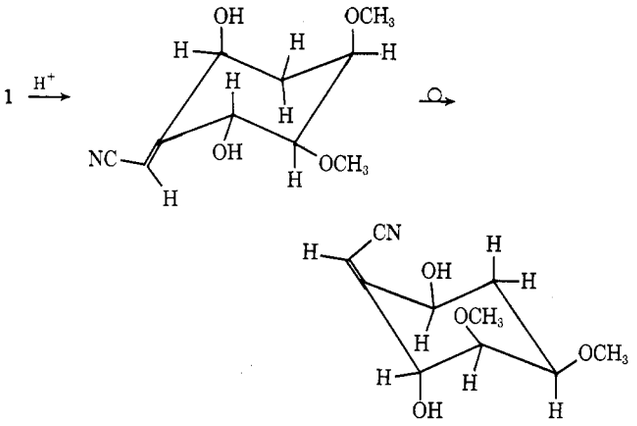
Scheme I



ial strain between the glucose and the methoxyl in this conformation. Such interaction in the vicinity of a double bond has been termed allylic 1,3 strain [$A^{(1,3)}$] by Johnson,[4] and he has pointed out that this can be of higher energy than 1,3-diaxial interaction in a cyclohexane system, even when the groups involved are of moderate size. The observed conformation of simmondsin is consistent with this theory.

Experimental Section

Melting points were measured on a Thomas-Hoover capillary apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer 257 instrument. Nmr spectra were measured on a Varian A-60 instrument or on a HA-100 spectrometer. Spin-decoupled spectra were obtained on the latter machine in the frequency mode. Elemental analyses were performed in this laboratory.

Treatment of Simmondsin with Acid. Simmondsin (4.40 g) dissolved in 1 *N* hydrochloric acid (50 ml) was refluxed for 1.5 hr. After cooling to room temperature, the mixture was concentrated under reduced pressure to a semisolid paste which was triturated with four 25-ml portions of ethyl acetate. Evaporation gave an oil (2.19 g) which was applied in ethyl acetate to a column (25 × 1000 mm) prepared with 190 g of silica gel (Mallinckrodt SilicAR CC-7, special) in chloroform. Elution was carried out at 60 ml/hr in a linear gradient from 100% chloroform to 20% methanol–chloroform (2 l.). Three major fractions were obtained: (i) between 370 and 580 ml (0.16 g), (ii) between 860 and 740 ml (0.33 g), and (iii) between 1040 and 1160 ml (1.31 g). Fraction iii was dissolved in ethyl acetate (40 ml) and extracted with 5% sodium hydrogen carbonate solution (3 × 30 ml). The organic layer was dried over magnesium sulfate and evaporated to give 0.32 g of crude lactone **2**, which was crystallized from benzene to give 0.17 g of material, mp 138–140°. *Anal.* Calcd for $C_{10}H_{14}O_5$: C, 59.34; H, 5.53. Found: C, 59.6; H, 5.57. The infrared spectrum, ν_{max} ($CHCl_3$), showed absorptions at 1665 (conjugated double bond in C-5 ring) and 1755 cm^{-1} (α,β-unsaturated, five-ring lactone). The nmr spectrum in deuterioacetone is shown in Table I.

Acidification of the aqueous extract from iii followed by extraction with ethyl acetate provided 2-hydroxy-5-methoxyphenylacetic acid (0.40 g). Fractions i and ii were shown to be respectively the lactone of the above phenolic acid and the corresponding methyl ester (formed during chromatography).[1]

Acknowledgments. We wish to thank Mrs. Mabry Benson for obtaining the 100-MHz nmr spectra and Miss G. E. Secor for elemental analysis.

Registry No.—**1b**, 51771-52-9; **2**, 52032-66-3.

