

**Collection of X-ray Data and Structure Determination.** Data were collected on a Rigaku AFC-6A diffractometer using Cu K $\alpha$  (1.5418 Å) radiation from a graphite-crystal monochromator. Least-squares refinement of the setting angles gave the following values for the cell parameters:  $a = 9.147 \pm 0.006$  Å,  $b = 20.925 \pm 0.01$  Å,  $c = 11.276 \pm 0.013$  Å,  $\beta = 109.33 \pm 0.06^\circ$ ,  $V = 2036.6$  Å<sup>3</sup>,  $M_r$ , 584.08, calculated density 1.90 g/cm<sup>3</sup>, space group  $Cc$ ,  $Z = 4$ . For the data collection, a monoclinic single crystal of approximate dimensions  $0.5 \times 0.5 \times 0.5$  mm was mounted on the diffractometer. Measurements were made at ambient temperature (ca. 293 K) with scan technique  $2\theta/\omega$ , scan rate 8 deg/min, and  $2\theta_{\max}$  135°. A total of 3980 independent reflections were collected, and 1500 reflections were used. The structure was solved by using the direct (MULTAN) method. The agreement factor was  $R = 0.080$ . Selected values of interatomic distances and of the distances to the best plane from the individual atoms are listed in Tables II and III. Complete listings of these parameters (Tables IV and V), positional and thermal parameters (Table VI), and  $F_o - F_c$  Table (Table VII) are available as supplementary materials.

**Acknowledgment.** This work was supported, in part, by a Grant-in-Aid for Scientific Research from the Japan Ministry of Education (No. 355372) and also by the Asahi Glass Foundation. We express our gratitude to M. Nakayama and T. Hori

of the Rigaku Corporation for the X-ray structure solution.

**Registry No.** **1a**, 78184-63-1; **1b**, 85848-84-6; **1c**, 85781-56-2; **1d**, 85848-83-5; **1d** (dichloromethano-monochloromethano derivative), 85781-73-3; **1e**, 85848-85-7; **1f**, 85781-57-3; **endo-1f** (chloromethano-dichloromethano derivative), 85781-70-0; **1g**, 78184-64-2; **1h**, 85849-45-2; **1i**, 36807-30-4; **2a**, 85848-89-1; **2b**, 85781-63-1; **2c**, 85781-66-4; **2d**, 85781-67-5; **endo-3**, 85781-62-0; **exo-3**, 85848-86-8; **4a** (X = Cl), 52126-70-2; **4a** (X = H), 52033-58-6; **5a** (X = Cl), 52033-55-3; **5a** (X = H), 52033-57-5; **5c** (X = H), 85781-64-2; **6a** (X = *endo*-Cl), 85848-87-9; **6a** (X = H), 78184-65-3; **6f** (X = *endo*-Cl), 85781-69-7; **6g** (X = *endo*-Cl), 85781-71-1; **6g** (X = *endo,exo*-Cl), 85848-88-0; **6h** (X = *endo*-Cl), 85781-72-2; **14c**, 85781-65-3; **29**, 85781-61-9; **30**, 85781-68-6; **1**, 85781-58-4; **II**, 85781-59-5; **III**, 85781-60-8; **Na**, 7440-23-5; **Na naph**, 3481-12-7; **K naph**, 4216-48-2; 1,2-dihydro-1,4,5,8-tetramethylnaphthalene, 4422-10-0.

**Supplementary Material Available:** Listings of interatomic distances, distances to the best plane from atoms, positional and thermal parameters, and observed and calculated structure factor amplitudes (23 pages). Ordering information is given on any current masthead page.

## Acid-Catalyzed and Photochemical Isomerization of Steroidal Cyclopropenes

Toshihiro Itoh and Carl Djerassi\*

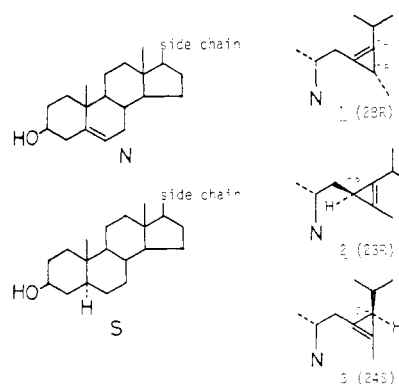
Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. Received September 20, 1982

**Abstract:** The acid-catalyzed and photochemical isomerization of two naturally occurring steroidal cyclopropenes, (28*R*)-calysterol (**1**) and (23*R*)-23*H*-isocalysterol (**2**), is described. Cyclopropene **1** on treatment with methanolic sulfuric acid afforded 23-ethylated cholesterol derivatives containing conjugated diene systems or methoxylated side chains. The sole production of C-23 ethylated sterols demonstrates that this cyclopropene undergoes acid-promoted bond cleavage only between C-24 and C-28. By contrast, methanolic sulfuric acid treatment of the isomeric cyclopropene **2** generated conjugated dienes with 24-methyl-24-homocholestane and 24-ethylcholestane side chains, together with their methoxylated derivatives. This implies that bond fission between C-23 and C-24, as well as C-23 and C-28, is operating in this instance, which is of mechanistic significance. Photolysis by direct irradiation of cyclopropenes **1** and **2** afforded isomerized cyclopropenes, which suggests that the reaction proceeded through an electronically excited singlet state via vinylcarbene intermediates. Among the fragmentation products from the photolysis were isolated the acetylenes 26,27-dinorcholestan-5-en-23-yn-3 $\beta$ -ol (**34**) and cholest-5-en-23-yn-3 $\beta$ -ol (**35**), which had been encountered earlier as the only naturally occurring steroidal acetylenes. Their generation can be rationalized by carbene elimination from the corresponding cyclopropenes.

### Introduction

Calysterol [23,28-cyclostigmasta-5,23(24)-dien-3 $\beta$ -ol, **1**, Chart I],<sup>1,2</sup> the principal sterol component of the marine sponge *Calyx niceaensis*, possesses one of the most intriguing functionalities—a cyclopropane ring—among the great variety of unusual side-chain substituents found in marine sterols.<sup>3</sup> Recently we determined the absolute configuration (28*R*) of calysterol<sup>2</sup> and isolated two novel steroidal cyclopropenes, (23*R*)-23*H*-isocalysterol [(23*R*)-23,28-cyclostigmasta-5,24(28)-dien-3 $\beta$ -ol, **2**]<sup>2</sup> and (24*S*)-24*H*-isocalysterol [(24*S*)-23,28-cyclostigmasta-5,23(28)-dien-3 $\beta$ -ol, **3**]<sup>4</sup> from *C. niceaensis*. The natural occurrence of cyclopropenes is extremely rare: sterculic and related acids<sup>5</sup> and the polyandrocarpidines<sup>6</sup> are the only heretofore known natural cyclopropenes aside from the calysterols **1–3**.

Chart I



Because of the strain associated with the unsaturated three-membered ring, the chemistry of cyclopropenes has attracted considerable interest.<sup>7–10</sup> Although some isomerization reactions

(1) Fattorusso, E.; Magno, S.; Mayol, L.; Santacrose, C.; Sica, D. *Tetrahedron* **1975**, *31*, 1715–1716.

(2) Li, L. N.; Li, H.-T.; Lang, R. W.; Itoh, T.; Sica, D.; Djerassi, C. *J. Am. Chem. Soc.* **1982**, *104*, 6726.

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

(4) Itoh, T.; Sica, D.; Djerassi, C. *J. Org. Chem.* **1983**, *48*, 890.

(5) Carter, F. L.; Frampton, V. L. *Chem. Rev.* **1964**, *64*, 497–525.

(6) Cheng, M. T.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 7409–7411.

(7) Closs, G. L. *Adv. Alicyclic Chem.* **1966**, *1*, 53–127.

(8) Wendisch, D. *Methoden Org. Chem. (Houben-Weyl)* **1971**, *IV/3*, 679.

Table I. Acid-Catalyzed Isomerization of (28*R*)-Calysterol (1) and 23-Ethylcholesta-5,23,28-trien-3 $\beta$ -ol (6)

compound <sup>a</sup>	rt <sub>R</sub>		1, %		6, %
	HPLC <sup>b</sup>	GLC <sup>c</sup>	H <sub>2</sub> SO <sub>4</sub> -MeOH	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> H-C <sub>6</sub> H <sub>6</sub>	H <sub>2</sub> SO <sub>4</sub> -MeOH
1 (28 <i>R</i> )	1.00	1.20 <sup>d</sup>	3 <sup>e</sup>	14 <sup>e</sup>	
4	0.89	1.16	8		4
5	0.94	1.54	6		2
6	0.92	1.60	6	70	12 <sup>e</sup>
7	1.03	1.54	3		5
8	1.05	1.57	8	1	3
9	0.55	1.96	14		18
10	0.56	1.97	16		21
11	0.63	2.03	4		6
12	0.63	2.03	4		6
13	0.73	2.20	8		8
14	0.79	2.17	10		9

<sup>a</sup> Wavy lines in this and in the subsequent tables imply that the stereochemistry is unknown. <sup>b</sup> rt<sub>R</sub> in this and in the subsequent tables is expressed relative to (28*R*)-calysterol (1) on an Altex column; eluent, methanol-water (95:5). <sup>c</sup> rt<sub>R</sub> in this and in the subsequent tables is expressed relative to cholesterol; 3% OV-17, column temperature 260 °C. <sup>d</sup> Several peaks arising from GLC decomposition products appeared after this peak. <sup>e</sup> Recovered starting material.

of calysterol (1) have been noted with silver nitrate<sup>11</sup> and acetic anhydride,<sup>12</sup> we were especially interested in a thorough investigation of acid-catalyzed and photochemical isomerization reactions of steroidal cyclopropenes in order to determine whether any of these naturally occurring marine sterols were artifacts of the isolation procedure. This paper describes the acid-catalyzed isomerization of the two naturally occurring steroidal cyclopropenes 1 and 2 with methanolic sulfuric acid and *p*-toluenesulfonic acid in benzene and their photochemical isomerization by direct irradiation.

