Later fractions gave 30.6 mg (16% yield) of β-santalol (2): IR (neat) 3333 (OH), 1664 (C=C), 877 cm^{-1} (=CH_2); NMR ($CDCl_3$) 1.05 (s, 3, CH_3), 1.78 (br s, 3, CH_3), 2.65 (br s, 1, CH), 4.12 (s, 2, CH_2O), 4.45 and 4.73 (2 s, 2, C=CH_2), 5.29 ppm (br t, 1, CH=C).

A mixture of 97.4 mg of **20**, 1 drop of triethylamine, and 10 mL of methanol was stirred at room temperature for 12 h. The solvents were removed by rotary evaporation, and the residue was placed on a vacuum pump at 0.1 mm for 3 h. This produced 85.8 mg of crude **2** (~80% purity by NMR).

Registry No. (±)-**2**, 27542-07-0; (±)-**4**, 85648-03-9; *d*-**9**, 3144-16-9; **10**, 41348-33-8; **11**, 17739-45-6; **12**, 85612-75-5; **13**, 85612-76-6; (±)-**15**, 85612-77-7; (±)-**16**, 85612-78-8; **17**, 85612-79-9; 2-bromoethanol, 540-51-2; dihydropyran, 110-87-2.

Reductive Transformation and Cyclopropanation of Mevinolin (6α-Methylcompactin). Generation of Chirality in the 1,4-Hydrostannation of a Cyclic Diene

C. H. Kuo,* A. A. Patchett, and N. L. Wendler

Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065

Received June 22, 1982

Conversion of mevinolin by direct reductive procedures as well as by indirect chemical transformations has permitted the preparation of the various di- and tetrahydro derivatives. Cyclopropanation of mevinolin and its derivatives has furnished mono- and dicyclopropanated analogues. These compounds are themselves bioactive to a varying degree as hypocholesterolemic agents.[2b]

Mevinolin or 6α-methylcompactin (1) isolated from *Aspergillus terreus*, is a potent HMG-CoA reductase inhibitor and as such is an effective hypocholesterolemic agent.[1,2a] Conversion of this substance by direct reductive procedures, as well as by indirect chemical transformations, has permitted preparation of the various di- and tetrahydro derivatives, themselves bioactive to a comparable degree with the parent compound.[2b]

Hydrogenation of mevinolin (1) in toluene solution by employing Wilkinson's catalyst produced a 9:1 mixture of 3,4-dihydro (2) and 3,5-dihydro (3) derivatives, respectively[3] (Scheme I), readily separable as their *tert*-butyldimethylsilyl ethers by HPLC. Hydrogenation of 1 in ethanol over palladium on calcium carbonate, on the other hand, proceeded in the opposite sense to a predominant extent to yield the 3,5-dihydro derivative **3** together with varying amounts of the 3,4-dihydro isomer. Depending on the catalyst, nearly exclusive formation of **3** is achievable by this technique. Finally, hydrogenation of 1 with platinum oxide in ethyl acetate yielded the tetrahydro derivative as a mixture (1:3) of *cis*- and *trans*-decalin isomers **4** and **5**, respectively. This mixture in the form of its *tert*-butyldimethylsilyl ethers could be separated by TLC or HPLC on silica gel to give the individual isomers in pure form.

An alternative reductive procedure which converts 1, in effect, exclusively to the 3,5-dihydro derivative **3** consists of the treatment of *tert*-butyldimethylsilyl)mevinolin **1b** with triethylsilane in methylene chloride[4] followed by protolysis with trifluoroacetic acid. This isomer, namely, **3a**, is important in the synthesis of the 4a,5-dihydro isomer vide infra.

The most elusive isomer to prepare synthetically is the 4a,5-dihydro system which also occurs as a congener together with mevinolin from the fermentation process.[5] Several routes to this dihydro compound via chemical sequences have been effected successfully; however, these approaches have all given, for the most part, the *cis*-octalin rather than the natural *trans*-octalin.

Three routes to 4a,5-dihydromevinolin were realized, and only one provided the natural trans isomer in ca. 10% yield. Thus, treatment of the *tert*-butyldimethylsilyl derivative of mevinolin (**1b**) with 1 equiv of osmium tetraoxide in pyridine yielded, on reductive workup, the 3α,4α-diol **6** (65% conversion yield) together with tetrol **7** (Scheme II). Assignment of the α-cis orientation of the hydroxyl functions is based on steric approach considerations, the α side of the molecule at the pertinent site appearing to be the more accessible. In addition, hydrogenation of both **6** and its corresponding acetonide derivative **6a** proceeded in the same directional sense. This was ascertained by the conversion of both series via the corresponding thionocarbonate derivative **9**, followed by pyrolysis at 110 °C in triethyl phosphite **6** and subsequent desilylation to give a 9:1 mixture of the cis vs. trans dihydro isomers **10a** and **11a**, respectively. The fact that the diol and its acetonide both hydrogenated in the same directional sense would appear to disallow any special orientation preference in the diol above and beyond a steric one. Significant, moreover, is the fact that hydrogenation of **6** in cyclohexane led virtually exclusively to **10**. Hydrogenation in nonpolar solvents is presumed to favor maximally the course of hydrogenation from the same side as the hydroxyl functions, a consequence completely contradicted in the present instance. It has further been observed that

(1) Alberts, A. W.; Chen, J.; Kuron, G.; Hunt, V.; Huff, J.; Hoffman, C.; Rothrock, J.; Lopez, M.; Joshua, H.; Harris, E.; Patchett, A.; Monaghan, R.; Currie, S.; Stapley, E.; Albers-Schonberg, G.; Hensens, O.; Hirschfield, J.; Hoogsteen, K.; Liesch, J.; Springer, J. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, (7), 3957.

(2) (a) Endo, A. *J. Antibiot.* **1979**, *32*, 852; **1980**, *33*, 334. (b) The results of biological studies on these and related systems will be published elsewhere.

(3) Numberical designations are those employed in ref 1 for the naphthanoid system.

