Mass Spectrometry in Structural and Stereochemical Problems. CCXL.[1] The Effect of a 14α-Angular Methyl Group upon the Mass Spectral Fragmentation of 11- and 7-Keto Steroids[2]

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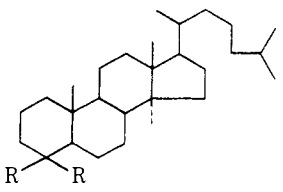
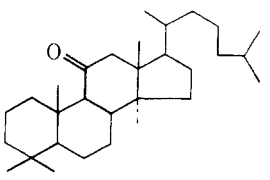
Abstract: Deuterium labeling of lanostan-11-one and lanostan-7-one has revealed the effect of a 14α-methyl group upon the mass spectral fragmentations of these tetracyclic triterpene ketones. The earlier proposed β cleavage of the 9–10 bond, associated with the principal peaks in the mass spectra of 11-keto steroids such as 5α-androstan-11-one and 5α-pregnan-11-one, is found to be relatively unimportant in the presence of a C-14 methyl substituent. Instead, the predominant fragmentations of lanostan-11-one involve the preferred α cleavage of the 11–12 bond with simultaneous homolytic fission of the highly substituted 13–14 bond. The fragmentation sequence is explained in terms of the greater substitution about ring D and the ionizations promoted by this additional methyl group. The effect of the 14α-methyl group on 7-keto steroids, on the other hand, is much smaller. As found for steroid hydrocarbons, the fragmentation is directed by the presence (or absence) of a C-17 side chain substituent. Cleavage across ring C (of the 8–14 and 11–12 bonds) is the main fragmentation sequence of 7-keto steroids with C-17 side chains and is associated with a reciprocal hydrogen transfer (H-9 being lost from the charged portion). Initial ionization of the 13–17 bond (and the 8–14 bond in 14α-methyl ketones) is postulated to accommodate the interatomic distances required for a McLafferty rearrangement and to account for the effect of a C-17 substituent. Synthetic procedures leading to the various deuterium-labeled analogs are outlined.

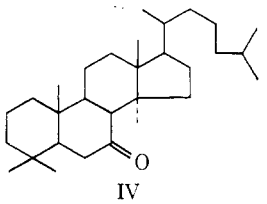
In our recent study[1] on the ring D cleavage of lanostane (I), we had occasion to prepare several deuterium-labeled analogs of lanostan-11-one (III) and lanostan-7-one (IV). The presence of the 14α-angular methyl substituent in lanostane (I) (and 14α-methylcholestane, II) was shown[1] to have a dramatic effect upon the fragmentation behavior of the steroid hydrocarbon. The increased substitution about ring D in this tetracyclic triterpene was found[1] to promote ionization of the 8–14 and 13–14 bonds, triggering alternative cleavages to those established for steroids[4,5] lacking the angular methyl group at C-14.



I, R = CH_3
II, R = H

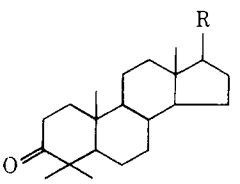


III

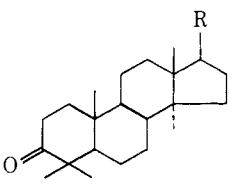


IV

It was therefore of interest to determine, for mechanistic reasons and for purposes of applicability of mass spectrometry to the tetracyclic triterpene field, whether 11- and 7-ketolanostanes (III and IV) would show major differences in their mass spectral fragmentations from those established for 11-[6–8] and 7-keto[6,9,10] steroids not containing a 14α-angular methyl substituent, particularly in light of the investigations on 4,4-dimethyl 3-keto steroids.[11] The mass spectrum of 4,4-dimethyl-5α-androstan-3-one (V) shows[11] almost exclusive ring A cleavage, while that of 4,4-dimethylcholestan-3-one (VI) shows[11] competing ring A and ring D cleavages. Lanostan-3-one (VII), on the other hand, shows[11] almost exclusive ring D cleavage, in accord with the greater substitution about this part of the molecule.



V, R = H
VI, R = C_8H_{17}



VII, R = C_8H_{17}

The spectrum (Figure 1) of lanostan-11-one (III) shows significant differences from that of 5α-androstan-11-one (VIII) and 5α-pregnan-11-one (IX), whose mass spectral fragmentations (see for instance Figure 2) have been elucidated[6–8] through extensive deuterium labeling. On the other hand, the spectra (Figures 4 and 5) of both lanostan-7-one (IV) and cholestan-7-one (X) are very similar but differ completely from that[9] of 5α-androstan-7-one (XI), whose mass spectral fragmentations have also been elucidated[9] through deuterium

(1) For paper CCXXXIX see R. R. Muccino and C. Djerassi, *J. Amer. Chem. Soc.*, in press.
(2) Financial support from the National Institutes of Health (Grants No. GM 06840 and AM 04257) is gratefully acknowledged.
(3) National Institutes of Health Postdoctoral Fellow 1971–1973.
(4) G. Eadon, S. Popov, and C. Djerassi, *J. Amer. Chem. Soc.*, **95**, 1282 (1973).
(5) L. Tökés, G. Jones, and C. Djerassi, *J. Amer. Chem. Soc.*, **90**, 5465 (1968).
(6) H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.*, **84**, 1430 (1962).
(7) D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2091 (1963).
(8) D. H. Williams and C. Djerassi, *Steroids*, **3**, 259 (1964).
(9) R. Beugelmans, R. H. Shapiro, L. J. Durham, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 2832 (1964).
(10) K. Biemann, "Mass Spectrometry," McGraw-Hill, New York, N. Y., 1962, Chapter 9.
(11) R. H. Shapiro and C. Djerassi, *Tetrahedron*, 1987 (1964).

Table I. Shifts[a] of Mass Spectral Peaks in Lanostan-11-one (III)

Lanostan-11-ones	Isotopic purity	M^+	$M - C_9H_{17}$	$M - C_{10}H_{18}$	$M - C_{15}H_{31}$	$M - C_{17}H_{31}O$
d_0 (III)		428	303	290	205	177
2,2,3,3-d_4 (XXIV)	5% d_3, 91% d_4, 4% d_5	432	303	290 (78%) 291 (22%)	209	181 (~70%)
6,6,7,7,8β-d_5 (XXII)	11% d_4, 86% d_5, 3% d_6	433	306 (91%) 304 (9%)	292 (66%) 293 (14%) 290 (20%)	210	182 (~70%)
7,7-d_2 (XVIII)	11% d_1, 89% d_2	430	304 (92%) 303 (8%)	292 (79%) 290 (21%)	207	179 (70%) 189 (30%)
8β-d_1 (XIX)	12% d_0, 88% d_1	429	303 (84%) 304 (16%)	290	206	178 (70%) 177 (30%)
9α,12,12-d_3 (XX)	6% d_2, 94% d_3	431	306 (93%) 305 (7%)	293 (46%) 292 (36%) 291 (18%)	205 (84%) 206 (9%) 207 (7%)	177 (70%) 178 (30%)

[a] The shift values are corrected for isotopic impurity as well as for ^{13}C contributions and are reliable to ±5% for all peaks except *m/e* 177, in which the uncertainty is ±10%. All spectra were measured at 70 eV on an Atlas CH-4 with E-413 ion source.

