Structural Probing of Ketone Catalysts for Asymmetric Epoxidation

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A series of chiral ketones derived from carbohydrates were investigated as catalysts for the asymmetric epoxidation. Fructose-derived ketones are found to be efficient catalysts. The studies show that the structural requirements for the ketone catalysts are very stringent and different types of olefins may require ketones with different structural arrangements. The current study allows us to further understand the chiral ketone catalyzed asymmetric epoxidation and provides some insight for the development of new catalysts.

Dioxiranes are remarkably versatile oxidizing agents which show encouraging potential for asymmetric synthesis, particularly asymmetric epoxidation. Dioxiranes can be generated *in situ* from Oxone (potassium peroxomonosulfate) and ketones.[1,2] In principle, only a catalytic amount of ketone is required, so with a chiral ketone there exist opportunities for catalytic asymmetric epoxidation.[3,4] Since the pioneering work reported by Curci in 1984,[3a] this area has received intensive interest. However, discovering efficient chiral ketone catalysts has proven to be a challenging problem.

In the search for efficient ketone catalysts for asymmetric epoxidation, both reactivity and selectivity are crucial issues to be considered. Scheme 1 shows a number of possible pathways involved in the catalytic cycle of the ketone mediated epoxidation. Achieving the desired outcome from this deceivingly simple looking reaction requires a delicate balance among all the possible pathways (**a**−**k**).[5] Intuitively speaking, high enantioselectivity is more likely to be achieved when the stereogenic centers are closer to the reacting center (carbonyl group) due to more efficient stereochemical communication between substrate and catalyst.[6] A potential problem associated with this type of ketone is the possible racemization of the chiral centers due to the acidity of the protons at α positions (path **e** in Scheme 1), which puts restrictions on the choice of groups.

Aside from the epimerization problem, the steric and electronic properties of the substituents are also extremely important for the reaction. If R_1 and R_2 are too large, the formation of tetrahedral intermediate **II** and/or dioxirane **IV** will be retarded. As a result, Oxone can decompose nonproductively via pathway **g**. The steric hindrance of R_1 and R_2 could also slow the reaction between dioxirane **IV** and the olefin, which would result in undesired consumption of the dioxirane via pathway **i** and/or **j** (many dioxiranes are short-lived).[7] On the other hand, if R_1 and R_2 are too small, the stereochemical communication between the olefin and the chiral centers

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(1) For general leading references on dioxiranes see: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205. (c) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**, *67*, 811. (d) Clennan, E. L. *Trends Org. Chem.* **1995**, *5*, 231. (e) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg.* **1996**, *105*, 581.

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(3) For leading references on asymmetric epoxidation mediated by chiral ketones see: (a) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun.* **1984**, 155. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett.* **1995**, *36*, 5831. (c) Reference 2h. (d) Brown, D. S.; Marples, B. A.; Smith, P.; Walton, L *Tetrahedron* **1995**, *51*, 3587. (e) Yang, D.; Yip, Y. C.; Tang, M. W.; Wong, M. K.; Zheng, J. H.; Cheung, K. K. *J. Am. Chem. Soc.* **1996**, *118*, 491. (f) Yang, D.; Wang, X.-C.; Wong, M.-K.; Yip, Y.-C.; Tang, M.-W. *J. Am. Chem. Soc.* **1996**, *118*, 11311. (g) Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S. G.; Jin, B. W. *Tetrahedron: Asymmetry* **1997**, *8*, 2921. (h) Adam, W.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1997**, *8*, 3995. (i) Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem.* **1997**, *62*, 8288. (j) Bergbreiter, D. E. *Chemtracts: Organ. Chem.* **1997**, *10*, 661. (k) Armstrong, A.; Hayter, B. R. *Chem. Commun.* **1998**, 621. (l) Dakin, L. A.; Panek, J. S. *Chemtracts: Organ. Chem.* **1998**, *11*, 531. (m) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1998**, *120*, 5943.

(4) (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Shi, Y. *J. Org. Chem.* **1997**, *62*, 2328. (c) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224. (d) Frohn, M.; Dalkiewicz, M.; Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 2948. (e) Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 3099. (f) Cao, G.-A.; Wang, Z.-X.; Tu, Y.; Shi. Y. *Tetrahedron Lett.* **1998**, *39*, 4425.

(5) For leading references on the discussion of the pathways see: refs 1, 2a−c,h.

(6) High enantioselectivity has been obtained for the epoxidation of 4,4′-substituted stilbenes using ketones in which the chiral element is actually away from the carbonyl group (see: refs 3e,f,m).

(7) For some leading references on the stability and decomposition of dioxiranes see: (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847. (b) Baumstark, A. L.; Beeson, M.; Vasquez, P. C. *Tetrahedron Lett.* **1989**, *30*, 5567. (c) Camporeale, M.; Fiorani, T.; Troisi, L.; Adam, W.; Curci, R.; Edwards, J. O. *J. Org. Chem.* **1990**, *55*, 93. (d) Adam, W.; Curci, R.; Gonzalez Nunez, M. E.; Mello, R. *J. Am. Chem. Soc.* **1991**, *113*, 7654. (e) Murray, R. W.; Singh, M.; Jeyaraman, R. *J. Am. Chem. Soc.* **1992**, *114*, 1346. (f) Singh, M.; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263. (g) Hull, L. A.; Budhai, L. *Tetrahedron Lett.* **1993**, *34*, 5039. (h) Ferrer, M.; Sanchez-Baeza, F.; Casas, J.; Messeguer, A. *Tetrahedron Lett.* **1994**, *35*, 2981. (i) Bouchard, J.; Maine, C.; Berry, R. M.; Argyropoulos, D. S. *Can. J. Chem.* **1996**, *74*, 232.

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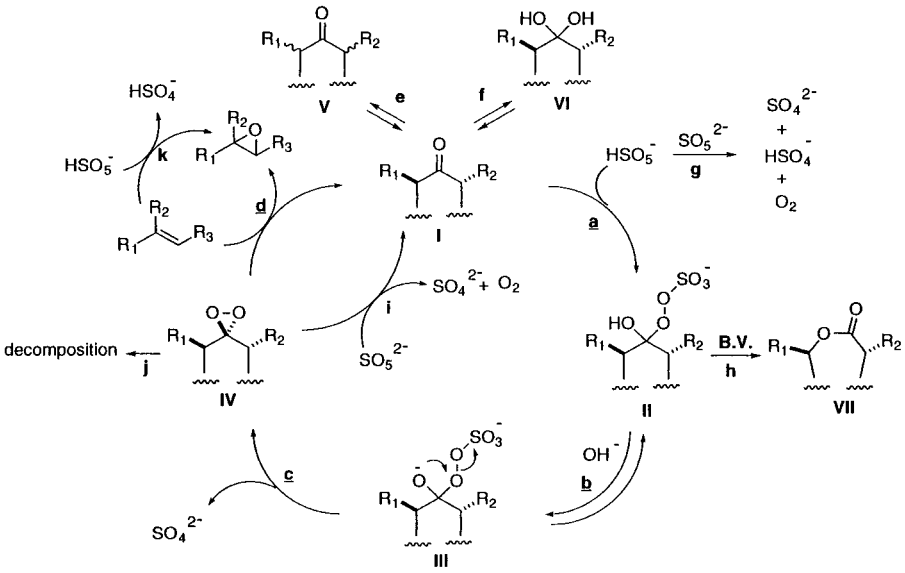
Scheme 1

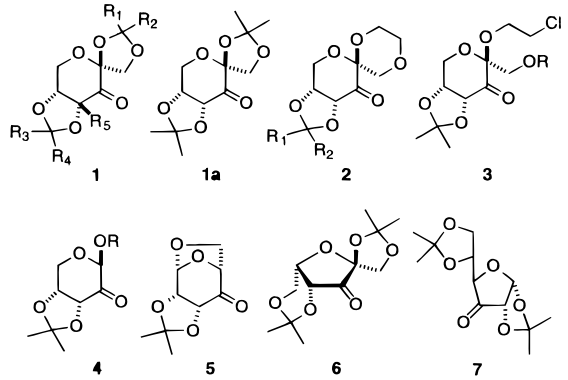


Pathways **a-k**: **(a)** Nucleophilic attack of the ketone by Oxone; **(b)** Deprotonation of the peroxy intermediate; **(c)** Formation of the dioxirane; **(d)** Epoxidation of an olefin by the dioxirane; **(e)** Epimerization of chiral centers of the ketone; **(f)** Hydration of the ketone; **(g)** Oxone self-decomposition; **(h)** Baeyer-Villiger reaction of the peroxy intermediate; **(i)** Consumption of the dioxirane by Oxone; **(j)** Self-decomposition of the dioxirane. **(k)** Epoxidation of the olefin by Oxone itself.

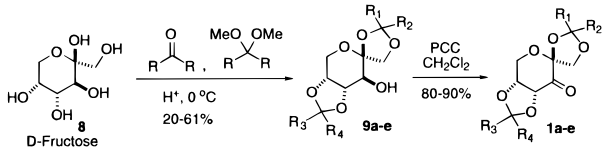
of the dioxirane may not be efficient enough to give high enantioselectivity.

Electronically, R_1 and R_2 are also important. Weak electron withdrawing abilities of R_1 and R_2 will not only result in inefficient formation of tetrahedral intermediate **II** (due to the poor electrophilicity of the carbonyl group), but also favor the detrimental Baeyer−Villiger reaction (pathway **h**). However, if R_1 and R_2 are too electron deficient, ketone **I** will largely exist in a hydrate form **VI**, which could potentially shut down the whole catalytic cycle. If ketone **I** is cyclic, the ring strain will also affect the reaction efficiency. These and the aforementioned factors put high structural stringency on chiral ketone catalysts in order for them to be effective in terms of both reactivity and selectivity.[8]

Recently we have found that a fructose-derived ketone (**1a**) has displayed some remarkably desirable features for asymmetric epoxidation of a variety of olefins.[4] This discovery has stimulated us to further probe the structural requirements for the chiral ketone catalysts by comparing the reactivity and selectivity of ketone **1a** with related ketones that could be readily prepared from carbohydrates. It was hoped that such a study would provide more understanding of the reaction and help in the development of new catalysts. In this paper we report our detailed studies.



Scheme 2



a) $R_1, R_2 = R_3, R_4$ = Me, Me b) $R_1, R_2 = R_3, R_4$ = Et, Et

c) $R_1, R_2 = R_3, R_4 = -(CH_2)_4-$ d) $R_1, R_2 = R_3, R_4 = -(CH_2)_5-$ e) $R_1, R_2 = R_3, R_4 = -(CH_2)_6-$

Results and Discussion

Ketones **1**−**7** were prepared from carbohydrates on the basis of the reported methods. Their syntheses are briefly outlined as follows: Ketones **1a**−**e** were prepared from D-fructose by direct ketalization and subsequent oxidation (Scheme 2).[4c,9] Ketones **1f**−**k** were prepared by selective deketalization of alcohol **9a** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[10] reketalization of the formed triol **10** with different ketones, and subsequent oxidation with pyridinium chlorochormate (PCC) (Scheme 3). Ketones **1l**,**m** were prepared by direction transketalization of ketones **1b**,**c** (Scheme 4). This direct ketalization was unsuccessful for the preparation of ketone **1n**, which was then prepared in a different way (Scheme 4). Selective deprotection of alcohol **9d** and reprotection of the resultant triol **12** gave alcohol **13**, which was subsequently oxidized to give ketone **1n**.

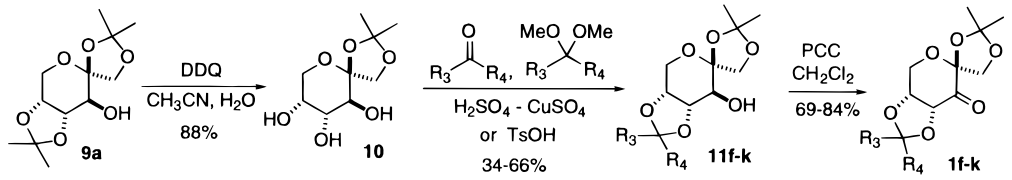
Ketones **2a**−**g** were also prepared from D-fructose (Scheme 5). Treating fructose with chloroethanol containing HCl gave tetraol **14**, which was refluxed in KOH−EtOH solution to give cyclized triol **15**.[11] Ketalization and subsequent oxidation of triol **15** gave ketones **2a**−**g**. Selective protection of the primary alcohol **14** with *tert*-butyldimethylsilyl chloride (TBSCl) led to triol **17**,

(8) For an extensive study and discussion on the ketone catalyst structures and reactivities see: ref 2h.

(9) Mio, S.; Kumagawa, Y.; Sugai, S. *Tetrahedron* **1991**, *47*, 2133.

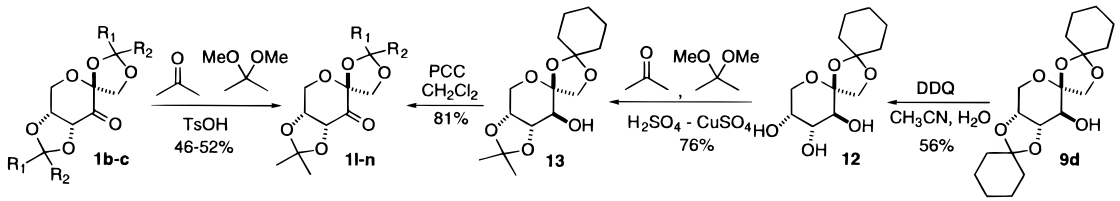
(10) Fernandez, J. M. G.; Mellet, C. O.; Marin, A. M.; Fuentes, J. *Carbohydr. Res.* **1995**, *274*, 263.

