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PLANT PREGNANES

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Key Word Index—Pregnanes; natural distribution; structure elucidation; stereochemistry.

Abstract—Various naturally occurring plant pregnanes have been reviewed. Different techniques used in their structure determination are described. The pregnanes isolated from plants until 1987 are compiled along with their physical and chemical data. Their biological importance is also discussed.

INTRODUCTION

Steroids are a class of naturally occurring organic substances that are of great importance in biology, medicine and chemistry. The group includes all sex hormones, adrenal cortical hormones, bile acids of vertebrates, moulting hormones of insects and many other physiologically active compounds of animal and plant origin. All steroids possess a tetracyclic carbon skeleton and differ in the number and nature of nuclear substituents and sometimes in the degree of unsaturation. According to the presence of different groups at different positions, the steroids can be divided into many sub-groups, viz. pregnanes, cardenolides [1], etc.

Cardenolides are well-known for the treatment of heart ailments and considerable work has been done on this type of compound. However, pregnanes which are the biological precursors [2, 3] of cardenolides, remained uninvestigated for a long time and detailed work was started only in the late forties. Although a few review articles on certain aspects of pregnanes [1–5] have appeared, no comprehensive review has been written. The present review deals with special structural features, spectroscopy and the biological activity of naturally occurring plant pregnanes.

Structural features of pregnanes

Pregnanes are C_{21} steroidal compounds having the usual perhydro-1,2-cyclopentanophenanthrene ring system with β-oriented angular methyl groups at C-10 and C-13 and a two-carbon atom side-chain at C-17 (**1**, Fig. 1). Usually pregnane derivative possess at 14β-configuration and bear a hydroxy group at this position. The configuration of pregnane derivatives at C-5 is usually α except for molecules containing a Δ^5-bond. Plant pregnanes also have a C-3 hydroxy group which is always β-oriented like in many other naturally occurring steroidal compounds.

Variations in the common steroidal skeleton (**1**) of pregnane derivatives from plants are also known; cyclic ethers have been reported which involve introduction of a new ring with C-20 (i.e. **2** and **3**). Hirundigenin [6] (**4**) has an unusual modified skeleton.

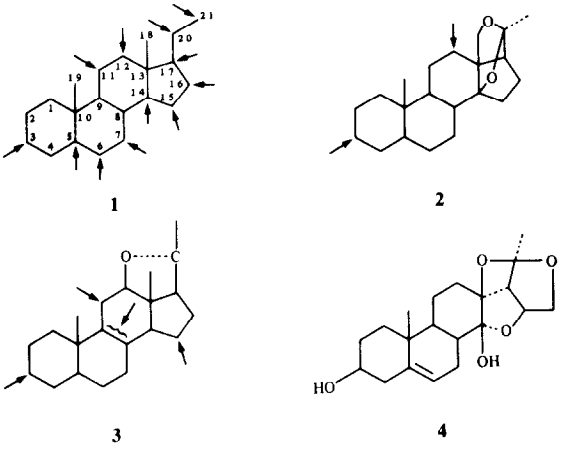


Fig. 1. Basic skeletons of pregnane derivatives.

Other characteristic features of pregnane genins reported so far may be summarized as follows: (i) Double bond at C-5 (Δ^5); (ii) fusion of rings B and C is always *trans*; (iii) fusion of rings C and D is *cis* when a hydroxy group is present at C-14 and *trans* when H is present at C-14; (iv) additional hydroxy groups at 5α, 6β, 7α, 8β, 11α. 12α, or 12β, 14β, 15α, 16α, 17α, or 17β, 20 and 21 which may be partially esterified; (v) carbonyl function at C-1, C-12, C-15 and C-20.

By analogy with known processes in animals and microorganisms, it may be assumed that in plants also,hydroxylation occurs [2] after the formation of the steroidal skeleton. This has been shown experimentally in the case of the hydroxy group at 12β. It is an interesting observation that in pregnanes of plant origin a hydroxy group at C-11 has an α-orientation while that on C-12 is β-oriented, a pattern opposite to that encountered in animal pregnanes.

Pregnane derivatives such as progesterone, aldosterone and the adrenocortical hormones occur in animals and play an important role as sex hormones. Isolation of some pregnane derivatives, viz. progesterone, pregnenolone

and a large number of highly hydroxylated C-21 steroids from plants in the early seventies aroused the interest of chemists and this was followed by a sudden burst of activity in this field.

Genins from Digitalis *genus (Digitanoles)*

The presence of the C_{21}-steroids as esters and their glycosides was demonstrated in the plant kingdom by Karrer [7]. The first compound diginin [7], was isolated in pure form from the leaves of *Digitalis purpurea* and it was for many years the only representative of this class. Subsequent work by Tschesche and Buschauer [8] on many other plants yielded other genins of this class which were named as digitanoles. They were found to occur along with cardiac glycosides. Later they were reported to occur not only in other species of *Digitalis*, e.g. *D. grandiflora* but also in the completely different genera of the Asclepiadaceae family.

The common steroidal pregnanes can be classified on the basis of the position of the oxygen function in its C_{21} moiety and, in exceptional cases, on the basis of their carbon framework, into the following four main groups.