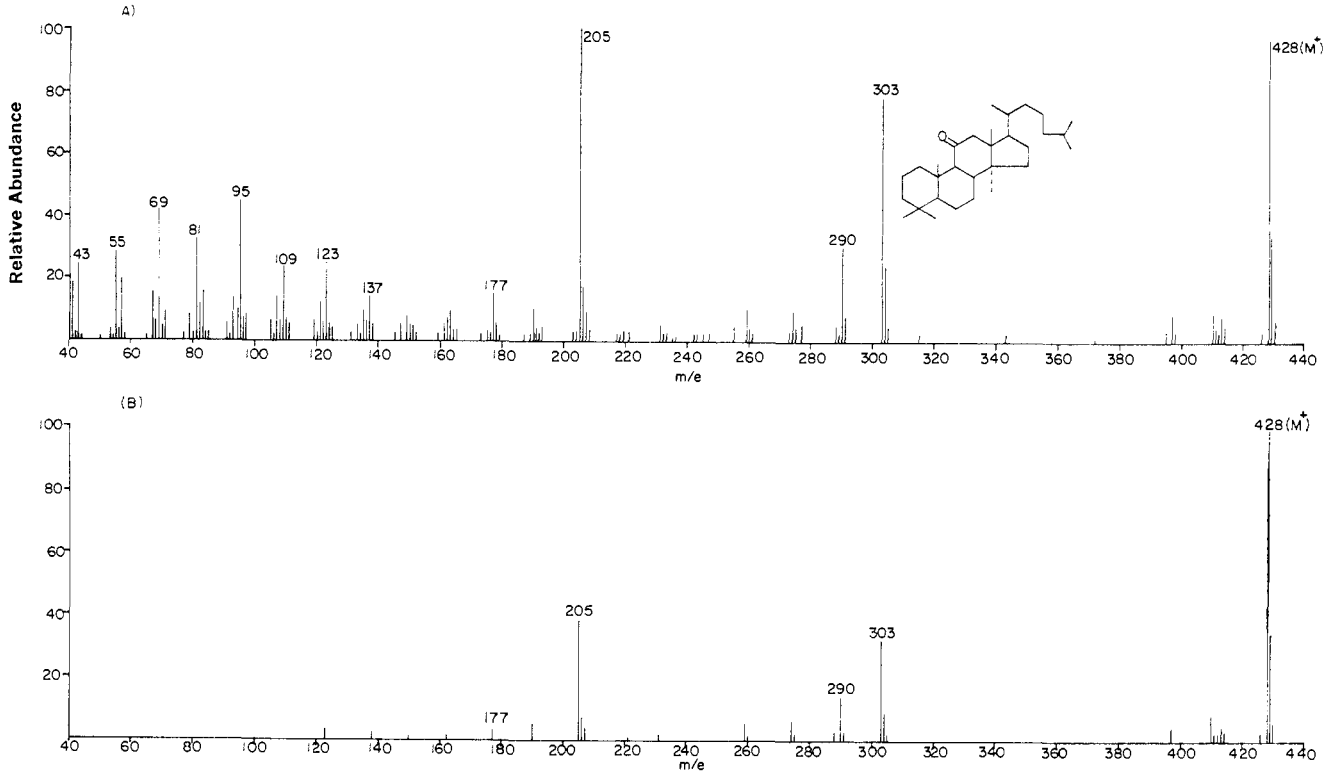
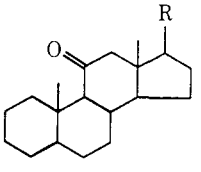
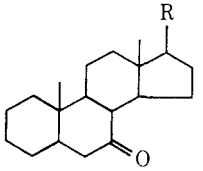


Figure 1. A. Mass spectrum (70 eV) of lanostan-11-one (III). B. Mass spectrum (15 eV) of lanostan-11-one (III).

labeling. The electron impact induced cleavages of 7-keto steroids bearing a C-17 side chain have thus far not been examined and thus provide an additional impetus for the present investigation.



VIII, R = H
IX, R = C_2H_5



X, R = C_8H_{17}
XI, R = H

Mass Spectral Fragmentation Processes of Lanostan-11-one (III). All carbon atoms on the A, B, and C rings, with the exception of positions 1 and 5, were labeled with deuterium. The isotopic purities and mass spectral shifts of the labeled analogs are summarized in Table I. The results of the metastable defocusing measurements are given in Table II.

Table II. Parent–Daughter Relationships[a] in the Fragmentation of Lanostan-11-one (III) Established by Defocused Measurement of Metastable Ions

Parent ions	Daughter ions			
	303	290	205	177
428	428s	428s	428s	
303				303w
290				290m
205				205s
177				

[a] Intensities are designated as <1%, w; 1% to 10%, m; >10%, s. Measurements were made on an MS-9 double-focusing mass spectrometer.

The base peak (*m/e* 205) in the spectrum of lanostan-11-one (Figure 1a and 1b) corresponds to cleavage across ring C (8–14 and 11–12 bonds) together with loss of one hydrogen. The cleavage processes associ-

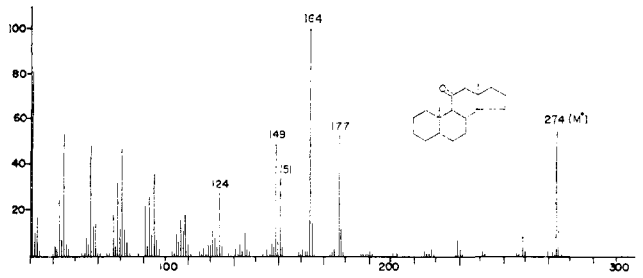
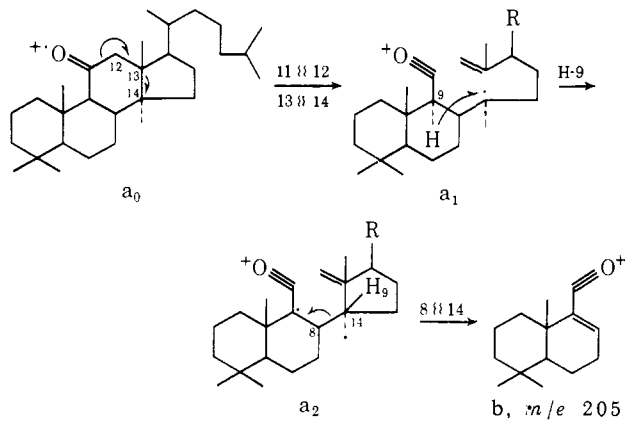


Figure 2. Mass spectrum (70 eV) of 5α-androstan-11-one (VIII).

