Reaction of 24,28-Epoxides of Sterol Side Chain with Boron Trifluoride Etherate[1]

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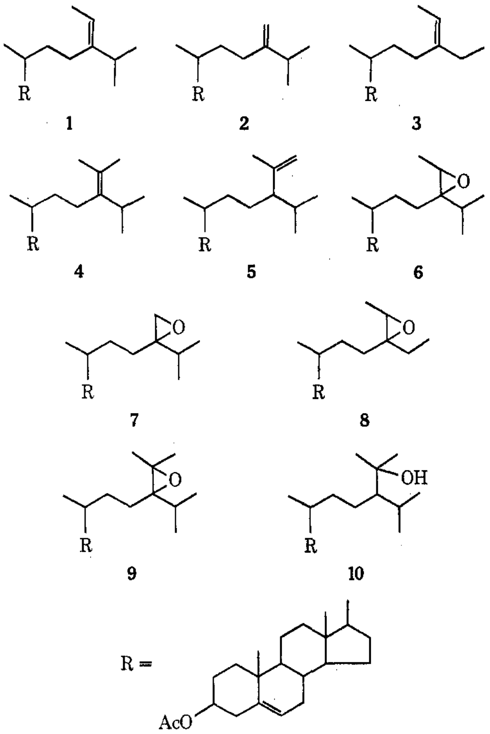
Brief treatment of 24,28-epoxystigmast-5-en-3β-yl acetate (6) with boron trifluoride etherate gave a fragmentation product, desmosteryl acetate (11, 35%), together with 24-acetylcholesteryl acetate (12, 45%) and 24-formyl-24-methylcholesteryl acetate (13, 12%). By contrast, when the analogous epoxides, 24,28-epoxyergost-5-en-3β-yl acetate (7), 24,28-epoxy-26-norstigmast-5-en-3β-yl acetate (8), and 24,28-epoxy-28-methylstigmast-5-en-3β-yl acetate (9) were treated with this reagent, no fragmentation reaction occurred, but 24-formylcholesta-3,5-diene (15, 12%), 24-acetyl-26-norcholesteryl acetate (14, 100%), and 24-acetyl 24-methylcholesteryl acetate (16, 22%) were obtained, respectively. The reactions of epoxide 6 with other Lewis acids and protonic acids are also described.

While the BF_3-catalyzed reaction of epoxides in the steroidal nucleus has been extensively studied,[2] the investigation of side-chain epoxides is relatively limited.[3] In continuation of our studies on the chemical reactivity of the side-chain double bond of fucosteryl acetate (1) (Chart I),[4] we have found a novel fragmentation reaction of 24,28-epoxystigmast-5-en-3β-yl acetate (6) to give desmosteryl acetate (11) by brief treatment with boron trifluoride etherate.[5] A similar reaction seems to occur in insects during the dealkylation of β-sitosterol to cholesterol, from the evidence that tritiated 24,28-epoxystigmast-5-en-3β-ol was shown to be effectively transformed into cholesterol in silkworm.[6]

CHART I



Details on the reactions of the epoxide will be described in this paper. Furthermore, to test the effect of structural variations of the epoxide on the fragmentation reaction, several analogous epoxides (7, 8, and 9) were prepared and their reaction with boron trifluoride etherate was examined. The influence of various acids on the reaction behavior was also tested.

Results and Discussion

Preparation of Epoxides.—The following epoxides were prepared: 24,28-epoxystigmast-5-en-3β-yl acetate (6), 24,28-epoxyergost-5-en-3β-yl acetate (7), 24,28-epoxy-26-norstigmast-5-en-3β-yl acetate (8), and 24,28-epoxy-28-methylstigmast-5-en-3β-yl acetate (9). 24-Methylenecholesteryl acetate (2) was synthesized by a Wittig reaction of 24-oxocholeteryl acetate,[7] prepared from fucosteryl acetate by ozonolysis. Similarly 26-norfucosteryl acetate (3) was obtained in 20% yield from 24-oxo-26-norcholesteryl acetate[4] by a Wittig reaction with ethylenetriphenylphosphorane. Treatment of 1, 2, or 3 with 1 equiv of *m*-chloroperbenzoic acid afforded the corresponding epoxides, 6, 7, and 8 in the yield of 75, 18, and 73%, respectively.

