***trans*-2-[2-(2-Pyridyl)vinyl]-4,7-dichlolofuro[2,3-*d*]pyridazine(Va) and *cis*-2-[2-Pyridyl)vinyl]-4,7-dichlorofuro[2,3-*d*]pyridazine(Vb)**——Compound(Va and Vb) were made as described above with IVa and IVb.

General Procedure for the Synthesis of 2-Aryl(or Heteryl)vinyl-4,7-dichlorofuro[2,3-*d*]pyridazine(VI—IX)——To a solution of 0.01 mole (III) and 0.01 mole (aromatic or heterocyclic aldehydes) in MeOH was added drop wise 10% Na_2CO_3 at room temperature. The precipitate was filtered off, purified by crystallization from AcOEt. These products are described in Table I.

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UDC 547.92.02.03 : 581.192 : 582.938

Studies on the Constituents of Asclepiadaceae Plants.XXIX.[1] Mass Spectra of C/D *cis* Pregnane Derivatives

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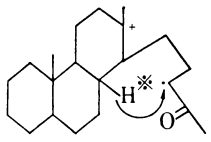
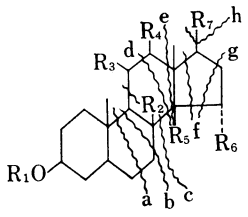
The mass spectra of various derivatives of C/D *cis* polyhydroxypregnane were examined and correlation between mass spectra and the structure was deduced. It was demonstrated that the location of a hydroxy group strongly influences the fragmentation of the skeleton of pregnane derivatives. On the basis of these experimental results, an attempt was made to interpret the mass spectra of related steroids. Tschesche[3] reported that the mass spectra of deacylkondurangogenin A (14β-hydroxy-20-keto-steroid)(X) was strongly affected by the configuration of a side chain at C-17 and giving characteristic differences in the mass spectra of such stereoisomers. The fragmentations reported are 17α-H compound: M^+-28, M^+-46, M^+-74, M^+-85, M^+-89, 17β-H compound: M^+-51, M^+-69, M^+-88, M^+-18, M^+-n·H_2O-$COCH_3$.

We examined the mass spectrum of a 17β-H compound, 3β-acetoxy-14β-hydroxy-5α, 17-isopregnan-20-one, but the spectrum indicated negligible fragment peaks of M^+-51, M^+-69, and M^+-88, while there were abundant fragment peaks of M^+-H_2O, M^+-H_2O-$COCH_3$, and M^+-H_2O-CH_3. Similarly the formation of ions *m/e* M^+-51, M^+-69, and M^+-88 could not be recognised in the mass spectrum of 3β, 11β, 12β-triacetoxy-14β-hydroxy-5α, 17-isopregnan-20-one (17β-H compound), but the peaks which should occur in the 17α-H compound, *m/e* M^+-28, M^+-44, M^+-74, and M^+-89, were detected.



I



II

Djerassi, *et al.*[4] reported that no difference was observed between the fragmentations of 17 epimers of 5α-pregnan-20-one isotopically labelled at C-8. A reasonable explanation is that the ionizations of both epimers occur through a common intermediate (I).

1) XXVIII: H. Mitsuhashi, K. Hayashi, and K. Tomimoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 828 (1970).
2) Location: *a*) Present address: *National Institute of Hygenic Sciences, Kamiyoga 1-18-1, Tokyo, 158, Japan*; *b*) *Kita-12-jo, Nishi-6-chome, Sapporo, Hokkaido, 060, Japan.*
3) T. Tschesche, P. Welzel, and H.W. Fehlhaber, *Tetrahedron*, **21**, 1797 (1965).
4) L. Tökes, R.T. La Londe, and C. Djerassi, *J. Org. Chem.*, **32**, 1020 (1967).

The mass spectra of about 30 polyhydroxypregnane derivatives were investigated (Table I), and the following plausible fragmentation mechanisms, a, b, c, d, e, f, g, and h, as shown by (II) are offered to rationalize some important peaks in the spectra.

