stirred at room temperature for 18 h while this pH was maintained. A few drops of acetone were added at midreaction to inhibit foaming. The reaction was acidified to pH 2 and the resulting precipitate isolated by filtration, carefully washed with H_2O, and dried under reduced pressure to give a tan powder 14 (240 mg): FABMS MH^+ m/z 969 calcd for $C_{41}H_{37}N_{12}O_{11}S_3$ 969.1867, found 969.1890; m/z 952 [M - OH], m/z 925 [M - CO_2], and m/z 908 [M - OH - CO_2]; t_R 108 s, using a RCM Nova C_{18} column (4 × 300 mm) developed isocratically at 2 mL/min with CH_3CN/H_2O, 0.5% aqueous NH_4OAc (38:62). This product was labile and resisted further purification and characterization.

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A Convergent Approach to the Dihydrotachysterol Diene System. Application to the Synthesis of Dihydrotachysterol$_2$ (DHT$_2$), 25-Hydroxydihydrotachysterol$_2$ (25-OH-DHT$_2$), 10(*R*),19-Dihydro-(5*E*)-3-epivitamin D$_2$, and 25-Hydroxy-10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$[†]

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Total synthesis of A-ring fragments of 10(*S*),19-dihydrovitamins D and 10(*R*),19-dihydro-(5*E*)-epivitamins D from (+)-(*S*)-carvone and (-)-(*R*)-carvone is described. These fragments were used for convergent synthesis of dihydrotachysterol$_2$ (DHT$_2$), 25-hydroxydihydrotachysterol$_2$, 10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$, and 25-hydroxy-10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$.

Introduction

Since the discovery that 1α,25-dihydroxyvitamin D$_3$ (**1**, Figure 1) modulates cell differentation and inhibits cell proliferation,[1] much effort has been put into the development of new vitamin D analogues of potential clinical interest.[2] The dihydrotachysterols **2a** and **2b** (Figure 1) have for a long time been used clinically as analogues of **1**[3,4] in relation of the role of the vitamin D in calcium metabolism. While their interest in this respect has declined due to the availability of 1α-hydroxylated vitamin D analogues,[5] their potential as antiproliferative drugs or as differentiation inducers remains. In spite of this, neither **2a** nor **2b**, nor their side-chain analogues, have been tested in these capacities.

We have previously reported a method for the preparation of dihydrotachysterols that is based on the regio- and stereoselective reduction of the 10,19-double bond of the corresponding 5,6-*trans*-vitamin D precursor (Scheme I).[3,6] However, this approach is inconvenient for pharmacological screening of numerous dihydrotachysterols and their hydroxylated or modified side-chain analogues, since it requires the individual preparation of each 5,6-*trans*-vitamin D precursor. We have therefore developed a strategy allowing the convergent assembly of a variety of side-chain analogues. We envisaged the diene system of dihydrotachysterol$_2$ (**2b**) and related derivatives as arising from a Wittig-Horner coupling between the α-anion of the unknown phosphine oxide **4** (contributing ring A) and the appropriate Grundmann ketone **5** (contributing the upper fragment).[7] We describe here the total synthesis of **4** and its enantiomer **6** and their use in the convergent synthesis of dihydrotachysterol$_2$ (DHT$_2$, **2b**), 25-hydroxydihydrotachysterol$_2$ (25-OH-DHT$_2$, **2c**), 10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$ (**2d**), and 25-hydroxy-10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$ (**2e**).

Synthesis of the Phosphine Oxide 4 and Its Enantiomer 6. Phosphine oxide **4** was synthesized from com-

[†] This work was taken in part from the Ph.D. thesis of Miguel A. Maestro (Universidad de Santiago, December 1989). This work was presented in part as a communication at the Eighth Workshop on Vitamin D, Paris, France, July 1991. See: Mouriño, A.; Granja, J.; Mascareñas, J. L.; Sarandeses, L.; Torneiro, M.; Maestro, M.; Fall, Y.; Castedo, L. Vitamin D - Gene Regulation, Structure-Function Analysis and Clinical Application, Norman, A. W., Bouillon, R., Thomasset, M., Eds.; Walter de Gruyter: New York-Berlin, 1991; p 199.

(1) For reviews, see: (a) Holick, M. F. 1α,25-(OH)$_2$-D$_3$, a Novel Hormone with Unlimited Potential. *Kidn. Int.* **1987**, *32*, 912-929. (b) Ostream, V. K.; DeLuca, H. F. *Steroids* **1987**, *49*, 73-102.

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(3) Cota, J. G.; Meilán, M. C.; Mouriño, A.; Castedo, L. *J. Org. Chem.* **1988**, *53*, 6094.

(4) The hydroxyl groups of **2a** and **2b** have the same orientation as the 1α-OH of **1**. See: Wecksler, W. R.; Norman, A. W. *Methods Enzymol.* **1980**, *67*, 494.

(5) Norman, A. W. *Vitamin D, The Calcium Homeostatic Hormone*; Academic Press: New York, 1979.

(6) For other approaches to the dihydrotachysterol diene system see: Solladié, G.; Hutt, J. *J. Org. Chem.* **1987**, *52*, 3560 and references cited therein.

(7) The Wittig-Horner coupling approach for the synthesis of vitamin D metabolites was first described by: Lythgoe, B. *Chem. Soc. Rev.* **1981**, 449.

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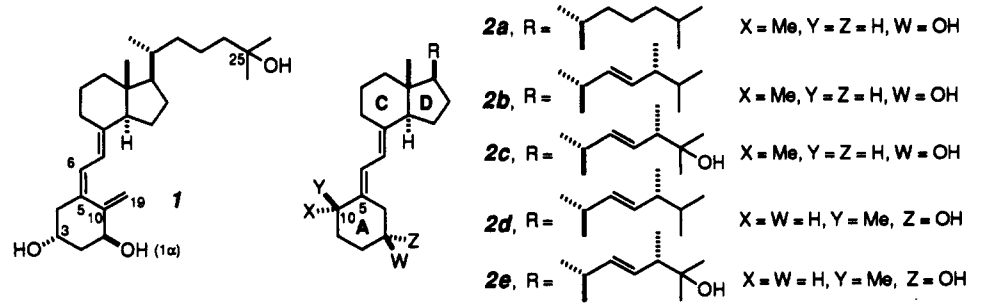
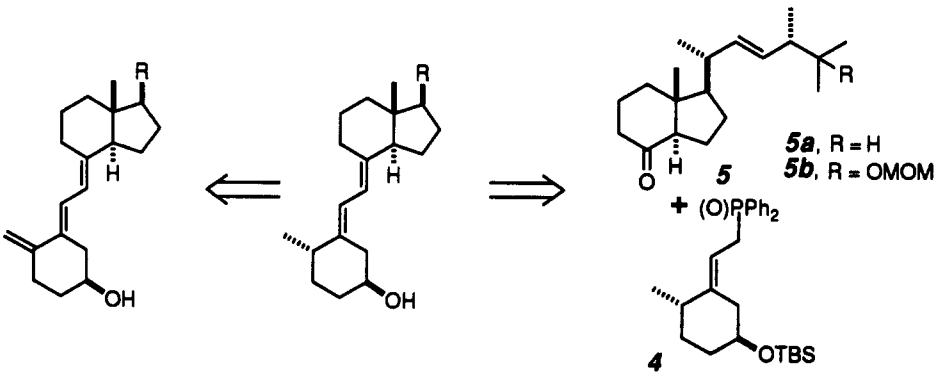
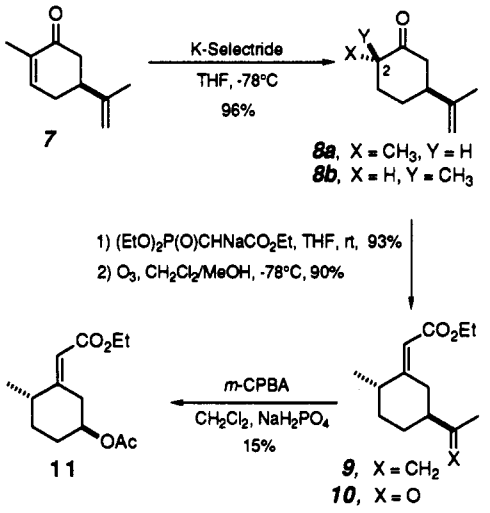


Figure 1.

