Stereospecific Synthesis of the Side Chain of the Steroidal Plant Sex Hormone Oogoniol

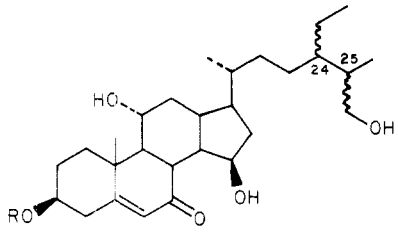
James R. Wiersig, Nada Waespe-Sarcevic, and Carl Djerassi*

Department of Chemistry, Stanford University, Stanford, California 94305

Received December 8, 1978

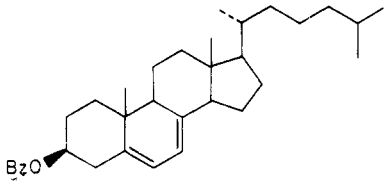
The determination of the configuration at C-24 of the revised structure of oogoniol (**19**), a sex hormone of the water mold *Achlya*, was accomplished by the stereospecific synthesis of the model compounds (24*S*)-stigmast-5-ene-3β,29-diol (**24**) and (24*R*)-stigmast-5-ene-3β,29-diol (**53**) which contain the oogoniol side chain. Diols **24** and **53** were prepared from esters **23** and **46**—products of the Claisen rearrangement of (23*E*,- and 23*Z*,22*S*)-6β-methoxy-3α,5-cyclo-5α-cholest-23-en-22-ol (**22** and **33**) with trimethyl orthoacetate. Comparison of the proton NMR spectral data of **24** and **53** with those of oogoniol proved that the stereochemistry at C-24 of the revised structure of oogoniol is 24*R*, and, therefore, that oogoniol has the stereostructure **56**.

Steroidal hormones have been shown to play an important role in the sexual reproductive process of the water mold *Achlya*.[1-8] This Oomycete genus is unique in this respect, and recent results strongly suggest that a complex hormonal control mechanism similar to those found in animal systems exists in *Achlya*.[6,8-12] The oogoniols induce the formation of oogonia, the female sex organs, in *Achlya*, and they were isolated in 1975 by McMorris and coworkers,[13] who proposed structures **1a–d** for the closely related steroids oogoniol-1, oogoniol-2, oogoniol-3, and oogoniol.



1a, R = $(CH_3)_2CHC{=}O$
b, R = $CH_3CH_2C{=}O$
c, R = $CH_3C{=}O$
d, R = H

The synthetic approach decided upon in our laboratory centered on oogoniol and was divided into two parts. The first focused on the nucleus of **1d**, and we have reported recently[14] the synthesis of 3β,11α,15β-trihydroxycholest-5-en-7-one (**3**), a compound containing the nuclear functionalities of oogoniol (**1d**) and an unsubstituted cholestane side chain, starting from 7-dehydrocholesterol benzoate (**2**). The second part involves the construction



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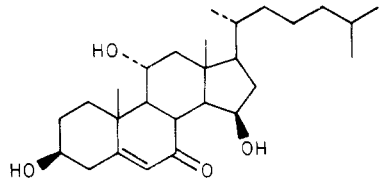

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of the side chain which should be stereospecific so that its stereochemistry and absolute configuration—two hitherto undetermined features—could be determined. We now report a successful solution to this second problem.

In designing our synthesis of the oogoniol side chain, we wanted to be able to stereospecifically synthesize all of the possible configurations in the side chain. Comparison of the proton and/or carbon nuclear magnetic resonance spectra of the synthetic models with the spectra of the authentic natural product would then permit determination of the configurations at C-24 and C-25. The Claisen rearrangement has proven to be an excellent method of introducing functionalities in a stereospecific and regiospecific manner,[15-17] and Sucrow et al.[18-22] have investigated its specific applicability to steroidal side chain allylic alcohols. Our general plan was to synthesize a suitable allylic alcohol (e.g., **5**) and expose it to triethyl orthopropionate (**6**) to yield a Claisen product (**7**), which could then easily be converted to the 24*R*,25*S* epimer **8** of the oogoniol side chain.

The starting material chosen for our synthesis (Scheme I) was the aldehyde **11**, which is readily available from stigmasterol (**9**) via its iso-methyl ether **10**.[23,24] Treatment

(1) L. Machlis in "The Fungi", Vol. II, G. C. Ainsworth and A. S. Sussman, Eds., Academic Press, New York, N.Y., 1966, p 415.
(2) A. W. Barksdale, *Science*, **166**, 831 (1969).
(3) L. Machlis, *Mycologia*, **64**, 235 (1972).
(4) G. W. Gooday, *Annu. Rev. Biochem.*, **43**, 35 (1974).
(5) M. J. Carlile and G. W. Gooday, *Cell. Surf. Rev.*, **5**, 219 (1978).
(6) G. Kochert, *Annu. Rev. Plant Physiol.*, **29**, 461 (1978).
(7) B. A. Knights, *Top. Horm. Chem.*, **1**, 251 (1978).
(8) C. G. Elliott, *Adv. Microb. Physiol.*, **15**, 121 (1977).
(9) P. A. Horgen, *Biochem. Biophys. Res. Commun.*, **75**, 1022 (1977).
(10) W. E. Timberlake, *Dev. Biol.*, **51**, 202 (1976).
(11) R. B. Sutherland and P. A. Horgen, *J. Biol. Chem.*, **252**, 8812 (1977).
(12) B. Groner, N. Hynes, A. E. Sippel, and G. Schultz, *Nature (London)*, **261**, 599 (1976).
(13) T. C. McMorris, R. Seshadri, G. R. Weihe, G. P. Arsenault, and A. W. Barksdale, *J. Am. Chem. Soc.*, **97**, 2544 (1975). For biosynthetic studies see T. C. McMorris and R. H. White, *Phytochemistry*, **16**, 359 (1977). **Note added in proof:** M. W. Preuss and T. C. McMorris, *J. Am. Chem. Soc.*, **101**, 3066 (1979), have shown that the $\Delta^{24(28)}$-dehydro analogues possess much higher biological activity.
(14) E. J. Taylor and C. Djerassi, *J. Org. Chem.*, **42**, 3571 (1977).
(15) G. B. Bennett, *Synthesis*, 589 (1977).
(16) S. J. Rhoads and N. R. Raulins, *Org. React.*, **22**, 1 (1975).
(17) F. E. Ziegler, *Acc. Chem. Res.*, **10**, 227 (1977).
(18) W. Sucrow and B. Girgensohn, *Chem. Ber.*, **103**, 750 (1970).
(19) W. Sucrow, B. Schubert, W. Richter, and M. Slopianka, *Chem. Ber.*, **104**, 3689 (1971).
(20) W. Sucrow, P. P. Caldeira, and M. Slopianka, *Chem. Ber.*, **106**, 2236 (1973).
(21) W. Sucrow, M. Slopianka, and P. P. Caldeira, *Chem. Ber.*, **108**, 1101 (1975).
(22) W. Sucrow and M. Slopianka, *Chem. Ber.*, **108**, 3721 (1975).

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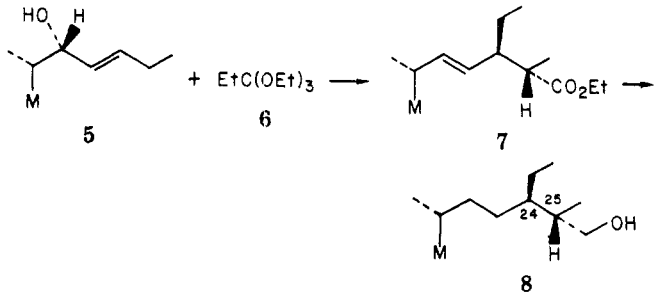
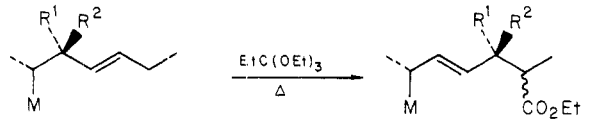


5 6 7 8

with 1-butynylmagnesium bromide gave a 1:1 mixture of the (22*R*)- (**12**) and (22*S*)- (**13**) 6β-methoxy-3α,5-cyclo-27-nor-5α-cholest-23-yn-22-ols. The epimeric alcohols were easily separable by column chromatography,[25] and their stereochemistry was proved by conversion to the known[20] acetates **14** and **15**, whose configurations at C-22 had been determined by Horeau analysis. Lithium aluminum hydride reduction of the acetylenic alcohols **12** and **13** gave the desired 22*S* and 22*R* allylic alcohols **16** and **5** with the 23*E* stereochemistry as established by NMR analysis.

Claisen rearrangement of the individual allylic alcohols **5** and **16** using triethyl orthopropionate[26,27] gave in both cases a mixture of two olefinic esters (**17** and **18**, re-

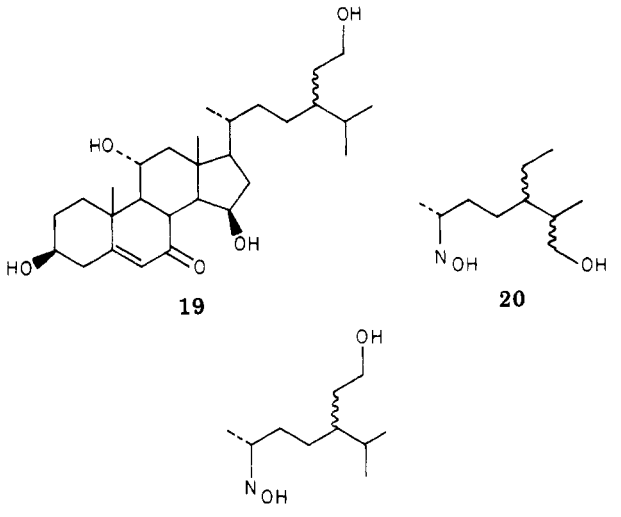


5, R¹ = OH, R² = H
16, R¹ = H, R² = OH

17, R¹ = H, R² = Et
18, R¹ = Et, R² = H

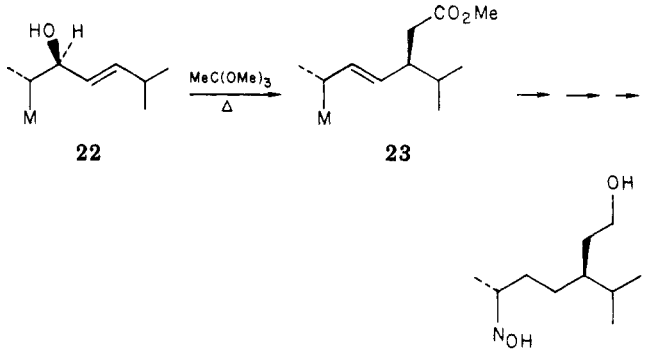
spectively) which were epimeric at C-25 and could not be separated by either thin-layer or column chromatography. Evidently both *E* and *Z* isomers of the intermediate ketene acetals are formed during the Claisen rearrangement when ethanol is lost from the mixed orthoester intermediates; consequently mixtures of C-25 epimers are formed. A description of the synthesis of **5** and **16** (Scheme I) and experimental details are available as supplementary material.

In order to achieve better stereochemical control during the Claisen rearrangement, we intended to employ Ireland's ester–enolate modification of the Claisen rearrangement.[28] However, at this stage McMorris and collaborators[29] revised the structure of oogoniol from **1d** to **19** because the ^{13}C NMR spectrum of oogoniol resembled more closely that of the model (24ξ)-stigmast-5-ene-3β,29-diol (**21**) than that of (24ξ,25ξ)-stigmast-5-ene-3β,26-diol (**20**).