## Results and Discussion

**Acid-Catalyzed Isomerization.** Table I summarizes the reaction products of (28*R*)-calysterol (1) and 23-ethylcholesta-5,23,28-trien-3 $\beta$ -ol (6) upon acid-catalyzed isomerization. Refluxing of cyclopropene 1 in 5% methanolic H<sub>2</sub>SO<sub>4</sub> for 3 h yielded the following conjugated dienes and methoxylated sterols: two stereoisomeric 23-ethylcholesta-5,22,24-trien-3 $\beta$ -ols (4 and 5); two stereoisomeric 23-ethylcholesta-5,23,28-trien-3 $\beta$ -ols (6 and 7); 23-ethylcholesta-5,23(28),24-trien-3 $\beta$ -ol (8); four stereoisomeric 28-methoxy-23-ethylcholesta-5,23-dien-3 $\beta$ -ols (9–12); two stereoisomeric 24-methoxy-23-ethylcholesta-5,23(28)-dien-3 $\beta$ -ols (13 and 14). Whereas exposure of calysterol 1 to 0.15% *p*-toluenesulfonic acid–C<sub>6</sub>H<sub>6</sub> at room temperature for 10 days afforded 23-ethylcholesta-5,23,28-trien-3 $\beta$ -ol (6) as the major product, the latter upon methanolic H<sub>2</sub>SO<sub>4</sub> isomerization gave the same mixture of conjugated dienes (4–8) and methanolysis products (9–14) as does calysterol (1). We conclude, therefore, that the diene 6 is the primary product of the acid-catalyzed isomerization of the cyclopropene 1.

Cyclopropenes readily undergo acid-promoted ring opening. Such an acid-catalyzed reaction has been rationalized<sup>7,8</sup> by invoking a rearrangement of the cyclopropene ring to an allylic carbonium ion, either by protonation of the double bond or by protonation of the cyclopropene single bond (e.g., 25). There are then two possible carbonium ions (26 and 28 in Scheme I) that

can be generated by protonation of cyclopropene 1: cation 26 by bond cleavage between C-24 and C-28, and cation 28 by bond fission between C-23 and C-28. Deprotonation of the cation then gives the conjugated diene sterols 4–8. On the other hand, nucleophilic attack by methanol affords the methoxy compounds 9–14. The intermediacy of the cation 28 would lead to 24-ethylsterols, which were conspicuously absent in the acid-catalyzed isomerization of the cyclopropene 1 (see Table I). This indicates that protonation by bond cleavage between C-23 and C-28, if it occurs at all, is very restricted, probably due to the steric hindrance by the bulky sterol ring, which makes it difficult for the proton donor to approach the cyclopropene ring plane.

As indicated above and summarized in Table I, comparison of the milder *p*-toluenesulfonic acid–C<sub>6</sub>H<sub>6</sub> treatment with the more drastic methanolic H<sub>2</sub>SO<sub>4</sub> conditions showed that the primary ring-opening product of the cyclopropene 1 is the diene 6, which arises by proton elimination of the cation 26.

The composition of the reaction mixture of the acid-catalyzed isomerization of (23*R*)-23*H*-isocalysterol (2) and (22*E*)-24-methyl-24-homocholesta-5,22,24-trien-3 $\beta$ -ol (18) is summarized in Table II. Methanolic H<sub>2</sub>SO<sub>4</sub> isomerization of 2 yielded the following ring-opening products: three stereoisomeric 24-methyl-24-homocholesta-5,20(22),23-trien-3 $\beta$ -ols (15–17); 24-ethylcholesta-5,20(22),23-trien-3 $\beta$ -ol (19); (22*E*)-24-ethylcholesta-5,22,24(28)-trien-3 $\beta$ -ol (21); (22*E*)-24-ethylcholesta-5,22,24-trien-3 $\beta$ -ol (22); 25-methoxy-24-methyl-24-homocholesta-5,23-dien-3 $\beta$ -ol (23); 28-methoxy-24-ethylcholesta-5,23-dien-3 $\beta$ -ol (24). When the isomerization of 2 was performed with the milder *p*-toluenesulfonic acid–C<sub>6</sub>H<sub>6</sub> reagent, the major product was the conjugated diene 18 accompanied by 24-ethylcholesta-5,23,28-trien-3 $\beta$ -ol (20) and (22*E*)-24-ethylcholesta-5,22,24(28)-trien-3 $\beta$ -ol (21) together with several other uncharacterized minor products. On methanolic H<sub>2</sub>SO<sub>4</sub> treatment 18 afforded the three stereoisomeric conjugated dienes 15–17, thus showing that the diene 18 is the principal initial isomerization product of the cyclopropene 2.

Again, two allylic carbonium ions can theoretically be produced by protonation of the cyclopropene 2 (Scheme II): cation 30 (possibly via 29)<sup>7</sup> formed by breaking the C-23 and C-24 bond, and cation 32 (possibly via 31)<sup>7</sup> arising from C-23 and C-28 bond fission. In the case of the cyclopropene 2, both cleavage processes operate, since the conjugated dienes 15–18, and the methoxy sterol 23 can arise from the cation 30, while sterols with the 24-

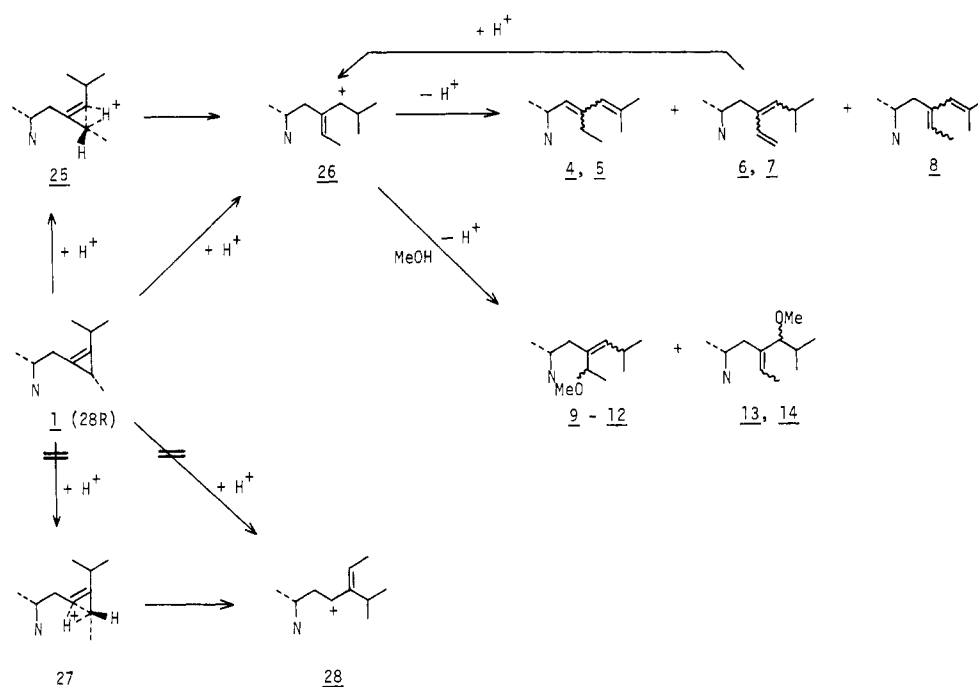
(9) Liebman, J. F.; Greenberg, A. *Chem. Rev.* 1976, 76, 311–365.

(10) Padwa, A. *Org. Photochem.* 1979, 4, 261–326.

(11) Fattorusso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Sica, D. *Gazz. Chim. Ital.* 1975, 105, 635–637.

(12) Fattorusso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Minale, L.; Riccio, R.; Scalona, O.; Sodano, G. *Gazz. Chim. Ital.* 1978, 108, 571–572.

Scheme I

Table II. Acid-Catalyzed Isomerization of (23*R*)-23*H*-Isocalysterol (**2**) and 24-Methyl-24-homocholesta-5,22,24-trien-3 $\beta$ -ol (**18**)

structure		rt <sub>R</sub>		2, %		18, %
		HPLC	GLC	H <sub>2</sub> SO <sub>4</sub> -MeOH	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> SO <sub>3</sub> H-C <sub>6</sub> H <sub>6</sub>	H <sub>2</sub> SO <sub>4</sub> -MeOH
	<b>2 (23<i>R</i>)</b>	1.14	1.62 <sup>a</sup>	2 <sup>b</sup>	2 <sup>b</sup>	
	<b>15</b>	0.93	1.87	29		30
	<b>16</b>	0.93	2.14	35		45
	<b>17</b>	0.97	1.63	2		6
	<b>18 (22<i>E</i>)</b>	0.95	1.82		72	
	<b>19</b>	0.87	1.92	7		
	<b>20</b>	0.99	1.86		4	
	<b>21 (22<i>E</i>)</b>	1.02	1.68	2	8	
	<b>22 (22<i>E</i>)</b>	1.04	2.03	11		
	<b>23</b>	0.75	2.44	6		
	<b>24</b>	0.60	2.56	1		

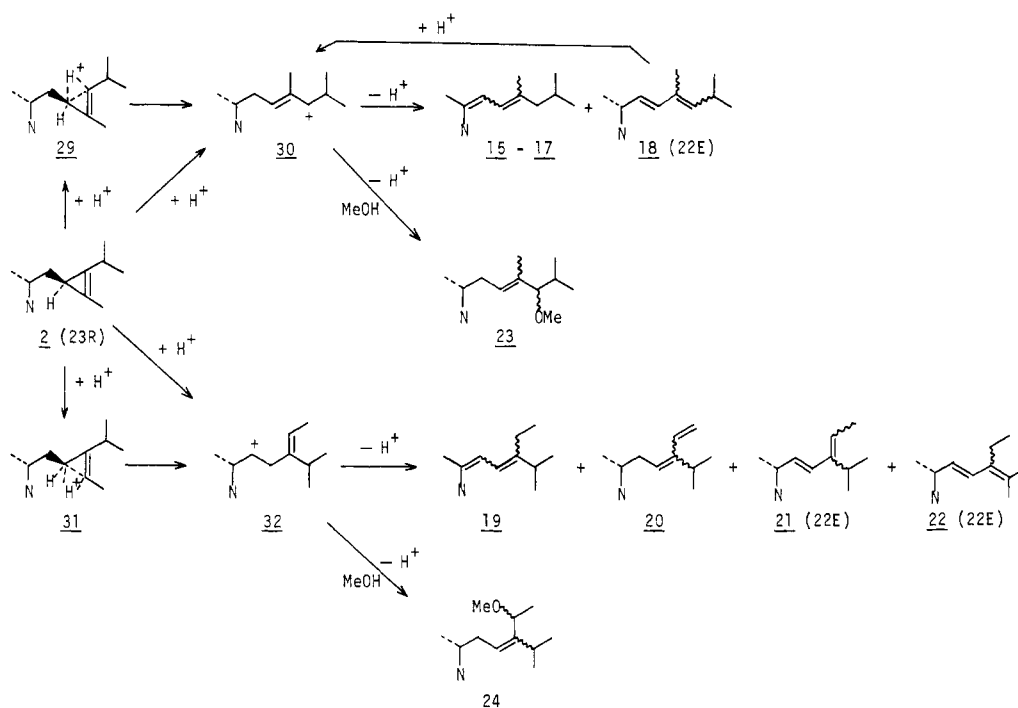
<sup>a</sup> Several peaks arising from GLC decomposition products appeared after this peak. <sup>b</sup> Recovered starting material.

ethylcholestone side chain (**19-22** and **24**) could be formed through the carbonium ion **32**.

