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MASS SPECTRA OF STEROIDAL ALKYL ETHERS—I*

C. R. NARAYANAN and A. K. LALA
National Chemical Laboratory, Poona 8, India

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Abstract—The mass spectral fragmentation of saturated and unsaturated steroidal methyl and ethyl ethers and ethers of 4,4-dimethyl steroids are studied and compared to the fragmentation of steroidal alcohols, trimethylsilyl ethers and ethylene ketals. Unlike the trimethylsilyl ether the small fragment containing the alkoxy group is neither the base peak nor a very strong peak in the spectrum. A significant peak occurs at $[M - ROH]^{+\cdot}$, however, sometimes even constituting the base peak of the spectrum. The fragmentations of the alkyl ethers are largely dependent on their environments. The present results also show the generalization that methyl ethers are better leaving groups than the corresponding alcohols in fragmentation processes, is not always valid.

IN VIEW of the recent publication by Idler *et al.*[1] on mass spectrometric studies of steroidal methyl ethers, we wish to report our work in the same field, which was nearly complete when the above publication reached us. We first deal with the two compounds which are common to both studies, viz. Cholestanyl and Cholesteryl methyl ethers, touching on points that have not been covered. Then we discuss the fragmentation of the new compounds we have studied, viz. methyl and ethyl ethers of saturated and α, β and β,γ-unsaturated steroids and 4,4-dimethyl steroids.

Cholestan-3β-yl-methyl ether (I)

Following the mass spectral fragmentation pattern of steroidal-3β-yl-trimethylsilyl ethers[2,3,4] we expected to observe in I, fragmentation as shown in Scheme 1. In 3,3-ethylene-dioxycholestane, besides the ion analogous to *a* in Scheme 1, cleavage of the C_2—C_3-bond and ring B is known to give two other strong ions (*b*) and (*c*) of *m/e* 113 and 125 respectively.[5] Fragmentation of I gave ions *a* (*m/e* 71), *b* (*m/e*, 84) and *c* (*m/e*, 97) only in a relative abundance of 15, 6 and 15% respectively. In cholest-5-en-3β-yl trimethylsilylsilyl ether the ion analogous to *a* forms the base peak of the spectrum[2] and in 3,3-ethylene dioxycholestane peaks analogous to these ions are very strong (100, 15 and 40% respectively).[5]

Very weak peaks are observed at $[M - 15]^+$, $[M - 32]^{+\cdot}$ and $[M - 47]^+$, corresponding to the loss of a methyl radical, methanol, and both a methyl radical and methanol, respectively. Similar eliminations are known to take place in 5α-cholestan-3β-ol,[6,7] but the intensities of these peaks are again very low. All these ions, though weak, have the corresponding metastable peaks (Table 1). Many strong peaks in the region *m/e* 270 to 210 in Fig. 1, indicate that ring D cleavages[8] are very facile (Scheme 2).

Cleavage of the C_{13}—C_{17}-bond followed by ring D fragmentation is found to be a low energy process. Thus ions corresponding to *A*, *B* and *C* give significant peaks in 5α-cholestane even at 14 eV.[9] Strong peaks are observed in this case for analogous ions. The tendency of the methoxy group to eliminate methanol as a neutral molecule

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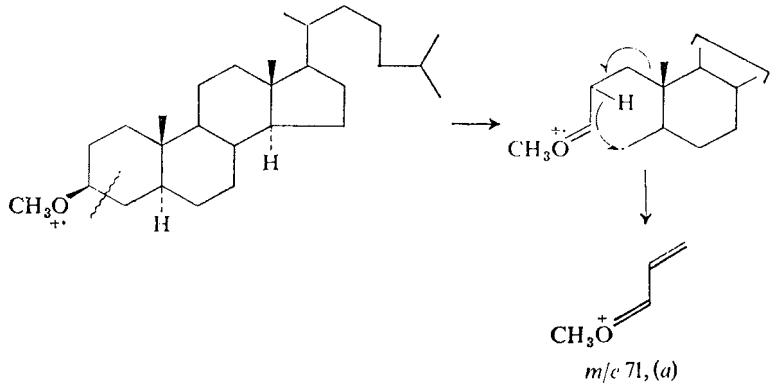
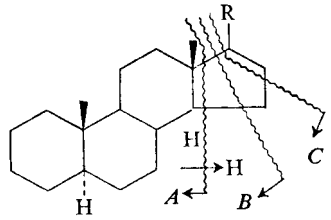


SCHEME 1



$R = C_8H_{17}$

$(A) = [M - 155]^+$, $(B) = [M - 154]^+$, $(C) = [M - 140]^+$

SCHEME 2

is also exhibited after these fragmentations. Intense peaks are thus observed at $[A - 32]^+$, $[B - 32]^{+\cdot}$ and $[C - 32]^{+\cdot}$. The peak with an intensity of 26% of the base peak at *m/e* 179 $[M - 223]^+$ is due to cleavage of the C/D rings.[9]

These results indicate that unlike the silyl ether or the ketal derivative, charge does not reside in the methoxy group, but elsewhere in the molecule and hence fragmentation is directed from there.

Cholest-5-en-3β-yl-methyl ether (II)

By analogy to the cleavage of cholest-5-en-3β-yl-trimethylsilyl ether,[2,3] we find that in II ion *a* has a relative intensity of only 37%, although this is the base peak in the corresponding silyl ether. The molecular ion is the base peak of the spectrum in this compound.

