C, and D. Analysis of the middle fraction by GC on a more polar column (Carbowax 20M, 100 °C, 15 mL/min N_2) resolved these three components. Preparative GC separation using similar conditions (Carbowax 20M, 160 °C, 25 mL/min N_2) gave pure samples of B, C, and D (18.0, 19.5, 22.0 min, peak area ~3:1:1).

Spectral Data. Lavandulol (B): EIMS *m/z* 154 (1), 152 (3), 150 (1), 139 (2), 137 (5), 136 (4), 124 (20), 123 (22), 121 (17), 111 (43), 109 (26), 93 (34), 91 (21), 81 (26), 79 (20), 77 (15), 69 (100), 68 (25), 67 (37), 41 (35); ^{1}H NMR ($CDCl_3$) δ 5.06 (1 H, complex multiplet), 4.91 (1 H, mult), 4.80 (1 H, mult), 3.52 (2 H, mult), 2.26 (1 H, mult), 2.06 (2 H, mult), 1.68 (6 H, mult), 1.59 (3 H, br s). **α-Necrodol (A):** high resolution MS: *m/z* 154.1353 (calcd for $C_{10}H_{18}O$, 154.1358); EIMS *m/z* 154 (7), 139 (46), 136 (6), 123 (100), 121 (50), 107 (26), 105 (25), 95 (18), 93 (36), 91 (38), 81 (71), 79 (30), 77 (22), 69 (11), 67 (22), 65 (10), 55 (18), 53 (12), 43 (14), 41 (20), 39 (14); CIMS *m/z* 155 (0.5), 154 (2), 153 (14), 139 (15), 138 (13), 137 (100), 135 (7), 122 (8), 95 (11), 81 (10); ^{1}H NMR ($CDCl_3$) δ 5.22 (1 H, qdd, *J* = 1.5, 2.0, 1.6), 3.61 (1 H, ddd, *J* = 10.7, 5.5, 4.0), 3.56 (1 H, ddd, *J* = 10.7, 5.5, 5.0), 2.28 (1 H, qdddd, *J* = 2.0, 5.5, 5.5, 6.8, 2.0, 1.8), 2.12 (1 H, qqdd, *J* = 7.3, 1.1, 1.8, 1.6), 1.65 (3 H, ddd, *J* = 2.0, 1.5, 1.1), 1.2 (1 H, dd, *J* = 5,4), 0.99 (3 H, s), 0.90 (3 H, s), 0.86 (3 H, d, *J* = 7.3); ^{1}H NMR (C_6D_6) δ 5.13 (1 H, qdd, *J* = 1.5, 2.0, 1.6), 3.42 (1 H, ddd, *J* = 12.6, 6.8), 3.36 (1 H, ddd, *J* = 12.6, 6.8), 2.17 (1 H, qdddd, *J* = 2.0, 6.8, 6.8, 2.0, 1.8), 2.04 (1 H, qqdd, *J* = 7.3, 1.1, 1.8, 1.5), 1.51 (3 H, ddd, *J* = 2.0, 1.5, 1.8), 0.96 (3 H, s), 0.88 (3 H, s), 0.77 (3 H, d, *J* = 7.3); noise-decoupled ^{13}C NMR (C_6D_6) δ 127.8, 123.9, 62.5, 56.3, 53.4, 42.6, 24.5, 23.4, 14.7, 11.9; IR ($CHCl_3$) 3620, 2960, 2875, 1443, 1385, 1365, 1070, 1005, 950 (vw), 860 (vw) cm^{-1}.

α-Necrodol *p*-Bromobenzoate. The methylene chloride extract from the defensive spray from 140 individuals was fractionated by preparative GC (OV-1) as previously described. The first fraction, containing mostly α-necrodol, was washed from the collection tube into a 300-μL cone-shaped vial with methylene chloride (2 × 100 μL). 4-(Dimethylamino)pyridine (1 mg, Aldrich) in methylene chloride (10 μL) was added followed by *p*-bromobenzoyl chloride (3 mg, Aldrich) also in methylene chloride (50 μL). The mixture was stirred at room temperature. After 5 min, a precipitate had started to form.

When the reaction was found to be complete (TLC), a large excess of *p*-bromobenzoyl chloride remained. Addition of water (100 μL) to the reaction mixture, followed by vigorous agitation, did not result in hydrolysis of the acid chloride. Concentrated ammonium hydroxide (50 μL) was then added and resulted in the formation of an insoluble precipitate. The methylene chloride layer was examined by TLC and no acid chloride was found. This layer was removed via syringe and the remaining aqueous suspension was extracted twice with methylene chloride (50 μL). The combined methylene chloride extracts were crudely fractionated on a silica gel column (4 mm × 10 cm, hexane/ethyl acetate, 9:1 vol) and the UV-active fractions corresponding to the aromatic ester were collected. This material was then subjected to preparative high pressure liquid chromatography (9 mm × 25 cm, 10-μm Partisil, 7.5 mL/min, hexane/methylene chloride, 89:11) to give the *p*-bromobenzoate ester of α-necrodol (**11**).

Spectral Data. α-Necrodol *p*-bromobenzoate (11): EIMS *m/z* 202 (2), 200 (2), 184 (14), 183 (15), 157 (7), 155 (8), 137 (9), 136 (57), 135 (10), 123 (19), 122 (10), 121 (100), 107 (5), 105 (6), 93 (6), 81 (9), 41 (7); CIMS *m/z* 339 (4.3), 337 (5.0), 185 (0.7), 183 (0.7), 183 (0.8), 153 (0.7), 138 (11), 137 (100), 121 (5), 81 (5); IR ($CHCl_3$) 3000 (w), 1960 (s), 1715 (s), 1400 (wl), 1380 (vw), 1365 (vw), 1273 (vs), 1120 (s), 1107 (s), 1070 (s), 1013 cm^{-1} (s); ^{1}H NMR ($CDCl_3$) δ 7.87 (2 H, m), 7.56 (2 H, m), 5.20 (1 H, qdd, *J* = 1.5, 2.0, 1.6), 4.3 (1 H, dd, 10.8, 7.0), 4.18 (1 H, dd, *J* = 10.8, 6.8), 2.60 (1 H, qdddd, *J* = 2.0, 7.0, 6.8, 2.0, 1.8), 2.15 (1 H, qqdd, *J* = 7.3, 1.1, 1.8, 1.6), 1.65 (3 H, ddd, *J* = 2.0, 1.5, 1.1), 1.00 (3 H, s), 0.98 (3 H, s), 0.98 (3 H, s), 0.88 (3 H, d, *J* = 7.3); ^{1}H NMR (C_6D_6) δ 5.10 (1 H, qdd) 4.13 (1 H, dd), 4.27 (1 H, dd), 2.49 (1 H, qdddd), 1.95 (1 H, qqdd), 1.50 (3 H, ddd), 0.88 (6 H, s), 0.75 (3 H, d); noise-decoupled ^{13}C NMR ($CDCl_3$) δ 145.6, 131.6, 129.5, 127.8, 65.5, 42.7, 52.6, 43.1, 24.7, 24.1, 15.2, 12.4.

β-Necrodol (E): EIMS *m/z* 154 (65), 139 (63), 136 (2), 121 (100), 109 (12), 107 (16), 105 (21), 95 (17), 93 (47), 91 (31), 81 (27), 79 (34), 87 (21), 69 (23), 67 (39), 55 (25), 53 (20), 43 (23), 41 (50), 39 (26); CIMS *m/z* 153 (8), 137 (100), 121 (9), 95 (10), 81 (7); ^{1}H NMR ($CDCl_3$) δ 4.84 (1 H, dddd, *J* = 2.2, 2.2, 2.2, 1.1), 4.77 (1 H, dddd, *J* = 2.2, 2.2, 2.2, 1.1), 3.75 (1 H, ddd, *J* = 10.3, 5.2, 4.8), 3.45 (1 H, ddd, *J* = 10.3, 8.5, 4.8), 2.58 (1 H, ddddd, *J* = 8.5, 17.3, 2.2, 2.2, 2.2), 2.25 (1 H, dddd, *J* = 17.3, 5.2, 2.2, 2.2), 2.14 (1 H, qddd, *J* = 7.0, 2.2, 2.2, 2.2), 1.84 (1 H, dddd, *J* = 8.5, 8.5, 5.2, 5.2), 0.917 (3 H, s), 0.915 (3 H, d, *J* = 7.0), 0.807 (3 H, s).

Acknowledgment. J.M. is deeply grateful to the N.I.H. Fogarty Scholar-in-Residence program for its hospitality during the preparation of this manuscript. The partial support of this research by N.I.H. research grants AI-12020 and AI-02908, and an N.I.H. Training grant (5-T32GM07273), as well as an unrestricted grant from the Schering Corporation, is acknowledged with pleasure. Initial phases of the study were carried out at the Archbold Biological Station, Lake Placid, FL.

Registry No. Octanoic acid, 124-07-2; decanoic acid, 334-48-5; (*Z*)-3-decenoic acid, 2430-93-5; (*Z*)-4-decenoic acid, 505-90-8; hexadecanoic acid, 57-10-3; octadecanoic acid, 57-11-4; lavandulol, 498-16-8; α-necrodol, 104104-38-3; β-necrodol, 104086-70-6.

Defense Mechanisms of Arthropods. 84. Synthesis of (−)-α-Necrodol and (−)-β-Necrodol: Novel Cyclopentanoid Terpenes from a Carrion Beetle

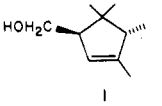
Robert T. Jacobs, Geoffrey I. Feutrill,† and Jerrold Meinwald*

Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301

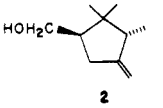
Received February 24, 1988

Syntheses of (−)-α-necrodol (1) and (−)-β-necrodol (2) from (+)-phenylcamphoric acid (**7a**) are described. In addition, several related compounds, (+)-*epi*-α-necrodol (**3**), (+)-*epi*-β-necrodol (**4**), and (+)-γ-necrodol (**5**), have been prepared. The absolute configuration of natural α-necrodol has been established as 3*R*,5*R* by comparison of its (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl ester with the ester derived from synthetic **1**.

The defensive spray of the red-lined carrion beetle, *Necrodes surinamensis*, contains two novel C_{10} alcohols, α- and β-necrodol, for which we have proposed the structures **1** and **2**, respectively.[1] The 1,2,2,3,4-pentamethylcyclopentane (necrodane) skeleton has not been described previously for any monoterpene, nor can it be derived



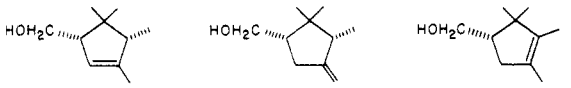
1



2

†Deceased July 4, 1987.

without rearrangement from cyclization of geranyl pyrophosphate. We undertook syntheses of structures **1** and **2** in order to confirm the necrodols' structures, to establish their relative and absolute configurations unambiguously, and to provide material for biological testing. We now report successful syntheses of (−)-α-necrodol (**1**) and (−)-β-necrodol (**2**), as well as syntheses of (+)-*epi*-α-necrodol (**3**), (+)-*epi*-β-necrodol (**4**), and (+)-γ-necrodol (**5**), closely related compounds not known from natural sources.



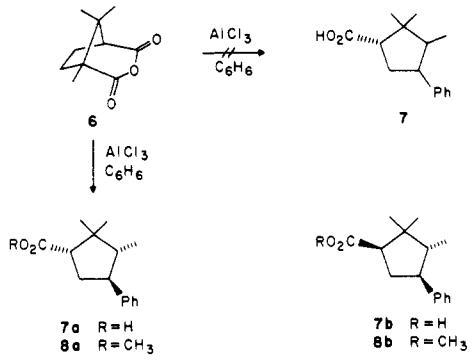
3 **4** **5**

An attractive starting material for the preparation of **1** and **2** appeared to be "phenylcamphoric acid", a compound readily obtained from camphoric anhydride (**6**) by treatment with aluminum chloride and benzene as shown in Scheme I.[2] After long controversy, phenylcamphoric acid had been assigned the structure and stereochemistry shown in formula **7b**.[3] However, when we prepared this compound as previously described, we found that the carboxyl substituent at C1 and the methyl group at C3, previously considered to be trans to each other, were actually cis.[4] This conclusion, supported by a single-crystal X-ray structure determination carried out on the corresponding methyl ester **8a**, established the structure and configuration of phenylcamphoric acid to be that represented by formula **7a**. To use methyl phenylcamphorate (**8a**) as an intermediate in our proposed syntheses, therefore, we needed to epimerize the methoxycarbonyl substituent, a transformation that had been reported previously to be unsuccessful.[5] Fortunately, we found that treatment of **8a** with sodium methoxide in methanol resulted in equilibration with the desired trans isomer **8b** after several days at reflux.

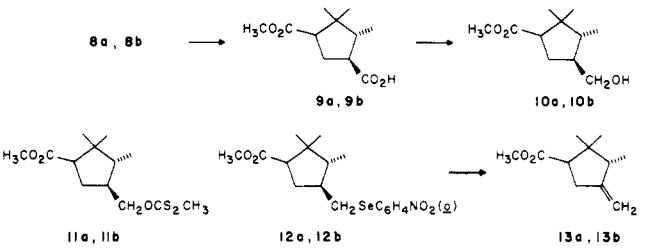
The progress of the epimerization could be monitored both by gas chromatographic and ^{1}H NMR spectroscopic techniques. The most striking spectral change in the epimer mixture was the increase in intensity of a pair of resonances in the ^{1}H NMR spectrum at δ = 0.92 and δ = 0.95 ppm, which were assigned to the geminal methyl groups of **8b**, accompanied by a corresponding decrease in intensity of the geminal methyl group resonances of **8a** (δ = 0.76 and δ = 1.16 ppm). Integration of these two sets of resonances gave the relative proportions of **8b** to **8a**. This pattern of the geminal methyl group resonances was not confined to **8a** and **8b** but was observed for most intermediates in the synthetic sequences and provided a simple criterion for the determination of both the identity and stereochemical purity of subsequent intermediates.

Separation of **8a** and **8b** was achieved by crystallization of **8a** from the equilibrium mixture, resulting in enhancement of the proportion of the desired trans isomer **8b** in the filtrate. By this procedure, an 80:20 mixture of **8b**:**8a** was obtained easily. Further purification by high pressure liquid chromatography (HPLC) gave a pure sample of **8b**.[6]

Scheme I



Scheme II



With both the cis and trans esters available, the syntheses of β-necrodol (**2**) and *epi*-β-necrodol (**4**) outlined in Scheme II were begun.[7] Oxidation of **8** with ruthenium tetraoxide in a biphasic system as described by Sharpless[8] gave the acid ester **9** in moderate yield. Treatment of **9** with borane/tetrahydrofuran reduced the carboxyl group to give hydroxy ester **10** in nearly quantitative yield. A variety of methods to convert **10** to the exocyclic olefin **13** were explored.

Treatment of **10** with phosphorus oxychloride in dry pyridine[9] gave only trace amounts of **13** after 2 days at reflux, a not entirely unexpected result, based on the known resistance of primary alcohols to phosphorus oxychloride dehydration. It was anticipated, however, that thermal eliminations of suitable derivatives of **10** would provide a more successful route to **13**.

Toward this end we first converted **10** to xanthate **11** by successive treatment with sodium hydride, carbon disulfide, and methyl iodide.[10] Surprisingly, the pyrolysis of **11** was found to take place only at temperatures in excess of 375 °C in a flow system. The isolation and subsequent purification of the volatile olefin **13** was difficult, owing to the large amounts of sulfur-containing byproducts produced in the pyrolysis. A more satisfactory sequence utilized the reaction of **10** with *o*-nitrophenylseleno cyanate and tri-*n*-butylphosphine in tetrahydrofuran to give selenide **12** in good yield.[11,12] The selenide

(1) (a) Eisner, T.; Meinwald, J. *Psyche* **1982**, *89*, 35. (b) Roach, B.; Eisner, T.; Meinwald, J. *J. Org. Chem.*, previous paper in this issue.

(2) (a) Burcker, E.; Stabil, C. *C.R. Acad. Sci., Paris* **1894**, *119*, 426. (b) Burcker, E. *Bull. Soc. Chim. Fr.* **1895**, *13*, 901.

(3) (a) Eijkman, J. F. *Chem. Weekbl.* **1907**, *4*, 727. (b) Eijkman, J. F. *Chem. Zent. II* **1907**, 2046. (c) Bantick, J. R.; Rothstein, E. *J. Chem. Soc. C* **1971**, 2512. (d) Bird, C. W.; Yeong, Y. C. *Tetrahedron* **1974**, *30*, 321.

(4) Jacobs, R.; Feutrill, G.; Meinwald, J. *Tetrahedron Lett.* **1983**, *24*, 2441.

(5) Mane, R. B.; Krishna Rao, G. S. *Ind. J. Chem.* **1974**, *12*, 932.

(6) It proved advantageous to use the 80:20 mixture of **8b**:**8a** for the preparation of **1** and **2**, as separation of the desired trans isomers from cis isomers was more efficient at later stages.

(7) As the cis isomer **7a** was obtained directly from camphoric anhydride and benzene, all reactions were performed first on cis material. Once the reaction conditions for each step had been optimized, purified trans material was carried through the synthetic scheme to generate either **1** or **2**.