The attempted preparation of 24-isopropylidenecholesteryl acetate (4) by a Wittig reaction of 24-oxocholesteryl acetate with isopropylidenetriphenylphosphorane failed, probably because of severe steric hindrance and the tetrasubstituted nature of the resulting olefin.[8] Therefore, an alternative route was explored. 24-Acetylcholesteryl acetate (12)[5] by a Grignard reaction with methylmagnesium iodide afforded 28-hydroxy-24-isopropylcholesteryl acetate (10) in 47% yield. Dehydration of 10 with phosphorus oxychloride gave a mixture of olefins (4 and 5, in a 1:3 ratio by glc analysis), which was directly (without separation) treated with a 0.5 equiv of *m*-chloroperbenzoic acid. The expected epoxide (9) and the olefin (5) were separated in yields of 28 and 48% by column chromatography of the crude product.

Reaction of Epoxides with Acids.—Treatment of 6 with an excess of boron trifluoride etherate in benzene for 10 sec at room temperature yielded desmosteryl acetate (11, 35%), 24-acetylcholesteryl acetate (12, 45%), and 24-formyl-24-methylcholesteryl acetate [13, 12%, 9.53 ppm (s, 1 H)]. A reasonable pathway of this reaction is the following (Scheme I). Regiospecific

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[1] This is part VI in the series of "Studies on Steroids." For part V see *Chem. Pharm. Bull.*, **21**, 457 (1973).

[2] D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanism," Elsevier, Amsterdam, 1968, Chapter 8, p 353.

[3] L. H. Briggs, J. P. Bartley, and P. S. Rutledge, *Tetrahedron Lett.*, 1237 (1970).

[4] N. Ikekawa, Y. Honma, N. Morisaki, and K. Sakai, *J. Org. Chem.*, **35**, 4145 (1970).

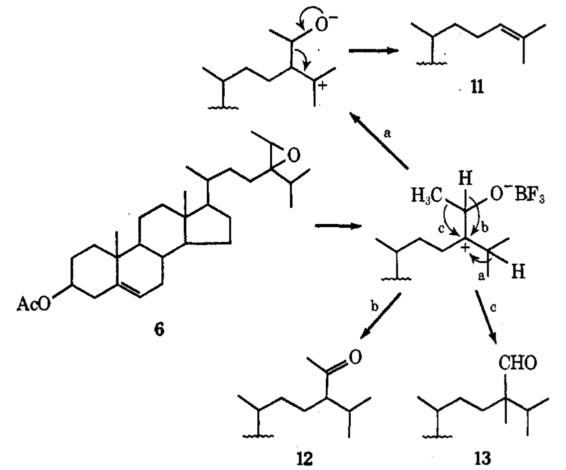
[5] N. Ikekawa, M. Morisaki, H. Ohtaka, and Y. Chiyoda, *Chem. Commun*, 1498 (1971).

[6] M. Morisaki, H. Ohtaka, M. Okubayashi, N. Ikekawa, Y. Horie, and S. Nakasone, *J. Chem. Soc., Chem. Commun.*, 1275 (1972).

[7] D. R. Idler and U. H. M. Fagerlund, *J. Amer. Chem. Soc.*, **79**, 1988 (1957).

[8] For a review of the Wittig reaction see A. Maercker, "Organic Reactions," Vol. 14, Wiley, New York, N. Y., 1965, p 270.