Additionally a strong ion was observed at $[M - 71]^+$. The origin of this ion would be analogous to the corresponding $[M - 129]^+$ ion in the mass spectrum of cholesteryl trimethylsilyl ether, as described by Djerassi *et al.*[3]

Unlike the fragmentation pattern of Cholestan-3β-yl-methyl ether (I), the $[M - CH_3OH]^{+\cdot}$ ion is very abundant (84%) in this case. Though there has been strong evidence in favour of 1,3 and 1,4-eliminations[6,10 to 13] in simple cyclic and steroidal alcohols, 1,2-eliminations[14 to 17] are not common. Such an elimination in II must be due to the ease of formation of a C_3—C_5-diene type of ion as has also been noted by Idler *et al.*[1] The intensity of the $[M - CH_3]^+$ peak then reduces and so

TABLE 1. METASTABLE IONS

Fragmentation	Compound No. (I)	(II)	(III)	(IV)	(V)	(VI)	(VII)	(IX)	(X)
$M \rightarrow [M - CH_3]$	372·5	386·5	358·2	372·0	370·5	—	370·2	—	—
	(372·5)	(386·5)	(358·5)	(372·5)	(370·6)		(370·5)		
$M \rightarrow [M - ROH]$	—	—	341·0	340·8	339·0	338·5	327·0	379·5	366·5
			(340·5)	(340·5)	(338·6)	(338·6)	(327·1)	(378·8)	(366·4)
$[M - CH_3] \rightarrow [(M - CH_3)—ROH]$	326·0	—	338·0	—	324·0	324·0	—	—	—
	(325·6)		(337·8)		(323·7)	(323·7)			
$[M - ROH] \rightarrow [(M - ROH)—CH_3]$	341·0	—	340·8	341·0	—	338·7	338·5	366·5	366·5
	(340·6)		(340·6)	(340·6)		(338·6)	(338·6)	(366·5)	(366·5)
$A \rightarrow [A - ROH]$	187·0	177·3							
	(187·1)	(177·1)							
$B \rightarrow [B - ROH]$	188·0	177·8							
	(188·1)	(178·0)							

The figures in parentheses represent the calculated, and the others the observed values of *m/e*.

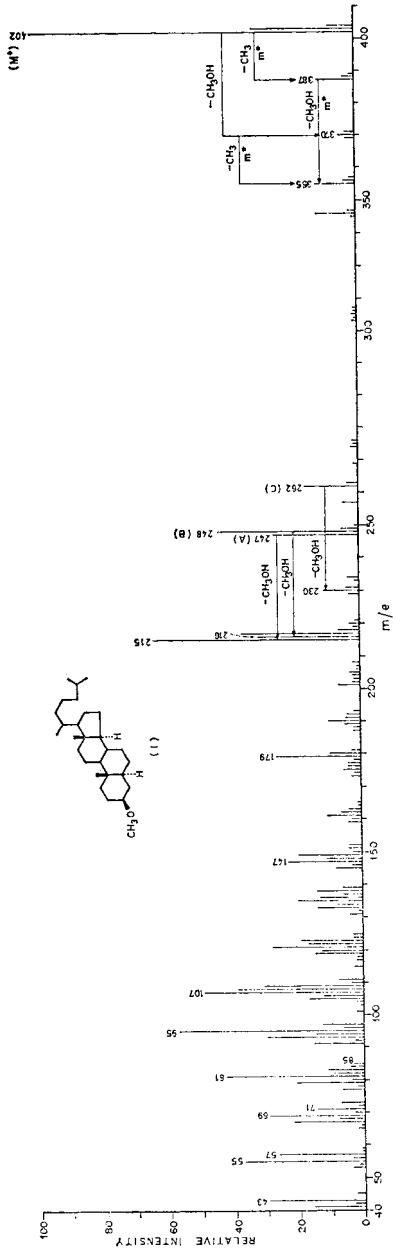
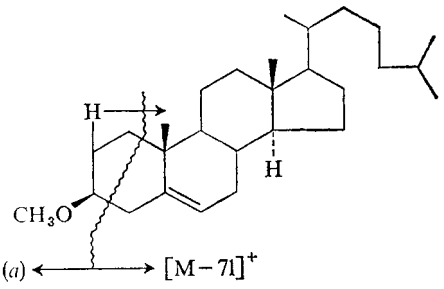

(M+) 402
-CH3OH
-CH3 m*
388
-CH3OH m*
370
-CH3 m*
355
262 (C)
248 (B)
247 (A)
-CH3OH
-CH2OH
-CH3OH m*
230
215
179
147
107
95
85
81
71
69
57
55
43
RELATIVE INTENSITY
m/e
(I)

FIG. 1

does the intensity of $[(M - CH_3) - CH_3OH]^+$, due to the facile 1,2-elimination of methanol. On the other hand the presence of the double bond at C_5—C_6 will initiate the ejection of the side chain,[18] followed by loss of methanol as a neutral molecule. Metastable ions are observed for most of the mass spectral fragmentations given here (Table 1). Ions corresponding to *A*, *B* and *C* and $(A - 32)^+$, $(B - 32)^{+\cdot}$ and $(C - 32)^+$ are also found, although of low intensity as expected.

Cholestan-3β-yl ethyl ether (III)

In this case also the relative intensity of ions corresponding to *a*, *b* and *c* i.e. of *m/e* 85, 98 and 111 respectively, remains low. Ions corresponding to $[M - ROH]^{+\cdot}$ and $[(M - ROH) - CH_3]^+$ or $[(M - CH_3) - ROH]^+$ also have, as in the case of the methyl ether, very low relative intensity (6 and 13% respectively).



SCHEME 3

This is not surprising in view of the fact that ring D cleavages would be very facile in this case. These cleaved ions were also seen after a subsequent loss of ethanol as a neutral molecule. Actually $[A - C_2H_5OH]^+$ is the base peak of the spectrum. Once the charge resides elsewhere in the molecule, the alkoxy groups show a strong tendency to be lost like the corresponding alcohols, as they no longer have to compete with reactions initiated by these, i.e. due to the presence of charge on the alkoxy group. Similarly there are strong peaks for ions $[B - C_2H_5OH]^{+\cdot}$ and $[C - C_2H_5OH]^{+\cdot}$. There are also many strong peaks in the low mass region, but it would not be proper to assign fragmentation patterns to these without performing deuterium exchange studies.

