Articles

Sequential Diastereoselective Addition and Palladium(II)-Catalyzed Allylic Acetate Transposition of *syn*- and *anti*-α-Acetoxy-β-silyl-(*E*)-hex-4-enoates with Achiral Acetals. Asymmetric Synthesis of Differentiated Syn and Anti 1,3-Diol Synthons

James S. Panek,* Michael Yang,† and Jason S. Solomon

Department of Chemistry, Metcalf Center for Science and Engineering, Boston University, Boston, Massachusetts 02215

Received September 11, 1992

syn- and *anti*-methyl α-acetoxy-β-(dimethylphenylsilyl)-(*E*)-hex-4-enoates, (2*R*,3*R*)-**8a** and (2*S*,3*R*)-**8b**, undergo highly diastereo- and enantioselective addition reactions with aldehydes and acetals **11** catalyzed by the action of trimethylsilyl trifluoromethanesulfonate (TMSOTf) generating α-acetoxy-β,γ-unsaturated esters (allylic acetates) **12**. A subsequent allylic acetate transposition promoted by dichloropalladium bisacetonitrile complex, $PdCl_2(MeCN)_2$ afforded the differentiated 1,3-diol synthons **13**.

Introduction

The 1,3-diol subunit is commonly found in many natural products of acetogenic and propionate biosynthetic origin and has often served as a focal point for the development of synthetic methodology. Indeed, a number of methods are available for the synthesis of stereochemically defined 1,3-diols; these methods range from directed reductions of β-hydroxy ketones[1] to nucleophilic opening of chiral epoxides.[2] Many of these methods have been reviewed by Oishi and Nakata.[3] Earlier reports from our laboratory have established the utility of functionalized (*E*)-crotylsilanes as carbon nucleophiles in highly diastereo- and enantioselective addition reactions to acetals and aldehydes. Those studies resulted in the development of a useful strategy for the asymmetric construction of homoallylic ethers,[4] tetrahydrofurans,[5] and γ-hydroxy-α-amino acid synthons.[6] Herein we disclose our results of experiments concerning the utility of related α-acetoxy (*E*)-crotylsilanes, (2*R*,3*R*)-**8a** and (2*S*,3*R*)-**8b**, in a sequential Lewis acid-promoted condensation and palladium(II)-catalyzed allylic acetate isomerization reaction with acetals and aldehydes. By implementation of the sequential asymmetric condensation and allylic ester transposition strategy the crotylsilane reagents described here provide a complementary approach to the stereocontrolled synthesis of *syn*- or *anti*-1,3-dihydroxy-2-methyl synthons (syn and anti 1,3-diol units).

Synthesis of the Chiral (*E*)-Crotylsilanes. The asymmetric synthesis of (2*R*,3*R*)-(*E*)-methyl 2-acetoxy-3-(dimethylphenylsilyl)hex-4-enoate (**8a**) and (2*S*,3*R*)-(*E*)-methyl 2-acetoxy-3-(dimethylphenylsilyl)hex-4-enoate (**8b**) is summarized in Schemes I and II. The preparation of crotylsilane **8a** was initiated by a catalytic hydrosilation[7a] of 3-butyn-2-ol employing bis(η-divinyltetramethyldisiloxane)tri-*tert*-butylphoshineplatinum(0) as the catalyst illustrated as A, which was prepared according to the procedure of Chandra and Lo.[7b] This process afforded a 8:1 mixture of the isomeric (*E*)-vinylsilanes **2a** and **2b** in a combined yield of 96%. The minor 1,1-disubstituted olefin **2b** was easily removed by chromatography on silica gel. The racemic (*E*)-vinylsilane **2a** was resolved using a

† Recipient of a Graduate Fellowship from the Organic Chemistry Division of the American Chemical Society 1992-1993 sponsored by Pfizer Inc.

(1) Anti 1,3-diols: (a) Evans, D. A.; Chapman, K. T. *Tetrahedron Lett.* **1986**, *27*, 5939-5942. (b) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560-3578. (c) Syn 1,3-diols: Evans, D. A.; Hoveyda, A. H. *J. Org. Chem.* **1990**, *55*, 5190-5192. Earlier reports of syn-selective reductions of β-hydroxy ketones: (d) Narasaka, K.; Pia, F.-C. *Chem. Lett.* **1980**, 1415-1418. (e) Narasaka, K.; Pai, F.-C. *Tetrahedron* **1984**, *40*, 2233-2238. (f) Kathawala, F. G.; Prager, B.; Prasad, K.; Repic, O.; Shapiro, M. J.; Stabler, R. S.; Widler, L. *Helv. Chim. Acta* **1986**, *69*, 803-805. (g) Kiyooka, S. I.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett.* **1986**, *27*, 3009-3012. (h) Bonadies, F.; Fabio, R. D.; Gubbiotti, A.; Mecozzi, S.; Bonini, C. *Tetrahedron Lett.* **1987**, *28*, 703-706. (i) Chen, K.-M.; Gunderson, K. G.; Hardtmann, G. E.; Prasad, K.; Repic, O.; Shapiro, M. J. *Chem. Lett.* **1987**, 1923-1926. (j) Hanamoto, T.; Hiyama, T. *Tetrahedron Lett.* **1988**, *29*, 6467-6470.

(2) Optically pure 1,3-diols from (2*R*,4*R*)- and (2*S*,4*S*)-1,2:4,5-diepoxypentane: (a) Rychnovsky, S. D.; Griesgraber, G.; Zeller, S.; Skalitzky, D. J. *J. Org. Chem.* **1991**, *56*, 5161-5169. For reports concerning the use of chiral crotylboronates in addition reactions to aldehydes for the synthesis of 1,3-dihydroxy and 1,3-dihydroxy-2-methyl arrays see: (b) Roush, W. R.; Hoong, L. K., Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109-4117. (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117-4126. (d) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339-6348. (e) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348-6359 and references cited therein. (f) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *426*, 489-594.

(3) Oishi, T.; Nakata, T. *Synthesis* **1990**, 635-645.

(4) (a) Aryl acetals: Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 6594-6600. (b) Hetero-substituted acetals: Panek, J. S.; Yang, M. *J. Org. Chem.* **1991**, *56*, 5755-5758. (c) Panek, J. S.; Yang, M.; Xu, F. *J. Org. Chem.* **1992**, *57*, 5790-5792.

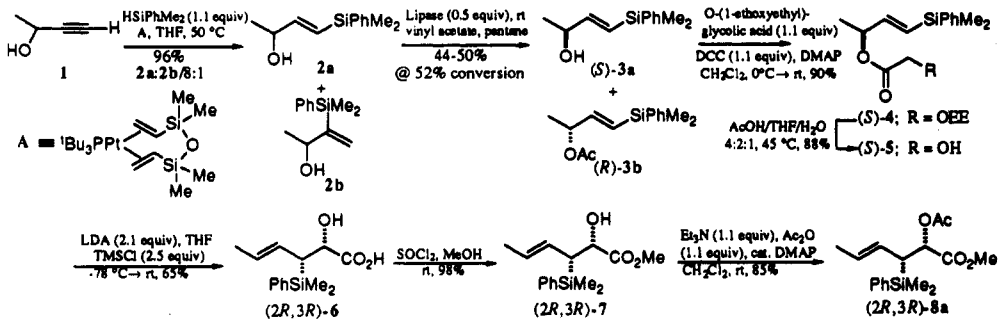
(5) Aldehydes: Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868-9870.

(6) Panek, J. S.; Yang, M.; Muler, I. *J. Org. Chem.* **1992**, *57*, 4063-4064.

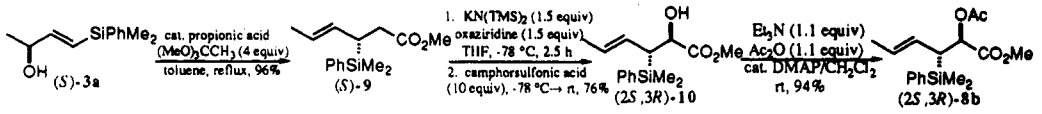
(7) (a) Murphy, P. J.; Spencer, J. L.; Procter, G. *Tetrahedron Lett.* **1990**, *31*, 1051-1054. (b) Chandra, G.; Lo, P. Y. *Organometallics* **1987**, *6*, 191-192.

0022-3263/93/1958-1003$04.00/0

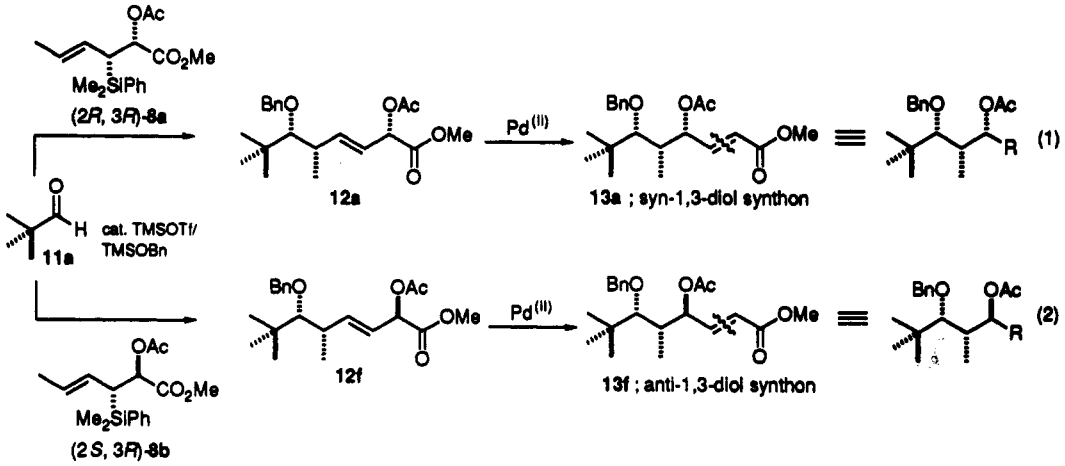
Scheme I. Synthesis of (2*R*,3*R*)-(*E*)-Methyl 2-Acetoxy-3-(dimethylphenylsilyl)hex-4-enoate



Scheme II. Synthesis of (2*S*,3*R*)-(*E*)-Methyl-2-Acetoxy-3-(dimethylphenylsilyl)hex-4-enoate



Scheme III



lipase-promoted resolution[8] to yield the (*S*)-alcohol **3a** in high enantiomeric purity after chromatographic separation from the enantiomeric (*R*)-acetate. A subsequent dicyclohexylcarbodiimide-promoted esterification with *O*-(1-ethoxyethyl)glycolic acid[9] produced the glycolate **4**. A mild aqueous acid hydrolysis produced the α-hydroxy ester **5**, the required Claisen substrate. As previously described,[10] an Ireland–Claisen rearrangement utilizing chelation-controlled reaction conditions promoted the formation of the (*Z*)-(*O*)-silylketene acetal which upon bond reorganization cleanly afforded the syn α-hydroxy (*E*)-crotylsilane **7** with >40:1 syn/anti diastereoselection after conversion to the methyl ester. Acylation of the secondary alcohol under standard conditions afforded **8a** in 43% overall yield (from **3a**) as a single diastereomer in highly scalemic form.

