154.71 (s, 8a- and 8a''-C), 162.65 (m, 4'- and 4'''-C), 162.70 (dd, J = 5, 5 Hz, 5- and 5''-C), 163.39 (m, 7- and 7''-C), 163.96 (td, J = 5, 5 Hz, 2- and 2''-C), 182.95 (br s, $W_{1/2}$ = 5 Hz, 4- and 4''-C); ^{1}H-^{13}C COSY (600 MHz, $CDCl_3$), data for the half monomer unit, 7-OCH_3/7-OCH_3, 4'-OCH_3/4'-OCH_3, 6-H/6-C, 3-H/3-C, 3'-H/3'-C, 2'-H/2'-C; long range ^{1}H-^{13}C COSY (COLOC, 600 MHz, $CDCl_3$), data for the half monomer unit, 7-OCH_3/7-C, 4'-OCH_3/4'-C, 6-H/8-C, 6-H/4a-C, 6-H/5-C, 6-H/7-C, 3-H/4a-C, 3-H/2-C, 3-H/4-C, 3'-H/5'-C, 3'-H/1'-C, 2'-H/6'-C, 2'-H/4'-C, 2'-H/2-C, 5-OH/6-C, 5-OH/4a-C, 5-OH/5-C; $[\alpha]^{27}_D$ -25.3° (c 0.3, MeOH); UV (EtOH) λ_{max} 324.2 nm (ϵ 40 900), 273.0 (41 400), 225.8 (51 800); CD (EtOH) λ_{ext} 362.0 nm ($\Delta\epsilon$ +25.6), 326.2 (-54.4), 267.5 (+21.3); MS m/z 594 (M^+, relative intensity 100), 433 (2), 297 (16), 135 (16), 77 (1); HRMS calcd for $C_{34}H_{26}O_{10}$ 594.152 58, found 594.152 99.

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Total Synthesis of (+)-Jatrophone

Qi Han and David F. Wiemer*

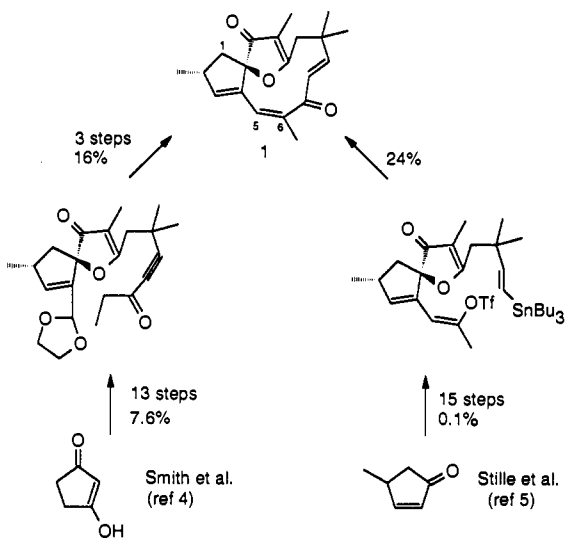
Contribution from the Department of Chemistry, University of Iowa, Iowa City, Iowa 52242.
Received February 24, 1992

Abstract: The first total synthesis of optically active (+)-jatrophone is described. A convergent sequence provides the natural enantiomer in just 12 steps from (*R*)-(+)-3-methyladipic acid. Key steps include formation of the jatrophone C-ring through a Wadsworth-Horner-Emmons variant, a Pd-catalyzed cross-coupling that incorporates the C5-C6 double bond with the required *Z*-stereochemistry, and formation of the macrocycle by condensation of an acetylenic aldehyde. This sequence provides a short, efficient, and stereocontrolled route to the complex diterpenoid (+)-jatrophone.

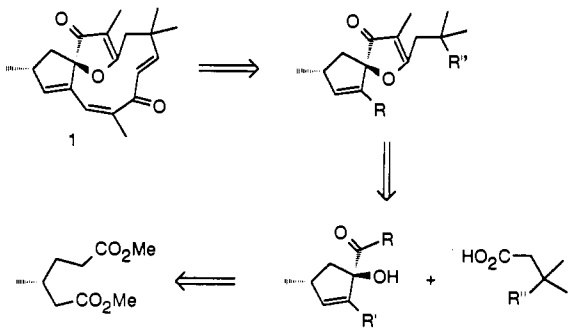
In 1970, Kupchan et al. first reported the isolation and characterization of the macrocyclic diterpenoid jatrophone (**1**),[1] a novel natural product with a new carbon skeleton and an unusual array of functionality. Significant antileukemic activity was reported for this compound, and subsequent studies unveiled that biological nucleophiles were trapped by a novel transannular cyclization.[2] In the intervening years a number of jatrophane diterpenoids have been characterized, including the kansuinines,[3a] the esulones,[3b,c] and euphornin[3d] and the euphoscopins,[3e] but as the prototypical jatrophane diterpenoid, jatrophone retains a special prestige.

The combination of an interesting skeleton and significant biological activity has stimulated several efforts to synthesize jatrophone. Despite the problems posed by the presence of two stereogenic centers, four carbon-carbon double bonds (including two that can isomerize), and an 11-membered ring, two successful routes to racemic jatrophone have been published.[4,5] While the two approaches differ substantially, both encountered significant difficulties with formation of the macrocyclic ring (Scheme I). In Smith's approach,[4] an aldol-type reaction was used to form the C5-C6 double bond in 23% yield. In the more recent example from Stille's laboratories,[5] a Pd-catalyzed carbonylation was employed to form both the C6-C7 and C7-C8 bonds in 24% yield. While these transformations did allow assembly of the natural product in both cases, it was tempting to speculate that a more efficient procedure could be found. Furthermore, the significant biological activity of the natural product places a premium on routes that would afford optically active materials.[6]

Scheme I



Scheme II



(1) (a) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Saenz Renauld, J. A.; Haltiwanger, R. C.; Bryan, R. F. *J. Am. Chem. Soc.* **1970**, *92*, 4476. (b) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 2295.

(2) Lillehaug, J. R.; Kleppe, K.; Sigel, C. W.; Kupchan, S. M. *Biochim. Biophys. Acta* **1973**, *327*, 92.

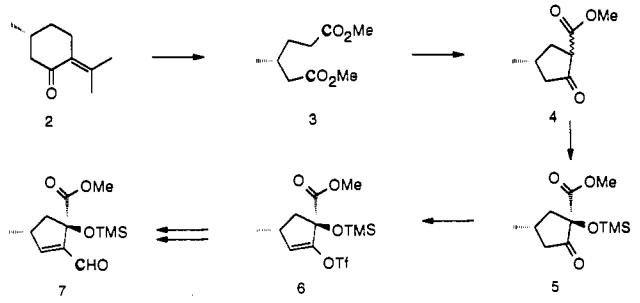
(3) (a) Uemura, D.; Hirata, Y.; Chen, Y.-P.; Hsu, H.-Y. *Tetrahedron Lett.* **1975**, 1697. (b) Manners, G. D.; Wong, R. Y. *J. Chem. Soc. Perkin Trans. I* **1985**, 2075. (c) Davis, D. G.; Manners, G. D. *Phytochemistry* **1987**, *26*, 727. (d) Sahai, R.; Rastogi, R. P.; Jakupovic, J.; Bohlmann, F. *Phytochemistry* **1981**, *20*, 1665. (e) Yamamura, S.; Kosemura, S.; Ohba, S.; Ito, M.; Saito, Y. *Tetrahedron Lett.* **1981**, 5315.

(4) Smith, A. B., III; Guaciaro, M. A.; Schow, S. R.; Wovkulich, P. M.; Toder, B. H.; Hall, T. W. *J. Am. Chem. Soc.* **1981**, *103*, 219, 4652. Smith, A. B., III. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: New York, 1984; p 223.

(5) Gyorkos, A. C.; Stille, J. K.; Hegedus, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 8465.