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Studies on Vitamin D and Its Analogs. I. Synthesis of 1α-Hydroxycholest-5-ene

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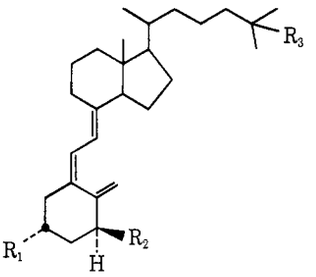
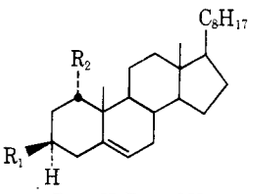
Received May 13, 1974

Vitamin D_3 (**1a**),[2] a steroidal hormone intimately associated with calcium transport, must be successively hydroxylated in the liver[3] and then in the kidney to produce the metabolite 1α,25-dihydroxyvitamin D_3 (**1b**)[4] before elic-



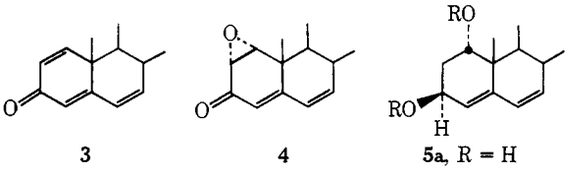
1a, R_1 = OH; R_2 = R_3 = H
b, R_1 = R_2 = R_3 = OH
c, R_2 = OH; R_1 = R_3 = H

iting its physiological action. Recent investigations have led to the suggestion that the 1α-hydroxyl contained in the carbon framework represented by structure 1 may be the critical functionality necessary for vitamin D activity.[5] If this is the case, an attractive substance for study is the analog **1c**, which lacks both the seemingly unnecessary 3β- and 25-hydroxyl groups of the natural system **1b**. Our ongoing studies directed toward synthesizing **1c** and related analogs required the availability of the hitherto unknown cholesterol isomer 1α-hydroxycholest-5-ene (**2a**). It is the purpose of this note to provide the details for its preparation.



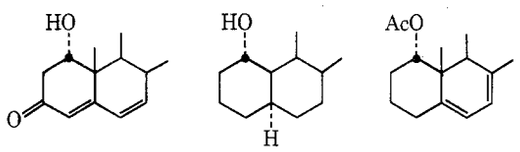
2a, R_1 = H; R_2 = OH
b, R_1 = OH; R_2 = H
c, R_1 = H; R_2 = OAc
d, R_1 = R_2 = OH
e, R_1 = OTs; R_2 = OH

The title compound **2a** has been prepared by two different routes. Cholesterol was converted as described previously to the epoxydienone **4** by successive treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[6] and alkaline hydrogen peroxide.[7] In the first route, **4** was reduced with lithium aluminum hydride yielding **5a** (62%), which upon subsequent reduction with lithium–ammonia pro-



3 **4** **5a**, R = H; **b**, R = Ac

duced the title compound **2a** (60%).[8] The structures of **5a** and its diacetate **5b** were evident from their spectral data and chemical behavior. Besides exhibiting nmr and ir spectral data appropriate for their assigned structures, **5a** and **5b** revealed uv bands at 232, 240, and 248 nm characteristic of other cholesta-4,6-dienes.[9] The orientation of the 3 substituent in **5a** and **5b** is presumably mainly β. A similar reduction of 4-cholesten-3-one gave mainly the 3β alcohol.[10] The dienediol **5a,** on selective oxidation at C-3 with DDQ, afforded **6** (92%). The latter revealed appropriate nmr, ir, and uv spectra and was convertible to **3** by isopropenyl acetate–acid treatment. Spectral data for **2a** and the monoacetate **2c** were also in accord with their assigned structures. The structure of **2a** was confirmed by its hydrogenation to the known alcohol **7**,[11] and furthermore, the acetate **2c** could be converted to 1α-acetoxycholesta-5,7-diene (**8**, 11%).[12]



6 **7** **8**

In the second route, the epoxydienone **4** was first converted to **2d** (49%) according to Barton, *et al.*, by lithium–ammonia reduction.[5d] The treatment of the latter with excess *p*-toluenesulfonyl chloride–pyridine afforded the monotosylate **2e** in almost quantitative yield. Lithium aluminum hydride reduction of **2e** afforded **2a** (72% based on **2d**) identical in every respect with the material prepared from **5a.**

