^{1}H NMR δ 5.28 (dd, J = 9.9, 3.9 Hz, 1H), 4.47−4.35 (m, 2H), 4.0 (dd, J = 9.9, 4.5 Hz, 1H), 3.7 (d, J = 9.6 Hz, 1H), 3.6 (d, J = 9.6 Hz, 1H), 2.94 (d, J = 4.5 Hz, 1H, OH), 2.77 (s, 1H, OH), 2.18 (s, 3H), 1.95 (dd, J = 14.4, 6.3 Hz, 1H), 1.67 (dd, J = 14.4, 8.1 Hz, 1H), 1.50 (s, 3H), 1.32, (s, 3H), 0.88 (s, 9H), 0.078 (s, 6H); ^{13}C NMR δ 171.4, 109.7, 74.63, 73.54, 72.67, 72.26, 70.21, 69.44, 34.8, 28.33, 26.14, 26.0, 21.39, 18.35, −5.35, −5.38. Anal. Calcd for $C_{18}H_{34}O_7Si$: C, 55.35; H, 8.77. Found: C, 55.44; H, 8.57.

To a solution of diol **23** (0.8 g, 2 mmol) and 2-methoxypropene (1.3 mL, 13.6 mmol) in dry CH_2Cl_2 (15 mL) was added camphorsulfonic acid (cat.) under N_2 at room temperature. After being stirred for 2 h, the reaction mixture was quenched with triethylamine (0.1 mL), concentrated, and purified by flash chromatography (hexane−ether, 10:1 to 5:1, v/v) (the silica gel was buffered with 1% triethylamine in hexane) to afford the acetate as a colorless syrup (0.81 g, 96%): ^{1}H NMR δ 5.43 (dd, J = 6.3, 3.6 Hz, 1H), 4.56−4.43 (m, 2H), 4.28 (d, J = 6.3 Hz, 1H), 3.7 (d, J = 10.5 Hz, 1H), 3.65 (d, J = 10.5 Hz, 1H), 2.11 (s, 3H), 2.04 (d, J = 6.0 Hz, 2H), 1.45 (s, 3H), 1.41(s, 6H), 1.32 (s, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

To a solution of the above acetate (0.81 g, 1.88 mmol) in dry THF (10 mL) was added dropwise a DIBAL-H solution (1.0 M in hexane, 6 mL) at −20 °C over 30 min. After being stirred at 0 °C for 3 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (3 mL), filtered, and washed with ether. The filtrate was concentrated and purified by flash chromatography (hexane−ether, 2:1, v/v) to give alcohol **24** as a colorless syrup (0.75 g, 94%): $[\alpha]^{25}_D = +10.0$ (c 0.24, $CHCl_3$); IR (NaCl) 3495 cm^{-1}; ^{1}H NMR δ 4.49−4.34 (m, 3H), 4.31 (d, J = 3.9 Hz, 1H), 3.65 (s, 2H), 2.61 (br s, 1H, OH), 2.07 (dd, J = 13.5, 5.7 Hz, 1H), 1.80 (dd, J = 13.5, 9.0 Hz, 1H), 1.50 (s, 3H), 1.41 (s, 6H), 1.38 (s, 3H), 0.91 (s, 9H), 0.084 (s, 3H), 0.077 (s, 3H); ^{13}C NMR δ 109.3, 108.5, 83.51, 75.98, 73.13, 71.46, 69.47, 67.28, 34.43, 28.02, 26.97, 26.95, 26.20, 24.55, 18.72, −5.13, −5.26. Anal. Calcd for $C_{19}H_{36}O_6Si$: C, 58.72; H, 9.34. Found: C, 58.71; H, 8.96.

Swern oxidation of alcohol **24** (0.70 g, 1.8 mmol) and purification by flash chromatography (hexane−ether, 5:1 to 2:1 v/v) gave ketone **6c** as a colorless syrup (0.63 g, 90%): $[\alpha]^{25}_D = +22.6$ (c 1.23, $CHCl_3$); IR (NaCl) 1752 cm^{-1}; ^{1}H NMR δ 5.05 (dd, J = 8.1, 1.2 Hz, 1H), 4.94 (ddd, J = 10.9, 8.1, 4.8 Hz, 1H), 4.33 (s, 1H), 3.64 (d, J = 10.4 Hz, 1H), 3.57 (d, J = 10.4, 1H), 2.09 (ddd, J = 14.1, 4.8, 1.2 Hz, 1H), 1.56 (s, 3H), 1.50 (s, 3H), 1.45 (ddd, J = 14.1, 10.9 Hz, 1H), 1.39 (s, 6H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR δ 203.4, 112.3, 110.1, 86.38, 81.26, 77.76, 73.48, 67.67, 36.69, 27.24, 27.05, 26.41, 25.99, 24.82, 18.47, −5.26, −5.44. HRMS for [**6c** + DCI(NH_3)], calcd for $C_{19}H_{38}NO_6Si$ (MNH_4^+) 404.2468, found 404.2488.

Preparation of Ketone 6d. DIBAL-H (1.0 M in hexane, 30 mL, 0.03 mol) was added dropwise to a solution of ester **19** (5.0 g, 12.1 mmol) in THF (30 mL) at −20 °C under N_2 over 30 min. After being stirred at 0 °C for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) and filtered. The cake was washed with ether. The filtrate was extracted with ether, washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 2:1, v/v) to give alcohol **25** as white crystals (4.3 g, 92.3%): $[\alpha]^{25}_D = -3.8$ (c 0.29, $CHCl_3$); IR (NaCl) 3484 cm^{-1}; ^{1}H NMR δ 4.43 (t, J = 4.5 Hz, 1H), 4.38 (ddd, J = 9.9, 7.8, 5.4 Hz, 1H), 4.32 (dd, J = 7.8, 4.5 Hz, 1H), 4.13 (d, J = 4.5 Hz, 1H), 3.64 (dd, J = 11.4, 6.6 Hz, 1H), 3.59 (dd, J = 11.4, 6.6 Hz, 1H), 2.10 (dd, J = 13.8, 5.4 Hz, 1H), 2.06 (t, J = 6.6 Hz, 1H, OH), 1.85 (dd, J = 13.8, 9.9 Hz, 1H), 1.48 (s, 3H), 1.43 (s, 3H), 1.40 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.11 (s, 6H); ^{13}C NMR δ 109.3, 108.2, 83.72, 77.81, 73.13, 71.19, 69.02, 68.51, 34.61, 27.74, 26.87, 26.65, 26.14, 24.24, 18.43, −4.31, −4.89. Anal. Calcd for $C_{19}H_{36}O_6Si$: C, 58.73; H, 9.33. Found: C, 58.84; H, 9.11.

Acetic anhydride (0.4 mL, 4.2 mmol) was added to a solution of **25** (0.9 g, 2.33 mol), triethylamine (0.9 mL, 6.46 mmol), and DMAP (cat.) in dry CH_2Cl_2 (5 mL). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 × 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated to give an acetate as a colorless syrup, which was then dissolved in a solution of TBAF in THF (1 M, 8 mL). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (4 x 15 mL), washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ethyl acetate, 5:1 to 2:1, v/v) to afford alcohol **26d** as white crystals (0.58 g, 86%): $[\alpha]^{25}_D = +7.4$ (c 0.27, $CHCl_3$); IR (NaCl) 3487, 1743 cm^{-1}; ^{1}H NMR δ 4.45−4.31 (m, 3H), 4.26 (d, J = 4.5 Hz, 1H), 4.19 (d, J = 11.6 Hz, 1H), 4.11 (d, J = 11.6 Hz, 1H), 2.61 (s, 1H, OH), 2.12 (m, 1H), 2.08 (s,

3H), 1.88 (m, 1H), 1.48 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H); ^{13}C NMR δ 170.9, 109.8, 108.7, 81.36, 76.58, 72.84, 71.13, 69.74, 67.22, 34.39, 27.96, 26.83, 26.53, 24.46, 21.08. Anal. Calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.64. Found: C, 57.13; H, 7.24.