Cholest-5-en-3β-yl-ethyl ether (IV)

The relative intensity of the ion corresponding to *a* in III, increases in IV from 37 to 42% (*m/e* 85). Additionally in IV there is a strong peak at $[M - 85]^+$, (90%). The general fragmentation of IV is similar to that discussed for III. Just as the intensity of the peak due to the loss of ethanol is higher than that due to the loss of methanol while going from cholestan-3β-ol methyl ether to cholestan-3β-ol-ethyl ether, it is found that here also, $[M - C_2H_5OH]^{+\cdot}$ is more intense than $[M - CH_3OH]^{+\cdot}$. This heteroannular diene type of ion ($\Delta^{3,5}$) is in fact the base peak of the spectrum in this case. The intensity of $[M - CH_3]^+$ is only 10%, although the intensity of $[(M - C_2H_5OH) - CH_3]^+$ is raised to 50%, probably due to the facile loss of ethanol followed by loss of a methyl radical. The loss of the side chain gives rise to an ion of 20% relative abundance, followed by loss of ethanol as a neutral molecule (35%).

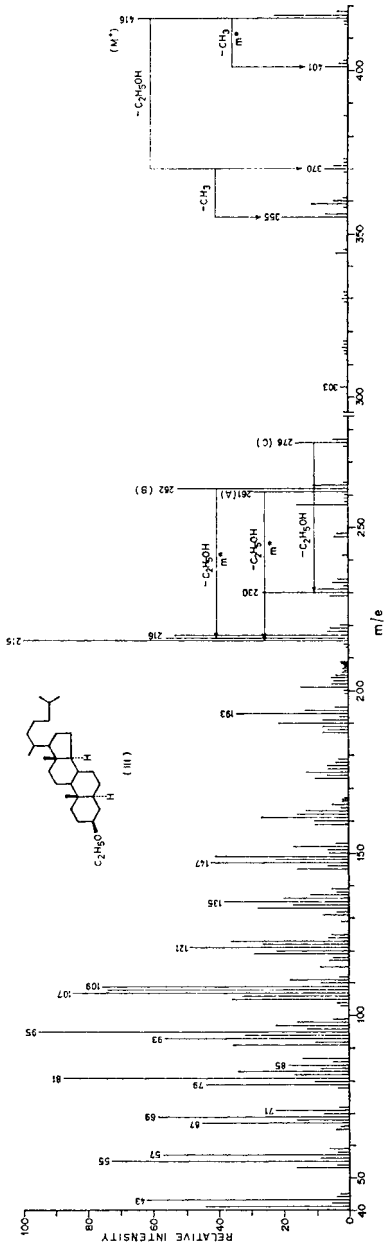


FIG. 2

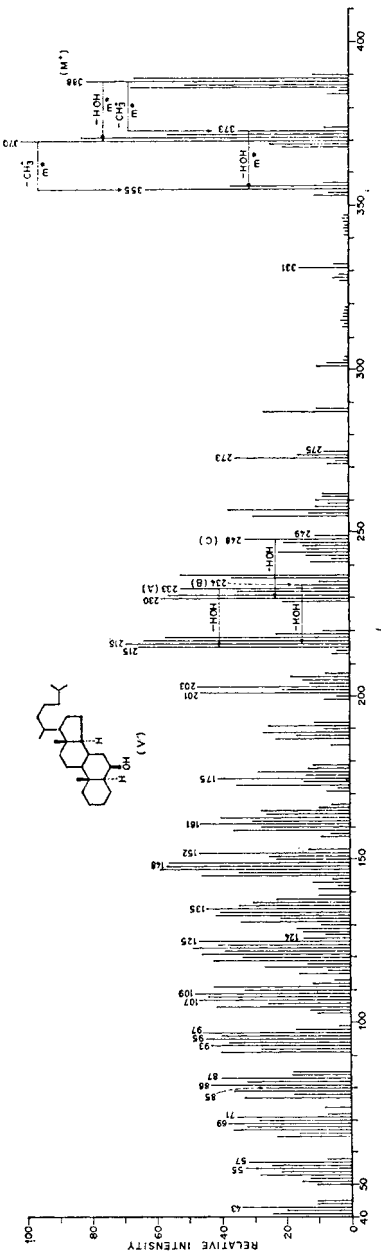


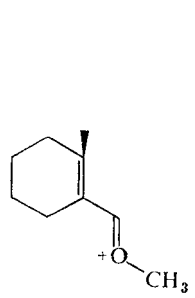
FIG. 3

Cholestan-6β-ol (V)

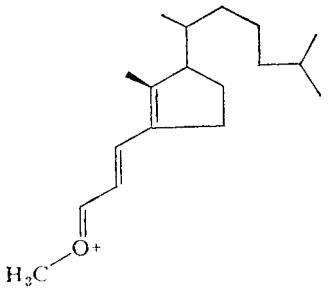
As the mass spectral fragmentation of this compound is not reported, we are reproducing the spectrum (Fig. 3). Its fragmentation pattern is very close to that of the corresponding methyl ether so only the latter is discussed in detail. Similarities and differences between the two are indicated, however.