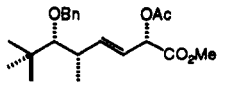
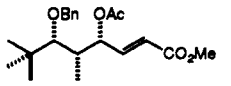
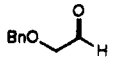
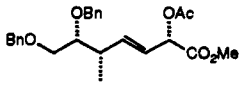
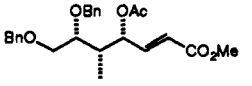
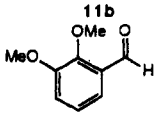
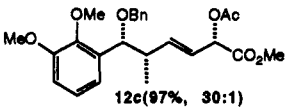
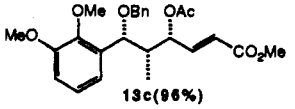
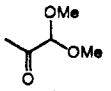
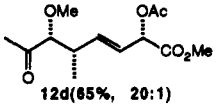
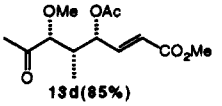
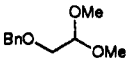
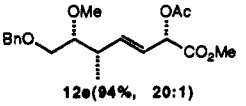
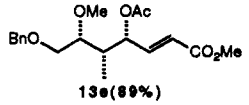
The synthesis of the *anti*-(*E*)-crotylsilane **8b** was initiated with an ortho ester Claisen rearrangement of (*S*)-**3a** which gave the optically active crotylsilane **9** in excellent yield with an ee of 93%.[11] This was followed by an asymmetric hydroxylation with *trans*-3-phenyl-2-(phenylsulfonyl)oxaziridine[12a] of the β-silyl enolate derived by the low-temperature deprotonation of **9** [KN(TMS)$_2$, oxzaridine, THF, −78 °C] to give the α-hydroxy ester **10** with complete stereocontrol.[12b,c] The *anti*-α-acetoxy (*E*)-crotylsilane (2*S*,3*R*)-**8b** was then obtained by a DMAP-catalyzed acylation.[13]

Enantioselective Addition Reactions to Acetals and in Situ Generated Oxonium Ions. The enantioselective condensation reactions can be carried out in two ways, by

(8) Sparks, M. A.; Panek, J. S. *Tetrahedron Lett.* **1991**, *33*, 4085–4088.
(9) Boger, D. L.; Curran, T. T. *J. Org. Chem.* **1992**, *57*, 2235–2244.
(10) Sparks, M. A.; Panek, J. S. *J. Org. Chem.* **1991**, *56*, 3421–3438.

(11) (a) Johnson, W. S.; Werthemann, L.; Barlett, W. R.; Brocksom, T. J.; Li, T.-t.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741–743. (b) Ee determination of the Claisen product **9** was accomplished by a Mosher analysis using the method of Trost et al. [cf. Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovek, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370–2374] on the (*R*)-*O*-acetyl mandelate esters of the primary alcohols derived from the reduction of the methyl ester of the (*E*)-crotylsilanes. Methyl ester reduction of **9** with LiAlH$_4$ (1.0 equiv/THF/0 °C) followed by esterification of the derived primary alcohol with (*R*)-*O*-acetylmandelic acid [1.5 equiv/DCC (1.5 equiv)/cat. DMAP/CH_2Cl_2] [cf. Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548–3551] afforded the new mandelate esters in 91% yields (two steps).
(12) (a) Vishwakarma, L. C.; Stringer, O. D.; Davis, F. A. *Org. Synth.* **1988**, *66*, 203–210. (b) Diastereoselective alkylation of β-silyl enolates, see: Panek, J. S.; Beresis, R.; Xu, F.; Yang, M. *J. Org. Chem.* **1991**, *56*, 7341–7344. (c) Asymmetric oxygenation of chiral imide enolates, see: Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346–4348.
(13) For an alternative approach to these structural types by an Ireland–Claisen rearrangement of (*Z*)-vinylsilanes, see: Panek, J. S.; Clark, T. D. *J. Org. Chem.* **1992**, *57*, 4323–4326.
(14) (a) Sakurai, H.; Sasaki, K.; Hayashi, J.; Hosomi, A. *J. Org. Chem.* **1984**, *49*, 2808–2809. (b) Imwinkelried, R.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 765–766. (c) Mukaiyama, T.; Ohshima, M.; Miyoshi, N. *Chem. Lett.* **1987**, 1121–1124. For the use of TMSOTf see: (d) Mekhalfia, A.; Marko', I. E. *Tetrahedron Lett.* **1991**, *32*, 4779–4782. (e) Marko', I. E.; Mekhalfia, A.; Bayston, D. J.; Adams, H. *J. Org. Chem.* **1992**, *57*, 2211–2213.

Table I. Enantioselective Additions of 2,3-*syn*-(*E*)-Crotylsilanes to Aldehydes and Acetals[a]

entry	aldehydes	crotylsilanes (methods[a] temp.)	major diastereomer[b] (%[c] 5,6-syn/anti ratio[d])	syn 1,3-diol[e] (%[c])
1	 11a	8a (A; -50 °C)	 12a(87%, 20:1)	 13a(91%)
2	 11b	8a (A; -35 °C)	 12b(51%, 20:1)	 13b(86%)
3	 11c	8a (A; -78 °C)	 12c(97%, 30:1)	 13c(96%)
4	 11d	8a (B; -35 °C)	 12d(65%, 20:1)	 13d(65%)
5	 11e	8a (B; -40 °C)	 12e(94%, 20:1)	 13e(89%)

[a] Method A: All reactions were run in CH_2Cl_2 (0.2–0.5 M) with 1.2 equiv of aldehyde and 1.0 equiv of TMSOTf (0.5 equiv of TMSOTf for the aromatic aldehyde) from −78 °C to the temperature indicated in the table for 12–20 h in the presence of TMSOBn (1.2 equiv). Method B: All reactions were run in CH_2Cl_2 (0.2–0.5 M) with 1.2 equiv of acetal and 1.0 equiv of TMSOTf (0.5 equiv of TMSOTf for aromatic acetals) from −78 °C to the temperature indicated in the table for 12–20 h. [b] The absolute stereochemistry of the major diastereomer assigned based on the anti addition [S_E' mechanism] of the optically pure (*E*)-crotylsilanes to the C=OMe$^+$ π-bond (96% de); cf. ref 4. [c] All yields are based on pure materials isolated by chromatography on SiO_2. [d] Ratio of products was determined by ^1H NMR (400 MHz) operating at S/N ratio of >200:1. [e] All the reactions of allylic acetate tranpositions were run in CH_2Cl_2 (0.2–0.5 M) with 0.2 equiv of $PdCl_2(CH_3CN)_2$ for 36 h at ambient temperature.

reaction with a preformed acetal or by a procedure involving the in situ generation and trapping of an oxonium ion.[4c,14] The action of a Lewis acid, trimethylsilyl trifluoromethanesulfonate (TMSOTf), and a silyl ether (Me_3SiOR) cleanly promotes the asymmetric addition directly from the corresponding aldehyde.[14d,e] The in situ process is illustrated in eqs 1 and 2. Thus, combining the chiral (*E*)-crotylsilane reagent (2*R*,3*R*)-**8a** or (2*S*,3*R*)-**8b** with trimethylacetaldehyde **11a** and the trimethylsilyl ether of benzyl alcohol (TMSOBn)[15] followed by the addition of TMSOTf led to the construction of homoallylic ethers **12a** and **12f**. A subsequent $Pd^{(II)}$-catalyzed allylic ester transposition with dichloropalladium bisacetonitrile[16] transferred the derived allylic acetate into the differentiated 1,3-diol derivatives **13a** and **13f**.[17] Mercury(II) and palladium(II) salts have found broad applications as catalysts for low-temperature sigmatropic rearrangements.[18] Recent studies by Overman,[19] Bosnich,[20] and others[21] have defined structural requirements and mechanistic features of Pd(II)-catalyzed allylic ester transpositions and Cope rearrangements and have demonstrated that these reactions proceed at an accelerated rate relative to their thermal variations. However, the cases we have examined in the present study indicate that the transposition was quite slow, generally requiring upwards of 35 h at room temperature to ensure efficient conversion to the α,β-unsaturated esters **13**.

The important results of the study describing the construction of syn and anti 1,3-diol equivalents using an enantioselective condensation and subsequent palladium(II)-catalyzed allylic ester transposition are summarized in Tables I and II. The data clearly indicate that both diastereomeric (*E*)-crotylsilanes **8a** and **8b** generally exhibit high levels of selectivity in the reactions with a range of acetals and aldehydes in the formation of the homoallylic ethers **12**. The use of a catalytic amount of dichloropalladium bisacetonitrile [$PdCl_2(MeCN)_2$, 0.2 equiv, CH_2Cl_2, rt] resulted in the efficient interchange of ester functionality with the formation of a differentiated 1,3-diol moiety and the generation of an α,β-unsaturated ester **13** with complete preservation of chirality (see entries 1–5, Table I, and entries 1 and 3–6 in Table II).[22] Surprisingly, the Lewis acid-promoted allylsilane addition reactions of acetaldehyde **11f** proceeded in good yield but with a complete loss of selectivity (entry 2, Table II).

Assignment of Stereochemistry for the (*E*)-Crotylsilane Condensation–Allylic Acetate Transposition: Preparation of 2,3-Diacetoxy-5-methoxy-4-methyl Hexopyranosides 15a and 15b. The stereochemical assignment for the palladium(II)-catalyzed acetate trans-

(15) Coles, B. F.; Walton, D. R. M. *Synthesis* **1975**, 390–391.

(16) (a) For transition metal catalyzed sigmatropic rearrangements, see: Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205–247. (b) Overman, L. E.; Campbell, C. B.; Knoll, F. M. *J. Am. Chem. Soc.* **1978**, *100*, 4822–4834. (c) Overman, L. E.; Campbell, C. B. *J. Org. Chem.* **1976**, *41*, 3338–3340.

(17) All new compounds were isolated as chromatographically pure materials and exhibited acceptable ^1H NMR, ^{13}C NMR, IR, MS, and HRMS spectral data.

(18) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579–586.

(19) For mechanistic studies of transition metal catalyzed Claisen rearrangements, see: (a) Overman, L. E.; Jacobsen, E. J. *J. Am. Chem. Soc.* **1982**, *104*, 7225–7231. (b) Overman, L. E.; Renaldo, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 3945–3949.

(20) (a) Auburn, P. R.; Whelan, J.; Bosnich, B. *Organometallics* **1986**, *5*, 1533–1537. (b) Schenck, T. G.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2058–2066.

(21) (a) Henry, P. M. *J. Am. Chem. Soc.* **1972**, *94*, 5200–5206. (b) Grieco, P. A.; Takigawa, T.; Bongers, S. L.; Tanaka, H. *J. Am. Chem. Soc.* **1980**, *102*, 7587–7588. (c) Saito, S.; Hamano, S.; Moriyama, H.; Okada, K.; Moriwake, T. *Tetrahedron Lett.* **1988**, *29*, 1157–1160.

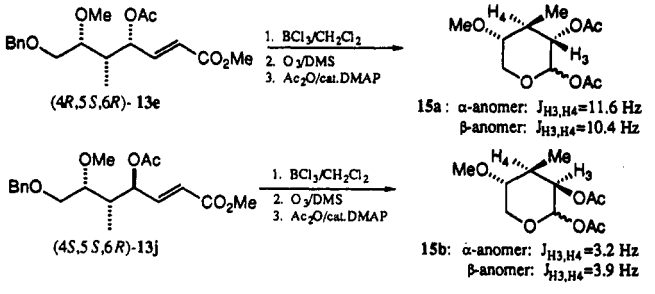
(22) (a) The crotylsilane additions are consistent with a stereospecific anti S_E' process as previously reported: Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962–4963. (b) the relative stereochemistry of the isomerization products **4e** and **4g** has been shown to be consistent with a suprafacial migration of the acetate group with respect to the olefin; see Experimental Section for details.