The pathway through which **5a** proceeds to **2a** can be considered to arise by initial cleavage of **5a** to a pentadienyl anion. It can then be presumed that the latter is protonated regioselectively to give 1α-hydroxy-4,6-cholestadiene, which upon further reduction gives **2a.** The reductive cleavage of the allylic hydroxyl is analogous to the known lithium reduction of 4-cholesten-3β-ol to 4-cholestene[10a] and the conversion of dienes to monoenes with lithium is well precedented.[8b,17]

Experimental Section

General. Infrared (ir) spectra (Nujol) were obtained with a Perkin-Elmer Model 137 or 621 spectrophotometer and ultraviolet (uv) spectra (95% ethanol) with a Beckman DB or Cary Model 14 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded with a Varian 60-MHz spectrometer with deuteriochloroform as solvent and tetramethylsilane (TMS, τ 10.00) as the internal standard. In most cases, C_{19} and C_{18} angular methyl singlets are expressed in hertz downfield from TMS.[11b] Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6D spectrometer. Microanalyses were performed by C. F. Geiger, Ontario, Calif. Melting points (Thomas-Hoover capillary melting point apparatus) are uncorrected. Low-boiling petroleum ether (30–60°) was used.

1,4,6-Cholestatrien-3-one (3). A known procedure,[6] DDQ (40 g) oxidation of cholesterol (20 g) in dry dioxane (500 ml) followed by purification by chromatography and then crystallization, afforded pure **3:** 11.0 g, 56%; mp 84–85° (lit.[13] mp 82–83°).

1α,2α-Oxido-4,6-cholestadien-3-one (4). A known procedure,[7] aqueous 30% hydrogen peroxide (25 ml)–aqueous 15% w/v sodium hydroxide (2 ml) treatment of **3** (11.0 g) in methanol (450 ml) followed by purification by crystallization, afforded pure **4:** 8.2 g, 72%; mp 106–107° (lit.[7b] mp 105–107°).

4,6-Cholestadiene-1α,3β-diol (5a). A solution of **4** (5.0 g, 0.013 mol) in dry ether (200 ml) was refluxed with lithium aluminum hydride (2.5 g, 0.066 mol) under anhydrous conditions for 4–5 hr. The mixture was ice cooled and then water (2.5 ml), aqueous sodium hydroxide (2.5 ml, 15% w/v), and water (7.5 ml) were added successively and cautiously to the well-stirred mixture. The precipitated aluminum salts were removed by filtration. The combined filtrate and washings were concentrated under vacuum to dryness. The residue was chromatographed over alumina (Woelm neutral III, 150 g). The product (3.8 g), which was eluted with benzene–ether (2:1), was crystallized from acetone–methanol to afford **5a** as stout needles (3.25 g, 62%): mp 120–121°; uv λ_{max} 248 nm (ϵ 15,400), 240 (23,800), and 232 (21,700); nmr τ 3.97 and 4.31 ($H_{6,7}$, AB q, $J_{AB} \simeq$ 10 Hz), 4.39 (H_1, d, $J \simeq$ 4 Hz), 5.71 and 6.06 ($H_{1\beta,3\alpha}$ br peaks), 9.09 (C_{21} CH_3, d, $J \simeq$ 6 Hz), 9.11 (C_{19} CH_3, s), 9.13 ($C_{26,27}$ 2 CH_3, d, $J \simeq$ 5.5 Hz), and 9.27 (C_{18} CH_3, s); ir ν_{max} 3400 cm^{-1} (OH).

Anal. Calcd for $C_{27}H_{44}O_2$: C, 80.94; H, 11.07. Found: C, 80.81; H, 11.21.

