were made by using tobacco mosaic virus (diameter = 180 Å), as a reference.

Arborol **3h** (20 mg) was dissolved in deionized water (1 mL) at 80 °C, allowed to gel at 25 °C, and then lyophilized for 24 h. A portion of the dried gel was transferred into a drop of water on a microscope slide. The reconstituted gel was viewed on a Leitz Ortholux II microscope equipped with polarized light optics. A λ-plate and λ/4-plate were inserted in the light path for color contrast; photographs were taken on Ektachrome film (Kodak) and are reproduced in black and white.

Viscometry. The solution was transfered into a Wells-Brookfield cone and plate, steady shear viscometer (Model LVDCP). Shear rates were adjusted from 450 to 2.25 Hz.

Gel-Solution Phase Transition. Aqueous solutions of **3h** (2.12, 4.34, 6.22, and 8.15 wt %) were prepared with use of water from a three-stage Millipore R/Q water purifier. The gels were heated above the phase transition (ca. 80 °C) filtered through Durapore 0.22-μm filters into precleaned fluorimeter cells. Portions of these samples were used for polarized light microscopy. Gel melting points were determined by the disappearance of birefringence between crossed polars on an Olympus BH-2 microscope using a Mettler FP800 thermally controlled stage, increasing the temperature 2 °C/min. The phase-transition temperatures were also observed by light scattering experiments performed at a scattering angle of 90°. The instrument consisted of a Hughes helium-neon laser, Pacific Precision Instruments Model 126 photon counting system, and Hamamatsu R928P photomultiplier. Temperature regulation was accomplished either by a Lauda RCS-6 bath or an Omega CN-2010 electrical temperature controller using a temperature ramp of 2 °C/min. Phase-transition temperatures were taken as a decrease of the scattered intensity to 10% of its initial value.

pH Stability of Gels. The pH of the solutions was measured with a Corning Model 7 pH meter with a combination electrode. The arborol (20 mg) was added to the solution (0.40 mL) and the mixture warmed until a homogeneous solution was obtained (ca. 80–90 °C). After solution was cooled to 25 °C, the occurrence of gel formation was noted. For data, see Table II.

Molecular Modeling. Calculations were performed on a Silicon Graphics IRIS 4D/50GT superworkstation with use of Polygen's QUANTA/CHARMm software.[6] Preliminary structures were input via CHEMNOTE and minimized by using initially the conjugate gradient and then the adopted-basis Newton-Raphson methods until the RMS deviation was <0.001 kcal/Å. Molecular dynamics were performed with 2000 steps (2.0 ps) of heating to 298 °C, 3000 steps (3.0 ps) of equilibration, and 20000 steps (20.0 ps) of stimulation. The lowest energy structures from molecular dynamics were minimized via adopted-basis Newton-Raphson until the RMS deviation was <0.001 kcal/Å.

Acknowledgment. We thank the National Science Foundation (G.R.N., Grant Nos. DMR 86-00929, 89-06792; M.J.S., Grant No. DCB 88-02011; P.S.R., Grant No. DMR 85-20027), the donors of the Petroleum Research Foundation, administered by the American Chemical Society, and the Florida High Technology and Industry Council, for partial support of this research.

Supplementary Material Available: The experimental procedures for 1,13-tridecanediol, 1,13-dibromotridecane, dimethyl pimelate, dimethyl dodecanedioate, and *N*-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide (**12**), spectral and analytical data for hexaesters **2**, [9]-*n*-[9] arborols **3**, tetraesters **4**, and [6]-*n*-[6] arborols **5**, and ^{13}C NMR data for the acetate derivatives (18 pages). Ordering information is given on any current masthead page.

Total Synthesis of (±)-*epi*-Jatrophone and (±)-Jatrophone Using Palladium-Catalyzed Carbonylative Coupling of Vinyl Triflates with Vinylstannanes as the Macrocycle-Forming Step

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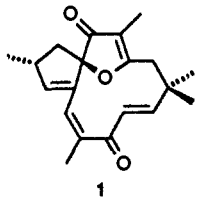
Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523. *Received April 19, 1990*

Abstract: Jatrophone is a macrocyclic diterpene which exhibits significant inhibitory activity in vivo and in vitro against various carcinomas. The synthesis of (±)-jatrophone and its epimer was completed with use of a palladium-catalyzed carbonylative coupling of a vinylic triflate with an organostannane as the key step. The synthesis of *epi*-jatrophone was first completed to establish the chemistry for jatrophone. The overall sequence for each synthesis required 16 steps starting from 4-methyl-2-cyclopenten-1-one. The overall yields were 0.83% and 0.28%, respectively.

Introduction

Jatrophone (**1**) is a macrocyclic diterpene first isolated from extracts of *Jatropha gossypiifolia* in 1970.[1] The structure of jatrophone was determined by NMR and X-ray studies.[2] This



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diterpene exhibits significant inhibitory activity in vivo against various carcinomas.[1,3] Jatrophone was first synthesized in 1981 by Amos B. Smith III and co-workers,[4] and this to date has been the only total synthesis reported. The key step in this synthesis of jatrophone involved a Mukaiyama titanium tetrachloride mediated cyclization of an acetal with a silyl enol ether.

As part of an ongoing study of palladium-catalyzed carbon-carbon bond-forming processes, an efficient carbonylative coupling

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† Deceased.

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(2) Kupchan, S. M.; Sigel, C. W.; Matz, M. J.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1976**, *98*, 2295.
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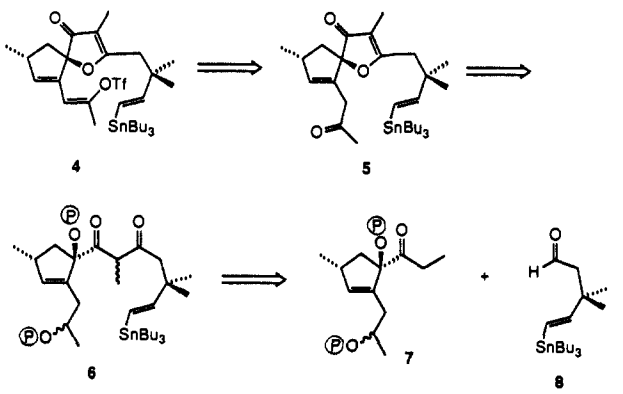
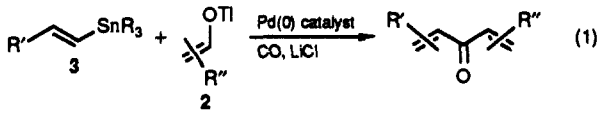
Scheme I

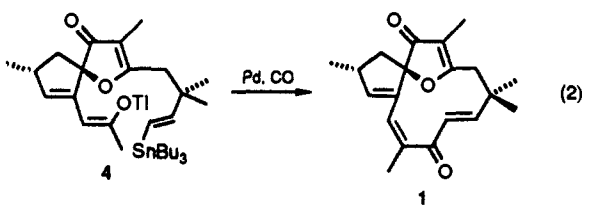


of vinylic triflates **2** with organostannanes **3** was recently developed in these laboratories[5] (eq 1). The reaction takes place under mild



(1)

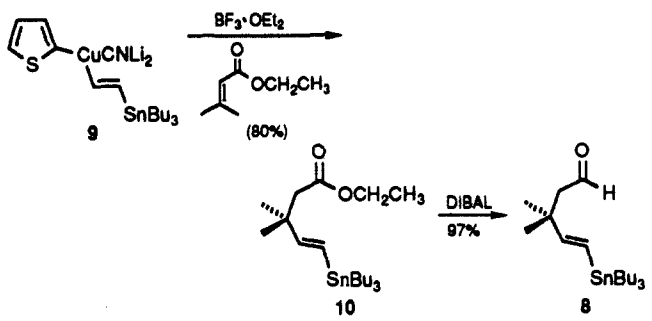
conditions and tolerates a variety of functional groups on both coupling partners. The use of this carbonylative coupling for forming the macrocyclic dienone portion of (±)-jatrophone is the subject of this paper (eq 2).



(2)

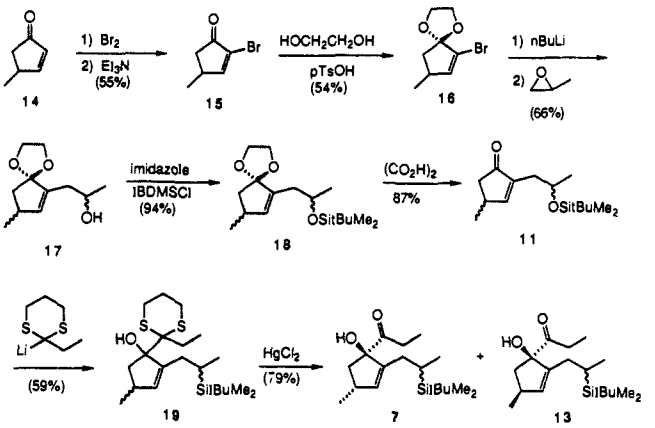
Results and Discussion

A retrosynthetic analysis of the requisite precursor **4** is shown in Scheme I. The vinylic triflate **4** may be obtained with use of established methods for generating enol triflates from ketones.[6] Compound **5** might be accessible by an acid-catalyzed cyclization–dehydration[4] of the corresponding diketone **6**. Compound **6** in turn may be obtained by an aldol condensation of **7** with the aldehyde bearing the vinyltin **8**, where **7** contains the two stereocenters required for the jatrophone molecule. Compound **8** was synthesized in the following manner: The conjugate addition of

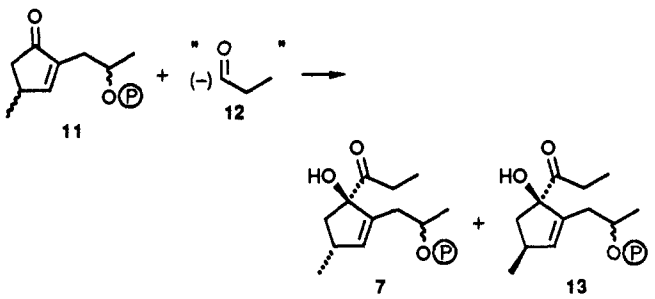


the thiophene-derived cuprate[7] **9** to ethyl 3,3-dimethylacrylate in the presence of boron trifluoride etherate (BF_3·OEt_2) afforded the ester **10**. Reduction of **10** with diisobutylaluminum hydride (DIBAL) gave the desired aldehyde **8** in an overall 78% yield. The proposed approach to compound **7** involved reaction of **11**

Scheme II

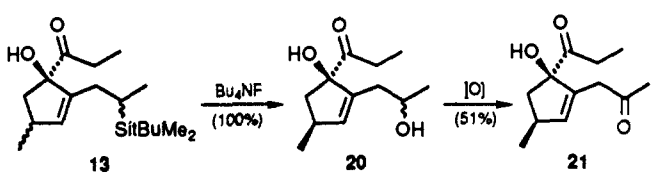


with acyl anion equivalent **12** to afford the desired ketone **7** and its isomer **13**. Compound **11** was synthesized by the bromination



of 4-methyl-2-cyclopenten-1-one[8] (**14**), followed by dehydrobromination to afford **15**.[9] Ketalization of **15** provided the α-bromo ketal **16**. Halogen–metal exchange of the bromide with *n*-butyllithium, followed by the addition of propylene oxide, gave alcohol **17** as a mixture of diastereoisomers.[10] Protection of alcohol **17** as the *tert*-butyldimethylsilyl ether **18**, followed by deprotection of the ketal, afforded the α,β-unsaturated ketone **11** in an overall 16% yield for the sequence.

