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A Diacetate Ketone-Catalyzed Asymmetric Epoxidation of Olefins

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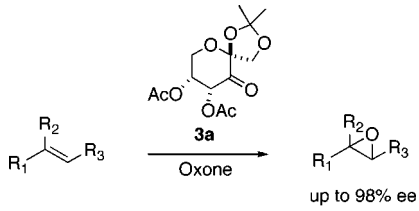
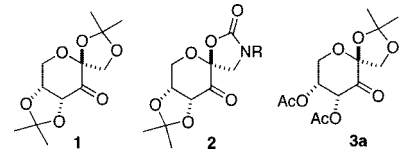


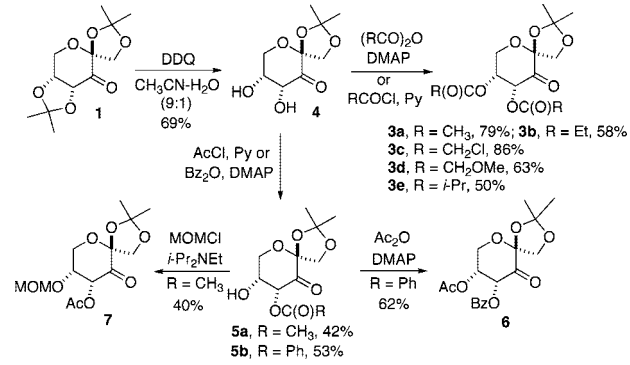
A fructose-derived diacetate ketone has been shown to be an effective catalyst for asymmetric epoxidation. High ee values have been obtained for a variety of trans and trisubstituted olefins including electron-deficient α,β-unsaturated esters as well as certain cis olefins.

Chiral ketones of various structures have been extensively investigated for asymmetric epoxidation of olefins in a number of laboratories.[1] In our studies, we have found that fructose-derived ketone **1** provides high ee values for a wide variety of trans and trisubstituted olefins,[2] and oxazolidinone ketone **2** can give high ee values for olefins which had not been effective with ketone **1**, including various cis olefins,[3a,c−e,g,k,l] styrenes,[3b−d,f] and certain trisubstituted[3h,j] and tetrasubstituted olefins.[3i,j] In our efforts to expand the substrate scope, we have reported that ketone **3a** is an effective epoxidation catalyst for a variety of electron-deficient α,β-unsaturated esters.[4] Replacing the fused ketal of **1** with more electron-withdrawing diacetates significantly enhances the ketone's reactivity and possibly reduces the decomposition via Baeyer−Villiger oxidation. Herein we wish to report our detailed studies on epoxidations with ketone **3a** and its related analogues.



Ketone **3a** can be synthesized from ketone **1** in two steps by selective deketalization with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[5] and subsequent acetylation with Ac_2O and a catalytic amount (2 mol %) of DMAP (Scheme 1).[4]

SCHEME 1



Ketone **3a** is highly electrophilic and can easily form a hydrate with water.[6] With this method, ketone **3a** can be obtained largely in ketone form by avoiding moisture. The β-acetate of ketone **3a** is prone to elimination to form an enone. To minimize this elimination, it is crucial to use only a small amount of DMAP (ca. 2 mol %) and to carefully control the reaction time in the acetylation step. Nevertheless, it was found that the resulting enone was barely active and had little impact on the asymmetric epoxidation. Alternatively, ketone **3a** can be readily prepared in hydrate form from ketone **1** by one-pot deketalization and acetylation with

(1) For leading reviews, see: (a) Denmark, S. E.; Wu, Z. *Synlett* **1999**, 847. (b) Frohn, M.; Shi, Y. *Synthesis* **2000**, 1979. (c) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488. (d) Yang, D. *Acc. Chem. Res.* **2004**, *37*, 497. (e) Wong, O. A.; Shi, Y. *Chem. Rev.* **2008**, *108*, 3958.

(2) (a) Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 9806. (b) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11224. (c) Shu, L.; Shi, Y. *Tetrahedron* **2001**, *57*, 5213.

