raphy gave an oligoribonucleotide building block.

Deprotection of the Fully Protected AUAp (18). Compound **18** (61 mg, 19.4 μmol) was dissolved in pyridine–water (2:1, v/v, 2.9 mL), and silver acetate (485 mg, 2.9 mmol) was added. After the mixture was stirred at 50 °C for 5 h, it was cooled and diluted with pyridine–water (2:1, v/v, 30 mL). The solution was treated with hydrogen sulfide gas at 0 °C until a clear supernatant had been obtained. The precipitate was removed by centrifugation, and the supernatant was passed through a column of Dowex 50 W × 2 (pyridinium form, 3 mL). The eluant was evaporated and coevaporated several times with pyridine to remove acetic acid. The residue was dissolved in pyridine (10 mL), and concentrated ammonia (50 mL) was added. After the solution was kept at room temperature for 18 h, it was evaporated under reduced pressure. The residue was coevaporated several times with water, and then dioxane (30 mL) was added. To the solution was added 0.02 M HCl (30 mL), and it was adjusted exactly to pH 2.0 by addition of 0.1 M HCl. After the mixture was stirred for 20 h, it was neutralized by addition of pyridine and extracted with CH_2Cl_2–H_2O. The aqueous layer was evaporated, and the residue was chromatographed on Whatman 3 MM papers with solvent to give AUAp (312 OD, 48%): UV λ_{max} 259. λ_{min} 229 nm; retention time, 11.9 min (method A).

Similarly, UUAp (168 OD, 32%) and pAUG (307 OD, 41%) nm, were obtained from **17** (17 μmol) and the fully protected pAUG (23 μmol), respectively. UUAp: λ_{max} 260 nm, λ_{min} 230 nm; retention time, 11.0 min (method A). pAUG: R_f 0.11 (solvent II, to pT); λ_{max} 257 nm, λ_{min} 228 nm; retention time, 5.6 min (method A).

Deprotection of the Fully Protected Tetramer 14. The fully protected tetramer **25** (18 mg, 5 μmol) was dissolved in a 1 M hydrazine solution in pyridine–acetic acid (3:1, v/v, 0.3 mL). After the mixture was stirred at room temperature for 20 min, the same workup as described in the synthesis of **7** was done. The mixture obtained after extraction was dissolved in pyridine–water (3:1, v/v, 0.6 mL), and silver acetate (125 mg, 0.75 mmol) was added. A workup similar to that described in the above experiment and the successive treatments with concentrated ammonia and 0.01 M HCl gave crude CAUG (100 OD, 47%). This crude tetramer was further purified by paper chromatography using concentrated ammonia–*n*-PrOH–H_2O (55:10:35, v/v/v) as the solvent for development. A single band at R_f 0.14 (to pU) was eluted (70 OD, 33%) similarly and analyzed by HPLC, which showed one peak: retention time, 11 min (method B).

Enzyme Assay. Each sample (10 OD) was incubated under the following conditions: spleen phosphodiesterase (10 μg, Boehringer), 0.01 M pyrophosphate buffer (pH 6.5, 100 μL), 0.05 M ammonium acetate (pH 6.5, 200 μL), 37 °C, 10 h; nuclease P_1 (10 μg, Yamasa), 0.02 M sodium acetate (pH 5.5, 100 μL), 37 °C, 4 h.

The degradation products were analyzed by paper electrophoresis or HPLC.

Acknowledgment. We heartily thank C. Sugimura for typewriting this manuscript. This work was supported by the Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture.

Supplementary Material Available: Table III showing ^1H NMR spectral data and elemental analyses of compounds **3–9** and Figure 1 showing the HLPC profile of AUAp (5 pages). Ordering information is given on any current masthead page.

Total Synthesis of (+)-Dihydromevinolin

Scott J. Hecker and Clayton H. Heathcock*

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received September 17, 1985*

Abstract: A total synthesis of (+)-dihydromevinolin (**2b**) is presented, as well as the preparation of three analogues (**62**, **63**, and **64**) for assessment of their biological activity. Base-promoted fragmentation of the tosylhydrazone (**20**) of key intermediate **6** affords acetylenic alcohol **23**. Partial hydrogenation and acetylation, followed by stereoselective epoxidation, provide oxirane **37**. Lewis acid mediated rearrangement followed by ozonolysis and epimerization furnishes keto aldehyde **49**, which contains the requisite stereochemistry at all six stereocenters of the octalin moiety. Selective reduction of the aldehyde affords keto alcohol **50**, which is elaborated to racemic diol **52** by the Shapiro olefin synthesis. Selective DCC-promoted esterification with (*R*)-(+)-*O*-methylmandelic acid provides diastereomers **53** and **54**, of which the desired isomer **54** is separated by fractional crystallization. Acylation and selective ester cleavage followed by Swern oxidation furnishes target intermediate **3b**. Coupling of **3b** with lactone synthon **4** affords enone **5b**, which is converted to ketone **58** by conjugate reduction. Acid-promoted lactonization of the major diol from hydride reduction of **58** furnishes **2b**, in 19 steps from pyranone **6**.

The mevinic acids compactin (**1a**),[1] mevinolin (**2a**),[2] dihydrocompactin (**1b**),[3] and dihydromevinolin (**2b**)[4] have attracted considerable synthetic attention[5-7] because of their significance as potent inhibitors of HMG CoA reductase, the enzyme that

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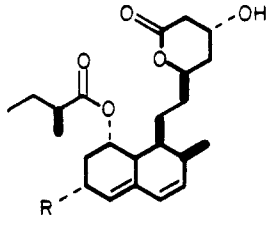
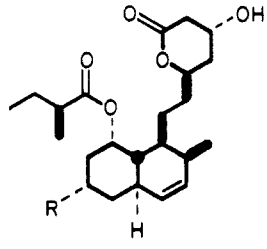
controls the rate-limiting step of cholesterol biosynthesis in many organisms. Efforts in this research group have led recently to a total synthesis of (+)-compactin (**1a**);[5j] we now report the successful application of methodology developed therein, as well as a new synthesis of the octalin moiety, in a total synthesis of (+)-dihydromevinolin (**2b**).

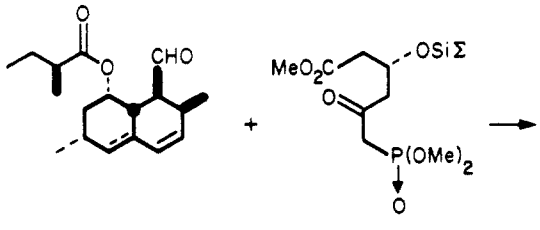


1a: R = H
2a: R = Me



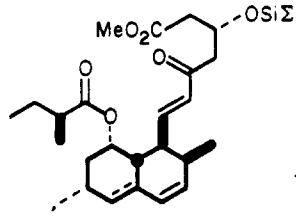
1b: R = H
2b: R = Me

The key coupling reaction that we used in the synthesis of **1a** involved condensation of keto phosphonate **4** with an appropriately substituted aldehyde, in which the key functionality of the natural product was already in place. We envisioned preparation of **2a** or **2b** by analogous condensation of **4** with **3a** or **3b** (eq 1). We



3a: 4a,5-dehydro
3b: 4a,5-dihydro

4

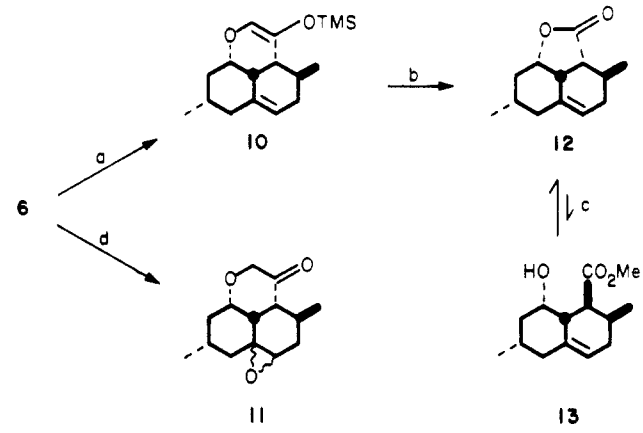


2a or **2b** (1)

5a: 4a,5-dehydro
5b: 4a,5-dihydro

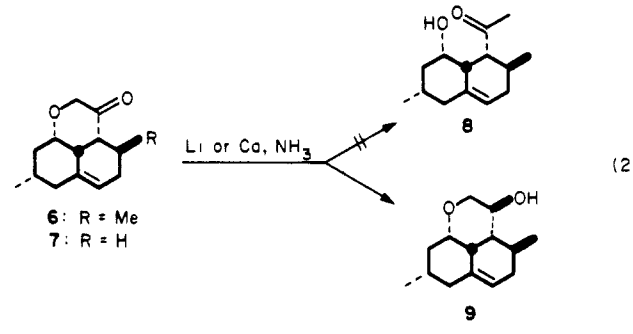
have already reported the highly stereoselective synthesis of pyranone **6** in seven steps from dihydroorcinol ethyl enol ether.[8] This paper details the conversion of **6** to aldehyde **3b**, further transformation to (+)-**2b**, and preparation of three analogues of dihydromevinolin for assessment of their biological activity.

Scheme I



(a) LDA, THF; TMSCl. (b) *t*-BuOOH, $MeO_2(acac)_2$, PhH; TFA, H_2O, THF. (c) NaOMe, MeOH. (d) mCPBA, CH_2Cl_2.

The most immediate need in achieving the desired transformation of **6** was an effective method for scission of the pyranone ring. Our first approach was reductive cleavage by dissolving metals. Although reductive cleavage of α-hydroxy and α-acetoxy ketones is known to be most successful when the leaving group occupies an axial position on a cyclohexanone ring (since this allows continuous overlap of the departing alkoxide with the developing allyloxy radical π-orbital), some success has been obtained with equatorial leaving groups.[9] The X-ray crystal structure of compound **7**[8] indicates that the O–C–C(O)–C dihedral angle in the system is 43.9° (optimal for cleavage = 90°); the chances for cleavage seemed good enough to warrant the attempt. In the event, reaction of **6** with lithium or calcium in liquid ammonia results in reduction to equatorial alcohol **9**; none of the desired cleavage product **8** is observed (eq 2). Clearly, protonation of the intermediate ketyl by solvent is much faster than the desired fragmentation process.