Addition of 2-lithio-2-ethyl-1,3-dithiane[11] provided alcohol **19** as a complex mixture of diastereoisomers. Removal of the dithiane functionality afforded the target molecule **7** and its isomer **13** in a 1:9 ratio. The overall yield for the two steps was 47% (Scheme II). The fact that **7** and **13** were diastereomeric at the methyl group was confirmed by treating the major isomer with tetrabutylammonium fluoride to afford diol **20** and subsequent oxidation of the secondary alcohol with use of Corey's procedure.[12] Spectral data of **21** were consistent with the formation of a single diastereomer.



The relative stereochemistry of the methyl group on the ring and the propanone appendage in compounds **7** and **13** was established on the basis of Smith's results,[4] where a similar intermediate was encountered. The preferred mode of addition of 2-lithio-2-ethyl-1,3-dithiane to **11** should occur on the face of the ketone opposite that of the methyl group. Thus, compound **13**

(5) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. Crisp, G. T.; Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 7500.
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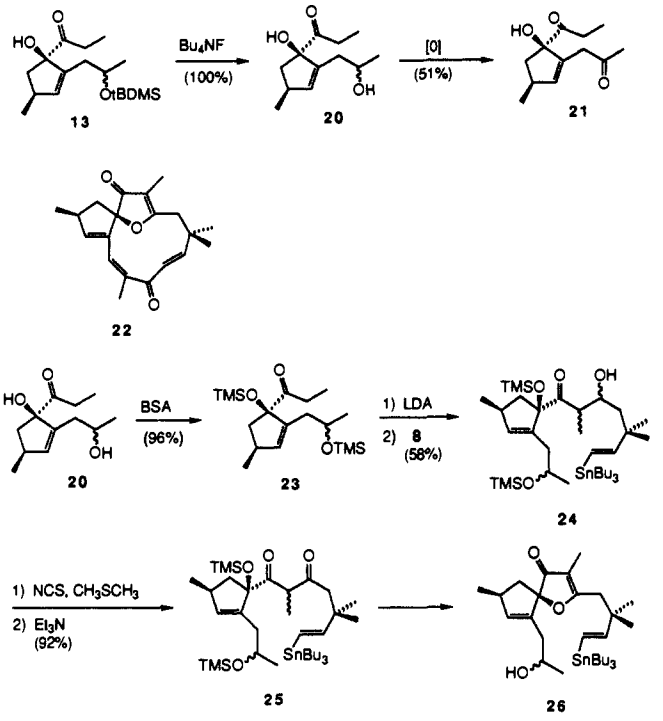
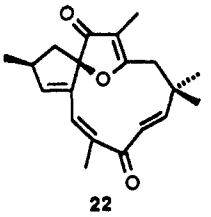
(11) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1975**, *40*, 231.
(12) Corey, E. J.; Kim, C. U. *Tetrahedron Lett.* **1974**, *3*, 287.

Scheme III

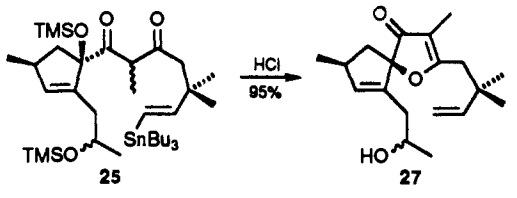


was most likely the major isomer. To establish the methodology for jatrophone itself, compound **13** was carried through the synthesis to generate *epi*-jatrophone (**22**).



Reaction of **20** with bis(trimethylsilyl)acetamide afforded the bis-protected diol **23**. Condensation of **23** with **8** afforded the alcohol **24** as a complex mixture of diastereoisomers. Oxidation of **24** afforded the diketone **25**. The overall yield for the three steps was 51% (Scheme III).

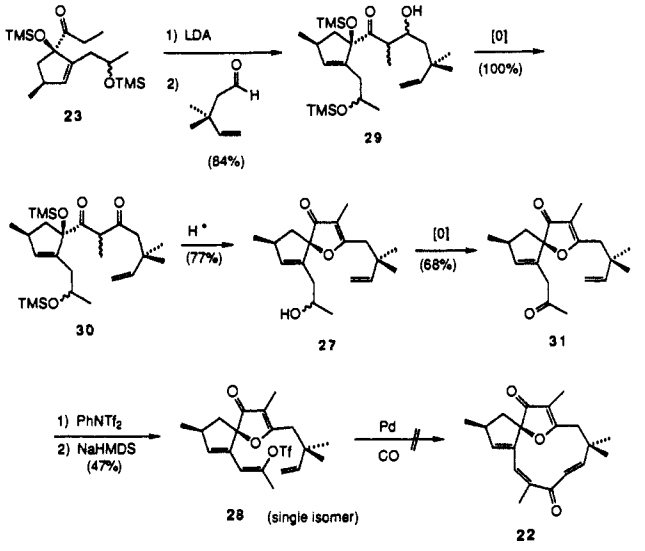
With **25** in hand, the next operation required formation of the 3(2*H*)-spirofuranone compound **26**. Treatment of **25** with a catalytic amount of hydrochloric acid[4] afforded a spirofuranone compound; however, a protiodestannylation had also taken place



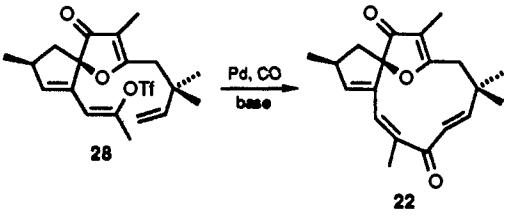
to afford not **26**, but instead compound **27** as the sole product. Because, at this stage, all attempts to form the spirofuranone resulted in loss of the vinylic tin moiety, an alternative approach to the key cyclization step was examined.

Vinylic triflates undergo palladium-catalyzed coupling with unactivated olefins in a Heck-type reaction,[13] and vinylic halides and aryl halides undergo coupling reaction with olefins in the presence of carbon monoxide to yield α,β-unsaturated ketones.[14] There were, however, no reports in the literature of the intramolecular carbonylative coupling of vinyl triflates with olefins.

Scheme IV

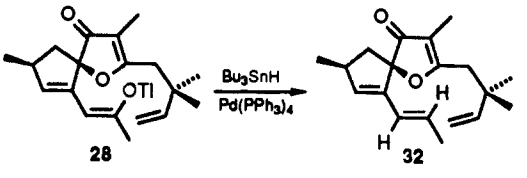


In view of this, the carbonylative coupling reaction of vinylic triflate **28** was examined as an alternative method for generating the macrocycle (eq 3).



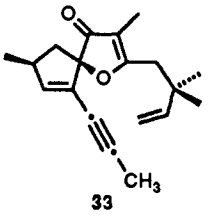
(3)

The synthesis of intermediates **28** is shown in Scheme IV. The stereochemistry of the enol triflate **28** was established by the palladium-catalyzed reduction of **28** to the olefin **32**[15] (eq 4).



(4)

Unfortunately, reaction of **28** with a number of palladium catalysts, under a variety of conditions, did not afford the desired cyclized product. Instead, compound **33** was the sole product observed.



Because the Heck-type coupling reaction was not successful, it was imperative that the spirofuranone compound **26** be generated without protiodestannylation taking place. This required the cyclization of **25** to be conducted under aprotic conditions. Such a requirement was fulfilled with an anhydrous fluoride ion source, tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TASF).[16] The desired furanone compound **26** was obtained in good yield. Subsequent oxidation of **26** afforded **34**, which was converted to the *Z*-vinylic triflate **35**. The overall yield for the three steps was

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(14) Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6761. Negishi, E.; O'Connor, B.; Zhang, Y. *J. Org. Chem.* **1988**, *53*, 5588.
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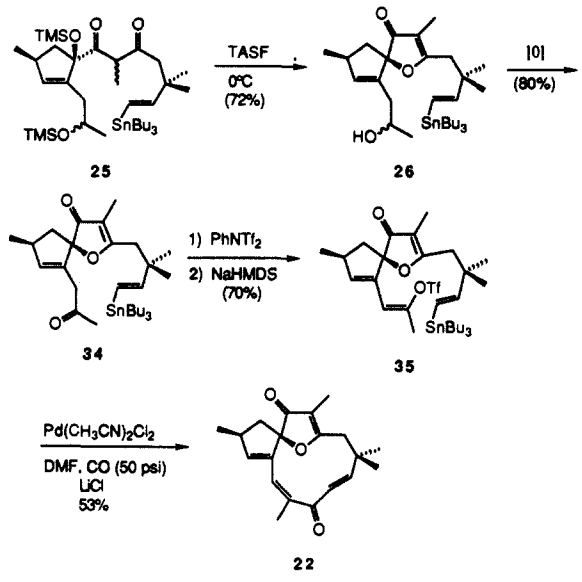
Scheme V



40%. Reaction of **35** with bis(acetonitrile)palladium(II) chloride and 3 equiv of lithium chloride in dimethylformamide at room temperature under 50 psi of carbon monoxide afforded *epi*-jatrophone (**22**) as a white crystalline solid in good yield (Scheme V). The physical data (^{1}H NMR, ^{13}C NMR, infrared, and high-resolution mass spectra) for compound **22** were identical in all respects to that reported for synthetic *epi*-jatrophone.[4] (±)-Jatrophone (**1**) itself was synthesized in a similar manner from the diastereoisomer **7** (Scheme VI).

