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MASS SPECTROMETRY OF STEROID SYSTEMS—IX*

STEREOCHEMISTRY OF 14-HYDROXYSTEROIDS

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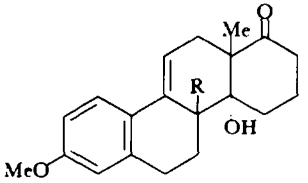
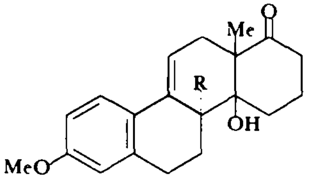
Abstract—The fragmentation behaviour of 14-hydroxy derivatives (I, II and III) of *rac*-dehydro-estrone and *rac*-dehydro-D-homoestrone under electron impact has been studied. Configuration of the compounds mentioned has been based on their mass spectra, the mass spectra of the corresponding dihydrogenated derivatives (VI–IX, XXVI and XXVII) and the products of thermal dehydration of the latter (obtained directly in the inlet balloon of mass spectrometer) as well as the mass spectra of the deuteroanalogs of VI–IX.

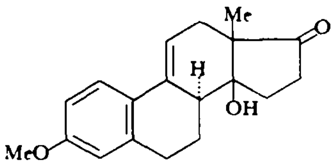
In the course of an investigation on the mass spectrometry of tertiary steroid alcohols[1] and *cis-trans*-isomers of polycyclic systems,[2-4] the mass spectra of 14-hydroxy derivatives of *rac*-estrone and *rac*-D-homoestrone[5] was studied.



I, R = H
IV, R = D



II, R = H
V, R = D



III

The mechanism of degradation of compounds I, II and III as well as their products of chemical transformations under electron impact has established the configuration of these compounds which up to now remained unclear.[5]

The mass spectra of ketols I and II (Figs 1a, b) differ strongly in intensity of the peak of tricyclic ion *a* (*m*/*e* 241) formed by cleavage of the bonds at the C and D ring fusion in the molecular ion together with elimination of the elements of the ring D

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[1] V. I. Zaretskii, N. S. Wulfson, V. G. Zaikin, S. N. Ananchenko, N. V. Leonov and I. V. Torgov, *Tetrahedron* **21**, 2469 (1965).

[2] V. I. Zaretskii, N. S. Wulfson, V. L. Sadovskaya, S. N. Ananchenko and I. V. Torgov, *Dokl. Akad. Nauk SSSR* **158**, 385 (1964).

[3] N. S. Wulfson, V. I. Zaretskii, V. L. Sadovskaya, A. V. Semenovsky, W. A. Smit and V. F. Kucherov, *Tetrahedron* **22**, 603 (1966).

[4] N. S. Wulfson, V. I. Zaretskii, V. L. Sadovskaya, S. N. Ananchenko, V. M. Rzheznikov and I. V. Torgov, *Tetrahedron* **22**, 1885 (1966).

[5] A. V. Zakharychev, I. Hora, S. N. Ananchenko and I. V. Torgov, *Tetrahedron Letters* 3585 (1966).

* Part VIII: V. I. Zaretskii, N. S. Wulfson and V. L. Sadovskaya, *Tetrahedron Letters* 3879 (1966).

† Laboratory of Mass Spectrometry.

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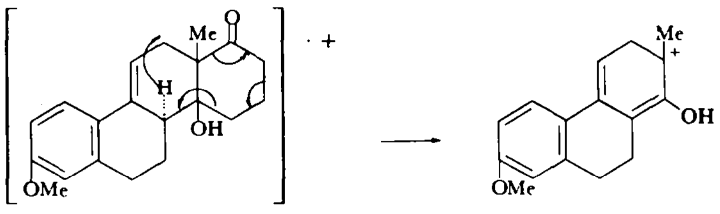

II

a, m/e 241

and the hydrogen atom from C-8 (this is confirmed by the absence from a shift of the peak with m/e 241 in the mass spectrum of V).

A similar type of fragmentation is characteristic of derivatives of $\Delta^{9(11)}$-dehydroestrone.[6] The presence of the 14-OH-group in the ion *a* is confirmed by the shift of the corresponding peak by a unit (to m/e 242) in the mass spectrum of 14-OD-analog of ketol II. The intensity of the peak with m/e 241 is low in the spectrum of ketol I, whereas it is more than 50% that from M^+ in the case of ketol II (Figs. 1a, b). A sharp increase in the intensity of the peak of the tricyclic fragment *a* in ketol II establishes the *cis*-C/D-configuration for the latter and the *trans*-C/D-configuration for ketol I. A similar dependence of the intensity of characteristic peaks on the mode of ring fusion was recorded for 14α- and 14β-D-homoequilenin,[2] the 8β- and 8α-D-homoestrone[2] series and certain other polycyclic systems.[3,4]

The mass spectra of ketols I and II also differ by the ratio of the intensities of the peaks M-18(m/e 294)/M^+. This value exceeds 1 in the case of ketol I, whereas it is only 1/3 in the spectrum of ketol II (see Figs. 1a, b and Table 1).

TABLE 1. THE INTENSITIES OF THE PEAKS M^+ AND M-18 IN THE MASS SPECTRA OF KETOLS I–III.

ketol	peak intensity %Σ		$\frac{M-18}{M^+}$
	M^+	M-18	
I	5·9	7·2	1·2
II	12·6	3·9	0·3
III	11·2	0·4	0·04

As this difference may be due to an alternate spatial disposition of the 14-OH-group and the corresponding H-atom which is eliminated from the molecular ion of I and II during dehydration, the mass spectra of 8-d_1-analogs of ketols I and II (IV and V, respectively) were studied. Practically a complete shift of the peak of M-18 ion by a unit (to m/e 295) proves that in both cases elimination of water proceeds without participation of the H-atom at C-8 (alternative process of 1,2-elimination[7] involving H-atom at C-15 is apparently also improbable). Therefore, dehydration involves

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[6] C. Djerassi, J. M. Wilson, H. Budzikiewicz and J. W. Chamberlin, *J. Am. Chem. Soc.* **84**, 4544 (1962).

[7] C. G. MacDonald, J. S. Shannon and G. Sugowdz, *Tetrahedron Letters* 807 (1963).