1α,3β-Diacetoxy-4,6-cholestadiene (5b). A mixture of **5a** (2 g, 0.005 mol), acetic anhydride (10 ml), and pyridine (10 ml) was heated on a steam bath for 3 hr. The cooled mixture was quenched with ice-cold water and then worked up in the usual way. The dark crystalline residue (2.3 g) thus obtained was purified by chromatography over alumina (Woelm neutral III) to afford 1.6 g (67%) of diacetate. Crystallization of this material from methanol afforded glistening needles: mp 178–179°; uv λ_{max} 232 nm (ϵ 23,100), 240 (25,600), and 248 (17,500); nmr τ 3.94 and 4.24 ($H_{6,7}$, AB q, $J_{AB} \simeq$ 10 Hz), 4.36–4.73 ($H_{3\alpha,4}$, m), 5.04 ($H_{1\beta}$, pseudo-t, $J \simeq$ 2.5 Hz), 7.94 ($AcCH_3$, s), 7.99 ($AcCH_3$, s), 9.02 (C_{19} CH_3, s), 9.07 (C_{21} CH_3, d, $J \simeq$ 5 Hz), 9.12 ($C_{26,27}$ 2 CH_3, d, $J \simeq$ 6 Hz), and 9.27 (C_{18} CH_3, s); ir ν_{max} 1725 cm^{-1} (C=O).

Anal. Calcd for $C_{31}H_{48}O_4$: C, 76.81; H, 9.98. Found: C, 76.93; H, 9.71.

1α-Hydroxy-4,6-cholestadien-3-one (6). An anhydrous mixture of dienediol **5a** (1.0 g, 0.0025 mol) and DDQ (0.90 g, 0.0040 mol) in purified dioxane (30 ml) was allowed to stand at ambient temperatures for 24 hr. The mixture was diluted with ether and then washed successively with 1 *M* aqueous sodium hydroxide and water. After drying (sodium sulfate) and filtration, concentration left a residue which on crystallization (aqueous acetone) afforded **6** (920 mg, 92%) as shiny flakes: mp 177°; uv λ_{max} 286 nm (ϵ 26,600);[14] ir ν_{max} 3470 (OH) and 1668 cm^{-1} (C=O); nmr τ 3.81 ($H_{6,7}$, br s, $W \simeq$ 2 Hz), 4.22 (H_4, br s, $W \simeq$ 2 Hz), 5.82 ($H_{1\beta}$, br m, $W \simeq$ 7 Hz), 7.14–7.44 ($H_{2\alpha,\beta}$, br m), 9.07 (C_{21} CH_3, d, $J \simeq$ 5 Hz), 9.13 ($C_{26,27}$ 2 CH_3, d, $J \simeq$ 6 Hz) [C_{19} CH_3, 67.0 Hz (calcd, 69.0); C_{18} CH_3, 45.5 Hz (calcd, 45.5)].[11b]

Anal. Calcd for $C_{27}H_{42}O_2$: C,81.35; H, 10.62. Found: C, 81.13; H, 10.36.

A mixture of **6** (100 mg), isopropenyl acetate (2 ml), and *p*-toluenesulfonic acid (10 mg) in benzene was refluxed for 4 hr. After sodium bicarbonate treatment to neutralize the acid, the mixture was worked up in the usual way with water and ether. The residue obtained after drying and concentrating the organic extract was chromatographed and then recrystallized to afford pure **3** with mp 83–84°.