Swern oxidation of alcohol **26d** (0.54 g, 1.72 mmol) and purification by flash chromatography (hexane−ether, 2:1 to 1:2, v/v) gave ketone **6d** as a white solid (0.53 g, 95%): mp 72.5−74 °C (recrystallized from hexane); $[\alpha]^{25}_D = +11.2$ (*c* 0.34, $CHCl_3$); IR (NaCl) 3464 (hydrate), 1748 cm^{-1}. **Ketone**: ^{1}H NMR δ 5.01 (dd, J = 8.4, 0.6 Hz, 1H), 4.90 (ddd, J = 10.2, 8.4, 4.5 Hz, 1H), 4.34 (s, 1H), 4.24 (d, J = 11.7 Hz, 1H), 4.04 (d, J = 11.7 Hz, 1H), 2.16 (ddd, J = 14.1, 4.5, 0.6 Hz, 1H), 2.08 (s, 3H), 1.55 (s, 3H), 1.50 (s, 3H), 1.45 (dd, J = 14.1, 10.2 Hz, 1H), 1.39 (s, 3H), 1.36 (s, 3H); ^{13}C NMR δ 203.3, 170.6, 112.9, 110.5, 84.33, 81.09, 77.74, 73.28, 67.55, 36.78, 27.04, 26.98, 26.15, 24.56, 20.89. **Hydrate**: ^{1}H NMR δ 4.50 (ddd, J = 10.6, 7.5, 5.7 Hz, 1H), 4.41 (d, J = 7.5 Hz, 1H), 4.25 (d, J = 11.5 Hz, 1H), 4.05 (d, J = 11.5 Hz, 1H), 4.11 (s, 1H), 2.08 (dd, J = 13.5, 5.7 Hz, 1H), 2.09 (s, 3H), 1.60 (dd, J = 13.5, 10.6 Hz, 1H), 1.50 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.39 (s, 3H); ^{13}C NMR δ 170.8, 110.5, 109.7, 94.12 (hydrate C), 81.9, 80.11, 76.33, 72.0, 68.87, 34.69, 27.46, 27.24, 26.03, 25.04, 21.05. Anal. Calcd for $C_{15}H_{22}O_7 \cdot 0.8H_2O$: C, 54.80; H, 7.10. Found: C, 54.79; H, 7.03.

Preparation of Ketone 6e. Benzoyl chloride (0.3 mL, 2.5 mmol) was added to a solution of alcohol **25** (0.77 g, 2 mmol), triethylamine (0.5 mL, 3.5 mmol), and DMAP (cat.) in dry CH_2Cl_2 (5 mL). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 × 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated to give the crude benzoate, which was then dissolved in a solution of TBAF in THF (1 M, 8 mL). After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ethyl acetate, 2:1, v/v) to give alcohol **26e** as a colorless syrup (0.75 g, 99%): IR (NaCl) 3508, 1723 cm^{-1}; ^{1}H NMR δ 8.08 (m, 2H), 7.55 (m, 1H), 7.43 (m, 2H), 4.52−4.35 (m, 6H), 2.68 (s, 1H, OH), 2.26 (dd, J = 14.1, 5.4 Hz, 1H), 2.06 (dd, J = 14.1, 8.7 Hz, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.42 (s, 3H), 1.39 (s, 3H); ^{13}C NMR δ 166.5, 133.2, 130.2, 130.0, 128.5, 109.8, 108.7, 81.57, 76.92, 72.91, 71.19, 70.23, 67.38, 34.57, 27.98, 26.79, 26.70, 24.38.

Swern oxidation of alcohol **26e** (0.73 g, 1.93 mmol) and purification by flash chromatography (hexane−ether, 2:1 to 1:2, v/v) gave ketone **6e** as a colorless syrup (0.71 g, 96%): $[\alpha]^{25}_D = +21.0$ (*c* 0.84, $CHCl_3$); IR (NaCl) 3468 (hydrate), 1749, 1724 cm^{-1}; ^{1}H NMR δ 8.04 (m, 2H), 7.57 (m, 1H), 7.45 (m, 2H), 5.07 (d, J = 8.4 Hz, 1H), 4.94 (ddd, J = 10.2, 8.4, 4.5 Hz, 1H), 4.50 (s, 1H), 4.42 (d, J = 11.4 Hz, 1H), 4.36 (d, J = 11.4 Hz, 1H), 2.27 (dd, J = 14.4, 4.5 Hz, 1H), 1.60 (dd, J = 14.4, 10.2 Hz, 1H), 1.58 (s, 3H), 1.52 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H); ^{13}C NMR δ 203.3, 166.1, 133.6, 130.0, 129.9, 128.7, 113.0, 110.5, 84.45, 81.45, 77.72, 73.33, 68.42, 36.93, 27.01, 27.0, 26.2, 24.56. Anal. Calcd for $C_{20}H_{24}O_7 \cdot H_2O$: C, 60.91; H, 6.64. Found: C, 60.85; H, 6.25.

Preparation of Ketone 6f. *p*-Toluenesulfonyl chloride (0.475 g, 2.5 mmol) was added to a solution of **25** (0.77 g, 2 mmol), pyridine (0.5 mL, 6.1 mmol), and DMAP (cat.) in dry CH_2Cl_2 (5 mL) at 0 °C. After being stirred at room temperature for 30 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3 x 20 mL), washed with water and brine, dried (Na_2SO_4), filtered, and concentrated to give the crude tosylate, which was then dissolved in a solution of TBAF in THF (1 M, 10 mL). After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ethyl acetate, 2:1, v/v) to give alcohol **26f** as white crystals (0.7 g, 82%): $[\alpha]^{25}_D = +3.1$ (*c* 0.89, $CHCl_3$); IR (NaCl) 3446, 1176, 1063, 986 cm^{-1}; ^{1}H NMR δ 7.81 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 4.42−4.34 (m, 2H), 4.29 (m, 1H), 4.22 (d, J = 5.1 Hz, 1H), 4.09 (d, J = 10.2 Hz, 1H), 4.03 (d, J = 10.2 Hz, 1H), 2.55 (s, 1H, OH), 2.45 (s, 3H), 2.03 (m, 1H), 1.79 (m, 1H), 1.44 (s, 3H), 1.39 (s, 3H), 1.35 (s, 3H), 1.31 (s, 3H); ^{13}C NMR δ 145.1, 130.0, 128.3, 128.3, 110.3, 108.8, 80.97, 76.11, 74.22, 72.79, 70.95, 67.23, 34.1, 28.06, 26.72, 26.48, 24.42, 21.84. Anal. Calcd for $C_{20}H_{28}O_8S$: C, 56.06; H, 6.59. Found: C, 55.98; H, 6.61.

Swern oxidation of alcohol **26f** (0.67 g, 1.55 mol) and purification by flash chromatography (hexane−ethyl acetate, 5:1 to 1:1, v/v) gave ketone **6f** as a colorless syrup (0.67 g, 100%): $[\alpha]^{25}_D = +4.3$ (*c* 0.81, $CHCl_3$); IR (NaCl) 3480 (hydrate), 1749, 1177, 990 cm^{-1}; ^{1}H NMR δ 7.79 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 4.91 (d, J = 8.1 Hz, 1H), 4.81 (ddd, J = 9.3, 8.1, 4.2 Hz, 1H), 4.33 (s, 1H), 4.07 (d, J = 10.2 Hz, 1H), 4.02 (d, J = 10.2 Hz, 1H), 2.44 (s, 3H), 2.07 (dd, J = 14.4, 4.2 Hz, 1H), 1.48 (dd, J = 14.4, 9.3 Hz, 1H), 1.49 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H), 1.31 (s, 3H); ^{13}C NMR δ 202.9, 145.5, 130.2, 130.0, 128.2, 113.3, 110.7, 83.95, 80.13, 77.57, 73.25, 71.91, 36.04, 27.21, 26.73, 26.26, 24.38, 21.81; HRMS for [**6f** + DCI(NH_3)], calcd for $C_{20}H_{30}NO_8S$ (MNH_4^+) 444.1692, found 444.1706.