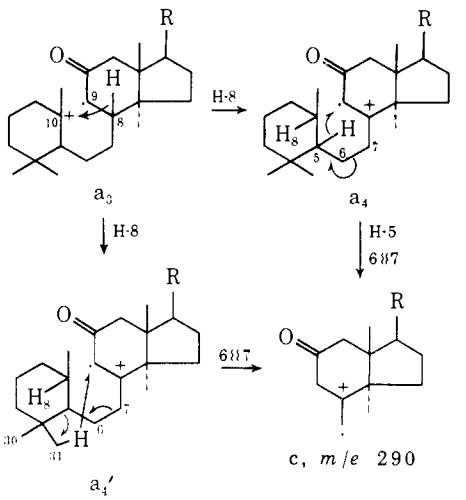
ated with the principal peaks in the spectra of 5α-androstan-11-one[7] (VIII, Figure 2) and 5α-pregnan-11-one[6,7] (IX) qualitatively correspond to the peaks in the higher mass region at *m/e* 290 and 303 (cleavage across ring B).

The deuterium labeling results (Table I) show the loss of C-12 and transfer of hydrogen from C-9 implicated in the mass 205 ion. The minor role that this type of ion plays in the spectra[6,7] of 11-keto steroids not containing a 14α-methyl group indicates that its formation is greatly enhanced by the increased substitution about ring D. An attractive mechanism involves parent ion a_1, generated by α cleavage of the 11–12 bond in a_0 and homolysis of the very highly substituted 13–14 bond and whose stability is enhanced by the 14α-methyl substituent. Transfer of the 9α-hydrogen ($a_1 \rightarrow a_2$) and homolytic rupture of the 8–14 bond would give the conjugated oxonium ion b, *m/e* 205.



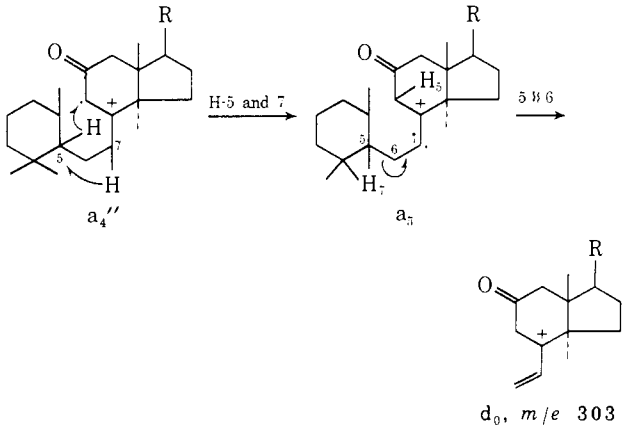
In the higher mass region, the peak at *m/e* 290 shows loss of ring A, C-6, and H-8 (see Table I). Analogous to the mechanism proposed[7] for the base peak in 5α-androstan-11-one (*m/e* 164 in Figure 2), β cleavage of the 9–10 bond (a_3) and transfer of the activated 8β hydrogen would give ion a_4. Random gain[7,12] (see Table I) of one hydrogen (such as $a_4 \rightarrow$ c) from ring A and rupture of the 6–7 bond would give ion c, *m/e* 290. As observed[7] for this type of cleavage in 5α-androstan-11-one (VIII), the C-2, -3, and -6 positions are minor contributors (see Table I) of hydrogen to the charge-retaining portion of the molecule. The position from which the most hydrogen was transferred in 5α-androstan-11-one (C-4, 0.68 atom)[7] cannot participate in lanostan-11-one, although the hydrogen atoms on C-30 and C-31 could be implicated ($a_4' \rightarrow$ c). However,

(12) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, San Francisco, Calif., 1964, Chapter 20.



labeling at these rather inaccessible C-30 and -31 positions would be necessary to substantiate these transfer mechanisms. Interestingly, 0.36 atom of deuterium is lost in the 9α,12,12-d_3 derivative (XX) [*vs.* 0.37–0.43 atom in the 5α-androstan-11-one[7] analog], while an additional 18% of this peak loses two deuterium atoms, in accord with the postulate that an appreciable amount of this cleavage is taking place through migration of two hydrogens in each direction.[7,12]

The homologous peak (13 mass units higher) at *m/e* 303 also exhibits loss of the 8β hydrogen and, in addition, one of the hydrogens at C-7. A reciprocal hydrogen transfer mechanism such as $a_4'' \rightarrow a_5$ could give, upon allylic rupture of the 5–6 bond, ion d_0, *m/e*



303. However, the much greater intensity of this mass 303 ion with respect to its lower homolog at *m/e* 290 (as compared to their analogs, *m/e* 177 and 164 in Figure 2, in the 5α-androstan-11-one spectrum[7]) indicates that a different sequence (triggered by the 14α-methyl group) is probably operating here. One attractive mechanism which combines the processes associated with formation of ions b and c involves the parent ion a_1'. Ionization of the activated 9–10 bond and transfer of the 8β hydrogen would give ion a_6. Migration of the tertiary 5α-hydrogen with simultaneous transfer of H-7 and homolytic fission of the 5–6 bond would give the conjugated dienyl oxonium ion d_1, *m/e* 303.

The peak at *m/e* 177 is associated with loss of C-12 and the 9α-hydrogen (see Table I) and, according to the metastable defocusing data (see Table II), is derived predominantly from a mass 205 precursor, *i.e.*, by loss of carbon monoxide from ion b. The remainder of

Table III. Shifts[a] of Mass Spectral Peaks in the Spectrum of Deuterated Lanostan-7-one (IV) Analogs

Lanostan-7-one	Isotopic purity	M^+	M − C_8H_{17}	M − C_9H_{16}	M − $C_{10}H_{20}$	M − $C_{11}H_{22}$	M − $C_{15}H_{29}$	M − $C_{16}H_{30}$	M − $C_{17}H_{31}$	M − $C_{10}H_{36}$
d_0 (IV)		428	315	304	288	273	219	206	193	164
6,6,8β-d_2 (XXVII)	17% d_2, 83% d_3	431	318	307	291	276	222	209	196	167
9α-d_1 (XXV)	6% d_0, 85% d_1, 9% d_2	429	316	305	289	274	219	206	194	165
11,11-d_2 (XXVI)	8% d_1, 86% d_2, 6% d_3	430	317	306	290	276	220	208	193	166

[a] See footnote *a* in Table I.