Scheme 3



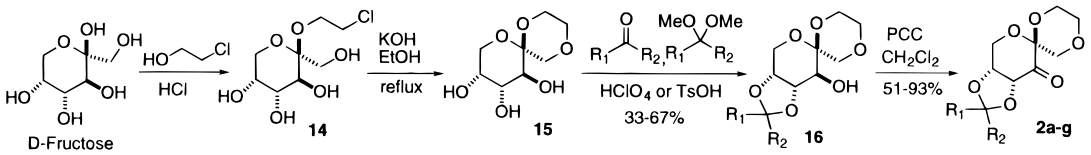
f) R_3, R_4 = Et, Et g) R_3, R_4 = Bn, Bn h) R_3, R_4 = -$(CH_2)_4$- i) R_3, R_4 = -$(CH_2)_5$- j) R_3, R_4 = Et, H k) R_3, R_4 = iPr, H

Scheme 4



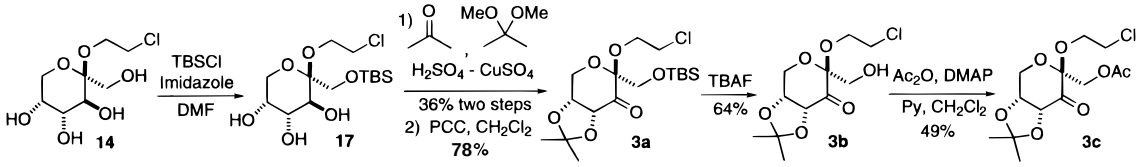
l) R_1, R_2 = Et, Et m) R_1, R_2 = -$(CH_2)_4$- n) R_1, R_2 = -$(CH_2)_5$-

Scheme 5

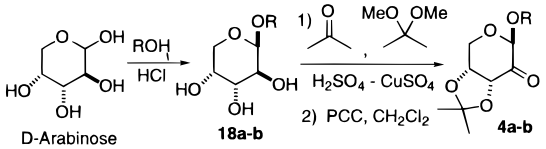


a) R_1, R_2 = Me, Me b) R_1, R_2 = Et, Et c) R_1, R_2 = Pr, Pr d) R_1, R_2 = Bn, Bn e) R_1, R_2 = Ph, Ph f) R_1, R_2 = -$(CH_2)_4$- g) R_1, R_2 = -$(CH_2)_5$-

Scheme 6

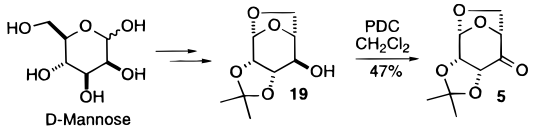


Scheme 7

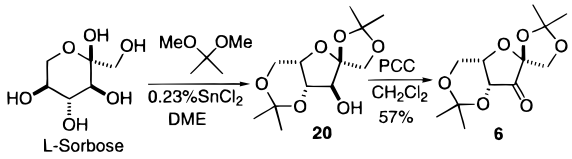


a) R = Me b) R = CH_2CH_2Cl

Scheme 8



Scheme 9



which was converted to ketones **3a**−**c** by a series of transformations as shown in Scheme 6.

Ketones **4a**,**b** were readily prepared from arabinose by glycosylations with methanol or chloroethanol, ketalizations, and subsequent oxidations (Scheme 7).[12] Ketone **5** was obtained by the oxidation of alcohol **19**, which was prepared from D-mannose in three steps using established procedures (Scheme 8).[13] Ketone **6** was prepared from L-sorbose, as shown in Scheme 9.[4c,14] Ketone **7** was prepared by the oxidation of commercially available diacetone-D-glucose according to the reported procedures.[15]

With these ketones in hand, we investigated their properties as epoxidation mediators. We tested five olefins representing *trans*-disubstituted, trisubstituted, *cis*, and terminal olefins (Table 1). All the epoxidations were carried out in CH_3CN at pH ∼ 10.5. The conversion of the olefin substrates and the enantiomeric excesses of the formed epoxides using these ketones are summarized

(11) (a) Chan, J. Y. C.; Cheong, P. P. L.; Hough, L.; Richardson, A. C. *J. Chem. Soc., Perkin Trans 1* **1985**, 1447. (b) Aamlid K. H.; Hough, L.; Richardson, A. C.; Hendry, D. *Carbohydr. Res.* **1987**, *164*, 373. (c) Hough, L.; McCarthy, K. C.; Richardson, A. C. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 450.

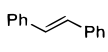
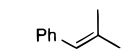
(12) Bennett, M.; Gill, G. B.; Pattenden, G.; Shuker, A. J.; Stapleton, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 929.

(13) (a) Zottola, M. A.; Alonso, R.; Vite, G. D.; Fraser-Reid, B. *J. Org. Chem*. **1989**, *54*, 6123. (b) Horton, D.; Jewell, J. S. *Carbohydr. Res*. **1966**, *2*, 251. (c) Horton, D.; Jewell, J. S. *Carbohydr. Res*. **1967**, *5*, 149.

(14) Chen, C.-C.; Whistler, R. L. *Carbohydr. Res*. **1988**, *175*, 265.

(15) (a) Anderson, F.; Samuelson, B. *Carbohydr. Res*. **1984**, *129*, C4. (b) Mazur, A.; Tropp, B. E.; Engel, R. *Tetrahedron* **1984**, *40*, 3949.

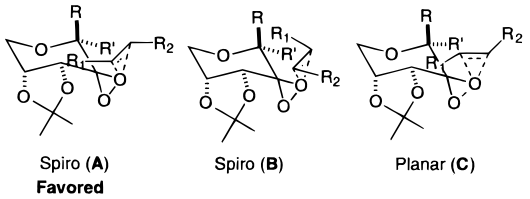
Table 1. Epoxidation of Olefins Catalyzed by Ketones 1−7[a]

entry	ketone	R_1, R_2	R_3, R_4	R_5	 conv.(ee)[b] (%)	 conv.(ee)[c] (%)	 conv.(ee)[d] (%)	 conv.(ee)[d] (%)	 conv.(ee)[c] (%)
1	**1a**	Me, Me	Me, Me	H	75 (97)	93 (92)	100 (72)	100 (15)	53 (51)
2	**1b**	Et, Et	Et, Et	H	16 (96)	32 (86)	40 (57)	26 (12)	17 (47)
3	**1c**	$-(CH_2)_4-$	$-(CH_2)_4-$	H	57 (99)	89 (94)	100 (68)	100 (30)	73 (47)
4	**1d**	$-(CH_2)_5-$	$-(CH_2)_5-$	H	41 (98)	51 (87)	80 (58)	59 (14)	43 (44)
5	**1e**	$-(CH_2)_6-$	$-(CH_2)_6-$	H	30 (98)	37 (91)	37 (66)	43 (17)	6 (51)
6	**1f**	Me, Me	Et, Et	H	38 (94)	91 (93)	98 (57)	92 (16)	19 (43)
7	**1g**	Me, Me	Bn, Bn	H	7 (93)	18 (66)	15 (29)	6 (3)(S)	0
8	**1h**	Me, Me	$-(CH_2)_4-$	H	52 (98)	95 (93)	100 (69)	100 (18)	56 (48)
9	**1i**	Me, Me	$-(CH_2)_5-$	H	59 (92)	100 (89)	100 (63)	77 (17)	46 (46)
10	**1j**	Me, Me	Et, H	H	38 (96)	79 (91)	100 (65)	79 (10)	55 (42)
11	**1k**	Me, Me	iPr, H	H	39 (95)	64 (89)	83 (61)	60 (7)	55 (53)
12	**1l**	Et, Et	Me, Me	H	36 (98)	81 (90)	77 (71)	77 (12)	24 (55)
13	**1m**	$-(CH_2)_4-$	Me, Me	H	66 (98)	100 (93)	100 (72)	92 (27)	57 (49)
14	**1n**	$-(CH_2)_5-$	Me, Me	H	59 (98)	100 (91)	100 (72)	93 (16)	50 (52)
15	**1o**	Me, Me	Me, Me	F	3 (11)	11 (5)	23 (12)	8 (32)	23 (12)
16	**2a**	Me, Me			34 (90)	44 (61)	65 (84)	38 (38)	30 (60)
17	**2b**	Et, Et			25 (85)	33 (61)	63 (76)	42 (42)	24 (49)
18	**2c**	Pr, Pr				28 (82)	43 (73)	29 (43)	13 (46)
19	**2d**	Bn, Bn			10 (82)	19 (56)	17 (29)	6 (21)	8 (39)
20	**2e**	Ph, Ph			10 (67)	26 (48)	36 (21)	30 (20)	8 (4)
21	**2f**	$-(CH_2)_4-$			34 (91)	36 (61)	81 (76)	39 (37)	29 (57)
22	**2g**	$-(CH_2)_5-$			35 (78)	52 (52)	80 (74)	42 (36)	31 (52)
23	**3a**	R = TBS			0	10 (40)	8 (17)	0	
24	**3b**	R = H			2 (nd)	8 (65)	6 (68)	0	
25	**3c**	R = Ac			6 (96)	5 (66)	11 (67)	5 (23)	8 (44)
26	**4a**	R = Me			10 (88)	15 (59)	17 (30)	14 (27)	13 (42)
27	**4b**	R = $(CH_2)_2Cl$			10 (90)	16 (67)	18 (29)	15 (29)	9 (41)
28	**5**				27 (74)	5 (41)	5 (35)	40 (10)	0
29	**6**				14 (75)[e]	41 (62)[e]	57 (20)(S)[e]	41 (15)[e]	46 (71)(S)[f]
30	**7**					4 (23)(S)[e]			

[a] All reactions were carried out with substrate (1 equiv), ketone (0.3 equiv), oxone (1.38 equiv), and K_2CO_3 (5.8 equiv) in CH_3CN−0.05 M $Na_2B_4O_7 \cdot 10H_2O$ of aqueous EDTA (4×10^{-4} M) solution (1.5:1, v/v) unless otherwise noted. The reactions were stopped after 1.5 h. [b] Enantioselectivity was determined by chiral HPLC (Chiralcel OD). The epoxide has the (*R*,*R*) configuration. [c] Enantioselectivity was determined by chiral GC (Chiraldex G-TA column). The epoxide has the (R,R) configuration unless otherwise noted. [d] Enantioselectivity was determined by chiral GC (Chiraldex G-TA column). The epoxide has the (R) configuration unless otherwise noted. [e] 1.0 equiv of ketone was used. [f] 1.5 equiv of ketone was used.

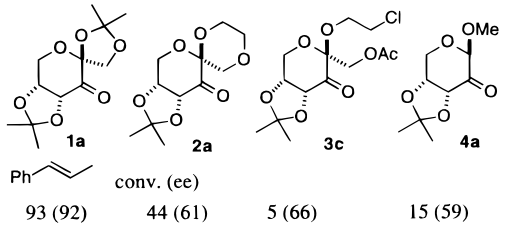
in Table 1. These five olefins show somewhat different responses toward the change of the catalyst structures.

The ketone structure has a profound impact on both the conversion and enantioselectivity of the epoxidation. Some selected results of the epoxidation of *β*-methylstyrene with ketones **1a**, **2a**, **3c**, and **4a** are shown in Scheme 10. These results demonstrate that the catalytic properties are dependent on the precise nature of the ketone substituents. The rigid spiro five-membered cyclic ketal of **1a** is superior to the six-membered cyclic ketal of **2a** and the acyclic groups of **3c** and **4a** in controlling the enantioselectivity of the epoxidation. The transition states spiro (**B**) and planar (**C**) are likely to be the



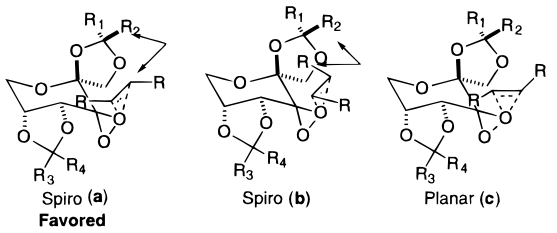
possible competing transition states for the favored spiro (**A**).[4c] The higher enantiomeric excess obtained with ketone **1a** could be due to that fact the five-membered spiro ketal moiety of the ketone strongly disfavors the spiro (**B**) transition state. On the other hand, the corresponding R and R′ structural units in ketones **2a**, **3c**, and **4a** are less efficient in discouraging the sprio (**B**)

Scheme 10



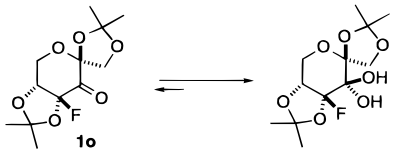
reaction mode. Ketone **1a** is also superior to ketones **2a**, **3c**, and **4a** with regard to the yield of the epoxidation. The experimental observations showed that ketone **1a** was more stable than ketones **2a**, **3c**, and **4a** under the epoxidation conditions. It is not clear how the spiro five-membered cyclic ketal of ketone **1a** enhances the stability of the ketone. A possibility is that the rigid conformational arrangement of the five-membered cyclic ketal slows down the Baeyer−Villiger reaction (a possible decomposition pathway for ketone catalysts).