Preparation of Ketone 6g. To an ice cold solution of **25** (0.776 g, 2 mmol) and 2,6-lutidine (0.35 mL, 3 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise trifluoromethanesulfonic anhydride (0.42 mL, 2.5 mmol) under N_2 over 10 min. After the resulting solution was stirred at 0 °C for 1 h, the solvent was removed under reduced pressure at 0 °C. The residue was dissolved in dry THF (3 mL), and to this solution was added dropwise TBAF (1 M in THF, 4 mL, 4 mmol) under N_2 at 0 °C. After being stirred at 0 °C for 30 min, the reaction mixture was diluted with ether (30 mL), quenched with saturated aqueous NH_4Cl (10 mL), extracted with ether (2 × 30 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a crude compound which was used directly for next step. An analytical sample was purified by flash chromatography (hexane−ether, 10:1 v/v): ^{1}H NMR δ 4.43 (s, 2H), 4.43 (dd, J = 4.5, 4.2 Hz, 1H), 4.34 (ddd, J = 9.6, 7.8, 5.5 Hz, 1H), 4.27 (dd, J = 7.8, 4.2 Hz, 1H), 4.10 (d, J = 4.5 Hz, 1H), 2.08 (dd, J = 13.2, 5.5 Hz, 1H), 1.81 (dd, J = 13.2, 9.6 Hz, 1H), 1.45 (s, 3H), 1.40 (s, 3H), 1.36 (s, 3H), 1.31 (s, 3H), 0.86 (s, 9H), 0.089 (s, 3H), 0.082 (s, 3H); ^{13}C NMR δ 110.6, 108.5, 81.01, 79.79, 76.82, 72.82, 70.55, 68.29, 34.2, 27.68, 26.58, 26.23, 26.05, 24.16, 18.36, −4.37, −4.94.

The above crude compound was dissolved in TBAF (1 M in THF, 10 mL), and the solution was stirred at room temperature for 1 h. The reaction mixture was then diluted with ether (50 mL) and quenched with saturated aqueous NH_4Cl (20 mL). The layers were separated, and the aqueous layer was extracted with ether (3 × 20 mL). The combined extracts were washed with water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 3:1 v/v) to give alcohol **26g** as a colorless oil (0.531 g, 96%): $[\alpha]^{23}_D = +9.0$ (*c* 0.99, $CHCl_3$); IR (NaCl) 3490 cm^{-1}; ^{1}H NMR δ 4.39 (dd, J = 47.5 (F), 9.6 Hz, 1H), 4.38 (dd, J = 47.5 (F), 9.6 Hz, 1H), 4.49−4.33 (m, 4H), 2.66 (s, 1H, OH), 2.05 (dd, J = 13.8, 5.4 Hz, 1H), 1.84 (dd, J = 13.8, 8.5 Hz, 1H), 1.50 (s, 3H), 1.44 (s, 3H), 1.41(s, 3H), 1.38 (s, 3H); ^{13}C NMR δ 109.9, 108.7, 87.13 (d, J = 178.9 Hz (F)), 81.87 (d, J = 16.6 Hz (F)), 75.15 (d, J = 5.3 Hz (F)), 72.87, 70.95 (d, J = 2.3 Hz (F)), 67.24, 33.13 (d, J = 4.5 Hz (F)), 27.99, 26.81, 26.35 (d, J = 3.8 Hz (F)), 24.43.

Swern oxidation of alcohol **26g** (0.525 g, 1.9 mmol) and purification by flash chromatography (hexane−ether 4:1 to 1:1 v/v) gave ketone **6g** as a colorless oil (0.52 g, 99%): $[\alpha]^{23}_D = +29.1$ (*c* 1.7, $CHCl_3$); IR (NaCl) 3464 (hydrate), 1750 cm^{-1}; ^{1}H NMR δ 5.04 (dd, J = 8.1, 0.9 Hz, 1H), 4.93 (ddd, J = 10.2, 8.1, 4.2 Hz, 1H), 4.45 (s, 1H), 4.39 (dd, J = 47.4 (F), 10.0 Hz, 1H), 4.38 (dd, J = 47.4 (F), 10.0 Hz, 1H), 2.12 (dd, J = 14.4, 4.2 Hz, 1H), 1.42 (ddd, J = 14.4, 10.2, 0.9 Hz, 1H), 1.57 (s, 3H), 1.52 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H); ^{13}C NMR δ 203.4, 113.1, 110.5, 84.95 (d, J = 180.4 Hz (F)), 84.81 (d, J = 18.9 Hz (F), 79.75 (d, J = 3.8 Hz (F)), 77.77, 73.27 (d, J = 1.5 Hz (F)), 35.3 (d, J = 3.8 Hz (F)), 27.13, 26.97, 26.09 (d, J = 3.0 Hz (F)), 24.55. Anal. Calcd for $C_{13}H_{19}O_5F$: C, 56.93; H, 6.98; F, 6.93. Found: C, 56.77; H, 6.91; F, 7.17.

Preparation of Ketone 6h. To an ice cold solution of ester **19** (2.11 g, 5 mmol) in dry THF (10 mL) was added dropwise CH_3MgBr (3 M in ether, 5 mL, 15 mmol) under N_2. After being stirred at 0 °C for 1 h, and then at room temperature for 4 h, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL) at 0 °C, extracted with ether (3 × 30 mL), washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 10:1 v/v) to give alcohol **27h** as white crystals (2.08 g, 100%): mp 79−80 °C; $[\alpha]^{23}_D = -13.6$ (*c* 0.59, $CHCl_3$); IR (NaCl) 3498 cm^{-1}; ^1H NMR δ 4.51 (dd, J = 4.8, 4.2 Hz, 1H), 4.46 (d, J = 4.2 Hz, 1H), 4.42 (ddd, J = 10.5, 7.8, 5.7 Hz, 1H), 4.34 (dd, J = 7.8, 4.8 Hz, 1H), 2.60 (s, 1H, OH), 2.05 (dd, J = 13.4, 5.7 Hz, 1H), 1.89 (dd, J = 13.4, 10.5 Hz, 1H), 1.47 (s, 3H), 1.41 (s, 6H), 1.33 (s, 3H), 1.29 (s, 3H), 1.21 (s, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 109.3, 108.0, 88.44, 77.18, 72.75, 72.17, 71.66, 68.41, 33.58, 28.14, 27.67, 26.84, 26.70, 26.44, 26.15, 24.43, 18.74, −4.21, −4.58. Anal. Calcd for $C_{21}H_{40}O_6Si$: C, 60.54; H, 9.68. Found: C, 60.44; H, 9.41.

Alcohol **27h** (2.08 g, 5 mmol) was dissolved in TBAF (1 M in THF, 10 mL), and the solution was stirred at room temperature for 15 min. The reaction solution was then diluted with ether (50 mL), washed with a saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 5:1 to 1:1 v/v) to give alcohol **28h** as white crystals (1.5 g, 99%): mp 103−105 °C; $[\alpha]^{23}_D = +15.0$ (*c* 0.54, $CHCl_3$); IR (NaCl) 3478 cm^{-1}; ^1H NMR δ 4.65 (dd, J = 3.9, 0.9 Hz, 1H), 4.54−4.40 (m, 3H), 2.88 (s, 1H, OH), 2.64 (s, 1H, OH), 2.09 (dd, J = 13.5, 6.0 Hz, 1H), 1.87 (ddd, J = 13.5, 10.2, 1.2 Hz, 1H), 1.52 (s, 3H), 1.44 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 1.23 (s, 3H); ^{13}C NMR δ 109.2, 108.6, 87.95, 75.32, 72.83, 72.11, 71.79, 66.22, 34.23, 28.24, 27.4, 27.08, 26.73, 25.58, 24.78.

