to J.C.). We also thank the NSF Chemical Instrumentation Program for their financial assistance in the purchase of a GC/MS and a PFT NMR apparatus and the University of California Research Expeditions Program for supporting our field work. We are also grateful to Mr. I. Papiashvili for his technical assistance with some of the spectroscopic work at UCSC and to Mr. K. Tabor and Ms. C. Weeks for their assistance in both the laboratory and field. The exact mass measurements were obtained by Dr. H. Webb at the UCSB Mass Spectrometry Laboratory, and the 360-MHz ^{13}C NMR were obtained at the Stanford Magnetic Resonance Laboratory supported by the NSF (Grant No. GR23633) and the National Institutes of Health (Grant No. RR00711).

Registry No. 1, 62681-06-5; 2, 75961-66-9; 3, 75961-67-0; 4, 74219-41-3; 5, 74145-73-6; 6, 74145-74-7; 7, 74183-98-5; 8, 74145-72-5; 9, 74145-71-4; 10, 74145-70-3; briarein B, 75961-58-9.

Synthesis of C_{19}-Functionalized 7-Dehydrocholesteryl Derivatives. Photochemical Transformation to Vitamin D_3 Analogues

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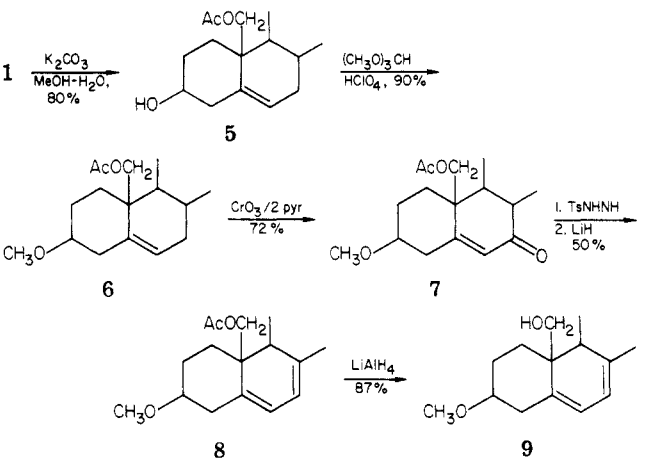
Received June 11, 1980

A series of C_{19}-substituted 7-dehydrocholesterol derivatives has been prepared in which the C_{19} substituent is hydroxyl, acetoxyl, methoxyl, or aldehydo. These compounds are cholesta-5,7-diene-3β,19-diol (4), cholesta-5,7-diene-3β,19-diol diacetate (3), cholesta-5,7-diene-3β,19-diol 3-acetate 19-methyl ether (19) and 3β-methoxycholesta-5,7-dien-19-al (10). In each case the synthesis proceeded from a Δ^5-steroid which was converted to the 7-keto-Δ^5 system. Then the derived tosylhydrazone was decomposed with lithium hydride to introduce the $\Delta^{7,8}$ double bond to complete the ring-B diene synthesis. Irradiation of 3 followed by thermally induced hydrogen migration yields the vitamin D_3 analogue with *E* stereochemistry at the C_{19} position. Likewise, photochemical ring-opening of 19 followed by the thermal hydrogen transfer yielded purely the C_{19} *E* isomer. This stereoselectivity is discussed. Irradiation of 4 proceeded with loss of the C_{19} functionality to yield 19-norcholesta-5(10),7-dien-3β-ol. The chiroptical effects of the homoannular cisoid dienes occurring in this study are discussed in terms of the diene quadrant rule.

The past decade has witnessed impressive advances in the biochemistry of vitamin D.[1] The hepatic metabolism of vitamin D_3 to its 25-hydroxylated derivative followed by renal 1α-hydroxylation to the active hormonal metabolite 1α,25-dihydroxyvitamin D_3 constitutes the basic enzymatic conversions of the vitamin D endocrine system.[2-5] Like other steroid hormones, the biochemical action of vitamin D_3 is believed to be regulated by a nuclear mechanism of gene expression and de novo protein synthesis.[6] A crucial step in this process is the binding of the steroid hormone 1α,25-dihydroxyvitamin D_3 to tissue specific intracellular binding proteins and translocation of this complex to the nucleus where it initiates the hormonal response.

Other steroidal endocrine systems have shown a great deal of sensitivity toward structural analogues of the active hormone. These effects can be directly attributed to variations in the ligand receptor protein interaction.[7] Analogues of greater binding affinity exhibit enhanced or selective biochemical activity while derivatives which bind to the receptor molecule without promoting translocation or nuclear activation possess "antihormonal" or antagonistic properties.

Scheme I



A clinically useful vitamin D antagonist has not been discovered, although effective antagonists of mineralocorticoids, estrogens, and androgens are used clinically for a wide range of disorders.[8,9] A great deal of synthetic work has accompanied the biochemical advances in the vitamin D field, but few reported examples exist of analogues which possess unique biological activities.[10] Furthermore, most synthetic work has been directed toward metabolites, i.e., A-ring- and side-chain-hydroxylated derivatives. We considered it of interest to synthesize C_{19}-functionalized analogues of vitamin D_3 and to determine their biological

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activity with respect to potential agonism or antagonism. The rationale is that receptor binding might occur with such an analogue, but subsequent steps might be blocked.

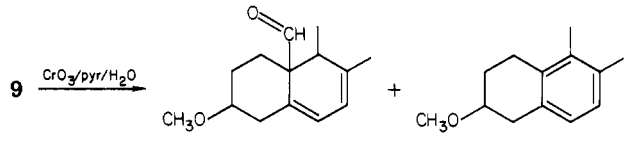
Synthetic Section

Photochemical ring opening followed by thermal 1,7 hydrogen shift converts the 7-dehydrocholesteryl system into the vitamin D series. The central synthetic problem in this study was the introduction of the C_7–C_8 double bond into a C_{19}-substituted cholesteryl derivative, which then could be transformed into the C_{19}-substituted vitamin D analogue.

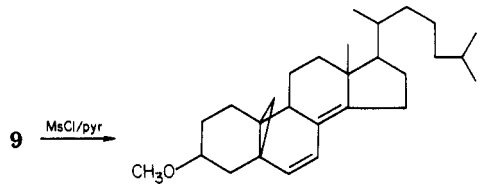
The customary procedure for conversion of a Δ^5 steroid into the corresponding $\Delta^{5,7}$ diene is allylic bromination–dehydrobromination.[11-13] In the case of cholest-5-ene-3β,19-diol diacetate (1),[14] application of this method with 1,3-dibromo-5,5-dimethylhydantoin–trimethyl phosphite[19] yielded a 1:1 mixture of the $\Delta^{4,6}$ and $\Delta^{5,7}$ dienes. Because of these unpromising results an alternative synthetic route for formation of the ring-B diene was sought. Success was achieved by using the method of Caglioti et al.[15] 7-Oxocholest-5-ene-3β,19-diol diacetate (2) was synthesized via allylic oxidation[16] of cholest-5-ene-3β,19-diol diacetate (1), followed by treatment with *p*-toluenesulfonylhydrazide and lithium hydride to yield cholesta-5,7-diene-3β,19-diol diacetate (3) in 55% from 1. Lithium aluminum hydride reduction of 3 gave the diol 4.