(3) (a) Tian, H.; She, X.; Shu, L.; Yu, H.; Shi, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11551. (b) Tian, H.; She, X.; Xu, J.; Shi, Y. *Org. Lett.* **2001**, *3*, 1929. (c) Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435. (d) Shu, L.; Wang, P.; Gan, Y.; Shi, Y. *Org. Lett.* **2003**, *5*, 293. (e) Shu, L.; Shi, Y. *Tetrahedron Lett.* **2004**, *45*, 8115. (f) Goeddel, D.; Shu, L.; Yuan, Y.; Wong, O. A.; Wang, B.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 1715. (g) Wong, O. A.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 3973. (h) Shen, Y.-M.; Wang, B.; Shi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 1429. (i) Shen, Y.-M.; Wang, B.; Shi, Y. *Tetrahedron Lett.* **2006**, *47*, 5455. (j) Wang, B.; Shen, Y.-M.; Shi, Y. *J. Org. Chem.* **2006**, *71*, 9519. (k) Burke, C. P.; Shi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4475. (l) Burke, C. P.; Shi, Y. *J. Org. Chem.* **2007**, *72*, 4093.

(4) Wu, X.-Y.; She, X.; Shi, Y. *J. Am. Chem. Soc.* **2002**, *124*, 8792.

(5) For leading references, see: (a) Fernandez, J. M. G.; Mellet, C. O.; Marin, A. M.; Fuentes, J. *Carbohydr. Res.* **1995**, *274*, 263. (b) Tu, Y.; Wang, Z.-X.; Frohn, M.; He, M.; Yu, H.; Tang, Y.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 8475.

(6) For other examples on ketone/hydrate, see: (a) Denmark, S. E.; Forbes, D. C.; Hays, D. S.; DePue, J. S.; Wilde, R. G. *J. Org. Chem.* **1995**, *60*, 1391. (b) Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem.* **1997**, *62*, 8288. (c) Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1997**, *62*, 8622. (d) Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S.-G.; Jin, B. W. *Tetrahedron: Asymmetry* **1997**, *8*, 2921. (e) Denmark, S. E.; Wu, Z. *J. Org. Chem.* **1998**, *63*, 2810. (f) Yang, D.; Yip, Y.-C.; Tang, M.-W.; Wong, M.-K.; Cheung, K.-K. *J. Org. Chem.* **1998**, *63*, 9888. (g) Yang, D.; Yip, Y.-C.; Jiao, G.-S.; Wong, M.-K. *J. Org. Chem.* **1998**, *63*, 8952. (h) Reference 5b. (i) Armstrong, A.; Hayter, B. R. *Tetrahedron* **1999**, *55*, 11119. (j) Carnell, A. J.; Johnstone, R. A. W.; Parsy, C. C.; Sanderson, W. R. *Tetrahedron Lett.* **1999**, *40*, 8029. (k) Reference 1a. (l) Wang, Z.-X.; Miller, S. M.; Anderson, O. P.; Shi, Y. *J. Org. Chem.* **1999**, *64*, 6443. (m) Armstrong, A.; Washington, I.; Houk, K. N. *J. Am. Chem. Soc.* **2000**, *122*, 6297. (n) Tian, H.; She, X.; Shi, Y. *Org. Lett.* **2001**, *3*, 715. (o) Stearman, C. J.; Behar, V. *Tetrahedron Lett.* **2002**, *43*, 1943. (p) Reference 3c. (q) Shu, L.; Shen, Y.-M.; Burke, C.; Goeddel, D.; Shi, Y. *J. Org. Chem.* **2003**, *68*, 4963. (r) Chan, W.-K.; Yu, W.-Y.; Che, C.-M.; Wong, M.-K. *J. Org. Chem.* **2003**, *68*, 6576. (s) Crane, Z.; Goeddel, D.; Gan, Y.; Shi, Y. *Tetrahedron* **2005**, *61*, 6409.

