Tetrahedron. Vol. 24, pp. 2339 to 2343. Pergamon Press 1968. Printed in Great Britain

MASS SPECTROMETRY OF STEROID SYSTEMS—XV[1]

DETERMINATION OF THE CONFIGURATION OF TERTIARY ALCOHOLS IN THE 17-ALKYL-ESTRADIOL AND 17-ALKYL-19-NORTESTOSTERONE SERIES

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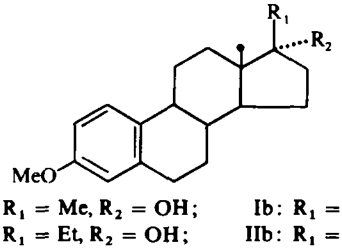
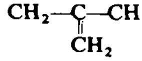
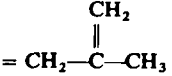
(*Received in the UK* 18 *July* 1967; *accepted for publication* 28 *August* 1967)

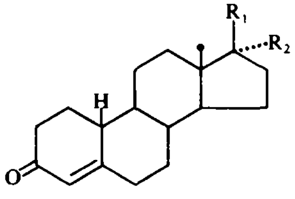
Abstract—The mass spectra of the epimeric tertiary alcohols of a number of 17-alkylestradiols and 17-alkyl-19-nortestosterones have been studied. The dehydration under electron impact of the alcohols with 17α-OH-group was found to proceed more easily than their β-OH-epimers.

In part III,[2] it was shown that the alcohols derived from 17a-alkyl-D-homoestradiol with the axial 17a-OH-group undergo dehydration on electron bombardment more readily than their e-OH-epimers. In the case of 17a-trideuteromethyl analogues, the M^+ ions resulting from dehydration of 17aα-compounds give rise to the fragments having the endocyclic double bond. At the same time the elimination of water from β-hydroxy-compounds results in ions with both *endo* and *exo*cyclic double bonds. This in turn decreases the intensity of the $M-H_2O—CH_3$ peak (which was found to be of a composite nature due to elimination of both angular and 17a-Me groups) in the spectrum of the 17aβ-epimer.

The mass spectra of the epimeric alcohol derivatives of 3-methoxy-17-alkyl-$\Delta^{1,3,5(10)}$-estratrien-17-ol (Ia, b–IIIa, b) and 17-alkyl-19-nortestosterone (IVa, b–Va, b) were studied in order to determine whether this regularity is retained by alcohols with the 5-membered ring D in which the 17α- and 17β-substituents possess axial and equatorial character in relation to ring C.



Ia: $R_1 = Me, R_2 = OH$; Ib: $R_1 = OH, R_2 = Me$
IIa: $R_1 = Et, R_2 = OH$; IIb: $R_1 = OH, R_2 = Et$
IIIa:  $R_1 = CH_2-\underset{\underset{CH_2}{\|}}{C}-CH_3$, $R_2 = OH$
IIIb: $R_1 = OH$,  $R_2 = CH_2-\overset{\overset{CH_2}{\|}}{C}-CH_3$



IVa: $R_1 = Me, R_2 = OH$
IVb: $R_1 = OH, R_2 = Me$
Va: $R_1 = Et, R_2 = OH$
Vb: $R_1 = OH, R_2 = Et$

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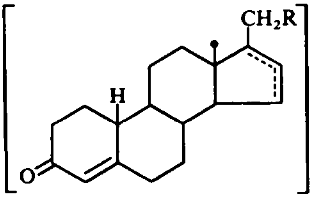
Contrary to D-homoalcohols the mass spectra of the epimers I–III differ only by the intensity ratio of the M-H_2O and M^+ peaks: in the spectra of alcohols with the 17α-OH group (Ia–IIIa) the value of the M-H_2O/M^+ ratio is larger than that of their β-OH-epimers (Ib–IIIb; Fig. 1, Table 1). This observation is in agreement with the fact that the α- and β-bonds at C-17 atom are axial and equatorial respectively.