In conclusion, the total syntheses of (±)-*epi*-jatrophone and (±)-jatrophone were completed with use of the palladium-catalyzed carbonylative coupling reaction as the key macrocycle-forming step. The overall yields were 0.83% and 0.28%, respectively. This approach compares favorably with previously reported syntheses of these compounds and illustrates the utility of this methodology in the total synthesis of highly functionalized molecules.

Experimental Section

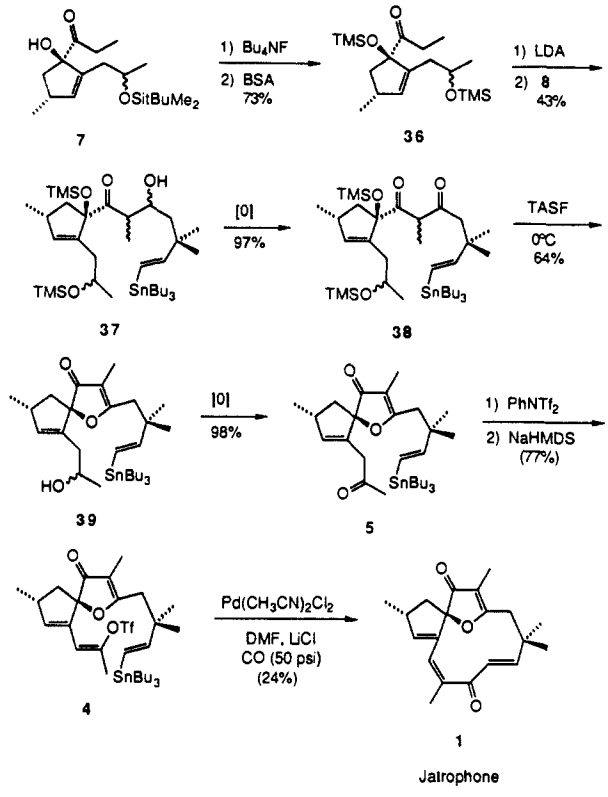
All reagents were used as obtained from commercial suppliers unless otherwise noted. Tetrahydrofuran (THF) was freshly distilled from potassium prior to use. Dimethylformamide and dichloromethane were distilled from calcium hydride. The following compounds were prepared according to literature procedures: tetrakis(triphenylphosphine)palladium(0),[17] bis(acetonitrile)palladium(II) chloride,[17] (*E*)-1,2-bis(tributylstannyl)ethylene,[18] *N*-phenyltriflimide,[19] 4-methyl-2-cyclopenten-1-one,[8] and 2-ethyl-1,3-dithiane.[11]

Column chromatography was performed on Absorbenzien Woelm (Universal Scientific) 62-200 silica gel.

^{1}H NMR and ^{13}C NMR spectra were obtained on either an IBM WP-270 (270 MHz, ^{1}H; 68 MHz, ^{13}C) or a Bruker AC300P (300 MHz, ^{1}H; 75 MHz, ^{13}C). The ^{13}C NMR spectra were obtained with deuteriochloroform (77.00 ppm) as the internal standard. The ^{1}H NMR spectra were obtained with tetramethylsilane (0.00 ppm) and/or deuteriochloroform (7.24 ppm) as the internal standard. Infrared spectra were recorded with a Beckman Model 4240 grating spectrophotometer or a Perkin-Elmer 1600 Series FTIR spectrophotometer. Low-resolution mass spectra (LRMS) were obtained on a VG Micromass 16F spectrometer. High-resolution mass spectra (HRMS) were performed by the Midwest Center for Mass Spectrometry, Lincoln, NE. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA.

Ethyl 3,3-Dimethyl-5-(tributylstannyl)-4-pentenoate (10). To a solution containing 1.04 g (1.72 mmol) of (*E*)-1,2-bis(tri-*n*-butylstannyl)-ethylene in 1.5 mL of THF under argon at −78 °C was added 1.15 mL (1.88 mmol) of a 1.63 M *n*-butyllithium solution in hexanes. The temperature was gradually increased to 0 °C over 4 h, maintained at 0 °C for 2 h, and then returned to −78 °C.

Scheme VI



In a second flask was added 0.14 mL (1.75 mmol) of thiophene (distilled from KOH) in 1.5 mL of THF at −78 °C under argon, followed by the addition of 1.15 mL (1.88 mmol) of a 1.63 M *n*-butyllithium solution in hexanes. After the solution was stirred at −78 °C for 30 min, the temperature was increased to 0 °C for 30 min and then returned to −78 °C. The pale yellow solution was then transferred via cannula to a third flask containing 0.15 g (1.67 mmol) of cuprous cyanide in 1.5 mL of ether at −78 °C under argon. The temperature was increased to 0 °C until a two-phase clear solution was formed. The flask was recooled to −78 °C, followed by the addition of the anion generated from (*E*)-1,2-bis(tributylstannyl)ethylene via cannula. The temperature was again increased to 0 °C for 15 min and then recooled to −78 °C. Boron trifluoride etherate (0.18 mL, 1.46 mmol) was then added, followed by the addition of 0.21 mL (1.51 mmol) of ethyl 3,3-dimethylacrylate. The mixture was slowly warmed to 0 °C over 3 h and maintained for 2 h. The reaction was quenched with a saturated ammonium chloride solution and extracted with ether. The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. Column chromatography of the residual brown oil on silica gel, first with hexanes as eluent to remove the tetrabutyltin generated in the reaction and then with 5% ethyl acetate/hexanes, afforded 0.54 g (80.3%) of product as a light yellow oil: IR (neat) ν 3000–2800, 1736, 1592, 1461, 1364, 1234, 1034 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.81–0.89 (m, 15 H ($CH_3CH_2)_3$), 1.10 (s, 6 H, $(CH_3)_2C$), 1.19–1.24 (t, 3 H, J = 7.1 Hz, OCH_2CH_3), 1.25–1.34 (m, 6 H, $(CH_2)_3$), 1.41–1.52 (m, 6 H, $(CH_2)_3$, 2.26 (s, 2 H, CH_2CO_2Et), 4.03–4.10 (q, 2 H, J = 7.1, 14.3 Hz, OCH_2CH_3), 5.79–5.94 (ABq, 2 H, J_{AB} = 19.3 Hz, CH=CH); ^{13}C NMR ($CDCl_3$) δ 9.42, 13.66, 14.31, 26.92, 27.20, 29.04, 38.29, 46.75, 59.86 (CH_2, CH_3), 122.21 (C=C), 156.73 (C=C), 171.92 (C=O). Anal. Calcd for $C_{21}H_{42}O_2Sn$: C, 56.65; H, 9.51. Found: C, 56.74; H, 9.56.

3,3-Dimethyl-5-(tributylstannyl)-4-pentenal (8). To a solution containing 0.22 g (0.49 mmol) of the tin ester **10** in 5 mL of CH_2Cl_2 under argon at −78 °C was added 0.65 mL (0.65 mmol) of a 1.0 M diisobutylaluminum hydride solution in hexanes slowly down the side of the flask. Stirring was continued for 1 h and the reaction quenched with MeOH. The mixture was warmed to room temperature and maintained for 20 min.

The solution was diluted with CH_2Cl_2 and passed through a plug of Celite. The filtrate was washed with water and the organic layer dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 25% ethyl acetate/hexanes gave 0.19 g (96.7 %) of product as clear colorless oil: IR (neat) ν 3000–2800, 2729, 1724, 1593, 1463, 1378, 996 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.83–0.89 (m, 15 H, $(CH_2CH_3)_3$), 1.11 (s, 6 H, $(CH_3)_2C$), 1.22–1.33 (m, 6 H, $(CH_2)_3$),

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1.41–1.52 (m, 6 H, $(CH_2)_3$), 2.30–2.31 (d, 2 H, J = 3.2 Hz, CH_2COH), 5.86–6.03 (AB q, 2 H, J_{AB} = 19.4 Hz, $CH{=}CH$), 9.66–9.68 (t, 1 H, J = 2.4 Hz, COH); ^{13}C NMR ($CDCl_3$) δ 9.47, 13.66, 27.17, 27.42, 29.04, 38.13, 54.54, (CH_2, CH_3), 124.04 (C=C), 155.90 (C=C), 203.57 (C=O). Anal. Calcd for $C_{19}H_{38}OSn$: C, 56.88; H, 9.55. Found: C, 57.10; H, 9.48.

(±)-2-Bromo-4-methyl-2-cyclopenten-1-one (15). To a 1-L three-neck flask equipped with two addition funnels and a mechanical stirrer were added 13.70 g (142.51 mmol) of (±)-4-methyl-2-cyclopenten-1-one (**8**) and 100 mL of carbon tetrachloride under argon. The solution was cooled to 0 °C, followed by the addition of 8.10 mL (157.22 mmol) of bromine in 100 mL of carbon tetrachloride over 1 h. Upon complete addition, 29.80 mL (213.80 mmol) of triethylamine in 100 mL of carbon tetrachloride was added over 1 h. The cooling bath was then removed and the reaction allowed to warm to room temperature over 2 h. The brown suspension was then filtered and the filter cake washed thoroughly with carbon tetrachloride. The filtrate was then washed successively with water (2×), saturated sodium bicarbonate solution (1×), and water (2×). The organic layer was dried over sodium sulfate. Removal of solvent and vacuum distillation of the residue gave 13.74 g (55.1%) of product as a white solid: bp 54–56 °C (0.01 mmHg); IR (neat) ν 3000–2800, 1719 (CO), 1586 (C=C), 1453, 1403, 1278, 1161, 923 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (d, 3 H, J = 7.2 Hz, CH_3CH), 2.07 (dd, 1 H, J = 1.9, 19.0 Hz, CH_2), 2.73 (dd, 1 H, J = 6.3, 19.0 Hz, CH_2), 2.85–3.00 (m, 1 H, $CHCH_3$), 7.64 (d, 1 H, J = 2.8 Hz, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ 19.89, 35.16, 41.06, (CH, CH_2, CH_3), 125.33 (C=C), 166.64 (C=C), 201.37 (C=O). Anal. Calcd for C_6H_7BrO: C, 41.17; H, 4.03; Br, 45.66. Found: C, 41.21; H, 4.05; Br, 45.74.