Table II. Enantioselective Additions of 2,3-*anti*-(*E*)-Crotysilanes to Aldehydes and Acetals[a]

entry	aldehydes	crotylsilane (methods[a] temp)	major diastereomer[b] (%[c] 5,6-syn/anti ratio[d])	anti 1,3-diol[e] (%[c])
1	11a	8b (A; -30 °C)	12f(30%, 15:1)	13f(78%)
2	11f	8b (A; -70 °C)	12g(91%, 2:1)	13g(98%)
3	11c	8b (A; -78 °C)	12h(75%, 30:1)	13h(95%)
4	11g	8b (B; -78 °C)	12i(80%, 10:1)	13i(93%)
5	11e	8b (B; -25 °C)	12j(54%, 20:1)	13j(96%)
6	11h	8b (B; -65 °C)	12k(90%, 30:1)	13k(88%)

[a] Method A: All reactions were run in CH_2Cl_2 (0.2–0.5 M) with 1.2 equiv of aldehyde and 1.0 equiv of TMSOTf (0.5 equiv of TMSOTf for the aromatic aldehyde) from −78 °C to the temperature indicated in the table for 12–20 h in the presence of TMSOBn (1.2 equiv). Method B: All reactions were run in CH_2Cl_2 (0.2–0.5 M) with 1.2 equiv of acetal and 1.0 equiv of TMSOTf (0.5 equiv of TMSOTf for aromatic acetals) from −78 °C to the temperature indicated in the table for 12–20 h. [b] The absolute stereochemistry of the major diastereomer assigned based on the anti addition [S_E' mechanism] of the optically pure (*E*)-crotylsilanes to the C=OMe$^+$ π-bond (96% de); cf. ref 4. [c] All yields are based on pure materials isolated by chromatography on SiO_2. [d] Ratio of products was determined by ^{1}H NMR (400 MHz) operating at S/N ratio of >200:1. [e] All the reactions of allylic acetate tranpositions were run in CH_2Cl_2 (0.2–0.5 M) with 0.2 equiv of $PdCl_2(CH_3CN)_2$ for 36 h at ambient temperature.

Scheme IV



position products **13e**/**13j** was accomplished by ^{1}H-NMR analysis and was based on the measurement of three-bond coupling constants of the vicinally related H_3 and H_4 protons. A first-order analysis was obtained by homonuclear decoupling experiments performed on the α and β-anomers of the derived hexopyranosides **15a** and **15b** respectively.

In order to assign the relative stereochemistry of the acetate transposition, diastereomers **13e** and **13j** were converted to the hexopyranosides **15a** and **15b**. The processes are illustrated in Scheme IV. Thus, diastereomer **13e** derived from (2*R*,3*R*)-**8a** and **13j** produced from (2*S*,3*R*)-**8b** were converted to the illustrated hexoses **15a** and **15b** in three steps. For each diastereomer the C7 benzyl group was removed with BCl_3 (1.3 equiv) −78 → 0 °C followed by quench with MeOH.[23] The α,β-unsaturated esters of the derived primary alcohols **14a** and **14b** were oxidatively cleaved by ozonolysis at low temperature [O_3, CH_2Cl_2, −78 °C; DMS (10 equiv)] followed by warming to room temperature to produce a 1:1 anomeric mixture of the pyranoside which was immediately subjected to standard acylation conditions (1.7 equiv of Ac_2O, 1.7 equiv of Et_3N, cat. DMAP) in CH_2Cl_2 to give the hexopyranoside **15** as a 1:1 mixture of anomeric acetates. Thus, the pyranoside **15a**, derived from the all-syn diastereomer **13e**, exhibited measured $^3J_{H3,H4}$ values of 11.6 and 10.4 Hz for the α and β anomers, respectively, indicating a trans diaxial relationship between the H_3 and H_4 protons and thus a syn relationship on the acyclic chain **13e**. Pyranoside **15b** was generated by the same reaction sequence and exhibited smaller $^3J_{H3,H4}$ values of 3.2 and 3.9 Hz for the α and β anomers, respectively, indicating a cis equatorial–axial relationship between the H_3 and H_4 protons and anti stereochemistry on **13j**. The stereochemical assignments confirmed that the transposition of the acetate was suprafacial with respect to the olefin and are consistent with the results of mechanistic studies of transition metal catalyzed Claisen rearrangements reported by Overman[19] and Bosnich.[20] No products arising from loss of π-facial selectivity in the acetate isomerization step could be detected chromatographically or by ^{1}H-NMR analysis.

In the context of acyclic diastereoselective reaction processes, the use of asymmetric allylsilane bond construction methodology together with the palladium(II)-catalyzed allylic ester transposition in addition reactions of α-acetoxy (*E*)-crotylsilanes to oxonium ions expands the scope of these reagents to include the asymmetric synthesis of stereochemically well-defined 1,3-diol syn-

(23) Williams, D. R.; Brown, D. L.; Benbow, J. W. *J. Am. Chem. Soc.* **1989**, *111*, 1923–1925.

thons. Further studies concerning the applications of these reagents in natural product synthesis will be reported in due course.

Experimental Section[24]

(±)-1-(Dimethylphenylsilyl)-1-buten-3-ol (2a). To a solution of 3-butyn-2-ol (10.0 g, 0.143 mol) dissolved in dry THF (0.25 M 570 mL) was added phenyldimethylsilane (21.4 g, 0.157 mol) and bis(η-divinyltetramethyldisiloxane)tri-*tert*-butylphosphineplatinum(0)[7b] (12 mg, 2.05 × 10^{-5} mol). The reaction mixture was then heated at reflux for 12 h with stirring. The solvent was then removed under reduced pressure to yield a colorless crude oil containing **2a** and **2b** in an 8:1 ratio. The crude oil was subjected to chromatography on silica gel whereupon the major regioisomer **2a** was eluted with 4% EtOAc/petroleum ether (PE) to afford 24.60 g (83.5%) of pure (**2a**): ^{1}H NMR δ 7.56–7.28 (m, 5 H), 6.22 (dd, 1 H, *J* = 4.9, 18.7 Hz), 5.99 (dd, 1 H, *J* = 1.3, 18.7 Hz), 4.34 (m, 1 H), 1.30 (d, 3 H, *J* = 6.5 Hz), 0.38 (s, 6 H); ^{13}C NMR δ 151.3, 133.8, 128.9, 127.6, 126.6, 125.9, 70.4, 22.8, -2.7(2c); IR (neat) ν_{max} 3380, 3080, 2960, 1730, 1620, 1430, 1250, 1110, 860 cm^{-1}; CIHRMS M + NH_4^+ (calcd for $C_{12}H_{22}NOSi$) 224.1470, (found) 224.1416.

(3*S*)-1-(Dimethylphenylsilyl)-1-buten-3-ol (3a) and (3*R*)-1-(Dimethylphenylsilyl)-1-buten-3-yl Acetate (3b). To a pentane solution of the racemic alcohol **2a** (10 g, 48.54 mmol, 0.2 M) was added a crude preparation of the lipase (5 g, 0.5 wt equiv of Amano AK) and freshly distilled vinyl acetate (242.7 mmol, 22.37 mL, 5.0 equiv). The heterogeneous mixture was vigorously stirred at rt for 4 h before the reaction mixture was filtered through a sintered glass funnel to recover the enzyme extract. The pentane was removed under reduced pressure and the products purified by flash chromatography on SiO_2 affording 5.65 g (47%) of (*S*)-**3a** and 4.40 g (44%) of (*R*)-**3b** as colorless oils. (*S*)-**3a**: ^{1}H NMR δ 7.56–7.28 (m, 5 H), 6.22 (dd, 1 H, *J* = 4.9, 18.7 Hz), 5.99 (dd, 1 H, *J* = 1.3, 18.7 Hz), 4.34 (m, 1 H), 1.30 (d, 3 H, *J* = 6.5 Hz), 0.38 (s, 6 H); ^{13}C NMR δ 151.3, 133.8, 128.9, 127.6, 126.6, 125.9, 70.4, 22.8, -2.7(2C); IR (neat) ν_{max} 3380, 3080, 2960, 1730, 1620, 1430, 1250, 1110, 860 cm^{-1}; CIMS (NH_3) *m/e* (relative intensity) 224 (M + NH_4, 100), 206 (M, 44); CIHRMS (NH_3) *m/e* M + NH_4 (calcd for $C_{12}H_{22}OSiN$ 224.1470, found 224.1416; $[\alpha]^{23}_D$ = +1.94° (*c* 1.65, $CHCl_3$). (*R*)-**3b**: ^{1}H NMR δ 7.5–7.3 (m, 5 H), 6.1 (dd, 1 H, *J* = 4.64, 18.8 Hz), 5.9 (dd, 1 H, *J* = 1.33, 18.8 Hz), 5.38 (m, 1 H), 2.08 (s, 3 H), 1.32 (d, 3 H, *J* = 6.5 Hz), 0.37 (s, 6 H); ^{13}C NMR δ 170.2, 146.6, 138.2, 133.8, 129.0, 128.0, 127.8, 127.7, 72.1, 64.1, 21.3, 20.3, 19.8, -2.7 (2 C); IR (neat) ν_{max} 3040, 2950, 1740, 1430, 1570, 1240, 1110, 1040, 830, 740 cm^{-1}; CIMS (NH_3) *m/e* (relative intensity) 209 (33), 179 (24), 171 (68), 135 (100), 117 (97); CIHRMS (NH_3) *m/e* M + NH_4^+ calcd for $C_{14}H_{20}O_2Si$ 248.1233, found 248.1299; $[\alpha]^{23}_D$ = +24.5° (*c* 1.0, $CHCl_3$).