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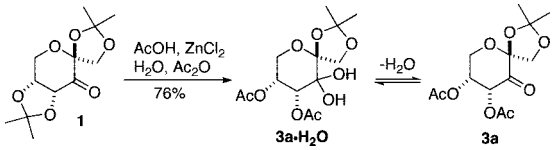
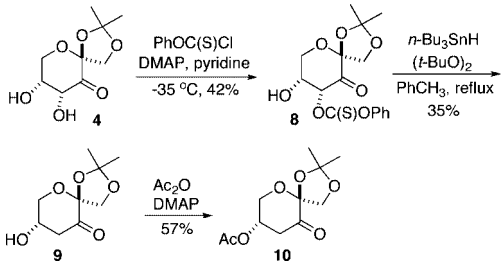
$ZnCl_2$, AcOH, and Ac_2O in water (Scheme 2).[7−9] However, if ketone **3a** is desired, it can be obtained from **3a**·H_2O by simply dissolving **3a**·H_2O in solvents such as EtOAc and stirring with Na_2SO_4 overnight at rt, followed by filtration

SCHEME 2



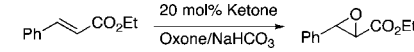
and concentration or by passing **3a**·H_2O through a short column of silica gel. In $CDCl_3$, the hydrate gradually converted into the ketone as judged by ^1H NMR (25% ketone at 10 min, 50% ketone at 30 min, 67% ketone at 1 h, 90% ketone at 2 h, 100% ketone at 11 h). In CD_3CN-D_2O (1.5:1, v/v), ca. 21% of the ketone was formed from the hydrate at 1 h (ca. 22% at 7 h). When the ketone was subjected to the same solvent mixture, ca. 26% of the ketone remained at 1 h (ca. 25% at 7 h). It appears that a similar amount of the ketone was present at around 1 h regardless of whether the ketone or its hydrate was used. Similar conversions and ee values were also obtained for the epoxidation with ethyl *trans*-cinnamate as test substrate when either the ketone or its hydrate was used. In addition to ketone **3a**, several analogues including diesters **3b−e** and **6**, as well as monoester ketones **5**, **7**, and **10**, were also prepared for the epoxidation studies (Schemes 1 and 3).

SCHEME 3



Ethyl *trans*-cinnamate was used for initial epoxidations with each of these ketones (20 mol %). As shown in Table 1, diacetate ketone **3a** was found to be among the most effective ketones in terms of both conversion and enantioselectivity. Various α,β-unsaturated esters were subsequently examined with ketone **3a** (20−30 mol %). As shown in Table 2, high ee values were obtained for substituted cinnamates and a variety of trisubstituted α,β-unsaturated esters (for more examples, see ref 4). While certain enones could give good

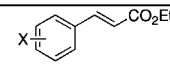
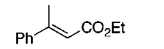
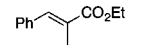
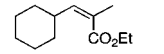
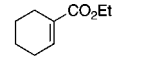
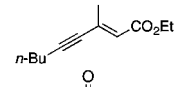
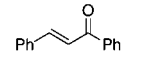
TABLE 1. Asymmetric Epoxidation of Ethyl *trans*-Cinnamate with Ketones 3, 5a, 6, 7, and 10[a]



entry	ketone	conv (%)	ee (%)
1[b]	**3a**	47	95
2[b]	**3b**	27	94
3[b]	**3c**	16	94
4[b]	**3d**	34	94
5[b]	**3e**	10	90
6[b]	**5a**	1	29
7[b]	**6**	10	91
8[b]	**7**	4	62
9[c]	**10**	5	42

[a] Method A: All reactions were carried out with substrate (0.5 mmol), ketone (0.1 mmol), Bu_4NHSO_4 (0.03 mmol), Oxone (2.5 mmol), and $NaHCO_3$ (7.75 mmol) in CH_3CN−aq. Na_2(EDTA) (4×10^{-4} M) (6.25 mL) (v/v, 1.5/1). A mixture of Oxone and $NaHCO_3$ was added portionwise over 4.5 h at 0 °C with stirring then for an additional 5.5 h at 0 °C. For entry 8, a mixture of Oxone and $NaHCO_3$ was added portionwise over 4.5 h at 0 °C with stirring then for an additional 7.5 h at 0 °C and for 12 h at room temperature. [b] The conversion and ee were determined by chiral GC (Chiraldex G-TA). [c] The conversion and ee were determined by chiral GC (Chiraldex B-DM).