TABLE 1. INTENSITIES OF THE M^+ AND M-H_2O PEAKS (% OF TOTAL IONIZATION) IN THE MASS SPECTRA OF Ia, b-IIIa, b

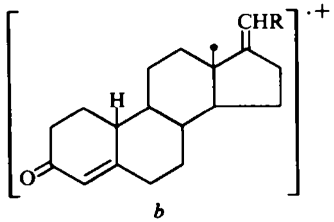
Compound	Ia	Ib	IIa	IIb	IIIa	IIIb
M^+	13	9·6	10·1	8·1	4	4·8
M-H_2O	5·8	1·4	4·1	1·7	2·5	1
M-H_2O/M^+ (%)	45	14	41	21	62	21

In the case of 17-alkyl-19-nortestosterones (IVa, b–Va, b) the difference in the value of the M-H_2O/M^+ ratio for the epimers is less, though, here also the dehydration of the 17α-hydroxy compounds proceeds more readily. The sharpest difference is observed in the value of the M-H_2O-Me(or Et)/M-H_2O ratio. A considerable diminution of this value for alcohols with the 17β-OH group as compared with their 17α-epimers (IVa, Va) is due to a different mechanism of dehydration of the corresponding molecular ions. It is likely, that as in the case of derivatives of 17a-alkyl-D-homoestradiol,[2,3] the dehydration process of IVa and Va is accompanied by elimination of an OH group and a H atom from ring D to produce the ion *a*, whereas in the case of their e-OH-epimers (IVb, Vb) the ion *b* with exocyclic double bond is formed together with the ion *a*. The loss of a 17-alkyl group is not possible in the case of ion *b* and hence the intensity of the M-H_2O-(17-alkyl) (*m/e* 255) peak is decreased (Fig. 2, Table 2).

Attention could be given to the reduced differences in the value of the M-H_2O-Et/M-H_2O ratio in the mass spectra of epimeric ethyltestosterones (Va, b). It is apparently concerned with the fact that in this particular case (contrary to methyltestosterones, IVa, b, in the spectra of which the M-Me peak is practically missing) the *m/e* 255 ion may arise from the molecular ion in two ways: either by successive abstraction of the OH and Et-radicals or as a result of elimination of these groups in the opposite sequence (cf. Figs 2a, b and 2c).



a

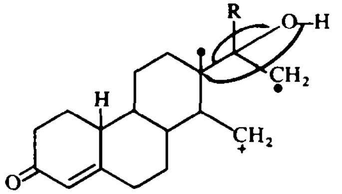


b

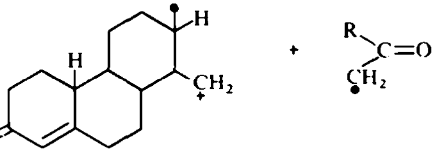
TABLE 2. INTENSITIES OF THE CHARACTERISTIC PEAKS (% OF TOTAL IONIZATION) IN THE MASS SPECTRA OF IVa, b AND Va, b

Compound	M^+	$M\text{-}H_2O$	$M\text{-}H_2O\text{-}Me(Et)$	$M\text{-}H_2O$ / M^+ %	$M\text{-}H_2O\text{-}Me(Et)$ / $M\text{-}H_2O$
IVa	9	3·2	6	36	1·8
IVb	5·7	1·0	0·3	17·4	0·3
Va	8·5	1·8	3·3	21	1·8
Vb	8·7	1·3	1·2	15	0·9

The mass spectra of IVa, b and Va, b reveal the intensive peak at *m/e* 231. The spectrum of OD-analogue of IVa demonstrates that the H atom from the 17-OH-group is responsible in giving rise the peak. However, in contrast to alcohols of D-homo-series[2] the intensity of the *m/e* 231 peak is independent of the configuration at the 17-centre.



M^+



m/e 231

We have also studied the mass spectra of epimeric 17a-methyl- and 17a-ethyl-D-homotestosterones. In this case no differences were observed in the spectra of the epimers. As we know, the absence of the distinctions in the mass spectra of these epimeric alcohols is one of the rare and hardly understandable cases.