The next goal was to vary the nature of the C_{19} functionality. A useful synthetic approach was formation of the C_3-methyl ether derivative of cholest-5,7-diene-3β,19-diol (4). This was accomplished by starting from cholest-5-ene-3β,19-diol diacetate (1). This was partial hydrolyzed to cholest-5-ene-3β,19-diol 19-acetate followed by methylation, allylic oxidation, $TsNHNH_2$–LiH treatment, and finally $LiAlH_4$ reduction (1 → 5 → 6 → 7 → 8 → 9; Scheme I). The next set of experiments was aimed at oxidation of the C_{19}-hydroxyl function in 9. Due to the sensitivity of the B-ring diene to acid, we initially used Sarett conditions[17] as modified by Ratcliffe and Rodehorst.[18] The principal product proved to be the B-ring aromatic derivative 11 obtained in low yield. Next we employed a less reactive variation of the Sarett conditions, which was suggested by work of Kalvoda et al.,[19] namely, the addition of water to the CrO_3–pyridine complex. A 10% yield of the desired aldehyde 10 was obtained along with 70% of the B-ring aromatic compound 11. Suppression of the carbon–carbon cleavage reaction, which according to work of Rocek et al. might result from Cr(IV) ion, was pursued by using Mn(II) ion as a scavenger for this species.[20] No material improvement in yield was achieved. Pyridinium chlorochromate gave essentially the same ratio of 10 to 11 in a slightly lower overall yield. Among milder oxidizing conditions, the Kornblum[22] method was not useful due to homoallylic participation (9 → 12). Oxidizing systems which failed altogether were the Parikh–Doering method,[23] the Pfitzner–Moffatt procedure,[24] and the Me_2SO–Ac_2O method.[25] Alternative synthetic strategies aimed at an improved yield of 10 led us to investigate introduction of the C_7–C_8 double bond after the formation of the C_{19}-aldehyde function. Keto aldehyde 14 was synthesized by the path 7 → 13 → 14 in good yield; in spite of the different steric environments of the two carbonyl groups in this molecule, the $TsNHNH_2$–LiH method failed to yield 10. Synthetic routes to 10 from the C_{19}-carboxylic acid derivative formed by oxidation of cholest-5-ene-3β,19-diol 3-methyl ether (15) or cholest-5-ene-3β,19-dial 3-methyl ether (16) are conceivable, but oxidation of the C_{19}-oxygenated function in either compound under Jones conditions led to partial destruction of the olefinic double bond and C_3-methyl ether. After much experimentation, a 10% yield of 10 represented the maximum we could achieve.

The C_{19}-methyl ether ring-B diene was synthesized in a straightforward manner from the previously described 17[26] by the usual procedure (17 → 18 → 19).



10 (10%) 11 (70%)



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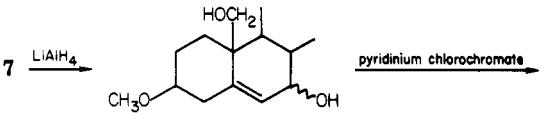

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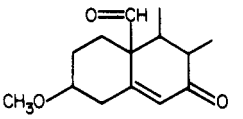

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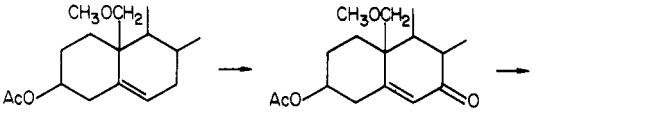
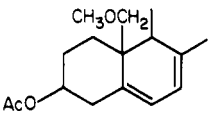


17 18



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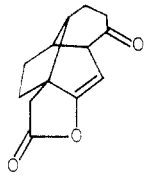
Spectral Properties of C_{19}-Substituted 7-Dehydrocholesteryl Derivatives. The ultraviolet spectrum of **10** displayed an intense homoconjugative interaction between the C_{19}-aldehyde and the diene as evidence by the n–π^* transition at 332 nm (ϵ 1630). The extinction coefficient of the carbonyl transition is some 20 times more intense than that for the monoene, λ_{max} 315 nm (ϵ 85), and 33 times more intense than that for the saturated analogue, λ_{max} 309 nm (ϵ 50). According to Cookson's view, the enhancement of the n–π^* transition is related to the distance in space between the carbonyl group and the β,γ-unsaturation.[27] A comparably large n–π^* enhancement is shown in the case of parasantanide (**20**), λ_{max} 300 (ϵ 1170), a molecule of rigid geometry in which the keto function and the olefinic group are optimally articulated in space for orbital mixing.[27] Cyclohex-3-enone (**21**) and norbornenone (**22**) are also illustrative.

Table I presents the circular dichroism data for several compounds encountered in this study. The negative chiroptical effect for the longer wavelength transition of



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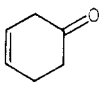
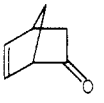


21 [277 nm (ϵ 107)]



22

7-dehydrocholesteryl acetate agrees with prediction based upon the recently enunciated diene quadrant rule for optically active homoannular cisoid dienes.[28] Figure 1 illustrates the inscription of the chromophore into the coordinate system of the quadrant. The diene double bonds fall into negative quadrants, and the axial allylic substituents at C_9 and C_{10}, R and R′, lie in positive quadrants. The sign and magnitude of the chiroptical effect is an algebraic sum of the diene contribution and the contribution from the axial allylic substituents at the termini of the homoannular cisoid diene. Empirically, it has been observed that the sign of the diene contribution is dominant in determining the observed sign of $\Delta\epsilon$ when R = R′ = CH_3 and when R = H and R′ = CH_3, but not when R = R′ = H. Therefore, in 7-dehydrocholesteryl acetate of *M* chirality, as well as **3**, **4**, and **19** of the same chirality, a negative sign of $\Delta\epsilon$ is expected and observed.

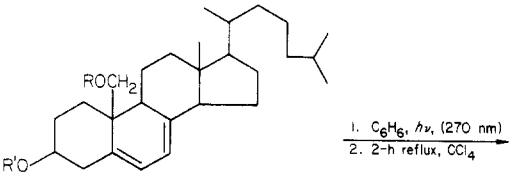
Photochemical Results. Photoconversion of 7-dehydrocholesterol into vitamin D_3 involves opening of the B-ring diene to the cisoid *ZcZ* triene previtamin followed by an intramolecular,[29] 1,7-antarafacial[30] hydrogen shift to yield the vitamin. The C_{19}-acetoxyl and methoxyl derivatives, cholesta-5,7-diene-3β,19-diol diacetate (**3**) and cholesta-5,7-diene-3β,19-diol 3-acetate 19-methyl ether (**19**), analogously yielded vitamin D_3 derivatives, **23** and **24**, respectively.[31a,b] Remarkably, in each case, only one of the two possible stereoisomers of the C_{19} carbon atom was formed, namely, the C_{19} *E* isomer.

The *E* configuration of **24** is based upon the fact that both the *E* and *Z* isomers are known in the related 3β-alcohol series.[32] The *Z* C_{19} OCH_3 group in this compound was assigned in the NMR spectrum ($CDCl_3$) at δ 3.43 and the *E* C_{19} OCH_3 appeared at δ 3.51. In the case of **24**, the OCH_3 resonance occurs at δ 3.51 which agrees with the relative deshielding associated with the *E* position. In the case of **23** only one isomer is known, namely, that one

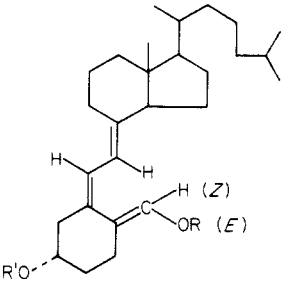
Table I. Chiroptical Effects for C_{19}-Substituted 7-Dehydrocholesteryl Derivatives[a]

compd	$\Delta\epsilon$ (γ_{max})
7-dehydrocholesteryl acetate	−10.8 (280), −11.4 (270)
cholesta-5,7-diene-3β,19-diol diacetate	−4.65 (282), −4.85 (273)
cholesta-5,7-diene-3β,19-diol (**4**)	−7.00 (282), −7.50 (273)
cholesta-5,7-diene-3β,19-diol 3-acetate 19-methyl ether (**19**)	−5.20 (282), −5.90 (272)
3β-methoxycholesta-5,7-dien-19-al (**10**)	−10.5 (332), 4.3 (284), +4.9 (275)

[a] Measurements were made with absolute ethanol as solvent.



3, R = Ac; R′ = Ac
19, R = CH_3; R′ = Ac



23, R = Ac; R′ = Ac
24, R = CH_3; R′ = Ac

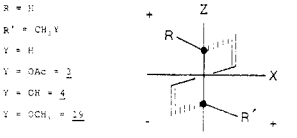
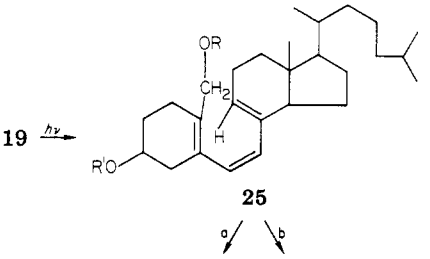


Figure 1. Quadrant diagram for the 7-dehydrocholesteryl system of *M* chirality.

