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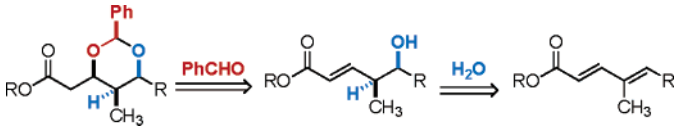
De Novo Synthesis of 2-Substituted *syn*-1,3-Diols via an Iterative Asymmetric Hydration Strategy

Md. Moinuddin Ahmed, Matthew S. Mortensen, and George A. O'Doherty*

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506

george.odoherty@mail.wvu.edu

Received June 10, 2006



The enantioselective syntheses of several protected 4-substituted *syn*-3,5-dihydroxy carboxylic esters have been achieved from the corresponding achiral (*E*,*E*)- or (*E*,*Z*)-1,3-dienoates. The route relies upon an enantio- and regioselective Sharpless dihydroxylation and a palladium-catalyzed reduction to form γ-substituted δ-hydroxy-1-enoates. The resulting δ-hydroxy-1-enoates are subsequently converted into benzylidene-protected 4-substituted *syn*-3,5-dihydroxy carboxylic esters in one step. The benzylidene-protected 3,5-dihydroxy carboxylic esters are produced in good overall yields (20−54%) and high enantiomeric excess (73−97% ee).

Introduction

As part of our continuing program focused on the de novo asymmetric synthesis of polyketide-based natural products,[1] we developed a sequential hydration approach (enantioselective hydration of **1** to **2** and a diastereoselective hydration of **2** to **3**) that converts achiral conjugated dienoates into enantiomerically enriched benzylidine-protected *syn*-3,5-dihydroxyesters.[2] The transformation relies upon a Sharpless asymmetric dihydroxylation followed by a Pd-π-allyl catalyzed allylic reduction to control both the regio- and enantioselectivity of the first hydration and an Evans hemiacetal addition to achieve diastereoselectivity in the second hydration.[3]

With the successful application of this approach to various 1,3-polyol natural products, we targeted the structurally more complex polyene-polyol macrolides (e.g., mycoticin A[4], Figure 1). Thus we required a strategy that would address two structural

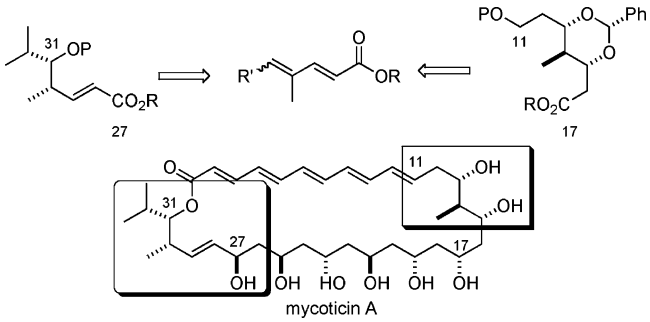


FIGURE 1. Asymmetric hydration approach to mycoticin A

motifs of mycoticin A. That is to say, we required access to both 2-methyl-1,3-diol (C-11 to C-17)[3,4] and δ-hydroxy-γ-methyl enoate (C-27 to C-31) subunits. Other approaches to δ-hydroxy-γ-methyl enoate synthons usually involve crotylation/metathesis, aldol/Wittig, or vinylogous aldol sequences; a few other more diverse strategies have been employed in recent years, as well.[5] Unfortunately, our initial studies on a new catalytic asymmetric approach using various carbon nucleophiles to install an alkyl group at C-4 was met with little success (i.e., replacing the palladium hydride with a palladium alkyl in the Pd-π-allyl intermediate **5**).

Alternatively, we envisioned that these two structural features could be prepared from C-4 substituted achiral dienoates by an iterative hydration approach (Scheme 1). This, of course, required that the initial asymmetric hydration reaction be stereospecific, which was demonstrated by substituting DCO_2H

(1) (a) Smith, C. M.; O'Doherty, G. A. *Org. Lett.* **2003**, *5*, 1959−1962. (b) Garaas, S. D.; Hunter, T. J.; O'Doherty, G. A. *J. Org. Chem.* **2002**, *67*, 2682−2685. (c) Hunter, T. J.; O'Doherty, G. A. *Org. Lett.* **2001**, *3*, 2777−2780. (d) Hunter, T. J.; O'Doherty, G. A. *Org. Lett.* **2002**, *4*, 4447−4450.

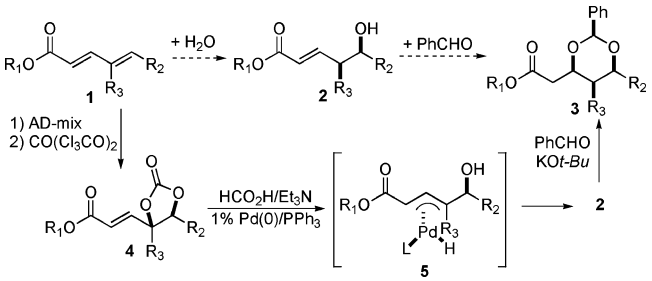
(2) Hunter, T. J.; O'Doherty, G. A. *Org. Lett.* **2001**, *3*, 1049−1052.

(3) Evans, D. A.; Gauchet-Prunet, J. A. *J. Org. Chem.* **1993**, *58*, 2446−2453.

(4) For total synthesis of mycoticin A, see: (a) Poss, C. S.; Rychnovsky, S. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 3360−3361. For formal syntheses and approaches toward mycoticin A, see: (b) Smith, A. B.; Pitram, S. M. *Org. Lett.* **1999**, *1*, 2001−2004. (c) Dreher, S. D.; Leighton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 341−342. For background on oxo polyene macrolide antibiotics, see: Rychnovsky, S. D. *Chem. Rev.* **1995**, *95*, 2021−2040. *Macrolide Antibiotics: Chemistry, Biology and Practice*, 2nd ed.; Omura, S., Ed.; Academic Press: New York, 2002.

