pyridinium)ethyl]-4-vinylpyridinium ditriflate (**6**, n = 1) [yield, 13%. ^{1}H NMR (DMSO-d_6): δ 3.4 (t, 2 H, NCH_2CH_2), 4.9 (t, 2 H, NCH_2), 5.98 (d, 1 H, J_{cis} = 10 Hz), 6.57 (d, 1 H, J_{trans} = 17 Hz), 7.05 (dd, 1 H, $CH{=}CH_2$), 8.05–8.95 (AB q, 4 H, vinyl py^{2,3,5,6}), 8.2–8.9 (AB q, 4 H, pyNH^{2,3,5,6}).

Addition of 0.02 mL of pyridine to the reaction mixture initiated conversion of **1a** to 1,6-polyionene (**6**), which was evidenced by the loss of ^{1}H NMR signals due to vinyl protons and the appearance of enhanced, broadened signals at δ 3.5 and 4.9 (CH_2-CH_2N). The half-life for polymerization was approximately 10 min.

Polymerization of 1-Alkyl-4-vinylpyridinium Triflates 1b–f. Polymerization of monomeric salts **1** was accomplished by three procedures: (a) thermally by heating at 100–125 °C for 15 min under vacuum in sealed ampules (Note: The salts **1** all polymerize when heated in air to their melting points.); (b) by treatment with 0.5 mol % of 2,2′-azobis(isobutyronitrile) (AIBN) in acetonitrile at 60–70 °C for 2–15 h; and (c) by treatment with excess 4-vinylpyridine or with 0.5 mol % of pyridine at room temperature for 1–12 h (Note: There is no detectable inclusion of **4** in the polymer when examined by ^{1}H NMR spectroscopy.).

The polymers were purified by dissolution in methanol followed by precipitation with cold ether. Spectral and elemental analyses were used to confirm polymer structure. IR spectra for **2** were very similar to those for related **1** except for broadening of bands at 1160 and 1260 cm^{-1} (CN str). ^{1}H NMR spectral assignments and elemental analyses are reported below for two representative homopolymers, **2c** and **2f**.

Poly(1-ethyl-4-vinylpyridinium triflate) (2c). ^{1}H NMR (DMSO-d_6): δ 1.6 (br s, 3 H, CH_3), 1.5–2.2 (br s, 3 H, backbone CH_2), 2.6 (br s, 1 H, backbone CH), 4.6 (br s, 2 H, NCH_2), 7.9 and 8.7 (br s, 4 H, py^{2,3,5,6}). Anal. Calcd for $C_{10}H_{12}F_3NO_3S$: C, 42.40; H, 4.24; N, 4.94. Found: C, 42.30; H, 4.23; N, 4.86.

Poly(1-dodecyl-4-vinylpyridinium triflate) (2f). ^{1}H NMR (DMSO-d_6): δ 0.9 (s, 3 H, CH_3), 1.3 (br s, 20 H, $(CH_2)_9CH_3$ and backbone CH_2), 2.0 (br s, 2 H, NCH_2CH_2), 2.3 (s, 1 H, backbone CH), 4.6 (br s, 2 H, NCH_2), 8.0 and 8.7 (br s, 4 H, py^{2,3,5,6}). Anal. Calcd for $C_{20}H_{32}F_3NO_3S$: C, 56.73; H, 7.56; N, 3.31. Found: C, 54.39; H, 6.80; N, 3.31.

^{1}H NMR Study of Alkylation of 4-Vinylpyridine with Ethyl Triflate. A solution of 0.026 g (0.25 mmol) of 4-vinylpyridine in 0.25 mL of $CDCl_3$ was added to 0.06 mL (0.45 mmol) of ethyl triflate in 0.25 mL of $CDCl_3$. ^{1}H NMR spectral analysis within 2 min revealed complete conversion of 4-vinylpyridine to the related pyridinium ions, **1a** and **1c**, via protonation (~33%) and alkylation (~67%). (Note: The ethyl triflate (Aldrich) was a commercial sample and it was used without purification.) The ^{1}H NMR spectrum included all signals appropriate for **1a** (see above), **1c** (see above), and excess ethyl triflate (δ 1.5, t, 3 H; 4.6, q, 2 H) as well as signals at δ 1.2 (t, 3 H) and 3.45 (q, 2 H), which were confirmed to be due to ethyl ether.

The alkylated and protonated products separated from solution after 5–10 min and were redissolved by addition of 0.5 mL of DMSO-d_6. New ^{1}H NMR signals at δ 1.5–1.8 and 4.3–4.5 accompanied addition of the DMSO-d_6. The spectrum of ethyl triflate in DMSO-d_6 includes signals at δ 1.7 (t, 3 H) and 4.4 (q, 2 H), which may be due to an ion formed by ethylation of DMSO.

Rates of Alkylation of 4-Vinylpyridine. Reaction progress in mixtures containing equimolar quantities (0.25–0.50 mmol) of 4-vinylpyridine and alkylating agent in 0.50 mL of deuterated solvent ($CDCl_3$ or DMSO-d_6) was followed by ^{1}H NMR spectroscopy at ~32 °C (NMR probe temperature). Signals in the 7.0–9.0 ppm (pyridine ring protons) and 4.2–4.6 ppm (N^+CH_2R) regions (TMS, internal standard) were integrated after different time intervals to obtain estimates of reaction half-lives ($t_{1/2}$). The results are summarized in Table II.

Acknowledgment. This work was supported by the Office of Naval Research and by Reilly Industries. We thank C. Parish for assistance with samples of monomeric and polymeric materials.

Supplementary Material Available: Preparation and characterization of 4-vinylpyridinium triflate (**1a**) and 1-alkyl-4-vinylpyridinium triflates (**1b**, **1c**, and **1f**) (2 pages). Ordering information is given on any current masthead page.

Synthesis of Optically Active Methylcyclopentanoids: Intermediates for the Assembly of Complex Diterpenoids

Brian T. Becicka, Frederick L. Koerwitz, Gary J. Drtina, Norman C. Baenziger, and David F. Wiemer*,[1]

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

Received February 7, 1990

A large number of diterpenoids can be classified as 4-methylcyclopentanoid derivatives, including compounds with the jatrophane, lathyrane, and tigliane (phorbol) skeletons. Three synthetic routes to 4-methylcyclopentanoids have been developed to obtain chiral, nonracemic synthons for assembly of the diterpenoids. These routes draw on the readily available monoterpenoids citronellol or pulegone as chiral resources, providing for synthesis of natural diterpenoid enantiomers without recourse to resolution.

Many plants of the spurge family (Euphorbiaceae) produce toxic or irritating substances that belong to a closely related group of diterpenoids, including jatrophane, lathyrane, and tigliane (phorbol) derivatives. Because of their often striking biological activities, this diterpenoid family has attracted considerable attention, and some of the less highly oxidized members have been prepared by total synthesis. In particular, a total synthesis of (±)-jatrophone (**1**) has been reported,[2] and the clever strategies of this approach were recently extended to syntheses of (+)-hydroxyjatrophones A (**2**) and B (**3**).[3] In the lathyrane family, (−)-bertyadionol (**4**) also has been prepared,[4] and

(1) Fellow of the Alfred P. Sloan Foundation, 1985–1989.

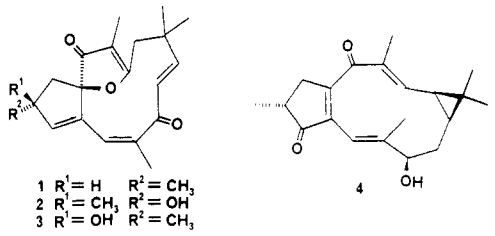
(2) Smith, A. B., III; Guaciaro, M. A.; Schow, S. R.; Wovkulich, P. M.; Toder, B. H.; Hall, T. W. *J. Am. Chem. Soc.* **1981**, *103*, 219.

(3) Smith, A. B., III; Lupo, A. T., Jr.; Ohba, M.; Chen, K. *J. Am. Chem. Soc.* **1989**, *111*, 6648.

(4) Smith, A. B., III; Dorsey, B. D.; Visnick, M.; Maeda, T.; Malamas, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 3110.