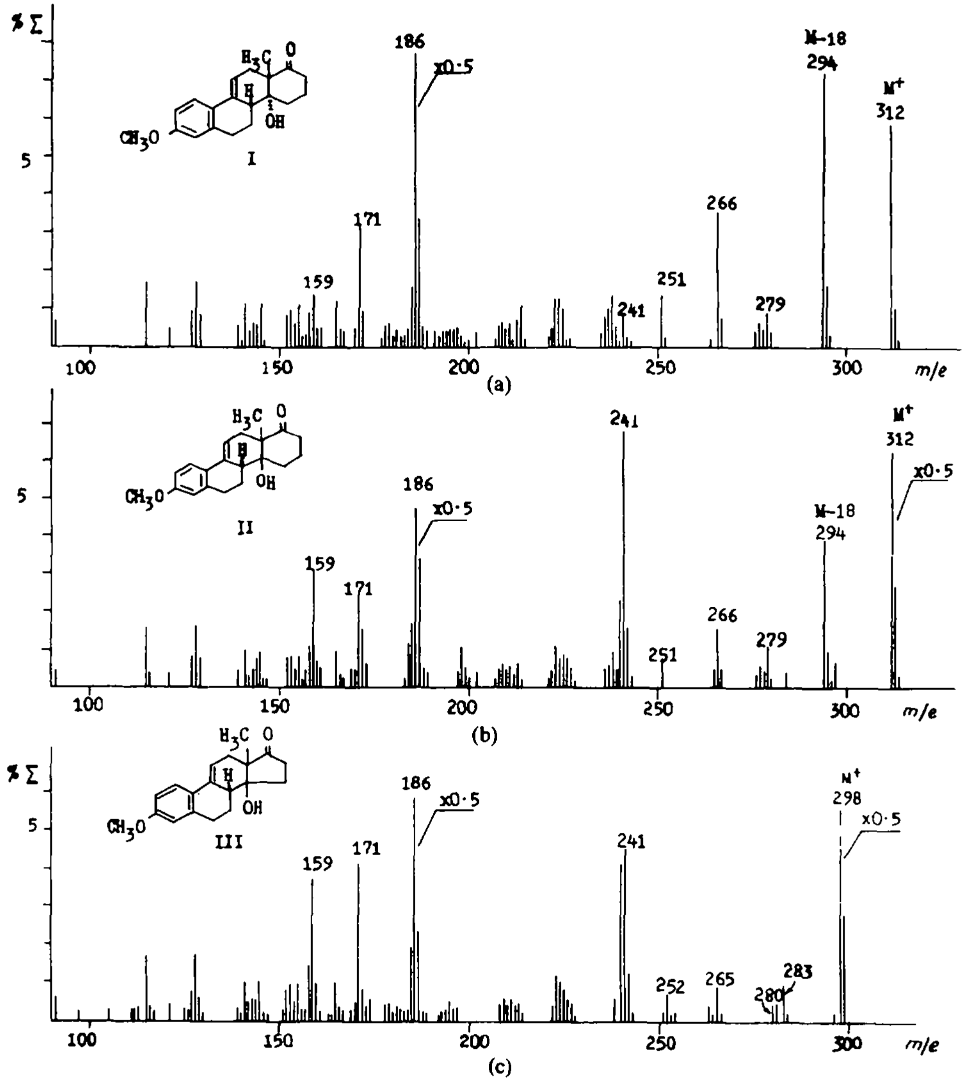


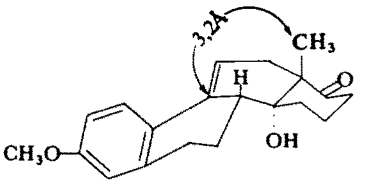
Fig. 1. Mass spectra (direct inlet system) of:

(a) $\Delta^{9(11)}$-dehydro-14α-hydroxy-D-homoestrone methyl ether (I);

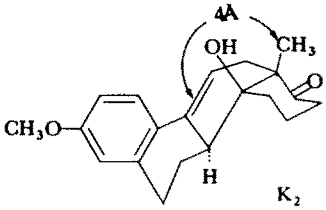
(b) $\Delta^{9(11)}$-dehydro-14β-hydroxy-8α-D-homoisoestrone methyl ether (II);

(c) $\Delta^{9(11)}$-dehydro-14β-hydroxy-8α-isoestrone methyl ether (III).

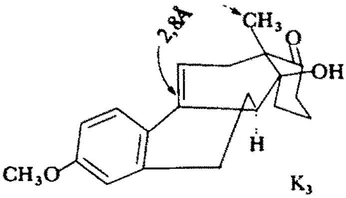
elimination of either the C_{12} hydrogen or one of H-atoms of ring D (from C-16). Consequently, the ease of dehydration of ketol I is due to the 14α-configuration of the 14-center (*trans*-C/D-junction, conformation K_1). In this case the 14-OH-group is axial to the rings C and D and elimination proceeds by removal of H-atoms from both possible positions. A low degree of dehydration of the molecular ion of ketol II may be due to the equatorial disposition of the 14-OH-group towards the ring which donates the H-atom in the course of dehydration under electron impact. This may happen only in the case of *cis*-C/D-ketol (14β-OH-configuration) since in any theoretically possible conformation of compound II (K_2 or K_3) the 14-OH-group is equatorial to one of the rings (C or D). More prominent dehydration of tertiary steroid alcohols with an axial OH-group under electron impact as compared with their e-OH-epimers has been recorded.[1] The most probable conformation of ketol II has been based on the hydrogenation of ketols I and II.



K_1

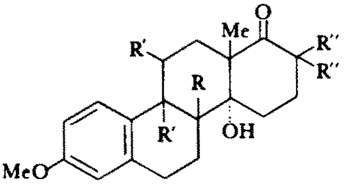


K_2

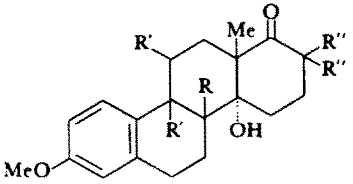


K_3

Earlier[5] hydrogenation of ketol I over 10%-Pd/$CaCO_3$ was shown to proceed stereospecifically yielding 72% of 14α-hydroxy-D-homoestrone methyl ether (VI) and only 5% of the C-9-isomer—9β-14α-hydroxy-D-homoisoestrone (VII).

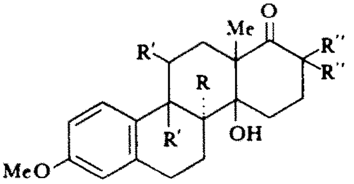


VI, R = R' = R'' = H
X, R = D, R' = H, R'' = H
XI, R = H, R' = D, R'' = H
XVII, R = H, R' = H, R'' = D

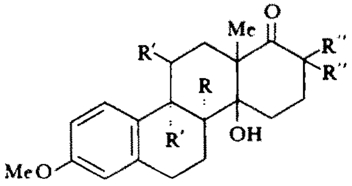


VII, R = R' = R'' = H
XII, R = H, R' = D, R'' = H
XVIII, R = H, R' = H, R'' = D

In contrast to ketol I, ketol II under these conditions, is hydrogenated non-stereospecifically yielding a mixture of isomers—dihydrogenated ketols VIII and IX.[5]