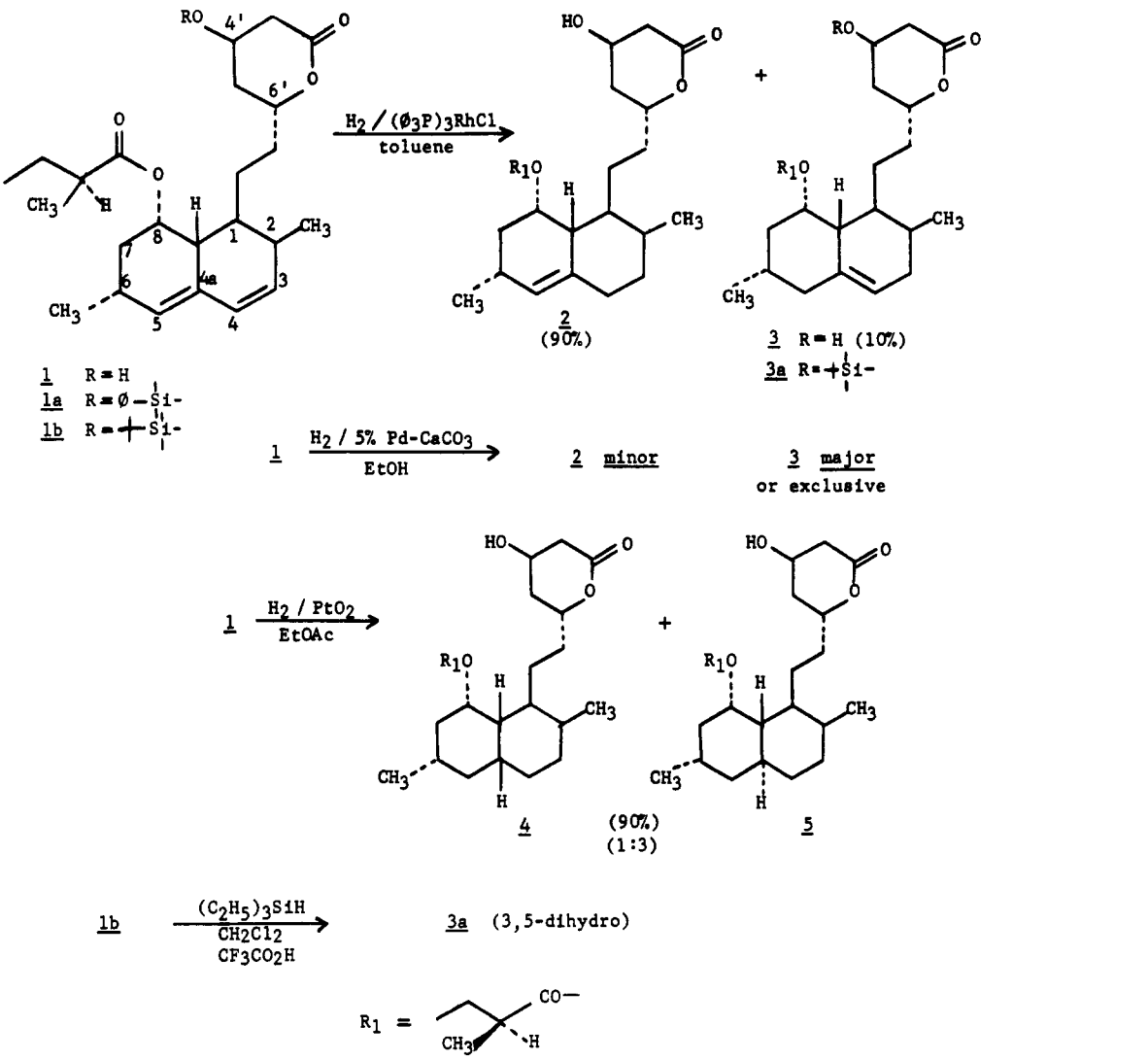
(4) Jogdao, P. S.; Bhide, G. V. *Steroids* **1980**, *35* (2), 133.

(5) Compare: Albers-Schonberg, G.; Joshua, H.; Lopez, M. B.; Hensens, O.D.; Springer, J. P.; Chen, J.; Ostrove, S.; Hoffman, C. H.; Alberts, A. W.; Patchett, A. A. *J. Antibiot.* **1981**, *34*, 507.

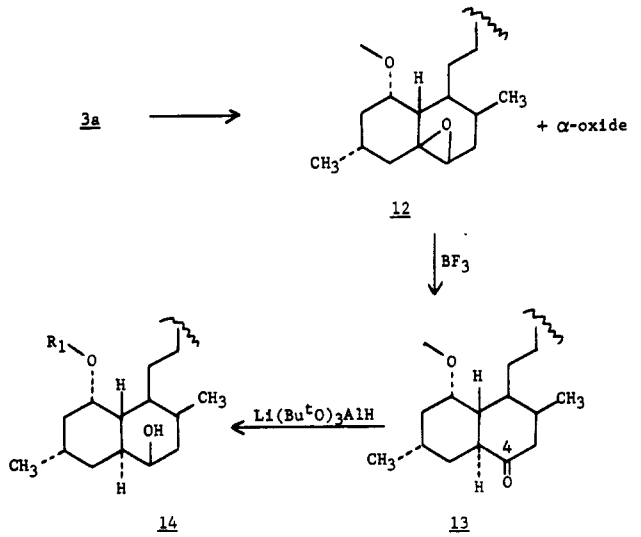
(6) Prinzbach, H.; Babsch, H. *Angew. Chem., Intl. Ed. Engl.* **1975**, *14*, 753.

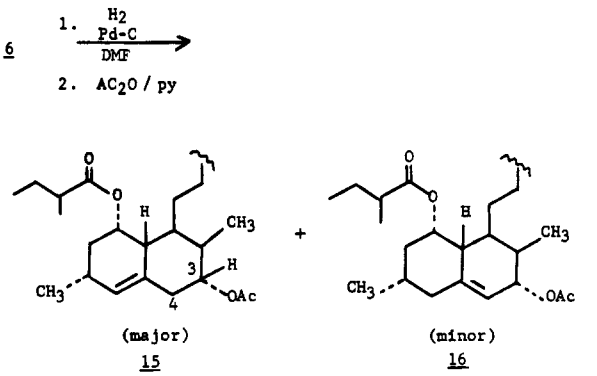
0022-3263/83/1948-1991$01.50/0

Scheme I



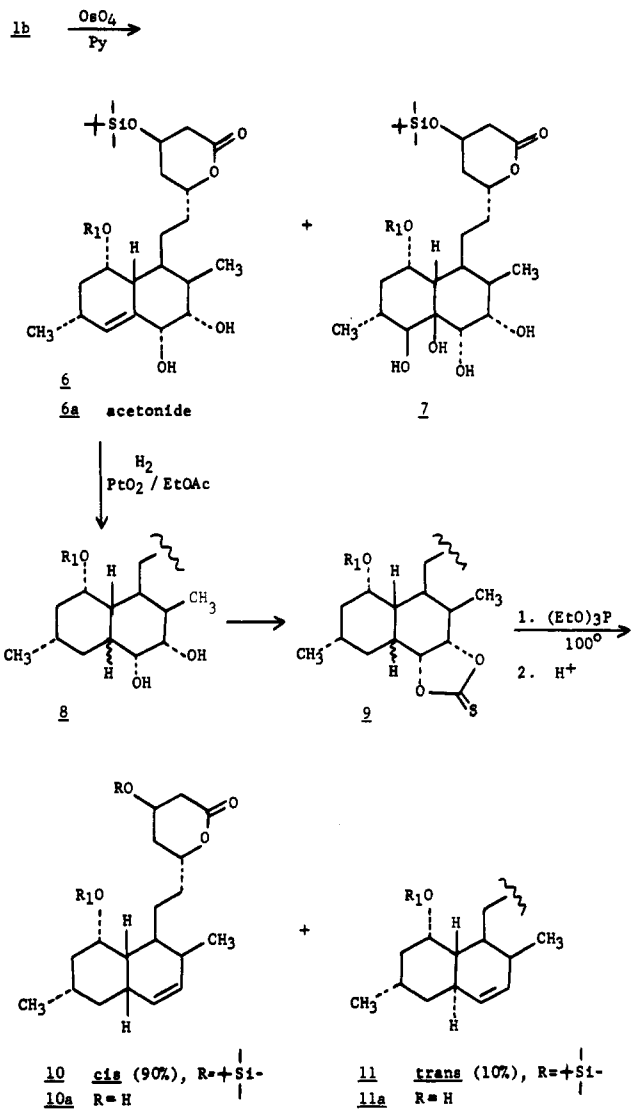
reaction independently at C-3 and C-4 proceeds via steric approach control with major attack α to the ring system; thus, reduction of the C-4 carbonyl group of **13** with lithium tri-*tert*-butoxyaluminum hydride occurs to a predominant extent to yield the 4β-hydroxy compound **14**. Similarly, the tosylhydrazone **18** is reduced with catecholborane to essentially an exclusive extent at C-3 from the α face, yielding, via **19**, the olefin **10** (Scheme III; see discussion below). These observations fortify the conclusion (see above) that OsO_4 hydroxylation, which is highly susceptible to steric approach control, does proceed in the case of mevinolin to give the glycol **6**. Final proof of the α orientation of the hydroxyl groups in the osmylation product **6** was derived from the hydrogenolysis of **6** with Pd/C in dimethyl formamide to yield **15**, after acetylation,





as the major compound together with the double-bond-rearranged system **16**. The small coupling constant of 3.42 Hz between the proton on the carbon bearing the acetoxyl substituent with its vicinal protons in a 200-MHz NMR spectrum dictates the acetoxyl group to be α in orientation in compliance with the molecular model display.