0002-7863/92/1514-7692$03.00/0

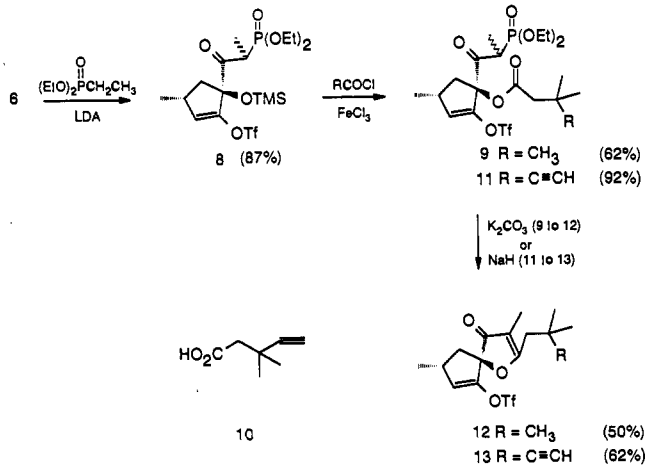
Scheme III



Our studies toward these diterpenoids have focused on routes that would afford the natural enantiomers through elaboration of common, nonracemic subunits. For (+)-jatrophone, our retrosynthetic analysis isolated both stereogenic centers in a highly substituted methylcyclopentanoid (Scheme II) and assumed that the remaining achiral portion of the molecule could be added in a highly convergent fashion. The achiral portion then would require a carboxyl group, for esterification of the cyclopentanoid hydroxyl group and subsequent condensation to form the 3-(2*H*)-furanone ring, as well as functionality to allow assembly of the macrocyclic ring.

Our synthetic strategy was designed to incorporate the natural C2 stereochemistry in early intermediates by extracting this key stereogenic center from readily available chiral pool reagents. Initially aldehyde **7** was targeted as the key intermediate. We have reported[7] preparation of this compound from commercially available (*R*)-(+)-3-methyladipic acid (or (+)-pulegone),[8] as summarized in Scheme III. However, discouraged by the low yields involved in formation of aldehyde **7** from compound **6**, and because if offered promise of a more efficient synthesis, we have reverted to use of optically active triflate **6** as the key intermediate. This decision has proven very fruitful: in this paper we report the first total synthesis of the complex diterpenoid (+)-jatrophone in its natural enantiomeric form.[9]

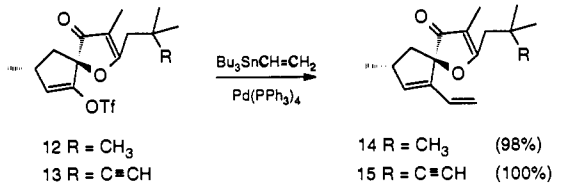
Reaction of triflate **6** with the anion of diethyl ethylphosphonate gave the expected[10] β-keto phosphonate **8** in good yield (87%).



Elaboration of compound **8** was planned through direct acylation of the TMS-protected alcohol according to a protocol we developed for formation of esters in the presence of β-keto phosphonates.[11] In a model reaction, treatment of compound **8** with *tert*-butylacetyl chloride and $FeCl_3$ gave β-keto phosphonate **9** cleanly, demonstrating that acylation could be accomplished efficiently in the presence of the triflate moiety. Accordingly, acetylenic acid **10**[12] was converted to the corresponding acid chloride and then allowed to react with compound **8** in a $FeCl_3$-catalyzed acylation yielding compound **11** (92%).

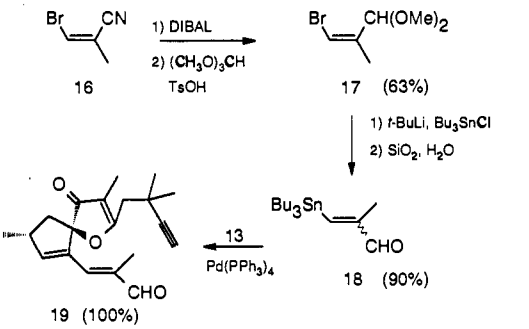
In our previous studies,[11] intramolecular condensation of phosphonates analogous to **11** was best accomplished by treatment with K_2CO_3 in DMF. Furthermore, the model compound **9** was shown to undergo the expected condensation smoothly under these conditions, yielding furanone **12**. However, when compound **11** was treated with K_2CO_3/DMF, the required furanone was isolated in just 20–30% yield. Fortunately, treatment of compound **11** with NaH/DME gave the desired product **13** in a more acceptable yield (62%).

An additional 4-carbon unit containing the C5–C6 double bond with the sensitive *Z*-stereochemistry must be incorporated through a Pd-catalyzed cross-coupling reaction to convert furanone **13** into the natural product.[13] Model reactions were conducted wherein furanone triflates **12** and **13** were treated with tributylvinyltin, $Pd(PPh_3)_4$, and LiCl in sealed tubes. Under these conditions the



vinyl-substituted compounds **14** and **15** were obtained in nearly quantitative yields. For preparation of jatrophone, reaction of triflate **13** with a more elaborate vinyltin reagent, including functionality to become the C7 carbonyl group, would be attractive. While vinyltin reagents substituted with electron-withdrawing groups often require more forceful conditions for a cross-coupling reaction, there are precedents for such transformations.[14] Therefore, the next objective became preparation of an appropriate vinyltin reagent.

Addition of bromine to methacrylonitrile, followed by treatment of the resulting dibromide with DBU, gave the expected vinyl bromide as a mixture of stereoisomers, from which the desired *Z*-isomer **16** was obtained by careful fractional distillation. After conversion of the cyano compound to acetal **17**, sequential treatment with *t*-BuLi, Bu_3SnCl, and moist SiO_2[15] gave the trialkyltin-substituted aldehyde **18**. Unfortunately, during this



sequence the olefin undergoes partial isomerization to the corresponding *E*-isomer. Furthermore, while this vinyltin reagent, as a 9:1 (*Z*:*E*) mixture of olefin stereoisomers, would undergo coupling with triflate **13**, the only product obtained was the *E*-aldehyde **19**. Isomerization to the less stable *Z*-isomer prior to

(6) Optically active hydroxyjatrophones have been prepared through resolution of a synthetic intermediate, cf: Smith, A. B., III; Lupo, A. T., Jr.; Ohba, M.; Chen, K. *J. Am. Chem. Soc.* **1989**, *111*, 6648.

(7) Becicka, B. T.; Koerwitz, F. L.; Drtina, G. J.; Baenziger, N. C.; Wiemer, D. F. *J. Org. Chem.* **1990**, *55*, 5613.

(8) (*R*)-(+)-3-Methyladipic acid can be prepared by oxidation of (*R*)-pulegone: Jackman, L. M.; Web, R. L.; Yick, H. C. J. *J. Org. Chem.* **1982**, *47*, 1824. This preparation has been incorporated into our undergraduate organic laboratory course to provide quantities of this key intermediate.

(9) Presented in part at the 26th Midwest Regional Meeting of the American Chemical Society, Omaha, NE, November 1991.

(10) Aboujaoude, E. E.; Collignon, N.; Savignac, P. *J. Organomet. Chem.* **1984**, *264*, 9. Coutrot, P.; Savignac, P.; Mathey, F. *Synthesis* **1978**, 36.

(11) (a) Sampson, P.; Roussis, V.; Drtina, G. J.; Koerwitz, F. L.; Wiemer, D. F. *J. Org. Chem.* **1986**, *51*, 2525. (b) Roussis, V.; Gloer, K. B.; Wiemer, D. F. *J. Org. Chem.* **1988**, *53*, 2011.

(12) Behrens, O. K.; Corse, J.; Huff, D. E.; Jones, R. G.; Soper, Q. F.; Whitehead, C. W. *J. Biol. Chem.* **1948**, *175*, 771.

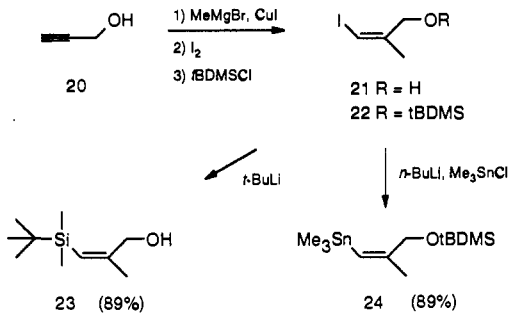
(13) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

(14) Renaldo, A. F.; Labadie, J. W.; Stille, J. K. *Org. Synth.* **1989**, *67*, 86.

(15) Baasov, T.; Sheves, M. *J. Am. Chem. Soc.* **1985**, *107*, 7524.