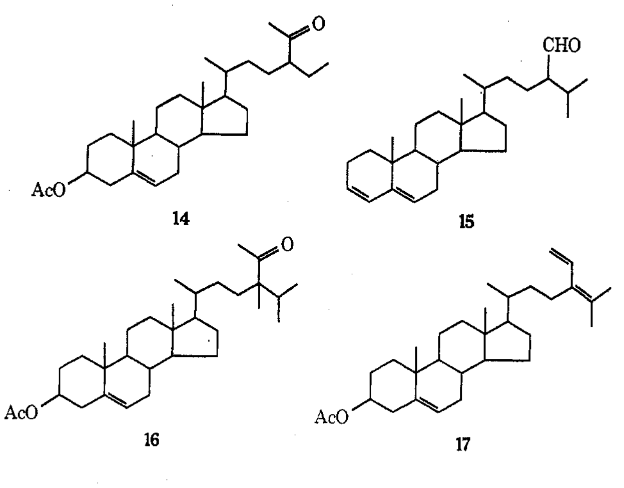
SCHEME I



epoxide ring opening of **6** would generate the tertiary carbonium ion at C-24, which, in turn, may be quenched in three ways: (a) migration of C-25 H with subsequent cleavage of C-24,28 bond to give **11**, (b) C-28 H shift to afford **12**, and (c) C-28 CH_3 shift to yield **13**. Rearrangement by route a would necessarily involve loss of acetaldehyde. Indeed, acetaldehyde was identified in the reaction mixture as its 2,4-dinitrophenylhydrazone by a glc analysis.

It was also suspected that the tertiary nature of the intermediate carbonium ion at C-25 may be one important factor in this fragmentation reaction.[9] This consideration appeared to be, at least partly, verified when similar treatment of epoxide (**8**) with boron trifluoride etherate was found to give 24-acetyl-26-norcholesteryl acetate (**14**) (Chart II) in theoretical yield,

CHART II



whereas, no 26-nordesmosteryl acetate was detected gas chromatographically.

In an attempt to assess the effect of a substituent at C-28 on this reaction, epoxides **7** and **9** were treated with boron trifluoride etherate. At room temperature, compound **7** reacted only sluggishly with boron trifluoride etherate. Starting material was recovered even on prolonged treatment (25 hr), while refluxing in benzene for 45 hr gave 24-formylcholesta-3,5-diene (**15**, 12%), uv 236.5 nm (ε 19,600), nmr δ 5.2–6.00 (m, 3 H) and 9.55 ppm (s, 1 H), as the sole isolable product, in addition to recovered starting compound. When compound **9** was treated with boron trifluoride etherate at room temperature for 10 sec, glc analysis of the product showed 24-acetyl-24-methylcholesteryl acetate (**16**), δ 1.97 (s, 3 H) and 2.00 ppm (s, 3 H), as the major component and a trace of **11**. The former was isolated in 22% yield by column chromatography on silicic acid.

Comparing the reactivity of four epoxides, it was found that the disubstituted one (**7**) reacted extremely slowly with boron trifluoride etherate compared with the tri- or tetrasubstituted epoxides (**6**, **8**, or **9**). Thus, even by refluxing the epoxide **7** in benzene for 30 hr, about half of unreacted starting material was recovered, whereas the other three epoxides were consumed completely within 10 sec at room temperature. All the isolated products (**11–16**) can be considered to be generated from the C-24 carbonium ion. This regiospecificity in the opening of the epoxide ring appears to be accomplished even in the case of **9**, which could give another tertiary carbonium ion at C-28. Another noteworthy feature of these reactions is the strong dependency of the fragmentation reaction on the substituents around the epoxide ring. Thus, only the epoxide **6**, but none of the analogous **7**, **8**, or **9**, seems to induce the fragmentation reaction.

Several Lewis acids and protonic acids were used to open the epoxide **6** in the hope of increasing the yield of desmosteryl acetate (**11**). However, the results summarized in Table I show that the optimum yield of **11** which never exceeded 35% was obtained with boron trifluoride etherate or $SnCl_4$.

When the epoxide **6** was refluxed with *p*-TsOH in benzene, a diene was obtained in 48% yield. The structure of this diene was deduced from its uv spectrum 235.5 nm (ε 18,600) and nmr 1.83 (s, 6H). The same diene **17** was generated from saringosteryl acetate[10] by dehydration with *p*-TsOH. A catalytic hydrogenation over PtO_2 gave tetrahydrofucosteryl acetate, proving no skeletal rearrangement during the reactions. The diene **17** seems to be a common reaction product of the epoxide **6** treated with protonic acids as shown in Table I.

Experimental Section[11]

24,28-Epoxystigmast-5-en-3β-yl Acetate (6).—A solution of 9.1 g of fucosteryl acetate[12] and 5.2 g of *m*-chloroperbenzoic acid in

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[9] J. M. Coxon, M. P. Hartshorn, and D. N. Kirk, *Tetrahedron*, **25**, 1603 (1969). B. N. Blackett, J. M. Coxon, M. P. Harshorn, and K. E. Richards, *Tetrahedron Lett.*, 1737 (1969); *Tetrahedron*, **25**, 4999 (1969). I. G. Guest and B. M. Marples, *J. Chem. Soc. C*, 1626 (1970).