Scheme II



(26) Compound **17** was prepared according to the procedure described in ref 14.
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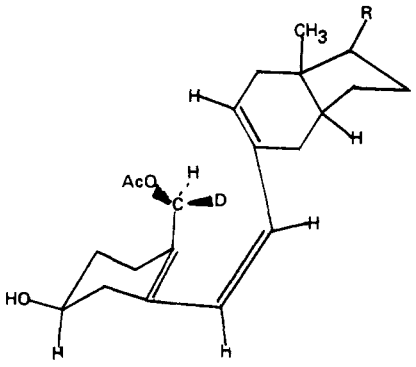
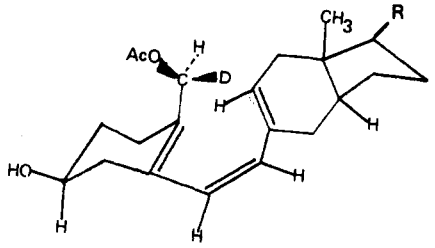
Chart I

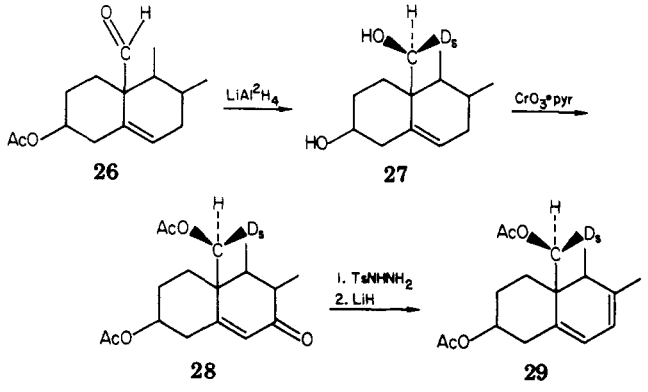


I



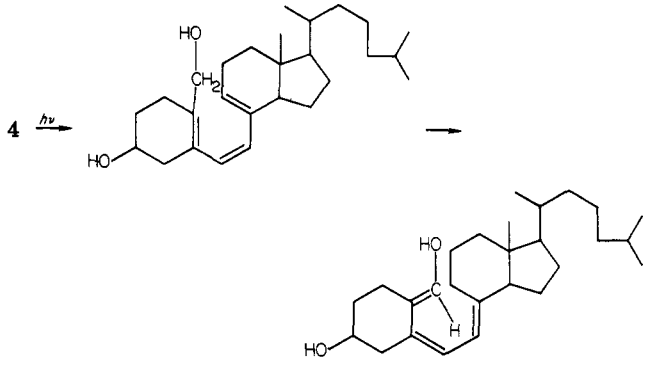
II

Scheme III

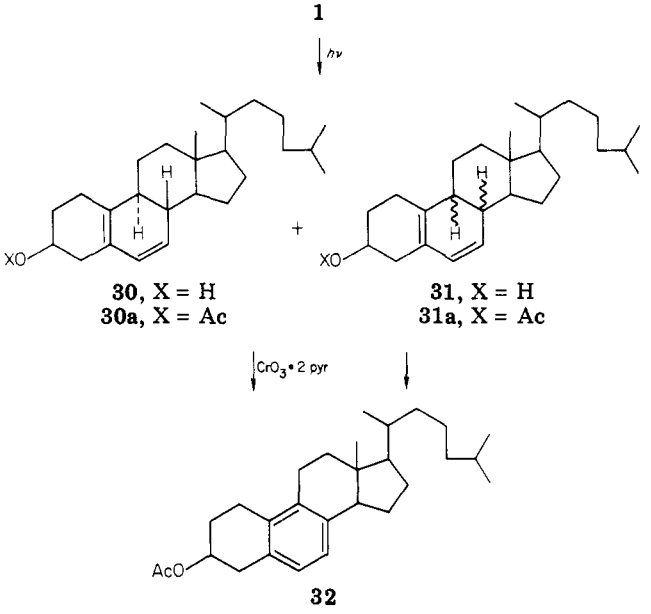


26 27 28 29

Scheme IV



Scheme V



30, X = H
30a, X = Ac
31, X = H
31a, X = Ac
32

obtained in the present study. We base the *E* C_{19} OAc configuration of the chemical shift of the *Z* C_{19} proton at 6.89 (C_6D_6) and 6.96 ppm (CD_2Cl_2). The analogous proton in vinyl acetate occurs at 7.25 ppm.[33] The *Z* C_{19} proton of **23** should experience relative shielding due to its position with respect to the adjacent diene system.

Akhtar and Gibbons have shown that the 1,7 hydrogen shift in the vitamin D_3 series is nonstereospecific.[34] Accordingly, one might expect both C_{19} *E* and *Z* isomers to form in **3** → **23** and **19** → **24**, contrary to what is actually observed. The observed stereospecific result could come about in two stereochemically distinct ways. First ring opening could yield the previtamin **25**, and one of the diastereotopic protons at C_{19} could be preferentially transferred to the C_9 position in a transition state involving one of the two possible twist senses of the cisoid triene (I or II, Scheme II). These differ in the sense of the chirality of the triene. In the case where the A ring lies below the place of the C and D rings, *P* chirality obtains. The opposite is true for the structure in which the A ring lies above the plane of the C and D rings.

Formation of the observed *E* isomer from (I) requires transfer of the *pro-S* C_{19} hydrogen to the C_9 α position while formation of the observed *E* isomer from II requires transfer of the *pro-R* C_{19} hydrogen to the C_9 β position. In order to probe this point the stereospecifically labeled C_{19}-*pro-S*-^2H compound **27** (Scheme III) was synthesized by $LiAl^2H_4$ reduction of **26**.[14] The incorporation of deuterium was 78%, and the *pro-S* stereochemistry has been established by work of Arigoni et al.[35] Conversion of **28** into diene **29** would not be expected to affect the stereochemistry at C_{19}.

If 1,7 hydrogen transfer involved the right-handed twist sense of the cisoid triene (case I, Chart I) then selective transfer of a deuterium atom should occur, and this would be detected by formation of the C_{19}-vinylic group with ~78% H. If a left-handed cisoid triene (case II) intervened, then a protium atom would be transferred and the C_{19}-vinylic group should contain ~22% H.

Irradiation of **29** (C_6H_6, ca. 280 nm) followed by heating at 80 °C for 18 h led to the vitamin analogue [9,19-^2H]-**29** with 26.4% hydrogen in the C_{19} *Z* position. This result is close to the predicted 22% value for the left-handed A

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ring above the C and D rings, 9β transfer of the *pro-R* hydrogen. This result indicates an overriding preference for case II geometry as the energetically most favored arrangement for the intramolecular hydrogen transfer.

Mazur et al.[36a] have studied the unsubstituted vitamin D_3–previtamin D_3 equilibrium and conclude that the preferred conformation for 1,7 hydrogen transfer is the right-handed twist sense of the *cis*-1,3,5-triene with the A ring lying below the plane of the C and D rings. Furthermore, they find a very large deuterium isotope effect, $k_H/k_D \approx 45$. Results in the two systems may not be strictly comparable since in the present case two opposing factors operate. In the left-handed conformation, a destabilizing steric interaction exists between C_{18} and C_{19}. In the right-handed conformation, formation of [^{2}H]-**23** requires transfer of a deuterium atom, and the large isotope effect mentioned above would inhibit this process.

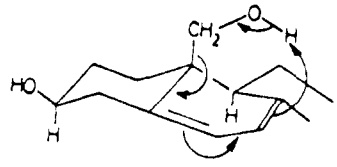
Irradiation of cholest-5,7-diene-3β,19-diol (**4**) was of interest because potentially an enol form might intervene in the hydrogen-transfer process (Scheme IV).

However, the photolysis of **4** followed a completely different course. Irradiation of **4** in benzene yielded **30** (Scheme V) as a crystalline product and **31** as an oil.[37] Both compounds formed acetate derivatives, **30a** and **31a**, respectively.