0022-3263/90/1955-5613$02.50/0

a variety of approaches to other lathyranes have been reported.[5]

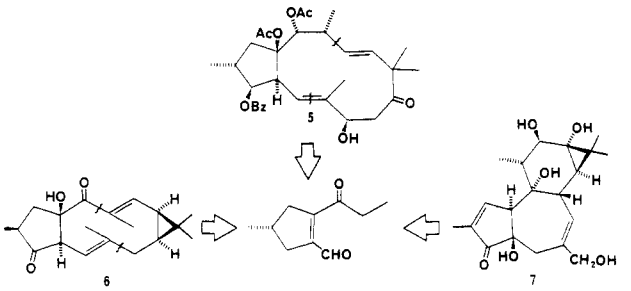


The skeletons of jatrophane (**5**), lathyrane (**6**), and tigliane (**7**) diterpenoids share a common 1,2-disubstituted 4-methylcyclopentane ring system, a feature that is fused to one or more additional rings in the various natural products and often highly functionalized. Our own interest in this family has been driven by a retrosynthetic analysis (Scheme I) that traces the common 1,2-disubstituted 4-methylcyclopentane system to a nearly symmetrical intermediate. From this perspective, syntheses of various members of this large family could utilize a common precursor. Furthermore, if the methylcyclopentane were prepared in optically active form, a single cyclopentanoid enantiomer could be used to obtain enantiomerically pure diterpenoids of either methine stereochemistry by using the C-1 and C-2 substituents to provide different portions of the diterpene skeleton (Scheme I). In pursuit of this objective, we have developed a variety of cyclopentanoid syntheses. In this paper we report three of these routes, all of which make use of readily available monoterpenoids to control the absolute stereochemistry of the methine position of 1,2-disubstituted 4-methylcyclopentanoids.

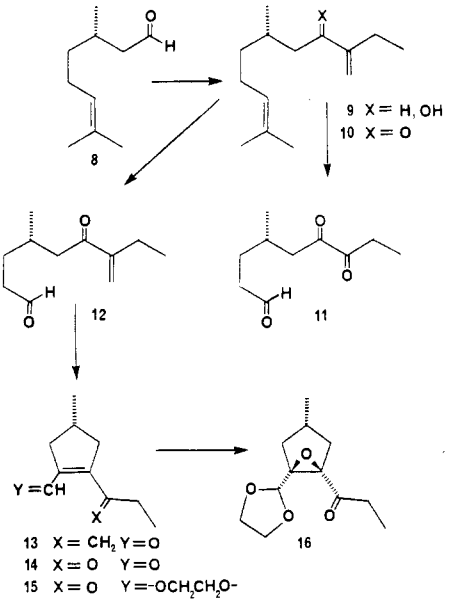
Our first route begins with (*S*)-citronellal (**8**) (Scheme II), which has been commercially available in moderate enantiomeric excess[6,7] or which can be prepared by oxidation of (*S*)-citronellol. Reaction of this aldehyde with the Grignard reagent derived from 2-bromo-1-butene gives a mixture of diastereomeric alcohols (**9**) in nearly quantitative yield. Upon treatment with pyridinium chlorochromate (PCC),[8] these alcohols are readily converted to the corresponding enone **10**. If this enone is treated with excess ozone, followed by reductive workup with dimethyl sulfide, both double bonds undergo oxidative cleavage. However, selective cleavage of the nonconjugated double bond can be achieved if the progress of the ozonolysis is carefully monitored by GC analysis, thereby limiting compound **10** to reaction with a single equivalent of ozone. By this approach, compound **10** can be converted to the desired enone aldehyde **12** efficiently, but this aldehyde proved sufficiently unstable that purification by column chromatography resulted in significantly lower isolated yields. Therefore, the unpurified material normally was carried directly into the next transformation, wherein treatment with piperidine and acetic acid resulted in cyclization to afford the cyclopentenoid aldehyde **13**.

Conversion of compound **13** into our immediate target,

Scheme I



Scheme II



the keto aldehyde **14**, requires oxidative cleavage of the terminal olefin. A variety of oxidants were examined, including OsO_4 and peracids, with frustrating results. Eventually, we discovered that treatment of the diene with a standard solution of ozone in CH_2Cl_2 (Rubin conditions)[9] would effect the desired transformation in modest yield, making keto aldehyde **14** available through a five-step sequence from citronellal.

Compound **14** embodies many of the goals established by our retrosynthetic analysis, and it may prove useful in synthesis of the targeted diterpenoids. This compound contains a stereogenic center, yet it escapes symmetry only by virtue of the nonequivalence of the formyl and propionyl substituents. In theory, compound **14** could be used to prepare diterpenoids of *either* absolute configuration at the methine carbon if the carbonyl groups were used as alternative portions of the skeleton. Furthermore, compound **14** could be obtained in optical purity if enantiomerically pure citronellal were employed in this route, because all transformations are remote from the single stereogenic center. However, the delicacy of the oxidative cleavages and the instability of the intermediate aldehydes exact a high toll on the overall yield. It also proved difficult to introduce substituents at the remaining allylic positions with regioselectivity. For example, after protection of the formyl group as its dioxolane derivative (**15**), we were unable to obtain the extended enolate that would allow regioselective oxidation of the cyclopentene ring.[10]

(5) (a) Braish, T. F.; Saddler, J. C.; Fuchs, P. L. *J. Org. Chem.* **1988**, *53*, 3647. (b) Saddler, J. C.; Fuchs, P. L. *J. Am. Chem. Soc.* **1981**, *103*, 2112. (c) Taylor, M. D.; Minaskanian, G.; Winzenberg, K. N.; Santone, P.; Smith, A. B., III *J. Org. Chem.* **1982**, *47*, 3960. (d) Maas, D. D.; Blagg, M.; Wiemer, D. F. *J. Org. Chem.* **1984**, *49*, 853. (e) Satoh, T.; Okuda, T.; Kaneo, Y.; Yamakawa, K. *Chem. Pharm. Bull.* **1984**, *32*, 1401.

(6) A preliminary description of this first route has appeared: Drtina, G. J.; Wiemer, D. F. *Tetrahedron Lett.* **1982**, *23*, 803.

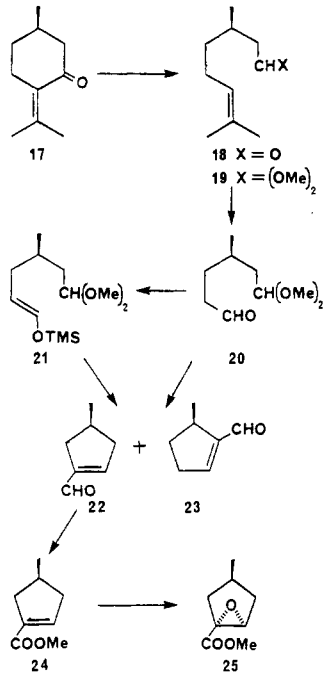
(7) The enantiomeric excess of the (*S*)-citronellal we purchased varied widely; experiments described here were done with a single batch of approximately 54% ee.

(8) (a) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (b) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682.

(9) Rubin, M. B. *J. Chem. Educ.* **1964**, *41*, 388. Meyer, W. L.; Cameron, D. D.; Johnson, W. S. *J. Org. Chem.* **1962**, *27*, 1130.

(10) Drtina, G. J. Ph.D. Thesis, University of Iowa, 1983.