Recently, Morelli, *et al.*, reported an interesting fragmentation reaction of 3-isopropyl-3,5-epoxy-*A*-norcholestane with boron trifluoride etherate: I. Morelli, S. Catalano, G. Moretts, and A. Marsili, *Tetrahedron Lett.*, 717 (1972). They proposed a mechanism proceeding through an oxetane intermediate. If a similar oxetane could be formed from **6**, 26-nordesmosteryl acetate should be one of the reaction products. However, we could not find, by glc analysis, any material having a shorter retention time than **11**. Further, if the oxetane were an intermediate of the reaction of **9**, desmosteryl should be the sole product.

[10] N. Ikekawa, K. Tsuda, and N. Morisaki, *Chem. Ind. (London)*, 1179 (1966).

[11] All melting points are uncorrected. Nmr spectra were recorded on a Varian T-60 spectrometer and mass spectra on a Hitachi RMU-6E and 7L spectrometer. Ir spectra were taken as KBr or liquid films on NaCl plates using a Hitachi EPI-G2 spectrometer, and uv spectra were obtained with an Hitachi ESP-3T spectrometer in ethanol solution. Glc analyses were performed on a Shimadzu GC-5APF gas chromatograph with a flame ionization detector.

[12] N. Ikekawa, N. Morisaki, K. Tsuda, and T. Yoshida, *Steroids*, **12**, 41 (1968).

TABLE I

PRODUCT DISTRIBUTION IN THE REACTION OF 24,28-EPOXYFUCOSTERYL ACETATE WITH VARIOUS ACIDS

Acids	Molar ratio of reagent	Solvent	Temp, °C	Time	Yields,[a] %			
					Desmo **11**	28-Keto **12**	24-Formyl **13**	24,28-Diene **17**
Lewis acids								
BF_3–Et_2O	4	Benzene[b]	25	10 sec	33.6	34.8	27.6	
BF_3–Et_2O	0.15	Benzene	25	10 sec	7.6	20.3	25.1	
BF_3Et_2O	0.15	Benzene	25	1 hr	29.7	28.4	28.4	
$SnCl_4$	4	Benzene	25	1 hr	30.4	42.0	17.6	
$ZnBr_2$	4	Benzene	80	1 hr	14.4	30.7	38.9	
$AlCl_3$	4	AcOH	25	10 sec	7.6	59.4	trace	
BF_3 gas	L.E.[c]	CCl_4	25	10 sec	10.9	29.7	22.5	
BF_3 gas	L.E.	CCl_4	0	10 sec	2.5	54.7	21.6	
Protonic acids								
p-TsOH	4	Benzene	25	1 hr	4.1	30.7	19.6	26.5
AcOH[d]			25	10 min	2.9	34.3	41.4	13.3
CF_3COOH	4	Hexane	25	1 hr	12.0	26.1	23.2	24.7
PPA	L.E.	Hexane	25	1 hr	12.8	39.4	14.5	29.2

[a] Estimated from the peak area of gas chromatogram (1.5% OV-1 on Gas-Chrom P, 80–100 mesh, 180 cm × 4 mm i.d.; column temperature, 270°; carrier gas, N_2; flow rate, 80 ml/min). [b] The reaction is strongly dependent on solvent. Ether in place of benzene gave a complex mixture of products, whereas *n*-hexane seemed to afford a similar product distribution as in the case of benzene. [c] Large excess. [d] The reagent was used as a solvent.

300 ml of chloroform was stirred for 5 min at 0°. The reaction mixture was washed with 1 *N* NaOH and then with water and dried over Na_2SO_4. After removal of the solvent, the product was chromatographed on silica gel. The fraction eluted with hexane–benzene (1:3) afforded the epoxide **6** (6.9 g), which was crystallized from acetone: mp 101–103°; nmr ($CDCl_3$) δ 0.67 (s, 3, C-18 H), 0.85–0.95 (m, 9), 1.01 (s, 3, C-19 H), 1.25 (d, 3, *J* = 6 Hz, C-29 H), 2.02 (s, 3, OAc), 2.88 (q, 1, *J* = 6 Hz, C-28 H), 4.60 (m, 1, C-3 H), 5.35 (m, 1, C-6 H); mass spectrum *m/e* 410 (M^+ − AcOH). *Anal.* Calcd for $C_{31}H_{50}O_3$: C, 79.10; H, 10.71. Found: C, 79.16; H, 10.63.