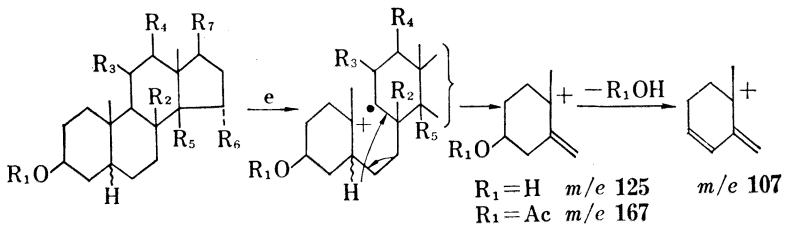
TABLE I

	R_1	R_2	R_3	R_4	R_5	R_6	R_7	Compounds
5α-H	Ac	H	H	H	H	H	α-$COCH_3$	5α-dihydropurpnigenin (I)
	Ac	H	H	H	OH	H	α-$COCH_3$	3β-acetoxy-14β-hydroxy-5α,14β,17α-pregnan-20-one (II)
	H	H	H	OH	OH	H	α-$COCH_3$	5α-dihydroramanone (III)
	Ac	H	β-Ac	Ac	H	H	α-$COCH_3$	3β,11β,12β-triacetoxy-5α,14β,17α-pregnan-20-one (IV)
	Ac	H	Ac	Ac	OH	H	α-$COCH_3$	3β,11β,12β-triacetoxy-5α,17α-pregnan-20-one (V)
	H	H	H	OH	OH	OH	β-$COCH_3$	3β,12β,14β,15α-tetrahydroxy-5α-pregnan-20-one (VI)
	H	H	H	OH	OH	OH	α-$COCH_3$	3β,12β,14β,15α-tetrahydroxy-5α-pregnan-20-one (VI)
	=O	H	H	=O	OH	OH	β-$COCH_3$	14β,15α-dihydroxy-5α-pregnane-3,12,20-trione (VII)
	H	H	H	H	OH	H	α-$CH(OH)CH_3$	3β,14β,20α-trihydroxy-5α,17α-pregnane (VIII)
	Ac	H	H	H	OH	H	α-$CH(OAc)CH_3$	3β,20-diacetoxy-14β-hydroxy-5α-pregnane (IX)
	H	H	α-OH	OH	OH	H	β-$CH(OH)CH_3$	deacylkondurangogenin A (X)[a]
	H	H	H	OH	OH	H	β-$CH(OH)CH_3$	5α-dihydroboucerin (XI)
	Ac	H	H	Ac	OH	H	β-$CH(OAc)CH_3$	5α-dihydroboucerin triacetate (XII)
	H	H	H	OH	OH	H	[β-OH, α-$CH(OH)CH_3$]	tomentogenin (XIII)
	Ac	H	H	Ac	OH	H	[β-OH, α-$CH(OAc)CH_3$]	tomentogenin triacetate (XIV)
	H	OH	H	OH	OH	H	[β-OH, α-$CH(OH)CH_3$]	5α-dihydrosarcostin (XV)
	H	H	β-H	OH	α-H	H	β-$COOCH_3$	methyl 3β,11α,12β-trihydroxy-5α-etianate[b] (XVI)
	Ac	H	β-Ac	Ac	α-H	H	β-$COCH_3$	3β,11β,12β-triacecetoxy-5α-pregnen-20-one (XVII)
	H	OH	H	OH	OH	H	[β-OH, α-$COCH_3$]	tayloron[c] (XVIII)
5β-H	Ac	H	H	H	OH	H	β-$COCH_3$	3β-acetoxy-14β-hydroxy-5β-pregnan-20-one[d] (XIX)
	Ac	H	H	H	OH	H	β-$COOCH_3$	methyl 3β-acetoxy-14β-hydroxy-5β-etianate[d] (XX)
	Ac	H	H	H		H	[$R_{5\beta}$β-O-CO-$R_{17\beta}$]	3β-acetoxy-14β-hydroxy 5β-etianic acid lactone[d] (XXI)
5β-OH	H	H	OH	H	OH	H	β- 	nigrescigenin (XXII)[d]
Δ5-	H	H	H	=O	OH	OH	β-$COCH_3$	purprogenin (XXIII)
	H	H	H	OH	OH	H	[β-OH, α-$CH(OH)CH_3$]	utendin (XXIV)
	H	OH	H	OH	OH	H	[β-OH, α-$CH(OH)CH_3$]	sarcostin (XXV)
	Ac	OH	H	Ac	OH	H	[β-OH, α-$CH(OAc)CH_3$]	sarcostin triacetate (XXVI)
	H	OH	H	OH	OH	H	[β-OH, α-$COCH_3$]	deacylmetaplexigenin (XXVII)
	H	H	OH	OH	OH	H	β-$CH(OH)CH_3$	drevogenin D[a] (XXVIII)
	H	H	OH	OH	OH	H	β-$COCH_3$	drevogenin P[a] (XXIX)
	H	H	OH	OH	OH	H	α-$COCH_3$	isodrevogenin P[a] (XXX)