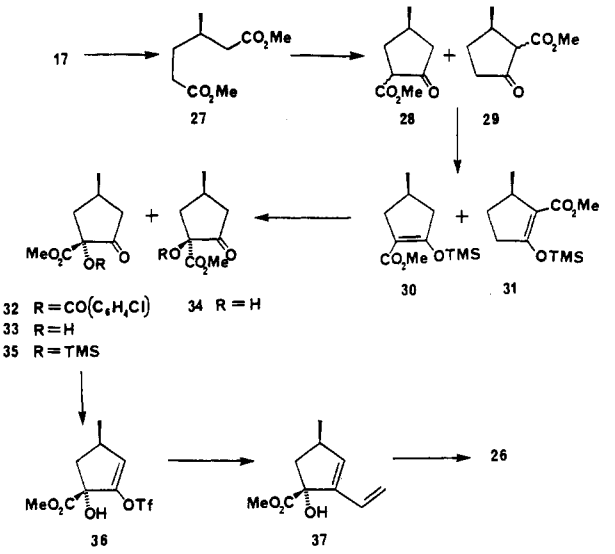
Scheme III



This enone does react rapidly with *m*-chloroperbenzoic acid (MCPBA), affording a single epoxide diastereomer **16**,[11] but regioselective opening of the epoxide also proved problematic. Accordingly, we have explored alternative preparations of methylcyclopentanoid systems to obtain more high functionalized intermediates.

To overcome the disadvantage imposed by the limited ee of most commercial (*S*)-citronellal, our alternate strategy employs (*R*)-pulegone (**17**) (Scheme III) as the ultimate chiral resource because it is available in very good optical purity. The next sequence begins with conversion of (*R*)-pulegone into (*R*)-citronellal (**18**) via (*R*)-citronellic acid.[12] After protection of aldehyde **18** as its dimethyl acetal **19**, ozonolysis and catalytic hydrogenation of the ozonide were carried out to prepare the selectively monoprotected dialdehyde **20**. To obtain the desired condensation product **22** without formation of the regioisomeric **23**, it was our intention to attempt an intramolecular aldol-type reaction under Mukaiyama conditions.[13] Indeed, treatment of compound **20** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) and trimethylsilyl chloride (TMSCl)[14] gives the expected enol ether **21** as an unstable oil, and further reaction with $TiCl_4$ results in cyclization. However, the regioselectivity of this reaction was less than expected, for the aldehydes **22** and **23** were formed in a ratio of about 9:1, and competing intermolecular reactions restricted the total yield to about 45%. Given the limited success of this sequence, we explored at some length the results of direct treatment of compound **20** with aqueous HCl.[15] While the cyclization is sensitive to both the concentration and quantity of acid used, conditions were discovered where the desired condensation dominates (a 19:1 ratio of compounds **22** to **23**). However, because it was prone to polymerization, the unpurified aldehyde was oxidized directly

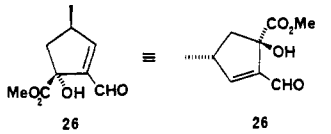
Scheme IV



to the methyl ester **24** by using SeO_2 in methanol.[16]

If one considers the carboxyl group of compound **24** as the effective equivalent of the propionyl group of compound **14**, then this approach yields the same enantiomeric series upon formylation at the β-position of the α,β-unsaturated ester. To introduce more functionality within the cyclopentane system, ester **24** was converted to an epoxide by treatment with MCPBA. Only one epoxide stereoisomer was formed by this reaction, which we assigned as shown in Scheme III (**25**) on the basis of our earlier work and literature precedent.[11] Unfortunately, our efforts to open this epoxide selectively at the β-position with a nucleophilic formyl equivalent went unrewarded. Conversion of epoxide **25** to a diol or α-ketol followed by introduction of the formyl group may be feasible, but in order to retain a short overall sequence, we decided to return once again to (*R*)-pulegone and pursue a closely related route.

A variation on the above strategy has been developed to obtain the more functionalized cyclopentanoid **26**, which can be viewed as an intermediate for (+)-jatrophone or, assuming oxidation with allylic transposition,[8b] (−)-bertyadionol. This route begins with conversion of (+)-pu-



legone to dimethyl 3-methyladipate (**27**).[17] Dieckmann condensation of this diester affords keto esters **28** and **29** in a 2.8:1 ratio,[18] but separation of the regioisomers was postponed until after introduction of an α-hydroxy substituent.

After preparation of the silyl enol ethers **30** and **31** (Scheme IV), oxidation could be effected either by treatment with MCPBA[19] or with catalytic OsO_4 and *N*-

(11) Henbest, H. B.; McCullough, J. J. *Proc. Chem. Soc.* **1962**, 74.
(12) Plesekm, J. *Collect. Czech. Chem. Commun.* **1957**, *22*, 644. Hubert, T. D.; Eyman, D. P.; Wiemer, D. F. *J. Org. Chem.* **1984**, *49*, 2279.
(13) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203. Alexakis, A.; Chapdelaine, M. J.; Posner, G. H.; Runquist, A. W. *Tetrahedron Lett.* **1978**, 4205.
(14) Tanaguchi, Y.; Inanaga, J.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3229.
(15) Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5045.
(16) Smith, C. W.; Holm, R. T. *J. Org. Chem.* **1957**, *22*, 746. Ishii, Y.; Muria, S.; Sonoda, N. *Technol. Rep. Osaka Univ.* **1976**, *26*, 623; *Chem. Abstr.* **1977**, *86*, 54738r. Kitahara, M.; Mitsui, T.; Hirayama, T. *Rikagaku Kenkyusho Hokoku* **1962**, *38*, 81; *Chem. Abstr.* **1963**, *58*, 13788a.
(17) Jackman, L. M.; Web, R. L.; Yick, H. C. *J. Org. Chem.* **1982**, *47*, 1824.
(18) Matthews, R. S.; Oliver, J. D.; Ward, J. F.; Eikhoff, D. J.; Strickland, L. C. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1485.
(19) Rubottom, G. M.; Vazquez, M. A.; Pelegrina, D. R. *Tetrahedron Lett.* **1974**, 4319.

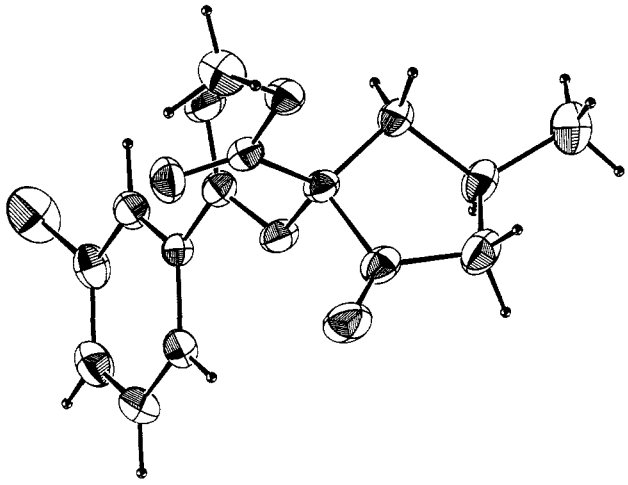


Figure 1. ORTEP drawing of compound **32**.

methylmorpholine *N*-oxide (NMMO).[20] We were surprised to find that oxidation with MCPBA gave the crystalline chlorobenzoate ester **32** as the major product. While this could be converted to the target alcohol **33** by transesterification with acidic methanol, its primary value lay in its crystalline form. A single-crystal X-ray analysis independently confirmed the absolute stereochemistry as shown in Figure 1. Oxidation of silyl enol ethers **30** and **31** with catalytic OsO_4 and NMMO gave a mixture of the desired alcohol **33** and its diastereomer **34** in a 58% yield and a 10:1 ratio, while leaving the regioisomeric enol ether **31** primarily unreacted. Isolation of the α-hydroxy ketone **33** could be accomplished by column chromatography, although separation of the diastereomers was more readily accomplished after further functionalization.

The alcohol **33** includes both of the stereogenic centers of (+)-jatrophone in their appropriate absolute stereochemistry. To complete this phase of our study, the alcohol **33** was protected as its TMS derivative **35**, which was converted to the vinyl triflate by treatment with lithium diisopropylamide (LDA) and *N*-phenyltriflimide,[21] and the TMS group was removed by hydrolysis. After a palladium-catalyzed cross coupling[22] of triflate **36** with tributylvinyltin gave diene **37**, a final oxidative cleavage of the terminal vinyl group ($OsO_4/NaIO_4$) provided the immediate target, aldehyde **26**.