Cholestan-6β-yl-methyl ether (VI)

Audier *et al.*[19] have reported the mass spectral fragmentation of 6,6-ethylenedioxycholestane. Corresponding rupture of the C_6—C_7 or the C_5—C_6-bond could give the fragment *d* or *e* from VI, though weak in intensity.



m/e 139, (43%)
(*d*)



m/e 263, (24%)
(*e*)

SCHEME 4

Both of these are actually found in the spectra of V and VI in low intensities. An interesting point to note here is that in the mass spectra of compounds V and VI, $[M - H_2O]^{+\cdot}$ and $[M - CH_3OH]^{+\cdot}$ are the base peaks, respectively. This is not surprising in view of the fact that a facile 1,3-elimination between the 6β-substituent and the C_8β-H can take place. A 1,4 elimination observed in cyclohexanols[10,11,12] may not take place in this case from the C_9α-H as they are *trans* diaxial in the rigid ring B. Elimination of water or methanol with a hydrogen atom from C_{19} cannot be discounted however, since it is favourably set in space. Subsequently a hydrogen atom may be transferred from C_8 to C_{19} analogous to the ring D cleavages.[8] The ring D fragmentation giving rise to ions *A*, *B* and *C* shows that the intensities of $[A - CH_3OH]^+$ and $[B - CH_3OH]^{+\cdot}$ are decreased in comparison to those in I and III. These observations support the involvement of the C_8β-H in the elimination of the 6β-substituent. For the formation of *A*, migration of a hydrogen atom from C_8 is needed[20] to some extent, and if this hydrogen atom is not readily available, the intensity of ions *A* and $[A - CH_3OH]^+$ are reduced by comparison. As a consequence, the C_{15}—C_{16}-bond would preferentially cleave to give rise to *C*, which would immediately lose methanol to give a strong $[C - CH_3OH]^{+\cdot}$ ion due to facile elimination of water or methanol. The additional fact that the $[C - ROH]^{+\cdot}$ peak is much more intense in V and VI as compared to I and III is also in line with the above proposals.

It may be noted further that the intensity of ions in the region *m/e* 270 to 210 is relatively high in VI as compared to V. This might be due to the fact that an axial

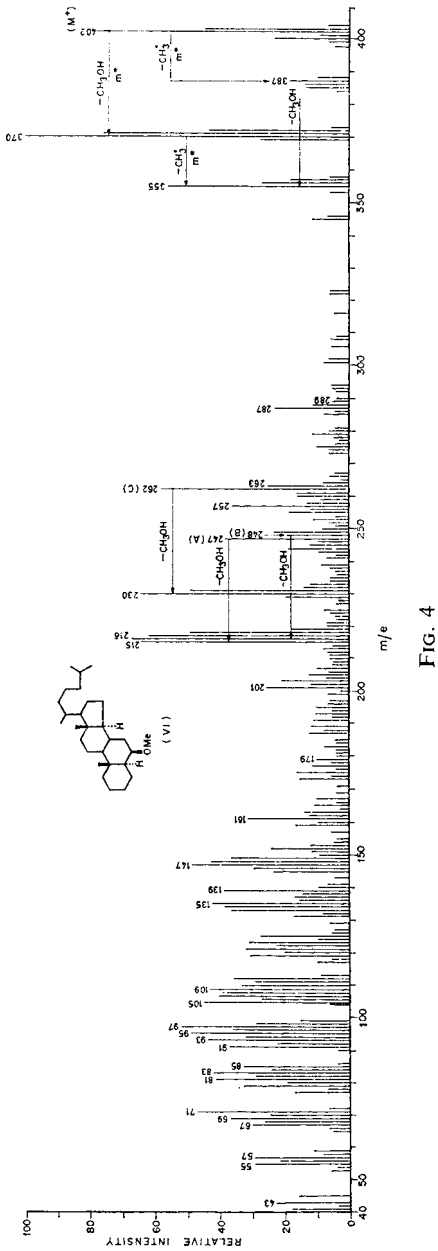


FIG. 4

FIG. 5

methoxy group introduces more crowding than an axial hydroxyl group and thus prefers to eliminate faster. Metastable ions for these fragmentations are given in Table 1.

Cholest-4-en-3β-yl-methyl ether (VII)

The presence of a double bond at C_4—C_5 does not favour C_3—C_4-bond cleavage, which would involve the formation of a vinyl free-radical. Cleavage of the C_2—C_3-bond followed by loss of ethylene[21] also seems to be a very weak process, since it gives rise to the ion $[M - 28]^{+\cdot}$ with a relative intensity of 15% only. In cholest-4-en-3β-yl trimethyl silyl ether the ion at *m/e* 143 is the base peak of the spectrum and the ion at *m/e* 142 and the molecular ion are the next highest peaks, forming 68% of the base peak. The ion $[M - (CH_3)_3SiOH]^+$ forms only 36% of the base peak.[4] In VII, however, the molecular ion is the base peak of the spectrum and [M − 32] the next highest peak (99%). The peak corresponding to *m/e* 143 in the silyl ether appears in VII, at *m/e* 85* where it is only 52% of the base peak. High resolution spectra of VII show that only half of this is due to the corresponding ion C_5H_9O (Table 2). The peak at *m/e* 84 corresponding to *m/e* 142 in the silyl ether forms only 33% of the base peak.

There is no direct proof to show that the present mode of fragmentation is not due to a thermal reaction. The corresponding allylic alcohol is known to undergo thermal dehydration.[22] The injection of a sample by direct inlet should show almost negligible thermal reaction, however, and the present spectra were all taken by injecting the sample by direct inlet. Additional support for the conclusion that the reaction may not be pyrolytic was obtained by taking a spectrum of this compound at low eV (30 eV) and low temperature (130°C). In this case $[M - CH_3OH]^{+\cdot}$ was the base peak of the spectrum and $[M]^+$ had a relative intensity of 50%. Thus the observed elimination of CH_3OH at low temperature and at low electron voltage, indicates that it is mainly an electron-impact process. A 1,2-elimination from C_2, or a 1,3-elimination from C-1 followed by loss of methyl radical could take place, giving rise to a conjugated 2,4 or 1(10), 4-diene, which would stabilize the resultant ion. The ion $[M - 47]^+$ may also come from the elimination of methanol after the ejection of a methyl radical.

