Colleagues for the 360-MHz ^1H NMR spectra (which were obtained at the Stanford NMR facility funded by NIH Grant RR-0711 and NSF Grant GP-23633), and Dr. James N. Shoolery (Varian Associates) for ^{13}C measurements and assignments.

Registry No. **6**, 80082-93-5; **7**, 80082-94-6; **8**, 55064-55-6; **9a**, 80082-95-7; **9b**, 80082-96-8; **10a**, 474-73-7; **10b**, 27460-26-0; **11a**, 80082-97-9; **11b**, 80082-98-0; **12a**, 80082-99-1; **12b**, 80083-00-7; **13a**, 80105-70-0; **13b**, 80083-01-8; **14a**, 80083-02-9; **14b**, 80083-03-0; **15a**, 80083-04-1; **15b**, 80083-05-2; **16**, 79396-52-4; **17a**, 80083-06-3; **17b**, 80083-07-4; **17b** acetate, 80083-08-5; **17c**, 80125-09-3; **17c** acetate, 80125-10-6; **18a**, 80083-09-6; **18b**, 80083-10-9; **18c**, 80125-11-7; **19a**, 80083-11-0; **19b**, 80083-12-1; **19c**, 80125-12-8; **20**, 80125-13-9; 6β-methoxy-3α,5-cyclocholestan-22-one, 80083-13-2.

Synthesis of Sterols with Cyclopropane-Containing Side Chains. Spectroscopic Properties and Absolute Configurations

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Received September 4, 1981

The synthesis of seven Δ^5 sterols with cyclopropane-containing side chains (**1–3** and **5–8**) by means of dichlorocarbene addition to the appropriate olefinic precursor is described. Separation of the diastereoisomeric mixtures of the primary dichlorinated adducts was accomplished by reverse-phase high-performance liquid chromatography. The effect of stereochemistry upon the NMR and mass spectroscopic properties of the diastereoisomerically pure sterols are reported, and their absolute configurations were determined either by X-ray crystal structure analysis of related precursors and/or by chemical and spectroscopic correlations.

Sterols with cyclopropane-containing side chains may be key intermediates in bioalkylation processes.[1,2] Indeed, speculations about their possible biosynthetic role had been advanced by Lederer[3] prior to the isolation of any such sterols in nature. Furthermore, they are useful as chemical tracers[4] in following complicated food chains in the marine environment. Our own studies in the marine sterol field,[1,2] especially those dealing with the occurrence of new cyclopropanated sterols,[5–8] prompted us to examine the synthesis of various suitable model compounds.[5,9–11] In order to examine the effect of stereochemical changes around the cyclopropane ring upon chemically or biologically induced isomerization or ring-opening reactions, we were especially interested in different cyclopropanated sterols with defined absolute configurations. In the present paper, we report the details of the synthesis and isolation of seven steroidal cyclopropanes, **1–3** and **5–8** (Chart I), which are of actual or potential relevance and of the hitherto unknown (23*Z*)-cholesta-5,23-dien-3β-ol (**19**).[12] These syntheses are also useful for the preparation of isotopically labeled analogues which may be required for biosynthetic studies. Additionally, we present their spectroscopic properties, notably the NMR data, which allow us to draw conclusions about the absolute configurations of **1** and **2** in comparison with **5** and **6**. Conformational assignments for the sterols **5–8** are based on an X-ray study of related trichloro steroids, which will be published elsewhere.[13]

Results and Discussion

The synthetically more attractive stereospecific routes[5,10,14,15] to diastereoisomerically pure, substituted, three-membered rings in the sterol side chain either failed

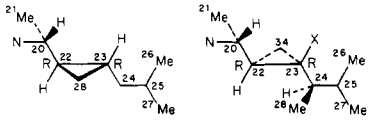
(1) Djerassi, C. *Pure Appl. Chem.* **1981**, *53*, 873–890 and references cited therein.

(2) Djerassi, C.; Theobald, N.; Kokke, W. C. M. C.; Pak, C. S.; Carlson, R. M. K. *Pure Appl. Chem.* **1979**, *51*, 1815–1828 and references cited therein.

(3) Lederer, E. *Q. Rev., Chem. Soc.* **1969**, *23*, 453–481.

(4) Carlson, R. M. K.; Tarchini, C.; Djerassi, C. In "Frontiers of Bioorganic Chemistry and Molecular Biology"; Ananchenko, S. N., Ed.; Pergamon Press: Oxford, 1980; pp 211–224.

(5) Blanc, P.-A.; Djerassi, C. *J. Am. Chem. Soc.* **1980**, *102*, 7113–7114. In this paper, we correctly showed that the absolute configuration of naturally occurring 23,23-methylenecholesterol (i) is opposite to that



i ii

(22*R*,23*R*,24*R*) of gorgosterol (ii, X = CH_3) and therefore identified the natural material as the 22*S*,23*S* isomer. In fact, this is a misapplication of the Cahn–Ingold–Prelog rules (*Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385–415): even though of opposite absolute configuration, the natural 22,23-methylenecholesterol (i) should really be referred to as 22*R*,23*R*. This is so because the 22*R* indication in the related sterols gorgosterol (ii, X = CH_3) and demethylgorgosterol (ii, X = H) is based on a higher priority of C-23 over C-20, which is for demethylgorgosterol due to methyl substitution on C-24; 23*R* then results from the priority of C-22 over C-24. However, *lack of the C-28 methyl group in 22,23-methylenecholesterol (i) leads to an inversion of the sequences around C-22 and C-23.* Regarding the 22-carbon atom, C-20 now assumes priority over C-23, while the sequence around C-23 is H < C-24 < C-28 < C-22. Apparently the *R,S* convention is subject to some uncertainty in the case of sterols with cyclopropane-containing side chains. The *R,S* notation for the 23-carbon atom in 23,24-methylenecholesterol, for example, depends on what priority is assigned to C-24 vs. C-20. In this particular case, we interpret the Cahn–Ingold–Prelog "always-outward" rule in terms of C-20 > C-24.

(6) Bohlin, L.; Gehrken, H. P.; Scheuer, P. J.; Djerassi, C. *Steroids* **1980**, *35*, 295–304.

(7) Ravi, B. N.; Kokke, W. C. M. C.; Delseth, C.; Djerassi, C. *Tetrahedron Lett.* **1978**, 4379–4380.

(8) (a) Hale, R. L.; Leclercq, J.; Tursch, B.; Djerassi, C.; Gross, R. A.; Weinheimer, A. J.; Gupta, K.; Scheuer, P. J. *J. Am. Chem. Soc.* **1970**, *92*, 2179–2180. (b) Ling, N. C.; Hale, R. L.; Djerassi, C. *Ibid.* **1970**, *92*, 5281–5282. (c) Sheikh, Y. M.; Djerassi, C.; Tursch, B. M. *J. Chem. Soc., Chem. Commun.* **1971**, 217–218.

(9) Tarchini, C.; Rohmer, M.; Djerassi, C. *Helv. Chim. Acta* **1979**, *62*, 1210–1216.

(10) Walkup, R. D.; Anderson, G. D.; Djerassi, C. *Tetrahedron Lett.* **1979**, 767–770.

(11) Sheikh, Y. M.; Leclercq, J.; Djerassi, C. *J. Chem. Soc., Perkin Trans. 1* **1974**, 909–914.

(12) For the isomeric (23*E*)-cholesta-5,23-dien-3β-ol see: (a) Fujimoto, Y.; Ikekawa, N. *Chem. Pharm. Bull.* **1976**, *24*, 825–828. (b) Fujimoto, Y.; Morisaki, M.; Ikekawa, N. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2302–2307.

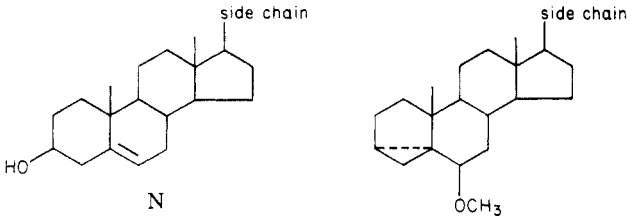
(13) Lang, R. W.; Djerassi, C.; Strong, P. D.; Swenson, D. C.; Duax. W. L. *Helv. Chim. Acta*, in press.

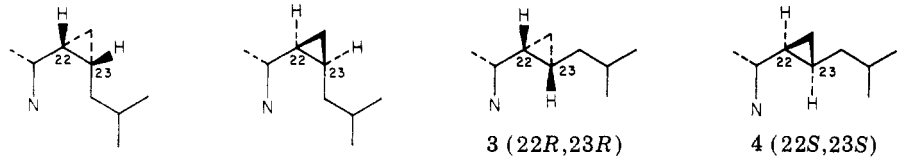
(14) Ishiguro, M.; Akaiwa, A.; Fujimoto, Y.; Sato, S.; Ikekawa, N. *Tetrahedron Lett.* **1979**, 763–766.

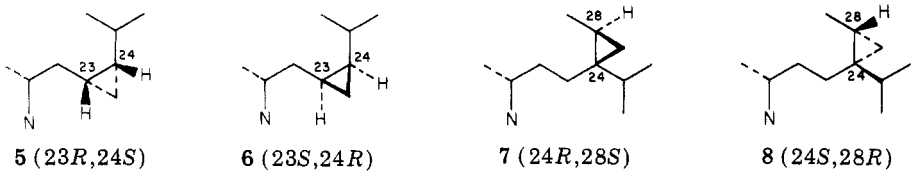
(15) Anderson, G. D.; Powers, T. J.; Djerassi, C.; Fajos, J.; Clardy, J. *J. Am. Chem. Soc.* **1975**, *97*, 388–394.

0022-3263/82/1947-0625$01.25/0

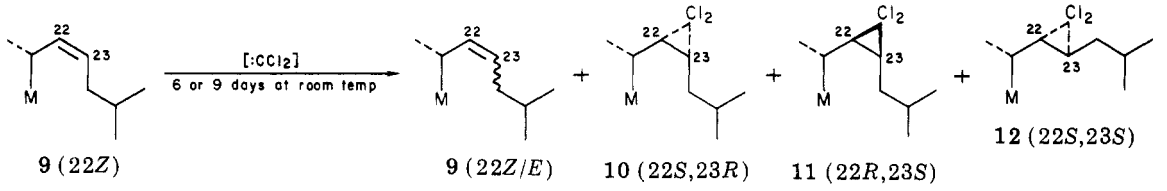
Chart I







Scheme I[a]



[a] The 9/10/11/12 ratio was 57:27:9:7 after 6 days and 47:36:10:7 after 9 days.