Among the ketones listed, ketone **1a** is an effective catalyst, particularly for *trans*-disubstituted olefins. To investigate the effect of the ketal moiety, analogues **1a**−**o** were prepared. The results in Table 1 indicate that the smaller R_2 is, the higher the reactivity and selectivity. These results are consistent with the notion that the main competing transition state for ketone **1** is planar (**c**) rather than spiro (**b**).[4c] The major transition state spiro (**a**) is disfavored when the size of R_2 increases due



to the steric interaction between the R_2 group and the olefin, leading to lower conversion and enantiomeric excess. The size of R_3 and R_4 also affects the yield and ee of the epoxidation. The exact reason for this trend is not entirely clear; R_3 and R_4 could affect the catalytic properties of the ketones by altering the catalyst conformation. Among ketones **1a**−**n**, ketone **1a** is probably the most effective and general catalyst considering the yield and enantiomeric excess of the formed epoxides as well as the preparation of the catalyst, although slightly higher ee's are obtained with ketones such as **1c**,**f**,**h**,**m**,**n** in certain cases (Table 1, entries 3, 6, 8, 13, and 14).

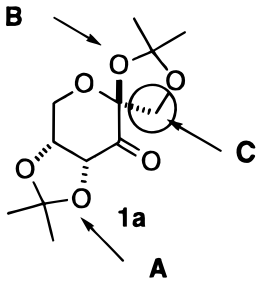
The fluoro group has been found to be a good activator for ketone catalysts.[16] For this reason, ketone **1o** was prepared and tested for the epoxidation. Surprisingly this ketone gave a very poor yield and ee of the epoxide product (Table 1, entry 15). The low catalytic activity of **1o** could be due to the fact that this ketone exists mainly in a hydrate form (eq 1). Another possibility is that the



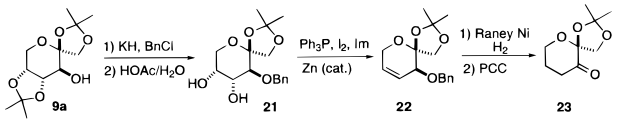
(1)

major transition state, spiro (**a**), is disfavored when F replaces H since F is bigger than H, consequently leading to both lower reactivity and enantioselectivity. The fluoro group has recently been found to be a sterically good controlling group for asymmetric induction,[3i,k] supporting the second explanation.

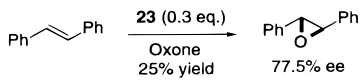
Ketone **1a** has a pseudo-C_2-symmetric element. Groups **A** and **B** are certainly important for the enantioselectivity. One interesting question is whether the methylene group **C** in **1a** plays any role in controlling enantioselectivity of the epoxidation. To explore this issue further, ketone **23** was prepared as shown in Scheme 11.[17−19] The



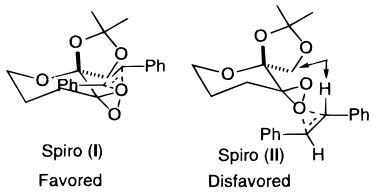
Scheme 11



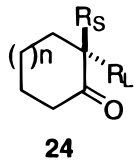
epoxidation of *trans*-stilbene with **23** gives 77.5% ee (eq 2)! The relatively high ee obtained is somewhat surprising, suggesting that the methylene group **C** plays an important role in controlling the epoxidation selectivity. This result could be explained by the two spiro transition states as shown. The spiro (**II**) transition state is disfavored probably due to the steric interaction between the hydrogen on the olefin and the methylene group (**C**).



(2)



Until this point, our logic in designing new ketone catalysts had mainly been introducing two groups on each side of the carbonyl group in a C_2 or pseudo C_2 symmetric fashion. The results from ketone **23** indicate that a chiral ketone like **24** which contains one chiral



center may potentially be a good chiral catalyst. The facial selectivity would be controlled by R_L, and R_S would control the competing reaction modes for the epoxidation. This type of ketone is currently under investigation.

In summary, among the many ketones studied, the results obtained with ketone **1** are extremely encouraging and represent significant progress in the area of chiral dioxirane mediated asymmetric epoxidation. However, there are still limitations with this system. The issues that need to be addressed include the following: (1) reducing the amount of the catalyst used; (2) enhancing the ee for certain trisubstituted olefins; and (3) developing new systems for terminal and electron-deficient olefins. To achieve these goals, new ketone catalysts need to be designed. The current studies show that the structural requirements for the ketone catalyst are very stringent. The precise understanding of all the factors involved in the reaction is difficult at the moment. The discovery of efficient ketone catalysts will be facilitated by studies in the areas of ketone structure and catalytic properties.

Experimental Section

General Methods. Oxone was purchased from Aldrich (it has been found that the oxidation activity of the purchased Oxone occasionally varies with different batches). All glass-

(16) For some examples discussing the effect of fluoro group on ketone catalysts see: (a) Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890. (b) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749. (c) Refs 2g, 3b,d,e,i,k.

(17) Kang, J.; Lim, G. J.; Yoon, S. K.; Kim, M. Y. *J. Org. Chem.* **1995**, *60*, 564.

(18) Lichtenthaler, F. W.; Doleschal, W.; Hahn, S. *Liebigs Ann. Chem.* **1985**, 2454.

(19) Izquierdo Cubero, I.; Plaza Lopez-Espinosa, M. T. *An. Quim.* **1990**, *86*, 554.

ware used for the epoxidation was carefully washed to be free of any trace metals which catalyze the decomposition of Oxone. High-resolution mass spectra were performed by the mass spectrometry facility of Colorado State University. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Preparation of Ketone 1a. For the detailed procedure for the synthesis of ketone **1a** see ref 4c.

Preparation of Ketone 1b.[20] To a solution of 3-pentanone (10.6 mL, 9.04 g, 105 mmol) and trimethyl orthoformate (8.8 mL, 8.5 g, 80 mmol) in methanol (50 mL) was added TsOH·H_2O (0.01 g). After the solution was heated at 60−70 °C for 3 h (during this time the formed methyl formate was distilled off), the bath temperature was raised to 90 °C and maintained at that temperature for 30 min to distill off the methanol. Upon cooling to room temperature, dioxane (100 mL) and D-fructose (7.2 g, 40 mmol) were added. The reaction mixture was cooled in an ice bath, and 0.1 mL of 70% perchloric acid was added. After being stirred for 6 h, the reaction was quenched by adding Et_3N and the product was concentrated. The resulting residue was dissolved in dichloromethane (50 mL), washed with brine, dried (Na_2SO_4), concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 2:1, v/v) to give alcohol **9b** as a syrup (7.81 g, 61%). $[\alpha]^{25}_D = -79.8$ (*c* 1, $CHCl_3$); IR 3434 cm^{-1}; ^1H NMR δ 4.19−4.25 (m, 2H), 4.16 (dd, J = 9.0, 1.2 Hz, 1H), 4.11 (br d, J = 12.9 Hz, 1H), 3.97 (d, J = 12.9 Hz, 1H), 3.95 (dd, J = 9.0, 1.2 Hz, 1H), 3.73 (d, J = 5.1, 1H), 2.12 (br s, 1H), 1.60−1.81 (m, 8H), 0.85−1.00 (m, 12H); ^{13}C NMR δ 115.9, 113.7, 104.3, 76.86, 73.18, 72.96, 70.81, 61.67, 30.19, 29.59, 28.94, 28.68, 8.76, 8.67, 8.02.

PCC (11.8 g, 55 mmol) was added portionwise over 15 min to a mixture of alcohol **9b** (7.52 g, 24 mmol) and powdered 3A molecular sieves (22 g, activated at 180−200 °C under vacuum) in dichloromethane (100 mL). After the reaction mixture was stirred for 3 h under nitrogen, it was filtered through Celite and washed carefully with ether. The filtrate was concentrated, and the residue was purified by being passed through a short silica gel column (hexane:ether, 1:1, v/v) to afford ketone **1b** as a syrup which solidified in the refrigerator after a few hours (6.03 g, 81%); mp 46.0−48.0 °C. $[\alpha]^{25}_D = -81.2$ (*c* 1, $CHCl_3$); IR 1747 cm^{-1}; ^1H NMR δ 4.71 (d, J = 5.9, 1H), 4.62 (d, J = 9.2 Hz, 1H), 4.58 (ddd, J = 5.9, 2.3, 0.9 Hz, 1H), 4.37 (dd, J = 13.5, 2.3 Hz, 1H), 4.13 (br d, J = 13.5 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 1.79 (q, J = 7.5 Hz, 2H), 1.65 (m, 6H), 0.96 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.5, Hz, 3H), 0.91 (t, J = 7.5 Hz, 3H), 0.82 (t, J = 7.5, Hz, 3H); ^{13}C NMR δ 197.5, 118.3, 114.9, 104.2, 77.71, 75.68, 70.62, 60.64, 30.14, 29.94, 29.14, 29.06, 8.56, 8.42, 8.40, 7.79. Anal. Calcd for $C_{16}H_{26}O_6$: C, 61.12; H, 8.34. Found: C, 61.36; H, 8.17.

Preparation of Ketone 1c. Perchloric acid (70%) (0.1 g) was added to a suspension of D-fructose (1.8 g, 10 mmol) in cyclopentanone (30 mL) and 1,1-dimethoxycyclopentane (2.86 g, 22 mmol) at 0 °C (ice bath). After being stirred under nitrogen at 0 °C for 6 h, the reaction mixture was neutralized with concentrated ammonium hydroxide and concentrated. The resulting residue was dissolved in CH_2Cl_2 (20 mL), washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 2:1, v/v), and followed by recrystallization (hexane) to give alcohol **9c** as white needles (1.15 g, 37%); mp 111.5−112.5 °C. $[\alpha]^{25}_D = -137.4$ (*c* 0.5, $CHCl_3$); IR 3455 cm^{-1}; ^1H NMR δ 4.16 (d, J = 8.7 Hz, 1H), 4.01−4.14 (m, 4H), 3.89 (d, J = 8.7 Hz, 1H), 3.63 (d, J = 6.1 Hz, 1H), 2.09 (br s, 1H), 1.60−2.00 (m, 16H); ^{13}C NMR δ 121.5, 119.4, 104.4, 77.16, 73.88, 72.44, 70.55, 61.04, 37.61, 37.56, 36.72, 36.42, 24.10, 23.76, 23.48, 23.04.

PCC (1.86 g, 8.6 mmol) oxidation of alcohol **9c** (1.0 g, 3.2 mmol) gave ketone **1c** as white crystals (0.83 g, 83%); mp 167.0−168.5 °C. $[\alpha]^{25}_D = -104.4$ (*c* 0.5, $CHCl_3$); IR 1745 cm^{-1}; ^1H NMR δ 4.73 (d, J = 5.5 Hz, 1H), 4.58 (d, J = 9.5 Hz, 1H), 4.44 (ddd, J = 5.5, 2.1, 0.9 Hz, 1H), 4.38 (dd, J = 13.4, 2.1 Hz, 1H), 4.12 (dd, J = 13.4, 0.9 Hz, 1H), 3.88 (d, J = 9.5 Hz, 1H), 1.60−2.10 (m, 16H); ^{13}C NMR δ 196.8, 123.2, 120.5, 104.0, 78.36, 75.78, 70.03, 60.46, 37.41, 37.04, 36.87, 36.16, 23.91, 23.71, 23.41, 23.21. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.66; H, 7.21.

Preparation of Ketone 1d.[21] To a solution of concentrated sulfuric acid (3 mL) in cyclohexanone (40 mL) at 0 °C was added powdered D-fructose (20.0 g, 111.1 mmol). The reaction mixture solidified after 40 min stirring at 0 °C. After standing at room temperature for an additional 24 h, the reaction mixture was dissolved in chloroform (150 mL) and washed with saturated Na_2CO_3, brine, saturated NH_4Cl, water, brine, and dried ($MgSO_4$), filtered, concentrated, and recrystallized (hexane) to give alcohol **9d** as white needles (13.6 g, 36%); mp 145.0−146.5 °C. $[\alpha]^{25}_D = -131.0$ (*c* 1, $CHCl_3$); IR 3467 cm^{-1}; ^1H NMR δ 4.22 (ddd, J = 5.7, 2.5, 0.8 Hz, 1H), 4.16−4.19 (m, 1H), 4.17 (d, J = 8.7 Hz, 1H), 4.13 (dd, J = 13.5, 2.5 Hz 1H), 4.03 (dd, J = 13.5, 0.8 Hz, 1H), 3.98 (d, J = 8.7 Hz, 1H), 3.65 (dd, J = 8.7, 7.0 Hz, 1H), 1.96 (d, J = 8.7 Hz, 1H), 1.38−1.80 (m, 20H); ^{13}C NMR δ 112.7, 110.3, 104.5, 77.23, 73.19, 72.15, 71.02, 61.17, 37.96, 36.09, 36.04, 35.46, 25.22, 25.21, 24.23, 24.14, 24.05, 23.89.

