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# Saponin and Sapogenol. XVIII.[1] 11-O-Arabinopyranosyl-metagenin and 11-O-Arabinopyranosyl-3-epi-metagenin from the Epigeous Part of *Metanarthecium luteo-viride* Maxim.

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Two arabinosides (designated as YM-I and YM-IV) were isolated along with their monoacetyl derivatives (YM-II and YM-III) from the less polar glycoside portion of the total glycoside mixture which was isolated from the epigeous part of *Metanarthecium luteo-viride* Maxim. (Liliaceae).

On the basis of chemical and physicochemical evidence including the synthesis of YM-IV pentaacetate (**4b**) from metagenin (**6**), the structure of YM-I has been elucidated to be 11-O-α-L-arabinopyranosyl-3-epi-metagenin (**3**), while the structure of YM-IV has been established as 11-O-α-L-arabinopyranosyl-metagenin (**4**).

By use of the soil bacterial hydrolysis method,[3] we have elucidated the structures of two new type prosapogenols: 2-O-acetyl-11-O-(2′,3′,4′-tri-O-acetyl-α-L-arabinopyranosyl)-3-epi-metagenin (**1**)[4] and 11-O-galactopyranosyl-nogiragenin (**2**),[5] which are characterized by having an O-glycoside moiety attached at C-11 of the steroidal aglycones. The total glycoside mixtures containing the parent saponins of **1** and **2** were respectively isolated from the epigeous and subterranean parts of *Metanarthecium luteo-viride* Maxim. (Japanese name: nogiran, Liliaceae). In a continuing study, we have attempted to isolate the parent saponin of **1** from the total glycoside mixture (=BEC[4]) of the epigeous part of the above plant and during the course of the study, we have isolated two arabinosides in addition to their monoacetyl derivatives, all of which are closely related to **1**. This paper provides detailed evidence which is consistent with the assignment of these two arabinosides as 11-O-α-L-arabinopyranosyl-3-epi-metagenin (**3**) and 11-O-α-L-arabinopyranosyl-metagenin (**4**), respectively.

Silica gel column chromatography of the glycoside mixture (BEC[4]) has led to the isolation of four glycosides (designated as YM-I, YM-II, YM-III, and YM-IV) from the less polar glycoside portion. YM-I (**3**), mp 300—303°, possesses hydroxyls and is a derivative of 25R spirostane as shown by its infrared (IR) spectrum. On acid hydrolysis, YM-I gave 3-epi-metagenin (**5**) and L-arabinose. Direct comparison (mixed mp, thin-layer chromatography (TLC), and IR) of YM-I with a desacetyl derivative of **1**[4] has demonstrated that YM-I is 11-O-α-L-arabinopyranosyl-3-epi-metagenin (**3**).

On the basis of the spectral properties and alkaline hydrolysis (see experimetal), YM-II and YM-III are presumed to be monoacetyl derivatives of YM-I (**3**) and YM-IV (**4**). However, the location of their acetyl groups has not yet been defined due to shortage of the material.

YM-IV (**4**), mp 297—300°, is also a derivative of 25R spirostane as shown by its IR spectrum. On acid hydrolysis, YM-IV furnished metagenin (**6**) and L-arabinose. Complete methylation of YM-IV with methyl iodide ($CH_3I$)–sodium hydride (NaH)–dimethyl sulfoxide (DMSO)[6] yielded a pentamethyl ether (**4a**) which, on acid treatment, was hydrolysed to a

1) Part XVII: I. Kitagawa, Y. Ikenishi, M. Yoshikawa, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **24**, 2470 (1976).
2) Location: *133-1, Yamada-kami, Suita, Osaka, 565, Japan.*
3) I. Yosioka, M. Fujio, M. Osamura, and I. Kitagawa, *Tetrahedron Letters*, **1966**, 6303.
4) I. Yosioka, K. Imai, Y. Morii, and I. Kitagawa, *Tetrahedron*, **30**, 2283 (1974).
5) I. Yosioka, Y. Morii, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **21**, 2092 (1973).
6) S. Hakomori, *J. Biochem.* (Tokyo), **55**, 205 (1964).

dimethyl ether of metagenin (**6a**). On oxidation with chromium trioxide–pyridine, the dimethyl ether (**6a**) was converted to a dimethyl ether ketone (**7**) which has been assigned as possessing a carbonyl function at C-11 of the spirostane skeleton on the basis of the molecular amplitude (A=+25.7) of its optical rotatory dispersion (ORD) curve[7] and the molar ellipticity ($[\theta]_{305}$ +1541) of its circular dichroism (CD) spectrum. Therefore, the dimethyl ether is considered to be 2,3-di-O-methyl-metagenin (**6a**).