19 **20** **21**

A stereospecific synthesis of the revised oogoniol side chain structure was still required since the C-24 stereochemistry could not be established on the basis of the reported[13,29] spectral measurements. Fortunately, the same Claisen rearrangement approach used for the generation of the original[13] oogoniol side chain could also be employed to produce the revised one (**19**). Specifically, the plan was to synthesize the allylic alcohol **22** and via Claisen re-



22 **23** **24**

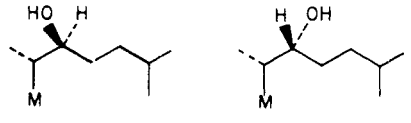
arrangement with trimethyl orthoacetate obtain a 28-methoxycarbonyl derivative (**23**) which could then easily be converted to the oogoniol side chain model **24**. The C-24 stereochemistry would be controlled simply by the stereochemistry of the Δ^{23} double bond in the starting alcohol **22**.

The starting material for the synthesis (Scheme II) was the aldehyde **11**, which is readily available from stigmasterol (**9**) via its iso-methyl ether (**10**).[23,24] Treatment with the vinyllithium reagent **25** derived from (*E*)-1-iodo-3-methyl-1-butene (**27**) gave, after chromatography, 50% of the crystalline 22*S* allylic alcohol **22** and 11% of the noncrystalline 22*R* epimer **26**. The *E* vinyl iodide **27** was prepared from commercially available 3-methyl-1-butyne (**35**) by reaction with catecholborane to give the catechol

(23) R. F. N. Hutchins, J. J. Thompson, and J. A. Svoboda, *Steroids*, **15**, 113 (1970).

(24) W. G. Salmond and M. C. Sobala, *Tetrahedron Lett.*, 1695 (1977).

(25) The relatively large difference in polarity between the epimeric alcohols (**12**, R_f 0.39; **13**, R_f 0.28 in 20% EtOAc/hexane) is noteworthy. The 22*R* (22α) alcohol **12** is the less polar epimer, which represents an inversion with respect to the usually observed polarities of epimeric pairs of 22-alcohols (see for example: J. P. Poyser, F. R. Hirtzbach, and G. Ourisson, *Tetrahedron*, **30**, 977 (1974); D. H. R. Barton, J. P. Poyser, and P. G. Sammes, *J. Chem. Soc., Perkin Trans. 1*, 53 (1974); J. P. Poyser and G. Ourisson, *ibid.*, 2061 (1974); ref 31). This is also a reversal of the polarities observed by Sucrow[20] in the 3β-acetoxy-Δ^5 analogues **14** and **15**. This reversal of behavior has previously been noted by Poyser and Ourisson, loc. cit., for the epimeric iso-methyl ethers **57** and **58**. This same behavior was noted in the other epimeric pairs of C-22 alcohols which we synthesized (vide infra). Apparently this behavior is a consequence of the iso-methyl ether functionality.



57 **58**

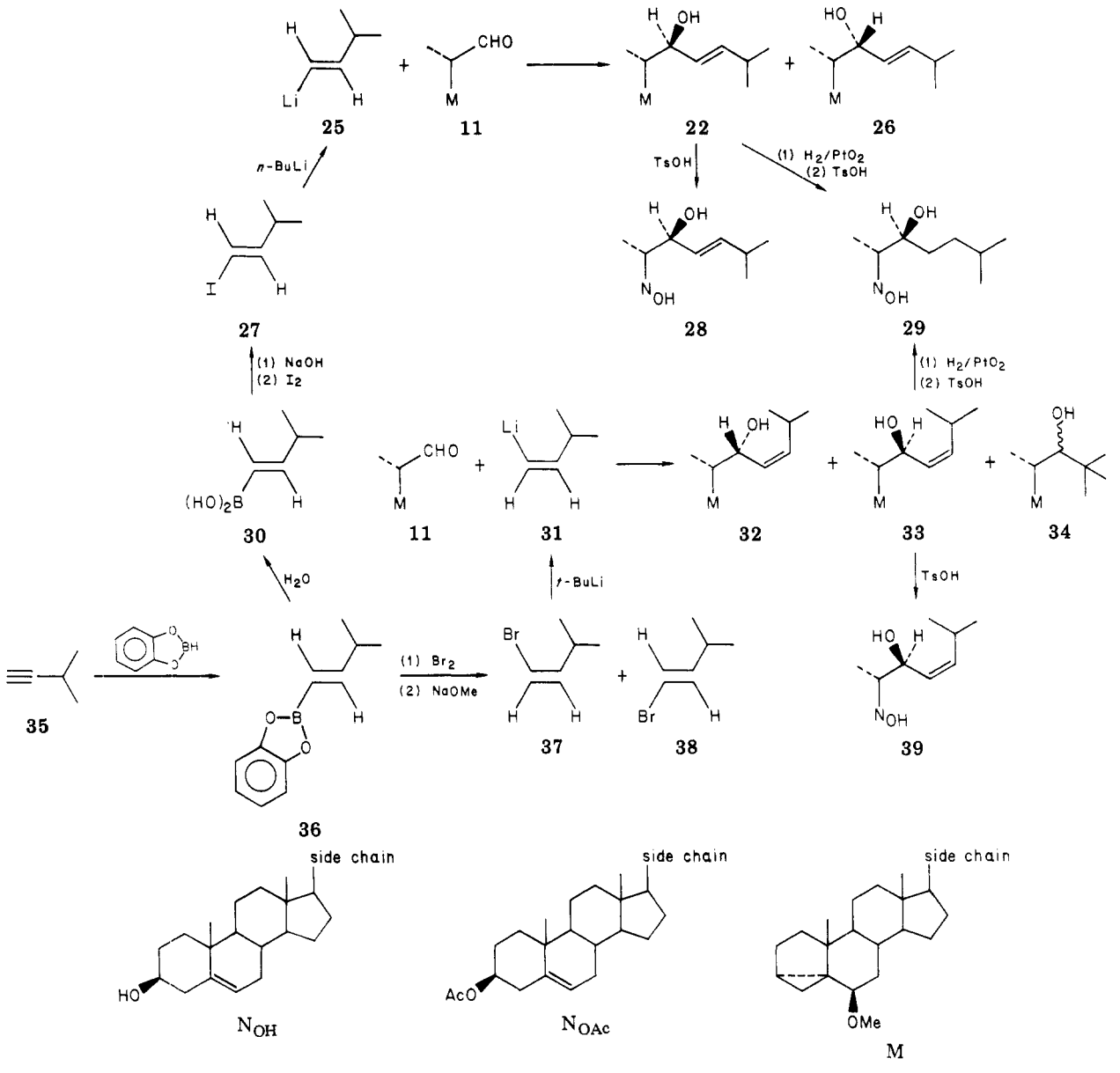
(26) I. J. Bolton, R. G. Harrison, and B. Lythgoe, *J. Chem. Soc. C*, 2950 (1971).

(27) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brockson, T. Li, D. J. Faulkner, and M. R. Petersen, *J. Am. Chem. Soc.*, **92**, 740 (1970).

(28) R. E. Ireland and R. H. Mueller, *J. Am. Chem. Soc.*, **94**, 5897 (1972); R. E. Ireland and A. K. Willard, *Tetrahedron Lett.*, 3975 (1975); R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Am. Chem. Soc.*, **98**, 2869 (1976).

(29) T. C. McMorris, S. R. Schow, and G. R. Weihe, *Tetrahedron Lett.*, 335 (1978).

Scheme II



ester **36**, hydrolysis to the boronic acid derivative **30**, and, finally, reaction with iodine in basic solution.[30] The *E* stereochemistry of the iodide **27** as well as of the Δ^{23} double bond in **22** was established by the appropriate signals in the olefinic region of their NMR spectra (see Experimental Section). Hydrogenation of **22** followed by regeneration of the 3β-hydroxy-Δ^5 system gave the known[31] (22*S*)-22-hydroxycholesterol **29**.

The preparation of the 23*Z*,22*S* allylic alcohol **33** proceeded in a similar manner (Scheme II). (*Z*)-1-Bromo-3-methyl-1-butene (**37**) was also generated from the catechol ester **36** by bromination at −40 °C followed by addition of sodium methoxide in methanol to produce a 63:37 mixture of *Z* and *E* vinyl bromides **37** and **38**. This was an unexpected result in view of Brown's report that this procedure produces exclusively *Z* vinyl bromides from terminal acetylenes.[32] The desired *Z* isomer was obtained in pure form by preparative gas chromatography. NMR spectral data were consistent with the literature data for this compound.[33]

The vinyllithium reagent **31** was prepared by reaction of the *Z* vinyl bromide **37** with *tert*-butyllithium at −120 °C in the Trapp solvent mixture.[34] Addition of the aldehyde **11** in tetrahydrofuran at −90 °C gave, after workup and chromatography, the 22*S* and 22*R* allylic alcohols **33** and **32** in 48 and 26% yield, respectively. In addition, we obtained a 12% yield of the alcohol **34**, which apparently arises by reaction of residual *tert*-butyllithium with the aldehyde **11**. The *Z* stereochemistry of the Δ^{23} double bond in **33** was again demonstrated by the olefinic region of the proton NMR spectrum. Proof of the configuration at C-22 was obtained by hydrogenation of the Δ^{23} double bond followed by regeneration of the 3β-hydroxy-Δ^5 system to yield the known[31] (22*S*)-22-hydroxycholesterol **29**.

Claisen rearrangement of the *E* (**22**) and *Z* (**33**) allylic alcohols with trimethyl orthoacetate in refluxing xylene gave in each case ca. 60% of a single (by TLC, GLC, and high-pressure LC) noncrystalline product, **23** and **46**, respectively (Scheme III). Consideration of the mech-

(30) H. C. Brown, T. Hamaoka, and N. Ravindran, *J. Am. Chem. Soc.*, **95**, 5786 (1973).
(31) E. P. Burrows, G. M. Hornby, and E. Caspi, *J. Org. Chem.*, **34**, 103 (1969).
(32) H. C. Brown, T. Hamaoka, and N. Ravindran, *J. Am. Chem. Soc.*, **95**, 6456 (1973).
(33) R. P. Gregson and R. N. Mirrington, *Aust. J. Chem.*, **29**, 2063 (1976).
(34) H. Neumann and D. Seebach, *Tetrahedron Lett.*, 4839 (1976).

Scheme III

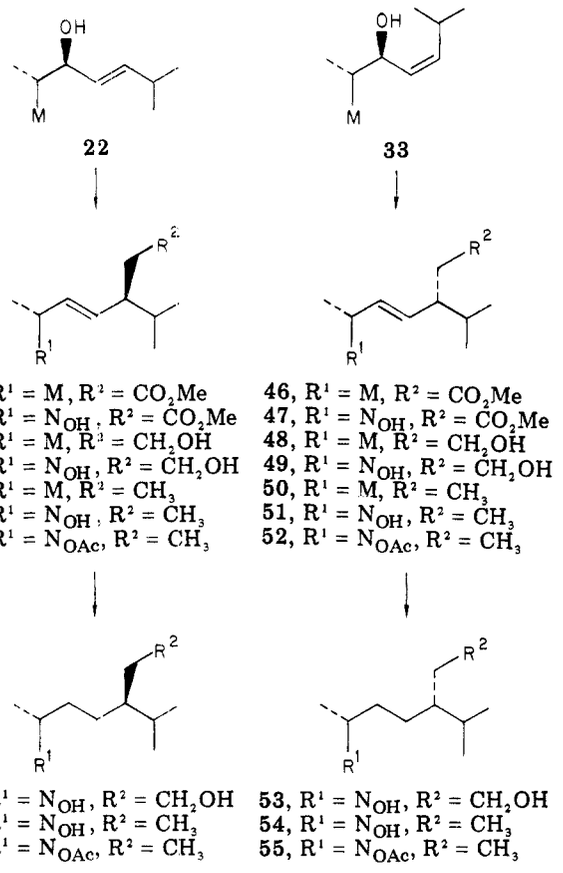


Table I. Methyl Group Chemical Shifts (360 MHz) of 23 and 46[a]

compd	C-18	C-19	C-21[b]	C-26[c]	C-27
23	0.718	1.020	0.966	0.838	0.876[c]
46	0.712	1.019	0.994	0.830	0.871[b]

[a] Solvent $CDCl_3$, internal standard Me_4Si. [b] Doublet, J = 6.6 Hz. [c] Doublet, J = 6.8 Hz.

anism of the Claisen rearrangement[15-17,35-37] suggests that the rearrangement of the E (22S) allylic alcohol **22** should proceed through the chair-like transition state which has the smallest number of nonbonded interactions (i.e., pseudoaxial substituents). The 24S configuration in **23** is predetermined by the initial 22S configuration, the E geometry of the Δ^{23} double bond, and the preferred transition state. Similarly, the Z (22S) allylic alcohol **33** should give the 24R compound **46**.