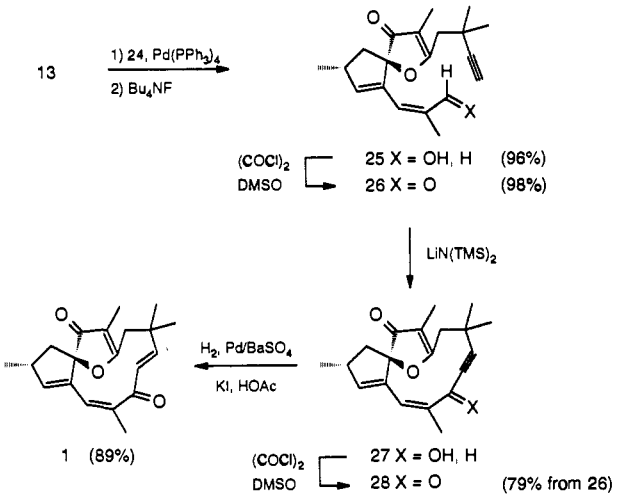
ring closure did not appear likely, and efforts to bring about ring closure of the *E*-isomer failed under a variety of conditions. On the basis of inspection of Dreiding models, the failure of compound **19** to cyclize is not surprising.

The successful route for assembly of the C5–C7 fragment began with the CuI-catalyzed addition of MeMgBr across the triple bond of propargyl alcohol (**20**), followed by reaction with iodine to obtain the vinyl iodide **21**.[16] After protection of this alcohol with



tBDMSCl, treatment of the resulting vinyl iodide **22** with *t*-BuLi in THF followed by addition of tributyltin chloride gave vinylsilane **23** as the major product. However, sequential reaction of vinyl iodide **22** with *n*-BuLi and Me_3SnCl in ether afforded the necessary vinyltin reagent, compound **24**.

The Pd-catalyzed coupling of vinyltin reagent **24** with triflate **13** gave the desired silyl ether in nearly quantitative yield. After deprotection of the hydroxyl group gave compound **25**, a Swern



oxidation afforded the desired *Z*-aldehyde **26** in 92% overall yield from triflate **13**. The *Z*-stereochemistry of the critical 5,6-double bond could be assigned with confidence by comparison of the NMR data for compound **26** with that from the corresponding *E*-isomer **19**.

To our delight, upon treatment with base under strictly anhydrous conditions, acetylenic aldehyde **26** undergoes a very clean macrocyclization. Out of concern for the stability of the resulting allylic and propargylic alcohol **27**, it was immediately oxidized under Swern conditions to ynone **28** (79% overall). Dreiding models make it clear that in acetylene **26** the degrees of freedom are severely restricted by both the spiro ring junction and the large number of sp^2 and sp centers, but the models do not establish the degree of conjugation between the C3–C4 and C5–C6 double bonds. An X-ray diffraction analysis of the crystalline aldehyde **26** was secured to gain further understanding.[17] As shown in

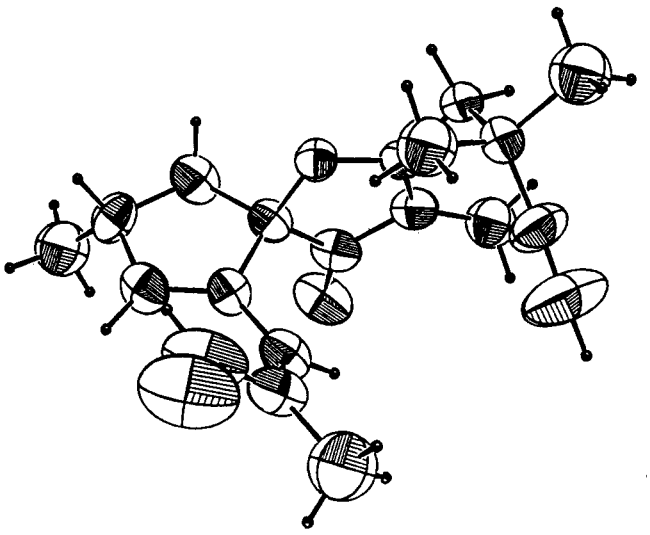


Figure 1. ORTEP drawing of compound **26**. Hydrogens are shown to clarify sp and sp^2 carbons.

Figure 1, in the solid state this material adapts a conformation wherein the aldehyde carbonyl group is some distance from the acetylene terminus, but the C3–C4 and C5–C6 double bonds display a torsional angle of about 45°. In solution, rotation along the C4–C5 and C10–C11 bonds must allow addition of the acetylide anion to this carbonyl group.

Because Smith has reported conversion of racemic ynone **28** to the racemic natural product (70%),[4] in one sense, formation of ynone **28** constitutes a formal synthesis of (+)-jatrophone. Our total synthesis of (+)-jatrophone was completed by employing Smith's procedure for reduction of the ynone to the natural product (H_2, $Pd/BaSO_4$ followed by KI in HOAc). Synthetic (+)-jatrophone produced in this fashion gave ^1H and ^{13}C NMR spectra identical to those previously recorded.[1,2,18] Furthermore, because the (+)-pulegone employed as the starting material was of high ee (>98% *R*), synthetic (+)-jatrophone of correspondingly high ee was expected. In fact, the rotation of synthetic material was +289°, virtually identical to that reported for the natural product (+292°).

This synthesis of (+)-jatrophone is the first to provide the optically active natural product, and it does so in a highly stereocontrolled fashion. Furthermore, a convergent sequence of just 11 steps from (*R*)-(+)-3-methyladipic acid to the known ynone **28** and an overall yield of over 15% for these steps make this approach highly efficient. A significant part of this attractive yield derives from the efficiency of the macrocyclization. Now that the viability of this approach to jatrophone has been demonstrated, similar strategies and derivatives of these optically active methyl cyclopentenoids[7] can be employed in syntheses of related diterpenoids in their natural enantiomeric form.

Experimental Section

Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use, and all reactions in this solvent were conducted under a positive pressure of an inert gas. CH_2Cl_2 was distilled from CaH_2, while pyridine was distilled from NaOH. Flash column chromatography was performed with Davisil Grade 633 silica gel (200–425 mesh). Unless otherwise noted, ^1H (300 or 360 MHz) and ^{13}C NMR spectra were recorded with $CDCl_3$ as solvent and either $(CH_3)_4Si$ or residual $CHCl_3$ as internal standard. Electron impact (EI) mass spectra were recorded at 70 eV; only selected ions are reported.

β-Keto Phosphonates 8. To an LDA solution prepared from 0.445 g (4.4 mmol) of diisopropylamine and 2.93 mL (1.5 M, 4.4 mmol) of BuLi in 10 mL of THF was added dropwise 0.73 g (4.4 mmol) of diethyl ethylphosphonate at −78 °C, and the reaction mixture was stirred for 40 min. The resulting solution was transferred by syringe to a solution of 0.752 g (2 mmol) of compound **6** in 10 mL of THF at −78 °C. After being stirred for 2 h, the reaction mixture was quenched by addition of

(16) Duboudin, J. G.; Jousseaume, B.; Bonakdar, A. *J. Organomet. Chem.* **1979**, *168*, 227.

(17) Crystallographic programs used are those of the SDP program package of Enraf-Nonius, which contains a version of MULTAN (P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978, 1980) and PLUTO78 (W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978).

(18) Guaciaro, M. A. Ph.D. Thesis, University of Pennsylvania, 1981.

0.3 mL of acetic acid in 20 mL of ether and then allowed to warm to room temperature. Solids were removed by filtration through silica gel and washed with ether. The filtrates were concentrated in vacuo and purified by chromatography on silica gel (gradient elution, 0 to 60% ethyl acetate in hexane) to give 0.886 g (87%) of compound **8** as a mixture of diastereomers in a 7:3 ratio.[19] For the major isomer: ^{1}H NMR δ 5.85 (d, J = 2.3 Hz, 1 H), 4.18–4.11 (m, 5 H), 3.05–2.95 (m, 1 H), 2.34 (dd, J = 14.8, 8.0 Hz, 1 H), 2.09 (dd, J = 14.8, 4.7 Hz, 1 H), 1.38 (d, J = 7.1 Hz, 3 H), 1.34 (t, J = 7.1 Hz, 3 H), 1.33 (t, J = 7.1 Hz, 3 H), 1.16 (d, J = 7.0 Hz, 3 H), 0.22 (s, 9 H); ^{13}C NMR δ 208.07, 147.05, 125.29, 118.25 (q, J = 320 Hz), 90.12, 62.62, 62.33, 43.13, 40.09, 33.41 (d, J = 132 Hz), 20.22, 16.28, 16.20, 12.12, 1.15. For the minor isomer: ^{1}H NMR δ 5.92 (d, J = 2.4 Hz, 1 H), 4.18–4.11 (m, 5 H), 3.05–2.95 (m, 1 H), 2.21 (dd, J = 14.6, 7.7 Hz, 1 H), 2.08 (dd, J = 14.8, 4.7 Hz, 1 H), 1.39 (d, J = 7.2 Hz, 3 H), 1.34 (t, J = 7.1 Hz, 6 H), 1.16 (d, J = 7.0 Hz, 3 H), 0.19 (s, 9 H); ^{13}C NMR δ 205.40, 146.87, 125.77, 118.60 (q, J = 320 Hz), 89.78, 62.62, 62.42, 42.13, 38.93 (d, J = 138 Hz), 33.48, 19.99, 16.20, 16.12, 12.03, 1.33. For both isomers: ^{19}F NMR −75.19; ^{31}P NMR 23.92; EIMS m/z (rel intensity) 510 (M^+, 0.01), 495 (3), 317 (76), 238 (47), 210 (30), 193 (17), 166 (23), 137 (15), 109 (20), 73 (100); HRMS calcd for $C_{16}H_{27}F_3O_8PSiS$ (M^+ − Me) 495.0886, found 495.0901. Anal. Calcd for $C_{17}H_{30}F_3O_8PSiS$: C, 39.99; H, 5.92. Found: C, 39.99; H, 5.95.