Just as observed in the isomerization of **1**, the isomerization of **2** by methanolic H<sub>2</sub>SO<sub>4</sub> afforded a more complicated reaction

mixture than by *p*-toluenesulfonic acid. The conjugated diene **18**, a ring-opening product of **2** without double-bond migration, was the most prominent product on *p*-toluenesulfonic acid isomerization while this sterol was not detected in the reaction mixture

Scheme II



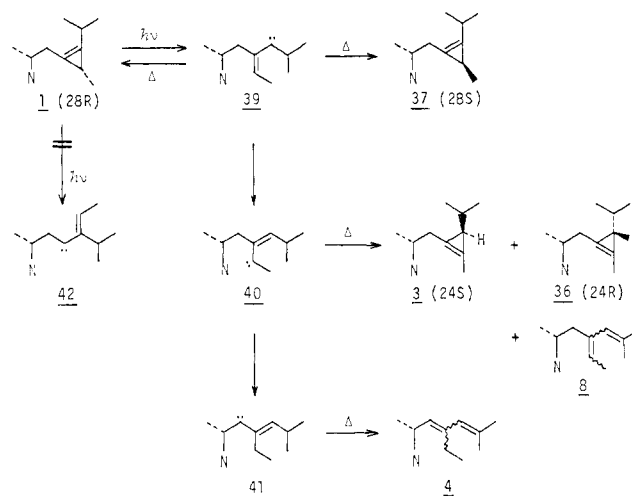
following methanolic  $\text{H}_2\text{SO}_4$  isomerization (Table II). This can be explained by assuming that the initially formed diene **18**, on methanolic  $\text{H}_2\text{SO}_4$  treatment, isomerizes further to the more stable highly alkyl-substituted conjugated dienes **15–17**.

Another noteworthy feature is the great contrast between cyclopropenes **1** and **2** in terms of the product ratio of conjugated diene vs. methyl ether in their reaction with methanolic  $\text{H}_2\text{SO}_4$ , viz., 1:1.8 for **1** as compared to >10:1 for **2**. Presumably very subtle steric features are responsible for the fact that deprotonation or methyl ether formations are equally feasible in the allyl cation **26** (Scheme I) derived from **1**, whereas deprotonation is greatly favored in cations **30** and **32** (Scheme II) generated by protonation of **2**.

**Photochemical Isomerization.** Table III summarizes the direct photolysis products of cyclopropenes **1** and **2**. Irradiation of **1** for 10 h under an argon atmosphere in isooctane with a 450-W medium-pressure lamp and a water-cooling quartz immersion well afforded the following products in addition to significant amounts of recovered starting material. They are the fragmentation products, 23,24-dinorchol-5-en-3 $\beta$ -ol (guneribol, **33**), and the two acetylenes 26,27-dinorchola-5-en-23-yn-3 $\beta$ -ol (**34**) and cholest-5-en-23-yn-3 $\beta$ -ol (**35**), as well as the conjugated dienes **4** and **8**, and, most interestingly, the isomerized cyclopropenes **3**, **36**, and **37**, accompanied by several other uncharacterized minor products. Irradiation of the cyclopropene **2** yielded again the fragmentation products **33–35**, as well as the isomerized cyclopropenes **1**, **3**, **36–38**.

The photochemical behavior of cyclopropene derivatives has been shown to be remarkably dependent on the multiplicity of the excited state involved.<sup>10</sup> Triplet states generated by sensitization techniques give high yields of cyclopropene dimers,<sup>13</sup> while singlet states generally react by  $\sigma$ -bond cleavage to give products in very low quantum yield, which are explicable in terms of the chemistry of vinylcarbenes.<sup>14,15</sup> The formation of the vinylcarbene in the direct irradiation can be viewed as the result of homolytic cleavage and simultaneous rotation of the disubstituted methylene

Scheme III



carbon. Both electrons occupy an in-plane  $\sigma$  orbital with only two electrons in the conjugated  $\pi$  orbital. The low efficiency for the electronically excited singlet-state reactivity has been explained by thermal recyclization of the carbene intermediate (through its conversion to a 1,3-diradical singlet state) to the cyclopropene, which yields a racemic mixture.<sup>16,17</sup>

The formation of the epimeric cyclopropene **37** by direct irradiation of **1** can be explained by the intervention of the vinylcarbene **39**, which upon thermal cyclization regenerates **1** and its epimer **37** (Scheme III). The other epimeric pair of cyclopropenes (**3** and **36**) and the diene **8** may arise from the vinylcarbene **40**, which could be generated from carbene **39**. Further transformation of the carbene intermediate **40** can lead to **41**, which could then give the diene **4**. There is an alternative vinylcarbene, a C-24 substituted one (**42**), which can be formed directly from cyclopropene **1** by irradiation. However, the fact that all of the conjugated dienes detected in the photolysis reaction

(13) Arnold, D. R.; Morchat, R. M. *Can. J. Chem.* **1977**, *55*, 393–406.

(14) Pincock, J. A.; Morchat, R.; Arnold, D. R. *J. Am. Chem. Soc.* **1973**, *95*, 7536–7538.

(15) There is evidence that vinylcarbenes are not necessarily intermediates in vinylcyclopropane rearrangements: Zimmerman, H. E.; Aasen, S. M. *J. Org. Chem.* **1978**, *43*, 1493–1506.

(16) York, E. J.; Dittmar, W.; Stevenson, J. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 2882–2883.

(17) Pincock, J. A.; Moutsokapas, A. A. *Can. J. Chem.* **1977**, *55*, 979–985.

**Table III.** Direct Photolysis of (28*R*)-Calysterol (**1**) and (23*R*)-23*H*-Isocalysterol (**2**)

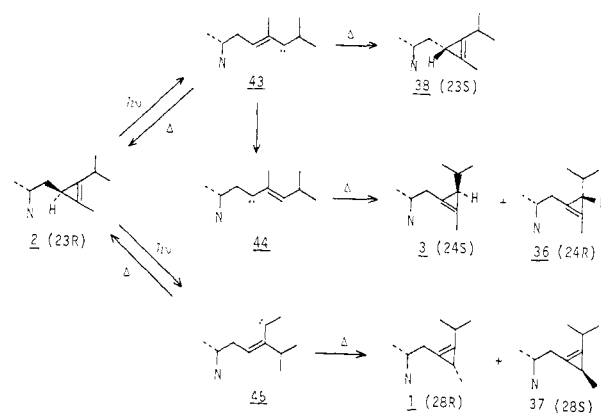
structure	$t_R^a$		1, %	2, %
	HPLC	GLC		
<b>1</b> (28 <i>R</i> )	1.00	1.20 <sup>a</sup>	51 <sup>b</sup>	3
<b>37</b> (28 <i>S</i> )	0.99	1.20 <sup>a</sup>	8	3
<b>2</b> (23 <i>R</i> )	1.14	1.62 <sup>a</sup>		34 <sup>b</sup>
<b>38</b> (23 <i>S</i> )	1.09	1.62 <sup>a</sup>		28
<b>3</b> (24 <i>S</i> )	0.98	1.30 <sup>a</sup>	2	3
<b>36</b> (24 <i>R</i> )	0.99	1.33 <sup>a</sup>	4	2
<b>4</b>	0.89	1.16	1	
<b>8</b>	1.06	1.57	1	
<b>33</b>	0.47	0.30	1	6
<b>34</b>	0.35	1.00	3	2
<b>35</b>	0.48	1.11	4	2

<sup>a</sup> Several peaks arising from GLC decomposition products appeared after this peak. <sup>b</sup> Recovered starting material.

mixture of **1** are only C-23 substituted ones (**4** and **8**) points to the sole intermediacy of carbene **39**.

The epimerization of cyclopropene **2** to afford **38** is explicable by the generation of the intermediate vinylcarbene **43** by direct photolysis (Scheme IV). The other two epimeric cyclopropenes, **3** and **36**, presumably arise from the precursor carbene **44**, which could be generated from **43**. Direct irradiation of **2** can also afford another vinylcarbene **45**, which would be the progenitor of the third epimeric pair (**1** and **37**) of cyclopropenes encountered in the photolysis of **2** (Table III).

The most probable process for the formation of the two acetylenic sterols, **34** and **35**, detected in the photolysis mixtures of cyclopropanes **1** and **2**, involves carbene elimination from the cyclopropanes (Scheme V). Such fragmentation is a widespread, though minor, photochemical reaction of cyclopropanes that give rise to carbenes and olefins.<sup>18,19</sup> It has been speculated that fragmentation proceeds via formation of a 1,3-diradical and subsequent homolysis to a carbene and olefin.<sup>18</sup> By analogy, one can postulate that acetylene **34** is generated via the diradical **46** from either **3** or **36**, which in turn are photolysis products of **1** and **2**. In the same manner, **35** could be formed via the diradical **47** from either **1** or **37**. The formation (see Table III) of the remaining fragmentation product, guneribol (**33**), is still mysterious. A possible route would be by bond cleavage between C-22 and C-23, accompanied by a 1,2-hydrogen migration to C-22 from C-28 (as for **1**) or C-24 (as for **3**), thus generating **33** and a carbene.

**Scheme IV**

In summary, direct photolysis of the steroidal cyclopropenes **1** and **2** results in isomerized cyclopropenes accompanied by several fragmentation products and conjugated dienes. In the photolysis of **2**, all six possible cyclopropane isomers of calysterol (**1**) are produced. The principal naturally occurring sterol component of the sponge *Calyx niceaensis* is (28*R*)-calysterol (**1**),<sup>1,2</sup> with (23*R*)-23*H*-isocalysterol (**2**)<sup>2</sup> being the next most abundant. We have recently demonstrated in the sponge<sup>4</sup> the presence (ca. 4% of the total sterols) of a third naturally occurring steroidal cyclopropene, (24*S*)-24*H*-isocalysterol (**3**). Since we have shown that steroidal cyclopropenes are susceptible to light, one may ask whether the cyclopropenes **2** and **3** are produced artificially from **1** during the isolation of the sterols from the sponge *C. niceaensis*.