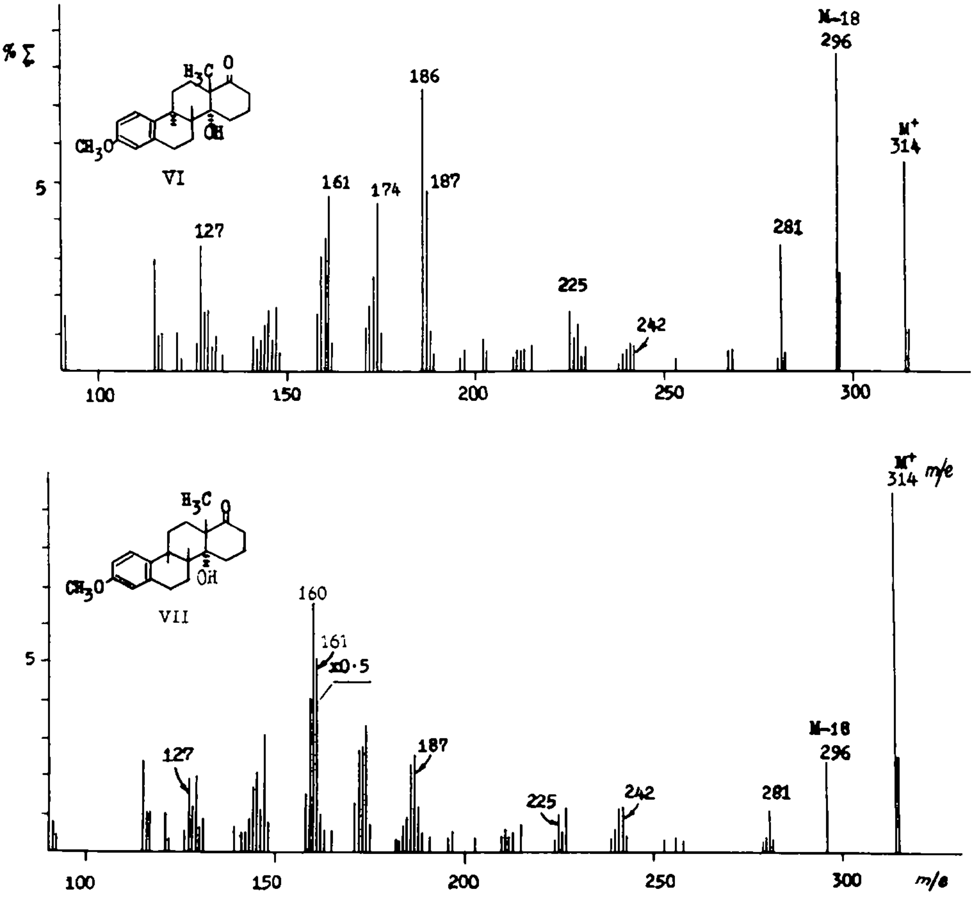
VIII, R = R' = R'' = H
XIII, R = D, R' = H, R'' = H
XIV, R = H, R' = D, R'' = H
XIX, R = H, R' = H, R'' = D



IX, R = R' = R'' = H
XV, R = D, R' = H, R'' = H
XVI, R = H, R' = D, R'' = H
XX, R = H, R' = H, R'' = D

Consideration of the Dreiding molecular models, reveals that in *anti-trans*-ketol I (conformation K_1) as well as in conformation K_3 of *anti-cis*-ketol II the angular Me group strongly shields the $\Delta^{9(11)}$-double bond from the side of β-region (the distance between Me group and double bond makes 3·2 Å and 2·8 Å, respectively) whereas in conformation K_2 of *anti-cis*-ketol II this distance is 4 Å. If conformation K_2 is assigned to ketol II and considering the taking into account a small degree of dehydration of the molecular ion of ketol II one may assume that in ketol I as well as in ketol II elimination of water under electron impact proceeds with involvement of one of the H-atoms from ring D.

Proof of the configuration of the 8-center in ketols I and II, as well as of the 9-center in their dihydro derivatives was obtained from the mass spectra of compounds VI–IX and the corresponding dehydro-D-homo-isoestrones prepared by thermal dehydration of the former *in vacuo* at 200° directly in a glass inlet balloon of a mass spectrometer.



(b)

FIG. 2 Mass spectra of:

(a) 14α-hydroxy-D-homoestrone methyl ether (VI) direct inlet system;

(b) 14α-hydroxy-9β-D-homoisoestrone methyl ether (VII) direct inlet system;

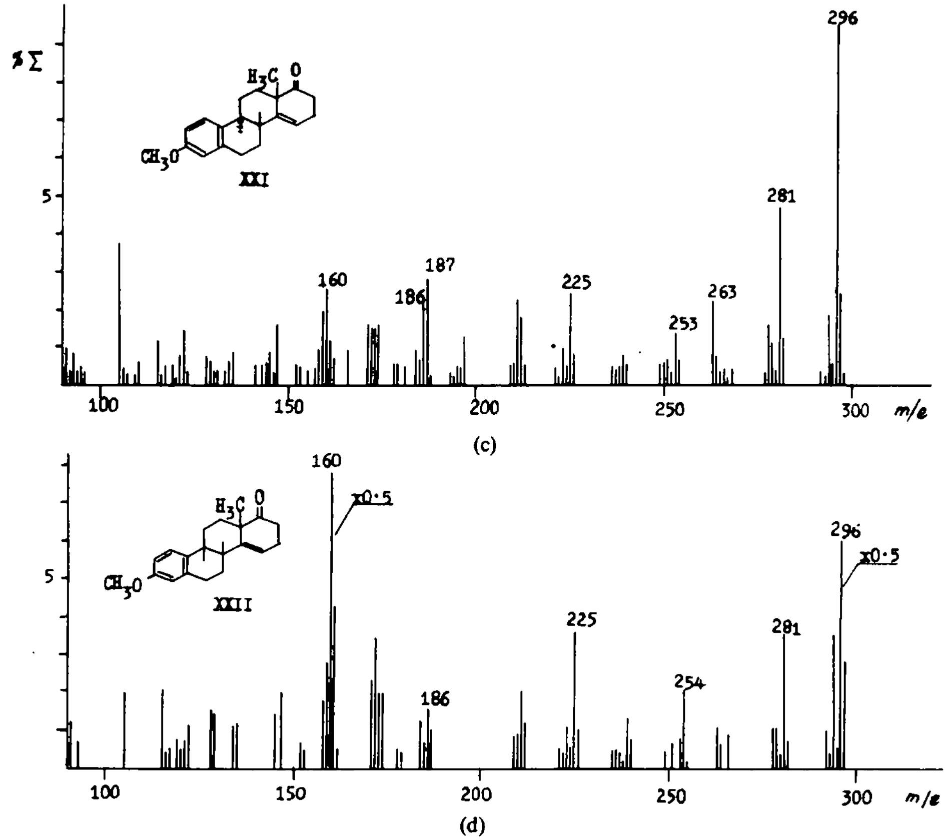


FIG. 2 (*continued*)

(c) $\Delta^{14(15)}$-dehydro-D-homoestrone methyl ether (XXI) obtained by thermal dehydration in hot inlet system;

(d) $\Delta^{14(15)}$-dehydro-9β-D-homoisoestrone methyl ether (XXII) obtained by thermal dehydration in hot inlet system.

The intensity of the peak of (M-18) ion (*m/e* 296) is much higher in the mass spectra of compounds VI and VIII when compared with the mass spectra of their corresponding C-9-isomers (VII and IX) (Figs. 2a, b and 3a, b). Compounds VI and VII, VIII and IX were obtained by hydrogenation of ketols I and II, respectively, and hence differ only by configuration of the C-9-center. One might, therefore, suppose that intense dehydration of the ion M^+ in compounds VI and VIII was due to *cis*-1,3-diaxial disposition of the 14-OH-group and the H-atom at C-9 (1,3-elimination of the elements of water under electron impact, cf.,[7, 8]), whereas an insignificant value of $M\text{-}18/M^+$ ratio in compounds VII and IX is connected with *trans*-ae-configuration of the 14- and 9-centers in the latter (Table 2). In order to trace the origin of the H-atom involved in water elimination under electron impact, the mass spectra of 8-d_1- and 9,11-d_2-analogs of compounds VI–IX were taken.