Reaction of 24,28-Epoxystigmast-5-en-3β-yl Acetate with Boron Trifluoride Etherate.—24,28-Epoxystigmast-5-en-3β-yl acetate (**6**, 270 mg) in 5 ml of dry benzene was treated with 0.5 ml of boron trifluoride etherate for 10 sec at room temperature. The solution was washed with saturated $NaHCO_3$, then with water, and dried over Na_2SO_4. The solvent was distilled off and the crude product was chromatographed on silica gel.

The fraction eluted with benzene–hexane (1:4) gave 95 mg of desmosteryl acetate, mp 114–116° (from acetone), identified by comparison with the authentic sample.

The fraction eluted with benzene–hexane (1:1) gave 32 mg of 24-formyl-24-methylcholesteryl acetate (**13**): mp 128–131° (from acetone); nmr ($CDCl_3$) δ 0.67 (s, 3, C-18 CH_3), 0.90 (s, 6), 0.96 (s, 3), 1.02 (s, 6), 2.03 (s, 3, OAc), 4.60 (m, 1, C-3 H), 5.40 (m, 1, C-6 H), 9.53 ppm (s, 1, CHO); ir 1710 cm^{-1}; mass spectrum *m/e* 410.3493 (M^+ − AcOH) (calcd 410.3548). Compound **13** (9 mg) in methanol (1 ml) was treated with excess $NaBH_4$ at room temperature for 30 min. After usual work-up, the 24-hydroxymethyl derivative was obtained: mp 129–132° (from methanol); nmr ($CDCl_3$) 0.67 (s, 3), 0.73 (s, 3), 0.77–0.97 (m, 6), 1.00 (s, 6), 2.03 (s, 3), 3.43 (s, 2, CH_2OH), 4.60 (m, 1), 5.37 ppm (m, 1).

The fraction eluted with benzene–hexane (3:1) gave 125 mg of 24-acetylcholesteryl acetate: mp 130–132° (from acetone); nmr ($CDCl_3$) δ 0.66 (s, 3), 0.85–1.05 (m, 12), 2.01 (s, 3), 2.08 (s, 3, C-24 Ac), 4.55 (m, 1), 5.33 ppm (m, 1); ir 1710, 1725 cm^{-1}. *Anal.* Calcd for $C_{31}H_{50}O_3$: C, 79.10; H, 10.71. Found: C, 79.05; H, 10.73.

Identification of Acetaldehyde.—To the reaction mixture of 24,28-epoxystigmast-5-en-3β-yl acetate (5 mg) with boron trifluoride etherate (5 μl) in benzene (1 ml), a solution of 2,4-dinitrophenylhydrazine (0.01 g) in diglyme (0.3 ml) and concentrated HCl (1 drop) was added. The mixture was extracted with benzene. The extract was analyzed by a glc using 1.5% OV-1 and 1.5% OV-17 on Chromosorb W, 80–100 mesh, as the column packings (column size, 180 cm × 4 mm i.d.; column temperature, 200°). One of the prominent peaks corresponded with the 2,4-dinitrophenylhydrazone of acetaldehyde.

26-Norfucosteryl Acetate (3).—A mixture of triphenylphosphinethyl bromide (0.5 g), *n*-butyllithium (1.5% w/v, 0.6 ml), and dry ether (6 ml) was shaken under nitrogen atmosphere in a pressure bottle for 30 min at room temperature. To the ylide solution, 24-oxo-26-norcholesteryl acetate[4] (185 mg) was added and the mixture was allowed to stand for 23 hr at 80°. After the usual work-up the product was acetylated with excess of acetic anhydride and pyridine and then chromatographed on silica gel. Elution with benzene–hexane (1:5) afforded 36 mg of **3**: mp 126–129° (from methanol–acetone); nmr ($CDCl_3$) δ 0.67 (s, 3), 0.99–1.10 (m, 9), 1.60 (d, 3, *J* = 7 Hz, C-29 CH_3), 2.00 (s, 3), 4.60 (m, 1), 5.17 (q, 1, *J* = 7 Hz, C-28 H), 5.40 ppm (m, 1); mass spectrum *m/e* 380.3416 (M^+ − AcOH) (calcd 380.3443). Elution with benzene–hexane (3:1) afforded 89 mg of starting material.

