24742-73-2; **42**, 24742-74-3; **43**, 24742-75-4; **46**, 24742-76-5; **47**, 24742-77-6; **50**, 6877-35-6; **52**, 24742-79-8; **53**, 24742-80-1; **57**, 24742-81-2; **60**, 24742-82-3; **61**, 24742-83-4; **62**, 24742-84-5; **63**, 24799-51-7; **64**, 24742-85-6; **65**, 24742-86-7; **66**, 24742-87-8; **67**, 468-99-5; **71**, 24742-89-0.

Terpenoids. LXVII.[1] Chemical Studies of Marine Invertebrates. VII.[2] Interrelation of Seychellogenin and Lanosterol through Lanostane-3β,11β,18-triol[3]

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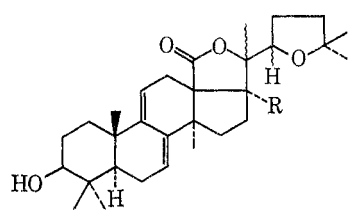
Received December 18, 1969

Seychellogenin (**9**) and lanosterol (**10**) were chemically correlated through a common intermediate, lanostane-3β,11β,18-triol (**21**). Seychellogenin was reduced to the triol **11**, whose 3,18-diacetate (**12**) was dehydrated and then hydrogenated to give a mixture of C-20 epimers of **15**. Subsequent chromium trioxide oxidation to the ene-dione **16**, followed by zinc reduction to **17** and removal of the C-7 functionality, gave 11-oxolanostane-3β,18-diol diacetate (**20**) and its C-20 epimer **19**. Reduction of **20** provided the desired triol **21**. Lead tetraacetate–iodine oxidation of 11β-hydroxylanostan-3β-yl acetate (**22**) and immediate reduction with lithium aluminum hydride yielded the 11β,18 ether **24** and the 11β,19 ether **25**. The former was oxidized to the lactone **27** and then reduced to the triol **21**, which was identical with the product of natural origin. The 11β,19 ether (**25**) was converted to lanostane-3β,11β,19-triol (**37**) which could be correlated with the known 11β,19-cyclolanostane-3β,11α-diol 3-acetate (**23**).

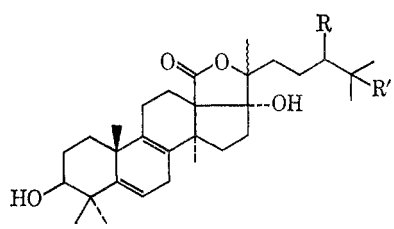
In recent years a number of triterpenoid saponins of toxic nature have been isolated from many species of sea cucumbers in the family *Holothuroidea* of the phylum *Echinodermata*. The first successful structural work was accomplished on the saponin mixture from the Cuvier glands of the Caribbean species *Actinopyga agassizi*.[5] Acid hydrolysis of the mixture yielded monosaccharides, sulfuric acid, and a mixture of triterpenoid aglycones, among them 22,25-oxidoholothurinogenin (**1**) and its deoxy analog **2**. In the saponin, an aglycone was found to be bound directly to a chain of four monosaccharides and to a sulfate ester. Enzymatic hydrolysis studies[6] have also led to some interesting speculations about the true nature of the triterpenoid portion when attached to the monosaccharide chain and the sulfate ester residue.

Chemical studies by our group established the structure of yet another aglycone, griseogenin (**3**), as an acid hydrolysis product from the body walls of the Brazilian sea cucumber *Halodeima grisea L.*[7] Structures **4** and **5** for the two sapogenins stichopogenin A_2 and stichopogenin A_4 from the Far Eastern sea cucumber *Stichopus japonicus* were assigned mainly on the basis of spectral evidence.[8]

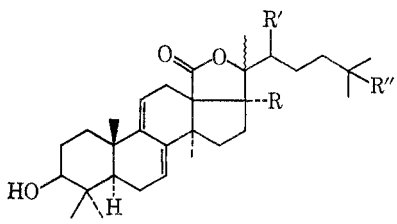
Thus all sea cucumber aglycones appear to possess a similar lanostane skeleton with structural variations in the side chain. Chemical and spectroscopic evidence all pointed to the correctness of the postulated struc-



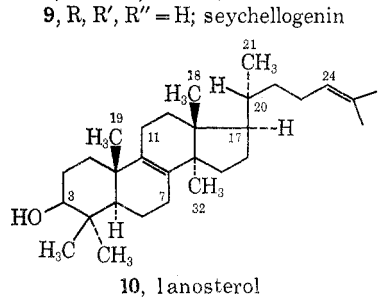
1, R = OH
2, R = H



4, R, R′ = double bond
5, R = H; R′ = OH



3, R, R′ = OH; R″ = H
6, R, R′ = H; R″ = OH
7, R, R′ = H; R″ = OMe
8, R = OH; R′ = H; R″ = OMe
9, R, R′, R″ = H; seychellogenin



10, lanosterol

(1) For part LXVI, see P. Roller and C. Djerassi, *J. Chem. Soc. C*, 1089 (1970).

(2) For part VI, see B. Tursch, R. Cloetens, and C. Djerassi, *Tetrahedron Lett.*, 467 (1970).

(3) Financial assistance from the National Institutes of Health Grant No. GM-06840 is gratefully acknowledged.

(4) (a) Taken in part from the Ph.D. Thesis of P. R., Stanford University, 1969; (b) Postdoctoral research associate, on leave from the Free University of Brussels, Brussels, Belgium.

(5) J. D. Chanley, T. Mezzetti, and H. Sobotka, *Tetrahedron*, **22**, 1857 (1966).

(6) J. D. Chanley and C. Rossi, *ibid.*, **25**, 1897, 1911 (1969).

(7) B. Tursch, I. S. deSouza Guimaraes, B. Gilbert, R. T. Aplin, A. M. Duffield, and C. Djerassi, *ibid.*, **23**, 761 (1967).

(8) G. B. Elyakov, T. A. Kuznetsova, A. K. Dzizenko, and Yu. N. Elkin, *Tetrahedron Lett.*, 1151 (1969).

tures, which, however, remained to be proved through a direct chemical correlation with lanosterol itself. Such occasion arose in our continuing study of marine toxins when we isolated[2,9] several new aglycones on acid hydrolysis of the saponins of the Indian Ocean sea cucumber *Bohadschia koellikeri*, namely koellikerigenin (**6**), ternaygenin (**7**), and praslinogenin (**8**) from the body walls, and seychellogenin (**9**) from the Cuvier glands. All were structurally related.

Seychellogenin (**9**), $C_{30}H_{46}O_3$, revealed the presence of a five-membered lactone ring (1755 cm^{-1}), one tertiary methyl group on an oxygen-bearing carbon (δ 1.40, CH_3-21), six additional methyl groups, one equatorial secondary hydroxyl group (δ 3.23, CH-3) which could be acetylated (δ 4.5), two vinylic protons (δ 5.25 and 5.56, CH-7 and CH-11), and a heteroannular diene (λ_{max} 237, 244, 252 nm; ϵ 11,000, 12,000, and 8000) commensurate with such a chromophore when contained in the fused-ring system of agnosterol.[10] The remaining four degrees of unsaturation are satisfied by structure **9**, containing four fused carbocyclic rings. Thus, seychellogenin appears to be the simplest possible holothurinogenin, being devoid of substituents on the side chain and lacking the hydroxyl group on C-17.

Seychellogenin was therefore chosen as the most convenient aglycone for an attempted chemical correlation with lanosterol (**10**), both because of its relative abundance in the particular species and because of its suitable structure. When compared with 24,25-dihydrolanosterol, the most distinguishing feature of seychellogenin appeared to be its functionalized character at carbon atoms 18 and 20. Our approach called for the derivation of a common intermediate from both seychellogenin and lanosterol using unambiguous chemical steps. Such an intermediate was obtained by removal of functionality of C-20[11] in a suitable derivative of seychellogenin as well as the conversion of its skeletal unsaturation to an 11-hydroxy derivative. At the same time lanosterol could be converted to an 11-hydroxy intermediate according to established methods[12,13] and subsequent application of one of the intramolecular hydrogen abstraction reactions[14] on the latter resulted in the introduction of functionality on C-18. The preparation of such a 3,11,18-trifunctionalized derivative from both sources is detailed below.

Seychellogenin (**9**) on lithium aluminum hydride reduction in tetrahydrofuran gave the triol **11**, which on acetylation under the usual conditions furnished the triol 3,18-diacetate **12** (Scheme I). Both substances were acid sensitive and their formulation is consonant with their spectral data.

Dehydration of the triol diacetate **12** with phosphorus oxychloride in pyridine gave a mixture of double-bond isomers;[15] separation of the two major olefins, **13** and **14**, was achieved in approximate yields of 35% each. The more polar $\Delta^{20(21)}$ isomer **13** was characterized by broad singlets at 4.75 and 4.87 ppm in the nmr spectrum corresponding to the two olefinic protons on C-21. In the case of the less polar $\Delta^{20(22)}$ olefin **14**, the vinylic methyl group (C-21) appeared as a broad three-proton singlet at 1.65 ppm.

Catalytic hydrogenation of either olefin **13** or **14** in ethyl acetate over platinum oxide gave a mixture of C-20 epimers **15** without affecting the skeletal unsaturation, as attested by its ultraviolet spectrum, λ_{max} 235, 242, and 251 nm. It is appropriate to remark at this stage that, while the dehydrogenation step leading to olefins **13** and **14** destroyed the asymmetric center on C-20, subsequent hydrogenation produced an approximately equal mixture of C-20 epimers, one of which had to possess the same configuration as lanosterol.