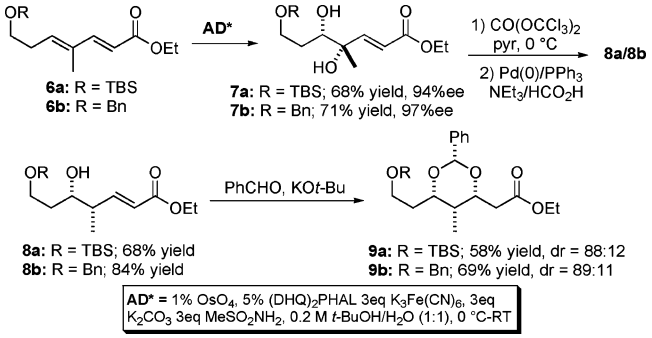
10.1021/jo061200h CCC: $33.50
Published on Web 09/08/2006

SCHEME 1. Asymmetric Iterative Hydration of C4-Methyl Dienoates



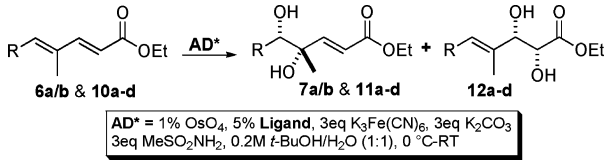
for HCO_2H (Scheme 1, R_3 = H; see Supporting Information). Then, we embarked on an effort to expand the asymmetric hydration methodology to include substituted dienoates (**1**) for the preparation of the 4-methyl-5-hydroxyenoates (**2**) and the benzylidine-protected 4-methyl-3,5-dihydroxy esters (**3**) via the substitution of cyclic carbonates **4** and Pd-π-allyl intermediates **5**.[6] Herein, we describe the successful development of a de novo asymmetric synthesis of these two structural motifs (**2** and **3**) from simple achiral dienoates (**1**).

SCHEME 2. Asymmetric Double Hydration of (*E*,*E*)-Dienoate



While we were initially concerned about the problems associated with enantio- and regioselectivity in both the osmium and palladium steps, the initial dienoates we chose to study (**6a/b**) proved to be very promising (Scheme 2).[7] Thus, exposure of dienoates **6a** and **6b** to Sharpless dihydroxylation conditions proceeded uneventfully (Table 1), providing diols **7a** and **7b** in good yields and excellent enantioselectivity. Similarly, the resulting diols were diastereoselectively converted to homoallylic alcohols **8a** and **8b** by conversion to a cyclic carbonate and reduction with $Et_3N{\cdot}HCO_2H$ (Table 2).[8] Finally, both homoallylic alcohols **8a** and **8b** were readily converted into the benzylidine-protected *syn*-3,5-dihydroxyester **9a** and **9b** by exposure to the Evans conditions (PhCHO, cat. KO*t*-Bu, Table 3).

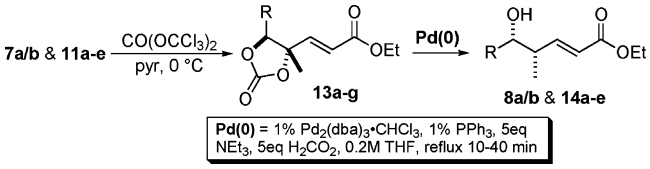
TABLE 1. Asymmetric dihydroxylation of (*E*,*E*)-Dienoates



entry	R	ligand	yield (%)	ee[a] (**11**)	ratio[b] (**11**:**12**)
a	CH_2iPr	**(DHQ)$_2$PHAL**	82	86	**(1:1)**
		DHQ-4-Me-2-Quin	75	73	(>99:1)
b	*i*Pr	**(DHQ)$_2$PHAL**	88	60	**(1.6:1)**
		DHQ-4-Me-2-Quin	60[c]	80	(16:1)
c	Ph	**(DHQ)$_2$PHAL**	77	*d*	**(1:2.5)**
		(DHQD)$_2$PHAL	78	*d*	**(1:2.5)**
		DHQ-4-Me-2-Quin[e]	60	90	(>99:1)
d	Me	(DHQ)$_2$PHAL	65	96	(>99:1)
		(DHQD)$_2$PHAL	68	99	(>99:1)
6a	$(CH_2)_2$OTBS	(DHQ)$_2$PHAL	68 (**7a**)	94	(>99:1)
		(DHQD)$_2$PHAL	70	98	(>99:1)
6b	$(CH_2)_2$OBn	(DHQ)$_2$PHAL	71 (**7b**)	97	(>99:1)
		(DHQD)$_2$PHAL	73	99	(>99:1)

[a] Determined by chiral HPLC. [b] Determined by ^{1}H NMR. [c] 3 equiv of $NaHCO_3$ used as buffer. [d] ee of minor isomer not determined. [e] 2% Os, 10% ligand.

TABLE 2. Diastereoselective carbonate reduction



entry	R	yield, % (**13**)	yield, % (**14**)	dr[a]
a	CH_2iPr	90	96	>95:5
b	*i*PR	84	98	>95:5
c	Ph	91	98	>95:5
d	Me	90	98	>95:5
e	**Me(*ent*-1)**[b]	90	98	>95:5
7a	(CH_2)OTBS	71 (**13f**)	95 (**8a**)	>95:5
7b	$(CH_2)_2$OBN	88 (**13g**)	96 (**8b**)	>95:5

[a] Determined by ^{1}H NMR. [b] Dienoate subjected to (DHQD)$_2$PHAL.

Unfortunately, when we investigated the scope of this reaction sequence we uncovered complications with the dihydroxylation step (Table 1). The simplest dienoate substrate (Table 1, entry d, R = Me)[9] underwent dihydroxylation using (DHQ)$_2$PHAL and (DHQD)$_2$PHAL with excellent enantio- and regioselectivity; however, the regioselectivities were diminished for branched-alkyl and aryl substituents (Table 1, entries a−c).[10] For instance, when dienoate **10c** (R = Ph) was dihydroxylated with the PHAL-linked dimeric ligands, the α,β-olefin **12c** was preferentially formed (2.5:1). To our delight, switching to a "first-

(5) For recent approaches to γ-methyl-δ-hydroxyenoates, see: ref 4 and (a) Chen, Y.-H.; McDonald, F. E. *J. Am. Chem. Soc.* **2006**, *128*, 4568−4569. (b) Jain, N. F.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 12475−12476. (c) Bluet, G.; Bazan-Tejeda, B.; Campagne, J. -M. *Org. Lett.* **2001**, *3*, 3807−3810. (d) Shirokawa, S.-i.; Kamiyama, M.; Nakamura, T.; Okada, M.; Nakazaki, A.; Hosokawa, S.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 13604−13605. (e) Roush, W. R.; Palkowitz, A. D. Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348−6359. (f) Rychnovsky, S. D.; Hoye, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 1753−1765. (g) Schlessinger, R. H.; Li, Y. -J. *J. Am. Chem. Soc.* **1996**, *118*, 3301−3302. (h) Enders, D.; Voith, M. *Synlett* **2002**, 29−32. (i) Denmark, S. E.; Fujimori, S. *J. Am. Chem. Soc.* **2005**, *127*, 8971−8973.