6: R = Me
7: R = H

(2)

We then turned our attention to oxidative cleavage of the enolsilane (**10**) of pyranone **6**, prepared regiospecifically by the action of LDA and chlorotrimethylsilane. Ozonolysis of **10** gave a complex mixture of products, undoubtedly due to overoxidation; although the enol silane is probably more nucleophilic than the trisubstituted olefin, oxidation of the latter is expected to be very rapid at −78 °C. In an attempt to avoid this problem by first functionalizing the olefin, compound **6** was epoxidized with *m*-CPBA (Scheme I). Stereoselectivity in this reaction is poor, affording a 60:40 mixture of epoxides **11**. Attempts at improving selectivity by the use of other epoxidation methods (Payne's reagent,[10] Bach's modification thereof[11]) were unsuccessful. Since

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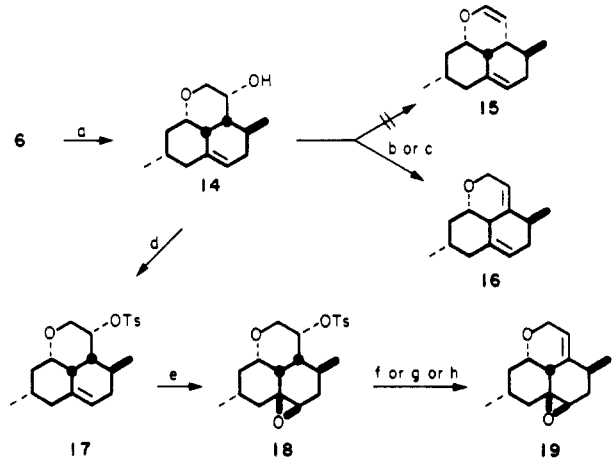
Scheme II



(a) L-Selectride, THF. (b) $SOCl_2$, pyridine. (c) $Et_3\overset{+}{N}SO_2\overset{-}{N}CO_2Me$. (d) p-TsCl, pyridine. (e) mCPBA, CH_2Cl_2. (f) DBU, CH_2Cl_2. (g) t-BuOK, t-BuOH. (h) DMSO, Δ.

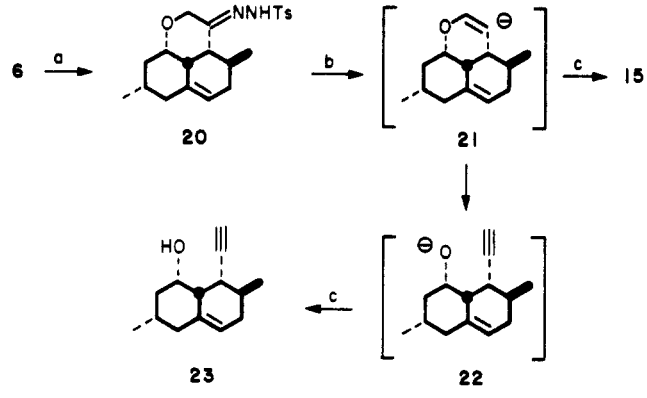
we were reluctant to work with a mixture of epoxides, other avenues were explored.

The Kaneda protocol[12] for oxidative cleavage of enol silanes in the presence of olefins was indeed somewhat successful at effecting the desired transformation (Scheme I). Treatment of **10** with *tert*-butyl hydroperoxide and catalytic $MoO_2(acac)_2$ at 60 °C for 1 h, followed by acidic workup, gave lactone **12** in 40% yield, along with a complex mixture of byproducts. Although the yield of **12** was poor, further studies were conducted to test its utility as an intermediate. In particular, it was hoped that conversion to hydroxy ester **13** by methanolysis and concomitant epimerization would be facile. However, **12** is unchanged by sodium methoxide in refluxing methanol. Complete H–D exchange of the proton α to the carbonyl could be effected within 3 h at room temperature with CD_3ONa/CD_3OD, and the lactone could easily be opened to the corresponding hydroxy carboxylate with NaOH; these results indicate that the equilibrium between **12** and **13** is heavily in favor of **12**.

Epoxidation of the olefin followed by ozonolytic cleavage of the pyranone ring still appeared to be a viable course, provided a more selective epoxidation protocol could be found. To this end, the reduction of ketone **6** to axial alcohol **14** was explored. Treatment of **6** with sodium borohydride in ethanol affords alcohols **9** and **14** in a ratio of 1:1. Selectivity is much better in L-Selectride:[13] isomer **14** is formed exclusively (Scheme II). Although *m*-CPBA epoxidation of **14** showed poor selectivity (3:2 ratio of epoxides), the direct elimination of alcohol **14** was explored; successful elimination toward the ether oxygen to give **15** would warrant further work to find an appropriate selective functionalization of the olefin of **14**. However, treatment of **14** with thionyl chloride in pyridine results exclusively in the formation of undesired elimination product **16**. Use of Burgess' salt (methyl(carbonylsulfamoyl)triethylammonium hydroxide inner salt)[14] gives the same result.

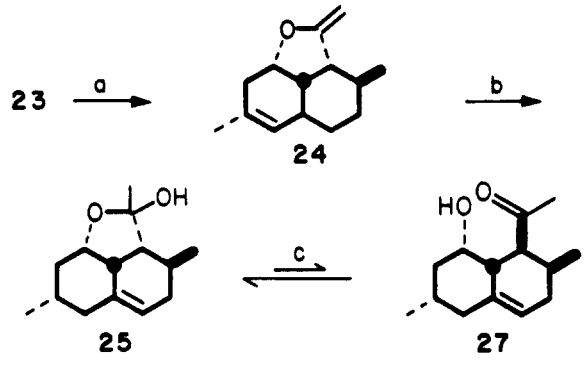
Since one-step elimination of alcohol **14** proceeds exclusively in the undesired direction, we sought to achieve the desired elimination by action of a hindered base on an appropriate derivative of the alcohol. To this end, tosylate **17** was prepared. Epoxidation of **17** with *m*-CPBA affords only the β-epoxide **18**; presumably the tosyl group effectively shields the α-face of the olefin. However, all attempts at elimination of tosylate **18** gave, as before, the product of elimination in the undesired direction of (**19**) (DBU/CH_2Cl_2, t-BuOK/t-BuOH, Me_2SO/heat).

Scheme III



(a) H_2NNHTs, MeOH. (b) n-BuLi, THF, Et_2O. (c) $[H^+]$.

Scheme IV



(a) t-BuOK, t-BuOH. (b) $[H^+]$, H_2O (c) NaOMe, MeOH.

The reason for the unexpected regioselectivity in elimination of alcohol **14** and its derivatives remains obscure. It is known that in simple cases of E2-like reactions in which the two possible products are a trisubstituted and a disubstituted olefin, mixtures of products are obtained, and more hindered bases afford more of the less substituted product.[15] It is clear that E1-like elimination of compounds **14** and **18** proceeds to give the more highly substituted olefin (Burgess' salt, tosylate pyrolysis in Me_2SO). This is not completely unexpected, althought one might have surmised that the two possible products would be somewhat comparable thermodynamically. The regiospecific elimination of tosylate **18** toward the more substituted position under E2-like conditions (hindered base) is more surprising. One possible explanation is that repulsion between the oxygen lone pairs and the approaching base causes elimination to proceed away from the oxygen, both in E1-like and E2-like cases.

At this point, attention was turned to the Shapiro reaction[16] as a method of modifying the pyranone ring (Scheme III). Tosylhydrazone **20** was prepared in 94% yield by treatment of ketone **6** with *p*-toluenesulfonohydrazide. Reaction of **20** with *n*-butyllithium produces intermediate vinyl anion **21**, which has two possible fates. Protonation of **21** by proton sources in the mixture (such as **20**) yields enol ether **15**; β-elimination followed by protonation yields acetylenic alcohol **23**. In practice, varying ratios of **15** and **23** have been obtained, depending upon reaction conditions. Although it has not been possible to generate enol ether **15** as the major product, addition of a THF solution of tosylhydrazone **20** slowly to a solution of *n*-butyllithium in ether/hexane provides **23** and **15** in a ratio of greater than 20:1; compound **23** can be isolated in a yield of 88%.

(12) Kaneda, K.; Ku, N.; Jitsukawa, K.; Teranishi, S. *Tetrahedron Lett.* **1981**, *22*, 2595.
(13) Brown, H. C.; Kirshnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.
(14) Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.
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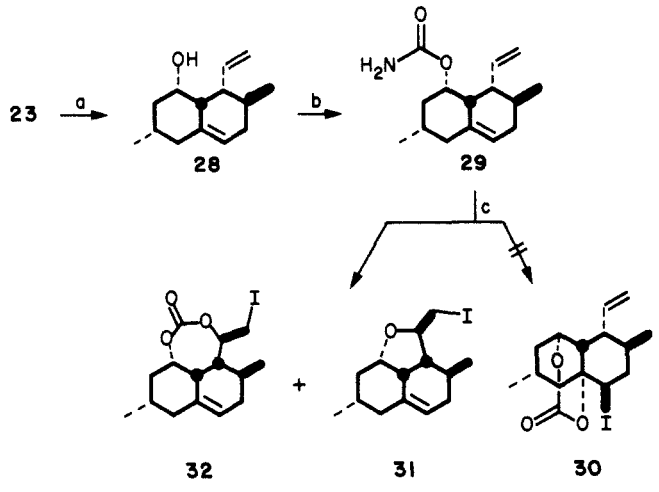
(16) Shapiro, R. H. *Org. React.* **1976**, *23*, 405.

Scheme V



(a) H_2, $Pd/BaSO_4$, quinoline. (b) $Cl_3CC(O)NCO$; MeOH, H_2O, K_2CO_3. (c) I_2, Et_2O, aq. $NaHCO_3$.

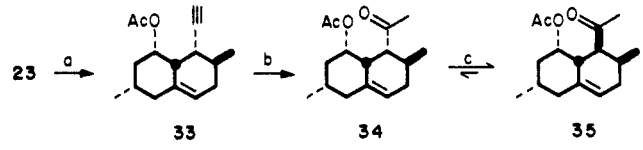
The chemistry of compound **23** proved to be quite interesting (Scheme IV). Treatment with a solution of potassium *tert*-butoxide in *tert*-butyl alcohol results in clean formation of sensitive enol ether **24**; brief treatment of **24** with aqueous acid affords a variable mixture of hemiketals **25**. Equilibration of **25** with methanolic sodium methoxide results in partial conversion to epimerized methyl ketone **27**, presumably via **8**. A 65:35 ratio of **25**:**27** is obtained; the results are identical when **27** is subjected to the same conditions.