(±)-6-Bromo-8-methyl-1,4-dioxaspiro[4.4]non-6-ene (16). To a solution containing 3.66 g (20.91 mmol) of **15** in 160 mL of benzene were added 2.90 mL (52.00 mmol) of ethylene glycol and 16 mg (0.08 mmol) of *p*-toluenesulfonic acid. The flask was equipped with a Dean–Stark trap, and the mixture was heated to reflux with azeotropic removal of water over 62 h. The flask was cooled, and the contents were transferred to a separatory funnel. The mixture was washed with water and the organic layer dried over sodium sulfate. The solvent was removed under reduced pressure and the residue passed through a plug of silica gel with 25% ethyl acetate/hexanes to give 2.50 g (54.6%) of product as a colorless liquid: IR (neat) ν 3000–2800, 1618 (C=C), 1454, 1329, 1304, 1208, 1031, 971 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, 3 H, J = 7.0 Hz, CH_3CH), 1.69 (dd, 1 H, J = 4.5, 13.8 Hz, CH_2), 2.36 (dd, 1 H, J = 7.6, 13.8 Hz, CH_2), 2.65–2.85 (m, 1 H, $CHCH_3$), 3.92–3.99 (m, 2 H, CH_2CH_2), 4.13–4.18 (m, 2 H, CH_2CH_2), 6.06 (d, 1 H, J = 2.4 Hz, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ 20.55, 36.11, 43.16, 65.68, 65.99, (CH, CH_2, CH_3), 117.40 (O–C–O), 123.40 (C=C), 142.19 (C=C).

6-(2-Hydroxypropyl)-8-methyl-1,4-dioxaspiro[4.4]non-6-ene (17). To a solution containing 72.00 mL (115.20 mmol) of a 1.60 M *n*-butyllithium solution in hexanes in 350 mL of THF under argon at −78 °C was added 20.74 g (94.67 mmol) of the ketal **16** in 150 mL of THF dropwise over 20 min. The solution was stirred at −78 °C for an additional 1.5 h, followed by the addition of 110.00 mL (1.57 mol) of propylene oxide in 150 mL of THF over 20 min. The mixture was allowed to warm to room temperature over 16 h, then quenched with a saturated ammonium chloride solution, and extracted with ether. The aqueous phase was thoroughly extracted with ether. The combined organic layers were dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 50% ethyl acetate/hexanes gave 12.36 g (65.8%) of product as an inseparable mixture of diastereomers: IR (neat) ν 3672–3089 (b, OH), 3000–2800, 1455, 1430, 1372, 1344, 1211, 1144, 1078, 959 cm^{-1}; ^1H NMR ($CDCl_3$) δ [1.00 (d, J = 7.03 Hz), 1.02 (d, J = 7.03 Hz), 3 H, CH_3CH], 1.14 (d, 3 H, J = 6.2 Hz, CH_3CH), [1.48 (dd, J = 3.2, 4.8 Hz), 1.52 (dd, J = 3.3, 4.8 Hz), 1 H, CH_2], 2.03–2.13 (m, 1 H, CH_2), 2.23 (dd, 1 H, J = 7.5, 13.6 Hz, CH_2), 2.24–2.33 (m, 1 H, CH_2), 2.55–2.73 (m, 1 H, $CHCH_3$), [3.23 (d, J = 2.8 Hz), 3.27 (d, J = 2.8 Hz), 1 H, OH], 3.84–3.99 (m, 5 H, OCH_2CH_2O, $CHOH$), 5.77 (bs, 1 H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ 20.89, 21.00, 22.91, 35.17, 35.25, 36.00, 36.22, 44.06, 44.13, 64.53, 64.61, 64.97, 67.02, 67.34, (CH, CH_2, CH_3), 119.51 (OCO), 138.56 (C=C), 138.64 (C=C), 141.65 (C=C), 141.75 (C=C). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.76; H, 9.23.

6-[2-[(*tert*-Butyldimethylsilyl)oxy]propyl]-8-methyl-1,4-dioxaspiro-[4.4]non-6-ene (18). To a solution containing 7.16 g (36.12 mmol) of alcohol **17** in 280 mL of DMF were added 3.69 g (54.20 mmol) of imidazole and 7.08 g (46.97 mmol) of *tert*-butyldimethylchlorosilane. The mixture was stirred at room temperature for 23 h and then quenched with water and extracted with ether. The organic layer was dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 25% ethyl acetate/hexanes gave 10.64 g (94.3%) of product as a mixture of diastereomers: IR (neat) ν 3000–2800, 1634 (C=C), 1471, 1460, 1376, 1357, 1254, 1210, 1129, 1090, 1001, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ −0.07 to +0.07 (m, 6 H, $(CH_3)_2Si$), 0.83–0.89 (m, 9 H, $(CH_3)_3CSi$), 1.01 (d, 3 H, J = 7.0 Hz, CH_3CH), [1.11 (d, J = 6.0 Hz), 1.12 (d, J = 6.0 Hz), 3 H, CH_3CH], 1.47 (dd, 1 H, J = 5.0, 13.6 Hz, CH_2), 2.00–2.09 (m, 1 H, CH_2), 2.21 (dd, 1 H, J = 7.5, 13.6 Hz, CH_2), 2.21–2.26 (m, 1 H, CH_2), 2.55–2.70 (m, 1 H, $CHCH_3$), 3.84–4.01 (m, 5 H, OCH_2CH_2O, $CHOH$), 5.65 (m, 1 H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ [−4.65, −4.60, −4.54, −4.51, (CH_3Si)], 18.14 $(CH_3)_3$-CSi, 20.97, 21.13, 23.49, 23.56, 25.65, 25.81, 25.93, 35.28, 36.40, 44.30, 64.64, 64.80, 65.08, 65.19, 67.71, 67.76, (CH, CH_2, CH_3), 120.12 (OCO), 138.90 (C=C), 138.95 (C=C), 139.37 (C=C), 139.47 (C=C). Anal. Calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.39; H, 10.35.

2-[2-[(*tert*-Butyldimethylsilyl)oxy]propyl]-4-methyl-2-cyclopenten-1-one (11). To a solution containing 10.64 g (34.05 mmol) of ketal **18** in 420 mL of methylene chloride were added 3.65 g (28.95 mmol) of oxalic acid dihydrate and 25 mL of water. The mixture was stirred at room temperature for 18 h, then diluted with water, and extracted with methylene chloride. The organic layer was dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 25% ethyl acetate/hexanes gave 7.94 g (86.9%) of product as a mixture of diastereomers: IR (neat) ν 3000–2800, 1706 (CO), 1635 (C=C), 1472, 1463, 1410, 1377, 1253, 1129, 1082, 1000, 836 cm^{-1}; ^1H NMR ($CDCl_3$) δ [−0.04 (s), −0.01 (s), 0.02 (s), 0.03 (s), 6 H, $(CH_3)_2Si$], [0.85 (s), 0.86 (s), 9 H, $(CH_3)_3CSi$], 1.10 (d, 3 H, J = 6.0 Hz, CH_3CH), [1.15 (d, J = 7.2 Hz), 1.16 (d, J = 7.2 Hz), 3 H, CH_3CH], 1.90 (dd, 1 H, J = 2.2, 18.6 Hz, CH_2), 2.23–2.27 (m, 2 H, CH_2), [2.53 (dd, J = 2.3, 6.3 Hz), 2.59 (dd, J = 2.3, 6.4 Hz), 1 H, CH_2], 2.80–2.92 (m, 1 H, CH_3CH), 3.97 (hex, 1 H, J = 6.1 Hz, $CHOH$), 7.26 (m, 1 H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ −4.85, −4.71, −4.57, −4.49, (CH_3Si), 17.98, 18.01, $((CH_3)_3C$-Si), 20.08, 20.28, 23.82, 25.77, 25.84, 33.45, 34.91, 34.95, 43.10, 43.15, 66.52, 66.73, (CH, CH_2, CH_3), 142.09 (C=C), 142.25 (C=C), 165.19 (C=C), 165.51 (C=C), 209.55 (C=O), 209.59 (C=O). Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 66.97; H, 10.47.

1-(2-Ethyl-1,3-dithianyl)-2-[2-[(*tert*-butyldimethylsilyl)oxy]propyl]-4-methyl-2-cyclopenten-1-ol (19). To a solution containing 5.80 g (39.11 mmol) of 2-ethyl-1,3-dithiane[11] in 250 mL of THF under argon at −40 °C was added 25.10 mL (37.15 mmol) of a 1.48 M *n*-butyllithium solution in hexanes. After the solution was stirred for 6 h at −40 °C, 7.00 g (26.07 mmol) of the α,β-unsaturated ketone **11** in 150 mL of THF was added dropwise over 1 h. The mixture was stirred at −40 °C for 5 h and then allowed to warm to room temperature over 6 h. The mixture was quenched with water and extracted with ether. The organic layer was dried over Na_2SO_4. The solvent was removed under reduced pressure and the excess 2-ethyl-1,3-dithiane removed via Kugelrohr distillation. The remaining yellow oil was purified by column chromatography on silica gel with 10% ethyl acetate/hexanes to give 6.43 g (59.2%) of product as a complex mixture of diastereomers: IR (neat) ν 3656–3233 (b, OH), 3000–2800, 1456, 1372, 1250, 1128, 1078, 994 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.04–0.09 (m, 6 H, $CH_3)_2Si$), 0.82–0.90 (m, 9 H, $(CH_3)_3CSi$), 0.95–1.05 (m, 3 H, CH_3CH), 1.05–1.18 (m, 6 H, CH_3CH, CH_3CH_2), 1.40–1.50 (m, 1 H, CH_2), 1.70–1.93 (m, 4 H, CH_2), 2.00–2.60 (mm, 2 H, CH_2), 2.63–3.25 (m, 6 H, CH, CH_2), [3.67 (s), 4.34 (s), 1 H, OH], [3.88–3.97 (m), 4.07–4.14 (m), 1 H, CH_3CHO], [5.45 (m), 5.50 (m), 5.57 (m), 1 H, $CH{=}C$]; HRMS for $C_{21}H_{40}O_2S_2Si$, calcd 416.2241, found 416.2234 (M^+), 398.2135 ($M - H_2O$)$^+$.

