

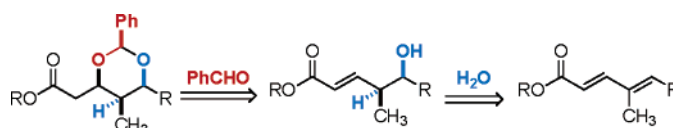
De Novo Synthesis of 2-Substituted *syn*-1,3-Diols via an Iterative Asymmetric Hydration Strategy

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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 benzylidene-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., mycotin A⁴, Figure 1). Thus we required a strategy that would address two structural

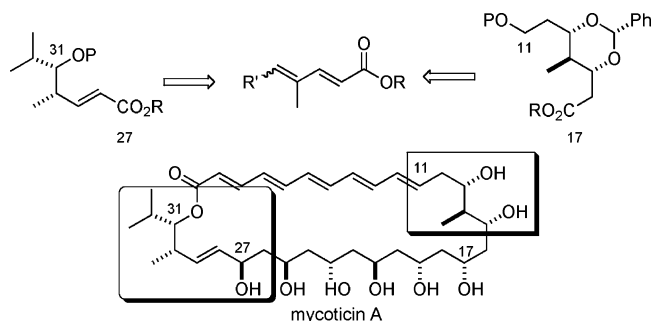


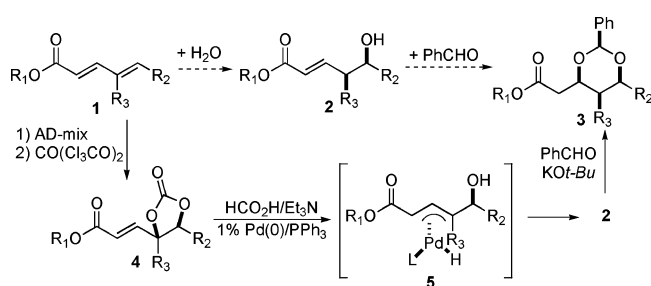
FIGURE 1. Asymmetric hydration approach to mycotin A

motifs of mycotin 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**).

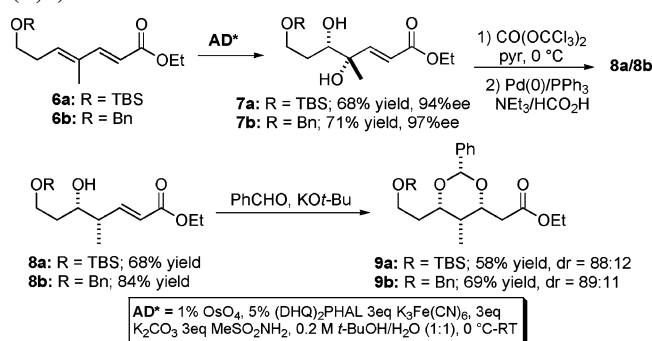
Alternatively, we envisioned that these two structural features could be prepared from C-4 substituted achiral dienoates by an iterative hydration approach (Scheme 1). This, of course, required that the initial asymmetric hydration reaction be stereospecific, which was demonstrated by substituting DCO₂H

(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 mycotin 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 mycotin 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.

SCHEME 1. Asymmetric Iterative Hydration of C4-Methyl Dienoates


for HCO₂H (Scheme 1, R₃ = H; see Supporting Information). Then, we embarked on an effort to expand the asymmetric hydration methodology to include substituted dienates (**1**) for the preparation of the 4-methyl-5-hydroxyenoates (**2**) and the benzylidene-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 dienates (**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 dienates we chose to study (**6a/b**) proved to be very promising (Scheme 2).⁷ Thus, exposure of dienates **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 Et₃N·HCO₂H (Table 2).⁸ Finally, both homoallylic alcohols **8a** and **8b** were readily converted into the

(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.