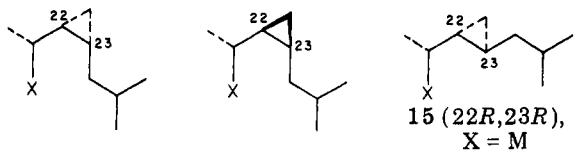
to give the desired isomer or provided it only in low yields after long reaction sequences. On the other hand, the use of classical, nonstereospecific carbene addition reactions[9,11,16] for the purpose of obtaining diastereoisomerically pure steroidal cyclopropanes from easily accessible olefinic precursors is only useful with an effective separation of diastereoisomeric product mixtures. As long as the corresponding olefinic precursor is available, a further advantage of carbene reactions is the fact that there is practically no restriction on producing three-membered rings in all the different positions of the sterol side chain. In all examples presented below, which were synthesized by the carbene addition route, the problem of diastereoisomeric product separation could easily be solved by using reverse-phase high-performance liquid chromatography (HPLC).

Synthesis of the 22,23-Methylene Sterols 1–3. High priority was given to a convenient synthesis of 22,23-methylenecholesterol, since the 22*R*,23*R* isomer **3** has recently been encountered[5] in nature. The starting olefin for the cyclopropanation reaction was (22*Z*)-6β-methoxy-3α,5-cyclo-5α-cholest-22-ene (**9**), which was synthesized from stigmasterol via its i-methyl ether[17] by a well-known six-step sequence[17-21] ending with the appropriate Wittig olefin generation.[20,21] By conducting this reaction in Me_2SO at room temperature (2 h),[20] the pure cis configuration (**9**) was produced almost exclusively. Dichlorocarbene, generated from chloroform under phase-transfer conditions[22,23] by use of benzyltriethylammonium chloride (BTEAC) in 50% aqueous sodium hydroxide, reacts only very slowly with dialkylated steroidal olefins at room temperature.[9,11,16] Thus after a 6-day reaction period, product analysis by reverse-phase HPLC showed that 57% of the starting material was still present in the reaction mixture and that the ratio of the three detectable adducts **10–12** was 65:20:15 (Scheme I). Even after 9 days, 47% of starting olefin as a 22*Z*/*E* mixture[24] was recovered. Repetitive application of the same reaction procedure, followed each time by reverse-phase HPLC separation, furnished the addition products **10–12** in reasonable overall yields.

Reduction of each of the dichloro adducts **10–12** with lithium in liquid ammonia[9] led to the dehalogenated cyclopropane methyl ethers **13–15**, which were transformed to the deprotected Δ^5-sterols **1–3** by acid-catalyzed hydrolysis.[25]

Synthesis of the 23,24-Methylene Sterols 5 and 6. For eventual comparison of the course of cyclopropane ring-opening reactions, we needed isomers of 22,23-methylenecholesterol (**1–4**) with a similar substitution

(16) Ikan, R.; Markus, A.; Goldschmidt, Z. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2423–2425.
(17) Steele, J. A.; Mosettig, E. *J. Org. Chem.* **1963**, *28*, 571–572.
(18) Partridge, J. J.; Faber, S.; Uskokovič, M. *Helv. Chim. Acta* **1964**, *57*, 764–771.
(19) Vanderah, D. J.; Djerassi, C. *J. Org. Chem.* **1978**, *43*, 1442–1448.
(20) Hutchins, R. F. N.; Thompson, M. J.; Svoboda, J. A. *Steroids* **1970**, *15*, 113–130.
(21) Sheikh, Y. M.; Djerassi, C. *Steroids* **1975**, *26*, 129–136.
(22) Makosza, M.; Wawrzniewicz, M. *Tetrahedron Lett.* **1969**, 4659–4662.
(23) Dehmlow, E. V. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 170–179.
(24) The *E*/*Z* ratio of the recovered starting material **9** was not determined separately. However, repeted carbene addition to the recovered olefin **9** gave the same product composition as encountered for pure (22*Z*)-**9**.
(25) Wiersig, J. R.; Waespe-Sarcevic, N.; Djerassi, C. *J. Org. Chem.* **1979**, *44*, 3374–3382.



13 (22*R*,23*S*), X = M
1 (22*R*,23*S*), X = N

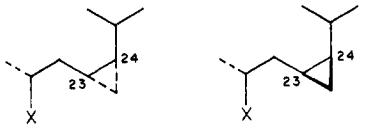
14 (22*S*,23*R*), X = M
2 (22*S*,23*R*), X = N

15 (22*R*,23*R*), X = M
3 (22*R*,23*R*), X = N

pattern. 6β-Methoxy-3α,5-cyclo-5α-cholest-23-yne (**16**) was synthesized by a slight modification of the literature procedure[26] and hydrogenated over Lindlar catalyst in ethyl acetate to give an easily separable (HPLC) mixture (9:1) of the pure cis olefin **17** and the saturated cholesterol i-methyl ether **18** in 88% overall yield (Scheme II).

In contrast to its 23*E* counterpart,[12] (23*Z*)-cholesta-5,23-dien-3β-ol (**19**), generated from **17** by conventional acid hydrolysis,[25] has not yet been described in the literature.

Dichlorocarbene addition to (23*Z*)-**17** under the same conditions as mentioned above for the 22*Z* analogue **9** yielded after 6 days the diasteroisomeric dichloro iso methyl ethers **20** and **21** as a 3:2 mixture (78%).[27] Separation was performed by reverse-phase HPLC, and the independently dehalogenated[9] steroidal cyclopropanes **22** and **23** were finally deprotected in the usual way[25] to the anticipated free sterols **5** and **6**.



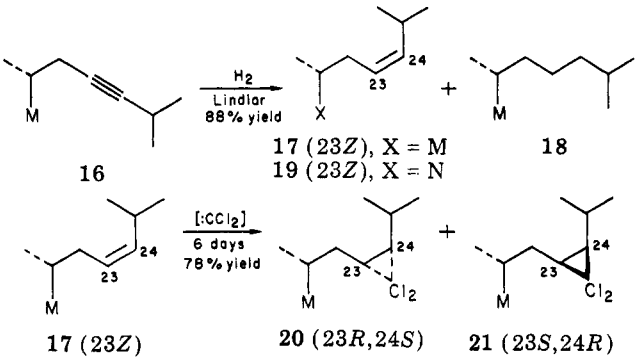
22 (23*R*,24*S*), X = M
5 (23*R*,24*S*), X = N

23 (23*S*,24*R*), X = M
6 (23*S*,24*R*), X = N

Synthesis of the 24,28-Methylene Sterols 7 and 8. The diastereoisomeric cyclopropanes **7** and **8** were of interest as conceivable biosynthetic intermediates[28] to naturally occurring 24-propylidenecholesterol; they were synthesized by a similar reaction sequence starting with natural fucosterol, which was isolated from the crude extract of the giant kelp *Macrocystis pyrifera*.[29] As expected for highly alkyl-substituted olefins, the dichlorocarbene addition to fucosterol i-methyl ether **24**[30] under phase-transfer conditions proceeded much faster than with the dialkylated analogue **9** and **17**, respectively. Thus after a 3-day reaction period, a 45:55 mixture of **25** and **26** was obtained (Scheme III) in almost quantitative yield and separated readily by HPLC. The dechlorination and deprotection of the i-methyl ether grouping proceeded in the usual way.[9,25] It should be mentioned that the saturated hydrocarbon analogue had been synthesized earlier[11] from $\Delta^{24(28)}$-fucostene but had led to an unseparable mixture of diastereoisomers.

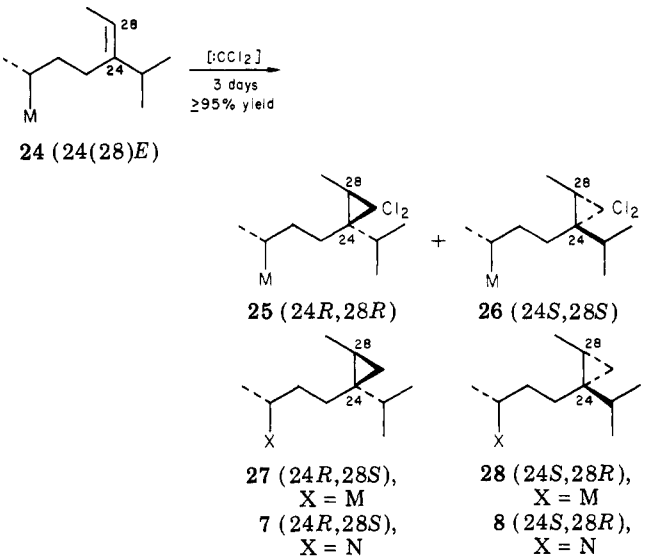
NMR and Mass Spectra of Isomeric Cyclopropanes. Inspection of the ^{1}H NMR (360 MHz, $CDCl_3$) chemical

Scheme II[a]



[a] The ratio of **17** or **19** to **18** was 9:1, and that of **20** to **21** was 3:2.

Scheme III[a]



[a] The ratio of **25** to **26** was 45:55.

shift data of the methyl group region of **1**–**8** (Table I) leads to the following conclusion. The position of the cyclopropane ring in the side chain has its most striking influence on the chemical shift values of the C-21 and the C-26 and C-27 methyl groups, respectively. In moving the cyclopropane ring from the 22,23-position (**1**–**4**) to the 23,24-position (**5**, **6**), the δ values of the C-21 methyl protons shift to higher field, whereas the C-26 and C-27 protons move to lower field. In addition, there is a low-field shift for the C-18 methyl group and, as expected, no measurable change of the C-19 signals. By changing the ring position from the 23,24- (**5**, **6**) to the 24,28-carbons (**7**, **8**), the signals for the C-18, C-21, C-26, and C-27 methyl groups all shift to higher field. As shown in Table I, within each cyclopropane substitution pattern, the individual diastereoisomers (e.g., **1** vs. **2** vs. **3** vs. **4**) can be differentiated readily by comparing their methyl group signals.