Swern oxidation of alcohol **28h** (1.5 g, 4.98 mmol) and purification by flash chromatography (hexane−ether 4:1 to 2:1 v/v) gave ketone **6h** as a colorless syrup (1.41 g, 97%): $[\alpha]^{23}_D = +54.8$ (*c* 1.22, $CHCl_3$); IR (NaCl) 3534, 1749 cm^{-1}; ^1H NMR δ 5.07 (dd, J = 8.1, 1.2 Hz, 1H), 4.98 (ddd, J = 11.1, 8.1, 5.1 Hz, 1H), 4.55 (s, 1H), 2.12 (dd, J = 14.1, 5.1 Hz, 1H), 1.97 (br s, 1H), 1.60 (s, 3H), 1.50 (s, 3H), 1.43 (s, 3H), 1.38 (s, 3H), 1.33 (dd, J = 14.1, 11.1 Hz, 1H), 1.25 (s, 3H), 1.11 (s, 3H); ^{13}C NMR δ 204.4, 112.1, 110.1, 91.28, 79.83, 78.04, 73.5, 72.27, 36.95, 27.4, 27.27, 26.68, 26.4, 24.74, 23.94. Anal. Calcd for $C_{15}H_{24}O_6$: C, 60.00; H, 8.05. Found: C, 59.89; H, 7.82.

Preparation of Ketone 6i. To a solution of ester **19** (0.64 g, 1.5 mmol) in dry THF (2.5 mL) was added dropwise PhMgBr (3 M in ether, 2 mL, 6 mmol) at 0 °C under N_2. The resulting mixture was stirred at room temperature for 3 h and then refluxed for 12 h. Upon cooling to 0 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 20 mL), washed with brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether, 8:1 v/v) to give alcohol **27i** as a white solid (0.9 g) (^1H NMR analysis showed it contained about 10% Ph-Ph): IR (NaCl) 3375, 1598, 1491 cm^{-1}; ^1H NMR δ 7.8 (dd, J = 8.4, 1.5 Hz, 2H), 7.53 (dd, J = 8.4, 1.5 Hz, 2H), 7.22−7.0 (m, 6H), 4.52 (dd, J = 5.4, 4.2 Hz, 1H), 4.42 (d, J = 4.2 Hz, 1H), 4.31 (ddd, J = 11.1, 7.5, 5.4 Hz, 1H), 4.20 (dd, J = 7.5, 5.4 Hz, 1H), 2.20 (dd, J = 14.4, 5.4 Hz, 1H), 1.56 (dd, J = 14.4, 11.1 Hz, 1H), 1.31 (s, 3H), 1.26 (s, 3H), 1.19 (s, 3H), 0.96 (s, 9H), 0.20 (s, 3H), 0.133 (s, 3H), 0.125 (s, 3H); ^{13}C NMR δ 145.9, 143.7, 130.2, 128.0, 127.6, 127.4, 126.9, 126.6, 110.7, 108.2, 87.92, 79.57, 77.38, 72.03, 71.72, 68.17, 36.28, 28.08, 26.94, 26.30, 26.24, 24.50, 18.78, −4.1, −4.63.

A solution of compound **27i** (0.72 g, 1.33 mmol) in TBAF (1 M in THF, 5 mL) was stirred at room temperature for 30 min and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with ether (3 × 30 mL), washed with water and brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether 5:1 to 2:1 v/v) to give alcohol **28i** as white crystals (0.51 g, 99% from **19**): mp 161−163 °C; $[\alpha]^{23}_D = -85.3$ (*c* 1.35, $CHCl_3$); IR (NaCl) 3374, 1598, 1491 cm^{-1}; ^1H NMR δ 7.91 (d, J = 7.2 Hz, 2H), 7.62 (d, J = 7.2 Hz, 2H), 7.35−7.10 (m, 6H), 5.10 (br s, 1H, OH), 4.67 (d, J = 4.2 Hz, 1H), 4.57 (dd, J = 5.1, 4.2 Hz, 1H), 4.50 (ddd, J = 10.8, 7.2, 6.0 Hz, 1H), 4.39 (dd, J = 7.2, 5.1 Hz, 1H), 3.6 (br s, 1H, OH), 2.38 (dd, J = 14.5, 6.0 Hz, 1H), 1.71 (dd, J = 14.5, 10.8 Hz, 1H), 1.45 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 0.28 (s, 3H); ^{13}C NMR δ 145.6, 143.5, 130.2, 128.0, 127.7, 127.4, 126.9, 126.8, 110.6, 108.9, 87.42, 79.82, 75.68, 71.89, 71.63, 65.65, 36.68, 28.2, 27.18, 26.04, 25.02. Anal. Calcd for $C_{25}H_{30}O_6$: C, 70.40; H, 7.09. Found: C, 70.52; H, 7.20.

Swern oxidation of alcohol **28i** (0.505 g, 1.18 mmol) and purification by flash chromatography (hexane−ether, 10:1 to 5:1 v/v) gave ketone **6i** as a white solid (0.49 g, 97%), which was recrystallized from hexane to give white crystals (0.45 g, 90%): mp 171.5−173 °C; $[\alpha]^{23}_D = -145.1$ (*c* 1.02, $CHCl_3$); IR (NaCl) 3406, 1750, 1599, 1493 cm^{-1}; ^1H NMR δ 7.74 (d, J = 7.2 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H), 7.4−7.13 (m, 6H), 4.83 (d, J = 6.3 Hz, 1H), 4.70 (ddd, J = 6.3, 6.0, 4.8 Hz, 1H), 4.45 (s, 1H), 3.92 (br s, 1H, OH), 2.50 (dd, J = 15.9, 4.8 Hz, 1H), 2.37 (dd, J = 15.9, 6.0 Hz, 1H), 1.58 (s, 3H), 1.51 (s, 3H), 1.35 (s, 3H), 0.57 (s, 3H); ^{13}C NMR δ 202.6, 144.7, 141.4, 129.1, 128.4, 127.5, 127.31, 127.3, 127.2, 113.3, 110.6, 90.81, 81.28, 80.66, 77.34, 74.69, 35.62, 28.18, 27.02, 25.99, 25.65. Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 71.0; H, 6.75.

Preparation of Ketone 6j. To a suspension of NaH (60% in mineral oil) (0.12 g, 2.7 mmol) in THF (1 mL) was added dropwise a solution of alcohol **27h** (0.36 g, 0.865 mmol) and MeI (1 mL, 16.1 mmol) in THF (2 mL) at room temperature under N_2, and the resulting mixture was stirred at 30 °C for 15 h. The reaction mixture was then quenched with solid NH_4Cl. After 30 min stirring, water was added. The mixture was extracted with ether (3 × 20 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue, which was then dissolved in TBAF (1 M in THF, 5 mL, 5 mmol). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 20 mL), washed with water and brine, dried (Na_2SO_4), and purified by flash chromatography (hexane−ether, 10:1 to 5:1 v/v) to give alcohol **28j** as white crystals (0.25 g, 91.5%): mp 48−49 °C; $[\alpha]^{23}_D = +7.1$ (*c* 0.34, $CHCl_3$); IR (NaCl) 3548 cm^{-1}; ^1H NMR δ 4.58 (dd, J = 3.0, 0.9 Hz, 1H), 4.42−4.26 (m, 3H), 3.15 (s, 3H), 2.02 (dd, J = 13.5, 5.7 Hz, 1H), 1.81 (ddd, J = 13.5, 10.5, 0.9 Hz, 1H), 1.44 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 1.29 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H); ^{13}C NMR δ 109.9, 108.1, 88.19, 78.04, 76.11, 72.7, 71.63, 66.67, 49.18, 33.73, 28.45, 27.38, 26.97, 24.48, 20.72, 19.83. Anal. Calcd for $C_{16}H_{28}O_6$: C, 60.74; H, 8.92. Found: C, 60.69; H, 8.83.