1α-Hydroxy-5-cholestene (2a) from 5a. A three-necked standard taper round-bottom flask equipped with a mechanical stirrer, a Dry Ice condenser, a nitrogen inlet, and an ammonia inlet was thoroughly dried and flushed with nitrogen. A solution of lithium metal (0.4 g, 0.06 mol) in ammonia (60 ml) was prepared under nitrogen in the usual manner. A solution of **5a** (0.518 g, 0.00129 mol) in dry, freshly distilled tetrahydrofuran (60 ml) was added to the Dry Ice–acetone cooled solution and then the mixture was stirred for 3 hrs after the cooling bath had been removed. Solid ammonium chloride (~0.5 g) was added and after the solution was stirred for 1 hr, saturated aqueous ammonium chloride was added. The ammonia was allowed to evaporate, water was added to dissolve the precipitated salts, and then the mixture was thoroughly extracted with ether. The ethereal extract was washed with water, dried (sodium sulfate), and then concentrated under vacuum to afford 0.509 g of a white solid. Silica gel column chromatography (petroleum ether–ether mixtures) gave 0.3 g (60%) of enol **2a.** Further purification by preparative tlc (silica gel H) and crystallization (95% ethanol) yielded very pure **2a:** mp 102–103°; nmr τ 4.34 (H_6, br, $W \simeq$ 10 Hz), 6.26 ($H_{1\beta}$, br, $W \simeq$ 8 Hz), 9.08 (C_{21} CH_3, d, $J \simeq$ 5 Hz), 9.14 ($C_{26,27}$ 2 CH_3, d, $J \simeq$ 6 Hz) [C_{19} CH_3, 60.5 Hz (calcd, 61.5) and C_{18} CH_3, 41.0 Hz (calcd, 42.0)];[11b] ir ν_{max} 3400 cm^{-1} (OH).

Anal. Calcd for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.71; H, 12.34.

1α-Acetoxy-5-cholestene (2c). The enol **2a** (1.5 g, 0.0039 mol) was treated with acetic anhydride (5 ml), pyridine (5 ml), and 4-dimethylaminopyridine (1.0 g)[5d] at room temperature and allowed to stand overnight. The mixture was treated with cold water and extracted with ether. The ethereal extract was washed successively with cold dilute hydrochloric acid, water, and aqueous sodium bicarbonate and finally dried over sodium sulfate. After filtration

and removal of the solvent under vacuum, the resulting dark red residue was passed through a column of silica gel with benzene as eluent. This gave 1.62 g of crude acetate which upon crystallization (95% ethanol) afforded **2c** as stout needles (1.40 g, 85%): mp 69–70°; nmr τ 4.69 (H_6, br, $W \simeq 10$ Hz), 5.13 ($H_{1\beta}$, br, $W \simeq 5.5$ Hz), 8.01 ($AcCH_3$, s), 9.11 (C_{21} CH_3, d, $J \simeq 5$ Hz), 9.16 ($C_{26,27}$ 2 CH_3, d, $J \simeq 6$ Hz) [C_{19} CH_3, 61.5 Hz (calcd, 63.5), C_{18} CH_3, 39.0 Hz (calcd, 40.5)];[11b] ir ν_{max} 1770 cm^{-1} (C=O).

Anal. Calcd for $C_{29}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 81.51; H, 11.20.

Hydrogenation of 2a. 1α-Hydroxy-5α-cholestane (7). A solution of **2a** (68 mg) in absolute ethanol containing a catalytic quantity of 10% palladium on carbon was hydrogenated at room temperature and pressure. After work-up, the product (mp 102–103°, lit.[11a] mp 103–105°) revealed an nmr spectrum[11b] identical with that published elsewhere.

1α-Acetoxy-5,7-cholestadiene (8). To a refluxing, magnetically stirred solution of **2c** (415 mg, 0.0097 mol) in a 1:1 mixture of benzene–hexane (90 ml) under anhydrous conditions was added 1,3-dibromo-5,5-dimethylhydantoin (145 mg, 0.00051 mol) at once. The mixture turned yellow and then finally colorless during the 15-min reflux period after adding the brominating agent. The mixture was ice cooled and filtered to remove the precipitated 5,5-dimethylhydantoin and the solid was rinsed thoroughly with cold petroleum ether. The combined filtrates were concentrated to dryness at room temperature on a rotary evaporator under vacuum. The yellow residual syrup in xylene (50 ml) was added dropwise under nitrogen to a refluxing, magnetically stirred solution of trimethyl phosphite (1.5 ml) in xylene (25 ml). After the addition (0.5 hr), the mixture was maintained at reflux for 1.0 hr. The cooled mixture was concentrated to dryness at water pump vacuum and then under high vacuum.