EXPERIMENTAL

The mass spectra were measured on the commercial instrument MX-1303, furnished with a system allowing direct sample inlet into the ion source at ionizing energy 70 eV and temp 90° (Ia, IIIa), 80° (IIa), 125° (IVa), 120° (IVb), 95° (Va), the temp being held constant to ± 1°. The sufficient reproducibility (±5%) of the mass spectra was achieved under these conditions.

Compounds Ia (m.p. 158–160°) and IIa (m.p. 132–135°) were prepared by the method Mori.[4] Compounds IVa (m.p. 165–171°) and Va (m.p. 118–121°) were obtained by reduction of Ia and IIa respectively with Li and alcohol in liquid ammonia.[5] Epimeric IIIb (m.p. 97–98°) and IIIa (m.p. 97–100·5°) were synthesized by addition of methylallyl magnesium chloride to estrone methyl ester, the 17β-hydroxy isomer being formed preferentially. The chemical part of the work will be published elsewhere.

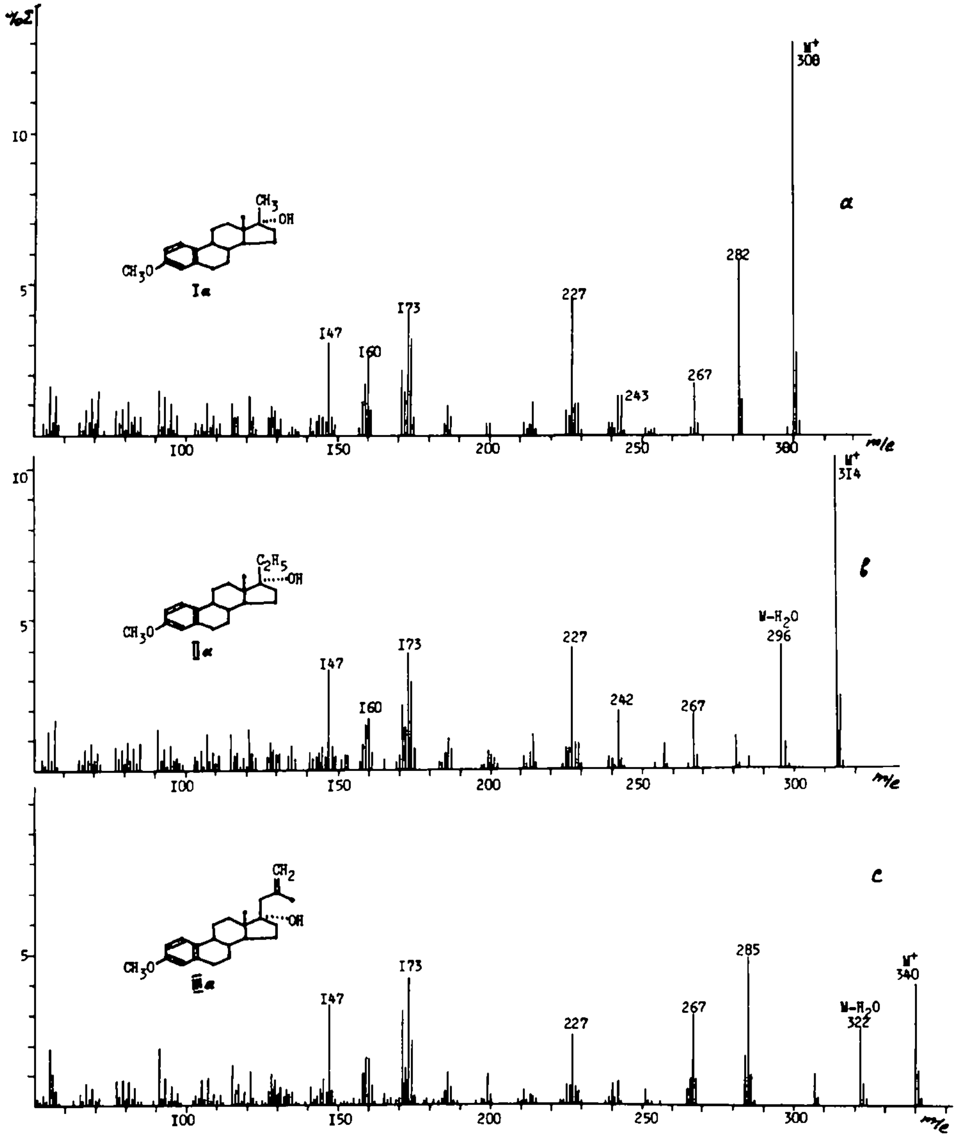


FIG. 1 Mass spectra of (a) Ia, (b) IIa, (c) IIIa.

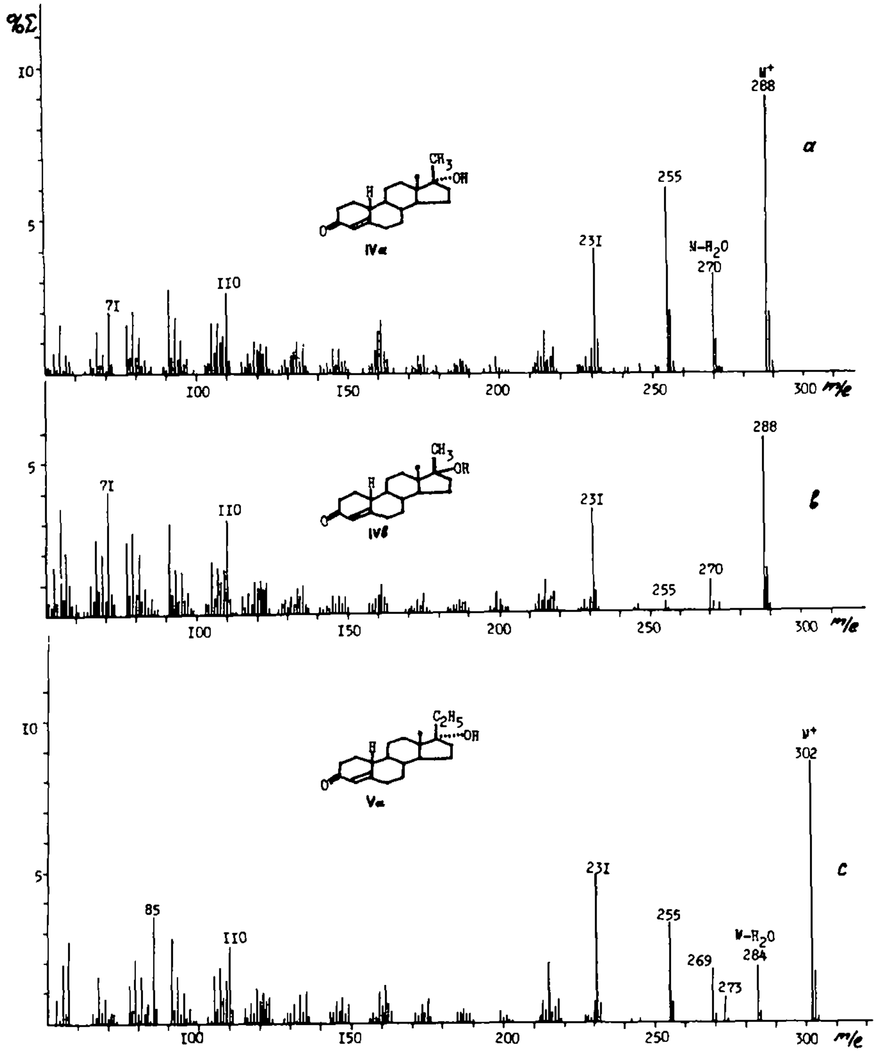


FIG. 2 Mass spectra of: (a) IVa, (b) IVb, (c) Va

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