These three routes to methylcyclopentanoids demonstrate the feasibility of using a stereogenic center derived from chiral pool terpenoids in construction of complex methylcyclopentanoids. For example, aldehyde **26** appears directly relevant to both (+)-jatrophone and (−)-bertyadionol, and other cyclopentenoids we have prepared, such as the vinyl triflate **34**, embody versatile functionality[22] which may allow the preparation of related natural products. Together, these routes should provide access to key portions of a number of diterpenoids in the jatrophane and lathyrane families and provide them with the natural absolute stereochemistry.

Experimental Section

Tetrahydrofuan (THF) was distilled from sodium/benzophenone immediately prior to use, and all reactions in this solvent were conducted under a positive pressure of an inert gas. Column chromatography was done on Merck grade 62 silica gel (60–200 mesh), while flash chromatography was performed with Davisil grade 633 silica gel (200–425 mesh). NMR spectra (^1H and ^{13}C) were recorded with $CDCl_3$ as both solvent and internal standard. Electron impact (EI) mass spectra were recorded at 70 eV; only selected ions are reported here.

6,10-Dimethyl-3-methylene-9-undecen-4-ol (9). A solution of 2-bromo-1-butene in THF was added to magnesium metal in the same solvent at room temperature. When formation of the Grignard reagent (0.19 mol in 150 mL of THF) was complete, the solution was cooled to 15 °C and (*S*)-citronellal (23.0 g, 0.15 mol in 30 mL of THF) was added at a rate such that the temperature never rose above 20 °C. After the addition was complete, the mixture was stirred at room temperature for 7 h. Saturated aqueous NH_4Cl was added dropwise until the mixture turned to a thick slush, which separated into a soft cake and clear supernatant upon standing overnight. After filtration, the filtrate was diluted with hexane (1 volume), washed with water, and dried (Na_2SO_4). Concentration in vacuo gave 32.0 g (100%) of the diastereomeric alcohols **9**: bp 86 °C (0.55 mm); ^1H NMR δ 5.10 (t, 1, J = 7.0 Hz), 5.01 (s, 1), 4.81 (s, 1), 4.22–4.13 (m, 1), 2.3–1.2 (m, 10), 1.68 (s, 3), 1.60 (s, 3), 1.07 (t, 3, J = 7.3 Hz), 0.93 (d, 3, J = 6.2 Hz); EIMS m/z (rel intensity) 210 (M^+, 1), 195 (2), 177 (14), 109 (64), 107 (100), 95 (85), 69 (86); HRMS calcd for $C_{14}H_{26}O$ 210.1984, found 210.1977.

(*S*)-6,10-Dimethyl-3-methylene-9-undecen-4-one (10). The diastereomeric alcohols **9** (4.56 g, 21.7 mmol) in CH_2Cl_2 (8 mL) were added to a stirred suspension of PCC (7.08 g, 32.9 mmol) and sodium acetate (0.54 g, 6.5 mmol) in the same solvent (30 mL). After 2 h, ether (30 mL) was added and the brown supernatant was decanted from the black residue. After rinsing of the residue with ether (3 × 20 mL) until it became granular, the combined supernatant and rinsings were washed with 1 N NaOH (3 × 100 mL), 1 N HCl (3 × 100 mL), 0.5 M $NaHCO_3$ (2 × 100 mL), and brine (2 × 50 mL). The brown residue was dissolved in 1 N NaOH and extracted with hexane, and the resulting extract was washed with 1 N HCl, 0.5 M $NaHCO_3$, and brine. The combined organic solutions were dried (Na_2SO_4) and concentrated to give 4.47 g of crude ketone **10**. Purification by column chromatography (silica gel, 3% EtOAc in hexane) gave 3.21 g (71%) of ketone **10**: bp 61 °C (0.15 mm); $[\alpha]^{22}_D$ −1.09° (c = 0.177, $CDCl_3$);[7] ^1H NMR δ 5.93 (s, 1), 5.68 (s, 2), 5.08 (t, 1, J = 7.0 Hz), 2.6–1.2 (m, 9), 1.66 (s, 3), 1.59 (s, 3), 1.02 (t, 3, J = 7.3 Hz), 0.90 (d, 3, J = 6.6 Hz); ^{13}C NMR 201.9, 151.0, 131.3, 124.5, 122.5, 45.2. 37.2, 29.8, 25.6, 25.5, 23.9, 19.9, 17.6, 12.7; EIMS m/z (rel intensity) 208 (M^+, 3), 193 (10), 180 (3), 125 (29), 110 (29), 109 (100), 95 (90), 83 (49), 69 (31); HRMS calcd for $C_{14}H_{24}O$ 208.1827, found 208.1831. Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.48; H, 11.16.

(*S*)-4-Methyl-7-methylene-6-oxononanal (12). Diene **10** (6.62 g, 31.5 mmol) in 2:1 CH_2Cl_2–ethanol (360 mL) at −78 °C was treated with ozone until 85% conversion was indicated by GC analysis of a quenched aliquot. Dimethyl sulfide (8 mL, 109 mmol) was added and the mixture allowed to warm to room temperature. After 5 h, the reaction mixture was concentrated, the residue was redissolved in ethyl acetate, and the solution was flash-filtered through silica gel. Concentration in vacuo gave material that could be used in subsequent reactions. Final purification by column chromatography (silica gel, 10% EtOAc in hexane) gave 2.71 g (47%) of pure aldehyde **12**: bp 76 °C (0.35 mm); $[\alpha]^{22}_D$ −2.08° (c = 0.0963, $CDCl_3$); ^1H NMR δ 9.77 (t, 1, J = 1.8 Hz), 5.95 (s, 1), 5.72 (s, 1), 2.66–1.50 (m, 9), 1.03 (t, 3, J = 7.3 Hz), 0.93 (d, 3, J = 6.2 Hz); ^{13}C NMR 202.2, 201.3, 150.8, 122.8, 44.8, 41.6, 29.3, 28.8, 23.8, 19.6, 12.7; EIMS m/z (rel intensity) 182 (M^+, 0.2), 138 (21), 125 (10), 98 (24), 83 (100), 55 (38). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.14; H, 9.64.

(*R*)-4-Methyl-2-(1-ethylethenyl)-1-cyclopentene-1-carboxaldehyde (13). Aldehyde **12** (2.56 g, 14.1 mmol) in anhydrous benzene (4 mL) was added to a boiling solution of piperidine (150 μL) and glacial acetic acid (150 μL) in benzene (12 mL). The mixture was heated at reflux for 20 min, a Dean–Stark apparatus being used for azeotropic removal of water (0.2 mL). After cooling to room temperature, the mixture was diluted with ether (45 mL), washed with 1 N HCl (3 × 4 mL), 1 N Na_2CO_3 (3 × 4 mL), and brine (2 × 4 mL), and then dried (Na_2SO_4). Concentration in vacuo gave an oil, which was purified by column chromatography (silica gel, 10% ethyl acetate in hexane) to obtain

(20) McCormick, J. P.; Tomasik, W.; Johnson, M. W.; *Tetrahedron Lett.* **1981**, *22*, 607.
(21) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.
(22) Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, *21*, 47.

1.00 g (44%) of cyclopentene aldehyde **13**: bp 60–65 °C (1.1 mm); $[\alpha]_D$ −5.79° (*c* = 0.105, $CDCl_3$); UV λ_{max} (CH_3OH) 260 nm; ^1H NMR δ 9.82 (s, 1), 5.15 (s, 1), 5.02 (s, 1), 3.0–2.5 (m, 5), 2.24 (q, 2, *J* = 7.3 Hz), 1.06 (d, 3, *J* = 6.2 Hz), 1.03 (t, 3, *J* = 7.3 Hz); ^{13}C NMR 189.9, 163.9, 145.3, 139.9, 115.9, 45.7, 38.3, 30.6, 27.9, 21.1, 12.5; EIMS *m/z* (rel intensity) 164 (M^+, 20), 163 (28), 149 (100), 136 (39), 135 (68), 107 (81), 93 (52), 91 (69), 79 (80), 77 (51); HRMS calcd for $C_{11}H_{16}O$ 164.1201, found 164.1192.