The residue dissolved in a small volume of petroleum ether was chromatographed (10% silver nitrate impregnated silica gel, 15 g; 1-cm diameter column, prepared with petroleum ether; 14-ml fractions) using ether–petroleum ether mixtures (0%, 200 ml; 2%, 350 ml; 4%, 500 ml; 10%, 100 ml) and the fractions were analyzed by examination of their uv spectra. Fractions 34–51 showed absorptions expected for the $\Delta^{4,6}$-diene and were not examined further. Fractions 52–75 contained mainly the $\Delta^{5,7}$-diene and these fractions were pooled and the solvent removed under vacuum. The residue (55 mg) was rechromatographed (silica gel, 8 g; 1-cm column prepared with petroleum ether; 30-ml fractions) using ether–petroleum ether mixtures (0%, 60 ml; 2%, 90 ml; 6%, 30 ml). Fraction 4 contained the desired provitamin acetate **8** (45 mg, 11%; mp 105–106°) uncontaminated by material with λ_{max} 311 nm which was not removed by the first chromatography.

In another experiment, further purification by preparative tlc followed by crystallization (ethanol) afforded **8** as colorless needles: mp 108–109°; nmr τ 4.32 and 4.61 ($H_{6,7}$, AB q, $J_{AB} \simeq 6$ Hz), 5.08 ($H_{1\beta}$, br, $W \simeq 6$ Hz), 7.92 ($AcCH_3$, s), 9.07 (C_{21} CH_3, d, $J \simeq 5$ Hz), 9.12 ($C_{26,27}$ 2 CH_3, d, $J \simeq 6$ Hz) [C_{19} CH_3, 59.0 Hz (calcd, 58.0); C_{18} CH_3, 37.5 Hz (calcd, 36.5)];[11b] uv λ_{max} 252 nm sh (ϵ 2700), 262 sh (6800), 271 (10,300), 281 (11,600), 293 (6800);[15] mass spectrum (80 eV) selected *m/e* (rel intensity) 428 (0.4), 427 (1.6), 426 (5) (parent), 366 (50), 253 (20), 226 (27), 211 (100 base), 199 (43), 183 (28), 168 (30), 158 (45), 143 (40), 131 (35), 43 (89).

1α-Hydroxycholesterol (2d).[5d,16] The epoxide **4** (3.0 g, 0.0076 mol) in tetrahydrofuran (100 ml) was treated with lithium (4.0 g, 0.58 mole) in ammonia (100 ml) for 3 hr as described above for the reduction of **5a.** Solid ammonium chloride (25 g) was added, the mixture was stirred for 1 hr, and then saturated aqueous ammonium chloride was added cautiously with vigorous stirring. The ammonia was allowed to evaporate and water was added to dissolve the precipitated salts. After extraction with ether, the combined ethereal extracts were washed with water, dried over sodium sulfate, filtered, and then concentrated under vacuum. The residue (3.05 g) was chromatographed over alumina (Woelm neutral III; 50% ethyl acetate–ethanol) to afford 1α-hydroxycholesterol (**2d,** 2.07 g). Crystallization (acetone) afforded 1.5 g (49%) of pure material: mp 156–157° (lit.[5d] mp 162–163°); $[\alpha]^{24}D$ −35° (*c* 8.72 mg/ml, $CHCl_3$); nmr τ 4.39 (H_6, br, $W \simeq 8$ Hz), 6.0 ($H_{3\alpha}$, very br, $W \gg 10$ Hz), 6.13 ($H_{1\beta}$, br, $W \simeq 7$ Hz), 9.07 (C_{21} CH_3, d, $J \simeq 5.5$ Hz), 9.13 ($C_{26,27}$ 2 CH_3, d, $J \simeq 6$ Hz) [C_{19} CH_3, 61.5 Hz (calcd, 62.0); C_{18} CH_3, 41.5 Hz (calcd, 42.0)].[11b]

The diacetate of this material was a liquid, but subsequent bromination–dehydrobromination according to the procedure described above for preparing **8** afforded the known crystalline 1α,3β-diacetoxy-5,7-cholestadiene (mp 113–114°, lit.[5d] mp 118–119°).