Genins without a C-8 *hydroxy group*

A well-known compound of this class, pregnenolone (**31**), which plays an important role as an intermediate in the biogenesis of steroidal hormones in animals, was also reported from plants. Tschesche [9] isolated pregnenolone (**31**) and its 5α-H dihydro compound in very small quantities from the roots of *Xysmolobium undulatum*. The natural occurrence of reduction products of pregnenolone has also been reported. Shibata [10] isolated the 16α-hydroxy and 17α-hydroxy substituted products of the reduced compound pregn-5-ene-3β,20α-diol (**33**) from the Chinese drug Pei Wujipai prepared from plants.

Benzoyl ramanon [11] which on de-esterification gave digipurpurogenin [12] (**29**), was isolated from the roots of *Metaplexis japonica*. Its 17-hydroxy derivative, pergularin [13] (**36**), was also isolated from the twigs and leaves of the same plant. Its C-20 keto reduction product is utendin [14, 15] (**37**) which on hydrogenation of the Δ^5-double bond yields tomentogenin [16, 17] (**38**). Conversion of tomentogenin diacetate into diacetyldihydro ramanon [**19**] by the serini reaction [20], confirmed the structural relationships between these four genins. Sasaki *et al.* [21] have also isolated kidjolanin [21], the cinnamoyl ester of pergularin. Calogenin [22], (**39**) the simplest pregn-5-ene-3β, 14β, 20ε-triol has recently been isolated from *Periploca calophylla* as a glycoside and its 20-keto derivative was reported [23] earlier from *Isoplexis isabelliana*. Baucerin [24] (**40**) which is 12-hydroxy calogenin, was found in *Stapelia grandiflora*. Reichstein and co-worker [25] isolated 5α,17α pregn-3β,14β-diol-20-one (**42**) and its 17β-isomer from *Trachycolymma fimbriatum*. Kasai *et al.* [26] have recently isolated 21-OMe-pregn-5-ene, 3β,14β,17β,21-tetrol-20-one (**41**), which has a C-17 dihydroxyacetone side chain, from *Periploca sepium*. Recently Seto *et al.* [27, 28] have reported five new pregnanes from *Marsdenia tomentosa*, and named them as tomentodin, tomentonin dehydrotomentosin deacyldehydrotomentodin and 12-*O*-acetyl tomentogenin. A novel pregnane, bregenin was reported by Khare *et al.* [29] from *Sarcostemma brevistigma*. A new acylated pregnane named cynafogenin [18] was isolated from *Cynanchum africanum*.

Genins with a C-8 *hydroxy group*

The first compound of this group, sarcostin (**44**) was obtained from *Sarcostemma australe* by Cornforth and Earl [30]. Its 12-*O*-cinnamoyl ester, penupogenin, was isolated from *Cynanchum caudatum* [31]. 12,20-Di-*O*-cinnamoyl sarcostin [32] was reported from *Periploca calophylla*. Glycopenu-pogenin and its 20-acetyl derivative were also isolated from *Cynanchum caudatum* [33] and *Marsdenia tomentosa* [34], respectively.

Mitsuhashi and co-workers reported various acyl derivatives of sarcostin from different plants, e.g. gagiminin from *Cynanchum caudatum* [35] and SG-A [12β-*O*-(2-methylbutyryl) 20-acetyl sarcostin], SG-B [20-*O*-(2-methylbutyryl) sarcostin], SG-C (20-*O*-tigloylsarcostin) and dihydrogagiminin from *Stephanotis japonica* [36].

Two new acylated sarcostin derivatives, Kidjoladinin (12β-*O*-tigloyl-20-*O*-acetyl sarcostin) and deacetyl kidjoladinin (12β-*O*-tigloyl sarcostin), were reported from *Marsdenia tomentosa* [34]. Tayloron (**45**) was obtained [37] from *Gongronema taylorri* along with 5α-H dihydrosarcostin (**46**) [38] which is formed by sodium borohydride reduction of tayloron. Metaplexigenin [39–41] and its deacylderivative (**1**) [42] were isolated from *Metaplexis japonica*. The latter compound was also found in *Cynanchum caudatum* and its sodium borohydride reduction gave sarcostin (**44**). Serini reaction of sarcostin acetate followed by deacetylation gave lineolon (**2**) [43] which was also isolated from *Pachycarpus lineolatus*. Mitsuhashi *et al.* [40, 44, 45] isolated its 17β-isomer, isolineolon (**3**) and its 12-benzoyl [41] derivative was also obtained from the same plant whereas its C-12 ester with Δ^2 3,4-dimethyl pentanoic acid, named as cynanchogenin, was reported by Mitsuhashi [39] in *Cynanchum caudatum*. Mitsuhashi *et al.* [46] isolated fukujusone which is 12-*O*-nicotinoylisolineolon, from *Adonis amurensis*. Gagaimol (**4**) [47], a 7-oxygenated pregnane, and its three polyoxyderivatives, dibenzoylgagaimol [48], gagaimol-7-methyl ether (**5**) [48] and 7β-methoxysarcostin (**6**) [48] were isolated from the roots of *Metaplexis japonica* and they are the first examples of polyoxypregnane derivatives having an oxygen function at the 7-position. Reichstein *et al.* [49] isolated from *Sarcostemma vinimale* 12,21-di-*O*-benzoylviminolone (**7**) which has a dihydroxyacetone C-17 side chain. A new pregnane sarcogenin and its 11-*O*-benzoyl derivative were isolated from *Sarcostemma brevistigma* by Khare *et al.* [50, 51]. Recently a novel pregnane having a C-15 hydroxy group (orgogenin) was also isolated from *Orthenthera viminea* by Khare *et al.* [52].