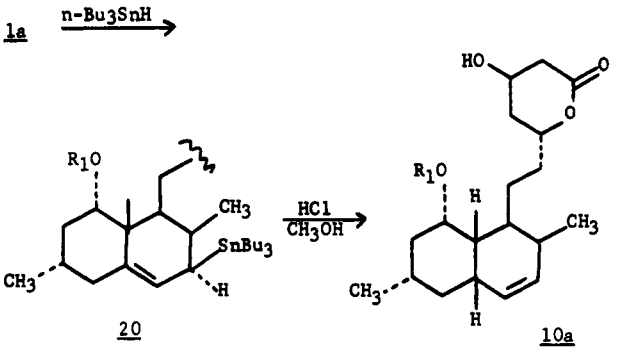
Scheme II



The second route to the 4a,5-dihydro system was achieved via the 3,5-dihydro isomer **3**. The latter as its *tert*-butyldimethylsilyl derivative **3a** was oxidized by CrO_3–3,5-dimethylpyrazole[7] to the corresponding $\Delta\alpha,\beta$-ketone **17** (Scheme III). Conversion of **17** in turn to its *p*-toluenesulfonylhydrazone followed by reduction with catecholborane according to the method of Kabalka[8] afforded the *cis*-4a,5-dihydro compound **10a** on desilylation.

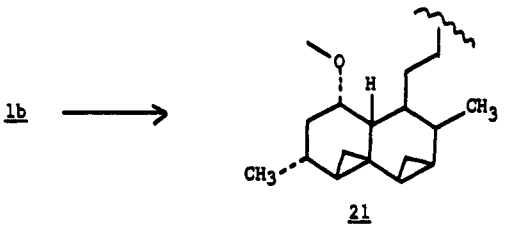
Parallel to Kabalka's observations[9] on the steric course of the reductive process with Δ^4-3-keto steroids, **18** is reduced from the sterically less hindered α side of the system to generate a transient diazene, **19**, which in turn delivers hydrogen via a cyclic sigmatropic process from the β face of the system with accompanying double bond migration.

A final route to the 4a,5-dihydro system proceeded from mevinolin itself in the form of its phenyldimethylsilyl derivative **1a**. The latter was submitted to 1,4-hydrostannation[10] with tri-*n*-butylstannane to yield 3β-(tributylstannyl)-3,5-dihydromevinolin **20**. The β orientation

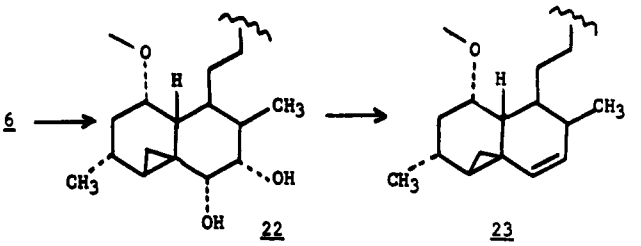


of the stannyl residue follows from the fact that the transannular hydrogen delivery in the cyclic S_E2' protolysis step[11] must occur from the β face, since treatment of **20** with anhydrous methanolic hydrogen chloride proceeded smoothly to generate **10a** in good yield. To our knowledge this is the first example of 1,4-hydrostannation of a cyclic diene whereby protolysis leads to generation of a chiral terminus.

Preparation of cyclopropyl derivatives of mevinolin was of interest for comparison with the hydromevinolins in biological activity. Thus, cyclopropanation of mevinolin via **1b** by various techniques including the Simmons–Smith reaction[12] and diazomethane–CuCl[13] afforded a dicyclopropyl derivative **21** in which the steric orientation of he



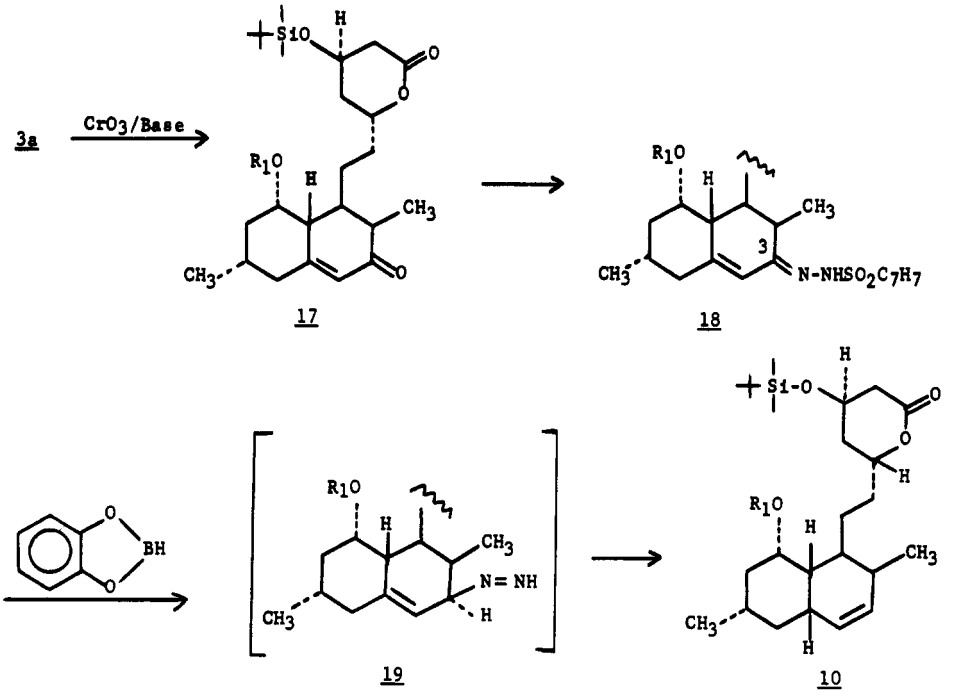
cyclopropyl groups could not be ascertained by spectroscopic means. The individual regioisomeric monocyclopropyl derivatives were prepared by a double bond blocking–deblocking sequence based on the diol and tetrol systems **6** and **7**, respectively. Thus, Simmons–Smith cyclopropanation of **6** afforded **22** which was in turn de-



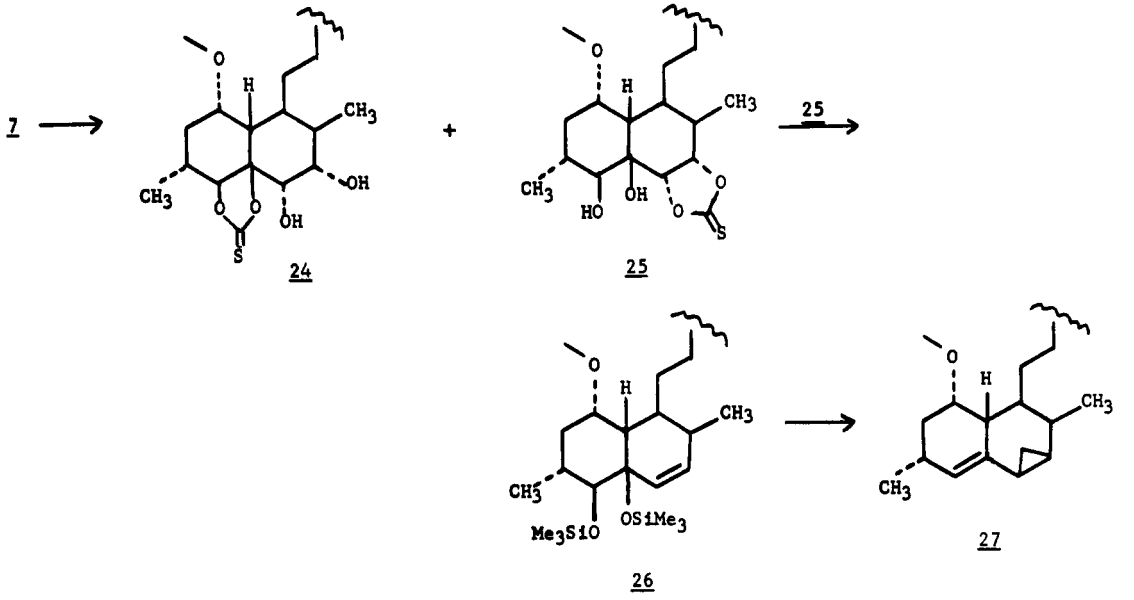
blocked by the technique already described for 8 → **10a** to give **23** as a crystalline compound. Again, the steric orientation could not be readily ascertained spectrocopically. The remaining regioisomeric monocyclopropyl derivative **27** was prepared from the tetrol **7** (Scheme IV). The latter on thionocarbonylation produced two separable monothionocarbonates **24** and **25**, respectively. **25** was trimethylsilylated and deblocked to yield **26** which is regioisomeric with **6** (H = Me_3Si). Application of the same sequence of cyclopropanation and deblocking to **26** as was applied to **22** produced the crystalline monocyclopropyl