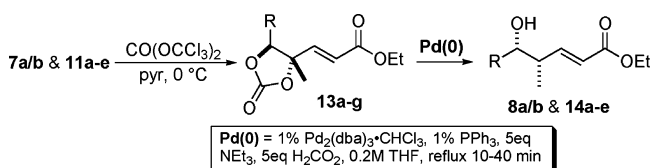
TABLE 1. Asymmetric dihydroxylation of (E,E)-Dienoates

AD* = 1% OsO₄, 5% Ligand, 3eq K₃Fe(CN)₆, 3eq K₂CO₃, 3eq MeSO₂NH₂, 0.2M *t*-BuOH/H₂O (1:1), 0 °C-RT

entry	R	ligand	yield (%)	ee ^a (11)	ratio ^b (11:12)
a	CH ₂ <i>i</i> Pr	(DHQ) ₂ PHAL	82	86	(1:1)
		DHQ-4-Me-2-Quin	75	73	(>99:1)
b	<i>i</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	<i>d</i>	(1:2.5)
		(DHQD) ₂ PHAL	78	<i>d</i>	(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 ¹H NMR. ^c 3 equiv of NaHCO₃ used as buffer. ^d ee of minor isomer not determined. ^e 2% Os, 10% ligand.

benzylidene-protected *syn*-3,5-dihydroxyester **9a** and **9b** by exposure to the Evans conditions (PhCHO, cat. KO^{*t*}-Bu, Table 3).

TABLE 2. Diastereoselective carbonate reduction


entry	R	yield, % (13)	yield, % (14)	dr ^a
a	CH ₂ <i>i</i> Pr	90	96	>95:5
b	<i>i</i> PR	84	98	>95:5
c	Ph	91	98	>95:5
d	Me	90	98	>95:5
e	Me(<i>ent</i> -1) ^b	90	98	>95:5
7a	(CH ₂) ₂ OTBS	71 (13f)	95 (8a)	>95:5
7b	(CH ₂) ₂ OBN	88 (13g)	96 (8b)	>95:5

^a Determined by ¹H NMR. ^b Dienoate subjected to (DHQD)₂PHAL.

Unfortunately, when we investigated the scope of this reaction sequence we uncovered complications with the dihydroxylation step (Table 1). The simplest dienate substrate (Table 1, entry d, R = Me)⁹ underwent dihydroxylation using (DHQ)₂PHAL and (DHQD)₂PHAL 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 dienate **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-

(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 iPr	75	90:10
b	iPr	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 CH₂Cl₂. 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% Pd₂(dba)₃·CHCl₃/PPh₃ in THF with 5 equiv of Et₃N·HCO₂H.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 benzylidene-protected *syn*-3,5-dihydroxyesters **15a–d**. With

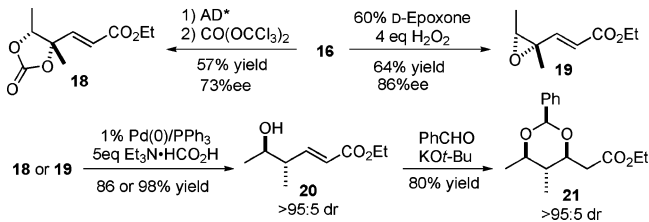
TABLE 4. Asymmetric dihydroxylation of (*E,Z*)-Dienoates^a

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 AD* = 1% OsO₄, 5% Ligand, 3eq K₃Fe(CN)₆, 3eq K₂CO₃, 3eq MeSO₂NH₂, 0.2M *t*-BuOH/H₂O (1:1), 0 °C-RT

^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 benzylidene 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)₂PYR (Table 4, entry 4).¹³ In an effort to further increase the enantioselectivity, a Shi epoxidation¹⁴ 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 benzylidene-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 Section¹⁶

General Procedure for Dihydroxylations. Into a round-bottom flask containing K₃Fe(CN)₆ (3 equiv), K₂CO₃ (3 equiv), MeSO₂-NH₂ (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 OsO₄ (1 mol %) immediately

(12) The ¹H NMR spectrum showed a qdd multiplicity ($J_{\text{HaHb}} = J_{\text{HbHc}} = 2.4$ 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 dienophile. 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 Na₂SO₄. After concentration the crude mixture was purified by silica gel column chromatography.

(+)-(E,4S,5S)-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), $[\alpha]_D^{25} +5.2$ (*c* 0.61, CH₂Cl₂); IR (neat, cm⁻¹) 3459(br), 2932, 2859, 1713, 1658, 1469, 1369, 1257, 1183, 1089, 987, 941, 836, 778, 728; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₆H₃₂O₅Si + Na]⁺ 355.1911, found 355.1909.