Both **30a** and **31a** upon oxidation with chromium trioxide in pyridine–methylene chloride yielded the known **32**.[38]

Diene **31** was shown to be a secondary photoproduct formed from irradiation of **30**. The structure of **30** was proved by an X-ray diffraction study[37] on the acetate **30a**.

A reasonable mechanism for the photofragmentation of **4** leading to **30** could involve intramolecular suprafacial hydrogen atom transfer of the following type shown for **4**. In support of this pathway is the observation that the



4

C_{19} *O*-deuterio analogue, [3,19-^{2}H]-**4**, undergoes the photorearrangement to yield a product shown by high-resolution mass spectrometry to contain one deuterium atom bound to carbon. The photoisomerization of **30** to **31** may involve an allowed conrotatory ring opening to yield triene **33** followed by disrotatory recyclization to yield either the 8α,9α or 8β,9β stereochemistry. A similar isomerization has been observed with 1,3-cholestadiene.[40]

A Dreiding mode of **30** reveals that the diene group exists as a conformationally rigid right-handed helix. A negative chiroptical effect was determined for this compound, i.e., $\Delta\epsilon_{266}$ −5.70. Likewise, the C_3-deoxy derivative **35** prepared as shown also showed a negative chiroptical effect, i.e., $\Delta\epsilon_{266}$ −5.20.

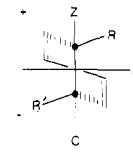
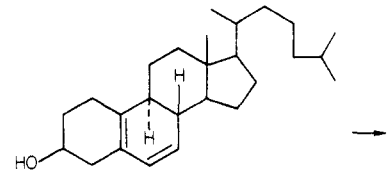
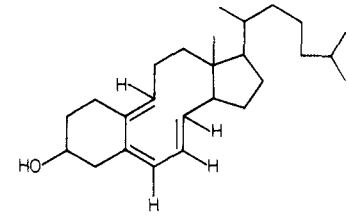


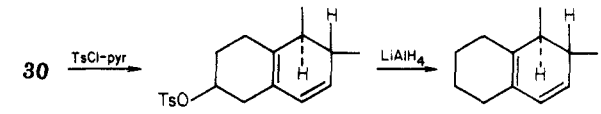
Figure 2. Quadrant diagram for the 19-norcholesta-5(10),6-dienyl system of *P* chirality.



30



33



34 **35**

The chiroptical effects of **31** and **35** may be understood in terms of the diene quadrant rule.

These two dienes may be inscribed in the quadrant diagram shown in Figure 2. The double bonds fall into positive sectors and the two axial allylic hydrogens, R = R′ = H, fall into negative compartments. Since axial allylic hydrogen has been shown empirically to dominate the chiroptical effect, the net result is negative.[28]

Various vitamin D analogues obtained in this study are currently being evaluated for physiological activity.[41]

Experimental Section

Cholest-5-ene-3β,19-diol diacetate (1) was prepared by the method of Moriarty and De Silva.[14]

Cholesta-5-ene-3β,19-diol 3-Acetate 19-(3,5-Dinitrobenzoate) (1a). Cholest-5-ene-3β,19-diol 3-acetate[14] (250 mg) was dissolved in 3 mL of pyridine, and 250 mg of 3,5-dinitrobenzoyl chloride, freshly recrystallized from petroleum ether, was added. The solution was heated to 75 °C for 1.5 h and then allowed to react 18 h at room temperature. At the end of this period, the reaction mixture was diluted with 50 mL of H_2O. The organic extracts were washed with portions of $NaHCO_3$ (2 × 50 mL), 3% HCl (1 × 50 mL), $NaHCO_3$ (1 × 50 mL), and H_2O (1 × 50 mL) and dried over $MgSO_4$. The solvent was removed in vacuo to yield 345 mg of an oil which was readily crystallized from acetone–methanol: mp 76.0–77.0 °C; [α] −33.3° (*c* 0.30); IR (Nujol) 3050, 1750, 1730, 1280 cm^{-1}; NMR δ 0.70 (s, 18-CH_3), 2.05 (s, 3-$OCOCH_3$), 4.70 (q, AB, *J* = 11 Hz, 19-CH_2), 4.95 (m, 3-CH), 5.80 (m, 6-CH), 9.25 (m, 19-$OCOC_6H_3(NO_2)_2$). Anal. Calcd for $C_{36}H_{50}N_2O_8$: C, 67.69; H, 7.89. Found: C, 67.56; H, 7.86.

7-Oxocholest-5-ene-3β,19-diol Diacetate (2). Chromium trioxide (dried over P_2O_5, 3.35 g) was added to 5.30 g of dry pyridine in 20 mL of rapidly stirred CH_2Cl_2. The solution was kept for 20 min at room temperature. A 1.8-g sample of **1** dissolved in 15 mL of CH_2Cl was added in one portion to the above solution which was stirred at room temperature for 17 h. At the end of

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this period an additional portion of CrO_3·2pyr complex, prepared from 1.05 g of CrO_3 and 1.65 g of pyridine in 75 mL of CH_2Cl_2, was added and the mixture allowed to stir for an additional 7 h. The organic layer was diluted with 600 mL of ether and washed with portions of saturated $NaHCO_3$ solution (3 × 75 mL), 3% HCl (2 × 75 mL), saturated $NaHCO_3$ solution (1 × 75 mL), and saturated NaCl solution (1 × 100 mL). The solution was dried over $MgSO_4$ and the solvent removed in vacuo to yield a brown oil which was chromatographed on 125 g of silica gel (benzene–ethyl acetate, 95:5), giving 1.35 g of **2** as a crystalline compound: mp 94.5–95.5 °C; $[\alpha]_D$ −127.8° (*c* 0.88); IR (Nujol) 1750, 1680, 980 cm^{-1}; UV 233 (ε 12 300); NMR δ 0.70 (s, 18-CH_3), 1.98 (s, 3-$OCOCH_3$), 2.02 (s, 19-$OCOCH_3$), 4.45 (q, AB, *J* = 11 Hz, 19-CH_2), 4.75 (m, 3-CH), 5.93 (s, 6-CH). Anal. Calcd for $C_{31}H_{48}O_5$: C, 74.37; H, 9.65. Found: C, 74.41; H, 9.73.

Cholesta-5,7-diene-3β,19-diol Diacetate (3). 7-Oxocholest-5-ene-3β,19-diol diacetate (**2**, 1.33 g) was refluxed with 600 mg of *p*-toluenesulfonylhydrazide, freshly recrystallized from petroleum ether, in 3 mL of MeOH for 1.0 h and then allowed to react overnight at room temperature. The reaction mixture was diluted with 25 mL of dry benzene, and the methanol was removed by azeotropic distillation at reduced pressure. A 1.9-g sample of LiH was added to the crude tosylhydrazone in 50 mL of dry benzene and the solution heated at reflux for 6.0 h. The cooled reaction mixture was filtered to remove insoluble lithium salts and the solvent removed in vacuo to yield an oil which was chromatographed on 45 g of silica gel (elution with benzene–ethyl acetate, 97:3) to yield 1.05 g of crystalline compound: mp 113.5–114.5 °C; $[\alpha]_D$ −103.2° (*c* 1.21); IR (Nujol) 1750, 1680, 1630, 850 cm^{-1}; UV 283 nm (ε 9020), 273 (8850); CD [θ] (λ, nm) −4.85 (273), −4.65 (282); NMR δ 0.75 (s, 18-CH_3), 2.10 (s, 3-$OCOCH_3$), 2.16 (s, 19-$OCOCH_3$), 4.35 (q, AB, *J* = 11 Hz, 19-CH_2), 5.58 (q, AB, *J* = 11 Hz, 6-CH and 7-CH). Anal. Calcd for $C_{31}H_{48}O_4$: C, 76.81; H, 9.98. Found: C, 76.81; H, 9.95.