The epimeric mixture **15** on oxidation with chromium trioxide in acetic acid yielded the expected ene–dione **16**, with an ultraviolet absorption, λ_{max} 271 nm (ϵ 7080), characteristic for such a chromophore.[12] Zinc reduction of the unsaturated diketone **16** in refluxing acetic acid gave in good yield the saturated diketone **17**. The two C-20 epimeric components could be barely distinguished on silica gel chromatoplates, and separation was not attempted at this stage. Removal of the 7-keto function was achieved by conversion to the 7-ethylene thioketal **18** followed by Raney Nickel desulfurization in refluxing ethanol. The product could be well separated into two components by preparative tlc. The less polar isomer was assigned the 11-oxo-20-epilanostane-3β,18-diol diacetate (**19**) structure while the more polar isomer corresponded to the natural epimer, 11-oxolanostane-3β,18-diol diacetate (**20**) as shown by its eventual correlation with lanosterol. The spectral data were in agreement with the assigned structures in that both epimers showed the expected infrared carbonyl band at 1737 cm^{-1} corresponding to the two ester functions and a low frequency band at 1700 cm^{-1} assigned to the C-11 carbonyl substituent.[16] The two-proton singlet at 4.00–4.02 ppm in the nmr spectrum of both epimers corresponded to the 18-acetoxymethylene protons and the two singlets at 1.13 and 1.08 ppm were assigned to methyls 19 and 32.[17] Furthermore, the spectra of both epimers exhibited an interesting pair of doublets at 2.45 and at 2.65 ppm, each integrating for one proton (J = 14 Hz). While in the well-studied case of 5α-androstan-11-one[18] the 12α and 12β protons appeared indistinguishable (A_2 singlet) at 2.27 ppm, the 18-acetoxy substituent in our case introduces sufficient molecular asymmetry to differentiate the C-12 axial and equatorial protons. Also, a broad low field doublet (J = 14 Hz), centered at 2.85 ppm, was tentatively assigned to the C-1 equatorial proton. Molecular models show that this γ-hydrogen atom lies in the nodal plane of the C-11 carbonyl group. Such paramagnetic shifts have ample precedent in the litera-

(9) For preliminary communication, see P. Roller, C. Djerassi, R. Cloetens, and B. Tursch, *J. Amer. Chem. Soc.*, **91**, 4918 (1969).

(10) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," Pergamon Press, Oxford, England, 1964, p 51.

(11) The plan of removal of the C-18 functionality from a derivative of seychellogenin was abandoned after preliminary work on the preparation and the reductive removal of the 18-tosylate, -iodide, and hydrazone derivatives indicated undue difficulties: see R. Cloetens, Ph.D. Thesis, Brussels, 1969.

(12) W. Voser, M. Montavon, H. H. Gunthard, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **33**, 1893 (1950).

(13) J. F. McGhie, M. K. Pradhan, and J. F. Calvalla, *J. Chem. Soc.*, 3176 (1952).

(14) K. Heusler and J. Kalvoda, *Angew. Chem., Int. Ed. Engl.*, 525 (1964).

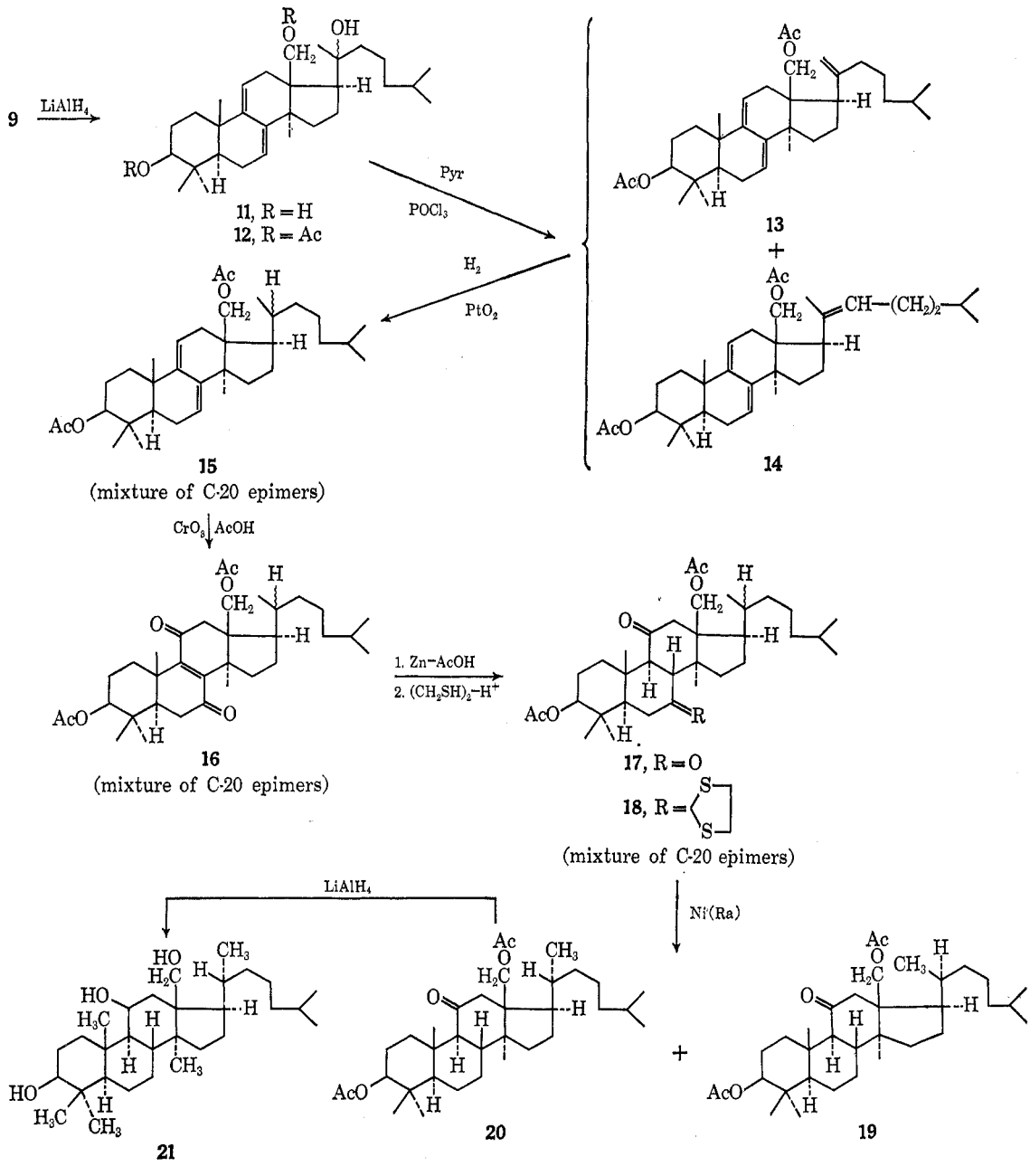
(15) J. S. Mills, *J. Chem. Soc.*, 2196 (1956).

(16) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy," Academic Press, New York, N. Y., 1963, p 436.

(17) F. Hemmert, B. Lacoume, J. Levisalles, and G. R. Pettit, *Bull. Soc. Chim. Fr.*, 976 (1966); F. Hemmert, A. Lablanche-Combier, B. Lacoume, and J. Levisalles, *ibid.*, 982 (1966).

(18) D. H. Williams, N. S. Bhacca, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2810 (1963).

SCHEME I



ture.[18,19] The principal mass spectral fragment (*m/e* 361) from the two epimeric ketones **19** and **20** can be rationalized in exact analogy to the well-studied case of 5α-androstan-11-one.[20]

Lithium aluminum hydride reduction of the more polar 11-keto-3,18-diacetate **20** gave on sublimation the sought after lanostane-3β,11β,18-triol (**21**), mp 228–229°. The spectral data are in full agreement with the structural assignment and will be detailed later.

The conversion of lanosterol to a 3,11,18-functionalized derivative was performed next. 11β-Hydroxylanostan-3β-yl acetate (**22**) was selected as the starting material and was prepared from lanosterol according to the method of Voser, *et al.*[12] Several methods were considered for the functionalization of the C-18 angular methyl group. Radical-type reactions involving intramolecular attack by an 11-oxy radical on a suitably located nonactivated carbon have been advantageously utilized in recent years to synthesize C-18 and/or C-19 substituted steroids.[14,21,22] However, in the case of the lanostane derivatives, both the photocyclization of the 11-ketolanostane[23,24] and the isomerization of the 11β-nitrite[25,26] yielded exclusively C-19 substituted products, which were not useful for our synthetic ob-

(19) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry, Illustrations from the Steroid Field," Holden-Day, San Francisco, Calif., 1964, p 66.

(20) D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2091 (1963).

(21) R. H. Hesse in "Advances in Free-Radical Chemistry," Vol. III, G. H. Williams, Ed., Academic Press, New York, N. Y., 1969.

(22) M. Akhtar in "Advances in Photochemistry," Vol. 2, W. A. Noyes, G. S. Hammond, and J. N. Pitts, Ed., Academic Press, New York, N. Y., 1964.