TABLE 2. Asymmetric Epoxidation of Olefins Catalyzed by Ketone 3a[a]

entry	substrate	yield (%)[b]	ee (%)	config.[j]
				
1[c]	X = H	73	96[f]	(+)-(2*S*,3*R*)[6c,11]
2[d]	X = *p*-Me	91	97[g]	(+)
3[e]	X = *p*-OMe	57	90[h]	(+)-(2*S*,3*R*)[12]
4[d]		93	96[i]	(+)-(2*S*,3*R*)[13]
5[c]		45	86[g]	(+)
6[c]		77	89[f]	(+)
7[d]		77	93[f]	(+)
8[d]		74	98[h]	(+)
9[c]		42	82[i]	(+)-(2*S*,3*R*)[14]

[a] Method A: All reactions were carried out with substrate (0.5 mmol), ketone **3a** (0.1−0.15 mmol), Bu_4NHSO_4 (0.03 mmol), Oxone (2.5 mmol), and $NaHCO_3$ (7.75 mmol) in CH_3CN−aq. Na_2(EDTA) (4×10^{-4} M) (6.25 mL) (v/v, 1.5/1). A mixture of Oxone and $NaHCO_3$ was added portionwise over 4.5 h at 0 °C with stirring then for an additional 7.5 h at 0 °C and for 12 h at rt. For entry 3 a mixture of Oxone and $NaHCO_3$ was added portionwise over 4.5 h at 0 °C and with stirring then for an additional 7.5 h at 0 °C. [b] Isolated yields. [c] 0.15 mmol **3a** used. [d] 0.125 mmol **3a** used. [e] 0.10 mmol **3a** used. [f] Determined by chiral GC (Chiraldex G-TA). [g] Determined by chiral HPLC (Chiralpak AD). [h] Determined by chiral HPLC (Chiralcel OD). [i] Determined by chiral HPLC (Chiralcel OB). [j] Determined by comparing the measured optical rotations with the reported ones.

(7) For a leading reference on selective deketalization with aqueous AcOH, see: Kang, J.; Lim, G. J.; Yoon, S. K.; Kim, M. Y. *J. Org. Chem.* **1995**, *60*, 564.
(8) For a leading reference on Lewis acid-catalyzed acetylation, see: Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *J. Org. Chem.* **2001**, *66*, 8926.
(9) For a related two-step procedure with AcOH−H_2O, Ac_2O−$ZnCl_2$ from ketone **1**, see: Nieto, N.; Molas, P.; Benet-Buchholz, J.; Vidal-Ferran, A. *J. Org. Chem.* **2005**, *70*, 10143.
(10) For leading reviews on various effective asymmetric epoxidation of electron-deficient olefins see: (a) Porter, M. J.; Skidmore, J. *Chem. Commun.* **2000**, 1215. (b) Lauret, C.; Roberts, S. M. *Aldrichim. Acta* **2002**, *35*, 47. (c) Kelly, D. R.; Roberts, S. M. *Biopolymers* **2006**, *84*, 74. (d) Shibasaki, M.; Kanai, M.; Matsunaga, S. *Aldrichim. Acta* **2006**, *39*, 31. (e) Díez, D.; Núñez, M. G.; Antón, A. B.; García, P.; Moro, R. F.; Garrido, N. M.; Marcos, I. S.; Basabe, P.; Urones, J. G. *Curr. Org. Synth.* **2008**, *5*, 186. (f) Lattanzi, A. *Curr. Org. Synth.* **2008**, *5*, 117.
(11) Cabon, O.; Buisson, D.; Larcheveque, M.; Azerad, R. *Tetrahedron: Asymmetry* **1995**, *6*, 2211.
(12) Yamamoto, M.; Hayashi, M.; Masaki, M.; Nohira, H. *Tetrahedron: Asymmetry* **1991**, *2*, 403.
(13) Abidi, S. L.; Wolfhagen, J. L. *J. Org. Chem.* **1979**, *44*, 433.
(14) Bougauchi, M.; Watanabe, S.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1997**, *119*, 2329.