Genins with a glycol group

Reichstein *et al.* [53–55] isolated drevogenin A, B, D (**9**) and P (**8**) from *Dregea volubilis* and drevogenin Q was isolated by Khare *et al.* [56] from *Marsdenia tenacissima*. Drevogenin P is the basic skeleton of all these genins and all of them contain a vicinal diol group at C-11α and C-12β. Drevogenin A is 11-*O*-isovaleryl-12-*O*-acetyl drevogenin P. Drevogenin B is deisovaleryl drevogenin A. These genins have a C-17β oriented methyl keto chain which undergoes isomerisation at C-17 with acid and alkali. 12,20-Di-*O*-benzoyl drevogenin D was isolated as

a glycoside by Khare *et al.* [57] from *Periploca calophylla* whereas tenasogenin and cissogenin were isolated from *Marsdenia tenacissima* [58, 59]. Tschesche [60, 61] isolated kondurangogenin by very careful acid hydrolysis of the glycosides from *Marsdenia condurango* and showed it to be 11-*O*-cinnamoyl 5α-dihydrodrevogenin P. Marsdenin (**11**) which is 8-hydroxydrevogenin P and its C-20 keto reduction product named as marsectohexol (**12**) were isolated by Reichstein [62] from *Marsdenia erecta*. Glycocynanchogenin (**13**) and glycocaudatin (**14**) containing the 12-*O*-ikemoyl group have a glycol arrangement at C-5 and C-6. These compounds were isolated by Mitsuhashi [63, 64] from *Cynanchum caudatum*. Stephanol (**16**), which is 17β-hydroxymarsectohexol has been reported by Fukuoka and Mitsuhashi [65, 66] in *Stephanotis japonica*. Glycosarcostin (**15**), another genin with a glycol arrangement at C-5 and C-6 was reported in *Cynanchum caudatum*, is dihydroxydihydrosarcostin [67]. Its 12,20-di-*O*-cinnamoyl derivative was isolated by Khare *et al.* [68] from *Orthenthera viminea*.

Unusual genins

Unlike the other genins of the Asclepiadaceae family stapelogenin (**18**), isolated [69, 70] from *Stapelia gigentia*, has an unusual C-21 skeleton in that C-18 and C-14 are attached to C-20 by an ether linkage. It contains the usual Δ^5-double bond and two β-oriented hydroxy groups at C-3 and C-14. Another example of an unusual genin is hirundigenin (**22**) isolated from *Vincetoxicum hirundinaria* by Reichstein *et al.* [6] which has a tetrahydrofuran unit as the D-ring and C-16 and C-18 are joined to C-20 through a five-membered cyclic ether linkage. Cellobioside (**20**), a novel glycoside isolated from safflower, has an unusual distribution of oxygen functions in its genin moiety [71]. The genin has a Δ^4-3-keto chromophore and an α-oriented hydroxy group at C-15 instead of the C-14 hydroxyl group commonly found in other pregnanes. The glycosidation is at the C-20 hydroxy group, which is also unusal. Asctuberogenin (**19**) has a structural resemblance to 5α-dihydrodiginigenin [1] except that the C-11 keto group is absent and there is a hydroxy group at C-8 or C-9. Flavascin (**17**) is unique in as much as it has a C-1 keto group [72]. Stephanthraniline C (**21**) isolated from the aerial parts of *Stephanotis japonica* by Mitsuhashi [73, 74], has a rare arrangement of hydroxy groups at C-3, C-8, C-14, C-15, C-16 and C-18, where C-18 is esterified.

Characterization of pregnane derivatives

About sixty pregnanes have been isolated from plants so far. No diagnostic tests or reactions for their identification, are yet known. Colour tests with non-specific reagents (chloroformic $SbCl_3$ and 50% H_2SO_4) although used widely for their detection, are not reliable. There are some well-known reagents which are used for the characterization of pregnanes, Liebermann–Burchardt for steroids [75], $NaIO_4$ for vicinal diol system [76], $NaBH_4$ for carbonyl function [77], NaOMe for ester group [32] and tetranitromethane for a double bond [78, 79].

In recent years physico-chemical and spectroscopic methods IR, ^{1}H NMR, ^{13}C NMR [80], UV and mass spectrometry have proved to be indispensable as they generally require micro quantities of the substances.

IR Spectroscopy of pregnanes

The principal value of IR spectroscopy in structural elucidation of pregnanes lies in the detection of a ketomethyl group at C-17 of the basic skeleton. The other groups which could be detected satisfactorily are hydroxyl [81], methyl and unsaturation. Pregnanes having keto methyl group exhibit carbonyl stretching vibration at 1670 cm^{-1} the methyl deformation band appears at 1360 cm^{-1}, and the stretching vibration of the OH groups is seen at 3350 cm^{-1}. Absorption bands for the trisubstituted Δ^5-double bond appear at 800 cm^{-1}. The ester group in pregnanes is revealed by a strong absorption band in the carbonyl stretching region at 1720 cm^{-1} and the complementary signal for the aliphatic and aromatic regions according to the nature of the ester group.