We consider this possibility unlikely for the following reasons. In the case of (23*R*)-23*H*-isocalysterol (**2**), we could not demonstrate its presence in the photolysis reaction mixture (Table III) of (28*R*)-calysterol (**1**) after careful HPLC fractionation followed by 360-MHz <sup>1</sup>H NMR examination. As to the cyclopropene **3**, if this sterol were generated artificially from **1** and/or **2** during isolation, we should also have been able to detect its epimer **36** in the sterol mixture of *C. niceaensis* because the photochemical isomerization is not stereospecific in the formation of 24*H*-isocalysterol (**3/36**) as demonstrated in our present study. We could not confirm the presence of **36** even after very careful isolation of sterols from the sponge *C. niceaensis*.<sup>4</sup>

The two acetylenic sterols **34** and **35** have previously been demonstrated to occur in the sponge *C. niceaensis*,<sup>20</sup> which represents the only recorded instance of the natural occurrence of a steroidal acetylene. Although these acetylenes are also photolysis products of the cyclopropenes **1** and **2**, we consider these acetylenes to be natural products because the sponge contains significant amounts of these sterols (17% of **34** and 12% of **35** in the sterol mixture), whereas we could not detect<sup>21</sup> in the sponge several of the other sterols (e.g., **4**, **8**, **33**, **36–38**) that are generated together with the two acetylenes in the photochemical isomerization of cyclopropenes **1** and **2** (Table III).

**Characterization of Sterols.** The presence of the 3β-hydroxy-Δ<sup>5</sup>-sterol nucleus in the isomerization products was revealed by a singlet signal at ca. δ 1.01 (in CDCl<sub>3</sub>) arising from the C-19 methyl group<sup>2</sup> accompanied by two methine multiplets at δ 3.53 (C-3αH) and 5.35 (C-6H) in the <sup>1</sup>H NMR spectra. The constitution of the side chains of these sterols was primarily established by the NMR spectroscopic analysis (Tables IV–VIII). Unless otherwise specified, the stereochemistry of the side chains of the conjugated diene and methoxy sterols remained undetermined in this study, and if not otherwise stated, all of the sterols possessing an asymmetric center at C-20 in the side chain have the 20*R* configuration.

**Conjugated Diene Sterols.** The UV spectra of sterols **4–8** and **15–22** showed absorption peaks at around 227–252 nm, indicating

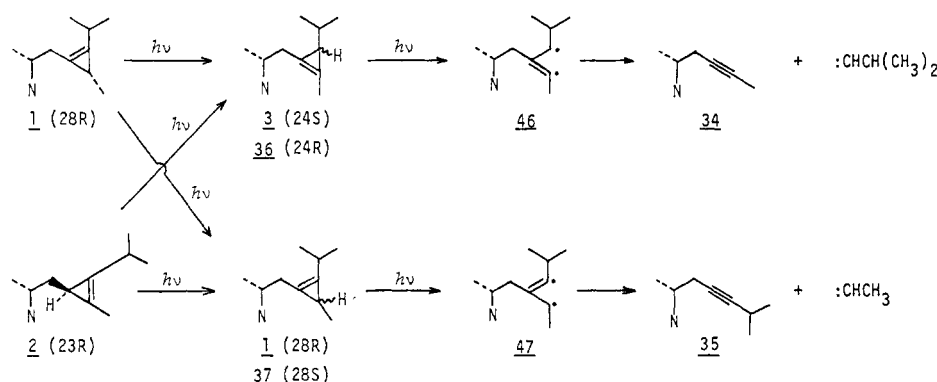
(18) Griffin, G. W. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 537–547.

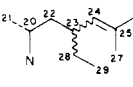
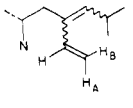
(19) Hixon, S. S. *Org. Photochem.* **1979**, *4*, 191–260.

(20) Steiner, E.; Djerassi, C.; Fattorusso, E.; Magno, S.; Mayol, L.; Santacrose, C.; Sica, D. *Helv. Chim. Acta* **1977**, *60*, 475–481.

(21) Itoh, T.; Djerassi, C., unpublished observation. The origin of the sponge was described in ref 4.

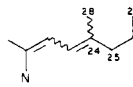
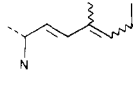
## Scheme V

Table IV.  $^1H$  NMR Data of 23-Ethylsterols with a Conjugated Diene System in the Side Chain

compound <sup>b</sup>	chemical shift <sup>a</sup>								
	C-18	C-19	C-21	C-26/C-27	C-29	C-20	C-22	C-24	C-28
 4	0.650	1.007	0.932 (d, 6.4) <sup>d</sup>	1.569 1.761	0.927 (t, 7.4)	2.22 (m)	4.954 (d, 9.7)	5.549	1.976 (q, 6.2)
5	0.732	1.016	0.999 (d, 6.7)	1.726 1.750	0.923 (t, 7.6)	2.40 (m)	4.917 (d, 9.5)	5.540	2.03 (m)
 6 <sup>c</sup>	0.687	1.008	0.820 (d, 6.5)	0.936 (d, 6.6)	A 4.911 (d, 11.1); B 5.099 (d, 17.9)			5.332 (d, 10.1)	6.256 (dd, 10.9, 17.5)
7 <sup>c</sup>	0.687	1.006	0.806 (d, 6.4)	0.962 (d, 7.0)	A 5.052 (d, 10.8); B 5.208 (d, 17.6)			5.120 (d, 9.7)	6.643 (dd, 11.0, 17.6)
8	0.659	1.007	0.822 (d, 6.3)	1.535 1.771	1.494 (d, 6.6)			5.426	5.221 (q, 6.8)

<sup>a</sup> The NMR data in this and in the subsequent tables are taken in  $CDCl_3$  with  $SiMe_4$  as internal standard at 360 MHz unless otherwise specified. The chemical shifts are given as  $\delta$  values. The signal is a singlet if no multiplicity is indicated. <sup>b</sup> All of the sterols in this and in the subsequent tables afforded two multiplets at  $\delta$  3.53 (1 H, C-3 $\alpha$ H) and 5.35 (1 H, C-6H). <sup>c</sup> Multiplet arising from C-25H was also observed at  $\delta$  2.60 for 6 and  $\delta$  2.76 for 7. <sup>d</sup>  $J$  values are given in hertz.

Table V.  $^1H$  NMR Data of 24-Methyl-24-homosterols with a Conjugated Diene System in the Side Chain

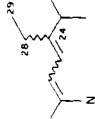
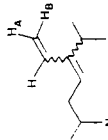
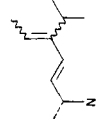
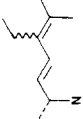
compound	chemical shift							
	C-18	C-19	C-21	C-28	C-29/C-30	C-22	C-23	C-25
15	0.565	1.008	1.761 1.783		0.881 (d, 6.5) 0.886 (d, 6.6)	6.049 (d, 11.4) 6.135 (d, 11.3)		2.034 (d, 7.3)
 16	0.579	1.010	1.708 1.763		0.863 (d, 6.4)	6.011 (d, 12.9) 6.046 (d, 12.0)		1.938 (d, 7.2)
17 <sup>a</sup>	0.656	1.009	1.698 1.813		0.826 (d, 6.8) 0.856 (d, 6.5)	6.054 (d, 10.6) 6.202 (d, 11.1)		
 18 <sup>b</sup> (22E)	0.704	1.008	1.044 (d, 6.6)	1.703	0.957 (d, 6.6) 0.961 (d, 6.6)	5.393 (dd, 8.6, 15.9)	5.936 (d, 15.6)	5.120 (d, 9.0)

<sup>a</sup> Recorded at 300 MHz. <sup>b</sup> Two multiplets at  $\delta$  2.13 (1 H, C-20) and 2.63 (1 H, C-26) were also observed.

the presence of a conjugated double-bond system in the side chain. Table IV contains the NMR data of five conjugated diene sterols with a 23-ethylated side chain (4–8). The structure of 23-ethylcholesta-5,22,24-trien-3 $\beta$ -ol was given for the sterol 4. Spin-decoupling experiments supported the structure. Irradiation at  $\delta$  2.22 (1 H, m, C-20) collapsed two doublets at  $\delta$  0.932 (3 H, C-21) and 4.954 (1 H, C-22) into singlets, whereas irradiation at  $\delta$  1.976 (2 H, q, C-28) collapsed the triplet at  $\delta$  0.927 (3 H, C-29) into a singlet. Sterol 5 displayed an NMR spectrum similar to that of 4 and was characterized as the stereoisomer of 4. Irradiation at  $\delta$  2.40 (1 H, m, C-20) collapsed two doublets at  $\delta$  0.999 (3 H, C-21) and 4.917 (1 H, C-22) into singlets, while irradiation at  $\delta$  0.923 (3 H, t, C-29) simplified the multiplet at

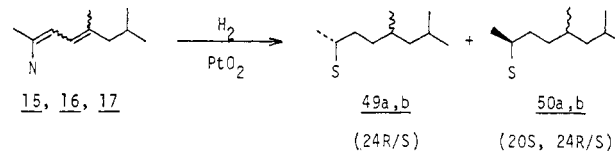
$\delta$  2.03 (2 H, C-28). Sterol 6 was shown to have the structure of 23-ethylcholesta-5,23,28-trien-3 $\beta$ -ol by NMR analysis, and this was supported by the spin-decoupling experiment. Irradiation at  $\delta$  2.60 (1 H, m, C-25) collapsed three doublets at  $\delta$  0.936 and 0.975 (each 3 H, C-26/C-27), and 5.332 (1 H, C-24) into singlets, while irradiation at  $\delta$  6.256 (1 H, dd, C-28) collapsed two doublets at  $\delta$  4.911 (1 H, C-29H<sub>A</sub>) and 5.099 (1 H, C-29H<sub>B</sub>) into singlets. Since the NMR signals of sterol 7 were closely related to those of 6, this was recognized as the stereoisomer of 6. Irradiation at  $\delta$  2.76 (1 H, m, C-25) collapsed three doublets at  $\delta$  0.962 and 0.982 (each 3 H, C-26/C-27) and 5.120 (1 H, C-24) into singlets, while irradiation at  $\delta$  6.643 (1 H, dd, C-28) simplified two doublets at  $\delta$  5.052 (1 H, C-29H<sub>A</sub>) and 5.208 (1 H, C-29H<sub>B</sub>). The NMR

Table VI.  $^1\text{H}$  NMR Data of 24-Ethylsterols with a Conjugated Diene System in the Side Chain

compound	C-18	C-19	C-21	C-26/C-27	C-29	chemical shift			
						C-22	C-23	C-25	C-28
 <b>19</b>	0.592	1.011	1.778	1.048 (d, 6.5)	1.017 (t, 7.7)	6.031 (d, 11.4) 6.078 (d, 11.4)		2.341 (sept, 7.1)	2.170 (q, 7.6)
 <b>20</b>	0.692	1.008	0.929 (d, 6.6)	1.052 (d, 7.0)	A 4.914 (dd, 1.8, 10.8); B 5.257 (dd, 1.8, 17.3)	5.468 (dd, 7.2, 8.1)		2.846 (sept, 7.0)	6.260 (dd, 11.1, 17.4)
 <b>21 (22E)</b>	0.705	1.011	1.037 (d, 6.7)	1.021 (d, 7.0) 1.031 (d, 7.0)	1.652 (d, 6.9)	5.508 (dd, 8.7, 15.8)	5.807 (d, 15.4)	2.843 (sept, 7.1)	5.389 (q, 6.9)
 <b>22 (22E)</b>	0.721	1.013	1.063 (d, 6.6)	1.749 1.777	0.944 (t, 7.5)	5.413 (dd, 8.6, 15.5)	6.259 (d, 15.6)		

analysis thus led to the structure of sterol **8** as 23-ethylcholesta-5,23(28),24-trien-3 $\beta$ -ol. Irradiation of a quartet at  $\delta$  5.221 (1 H, C-28) collapsed a doublet at  $\delta$  1.494 (3 H, C-29) into singlet, and thus the decoupling experiment supported the structure. The mass spectral data are consistent with this structure. The base peak at  $m/z$  110 ( $\text{C}_8\text{H}_{14}^+$ ) originates from a McLafferty rearrangement<sup>22</sup> involving cleavage of the 20,22-bond with one H transfer from C-17. The other diagnostic ion due to this cleavage appeared at  $m/z$  300 ( $\text{C}_{21}\text{H}_{32}\text{O}^+$ ). Conjugated diene sterols **4-8** afforded (23*R*)- and (23*S*)-23-ethyl-5 $\alpha$ -cholestan-3 $\beta$ -ols (**48a,b**) on hydrogenation, confirming the 23-ethyl substitution.

