$(Cp)(CO)_2I$ firmly establishes silver ion involvement in organotransition-metal chemistry. Silver ion involvement has also been established in chloride ion abstractions from $Ru(CO)_2(dppm)Cl_2$ and apparently involves one-end dissociation of the bidentate phosphine.[37] Of greater novelty, the present findings with $IrCl(CO)(PPh_3)_2$ show that in the case of coordinatively unsaturated complexes, silver adduct formation may involve metal-to-silver bonding rather than halide-bridge bonding. This had been proposed in the $Ru(CO)_2(dppm)Cl_2$ system cited above. Interestingly, the crystal structure of the $Ag(PPh_3)^+$ adduct of $[PtCl_2(C_6F_5)_2]^{2-}$ shows a hybrid, nonclassical structure; the silver atom is bonded primarily to chlorine (Ag-Cl = 2.47 Å) but also to platinum (Ag-Pt = 2.79 Å).[38] Whether metal-metal-bonded adducts are actual intermediates in silver metathesis reactions remains to be determined but they must certainly be considered, particularly in d^8 square-planar complexes where the filled d_{z^2} orbital can apparently confer a high basicity on the metal.

Of much wider impact is the very active role that weakly coordinating anions play in silver salt metathesis reactions. It seems likely that in a large number of silver-assisted ionizations the nucleophilicity Y^- will be rate determining:[39]

$$M\text{-}X + AgY \xrightarrow{\text{fast}} [M\text{-}X\text{-}Ag]Y \xrightarrow{\text{slow}} AgX + MY$$

In organic chemistry, these reactions have been referred to as $Y^-\text{-}S_N1\text{-}Ag^+$ when they lead to carbocation ion formation[8] but there can clearly be many variants with respect to the nature of [M-X-Ag]Y and the precise role of Y in influencing the outcome of a reaction and its rate. The lack of metathesis when, for example, $IrCl(CO)(PPh_3)_2$ or Ph_3SiCl[40] is treated with $Ag(B_{11}CH_{12})$ compared to the rapid reaction with the corresponding perchlorate is taken as a kinetic result rather than a thermodynamic one. The existence of $Fe(Cp)(CO)_2(B_{11}CH_{12})$ and its essentially normal stereochemistry argues against the notion that the carborane anion is too bulky to form metathesis products. Rather, its low nucleophilicity relative to perchlorate seems to be the reason for decreased reactivity. This is probably the result of a unique characteristic. The anion is large and has no lone pairs of electrons. Only tetraphenylborate rivals this although its electron-rich arene rings are well-known to act as ligands. Future work will endeavor to put these concepts on a more quantitative basis.

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Supplementary Material Available: Table SI, complete crystallographic details of the structure solution of $FeCp(CO)_2(B_{11}CH_{12})$, Table SII, anisotropic thermal parameters, and Tables SIII-SV, complete tabulations of bond distances and bond angles (7 pages); tables of observed and calculated structure amplitudes (15 pages). Ordering information is given on any current masthead page.

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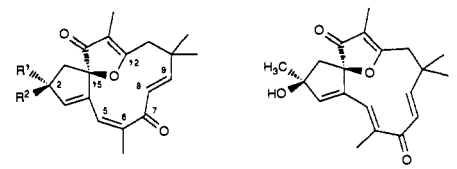
Total Synthesis of (+)-Hydroxyjatrophone A and (+)-Hydroxyjatrophone B

Amos B. Smith, III,* Andrew T. Lupo, Jr., Masashi Ohba, and Kwunmin Chen

Contribution from the Department of Chemistry, The Laboratory for Research on the Structure of Matter, and The Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received October 17, 1988. Revised Manuscript Received April 11, 1989*

Abstract: A full account of the first total synthesis of (+)-hydroxyjatrophone A (**2**) and (+)-hydroxyjatrophone B (**3**), two antileukemic diterpene macrocycles isolated from *Jatropha gossypiifolia*, is presented. Central to the synthetic strategy was an intramolecular Mukaiyama acetal-aldol reaction that generated the 11-membered ring. Of paramount interest with respect to the hydroxyjatrophones was the compatibility of the highly sensitive, tertiary allylic hydroxyl group with the required end-game transformations. Completion of this synthetic venture dramatically demonstrates the versatility of our jatrophone synthetic strategy.

In 1983 we reported, in collaboration with Cordell, the structures of hydroxyjatrophones A, B, and C (**2-4**),[1] three new antileukemic diterpene macrocycles, isolated from *Jatropha gossypiifolia*, a plant used ethnomedically for the treatment of cancer.[2] This work reflected one aspect of our longstanding interest in the secondary metabolites of *J. gossypiifolia*, which has also resulted in the first (and to this date the only) total synthesis of (±)-jatrophone (**1**),[3] as well as the total synthesis of the structurally related jatropholones A and B.[4]



Jatrophone (1): $R' = CH_3$, $R^2 = H$
Hydroxyjatrophone A (2): $R' = OH$, $R^2 = CH_3$
Hydroxyjatrophone B (3): $R' = CH_3$, $R^2 = OH$
Hydroxyjatrophone C (4)

A central underlying theme of our synthetic program is the development and execution of strategies that are not single target

* To whom correspondence should be addressed at the Department of Chemistry.

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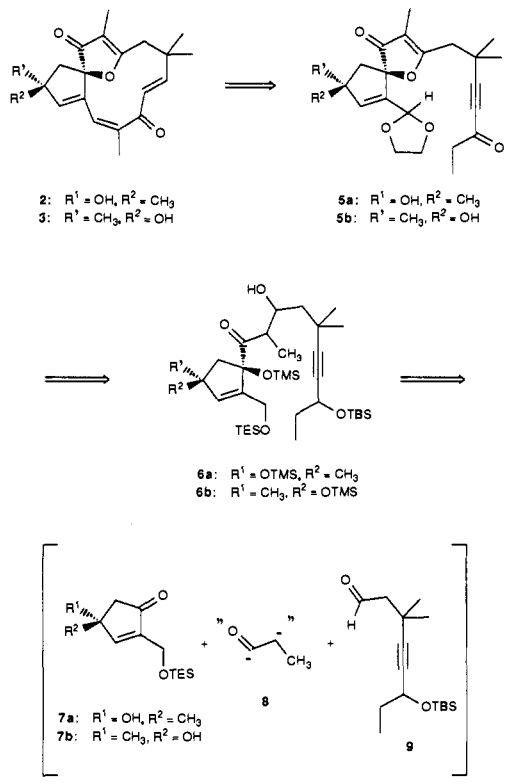
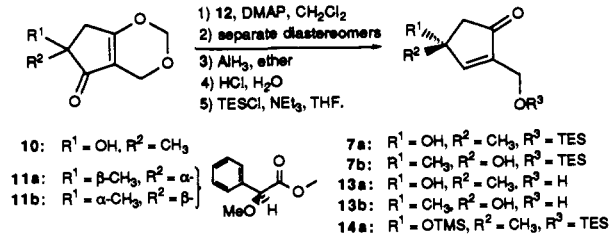
Scheme I



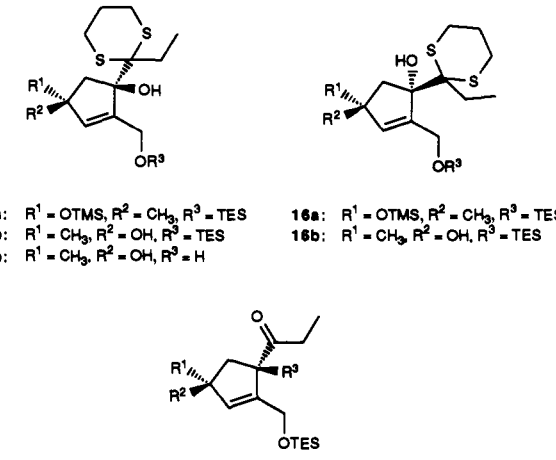
oriented but instead permit construction of entire families of natural products. Given our success in the jatrophone area, we were intrigued by the possibility of extending and streamlining our initial strategy to accommodate other members of this class. Of paramount interest with respect to hydroxyjatrophones A (**2**) and B (**3**) was the stability of the tertiary allylic C(2)-hydroxyl group vis-à-vis the required end-game transformations.

The cornerstone of our jatrophone strategy is the use of an intramolecular Mukaiyama acetal–aldol[5] reaction to construct the 11-membered ring. Thus, for hydroxyjatrophone A (**2**) we required 3(2*H*)-furanone **5a** (Scheme I). Execution of the Mukaiyama cyclization, followed by elimination of ethylene glycol and net trans hydrogenation of the C(8,9)-acetylene, would provide **2**. Advanced intermediate **5a** in turn was envisioned to arise from β-hydroxy ketone **6a** via oxidation at C(5), C(12), and C(7) (jatrophone numbering), an acid-promoted cyclization to form the 3(2*H*)-furanone, and finally conversion of the aldehyde to the corresponding acetal. Ultimately, **6a** would derive from three components: cyclopentenone **7a**, a synthetic equivalent for dianion **8**, and aldehyde **9**.[3] Analysis of hydroxyjatrophone B (**3**) is similar to that of A (**2**), except for the requirement of the enantiomeric cyclopentenone **7b**. Examination of the structure of **6a** reveals that attack of the acyl anion equivalent **8** must occur syn to the hydroxy substituent at C(2) of **7a**. Conversely for the preparation of **6b**, nucleophilic attack must occur anti to the C(2)-hydroxyl of **7b**. We anticipated that the required facial selectivity could be achieved by either modification of the steric bulk of the C-(2)-hydroxy protecting group and/or via hydroxyl directed nucleophilic acylation.

Preparation of the enantiomeric cyclopentenones **7a** and **7b** began with tertiary alcohol (±)-**10**, readily available in three steps from 1,3-cyclopentanedione.[6] Treatment of (±)-**10** with (*S*)-(+)-*O*-methylmandeloyl chloride (**12**,[7] DMAP, CH_2Cl_2, room temperature (rt)) gave diastereomeric esters **11a** and **11b** (1:1, 83% yield), which proved readily separable by flash chromatography. Treatment of **11a** with aluminum hydride (ether, 0 °C)[8] followed by an acid-promoted hydrolysis–rearrangement (HCl, H_2O, rt) and selective triethylsilylation (TESCl, NEt_3, THF, rt) then afforded homochiral cyclopentenone (−)-**7a** (60% from **11a**). In a similar fashion (+)-**7b** was obtained from **11b** (63%).[9]



Continuing with the synthesis, treatment of (+)-**7b** with 2-lithio-2-ethyl-1,3-dithiane[10] (THF, −65 °C) provided diastereomeric diols **15b** and **16b** (18:1, 95% yield); a single-crystal X-ray analysis of the triol **17b**, obtained by fluoride treatment of **15b** (*n*-bu_4NF, THF, rt), secured the syn relationship of the two tertiary hydroxyl groups.



(1) Taylor, M. D.; Smith, III, A. B.; Furst, G. T.; Gunasekara, S. R.; Bevelle, C. A.; Cordell, G. A.; Kupchan, S. M.; Uchida, H.; Branfman, A. R.; Dailey, Jr., R. G.; Sneden, A. T. *J. Am. Chem. Soc.* **1983**, *105*, 3177. For previous studies of *Jatropha gossypiifolia* see: (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.

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(4) (a) Smith, III, A. B.; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. *J. Org. Chem.* **1985**, *50*, 3239. (b) Smith, III, A. B.; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. *J. Am. Chem. Soc.* **1986**, *108*, 3040.