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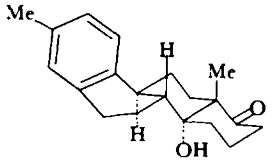
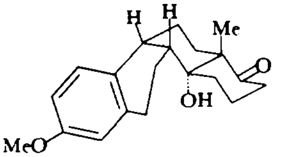
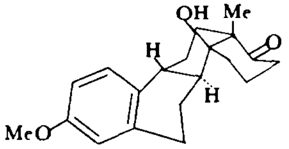
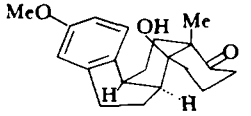
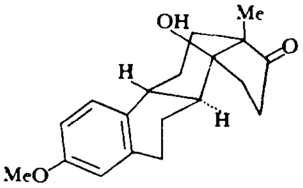
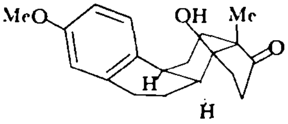
[8] J. Karliner, H. Budzikiewicz and C. Djerassi, *J. Org. Chem.* 31, 710 (1966).

Table 2. The intensities of the peaks of (M-18) ions in the mass spectra of compounds VI–IX, XXVI and XXVII and of ion *b* (*m*/*e* 160) in the spectra of the products of thermal dehydration of these compounds.

Compound	Conformational formula	$\frac{\text{M-H}_2\text{O}}{\text{M}^+}$	$\frac{b}{\text{M}^+ \text{ of dehydroestrone}}$
VI		1·5	0·2
VII		0·2	1·3
VIII		2·3	0·2
IX		0·2	1·2
XXVI		2·0	0·1
XXVII		0·8	0·4

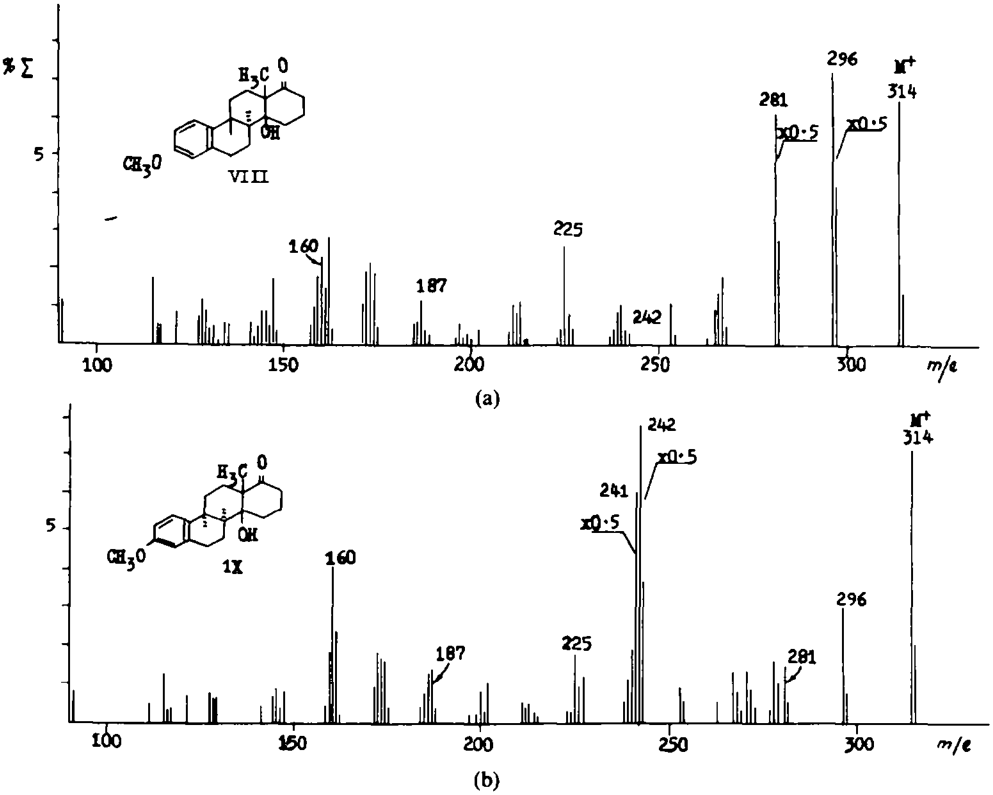


FIG. 3 Mass spectra of:

(a) 14β-hydroxy-8α,9β-D-homoisoestrone methyl ether (VIII) direct inlet system;

(b) 14β-hydroxy-8α,9α-D-homoisoestrone methyl ether (IX) direct inlet system;

An almost complete shift of the peak M-18 by a unit (to *m/e* 297) in the mass spectra of 8-d_1-compounds X, XIII and XV proves that the H-atom at C-8 is not involved in dehydration. At the same time a comparison of the mass spectra of 9,11-d_2-compounds XI, XII, XIV and XVI reveals that 50–94% of hydrogen lost in the form of water originates from the 9-position (Tables 3 and 4), e.g. 1,3-elimination of water takes place.[8] A possibility that the H-atom at C-11 is involved in dehydration may be neglected since in the case of 1,4-elimination of water the ring C should have a "Boat" conformation which is unlikely as has been exemplified by cyclohexanol.[7] In polycyclic systems, 1,4-elimination of water does not appear to take place even in the conformationally more labile side ring D. This is confirmed by the shift of the peak M-18 by two units (to *m/e* 298) in the spectra of 17,17-d_2-analogs (XVII–XX).

Participation of the H-atom at C-9 in the dehydration of ketols VI–IX (an extent of its involvement being as high as 70–94% (Table 4) in compounds VI and VIII) confirms that a higher degree of dehydration of the molecular ion in compounds VI and VIII is connected with a more favourable 1,3-*cis*-disposition of the 14-OH-group and the H-atom at C-9. A low degree of dehydration of compounds VII and IX is due to a 1,3-*trans*-disposition of these groups. In other words, compounds VI and IX should be referred to as the 9α-, and compounds VII and VIII as the 9β-series.