(1*R*,4*S*)-1-(1-Oxopropyl)-2-[2-[(*tert*-butyldimethylsilyl)oxy]propyl]-4-methyl-2-cyclopenten-1-ol (13). To a solution containing 3.83 g (9.19 mmol) of the dithiane-protected ketone **19** in 112 mL of acetonitrile and 25 mL of water were added 1.84 g (18.38 mmol) of calcium carbonate and 5.00 g (18.42 mmol) of mercuric chloride under argon. The mixture was heated to 50 °C for 8 h. The flask was cooled, and the contents were filtered through a plug of Celite. The solid was washed thoroughly with benzene and the filtrate washed successively with brine and water. The organic layer was dried over Na_2SO_4. Removal of solvent and repeated column chromatography on silica gel of the residue with 10% ethyl acetate/hexanes gave 2.13 g (71.0%) of the 1*R*,4*S* product as a mixture of diastereomers at the silyloxy carbon and 0.24 g (8.00%) of the 1*R*,4*R* product as a mixture of diastereomers at the silyloxy carbon. 1*R*,4*S*: IR (neat) ν 3467 (b, OH), 3000–2800, 1704 (CO), 1472, 1462, 1410, 1377, 1287, 1255, 1084, 1001 cm^{-1}; ^1H NMR ($CDCl_3$) δ [0.02 (s), 0.03 (s), 0.04 (s), 6 H, $(CH_3)_2Si$], [0.85 (s), 0.86 (s), 9 H, $(CH_3)_3CSi$], [1.04 (t, J = 7.3 Hz), 1.06 (t, J = 7.3 Hz), 3 H, CH_3CH_2], 1.10–1.14 (m, 6 H, CH_3CH, CH_3CHO), [1.51 (dd, J = 6.8, 14.1 Hz), 1.55 (dd, J = 6.5, 14.1 Hz), 1 H, CH_2], 1.90–2.01 (m, 2 H, CH_2), 2.35–2.50 (m , 2 H, CH_2), 2.70–2.90 (m, 1 H, $CHCH_3$), 3.97 (hex, 1 H, J = 6.0, Hz, CHO), [4.45 (s), 4.74 (s), 1 H, OH], 5.69 (m, 1 H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ −4.65, −4.60, −4.49, −4.46 (CH_3Si), 7.89, 8.00, 18.12, $((CH_3)_3CSi)$, 21.57, 21.60, 23.19, 23.28, 25.90, 28.41, 28.87, 37.06, 37.39, 38.19, 38.33, 45.23, 67.34, 67.78, 91.69, 92.09, (CH, CH_2, CH_3), 138.21 (C=C), 138.70 (C=C), 140.66 (C=C), 141.22 (C=C), 213.45 (C=O), 214.02

(C=O). Anal. Calcd for $C_{18}H_{34}O_3Si$: C, 66.20; H, 10.50. Found: C, 66.32; H, 10.54.

(1*R*,4*R*)-1-(1-Oxopropyl)-2-[2-[(*tert*-butyldimethylsilyl)oxy]-propyl]-4-methyl-2-cyclopenten-1-ol (7). 1*R*,4*R*: ^{1}H NMR ($CDCl_3$) δ [0.00 (s), 0.02 (s), 0.04 (s), 0.05 (s), 6 H, $(CH_3)_2Si$], [0.84 (s), 0.86 (s), 9 H, $(CH_3)_3CSi$], 1.01–1.07 (m, 3 H, CH_3CH_2), 1.08–1.16 (m, 6 H, CH_3CH, CH_3CHO), [1.69 (dd, J = 5.7, 14.1 Hz), 1.77 (dd, J = 5.7, 14.1 Hz), 1 H, CH_2], 1.85–2.05 (m, 1 H, CH_2), 2.05–2.30 (m, 2 H, CH_2), 2.38–2.70 (m, 2 H, CH_2), [2.73–2.90 (m), 3.00–3.10 (m), 1 H, CH_3CH], 3.94–4.03 (m, 1 H, CHO), [4.32 (s), 4.84 (s), 1 H, OH], 5.65 (m, 1 H, CH=C). Anal. Calcd for $C_{18}H_{34}O_3Si$: C, 66.20; H, 10.50. Found: C, 66.31; H, 10.55.

(1*R*,4*S*)-1-(1-Oxopropyl)-2-(2-hydroxypropyl)-4-methyl-2-cyclopenten-1-ol (20). To a solution containing 0.20 g (0.61 mmol) of **13** in 50 mL of THF under argon was added 1.00 mL (1.00 mmol) of a 1.0 M solution of tetrabutylammonium fluoride in THF at 0 °C. Stirring at 0 °C was continued for 5 min and then increased to room temperature and continued for 20 min. The mixture was diluted with ethyl acetate and quenched with water. The organic phase was separated and dried over Na_2SO_4. Removal of solvent and column chromatography of the residual oil on silica gel with 50% ethyl acetate/hexanes gave 0.13 g (100%) of product: IR (neat) ν 3411 (b, OH), 3000–2800, 1704 (CO), 1457, 1375, 1344, 1148, 1107, 1078, 1054, 938 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ [1.06 (t, J = 7.3 Hz), 1.07 (t, J = 7.3 Hz), 3 H, CH_3CH_2], 1.12–1.16 (m, 6 H, CH_3CH, CH_3CHOH), [1.54 (dd, J = 2.3, 6.4 Hz), 1.58 (dd, J = 2.3, 6.4 Hz), 1 H, CH_2], [1.64–1.73 (m), 2.04–2.13 (m), 1 H, CH_2], [1.93–2.00 (m), 2.19–2.26 (m), 1 H, CH_2], 2.33–2.54 (m, 3 H), [2.66 (bs), 3.31 (bs), 1 H, OH], 2.74–2.87 (m, 1 H, $CHCH_3$), [3.71–3.78 (m), 3.83–3.95 (m), 1 H, $CHOHCH_3$], [4.67 (s), 4.80 (s), 1 H, OH], 5.81 (bs, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 7.85, 21.37, 21.56, 22.72, 23.36, 28.30, 28.35, 36.92, 37.14, 38.02, 38.07, 45.10, 45.18, 65.34, 67.86, 91.26, 91.53 (CH, CH_2, CH_3), 139.64 (C=C), 140.04 (C=C), 140.31 (C=C), 141.60 (C=C, diastereomers), 213.00 (C=O), 213.16 (C=O). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.70; H, 9.60.

1-(1-Oxopropyl)-2-(2-oxopropyl)-4-methyl-2-cyclopenten-1-ol (21). To a solution containing 0.028 g (0.21 mmol) of *N*-chlorosuccinimide in 1 mL of toluene was added, at 0 °C, 0.020 mL (0.27 mmol) of dimethyl sulfide under argon. The mixture was cooled to −25 °C for 15 min. A solution of 0.016 g (0.075 mmol) of **20** in 1.5 mL of toluene was added and stirring continued for 3 h at −25 °C, followed by the addition of 0.03 mL (0.22 mmol) of triethylamine in 1 mL of toluene dropwise. The cooling bath was removed, the reaction warmed to room temperature, and stirring continued for 30 min. The mixture was diluted with ether and washed with water. The organic layer was dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 50% ethyl acetate/hexanes gave 0.0080 g (50.7%) of product: IR (neat) ν 3678–3167 (b, OH), 3000–2800, 1704 (CO), 1650 (C=C), 1616, 1456, 1164, 1108 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (t, 3 H, J = 7.2 Hz, CH_3CH_2), 1.14 (d, 3 H, J = 6.9 Hz, CH_3CH), 1.53 (dd, 1 H, J = 7.3, 14.0 Hz, CH_2), 2.12 (s, 3 H, CH_3C=O), 2.35–2.50 (m, 2 H), 2.61 (dq, 1 H, J = 7.3, 18.2 Hz, CH_2CH_3), 2.82–2.90 (m, 1 H, $CHCH_3$), 2.93–3.08 (m, 2 H, CH_2O), 4.55 (s, 1 H, OH), 5.80 (q, 1 H, J = 1.4 Hz, CH=C); ^{13}C NMR ($CDCl_3$) δ 7.72, 21.22, 28.27, 29.60, 38.02, 41.31, 45.70, (CH, CH_2, CH_3), 90.92 (COH), 137.64 (C=C), 140.20 (C=C), 206.20 (C=O), 212.77 (C=O); LRMS for $C_{12}H_{18}O_3$, calcd 210, found m/z (relative intensity) 210 (M^+, 5), 209 ($M^+ - 1$, 36), 192 ($M^+ - H_2O$, 13), 174 (8), 153 ($M^+ - C_3H_5O$, 25), 149 (14), 138 (61), 135 (25), 121 (18), 110 (16), 95 (100), 93 (46), 67 (60), 57 (46). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.35; H, 8.68.