The cyclopropane protons are generally well separated in the high-field region of the ^{1}H NMR spectrum and can therefore be assigned easily (see Experimental Section). Their signals are sensitive to the substitution pattern (*E*/*Z* configuration) at the three-membered ring (e.g., *Z* for **1** and **2** vs. *E* for **3**), but diastereoisomers can only be differentiated when there is a major change in the chemical environment. Thus, there is no significant shift difference in the cyclopropane proton signals of the diastereoisomeric sterols **7** and **8**, whereas reasonable differences in **1** and **2** as well as in **5** and **6** are observed, which we were able to use (vide infra) to assign the absolute configuration of

(26) Steiner, E.; Djerassi, C.; Fattorusso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Sica, D. *Helv. Chim. Acta* **1977**, *60*, 475–481.
(27) When dibenzo-18-crown-6 catalysis was used for the dichlorocarbene reaction (see: Makosza, M.; Ludwikow, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 665–666), the starting material was recovered almost quantitatively.
(28) Rohmer, M.; Kokke, W. C. M. C.; Fenical, W.; Djerassi, C. *Steroids* **1980**, *35*, 219–231.
(29) Shimadate, T.; Rosenstein, F. U.; Kircher, H. W. *Lipids* **1977**, *12*, 241–250.
(30) Kokke, W. C. M. C.; Pak, C. S.; Fenical, W.; Djerassi, C. *Helv. Chim. Acta* **1979**, *62*, 1310–1318.

Table I. Methyl Group Region ^{1}H NMR (360 MHz, $CDCl_3$) Chemical Shifts

compd	chemical shift[a] C-18	C-19	C-21	C-26, C-27	C-29
1 (22*R*,23*S*)	0.652	1.013	1.013 (s!)	0.933 (6.54)	
2 (22*S*,23*R*)	0.657	1.009	1.025 (6.02)	0.930/0.922 (6.61/6.31)	
3 (22*R*,23*R*)	0.622	1.004	0.995 (6.55)	0.913/0.890 (6.82/6.86)	
4[b] (22*S*,23*S*)	0.626	1.006	0.951 (6.6)	0.894 (6.6)	
5 (23*R*,24*S*)	0.695	1.010	0.946 (6.20)	1.011/0.986 (5.92/6.28)	
6 (23*S*,24*R*)	0.694	1.009	0.974 (5.67)	1.036/0.989 (6.48/5.26)	
7 (24*R*,28*S*)	0.674	1.007	0.919 (6.46)	0.834/0.806 (6.89/6.89)	1.034 (6.29)
8 (24*S*,28*R*)	0.673	1.007	0.915 (6.46)	0.833/0.826 (6.89/6.89)	1.043 (6.22)
19 (23*Z*)	0.686	1.007	0.916 (6.5)	0.933 (6.5)	

[a] Given as δ values; J values are given in parentheses in hertz. [b] Synthesis described in ref 5, where the Cahn-Ingold-Prelog notation was applied incorrectly.

Table II. ^{13}C NMR Chemical Shifts of Side-Chain Carbon Atoms

compd	chemical shift[a] C-20	C-21	C-22	C-23	C-24	C-25	C-26, C-27	C-28	C-29	C-30
1 (22*R*,23*S*)	33.08	21.05	24.47	16.96	39.45	29.07	22.45, 23.12	9.80		
2 (22*S*,23*R*)	36.32	20.84	23.73	12.72	37.37	29.17	22.54, 22.92	13.36		
3 (22*R*,23*R*)	40.24	19.93	26.71	14.65	44.28	28.68	22.50, 23.00	14.56		
5 (23*R*,24*S*)	36.69	18.89	34.06	13.34	24.58	28.64	22.72, 23.02	10.45		
6 (23*S*,24*R*)	37.37	18.82	34.98	14.05	23.42	28.15	23.14, 23.14	11.44		
7 (24*R*,28*S*)	36.51	18.77	33.96	25.60	27.85	33.83	19.43, 19.49	14.28	15.73	17.45
8 (24*S*,28*R*)	36.60	18.70	34.19	25.48	28.01	34.33	19.28, 19.68	14.35	16.07	17.82
19 (23*Z*)	36.33	18.65	33.61	125.60	138.23	26.53	22.97, 23.09			

[a] Given as δ values.

Table III. Main Mass Spectral Fragments of Steroidal Cyclopropanes[a]

1 (22*R*,23*S*), 2 (22*S*,23*R*), 3 (22*R*,23*R*), 4[b] (22*S*,23*S*)	5 (23*R*,24*S*), 6 (23*S*,24*R*)	7 (24*R*,28*S*), 8 (24*S*,28*R*)
398 (20, M^+)[c]	398 (70, M^+)[c]	426 (60, M^+)[c]
383 (6, M − CH_3)	383 (15, M − CH_3)	411 (11, M − CH_3)
380 (20, M − H_2O)	380 (25, M − H_2O)	408 (25, M − H_2O)
365 (7, M − CH_3 − H_2O)	365 (12, M − CH_3 − H_2O)	393 (16, M − CH_3 − H_2O)
315 (28)	342 (28, M − C_4H_8!)	384 (5, M − C_3H_6!)
314 (100, M − C_6H_{12}!)	328 (13, M − C_5H_{10}!)	314 (46, M − C_8H_{16}!)
299 (20, 314 − CH_3)	324 (10)	299 (35)
296 (20, 314 − H_2O)	300 (21)	271 (45)
281 (30, 314 − CH_3 − H_2O)	287 (10)	255 (17)
271 (35)	273 (13)	213 (27)
255 (10)	271 (65)	69 (100)
253 (10)	255 (15)	
	253 (10)	
	55 (100)	

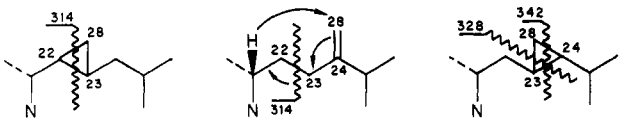
[a] Low-resolution data obtained at 70 eV. [b] Reference 5. [c] Values given as m/z (average intensity, fragments).

1 and 2 by comparison to that of 5 and 6.

^{13}C NMR Spectra. The ^{13}C NMR chemical shift values of the side-chain carbons (Table II) were assigned on the basis of comparable literature data.[31] However, in the absence of reference ^{13}C NMR values of steroidal cyclopropanes our assignments are subject to some uncertainty. Nevertheless, it is clear from Table II that, compared to the ^{1}H NMR shifts (Table I), the ^{13}C NMR spectra are much more sensitive to diastereoisomeric substitution. There is no doubt about the correct attribution of the high-field-shifted C-28 signal, which we use below for assignment of absolute configurations.

Mass Spectra. The mass spectra of the steroidal cyclopropanes 1–8 are characterized by important ions which depend upon the position (but not the stereochemistry) of the three-membered ring in the side chain. Characteristic features of the mass spectra of the regioisomers are summarized in Table III and lead to interesting conclusions, based in part on earlier generalizations of the mass spectral fragmentations of sterols[32] and of simple cyclopropanes.[33]

For instance, the mass spectrum of the 22,23-methylene sterols 1–4 is exceptionally similar to that of 24-methylenecholesterol (29), both having a base peak at m/z



1-4 29 5, 6

314, a feature which can easily lead to misinterpretations. In 24-methylenecholesterol (29) such a peak is associated with a McLafferty rearrangement[34] of the $\Delta^{24(28)}$ double bond, whereas in the steroidal cyclopropanes 1–4 it is due to the fission[8,33] of the C-22/C-23 and C-22/C-28 bonds.

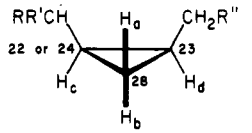
(31) For reviews of this topic, see: (a) Tsuda, M.; Schroepfer, G. J., Jr. *Chem. Phys. Lipids* **1979**, *25*, 49–68. (b) Blunt, J. W.; Stothers, J. B. *Org. Magn. Reson.* **1977**, *9*, 439–464.

(32) Djerassi, C. *Pure Appl. Chem.* **1978**, *50*, 171–184 and references cited therein.

(33) Dias, J. R.; Djerassi, C. *Org. Mass. Spectr.* **1973**, *7*, 753–770.

(34) Massey, I. J.; Djerassi, C. *J. Org. Chem.* **1979**, *44*, 2448–2456.

Table IV. ^{1}H NMR (360 MHz, $CDCl_3$) Chemical Shifts of the Cyclopropane Protons of Comparable Sterols



compd	chemical shift[a]			
	H_a, C-28	H_b, C-28	H_c, C-22 or C-24	H_d, C-23
1 (22*R*,23*S*)	−0.38 (ddd, 5, 5, 5)	0.57 (ddd, 5, 8.5, 8.5)	0.50 (dddd, 5.5, 8.5, 8.5, 8.5)	~0.75 (m)
2 (22*S*,23*R*)	−0.10 (ddd, 4.5, 4.5, 4.5)	~0.63 (ddd)	0.42 (dddd, 5.5, 8.5, 8.5, 8.5)	0.75 (m)
5 (23*R*,24*S*)	−0.33 (ddd, 5, 5, 5)	0.55 (ddd, 5, 8.5, 8.5)	0.43 (dddd, 5.5, 8.5, 8.5, 8.5)	~0.79 (m)
6 (23*S*,24*R*)	−0.26 (ddd, 4.5, 4.5, 4.5)	~0.61 (ddd)	0.36 (dddd, 5.5, 8.5, 8.5, 8.5)	0.79 (m)

[a] Given as δ values; multiplicity and *J* values in hertz are given in parentheses.

The mass spectra of the 23,24 regioisomers **5** and **6** show two diagnostic peaks which could be assigned to a cyclopropane ring fragmentation. The one with the higher intensity at m/z 342 originates from the loss of C_4H_8 (C-24 to C-27), while the peak of lower intensity at m/z 328 is due to the simultaneous fission of C-23/C-24 and C-23/C-28.

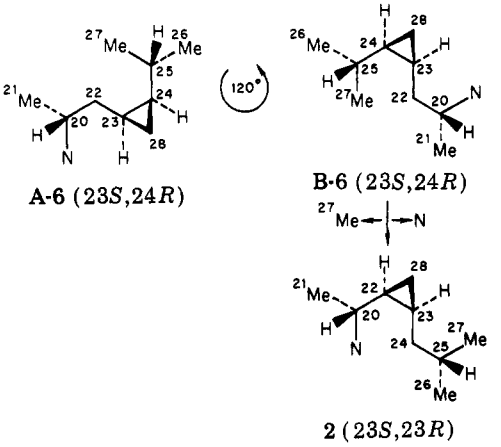
The mass spectroscopic fragmentation pattern of the cyclopropanated sterols **7** and **8** shows a very low intensity peak at m/z 384 attributable to the fission of the two three-membered-ring bonds around C-24. A fragment peak of higher intensity is m/z 314 which is associated with the fission of the 22,23 single bond and concomitant hydrogen migration, similar to the McLafferty rearrangement[34] observed in 24-methylenecholesterol (**29**).

