(br s, 1 H, NH). The crude mixture of carbamates was dissolved in an 80% solution of acetic acid in water (2 mL) and the reaction mixture stirred at 80 °C for 0.5 h. The volatiles were removed in vacuo, and the residue was subjected to flash chromatography. The major product was the cyclic carbonate **15** (18 mg, 16% from **13a**): colorless gum; TLC R_f 0.27 (H); IR (neat) 3430, 1790, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.13 (d, 3 H, J = 6.3 Hz, CH_3-6), 1.23 (s, 3 H, CH_3-8), 1.91 (m, 1 H, H-6), 2.70 (m, 1 H, OH), 3.42 (s, 3 H, OCH_3), 3.64 (dd, 1 H, $J_{1,2}$ = 4.2, $J_{2,3}$ = 9.0 Hz, H-2), 3.70 (m, 3 H, H-5, CH_2-9), 4.08 (t, 1 H, J = 9.0 Hz, H-3), 4.69 (AB q, 2 H, J = 10.8 Hz, $\Delta\delta$ = 0.07 ppm, PhCH_2), 4.71 (d, 1 H, J = 4.2 Hz, H-1), 4.72 (AB q, 2 H, J = 12.1 Hz, $\Delta\delta$ = 0.07 ppm, PhCH_2), 5.02 (s, 1 H, H-7), 5.14 (t, 1 H, J = 9.0 Hz, H-4), 7.20–7.94 (m, 15 H, PhCH$_2$ × 2, PhCO$_2$). The material was treated with a solution of sodium methoxide (0.10 mL of a 1.5 M solution, 0.15 mmol) in dry methanol. After it was stirred at room temperature for 4 h, the reaction mixture was neutralized with 2 N hydrochloric acid in methanol and the solvent evaporated in vacuo. The residue was triturated with ethyl acetate, filtered, and concentrated in vacuo, and the product **6c** (11 mg, 78%) was acetylated (see the General Procedures). The triacetate **6d** had the following physical characteristics: TLC R_f 0.12 (C); IR (neat) 3450, 1720, (br) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (d, 3 H, J = 7.0 Hz, CH_3-6), 1.11 (s, 3 H, CH_3-8), 1.84, 1.89, and 2.06 (all s, 3 H each, CH_3CO_2 × 3), 2.08 (s, 1 H, OH), 3.29 (s, 3 H, OCH_3), 3.49 (m, 2 H, H-2, H-5), 3.80 (t, 1 H, J = 9.9 Hz, H-3), 3.86 (br s, 2 H, CH_2-9), 4.26 (d, 1 H, J = 3.3 Hz, H-1), 4.65 (AB q, 2 H, J = 11.7 Hz, $\Delta\delta$ = 0.16 ppm, PhCH_2), 4.70 (AB q, 2 H, J = 11.7 Hz, $\Delta\delta$ = 0.23 ppm, PhCH_2), 5.16 (dd, 1 H, $J_{3,4}$ = 9.9, $J_{4,5}$ = 10.8 Hz, H-4), 5.26 (br s, 1 H, H-7), 7.27 (m, 10 H, PhCH$_2$ × 2). Anal. Calcd for $C_{32}H_{42}O_{11}$: C, 63.77; H, 7.03. Found: C, 63.64; H, 7.21.

For **16** (5 mg, 5.0% from **13a**): colorless gum; TLC R_f 0.23 (H); IR (neat) 3400, 1705 (br), 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.13 (d, 3 H, J = 7.2 Hz, CH_3-6), 1.30 (s, 3 H, CH_3-8), 2.26 (m, 1 H, OH) 2.42 (m, 1 H, H-6), 3.47 (d AB q, 2 H, $J_{9,OH}$ = 6.0, J_{gem} = 10.8 Hz, $\Delta\delta$ = 0.07 ppm, CH_2-9), 3.91 (dd, 1 H, $J_{4,5}$ = 3.9, $J_{5,6}$ = 9.3 Hz, H-5), 4.85 (d, 1 H, J = 7.2 Hz, H-7), 5.23 (AB q, 2 H, J = 10.8 Hz, $\Delta\delta$ = 0.14 ppm, PhCH_2), 6.02 (d, 1 H, J = 7.8 Hz, H-3), 6.16 (dd, 1 H, $J_{3,4}$ = 10.8, $J_{4,5}$ = 3.9 Hz, H-4), 6.91 (br s, 1 H, NH), 7.24–8.07 (m, 15 H, PhCH$_2$, PhCO$_2$, PhNH), 9.35 (s, 1 H, CHO).