Even in this compound ion $[M - C_8H_{17}]^+$ and further loss of methanol are observed. To check the correctness of this statement, cholest-4-ene was prepared and its fragmentation studied. As expected its mass spectrum showed a moderate peak for $[M - C_8H_{17}]^+$. Fragmentations initiated from ring D as *A*, *B* and *C* each with a loss of 32 mass units are also observed in low intensity.

4,4-*Dimethyl steroids*

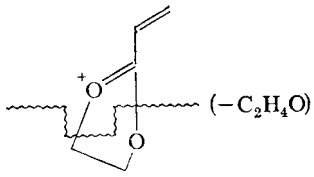
In the mass spectral fragmentation of an unsaturated-pentacyclic triterpene methyl ether, arundoin, Martin-Smith *et al.*[23,24] observed significant differences on changing the inlet system for injection of the sample. Whereas in a direct inlet system, the $[M - CH_3OH]^{+\cdot}$ ion is very weak, it becomes intense when a heated inlet system is used. This suggests that electron-impact reactions are accompanied by thermal reactions. This would be expected to be negligible, however, when a direct

* This was kindly pointed out to us by a referee.

inlet system is used. We therefore investigated the mass spectral fragmentation of the following 4,4-dimethyl steroids using a direct inlet system only.

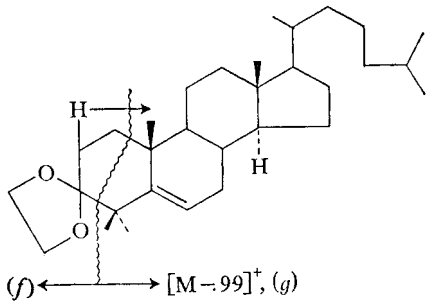
3,3-*Ethylenedioxy*-4,4-*dimethyl-cholest*-5-*ene* (*VIII*)

Ion *f* (*m/e* 99) was observed as expected from 3,3-ethylenedioxy steroids and was found to be the base peak of the spectrum. Due to the absence of a hydrogen atom at C_4, cleavage of the C_2—C_3-bond does not take place and therefore no peak due to this cleavage[5] is observed. There is a small peak at *m/e* 412 (13%), probably due to the loss of C_2H_4O from the ketal moiety. A metastable ion at *m/e* 372·0 suggests that this ion comes from the molecular ion. Such a loss of C_2H_4O[25] is not found in the mass spectral fragmentation of the 3,3-ethylenedioxy derivative of 5α-cholestan-4-one, although the corresponding ion by loss of C_2H_4S is found to be formed in its hemi-thio-ketal and thio-ketal derivatives.[25]



m/e 99, (*f*)

SCHEME 5



SCHEME 6

A similar loss of C_2H_4O also occurs from the *m/e* 99 ion giving rise to a peak at *m/e* 55 (96%). High resolution spectra show that about one third of this peak is due to C_3H_3O (see Table 2). Perhaps the most interesting part of the spectrum is a strong peak at $[M - 99]^+$, (56%). This may be ascribed to fragmentations similar to those described by Djerassi *et al.* in the case of 4,4-dimethyl androst-5 en-3β-yl-trimethyl-silyl ether.[3]

4,4-*Dimethyl cholest*-5-*en*-3β-*ol* (*IX*)

In this case the molecular ion is the base peak of the spectrum, as there is no substituent which can direct fragmentations like a ketal group. Loss of a methyl

group from the molecular ion leading to the ion *m/e* 399 (75%) is followed by loss of water as a neutral molecule. On the other hand due to the presence of the 4,4-dimethyl group, the expected 1,2-dehydration cannot take place to give a hetero-annular diene type of ion. The still abundant $[M - H_2O]^{+\cdot}$ ion (91%) is attributable to 1,3-elimination taking place between the 3β-OH and one of the hydrogen atoms of the C_4-methyl groups. This may then be followed by elimination of CH_2 permitting the resultant ion to stabilize as an allyl free radical. Such an involvement of a methyl group in elimination of water has been reported previously in 1-monomethyl and 1,1-dimethyl 3β-substituted steroids.[13] On the other hand 1,3-elimination from the hydrogen atom of C_1 may take place followed by the loss of an angular methyl group giving rise to a heteroannular 1(10), 5-diene.

TABLE 2. HIGH RESOLUTION DATA

Compound	*m/e* at low resolution	Fragment as per high resolution	Ratio of peaks
Cholest-4-ene-3β-yl-methyl ether (VII)	85	C_5H_9O	1
		C_6H_{13}	1
3,3-ethylenedioxy cholest-5-ene (VIII)	57	C_4H_9	Singlet
3,3-ethylenedioxy cholest-5-ene (VIII)	55	C_4H_7	7
		C_3H_3O	4

The ions $[M - H_2O]^{+\cdot}$ (*m/e* 396) and $[(M - H_2O) - CH_3]^+$ (*m/e* 381) each have a relative intensity of 92%, which is a measure of their relative stability. The positive charge developed at C_3 in these cases is stabilized as a homoallylic carbonium ion. If a methyl group then shifts from C_4 to C_3, the carbonium ion would be shifted to C_4 and would again be stabilized as an allylic carbonium ion. There is a strong peak (67%) at *m/e* [M − 57], which corresponds to the strong peak at $[M - 129]^+$ in steroidal 3β-trimethylsilyl ethers and hence should be formed by an analogous process 3.