1α-Hydroxycholesteryl Tosylate (2e). The diol **2d** (1.0 g, 0.0025 mol) and *p*-toluenesulfonyl chloride (1.0 g, 0.0052 mol) dissolved in dry pyridine (5 ml) were allowed to stand overnight in the freezer (<0°). After addition of a small volume of cold water to the reaction mixture and then addition of ether, the ethereal phase was washed with cold water, dried (sodium sulfate), and concentrated to afford a crystalline residue (1.35 g). This material, which was mainly **2e,** was used in the next step without further purification. In another experiment, crystallization (acetone–petroleum ether) afforded a sample: mp 147° dec; nmr τ 2.18 and 2.65 (4 H, aryl ring, AB q, $J_{AB} \simeq 8$ Hz), 4.45 (H_6, br, $W \simeq 10$ Hz), 5.2 ($H_{3\alpha}$, very br, $W \gg 10$ Hz), 6.18 ($H_{1\beta}$, br, $W \simeq 8$ Hz), 7.54 ($ArCH_3$, s), 9.02 (C_{19} CH_3, s), 9.07 (C_{21} CH_3, d, $J \simeq 5$ Hz), 9.12 ($C_{26,27}$ 2 CH_3, d, $J \simeq 6$ Hz), and 9.33 (C_{18} CH_3, s).

Anal. Calcd for $C_{34}H_{52}O_4S$: C, 73.33; H, 9.41. Found: C, 73.02; H, 9.48.

1α-Hydroxy-5-cholestene (2a) from 2e. The crude **2e** (1.35 g) from the immediately preceding step in ether (80 ml) was treated in the usual way with lithium aluminum hydride (908 mg, 0.0239 mol). The reaction mixture was worked up as described above and then the ensuing crude alcohol was purified by chromatography (silica gel, 25 g, petroleum ether–benzene mixtures as eluent to afford **2a** (mp 99–100°, 705 mg, 72% based on **2d**), which proved homogeneous by tlc. Further purification by crystallization (95% ethanol) afforded stout needles mp 102–103°. This material was identical (nmr, melting point, tlc) with **2a** prepared in the different manner described above.[17]

Registry No.—**2a,** 52032-61-8; **2c,** 52932-62-9; **2d,** 26358-75-8; **2e,** 52032-63-0; **3,** 3464-60-6; **4,** 28893-44-9; **5a,** 51525-89-4; **5b,** 52032-64-1; **6,** 52032-65-2; **8,** 52109-45-2; DDQ, 84-58-2.

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(1) (a) Department of Biochemistry. (b) Supported by U. S. Public Health Service grants AM-09012 and AM-14,750 to A. W. N. (c) Recipient of USPHS Career Development Award 1-KD-AM-13,654. (d) Department of Chemistry. (e) Supported by an Intramural Research Fund Grant, University of California, Riverside, and by a grant from the U. S. Public Health Service (AM-16595).

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(14) See ref 9; 4,6-dien-3-ones show λ_{max} 281–284 nm (ϵ 25,000–30,000).

(15) This spectrum is characteristic of provitamin D. See ref 2, p 93, as well as ref 9.

(16) For other reported preparations of **2d,** see (a) B. Pelc and E. Kodicek, *J. Chem. Soc.,* 1624 (1970); (b) E. J. Semmler, M. F. Holick, H. K. Schnoes, and H. F. DeLuca, *Tetrahedron Lett.,* 4147 (1972); (c) C. Kaneko, S. Yamada, A. Sugimoto, and M. Ishikawa, *ibid.,* 2339 (1973); (d) M. Morisaki, K. Bannai, and N. Ikekawa, *Chem. Pharm. Bull.,* **21,** 1853 (1973); (e) A. Fürst, L. Labler, W. Meier, and K.-H. Pfoertner, *Helv. Chim. Acta,* **56,** 1708 (1973).

(17) Since the submission of this manuscript, 3-deoxy-1α-hydroxyvitamin D_3 (**1c**) has been found to be highly biologically active in stimulating intestinal calcium transport in vitamin D deficient chicks.