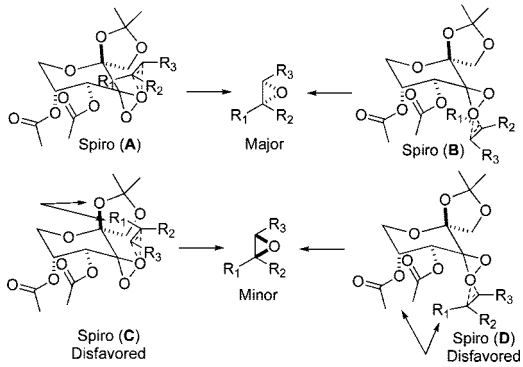


FIGURE 1. Possible competing spiro transition states for the epoxidation of trans and trisubstituted olefins with ketone **3a**.

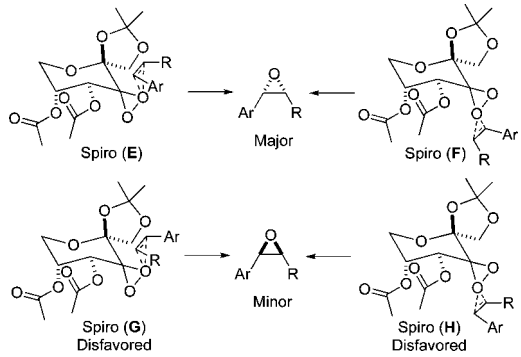
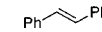
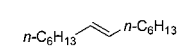
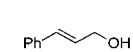
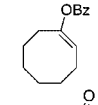
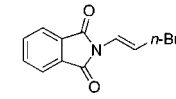
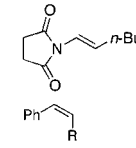
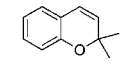
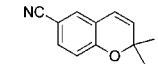
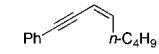
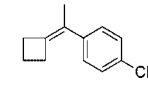


FIGURE 2. Possible competing spiro transition states for the epoxidation of cis olefins with ketone **3a**.

ee values (Table 2, entry 9), ketone **3a** is less effective for enones in general.[10]

The epoxidation with other types of olefins was also investigated.[15] Studies with *trans*-β-methylstyrene showed that a smaller amount of ketone catalyst (10 mol %) was required when the epoxidation was carried out at a slightly higher pH (around 8.75 to 9.50) with slow addition of Oxone and K_2CO_3 solutions (method B). This protocol is usually effective for relatively reactive substrates. The epoxidation with ketone **3a** gave good to high ee values for various trans and trisubstituted olefins including less reactive trans enimides (Table 3, entries 1−9). High ee values were obtained for certain cis olefins such as aromatic conjugated olefins with bulky R groups (Table 3, entries, 14−17). Low ee values were obtained for terminal and tetrasubstituted olefins tested (Table 3, entries 19−21). Figures 1 and 2 list a few possible competing spiro transition states for trans, trisubstituted, and cis olefins.[16] On the basis of the determined configurations of some epoxide products in Tables 2 and 3, the epoxidation for trans and trisubstituted olefins likely proceeds via spiro transition state **A** with possible contribution from **B** (Figure 1) (at least in these cases). For conjugated aromatic cis olefins, the epoxidation appears to proceed via spiro transition state **E** with possible contribution from **F** based on the configurations determined (Table 3).

TABLE 3. Asymmetric Epoxidation of Olefins Catalyzed by Ketone 3a[a,b]