Cholesta-5,7-diene-3β,19-diol (4). One gram of lithium aluminum hydride was added to 75 mL of dry Et_2O. To this rapidly stirred solution was added 1.6 g of **3** in 10 mL of Et_2O dropwise. The solution was heated to reflux for 2.0 h and cooled to 0 °C, and the excess lithium aluminum hydride was decomposed by dropwise addition of H_2O. The insoluble lithium salts were filtered and washed several times with Et_2O. The organic solution was dried over $MgSO_4$ and the solvent removed in vacuo to yield 1.20 g of a crystalline residue which was recrystallized from MeOH: mp 174.5–175.0 °C; $[\alpha]_D$ −59.1° (*c* 0.77); IR (Nujol) 3570, 1680, 1630, 1070 cm^{-1}; UV 284 nm (ε 10 100), 272 (9800); CD [θ] (λ, nm) −7.50 (273), −7.00 (282); NMR δ 0.70 (s, 18-CH_3), 3.6 (m, 3-CH), 3.65 (q, AB, *J* = 11 Hz, 19-CH_2), 5.58 (q, AB, *J* = 6 Hz, 6-CH and 7-CH). Anal. Calcd for $C_{22}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.90; H, 11.21.

Cholest-5-ene-3β,19-diol 19-Acetate (5). Cholest-5-ene-3β,19-diol diacetate (**1**, 329 g) was dissolved in 260 mL of anhydrous methanol by briefly heating the solution to reflux. To this solution, at room temperature, was added 0.675 g of $KHCO_3$ in 32.6 mL of H_2O and the mixture heated to reflux for 1.0 h. The reaction was then concentrated in vacuo, diluted with 100 mL of H_2O, and extracted with portions of ether (3 × 75 mL). The combined extracts were then washed with portions of H_2O (2 × 100 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo to give a clear oil which was chromatographed on silica gel; elution with hexane–ethyl acetate (70:30) yielded 2.53 g of an oil which was crystallized from acetone: mp 103.5–104.5 °C; $[\alpha]_D$ −125.0° (*c* 0.32); IR (neat) 3420, 1750, 1230, 1040 cm^{-1}; NMR δ 0.70 (s, 18-CH_3), 2.05 (s, 19-$OCOCH_3$), 3.50 (m, 3-CH), 4.22 (q, AB, *J* = 12 Hz, 19-CH_2), 5.60 (m, 6-CH). Anal. Calcd for $C_{29}H_{48}O_3$: C, 78.32; H, 10.80. Found: C, 78.16; H, 10.84.

Cholest-5-ene-3β,19-diol 3-Methyl Ether 19-Acetate (6). Cholest-5-ene-3β,19-diol 19-acetate (**5**, 2.50 g) was dissolved in 25 mL of trimethyl orthoformate, and 0.73 mL of perchloric acid was added. The mixture was stirred for 10 min. At the end of this period the reaction mixture was poured into 150 mL of saturated $NaHCO_3$ solution and extracted with portions of ether (3 × 75 mL). The combined extracts were washed with portions of H_2O (2 × 50 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting oil was chromatographed on 50 g of silica gel; elution with hexane–ethyl acetate (90:10) yielded 2.51 g of an oil which was crystallized from methanol–acetone: mp 46.0–47.0 °C; $[\alpha]_D$ −100.0° (*c* 0.45); IR (neat) 1740, 1230, 1100, 1040 cm^{-1}; NMR δ 0.70 (s, 18-CH_3), 2.02 (s, 19-$OCOCH_3$), 3.25 (m, 3-CH), 3.33 (s, 3-OCH_3)$_3$, 4.22 (q, AB, *J* = 12 Hz, 19-CH_2), 5.60 (m, 6-CH). Anal. Calcd for $C_{30}H_{50}O_3$: C, 78.55; H, 10.99. Found: C, 78.65; H, 11.12.

7-Oxocholest-5-ene-3β,19-diol 3-Methyl Ether 19-Acetate (7). Chromium trioxide (4.9 g) was added to 7.75 g of dry pyridine in 220 mL of rapidly stirring CH_2Cl_2. The solution stirred for 20 min at room temperature. A 2.5-g sample of **6** in 10 mL of CH_2Cl_2 was added in one portion, and the reaction continued for 17 h. At the end of this period an additional portion of CrO_3·2pyr complex, prepared from 1.52 g of chromium trioxide and 2.4 g pyridine in 100 mL of CH_2Cl_2, was added and the mixture allowed to stir for 7 h longer. The solution was diluted with 600 mL of ether and washed with portions of saturated $NaHCO_3$ solution (3 × 75 mL), 3% HCl (2 × 75 mL), saturated $NaHCO_3$ solution (1 × 100 mL), and saturated NaCl solution (1 × 100 mL). The solution was dried over $MgSO_4$ and the solvent removed in vacuo to yield a brown oil which was chromatographed on 110 g of silica gel; elution with hexane–ethyl acetate (75:25) yielded 1.78 g of a crystalline compound: mp 95.0–96.5 °C; $[\alpha]_D$ −167.5° (*c* 0.35); IR (Nujol) 1740, 1670, 1230, 1100, 1040 cm^{-1}; UV 236 nm (ε 10 600); NMR δ 0.70 (s, 18-CH_3), 2.02 (s, 19-$OCOCH_3$), 3.28 (m, 3-CH), 3.40 (s, 3-OCH_3), 4.45 (q, AB, *J* = 11 Hz, 19-CH_2), 5.90 (s, 6-CH). Anal. Calcd for $C_{30}H_{48}O_4$: C, 76.22; H, 10.24. Found: C, 76.27; H, 10.23.

Cholesta-5,7-diene-3β,19-diol 3-Methyl Ether 19-Acetate (8). 7-Oxocholest-5-ene-3β,19-diol 3-methyl ether 19-acetate (**7**, 1.70 g) and 930 mg of *p*-toluenesulfonylhydrazide in 2.0 mL of methanol was kept at reflux for 1.0 h and then kept at room temperature overnight. The methanol was removed from the reaction mixture by azeotropic distillation with benzene and the crude oily tosylhydrazone dissolved in 50 mL of benzene. A 2.5-g sample of LiH was added, the solution was kept at reflux to remove the insoluble lithium salts, and the solvent was removed in vacuo. The resulting oil was chromatographed on 50 g of silica gel; elution with hexane–ethyl acetate (90:10) yielded 845 mg of an oil which was crystallized from MeOH: mp 75.0–76.0 °C; $[\alpha]_D$ −183.3° (*c* 0.30); IR (neat) 1740, 1660, 1100, 1040 cm^{-1}; UV 283 nm (ε 10 000), 272 (9800); NMR δ 0.68 (s, 18-CH_3), 1.98 (s, 19-$OCOCH_3$), 3.25 (m, 3-CH), 3.35 (s, 3-OCH_3), 4.28 (q, AB, *J* = 11 Hz, 18-CH_2), 5.50 (q, AB, *J* = 6 Hz, 6-CH and 7-CH). Anal. Calcd for $C_{30}H_{48}O_3$: C, 78.89; H, 1059. Found: 78.83; H, 10.52.

Later fractions, hexane–ethyl acetate (86:14), contained 465 mg of an unidentified byproduct.

Cholesta-5,7-diene-3β,19-diol 3-Methyl Ether (9). Cholesta-5,7-diene-3β,19-diol 3-methyl ether 19-acetate (**8**, 820 mg) was dissolved in a minimum volume of ether and added dropwise to a magnetically stirred solution of 600 mg of $LiAlH_4$ in 70 mL of dry ether. The solution was then kept at a reflux for 1.0 h and cooled to 0 °C, and the excess reagent was carefully decomposed by addition of water. The mixture was filtered, and the salts were thoroughly washed with ether. The resulting solution was dried with $MgSO_4$ and the solvent removed in vacuo to give 700 mg of crystalline product which was purified by recrystallization from acetone: mp 150.0–151.0 °C; $[\alpha]_D$ −36.8° (*c* 0.34); IR (Nujol) 3470, 1680, 1100, 1040 cm^{-1}; UV 284 nm (ε 8500), 274 (8400); NMR δ 0.69 (s, 18-CH_3), 3.24 (m, 3-CH), 3.35 (s, 3-OCH_3), 3.72 (q, AB, *J* = 11 Hz, 19-CH_2), 5.57 (q, AB, *J* = 6 Hz, 6-CH and 7-CH). Anal. Calcd for $C_{28}H_{46}O_2$: C, 81.10; H, 11.18. Found: C, 81.31; H, 11.28.