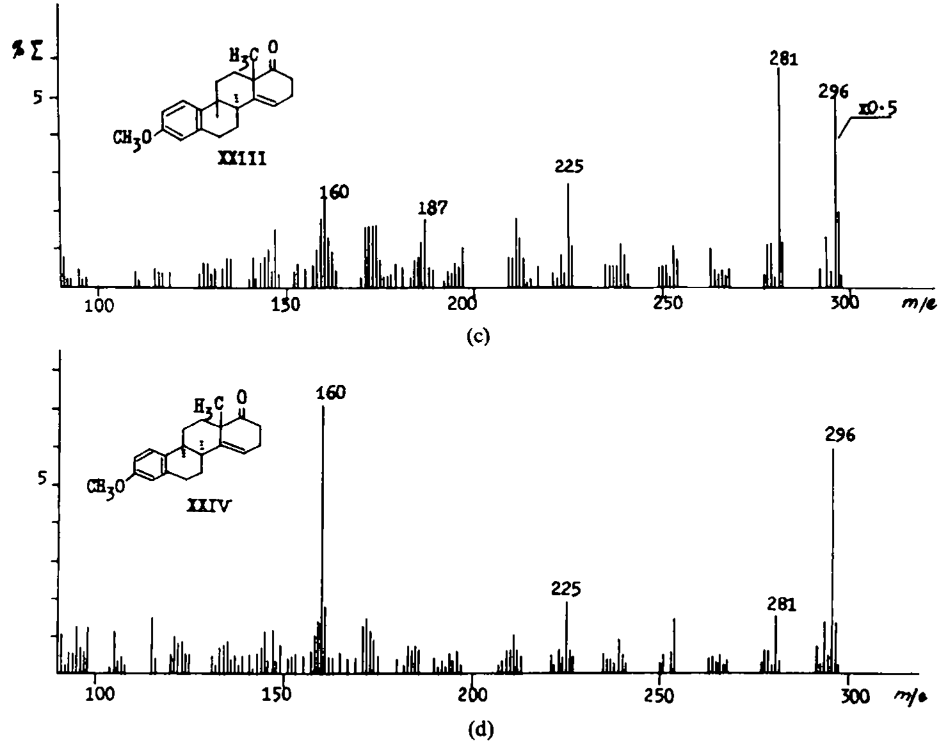


FIG. 3 (*continued*)

(c) $\Delta^{14(15)}$-dehydro-8α,9β-D-homoisoestrone methyl ether (XXIII) obtained by thermal dehydration in hot inlet system;

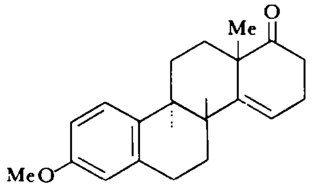
(d) $\Delta^{14(15)}$-dehydro-8α,9α-D-homoisoestrone methyl ether (XXIV) obtained by thermal dehydration in hot inlet system.

The configuration of the 9-center in compounds VI–IX established in such way is in a perfect agreement with the chemical data on the stereochemistry of hydrogenation.[5]

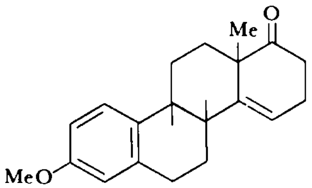
The configuration of the C-8-center in compounds VI–IX and, therefore, in parent ketols I and II has been determined by a comparison of the mass spectra of dehydro-D-homo-isoestrones prepared by thermal dehydration of compounds VI–IX.

The mass spectra of compounds XXII and XXIV obtained by dehydration of VII and IX differ widely from those of compounds XXI and XXIII prepared by dehydration of VI and VIII in a higher intensity of the peak of ion *b* (*m*/*e* 160) (Figs. 2c, d and 3c, d).

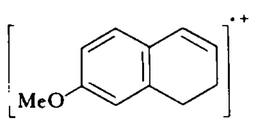
The difference may be due to the presence of a $\Delta^{8(14)}$-double bond (which is blocking a breakdown of C–C-bond 8–14) in a corresponding dehydro-D-homoestrone as well as the passing from *cis*-B/C- to *trans*-B/C-fused $\Delta^{14(15)}$-dehydro derivatives. The mass spectra of the products of thermal dehydration prepared under similar conditions from 8-d_1- and 9,11-d_2-analogs of compounds VI–IX revealed that thermal dehydration of the 14-hydroxy compounds VI–IX did not involve hydrogen atoms from the ring C and, therefore, 1,2-elimination of water resulting in formation of $\Delta^{14(15)}$-dehydro derivatives XXI–XXIV took place in these conditions. The structure of these compounds is also confirmed by a comparison of their mass spectra with the spectra of authentic compounds, as well as with the spectrum of $\Delta^{8(14)}$-dehydro-9β-iso-D-homoestrone methyl ether (XXV) obtained by an independent method[5] (Figs 5a, b, c).



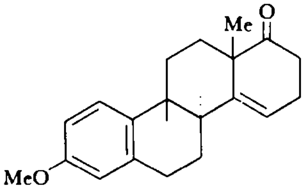
XXI



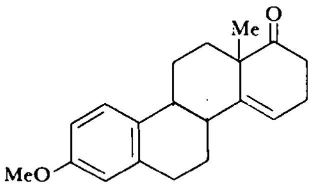
XXII



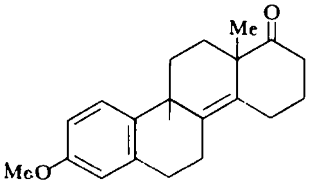
b, m/e 160



XXIII



XXIV



XXV

Table 3. The shifts of the peaks M^+ and M-18 in the mass spectra of 9,11-d_2-compounds XI, XII, XIV and XVI.

Compound	M^+		M-18	
VI–IX	314		296	
XI	314	8%	296	17%
	315	28%	297	57%
	316	50%	298	22%
	317	14%	299	4%
XII	314	5%	296	10%
	315	16%	297	20%
	316	36%	298	35%
	317	34%	299	25%
	318	9%	300	10%
XIV	314	10%	296	21%
	315	27%	297	54%
	316	46%	298	21%
	317	17%	299	4%
XVI	314	13%	296	17%
	315	30%	297	38%
	316	47%	298	37%
	317	10%	299	8%

TABLE 4. THE GENESIS OF THE H-ATOM INVOLVED IN DEHYDRATION OF COMPOUNDS VI–IX UNDER ELECTRON IMPACT.

Compound	H-atom lost from C-9, %[a]	H-atom lost from other positions except C-8, %[a]
VI	70	30
VII	52	48
VIII	94	6
IX	50	50

[a] When taking into consideration that the isotopic effect makes ~0·8[8].