The two Claisen rearrangement products **23** and **46** could be differentiated easily by 360-MHz proton NMR spectroscopy as indicated in the table of chemical shifts of the methyl groups (Table I). The most noticeable feature is the large downfield shift of the C-21 methyl group in the 24R (24β) compound **46**. This same relative shift has been noted in other C-24 epimeric steroids.[38] The E geometry of the Δ^{23} double bond was indicated by the appropriate coupling constants (see Experimental Section) and by an infrared band at ~970 cm^{-1}. The esters **23** and **46** were characterized further by regenerating the 3β-hydroxy-Δ^5 system to give the solid derivatives **40** and **47**.

(35) H. J. Hansen and H. Schmid, *Chem. Br.*, **5**, 111 (1969).
(36) D. J. Faulkner and M. R. Peterson, *J. Am. Chem. Soc.*, **95**, 553 (1973).
(37) H. J. Hansen and H. Schmid, *Tetrahedron*, **30**, 1959 (1974).
(38) N. Theobald and C. Djerassi, *Tetrahedron Lett.*, 4369 (1978), and references cited therein.

Table II. Methyl Group Chemical Shifts of 24, 53, and 1a[a]

compd	C-18	C-19	C-21[b]	C-26	C-27
24[c]	0.678	1.008	0.921	0.842[d]	0.850[d]
53[c]	0.677	1.009	0.923	0.826[d]	0.858[e]
1a[f]				0.827	0.859

[a] Solvent $CDCl_3$, internal standard Me_4Si. [b] Doublet, J = 6.5 Hz. [c] 360-MHz spectrum. [d] Doublet, J = 6.8 Hz. [e] Doublet, J = 6.9 Hz. [f] 220-MHz spectrum.[29]

In order to fully characterize the stereochemistry at C-24, we converted the Claisen rearrangement esters **23** and **46** to known compounds (Scheme III). The rearrangement product **23** from the E allylic alcohol **22** was converted into stigmasterol (**9**) and sitosterol (**44**) and their acetates (**43** and **45**), and the rearrangement product **46** from the Z allylic alcohol **33** was converted into poriferasterol (**51**) and clionasterol (**54**) and their acetates (**52** and **55**).

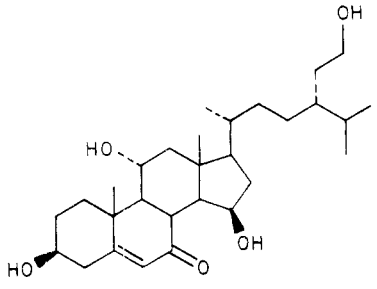
Lithium aluminum hydride reduction of the methyl esters **23** and **46** gave approximately 85% of the noncrystalline 29-hydroxy compounds **41** and **48**, respectively. The proton NMR spectra of **41** and **48** are characterized by a small downfield shift of the C-21 methyl group and a small upfield shift of the C-26 and C-27 methyl groups in the spectrum of the 24R epimer **48** (see Experimental Section). Regeneration of the Δ^5-3β-hydroxy system gave the crystalline diol derivatives **42** and **49** from **41** and **48**, respectively. Conversion of the primary alcohol function to the mesylate[39] and lithium aluminum hydride reduction led to stigmasteryl iso-methyl ether (**10**) and poriferasteryl iso-methyl ether (**50**) from **41** and **48**, respectively. The iso-methyl ethers **10** and **50** were cleaved to the crystalline stigmasterol (**9**) and poriferasterol (**51**) and then converted to their acetates **43** and **52**. The physical constants of the synthetic compounds show good agreement with the known literature values (see Experimental Section). In addition, the 360-MHz proton NMR spectra of **43**, **52**, and authentic stigmasteryl acetate show clearly that **43** is identical with stigmasteryl acetate; **52** shows a significantly different peak pattern.

Hydrogenation of the iso-methyl ethers **10** and **50** over platinum oxide gave the saturated derivatives which were converted to sitosterol (**44**), clionasterol (**54**), and their acetates (**45** and **55**). Comparison of the physical constants of the synthetic compounds with the known literature values confirms our structure assignment (see Experimental Section). It can safely be concluded from all of the above data that the Claisen rearrangement product **23** of the E (22S) allylic alcohol **22** possesses the 24S stereochemistry, while the Claisen rearrangement product **46** of the Z (22S) allylic alcohol **33** has the 24R stereochemistry.

The synthesis of the two side chain models of oogoniol could now be concluded. Hydrogenation of the 29-hydroxy compounds **41** and **48** over platinum oxide followed by regeneration of the 3β-hydroxy-Δ^5 system gave the two crystalline diols **24** and **53**, respectively. The 360-MHz proton NMR spectra of the two diols were recorded, and the chemical shifts of the methyl groups are listed in Table II. While the chemical shifts of the C-18, C-19, and C-21 methyls are almost identical, there is a large difference in the shifts of the C-26 and C-27 methyls. In one case (**53**) the doublets are cleanly separated, and in the other case (**24**), the doublets overlap each other. The 100-MHz spectra are also clearly different, although it is much more difficult to assign peaks.

(39) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).

Comparison of the C-26 and C-27 chemical shifts of **29** and **50** with the published[29] values (220-MHz spectra) for oogoniol-1 (**1a**) and oogoniol-2 (**1b**) (see Table II) clearly indicates that the side chain of **53** is the same as the side chain of oogoniol. Oogoniol, therefore, has the same configuration at C-24 (i.e., 24*R* = 24β) as clionasterol (**54**), thus leading to the complete stereostructure **56**.[40]



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The configuration at C-24 is consistent with the general pattern which has been observed for other 24-alkyl phytosterols. In general, algae[41] and fungi produce sterols with 24β configurations, while most higher plants produce sterols with 24α configurations.[42]

Experimental Section

General Procedures. Low-resolution mass spectra were obtained at 70 eV by Mr. R. G. Ross on an AEI MS-9 mass spectrometer with a source temperature of 200 °C using a direct-inlet system for solids and a heated-inlet system (150 °C) for liquids. Low-resolution GC/MS spectra were obtained on a Varian MAT-44 GC/MS system using a 2.7 mm i.d. × 2 m spiral glass column containing 3% SP-2250 on Supelcoport 100/120 (Supelco Inc.) with an oven temperature of 270 °C. Due to the mass discrimination characteristics of the MAT-44, no relative intensities are given for these spectra. High-resolution mass spectra were recorded by Miss A. Wegmann on a Varian MAT-711 double-focusing mass spectrometer using a direct-inlet system for sample introduction and a PDP-11/45 computer for data acquisition and reduction.

Nuclear magnetic resonance spectra were recorded on a Varian Associates T-60 NMR spectrometer (^{1}H NMR), a Varian Associates XL-100-15 NMR spectrometer equipped with a Nicolet TT 1010-A computer (^{1}H and ^{13}C NMR), and a Bruker HXS-360 NMR spectrometer equipped with a Nicolet TT 1010-A computer (^{1}H NMR). All NMR spectra were taken in $CDCl_3$ solution with Me_4Si as the internal reference unless otherwise indicated. The XL-100 spectra (^{1}H and ^{13}C) were determined by Lee C. Garver, and the 360-MHz spectra were determined by Dr. L. J. Durham.

Elemental analyses were performed by Mr. E. H. Meier, Microanalytical Laboratory, Department of Chemistry, Stanford University. Melting points are uncorrected and were determined on a Kofler hot-stage apparatus. Infrared spectra were obtained on a Perkin-Elmer 700A infrared spectrometer as thin films or as solid dispersions in KBr. Optical rotations were measured on a Perkin-Elmer Model 141 spectropolarimeter for solutions in chloroform.

Routine analytical gas–liquid chromatography (GLC) was performed on a Hewlett-Packard Model 402 high-efficiency gas chromatograph equipped with a flame ionization detector, using 4 mm i.d. × 1.7 m U-shaped glass columns packed with either 1% OV-25, 3% OV-17, or 3% OV-225 on 100/120 mesh Gas-Chrom Q (Applied Science, Inc.). Helium was used as the carrier gas at a flow rate of 75–80 mL/min. Preparative GLC was performed on a Varian Aerograph Series 2700 gas chromatograph using a 10 ft × $^3/_8$ in. aluminum column packed with 20% SE-30 on 45/60 mesh Chromosorb P at a column temperature of 80 °C and using helium as the carrier gas.

Analytical thin-layer chromatography (TLC) was performed on 2.5 cm × 10 cm TLC plates precoated with a 0.25 mm thick layer of silica gel GF (Analtech, Inc.). The plates were visualized by spraying with a 2% solution of cerium(IV) sulfate in 2 N sulfuric acid followed by heating. Preparative TLC was done on 0.75 mm thick HF 254 + 366 (type 60) silica gel (E. Merck) plates (20 cm × 20 cm). The bands were detected either visually or by viewing under ultraviolet light. Column chromatography was carried out on E. Merck neutral, activity II alumina, E. Merck silica gel 60 (70–230 mesh ASTM), and E. Merck TLC grade silica gel HF 254 + 366 (type 60).

Preparative high-pressure liquid chromatography (LC) was performed by using a Haskel Model 28030 miniaturized air-driven hydraulic pump, a 0–5000-psi Ashroft gauge, and a Waters Associates Model R401 differential refractometer. The separations were carried out on a Whatman Partisil M9 10/50 ODS-2 column (50 cm × 8 mm i.d.), using absolute methanol as the mobile phase.

The progress of all reactions and column chromatographies was monitored by TLC and/or GLC.

3-Methyl-1-butyne (**35**) was obtained from the Farchan Division, Story Chemical Corp. Dry THF was obtained by distillation from Na–benzophenone. Triethylamine and methanesulfonyl chloride were distilled before use.

Regeneration of the 3β-hydroxy-Δ^5 system from the 3α,5α-cyclo-6β-methoxy system was accomplished by dissolving the iso-methyl ether compound in dioxane (ca. 1 mL/10 mg of compound) followed by addition of water until the stirred solution became cloudy (ca. 0.5 mL/10 mg of compound).[43] A small crystal of *p*-toluenesulfonic acid monohydrate was added, and the solution was heated at 100 °C for 1 h. Water was added until the solution just clouded, and it was allowed to cool. Filtration followed by recrystallization gave the desired product.

(20*S*)-6β-Methoxy-3α,5-cyclo-5α-pregnane-20-carboxaldehyde (11). The aldehyde 11 was prepared according to literature procedures[23,24] from stigmasterol (**9**) via its iso-methyl ether **10**. Apparently the aldehyde is not as unstable as previously reported,[44] since it could be chromatographed (silica gel, 5% EtOAc/hexane, fractions collected under N_2) to give the pure aldehyde as a white crystalline solid: mp 82–83 °C; $[\alpha]_D^{20}$ +42°; NMR (60 MHz, CCl_4) δ 0.3–0.7 (2 H, m, 4-H), 0.78 (3 H, s, 18-CH_3), 0.98 (3 H, s, 19-CH_3), 1.09 (3 H, d, 21-CH_3, J = 7 Hz), 2.68 (1 H, m, 6α-H, $w_{1/2}$ ca. 7 Hz), 3.25 (3 H, s, OCH_3), 9.53 (1 H, d, CHO, J = 2.5 Hz); mass spectrum (MAT-44) m/z 344 (25%, M^+), 289 (100, M – C_4H_7 (ring A fission)); IR (film) 1722 cm^{-1}.