(±)-(1*R*,4*S*)-1-(1-Oxopropyl)-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)oxy]-2-cyclopentene (23). To a solution containing 0.53 g (2.48 mmol) in 70 mL of DMF under argon was added 6.00 mL (24.27 mmol) of bis(trimethylsilyl)acetamide. The mixture was heated to 65 °C for 23 h, then cooled in an ice bath, and carefully quenched with water. The organic layer was separated and the aqueous layer thoroughly extracted with ether. The combined organic layers were dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 10% ethyl acetate/hexanes gave 0.85 g (96.1%) of product as a mixture of diastereomers: IR (neat) ν 3000–2800, 1720 (CO), 1456, 1377, 1250, 1127, 1086, 1003, 909, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ [0.05 (s), 0.06 (s), 0.09 (s), 0.10 (s), 18 H, $(CH_3)_3Si)_2$], [0.96 (t, J = 7.3 Hz), 0.97 (t, J = 7.3 Hz), 3 H, CH_3CH_2], 1.04–1.10 (m, 6 H, CH_3CH, CH_3CHO), [1.42 (dd, J = 6.8, 13.2 Hz), 1.43 (dd, J = 7.4, 13.2 Hz), 1 H, CH_2], 1.89–2.14 (m, 2 H, CH_2), 2.40–2.56 (m, 3 H, CH_2), 2.70–2.80 (m, 1 H, $CHCH_3$), [3.81 (hex, J = 6.3 Hz), 3.93–4.03 (m), 1 H, CHO], 5.30–5.55 (m, 1 H, CH=C); ^{13}C NMR ($CDCl_3$) δ 0.18, 0.25 $(CH_3)_3Si$, 2.17 $(CH_3)_3Si$, 7.94, 21.29, 21.38, 23.18, 23.71, 30.00, 30.27, 37.10, 37.89, 38.14, 38.18, 46.61, 46.79, 67.10, 67.49, 95.00, 95.13, (CH, CH_2, CH_3), 136.06 (C=C), 136.56 (C=C), 142.15 (C=C), 142.25 (C=C), 212.92 (C=O). Anal. Calcd for $C_{18}H_{36}O_3Si_2$: C, 60.62; H, 10.18. Found: C, 60.73; H, 10.18.

(±)-(1*R*,4*S*)-1-[2-Methyl-3-hydroxy-5,5-dimethyl-7-(tributylstannyl)-1-oxo-6-heptenyl]-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)oxy]-2-cyclopentene (24). To a solution containing 0.22 mL (1.57 mmol) of diisopropylamine in 3 mL of THF under argon at −78 °C was added 1.00 mL (1.48 mmol) of a 1.48 M *n*-butyllithium solution in hexanes. Stirring at −78 °C was continued for 1.5 h, followed by the addition of 0.40 g (1.12 mmol) of ketone **23** in 2 mL of THF dropwise. The mixture was warmed to −10 °C over 3.5 h, followed by the addition of 0.66 g (1.65 mmol) of the tin aldehyde **8** in 2 mL of THF dropwise. The reaction went from colorless to yellow. Stirring was continued for 20 min, followed by the addition of a saturated NH_4Cl solution. Th organic layer was separated and the aqueous layer washed with ether. The combined organic layers were dried over Na_2SO_4. Removal of solvent and column chromatography of the residue on silica gel with 5% ethyl acetate/hexanes gave 0.49 g (57.7%) of product as a complex mixture of nine diastereomers: IR (neat) ν 3529 (b, OH), 3000–2800, 1698 (CO), 1592 (C=C), 1458, 1415, 1376, 1338, 1161, 1124, 1074 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.05–0.15 (m, 18 H, $(CH_3)_3Si$), 0.81–0.90 (m, 15 H, $(CH_3CH_2)_3$), 0.96–1.15 (m, 15 H, CH_3CHO, CH_3CH, $(CH_3)_2C$), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.41–1.51 (m, 7 H, $(CH_2)_3$, CH), 1.80–2.20 (m, 3 H, CH_2), 2.40–2.60 (m, 2 H, CH_2), 2.62–2.80 (m, 2 H, CH_2), 2.80–3.10 (m, 1 H, $CHCH_3$), [3.70–3.82 (m), 3.95–4.05 (m), 2 H, $(CHO)_2$], 5.58–5.61 (m, 1 H, CH=C), 5.90 (mAB_q, 2 H, J_{AB} = 19.5 Hz, CH=CH). Anal. Calcd for $C_{37}H_{74}O_4Si_2Sn$: C, 58.64; H, 9.84. Found: C, 58.53; H, 9.89.

(±)-(1*R*,4*S*)-1-[2-Methyl-5,5-dimethyl-7-(tributylstannyl)-1,3-dioxo-6-heptenyl]-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)-oxy]-2-cyclopentene (25). To a solution containing 0.25 g (.187 mmol) of *N*-chlorosuccinimide in 35 mL of toluene at −25 °C was added 0.18 mL (2.45 mmol) of dimethylsulfide. The mixture was stirred at −25 °C for 30 min, followed by the addition of 0.35 g (0.46 mmol) of alcohol **24** in 18 mL of toluene over 10 min. Stirring was continued for 3 H, followed by the addition of 0.28 mL (2.01 mmol) of triethylamine in 18 mL of toluene dropwise. The cold bath was removed, and the contents were warmed to room temperature and maintained for an additional 30 min. The mixture was diluted with water and extracted with ether. The organic layer was dried over Na_2SO_4. Removal of solvent and column chromatography of the yellow oil on silica gel with 10% ethyl acetate/hexanes gave 0.32 g (92.0%) of product as a mixture of diastereomers. This intermediate was not fully characterized but instead carried on to the next step: IR (neat) ν 3000–2800, 1730 (CO), 1705 (CO), 1592 (C=C), 1456, 1376, 1251, 1127, 1082, 1001 cm^{-1}; ^{1}H NMR (CDC_3) δ 0.06–0.15 (m, 18 H, $(CH_3)_3Si$), 0.81–0.92 (m, 15 H, $(CH_3CH_2)_3$), 1.02–1.20 (m, 15 H, $(CH_3CH)_2$), CH_3CHO, $(CH_3)_2C$), 1.22–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.52 (m, 6 H, $(CH_2)_3$), 1.94–2.18 (m, 3 H, CH_2), 2.30–2.68 (m, 3 H, CH_2), 2.80–2.90 (m, 1 H, $CHCH_3$), [3.70 (m) 3.90 (m), 4.00 (m), 2 H, CHO, $CHCO$)], [5.53 (m), 5.56 (m), 5.60 (m), 1 H, CH=C), 5.89 (AB_q, 2 H, J = 19.4 Hz, CH=CH).

Attempted Formation of the 3(2*H*)-Spirofuranone Alcohol 26 under Protic Conditions (Protiodestannylation Product 27). To a solution containing 0.18 g (0.24 mmol) of the diketone **25** and 8 mL of THF under argon were added a few drops of 2 N hydrochloric acid. The reaction was monitored by thin-layer chromatography until no starting material remained. The mixture was diluted with ether and washed with a saturated sodium chloride solution. The organic layer was dried over Na_2SO_4. Removal of solvent gave a pale yellow oil, which was purified by column chromatography on silica gel with 50% ethyl acetate/hexanes to afford 0.069 g (95.4%) of the spirofuranone with the tin cleaved as a mixture of diastereomers: IR (neat) ν 3442 (b, OH), 3000–2800, 1695 (CO), 1616 (C=C), 1455, 1435, 1403, 1372, 1239, 1192, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08 (d, 3 H, J = 6.2 Hz, CH_3CH), 1.09 (d, 3 H, J = 6.2 Hz, CH_3CH), 1.12 (bs, 6 H, $(CH_3)_2C$), 1.58–1.66 (m, 1 H, CH_2), 1.65 (s, 3 H), CH_3C=C), 1.80–2.03 (m, 3 H, CH_2), 2.37–2.58 (m, 3 H, CH_2), 2.84–2.93 (m, 1 H, $CHCH_3$), [3.49 (hex, J = 6.4 Hz), 3.70–3.80 (m), 1 H, $CHOH$], 4.90–4.98 (m, 2 H, CH_2C), 5.84 (dd, 1 H, J = 10.6, 17.4 Hz, CH=CH_2), [5.93–5.94 (m), 5.95–5.96 (m), 1 H, CH=C). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.02; H, 9.24.

Preparation of the 3(2*H*)-Furanone Alcohol 26 under Aprotic Conditions. To a solution containing 0.32 g (0.42 mmol) of the diketone **25** in 21 mL of THF at 0 °C under an argon atmosphere was added 0.12 g (0.44 mmol) of tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F) in 9 mL of THF dropwise. The mixture was stirred at 0 °C for 19 h. The mixture was transferred to a separatory funnel containing ether and water. The organic layer was separated and the aqueous layer washed with ether. The combined organic layers were dried over Na_2SO_4. Removal of solvent under reduced pressure afforded a pale yallow oil, which was purified further by column chromatography on silica gel with 25% ethyl acetate/hexanes to give 0.18 g (72.2%) of product as a colorless oil: IR (neat) ν 3440 (b, OH), 3000–2800, 1698 (CO), 1622

(C=C), 1456, 1402, 1372, 1288, 1203, 1074 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.78–0.88 (m, 15 H, $(CH_3CH_2)_3$), 1.06–1.11 (m, 12 H, CH_3CH, CH_3CHO, $CH_3C{=}C$, $(CH_3)_2C$), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.37–1.50 (m, 6 H, $(CH_2)_3$), 1.64 (s, 3 H, $CH_3C{=}C$), 1.58–1.66 (m, 1 H, CH_2), 1.80–2.02 (m, 3 H, CH_2), 2.30–2.59 (m, 3 H, CH_2), 2.85–2.95 (m, 1 H, $CHCH_3$), [3.49 (q, J = 6.3 Hz), 3.65–3.82 (m), 1 H, $CHOH$], 5.75–6.05 (m, 3 H, $CH{=}C$, $CH{=}CH$). Anal. Calcd for $C_{31}H_{54}O_3Sn$: C, 62.74; H, 9.17. Found: C, 62.80; H, 9.20.