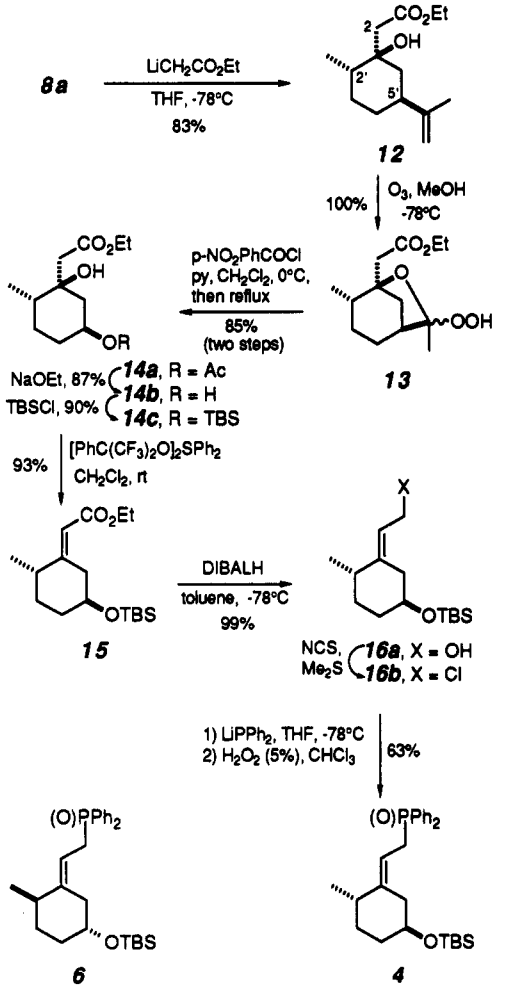
Scheme I



Scheme II



Scheme III



mercially available (+)-(*S*)-carvone (**7**)[8] as follows. Compound **7** was converted on a multigram scale into the known[9] dihydrocarvones **8a** (79%) and **8b** (17%) following Ganem's procedure.[10] Initially, we attempted to synthesize **11**, the acetate precursor of **4**, through the steps depicted in Scheme II.[11]

Unfortunately, the Baeyer–Villiger buffered oxidation of the methyl ketone moiety of **10** took place in low yield (10–15%) due to the presence of the conjugated double bond. This result led us to undertake the alternative route depicted in Scheme III, in which the conjugated double bond is introduced after the acetoxy group.

(8) This compound has already been used for the synthesis of the A-ring precursor of important vitamin D metabolites, see: (a) Castedo, L.; Mascareñas, J. L.; Mouriño, A. *Tetrahedron Lett.* **1987**, *28*, 2099. (b) Hatakeyama, S.; Numata, H.; Osanai, K.; Takano, S. *J. Org. Chem.* **1989**, *54*, 3515.

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(11) While this manuscript was in preparation a related synthesis of **11** using this route has appeared: Rookhuizen, R. B.; Hanekamp, J. C.; Bos, H. J. T. *Tetrahedron Lett.* **1992**, *33*, 1633. However, after several attempts we have not been successful in carrying out the transformation **9** → **11** using the Criegee rearrangement.

Reaction of **8a** with the α-carbanion of EtOAc[12] gave the tertiary alcohol **12** (83%) and its C-1′ epimer (12%).[13] The absence of the C-2 epimer was demonstrated by subjecting **8b** to the same reaction conditions, upon which two different tertiary alcohols were obtained. The stereochemistry of **12** was established in the next step, in which, interestingly and serendipitously, ozonolysis in MeOH[14] yielded a 1:1 ratio of the hydroperoxy ketals **13** (100%) through intramolecular attack by the tertiary hydroxyl group (we had expected intermolecular attack by MeOH[15] on the preformed ozonide). Acylation of **13** with 4-nitrobenzoyl chloride[14] and subsequent Criegee rearrangement[16] gave the desired acetate **14a** (85%).

Deprotection of **14a** (NaOEt, EtOH) and reprotection (TBSCl, imidazole) afforded the *tert*-butyldimethylsilyl ether **14c** (90% over the two steps), but the reaction of the mesylate of **14c** with LDA, instead of affording **15**, yielded a complex mixture including *E* and *Z* isomers and starting mesylate; the cause of this behavior is attributed to the equatorial orientation of the nucleofuge. Attempts to lock the leaving group in the axial orientation through ketal or methyl orthoformate formation via **14b** were also unsuccessful. Finally, dehydration of **14c** via an E1 mechanism[17] using Martin's sulfurane succeeded in giving the (*E*)-α,β-unsaturated ester **15** (93%). The stereochemistry of the α,β-unsaturated ester moiety was confirmed by comparison of its acetate with the same compound as prepared by the low-yielding route of Scheme II.

Reduction of **15** with DIBALH afforded the allyl alcohol **16a** (99%), which was transformed into the desired phosphine oxide **4** by a known sequence (NCS, Me_2S; $LiPPh_2$; H_2O_2, 63%)[18] (10 steps, 32% overall yield). The synthesis of **6** was effected by the same sequence of reactions starting from commercially available (+)-(2*R*,5*R*)-dihydrocarvone.

Synthesis of Dihydrotachysterol$_2$ (DHT$_2$, 2b) and Related Compounds. We next investigated the feasibility of the proposed convergent synthesis of dihydrotachysterols (Scheme I). Reaction of **4** with *n*-BuLi gave the corresponding α-anion, which was coupled with the ketone **5a** to provide, after deprotection (*n*-Bu_4NF), the desired dihydrotachysterol$_2$ (DHT$_2$, **2b**, 74%, two steps, Figure 1), as was confirmed by comparison (^1H and ^{13}C NMR, UV, and TLC) with an authentic sample.[3] Similarly, coupling the α-anion of **4** with ketone **5b** followed by deprotection (AG-50WX4 ion-exchange resin) gave 25-hydroxydihydrotachysterol$_2$[19] (25-OH-DHT$_2$, **2c**, 84%). The phosphine oxide **6** was used to prepare the new dihydrovitamins **2d** (70%) and **2e** (80%).

In conclusion, an efficient convergent approach to dihydrotachysterol and related dihydrovitamins D has been developed. Further applications of this method to the preparation of other side-chain-modified derivatives of DHT$_2$ and DHT$_3$ is underway, as is the biological testing of the compounds already prepared.

Experimental Section

General Procedures. NMR spectra were recorded at 250, 300, or 400 MHz for ^1H (δ, Me_4Si, $CDCl_3$ except otherwise stated) and 62.83, 75.73, or 100.63 MHz for ^{13}C (δ, $CDCl_3$, carbon multiplicities assigned by DEPT techniques) except when otherwise stated. Low-resolution and high-resolution electron impact mass spectrum data (EI-LRMS and EI-HRMS) were obtained at 70 eV unless otherwise stated. Optical rotations were measured with Na 589-nm irradiation at 20 °C. Melting points are uncorrected. Kugelrohr distillation oven temperatures (ot) refer to the external air bath temperature. Silica gel flash chromatography purifications were performed on silica gel (230–400 mesh) as described by Stille.[20] Ozone was generated in a laboratory ozonizer. TLC was performed on plates of silica gel (2 × 5 cm, 0.2-mm thickness). Components were located by observation of the plates under UV light and/or by treating the plates with a phosphomolybdic acid reagent followed by heating. All reactions were performed under dry, deoxygenated argon except when otherwise stated. All glassware was dried at 150 °C overnight, assembled hot, and allowed to cool in a stream of dry argon. All transfers of liquid solutions and solvents were performed by syringe techniques or via a cannula. All solvents were freshly distilled from the appropriate drying agent before use. Et_2O, THF, toluene, and benzene were distilled from sodium benzophenone ketyl under argon. CCl_4 and CH_2Cl_2 were distilled from P_2O_5 under argon. Pyridine was distilled first from KOH and later from CaH_2 under argon. DMF was distilled from P_2O_5 under reduced pressure and stored over 4-Å molecular sieves. EtOAc, hexanes, and Me_2S were distilled from CaH_2 under nitrogen. Diisopropylamine was distilled twice from CaH_2 under nitrogen and stored over 4-Å molecular sieves. MeOH was distilled from Mg under argon. *m*-CPBA was crystallized from CH_2Cl_2.[21] Concentrations were carried out in a rotatory evaporator. Drying was carried out with anhydrous Na_2SO_4. All the new compounds exhibited satisfactory low-resolution MS data as well as combustion analysis or appropriate exact mass data of the molecular ions.