(7) Kok, P.; CeClerq, P.; Van deWalle, M. E. *J. Org. Chem.* **1979**, *44*, 4553.
(8) Kabalka, G. W.; Yang, D. T. C.; Baker, J. D., Jr. *J. Org. Chem.* **1976**, *41*, 574.
(9) Yang, D. T. C.; Kabalka, G. W. *Org. Prep. Proc. Int.* **1977**, *9*, 85.
(10) Neumann, W. P.; Sommer, R. *Angew. Chem., Intl. Ed. Engl.* **1964**, 3 (2), 133; *Justus Liebigs Ann. Chem.* **1967**, *701*, 28. We thank Prof. B. M. Trost of the University of Wisconsin for discussions concerning this reaction.
(11) Kuivila, H. G.; Verdone, J. A. *Tetrahedron Lett.* **1964**, 119.
(12) LeGoff, E. *J. Org. Chem.* **1964**, *29*, 2048. Harrison, I. T.; Rawson, R. J.; Turnbull, P.; Fried, J. H. *Ibid.* **1971**, *36*, 3515.
(13) Pincock, R. E.; Wells, J. I. *J. Org. Chem.* **1964**, *29*, 965.

Scheme III



Scheme IV



derivative 27 of unknown stereochemistry.

Experimental Section

Spectra were recorded on the following instruments: IR, Perkin-Elmer 727B; mass spectra, Varian MAT-731; ^{1}H NMR, Varian T-60, Varian XL-200, and Varian SC-300 spectrometers with Me_4Si as an internal standard. Melting points were taken on a microscope hot-stage apparatus and are uncorrected. TLC was carried out on silica gel coated glass plates (Analtech). Column chromatography was effected by the "dry column technique" with proper elution systems predetermined by TLC probes, and fractions were collected automatically.

6(*R*)-[2-[1,2,3,4,6,7,8,8a(*R*)-Octahydro-2(*S*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (2). (A) A mixture of mevinolin (1; 50 mg, 0.124 mmol) and tris(triphenylphosphine)chlororhodium (114.35 mg) in 10 mL of dry toluene was hydrogenated at 1 atm of H_2 and 25 °C for 6 days, with a total uptake of 14.6 mL of hydrogen. The mixture was evaporated in vacuo and the solid residue removed by filtration with acetone and purified by PTLC on silver nitrate impregnated silica plates[14] (10% ethyl acetate–ether) to give 22.3 mg of 2: R_f 0.74; MS, m/z 406 (M^+), 304, 286; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.37 (m, 1 H), 4.62 (m, 1 H), 5.34 (dt, J = 2.5 Hz, 1 H), 5.41 (m, 1 H).

(B) A solution of compound 1 (1.21 g, 3 mmol) in 80 mL of toluene together with 1.21 g of tris(triphenylphosphine)chlororhodium (prereduced in 20 mL of toluene) was hydrogenated at 40 °C at 2.7 atm of H_2 for 24 h. The reaction mixture was concentrated in vacuo, taken up in 50 mL of ether, treated with Norit and evaporated to give 2.3 g of an oil. The product was chromatographed on 250 g of silica gel and eluted with 30% acetone–hexane. Single-spot material (R_f 0.48, 650 mg) was isolated. This

(14) Sliwowski, J. K.; Caspi, E. *J. Steroid Biochem.* 1977, *8*, 47.

product was transparent in the UV and gave an m/z 406 (M^+) mass spectral signal. Anal. Calcd for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 71.17; H, 9.41.

The ^{13}C NMR of this product demonstrated it to be approximately a 9:1 mixture[15] of **2** and compound **3**. Several crystallizations from acetone–hexane gave compound **2** as needles of constant melting point, 113–115 °C. The *tert*-butyldimethylsilyl derivatives of **2** and **3** could be separated quantitatively by HPLC on a Lichroprep Si-60 column by eluting with 2% acetonitrile in methylene chloride; the 3,4-dihydro compound **2** precedes the 3,5-dihydro derivative **3**. Hydrolytic desilylation provided pure **2**, mp 114–115 °C. Anal. Found: C, 71.17; H, 9.42.

6(*R*)-[2-[1,2,3,5,6,7,8,8a(*R*)-Octahydro-2(*S*),6(*R*)-dimethyl-8(*R*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (3). A solution of 80.91 mg (0.2 mmol) of mevinolin (**1**) in 10 mL of absolute ethanol was hydrogenated in the presence of an equal weight of 5% Pd on $CaCO_3$ at 1 atm of H_2 until an uptake of 1 molar equiv of hydrogen was observed. The catalyst was removed by filtration, and the filtrate was evaporated to give 81 mg of product, which after preparative TLC (10% EtOAc/Et_2O) afforded 7 mg of **2** and 72 mg of **3**: MS, m/z 406 (M^+), 304, 286; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.38 (m, 1 H), 4.64 (m, 1 H), 5.28 (dt, J = 3.5 Hz, 1 H), 5.48 (m, 1 H). Anal. Calcd for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 70.85; H, 9.74.

The conversion of **1b** to **3a** via hydrosilylation–protolysis was accomplished by dropwise addition of triethylsilane (0.16 mL, 1 mmol) and CF_3CO_2H (0.25 mL) to a stirred solution of **1b** (259.4 mg, 0.5 mmol) in dry methylene chloride (2.5 mL) at 25 °C under argon. After being stirred at room temperature for 24 h, the yellow mixture was evaporated to an oil. PTLC (2% acetone/$CHCl_3$) provided 97 mg of **3a** [MS, m/z 520 (M^+), 418, 361; ^1H NMR ($CDCl_3$) δ 4.27 (m, 1 H, H_4', 4.63 (m, 1 H, H_6'), 5.27 (m, 1 H, H_8), 5.47 (m, 1 H, H_4)] and 50 mg of the desilylated product **3** [IR ($CHCl_3$) 3450, 1720 cm^{-1}], which on resilylation (cf. preparation of **1b**) gave an additional 55 mg of **3a**.

6(*R*)-[2-[1,2,3,4,4a(*R* and *S*),5,6,7,8,8a(*S*)-Decahydro-2(*S*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (4 and 5). A mixture of 80.91 mg (0.2 mmol) of **1** in 10 mL of ethyl acetate and an equal weight of platinum oxide was hydrogenated at 1 atm. Two moles of hydrogen was consumed in 1 h. The catalyst was removed by filtration through a bed of Celite and the filtrate concentrated to an oily residue. The trans and cis isomers were separated by preparative layer chromatography on silica plates (10% ethyl acetate–ether, bands detected by water spray). The trans isomer **5** (60 mg, with slight contamination of **2**) appears as the more polar spot compared to the cis isomer **4** (19 mg). Further purification by preparative TLC (20% acetone/CH_2Cl_2) provided 50 mg of the trans isomer **5**: mp 126–127 °C; MS, m/z 408 (M^+), 323, 306; ^1H NMR (300 MHz, $CDCl_3$) δ 4.38 (m, 1 H, H_4'), 4.60 (m, 1 H, H_6'), 5.22 (dt, J = 2.5 Hz, C_8 methine). For the cis isomer **4**: mp 64–66 °C; MS, m/z 408 (M^+), 323, 306; ^1H NMR (300 MHz, $CDCl_3$) δ 4.42 (m, 1 H, H_4'), 4.70 (m, 1 H, H_6'), 4.86 (dt, J = 13 Hz, 1 H, C_8 methine). Anal. Calcd for $C_{24}H_{40}O_5$: C, 70.55; H, 9.87. Found for **5**: C, 70.61; H, 9.93. Found for **4**: C, 70.60; H, 10.32.