Preparation of the 3(2*H*)-Furanone Ketone 34. To a solution containing 0.090 g (0.67 mmol) of *N*-chlorosuccinimide under argon in 12 mL of toluene at −25 °C was added 0.070 mL (0.95 mmol) of dimethyl sulfide. Stirring at −25 °C was continued for 30 min, followed by the addition of 0.10 g (0.17 mmol) of alcohol **26** in 6 mL of toluene over a period of 5 min. After the solution was stirred at −25 °C for 3 h, 0.11 mL (0.79 mmol) of triethylamine in 5 mL of toluene was added dropwise. The cold bath was removed, the mixture allowed to warm to room temperature, and stirring continued for 30 min. The contents were diluted with water and then extracted with ether. The organic layer was dried over Na_2SO_4. Removal of solvent afforded an oily residue, which was purified by column chromatography on silica gel with 50% ethyl acetate/hexanes to give 0.080 g (79.6%) of product as an oil: IR (neat) ν 3000–2800, 1714 (CO), 1698 (CO), 1625 (C=C), 1463, 1400, 1371, 1202, 1073 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81–0.88 (m, 15 H, $(CH_3CH_2)_3$), 1.09 (s, 6 H, $(CH_3)_2C$), 1.12 (d, 3 H, J = 7.0 Hz, CH_3CH), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.50 (m, 6 H, $(CH_2)_3$), 1.63 (dd, 1 H, J = 4.4, 13.5 Hz, CH_2), 1.63 (s, 3 H, $CH_3C{=}C$), 2.10 (s, 3 H, $CH_3C{=}O$), 2.32 (d, 1 H, J = 13.3 Hz, CH_2), 2.49 (dd, 1 H, J = 7.7, 13.6 Hz, CH_2), 2.55 (d, 1 H, J = 13.3 Hz), 2.75 (d, 1 H, J = 15.3 Hz, CH_2), 2.87 (d, 1 H, J = 15.3 Hz, CH_2), 2.90–3.00 (m, 1 H, $CHCH_3$), 5.85 (d, 1 H, J = 19.2 Hz, $CH{=}CH$), 5.96 (d, 1 H, J = 19.2 Hz, $CH{=}CH$), 6.00–6.02 (m, 1 H, $CH{=}C$); ^{13}C NMR ($CDCl_3$) δ 6.48, 9.36, 13.68, 21.13, 26.99, 27.20, 27.55, 28.77, 29.02, 38.00, 40.36, 41.11, 42.22, 42.43, (CH, CH_2, CH_3), 99.22 (CO), 111.92 (C=C), 122.91 (C=C), 133.19 (C=C), 143.01 (C=C), 156.39 (C=C), 186.15 (C=C), 205.07 (C=O), 205.54 (C=O). Anal. Calcd for $C_{31}H_{52}O_3Sn$: C, 62.95; H, 8.86. Found: C, 63.06; H, 8.88.

Preparation of the 3(2*H*)-Furanone Vinylic Triflate 35. To a solution containing 0.076 g (0.13 mmol) of ketone **34** in 10 mL of THF was added 0.050 g (0.14 mmol) of *N*-phenyltriflimide under an argon atmosphere. The temperature was reduced to −78 °C, followed by the addition of 0.10 mL (0.10 mmol) of a 1.0 M sodium bis(trimethylsilyl)amide solution in THF. The solution was stirred at −78 °C for 10 min, then quenched with water, and extracted with ether. The organic layer was dried over Na_2SO_4. Removal of solvent under reduced pressure afforded a pale yellow oil, which was purified by column chromatography on silica gel with 25% ethyl acetate/hexanes to give 0.050 g (53.6%) of product as white needles and 0.018 g (23.68%) of the starting ketone **34**. Yield based on recovered starting material is 70.47%. This intermediate was not fully characterized but instead carried on to the next step: ^1H NMR ($CDCl_3$) δ 0.81–0.89 (m, 15 H, $(CH_3CH_2)_3$), 1.09 (s, 3 H, $(CH_3)_2C$), 1.10 (s, 3 H, $(CH_3)_2C$), 1.15 (d, 3 H, J = 7.1 Hz, CH_3CH), 1.24–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.50 (m, 6 H, $(CH_2)_3$), 1.63 (dd, 1 H, J = 7.8, 9.3 Hz, CH_2), 1.65 (s, 3 H, $CH_3C{=}C$), 2.07 (s, 3 H, CH_3COTf), 2.45 (dd, 1 H, J = 7.7, 13.6 Hz, CH_2), 2.49 (bs, 2 H), 2.95–3.08 (m, 1 H, $CHCH_3$), 4.98 (d, 1 H, J = 1.1 Hz, $CH{=}COTf$), 5.86 (d, 1 H, J = 19.3 Hz, $CH{=}CH$), 5.97 (d, 1 H, J = 19.3 Hz, $CH{=}CH$), 6.53 (d, 1 H, J = 2.4 Hz, $CH{=}C$).

***epi*-Jatrophone (22).** To a Fischer–Porter tube were added 0.030 g (0.042 mmol) of vinylic triflate **35** in 10 mL of DMF and 0.011 g (0.26 mmol) of LiCl. The solution was bubbled with carbon monoxide for 30 min. This was followed by the addition of 0.001 g (0.004 mmol) of bis(acetonitrile)palladium(II) chloride in 3 mL of DMF. The tube was then pressurized to 50 psi and the mixture stirred at room temperature for 13 h, after which time palladium black had precipitated out of solution. The tube was vented and the solution taken up in ether and washed with water. The organic layer was dried over Na_2SO_4. Removal of solvent under reduced pressure afforded an oily residue that was purified by column chromatography on silica gel with 25% ethyl acetate/hexanes to give 0.007 g (53.4%) of product as a white crystalline solid. All spectral data matched that of the literature:[4] IR (neat) ν 3000–2800, 1696 (CO), 1659 (CO), 1620 (C=C), 1449, 1400, 1371, 1232, 1200, 1161, 1109, 1074 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, 3 H, J = 7.0 Hz, CH_3CH), 1.21 (s, 3 H, $(CH_3)_2C$), 1.36 (s, 3 H, $(CH_3)_2C$), 1.63 (d, 1 H, J = 14.0 Hz, CH_2), 1.70 (d, 3 H, J = 0.8 Hz, $CH_3C{=}C$), 1.86 (d, 3 H, J = 1.7 Hz, $CH_3C{=}C$), 2.43 (dd, 1 H, J = 0.9, 15.3 Hz, CH_2), 2.52 (dd, 1 H, J = 7.7, 14.0 Hz, CH_2), 2.83 (m, 1 H, $CHCH_3$), 2.81–2.86 (d, 1 H, J = 15.3 Hz, CH_2), 5.73–5.76 (m, 1 H, $CH{=}CCH_3$), 5.86 (t, 1 H, J = 2.5 Hz, $CH{=}C$), 6.00 (d, 1 H, J = 16.2 Hz, $CH{=}CH$), 6.40 (d, 1 H, J = 16.2 Hz, $CH{=}CH$); ^{13}C NMR ($CDCl_3$) δ 6.02, 20.23, 20.75, 26.78, 30.34, 36.73, 38.65, 40.64, 40.89, (CH, CH_2, CH_3), 99.07 (CO), 112.41, 123.80, 129.02, 136.93, 142.25, 146.60, 158.78, 183.43 (C=C), 202.04 (C=O), 204.56 (C=O); HRMS for $C_{20}H_{24}O_3$, calcd 312.1726, found 312.1722 (M^+).

(±)-(1*R*,4*R*)-1-(1-Oxopropyl)-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)oxy]-2-cyclopentene (36). With use of a procedure identical with that for **23**, 0.30 g (1.41 mmol) of the diol afforded 0.36 g (72.8%) of the bis(trimethylsilyl)-protected diol: IR (neat) ν 3000–2800, 1716 (CO), 1685 (CO), 1456, 1407, 1378, 1339, 1250, 1126, 1005 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.06–0.11 (m, 18 H, $((CH_3)_3Si)_2$), 0.98–1.03 (m, 3 H, CH_3CH_2), 1.05–1.12 (m, 6 H, CH_3CH, CH_3CHO), 1.81 (dd, 1 H, J = 5.2, 14.2 Hz, CH_2), 1.87–2.15 (m, 2 H), 2.11 (dd, 1 H, J = 8.1, 14.2 Hz, CH_2), 2.41–2.70 (m, 2 H, CH_2), 2.85–3.00 (m, 1 H, $CHCH_3$), [3.75–3.86 (m), 3.90–4.00 (m), 1 H, CHO], 5.53–5.58 (m, 1 H, $CH{=}C$); HRMS for $C_{18}H_{36}O_3Si_2$, calcd 356.2204, found 356.2230 (M^+), 314.1963 $(M - Me)^+$, 299.1857 $(M - C_3H_5O)^+$.

(±)-(1*R*,4*R*)-1-[2-Methyl-3-hydroxy-5,5-dimethyl-7-(tributylstannyl)-1-oxo-6-heptenyl]-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)oxy]-2-cyclopentene (37). With the same procedure as that for **24**, 0.35 g (0.98 mmol) of the bis(trimethylsilyl)-protected diol **36** and 0.58 g (1.45 mmol) of the aldehyde **8** afforded 0.32 g (43.1%) of product as a complex diastereomeric mixture: IR (neat) ν 3528 (b, OH), 3000–2800, 1699 (CO), 1592 (C=C), 1457, 1377, 1251, 1124, 1072, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.05–0.15 (m, 18 H, $((CH_3)_3Si)_2$), 0.78–0.88 (m, 15 H, $(CH_3CH_2)_3$, 1.00–1.18 (m, 15 H, CH_3CHO, $(CH_3)_2C$, $(CH_3CH)_2$), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.41–1.54 (m, 6 H, $(CH_2)_3$), 1.65–1.89 (m, 1 H, CH_2), 1.90–2.31 (m, 4 H, CH_2), 2.40–3.27 (m, 4 H, CH_2), 3.68–4.08 (m, 2 H, $CHOH$, $CHO(TMS)$), 5.53–5.62 (m, 1 H, $CH{=}C$), 5.80–6.02 (m, 2 H, $CH{=}CH$); HRMS for $C_{37}H_{74}{}^{16}O_4Si_2{}^{120}Sn$, calcd 758.4149, found 697.3393 ($[M - C_4H_9]^+$, $C_{33}H_{65}{}^{16}O_4Si_2{}^{116}Sn$), 701.3400 ($[M - C_4H_9]^+$, $C_{33}H_{65}{}^{16}O_4Si_2{}^{120}Sn$).