^{1}H NMR spectroscopy

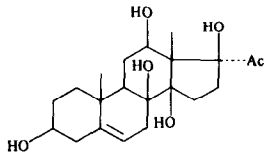
In recent years the introduction of NMR spectroscopy has provided a very reliable tool for structure determination. With the help of high frequency ^{1}H NMR spectroscopy it is possible to pinpoint the position of functional groups in the pregnane moiety. ^{1}H NMR spectra of pregnanes usually contain two singlets of three proton each in the region δ0.8–1.5 for two tertiary angular methyl groups present at C-10 and C-13. Two different types of pregnanes containing either a hydroxyethyl or an acetyl group at C-17 can be distinguished easily by the presence of a doublet (6–8 Hz) of three protons around δ1.0 or a singlet of three protons at δ2.1, respectively. The prominent signal for the Δ^5 vinylic proton appears as a multiplet at δ5.3–5.5. The signals for the methylene protons of pregnane appear as multiplets in the region δ1.5–2.5. The signal of a methine proton of a hydroxylated carbon gives its expected signal in the region δ3.0–4.0. The methine protons deshielded by esters of benzoic [57], cinnamic [32], valeric, isovaleric, tiglic [36], nicotinic [46] ikemic [63, 64] or anthranilic acids appear 1 ppm downfield to their corresponding hydroxy precursor. The positions of ester functions in the pregnane moiety can be established by double resonance experiments. The number of hydroxy groups could be fixed by the addition of TAI reagent or by D_2O exchange.

Mass spectrometry of pregnanes

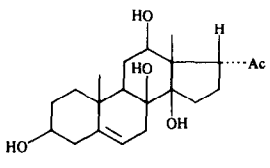
Mass spectrometry has proved to be a useful tool for assigning the position of the substituent groups in various derivatives of *cis*-C/D-polyhydroxy pregnanes. It was demonstrated that the fragmentation of pregnane derivatives was strongly influenced by the location of hydroxy group. Mitsuhashi *et al.* [82] also deduced a correlation between the structure and fragmentation pattern of pregnanes which was very helpful in the elucidation of their structures. Some representative fragmentation routes are presented in Scheme 1.

(a). Pregnanes having a 3-OR-Δ^5 system (R=H or acyl) undergo retro-Diels–Alder fission followed by elimination of ROH and Me radical to give prominent peaks. Similarly, retro-Diels–Alder cleavage is observed in 11-OR pregnanes (R=H or acyl) after elimination of the oxygen function as ROH.

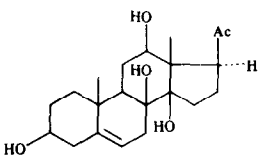
(b). Tschesche *et al.* [83] found that 14β-hydroxy pregnanes having 20-keto 17β-side chain undergo D-ring



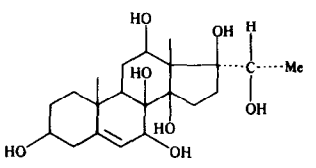
Deacylmetaplexigenin **1**
222–225° [+ 41.3 MeOH]



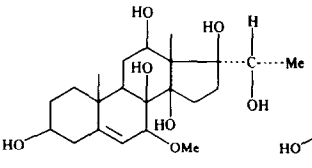
Lineolon **2**
233–239° [+ 13 MeOH]



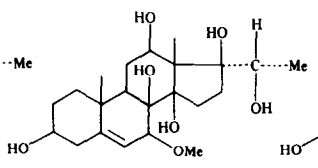
Isolineolon **3**
248–250° [+ 88.8 MeOH]



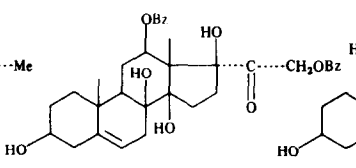
Gagaimol **4**
274–227°



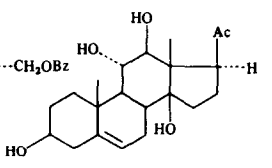
Gagaimol - 7 - methyl ether **5**
153 / 239° [- 30 MeOH]



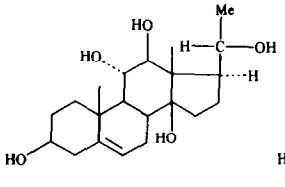
7β- Methoxysarcostin **6**
210–218° [+ 44 MeOH]



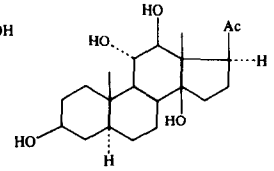
DI - *O* - benzoyl viminolone amorph **7**
[- 53 MeOH]



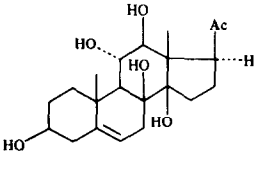
Drevogenin - P **8**
122–130° / 210 – 214° or 185–190° [-34.4 MeOH]



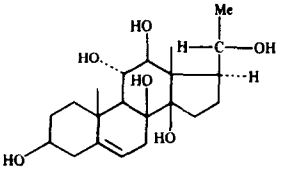
Drevogenin - D **9**
227–230° [- 10.2 MeOH]



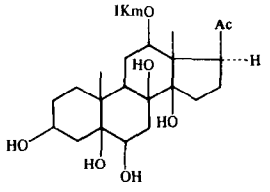
Deacyl kondurangogenin A **10**
164–170° / 195 - 200°