Table V contains NMR data of four 24-methyl-24-homocholesterols, **15-18**, with a conjugated double-bond system in the side chain. The structures of sterols **15-17** were elucidated as the stereoisomeric 24-methyl-24-homocholesta-5,20(22),23-trien-3 $\beta$ -ols. Hydrogenation of sterols **15-17** afforded four saturated 24-methyl-24-homosterols in almost equal proportions. Two (GLC,  $r_{\text{t}}$  (related retention time) 1.44) of them were identified as (24*R*)- and (24*S*)-24-methyl-24-homo-5 $\alpha$ -cholestan-3 $\beta$ -ols (**49a,b**).<sup>2</sup> The other two sterols, **50a,b**, exhibited NMR spectra similar to those of **49a,b**, whereas these moved faster in GLC ( $r_{\text{t}}$  1.24) than the latter. No selectivity is to be expected in the hydrogenation of the  $\Delta^{20(22)}$  bond to afford the 20*R* and 20*S* isomers, as is observed in the hydrogenation of the 24-methyl- $\Delta^{23}$  bond, which gives a mixture of 24*R/S* isomers; also it is known that a (20*S*)-sterol elutes faster than its 20*R* isomer (the separation factor of 20*S*/20*R*  $\approx$  0.9) in GLC.<sup>23,24</sup> Thus the sterols **50a,b**



could have the structures (20*S*,24*R*)- and (20*S*,24*S*)-24-methyl-24-homo-5 $\alpha$ -cholestan-3 $\beta$ -ols, and the hydrogenation evidence supports the structures of the conjugated diene sterols **15-17**. Sterol **18** was assigned the structure (22*E*)-24-methyl-24-homocholesta-5,22,24-trien-3 $\beta$ -ol. Irradiation at  $\delta$  2.13 (1 H, m, C-20) collapsed the doublet at  $\delta$  1.044 (3 H, C-21) into a singlet and the double doublet at  $\delta$  5.393 (1 H,  $J$  = 8.6, 15.9 Hz, C-22) into a doublet ( $J$  = 15.9 Hz). The other coupling partner of the dd signal ( $\delta$  5.393, C-22) must then be the methine proton at C-23 ( $\delta$  5.936, d,  $J$  = 15.6 Hz), and the coupling constants ( $\approx$  16 Hz) of these signals imply that the proton at C-22 and C-23 are trans oriented (22*E*). Irradiation at  $\delta$  2.63 (1 H, m, C-26H) collapsed three doublets at  $\delta$  0.957 and 0.961 (each 3 H, C-29/C-30) and 5.120 (1 H, C-25) into singlets. Hydrogenation of **18** afforded the fully saturated sterols **49a,b**.

The NMR data of the four 24-ethylcholesterols **19-22** with the conjugated diene systems in the side chain are shown in Table VI. The structure of sterol **19** was assigned as 24-ethylcholesta-5,20(22),23-trien-3 $\beta$ -ol, while sterol **20** was shown to have the structure 24-ethylcholesta-5,23,28-trien-3 $\beta$ -ol. Irradiation of the septet at  $\delta$  2.846 (1 H, C-25) collapsed the doublet at  $\delta$  1.052 (6 H, C-26/C-27) into a singlet. Sterol **21** was characterized as (22*E*)-24-ethylcholesta-5,22,24(28)-trien-3 $\beta$ -ol. The 22*E* stereochemistry was based on the coupling constant of the doublet due to the C-23 methine proton ( $J$  = 15.4 Hz), which is consistent with one of the coupling constants of the dd signal of the C-22 methine proton ( $J$  = 8.7, 15.8 Hz), the coupling partner of C-23H. Irradiation of the septet at  $\delta$  2.843 (1 H, C-25) simplified two doublets at  $\delta$  1.021 and 1.031 (each 3 H, C-26/C-27) into singlets. Sterol **22** was characterized as (22*E*)-24-ethylcholesta-5,22,24-trien-3 $\beta$ -ol. The 22*E* configuration was deduced from the coupling

(22) (a) Massey, I. J.; Djerassi, C. *J. Org. Chem.* **1979**, *44*, 2448-2456.  
(b) Wyllie, S. G.; Djerassi, C. *Ibid.* **1968**, *33*, 305-313.

(23) Nes, W. R.; Varkey, T. E.; Krevitz, K. *J. Am. Chem. Soc.* **1977**, *99*, 260-262.

(24) Itoh, T.; Tani, H.; Fukushima, K.; Tamura, T.; Matsumoto, T. *J. Chromatogr.* **1982**, *234*, 65-76.

Table VII.  $^1\text{H}$  NMR Data of Methoxylated Sterols

compound	chemical shift								
	C-18	C-19	C-21	C-26/C-27	C-29	C-24	C-25	C-28	OMe
9	0.696	1.010	0.882	0.905 (d, 6.7)	1.202	5.289	2.530	3.583	3.215
10	0.695	1.008	0.861	0.918 (d, 6.6)	1.217	5.254	2.552	3.594	3.207
11 <sup>a</sup>	0.716	1.011	0.868	0.925 (d, 6.2)	1.209	5.042	2.716	4.110	3.191
12 <sup>a</sup>			(d, 6.5)	0.942 (d, 6.0)	(d, 6.4)	(d, 11.1)	(d, sept, 9.7, 6.4)	(q, 6.6)	
			0.895	0.959 (d, 6.1)	1.221	5.072		4.168	
13	0.694	1.011	0.891	0.856 (d, 6.7)	1.644	3.096		5.524	3.179
14	0.689	1.007	0.882	0.720 (d, 6.8)	1.642	2.938		5.483	3.190
23 <sup>b</sup>	0.695	1.011	0.926	0.731 (dd, 2.5, 6.8) <sup>c</sup>	(d, 6.8)		2.937	1.482	3.160
			(d, 6.5)	0.986 (d, 6.5) <sup>c</sup>			(d, 9.0)		
24 <sup>d</sup>	0.690	1.007	0.917	1.011 (dd, 1.2, 7.0)	1.236		2.714	3.701	3.194
			(d, 6.5)	1.067 (d, 7.0)	(dd, 1.7, 6.5)		(d, sept, 2.8, 7.2)	(q, 6.4)	

<sup>a</sup> The isomeric pair **11** and **12** was not separated. <sup>b</sup> Recorded at 300 MHz. Two signals at  $\delta$  1.72 (1 H, m, C-26H) and 5.303 (1 H, t,  $J = 7.0$  Hz, C-23H) were also observed. <sup>c</sup> Signals from C-29/C-30 methyl protons. <sup>d</sup> Triplet signal at  $\delta$  5.360 (1 H,  $J = 11.5$  Hz, C-23H) was also observed.

Table VIII.  $^1\text{H}$  NMR Data of Steroidal Cyclopropenes

compound	chemical shift						
	C-18	C-19	C-21	C-26/C-27	C-29	C-25	C-28
1 (28R) <sup>a</sup>	0.700	1.010	0.965	1.097 (d, 6.8)	0.999	2.694	1.330
			(d, 6.6)	1.105 (d, 6.8)	(d, 4.5)	(sept, 6.8)	(q, 4.1)
37 (28S) <sup>b</sup>	0.698	1.012	0.984	1.102 (d, 6.9)	1.019	2.701	1.330
			(d, 6.4)	1.107 (d, 6.9)	(d, 4.8)	(sept, 6.8)	(q, 5.0)
2 (23R) <sup>a</sup>	0.692	1.010	1.006	1.099 (d, 6.8)	1.994	2.687	
			(d, 6.0)	1.151 (d, 6.8)	(d, 1.4)	(d, sept, 1.4, 6.4)	
38 (23S)	0.686	1.010	1.009	1.093 (d, 6.9)	2.013	2.630	
			(d, 6.5)	1.118 (d, 6.9)	(d, 1.1)	(d, sept, 1.2, 7.2)	
3 (24S) <sup>c</sup>	0.703	1.011	0.968	0.785 (d, 6.8)	2.021		
			(d, 6.6)	0.792 (d, 6.8)	(t, 1.4)		
36 (24R) <sup>b</sup>	0.703	1.012	0.984	0.782 (d, 6.8)	2.001		
			(d, 6.4)	0.806 (d, 6.8)	(t, 1.4)		

<sup>a</sup> Reference 2. <sup>b</sup> The two isomers **36** and **37** were not separated. <sup>c</sup> Reference 4. Doublet signal at  $\delta$  1.168 (1 H,  $J = 4.4$  Hz, C-24) also was observed.

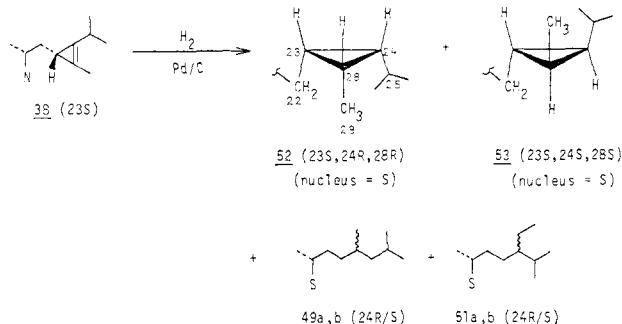
constant of the C-23H (d,  $J = 15.6$  Hz) and C-22H (dd,  $J = 8.6, 15.5$  Hz) signals. Sterols **20–22** gave (24R)- and (24S)-24-ethyl-5 $\alpha$ -cholestan-3 $\beta$ -ols (**51a,b**) on hydrogenation.