entry	substrate	method (h)	yield[c] (ee) (%)	config.[d]
1		A (24)	75 (86[e])	(+)-(*R*,*R*)[2b]
		B (8)	81 (86[e])	
2		A (24)	68 (92[f])	(+)-(*R*,*R*)[2b]
		B (16)	63 (93[f])	
3		B (8)	53 (88[g])	(+)-(*R*,*R*)[2b]
4		B (8)	73 (79[f])	(+)-(*R*,*R*)[17]
5		A (24)	93 (86[f])	(+)-(*R*,*R*)[2b]
		B (8)	46 (88[f])	
6		A (24)	92 (92[e])	(+)-(*R*,*R*)[2b]
		B (8)	82 (92[e])	
7		B (8)	97 (95[f])	(+)-(*R*,*R*)[18]
8		A (14)	95 (75[h])	(+)
9		A (14)	78 (86[e])	(+)
10	R = Me	B (8)	81 (49[e])	(+)-(1*S*,2*R*)[3c]
11	R = CH_2OH	B (8)	85 (47[i])	(+)-(2*R*,3*S*)[19]
12	R = CH_2OTBS	B (8)	62 (70[e])	(+)
13	R = CH_2TMS	B (8)	81 (65[e])	(+)
14	R = TMS	B (8)	54 (80[e])	(+)
15	R = TBS	B (24)	60 (90[e])	(+)
16		B (8)	75 (88[f])	(-)-(*S*,*S*)[3g]
17		B (8)	73 (90[f])	(-)-(*S*,*S*)[3g]
18		B (8)	50 (62[e])	(+)-(2*R*,3*S*)[31]
19		B (8)	77 (27[e])	(-)-(*S*)[2b]
20		B (8)	72 (6[f])	(+)-(*S*)[20]
21		B (8)	63 (67[e])	(-)-(*S*)[3i]

[a] Method A: All reactions were carried out with olefin (0.5 mmol), ketone **3a** (0.125 mmol), Bu_4NHSO_4 (0.03 mmol), Oxone (2.5 mmol), and $NaHCO_3$ (7.75 mmol) in CH_3CN−aq. Na_2(EDTA) (4×10^{-4} M) (6.25 mL) (v/v, 1.5/1). For entries 1, 2, 5, and 6, a mixture of Oxone and $NaHCO_3$ was added portionwise over 4.5 h at 0 °C with stirring then for an additional 7.5 h at 0 °C and for 12 h at rt. For entries 8 and 9, a mixture of Oxone and $NaHCO_3$ was added portionwise over 3 h at 0 °C with stirring for another 11 h at 0 °C. [b] Method B: All epoxidations were carried out with substrate (0.5 mmol), ketone **3a**·H_2O (0.046 mmol) (0.1 mmol for entries 14 and 15), Oxone (1.01 mmol), and K_2CO_3 (2.02 mmol) in CH_3CN−DMM (9 mL) (v/v, 1/2), and buffer (0.05 M Na_2HPO_4/0.05 M KH_2PO_4, pH 7.0, 3 mL) at 0 °C for 8, 16, or 24 h. [c] Isolated yields. [d] Determined by comparing the measured optical rotations with the reported ones. [e] Determined by chiral GC (Chiraldex B-DM). [f] Determined by chiral HPLC (Chiralcel OD). [g] The epoxide was opened (NaOMe−MeOH), the resulting alcohol was converted to its benzoate, enantioselectivity was determined by chiral HPLC (Chiralcel OD-H). [h] Determined by chiral HPLC (Chiralpak AD-H). [i] Determined by chiral HPLC (Chiralcel OD-H).

(15) For recent epoxidation examples catalyzed by ketone **3a**, see: (a) ref 9. (b) Nieto, N.; Munslow, I. J.; Fernández-Pérez, H.; Vida-Ferran, A. *Synlett* **2008**, 2856. (c) Hirooka, Y.; Nitta, M.; Furuta, T.; Kan, T. *Synlett* **2008**, 3234.

(16) Some planar transition states may also be competing. However, the extent of their involvement awaits further studies.

(17) Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 3099.

(18) Zhu, Y.; Shu, L.; Tu, Y.; Shi, Y. *J. Org. Chem.* **2001**, *66*, 1818.

(19) Denis, J. N.; Greene, A. E.; Serra, A. A.; Luche, M. J. *J. Org. Chem.* **1986**, *51*, 46.

(20) Capriati, V.; Florio, S.; Luisi, R.; Salomone, A. *Org. Lett.* **2002**, *4*, 2445.