(−)-(2*S*,5*S*)-Dihydrocarvone (8a) and (−)-(2*R*,5*S*)-Dihydrocarvone (8b). A solution of (+)-(*S*)-carvone (**7**, 7.06 g, 47 mmol) in THF (40 mL) was cooled at −78 °C under argon and, after 5 min, a solution of potassium tri-*sec*-butylborohydride in THF (K-Selectride, 47 mL, 1 M, 47 mmol) was added dropwise. The solution was stirred for 1 h at −78 °C and 15 min at rt and transferred to an Erlenmeyer flask containing NaOH (10%, 130 mL). An aqueous solution of H_2O_2 (30%, 100 mL) was carefully added via a syringe (**CAUTION**: gas evolution), and the mixture was stirred for 3 h. The aqueous phase was extracted with EtOAc/hexanes (3 × 20 mL), and the combined organic layers were washed with an aqueous solution of Na_2SO_3 (50 mL), dried, and filtered. Concentration afforded an oil which was purified by MPLC (silica gel 230–400 mesh, 5 × 60 cm, 2% EtOAc/hexanes) to afford **8a** (5.72 g, 79%) and its epimer **8b** (1.14 g, 17%) as colorless oils.

Compound 8a: $[\alpha]_D$ = −16.5° (neat); ^1H NMR (250 MHz) δ 4.75 (2 H, m, H2′), 1.74 (3 H, br s, CH_3-C1′), 1.04 (3 H, d, J = 6.5 Hz, CH_3-C2); ^{13}C NMR (62 MHz) δ 212.7, 147.7, 109.6, 47.0, 46.8, 44.7, 34.9, 30.7, 20.4, 14.2; IR (film) 3090 (=CH, w), 1720 (C=O, s), 1650 (C=C, m) cm^{-1}.

Compound 8b: ^1H NMR (250 MHz) δ 4.83 (1 H, br s, H2′), 4.70 (1 H, br s, H2′), 1.73 (3 H, br s, CH_3-C1′), 1.09 (3 H, d, J = 6.9 Hz, CH_3-C2); ^{13}C NMR (62 MHz) δ 213.9, 146.9, 111.4, 44.5, 44.0, 43.8, 30.5, 26.2, 21.4, 15.4; IR (film) 3090 (=CH, w), 1710 (C=O, s), 1640 (C=C, m) cm^{-1}.

(2*E*)-Ethyl [(2′*S*,5′*S*)-2′-Methyl-5′-(1″-methylethenyl)-cyclohexylidene]ethanoate (9). NaH (2 g, 80% in paraffin, 69 mmol) was placed in a flask, washed with dry hexanes (3 × 20

(12) Bruderer, H.; Knopp, D.; Daly, J. J. *Helv. Chim. Acta* **1977**, *60*, 1935.

(13) Reaction of **8a** with $BrZnCH_2CO_2Et$ or 2-(lithiomethyl)-1,3-dioxane was unsuccessful.

(14) Anhydrous conditions were important to avoid ketone formation.

(15) For an example of intermolecular trapping of an ozonide with MeOH, see: Schreiber, S. L.; Liew, W. *Tetrahedron Lett.* **1983**, *24*, 2363.

(16) (a) Criegee, R. *Ann.* **1948**, *560*, 127. (b) Hedaya, E.; Winsteid, S. *J. Am. Chem. Soc.* **1967**, *89*, 1661. (c) Baggiolini, E. G.; Hennessy, B. M.; Iacobelli, J. A.; Uskokovic, M. R. *Tetrahedron Lett.* **1987**, *28*, 2095.

(17) Arhart, R. J.; Martin, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 5003. See also: *Aldrichimica Acta* **1985**, *18*, 81.

(18) Mascareñas, J. L.; Mouriño, A.; Castedo, L. *J. Org. Chem.* **1986**, *51*, 1269 and references cited therein.

(19) For more complicated route to this compound see: Rookhuizen, R. B.; Bosch, R.; Castedo, L.; Cota, J. G.; Granja, J.; Maestro, M. A.; de Marigorta, E. M.; Mouriño, A. *Vitamin D, Molecular, Cellular and Clinical Endocrinology*; Norman, A. W., Schaefer, K., Grigoleit, H.-G., Herrath, D. v., Eds.; Walter de Gruyter: Berlin–New York, 1988; p 68. This compound was isolated from rats as a hydroxylated metabolite of DHT$_2$: Bosch, R.; Versluis, C.; Terlouw, J. K.; Thijssen, J. H. H.; Duursma, S. A. *J. Steroid Biochem.* **1985**, *23*, 223. Unpublished results show that this compound is more active than the clinically still used DHT$_2$.

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(21) Taylor, T. D.; Miksztal, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 2270.

mL), and decanted, and liquids were removed with a syringe. THF (35 mL) was added, and the suspension was cooled to 0 °C. $(EtO)_2P(O)CH_2CO_2Et$ (14.13 g, 12.5 mL, 63 mmol) was added dropwise. The reaction mixture was stirred at 40 °C for 5 min and 30 min at rt. A solution of **8a** (4.2 g, 27.63 mmol) in THF (10 mL) was added dropwise. The reaction was stirred for 48 h at rt. It was poured into aqueous saturated solution of $NaHCO_3$ (100 mL). The organic phase was washed with aqueous $NaHCO_3$ (3 × 30 mL) and brine (2 × 10 mL), dried, filtered, and concentrated. The resulting oil was purified by flash column chromatography (30 × 3 cm, hexanes) to give 5.7 g of **9** [93%, R_f = 0.8 (20% EtOAc/hexanes)]: ^{1}H-NMR (250 MHz) δ 5.57 (1 H, s, H1), 4.73 (2 H, s, H2″), 4.15 (2 H, q, J = 7.2 Hz, OCH_2), 4.00 (1 H, dt, J = 12.5, 2 Hz, H6′α), 1.75 (3 H, s, CH_3-C1″), 1.28 (3 H, t, J = 7.2 Hz, OCH_2CH_3), 1.06 (3 H, d, J = 6.5 Hz, CH_3-C2″); ^{13}C-NMR (62 MHz) δ 167.3, 165.8, 149.3, 110.9, 108.8, 59.5, 47.0, 39.5, 36.8, 35.5, 31.5, 20.8, 17.8, 14.3; IR (film) 3080 (=CH, w), 1720 (C=O, s) cm^{-1}.