(*S*)-4-Methyl-2-(1-oxopropyl)-1-cyclopentene-1-carboxaldehyde (14). Cyclopentene aldehyde **13** (791 mg, 4.82 mmol) in CH_2Cl_2 (10 mL) at −78 °C was treated with CH_2Cl_2 (225 mL) saturated with ozone at −78 °C. After 20 min, dimethyl sulfide (5 mL) was added. The resulting mixture was kept at −78 °C for 2 h and then allowed to warm to room temperature. After 4 h, the mixture was filtered through potassium carbonate and concentrated in vacuo. The resulting product is suitable for subsequent reactions without further purification. A sample for spectral analysis was obtained by column chromatography (silica gel, 8% ethyl acetate in hexane): $[\alpha]^{23}_D$ +1.18° (*c* = 0.040, $CDCl_3$); ^1H NMR δ 10.13 (s, 1), 2.9–2.3 (m, 7), 1.13 (t, 3, *J* = 7.0 Hz), 1.10 (d, 3, *J* = 6.2 Hz); ^{13}C NMR 201.3, 190.0, 153.4, 147.3, 43.6, 38.8, 35.7, 30.8, 21.0, 7.3; EIMS *m/z* (rel intensity) 166 (M^+, 77), 151 (97), 137 (61), 109 (100), 96 (49), 81 (74), 70 (65); HRMS calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0992.

(*S*)-1-[2-(1,3-Dioxolan-2-yl)-4-methyl-1-cyclopenten-1-yl]-1-propanone (15). Ethylene glycol (3 mL) and oxalic acid (220 mg, 2.44 mmol) were added to an acetonitrile solution (80 mL) of unpurified aldehyde **14**. After 10 min, 1 N NaOH (20 mL) was added to the vigorously stirred reaction mixture. Concentration in vacuo afforded an emulsion, which was diluted with water and extracted with 1:1 hexane–ether (3 × 50 mL). The combined organic extracts were washed with brine and dried (K_2CO_3). Concentration in vacuo gave 341 mg (34% overall from **13**) of acetal **15**, sufficiently pure for use in subsequent reactions. A pure sample was obtained by column chromatography (silica gel, 15% EtOAc in hexane): $[\alpha]^{27}_D$ + 4.21° (*c* = 0.0107, $CDCl_3$); UV λ_{max} (CH_3OH) 243 nm; ^1H NMR δ 5.89 (s, 1), 3.9–3.8 (m, 4), 2.81–2.36 (m, 5), 2.45 (q, 2, *J* = 7.2 Hz), 1.01 (d, 3, *J* = 6.6 Hz), 1.00 (t, 3, *J* = 7.3 Hz); ^{13}C NMR 201.8, 148.4, 140.8, 98.5, 65.5, 42.6, 39.8, 35.5, 30.6, 21.1, 7.5; EIMS *m/z* (rel intensity) 210 (M^+, 3), 181 (18), 165 (18), 153 (100), 109 (52); HRMS calcd *m/z* for $C_{12}H_{18}O_3$ 210.1252, found 210.1252.

(1*R*)-(1α,3α,5α)-1-[5-(1,3-Dioxolan-2-yl)-3-methyl-6-oxabicyclo[3.1.0]hex-1-yl]-1-propanone (16). Solid MCPBA (453 mg, 2.10 mmol) was added in one portion to a $CHCl_3$ solution (50 mL) of unpurified acetal **15** (341 mg, 1.62 mmol), and the resulting mixture was stirred at room temperature overnight. Treatment with 0.5 N NaOH (20 mL) gave an organic layer, which was washed with 0.5 N NaOH (2 × 25 mL) and brine and then dried (K_2CO_3). Concentration in vacuo followed by column chromatography (silica gel, $CHCl_3$) gave 219 mg (60%) of pure epoxide **16**: $[\alpha]^{25}_D$ + 3.88° (*c* = 0.0129, $CDCl_3$); ^1H NMR δ 5.01 (s, 1), 4.0–3.8 (m, 4), 2.7–1.5 (m, 7), 1.06 (t, 3, *J* = 7.2 Hz), 1.04 (d, 3, *J* = 6.1 Hz); ^{13}C NMR 206.9, 100.9, 73.4, 72.6, 65.2, 37.0, 34.3, 32.9, 27.3, 18.4, 7.0; EIMS *m/z* (rel intensity) 226 (M^+, 1), 169 (29), 126 (8), 99 (52), 73 (100); HRMS calcd *m/z* for $C_{12}H_{18}O_4$ 226.1205, found 226.1209.

Citronellal Dimethyl Acetal (19). Trimethyl orthoacetate (8.8 mL, 0.08 mol) was added (45 min) to a solution of (*R*)-citronellal (11.3 g, 0.073 mol) and pyridinium *p*-toluenesulfonate (550 mg, 2.1 mmol) in MeOH (11 mL) at reflux. The resulting solution was stirred at reflux overnight. The reaction mixture was quenched by addition of 0.1 M NaOMe–MeOH (30 mL), diluted with ether (50 mL), and washed with water (50 mL) and brine (2 × 35 mL). After the aqueous layers were combined and extracted with ether (2 × 35 mL), the ether layers were combined and dried ($MgSO_4$). Concentration in vacuo and purification by bulb-to-bulb distillation gave **19** (11.61 g, 80%): ^1H NMR data identical with reported data;[23] ^{13}C NMR 131.1, 124.6, 103.0, 52.6, 52.0, 39.3, 37.3, 28.7, 25.6, 25.3, 19.6, 17.5; EIMS *m/z* (rel intensity) 200 (M^+, 0.1), 185 (0.4), 168 (6), 121 (74), 95 (35), 75 (100), 58 (29).

Aldehyde Acetal 20.[23] A solution of acetal **19** (5.6 g, 0.028 mol) in MeOH (75 mL) at −78 °C was treated with ozone as reported, but then was treated with H_2 at 35 psi for 45 min in the presence of a 5% Pd–C catalyst. Filtration and concentration of the filtrate in vacuo provided compound **20** (4.76 g, 97%).

(*S*)-4-Methyl-1-cyclopentenecarboxaldehyde (22).[24] 1,8-Diazabicyclo[5.4.0]undec-7-ene (6.19 mL, 41.4 mmol) was added via syringe to a solution of aldehyde acetal **20** (6 g, 34.5 mmol) in CH_2Cl_2 (35 mL) at room temperature. After 5 min, TMSCl (4.82 g, 37.95 mmol) was added dropwise, and the reaction mixture was then heated to reflux. After 3 h the mixture was diluted with CH_2Cl_2 (30 mL), washed with 1% HCl solution (2 × 50 mL), saturated $NaHCO_3$ (2 × 50 mL), and brine (50 mL), and dried ($MgSO_4$). Concentration in vacuo gave **21** (7.6 g, ca. 89%) as an unstable oil [EIMS *m/z* (rel intensity) 246 (M^+, 0.1), 156 (20), 115 (90), 99 (17), 85 (19), 75 (75), 73 (100), 59 (18)].

A solution of the enol ether **21** in CH_2Cl_2 (7.97 g in 30 mL) was added to a solution of $TiCl_4$ (5.36 mL) in CH_2Cl_2 (190 mL) at −20 °C (cryostat) via syringe pump over 24 h. After 24 h the reaction mixture was allowed to warm to 0 °C and stirred for 4 h, at which time the reaction was determined to be complete by GC analysis. The reaction mixture was quenched by adding a solution of saturated K_2CO_3 (60 mL). After 1 h, the resulting layers were separated and the aqueous layer was extracted with ether (3 × 75 mL). The organic layers were combined and dried ($MgSO_4$). Concentration in vacuo and purification by column chromatography gave aldehydes **22** and **23** (1.64 g, 46%) as a 9:1 mixture of regioisomers. Aldehyde **22**: ^1H NMR δ 9.75 (s, 1), 6.83–6.81 (m, 1), 2.83–2.66 (m, 2), 2.55–2.45 (m, 1), 2.25–2.04 (m, 2), 1.07 (d, 3, *J* = 6.9 Hz); ^{13}C NMR 190.2, 152.3, 145.5, 41.9, 36.6, 32.3, 21.6; EIMS *m/z* (rel intensity) 110 (M^+, 31) 95 (52), 81 (100), 67 (63), 53 (43), 41 (39).