**Methoxylated Sterols.** Table VII shows NMR data of eight sterols, **9–14**, **23**, and **24**, which possess a methoxy group in the side chain. These sterols exhibited a molecular ion ( $M^+$ ) at  $m/z$  442 ( $\text{C}_{30}\text{H}_{50}\text{O}^+$ ) accompanied by a peak at  $m/z$  410 ( $\text{C}_{29}\text{H}_{48}\text{O}^+$ ,  $M^+ - \text{MeOH}$ ), suggesting the presence of a methoxy group, which was substantiated by the occurrence of the methyl singlet at around  $\delta$  3.2 in the NMR spectra. That the methoxy group is located in a monounsaturated side chain was supported by the existence of a diagnostic ion at  $m/z$  371 ( $\text{C}_{19}\text{H}_{27}\text{O}^+$ ,  $M^+ - \text{side chain} - 2\text{H}$ ) in the mass spectra. Sterols **9** and **10** were characterized as the stereoisomeric 28-methoxy-23-ethylcholesta-5,23-dien-3 $\beta$ -ols. Although sterols **11** and **12** occurred as a mixture (1:1) and were not separated, the NMR data of this mixture serve to characterize it as the stereoisomers of the methoxy sterols **9** and **10**. The

structure of sterols **13** and **14** were assigned as the stereoisomeric 24-methoxy-23-ethylcholesta-5,23(28)-dien-3 $\beta$ -ols. These sterols yielded a fragment ion at  $m/z$  399 ( $\text{C}_{27}\text{H}_{43}\text{O}_2^+$ ) as the base peak in the mass spectra formed by 24,25-bond cleavage and elimination of a terminal isopropyl group from the molecular ion. The structure 25-methoxy-24-methyl-24-homocholesta-5,23-diene-3 $\beta$ -ol was established for the sterol **23**. Irradiation of the dd methyl signal at  $\delta$  0.731 (C-29 or C-30) simplified the multiplet at  $\delta$  1.72 (1 H, C-26). Furthermore, irradiation at  $\delta$  1.72 (m) collapsed the doublets at  $\delta$  0.986 (3 H, C-30 or C-29) and 2.937 (1 H, C-25) into singlets accompanied with a simplification of the multiplet at  $\delta$  1.72. Thus the spin-decoupling experiment supported the structure **23**. The mass spectral data are consistent with this structure since the base peak corresponded to an ion at  $m/z$  399 ( $M^+ - \text{C}_3\text{H}_7$ ) as was observed for sterols **13** and **14**. Sterol **24** was assigned the 28-methoxy-24-ethylcholesta-5,23-dien-3 $\beta$ -ol structure.



**Steroidal Cyclopropenes.** The NMR data of six steroidal cyclopropenes, **1**–**3** and **36**–**38**, are shown in Table VIII. The structure elucidation and the assignment of NMR signals of (28*R*)-calysterol (**1**),<sup>2</sup> (23*R*)-23*H*-isocalysterol (**2**),<sup>2</sup> and (24*S*)-24*H*-isocalysterol (**3**)<sup>4</sup> were described in our previous articles. That sterol **38** is the stereoisomer at C-23 (i.e., 23*S*) of the steroidal cyclopropene **2** (23*R*) can be recognized by the similarity of its NMR pattern with that of **2**. Irradiation of the center of the double septet at  $\delta$  2.630 (1 H,  $J = 1.2, 7.2$  Hz, C-25) simplified the two doublets at  $\delta$  1.093 and 1.118 (each 3 H and  $J = 6.9$  Hz, C-26/C-27) and collapsed the low-field shifted olefinic methyl doublet at  $\delta$  2.013 ( $J = 1.1$  Hz, C-29) into a singlet, indicating that the coupling partner of the C-29 methyl protons is the C-25 methine proton; the magnitude of the coupling is consistent with that of  $^4J$  (H, H) coupling. Therefore, the C-29 methyl group is linked to the cyclopropene functionality.<sup>2,4</sup> In order to confirm the stereochemistry (23*S*) of cyclopropene **38**, it was subjected to catalytic hydrogenation over palladium/charcoal. Assuming syn hydrogenation to be operative on both sides of the double bond of **38**, one may encounter two possible diastereoisomeric cyclopropanes, (23*S*,24*R*,28*R*)- (**52**) and (23*S*,24*S*,28*S*)-23,24-dihydrocalysterols (**53**). On the assumption that steric factors (hydrogen attack opposite to the C-23 alkyl rest) would play the dominant stereochemical role,<sup>25</sup> the all-cis-substituted cyclopropane **52** (23*S*,24*R*,28*R*) would be expected to be the kinetically controlled major product. Indeed, cyclopropane **38** yielded cyclopropane **52**<sup>2</sup> as the major (53%) hy-



drogenation product accompanied by the cyclopropane **53** (23*S*,24*S*,28*S*; 11%) and four ring-opening products, (24*R*)- (11%) and (24*S*)- (11%) 24-methyl-24-homo-5 $\alpha$ -cholestan-3 $\beta$ -ols (**49a,b**) and (24*R*)- (6%) and (24*S*)- (6%) 24-ethyl-5 $\alpha$ -cholestan-3 $\beta$ -ols (**51a,b**). From the hydrogenation evidence we can conclude that cyclopropene **38** has the 23*S* configuration and hence the structure (23*S*)-23*H*-isocalysterol is given for this sterol. The stereochemistry of the new cyclopropane **53** (HPLC,  $r_t$  1.79; GLC,  $r_t$  1.39) was deduced from the similarity of its NMR data (see Experimental Section) with those of the known cyclopropane possessing the completely opposite configuration from that of **53**, (23*R*,24*R*,28*R*)-23,24-dihydrocalysterol (HPLC,  $r_t$  1.89; GLC,  $r_t$  1.38).<sup>2</sup>

Cyclopropenes **36** and **37** did not separate even after several HPLC fractionations on an Altex column, and the structure of these cyclopropenes was assigned as the mixture. One of the constituents could be characterized as the 24*R* isomer of cyclopropene **3** (24*S*), i.e., (24*R*)-24*H*-isocalysterol (**36**), because it exhibited an NMR pattern very similar to that of **3** (Table VIII); we have already shown before with the stereoisomeric pair of cyclopropenes **2** and **38** that these show nearly identical NMR patterns. With this in mind, since the other constituent cyclopropene exhibited an NMR pattern so similar to that of cyclopropene **1** (28*R*), the new sterol could be assigned the (28*S*)-calysterol (**37**) structure.

**Shorter Side Chain Sterols.** Three shorter side chain sterols, goneribol (**33**), 26,27-dinorcholest-5-en-23-yn-3 $\beta$ -ol (**34**), and cholest-5-en-23-yn-3 $\beta$ -ol (**35**) were identified by direct comparison

of their chromatographic and spectroscopic data with those of authentic **33**,<sup>26</sup> **34**,<sup>20</sup> and **35**,<sup>20</sup> respectively.

## Experimental Section

**General Methods and Materials.** GLC was performed on a Hewlett-Packard 402 A chromatograph equipped with a flame-ionization detector (carrier gas He, temperature 260 °C). A glass column (1.8 m  $\times$  2 mm i.d.) containing 3% OV-17/GCQ was used for analytical purpose and a glass column (1.8  $\times$  6 mm i.d.) containing 3% OV-25/GCQ equipped with effluent splitter (1:4) for preparative work. Relative retention times ( $r_t$ ) were expressed relative to cholesterol. Low-resolution mass spectra were recorded on a Ribermag GLC-MS system with fused silica capillary column and a SADR data system. High-resolution mass spectra were recorded on a Varian MAT-711 double-focusing spectrometer equipped with a PDP-11/45 computer. <sup>1</sup>H NMR spectra were recorded on a Bruker HXS-360 (360 MHz) or on a Nicolet NMC-300 (300 MHz) spectrometer in CDCl<sub>3</sub> with SiMe<sub>4</sub> as internal standard. Preparative HPLC was carried out on a Waters Associates HPLC system (M 6000 pump, R 403 differential refractometer) with an Altex Ultrasphere ODS 5  $\mu$ m (25 cm  $\times$  10 mm i.d., two columns in series) reverse-phase column with methanol/water (95:5) as the eluent. The  $r_t$  were expressed relative to (28*R*)-calysterol (**1**). UV spectra (ethanol) were recorded on a Cary-14 spectrophotometer. (28*R*)-Calysterol (**1**) and (23*R*)-23*H*-isocalysterol (**2**) used in this study were isolated from the marine sponge *Calyx niceensis*.

**Acid-Catalyzed and Photochemical Isomerization.** **Acid-Catalyzed Isomerization.** (a) Isomerization by sulfuric acid/methanol: Sterol (20 mg) in sulfuric acid (0.5 mL)/methanol (10 mL) was refluxed under an atmosphere of argon for 3 h. The product, extracted with diethyl ether, was neutralized by washing with sodium bicarbonate solution, filtered through Florisil, and fractionated by HPLC on an Altex column. (b) Isomerization by *p*-toluenesulfonic acid/benzene: Sterol (20 mg) in 0.15% *p*-toluenesulfonic acid/benzene (10 mL) was allowed to stand in an argon atmosphere at room temperature in the dark for 10 days. The product was then worked up as described above and fractionated by HPLC.

**Photochemical Isomerization.** Sterol (30 mg) in isooctane (50 mL, spectroscopic grade) in an argon atmosphere was irradiated with an ACE-Hanovia 450-W medium-pressure mercury lamp and a water-cooling quartz immersion well for 10 h. The product was filtered through Florisil and fractionated by HPLC.