PCC (17.46 g, 81 mmol) oxidation of alcohol **9d** (10.2 g, 30 mmol) gave **1d** as a white solid (8.11 g, 80%); mp 154.0−155.5 °C. $[\alpha]^{25}_D = -107.7$ (*c* 1, $CHCl_3$); IR 1747 cm^{-1}; ^1H NMR δ 4.75 (d, J = 5.7 Hz, 1H), 4.59 (d, J = 9.5 Hz, 1H), 4.55 (ddd, J = 5.7, 2.2, 0.8 Hz, 1H), 4.39 (dd, J = 13.5, 2.2 Hz, 1H), 4.13 (d, J = 13.5 Hz, 1H), 3.98 (d, J = 9.5 Hz, 1H), 1.79 (t, J = 6.1 Hz, 2H), 1.57−1.68 (m, 14H), 1.41 (br s, 4H); ^{13}C NMR δ 197.5, 114.8, 111.5, 103.9, 77.78, 75.73, 69.79, 60.46, 36.94, 36.36, 35.65, 35.49, 25.11, 25.07, 24.15, 24.10, 23.95, 23.91. Anal. Calcd for $C_{18}H_{26}O_6$: C, 63.89; H, 7.74. Found: C, 63.96; H, 7.72.

Preparation of Ketone 1e. Alcohol **9e** was prepared in a way similar to that of alcohol **1b** using cycloheptanone (23.6 mL, 22.4 g, 200 mmol), trimethyl orthoformate (11.3 mL, 10.6 g, 100 mmol), methanol (50 mL), TsOH·H_2O (0.05 g), dioxane (50 mL), D-fructose (9.0 g, 50 mmol), and 1 mL of 70% perchloric acid. Alcohol **9e** was obtained as a white solid (3.64 g, 19.8%); mp 143.0−144.0 °C. $[\alpha]^{25}_D = -109.7$ (*c* 0.2, $CHCl_3$); IR 3437 cm^{-1}; ^1H NMR δ 4.07−4.18 (m, 4H), 3.99 (d, J = 13.2 Hz, 1H), 3.93 (d, J = 8.9 Hz, 1H), 3.65 (d, J = 6.1 Hz, 1H), 1.78−2.0 (m, 9H), 1.57 (br s, 16H); ^{13}C NMR δ 116.7, 114.3, 104.4, 77.10, 73.09, 72.19, 70.72, 61.17, 41.41, 39.56, 38.99, 38.39, 29.59, 29.47, 29.18, 29.11, 22.84, 22.40, 22.35.

PCC (3.4 g, 16 mmol) oxidation of alcohol **9e** (2.51 g, 6.8 mmol) gave ketone **1e** as a white solid (2.25 g, 90%); mp 136.5−137.5 °C. $[\alpha]^{25}_D = -88.9$ (*c* 0.6, $CHCl_3$); IR 1742 cm^{-1}; ^1H NMR δ 4.68 (d, J = 5.6 Hz, 1H), 4.52 (d, J = 9.5 Hz, 1H), 4.46 (ddd, J = 5.6, 2.1, 0.8 Hz, 1H), 4.33 (dd, J = 13.4, 2.1 Hz, 1H), 4.08 (d, J = 13.4 Hz, 1H), 3.91 (d, J = 9.5 Hz, 1H), 1.40−2.00 (m, 24H); ^{13}C NMR δ 197.5, 118.8, 115.5, 104.0, 77.50, 75.74, 69.86, 60.43, 40.26, 39.48, 38.83, 38.73, 29.48, 29.07, 25.58, 22.46, 22.44, 22.25. Anal. Calcd for $C_{20}H_{30}O_6$: C, 65.55; H, 8.27. Found: C, 65.81; H, 8.17.

Preparation of Ketone 1f. To a solution of alcohol **9a** (13.34 g, 51 mmol) (for the preparation see ref 4c) in 150 mL of acetonitrile−water (9:1, v/v) was added DDQ[10] (1.13 g, 5 mmol). After the mixture was stirred at room temperature for 6 h, the solvent was evaporated. The resulting reddish residue was dissolved in ethyl acetate, dried (Na_2SO_4), and concentrated to give alcohol **10** as a reddish solid (9.98 g, 88%).

To a solution of 3,3-dimethoxylpentane (4.41 g, 33 mmol) in 3-pentanone (22 mL) were added $CuSO_4$ (1.0 g) and concentrated H_2SO_4 (0.05 g).[12] After the mixture was stirred for 5 min, alcohol **10** (2.97 g, 13.5 mmol) was added. After being stirred an additional 3.5 h at room temperature, the reaction mixture was neutralized with Et_3N (0.8 mL), filtered, concentrated, and purified by flash chromatography (hexane: ether, 20:1 to 2:1, v/v) to afford alcohol **11f** as a syrup (2.39 g, 61%). $[\alpha]^{25}_D = -117.2$ (*c* 0.5, $CHCl_3$); IR 3468 cm^{-1}; ^1H NMR δ 4.22 (ddd, J = 6.3, 2.7, 0.9 Hz, 1H), 4.18 (dd, J = 6.3, 6.0 Hz, 1H), 4.17 (d, J = 8.9, 1 Hz, 1H), 4.10 (dd, J = 13.2, 2.7 Hz, 1H), 3.98 (dd, J = 13.2, 0.9 Hz, 1H), 3.97 (d, J = 8.9 Hz, 1H),

(20) Napolitano, E.; Fiaschi, R.; Mastrorilli, E. *Synthesis* **1986**, 122.

(21) James, K.; Tatchell, A. R.; Ray, P. K. *J. Chem. Soc. C* **1967**, 2681.

3.71 (d, J = 6.0 Hz, 1H), 2.05 (br s, 1H), 1.70−1.79 (m, 2H), 1.63 (q, J = 7.5 Hz, 2H), 1.51 (s, 3H), 1.44 (s, 3H), 0.96 (t, J = 7.5, 3H), 0.90 (t, J = 7.5, 3H); ^{13}C NMR δ 113.7, 111.8, 104.5, 77.01, 73.22, 72.77, 70.64, 61.47, 30.23, 28.72, 26.71, 26.37, 8.76, 8.67.

PCC (4.10 g, 19.0 mmol) oxidation of alcohol **11f** (2.03 g, 7.0 mmol) gave ketone **1f** as a white solid (1.61 g, 79%); mp 52.0−53.0 °C. $[\alpha]^{25}_D$ = −83.1 (*c* 1, $CHCl_3$); IR 1750 cm^{-1}; ^{1}H NMR δ 4.68 (d, J = 6.0 Hz, 1H), 4.59 (dd, J = 9.3, 0.6 Hz, 1H), 4.57 (dd, J = 6.0, 2.2 Hz, 1H), 4.35 (dd, J = 13.5, 2.2 Hz, 1H), 4.12 (dd, J = 13.5, 0.6 Hz, 1H), 3.98 (dd, J = 9.3, 0.6 Hz, 1H), 1.61−1.70 (m, 4H), 1.55 (s, 3H), 1.40 (s, 3H), 0.92 (t, J = 7.4, 3H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR δ 197.5, 114.9, 114.0, 104.2, 76.67, 75.69, 70.48, 60.64, 29.91, 29.18, 26.72, 26.13, 8.56, 8.36. Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.51; H, 7.58.

Preparation of Ketone 1g. To a solution of 2,2-dimethoxy-1,3-diphenylpropane (5.12 g, 20 mmol) in dioxane (50 mL) were added $CuSO_4$ (1.5 g) and concentrated H_2SO_4 (0.12 g), followed by alcohol **10** (3.30 g, 15 mmol). After being stirred 3 h at room temperature under nitrogen, the reaction mixture was neutralized with Et_3N, filtered, concentrated, and purified by flash chromatography (hexane:ether, 17:1 to 2:1, v/v) to give alcohol **11g** as a white solid (2.94 g, 48%); mp 133.5−134.5 °C. $[\alpha]^{25}_D$ = −92.1 (*c* 0.3**,** $CHCl_3$); IR 3458 cm^{-1}; ^{1}H NMR δ 7.29 (m, 10H), 3.60−3.88 (m, 6H), 2.88−3.10 (m, 4H), 2.38 (m, 1H), 1.65 (d, J = 9.4 Hz, 1H), 1.42 (s, 3H), 1.35 (s, 3H).

PCC (4.01 g, 18.6 mmol) oxidation of alcohol **11g** (2.84 g, 6.9 mmol) gave ketone **1g** as a syrup (1.96 g, 69%). $[\alpha]^{25}_D$ = −9.5 (*c* 0.7, $CHCl_3$); IR 1748 cm^{-1}; ^{1}H NMR δ 7.45−7.20 (m, 10H), 4.50 (d, J = 9.5 Hz, 1H), 4.44 (d, J = 6.1 Hz, 1H), 4.08 (dd, J = 13.5, 2.1 Hz, 1H), 3.98 (d, J = 13.5 Hz, 1H), 3.88 (d, J = 9.5 Hz, 1H), 3.58 (ddd, J = 6.1, 2.1, 1.0 Hz, 1H), 3.00 (d, J = 14.1 Hz, 1H), 2.94 (d, J = 14.1 Hz, 1H), 2.93 (d, J = 14.0 Hz,1H), 2.84 (d, J = 14.0 Hz, 1H), 1.48 (s, 3H), 1.34 (s, 3H); ^{13}C NMR δ 197.0, 136.2, 136.1, 131.1, 131.0, 128.2, 126.8, 114.0, 112.9, 104.0, 78.52, 75.87, 70.33, 60.30, 46.21, 43.94, 26.70, 26.09. Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 70.18; H, 6.31.

Preparation of Ketone 1h. To a solution of 1,1-dimethoxycyclopentane (3.9 g, 30 mmol) in cyclopentanone (20 mL) was added a solution of $CuSO_4$ (6.0 g) and concentrated H_2SO_4 (0.2 g) in dioxane (20 mL). Upon stirring for 5 min, alcohol **10** (5.50 g, 25 mmol) was added. After being stirred l.5 h at room temperature, the reaction mixture was neutralized with Et_3N (1.0 mL), filtered, concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 3:2) to give alcohol **11h** as a solid (2.45 g, 34%); mp 108.0−109.5 °C. $[\alpha]^{25}_D$ = −129.5 (*c* 1.0, $CHCl_3$); IR 3462 cm^{-1}; ^{1}H NMR δ 4.19 (d, J = 8.7 Hz, 1H), 4.01−4.15 (m, 4 H), 3.98 (d, J = 8.7 Hz, 1H), 3.61 (m, 1H), 2.00 (m, 3H), 1.60 (m, 6H), 1.52 (s, 3H), 1.45 (s, 3H); ^{13}C NMR δ 119.5, 112.2, 104.9, 77.31, 73.94, 72.36, 70.38, 60.70, 37.66, 26.62, 26.53, 23.80, 23.53.

PCC (1.85 g, 19 mmol) oxidation of alcohol **11h** (0.91 g, 3.2 mmol) gave ketone **1h** as a white solid (0.69 g, 76%); mp 162.0−162.5 °C. $[\alpha]^{25}_D$ = −106.4 (*c* 1, $CHCl_3$); IR 1743 cm^{-1}; ^{1}H NMR δ 4.72 (d, J = 5.3 Hz, 1H), 4.61 (d, J = 9.5 Hz, 1H), 4.36−4.44 (m, 2H), 4.13 (d, J = 13.1 Hz, 1H), 3.98 (d, J = 9.5 Hz, 1H), 1.65−2.05 (m, 8H), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 196.8, 120.5, 114.0, 104.3, 78.38, 75.80, 70.13, 60.22, 37.44, 37.07, 26.72, 26.23, 23.75, 23.44. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 58.96; H, 7.26.

Preparation of Ketone 1i. To a mixture of alcohol **10** (2.91 g, 13.2 mmol) in cyclohexanone (30 mL) and 1,1-dimethoxycyclohexane (5.0 mL) were added $CuSO_4$ (5.0 g) and concentrated H_2SO_4 (0.05 g). After being stirred for 50 min at room temperature under nitrogen, the reaction mixture was neutralized with Et_3N (1.0 mL), filtered, concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 3:2) to give alcohol **11i** as a white solid (2.60 g, 66%); mp 96.5−98.0 °C. $[\alpha]^{25}_D$ = −125.2 (*c* 0.5, $CHCl_3$); IR 3454 cm^{-1}; ^{1}H NMR δ 4.20 (ddd, J = 6.0, 2.4, 0.9 Hz, 1H), 4.18 (d, J = 8.7 Hz, 1H), 4.12 (dd, 6.6, 6.0 Hz, 1H), 4.11 (dd, J = 13.2, 2.4 Hz, 1H), 4.02 (d, J = 13.2 Hz, 1 H), 3.97 (d, J = 8.7, 1H), 3.66 (br s, 1H), 2.11 (br s, 1H), 1.55−1.76 (m, 8H), 1.52 (s, 3H), 1.44 (s, 3H), 1.37−1.45 (m, 2H); ^{13}C NMR δ 112.0, 110.3, 104.7, 77.01, 73.11, 72.53, 70.92, 61.06, 37.90, 35.38, 26.63, 26.45, 25.20, 24.20, 23.86.