3β-Methoxy-7-oxocholest-5-en-19-al (14). 7-Oxocholest-5-ene-3β,19-diol 3-methyl ether 19-acetate (**7**, 0.775 g) in a small amount of ether was added dropwise to a refluxing solution of 1.2 g of $LiAlH_4$ in 100 mL of ether and reflux continued for 2.0 h. The solution was then cooled in an ice bath, and the excess reagent was decomposed by addition of H_2O. The lithium salts were filtered, the organic solution was dried over $MgSO_4$, and the solvent was removed in vacuo to yield 715 mg of an oil which crystallized upon trituration with ether. The IR spectrum of the crystalline mixture showed no carbonyl absorption.

A 1.1-g sample of pyridinium chlorochromate was suspended in 15 mL of rapidly stirred CH_2Cl_2. A 0.710-g sample of the epimeric diols was added in a small amount of CH_2Cl_2 and stirring continued for 2.0 h at ambient temperature. The solution was then diluted with 100 mL of ether, washed with portions of saturated $NaHCO_3$ solution (2 × 60 mL), 3% HCl (1 × 60 mL),

saturated $NaHCO_3$ solution (1 × 60 mL), and H_2O (1 × 100 mL), and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting material was crystallized from acetone to yield 500 mg of **14**: mp 137.0–138.0 °C; $[\alpha]_D$ −237.5° (*c* 0.40); IR (Nujol) 1730, 1680, 1100 cm^{-1}; UV 315 nm (ε 240), 241 (8800); NMR δ 0.67 (s, 18-CH_3), 3.25 (m, 3-CH), 3.35 (s, 3-OCH_3), 6.03 (s, 6-CH), 9.80 (s, 19-CH). Anal. Calcd for $C_{28}H_{44}O_3$: C, 78.45; H, 10.35. Found: C, 78.58; H, 10.51.

Attempted Synthesis of 3β-Methoxycholesta-5,7-dien-19-al (10). 7-Oxocholest-5-en-3β,19-al 3-methyl ether (**14**, 445 mg) was dissolved in 1.1 mL of $CHCl_3$ along with 200 mg of freshly recrystallized *p*-toluenesulfonylhydrazide. The solution was stirred at room temperature for 24 h. The crude solid mass was isolated from the $CHCl_3$ by azeotropic distillation with benzene and taken up in 65 mL of benzene. A 900-mg sample of LiH was added, and the solution refluxed by 4.5 h. At the end of this period, the insoluble lithium salts were removed by filtration, and the solvent was removed in vacuo. The resulting oil was shown to be a complex mixture by TLC, and UV analysis revealed that none of the 5,7-diene had been formed.

Cholest-5-ene-3β,19-diol 3-Methyl Ether (15). Cholest-5-ene-3β,19-diol 3-methyl ether 19-acetate (**6**, 1.1 g) was dissolved in a small amount of Et_2O and added dropwise to a refluxing solution of 800 mg of $LiAlH_4$ in 70 mL of Et_2O. The solution was refluxed for 1.0 h and cooled in an ice bath, and the excess reagent was carefully decomposed by the addition of H_2O. The lithium salts were filtered and washed with several portions of ether. The organic solution was dried over $MgSO_4$ and the solvent removed in vacuo to yield a crude solid residue which was crystallized from acetone to yield 0.885 g of **15**: mp 168.0–169.0 °C; $[\alpha]_D$ −29.2° (*c* 0.30); IR (Nujol) 3470, 1100 cm^{-1}; NMR 0.75 (s, 18-CH_3), 3.20 (m, 3-CH), 3.35 (s, 3-OCH_3), 3.80 (q, AB, *J* = 11 Hz, 19-CH_2), 5.80 (m, 6-CH). Anal. Calcd for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 80.87; H, 11.76.

7-Oxocholest-5-ene-3β,19-diol 3-Acetate 19-Methyl Ether (18). Chromium trioxide (3.53 g) was added to 5.58 g of pyridine in 150 mL of rapidly stirring CH_2Cl_2. The solution was allowed to react for 20 min at room temperature, and 1.80 g of **17** in 10 mL of CH_2Cl_2 was added in one portion. The mixture was allowed to react for 17 h at room temperature with constant stirring. At the end of this period an additional portion of CrO_3·2pyr complex, prepared from 1.10 g of CrO_3 and 1.73 g of pyridine in 80 mL of CH_2Cl_2, was added and stirring continued for 7 h longer. The organic layer was diluted with 600 mL of ether and the mixture washed with portions of saturated $NaHCO_3$ solution (3 × 75 mL), 3% HCl (2 × 75 mL), saturated $NaHCO_3$ solution (1 × 75 mL), and saturated NaCl solution (1 × 100 mL). The solution was dried over $MgSO_4$ and the solvent removed in vacuo to yield a brown oil which was chromatographed on 110 g of silica gel; elution with hexane–ethyl acetate (83:17) gave 1.23 g of a crystalline compound: mp 153.5-154.5 °C; $[\alpha]_D$ −125.0° (*c* 0.5); IR (Nujol) 1750, 1680, 1100, 1020 cm^{-1}; UV 233 nm (ε 12 000); NMR 0.72 (s, 18-CH_3), 2.03 (s, 3-$OCOCH_3$), 3.35 (s, 19-OCH_3), 3.50 (q, AB, *J* = 9 Hz, 19-CH_2), 4.75 (m, 3-CH).

Cholesta-5,7-diene-3β,19-diol 3-Acetate 19-Methyl Ether (19). 7-Oxocholest-5-ene-3β,19-diol 3-acetate 19-methyl ether (**18**, 1.23 g) was kept at reflux with 590 mg of *p*-toluenesulfonylhydrazide in 2.0 mL of methanol for 1.0 h, and the mixture was then allowed to react at room temperature overnight. The reaction mixture was diluted with 25 mL of benzene, and the methanol was removed by azeotropic distillation at reduced pressure. A 1.8-g sample of LiH was added to the crude tosylhydrazone in 60 mL of dry benzene and the solution heated to reflux for 4.0 h. The cooled reaction mixture was filtered to remove the lithium salts and the solvent removed in vacuo to yield an oil which was chromatographed on 45 g of silica gel; elution with hexane–ethyl acetate (92:8) gave 780 mg of a crystalline compound: mp 113.5–114.5 °C; $[\alpha]_D$ −95.7° (*c* 0.47); IR (Nujol) 1750, 1650, 1100 cm^{-1}; UV 282 nm (ε 8400), 273 (8400), CD [Θ] (λ, nm) −5.90 (272), −5.20 (282); NMR δ 0.60 (s, 18-CH_3), 2.00 (s, 3-$OCOCH_3$), 3.25 (s, 19-OCH_3), 3.40 (q, AB, *J* = 10 Hz, 19-CH_2), 4.75 (m, 3-CH), 5.55 (q, AB, *J* = 7 Hz, 6-CH and 7-CH). Anal. Calcd for $C_{38}H_{48}O_3$: C, 78.89; H, 10.59. Found: C, 78.99; H, 10.82.

19-Acetoxyvitamin D_3 3-Acetate (23). Three 200-mg portions of **3** were each irradiated in 220 mL of degassed benzene for 16 min, with the solution constantly being flushed with N_2. The portions were combined, and the solvent was removed in vacuo to yield a clear oil which was chromatographed on 125 g of Florisil. The initial fraction eluted with 95:5 hexane–ethyl acetate contained a mixture of the vitamin **23** and previtamin analogues, as oils, totaling 292 mg. Later fractions contained a mixture of the previtamin and starting material totaling 120 mg, which was saved for rechromatography, with the final fractions yielding 100 mg of pure starting material. A 292-mg sample of the vitamin and previtamin analogues was dissolved in 70 mL of degassed CCl_4 and the mixture heated to reflux under N_2 for 2.0 h. The solvent was removed in vacuo, and the resulting oil was chromatographed on 65 g of Florisil. Elution with hexane–ethyl acetate (95:5) yielded 195 mg of the vitamin **23** as an oil. Analysis of individual fractions was done further by high-pressure LC using a Du Pont Zorbex-Sil, 6.2 mm × 25 mm column with 0.25% isopropyl alcohol–hexane. Further NMR spectra were determined on a Bruker WR-270 instrument operating in the Fourier transform mode. Chemical shifts with $CHCl_3$ as an internal standard are relative to Me_4Si and are in parts per million. The *Z* C_{19} proton appears at 6.89 ppm (C_6D_6) and 6.96 ppm (CH_2Cl_2): mass spectrum, *m/e* 485 (M^+), 425 (M^+ − $HOCOCH_3$); [α] 22.2° (*c* 0.9); IR (neat) 1750, 1680, 920, 800 cm^{-1}; UV 266 nm (ε 16 400); NMR (CCl_4) 0.60 (s, 18-CH_3), 2.02 (s, 3-$OCOCH_3$), 2.20 (s, 19-$OCOCH_3$), 4.96 (m, 3-CH), 6.17 (q, AB, *J* = 11 Hz, 6-CH and 7-CH), 7.07 (s, 19-CH).