(3*S*)-(*E*)-1-(Dimethylphenylsilyl)-1-buten-3-yl Hydroxyacetate (5). A solution of (*S*)-**3a** (2 g, 9.7 mmol) in 20 mL of CH_2Cl_2 (0.5 M) at 0 °C under N_2 was treated with *O*-(1-ethoxyethyl)glycolic acid[9] (1.1 equiv, 1.6 g, 10.7 mmol) and cat. DMAP (ca. 5 mg). To the stirred solution was then added DCC (1.1 equiv, 2.2 g, 10.7 mmol). Immediately after addition of DCC a white suspension of urea precipitated out of solution. The solution was allowed to warm to rt over 16 h before the suspension of urea was filtered through a pad of Celite using a sintered glass funnel. The solvent of the filtrate was removed in vacuo to produce crude **4** as a yellow oil. The crude oil product **4** (3.5 g, 10.3 mmol) was further dissolved in 20 mL of AcOH/THF/H_2O mixture with a ratio 4:2:1, respectively. The reaction mixture was left at 45 °C and refluxed for 4 h before it was quenched with a saturated solution of $NaHCO_3$ (25 mL). The organic layer was extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried over Na_2SO_4, and the solvents and volatiles were removed under reduced pressure to give the crude product **5**. The crude mixture was flash-chromatographed on silica gel (15% EtOAc/PE eluant) to afford 2.03 g (88%) of pure **5** as a clear, viscous oil: ^{1}H NMR δ 7.55–7.38 (m, 5 H), 6.01 (dd, 1 H, *J* = 4.3, 19.0 Hz), 6.03 (d, 1 H, *J* = 19.0 Hz), 5.51 (m, 1 H), 4.20 (s, 2 H), 2.79 (broad s, OH), 11.39 (d, 3 H, *J* = 6.5 Hz), 0.40 (s, 6 H); ^{13}C NMR δ 172.6, 145.5, 137.9, 133.7, 129.2, 129.0, 127.8, 73.7, 60.7, 19.8, -2.8 (2 C); IR (neat) ν_{max} 3430, 2950, 1730, 1420, 1210, 1100 cm^{-1}; CIMS (NH_3) *m/e* (relative intensity) 382 (M + NH_4^+, 57), 206 (11), 189 (100), 145 (59), 131 (55); CIHRMS (NH_3) *m/e* M + NH_4^+ calcd for $C_{14}H_{24}O_3SiN$ 282.1526, found 282.1536); $[\alpha]^{23}_D$ = +27.4° (*c* 4.00, $CHCl_3$).

(2*R*,3*R*)-(*E*)-3-(Dimethylphenylsilyl)-2-hydroxyhex-4-enoic Acid (6). To a solution of diisopropylamine (12.22 mmol, 1.71 mL) in 23 mL of freshly distilled THF at 0 °C was added nBuLi (11.51 mmol, 5.75 mL, 2.0 M in hexanes). The solution was stirred at 0 °C for 30 min before being cooled to -78 °C and adding a solution of TMSCl (10.8 equiv, 77.65 mmol, 9.85 mL) and pyridine (11.9 equiv, 85.56 mmol, 6.92 mL) in 17 mL of dry THF. After 5 min a solution of **5** (1.9 g, 7.19 mmol, in 47.9 mL of dry THF) was added. The solution was stirred at -78 °C for 5 min before being warmed to 0 °C for 1 h. The solution was then diluted with 10% aqueous HCl (50 mL). The solution was extracted with EtOAc (2 × 50 mL) and dried ($MgSO_4$) and the solvent removed in vacuo to afford a crude yellow oil. Purification on SiO_2 (30% EtOAc/PE eluant) afforded 1.24 g (65%) of the pure **6** as a clear oil in a syn/anti ratio of 40:1 as determined by ^{1}H NMR analysis: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.26 (m, 5 H), 5.37 (m, 2 H), 4.26 (dd, 1 H, *J* = 6.8, 4.8 Hz), 2.68 (d, 1 H, *J* = 6.8 Hz, OH), 2.28 (dd, 1 H, *J* = 4.8, 9.8 Hz), 1.69 (d, 3 H, *J* = 5.2 Hz), 0.34 (s, 3 H), 0.32 (s, 3 H); ^{13}C NMR δ 174.7, 137.5, 134.2, 129.1, 127.6, 127.3, 126.5, 72.3, 51.9, 39.7, 18.1, -3.3, -3.7; IR ($CHCl_3$) ν_{max} 3500–2500 (b), 1700, 1250, 1120, 830 cm^{-1}; CIMS (NH_3) *m/e* (relative intensity) 278 (M + NH_4^+, 17), 264 (100), 201 (13); CIHRMS (NH_3) *m/e* M + NH_4^+ calcd for $C_{14}H_{20}O_3SiN$ 278.1212 found 278.1215.

(2*R*,3*R*)-(*E*)-Methyl 3-(Dimethylphenylsilyl)-2-hydroxyhex-4-enoate (7). A solution of methanol (50 mL) and **6** (1.9 g, 7.19 mmol) was cooled to 0 °C and treated dropwise with $SOCl_2$ (10.78 mmol, 1.28 mL) over 10 min. After the addition was complete, the reaction mixture was allowed to warm to rt over 3 h. When the starting acid (**6**) was consumed as evidenced by TLC analysis, the methanol was evaporated under reduced pressure. Immediate purification of the crude product on SiO_2 (10% EtOAc/PE eluant) afforded 1.86 g (98%) the desired methyl ester **7**: ^{1}H NMR δ 7.53–7.27 (m, 5 H), 5.43–5.33 (m, 2 H), 4.23 (d, 1 H, *J* = 4.9 Hz), 3.56 (s, 3 H), 2.25 (dd, 1 H, *J* = 4.9, 9.8 Hz), 1.69 (d, 3 H, *J* = 5.1 Hz), 0.35 (s, 3 H), 0.34 (s, 3 H); ^{13}C NMR δ 174.8, 137.5, 134.2, 129.0, 127.6, 127.2, 126.5, 72.3, 51.9, 39.7, 18.1, -3.3, -3.7; CIMS (NH_3) *m/e* (relative intensity) 296 (M + NH_4^+, 100), 261 (20), 201 (26); CIHRMS (NH_3) *m/e* M + NH_4^+ calcd for $C_{15}H_{26}O_3SiN$ 296.1682), found 296.1682; $[\alpha]^{23}_D$ = +8.22° (*c* 1.72, $CHCl_3$).

(2*R*,3*R*)-(*E*)-Methyl 2-acetoxy-3-(dimethylphenylsilyl)-hex-4-enoate (8a) obtained by DMAP-catalyzed acylation: ^{1}H NMR δ 7.50–7.35 (m, 5 H), 5.33–5.26 (m, 2 H), 4.97 (d, 1 H, *J* = 7.1 Hz), 3.55 (s, 3 H), 2.35 (dd, 1 H, *J* = 7.1, 9.2 Hz), 1.98 (s, 3 H), 1.66 (d, 3 H, *J* = 6.1 Hz), 0.35 (s, 6 H); ^{13}C NMR δ 170.5, 170.3, 137.1, 134.0, 129.1, 127.6, 126.7, 125.8, 74.1, 51.7, 35.8, 20.5, 18.1, -3.2, -3.9; IR (neat) ν_{max} 3010, 1740, 1200, 750 cm^{-1}; CIMS (NH_3) *m/e* (relative intensity) 338 (M + NH_4^+, 100), 261 (53); CIHRMS M + NH_4^+ calcd for $C_{17}H_{28}NO_4Si$ 338.1788, found 338.1787; $[\alpha]^{23}_D$ = -1.06° (*c* 1.31, $CHCl_3$).

(3*S*,4*E*)-Methyl 3-(Dimethylphenylsilyl)-4-hexenoate (9). A stirred solution of **3a** (8 g, 38.8 mmol) in 78 mL of dry toluene (0.5 M) was treated with trimethyl orthoacetate (20 mL, 155 mmol) and freshly distilled propionic acid (0.3 mL, 3.8 mmol) at rt. The reaction mixture was refluxed for 16 h and then was allowed to cool to rt before it was quenched with a saturated solution of $NaHCO_3$ (40 mL). The mixture solution was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were dried over Na_2SO_4, and the solvents and volatiles were removed under reduced pressure to give the crude crotylsilane **9**. The

(24) General Experimental Section. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 and 67 MHz in $CDCl_3$ at ambient temperature. The reaction solvent, CH_2Cl_2, and triethylamine (Et_3N) were distilled from CaH_2. All extraction and chromatographic solvents, ethyl acetate (EtOAc), ethyl ether (Et_2O), and petroleum ether (P.E.) were distilled prior to use. Unless otherwise noted, nonaqueous reactions were carried out in flame- or oven-dried glassware under a dry nitrogen atmosphere. TMSOTf and $PdCl_2(MeCN)_2$ were both purchased from Aldrich Chemical Co., Inc. Analytical TLC was performed on Whatman Reagent 0.25-mm silica gel 60-A plates. Flash chromatography was performed as previously described (cf. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.)

crude mixture was flash chromatographed on silica gel (10% EtOAc/PE eluant) to afford 8.6 g (85%) of pure **9** as a clear, viscous oil: ^{1}H NMR δ 7.49–7.35 (m, 5 H), 5.28 (m, 2 H), 3.57 (s, 3 H), 2.33 (dd, 1 H, J = 6.3, 14.5 Hz), 2.27 (dd, 1 H, J = <1.0, 14.5 Hz), 2.20 (m, 1 H), 1.64 (d, 3 H, J = 4.7 Hz), 0.28 (s, 9 H); ^{13}C NMR δ 173.9, 136.8, 133.9, 129.8, 129.1, 127.7, 123.8, 51.4, 34.3, 28.7, 18.1, –4.5, –5.5; CIMS (NH_3), m/e (relative intensity) 280 (M + NH_4^+, 48), 263 (M^+, 39), 184 (100), 151 (40); CIHRMS (NH_3) m/e M + NH_4^+ calcd for $C_{15}H_{28}O_2SiN$ 280.1733, found 280.1734; $[\alpha]^{23}_D$ = –17.0° (c 1.0, CH_2Cl_2).

(2*S*,3*R*)-(*E*)-Methyl 3-(Dimethylphenylsilyl)-2-hydroxyhex-4-enoate (10). A stirred solution of **9** (1.34 g, 5.11 mmol) in 10.2 mL of dry THF (0.5 M) was cooled to –78 °C and then treated with a 0.5 M solution of potassium bis(trimethylsilyl)-amide (15.3 mL, 7.65 mmol) in toluene. After the solution was stirred for 40 min at –78 °C, *trans*-3-phenyl-2-(phenylsulfonyl)-oxaziridine[12a] (2.00 g, 7.66 mmol) dissolved in 51.1 mL of dry THF (0.5 M) was added to the yellow solution of the β-silyl enolate and stirred at –78 °C for 2.5 h. Following this period, camphorsulfonic acid (5.94 g, 25.5 mmol) dissolved in 51.1 mL of dry THF (0.2 M), was added to the reaction mixture at –78 °C and stirred for an additional 16 h while the mixture was gradually warmed to rt. The white, heterogeneous mixture was then diluted with 20 mL of a saturated solution of NH_4Cl, stirred for 5 min, and extracted with Et_2O (2 × 30 mL). The combined organic layers were dried over Na_2SO_4, and the solvents and volatiles were removed under reduced pressure to give the crude α-hydroxylated ester. The crude mixture was flash-chromatographed on silica gel (4% EtOAc/PE eluant) to afford 1.07 g (76%) of pure **10** as a colorless oil: ^{1}H NMR δ 7.56–7.54 (m, 2 H), 7.35–7.32 (m, 3 H), 5.40–5.26 (m, 2 H), 4.20 (d, 1 H, J = 2.4 Hz), 3.65 (s, 3 H), 2.75 (bs, 1 H), 2.08 (dd, 1 H, J = 2.4, 10.0 Hz), 1.61 (d, 3 H, J = 6.4 Hz), 0.38 (s, 3 H), 0.30 (s, 3 H); ^{13}C NMR δ 175.7, 137.7, 134.1, 129.0, 127.6, 126.9, 125.0, 71.7, 52.2, 38.2, 18.2, –3.8, –4.2; IR (neat) ν_{max} 3500, 2980, 1735 cm^{-1}; CIMS (NH_3 gas) 296 (M + NH_4), 261, 201, 126; CIHRMS M + NH_4^+ calcd for $C_{15}H_{26}NO_3Si$ 296.1682, found 296.1675; $[\alpha]^{23}_D$ = –81.6° (c 1.0, CH_2Cl_2).