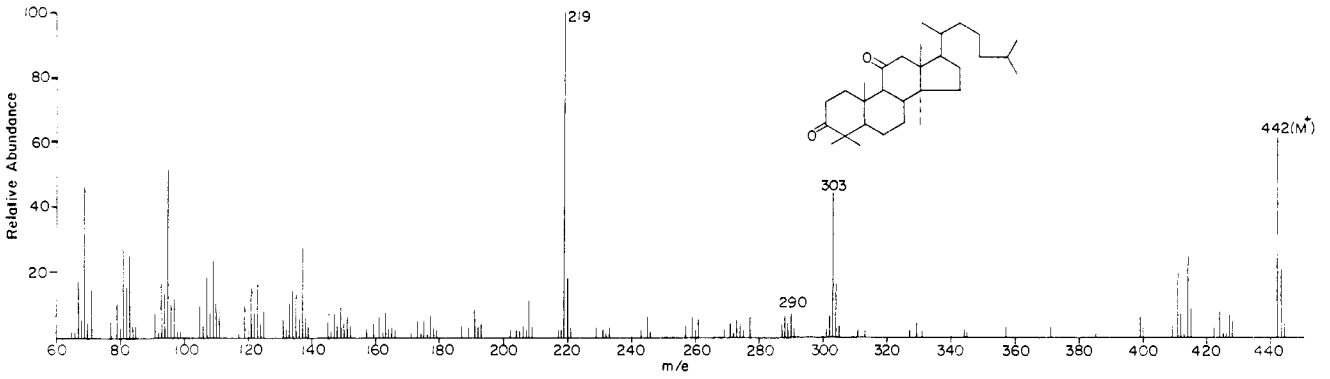
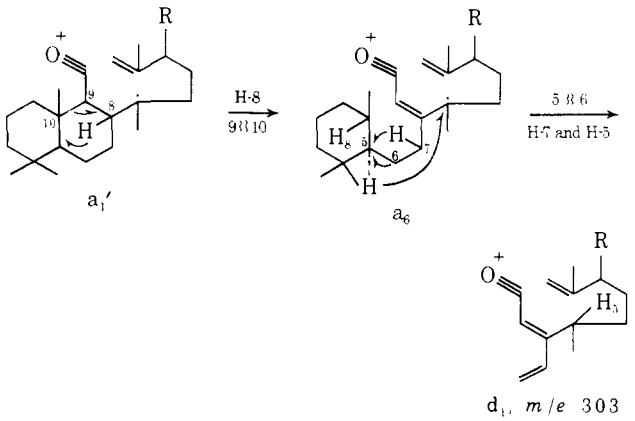
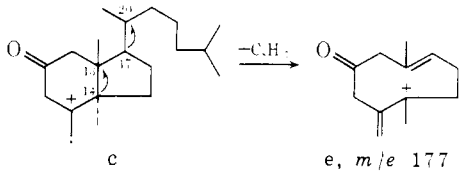


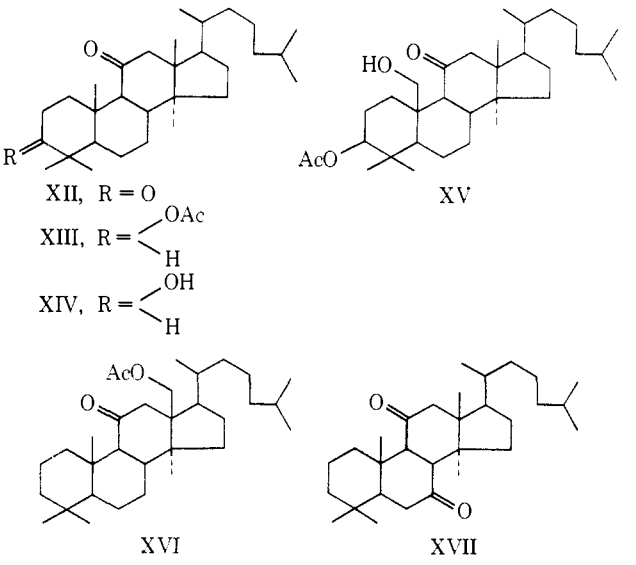
Figure 3. Mass spectrum (70 eV) of lanostane-3,11-dione (XII).



the mass 177 ion is derived (see Tables I and II) from a *m/e* 290 precursor; loss of the side chain in ion c would give ion e, *m/e* 177.



Interestingly, the spectrum (Figure 3) of lanostane-3,11-dione (XII) shows that the fragmentation sequence directed by the 11-keto function is essentially unaffected by the presence of a 3-carbonyl group. Thus, in the higher mass region, *m/e* 303 and 290 remained unchanged because of the loss of ring A while the base peak (*m/e* 219) is shifted 14 mass units higher due to the retention of ring A. Similarly, the spectra (see Experimental Section) of 3-acetoxylanostan-11-one (XIII) and lanostan-3β-ol-11-one (XIV) show unshifted peaks at *m/e* 303 and 290 and base peaks at *m/e* 263 and 221, respectively. Furthermore, this fragmentation behavior applies even to some angularly substituted derivatives. Thus, 3β-acetoxylanostan-19-ol-11-one (XV)[13] displays unshifted peaks at *m/e* 303 and 290 and a very intense peak at *m/e* 279, while 18-acetoxylanostan-11-one (XVI)[1] exhibits intense peaks at *m/e* 348 and 361 (shifted 2 mass units higher in the 18,18-d_2 derivative[1]) and a moderate unshifted peak at *m/e* 205. While not displaying these characteristic peaks in the higher mass region, lanostane-7,11-dione (XVII) has its base peak at *m/e* 219 (shifted 3 mass units higher in the 6,6,8β,9α,12,12-d_6 derivative). We conclude, therefore, that the 11-keto function can be a useful "triggering group" in certain bifunctional lanostanes and has a much more dominant effect upon the molecule's fragmentation than does an 11-keto group in ordinary steroids.[6-7]



Mass Spectral Fragmentation Processes of Lanostan-7-one (IV). The isotopic purities and mass spectral shifts of the deuterated lanostan-7-ones are summarized in Table III. The spectra of lanostan-7-one (IV) and cholestan-7-one[6] (X) are reproduced in Figures 4 and 5,

(13) P. Roller, B. Tursch, and C. Djerassi, *J. Org. Chem.*, 35, 2585 (1970).