Ethyl (22*E*,24*S*,25ξ)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-26-oate (18). The 22*S* alcohol **16** (0.940 g, 2.34 mmol), triethyl orthopropionate (0.94 g, 5.3 mmol), and two drops of propionic acid were heated under reflux in 10 mL of dry xylene for 3 h.[26,27] Removal of the solvent and excess reagent under reduced pressure gave an oily residue which was purified by column chromatography (alumina, 17% EtOAc/hexane) to give the oily ethyl ester **18** (0.736 g, 63%). GC analysis (3% OV-225, 230 °C) showed that the product was a mixture of two compounds in a ratio of 4:5: NMR (60 MHz) δ 0.3–0.7 (2 H, m, 4-H), 0.73 (3 H, s, 18-CH_3), 1.01 (3 H, s, 19-CH_3), 2.77 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.32 (3 H, s, OCH_3), 4.10 and 4.13 (2 H, 2 quartets, OCH_2CH_3, C-25 epimers, J = 7 Hz), 4.9–5.3 (2 H, m, 22-H and 23-H); mass spectrum (MAT-711) m/z 484.3938 ($C_{32}H_{52}O_3$, 18%, M^+), 469.3726 ($C_{31}H_{49}O_3$, 21, M – CH_3), 452.3673 ($C_{31}H_{48}O_2$, 89, M – CH_3OH), 429.3317 ($C_{28}H_{45}O_3$, 38, M – C_4H_7 (ring A fission)), 313.2503 ($C_{22}H_{33}O$, 14, M – $C_{10}H_{19}O_2$ (C(20)–C(22) fission + 2 H), 283.2401 ($C_{21}H_{31}$, 24, M – (CH_3OH and C(20)–C(22) fission)), 255.2116 ($C_{19}H_{27}$, 53, M – (CH_3OH + side chain)), 253.1993 ($C_{19}H_{25}$, 71, M – (CH_3OH + side chain + 2 H)), 227.1785 ($C_{17}H_{23}$, 38, M – (CH_3OH + side chain + (C(16)–C(17) unit) + 1 H)), 224.1766 ($C_{14}H_{24}O_2$, 32, side chain + (C(16)–C(17) unit)), 213.1688 ($C_{16}H_{21}$, 24, M – (CH_3OH + ring D fission + 1 H)), 95.0860 (C_7H_{11}, 100); IR (film) 1725, 970 cm^{-1}.

Ethyl (22*E*,24*R*,25ξ)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-26-oate (17). The 22*R* alcohol **5** (0.410 g) was re-

(40) After completion of our work, we were informed by Professor T. C. McMorris (University of California, San Diego) that he had reached the same stereochemical conclusion on the basis of independent evidence.

(41) G. W. Patterson, *Lipids*, 6, 120 (1971).

(42) L. J. Goad and T. W. Goodwin, *Prog. Phytochem.*, 3, 113 (1972).

(43) J. J. Partridge, S. Faber, and M. R. Uskokovic, *Helv. Chim. Acta*, 57, 764 (1964).

(44) G. D. Anderson, T. J. Powers, C. Djerassi, J. Fayos, and J. Clardy, *J. Am. Chem. Soc.*, 97, 388 (1975).

arranged in the same manner as **16** to give, after chromatography, the oily ester **17** (0.356 g, 70%). GC analysis (3% OV-225, 230 °C) showed the presence of two compounds in a ratio of 4:5: NMR (60 MHz) same as that for **18**; mass spectrum (MAT-711) *m/z* 484.3881 ($C_{32}H_{52}O_3$, 9%, M^+), 469.3677 ($C_{31}H_{49}O_3$, 25, M - CH_3), 452.3615 ($C_{31}H_{48}O_2$, 97, M - CH_3OH), 429.3339 ($C_{28}H_{45}O_3$, 35, M - C_4H_7 (ring A fission)), 313.2504 ($C_{22}H_{33}O$, 25, M - $C_{10}H_{19}O_2$ (C(20)–C(22) fission + 2 H)), 283.2420 ($C_{21}H_{31}$, 29, M - (CH_3OH and C(20)–C(22) fission)), 255.2088 ($C_{19}H_{27}$, 65, M - (CH_3OH + side chain)), 253.1924 ($C_{19}H_{25}$, 100, M - (CH_3OH + side chain + 2 H)), 227.1828 ($C_{17}H_{23}$, 39, M - (CH_3OH + side chain + (C(16)–C(17) unit) + 1 H)), 224.1748 ($C_{14}H_{24}O_2$, 33, side chain + (C(16)–C(17) unit)), 213.1612 ($C_{16}H_{21}$, 31, M - (CH_3OH + ring D fission + 1 H)); IR 1725, 970 cm^{-1}.

(*E*)-(3-Methyl-1-butenyl)boranediol (30). Catecholborane (12.0 g, 0.10 mol) and 3-methyl-1-butyne (**35**, 10.2 mL, 0.10 mol) were combined under argon at 5 °C in a Fisher–Porter bottle.[30] The bottle was sealed, and the solution was stirred for 30 min at room temperature and 2 h at 70 °C. After the solution cooled to room temperature, the benzodioxaborole **36** was hydrolyzed by pouring it into 100 mL of water and stirring at room temperature for 3 h. After the mixture was cooled in an ice bath, the white solid was collected by filtration and thoroughly washed with ice-cold water to remove catechol. Air-drying gave 8.2 g (72%) of the diol **30**: mp 44–46 °C (H_2O); NMR (60 MHz, $(CD_3)_2CO$) δ 0.97 (6 H, d, $(CH_3)_2CH$, J = 6.5 Hz), 2.32 (1 H, br septet, $(CH_3)_2CH$, $J \approx 6$ Hz), 2.88 (water of hydration), 5.31 (1 H, dd, $(HO)_2BCH{=}C$, J = 1 and 18 Hz), 6.50 (1 H, dd, $CHCH{=}C$, J = 6 and 18 Hz), 6.57 (2 H, s, $B(OH)_2$).

(*E*)-1-Iodo-3-methyl-1-butene (27). The boranediol **30** (3.9 g, 34 mmol) was dissolved in 35 mL of ether and cooled to 0–5 °C in an ice bath.[30] To the stirred solution was added aqueous NaOH solution (34 mL of 3 N) followed by a cold solution of elemental iodine (10.4 g, 41 mmol) in 100 mL of ether. After being stirred for 30 min at 0 °C, the solution was allowed to warm to room temperature, and the excess iodine was destroyed with aqueous sodium thiosulfate solution. The aqueous layer was separated and extracted with ether (1 × 50 mL). The combined organic layers were washed with water and saturated NaCl solution and dried over anhydrous $MgSO_4$. Removal of the solvent at atmospheric pressure followed by distillation at reduced pressure gave the pure iodide: bp 54–56 °C (50 mm); NMR (60 MHz, CCl_4) δ 1.07 (6 H, d, $(CH_3)_2CH$, J = 7 Hz), 2.29 (1 H, br septet, $(CH_3)_2CH$, $J \approx 7$ Hz), 5.92 (1 H, d, $ICH{=}C$, J = 14.5 Hz), 6.47 (1 H, dd, $CHCH{=}C$, J = 7 and 14.5 Hz).

(22*S*,23*E*)-6β-Methoxy-3α,5-cyclo-5α-cholest-23-en-22-ol (22). The vinyllithium reagent **25** was prepared by addition of a solution of *n*-butyllithium in hexane (5.9 mL of a 1.36 M solution, 8.0 mmol) to a stirred solution of the vinyl iodide **27** (1.42 g, 7.25 mmol) in dry ether (15 mL) at −75 °C.[45] The mixture was stirred at −60 °C for 20 min and then cooled to −75 °C. A solution of the aldehyde **11** (2.00 g, 5.8 mmol) in 15 mL of dry ether was added dropwise to the stirred solution of vinyllithium reagent.[45] The mixture was stirred for 30 min at −75 °C, allowed to warm to −20 °C, and hydrolyzed by careful addition of saturated, aqueous NH_4Cl solution (15 mL). The stirred mixture was allowed to warm to room temperature, and 10 mL of water was added. The aqueous layer was separated and extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated aqueous NaCl solution (2 × 20 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent afforded an oily residue which was purified by column chromatography (TLC grade silica gel, 5% EtOAc/hexane) to give first crystalline **22**: 1.20 g, 50%; R_f 0.54 (20% EtOAc/hexane); mp 116.0–116.5 °C ($MeOH/H_2O$); NMR (100 MHz) δ 0.43 (1 H, dd, 4α-H, J = −5 and 8 Hz), 0.65 (1 H, t, 4β-H, J = 5 Hz), 0.732 (3 H, s, 18-CH_3), 0.890 (3 H, d, 21-CH_3, J = 5.9 Hz), 0.995 (6 H, d, 26-CH_3 and 27-CH_3, J = 6.6 Hz), 1.028 (3 H, s, 19-CH_3), 2.26 (1 H, br septet, 25-H, $J \approx 7$ Hz), 2.77 (1 H, m, 6α-H, $w_{1/2}$ ca. 5 Hz), 3.323 (3 H, s, OCH_3), 4.21 (1 H, br t, 22-H, J = 4.5 Hz), 5.40 (1 H, dd, 23-H, J = 4 and 15.5 Hz), 5.62 (1 H, dd, 24-H, J = 5 and 15.5 Hz); mass spectrum (MAT-711) *m/z* 414.3487 ($C_{28}H_{46}O_2$, 5%, M^+), 359.2952 ($C_{24}H_{39}O_2$, 17, M - C_4H_7 (ring A fission)), 316.2737 ($C_{22}H_{36}O$, 29, M - $C_6H_{10}O$ (C(20)–C(22) fission - 1 H)), 301.2528 ($C_{21}H_{33}O$, 11, M - (C(20)–C(22) fission - 1 H + CH_3)), 284.2504 ($C_{21}H_{32}$, 100, M - (C(20)–C(22) fission - 1 H + CH_3OH)), 283.2429 ($C_{21}H_{31}$, 75, M - (CH_3OH and (C(20)–C(22) fission)), 269.2237 ($C_{20}H_{29}$, 13, M - (C(20)–C(22) fission - 1 H + CH_3 + CH_3OH)), 261.2194 ($C_{18}H_{29}O$, 12, M - (side chain + (C(16)–C(17) unit) - 1 H)), 255.2116 ($C_{19}H_{27}$, 19, M - (CH_3OH + side chain)), 253.1956 ($C_{19}H_{25}$, 25, M - (CH_3OH + side chain + 2 H)), 227.1775 ($C_{17}H_{23}$, 13, M - (CH_3OH + side chain + (C(16)–C(17) unit) + 1 H)), 215.1787 ($C_{16}H_{23}$, 19, M - (CH_3OH + ring D fission - 1 H)), 213.1629 ($C_{16}H_{21}$, 38, M - (CH_3OH + ring D fission + 1 H)). Further elution afforded 0.26 g (11%) of a noncrystalline compound (R_f 0.41, 20% EtOAc/hexane) which, based on analogy, is probably **(22*R*,23*E*)-6β-methoxy-3α,5-cyclo-5α-cholest-23-en-22-ol (26).**

(22*S*,23*E*)-Cholesta-5,23-diene-3β,22-diol (28). Alcohol **22** was converted to the diol **28** by reaction with *p*-TsOH in aqueous dioxane: mp 157.5–159 °C ($MeOH/H_2O$); NMR (100 MHz) δ 0.697 (3 H, s, 18-CH_3), 0.896 (3 H, d, 21-CH_3, J = 5.8 Hz), 0.996 (6 H, d, 26-CH_3 and 27-CH_3, J = 6.7 Hz), 1.010 (3 H, s, 19-CH_3), 3.51 (1 H, br m, 3α-H, $w_{1/2}$ ca. 25 Hz), 4.10 (1 H, m, 22-H, $w_{1/2}$ ca. 10 Hz), 5.36 (1 H, m, 6-H, $w_{1/2}$ ca. 9 Hz), 5.40 (1 H, m, 23-H), 5.62 (1 H, dd, 24-H, J = 5 and 15.5 Hz); mass spectrum (MS-9) *m/z* 400 (1%, M^+), 302 (42, M - $C_6H_{10}O$ (C(20)–C(22) fission - 1 H)), 301 (15, M - (C(20)–C(22) fission)), 284 (60, M - (C(20)–C(22) fission - 1 H + H_2O)), 283 (38, M - (C(20)–C(22) fission + H_2O)), 271 (9, M - (side chain + 2 H)), 269 (18, M - (C(20)–C(22) fission - 1 H + H_2O + CH_3)), 217 (10), 215 (21, M - (ring D fission - 1 H + H_2O)), 213 (29, M - (ring D fission + 1 H + H_2O)), 99 (100).