Swern oxidation of alcohol **28j** (0.316 g, 1 mmol) and purification by flash chromatography (hexane−ether 10:1 to 5:1 v/v) gave ketone **6j** as white crystals (0.3 g, 95%): mp 41−43 °C; $[\alpha]^{23}_D = +54.8$ (*c* 2.2, $CHCl_3$); IR (NaCl) 1752 cm^{-1}; ^1H NMR δ 5.05 (dd, J = 8.1, 1.5 Hz, 1H), 4.98 (ddd, J = 11.1, 8.1, 4.6 Hz, 1H), 4.50 (s, 1H), 3.20 (s, 3H), 2.15 (dd, J = 13.8, 4.6 Hz, 1H), 1.57 (s, 3H), 1.50 (s, 3H), 1.49 (dd, J = 13.8, 11.1 Hz, 1H), 1.39 (s, 3H), 1.37 (s, 3H), 1.19 (s, 3H), 1.10 (s, 3H); ^{13}C NMR δ 204.6, 112.5, 109.8, 91.24, 80.18, 77.94, 77.17, 73.55, 49.66, 36.55, 27.59, 27.28, 26.66, 24.77, 20.6, 20.1. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34. Found: C, 60.92; H, 8.13.

Preparation of Ketone 6k. To a solution of diol **18** (1.2 g, 3.2 mmol) and 3-methoxy-2-pentene[34] (1 mL, 7.5 mmol) in dry

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CH_2Cl_2 (5 mL) was added camphorsulfonic acid (cat.). After being stirred at room temperature for 2 h, the reaction mixture was quenched with 0.1 mL of Et_3N, and the solvents were evaporated under reduced pressure. The residue was purified by flash chromatography (hexane−ether, 10:1 to 8:1 v/v) to give compound **29** as white crystals (1.1 g, 78%): mp 50−52 °C; $[\alpha]^{23}_D = -10.5$ (*c* 1.5, $CHCl_3$); IR (NaCl) 1741 cm^{-1}; ^1H NMR δ 4.78 (d, $J = 4.5$ Hz, 1H), 4.43 (ddd, $J = 7.8$, 7.8, 6.6 Hz, 1H), 4.30 (dd, $J = 7.8$, 3.9 Hz, 1H), 4.23 (dd, $J = 4.5$, 3.9 Hz, 1H), 3.77 (s, 3H), 2.38 (dd, $J = 11.7$, 7.8 Hz, 1H), 2.32 (dd, $J = 11.7$, 6.6 Hz, 1H), 1.69 (qd, $J = 7.5$, 1.8 Hz, 2H), 1.51 (q, $J = 7.5$ Hz, 2H), 1.46 (s, 3H), 1.32 (s, 3H), 0.92 (t, $J = 7.5$ Hz, 3H), 0.91 (s, 9H), 0.84 (t, $J = 7.5$ Hz, 3H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR δ 173.6, 113.9, 108.2, 82.03, 77.6, 73.01, 70.37, 69.35, 52.79, 34.04, 28.35, 27.97, 26.06, 25.85, 23.84, 18.33, 8.79, 7.68, −4.5, −4.80.

A solution of **29** (0.27 g, 0.61 mmol) in TBAF (1 M in THF, 3 mL, 3 mmol) was stirred at room temperature for 30 min and then quenched with ether and saturated aqueous NH_4Cl. The aqueous layer was extracted twice with ether. The combined extracts were washed with brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether 2:1 to 1:1 v/v) to give alcohol **30** as a colorless syrup (0.2 g, 99%): $[\alpha]^{23}_D = -9.6$ (*c* 2.0, $CHCl_3$); IR (NaCl) 3470, 1742 cm^{-1}; ^1H NMR δ 4.95 (d, $J = 5.7$ Hz, 1H), 4.48 (ddd, $J = 7.8$, 7.2, 4.8 Hz, 1H), 4.41 (dd, $J = 7.8$, 3.6 Hz, 1H), 4.09 (dt, $J = 5.7$, 3.6 Hz, 1H), 3.80 (s, 3H), 2.53 (dd, $J = 3.6$, 1.2 Hz, 1H, OH), 2.47 (dd, $J = 14.1$, 7.2 Hz, 1H), 2.19 (dd, $J = 14.1$, 4.8 Hz, 1H), 1.70 (q, $J = 7.5$ Hz, 2H), 1.53 (q, $J = 7.5$ Hz, 2H), 1.46 (s, 3H), 1.34 (s, 3H), 0.91 (t, $J = 7.5$ Hz, 3H), 0.85 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 173.4, 114.1, 108.7, 81.58, 76.51, 73.1, 70.65, 69.17, 52.95, 33.81, 28.67, 28.48, 25.59, 23.70, 8.75, 7.57.

Swern oxidation of alcohol **30** (0.164 g, 0.5 mmol) and purification by flash chromatography (hexane−ether, 5:1 to 1:1 v/v) gave ketone **6k** as a colorless syrup (0.155 g, 95%): $[\alpha]^{23}_D = -6.3$ (*c* 2.1, $CHCl_3$); IR (NaCl) 3486, 3381 (hydrate), 1746 cm^{-1}; ^1H NMR δ 5.09 (s, 1H), 4.9−4.8 (m, 2H), 3.82(s, 3H), 2.19 (d, $J = 7.5$ Hz, 2H), 1.79 (q, $J = 7.5$ Hz, 2H), 1.57 (q, $J = 7.5$ Hz, 2H), 1.5 (s, 3H), 1.35 (s, 3H), 0.98 (t, $J = 7.5$ Hz, 3H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 202.8, 171.5, 117.5, 111.1, 84.93, 79.40, 77.22, 73.60, 53.30, 35.99, 28.74, 28.23, 25.79, 24.06, 8.53, 7.95. Anal. Calcd for $C_{16}H_{24}O_7$: C, 58.53; H, 7.37. Found: C, 58.55; H, 7.20.

Preparation of Ketone 6l. To a solution of ester **29** (0.22 g, 0.5 mmol) in dry THF (2 mL) was added dropwsie DIBAL-H (1 M in hexane, 1.1 mL, 1.1 mmol) at −20 °C under N_2. Upon stirring at 0 °C for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, filtered, and washed with ether. The filtrate was evaporated to give a white solid (0.19 g). The crude product was dissolved in dry CH_2Cl_2 (2 mL), and to this solution were added Ac_2O (0.1 mL, 1.06 mmol), Et_3N (0.15 mL, 1.08 mmol), and DMAP (cat.). After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue, which was then dissolved in TBAF (1 M in THF, 3 mL). After being stirred at room temperature for 30 min, the reaction mixture was diluted with ether, washed with brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether 3:1 to 1:1, v/v) to give an alcohol as a colorless syrup (0.16 g, 93%): $[\alpha]^{23}_D = +16.9$ (*c* 2.0, $CHCl_3$); IR (NaCl) 3496, 1747 cm^{-1}; ^1H NMR δ 4.48 (ddd, $J = 9.0$, 7.5, 5.7 Hz, 1H), 4.40 (dd, $J = 7.5$, 4.5 Hz, 1H), 4.34 (t, $J = 4.5$ Hz, 1H), 4.26 (d, $J = 4.5$ Hz, 1H), 4.22 (d, $J = 11.5$ Hz, 1H), 4.13 (d, $J = 11.5$ Hz, 1H), 2.56 (br s, 1H, OH), 2.18 (dd, $J = 14.1$, 5.7 Hz, 1H), 2.10 (s, 3H), 1.94 (dd, $J = 14.1$, 9.0 Hz, 1H), 1.68 (q, $J = 7.5$ Hz, 2H), 1.65 (q, $J = 7.5$ Hz, 2H), 1.51 (s, 3H), 1.38 (s, 3H), 0.92 (t, $J = 7.5$ Hz, 3H), 0.88 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 170.9, 113.6, 108.5, 80.86, 76.45, 72.81, 70.94, 70.01, 67.47, 34.34, 29.62, 28.77, 26.57, 24.16, 21.05, 8.83, 8.35.