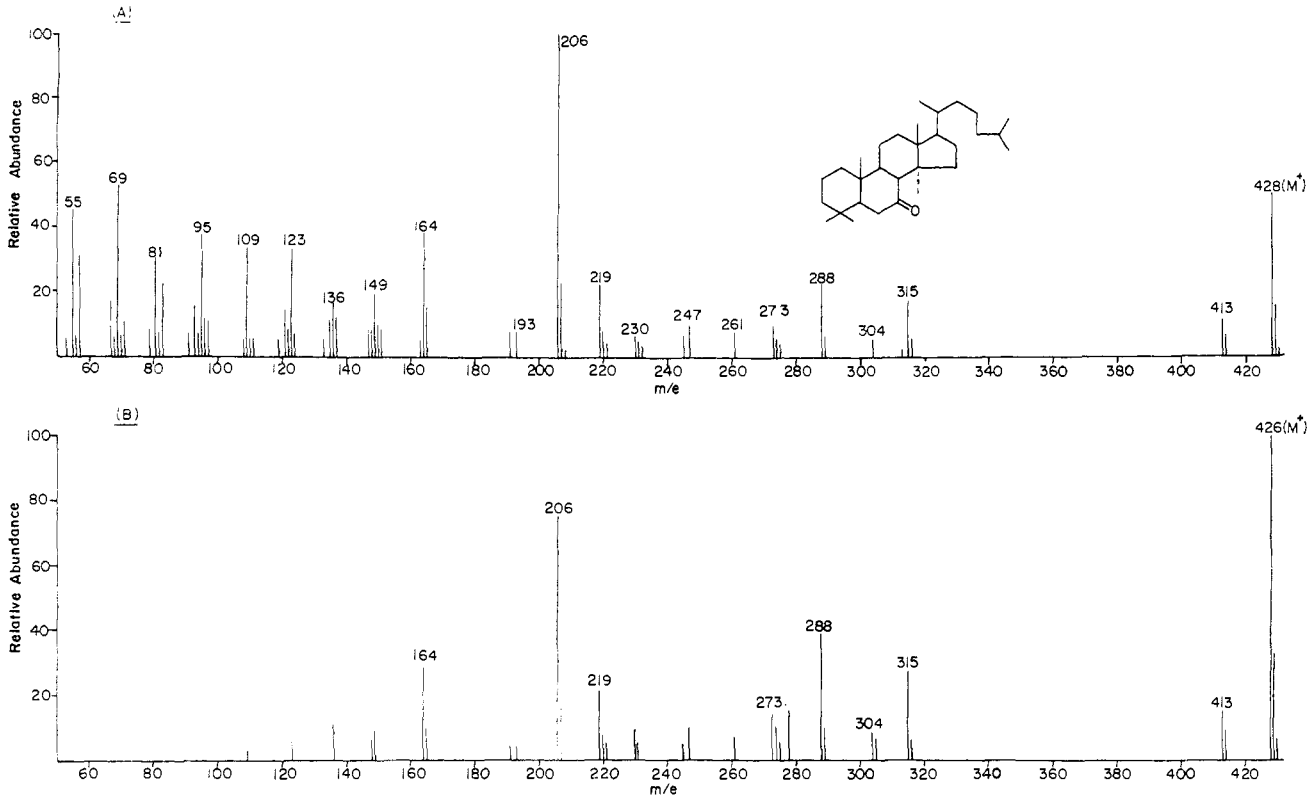


Figure 4. A. Mass spectrum (70 eV) of lanostan-7-one (IV). B. Mass spectrum (15 eV) of lanostan-7-one (IV).

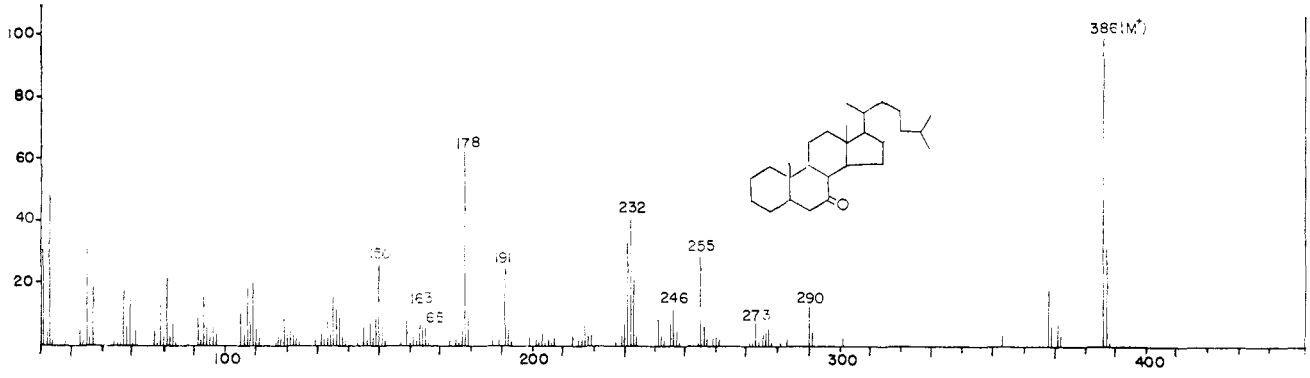


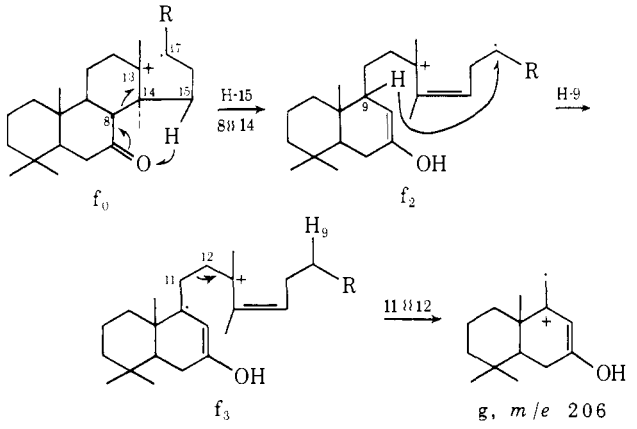
Figure 5. Mass spectrum (70 eV) of cholestan-7-one (X).

and are qualitatively similar (taking into account the expected mass shifts to accommodate the extra methyl groups). The principal peaks in the spectra of these 7-keto steroids having a C-17 side chain (IV and X) predominantly involve loss of parts of ring C and D. Loss of ring A, on the other hand, is the major cleavage pattern[9] in the spectrum of 5α-androstan-7-one (XI), which lacks a C-17 substituent.

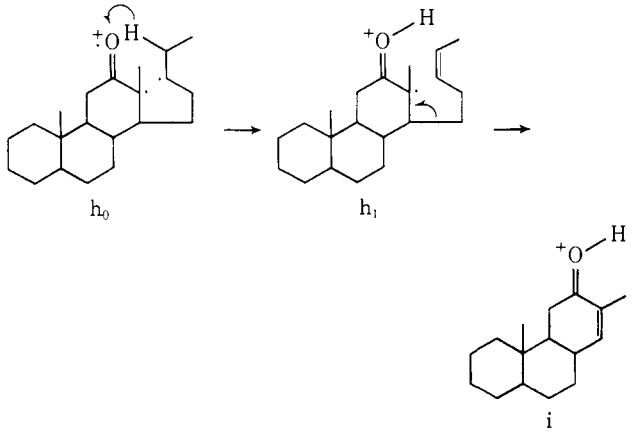
The base peak in the spectrum (Figure 4) of lanostan-7-one (*m/e* 206) involves cleavage across ring C (of the 8–14 and 11–12 bonds) and formally requires no net hydrogen transfer. However, as proposed earlier[6,10] for the principal fragmentation mode of cholestan-7-one (X) (*m/e* 178, Figure 5), this process exhibits loss of the 9α-hydrogen and thus must involve a reciprocal hydrogen transfer process. Abstraction of H-15 has been suggested[6,10] Prior ionization of the 13–17 bond (f_0) could be postulated to optimize the interatomic distances involved between oxygen and hydrogen (H-15) and would account for the different fragmentation pathways observed for 7-keto steroids lacking a C-17 side chain. Fission of the 13–17 bond in steroid hydrocarbons bearing a side chain (cholestane and pregnane) is a favored process,[4,5] while ring A fission prevails[14] in the absence of a C-17 substituent (androstane). The ring D cleavage peaks observed (see below) in the spectra of side chain bearing 7-keto steroids substantiate this proposal and indicate that the 7-keto function does not strongly direct the fragmentation of the molecule. Abstraction of H-15 and cleavage of the activated 8–14 bond would give f_2. Transfer of the 9α-hydrogen and rupture of the 11–12 bond (f_3) would give the conjugated ion g, *m/e* 206.