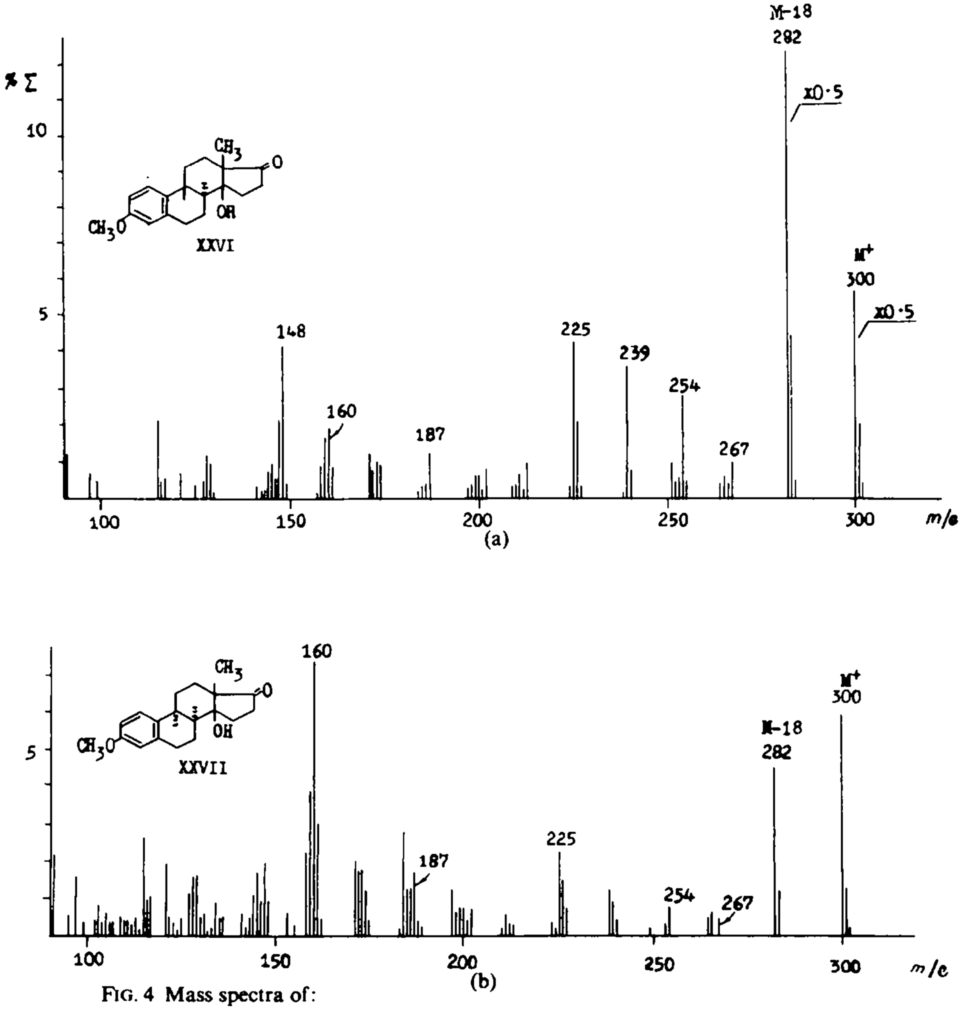
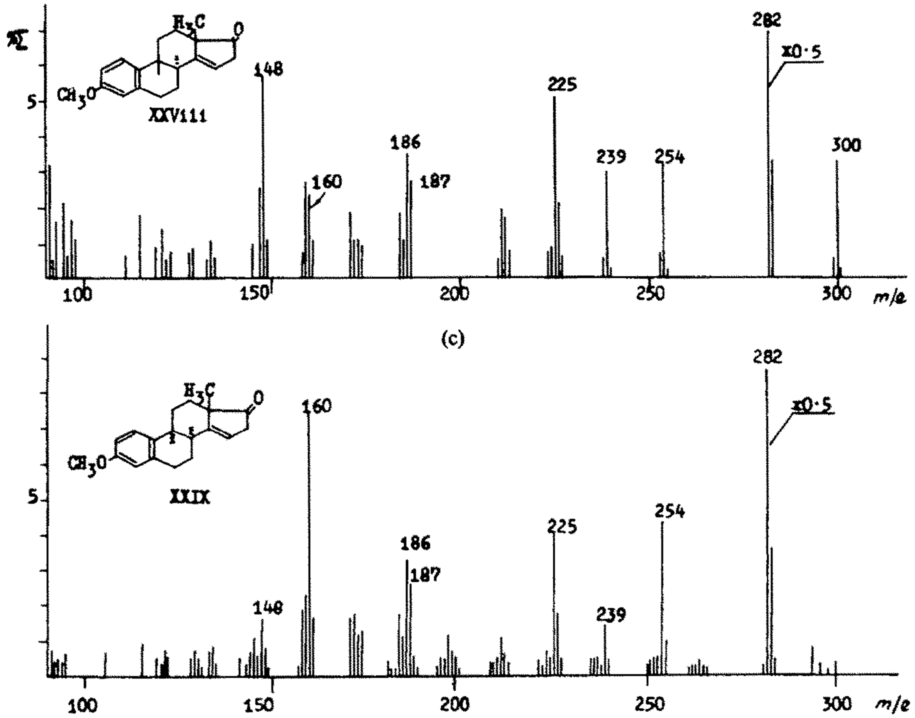


FIG. 4 Mass spectra of:

(a) 14β-hydroxy-8α,9β-isoestrone methyl ether (XXVI) direct inlet system;

(b) 14β-hydroxy-8α-isoestrone methyl ether (XXVII) direct inlet system;



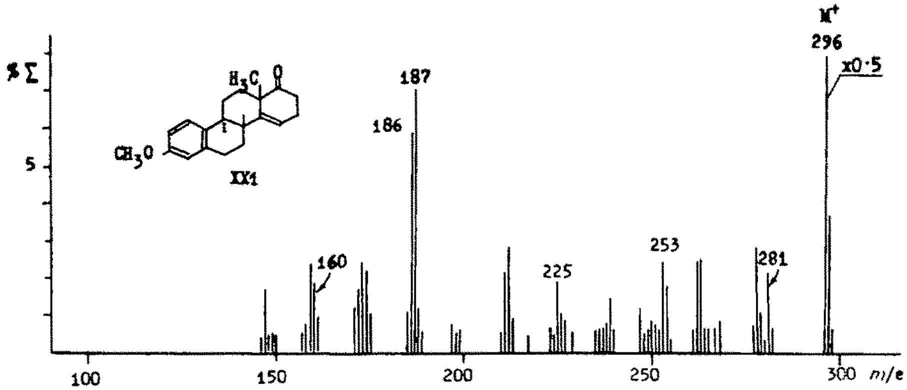
(c)

(d)

FIG. 4 *(continued)*

(c) $\Delta^{14(15)}$-dehydro-8α,9β-isoestrone methyl ether (XXVIII) obtained by thermal dehydration in hot inlet system;