(22*S*)-Cholest-5-ene-3β,22-diol (29). Alcohol **22** (30 mg, 0.072 mmol) was hydrogenated[46] at atmospheric pressure over PtO_2 (10 mg) in 10 mL of ethyl acetate. After the catalyst was removed by filtration through Celite, the solvent was evaporated to leave the saturated noncrystalline alcohol. The 3β-hydroxy-Δ^5 system was regenerated in the usual manner (aqueous dioxane, *p*-TsOH) to give the crystalline diol **29** (25 mg, 86%): mp 180–182 °C (MeOH); $[\alpha]_D^{20}$ −53° (*c* 0.55) (lit.[31] mp 180 °C (MeOH), lit.[31] $[\alpha]_D$ −54°); NMR (100 MHz) δ 0.697 (3 H, s, 18-CH_3), 0.893 (9 H, d, 21-CH_3, 26-CH_3, and 27-CH_3, J = 6.1 Hz), 1.013 (3 H, s, 19-CH_3), 3.30–3.75 (2 H, br m, 22-H and 3α-H), 5.35 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz); mass spectrum (MS-9) *m/z* 402 (15%, M^+), 384 (9, M - H_2O), 369 (6, M - (H_2O + CH_3)), 351 (5, M - (2H_2O + CH_3)), 302 (10, M - $C_6H_{12}O$ (C(20)–C(22) fission - 1 H)), 287 (7, M - $C_7H_{15}O$ (C(20)–C(22) fission - 1 H + CH_3)), 284 (8, M - $C_6H_{14}O_2$ (C(20)–C(22) fission - 1 H + H_2O)), 273 (10, M - side chain), 269 (9, M - (C(20)–C(22) fission - 1 H + CH_3 + H_2O)), 217 (8), 215 (8, M - (ring D fission - 1 H + H_2O)), 213 (12, M - (ring D fission + 1 H + H_2O)), 55 (100). For further characterization (because (22*R*)-cholest-5-ene-3β,22-diol has[31] mp 186 °C and $[\alpha]_D$ −39°) the diol **29** was converted to its diacetate **((22*S*)-cholest-5-ene-3β,22-diol diacetate)** with acetic anhydride and pyridine: mp 143–145 °C (MeOH); $[\alpha]_D^{20}$ −58° (*c* 0.30) (lit.[31] mp 145–146 °C, lit.[31] $[\alpha]_D$ −59°) (lit.[31] values for (22*R*)-cholest-5-ene-3β,22-diol diacetate: mp 101.5–103 °C (MeOH); $[\alpha]_D$ −37.5°); NMR (100 MHz) δ 0.684 (3 H, s, 18-CH_3), 0.872 (6 H, d, 26-CH_3 and 27-CH_3, J = 6.3 Hz), 0.964 (3 H, d, 21-CH_3, J = 6.8 Hz), 1.016 (3 H, s, 19-CH_3), 2.026 (3 H, s, OAc), 2.036 (3 H, s, OAc), 4.62 (1 H, br m, 3α-H, $w_{1/2}$ ca. 24 Hz), 4.94 (1 H, br t, 22-H, J = 6 Hz), 5.38 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz).

(*Z*)- and (*E*)-1-Bromo-3-methyl-1-butene (37 and 38). (*E*)-2-(3-Methyl-1-butenyl)-1,3,2-benzodioxaborole (**36**, 0.110 mol) was prepared as described above in the preparation of **30**. The solution was transferred under argon to a round-bottomed flask and 140 mL of CH_2Cl_2 was added. The solution was cooled to −40 °C and bromine (35.2 g, 0.220 mol) was added dropwise over a period of 20 min.[32] After the dark orange suspension was stirred for 1 h, 220 mL of a 2 M solution of NaOMe in methanol was slowly added, and the resulting mixture was stirred for 30 min at −40 °C. The cooling bath was removed, and the mixture was

(45) G. Cahiez, D. Bernard, and J. F. Normant, *Synthesis*, 245 (1976).

(46) The hydrogenations of the allylic alcohols were originally done with PtO_2 as the catalyst; however, when a new batch of PtO_2 was tried, the hydrogenations could not be repeated. Apparently the new batch was much more active because it led to cleavage of the methoxy and cyclopropane moieties. Use of 5% rhodium on carbon gave fast and clean hydrogenation of the Δ^{23} double bond.

allowed to warm to room temperature. After addition of 110 mL of water, the aqueous layer was separated and extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layers were washed with water (1 × 50 mL) and saturated aqueous NaCl solution (1 × 50 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent at atmospheric pressure followed by distillation gave 11.5 g (70%) of a clear, colorless liquid (bp 99–110 °C) which was shown by GC to be a 63:37 mixture of *Z* and *E* vinyl bromides. Pure **37** and **38** were obtained by preparative GLC. **(*Z*)-1-Bromo-3-methyl-1-butene (37)**[33] (shorter retention time): NMR (100 MHz) δ 1.02 (6 H, d, $(CH_3)_2CH$, *J* = 7 Hz), 2.82 (1 H, d of septets, $(CH_3)_2CH$, *J* = 7 and 8 Hz), 5.89 (1 H, dd, CHCH=CHBr, *J* = 7 and 8 Hz), 6.02 (1 H, d, CH=CHBr, *J* = 7 Hz); mass spectrum (MS-9) *m/z* 150/148 (3%, M^+), 135/133 (8, M – CH_3), 69 (100, M – Br), 53 (68, (M – CH_3) – HBr), 51 (15), 50 (10), 41 (91, (M – Br) – C_2H_4), 39 (38, (M – Br – C_2H_4) – H_2). **(*E*)-1-Bromo-3-methyl-1-butene (38)**[33] (longer retention time): NMR (100 MHz) δ 1.02 (6 H, d, $(CH_3)_2CH$, *J* = 7 Hz), 2.34 (1 H, septet, $(CH_3)_2CH$, *J* = 7 Hz), 5.96 (1 H, d, CH=CHBr, *J* = 13 Hz), 6.16 (1 H, dd, CHCH=CHBr, *J* = 6 and 13 Hz); mass spectrum (MS-9) *m/z* 150/148 (4%, M^+), 135/133 (10, M – CH_3), 69 (100, M – Br), 53 (69, (M – CH_3) – HBr), 51 (12), 50 (8), 41 (84, (M – Br) – C_2H_4), 39 (31, (M – Br – C_2H_4) – H_2). The mass spectra for **37** and **38** differ significantly from the reported[33] spectra which show a base peak at *m/z* 85 for **37** and at *m/z* 147 for **38**.

(22*S*,23*Z*)-6β-Methoxy-3α,5-cyclo-5α-cholest-23-en-22-ol (33). (*Z*)-(3-Methyl-1-butenyl)lithium (**31**) was prepared by dropwise addition of a solution of *tert*-butyllithium in pentane (5.64 mL of a 1.62 M solution, 9.14 mmol) to a stirred solution of the *Z* vinyl bromide **37** (0.65 g, 4.4 mmol) under argon in 18 mL of Trapp mixture (THF/Et_2O/pentane (4:1:1)) cooled to –120 °C with a methylcyclohexane–liquid N_2 bath.[34] The temperature was maintained between –120 and –115 °C for 1 h and then allowed to increase to –90 °C. A solution of the aldehyde **11** (1.20 g, 3.48 mmol) in 6 mL of THF was added dropwise over a period of 5 min and stirring was continued for 15 min at –75 °C. After the solution was allowed to warm to room temperature, it was hydrolyzed by careful addition of saturated aqueous NH_4Cl solution. Workup in the usual manner gave an oily residue which was purified by column chromatography (TLC grade silica gel, 5% EtOAc/hexane) to give first **(22ξ)-6β-methoxy-23,23-dimethyl-3α,5-cyclo-5α-cholan-22-ol (34):** 170 mg, 12%; R_f 0.59 (20% EtOAc/hexane); mp 130–131 °C (MeOH/H_2O); NMR (100 MHz) δ 0.43 (1 H, dd, 4α-H, *J* = –5.0 and 8.1 Hz), 0.65 (1 H, dd, 4β-H, *J* = –4.9 and 3.6 Hz), 0.753 (3 H, s, 18-CH_3), 0.925 (9 H, s, $(CH_3)_3C$), 0.95 (3 H, d, 21-CH_3, *J* = 5.5 Hz), 1.022 (3 H, s, 19-CH_3), 2.78 (1 H, br t, 6α-H, *J* = 2.5 Hz), 3.28 (1 H, d, 22-H, *J* ≈ 4 Hz), 3.324 (3 H, s, OCH_3); mass spectrum (MAT-711) *m/z* 402.3520 ($C_{27}H_{46}O_2$, 27%, M^+), 387.3281 ($C_{26}H_{43}O_2$, 11, M – CH_3), 370.3242 ($C_{26}H_{42}O$, 19, M – CH_3OH), 347.2934 ($C_{23}H_{39}O_2$, 20, M – C_4H_7 (ring A fission)), 345.2791 ($C_{23}H_{37}O_2$, 22, M – *t*-Bu), 313.2538 ($C_{22}H_{33}O$, 100, M – (*t*-Bu + CH_3OH)), 295.2433 ($C_{22}H_{31}$, 34, M – (*t*-Bu + CH_3OH + H_2O)), 284.2501 ($C_{21}H_{32}$, 10, M – (CH_3OH and C(20)–C(22) fission – 1 H)), 255.2109 ($C_{19}H_{27}$, 15, M – (side chain + CH_3OH)), 227.1798 ($C_{17}H_{23}$, 11, M – (side chain + CH_3OH + (C(16)–C(17) unit) + 1 H)), 213.1634 ($C_{16}H_{21}$, 10, M – (CH_3OH + ring D fission + 1 H)). Continued elution afforded, as a glass, 690 mg (48%) of the 22*S* alcohol **33**: R_f 0.52 (20% EtOAc/hexane); NMR (100 MHz) δ 0.43 (1 H, dd, 4α-H, *J* = –5 and 8 Hz), 0.65 (1 H, m 4β-H), 0.723 (3 H, s, 18-CH_3), 0.958 (3 H, d, 26-CH_3, *J* = 6.6 Hz), 0.976 (3 H, d, 27-CH_3, *J* = 6.6 Hz), 0.995 (3 H, d, 21-CH_3, *J* = 5.8 Hz), 1.024 (3 H, s, 19-CH_3), 2.77 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.327 (3 H, s, OCH_3), 4.55 (1 H, d, 22-H, *J* = 7.4 Hz), 5.22 (1 H, dd, 24-H, *J* = 9.1 and 11.1 Hz), 5.43 (1 H, dd, 23-H, *J* = 7.4 and 11.0 Hz); mass spectrum (MAT-44) *m/z* 414 (M^+), 382 (M – CH_3OH), 359 (M – C_4H_7 (ring A fission)), 316 (M – (C(20)–C(22) fission – 1 H)), 315 (M – (C(20)–C(22) fission)), 301 (M – (C(20)–C(22) fission – 1 H + CH_3)), 284 (M – (C(20)–C(22) fission – 1 H + CH_3OH)), 283 (M – (C(20)–C(22) fission + CH_3OH)), 269 (M – (C(20)–C(22) fission – 1 H + CH_3 + CH_3OH)), 261 (M – (side chain + (C(16)–C(17) unit) – 1 H), 255 (M – (side chain + CH_3OH)), 253 (M – (side chain + CH_3OH + 2 H)), 227 (M – (CH_3OH + side chain + (C(16)–C(17) unit) + 1 H)), 215 (M – (CH_3OH + ring D fission – 1 H)), 213 (M – (CH_3OH + ring D fission + 1 H)). Further elution gave 370 mg (26%) of a noncrystalline compound (R_f 0.41 (20% EtOAc/hexane)) which, based on analogy and spectra, is **(22*R*,23*Z*)-6β-methoxy-3α,5-cyclo-5α-cholest-23-en-22-ol (32):** NMR (100 MHz) δ 0.42 (1 H, dd, 4α-H, *J* = –4.9 and 8.1 Hz), 0.65 (1 H, dd, 4β-H, *J* = –4.9 and 3.8 Hz), 0.754 (3 H, s, 18-CH_3), 0.976 (3 H, d, 26-CH_3, *J* = 6.7 Hz), 0.990 (6 H, d, 21-CH_3 and 27-CH_3, *J* = 6.2 Hz), 2.77 (1 H, br t, 6α-H, *J* ≈ 2 Hz), 3.318 (3 H, s, OCH_3), 4.47 (1 H, dd, 22-H, *J* = 3.4 and 7.8 Hz), 5.36 (2 H, complex m, 23-H and 24-H); mass spectrum (MAT-44) *m/z* 414 (M^+), rest of spectrum same as that for **33**.