19-Methoxyvitamin D_3 3-Acetate (24). Three 20-mg portions of **19** were each irradiated in 220 mL of degassed benzene for 16 min, with the solution constantly being flushed with N_2. The portions were combined and the solvent removed in vacuo to yield a clear oil which was chromatographed on 125 g of Florisil. The initial fractions were eluted with hexane–ethyl acetate (95:5) and contained 225 mg of the starting material and an 80-mg mixture of the precalciferol$_3$ analogue and starting material. Later fractions contained 220 mg of the pure previtamin analog. A 220-mg sample of the previtamin derivative was dissolved in 80 mL of degassed CCl_4 and heated to reflux under N_2 for 2.0 h. The solvent was removed in vacuo and the resulting oil chromatographed on 65 g of Florisil; elution with hexane–ethyl acetate (95:5) yielded 135 mg of the vitamin derivative **24** as an oil. Analysis by high-pressure LC showed the presence of only **24** from the thermal reaction. NMR on a Bruker WR 270 instrument using $CDCl_3$ as solvent showed the *E* C_{19} OCH_3 at δ 3.51 ppm: mass spectrum, *m/e* 457 (M^+), 397 (M^+ − HOCOCH); $[\alpha]_D$ −25.0° (*c* 0.60); IR (neat) 1750, 1660, 1240, 1130, 1080, 1080, 1030 cm^{-1}; UV 273 nm (ε 9700); NMR δ 0.55 (s, 18-CH_3), 2.02 (s, 3-$OCOCH_3$), 3.64 (s, 19-OCH_3), 4.90 (m, 3-CH), 6.05 (m, 19-CH + 6-CH and 7-CH).

19-Deuteriocholest-5-ene-3β,19-diol Diacetate (29). A 450-mg sample of 3-hydroxycholest-5-en-19-al (**26**)[14] was dissolved in 40 mL of ether (dried and distilled from $LiAlH_4$) and cooled to 0 °C. A 200-mg sample of $LiAlD_4$ was added in one portion, and the solution was warmed to room temperature and kept at reflux for 2.0 h. The excess reagent was decomposed by the dropwise addition of H_2O, the insoluble salts were removed by filtration, the organic solution was dried over $MgSO_4$, and the solvent was removed in vacuo. The crude crystalline material was acetylated with 2 mL of Ac_2O in 1.0 mL of pyridine at 80 °C for 2.0 h. The labeled diacetate was converted to the diene by using the same conditions as those used for the conversion of **1** to **3**. The *pro-S* proton appeared at 3.89 ppm and the *pro-R* proton appeared at 4.59 ppm. The percent incorporation was 78%. After irradiation as above, the previtamin was thermally isomerized at 80 °C (18 h in CCl_4) to the vitamin. The chemical shift of the C_{19} *Z* proton in [9,19-^{2}H]-**29** appeared at 6.89 ppm. Its intensity was compared with the 3α-proton at 4.74 ppm and was determined to be 26.4%.

Irradiation of 19-Hydroxy-7-dehydrocholesterol (4). Three 200-mg portions of **4** were each irradiated in 200 mL of degassed benzene for 15 min under N_2. The solvent was removed in vacuo from the combined photolysates, giving a clear oil which was chromatographed on 125 g of Florisil. The initial fractions, eluted with hexane–ethyl acetate (90:10), consisted of 50 mg of **31** as a homogeneous oil which could not be crystallized: mass spectrum, *m/e* 370 (M^+); IR (neat) 3420, 1660, 1040 cm^{-1}; UV 266 nm (ε 4000); NMR 0.80 (s, 180 CH_3), 4.05 (m, 3-CH), 5.73 (pseudo s, 6-CH and 7-CH). Later fractions yielded 335 mg of **30** as an oil which was crystallized from acetone–methanol: mp 91.0–91.5 °C; $[\alpha]_D$ −93.5 (0.28); IR (Nujol) 3400, 1670, 1040 cm^{-1}; UV 266 nm

(ε 4420); CD [θ] (λ, nm) −4.68 (266); NMR δ 0.73 (s, 17-CH_3), 405 (m, 3-CH), 5.83 (pseudo s, 6-CH and 7-CH); mass spectrum, *m/e* 370 (M^+). Anal. Calcd for $C_{26}H_{42}O$: C, 84.26; H, 11.42. Found: C, 84.07; H, 11.24.

19-Norcholesta-5,7,9-trien-3β-ol Acetate (32). A 20.5-g sample of 7-dehydrocholesteryl acetate was dissolved in 50 mL of dry benzene, and 22.0 g of diethyl azodicarboxylate was added. The solution was heated to reflux for 7.0 h under N_2. The solvent and excess dienophile were removed at 2.5 mm pressure, yielding 16.3 g of the ene adduct. This was crystallized from petroleum ether.

An 8.0-g sample of the ene adduct was placed in a 100-mL, round-bottomed flask, evacuated to 1.5 mm pressure and heated to 215 °C for 2.0 h. A 1.55-g sample of diethyldicarboxyhydrazine was collected after it condensed on the cooler parts of the apparatus. The resulting crude brown oil was chromatographed on 300 g of Florisil, and 796 mg of **32** was eluted with benzene–$CHCl_3$ (4:1) and crystallized from methanol; mp 69.0–71.0 °C (lit.[38] mp 70.0–71.5 °C).

19-Norcholesta-5(10),6-dien-3β-ol Acetate (30a). 19-Norcholesta-5(10),6-dien-3β-ol (**30**, 125 mg) was dissolved in 0.5 mL of acetic anhydride and 0.5 mL of dry pyridine. The solution was stirred overnight at room temperature under N_2, poured into ice–H_2O, and extracted with portions of ether (3 × 30 mL). The organic extracts were washed with portions of saturated $NaHCO_3$ solution (2 × 50 mL), 3% HCl (2 × 50 mL), saturated $NaHCO_3$ solution (1 × 50 mL), and H_2O (1 × 50 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo to yield 223 mg of an oil which was crystallized from acetone–methanol: mp 94.0–94.5 °C; $[\alpha]_D$ −119.3° (*c* 0.66); IR (KBr) 1750, 1660, 1240, 1030, 800 cm^{-1}; UV 266 nm (ε 4400); CD [θ] (λ, nm) −4.68 (266); NMR δ 0.72 (s, 18-CH_3), 2.05 (s, 3-CCH_3), 4.95 (m, 3-CH), 5.72 (pseudo s, 6-CH and 7-CH); mass spectrum, *m/e* 412 (M^+), 352 (M^+ − $HOCOCH_3$). Anal. Calcd for $C_{28}H_{44}O_2$: C, 81.50; H, 10.75. Found: C, 81.43; H, 10.92.

3,19-Di-*O*-deuterio-19-hydroxy-7-dehydrocholesterol ([3,19-^{2}H]-4). A 200-mg sample of **4** was dissolved in a small amount of $CHCl_3$ in a 10-mL separatory funnel. The organic solution was washed with portions of 99.9% D_2O (4 × 4 mL) and the solvent removed in vacuo. The crude crystalline material was dried over P_2O_5 at 1.0 mm for 18 h and then recrystallized twice from 99.5% EtOD. The IR of the resulting crystals showed that extensive deuterium exchange had taken place: IR (Nujol) 2620 (OD), 1020 cm^{-1}.