Swern oxidation of the above alcohol (0.12 g, 0.35 mmol) and purification by flash chromatography (hexane−ether 5:1 to 2:1) gave ketone **6l** as a colorless syrup (0.105 g, 88%): $[\alpha]^{23}_D = +24.4$ (*c* 1.0, $CHCl_3$); IR (NaCl) 3473 (hydrate), 1749 cm^{-1}; ^1H NMR δ 5.03 (dd, $J = 8.4$, 0.9 Hz, 1H), 4.95 (ddd, $J = 9.9$, 8.4, 4.3 Hz, 1H), 4.33 (s, 1H), 4.26 (d, $J = 11.4$ Hz, 1H), 4.06 (d, $J = 11.4$ Hz, 1H), 2.20 (dd, $J = 14.1$, 4.3 Hz, 1H), 2.09 (s, 3H), 1.80 (q, $J = 7.5$ Hz, 2H), 1.66 (qd, $J = 7.5$, 1.8 Hz, 2H), 1.53 (s, 3H), 1.51 (dd, $J = 14.1$, 9.9 Hz, 1H), 1.38 (s, 3H), 1.0 (t, $J = 7.5$ Hz, 3H), 0.89 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 203.5, 170.6, 117.2, 110.3, 84.0, 80.90, 77.55, 73.3, 67.82, 36.83, 29.19, 27.94, 26.86, 24.44, 20.89, 8.71, 8.67. Anal. Calcd for $C_{17}H_{26}O_7$: C, 59.64; H, 7.65. Found: C, 59.38; H, 7.40.

Preparation of Ketone 6m. To an ice cold solution of **29** (0.442 g, 1 mmol) in dry THF (1.5 mL) was added dropwise CH_3MgBr (3 M in ether, 1.35 mL, 4.1 mmol) at 0 °C under N_2. After being stirred at 0 °C for 30 min and then at room temperature for 5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 20 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue, which was then dissolved in TBAF (1 M, in THF, 5 mL). After stirring at room temperature for 30 min, the reaction mixture was diluted with ether, washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 3:1 to 1:1 v/v) to give an alcohol as white crystals (0.31 g, 94%): mp 105−107 °C; $[\alpha]^{23}_D = +19.3$ (*c* 0.92, $CHCl_3$); IR (NaCl) 3450 cm^{-1}; ^1H NMR δ 4.61 (d, $J = 4.2$ Hz, 1H), 4.55−4.45 (m, 2H), 4.40 (dd, $J = 7.5$, 5.1 Hz, 1H), 2.94 (s, 1H, OH), 2.74 (s, 1H, OH), 2.10 (dd, $J = 13.8$, 6.3 Hz, 1H), 1.89 (dd, $J = 13.8$, 10.2 Hz, 1H), 1.75−1.50 (m, 4H), 1.51 (s, 3H), 1.40 (s, 3H), 1.30 (s, 3H), 1.22 (s, 3H), 0.91 (t, $J = 7.5$ Hz, 3H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 113.1, 108.5, 87.33, 74.93, 72.88, 72.06, 71.76, 66.12, 34.36, 29.96, 27.92, 26.99, 26.69, 25.61, 24.69, 9.19, 8.99. Anal. Calcd for $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.83; H, 9.10.

Swern oxidation of the above alcohol (0.18 g, 0.545 mmol) and purification by flash chromatography (hexane−ether 5:1 to 2:1) gave ketone **6m** as a colorless syrup (0.175 g, 98%): $[\alpha]^{23}_D = +37.5$ (*c* 1.7, $CHCl_3$); IR (NaCl) 3523, 1749 cm^{-1}; ^1H NMR δ 5.08 (dd, $J = 8.4$, 1.2 Hz, 1H), 5.02 (ddd, $J = 10.2$, 8.4, 4.8 Hz, 1H), 4.52 (s, 1H), 2.15 (ddd, $J = 13.8$, 4.8, 1.8 Hz, 1H), 1.95 (br s, 1H, OH), 1.84 (q, $J = 7.5$ Hz, 2H), 1.76 (dq, $J = 14.1$, 7.5 Hz, 1H), 1.67 (dq, $J = 14.1$, 7.5 Hz, 1H), 1.51 (s, 3H), 1.39 (s, 3H), 1.36 (dd, $J = 13.8$, 10.2 Hz, 1H), 1.27 (s, 3H), 1.11 (s, 3H), 1.0 (t, $J = 7.5$ Hz, 3H), 0.88 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR δ 204.6, 116.4, 110.0, 90.93, 79.53, 77.94, 73.62, 72.43, 37.12, 29.44, 27.41, 27.26, 26.49, 24.73, 23.99, 9.24, 8.89. Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.59. Found: C, 62.27; H, 8.23.

Preparation of Ketone 6n. To a solution of **16** (2.74 g, 12 mmol) in DMF (20 mL) were added imidazole (1.36 g, 20 mmol), *tert*-butyldiphenylsilyl chloride (4.15 g, 15 mmol), and DMAP (cat.) at room temperature. After stirring at room temperature for 5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 50 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue, which was then dissolved in 80% aqueous acetic acid (30 mL). After being stirred at 50 °C for 2 h and cooled to room temperature, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, extracted with ether (3 × 50 mL), washed twice with saturated aqueous $NaHCO_3$ and then water and brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 1:2 v/v) to give diol **31** as a colorless syrup (4.65 g, 91.5%): $[\alpha]^{23}_D = +83.4$ (*c* 1.0, $CHCl_3$); IR (NaCl) 3454, 1722 cm^{-1}; ^1H NMR δ 7.72−7.67 (m, 4H), 7.50−7.37 (m, 6H), 6.51 (m, 1H), 4.40 (m, 1H), 3.87 (m, 1H), 3.71 (s, 3H), 3.68 (m, 1H), 2.60 (dd, $J = 16.2$, 6.0 Hz, 1H), 2.44 (ddt, $J = 16.2$, 7.2, 2.1 Hz, 1H), 1.11 (s, 9H); ^{13}C NMR δ 166.8, 137.1, 136.0, 135.8, 132.8, 132.6, 130.5, 130.4, 129.5, 128.2, 128.1, 70.85, 70.33, 68.85, 52.12, 29.64, 27.12, 19.42. Anal. Calcd for $C_{24}H_{30}O_5Si$: C, 67.58; H, 7.09. Found: C, 67.37; H, 7.09.

A solution of diol **31** (1.704 g, 4 mmol), 3-methoxy-2-pentene (0.5 g, 5 mmol), and camphorsulfonic acid (cat.) in dry CH_2Cl_2

(33) Akhtar, M. N.; Boyd, D. R.; Hamilton, J. G. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2437.

(34) Newman, M. S.; Vander Zwan, M. C. *J. Org. Chem.* **1973**, *38*, 2910.

(10 mL) was stirred at room temperature for 30 min. The reaction mixture was then quenched with several drops of Et_3N. The solvents were evaporated, and the residue was purified by flash chromatography (hexane−ether, 10:1 to 8:1 v/v) to give compound **32** as a colorless oil (1.91 g, 96%): IR (NaCl) 1741 cm^{-1}; ^1H NMR δ 7.80 (dd, J = 7.8, 1.5 Hz, 2H), 7.68 (dd, J = 7.8, 1.5 Hz, 2H), 7.48−7.34 (m, 6H), 7.02 (m, 1H), 4.32 (ddd, J = 7.5, 4.2, 1.8 Hz, 1H), 4.18 (ddd, J = 7.5, 3.9, 1.5 Hz, 1H), 4.09 (dt, J = 3.9, 2.1 Hz, 1H), 3.74 (s, 3H), 2.94 (d, J = 16.2 Hz, 1H), 1.7−1.4 (m, 5H), 1.10 (s, 9H), 0.86 (t, J = 7.5 Hz, 3H), 0.79 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 166.3, 144.2, 136.1, 136.0, 134.2, 133.3, 130.1, 130.0, 128.1, 128.0, 127.8, 112.4, 77.27, 73.01, 71.25, 52.01, 28.82, 28.42, 27.36, 27.03, 19.51, 8.96, 7.79.