Methyl 4-*O*-Acetyl-2,3,7-tri-*O*-benzyl-6-deoxy-6,8-di-*C*-methyl-L-*arabino*-α-D-*gluco*-nono-1,5-pyranoside (7a). *N*-Methylmorpholine *N*-oxide (0.02 mL, 60 wt % in water, 0.10 mmol) and osmium tetraoxide (0.6 mL, 2.5 wt % in *tert*-butyl alcohol, 0.006 mmol) were added to a solution of **9c** (31 mg, 0.054 mmol) in acetone (2 mL). The reaction mixture was stirred for 12 h at room temperature. Sodium bisulfite (0.02 mL of N solution) was added, and the mixture was stirred for an additional 0.5 h. Most of the solvent was evaporated in vacuo, and the residue was diluted with water (2 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography gave the diol **7a** (28 mg, 85%) as a clear gum: TLC R_f 0.25 (D); $[\alpha]^{25}_D$ +4.2 (*c* 0.51, $CHCl_3$); IR (neat) 3500, 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 1.0 (s, 3 H, CH_3-8), 1.07 (d, 3 H, J = 7.5 Hz, CH_3-6), 1.65 (t, 1 H, J = 6.2 Hz, 9-OH), 1.85 (s, 3 H, CH_3CO_2), 2.41 (m, 1 H, H-6), 2.31 (s, 1 H, 8-OH), 3.19 (dd, 1 H, $J_{9a,OH}$ = 6.2, J_{gem} = 10.5 Hz, H-9a), 3.36 (s, 3 H, OCH_3), 3.55 (m, 3 H, H-2, H-7, H-9b), 3.63 (dd, 1 H, $J_{4,5}$ = 9.6, $J_{5,6}$ = 2.0 Hz, H-5), 3.84 (t, 1 H, J = 10.0 Hz, H-3), 4.49 (AB q, 2 H, J = 12.0 Hz, $\Delta\delta$ = 0.20 ppm, PhCH_2), 4.53 (d, 1 H, J = 3.3 Hz, H-1), 4.66 (AB q, 2 H, J = 10.0 Hz, $\Delta\delta$ = 0.14 ppm, PhCH_2), 4.73 (AB q, 2 H, J = 11.0 Hz, $\Delta\delta$ = 0.20 ppm, PhCH_2), 4.92 (t, 1 H, J = 10.0 Hz, H-4), 7.42 (m, 15 H, PhCH$_2$ × 3). Anal. Calcd for $C_{35}H_{44}O_9$: C, 69.06; H, 7.29. Found: C, 69.03; H, 7.37.

Methyl 2,3-Di-*O*-benzyl-6-deoxy-6,8-di-*C*-methyl-L-*arabino*-α-D-*gluco*-nono-1,5-pyranoside (7d). Allylic alcohol **9b** (72 mg, 0.13 mmol) was treated under similar hydroxylation conditions to those described for the preparation of **7a**. The reaction was completed within 2 h and afforded triol **7c** (65 mg, 85%). Triol **7d** (65 mg, 0.11 mmol) was debenzoylated by using sodium methoxide according to the procedure described for the preparation of **6a**, and the resulting tetrol **7d** was acetylated (see the General Procedures). The triacetate **7e** had the following physical properties: TLC R_f 0.14 (C); IR (neat) 3500, 1635 (br) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, 3 H, J = 6.6 Hz, CH_3-6), 1.08 (s, 3 H, CH_3-8), 1.85, 1.87, and 2.08 (all s, 3 H each, CH_3CO_2 × 3), 2.19 (m, 1 H, H-6), 2.51 (s, 1 H, OH), 3.30 (s, 3 H, OCH_3), 3.52 (dd, 1 H, $J_{1,2}$ = 3.3, $J_{2,3}$ = 9.8 Hz, H-2), 3.55 (dd, 1 H, $J_{4,5}$ = 9.8, $J_{5,6}$ = 3.3 Hz, H-5), 3.80 (AB q, 2 H, J = 11.1 Hz, $\Delta\delta$ = 0.24 ppm, CH_2-9), 3.81 (t, 1 H, J = 9.8 Hz, H-3), 4.34 (d, 1 H, J = 3.3 Hz, H-1), 4.64 (AB q, 2 H, J = 12.0 Hz, $\Delta\delta$ = 0.13 ppm, PhCH_2), 4.67 (AB q, 2 H, J = 12.0 Hz, $\Delta\delta$ = 0.23 ppm, PhCH_2), 5.13 (t, 1 H, J = 9.8 Hz, H-4), 5.29 (br s, 1 H, H-7), 7.24 (m, 10 H, PhCH$_2$ × 2). Anal. Calcd for $C_{32}H_{42}O_{11}$: C, 63.77; H, 7.03. Found: C, 63.69; H, 7.29.

Registry No. **1a**, 110045-79-9; **1b**, 110045-80-2; **2a**, 110045-81-3; **2b**, 110045-90-4; **3a**, 110045-82-4; **4a**, 110045-83-5; **4b**, 110045-85-7; **4c**, 110045-86-8; **5**, 110045-84-6; **6a**, 110045-87-9; **6b**, 110045-88-0; **6c**, 110046-03-2; **6d**, 110046-04-3; **7a**, 110046-06-5; **7b**, 110045-89-1; **7c**, 110046-07-6; **7d**, 110046-08-7; **7e**, 110046-09-8; **8a**, 110045-91-5; **8b**, 110045-92-6; **9a**, 110045-93-7; **9b**, 110045-94-8; **9c**, 110045-95-9; **10** (isomer 1), 110045-96-0; **10** (isomer 2), 110045-97-1; **12** (isomer 1), 110045-98-2; **12** (isomer 2), 110046-10-1; **13a**, 110045-99-3; **13b**, 110046-00-9; **13c**, 110046-01-0; **15**, 110046-02-1; **16**, 110046-05-4; vinylmagnesium bromide, 1826-67-1.

Minor and Trace Sterols from Marine Invertebrates. 58.[1] Stereostructure and Synthesis of New Sponge Sterols Jaspisterol and Isojaspisterol

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Two new trace sterols, jaspisterol and isojaspisterol, were isolated from the Australian sponge *Jaspis stellifera*. The structures, geometry, and stereochemistry were determined by synthesis and spectroscopic methods. Jaspisterol (**26**) and isojaspisterol (**25**) correspond to further variations of the aplysterol side chain.

While studying the biosynthesis of marine sterols in the Australian sponge *Jaspis stellifera*, we encountered a new trace sterol fraction, which was highly radioactive when carbon-14-labeled epicodisterol (**1**) was fed to the sponge.[2] In order to interpret our incorporation results, the composition of this fraction had to be determined. We now

(1) For preceding paper, see: Cho, J.-H.; Djerassi, C. *J. Chem. Soc. Perkin Trans. 1* **1987**, 1307–1318.

(2) Cho, J.-H.; Thompson, J. E.; Stoilov, I. L.; Silva, C.; Djerassi, C., manuscript in preparation. 25% of the radioactivity accumulated in the jaspisterol fraction when carbon-14-labeled epicodisterol (**1**) was fed to the sponge, whereas no radioactivity was encountered when radiolabeled codisterol (**2**) was fed.