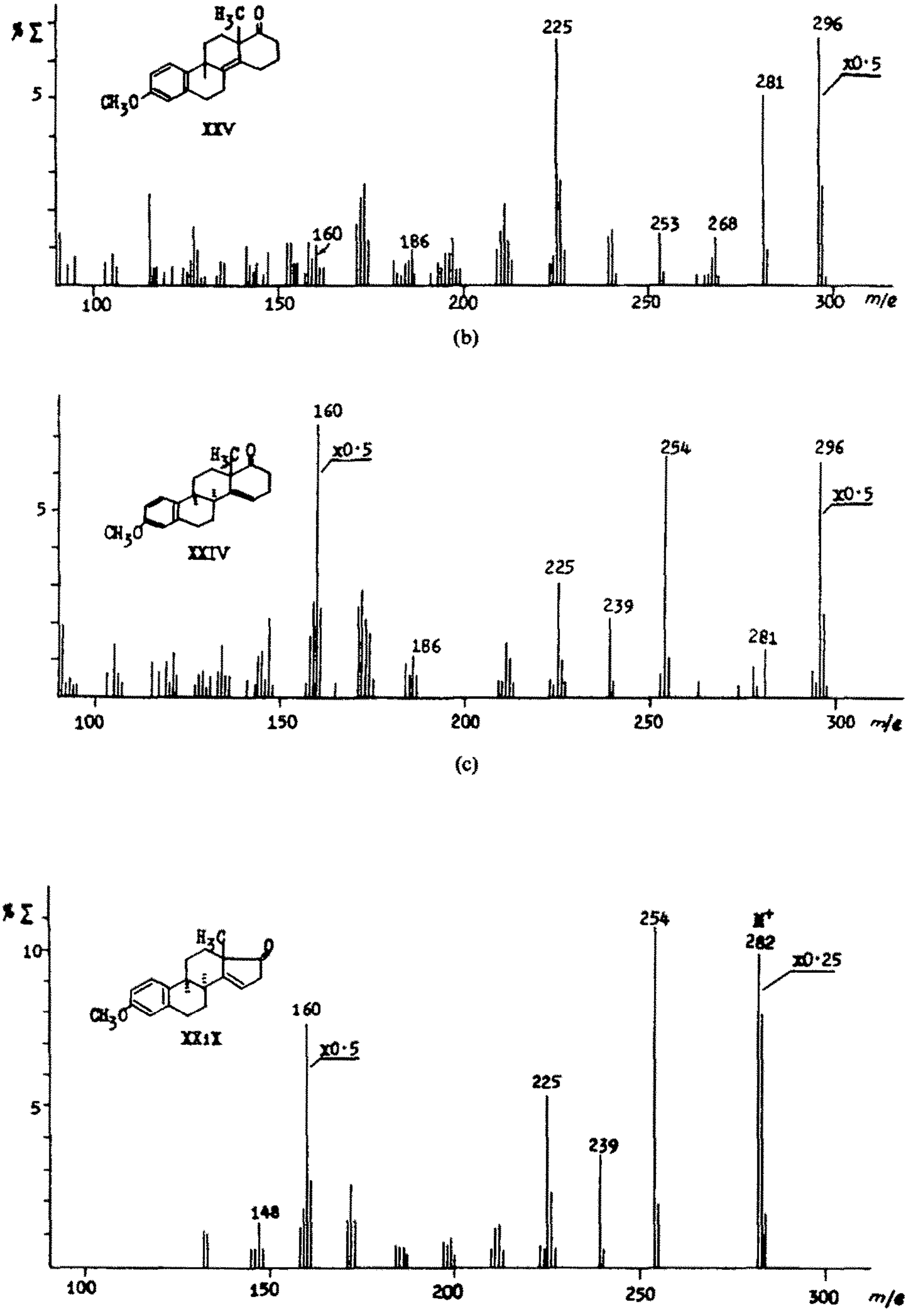
(d) $\Delta^{14(15)}$-dehydro-8α-isoestrone methyl ether (XXIX) obtained by thermal dehydration in hot inlet system.



(a)

FIG. 5 Mass spectra, direct inlet system, of:

(a) $\Delta^{14(15)}$-dehydro-D-homoestrone methyl ether (XXI);



(b)

(c)

(d)

FIG. 5 (*continued*)

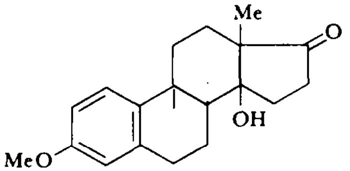
(b) $\Delta^{8(14)}$-dehydro-9β-D-homoisoestrone methyl ether (XXV);
(c) $\Delta^{14(15)}$-dehydro-8α-D-homoisoestrone methyl ether (XXIV);
(d) $\Delta^{14(15)}$-dehydro-8α-isoestrone methyl ether (XXIX).

A higher intensity of the peak with *m/e* 160 in the spectra of compounds XXII and XXIV when compared with that in the spectra of compounds XXI and XXIII is thus due to *cis*-junction of the rings B and C in the former. A similar regularity in an alteration of the intensity of fragment *b* (*m/e* 160) by passing from B/C-*trans*- to B/C-*cis*-structure was noted earlier for D-homoestrone methyl ether and its 8α-isomer.[2]

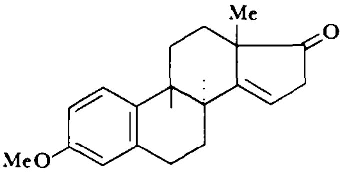
Thus, in compounds VI and VII, as well as in initial ketol I, the 8-H-atom is in β-position, whereas 8α-configuration is to be assigned for ketols VIII, IX and II.

The structure of $\Delta^{9(11)}$-dehydro-14-hydroxy-8α-isoestrone (III) and the stereochemistry of the 8-center in its molecule has been based on chemical data.[5] However, the configuration of the 14-center in this compound has been suggested only on the basis of general considerations.

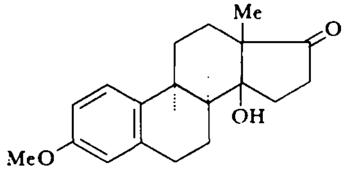
In the mass spectrum of ketol III (Fig. 1c) the peak of M-18 ion (*m/e* 280) has very low intensity (~4% of M^+, Table 1). The similarity with ketols of the D-homo series (I and II) together with the published data[9] suggested that in this compound the OH-group has the 14β-configuration. Further proof of this configuration was obtained from the mass spectra of 9,11-dihydro derivatives (XXVI and XXVII) of ketol III, as well as the spectra of the products of their thermal dehydration (XXVIII and XXIX, respectively).



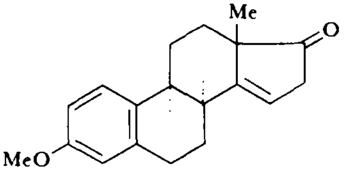
XXVI



XXVIII



XXVII



XXIX

Indeed, in the mass spectrum of XXVII, the 8α,9α-configuration of which was unambiguously proved by chemical methods,[5] the intensity of the peak of M-18 ion (*m/e* 282) is much lower than that in the spectrum of its 9β-isomer (XXVI, Figs. 4a, b) and, therefore, similarly to compounds of the D-homo-series, compounds XXVI, XXVII and ketol III may be assigned to the 14β-series.

The spectra of dehydroisoestrones XXVIII and XXIX obtained by thermal dehydration of compounds XXVI and XXVII (Figs. 4c, d) are in a complete agreement with *trans*-B/C- (XXVI, 8α,9β-) and *cis*-B/C-junction (XXVII, 8α,9α-) of these compounds.

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[9] R. Tschesche, P. Welzel and H.-W. Fehlhaber, *Tetrahedron* **21**, 1797 (1965).

EXPERIMENTAL

Mass spectra of I–XX and XXV–XXIX were taken on the commercial mass spectrometer MX-1303 by using a direct inlet system, at a temp 120–140° for 14-OH-compounds and 90–100° for dehydroestrone derivs (the temp being held constant to $\pm 1°$) and electron energy 70 eV. Mass spectra of XXI–XXIV were taken by using glass inlet system (200°, 30 eV) after heating VI–IX, respectively, directly in a glass inlet balloon of the mass spectrometer *in vacuo* at 200° during 2 hr.

6-*Methoxytetralone*-1-2-d_2 (XXX). To a soln of 6-methoxytetralone-1 (200 mg) in THF (13 ml), D_2O (0·5 ml), C_2H_5OD (0·5 ml) and Na (0·003 g) was added and the mixture was boiled for 6 hr. The residue after evaporation *in vacuo* was extracted with Chf yielding XXX (m.p. 76°) after evaporation. Mass spectrum: *m/e* 177 (d_1), 17%; *m/e* 178 (d_2), 83%.