PCC (5.06 g, 23.5 mmol) oxidation of alcohol **11i** (2.60 g, 8.7 mmol) gave ketone **1i** as a white solid (1.89 g, 73%); mp 106.5−108.0 °C. $[\alpha]^{25}_D$ = −105.5 (*c* 0.5**,** $CHCl_3$); IR 1750 cm^{-1}; ^{1}H NMR δ 4.72 (d, J = 5.6 Hz, 1H), 4.60 (d, J = 9.5 Hz, 1H), 4.55 (ddd, J = 5.6, 2.2, 0.9 Hz, 1H), 4.37 (dd, J = 13.4, 2.2 Hz, 1H), 4.13 (d, J = 13.4, 1H), 3.98 (d, J = 9.5 Hz, 1H), 1.34−1.70 (m, 10H), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 197.4, 113.9, 111.5, 104.3, 77.71, 75.66, 70.21, 60.43, 36.90, 35.61, 26.67, 26.16, 25.09, 24.07, 23.91. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.42; H, 7.47.

Preparation of Ketone 1j. To a mixture of $CH(OMe)_3$ (2.2 mL, 2.12 g, 20 mmol), alcohol **10** (2.20 g, 10 mmol), and propanal (11.6 g, 200 mmol) in THF (40 mL) was added TsOH·H_2O (0.5 g) at room temperature. After being stirred overnight, the reaction mixture was neutralized with Et_3N, concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 4:3, v/v) to give alcohol **11j** as a white solid (1.20 g, 46%); mp 98.0−99.0 °C. $[\alpha]^{25}_D$ = −131.9 (*c* 1.0, $CHCl_3$); IR 3468 cm^{-1}; ^{1}H NMR δ 4.96 (t, J = 4.9 Hz, 1H), 4.18 (d, J = 8.8 Hz, 1H), 4.13 (dd, J = 13.6, 2.4 Hz, 1H), 4.10 (t, J = 6.0, 1H), 4.04−4.10 (m, 2H), 3.97 (d, J = 8.8 Hz, 1H), 3.60 (dd, J = 6.3, 6.0 Hz, 1H), 2.25 (d, J = 7.8, 1H), 1.70−1.80 (m, 2H), 1.51 (s, 3H), 1.44 (s, 3H), 1.00 (t, J = 7.5 Hz, 3H); ^{13} C NMR δ 112.1, 106.3, 104.7, 76.81, 75.25, 72.52, 71.18, 60.74, 27.96, 26.63, 26.46, 8.51.

PCC (2.2 g, 10.3 mmol) oxidation of alcohol **11j** (1.0 g, 3.8 mmol) gave ketone **1j** as a solid (0.83 g, 84%). IR 3482 (hydrate OH), 1750 cm^{-1}; ^{1}H NMR δ 5.02 (t, J = 4.9 Hz, 1H), 4.69 (d, J = 5.9 Hz, 1H), 4.60 (d, J = 9.6 Hz, 1H), 4.44 (ddd, J = 5.9, 2.1, 0.9 Hz, 1H), 4.40 (dd, J = 13.2, 2.1 Hz, 1H), 4.18 (dd, J = 13.2, 0.9 Hz, 1H), 3.99 (d, J = 9.6 Hz, 1H), 1.62−1.82 (m, 2H), 1.55 (s, 3H), 1.40 (s, 3H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR 196.4, 114.1, 107.0, 104.2, 79.61, 75.20, 70.29, 60.12, 27.60, 26.73, 26.19, 8.21. Anal. Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 55.93; H, 7.11.

Preparation of Ketone 1k. To a mixture of $CH(OEt)_3$ (3 mL, 2.65 g, 18 mmol) and TsOH·H_2O (0.2 g) in dioxane (30 mL) at 0 °C was added isobutanal (10 mL) at room temperature. After stirring for 1 h, **10** (2.2 g, 10 mmol) was added. After 4 h, another batch of $CH(OEt)_3$ (2.0 mL, 12 mmol) was added. The reaction mixture was stirred for another 2 h, neutralized with Et_3N (1 mL), concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 3:2, v/v) to give alcohol **11k** as a white solid (1.48 g, 54%); mp 86.5−88.5 °C. $[\alpha]^{25}_D$ = −127.1 (*c* 0.6, $CHCl_3$); IR 3452 cm^{-1}; ^{1}H NMR δ 4.71 (d, J = 5.4 Hz, 1H), 4.18 (d, J = 8.8 Hz, 1H), 4.03−4.16 (m, 4H), 3.97 (d, J = 8.8 Hz, 1H), 3.62 (d, J = 6.2 Hz, 1H), 1.85 (m, 1H), 1.51 (s, 3H), 1.45 (s, 3H), 1.00 (d, J = 6.9 Hz, 3H), 0.98 (d, J = 6.9 Hz, 3H); ^{13}C NMR δ 112.0, 109.1, 104.7, 76.77, 75.11, 72,59, 70.92, 60.89, 32.51, 26.67, 26.44, 17.38, 17.34.

PCC (1.93 g, 9.0 mmol) oxidation of alcohol **11k** (0.91 g, 3.3 mmol) gave ketone **1k** as a solid (0.64 g, 71%); mp 58.5−60.0 °C. $[\alpha]^{25}_D$ = −87.0 (*c* 0.5, $CHCl_3$); IR 3482 (hydrate OH), 1749 cm^{-1}; ^{1}H NMR δ 4.77 (d, J = 5.4 Hz, 1H), 4.66 (d, J = 5.9 Hz, 1H), 4.59 (d, J = 9.6 Hz,1H), 4.36−4.57 (m, 2H), 4.16 (d, J = 13.4 Hz, 1H), 3.98 (d, J = 9.6 Hz, 1H), 1.84 (m, 1H), 1.55 (s, 3H), 1.40 (s, 3H), 0.99 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H); ^{13}C NMR δ 196.3, 114.0, 109.8, 104.2, 79.33, 75.07, 70.38, 60.24, 32.31, 26.73, 26.17, 17.14, 16.94. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.43. Found: C, 57.28; H, 7.42.

Preparation of Ketone 1l. TsOH·H_2O (0.6 g) was added to a solution of ketone **1b** (1.47 g, 4.7 mmol) in acetone (60 mL). After being stirred for 0.5 h at room temperature, 2,2-dimethoxypropane (2.0 mL, 1.69 g, 16 mmol) was added. The mixture was stirred at room temperature for 3.5 h, neutralized with Et_3N, concentrated, and purified by flash chromatography (hexane:ether, 15:1 to 10:1, v/v) to afford ketone **1l** as a syrup (0.62 g, 46%). $[\alpha]^{25}_D$ = −111.4 (*c* 1.1, $CHCl_3$); IR 1749 cm^{-1}; ^{1}H NMR δ 4.76 (d, J = 5.5 Hz, 1H), 4.63 (d, J = 9.4 Hz, 1H), 4.56 (ddd, J = 5.5, 2.2, 0.9 Hz, 1H), 4.42 (dd, J = 13.5, 2.2 Hz, 1H), 4.13 (d, J = 13.5 Hz, 1H), 3.96 (d, J = 9.4 Hz, 1H), 1.80 (q, J = 7.4, 2H), 1.63 (q, J = 7.4, 2H), 1.46 (s, 3H), 1.40 (s,

3H), 0.96 (t, J = 7.4 Hz, 3H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR δ 197.2, 118.3, 110.7, 104.3, 78.11, 76.05, 70.36, 60.34, 30.12, 29.06, 27.32, 26.23, 8.42, 7.75. Anal. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.81; H, 7.80.

Preparation of Ketone 1m. TsOH·H_2O (0.25 g) was added to a solution of ketone **1c** (0.62 g, 2.0 mmol) in acetone (30 mL). After being stirred for 0.5 h at room temperature, 2,2-dimethoxypropane (1.0 mL, 0.84 g, 8 mmol) was added. The mixture was stirred at room temperature for 3.5 h, neutralized with Et_3N, concentrated, and purified by chromatography to give ketone **1m** as a solid (0.30 g, 52%); mp 152.0−153.5 °C. $[\alpha]^{25}_D$ = −118.5 (*c* 0.5, $CHCl_3$); IR 1747 cm^{-1}; ^{1}H NMR δ 4.76 (d, J = 5.6 Hz, 1H), 4.60 (d, J = 9.4 Hz, 1H), 4.58 (ddd, J = 5.6, 2.1, 0.9 Hz, 1H), 4.41 (dd, J = 13.5, 2.1 Hz, 1H), 4.15 (d, J = 13.5 Hz, 1H), 3.90 (d, J = 9.4 Hz, 1H), 1.60−2.00 (m, 8H), 1.46 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 197.2, 123.3, 110.9, 104.0, 78.16, 76.11, 70.17, 60.57, 36.93, 36.22, 27.37, 26.28, 23.96, 23.26; Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 58.95; H, 7.28.

Preparation of Ketone 1n. To a solution of alcohol **9d** (5.10 g, 15 mmol) in acetonitrile−water (100 mL, 9:1, v/v) was added DDQ[10] (0.64 g, 3 mmol). After being stirred at room temperature for 3 h, the reaction mixture was concentrated to a reddish residue. After being washed with ethyl acetate, the residue was dried under vacuum to give alcohol **12** as a reddish solid (2.19 g, 56%), which could be directly used for the next reaction.

To a mixture of crude alcohol **12** (2.19 g, 8.4 mmol), 2,2-dimethoxypropane (2.0 mL, 1.69 g, 18 mmol), $CuSO_4$ (5.0 g), and acetone (40 mL) was added concentrated H_2SO_4 (0.06 g). After being stirred for 1.5 h at room temperature, the reaction mixture was neutralized with Et_3N (1 mL), filtered, concentrated, and purified by flash chromatography (hexane:ether, 10:1 to 3:2) to afford alcohol **13** as a solid (1.92 g, 76%); mp 100.0−101.0 °C. $[\alpha]^{25}_D$ = −134.1 (*c* 0.3, $CHCl_3$); IR 3469 cm^{-1}; ^{1}H NMR δ 4.22 (ddd, J = 5.8, 2.4, 0,9 Hz, 1H), 4.17 (d, J = 8.7 Hz, 1H), 4.13 (dd, J = 13.5, 2.4 Hz, 1H), 4.13 (dd, J = 7.0, 5.8 Hz, 1H), 4.01 (d, J = 13.5 Hz, 1H), 3.97 (d, J = 8.7 Hz, 1H), 3.66 (dd, J = 8.6, 7.0 Hz, 1H), 1.96 (d, J = 8.6 Hz, 1H), 1.80−1.37 (m, 10H), 1.54 (s, 3H), 1.37 (s, 3H); ^{13}C NMR δ 112.8, 109.6, 104.4, 77.69, 73.61, 72.15, 70.70, 61.07, 36.10, 36.04, 28.19, 26.20, 25.20, 24.14, 24.05.

PCC (3.05 g, 14.1 mmol) oxidation of alcohol **13** (1.57 g, 5.2 mmol) gave ketone **1n** as a white solid (1.26 g, 81%); mp 99.5−101.0 °C. $[\alpha]^{25}_D$ = −119.8 (*c* 0.5, $CHCl_3$); IR 1750 cm^{-1}; ^{1}H NMR δ 4.76 (d, J = 5.6 Hz, 1H), 4.60 (d, J = 9.5 Hz, 1H), 4.56 (ddd, J = 5.6, 2.2, 0.9 Hz, 1H), 4.41 (dd, J = 13.5, 2.2 Hz, 1H), 4.12 (dd, J = 13.5, 0.9 Hz, 1H), 3.99 (d, J = 9.5 Hz, 1H), 1.80 (t, J = 6.1 Hz, 2H), 1.40−1.70 (m, 8H), 1.64 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 197.2, 114.9, 110.8, 104.0, 78.17, 76.13, 69.81, 60.34, 36.39, 35.54, 27.38, 26.29, 25.09, 24.17, 23.93; Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.50; H, 7.52.

Preparation of Ketone 1o.[22] To a solution of diisopropylamine (0.36 mL, 0.27 g, 2.7 mmol) in THF (5 mL) was added nBuLi (1.6 M) (1.6 mL, 2.6 mmol) at 0 °C. Upon stirring for an additional 30 min, the reaction mixture was cooled to −78 °C, whereupon a solution of ketone **1a** (0.510 g, 2 mmol) in THF (2 mL) was added. After stirring for 30 min, hexamethylphosphoramide (HMPA) (2 mL) was added. After the reaction mixture was stirred for another 1 h, a solution of $(PhSO_2)_2NF$ (0.82 g, 2.6 mmol) in THF (2 mL) was added. The reaction mixture was stirred at −78 °C for 1 h, then warmed to room temperature, quenched with aqueous NH_4Cl, extracted with ether (2 × 20 mL), washed with water and brine, dried (Na_2SO_4), concentrated, and purified by flash chromatography (hexane:ethyl acetate, 2:1) to provide ketone **1o** (0.278 g, 45%). IR 3472 (hydrate OH), 1774 cm^{-1}; ^{1}H NMR δ 4.53 (d, J = 9.4 Hz, 1H), 4.52 (dd, J = 15.8, 2.2 Hz, 1H), 4.31(s, 1H), 4.25 (dd, J = 12.9, 2.2 Hz, 1H), 3.86 (d, J = 9.4 Hz, 1H), 3.64 (dd, J = 12.9, 3.9 Hz, 1H), 3.14 (s, 1H), 1.55 (s, 3H), 1.50 (s, 6H), 1.47 (s, 3H); ^{13}C NMR δ 201.4, 115.2, 111.2, 105.1, 91.9, 80.9, 72.0, 65.3, 27.6, 26.5, 26.4, 25.3. HRMS. Calcd for $C_{12}H_{19}FO_7$ (hydrate) ($M^+ + 1$): 295.1193. found: 295.1190.