(2*E*)-Ethyl [(2′*S*,5′*S*)-5′-Acetyl-2′-methylcyclohexylidene]ethanoate (10). A solution of the hydroxy ester **9** (0.4 g, 1.8 mmol) in dry CH_2Cl_2 (25 mL) and dry methanol (10 mL) was placed in a dry ozonation vessel (three-necked round-bottom flask) provided with a magnetic stirring bar. The solution was cooled to −78 °C while being purged with nitrogen. The nitrogen flow as replaced by a slow stream of ozone until the solution turned gray-blue (~8 min). The ozone was replaced by nitrogen until no ozone remained in solution (KI test, ~1 h). $(EtO)_3P$ (2 mL) was added carefully, and the solution was allowed to reach rt. Concentration gave a residue that was flash chromatographed (15 × 1.5 cm, eluent: 1% EtOAc/hexanes) to afford 0.363 g of **10** [90%, R_f = 0.4 (20% EtOAc/hexanes)]: ^{1}H-NMR (250 MHz) δ 5.62 (1 H, s, H2), 4.15 and 4.10 (2 H, q, J = 7.2 Hz, and 1 H, dt, J = 12.5, 1.3 Hz, overlapped OCH_2 and H6′α), 2.20 (3 H, s, CH_3CO), 1.30 (3 H, t, J = 7.2 Hz, OCH_2CH_3), 1.08 (3 H, d, J = 6.5 Hz, CH_3-C2′); ^{13}C-NMR (62 MHz) δ 210.5, 167.1, 141, 111.9, 59.7, 52.5, 39.1, 36.1, 32.5, 28.8, 27.9, 17.7, 14.2; IR (film) 1715 (C=O, s) cm^{-1}.

(2*E*)-Ethyl [(2′*S*,5′*S*)-5′-Acetoxy-2′-methylcyclohexylidene]ethanoate (11). A solution of *m*-CPBA[21] (0.37 g, 2.14 mmol) in $CHCl_3$ (3.5 mL) was cooled at 0 °C, and a solution of **10** (0.12 g, 0.53 mmol) in $CHCl_3$ (1.5 mL) and KH_2PO_4 (0.6 g) were added. The suspension was stirred for 96 h at rt. An aqueous saturated solution of Na_2SO_3 (10 mL) was added, and the mixture was stirred overnight. The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase was washed with water (2 × 5 mL), an aqueous saturated solution of $NaHCO_3$ (3 × 5 mL), and brine (2 × 5 mL), dried, filtered, and concentrated. The residue was purified by flash column chromatography (10 × 1.5 cm, 0.5% EtOAc/hexanes) to give 18 mg of **11** [15%, R_f = 0.5 (20% EtOAc/hexanes), colorless liquid]: ^{1}H-NMR (250 MHz) δ 5.67 (1 H, s, H2), 4.77 (1 H, tt, J = 10.1, 4.3 Hz, H5′), 4.16 (2 H, q, J = 7.1 Hz, OCH_2), 3.90 (1 H, ddd, J = 11.3, 4.3, 1.7 Hz, H6′α), 2.03 (3 H, s, CH_3CO_2), 1.28 (3 H, t, J = 7.1 Hz, OCH_2CH_3), 1.09 (3 H, d, J = 6.6 Hz, CH_3-C2′); ^{13}C-NMR (62 MHz) δ 170.2, 166.7, 160.6, 113.9, 72.5, 59.8, 38.6, 34.5, 32.1, 30.3, 21.2, 17.5, 14.2; IR (film) 1745 (C=O, s), 1720 (C=O, s) cm^{-1}; UV (EtOH 95%) λ_{max} 218 nm (ε 10000).

Ethyl [(1′*R*,2′*S*,5′*S*)-1′-Hydroxy-2′-methyl-5′-(1″-methylethenyl)cyclohexyl]ethanoate (12) and Its Epimer at C-1′. A solution of lithium hexamethyldisilazane (LHMDS) was prepared by adding *n*-BuLi (14.67 mL, 2.28 M in hexanes, 33.46 mmol) to a solution of hexamethyldisilazane (7 mL, 33.5 mmol) in Et_2O (30 mL) at 0 °C. After 10 min the suspension was allowed to reach rt and then refluxed for 30 min. The solvents were removed by distillation. The white solid was dissolved in THF (30 mL) and cooled to −78 °C. A solution of dry EtOAc (3 mL, 30.78 mmol) in Et_2O (30 mL) was added dropwise. The solution was stirred for 40 min. A solution of dihydrocarvone **8a** (4.075 g, 26.77 mmol) in Et_2O (10 mL) was added. The solution was stirred for 1 h, allowed to come to rt, and stirred for 10 h. The reaction was quenched by the addition of H_2O (7 mL). The mixture was poured into brine (100 mL). The organic phase was washed with brine (3 × 30 mL), and the combined aqueous extracts were extracted with Et_2O (2 × 10 mL). The combined organic layers were dried, filtered, and concentrated. The residue was flash chromatographed (3 × 30 cm, 2% EtOAc/hexanes) to afford 6.68 g of **12** [83%, R_f = 0.77 (25% EtOAc/hexanes), ot 92 °C (6 mmHg), colorless oil] and 0.97 g of its C-1′ epimer [12%, R_f = 0.70 (25% EtOAc/hexanes), colorless oil].

Compound 12: $[\alpha]_D$ = −2.61° (c = 5.6, $CHCl_3$); ^{1}H NMR (400 MHz) δ 4.67 (2 H, m, H2″), 4.18 (2 H, q, J = 7.1 Hz, OCH_2), 2.72 (1 H, d, J = 15.2 Hz, H2), 2.26 (1 H, d, J = 15.2 Hz, H2), 1.70 (3 H, t, J = 1 Hz, CH_3-C1″), 1.28 (3 H, J = 7.1 Hz, OCH_2CH_3), 0.93 (3 H, d, J = 6.7 Hz, CH_3-C2′); ^{13}C NMR (100 MHz) δ 173.4, 150.2, 108.4, 71.9, 60.7, 44.4, 42.6, 39.80, 39.76, 31.5, 30.4, 21.0, 15.4, 14.2; IR (film) 3520 (OH, br), 3080 (=CH, w), 1715 (C=O, s), 1650 (C=C, m) cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.71; H, 10.05.

Epimer of 12: ^{1}H NMR (250 MHz) δ 4.61 (2 H, m, H2″), 4.12 (2 H, dq, J = 7.1, 4.5 Hz, OCH_2), 2.50 (1 H, d, J = 14.9 Hz, H2), 2.38 (1 H, dd, J = 14.9, 1.5 Hz, H2), 1.62 (3 H, br s, CH_3-C1″), 1.21 (3 H, J = 7.1 Hz, OCH_2CH_3), 0.86 (3 H, d, J = 6.6 Hz, CH_3-C2′); ^{13}C NMR (62 MHz) δ 173.6, 148.9, 108.6, 73.3, 60.5, 43.7, 42.5, 41.3, 36.3, 31.2, 30.9, 20.4, 14.7, 14.0; IR (film) 3520 (OH, br), 3080 (=CH, w), 1720 (C=O, s), 1645 (C=C, m) cm^{-1}.

Ethyl [(1′*R*,2′*R*,5′*S*)-1′-Hydroxy-2′-methyl-5′-(1″-methylethenyl)cyclohexyl]ethanoate and Its Epimer at C-1′. These compounds were prepared as above in 78% and 17% yields, respectively, starting from (−)-(2*R*,5*S*)-dihydrocarvone (**8b**).

Ethyl [(1′*R*,2′*R*,5′*S*)-1′-hydroxy-2′-methyl-5′-(1″-methylethenyl)cyclohexyl]ethanoate: ^{1}H NMR (250 MHz) δ 4.69 (2 H, m, H2″), 4.15 (2 H, qd, J = 7.1, 1.2 Hz, OCH_2), 2.72 and 2.64 (2 H, AB system, J = 15.4 Hz, H2), 1.70 (3 H, m, CH_3-C1″), 1.26 (3 H, J = 7.1 Hz, OCH_2CH_3), 1.02 (3 H, d, J = 7.1 Hz, CH_3-C2′); ^{13}C NMR (62 MHz) δ 173.2, 149.2, 108.8, 73.1, 60.6, 42.6, 42.1, 37.1, 36.9, 29.5, 24.7, 20.1, 14.1, 13.5.