4,4-*Dimethyl-cholest-5 en-3β-yl-methyl ether (X)*

In this case the loss of a methyl group or methanol is considerably reduced. Unlike the other cases, $[M - 71]^+$ is the base peak of the spectrum. As before this is analogous to the $[M - 129]^+$ ion in similar steroidal trimethylsilyl ethers as reported by Djerassi *et al.*[3] This electron-impact reaction seems to be very facile in this case as compared to other cases. In VIII the resonance stablized oxonium ion *f*, (*m/e* 99), suppresses all other fragmentations. In the case of IX, however, the tendency of the hydroxyl group (weak Lewis base), is to eliminate as water competes with the formation of an ion analogous to *f*. But the tendency of the methoxy group to eliminate as methanol, as compared to water in the corresponding alcohol would be less (relatively strong Lewis base), unless the charge has resided elsewhere prior to elimination of methanol. The methoxy or alkoxy compound thus shows to some extent, a tendency

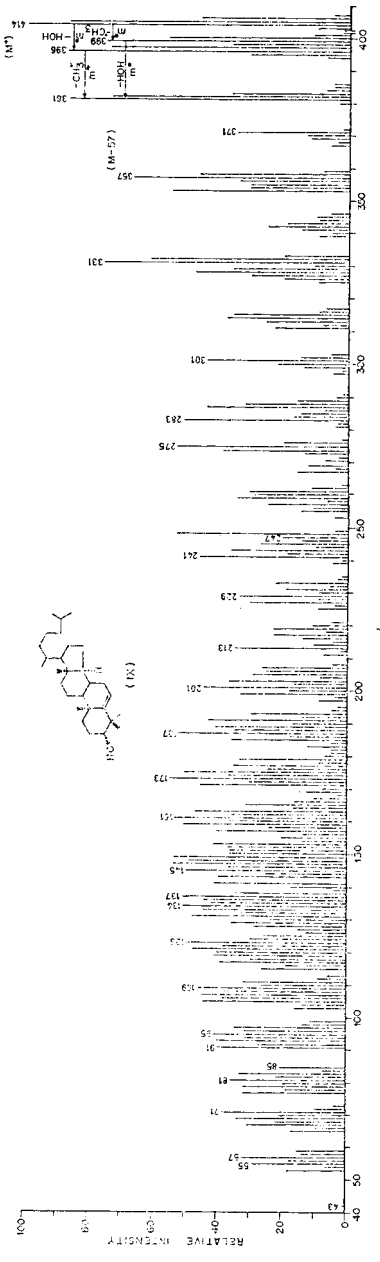


FIG. 6

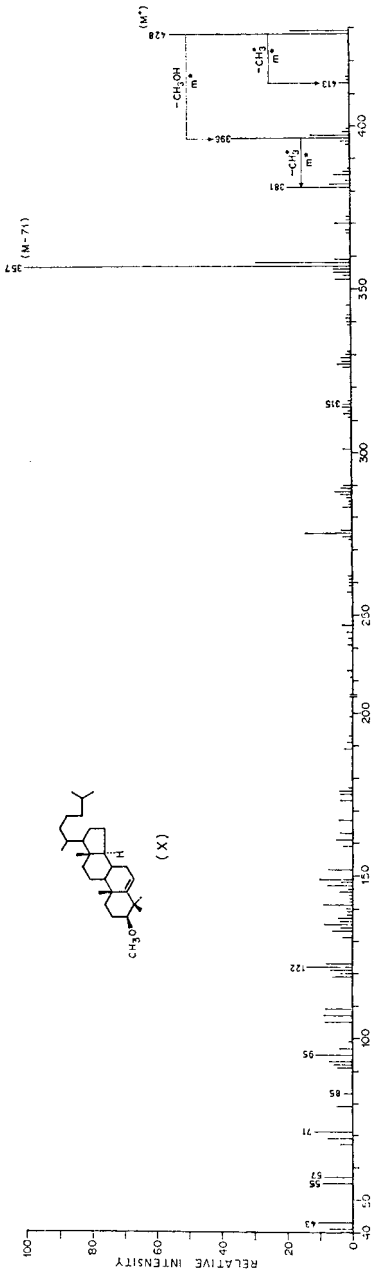
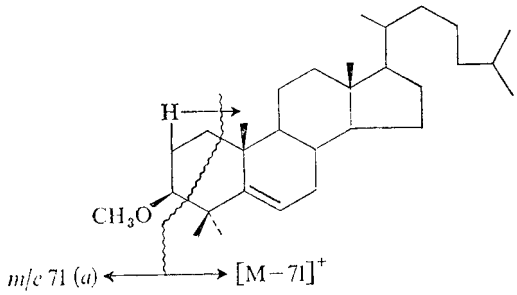


FIG. 7



SCHEME 7

to direct fragmentations similar to the corresponding trimethylsilyl ethers or ethylene dioxy compounds and hence the alkoxy group lies as an intermediate between the trimethylsilyl ethers and ethylene dioxy groups on the one side and the hydroxyl group on the other. These two competing reactions in X suppress the formation of the $[M]^+$, $[M-15]^+$, $[M-32]^{+\cdot}$ and $[M-47]^+$ ions and instead the process formulated above becomes more facile.

Cholesta-4-ene-3β,6β-diol-3-methyl ether-6-acetate (XI)

It is known that under electron-impact, acetates of cyclic compounds show a higher tendency to lose acetic acid as compared to the tendency to lose a molecule of water from the alcohols of the same compounds.[26] Although the pathways for the loss of water and methanol are similar, that for the loss of acetic acid is considered to be somewhat different.[20] We therefore prepared this compound with the two allylic groups to compare the tendencies to lose acetic acid and methanol by their respective pathways upon electron-impact. On fragmentation, the molecular ion is found to be relatively weak, (48%), and $[M-60]^+$ is the base peak of the spectrum. It may be recalled that 4-Cholesten-3β-ol-methyl ether (VII), gave the $[M-CH_3OH]^{+\cdot}$ peak with a relative intensity of 99% on fragmentation. In the present case, however, there is almost no peak at $[M-32]^{+\cdot}$. This demonstrates the overwhelming facility for the loss of acetic acid. There is a small peak of $[(M-CH_3COOH)-CH_3]^+$ (22%), indicating the loss of a methyl group after the loss of acetic acid or *vice versa*.