Esters 9. *tert*-Butylacetyl chloride (33 mg, 0.24 mmol) was added dropwise to a stirred solution of compound **8** (102 mg, 0.20 mmol) and $FeCl_3$ (43 mg, 0.26 mmol) in anhydrous CH_2Cl_2 (2 mL) at 0 °C. After being stirred at 0 °C overnight, the reaction mixture was diluted with 20 mL of CH_2Cl_2, washed with 1 M HCl (3 × 5 mL), saturated $NaHCO_3$ (2 × 5 mL), and brine (5 mL), and then dried over $MgSO_4$. After concentration in vacuo, purification by flash chromatography (20 to 40% ethyl acetate in hexane) gave 73 mg (68.1%) of compound **9** as a mixture of diastereomers in a 5:4 ratio. For the major isomer: ^{1}H NMR δ 6.05 (d, J = 2.3 Hz, 1 H), 4.13 (q, J = 7.2 Hz, 4 H), 3.81 (dq, J = 21.1, 7.1 Hz, 1 H), 3.16–3.07 (m, 1 H), 2.60 (dd, J = 14.6, 7.5 Hz, 1 H), 2.28 (s, 2 H), 2.22 (dd, J = 14.6, 5.1 Hz, 1 H), 1.43 (d, J = 7.0 Hz, 3 H), 1.32 (t, J = 7.0 Hz, 6 H), 1.19 (d, J = 7.2 Hz, 3 H), 1.05 (s, 9 H); ^{19}F NMR −74.2. For the minor isomer: ^{1}H NMR δ 6.09 (d, J = 2.4 Hz, 1 H), 4.14 (q, J = 7.2 Hz, 4 H), 3.59 (dq, J = 19.5, 7.1 Hz, 1 H), 3.16–3.07 (m, 1 H), 2.60 (dd, J = 14.6, 5.0 Hz, 1 H), 2.44 (dd, J = 14.8, 7.9 Hz, 1 H), 2.26 (s, 2 H), 1.45 (d, J = 7.1 Hz, 3 H), 1.22 (d, J = 7.2 Hz, 3 H), 1.33 (t, J = 7.0 Hz, 6 H), 1.05 (s, 9 H); ^{19}F NMR −74.0. For both isomers: ^{31}P NMR δ 22.5; EIMS m/z (rel intensity) 491 (M^+ − OEt, 0.01), 438 (0.33), 305 (20), 193 (100), 166 (83), 137 (33), 109 (33), 99 (23), 69 (14), 57 (81).

3,3-Dimethyl-4-pentynoic Acid (10). The acetylenic acid was prepared from the corresponding malonate according to a known procedure:[12] bp 76–78 °C/2 mm; ^{1}H NMR δ 2.52 (s, 2 H), 2.18 (s, 1 H), 1.39 (s, 6 H); ^{13}C NMR δ 177.02, 89.73, 68.56, 46.65, 29.42, 29.03; EIMS m/z (rel intensity) 126 (M^+, 4), 125 (18), 111 (71), 98 (17), 83 (46), 67 (100), 45 (19).

Preparation of Esters 11. A mixture of acetylenic acid **10** (1.26 g, 10 mmol) and oxalyl chloride (1.30 g, 10 mmol, flash distilled from PCl_5) was stirred in anhydrous CH_2Cl_2 (40 mL) at room temperature overnight. After concentration in vacuo, distillation gave 1.4 g (97%) of the corresponding acid chloride (bp 80 °C/40 mm). This compound was not further characterized but instead carried directly to the next reaction.

As described for the preparation of compound **9**, the acid chloride (235 mg, 1.63 mmol) was allowed to react with compound **8** (443 mg, 0.87 mmol) and $FeCl_3$ (220 mg, 1.36 mmol) in anhydrous CH_2Cl_2 (20 mL) at −20 °C. A parallel workup and purification by flash chromatography (20% ethyl acetate in hexane) gave 432 mg (92%) of compound **11** as a 6:4 mixture of two diastereomers. For the major isomer: ^{1}H NMR δ 6.06 (d, J = 2.3 Hz, 1 H), 4.17–4.11 (m, 4 H), 3.91 (dq, J = 22.1, 7.1 Hz, 1 H), 3.18–3.09 (m, 1 H), 2.60–2.50 (m, 1 H), 2.55 (s, 2 H), 2.24–2.15 (m, 1 H), 2.18 (s, 1 H), 1.38 (s, 6 H), 1.47–1.20 (m, 9 H), 1.18 (d, J = 7.1 Hz, 3 H); ^{19}F NMR −73.98. For the minor isomer: ^{1}H NMR δ 6.09 (d, J = 2.4 Hz, 1 H), 4.17–4.11 (m, 4 H), 3.65 (dq, J = 19.5, 7.1 Hz, 1 H), 3.18–3.09 (m, 1 H), 2.60–2.65 (m, 1 H), 2.53 (s, 2 H), 2.24–2.15 (m, 1 H), 2.15 (s, 1 H), 1.47–1.20 (m, 9 H), 1.37 (s, 6 H), 1.19 (d, J = 7.1 Hz, 3 H); ^{19}F NMR −74.14. For both isomers: ^{31}P NMR 21.8; EIMS m/z (rel intensity) 438 (1), 376 (1), 305 (12), 193 (100), 166 (49), 137 (34), 109 (47), 69 (12), 67 (40), 65 (13); HRMS calcd for $C_{21}H_{30}O_9F_3PSNa$ 569.1198, found 569.1193.

3(2*H*)-Furanone 12. A mixture of 73 mg (0.14 mmol) of compound **9** and 47 mg (0.34 mmol) of K_2CO_3 in DMF (3 mL) was stirred at room temperature for 30 min and then heated at reflux for 12 h. After being cooled to room temperature, the reaction mixture was diluted with ethyl acetate. Solids were removed by filtration through silica gel and washed with ether. Concentration in vacuo gave a residue that was finally purified by thin layer chromatography (10% ethyl acetate in hexane) to give 26 mg (50%) of compound **12**: ^{1}H NMR δ 6.07 (d, J = 2.3 Hz, 1 H), 3.12–3.06 (m, 1 H), 2.45 (d, J = 13.2 Hz, 1 H), 2.37 (d, J = 13.2 Hz, 1 H), 2.34 (dd, J = 14.1, 7.7 Hz, 1 H), 1.97 (dd, J = 14.1, 4.7 Hz, 1 H), 1.69 (s, 3 H), 1.26 (d, J = 7.0 Hz, 3 H), 1.04 (s, 9 H); EIMS m/z (rel intensity) 382 (M^+, 1), 367 (1), 326 (5), 249 (40), 193 (58), 165 (20), 151 (20), 81 (33), 69 (55), 57 (100); HRMS calcd for $C_{16}H_{21}O_5SF_3$ 382.1067, found 382.1081.