The structure **6a** has been further substantiated by the following unambiguous derivation from metagenin (**6**). Thus, treatment of **6** with dry acetone–anhydrous cupric sulfate gave

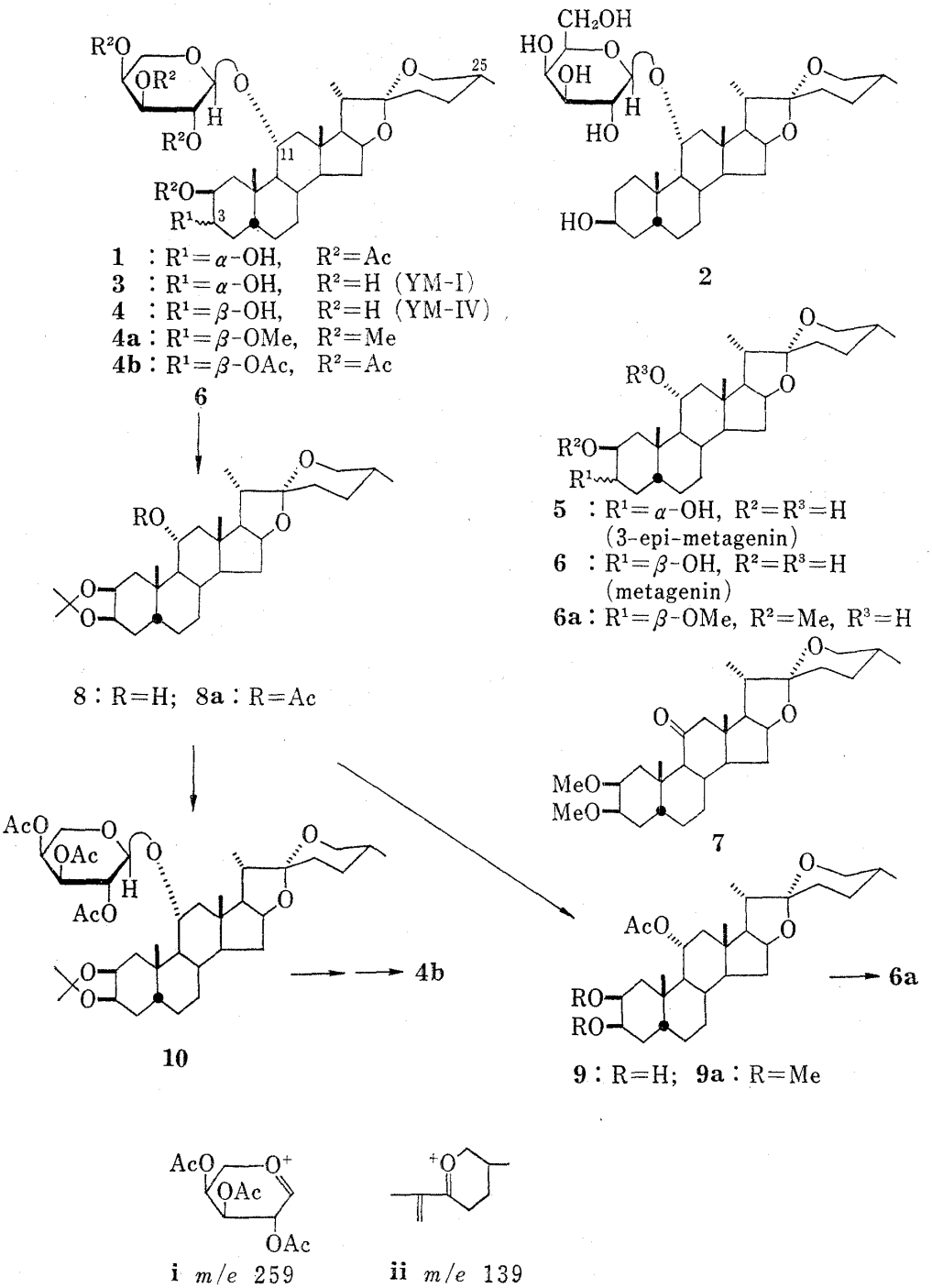


Chart 1

7) K. Takeda and H. Minato, *Steroids*, **1**, 345 (1963).