Cyclopentenal 22 via HCl-Catalyzed Cyclization. To a solution of acetal **20** (4.76 g, 0.027 mol) in THF (120 mL) at room temperature was added a solution of 1 N HCl (2.5 mL). After being stirred for 7.5 h, the reaction mixture was diluted with ether (60 mL) and washed with saturated $NaHCO_3$ (60 mL), water (60 mL), and brine (60 mL). The aqueous layers were combined and extracted with ether (50 mL), and the combined ether layers were dried ($MgSO_4$). Concentration in vacuo gave 4.5 g of compounds **22** and **23** (ca. 95:5), material that was used in the following reaction without further purification.

Methyl (*S*)-4-Methyl-1-cyclopentenecarboxylate (24). To a solution of unpurified cyclopentenal **22** (4.5 g, ca. 0.027 mol) and SeO_2 (1.54 g, 0.014 mol) in MeOH (140 mL) at 0 °C was added H_2O_2 (0.042 mol, 30% in H_2O). The reaction mixture was allowed to warm to room temperature and stirred for 5.5 h. The reaction mixture was then diluted with ether (100 mL) and washed with saturated $NaHCO_3$ (2 × 65 mL), water (2 × 50 mL), and brine (60 mL). The aqueous layers were combined and extracted with ether (75 mL), and the combined ether layers were dried ($MgSO_4$). Concentration in vacuo and purification by flash chromatography (silica, hexane 55%, ethyl acetate 45%) provided compound **24** (975 mg, 26% overall from aldehyde acetal **20**): $[\alpha]^{28}_D$ +3.18° (*c* = 0.027, Et_2O); ^1H NMR δ 6.68 (t, 1, *J* = 1.9 Hz), 3.71 (s, 3), 2.76–2.61 (m, 2), 2.47–2.41 (m, 1), 2.19–2.04 (m, 2), 1.04 (d, 3, *J* = 6.9 Hz); ^{13}C NMR 165.7, 142.8, 135.4, 51.2, 41.5, 39.5, 32.1, 21.4; EIMS *m/z* (rel intensity) 140, (M^+, 4), 125 (4), 109 (9), 79 (71), 65 (42), 59 (73), 53 (100); HRMS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0824.

Methyl (1*R*,2*R*,4*S*)-4-Methyl-6-oxabicyclo[3.1.0]hexanecarboxylate (25). To a solution of ester **24** in anhydrous $CHCl_3$ at room temperature was added a solution of MCPBA (905 mg, 4.46 mmol) in $CHCl_3$ (10 mL). The resulting mixture was then stirred for 17 h. A white precipitate formed and was removed by filtration. The resulting solution was diluted with $CHCl_3$ and washed with 0.5 N NaOH (35 mL), saturated $NaHCO_3$ (2 × 35 mL), and brine (35 mL). The aqueous layers were extracted with $CHCl_3$, and the combined $CHCl_3$ solutions were dried ($MgSO_4$). Concentration in vacuo gave epoxide **25** as a clear oil (464 mg, 80%): $[\alpha]^{28}_D$ −2.93° (*c* = 0.134, Et_2O); ^1H NMR δ 3.79 (s, 3), 2.29–2.17 (m, 2), 1.94–1.87 (m, 1), 1.81–1.72 (m, 2), 1.39–1.32 (m, 1), 1.02 (d, 3, *J* = 6.8 Hz); ^{13}C NMR 169.9, 63.6, 62.3, 52.3, 35.8, 35.2, 26.9, 18.7; EIMS *m/z* (rel intensity) 156 (M^+, 0.1), 141 (0.1), 97 (4), 69 (32), 59 (63), 41 (100); HRMS calcd for $C_8H_{12}O_3$ 156.0787,

(23) Naruse, Y.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 6021.

(24) Bloch, R.; Bouket, J.-L.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1969**, 489.

found 156.0787. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.56; H, 7.87.

Methyl (4*R*)-2-Oxo-4- and (5*R*)-2-Oxo-5-methylcyclopentanecarboxylate (28 and 29).[18] A Dieckmann condensation was used to prepare keto esters **28** and **29** from dimethyl (*R*)-3-methyladipate[17] ($[\alpha]^{24}_D$ +4.7° (*c* = 0.0710, $CHCl_3$)) in 83% yield. Analysis of the high-field ^1H NMR spectrum of the product mixture indicated the formation of three isomers: two diastereomers of keto ester **28** and one of its regioisomer **29**. Integration of the methyl ester resonances or the aliphatic methyl resonances indicated a ratio of about 2.8:1 in favor of compounds **28**.

Methyl (*R*)-4-Methyl-2-[(trimethylsilyl)oxy]-1-cyclopentenecarboxylate (30). A mixture of keto esters **28** and **29** (5.01 g, 32.1 mmol) was dissolved in THF, and a catalytic amount of $(n\text{-Bu})_4NF$ (0.01 equiv) was added. The silyl ketene acetal of methyl propionate[25] was added (5 mL), and after 15 min at room temperature the reaction was monitored by GC. An additional 1 mL of the silyl ketene was added every 15 min until the silylation was complete. The reaction mixture was diluted with pentane (25 mL) and filtered through a cotton plug. After concentration in vacuo, the product was purified by distillation, giving 7.15 g (98%) of silyl enol ether **30** (along with its regioisomer) as a clear oil: bp 60 °C (0.6 mm); ^1H NMR (**30**) δ 3.57 (s), 0.95 (d, *J* = 6.8 Hz); (**31**) δ 3.58 (s), 1.01 (d, *J* = 6.7 Hz); ^{13}C NMR (**30**) 165.2, 163.9, 107.6, 50.3, 43.9, 37.1, 28.0, 21.5, 0.3; (**31**) 165.2, 164.7, 113.9, 50.1, 36.3, 34.1, 27.7, 20.6, 0.3.

Chlorobenzoate Ester (32). A solution of MCPBA (2.07 g, 8.8 mmol; 73% peracid) in 80 mL of CH_2Cl_2 was added dropwise to a solution of the silyl ethers **30** and **31** (1.00 g, 4.38 mmol) in 40 mL of anhydrous CH_2Cl_2 at 0 °C. Once the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The resulting precipitate (chlorobenzoic acid) was removed by filtration and the filtrate washed with saturated sodium carbonate (3 × 30 mL). After treatment of the organic layer with $MgSO_4$, concentration in vacuo gave 1.2 g of a yellow oil. Purification by flash column chromatography (9:1 hexane–EtOAc) gave 0.532 g (40%) of a yellow oil, which crystallized upon storage in a refrigerator: $[\alpha]^{23}_D$ +56.7° (*c* = 0.0127, $CHCl_3$); ^1H NMR δ 7.98 (d, 1, *J* = 1.7 Hz), 7.90 (d, 1, *J* = 7.8 Hz), 7.54 (d, 1, *J* = 8.0 Hz), 7.37 (dd, 1, *J* = 7.9, 7.9 Hz), 3.79 (s, 3), 2.80 (ddd, 1, *J* = 2, 6, 13 Hz), 2.69 (ddd, 1, *J* = 18, 7, 2 Hz), 2.58 (m, 1), 2.46 (dd, 1, *J* = 10, 18 Hz), 2.23 (dd, 1, *J* = 13, 9 Hz), 1.2 (d, 3, *J* = 6 Hz); ^{13}C NMR 206.7, 167.7, 163.8, 134.6, 133.7, 130.6, 130.0, 129.8, 128.1, 85.3, 77.5, 53.3, 45.6, 41.7, 27.6, 20.4; EIMS *m/z* (rel intensity) 310 (M^+, 1), 171 (5), 139 (100), 111 (24), 59 (7). Anal. Calcd for $C_{15}H_{15}O_5Cl$: C, 57.98; H, 4.87. Found: C, 57.86; H, 4.88.