Preparation of Ketone 2a. Perchloric acid (70%) (1 mL) was added to a mixture of alcohol **15** (10.8 g, 52 mmol) (for preparation see ref 11a) and 2,2-dimethoxypropane (8.0 mL, 65 mmol) in acetone (100 mL) at 0 °C. After being stirred under nitrogen at this temperature overnight, the reaction mixture was neutralized with concentrated NH_4OH solution and concentrated. The resulting residue was dissolved in dichloromethane (100 mL), washed with brine, dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (ethyl acetate:hexane, 3:1 to 1:1, v/v) to give alcohol **16a** as a solid (4.22 g, 33%); mp 110.5−111.5 °C. $[\alpha]^{25}_D$ = −141.3 (*c* 1, $CHCl_3$); IR 3441 cm^{-1}; ^{1}H NMR δ 4.25 (dd, J = 5.7, 2.4 Hz, 1H), 4.17 (dd, J = 6.9, 5.7 Hz, 1H), 4.08 (d, J = 13.2 Hz, 1H), 4.03 (ddd, J = 11.4, 11.4, 3.0 Hz, 1H), 3.94 (dd, J = 13.2, 2.4 Hz, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.78 (dd, J = 11.4, 3.0 Hz, 1H), 3.71 (ddd, J = 11.4, 11.4, 2.5 Hz, 1H), 3.67 (d, J = 12.0 Hz, 1H), 3.59 (dd, J = 11.4, 2.5 Hz, 1H), 3.44 (dd, J = 7.2, 6.9 Hz, 1H), 2.26 (d, J = 7.2 Hz, 1H), 1.54 (s, 3H), 1.37 (s, 3H); ^{13}C NMR δ 109.6, 95.06, 76.74, 73.69, 71.56, 69.12, 65.74, 60.47, 60.01, 28.20, 26.23.

PCC (5.82 g, 27 mmol) oxidation of alcohol **16a** (2.46 g, 10 mmol) gave ketone **2a** as a white solid (2.04 g, 84%); mp 137.5−138.5 °C. $[\alpha]^{25}_D$ = −105.6 (*c* 1.3, $CHCl_3$); IR 1750 cm^{-1}; ^{1}H NMR δ 4.74 (d, J = 5.7 Hz, 1H), 4.58 (ddd, J = 5.7, 2.0, 1.2 Hz, 1H), 4.22 (dd, J = 13.0, 2.0 Hz, 1H), 4.16 (d, J = 13.0 Hz, 1H), 4.06 (m, 1H) 3.90 (d, J = 12.6 Hz, 1H), 3.58−3.83 (m, 3H), 3.76 (d, J = 12.6 Hz, 1H), 1.45 (s, 3H), 1.39 (s, 3H); ^{13}C NMR δ 199.3, 110.7, 93.94, 78.72, 75.70, 67.23, 65.58, 60.49, 59.42, 27.36, 26.28. Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 53.91; H, 6.89.

Preparation of Ketone 2b. To a solution of 3-pentanone (3.44 g, 40 mmol) and trimethyl orthoformate (4.4 mL, 4.24 g, 40 mmol) in methanol (10 mL) was added TsOH·H_2O (0.05 g). After the solution was heated at 50−60 °C for 2 h (during this time the methyl formate formed was distilled off), the bath temperature was raised to 80 °C to distill off the methanol. Upon cooling to room temperature, a solution of alcohol **15** (6.18 g, 30 mmol) in THF (100 mL) was added, followed by 4 drops of 70% perchloric acid. After being stirred at room temperature overnight, the reaction mixture was neutralized with concentrated NH_4OH and concentrated. The resulting residue was dissolved in dichloromethane (200 mL), washed with brine, dried over sodium sulfate, concentrated, and purified by flash chromatography (hexane:ether, 20:1 to 3:2, v/v) to give alcohol **16b** as a solid (5.08 g, 62%); mp 79.5−80.5 °C. $[\alpha]^{25}_D$ = −127.8 (*c* 0.5, $CHCl_3$); IR 3451 cm^{-1}; ^{1}H NMR δ 4.26 (dd, J = 6.3, 3.0, Hz, 1H), 4.20 (dd, J = 6.3, 6.0 Hz, 1H), 4.06 (d, J = 13.2 Hz, 1H), 4.03 (ddd, J = 11.4, 11.4, 3.0 Hz, 1H), 3.90 (dd, J = 13.2, 2.7 Hz, 1H), 3.87 (d, J = 11.7 Hz, 1H), 3.76 (dd, J = 11.4, 3.0 Hz, 1H), 3.71 (ddd, J = 11.4, 11.4, 2.4 Hz, 1H), 3.66 (d, J = 11.7 Hz, 1H), 3.58 (dd, J = 11.4, 2.4 Hz, 1H), 3.47 (t, J = 6.0 Hz, 1H), 2.69 (d, J = 6.0 Hz, 1H), 1.76 (m, 2H), 1.63 (q, J = 7.5, 2H), 0.97 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H); ^{13}C NMR δ 113.5, 94,77, 76.34, 73.34, 71,36, 69.22, 65,62, 60,34, 60.18, 30.20, 28.65, 8.66, 8.62.

PCC (10.52 g, 48.8 mmol) oxidation of alcohol **16b** (5.00 g, 27.4 mmol) gave **2b** as a white solid (3.98 g, 80%); mp 81.0−82.0 °C. $[\alpha]^{25}_D$ = −70.4 (*c* 1.1, $CHCl_3$); IR 1750 cm^{-1}; ^{1}H NMR δ 4.69 (d, J = 6.1 Hz, 1H), 4.62 (dt, J = 6.1, 1.6 Hz, 1H), 4.19 (d, J = 1.6 Hz, 2H), 4.08 (td, J = 11.3, 3.1 Hz, 1H), 3.94 (d, J = 12.5 Hz, 1H), 3.84−3.60 (m, 3H), 3.76 (d, J = 12.5 Hz, 1H), 1.67 (q, J = 7.5 Hz, 4H), 0.93 (t, J = 7.5 Hz, 6H); ^{13}C NMR δ 199.2, 114.8, 93.94, 78.18, 75.29, 67.31, 65.58, 60.38, 59.65, 29.87, 29,12, 8.58, 8,39. Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.58; H, 7.45.

Preparation of Ketone 2c. To a solution of 4-heptanone (11.4 g, 100 mmol) and trimethyl orthoformate (4.24 g, 40 mmol) in methanol (50 mL) was added TsOH·H_2O (0.01 g). After the solution was heated at 50−70 °C for 2 h (during this time the methyl formate formed was distilled off), the bath temperature was raised to 100 °C to distill off the methanol. Upon cooling to room temperature, a solution of alcohol **15** (8.80 g, 43 mmol) in dioxane (60 mL) was added, followed by

(22) Differding, E.; Ofner, H. *Synlett* **1991**, 187.

$CuSO_4$ (6.0 g) and concentrated H_2SO_4 (0.2 g). After being stirred at room temperature overnight, the reaction mixture was neutralized with concentrated NH_4OH, concentrated, and purified by flash chromatography (hexane:ether, 50:1 to 3:1, v/v) to give alcohol **16c** as a white solid (5.56 g, 43%); mp 85.5−86.5 °C. $[\alpha]^{25}_D = -127.0$ (*c* 0.6, $CHCl_3$); IR 3449 cm^{-1}; ^1H NMR δ 4.24 (dd, *J* = 6.2, 2.7 Hz, 1H), 4.18 (dd, *J* = 6.3, 6.2 Hz, 1H), 4.05 (d, *J* = 13.4 Hz, 1H), 4.04 (ddd, *J* = 11.4, 11.4, 3.3 Hz, 1H), 3.91 (dd, *J* = 13.4, 2.7 Hz, 1H), 3.85 (d, *J* = 11.9 Hz, 1H), 3.78 (dd, *J* = 11.7, 3.3 Hz, 1H), 3.69 (ddd, 11.7, 11.4, 2.7 Hz, 1H), 3.68 (d, *J* = 11.9 Hz, 1H), 3.59 (dd, *J* = 11.4, 2.7, Hz, 1H), 3.46 (dd, *J* = 6.3, 5.9 Hz, 1H), 2.33 (br s, 1H), 1.31−1.73 (m, 8H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 112.9, 94.77, 76.31, 73.32, 71.45, 69.46, 65.76, 60.49, 60.34, 40.45, 38.92, 17.82, 17.68, 14.61.

PCC (9.12 g, 42.3 mmol) oxidation of alcohol **16c** (4.73 g, 15.7 mmol) gave ketone **2c** as a syrup (3.89 g, 83%). $[\alpha]^{25}_D = -65.0$ (*c* 1.1, $CHCl_3$); IR 1751 cm^{-1}; ^1H NMR δ 4.66 (d, *J* = 6.3 Hz, 1H), 4.50 (ddd, *J* = 6.3, 1.5, 1.5 Hz, 1H), 4.17 (d, *J* = 1.5 Hz, 2H), 4.06 (td, *J* = 11.1, 3.2 Hz, 1H), 3.92 (d, *J* = 12.6 Hz, 1H), 3.80 (dd, *J* = 11.7, 3.2 Hz, 1H), 3.75 (d, *J* = 12.6 Hz, 1H), 3.70 (ddd, 11.7, 11.0, 2.7 Hz, 1H), 3.62 (dd, *J* = 11.1, 2.7 Hz, 1H), 1.62 (m, 4H), 1.40 (m, 4H), 0.912 (t, *J* = 7,3 Hz, 3H), 0.907 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 199.2, 114.1, 94.03, 78.09, 75.26, 67.42, 65.62, 60.44, 59.74, 39.89, 39.22, 17.65, 17.44, 14.55. Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.93; H, 8.15.

Preparation of Ketone 2d. Alcohol **16d** was prepared in a way similar to that of alcohol **16b** using 1,3-diphenylacetone (2.1 g, 10 mmol), trimethyl orthoformate (1.2 mL, 1.15 g, 11 mmol), methanol (10 mL), $TsOH\cdot H_2O$ (0.01 g), alcohol **15** (3.10 g, 15 mmol), THF (100 mL), and 3 drops of 70% perchloric acid. Alcohol **16d** was obtained as a solid (2.36 g, 59%); mp 180.0−181.0 °C. $[\alpha]^{25}_D = -86.2$ (*c* 0.5, $CHCl_3$); IR 3419 cm^{-1}; ^1H NMR δ 7.30 (m, 10H), 3.98 (d, *J* = 13.2 Hz, 1H), 3.90 (dd, *J* = 6.9, 6.6 Hz, 1H), 3.84 (td, *J* = 11.4, 3.2 Hz, 1H), 3.71 (dd, *J* = 6.6, 2.9 Hz, 1H), 3.67 (dd, *J* = 11.7, 3.2 Hz, 1H), 3.64 (dd, *J* = 13.2, 2.9 Hz, 1H), 3.56 (ddd, *J* = 11.7, 11.4, 2.7 Hz, 1H), 3.55 (d, *J* = 12.0 Hz, 1H), 3.45 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.16 (d, *J* = 12.0 Hz, 1H), 3.05 (d, *J* = 13.8 Hz, 1H), 3.03 (d *J* = 13.8 Hz, 1H), 2.98 (d, *J* = 13.8 Hz, 1H), 2.91 (d, *J* = 13.8 Hz, 1H), 1.87 (dd, *J* = 8.0, 6.9 Hz, 1H), 1.72 (d, *J* = 8.0, Hz, 1H); ^{13}C NMR δ 136.7, 136.3, 131.7, 130.8, 128.4, 128.1, 126.8, 111.5, 94.76, 77.47, 73.86, 70.51, 68.46, 65.54, 60.21, 59.49, 45.49, 44.53.

PCC (2.34 g, 10.4 mmol) oxidation of alcohol **16d** (1.8 g, 4.5 mmol) gave ketone **2d** as a solid (1.68 g, 93%); mp 131.0−131.5 °C. $[\alpha]^{25}_D = -6.3$ (*c* 0.7, $CHCl_3$); IR 1749 cm^{-1}; ^1H NMR δ 7.20−7.45 (m, 10H), 4.45 (d, *J* = 6.3 Hz, 1H), 4.05 (d, *J* = 13.2 Hz, 1H), 3.97 (ddd, *J* = 11.4, 11.1, 3.0 Hz, 1H), 3.90 (dd, *J* = 13.2, 2.4 Hz, 1H), 3.87 (d, *J* = 12.4 Hz, 1H), 3.76 (dd, *J* = 11.7, 3.0 Hz, 1H), 3.66 (ddd, *J* = 11.7, 11.4, 2.4 Hz, 1H), 3.65 (d, *J* = 12.4 Hz, 1H), 3.62 (dd, *J* = 6.3, 2.4 Hz, 1H), 3.54 (dd, *J* = 11.1, 2.4 Hz, 1H), 2.98 (d, *J* = 13.8 Hz, 1H), 2.93 (d, *J* = 13.8 Hz, 1H), 2.91 (d, *J* = 13.9 Hz, 1H), 2.82 (d, *J* = 13.9 Hz, 1H); ^{13}C NMR δ 198.9, 136.2, 136.0, 131.0, 130.9, 128.2, 128.1, 126.7, 112.5, 93.63, 79.03, 75.45, 66.99, 65.39, 60.22, 59.23, 46.13, 43.63. Anal. Calcd for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.46; H, 5.88.