R_1	R_2	R_3	R_4	R_5	R_6	R_7	Compounds
H	H	H	OH	OH	H	α-$COCH_3$	ramanone (XXXI)
H	H	H	OH	OH	H	β-$COCH_3$	isoramanone (XXXII)
H	OH	H	OH	OH	H	α-$COCH_3$	lineolon (XXXIII)
H	OH	H	OH	OH	H	β-$COCH_3$	isolineolon (XXXIV)
H	OH	OH	OH	OH	H	α-$COCH_3$	marsdenin (XXXV)
H	OH	OH	OH	OH	H	[β-OH, α-$CH(OH)CH_3$	stephanol (XXXVI)
H	OH	H	OH	OH	H	=O	sarcostin ketone (XXXVII)

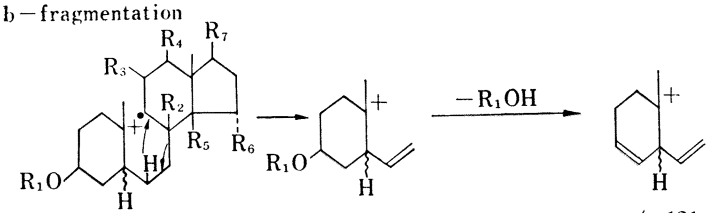
a) H.H. Sauer, Ek. Weiss, and T. Reichstein, *Helv. Chim. Acta*, **48**, 857 (1965).
b) H.H. Sauer, Ek. Weiss, and T. Reichstein, *Helv. Chim. Acta*, **49**, 1632 (1966).
c) K.A. Jaeggi, Ek. Weiss, W. Wehrli, and T. Reichstein, *Helv. Chim. Acta*, **50**, 1201 (1966).
d) U. Eppenberga, V. Vetter, and T. Reichstein, *Helv. Chim. Acta*. **49**, 1505 (1966).

a−fragmentation



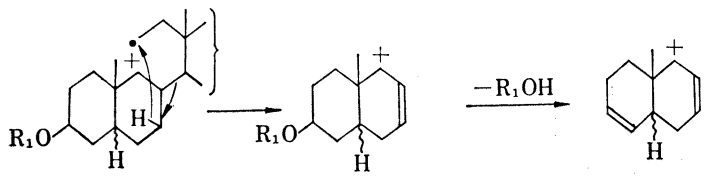
R_1=H *m/e* 125 *m/e* 107
R_1=Ac *m/e* 167