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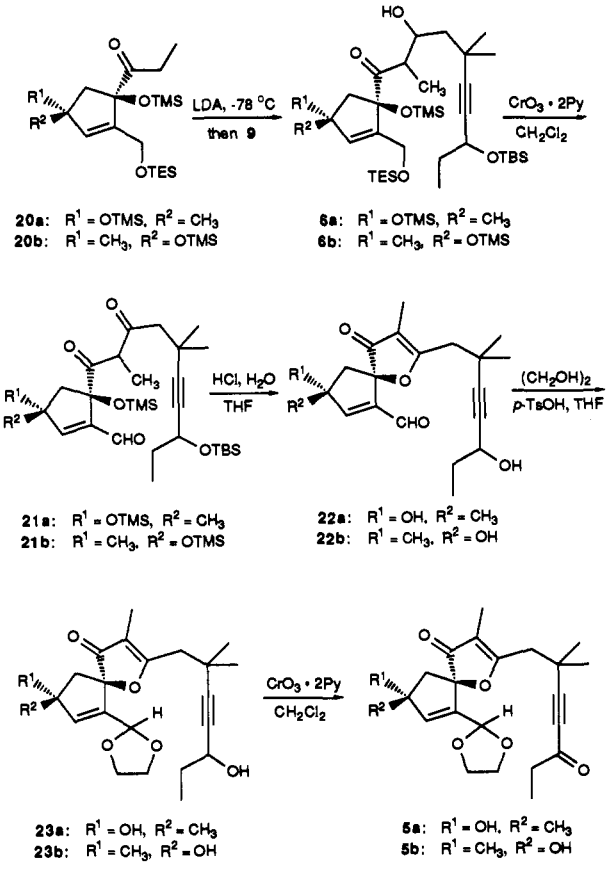
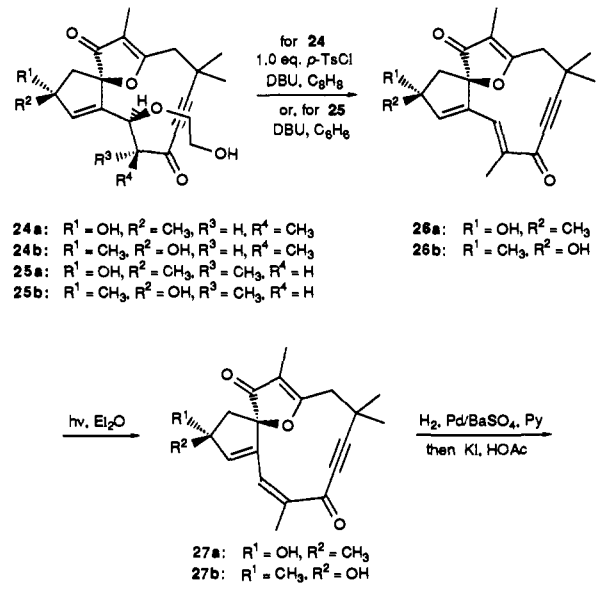
(9) Chiral shift ^1H NMR studies demonstrated that both (−)-**7a** and (+)-**7b** were obtained in greater than 95% enantiomeric excess; single-crystal X-ray analysis of **11a** permitted assignment of the absolute configurations as (*R*)-(−)-**7a** and (*S*)-(+)-**7b**.

(10) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231.

Scheme II



Scheme III



With a highly stereocontrolled route to **15b** in hand, efforts were then directed toward the synthesis of (+)-hydroxyjatrophone B (**3**). Hydrolysis of the dithiane moiety was effected by treatment with mercury(II) perchlorate[11] in the presence of diisopropylamine [3.0 equiv of i-Pr_2NH, 2.3 equiv of $Hg(ClO_4)_2 \cdot 3H_2O$, THF, rt] thereby providing diol–ketone **19b**. The presence of diisopropylamine is crucial to the success of this reaction; in its absence extensive decomposition of **15b** was observed. In particular, the conditions used in the jatrophone synthesis (MeI, $CaCO_3$, MeCN, H_2O)[3] were unacceptable for this substrate due to the hydrolytic lability of the primary, allylic triethylsilyl ether. Bissilylation (TMSCl, NEt_3, DMF, rt) of diol–ketone **19b** then provided the trissilyl-protected triol **20b**.

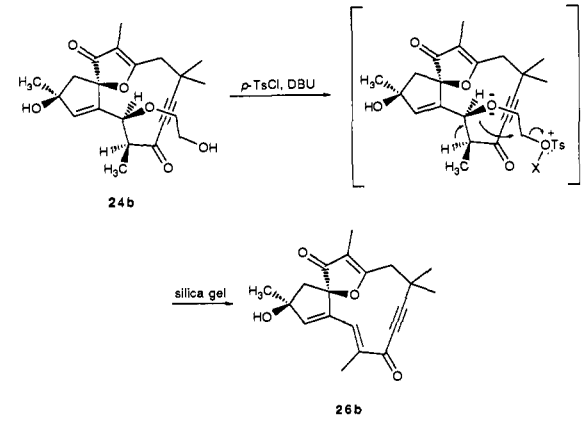
Generation of the enolate of ketone **20b** (LDA, THF, −78 °C), followed by addition of the aldehyde (±)-**9** (−78 °C) then led to a diastereomeric mixture of aldol products **6b**, which upon treatment with Collins' reagent (18 equiv of $CrO_3 \cdot 2Py$, CH_2Cl_2, rt) resulted in oxidation of the C(5)-triethylsilyl ether to the aldehyde in addition to oxidation of the secondary alcohol at C(12) (jatrophone numbering) to provide enal–dione **21b** (Scheme II). The triethylsilyl protecting group at C(5) thus satisfied three important requirements: (1) flash chromatographic stability of the silylated intermediates; (2) moderate steric bulk; in the earlier jatrophone studies[3] a very bulky (*tert*-butyldimethylsilyl)oxy group at C(5) precluded enolate formation as required for aldol reaction with aldehyde **9**; and (3) susceptibility to direct oxidation to the corresponding aldehyde; in the jatrophone work[3] the corresponding primary allylic trimethylsilyl ether was oxidized in this fashion. Subsequent acid-promoted cyclization and desilylation (HCl, H_2O, rt) of **21b** provided 3(2*H*)-furanone **22b** in excellent yield (31%, six steps from **7b**). Finally, advanced intermediate **5b** was obtained by acid-catalyzed ketalization of the C(5)-aldehyde under mild conditions (100 equiv of $HOCH_2CH_2OH$, 0.05 equiv of *p*-TsOH, THF, rt)[12] and then Collins oxidation (12 equiv of $CrO_3 \cdot 2Py$, CH_2Cl_2, rt).

Turning next to the critical intramolecular Mukaiyama reaction, generation of the enol silyl ether of ketone **5b** [(a) LDA, THF, −78 °C; (b) excess TMSCl, 0 °C, 1.5 h], followed by treatment with titanium tetrachloride (CH_2Cl_2, −78 °C) provided two diastereomeric β-alkoxy ketones, **24b** and **25b** (2.5:1, 65% yield; Scheme III). At this point only two operations remained to complete the synthesis of (+)-hydroxyjatrophone B (**3**); these were (A) elimination of ethylene glycol to provide the C(5,6)-cis double bond and (B) conversion of the alkyne moiety into the C(8,9)-trans double bond. In our jatrophone synthesis, elimination of ethylene glycol, providing ultimately the C(5,6)-cis-olefin geometry, was accomplished only after prolonged treatment with *p*-toluenesulfonic acid. As anticipated, the tertiary, allylic hydroxyl group at C(2) of **24b** was incompatible with such conditions; treatment of **24b** with *p*-toluenesulfonic acid led to extensive C(2)-hydroxyl elimination. However, after considerable experimentation, we found that treatment of the major diastereomer **24b** with *p*-toluenesulfonyl chloride and diazabicycloundecane followed by flash chromatography on silica provided the C(5,6)-trans-olefin **26b**.[13] Interestingly, the minor isomer **25b** [epimeric at C(6)] reacted quite efficiently with DBU (benzene, 10 °C, 10 min) to provide the same olefin **26b**, without prior conversion to the corresponding tosylate. Photoisomerization of the C(5,6) double bond (*hν*, 254

(11) Nagao, Y.; Fujita, E.; Kaneko, K. *Chem. Pharm. Bull.* **1978**, *26*, 3743.

(12) More vigorous conditions led to extensive elimination of the C(2)-hydroxyl providing the corresponding exocyclic olefin.

(13) Thin-layer chromatographic analysis of this reaction revealed the formation of an intermediate, presumably the corresponding tosylate, which decomposed upon flash chromatography to provide the desired C(5,6)-olefin.



nm, ether, rt) of **26b**, an extremely efficient process, then provided the C(5,6)-cis-olefin **27b** in near quantitative yield.

Completion of (+)-hydroxyjatrophone B (**3**) was accomplished as in our earlier jatrophone studies: semihydrogenation of the alkyne ($Pd/BaSO_4$, pyridine, H_2)[14] and isomerization of the C(8,9)-double bond (KI, HOAc). Synthetic (+)-hydroxyjatrophone B (**3**) was identical in all respects (500-MHz ^1H NMR, HRMS, optical rotation, and TLC mobility in six solvent systems) with a sample of natural material.[1]

The synthesis of (+)-hydroxyjatrophone A (**2**) proceeded in a similar fashion from cyclopentenone (−)-**7a**. Silylation (TMSCl, NEt_3, DMF, rt) provided the corresponding tertiary silyl ether **14a**, which when treated with 2-lithio-2-ethyl-1,3-dithiane[10] (benzene, 10 °C) gave two diastereomeric adducts **15a** and **16a** (1:2,[15] 85% yield). Hydrolysis of the dithiane moiety of **15a**, followed by silylation of the remaining tertiary hydroxyl led to the tris-protected triol **20a** (20% overall from **7a**). The remaining transformations, as described for the construction of **3**, proceeded without incident to provide synthetic (+)-hydroxyjatrophone A (**2**), identical in all respects with an authentic sample (see Experimental Section).

In summation, the first total syntheses of (+)-hydroxyjatrophone A (**2**) and (+)-hydroxyjatrophone B (**3**) have been achieved from (*R*)-(−)-**7a** and (*S*)-(+)-**7b**, respectively. These efforts not only demonstrate further the versatility of our jatrophone synthetic strategy but in addition provide confirmation of the assigned absolute configurations of hydroxyjatrophones A (**2**) and B (**3**).[1] Future studies directed toward hydroxyjatrophone C (**4**) will be reported in due course.

Experimental Section

Materials and Methods. Reactions were carried out under an argon atmosphere, using dry freshly distilled solvents, under anhydrous conditions in vacuum-flamed glassware, unless otherwise noted. Diethyl ether and THF were distilled under nitrogen from sodium/benzophenone, while benzene and dichloromethane were distilled from calcium hydride. Diisopropylamine, triethylamine, and pyridine were distilled from calcium hydride and stored over KOH. *n*-Butyllithium in hexanes was purchased from Aldrich and standardized by titration with diphenylacetic acid. All reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Flash column chromatography was performed with the solvents indicated using silica gel-60 (particle size 0.040–0.063 mm) supplied by E. Merck. The purity of the products on which yields are reported was determined to be ≥95% on the basis of ^1H NMR spectral and/or chromatographic analyses, unless stated otherwise. All melting points are uncorrected. Proton NMR were recorded at 500 MHz. Carbon-13 NMR spectra were obtained at 125 MHz. The single-crystal X-ray structures were determined by Dr. Patrick Carroll of the University of Pennsylvania with a CAD-4 automated diffractometer.

3,3-Dimethyl-6-hydroxy-4-octynoic Acid. To a mixture of 160 mL of dry THF and 14.3 mL (102 mmol) of dry diisopropylamine under nitrogen atmosphere at −10 °C was added 45.3 mL (90.6 mmol, 2.2 M) of *n*-butyllithium. The mixture was stirred for 20 min at −10 °C and cooled to −78 °C. 3,3-Dimethyl-4-pentynoic acid[16] (4.97 g, 39.4 mmol) in dry HMPA (31.5 mL, 181 mmol) was then added over a 15-min period. The mixture was stirred 75 min at −78 °C and a solution of freshly distilled propanal (7.0 mL, excess) in dry THF (10 mL) was added over a 10-min period. The resultant yellow mixture was stirred an additional 45 min at −78 °C; the cooling bath was then removed, and stirring was continued for 1 h. The reaction mixture was poured into 150 mL of 1.5 N NaOH. The organic layer was extracted thoroughly with additional NaOH; the basic aqueous extracts were combined with ether and cooled to 0 °C. A solution of concentrated H_2SO_4:ice water (1:5) was added slowly; acidification (pH paper) was characterized by a color change of yellow to cloudy white. After thorough extraction with ether, the combined organic layers were washed with 1 N HCl, water, and brine. Removal of solvent in vacuo gave 7.14 g of a viscous yellow oil, which was used without purification in the following step; IR (CCl_4, cm^{-1}) 3500–3350 (br s), 1710 (s); NMR (60 MHz, CCl_4) δ 4.28 (t, *J* = 6 Hz, 1 H), 2.49 (s, 2 H), 1.70 (m, 2 H), 1.37 (s, 6 H), 0.99 (t, *J* = 6 Hz, 3 H).