24,28-Epoxy-26-norstigmast-5-en-3β-yl Acetate (8).—26-Norfucosteryl acetate (30 mg) in 1 ml of chloroform was treated with 17 mg of *m*-chloroperbenzoic acid at 0° for 3 min. The product was chromatographed on silica gel. Elution with benzene–hexane (1:5) afforded 5 mg of recovered starting material. Elution with benzene–hexane (1:1) afforded 22 mg of **8**: mp 135–137° (from methanol–acetone); nmr ($CDCl_3$) δ 0.67 (s, 3), 0.87–1.10 (m, 9), 1.27 (d, 3, *J* = 6 Hz, C-29 CH_3), 2.02 (s, 3), 2.83 (q, 1, *J* = 6 Hz, C-28 H), 4.60 (m, 1), 5.40 ppm (m, 1); mass spectrum *m/e* 396.3371 (M^+ − AcOH) (calcd 396.3392).

Reaction of 8 with Boron Trifluoride Etherate.—**8** (10 mg) in dry benzene (2 ml) was treated with 10 μl of boron trifluoride etherate for 10 sec at room temperature. The solution was washed with saturated $NaHCO_3$, then with water, and dried over Na_2SO_4. Removal of the solvent afforded 10 mg of 24-acetyl-26-norcholesteryl acetate as a sole product: mp 133.5–134.5°; nmr ($CDCl_3$) δ 0.67 (s, 3), 0.83–1.10 (m, 9), 2.03 (s, 3), 2.10 (s, 3, C-24 Ac), 4.60 (m, 1), 5.40 ppm (m, 1); mass spectrum *m/e* 396.3371 (M^+ − AcOH) (calcd 396.3392).

24,28-Epoxy-24-methylenecholesteryl Acetate (7).—24-Methylenecholesteryl acetate (**2**) was prepared from 24-oxocholesteryl acetate with triphenylphosphinemethyl bromide by a Wittig reaction. The yield was increased to 85% by heating the reaction mixture at 120° for 24 hr, instead of room temperature as reported.[7]

2 (1 g) in 50 ml of chloroform was treated with *m*-chloroperbenzoic acid (450 mg) at 0° for 3.5 hr. After the usual work-up the product was chromatographed on silical gel. Elution with benzene–hexane (1:2) afforded 200 mg of the starting material. Elution with benzene–hexane (1:1) afforded 190 mg of **7**: mp 134–136° (from methanol); nmr (CCl_4) δ 0.67 (s, 3), 0.80–1.02 (m, 12), 1.93 (s, 3), 2.39 (s, 2, C-28 H), 4.48 (m, 1), 5.42 ppm (m, 1). *Anal.* Calcd for $C_{30}H_{48}O_3$: C, 78.89; H, 10.59. Found: C, 78.99; H, 10.63.

Reaction of 7 with Boron Trifluoride Etherate.—A solution of 100 mg of **7** and 110 μl of boron trifluoride etherate in 20 ml of benzene was refluxed for 45 hr. After the usual work-up, the crude product was chromatographed on silica gel column. Elution with benzene–hexane (1:6) afforded 9.4 mg of 24-formylcholesta-3,5-diene (**15**): mp 94–99° (amorphous); nmr ($CDCl_3$) δ 0.67 (s, 3), 0.87–1.03 (m, 12), 5.62–6.0 (m, 3, C-3,4,6 H), and 9.55 ppm (s, 1, 24-CHO); uv max 236.5 nm (ε 19,600); ir 1715

cm^{-1}; mass spectrum m/e 396 (M^+). Elution with benzene–hexane (2:1) afforded 12 mg of the starting material.