In summary, several fructose-derived diester and monoester ketones were investigated for asymmetric epoxidation. Diacetate ketone **3a** has been found to be the most effective catalyst among those ketones investigated. High ee values have been obtained for a variety of trans and trisubstituted olefins as well as certain cis olefins. While it is generally less enantioselective than ketone **1** for trans and trisubstituted olefins and less enantioselective than ketone **2** for cis olefins, ketone **3a** is more effective than **1** and **2** for electron-deficient olefins, thus providing a complementary epoxidation system to ketones **1** and **2**. Future efforts will be devoted to further understanding the structural effect of ketones on catalysis and developing more effective catalytic systems.

Experimental Section

Representative Synthesis of Ketone 3a. To a solution of ketone **1** (6.90 g, 26.7 mmol) in CH_3CN-H_2O (v/v, 9/1) (90 mL) was added DDQ (0.60 g, 2.60 mmol) at rt. Upon being stirred at rt for 7 h, the reaction mixture was concentrated, dissolved in EtOAc (80 mL), dried (Na_2SO_4), filtered, concentrated, and purified by flash chromatography (silica gel, hexane/EtOAc = 1/0 to 1/1) to give **4** as a white solid (4.00 g, 69% yield). Mp 107−110 °C; $[\alpha]^{25}_D$ −140.0 (*c* 0.80, MeOH); IR (film) 3469, 3402, 1747 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.74 (d, J = 4.2 Hz, 1H), 4.68 (d, J = 9.6 Hz, 1H), 4.39 (m, 1H), 4.32 (d, J = 12.9 Hz, 1H), 4.00 (d, J = 9.6 Hz, 1H), 3.98 (dd, J = 12.9, 2.4 Hz, 1H), 3.29 (m, 2H), 1.54 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 113.6, 104.5, 74.4, 73.8, 69.7, 63.6, 26.6, 26.4.

To a solution of **4** (3.51 g, 16.10 mmol) and DMAP (0.039 g, 0.32 mmol) in dry DCM (150 mL) was added dropwise Ac_2O (4.97 g, 48.70 mmol) at 0 °C over 20 min. After being stirred at rt for 16 h (monitored by TLC), the reaction mixture was filtered through a short silica gel column. The filtrate was concentrated and purified by flash chromatography (silica gel, hexane/EtOAc = 1/0 to 3/1) to give ketone **3a** as colorless syrup (3.84 g, 79% yield). $[\alpha]^{25}_D$ −103.0 (*c* 0.98, $CHCl_3$); IR (film) 1750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 (d, J = 3.9 Hz, 1H), 5.62−5.60 (m, 1H), 4.70 (d, J = 9.6 Hz, 1H), 4.44 (d, J = 13.2 Hz, 1H), 3.99 (d, J = 9.6 Hz, 1H), 3.96 (dd, J = 13.2, 2.1 Hz, 1H), 2.18 (s, 3H), 2.13 (s, 3H), 1.55 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.0, 170.4, 169.6, 114.1, 105.2, 74.2, 72.3, 69.6, 62.7, 26.6, 26.2, 21.0, 20.6; HRMS calcd for $C_{13}H_{19}O_8$ (M + 1) 303.1080, found 303.1087.

One-Pot Synthesis of Ketone 3a. AcOH (17.5 mL) and deionized water (4.3 mL) were added to a mixture of ketone **1** (12.90 g, 50.0 mmol) and $ZnCl_2$ (0.17 g, 1.25 mmol) in a 250 mL round-bottomed flask equipped with a Teflon-coated magnetic stir bar. After the resulting suspension was stirred at rt for 8−10 h, Ac_2O (64.9 g, 635.8 mmol) was added into the reaction flask. After the resulting mixture was stirred at rt for 16 h, deionized water (30 mL) was added. After being stirred at rt for 20 min, the reaction mixture was concentrated in vacuo (130 mmHg, 55 °C) until about 20 mL of solution remained. The resulting solution was transferred to a 100 mL beaker, and 10 mL of deionized water was used to rinse the flask and transferred to the beaker. After being shaken slightly for 5 min, the mixture was then placed in an ice bath for 2 h, and the solid (mud-like) precipitated. The solid was filtered through a Büchner funnel, washed by ice-cold H_2O (5 mL) and ice-cold hexane (20 mL), and dried under vacuum pump (10−20 mmHg) overnight to give ketone **3a**·H_2O as a white solid (12.2 g, 76% yield). Mp 81−84 °C; $[\alpha]^{25}_D$ −112.0 (*c* 1.05, $CHCl_3$); IR (film) 3436, 1736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (ketone) δ 5.89 (d, J = 4.0 Hz, 1H), 5.60−5.62 (m, 1H), 4.70 (d, J = 9.6 Hz, 1H), 4.44 (dd, J = 13.2, 1.2 Hz, 1H), 3.99 (d, J = 9.6 Hz, 1H), 3.96 (dd, J = 13.2, 2.0 Hz, 1H), 2.17 (s, 3H), 2.12 (s, 3H), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (ketone) δ 192.0, 170.4, 169.6, 114.1, 105.2, 74.2, 72.3, 69.6, 62.7, 26.6, 26.2, 21.0, 20.6. Anal. Calcd for $C_{13}H_{20}O_9$ (hydrate): C, 48.75; H, 6.29. Found: C, 49.14; H, 6.12.