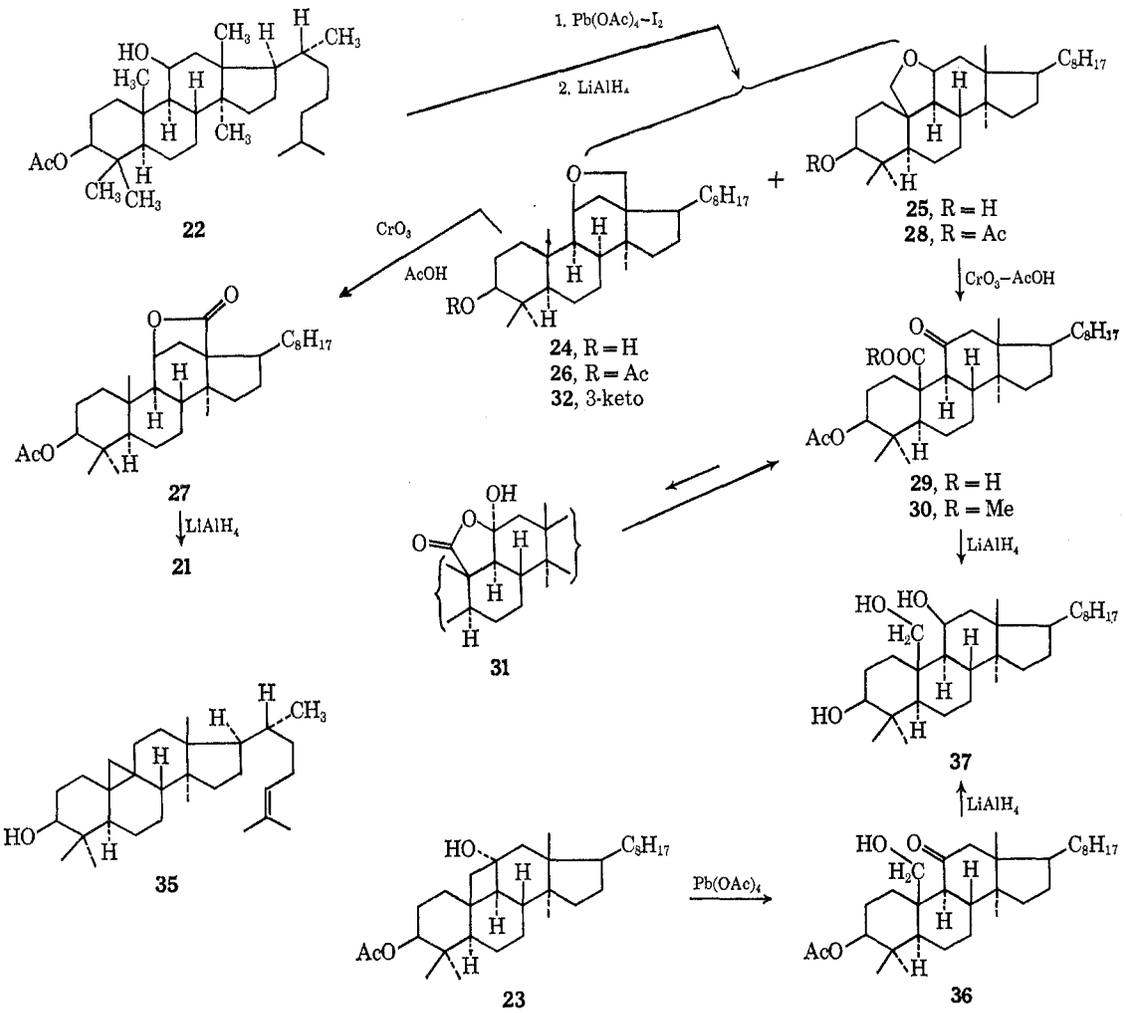
(23) R. Imhof, W. Graf, H. Wehrli, and K. Schaffner, *Chem. Commun.*, 852 (1969).

(24) E. Altenburger, H. Wehrli, and K. Schaffner, *Helv. Chim. Acta*, **48**, 704 (1965).

(25) D. H. R. Barton, D. Kumari, P. Wetzel, L. J. Danks, and J. F. McGhie, *J. Chem. Soc. C*, 332 (1969).

(26) D. H. R. Barton, R. P. Budhiraja, and J. F. McGhie, *ibid.*, 336 (1969).

SCHEME II



jectives. Our choice of the proper reagent was lead tetraacetate. Oxidations with this reagent on 11β-hydroxy steroids have been reported[27] to give mainly the 11-keto derivative (54%) and in addition small quantities of the 11β,19, 11β,18, and 1β,11α ethers. The Swiss group also found[28] that in the presence of iodine the above reaction produces a complex mixture of presumably ethers, α-iodo ethers, and hemiacetals in which C-18 and C-19 were attacked to about equal extent and after silver acetate oxidation the corresponding ethers and hemiacetals were isolated in 5–10% yields each.

In our envisaged synthetic sequence, it seemed advantageous to reduce the products of multiple attack, such as iodo ethers, to ethers and the overoxidized components, such as hemiacetals, to polar triols immediately after lead tetraacetate–iodine treatment. Thus, refluxing 11β-hydroxylanostan-3β-yl acetate (**22**) with lead tetraacetate and iodine in cyclohexane–acetic acid under illumination followed by lithium aluminum hydride reduction gave a mixture that could be easily separated into an ether-containing fraction and into more polar fractions containing mixtures of polyols. Preparative tlc of the ether-containing fraction gave two components identified as 11β,18-epoxylanostan-3β-ol (**24**) and 11β,19-epoxylanostan-3β-ol (**25**) in 32 and 8% overall yields, respectively. Acetylation of **24** followed by oxidation of the acetate **26** with chromium trioxide in acetic acid gave the corresponding lactone **27** in 35% yield. On the other hand, the oxidation of 11β,19-epoxylanostan-3β-yl acetate (**28**) resulted in formation of acidic material formulated as **29**. The latter on esterification with diazomethane gave 3β-acetoxy-11-oxolanostan-19-oic acid methyl ester (**30**). Aside from the analytical data, spectrocsopic information was available to support the structural assignments.

The oxo acid **29**, obtained by chromium trioxide oxidation of the 11β,19-epoxy acetate **28**, exhibited no lactone absorption around 1760 cm^{-1} in the infrared spectrum in chloroform, thus excluding the presence of a cyclized form such as **31**. Furthermore, the presence of an intense band at 1708^{-1}, assigned to the 11-keto function,[16] confirms the observation that in fact the oxo acid **29** is entirely in the open form in solution. See Scheme II.

The nmr spectra of the 11β,18-ether alcohol **24**, its acetate **26**, and its 3-keto derivative **32** exhibit a two-proton singlet at 3.63–3.67 ppm, attributable to the methylene protons on C-18. By comparison, the analogous protons of 11β,18-epoxy-5α-pregnane-3β,20β-diol diacetate (**33**) have been found[27] to appear nonequivalent, illustrating the effect of the nearby 20-acetate group. On the other hand, the C-19 methylene

(27) K. Heusler, J. Kalvoda, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **46**, 352 (1963).

(28) J. Kalvoda, K. Heusler, G. Anner, and A. Wettstein, *ibid.*, **46**, 618 (1963).

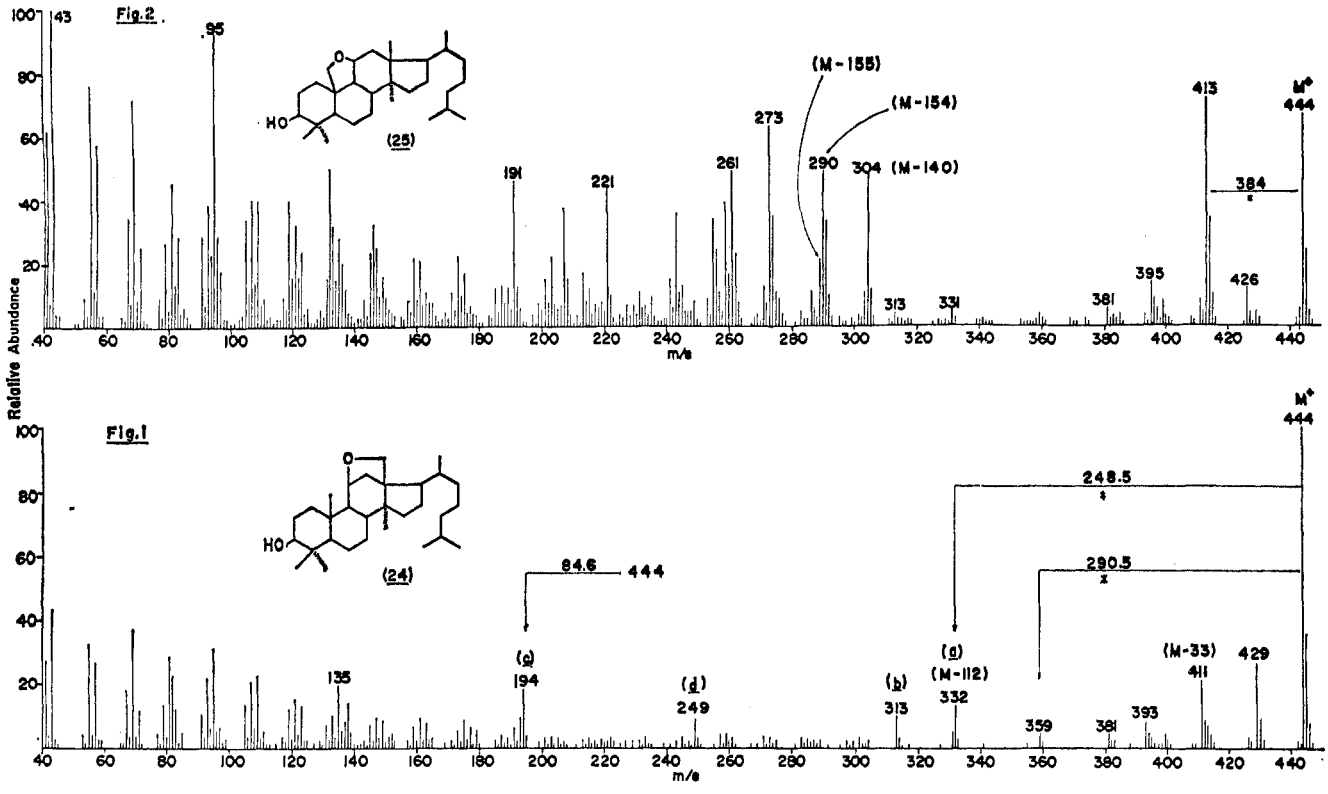
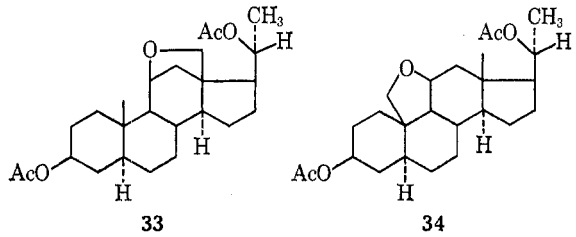


Figure 1.—Mass spectrum of 11β,18-epoxylanostan-3β-ol (24).
Figure 2.—Mass spectrum of 11β,19-epoxylanostan-3β-ol (25).