0022-3263/87/1952-4517$01.50/0

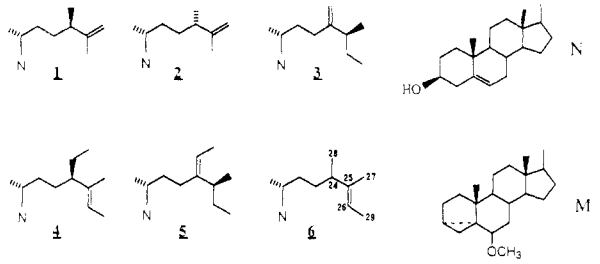
Table I. Selected 300-MHz ^{1}H NMR Data ($CDCl_3$) for Jaspisterol (26), Isojaspisterol (25), and Their Stereoisomers (23, 24)[a]

compd	C-18	C-19	C-21	C-24	C-26	C-27	C-28	C-29
23	0.668	1.004	0.913 (d, 6.3)	2.550	5.173	1.544	0.931 (d, 6.8)	1.554[b]
24	0.667	1.005	0.904 (d, 6.3)	2.000	5.186	1.500	0.943 (d, 6.8)	1.560 (d, 6.6)
25	0.667	1.003	0.904 (d, 6.5)	2.550	5.180	1.543	0.938 (d, 6.8)	1.562[b]
25[d]	0.667	1.005	0.906 (d, 6.5)	2.550	5.180	1.545	0.938 (d, 6.9)	c
26	0.667	1.005	0.898 (d, 6.6)	2.000	5.186	1.486	0.949 (d, 6.5)	1.558 (d, 7.1)
26[d]	0.667	1.006	0.899 (d, 6.2)	2.000	5.188	1.487	0.949 (d, 7.0)	c

[a] Chemical shifts are given in parts per million; J values (in parentheses) are in hertz. [b] The J value could not be determined because of overlap with the water peak. [c] Chemical shifts could not be determined because of overlap with the water peak. In C_6D_6, the doublet (J = 6.9 Hz) occurred at 1.588 ppm. [d] Natural sterol.

report the isolation, structure elucidation, and stereochemical assignment of two new trace sterols, which we have named jaspisterol and isojaspisterol.

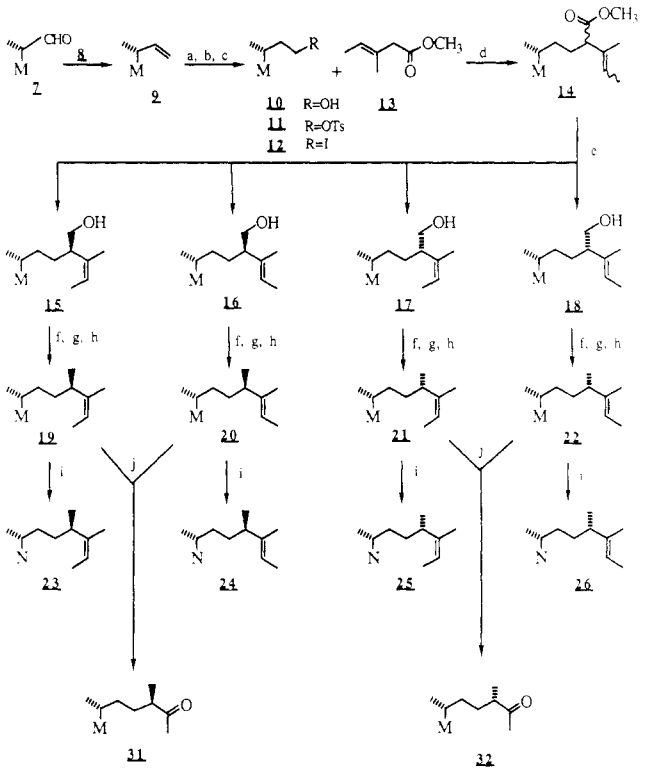
Fractionation of the sterol mixture of *J. stellifera* by reverse-phase HPLC afforded 1% of inseparable jaspisterol and isojaspisterol along with known sterols such as 24-(28)-dehydroaplysterol (**3**), stelliferasterol (**4**), and isostelliferasterol (**5**), which had been described previously.[3]



The high-resolution mass spectrum of jaspisterol and isojaspisterol showed a molecular ion corresponding to $C_{29}H_{48}O$ and a fragmentation pattern typical of the cholesterol nucleus.[4] The diagnostic fragmentation peaks at m/z 328.2782 ($C_{23}H_{36}O$) and 314.2605 ($C_{22}H_{34}O$) suggested the presence of unsaturation around C-25 in the side chain.[5] The 300-MHz ^{1}H NMR spectra of jaspisterol and isojaspisterol (Table I) displayed two doublets in the 0.90 and 0.94 ppm regions due to the secondary methyl groups (C-21, C-28) and two singlets for the C-18 (0.667 ppm) and C-19 (1.005 ppm) methyl substituents, respectively. If the above mass spectroscopic evidence for a $\Delta^{25(26)}$ double bond is accepted, then one vinyl methyl signal (1.487 ppm) can be assigned to C-27 and another vinyl methyl signal, which overlaps with the water peak, to C-29.[6] These data, along with basic biosynthetic considerations,[2] led to the formulation of jaspisterol and isojaspisterol as 24,26-dimethylcholesta-5,25(26)-dien-3β-ol (**6**) without a stereochemical assignment. Since no such side chain had been encountered previously, we embarked on an unambiguous synthesis (Scheme I) to confirm its structure and stereochemistry.