(22*S*,23*Z*)-Cholesta-5,23-diene-3β,22-diol (39). Alcohol **33** was reacted with *p*-TsOH in aqueous dioxane to give the diol **39**: mp 183–184 °C (dioxane/H_2O); NMR (100 MHz) δ 0.691 (3 H, s, 18-CH_3), 0.956 (3 H, d, 26-CH_3, *J* = 6.7 Hz), 0.978 (6 H, d, 21-CH_3 and 27-CH_3, *J* = 6.7 Hz), 1.011 (3 H, s, 19-CH_3), 2.60 (1 H, d of septets, *J* = 6.8 and 9.0 Hz), 3.34–3.76 (1 H, m 3α-H), 4.55 (1 H, dd, 22-H, *J* = 4.4 and 7.0 Hz), 5.23 (1 H, dd, 24-H, *J* = 8.9 and 11.1 Hz), 5.38 (1 H, m, 6-H), 5.43 (1 H, dd, 23-H, *J* = 7.2 and 11.2 Hz); mass spectrum (MAT-711) *m/z* 400.3339 ($C_{27}H_{44}O_2$, 6%, M^+), 302.2618 ($C_{21}H_{34}O$, 63, M – $C_6H_{10}O$ (C(20)–C(22) fission – 1 H)), 301.2536 ($C_{21}H_{33}O$, 25, M – (C(20)–C(22) fission)), 284.2490 ($C_{21}H_{32}$, 48, M – (C(20)–C(22) fission – 1 H + H_2O)), 283.2427 ($C_{21}H_{31}$, 62, M – (C(20)–C(22) fission + H_2O)), 271.2062 ($C_{19}H_{27}O$, 10, M – (side chain + 2 H)), 269.2248 ($C_{20}H_{29}$, 11, M – (C(20)–C(22) fission – 1 H + H_2O + CH_3)), 241.1947 ($C_{18}H_{25}$, 11, M – $C_9H_{19}O_2$), 227.1804 ($C_{17}H_{23}$, 11, M – (side chain + (C(16)–C(17) unit) + H_2O + 1 H)), 217.1966 ($C_{16}H_{25}$, 11, M – $C_{11}H_{19}O_2$), 215.1796 ($C_{16}H_{23}$, 18, M – (ring D fission – 1 H + H_2O)), 213.1633 ($C_{16}H_{21}$, 30, M – (ring D fission + 1 H + H_2O)), 81.0771 (C_6H_9, 100).

(22*S*)-Cholest-5-ene-3β,22-diol (29). Conversion of alcohol **33** to **29** was accomplished as described above for the conversion of **22** to **29**:[46] mp 179–181 °C (MeOH); $[\alpha]_D^{20}$ –54° (*c* 0.45); the NMR spectrum and mass spectrum were identical with those of **29** prepared from **22**. Diol **29** was converted to the diacetate as before: mp 144–146 °C (MeOH); $[\alpha]_D^{20}$ –57° (*c* 0.25); the NMR spectrum was identical with that obtained for the diacetate derived from **22**.

Methyl (22*E*,24*S*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-29-oate (23). The *E* allylic alcohol **22** (100 mg, 0.241 mmol), trimethyl orthoacetate (0.31 mL, 290 mg, 2.4 mmol), and 2 μL of propionic acid were heated in refluxing xylenes (0.5 mL) for 3 h, when the reaction was shown to be complete by GLC and TLC.[26,27] The reaction mixture was cooled and then concentrated under vacuum. The oily residue was purified by preparative TLC (20% EtOAc/hexane) to give the noncrystalline ester **23**: 70 mg, 62%; NMR (360 MHz) δ 0.43 (1 H, dd, 4α-H, *J* = –5 and 8 Hz), 0.65 (1 H, t, 4β-H, *J* = 5 Hz), 0.718 (3 H, s, 18-CH_3), 0.838 (3 H, d, 26-CH_3, *J* = 6.8 Hz), 0.876 (3 H, d, 27-CH_3, *J* = 6.8 Hz), 0.966 (3 H, d, 21-CH_3, *J* = 6.6 Hz), 1.020 (3 H, s, 19-CH_3), 1.88 (1 H, dt, 7-H, *J* = 3.0 and 13 Hz), 1.95 (1 H, dt, 7-H, *J* = 3.5 and 13 Hz), 1.96–2.08 (1 H, m, 20-H), 2.16–2.31 (2 H, m, 24-H and 28-H), 2.42 (1 H, dd, 28-H, *J* = 3.5 and 12.5 Hz), 2.77 (1 H, m, 6α-H, $w_{1/2}$ ca. 7 Hz), 3.322 (3 H, s, CH_3OCH), 3.622 (3 H, s, CO_2CH_3), 5.12 (1 H, dd, 22-H, *J* = 7.5 and 15 Hz), 5.23 (1 H, dd, 23-H, *J* = 9 and 15 Hz); IR 1750, 970 cm^{-1}.

Methyl (22*E*,24*S*)-3β-Hydroxystigmasta-5,22-dien-29-oate (40). The iso-methyl ether protecting group in **23** was removed in the usual way to give **40**: mp 120–121 °C (MeOH/H_2O); NMR (100 MHz) δ 0.683 (3 H, s, 18-CH_3), 0.834 (3 H, d, 26-CH_3, *J* = 6.7 Hz), 0.872 (3 H, d, 27-CH_3, *J* = 6.7 Hz), 0.972 (3 H, d, 21-CH_3, *J* = 6.7 Hz), 1.005 (3 H, s, 19-CH_3), 3.30–3.65 (1 H, m, 3α-H), 3.618 (3 H, s, CO_2CH_3), 5.05–5.40 (3 H, m, 6-H, 22-H, and 23-H); mass spectrum (MAT-711) *m/z* 456.3591 ($C_{30}H_{48}O_3$, 100%, M^+), 441.3345 ($C_{29}H_{45}O_3$, 14, M – CH_3), 438.3483 ($C_{30}H_{46}O_2$, 33, M – H_2O), 423.3232 ($C_{29}H_{43}O_2$, 12, M – (H_2O + CH_3)), 314.2625 ($C_{22}H_{34}O$, 22), 301.2518 ($C_{21}H_{33}O$, 12, M – (C(20)–C(22) fission)), 300.2428 ($C_{21}H_{32}O$, 14, M – (C(20)–C(22) fission + 1 H)), 299.2364 ($C_{21}H_{31}O$, 49), 283.2425 ($C_{21}H_{31}$, 25, M – (C(20)–C(22) fission + H_2O)), 272.2122 ($C_{19}H_{28}O$, 18, M – (side chain + 1 H)), 271.2066 ($C_{19}H_{27}O$, 60, M – (side chain + 2 H)), 255.2125 ($C_{19}H_{27}$, 49, M – (side chain + H_2O)), 213.1645 ($C_{16}H_{21}$, 25, M – (ring D fission + 1 H + H_2O)).

Methyl (22*E*,24*R*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-29-oate (46). The *Z* allylic alcohol **33** (125 mg, 0.301 mmol) was treated with trimethyl orthoacetate (0.38 mL, 360 mg, 3.0 mmol) and propionic acid (3 μL) in xylenes (0.75 mL) as described above for the preparation of **23**. After purification by preparative

TLC, 99 mg (70%) of the oily ester was obtained: NMR (360 MHz) δ 0.42 (1 H, dd, 4α-H, J = -5 and 8 Hz), 0.65 (1 H, t, 4β-H, J = 5 Hz), 0.712 (3 H, s, 18-CH_3), 0.830 (3 H, d, 26-CH_3, J = 6.8 Hz), 0.871 (3 H, d, 27-CH_3, J = 6.6 Hz), 0.994 (3 H, d, 21-CH_3, J = 6.6 Hz), 1.019 (3 H, s, 19-CH_3), 1.88 (1 H, dt, 7-H, J = 3 and 13 Hz), 1.95 (1 H, dt, 7-H, J = 3.5 and 13 Hz), 1.97–2.08 (1 H, m, 20-H), 2.18–2.35 (2 H, m, 24-H and 28-H), 2.40 (1 H, dd, 28-H, J = 3.5 and 12.5 Hz), 2.77 (1 H, m, 6α-H, $w_{1/2}$ ca. 7 Hz), 3.322 (3 H, s, CH_3OCH), 3.622 (3 H, s, CO_2CH_3), 5.12 (1 H, dd, 22-H, J = 7.5 and 15 Hz), 5.27 (1 H, dd, 23-H, J = 9 and 15 Hz); IR 1750, 970 cm^{-1}.

Methyl (22*E*,24*R*)-3β-Hydroxystigmasta-5,22-dien-29-oate (47). Regeneration of the 3β-hydroxy-Δ^5 system in **46** in the usual way gave **47**: mp 141.5–143 °C (acetone/H_2O); NMR (100 MHz) δ 0.678 (3 H, s, 18-CH_3), 0.830 (3 H, d, 26-CH_3, J = 6.7 Hz), 0.870 (3 H, d, 27-CH_3, J = 6.7 Hz), 1.000 (3 H, d, 21-CH_3, J = 6.6 Hz), 1.006 (3 H, s, 19-CH_3), 3.3–3.7 (1 H, br m, 3α-H), 3.622 (3 H, s, CO_2CH_3), 5.08–5.42 (3 H, m, 6-H, 22-H, and 23-H); mass spectrum (MAT-711) m/z 456.3584 ($C_{30}H_{48}O_3$, 58, M^+), 441.3394 ($C_{29}H_{45}O_3$, 10, M - CH_3), 438.3537 ($C_{30}H_{46}O_2$, 20, M - H_2O), 423.3264 ($C_{29}H_{43}O_2$, 14, M - (H_2O + CH_3)), 314.2629 ($C_{22}H_{34}O$, 14), 300.2430 ($C_{21}H_{32}O$, 10, M - (C(20)–C(22) fission + 1 H)), 299.2367 ($C_{21}H_{31}O$, 38), 283.2429 ($C_{21}H_{31}$, 18, M - (C(20)–C(22) fission + H_2O)), 272.2120 ($C_{19}H_{28}O$, 17, M - (side chain + 1 H)), 271.2054 ($C_{19}H_{27}O$, 41, M - (side chain + 2 H)), 255.2114 ($C_{19}H_{27}$, 34, M - (side chain + H_2O)), 253.1971 ($C_{19}H_{25}$, 13, M - (side chain + H_2O + 2 H)), 213.1683 ($C_{16}H_{21}$, 23, M - (ring D fission + 1 H + H_2O), 81.0707 (C_6H_9, 100).