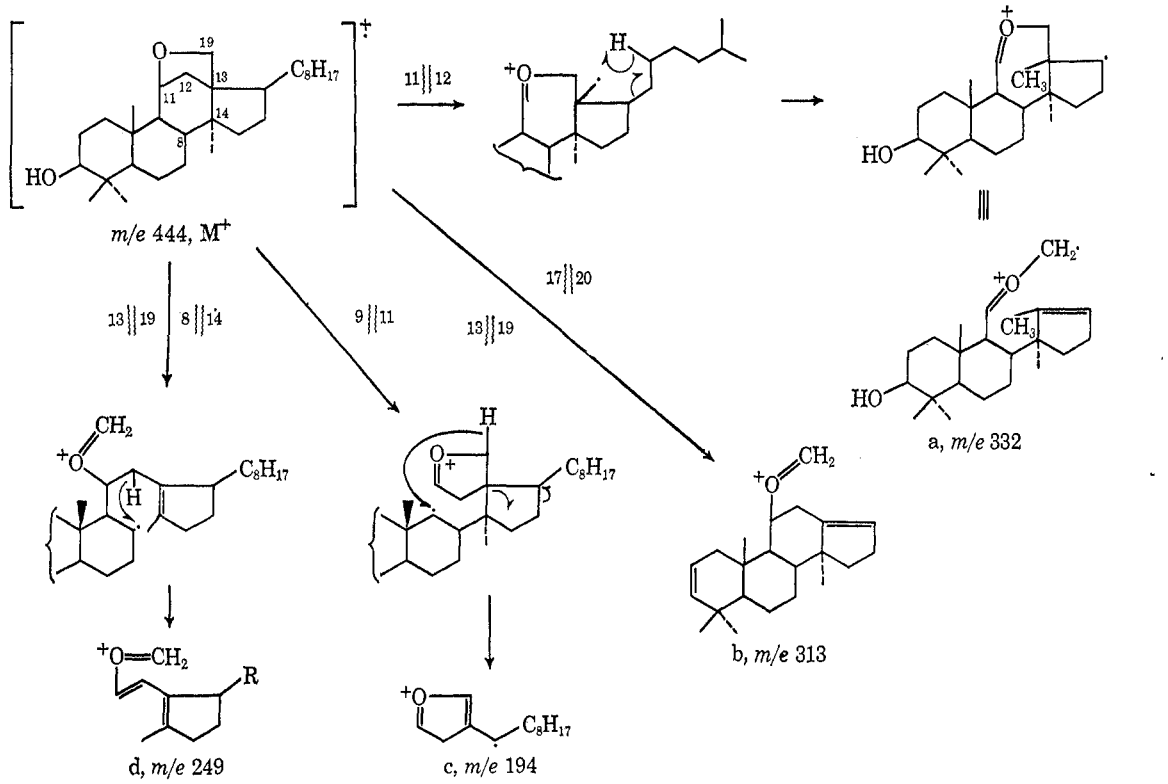
33 34

protons of the 11β,19-ether alcohol **25** and of its acetate **28** appeared each as a pair of doublets centered at 3.82 and 3.64 ppm (J = 8 Hz). In addition, the lower field doublet is further split (J = 1.5 Hz) into doublets probably by coupling with the 4β-methyl protons. In contrast to such spatial dissymmetry in these 11β,19-lanostane ethers, the 19-methylene protons of the steroid analog **34** are reported to be equivalent. It is worthy of note that an almost diagnostic sharp doublet (J = 6 Hz) appears for the 11β,18 ethers **24**, **26**, and **32** and 18,11β-lactone **27** as well as for the steroidal 11β,18 ether **33** and an earlier reported[28] 11β,18-steroidal lactone, centered at 4.27–4.30 ppm for ethers and at 4.80–4.93 ppm for the lactones. Indeed, molecular models show a dihedral angle of 45° between the 11α and 12β protons, and therefore it may be reasonable to assign the observed spin coupling to these protons. The dihedral angle was estimated to be 75 to 83° for proton pairs 11α,9α and 11α,12α on the basis of molecular models, and accordingly no coupling is associated with them. In this connection the 3β-acetoxylanostane-18,11β-lactone (**27**) also shows a one-proton quartet centered at 2.52 ppm ($J_{12\beta,11\alpha}$ = 6 Hz, $J_{12\alpha,12\beta}$ = 12.5 Hz) and assigned to the C-12 (β) equatorial proton. The latter is obviously coupled with the 11α proton in agreement with the above-cited observations. Such a low field quartet (at 2.61 ppm) has been found earlier[29] for the 1β-equatorial proton of a steroidal 19,2β-lactone, and its position was verified by double and triple resonance techniques. The 11α protons in the 11β,19-epoxylanostanes **25** and **28**, as well as in the analogous steroidal ether **34**, appear as multiplets at 4.13 and 4.25 ppm, respectively.

The mass spectra (Figures 1 and 2) of the above lanostane ethers deserve some comment. Interestingly, both the 11β,18-ether alcohol **24** and its acetate **26**, as well as the 3-keto derivative **32**, show the molecular ion as base peak. No significant change was observed in the spectrum of the hydroxy compound at low voltage (12 and 15 eV). All three 11,18-ether derivatives show a loss of 33 mass units, corresponding to the combined loss of methyl and water. A possible diagnostic fragment for the 11β,18 ethers, corresponding to the loss of 112 mass units, could be formulated, for example as fragment a for the 3-hydroxy derivative **24**, resulting from the elimination of the side chain and appropriate metastable peaks were observed for this transition. Such fragmentation is not observed in the case of the 11β,19 ether **25** and its acetate **28**. Also, concomitant elimination of the 3β substituent and loss of the side chain lead to a fragment b (m/e 313) found in both the 11β,18-ether alcohol **24** and its acetate **26**, while in the 3-keto compound only the loss of the side chain (M − 113) was observed. One of the possible formulations for a significant fragment (m/e 194), common to all the above 11,18 ethers, is depicted by formula c. The loss of one C-18 hydrogen is proposed on the basis of the spectrum of the 18,18-dideuterio derivative. Our proposed mechanism provides for a fully

(29) N. Bhacca, M. E. Wolff, and R. Kwok, *J. Amer. Chem. Soc.*, **84**, 4976 (1962).

SCHEME III



conjugated radical ion and its direct formation from the respective molecular ions of the various derivatives is indicated by the presence of proper metastable ions. Lastly, an ion of mass 249, observed in the spectra of all 11,18 ethers, could be formulated as fragment d, but no further evidence indicates its mode of formation or its structural formulation (Scheme III).

In contrast to the relatively simple mass spectra of the 11,18 ethers, the isomeric 11,19 ethers undergo very extensive fragmentation. Characteristically ring-D fragmentation processes resulting in loss of 155, 154, and 140 mass units are prevalent. Fragmentation modes arising from ring D cleavages have been studied[30] in detail in our laboratory.

To complete our synthetic scheme, the 3β-acetoxylanostane-18,11β-lactone (**27**) was reduced with lithium aluminum hydride to yield lanostane-3β,11β,18-triol (**21**), which proved to be identical with the triol derived from the sea cucumber aglycone seychellogenin (**9**) on the basis of mixture melting point, rotation, and identity of all spectral characteristics.

Although the chemical and spectroscopic properties of the minor lead tetraacetate product, 11β,19-epoxylanostan-3β-ol (**25**), were consistent with its structure, unambiguous chemical proof appeared to be in order. A suitable material was the known[23] 11β,19-cyclolanostane-3β,11α-diol 3-acetate (**23**) whose structure had been proved[23,31] unambiguously by chemical correlation with cycloartenol (**35**). Thus lead tetraacetate oxidation of the cyclobutanol **23** yielded the known[23] 3β,19-dihydroxylanostan-11-one 3-acetate (**36**), which by lithium aluminum hydride reduction gave lanostane-3β,11β,19-triol (**37**). This triol was identical in all respects with the lithium aluminum hydride reduction product of the oxo-acid ester **30**.

In conclusion, the successful interconversion of seychellogenin and lanosterol establishes the complete structure of the marine sapogenin and its stereochemistry at every position but C-20. It is safe to assume, therefore, that all other holothurinogenins with hydroxyl groups at C-17 (**1**,[5,6] **3**,[7] **4**,[8] **5**,[8] **8**,[9]) are also based on a lanostane skeleton.

Experimental Section

Melting points were measured on a Kofler hot-stage microscope and are uncorrected. All rotations were determined using chloroform as solvent. Infrared spectra were obtained using Perkin-Elmer infracord or Model 421 recording spectrophotometers. Ultraviolet spectra were measured in 95% ethanol on a Cary-14 recording spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian T-60, A-60, or HA-100 spectrometer under the supervision of Dr. L. J. Durham. In all cases deuteriochloroform was employed as solvent and tetramethylsilane (δ 0.00 ppm) as internal reference. The visually most intense signal in the methyl region (δ 0.5–1.5) is underlined in the presentation of data. Microanalyses were carried out by Messrs. E. Meier and J. Consul. Mass spectra (70 eV) were obtained by Dr. A. M. Duffield, Mr. R. Ross, and Mr. R. T. Conover with an AEI MS-9 mass spectrometer and in some instances with an Atlas CH-4 mass spectrometer, both equipped with a direct inlet system. Column chromatographies were performed using Davison 60–200 mesh silica gel. Analytical scale thin layer chromatography (tlc) was carried out on 5 × 20 cm, 250-μ silica gel HF plates. Substances were visualized on these plates either by exposure to iodine vapor or by spraying with ceric sulfate solution (2% in 2 *N* sulfuric acid) followed by brief heating on a hot plate. Materials were located on the preparative silica gel plates by iodine vapor or, alternatively, by vertical spotting of ceric sulfate solution, followed by activation of the strip with hot wire from above.

Seychellogenin (**9**).—The isolation, acid hydrolysis of the crude saponins, and the purification of seychellogenin have been described previously.[9,11] Physical properties of seychellogenin: mp (after sublimation) 234–238°; $[\alpha]^{26}D$ −7° (*c* 1.6); ir ($CHCl_3$)

(30) L. Tökés, G. Jones, and C. Djerassi, *J. Amer. Chem. Soc.*, **90**, 5465 (1968).