3(2*H*)-Furanone 13. NaH (36.7 mg, 80% in mineral oil, 1.22 mmol) was washed with anhydrous pentane (3 × 1 mL) and then suspended in DME (2 mL). To this suspension was added dropwise compound **11** (268 mg, 0.49 mmol) in 3 mL of DME at −10 °C, and the resulting mixture was warmed to room temperature over 15 min. After 1 h at reflux, the reaction mixture was allowed to cool to room temperature and diluted with ether. Standard workup gave a residue that was purified by chromatography on silica gel (10% ethyl acetate in hexane) to give 120 mg (62.4%) of compound **13**: $[\alpha]_D$ = 16.6° [c = 1.67 (EtOH)]; ^{1}H NMR δ 6.09 (d, J = 2.4 Hz, 1 H), 3.15–3.08 (m, 1 H), 2.77 (d, J = 13.4 Hz, 1 H), 2.61 (d, J = 13.4 Hz, 1 H), 2.38 (dd, J = 14.2, 7.7 Hz, 1 H), 2.14 (s, 1 H), 1.98 (dd, J = 14.2, 4.7 Hz, 1 H), 1.74 (s, 3 H), 1.36 (s, 6 H), 1.26 (d, J = 7.0 Hz, 3 H); ^{13}C NMR δ 201.11, 184.60, 142.94, 129.70, 118.29 (q, J = 320.2 Hz), 112.69, 93.69, 89.45, 69.05, 41.28, 40.54, 34.06, 31.62, 29.69, 29.32, 20.49, 6.39; EIMS m/z (rel intensity) 393 (M^+ + 1, 0.23), 326 (1), 256 (59), 241 (77), 165 (5), 147 (27), 136 (74), 121 (24), 69 (87), 67 (100); HRMS calcd for $C_{17}H_{20}O_5SF_3$ (M^+ + 1) 393.0984, found 393.0960. Anal. Calcd for $C_{17}H_{19}O_5SF_3$: C, 52.04; H, 4.88. Found: C, 52.17; H, 4.98.

Preparation of Olefin 14. A Rotaflo tube was charged with 0.9 mg (0.8 μmol) of $Pd(PPh_3)_4$, 4.4 mg (0.102 mmol) of LiCl, 2.5 mg (7.9 μmol) of vinyltributylstanane, and 3 mg (7.9 μmol) of compound **12** in THF (1 mL), flushed with N_2, and then sealed. The reaction mixture was stirred at room temperature for 15 min and then heated at 80 °C (oil bath) overnight. After being cooled to room temperature, the mixture was diluted with hexane and the solids were removed by filtration. Evaporation of the solvents gave a residue that was purified by chromatography on silica gel (0 to 10% ethyl acetate in hexane) to give 2 mg (98%) of compound **14** as a colorless oil: ^{1}H NMR δ 6.15 (dd, J = 17.7, 11.2 Hz, 1 H), 6.11 (br, 1 H), 4.95 (d, J = 11.2 Hz, 1 H), 4.90 (d, J = 17.4 Hz, 1 H), 3.11–3.04 (m, 1 H), 2.39 (s, 2 H), 2.23 (dd, J = 13.8, 7.1 Hz, 1 H), 1.87 (dd, J = 13.8, 6.4 Hz, 1 H), 1.72 (s, 3 H), 1.15 (d, J = 7.1 Hz, 3 H), 1.01 (s, 9 H); EIMS m/z (rel intensity) 260 (M^+, 12), 245 (4), 203 (17), 189 (5), 161 (100), 147 (11), 133 (8), 105 (10), 91 (18), 57 (60).

Preparation of Olefin 15. As described for the preparation of compound **14**, a Rotaflo tube was charged with 13.3 mg (0.012 mmol) of $Pd(PPh_3)_4$, 43.5 mg (1.02 mmol) of LiCl, 38.0 mg (0.120 mmol) of vinyltributylstanane, and 47.0 mg (0.12 mmol) of compound **13** in THF (5 mL). Standard reaction conditions and workup gave 33 mg (100%) of compound **15** as a colorless oil: $[\alpha]_D$ = 46.3° [c = 2.4 ($CDCl_3$)]; ^{1}H NMR δ 6.18 (dd, J = 17.8, 11.4 Hz, 1 H), 6.13 (br, 1 H), 4.97 (d, J = 11.2 Hz, 1 H), 4.95 (d, J = 17.8 Hz, 1 H), 3.14–3.06 (m, 1 H), 2.71 (d, J = 13.2 Hz, 1 H), 2.63 (d, J = 13.2 Hz, 1 H), 2.28 (dd, J = 13.9, 7.2 Hz, 1 H), 2.12 (s, 1 H), 1.89 (dd, J = 13.9, 6.4 Hz, 1 H), 1.79 (s, 3 H), 1.37 (s, 3 H), 1.34 (s, 3 H), 1.18 (d, J = 7.0 Hz, 3 H); ^{13}C NMR δ 205.56, 183.39, 145.48, 138.40, 129.15, 115.63, 113.04, 98.66, 89.86, 69.05, 45.50, 41.47, 37.90, 31.88, 29.94, 29.47, 19.94, 6.62; EIMS m/z (rel intensity) 270 (M^+, 12), 255 (4), 227 (7), 203 (29), 161 (100), 147 (14), 134 (42), 119 (60), 105 (51), 67 (67); HRMS calcd for $C_{18}H_{22}O_2$ 270.1620, found 270.1595.

(*Z*)-3-Bromomethacrylonitrile (16). To a stirred solution of methacrylonitrile (9.0 g, 0.134 mol) in CH_2Cl_2 (30 mL) was added dropwise 6.9 mL (0.134 mol) of bromine at −10 °C. After being stirred at room temperature for 1 h, the reaction mixture was diluted with 200 mL of CH_2Cl_2, washed with Na_2SO_3 solution and water, and dried over $MgSO_4$. Concentration in vacuo and subsequent distillation gave 30.0 g (100%) of the dibromide: bp 66–67 °C/2.2 mm; ^{1}H NMR δ 4.01 (d, J = 10.6 Hz, 1 H), 3.75 (d, J = 10.6 Hz, 1 H), 2.19 (s, 3 H); ^{13}C NMR δ 118.00, 40.43, 38.07, 29.69.

To a stirred solution of the dibromide (30.0 g, 0.13 mol) in CH_2Cl_2 (30 mL) was added slowly 20.0 g (0.13 mol) of DBU at −10 °C. After being stirred at room temperature for 1 h, the reaction mixture was diluted with CH_2Cl_2, washed with 1 N HCl (3 × 20 mL) and water, and dried over $MgSO_4$. Concentration gave a mixture of *Z*- and *E*-isomers[20] in a 7:3 ratio as determined by GC analysis. Repeated distillation (3 times) through a 50-cm Vigreux column gave a total of 10.0 g (51%) of

(19) We thank Dr. B. T. Becicka for his preparation of this compound: cf. Becicka, B. T. Ph.D. Thesis, University of Iowa, 1991.

(20) Patel, B. A.; Kim, J. I.; Bender, D. D.; Kao, L.-C.; Heck, R. F. *J. Org. Chem.* **1981**, *46*, 1061.

3-bromomethacrylonitrile (**16**), 97.6% *Z*-isomer by GC analysis: bp 68–70 °C/14 mmHg; ^{1}H NMR δ 6.85 (q, *J* = 1.7 Hz, 1 H), 2.03 (d, *J* = 1.7 Hz, 3 H); ^{13}C NMR δ 120.52, 117.11, 116.90, 20.67; EIMS *m/z* (rel intensity) 147 (M^+ + 2, 45), 145 (M^+, 45), 120 (5), 118 (5), 95 (4), 93 (6), 81 (6), 79 (6), 66 (100).

After 2 weeks at room temperature, the sample was a 70:30 mixture of *Z*- and *E*-isomers, based on ^{1}H NMR analysis. For the *E*-isomer: bp 57–60 °C/14 mmHg; ^{1}H NMR δ 7.17 (q, *J* = 1.4 Hz, 1 H), 2.03 (d, *J* = 1.5 Hz, 3 H); ^{13}C NMR δ 125.71, 115.51, 115.34, 18.03; EIMS *m/z* (rel intensity) 147 (M^+ + 2, 40), 145 (M^+, 40), 120 (6), 118 (6), 95 (4), 93 (5), 81 (5), 79 (5), 66 (100).