CONCLUSION

All the compounds studied had a fully saturated C_8H_{17} side chain and unsaturation or substitution in ring A or B. In the spectra of all these compounds, peaks at *m/e*, 43, 57, 71 and 85 in the low mass region were observed with varying intensities. High resolution spectra of compounds VII and VIII have shown that peaks at *m/e* 57 and 85 are partly due to C_4H_9 and C_6H_{13} respectively. In the mass spectra of cholest-5-ene all these peaks are observed with intensities varying from 3 to 10% or more, whereas in that of androst-5-ene taken under the same conditions, these are all absent. It therefore follows that at least to some extent these peaks are due to the successive cleavage of the side chain starting from the terminal isopropyl group (C_3H_7),[27] as is found in analogous hydrocarbon chains.

In the spectra of steroidal alkyl ethers, the $[M-ROH]^{+\cdot}$ ion, i.e. here the

$[M - CH_3OH]^{+\cdot}$ or the $[M - C_2H_5OH]^{+\cdot}$ ion, shows a significant peak, sometimes even becoming the base peak. The intensity of this peak, however, varies with the environment of the alkoxy group. If there is any other group or position in the steroid skeleton which would need less energy for its fragmentation, that may go first giving rise to the thermodynamically more stable ion. In some cases stereochemistry plays an important role and the fragmentation pattern is directed by the stereochemistry of the alkoxy group in the steroid skeleton. This can be illustrated by comparing the spectra of I and VI. In VI the sterically favoured 1-3 or 1,4 elimination between 6β-OCH_3 and the C_8 or C_{19}-H respectively is very fast since it relieves steric crowding and therefore $[M - CH_3OH]^{+\cdot}$ becomes the base peak of the spectrum. In compound I, however, there is no such crowding nor a sterically favoured hydrogen atom, and hence the usual ring D cleavage, which has been experimentally demonstrated as a low energy process[9] takes precedence.

On comparing the spectra of the alcohols and their methyl ethers studied, it cannot be stated as a general rule that the tendency of a methoxy group to eliminate is greater as compared to that of the corresponding hydroxy group, as has been sometimes made out.[28] For example in the case of cholestan-6β-ol, and 6β-yl-methyl ether, $[M - H_2O]^{+\cdot}$ and $[M - CH_3OH]^{+\cdot}$ are the base peaks of the respective spectra, and in the case of cholestan 3β-ol, $[M - H_2O]^{+\cdot}$ is 13% of the base peak, whereas in cholestan-3β-yl methyl ether, $[M - CH_3OH]^{+\cdot}$ is only 6% of the base peak. Such a rule would usually hold good if the charge resided elsewhere in the ring, and the fragmentation thus directed often takes place. In such cases, the elimination of CH_3OH or C_2H_5OH as a neutral molecule is more abundant as compared to the loss of water in the corresponding alcohol. This can be elucidated from the mass spectra of cholestanol, and its methyl and ethyl ethers. In cholestanol the elimination of water after ring D fragmentation i.e. $[A - H_2O]^+$ is 14% whereas in cholestanyl methyl ether $[A - CH_3OH]^+$ is 65% and in cholestanyl ethyl ether $[A - C_2H_5OH]^+$ is the base peak of the spectrum. Such a generalization is also supported by Spiteller's[28] observations on the mass spectral fragmentation of 17α-ethyl-17β-methoxy-5-α-androstan-3-one. The elimination of methanol as compared to water in its 17β-hydroxy derivatives is intensified, since the charge now resides preferentially on C_{13} due to C_{13}—C_{17}-bond cleavage. Such an influence of the methoxy group predominates only so long as the elimination of methanol from the molecular ion is neither sterically nor thermodynamically favoured. The introduction of a double bond (II, IV and VII) completely changes the mode of fragmentation and a thermodynamically favoured elimination of methanol from the molecular ion then becomes the most facile electron-impact reaction.

EXPERIMENTAL

Mass spectra of all compounds were taken on a CEC 21-110B double focusing mass spectrometer at a source temperature of 140 to 180°C. A direct inlet system was used in all cases, to minimize thermal reactions. Rotations were taken in 1% solution in $CHCl_3$. Purity of compounds was checked by t.l.c. and i.r. and n.m.r. spectra.

Compounds I, III and VII were prepared as reported by Narayanan and Iyer,[29] II and IV as reported by Dusza *et al.*[30] and V and VI as reported by Jones *et al.*[31]

4,4-*Dimethyl-cholesta-5-en-3β-ol* (IX). Cholesta-4-ene-3-one was alkylated by the procedure of Mukherjee and Dutta[32] using potassium-t-amylate and methyl iodide to give 4,4-dimethyl cholest-5-ene-3-one (XII) in 80% yield. Compound XII so obtained was reduced with lithium aluminium hydride according to the procedure of Woodward *et al.*[33] to give IX, m.p. 150 to 51°C, $(\alpha)_D$, −64°.

4,4-*Dimethyl-cholest-5-ene-3β-ol methyl ether* (*X*). In an atmosphere of nitrogen, 4,4-dimethyl cholesta-5-ene-3β-ol (700 mg) was dissolved in dry benzene (40 ml) and potassium metal (700 mg) was added and refluxed for 3 hrs with vigorous stirring. The reaction mixture was then cooled to room temperature and methyl iodide (20 ml) was added. It was then further stirred and refluxed as before for another 3 hrs, during which time the potassium iodide gradually separated out. Methanol was then added to the cooled reaction mixture and the solvent removed *in vacuo*. The residue was extracted with chloroform and chromatographed on a column of activated neutral alumina (30 gms). First petroleum ether eluate (100 ml) gave 10 mg of an unidentified material, probably a hydrocarbon. Further petroleum ether eluates (1000 ml) gave 120 mgs of a pure compound (single spot in t.l.c., which on crystallization from methanol gave 72 mg of the required compound m.p. 113 to 114°, $(\alpha)_D$, −31°. (Found: C, 83·54; H, 12·01. $C_{30}H_{52}O$ requires C, 84·04; H, 12·23%) (n.m.r.: δ, 5·5 (1 H), δ, 3·36, *S* (3 H), δ, 2·65, *m* (1 H).