3,3-Dimethyl-6-((*tert*-butyldimethylsilyl)oxy)-4-octynoic acid, *tert*-Butyldimethylsilyl Ester. The hydroxy acid prepared above was taken up in 200 mL of DMF. Imidazole (15.8 g, 233 mmol) and *tert*-butyldimethylsilyl chloride[17] (17.5 g, 116 mmol) were added, and the mixture was stirred 21 h at 45 °C (oil bath) under nitrogen atmosphere. After cooling to room temperature, the mixture was poured into 600 mL of pentane:water (1:1). The aqueous layer was extracted with pentane; the combined pentane extracts were washed with water and brine. Removal of solvent in vacuo and distillation (short path with Vigreux column, 0.05 mmHg, 113–120 °C) gave 12.3 g (76.4%) of a colorless oil. An analytical sample was prepared by preparative TLC [hexane:CH_2Cl_2 (1:1), R_f 0.50–0.65], followed by distillation (kugelrohr, 0.20 mmHg, 120–135 °C); IR (CCl_4, cm^{-1}) 1720 (s); NMR (60 MHz, CCl_4) δ 4.15 (t, *J* = 6 Hz, 1 H), 2.35 (d, *J* = 3 Hz, 2 H), 1.48 (q, *J* = 6 Hz, 2 H), 1.28 (d, m, *J* = 2 Hz, 6 H), 0.88 (t, *J* = 6 Hz, 3 H), 0.85 (s, 18 H), 0.06 (s, 3 H), 0.03 (s, 9 H).

Anal. Calcd for $C_{22}H_{44}O_3Si_2$: C, 63.97; H, 10.75. Found: C, 63.69; H, 10.74.

3,3-Dimethyl-6-((*tert*-butyldimethylsilyl)oxy)-4-octyn-1-ol. A solution of 4.35 g (10.5 mmol) of the above silyl ester in 80 mL of dry ether was added dropwise to a suspension of 4.35 g (114 mmol) of $LiAlH_4$ in 200 mL of dry ether under nitrogen atmosphere. The mixture was heated at reflux 3.5 h and cooled in an ice bath. Sodium sulfate decahydrate ($Na_2SO_4 \cdot 10H_2O$) was added to quench the reaction. The solid mass was filtered and washed thoroughly with ether. The filtrate was concentrated in vacuo to afford 3.95 g of colorless oil, which was distilled (kugelrohr, 0.05 mmHg, 110–120 °C) to give 2.72 g (91.2%) of a colorless oil. An analytical sample was prepared via preparative TLC [CH_2Cl_2:hexane (1:1), R_f 0.30–0.35] and kugelrohr distillation; IR (CCl_4, cm^{-1}) 3650–3350 (br), 2230 (w); NMR (60 MHz, CCl_4) δ 4.17 (t, *J* = 6 Hz, 1 H), 3.65 (t, *J* = 7 Hz, 2 H), 1.80 (s, 2 H), 1.55 (m, 3 H), 1.15 (s, 6 H), 0.87 (t, *J* = 7 Hz, 3 H), 0.83 (s, 9 H), 0.03 (s, 3 H), 0.01 (s, 3 H).

Anal. Calcd for $C_{16}H_{32}O_2Si$: C, 67.43; H, 11.33. Found: C, 67.30; H, 11.30.

3,3-Dimethyl-6-((*tert*-butylmethylsilyl)oxy)-4-octyn-1-al (9). To a solution of 4.05 g (51.3 mmol) of dry pyridine in 75 mL of dry CH_2Cl_2 under nitrogen atmosphere at room temperature was added 2.50 g (25.0 mmol) of dry CrO_3. After stirring 15 min, a solution of 1.01 g (3.57 mmol) of the above alcohol in 5 mL of dry CH_2Cl_2 was added. Stirring was continued for 30 min. The mixture was decanted, the residue was washed with 200 mL ether in portions, and the combined organic fractions were washed with 5% NaOH, water, 10% HCl, saturated $NaHCO_3$, and brine. Removal of solvent in vacuo and distillation (kugelrohr, 0.10 mmHg, 85–93 °C) gave 965 mg (96.4%) of **9** as a colorless oil. An analytical sample was prepared by preparative TLC [hexane:CH_2Cl_2 (3:1), R_f 0.55–0.70] and kugelrohr distillation; IR (CCl_4, cm^{-1}) 2722 (s), 1717 (s); NMR (60 MHz, CCl_4) δ 9.72 (t, *J* = 3 Hz, 1 H), 4.20 (t, *J* = 6 Hz, 1 H), 2.29 (app d, *J* = 3 Hz, 2 H), 1.53 (app q, *J* = 7 Hz, 2 H), 1.23 (s, 6 H), 0.90 (t, *J* = 7 Hz, 3 H), 0.83 (s, 9 H), 0.06 (s, 3 H), 0.03 (s, 3 H).

Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.02; H, 10.70. Found: C, 68.06; H, 10.80.

Diastereomeric Mandelate Esters 11a and 11b. To a solution of the vinylogous ether (±)-**10**[6] (5.10 g, 30.0 mmol), pyridine (7.5 mL, 92.7 mmol), and 4-(dimethylamino)pyridine (0.750 g, 6.14 mmol) in methylene chloride (75 mL) was added a solution of (*S*)-(+)-*O*-methylmandeloyl chloride (**12**,[7] 7.94 g, 43.0 mmol) in methylene chloride (15 mL) over the course of 10 min. The mixture was stirred at 0 °C for 5 min and then at room temperature for 2.5 h. To the mixture was added ether (300 mL) and methylene chloride (50 mL), and the resulting solution was washed successively with 1 N hydrochloric acid (2 × 50 mL), 10% aqueous sodium carbonate (50 mL), and saturated aqueous sodium chloride (50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to give a yellow, oily residue, which was purified by flash chromatography (gradient elution: ether/petroleum ether/CH_2Cl_2, 1:2:5 to 1:0:5) to provide two compounds. The first to elute was the *R,S* diastereomer **11a** as a white solid (4.30 g, 45%). An analytical sample was obtained by recrystallization from hexanes/acetone: mp 98.0–100.0 °C; IR ($CHCl_3$) 3010 (m), 1745 (m), 1715 (m), 1640 (s), 1440 (m), 1310 (m), 1195 (m), 900 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.30–7.45 (m, 5 H), 5.25 (s, 2 H), 4.78 (s, 1 H), 4.35–4.55 (m, 2 H), 3.44 (s, 3 H), 2.68–2.93 (ABq, J_{AB} = 17.5 Hz, 2 H), 1.51 (s, 3 H): $[\alpha]_D$ +3.0° (*c* 1.00, $CHCl_3$); HRMS *m/z* ($M^+ + H$)

(14) Fieser, L.; Fieser, M. *Reagents for Organic Synthesis*, Wiley: New York, 1967; Vol. 1, p 566. See also: Hutchins, R. O.; Hutchins, M. G. K. *The Chemistry of Triple-bonded Functional Groups*, Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1983; Suppl. C, Part 1; p 571, and references therein.

(15) Efforts to enhance the stereoselectivity of this process are currently underway.

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

(17) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

319.1195 (calcd for $C_{17}H_{19}O_6$, 319.1182).

Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.32; H, 5.74.

The next to elute was the *S,S* diastereomer **11b** as a white solid (4.0 g, 43%). An analytical sample was obtained by recrystallization from hexanes/acetone: mp 79–80 °C; IR ($CHCl_3$) 3010 (m), 1745 (m), 1710 (m), 1640 (s), 1435 (m), 1310 (m), 1195 (m), 900 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.30–7.45 (m, 5 H), 5.26 (s, 2 H), 4.79 (s, 1 H), 4.40–4.60 (m, 2 H), 3.41 (s, 3 H), 2.55–2.83 (ABq, J_{AB} = 17.6 Hz, 2 H), 1.44 (s, 3 H); $[\alpha]_D$ +130.6° (*c* 1.47, $CHCl_3$); HRMS *m/z* (M^+ + H) 319.1166 (calcd for $C_{17}H_{19}O_6$, 319.1182).

Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 64.52; H, 5.81.

(4*R*)-(−)-4-Hydroxy-4-methyl-2-(((triethylsilyl)oxy)methyl)-2-cyclopentenone (7a). To a flask containing ether (20 mL) was added a solution of aluminum hydride in ether[8] (0.14 M, 73.4 mL, 10.7 mmol). The mixture was cooled to 0 °C, and a solution of the mandelate ester **11a** (1.26 g, 3.96 mmol) in ether (20 mL) was added slowly (15 min). Following the addition, the mixture was stirred at 0 °C for an additional 15 min, and then tetrahydrofuran (120 mL) and 6 N aqueous hydrochloric acid (4.74 mL) were added. The mixture was stirred for an additional 20 min while the mixture warmed to room temperature. The layers were separated and the aqueous layer was extracted with methylene chloride (3 × 60 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and evaporated to provide a yellow, oily residue that was filtered through a small column of silica gel to provide the crude diol **13a**. To a solution of the crude diol **13a** and triethylamine (620 μL, 4.45 mmol) in tetrahydrofuran (10 mL) was added chlorotriethylsilane (1.0 mL, 5.94 mmol). The mixture was stirred at room temperature for 30 min, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography to provide (4*R*)-(−)-4-hydroxy-4-methyl-2-(((triethylsilyl)oxy)methyl)-2-cyclopentenone (**7a**) as a colorless oil (609 mg, 60%). An analytical sample was obtained by reduced pressure distillation (bp 128–130 °C, 0.4 mmHg): IR ($CHCl_3$) 3580 (w), 2950 (m), 2870 (m), 1705 (s), 1120 (m), 1000 (m) cm^{-1}; UV (EtOH) λ_{max} 220 (ϵ 7800) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 2.0, 2.0 Hz, 1 H), 4.37 (d, *J* = 2.0 Hz, 2 H), 2.63 (ABq, J_{AB} = 18.5 Hz, $v_0\delta$ = 15.0 Hz, 2 H), 1.73 (s, 1 H), 1.56 (s, 3 H), 0.98 (t, *J* = 8.0 Hz, 9 H), 0.64 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.2, 159.6, 145.7, 74.7, 57.2, 51.8, 27.7, 6.7, 4.3 ppm; $[\alpha]_D$ −24.9° (*c* 1.00, $CHCl_3$); HRMS *m/z* (M^+ + H) 257.1582 (calcd for $C_{13}H_{25}O_3Si$, 257.1573).

(4*S*)-(+)-4-Hydroxy-4-methyl-2-(((triethylsilyl)oxy)methyl)-2-cyclopentenone (7b). The mandelate ester **11b** (0.526 g, 1.65 mmol) was treated in the same manner as described for the preparation of cyclopentenone **7a**. Obtained in this manner was (4*S*)-(+)-4-hydroxy-4-methyl-2-(((triethylsilyl)oxy)methyl)-2-cyclopentenone (**7b**) as a colorless oil (265 mg, 63%). An analytical sample was obtained by reduced pressure distillation (bp 128–130 °C, 0.4 mmHg): IR ($CHCl_3$) 3580 (w), 2950 (m), 2870 (m), 1705 (s), 1120 (m), 1000 (m) cm^{-1}; UV (EtOH) λ_{max} 220 (ϵ 7600) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 2.0, 2.0 Hz, 1 H), 4.37 (d, *J* = 2.0 Hz, 2 H), 2.63 (ABq, J_{AB} = 18.5 Hz, $v_0\delta$ = 15.0 Hz, 2 H), 1.73 (s, 1 H), 1.56 (s, 3 H), 0.98 (t, *J* = 8.0 Hz, 9 H), 0.64 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.2, 159.6, 145.7, 74.7, 57.2, 51.8, 27.7, 6.7, 4.3 ppm; $[\alpha]_D$ +25.3° (*c* 1.00, $CHCl_3$); HRMS *m/z* (M^+ + H) 257.1546 (calcd for $C_{13}H_{25}O_3Si$, 257.1573).