The starting material, 3α,5-cyclo-6β-methoxy-23-iodonorcholane (**12**), is a known compound;[3,7] however, it is now synthesized by a more efficient route. The known[8] aldehyde **7** was condensed with methylidenetriphenylphosphorane (**8**) to yield the olefin **9**, which was subjected to hydroboration to provide **10**, tosylation to provide **11**, and iodide formation to provide the 23-iodide **12** in good yield. The anion of methyl *trans*-3-methyl-3-pentenoate (**13**)[9] was treated with 3α,5-cyclo-6β-methoxy-23-iodonorcholane (**12**) to afford in 98% yield the α-alkylated product **14** as a mixture of four isomers. Subsequent reduction of this ester with lithium aluminum hydride produced the alcohol as an isomeric mixture, whose four components (**15**–**18**) were readily separated by normal-phase silica gel HPLC. Each alcohol was converted into the desired free sterol (**23**–**26**) by tosylation, iodide formation, sodium borohydride reduction, and, finally, deprotection of the individual i-methyl ethers (**19**–**22**). The ^{1}H NMR spectral data of the four jaspisterol isomers, two of which were identified with natural jaspisterol and iso-

Scheme I[a]



[a] (a) B_2H_6, 80%; (b) TsCl/Py; (c) NaI/acetone, reflux, overall (b), (c) 72%; (d) LDA, THF/10% HMPA, −70 °C → room temperature, 98%; (e) $LiAlH_4$, 94%; (f) TsCl/Py; (g) NaI/acetone, reflux; (h) $NaBH_4$; (i) p-TsOH, (f), (g), (h), (i) 62%; (j) O_3, −70 °C, 85%.

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(6) The 300-MHz ^{1}H NMR spectrum of natural jaspisterol and isojaspisterol in C_6D_6 indicates two kinds of vinyl methyl signals. One (C-27) is a singlet (1.526 ppm), in Table I, **25** and **26** show this singlet at two different positions (1.545 and 1.486 ppm) in $CDCl_3$, and the other (C-29) a doublet (1.588 ppm, J = 6.9 Hz).

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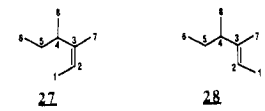
Table II. Selected ^{13}C NMR (400 MHz) Chemical Shifts of 23–26 in $CDCl_3$

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
27(Z)[a]	12.8	119.4	139.6	35.9	28.2	12.3	17.9	18.9
28(E)[a]	13.2	118.2	139.9	45.4	28.5	12.3	12.1	19.7
compd	C-29	C-26	C-25	C-24	C-23	C-22	C-27	C-28
23	12.97	118.33	140.07	36.00	31.20	33.94	18.14	19.10
24	13.31	117.10	140.31	43.21	31.38	33.99	12.27	19.71
25	13.04	118.56	139.70	35.74	31.12	33.71	18.02	18.83
26	13.29	117.53	139.72	43.20	31.15	33.93	11.99	20.25

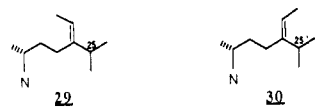
[a] These chemical shifts were obtained from ref 10.

jaspisterol, are summarized in Table I.

The geometry of the $\Delta^{25(26)}$ double bond in jaspisterol (**26**), isojaspisterol (**25**), and their C-24 epimers (**23,24**) was determined by comparing their ^{13}C NMR spectra (Table II) with those of (*Z*)- and (*E*)-3,4-dimethyl-2-hexene (**27,28**).[10] Compounds **27** and **28** are reasonable models



27 **28**



29 **30**

for the jaspisterol isomers **23–26** because their side chains starting with C-24 (see **6**) have the same environment as those of the reference olefins **27** and **28**. The chemical shift of C-4 in the *Z*-olefin **27** appears at higher field (35.9 ppm) than that (45.4 ppm) of the *E*-isomer **28**. The same observation was made in comparing the chemical shift (35.8 ppm) of C-24 in isomers **23** and **25** with that (43.2 ppm) in **24** and **26**. Furthermore, the chemical shift of C-7 in the *Z*-olefin **27** appears at lower field (17.9 ppm) than that (12.1 ppm) of the *E*-isomer **28**. Again, the same observation was made in comparing the chemical shift (18.1 ppm) of C-27 in **23** and **25** with that (12.1 ppm) in **24** and **26**. On the basis of these ^{13}C NMR spectral data, the jaspisterol isomers **23** and **25** must have the *Z* stereochemistry whereas isomers **24** and **26** belong to the *E* series.

These assignments of the 25–26 double bond geometry in jaspisterol (**26**), isojaspisterol (**25**), and their C-24 epimers (**23,24**) were further confirmed by comparing the ^1H NMR spectral data of the methine allylic proton (C-24) with that (C-25) of fucosterol (**29**) and isofucosterol (**30**). The chemical shift of the isopropyl methine proton (C-25) in isofucosterol (**30**)[11] is at a lower field (2.8 ppm) than that (2.2 ppm) of fucosterol (**29**).[12] Since the chemical shift of the C-24 proton in **23** and **25** occurs at 2.55 ppm whereas it is found at 2.00 ppm in **24** and **26**, the C24–C25 bond in isomers **23** and **25** should be cis oriented to the C26–C29 bond, thereby implying the *Z* configuration for the $\Delta^{25(26)}$ double bond in **23** and **25** and the *E* configuration in **24** and **26**.

In order to assign the absolute stereochemistry of the 24-methyl group in the jaspisterol isomers **23–26**, chemical degradation to a compound of known stereochemistry was performed. Ozonolysis of the i-methyl ethers **19** and **20** yielded the known (24*R*)-3α,5-cyclo-6β-methoxy-24-methyl-27-norcholestan-25-one (**31**),[13] thereby requiring the 24*R* configuration for the sterols **23** and **24**, while (24*S*)-3α,5-cyclo-6β-methoxy-24-methyl-27-norcholestan-25-one (**32**)[13] was obtained from the i-methyl ethers **21** and **22**, thus leading to the 24*S* configuration for **25** and **26**. Finally, the mixture of natural jaspisterol (**26**) and isojaspisterol (**25**) was converted into i-methyl ethers via a known method. Ozonolysis of this mixture afforded exclusively the 24*S* ketone (**32**), thus proving that natural jaspisterol (**26**) has the same C-24 stereochemistry as natural isojaspisterol (**25**).