(8) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

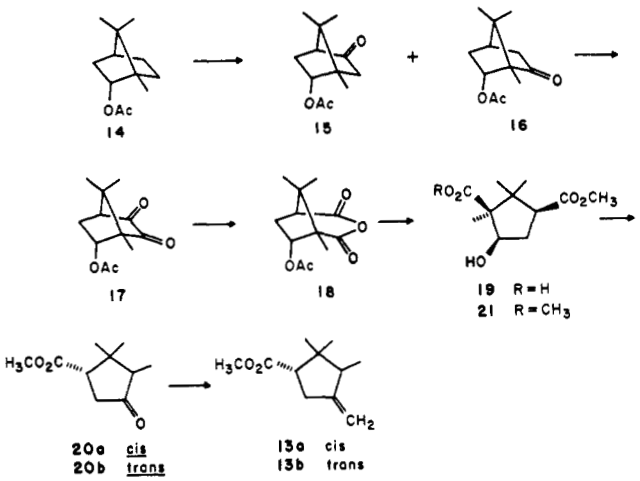
(9) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*, Vol. 1; Wiley: New York, 1967; pp 876–882.

(10) Nace, H. R. *Org. React.* **1962**, *12*, 57.

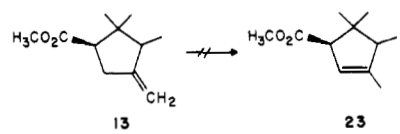
(11) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

(12) In addition, it was possible to efficiently separate epimeric selenides **12a** and **12b** by column chromatography, making possible use of the 80:20 mixture of **8b**:**8a** discussed earlier as a precursor to β-necrodol.

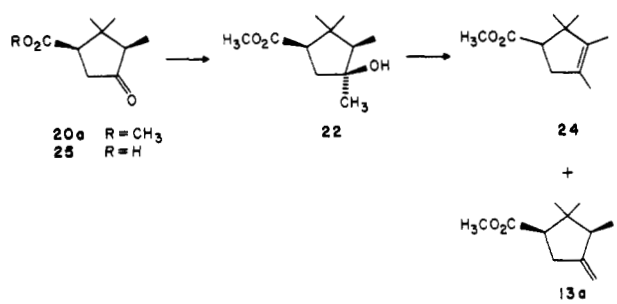
Scheme III



Scheme IV



Scheme V



was oxidized with *m*-chloroperoxybenzoic acid, and the resultant selenoxide was warmed with diisopropylamine to give olefin **13** in high yield.[13] Reduction of **13b** with lithium aluminum hydride gave (−)-β-necrodol (**2**); **13a** gave (+)-*epi*-β-necrodol (**4**). The trans isomer **2** was found to be indistinguishable from natural β-necrodol on the basis of its ^{1}H NMR spectrum and gas chromatographic behavior. On the other hand, the cis isomer **4** was found to differ clearly from the natural product on the basis of both spectroscopic and chromatographic criteria.

An independent synthesis of (+)-*epi*-β-necrodol (**4**), developed simultaneously with the above work, is outlined in Scheme III. Starting from commercially available *l*-bornyl acetate (**14**), oxidation with chromium trioxide in acetic acid[14-16] gave 5-ketobornyl acetate (**15**), accompanied by small amounts of 6-ketobornyl acetate (**16**). This mixture was separated from unreacted **14** and further oxidized with selenium dioxide to give the diketone **17**.[14] Treatment of **17** with 30% hydrogen peroxide gave the cyclic anhydride **18**,[14] which was opened selectively with a saturated methanolic hydrogen chloride solution to give monoester **19**.[17] This sequence was accompanied by methanolysis of the acetate substituent; prolonged reaction times gave the corresponding diester **21**. Treatment of **19** with chromic acid in a biphasic system,[18] followed by decarboxylation of the resultant β-keto acid in refluxing benzene, gave the epimerically pure ketone **20**, which was assigned a cis configuration (**20a**) on the basis of NOE difference spectra, as well as by comparison of later products with those obtained from the methyl phenylcamphorate route.

Methylenation of **20a** was found to be difficult, as might be expected on the basis of previously reported experience with attempted methylenations of cyclopentanones.[19,20] These failures have been attributed to the formation of enolates under the strongly basic conditions of conventional Wittig reactions. Thus, treatment of **20a** with the phosphorane derived from methyltriphenylphosphonium bromide under a variety of conditions resulted in the isolation of starting material in each case. An alternative procedure for methylenation of ketones using Tebbe's reagent[21,22] gave an intractible mixture, presumably due to competitive attack of the reagent on the ester function of **20a**.

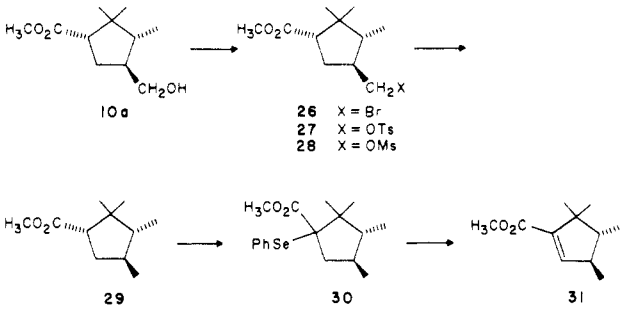
Success was ultimately realized through the use of Nozaki's recently described reagent prepared from methylene bromide, zinc dust, and titanium tetrachloride.[23] This reagent has been reported to give good yields in cases where conventional Wittig conditions had failed.[24] Application of this procedure to **20a** gave olefin **13a** in high yield. This product was found to be indistinguishable spectroscopically and chromatographically from a sample of **13a** prepared from methyl phenylcamphorate, confirming the cis disposition of the methoxycarbonyl and methyl substituents in ketone **20a**.

The epimerization of **20a** with sodium methoxide in methanol at room temperature resulted in an equilibrium mixture of **20a**:**20b** in the ratio of 3:1, respectively, as determined by the integration of the methyl resonances in the ^{1}H NMR spectrum of the mixture. Treatment of this mixture as described for pure **20a** gave a mixture of unsaturated esters, **13**, which were inseparable by gas chromatography under a variety of conditions. Reduction of this mixture with lithium aluminum hydride gave a mixture of (+)-*epi*-β-necrodol (**4**) and β-necrodol (**2**), which were separated by gas chromatography. The purified (+)-β-necrodol (**2**) prepared in this manner was indistinguishable from the natural product and the material derived from methyl phenylcamphorate on the basis of both ^{1}H NMR and chromatographic criteria. This result is to be expected from the epimerization of ketone **20a** at C4.

With these syntheses of β-necrodol completed, a direct isomerization of the exocyclic double bond to the desired endocyclic double bond present in α-necrodol as shown in Scheme IV was attractive. We felt that the best chance of success for this transformation would involve use of a transition-metal catalyst. Several organometallic catalysts

(13) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelbaum, D. F. *J. Org. Chem.* **1978**, *43*, 1697.
(14) Tiovonen, N. J.; Hirsjarvi, P.; Melaja, A.; Kainulainen, A.; Halonen, A.; Pulkkinen, E. *Acta. Chem. Scand.* **1949**, *3*, 991.
(15) Bredt, J.; Goeb, A. *J. Prakt. Chem., Ser. II* **1920**, *101*, 273.
(16) (a) Allen, M. S.; Darby, N.; Salisbury, P.; Money, T. *J. Chem. Soc., Chem. Commun.* **1977**, 358. (b) Allen, M. S.; Lamb, N.; Money, T.; Salisbury, P. *J. Chem. Soc., Chem. Commun.* **1979**, 112.
(17) Marquet, A.; Dvolaitzky, M.; Arigoni, D. *Bull. Soc. Chim. Fr.* **1966**, 2956.
(18) Brown, H. C.; Garg, C. P.; Liu, K.-T. *J. Org. Chem.* **1971**, *36*, 387.
(19) Gewali, M. B.; Ronald, R. C. *J. Org. Chem.* **1982**, *47*, 2792.
(20) Schlessinger, R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 1116.
(21) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.
(22) Pine, S. H.; Zahler, R.; Evans, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 3270.
(23) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1978**, 2417.
(24) (a) Mincione, E.; Pearson, A. J.; Bovicelli, P.; Chandler, M.; Heywood, G. C. *Tetrahedron Lett.* **1981**, 2929. (b) Hoffmann, H. M. R.; Vathke, H. *Chem. Ber.* **1980**, *113*, 3416.

Scheme VI

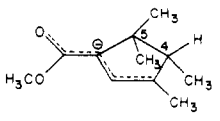


are reported to isomerize double bonds under a variety of conditions.[25] We were most encouraged by the reported successes of complexes of palladium(II), rhodium(I), and rhodium(III). We chose, therefore, to employ a representative complex of each of these metals in our system. Unfortunately, treatment of olefin **13** with each of these catalysts under conditions previously reported to effect double-bond isomerizations gave no useful result, even after extended periods of time at elevated temperatures. An independent route to α-necrodol (**1**) was, therefore, required.

One approach, aimed at introduction of the double bond in α-necrodol via an elimination pathway is outlined in Scheme V. Treatment of keto ester **20** or the corresponding keto acid **25** with either methyllithium or methylmagnesium bromide in tetrahydrofuran or ether under a variety of conditions led to mixtures of products, presumably due to comparable rates of attack of the organometallic reagent on the ester and ketone functionality. Under optimized conditions, a 60% yield of **22** was obtained after chromatography. Treatment of **22** with phosphorus oxychloride and pyridine gave a mixture of tetrasubstituted olefin **24** and exocyclic olefin **13a**, but none of the desired **23**, as judged by ^{1}H NMR spectroscopy.

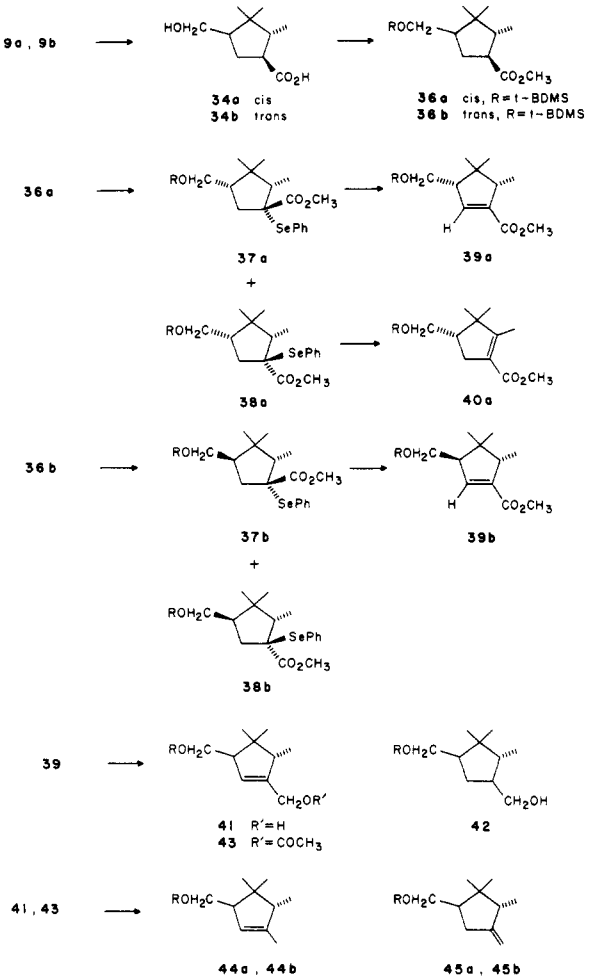
Another approach that appeared promising was the introduction of a double bond conjugated to the ester substituent, followed by deconjugation, as shown in Scheme VI. Preparation of the desired, α,β-unsaturated ester **31** was achieved in four steps from alcohol **10a**. Conversion of **10a** to the corresponding bromide **26**, tosylate **27**, or mesylate **28** was accomplished by standard methodology; the tosylate **27** was obtained in the highest yield. Reduction of **27** with sodium cyanoborohydride in hexamethylphosphoramide yielded ester **29**.[26] Phenylselenylation of **29** was accomplished via its (trimethylsilyl)ketene acetal (generated from the enolate of **29**) to give diastereomerically pure selenide **30**. Oxidation and subsequent elimination, as described earlier for **12**, gave the α,β-unsaturated ester **31** in good yield.

The deconjugation of α,β-unsaturated esters via delocalized enolates such as **32** has been reported.[27] However,



32

Scheme VII



all attempts to apply this methodology to **31** failed, yielding only recovered starting material. Furthermore, quenching of the reaction mixtures with various deuterium sources (CH_3CO_2D, CH_3OD, D_2O) showed no deuterium incorporation in the recovered starting material, indicating that enolate **32** had not been formed. These results were obtained by using a variety of dialkylamide bases at several temperatures and reaction times. These results can be rationalized by examination of enolate **32** as drawn below. It is clearly seen that the effect of placing three sp^2 centers in the five-membered ring forces the ring to become planar, which results in eclipsing of bonds on carbon atoms 4 and 5. Examination of this conformation suggests that it is highly strained and should be very difficult to generate.

The successful introduction of the double bond in **31** suggested a route to α-necrodol that is outlined in Scheme VII. Treatment of **9** with lithium metal in liquid ammonia gave hydroxy acid **34** in nearly quantitative yield. At this point, trans hydroxy acid **34b** could be crystallized from the 80:20 mixture of **34b**:**34a**, although the recovery of pure **34b** was not as high as expected. Following esterification with diazomethane, protection of the hydroxyl group as its *tert*-butyldimethylsilyl ether gave **36** in excellent yield.

It was expected that selenenylation of **36** via its (trimethylsilyl)ketene acetal would lead to a mixture of two diastereomeric selenides **37** and **38**, resulting from selenenylation from the α and β faces of the cyclopentanoid ring, respectively. In the case of *cis*-**36a**, a 1:1 mixture of the

(25) (a) Cramer, R.; Lindsey, R. V. *J. Am. Chem. Soc.* **1966**, *88*, 3534. (b) Bond, J. C. *Discuss. Faraday Soc.* **1966**, *41*, 200. (c) Harrod, J. F.; Chalk, A. J. *J. Am. Chem. Soc.* **1964**, *86*, 1776. (d) Harrod, J. F.; Chalk, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 3491. (e) Birch, A. J.; Subba Rao, G. *Tetrahedron Lett.* **1968**, 3797. (f) Andreiux, J.; Barton, D. H. R.; Patin, H. *J. Chem. Soc., Perkin Trans. I* **1977**, 359.

(26) Hutchins, R. O.; Maryanoff, B. E.; Milewski, C. A. *J. Chem. Soc., Chem. Commun.* **1971**, 1097.

(27) (a) Rathke, M. W.; Sullivan, D. *Tetrahedron Lett.* **1972**, 4249. (b) Hermann, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433.

selenides **37a** and **38a**, separable by careful chromatography, was obtained. It was not readily apparent from spectral data which compound was the desired **37a** and which was **38a**. Since selenoxide eliminations are known to proceed via a syn transition state,[13] it was clear that **37a** should yield the α,β-unsaturated ester **39a** upon oxidation and elimination, whereas **38a** should give the α,β-unsaturated ester **40a**, perhaps accompanied by small amounts of **39a**. Oxidation of pure samples of the lower R_f[28] and the higher R_f[28] selenides with *m*-chloroperoxybenzoic acid, followed by warming with diisopropylamine, gave **39a** and **40a**, respectively, making clear the stereochemistry of the precursors. These two unsaturated esters were easily distinguished by ^{1}H NMR spectroscopy; **39a** shows a single vinylic proton resonance at δ = 6.66 ppm, whereas **40a** shows an allylic methyl resonance at δ = 1.96 ppm.

Selenylation of *trans*-**36b** gave the desired selenide **37b**, with only traces of **38b** being produced. This difference in selectivity for α-face selenenylation between **36a** and **36b**, while convenient, was not anticipated. Oxidation and subsequent elimination as described above gave **39b** from **37b**, characterized by a ^{1}H NMR spectrum that exhibited a vinylic proton resonance at δ = 6.59 ppm.

Having generated the trisubstituted double bond in **39**, it remained only to convert the methoxycarbonyl substituent to a methyl group and to deprotect the hydroxyl group to complete our synthesis. Reduction of **39** with lithium ethoxyaluminum hydride[29] gave allylic alcohol **41** contaminated with approximately 10% of the saturated alcohol **42**, resulting from conjugate reduction of the α,β-unsaturated ester. These two alcohols were separated by HPLC on silica gel.

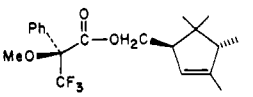
Two methods were employed to convert **41** to the desired olefin **44**. The one-pot procedure of Corey,[30] involving conversion of an allylic alcohol into its sulfate ester by treatment with sulfur trioxide/pyridine, followed by reduction with lithium aluminum hydride gave **44** in rather low yield. A more satisfactory sequence involved the conversion of **41** into its acetate **43**, followed by treatment with lithium metal in liquid ammonia.[31] A minor disadvantage in this case was that the reduction was accompanied by a small amount of double-bond isomerization to give the exocyclic olefin **45**. In spite of the required preparative gas chromatographic separation of **44** from **45**, larger quantities of **44** could be prepared by this route.