(*Z*)-1-Bromo-3,3-dimethoxy-2-methyl-1-propene (17). To a stirred solution of the *Z*-vinyl bromide **16** (4.13 g, 28 mmol) in CH_2Cl_2 (60 mL) was added 33.7 mL (1 M, 33.7 mmol) of DIBAL in CH_2Cl_2 at −78 °C. After the resulting mixture was stirred for 2 h, 0.6 mL of water and 20 g of silica gel were added at −78 °C. The reaction mixture was allowed to warm slowly to 0 °C and stirred for 12 h. Solids were removed by filtration. The filtrate was dried over $MgSO_4$ and then flash distilled at room temperature in vacuo to give a solution of (*Z*)-3-bromo-2-methacrolein in CH_2Cl_2: ^{1}H NMR ($CDCl_3/CH_2Cl_2$) δ 10.11 (s, 1 H), 7.24 (q, *J* = 1.4 Hz, 1 H), 1.84 (d, *J* = 1.5 Hz, 3 H); ^{13}C NMR ($CDCl_3/CH_2Cl_2$) δ 191.70, 138.02, 122.34, 18.50; EIMS *m/z* (rel intensity) 150 (M^+ + 2, 100), 148 (M^+, 100), 122 (10), 121 (27), 120 (14), 119 (32), 95 (7), 93 (9), 69 (59). After the solution was kept in a refrigerator for 1 week, 10% isomerization to the *E*-isomer was observed on the basis of ^{1}H NMR analysis: ^{1}H NMR δ 9.49 (d, *J* = 1.7 Hz, 1 H), 7.44 (s, 1 H), 1.90 (d, *J* = 1.5 Hz, 3 H); ^{13}C NMR δ 189.99, 144.75, 133.04, 16.03; EIMS *m/z* (rel intensity) 150 (M^+ + 2, 97), 148 (M^+, 100), 122 (5), 121 (13), 120 (6), 119 (16), 95 (4), 93 (6), 69 (26).

Without further purification, the aldehyde solution was added to a stirred solution of trimethyl orthoformate (40 g) and TsOH (5.4 g, 27 mmol) at room temperature, and the resulting mixture was stirred for 15 min. After being cooled to −10 °C, the reaction mixture was poured into a solution of aqueous K_2CO_3 (4 g in 40 mL). The organic layer was separated, washed with water (2 × 20 mL) and brine (20 mL), and finally dried over $MgSO_4$. After concentration in vacuo, the residue was distilled at reduced pressure to give 3.47 g (63.3%) of compound **17** as a mixture of *Z*- and *E*-isomers[20] in a 9:1 ratio (bp 38–39 °C/2 mm): ***Z*-17**: ^{1}H NMR δ 6.12 (q, *J* = 1.6 Hz, 1 H), 5.17 (s, 1 H), 3.41 (s, 6 H), 1.77 (d, *J* = 1.6 Hz, 3 H); ^{13}C NMR δ 138.48, 104.17, 103.55, 54.92, 16.62; EIMS *m/z* (rel intensity) 195 (1), 193 (M^+ − 1, 1) 165 (77), 163 (75), 135 (6), 133 (7), 115 (83), 95 (12), 93 (10), 83 (8), 75 (100), 69 (15), 55 (25), 53 (26). ***E*-17**: ^{1}H NMR δ 6.43 (t, *J* = 1.3 Hz, 1 H), 4.63 (s, 1 H), 3.29 (s, 6 H), 1.77 (d, *J* = 1.4 Hz, 3 H); ^{13}C NMR δ 138.17, 107.79, 104.23, 52.82, 14.99; EIMS *m/z* (rel intensity) 196 (M^+ + 2, 0.2), 194 (M^+, 0.2), 182 (1), 180 (1), 166 (37), 164 (37), 115 (53), 75 (100).

Preparation of Tributyltin Aldehyde 18. To a stirred solution of compound **17** (220 mg, 1.13 mmol, *Z*:*E* ratio of 9:1) in THF (5 mL) was added dropwise 1.46 mL (1.7 M, 2.48 mmol) of *t*-BuLi at −78 °C. After the solution was stirred for 1 h, Bu_3SnCl was added and the resulting mixture was allowed to warm to room temperature over 2 h. The reaction mixture was diluted with ether (30 mL), washed with saturated NH_4Cl (2 × 20 mL) and water (2 × 10 mL), and then dried over $MgSO_4$. After evaporation of the ether, the desired tin acetal was obtained as a 9:1 mixture of *Z*- and *E*-isomers.

For the *Z*-isomer: ^{1}H NMR δ 5.88 (q, *J* = 1.2 Hz, 1 H), 4.67 (s, 1 H), 3.25 (s, 6 H), 1.85 (d, *J* = 1.3 Hz, 3 H), 1.56–1.44 (m, 6 H), 1.39–1.24 (m, 6 H), 0.97–0.82 (m, 15 H); ^{13}C NMR δ 148.78, 130.05, 104.30, 51.88, 29.16, 27.40, 22.49, 13.64, 11.25; EIMS *m/z* (rel intensity) 350 (2), 320 (1), 236 (1), 205 (1), 151 (5), 121 (4), 115 (100), 85 (14), 75 (4), 53 (28); HRMS calcd for $C_{18}H_{37}O_2Sn$ 405.1816, found 405.1809.

For the *E*-isomer: ^{1}H NMR δ 5.96 (s, 1 H), 4.53 (s, 1 H), 3.30 (s, 6 H), 1.74 (s, 3 H), 1.56–1.44 (m, 6 H), 1.39–1.24 (m, 6 H), 0.97–0.82 (m, 15 H); ^{13}C NMR δ 149.30, 127.63, 107.75, 53.25, 29.15, 27.22, 19.08, 13.58, 10.01; EIMS *m/z* (rel intensity) 350 (2), 294 (2), 189 (2), 177 (5), 151 (7), 141 (6), 115 (100), 85 (30), 75 (17), 53 (24).

After the unpurified acetal was stirred with 1.0 g of silica gel in moist ether for 30 min at room temperature, the silica gel was removed by filtration. The filtrate was concentrated and purified by chromatography on silica gel (5% ethyl acetate in hexane) to give 366 mg (90%) of compound **18** as a 9:1 mixture of *Z*- and *E*-isomers.

For ***Z*-18**: ^{1}H NMR δ 9.48 (s, 1 H), 7.40 (q, *J* = 1.4 Hz, 1 H), 1.98 (d, *J* = 1.3 Hz, 3 H), 1.53–1.46 (m, 6 H), 1.31 (q, *J* = 7.3 Hz, 6 H), 1.01 (t, *J* = 7.3 Hz, 6 H), 0.89 (t, *J* = 7.3 Hz, 9 H); ^{13}C NMR δ 194.89, 157.08, 152.38, 28.93, 27.13, 18.82, 13.52, 11.28; EIMS *m/z* (rel intensity) 303 (M^+ − Bu, 100), 247 (68), 189 (72), 177 (33), 161 (33), 135 (29), 121 (53), 57 (32), 53 (85); HRMS calcd for $C_{12}H_{23}OSn$ (M^+ − Bu) 303.0770, found 303.0766. For ***E*-18**: ^{1}H NMR δ 9.42 (s, 1 H), 7.31 (q, *J* = 0.7 Hz, 1 H), 1.88 (d, *J* = 0.7 Hz, 3 H), 1.53–1.45 (m, 6 H), 1.30 (q, *J* = 7.2 Hz, 6 H), 1.02 (t, *J* = 7.2 Hz, 6 H), 0.88 (t, *J* = 7.2 Hz, 9 H); ^{13}C NMR δ 193.87, 157.80, 154.21, 29.03, 27.21, 16.01, 13.52, 10.17; EIMS *m/z* (rel intensity) 303 (M^+ − Bu, 71), 247 (100), 189 (85), 177 (28), 161 (25), 137 (22), 121 (51), 53 (96).

Preparation of *E*-Aldehyde 19. As described for compound **14**, a Rotaflo tube was charged with 3 mg (0.003 mmol) of $Pd(PPh_3)_4$, 20 mg (0.465 mmol) of LiCl, 18.9 mg (0.053 mmol) of tin reagent **18**, and 20.5 mg (0.052 mmol) of triflate **13** in THF (1 mL). Standard reaction conditions and workup, and purification by chromatography on silica gel (0 to 10% ethyl acetate in hexane), gave 17 mg (100%) of compound **19**: ^{1}H NMR δ 9.32 (s, 1 H), 6.51 (s, 1 H), 6.25 (s, 1 H), 3.29–3.22 (m, 1 H), 2.77 (d, *J* = 13.3 Hz, 1 H), 2.58 (d, *J* = 13.3 Hz, 1 H), 2.35 (dd, *J* = 14.1, 7.6 Hz, 1 H), 2.12 (s, 1 H), 1.95 (dd, *J* = 14.1, 5.6 Hz, 1 H), 1.93 (s, 3 H), 1.78 (s, 3 H), 1.37 (s, 3 H), 1.34 (s, 3 H), 1.29 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR δ 204.74, 194.55, 184.62, 149.59, 141.66, 139.53, 135.60, 113.12, 99.93, 89.60, 69.35, 42.03, 41.55, 39.80, 31.96, 30.28, 29.60, 20.20, 11.40, 6.63; EIMS *m/z* (rel intensity) 312 (M^+, 2), 297 (2), 283 (6), 269 (2), 245 (14), 203 (15), 186 (10), 176 (59), 147 (100), 67 (66); HRMS calcd for $C_{20}H_{24}O_3$ 312.1725, found 312.1751.