(31) S. Corsano and G. Nicita, *Ric. Sci.*, **37**, 351 (1967).

3300 (OH) and 1755 cm^{-1} (lactone C=O); uv max 237 nm sh (ϵ 11,000), 244 (12,000), and 252 nm sh (8200); nmr δ 0.83 + 0.90 + 0.92 + 1.01 + 1.11 (CH_3-19, -26, -27, -30, -31, -32), 1.40 (CH_3-21), 2.55 (broad d, 2, CH_2-12), 3.23 (m, 1, CH-3), 5.25 and 5.62 (m, 1 each, CH-7 and CH-11); mass spectrum (rel intensity) *m/e* 456 (20, M + 2, probably dihydro contaminant), 454 (100, M^+), 441 (5), 439 (5), 421 (48), 411 (6), 395.33055 (62, $C_{28}H_{43}O$ requires 395.33137), 393 (11), 377.32070 (18, $C_{28}H_{41}$ requires 377.32081), 368.27022 (34, $C_{25}H_{36}O_2$ requires 368.27152), 367.26405 (88, $C_{25}H_{35}O_2$ requires 367.26369), 283 (15), and 43 (100).

Anal. Calcd for $C_{30}H_{46}O_3$: mol wt, 454.34404. Found: mol wt (mass spectrometry), 454.34468.

Seychellogenin 3β-Acetate.—Seychellogenin (**9**, 100 mg) was acetylated with 1:1 acetic acid–pyridine (6 ml) at room temperature overnight. After the usual work-up seychellogenin 3β-acetate was obtained: mp 214–217° (from acetone–ethanol); $[\alpha]^{24}D$ +21° (*c* 0.9); ir (KBr) 1763 (lactone C=O), 1736 (ester C=O), 1650 and 1240 cm^{-1}; uv max 237 nm sh (ϵ 11,500), 244 (12,700), and 252 sh (9100); nmr δ 0.83 + 9.91 + 0.95 + 0.98 + 1.01 + 1.13 (CH_3-19, -26, -27, -30, -31, -32), 1.40 (s, 3, CH_3-21), 2.05 (s, 3, $OCOCH_3$), 2.5 (broad d, 2, CH_2-12), 4.5 (m, 1, CH-3), 5.2 and 5.5 (m, 1, each CH-7 and CH-11); mass spectrum *m/e* (rel intensity) 498 (18, M + 2, dihydro impurity), 496 (100, M^+), 481 (3, M − CH_3), 453 [6, M − (CH_3 + H_2O)], 437 [83, M − (CO_2 + CH_3)], 463 (9, M − AcOH), 421 [74, M − (AcOH + CH_3)], 393 (11), 377 [23, M − (CH_3 + CO_2 + AcOH)], 368 (38), 367 (98, ring-A fragmentation), 325 [15, M − (CO_2 + CH_3 + side chain)], and 43 (96).

Anal. Calcd for $C_{32}H_{48}O_4$: C, 77.38; H, 9.74. Found: C, 77.21; H, 9.75.

Lithium Aluminum Hydride Reduction of Seychellogenin (9).—Seychellogenin (130 mg) was reduced with lithium aluminum hydride (200 mg) in tetrahydrofuran (20 ml) at reflux temperature over a period of 4 hr. After work-up with saturated sodium sulfate solution, the triol **11** was crystallized from chloroform–methanol: mp 172–173° (transition at 161–170°); $[\alpha]^{24}D$ +47° (*c* 0.6); ir ($CHCl_3$) 3620 (sharp), 3390 (broad), and 1050 cm^{-1}; uv max 236, 243, and 252 nm; nmr δ 1.31 + 1.25 + 0.98 + 0.92 + 0.87 + 0.83 (CH_3-19, -21, -26, -27, -30, -31, -32), 3.1–3.5 (*m*, CH_2-18 and CH-3), 5.4 (*m*, CH-7 and CH-11); mass spectrum (rel intensity) *m/e* 458 (1, M^+), 440 (10, M − H_2O), 425 [9, M − (H_2O + CH_3)], 422 [19, M − (H_2O + H_2O)], 409 [100, M − (H_2O + CH_2OH)], 407 [19, M − (H_2O + H_2O + CH_3)], and 355 (10, M − C_6H_{13} side chain).

Anal. Calcd for $C_{30}H_{50}O_3$: mol wt, 458. Found: mol wt (mass spectrometry), 458.

Acetylation of the Triol 11.—The triol **11** (140 mg) was acetylated in a 1:1 mixture of pyridine–acetic anhydride (16 ml) at room temperature overnight. After the usual work-up and preparative tlc (silica gel HF, 10% ethyl acetate–benzene, R_f 0.4) the triol diacetate **12** (110 mg) could be crystallized from benzene–hexane (containing a trace of pyridine): mp 139–144°; $[\alpha]^{26}D$ +67° (*c* 1.3); ir (KBr) 3550 (sharp), 3490 (broad), 1737, 1375, and 1240 cm^{-1}; uv max 235 nm (ϵ 13,400), 243 (15,400), and 252 (10,200); nmr δ 0.83 + 0.88 + 0.92 + 0.95 + 1.02 (18, CH_3-19, -26, -27, -30, -31, -32), 1.32 (s, 3, CH_3-21), 2.02 (s, 6, $OCOCH_3$), AB quartet at 4.20 and 3.79 (1 each, *J* = 11 Hz, CH_2-18), 4.54 (m, 1, CH-3), 5.2–5.7 (broad, m, 2, CH-7 and CH-11); mass spectrum (rel intensity) *m/e* 542 (1, M^+), 524 (18), 509 [7, M − (H_2O + CH_3)], 482 (7, M − AcOH), 464 [35, M − (H_2O + AcOH)], 451 [70, M − (H_2O + CH_2OAc)], 449 [48, M − (H_2O + AcOH + CH_3)], 411 (20), 407 [14, M − (AcOH + CH_2OAc + H_2O)], 397 [30, M − (AcOH + C_6H_{13})], 389 [20, M − (2AcOH + H_2O + CH_3)], 69 (10), and 43 (235, base peak).

Anal. Calcd for $C_{34}H_{54}O_5$: C, 75.23; H, 10.03. Found: C, 75.30; H, 10.03.

Reduction of seychellogenin (**9**) with lithium aluminum deuteride followed by acetylation gave the corresponding C_{18}-dideuterio derivative, the spectrum of which exhibited the following peaks: *m/e* 544 (1, M^+), 526 (26), 511 (5), 484 (20), 466 (20), 465 (23), 451 (100), 449 (2), 437 (16), 413 (19), 409 (17), 401 (26), 399 (62), 391 (25), and 43 (183, base peak).

Dehydration of 3β,18-Diacetoxy-20ξ-hydroxylanosta-7,9(11)-diene (12).—The triol diacetate **12** (94 mg) in pyridine (18 ml) was treated with phosphorus oxychloride[15] (3 ml) at room temperature for 1 day. After the excess reagent was destroyed with water, ether extraction gave a mixture of products which were separated on silver nitrate impregnated silica gel HF plates (1.1% ethyl acetate–benzene, developed twice). The less polar isomer, 3β,18-diacetoxylanosta-7,9(11),20(22)-triene (**14**) (R_f 0.65, 28 mg, 30%), was crystallized from dichloromethane–methanol: mp 120–122°; $[\alpha]^{26}D$ +18° (*c* 0.9); ir ($CHCl_3$) 1735 and 1255 cm^{-1}; uv max 235 nm (ϵ 11,700), 242 (13,900), and 251 (9000); nmr δ 0.81 + 0.87 + 0.90 + 0.92 + 0.95 + 1.00 (CH_3-19, -26, -27, -30, -31, -32), 1.65 (s, half width = 3 Hz, 3, CH_3-21), 1.88 (s, 3, CH_3OCO-18), 2.03 (s, 3, CH_3OCO-3), AB quartet at 3.76 and 3.50 (1 each, *J* = 11 Hz, CH_2-18), 4.50 (m, 1, CH-3) 5.15–5.55 (broad m, 3, CH-7, CH-11, and CH-22); mass spectrum (rel intensity) *m/e* 524 (27, M^+), 509 (5, M − CH_3), 464 [52, M − AcOH), 451 (90, M − CH_2OAc), 449 [63, M − (CH_2OAc + AcOH)], 411 (26), 407 (15), 391 (40), 389 (41), 355 (18), 35 (16), 315 (76), 313 (95), 312 (25), 255 (50), 69 (100), and 43 (224, base peak).

Anal. Calcd for $C_{34}H_{52}O_4$: mol wt, 524. Found: mol wt (mass spectrometry), 524.

The more polar olefin, 3β,18-diacetoxylanosta-7,9(11),20(21)-triene (**13**) (R_f 0.53, 34 mg, 37%), was crystallized from chloroform–methanol: mp 130–131°; $[\alpha]^{26}D$ +28° (*c* 0.5); ir ($CHCl_3$) 1735, 1650, 893 (C=CH_2), and 1250 cm^{-1} uv max 235 nm (ϵ 12,100), 242 (14,200) and 251 (9300); nmr δ 0.83 + 0.88 + 0.93 + 0.95 + 1.01 (CH_3-19, -26, -27, -30, -31, -32), 1.88 (s, 3, CH_3OCO-18), 2.04 (s, 3, CH_3OCO-3), AB quartet at 3.85 and 3.50 (1 each, *J* = 11 Hz, CH_2-18), 4.55 (m, 1, CH-3), 4.80 (broad d, 2, *J* = 5 Hz, CH_2-21), 5.45 (broad m, 2, CH-7 and CH-11); mass spectrum (rel intensity) *m/e* 524 (34, M^+), 509 (7), 464 (61), 451 (90), 449 (68), 411 (53), 407 (16), 391 (36), 389 (47), 379 (15), 355 (22), 351 (18), 315 (31), 313 (61), 312 (35), 255 (37), 69 (100), and 43 (242, base peak).