(3*S*,5*R*)-(−)-3,5-Dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-3-methyl-1-(((triethylsilyl)oxy)methyl)cyclopentene (15b). To a solution of 2-ethyl-1,3-dithiane[10] (1.83 mL, 13.5 mmol) in tetrahydrofuran (25 mL) at −65 °C was added *n*-butyllithium in hexanes (2.48 M, 5.0 mL, 12.4 mmol) slowly over the course of 5 min. The mixture was stirred at −65 °C for 5 min, warmed to −15 °C, and stirred at this temperature for 2.5 h. The mixture was then cooled to −65 °C, and a solution of (4*S*)-(+)-4-hydroxy-4-methyl-2-(((triethylsilyl)oxy)methyl)-2-cyclopentenone (**7b**, 1.19 g, 4.64 mmol) in tetrahydrofuran (5 mL) was added. The mixture was allowed to warm slowly to 0 °C (1 h), and then saturated aqueous ammonium chloride (2.5 mL) was added. To a separatory funnel containing chloroform (175 mL) and water (10 mL) was added the reaction mixture. The mixture was shaken, the layers were separated, and the aqueous layer was extracted with chloroform (3 × 25 mL). The organic layers were combined, dried over anhydrous sodium sulfate, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography (gradient elution: acetone/$CHCl_3$; 2% acetone to 10% acetone) to provide two products. The first to elute was (3*S*,5*S*)-(+)-3,5-dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-3-methyl-1-(((triethylsilyl)oxy)methyl)cyclopentene (**16b**) as a viscous, colorless oil (0.097 g, 5%): IR ($CHCl_3$) 3580 (w), 3440 (br, w), 2950 (m), 2870 (m), 1455 (w), 1410 (w), 1370 (w), 1280 (m), 1000 (m) cm^{-1}; UV (EtOH) λ_{max} 245 (ϵ 880), 209 (ϵ 2370) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 5.79 (d, *J* = 0.9 Hz, 1 H), 4.81 (d, *J* = 13.1 Hz, 1 H), 4.50 (dd, *J* = 13.1, 0.9 Hz, 1 H), 3.79 (s, 1 H), 2.89 (m, 4 H), 2.68 (d, *J* = 14.9 Hz, 1 H), 2.24 (d, *J* = 14.9 Hz, 1 H), 2.15 (m, 2 H), 2.03 (m, 1 H), 1.87 (m, 2 H), 1.47 (s, 3 H), 1.21 (t, *J* = 7.3 Hz, 3 H), 0.99 (t, *J* = 8.0 Hz, 9 H), 0.66 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 145.4, 138.7, 92.8, 78.2, 62.2, 61.3, 54.0, 30.9, 28.6, 26.5, 24.3, 11.0, 6.8, 4.3 ppm; $[\alpha]_D$ +17.2° (*c* 1.00, $CHCl_3$); HRMS *m/z* (M^+ − H) 403.1780 (calcd for $C_{19}H_{35}O_3S_2Si$, 403.1797).

The second compound to elute was the diastereomeric (3*S*,5*R*)-(−)-**15b** as a viscous, colorless oil (1.74 g, 93%): IR ($CHCl_3$) 3580 (w), 3440 (br, w), 2950 (m), 2860 (m), 1450 (w), 1410 (w), 1370 (w), 1140 (m) cm^{-1}; UV (EtOH) λ_{max} 246 (ϵ 1140), 227 (ϵ 1320), 210 (ϵ 2430) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 5.87 (s, 1 H), 4.63 (ABq, J_{AB} = 13.7 Hz, $v_0\delta$ = 67.6 Hz, 2 H), 3.47 (br s, 1 H), 2.86 (br m, 4 H), 2.51 (d, *J* = 14.5 Hz, 1 H), 2.14 (d, *J* = 14.5 Hz, 1 H), 2.10 (br s, 1 H), 2.01 (br m, 2 H), 1.86 (br s, 2 H), 1.41 (s, 3 H), 1.20 (t, *J* = 7.4 Hz, 3 H), 1.00 (t, *J* = 8.0 Hz, 9 H), 0.66 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 148.4, 137.9, 78.3, 61.5, 60.2, 52.1, 30.3, 26.9, 26.2, 24.5, 11.0, 6.8, 4.4 ppm; $[\alpha]_D$ −9.7° (*c* 1.00, $CHCl_3$); HRMS *m/z* (M^+ − H) 403.1758 (calcd for $C_{19}H_{35}O_3S_2Si$, 403.1797).

(3*S*,5*R*)-3,5-Dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-1-(hydroxymethyl)-3-methylcyclopentene (17b). To a solution of (3*S*,5*R*)-(−)-3,5-dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-3-methyl-1-(((triethylsilyl)oxy)methyl)cyclopentene (**15b**, 101 mg, 0.25 mmol) in tetrahydrofuran (1.0 mL) at room temperature was added a solution of tetra-*n*-butylammonium fluoride trihydrate (118 mg, 0.375 mmol) in tetrahydrofuran (400 μL). The reaction was stirred at room temperature for 5 min, and the solvents were removed in vacuo. The residue was purified by flash chromatography (gradient elution: acetone/EtOAc; 1:9 to 1:4) to provide (3*S*,5*R*)-3,5-dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-1-(hydroxymethyl)-3-methylcyclopentene (**17b**) as a white solid (52 mg, 72%). Recrystallization from EtOAc provided white crystals suitable for single-crystal X-ray analysis: mp 152.0–154.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 5.85 (d, *J* = 0.6 Hz, 1 H), 4.72 (br d, *J* = 13.7 Hz, 1 H), 4.45 (br dd, *J* = 13.7, 5.7 Hz, 1 H), 3.73 (br s, 1 H), 3.10–2.80 (m, 4 H), 2.67 (s, 1 H), 2.51 (d, *J* = 14.8 Hz, 1 H), 2.15 (d, *J* = 14.8 Hz, 1 H), 2.10–1.80 (m, 4 H), 1.68 (s, 1 H), 1.40 (s, 3 H), 1.20 (t, *J* = 7.4 Hz, 3 H).

(3*S*,5*R*)-(−)-3,5-Dihydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (19b). To a solution of (3*S*,5*R*)-(−)-3,5-dihydroxy-5-(2-ethyl-1,3-dithian-2-yl)-3-methyl-1-(((triethylsilyl)oxy)methyl)cyclopentene (**15b**, 1.57 g, 3.88 mmol) and diisopropylamine (1.65 mL, 11.8 mmol) in tetrahydrofuran (100 mL) was added dropwise a solution of mercury(II) perchlorate trihydrate[11] in tetrahydrofuran (0.50 M, 18.0 mL, 9.00 mmol). The addition required 50 min, after which the mixture was stirred for an additional 10 min. The mixture was then filtered with suction, the grey solid was washed with ether (750 mL), and the combined organic layers were washed with 5% aqueous sodium bicarbonate (80 mL) and saturated aqueous sodium chloride (50 mL). The organic layer was dried over anhydrous potassium carbonate, filtered, and evaporated to give an oily residue that was purified by flash chromatography (EtOAc/hexanes, 1:1) to provide (3*S*,5*R*)-(−)-3,5-dihydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**19b**) as a colorless oil (0.941 g, 77%): IR ($CHCl_3$) 3580 (w), 3440 (br, w), 2950 (m), 2870 (m), 1705 (m), 1455 (w), 1380 (w), 1110 (m), 1070 (m), 1000 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (s, 1 H), 4.51 (s, 1 H), 4.19 (ABX, J_{AB} = 13.1 Hz, $v_0\delta$ = 15.3 Hz, J_{AX} = 1.4 Hz, J_{BX} = 1.4 Hz, 2 H), 2.56 (m, 2 H), 2.41 (d, *J* = 14.9 Hz, 1 H), 2.07 (d, *J* = 14.9 Hz, 1 H), 2.01 (s, 1 H), 1.50 (s, 3 H), 1.10 (t, *J* = 7.2 Hz, 3 H), 0.94 (t, *J* = 8.0 Hz, 9 H), 0.59 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 212.3, 145.7, 138.0, 88.8, 80.6, 58.8, 53.0, 29.1, 26.6, 7.9, 6.6, 4.1 ppm; $[\alpha]_D$ −88.8° (*c* 1.00, $CHCl_3$); HRMS *m/z* (M^+ + NH_4) 332.2233 (calcd for $C_{16}H_{34}O_4NSi$, 332.2257).

(3*S*,5*R*)-(−)-3,5-Bis((trimethylsilyl)oxy)-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (20b). To a solution of (3*S*,5*R*)-(−)-3,5-dihydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**19b**, 0.895 g, 2.85 mmol) and triethylamine (2.4 mL, 17.2 mmol) in dimethylformamide (15 mL) at room temperature was added chlorotrimethylsilane (1.8 mL, 14.2 mmol). The mixture was stirred at room temperature for 30 min and then transferred to a separatory funnel containing hexanes (400 mL) and 5% aqueous sodium bicarbonate (50 mL). The mixture was shaken, the layers were separated, and the organic layer was washed with saturated aqueous sodium chloride (50 mL). The organic layer was dried over anhydrous potassium carbonate, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography (gradient elution: 2% ether in petroleum ether to 10% ether in petroleum ether) to provide (3*S*,5*R*)-(−)-3,5-bis((trimethylsilyl)oxy)-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**20b**) as a colorless oil (1.21 g, 93%): IR ($CHCl_3$) 2960 (m), 2870 (m), 1715 (m), 1455 (w),

1250 (s), 1130 (m), 1080 (m), 1000 (m), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (dd, J = 1.4, 1.4 Hz, 1 H), 4.11 (ABX, J_{AB} = 14.1 Hz, $v_0\delta$ = 61.2 Hz, J_{AX} = 1.4 Hz, J_{BX} = 1.4 Hz, 2 H), 2.60 (m, 2 H), 2.48 (d, J = 14.3 Hz, 1 H), 2.25 (d, J = 14.3 Hz, 1 H), 1.49 (s, 3 H), 1.02 (t, J = 7.2 Hz, 3 H), 0.96 (t, J = 8.0 Hz, 9 H), 0.60 (q, J = 8.0 Hz, 6 H), 0.17 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 213.8, 145.6, 136.2, 91.3, 82.7, 58.4, 55.2, 30.9, 29.2, 7.8, 6.7, 4.3, 2.3, 1.9 ppm; $[\alpha]_D$ -73.0° (c 1.00, $CHCl_3$); HRMS m/z ($M^+ - CH_3$) 443.2497 (calcd for $C_{21}H_{43}O_4Si_3$, 443.2469).

Anal. Calcd for $C_{22}H_{46}O_4Si_3$: C, 57.59; H, 10.10. Found: C, 57.39; H, 9.79.

β-Hydroxy Ketone 6b. To a cooled (-45 °C) solution of diisopropylamine (0.500 mL, 3.57 mmol) in tetrahydrofuran (30 mL) was added a solution of *n*-butyllithium in hexanes (2.48 M, 1.25 mL, 3.10 mmol). The mixture was stirred at -45 °C for 1 h and cooled to -78 °C, and then a solution of (3*S*,5*R*)-(-)-3,5-bis((trimethylsilyl)oxy)-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**20b**, 1.17 g, 2.55 mmol) in tetrahydrofuran (6 mL) was added dropwise over the course of 5 min. The reaction mixture was stirred at -78 °C for 3 h, and then a solution of aldehyde (±)-(**9**) (1.01 g, 3.57 mmol) in tetrahydrofuran (6 mL) was added dropwise over the course of 5 min. The mixture was stirred at -78 °C for 30 min, and then saturated aqueous ammonium chloride (0.75 mL) was added. The mixture was brought to room temperature and transferred to a separatory funnel containing ether (500 mL) and methylene chloride (250 mL). The mixture was washed successively with water (100 mL) and saturated aqueous sodium chloride (100 mL). The organic layer was dried with anhydrous sodium sulfate, filtered, and evaporated to give an oily residue that was purified by flash chromatography (gradient elution: 0.5% ether in CH_2Cl_2 to 1.0% ether in CH_2Cl_2) to provide the β-hydroxy ketone **6b**, a complex diastereomeric mixture, as a viscous, colorless oil (1.36 g, 72%): IR ($CHCl_3$) 3620 (w), 2950 (s), 2870 (s), 1705 (m), 1460 (m), 1250 (s), 1110 (s), 1000 (s), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (s 1 H), 4.27 (dd, J = 6.3, 6.3 Hz, 1 H), 4.20-3.95 (m, 3 H), 3.30-3.00 (m, 2 H), 2.65-2.20 (m, 2 H), 1.70-0.85 (m, 28 H), 0.91 (s, 9 H), 0.62 (m, 6 H), 0.21 (s, 9 H), 0.14 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H).