Dihydroxylation of **32** (1.7 g, 3.44 mmol) was performed in a manner similar to that of **17**. Diol **33** was obtained as a colorless syrup (1.68 g, 93%) after purification by flash chromatography (hexane−ether, 1:1 v/v): $[\alpha]^{23}_D$ = −20.1 (*c* 1.07, $CHCl_3$); IR (NaCl) 3485, 1739 cm^{-1}; ^1H NMR δ 7.77 (dd, J = 7.9, 1.5 Hz, 2H), 7.70 (dd, J = 7.9, 1.5 Hz, 2H), 7.47−7.33 (m, 3H), 7.29−7.11 (m, 3H), 4.25 (dd, J = 9.3, 4.8 Hz, 1H), 4.11 (td, J = 8.0, 4.3 Hz, 1H), 4.07 (dd, J = 9.3, 3.9 Hz, 1H), 4.02 (dd, J = 4.3, 3.9 Hz, 1H), 3.80 (s, 3H), 3.10 (s, 1H, OH), 2.06 (d, J = 4.8 Hz, 1H, OH), 1.95 (d, J = 8.0 Hz, 2H), 1.85 (dq, J = 14.1, 7.5 Hz, 1H), 1.70 (dq, J = 14.1, 7.5 Hz, 1H), 1.45 (qd, J = 7.5, 2.4 Hz, 2H), 1.11 (s, 9H), 0.98 (t, J = 7.5 Hz, 3H), 0.85 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 174.5, 136.2, 136.0, 133.8, 133.5, 130.2, 130.1, 128.1, 127.8, 113.9, 77.18, 76.64, 72.85, 72.38, 71.95, 53.43, 36.6, 30.91, 27.98, 27.2, 19.66, 9.06, 8.97. Anal. Calcd for $C_{29}H_{40}O_7Si$: C, 65.89; H, 7.63. Found: 65.60; H, 7.40.

A solution of diol **33** (1.6 g, 3.06 mmol), 2-methoxypropene (0.5 mL, 5.2 mmol), and camphorsulfonic acid (cat.) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 2 h and then quenched with several drops Et_3N. Upon removing solvents under reduced pressure, the residue was purified by flash chromatography (hexane−ether, 10:1 v/v) to give compound **34** as a colorless oil (1.65 g, 96%): $[\alpha]^{23}_D$ = −21.1 (*c* 1.56, $CHCl_3$); IR (NaCl) 1741 cm^{-1}; ^1H NMR δ 7.85−7.7 (m, 4H), 7.45−7.3 (m, 6H), 4.58 (d, J = 5.4 Hz, 1H), 4.28 (ddd, J = 7.8, 7.8, 4.8 Hz, 1H), 4.22 (dd, J = 5.4, 4.2 Hz, 1H), 4.15 (dd, J = 7.8, 4.2 Hz, 1H), 3.70 (s, 3H), 2.55 (dd, J = 13.8, 7.8 Hz, 1H), 2.06 (dd, J = 13.8, 4.8 Hz, 1H), 1.72 (q, J = 7.5 Hz, 2H), 1.56 (q, J = 7.5 Hz, 2H), 1.33 (s, 3H), 1.17 (s, 3H), 1.11 (s, 9H), 0.92 (t, J = 7.5 Hz, 3H), 0.86 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 172.9, 136.5, 136.3, 134.0, 133.7, 130.1, 129.7, 127.7, 127.5, 112.8, 110.1, 82.07, 77.28, 73.06, 70.78, 70.69, 52.66, 33.84, 27.92, 27.27, 27.22, 25.63, 25.10, 19.49, 8.90, 8.80.

A solution of **34** (0.5 g, 0.89 mmol) in TBAF (1 M in THF, 3 mL) was stirred at room temperature for 1 h and then diluted with ether and saturated aqueous NH_4Cl. The ether layer was separated, and the aqueous layer was extracted twice with ether. The combined extracts were washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane−ether, 2:1 to 1:1 v/v) to give the alcohol as a colorless syrup (0.12 g, 41%): $[\alpha]^{23}_D$ = −6.0 (*c* 0.5, $CHCl_3$); IR (NaCl) 3530, 1742 cm^{-1}; ^1H NMR δ 4.91 (d, J = 4.0 Hz, 1H), 4.41 (ddd, J = 8.7, 8.1, 6.3 Hz, 1H), 4.33 (t, J = 4.0 Hz, 1H), 4.35−4.25 (m, 1H), 3.81 (s, 3H), 2.68 (br s, 1H, OH), 2.34 (dd, J = 13.8, 6.3 Hz, 1H), 2.27 (dd, J = 13.8, 8.7 Hz, 1H), 1.74 (q, J = 7.5 Hz, 2H), 1.64 (q, J = 7.5 Hz, 2H), 1.44 (s, 3H), 1.29 (s, 3H), 0.93 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 173.6, 112.5, 110.1, 82.12, 76.60, 72.42, 70.19, 67.96, 53.11, 33.82, 28.28, 27.86, 26.89, 24.63, 8.84, 7.91.

Swern oxidation of the above alcohol (0.03 g, 0.09 mmol) and purification by flash chromatography (hexane−ether, 5:1 to 1:1 v/v) gave ketone **6n** as a colorless syrup (0.028 g, 94%): $[\alpha]^{23}_D$ = −1.26 (*c* 0.87, $CHCl_3$); IR (NaCl) 3491 (hydrate), 1754 cm^{-1}; ^1H NMR δ 5.02 (d, J = 8.4 Hz, 1H), 4.88 (ddd, J = 10.0, 8.4, 4.5 Hz, 1H), 4.75 (s, 1H), 3.81 (s, 3H), 2.38 (dd, J = 14.4, 4.5 Hz, 1H), 1.78 (dd, J = 14.4, 10.0 Hz, 1H), 1.73 (q, J = 7.5 Hz, 2H), 1.63 (q, J = 7.5 Hz, 2H), 1.58 (s, 3H), 1.34 (s, 3H), 0.91 (t, J = 7.5 Hz, 3H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 202.3, 171.5, 114.9, 113.7, 85.12, 80.21, 77.28, 73.27, 53.44, 36.19, 28.79, 28.49, 26.47, 24.63, 8.72, 7.70; HRMS for $C_{16}H_{25}O_7$ (M^+ + 1) calcd: 329.1600, found 329.1606.

Preparation of Ketone 6o. To a solution of **34** (0.5 g, 0.89 mmol) in dry THF (2 mL) was added dropwsie DIBAL-H (1M in hexane, 2.0 mL, 2 mmol) at −20 °C under N_2. Upon stirring at 0 °C for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, filtered, and washed with ether. The filtrate was concentrated to give a colorless syrup, which was then dissolved in dry CH_2Cl_2 (2 mL). To this solution were added Ac_2O (0.15 mL, 1.59 mmol), Et_3N (0.2 mL, 1.43 mmol), and DMAP (cat.). After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue. The resulting residue was dissolved in TBAF (1 M in THF, 3 mL). After being stirred at room temperature for 30 min, the reaction mixture was diluted with ether, washed with brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether, 3:1 to 1:1 v/v) to give an alcohol as a colorless syrup (0.22 g, 73%): $[\alpha]^{23}_D$ = +9.5 (*c* 1.0, $CHCl_3$); IR (NaCl) 3464, 1746 cm^{-1}; ^1H NMR δ 4.39 (t, J = 4.5 Hz, 1H), 4.37−4.26 (m, 2H), 4.24 (d, J = 4.5 Hz, 1H), 4.16 (d, J = 11.5 Hz, 1H), 4.06 (d, J = 11.5 Hz, 1H), 2.72 (br s, 1H, OH), 2.11 (dd, J = 13.5, 5.1 Hz, 1H), 2.04 (s, 3H), 1.79 (dd, J = 13.5, 9.6 Hz, 1H), 1.69 (qd, J = 7.5, 2.4 Hz, 2H), 1.60 (q, J = 7.5 Hz, 2H), 1.37 (s, 3H), 1.35 (s, 3H), 0.88 (t, J = 7.5 Hz, 3H), 0.85 (t, J = 7.5 Hz. 3H); ^{13}C NMR δ 170.8, 112.4, 109.4, 81.21, 76.17, 72.51, 70.81, 69.67, 67.05, 34.29, 28.66, 28.45, 27.60, 26.09, 20.97, 8.74, 7.83.