Anal. Calcd for $C_{34}H_{52}O_4$: mol wt, 524.38654. Found: mol wt (mass spectrometry), 524.38714.

Catalytic Hydrogenation of the $\Delta^{20(21)}$ Olefin 13. The olefin **13** (127 mg) in ethyl acetate (25 ml) was hydrogenated with 120 mg of platinum oxide at room temperature for 4 hr giving the C-20 epimeric mixture **15**: mp 97–105°; $[\alpha]^{27}D$ +43° (*c* 1.2); ir (KBr) 1738 and 1240 cm^{-1}; uv max 235 nm (ϵ 10,500), 242 (12,300), and 251 (8100); nmr δ 0.82 + 0.88 + 0.90 + 0.93 + 0.96 (CH_3-19, -21, -26, -27, -30, -31, -32), 1.98 (s, 3, CH_3OCO-18), 2.04 (s, 3, CH_3OCO-3), 3.75 (broad s, 2, half width = 3 Hz, CH_2-18), 4.5 (m, 1, CH-3), and 5.4 (broad m, ~1.5, CH-7 and CH-11); mass spectrum (rel intensity) *m/e* 528 (12, M′+, dihydro compound], 526 (13, M^+), 468 (12, M′ − AcOH), 466 (46, M − AcOH), 453 (34), 451 (12), 411 (7), 393 [100, M − (AcOH + CH_2OAc)], 391 (27), 353 (38), 297 (38), 257 (65), 171 (39), 145 (40), 69 (64) and 43 (145).

Anal. Calcd for $C_{34}H_{54}O_4$: mol wt, 526. Found: mol wt (mass spectrometry), 526.

Catalytic Hydrogenation of the $\Delta^{20(22)}$ Olefin 14.—Hydrogenation of the olefin **14** (18 mg) in ethyl acetate (15 ml) with 25 ml of platinum oxide at room temperature for 24 hr yielded the diacetate **15** (18 mg), identical with that reported above on the basis of mass spectral, ultraviolet, and thin layer chromatographic comparison.

Chromium Trioxide Oxidation of 3β,18-Diacetoxy-20ξ-lanosta-7,9(11)-diene (15).—The diene **15** (120 mg) in acetic acid (1 ml) was treated with chromium trioxide solution (200 mg, in 1 ml 8:2 acetic acid–water) at 60° over a period of 1 hr. The mixture was allowed to stand at room temperature for a further 2 hr and then poured onto ice (200 ml) and extracted with ether. The product (140 mg) resulting after removal of solvent was purified by tlc (silica gel HF, 5% ethyl acetate–benzene, developed three times). The uv-active fraction (R_f 0.55, 55 mg, 45%) was identified as 3β,18-diacetoxy-20ξ-lanost-8-ene-7,11-dione (**16**): mp 105–109° (diethyl ether–methanol); $[\alpha]^{27}D$ +82° (*c* 1.0) ir (KBr) 1736, 1671, and 1240 cm^{-1}; uv max 271 nm (ϵ 7080); nmr δ 0.81 + 0.90 + 0.93 + 1.20 + 1.28 (CH_3-19, -21, -26, -27, -30, -31, -32), 2.03 and 2.00 (s, 3, each, CH_3OCO-3 and -18), coalescing AB quartet at 3.92 and 3.98 (2, CH_2-18) and 4.53 (q, 1, *J* = 6.5 and 9 Hz, CH-3); mass spectrum (rel intensity) *m/e* 556 (100, M^+), 528 (2), 514 (13), 496 (93, M − AcOH), 481 (14), 468 (9), 436 (10), 384 (14), 383 (13), 287 (20), 187 (22), 121 (20), and 43 (75).

Anal. Calcd for $C_{34}H_{52}O_6$: mol wt, 556. Found: mol wt (mass spectrometry), 556.

Zinc–Acetic Acid Reduction of Ene–Dione 16.—Zinc dust (200 mg) was added to a solution of the ene–dione **16** (53 mg) in refluxing glacial acetic acid (10 ml) over a period of 30 min. After refluxing for 5 hr, the reaction mixture was poured onto ice and extracted with ether. Purification of the product by tlc (silica

gel HF, 5% ethyl acetate–benzene, developed three times) gave a C-20 epimeric mixture of 7,11 diketone **17** (41 mg, 77%) as an amorphic solid: $[\alpha]^{26}D$ +36° (*c* 1.1); ir (KBr) 1735, 1704, and 1240 cm^{-1}; nmr δ 0.82 + 0.85 + 0.92 (CH_3-21, -26, -27, -30, -31), 1.24 and 1.32 (s, 3 each, CH_3-19 and -32), 2.04 (s, 6, CH_3OCO-3 and -18), 4.05 (t, 2, CH-$_2$18), 4.53 (q, 1, *J* = 6.5 and 9 Hz, CH-3); mass spectrum (rel intensity) *m/e* 558 (100, M^+), 516 (4), 498 (10), 485 (10), 483 (11), 456 (25), 455 (7), 423 (15), 385 (5), 357 (5), 303 (5), 275 (7), 251 (5), 219 (7), 207 (6), 191 (14), 121 (23), and 43 (56).

Anal. Calcd for $C_{34}H_{54}O_6$: mol wt, 588. Found: mol wt (mass spectrometry), 558.

Preparation of 7-Ethylene Thioketal 18.—The diketone **17** (40 mg) in ethanedithiol (70 drops) and boron trifluoride–etherate (25 drops) was stirred for 2 hr at room temperature, the mixture diluted with benzene, and washed with aqueous sodium hydroxide solution (4%) followed by saturated sodium chloride solution. Evaporation of the solvent yielded a yellow gum (45 mg), which, on thin layer chromatoplates (silica gel HF, 2% ethyl acetate–benzene, developed twice) indicated very little starting material and two distinct major components with R_f values 0.41 and 0.27 assigned to the C-20 epimeric mixture of 3,18-diacetoxy-20ξ-lanostane-7,11-dione 7-ethylene thioketals (**18**): nmr (on crude mixture in pyridine) δ 0.83 + 0.90 + 0.96 (CH_3-21, -26, -27, -30, 31), 1.26 (s, 3, CH_3-19), 1.50 (s, 3, CH_3-32), 2.02 and 2.08 (s, 3 each, CH_3OCO-3, and -18), 3.27 (s, 4, $-SCH_2CH_2S-$) and 4.2–4.9 (broad m, 3, CH_2-18 and CH-3).

Anal. Calcd for $C_{36}H_{58}O_5S_2$: mol wt 634. Found: mol wt (mass spectrometry), 634.

Raney Nickel Desulfurization of 7-Ethylene Thioketal 18.—Excess Raney nickel[32] was added to a solution (diethyl ether–ethanol, 2:3, 20 ml) of the crude 7-ethylene thioketal **18** (40 mg). After 4-hr refluxing additional Raney nickel was added and refluxing was continued for 24 hr. The reaction mixture was filtered through celite and on evaporation of the solvent, a pale yellow gum resulted (44 mg). Preparative tlc (silica gel HF, 2% ethyl acetate–benzene, developed three times) yielded two well-separated components (R_f 0.44 and 0.29).

The less polar component, 3β,18-diacetoxy-20-epilanostan-11-one (**19**) (R_f 0.44, 10.3 mg, 27%), was crystallized from acetone–hexane: mp 140.5–143°; $[\alpha]^{27}D$ +38° (*c* 1.1); ir (KBr) 1737, 1700, 1240, and 1030 cm^{-1}; nmr δ 0.83 + 0.84 + 0.87 + 0.88 + 1.08 + 1.13 (CH_3-19, -21, -26, -27, -30, -31, -32), 203 (s, 6, CH_3OCO-3 and -18), AB quartet at 2.67 and 2.46 (1 each, *J* = 14 Hz, CH_2-12), broad doublet centered at 2.8 (1, CHβ-1), 4.00 (s, 2, CH_2-18), 4.47 (s, 1, CH-3); mass spectrum (rel intensity) *m/e* 544 (18, M^+), 502 (1), 484 (48), 471 (20), 442 (8), 441 (11), 411 (11), 399 (12), 361 (100), 348 (13), 301 (14), 275 (11), 263 (29), 193 (17), 135 (33), and 43 (69).

Anal. Calcd for $C_{34}H_{56}O_6$: mol wt, 544.41275. Found: mol wt (mass spectrometry), 544.41228.

The more polar component, 3β,18-diacetoxylanostan-11-one (**20**) (R_f 0.29, 13.4 mg, 34%), was crystallized from ether–hexane: mp 130–131°; $[\alpha]^{26}D$ +53° (*c* 1.4); ir (KBr) 1735, 1700, 1240, and 1025 cm^{-1}; nmr δ 0.83 + 0.84 + 0.87 + 0.89 (CH_3-21, -26, -27, -30, -31), 1.08 and 1.13 (s, 3, each, CH_3-32, -19), 2.03 (CH_3OCO-3 and -18) a pair of doublets at 2.45 and 2.65 (d, 1 each, *J* = 14 Hz, CH_2-12), 2.85 (broad d, 1, CHβ-1) 4.02 (broad s, 2, CH_2-18), 4.47 (m, 1, CH-3); mass spectrum (rel intensity) *m/e* 544 (25, M^+), 502 (2), 484 (40), 471 (20), 442 (8), 441 (10), 411 (9), 399 (10), 361 (100), 348 (11), 301 (8), 275 (8), 263 (35), 175 (14), 135 (30), and 43 (53).

Anal. Calcd for $C_{34}H_{56}O_5$: mol wt, 544.41275. Found: mol wt (mass spectrometry), 544.41228.