The observed abstraction of deuterium from C-20 in 12-keto steroids[15] ($h_0 \rightarrow h_1 \rightarrow i$) has similarly been ra-

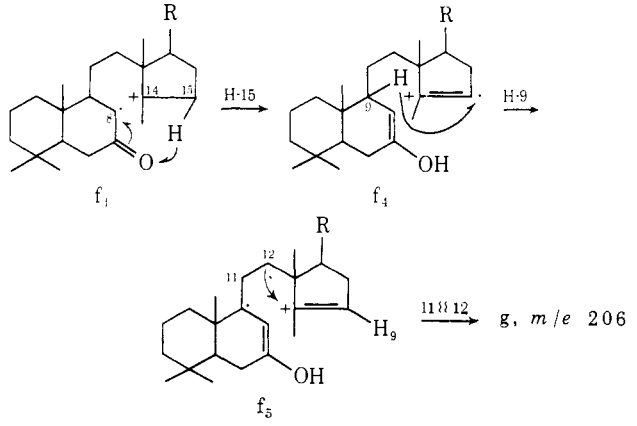
(14) L. Tökés and C. Djerassi, *J. Amer. Chem. Soc.*, **91**, 5017 (1969).
(15) C. Djerassi and L. Tökés, *J. Amer. Chem. Soc.*, **88**, 536 (1966).



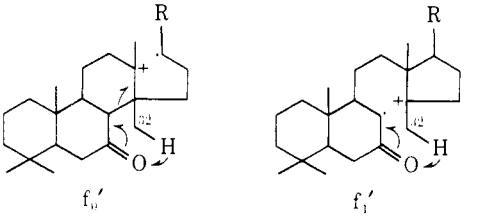
tionalized on the basis of prior ionization of the 13–17 bond.



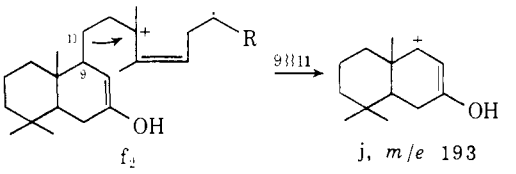
The greater intensity of this mass 206 ion in the spectrum of lanostan-7-one (as compared to its analog, *m/e* 178, in the spectrum of cholestan-7-one) could be attributed to an alternative mode of genesis. Fission of the highly substituted 8–14 bond in lanostane (and 14α-methylcholestane) has been found[1] to be a very favored process and would substantiate the formation of f_1. Abstraction of H-15, transfer of the 9α hydrogen, and fission of the 11–12 bond ($f_1 \rightarrow f_4 \rightarrow f_5$) as before would give ion g, *m/e* 206.



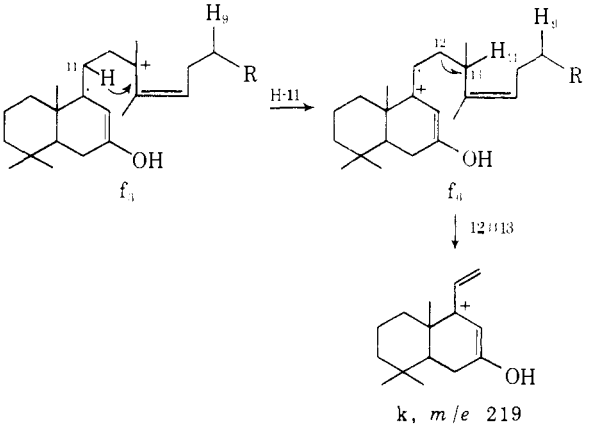
Abstraction from the C-32 position (f_0' and f_1') as well as the C-15 position is possible in lanostan-7-one. However, deuterium labeling at the rather inaccessible C-15 and -32 positions would be required to substantiate these proposals.



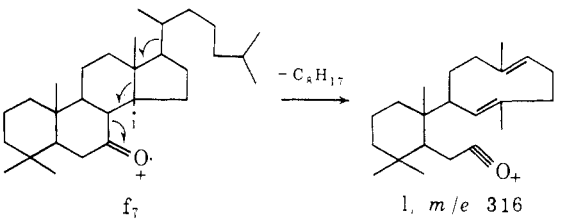
The deuterium labeling data support the earlier proposals[6,10] for the weaker peaks (see Figure 4, *m/e* 193 and 219) accompanying the intense mass 206 ion. The homologous peak (13 mass units lower) at *m/e* 193 indeed shows retention of C-6, -8, and -9 and loss of C-11 (see Table III); allylic cleavage of the 9–11 bond in ion f_2 would generate ion j, *m/e* 193.



The homologous peak (12 mass units higher) at *m/e* 219 exhibits loss of one hydrogen each from C-9 and C-11 (Table III); transfer of the activated H-11 in ion f_3 and allylic cleavage of the 12–13 bond would generate the conjugated ion k, *m/e* 219.

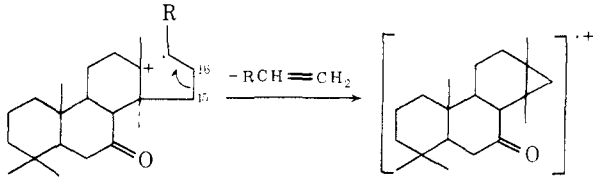


The ring D cleavages proposed[6] for the peaks in the higher mass region (*m/e* 232, 246, and 273 in Figure 5) of cholestan-7-one (X) are substantiated both by the retention of all deuterium labels in the B and C rings and by the appropriate shift of peaks 42 mass units higher in the spectrum (Figure 4) of lanostan-7-one (IV). The peak at *m/e* 316 corresponds to loss of the side chain and can be rationalized through α cleavage of the 7–8 bond with simultaneous homolytic cleavage of the very highly substituted 13–14 bond and rupture of the activated 17–20 bond ($f_7 \rightarrow$ l).

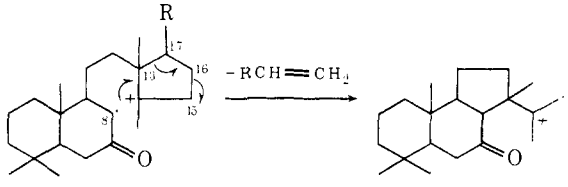


The peak at *m/e* 288 represents a partial ring D cleavage process which, in lanostane, has been shown[4] to occur through two pathways. Rupture of the acti-

vated 15–16 bond (in f_0) would generate the cyclopropyl ion m_1, *m/e* 288. Alternatively, fission of the 13–17 and 15–16 bonds (in f_1) and formation of an 8–13 bond would generate the ion m_2, *m/e* 288.