Preparation of Ketone 2e. Alcohol **16e** was prepared in a way similar to that of alcohol **16b** using benzophenone (4.86 g, 27 mmol), trimethyl orthoformate (3.1 mL, 3.0 g, 28 mmol), methanol (20 mL), $TsOH\cdot H_2O$ (0.02 g), alcohol **15** (6.18 g, 30 mmol), THF (150 mL), and 3 drops of 70% perchloric acid. Alcohol **16e** was obtained as a syrup (7.24 g, 67%). $[\alpha]^{25}_D = -48.6$ (*c* 1.2, $CHCl_3$); IR 3445 cm^{-1}; ^1H NMR δ 7.50−7.56 (m, 4H), 7.20−7.36 (m, 6H), 4.35 (dd, *J* = 6.9, 6.3 Hz, 1H), 4.23(d, *J* = 13.2 Hz, 1H), 4.15 (dd, *J* = 6.3, 2.9 Hz, 1H), 4.02 (ddd, *J* = 11.4, 11.4, 3.3 Hz, 1H), 3.92 (dd, *J* = 13.2, 2.9 Hz, 1H), 3.80 (d, *J* = 12.0 Hz, 1H), 3.75 (dd, *J* = 11.4. 3.3 Hz, 1H), 3.66 (ddd, *J* = 11.4, 11.4, 2.7 Hz, 1H), 3.58 (d, *J* = 12.0 Hz, 1H), 3.57 (dd, *J* = 11.4, 2.7 Hz, 1H), 3.43 (dd, *J* = 7.2, 6.9 Hz, 1H), 2.37 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR δ 143.3, 142.7, 128.3, 128.2, 126.3, 126.2, 126.1, 109.6, 95.02, 77.42, 74.10, 71.01, 69.08, 65.68, 60.44, 59.78.

PCC (4.0 g, 18.6 mmol) oxidation of alcohol **16e** (2.79 g, 7.5 mmol) gave ketone **2e** as a white solid (1.43 g, 51%); mp 193.5−194.5 °C. IR 1752 cm^{-1}; ^1H NMR δ 7.2−7.6 (m, 10H), 4.79 (d, *J* = 6.6 Hz, 1H), 4.53 (dd, *J* = 6.6, 2.1 Hz, 1H), 4.32 (d, *J* = 13.4 Hz, 1H), 4.18 (dd, *J* = 13.4, 2.1 Hz, 1H), 4.07 (td, *J* = 11.2, 3.2 Hz, 1H), 3.85 (d, *J* = 12.3 Hz, 1H), 3.78 (dd, *J* = 12.0, 3.2 Hz, 1H), 3.70 (d, *J* = 12.3 Hz, 1H), 3.68 (ddd, *J* = 12.0, 11.4, 2.4 Hz, 1H), 3.59 (dd, *J* = 11.4, 2.4 Hz, 1H); ^{13}C NMR δ 197.8, 141.9, 140.9, 128.8, 128.5, 128.4, 128.2, 126.8, 126.5, 110.8, 94.17, 78.58, 75.63, 67.47, 65.60, 60.44, 59.55. Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.34; H, 5.85.

Preparation of Ketone 2f. Alcohol **16f** was prepared in a way similar to that of alcohol **16b** using cyclopentanone (5.04 g, 60 mmol), trimethyl orthoformate (4.4 mL, 4.24 g, 40 mmol), methanol (20 mL), $TsOH\cdot H_2O$ (0.05 g), alcohol **15** (8.24 g, 40 mmol), THF (100 mL), and 4 drops of 70% perchloric acid. Alcohol **16f** was obtained as a solid (5.97 g, 52%); mp 131.0−132.5 °C. $[\alpha]^{25}_D = -133.1$ (*c* 0.5, $CHCl_3$); IR 3444 cm^{-1}; ^1H NMR δ 4.08−4.14 (m, 3H), 4.02 (td, *J* = 11.4, 3.2, 1H), 3.95 (dd *J* = 13.5, 2.6, 1H), 3.90 (d, *J* = 11.8, 1H), 3.77 (dd, *J* = 11.4, 3.2, 1H), 3.71 (dd, *J* = 11.4, 2.6, 1H), 3.69 (td, *J* = 11.8, 2.6, 1H), 3.65 (d, *J* = 11.8 Hz, 1H), 3.59 (dd, 11.4, 2.6, Hz, 1H), 3.39 (m, 1H), 2.12 (br s, 1H), 1.96 (m, 2H), 1.74 (m, 6H); ^{13}C NMR δ 119.2, 95.25, 76.33, 73.97, 71.36, 68.57, 65.56, 60.28, 59.59, 37.65, 37.59, 23.69, 23.43.

PCC (9.92 g, 46 mmol) oxidation of alcohol **16f** (5.48 g, 20 mmol) gave ketone **2f** as a white solid (4.29 g, 78%); mp 98.0−100 °C. $[\alpha]^{25}_D = -88.5$ (*c*, 1.1, $CHCl_3$); IR 1751 cm^{-1}; ^1H NMR δ 4.73 (d, *J* = 5.8 Hz, 1H), 4.46 (ddd, *J* = 5.8, 1.8, 0.6 Hz, 1H), 3.60−4.25 (m, 8H), 1.61−2.05 (m, 8H); ^{13}C NMR δ 198.8, 120.3, 93.85, 78.97, 75.40, 67.16, 65.55, 60.45, 59.34, 37.47, 37.04, 23.71, 23.40. Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.62; H, 6.81.

Preparation of Ketone 2g. Alcohol **16g** was prepared in a way similar to that of alcohol **16b** using cyclohexanone (5.88 g, 61 mmol), trimethyl orthoformate (4.4 mL, 4.24 mmol), methanol (20 mL), $TsOH\cdot H_2O$ (0.05 g), alcohol **15** (8.24 g, 40 mmol), THF (100 mL), and 4 drops of 70% perchloric acid. Alcohol **16g** was obtained as a solid (7.64 g, 66%); mp 138.0−139.5 °C. $[\alpha]^{25}_D = -128.6$ (*c* 0.5, $CHCl_3$), IR 3452 cm^{-1}; ^1H NMR δ 4.23 (ddd, *J* = 5.7, 2.4, 0.6 Hz, 1H), 4.17 (dd, *J* = 6.9, 5.7 Hz, 1H), 4.10 (d, *J* = 13.2 Hz, 1H), 4.02 (ddd, *J* = 11.4, 11.1, 3.6 Hz, 1H), 3.92 (dd, *J* = 13.2, 2.4 Hz, 1H), 3.88 (d, *J* = 11.9 Hz, 1H), 3.78 (dd, *J* = 11.7, 3.6 Hz, 1H), 3.71 (ddd, *J* = 11.7, 11.4, 2.4 Hz, 1H), 3.65 (d, *J* = 11.9 Hz, 1H), 3.59 (dd, *J* = 11.1, 2.4 Hz, 1H), 3.43 (dd, *J* = 7.2, 6.9 Hz, 1H), 2.53 (d, *J* = 7.2 Hz, 1H), 1.76−1.58 (m, 8H), 1.43−1.38 (m, 2H); ^{13}C NMR δ 110.2, 95.05, 76.24, 73.21, 71.81, 68.95, 65.64, 60.34, 59.96, 37.93, 35.41, 25.11, 24.14, 23.78.

PCC (9.92 g, 46 mmol) oxidation of alcohol **16g** (5.76 g, 20 mmol) gave ketone **2g** as a white solid (4.98 g, 86%); mp 136.0−137.0 °C. $[\alpha]^{25}_D = -75.9$ (*c* 1, $CHCl_3$); IR 1750 cm^{-1}; ^1H NMR δ 4.73 (d, *J* = 5.6 Hz, 1H), 4.59 (dt, *J* = 5.6, 1.5 Hz, 1H), 4.19 (d, *J* = 1.5 Hz, 2H), 4.07 (td, *J* = 11.2, 3.2 Hz, 1H), 3.90 (d, *J* = 12.6 Hz, 1H), 3.60−3.84 (m, 3H), 3.76 (d, *J* = 12.6 Hz, 1H), 1.62 (m, 8H), 1.40 (m, 2H); ^{13}C NMR δ 199.5, 111.3, 93.93, 78.26, 75.28, 67.25, 65.55, 60.42, 59.53, 36.91, 35.61, 25.07, 24.05, 23.90. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.21; H, 7.03.

Preparation of Ketone 3a. *tert*-Butyldimethylsilyl chloride (22.61 g, 150 mmol) was added to a mixture of alcohol **14** (36.32 g, 150 mmol), dimethylaminopropylamine (DMAP) (1.0 g), and imidazole (10.8 g, 150 mmol) in DMF (200 mL) at room temperature. After being stirred overnight, the reaction mixture was concentrated to give a residue which was treated with ethyl acetate (400 mL). After filtration, the filtrate was dried (Na_2SO_4) and concentrated to give alcohol **17** as a syrup.

The syrup was mixed with acetone (800 mL), 2,2-dimethoxypropane (70 mL, 57 mmol), $CuSO_4$ (180 g), and concentrated H_2SO_4 (2.8 g). After being stirred at room temperature for 40 min, the reaction mixture was neutralized with Et_3N, filtered, and concentrated. The resulting residue was dissolved in ethyl acetate (300 mL), washed with brine, dried (Na_2SO_4), concentrated, and purified by flash chromatography (hexane:ether,

100:0 to 10:1, v/v) to give an alcohol as a syrup (21.28 g, 36%). $[\alpha]^{25}_D = -76.8$ (*c* 0.9, $CHCl_3$); IR 3500 cm^{-1}; ^1H NMR δ 4.34 (dd, *J* = 6.2, 6.0 Hz, 1H), 4.25 (ddd, *J* = 6.2, 2.4, 0.9 Hz, 1H), 4.05 (dd, *J* = 13.1, 2.4 Hz, 1H), 3.97 (dd, *J* = 6.0, 2.8 Hz, 1H), 3.64−3.89 (m, 7H), 3.20 (d, *J* = 2.5 Hz, 1H), 1.52 (s, 3H), 1.36 (s, 3H), 0.90 (s, 9H), 0.095 (s, 3H), 0.085 (s, 3H); ^{13}C NMR δ 109.3, 98.12, 75.45, 72.75, 70.45, 64.30, 61.47, 61.05, 43.33, 27.55, 25,99, 25.62, 18.36, −5.34, −5.39.

PCC (25.32 g, 117.5 mmol) oxidation of the above alcohol (20.25 g, 51 mmol) gave ketone **3a** as a syrup (15.86 g, 78%). $[\alpha]^{25}_D = -89.3$ (*c* 1, $CHCl_3$); IR 1757 cm^{-1}; ^1H NMR δ 4.85 (d, *J* = 5.8 Hz, 1H), 4.59 (dd, *J* = 5.8, 2.1 Hz, 1H), 4.38 (dd, *J* = 13.4, 2.1 Hz, 1H), 4.06 (dt, *J* = 10.5, 4.5 Hz, 1H), 4.06 (d, *J* = 13.4 Hz, 1H), 4.03 (d, *J* = 11.7 Hz, 1H), 3.91 (dt, *J* = 10.5, 6.3 Hz, 1H), 3.74 (d, *J* = 11.7 Hz, 1H), 3.71 (dd, *J* = 6.3, 4.5 Hz, 2H), 1.48 (s, 3H), 1.38 (s, 3H), 0.87 (s, 9H), 0.092 (s, 3H), 0.085 (s, 3H); ^{13}C NMR δ 198.7, 110.5, 99.53, 78.79, 76.12, 63.07, 61.53, 60.01, 43.29, 27.36, 26.24, 25.99, 18.47, −5.29, −5.41. Anal. Calcd for $C_{17}H_{31}O_6ClSi$: C, 51.69; H, 7.91. Found: C, 51.90; H, 8.03.

Preparation of Ketone 3b. To a solution of ketone **3a** (1.98 g, 5.0 mmol) in pyridine (2 mL) and water (2 mL) was added tetrabutylammonium fluoride (TBAF) (10 mL, 1 M in THF). After being stirred at room temperature for 15 min, the reaction mixture was poured into water (10 mL), extracted with chloroform, washed with brine, dried over sodium sulfate, concentrated, and purified by flash chromatography (hexane: ether, 10:1 to 1:1, v/v) to give ketone **3b** as a syrup (0.90 g, 64%). $[\alpha]^{25}_D = -134.7$ (*c* 1.6, $CHCl_3$); IR 3497, 1751 cm^{-1}; ^1H NMR δ 4.82 (d, *J* = 5.6 Hz, 1H), 4.58 (ddd, *J* = 5.6, 2.2, 1.0 Hz, 1H), 4.50 (dd, *J* = 13.3, 2.2 Hz, 1H), 4.12 (d, *J* = 13.3 Hz, 1H), 4.03 (dt, *J* = 10.5, 4.3 Hz, 1H), 3.86−3.98 (m, 2H), 3.68−3.78 (m, 1H), 3.75 (dd, *J* = 4.3, 1.0 Hz, 1H), 3.73 (d, *J* = 4.3 Hz, 1H), 2.23 (bs, 1H), 1.46 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 201.4, 110.6, 98.91, 78.11, 75.63, 62.84, 61.08, 59.67, 43.15, 27.36, 26.21. Anal. Calcd for $C_{11}H_{17}O_6Cl$: C, 47.07; H, 6.10. Found: C, 46.98; H, 6.18.