Vinylsilane 23. To a solution of compound **22**[16,21] (0.123 g, 0.394 mmol) in THF (3 mL) was added *t*-BuLi (0.56 mL, 0.95 mmol, 1.7 M) at −78 °C over 30 min. The resulting mixture was stirred at −78 °C for 1 h, and then it was allowed to warm to room temperature. The mixture was diluted with ether (10 mL), washed with saturated NH_4Cl (2 × 5 mL), water (5 mL), and brine, and then dried over $MgSO_4$. Concentration in vacuo gave 65 mg (89%) of compound **23**: ^{1}H NMR δ 5.43 (br s, 1 H), 4.12 (s, 2 H), 1.96 (d, *J* = 1.3 Hz, 3 H), 1.59 (s, 1 H), 0.88 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR δ 154.32, 125.37, 66.03, 26.33, 24.40, 16.72, −3.96; EIMS *m/z* (rel intensity) 171 (M^+ − Me, 0.13), 129 (M^+ − *t*-Bu, 26), 111 (32), 101 (34), 87 (13), 75 (100), 73 (17), 61 (60); IR 3649, 3635, 3630, 3619, 2954, 2929, 2857, 1742, 1653, 1635. Anal. Calcd for $C_{10}H_{22}OSi$: C, 64.45; H, 11.90. Found: C, 64.38; H, 11.85.

Vinyltin 24. To a solution of compound **22**[16,21] (0.62 g, 2 mmol) in anhydrous ether (10 mL) was added *n*-BuLi (1.6 M, 2.8 mL, 4.4 mmol) at −78 °C over 30 min, and the resulting mixture was stirred for 1.5 h. After a solution of Me_3SnCl (0.8 g, 4 mmol) in ether (5 mL) was added, the reaction mixture was stirred at −78 °C for 3 h. The volatile materials were removed in vacuo and the residue was diluted with ether, washed with water, and dried over $MgSO_4$. After concentration, 0.62 g (89%) of compound **24** was obtained. This tin reagent was not further purified but instead was carried directly to the next step. **24**: ^{1}H δ 5.60 (q, *J* = 1.3 Hz, 1 H), 4.08 (s, 2 H), 1.90 (d, *J* = 1.4 Hz, 3 H), 0.92 (s, 9 H), 0.14 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR δ 153.76, 125.05, 68.74, 26.07, 23.66, 18.50, −5.19, −8.23; EIMS *m/z* (rel intensity) 336 (9), 334 (4), 239 (11), 185 (32), 165 (45), 143 (20), 135 (16), 113 (9), 75 (23), 73 (100); HRMS calcd for $C_{13}H_{30}OSiSn$ 335.0853 (M^+ − Me), found 335.0859.

Preparation of *Z*-Alcohol 25. As described for the preparation of compound **14**, a Rotaflo tube was charged with 6 mg (0.005 mmol) of $Pd(PPh_3)_4$, 35 mg (0.824 mmol) of LiCl, 19 mg (0.054 mmol) of tin reagent **24**, and 20 mg (0.051 mmol) of triflate **13** in THF (1 mL). Application of standard reaction conditions and workup, and purification by column chromatography on silica gel (hexane then CH_2Cl_2), gave 22 mg (100%) of the silyl ether of compound **25** as a colorless oil: ^{1}H NMR δ 5.81 (s, 1 H), 5.26 (q, *J* = 1.3, Hz, 1 H), 4.31 (d, *J* = 12.4 Hz, 1 H), 4.16 (d, *J* = 12.4 Hz, 1 H), 3.14–3.08 (m, 1 H), 2.70 (d, *J* = 13.2 Hz, 1 H), 2.59 (d, *J* = 13.2 Hz, 1 H), 2.26 (dd, *J* = 14.0, 7.5 Hz, 1 H), 2.12 (s, 1 H), 1.85 (dd, *J* = 14.0, 5.5 Hz, 1 H), 1.77 (d, *J* = 1.3 Hz, 3 H), 1.73 (s, 3 H), 1.34 (s, 3 H), 1.33 (s, 3 H), 1.20 (d, *J* = 7.0 Hz, 3 H), 0.90 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR δ 205.38, 183.76, 142.84, 142.61, 136.06, 117.17, 112.65, 100.63, 89.92, 68.91, 62.77, 42.41, 41.45, 38.62, 31.76, 29.77, 29.39, 25.89, 21.48, 20.65, 18.31, 6.57, −5.34; EIMS *m/z* (rel intensity) 429 (M^+ + 1, 0.01), 320 (2), 262 (1), 234 (2), 188 (6), 149 (3), 115 (7), 75 (32), 73 (100), 67 (25).

To a solution of the silyl ether (20.5 mg, 0.048 mmol) in THF (1 mL) was added dropwise 0.058 mL (1 M, 0.058 mmol) of Bu_4NF in THF at 0 °C. After 5 min at 0 °C, the reaction mixture was allowed to warm to room temperature, stirred for an additional 40 min, and then quenched by addition of 3 drops of saturated NH_4Cl solution. After concentration in vacuo, the residue was diluted with ether and washed with water, and then the ether layer was dried over $MgSO_4$. Evaporation of the ether gave 17.5 mg of a product which was further purified by chromatography on silica gel (20% ethyl acetate in hexane) to give 14.5 mg (96.1%) of compound **25**: $[\alpha]_D$ = 89.1° [*c* = 0.64 (EtOH)]; ^{1}H NMR δ 5.85 (br s, 1 H), 5.37 (br s, 1 H), 4.31 (d, *J* = 12.2 Hz, 1 H), 4.05 (d, *J* = 12.2 Hz, 1 H), 3.14–3.08 (m, 1 H), 2.71 (d, *J* = 13.4 Hz, 1 H), 2.60 (d, *J*

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= 13.4 Hz, 1 H), 2.28 (dd, J = 14.1, 7.3 Hz, 1 H), 2.14 (br, 1 H), 2.13 (s, 1 H), 1.87 (dd, J = 14.1, 5.8 Hz, 1 H), 1.81 (d, J = 1.5 Hz, 3 H), 1.72 (s, 3 H), 1.37 (s, 3 H), 1.35 (s, 3 H), 1.20 (d, J = 7.0 Hz, 3 H); ^{13}C NMR δ 205.90, 184.24, 143.15, 142.10, 135.72, 118.60, 112.74, 100.84, 89.78, 68.99, 62.06, 42.57, 41.44, 38.62, 31.71, 29.71, 29.52, 21.49, 20.46, 6.47; EIMS m/z (rel intensity) 314 (M^+, 1), 285 (16), 259 (2), 247 (4), 231 (5), 191 (12), 177 (27), 136 (54), 67 (95); HRMS calcd for $C_{20}H_{26}O_3$ 314.1883, found 314.1879.

Preparation of *Z*-Aldehyde 26. *Z*-Alcohol **25** (52 mg, 0.166 mmol) in CH_2Cl_2 (1 mL) was treated with 2 equiv of Swern's reagent (prepared from oxalyl chloride (42 mg, 0.33 mmol) and DMSO (0.08 mL) in CH_2Cl_2 (1 mL)), and the resulting mixture was stirred for 15 min at −78 °C. After 0.5 mL of Et_3N was added, the reaction mixture was stirred for 5 min at −78 °C and then allowed to warm to room temperature. After removal of the volatile materials in vacuo, the residue was purified by chromatography on silica gel (10% ethyl acetate in hexane) to give 51 mg (98.7%) of *Z*-aldehyde **26**: mp 80.5–81 °C; $[\alpha]_D$ = 89.1° [c = 0.32 (EtOH)]; ^{1}H NMR δ 9.96 (s, 1 H), 6.52 (q, J = 1.5 Hz, 1 H), 6.13 (br, 1 H), 3.22–3.16 (m, 1 H), 2.72 (d, J = 13.3 Hz, 1 H), 2.58 (d, J = 13.3 Hz, 1 H), 2.38 (dd, J = 14.1, 7.5 Hz, 1 H), 2.11 (s, 1 H), 1.98 (dd, J = 14.1, 5.6 Hz, 1 H), 1.79 (d, J = 1.2 Hz, 3 H), 1.75 (s, 3 H), 1.34 (s, 3 H), 1.33 (s, 3 H), 1.25 (d, J = 7.1 Hz, 3 H); ^{13}C NMR δ 204.45, 192.12, 184.26, 149.67, 141.60, 136.79, 133.87, 112.81, 99.27, 89.52, 69.11, 42.68, 41.42, 39.04, 31.73, 29.86, 29.61, 20.15, 16.48, 6.50; EIMS m/z (rel intensity) 312 (M^+, 6), 297 (3), 284 (5), 269 (10), 245 (5), 203 (18), 189 (25), 175 (25), 161 (22), 67 (70); HRMS calcd for $C_{20}H_{24}O_3$ 312.1725, found 312.1720.