At this point, attention was turned to elaboration of the olefin into the requisite diene of **2a** by a carbonate cyclization[17] (Scheme V). To this end, acetylene **23** was hydrogenated over Lindlar catalyst[18] to afford diene alcohol **28** in quantitative yield. This compound was converted to carbamate **29** in 96% yield by the action of trichloroacetyl isocyanate followed by aqueous methanolic potassium carbonate.[19] Iodocarbonate cyclization of carbamate **29** was expected to give desired cyclization product **30** for two reasons. First, the trisubstituted olefin would be expected to be much more reactive toward electrophiles than the monosubstituted olefin. Second, formation of a seven-membered ring is required if cyclization is to take place on the monosubstituted double bond, whereas a six-membered ring is formed in the desired pathway.

Nevertheless, treatment of carbamate **29** with iodine in a two-phase medium (Et_2O/saturated aqueous $NaHCO_3$) results in slow conversion to two products, **31** and **32**, isolated in yields of 48% and 20%, respectively. The stereochemical assignment at the new center is based on what is presumed to be the lowest energy transition state. Tetrahydrofuran **31** may either be formed by hydrolysis of the carbamate and subsequent cyclization of the resultant alcohol, or directly from **29** by attack of the proximal oxygen on the intermediate iodonium ion, with loss of cyanic acid. In any case, isolation of seven-membered ring carbamate **32**, and *none* of the desired product **30**, indicates that the transition state for formation of **30** is too sterically hindered for the reaction to proceed at a reasonable rate. This is not unduly surprising, given that all six substitutents on the decalin system of **30** must be axial in order for it to exist in a chair–chair conformation.

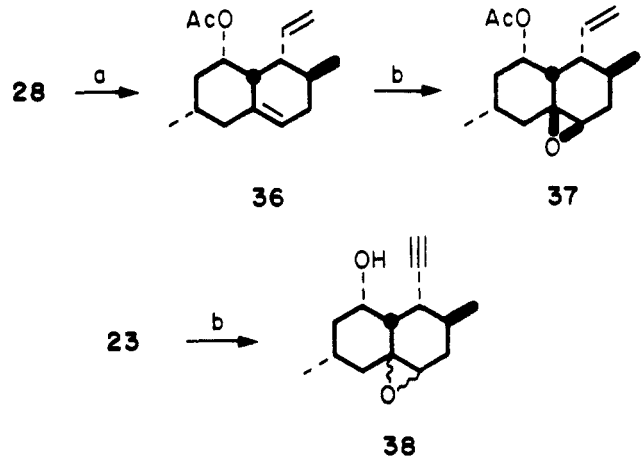
Our attempts at modification of the carbon–carbon double bond of **23** were postponed at this point, pending verification that the stereochemistry required at C-1 could be obtained by epimerization of an appropriate intermediate. Thus, alcohol **23** was acetylated to afford acetate **33**, and the ethynyl moiety was then hydrated under the conditions of Newman[20] (Dowex 50/HgO, MeOH, H_2O) to afford methyl ketone **34** (78%) (Scheme VI).

Scheme VI



(a) Ac_2O, pyridine, DMAP. (b) DOWEX 50 · HgO, MeOH, H_2O. (c) DBU, CH_2Cl_2.

Scheme VII

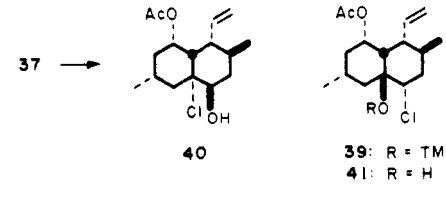


(a) Ac_2O, pyridine, DMAP. (b) mCPBA, CH_2Cl_2.

At this point, a protocol was needed that would effect epimerization to the ketone while leaving the acetate group intact. Heating a solution of **34** in neat diazabicyclo[5.4.0]undec-7-ene (DBU) at 95 °C for 2 days nicely accomplishes this goal, giving a favorable equilibrium ratio for **35**:**34** of 94:6. The major, desired isomer can be separated from the minor one by chromatography and is isolated in 76% yield.

Dienic ester **36** (prepared from alcohol **28**) is stereoselectively epoxidized on the β-face of the more substituted double bond, giving **37** (Scheme VII). The initial stereochemical assignment was made by comparison with the epoxidation of acetylenic alcohol **23**, which affords a 4:1 ratio of epoxides **38** (stereochemistry unassigned). The conversion of **23** to **36** would be expected to create more steric hindrance to epoxidiation on the α-face of the molecule and therefore provide more of the β-isomer. Since epoxidation of **23** gives a mixture, while that of **36** gives one compound, it is reasonable to conclude that **37** is the β-epoxide. This assignment was later confirmed by X-ray crystallographic analysis of a compound derived from **37** (vide infra).

Treatment of **37** with chlorotrimethylsilane and a catalytic amount of triphenylphosphine in dichloromethane was expected to provide silylated chlorohydrin **39** (eq 3).[21] Instead, however,



(3)

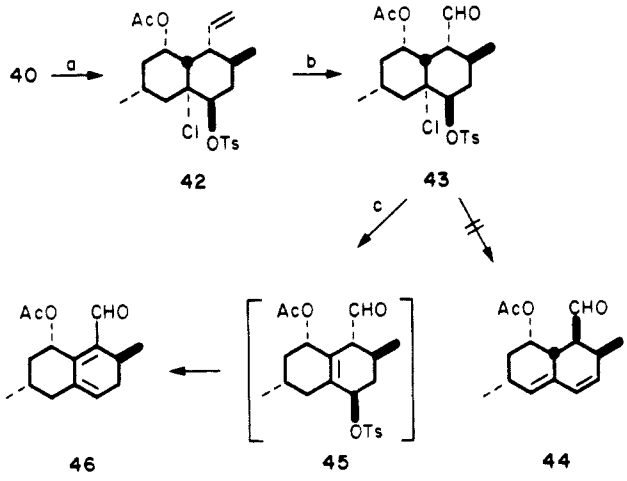
a mixture of chlorohydrins **40** and **41** was obtained in a ratio of about 6:1. Clearly, adventitious water was causing formation of HCl in situ, although all attempts to exclude moisture gave essentially identical results. Presumably, reaction with HCl is several orders of magnitude faster than reaction with chlorotrimethyl-

(17) Bartlett, P. A.; Meadows, J. D.; Brown, E. G.; Morimoto, A.; Jernstedt, K. K. *J. Org. Chem.* **1982**, *47*, 4013.
(18) (a) Lindlar, H. *Helv. Chim. Acta* **1952**, *35*, 446. (b) Cram, D. J.; Allinger, N. C. *J. Am. Chem. Soc.* **1956**, *78*, 2518.
(19) Kishi, Y.; Minami, N.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1109.
(20) Newman, M. S. *J. Am. Chem. Soc.* **1953**, *75*, 4740.
(21) Andrews, G. C.; Crawford, T. C.; Contrillo, L. G. *Tetrahedro Lett.* **1981**, 3803.

Table I. Formation of Chlorohydrins **40** and **41** from **37** (Equation 3)

conditions	ratio 40:41
TMSCl, PPh_3 (cat.), CH_2Cl_2	6:1
Pyr·HCl, *p*-TSOH·H_2O, CH_2Cl_2	3:2
HCl (conc.), CH_2Cl_2	1:1
HCl(conc.), PPh_3 (cat.), CH_2Cl_2	1:1
HCl (anhydrous), CH_2Cl_2	1:1

Scheme VIII



(a) *p*-TsCl, pyridine. (b) O_3; Me_2S. (c) DBU, CH_3CN.

silane, so that even a trace amount of HCl leads exclusively to chlorohydrin formation.

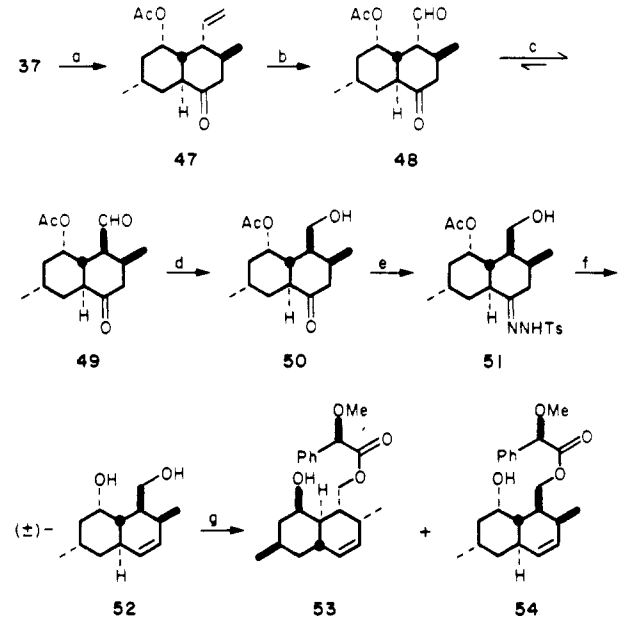
Since chlorohydrin **40** appeared to be a viable intermediate for synthesis of the requisite diene moiety, a number of attempts were made to improve the regioselectivity of the epoxide opening. As shown in Table I, standard sources of HCl gave nearly equal amounts of the regioisomeric chlorohydrins; in retrospect, the ratio of 6:1 obtained with the initial conditions was quite fortuitous.

Before proceeding further with possible improvements in this hydrochlorination reaction, we began to explore the potential utility of compound **40** as a synthon for construction of the hexahydronaphthalene moiety of **2a** (Scheme VIII). Sulfonylation of secondary alcohol **40** provides tosylate **42** (67%), which is ozonized cleanly to afford aldehyde **43** (89%). At this point, the stage was set for the execution, in one pot, of two eliminations and an epimerization, providing highly desirable diene aldehyde **44**. If this sequence was successful, then the appropriate acyl side chain (instead of acetate) could be incorporated at the stage of protection of alcohol **28**. In the event, treatment of **43** with DBU in acetonitrile affords dienal **46** as the sole isolable product (41%), presumably via intermediate **45**. This result did not bode well for the establishment of the requisite diene functionality of **2a** by anti elimination of a leaving group bearing the configuration at the ring juncture.

A side reaction which had been observed in the hydrochlorination of epoxide **37** was the formation of ketone **47** (Scheme IX). Although **37** was originally treated as an annoying byproduct, it has the necessary trans ring juncture for a synthesis of **2b** and also contains a suitable handle for formation of the carbon–carbon double bond in a regioselective fashion. The first order of business was to obtain ketone **47** in good yield. We were gratified to find that treatment of a benzene solution of **37** with boron trifluoride etherate results in rapid and quantitative conversion to the desired ketone.