b−fragmentation

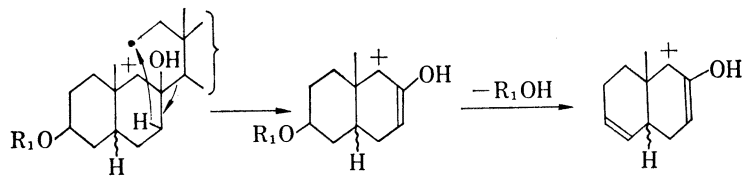


R_1=H *m/e* 139 *m/e* 121
R_1=Ac *m/e* 181

c−fragmentation



R_1=H *m/e* 165 *m/e* 147
R_1=Ac *m/e* 207



R_1=H *m/e* 181 *m/e* 163
R_1=Ac *m/e* 223

Chart 1

1) Fragmentations a,b, and c

1-i: 5H-Pregnane Derivative——The breakdown paths of 5H-polyhydroxypregnane derivatives, functional groups of which located in various positions are indicated in Chart 1, follow the pattern discussed by Djerassi, *et al.*[4,5]

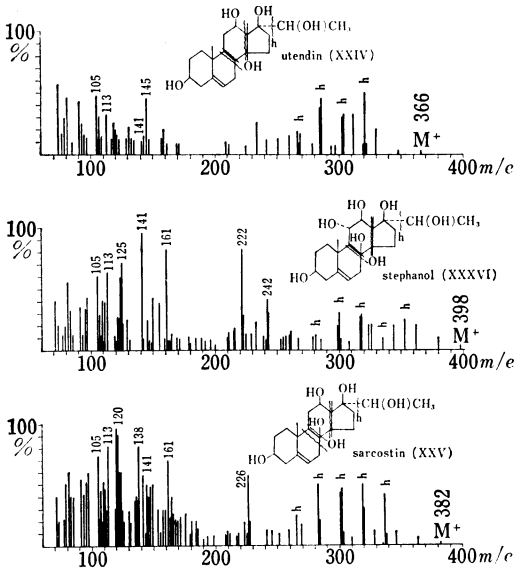


Fig. 1. Mass Spectra of Utendin, Stephanol and Sarcostin

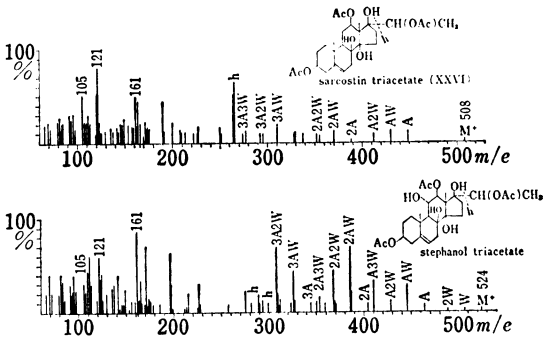


Fig. 2. Mass Spectra of Sarcostin Triacetate and Stephanol Triacetate

W=-H_2O, A=-CH_2COOH

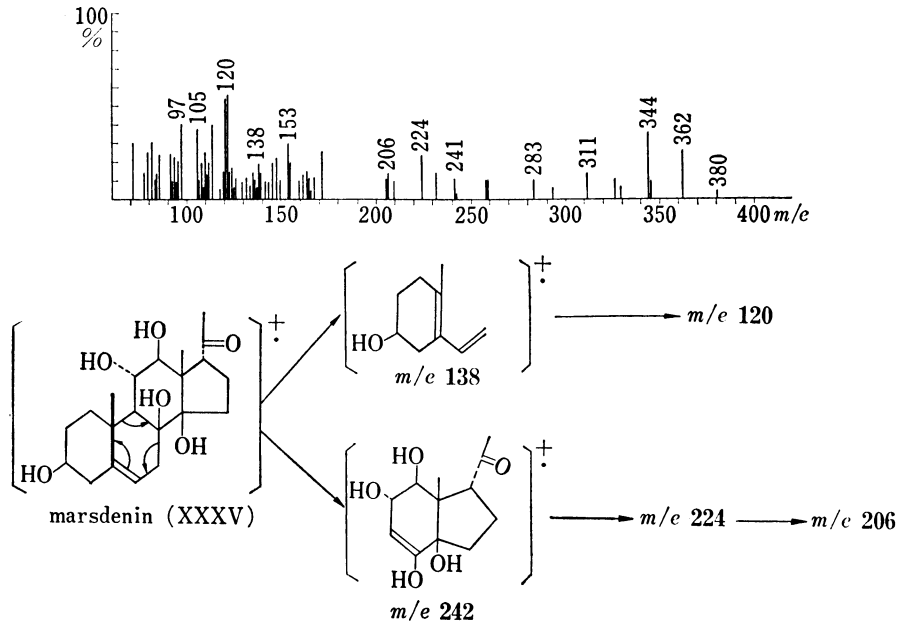


Fig. 3. Mass Specrum of Marsdenin

5) H. Budzikiewicz, C. Djerassi, and Dudley H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., 1964.