Epimer at C-1′: ^{1}H NMR (250 MHz) δ 4.68 (2 H, m, H2″), 4.17 (2 H, dq, J = 7.1, 2.5 Hz, OCH_2), 2.47 and 2.39 (2 H, AB system, J = 15.7 Hz, H2), 1.70 (3 H, t, J = 1.1 Hz, CH_3-C1″), 1.28 (3 H, J = 7.2 Hz, OCH_2CH_3), 0.92 (3 H, d, J = 7.3 Hz, CH_3-C2′); ^{13}C NMR (62 MHz) δ 173.1, 150.3, 108.4, 73.2, 60.6, 44.2, 39.5, 37.1, 36.7, 28.2, 24.8, 20.9, 15.6, 14.0.

Ethyl [(1′*S*,2′*S*,5′*S*)-6-Hydroperoxy-2′,6′-dimethylbicyclo[3.2.1]-7′-oxaoctyl]ethanoate (13). A solution of the hydroxy ester **12** (1.60 g, 6.67 mmol) in dry methanol (100 mL, HPLC grade) was placed in a dry ozonation vessel (three-necked round-bottom flask) provided with a magnetic stirring bar. The solution was cooled to −78 °C while being purged with nitrogen. The nitrogen flow was replaced by a slow stream of ozone until the solution turned gray-blue (~30 min). The ozone was replaced by nitrogen until no ozone remained in solution (KI test, ~1 h). The solution was allowed to reach rt. Concentration in the same reaction flask under anhydrous conditions (argon, vacuum pump) afforded, after high-vacuum drying, the crude hydroperoxy ketals **13** [100%, R_f = 0.32 (30% EtOAc/hexanes), colorless oil] which were used directly in the next reaction: ^{1}H NMR (250 MHz, CD_2Cl_2) δ 4.11 (2 H, q, J = 7.1 Hz, OCH_2), 3.20 (3 H, d, J = 2 Hz, CH_3-C1″), 2.63 (1 H, d, J = 15.2 Hz, H2), 2.23 (1 H, d, J = 15.2 Hz, H2), 1.21 (3 H, J = 7.1 Hz, OCH_2CH_3), 0.85 (3 H, d, J = 6.7 Hz, CH_3-C2′): ^{13}C NMR (62 MHz, CD_2Cl_2) δ 173.7, 108.1, 92.9, 72.2, 61.0, 48.9, 44.8, 40.2, 39.1, 37.6, 30.5, 27.7, 15.7, 14.3; IR (film) 3420 (OOH, br), 1710 (C=O, s) cm^{-1}.

Ethyl [(1′*R*,2′*S*,5′*S*)-5′-Acetoxy-1′-hydroxy-2′-methylcyclohexyl]ethanoate (14a). In the same three-necked round-bottom flask was prepared a solution of the crude hydroperoxy ketals **13** (1.8 g, 6.92 mmol) and DMAP (trace) in CH_2Cl_2 (100 mL). The solution was cooled to 0 °C. A solution of 4-nitrobenzoyl chloride (3.71 g, 20 mmol, purified twice by high vacuum pump distillation) in CH_2Cl_2 (80 mL) and a solution of pyridine (2.37 g, 2.5 mL, 30 mmol) in CH_2Cl_2 (50 mL) were successively added. The solution was stirred for 1 h at 0 °C and for 2 h at rt and then refluxed smoothly for 12 h. The mixture was poured into a saturated aqueous solution of $NaHCO_3$ (200 mL) and extracted with CH_2Cl_2 (5 × 20 mL). The combined organic layers were dried, filtered, and concentrated. The residue was flash chromatographed (3 × 30 cm, 6% EtOAc/hexanes) to give 1.42 g of **14a** [85% (two steps), R_f = 0.60 (30% EtOAc/hexanes), colorless oil, $[\alpha]_D$ = −16.77° (c = 1.3, $CHCl_3$)]; ^{1}H NMR (400 MHz) δ 5.05 (1 H, tt, J = 11.2, 4.5 Hz, H5′), 4.18 (2 H, q, J = 7.1 Hz OCH_2), 2.68 (1 H, d, J = 15.3 Hz, H2), 2.29 (1 H, d, J = 15.2 Hz, H2), 2.01 (3 H, s, CH_3CO_2), 1.28 (3 H, J = 7.1 Hz, OCH_2CH_3), 0.93 (3 H, d, J = 6.7 Hz, CH_3-C2′); ^{13}C NMR (100

MHz) δ 172.9, 170.4, 72.6, 70.4, 60.8, 44.2, 42.3, 39.3, 31.5, 28.2, 23.8, 14.6, 14.2; IR (film) 3510 (OH, br), 1735 (C=O, s), 1715 (C=O, s) cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.19; H, 8.64.

Ethyl [(1′*R*,2′*S*,5′*S*)-1′,5′-Dihydroxy-2′-methylcyclohexyl]ethanoate (14b). An ethanolic solution of NaOEt (0.2 M, 52 mL) was added dropwise to a 0 °C stirred solution of the hydroxy acetate **14a** (0.90 g, 3.47 mmol) in EtOH (15 mL). The mixture was stirred for 3 h. Glacial acetic acid was added until pH = 6. The mixture was filtered and concentrated. The residue was purified by flash chromatography (2 × 15 cm, 25% EtOAc/hexanes) to afford 0.655 g of **14b** [87%, R_f = 0.50 (80% EtOAc/hexanes), colorless oil, $[\alpha]_D$ = +4.25° (*c* = 1.2, $CHCl_3$)]; ^{1}H NMR (400 MHz) δ 4.18 (2 H, q, *J* = 7.1 Hz, OCH_2), 3.97 (1 H, tt, *J* = 11.1, 4.4 Hz, H5′), 2.68 (1 H, d, *J* = 15.2 Hz, H2), 2.28 (1 H, d, *J* = 15.2 Hz, H2), 1.29 (3 H, *J* = 7.1 Hz, OCH_2CH_3), 0.92 (3 H, d, *J* = 6.6 Hz, CH_3-C2′); ^{13}C NMR (100 MHz) δ 173.4, 72.8, 67.2, 60.8, 46.2, 44.2, 39.3, 35.4, 28.6, 14.2, 13.2; IR (film) 3410 (OH, br), 1715 (C=O, s) cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.03; H, 9.46.

Ethyl [(1′*R*,2′*S*,5′*S*)-5′-[(*tert*-Butyldimethylsilyl)oxy]-1′-hydroxy-2′-methylcyclohexyl]ethanoate (14c). A solution of **14b** (0.595 g, 2.75 mmol) in DMF (25 mL) was treated with TBSCl (0.835 g, 5.5 mmol) and imidazole (0.758 g, 11.11 mmol). The solution was stirred in the dark for 24 h and then poured into ice–water. The mixture was extracted with EtOAc (5 × 15 mL). The combined organic extracts were washed with water (2 × 10 mL), dried, filtered, and concentrated. The oily residue was purified by flash chromatography (2 × 20 cm, 1% EtOAc/hexanes) to give 0.818 g of **14c** [90%, R_f = 0.60 (10% EtOAc/hexanes), colorless oil, $[\alpha]_D$ = −7.63° (*c* = 2.15, $CHCl_3$)]; ^{1}H NMR (400 MHz) δ 4.18 (2 H, dq, *J* = 7.1, 2.6 Hz, OCH_2), 3.95 (1 H, tt, *J* = 10.7, 4.4 Hz, H5′), 2.66 (1 H, d, *J* = 15.3 Hz, H2), 2.27 (1 H, d, *J* = 15.2 Hz, H2), 1.29 (3 H, *J* = 7.1 Hz, OCH_2CH_3), 0.90 (3 H, d, *J* = 6.7 Hz, CH_3-C2′), 0.87 [9 H, s, $(CH_3)_3C$], 0.049 (3 H, s, CH_3Si), 0.045 (3 H, s, CH_3Si); ^{13}C NMR (75 MHz) δ 173.5, 72.9, 67.9, 60.7, 46.6, 44.2, 39.3, 35.6, 28.6, 25.9, 18.2, 14.7, 14.2, −4.5, −4.6; IR (film) 3510 (OH, br), 1715 (C=O, s) cm^{-1}. Anal. Calcd for $C_{17}H_{34}O_4Si$: C, 61.76; H, 10.39. Found: C, 61.89; H, 10.50.