Lithium Aluminum Hydride Reduction of 3β,18-Diacetoxylanostan-11-one (20).—The 11 ketone **20** was reduced with excess lithium aluminum hydride in tetrahydrofuran (4 ml) at reflux temperature overnight. After work-up with saturated sodium sulfate solution, the triol **21** (14 mg) was obtained: mp 228–229° (after sublimation at 2 × 10^{-5} mm, approx 170°); $[\alpha]^{26}D$ +43° (*c* 1.0); ir 3410 and 1030 cm^{-1}; nmr δ 0.82 + 0.90 + 0.97 (CH_3-21, -26, -27, -30, -31, -32), 1.18 (s, 3, CH_3-19), 3.25 (m, 1, CH-3), 3.7 (m, 2, CH_2-18), 4.26 (m, 1, CH-11); mass spectrum (rel intensity) *m/e* 444 (18, M − H_2O), 429 (20), 414 (37), 413 (15), 411 (26), 399 (18), 395, 393, 381 (10), 301 (88), 283 (21), 220 (23), and 193 (100 base peak).

(32) A. A. Pavlic and H. Adkins, *J. Amer. Chem. Soc.*, **68**, 1471 (1946).

Mixture melting point (227–229°), comparison of the physical data, and identical tlc behavior (R_f 0.40, silica gel HF, 4:1 hexane–acetone, developed three times) established its identity with the triol **21** derived from lanosterol.

Lead Tetraacetate–Iodine–Lithium Aluminum Hydride Reaction on 11β-Hydroxylanostan-3β-yl Acetate (22).[33]—Lead tetraacetate (3.0 g), glacial acetic acid (40 ml), and iodine (1.5 g) in cyclohexane (dry) (80 ml), was stirred for 10 min at room temperature. A cyclohexane solution (150 ml) of 11β-hydroxylanostan-3β-yl acetate (**22**)[12] (3.0 g, mp 215–216°) was added and the reaction mixture irradiated and kept at reflux temperature by means of a 500-W tungsten lamp. After 10 hr, additional lead tetraacetate (2.0 g) and iodine (1.0 g) were added, and the addition of lead tetraacetate (2.0 g) was repeated after 10 hr more. In 6 hr the reaction mixture was cooled, diluted with cyclohexane (500 ml), and washed successively with sodium thiosulfate solution (10%, 3 × 100 ml), saturated sodium bicarbonate solution, and saturated sodium chloride solution. Brief drying over anhydrous magnesium sulfate and evaporation of the solvent under reduced pressure yielded a pale yellow gum (4.25 g). This oxidation mixture was reduced with lithium aluminum hydride (5.0 g) in ether (150 ml) at reflux temperature for 10 hr. After work-up with saturated sodium sulfate solution, the amorphous residue (2.70 g) was chromatographed over silica gel [300 g, pretreated with 15% water, eluent hexane–acetone (6:1)]. The initial fractions (1.30 g) contained a mixture of two compounds and the subsequent fractions contained up to 12 components on the basis of analytical tlc (silica gel HF, 4:1 hexane–acetone, developed twice). Preparative tlc (silica gel HF, 9:1 hexane–acetone, four times) on the initial fractions yielded two ethers (R_f 0.42 and 0.30).

(1) 11β,18-Epoxylanostan-3β-ol (**24**) (R_f 0.42, 870 mg, 32%): mp 196–197° (from methanol–chloroform); $[\alpha]^{24}D$ +81° (*c* 1.2); ir (KBr) 3410 and 1020 cm^{-1}; nmr δ 0.73 + 0.82 + 0.86 + 0.88 + 0.95 + 1.02 (CH_3-19, 21, -26, -27, -30, -31, -32), 3.18 (q, 1, *J* = 6.5 and 9 Hz, CH-3), 3.63 (s, 2, CH_2-18), and 4.27 (d, $J_{11\alpha,12\beta}$ = 6 Hz, CH-11); for mass spectrum, see Figure 1.

Anal. Calcd for $C_{30}H_{52}O_2 \cdot {}^1/_2CH_3OH$: C, 79.50; H, 11.81. Found: C, 79.60; H, 11.69.

(2) 11β,19-Epoxylanostan-3β-ol (**25**) (R_f 0.30, 223 mg, 8%): mp 174–175° (from chloroform–methanol); $[\alpha]^{27}D$ +55° (*c* 1.1); ir (KBr) 3440, 1040, and 1010 cm^{-1}; nmr δ 0.61 + 0.68 + 0.81 + 0.86 + 0.91 + 0.91 (CH_3-18, -21, -26, -27, -30, -31, -32), 3.26 (q, 1, *J* = 5.5 and 9 Hz, CH-3), AB quartet at 3.82 and 3.64 (doublet, 1 each, *J* = 8 Hz, 3.82 is pair of narrow doublets, *J* = 1.5 Hz) and 4.13 (m, 1, CH-11); for mass spectrum, see Figure 2.

Anal. Calcd for $C_{30}H_{52}O_2$: C, 81.02; H, 11.79. Found: C, 80.85; H, 11.69.

11β,18-Epoxylanostan-3-one (32).—11β,18-Epoxylanostan-3β-ol (**24**) (30 mg) was treated with a pyridine (1 ml) solution of chromium trioxide (30 mg) at room temperature for 5 hr. After the usual work-up, the ketone **32** was crystallized from acetone–methanol: mp 116–117°; $[\alpha]^{24}D$ +78° (*c* 1.4); ir (KBr) 1705 (C=O), 1030, and 1020 cm^{-1}; nmr δ 0.82 + 0.88 + 0.91 + 1.04 (CH_3-21, -26, -27, -30, -31, -32), 1.16 (s, 3, CH_3-19), 3.67 (s, 2, CH_2-18), 4.28 (d, 1, $J_{11\alpha,12\beta}$ = 6 Hz); mass spectrum (rel intensity) *m/e* 442 (84, M^+), 427 (23), 424 (2), 411 (10), 409 (23, 427 → 409, m* 392.5), 397 (7), 357 (7, 442 → 357, m* 288.5), 330 (24, 442 → 330, m* 246.2), 329 (14), 311 (10), 299 (7), 249 (12), 194 (23, 442 → 194, m* 85.2), 193 (14), and 43 (100).

Anal. Calcd for $C_{30}H_{50}O_2$: C, 81.39; H, 11.38. Found: C, 81.30; H, 11.40.

2,2-Dideuterio-11,18-epoxylanostan-3-one.—The ketone **32** (10 mg) was stirred in an aliquot of sodium (100 mg), deuterium oxide (1 ml), and dioxane (2 ml). After 1 day the solvent evaporated under reduced pressure and the exchange repeated with deuterium oxide (1 ml) and dioxane (2 ml) for an additional day. Then the solvent was again evaporated, deuterium oxide (3 ml) was added, and the solution was extracted with chloroform. The product was purified by tlc (silica gel HF, 5% ethyl acetate–benzene, developed twice, R_f 0.4) and crystallized from methanol–chloroform: mp 114–116°; approximate isotopic distribution 1% d_0, 9% d_1, and 90% d_2; mass spectrum (rel intensity) *m/e*

(33) We employed a modification of the procedure of Barton and coworkers (ref 26), who recorded the isolation of 11β,19-epoxylanostan-3β-ol (**25**), mp 177–182°, $[\alpha]D$ +52°, and its 3-acetate (**28**), mp 162–165°, $[\alpha]D$ +61°. Identity of our product was established by direct comparison in Professor Barton's laboratory.

444 (100, M^+), 429 (29), 413 (14), 411 (30), 399 (9), 359 (7), 332 (29), 331 (17), 313 (12), 249 (16), 194 (27), 193 (17), and 43 (46).

11β,18-Epoxylanostan-3β-yl Acetate (26).—The 3-hydroxy 11,18 ether **24** was acetylated in 1:1 pyridine–acetic anhydride at room temperature overnight. The product, 11β,18-epoxylanostan-3β-yl acetate (**26**), was crystallized from chloroform–methanol: mp 185.5–186.5°; $[\alpha]^{24}D$ +89° (*c* 1.2); ir (KBr) 1735, 1240, and 1020 cm^{-1}; nmr δ 0.81 + 0.82 + 0.87 + 0.89 + 10.5 (CH_3-19, -21, -26, -27, -30, -31, -32), 2.02 (s, 3, CH_3-OCO-3), 3.65 (s, 2, CH_2-18), 4.27 (d, 1, $J_{11\alpha,12\beta}$ = 6 Hz, CH-11), 4.5 (m, 1, CH-3); mass spectrum (rel intensity) *m/e* 486 (100, M^+), 741 (41), 468 (5), 455 (12), 453 (20, 471 → 453, m* 436), 426 (10), 411 (43, 471 → 411, m* 359), 401 (5, 486 → 401 m* 330), 393 (33, 471 → 393, m* 328), 383 (11), 374 (26, 486 → 374, m* 288), 313 (20), 249 (14), 194 (32, 486 → 194, m* 77.4), 193 (18), and 43 (100).

Anal. Calcd for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18. Found: C, 78.73; H, 10.96.

3β-Acetoxylanostane-18,11β-lactone (27).—The ether **26** (200 mg) in acetic acid (1 ml) was treated with chromium trioxide solution (180 mg, in 2 ml of 80% aqueous acetic acid) at room temperature for 5 hr. After the usual work-up, preparative tlc (silica gel HF, 5:1 hexane–acetone) provided the starting material 11β,18-epoxylanostan-3β-yl acetate (**26**) (R_f 0.70, 70 mg), mp 185.5–186.5, and 3β-acetoxylanostane-18,11β-lactone (**27**) (R_f 0.59, 47 mg, 35%): mp 222–222.5° (from chloroform–acetone); $[\alpha]^{24}D$ +73° (*c* 1.3); ir (KBr) 1762 (five-membered lactone), 1736 (acetate), 1240 and 1030 cm^{-1}; nmr δ 0.79 + 0.83 + 0.85 + 0.87 + 0.89 + 0.93 + 1.03 (CH_3-19, -21, -26, -27, -30, -31, -32), 2.04 (s, 3, CH_3OCO-3), 2.52 (q, 1, *J* = 6 and 12.5 Hz, CH-12β), 4.47 (q, 1, *J* = 6.5 and 9 Hz, CH-3), 4.93 (d, 1, $J_{11\alpha,12\beta}$ = 6 Hz, CH-11); nmr (C_6D_6) δ 0.69 + 0.85 + 0.88 + 0.95 + 0.97 (CH_3-19, -21, -26, -27, -30, -31, -32), 1.75 (s, 3, CH_3OCO-3), 2.27 (q, 1, *J* = 6 and 12.5 Hz, CH-12β), 4.26 (d, 1, $J_{11\alpha,12\beta}$ = 6 Hz, CH-11), 4.58 (q, 1, *J* = 6.5 and 9 Hz, CH-3); mass spectrum (rel intensity) *m/e* 500 (32, M^+), 485 (26), 482 (3), 455 (8), 440 (22), 425 (39), 397 (12), 385 (7), 371 (15), 347 (48), 343 (58), 327 (7), 311 (8), 288 (32), 287 (29), 283 (26), 237 (22), 193 (25), 176 (28), 135 (39), and 43 (100).