28-Hydroxy-24-isopropylcholesteryl Acetate (10).—A solution of 250 μl of methyl iodide in 1 ml of dry ether was added dropwise to 96 mg of magnesium turnings under nitrogen atmosphere. After the spontaneous reaction began, another 5 ml of dry ether was added, and the mixture was stirred for 45 min. To the solution 800 mg of **12** in 5 ml of ether was added dropwise in 15 min and the solution was refluxed for 1.5 hr. After the usual work-up, the product was acetylated with excess acetic anhydride and pyridine and chromatographed on silica gel. Elution with benzene–hexane (2:1) afforded 237 mg of the starting material. Elution with benzene–hexane (10:1) afforded 28-hydroxy-24-isopropylcholesteryl acetate (**10**, 387 mg): mp 132–135° (from acetone); nmr (CCl_4) δ 0.62 (s, 3), 0.73–1.00 (m, 12), 1.07 (s, 6, C-29 CH_3, C-30 CH_3), 1.89 (s, 3), 4.50 (m, 1), 5.30 (m, 1); mass spectrum m/e 426.3849 ($M^+ -$ AcOH) (calcd 426.3861).

24,28-Epoxy-28-methylstigmast-5-en-3β-yl Acetate (9).—To the solution of 150 mg of **10** in 3 ml of pyridine, 0.3 ml of phosphorus oxychloride was added, and the mixture was allowed to stand overnight at room temperature. After the usual work-up, the product was dissolved in 10 ml of chloroform and treated with 35 mg of *m*-chloroperbenzoic acid at 0° for 10 min. The product was chromatographed on silica gel. Elution with benzene–hexane (1:10) afforded 82 mg of 24-isopropylcholesta-5,28-dien-3-ol acetate (**5**): mp 128–131° (from acetone); nmr (CCl_4) δ 0.63 (s, 3), 0.80–1.03 (m, 12), 1.53 (s, 3), 1.90 (s, 3), 4.55 (m, 1), 4.59 (s, 1, C-29 H), 4.70 (s, 1, C-29 H), 5.33 ppm (m, 1); mass spectrum m/e 408.3724 ($M^+ -$ AcOH) (calcd 408.375). Elution with benzene–hexane (3:1) afforded 48 mg of **9**: mp 103–105° (amorphous); nmr (CCl_4) δ 0.67 (s, 3), 0.83–1.13 (m, 12), 1.22 (s, 3), 1.26 (s, 3), 1.95 (s, 3), 4.55 (m, 1), 5.30 ppm (m, 1); mass spectrum m/e 424.3671 ($M^+ -$ AcOH) (calcd 424.3704).

Reaction of 9 with Boron Trifluoride Etherate.—**9** (30 mg) in 6 ml of benzene was treated with boron trifluoride etherate (30 μl) for 10 sec at room temperature. After the usual work-up, the product was chromatographed on silica gel. Elution with benzene–hexane (1:3) afforded 6.6 mg of 24-acetyl-24-methylcholesteryl acetate (**16**): mp 115–120° (from methanol); nmr ($CDCl_3$) δ 0.67 (s, 3), 0.80 (s, 3), 0.90 (s, 6), 1.00 (s, 6), 1.97 (s, 3), 2.00 (s, 3, C-24 Ac), 4.60 (m, 1), 5.40 ppm (m, 1); ir 1690, 1715 cm^{-1}; mass spectrum m/e 424.3671 ($M^+ -$ AcOH) (calcd 424.3704).

24-Ethylcholesta-5,24,28-trien-3β-ol Acetate (17).—A solution of 1 g of **6** and 65 mg of *p*-toluenesulfonic acid in 30 ml of benzene was refluxed for 30 min. After usual work-up of the mixture, the crude product was chromatographed on silica gel. The fraction eluted with benzene–hexane (1:1) gave 487 mg of **17**: mp 109–111°; nmr ($CDCl_3$) δ 0.69 (s, 3), 1.02 (s, 6), 1.83 (m, 6, C-26 and C-27 CH_3), 2.02 (s, 3), 4.60 (m, 1), 4.80–5.06 (m, 2, C-29 H_2), 5.38 (m, 1, C-28 H), 5.64 ppm (m, 1); uv max 235.5 nm (ϵ 18,600); mass spectrum m/e 452.3677 (M^+) (calcd 452.3654).