6(*R*)-[2-[1,2,6,7,8,8a(*R*)-Hexahydro-2(*S*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (1b). A solution of mevinolin (**1**; 1.556 g, 2.86 mmol), *tert*-butyldimethylsilyl chloride (1.292 g, 8.57 mmol), and imidazole (1.216 g, 17.86 mmol) in 10 mL of dry dimethylformamide was heated at 35 °C under nitrogen for 5 h. The mixture was diluted with a large volume of ethyl acetate–benzene (1:1) and washed with water several times. The organic phase was dried over anhydrous Na_2So_4 and evaporated in vacuo to 1.48 g of **1b** as an oil: ^1H NMR ($CDCl_3$) δ 0.1 (s, 6 H), 0.9 (s), 2.58 (d, J = 4 Hz), 4.30 (m, 1 H), 4.60 (m, 1 H), 5.35 (m, 1 H), 5.57 (m, 1 H), 5.7–6.2 (m, 2 H); MS, m/z 518 (M^+), 359, 341, 284.

6(*R*)-[2-[1,2,3,4,6,7,8,8a(*R*)-Octahydro-2(*R*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3(*S*),4-(*R*)-dihydroxy-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (6). A solution of osmium tetraoxide (0.6502 g, 2.56 mmol) in dry pyridine (2 mL) was added dropwise to a stirred solution of the silyl derivative **1b** (1.327 g, 2.56 mmol) in a mixture of benzene (4 mL) and pyridine (2 mL) at 5 °C under nitrogen. A dark brown mixture formed almost instantaneously after the addition was complete. The mixture was stirred at 25 °C for 16 h, followed by addition of a chilled solution of sodium bisulfite (1.171 g) in H_2O (19 mL) and pyridine (13 mL) to give a brown precipitate. After being stirred at room temperature for 1.5 h, the mixture was evaporated in vacuo and extracted with ethyl acetate. The organic phase was washed with water and salt solution, dried over anhydrous Na_2SO_4, and concentrated to 2.03 g of a residue. Chromatographic purification (30% acetone/$CHCl_3$) provided 504.8 mg of the unreacted starting material **1b** and 320 mg of the tetrol **7** [mp 180–181 °C; IR ($CHCl_3$) 3580–3200, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.1 (s, 6 H), 0.9 (s), 2.57 (d, J = 4 Hz), 3.85 (m), 4.1–4.9 (m), 5.2–5.9 (m); MS, m/z 568 ($M^+ - H_2O$), 550 (568 – H_2O), 467 (568 – 101, ester side chain)] and 567 mg of the glycol **6**: IR ($CHCl_3$) 3580–3300, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.1 (6 H), 0.9 (s), 2.57 (d, J = 4 Hz), 3.83 (m, 1 H), 4.1–4.9 (m, 3 H), 5.33 (m, 1 H), 5.90 (m, 1 H); MS, m/z 552 (M^+), 477, 450, 432, 393. The corresponding acetonide of the *cis*-glycol **6** was prepared by treating **6** (300 mg) in dry acetone (8 mL) with anhydrous copper sulfate (300 mg). The mixture was stirred under nitrogen at 25 °C for 72 h. Inorganic material was removed by filtration and the filtrate evaporated to an oil. Preparative layer chromatography with 50% ethyl acetate–hexane provided 177 mg of acetonide **6a**: MS, m/z 592 (M^+), 577; ^1H NMR ($CDCl_3$) acetonide methyls appear at δ 1.45 and 1.55, other pertinent resonances at δ 3.8–5.0 (m, 4 H), 5.24 (m, 1 H), 5.85 (m, 1 H).

6(*R*)-[2-[1,2,3,4,4a,5,6,7,8,8a(*R*)-Decahydro-2(*R*),6-(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3-(*S*),4(*R*)-dihydroxy-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (8). A solution of the glycol **6** (565 mg, 1.02 mmol) in ethyl acetate (15 mL) was hydrogenated at room temperature under 1 atm of H_2 with an equal weight of platinum oxide as catalyst. The uptake of hydrogen ceased after 1 h. The catalyst was removed by filtration, and the solvent was evaporated in vacuo to yield 570 mg of a foam, **8**, having predominantly the *cis*-decalin ring juncture (see discussion): IR ($CHCl_3$) 3650–3300, 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.1 (s, 6 H), 0.9 (s), 2.57 (d, J = 4 Hz), 3.77 (m,

(15) The two isomers can be readily distinguished by ^{13}C NMR in $CDCl_3$ by the chemical shifts of C_5 (compound **2**) and C_4 (compound **3**) together with that of C_8 and by their ratios of comparison of their relative peak heights: compound **2**, C_5 (125.7), C_8 (69.1); compound **3**; C_4 (122.2), C_8(72.1).

2 H), 4.3 (m), 4.4–5.2 (m, 2 H); MS, m/z 554 (M^+), 536, 524, 452, 434.

6(*R*)-[2-[1,2,3,4,4a,5,6,7,8,8a(*R*)-Decahydro-2(*R*),6-(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3-(*S*),4(*R*)-(thioxomethylenedioxy)-1(*S*)-naphthyl]-ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (9). A mixture of the saturated *cis*-glycol 8 (146.8 mg, 0.265 mmol) and 1,1′-thiocarbonyldiimidazole (70.74 mg, 0.397 mmol) in 2 mL of dry toluene was refluxed for 30 min. After removal of the solvent at reduced pressure, the residue was extracted into methylene chloride and washed with water and salt solution. The organic phase was dried over anhydrous Na_2SO_2 and evaporated to dryness. Preparative layer chromatography (5% acetone–Chf) provided the cyclic thionocarbonate 9: 118 mg (75.4%); R_f 0.42; MS, m/z 596 (M^+), 537; ^1H NMR ($CDCl_3$) δ 0.1 (s, 6 H), 0.9 (s), 2.57 (d, J = 4 Hz). 4.15–5.3 (m, 5 H).

6(*R*)-[2-[1,2,4a(*S* and *R*),5,6,7,8,8a(*S*)-Octahydro-2-(*S*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (10 and 11). A mixture of the cyclic thionocarbonate 9 (101 mg, 0.169 mmol) and triethyl phosphite (2.5 mL) was heated at reflux under nitrogen for 140 h. The solvent was removed in vacuo, and preparative layer chromatography of the residue (2% acetone—Chf) provided 56 mg of an olefin (63%). The infrared spectrum showed the absence of hydroxyl functionality, and the ester carbonyl group appeared as a strong band at 1720 cm^{-1}: MS, m/z 521 (M^+), 464, 418; ^1H NMR ($CDCl_3$) δ 0.1 (s, 6 H), 0.9 (s), 2.6 (d, J = 4 Hz), 4.2–5.3 (m, 3 H), 5.58 (m, J = 9.8 Hz, 2 H).