(6) Tsuji has demonstrated a diastereoselective Pd-catalyzed reduction of trisubstituted vinyl epoxides, see: Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am. Chem. Soc.* **1989**, *111*, 6280−6287.

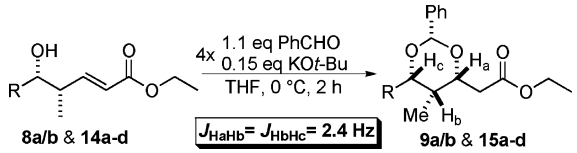
(7) (a) Tholander, J.; Carreira, E. M. *Helv. Chim. Acta* **2001**, *84*, 613−622. b) Smith, A. B.; Walsh, S. P.; Frohn, M.; Duffey, M. O. *Org. Lett.* **2005**, *7*, 139−142.

(8) Lower yields for the TBS series were due to minor loss of the TBS group in the carbonate-forming step.

(9) Carreira has prepared **19** by a three step sequence from **6d**, see: ref 7a.

(10) The regioselectivity of the asymmetric dihydroxylation of di- and trienoates has been studied by Sharpless and our group, see: (a) Berker, H.; Soler, M. A.; Sharpless, K. B. *Tetrahedron* **1995**, *51*, 1345. and (b) Zhang, Y.; O'Doherty, G. A. *Tetrahedron* **2005**, *61*, 1345−1376.

TABLE 3. Diastereoselective hydration of δ-Hydroxyenoates



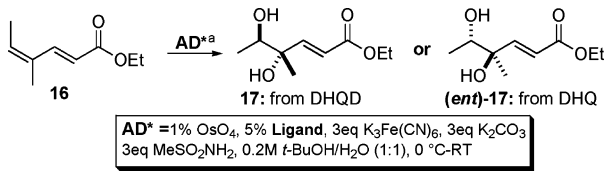
entry	R	yield, % (**15**)	dr
a	CH_2*i*Pr	75	90:10
b	*i*Pr	57	89:11
c	Ph	33	90:10
d	Me	63	90:10
8a	$(CH_2)_2$OTBS	58 (**9a**)	88:12
8b	$(CH_2)_2$OBn	69 (**9b**)	89:11

generation" dihydroxylation ligand, DHQ-4-Me-2-quinolyl ether (DHQ-MEQ), eliminated this problem and gave the desired diol with excellent selectivity in all three cases (entries a−c, Table 1) with greatly improved regio- (>16:1) and enantioselectivity (73−90 % ee) for the diols **11a**−**c**.

The palladium-catalyzed reduction proved to be very tolerant to a variety of functionalities, giving excellent yields and selectivities in all cases. As with the diols **7a/b**, the diastereomerically pure diols **11a**−**e** were converted into the corresponding cyclic carbonates **13a**−**e** (Table 2) in excellent yields using triphosgene and pyridine in CH_2Cl_2. We next examined the Pd-catalyzed reduction of the (*E*,*E*)-allylic carbonates **13a**−**e**. After some experimentation it was found that the optimal conditions were 1% $Pd_2(dba)_3$·$CHCl_3$/PPh_3 in THF with 5 equiv of Et_3N·HCO_2H.[11] In all case the carbonates were cleanly converted into homoallylic alcohols in excellent yields (>95%). It is worth noting that we have been able to use this procedure for the preparation of multigram quantities of **14b** (i.e., several 10 g batches).

Both to demonstrate the synthetic utility of this oxidation/reduction sequence and to assign the stereochemistry of the asymmetric hydration reaction, the homoallylic alcohols **14a**−**d** were converted into the 1,3-*syn* diols **15a**−**d**. Thus exposure of alcohols **14a**−**d** to the Evans 1,3-*syn* diol protocol provided the benzylidine-protected *syn*-3,5-dihydroxyesters **15a**−**d**. With

TABLE 4. Asymmetric dihydroxylation of (*E*,*Z*)-Dienoates[a]

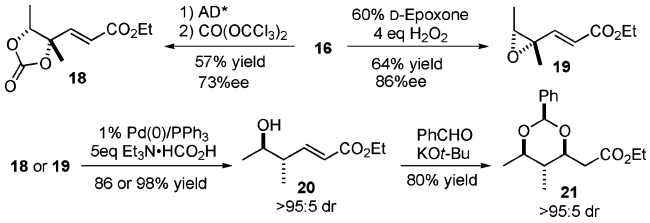


entry	ligand	yield, % (**17**)	ee[b], %
1	**$(DHQ)_2$PHAL**	63	**56**
2	**$(DHQD)_2$PHAL**	35	**70**
3	DHQ-4-Me-2-Quin	50	49
4	**$(DHQD)_2$PYR**	64	**73**
5	DHQD-9-phen	47	64
6	$(DHQD)_2$AQN	35	61
7	DHQD-4-CLB	38	30

[a] **17** is major from DHQD ligands whereas **(*ent*)-17** is major from DHQ ligands. [b] Determined by chiral HPLC.

(11) This constitutes a reduction in the ratio of Pd versus phosphine to our optimized conditions for the des-methyl substrates but is in accordance with Tsuji's vinyl epoxide reduction, albeit with significantly lower catalyst loadings; see ref 6.

SCHEME 3. Shi Epoxidation of (*E*,*Z*)-Dienoates



the exception of the phenyl-substituted substrate **14c**, the benzylidine acetals were formed in good yields (57−75%, Table 3).[12]

We next set out to test the stereospecificity of the overall transformation (**6**/**10** to **9**/**15**). To do so we chose the (*Z*,*E*)-methyl-substituted dienoate **16** (cf., Table 4 and Scheme 3). Once again the initial dihydroxylation proved to be problematic. While no regioisomers were detected, the enantioselectivities were unsatisfactory using the PHAL-linked dimeric ligands (Table 4, entries 1 and 2).