Swern oxidation of the above alcohol (0.18 g, 0.52 mmol) and purification by flash chromatography (hexane−ether, 3:1 to 2:1 v/v) gave ketone **6o** as a colorless syrup (0.171 g, 97%): $[\alpha]^{23}_D$ = +19.3 (*c* 1.0, $CHCl_3$); IR (NaCl) 3472 (hydrate), 1751 cm^{-1}; ^1H NMR δ 5.09 (dd, J = 8.4, 0.9 Hz, 1H), 4.94 (ddd, J = 10.8, 8.4, 4.5 Hz, 1H), 4.32 (s, 1H), 4.26 (d, J = 11.7 Hz, 1H), 4.04 (d, J = 11.7 Hz, 1H), 2.22 (dd, J = 14.0, 4.5 Hz, 1H), 2.10 (s, 3H), 1.75 (qd, J = 7.5, 1.5 Hz, 2H), 1.66 (qd, J = 7.5, 2.4 Hz, 2H), 1.58 (s, 3H), 1.41 (s, 3H), 1.39 (dd, J = 14.0, 10.8 Hz, 1H), 0.92 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 203.4, 170.5, 114.6, 112.9, 84.3, 81.19, 77.82, 73.35, 67.47, 36.71, 29.15, 28.7, 26.98, 26.05, 20.91, 8.78, 7.66. Anal. Calcd for $C_{17}H_{26}O_7$: C, 59.64; H, 7.65. Found: C, 59.55; H, 7.44.

Preparation of Ketone 6p. To an ice cold solution of **34** (0.51 g, 0.9 mmol) in dry THF (1 mL) was added dropwise CH_3MgBr (3 M in ether, 1 mL, 3 mmol) under N_2. After being stirred at 0 °C for 30 min and then at room temperature for 4 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether (3 × 20 mL), washed with brine, dried (Na_2SO_4), filtered, and concentrated to give a residue. The resulting residue was dissolved in TBAF (1 M, in THF, 3 mL). After being stirred at room temperature for 30 min, the reaction mixture was diluted with ether, washed with brine, dried (Na_2SO_4), filtered, and purified by flash chromatography (hexane−ether, 3:1 to 2:1 v/v) to give an alcohol as a colorless syrup (0.28 g, 93%): $[\alpha]^{23}_D$ = +15.2 (*c* 1.1, $CHCl_3$); IR (NaCl) 3454 cm^{-1}; ^1H NMR δ 4.64 (d, J = 4.2 Hz, 1H), 4.51 (dd, J = 4.8, 4.2 Hz, 1H), 4.48 (ddd, J = 10.5, 7.5, 6.0 Hz, 1H), 4.39 (dd, J = 7.5, 4.8 Hz, 1H), 2.95 (br s, 1H, OH), 2.66 (br s, 1H, OH), 2.09 (dd, J = 13.5, 6.0 Hz, 1H), 1.87 (dd, J = 13.5, 10.5 Hz, 1H), 1.76 (qd, J = 7.5, 4.2 Hz, 2H), 1.67 (q, J = 7.5 Hz, 2H), 1.42 (s, 6H), 1.30 (s, 3H), 1.22 (s, 3H), 0.95 (t, J = 7.5 Hz, 3H), 0.92 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 112.4, 109.1, 87.94, 75.30, 72.8, 72.07, 71.69, 66.54, 34.01, 28.94, 28.85, 28.26, 27.4, 26.78, 25.66, 8.87, 7.97.

Swern oxidation of the above alcohol (0.25 g, 0.758 mmol) and purification by flash chromatography (hexane−ether 5:1 to 2:1, v/v) gave ketone **6p** as a colorless syrup (0.24 g, 97%): $[\alpha]^{23}_D$ = +38.5 (*c* 1.7, $CHCl_3$); IR (NaCl) 3530, 1750 cm^{-1}; ^1H NMR δ 5.09 (dd, J = 8.1, 1.2 Hz, 1H), 5.01 (ddd, J = 10.6, 8.1, 4.8 Hz, 1H), 4.55 (s, 1H), 2.15 (dd, J = 14.1, 4.8 Hz, 1H), 2.03 (br s, 1H, OH), 1.73 (q, J = 7.5 Hz, 2H), 1.66 (qd, J = 7.5, 2.7 Hz, 2H), 1.61 (s, 3H), 1.43 (s, 3H), 1.36 (dd, J = 14.1, 10.6 Hz, 1H), 1.26 (s, 3H), 1.12 (s, 3H), 0.93 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 204.6, 114.2, 112.0, 91.25, 79.80, 78.05, 73.65, 72.28, 36.69, 29.31, 28.75, 27.42, 26.65, 26.36,

23.90, 8.75, 7.63; HRMS for $C_{17}H_{29}O_6$ ($M^+ + 1$) calcd 329.1964, found 329.1966.

General Procedure for Asymmetric Epoxidation. To a stirred mixture of *trans*-β-methylstyrene (0.047 g, 0.4 mmol), ketone **6h** (0.0062 g, 0.02 mmol), and tetrabutylammonium hydrogen sulfate (5 mg, 0.016 mmol) in DME (5 mL) was added 3 mL of buffer [prepared by mixing 100 mL of 0.1 M aqueous K_2CO_3 with 0.5 mL of acetic acid (pH 9.3)]. The mixture was then cooled to about −15 °C (inside) (outside is about −15 to −20 °C) via a NaCl−ice bath. A solution of Oxone (0.34 g, 0.55 mmol) in aqueous Na_2EDTA (4×10^{-4} M, 1.6 mL) and a solution of K_2CO_3 (0.32 g, 2.31 mmol) in water (1.6 mL) were added dropwise simultaneously via two separate syringe pumps over a period of 4 h. Upon quenching with pentane and water, the reaction mixture was extracted with pentane (3×10 mL), washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (the silica gel was buffered with 1% Et_3N in pentane) (pentane−ether 1:0 to 50:1 then 2:1 v/v) to afford (*R*,*R*)-β-methylstyrene oxide as colorless liquid (0.05 g, 94% yield, 80% ee determined by chiral GC analysis with Chiraldex G-TA column).

For this particular ketone catalyst (**6h**), lactone **35a** was also isolated as a colorless oil (0.0054 g, 86%): $[\alpha]^{23}_D = +7.2$ (*c* 1.42, $CHCl_3$); IR (NaCl) 3510, 1740 cm^{-1}; ^1H NMR δ 6.81 (d, $J = 3.9$ Hz, 1H), 5.05 (d, $J = 1.5$ Hz, 1H), 4.60 (ddd, $J = 10.0, 5.4, 3.9$ Hz, 1H), 2.46 (ddd, $J = 14.4, 5.4, 1.5$ Hz, 1H), 1.92 (br s, 1H, OH), 1.79 (dd, $J = 14.4, 10.0$ Hz, 1H), 1.57 (s, 3H), 1.56 (s, 3H), 1.46 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.24 (s, 3H); ^{13}C NMR δ 166.5, 112.7, 111.6, 99.21, 87.81, 79.70, 77.48, 72.97, 34.52, 31.76, 28.22, 26.60, 24.34, 22.83, 14.30; HRMS for $C_{15}H_{24}O_7$ (M^+) calcd 316.1522, found 316.1516.

General Procedure for Baeyer−Villiger Reactions Using *m*-CPBA. To a stirred solution of ketone (0.1 mmol) in CH_2Cl_2 were added $NaHCO_3$ (0.01 g, 0.11 mmol) and *m*-CPBA (50 mg, 0.2 mmol) at 0 °C. After being stirred at 0 °C for 40 min, the reaction mixture was diluted with hexane (5 mL) and filtered. The filtrate was concentrated, and the residue was dissolved in 0.5 mL of $CDCl_3$. Upon the removal of any solid by filtration, the solution was analyzed by ^1H and ^{13}C NMR.

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Supporting Information Available: X-ray structural data of ketones **6b** and **6i** containing atomic coordinates and bond lengths and angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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