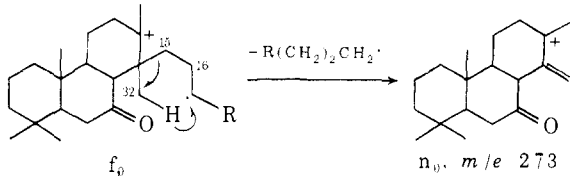


f_0 m, *m/e* 288

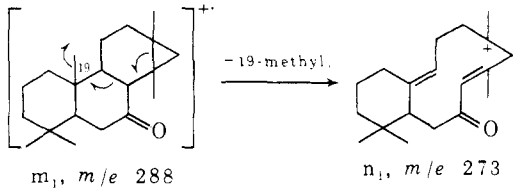


f_1 m_2, *m/e* 288

The peak at *m/e* 273 corresponds to ring D cleavage which in lanostane[1] has been shown to occur through a number of pathways. Applied to lanostan-7-one (IV), the two most prominent peaks would involve abstraction of hydrogen from C-32 in ion f_0 with cleavage of the 15–16 bond (yielding ion n_0) and expulsion of the C-19 angular methyl group from cyclopropyl ion m_1 (yielding ion n_1).

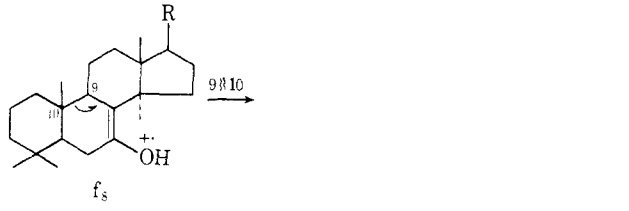


f_0 n_0, *m/e* 273

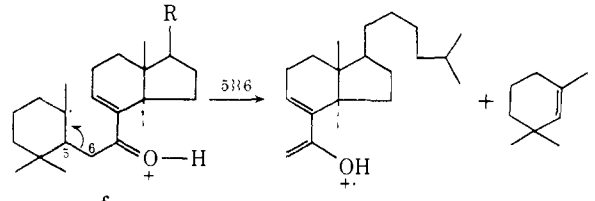


m_1, *m/e* 288 n_1, *m/e* 273

The mechanism[16] associated with the base peak in 5α-androstan-7-one[9] (XI) (cleavage across the 5–6 and 9–10 bonds) is substantiated by the *m/e* 304 peak in the spectrum of lanostan-7-one (loss of ring A along with the 4,4-demethyl groups and retention of all deuterium labels and the 14α-methyl group). An analogous peak (*m/e* 290 in Figure 5) appears in the spectrum[6] of cholestan-7-one.

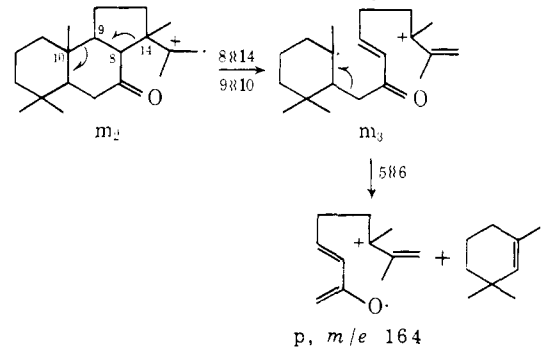


f_8



f_9 o, *m/e* 304

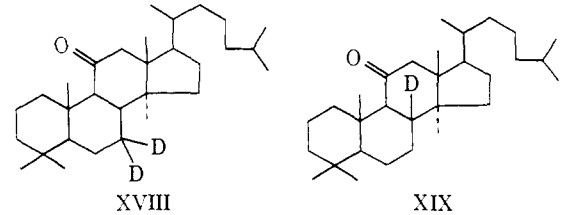
The intense peak at *m/e* 164 (Figure 4) also completely retains the deuterium labels in rings B and C. Because of its low mass, loss of parts of ring A and ring D is required and, in fact, an attractive mechanism involves the partial ring D cleavage ion m_2. Allylic rupture of the 8–14 bond with simultaneous fission of the activated 9–10 bond would give ion m_3. Cleavage of the 5–6 bond in m_3 (analogous to $f_8 \rightarrow 0$) would then afford ion p, *m/e* 164 (which could cyclize in a number of ways). An analogous peak (*m/e* 160) is found in the spectrum (Figure 5) of cholestan-7-one (X).



m_2 m_3 p, *m/e* 164

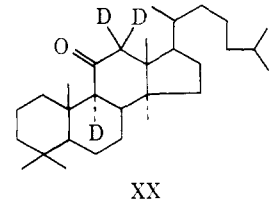
In conclusion, the effect of a 14α-methyl group upon the mass spectral fragmentations of 7-keto steroids can be viewed as the effect of the C-14 substituent upon the initial fragmentations of the hydrocarbon portion of the molecule. This behavior is clearly illustrated by the dramatic effect of a C-17 side chain, whose presence directs ring D fragmentation and whose absence allows ring A fragmentation, an observation paralleled in the steroid hydrocarbons.[5,14] This is in sharp contrast with the 11-keto steroids, where the strong directing ability of the 11-keto function is affected directly by the 14α-methyl group.

Preparation of Deuterium Labeled Lanostan-11-ones and Lanostan-7-ones. The synthesis of lanostan-11-one-*7,7-d*$_2$[1] (XVIII) and lanostan-11-one-*8β-d*$_1$[1] (XIX) has already been described.



XVIII XIX

Base-catalyzed equilibration of lanostan-11-one (III)[1] with methanol-*O-d* provided lanostan-11-one-*9β,12,12-d*$_3$ (XX).



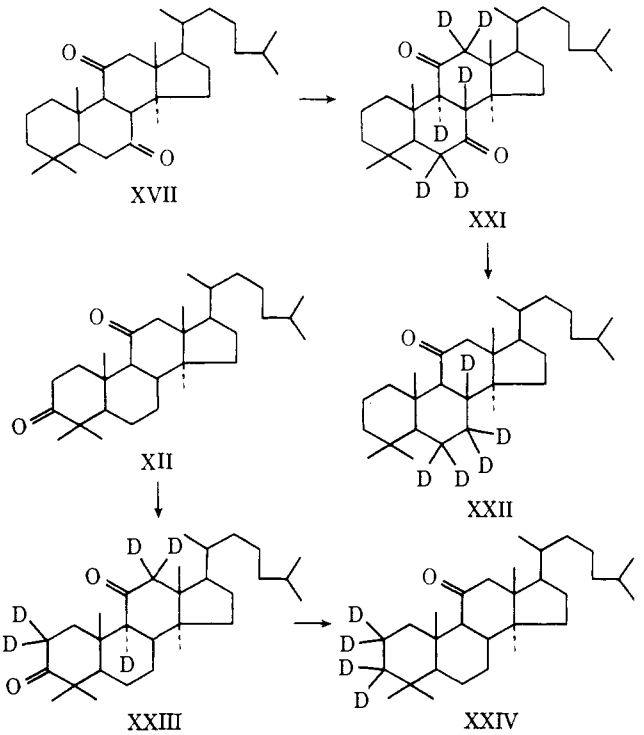
XX

Lanostane-7,11-dione (XVII),[17] after equilibration with methanol-*O-d* to lanostane-7,11-dione-*6,6,8β,-9α,12,12-d*$_6$ (XXI) gave, upon mild deuterio-Clemmensen reduction[1] and back exchange, lanostan-11-one-