Finally, cleavage of the silyl ether **44b** with tetra-*n*-butylammonium fluoride in tetrahydrofuran gave (−)-α-necrodol (**1**); **44a** gave (+)-*epi*-α-necrodol (**3**). The trans compound **1** was found to be indistinguishable from natural α-necrodol on the basis of its ^{1}H NMR spectrum and gas chromatographic behavior. On the other hand, the cis compound **3** was found to differ clearly from the natural product on the basis of both spectroscopic and chromatographic criteria.

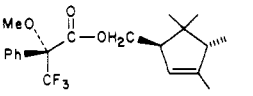
Using the reaction sequence described above, **40** was converted to the olefin **5**, which we have designated "γ-necrodol". While the secretion in which **1** and **2** were found does contain some apparently closely related but as yet unidentified compounds in very small amounts, **3**, **4**, and **5** do not correspond to any of these unidentified natural products, as judged by GLC co-injections of synthetic samples with the native *N. surinamensis* secretion.

With the synthesis of **1** and **2** completed, it remained only to determine the absolute configuration of the natural products. Since the anhydride of (+)-camphoric acid used as our starting material is known to have the absolute configuration shown in formula **6**, it follows from a consideration of the above-described reaction sequences that the necrodols we have prepared from it have the absolute configurations represented by formulas **1**–**5**. To determine the absolute configurations of the natural materials, it was necessary only to compare the natural compounds with the optically active synthetic samples. With only submilligram amounts of the more abundant natural α-isomer available, however, a good direct comparison of optical rotations was not practical. We chose, therefore, to make use of a method developed by Mosher for the determination of the optical purity of chiral alcohols.[32]

Condensation of (+)- and (−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPCl) with synthetic (−)-α-necrodol (**1**) gave the esters **49** and **50**, respectively.



49



50

Mixtures of these esters proved inseparable under a variety of gas chromatographic conditions (using both packed and capillary columns). Attempted HPLC separation was similarly unsuccessful.[33] The ^{1}H NMR spectra of **49** and **50** showed only subtle differences, clearly insufficient as a basis for reliable distinction. Fortunately, ^{19}F NMR spectroscopy at 282.5 MHz provided a solution to this problem. At this frequency, and at a concentration of 100 μg/mL,[34] the trifluoromethyl group singlets of **49** and **50** were found to be separated by 0.014 ppm (3.95 Hz).

The small amount of natural α-necrodol available dictated that only one ester could be prepared. Addition of the ester prepared from natural α-necrodol and (+)-MTPCl to a solution containing equal amounts of **49** and **50** resulted in enhancement of the downfield ^{19}F signal characteristic of **49**. These results indicate that the absolute configuration of natural α-necrodol is the same 3*R*,5*R* as that of synthetic (−)-α-necrodol, as represented in formula **1**.[35]

Experimental Section

All solvents used were reagent grade. Methylene chloride, ethyl acetate, hexamethylphosphoramide, diisopropylamine, and dicyclohexylamine were distilled from calcium hydride. Benzene and toluene were distilled from sodium/benzophenone. Tetrahydrofuran was distilled from potassium/benzophenone immediately prior to use. All reactions requiring anhydrous conditions were conducted under an atmosphere of nitrogen or argon in flame-dried glassware. *n*-Butyllithium and methyllithium (Aldrich) were standardized by titration using diphenylacetic acid indicator.[36]

Analytical thin-layer chromatography (TLC) was performed with precoated (0.25 mm) silica gel plates (Baker). Visualization was achieved by staining with phosphomolybdic acid (3% in ethanol). Flash chromatography[37] was performed on Baker flash

(28) The terms "lower R_f" and "higher R_f" refer to the relative mobilities of **37a** and **38a** on silica gel using ethyl acetate/petroleum ether mixtures as eluant.

(29) Davidson, R. S.; Gunther, W. H. H.; Waddington-Feather, S. M.; Lythgoe, B. *J. Chem. Soc.* **1964**, 4907.

(30) Corey, E. J.; Achiwa, K. *J. Org. Chem.* **1969**, *34*, 3667.

(31) Birch, A. J.; Subba Rao, G. *Adv. Org. Chem.* **1962**, *8*, 1.

(32) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(33) For cases where HPLC has separated MTPA esters, see: (a) Mori, K.; Otsuka, T.; Oga, M. *Tetrahedron* **1984**, *40*, 299. (b) Mori, K.; Otsuka, T. *Tetrahedron* **1983**, *39*, 3267.

(34) The exact chemical shift of the trifluoromethyl singlet was found to be concentration dependent.

(35) It is likely that natural β-necrodol also has the 3*R*,5*R* configuration, although a shortage of natural material prevented us from carrying out a similar analysis on this isomer.

(36) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

silica gel. Preparative thin-layer chromatography was performed on precoated (1 mm) Analtech silica gel plates (20 cm × 20 cm).

Preparative gas chromatography was performed on a Varian 2100 instrument. High-pressure liquid chromatography (HPLC) was performed on a system consisting of a Waters M6000A pump, Rheodyne 7120 injection valve fitted with a 20-μL (analytical) or 100-μL (semipreparative) sample loop, Perkin-Elmer LC-65T variable wavelength ultraviolet detector, and Waters R401 refractive index detector. Reverse-phase separations were performed on octadecylsilyl bonded phase (4.6 or 10 mm × 25 cm). Nuclear magnetic resonance (NMR) spectra were recorded on either a Bruker WM-300 (300 MHz for ^{1}H NMR, 282.5 MHz for ^{19}F NMR) spectrometer or a JEOL FX-90Q (22.5 MHz for ^{13}C NMR) spectrometer in deuteriochloroform. Chemical shifts are reported in parts per million (δ scale) downfield from tetramethylsilane (^{1}H and ^{13}C) or external trifluoroacetic acid (^{19}F). Infrared spectra were recorded on a Perkin-Elmer 299B spectrophotometer. Low-resolution mass spectra were obtained on either a Finnigan 3300 mass spectrometer interfaced to a Systems Industries 150 data system or an AEI MS 902 instrument interfaced to a VG Datasystem 2040. Electron impact spectra (EIMS) were recorded at 70 eV and chemical ionization spectra (CIMS) were recorded with methane as the reagent gas. High-resolution mass spectra (HRMS) were obtained on the AEI MS 902 instrument. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter.

Methyl phenylcamphorate (**8a**) was prepared from camphoric anhydride (**6**) as described earlier.[2-4] Camphoric anhydride (**6**) was prepared from commercial (1*R*,3*S*)-(+)-camphoric acid (Aldrich) by treatment with acetyl chloride.

Methyl *epi*-Phenylcamphorate (8b). A solution of sodium methoxide in methanol was prepared by reaction of sodium metal (400 mg, 18 mmol) with methanol (500 mL). Methyl phenylcamphorate (15.0 g, 20 mmol) was added to the solution, and the reaction was heated at reflux for 5 days. The solvent was evaporated and the residue was partitioned between ether (200 mL) and water (100 mL). The ethereal extract was washed with saturated aqueous sodium chloride (50 mL), dried, and evaporated. The partially crystalline residue was recrystallized from methanol, yielding recovered methyl phenylcamphorate (**8a**) as colorless needles. The filtrate was thus enriched in the desired trans epimer **8b**. Further enrichment by slow crystallization of methyl phenylcamphorate (**8a**) from the oily residue afforded an approximately 4:1 mixture of trans to cis epimers. High-pressure liquid chromatography as described[4] afforded the pure trans epimer **8b** as a clear liquid (bp 210 °C/0.07 Torr).

8b: ^{1}H NMR δ 0.65 (d, *J* = 6.8 Hz, 3 H), 0.92 (s, 3 H), 0.95 (s, 3 H), 1.80 (dq, *J* = 11.5, 6.8 Hz, 1 H), 2.12 (m, 2 H), 2.56 (m, 2 H), 3.65 (s, 3 H), 7.22 (m, 5 H); ^{13}C NMR: δ 11.8 (q), 24.5 (q), 24.6 (q), 35.4 (t), 44.5 (s), 50.8 (d), 51.1 (d), 51.5 (q), 54.4 (d), 126.1 (d), 127.7 (d), 128.2 (d), 144.2 (s), 176.2 (s); IR (film) 3030, 2980, 1732, 1602, 1256 cm^{-1}; EIMS *m/z* 246 (38), 186 (24), 167 (15), 169 (68), 145 (35), 132 (17), 117 (67), 115 (28), 104 (100); HRMS found 246.1619, calcd 246.1620 for $C_{16}H_{22}O_2$; $[\alpha]_D$ −16.1 ± 0.1° (*c* = 1.55, $CHCl_3$).

(1*S*,3*S*,5*R*)-3-(Carbomethoxy)-4,4,5-trimethylcyclopentanecarboxylic Acid (9a). A solution of methyl phenylcamphorate (**8a**) (8.15 g, 33.1 mmol) in carbon tetrachloride (120 mL) was added to a vigorously stirred suspension of sodium periodate (99.0 g, 463 mmol) in acetonitrile (120 mL) and water (180 mL). Ruthenium dioxide (100 mg, 0.75 mmol) was added, and the biphasic mixture was stirred vigorously (mechanical stirrer) for 72 h. The mixture was filtered and the precipitate washed with ether (100 mL). The filtrate was then refiltered through a pad of Celite to remove the precipitated ruthenium salts. This filtrate was extracted with ether (3 × 100 mL) and the combined ethereal layer was extracted with saturated aqueous sodium bicarbonate (2 × 200 mL). The aqueous extract was acidified to pH 3 with 12 M hydrochloric acid and then extracted with ether (2 × 150 mL). The ethereal extract was dried and evaporated to yield the crude acid ester **9a** (4.84 g, 22.6 mmol) as a white foam. Recrystallization from petroleum ether at −78 °C gave a white powder (4.43 g, 20.7 mmol, 62%) mp 70–71 °C. The 3*R* isomer **9b** was prepared in an analogous manner from methyl *epi*-phenylcamphorate (**8b**).

9a: ^{1}H NMR δ 0.65 (s, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 1.11 (s, 3 H), 1.89 (dq, *J* = 10.5, 6.8 Hz, 1 H), 2.08 (ddd, *J* = 5.6, 9.5, 13.8 Hz, 1 H), 2.38 (ddd, *J* = 10.0, 11.0, 13.8 Hz, 1 H), 2.53 (ddd, *J* = 5.6, 10.5, 11.0 Hz, 1 H), 2.65 (dd, *J* = 9.5, 10.0 Hz, 1 H), 3.67 (s, 3 H), 11.2 (br s, 1 H); ^{13}C NMR δ 12.6 (q), 16.5 (q), 26.3 (q), 28.6 (t), 45.3 (s), 48.0 (d), 49.8 (d), 51.2 (q), 54.3 (d), 173.6 (s), 182.6 (s); IR (CCl_4) 3000, 1740 cm^{-1}; EIMS *m/z* 215 (8), 214 (1), 196 (30), 168 (33), 154 (25), 142 (46), 128 (100), 109 (88); HRMS found 214.1216, calcd 214.1205 for $C_{11}H_{18}O_4$; $[\alpha]_D$ +26.1 ± 0.1° (*c* = 1.18 $CHCl_3$).

9b: ^{1}H NMR δ 0.91 (s, 3 H), 0.94 (s, 3 H), 0.96 (d, *J* = 6.8 Hz, 3 H), 2.07 (dq, *J* = 10.2, 6.8 Hz, 1 H), 2.18 (m, 2 H), 2.59 (m, 2 H), 3.69 (s, 3 H); ^{13}C NMR δ 13.1 (q), 24.0 (q), 24.0 (q), 29.9 (t), 45.0 (s), 46.3 (d), 49.9 (d), 51.6 (q), 54.8 (d), 176.1 (s), 180.6 (s); IR (CCl_4) 3050, 2960, 1736, 1704, 1222 cm^{-1}; EIMS *m/z* 215 (1), 183 (19), 168 (58), 153 (35), 128 (85), 110 (49), 109 (91), 108 (48), 95 (34), 93 (34), 87 (45), 67 (42), 55 (60), 41 (100); HRMS found 183.1041, calcd 183.1021 for $C_{10}H_{15}O_3$ (M − CH_3O)$^+$; $[\alpha]_D$ −22.0 ± 0.1° (*c* = 1.4, $CHCl_3$).

(1*S*,3*S*,4*R*)-Methyl 3-(Hydroxymethyl)-4,5,5-trimethylcyclopentanecarboxylate (10a). The acid ester **9a** (4.43 g, 20.7 mmol) was dissolved in dry THF (100 mL). This solution was cooled to 0 °C and borane/tetrahydrofuran (30 mL of a 1.0 M solution, 30 mmol) was added. The reaction mixture was stirred at 0 °C for 3 h and then quenched by careful addition of water (50 mL). The excess THF was removed in vacuo, and the aqueous residue was extracted with ether (3 × 100 mL). The combined ethereal extracts were washed with water (2 × 50 mL) and saturated aqueous sodium chloride (50 mL), then dried, and evaporated to afford the hydroxy ester **10a** (3.85 g, 19.2 mmol, 93%) as a clear liquid (bp 190 °C/0.05 Torr). The 3*R* isomer **10b** was prepared analogously from **9b**.

10a: ^{1}H NMR δ 0.66 (s, 3 H), 0.87 (d, *J* = 6.8 Hz, 3 H), 1.07 (s, 3 H), 1.36 (dq, *J* = 10.2, 6.8 Hz, 1 H), 1.62 (ddd, *J* = 5.6, 9.2, 13.6 Hz, 1 H), 1.80 (ddddd, *J* = 4.6, 5.6, 6.6, 10.2, 10.4 Hz, 1 H), 2.27 (ddd, *J* = 9.8, 10.4, 13.6 Hz, 1 H), 2.48 (dd, *J* = 9.2, 9.8 Hz, 1 H), 3.47 (dd, *J* = 6.6, 10.5 Hz, 1 H), 3.65 (dd, *J* = 4.6, 10.5 Hz, 1 H), 3.66 (s, 3 H); ^{13}C NMR δ 12.6 (q), 16.7 (q), 26.5 (q), 28.4 (t), 45.2 (s), 45.2 (d), 46.3 (d), 51.2 (q), 54.9 (d), 65.7 (t), 174.0 (s); IR (CCl_4) 3440, 2980, 1740, 1205, 1165 cm^{-1}; EIMS *m/z* 200 (1), 185 (5), 182 (2), 170 (30), 167 (22), 123 (38), 122 (39), 109 (38), 107 (57); CIMS *m/z* 201 (17), 183 (65), 169 (17), 151 (57), 123 (100); HRMS found 200.1415, calcd 200.1412 for $C_{11}H_{20}O_3$; $[\alpha]_D$ +44.9 ± 0.1° (*c* = 1.0, $CHCl_3$).

10b: ^{1}H NMR δ 0.84 (d, *J* = 6.7 Hz, 3 H), 0.89 (s, 3 H), 1.64 (m, 1 H), 1.72 (m, 1 H), 1.78 (m, 1 H), 2.04 (m, 1 H), 2.50 (m, 1 H), 3.64 (s, 3 H), 3.65 (dd, *J* = 8.5, 11.0 Hz, 1 H), 3.74 (dd, *J* = 3.6, 11.0 Hz, 1 H); ^{13}C NMR δ 12.7 (q), 23.6 (q), 24.0 (q), 29.6 (t), 43.2 (d), 45.3 (s), 46.8 (d), 51.1 (q), 54.2 (d), 64.7 (t), 177.1 (s); IR (CCl_4) 3450, 2980, 1738, 1204 cm^{-1}; EIMS: *m/z* 182 (3), 170 (62), 167 (26), 150 (31), 123 (48), 115 (84), 107 (53), 96 (100); CIMS *m/z* 201 (1), 183 (33), 169 (14), 151 (35), 123 (100); HRMS found 182.1309, calcd 182.1307 for $C_{11}H_{18}O_2$ [M − H_2O]$^+$; $[\alpha]_D$ −21.6 ± 0.1° (*c* = 0.8, $CHCl_3$).

(1*S*,3*S*,4*R*)-Methyl 3-(Hydroxymethyl)-4,5,5-trimethylcyclopentanecarboxylate Xanthate (11a). To a suspension of sodium hydride (15 mg, 0.63 mmol) in benzene (5 mL) was added the alcohol **10a** (100 mg, 0.50 mmol) dissolved in benzene (1 mL). The reaction mixture was stirred at room temperature for 6 h, and then carbon disulfide (380 mg, 5.0 mmol) was added and the mixture stirred for an additional 24 h. Methyl iodide (710 mg, 5.0 mmol) was added, and the reaction was stirred for 24 h. The solvent was evaporated and the residue was purified by column chromatography (1:3 ethyl acetate/petroleum ether) to afford the xanthate **11a** (120 mg, 0.41 mmol, 83%) as a clear oil, which slowly crystallized (mp 75–76 °C, MeOH).