Enal-Dione 21b. To a solution of pyridine (5.35 mL, 66.2 mmol) in methylene chloride (75 mL) at room temperature was added portionwise chromium trioxide (3.28 g, 32.8 mmol) over the course of 5 min. The mixture was stirred for 20 min and then a solution of the β-hydroxy ketone **6b** (1.35 g, 1.82 mmol) in methylene chloride (5 mL) was added. The mixture was stirred at room temperature for 6 h, and then ether was added (300 mL). The mixture was washed successively with 5% aqueous sodium bicarbonate (5 × 100 mL) and saturated aqueous sodium chloride (100 mL). The resulting brown suspension was dried over anhydrous sodium sulfate, filtered, and evaporated to give a dark red residue that was purified by flash chromatography [(a) 10% ether in petroleum ether and (b) gradient elution: acetone/$CHCl_3$/hexanes; 1:19:40 to 1:19:20] to provide enal-dione **21b** as a viscous, colorless oil (0.810 g, 72%): IR ($CHCl_3$) 2950 (s), 2850 (m), 1725 (m), 1705 (m), 1690 (s), 1460 (m), 1345 (m), 1250 (s), 1140 (m), 1050 (m), 1000 (m), 840 (s) cm^{-1}; UV (EtOH) λ_{max} 220 (ϵ 10700), 204 (ϵ 10800) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 9.66 (s, 1 H), 6.75 (s, 1 H), 4.61 (m, 1 H), 4.26 (dd, J = 6.3, 6.3 Hz, 1 H), 3.00-2.15 (m, 4 H), 1.70-1.55 (m, 2 H), 1.60 (s, 3 H), 1.40-1.30 (m, 6 H), 1.23 (d, J = 7.1 Hz, 3 H), 1.00-0.85 (m, 3 H), 0.91 (s, 9 H), 0.25-0.10 (m, 24 H); HRMS m/z ($M^+ + NH_4$) 640.3816 (calcd for $C_{32}H_{62}O_6NSi_3$, 640.3885).

3-(2*H*)-Furanone-Aldehyde 22b. To a solution of enal-dione **21b** (0.810 g, 1.44 mmol) in tetrahydrofuran (75 mL) was added 1 N aqueous hydrochloric acid (27.5 mL). The mixture was stirred at room temperature for 66 h, and then ether (150 mL), methylene chloride (200 mL), and solid sodium chloride (10 g) were added. The mixture was shaken vigorously, the layers were separated, and the organic layer was washed successively with saturated aqueous sodium bicarbonate (50 mL) and saturated aqueous sodium chloride (50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and evaporated to give a colorless, oily residue that was purified by flash chromatography to provide 3-(2*H*)-furanone-aldehyde **22b** as a colorless gum (0.407 g, 90%): IR ($CHCl_3$) 3640 (w), 3400 (br, w), 2970 (m), 1695 (s), 1625 (s), 1400 (w), 1370 (m) cm^{-1}; UV (EtOH) λ_{max} 278 (ϵ 10300), 206 (ϵ 10400) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 9.67 (s, 1 H), 7.03 (s, 1 H), 4.26 (m, 1 H), 2.70-2.25 (m, 6 H), 1.78 (s, 3 H), 1.75-1.60 (m, 2 H), 1.64 (s, 3 H), 1.40-1.25 (m, 6 H), 0.97 (m, 3 H); $[\alpha]_D$ -18.6° (c 1.01, $CHCl_3$); HRMS m/z ($M^+ + NH_4$) 364.2094 (calcd for $C_{20}H_{30}O_5N$, 364.2124).

Acetal-Alcohol 23b. To a solution of 3-(2*H*)-furanone-aldehyde **22b** (139 mg, 0.40 mmol) and ethylene glycol (2.25 mL, 40.0 mmol) in tetrahydrofuran (100 mL) was added *p*-toluenesulfonic acid monohydrate (3.8 mg, 0.02 mmol). The reaction mixture was stirred at room temperature for 2 h, and then the solvents were removed slowly (1 h) by vacuum distillation. To the residue was added saturated aqueous sodium bicarbonate (8 mL) and ether (60 mL), and the mixture was vigorously shaken. The layers were separated, and the aqueous layer was extracted with ether (10 mL). The combined organic layers were dried over anhydrous potassium carbonate, filtered, and evaporated to give a colorless gum that was purified by flash chromatography (ether/EtOAc; 9:1) to provide acetal-alcohol **23b** as a colorless gum (115 mg, 74%): IR ($CHCl_3$) 3640 (w), 3420 (br, w), 2970 (m), 1695 (m), 1625 (s), 1400 (m), 1370 (m), 1100 (m) cm^{-1}; UV (EtOH) λ_{max} 278 (ϵ 10200), 203 (ϵ 8300) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 6.26 (d, J = 3.1 Hz, 1 H), 5.48 (m, 1 H), 4.24 (m, 1 H), 3.98-3.78 (m, 4 H), 2.75-2.15 (m, 6 H), 1.74 (s, 3 H), 1.70-1.60 (m, 2 H), 1.57 (s, 3 H), 1.35 (s, 3 H), 1.35 (s, 3 H), 0.97 (t, J = 7.3 Hz, 3 H); $[\alpha]_D$ -26.5° (c 1.00, $CHCl_3$); HRMS m/z (M^+ - OH) 373.1966 (calcd for $C_{22}H_{29}O_5$, 373.2015).

Acetal-Ketone 5b. To a solution of pyridine (0.590 mL, 7.29 mmol) in methylene chloride (8 mL) was added chromium trioxide (360 mg, 3.60 mmol) in one portion. The mixture was stirred at room temperature for 20 min, and then a solution of acetal-alcohol **23b** (115 mg, 0.295 mmol) in methylene chloride (1.5 mL) was added. The mixture was stirred at room temperature for 15 min, and then ether (50 mL) and 5% aqueous sodium hydroxide (10 mL) were added. The mixture was vigorously shaken, the layers were separated, and the organic layer was washed successively with 5% aqueous sodium hydroxide (2 × 10 mL), 1 N aqueous hydrochloric acid (10 mL), saturated aqueous sodium bicarbonate (10 mL), and saturated aqueous sodium chloride (10 mL). The organic layer was dried over anhydrous potassium carbonate, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography [(a) gradient elution EtOAc/hexanes 3:2 to 3:1 and (b) ether] to provide acetal-ketone **5b** as a colorless gum (89 mg, 78%): IR ($CHCl_3$) 3600 (w), 2970 (m), 2200 (m), 1695 (m), 1670 (s), 1625 (s), 1400 (m), 1370 (m) cm^{-1}; UV (EtOH) λ_{max} 278 (ϵ 11100), 212 (ϵ 10000) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 6.26 (s, 1 H), 5.41 (s, 1 H), 3.95-3.75 (m, 4 H), 2.71 (s, 2 H), 2.53 (q, J = 7.4 Hz, 2 H), 2.48 (d, J = 14.2 Hz, 1 H), 2.23 (d, J = 14.2 Hz, 1 H), 2.00 (s, 1 H), 1.75 (s, 3 H), 1.58 (s, 3 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 1.12 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 204.1, 188.4, 181.5, 143.4, 140.0, 112.6, 98.7, 97.8, 95.0, 80.7, 80.2, 64.8, 64.5, 51.2, 40.8, 38.7, 32.0, 28.8, 28.8, 27.4, 8.0, 6.5 ppm; $[\alpha]_D$ -45.1° (c 1.00, $CHCl_3$); HRMS m/z (M^+ - OH) 371.1842 (calcd for $C_{22}H_{27}O_5$, 371.1858).

Intramolecular Mukaiyama Acetal Aldol Reaction of Acetal-Ketone 5b. To a solution of diisopropylamine (27 μL, 0.193 mmol) in tetrahydrofuran (1.4 mL) at -45 °C was added a solution of *n*-butyllithium in hexanes (2.82 M, 62 μL, 0.174 mmol). The mixture was stirred at -45 °C for 1 h and cooled to -78 °C, and then a solution of acetal-ketone **5b** (27.2 mg, 0.070 mmol) in tetrahydrofuran (250 μL) was added. The mixture was stirred at -78 °C for 1 h, and then chlorotrimethylsilane (58 μL, 0.457 mmol) was added. The mixture was stirred at -78 °C for 15 min, warmed to 0 °C (15 min), and then stirred at this temperature for an additional 1.5 h. The solvents were removed by vacuum distillation, and to the residue was added methylene chloride (1.4 mL). The solution was cooled to -78 °C, and a solution of titanium tetrachloride in methylene chloride (1.0 M, 140 μL, 0.140 mmol) was added. The mixture was stirred at -78 °C for 1 h, and then ether (4 mL) and saturated aqueous sodium carbonate (800 μL) were added simultaneously and with vigorous stirring. The mixture was brought to room temperature, and water (500 μL) was added. The mixture was shaken vigorously, the layers were separated, and the aqueous layer was extracted with ether (2 × 4 mL) and methylene chloride (4 mL). The combined organic layers were dried over anhydrous potassium carbonate, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography (EtOAc) and preparative thin-layer chromatography (500 μm, 20 cm × 20 cm, $CHCl_3$/acetone; 3:1) to provide two compounds. The less polar product, 6α-methyl diastereomer **25b**, was isolated as a colorless glass (4.5 mg, 17%): IR ($CHCl_3$) 3580 (w), 3460 (br, w), 3000 (m), 2980 (m), 2920 (m), 2200 (m), 1680 (s), 1615 (s), 1450 (m), 1370 (m), 1080 (m) cm^{-1}; UV (EtOH) λ_{max} 278 (ϵ 7600), 219 (ϵ 6800), 202 (ϵ 8700) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 5.95 (s, 1 H), 3.78 (d, J = 6.7 Hz, 1 H), 3.50 (m, 1 H), 3.50-3.30 (m, 4 H), 2.83 (d, J = 13.1 Hz, 1 H), 2.64 (d, J = 13.1 Hz, 1 H), 2.44 (d, J = 13.6 Hz, 1 H), 2.25 (d, J = 13.6 Hz, 1 H), 2.10 (dd, J = 6.6, 6.6 Hz, 1 H), 1.78 (s, 1 H), 1.76 (s, 3 H), 1.64 (s, 3 H), 1.43 (s, 3 H), 1.42 (s, 3 H), 1.14 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 206.3, 188.0, 182.1, 143.6, 139.6, 111.0, 103.6, 95.3, 84.7, 82.2, 80.0, 73.9, 61.8, 54.2, 51.1, 42.6, 33.4, 29.6, 29.2, 28.4, 14.3, 7.2 ppm; $[\alpha]_D$ -296° (c 0.750, $CHCl_3$); HRMS m/z ($M^+ + H$) 389.1965 (calcd for $C_{22}H_{29}O_6$, 389.1966).

The more polar product, 6β-methyl diastereomer **24b**, was also isolated as a colorless glass (13 mg, 48%): IR ($CHCl_3$) 3580 (w), 3440 (br, w), 3000 (m), 2970 (m), 2920 (m), 2190 (m), 1685 (s), 1625 (s), 1400 (m), 1370 (m), 1050 (m), 1000 (m) cm^{-1}; UV (EtOH) λ_{max} 279 (ϵ 7300), 203

(ε 9100) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.10 (d, J = 1.3 Hz, 1 H), 4.70 (br s, 1 H), 3.65 (m, 2 H), 3.52 (m, 2 H), 2.93 (d, J = 13.6 Hz, 1 H), 2.58 (d, J = 13.6 Hz, 1 H), 2.50 (br s, 1 H), 2.46 (d, J = 13.7 Hz, 1 H), 2.40 (br s, 1 H), 2.29 (d, J = 13.7 Hz, 1 H), 1.88 (s, 1 H), 1.73 (s, 3 H), 1.64 (s, 3 H), 1.59 (s, 3 H), 1.43 (s, 3 H), 1.02 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.4, 188.2, 183.3, 141.7, 141.2, 112.3, 104.7, 95.7, 83.2, 80.5, 77.6, 71.8, 61.7, 54.0, 51.1, 41.5, 32.9, 30.0, 29.4, 27.8, 8.8, 6.4 ppm; $[\alpha]_D$ −35.4° (c 0.750, $CHCl_3$); HRMS m/z (M^+ + H) 389.1946 (calcd for $C_{22}H_{29}O_6$, 389.1966).

C(5,6)-Trans-Olefin 26b. Method A: From 6β-Methyl Diastereomer 24b. To a cooled (10 °C) solution of the 6β-methyl diastereomer **24b** (7.8 mg, 0.020 mmol) and diazabicycloundecane (45 μL, 0.30 mmol) in benzene (1.0 mL) was added a solution of p-toluenesulfonyl chloride in benzene (0.10 M, 200 μL, 0.020 mmol). The mixture was brought to room temperature slowly (30 min) and then stirred at this temperature for 20 h. The solvents were removed in vacuo, and the residue was purified by flash chromatography (EtOAc/hexanes; 3:2) to provide the C(5,6)-trans-olefin **26b** (4.8 mg, 74%).