**Catalytic Hydrogenation of Conjugated Diene Sterols.** Hydrogenation of conjugated diene sterols ( $\approx 1$  mg) was performed in ethanol (4 mL) over PtO<sub>2</sub> catalyst (10 mg) at atmospheric pressure and temperature for 16 h. The hydrogenation product was filtered through Florisil and fractionated by HPLC on an Altex column. Conjugated diene sterols **4**–**8** afforded a 1:1 mixture of fully saturated 23-ethylsterols upon hydrogenation, (23 $\xi$ )-23-ethylcholestanol (HPLC,  $r_t$  1.94; GLC,  $r_t$  1.28; **48a,b**) and (23 $\xi$ )-23-ethylcholestanol (HPLC,  $r_t$  2.02; GLC,  $r_t$  1.33; **48b,a**), which were identified by comparison of chromatographic and spectral data with those of authentic compounds.<sup>2</sup>

Hydrogenation of sterols **15**–**17** afforded four fully saturated 24-methyl-24-homosterols, (24 $\xi$ )-24-methyl-24-homocholestanol (HPLC,  $r_t$  2.09; GLC,  $r_t$  1.44, 25%; **49a,b**), (24 $\xi$ )-24-methyl-24-homocholestanol (HPLC,  $r_t$  2.11; GLC,  $r_t$  1.44, 25%; **49b,a**), (20*S*,24 $\xi$ )-24-methyl-24-homocholestanol (HPLC,  $r_t$  2.02; GLC,  $r_t$  1.24, 23%; **50a,b**), and (20*S*,24 $\xi$ )-24-methyl-24-homocholestanol (HPLC,  $r_t$  2.06; GLC,  $r_t$  1.24, 27%; **50b,a**), while hydrogenation of sterol **18** yielded a 1:1 mixture of fully saturated sterols **49a,b** and **49b,a**. These sterols were identified by comparison of their chromatographic and spectral data with those of authentic sterols.<sup>2</sup> Sterols **20**–**22** gave a 1:1 mixture (HPLC,  $r_t$  2.16; GLC,  $r_t$  1.59) of (24*R*)- and (24*S*)-24-ethylcholestanols (**51a,b**) upon hydrogenation. Identification of these sterols was achieved by comparison of chromatographic and spectral data with those of authentic compounds.<sup>2</sup>

**Catalytic Hydrogenation of (23*S*)-23*H*-Isocalysterol (**38**).** Hydrogenation of cyclopropene **38** (5 mg) was performed in ethanol (5 mL) over 10% Pd/C (5 mg) at 2 atm of H<sub>2</sub> and room temperature for 30 h. The product was filtered through Florisil and fractionated by HPLC. This hydrogenation yielded two cyclopropanes, (23*S*,24*R*,28*R*)-23,24-dihydrocalysterol (HPLC,  $r_t$  1.91; GLC,  $r_t$  1.91, 53%, **52**) and (23*S*,24*S*,28*S*)-23,24-dihydrocalysterol (HPLC,  $r_t$  1.79; GLC,  $r_t$  1.39, 11%, **53**), and four ring-opened products, a 1:1 mixture each of (24*R*)- and (24*S*)-24-methyl-24-homocholestanols (**49a,b**, 22%) and (24*R*)- and (24*S*)-24-ethylcholestanols (**51a,b**, 12%). Identification of **49a,b**, **51a,b**, and **52** was accomplished by comparison of their chromatographic and

(25) Lukina, M. Y.; Nesmeyanova, O. A.; Rudashevskaya, T. Y. *Dokl. Akad. Nauk SSSR* **1967**, *174*, 1101–1104.

(26) Carlson, R. M. K.; Popov, S.; Massey, I. J.; Delseth, C.; Ayanoglu, E.; Varkony, T. H.; Djerassi, C. *Bioorg. Chem.* **1978**, *7*, 453–479.

spectral data with those of authentic specimens.<sup>2</sup>

**Physical Data.** For  $r_{\text{H}}$  in HPLC and GLC see Tables I–III, and for  $^1\text{H}$  NMR see Tables IV–VIII. The mass spectral (MS) data [ $m/z$  (assignment, relative intensity)] of the new sterols, the UV data of the conjugated diene sterols, and some experimental data are given below.

**Conjugated Diene Sterols.** **23-Ethylcholesta-5,22,24-trien-3 $\beta$ -ol (4):**  $m/z$  410.355 91 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 23%, calcd 410.354 85), 395.328 41 ( $\text{C}_{28}\text{H}_{43}\text{O}$ , 0.5), 392.342 93 ( $\text{C}_{29}\text{H}_{44}$ , 0.3), 300.243 63 ( $\text{C}_{21}\text{H}_{32}\text{O}$ , 6), 285.220 72 ( $\text{C}_{20}\text{H}_{29}\text{O}$ , 2), 282.232 11 ( $\text{C}_{21}\text{H}_{30}$ , 2), 271.206 74 ( $\text{C}_{19}\text{H}_{27}\text{O}$ , 9), 267.211 67 ( $\text{C}_{20}\text{H}_{27}$ , 3), 255.212 89 ( $\text{C}_{19}\text{H}_{27}$ , 3), 230.167 82 ( $\text{C}_{16}\text{H}_{22}\text{O}$ , 2), 215.178 52 ( $\text{C}_{16}\text{H}_{23}$ , 0.4), 137.134 53 ( $\text{C}_{10}\text{H}_{17}$ , 70), 110.110 16 ( $\text{C}_8\text{H}_{14}$ , 100);  $\text{UV}_{\text{max}}$   $\lambda$  230 nm.

**23-Ethylcholesta-5,22,24-trien-3 $\beta$ -ol (5):**  $m/z$  410.353 74 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 31%), 395 (0.5), 392 (2), 300 (8), 285 (4), 282 (4), 271 (16), 267 (3), 255 (4), 230 (1), 215 (1), 213 (2), 137 (99), 110 (100);  $\text{UV}_{\text{max}}$   $\lambda$  229 nm.

**23-Ethylcholesta-5,23,28-trien-3 $\beta$ -ol (6):**  $m/z$  410.354 64 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 8%), 395 (6), 392 (0.6), 377 (0.6), 367 (9), 300 (25), 285 (8), 283 (5), 282 (5), 271 (100), 267 (8), 253 (7), 241 (4), 230 (2), 215 (4), 213 (5);  $\text{UV}_{\text{max}}$   $\lambda$  232 nm.

**23-Ethylcholesta-5,23,28-trien-3 $\beta$ -ol (7):**  $m/z$  410.357 30 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 6%), 395 (4), 392 (2), 267 (2), 300 (23), 285 (9), 283 (7), 282 (4), 271 (100), 267 (13), 253 (7), 241 (3), 230 (2), 215 (4), 213 (4);  $\text{UV}_{\text{max}}$   $\lambda$  235 nm.

**23-Ethylcholesta-5,23(28),24-trien-3 $\beta$ -ol (8):**  $m/z$  410.355 17 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 5%), 395 (0.3), 392 (0.3), 300 (9), 285 (3), 282 (4), 271 (8), 267 (5), 253 (1), 230 (1), 215 (1), 110 (100);  $\text{UV}_{\text{max}}$   $\lambda$  227 nm.

**24-Methyl-24-homocholesta-5,20(22),23-trien-3 $\beta$ -ol (15).** Since this sterol formed a homogeneous mixture with sterol 16 in HPLC, separation of this sterol from 16 was achieved by preparative GLC. Determination of NMR before and after GLC revealed that no isomerization occurred during GLC separation;  $m/z$  410.357 19 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 100%), 395 (1), 392 (2), 377 (2), 325 (1), 299 (2), 272 (13), 271 (9), 229 (9), 213 (4), 211 (5), 164 (60), 138 (78), 108 (81);  $\text{UV}_{\text{max}}$   $\lambda$  252 nm.

**24-Methyl-24-homocholesta-5,20(22),23-trien-3 $\beta$ -ol (16):**  $m/z$  (GLC–MS) 410 ( $\text{M}^+$ , 12), 392 (0.1), 377 (1), 325 (0.5), 299 (0.2), 272 (6), 271 (5), 229 (4), 211 (5), 164 (47), 138 (99), 108 (100);  $\text{UV}_{\text{max}}$   $\lambda$  252 nm.

**24-Methyl-24-homocholesta-5,20(22),23-trien-3 $\beta$ -ol (17):**  $m/z$  410.352 40 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 100%), 395 (2), 392 (1), 325 (2), 300 (3), 299 (4), 271 (50), 267 (3), 253 (5), 229 (6), 213 (5), 164 (39), 138 (61), 108 (61);  $\text{UV}_{\text{max}}$   $\lambda$  252 nm.

**(22E)-24-Methyl-24-homocholesta-5,22,24-trien-3 $\beta$ -ol (18):**  $m/z$  410.354 50 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 38%), 395 (3), 392 (3), 377 (1), 300 (38), 285 (10), 282 (9), 271 (100), 267 (11), 255 (22), 253 (8), 230 (3), 213 (6), 137 (60), 109 (44);  $\text{UV}_{\text{max}}$   $\lambda$  234 nm.

**24-Ethylcholesta-5,20(22),23-trien-3 $\beta$ -ol (19):**  $m/z$  410.351 24 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 100%), 395 (1), 377 (1), 272 (8), 271 (8), 255 (2), 239 (1), 229 (5), 211 (4), 164 (45), 138 (57), 121 (61);  $\text{UV}_{\text{max}}$   $\lambda$  252 nm.

**24-Ethylcholesta-5,23,28-trien-3 $\beta$ -ol (20):**  $m/z$  410.353 01 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 12%), 300 (21), 293 (8), 271 (100), 255 (12), 253 (8), 215 (16);  $\text{UV}_{\text{max}}$   $\lambda$  231 nm.

**(22E)-24-Ethylcholesta-5,22,24(28)-trien-3 $\beta$ -ol (21):**  $m/z$  410.352 42 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 32%), 395 (2), 392 (3), 300 (23), 285 (9), 283 (8), 282 (8), 271 (100), 267 (9), 255 (15), 230 (5), 215 (6), 137 (35), 110 (42);  $\text{UV}_{\text{max}}$   $\lambda$  234 nm.

**(22E)-24-Ethylcholesta-5,22,24-trien-3 $\beta$ -ol (22):**  $m/z$  410.355 57 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 41%), 392 (3), 377 (1), 314 (2), 300 (4), 283 (6), 271 (29), 255 (6), 253 (4), 239 (2), 215 (2), 213 (4), 137 (58), 110 (100);  $\text{UV}_{\text{max}}$   $\lambda$  243 nm.

**Methoxylated Sterols.** **28-Methoxy-23-ethylcholesta-5,23-dien-3 $\beta$ -ol (9):**  $m/z$  442.381 14 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 24%, calcd 442.381 06), 410.354 63 ( $\text{C}_{29}\text{H}_{46}\text{O}$ , 9), 399.325 73 ( $\text{C}_{27}\text{H}_{43}\text{O}_2$ , 78), 395.329 22 ( $\text{C}_{28}\text{H}_{43}\text{O}$ , 6), 367.300 81 ( $\text{C}_{26}\text{H}_{39}\text{O}$ , 10), 301.352 39 ( $\text{C}_{21}\text{H}_{32}\text{O}$ , 44), 300.246 65 ( $\text{C}_{21}\text{H}_{32}\text{O}$ , 92), 283.240 85 ( $\text{C}_{21}\text{H}_{31}$ , 58), 282.234 42 ( $\text{C}_{21}\text{H}_{30}$ , 20), 271.205 19 ( $\text{C}_{19}\text{H}_{27}\text{O}$ , 100), 253.193 80 ( $\text{C}_{19}\text{H}_{25}$ , 7), 241.196 58 ( $\text{C}_{16}\text{H}_{25}$ , 12), 227.179 27 ( $\text{C}_{17}\text{H}_{23}$ , 9), 215.179 09 ( $\text{C}_{16}\text{H}_{23}$ , 21).