11a: ^{1}H NMR δ 0.67 (s, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 1.10 (s, 3 H), 1.43 (dq, *J* = 10.2, 6.8 Hz, 1 H), 1.63 (m, 1 H), 2.13 (m, 1 H), 2.34 (m, 1 H), 2.53 (m, 1 H), 2.54 (s, 3 H), 3.67 (s, 3 H), 4.45 (dd, *J* = 6.8, 10.7 Hz, 1 H), 4.58 (dd, *J* = 5.0, 10.7 Hz, 1 H); ^{13}C NMR δ 12.6 (q), 16.7 (q), 18.9 (q), 26.5 (q), 28.7 (t), 41.9 (d), 45.1 (t), 45.1 (s), 48.1 (d), 51.2 (q), 53.9 (d), 173.8 (s), 215.8 (s); IR (KBr) 2980, 2940, 1720, 1315, 1292, 1250, 1200 cm^{-1}; EIMS *m/z* 182 (14), 167 (39), 123 (81), 122 (30), 107 (100); CIMS *m/z* 259 (4), 184 (8), 183 (65), 151 (72), 123 (100); $[\alpha]^{20}_D$ +38.8 ± 0.1° (*c* = 1.8, $CHCl_3$).

(37) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(1*S*,3*S*,4*R*)-Methyl 3-[[(*o*-Nitrophenyl)seleno]methyl]-4,5,5-trimethylcyclopentanecarboxylate (12a). The hydroxy ester **10a** was dissolved in tetrahydrofuran (50 mL) and *o*-nitrophenylseleno cyanate (2.20 g, 11.1 mmol) was added. Tri-*n*-butylphosphine (2.8 mL, 11.4 mmol) was added dropwise, resulting in a brick red solution that slowly turned bright yellow over 3 h. The solvent was evaporated and the crude selenide isolated by chromatography on silica gel (5 cm × 45 cm column, 2:1 hexane/ethyl acetate). The selenide **24a** crystallized as yellow needles (2.70 g, 7.02 mmol, 74%), mp 87–88 °C (hexane). The 3*R* isomer **12b** was prepared analogously from **10b**.

12a: ^{1}H NMR δ 0.66 (s, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 1.11 (s, 3 H), 1.43 (dq, *J* = 10.3, 6.7 Hz, 1 H), 1.64 (ddd, *J* = 6.1, 9.2, 13.6 Hz, 1 H), 2.03 (ddddd, *J* = 3.8, 6.1, 9.6, 9.6, 10.3 Hz, 1 H), 2.44 (ddd, *J* = 9.6, 9.8, 13.6 Hz, 1 H), 2.56 (dd, *J* = 9.2, 9.8 Hz, 1 H), 2.74 (dd, *J* = 9.6, 10.8 Hz, 1 H), 3.15 (dd, *J* = 3.8, 10.8 Hz, 1 H), 3.66 (s, 3 H), 7.29 (m, 1 H), 7.49 (m, 2 H), 8.26 (m, 1 H); ^{13}C NMR δ 12.3 (q), 16.9 (q), 26.9 (q), 32.0 (t), 32.3 (t), 41.7 (d), 45.4 (s), 51.2 (q), 52.3 (d), 53.9 (d), 125.3 (d), 126.3 (d), 129.0 (d), 133.4 (d), 133.6 (s), 146.5 (s), 173.9 (s); IR (CCl_4) 2980, 1740, 1595, 1570, 730 cm^{-1}; EIMS *m*/*z* 387 (1), 385 (5), 383 (2), 381 (1), 183 (13), 151 (17), 123 (100); HRMS found 383.0793, calcd 383.0801 for $C_{17}H_{23}NO_4{}^{78}Se$; $[\alpha]_D$ +19.6 ± 0.1° (*c* = 1.2, $CHCl_3$).

12b: ^{1}H NMR δ 0.90 (s, 3 H), 0.91 (s, 3 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 1.62 (dq, *J* = 10.1, 6.9 Hz, 1 H), 1.75 (ddd, *J* = 5.6, 8.0, 13.4 Hz, 1 H), 1.90 (ddddd, *J* = 3.6, 8.0, 8.3, 10.1, 10.5 Hz, 1 H), 2.19 (ddd, *J* = 8.1, 8.3, 13.4 Hz, 1 H), 2.53 (dd, *J* = 5.6, 8.1 Hz, 1 H), 2.87 (dd, *J* = 10.5, 10.7 Hz, 1 H), 3.20 (dd, *J* = 3.6, 10.7 Hz, 1 H), 3.64 (s, 3 H), 7.28 (m, 1 H), 7.51 (m, 2 H), 8.26 (m, 1 H); ^{13}C NMR δ 12.6 (q), 24.1 (q), 24.3 (q), 31.6 (t), 33.6 (t), 43.5 (d), 45.2 (s), 49.2 (d), 51.2 (q), 54.2 (d), 125.2 (d), 126.3 (d), 129.0 (d), 133.4 (d), 134.0 (s), 146.7 (s), 176.0 (s); IR (CCl_4) 2980, 1732, 1595, 1568, 1168 cm^{-1}; EIMS *m*/*z* 385 (3), 383 (3), 255 (4), 183 (36), 123 (100); HRMS found 383.0800, calcd 383.0801 for $C_{17}H_{23}NO_4{}^{78}Se$; $[\alpha]_D$ +7.6 ± 0.1° (*c* = 0.5, $CHCl_3$).

(1*S*,3*R*)-Methyl 3-Methylene-4,5,5-trimethylcyclopentanecarboxylate (13a). The selenide **12a** (450 mg, 1.17 mmol) was dissolved in dry dichloromethane (5.0 mL) and the solution was cooled to −10 °C. *m*-Chloroperoxybenzoic acid (400 mg, 2.3 mmol) was added and the mixture stirred for 1 h. Diisopropylamine (1.0 mL) was added, and the mixture was heated at reflux for 1 h. The solvent was evaporated, and the residue was slurried in pentane and passed through a short silica plug to afford a yellow oil. This material was purified by bulb-to-bulb distillation to give the alkene **13a** (150 mg, 0.82 mmol, 70%), bp 70–75 °C/0.7 Torr). The 3*R* isomer **13b** was prepared analogously from **12b**.

13a: ^{1}H NMR δ 0.56 (s, 3 H), 0.92 (d, *J* = 6.8 Hz, 3 H), 1.14 (s, 3 H), 2.15 (m, 3 H), 3.65 (s, 3 H), 4.75 (m, 1 H), 4.86 (m, 1 H); ^{13}C NMR δ 10.6 (q), 16.1 (q), 26.2 (q), 32.3 (t), 44.2 (s), 50.2 (d), 51.2 (q), 52.9 (d), 104.8 (t), 153.4 (s), 173.8 (s); IR (CCl_4) 3080, 2980, 1738, 1660, 1169, 782 cm^{-1}; EIMS *m*/*z* 182 (16), 167 (42), 150 (26), 123 (46), 107 (100); HRMS found 182.1292, calcd 182.1307 for $C_{11}H_{18}O_2$; $[\alpha]_D$ +68.0 ± 0.1° (*c* = 1.0, $CHCl_3$).

13b: ^{1}H NMR δ 0.85 (s, 3 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.94 (s, 3 H), 2.38 (br q, *J* = 6.9 Hz, 1 H), 2.45 (m, 2 H), 2.74 (m, 1 H), 3.67 (s, 3 H), 4.78 (br d, *J* = 2.2 Hz, 1 H), 4.84 (br d, *J* = 2.2 Hz, 1 H); ^{13}C NMR δ 12.6 (q), 23.4 (q), 23.8 (q), 33.2 (t), 44.4 (s), 47.2 (d), 51.2 (q), 52.3 (d), 105.1 (t), 154.9 (s), 175.8 (s); IR (CCl_4) 2980, 2860, 1732, 1652, 1212, 880 cm^{-1}; EIMS: *m*/*z* 182 (6), 167 (79), 151 (11), 123 (21), 107 (100); HRMS found 182.1301, calcd 182.1307 for $C_{11}H_{18}O_2$; $[\alpha]_D$ −13.9 ± 0.1° (*c* = 0.9, $CHCl_3$).

(1*S*,4*R*)-1-(Hydroxymethyl)-3-methylene-4,5,5-trimethylcyclopentane (*epi*-β-Necrodol) (4). The ester **13a** (200 mg, 1.1 mmol), dissolved in ether (5.0 mL), was added dropwise to a stirred suspension of lithium aluminum hydride (200 mg, 5.5 mmol) in ether (5.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 6 h. After this time, the reaction was quenched by sequential addition of water (0.2 mL), 15% aqueous sodium hydroxide (0.2 mL), and water (0.6 mL). The white precipitate was filtered and washed with ether (10 mL). The filtrate was evaporated to yield *epi*-β-necrodol (**4**) (158 mg, 1.0 mmol, 93%) as a clear liquid (bp 200 °C/34 Torr). (−)-β-Necrodol (**2**) was prepared analogously from **13b**.

4: ^{1}H NMR δ 0.51 (s, 3 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 1.04 (s, 3 H), 1.82 (m, 1 H), 2.02 (m, 2 H), 2.65 (m, 1 H), 3.53 (m, 1 H), 3.76 (m, 1 H), 4.73 (m, 1 H), 4.82 (m, 1 H); ^{13}C NMR δ 10.4 (q), 14.8 (q), 26.8 (q), 34.4 (t), 42.1 (s), 50.2 (d), 50.6 (d), 64.3 (t), 104.3 (t), 154.8 (s); IR (CCl_4) 3620, 3380, 3078, 2960, 1658, 1470, 1380, 1070, 1038, 880 cm^{-1}; EIMS *m*/*z* 154 (3), 139 (65), 121 (100), 93 (44), 81 (30), 79 (30); HRMS found 154.1343, calcd 154.1358 for $C_{10}H_{18}O$; $[\alpha]_D$ +53.9 ± 0.1° (*c* = 1.5, $CHCl_3$).

2: ^{1}H NMR δ 0.80 (s, 3 H), 0.91 (d, *J* = 7.0 Hz, 3 H), 0.92 (s, 3 H), 1.84 (dddd, *J* = 5.3, 5.4, 8.6, 8.6 Hz, 1 H), 2.14 (qddd, *J* = 7.0, 2.2, 2.2, 2.2 Hz, 1 H), 2.25 (dddd, *J* = 2.2, 2.2, 5.3, 17.5 Hz, 1 H), 2.58 (ddddd, *J* = 2.2, 2.2, 2.2, 8.6, 17.5 Hz, 1 H), 3.45 (dd, *J* = 8.6, 10.3 Hz, 1 H), 3.75 (dd, *J* = 5.4, 10.3 Hz, 1 H), 4.77 (dddd, *J* = 2.2, 2.2, 2.2, 2.3 Hz, 1 H), 4.84 (dddd, *J* = 2.2, 2.2, 2.2, 2.3 Hz, 1 H); ^{13}C NMR δ 13.5 (q), 23.1 (q), 23.8 (q), 33.9 (t), 42.2 (s), 48.4 (d), 48.8 (d), 64.3 (t), 105.1 (t), 156.1 (s); IR (CCl_4) 3630, 3350, 3078, 2980, 1658, 1266, 880 cm^{-1}; EIMS *m*/*z* 154 (1), 139 (64), 123 (14), 121 (99); HRMS found 154.1361, calcd 154.1358 for $C_{10}H_{18}O$; $[\alpha]_D$ −11.2 ± 0.1° (*c* = 0.6, $CHCl_3$).

(1*S*,4*S*,6*R*)-6-Acetoxy-1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dione (17). *l*-Bornyl acetate (Aldrich) (10.0 g, 50.9 mmol) in acetic acid (25 mL) and acetic anhydride (20 mL) containing sodium acetate (0.1 g) was heated to 60 °C on a water bath and stirred with a mechanical stirrer. A solution of chromium trioxide (22 g) in acetic anhydride (60 mL) was added at a rate sufficient to maintain the reaction temperature at 100–120 °C. After the addition was complete, the heating and stirring was continued for 1 h; then the cooled mixture was poured into water and extracted with ether. The extracts were washed with 20% aqueous ammonium hydroxide until the washings were basic and then with water, dried, and evaporated to give a pale yellow oil (9.3 g). The mixture was fractionated and the fraction bp 105 °C/2 mmHg (4.9 g) solidified on standing. An NMR spectrum of this fraction indicated that it consisted mainly of 5-ketobornyl acetate and was not purified further.

This material was dissolved in acetic anhydride (5 mL), then pulverized selenium dioxide (5.9 g) was added, and the mixture was stirred at 140–145 °C for 8 h. It was then poured into water and extracted with ether. The extract was washed with aqueous sodium bicarbonate solution and then with water, dried, and evaporated to give an oil (2.7 g). This was dissolved in hot hexanes, decanted from the dark residue, and allowed to crystallize. Recrystallization gave the dione **17** (2.3 g, 10.3 mmol, 20%) as coarse yellow needles, mp 109 °C (lit.[14] mp 109 °C).

17: ^{1}H NMR δ 0.91 (s, 3 H), 1.11 (s, 3 H), 1.12 (s, 3 H), 1.53 (dd, *J* = 3.1, 15.1 Hz, 1 H), 1.98 (s, 3 H), 2.75 (m, 1 H), 2.86 (m, 1 H), 5.18 (dd, *J* = 3.1, 7.5 Hz, 1 H); IR (CH_2Cl_2) 2960, 1775, 1755, 1745, 1378, 1220, 1080, 1040, 1008, 985 cm^{-1}; EIMS *m*/*z* 224 (13), 154 (14), 153 (14), 139 (18), 109 (16), 108 (74); $[\alpha]_D$ −188.0 ± 0.1° (*c* = 1.0, EtOH) (lit.[14] $[\alpha]_D$ −191.4 °C).

(1*S*,2*R*,4*S*)-2-Acetoxy-1,5,5-trimethylcyclopentane-1,4-dicarboxylic Acid Anhydride (18). The dione **17** (900 mg, 4.01 mmol) was dissolved in acetic acid (5.4 mL) and 30% H_2O_2 (3.6 mL) was added dropwise. The solution was allowed to stand until it became colorless (2 h) and then water was added to induce crystallization. The product was filtered, washed with water, and dried to afford **18** (670 mg, 2.79 mmol, 70%) as colorless needles, mp 111–112 °C.

18: ^{1}H NMR δ 1.05 (s, 3 H), 1.10 (s, 3 H), 1.28 (s, 3 H), 1.82 (m, 1 H), 2.05 (s, 3 H), 2.83 (m, 2 H), 5.22 (m, 1 H); ^{13}C NMR δ 12.5 (q), 20.6 (q), 20.6 (s), 21.3 (q), 32.5 (q), 43.9 (t), 52.5 (d), 58.4 (s), 77.8 (d), 168.1 (s), 168.8 (s), 169.9 (s); IR ($CHCl_3$) 2980, 1818, 1770, 1750, 1265, 1240 cm^{-1}; EIMS *m*/*z* 240 (1), 198 (4), 115 (20), 109 (12), 108 (69), 99 (30).

(1*S*,2*R*,4*S*)-2-Hydroxy-1,5,5-trimethyl-4-carbomethoxycyclopentanecarboxylic Acid (19). The anhydride **18** (2.5 g, 10.4 mmol) was dissolved in methanol (75 mL) containing HCl (3.6 g) and left to stand for 12 h. The solution was concentrated to 20 mL and diluted with water (50 mL). The mixture was extracted with ether, and the extract was washed with water, dried, and evaporated to give a white solid, which was recrystallized from benzene to afford **19** (2.0 g, 8.69 mmol, 84%) as white plates, mp 152 °C.

19: ^{1}H NMR δ 1.10 (s, 3 H), 1.20 (s, 3 H), 1.29 (s, 3 H), 2.30 (m, 2 H), 2.80 (dd, *J* = 7.4, 9.6 Hz, 1 H), 3.72 (s, 3 H), 4.16 (dd, *J* = 2.5, 6.3 Hz, 1 H); ^{13}C NMR δ 20.7 (q), 22.1 (q), 24.6 (q), 33.5 (t), 46.8 (s), 50.4 (d), 51.8 (q), 58.9 (s), 78.8 (d), 174.1 (s), 174.2 (s); IR (KBr) 3220, 2980, 2540 (br), 1745, 1680, 1280, 1235, 1200

cm^{-1}; EIMS m/z: 231 (9), 213 (12), 181 (14), 153 (18), 116 (100), 115 (63), 107 (22); CIMS m/z 231 (11), 213 (57), 181 (100), 167 (60), 153 (43); $[\alpha]^{20}_D$ +12.8 ± 0.1° (c = 1.0, EtOH).

(1*S*,3*S*)-Methyl 4-Oxo-2,2,3-trimethylcyclopentanecarboxylate (20a). The alcohol **19** (700 mg, 3.04 mmol) in ether (17.5 mL) was added to a solution of chromic acid (1.1 M, 14 mL). The reaction was stirred vigorously for 6 h; then the ether layer was separated and the aqueous layer extracted with ether (20 mL). The combined ethereal extract was washed with water (10 mL), dried, and evaporated to give an oil. This crude product was not purified further, but rather dissolved in benzene (20 mL), and the solution was heated to reflux for 18 h. The benzene was evaporated to give an oil, which crystallized on standing. Recrystallization from water gave the ketone **20a** (510 mg, 2.77 mmol, 91%) as colorless needles, mp 52–54 °C.