1-*Vinyl-6-methoxytetralol*-1-2-d_2 (XXXI). This carbinol was obtained in quantitative yield from XXX and vinyl magnesium bromide by the Norman reaction,[10] $n_D^{20} = 1·5250$, mass spectrum: *m/e* 205 (d_1), 10%; *m/e* 206 (d_2), 90%.

3-*Methoxy*-$\Delta^{1\ 3\ 5(10)\ 9(11)}$-8, 14-*seco*-8-$d_2$-D-*homoestratetraendione*-14, 17a (XXXII). A mixture of XXXI (2 g), methyldihydroresorcinol (2 g), MeOH (25 ml), KOH (0·15 g) and water (5 ml) was boiled for 6 hr. After cooling the mixture was diluted with a half volume of water and extracted with AcOEt. The extract was washed with 5%-Na_2CO_3aq, then with water to neutral, dried over $MgSO_4$ and evaporated. The residue was washed with cold ether and recrystallized from MeOH, yielding 1·4 g of XXXII, m.p. 89°, mass spectrum: *m/e* 313 (d_1), 10%; *m/e* 314 (d_2), 90%.

3-*Methoxy*- $\Delta^{1,3,5(10),9(11)}$-14α-*hydroxy*-8β-d_1-D-*homoestratetraenone*-17a (IV) *and* 3-*methoxy*- $\Delta^{1,3,5(10),9(11)}$-14β-*hydroxy*-8α-d_1-D-*homoestratetraenone*-17a (V). Diketone XXXII (800 mg) was dissolved in the mixture of MeOH (8 ml) and THF (5 ml), acid resin "KY-2" (240 mg) was added and the mixture was stirred for 12 hr at 20°. The resin was removed, the filtrate was evaporated and the residue was chromatographed on Al_2O_3 (III–IV act.) on the plate (23 × 28), $d = 2–3$ mm. Benzene was used for developing, zone indication was carried out in UV-light. After elution from the starting zone with ether, evaporation and crystallization of the residue from AcOEt 70 mg of IV was obtained, m.p. 216–218° and chromatographically pure. Mass spectrum: *m/e* 312 (d_0), 5%; *m/e* 313 (d_1), 95%.

A similar treatment of the middle zone yielded a mixture which was rechromatographed using the procedure described above. After rechromatography and recrystallization from AcOEt 160 mg of V was obtained, m.p. 168–170° and chromatographically pure. Mass spectrum: *m/e* 313 (d_1), 100%.

3-*Methoxy*- $\Delta^{1,3,5(10)}$-14α-*hydroxy*-8β-d_1-9α-D-*homoestratrienone*-17a (X). Ketol IV (70 mg) was dissolved in THF (10 ml) and hydrogenated over 10%-Pd/$CaCO_3$ until uptake of H ceased. After removing the catalyst the soln was evaporated and the residue was recrystallized from MeOH yielding X, m.p. 200–202° and chromatographically pure. Mass spectrum: *m/e* 315 (d_1), 100%.

3-*Methoxy*- $\Delta^{1,3,5(10)}$-14β-*hydroxy*-8α-d_1-9β-D-*homoestratrienone*-17a (XIII) and 3-*methoxy*- $\Delta^{1,3,5(10)}$-14β-*hydroxy*-8α-d_1-9α-D-*homoestratrienone*-17a (XV). Ketol V (160 mg) was hydrogenated over 10%-Pd/$CaCO_3$. The residue after routine treatment was chromatographed on a column with Al_2O_3 (II–III act., 5 g). In the course of elution with pet. ether, control of the fractions was carried out by means of thin layer binderless chromatography on Al_2O_3. After evaporation of the first fractions and two-fold crystallization from MeOH ketol XIII (7 mg) was obtained, m.p. 182–184° and chromatographically pure. Mass spectrum: *m/e* 315 (d_1), 100%. A mixture of XIII and XV (145 mg) was obtained from the middle fractions. Ketol XV (2 mg) was isolated after usual treatment of the end fractions: m.p. 209–213° and chromatographically pure. Mass spectrum: *m/e* 315 (d_1), 100%.

3-*Methoxy*- $\Delta^{1,3,5(10)}$-14α-*hydroxy*-8β-H-9α,11-d_2-D-*homoestratrienone*-17a (XI) and 3-*methoxy*- $\Delta^{1\ 3\ 5(10)}$-14α-*hydroxy*-8β-H-9β,11-d_2-D-*homoestratrienone*-17a (XII). A mixture of I[5] (200 mg), AcOEt (10 ml) and THF (4 ml) was stirred over 10%–Pd/$CaCO_3$ at 20° in an atmosphere of deuterium until gas uptake ceased. A usual treatment and crystallization from AcOEt yielded XI (72 mg), m.p. 188–190°. An analytical sample has m.p. 190–191°. Mass spectrum: *m/e* 314 (d_0), 8%; *m/e* 315 (d_1), 28%; *m/e* 316 (d_2), 50%; *m/e* 317 (d_3), 14%.

The deuterium content in M^+ remained unchanged after treatment of XI in boiling MeOH for 1 hr. The mother liquor after isolation of XI was evaporated to dryness and the residue chromatographed on a column with Al_2O_3 (II–III act., 8 g). Elution with benzene and evaporation of the eluate yielded crystals ketol XII. After successive washing with ether, AcOEt and again with ether it was chromatographically

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[10] S. N. Ananchenko, V. Ye. Limanov, V. N. Leonov, V. M. Rzheznikov and I. V. Torgov, *Tetrahedron* **18**, 1355 (1962).

pure, m.p. 169–171° (20 mg). Mass spectrum: *m/e* 314 (d_0), 5%; *m/e* 315 (d_1), 16%; *m/e* 316 (d_2), 36%; *m/e* 317 (d_3), 34%; *m/e* 318 (d_4), 9%.

3-*Methoxy*- $\Delta^{1,3,5(10)}$-14β-*hydroxy*-8α-H-9α,11d_2-D-*homoestratrienone*-17a (XVI) *and* 3-*methoxy*- $\Delta^{1,3,5(10)}$-14β-*hydroxy*-8α-H-9β,11-d_2-D-*homoestratrienone*-17a (XIV). Ketol II[5] (300 mg) was treated with deuterium gas over 10%-Pd/$CaCO_3$ as above. After the usual treatment and recrystallization from a large volume of AcOEt, XVI was isolated; m.p. 223–225° and chromatographically pure. Mass spectrum: *m/e* 314 (d_0), 13%; *m/e* 315 (d_1), 30%; *m/e* 316 (d_2), 47%; *m/e* 317 (d_3), 10%. The mother liquor was evaporated and the residue was chromatographed on a column with Al_2O_3 (II–III act., 10 g). Elution with benzene followed by evaporation of the eluate and washing the residue with ether yielded XIV (15 mg), m.p. 160–162° and chromatographically pure. Mass spectrum: *m/e* 314 (d_0), 10%; *m/e* 315 (d_1), 27%; *m/e* 316 (d_2), 46%; *m/e* 317 (d_3), 16%.