We again turned to the DHQ-MEQ ligand, but this time we were met with lower ee (Table 4, entry 3). A screening of commercially available AD ligands was conducted in which the optimum ligand was determined to be $(DHQD)_2$PYR (Table 4, entry 4).[13] In an effort to further increase the enantioselectivity, a Shi epoxidation[14] was attempted on **16** (Scheme 3). Indeed, epoxide **19** was formed in greater enantioexcess and was subjected to identical Pd-reduction conditions as the carbonate **18**. Both **18** and **19** behaved similarly in the reaction giving excellent dr with the epoxide opening having higher yield (98% vs 86%). Finally, the conversion of **20** to the *anti*-methyl diastereomer **21** occurred in 80% yield and diastereoselectivity (>95:5) via the Evans protocol.[15]

In summary, we have demonstrated the utility of our asymmetric bis-hydration methodology for the stereospecific conversion of both (*E*,*E*)- and (*E*,*Z*)-dienoates into either C-4 diastereomer of benzylidine-protected *syn*-3,5-dihydroxy esters (**9**, **15** and **21**).[9] Key to this development was the control of regioselectivity in both the osmium-catalyzed asymmetric dihydroxylation and palladium-catalyzed reduction reactions. Further development to improve the enantioselectivity of the oxidation of the (*E*,*Z*)-dienoates and its application toward natural product synthesis is ongoing.

Experimental Section[16]

General Procedure for Dihydroxylations. Into a round-bottom flask containing $K_3Fe(CN)_6$ (3 equiv), K_2CO_3 (3 equiv), $MeSO_2NH_2$ (3 equiv), and $(DHQ)_2$-PHAL (5 mol %) was added *t*-BuOH and water (1:1, 0.2 M). The mixture was stirred at 0 °C for 5 min, and then to this solution was added OsO_4 (1 mol %) immediately

(12) The ^{1}H NMR spectrum showed a qdd multiplicity ($J_{HaHb} = J_{HbHc} = 2.4$ Hz) for the proton at C-4, indicating the all-*syn* stereochemistry of both **14** and **15**, see supporting information.

(13) It is noteworthy that the dihydroxylation of **16** appears to proceed with the opposite facial selectivity to the analogous (*E*,*E*)-diene, but this result is consistent with the Sharpless mnemonic; see: Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547.

(14) Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488−496.

(15) In general, the all-equatorial diastereomer **21** forms with even greater stereocontrol than **15**.

(16) Presented in this Experimental Section are the general experimental procedures and spectral data for all new compounds. Complete experimental procedures and spectral data for all compounds are presented in Supporting Information.

followed by addition of dienoate. The reaction was stirred vigorously at 0 °C for 2−18 h. Ethyl acetate was added to the reaction mixture followed by quenching with solid sodium sulfite. The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine and then dried over Na_2SO_4. After concentration the crude mixture was purified by silica gel column chromatography.

(+)-(*E*,4*S*,5*S*)-Ethyl 7-(*tert*-Butyldimethylsilyloxy)-4,5-dihydroxy-4-methylhept-2-enoate (7a). After flash column chromatography (30% EtOAc/hexanes) the reaction yielded 380 mg (68%) of diol as a clear, colorless oil. R_f = 0.10 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +5.2 (*c* 0.61, CH_2Cl_2); IR (neat, cm^{-1}) 3459(br), 2932, 2859, 1713, 1658, 1469, 1369, 1257, 1183, 1089, 987, 941, 836, 778, 728; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.99 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.6 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.90 (m, 2H), 3.74 (dd, J = 6, 6 Hz, 1H), 1.99 (brs, 2H), 1.71 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H), 1.25 (s, 3H), 0.88 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.6, 152.3, 120.2, 77.2, 74.6, 62.5, 60.3, 32.2, 25.7 (3C), 22.8, 18.0, 14.1, −5.6 (2C); HRMS (ESI) calcd for $[C_{16}H_{32}O_5Si + Na]^+$ 355.1911, found 355.1909.

(+)-(*E*,4*S*,5*S*)-Ethyl 7-(Benzyloxy)-4,5-dihydroxy-4-methylhept-2-enoate (7b). After purification by flash column chromatography (50% EtOAc/hexanes) the diol was obtained in 71% yield as a clear, colorless oil. R_f = 0.11 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +5.2 (*c* 2.0, CH_2Cl_2); IR (neat, cm^{-1}) 3461(br), 2931, 2860, 1715, 1453, 1367, 1282, 1186, 1095, 1031, 987, 698; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.35 (m, 3H), 7.30 (m, 2H), 6.99 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.6 Hz, 1H), 4.52 (s, 2H), 4.18 (q, J = 7.2 Hz, 2H), 3.75 (m, 2H), 3.68 (m, 1H), 3.51 (s, 1H), 2.71 (s, 1H), 1.81 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5, 152.0, 138.1, 128.5 (2C), 127.9, 127.7 (2C), 120.3, 76.7, 74.6, 73.5, 69.2, 60.4, 30.2, 22.8, 14.2; HRMS (ESI) calcd for $[C_{17}H_{24}O_5 + Na]^+$ 331.1515, found 331.1516.

(−)-(*E*,4*S*,5*S*)-Ethyl 4,5-Dihydroxy-4,7-dimethyloct-2-enoate (11a). After purification by flash column chromatography (50% EtOAc/hexanes) the reaction yielded 44 mg (75%) of diol as a clear oil with no detectable regioisomer. R_f = 0.15 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −21.7 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3460, 2957, 2870, 1701, 1656, 1466, 1368, 1307, 1282, 1189, 1034, 988, 869, 766, 743, 652; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.95 (d, J = 15.6 Hz, 1H), 6.10 (d, J = 15.6 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.56 (ddd, J = 10.8, 4.2, 2.4 Hz, 1H), 2.53 (brs, 1H), 2.31 (brs, 1H), 1.80 (m, 1H), 1.38 (ddd, J = 13.8, 10.8, 3.6 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H),1.26 (s, 3H), 1.20 (ddd, J = 13.8, 10.2, 4.2 Hz, 1H), 0.94 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.6, 151.9, 120.6, 75.4, 74.7, 60.5, 39.7, 24.6, 23.8, 21.8, 21.2, 14.1; HRMS (ESI) calcd for $[C_{12}H_{22}O_4 + Na]^+$ 253.1410, found 253.1402.

(−)-(*E*,4*S*,5*S*)-Ethyl 4,5-Dihydroxy-4,6-dimethylhept-2-enoate (11b). After purification by silica gel column chromatography (30% EtOAc/hexanes) the reaction yielded 72 mg (60%) of diols as a 16:1 mixture of regioisomers. R_f = 0.11 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −3.0 (*c* 0.5, CH_2Cl_2); IR (neat, cm^{-1}) 3448, 2962, 2874, 1698, 1655, 1467, 1368, 1303, 1279, 1179, 1096, 1031, 984, 869, 725, 679; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.89 (d, J = 15.6 Hz, 1H), 5.99 (d, J = 15.6 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.27 (dd, J = 4.8, 3.6 Hz, 1H), 2.32 (s, 1H), 1.95 (d, J = 4.8 Hz, 1H), 1.86 (m, 1H), 1.22 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.8, 153.4, 120.2, 80.1, 75.6, 60.7, 29.0, 23.1, 22.0, 16.6, 14.4; HRMS (ESI) calcd for $[C_{11}H_{20}O_4 + Na]^+$ 239.1253, found 239.1249.