Compound **17** (50 mg) was dissolved in 1 ml of acetic acid and hydrogenated over 5 mg of platinum dioxide. Three mole equivalents of hydrogen was absorbed over a period of 1 hr. After removal of the catalyst, the filtrate was made alkaline with NaOH solution and the precipitate crystallized from acetone, mp 123–126°. The melting point and ir and nmr spectra were identical with those of tetrahydrofucosteryl acetate prepared from fucosteryl acetate by the same procedure.

Compound **17** was unstable to light. After a 1-day exposure to light in the laboratory, the major part had decomposed, but it was stable when refrigerated in a dark bottle.

Dehydration of Saringosteryl Acetate.—A solution of 517 mg of saringosteryl acetate and 27 mg of *p*-toluenesulfonic acid in 15 ml of benzene was refluxed for 30 min. After the usual work-up, the crude product was chromatographed on silica gel. The fraction eluted with benzene–hexane (1:3) afforded prisms from acetone of mp 109–111°. The compound's melting point, mixture melting point, and nmr spectrum agreed with those of compound **17**.

Registry No.—**3**, 38863-83-1; **5**, 38863-84-2; **6**, 35458-70-9; **7**, 35458-74-3; **8**, 38863-87-5; **9**, 38863-88-6; **10**, 38863-89-7; **11**, 2665-04-5; **12**, 38863-91-1; **13**, 38863-92-2; **13** (24-hydroxymethyl derivative), 38863-93-3; **14**, 38863-94-4; **15**, 38863-95-5; **16**, 38863-96-6; **17**, 38863-97-7; fucosteryl acetate, 6035-62-7; boron trifluoride etherate, 109-63-7; 24-oxo-26-norcholesteryl acetate, 26308-99-6; 24-oxocholesteryl acetate, 20981-59-3.

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Stereospecific Synthesis of Cis and Trans Epoxides from the Same Diol

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From the benzaldehyde acetal of *meso*-2,3-butanediol, isomerically pure *cis*-2,3-epoxybutane was synthesized by treatment with *N*-bromosuccinimide in carbon tetrachloride, followed by treatment with potassium hydroxide; isomerically pure *trans*-2,3-epoxybutane was synthesized by treatment with *N*-bromosuccinimide in water, followed by treatment with *p*-toluenesulfonyl chloride, followed by treatment with potassium hydroxide. From these reactions and the treatment of other cyclic acetals with *N*-bromosuccinimide, the reaction was shown to be ionic, kinetically regiospecific, and specific for the acetal carbon.

The recently reported stereospecific syntheses of halohydrin esters and epoxides by Newman and Chen[2] prompt us to report our preliminary results on a related stereospecific epoxide synthesis. Treatment of the readily accessible acetal of benzaldehyde and *meso*-2,3-butanediol[3] with *N*-bromosuccinimide[4] (NBS) in carbon tetrachloride containing a trace of HBr followed by treatment of the resulting bromohydrin ester[5] with potassium hydroxide in ethylene glycol gives *cis*-2,3-epoxybutane isomerically pure by nmr (Scheme I). Treatment of the same acetal with NBS in water, followed by treatment of the tosylate derived from the resulting glycol monoester with potassium hydroxide in ethylene glycol and 1,2-dimethoxyethane, gives *trans*-2,3-epoxybutane isomerically pure by nmr (Scheme II).

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(1) Participant in ACS Seed Catalyst Program, summer, 1971.

(2) M. S. Newman and C. H. Chen, *J. Amer. Chem. Soc.*, **94**, 2149 (1972).

(3) D. Gagnaire and J.-B. Robert, *Bull. Soc. Chim. Fr.*, 3646 (1965).

(4) For other examples of bromination of 1,3-dioxolanes, see ref 6 and papers cited therein; T. L. Hullar and S. B. Siskin, *J. Org. Chem.*, **35**, 225 (1970), and M. M. Ponpipom and S. Hanessian, *Can. J. Chem.*, **50**, 253 (1972), for uses in sugar and nucleoside chemistry; and D. H. R. Barton, L. Bould, D. L. C. Clive, P. D. Magnus, and T. Hase, *J. Chem. Soc. C*, 2204 (1971).

(5) Satisfactory ir, nmr, and low-resolution mass spectral data were obtained for each new compound. A satisfactory elemental analysis was obtained for compound **1**; all other compounds gave satisfactory high-resolution mass spectra.