Determination of the Absolute Configuration. Although there exist remarkable differences in physical and spectroscopic properties of steroidal cyclopropanes (see Experimental Section), the determination of the absolute configuration at the three-membered ring for all practical purposes can be accomplished only by X-ray analysis. Therefore, the assignment of the chiral centers C-23,24 in **5** and **6**, and of C-24,28 in **7** and **8** was achieved by correlation with two crystal structure analyses of related trichloro steroids.[13] The absolute configuration of the 22*R*,23*R* isomer **3** could easily be assigned by comparison with the earlier reported[5] NMR data of an authentic sample, which had been synthesized stereospecifically and related to another X-ray standard.[15]

The absolute configuration of the steroidal cyclopropanes **1** and **2** was accomplished by chemical and spectroscopic correlations with the configurations of **5** and **6**. If we consider the structure A of (23*S*,24*R*)-**6** in Scheme IV and turn the molecule in the plane of the paper around 120°, we do not change its stereochemistry (cf. B in Scheme IV). If we now equate the whole steroid nucleus (N) to a methyl group and replace the C-27 methyl group of **B-6** with the nucleus N we obtain structure **2** (Scheme IV), whose absolute configuration would then have to be 22*S*,23*R*. Accepting that this is only a rough approximation, it should nevertheless be possible to find parallels in the chemical and spectroscopic properties of **2** compared to **6**, as well as of (22*R*,23*S*)-**1** compared to (23*R*,24*S*)-**5**.

First we consider the ^{1}H NMR chemical shifts of the cyclopropane protons (Table IV), because the influence of the postulated substitution interchange on their chemical environment would seem to be the lowest. As can be seen from Table IV, H_a on C-28 is shifted to higher field in **1** and **5** but to lower field in **2** and **6**. A similar consistency is noted for H_b on C-28 in that the higher field δ values belong to **1** and **5** and the lower field signals to **2** and **6**. The proton H_c, which is connected to C-22 in **1** and **2** and to C-24 in **5** and **6**, shows an opposite shift mode

Scheme IV



for the comparable sterols. Here, the low-field signals are associated with **1** and **5** and the high-field ones with **2** and **6**. Due to its complexity, H_d on C-23 is difficult to assign, but nevertheless it shows no significant shift differences in the four samples.

Next we turn to the assignment of the three-membered-ring carbon atoms in the ^{13}C NMR spectrum of steroidal cyclopropanes (see Table II), where the only well-separated signal in the high-field region is due to the C-28 resonance. Just like the chemical shift mode of the methylene protons at C-28 in the ^{1}H NMR spectrum (see above), the ^{13}C NMR signals for C-28 in **1** and **5** are also shifted to higher field compared to C-28 in **2** and **6**.

In addition to these consistent NMR spectroscopic relations, we can also point to a chemical one. When the 23*S*,24*R* isomer **6** is written as **B-6** (Scheme IV) and compared to the 22*S*,23*R* isomer **2**, it is clear that both result from top-side attack of the carbene to the *Z* double bond. Both **6** and **2** are minor products compared to **5** and **1**, which result from bottom-side approach of the reagent.[35] The stereoselectivity is especially pronounced (4:1 ratio) in the case of the 22,23-methylene sterols **1** and **2** (compared to a 3:2 ratio of **5** and **6**) and may be a reflection of the closer proximity of the bulky sterol nucleus in the former.[36]

Conclusion

The synthesis of diastereoisomerically pure, substituted, three-membered rings in different positions of the sterol

(35) In case of the major (and solely detectable) trans adduct (22*R*,23*R*)-**3**, the carbene addition also takes place from the bottom side as it is the case with the dominant cis adduct (22*R*,23*S*)-**1**.

(36) For the stereoselectivity of some electrophilic additions to the steroidal C-22 double bond, see: Ishiguro, M.; Ikekawa, N. *Chem. Pharm. Bull.* **1975**, *23*, 2860–2866.

side chain can be effected conviently and in good yield by dichlorocarbene addition to the readily available olefinic precursors coupled with reverse-phase high-performance liquid chromatography. It is noteworthy that during the long addition time for the pure cis-oriented Δ^{22}-steroidal olefin **9**, E/Z isomerization occurs, which explains why three (**10**–**12**) rather then just two (**10**, **11**) adducts are generated.

Determination of the absolute configuration at the three-membered-ring moiety has be done by either physical (X-ray), spectroscopic (NMR), and/or stereochemical correlations.

Experimental Section

General Procedures. Low-resolution 70-eV mass spectra were obtained with a Finnigan MAT-44 spectrometer with a source temperature of 160 °C with a direct-inlet system. High-resolution mass spectra were recorded on a Finnigan MAT-711 double-focusing spectrometer with a direct-inlet system for sample introduction and a PDP-11/45 computer for data acquisition and reduction.

Nuclear magnetic resonance spectra (NMR) were recorded on a Varian Associates XL-100-15 spectrometer equipped with a Nicolet TT 1010-A computer (^{1}H NMR), a Bruker HXS-360 spectrometer equipped with a Nicolet TT 1010-A computer (^{1}H NMR), and a Varian FT 80 A spectrometer (^{13}C NMR). All NMR spectra were taken in $CDCl_3$ solution with Me_4Si as the internal reference unless otherwise indicated. The ^{1}H NMR spectra were determined by Dr. L. J. Durham, and the ^{13}C NMR spectra were recorded by Dr. J. N. Shoolery (Varian Associates).

Elemental analyses were performed by Mr. E. H. Meier of our Microanalytical Laboratory. Melting points are uncorrected and were determined on a Thomas-Hoover "Unimelt" capillary melting point apparatus. Optical rotations (α) were measured on a Autopol III (Rudolph Research) polarimeter at 546 and 589 nm, respectively, by using a thermostated (20 °C) 1.00-dm microcell and chloroform as the solvent.

Analytical gas–liquid chromatography (GLC) was performed on a Hewlett-Packard Model 402 A chromatograph equipped with a flame-ionization detector and a U-shaped glass column (4 mm i.d. × 1.8 m) packed with 3% OV-17 on GCQ (100–120 mesh). The oven temperature was 260 °C with helium as the carrier gas at a flow rate of 100 mL/min. Capillary GLC was processed on a Carlo Erba Fractovap 4160 chromatograph equipped with a glass capillary column (0.317 mm i.d. × 15 m) packed with SE-54. The oven temperature was 235 °C with hydrogen as the carrier gas at a pressure of 0.6 kg/cm^2.

Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} precoated (0.2 mm) aluminum sheets (E. Merck). The TLC sheets were developed in hexane–ethyl acetate (5:1) and visualized by spraying with a ceric sulfate solution (25 g in 1 L of 25% sulfuric acid) followed by heating. Column chromatography was carried out on E. Merck silica gel 60 (70–230-mesh ASTM) with hexane–ethyl acetate (9:1) as the eluent.

High-performance liquid chromatography (HPLC) was used for preparative-scale separation of diastereoisomeric sterol mixtures as well as for monitoring of product purification and was performed by using a Waters Associated HPLC unit (M 6000 pump, UK 6 injector, R 403 differential refractometer) and two different reverse-phase columns: Whatman Partisil M9 10/50 ODS-2 (9 mm i.d. × 50 cm), with absolute methanol as the mobile phase; Altex Ultrasphere ODS 5-μm (10 mm i.d. × 25 cm), with methanol/water (95:5) as the mobile phase. The flow rate was 5 mL/min, and the injection volume was 3–6 mL of a saturated methanol solution.

The progress of all reactions and of column chromatography was monitored by TLC and/or GLC. All solvents were purified as necessary before use according to standard procedures. Abbreviations are as follows: t_R = retention time, RV = rotary evaporator.

Regeneration of the 3β-hydroxy-Δ^5 system from the 3α,5α-cyclo-6β-methoxy system was always accomplished by dissolving 10 mg of the i-methyl ether derivative in 10 mL of dioxane/water (5:1). A small amount of *p*-toluenesulfonic acid monohydrate (ca. 5 mg/10 mg of compound) was added, and the solution was heated under reflux for 30–45 min (TLC monitoring).[25] The solvents were evaporated in a rotary evaporator (RV) at reduced pressure until the appearance of a white precipitate. Cold water was added, and the desired product was collected by filtration and then recrystallized.

(22*Z*)-6β-Methoxy-3α,5-cyclo-5α-cholest-22-ene (9). (20*S*)-6β-Methoxy-3α,5-cyclo-5α-pregnane-20-carboxaldehyde was prepared from the corresponding primary alcohol[18] by oxidation under mild conditions with Collins reagent.[19] Wittig reaction with the appropriate phosphorane in Me_2SO[20] furnished after a 2-h reaction time at room temperature and column chromatography the pure Z isomer of the Δ^{22}-steroidal i-methyl ether **9**. HPLC analysis (ODS-2) of the noncrystalline compound showed only one peak: t_R = 42 min; ^{1}H NMR (360 MHz) δ 5.18 (m, 2 H, C-22 and C-23), 3.324 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 1.028 (s, 3 H, C-19), 0.950 (d, J = 6.60 Hz, 3 H, C-21), 0.906 (d, J = 6.60 Hz, 3 H) and 0.890 (d, J = 6.60 Hz, 3 H) C-26 and C-27, 0.756 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.44 (dd, J = 5 and 8 Hz, 1 α H, C-4); high-resolution mass spectrum, m/z (relative intensity) 398.3547 (M^+, 13, calcd for $C_{28}H_{46}O$ 398.3549), 383.3290 ($C_{27}H_{43}O$, 12, M – CH_3), 366.3277 ($C_{27}H_{42}$, 28, M – CH_3OH), 351.3031 ($C_{26}H_{39}$, 8), 343.2993 ($C_{24}H_{39}O$, 18, M – A ring), 255.2118 ($C_{19}H_{27}$, 23), 57.0707 (C_4H_9, 100).

Dichlorocarbene Addition to 9. To a vigorously stirred solution of the i-methyl ether **9** (405 mg, 1.02 mmol) and of benzyltriethylammonium chloride (BTEAC; 150 mg, 0.66 mmol) in chloroform (15 mL) was added slowly an aqueous solution of sodium hydroxide (50%, 15 mL). The mixture was stirred for 9 days at room temperature, diluted with water, and extraced with chloroform. The extract after being washed with water and brine was dired over potassium carbonate and evaporated in an RV at reduced pressure. After purification of the crude material by column chromatography, the product separation was realized by HPLC (Altex ODS). Four fractions, A-D, in a ratio 47:36:10:7 were collected,[37] and the analytical data for these addition products are listed herewith.