Methyl (1*R*,4*R*)-1-Hydroxy-4-methyl-2-oxocyclopentanecarboxylate (33). *N*-Methylmorpholine *N*-oxide (NMMO, 284 mg, 2.1 mmol) was added to a mixture of acetone (3 mL), water (4 mL), and OsO_4 (0.04 mmol as a 0.02 M solution in *t*-BuOH). The resulting mixture was cooled to −15 °C, and crude silyl enol ether **30** (456 mg, 2 mmol in 3 mL of acetone) was added in one portion. After the reaction had warmed to room temperature, sodium bisulfite and Florisil (3 g) was added. The resulting slurry was stirred for 15 min and filtered through a pad of Celite, and the pad was washed with acetone (3 × 10 mL). The combined filtrates were neutralized with 1 M H_2SO_4 and concentrated in vacuo. The remaining aqueous solution was acidified (to pH 2), saturated with sodium chloride, and extracted with ethyl acetate (4 × 15 mL). The combined organic solutions were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography (9:1 hexane–EtOAc) yielded 200 mg (58%) of a mixture of the desired hydroxy keto ester **33** and its diastereomer **34** in a 10:1 ratio. (Other fractions yielded 71.1 mg (22%) of keto esters **28** and **29** in a 1:10 ratio and 17.8 mg (5%) of the hydroxylated regioisomers.) Compound **33**: $[\alpha]^{24}_D$ + 45.1° (*c* = 0.0317, $CHCl_3$); ^1H NMR δ 3.77 (s, 3), 2.58 (ddd, 1, *J* = 2.4, 7.0, 17.9 Hz), 2.49 (m, 1), 2.20 (ddd, 1, *J* = 2.4, 6.3, 13.8 Hz), 2.00 (dd, 1, *J* = 11.6, 17.9 Hz), 1.97 (dd, 1, *J* = 11.6, 14.2 Hz), 1.14 (d, 3, *J* = 6.5 Hz); ^{13}C NMR 212.0, 172.2, 80.8, 53.2, 45.1, 43.1, 28.3, 20.0; EIMS *m/z* (rel intensity) 172 (M^+, 24), 140 (16), 116 (41), 112 (42), 102 (30), 74 (100), 56 (81). Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.03. Found: C, 55.79; H, 7.19.

Methyl (1*R*,4*R*)-4-Methyl-2-[[(trifluoromethyl)sulfonyl]oxy]-1-hydroxy-2-cyclopentenecarboxylate (36). A 10:1 mixture of alcohols **33** and **34** (7.35 g, 42.7 mmol) in DMF (80 mL) was treated with imidazole (5.82 g, 85.5 mmol) and $(CH_3)_3SiCl$ (10.85 mL, 85.5 mmol) at room temperature. After 1 h, ether was added (300 mL) and the organic layer was washed with water (4 × 40 mL) and brine and dried ($MgSO_4$). Concentration in vacuo yielded a crude oil. Distillation (75 °C, 0.8 mm) gave 10.40 g (100%) of the TMS ether **35**: ^1H NMR δ 3.73 (s, 3), 2.57 (ddd, 1, *J* = 2.6, 7.3, 18.3 Hz), 2.43 (m, 1), 2.21 (ddd, 1, *J* = 2.6, 6.0, 13.4 Hz), 1.95 (dd, 1, *J* = 11.1, 18.3 Hz), 1.91 (dd, 1, *J* = 11.6, 13.4 Hz), 1.14 (d, 3, *J* = 6.5 Hz), 0.13 (s, 9); ^{13}C NMR 210.2, 171.4, 82.8, 51.8, 46.0, 44.6, 27.7, 19.4, 1.1; EIMS *m/z* (rel intensity) 244 (M^+, 2), 229 (6), 201 (56), 169 (41), 159 (66), 89 (78), 73 (48), 59 (33).

The silyl ether **35** (2.00 g, 8.19 mmol) in THF (5 mL) was added to LDA (8.19 mmol) in 10 mL of THF at −70 °C, and the resulting solution was stirred for 15 min. *N*-Phenyltriflimide (3.00 g, 8.40 mmol) was added, and the mixture was allowed to warm to room temperature. After it was stirred for 1 h, the reaction mixture was diluted with ether (50 mL) and washed twice with 1 M HCl and once with brine. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to afford 5.01 g of crude product. Upon treatment with 1 M HCl and THF in a two-phase system, the TMS ether was cleaved. Final purification by flash chromatography gave 1.57 g (66%) of compound **36**: $[\alpha]^{24}_D$ −33.0° (*c* = 0.1036, $CHCl_3$); ^1H NMR δ 5.91 (d, 1, *J* = 2.4 Hz), 3.84 (s, 3), 3.05 (m, 1), 2.33 (dd, 1, *J* = 8.1, 14.0 Hz), 2.03 (dd, 1, *J* = 4.4, 14.0 Hz), 1.16 (d, 3, *J* = 7.1 Hz); ^{13}C NMR 172.9, 146.2, 126.9, 118.3 (q, J_{CF} = 320.5 Hz), 82.0, 53.5, 43.6, 33.3, 19.9; EIMS *m/z* (rel intensity) 286 (M^+ − 18, 0.1), 245 (100), 69 (43), 67 (31), 59 (7). Anal. Calcd for $C_9H_{11}F_3O_6S$: C, 35.33; H, 3.64. Found: C, 35.56; H, 3.78.

2-Ethenyl-1-hydroxy-4-methyl-2-cyclopentenecarboxylic Acid, Methyl Ester (37). The vinyl triflate **36** (325 mg, 1.07 mmol) was added to a solution of LiCl (318 mg, 7.5 mmol) and $Pd(Ph_3P)_4$ (12.7 mg, 0.011 mmol) in THF (20 mL). The mixture was stirred at room temperature for 15 min, tributylvinyltin (338 mg, 1.07 mmol) was added, and the mixture was heated to reflux. After 6 h at reflux, TLC analysis indicated complete consumption of the vinyl triflate. The reaction mixture was allowed to cool, diluted with ether (50 mL), and washed with 1 M HCl (2 × 15 mL), water, and brine. The organic layer was dried ($MgSO_4$) and concentated in vacuo to afford 853 mg of a crude oil. This material was purified by flash chromatography (hexane followed by 5% EtOAc), to afford diene **37** (167 mg, 86%): $[\alpha]^{23}_D$ −46.5° (*c* = 0.0154, $CHCl_3$); ^1H NMR δ 6.26 (dd, 1, *J* = 11.3, 17.9 Hz), 5.93 (d, 1, *J* = 2.2 Hz), 5.10 (d, 1, *J* = 17.9 Hz), 5.02 (d, 1, *J* = 11.3 Hz), 3.78 (s, 3), 3.08 (m, 1), 2.31 (dd, 1, *J* = 7.8, 13.8 Hz), 1.96 (dd, 1, *J* = 5.6, 13.8 Hz), 1.10 (d, 3, *J* = 7.1 Hz); EIMS *m/z* (rel intensity) 182 (M^+, 2), 164 (25), 149 (2), 123 (100), 79 (57), 77 (54); HRMS calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0963.

Methyl (1*R*,4*R*)-2-Formyl-1-hydroxy-4-methyl-2-cyclopentenecarboxylate (26). A catalytic amount of osmium tetraoxide (0.004 mmol as a 0.02 M solution in *t*-BuOH) was added to diene **37** (65 mg, 0.36 mmol) in acetone–water [(3 mL):(1 mL)], and the solution was stirred for 15 min at room temperature. Over 1 h, sodium periodate (147 mg, 0.72 mmol) dissolved in 2 mL of water was added to the solution. Following the addition, the reaction mixture was stirred at room temperature until TLC analysis indicated consumption of starting material. The solution was extracted with EtOAc (5 × 5 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated to afford 93 mg of crude product. Purification by flash column chromatography (silica gel, 9:1 hexane–EtOAc) gave 22 mg (32%) of compound **26**: $[\alpha]^{24}_D$ + 8.34° (*c* = 0.0127, $CHCl_3$); ^1H NMR δ 9.67 (s, 1), 6.92 (d, 1, *J* = 2.2 Hz), 3.76 (s, 3), 3.30 (m, 1), 2.34 (dd, 1, *J* = 7.5, 13.9 Hz), 1.97 (dd, 1, *J* = 6.2, 13.9 Hz), 1.21 (d, 3, *J* = 7.2 Hz); ^{13}C NMR 188.2, 174.9, 160.0, 129.0, 82.2, 53.1, 46.4, 39.2, 18.9; EIMS *m/z* (rel intensity) 169 (M^+ − 15, 0.1), 166 (M^+ − 18, 2), 125 (100), 97 (19). Anal. Calcd for $C_9H_{12}O_4$: C, 58.96; H, 6.57. Found: C, 58.57; H, 6.87.