The "24*S*" stereochemistry of natural jaspisterol (**26**) and isojaspisterol (**25**) is surprising because, on the basis of our incorporation experiments, it appeared that epicodisterol (**1**) was their biosynthetic precursor.[2] If so, jaspisterol (**26**) and isojaspisterol (**25**) ought to have the "24*R*" stereochemistry like epicodisterol (**1**). The most likely explanation is that the actual radioactivity is associated with still another unknown trace sterol, which accidently has the same retention time as jaspisterol (**26**) and isojaspisterol (**25**). A more remote possibility is that we are dealing with an unusual inversion of the C-24 stereochemistry during one of the biosynthetic steps. Further incorporation studies are under way to explore this possibility, but these have no bearing on the validity of the presently reported structural and stereochemical assignments, which are unequivocal.

Experimental Section

General Methods. High-performance liquid chromatography (HPLC) was carried out on a Waters Associates HPLC system (M 6000 pump, UK6 injector, R403 differential refractometer). For reverse-phase HPLC, two Altex Ultrasphere ODS 5-μm columns (25 cm × 10 mm i.d.) in series with 15 mmol of silver nitrate in methanol or methanol as the mobile phase were used for the fractionation of the sterol mixture and for purification of synthetic sterol intermediates. The flow rate was 3 mL/min. Cholesterol was used as the standard for relative retention time (RRT) in HPLC and in GC. Normal-phase HPLC was performed on a silica gel column (Beckman Ultrasil-Si, 25 cm × 10 mm i.d.) with 7% ethyl acetate in hexanes as the mobile phase. Analytical gas–liquid chromatography was performed on a Hewlett-Packard 402A gas chromatograph instrument with a flame-ionization detector and a U-shaped glass column (1.8 m × 2 mm i.d.) packed with 3% OV-17 on Gas-Chrom Q. The oven temperature was 260 °C with helium as the carrier gas. Fourier transform ^1H NMR spectra were recorded on a Nicolet Magnetic Corp. NMC-300 spectrometer equipped with a 1280 data system. Fourier ^{13}C NMR spectra were recorded on a Varian XL-400 spectrometer. All NMR spectra were referenced to either $CHCl_3$ (7.259 ppm) or C_6H_6 (7.150 ppm). Low-resolution mass spectra were recorded on a Hewlett-Packard 5970 series mass spectrometer system with a 5890A GC for sample introduction and a Hewlett-Packard 9133 system for data acqusion. High-resolution mass spectra were recorded on an MS-50 instrument by a direct probe inlet system at the University of California at Berkeley. Melting points were determined on a Koffler hot-stage apparatus and are uncorrected.

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Specific rotations were recorded in chloroform at 20 °C on a Rudolph Research Autopol III automatic polarimeter equipped with a thermostated 1.00 dm microcell. Commercial reagents and solvents were analytical grade or were purified by standard procedures[14] prior to use.

Isolation of Jaspisterol (26) and Isojaspisterol (25). The chloroform/methanol (1:1) extract of *J. stellifera* was fractionated on an open silica gel column (eluent, hexanes/ether, 6:1). The sterol fractions (R_f cholesterol by TLC) were combined and subjected to reverse-phase HPLC to give, along with previously described sterols,[3] an inseparable[15] mixture (1%) of jaspisterol (**26**) and isojaspisterol (**25**) in a ratio of 2:1 as determined by ^{1}H NMR (see Table I): HPLC RRT (0.96) (Altex Ultrasphere ODS-5, methanol); high-resolution mass spectrum, m/z (relative intensity) 412.3711 (M^+, 98; calcd for $C_{29}H_{48}O$ 412.3705), 397.3472 ($C_{28}H_{45}O$, 23), 379.3375 ($C_{28}H_{43}$, 28), 328.2792 ($C_{23}H_{36}O$, 30), 314.2605 ($C_{22}H_{34}O$, 49), 299.2377 ($C_{21}H_{31}O$, 85), 271.2047 ($C_{19}H_{27}O$, 55), 255.2116 ($C_{19}H_{27}$, 24), 213.1633 ($C_{16}H_{21}$, 41), 83.0854 (C_6H_{11}, 100). Since jaspisterol (**26**) and isojaspisterol (**25**) could not be separated by HPLC, the other relevant physical data were secured with synthetic material.

20(*R*)-3α,5-Cyclo-6β-methoxy-22-cholene (9). To a stirred suspension of methyltriphenylphosphonium iodide (1.22 g, 3.0 mmol) in dry ether (10 mL) at 0 °C was added *n*-butyllithium (1.6 M) dropwise until a clear solution was obtained. To this ylide solution was then added the 22-aldehyde **7** (975 mg, 2.8 mmol) in ether (5 mL), and the reaction mixture was stirred for 2 h at room temperature. The reaction was quenched with water, ether was added, and the organic layer was separated and evaporated. The residue was chromatographed on silica gel (eluent, hexanes/ether, 20:1) to provide the olefin **9** (901 mg, 93%): ^{1}H NMR (300 MHz) δ 5.67 (1 H, m, C-22), 4.85 (2 H, m, C-23), 3.321 (3 H, s, OCH_3), 1.031 (3 H, d, J = 5.3 Hz, C-21), 1.022 (3 H, s, C-19), 0.740 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity), 342.25 (M^+, 28), 327.25 (71), 310.25 (50), 287.20 (100), 284.20 (13), 255.20 (18).