(2*S*,3*R*)-(*E*)-Methyl 2-Acetoxy-3-(dimethylphenylsilyl)-hex-4-enoate (8b). A stirred solution of **10** (784 mg, 2.82 mmol) in dry CH_2Cl_2 (5.64 mL) was cooled to 0 °C and treated with triethylamine (388 μL, 3.38 mmol), acetic anhydride (471 μL, 3.38 mmol) and a catalytic amount of DMAP (ca. 1–3 mg). The reaction mixture was allowed to warm to rt over 3 h and stirred for an additional 3 h. After this period the reaction was quenched with a saturated solution of $NaHCO_3$ (10 mL) and the organic layer extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over Na_2SO_4 and filtered, and the solvents and volatiles were removed under reduced pressure to give the crude α-acetoxy ester. The crude product mixture was flash chromatographed on silica gel (4% EtOAc/PE eluant) to afford 0.848 g (94%) of pure **8b** as a colorless oil: ^{1}H NMR δ 7.43–7.41 (m, 2 H), 7.33–7.28 (m, 3 H), 5.47–5.40 (m, 2 H), 4.93 (d, 1 H, J = 3.2 Hz), 3.58 (s, 3 H), 2.24 (dd, 1 H, J = 3.3, 10.3 Hz), 2.01 (s, 3 H), 1.61 (d, 3 H, J = 6.6 Hz), 0.31 (s, 3 H), 0.29 (s, 3 H); ^{13}C NMR δ 169.9, 169.8, 136.3, 133.5, 129.1, 127.6, 127.0, 124.8, 73.3, 51.7, 35.4, 20.3, 17.9, –4.2, –4.6; IR (neat) ν_{max} 3000, 2980, 1735, 1420, 1380 cm^{-1}; CIHRMS M + NH_4^+ calcd for $C_{17}H_{28}NO_4Si$ 338.1788, found 338.1787; $[\alpha]^{23}_D$ = –55.5° (c 0.75, CH_2Cl_2).

Representative Experimental Procedure for the Diastereoselective Addition of Chiral (*E*)-Crotylsilanes to in Situ Generated Oxonium Ions. Method A. (*E*)-(2*S*,5*S*,6*R*)-Methyl 2-Acetoxy-6-(benzyloxy)-6-(2,3-dimethoxyphenyl)-5-methylhex-3-enoate (12c). A solution of 2,3-dimethoxybenzaldehyde (78 mg, 0.47 mmol), trimethylsilyl benzyl ether (85 mg, 0.47 mmol), and **8a** (150 mg, 0.47 mmol) in 1.0 mL of dry CH_2Cl_2 (0.5 M) was cooled to –78 °C and treated with TMSOTf (40 μL, 0.23 mmol). The reaction mixture was stirred at –78 °C for 18 h before being diluted with a solution of $NaHCO_3$. This mixture was stirred for 2 min before extraction with Et_2O (2 × 5 mL). The combined organic layers were dried with $MgSO_4$ and filtered and the solvent removed under reduced pressure to give crude **12c**. The crude oil was flash chromatographed on silica gel (15% EtOAc/PE eluant) to afford 200 mg (97%) of pure **12c** as a colorless oil: ^{1}H NMR δ 7.32–7.26 (m, 5 H), 7.06 (t, 1 H, J = 8 Hz), 6.98 (d, 1 H, J = 6.4 Hz), 6.83 (d, 1 H, J = 6.8 Hz), 5.87 (dd, 1 H, J = 7.6, 15.6 Hz), 5.43 (dd, 1 H, J = 7.2, 15.6 Hz), 5.29 (d, 1 H, J = 7.6 Hz), 4.66 (d, 1 H, J = 6.8 Hz), 4.42 and 4.24 (AB q, 2 H, J_{AB} = 12 Hz), 3.87 (s, 3 H), 3.77 (s, 3 H), 3.65 (s, 3 H), 2.65–2.63 (m, 1 H), 2.04 (s, 3 H), 1.09 (d, 3 H, J = 6.4 Hz); ^{13}C NMR δ 170.1, 169.3, 152.3, 147.3, 139.9, 138.6, 133.9, 128.2, 127.6, 127.4, 123.8, 121.7, 119.6, 111.2, 78.2, 73.2, 70.7, 60.5, 55.6, 52.3, 42.6, 20.6, 15.1; IR (CH_2Cl_2) ν_{max} 3050, 2950, 1730, 1600, 1490, 1430, 1280, 1230 cm^{-1}; CIMS (NH_3 gas) 460 (M + NH_4), 365, 335, 275, 257, 243, 229, 165, 151, 91; CIHRMS M + NH_4^+ (calcd for $C_{25}H_{34}NO_7$ 460.2335, found 460.2329; $[\alpha]^{23}_D$ = +58.2° (c 1.5, CH_2Cl_2).

Representative Procedure for the Diastereoselective Addition of Chiral (*E*)-Crotylsilanes to a Preformed Acetal. Method B. (*E*)-(2*S*,5*S*,6*R*)-Methyl 2-Acetoxy-7-(benzyloxy)-6-methoxy-5-methylhept-3-enoate (12e). A solution of the α-(benzyloxy)acetaldehyde dimethoxy acetal[4b] (32 mg, 0.1 mmol) in 0.5 mL of dry CH_2Cl_2 (0.2 M) was cooled to –78 °C and treated with trimethylsilyl trifluoromethanesulfonate (TMSOTf; 18 μL, 0.10 mmol). The light yellow solution was stirred for 5 min, and **8a** (30 mg, 0.09 mmol) was added as a solution in CH_2Cl_2 (0.5 mL). The temperature of the reaction mixture was increased slowly from –78 to –40 °C over 3 h. The resulting mixture was stirred for 20 h and diluted with saturated $NaHCO_3$ solution. This solution was stirred for 2 min before extraction with Et_2O (2 × 10 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was flash chromatographed on silica gel (10% EtOAc/PE eluant) to afford 30 mg (94%) of pure **12e** as a colorless oil: ^{1}H NMR δ 7.32–7.26 (m, 5 H), 5.89 (dd, 1 H, J = 8, 15.6 Hz), 5.55 (dd, 1 H, J = 7.2, 15.6 Hz), 5.36 (d, 1 H, J = 7.2 Hz), 4.49 (s, 2 H), 3.70 (s, 3 H), 3.53–3.49 (m, 1 H), 3.41 (s, 3 H), 3.43–3.39 (m, 1 H), 3.19–3.18 (m, 1 H), 2.52–2.50 (m, 1 H), 2.12 (s, 3 H), 1.03 (d, 3 H, J = 6.8 Hz); ^{13}C NMR δ 170.1, 169.4, 139.4, 138.2, 128.3, 127.6, 127.5, 121.8, 83.5, 73.4, 73.1, 70.2, 58.5, 52.4, 38.3, 20.7, 15.0; IR (CH_2Cl_2) ν_{max} 3050, 1730, 1490, 1430, 1280, 1230 cm^{-1}; CIMS (NH_3 gas) 368 (M + NH_4), 291, 259, 216, 199, 169, 164, 126, 92, 91, 58, 43; CIHRMS M + NH_4^+ calcd for $C_{19}H_{30}NO_6$ 368.2073, found 368.2062; $[\alpha]^{23}_D$ = +28.6° (c 1.5, CH_2Cl_2).

(*E*)-(2*S*,5*S*,6*R*)-Methyl 2-acetoxy-6-(benzyloxy)-5,7,7-trimethyloct-3-enoate (12a): ^{1}H NMR δ 7.33–7.25 (m, 5 H), 6.00 (dd, 1 H, J = 7.6, 15.6 Hz), 5.51 (dd, 1 H, J = 7.2, 15.6 Hz), 5.39 (d, 1 H, J = 7.2 Hz), 4.55 and 4.46 (AB q, 2 H, J_{AB} = 11.2 Hz), 3.72 (s, 3 H), 2.99 (d, 1 H, J = 3.6 Hz), 2.52–2.48 (m, 1 H), 2.12 (s, 3 H), 1.11 (d, 3 H, J = 6.8 Hz), 0.94 (s, 9 H); ^{13}C NMR δ 170.3, 169.5, 144.3, 139.1, 128.3, 127.4, 127.2, 119.9, 90.0, 75.2, 73.3, 52.6, 38.3, 37.1, 27.3, 20.8, 15.5; IR (CH_2Cl_2) ν_{max} 2950, 1710, 1430, 1220, 900 cm^{-1}; CIMS (NH_3 gas) 380 (M + NH_3), 195, 177, 91, 57, 43; CIHRMS M + NH_4^+ calcd for $C_{21}H_{35}NO_5$ 381.2515, found 381.2511; $[\alpha]^{23}_D$ = +57.2° (c 0.75, CH_2Cl_2).

(*E*)-(2*S*,5*S*,6*R*)-Methyl 2-acetoxy-6,7-bis(benzyloxy)-5-methylhept-3-enoate (12b): ^{1}H NMR δ 7.34–7.25 (m, 10 H), 5.92 (dd, 1 H, J = 8, 15.6 Hz), 5.56 (dd, 1 H, J = 7.2, 15.6 Hz), 5.36 (d, 1 H, J = 6.8 Hz), 4.69 and 4.53 (AB q, 2 H, J_{AB} = 11.6 Hz), 4.50 (s, 2 H), 3.70 (s, 3 H), 3.68–3.46 (m, 3 H), 2.57–2.55 (m, 1 H), 2.12 (s, 3 H), 1.05 (d, 3 H, J = 6.8 Hz); ^{13}C NMR δ 170.1, 169.4, 139.7, 138.6, 138.2, 133.9, 128.4, 128.3, 127.8, 127.6, 127.5, 121.8, 81.3, 73.4, 73.2, 72.8, 71.0, 52.5, 38.7, 20.7, 15.0; IR (CH_2Cl_2) ν_{max} 3010–2850, 1730, 1460, 1370, 1280–1240, 730 cm^{-1}; CIMS (NH_3 gas) 444 (M + NH_4), 367, 275, 259, 216, 185, 181, 149, 127, 126, 91; CIHRMS M + NH_4^+ calcd for $C_{25}H_{34}NO_6$ 444.2386, found 444.2376; $[\alpha]^{23}_D$ = +20.9° (c 0.7, CH_2Cl_2).