Fraction A. HPLC t_R = 63 min. According to its mass spectrum, this fraction represents the unreacted starting material **9** whose E/Z distribution was not further determined.

Fraction B. (22*S*,23*R*)-22,23-(Dichloromethylene)-6β-methoxy-3α,5-cyclo-5α-cholestane (10): HPLC t_R = 67 min; ^{1}H NMR (360 MHz) δ 3.324 (s, 3 H, OCH_3), 2.78 (m, 1 H, C-6), 1.212 (d, J = 3.07 Hz, 3 H, C-21), 1.023 (s, 3 H, C-19), 1.008 (d, J = 6.75 Hz, 3 H) and 0.997 (d, J = 6.67 Hz, 3 H) C-26 and C-27, 0.706 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.44 (dd, J = 5, 8 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 480 (M^+, 1), 465 (2, M – CH_3), 448 (2, M – CH_3OH), 425 (5, M – A ring), 397 (6), 328 (17, M – $C_6H_{10}Cl_2$), 313 (4), 296 (17), 285 (15), 281 (7), 255 (20), 253 (100).

Fraction C. (22*R*,23*S*)-22,23-(Dichloromethylene)-6β-methoxy-3α,5-cyclo-5α-cholestane (11): HPLC t_R = 74 min; ^{1}H NMR (360 MHz) δ 3.328 (s, 3 H, OCH_3), 2.78 (m, 1 H, C-6), 1.026 (s, 3 H, C-19), 0.993 d, J = 6.57 Hz, 3 H, C-21), 0.993 (d, J = 6.57 Hz, 3 H) and 0.983 (d, J = 6.64 Hz, 3 H) C-26 and C-27, 0.749 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.44 (dd, J = 5, 8 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 480 (M^+, 2), 465 (3, M – CH_3), 448 (4, M – CH_3OH), 425 (8, M – A ring), 328 (18, M – $C_6H_{10}Cl_2$), 313 (6), 296 (22), 285 (20), 281 (10), 255 (25), 253 (100).

Fraction D. (22*S*,23*S*)-22,23-(Dichloromethylene)-6β-methoxy-3α,5-cyclo-5α-cholestane (12): HPLC t_R = 79 min; ^{1}H NMR (360 MHz) δ 3.330 (s, 3 H, OCH_3), 2.780 (m, 1 H, C-6), 1.027 (s, 3 H, C-19), 1.016 (d, J = 7.0 Hz, 3 H, C-21), 0.979 (d, J = 6.57 Hz, 3 H) and 0.967 (d, J = 6.62 Hz, 3 H) C-26 and C-27, 0.740 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.44 (dd, J = 5, 8 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 480 (M^+, 2), 465 (3, M – CH_3), 448 (4, M – CH_3OH), 425 (8, M – A ring), 328 (15, M – $C_6H_{10}Cl_2$), 313 (6), 296 (16), 285 (15), 281 (10), 255 (25), 253 (100).

(22*R*,23*S*)-22,23-Methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (13). Dehalogenation of the dichloro i-methyl ether

(37) An aliquot of the reaction mixture which was worked up in the same manner after 6 days was shown by HPLC analysis to contain an *A–D* ratio of 57:27:9:7.

10 was accomplished by using lithium in liquid ammonia according to the literature[9] procedure. A workup in the usual fashion[9] furnished the desired compound 13 in almost quantitative yield: mass spectrum, m/z (relative intensity) 412 (M^+, 10), 397 (10, M – CH_3), 380 (21, M – CH_3OH), 357 (35, M – A ring), 343 (9), 328 (58, M – C_6H_{12}), 313 (21), 296 (54), 255 (40), 253 (100).

(22*S*,23*R*)-22,23-Methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (14). Repetition of the above reduction on the dichloro compound 11 gave the anticipated i-methyl ether 14 in almost quantitative yield: mass spectrum, m/z (relative intensity) 412 (M^+, 5), 397 (6, M – CH_3), 380 (6, M – CH_3OH), 357 (13, M – A ring), 343 (2), 328 (40, M – C_6H_{12}), 313 (15), 296 (40), 255 (25), 253 (100).

(22*R*,23*R*)-22,23-Methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (15). Reduction of 12 as mentioned above yielded the desired i-methyl ether 15 in almost quantitative yield: mass spectrum, m/z (relative intensity) 412 (M^+, 22), 397 (23, M – CH_3), 380 (27, M – CH_3OH), 357 (59, M – A ring), 328 (73, M – C_6H_{12}), 313 (35), 296 (71), 255 (33), 253 (100).

(22*R*,23*S*)-22,23-Methylenecholest-5-en-3β-ol (1). The i-methyl ether protecting group in 13 was removed in the usual way to give 1: mp 143–144 °C ($MeOH/H_2O$); $[\alpha]^{20}_{589}$ –86.0°, $[\alpha]^{20}_{546}$ –102.3° (*c* 6.0 mg/mL, $CHCl_3$); HPLC t_R (Altex ODS) = 48 min; ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.013 (s!, 3 H, C-21), 1.013 (s, 3 H, C-19), 0.933 (d, J = 6.54 Hz, 6 H, C-26 and C-27), ~0.75 (m, 1 H, C-23), 0.652 (s, 3 H, C-18), 0.57 (ddd, J = 5, 8.5, 8.5 Hz, 1 H, C-28), 0.50 (dddd, J = 5.5, 8.5, 8.5, 8.5 Hz, 1 H, C-22), –0.38 (ddd, J = 5, 5, 5 Hz, 1 H, C-28); ^{13}C NMR δ 37.32 (C-1), 31.72 (C-2), 71.79 (C-3), 42.37 (C-4), 140.83 (C-5), 121.64 (C-6), 31.91 (C-7), 32.09 (C-8), 50.34 (C-9), 36.55 (C-10), 21.15 (C-11), 39.83 (C-12), 42.47 (C-13), 58.78 (C-14), 24.20 (C-15), 27.25 (C-16), 56.72 (C-17), 12.23 (C-18), 19.36 (C-19), 33.08 (C-20), 21.05 (C-21), 24.47 (C-22), 16.96 (C-23), 39.45 (C-24), 29.07 (C-25), 22.45 (C-26), 23.12 (C-27), 9.80 (C-28); high-resolution mass spectrum, m/z (relative intensity) 398.3531 (M^+, 20, calcd for $C_{28}H_{46}O$ 398.3549), 383.3337 ($C_{27}H_{43}O$, 7, M – CH_3), 380.3443 ($C_{28}H_{44}$, 34, M – H_2O), 365.3248 ($C_{27}H_{41}$, 10, M – CH_3 – H_2O), 315.2624 ($C_{22}H_{35}O$, 29), 314.2560 ($C_{22}H_{34}O$, 100, M – C_6H_{12}!), 299.2365 ($C_{21}H_{31}O$, 19), 296.2480 ($C_{22}H_{32}$, 34), 285.2200 ($C_{20}H_{29}O$, 16), 281.2265 ($C_{21}H_{29}$, 42), 272.2122 ($C_{19}H_{28}O$, 52), 271.2047 ($C_{19}H_{27}O$, 43), 255.2105 ($C_{19}H_{27}$, 13), 253.1942 ($C_{19}H_{25}$, 19).

(22*S*,23*R*)-22,23-Methylenecholest-5-en-3β-ol (2). The 3β-hydroxy-Δ⁵ system was regenerated from 14 in the usual manner to give the crystalline sterol 2: mp 190–192 °C ($MeOH/H_2O$); $[\alpha]^{20}_{589}$ –21.21°, $[\alpha]^{20}_{546}$ –26.26° (*c* 9.9 mg/mL, $CHCl_3$); HPLC t_R (Altex ODS) = 50 min; ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.025 (d, J = 6.02 Hz, 3 H, C-21), 1.009 (s, 3 H, C-19), 0.930 (d, J = 6.61 Hz, 3 H) and 0.922 (d, J = 6.31 Hz, 3 H) C-26 and C-27, 0.75 (m, 1 H, C-23), 0.657 (s, 3 H, C-18), ~0.63 (ddd, 1 H, C-28), 0.42 (dddd, J = 5.5, 8.5, 8.5, 8.5 Hz, 1 H, C-22), –0.10 (ddd, J = 4.5, 4.5, 4.5 Hz, 1 H, C-28); ^{13}C NMR δ 37.32 (C-1), 31.73 (C-2), 71.80 (C-3), 42.38 (C-4), 140.82 (C-5), 121.66 (C-6), 31.91 (C-7), 32.06 (C-8), 50.32 (C-9), 36.54 (C-10), 21.14 (C-11), 39.81 (C-12), 42.65 (C-13), 58.99 (C-14), 24.35 (C-15), 28.15 (C-16), 56.51 (C-17), 11.92 (C-18), 19.36 (C-19), 36.32 (C-20), 20.84 (C-21), 23.73 (C-22), 12.72 (C-23), 37.37 (C-24), 29.17 (C-25), 22.54 (C-26), 22.92 (C-27), 13.36 (C-28); high-resolution mass spectrum, m/z (relative intensity) 398.3538 (M^+, 17, calcd for $C_{28}H_{46}O$ 398.3549), 383.3285 ($C_{27}H_{43}O$, 6, M – CH_3), 380.3439 ($C_{28}H_{44}$, 15, M – H_2O), 365.3219 ($C_{27}H_{41}$, 5, M – CH_3 – H_2O), 315.2643 ($C_{22}H_{35}O$, 26), 314.2615 ($C_{22}H_{34}O$, 100, M – C_6H_{12}!), 299.2379 ($C_{21}H_{31}O$, 20), 296.2515 ($C_{22}H_{32}$, 20), 281.2258 ($C_{21}H_{29}$, 25), 272.2116 ($C_{19}H_{28}O$, 18), 271.2063 ($C_{19}H_{27}O$, 41), 255.2119 ($C_{19}H_{27}$, 8), 253.1965 ($C_{19}H_{25}$, 11).