Method B: From 6α-Methyl Diastereomer 25b. To a cooled (10 °C) solution of the 6α-methyl diastereomer **25b** (2.3 mg, 0.0060 mmol) in benzene (360 μL) was added diazabicycloundecane (13.5 μL, 0.090 mmol). The mixture was stirred while warming to room temperature (5 min), and the solvents were removed by vacuum distillation. The residue was purified by flash chromatography (EtOAc/hexanes; 3:2) to provide olefin **26b** (1.7 mg, 72%): IR ($CHCl_3$) 3580 (w), 3000 (m), 2960 (m), 2905 (m), 2190 (m), 1695 (s), 1650 (s), 1620 (s), 1360 (m), 1070 (m), 1060 (m), 1000 (m) cm^{-1}; UV (EtOH) λ_{max} 283 (ε 13900), 241 (ε 8000), 201 (ε 8400) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (dd, J = 1.2, 1.2 Hz, 1 H), 6.29 (s, 1 H), 2.90 (d, J = 13.8 Hz, 1 H), 2.65 (d, J = 13.8 Hz, 1 H), 2.58 (d, J = 13.7 Hz, 1 H), 2.29 (d, J = 13.7 Hz, 1 H), 1.94 (d, J = 1.2 Hz, 3 H), 1.90 (s, 1 H), 1.83 (s, 3 H), 1.81 (s, 3 H), 1.55 (s, 3 H), 1.48 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 204.2, 183.8, 182.2, 141.8, 140.2, 138.0, 136.1, 114.3, 105.7, 97.6, 82.5, 82.2, 48.2, 42.9, 34.9, 31.0, 30.7, 28.6, 12.0, 7.9 ppm; $[\alpha]_D$ +16.8° (c 0.250, $CHCl_3$); HRMS m/z (M^+ + H) 327.1617 (calcd for $C_{20}H_{23}O_4$, 327.1596).

C(5,6)-Cis-Olefin 27b. A solution of the C(5,6)-trans-olefin **26b** (3.3 mg, 0.01 mmol) in ether (3 mL) was irradiated with ultraviolet light from a Mineralight lamp, No. UVS-11 (254 nm) at room temperature for 7 h. The solvent was removed in vacuo, and the residue was purified by flash chromatography to provide the C(5,6)-cis-olefin **27b** as a colorless, viscous oil (3.2 mg, 97%): IR ($CHCl_3$) 3580 (w), 3000 (m), 2970 (m), 2910 (m), 2200 (m), 1685 (s), 1670 (s), 1625 (s), 1370 (m), 1300 (m), 1080 (m), 910 (w) cm^{-1}; UV (EtOH) λ_{max} 284 (ε 7900), 225 (ε 6900), 203 (ε 7900) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.98 (d, J = 2.1 Hz, 1 H), 5.71 (dq, J = 2.1, 1.7 Hz, 1 H), 2.91 (d, J = 14.5 Hz, 1 H), 2.60 (d, J = 14.5 Hz, 1 H), 2.44 (d, J = 14.1 Hz, 1 H), 2.12 (d, J = 14.1 Hz, 1 H), 1.96 (s, 1 H), 1.88 (d, J = 1.7 Hz, 3 H), 1.75 (s, 3 H), 1.49 (s, 3 H), 1.47 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 203.2, 184.0, 182.6, 146.4, 145.5, 139.5, 121.1, 112.3, 106.4, 97.4, 84.5, 80.7, 49.4, 41.7, 32.7, 29.5, 29.4, 25.5, 19.7, 6.2 ppm; $[\alpha]_D$ +56.3° (c 0.250, $CHCl_3$); HRMS m/z (M^+ + H) 327.1580 (calcd for $C_{20}H_{23}O_4$, 327.1596).

(+)-Hydroxyjatrophone B (3). A vial containing a suspension of $Pd/BaSO_4$ (15 mg) in pyridine (300 μL) was purged with H_2 via balloon. The mixture was stirred at room temperature for 10 min, during which time the color of the mixture changed from brown to black. The balloon was removed and a solution of the C(5,6)-cis-olefin **27b** (3.0 mg, 0.0090 mmol) in pyridine (300 μL) was added. The mixture was stirred for 2 min and then filtered through a small column of silica gel (1.0 × 4.5 cm) with the aid of ether (20 mL). The filtrate was evaporated, and to a solution of the residue in acetic acid (500 μL) was added solid potassium iodide (5 mg). The mixture was stirred at room temperature for 10 min, and then the solvent was evaporated in vacuo. The residue was dissolved in methylene chloride (1.0 mL), and then this solution was dried over anhydrous potassium carbonate, filtered, and evaporated. The resulting residue was purified by thin-layer chromatography (250 μm; 5 × 20 cm; ether) to provide two compounds. The lower R_f compound was the starting material; **27b** (1.5 mg). The higher R_f compound was (+)-hydroxyjatrophone B (**3**) isolated as a colorless, viscous oil (1.0 mg, 67% based on starting material recovery): ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.49 (d, J = 16.2 Hz, 1 H), 6.04 (d, J = 16.2 Hz, 1 H), 5.88 (d, J = 1.9 Hz, 1 H), 5.79 (s, 1 H), 2.90 (d, J = 14.7 Hz, 1 H), 2.46 (d, J = 14.7 Hz, 1 H), 2.39 (d, J = 14.3 Hz, 1 H), 2.04 (d, J = 14.3 Hz, 1 H), 1.91 (d, J = 1.4 Hz, 3 H), 1.76 (s, 3 H), 1.68 (br s, 1 H), 1.45 (s, 3 H), 1.38 (s, 3 H), 1.27 (s, 3 H); $[\alpha]_D$ +230° (c 0.070, $CHCl_3$); TLC R_f 0.32 (Et_2O), 0.40 (EtOAc:hexanes, 3:1), 0.42 ($CHCl_3$:acetone, 4:1), 0.27 (hexanes:acetone, 2:1), 0.36 (CH_2Cl_2:EtOH, 9:1), 0.27 (benzene:EtOH, 19:1). HRMS m/z (M^+ + H) 329.1753 (calcd for $C_{20}H_{25}O_4$, 329.1754).

Synthetic (+)-hydroxyjatrophone B (**3**) was in all respects (500-MHz ^{1}H NMR, HRMS, optical rotation, and TLC mobility in six solvent systems) identical with an authentic sample of the natural material.[1]

(4*R*)-(−)-4-Methyl-2-(((triethylsilyl)oxy)methyl)-4-((trimethylsilyl)oxy)-2-cyclopentenone (14a). To a cooled (0 °C) solution of (4*R*)-(−)-4-hydroxy-4-methyl-2-((triethylsilyloxy)methyl)-2-cyclopentenone (**7a**, 256.4 mg, 1.0 mmol) and triethylamine (560 μL, 4.0 mmol) in dimethylformamide (5 mL) was added chlorotrimethylsilane (320 μL, 2.5 mmol). The mixture was stirred at 0 °C for 10 min, warmed to room temperature, and stirred at this temperature for 2 h. The reaction mixture was transferred to a separatory funnel containing hexanes (150 mL) and 5% aqueous sodium bicarbonate (20 mL), the resulting mixture was shaken vigorously, and the layers were separated. The organic layer was washed with saturated aqueous sodium chloride (25 mL), dried over anhydrous sodium sulfate, filtered, and evaporated to give an oily residue that was purified by flash chromatography (hexanes/EtOAc; 15:1) to provide (4*R*)-(−)-4-methyl-2-(((triethylsilyl)oxy)methyl)-4-((trimethylsilyl)oxy)-2-cyclopentenone (**14a**) as a colorless oil (298 mg, 91%): IR ($CHCl_3$) 2970 (m), 2905 (m), 2875 (m), 1700 (s), 1250 (m), 1120 (m), 1000 (m), 840 (s) cm^{-1}; UV (EtOH) λ_{max} 220 (ε 7300) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 1.9, 1.9 Hz, 1 H), 4.36 (m, 2 H), 2.61 (ABq, J_{AB} = 18.3 Hz, $v_0\delta$ = 56.2 Hz, 2 H), 1.52 (s, 3 H), 0.98 (t, J = 8.0 Hz, 9 H), 0.64 (q, J = 8.0 Hz, 6 H), 0.13 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.4, 160.7, 144.7, 76.6, 57.2, 52.8, 29.3, 6.7, 4.3, 2.1 ppm; $[\alpha]_D$ −10.8° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 329.1968 (calcd for $C_{16}H_{33}O_3Si_2$, 329.1970).

(3*R*,5*R*)-(+)-5-(2-Ethyl-1,3-dithian-2-yl)-5-hydroxy-3-methyl-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (15a). To a solution of 2-ethyl-1,3-dithiane[10] (3.60 mL, 26.6 mmol) in tetrahydrofuran (45 mL) at −65 °C was added n-butyllithium in hexanes (2.65 M, 8.0 mL, 21.2 mmol) slowly over the course of 5 min. The mixture was stirred at −65 °C for 5 min, warmed to −15 °C, and stirred at this temperature for 2.5 h. The solvents were removed in vacuo (0.2 mmHg, 0–10 °C), and benzene (60 mL) was added. To this solution of 2-lithio-2-ethyl-1,3-dithiane in benzene at 10 °C was added a solution of (4*R*)-(−)-4-methyl-2-(((triethylsilyl)oxy)methyl)-4-((trimethylsilyl)oxy)-2-cyclopentenone (**14a**, 3.45 g, 10.5 mmol) in benzene (10 mL). The mixture was stirred at 10 °C for 5 min, and then 5 M aqueous ammonium chloride (2 mL) was added. To a separatory funnel containing chloroform (450 mL) and water (75 mL) was added the reaction mixture. The mixture was shaken, the layers were separated, and the organic layer was washed with saturated aqueous sodium chloride (75 mL), dried over anhydrous sodium sulfate, filtered, and evaporated to give a yellow, oily residue that was purified by flash chromatography (gradient elution: petroleum ether/ether; 19:1 to 9:1) to provide two products. The first to elute was (3*R*,5*S*)-(+)-(2-ethyl-1,3-dithian-2-yl)-5-hydroxy-3-methyl-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (**16a**) as a viscous, colorless oil (3.78 g, 57%): IR ($CHCl_3$) 3450 (br, w), 2950 (m), 2870 (m), 1450 (w), 1410 (w), 1370 (w), 1245 (m), 1120 (m), 1000 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (s, 1 H), 4.76 (br m, 1 H), 4.62 (dd, J = 15.3, 1.8 Hz, 1 H), 3.05–2.70 (br m, 5 H), 2.43 (d, J = 14.2 Hz, 1 H), 2.20 (d, J = 14.2 Hz, 1 H), 2.10–1.75 (br m, 4 H), 1.44 (s, 3 H), 1.19 (t, J = 7.4 Hz, 3 H), 1.01 (t, J = 8.0 Hz, 9 H), 0.67 (q, J = 8.0 Hz, 6 H), 0.13 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 149.8, 136.0, 80.8, 77.2, 61.4, 59.3, 53.7, 30.2, 27.9, 27.0, 26.4, 24.8, 11.0, 6.9, 4.5, 2.4 ppm; $[\alpha]_D$ +1.2° (c 1.00, $CHCl_3$); HRMS m/z (M^+ − H) 475.2192 (calcd for $C_{22}H_{43}O_3S_2Si_2$, 475.2190).

The second compound to elute was the diastereomeric (3*R*,5*R*)-(+)-**15a** as a viscous, colorless oil (1.85 g, 28%): IR ($CHCl_3$) 3450 (br, w), 2460 (m), 2375 (m), 1450 (w), 1410 (w), 1370 (w), 1245 (m), 1115 (m), 1000 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (s, 1 H), 4.68 (d, J = 13.4 Hz, 1 H), 4.45 (d, J = 13.4 Hz, 1 H), 3.56 (br s, 1 H), 3.07 (br m, 2 H), 2.82 (m, 2 H), 2.68 (d, J = 14.4 Hz, 1 H), 2.17 (d, J = 14.4 Hz, 1 H), 2.02–1.86 (br m, 4 H), 1.48 (s, 3 H), 1.18 (t, J = 7.4 Hz, 3 H), 0.99 (t, J = 8.0 Hz, 9 H), 0.65 (q, J = 8.0 Hz, 6 H), 0.12 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 145.0, 138.9, 80.7, 62.0, 61.7, 54.8, 30.8, 30.5, 27.5, 26.7, 24.3, 10.7, 6.8, 4.5, 2.3 ppm; $[\alpha]_D$ +26.6° (c 1.00, $CHCl_3$); HRMS m/z (M^+ − H) 475.2192 (calcd for $C_{22}H_{43}O_3S_2Si_2$, 475.2190).