6(*R*)-[2-[1,2,4a(*S* and *R*),5,6,7,8,8a(*S*)-Octahydro-2-(*S*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (10a and 11a). The monoolefin silyl ether obtained above (50 mg, 0.096 mmol) was stirred at room temperature in a 1.5-mL solution of acetic acid/water/tetrahydrofuran (3:1:1) plus one drop of 2.5 N aqueous hydrochloric acid. The progress of the hydrolysis was monitored by TLC. After 9 h the reaction mixture no longer contained starting material and was evaporated in vacuo to dryness. Preparative layer chromatography (10% acetone–Chf) produced 28.5 and 4.0 mg of the cis and the trans alcohols **10a** and **11a**, respectively. For **10a**: MS, m/z 406 (M^+), 304, 286; ^1H NMR ($CDCl_3$) δ 0.7–2.5 (m, 33 H), 2.7 (d, J = 5 Hz, 2 H), 4.2–5.12 (m, 3 H), 5.58 (m, J = 9.8 Hz, 2 H). Its 300-MHz ^1H NMR displayed vicinal coupling constants of 4.6 and 4.8 Hz between the vinyl protons and protons at the 2- and 4a-positions. Each olefinic hydrogen appeared as a double of doublets in benzene solution. **11a** exhibited m/z 304 and 286, with the 300-MHz ^1H NMR (C_6D_6) showing coupling constants of near 0 and 5 Hz, respectively, between the vinyl protons and protons at the 2- and 4a-positions as a double of doublets.

6(*R*)-[2-[1,2,3,4,4a(*S*),5,6,7,8,8a(*R*)-Decahydro-2-(*S*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-4(*R*)-hydroxy-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (14). A solution of **3a** (657.4 mg, 1.26 mmol) in methylene chloride (5 mL) was cooled to 4 °C. Sodium bicarbonate (powder, 212.1 mg, 2.53 mmol) was added, followed by addition of a solution of *m*-chloroperbenzoic acid (250.5 mg, 1.26 mmol) over 10 min at 4 °C. Heavy precipitation occurred within 30 min. After 5 h at 4 °C, a solution of 10% aqueous sodium sulfite was added until a starch–iodide test was negative. The organic phase was then washed suuccessively with 5% $KHCO_3$, H_2O, and salt solution. After the organic phase was dried (Na_2SO_4) and the solvent evaporated, the mixture (635 mg) was chromatographed on a SiO_2 column (30% EtOAc–hexane) to give the β-oxide **12** [162 mg; MS, m/z 536 (M^+), 451, 434; ^1H NMR (300 MHz, $CDCl_3$) δ 3.04 (br s, $J \simeq$ 2 Hz, 1 H, methine of the epoxide)] and the α-oxide: 362 mg; MS, m/z 536 (M^+) 451, 434; ^1H NMR (300 MHz, $CDCl_3$) δ 3.0 (d, J = 5 Hz, methine of the epoxide ring).

Boron trifluoride ethereate (0.1 mL) was added to a stirred solution of the β-oxide **12** (124 mg) in 2 mL of benzene–ether (1:1) at 2 °C under N_2. After 2 h a large volume of ether was added followed by cold 5% aqueous $KHCO_3$ and dilution with an equal volume of EtOAc. The organic phase was further washed with additional 5% $KHCO_3$ solution, H_2O, and salt solution. After the mixture was dried and the solvent evaporated, there was afforded 109.5 mg of the trans ketone **13**: MS, m/z 536 (M^+), 479, 434; ^1H NMR ($CDCl_3$) δ 4.1–4.9 (m, 2 H, 2 methines in the lactone ring), 5.30 (m, 1 H, C_8 methine).

Reduction of the ketone was carried out by dropwise addition of a solution of lithium tri-*tert*-butoxyaluminum hydride (194.23 mg, 0.76 mmol) in 2.5 mL of dry THF to a stirred solution of the trans ketone **13** (205 mg, 0.38 mmol) in 1.5 mL of THF at 0 °C under N_2. After 5 h at 0 °C, a saturated aqueous solution of NaH_2PO_4 was added and the reaction mixture concentrated in vacuo to remove the THF. After the usual extractive (EtOAc) workup, PTLC purification (5% acetone–Chf) provided the alcohol **14** (119 mg). The infrared spectrum shows the presence of a hydroxyl group and an ester carbonyl band at 1720 cm^{-1}: MS, m/z 538 (M^+), 505, 481, 463, 418; ^1H NMR (200 MHz, $CDCl_3$) δ 2.56 (d, J = 4 Hz, C_3' methylene), 3.86 (br s, 1 H, H_4), 4.30 (m, 1 H, H_4'), 4.60 (m, 1 H, H_6'), 5.26 (m, 1 H, H_8).

6(*R*)-[2-[1,2,3,4,6,7,8,8a(*R*)-Octahydro-2(*R*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3(*R*)-acetoxy-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (15). The diol **6** (136.8 mg) was hydrogenated in dry dimethylformamide with an equal weight amount of 10% pd/C as the catalyst. After 1 molar equiv of hydrogen was consumed, the catalyst was removed by filtration and the product isolated via extractive workup with EtOAc (yield 180.2 mg). Preparative layer chromatography (10% acetone–CH_2Cl_2) gave 86 mg of a mixture of alcohols of **15** (major) and **16**: MS, m/z 536 (M^+), 434, 359; NMR exhibited two kinds of vinylic protons. For ease of separation, the mixture was acetylated with acetic anhydride (0.2 mL) in dry pyridine (0.5 mL) at 25 °C for 16 h. After the usual isolation procedure and thin-layer chromatographic separation, the bond isomerized isomer **16** was isolated (33.7 mg) together with the homoallylic acetate **15**: 54.4 mg; ^1H NMR (200 MHz, $CDCl_3$) δ 4.30 (m, 1 H, H_4'), 4.58 (m, 1 H, H_6'), 4.83 (1 H, m, J = 3.42 Hz, H_3), 5.40 (m, 2 H, H_8 + vinylic proton).

6(*R*)-[2-[1,2,3,5,6,7,8,8a(*R*)-Octahydro-2(*R*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3-[[(4-methylphenyl)sulfonyl]hydrazono]-1(*S*)-naphthyl]-ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (18). To a stirred suspension of chromic anhydride (5.24 g, 52.40 mmol) in dry dichloromethane at −20 °C under N_2 atmosphere was added 3,5-dimethylpyrazole (5.037 g, 52.40 mmol). After the mixture was stirred at −20 °C for 20 min, a solution of 1.819 g (3.49 mmol) of the alkene **3a** in 7 mL of dichloromethane was added and the mixture stirred at −10 °C for 4 h. Evaporation of the reaction mixture produced a reddish

brown residue which was extracted with benzene. The latter was washed with 5% $KHCO_3$, H_2O, saturated aqueous NaH_2PO_4, and salt solution. The organic phase was dried over magnesium sulfate and concentrated in vacuo to give 1.9 g of a gummy solid. The latter was chromatographed on 100 g of silica gel and eluted with 50% ethylacetate–hexane to provide 725 mg of the α,β-unsaturated ketone **17**: IR ($CHCl_3$) 1720, 1660 cm^{-1}; UV (MeOH) λ_{max} 239 μm (ϵ 8290); ^1H NMR ($CDCl_3$) δ 4.27 (perturbed t, 1 H), 4.57 (m, 1 H), 5.40 (m, 1 H), 5.87 (br s, 1 H); MS, m/z 534 (M^+), 477.

The tosylhydrazone derivative **18** was obtained by treatment of **17** (285.2 mg, 0.53 mmol) with tosylhydrazine (145.3 mg, 1.07 mmol) in glacial acetic acid (1.5 mL) at room temperature under nitrogen. The mixture was evaporated to a foam after 4 h and the product isolated by methylene chloride extraction and purification by PTLC on silica gel (50% ethyl acetate–hexane), to yield 175 mg of tosylhydrazone **18**: IR ($CHCl_3$) 3200, 1720, 1635, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08 (s), 2.7–3.2 (m), 4.1–4.9 (m, 2 H), 5.3, 5.9, 6.13 (each br s, one proton for each signal), 7.1–8.0 (m, 3 H).