(±)-(1*R*,4*R*)-1-[2-Methyl-5,5-dimethyl-7-(tributylstannyl)-1,3-dioxo-6-heptenyl]-2-[2-[(trimethylsilyl)oxy]propyl]-4-methyl-1-[(trimethylsilyl)oxy]-2-cyclopentene (38). With the same procedure as that for **25**, 0.29 g (0.38 mmol) of the alcohol **37** afforded 0.28 g (97.5%) of the diketone as a mixture of diastereomers. This intermediate was not fully characterized but instead taken on to the next step: IR (neat) ν 3000–2800, 1728 (CO), 1705 (CO), 1592 (C=C), 1456, 1376, 1343, 1251, 1126, 1089, 1001, 909 cm^{-1}; HRMS for $C_{37}H_{72}{}^{16}O_4Si_2{}^{120}Sn$, calcd 756.3993, found 695.3271 ($[M - C_4H_9]^+$, $C_{33}H_{63}{}^{16}O_4Si_2{}^{116}Sn$), 699.3287 ($[M - C_4H_9]^+$, $C_{33}H_{63}{}^{16}O_4Si_2{}^{120}Sn$).

Formation of the 3(2*H*)-Furanone Alcohol Precursor to (±)-Jatrophone (39). With the same procedure as that of **26**, 0.27 g (0.36 mmol) of the diketone **38** and 0.10 g (0.36 mmol) of (TAS-F) afforded 0.14 g (63.7%) of the furanone alcohol as a mixture of diastereomers: IR (neat) ν 3444 (b, OH), 3000–2800, 1698 (CO), 1614 (C=C), 1456, 1402, 1373, 1203, 1075, 992 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81–0.89 (m, 15 H, $(CH_3CH_2)_3$), 1.06–1.16 (m, 12 H, CH_3CH, CH_3CHO, $CH_3C{=}C$, $(CH_3)_2C$), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.48 (m, 6 H, $(CH_2)_3$), 1.66 (s, 3 H, $CH_3C{=}C$), 1.75–2.05 (m, 3 H, CH_2), 2.10–2.26 (m, 1 H, CH_2), 2.30–2.63 (m, 3 H, CH_2), 2.85–3.08 (m, 1 H, $CHCH_3$), [3.44–3.62 (m), 3.65–3.81 (m), 1 H, $CHOH$], 5.81–6.02 (m, 3 H, $CH{=}C$, $CH{=}CH$); HRMS for $C_{31}H_{54}{}^{16}O_3{}^{120}Sn$, calcd 594.3096, found 533.2275 ($[M - C_4H_9]^+$, $C_{27}H_{45}{}^{16}O_3{}^{116}Sn$), 537.2359 ($[M^+ - C_4H_9]^+$, $C_{27}H_{45}{}^{16}O_3{}^{120}Sn$).

Preparation of the 3(2*H*)-Furanone Ketone Precursor to (±)-Jatrophone (5). With a procedure identical with that for **34**, 0.12 g (0.20 mmol) of alcohol **39** afforded 0.090 g (75.7%) of product: IR (neat) ν 3000–2800, 1716 (CO), 1698 (CO), 1625 (C=C), 1458, 1400, 1371, 1219, 1073, 993 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.79–0.89 (m, 15 H, $(CH_3CH_2)_3$), 1.077 (s, 3 H, $(CH_3)_2C$), 1.082 (s, 3 H, $(CH_3)_2C$), 1.16 (d, 3 H, J = 7.0 Hz, CH_3CH), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.48 (m, 6 H, $(CH_2)_3$), 1.64 (, 3 H, $CH_3C{=}C$), 1.82 (dd, 1 H, J = 5.4, 14.0 Hz, CH_2), 2.10 (s, 3 H, $CH_3C{=}O$), 2.17–2.25 (dd, 1 H, J = 7.5, 14.0 Hz, CH_2), 2.33 (d, 1 H, J = 13.2 Hz, CH_2), 2.53 (d, 1 H, J = 13.2 Hz, CH_2), 2.74 (d, 1 H, J = 15.5 Hz, CH_2), 2.88 (d, 1 H, J = 15.5 Hz, CH_2), 3.00–3.05 (m, 1 H, $CHCH_3$), 5.83 (d, 1 H, J = 19.3 Hz, $CH{=}CH$), 5.95 (d, 1 H, J = 19.3 Hz, $CH{=}CH$), 6.00 (m, 1 H, $CH{=}C$); HRMS for $C_{31}H_{52}{}^{16}O_3{}^{116}Sn$, calcd 588.2937, found 531.2195 ($[M - C_4H_9]^+$, $C_{27}H_{43}{}^{16}O_3{}^{116}Sn$), 533.2204 ($[M - C_4H_9]^+$, $C_{27}H_{43}{}^{16}O_3{}^{118}Sn$).

Preparation of 3(2*H*)-Furanone Vinylic Triflate Precursor to (±)-Jatrophone (4). With the same procedure as that given for the vinylic triflate precursor **35** to *epi*-jatrophone, 0.054 g (0.091 mmol) of ketone **5** gave 0.032 g (48.6%) of product and 0.020 g (37.0%) of starting material. Yield based on recovered starting material is 76.94%. This intermediate was not fully characterized but instead carried out to the next step: ^1H NMR ($CDCl_3$) δ 0.81–0.89 (m, 15 H, $(CH_3CH_2)_3$), 1.07 (s, 3 H, $(CH_3)_2C$), 1.09 (s, 3 H, $(CH_3)_2C$), 1.18 (d, 3 H, J = 7.1 Hz, CH_3CH), 1.21–1.33 (m, 6 H, $(CH_2)_3$), 1.40–1.50 (m, 6 H, $(CH_2)_3$), 1.66 (s, 3 H), $CH_3C{=}C$), 1.80 (dd, 1 H, J = 5.8, 14.0 Hz, CH_2), 2.07 (s, 3 H, CH_3COTf), 2.14–2.22 (m, 2 H, CH_2), 2.40–2.53 (m, 1 H, CH_2), 3.06–3.19 (m, 1 H, $CHCH_3$), 4.98 (d, 1 H, J = 1.0 Hz, $CH{=}COTf$),

5.84 (d, 1 H, J = 19.2 Hz, CH=CH), 5.96 (d, 1 H, J = 19.2 Hz, CH=CH), 6.51 (d, 1 H, J = 2.0 Hz, CH=C).

(±)-Jatrophone (1). With the same procedure as that given for *epi*-jatrophone (**22**), 0.020 g (0.027 mmol) of the vinyl triflate **4** afforded 0.002 g (23.7%) of jatrophone as a white crystalline solid. All spectral data matched that reported in the literature:[4] IR (neat) ν 3000–2800, 1696 (CO), 1659 (CO), 1621 (C=C), 1450, 1398, 1371, 1231, 1160, 1107, 1063 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.06 (d, 3 H, J = 7.1 Hz, CH_3CH), 1.21 (s, 3 H, (CH_3)$_2$C), 1.33 (s, 3 H, (CH_3)$_2$C), 1.72 (d, 3 H, J = 0.7 Hz, CH_3C=C), 1.84 (dd, 1 H, J = 5.7, 13.5 Hz, CH_2), 1.85 (d, 3 H, J = 1.6 Hz, CH_3C=C), 2.12 (dd, 1 H, J = 5.8, 13.6 Hz, CH_2), 2.37 (dd, 1 H, J = 0.7, 14.8 Hz, CH_2), 2.83 (d, 1 H, J = 14.7 Hz, CH_2), 2.92–2.96 (m, 1 H, CHCH$_3$), 5.77–5.80 (m, 2 H, CH=C, CH=CCH3), 5.97 (d, 1 H, J = 16.3 Hz, CH=CH), 6.42 (d, 1 H, J = 16.3 Hz, CH=CH); ^{13}C NMR ($CDCl_3$) δ 6.13, 18.98, 20.78, 26.92, 30.42, 36.64, 38.35, 41.24, 42.47, (CH, CH_2, CH_3), 99.78 (CO), 112.42, 123.76, 128.73, 137.09, 141.77, 147.13, 159.04, 183.25 (C=C), 202.03 (C=O), 203.93 (C=O); HRMS for $C_{20}H_{24}O_3$, calcd 312.1726, found 312.1725.

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Supplementary Material Available: Experimental details for the reactions reported in Scheme IV (5 pages). Ordering information is given on any current masthead page.

Effect of Allylic Substituents on the Face Selectivity of Diels–Alder Reactions of Semicyclic Dienes

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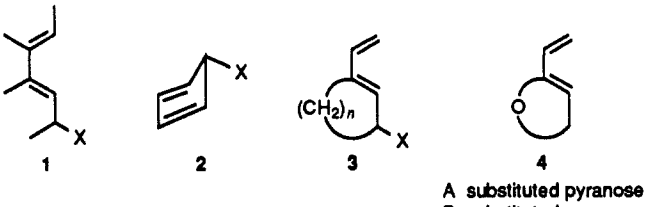
Abstract: Vinylcyclohexenes substituted allylically on the cyclohexene ring were examined as substrates in the Diels–Alder cycloaddition. In the octalin cycloaddition products, the relative stereochemistry of the one angular hydrogen relative to that of the allylic substituent was examined as a measure of the control of face selectivity by the substituent. In the 17 examples reported where the competition for control was between OH–H, MeO–H, (TMS)O–H, OH–CH_3, OMe–CH_3, and (TMS)O–CH_3, the simplest rationale was that size alone controlled the face selectivity of the Diels–Alder cycloaddition.

Introduction

High regiospecificity and stereoselectivity along with the simultaneous creation of multiple chiral centers make the Diels–Alder reaction an important process in organic synthesis.[2] Heteroatom substitution at the allylic position of a diene has a pronounced effect on diastereofacial selection. Attempts have been made to rationalize the observed diastereoselectivity.[3-8] Experiments involving the use of dienes with a stereogenic allylic carbon can be divided into three categories. Acyclic dienes of type **1**[5-11] (X = O, N, Si) have essentially free rotation of the allylic



1 2 3 4

A substituted pyranose
B substituted pyranose

center, while in cyclic dienes **2**,[12] **3**,[13] and **4**[14] the allylic substituents are restricted in their degree of conformational flexibility. Recent work at Hunter documented a series of Diels–Alder reactions using

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