20a: ^{1}H NMR δ 0.68 (s, 3 H), 0.95 (d, J = 6.9 Hz, 3 H), 1.30 (s, 3 H), 2.03 (q, J = 6.9 Hz, 1 H), 2.45 (dd, J = 8.6, 19.5 Hz, 1 H), 2.68 (dd, J = 11.1, 19.5 Hz, 1 H), 2.85 (dd, J = 8.6, 11.1 Hz, 1 H), 3.73 (s, 3 H); ^{13}C NMR δ 7.3 (q), 17.1 (q), 26.9 (q), 37.9 (t), 42.4 (s), 50.2 (d), 51.6 (q), 56.5 (d), 172.3 (s), 216.2 (s); IR ($CHCl_3$) 2980, 1740, 1240, 1200 cm^{-1}; EIMS m/z 184 (5), 169 (32), 153 (4), 114 (100); HRMS found 184.1103, calcd 184.1099 for $C_{10}H_{16}O_3$; $[\alpha]^{23}_D$ +105.0 ± 0.1° (c = 1.0, EtOH).

(1*S*,3*R*)-Methyl 2,2,3-Trimethyl-4-methylenecyclopentanecarboxylate (13a) from 20a. A solution of titanium tetrachloride in dichloromethane (1.1 mL of a 1.0 M solution) was added dropwise to a suspension of zinc dust (200 mg) and methylene bromide (261 mg, 1.50 mmol) in tetrahydrofuran (5 mL) at room temperature. The mixture was stirred for 30 min; then the ketone **20a** (100 mg, 0.54 mmol) in tetrahydrofuran was added dropwise. The reaction was stirred at room temperature for 48 h and then quenched by addition of water (5 mL). The mixture was extracted with pentane (20 mL), and the pentane extract was washed with water (5 mL), dried, and evaporated. Purification of the residue by preparative TLC (4:1 pentane/dichloromethane, R_f ~0.3) gave the olefin **13a** (57 mg, 0.31 mmol, 58%) as a clear oil. This product had spectra identical with those of the material prepared earlier from methyl phenylcamphorate.

Epimerization of 20a. The ketone **20a** (466 mg, 2.53 mmol) was dissolved in methanol (10 mL) containing sodium metal (300 mg). After being stirred overnight at room temperature, the solution was poured into ether (50 mL) and then washed with water (10 mL). The aqueous layer was extracted with ether (20 mL); then the combined ether extracts were washed with water, dried, and evaporated to give a mixture of epimers **20a** and **20b** (377 mg, 2.04 mmol, 81%) as a colorless oil. Integration of the methoxyl resonances in the ^{1}H NMR spectrum of this mixture showed the mixture to be approximately 3:1 **20a**/**20b**, respectively. All attempts at separation of these epimers were unsuccesful (GC, HPLC, TLC). Treatment of this mixture with the titanium tetrachloride/zinc dust/methylene dibromide reagent as described for **20a** gave an approximately 3:1 mixture of olefins **13a** and **13b** (240 mg, 1.32 mmol, 65%) as a clear oil. These compounds had identical GC behavior (co-injection) as authentic samples of **13a** and **13b** prepared from methyl phenylcamphorate.

Attempted Olefin Isomerizations of (1*S*,3*R*)-Methyl 3-methylene-4,5,5-trimethylcyclopentanecarboxylate (13a) with Transition-Metal Catalysis. Method A. To a solution of **13a** (10 mg, 0.05 mmol) in d_6-benzene (500 μL) was added bis(triphenylphosphine)palladium(II) chloride (1 mg). The reaction was allowed to stand at room temperature and was monitored by ^{1}H NMR. No change was observed after 10 h at room temperature. Subsequent heating of the solution to 50 °C for 4 days also resulted in no observable change.

Method B. The exocyclic olefin **13a** (10 mg, 0.05 mmol) was treated with bis(triphenylphosphine)rhodium(I) chloride as described in method A. No olefin isomerization was observed after 4 days at 50 °C.

Method C. The exocyclic olefin **13a** (10 mg, 0.05 mmol) was dissolved in methanol (500 μL) and rhodium(III) chloride (1 mg) was added. The reaction mixture was stirred at room temperature for 48 h, then diluted with ether (2 mL), and filtered. The filtrate was evaporated and examined by ^{1}H NMR. This showed **13a** as the only product.

(3*S*,5*S*)-3-(Methoxycarbonyl)-1,4,4,5-tetramethylcyclopentanol (22). A solution of keto ester **20a** (238 mg, 1.29 mmol) in tetrahydrofuran (10 mL) was cooled to −78 °C and methyllithium (0.52 mL of a 2.4 M solution in ether, 1.25 mmol) was added dropwise. After being stirred for 30 min at −78 °C, the reaction mixture was warmed to room temperature and immediately quenched with water (5 mL). The solvent was evaporated and the residue was partitioned between water (10 mL) and ether (50 mL). The ethereal extract was washed with water (10 mL) and saturated aqueous sodium chloride (10 mL), then dried, and evaporated. Flash chromatography (1:1 ethyl acetate/hexanes) of the residue gave the hydroxy ester **22** (158 mg, 0.79 mmol, 61%) as a clear oil.

22: ^{1}H NMR δ 0.84 (s, 3 H), 0.88 (d, J = 7.2 Hz, 3 H), 1.12 (s, 3 H), 1.26 (s, 3 H), 1.41 (q, J = 7.2 Hz, 1 H), 2.01 (dd, J = 9.2, 14.3 Hz, 1 H), 2.27 (dd, J = 8.2, 14.3 Hz, 1 H), 2.56 (dd, J = 8.2, 9.2 Hz, 1 H), 3.70 (s, 3 H); EIMS m/z 182 (7), 167 (21), 130 (88), 123 (18), 107 (37), 98 (23), 87 (100); CIMS m/z 201 (2), 183 (100), 169 (13), 151 (18), 130 (23), 123 (74).

(1*S*,3*S*,4*R*)-Methyl 3-(Bromomethyl)-4,5,5-trimethylcyclopentanecarboxylate (26). The hydroxy ester **10a** (543 mg, 2.71 mmol) was dissolved in benzene (5 mL) and pyridine (5 mL). Phosphorus tribromide (1.46 g, 5.4 mmol) was added to the stirred solution and the resulting reaction mixture was stirred at room temperature for 18 h. The reaction mixture was then cooled to 0 °C and quenched with water (10 mL). The aqueous mixture was extracted with ether (50 mL); the ethereal extract was washed with 1 M aqueous nickel(II) chloride (15 mL), water (10 mL), and saturated aqueous sodium chloride (10 mL), dried, and evaporated to give a clear oil. Chromatography on silica gel (1:1 ether/petroleum ether) gave the bromide **26** (300 mg, 1.14 mmol, 42%) as white needles (mp 37–38 °C, petroleum ether).

26: ^{1}H NMR δ 0.64 (s, 3 H), 0.84 (d, J = 6.8 Hz, 3 H), 1.07 (s, 3 H), 1.45 (dq, J = 10.4, 6.8 Hz, 1 H), 1.70 (ddd, J = 5.6, 9.5, 13.8 Hz, 1 H), 2.00 (ddddd, J = 3.6, 5.6, 6.6, 10.0, 10.4 Hz, 1 H), 2.31 (ddd, J = 9.6, 10.0, 13.8 Hz, 1 H), 2.52 (dd, J = 9.5, 9.6 Hz, 1 H), 3.35 (dd, J = 6.6, 10.0 Hz, 1 H), 3.55 (dd, J = 3.6, 10.0 Hz, 1 H), 3.65 (s, 3 H); ^{13}C NMR δ 12.1 (q), 17.1 (q), 26.7 (q), 30.5 (t), 39.2 (d), 44.8 (t), 45.5 (s), 49.3 (d), 51.3 (q), 53.7 (d), 174.8 (s); IR (CH_2Cl_2) 2950, 1725, 1270 cm^{-1}; EIMS m/z 262 (0.2), 247 (0.6), 233 (2.5), 231 (2.6), 183 (18), 151 (45), 123 (100), 115 (14), 113 (23); CIMS m/z 265 (95), 263 (95), 233 (11), 231 (11), 183 (100), 151 (41), 123 (59); HRMS found 262.0563, calcd 267.0569 for $C_{11}H_{19}{}^{79}BrO_2$; $[\alpha]^{20}_D$ +48.7 ± 0.1° (c = 1.4, $CHCl_3$).

(1*S*,3*S*,4*R*)-Methyl 3-[[(*p*-Tolylsulfonyl)oxy]methyl]-4,5,5-trimethylcyclopentanecarboxylate (27). The hydroxy ester **10a** (2.70 g, 13.5 mmol) was dissolved in pyridine (30 mL) and treated with *p*-toluenesulfonyl chloride (3.25 g, 16.9 mmol) and 4-(dimethylamino)pyridine (40 mg, 0.32 mmol). The reaction mixture was stirred at room temperature for 1 h and then was quenched by addition of water (20 mL) and 2 M aqueous hydrochloric acid (30 mL). The product was extracted into ether (3 × 50 mL); the combined ethereal extract was washed successively with 1 M aqueous hydrochloric acid (2 × 50 mL), 1 M aqueous nickel(II) chloride (50 mL), water (50 mL), and saturated aqueous sodium chloride (25 mL), then dried, and evaporated to give the tosylate **27** (4.0 g, 11.3 mmol, 84%) as a pale yellow liquid (bp 245 °C/0.04 Torr).

27: ^{1}H NMR δ 0.61 (s, 3 H), 0.79 (d, J = 6.8 Hz, 3 H), 1.04 (s, 3 H), 1.34 (dq, J = 10.4, 6.8 Hz, 1 H), 1.51 (ddd, J = 5.5, 9.2, 13.8 Hz, 1 H), 1.90 (ddddd, J = 4.6, 5.5, 6.1, 10.4, 10.4 Hz, 1 H), 2.21 (ddd, J = 10.2, 10.4, 13.8 Hz, 1 H), 2.43 (dd, J = 9.2, 10.2 Hz, 1 H), 2.43 (s, 3 H), 3.64 (s, 3 H), 3.89 (dd, J = 6.1, 9.5 Hz, 1 H), 4.00 (dd, J = 4.6, 9.5 Hz, 1 H), 7.32 (d, J = 8.3 Hz, 2 H), 7.76 (d, J = 8.3 Hz, 2 H); ^{13}C NMR δ 12.2 (q), 16.6 (q), 21.5 (q), 26.4 (q), 28.0 (t), 42.1 (d), 45.0 (s), 47.1 (d), 51.2 (q), 53.7 (d), 72.7 (t), 127.7 (d), 129.8 (d), 132.9 (s), 144.7 (s), 173.7 (s); IR (film) 2950, 2860, 1725, 1595, 1288, 1210 cm^{-1}; EIMS m/z 354 (5), 322 (8), 183 (14), 182 (63), 167 (100), 155 (24), 150 (49), 123 (67), 122 (77), 109 (23); CIMS m/z 355 (1), 323 (28), 183 (100), 151 (63), 123 (71); HRMS found 354.1495, calcd 354.1501 for $C_{18}H_{26}SO_5$; $[\alpha]^{20}_D$ +26.8 ± 0.1° (c = 1.0, $CHCl_3$).

(1*S*,3*S*,4*R*)-Methyl 3-[[(Methylsulfonyl)oxy]methyl]-4,5,5-trimethylcyclopentanecarboxylate (28). The hydroxy ester **10a** (530 mg, 2.65 mmol) was dissolved in pyridine (5 mL) and treated with methanesulfonyl chloride (1.52 g, 13.2 mmol). The reaction mixture was stirred for 16 h at room temperature and then was quenched with water (5 mL). The solution was

partitioned between water (10 mL) and ether (50 mL). The ethereal extract was washed successively with 1 M aqueous nickel(II) chloride (10 mL), water (10 mL), and saturated aqueous sodium chloride (10 mL), then dried, decolorized (charcoal), and evaporated to give the mesylate **28** (614 mg, 2.20 mmol, 83%) as a pale yellow oil (bp 185 °C/0.07 Torr).

28: ^{1}H NMR δ 0.66 (s, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 1.09 (s, 3 H), 1.42 (dq, J = 10.4, 6.8 Hz, 1 H), 1.64 (ddd, J = 5.4, 9.2, 13.8 Hz, 1 H), 2.02 (ddddd, J = 4.8, 5.4, 6.4, 10.4, 10.4 Hz, 1 H), 2.32 (ddd, J = 10.2, 10.4, 13.8 Hz, 1 H), 2.51 (dd, J = 9.2, 10.2 Hz, 1 H), 2.99 (s, 3 H), 3.66 (s, 3 H), 4.09 (dd, J = 6.4, 9.6 Hz, 1 H), 4.20 (dd, J = 4.8, 9.6 Hz, 1 H); ^{13}C NMR δ 12.4 (q), 16.7 (q), 26.5 (q), 28.3 (q), 37.3 (t), 42.3 (d), 45.1 (s), 47.4 (d), 51.3 (q), 53.8 (d), 72.2 (t), 173.8 (s); IR (film) 2960, 1730, 1220 cm^{-1}; EIMS m/z 279 (7), 247 (12), 182 (20), 167 (100), 150 (28), 123 (100), 122 (100), 107 (90); CIMS m/z 279 (4), 247 (20), 183 (100), 151 (90), 123 (76); HRMS found 279.1261, calcd 279.1266 for $C_{12}H_{23}SO_5$ $(M + H)^+$; $[\alpha]^{20}_D$ +32.2 ± 0.1° (c = 0.9, $CHCl_3$).

(1*S*,3*R*,4*S*)-Methyl 2,2,3,4-Tetramethylcyclopentanecarboxylate (29). The tosylate **27** (4.0 g, 11.2 mmol) was dissolved in dry hexamethylphosphoramide (15 mL) and sodium cyanoborohydride (2.9 g, 46.1 mmol) was added. The reaction mixture was heated and stirred at 105 °C for 24 h. The cooled reaction mixture was quenched by addition of 1 M hydrochloric acid (*Caution*: *HCN evolved*!) (20 mL). The aqueous solution was washed with ether (3 × 50 mL); the combined ethereal extract was washed with 1 M aqueous hydrochloric acid (2 × 30 mL), water (10 mL), and saturated aqueous sodium chloride (30 mL), then dried, and evaporated. The residue was slurried in petroleum ether (50 mL) and filtered through a short plug of silica gel. The filtrate was evaporated to afford ester **29** (1.43 g, 7.7 mmol, 68%) as a clear liquid (bp 145 °C/0.1 Torr).

29: ^{1}H NMR δ 0.62 (s, 3 H), 0.80 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.6 Hz, 3 H), 1.06 (s, 3 H), 1.10 (dq, J = 7.0, 6.8 Hz, 1 H), 1.33 (ddd, J = 6.7, 9.8, 13.5 Hz, 1 H), 1.64 (dddq, J = 6.7, 7.0, 10.1, 6.6 Hz, 1 H), 2.29 (ddd, J = 8.9, 10.1, 13.5 Hz, 1 H), 2.51 (dd, J = 8.9, 9.8 Hz, 1 H), 3.65 (s, 3 H); ^{13}C NMR δ 11.7 (q), 16.8 (q), 19.8 (q), 27.1 (q), 33.3 (t), 37.4 (d), 45.2 (s), 50.9 (q), 53.4 (d), 53.8 (d), 174.6 (s); IR (film) 2960, 2860, 1735, 1195 cm^{-1}; EIMS m/z 184 (4), 169 (2), 153 (6), 125 (5), 115 (42), 114 (12), 109 (22); CIMS m/z 186 (31), 185 (100), 169 (7), 153 (25), 151 (12), 137 (26), 123 (18); $[\alpha]^{20}_D$ +20.2 ± 0.1° (c = 1.2, $CHCl_3$).

(3*R*,4*R*)-Methyl 1-(Phenylseleno)-2,2,3,4-tetramethylcyclopentanecarboxylate (30). A solution of n-butyllithium (2.2 mL of a 1.58 M solution in hexanes, 3.48 mmol) and dicyclohexylamine (637 mg, 3.52 mmol) in tetrahydrofuran (10 mL) was stirred at −78 °C for 1 h. A solution of ester **29** (524 mg, 2.80 mmol) in tetrahydrofuran (5 mL) was added to the reaction mixture and the mixture was slowly warmed to −20 °C. After 30 min at −20 °C, the reaction was cooled to −78 °C and trimethylsilyl chloride (450 mg, 4.14 mmol) was added. The temperature was raised to 0 °C for 30 min and then lowered to −78 °C, and a solution of phenylselenenyl chloride (650 mg, 3.40 mmol) in tetrahydrofuran (5 mL) was added. The reaction mixture was then slowly warmed to room temperature and stirred for 1 h. The solvent was evaporated; the residue was slurried in petroleum ether (20 mL), filtered, and washed with petroleum ether (20 mL). The filtrate was evaporated and the residue purified by flash chromatography (1:8 ether/petroleum ether) to give the selenide **30** (500 mg, 1.40 mmol, 50%) as white plates (mp 59–60 °C, MeOH).