6(*R*)-[2-[1,2,4a(*S*),5,6,7,8,8a(*S*)-Octahydro-2(*S*),6-(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(*tert*-butyldimethylsilyl)oxy]-2*H*-pyran-2-one (10). To a stirred solution of tosylhydrazone **18** (315 mg, 0.451 mmol) in 1.2 mL of dry chloroform at 0 °C under nitrogen was added catecholborane (0.056 mL, 0.496 mmol) dropwise, and the reduction was allowed to proceed at 0 °C for 2 h. Sodium acetate trihydrate (184 mg, 1.352 mmol) was added, and the mixture was brought to a gentle reflux for 1 h. At the end of this period, the solid material was filtered from the chloroform, and the filtrate was evaporated to a foam. Preparative thin-layer chromatography (2% acetone–Chf) produced 159.2 mg of the isomerized olefin **10** [NMR in $CDCl_3$ was identical with that of the cis compound obtained from the transformation **9** → **10** and had pertinent resonances at δ 2.6 (d, J = 4 Hz), 4.2–5.3 (m, 3 H), and 5.58 (m, J = 9.8 Hz, 2 H); MS, m/z 521 (M^+), 464] and 30.6 mg of the unisomerized olefin **3** by NMR and mass spectral comparison.

6(*R*)-[2-[1,2,6,7,8,8a(*R*)-Hexahydro-2(*S*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy)-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[[phenyldimethylsilyl)oxy]-2*H*-pyran-2-one (1a). A mixture of mevinolin (**1**; 1.011 g, 2.5 mmol), phenyldimethylchlorosilane (1.241 mL, 7.5 mmol), and imidazole (1.064 g, 15.63 mmol) in 10 mL of dry dimethylformamide was kept at 35 °C under nitrogen for 5 h. After cooling, the mixture was diluted with a large volume of ethyl acetate–benzene (1:1) and washed successively with water and salt solution. The organic extract was dried over anhydrous sodium sulfate and evaporated to 2.32 g of an oil which was chromatographed on 23 g of silica gel (2% acetone–Chf) to provide 1.151 g of **1a**: IR ($CHCl_3$) no OH absorption, ester carbonyl absorption at 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.18 (distorted t, 1 H), 4.53 (m, 1 H), 5.2–6.2 (m, 4 H); MS, m/z 538 (M^+), 469, 452, 436.

6(*R*)-[2-[1,2,3,5,6,7,8,8a(*R*)-Octahydro-2(*R*),6(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3(*R*)-(tributylstannyl)-1(*R*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-[(phenyldimethylsilyl)oxy]-2*H*-pyran-2-one (20). A mixture of diene **1a** (223.5 mg, 0.415 mmol) tri-*n*-butytin hydride (0.6 mL), and 2,2′-azobis(2-methylpropionitrile) (6 mg) in 0.5 mL of cyclohexane was refluxed for 47 h. Heating was arbitrarily terminated at the end of this period, and products were isolated by preparative thin-layer chromatography, (20% ethyl acetate–hexane) to provide 51 mg of **20** [IR ($CHCl_3$) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.23 (distorted t, 1 H), 4.55 (m, 1 H), 5.23 (m, 1 H), 5.47 (m, 1 H), 7.43 (m, 5 H); MS, m/z 830 (M^+ as group isotopes)] together with 67 mg of the starting diene **1a** and 4 mg of the desilylated hydrolysis product, possessing no aryl proton resonance in NMR. The mass spectrum showed m/z 696 (M^+ as group isotopes).

6(*R*)-[2-[1,2,4a(*S*),5,6,7,8,8a(*S*)-Octahydro-2(*S*),6-(*S*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (10a). A mixture of the tributylstannate **20** (155 mg, 0.187 mmol) and 0.68 mL of 0.278 M methanolic hydrogen chloride was stirred under nitrogen at 25 °C for 1 h. Evaporation to dryness followed by flushing twice with benzene provided an oil residue which was purified by preparative TLC (40% EtOAc–hexane) to provide 29.5 mg of the hydroxymethyl ester of **10a**: IR ($CHCl_3$) 3355, 1710, 1459, 1439 cm^{-1}; NMR ($CDCl_3$) pertinent vinylic protons appear as multiplet centered at δ 5.57 with J_{AB} = 9.8 Hz, and 29 mg of the hydroxylacetone **10a**; IR ($CHCl_3$) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.7 (d, J = 5 Hz), 4.2–5.2 (m, 3 H), 5.58 (m, J_{AB} = 9.8 Hz, 2 H); MS, m/z 406 (M^+), 304, 286. The open hydroxy ester of **10a** was converted quantitatively to the hydroxy lactone **10a** by refluxing it in toluene with slow distillation of the solvent until TLC showed total conversion.

6(*R*)-[2-[1,2,3,4,4a,5,6,7,8,8a(*R*)-Decahydro-2(*R*),6-(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3,4:4a,5-dicyclopropano-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4(*R*)-hydroxy-2*H*-pyran-2-one (21). Zinc–copper couple was prepared by adding zinc dust (0.7 g) to a hot (oil bath temperature ~95 °C) rapidly stirred solution of $Cu(OAc)_2 \cdot H_2O$ (40 mg) in glacial HOAc (1 mL). After 1 min, all of the copper had deposited on the zinc. The couple was allowed to settle for 1 min; supernatant HOAc was removed by syringe. The dark reddish gray couple was then washed with HOAc followed by ether until no longer acidic to litmus paper. To this couple (ca. 749 mg), suspended and stirred in ether (3 mL) was added diiodomethane (0.59 mL) followed by heating under reflux in a nitrogen atmosphere for 1 h to yield a reddish reaction mixture. The mixture was cooled to room temperature, and the diene **1b** (158 mg, 0.305 mmol) in ether (1.68 mL) was added. The reaction mixture was stirred at ambient temperature for 24 h, diluted with benzene, and finally filtered through a bed of Celite. The filtrate was washed successively with aqueous NH_4Cl and $NaHSO_3$ solutions, followed by water and salt solution, dried over Na_2SO_4, and evaporated to an oil. The latter afforded, after PTLC purification (20% EtOAc–hexane), 23 mg of product [^1H NMR (300 MHz, $CDCl_3$) δ 0.2–0.6 (m), 4.28 (m, 1 H), 4.60 (m, 1 H), 4.90 (m, 1 H); MS, m/z 547 (M^+) 489, 444; IR ($CHCl_3$) 1720 cm^{-1}] which on hydrolysis of the TBDMS ether with a mixture of glacial HOAc–H_2O–THF (3:1:1) plus 2 drops of 2.5 N HCl at room temperature for 2 h gave 17 mg of **21**: IR ($CHCl_3$) 3600–3250 (OH), 1720 cm^{-1} (ester carbonyl); MS, m/z 330 (M − 102, ester side chain); ^1H NMR (200 MHz, $CDCl_3$) δ 0.2–0.8 (m, cyclopropylmethylene), 4.4 (m, 1 H), 4.62 (m, 1 H), 4.97 (m, 1 H); mass spectrum, calcd for $C_{26}H_{40}O_5$ m/z 432.2873, found 432.2860 (M^+).

6(*R*)-[2-[1,2,4a,5,6,7,8,8a(*R*)-Octahydro-2(*S*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-4a,5-cyclopropano-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4-(*R*)-hydroxy-2*H*-pyran-2-one (23). Method A. Cuprous chloride (275 mg) was added to a stirred solution of the diene **1b** (1.29 g, 2.49 mmol) in dry ether (25 mL), and

a stream of N_2 carrying excess diazomethane was passed through at 0 °C for 2 h. The reaction mixture changed color from light green to reddish brown. NMR analysis of an aliquot indicate ca. 23% conversion. The reaction mixture was then allowed to stir at room temperature and diazomethane slowly passed into the reaction mixture for an additional 8 h. The reaction was worked up by filtering off the inorganic salt and concentrating it to an oil. The NMR spectrum indicated ca. 30% conversion.