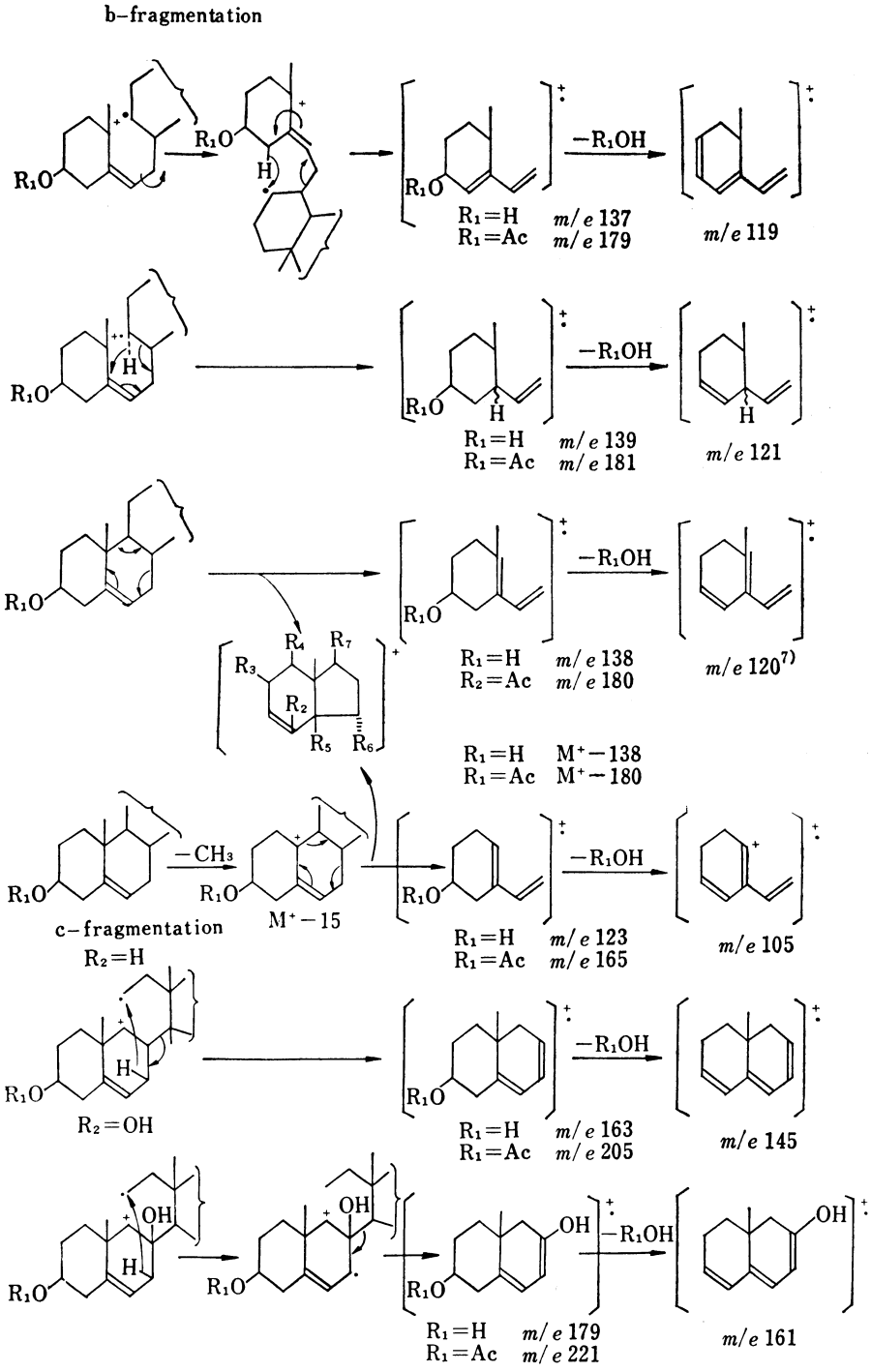


Chart 2

6) G. Galli and S. Moroni, *Steroids*, **10**, 189 (1967).

The main features of the mass spectrum of the compound which posesses R_1=H or Ac, R_{2-6}–H, OH, or OAc are the appearance of the prominent peaks at *m/e* 107 and 121. An effect of R_2 was found in the intensities of the peaks at *m/e* 147 and *m/e* 163 (Chart 1 and Table II), though the presence of fairly strong peaks at *m/e* 163 (57%) in the spectrum of tomentogenin (R_2–H) (XIII) and at *m/e* 147 (48%) of dihydrosarcostin (R_2–OH) (XV) suggest the existence of a different mechanism other than fragementation c.

1-ii: Δ^5-Pregnane Derivative——In the mass spectrum of a Δ^5-pregnane (Chart 2), such as sarcostin (XXV), the prominent peaks are *m/e* 105, 119, 120, and 121. The spectrum contains additional characteristic peaks at *m/e* 145 (R_2=H) and *m/e* 161 (R_2=OH). Intensity of the peaks of *m/e* 105 and 120 is related to the substituents R_1, R_3, and R_4. In the compound where R_3=R_4=OH, the peak at *m/e* 105 is more prominent than *m/e* 120, while in the compound with R_1=R_4=OH, the intensity of the two peaks are reversed.