20(*R*)-3α,5-Cyclo-6β-methoxy-22-(hydroxymethyl)cholane (10). To the olefin **9** (900 mg, 2.63 mmol) in dry tetrahydrofuran (5 mL) at 0 °C under argon was added 4 mL of 1 M borane in THF. After 2 h, 5 mL of 6 N NaOH solution was added, followed by 70 mL of 30% H_2O_2. The organic layer was separated and evaporated. Silica gel column chromatography of the organic residue gave the 23-alcohol **10** (758 mg, 80%): ^{1}H NMR (300 MHz) δ 3.323 (3 H, s, OCH_3), 1.023 (3 H, s, C-19), 0.955 (3 H, d, J = 6.5 Hz, C-21), 0.733 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 360.25 (M^+, 27), 345.25 (82), 328.25 (50), 305.25 (100), 302.20 (18), 255.20 (14), 213.20 (11).

20(*R*)-3α,5-Cyclo-6β-methoxy-22-(iodomethyl)cholane (12). The 23-alcohol **10** (755 mg, 2.10 mmol) was dissolved in dry pyridine (3 mL), and *p*-toluenesulfonyl chloride (600 mg) was added. After 24 h at room temperature, the reaction mixture was diluted with ether, washed with saturated potassium bicarbonate, and purified by chromatography on a short silica gel column (eluent, hexanes/ether, 7:1). The tosylate **11** (883 mg) was dissolved in acetone, and sodium iodide (600 mg) was added, followed by heating under reflux for 17 h. The reaction mixture was concentrated; silica gel column chromatography of the residue afforded the 23-iodide **12** (710 mg, 72% from **10**): ^{1}H NMR (300 MHz) δ 3.323 (3 H, s, OCH_3), 1.022 (3 H, s, C-19), 0.926 (3 H, d, J = 6.2 Hz, C-21), 0.735 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 470.30 (M^+, 30), 455.30 (58), 438.30 (61), 423.15 (12), 415.15 (100), 412.25 (18).

(24ζ,25(26)*E*,*Z*)-3α,5-Cyclo-6β-methoxy-24-carbomethoxy-26-methylcholest-25(26)-ene (14). Methyl *trans*-3-methyl-3-pentenoate[9] (166 μL, 1.23 mmol) was added to 1.23 mmol of lithium diisopropylamide in dry tetrahydrofuran (8 mL) and hexamethylphosphoramide (1 mL), and the solution was stirred for 30 min at −70 °C, followed by the addition via a syringe of 3α,5-cyclo-6β-methoxy-23-iodonorcholane (**12**; 383 mg, 0.82 mmol) in dry tetrahydrofuran (2 mL). The reaction mixture was allowed to warm slowly to room temperature while stirring and then stirred for an additional 5 h. The reaction was quenched with 0.5 mL of water and concentrated in vacuo to give the α-alkylation product **14**, which was purified by silica gel column chromatography (eluent, hexanes/ether, 10:1): yield 375 mg (98%); ^{1}H NMR (300 MHz) δ 3.656 (3 H, s, CO_2CH_3), 3.319 (3 H, s, OCH_3), 1.623 (3 H, d, J = 6.5 Hz, C-30), 1.594 (3 H, s, C-27), 1.015 (3 H, s, C-19), 0.922, 0.915 (3 H, d, J = 6.5 Hz, C-21), 0.700 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 470.50 (M^+, 33), 455.50 (46), 438.40 (45), 415.40 (84), 253.10 (17), 55.05 (100).

Reduction of 14. Lithium aluminum hydride (70 mg, 1.6 mmol) was added to the α-alkylation product **14** (375 mg, 0.80 mmol) in dry ether (10 mL). The reaction mixture was stirred at room temperature for 30 min, and the excess lithium aluminum hydride was destroyed by addition of ethyl acetate and water. Filtration and evaporation of the solvent in vacuo gave the crude product that was fractionated by HPLC over silica gel (eluent, hexanes/ethyl acetate, 93:7) to provide four components (**15**–**18**) described below in the order of elution; total yield (94%, **15**:**16**:**17**:**18** = 2:2:1:1).

Fraction 1. (24*S*,25(26)*Z*)-3α,5-Cyclo-6β-methoxy-24-(hydroxymethyl)-26-methylcholest-25(26)-ene (15): ^{1}H NMR (300 MHz) δ 3.321 (3 H, s, OCH_3), 1.616 (3 H, d, J = 6.5 Hz, C-29), 1.579 (3 H, s, C-27), 1.016 (3 H, s, C-19), 0.911 (3 H, d, J = 6.5 Hz, C-21), 0.701 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 442.40 (M^+, 39), 427.40 (63), 410.40 (51), 395.25 (11), 387.25 (100), 313.25 (13), 255.20 (14), 253.10 (14), 213.10 (12).

Fraction 2. (24*S*,25(26)*E*)-3α,5-Cyclo-6β-methoxy-24-(hydroxymethyl)-26-methylcholest-25(26)-ene (16). ^{1}H NMR (300 MHz) δ 3.321 (3 H, s, OCH_3), 1.653 (3 H, d, J = 6.6 Hz, C-29), 1.573 (3 H, s, C-27), 1.016 (3 H, s, C-19), 0.902 (3 H, d, J = 6.6 Hz, C-21), 0.699 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 442.30 (M^+, 32), the fragment peaks occur at the same m/z values as cited for fraction 1.

Fraction 3. (24*R*,25(26)*Z*)-3α,5-Cyclo-6β-methoxy-24-(hydroxymethyl)-26-methylcholest-25(26)-ene (17). ^{1}H NMR (300 MHz) δ 3.317 (3 H, s, OCH_3), 1.614 (3 H, d, J = 6.8 Hz, C-29), 1.580 (3 H, s, C-27), 1.014 (3 H, s, C-19), 0.902 (3 H, d, J = 6.5 Hz, C-21), 0.702 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 442.40 (M^+, 31), the fragment peaks occur at the same m/z values as cited for fraction 1.