(2*E*)-Ethyl [(2′*S*,5′*S*)-5′-[(*tert*-Butyldimethylsilyl)oxy]-2′-methylcyclohexylidene]ethanoate (15). A solution of **14c** (1.0 g, 3.03 mmol) in CCl_4 (15 mL) was rapidly added to a stirred solution of [bis[2,2,2-trifluoro-1-phenyl-1-(trifluoromethyl)ethoxy]diphenylsulfurane (2.5 g, 3.71 mmol) in CCl_4 (100 mL) at rt. The reaction mixture was stirred for 70 h and poured into water (1 × 50 mL). The organic phase was washed with brine (1 × 50 mL), dried, filtered, and concentrated. The crude product was purified by flash chromatography (2 × 20 cm, hexanes) to afford **15** [0.878 g, 93%, R_f = 0.80 (10% EtOAc/hexanes), colorless oil, $[\alpha]_D$ = −14.16° (*c* = 1.6, $CHCl_3$)]: ^{1}H NMR (400 MHz) δ 5.59 (1 H, br s, H2), 4.16 (2 H, q, *J* = 7.1 Hz, OCH_2), 3.90 (1 H, ddd, *J* = 12.5, 4.2, 1.7 Hz, H6′α), 1.28 (3 H, *J* = 7.1 Hz, OCH_2CH_3), 1.05 (3 H, d, *J* = 6.6 Hz, CH_3-C2′), 0.89 [9 H, s, $(CH_3)_3C$], 0.09 (3 H, s, CH_3Si), 0.08 (3 H, s, CH_3Si); ^{13}C NMR (100 MHz) δ 167.0, 162.5, 112.5, 71.8, 59.7, 39.4, 38.8, 35.0, 32.8, 25.9, 18.2, 17.6, 14.4, −4.6, −4.9; IR (film) 1715 (C=O, s), 1645 (C=C, s) cm^{-1}; UV (EtOH 95%) λ_{max} 223 nm (ε 14 500). Anal. Calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.52; H, 10.59. The stereochemistry of the α,β-unsaturated ester moiety was established by ^{1}H NMR nOe difference experiments between the vinylic proton and the exocyclic methyl group.

(2*E*)-2-[(2′*S*,5′*S*)-5′-[(*tert*-Butyldimethylsilyl)oxy]-2′-methylcyclohexylidene]ethanol (16a). A solution of DIBALH in toluene (6.5 mL, 1.2 M, 7.8 mmol) was slowly added (ca. 10 min) to a −78 °C cooled solution of **15** (0.80 g, 2.56 mmol) in toluene (20 mL). The solution was stirred for 1 h and then poured into a stirred aqueous solution of potassium sodium tartrate (1 M, 150 mL). The mixture was stirred for 30 min. The aqueous phase was extracted with EtOAc (5 × 10 mL). The combined organic extracts were washed with water (1 × 50 mL) and brine (1 × 50 mL), dried, and filtered. Concentration gave an oil that was flash chromatographed (2 × 20 cm, 5% EtOAc/hexanes) to give 0.684 g of **16a** [99%, R_f = 0.50 (20% EtOAc/hexanes), colorless oil, $[\alpha]_D$ = +14.27° (*c* = 4.1, $CHCl_3$)]: ^{1}H NMR (400 MHz) δ 5.40 (1 H, br t, *J* = 7 Hz, H2), 3.56 (1 H, tt, *J* = 9.9, 4.2 Hz, H5′), 1.03 (3 H, d, *J* = 6.2 Hz, CH_3-C2′), 0.89 [9 H, s, $(CH_3)_3C$], 0.07 (3 H, s, CH_3Si), 0.06 (3 H, s, CH_3Si); ^{13}C NMR (100 MHz) δ 144.8, 119.8, 71.8, 58.8, 38.7, 37.4, 35.1, 33.0, 25.9, 18.2, 17.7, −4.6, −4.7; IR (film) 3335 (OH, br), 1655 (C=C, w) cm^{-1}. Anal. Calcd for $C_{15}H_{30}O_2Si$: C, 66.61; H, 11.18. Found: C, 66.60; H, 11.28.

(2*E*)-[2-[(2′*S*,5′*S*)-5′-[(*tert*-Butyldimethylsilyl)oxy]-2′-methylcyclohexylidene]ethyl]diphenylphosphine Oxide (4). A mixture of NCS (1.42 g, 10.65 mmol, crystallized from benzene and high vacuum dried) in CH_2Cl_2 (30 mL) and DMF (30 mL) was stirred at rt for 10 min. The resulting solution was cooled to 0 °C followed by the slow addition of dimethyl sulfide (1.56 mL, 21.29 mmol). The resulting white precipitate was stirred for 15 min and then cooled to −25 °C. A solution of the allylic alcohol **16a** (1.15 g, 4.26 mmol) in CH_2Cl_2 (30 mL) was added. The resulting solution was warmed to 0–10 °C (2 h) and poured into a separatory funnel containing ice-cold brine. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried, filtered, and concentrated without heating. The crude allylic chloride **16b** was used immediately without purification. A solution of *n*-BuLi in hexanes (7 mL, 1.52 M, 10.65 mmol) was added to a −10 °C cooled solution of diphenylphosphine (1.98 g, 1.85 mL, 10.65 mmol) in THF (40 mL). The resulting red solution was stirred at 0 °C for 30 min and slowly added to a −60 °C cooled solution of the above crude allylic chloride **16b** in THF (50 mL). The pale yellow solution was further stirred for 1 h and then quenched by the addition of one drop of water. Concentration afforded a residue that was diluted with $CHCl_3$ (60 mL). The solution was transferred to a separatory funnel and vigorously shaken with an aqueous solution of H_2O_2 (200 mL, 5%) for 1 h. The organic layer was washed with an aqueous solution of Na_2SO_3 (10%, 100 mL), dried, filtered, and concentrated. The crude product was purified by flash chromatography (2 × 20 cm, 25% EtOAc/hexanes) to afford 1.22 g of the phosphine oxide **4** [63% (3 steps), R_f = 0.38 (40% EtOAc/hexanes), mp = 76.7–77.6 °C, white powder, $[\alpha]_D$ = −1.54° (*c* = 2.4, $CHCl_3$)]: ^{1}H NMR (400 MHz) δ 7.76–7.68 (4 H, m, Ar), 7.56–7.43 (6 H, m, Ar), 5.21 (1 H, dd, *J* = 14.3, 7.7 Hz, H2), 3.27 (1 H, tt, *J* = 10.2, 4.4 Hz, H5′), 0.92 (3 H, d *J* = 6.6 Hz, CH_3-C2′), 0.87 [9 H, s, $(CH_3)_3C$], 0.03 (3 H, s, CH_3Si), 0.02 (3 H, s, CH_3Si); ^{13}C NMR (100 MHz) δ 145.5, 133.2, 132.2, 131.7, 131.2, 128.5, 108.8, 71.3, 38.9, 37.6, 35.4, 33.1, 30.4, 25.9, 18.1, 17.7, −4.3, −4.6; IR ($CHCl_3$) 3060 (=CH, w), 1655 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 204 nm (ε 43 000), λ_{sh} 220 nm (ε 26 500). Anal. Calcd for $C_{27}H_{39}O_2PSi$: C, 71.33; H, 8.65. Found: C, 71.33; H, 8.82.

Preparation of the Phosphine Oxide 6. This compound (enantiomer of **4**) was prepared as described above starting from (+)-(2*R*,5*R*)-dihydrocarvone.