metagenin acetonide (**8**)[8] which was then converted to a monoacetonide acetate (**8**) by ordinary acetylation with acetic anhydride and pyridine. Removal of the acetonide protecting group of **8a** by treatment with 50% aqueous acetic acid gave 11-O-acetyl-metagenin (**9**), which was methylated with $CH_3I$ and silver oxide.[9] The acetoxyl group at C-11 remained intact during the methylation, and the resulting 2,3-di-O-methyl-11-O-acetyl-metagenin (**9a**) was then treated with alkali to furnish 2,3-di-O-methyl-metagenin (**6a**) which was found to be identical (TLC and IR) to the dimethyl ether obtained from YM-IV. Therefore, the structure of YM-IV has been elucidated to be 11-O-L-arabinosyl-metagenin.

As for the structure of the arabinoside portion in YM-IV, the following proton magnetic resonance (PMR) examination of YM-IV pentaacetate (**4b**) has been conclusive. Acetylation of YM-IV with acetic anhydride and pyridine gave **4b** which possesses no free hydroxyl (IR). The PMR spectrum of **4b** shows a doublet ($J$=8 Hz)[10] at $\delta$ 4.44 which is assignable to the anomeric proton, and therefore the arabinoside moiety in YM-IV has been assigned as being attached at 11α–OH of metagenin with the α anomeric configuration (Cl form). Furthermore, a detailed PMR study including decoupling experiments of **4b** and comparison with the PMR spectrum of **1**[4] (Table I) has revealed that the structure of YM-IV is now assigned as 11-O-α-L-arabinopyranosyl–metagenin (**4**).

Table I. Comparison of the PMR Data of **1** and **4b**[a] (taken in $CDCl_3$, $\delta$ Values at 100 MHz, $J$ Values in Hz)

| | 10-C<u>H</u>$_3$ | 13-C<u>H</u>$_3$ | 20-C<u>H</u>$_3$ | 25-C<u>H</u>$_3$ | OAc | >C<u>H</u>OAc |
|---|---|---|---|---|---|---|
| **1**[4] | 1.10 (s) | 0.77 (s) | 1·00 (d, $J$=6) | 0.79 (d, $J$=5.5) | 1.98, 2.00, 2.14 2.16 (3H each, all s) | 4.6—5.1 (3H) |
| **4b** | 1.14 (s) | 0.76 (s) | 0.99 (d, $J$=6) | 0.79 (d, $J$=5.5) | 1.98 (6H), 2.03, 2.05 2.13 (3H, each) (all s) | 4.7—5.1 (3H)[b] |

| | 1α-<u>H</u> | 3-<u>H</u> | 1′-<u>H</u> | 4′-<u>H</u> | 5′-<u>H</u>$_2$ |
|---|---|---|---|---|---|
| **1**[4] | 3.00 (d.d, $J$=12.5, 4) | *ca.* 3.5 | 4.44 (d, $J$=8)[10] | 5.19 (m) | 3.58 (1H, A part in ABX, $J_{AB}$=13, $J_{AX}$<1) 4.02 (1H, B part in ABX, $J_{AB}$=13, $J_{BX}$=2) |
| **4b** | 2.76 (d.d, $J$=12, 4) | 5.46 (m) | 4.44 (d, $J$=8)[10,b] | 5.20 (m)[b] | 3.58 (1H, A part in ABX, $J_{AB}$=13, $J_{AX}$<1) 4.01 (1H, B part in ABX, $J_{AB}$=13, $J_{BX}$=2)[b] |

*a*) abbreviations: d=doublet, d.d=doublet of doublet, m=multiplet, s=singlet
*b*) The assignments were supported by the decoupling experiments.

YM-IV (**4**) corresponds to a deacetylated derivative of a minor component of the prosapogenol mixture (=NE-1[4]) which was previously obtained by the soil bacterial hydrolysis of the total glycoside mixture (BEC[4]) of the epigeous part of the plant although the isolation of **4** in a pure state was not achieved at that time. It should be added here that, although the parent saponins of NE-1 have not yet been isolated, BEC containing the parent saponins has been clarified by the present work to contain two monoarabinosides (YM-1 (**3**), YM-IV (**4**)) and their monoacetates (YM-II, YM-III) whose structures are very alike to those of NE-1. The elucidation of the parent saponins of NE-1 will be a subject of the further study.