(+)-(E,4S,5S)-Ethyl 7-(Benzoyloxy)-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), $[\alpha]_D^{25} +5.2$ (*c* 2.0, CH₂Cl₂); IR (neat, cm⁻¹) 3461(br), 2931, 2860, 1715, 1453, 1367, 1282, 1186, 1095, 1031, 987, 698; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₇H₂₄O₅ + Na]⁺ 331.1515, found 331.1516.

(-)-(E,4S,5S)-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), $[\alpha]_D^{25} -21.7$ (*c* 1.0, CH₂Cl₂); IR (neat, cm⁻¹) 3460, 2957, 2870, 1701, 1656, 1466, 1368, 1307, 1282, 1189, 1034, 988, 869, 766, 743, 652; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₂H₂₂O₄ + Na]⁺ 253.1410, found 253.1402.

(-)-(E,4S,5S)-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), $[\alpha]_D^{25} -3.0$ (*c* 0.5, CH₂Cl₂); IR (neat, cm⁻¹) 3448, 2962, 2874, 1698, 1655, 1467, 1368, 1303, 1279, 1179, 1096, 1031, 984, 869, 725, 679; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₁H₂₀O₄ + 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), $[\alpha]_D^{25} +15.7$ (*c* 1.2, CH₂Cl₂); IR (neat, cm⁻¹) 3436, 2981, 1699, 1656, 1453, 1368, 1304, 1278, 1182, 1094, 1026, 985, 910, 868, 721, 700; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₄H₁₈O₄ + Na]⁺ 273.1097, found 273.1091

(+)-(E,4R,5S)-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), $[\alpha]_D^{25} +2.5$ (*c* 1.00, CH₂Cl₂); IR (neat, cm⁻¹) 3434 (br), 2980, 2936, 1699, 1655, 1449, 1368, 1303, 1276, 1181, 1090, 1033, 985, 920, 887, 729; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 CH₂Cl₂ (0.4 M) in an ice bath was added pyridine (5 equiv). Triphosgene (1.1 equiv) in CH₂Cl₂ (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 CuSO₄ 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 Na₂SO₄ and concentrated. The crude mixture was then purified by flash column chromatography.

(+)-(E)-Ethyl 3-((4S,5S)-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), $[\alpha]_D^{25} +35.6$ (*c* 1.0, CH₂Cl₂); IR (neat, cm⁻¹) 2961, 1799, 1719, 1663, 1468, 1385, 1367, 1309, 1280, 1232, 1177, 1088, 1063, 1013, 982, 870, 774; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₃H₂₀O₅ + Na]⁺ 279.1202, found 279.1204.

(+)-(E)-Ethyl 3-((4S,5S)-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), $[\alpha]_D^{25} +18.3$ (*c* 1.0, CH₂Cl₂); IR (neat, cm⁻¹) 2973, 1801, 1720, 1663, 1472, 1368, 1281, 1245, 1175, 1109, 1062, 1027, 982, 839, 774; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₂H₁₈O₅ + Na]⁺ 265.1046, found 265.1050.

(-)-(E)-Ethyl 3-((4S,5S)-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), $[\alpha]_D^{25} -24.9$ (*c* 1.3, CH₂Cl₂); IR (neat, cm⁻¹) 2984, 1802, 1718, 1663, 1456, 1367, 1308, 1288, 1245, 1180, 1088, 1069, 1044, 1028, 979, 771, 700; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₅H₁₆O₅ + 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), $[\alpha]_D^{24} +12.7$ (*c* 1.00, CH₂Cl₂); IR (neat, cm⁻¹) 2987, 2941, 2301, 1821, 1726, 1664, 1446, 1390, 1348, 1312, 1235, 1183, 1086, 1034, 868, 774, 630; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₀H₁₄O₅ + 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), $[\alpha]_D^{24} -52.2$ (*c* 1.00, CH₂Cl₂); IR (neat) 2956, 2858, 1813, 1723, 1665, 1469, 1388, 1309, 1258, 1179, 1088, 1033, 982, 835, 777, 721; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₇H₃₀O₆Si + Na]⁺ 381.1703, found 381.1718.