Anal. Calcd for $C_{32}H_{52}O_4$: C, 76.75; H, 10.47. Found: C, 76.91; H, 10.27.

Lanostane-3β,11β,18-triol (21).—The lactone **27** (35 mg) was reduced with excess lithium aluminum hydride in tetrahydrofuran (3 ml) at room temperature overnight. Work-up with saturated sodium sulfate solution gave lanostane-3β,11β,18-triol (**21**) (32 mg): mp 227–229° (after sublimation at 2 × 10^{-5} mm, *ca.* 170°); $[\alpha]^{27}D$ +43° (*c* 1.1); ir (KBr) 3410 and 1035 cm^{-1}; nmr δ 0.82 + 0.90 + 0.97 (CH_3-21, -26, -27, -30, -31, -32), 1.18 (s, 3, CH_3-19), 3.25 (m, 1, CH-3), 3.70 (q poor, 2, CH_2-18), 4.26 (m, 1, CH-11), 3.70 + 2.20 + 1.69 (all three singlets exchange in D_2O, HO-3, -11, -18); mass spectrum (rel intensity) *m/e* 444 (11), 429 (9), 414 (43), 413 (13), 411 (10), 399 (16), 395, 393, 381 (6), 301.2537 (85, $C_{21}H_{33}O$ requires 301.2531), 283.2471 (15, $C_{21}H_{31}$ requires 283.2426), 220 (23), and 193.1944 (100, $C_{14}H_{25}$ requires 193.1956).

Anal. Calcd for $C_{30}H_{54}O_3$: C, 77.87; H, 11.76. Found: C, 77.69; H, 11.59.

3β-Acetoxylanostane-18,11β-lactone (**27**) was reduced in a similar manner with lithium aluminum deuteride giving 18,18-dideuteriolanostane-3β,11β,18-triol: mass spectrum (rel intensity) *m/e* 446 (8, M − H_2O), 431 (8), 414 (48), 413 (18), 399 (13), 395 (9), 301 (83), 283 (15), 220 (20), 193 (100, base peak), and 43 (73).

The above 18,18-dideuteriolanostane-3β,11β,18-triol was stirred with *p*-toluenesulfonyl chloride[34] in pyridine at room temperature overnight and the crude product was treated with sodium naphthalide[35] in tetrahydrofuran. Preparative tlc (silica gel HF, 4:1 hexane–acetone, R_f 0.40) gave a small yield of 18,18-dideuterio-11β,18-epoxylanostan-3β-ol: mass spectrum (rel intensity) *m/e* 446 (100 M^+), 431 (26), 413 (32), 381 (6), 361 (4), 334 (16), 315 (12), 251 (12), 195 (25), and 193 (12).

11β,19-Epoxylanostan-3β-yl Acetate (28).—The 3β alcohol **25** was acetylated in 1:1 pyridine–acetic anhydride at room temperature overnight. The acetate **28** was crystallized from chloroform–methanol: mp 165–166°; $[\alpha]^{25}D$ +62° (*c* 1.2); ir (KBr) 1737, 1245, and 1020 cm^{-1}; nmr δ 0.70 + 0.81 + 0.84 + 0.90 (CH_3-18, -21, -26, -27, -30, -31, -32), 2.03 (s, 3, CH_3-OCO-3), AB quartet at 3.65 and 3.83 (1 each, *J* = 8 Hz, CH_2-19), 4.13 (m, 1, CH-11), 4.53 (m, 1, CH-3); mass spectrum (rel intensity) *m/e* 486 (29, M^+), 471 (3), 455 (32), 426 (18), 411 (7), 396 (33), 395 (27), 381 (8), 373 (6), 346 (43), 332 (50), 331 (20), 315 (29), 303 (37), 301 (31), 286 (28), 273 (33), 263 (43), 255 (72), 243 (53), 207 (38), 203 (48), 95 (100), and 43 (97).

Anal. Calcd for $C_{32}H_{54}O_3$: C, 78.96; H, 11.18. Found: C, 78.86; H, 11.34.

Chromium Trioxide Oxidation of 11β,19-Epoxylanostan-3β-yl Acetate (28).—The ether **28** (35 mg) in acetic acid (1 ml) was treated with chromium trioxide (20 mg in 1 ml of 80% aqueous acetic acid) at room temperature for 4 hr. The excess reagent was decomposed with 2-propanol and the resulting 3β-acetoxy-11-oxolanostan-19-oic acid (**29**) was isolated by preparative tlc (silica gel HF, 4:1 hexane–acetone, developed twice, R_f 0.3, 18 mg): mp 185–188° (from chloroform–acetone); ir ($CHCl_3$) 3540, 2900–3300 (broad), 1730, 1708 (11 ketone), and 1250 cm^{-1}; mass spectrum (rel intensity) *m/e* 516 (5, M^+), 498 (7, M − H_2O), 472 (2), 456 (80, M − AcOH), 438 (23, M − (AcOH + H_2O)], 410 [100, M − (AcOH + CO_2H_2)], 395 (10), 393 (16), 377 (7), and 95 (68).

Anal. Calcd for $C_{32}H_{52}O_5$: mol wt, 516. Found: mol wt (mass spectrometry), 516.

The above acid was further characterized by converting it to the methyl ester **30** with diazomethane in ether: mp 140–142° (from ether); $[\alpha]^{25}D$ +74° (*c* 0.5); ir ($CHCl_3$) 1735–1700 and 1240 cm^{-1}; nmr δ 0.72 + 0.80 + 0.85 + 0.90 + 1.04 (CH_3-18, -21, -26, -27, -30, -31, -32), 2.04 (s, 3, CH_3OCO-3), 3.70 (s, 3, $COOCH_3$-19); mass spectrum (rel intensity) *m/e* 530 (11, M^+), 512 (17, M − H_2O), 498 (4), 470 (8, M − AcOH), 456 [60, M − (CO_2Me + CH_3)], 438 (20), 410 (64), 393 (89), 392 (28), 377 (8), and 303 (12).

Anal. Calcd for $C_{33}H_{54}O_5$: mol wt, 530.397. Found: mol wt (mass spectrometry), 530.392.

Lithium Aluminum Hydride Reduction of 3β-Acetoxy-11-oxolanostane-19-carboxylic Acid Methyl Ester 30.—The ester **30** (25 mg) was reduced with lithium aluminum hydride in tetrahydrofuran at reflux temperature for 5 hr. After the usual work-up with saturated sodium sulfate solution, preparative tlc (silica gel HF, 4:1 hexane–acetone, three times) gave lanostane-3β,11β,-19-triol (**37**) (15 mg, R_f 0.23): mp 237–238°; $[\alpha]^{25}D$ +41° (*c* 0.9); ir (KBr) 3390 and 1030 cm^{-1}. Mixture melting point determination (mp 237–238°) and comparison of its specific rotation and ir spectrum, as well as its identical tlc behavior (in the above system), confirmed its identity with lanostane-3β,11β,-19-triol (**37**) characterized below.

Lanostane-3β,11β,19-triol (37).—3β-Acetoxy-lanostan-19-ol-11-one[23] (**36**) (53 mg, mp 163–165°; $[\alpha]^{26}D$ +54°; lit.[23] mp 157–158°, $[\alpha]D$ +53°, nmr identical) was reduced with lithium aluminum hydride in tetrahydrofuran (4 ml). After the usual work-up and purification (same as above) lanostane-3β,11β,19-triol (**37**) (21 mg) was isolated: mp 237–239° (from chloroform–methanol); $[\alpha]^{25}D$ +43° (*c* 0.5); ir (KBr) 3390 and 1030 cm^{-1}; nmr 0.79 + 0.91 + 1.00 + 1.02 (CH_3-18, -21, -26, -27, -30, -31, -32), 3.27 (broad m, 1, CH-3), 3,82 (s, 2, CH_2-19), 4.20 (narrow m, 1, CH-11); mass spectrum spectrum (rel intensity) *m/e* 462 (1, M^+), 444 (17), 426 (55), 414 (100), 413 (48), 411 (20), 399 (64), 396 (32), 395 (22), 381 (26), 353 (7), and 239 (10).

Anal. Calcd for $C_{30}H_{54}O_3 \cdot {}^1/_2CH_3OH$: C. 76.51; H, 11.79. Found: C, 76.61; H, 11.80.

Registry No.—**9**, 24041-68-7; **9** 3β-acetate, 24041-70-1; **11**, 25116-58-9; **12**, 25116-59-0; **13**, 24041-73-4; **14**, 25116-61-4; **15**, C-20 (*R*), 24041-75-6; **15**, C-20 (*S*), 24041-74-5; **16**, C-20 (*R*), 24041-81-4; **16**, C-20 (*S*), 24041-76-7; **17**, C-20 (*R*), 25116-64-7; **17**, C-20 (*S*), 25158-18-3; **18**, C-20 (*R*), 25158-19-4; **18**, C-20 (*S*), 25158-20-7; **19**, 24041-77-8; **20**, 24041-78-9; **21**, 24041-79-0; **24**, 25116-67-0; **25**, 22417-94-3; **26**, 25116-68-1; **27**, 24041-80-3; **28**, 22417-93-2; **29**, 25116-71-6; **30**, 25116-72-7; **32**, 25116-73-8; **32** (2,2-dideuterio), 25116-74-9; **37**, 25116-75-0.

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