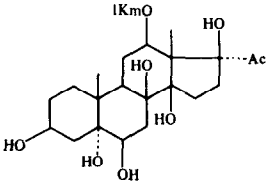
Marsdenin **11**
220–224° [+ 81.6 MeOH]



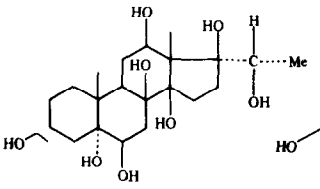
Marsectohexol **12**
312–315° [+ 47.4 pyridine]



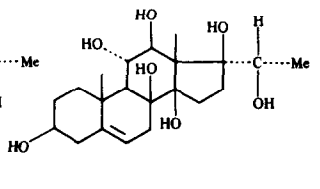
Glycocynanchogenin **13**
267–277° [- 41.5 MeOH]



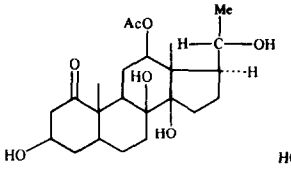
Glycocaudatin **14**
286–293° [- 22.3 MeOH]



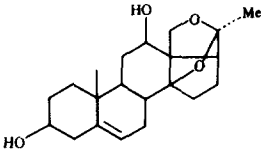
Glycosarcostin **15**
268–275° [+ 24.3 MeOH]



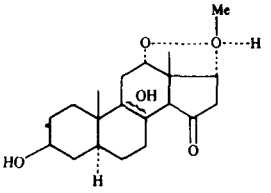
Stephanol **16**
222.5 - 225° [+ 37.3 MeOH]



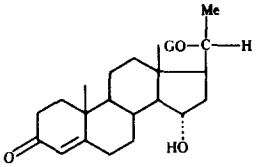
Flavescin **17**
252–254 [+ 121 MeOH]



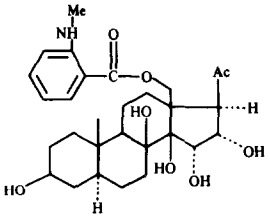
Stapelogenin **18**
295–300° [- 45.7 MeOH]



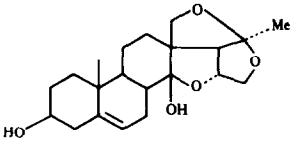
Asctuberogenin **19**



Cellobioside **20**



Stephanthraniline amorph **21**
[+ 4.2 $CHCl_3$]



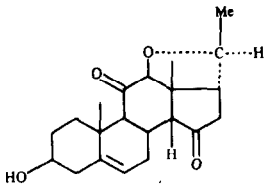
Hirundigenin **22**
190–195° [- 44.8 $CHCl_3$]

Bz: Benzoyl
IKm: Ikomyl
G: Sugar
Ac: Acetyl

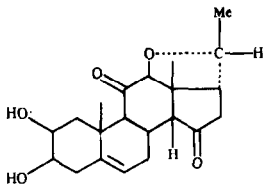
cleavage with the loss of an ethylene molecule. The fragmentation is highly stereoselective and is independent of the presence or absence of other functional groups in the molecule. Compounds with a 17α-side chain do not show this fragmentation.

ORD

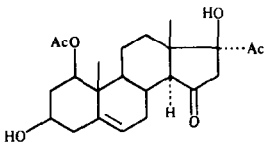
The stereochemistry at C-20 of pregnanes having a –CHOH–Me side-chain baffled chemists for a long time until Nagai [84] reported that 20-*O*-*ortho*-nitrobenzoates show a Cotton effect at *ca* 330 nm due to $n \rightarrow \pi^*$ transition



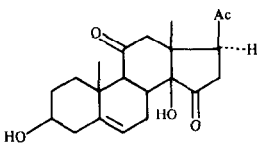
Digitigenin **23**
115°[· 226 Me_2CO]



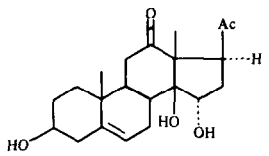
Digifologenin **24**
110–115°[· 270 Me_2CO]



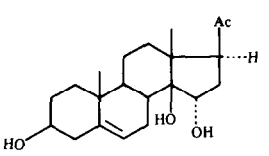
Digacetigenin **25**
166–170°



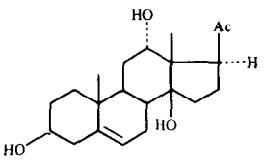
γ-Digiprogenin **26**
250–253°[· 72.5]



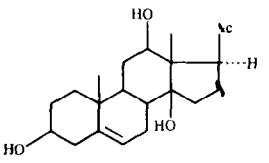
Purprogenin **27**
249–252°[+ 60 MeOH]



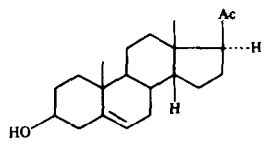
Purpnigenin **28**
239–243°[+ 21.1 MeOH]



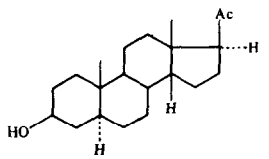
Digipurpurogenin-I **29**
165–175°[+ 51 $CHCl_3$]