30: ^{1}H NMR δ 0.78 (s, 3 H), 0.86 (d, J = 6.8 Hz, 3 H), 1.08 (d, J = 6.6 Hz, 3 H), 1.30 (s, 3 H), 1.63 (dd, J = 4.6, 16.8 Hz, 1 H), 1.63 (dddq, J = 4.6, 9.8, 12.3, 6.6 Hz, 1 H), 2.06 (dq, J = 9.8, 6.8 Hz, 1 H), 2.66 (dd, J = 12.3, 16.8 Hz, 1 H), 3.64 (s, 3 H), 7.24–7.50 (m, 5 H); ^{13}C NMR δ 12.5 (q), 18.2 (q), 20.3 (q), 23.5 (q), 36.4 (t), 39.5 (d), 48.8 (s), 50.4 (d), 51.6 (q), 66.0 (s), 127.9 (s), 128.7 (d), 128.9 (d), 137.7 (d), 173.7 (s); IR (CCl_4) 3060, 2980, 2880, 1725, 1580, 1260, 1210 cm^{-1}; EIMS m/z 340 (3), 338 (2), 183 (12), 157 (15), 124 (12), 123 (100); CIMS m/z 341 (4), 339 (6), 338 (6), 337 (5), 336 (4), 282 (12), 280 (49), 278 (27), 277 (15), 276 (15), 183 (49), 123 (100); HRMS found 338.0939, calcd 338.0950 for $C_{17}H_{24}O_2{}^{78}Se$, found 340.0935, calcd 340.0941 for $C_{17}H_{24}O_2{}^{80}Se$; $[\alpha]^{20}_D$ −85.2 ± 0.1° (c = 1.7, $CHCl_3$).

(3*R*,4*R*)-Methyl 3,4,5,5-Tetramethylcyclopentenecarboxylate (31). The selenide **31** (500 mg, 1.40 mmol) was dissolved in methylene chloride (5 mL) and the solution was cooled to −10 °C. m-Chloroperoxybenzoic acid (350 mg, 2.03 mmol) was added, and the reaction was stirred for 0.5 h at −10 °C. Diisopropylamine (1.0 mL) was added, and the mixture was warmed to reflux for 0.5 h. The solvent was evaporated, and the residue was filtered through a short plug of silica gel. Evaporation of the filtrate gave the unsaturated ester **31** (210 mg, 1.16 mmol, 83%) as a clear liquid (bp 120 °C/0.5 Torr).

31: ^{1}H NMR δ 0.91 (d, J = 7.0 Hz, 3 H), 0.94 (s, 3 H), 1.06 (d, J = 7.0 Hz, 3 H), 1.16 (s, 3 H), 1.39 (dq, J = 9.8, 7.0 Hz), 2.26 (br ddq, J = 1.7, 9.8, 7.0 Hz, 1 H), 3.69 (s, 3 H), 6.53 (d, J = 1.7 Hz, 1 H); ^{13}C NMR δ 11.3 (q), 17.3 (q), 20.2 (q), 26.0 (q), 44.2 (d), 47.0 (s), 50.8 (q), 53.1 (d), 143.0 (s), 147.7 (d), 165.4 (s); IR (film) 2980, 2860, 1720, 1615, 1550, 1256, 1238, 1052 cm^{-1}; EIMS m/z 182 (12), 167 (67), 151 (11), 123 (18), 108 (11), 107 (100); CIMS m/z 183 (100), 181 (12), 167 (12), 151 (14), 123 (8); HRMS found 182.1310, calcd 182.1307 for $C_{11}H_{18}O_2$; $[\alpha]^{20}_D$ +85.6 ± 0.1° (c = 0.8, $CHCl_3$).

Attempted Deconjugation of Methyl 3,4,5,5-Tetramethylcyclopentenecarboxylate (31). A solution of n-butyllithium (345 μL of a 1.55 M solution in hexanes, 0.53 mmol) and diisopropylamine (54 mg, 0.54 mmol) in tetrahydrofuran (2 mL) was stirred at −78 °C for 1 h. Hexamethylphosphoramide (100 μL) was added and the resulting solution was stirred at −78 °C for 0.5 h. The ester **31** (50 mg, 0.27 mmol) dissolved in tetrahydrofuran (0.5 mL) was added, and the reaction mixture was slowly warmed to −20 °C and stirred for 1 h. The reaction was cooled to −78 °C and quenched with acetic acid (50 μL). The solvent was evaporated and the residue was purified by flash chromatography (1:8 ether/petroleum ether) to give a clear oil (38 mg, 0.21 mmol, 76%). Gas chromatographic and ^{1}H NMR spectroscopic examination of this oil showed it to be recovered **31** with less than 2% of the deconjugated ester **33**. Use of deuterated acetic acid to quench the reaction showed no deuterium incorporation in the recovered starting material (^{1}H NMR).

(1*S*,3*S*,5*R*)-3-(Hydroxymethyl)-4,4,5-trimethylcyclopentanecarboxylic Acid (34a). To a stirred solution of lithium metal (1.0 g, 0.14 mmol) in liquid ammonia (350 mL) were added the acid ester **9a** (3.2 g, 14.9 mmol) in tetrahydrofuran (15 mL) and methanol (1.4 mL) via syringe pump over 30 min. The mixture was then warmed to reflux for 2 h and then quenched by addition of enough methanol to discharge the blue color. The excess ammonia was evaporated, and the residue was diluted with saturated aqueous ammonium chloride (100 mL) and extracted with ether (2 × 150 mL). The combined ethereal extract was dried, filtered, and evaporated to yield the hydroxy acid **34a** (2.34 g, 12.6 mmol, 84%) as a white powder, mp 111–112 °C (ethyl acetate/hexane).

(1*S*,3*R*,5*R*)-3-(Hydroxymethyl)-4,4,5-trimethylcyclopentanecarboxylic Acid (34b). A 1:4 mixture of acid esters **9a** and **9b**, respectively, (2.0 g, 9.5 mmol) was reduced with a solution of lithium metal in liquid ammonia as described for **9a** to yield a mixture of hydroxy acids **34a** and **34b** (1.8 g, 9.1 mmol, 96%) as a semisolid mass. The residue was slurried in 2:1 hexane/ethyl acetate and filtered to give the pure hydroxy acid **34b** (350 mg, 1.75 mmol) as a white powder (mp 124–125 °C). The filtrate was evaporated to give an oil (1.4 g, 7.3 mmol), which was a mixture of **34a** and **34b** (1:3, respectively) and would not crystallize despite repeated attempts.

34a: ^{1}H NMR [$(CD_3)_2CO$] δ 0.64 (s, 3 H), 0.91, (d, J = 6.8 Hz, 3 H), 1.01 (s, 3 H), 1.63 (dq, J = 11.0, 6.8 Hz, 1 H), 1.81 (m, 2 H), 2.07 (ddd, J = 5.4, 8.7, 13.5 Hz, 1 H), 2.37 (ddd, (J = 5.4, 10.9, 11.0 Hz), 1 H), 3.43 (dd, J = 8.6, 9.6 Hz, 1 H), 3.65 (dd, J = 5.7, 9.6 Hz, 1 H), 10.4 (br s, 2 H); ^{13}C NMR [$(CD_3)_2CO$] δ 12.2 (q), 14.8 (q), 26.3 (q), 31.2 (t), 43.0 (s), 48.0 (d), 50.2 (d), 52.1 (d), 63.2 (t), 177.8 (s); IR (CCl_4) 3260, 2980, 1675, 1290 cm^{-1}; EIMS m/z 168 (1), 156 (14), 153 (17), 125 (23), 123 (42); CIMS m/z 169 (26), 151 (20), 123 (100); HRMS found 168.1144, calcd 168.1150 for $C_{10}H_{16}O_2$ $(M - H_2O)^+$; $[\alpha]_D$ +24.1 ± 0.1° (c = 1.1, MeOH).

34b: ^{1}H NMR δ 0.82 (s, 3 H), 0.93 (d, J = 7.0 Hz, 3 H), 0.94 (s, 3 H), 1.78 (m, 2 H), 1.96 (dq, J = 10.2, 7.0 Hz, 1 H), 2.19 (m, 1 H), 2.43 (m, 1 H), 3.56 (dd, J = 7.1, 10.7 Hz), 3.72 (dd, J = 4.8, 10.7 Hz, 1 H), 6.5 (br s, 2 H); ^{13}C NMR δ 13.5 (q), 23.0 (q), 24.3 (q), 30.7 (t), 43.0 (s), 47.8 (d), 49.6 (d), 51.1 (d), 64.4 (t), 182.4 (s); IR (Nujol mull) 3350, 3000, 1702, 1306, 1260, 1204, 1022 cm^{-1}; EIMS m/z 168 (4), 156 (23), 140 (10), 123 (20), 109 (37); CIMS m/z 169 (32), 123 (100), 109 (4); HRMS found 168.1152, calcd

168.1150 ($M - H_2O)^+$; $[\alpha]_D$ −1.7 ± 0.1° (*c* = 0.9, MeOH).

(1*S*,3*S*,5*R*)-Methyl 3-(Hydroxymethyl)-4,4,5-trimethylcyclopentanecarboxylate (35a). The hydroxy acid **34a** (1.0 g, 5.37 mmol) was dissolved in 5:1 ether/methanol (25 mL) and the solution was cooled to 0 °C. Diazomethane was bubbled through the solution until a bright yellow color persisted. This solution was warmed to room temperature for 30 min, and the excess diazomethane was removed under a stream of nitrogen. Evaporation of the solution afforded the hydroxy ester **35a** (1.07 g, 5.34 mmol, 99%) as a clear liquid (bp 135–140 °C/0.03 Torr). Methyl ester **35b** was prepared analogously from **34b**.

35a: ^{1}H NMR δ 0.59 (s, 3 H), 0.87 (d, *J* = 6.9 Hz, 3 H), 0.99 (s, 3 H), 1.45 (br s, 1 H), 1.61 (ddd, *J* = 10.6, 10.9, 13.3 Hz, 1 H), 1.80 (dq, *J* = 10.8, 6.9 Hz, 1 H), 1.88 (m, 1 H), 3.48 (dd, *J* = 8.1, 10.5 Hz, 1 H), 3.65 (s, 3 H), 3.71 (dd, *J* = 5.6, 10.5 Hz); ^{13}C NMR δ 12.3 (q), 15.1 (q), 26.2 (q), 30.8 (t), 43.0 (s), 48.0 (d), 49.8 (d), 51.6 (q), 51.7 (d), 64.0 (t), 177.3 (s); IR (film) 3440, 2980, 1740, 1175, 1075, 1008 cm^{-1}; EIMS *m/z* 200 (4), 182 (8), 170 (18), 167 (21), 142 (24), 123 (92), 122 (84); CIMS *m/z* 201 (4), 183 (22), 151 (37), 123 (100); HRMS found 200.1415, calcd 200.1412 for $C_{11}H_{20}O_3$, found 182.1298, calcd 182.1307 for $C_{11}H_{18}O_2$ ($M - H_2O)^+$; $[\alpha]_D$ +25.7 ± 0.1° (*c* = 1.0, $CHCl_3$).

35b: ^{1}H NMR δ 0.81 (s, 3 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.94 (s, 3 H), 1.68 (m, 1 H), 1.74 (m, 1 H), 1.92 (dq, *J* = 10.0, 6.9 Hz, 1 H), 2.14 (m, 1 H), 2.42 (ddd, *J* = 7.8, 9.8, 10.0 Hz, 1 H), 3.52 (dd, *J* = 6.2, 10.4 Hz, 1 H), 3.66 (s, 3 H), 3.67 (dd, *J* = 1.5, 10.4 Hz, 1 H); ^{13}C NMR δ 13.4 (q), 22.8 (q), 24.3 (q), 30.9 (t), 42.4 (s), 47.6 (d), 49.3 (d), 51.0 (d), 51.5 (q), 64.0 (t), 177.6 (s); IR (film) 3450, 2980, 1736, 1260, 1078 cm^{-1}; EIMS *m/z* 185 (3), 182 (1), 170 (27), 168 (13), 142 (22), 127 (10), 123 (22); CIMS *m/z* 201 (100), 183 (89), 169 (42), 151 (24); HRMS found 182.1303, calcd 182.1307 for $C_{11}H_{18}O_2$ ($M - H_2O)^+$; $[\alpha]_D$ +8.1 ± 0.1° (*c* = 1.0, $CHCl_3$).

(1*S*,3*S*,5*R*)-Methyl 3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,4,5-trimethylcyclopentanecarboxylate (36a). The hydroxy ester **35a** (640 mg, 3.20 mmol) dissolved in tetrahydrofuran (20 mL) was treated with *tert*-butyldimethylsilyl chloride (625 mg, 4.14 mmol), imidazole (700 mg, 10.3 mmol), and 4-(dimethylamino)pyridine (40 mg, 0.32 mmol). The resulting reaction mixture was stirred at room temperature for 3 h and filtered, and the filtrate was evaporated to yield a gummy residue. This was partitioned between water (20 mL) and methylene chloride (50 mL). The organic phase was washed with water (10 mL), dried, filtered, and evaporated to yield the silyl ether **36a** (960 mg, 3.05 mmol, 95%) as a clear liquid (bp 180 °C/0.13 Torr). Ester **36b** was prepared analogously from **35b**.

36a: ^{1}H NMR δ 0.02 (s, 6 H), 0.59 (s, 3 H), 0.86 (d, *J* = 6.9 Hz, 3 H), 0.86 (s, 9 H), 0.98 (s, 3 H), 1.54 (ddd, *J* = 9.8, 11.0, 13.1 Hz, 1 H), 1.79 (dq, *J* = 10.9, 6.9 Hz, 1 H), 1.88 (dddd, *J* = 6.2, 7.1, 9.2, 9.8 Hz, 1 H), 2.01 (ddd, *J* = 5.6, 9.2, 13.1 Hz, 1 H), 2.37 (ddd, *J* = 5.6, 10.9, 11.0 Hz, 1 H), 3.46 (dd, *J* = 7.1, 10.1 Hz, 1 H), 3.62 (dd, *J* = 6.2, 10.1 Hz, 1 H), 3.65 (s, 3 H); ^{13}C NMR δ −5.4 (q), 12.3 (q), 15.1 (q), 18.2 (s), 25.9 (q), 26.4 (q), 30.6 (t), 42.9 (s), 48.0 (d), 49.9 (d), 51.2 (q), 51.6 (d), 63.9 (t), 177.4 (s); IR (film) 2980, 1738, 1260 cm^{-1}; EIMS *m/z* 257 (6), 123 (100), 119 (33); HRMS found 257.1566, calcd 257.1573 for $C_{13}H_{25}O_3Si$ ($M - C_4H_9)^+$; $[\alpha]_D$ +9.2 ± 0.1° (*c* = 2.1, $CHCl_3$).

36b: ^{1}H NMR δ 0.00 (s, 6 H), 0.80 (s, 3 H), 0.86 (d, *J* = 6.8 Hz, 3 H), 0.86 (s, 9 H), 0.90 (s, 3 H), 1.64 (m, 1 H), 1.78 (m, 1 H), 1.87 (dq, *J* = 10.5, 6.8 Hz, 1 H), 2.07 (m, 1 H), 2.35 (m, 1 H), 3.44 (dd, *J* = 7.4, 9.9 Hz, 1 H), 3.62 (dd, *J* = 5.6, 9.9 Hz, 1 H), 3.65 (s, 3 H); ^{13}C NMR δ −5.6 (q), 13.4 (q), 18.0 (s), 23.1 (q), 24.7 (q), 25.8 (q), 31.1 (t), 41.8 (s), 47.4 (d), 49.4 (d), 50.8 (d), 51.2 (q), 64.1 (t), 176.5 (s); IR (film) 2980, 1740, 1256 cm^{-1}; EIMS *m/z* 283 (5), 258 (19), 257 (99), 225 (9), 123 (19); CIMS *m/z* 315 (35), 299 (52), 283 (30), 157 (73), 183 (100), 151 (13), 123 (39); HRMS found 257.1568, calcd 257.1573 for $C_{13}H_{25}O_3Si$ ($M - C_4H_9)^+$; $[\alpha]_D$ −1.4 ± 0.1° (*c* = 0.8, $CHCl_3$).

Selenylation of 36a. A solution of *n*-butyllithium (2.4 mL of a 1.55 M solution in hexane, 3.72 mmol) and dicyclohexylamine (682 mg, 3.76 mmol) in tetrahydrofuran (25 mL) was stirred at −78 °C for 1 h. A solution of the silyl-protected methyl ester **36a** (850 mg, 2.70 mmol) in tetrahydrofuran (4.0 mL) was then added and the reaction mixture was warmed to −23 °C for 1 h. After being cooled to −78 °C, the reaction mixture was treated with trimethylsilyl chloride (536 mg, 4.94 mmol) and the temperature was raised to 0 °C for 1 h. The solution was cooled to −78 °C, a solution of phenylselenyl chloride (750 mg, 3.92 mmol) in tetrahydrofuran (4.0 mL) was added, and the entire mixture was slowly warmed to room temperature and stirred for 1 h. The solvent was evaporated, the residue was slurried in petroleum ether (20 mL) and filtered, and the solid was washed with petroleum ether (10 mL). The filtrate was evaporated and the residue purified by flash chromatography (20:1 petroleum ether/ether) to give the epimeric selenides **37a** (510 mg, 1.15 mmol) and **38a** (462 mg, 1.04 mmol) as pale yellow oils. Selenide **37b** was formed essentially stereospecifically by analogous reaction of **36b**.