(+)-(*S*,*E*)-Ethyl 4-Hydroxy-4-((S)-hydroxy(phenyl)methyl)-pent-2-enoate (11c). After purification by flash column chromatography (50% EtOAc/hexanes) the reaction yielded 490 mg (60%) of diol as a clear, yellow oil. R_f = 0.10 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +15.7 (*c* 1.2, CH_2Cl_2); IR (neat, cm^{-1}) 3436, 2981, 1699, 1656, 1453, 1368, 1304, 1278, 1182, 1094, 1026, 985, 910, 868, 721, 700; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.33 (m, 5H), 7.01 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.6 Hz, 1H), 4.60 (d, J = 3.0 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 2.70 (s, 1H), 2.47 (s, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5 151.8, 138.9, 128.2, 128.1 (2C), 127.5 (2C), 120.5, 79.2, 75.5, 60.4, 22.9, 14.1; HRMS (ESI) calcd for $[C_{14}H_{18}O_4 + Na]^+$ 273.1097, found 273.1091

(+)-(*E*,4*R*,5*S*)-Ethyl 4,5-dihydroxy-4-methylhex-2-enoate (17). After purification by flash column chromatography (30% EtOAc/hexanes) the reaction yielded 153 mg (64%) of diol as a clear, colorless oil. R_f = 0.10 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +2.5 (*c* 1.00, CH_2Cl_2); IR (neat, cm^{-1}) 3434 (br), 2980, 2936, 1699, 1655, 1449, 1368, 1303, 1276, 1181, 1090, 1033, 985, 920, 887, 729; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.97 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.6 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.71 (q, J = 6.6 Hz, 1H), 2.64 (brs, 1H), 2.28 (brs, 1H), 1.31 (s, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.17 (dd, J = 6.6, 1.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.7, 150.0, 121.2, 75.6, 74.0, 60.7, 24.6, 18.2, 14.4.

General Procedure for Carbonate Formation. To diol in CH_2Cl_2 (0.4 M) in an ice bath was added pyridine (5 equiv). Triphosgene (1.1 equiv) in CH_2Cl_2 (0.4 M, total reaction concentration equals 0.2 M) was added via syringe, and the reaction was allowed to stir for 5 min until determined complete by TLC (UV, PMA stain). The reaction was diluted with diethyl ether and was placed in a separatory funnel. The crude mixture, including salts, was washed vigorously with a saturated aqueous $CuSO_4$ solution until all salts dissolved. The layers were then separated, and the organic layer was washed with brine. After separation the organic layer was dried over Na_2SO_4 and concentrated. The crude mixture was then purified by flash column chromatography.

(+)-(*E*)-Ethyl 3-((4*S*,5*S*)-5-Isobutyl-4-methyl-2-oxo-1,3-dioxolan-4-yl)acrylate (13a). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 90% yield as a clear, colorless oil. R_f = 0.26 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +35.6 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2961, 1799, 1719, 1663, 1468, 1385, 1367, 1309,1280, 1232, 1177, 1088, 1063, 1013, 982, 870, 774; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.85 (d, J = 15.6 Hz, 1H), 6.16 (d, J = 15.6 Hz, 1H), 4.41 (dd, J = 10.8, 2.4 Hz, 1H), 4.22 (q, J = 7.2 Hz, 2H), 1.84 (m, 1H), 1.71 (m, 1H), 1.46 (s, 3H), 1.32 (m, 1H), 1.30 (t, J = 7.2 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 153.2, 144.0, 122.3, 84.15, 82.0, 61.0, 37.4, 25.1, 23.1, 21.5, 19.2, 14.1; HRMS (ESI) calcd for $[C_{13}H_{20}O_5 + Na]^+$ 279.1202, found 279.1204.

(+)-(*E*)-Ethyl 3-((4*S*,5*S*)-5-Isopropyl-4-methyl-2-oxo-1,3-dioxolan-4-yl)acrylate (13b). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 84% yield as a clear, colorless oil. R_f = 0.22 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +18.3 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2973, 1801, 1720, 1663, 1472, 1368, 1281, 1245, 1175, 1109, 1062, 1027, 982, 839, 774; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.84 (d, J = 15.6 Hz, 1H), 6.20 (d, J = 15.6 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.98 (d, J = 9.6 Hz, 1H), 2.04 (m, 1H), 1.54 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.11 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.6, 153.1, 144.5, 123.0, 89.1, 84.5, 61.2, 28.2, 19.8, 19.1, 18.7, 14.3; HRMS (ESI) calcd for $[C_{12}H_{18}O_5 + Na]^+$ 265.1046, found 265.1050.

(−)-(*E*)-Ethyl 3-((4*S*,5*S*)-4-Methyl-2-oxo-5-phenyl-1,3-dioxolan-4-yl)acrylate (13c). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 91% yield as a clear, colorless oil. R_f = 0.21 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −24.9 (*c* 1.3, CH_2Cl_2); IR (neat, cm^{-1}) 2984, 1802, 1718, 1663, 1456, 1367, 1308, 1288, 1245, 1180, 1088, 1069, 1044, 1028, 979, 771, 700; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.43 (m, 3H), 7.28 (m, 2H), 7.01 (d, J = 15.6 Hz, 1H), 6.20 (d, J = 15.6 Hz, 1H), 5.47 (s, 1H), 4.26 (qd, J = 7.2, 1.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 153.0, 144.5, 132.2, 129.5, 128.9 (2C), 125.5 (2C), 122.6, 85.2, 84.4, 61.1, 20.9, 14.1; HRMS (ESI) calcd for $[C_{15}H_{16}O_5 + Na]^+$ 299.0889, found 299.0897.