A 170-mg sample of the dideuterio 5,7-diene was irradiated, purified, acetylated, and crystallized in the usual manner. The resulting compound showed one deuterium bound to carbon by high-resolution mass spectrometry: *m/e* 413 (M^+).

19-Norcholesta-5(10),6-dien-3β-ol *p*-Toluenesulfonate (34). 19-Norcholesta-5(10),6-dien-3β-ol (**30**, 60 mg) was dissolved in a small amount of pyridine, and 60 mg of freshly recrystallized tosyl chloride was added. The reaction was stirred at room temperature for 3.0 h, diluted with ice–H_2O, and extracted with portions of Et_2O (3 × 25 mL). The organic extracts were washed with portions of saturated $NaHCO_3$ solution (2 × 30 mL), 3% HCl (2 × 30 mL), saturated $NaHCO_3$ solution (1 × 30 mL), and H_2O (1 × 50 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo. The crude crystalline product was purified by recrystallization from acetone to give 88 mg of **34**: mp 100.0–101.0 °C dec; $[\alpha]_D$ −53.4° (*c* 0.42); IR (Nujol) 1660, 1180, 1170, 1040 cm^{-1}; UV 266 nm (ε 4400), 224 (13 800); NMR δ 0.68 (s, 18-CH_3), 2.45 (s, 3-$SO_2C_6H_4$-*p*-CH_3), 4.75 (m, 3-CH), 5.67 (pseudo d, 6-CH and 7-CH), 7.65 (m, AA′BB′, 3-$SO_2C_6H_4$-*p*-Me). Anal. Calcd for $C_{33}H_{48}SO_3$: C, 75.53; H, 9.22; S, 6.10. Found: C, 75.77; H, 9.04; S, 6.25.

3-Deoxy-19-norcholesta-5(10),6-diene (35). 19-Norcholesta-5(10),6-dien-3β-ol *p*-toluenesulfonate (**34**, 60 mg) was dissolved in a small amount of Et_2O and the mixture added to a refluxing solution of 300 mg of $LiAlH_4$ in 50 mL of Et_2O. The reaction was refluxed under N_2 overnight and cooled to 0.5 °C in an ice bath, and the excess reagent was decomposed by the dropwise addition of H_2O. The salts were removed by filtration, the Et_2O solution dried with $MgSO_4$, and the solvent removed in vacuo. The crude oil was chromatographed on 20 g of silica gel (hexane–ethyl acetate, 99.1) to yield 32 mg of **35** as an oil: mass spectrum, *m/e* 354 (M^+); $[\alpha]_D$ −84.2° (*c* 0.46); IR (neat) 2950, 1650, 1460, 1370 cm^{-1}; UV 266 nm (ε 5190); CD [θ] (λ, nm) 5.22 (266); NMR δ 0.65 (s, 18-CH_2), 5.70 (pseudo s, 6-CH and 7-CH).

CrO_3·2pyr Oxidation of 30a. A 120-mg sample of dry CrO_3 was added to an efficiently stirred solution of 0.19 g of dry pyridine in 30 mL of CH_2Cl_2. An 80-mg sample of **30a** was dissolved in 3 mL of CH_2Cl_2 and the mixture added to the reaction mixture in one portion. The solution was stirred for 15 min at room temperature and then diluted with 100 mL of ether. The organic solution was washed with portions of saturated $NaHCO_3$ solution (3 × 30 mL), 3% HCl (2 × 30 mL), saturated $NaHCO_3$ solution (1 × 50 mL), and saturated NaCl solution (1 × 50 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting 80 mg of brown oil was crystallized from methanol; mp 69.0–70.0 °C. The crystalline product was identical in all respects with **32**.

19-Nor-8ξ,9ξ-cholesta-5(10),6-dien-3β-ol Acetate (31a). A 73-mg sample of **31** was dissolved in 0.5 mL of pyridine and 0.3 mL of acetic anhydride. The solution was allowed to react overnight at room temperature under N_2. The mixture was then poured in 100 mL of ice–N_2O and extracted with ether (3 × 30 mL). The organic extracts were washed with ether (2 × 30 mL). The organic extracts were washed with portions of saturated $NaHCO_3$ solution (2 × 30 mL), 3% HCl (2 × 30 mL), saturated $NaHCO_3$ solution (1 × 40 mL), and H_2O (1 × 40 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting 75 mg of an oil, which was shown to be homogeneous, resisted crystallization from a variety of solvents: mass spectrum, *m/e* 412 (M^+), 352 (M^+ − HOCOCH); $[\alpha]_D$ −102.8° (*c* 0.45); IR (neat) 1750, 1660, 1230, 1030 cm^{-1}; UV 266 nm (ε 4000); CD [θ] (λ, nm) −7.60 (266); NMR δ 0.80 (s, 18-CH_3), 2.04 (s, 3-$OCOCH_3$), 4.85 (m, 3-CH), 5.75 (pseudo s, 6-CH and 7-CH).

CrO_3·2pyr Oxidation of (31a). A 93-mg sample of CrO_3 was added to 0.104 g of dry pyridine in 30 mL of CH_2Cl_2, and the solution was stirred for 15 min. At the end of this period, 62 mg of **31a** in 3 mL of CH_2Cl_2 was added in one portion and the reaction continued for 20 min. The crude mixture was diluted with 90 mL of ether and washed with portions of saturated $NaHCO_3$ solution (3 × 30 mL), 3% HCl (2 × 30 mL), and H_2O (1 × 50 mL) and dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting 55 mg of an oil was crystallized from methanol; mp 68.0–70.0 °C. The crystalline material was identical with **32**.

3β-Methoxycholesta-5,7-dien-19-al (10). A 100-mg sample of **9** in 3.7 mL of pyridine was added to a stirred solution of 0.278 g of CrO_3, 2.32 mL of H_2O, and 4.63 mL of pyridine. The stirred solution was heated to 70 °C for 2.0 h and then poured into ice–H_2O. The aqueous suspension was extracted with Et_2O (3 × 30 mL), and the organic layers were washed with portions of H_2O (2 × 100 mL), 3% HCl (1 × 100 mL), and H_2O (1 × 100 mL) and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude oil, which was shown to be a three-component system by TLC, was chromatographed on 25 g of silica gel. The first component, eluted in hexane–ethyl acetate (94:6), totaled 10 mg and was identified as **10**: mp 128.0–129.0 °C; $[\alpha]_D$ −521.0° (*c* 0.24); IR (Nujol) 1750, 1650, 1100, 1040 cm^{-1}; UV 332 nm (ε 1630), 285 (7500), 275 (8200); CD [θ] (λ, nm) −10.5 (332), +4.3 (285), +4.9 (275); NMR 0.62 (s, 18-CH_3), 3.33 (s, 3-OCH_3), 3.65 (m, 3-CH), 5.80 (q, AB, J = 6 Hz, 6-CH and 7-CH), 9.4 (s, 19-CH). Anal. Calcd for $C_{28}H_{44}O_2$: C, 81.50; H, 10.75. Found: C, 81.42; H, 10.60.

Registry No. **1**, 21072-68-4; **1** 3-monoacetate, 750-59-4; **1a**, 76010-20-3; **2**, 40272-38-6; **3**, 13640-06-7; **4**, 59446-44-5; **4** di-*O*-deuterio, 76010-21-4; **5**, 73532-71-5; **6**, 73532-72-6; **7**, 76010-22-5; **8**, 76024-66-3; **9**, 76010-23-6; **10**, 76010-24-7; **14**, 76010-25-8; **15**, 21072-63-9; **17**, 1108-65-2; **18**, 76010-26-9; **19**, 76010-27-0; **23**, 73245-72-4; **24**, 76010-28-1; **26**, 1107-90-0; **29**, 76010-29-2; **30**, 59446-45-6; **30a**, 59462-94-1; **31**, 76035-34-2; **31a**, 76035-35-3; **32**, 1253-99-2; **34**, 76010-30-5; **35**, 76010-31-6; 35-dinitrobenzoyl chloride, 99-33-2; 7-dehydrocholesteryl acetate, 1059-86-5.