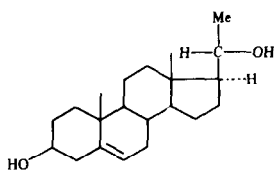
Digipurpurogenin-II **30**
226–234°[+ 40 MeOH]



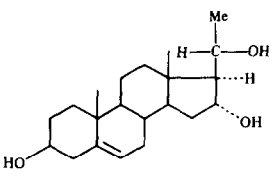
Pregnenolone **31**
186–192°[+ 25]



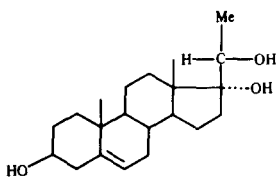
5α-Pregnanolone **32**
195–198°[+ 93]



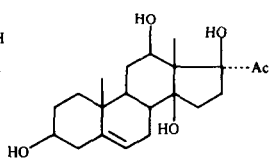
Pregn-5-ene-3β·20α-diol **33**
182°[· 55.5 $CHCl_3$]



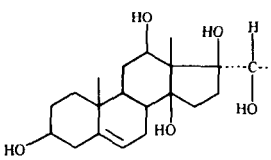
Pregn-5-ene-3β.16α,20α-triol **34**
251°[· 65.0 C_2H_5OH]



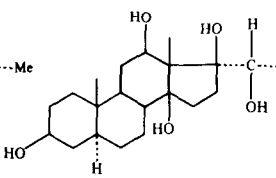
Pregn-5-ene 3β, 17α,20α triol **35**
230°[· 69.2 C_2H_5OH]



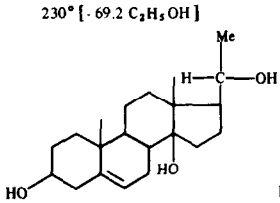
Pergularin **36**
220–234°[· 33 MeOH]



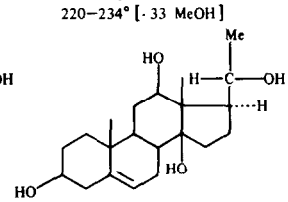
Utendin **37**
247–251°[+ 9.6 MeOH]



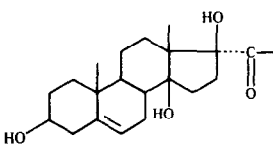
Tomentogenin **38**
256.5–259.5°[+ 40 MeOH]



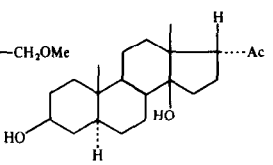
Calogenin **39**
202°[· 205]



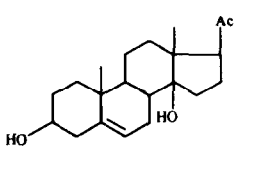
Baucerin **40**
239–247°[+3.7 MeOH]



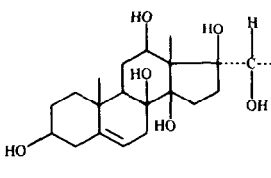
21-OMe-pregn-5-ene-3β, 14β, 17β, triol-20-one **41**
239°[· 46.5 $CHCl_3$]



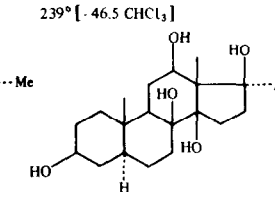
5α, 17α-pregnane-3β,14β diol-20-one **42**
218–222°[· 47.2 Me_2CO]



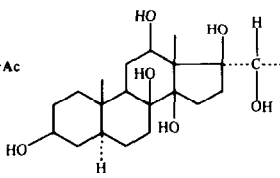
3β, 14β,Dihydroxy-pregn-5-ene-20-one **43**
190–218°[+ 12 MeOH]



Sarcostin **44**
150 / 260–283°[+ 67 MeOH]