The sample for single crystal diffraction analysis was obtained by recrystallization from 25% ether in pentane at room temperature.

(+)-8,9-Dehydrojatrophone (28).[4] Aldehyde **26** (6.4 mg, 0.02 mmol) was washed with anhydrous benzene (4 × 2 mL) and then dried under vacuum for 5 h. After the aldehyde was dissolved in THF (4 mL), $LiN(TMS)_2$ (28 μL, 1 M in THF, 0.028 mmol) was added dropwise at room temperature. The resultant mixture was stirred for 5 h and then quenched by addition of saturated NH_4Cl (3 μL). After concentration in vacuo, the residue was diluted with ether and then filtered through silica gel to give compound **27**: ^{1}H NMR δ 5.73 (q, J = 1.8 Hz, 1 H), 5.42–5.38 (m, 2 H), 3.11–3.04 (m, 1 H), 2.66 (d, J = 12.7 Hz, 1 H), 2.38 (d, J = 12.7 Hz, 1 H), 2.16 (dd, J = 6.5, 13.8 Hz, 1 H), 1.96 (br, 1 H), 1.79 (dd, J = 7.3, 13.8 Hz, 1 H), 1.71 (d, J = 1.4 Hz, 3 H), 1.62 (s, 3 H), 1.23 (s, 3 H), 1.19 (d, J = 1.8 Hz, 3 H), 1.10 (d, J = 7.0 Hz, 3 H); ^{13}C NMR δ 205.34, 183.84, 143.80, 143.06, 136.05, 118.20, 111.77, 100.91, 90.81, 85.91, 61.14, 44.21, 44.14, 38.35, 33.55, 29.75, 29.23, 19.63, 16.86, 6.78; EIMS m/z (rel intensity) 312 (M^+, 13), 297 (11), 284 (3), 279 (4), 269 (16), 251 (9), 241 (15), 227 (17), 213 (26), 199 (21), 173 (33), 161 (30), 145 (26), 128 (40), 115 (34), 105 (29), 53 (100).

Without further purification, compound **27** in CH_2Cl_2 (0.5 mL) was added to 4 equiv of Swern's reagent, and the resulting mixture was stirred for 15 min at −78 °C. After 0.4 mL of Et_3N was added, the reaction mixture was stirred for 5 min at −78 °C and then allowed to warm to room temperature. After concentration in vacuo at room temperature, the residue was purified by chromatography on silica gel (3% ether in pentane) to give 5.0 mg (79%) of crystalline ynone **28**:[4] $[\alpha]_D$ = 123° [c = 0.13 (EtOH)]; ^{1}H NMR δ 5.87 (d, J = 1.7 Hz, 1 H), 5.74 (q, J = 1.5 Hz, 1 H), 3.18–3.04 (m, 1 H), 2.85 (d, J = 14.6 Hz, 1 H), 2.51 (d, J = 14.6 Hz, 1 H), 2.20 (dd, J = 13.4, 5.7 Hz, 1 H), 1.88 (dd, J = 13.4, 8.0 Hz, 1 H), 1.82 (d, J = 1.7 Hz, 3 H), 1.70 (d, J = 0.4 Hz, 3 H), 1.43 (s, 3 H), 1.36 (s, 3 H), 1.10 (d, J = 7.1 Hz, 3 H); ^{13}C NMR δ 203.91, 184.84, 182.71, 147.79, 144.68, 136.53, 123.00, 111.79, 105.53, 99.30, 84.40, 43.65, 41.56, 38.44, 32.54, 29.60, 29.50, 19.59, 18.99, 6.19; EIMS m/z (rel intensity) 310 (M^+, 10), 295 (20), 282 (7), 267 (29), 253 (10), 239 (28), 227 (34), 211 (36), 197 (29), 187 (34).

(+)-Jatrophone (1). According to the procedure of Smith et al.,[4] a suspension of 18 mg of 5% $Pd/BaSO_4$ in anhydrous pyridine (0.5 mL) was treated with H_2 at room temperature for 10 min, and then the H_2 reservoir was removed. After a solution of ynone **28** (1.5 mg) in pyridine (1 mL) was added, the resultant reaction mixture was stirred for 8 min and diluted with 10 mL of ether. The solids were removed by suction filtration, and the filtrate was evaporated to give an oil, which was treated with a mixture of 10 mg of KI and 1.0 mL of acetic acid at room temperature for 30 min. After removal of acetic acid in vacuo, GC analysis indicated an 89% yield of jatrophone (**1**), which was further purified by TLC (CH_2Cl_2:ether = 10:1) to give 1.1 mg of compound **1**: $[\alpha]_D$ = 289° [c = 0.0706 (EtOH)]; lit.[1] $[\alpha]_D$ = +292° (EtOH); ^{1}H NMR δ 6.42 (d, J = 16.2 Hz, 1 H), 5.97 (d, J = 16.2 Hz, 1 H), 5.80–5.78 (m, 1 H), 5.77 (q, J = 1.7 Hz, 1 H), 2.96–2.92 (m, 1 H), 2.84 (d, J = 14.8 Hz, 1 H), 2.38 (d, J = 14.8 Hz, 1 H), 2.12 (dd, J = 13.6, 5.9 Hz, 1 H), 1.85 (d, J = 1.6 Hz, 3 H), 1.84 (dd, J = 13.6, 5.5 Hz, 1 H), 1.72 (d, J = 0.6 Hz, 3 H), 1.33 (s, 3 H), 1.21 (s, 3 H), 1.06 (d, J = 7.1 Hz, 3 H); ^{13}C NMR δ 203.86, 201.94, 183.19, 158.95, 147.09, 141.77, 137.12, 128.72, 123.74, 112.40, 99.77, 42.45, 41.24, 38.33, 36.62, 30.39, 26.90, 20.70, 18.95, 6.08; EIMS m/z (rel intensity) 312 (M^+, 3), 297 (1), 284 (3), 269 (3), 259 (6), 242 (6), 227 (8), 213 (9), 199 (7), 189 (37), 173 (35); HRMS calcd for $C_{20}H_{24}O_3$ 312.1725, found 312.1732.

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Registry No. 1, 29444-03-9; **2**, 89-82-7; **3**, 4463-74-5; **3** acid, 623-82-5; **6**, 142843-46-7; **8** (isomer 1), 142843-47-8; **8** (isomer 2), 142926-23-6; **9** (isomer 1), 142843-48-9; **9** (isomer 2), 142926-24-7; **10**, 67099-40-5; **10** acid chloride, 142843-49-0; **11** (isomer 1), 142843-50-3; **11** (isomer 2), 142926-25-8; **12**, 142843-51-4; **13**, 142843-52-5; **14**, 142843-53-6; **15**, 142843-54-7; **16**, 28976-76-3; (*E*)-**16**, 28976-77-4; **17**, 76252-02-3; (*E*)-**17**, 76232-48-9; **17** aldehyde, 84695-31-8; (*E*)-**17** aldehyde, 142843-55-8; (*E*)-**18**, 142843-57-0; (*Z*)-**18**, 142843-56-9; (*E*)-**18** dimethyl acetal, 142843-59-2; (*Z*)-**18** dimethyl acetal, 142843-58-1; **19**, 142843-60-5; **22**, 110046-90-7; **23**, 142843-61-6; **24**, 142843-62-7; **25**, 142843-63-8; **25** TBDMS ether, 142843-64-9; **26**, 142926-26-9; **27**, 142843-65-0; **28**, 142843-66-1; $CH_2{=}C(CH_3)CN$, 126-98-7; $BrCH_2C{-}Br(CH_3)CN$, 142843-67-2.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **11**, **15**, **18**, **19**, and **24–27** (16 pages). Ordering information is given on any current masthead page.