(+)-(*E*)-Ethyl 3-((4*S*,5*S*)-4,5-Dimethyl-2-oxo-1,3-dioxolan-4-yl)acrylate (13d). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 90% yield as a clear, colorless oil. $R_f = 0.25$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +12.7 (*c* 1.00, CH_2Cl_2); IR (neat, cm^{-1}) 2987, 2941, 2301, 1821, 1726, 1664, 1446, 1390, 1348, 1312, 1235, 1183, 1086, 1034, 868, 774, 630; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.86 (d, $J = 16.2$ Hz, 1H), 6.15 (d, $J = 16.2$ Hz, 1H), 4.54 (q, $J = 6.6$ Hz, 1H), 4.22 (q, $J = 6.6$ Hz, 2H), 1.48 (s, 3H), 1.41 (d, $J = 6.6$ Hz, 3H), 1.30 (t, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 153.1, 144.0, 122.3, 84.1, 79.6, 61.0, 19.1, 14.3, 14.1; HRMS (ESI) calcd for $[C_{10}H_{14}O_5 + Na]^+$ 237.0733, found 237.0726.

(−)-(*E*)-Ethyl 3-((4*S*,5*S*)-5-(2-(*tert*-Butyldimethylsilyloxy)-ethyl)-4-methyl-2-oxo-1,3-dioxolan-4-yl)acrylate (13f). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 71% yield as a clear, colorless oil. $R_f = 0.50$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −52.2 (*c* 1.00, CH_2Cl_2); IR (neat) 2956, 2858, 1813, 1723, 1665, 1469, 1388, 1309, 1258, 1179, 1088, 1033, 982, 835, 777, 721; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.89 (d, $J = 15.6$ Hz, 1H), 6.15 (d, $J = 15.6$ Hz, 1H), 4.59 (dd, $J = 9.6$, 3.6 Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.77 (m, 2H), 1.87 (m, 2H), 1.49 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 153.1, 144.1, 122.2, 83.9, 80.3, 61.0, 58.5, 32.1, 25.8 (3C), 19.6, 18.2, 14.1, −5.5 (2C); HRMS (ESI) calcd for $[C_{17}H_{30}O_6Si + Na]^+$ 381.1703, found 381.1718.

(−)-(*E*)-Ethyl 3-((4*S*,5*S*)-5-(2-(Benzyloxy)ethyl)-4-methyl-2-oxo-1,3-dioxolan-4-yl)acrylate (13 g). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 88% yield as a clear, colorless oil. $R_f = 0.23$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −23. 8 (*c* 2.3, CH_2Cl_2); IR (neat, cm^{-1}) 2985, 2863, 1810, 1720, 1662, 1556, 1495, 1454, 1382, 1188, 1090, 985, 773, 741;; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.35 (m, 3H), 7.31 (m, 2H), 6.88 (d, $J = 15.6$ Hz, 1H), 6.15 (d, $J = 15.6$ Hz, 1H), 4.62 (t, $J = 7.2$ Hz, 1H), 4.51 (dd, $J = 27.0$, 6.0 Hz, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.63 (m, 2H), 1.95 (dd, $J = 12.6$, 6.0 Hz, 2H), 1.48 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.3, 153.0, 144.1, 137.5, 128.4 (2C), 127.8, 127.7 (2C), 122.2, 84.0, 80.5, 73.4, 65.4, 61.0, 29.6, 19.5, 14.1; HRMS (ESI) calcd for $[C_{18}H_{22}O_6 + Na]^+$ 357.1308, found 357.1290.

(−)-(*E*)-Ethyl 3-((4*R*,5*S*)-4,5-Dimethyl-2-oxo-1,3-dioxolan-4-yl)acrylate (18). The crude mixture was purified by flash column chromatography (20% EtOAc/hexanes) to yield carbonate in 89% yield as a clear, colorless oil. $R_f = 0.20$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −30.2 (*c* 0.65, CH_2Cl_2); IR (neat, cm^{-1}) 2985, 2940, 1793, 1717, 1662, 1594, 1448, 1387, 1367, 1310, 1287, 1225, 1180, 1097, 1074, 1000, 905, 870, 773, 732, 685; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.76 (d, $J = 15.6$ Hz, 1H), 6.19 (d, $J = 15.6$ Hz, 1H), 4.55 (dd, $J = 6.6$, 6.6 Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 1.60 (s, 3H), 1.32 (d, $J = 6.6$ Hz, 3H), 1.30 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 165.4, 153.3, 142.1, 123.2, 84.4, 81.9, 61.2, 24.4, 16.1, 14.3; HRMS (ESI) calcd for $[C_{10}H_{14}O_5 + Na]^+$ 237.0733, found 237.0736.

General Procedure for Pd-Catalyzed Carbonate Reduction. To a flask containing carbonate in THF (0.2 M) were added $Pd_2(dba)_3 \cdot CHCl_3$ (1 mol %), PPh_3 (1 mol %), Et_3N (5 equiv) and finally formic acid (5 equiv). The reaction was then refluxed for 20−40 min at which time it was determined complete by TLC (UV, anisaldehyde). The reaction was then allowed to cool to room temperature, diluted with ether, and filtered through a plug of silica gel to remove Pd(0) before concentration. The crude mixture was then concentrated and subjected to flash column chromatography.

(−)-(*E*,4*S*,5*S*)-Ethyl 7-(*tert*-Butyldimethylsilyloxy)-5-hydroxy-4-methylhept-2-enoate (8a). The crude mixture was concentrated and subjected to flash column chromatography (20% EtOAc/hexanes) to yield δ-hydroxy enoate in 95% yield as a clear, colorless oil. $R_f = 0.45$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −16.5 (*c* 0.63, CH_2Cl_2); IR (neat, cm^{-1}) 3499 (br), 2955, 2859, 1720, 1651, 1463, 1368, 1256, 1181, 1144, 1093, 1038, 986, 835, 777, 726; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.93 (dd, $J = 16.2$, 7.8 Hz, 1H), 5.84 (dd, $J = 16.2$, 1.2 Hz, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 3.89 (m, 1H), 3.78 (m, 2H), 2.41 (m, 1H), 1.61 (m, 2H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.10 (d, $J = 7.2$ Hz, 3H), 0.88 (s, 9H), 0.07 (d, $J = 1.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.6, 150.9, 121.4, 75.1, 63.0, 60.2, 42.7, 35.4, 25.8 (3C), 18.0, 14.7, 14.2, −5.6 (2C); HRMS (ESI) calcd for $[C_{16}H_{32}O_4Si + Na]^+$ 339.1962, found 339.1954.