(22*E*,24*S*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-29-ol (41). Ester **23** (30 mg, 0.064 mmol) was reduced with $LiAlH_4$ (50 mg, 1.3 mmol) in ether (10 mL). After 1 h of refluxing, the reaction was worked up in the usual way. Purification by high-pressure liquid chromatography gave 23 mg (82%) of the oily alcohol **41**: NMR (100 MHz) δ 0.42 (1 H, dd, 4α-H, J = -5 and 8 Hz), 0.64 (1 H, t, 4β-H, J = 5 Hz), 0.733 (3 H, s, 18-CH_3), 0.828 (3 H, d, 26-CH_3, J = 6.5 Hz), 0.869 (3 H, d, 27-CH_3, J = 6.5 Hz), 1.010 (3 H, d, 21-CH_3, J = 6.5 Hz), 1.023 (3 H, s, 19-CH_3), 2.76 (1 H, m, 6α-H, $w_{1/2}$ ca. 5 Hz), 3.319 (3 H, s, OCH_3), 3.62 (2 H, br t, 29-H, J = 6.5 Hz), 5.16 (2 H, m, 22-H and 23-H).

(22*E*,24*S*)-Stigmasta-5,22-diene-3β,29-diol (42). Cleavage of the iso-methyl ether moiety of **41** gave the diol **42**: mp 178–179 °C (acetone); NMR (100 MHz) δ 0.699 (3 H, s, 18-CH_3), 0.826 (3 H, d, 26-CH_3, J = 6.6 Hz), 0.868 (3 H, d, 27-CH_3, J = 6.5 Hz), 1.010 (3 H, s, 19-CH_3), 1.018 (3 H, d, 21-CH_3, J = 6.5 Hz), 3.3–3.8 (3 H, br m, 3α-H and 29-H), 4.96–5.42 (3 H, m, 6-H, 22-H, and 23-H); mass spectrum (MAT-711) m/z 428.3681 ($C_{29}H_{48}O_2$, 100%, M^+), 413.3397 ($C_{28}H_{45}O_2$, 11, M - CH_3), 410.3536 ($C_{29}H_{46}O$, 46, M - H_2O), 314.2616 ($C_{22}H_{34}O$, 22), 301.2528 ($C_{21}H_{33}O$, 12, M - (C(20)–C(22) fission)), 299.2379 ($C_{21}H_{31}O$, 45, M - (C(20)–C(22) fission + 2 H)), 283.2413 ($C_{21}H_{31}$, 18, M - (C(20)–C(22) fission + H_2O)), 272.2119 ($C_{19}H_{28}O$, 32, M - (side chain + 1 H)), 271.2064 ($C_{19}H_{27}O$, 58, M - (side chain + 2 H)), 258.1987 ($C_{18}H_{26}O$, 13), 255.2104 ($C_{19}H_{27}$, 47, M - (side chain + H_2O)), 229.1960 ($C_{17}H_{25}$, 16), 213.1668 ($C_{16}H_{21}$, 26, M - (ring D fission + 1 H + H_2O)).

(22*E*,24*R*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-en-29-ol (48). Reduction of ester **46** (30 mg, 0.064 mmol) with $LiAlH_4$ (50 mg, 1.3 mmol) in refluxing ether (10 mL) gave, after the usual workup and purification by high-pressure liquid chromatography, 24 mg (85%) of the noncrystalline alcohol **48**: NMR (100 MHz) δ 0.43 (1 H, dd, 4α-H, J = -5 and 8 Hz), 0.65 (1 H, t, 4β-H, J = 5 Hz), 0.730 (3 H, s, 18-CH_3), 0.820 (3 H, d, 26-CH_3, J = 6.5 Hz), 0.865 (3 H, d, 27-CH_3, J = 6.4 Hz), 1.020 (3 H, d, 21-CH_3, J = 6.5 Hz), 1.022 (3 H, s, 19-CH_3), 2.76 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.319 (3 H, s, OCH_3), 3.63 (2 H, dt, 29-H, J = 2.5 and 6.5 Hz), 5.05 (1 H, dd, CH=CH, J = 7 and 15 Hz), 5.25 (1 H, dd, CH=CH, J = 7.5 and 15 Hz).

(22*E*,24*R*)-Stigmasta-5,22-diene-3β,29-diol (49). Reaction of **48** with *p*-TsOH in hot aqueous dioxane gave the crystalline diol **49**: mp 188.5–190.0 °C (acetone); NMR (100 MHz) δ 0.695 (3 H, s, OCH_3), 0.820 (3 H, d, 26-CH_3, J = 6.5 Hz), 0.866 (3 H, d, 27-CH_3, J = 6.5 Hz), 1.009 (3 H, s, 19-CH_3), 1.027 (3 H, d, 21-CH_3, J = 6.4 Hz), 3.25–3.80 (3 H, br m, 29-H and 3α-H), 5.05–5.45 (3 H, m, 6-H, 22-H, and 23-H); mass spectrum (MAT-711) m/z 428.3648 ($C_{29}H_{48}O_2$, 49%, M^+), 410.3518 ($C_{29}H_{46}O$, 30, M - H_2O), 314.2615 ($C_{22}H_{34}O$, 14), 299.2369 ($C_{21}H_{31}O$, 44, M - (C(20)–C(22) fission + 2 H)), 283.2412 ($C_{21}H_{31}$, 13, M - (C(20)–C(22) fission + H_2O)), 272.2135 ($C_{19}H_{28}O$, 17, M - (side chain + 1 H)), 271.2058 ($C_{19}H_{27}O$, 40, M - (side chain + 2 H)), 258.1982 ($C_{18}H_{26}O$, 12), 255.2099 ($C_{19}H_{27}$, 27, M - (side chain + H_2O)), 253.1947 ($C_{19}H_{25}$, M - (side chain + 2 H + H_2O)), 229.1934 ($C_{17}H_{25}$, 12), 215.1816 ($C_{16}H_{23}$, 12, M - (ring D fission - 1 H + H_2O)), 213.1656 ($C_{16}H_{21}$, 25, M - (ring D fission + 1 H + H_2O)), 211.1501 ($C_{16}H_{19}$, 13), 81.0707 (C_6H_9, 100).

(22*E*,24*S*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-ene (10). To a stirred solution of alcohol **41** (18.0 mg, 0.0406 mmol) and triethylamine (25 μL, 18 mg, 0.18 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C and under N_2 was added methanesulfonyl chloride (10 μL, 15 mg, 0.13 mmol).[39] Stirring was continued for 30 min at 0 °C, after which the reaction was shown to complete by TLC. The solvent and excess reactants were removed at reduced pressure. THF (3 mL) and $LiAlH_4$ (100 mg) were added to the crude mesylate, and the mixture was stirred for 2 h at room temperature. After the usual workup, 17.0 mg (98%) of **10** was obtained (>99% pure by GLC): NMR (100 MHz) δ 0.42 (1 H, dd, 4α-H, J = -5 and 8 Hz), 0.65 (1 H, t, 4β-H, J = 4 Hz), 0.733 (3 H, s, 18-CH_3), 0.75–0.90 (9 H, m, 26-CH_3, 27-CH_3, and 29-CH_3), 1.014 (3 H, d, 21-CH_3, J = 6.5 Hz), 1.024 (3 H, s, 19-CH_3), 2.78 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.319 (3 H, s, OCH_3), 5.10 (2 H, m, 22-H and 23-H). An authentic sample of **10** prepared[23,24] from (22*E*,24*S*)-stigmasta-5,22-dien-3β-ol (**9**) had the following NMR spectrum: NMR (100 MHz) δ 0.42 (1 H, dd, 4α-H, J = -5.0 and 8.0 Hz), 0.64 (1 H, dd, 4β-H, J = 3.8 and -5.0 Hz), 0.735 (3 H, s, 18-CH_3), 0.75–0.90 (9 H, m, 26-CH_3, 27-CH_3, and 29-CH_3), 1.014 (3 H, d, 21-CH_3, J = 6.5 Hz), 1.025 (3 H, s, 19-CH_3), 2.78 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.319 (3 H, s, OCH_3), 5.10 (2 H, m, 22-H and 23-H). The region 0.79–0.84 ppm shows a much better resolution of peaks for **10**, both "synthetic" and "authentic", than for the 24*R*-epimer **50**. A similar difference has been noted[47] for the 3β-hydroxy-Δ^5 compounds **9** and **51**. The spectra of synthetic and authentic **10** are identical in this region and very much different from that of **50** in this region.

(22*E*,24*R*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-22-ene (50). Alcohol **48** (18.0 mg, 0.0406 mmol) was converted to **50** in 97% yield as described above for the preparation of **10** from **41**: NMR (100 MHz) δ 0.42 (1 H, dd, 4α-H, J = -5 and 8 Hz), 0.64 (1 H, t, 4β-H, $J \approx$ 5 Hz), 0.734 (3 H, s, 18-CH_3), 0.75–0.90 (9 H, m, 26-CH_3, 27-CH_3, and 29-CH_3), 1.016 (3 H, d, 21-CH_3, J = 6.6 Hz), 1.024 (3 H, s, 19-CH_3), 2.78 (1 H, m, 6α-H, $w_{1/2}$ ca. 6 Hz), 3.319 (3 H, s, OCH_3), 5.11 (2 H, m, 22-H and 23-H). The region 0.79–0.84 ppm is a broadened singlet which is much different from the same region of **10**.

(22*E*,24*S*)-Stigmasta-5,22-dien-3β-ol (9). Reaction of synthetic **10** (16 mg, 0.037 mmol) with *p*-TsOH in refluxing aqueous dioxane gave **9**: 14.5 mg, 95%; mp 169–170 °C (MeOH) (lit.[47] mp 169–170 °C).

(22*E*,24*S*)-Stigmasta-5,22-dien-3β-yl Acetate (43). Acetylation of **9** with acetic anhydride in pyridine gave the acetate **43**: mp 144–145 °C (MeOH) (lit.[48] mp 144 °C); NMR (360 MHz) δ 0.696 (3 H, s, 18-CH_3), 0.795 (3 H, d, 26-CH_3, J = 6.7 Hz), 0.804 (3 H, t, 29-CH_3, J = 7.1 Hz), 0.846 (3 H, d, 27-CH_3, J = 6.2 Hz), 1.021 (3 H, s, 19-CH_3), 1.021 (3 H, d, 21-CH_3, J = 6.4 Hz), 2.032 (3 H, s, CH_3CO_2), 2.31 (2 H, d, 4-H, J = 8 Hz), 4.61 (1 H, m, 3α-H, $w_{1/2}$ ca. 17 Hz), 5.01 (1 H, dd, 22-H or 23-H, J = 9 and 15 Hz), 5.15 (1 H, dd, 23-H or 22-H, J = 9 and 15 Hz), 5.37 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz). An authentic sample of **43** prepared from natural **9** had a 360-MHz NMR spectrum completely identical with that for synthetic **43** and much different from that of **52** in the methyl region.