3,3-*Ethylenedioxy*-4,4-*dimethyl-cholest*-5-*ene* (*VIII*)[34]. To 4,4-dimethyl-cholest-5-en-3-one (100 mg), a mixture of ethylene glycol (0·2 ml), triethyl *ortho*formate (0·5 ml) and *para*toluene sulphonic acid (5 mgs) were added. The reaction mixture was warmed at 125 to 135°C for 1 hr. It was then dumped in 100 ml of cold sodium bicarbonate solution and filtered and washed thoroughly with water. One crystallization from ether/methanol gave pure VIII, m.p. 127°C $(\alpha)_D$ −74°. I.r. showed no absorption in the 1500 to 2000 cm^{-1} region. n.m.r.: δ, 5·42 (1 H), δ, 3·87 (4 H) (ethylene dioxy protons). Found: C, 81·8; H, 11·8%. $C_{31}H_{52}O_2$ requires C, 81·52; H, 11·5%.

REFERENCES

1. D. R. Idler, L. M. Safe and S. H. Safe, *Steroids* **16,** 231 (1970).
2. P. Eneroth, K. Hellstrom and R. Ryhage, *J. Lipid Res.* **5,** 245 (1964).
3. J. Diekman and C. Djerassi, *J. Org. Chem.* **32,** 1005 (1967).
4. C. J. W. Brooks, E. C. Horning and J. S. Young, *Lipids* **3,** 391 (1968).
5. G. V. Mutzenbecher, Z. Pelah, D. H. Williams, H. Budzikiewicz and C. Djerassi, *Steroids* **2,** 475 (1963).
6. J. Karliner, H. Budzikiewicz and C. Djerassi, *J. Org. Chem.* **31,** 710 (1966).
7. C. Beard, J. M. Wilson, H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.* **86,** 269 (1964).
8. L. Tokes, G. Jones and C. Djerassi, *J. Am. Chem. Soc.* **90,** 5465 (1968).
9. K. Hirota and R. Nakane, *Tetrahedron Letters* 5909 (1968).
10. C. E. Brion and L. D. Hall, *J. Am. Chem. Soc.* **88,** 3661 (1966).
11. C. G. Macdonald, J. S. Shannon and G. Sugowdz, *Tetrahedron Letters* 807 (1963).
12. H. Budzikiewicz, Z. Pelah and C. Djerassi, *Monatsh. Chem.* **95,** 158 (1964).
13. H. Egger and G. Spiteller, *Monatsh. Chem.* **97,** 579 (1966).
14. V. I. Zaretskii, N. S. Wulfson, V. G. Zaikin, S. N. Ananchenko, V. N. Leonov and I. V. Torgov, *Tetrahedron* **22,** 2469 (1965).
15. V. I. Zaretskii, N. S. Wulfson, V. G. Zaikin, L. M. Kogan, N. E. Voishvillo and I. V. Torgov, *Tetrahedron* **22,** 1399 (1966).
16. N. S. Wulfson, V. I. Zaretskii, V. L. Sadovskaya, A.V. Zakharychev, S. N. Ananchenko and I. V. Torgov, *Tetrahedron* **23,** 3667 (1967).
17. M. F. Grostic and K. L. Rinehart, Jr., *J. Org. Chem.* **33,** 1740 (1968).
18. C. Djerassi, *Pure Appl. Chem.* **21,** 205 (1970).
19. H. Audier, J. Bottin, A. Diara, M. Fetizon, P. Foy, M. Golfier and W. Vetter, *Bull. Soc. Chim. France* 2292 (1964).
20. M. Spiteller-Friedmann and G. Spiteller, *Fortschr. Chem. Forsch.* **12,** 440 (1969).
21. P. Toft and A. J. Liston, *Steroids* **12,** 447 (1968).
22. R. A. Okerholm, P. I. Brecher and H. H. Wotiz, *Steroids* **12,** 435 (1968).
23. T. A. Bryce, M. Martin-Smith, G. Osske, K. Schreiber and G. Subramanian, *Tetrahedron* **23,** 1283 (1967).
24. T. A. Bryce, G. Eglinton, R. J. Hamilton, M. Martin-Smith and G. Subramanian, *Phytochemistry* **6,** 727 (1967).
25. C. Fenselau, L. Milewich and C. H. Robinson, *J. Org. Chem.* **34,** 1374 (1969).
26. M. A. Baldwin, A. G. Loudon, A. Maccoll and C. W. L. Bevan, *J. Chem. Soc.* (*C*) 1026 (1967).
27. R. I. Reed, *J. Chem. Soc.* 3432 (1958).

28. M. Spiteller-Friedmann and G. Spiteller, *Org. Mass. Spectrom.* **1**, 231 (1968).
29. C. R. Narayanan and K. N. Iyer, *J. Org. Chem.* **30**, 1734 (1965).
30. J. P. Dusza, J. P. Joseph and S. Bernstein, *Steroids* **8**, 495 (1966).
31. D. N. Jones, J. R. Lewis, C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.* 2876 (1955).
32. S. L. Mukherjee and P. C. Dutta, *J. Chem. Soc.* 67 (1960).
33. R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives and R. B. Kelly, *J. Chem. Soc.* 1131 (1957).
34. This compound was first prepared by Mr S. A. Ibiyemi, MSc Thesis, Ahmadu Bello University, Nigeria, 1968.