(−)-(*E*,4*S*,5*S*)-Ethyl 7-(Benzyloxy)-5-hydroxy-4-methylhept-2-enoate (8b). The crude mixture was concentrated and subjected to flash column chromatography (20% EtOAc/hexanes) to yield δ-hydroxy enoate in 96% yield as a clear, colorless oil. $R_f = 0.23$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −18.9 (*c* 1.20, CH_2Cl_2); IR (neat, cm^{-1}) 3486 (br), 2932, 2854, 1725, 1646, 1467, 1273, 1193, 1107, 1090, 741, 705; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.31 (m, 5H), 6.95 (dd, $J = 15.6$, 7.8 Hz, 1H), 5.84 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.51 (s, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.74 (m, 2H), 3.64 (ddd, $J = 12.6$, 6.6, 2.4 Hz, 1H), 3.01 (d, $J = 3.0$ Hz, 1H), 2.43 (sextet, $J = 6.6$ Hz, 1H), 1.73 (q, $J = 6.0$ Hz, 2H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.11 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5, 150.7, 137.7, 128.4 (2C), 127.8, 127.7 (2C), 121.5, 74.4, 73.4, 69.4, 60.2, 42.6, 33.6, 14.6, 14.2; HRMS (ESI) calcd for $[C_{17}H_{24}O_4Si + Na]^+$ 315.1566, found 315.1568.

(−)-(*E*,4*S*,5*S*)-Ethyl 5-Hydroxy-4,7-dimethyloct-2-enoate (14a). The crude mixture was concentrated and subjected to flash column chromatography (20% EtOAc/hexanes) to yield δ-hydroxy enoate in 96% yield as a clear, colorless oil. $R_f = 0.27$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −43.7 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 3436 (br), 2957, 2871, 1702, 1651, 1467, 1368, 1272, 1182, 1150, 1095, 1034, 989, 865, 729; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.95 (dd, $J = 15.6$, 7.8 Hz, 1H), 5.86 (dd, $J = 15.6$, 1.8 Hz, 1H), 4.21 (q, $J = 7.2$ Hz, 2H), 3.67 (ddd, $J = 9.0$, 8.4, 5.4 Hz, 1H), 2.40 (sextet, $J = 7.2$ Hz, 1H), 1.77 (m, 2H), 1.57 (brs, 1H), 1.35 (m, 1H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.08 (d, $J = 7.2$ Hz, 3H), 0.94 (d, $J = 6.6$ Hz, 3H), 0.90 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5, 150.9, 121.6, 72.4, 60.2, 43.4, 42.8, 24.6, 23.6, 21.6, 14.2, 13.8; HRMS (ESI) calcd for $[C_{12}H_{22}O_3 + Na]^+$ 237.1461, found 237.1460.

(−)-(*E*,4*S*,5*S*)-Ethyl 5-Hydroxy-4-methylhex-2-enoate (14d). The crude mixture was concentrated and subjected to flash column chromatography (20% EtOAc/hexanes) to yield δ-hydroxy enoate in 98% yield as a clear, colorless oil. $R_f = 0.40$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −29.8 (*c* 0.77, CH_2Cl_2); IR (neat, cm^{-1}) 3410 (br), 2971, 2850, 1716, 1650, 1273, 1183, 1155, 1093, 1034; ^1H NMR ($CDCl_3$, 600 MHz) δ 6.93 (dd, $J = 15.6$, 7.8 Hz, 1H), 5.86 (dd, $J = 15.6$, 1.2 Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.77 (m, 1H), 2.39 (m, 1H), 1.58 (brs, 1H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.16 (d, $J = 6.6$ Hz, 3H), 1.08 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 166.5, 150.4, 121.8, 70.5, 60.2, 43.7, 20.4, 14.4, 14.2; HRMS (ESI) calcd for $[C_9H_{16}O_3 + Na]^+$ 195.0991, found 195.1000.

General Procedure for Evans' Hemiacetal Addition. Enoate was dissolved in THF (0.2 M) and cooled to 0 °C. To the solution were added benzaldehyde (1.1 equiv) and potassium *tert*-butoxide (0.15 equiv). The addition of base and aldehyde was repeated three times at 20 min intervals. The reaction was allowed to stir at 0 °C and was quenched after 1 h by adding pH 7 buffered phosphate solution. The layers were separated, and the aqueous layer was extracted with Et_2O. The organic layers were combined, washed with brine, and dried over Na_2SO_4, and the solvent was removed under reduced pressure. The product was purified by silica gel chromatography.

(−)-Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-6-(2-(*tert*-Butyldimethylsilyloxy)-ethyl)-5-methyl-2-phenyl-1,3-dioxan-4-yl)acetate (9a). The product was purified by silica gel chromatography eluting with 5% EtOAc/hexanes to yield benzylidine acetal in 58% yield as a clear, colorless oil. $R_f = 0.62$ (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −27.5 (*c* 0.50, CH_2Cl_2); IR (neat, cm^{-1}) 2955, 2930, 2858, 1738, 1461, 1390, 1349, 1314, 1254, 1182, 1098, 1064, 1027, 941, 835, 776, 697; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.49 (m, 2H), 7.34 (m, 3H), 5.58 (s, 1H), 4.43 (ddd, $J = 7.8$, 6.0, 2.4 Hz, 1H), 4.16 (dq, $J = 7.2$, 1.2 Hz, 2H), 4.13 (ddd, $J = 8.4$, 3.0, 3.0 Hz, 1H), 3.78 (m, 1H), 3.73 (m,

1H), 2.71 (dd, J = 15.6, 8.4 Hz, 1H), 2.48 (dd, J = 15.6, 6.0 Hz, 1H), 1.87 (m, 1H), 1.66 (m, 1H), 1.58 (qdd, J = 7.2, 2.4, 2.4 Hz, 1H), 1.26 (t, J = 7.2 Hz, 3H), 1.01 (d, J = 7.2, Hz, 3H), 0.91 (d, J = 1.2 Hz, 9H), 0.06 (d, J = 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.0, 138.6, 128.6, 128.1 (2C), 126.1 (2C), 101.5, 77.3, 77.1, 60.5, 59.2, 38.1, 35.8, 34.6, 25.9 (3C), 18.3, 14.1, 6.2, −5.3-(2C); HRMS (ESI) calcd for $[C_{23}H_{38}O_5 + Na]^+$ 445.2380, found 445.2398.