Fraction 4. (24*R*,25(26)*E*)-3α,5-Cyclo-6β-methoxy-24-(hydroxymethyl)-26-methylcholest-25(26)-ene (18). ^{1}H NMR (300 MHz) δ 3.316 (3 H, s, OCH_3), 1.632 (3 H, d, J = 6.7 Hz, C-29), 1.568 (3 H, s, C-27), 1.014 (3 H, s, C-19), 0.892 (3 H, d, J = 6.5 Hz, C-21), 0.698 (3 H, s, C-18); high-resolution mass spectrum, m/z (relative intensity 442.3822, (M^+, 48; calcd for $C_{30}H_{50}O_2$ 442.3798), 427.3574 ($C_{29}H_{47}O_2$, 71), 410.3578 ($C_{29}H_{46}O$, 68), 395.3304 ($C_{28}H_{43}O$, 14), 387.3251 ($C_{26}H_{43}O_2$, 100), 313.2560 ($C_{22}H_{33}O$, 27), 255.2107 ($C_{19}H_{27}$, 35), 253.1958 ($C_{19}H_{25}$, 54), 213.1631 ($C_{16}H_{21}$, 31).

i-Methyl Ether Jaspisterol Isomer (19–22). Each 24-hydroxymethyl i-methyl ether (**15**–**18**) was converted into the corresponding jaspisterol derivative (**19**–**22**) by a known procedure.[16]

(24*R*,25(26)*Z*)-3α,5-Cyclo-6β-methoxy-24,26-dimethylcholest-25(26)-ene (19) from 15: ^{1}H NMR (300 MHz) δ 3.322 (3 H, s, OCH_3), 1.562 (3 H, s, C-27), 1.550 (3 H, d, J = 4.9 Hz, C-29), 1.018 (3 H, s, C-19), 0.932 (3 H, d, J = 7.0 Hz, C-28), 0.909 (3 H, d, J = 6.8 Hz, C-21), 0.705 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 426.40 (M^+, 26), 411.40 (32), 394.35 (25), 371.25 (45), 55.10 (100).

(24*R*,25(26)*E*)-3α,5-Cyclo-6β-methoxy-24,26-dimethylcholest-25(26)-ene (20) from 16: ^{1}H NMR (300 MHz) δ 3.320 (3 H, s, OCH_3), 1.558 (3 H, d, J = 6.5 Hz, C-29), 1.499 (3 H, s, C-27), 1.017 (3 H, s, C-19), 0.943 (3 H, d, J = 6.9 Hz, C-28), 0.896 (3 H, d, J = 6.5 Hz, C-21), 0.701 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 426.40 (M^+, 28), 4111.40 (37), 371.25 (61), 55.10 (100).

(24*S*,25(26)*Z*)-3α,5-Cyclo-6β-methoxy-24,26-dimethylcholest-25(26)-ene (21) from 17: ^{1}H NMR (300 MHz) δ 3.318 (3 H, s, OCH_3), 1.567 (3 H, s, C-27), 1.556 (3 h, d, J = 6.9 Hz, C-29), 1.016 (3 H, s, C-19, 0.938 (3 H, d, J = 6.9 Hz, C-28), 0.899 (3 H, d, J = 6.5 Hz, C-21), 0.703 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 326.40 (M^+, 34), 411.40 (64),

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(15) Other solvent systems, such as CH_3CN/EtOAc/MeOH (22:9:9) also failed to separate the *E*- and *Z*-isomers **25** and **26**. They were partially separable by GC; RRT 1.31 for **26** and RRT 1.32 for **25** (Carlo Erba Capillary GC; SE 54, 30 m, 280 → 290 °C, 1 °C/min increase).

394.25 (82), 371.25 (91), 55.10 (100).

(24*S*,25(26)*E*)-3α,5-Cyclo-6β-methoxy-24,26-dimethylcholest-25(26)-ene (22) from 18: ^{1}H NMR (300 MHz) 3.318 (3 H, s, OCH_3), 1.557 (3 H, d, J = 6.5 Hz, C-29), 1.483 (3 H, s, C-27), 1.016 (3 H, s, C-19), 0.947 (3 H, d, J = 6.9 Hz, C-28), 0.890 (3 H, d, J = 6.6 Hz, C-21), 0.700 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 426.40 (M^+, 30), 411.40 (41), 394.25 (37), 371.25 (70), 55.10 (100).

Jaspisterol (26), Isojaspisterol (25), and Their Isomers (23, 24). Each i-methyl ether (**19–22**) was hydrolyzed to the corresponding jaspisterol isomers (**23–26**) by a known procedure.[16]

(24*R*,25(26)*Z*)-24,26-Dimethylcholesta-5,25(26)-dien-3β-ol (23) from 19: mp 129–130 °C (MeOH); $[\alpha]^{20}_D$ −12.3° (*c* 12.5, $CHCl_3$); GC RRT (1.73); HPLC RRT (0.96); for ^{1}H NMR (300 MHz and ^{13}C NMR (400 MHz) data, see Tables I and II; low-resolution mass spectrum, m/z (relative intensity) 412.40 (M^+, 32), 379.15 (10), 328.15 (16), 314.15 (17), 299.15 (35), 271.15 (28), 255.15 (16), 213.15 (25), 55.05 (100).