(3*R*,5*R*)-(−)-5-hydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (18a). A solution of (3*R*,5*R*)-(+)-5-(2-ethyl-1,3-dithian-2-yl)-5-hydroxy-3-methyl-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (**15a**) (1.85 g, 3.88 mmol) and diisopropylamine (1.63 mL, 11.6 mmol) in tetrahydrofuran (100 mL) was treated with mercury(II) perchlorate trihydrate[11] (8.75 mmol) as described for the ketone **18b**. The crude product was purified by flash chromatography (5% acetone in $CHCl_3$) to provide two compounds. The first to elute was (3*R*,5*R*)-(−)-5-hydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (**18a**) as a colorless oil (806 mg, 54%): IR ($CHCl_3$) 3450 (w), 2960 (m), 2870 (m), 1700 (m), 1455 (w),

1415 (w), 1370 (w), 1250 (m), 1105 (m), 1000 (m), 840 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (s, 1 H), 4.45 (s, 1 H), 4.12 (ABq, J_{AB} = 13.1 Hz, $v_0\delta$ = 40.4 Hz, 2 H), 2.95 (dq, J = 18.4, 7.3 Hz, 1 H), 2.58 (dq, J = 18.4, 7.3 Hz, 1 H), 2.39 (d, J = 14.6 Hz, 1 H), 2.05 (d, J = 14.6 Hz, 1 H), 1.53 (s, 3 H), 1.09 (t, J = 7.3 Hz, 3 H), 0.94 (t, J = 8.0 Hz, 9 H), 0.58 (q, J = 8.0 Hz, 6 H), 0.15 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 212.9, 145.4, 137.9, 88.2, 83.3, 58.5, 54.2, 30.3, 28.9, 7.8, 6.6, 4.2, 2.2 ppm; $[\alpha]_D$ −65.7° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 387.2387 (calcd for $C_{19}H_{39}O_4Si_2$, 387.2389).

The second compound to elute was the corresponding diol, (3*R*,5*R*)-(−)-3,5-dihydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**19a**) as a colorless oil (342 mg, 28%): IR ($CHCl_3$) 3580 (w), 3450 (br, w), 3000 (m), 2960 (m), 2870 (m), 1700 (m), 1455 (w), 1410 (w), 1370 (w), 1100 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (s, 1 H), 4.46 (s, 1 H), 4.22 (s, 2 H), 2.85 (ABX_3, J_{AB} = 18.9 Hz, J_{AX} = 7.2 Hz, J_{BX} = 7.2 Hz, $v_0\delta$ = 45.9 Hz, 2 H), 2.58 (s, 1 H), 2.33 (d, J = 14.4 Hz, 1 H), 2.07 (d, J = 14.4 Hz, 1 H), 1.50 (s, 3 H), 1.10 (t, J = 7.2 Hz, 3 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.61 (q, J = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) 215.7, 144.9, 137.4, 90.1, 80.2, 59.6, 53.4, 30.4, 28.2, 7.5, 6.6, 4.1 ppm; $[\alpha]_D$ −94.5° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 315.1992 (calcd for $C_{16}H_{31}O_4Si_2$, 315.1991).

(3*R*,5*R*)-(−)-3,5-Bis((trimethylsilyl)oxy)-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (20a). Method A: From (3*R*,5*R*)-(−)-5-Hydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)-3-((trimethylsilyl)oxy)cyclopentene (18a). A solution of the alcohol **18a** (806 mg, 2.08 mmol) and triethylamine (1.16 mL, 8.32 mmol) in dimethylformamide (10 mL) was treated with chlorotrimethylsilane (0.660 mL, 5.20 mmol) as described for the silyl ether **20b**. The crude residue was purified by flash chromatography (2% ether in petroleum ether) to provide (3*R*,5*R*)-(−)-3,5-bis((trimethylsilyl)oxy)-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (**20a**) as a colorless oil (896 mg, 94%).

Method B: From (3*R*,5*R*)-(−)-3,5-Dihydroxy-3-methyl-5-(1-oxopropan-1-yl)-1-(((triethylsilyl)oxy)methyl)cyclopentene (19a). A solution of the diol **19a** (342 mg, 1.09 mmol) and triethylamine (0.910 mL, 6.53 mmol) in dimethylformamide (5 mL) was treated with chlorotrimethylsilane (0.690 mL, 5.44 mmol) as described for the silyl ether **20b**. The crude residue was purified by flash chromatography (2% ether in petroleum ether) to provide silyl ether **20a** as a colorless oil (421 mg, 84%): IR ($CHCl_3$) 2960 (m), 1720 (m), 1450 (w), 1370 (w), 1310 (w), 1250 (m), 1000 (m), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.90 (s, 1 H), 4.07 (ABX, J_{AB} = 14.4 Hz, J_{AX} = 1.1 Hz, J_{BX} = 1.8 Hz, $v_0\delta$ = 64.4 Hz, 2 H), 2.77 (dq, J = 18.0, 7.3 Hz, 1 H), 2.49 (d, J = 14.3 Hz, 1 H), 2.45 (dq, J = 18.0, 7.3 Hz, 1 H), 2.03 (d, J = 14.3 Hz, 1 H), 1.51 (s, 3 H), 1.04 (t, J = 7.3 Hz, 3 H), 0.96 (t, J = 8.0 Hz, 9 H), 0.60 (q, J = 8.0 Hz, 6 H), 0.14 (s, 9 H), 0.12 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) 210.9, 146.9, 135.0, 91.7, 83.4, 58.5, 55.3, 30.5, 29.6, 8.1, 6.7, 4.3, 2.3, 2.2 ppm; $[\alpha]_D$ −40.9° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 459.2782 (calcd for $C_{22}H_{47}O_4Si_3$, 459.2784).

β-Hydroxy Ketone 6a. The ketone **20a** (1.16 g, 2.53 mmol) was treated with lithium diisopropylamide (3.05 mmol, 1.22 equiv) followed by the aldehyde (±)-**9** (1.0 g, 3.54 mmol) as described for the β-hydroxy ketone **6b**. The crude product was purified by flash chromatography (gradient elution: CH_2Cl_2 to 2% ether in CH_2Cl_2) to provide the β-hydroxy ketone **6a**, a complex diastereomeric mixture, as a colorless oil (1.42 g, 76%): IR ($CHCl_3$) 3520 (w), 2960 (s), 2870 (m), 1700 (m), 1455 (m), 1315 (m), 1250 (s), 1100 (s), 840 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.94 (m, 1 H), 4.30–3.95 (m, 4 H), 3.40–3.15 (m, 2 H), 2.80–2.65 (m, 1 H), 2.10–2.00 (m, 1 H), 1.70–1.45 (m, 17 H), 1.30 (m, 6 H), 1.20–1.05 (m, 4 H), 1.10–0.85 (m, 10 H), 0.70–0.60 (m, 6 H), 0.20–0.00 (m, 24 H).

Enal–Dione 21a. The β-hydroxy ketone **6a** (1.42 g, 1.92 mmol) was treated with chromium trioxide pyridine complex (34.5 mmol, 18.0 equiv) as described for the enal–dione **21b**. The crude product was purified by flash chromatography (ether/petroleum ether, 1:9) to provide enal dione **21a** as a colorless oil (524 mg, 44%): IR ($CHCl_3$) 2980 (m), 2860 (m), 1730 (m), 1705 (m), 1690 (m), 1440 (w), 1340 (w), 1250 (s), 1130 (m), 1000 (m), 840 (s) cm^{-1}; UV (EtOH) λ_{max} 216 (ϵ 9700) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 9.68 (m, 1 H), 6.87 (m, 1 H), 4.39 (m, 1 H), 4.25 (m, 1 H), 2.90–2.70 (m, 2 H), 2.65–2.40 (m, 1 H), 2.15–2.00 (m, 1 H), 1.70–1.50 (m, 5 H), 1.40–1.25 (m, 9 H), 1.00–0.85 (m, 12 H), 0.20–0.00 (m, 24 H); HRMS m/z (M^+ + NH_4) 640.3920 (calcd for $C_{32}H_{62}O_6NSi_3$, 640.3885).

3-(2*H*)-Furanone–Aldehyde 22a. The enal–dione **21a** (524 mg, 0.841 mmol) was treated with aqueous hydrochloric acid as described for the 3-(2*H*)-furanone–aldehyde **22b**. The crude product was purified by flash chromatography (EtOAc/hexanes; 4:1) to provide the 3-(2*H*)-furanone–aldehyde **22a** as a colorless, viscous oil (263 mg, 90%): IR ($CHCl_3$) 3580 (w), 2970 (s), 2840 (m), 1700 (m), 1615 (s), 1455 (m), 1370 (m) cm^{-1}; UV (EtOH) λ_{max} 277 (ϵ 10700), 209 (ϵ 10800) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 9.65 (s, 1 H), 7.09 (s, 1 H), 4.27 (m, 1 H), 3.96 (s, 1 H), 2.80–2.65 (m, 2 H), 2.29 (ABq, J_{AB} = 13.6 Hz, $v_0\delta$ = 46.9 Hz, 2 H), 2.15–2.05 (m, 1 H), 1.79 (s, 3 H), 1.75–1.60 (m, 2 H), 1.59 (s, 3 H), 1.40–1.30 (m, 6 H), 0.97 (t, J = 7.4 Hz, 3 H); $[\alpha]_D$ −100.4° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 347.1858 (calcd for $C_{20}H_{27}O_5$, 347.1860).

Acetal–Alcohol 23a. The 3-(2*H*)-furanone–aldehyde **22a** (243 mg, 0.70 mmol) was treated with ethylene glycol (3.9 mL, 70.0 mmol) and *p*-toluenesulfonic acid (6.5 mg, 0.035 mmol) as described for the acetal–alcohol **23b**. The crude product was purified by flash chromatography (4% ethanol in CH_2Cl_2) to provide the acetal–alcohol **23a** as a colorless oil (193 mg, 71%): IR ($CHCl_3$) 3580 (w), 3450 (w), 3010 (m), 2970 (m), 2920 (m), 1685 (m), 1615 (s), 1400 (m), 1370 (m), 1110 (m), 1030 (m) cm^{-1}; UV (EtOH) λ_{max} 279 (ϵ 9350), 204 (ϵ 6180) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (s, 1 H), 5.55 (m, 1 H), 4.23 (m, 1 H), 4.05–3.70 (m, 4 H), 3.91 (s, 1 H), 2.80–2.57 (m, 2 H), 2.32–2.15 (m, 3 H), 1.77 (s, 3 H), 1.70–1.60 (m, 2 H), 1.49 (s, 3 H), 1.45–1.35 (m, 6 H), 1.02–0.95 (m, 3 H); $[\alpha]_D$ −69.0° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 391.2121 (calcd for $C_{22}H_{31}O_6$, 391.2122).

Acetal–Ketone 5a. The acetal–alcohol **23a** (185.5 mg, 0.475 mmol) was treated with chromium trioxide–pyridine complex (5.70 mmol, 12.0 eq) as described for the acetal–ketone **5b**. The crude product was purified by flash chromatography (gradient elution; ether to 10% EtOAc in ether) to provide the acetal–ketone **5a** as a colorless oil (126 mg, 68%): IR ($CHCl_3$) 3450 (br, w), 3000 (m), 2970 (m), 2100 (w), 1670 (s), 1620 (s), 1400 (m), 1370 (m), 1110 (m), 1030 (m) cm^{-1}; UV (EtOH) λ_{max} 279 (ϵ 9460), 216 (ϵ 9400), 205 (ϵ 10200) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (s, 1 H), 5.46 (s, 1 H), 3.98–3.70 (m, 5 H), 2.75 (ABq, J_{AB} = 13.6 Hz, $v_0\delta$ = 8.0 Hz, 2 H), 2.53 (q, J = 7.3 Hz, 2 H), 2.22 (ABq, J_{AB} = 13.2 Hz, $v_0\delta$ = 61.1 Hz, 2 H), 1.77 (s, 3 H), 1.49 (s, 3 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 1.13 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 206.2, 188.3, 183.5, 142.0, 141.0, 112.2, 98.3, 97.5, 96.3, 80.7, 78.5, 64.9, 64.2, 48.8, 40.9, 38.7, 32.1, 29.0, 28.6, 25.7, 8.0, 6.5 ppm; $[\alpha]_D$ −103.1° (c 1.00, $CHCl_3$); HRMS m/z (M^+ + H) 389.1964 (calcd for $C_{22}H_{29}O_6$, 389.1966).