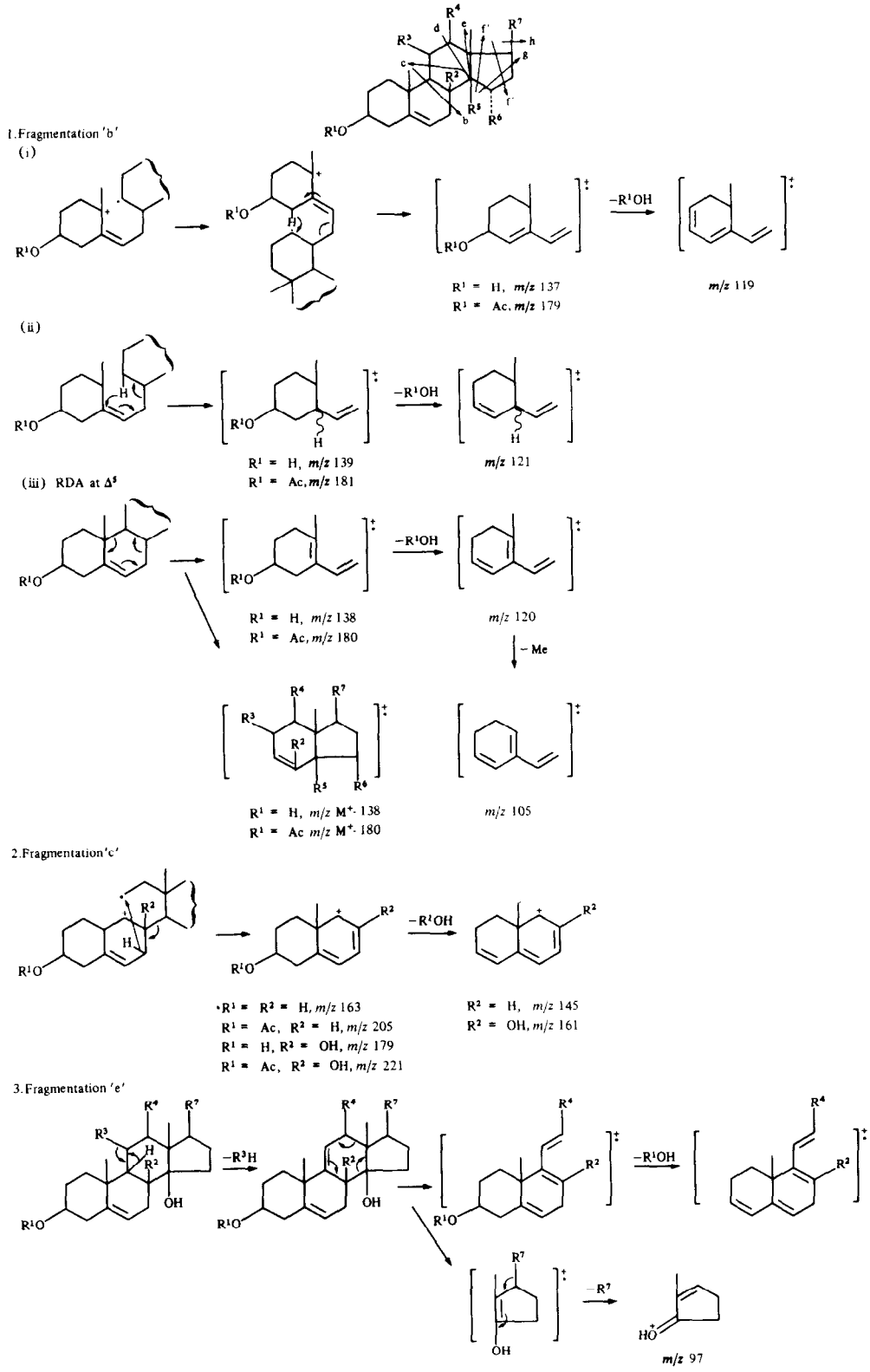


Tayloron **45**
195–200°[+ 40.6 MeOH]