37a: ^{1}H NMR δ −0.02 (s, 6 H), 0.84 (s, 9 H), 0.88 (s, 3 H), 0.98 (s, 3 H), 1.22 (d, *J* = 7.0 Hz, 3 H), 1.64 (dddd, *J* = 6.6, 7.0, 10.2, 13.0 Hz, 1 H), 1.82 (dd, *J* = 13.0, 14.1 Hz, 1 H), 2.00 (q, *J* = 7.0 Hz, 1 H), 2.62 (dd, *J* = 7.0, 14.1 Hz, 1 H), 3.46 (dd, *J* = 6.6, 10.2 Hz, 1 H), 3.58 (s, 3 H), 3.62 (dd, *J* = 10.2, 10.2 Hz, 1 H), 7.25–7.56 (m, 5 H); ^{13}C NMR δ −5.4 (q), 11.6 (q), 16.0 (q), 18.2 (s), 25.9 (q), 27.5 (q), 40.1 (t), 43.6 (s), 51.4 (q), 52.1 (d), 52.7 (d), 57.9 (s), 63.3 (t), 127.9 (s), 128.7 (d), 128.8 (d), 137.4 (d), 175.4 (s); IR (CCl_4) 2980, 1722, 1580, 1252, 1206 cm^{-1}; EIMS *m/z* 472 (10), 471 (14), 470 (40), 468 (23), 415 (24), 414 (25), 413 (100), 411 (51), 255 (46), 181 (16), 121 (51); HRMS found 468.1764, calcd 468.1764 for $C_{23}H_{38}O_3{}^{78}SeSi$, found 470.1754, calcd 470.1755 for $C_{23}H_{38}O_3{}^{80}SeSi$; $[\alpha]_D$ −21.1 ± 0.1° (*c* = 1.7, $CHCl_3$).

38a: ^{1}H NMR δ 0.03 (s, 6 H), 0.57 (s, 3 H), 0.85 (s, 9 H), 0.90 (d, *J* = 7.4 Hz, 3 H), 0.93 (s, 3 H), 1.62 (dddd, *J* = 6.3, 7.3, 7.3, 12.3 Hz, 1 H), 2.03 (q, *J* = 7.4 Hz, 1 H), 2.15 (dd, *J* = 7.3, 14.7 Hz, 1 H), 2.51 (dd, *J* = 12.3, 14.7 Hz, 1 H), 3.43 (dd, *J* = 7.3, 10.2 Hz, 1 H), 3.60 (dd, *J* = 6.3, 10.2 Hz, 1 H), 3.63 (s, 3 H), 7.25–7.60 (m, 5 H); ^{13}C NMR δ −5.4 (q), 10.2 (q), 15.4 (q), 18.2 (s), 25.9 (q), 27.6 (q), 39.6 (t), 43.3 (s), 50.1 (d), 52.1 (q), 57.2 (d), 58.2 (s), 63.3 (t), 128.8 (s), 128.8 (d), 128.9 (d), 137.1 (d), 174.3 (s); IR (CCl_4) 2980, 1730, 1580, 1252, 1066 cm^{-1}; EIMS *m/z* 468 (1), 412 (25), 410 (15), 256 (16), 181 (12), 121 (35); HRMS found 468.1764, calcd 468.1764 for $C_{23}H_{38}O_3{}^{78}SeSi$; $[\alpha]_D$ +2.9 ± 0.1° (*c* = 1.4, $CHCl_3$).

37b: ^{1}H NMR δ 0.00 (s, 6 H), 0.85 (s, 9 H), 0.86 (s, 3 H), 1.11 (s, 3 H), 1.21 (d, *J* = 7.2 Hz, 3 H), 1.72 (dd, *J* = 11.2, 14.3 Hz, 1 H), 1.96 (dd, *J* = 6.3, 14.3 Hz, 1 H), 2.11 (q, *J* = 7.2 Hz, 1 H), 2.26 (dddd, *J* = 6.3, 6.3, 7.1, 11.2 Hz), 3.47 (*J* = 7.1, 10.0 Hz), 1 H), 3.56 (s, 3 H), 3.62 (dd, *J* = 6.3, 10.0 Hz, 1 H), 7.23–7.55 (m, 5 H); ^{13}C NMR δ −5.5 (q), 12.5 (q), 18.2 (s), 25.4 (q), 26.0 (q), 26.9 (q), 37.8 (t), 41.3 (s), 49.5 (d), 51.7 (q), 51.9 (d), 61.0 (s), 63.4 (t), 127.2 (s), 128.6 (d), 129.0 (d), 137.8 (d), 174.4 (s); IR (CCl_4) 2980, 1722, 1250, 838 cm^{-1}; EIMS *m/z* 472 (3), 470 (6), 468 (6), 466 (5), 415 (14), 413 (51), 411 (29), 409 (9), 314 (15), 281 (20), 256 (27), 181 (57), 157 (32), 121 (100); HRMS found 468.1754, calcd 468.1764 for $C_{23}H_{38}O_3{}^{78}SeSi$, found 470.1758, calcd 470.1755 for $C_{23}H_{38}O_3{}^{80}SeSi$; $[\alpha]_D$ −4.9 ± 0.1° (*c* = 0.5, $CHCl_3$).

(3*S*,5*R*)-Methyl 3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,4,5-trimethylcyclopentenecarboxylate (39a). The selenide **37a** (500 mg, 1.06 mmol) was dissolved in methylene chloride (10 mL) and the solution was cooled to −10 °C. *m*-Chloroperoxybenzoic acid (380 mg, 2.21 mmol) was added, and the reaction mixture was stirred for 0.5 h at −10 °C. Diisopropylamine (0.45 mL) was added, and the mixture was warmed to reflux for 0.5 h. The solvent was evaporated, yielding a residue that was purified by flash chromatography (20:1 petroleum ether/ether) to yield the unsaturated ester **39a** (245 mg, 0.86 mmol, 81%) as a pale yellow liquid (bp 180–185 °C/0.13 Torr). Unsaturated ester **39b** was prepared and analogously from **37b**.

39a: ^{1}H NMR δ 0.02 (s, 6 H), 0.84 (s, 3 H), 0.87 (s, 9 H), 1.03 (d, *J* = 6.1 Hz, 3 H), 1.04 (s, 3 H), 2.42 (br ddd, *J* = 2.0, 6.3, 7.8 Hz, 1 H), 2.46 (br q, *J* = 6.1 Hz, 1 H), 3.52 (dd, *J* = 7.8, 9.9 Hz, 1 H), 3.66 (dd, *J* = 6.3, 9.9 Hz, 1 H), 3.70 (s, 3 H), 6.66 (br d, *J* = 2.0 Hz, 1 H); ^{13}C NMR δ −5.4 (q), 15.1 (q), 18.3 (s), 25.9 (q), 26.4 (q), 30.1 (q), 42.8 (s), 49.4 (d), 51.1 (q), 58.2 (d), 63.4 (t), 139.7 (s), 144.0 (d), 165.9 (s); IR (film) 2970, 2830, 1720, 1628, 1268, 886, 820 cm^{-1}; EIMS *m/z* 255 (53), 121 (50); CIMS *m/z* 298 (18), 282 (11), 256 (21), 182 (13), 181 (100), 121 (23); HRMS found 255.1414, calcd 255.1417 for $C_{13}H_{23}O_3Si$ ($M - C_4H_9)^+$; $[\alpha]_D$ +84.1 ± 0.1° (*c* = 1.0, $CHCl_3$).

39b: ^{1}H NMR δ 0.03 (s, 6 H), 0.87 (s, 9 H), 0.88 (s, 3 H), 0.98 (d, *J* = 7.1 Hz, 3 H), 1.03 (s, 3 H), 2.47 (dq, *J* = 0.8, 7.1 Hz, 1 H), 2.61 (ddd, *J* = 1.8, 6.5, 10.0 Hz, 1 H), 3.56 (dd, *J* = 8.1, 10.0 Hz, 1 H), 3.65 (dd, *J* = 6.5, 8.1 Hz, 1 H), 3.71 (s, 3 H), 6.59 (dd, *J* = 0.8, 1.8 Hz); ^{13}C NMR δ −5.4 (q), 14.0 (q), 18.2 (s), 23.8 (q), 24.1 (q), 25.9 (q), 43.3 (s), 50.1 (d), 51.2 (q), 56.0 (d), 61.5 (t), 140.6

(s), 143.3 (d), 165.8 (s); IR (film) 2980, 2860, 1720, 1632, 1256, 840 cm^{-1}; EIMS *m/z* 257 (8), 255 (44), 121 (63), 119 (43); CIMS *m/z* 296 (15), 280 (12), 254 (21), 181 (73), 149 (11), 121 (37); HRMS found 255.1431, calcd 255.1416 for $C_{13}H_{23}O_3Si$ $(M - C_4H_9)^+$; $[\alpha]_D$ $-45.2 \pm 0.1°$ (*c* = 0.8, $CHCl_3$).

(3*S*,5*R*)-1-(Hydroxymethyl)-3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,4,5-trimethylcyclopentene (41a). The unsaturated ester **39a** (250 mg, 0.80 mmol) was dissolved in tetrahydrofuran (8.0 mL) and the stirred solution was cooled to 0 °C. To this solution was added a suspension of lithium ethoxyaluminum hydride in tetrahydrofuran (1.0 mL of a 1.1 M suspension). After 0.5 h at 0 °C, a further portion of lithium ethoxyaluminum hydride (0.5 mL of a 1.1 M suspension) was added to the reaction mixture. After an additional 0.5 h, the reaction was quenched by sequential addition of water (60 μL), 15% aqueous sodium hydroxide (60 μL), and water (180 μL). The mixture was stirred 10 min and then dried (Na_2SO_4). The reaction mixture was filtered, the precipitate was washed with ether (10 mL), and the combined filtrate was evaporated. High pressure liquid chromatography of the residue (μ-Porasil, 5% ethyl acetate/hexane, 2.0 mL/min) indicated that the residue was a 6:1 mixture of the desired allylic alcohol **41a** and the saturated alcohol **42**, respectively. Preparative HPLC of the mixture gave the pure alcohol **41a** (180 mg, 0.63 mmol, 79%) as a clear oil. Allylic alcohol **41b** was prepared analogously from ester **39b**.

41a: ^1H NMR δ 0.02 (s, 6 H), 0.75 (s, 3 H), 0.87 (s, 9 H), 0.90 (d, *J* = 7.4 Hz, 3 H), 1.07 (s, 3 H), 2.34 (br q, *J* = 7.4 Hz, 1 H), 2.42 (br ddd, *J* = 0.6, 6.9, 7.3 Hz, 1 H), 3.49 (dd, *J* = 7.3, 9.9 Hz, 1 H), 3.59 (dd, *J* = 6.9, 9.9 Hz, 1 H), 4.13 (m, 2 H), 5.50 (br d, *J* = 0.6 Hz, 1 H); ^{13}C NMR δ −5.4 (q), 12.9 (q), 17.5 (q), 18.2 (s), 25.9 (q), 29.3 (q), 43.9 (s), 50.2 (d), 57.1 (d), 61.1 (t), 63.8 (t), 125.7 (d), 147.0 (s); IR (film) 3350, 2980, 2860, 1650, 1260, 840 cm^{-1}; EIMS *m/z* 241 (16), 211 (31), 149 (20), 135 (52), 121 (33); CIMS *m/z* 285 (5), 267 (8), 151 (14), 135 (100), 121 (23); $[\alpha]_D$ $+20.1 \pm 0.1°$ (*c* = 1.9, $CHCl_3$).

41b: ^1H NMR δ 0.01 (s, 6 H), 0.87 (s, 9 H), 0.89 (d, *J* = 7.4 Hz, 3 H), 0.92 (s, 3 H), 0.95 (s, 3 H), 2.26 (br q, *J* = 7.4 Hz, 1 H), 2.38 (br dd, *J* = 6.4, 7.4 Hz, 1 H), 3.51 (dd, *J* = 7.4, 9.8 Hz, 1 H), 3.61 (dd, *J* = 6.4, 9.8 Hz, 1 H), 4.13 (br s, 2 H), 5.46 (br s, 1 H); ^{13}C NMR δ −5.4 (q), 12.8 (q), 18.2 (s), 23.6 (q), 24.4 (q), 25.9 (q), 43.0 (s), 49.8 (d), 55.5 (d), 60.9 (t), 62.9 (t), 125.1 (d), 148.0 (s); IR (film) 3350, 2980, 2824, 1640, 1100, 834 cm^{-1}; EIMS *m/z* 282 (2), 255 (23), 227 (4), 137 (27), 135 (52), 121 (44), 119 (31), 109 (21); CIMS *m/z* 267 (10), 181 (26), 153 (14), 137 (42), 135 (100), 121 (18), 109 (21); HRMS found 227.1468, calcd 227.1467 for $C_{12}H_{23}O_2Si$ $(M - C_4H_9)^+$; $[\alpha]_D$ $-22.5 \pm 0.1°$ (*c* = 1.5, $CHCl_3$).

(3*S*,5*R*)-1-(Acetoxymethyl)-3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-4,4,5-trimethylcyclopentene (43a). A solution of allylic alcohol **41a** (40 mg, 0.14 mmol) in methylene chloride (2 mL) was treated with triethylamine (0.1 mL) and acetic anhydride (0.1 mL). The mixture was stirred at room temperature for 4 h and thenm partitioned between water (5 mL) and ether (10 mL). The ethereal extract was dried, filtered, and evaporated. The residue after evaporation was purified by preparative TLC (R_f = 0.58, 8:1 petroleum ether/ether) to give the acetate **43a** (38 mg, 0.12 mmol, 85%) as a clear oil. Acetate **43b** was prepared analogously from **41b**.

43a: ^1H NMR δ 0.02 (s, 6 H), 0.75 (s, 3 H), 0.87 (s, 9 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 1.07 (s, 3 H), 2.05 (s, 3 H), 2.34 (br q, *J* = 7.0 Hz, 1 H), 2.44 (m, 1 H), 3.49 (dd, *J* = 7.6, 9.9 Hz, 1 H), 3.59 (dd, *J* = 6.8, 9.9 Hz, 1 H), 4.57 (br s, 2 H), 5.56 (br s, 1 H); ^{13}C NMR δ −5.4 (q), 12.9 (q), 17.5 (q), 18.2 (s), 20.9 (q), 25.9 (q), 29.2 (q), 43.9 (s), 50.4 (d), 57.2 (d), 62.2 (t), 63.5 (t), 128.8 (d), 141.7 (s), 170.7 (s); IR (film) 2980, 2860, 1750, 1240, 840 cm^{-1}; EIMS *m/z* 209 (7), 135 (100), 122 (29), 121 (21), 117 (99), 107 (30); CIMS *m/z* 267 (10), 135 (100), 117 (7); $[\alpha]_D$ $+43.6 \pm 0.1°$ (*c* = 1.1, $CHCl_3$).

43b: ^1H NMR δ 0.01 (s, 6 H), 0.86 (s, 9 H), 0.88 (d, *J* = 7.3 Hz, 1 H), 0.93 (s, 3 H), 0.95 (s, 3 H), 2.04 (s, 3 H), 2.25 (br q, *J* = 7.3 Hz, 1 H), 2.39 (br dd, *J* = 6.2, 7.2 Hz, 1 H), 3.52 (dd, *J* = 7.2, 9.8 Hz, 1 H), 3.61 (dd, *J* = 6.2, 9.8 Hz, 1 H), 4.57 (br s, 2 H), 5.57 (br s, 1 H); ^{13}C NMR δ −5.5 (q), 12.6 (q), 18.2 (s), 21.0 (q), 23.5 (q), 24.5 (q), 25.9 (q), 43.0 (s), 50.1 (d), 55.7 (d), 62.2 (t), 62.7 (t), 128.5 (d), 142.7 (s), 170.8 (s); IR (CCl_4) 2980, 2860, 1740, 1252, 840 cm^{-1}; EIMS *m/z* 211 (7), 109 (4), 137 (21), 135 (96), 122 (24), 121 (20), 117 (100); CIMS *m/z* 269 (2), 267 (9), 251 (5), 159 (10), 137 (23), 135 (100); $[\alpha]_D$ $-45.7 \pm 0.1°$ (*c* = 0.3, $CHCl_3$).

(3*S*,5*R*)-3-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-1,4,4,5-tetramethylcyclopentene (44a). Method A. From Allylic Alcohol 41a. A solution of allylic alcohol **41a** (25 mg, 0.09 mmol) in tetrahydrofuran (0.5 mL) was added to a stirred suspension of sulfur trioxide/pyridine (22 mg, 0.14 mmol) in tetrahydrofuran (2.0 mL) at 0 °C. After 1 h at 0 °C, TLC of the reaction mixture indicated complete conversion to the sulfate ester, and a suspension of lithium aluminum hydride (21 mg, 0.55 mmol) in tetrahydrofuran (1.0 mL) was added to the reaction mixture. The mixture was warmed slowly to room temperature and was stirred for 20 h. The reaction mixture was quenched by sequential addition of water (20 μL), 15% aqueous sodium hydroxide (20 μL), and water (60 μL) and then filtered. The precipitate was washed with ether (5 mL) and the filtrate was evaporated. The residue after evaporation was purified by preparative TLC (R_f = 0.75, 8:1 petroleum ether/ether) to afford **44a** (11 mg, 0.04 mmol, 44%) as a clear oil.