The remaining transformations for conversion of ketone **47** to requisite synthon **3b** were carried out with little difficulty (Scheme IX). Ozonolysis of **47** followed by dimethyl sulfide reduction of the ozonide affords aldehyde **48** (85%) which is rapidly epimerized with 10% DBU in dichloromethane to afford a 95:5 ratio of aldehydes **49** and **48**; the desired isomer **49** is isolated by column

Scheme IX



(a) $BF_3 \cdot Et_2O$, PhH. (b) O_3, CH_2Cl_2; Me_2S. (c) DBU, CH_2Cl_2. (d) $Li(t\text{-}BuO)_3AlH$, THF. (e) H_2NNHTs, MeOH, HCl(cat.). (f) MeLi, Et_2O, TMEDA; KOH, MeOH. (g) (R)-(+)-PhCH(OMe)CO_2H, DCC, DMAP, CH_2Cl_2.

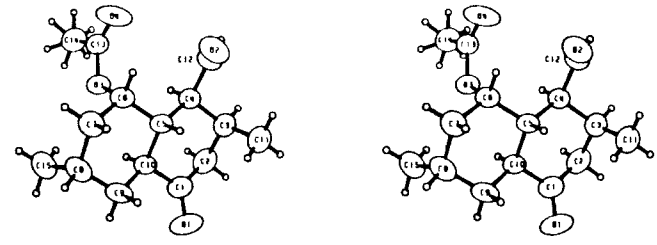


Figure 1. ORTEP stereoscopic projection of compound **49**.

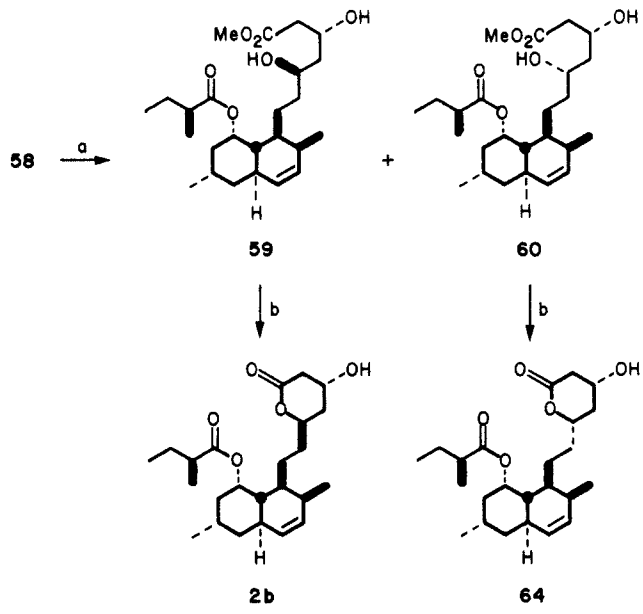
chromatography in 91% yield. Single-crystal X-ray structure determination of compound **49** established that we had indeed succeeded in setting the appropriate stereochemistry at all six asymmetric centers (Figure 1). The aldehyde functionality is selectively reduced with $Li(t\text{-}BuO)_3AlH$ to provide alcohol **50** (93%), which is subjected to the Shapiro modification[16] of the Bamford–Stevens reaction[22] to afford diol **52**. Specifically, treatment of **50** with *p*-toluenesulfonohydrazide in methanol under acid catalysis affords tosylhydrazone **51** (85%); reaction of **51** with methyllithium in ether/tetramethylethylenediamine, followed by treatment with potassium hydroxide in methanol (to completely remove the acetoxy group), affords racemic diol **52** in 77% yield.

Resolution of the octalin moiety is conveniently performed at this stage of the synthetic sequence. Selective esterification of **52** with (*R*)-(+)-*O*-methylmandelic acid (DCC, DMAP, CH_2Cl_2; 91%) proceeds smoothly to provide a 1:1 ratio of diastereomeric esters **53** and **54**. Although they can be separated by HPLC, we were gratified to discover that fractional crystallization provides the diastereomer of lower R_f in purity of greater than 98% de.

The initial assignment of the structures of **53** and **54** was made on the basis of the optical rotations of the two diastereomers. The principle of optical superposition, attributed in its original form to van't Hoff, states that two or more asymmetric centers in an optically active compound contribute independently to the total molecular rotation.[23] Although this principle is not valid when the asymmetric centers are close together, it does hold reasonably

(22) Bamford, W. R.; Stevens T. S. *J. Chem. Soc.* **1952**, 4735.
(23) van't Hoff, J. H. *Die Lagerung der Atoms in Raume*; Vieweg-Verlag: Brunswick, Germany, 1893; p 119. Guye, P. A.; Gautier, M. *Compt. Rend.* **1894**, 119, 740, 953.

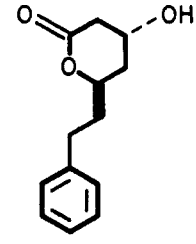
Scheme X



(a) $NaBH_4$, MeOH. (b) p-TsOH · H_2O, PhH.

well when the stereocenters are separated by a number of saturated atoms. The rule has been successfully applied to structure assignments of steroids, polycyclic terpenes, and carbohydrates.[24]

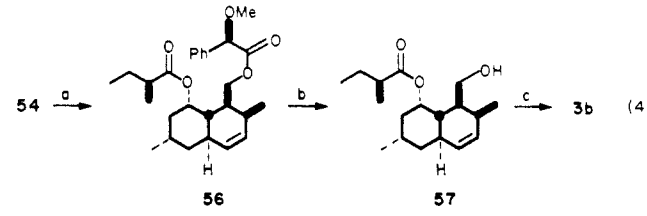
The specific rotation of (+)-dihydromevinolin (**2b**) is +148.6° (c 0.52, acetonitrile),[4] while that of lactone **55** is +48.8° (c 0.20, $CHCl_3$).[61] If the principle of superposition holds, then the octalin



55

moiety of **2b** should make a contribution to the overall rotation of about +100°.[25] Of the two *O*-methylmandelate esters, the less polar (higher R_f) one has a specific rotation of −19.9° (c 1.28, $CHCl_3$), while the more polar one has a specific rotation of +130° (c 1.24, $CHCl_3$). The (*R*)-*O*-methylmandelate ester would be expected to make a strong, positive contribution to the rotation.[26] To a first approximation, it seems reasonable to conclude that the specific rotations of the two *O*-methylmandelate esters are generated by independent contributions of +55° for the resolving moiety and ±75° for the two enantiomers of the octalin portion. With this reasoning, we assigned structure **53** to the less polar diastereomer and **54** to the more polar diastereomer. This assignment was corroborated by the fact that compound **57** (vide infra) exhibited a specific rotation of +136° (c 0.887, $CHCl_3$) and was confirmed by the ultimate conversion of **57** to **2b**.

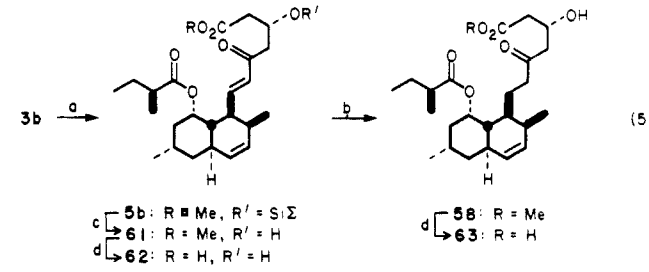
With ester **54** in hand, we proceeded with the synthesis (eq 4). Since the primary alcohol is conveniently protected, the secondary alcohol may be acylated with (*S*)-2-methylbutyric anhydride[5a] (pyridine, DMAP; 96%) to afford diester **56**. The *O*-methylmandelate ester is then selectively removed (KOH, MeOH; 96%), giving monoester **57**. Swern oxidation[27] provides key intermediate **3b** in 92% yield.



(4)

(a) (S)-2-methylbutyric anhydride, pyridine, DMAP. (b) KOH, MeOH (c) $(ClCO)_2$, DMSO, CH_2Cl_2; Et_3N.

The completion of the synthesis of **2b** proceeds in direct analogy to our previously reported synthesis of (+)-compactin (**1a**) (eq 5). Coupling of **3b** with keto phosphonate **4** under the conditions of Roush and Masamune[28] (DBU, LiCl, Me_2SO) provides enone **5b** in 45% yield, along with 42% of a mixture of recovered **3b** and its α-epimer. Only one isomer of coupled material was obtained;



(5)

(a) 4, LiCl, DBU, DMSO. (b) Et_3SiH, $(PPh_3)_3RhCl$, PhH; HF, CH_3CN. (c) HF, CH_3CN. (d) KOH, MeOH.

however the isolation of epimerized **3b** raises a question regarding the stereochemistry at C-1 of the coupled product. Our intuition suggested that the equatorial aldehyde **3b** would be likely to be more reactive than its axial epimer; conversion to **2b** and comparison with an authentic sample showed that this was indeed the case.

Conjugate reduction of **5b** ($(PPh_3)_3RhCl$, Et_3SiH, PhH),[29] followed (in the same pot) by desilylation of both the intermediate enol silane and the protected alcohol, is cleanly effected in 76% yield, affording saturated β-hydroxy ketone **58**. Compound **58** is reduced with sodium borohydride to provide a mixture of diol diesters **59** and **60** in a ratio of 65:35 (Scheme X), which are separable by careful column chromatography (94% yield). The major, higher R_f diastereomer **59** is lactonized with p-toluenesulfonic acid in benzene to afford (+)-**2b**. This synthetic specimen had an HPLC retention time and ^1H NMR spectrum which showed it to be identical with an authentic sample of (+)-**2b** generously provided by Dr. A. A. Patchett of Merck, Sharp & Dohme Research Laboratories. In addition, the activity of our synthetic **2b** in inhibition of HMG CoA reductase was found, within experimental error, to be identical with that of the natural material.

In order to explore the molecular basis of the inhibitory action of **2b**, we have also prepared three analogues for assessment of their biological activity (eq 5). Thus, desilylation of **5b** affords **61**, which is saponified to provide enone acid **62**. In similar fashion, saponification of **58** affords keto acid **63**. Finally, diol diester **60** is lactonized with p-toluenesulfonic acid in benzene to give 5-epidihydromevinolin (**64**) (Scheme X). The results of biological evaluation of compounds **62**, **63**, and **64**, as well as other analogues, will be reported in a future publication.

In summary, (+)-dihydromevinolin (**2b**) has been prepared by total synthesis. The successful route requires 19 steps (**6** → **20**

(24) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill; New York, 1962; pp 110–114.