A portion (313 mg) of the above mixture was hydrolyzed in the usual manner (glacial HOAc–H_2O–THF (3:1:1) + 3 drops of 2.5 N HCl at 25 °C for 16 h) to give, after PTLC (Ag^+-impregnated plates, 10% EtOAc/Et_2O), the monocyclopropyl compound **23**: 36.2 mg; IR ($CHCl_3$) 3650–3300 (OH, 1720 cm^{-1} (carbonyl); MS, m/z 316 (M^+ – 102, the ester side chain); ^1H NMR (200 MHz, $CDCl_3$) δ 0.44, 0.76 (cyclopropylmethylene), 4.4 (m, 1 H, H_4'), 4.63 (m, 1 H, H_6'), 4.95 (d, J = 9.5 Hz, 1 H, H_4), 5.09 (m, 1 H, H_8), 5.69 (dd, J = 9.5, 6 Hz, 1 H, H_3).

Method B. Cyclopropanation with Zn–Cu couple (2.2 g) and diiodomethane (1.82 mL) on the *cis*-glycol **6** (762 mg) under the same reaction conditions as described for the formation of **21** gave two isomers, major (175 mg) and minor (32 mg), in addition of 250 mg of starting material. For the major isomer **22**: IR ($CHCl_3$) 3540 (OH), 1721 (C=O) cm^{-1}; MS, m/z 509 (M^+ – 57, *t*-Bu), 491 (509 – 18, H_2O), 447 (M^+ – 18 – 101, H_2O + ester side chain); NMR ($CDCl_3$) resonane due to cyclopropyl moiety present.

Thionocarbonylation of the above-obtained diol (141.3 mg) with 1,1′-thiocarbonyldiimidazole (74.64 mg) in dry toluene (2 mL) at reflux for 1 h afforded, after PTLC (5% acetone–Chf), 96 mg of the thionocarbonate derivative: IR ($CHCl_3$) 1721, 1099, 980, 926, 870 cm^{-1}; MS, m/z 609 (M^+), 552 (M^+ – 57, *t*-Bu); ^1H NMR ($CDCl_3$) multiple resonance δ 0.2–0.6.

Thermal elimination of the above thionocarbonate was effected with triethyl phosphite (2.5 mL) by heating at 114 °C for 5 days to afford the recovered starting material (8 mg) and the cyclopropanated monoolefin TBDMS ether of **23**: 43 mg; IR ($CHCl_3$) 1720 cm^{-1}; MS, m/z 476 (M – 57), 374 (476 – 102 ester side chain); ^1H NMR ($CDCl_3$) 2 vinylic protons appear at δ 4.90 (d, J = 10 Hz), 5.63 (1 H, dd, J = 10, 5 Hz).

Hydrolysis of the above compound with glacial HOAc–H_2O–THF (3:1:1) plus 2 drops of 2.5 N HCl (1.6 mL) a room temperature for 3.5 h gave the alcohol **23**: 23 mg; mp 75–78 °C; MS, m/z 418 (M^+), 317 (M – 101, ester side chain); NMR spectrum identical with that of the product obtained by the diazomethane–cuprous chloride route; mass spectrum, calcd for $C_{25}H_{38}O_5$ m/z 418.2717, found 418.2699 (M^+).

6(*R*)-[2-[1,2,3,4,6,7,8,8a(*R*)-Octahydro-2(*R*),6(*R*)-dimethyl-8(*S*)-[[2(*S*)-methylbutyryl]oxy]-3,4-cyclopropano-1(*S*)-naphthyl]ethyl]-3,4,5,6-tetrahydro-4-(*R*)-hydroxy-2*H*-pyran-2-one (27). The TBDMS-protected tetraol **7** (1.5 g, 2.56 mmol) was thionocarbonylated by heating at 130 °C with 1,1′-thiocarbonyldiimidazole (552.2 mg, 3.09 mmol) in 14 mL of dry toluene for 2 h. After the usual extractive (CH_2Cl_2) workup and chromatographic purification (50% EtOAc–hexane) provided a ca. 1:1 ratio of **24**/**25** (924 mg/916 mg) in addition to a small amount of the bis-thionocarbonated material. ^1H NMR of **24** (200 MHz, $CDCl_3$) δ 3.8–3.9 (m, 2 H, C_3 and C_4 methines), 4.32 (m, 1 H, H_4'), 4.68 (m, H_6'), 4.79 (d, J = 10 Hz, H_5), 5.22 (m, 1 H, H_8). ^1H NMR of **26** (200 MHz, $CDCl_3$) δ 4.30 (m, 1 H, H_4'), 4.60 (m, 1 H, H_6'), 5.02 (2 H, C_3 and C_4 methines), 5.24 (m, 1 H, H_8).

The diol **24** (268.4 mg, 0.427 mmol) was heated with Tri-Sil "TBT" (0.6 mL, Pierce Co.) under N_2 at 95 °C for 8 h. The silylated product was isolated by evaporation and extraction of the residue with EtOAc followed by washing the organic extract with water and brine and then by drying (Na_2SO_4) and concentration to give 340 mg of a thick oil. Thermal elimination of the latter in 4 mL of triethyl phosphite of 150 °C for 8 h, followed by chromatographic isolation provided **26**: 255 mg; IR no hydroxy absorption, carbonyl band at 1725 cm^{-1}; MS, m/z 696 (M^+), 639 (M – 57), 594 (M – 102); ^1H NMR ($CDCl_3$) δ 3.4 (d, 1 H), 4.0–5.0 (m, 2 H), 5.2–5.8 (m, 3 H). Hydrolysis of **26** (glacial HOAc/H_2O/THF, 3:1:1; 9 mL) at 25 °C for 7 h provided the free glycol with the TBDMS protecting group remaining intact. By use of general conditions for cyclopropanation (see above; Zn–Cu couple, CH_2I_2 in ether) followed by thionocarbonylation, thermal elimination [$(EtO)_3P$, 165 °C, 1 h], and hydrolysis (glacial HOAc/H_2O/THF, 3:1:1 with no added 2.5 N HCl at 25 °C for 5 days), the monocyclopropyl hydroxylactone **27** was obtained: 22 mg; 138–140 °C; IR ($CHCl_3$), 3600–3200 (OH), 1720 cm^{-1} (C=O). MS, m/z 418 (M^+), 316 (M – 102, ester side chain); ^1H NMR (200 MHz, $CDCl_3$) δ 0.22 and 0.61 (2 m, each integrates for 1 H), 4.40 (m, 1 H, H_4'), 4.60 (m, 1 H, H_6'), 5.22 (m, 1 H, H_8), 5.64 (m, 1 H, vinylic proton). Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.52; H, 9.66.

Acknowledgment. We are indebted to Dr. B. H. Arison and R. A. Reamer of these laboratories for determining 300-MHz ^1H NMR and ^{13}C NMR, respectively.

Registry No. **1**, 75330-75-5; **1a**, 85613-98-5; **1b**, 79691-11-5; **2**, 79902-20-8; **3**, 79691-09-1; **3a**, 85613-99-6; **4**, 85648-15-3; **5**, 79691-10-4; **6**, 85614-00-2; **6a**, 85614-01-3; **7**, 85614-02-4; **8** (isomer 1), 85614-03-5; **8** (isomer 2), 85648-16-4; **9**, 85614-04-6; **10**, 85614-05-7; **10a**, 85699-75-8; **10a** hydroxy methyl ester, 85614-06-8; **11**, 85648-17-5; **11a**, 85648-18-6; **12** α-oxide, 85614-07-9; **12** β-oxide, 85648-19-7; **13**, 85614-08-0; **14**, 85614-09-1; **15**, 85614-10-4; **16**, 85614-11-5; **17**, 85614-12-6; **18**, 85614-13-7; **20**, 85629-01-2; **21**, 85614-14-8; **22**, 85614-15-9; **22** thionocarbonate, 85614-16-0; **23**, 85614-17-1; **23** TBDMS ether, 85614-18-2; **24**, 85614-19-3; **25**, 85614-20-6; **26**, 85614-21-7; **26** free glycol, 85614-22-8; **27**, 85614-23-9; 1,1′-thiocarbonyldiimidazole, 6160-65-2; diiodomethane, 75-11-6.