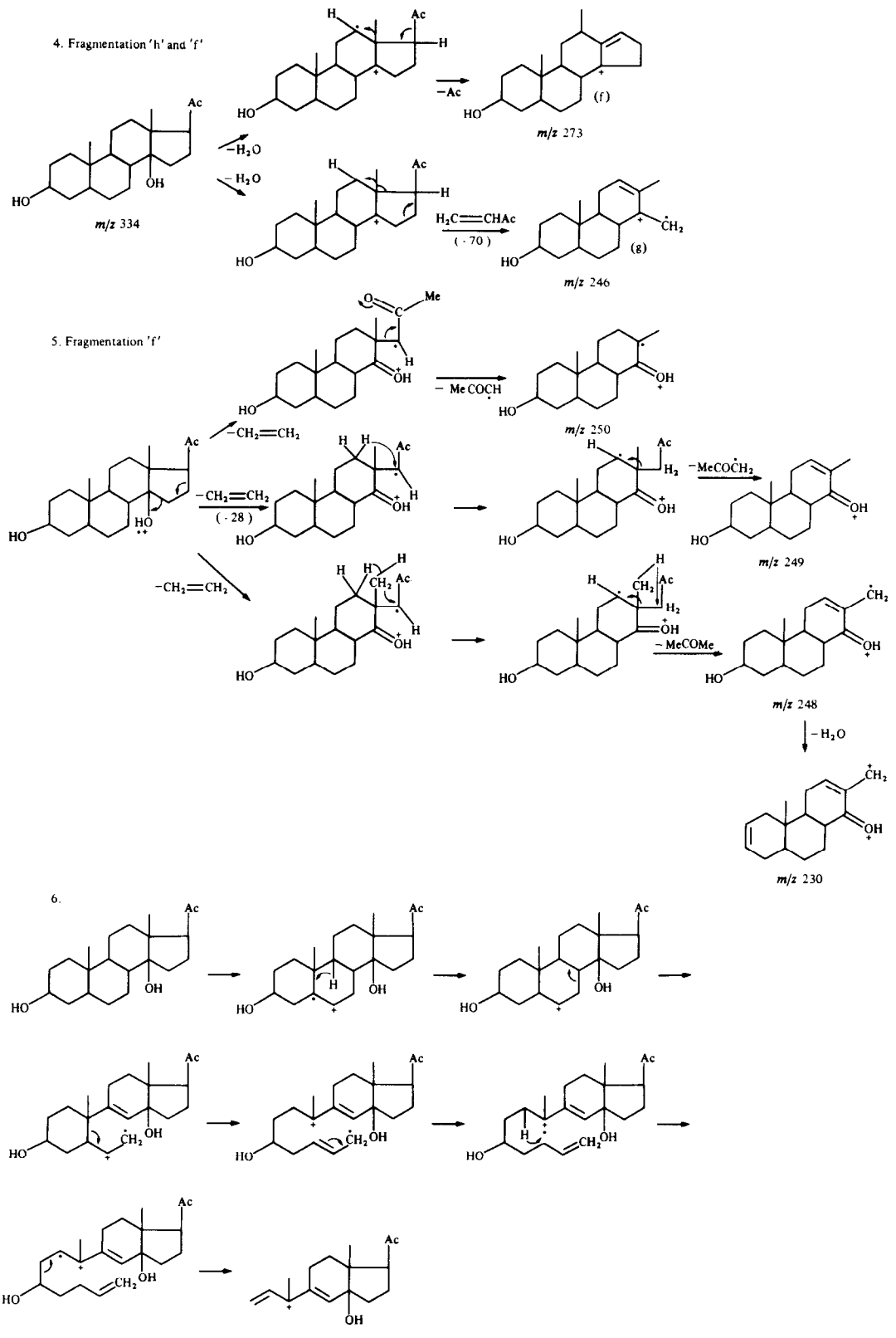


5α-Dihydrosarcostin **46**
269–272°[+ 51.7 MeOH]

of the aromatic nitro group. The effect is negative in the case of 20-*O-ortho*-nitrobenzoates with the *R*-configuration and positive for those with the *S*-configuration. It has been reported that polar functional groups present around the *ortho*-nitrobenzoyl group, e.g. 17-OH, strongly influence this effect. This property has been used to assign the absolute configuration of the C-20 carbinol group in sarcostin, utendin and tomentogenin [81].


1.Fragmentation 'b'
(i)
R^1 = H, *m/z* 137
R^1 = Ac, *m/z* 179
m/z 119
(ii)
R^1 = H, *m/z* 139
R^1 = Ac, *m/z* 181
m/z 121
(iii) RDA at Δ^5
R^1 = H, *m/z* 138
R^1 = Ac, *m/z* 180
m/z 120
– Me
R^1 = H, *m/z* $M^{+\cdot}$ 138
R^1 = Ac *m/z* $M^{+\cdot}$ 180
m/z 105
2.Fragmentation 'c'
R^1 = R^2 = H, *m/z* 163
R^1 = Ac, R^2 = H, *m/z* 205
R^1 = H, R^2 = OH, *m/z* 179
R^1 = Ac, R^2 = OH, *m/z* 221
R^2 = H, *m/z* 145
R^2 = OH, *m/z* 161
3.Fragmentation 'e'
m/z 97

Scheme 1.


4. Fragmentation 'h' and 'f'
m/z 334
m/z 273
m/z 246
5. Fragmentation 'f'
m/z 250
m/z 249
m/z 248
m/z 230
6.

Scheme 1.

A characteristic feature of a 17-keto methyl pregnane in the absence of any other substituent at C-17 but a C-14 β-hydroxyl group, is their property of undergoing α/β-isomerisation in acid or alkali conditions to give predominantly the more stable 17α-side chain. It is further reported that when C-17 has a substituent group this is always a β-hydroxyl group resulting in an α-configuration of the C-17 side-chain. Their orientation has been unambiguously determined from their Cotton effect in ORD, e.g. the 17β-keto methyl side-chain shows a positive effect whereas the 17α-side chain shows a negative effect.

UV spectroscopy

The absence of a conjugated system in pregnanes has limited the use of UV spectroscopy in this field. However, the technique has proved valuable in the study of pregnane esters containing α, β unsaturated and/or aromatic acids. UV spectroscopy has also been used [85] for determining the number of ester groups in the pregnane moiety and is proving useful in ascertaining the stereochemistry [86, 87] of pregnanes by formation of their derivatives.

BIOLOGICAL ACTIVITY

Pregnane ester glycosides closely resemble cardiac glycosides which are important in medicinal chemistry [8] due to their digitalis-like effect on cardiac muscles and their application in the therapy of auricular fibrillation and in many types of congestive heart failure. Biogenetic studies have revealed that pregnane derivatives are biological precursors [2] of cardiac butenolides and therefore these substances can be isolated from plants only in very small quantities. Moreover, using modern pharmacological methods only a few of these compounds have shown specific biological activity.

Condurango glycosides Ao & Co from the bark of *Marsdenia condurango* have been used as aromatic bitter stomachics in popular medicine and also against cancer or syphilis in folk remedies. According to the reports on the anti-tumour screening by CCNSC the extract of this plant was evaluated for failure against Sarcoma-180, Adenocarcinoma 755, human sarcoma HS-1 and KB system [88]. Ahsan [86] reported that the polyoxy pregnane glycoside amplexoeside A, from an Asclepiadaceae plant *Asclepias amplexcicaulis*, showed a cancer inhibitory activity in the KB assay. Generally Asclepiadaceae plants are abundant in esterified polyoxy pregnane glycosides which therefore promise a source of antitumour agents [88]. Seven new glycosides were isolated from *Dregea volubilis* [87] out of which Ap_1 and Ao_1 showed activity against tumour (Ehrlich carcinoma). *Dregea volubilis* also showed activity against melanoma B-16 [87] and pregnane glycosides C_GAo, C_GCo, C_GBo, C_GDo, 20-*O*-methyl C_GDo and 20-iso-*O* methyl-C_GDo from *Marsdenia condurango* were found to be active against Ehrlich ascites carcinoma *in vitro* [89].

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