(25) This approximation ignores differences in solvent and concentration between the reported rotations and our observed rotations; these effects should be minor. In addition, we are ignoring the contribution of the (*S*)-2-methylbutyryl ester; (*S*)-2-methylbutyric acid gives $[\alpha]^{25}$ +18° (neat).

(26) (*S*)-(−)-Methyl *O*-methylmandelate has $[\alpha]^{25}$ −124° (neat). Barth, G.; Voelter, W.; Mosher, H. S.; Bunnenberg, E.; Djerassi, C. *J. Am. Chem. Soc.* **1970**, *92*, 875.

(27) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(28) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, 2183.

(29) Ojima, J.; Kogure, T.; Nagai, Y. *Tetrahedron Lett.* **1972**, 5035.

→ **23** → **28** → **36** → **37** → **47** → **48** → **49** → **50** → **51** → **52** → **54** → **56** → **57** → **3b** → **5b** → **58** → **59** → **2b**). The synthesis also provided the 5-epi compound **64** and the related acids **62** and **63** for biological evaluation.

Experimental Section[30]

Following are experimental details for all reactions involved in the direct transformation of the tricyclic pyranone **6** into (+)-dihydromevinolin (**2b**), its C-5 epimer **64** and the related acids **62** and **63**. Experimental details for the preparation of compounds **9-14**, **16-19**, **24**, **25**, **27**, **29-35**, **39**, **41**, **43**, and **46** are given in the supplemental material (see paragraph at end of paper). Coupling constants are in hertz, and IR values are in inverse centimeters. Specific rotations, $[\alpha]$, were measured at the sodium D line.

(3a*RS*,4*SR*,8*SR*,9a*SR*,9b*RS*)-2,3,3a,4,5,7,8,9,9a,9b-Decahydro-4,8-dimethyl-3-oxonaphtho[1,8-*bc*]pyran *p*-Toluenesulfonylhydrazone (20). To a stirring solution of ketone **6** (945 mg, 4.30 mmol) in methanol (3 mL) was added a solution of *p*-toluenesulfonohydrazide (959 mg, 5.15 mmol) in methanol. White crystals began to form within minutes. The mixture was stirred at room temperature for 18 h and was cooled to 0 °C. The crystals were removed by filtration, washed with ice-cold methanol and hexane, and dried in vacuo to afford 1.56 g (94%) of white crystalline solid **20**, mp 155–156 °C dec. IR ($CHCl_3$): 2960, 2930, 1600, 1170, 915. ^1H NMR: δ 0.70 (d, 3, J = 7), 0.96 (d, 3 J = 7), 1.4–1.6 (m, 2), 1.7–1.9 (m, 3), 2.0–2.4 (m, 4), 2.45 (s, 3), 2.46 (m, 1), 3.62 (m, 1), 3.99 (d, 1, J = 16), 4.44 (d, 1, J = 16), 5.45 (m, 1), 7.14 (br s, 1), 7.33 (d, 2, J = 8), 7.85 (d, 2, J = 8). Anal. Calcd for $C_{21}H_{28}N_2O_3S$: C, 64.92; H, 7.26; N, 7.21. Found: C, 64.85; H, 7.29; N, 7.19.

(1*RS*,2*SR*,6*SR*,8*SR*,8a*RS*)-1,2,3,5,6,7,8,8a-Octahydro-2,6-dimethyl-1-ethynyl-8-hydroxynaphthalene (23). To a stirring solution of *n*-butyllithium (15.7 mmol) in a mixture of hexane (10 mL) and ether (15 mL) at 0 °C was added dropwise (1.0 mL/min, syringe pump) a solution of tosylhydrazone **20** (1.52 g, 3.92 mmol) in THF (25 mL). When the addition was complete, the mixture was stirred for 1 h at 2 °C and was quenched with H_2O (20 mL). The organic layer was removed, and the aqueous layer was extracted with ether. The combined organic portions were dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator. ^1H NMR analysis of the crude reaction mixture showed a ≥20:1 ratio of acetylene **23** to enol ether **15**. The crude product was subjected to flash chromatography[32] on silica gel (1:30 ether/hexane) to afford 684 mg (86%) of **23** as white crystals, mp 39–41 °C. IR ($CHCl_3$): 3600, 3320, 2935, 2120, 1605, 1460, 1370, 1100. ^1H NMR: δ 1.06 (d, 3, J = 8), 1.09 (d, 3, J = 7), 1.5–2.4 (m, 10), 2.23 (d, 1, J = 2.5), 2.44 (ddd, 1, J = 2.5, 7, 11), 4.52 (m, 1), 5.60 (m, 1). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 81.97; H, 10.00.

(1*RS*,2*SR*,6*SR*,8*SR*,8a*RS*)-1,2,3,5,6,7,8,8a-Octahydro-2,6-dimethyl-8-hydroxy-1-ethenylnaphthalene (28). Palladium on $BaSO_4$ (5%, 6.6 mg) was treated with quinoline (6.7 μL) and slurried in ether (1 mL). To this mixture was added acetylenic alcohol **23** (107 mg, 0.527 mmol). The flask was flushed with hydrogen and stirred under a hydrogen atmosphere for 50 h. Ether was added, and the mixture was filtered through Celite, washed with 1 M aqueous H_3PO_4 (10 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, affording 107.5 mg (99%) of **28** as a colorless oil. IR ($CHCl_3$): 3615, 2925, 1640, 1460, 1385, 920. ^1H NMR: δ 0.82 (d, 3, J = 6), 1.07 (d, 3, J = 7), 1.22 (m, 1), 1.5–1.9 (m, 3), 1.9–2.4 (m, 7), 4.15 (m, 1), 5.01–5.09 (m, 2), 5.63–5.66 (m, 1), 5.92 (ddd, 2, J = 20.0, 10.9, 9.0). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.71; H, 10.81.

(1*RS*,2*SR*,6*SR*,8*SR*,8a*RS*)-1,2,3,5,6,7,8,8a-Octahydro-8-(acetyloxy)-2,6-dimethyl-1-ethenylnaphthalene (36). To a stirring solution of alcohol **28** (542 mg, 2.63 mmol) and 4-(dimethylamino)pyridine (16 mg, 0.13 mmol) in pyridine (2.6 mL) was added acetic anhydride (0.745 mL, 7.89 mmol). The mixture was heated at 60 °C for 7 h and was cooled to room temperature. Ether (30 mL) was added, and the mixture was washed with 1 M aqueous H_3PO_4 (2 × 20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by flash chromatography[32] on silica gel (20 g, 1:50 ether/hexane) to afford 604 mg (92%) of **36** as a clear, colorless oil. IR ($CHCl_3$): 2970, 2935, 1732, 1390, 1035, 925. ^1H NMR: δ 0.80 (d, 3, J = 6), 0.97 (d, 3, J = 7), 1.6–2.4 (m, 10), 2.01 (s, 3), 5.05 (m, 2), 5.15 (m, 1), 5.55 (m, 2). Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.53; H, 9.82.

(1*RS*,2*SR*,4*RS*,4a*SR*,6*RS*,8*SR*,8a*SR*)-8-(Acetyloxy)-2,6-dimethyl-4,4a-epoxy-1-ethenyldecahydronaphthalene (37). To a stirring solution of compound **36** (277 mg, 1.12 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added *m*-CPBA (313 mg, 80–85% *m*-CPBA, 1.5 mmol). After 1 h at 0 °C, CH_2Cl_2 (15 mL) was added, and the mixture was washed with 10% aqueous Na_2SO_3 (15 mL) and saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and filtered. The solvent was removed with rotary evaporator, and the crude product was purified by flash chromatography[32] on silica gel (6 g, 1:9 ether/hexane) to afford 281 mg (95%) of **37** as a clear, colorless oil. IR ($CHCl_3$): 2965, 2940, 1735, 1388, 928. ^1H NMR: δ 0.76 (d, 3, J = 6), 1.12 (d, 3, J = 7), 1.34 (m, 1), 1.5–1.9 (m, 4), 2.04 (s, 3), 2.0–2.3 (m, 5), 3.12 (d, 1, J = 4), 5.05 (m, 2), 5.38 (m, 1), 5.45 (m, 1). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.58; H, 9.16.

(1*RS*,2*SR*,4a*SR*,6*SR*,8*SR*,8a*RS*)-8-(Acetyloxy)-2,6-dimethyl-1-ethenyl-4-oxodecahydronaphthalene (47). To a stirring solution of epoxide **37** (105.7 mg, 0.400 mmol) in benzene (2 mL) at 10 °C was added boron trifluoride etherate (2.8 mg, 0.02 mmol). The mixture was allowed to warm to room temperature and was stirred for 11 h. Ether (20 mL) was added, and the mixture was washed with saturated aqueous $NaHCO_3$ (15 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator to afford 105.6 mg (100%) of **47** as white crystals, mp 90–92 °C. IR ($CHCl_3$): 2940, 1735, 1710, 1260, 1035. ^1H NMR: δ 0.99 (d, 3, J = 7), 1.06 (d, 3, J = 7), 1.5–1.8 (m, 3), 1.9–2.3 (m, 6), 1.97 (s, 3), 2.72 (m, 1), 2.84 (dt, 1, J = 3, 12), 4.96 (d, 1, J = 10), 5.01 (d, 1, J = 17), 5.15 (m, 1), 6.33 (dt, 1, J = 17, 10). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.53; H, 9.21.

(1*RS*,2*SR*,4a*SR*,6*SR*,8*SR*,8a*RS*)-8-(Acetyloxy)-2,6-dimethyl-1-formyl-4-oxodecahydronaphthalene (48). A stream of ozone (Wellsbach ozone generator Model H-30) was passed into a solution of compound **47** (499 mg, 1.89 mmol) in CH_2Cl_2 (10 mL). At the appearance of a blue color in the solution, the gas flow was stopped, and dimethyl sulfide (6 mL) was added. The mixture was allowed to warm to room temperature and was heated at 40 °C for 18 h. Dichloromethane (20 mL) was added, and the mixture was washed with water (20 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by flash chromatography[32] on silica gel (12 g, 2:3 ether/hexane) to afford 429 mg (85%) of **48** as white crystals, mp 73–75 °C. IR ($CHCl_3$): 2980, 1745, 1715, 1390, 1125, 1030. ^1H NMR: δ 1.06 (d, 6, J = 7), 1.5–1.7 (m, 2), 2.01 (s, 3), 1.8–2.6 (m, 7), 2.90 (dd, 1, J = 6, 14), 3.09 (dt, 1, J = 3, 12), 5.11 (m, 1), 10.16 (d, 1, J = 4.5). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.71; H, 8.23.