**28-Methoxy-23-ethylcholesta-5,23-dien-3 $\beta$ -ol (10):**  $m/z$  442.381 85 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 13%), 427 (2), 410 (14), 399 (46), 395 (9), 381 (2), 367 (7), 301 (22), 300 (46), 283 (36), 271 (100), 253 (9), 241 (7), 229 (7), 215 (11), 110 (52).

**Mixture of Two Stereoisomeric 28-Methoxy-23-ethylcholesta-5,23-dien-3 $\beta$ -ols (11, 12):**  $m/z$  442.381 39 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 6%), 410 (7), 399 (6), 395 (4), 367 (2), 353 (1), 301 (11), 300 (31), 285 (7), 283 (13), 282 (10), 271 (37), 253 (3), 241 (4), 215 (6), 110 (87), 73 (100).

**24-Methoxy-23-ethylcholesta-5,23(28)-dien-3 $\beta$ -ol (13):**  $m/z$

442.382 50 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 8%), 410 (3), 399 (100), 367 (74), 349 (29), 300 (5), 285 (4), 283 (4), 271 (30), 253 (6), 241 (4), 215 (5), 183 (14), 127 (40), 99 (69).

**24-Methoxy-23-ethylcholesta-5,23(28)-dien-3 $\beta$ -ol (14):**  $m/z$  442.378 68 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 6%), 410 (3), 399 (100), 367 (64), 349 (26), 300 (8), 271 (33), 255 (5), 253 (4), 229 (5), 215 (5), 213 (7).

**25-Methoxy-24-methyl-24-homocholesta-5,23-dien-3 $\beta$ -ol (23):**  $m/z$  442.384 35 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 2%), 427 (1), 410 (3), 399 (100), 386 (5), 381 (3), 368 (1), 367 (3), 349 (2), 301 (2), 283 (7), 271 (5), 255 (3), 241 (2).

**28-Methoxy-24-ethylcholesta-5,23-dien-3 $\beta$ -ol (24):**  $m/z$  442.379 08 ( $\text{M}^+$ ,  $\text{C}_{30}\text{H}_{50}\text{O}_2$ , 22%), 427 (9), 410 (37), 399 (54), 395 (4), 377 (2), 367 (6), 314 (13), 301 (21), 300 (14), 283 (40), 371 (100), 255 (4), 241 (7), 215 (17), 127 (85).

**Steroidal Cyclopropanes and Other Sterols.** **Mixture of (24R)-24H-Isocalysterol (36) and (28S)-Calysterol (37):**  $m/z$  410.363 77 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 18%), 395 (7), 392 (4), 377 (4), 367 (100), 349 (4), 300 (23), 271 (99), 267 (17), 253 (17), 231 (9), 213 (15), 110 (80), 95 (78).

**(23S)-23H-Isocalysterol (38):**  $m/z$  410.355 64 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 22%), 392.343 71 ( $\text{C}_{29}\text{H}_{44}$ , 2), 314.261 15 ( $\text{C}_{22}\text{H}_{34}\text{O}$ , 5), 300.239 16 ( $\text{C}_{21}\text{H}_{32}\text{O}$ , 7), 283.242 07 ( $\text{C}_{21}\text{H}_{31}$ , 22), 271.206 92 ( $\text{C}_{19}\text{H}_{27}\text{O}$ , 100), 253.194 86 ( $\text{C}_{19}\text{H}_{25}$ , 10), 241.191 72 ( $\text{C}_{18}\text{H}_{25}$ , 5), 227.181 20 ( $\text{C}_{17}\text{H}_{23}$ , 5), 215.178 85 ( $\text{C}_{16}\text{H}_{23}$ , 7), 213.164 05 ( $\text{C}_{16}\text{H}_{21}$ , 8), 96.093 63 ( $\text{C}_7\text{H}_{12}$ , 87), 95.086 65 ( $\text{C}_7\text{H}_{11}$ , 61).

**(20S,24E)-24-Methyl-24-homocholestan-3 $\beta$ -ol (50a,b):**  $^1\text{H}$  NMR (300 MHz)  $\delta$  0.651 (3 H, s, C-18), 0.804 (3 H, s, C-19), 0.799 ( $J = 6.6$  Hz), 0.816 ( $J = 7.1$  Hz), 0.839 ( $J = 6.6$  Hz), and 0.862 ( $J = 7.0$  Hz), (each 3 H, d, C-21, C-28, C-29, C-30), 3.59 (1 H, m, C-3 $\alpha$ ); MS,  $m/z$  416.401 05 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{46}\text{O}$ , 100%, calcd 416.401 79), 401.378 85 ( $\text{C}_{28}\text{H}_{44}\text{O}$ , 14), 398.386 96 ( $\text{C}_{29}\text{H}_{50}$ , 10), 383.368 35 ( $\text{C}_{28}\text{H}_{47}$ , 6), 290.300 66 ( $\text{C}_{21}\text{H}_{38}$ , 5), 275.272 36 ( $\text{C}_{20}\text{H}_{35}$ , 2), 257.226 24 ( $\text{C}_{19}\text{H}_{29}$ , 4), 248.215 41 ( $\text{C}_{17}\text{H}_{28}\text{O}$ , 6), 234.197 93 ( $\text{C}_{16}\text{H}_{26}\text{O}$ , 39), 233.192 41 ( $\text{C}_{16}\text{H}_{25}\text{O}$ , 39).

**(20S,24E)-24-Methyl-24-homocholestan-3 $\beta$ -ol (50b,a):**  $^1\text{H}$  NMR (300 MHz)  $\delta$  0.648 (3 H, s, C-18), 0.805 (3 H, s, C-19), 0.804 ( $J = 6.3$  Hz), 0.825 ( $J = 6.2$  Hz), 0.837 ( $J = 7.0$ ) and 0.861 ( $J = 7.2$  Hz), (each 3 H, d, C-21, C-28, C-29, C-30), 3.59 (1 H, m, C-3 $\alpha$ ); MS (GLC–MS),  $m/z$  416 ( $\text{M}^+$ , 82), 401 (16), 398 (6), 383 (6), 290 (10), 273 (3), 257 (3), 248 (10), 233 (100), 215 (82).

**(23S,24S,28S)-23,28-Dihydrocalysterol-3 $\beta$ -ol (53):**  $^1\text{H}$  NMR (360 MHz)  $\delta$  0.651 (3 H, s, C-18), 0.801 (3 H, s, C-19), 0.980 (3 H, d,  $J = 6.2$ , C-21 Hz), 0.931 and 0.998 (each 3 H, d,  $J = 6.5$ , C-26, C-27 Hz), 1.031 (3 H, d,  $J = 6.3$ , C-29 Hz), 0.07, and 0.14 (each 1 H, m, C-23, C-24), 0.40 (1 H, m, C-28), 3.59 (1 H, m, C-3 $\alpha$ ). That the multiplet at  $\delta$  0.40 (1 H) is due to C-28H was supported by the following spin-decoupling experiment. Irradiation at  $\delta$  1.031 (3 H, d) simplified the multiplet at  $\delta$  0.40 (1 H), while irradiation of this multiplet collapsed the doublet at  $\delta$  1.031 into a singlet and simplified two multiplets at  $\delta$  0.07 (1 H) and 0.14 (1 H). MS,  $m/z$  414.383 86 ( $\text{M}^+$ ,  $\text{C}_{29}\text{H}_{50}\text{O}$ , 12%, calcd 414.386 14), 399.362 97 ( $\text{C}_{28}\text{H}_{47}\text{O}$ , 3), 396.376 85 ( $\text{C}_{29}\text{H}_{48}$ , 1), 371.330 77 ( $\text{C}_{26}\text{H}_{43}\text{O}$ , 2), 358.318 48 ( $\text{C}_{25}\text{H}_{42}\text{O}$ , 3), 316.277 74 ( $\text{C}_{22}\text{H}_{36}\text{O}$ , 28), 302.261 77 ( $\text{C}_{21}\text{H}_{34}\text{O}$ , 34), 287.238 08 ( $\text{C}_{20}\text{H}_{31}\text{O}$ , 10), 285.259 54 ( $\text{C}_{21}\text{H}_{33}$ , 19), 273.211 25 ( $\text{C}_{19}\text{H}_{29}\text{O}$ , 100), 257.227 22 ( $\text{C}_{19}\text{H}_{29}$ , 11), 255.210 73 ( $\text{C}_{19}\text{H}_{27}$ , 9), 233.190 79 ( $\text{C}_{16}\text{H}_{25}\text{O}$ , 9), 229.196 09 ( $\text{C}_{17}\text{H}_{25}$ , 5), 215.178 91 ( $\text{C}_{16}\text{H}_{23}$ , 9).

**Acknowledgment.** Financial support was provided by NIH Grants GM-06840 and GM-28352. We thank L. N. Li for preliminary experiments, Dr. W. C. M. C. Koke for valuable suggestions, A. Wegmann for mass spectral measurements, Dr. L. Durham for the 360-MHz NMR spectra, and Dr. B. V. Crist for the 300-MHz NMR spectra. Use of the 360-MHz NMR spectrometer was made possible by grants from NSF (GP-23633) and NIH (RR-0711) and the 300-MHz NMR spectrometer by a grant from NSF (CHE81-09064).

**Registry No.** 1, 57331-04-1; 2, 83511-84-6; 3, 84582-62-7; 4, 85735-27-9; 5, 85735-28-0; 6, 85735-29-1; 7, 85735-30-4; 8, 85735-31-5; 9, 85735-32-6; 10, 85735-33-7; 11, 85735-34-8; 12, 85735-35-9; 13, 85735-36-0; 15, 85735-37-1; 18, 85735-38-2; 19, 85735-39-3; 20, 85735-40-6; 21, 85735-41-7; 22, 85735-42-8; 23, 85735-43-9; 24, 85735-44-0; 33, 1042-59-7; 34, 63015-89-4; 35, 63015-91-8; 36, 85798-17-0; 37, 85798-18-1; 38, 85798-19-2; 48a, 83542-21-6; 48b, 83572-16-1; 49a, 83542-23-8; 49b, 83542-22-7; 50a, 85798-20-5; 50b, 85798-21-6; 51a, 83-45-4; 51b, 55529-51-6; 52, 83542-17-0; 53, 85798-22-7.