As for the peaks at *m/e* 145 and *m/e* 161 which may be resulted from the fragmentation c, the former is always more intense than the latter when R_2=H (Table III), and this phenomenon is also observed in the 5α-H compounds. However, the peak at *m/e* 145 is not negligeble in the spectra of the compounds with R_2=OH. Therefore, the formation of this peak may be originate from other decomposition routes which has no relation to R_2-group.

In the case of acetylated derivative, the intensity of the peaks at *m/e* 145 (R_2–H) and 161 (R_2–OH) increased remarkably, as seen in sarcostin (XXV), stephanol (XXXVI) and their acetates (Fig. 1,2, and 3).

2) Fragmentation e

It has been observed that this fragmentation mode occurs in 11α, 12β-oxygenated pregnane (Chart 3). The first step is *cis* elimination of 11α-OR and 9α-H, then the ion decomposes further by retro-Diels-Alder fragmentation induced by 9—11 double bond.[7] It was observed that the retro-Diels-Alder fragmentation of ring B occurs predominantly in the spectrum of Δ^5-11α,12β-oxygenated pregnane.

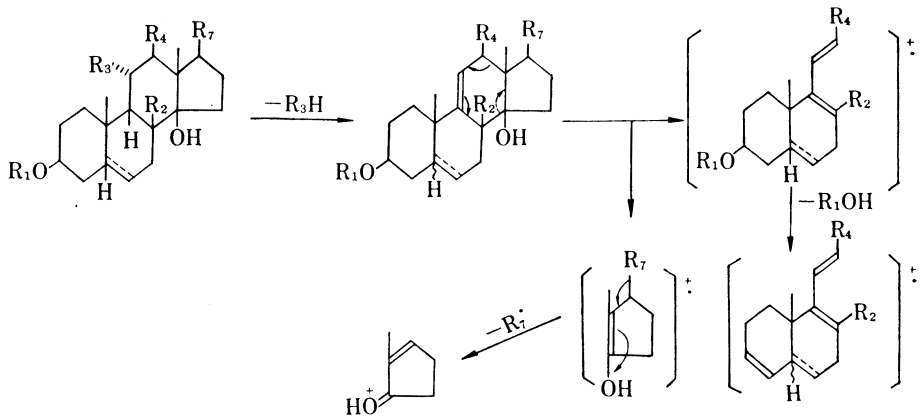


Chart 3

3) Fragmentation f (f')