(22*R*,23*R*)-22,23-Methylenecholest-5-en-3β-ol (3). Cleavage of the i-methyl ether moiety of 15 gave the desired steroidal cyclopropane 3:[38] mp 179–180 °C ($MeOH/H_2O$); $[\alpha]^{20}_{589}$ –61.27°, $[\alpha]^{20}_{546}$ –76.06° (*c* 7.1 mg/mL, $CHCl_3$); HPLC t_R (Altex ODS) = 62 min; ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.004 (s, 3 H, C-19), 0.995 (d, J = 6.55 Hz, 3 H, C-21), 0.913 (d, J = 6.82 Hz, 3 H) and 0.890 (d, J = 6.86 Hz, 3 H) C-26 and C-27, 0.622 (s, 3 H, C-18), 0.38 (m, 2 H, C-23 and C-24), 0.20 (m, 2 H, C-28); ^{13}C NMR δ 37.33 (C-1), 31.75 (C-2), 71.81 (C-3), 42.39 (C-4), 140.82 (C-5), 121.66 (C-6), 31.93 (C-7), 32.06 (C-8), 50.33 (C-9), 36.56 (C-10), 21.14 (C-11), 39.72 (C-12), 42.39 (C-13), 58.46 (C-14), 24.34 (C-15), 27.74 (C-16), 56.53 (C-17), 11.87 (C-18), 19.37 (C-19), 40.24 (C-20), 19.93 (C-21), 26.71 (C-22), 14.65 (C-23), 44.28 (C-24), 28.68 (C-25), 22.50 (C-26), 23.00 (C-27), 14.56 (C-28); high-resolution mass spectrum, m/z (relative intensity) 398.3526 (M^+, 23, calcd for $C_{28}H_{46}O$ 398.3549), 383.3297 ($C_{27}H_{43}O$, 6, M – CH_3), 380.3432 ($C_{28}H_{44}$, 18, M – H_2O), 365.3241 ($C_{27}H_{41}$, 6, M – CH_3 – H_2O), 315.2636 ($C_{22}H_{35}O$, 27), 314.2612 ($C_{22}H_{34}O$, 100, M – C_6H_{12}!), 299.2384 ($C_{21}H_{31}O$, 18), 296.2511 ($C_{22}H_{32}$, 12), 281.2258 ($C_{21}H_{29}$, 25), 272.2108 ($C_{19}H_{28}O$, 11), 271.2052 ($C_{19}H_{27}O$, 29), 255.2109 ($C_{19}H_{27}$, 9), 253.1938 ($C_{19}H_{25}$, 9).

6β-Methoxy-3α,5-cyclo-5α-cholest-23-yne (16). Lowering the reaction temperature for generating the lithium acetylide by use of a solvent mixture (dioxane/pentane, 5:1) is a very efficient modification of the coupling reaction[26] to the desired compound 16. Thus 3-methylbut-1-yne[39] (1.022 g, 15 mmol) was dissolved in a flask containing the ice-cold solvent mixture (60 mL) under an argon atmosphere. A 1.5 M solution of *n*-butyllithium in hexane (10 mL) was added at a rate that maintains the reaction temperature below 5 °C. After being stirred further in an ice bath for 1 h, the mixture was allowed to warm to room temperature, the appropriate steroidal *p*-toluenesulfonate[18] (3.00 g, 6 mmol) added, and the mixture heated to reflux. The reaction was almost complete after 48 h (TLC monitoring). The usual workup procedure[26] and recrystallization from hot ethyl acetate yielded 2.17 g (91%) of analytically pure 16: mp 97–99 °C (AcOEt); $[\alpha]^{20}_{589}$ +55.15°, $[\alpha]^{20}_{546}$ +65.05° (*c* 10.3 mg/mL, $CHCl_3$) [lit.[26] mp 97–99 °C (AcOEt), lit.[26] $[\alpha]_{589}$ +57.08° (*c* 10 mg/mL, $CHCl_3$)]; HPLC t_R (ODS-2) = 29 min; GLC relative t_R (OV-17) = 0.486 (cholesterol); ^1H NMR (100 MHz) δ 3.31 (s, 3 H, OCH_3), 2.77 (t, J = 2.55 Hz, 1 H, C-6), 1.13 (d, J = 6.75 Hz, 6 H, C-26 and C-27), 1.04 (d, J = 6.25 Hz, 3 H, C-21), 1.01 (s, 3 H, C-19), 0.71 (s, 3 H, C-18); mass spectrum m/z (relative intensity) 396 (M^+, 74), 381 (67, M – CH_3), 364 (93, M – CH_3OH), 349 (15, M – CH_3 – CH_3OH), 341 (100, M – A ring), 338 (20), 283 (11), 255 (13), 253 (30), 227 (24), 215 (15), 213 (39).

Anal. Calcd for $C_{28}H_{44}O$: C, 84.79; H, 11.18. Found: C, 84.54; H, 11.06.

(23*Z*)-6β-Methoxy-3α,5-cyclo-5α-cholest-23-ene (17). A solution of the i-methyl ether 16 (397 mg, 1 mmol) in ethyl acetate (50 mL) was hydrogenated at normal pressure and room temperature over Lindlar catalyst (200 mg). The reaction was almost complete after 30 min (GLC monitoring: SE-54). The black suspension was filtered by passing over Celite, and the solvent was evaporated in an RV at reduced pressure to give a 9:1 mixture of the desired 17 and cholesterol i-methyl ether 18, which was identified by comparison with an authentic sample. The mixture was separated by HPLC (ODS-2) to yield 350 mg (88%) of pure (23*Z*)-17: ^1H NMR (360 MHz) δ 5.220 (m, 2 H, C-23 and C-24), 3.324 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 2.57 (m, 1 H, C-25), 1.021 (s, 3 H, C-19), 0.933 (d, J = 7.0 Hz, 6 H, C-26 and C-27), 0.913 (d, J = 7.0 Hz, 3 H, C-21), 0.723 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.44 (dd, J = 5, 9 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 398 (M^+, 60), 383 (58, M – CH_3), 366 (61, M – CH_3OH), 351 (11), 343 (100, M – A ring), 340 (13), 314 (15), 285 (47), 283 (77), 255 (25), 253 (47).

(23*Z*)-Cholesta-5,23-dien-3β-ol (19). Regeneration of the 3β-hydroxy-Δ⁵ system in 17 in the usual way gave the desired cis compound 19: mp 137.5 °C (MeOH); $[\alpha]^{20}_{589}$ –53.89°, $[\alpha]^{20}_{546}$ –65.00° (*c* 9.0 mg/mL, $CHCl_3$); HPLC t_R (ODS-2) = 38 min; ^1H NMR (360 MHz) δ 5.40–5.18 (m, 3 H, C-6, C-23, and C-24), 3.53 (m, 1 α H, C-3), 2.57 (m, 1 H, C-25), 1.007 (s, 3 H, C-19), 0.933 (d, J = 6.5 Hz, 6 H, C-26 and C-27), 0.916 (d, J = 6.5 Hz, 3 H, C-21), 0.686 (s, 3 H, C-18); ^{13}C NMR δ 37.16 (C-1), 31.53 (C-2), 71.65 (C-3), 42.18 (C-4), 140.66 (C-5), 121.54 (C-6), 31.85 (C-7), 31.85 (C-8), 50.02 (C-9), 36.40 (C-10), 20.96 (C-11), 39.59 (C-12),

(38) The physical and spectroscopic properties of natural 22,23-methylenecholesterol (reported in ref 5) are given as follows: mp 165 °C; $[\alpha]_{589}$ –104.6° ($CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$) δ 5.35 (m, 1 H, C-6), 1.004 (s, 3 H, C-19), 0.995 (d, J = 6.6 Hz, 3 H, C-21), 0.913 (d, J = 6.9 Hz, 3 H) and 0.889 (d, J = 6.8 Hz, 3 H, C-26 and C-27), 0.621 (s, 3 H, C-18), 0.40–0.36 (m, 2 H) and 0.22–0.18 (m, 2 H) four cyclopropane protons; high-resolution mass spectrum, m/z 398.355 01 (M^+, calcd for $C_{28}H_{46}O$ 398.354 86), 314 (100, M – C_6H_{12}).

(39) 3-Methylbut-1-yne was obtained from the Farchan Division, Story Corp.

42.18 (C-13), 56.64 (C-14), 24.21 (C-15), 28.19 (C-16), 55.92 (C-17), 11.78 (C-18), 19.28 (C-19), 36.33 (C-20), 18.65 (C-21), 33.61 (C-22), 125.60 (C-23), 138.23 (C-24), 26.53 (C-25), 22.97 (C-26), 23.09 (C-27); high-resolution mass spectrum, m/z (relative intensity) 384.3411 (M^+, 100, calcd for $C_{27}H_{44}O$ 384.3392), 369.3159 ($C_{26}H_{41}O$, 18, M – CH_3), 366.3303 ($C_{27}H_{42}$, 22, M – H_2O), 351.3058 ($C_{26}H_{39}$, 10, M – CH_3 – H_2O), 301.2533 ($C_{21}H_{33}O$, 67), 300.2455 ($C_{21}H_{32}O$, 38), 284.2460 ($C_{21}H_{32}$, 19), 283.2426 ($C_{21}H_{31}$, 81), 272.2109 ($C_{19}H_{28}O$, 25), 271.2048 ($C_{19}H_{27}O$, 96), 255.2119 ($C_{19}H_{27}$, 7), 253.1967 ($C_{19}H_{25}$, 6), 215.1790 ($C_{16}H_{23}$, 24), 213.1637 ($C_{16}H_{21}$, 15).

Dichlorocarbene Addition to 17. The i-methyl ether **17** (380 mg, 0.95 mmol) was treated with dichlorocarbene under phase-transfer conditions as described above for **9**. After a reaction time of 6 days and the usual workup, the prepurified (column chromatography) reaction mixture was separated by HPLC (ODS-2). Two fractions (78% yield; A and B, 3:2) were collected whose analytical data are listed below.

Fraction A. (23*R*,24*S*)-23,24-(Dichloromethylene)-6β-methoxy-3α,5-cyclo-5α-cholestane (20): mp 118–120 °C (MeOH/H_2O); HPLC t_R = 40 min; ^1H NMR (360 MHz) δ 3.326 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 1.106 (d, J = 6.43 Hz, 3 H) and 1.056 (d, J = 6.56 Hz, 3 H) C-26 and C-27, 1.027 (s, 3 H, C-19), 0.945 (d, J = 6.63 Hz, 3 H, C-21), 0.762 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.43 (dd, J = 5, 9 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 480 (M^+, 58), 465 (57, M – CH_3), 448 (83, M – CH_3OH), 425 (100, M – A ring), 327 (25), 285 (18), 255 (68), 253 (85), 229 (32), 213 (77).

Fraction B. (23*S*,24*R*)-23,24-(Dichloromethylene)-6β-methoxy-3α,5-cyclo-5α-cholestane (21): HPLC t_R = 44 min; ^1H NMR (360 MHz) δ 3.326 (s, 3 H, OCH_3), 2.78 (m, 1 H, C-6), 1.105 (d, J = 6.43 Hz, 3 H) and 1.073 (d, J = 6.55 Hz, 3 H) C-26 and C-27, 1.026 (s, 3 H, C-19), 0.979 (d, J = 6.55 Hz, 3 H, C-21), 0.740 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.43 (dd, J = 5, 9 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 480 (M^+, 59), 465 (53, M – CH_3), 448 (100, M – CH_3OH), 425 (95, M – A ring), 327 (20), 285 (12), 255 (60), 253 (74), 229 (37), 213 (68).