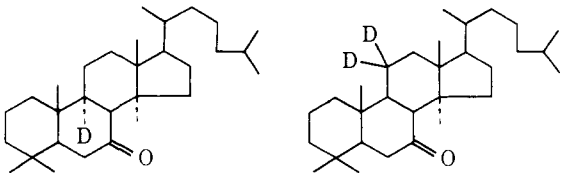
(16) J. Glitzwiller and C. Djerassi, *Helv. Chim. Acta*, **49**, 2108 (1966).

(17) C. Daree, J. F. McGhie, and F. Kurzer, *J. Chem. Soc.*, 988 (1948).

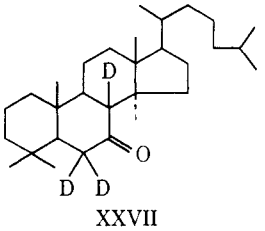
6,6,7,7,8β-d$_5$ (XXII). In the same manner, lanostane-3,11-dione[18] (XII), after equilibration to lanostane-3,11-dione-*2,2,9α,12,12-d*$_5$ (XXIII), gave lanostan-11-one-*2,2,3,3-d*$_4$ (XXIV).



The synthetic routes to lanostan-7-one-*9α-d*$_1$ (XXV) and lanostan-7-one-*11,11-d*$_2$ (XXVI) have been reported.[1]



Alkaline equilibration of lanostan-7-one (IV)[1] with methanol-*O-d* afforded lanostan-7-one-*6,6,8β-d*$_3$ (XXVII).



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

Experimental Section

Melting points are uncorrected and were determined in unsealed capillaries on a Thomas Hoover melting point apparatus. Mass spectra were determined by Richard Conover and Robert Ross on an Atlas CH-4 spectrometer with an E-413 ion source using the direct inlet procedure, or on an MS-9 double focusing mass spectrometer. All labeled samples except those containing labile deuteriums were purified by preparative vpc on a Hewlett-Packard 402 gas chromatograph using an OV 25 (3%) on Gas Chrom Q 100–120 mesh column, prior to mass spectral analysis. Recrystallizations were done from ether–methanol.

Lanostan-11-one-*9α,12,12-d*$_3$ (XX). Lanostan-11-one (III, 25 mg) was heated to reflux in 4 ml of methanol-*O-d*. Sodium (~50 mg), previously dissolved in methanol-*O-d* (1 ml), was then added, and heating under reflux continued overnight. The methanol-*O-d* was carefully distilled off and replaced with 5 ml of fresh methanol-*O-d*, and the heating continued overnight. The methanol-*O-d* was again removed by distillation, and the product was taken up in anhydrous ether (10 ml, distilled from sodium) and washed with deuterium oxide (3 × 2 ml). Drying (magnesium sulfate) and concentrating yielded 24 mg (96%) of lanostan-11-one-*9α,12,12-d*$_3$ (XX), mp 92–95°. (For isotopic purity, see Table I.)

Lanostane-7,11-dione-*6,6,8β,9α,13,13-d*$_6$ (XXI). Lanostane-7,11-dione (XVII, 50 mg)[7] was equilibrated with methanol-*O-d* as described for the preparation of XX to give lanostane-7,11-dione-*6,6,8β,9α,12,12-d*$_6$ (XXI, 48 mg): mp 139–141° (lit.[17] mp 140–142°); mass spectrum (rel intensity) 448 (100, M$^+$), 430 (90, M − H_2O), 415 (42), 401 (20), 277 (76), 247 (20), 222 (100); mass spectrum (rel intensity) of the unlabeled derivative XVII, 442 (100, M$^+$), 426 (90, M − H_2O), 411 (44), 397 (20), 274 (80), 245 (30), 219 (100).

Lanostan-11-one-*6,6,7,7,8β-d*$_5$ (XXII). Lanostane-7,11-dione-*6,6,8β,9α,12,12-d*$_6$ (XXI, 45 mg) was added to a previously mixed solution[1] of acetyl chloride (5 ml, freshly distilled) and deuterium oxide (10 ml). Amalgamated zinc (1 g) was added and the reaction slowly brought to reflux temperature. Heating was continued for 12 hr. After back exchange in 5% potassium hydroxide–methanol solution (refluxing overnight), the product was chromatographed on alumina (10 g, activity II). Elution with 20% benzene–hexane gave 22 mg of lanostan-11-one-*6,6,7,7,8β-d*$_5$ (XXII), mp 90–92°. (For isotopic purity, see Table I.)

Lanostane-3,11-dione-*2,2,9α,12,12-d*$_5$ (XXIII). Lanostane-3,11-dione (XII, 50 mg)[18] was equilibrated with methanol-*O-d* as described for the preparation of XX to give 47 mg of lanostane-3,11-dione-*2,2,9α,12,12-d*$_5$ (XXIII), mp 117–119° (lit.[17] mp 120–122°); mass spectrum (rel intensity) 447 (61, M$^+$), 432 (7, M − CH_3), 424 (8, M − H_2O), 306 (44), 293 (8), 221 (100); for mass spectrum of unlabeled derivative XII, see Figure 3.

Lanostan-11-one-*2,2,3,3-d*$_4$ (XXIV). Lanostane-3,11-dione-*2,2,9α,12,12-d*$_5$ (XXIII, 43 mg) was reduced under deuterio-Clemmensen conditions in the manner described for the preparation of XXII. After workup, the yield was 19 mg of lanostan-11-one-*2,2,3,3-d*$_4$ (XXIV), mp 91–93°. (For isotopic purity, see Table I).

Lanostan-7-one-*6,6,8β-d*$_3$ (XXVII). Lanostan-7-one[1] (IV, 25 mg) was equilibrated with methanol-*O-d* in the manner described for the preparation of XX. The yield was 23 mg (92%) of lanostan-7-one-*6,6,8β-d*$_3$ (XXVII), mp 115–117°. (For isotopic purity, see Table III.)

3β-Acetoxylanostan-11-one[18] (XIII). Mass spectrum (rel intensity) 486 (28, M$^+$), 471 (1, M − CH_3), 325 (26), 411 (6), 383 (5), 303 (73), 290 (16), 263 (100).

Lanostan-3β-ol-11-one[18] (XIV). Mass spectrum (rel intensity) 444 (58, M$^+$), 429 (5, M − CH_3), 426 (8, M − H_2O), 413 (4), 411 (3), 303 (43), 290 (25), 275 (11), 235 (7), 221 (100).