(1*SR*,2*SR*,4a*SR*,6*SR*,8*SR*,8a*RS*)-8-(Acetyloxy)-2,6-dimethyl-1-formyl-4-oxodecahydronaphthalene (49). To a solution of aldehyde **48** (70.7 mg, 0.266 mmol) in CH_2Cl_2 (2 mL) at room temperature was added DBU (0.2 mL). The mixture was stirred at room temperature for 1 h and was cooled to 0 °C. After 1 h at 0 °C, the mixture was poured into a mixture of 1 M aqueous H_3PO_4 (10 mL) and CH_2Cl_2 (10 mL). The organic layer was removed, washed with 1 M aqueous H_3PO_4 (10 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator to afford 70.0 mg (99%) of a mixture of aldehydes **49** and **48** (ratio 20:1 by ^1H NMR). The major isomer **49** was separated from the minor one by flash chromatography[32] on silica gel (1.7 g, 1:1 ether/hexane), affording 64.3 mg (91%) of **49** as white crystals, mp 142–145 °C. IR ($CHCl_3$): 2980, 2945, 1735, 1715, 1390, 1380, 1030. ^1H NMR: δ 0.85 (d, 3, J = 7), 1.05 (d, 3, J = 7), 1.5–2.0 (m, 4), 2.08 (s, 3), 2.12 (m, 1), 2.22 (dt, 1, J = 2.3, 12), 2.32 (dd, 1, J = 3, 13), 2.6–2.9 (m, 3), 2.93 (ddd, 1, J = 1.5, 4, 11), 5.26 (m, 1), 9.68 (d, 1, J = 1.5). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.43; H, 8.44.

(1*SR*,2*SR*,4a*SR*,6*SR*,8*SR*,8a*RS*)-8-(Acetyloxy)-2,6-dimethyl-1-(hydroxymethyl)-4-oxodecahydronaphthalene (50). To a stirring solution of Li(*t*-BuO)$_3$AlH (56.1 mg, 0.221 mmol) in THF (1.5 mL) at −78 °C was added a solution of aldehyde **49** (49.0 mg, 0.184 mmol) in THF (0.5 mL). After being stirred for 5 min at −78 °C, the mixture was warmed to 0 °C and stirred for 15 min. To this mixture was added 15% aqueous NaOH (0.5 mL); after stirring for 10 min, $MgSO_4$ was added, and the mixture was filtered through Celite. The solvent was removed with a rotary evaporator, and the crude product was triturated with 1:1 EtOAc/hexane to afford 45.7 mg (93%) of **50** as white crystals, mp 118–120 °C. IR ($CHCl_3$): 3640, 3500, 2980, 2945, 1730, 1715, 1390, 1370, 1035. ^1H NMR: δ 0.86 (d, 3, J = 7), 1.04 (d, 3, J = 7), 1.4–1.7 (m, 4), 1.8–2.0 (m, 2), 2.10 (s, 3), 2.1–2.3 (m, 3), 2.5–2.8 (m, 3), 3.55 (t, 1, J = 12), 3.77 (dd, 1, J = 6, 12), 5.14 (m, 1). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.22; H, 9.07.

***p*-Toluenesulfonylhydrazone of Compound 50 (51).** One drop (Pasteur pipet) of a 1 M solution of HCl in MeOH was added to a solution of compound **50** (99.0 mg, 0.369 mmol) and *p*-toluenesulfonohydrazide

(30) ^1H NMR spectra were determined at 200, 250, or 300 MHz. Unless otherwise specified, all NMR spectra were recorded in $CDCl_3$, and the chemical shifts are expressed in ppm downfield from tetramethylsilane. Data are presented in the order: multiplicity, number of hydrogens, coupling constant in hertz.

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(82.5 mg, 0.443 mmol) in MeOH (0.5 mL). The mixture was placed in a 0 °C freezer for 15 h, during which time crystals formed. The mother liquor was removed by pipet, and the crystals were washed twice with ice-cold MeOH and dried in vacuo to afford 137.5 mg (85%) of **51** as a white solid, mp 111–113 °C. IR ($CHCl_3$): 2985, 2940, 1735, 1390, 1175, 1035, 915. ^1H NMR: δ 0.70 (d, 3, J = 7), 1.02 (d, 3, J = 7), 1.2–1.6 (m, 4), 1.8–2.2 (m, 5), 2.05 (s, 3), 2.3–2.6 (m, 3), 2.44 (s, 3), 3.42 (dd, 1, J = 8, 10), 3.62 (dd, 1, J = 5, 10), 5.05 (m, 1), 7.26 (br s, 1), 7.30 (d, 2, J = 8), 7.83 (d, 2, J = 8). Anal. Calcd for $C_{22}H_{32}N_2O_5S$: C, 60.53; H, 7.39; N, 6.42. Found: C, 60.29; H, 7.30; N, 6.29.

(1*SR*,2*SR*,4a*RS*,6*SR*,8*SR*,8a*SR*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-8-hydroxy-1-(hydroxymethyl)naphthalene (52). To a stirring solution of hydrazone **51** (44.2 mg, 0.101 mmol) in TMEDA (2 mL) at 0 °C was added dropwise a solution of methyllithium in ether (0.72 mL, 1.4 M, 1.01 mmol). After being stirred at 0 °C for 10 min, the mixture was warmed to 40 °C and was stirred at that temperature for 2 h. The mixture was cooled to 0 °C, water (0.1 mL) was added, and the cooling bath was removed. To the resulting solution was added a solution of KOH in methanol (2 M, 2 mL), and the mixture was stirred for 15 min. Ether (15 mL) was added, and the mixture was washed with water (10 mL), 1 M aqueous H_3PO_4 (25 mL), and brine (10 mL), dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by flash chromatography[32] on silica gel (2 g, 1:1 ether/hexane) to afford 16.4 mg (77%) of **52** as a white solid, mp 109–111 °C. IR ($CHCl_3$): 3620, 3460, 2980, 2940, 1465, 1380, 1030. ^1H NMR: δ 0.80 (d, 3, J = 7), 1.21 (d, 3, J = 7), 1.1–1.4 (m, 2), 1.39 (m, 2), 1.79 (m, 2), 2.02 (m, 2), 2.3–2.6 (m, 2), 2.85 (m, 1), 3.66 (dd, 1, J = 3, 10), 3.75 (t, 1, J = 10), 4.21 (m, 1), 5.38 (br d, 1, J = 10), 5.55 (ddd, 1, J = 2.6, 4.6, 10). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 73.97; H, 10.55.

(1*SR*,2*SR*,4a*RS*,6*SR*,8*SR*,8a*SR*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-8-hydroxy-1-([(*R*)-(*O*-methylmandelyl)oxy]methyl)naphthalene (53 and 54). To a stirring solution of diol **52** (180.3 mg, 0.859 mmol), (*R*)-(+)-*O*-methylmandelic acid[33] (142.5 mg, 0.859 mmol), and DMAP (10.5 mg, 0.086 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added 1,3-dicyclohexylcarbodiimide (176.9 mg, 0.859 mmol). The mixture was allowed to warm to room temperature gradually over 3 h. Ether (30 mL) was added, and the mixture was filtered. The filtrate was washed with 1 M aqueous H_3PO_4 (15 mL) and saturated aqueous $NaHCO_3$ (15 mL) and was dried ($MgSO_4$) and filtered. The solvent was removed with a rotary evaporator and the crude product was purified by flash chromatography[32] (9 g of silica gel, 1:3 ether/hexane) to afford 279 mg (91%) of esters **53** and **54**. Combustion analysis was carried out on a mixture of **53** and **54**. Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.82; H, 8.54.

The diastereomers are separable by HPLC;[34] however, compound **54** is more conveniently isolated by fractional crystallization from 1:4 ether/hexane followed by trituration with 1:30 ether/hexane. In this way, 103 mg of pure **54** was obtained.

Compound 53. $[\alpha]^{25}$–19.9° (c 1.28, $CHCl_3$). IR ($CHCl_3$): 3570, 2920, 1740, 1110. ^1H NMR: δ 0.79 (d, 3, J = 7), 1.20 (d, 3, J = 7), 1.1–1.4 (m, 2), 1.5–1.7 (m, 3), 1.9–2.2 (m, 3), 2.25 (m, 1), 2.50 (m, 1), 3.39 (s, 3), 3.88 (m, 1), 4.15 (m, 2), 4.76 (s, 1), 5.36 (br d 1, J = 10), 5.53 (m, 1), 7.4 (m, 5).

Compound 54. mp 109–111 °C. $[\alpha]^{25}$ +130° (c 1.24, $CHCl_3$. IR ($CHCl_3$): 3570, 2920, 1740, 1110. ^1H NMR: δ 0.72 (d, 3, J = 7), 1.21 (d, 3, J = 7), 1.1–1.4 (m, 2), 1.5–1.8 (m, 3), 1.9–2.2 (m, 3), 2.25 (m, 1), 2.51 (m, 1), 3.40 (s, 3), 3.95 (m, 1), 4.16 (d, 2, J = 7), 4.77 (s, 1), 5.36 (br d, 1, J = 10), 5.53 (m, 1), 7.4 (m, 5).