Dihydrotachysterol$_2$ *tert*-Butyldimethylsilyl Ether. A solution of *n*-BuLi in hexanes (0.25 mL, 1.52 M, 0.38 mmol) was added slowly to a −78 °C cooled solution of the phospine oxide **4** (0.173 g, 0.38 mmol) in THF (5 mL). The resulting red solution was stirred for 30 min. A solution of the ketone **5a** (0.10 g, 0.36 mmol) in THF (3 mL) was then added. The resulting solution was stirred for 2 h at −70 °C and then allowed to reach rt (2 h). The reaction was quenched by the addition of a drop of water. Concentration gave a residue that was redissolved in EtOAc/hexanes, washed with an aqueous saturated solution of $NaHCO_3$ (30 mL) and brine (25 mL), dried, and filtered. Concentration gave an oil that was flash chromatographed (1.5 × 15 cm, 2% EtOAc/hexanes) to give 0.156 g of the protected dihydrotachysterol$_2$ (85%, thick colorless oil): ^{1}H NMR (400 MHz) δ 6.11 and 5.92 (2 H, AB system, *J* = 11.2 Hz, H6 and H7), 5.21 (2 H, m, H23 and H22), 3.53 (1 H, tt, *J* = 10.3, 4.2 Hz, H3), 1.07 (3 H, d, *J* = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, *J* = 6.6 Hz, CH_3-C21), 0.93 (3 H, d, *J* = 6.8 Hz, CH_3-C28), 0.90 [9 H, s, $(CH_3)_3C$], 0.85 (3 H, d, *J* = 6.4 Hz, CH_3-C26 or C27), 0.83 (3 H, d, *J* = 6.6 Hz, CH_3-C27 or C26), 0.58 (3 H, s, CH_3-C18), 0.08 (3 H, s, CH_3Si), 0.07 (3 H, s, CH_3Si); ^{13}C NMR (100 MHz) δ 141.6, 141.1, 135.7, 132.0, 115.9, 115.7, 72.0, 56.54, 56.50, 45.5, 42.9, 40.49, 40.47, 39.4, 37.8, 35.7, 33.9, 33.1, 28.9, 27.9, 26.0, 23.5, 22.2, 21.1, 20.0, 19.7, 18.3, 17.8, 17.7, 12.3, −4.6, −4.7; IR ($CHCl_3$) 3075 (=CH, w), 1620 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 260 nm (ε 33 600), 251 nm (ε 48 800), 242 nm (ε 43 400).

Dihydrotachysterol$_2$ (2b). A solution of *n*-Bu_4NF in THF (0.26 mL, 1 M, 0.26 mmol) was added to a solution of the protected dihydrotachysterol (0.13 g, 0.25 mmol) in THF (2 mL) at rt. The solution was stirred for 1 h. Water (1 mL) was added. The

mixture was stirred for 1 h and diluted with Et_2O (10 mL). The aqueous phase was extracted with Et_2O (2 × 5 mL). The combined organic layers were dried, filtered, and concentrated. The oily residue was flash chromatographed (1.5 × 10 cm, 10% EtOAc/hexanes) to afford dihydrotachysterol$_2$ (**2b**, 85 mg, 86%, white powder) that was identified by comparison (^{1}H NMR, ^{13}C NMR, UV, and TLC) with an authentic sample: ^{1}H NMR (400 MHz) δ 6.17 and 5.90 (2 H, AB system, J = 11.1 Hz, H6 and H7), 5.21 (2 H, m, H23 and H22), 3.62 (1 H, tt, J = 10.1, 4.3 Hz, H3), 1.10 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, J = 6.6 Hz, CH_3-C21), 0.93 (3 H, d, J = 6.9 Hz, CH_3-C28), 0.85 (3 H, d, J = 6.4 Hz, CH_3-C26 or C27), 0.83 (3 H, d, J = 6.6 Hz, CH_3-C27 or C26), 0.57 (3 H, s, CH_3-C18); ^{13}C NMR (100 MHz) δ 142.2, 139.8, 135.6, 132.0, 116.9, 115.6, 70.9, 56.5, 45.6, 42.9, 40.44, 40.40, 38.3, 37.7, 34.9, 33.2, 33.1, 28.9, 27.8, 23.5, 22.3, 21.1, 20.0, 19.7, 17.8, 17.7, 12.3; UV (EtOH 95%) λ_{max} 260 nm (ε 21 500), 252 nm (ε 37 000), 242 nm (ε 29 500).

25-[(Methoxymethyl)oxy]dihydrotachysterol$_2$ *tert*-Butyldimethylsilyl Ether. Following the same procedure as used in the synthesis of dihydrotachysterol$_2$ *tert*-butyldimethylsilyl ether, a solution of the lithiated phospine oxide **4** (0.173 g, 0.38 mmol) was treated with ketone **5b** (0.120 g, 0.36 mmol) in THF. Workup and concentration gave an oil that was flash chromatographed (1.5 × 15 cm, 5% EtOAc/hexanes) to give 0.181 g of the protected 25-OH-DHT$_2$ (88%, thick colorless oil): ^{1}H NMR (250 MHz) δ 6.10 and 5.92 (2 H, AB system, J = 11.2 Hz, H6 and H7), 5.29 (2 H, m, H23 and H22), 4.72 (2 H, s, OCH_2O), 3.52 (1 H, tt, J = 9.8, 4.2 Hz, H3), 3.37 (3 H, s, OCH_3), 1.18 (3 H, s, CH_3-C26 or C27), 1.14 (3 H, s, CH_3-C27 or C26), 1.06 (3 H, d, J = 6.5 Hz, CH_3-C19), 1.02 (3 H, d, J = 6.2 Hz, CH_3-C21), 0.99 (3 H, d, J = 6.8 Hz, CH_3-C28), 0.90 [9 H, s, $(CH_3)_3C$], 0.57 (3 H, s, CH_3-C18), 0.07 (3 H, s, CH_3Si), 0.06 (3 H, s, CH_3Si); ^{13}C NMR (62 MHz) δ 141.4, 141.2, 137.3, 129.8, 116.0, 115.9, 91.0, 78.2, 71.9, 56.5, 55.0, 46.7, 45.5, 40.5, 40.4, 39.3, 37.8, 35.6, 33.8, 29.6, 28.8, 27.8, 25.9, 24.7, 23.5, 23.0, 22.2, 20.8, 18.2, 17.7, 15.1, 12.3, −4.7, −4.8; IR ($CHCl_3$) 3060 (=CH, w), 1615 (C=C, m) cm^{-1}; UV (EtOH 95%) λ_{max} 261 nm (ε 18 500), 252 nm (ε 26 500), 242 nm (ε 20 000), λ_{sh} 236 nm (ε 14 500).

25-Hydroxydihydrotachysterol$_2$ (2c). AG-50WX4 ion-exchange resin (1.5 g, prewashed with deoxygenated methanol) was added to a solution of the above protected 25-OH-DHT$_2$ (120 mg, 0.21 mmol) in deoxygenated methanol (5 mL). The mixture was stirred for 12 h at rt, filtered, and concentrated. The residue was dissolved in EtOAc, washed with brine (3 × 20 mL), dried, and filtered. Removal of the solvents afforded a residue that was flash chromatographed (1.5 × 10 cm, 30% EtOAc/hexanes) to give 25-OH-DHT$_2$ (**2c**, 82 mg, 95%, white foam): ^{1}H NMR (250 MHz) δ 6.15 and 5.89 (2 H, AB system, J = 11.1 Hz, H6 and H7), 5.33 (2 H, m, H23 and H22), 3.60 (1 H, tt, J = 10.3, 4.2 Hz, H3), 1.13 (3 H, s, CH_3-C26 or C27), 1.13 (3 H, s, CH_3-C27 or C26), 1.09 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.04 (3 H, d, J = 7.7 Hz, CH_3-C21), 1.01 (3 H, d, J = 7.8 Hz, CH_3-C28), 0.56 (3 H, s, CH_3-C18); ^{13}C NMR (62 MHz) δ 142.0, 139.9, 139.1, 129.1, 116.9, 115.7, 72.3, 70.9, 56.4, 56.2, 48.2, 45.6, 40.4, 38.2, 37.7, 34.9, 33.2, 28.9, 27.8, 26.4, 23.5, 22.3, 21.0, 19.7, 17.8, 15.7; IR (CCl_4) 3605 (w, free OH), 3445 (br, ass. OH), 3010 (=CH, w), 1615 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 260 nm (ε 21 500), 252 nm (ε 33 000), 242 nm (ε 29 500).