Preparation of Ketone 3c. To a mixture of ketone **3b** (1.40 g, 5 mmol), DMAP (0.20 g), and pyridine (6 mL) in dichloromethane (15 mL) was added acetic anhydride (4.0 mL, 42.4 mmol). After being stirred overnight, the reaction mixture was poured into ice water (20 mL), extracted with dichloromethane, washed with brine, dried over sodium sulfate, concentrated, and purified by flash chromatography to give ketone **3c** as a syrup (0.89 g, 55%). $[\alpha]^{25}_D = -120.0$ (*c* 0.5, $CHCl_3$); IR 1752 cm^{-1}; ^1H NMR δ 4.82 (d, *J* = 5.9 Hz, 1H), 4.60 (ddd, *J* = 5.9, 2.0, 0.9 Hz, 1H), 4.43 (d, *J* = 12.3 Hz, 1H), 4.40 (dd, *J* = 13.5, 2.0 Hz, 1H), 4.32 (d, *J* = 12.3 Hz, 1H), 4.13 (d, *J* = 13.5, Hz, 1H), 3.80−4.00 (m, 2H), 3.68−3.75 (m, 2H), 2.08 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 198.1, 170.3, 110.8, 98.81, 78.05, 75.63, 62.87, 60.76, 60.00, 42.94, 27.24, 26.21, 20.94. Anal. Calcd for $C_{13}H_{19}O_7Cl$: C, 48.38; H, 5.93. Found: C, 48.45; H, 6.23.

Preparation of Ketone 4a. Ketone **4a** was prepared on the basis of a reported procedure;[12] mp 100.0−101.0 °C. $[\alpha]^{25}_D = -194.6$ (*c* 0.5, $CHCl_3$); IR 1749 cm^{-1}; ^1H NMR δ 4.71 (s, 1H), 4.69 (d, *J* = 5.7 Hz, 1H), 4.54 (ddd, *J* = 5.7, 1.9, 1.3 Hz, 1H), 4.24 (dd, *J* = 12.7, 1.9 Hz, 1H), 4.08 (dd, *J* = 12.7, 1.3 Hz, 1H), 3.49 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H); ^{13}C NMR δ 199.0, 110.7, 101.1, 78.70, 75.61, 58.60, 55.93, 27.36, 26.32. HRMS. Calcd for $C_9H_{15}O_5$ ($M^+ + 1$). 203.0919. Found: 203.0924.

Preparation Of Ketone 4b. Concentrated H_2SO_4 (0.1 g) was added to a mixture of 2-chloroethyl arabinoside **18b**[11c] (6.02 g, 31 mmol), 1,1-dimethoxypropane (5 mL, 4.35 g, 41 mmol), and $CuSO_4$ (10 g) in acetone (100 mL). After being stirred overnight, the reaction mixture was filtered, concentrated, purified by flash chromatography (hexane:ether, 20:1 to 2:1, v/v) to give an alcohol as a white solid (5.87 g, 81%); mp 69.5−71.0 °C. $[\alpha]^{25}_D = -171.0$ (*c* 0.6, $CHCl_3$); IR 3449 cm^{-1}; ^1H NMR δ 4.87 (d, *J* = 3.9 Hz, 1H), 4.25 (ddd, *J* = 6.0, 2.4, 1.2 Hz, 1H), 4.21 (t, *J* = 6.0, Hz, 1H), 4.05 (dd, *J* = 13.2, 2.4 Hz, 1H), 4.01 (dt, *J* = 11.1, 5.4 Hz, 1H), 3.91 (dd, *J* = 13.2, 1.2 Hz, 1H), 3.81 (dd, *J* = 6.0, 4.8 Hz, 1H), 3.75−3.85 (m, 1H), 3.70 (m, 2H), 2.29 (br s, 1H), 1.53 (s, 3H), 1.37 (s, 3H); ^{13}C NMR δ 109.4, 98.17, 75.89, 72,98, 70.02, 68.46, 60.14, 43.01, 28.02, 26.04.

PCC (13.58 g, 63 mmol) oxidation of the above alcohol (5.87 g, 23.2 mmol) gave ketone **4b** as a white solid (1.63 g, 28%) (recrystallized from diisopropyl ether); mp 64.0−65.0 °C. $[\alpha]^{25}_D = -165.0$ (*c* 1, $CHCl_3$); IR 1734 cm^{-1}; ^1H NMR δ 4.87 (s, 1H), 4.72 (d, *J* = 5.6 Hz, 1H), 4.56 (ddd, *J* = 5.6, 2.1 Hz, 1H), 4.39 (dd, *J* = 13.4, 2.1 Hz, 1H), 4.10 (d, *J* = 13.4 Hz, 1H), 4.03 (dt, *J* = 11.0, 5.9 Hz, 1H), 3.85 (dt, *J* = 11.0, 4.9 Hz, 1H), 3.70 (dd, *J* = 5.9, 4.9 Hz, 2H), 1.47 (s, 3H), 1,40 (s, 3H); ^{13}C NMR δ 198.5, 110.8, 100.1, 77.66, 75.52, 68.81, 59.06, 42.67, 27.36, 26.31. Anal. Calcd for $C_{10}H_{15}O_5Cl$: C, 47.91; H, 6.03. Found: C, 48.00; H, 6.24.

Preparation of Ketone 5. To a mixture of PDC (15 g, 40 mmol) and powdered molecular sieve (15 g) in CH_2Cl_2 (100 mL) was added a solution of alcohol **19** (1.6 g, 8.0 mmol) (prepared from D-mannose on the basis of a reported procedure[13]) in CH_2Cl_2 (30 mL). Upon stirring for 4 h, the reaction mixture was filtered through Celite, concentrated, and recrystallized from ether−hexane to give ketone **5** as clear needles (0.81 g, 47%); mp 80.5−82.0 °C. $[\alpha]^{25}_D = -74.3$ (*c* 0.3, $CHCl_3$); IR 1747 cm^{-1}; ^1H NMR δ 5.65 (d, *J* = 3.1 Hz, 1H), 4.61 (d, *J* = 5.6 Hz, 1H), 4.52 (dd, *J* = 7.6, 3.1 Hz, 1H), 4.47 (d, *J* = 7.6 Hz, 1H), 4.04 (d, *J* = 7.9 Hz, 1H), 3.90 (dd, *J* = 7.9, 5.6, Hz, 1H), 1.53 (s, 3H), 1.37 (s, 3H); ^{13}C NMR δ 201.4, 113.3, 99.58, 77.23, 76.59, 75.77, 67.27, 26.42, 25.67. HRMS. Calcd for $C_9H_{13}O_5$ ($M^+ + 1$): 201.0763. Found: 201.0766.

Preparation of Ketone 6. To a solution of 1,2:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (1.3 g, 5 mmol) (see ref 4c) in dry CH_2Cl_2 (10 mL) were added 3A molecular sieve powder (1.7 g) and PCC (2.2 g, 10 mmol). Upon stirring at room temperature for 30 min, the reaction mixture was diluted with ether (50 mL), filtered through a glass funnel with a thin silica gel layer, and washed with ether. The filtrate was concentrated and purified by flash chromatography (hexane:ethyl acetate, 2:1) to give a syrup (1 g) which was recrystallized from hexane to afford ketone **6** as white crystals (0.8 g, 57%); mp 82−84 °C. $[\alpha]^{25}_D = -48.4$ (*c* 0.71, $CHCl_3$); IR and NMR data showed ketone **6** existed in hydrate form; IR 3385, 1785 cm^{-1}; ^1H NMR δ 4.42 (d, *J* = 9.6 Hz, 1H), 4.35 (br s, 1H, OH), 3.90−4.13 (m, 5H), 3.61 (br s, 1H, OH), 1.54, 1.47, 1.44, 1.42 (s, each 3H); ^{13}C NMR δ 111.2, 111.2, 100.3, 98.24, 72.86, 71.16, 70.33, 60.91, 28.91, 26.5, 25.65, 19.52. Anal. Calcd for $C_{11}H_{16}O_6 \cdot 0.5H_2O$: C, 52.16; H, 6.76. Found: C, 52.11; H, 7.01.

Preparation of Ketone 23.[17−19] To a mixture of diol **21**[17] (15.23 g, 52 mmol), PPh_3 (51.96 g, 198 mmol), imidazole (26.21 g, 385 mmol), and zinc (0.2 g) in toluene (250 mL) was added I_2 (26.21 g, 103 mmol) over 45 min under refluxing. After 1 h another batch of zinc (0.2 g) was added. Upon stirring for an additional 3.5 h, the reaction mixture was cooled, filtered, concentrated, and purified by flash chromatography to give compound **22** (10.28 g 76%) as a syrup which solidified in the refrigerator. $[\alpha]^{25}_D = +14.3$ (*c* 0.6, $CHCl_3$); IR 3063, 3033, 2987, 2936, 2884, 2854, 1654, 1606, 1497, 1454, 1382 cm^{-1}; ^1H NMR δ 7.30 (m, 5H), 5.87 (m, 2H), 4.76 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.35 (m, 1H), 4.02−4.10 (m, 2H), 4.01 (d, *J* = 8.7 Hz, 1H), 3.87 (d, *J* = 8.7 Hz, 1H), 1.54 (s, 3H), 1.45 (s, 3H); ^{13}C NMR δ 128.6, 128.1, 128.0, 127.8, 123.9, 114.2, 112.2, 102.6, 72.13, 71.29, 70.40, 61.75, 27.50. 26.21.

Compound **22** (2.09 g, 8 mmol) was hydrogenated[19] in MeOH (50 mL) using Raney Ni (10 g) under H_2 at room temperature for 24 h. The reaction mixture was filtered, concentrated, and purified by flash chromatography (Et_2O:hexanes, 1:8 to 1:2) to give an alcohol (1.05 g, 69%) as a syrup which solidified in the refrigerator. $[\alpha]^{25}_D = -89.8$ (*c* 0.3, $CHCl_3$); IR 3460 cm^{-1}; ^1H NMR δ 4.18 (d, *J* = 8.8 Hz, 1H), 3.89 (d, *J* = 8.8 Hz, 1H), 3.78 (td, *J* = 11.4, 3.1 Hz, 1H), 3.63 (ddt, *J* = 11.2, 4.5, 1.6 Hz, 1H), 3.48 (dd, *J* = 11.4, 5.5 Hz, 1H), 2.03, (m, 1H), 1.56−1.77 (m, 4H), 1.53 (s, 3H), 1.44 (s, 3H); ^{13}C NMR δ 111.5, 105.4, 72.44, 67.74, 61.54, 29.83, 26.83, 26.71, 25.22.

To a mixture of the above alcohol (0.9 g, 4.8 mmol), molecular sieve (5.5 g) in CH_2Cl_2 (20 mL) was added PCC (2.78 g, 12.9 mmol) over 20 min. Upon stirring at room temperature for 3 h, the reaction mixture was diluted with ether and

filtered through silicon gel and Celite to give ketone **23** as a liquid (0.72 g, 81%). $[\alpha]^{25}_D = -62.3$ (*c* 0.7, $CHCl_3$); IR 1734 cm^{-1}; ^1H NMR δ 4.60 (d, J = 9.2 Hz, 1H), 4.23 (td, *J* = 11.6, 3.1 Hz, 1H), 3.84 (d, *J* = 9.2 Hz), 3.80 (m, 1H), 2.82 (ddd, *J* = 14.7, 12.7, 6.7 Hz, 1H), 2.52 (m, 1H), 2.00−2.25 (m, 2H), 1.54 (s, 3H), 1.38 (s, 3H); ^{13}C NMR δ 200.9, 113.1, 104.5, 70.19, 61.4, 36.74, 27.98, 26.88, 26.30. HRMS. Calcd for $C_9H_{15}O_4$ ($M^+ + 1$): 187.0970. Found: 187.0975.

General Epoxidation Procedure. To a 100 mL three-neck round-bottom flask, were added buffer (0.05 M $Na_2B_4O_7 \cdot 10H_2O$ in 4×10^{-4} M aqueous Na_2EDTA, 10 mL), acetonitrile (15 mL), *trans*-β-methylstyrene (0.118 g, 1 mmol), tetrabutylammonium hydrogen sulfate (0.015 g, 0.04 mmol), and ketone **1a** (0.0774 g, 0.3 mmol). The reaction mixture was cooled by an ice bath. A solution of Oxone (0.85 g, 1.38 mmol) in aqueous Na_2EDTA (4×10^{-4} M, 6.5 mL) and a solution of K_2CO_3 (0.8 g, 5.8 mmol) in water (6.5 mL) were added dropwise through two syringe pumps or two separate addition funnels over a period of 1.5 h (under this condition, the reaction pH is around 10.5. It is recommended that both Oxone and K_2CO_3 be added uniformly over 1.5 h). At this point, the reaction was immediately quenched by addition of pentane and water. The mixture was extracted with pentane (3×30 mL), washed with brine, dried over Na_2SO_4, purified by flash chromatography [the silica gel was buffered with 1% Et_3N in pentane, pentane: ether (1:0 to 50:1, v/v) was used as eluent] to afford *trans*-β-methylstyrene oxide as colorless liquid (0.124 g, 93% yield, 92% ee).

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