(23*R*,24*S*)-23,24-Methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (22). Dehalogenation of the dichloro i-methyl ether **20** was accomplished as described above for the preparation of **13** from **10**. A workup in the usual way gave **22** in almost quantitative yield: mass spectrum, m/z (relative intensity) 412 (M^+, 70), 397 (59, M – CH_3), 380 (100, M – CH_3OH), 357 (98, M – A ring), 324 (16), 301 (11), 285 (34), 259 (40), 255 (55), 253 (95), 229 (31), 227 (43), 215 (31), 213 (75).

(23*S*,24*R*)-23,24-Methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (23). Repetition of the dehalogenation reaction on **21** furnished the desired i-methyl ether **23** in almost quantitative yield: mass spectrum, m/z (relative intensity) 412 (M^+, 49), 397 (43, M – CH_3), 380 (74, M – CH_3OH), 357 (69, M – A ring), 324 (6), 301 (6), 285 (40), 259 (30), 255 (40), 253 (100), 229 (21), 227 (30), 215 (21), 213 (62).

(23*R*,24*S*)-23,24-Methylenecholest-5-en-3β-ol (5). The i-methyl ether protecting group in **22** was removed in the usual way to give **5**: mp 192–194 °C (MeOH); $[\alpha]^{20}_{589}$ –15.07°, $[\alpha]^{20}_{549}$ –17.46° (*c* 6.3 mg/mL, $CHCl_3$); HPLC t_R (ODS-2) = 41 min; ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.010 (s, 3 H, C-19), 1.011 (d, J = 5.92 Hz, 3 H) and 0.986 (d, J = 6.28 Hz, 3 H) C-26 and C-27, 0.946 (d, J = 6.20 Hz, 3 H, C-21), ~0.79 (m, 1 H, C-23), 0.695 (s, 3 H, C-18), 0.55 (ddd, J = 5, 8.5, 8.5 Hz, 1 H, C-28), 0.43 (dddd, J = 5.5, 8.5, 8.5, 8.5 Hz, 1 H, C-24), –0.33 (ddd, J = 5, 5, 5 Hz, 1 H, C-28); ^{13}C NMR δ 37.16 (C-1), 31.55 (C-2), 71.66 (C-3), 42.19 (C-4), 140.66 (C-5), 121.54 (C-6), 31.73 (C-7), 31.73 (C-8), 50.05 (C-9), 36.39 (C-10), 20.98 (C-11), 39.69 (C-12), 42.27 (C-13), 56.75 (C-14), 24.16 (C-15), 28.26 (C-16), 56.17 (C-17), 11.77 (C-18), 19.27 (C-19), 36.69 (C-20), 18.89 (C-21), 34.06 (C-22), 13.34 (C-23), 24.58 (C-24), 28.64 (C-25), 22.72 (C-26), 23.02 (C-27), 10.45 (C-28); high-resolution mass spectrum, m/z (relative intensity) 398.3569 (M^+, 84, calcd for $C_{28}H_{46}O$ 398.3549), 383.3324 ($C_{27}H_{43}O$, 14, M – CH_3), 380.3440 ($C_{28}H_{44}$, 27, M – H_2O), 365.3227 ($C_{27}H_{41}$, 14, M – CH_3 – H_2O), 342.2907 ($C_{24}H_{38}O$, 34, M – C_4H_8!), 328.2473 ($C_{23}H_{36}O$, 15, M – C_5H_{10}!), 324.2817 ($C_{24}H_{36}$, 11, M – C_4H_8 – H_2O), 313.2836 ($C_{23}H_{37}$, 13), 310.2701 ($C_{23}H_{34}$, 6, M – C_5H_{10} – H_2O), 300.2454 ($C_{21}H_{32}O$, 21, M – C_7H_{14}), 287.2766 ($C_{21}H_{35}$, 11), 283.2440 ($C_{21}H_{31}$, 14), 273.2207 ($C_{19}H_{29}O$, 13), 271.2065 ($C_{19}H_{27}O$, 59), 255.2115 ($C_{19}H_{27}$, 15), 253.1940 ($C_{19}H_{25}$, 10), 231.2098 ($C_{17}H_{27}$, 11), 215.1801 ($C_{16}H_{23}$, 11), 213.1646 ($C_{16}H_{21}$, 23), 55.0554 (C_4H_7, 100).

(23*S*,24*R*)-23,24-Methylenecholest-5-en-3β-ol (6). The 3β-hydroxy-Δ⁵ system was regenerated from **23** in the usual manner to give the crystalline sterol **6**: mp 154.5 °C (MeOH); $[\alpha]^{20}_{589}$ –55.5°, $[\alpha]^{20}_{546}$ –65.9° (*c* 5.1 mg/mL, $CHCl_3$); HPLC t_R (ODS-2) = 45 min; ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.036 (d, J = 6.48 Hz, 3 H) and 0.989 (d, J = 5.26 Hz, 3 H) C-26 and C-27, 1.009 (s, 3 H, C-19), 0.974 (d, J = 5.67 Hz, 3 H, C-21), 0.79 (m, 1 H, C-23), 0.694 (s, 3 H, C-18), ~0.61 (ddd, 1 H, C-28), 0.36 (dddd, J = 5.5, 8.5, 8.5, 8.5 Hz, 1 H, C-24), –0.26 (ddd, J = 4.5, 4.5, 4.5 Hz, 1 H, C-28); ^{13}C NMR δ 37.16 (C-1), 31.55 (C-2), 71.65 (C-3), 42.20 (C-4), 140.66 (C-5), 121.55 (C-6), 31.82 (C-7), 31.82 (C-8), 50.03 (C-9), 36.39 (C-10), 20.99 (C-11), 39.70 (C-12), 42.28 (C-13), 56.67 (C-14), 24.21 (C-15), 28.27 (C-16), 56.45 (C-17), 11.71 (C-18), 19.27 (C-19), 37.37 (C-20), 18.82 (C-21), 34.98 (C-22), 14.05 (C-23), 23.42 (C-24), 28.15 (C-25), 23.14 (C-26), 23.14 (C-27), 11.44 (C-28); high-resolution mass spectrum, m/z (relative intensity) 398.3569 (M^+, 60, calcd for $C_{28}H_{46}O$ 398.3549), 383.3301 ($C_{27}H_{43}O$, 17, M – CH_3), 380.3437 ($C_{28}H_{44}$, 19, M – H_2O), 365.3231 ($C_{27}H_{41}$, 10, M – CH_3 – H_2O), 342.2920 ($C_{24}H_{38}O$, 22, M – C_4H_8!), 328.2788 ($C_{23}H_{36}O$, 10, M – C_5H_{10}!), 324.2789 ($C_{24}H_{36}$, 8, M – C_4H_8 – H_2O), 313.2893 ($C_{23}H_{37}$, 9), 310.2662 ($C_{23}H_{34}$, 4, M – C_5H_{10} – H_2O), 300.2458 ($C_{21}H_{32}O$, 21, M – C_7H_{14}), 287.2733 ($C_{21}H_{35}$, 8), 283.2423 ($C_{21}H_{31}$, 12), 273.2187 ($C_{19}H_{29}O$, 14), 271.2066 ($C_{19}H_{27}O$, 74), 255.2109 ($C_{19}H_{27}$, 14), 253.1942 ($C_{19}H_{25}$, 10), 231.2120 ($C_{17}H_{27}$, 10), 215.1801 ($C_{16}H_{23}$, 10), 213.1645 ($C_{16}H_{21}$, 16), 55.0553 (C_4H_7, 100).

(24(28)*E*)-6β-Methoxy-3α,5-cyclo-5α-stigmast-24(28)-ene (24). Natural fucosterol which was isolated[29] from the crude extract of the giant kelp *Macrocystis pyrifera* was transformed to its i-methyl ether **24** in two well-known steps:[30] HPLC t_R (ODS-2) = 59 min; GLC relative t_R (OV-17) = 0.760 (cholesterol); ^1H NMR (360 MHz) δ 5.18 (q, J = 6.7 Hz, 1 H, C-28), 3.326 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 1.572 (d, J = 6.82 Hz, 3 H, C-29), 1.024 (s, 3 H, C-19), 0.980 (d, J = 7 Hz, 6 H, C-26 and C-27), 0.724 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.43 (dd, J = 5 and 8 Hz, 1 α H, C-4); mass spectrum, m/z (relative intensity) 426 (M^+, 19), 411 (53, M – CH_3), 394 (25, M – CH_3OH), 371 (100, M – A ring), 328 (85), 313 (43), 296 (70), 285 (18), 281 (20), 273 (40), 255 (23), 253 (45).

Dichlorocarbene Addition to 24. The i-methyl ether **24** (590 mg, 1.38 mmol) was treated with dichlorocarbene under phase-transfer conditions as described above for **9** and **17**, respectively. After a reaction time of 3 days and the usual workup, the prepurified (column chromatography) reaction mixture was separated by HPLC (Altex ODS). Two fractions (A and B, 45:55) yielding together ≥95% addition products were collected, and the analytical data for these addition products are listed below.

Fraction A. (24*R*,28*R*)-24,28-(Dichloromethylene)-24-ethyl-6β-methoxy-3α,5-cyclo-5α-cholestane (25): mp 165–168 °C (MeOH/H_2O); HPLC t_R (ODS-2) = 58 min, t_R (Altex ODS) = 102 min; ^1H NMR (360 MHz) δ 3.324 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 1.154 (s, 3 H, C-29), 1.134 (d, J = 6.88 Hz, 3 H) and 1.028 (d, J = 6.49 Hz, 3 H) C-26 and C-27, 1.019 (s, 3 H, C-19), 0.913 (d, J = 6.47, 3 H, C-21), 0.710 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.43 (dd, J = 5, 9 Hz, 1 α H, C-4); mass spectrum m/z (relative intensity) 508 (M^+, 5), 493 (25, M – CH_3), 476 (10, M – CH_3OH), 453 (49, M – A ring), 398 (44, M – $C_3H_4Cl_2$!), 383 (79, 398 – CH_3), 351 (25), 343 (72, 398 – A ring), 314 (27), 285 (98), 253 (100).