Intramolecular Mukaiyama Acetal Aldol Reaction of Acetal–Ketone 5a. The acetal–ketone **5a** (97.1 mg, 0.250 mmol) was treated successively with lithium diisopropylamide (0.610 mmol, 2.44 equiv), chlorotrimethylsilane (200 μL, 1.58 mmol), and titanium tetrachloride (0.500 mmol, 2.0 equiv) as described for the β-alkoxy ketones **24b** and **25b**. The crude product was purified by flash chromatography (EtOAc) to give the β-alkoxy ketones **24a** and **25a** (3:1 diastereomeric mixture) as a white foam (46.2 mg, 48%): IR ($CHCl_3$) 3580 (w), 3450 (br, w), 3000 (m), 2970 (m), 2920 (m), 2095 (w), 1670 (s), 1615 (s), 1400 (m), 1370 (m), 1180 (m), 1100 (m), 1050 (m) cm^{-1}; UV (EtOH) λ_{max} 281 (ϵ 8400), 219 (ϵ 8220), 204 (ϵ 9840) nm; ^1H NMR (500 MHz, $CDCl_3$) δ major diastereomer **24a**: 6.20 (d, J = 1.2 Hz, 1 H), 4.86 (s, 1 H), 4.10 (s, 1 H), 3.75–3.30 (m, 5 H), 3.01 (d, J = 13.9 Hz, 1 H), 2.59 (d, J = 13.9 Hz, 1 H), 2.36 (d, J = 12.9 Hz, 1 H), 2.21 (d, J = 12.9 Hz, 1 H), 1.89 (br s, 1 H), 1.74 (s, 3 H), 1.67 (s, 3 H), 1.53 (s, 3 H), 1.46 (s, 3 H), 0.95 (d, J = 6.8 Hz, 3 H). Minor diastereomer **25a**: 6.07 (s, 1 H), 4.86 (s, 1 H), 4.00 (s, 1 H), 3.75–3.30 (m, 5 H), 2.77 (ABq, J_{AB} = 13.0 Hz, $v_0\delta$ = 78.4 Hz, 2 H), 2.20 (s, 1 H), 2.20 (ABq, J_{AB} = 13.0 Hz, $v_0\delta$ = 50.6 Hz, 2 H), 1.80 (s, 3 H), 1.67 (s, 3 H), 1.48 (s, 3 H), 1.46 (s, 3 H), 1.08 (d, J = 6.9 Hz, 3 H); HRMS m/z (M^+ + H) 389.1964 (calcd for $C_{22}H_{29}O_6$, 389.1966).

C(5,6)-Trans-Olefin 26a. The diastereomeric mixture of β-alkoxy ketones **24a** and **25a** (19.4 mg, 0.050 mmol) was treated with diazabicycloundecane (115 μL, 0.77 mmol) and *p*-toluenesulfonyl chloride (9.5 mg, 0.05 mmol) as described for the C(5,6)-trans-olefin **26b**. The crude product was purified by flash chromatography (ether:petroleum ether; 6:1) to provide the C(5,6)-trans-olefin **26a** as a colorless oil (5.4 mg, 33%): IR ($CHCl_3$) 3010 (m), 2950 (m), 2180 (m), 1650 (s), 1615 (s), 1400 (m), 1375 (m), 1200 (m) cm^{-1}; UV (EtOH) λ_{max} 280 (ϵ 6050), 213 (ϵ 12100), 192 (ϵ 7500) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (m, 1 H), 6.33 (s, 1 H), 4.36 (s, 1 H), 2.93 (d, J = 13.8 Hz, 1 H), 2.68 (d, J = 13.8 Hz, 1 H), 2.26 (ABq, J_{AB} = 13.3 Hz, $v_0\delta$ = 7.4 Hz, 2 H), 1.90 (d, J = 1.2 Hz, 3 H), 1.87 (s, 3 H), 1.59 (s, 3 H), 1.56 (s, 3 H), 1.50 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 205.8, 185.8, 181.9, 141.5, 140.0, 138.1, 137.5, 114.3, 105.3, 99.7, 82.1, 80.2, 46.1, 42.9, 35.0, 30.9, 30.6, 26.1, 11.8, 7.8 ppm; HRMS m/z (M^+ + H) 327.1600 (calcd for $C_{20}H_{23}O_4$, 327.1596).

C(5,6)-Cis-Olefin 27a. The C(5,6)-trans-olefin **26a** (4.0 mg, 0.012 mmol) was irradiated with ultraviolet light (254 nm) as described for the C(5,6)-cis-olefin **27b**. The crude product was purified by flash chromatography (EtOAc:hexanes; 2:1) to provide the C(5,6)-cis-olefin **27a** as a colorless oil (3.8 mg, 95%): IR ($CHCl_3$) 2900 (m), 2210 (m), 1680 (s), 1610 (s), 1380 (m), 1210 (s), 1190 (m) cm^{-1}; UV (EtOH) λ_{max} 291 (ϵ 12400), 222 (ϵ 12500), 204 (ϵ 13500) nm; ^1H NMR (500 MHz,

$CDCl_3$) δ 5.96 (d, J = 2.1 Hz, 1 H), 5.73 (dq, J = 2.1, 1.7 Hz, 1 H), 2.92 (d, J = 14.9 Hz, 1 H), 2.60 (d, J = 14.9 Hz, 1 H), 2.42 (d, J = 13.6 Hz, 1 H), 2.25 (d, J = 13.6 Hz, 1 H), 2.10 (s, 1 H), 1.87 (d, J = 1.7 Hz, 3 H), 1.73 (s, 3 H), 1.56 (s, 3 H), 1.49 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 203.3, 184.0, 183.4, 147.5, 145.5, 137.0, 121.3, 111.8, 106.7, 97.4, 84.6, 81.4, 50.4, 41.9, 32.4, 29.4, 29.2, 26.9, 19.8, 6.1 ppm; HRMS m/z (M^+ + H) 327.1608 (calcd for $C_{20}H_{23}O_4$, 327.1596).

(+)-Hydroxyjatrophone A (2). The C(5,6)-cis-olefin **27a** (3.8 mg, 0.012) was semihydrogenated ($Pd/BaSO_4$) and isomerized (KI, HOAc) as described for (+)-hydroxyjatrophone B (3). The crude product was purified by preparative thin-layer chromatography (500 μm; 3 × 20 cm; EtOAc:hexanes; 3:1) to provide (+)-hydroxyjatrophone A (2) as a colorless oil (1.6 mg, 42%): ^1H NMR (500 MHz, $CDCl_3$) δ 6.45 (d, J = 16.2 Hz, 1 H), 6.02 (d, J = 16.2 Hz, 1 H), 5.86 (d, J = 2.0 Hz, 1 H), 5.81 (dq, J = 2.0, 1.7 Hz, 1 H), 2.88 (d, J = 15.1 Hz, 1 H), 2.47 (dd, J = 15.1, 0.6 Hz, 1 H), 2.38 (d, J = 13.8 Hz, 1 H), 2.17 (d, J = 13.8 Hz, 1 H), 1.91 (d, J = 1.7 Hz, 3 H), 1.90 (s, 1 H), 1.74 (d, J = 0.6 Hz, 3 H), 1.46 (s, 3 H), 1.39 (s, 3 H), 1.25 (s, 3 H); HRMS m/z (M^+ + H) 328.1673 (calcd for $C_{20}H_{25}O_4$, 328.1674); $[\alpha]_D$ +277° (c 0.100, $CHCl_3$); TLC R_f 0.30 (Et_2O), 0.35 (EtOAc:hexanes, 3:1), 0.24 ($CHCl_3$:acetone, 4:1), 0.24 (hexanes:acetone, 2:1), 0.36 (CH_2Cl_2:EtOH, 9:1), 0.31 (benzene, EtOH, 19:1).

Synthetic (+)-hydroxyjatrophone A (2) was in all respects (500 MHz ^1H NMR, HRMS, optical rotation and TLC mobility in six solvent systems) identical with an authentic sample of the natural product.[1]

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On the Controlled Oxidative Coupling of Glycals: A New Strategy for the Rapid Assembly of Oligosaccharides

Richard W. Friesen and Samuel J. Danishefsky*

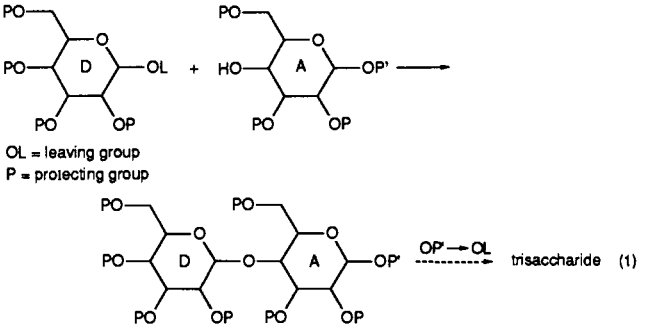
Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06511. *Received November 9, 1988. Revised Manuscript Received February 24, 1989*

Abstract: Controlled oxidative coupling of various glucal triethers with glucals containing a single hydroxy group (either at C4 or C3) and acyloxy groups at the other two positions has been demonstrated. The process is readily reiterated. A concise route to α-linked oligosaccharides has been developed.

The ability to couple carbohydrate entities to produce glycosides or higher oligomers is one of the important goals of synthetic organic chemistry.[1] The roles of oligosaccharides as energy storage sources, as structural building blocks, as modifiers of protein folding, as immunological determinants, and as apparent accessories (conjugating agents) to various steroidal hormones and antibiotics are well-known.[2]

Considerable progress has been achieved in the fashioning of the glycosidic bond and in the synthesis of various oligosaccharide patterns.[1] The application of enzymatic techniques at the preparative level has brought with it much progress.[3] The development of more sophisticated blocking and deblocking strategies in glycosyl acceptors, and more efficacious anomeric activating groups for glycosyl donors, have each brought forth improvements in the synthesis of oligosaccharides.[4] While cognizant of these encouraging developments, we have in the course of several synthetic ventures perceived a need for fresh departures in this field, particularly as regards operational conciseness.

Virtually all current glycosylations conserve the oxidation level of both coupling components.[1] Consider the merger of two hexose residues as shown in eq 1. Typically the glycosyl acceptor (A)



enters the reaction with a single free hydroxyl group and four OP appendages (P = protecting groups). The donor D must be equipped with a displaceable group at its anomeric carbon and is presented for coupling with four masked hydroxylic centers. If the AD disaccharide is eventually to function as a glycosyl donor, for elongation to an oligosaccharide, its reducing end must be furnished with glycosyl-donating (i.e., a leaving group) capabilities. Provision for this, in the form of a unique blocking group at the anomeric center of the original A acceptor, was necessary (see unique P′ function in A, which is suitable for conversion to the OL group of AD in eq 1).

The experiments described herein were organized around a new idea involving oxidative coupling of glycals (see eq 2). Manipulations at the anomeric centers are unnecessary since coupling is actuated by attack of the oxidant at the donor[5] glycal. The free hydroxyl function in the acceptor[5] glycal must be differentiated from two (rather than four) other alcohols that must be

(1) For two recent reviews of glycosylation, see: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(2) For an entry to the biological roles of various carbohydrates, see: Kennedy, J. F.; White, C. A. *Bioactive Carbohydrates in Chemistry, Biochemistry and Biology*; Halsted Press: New York, 1983.

(3) For leading references to enzyme-catalyzed carbohydrate synthesis, see: Wong, C.-H.; Drueckhammer, D. G.; Durrwachter, J. R.; Lacher, B.; Chauvet, C. J.; Wang, Y.-F.; Sweers, H. M.; Smith, G. L.; Yang, L. J.-S.; Hennen, W. J. In "*Trends in Synthetic Carbohydrate Chemistry*", Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium *Series 386*; American Chemical Society: Washington, DC, 1989; Chapter 18.

(4) See ref 1, as well as: El Khadem, H. S. *Carbohydrate Chemistry: Monosaccharides and Their Oligomers*; Academic Press: San Diego, CA, 1988, Chapter 7.

(5) In this paper, the donor glycal will be that hexose which supplies what becomes the anomeric carbon of the new glycosidic bond. The acceptor glycal will be that hexose which is incorporated into the new glycoside via its free hydroxyl moiety.

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