(22*E*,24*R*)-Stigmasta-5,22-dien-3β-ol (51). Regeneration of the 3β-hydroxy-Δ^5 system in **50** gave **51** in 93% yield; mp 156–157.5 °C (MeOH) (lit.[48] mp 156 °C).

(22*E*,24*R*)-Stigmasta-5,22-dien-3β-yl Acetate (52). Poriferasterol (**51**) was acetylated with acetic anhydride in pyridine to give the acetate **52**: mp 146–147.5 °C (MeOH) (lit.[48] mp 147 °C); NMR (360 MHz) δ 0.695 (3 H, s, 18-CH_3), 0.791 (3 H, d, 26-CH_3, J = 6.3 Hz), 0.811 (3 H, t, 29-CH_3, J = 7.3 Hz), 0.844 (3 H, d, 27-CH_3, J = 6.6 Hz), 1.021 (3 H, s, 19-CH_3), 1.024 (3 H, d, 21-CH_3, J = 6.3 Hz), 2.032 (3 H, s, CH_3CO_2), 2.32 (2 H, d, 4-H,

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J = 8 Hz), 4.61 (1 H, m, 3α-H, $w_{1/2}$ ca. 17 Hz), 5.02 (1 H, dd, 22-H or 23-H, J = 9 and 15 Hz), 5.16 (1 H, dd, 23-H or 22-H, J = 9 and 15 Hz), 5.37 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz).

(24*R*)-Stigmast-5-en-3β-ol (44). Hydrogenation of **10** (8.0 mg, 0.019 mmol) over PtO_2 in ethyl acetate followed by cleavage of the iso-methyl ether functionality gave the crystalline β-sitosterol (**44**): 7.1 mg, 90%; mp 137–138.5 °C (MeOH) (lit.[49] mp 137–138 °C).

(24*R*)-Stigmast-5-en-3β-yl Acetate (45). Acetylation of **44** with acetic anhydride in pyridine gave the acetate **45**: mp 121.5–122.5 °C (MeOH) (lit.[49] mp 120.5–121.5 °C); NMR (100 MHz) δ 0.680 (3 H, s, 18-CH_3), 0.814 (3 H, d, 26-CH_3, J = 6.7 Hz), 0.834 (3 H, d, 27-CH_3, J = 6.8 Hz), 0.848 (3 H, t (center and right leg overlap with 26-CH_3 doublet), J = 6.5 Hz), 0.920 (3 H, d, 21-CH_3, J = 5.8 Hz), 1.018 (3 H, s, 19-CH_3), 2.024 (3 H, s, CH_3CO_2), 4.4–4.8 (1 H, br m, 3α-H), 5.38 (1 H, m, 6-H, $w_{1/2}$ ca. 9 Hz).

(24*S*)-Stigmast-5-en-3β-ol (54). The iso-methyl ether **50** (8.0 mg, 0.019 mmol) was hydrogenated over PtO_2 in ethyl acetate and then cleaved with p-TsOH in aqueous dioxane to give clionasterol (**54**): mp 139–140 °C (MeOH) (lit.[50] mp 139.5–140 °C).

(24*S*)-Stigmast-5-en-3β-yl Acetate (55). Clionasterol (**54**) was acetylated in the usual way to give the 3β-acetate **55**: mp 142–142.5 °C (MeOH) (lit.[50] mp 140–141 °C); NMR (100 MHz) δ 0.679 (3 H, s, 18-CH_3), 0.813 (3 H, d, 26-CH_3, J = 6.8 Hz), 0.830 (3 H, d, 27-CH_3, J = 6.7 Hz), 0.847 (3 H, t (center and right leg overlag with 26-CH_3 doublet), 29-CH_3, J = 6.6 Hz), 0.925 (3 H, d, 21-CH_3, J = 5.8 Hz), 1.019 (3 H, s, 19-CH_3), 2.024 (3 H, s, CH_3CO_2), 4.4–4.8 (1 H, br m, 3α-H), 5.38 (1 H, m, 6-H, $w_{1/2}$ ca. 8 Hz).

(24*S*)-Stigmast-5-ene-3β,29-diol (24). Hydrogenation of alcohol **41** (22 mg, 0.050 mmol) over PtO_2 in ethyl acetate followed by regeneration of the 3β-hydroxy-Δ^5 system with p-TsOH in aqueous dioxane gave the desired diol **24**: mp 175.5–176.5 °C (acetone); NMR (360 MHz) δ 0.678 (3 H, s, 18-CH_3), 0.842 (3 H, d, 26-CH_3, J = 6.8 Hz), 0.850 (3 H, d, 27-CH_3, J = 6.8 Hz), 0.921 (3 H, d, 21-CH_3, J = 6.5 Hz), 1.008 (3 H, s, 19-CH_3), 1.68 (1 H, m, 24-H), 1.77–1.89 (3 H, m, 28-H + ?), 1.93–2.05 (2 H, m, 7-H), 2.23 (1 H, t, 4β-H, $J \approx$ 13 Hz), 2.30 (1 H, dd, 4α-H, J = 6 and 13 Hz), 3.53 (1 H, m, 3α-H, $w_{1/2}$ ca. 26 Hz), 3.65 (2 H, m, 29-H, $w_{1/2}$ ca. 17 Hz), 5.35 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz); ^{13}C NMR 37.28 (C-1), 31.68 (C-2), 71.70 (C-3), 42.30 (C-4), 140.59 (C-5), 121.44 (C-6), 31.94 (C-7), 31.94 (C-8), 50.13 (C-9), 36.49 (C-10), 21.12 (C-11), 39.79 (C-12), 42.30 (C-13), 56.72 (C-14), 24.31 (C-15), 28.27 (C-16), 56.02 (C-17), 11.92 (C-18), 19.39 (C-19), 36.11 (C-20), 18.83 (C-21), 33.96 (C-22), 27.10 (C-23), 40.84 (C-24), 29.85 (C-25), 19.10 and 19.28 (C-26 and C-27), 34.15 (C-28), 61.96 (C-29); mass spectrum (MAT-711) m/z 430.3814 ($C_{29}H_{50}O_2$, 100%, M^+), 415.3570 ($C_{28}H_{47}O_2$, 21, M – CH_3), 412.3677 ($C_{29}H_{48}O$, 54, M – H_2O), 397.3469 ($C_{28}H_{45}O$, 13, M – (CH_3 + H_2O)), 345.3158 ($C_{24}H_{41}O$, 17, M – (complex ring A and B fission)[51]), 319.2996 ($C_{22}H_{39}O$, 25, M – (complex ring A and B fission)[51]), 273.2222 ($C_{19}H_{29}O$, 15, M – (side chain)), 55.2105 ($C_{19}H_{27}$, 18, M – (side chain + H_2O)), 213.1658 ($C_{16}H_{21}$, 19, M – (ring D fission + 1 H + H_2O)).

Anal. Calcd for $C_{29}H_{50}O_2$: C, 80.87; H, 11.70. Found: C, 80.53; H, 11.48.

(24*R*)-Stigmast-5-ene-3β,29-diol (53). Alcohol **48** (23 mg, 0.052 mmol) was hydrogenated over PtO_2 in ethyl acetate and reacted with p-TsOH in hot aqueous dioxane to give the diol **53**: 20 mg, 89%; mp 174–175 °C (acetone); NMR (360 MHz) δ 0.677 (3 H, s, 18-CH_3), 0.826 (3 H, d, 26-CH_3, J = 6.8 Hz), 0.858 (3 H, s, 27-CH_3, J = 6.9 Hz), 0.923 (3 H, s, 21-CH_3, J = 6.5 Hz), 1.009 (3 H, s, 19-CH_3), 1.71 (1 H, m, 24-H), 1.77–1.89 (3 H, m, 28-H + ?), 1.93–2.05 (2 H, m, 7-H), 2.23 (1 H, t, 4β-H, $J \approx$ 13 Hz), 2.30 (1 H, dd, 4α-H, J = 6 and 13 Hz), 3.53 (1 H, m, 3α-H, $w_{1/2}$ ca. 24 Hz), 3.66 (2 H, m, 29-H, $w_{1/2}$ ca. 31 Hz), 5.35 (1 H, m, 6-H, $w_{1/2}$ ca. 10 Hz); ^{13}C NMR δ 37.28 (C-1), 31.69 (C-2), 71.71 (C-3), 42.31 (C-4), 140.58 (C-5), 121.44 (C-6), 31.94 (C-7), 31.94 (C-8), 50.14 (C-9), 36.49 (C-10), 21.12 (C-11), 39.80 (C-12), 42.31 (C-13), 56.73 (C-14), 24.32 (C-15), 28.26 (C-16), 56.03 (C-17), 11.92 (C-18), 19.40 (C-19), 36.20 (C-20), 18.85 (C-21), 33.92 (C-22), 27.39 (C-23), 40.75 (C-24), 29.33 (C-25), 18.50 and 19.66 (C-26 and C-27), 33.84 (C-28), 62.03 (C-29); mass spectrum (MAT-711) m/z 430.3805 ($C_{29}H_{50}O_2$, 100%, M^+), 415.3612 ($C_{28}H_{47}O_2$, 18, M – CH_3), 412.3705 ($C_{29}H_{48}O$, 54, M – H_2O), 397.3491 ($C_{28}H_{45}O$, 15, M– (CH_3 + H_2O)), 345.3150 ($C_{24}H_{41}O$, 20, M – (complex ring A and B fission)[51]), 319.2990 ($C_{22}H_{39}O$, 27, M – (complex ring A and B fission)[51]), 273.2210 ($C_{19}H_{29}O$, 16, M – (side chain)), 255.2130 ($C_{19}H_{27}$, 18, M – (side chain + H_2O)), 213.1643 ($C_{16}H_{21}$, 25, M – (ring D fission + 1 H + H_2O)).

Anal. Calcd for $C_{29}H_{50}O_2$: C, 80.87; H, 11.70. Found: C, 80.55; H, 11.50.

Acknowledgment. The authors gratefully acknowledge financial support from the National Institutes of Health (Grant No. GM-06840). In addition we are grateful for the use of the 360-MHz NMR spectrometer at the Stanford Magnetic Resonance Laboratory supported by NSF Grant No. GR 23633 and NIH Grant No. RR 00711. We also acknowledge NSF Grant No. GP-28142 and NSF Grant No. CHE 77-08810 for access to the Varian XL-100-15 NMR spectrometer at Stanford. Finally, we thank the Upjohn Company for a generous supply of stigmasterol.

Registry No. 5, 70813-66-0; **9**, 83-48-7; **10**, 53603-94-4; **11**, 25819-77-6; **13**, 70813-67-1; **16**, 70813-68-2; **17**, 70813-69-3; **18**, 70832-43-8; **22**, 70813-70-6; **23**, 70813-71-7; **24**, 70832-44-9; **25**, 917-57-7; **26**, 70813-72-8; **27**, 593-66-8; **28**, 70813-73-9; **29**, 70813-74-0; **29** diacetate, 17955-05-4; **30**, 70813-75-1; **31**, 70813-76-2; **32**, 70813-77-3; **33**, 70813-78-4; **34**, 70813-79-5; **35**, 598-23-2; **36**, 274-07-7; **37**, 16416-44-7; **38**, 16416-41-4; **39**, 70813-80-8; **40**, 70813-81-9; **41**, 70813-82-0; **42**, 70813-83-1; **43**, 4651-48-3; **44**, 83-46-5; **45**, 915-05-9; **46**, 70832-45-0; **47**, 70832-46-1; **48**, 70832-47-2; **49**, 70832-48-3; **50**, 70832-49-4; **51**, 481-16-3; **52**, 4651-49-4; **53**, 70832-50-7; **54**, 83-47-6; **55**, 915-05-9; **56**, 66786-17-2.

Supplementary Material Available: A description of the synthesis of **5** and **16** (Scheme I) and experimental details (5 pages). Ordering information is given on any current masthead page.

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