Acknowledgment. The financial support of the Sloan Foundation and the National Institutes of Health (CA

(25) Kita, Y.; Yasuda, H.; Haruta, J.; Segawa, J.; Tamura, Y. *Synthesis* **1982**, 1089.

33743) is gratefully acknowledged.

Registry No. **5**, 81542-94-1; **6**, 62820-13-7; **7**, 67707-87-3; **8**, 5949-05-3; **9** (isomer 1), 82507-56-0; **9** (isomer 2), 82507-57-1; **10**, 82507-58-2; **12**, 82507-44-6; **13**, 82507-45-7; **14**, 82507-46-8; **15**, 128471-61-4; **16**, 128571-81-3; **17**, 89-82-7; **18**, 2385-77-5; **19**, 128471-62-5; **20**, 128471-63-6; **21**, 128471-64-7; **22**, 128471-65-8; **23**, 128571-82-4; **24**, 128471-66-9; **25**, 128471-67-0; **26**, 128471-68-1; **27**, 4463-74-5; **28** (isomer 1), 128571-83-5; **28** (isomer 2), 128571-85-7; **29**, 80796-76-5; **30**, 128471-69-2; **31**, 128471-70-5; **32**, 128471-71-6; **33**, 128471-72-7; **34**, 128571-84-6; **35**, 128471-73-8; **36**, 128471-74-9; **37**, 128471-75-0; $CH_3CH{=}C(OMe)OTMS$, 34880-70-1.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds **9**, **13–16**, **22**, and **24** and crystal data for compound **32** (22 pages). Ordering information is given on any current masthead page.

Olefin Synthesis by Vanadium(V)-Induced Oxidative Decarboxylation–Deoxygenation of 3-Hydroxy Carboxylic Acids

Ingrid K. Meier and Jeffrey Schwartz*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544-1009

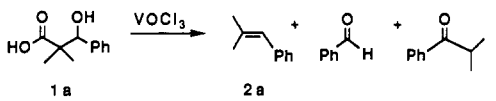
Received March 19, 1990

Oxidative decarboxylation of 3-hydroxy carboxylic acids can be effected with various V(V) complexes. This process likely yields an intermediate 1,4-metalla diradical. β-Elimination from this intermediate gives olefin and regenerates V(V), likely as VO_2Cl. Thus, although the overall process involves no net change in oxidation state for vanadium, the decarboxylation process is oxidatively induced. Intramolecular trapping of the intermediate yields glycolate and then C–C cleavage products, and skeletal rearrangement gives ketonic products. Qualitatively, rates for oxidative decarboxylation of the acids and the stereospecificity of formation of olefinic products depend on the electron-withdrawing ability of groups attached to vanadium. Methodology is described for the preparation of tri- and tetrasubstituted olefins in high yield from appropriate 3-hydroxy carboxylic acid precursors.

3-Hydroxy carboxylic acids are easily obtained products of "aldol" condensation processes. In concept, removing hydroxyl and carboxyl functionality from these "aldol" products enables the preparation of olefins from carbonyl precursors; in fact, several methods exist to realize this overall transformation.[1-3] One previously unexplored option for this transformation involves oxidatively removing the carboxylate unit and then β-elimination of the hydroxyl-derived fragment. Although oxidative decarboxylation of 2-hydroxy carboxylic acids is well known,[4] no investigation of 3-hydroxy carboxylic acids had been reported prior to our initial report.[5] At that time, we noted that readily available $VOCl_3$ or its simple derivatives could react with "aldol" acids to give olefins in a straightforward, synthetically useful way.

The Simple Reaction between $VOCl_3$ and 3-Hydroxy Carboxylic Acids. When $VOCl_3$ was added to a suspension of hydroxy acid **1a** (1 equiv) in anhydrous chlorobenzene at room temperature followed by heating to reflux, **2a** (61%) and benzaldehyde (37%) were obtained

Scheme I



(Scheme I). When solvents such as acetonitrile, dimethyl sulfoxide, or tetrahydrofuran (THF) were used, little olefin, but much isobutyrophenone, was produced.[6] When toluene was used, a major product observed by GC/MS (ca. 60%) showed solvent incorporation, though the structure of this product was not identified.[7] Unreactive, high-boiling chlorobenzene was the solvent of choice.

Several problems characterize the simple $VOCl_3$ system (Table I) including dehydration, double-bond migration, and E/Z isomerization. Dehydration, either proton (2 equiv of HCl are produced in the reaction) or Lewis acid catalyzed ($VOCl_3$ is a strong Lewis acid), can occur in 3-hydroxy carboxylic acids which are not disubstituted in the 2-position. For example, **1f** gave 3,3-diphenyl-2-propenoic acid (8) as the major product. When pure **2c*E*** was added to a reaction of $VOCl_3$ and 3-hydroxy carboxylic acid **1a** which was in progress, it rapidly E/Z isomerized; product olefins are thus unstable to these reaction conditions. However, when **2c** (E/Z = 0.74) was added to an ongoing reaction between $VOCl_3$ and **1a** to which 1 equiv of Proton Sponge (1,8-bis(dimethylamino)naphthalene)

(1) (a) Adam, W.; Baeza, J.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2000. (b) Noyce, D. S.; Banitt, E. H. *J. Org. Chem.* **1966**, *32*, 4043. (c) Krapcho, A. P.; Jahngen, E. G. E., Jr. *Ibid.* **1974**, *39*, 1650. (d) Schollkopf, U.; Hoppe, I. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 765. (e) Mageswaran, S.; Sultanbawa, M. U. S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 884. (f) Imai, T.; Nishida, S. *J. Org. Chem.* **1980**, *45*, 2354.

(2) Mulzer, J.; Lammer, O. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 628.

(3) Hara, S.; Taguchi, H.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* **1975**, 1545.

(4) For examples of oxidative decarboxylation of 2-hydroxy carboxylic acids with V(V), see: (a) Jones, J. R.; Waters, W. A.; Littler, J. S. *J. Chem. Soc., London* **1961**, 630. (b) Mehrotra, R. N. *J. Chem. Soc. B* **1968**, 642. (c) Paul, S. D.; Pradhan, D. G. *Indian J. Chem.* **1972**, *10*, 562. (d) Virtanen, P. O. I.; Karppinen, S. *Finn. Chem. Lett.* **1984**, 34. (e) Kalidoss, P.; Srinivasan, V. S. *J. Chem. Soc., Dalton, Trans.* **1984**, 2631. (f) Micera, G.: Deiana, S.; Dessi, A.; Pusino, A.; Gessa, C. *Inorg. Chim. Acta* **1986**, *120*, 49.

(5) Meier, I. K.; Schwartz, J. *J. Am. Chem. Soc.* **1989**, *111*, 3069.

(6) Such solvents form adducts with $VOCl_3$. See: (a) Funk, V. H.; Weiss, W.; Zeising, M. *Z. Anorg. Allg. Chem.* **1958**, *296*, 36. (b) Baker, K. L.; Edwards, D. A.; Fowles, G. W. A.; Williams, R. G. *J. Inorg. Nucl. Chem.* **1967**, *29*, 1881. (c) Miles, S. J.; Wilkins, J. D. *Ibid.* **1975**, *37*, 2271.

(7) Such solvents form charge transfer complexes with $VOCl_3$. See: H.-L.; Krauss, H.-L.; Gnatz, G. *Chem. Ber.* **1962**, *95*, 1023. (b) Krauss, H.-L.; Deffner, U. *Z. Naturforsch.* **1964**, *19b*, 1.

(8) Cornforth, D. A.; Opara, A. E.; Read, G. *J. Chem. Soc. C* **1969**, 2799.

0022-3263/90/1955-5619$02.50/0