The fragmentation occurs only in the case of side-chain R_7=$COCH_3$ and the fragmentation f' has been found only in the case of R_7–CH(OR)CH_3(R=H, Ac) (Chart 4). The fragmen-

7) R.I. Reed, *J. Chem. Soc.*, **1958**, 3432.

tation f is prominent in the spectra of pregnane derivatives, 3β-acetoxy-5β-H-14β-hydroxy-pregnan-20-one (XIX) (47%), isodrevogenin P (XXX) (7%), and drevogenin P (XXIX) (100%). Also the fragmentation f′ is observed in the spectrum of drevogenin D (XXVIII) (13%).

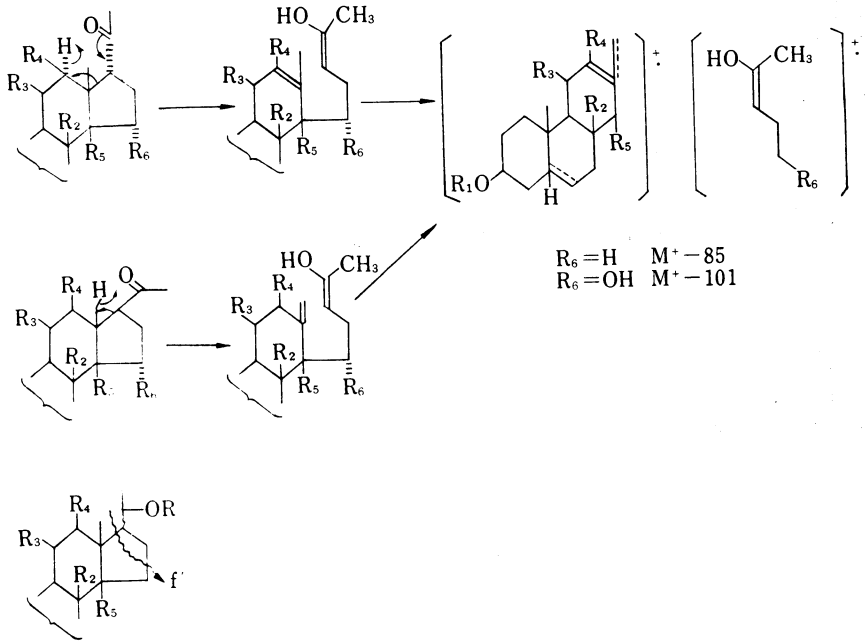


Chart 4

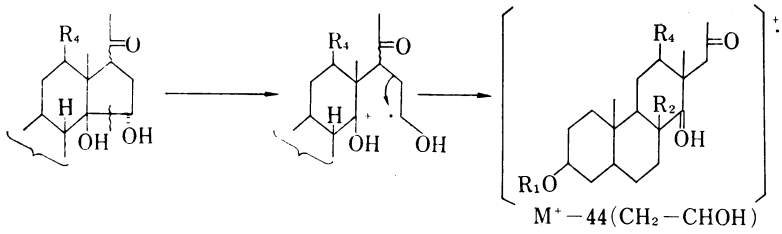


Chart 5

4) Fragmentation g

In the spectra of 14β, 15α-glycol derivatives, the fragment g is the prominent peak and occurs at *m/e* **M**$^+$-44 (Chart 5). This characteristic fragmentation is observed for example in the spectrum of purpurogenin[8] (XXIII) and 14β, 15α-dihydroxy-5α-pregnane-3,12,20-trione.[9]

8) U. Eppenberger, W. Vetter, and T. Reichstein, *Helv. Chim. Acta*, **49**, 1519 (1966).
9) M. Fukuoka, abstracted from the Ph. D. thesis, "Study of C/D *cis*-Polyhydroxypregnane Derivatives," Hokkaido University, March, 1968, p. 24.