(24*R*,25(26)*E*)-24,26-Dimethylcholesta-5,25(26)-dien-3β-ol (24) from 20: mp 135–136 °C (MeOH); $[\alpha]^{20}_D$ −53.8° (*c* 5.1, $CHCl_3$); GC RRT (1.77); HPLC RRT (0.96); for ^{1}H NMR (300 MHz) and ^{13}C NMR (400 MHz) data, see Tables I and II; low-resolution mass spectrum, m/z (relative intensity) 412.40 (M^+, 30), 328.15 (17), 314.15 (21), 299.15 (36), 271.15 (26), 255.15 (14), 213.10 (26), 55.05 (100).

(24*S*,25(26)*Z*)-24,26-Dimethylcholesta-5,25(26)-dien-3β-ol (Isojaspisterol, 25) from 21: mp 130–131 °C (MeOH); $[\alpha]^{20}_D$ −52.8° (*c* 8.0, $CHCl_3$); GC RRT (1.73); HPLC RRT (0.96); for ^{1}H NMR (300 MHz) and ^{13}C NMR (400 MHz) data, see Tables I and II; low-resolution mass spectrum, m/z (relative intensity) 412.40 (M^+, 35), 328.15 (21), 314.15 (19), 299.15 (28), 271.15 (35), 255.15 (14), 213.00 (28), 55.05 (100).

(24*S*,25(26)*E*)-24,26-Dimethylcholesta-5,25(26)-dien-3β-ol (Jaspisterol, 26) from 22: mp 113–114 °C (MeOH); $[\alpha]^{20}_D$ −44.1° (*c* 10.3, $CHCl_3$); GC RRT (1.74); HPLC RRT (0.96); for ^{1}H NMR (300 MHz) and ^{13}C NMR (400 MHz), see Tables I and II; high-resolution mass spectrum, m/z (relative intensity) 412.3694 (M^+, 86; calcd for $C_{29}H_{48}O$ 412.3705), 397.3486 ($C_{28}H_{45}O$, 21), 379.3361 ($C_{28}H_{43}$, 22), 328.2791 ($C_{23}H_{36}O$, 26), 314.2618 ($C_{22}H_{34}O$, 30), 299.2383 ($C_{21}H_{31}O$, 71), 271.2054 ($C_{19}H_{27}O$, 44), 255.2101 ($C_{19}H_{27}$, 23), 213.1633 ($C_{16}H_{21}$, 33), 83.0867 (C_6H_{11}, 100).

Ozonolysis of Isomeric Jaspisterol i-Methyl Ethers (19–22). A saturated solution of ozone in methylene chloride (5 mL) at −70 °C was added to each jaspisterol isomer i-methyl ether (**19–22**) at −70 °C, and the mixtures were stirred at the same temperature for 5 min. Excess ozone was destroyed by the addition of methyl sulfide. Concentration and separation by silica gel column chromatography gave the corresponding carbonyl compound (**31** or **32**), which was further purified by reverse-phase HPLC.

(24*R*)-3α,5-Cyclo-6β-methoxy-24-methyl-27-norcholestan-25-one (31)[13] from 19 and 22: ^{1}H NMR (300 MHz) δ 3.320 (3 H, s, OCH_3), 2.128 (3 H, C-26), 1.065 (3 H, d, J = 6.9 Hz, C-28), 1.017 (3 H, s, C-19), 0.917 (3 H, d, J = 6.6 Hz, C-21), 0.708 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity 414.50 (M^+, 29), 399.25 (42), 382.25 (100), 367.25 (24), 359.25 (71), 213.10 (34).

(24*S*)-3α,5-Cyclo-6β-methoxy-24-methyl-27-norcholestan-25-one (32)[13] from 21 and 22: ^{1}H NMR (300 MHz) δ 3.320 (3 H, s, OCH_3), 2.123 (3 H, s, C-26), 1.077 (3 H, d, J = 6.9 Hz, C-28), 1.016 (3 H, s, C-19), 0.918 (3 H, d, J = 6.5 Hz, C-21), 0.705 (3 H, s, C-18); low-resolution mass spectrum, m/z (relative intensity) 414.50 (M^+, 41), 399.25 (58), 382.25 (100), 367.25 (24), 359.25 (81), 213.10 (21).

Ozonolysis of Natural Jaspisterol (26) and Isojaspisterol (25). Ozonolysis of the mixture of i-methyl ethers, which was derived from natural jaspisterol (**26**) and isojaspisterol (**25**), was performed by the same procedure as above. The 300-MHz ^{1}H NMR spectrum of the product was same as that of **32**.

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C-Nucleosides. 6. Synthesis of 5-Methoxy-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)furan-2(5*H*)-one and Its Ring Transformation

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Synthesis of the versatile and stable C-nucleoside precursor 5-hydroxy-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)furan-2(5*H*)-one (**2**) was achieved by oxidation of glycosyl furan (**1**) with Jones reagent. Treatment of **2** with triethylamine in benzene afforded the elimination product **5** in 81% yield. Methoxylation of **2** with hydrochloric acid in methanol afforded (5*R*)- and (5*S*)-5-methoxy-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-furan-2(5*H*)-one (**6a** and **6b**). The conversion of the furanone ring into pyridazinone and *N*-aminopyrrolinone was performed by treatment of **6a,b** with hydrazine hydrate to give **11** and **12**. Deblocking of **11** and **12** gave **13** and **17**. Compounds **6a,b** were reacted with hydroxylamine-*O*-sulfonic acid (HOSA) in methanol to form **18** in 72% yield. Deblocking of **18** gave 3-β-D-ribofuranosyl-6*H*-1,2-oxazin-6-one (**20**). Finally, reaction of **6a,b** with ammonia in dioxane gave the known epimers of protected pyrrolinone **22**.

It has been demonstrated that certain five- and six-membered α,β-unsaturated lactone derivatives possess, in addition to other pharmacological properties,[1] tumor-inhibitory activity.[2] Moreover, they have proven to be versatile synthetic intermediates, suitable for the elaboration of other heterocyclic systems.[3] We were interested

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