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-8-[(*S*)-(2-methylbutyryl)oxy]-1-([(*R*)-(*O*-methylmandelyl)oxy]methyl)-naphthalene (56). To a stirring solution of compound **54** (37.3 mg, 0.104 mmol) and DMAP (2.0 mg, 0.016 mmol) in pyridine (0.3 mL) was added (*S*)-2-methylbutyric anhydride.[5a] The mixture was heated at 50 °C for 200 min and was cooled to room temperature. Ether (20 mL) was added, and the mixture was washed with 1 M aqueous H_3PO_4 (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The ether solution was dried ($MgSO_4$) and the solvent was removed with a rotary evaporator. The crude product was purified by flash chromatography[32] on silica gel (2 g, 1:4 ether/hexane) to afford 44.1 mg (96%) of diester **56**. IR ($CHCl_3$): 2975, 1750, 1725, 1960, 1190. ^1H NMR δ 0.61 (d, 3, J = 7), 0.87 (t, 3, J = 7), 0.92 (m, 1), 1.07 (d, 3, J = 7), 1.12 (d, 3, J = 7), 1.2–1.8 (complex, 5), 1.85 (m, 1), 1.9–2.2 (m, 3), 2.36 (m, 1), 2.47 (m, 1), 3.40 (s, 3), 3.90 (t, 1, J = 11), 4.10 (dd, 1, J = 4, 11), 4.72 (s, 1), 4.90 (m, 1), 5.34 (br d, 1, J = 10), 5.54 (m, 1), 7.38 (m, 5). HRMS Calcd for $C_{27}H_{38}O_5$: 442.2719. Found: 442.2725.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-1-(hydroxymethyl)-8-[(*S*)-(2-methylbutyryl)oxy]naphthalene (57). To a solution of compound **56** (42.9 mg, 0.0971 mmol) in methanol (0.2 mL) was added a solution of KOH in methanol (0.1 M, 1.94 mL, 0.194 mmol). The mixture was allowed to stand at room temperature for 8.5 h. Ether (20 mL) was added, and the mixture was washed with water (10 mL) and brine (10 mL). The combined aqueous washings were extracted with ether (10 mL), and the combined organic phases were dried ($MgSO_4$) and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by flash chromatography[32] on silica gel (2 g, 1:3 ether/hexane) to afford a product which was contaminated with (*R*)-methyl *O*-methylmandelate. The impurity was removed with a high-vacuum pump (2 h), affording 27.4 mg (96%) of **57** as a colorless oil. $[\alpha]^{24}$ +136° (c 0.887, $CHCl_3$). IR ($CHCl_3$): 3620, 3480, 2980, 1720, 1460, 1195, 925. ^1H NMR: δ 0.92 (t, 3 J = 7), 0.93 (d, 3, J = 7), 1.10 (d, 3, J = 7), 1.15 (d, 3, J = 7), 1.1–2.1 (complex, 10), 2.38 (m, 1), 2.54 (m, 2), 3.50 (t, 1, J = 10), 3.66 (dd, 1, J = 5, 10), 5.05 (m, 1), 5.38 (br d, 1, J = 10), 5.45 (m, 1). HRMS Calcd for $C_{18}H_{30}O_3$: 294.2195. Found: 294.2205.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-1-formyl-8-[(*S*)-(2-methylbutyryl)oxy]naphthalene (3b). According to the Swern protocol,[27] to a stirring solution of oxalyl chloride (38.8 mg, 0.306 mmol) in CH_2Cl_2 (0.7 mL) at −60 °C was added a solution of Me_2SO (47.8 mg, 0.611 mmol) in CH_2Cl_2 (0.15 mL). The solution was stirred for 2 min at −60 °C, and a solution of alcohol **57** (72.8 mg, 0.248 mmol) in CH_2Cl_2 (0.25 mL) was added. After stirring for 15 min at −60 to −50 °C, triethylamine (129 mg, 1.27 mmol) was added; the mixture was stirred for 5 min at the same temperature and was allowed to warm to room temperature. Ether (20 mL) was added, and the mixture was washed with 1 M aqueous H_3PO_4, saturated aqueous $NaHCO_3$, and brine. The ether solution was dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator. The crude product was purified by flash chromatography[32] on silica gel (2 g, 1:4 ether/hexane) to afford 66.7 mg (92%) of **3b** as a colorless oil. IR ($CHCl_3$): 2970, 2940, 1725, 1605, 1460. ^1H NMR: δ 0.88 (t, 3, J = 7), 0.96 (d, 3, J = 7), 1.11 (d, 3, J = 7), 1.12 (d, 3, J = 7), 1.4–2.0 (complex, 7), 2.10 (m, 1), 2.33 (m, 1), 2.47 (m, 1), 2.67 (m, 2), 5.34 (m, 1), 5.43 (br d, 1, J = 10), 5.61 (ddd, 1, J = 2.8, 4, 10), 9.72 (d, 1, J = 2.5). HRMS Calcd for $C_{18}H_{28}O_3$: 292.2038. Found: 292.2055.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,5′*R*,2″*S*)-Methyl 1,2,4a,5,6,7,8,8a-Octahydro-5′-(*tert*-butyldimethylsilyloxy)-2,6-dimethyl-8-[(2-methyl-1-oxobutyl)oxy]-3′-oxo-1-naphthalenehept-1′-enoate (5b). To a stirring solution of LiCl (ca. 15 mg) in a solution of aldehyde **3b** (66.4 mg, 0.227 mol) and keto phosphonate **4** (135.5 mg, 0.355 mmol) in Me_2SO (0.15 mL) was added DBU (34.6 mg, 0.227 mmol). A yellow-brown color developed, and the solids gradually dissolved over 1 h. The mixture was stirred at room temperature for 39 h and was partitioned between ether (20 mL) and 1 M aqueous H_3PO_4 (10 mL). The organic phase was washed with brine, dried ($MgSO_4$), and filtered, and the solvent was removed with a rotary evaporator. The crude product was subjected to column chromatography on silica gel (6 g, 1:4 to 1:9 ether/hexane; EtOAc) to afford, in order of elution, 28.0 mg (42%) of recovered aldehyde **3b** and its α-epimer, 56.3 mg (45%) of enone **5b**, and 55.7 mg of recovered keto phosphonate **4**.

Compound 5b. IR ($CHCl_3$): 2960, 2935, 1730, 1670, 1460. ^1H NMR: δ 0.04 (s, 3), 0.06 (s, 3), 0.83 (s, 9), 0.89 (t, 3, J = 7) 0.96 (d, 3, J = 7), 1.10 (t, 6, J = 7), 1.3–1.8 (complex, 6), 1.88 (m, 1), 2.08 (m, 1), 2.30 (m, 2), 2.43 (dd, 1, J = 6.5, 15), 2.55 (m, 3), 2.71 (dd, 1, J = 6, 16), 2.81 (dd, 1, J = 6, 16), 3.66 (s, 3), 4.62 (m, 1), 4.92 (m, 1), 5.43 (br d, 1, J = 10), 5.62 (ddd, 1, J = 2.5, 4.5, 10), 5.99 (d, 1, J = 16), 6.76 (dd, 1, J = 10, 16). HRMS Calcd for $C_{31}H_{52}O_6Si$: 548.3533. Found: 548.3513.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,5′*R*,2″*S*)-Methyl 1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-5′-hydroxy-8-[(2-methyl-1-oxobutyl)oxy]-3′-oxo-1-naphthaleneheptanoate (58). To compound **5b** (49.9 mg, 0.0911 mmol) in a 10-mL round-bottomed flask was added a solution of $(PPh_3)_3RhCl$ in benzene (1.9 mg/mL, 1.0 mL). Triethylsilane (0.50 mL) was added, and the mixture was heated at 70 °C for 40 min. After cooling to room temperature, the mixture was concentrated with a rotary evaporator followed by high vacuum (10 min). The residue was taken up in 1:19 48% aqueous HF/CH_3CN (6 mL) and was stirred at room temperature for 50 min. Ether (15 mL) was added, and the mixture was washed carefully with saturated aqueous $NaHCO_3$ (15 mL). The ether solution was dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator. The crude product was purified by flash chromatography[32] on silica gel (2 g, 1:1 ether/hexane) to afford 30.2 mg (76%) of **58** as a clear, colorless oil. IR ($CHCl_3$): 3540, 2970, 2880, 1722, 1605, 1195 cm^{-1}. ^1H NMR: δ 0.82 (d, 3, J = 7), 0.89 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.13 (d, 3, J = 7), 1.2–2.5 (complex), 2.50 (d, 2, J = 6), 2.60

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(34) Parameters for HPLC: one μ Porasil semipreparative column; 5–10 mg/injection; 30% ether/hexanes; 5.0 mL min^{-1}; t_R of compound **53**, 8.8 min; compound **54**, 10.9 min.

(d, 2, J = 6), 3.39 (d, 1, J = 4), 3.70 (s, 3), 4.44 (m, 1), 5.19 (m, 1), 5.38 (br d, 1, J = 10), 5.62 (ddd, 1, J = 2.5, 4.7, 10). Mass spectrum (70 eV), m/z 334 (M − 102), 43 (base).

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,3′*R*,5′*R*,2″*S*)-Methyl 1,2,4a,5,6,7,8,8a-Octahydro-3′,5′-dihydroxy-2,6-dimethyl-8-[(2-methyl-1-oxobutyl)oxy]-1-naphthaleneheptanoate (59) and (1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,3′*S*,5′*R*,2″*S*)-Methyl 1,2,4a,5,6,7,8,8a-Octahydro-3′,5′-dihydroxy-2,6-dimethyl-8-[(2-methyl-1-oxobutyl)oxy]-1-naphthaleneheptanoate (60). To a stirring solution of compound **58** (26.8 mg, 0.0615 mmol) in methanol (1 mL) at −24 °C was added $NaBH_4$. The mixture was allowed to warm to −8 °C over 30 min at which point was added a mixture of ether (3 mL) and saturated aqueous $NaHCO_3$ (3 mL). After the solution was warmed to room temperature and stirred for 45 min, additional ether was added, and the organic layer was separated, dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, affording 26.8 mg (100%) of a mixture of **58** and **59** (ratio 65:35 by ^1H NMR analysis). The crude product was purified by column chromatography (2.3 g, 1:4 EtOAc/hexane), affording 10.4 mg (39%) of compound **59**, 8.9 mg (33%) of a mixture of **59** and **60**, and 6.1 mg (23%) of compound **60**.

Compound 59. IR ($CHCl_3$): 3500, 2970, 2940, 1720, 1440. ^1H NMR: δ 0.83 (d, 3, J = 7), 0.89 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.12 (d, 3, J = 7), 1.0–2.4 (complex, 18), 2.48 (d, 2, J = 6), 3.35 (m, 1), 3.71 (s, 3), 3.80 (m, 2), 4.26 (m, 1), 5.21 (m, 1), 5.37 (br d, 1, J = 10), 5.64 (ddd, 1, J = 2.6, 5, 10). HRMS Calcd for $C_{25}H_{42}O_6$: 438.2981. Found: 438.2958.

Compound 60. IR ($CHCl_3$): 3500, 2940, 1720, 1460, 1440. ^1H NMR: δ 0.82 (d, 3, J = 7), 0.91 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.13 (d, 3, J = 7), 1.0–2.6 (complex, 20), 3.42 (m, 1), 3.71 (s, 3), 3.85 (m, 1), 4.1–4.4 (m, 2), 5.19 (m, 1), 5.37 (br d, 1, J = 10), 5.64 (ddd, 1, J = 2.6, 5, 10).