(−)-Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-6-(2-(Benzyloxy)ethyl)-5-methyl-2-phenyl-1,3-dioxan-4-yl)acetate (9b). The product was purified by silica gel chromatography eluting with 5% EtOAc/hexanes to yield benzylidine acetal in 69% yield as a clear, colorless oil. R_f = 0.39 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −20.5 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2978, 2869, 1735, 1496, 1454, 1369, 1350, 1264, 1182, 1151, 1100, 1066, 1027, 754, 697; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.33 (m, 10H), 5.5 (s, 1H), 4.54 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 12.0, Hz, 1H), 4.42 (ddd, J = 8.4, 5.4, 2.4 Hz, 1H), 4.18 (qd, J = 7.2, 1.8 Hz, 1H), 4.17 (ddd, J = 8.4, 3.6, 2.4 Hz, 1H), 4.15 (qd, J = 7.2, 1.8 Hz, 1H), 3.65 (ddd, J = 13.2, 9.0, 4.8 Hz, 1H), 3.59 (ddd, J = 12.0, 9.0, 6.0 Hz, 1H), 2.71 (dd, J = 15.6, 7.8 Hz, 1H), 2.47 (dd, J = 15.6, 5.4 Hz, 1H), 1.97 (m, 1H), 1.76 (m, 1H), 1.58 (qdd, J = 6.6, 2.4, 2.4 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.9, 138.6, 138.4, 128.6, 128.3 (2C), 128.1 (2C), 127.6 (2C), 127.5, 126.1 (2C), 101.4, 77.5, 77.2, 73.0. 66.4, 60.5, 38.1, 34.5, 33.1, 14.1, 6.1; HRMS (ESI) calcd for $[C_{24}H_{30}O_5 + Na]^+$ 421.1985, found 421.2014.

(−)-Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-6-Isobutyl-5-methyl-2-phenyl-1,3-dioxan-4-yl)acetate (15a). The product was purified by silica gel chromatography eluting with 5−10% EtOAc/hexanes to yield benzylidine acetal in 75% yield as a clear, colorless oil. R_f = 0.39 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ −7.3 (*c* 0.50, CH_2Cl_2); IR (neat, cm^{-1}) 2955, 2870, 1734, 1456, 1391, 1368, 1349, 1259, 1180, 1102, 1056, 1021, 993, 922, 853, 755, 696; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.48 (m, 2H), 7.33 (m, 3H), 5.58 (s, 1H), 4.42 (ddd, J = 7.8, 5.4, 2.4 Hz, 1H), 4.16 (q, J = 7.2 Hz, 2H), 3.99 (ddd, J = 8.4, 4.8, 2.4 Hz, 1H), 2.71 (dd, J = 15.6, 7.8 Hz, 1H), 2.48 (dd, J = 15.6, 6.0 Hz, 1H), 1.78 (m, 1H), 1.64 (m, 1H), 1.54 (qdd, J = 7.2, 2.4, 2.4 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H), 1.26 (m, 1H), 0.99 (d, J = 7.2 Hz, 3H), 0.95 (d, J = 6.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.1, 138.7, 128.5, 128.1 (2C), 126.0 (2C), 101.4, 79.0, 77.4, 60.5, 41.5, 38.1, 34.6, 24.3, 23.0, 22.6, 14.2, 6.0; HRMS (ESI) calcd for $[C_{19}H_{28}O_4 + Na]^+$ 343.1879, found 343.1880.

(+)-Ethyl 2-((2*R*,4*R*,5*S*,6*R*)-5-Methyl-2,6-diphenyl-1,3-dioxan-4-yl)acetate (15c). The product was purified by silica gel chromatography eluting with 10% EtOAc/hexanes to yield benzylidine acetal in 33% yield as a clear, colorless oil. R_f = 0.26 (4:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +11.1 (*c* 1.0, CH_2Cl_2); IR (neat, cm^{-1}) 2982, 2165, 1734, 1497, 1452, 1348, 1260, 1183, 1135, 1100, 1052, 1027, 993, 755, 698; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.59 (d, J = 7.2 Hz, 1H), 7.37 (m, 9H), 5.79 (s, 1H), 5.15 (d, J = 2.4 Hz, 1H), 4.65 (ddd, J = 7.8, 6.0, 2.4 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 2.76 (dd, J = 15.6, 8.4 Hz, 1H), 2.53 (dd, J = 15.6, 6.0 Hz, 1H), 1.97 (qdd, J = 6.6, 2.4, 2.4 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), 0.79 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.9, 140.1, 138.5, 128.8, 128.1 (2C), 128.1 (2C), 127.0, 126.2 (2C), 125.3 (2C), 101.5, 81.7, 77.1, 60.6, 38.2, 36.6, 14.2, 6.1; HRMS (ESI) calcd for $[C_{21}H_{24}O_4 + Na]^+$ 363.1566, found 363.1562.

(+)-Ethyl 2-((2*S*,4*R*,5*R*,6*S*)-5,6-Dimethyl-2-phenyl-1,3-dioxan-4-yl)acetate (15d). The product was purified by silica gel chromatography eluting with 10% EtOAc/hexanes to yield benzylidine acetal in 63% yield as a clear, colorless oil. R_f = 0.42 (9:1 hexanes/EtOAc), $[\alpha]^{24}_D$ +21.6 (*c* 1.00, CH_2Cl_2); IR (neat, cm^{-1}) 3453, 3066, 3037, 2980, 2935, 2890, 2360, 1958, 1882, 1732, 1496, 1375, 1263, 1183, 1062, 918, 851, 757, 699, 650, 584; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (m, 2H), 7.33 (m, 3H), 5.58 (s, 1H), 4.40 (ddd, J = 7.8, 6.0, 2.4 Hz, 1H), 4.14 (dq, J = 7.2, 2.4 Hz, 2H), 4.10 (dq, J = 6.6, 2.4 Hz, 1H), 2.69 (dd, J = 15.6, 7.8 Hz, 1H), 2.48 (dd, J = 15.6, 6.0 Hz, 1H), 1.54 (qdd, J = 7.2, 2.4, 2.4 Hz, 1H), 1.27 (d, J = 6.6 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H), 1.01 (d, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 170.9, 138.5, 128.6, 128.1 (2C), 126.1 (2C), 101.6, 77.2, 76.4, 60.4, 37.9, 35.4, 18.5, 14.1, 5.5; HRMS (ESI) calcd for $[C_{16}H_{22}O_4 + Na]^+$ 301.1410, found 301.1422.

Acknowledgment. We are grateful to NIH (GM63150) and NSF (CHE-0415469) for the support of our research program and NSF-EPSCoR (0314742) for a 600 MHz NMR and a LTQ-FT Mass Spectrometer at WVU.

Supporting Information Available: Complete experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061200H