(*E*)-(2*S*,5*S*,6*R*)-Methyl 2-acetoxy-6-methoxy-5-methyl-7-oxooct-3-enoate (12d): ^{1}H NMR δ 5.88 (dd, 1 H, J = 8, 15.6 Hz), 5.60 (dd, 1 H, J = 6.8, 15.6 Hz), 5.41 (d, 1 H, J = 6.8 Hz), 3.76 (s, 3 H), 3.41 (d, 1 H, J = 6.0 Hz), 3.36 (s, 3 H), 2.61–2.58 (m, 1 H), 2.16 (s, 3 H), 2.12 (s, 3 H), 1.06 (d, 3 H, J = 6.8 Hz); ^{13}C NMR δ 210.5, 170.0, 169.2, 137.5, 122.8, 90.7, 72.7, 58.9, 52.6, 39.3, 26.3, 20.7, 15.0; IR (CH_2Cl_2) ν_{max} 2900, 1730, 1420, 1250, 1100, 900 cm^{-1}; CIMS (NH_3 gas) 290 (M + NH_4), 213, 181, 169, 109, 95, 87, 43; CIHRMS M + NH_4^+ calcd for $C_{13}H_{24}NO_6$ 290.1604, found 290.1597; $[\alpha]^{23}_D$ = +36.2° (c 0.5, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*R*)-Methyl 2-acetoxy-6-(benzyloxy)-5,7,7-trimethyloct-3-enoate (12f): ^{1}H NMR δ 7.34–7.23 (m, 5 H), 6.00 (dd, 1 H, J = 7.3, 15.6 Hz), 5.48 (dd, 1 H, J = 7.6, 15.6 Hz), 5.36 (d, 1 H, J = 7.3 Hz), 4.54 and 4.43 (AB q, 2 H, J_{AB} = 11.2 Hz), 3.66 (s, 3 H), 2.99 (d, 1 H, J = 3.4 Hz), 2.58–2.45 (m, 1 H), 2.11 (s, 3 H), 1.08 (d, 3 H, J = 6.9 Hz), 0.91 (s, 9 H); ^{13}C NMR δ 170.2,

169.5, 144.5, 144.4, 139.0, 128.3, 127.4, 119.7, 89.7, 74.9, 73.4, 52.5, 40.0, 37.1, 27.2, 20.8, 15.2; IR (CH_2Cl_2) ν_{max} 2950, 1750, 1400, 1250, 900 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{21}H_{35}NO_5$ 381.2515, found 381.2511; $[\alpha]^{23}_D$ = −31.2° (*c* 1.25, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*S*)-Methyl 2-acetoxy-6-(benzyloxy)-5-methylhept-3-enoate (12g): ^{1}H NMR δ 7.32–7.24 (m, 5 H), 5.97 (dd, 1 H, *J* = 7.3, 15.6 Hz), 5.56 (dd, 1 H, *J* = 7.1, 15.6 Hz), 5.40 (d, 1 H, *J* = 7.3 Hz), 4.50 and 4.45 (AB q, 2 H, J_{AB} = 11.7 Hz), 3.72 (s, 3 H), 3.41–3.38 (m, 1 H), 2.48–2.39 (m, 1 H), 2.14 (s, 3 H), 1.10 (d, 3 H, *J* = 6.1 Hz), 1.04 (d, 3 H, *J* = 6.8 Hz); IR (CH_2Cl_2) ν_{max} 3050, 2970, 2290, 1740, 1420, 1250, 890 cm^{-1}; ClMS (NH_3 gas) 338 (M + NH_4), 321, 278, 262, 261, 243, 216, 185, 153, 126, 91, 83, 67, 43; ClHRMS M + NH_4^+ calcd for $C_{18}H_{28}NO_5$ 338.1967, found 338.1955; $[\alpha]^{23}_D$ = 53.3° (*c* 1.05, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*R*)-Methyl 2-acetoxy-6-(benzyloxy)-6-(2,3-dimethoxyphenyl)-5-methylhex-3-enoate (12h): ^{1}H NMR δ 7.31–7.24 (m, 5 H), 7.07–7.00 (m, 2 H), 6.84–6.82 (m, 1 H), 5.90 (dd, 1 H, *J* = 7.1, 15.5 Hz), 5.43 (dd, 1 H, *J* = 7.1, 15.5 Hz), 5.31 (d, 1 H, *J* = 6.4 Hz), 4.66 (d, 1 H, *J* = 6.4 Hz), 4.42 and 4.23 (AB qm 2 H, J_{AB} = 11.8 Hz), 3.86 (s, 3 H), 3.76 (s, 3 H), 3.67 (s, 3 H), 2.65–2.62 (m, 1 H), 2.09 (s, 3 H), 1.07 (d, 3 H, *J* = 6.6 Hz); ^{13}C NMR δ 170.1, 169.3, 152.3, 147.3, 140.0, 138.6, 133.8, 128.2, 127.6, 127.4, 123.7, 121.6, 119.6, 111.2, 78.1, 73.1, 70.7, 60.4, 55.6, 52.3, 42.3, 20.6, 14.7; IR (CH_2Cl_2) ν_{max} 3050, 2980, 2295, 1725, 1420, 1260, 900 cm^{-1}; ClMS (NH_3 gas) 460 (M + NH_4), 383, 365, 335, 305, 275, 243, 229, 213, 165, 126, 91, 83, 43; ClHRMS M + NH_4 (calcd for $C_{25}H_{34}NO_7$ 460.2335, found 460.2326; $[\alpha]^{23}_D$ = −20.1° (*c* 2.05, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*R*)-Methyl 2-acetoxy-6-methoxy-5-methyl-6-phenylhex-3-enoate (12i): ^{1}H NMR δ 7.37–7.22 (m, 5 H), 5.85 (dd, 1 *H*, *J* = 7.3, 15.1 Hz), 5.40 (dd, 1 H, *J* = 7.3, 15.1 Hz), 5.38 (t, 1 H, *J* = 7.3 Hz), 3.99 (d, 1 H, *J* = 6.6 Hz), 3.74 (s, 3 H), 3.25 (s, 3 H), 2.61–2.57 (m, 1 H), 2.14 (s, 3 H), 1.09 (d, 3 H, *J* = 6.7 Hz); ^{13}C NMR δ 170.0, 169.3, 139.8, 139.0, 127.5, 127.4, 122.0, 120.8, 87.3, 72.9, 57.0, 52.4, 43.0, 20.6, 15.2; IR (CH_2Cl_2) ν_{max} 3050, 2970, 2395, 1720, 1420, 1440, 1260, 895 cm^{-1}; ClMS (NH_3 gas) 324 (M + NH), 215, 155, 122, 121, 105, 91; ClHRMS M + NH_4^+ calcd for $C_{17}H_{26}NO_5$ 324.1810, found 324.1796; $[\alpha]^{23}_D$ = −35.5° (*c* 1.80, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*R*)-Methyl 2-acetoxy-7-(benzyloxy)-6-methoxy-5-methylhept-3-enoate (12j): ^{1}H NMR δ 7.35–7.24 (m, 5 H), 5.93 (dd, 1 H, *J* = 7.6, 15.6 Hz), 5.52 (dd, 1 H, *J* = 7.6 15.6 Hz) 5.37 (d, 1 H, *J* = 7.1 Hz), 4.49 (s, 2 H), 3.70 (s, 3 H), 3.51–3.42 (m, 2 H), 3.41 (s, 3 H), 3.37–3.21 (m, 1 H), 2.58–2.52 (m, 1 H), 2.12 (s, 3 H), 1.02 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR δ 170.1, 169.4, 139.4, 138.2, 137.8, 128.3, 127.5, 121.8, 83.4, 73.3, 73.1, 70.3, 58.5, 52.4, 38.2, 20.6, 14.9; IR (CH_2Cl_2) ν_{max} 3050, 2995, 2300, 1750, 1425, 1255, 895 cm^{-1}; ClMS (NH_3 gas) 368 (M + NH_4), 291, 259, 226, 199, 169, 164, 126, 92, 91, 58, 43; ClHRMS M + NH_4^+ calcd for $C_{19}H_{30}NO_6$ 368.2073, found 368.2062; $[\alpha]^{23}_D$ = −51.1° (*c* 1.85, CH_2Cl_2).

(*E*)-(2*R*,5*S*,6*R*)-Methyl 2-acetoxy-6-(2,5-dimethoxy-3-nitrophenyl)-6-methoxy-5-methylhex-3-enoate (12k): ^{1}H NMR δ 7.26 (d, 1 H, *J* = 3.2 Hz), 7.10 (d, 1 H, *J* = 3.2 Hz), 5.82 (dd, 1 H, *J* = 7.7, 15.4 Hz), 5.38 (dd, 1 H, *J* = 7.1, 15.4 Hz), 5.29 (d, 1 H, *J* = 7.1 Hz), 4.38 (d, 1 H, *J* = 6.3 Hz), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.68 (s, 3 H), 3.22 (s, 3 H), 2.53–2.48 (m, 1 H), 2.08 (s, 3 H), 1.04 (d, 3 H, *J* = 6.7 Hz); ^{13}C NMR δ 170.0, 169.2, 155.2, 145.5, 143.6, 138.5, 138.0, 122.6, 118.6, 109.1, 80.4, 72.8, 62.7, 57.4, 55.9, 52.4, 42.9, 20.5, 15.0; IR (CH_2Cl_2) ν_{max} 3060, 2980, 2320, 1760, 1435, 1270, 910 cm^{-1}; ClMS (NH_3 gas) 429 (M + NH_4), 411, 368, 352, 320, 288, 285, 227, 211, 169, 149, 138, 91, 45; ClHRMS M + NH_4 calcd for $C_{19}H_{29}N_2O_9$ 429.1873, found 429.1887; $[\alpha]^{23}_D$ = +20.4° (*c* 2.50, CH_2Cl_2).

Representative Procedure for the Palladium(II)-Catalyzed Allylic Acetate Transpositions of the Allylic Acetates 12a–k. (*E*)-(4*S*,5*S*,6*R*)-Methyl 4-Acetoxy-6-(benzyloxy)-6-(2,3-dimethoxyphenyl)-5-methylhex-2-enoate (13h). A stirred solution of **12h** (38 mg, 0.086 mmol) in 1 mL of dry CH_2Cl_2 (0.09 M) was treated with $PdCl_2(CH_3CN)_2$ (2.2 mg, 0.0084 mmol, 0.2 equiv) in two portions of 1.1 mg at 10-h intervals over 36 h at rt. The reaction mixture was then filtered through a SiO_2 plug washing several times with CH_2Cl_2 (ca. 10 mL). The solvent was removed under reduced pressure to afford 36 mg (95%) of pure **13h** as a colorless oil: ^{1}H NMR δ 7.32–7.23 (m, 5 H), 7.08–7.0-1 (m, 2 H), 7.00–6.83 (m, 2 H), 5.93 (d, 1 H, *J* = 15.6 Hz), 5.39 (t, 1 H, *J* = 7.1 Hz), 4.88 (d, 1 H, *J* = 3.2 Hz), 4.43 and 4.18 (AB q, 2 H, J_{AB} = 11.7 Hz), 3.85 (s, 3 H), 3.80 (s, 3 H), 3.68 (s, 3 H), 2.09–2.06 (m, 1 H), 1.95 (s, 3 H), 0.83 (d, 3 H, *J* = 7.1 Hz); ^{13}C NMR δ 169.7, 166.4 152.6, 144.9, 138.14, 133.8, 128.2, 128.0, 128.3, 127.6, 123.7, 122.1, 119.5, 111.3, 74.4, 74.1, 70.9, 60.4, 55.7, 51.6, 42.7, 20.9, 9.4; IR (CH_2Cl_2) ν_{max} 3050, 2980, 2300, 1725, 1420, 1260, 895 cm^{-1}; ClMS (NH_3 gas) 442, 370, 335, 291, 274, 257, 215, 185, 165, 151, 125, 91; ClHRMS M + NH_4^+ calcd for $C_{25}H_{34}NO_7$ 460.2335, found 460.2326; $[\alpha]^{23}_D$ = −7.25° (*c* 0.8, CH_2Cl_2).