(+)-Dihydromevinolin (2b). To a stirring solution of compound **59** (9.6 mg, 0.022 mmol) in benzene (2 mL) at room temperature was added p-TsOH·H_2O (3.2 mg, 0.019 mmol). After 40 min, the mixture was concentrated with a rotary evaporator, and fresh benzene (2 mL) was added. After the mixture stirred for 15 min, a small amount of solid $NaHCO_3$ was added, and the mixture was stirred for 2 min. Ethyl acetate (10 mL) was added, and the mixture was washed with water and brine, dried ($MgSO_4$), and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by column chromatography on silica gel (1 g, 2:3 EtOAc/hexane) to afford 7.6 mg (85%) of slightly impure **2b**. Further purification by HPLC[35] afforded 5.8 mg of **2b** as a colorless oil whose ^1H NMR spectrum showed it to be identical with an authentic sample. ^1H NMR: δ 0.84 (d, 3, J = 7), 0.90 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.13 (d, 3, J = 7), 1.2–2.1 (complex, 16), 2.35 (m, 2), 2.48 (m, 1), 2.60 (ddd, 1, J = 1.4, 4, 18), 2.74 (dd, 1, J = 5, 18), 4.38 (m, 1), 4.61 (m, 1), 5.21 (m, 1), 5.38 (br d, 1, J = 10), 5.65 (ddd, 1, J = 2.6, 5, 10). HRMS Calcd for $C_{24}H_{38}O_5$: 406.2719. Found: 406.2727.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,5′*R*,2″*S*)-Methyl 1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-5′-hydroxy-8-[(2-methyl-1-oxobutyl)oxy]-3′-oxo-1-naphthalenehept-1′-enoate (61). Compound **5b** (6.5 mg, 0.012 mmol) was taken up in a solution of 48% aqueous HF in acetonitrile (1:19, 1 mL). After 45 min at room temperature, ether (10 mL) was added, and the mixture was washed carefully twice with saturated aqueous $NaHCO_3$ and dried ($MgSO_4$). After filtration, the solvent was removed with a rotary evaporator and the crude product was subjected to flash chromatography[32] on silica gel (1 g, 1:1 ether/hexane) to afford 4.9 mg (96%) of **61** as a clear, colorless oil. IR ($CHCl_3$): 3520, 2980, 1730, 1670, 1460, 1440. ^1H NMR δ 0.89 (t, 3, J = 7), 0.96 (d, 3, J = 7), 1.09 (d, 3, J = 7), 1.12 (d, 3, J = 7), 1.3–1.9 (complex, 7), 2.08 (m, 1), 2.30 (m, 2), 2.55 (m, 2), 2.55 (d, 2, J = 6), 2.70 (dd, 1, J = 4, 16), 2.82 (dd, 1, J = 8, 16), 3.59 (d, 1, J = 4), 3.71 (s, 3), 4.46 (m, 1), 4.95 (m, 1), 5.44 (br d, 1, J = 10), 5.63 (ddd, 1, J = 2.6, 4.5, 10), 5.99 (d, 1, J = 16), 6.80 (dd, 1, J = 10, 16). HRMS Calcd for $C_{25}H_{38}O_6$: 434.2668. Found: 434.2673.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*,5′*R*,2″*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-5′-hydroxy-8-[(2-methyl-1-oxobutyl)oxy]-3′-oxo-1-naphthalenehept-1′-enoic Acid (62). Compound **61** (4.6 mg, 0.011 mmol) was taken up in a solution of KOH in methanol (0.1 M, 0.3 mL) at room temperature. After 1 h, ether (5 mL) was added, and the organic solution was extracted with saturated aqueous $NaHCO_3$ (2 × 5 mL). The combined aqueous portions were acidified with 1 M aqueous H_3PO_4 (15 mL) and were extracted with EtOAc (2 × 10 mL). The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator, affording 2.7 mg (61%) of compound **62** as a clear, colorless oil. The ^1H NMR spectrum of this material showed it to be pure. IR ($CHCl_3$): 3510, 2980, 2940, 1720, 1670, 1200. ^1H NMR δ 0.89 (t, 3, J = 7), 0.96 (d, 3, J = 7), 1.09 (d, 3, J = 7), 1.12 (d, 3, J = 7), 1.2–1.9 (complex, 10), 2.09 (m, 1), 2.30 (m, 2), 2.55 (m, 1), 2.60 (d, 2, J = 6), 2.71 (dd, 1, J = 4, 16), 2.86 (dd, J = 8, 16), 4.50 (m, 1), 4.97 (m, 1), 5.44 (br d, 1, J = 10), 5.63 (ddd, 1, J = 2.6, 4.5, 10), 6.00 (d, 1, J = 16), 6.82 (dd, 1, J = 10, 16). HRMS Calcd for $C_{24}H_{36}O_6$: 420.2512. Found: 420.2511.

(1*S*,2*R*,4a*R*,6*S*,8*S*,8a*R*,5′*R*,2″*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2,6-dimethyl-5′-hydroxy-8-[(2-methyl-1-oxobutyl)oxy]-3′-oxo-1-naphthaleneheptanoic Acid (63). Compound **58** was taken up in a solution of KOH in MeOH–water (0.1 M, 2:1, 0.3 mL) at room temperature. After 45 min, ether (10 mL) was added, and the organic solution was extracted with saturated aqueous $NaHCO_3$ (2 × 5 mL). The combined organic portions were acidified with 1 M aqueous H_3PO_4 (15 mL) and were extracted with EtOAc (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and filtered, and the solvent was removed with a rotary evaporator to afford 2.7 mg (82%) of compound **63** as a colorless oil. The ^1H NMR spectrum of this material showed it to be pure. IR ($CHCl_3$): 3510, 2975, 2940, 1720, 1200. ^1H NMR: δ 0.82 (d, 3, J = 7), 0.89 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.14 (d, 3, J = 7), 1.1–1.8 (complex, 11), 1.92 (m, 1), 2.05 (m, 1), 2.2–2.5 (m, 4), 2.55 (d, 2, J = 6), 2.64 (d, 2, J = 6), 4.46 (m, 1), 5.21 (m, 1), 5.39 (br d, 1, J = 10), 5.63 (ddd, 1 J = 2.5, 5, 10). Mass spectrum (70 eV), m/e 160 (base), 320 (M − 102), 404 (M − 18).

5-Epidihydromevinolin (64). To a stirring solution of compound **60** (4.3 mg, 0.0098 mmol) in benzene (1 mL) at room temperature was added p-TsOH·H_2O (2.8 mg, 0.015 mmol). After 25 min, the mixture was concentrated with a rotary evaporator, and an additional 1 mL of fresh benzene was added. After stirring for 25 min more, a small amount of solid $NaHCO_3$ was added, the mixture was stirred for 5 min, and EtOAc (10 mL) was added. The mixture was washed with water and brine and was dried ($MgSO_4$) and filtered. The solvent was removed with a rotary evaporator, and the crude product was purified by column chromatography on silica gel (1 g, 2:3 EtOAc/hexane) to afford 3.4 mg (85%) of compound **64** as a clear, colorless oil. IR ($CHCl_3$): 3450, 2980, 2950, 1720, 1460, 1385. ^1H NMR: δ 0.84 (d, 3, J = 7), 0.90 (t, 3, J = 7), 1.09 (d, 3, J = 7), 1.13 (d, 3, J = 7), 1.1–2.2 (complex, 16), 2.2–2.5 (m, 4), 2.89 (ddd, 1, J = 1.2, 6, 17), 4.2 (m, 2), 5.18 (m, 1), 5.39 (br d, 1, J = 10), 5.64 (ddd, 1, J = 2.6, 5, 10). HRMS Calcd for $C_{24}H_{38}O_5$: 406.2719. Found: 406.2725.

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Registry No. 2b, 77517-29-4; **3b** (isomer 1), 101761-34-6; **3b** (isomer 1), 101761-37-9; **4**, 96555-58-7; **5b**, 101761-35-7; (±)-**6**, 99342-52-6; (±)-**8**, 101760-94-5; (±)-**9**, 101760-99-0; (±)-**10**, 101761-00-6; (±)-**11** (isomer 1), 101761-01-7; (±)-**11** (isomer 2), 101833-99-2; (±)-**12**, 101761-02-8; (±)-**13**, 101760-95-6; (±)-**14**, 101834-00-8; (±)-**14** (epoxide) (isomer 1), 101761-04-0; (±)-**14** (epoxide) (isomer 2), 101834-01-9; (±)-**15**, 101760-96-7; (±)-**16**, 101761-03-9; (±)-**17**, 101761-05-1; (±)-**18**, 101761-06-2; (±)-**19**, 101761-07-3; (±)-**20**, 101773-26-6; (±)-**23**, 101761-22-2; (±)-**24**, 101761-08-4; (±)-**25** (isomer 1), 101761-09-5; (±)-**25** (isomer 2), 101834-02-0; (±)-**27**, 101761-10-8; (±)-**28**, 101761-11-9; (±)-**29**, 101761-12-0; (±)-**30**, 101760-97-8; (±)-**31**, 101760-14-2; (±)-**32**, 101761-13-1; (±)-**33**, 101761-15-3; (±)-**34**, 101761-16-4; (±)-**35**, 101761-17-5; (±)-**36**, 101761-23-3; (±)-**37**, 101761-24-4; (±)-**38** (isomer 1), 101761-18-6; (±)-**38** (isomer 2), 101834-03-1; **39**, 101761-42-6; (±)-**40**, 101771-82-8; (±)-**41**, 101761-43-7; (±)-**42**, 101761-19-7; (±)-**43**, 101761-20-0; (±)-**44**, 101760-98-9; (±)-**46**, 101761-21-1; (±)-**47**, 101761-25-5; (±)-**48**, 101761-26-6; (±)-**49**, 101761-27-7; (±)-**50**, 101761-28-8; (±)-**51**, 101761-29-9; (±)-**52**, 101761-30-2; **53**, 101761-31-3; **54**, 101773-25-5; **56**, 101761-32-4; **57**, 101761-33-5; **58**, 101761-38-0; **58** (TBDMS ether), 101761-36-8; **59**, 101834-04-2; **60**, 101834-05-3; **61**, 101761-39-1; **62**, 101761-40-4; **63**, 101761-41-5; **64**, 101834-06-4; (*R*)-(+)-PhCH(OMe)CO_2H, 3966-32-3; (*S*)-2-methylbutyric anhydride, 84131-91-9.

Supplementary Material Available: Crystal data for compound **49** and experimental details for the preparation and characterization of compounds **9–14**, **16–19**, **24**, **25**, **27**, **29**, **30–35**, **39**, **41**, **43**, and **46** (24 pages). See any current masthead page for ordering information.

(35) Parameters for HPLC: one μ Porasil semipreparative column; 1.5 mg/injection; 1:1 EtOAc/hexane; 5.0 mL min^{-1}; t_R 10.2 min.