10(*R*),19-Dihydro-(5*E*)-3-epivitamin D$_2$ *tert*-Butyldimethylsilyl Ether. Following the same procedure as used in the synthesis of dihydrotachysterol$_2$ *tert*-butyldimethylsilyl ether, a solution of the lithiated phospine oxide **6** (0.110 g, 0.24 mmol) was treated with the ketone **5a** (65 m g, 0.23 mmol) in THF. Workup and concentration gave an oil that was flash chromatographed (1.5 × 10 cm, 1% EtOAc/hexanes) to give 96 mg of the protected dihydrovitamin D (82%, thick colorless oil): ^{1}H NMR (250 MHz) δ 6.06 and 5.89 (2 H, AB system, J = 10.8 Hz, H6 and H7), 5.21 (2 H, m, H23 and H22), 3.53 (1 H, tt, J = 10.4, 4.2 Hz, H3), 1.06 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, J = 6.6 Hz, CH_3-C21), 0.93 (3 H, d, J = 6.9 Hz, CH_3-C28), 0.91 [9 H, s, $(CH_3)_3C$], 0.85 (3, H, d, J = 6.7 Hz, CH_3-C26 or C27), 0.83 (3 H, d, J = 6.8 Hz, CH_3-C27 or C26), 0.57 (3 H, S, CH_3-C18), 0.09 (3 H, s, CH_3Si), 0.08 (3 H, s, CH_3Si); ^{13}C NMR (62 MHz) δ 141.4, 140.9, 135.8, 132.0, 116.0, 115.8, 72.0, 56.5, 45.5, 42.9, 40.4, 39.4, 37.6, 35.7, 33.7, 33.1, 29.6, 28.8, 27.8, 25.9, 23.4, 22.2, 21.1, 19.9, 19.6, 18.3, 17.7, 17.6, 12.2, −4.7, −4.8; IR ($CHCl_3$) 3080 (=CH, w), 1620 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 261 nm (ε 16 000), 252 nm (ε 25 000), 243 nm (ε 22 000), λ_{sh} 236 nm (ε 15 500).

10(*R*),19-Dihydro-(5*E*)-3-epivitamin D$_2$ (2d). A solution of *n*-Bu_4NF in THF (0.20 mL, 1 M, 0.20 mmol) was added to a solution of the above protected dihydrovitamin D (80 mg, 0.16 mmol) in THF (2 mL) at rt. Workup and concentration afforded an oil that was flash chromatographed (1 × 10 cm, 10% EtOAc/hexanes) to afford 54 mg of **2d** (85%, white foam): ^{1}H NMR (250 MHz) δ 6.14 and 5.88 (2 H, AB system, J = 10.8 Hz, H6 and H7), 5.20 (2 H, m, H23 and H22), 3.65 (1 H, tt, J = 10, 4.2 Hz, H3), 1.08 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, J = 6.6 Hz, CH_3-C21), 0.92 (3 H, d, J = 6.8 Hz, CH_3-C28), 0.84 (3 H, d, J = 6.8 Hz, CH_3-C26 or C27), 0.82 (3 H, d, J = 6.7 Hz, CH_3-C27 or C26), 0.57 (3 H, s, CH_3-C18); ^{13}C NMR (62 MHz) δ 142.0, 139.5, 135.7, 132.1, 117.2, 115.8, 70.7, 56.5, 45.6, 42.9, 40.4, 38.8, 37.7, 34.7, 33.1, 32.9, 28.8, 27.7, 23.4, 22.3, 21.1, 19.9, 19.6, 17.7, 17.6, 12.3; IR ($CHCl_3$) 3075 (=CH, w), 1620 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 261 nm, 252 nm, 243 nm.

25-[(Methoxymethyl)oxy]-10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$ *tert*-Butyl Dimethylsilyl Ether. A solution of the lithiated phospine oxide **6** (0.140 g, 0.31 mmol) was treated with the ketone **5b** (0.104 g, 0.31 mmol) in THF. Workup and concentration gave an oil that was flash chromatographed (1.5 × 15 cm, 5% EtOAc/hexanes) to give 0.154 g of the protected dihydrovitamin D (87%, thick colorless oil): ^{1}H NMR (250 MHz) δ 6.06 and 5.88 (2 H, AB system, J = 11.1 Hz, H6 and H7), 5.32 (2 H, m, H23 and H22), 4.72 (2 H, s, OCH_2O), 3.52 (1 H, tt, J = 10.6, 4.2 Hz, H3), 3.37 (3 H, s, OCH_3), 1.18 (3 H, s, CH_3-C26 or C27), 1.14 (3 H, s, CH_3-C27 or C26), 1.05 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, J = 6.0 Hz, CH_3-C21), 0.99 (3 H, d, J = 6.8 Hz, CH_3-C28), 0.90 [9 H, s, $(CH_3)_3C$], 0.56 (3 H, s, CH_3-C18), 0.08 (3 H, s, CH_3Si), 0.07 (3 H, s, CH_3Si); ^{13}C NMR (62 MHz) δ 141.3, 141.0, 137.3, 129.7, 116.0, 115.8, 90.9, 78.3, 72.0, 56.4, 55.1, 46.6, 45.5, 40.5, 40.4, 39.4, 37.6, 35.7, 33.7, 29.9, 28.8, 27.8, 25.9, 24.7, 23.4, 23.0, 22.2, 20.8, 18.3, 17.7, 15.2, 12.2, −4.7, −4.8; IR ($CHCl_3$) 3065 (=CH, w), 1620 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 261 nm (ε 21 000), 252 nm (ε 32 500), 243 nm (ε 28 500), λ_{sh} 237 nm (ε 20 000).

25-Hydroxy-10(*R*),19-dihydro-(5*E*)-3-epivitamin D$_2$ (2e). AG-50WX4 ion-exchange resin (1.4 g, prewashed with deoxygenated methanol) was added to a solution of the above protected dihydrovitamin D (110 mg, 0.19 mmol) in deoxygenated methanol (5 mL), filtered, and concentrated. The residue was dissolved in EtOAc, washed with brine (3 × 20 mL), dried, and filtered. Concentration afforded a residue that was flash chromatographed (1.5 × 10 cm, 30% EtOAc/hexanes) to give 82 mg of **2e** (92%, white foam): ^{1}H NMR (250 MHz) δ 6.13 and 5.88 (2 H, AB system, J = 11.3 Hz, H6 and H7), 5.34 (2 H, m, H23 and H22), 3.64 (1 H, tt, J = 9.9, 4.3 Hz, H3), 1.17 (3 H, s, CH_3-C26 or C27), 1.13 (3 H, s, CH_3-C27 or C26), 1.08 (3 H, d, J = 6.6 Hz, CH_3-C19), 1.03 (3 H, d, J = 6.6 Hz, CH_3-C21), 1.00 (3 H, d, J = 6.8 Hz, CH_3-C28), 0.57 (3 H, s, CH_3-C18); ^{13}C NMR (62 MHz) δ 141.8, 139.7, 139.0, 129.3, 117.1, 115.9, 72.4, 70.7, 56.4, 56.3, 48.1, 45.6, 40.4, 40.3, 38.2, 37.7, 34.7, 32.9, 29.6, 28.8, 27.7, 26.9, 26.4, 23.4, 22.3, 20.9, 17.7, 15.5, 12.3; IR ($CHCl_3$) 3080 (=CH, w), 1620 (C=C, w) cm^{-1}; UV (EtOH 95%) λ_{max} 261 nm, 252 nm, 243 nm.

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Supplementary Material Available: Spectral data (^{1}H and ^{13}C NMR, IR, UV, EI-LRMS, and EI-HRMS), ^{1}H and ^{13}C NMR spectra, and the ^{1}H NMR NOE difference experiment over **15** (25 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masterhead page for ordering information.