(-)-(*E*)-Ethyl 3-((4*S*,5*S*)-5-(2-(Benzoyloxy)ethyl)-4-methyl-2-oxo-1,3-dioxolan-4-yl)acrylate (**13g**). 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), $[\alpha]_D^{24} -23.8$ (*c* 2.3, CH₂Cl₂); IR (neat, cm⁻¹) 2985, 2863, 1810, 1720, 1662, 1556, 1495, 1454, 1382, 1188, 1090, 985, 773, 741; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₈H₂₂O₆ + 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), $[\alpha]_D^{24} -30.2$ (*c* 0.65, CH₂Cl₂); 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 (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₀H₁₄O₅ + 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 Pd₂(dba)₃·CHCl₃ (1 mol %), PPh₃ (1 mol %), Et₃N (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), $[\alpha]_D^{24} -16.5$ (*c* 0.63, CH₂Cl₂); IR (neat, cm⁻¹) 3499 (br), 2955, 2859, 1720, 1651, 1463, 1368, 1256, 1181, 1144, 1093, 1038, 986, 835, 777, 726; ¹H NMR

(CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₆H₃₂O₄Si + Na]⁺ 339.1962, found 339.1954.

(-)-(*E*,4*S*,5*S*)-Ethyl 7-(Benzoyloxy)-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), $[\alpha]_D^{24} -18.9$ (*c* 1.20, CH₂Cl₂); IR (neat, cm⁻¹) 3486 (br), 2932, 2854, 1725, 1646, 1467, 1273, 1193, 1107, 1090, 741, 705; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₇H₂₄O₄Si + 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), $[\alpha]_D^{24} -43.7$ (*c* 1.0, CH₂Cl₂); IR (neat, cm⁻¹) 3436 (br), 2957, 2871, 1702, 1651, 1467, 1368, 1272, 1182, 1150, 1095, 1034, 989, 865, 729; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₁₂H₂₂O₃ + 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), $[\alpha]_D^{24} -29.8$ (*c* 0.77, CH₂Cl₂); IR (neat, cm⁻¹) 3410 (br), 2971, 2850, 1716, 1650, 1273, 1183, 1155, 1093, 1034; ¹H NMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 [C₉H₁₆O₃ + 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 Et₂O. The organic layers were combined, washed with brine, and dried over Na₂SO₄, 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 benzylidene acetal in 58% yield as a clear, colorless oil. $R_f = 0.62$ (4:1 hexanes/EtOAc), $[\alpha]_D^{24} -27.5$ (*c* 0.50, CH₂Cl₂); IR (neat, cm⁻¹) 2955, 2930, 2858, 1738, 1461, 1390, 1349, 1314, 1254, 1182, 1098, 1064, 1027, 941, 835, 776, 697; ¹H NMR (CDCl₃, 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 $[\text{C}_{23}\text{H}_{38}\text{O}_5 + \text{Na}]^+$ 445.2380, found 445.2398.

(-)-Ethyl 2-((2S,4R,5R,6S)-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 benzyldine acetal in 69% yield as a clear, colorless oil. $R_f = 0.39$ (4:1 hexanes/EtOAc), $[\alpha]_D^{24} -20.5$ (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; ^1H 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 $[\text{C}_{24}\text{H}_{30}\text{O}_5 + \text{Na}]^+$ 421.1985, found 421.2014.

(-)-Ethyl 2-((2S,4R,5R,6S)-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 benzyldine acetal in 75% yield as a clear, colorless oil. $R_f = 0.39$ (4:1 hexanes/EtOAc), $[\alpha]_D^{24} -7.3$ (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; ^1H 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 $[\text{C}_{19}\text{H}_{28}\text{O}_4 + \text{Na}]^+$ 343.1879, found 343.1880.

(+)-Ethyl 2-((2R,4R,5S,6R)-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 benzyldine acetal in 33% yield as a clear, colorless oil. $R_f = 0.26$ (4:1 hexanes/EtOAc), $[\alpha]_D^{24} +11.1$ (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; ^1H 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 $[\text{C}_{21}\text{H}_{24}\text{O}_4 + \text{Na}]^+$ 363.1566, found 363.1562.

(+)-Ethyl 2-((2S,4R,5R,6S)-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 benzyldine acetal in 63% yield as a clear, colorless oil. $R_f = 0.42$ (9:1 hexanes/EtOAc), $[\alpha]_D^{24} +21.6$ (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; ^1H 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 $[\text{C}_{16}\text{H}_{22}\text{O}_4 + \text{Na}]^+$ 301.1410, found 301.1422.

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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>.

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