Representative Asymmetric Epoxidation Procedure with Oxone and $NaHCO_3$ (Method A) (Table 2, Entry 2). Aqueous $Na_2(EDTA)$ (1×10^{-4} M, 2.5 mL) and a catalytic amount of tetrabutylammonium hydrogen sulfate (0.010 g, 0.03 mmol) were added to a solution of ethyl *trans*-4-methylcinnamate (0.095 g, 0.5 mmol) in CH_3CN (2.5 mL) with vigorous stirring at 0 °C. A mixture of Oxone (1.537 g, 2.5 mmol) and $NaHCO_3$ (0.651 g, 7.75 mmol) was pulverized, and a small portion of this mixture was added to the reaction mixture to bring the pH to >7.0. Then a solution of ketone **3a** (0.038 g, 0.125 mmol) in CH_3CN (1.25 mL) was added. The rest of the Oxone and $NaHCO_3$ was added to the reaction mixture portionwise over a period of 4.5 h. After being stirred for an additional 7.5 h at 0 °C and 12 h at rt, the resulting mixture was diluted with water and extracted with ethyl acetate. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography (silica gel, hexane/EtOAc = 1/0 to 95/5) to give the epoxide as a colorless oil (0.094 g, 91% yield, 97% ee).

[For Table 2 entry 3, 7.5 mL of CH_3CN and 5.0 mL of aqueous $Na_2(EDTA)$ (1×10^{-4} M) were used due to the poorer solubility of the substrate. For Table 2 entry 3 as well as Table 3, the silica gel was buffered with 1% Et_3N in hexane.]

Representative Asymmetric Epoxidation Procedure with Oxone and K_2CO_3 (Method B) (Table 3, Entry 1). To a solution of olefin (0.059 g, 0.5 mmol), ketone **3a** (hydrate form) (0.015 g, 0.046 mmol), and tetrabutylammonium hydrogen sulfate (0.01 g, 0.03 mmol) in MeCN−DMM (v/v, 1/2) (9 mL) was added buffer (0.05 M aq Na_2HPO_4−0.05 M aq KH_2PO_4, pH 7.0) (3 mL) with stirring. Upon cooling to 0 °C, a solution of Oxone (0.212 M in 4×10^{-4} M aq EDTA, 4.8 mL) and a solution of K_2CO_3 (0.42 M in 4×10^{-4} M aq EDTA, 4.8 mL) were added dropwise simultaneously and separately over 8 h via syringe pump. The reaction was quenched by addition of pentane and extracted with pentane. The combined organic layers were dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography (silica gel was buffered with 1% Et_3N in organic solvent, first pentane, then pentane/Et_2O = 20/1) to give the epoxide as a colorless oil (0.054 g, 81% yield, 86% ee).

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Supporting Information Available: The synthesis and characterization of ketones **3**, **4**, **5**, **6**, **7**, **9**, and **10**; the characterization of epoxides, the X-ray structure of ketone **5a**, the NMR spectra of ketones and epoxides, and the data for the determination of the enantiomeric excess of the epoxides obtained with ketone **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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