Fraction B. (24*S*,28*S*)-24,28-(Dichloromethylene)-24-ethyl-6β-methoxy-3α,5-cyclo-5α-cholestane (26): HPLC t_R (ODS-2) = 59 min, t_R (Altex ODS) = 106 min; ^1H NMR (360 MHz) δ 3.327 (s, 3 H, OCH_3), 2.77 (m, 1 H, C-6), 1.168 (s!, C-29), 1.127 (d, J = 6.95 Hz, 3 H) and 1.033 (d, J = 6.95 Hz, 3 H) C-26 and C-27, 1.020 (s, 3 H, C-19), 0.924 (d, J = 5.92 Hz, 3 H, C-21), 0.709 (s, 3 H, C-18), 0.65 (t, J = 5 Hz, 1 β H, C-4), 0.43 (dd, J = 5 and 9 Hz, 1 α H, C-4); high-resolution mass spectrum, m/z (relative intensity) 508.3254 (M^+, 4, calcd for $C_{31}H_{50}Cl_2O$ 508.3238), 493.3004 ($C_{30}H_{47}Cl_2O$, 4, M – CH_3), 476.2988 ($C_{30}H_{46}Cl_2$, 9, M – CH_3OH), 453.2669 ($C_{27}H_{43}Cl_2O$, 15, M – A ring), 398.3548 ($C_{28}H_{46}O$, 37, M – $C_3H_4Cl_2$!), 383.3321 ($C_{27}H_{43}O$, 46, 398 – CH_3), 351.3032 ($C_{26}H_{39}$, 20), 343.2980 ($C_{24}H_{39}O$, 35, 398 – A ring), 314.2580 ($C_{22}H_{34}O$, 26), 285.2209 ($C_{20}H_{29}O$, 100), 253.1961 ($C_{19}H_{25}$, 99).

(24*R*,28*S*)-24-Ethyl-24,28-methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (27). Dehalogenation of the dichloro i-methyl ether **25** to **27** was accomplished as described above (**10** → **13**): mass spectrum *m/z* (relative intensity) 440 (M^+, 10), 425 (31, M − CH_3), 408 (17, M − CH_3OH), 385 (47, M − A ring), 313 (9), 285 (9), 281 (7), 255 (17), 253 (30), 55 (100).

(24*S*,28*R*)-24-Ethyl-24,28-methylene-6β-methoxy-3α,5-cyclo-5α-cholestane (28). Repetition of the dehalogenation reaction on **26** yielded **28**: mass spectrum, *m/z* (relative intensity) 440 (M^+, 29), 425 (46, M − CH_3), 408 (37, M − CH_3OH), 385 (83, M − A ring), 313 (13), 285 (13), 281 (9), 255 (18), 253 (32), 55 (100).

(24*R*,28*S*)-24-Ethyl-24,28-methylenecholest-5-en-3β-ol (7). The i-methyl ether protecting group in **27** was removed in the usual way to give **7**: mp 136–138 °C ($MeOH/H_2O$); $[\alpha]^{20}_{589}$ −38.0°, $[\alpha]^{20}_{546}$ −45.8° (*c* 15.9 mg/mL, $CHCl_3$); ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.034 (d, *J* = 6.29 Hz, 3 H, C-29), 1.007 (s, 3 H, C-19), 0.919 (d, *J* = 6.46 Hz, 3 H, C-21), 0.834 (d, *J* = 6.89 Hz, 3 H) and 0.806 (d, *J* = 6.89 Hz, 3 H) C-26 and C-27, 0.674 (s, 3 H, C-18), 0.60 (m, 1 H, C-28), 0.39 (dd, *J* = 4.5 and 8.8 Hz, 1 H, C-30), −0.23 (dd, *J* = 4.5 and 5.4 Hz, 1 H, C-30); ^{13}C NMR δ 37.16 (C-1), 31.55 (C-2), 71.68 (C-3), 42.20 (C-4), 140.65 (C-5), 121.57 (C-6), 31.81 (C-7), 31.81 (C-8), 50.04 (C-9), 36.39 (C-10), 20.98 (C-11), 39.65 (C-12), 42.20 (C-13), 56.67 (C-14), 24.20 (C-15), 28.16 (C-16), 55.92 (C-17), 11.73 (C-18), 19.28 (C-19), 36.51 (C-20), 18.77 (C-21), 33.96 (C-22), 25.60 (C-23), 27.85 (C-24), 33.83 (C-25), 19.43 (C-26), 19.49 (C-27), 14.28 (C-28), 15.73 (C-29), 17.45 (C-30); high-resolution mass spectrum, HRMS *m/z* (relative intensity) 426.3885 (M^+, 60, calcd for $C_{30}H_{50}O$ 426.3862), 411. 3632 ($C_{29}H_{47}O$, 11, M − CH_3), 408.3740 ($C_{30}H_{48}$, 24, M − H_2O), 393.3506 ($C_{29}H_{45}$, 17, M − CH_3 − H_2O), 384.3391 ($C_{27}H_{44}O$, 5, M − C_3H_6!), 365.3185 ($C_{27}H_{41}$, 11), 341.3184 ($C_{25}H_{41}$, 8), 314.2646 ($C_{22}H_{34}O$, 48), 299.2399 ($C_{21}H_{31}O$, 36), 281.2277 ($C_{21}H_{29}$, 14), 271.2061 $C_{19}H_{27}O$, 47), 255.2122 ($C_{19}H_{27}$, 18), 213.1628 ($C_{16}H_{21}$, 31), 69.0703 (C_5H_9, 100).

(24*S*,28*R*)-24-Ethyl-24,28-methylenecholest-5-en-3β-ol (8). The 3β-hydroxy-Δ^5 system was regenerated from **28**, in the usual manner to give the crystalline sterol **8**: mp 126–128 °C ($MeOH/H_2O$); $[\alpha]^{20}_{589}$ −34.8°, $[\alpha]^{20}_{546}$ −40.8° (*c* 5.0 mg/mL, $CHCl_3$); ^1H NMR (360 MHz) δ 5.36 (m, 1 H, C-6), 3.53 (m, 1 α H, C-3), 1.043 (d, *J* = 6.22 Hz, 3 H, C-29), 1.007 (s, 3 H, C-19), 0.915 (d, *J* = 6.46 Hz, 3 H, C-21), 0.833 (d, *J* = 6.89 Hz, 3 H) and 0.826 (d, *J* = 6.89 Hz, 3 H) C-26 and C-27, 0.673 (s, 3 H, C-18), 0.61 (m, 1 H, C-28), 0.36 (dd, *J* = 4.5, 8.8 Hz, 1 H, C-30), −0.24 (dd, *J* = 4.5, 5.4 Hz, 1 H, C-30); ^{13}C NMR δ 37.16 (C-1), 31.53 (C-2), 71.67 (C-3), 42.18 (C-4), 140.64 (C-5), 121.56 (C-6), 31.85 (C-7), 31.85 (C-8), 50.04 (C-9), 36.40 (C-10), 20.98 (C-11), 39.66 (C-12), 42.18 (C-13), 56.67 (C-14), 24.20 (C-15), 28.16 (C-16), 55.74 (C-17), 11.72 (C-18), 19.28 (C-19), 36.60 (C-20), 18.70 (C-21), 34.19 (C-22), 25.48 (C-23), 28.01 (C-24), 34.33 (C-25), 19.28 (C-26), 19.68 (C-27), 14.35 (C-28), 16.07 (C-29), 17.82 (C-30); high-resolution mass spectrum, *m/z* (relative intensity) 426.3842 (M^+, 63, calcd for $C_{30}H_{50}O$ 426.3862), 411.3667 ($C_{29}H_{47}O$, 12, M − CH_3), 408.3785 ($C_{30}H_{48}$, 26, M − H_2O), 393.3543 ($C_{29}H_{45}$, 17, M − CH_3 − H_2O), 384.3358 ($C_{27}H_{44}O$, 4, M − C_3H_6!), 365.3220 ($C_{27}H_{41}$, 8), 341.3195 ($C_{25}H_{41}$, 9), 314.2592 ($C_{22}H_{34}O$, 42), 299.2380 ($C_{21}H_{31}O$, 33), 271.2053 ($C_{19}H_{27}O$, 43), 255.2110 ($C_{19}H_{27}$, 16), 213.1667 ($C_{16}H_{21}$, 22), 69.0703 (C_5H_9, 100).

Acknowledgment. Financial support by the National Institutes of Health (Grants No. GM-06840 and AM-04257) is gratefully acknowledged. In addition we are grateful for the use of the NMR/MS center at the Stanford 360-MHz facility (NSF Grant No. GP-23633 and NIH Grant No. RR-0711). We are especially indebted to Dr. James N. Shoolery of Varian Associates for running ^{13}C NMR spectra and for helpful discussions. We thank Dr. Lois J. Durham for the ^1H NMR spectra and Ms. A. Wegmann for mass spectral determinations. We are also indebted to Dr. W. C. M. C. Kokke for assistance in the HPLC separations, to Dr. Gunter Barth for helpful discussions, and to Dr. Jaroslav Kramar for preliminary chemical experiments. We thank Dr. H. Jones (Merck Sharp & Dohme) for a gift of the crude giant kelp extract and the Upjohn Co. for a generous supply of stigmasterol. R.W.L. thanks the Swiss National Science Foundation for a postdoctoral fellowship.

Registry No. **1**, 80227-02-7; **2**, 80227-03-8; **3**, 75871-95-3; **4**, 75917-89-4; **5**, 80186-22-7; **6**, 80227-04-9; **7**, 80186-23-8; **8**, 80227-05-0; (22*Z*)-**9**, 25819-78-7; (22*E*)-**9**, 25819-80-1; **10**, 80186-24-9; **11**, 80227-06-1; **12**, 80227-07-2; **13**, 80186-25-0; **14**, 80227-08-3; **15**, 80227-09-4; **16**, 63015-93-0; **17**, 80186-26-1; **18**, 2867-93-8; **19**, 80227-10-7; **20**, 80186-27-2; **21**, 80227-11-8; **22**, 80186-28-3; **23**, 80227-12-9; **24**, 68844-30-4; **25**, 80186-29-4; **26**, 80227-13-0; **27**, 80186-30-7; **28**, 80227-14-1; (20*S*)-6β-methoxy-3α,5-cyclo-5α-pregnane-20-carboxaldehyde, 25819-77-6; 3-methylbut-1-yne, 598-23-2; 6β-methoxy-(20*S*)-methyl-3α,5-cyclo-5α-pregnan-21-ol *p*-toluenesulfonate, 51231-24-4; fucosterol, 17605-67-3.