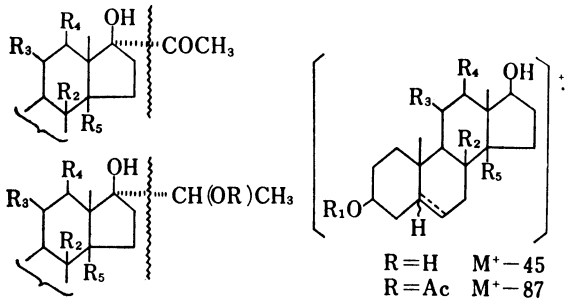


Chart 6

5) Fragmentation h

The pregnane drivatives of type $C_{(17)}\langle^{H}_{COCH_3}$ give both fragmentations f and h, but the compound with $C_{(17)}\langle^{OH}_{COCH_3}$ only fragmentation h is observed. It is interesting to note that in the spectrum of the compound of $C_{(17)}\langle^{OH}_{CH(OR)CH_3}$ the ion arising through fragmentation h is very strong (Fig. 1) (Chart 6). Tschesche[10] reported this fragmentation h in the spectrum of the compound R=C_6H_5·CO-.

Experimental

Mass spectra were measured on a Hitachi RMU-6 Mass spectrometer.

Fragmentation of 5α-H-Derivatives——The observed and calculated data of 5α-H-pregnane derivatives are listed in Table II.

C/D cis Δ^5-Polyhydroxypregnane Derivatives——The fragmentations b and c of Δ^5-derivatives are shown in Table III.

Table II

Compound *m/e* %[a]	107	121	125	139	147	163	165
Dihydrodrevogenin D[b] (XXVIII+2H)	61	34	46	7	37	13	12
Deacylkondurangogenin A[c] (X)	50	43	19	15	43	15	14
Tomentogenin (XIII)	83	75	59	30	73	57	31
Dihydrosarcostin (XV)	66	59	45	29	48	41	28
Dihydroboucerin (XI)	76	67	58	19	80	21	40
Tayloron (XVIII)	32	19	10	8	11	3	12

a) percentage to the base peak
b) (2H=5α-H-dihydro-)
c) H.H. Sauer, E.K. Weiss, and T. Reichstein, *Helv. Chim. Acta*, **48**, 857 (1965).

Table III

Compound *m/e* %	119	120	121	145	161	Fragments originated from retro D.A.
Ramanone (XXXI)	20	27	17	34	5	9 (M-139)
Isoramanone (XXXII)	12	12	10	19	6	3 (M-139)
Utendin (XXIV)	25	19	17	16	8	0
Drevogenin D (XXVIII)	26	24	21	45	11	32 (M-138)-H_2O
Drevogenin P (XXIX)	22	16	16	35	8	15 (M-138)-H_2O
Isodrevogenin P (XXX)	7	5	4	7	0	100 (M-138)-H_2O
Lineolon (XXXIII)	30	90	40	32	37	17 (M-138)-H_2O
Isolineolon (XXXIV)	18	93	27	17	18	100 (M-138)
Sarcostin (XXV)	31	79	76	54	70	57 (M-138)-H_2O
Deacyl-metaplexigenin (XXVII)	50	53	74	68	35	24 (M-139), 17 (M-139)-H_2O
Marsdenin (XXXV)	13	45	47	19	13	23 (M-138)-H_2O, 14 (M-138)-$2H_2O$
Stephanol (XXXVI)	13	8	28	50	70	0
Sarcostin ketone (XXXVII)	21	62	30	20	16	19 (M-138)-H_2O

Acknowledgment The authors are grateful to Miss Y. Imai for the measurement of the mass spectra.

10) R. Tschesche and G. Marwede, *Tetrahedron Letters*, **1967**, 1359.