Method B. From Allylic Acetate 43a. A solution of the allylic acetate **43a** (40 mg, 0.12 mmol) in tetrahydrofuran (0.75 mL) and methanol (10 μL) was added to a stirred solution of lithium metal (50 mg) in liquid ammonia (5 mL) at −78 °C. The mixture was warmed to reflux for 1 h and then quenched by addition of sufficient methanol to discharge the blue color. The excess ammonia was evaporated, and the residue was partitioned between ether (10 mL) and saturated aqueous ammonium chloride (5 mL). The ethereal extract was washed with saturated aqueous sodium chloride (5 mL), dried, filtered, and evaporated. The residue (28 mg, 0.10 mmol, 85%) was analyzed by gas chromatography (3% OV-101, 150 °C), which showed it to be a 7:1 mixture of **44a** and **45a** (t_R = 8.5, 9.2 min, respectively). Preparative gas chromatography (3.5 m × 8 mm 3% OV-101, 150 °C) gave a pure sample of **44a**. The trans isomer **44b** was prepared analogously from **43b** by method B.

44a: ^1H NMR δ 0.02 (s, 6 H), 0.72 (s, 3 H), 0.84 (d, *J* = 7.4 Hz, 3 H), 0.84 (s, 9 H), 1.05 (s, 3 H), 1.62 (ddd, *J* = 1.0, 1.0, 1.6 Hz, 3 H), 2.12 (br q, *J* = 7.4 Hz, 1 H), 2.34 (m, 1 H), 3.45 (dd, *J* = 7.5, 9.8 Hz, 1 H), 3.55 (dd, *J* = 7.1, 9.8 Hz, 1 H), 5.18 (br d, *J* = 1.6 Hz, 1 H); ^{13}C NMR δ −5.3 (q), 13.1 (q), 15.1 (q), 17.6 (q), 18.3 (s), 26.0 (q), 29.7 (q), 43.6 (s), 53.1 (d), 57.3 (d), 64.2 (t), 124.5 (d), 143.3 (s); IR ($CDCl_3$) 3020, 2980, 1652, 1260, 840 cm^{-1}; EIMS *m/z* 211 (36), 135 (69), 123 (60), 107 (9); HRMS found 211.1514, calcd 211.1518 for $C_{12}H_{23}OSi$ $(M - C_4H_9)^+$; $[\alpha]_D$ $+37.3 \pm 0.1°$ (*c* = 1.7, $CHCl_3$).

44b: ^1H NMR δ 0.02 (s, 6 H), 0.84 (d, *J* = 7.3 Hz, 1 H), 0.87 (s, 9 H), 0.91 (s, 3 H), 0.92 (s, 3 H), 1.63 (dd, *J* = 1.6, 1.9 Hz, 3 H), 2.05 (dq, *J* = 1.9, 7.3 Hz, 1 H), 2.31 (qdd, *J* = 1.6, 6.6, 7.3 Hz, 1 H), 3.47 (dd, *J* = 7.3, 9.8 Hz, 1 H), 3.57 (dd, *J* = 6.6, 9.8 Hz, 1 H), 5.15 (q, *J* = 1.9 Hz, 1 H); ^{13}C NMR δ −5.4 (q), 12.5 (q), 15.2 (q), 18.2 (s), 23.8 (q), 24.8 (q), 25.9 (q), 42.8 (s), 52.9 (d), 56.0 (d), 63.3 (t), 124.3 (d), 144.2 (s); IR (CH_2Cl_2) 2980, 2964, 2878, 1640, 1250, 838 cm^{-1}; EIMS *m/z* 211 (4), 136 (4), 135 (64), 123 (48), 121 (50); CIMS *m/z* 269 (3), 267 (5), 253 (25), 211 (36), 137 (100), 135 (20); HRMS found 211.1512, calcd 211.1518 for $C_{12}H_{23}OSi$ $(M - C_4H_9)^+$; $[\alpha]_D$ $-82.6 \pm 0.1°$ (*c* = 1.0, $CHCl_3$).

(3*S*,5*R*)-3-(Hydroxymethyl)-1,4,4,5-tetramethylcyclopentene (*epi*-α-Necrodol) (3). A solution of silyl ether **44a** (40 mg, 0.15 mmol) in tetrahydrofuran was cooled to 0 °C and tetra-*n*-butylammonium fluoride in tetrahydofuran (200 μL of a 1.0 M solution, 0.20 mmol) was added. The reaction mixture was warmed to room temperature and was stirred for 6 h. The product was isolated by preparative TLC (4:1 petroleum ether/ether) of the crude reaction mixture. The band of R_f = 0.26 gave *epi*-α-necrodol (**3**) (22 mg, 0.14 mmol, 95%) as a clear oil. α-Necrodol (**1**) was prepared analogously from **44b**.

3: ^1H NMR δ 0.80 (s, 3 H), 0.85 (d, *J* = 7.3 Hz, 3 H), 1.05 (s, 3 H), 1.65 (br d, *J* = 1.5 Hz, 3 H), 2.09 (dq, *J* = 2.0, 7.3 Hz, 1 H), 2.33 (dddd, *J* = 2.0, 2.1, 5.7, 6.0 Hz, 1 H), 3.49 (dd, *J* = 5.7, 10.8 Hz, 1 H), 3.61 (dd, *J* = 6.0, 10.8 Hz, 1 H), 5.21 (dd, *J* = 1.5, 2.1 Hz); ^{13}C NMR δ 13.6 (q), 15.2 (q), 18.3 (q), 30.6 (q), 43.2 (s), 53.1 (d), 57.6 (d), 63.7 (t), 123.1 (d), 145.3 (s); IR ($CDCl_3$) 3620, 3030, 2980, 2880, 1378, 1018 cm^{-1}; EIMS *m/z* 154 (6), 139 (5), 123 (100), 121 (6); CIMS *m/z* 155 (1), 153 (11), 137 (100), 123 (16); HRMS found 154.1366, calcd 154.1358 for $C_{10}H_{18}O$; $[\alpha]_D$ $+24.5 \pm 0.1°$ (*c* = 0.9, $CHCl_3$).

1: ^1H NMR δ 0.85 (d, *J* = 7.3 Hz, 3 H), 0.90 (s, 3 H), 0.99 (s, 3 H), 1.65 (br d, *J* = 1.5 Hz, 3 H), 2.12 (br dq, *J* = 1.8, 7.3 Hz,

1 H), 2.28 (m, 1 H), 3.59 (ABX, J_{AB} = 10.7, J_{AX} = 5.5, J_{BX} = 5.5 Hz, 2 H), 5.22 (br qd, J = 1.5, 1.8 Hz, 1 H); ^{13}C NMR δ 11.9 (q), 15.2 (q), 23.6 (q), 25.0 (q), 43.0 (s), 52.1 (d), 56.5 (d), 63.2 (t), 123.2 (d), 145.7 (s); IR ($CDCl_3$) 3620, 2960, 1468, 1386, 1070, 1008, 860 cm^{-1}; EIMS m/z 154 (9), 139 (19), 123 (22), 121 (8), 107 (5), 105 (9), 95 (18), 93 (18), 91 (19), 81 (100); CIMS m/z 155 (3), 154 (2), 153 (11), 139 (10), 137 (100); HRMS found 154.1366, calcd 154.1358 for $C_{10}H_{18}O$; $[\alpha]_D$ −76.5 ± 0.1° (c = 0.2, $CHCl_3$).

(4*S*)-Methyl 4-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2,3,3-trimethyl-1-cyclopentenecarboxylate (40). A solution of selenide **38a** (50 mg, 0.11 mmol) was oxidized with *m*-chloroperoxybenzoic acid (30 mg, 0.17 mmol) at −10 °C and treated as described for **37a** to give the tetrasubstituted olefin **40** (30 mg, 0.10 mmol, 87%) as a clear oil.

40: ^{1}H NMR δ 0.03 (s, 6 H), 0.86 (s, 3 H), 0.87 (s, 9 H), 1.10 (s, 3 H), 1.96 (dd, J = 1.6, 2.2 Hz, 3 H), 2.01 (dddd, J = 6.1, 6.4, 6.8, 7.4 Hz, 1 H), 2.17 (ddq, J = 6.1, 13.8, 2.2 Hz, 1 H), 2.57 (ddq, J = 7.4, 13.8, 1.6 Hz, 1 H), 3.58 (dd, J = 6.8, 10.2 Hz, 1 H), 3.68 (dd, J = 6.4, 10.2 Hz, 1 H), 3.69 (s, 3 H); ^{13}C NMR δ −5.5 (q), 11.8 (q), 18.2 (s), 19.3 (q), 25.9 (q), 26.3 (q), 33.9 (t), 43.0 (s), 49.4 (d), 50.8 (q), 63.5 (t), 124.4 (s), 163.0 (s), 167.0 (s); IR ($CDCl_3$) 2980, 2860, 1718, 1646, 1246, 840 cm^{-1}; EIMS m/z 255 (100), 121 (85), 119 (46); HRMS found 255.1417, calcd 255.1417 for $C_{13}H_{23}O_3Si$ $(M - C_4H_9)^+$; $[\alpha]_D$ +10.3 ± 0.1° (c = 1.8, $CHCl_3$).

(4*S*)-4-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-1-(hydroxymethyl)-2,2,3-trimethylcyclopentene (46). A solution of ester **40** (225 mg, 0.72 mmol) in ether (5 mL) was added to a stirred suspension of lithium aluminum hydride (100 mg, 2.63 mmol) in ether (10 mL) at 0 °C. The reaction was then stirred at 0 °C for 30 min and then quenched by sequential addition of water (100 μL), aqueous sodium hydroxide (100 μL), and water (300 μL). The white precipitate was filtered and washed with ether (10 mL). The filtrate was evaporated to yield the allylic alcohol **46** (169 mg, 0.60 mmol, 83%) as a clear oil.

46: ^{1}H NMR δ 0.02 (s, 6 H), 0.83 (s, 3 H), 0.88 (s, 9 H), 1.05 (s, 3 H), 1.48 (br s, 3 H), 2.02 (m, 2 H), 2.42 (m, 1 H), 3.55 (dd, J = 7.0, 10.0 Hz, 1 H), 3.70 (dd, J = 6.9, 10.0 Hz, 1 H), 4.16 (m, 2 H); ^{13}C NMR δ −5.4 (q), 9.3 (q), 18.2 (s), 19.6 (q), 25.9 (q), 26.8 (q), 34.9 (t), 47.9 (s), 50.2 (d), 59.5 (t), 63.9 (t), 131.4 (s), 143.4 (s); IR (film) 3400, 2978, 2850, 1250, 832 cm^{-1}; EIMS m/z 227 (4), 137 (14), 135 (53), 121 (14), 109 (34), 107 (35); CIMS m/z 267 (41), 137 (22), 135 (100), 121 (17), 109 (64), 107 (10); HRMS found 227.1468, calcd 227.1467 for $C_{12}H_{23}O_2Si$ $(M - C_4H_9)^+$; $[\alpha]_D$ +1.9 ± 0.1° (c = 1.3, $CHCl_3$).

(4*S*)-1-(Acetoxymethyl)-4-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2,3,3-trimethylcyclopentene (47). Allylic alcohol **46** (20 mg, 0.07 mmol) was acetylated as described for **41a** to afford the acetate **47** (21 mg, 0.06 mmol, 92%) as a clear oil.

47: ^{1}H NMR δ 0.02 (s, 6 H), 0.83 (s, 3 H), 0.88 (s, 9 H), 1.05 (s, 3 H), 1.55 (br s, 3 H), 2.02 (m, 1 H), 2.03 (s, 3 H), 2.32 (m, 1 H), 3.56 (dd, J = 7.0, 10.0 Hz, 1 H), 3.70 (dd, J = 6.9, 10.0 Hz, 1 H), 4.57 (br s, 2 H); ^{13}C NMR δ −5.4 (q), 9.4 (q), 18.2 (s), 19.6 (q), 20.9 (q), 25.9 (q), 26.8 (q), 35.2 (t), 47.9 (s), 50.1 (d), 61.3 (t), 63.8 (t), 126.9 (s), 145.9 (s), 171.1 (s); IR (film) 2980, 1960, 1860, 1748, 1234, 840 cm^{-1}; EIMS m/z 267 (2), 135 (100), 121 (10), 119 (15), 117 (67), 107 (16); CIMS m/z 266 (46), 135 (100), 109 (29), 75 (13); $[\alpha]_D$ +1.9 ± 0.1° (c = 0.8, $CHCl_3$).

(4*S*)-4-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-1,2,2,3-tetramethylcyclopentene (48). Method A. From Allylic Alcohol 46. The allylic alcohol **46** (1.0 g, 3.51 mmol) was converted to its sulfate ester and reduced as described for **41a** to give **48** (625 mg, 2.33 mmol, 66%) as a clear oil.

Method B. From Allylic Acetate 47. The allylic acetate **47** (20 mg, 0.06 mmol) was reduced with lithium/ammonia as described for **43a** to give **48** (14 mg, 0.05 mmol, 85%) as a clear oil.

48: ^{1}H NMR δ 0.03 (s, 6 H), 0.78 (s, 3 H), 0.88 (s, 9 H), 1.02 (s, 3 H), 1.45 (br s, 3 H), 1.56 (br s, 3 H), 1.94 (m, 2 H), 2.16 (m, 1 H), 3.55 (dd, J = 7.3, 10.0 Hz, 1 H), 3.69 (dd, J = 6.8, 10.0 Hz, 1 H); ^{13}C NMR δ −5.3 (q), 9.2 (q), 14.2 (q), 18.3 (s), 19.8 (q), 26.0 (q), 27.3 (q), 39.2 (t), 47.6 (s), 50.4 (d), 64.3 (t), 128.0 (s), 138.4 (s); IR (film) 2965, 2920, 1250, 836, 810 cm^{-1}; EIMS m/z 211 (38), 137 (19), 136 (80), 135 (87), 121 (100), 107 (12); HRMS found 211.1520, calcd 211.1518 for $C_{12}H_{23}OSi$ $(M - C_4H_9)^+$; $[\alpha]_D$ +3.7 ± 0.1° (c = 1.1, $CHCl_3$).

(4*S*)-4-(Hydroxymethyl)-1,2,2,3-tetramethylcyclopentene (γ-Necrodol) (5). A solution of silyl ether **48** (250 mg, 0.93 mmol) in tetrahydrofuran (5 mL) was cooled to 0 °C and treated with tetra-*n*-butylammonium fluoride (1.2 mL of a 1 M solution). The reaction was slowly warmed to room temperature and stirred for 18 h. Workup as described for **44a** gave γ-necrodol (**5**) (115 mg, 0.75 mmol, 80%) as a clear oil.

5: ^{1}H NMR δ 0.80 (s, 3 H), 1.03 (s, 3 H), 1.45 (br s, 3 H), 1.57 (br s, 3 H), 1.97 (m, 2 H), 2.28 (m, 1 H), 3.60 (m, 1 H), 3.75 (m, 1 H); ^{13}C NMR δ 9.1 (q), 14.1 (q), 19.9 (q), 27.2 (q), 39.3 (t), 47.5 (s), 50.4 (d), 64.3 (t), 127.9 (s), 138.6 (s); IR (film) 3050, 2980, 2960, 1245, 995 cm^{-1}; EIMS m/z 154 (28), 139 (100), 123 (15), 121 (67), 109 (25), 105 (18); CIMS m/z 155 (2), 154 (10), 153 (15), 139 (21), 138 (12), 137 (100), 81 (12); HRMS found 154.1368, calcd 154.1358 for $C_{10}H_{18}O$; $[\alpha]_D$ +15.1 ± 0.1° (c = 1.2, $CHCl_3$).

Preparation and Analysis of α-Methoxy-α-(trifluoromethyl)phenylacetate Esters of α-Necrodol (49, 50). A solution of synthetic **1** (100 μg) in dichloromethane (100 μL) was treated with α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPCl) (2 mg) and pyridine (50 μL). After 18 h at room temperature, the crude mixture was purified by preparative TLC (250-μm SiO_2, 10:1 petroleum ether/ether). The ester (R_f = 0.5) was removed from the gel with dichloromethane (2 mL), the suspension was filtered, and the solvent was evaporated. The residue (100 μg) was dissolved in deuteriochloroform (0.5 mL) and analyzed by ^{19}F NMR at 305 K.

49: ^{19}F NMR δ 6.207 (1752.9 Hz).

50: ^{19}F NMR δ 6.193 (1747.3 Hz).

The analogous ester prepared from natural **1** and (+)-MTPCl showed a ^{19}F NMR spectrum indistinguishable from the ^{19}F NMR spectrum of **49**.

Acknowledgment. We gratefully acknowledge partial support of this research by the National Institutes of Health (Grant No. AI-12020). We thank the International Paper Company Foundation for a J. Stanford Smith Fellowship to R.T.J. Acknowledgment is given to the National Science Foundation Instrumentation Program (Grant No. CHE 7904825 and PCM 8018643) for support of the Cornell Nuclear Magnetic Resonance Facility. The hospitality of the N.I.H. Fogarty Scholar-in-Residence program during the preparation of this manuscript is acknowledged with pleasure.

Note Added in Proof: Since the completion of this work, successful syntheses of β-necrodol (**2**) and *epi*-β-necrodol (**4**) have been reported from the laboratories of Oppolzer,[38] Trost,[39] and Schulte-Elte.[40]

(38) Oppolzer, W.; Schneider, P. *Helv. Chim. Acta* **1986**, *69*, 1817.
(39) Trost, B. M.; Braslau, R. *Tetrahedron Lett.* **1988**, *29*, 1231.
(40) Schulte-Elte, K. H.; Pamingle, H. *Helv. Chim. Acta* **1989**, *72*, 1158.