(*E*)-(4*R*,5*S*,6*R*)-Methyl 4-acetoxy-6-(benzyloxy)-5,7,7-trimethyloct-2-enoate (13a): ^{1}H NMR δ 7.33–7.25 (m, 5 H), 6.91 (dd, 1 H, *J* = 5.2, 16 Hz), 5.93 (d, 1 H, *J* = 16 Hz), 5.33 (t, 1 H, *J* = 5.2 Hz), 4.54 and 4.41 (AB q, 2 H, J_{AB} = 11.2 Hz), 3.68 (s, 3 H), 2.98 (d, 1 H, *J* = 2 Hz), 2.22–2.18 (m, 1 H), 2.10 (s, 3 H), 1.02 (d, 3 H, *J* = 7.2 Hz), 0.91 (s, 9 H); ^{13}C NMR δ 170.3, 160.5, 144.5, 139.2, 128.2, 127.2, 127.0, 121.9, 85.7, 76.4, 74.2, 51.7, 38.1, 26.3, 26.2, 21.0, 11.1; IR (CH_2Cl_2) ν_{max} 2950, 2100, 1730, 1670, 1380, 1220, 900 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{21}H_{35}NO_5$ 381.2515, found 381.2503; $[\alpha]^{23}_D$ = +24.4° (*c* 0.7, CH_2Cl_2).

(*E*)-(4*R*,5*S*,6*R*)-Methyl 4-acetoxy-6,7-bis(benzyloxy)-5-methylhept-2-enoate (13b): ^{1}H NMR δ 7.38–7.25 (m, 10 H), 6.88 (dd, 1 H, *J* = 5.2, 15.6 Hz), 5.87 (dd, 1 H, *J* = 1.6, 15.6 Hz), 5.50–5.47 (m, 1 H), 4.70 and 4.45 (AB q, 2 H, *J* = 11.6 Hz), 4.54 and 4.51 (AB q, 2 H, J_{AB} = 12.4 Hz), 3.69 (s, 3 H), 3.68–3.56 (m, 3 H), 2.15–2.12 (m, 1 H), 2.04 (s, 3 H), 1.01 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR δ 169.8, 166.2, 144.8, 138.5, 137.9, 128.4, 128.2, 127.7, 127.6, 127.4, 127.3, 121.3, 77.8, 74.0, 73.4, 72.1, 70.6, 51.5, 39.1, 20.9, 9.9; IR (CH_2Cl_2) δ_{max} 3005, 2900, 1720, 1680, 1450, 1370, 1250 cm^{-1}; CIMS (NH_3 gas) 444 (M + NH_4), 367, 319, 275, 229, 181, 169, 127, 126, 91; ClHRMS M + NH_4^+ calcd for $C_{25}H_{34}NO_6$ 444.2386, found 444.2394; $[\alpha]^{23}D$ = +11.3° (*c* 0.6, CH_2Cl_2).

(*E*)-(4*R*,5*S*,6*R*)-Methyl 4-acetoxy-6-(benzyloxy)-6-(2,3-dimethoxyphenyl)-5-methylhex-2-enoate (13c): ^{1}H NMR δ 7.34–7.26 (m, 5 H), 7.07–6.97 (m, 2 H), 6.91 (dd, 1 H, *J* = 5.6, 15.6 Hz), 6.84 (d, 1 H, *J* = 8 Hz), 5.84 (d, 1 H, *J* = 15.6 Hz), 5.35 (t, 1 H, *J* = 5.6 Hz), 4.80 (d, 1 H, *J* = 4 Hz), 4.39 and 4.20 (AB q, 2 H, J_{AB} = 11.6 Hz), 3.86 (s, 3 H), 3.67 (s, 3 H), 2.15–2.10 (m, 1 H), 2.03 (s, 3 H), 0.97 (d, 3 H, *J* = 6.8 Hz); ^{13}C NMR δ 169.8, 166.3, 152.6, 146.8, 145.0, 133.8, 128.3, 128.2, 127.6, 127.4, 123.8, 121.1, 119.3, 111.6, 75.4, 74.5, 70.7, 60.4, 55.7, 51.5, 42.9, 20.9, 9.5; IR (CH_2Cl_2) ν_{max} 3010–2800, 1720, 1650, 1590, 1480, 1370, 1250 cm^{-1}; CIMS (NH_3 gas) 442, 370, 335, 274, 257, 215, 185, 165, 91; ClHRMS M + NH_4^+ calcd for $C_{25}H_{34}NO_7$ 460.2335, found 460.2321; $[\alpha]^{23}_D$ = +14.3° (*c* 3.35, CH_2Cl_2).

(*E*)-(4*R*,5*S*,6*R*)-Methyl 4-acetoxy-6-methoxy-5-methyl-7-oxooct-2-enoate (13d): ^{1}H NMR δ 6.86 (dd, 1 H, *J* = 6, 15.6 (d, 1 H, *J* = 15.6 Hz), 5.40 (t, 1 H, *J* = 6.4 Hz), 3.73 (s, 3 H), 3.58 (d, 1 H, *J* = 3.2 Hz), 3.29 (s, 3 H), 3.22–3.20 (m, 1 H), 2.14 (s, 3 H), 2.08 (s, 3 H), 0.93 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR δ 210.3, 172.8, 169.7, 143.6, 122.3, 86.7, 73.9 58.6, 51.8, 39.9, 33.6, 26.3, 10.1; IR (CH_2Cl_2) ν_{max} 2900, 1720, 1420, 1370, 1250, 1100, 900 cm^{-1}; CiMS (NH_3 gas) 290 (M + NH_4), 229, 213, 181, 169, 109, 95 87, 43; ClHRMS M + NH_4^+ calcd for $C_{13}H_{24}NO_6$ 290.160.4, found 290.1590; $[\alpha]^{23}_D$ = +5.3° (*c* 0.2, CH_2Cl_2).

(*E*)-(4*R*,5*S*,6*R*)-Methyl 4-acetoxy-7-(benzyloxy)-6-methoxy-5-methylhept-2-enoate (13e): ^{1}H NMR δ 7.32–7.27 (m, 5 H), 6.86 (dd, 1 H, *J* = 5.2, 15.6 Hz), 5.89 (d, 1 H, *J* = 15.6 Hz), 5.44 (t, 1 H, *J* = 5.6 Hz), 4.52 and 4.47 (AB q, 2 H, J_{AB} = 12 Hz), 3.71 (s, 3.51–3.47 (m, 2 H), 3.39–3.34 (m, 1 H), 3.32 (s, 3 H), 2.11–2.03 (m, 1 H), 2.04 (s, 3 H), 0.92 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR δ 169.9, 166.4, 144.9, 137.9, 128.4, 127.7, 127.6, 121.3, 79.7, 74.1, 73.4, 70.0, 58.1, 51.7, 38.9, 21.0, 9.7; IR (CH_2Cl_2) ν_{max} 3050, 2980, 2400, 1730, 1600, 1410, 1280, 900 cm^{-1}; CIMS (NH_3 gas) 368 (M + NH_4), 291, 259, 229, 199, 169, 109, 91; ClHRMS M + NH_4 calcd for $C_{19}H_{30}NO_6$ 368.2073, found 368.2062; $[\alpha]^{23}_D$ = −6.2° (*c* 1.15, CH_2Cl_2).

(*E*)-(4*S*,5*S*,6*R*)-Methyl 4-acetoxy-6-(benzyloxy)-5,7,7-trimethyloct-2-enoate (13f): ^{1}H NMR δ 7.35–7.25 (m, 5 H), 6.81 (dd, 1 H, *J* = 6.1, 15.8 Hz), 5.94 (d, 1 H, *J* = 15.8 Hz), 5.29 (m, 1 H), 4.62 and 4.49 (AB q, 2 H, J_{AB} = 11.3 Hz), 3.72 (s, 3 H), 3.00 (d, 1 H, *J* = 2.5 Hz), 2.14–2.08 (m, 1 H), 2.07 (s, 3 H), 0.97 (d, 3 H, *J* = 7.1 Hz), 0.94 (s, 9 H); ^{13}C NMR δ 170.0, 166.2, 144.8, 139.1, 128.2, 127.3, 127.1, 122.5, 84.8, 76.5, 74.6, 51.7, 37.8, 37.0, 26.6, 21.0, 12.4; IR (CH_2Cl_2) ν_{max} 3050, 3000, 2400, 1720, 1600, 1420 cm^{-1}; ClHRMS M = NH_4^+ calcd for $C_{21}H_{35}NO_5$ 381.2515, found 381.2503; $[\alpha]^{23}_D$ = +24.4° (*c* 0.7, CH_2Cl_2).

(*E*)-(4*S*,5*R*,6*S*)-Methyl 4-acetoxy-6-(benzyloxy)-5-methylhept-2-enoate (13g): ^{1}H NMR δ 7.33–7.24 (m, 5 H), 6.86 (dd, 1 H, J = 6.3, 15.7 Hz), 5.95 (d, 1 H, J = 15.4 Hz), 5.39 (t, 1 H, J = 6.8 Hz), 4.55 and 4.32 (AB q, 2 H, J_{AB} = 11.7 Hz), 3.70 (s, 3 H), 3.70–3.65 (m, 1 H), 1.97 (s, 3 H), 1.74–1.83 (m, 1 H), 1.20 (d, 3 H, J = 6.2 Hz), 0.92 (d, 3 H, J = 7.1 Hz); IR (CH_2Cl_2) ν_{max} 3050, 2970, 2290, 1740, 1420, 1250, 890 cm^{-1}; ClMS (NH_3 gas) (M + NH_4), 321, 289, 262, 261, 229, 217, 181, 154, 111, 91, 83, 43; ClHRMS M + NH_4^+ calcd for $C_{19}H_{28}NO_5$ 338.1967, found 338.1954 $[\alpha]^{23}_D$ = +8.2° (*c* 0.85, CH_2Cl_2).

(*E*)-(4*S*,5*S*,6*R*)-Methyl 4-acetoxy-6-methoxy-5-methyl-6-phenylhex-3-enoate (13i): ^{1}H NMR δ 7.49–7.37 (m, 5 H), 6.96 (dd, 1 H, J = 6.1, 15.6 Hz), 6.06 (d, 1 H, J = 15.9 Hz), 5.51 (t, 1 H, J = 6.4 Hz), 4.35 (d, 1 H, J = 4.2 Hz), 3.85 (s, 3 H), 3.33 (s, 3 H), 2.22 (s, 3 H), 2.21–2.13 (m, 1 H), 0.94 (d, 3 H, J = 6.8 Hz); ^{13}C NMR δ 170.0, 166.4, 144.2, 140.0, 128.3, 127.5, 126.8, 122.4, 82.7, 74.1, 57.3, 51.7, 44.1, 21.0, 9.5; IR (CH_2Cl_2) ν_{max} 3050, 2970, 2395, 1720, 1420, 1440, 1260, 895 cm^{-1}; ClMS (NH_3 gas) 324 (M + NH_4), 290, 275, 246, 215, 105, 149, 122, 91, 83, 43; ClHRMS M + NH_4^+ calcd for $C_{17}H_{26}NO_5$ 324.1810, found 324.1806; $[\alpha]^{23}_D$ = +9.1° (*c* 0.55, CH_2Cl_2).

(*E*)-(4*S*,5*S*,6*R*)-Methyl 4-acetoxy-7-(benzyloxy)-6-methoxy-5-methylhept-2-enoate (13j): ^{1}H NMR δ 7.36–7.27 (m, 5 H), 6.83 (dd, 1 H, J = 6.4, 15.8 Hz), 5.96 (d, 1 H, J = 15.7 Hz), 5.37 (t, 1 H, J = 7.1 Hz), 4.55 and 4.49 (AB q, 2 H, J_{AB} = 12.0 Hz), 3.72 (s, 3 H), 3.68–3.57 (m, 1 H), 3.51–3.43 (m, 2 H), 3.37 (s, 3 H), 2.08 (s, 3 H), 2.07–2.01 (m, 1 H), 0.83 (d, 3 H, J = 10.1 Hz); ^{13}C NMR δ 169.8, 166.4, 144.5, 138.0, 128.4, 127.6, 122.7, 78.6, 73.9, 73.5, 70.8, 59.0, 51.7, 39.0, 29.7, 21.0, 9.4; IR (CH_2Cl_2) ν_{max} 3050, 2995, 2300, 1750, 1425, 900 cm^{-1}; ClHRMS M + NH_4 calcd for $C_{19}H_{30}NO_6$ 368.2073, found 368.2066 $[\alpha]^{23}_D$ = −1.8° (*c* 1.00, CH_2Cl_2).

(*E*)-(4*S*,5*S*,6*R*)-Methyl 4-acetoxy-6-(2,5-dimethoxy-3-nitrophenyl)-6-methoxy-5-methylhex-2-enoate (13k): ^{1}H NMR δ 7.26 (d, 1 H, J = 3.2 Hz), 7.14 (d, 1 H, J = 3.2 Hz), 6.86 (dd, 1 H, J = 6.2, 15.6 Hz), 6.00 (d, 1 H, J = 15.6 Hz), 5.46 (t, 1 H, J = 6.4 Hz), 4.38 (d, 1 H, J = 4.6 Hz), 3.84 (s, 3 H), 3.82 (s, 3 H), 3.72 (s, 3 H), 3.22 (s, 3 H), 2.12 (s, 3 H), 2.07–2.08 (m, 1 H), 0.73 (d, 3 H, J = 7.3 Hz); ^{13}C NMR δ 169.7, 166.3, 155.2, 144.9, 144.2, 143.7, 137.7, 122.7, 119.1, 108.6, 76.8, 74.2, 62.5, 57.7, 56.0, 51.7, 42.1, 21.0, 9.0; IR (CH_2Cl_2) ν_{max} 3060, 2980, 2320, 1750, 1435, 1270, 890 cm^{-1}; ClHRMS M + NH_4 calcd for $C_{19}H_{29}N_2O_9$ 429.1873, found 429.1861; $[\alpha]^{23}_D$ = +33.8° (*c* 1.85, CH_2Cl_2).

Representative Procedure for the Debenzylation: (*E*)-(4*R*,5*S*,6*R*)-Methyl 4-Acetoxy-6-methoxy-5-methyl-7-hydroxyhept-2-enoate (14a). A solution of **13e** (15 mg, 0.04 mmol) in 0.5 mL of CH_2Cl_2 was cooled to −78 °C and sequentially treated with a 1.0 M hexane solution of BCl_3 (0.1 mL, 0.12 mmol, 1.3 equiv). The resulting solution was then allowed to warm to 0 °C over 3 h. The reaction was cooled to −78 °C and diluted with 2 mL of MeOH. This solution was stirred for 2 min before extraction with Et_2O (2 × 10 mL). The combined organic layers were dried with $MgSO_4$ and filtered and the solvent removed under reduced pressure. The crude product was flash chromatographed on silica gel (20% EtOAc/PE eluant) to afford 8.5 mg (82%) of pure **14a** as a colorless oil: ^{1}H NMR δ 7.00 (dd, 1 H, J = 5.2, 16 Hz), 6.03 (dd, 1 H, J = 1.6, 16 Hz), 5.64–5.61 (m, 1 H), 3.86 (s, 3 H), 3.83 (dd, 1 H, J = 4, 11.6 Hz), 3.70 (dd, 1 H, J = 5.6, 11.6 Hz), 3.50 (s, 3 H), 3.49–3.30 (m, 1 H), 2.27–2.24 (m, 1 H), 2.22 (s, 3 H), 1.12 (d, 3 H, J = 7.2 Hz); ^{13}C NMR δ 169.9, 166.4, 145.0, 121.4, 82.3, 73.0, 61.6, 58.2, 51.8, 38.1, 33.7, 10.4; IR (CH_2Cl_2) ν_{max} 3540, 3100, 3000, 2300, 1730, 1600, 1430, 1250, 900 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{12}H_{24}NO_6$ 278.1604, found 278.1612; $[\alpha]^{23}_D$ = −9.2° (*c* 0.25, CH_2Cl_2).

(*E*)-(4*S*,5*S*,6*R*)-Methyl 4-acetoxy-7-hydroxy-6-methoxy-5-methylhept-2-enoate (14b): ^{1}H NMR δ 6.80 (dd, 1 H, J = 6.3, 15.7 Hz), 5.95 (dd, 1 H, J = 1.3, 15.7 Hz), 5.37 (t, 1 H, J = 6.1 Hz), 3.71 (s, 3 H), 3.67–3.63 (m, 1 H), 3.42–3.34 (m, 1 H), 3.38 (s, 3 H), 3.32–3.29 (m, 1 H), 2.12–1.99 (m, 1 H), 2.07 (s, 3 H), 0.88 (d, 3 H, J = 7.1 Hz); ^{13}C NMR δ 169.8, 166.3, 144.1, 122.7, 81.0, 73.8, 59.0, 51.7, 62.5, 38.5, 20.9, 10.1; IR (CH_2Cl_2) ν_{max} 3550, 2890, 1650, 1180, 825 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{12}H_{24}NO_6$ 278.1604, found 278.1603; $[\alpha]^{23}_D$ = +13.94° (*c* 1.70, CH_2Cl_2).

Representative Procedure for the Ozonolysis: (3*S*,4*R*,5*R*)-2,3-Diacetoxy-5-methoxy-4-methylpyranose (15a). A solution of **14a** (20 mg, 0.08 mmol) in 5 mL of CH_2Cl_2 was treated with a stream of ozone until the reaction was complete as determined by TLC analysis (5 min) at −78 °C. Dimethyl sulfide (41 μL, 0.8 mmol) was added, and the solution was allowed to warm to rt. After 15 h at 23 °C, the solvent was removed under reduced pressure and the crude pyranoside was dissolved in 0.5 mL of CH_2Cl_2. The solution was treated with Et_3N (13 μL, 0.14 mmol), Ac_2O (20 μL, 0.14 mmol), and a catalytic amount of DMAP (1–3 mg). The mixture was stirred for 6 h at 23 °C and then diluted with saturated $NaHCO_3$ solution. This solution was stirred for 2 min before extraction with Et_2O (2 × 5 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was flash chromatographed on silica gel (10% EtOAc/PE eluant) to afford total 17 mg (89%) of α- and β-anomers of **15a** as a colorless oil. α-Anomer: ^{1}H NMR δ 6.08 (d, 1 H, J = 3.6 Hz), 4.64 (dd, 1 H, J = 3.2, 11.6 Hz), 3.87 (dd, 1 H, J = 5.2, 10.8 Hz), 3.51 (t, 1 H, J = 10.8 Hz), 3.41 (s, 3 H), 3.04–3.01 (m, 1 H), 2.10 (s, 3 H), 2.07–2.05 (m, 1 H), 2.02 (s, 3 H), 1.02 (d, 3 H, J = 6.4 Hz); ^{13}C NMR δ 170.4, 169.5, 88.7, 83.8, 78.9, 72.0, 62.3, 58.6, 36.1, 33.7, 13.3; IR (CH_2Cl_2) ν_{max} 1740, 1650, 1420, 1380, 1250, 1100, 900 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{11}H_{22}NO_6$ 264.1447, found 264.1325; $[\alpha]^{23}_D$ = −51.3° (*c* 0.4, CH_2Cl_2). β-Anomer: ^{1}H NMR δ 5.68 (d, 1 H, J = 7.2 Hz), 4.84 (dd, 1 H, J = 7.6, 10.4 Hz), 4.10 (dd, 1 H, J = 4.8, 11.6, Hz), 3.43–3.36 (m, 1 H), 3.40 (s, 3 H), 3.04–3.01 (m, 1 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 2.03–1.81 (m, 1 H), 1.05 (d, 3 H, J = 6.4 Hz); ^{13}C NMR δ 170.0, 169.6, 93.7, 78.7, 72.2, 66.1, 58.5, 40.0, 33.6, 21.0, 13.9; IR (CH_2Cl_2) ν_{max} 1740, 1650, 1420, 1380, 1250, 1100, 900 cm^{-1}; ClMS (NH_3 gas) 264 (M + NH_4), 204, 187, 144, 115, 103, 83, 58, 43; ClHRMS M + NH_4^+ calcd for $C_{11}H_{22}NO_6$ 264.1484; $[\alpha]^{23}_D$ = +2° (*c* 0.4, CH_2Cl_2).

(3*R*,4*R*,5*R*)-2,3-Diacetoxy-5-methoxy-4-methylpyranose (15b). α-Anomer: ^{1}H NMR δ 5.85 (d, 1 H, J = 1.8 Hz), 4.86 (t, 1 H, J = 2.3 Hz), 3.91 (dd, 1 H, J = 4.9, 11.1 Hz), 3.47 (t, 1 H, J = 10.7 Hz), 3.40 (s, 3 H), 3.37–3.23 (m, 1 H), 2.14–2.05 (m, 1 H), 2.11 (s, 3 H), 2.09 (s, 3 H), 1.02 (d, 3 H, J = 6.6 Hz); ^{13}C NMR δ 170.2, 168.9, 76.5, 75.8, 71.9, 62.8, 58.4, 34.6, 20.9, 20.8, 12.6; IR (CH_2Cl_2) ν_{max} 3050, 2990, 2305, 1750, 1425, 1260, 895 cm^{-1}; ClHRMS M + NH_4^+ calcd for $C_{11}H_{22}NO_6$ 264.1447, found 264.1456; $[\alpha]^{23}_D$ = −10.0° (*c* 0.55, CH_2Cl_2). The β-anomer was extremely difficult to separate from its diastereoisomer by flash chromatography on silica gel, and the data reported below was therefore obtained on 1:5 diastereomeric mixture analysis by ^{1}H NMR: ^{1}H NMR δ 5.79 (d, 1 H, J = 2.0 Hz), 5.17 (t, 1 H, J = 2.4 Hz), 4.14 (dd, 1 H, J = 4.2, 11.7 Hz), 3.45–3.39 (m, 1 H), 3.39 (s, 3 H), 3.35–3.22 (m, 1 H), 2.12 (s, 3 H), 2.08–2.05 (m, 1 H), 2.06 (s, 3 H), 1.05 (d, 3 H, J = 7.0 Hz).

Acknowledgment. This work has been financially supported by the National Institutes of Health (CA47249). Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research (ACS-PRF No. 25590). We are grateful to Mr. Michael Creech for performing mass spectral measurements.

Supplementary Material Available: ^{1}H NMR spectra for compounds **12a–12k** and **13a–13k** (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.