Finally, the structure **4** for YM-IV has been further supported by the following synthesis. For the synthesis of O-glycosides of steroids and triterpenoids, the Koenigs–Knorr method[11]

8) K. Takeda, T. Okanishi, K. Hamamoto, A. Shimaoka, and N. Maezono, *Yakugaku Zasshi*, **77**, 175 (1957).
9) R. Kuhn, H. Egge, R. Brossmer, A. Gauhe, P. Klesse, W. Lochinger, R. Röhm, H. Trischmann, and D. Tschampel, *Angew. Chem.*, **72**, 805 (1960).
10) The doublet is observed with additional fine splitting due to virtual long-range coupling.[4]
11) W. Koenigs and E. Knorr, *Chem. Ber.*, **34**, 957 (1901).

and its modifications[12] have generally been used.[13] In addition to them, a method utilizing an orthoester intermediate of the carbohydrate moiety (with or without isolation of the intermediate) has been announced to be especially useful for the synthesis of glycosides in which the oxygen functions at C-1′ and C-2′ in the carbohydrate portion are *trans* and also to be effective for the synthesis of glycosides containing a less reactive aglycone.[13,14]

We have initially undertaken some preliminary experiments under the ordinary Koenigs–Knorr and several other conditions (using condensation reagents such as cadmium carbonate,[12a] silver carbonate,[12b] and triethylamine–tetraethylammonium bromide[15]) to introduce an arabinoside moiety at the rather sterically crowded 11α–OH of metagenin acetonide (**8**). However, the desired glycosidation was not effected, but instead the acetonide protecting group in **8** was noted to be labile under these reaction conditions.

After all, it has been found that reaction of metagenin acetonide (**8**) under cooled conditions with 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide and silver perchlorate in dry benzene followed by dry pyridine treatment[16] affords an arabinoside derivative (**10**) which retains the acetonide protecting group. Although the starting material (**8**) was recovered in large percentage, the product (**10**) was isolated and treated with 50% aqueous acetic acid to remove the acetonide group. The triacetate thus obtained was acetylated with acetic anhydride and pyridine to furnish its peracetate which was found to be identical to YM-IV pentaacetate (**4b**) by mixed mp, TLC, IR, and PMR.

## Experimental[17]

**Isolation of YM-I (3), YM-II, YM-III, and YM-IV (4)**——The glycoside mixture (=BEC[4], 35 g) obtained from the epigeous part of the plant was chromatographed on silica gel (Merck, 0.05—0.2 mm, 1500 g) eluting with a $CHCl_3$–MeOH mixture to furnish four arabinosides YM-II (76 mg, eluted with 8—10 v/v% MeOH in $CHCl_3$), YM-III (30 mg, with 10 v/v% MeOH in $CHCl_3$), YM-IV (111 mg, with 13 v/v % MeOH in $CHCl_3$), and YM-I (52 mg, with 20 v/v% MeOH in $CHCl_3$).

YM-II, mp 234—236° (from $CHCl_3$–MeOH), $[\alpha]_D^{20}$ −55° ($c$=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{54}O_{10}\cdot 1/2H_2O$: C, 64.48; H, 8.80. Found: C, 64.71; H, 8.62. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3470 (OH), 1713, 1259 (OAc), 974, 914, 892, 857 (intensity at 914<at 892, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.74 (3H, s, 13-C$\underline{H}_3$), 0.79 (3H, d, $J$=5.5 Hz, 25-C$\underline{H}_3$), 0.98 (3H, d, $J$=5.5 Hz, 20-C$\underline{H}_3$), 1.07 (3H, s, 10-C$\underline{H}_3$), 2.08 (3H, s, OAc), 5.18 (1H, m, >C$\underline{H}$–OAc). Hydrolysis of YM-II (7 mg) with 5% KOH–EtOH (2 ml) under reflux for 30 min followed by treatment with Amberlite IRC-50 and crystallization from MeOH gave YM-I (4 mg) which was identical to the authentic sample described below by TLC and IR.

YM-III, mp 166—169° ($CHCl_3$–MeOH). *Anal.* Calcd. for $C_{34}H_{54}O_{10}\cdot 1/2H_2O$: C, 64.48; H, 8.80. Found: C, 64.83; H, 9.10. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400 (OH), 1733, 1241 (OAc), 980, 920, 897, 866 (920<897, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.71 (3H, s, 13-C$\underline{H}_3$), 1.04 (3H, s, 10-C$\underline{H}_3$), 2.02 (3H, s, OAc), 4.6—5.1 (1H, m, >C$\underline{H}$–OAc). Alkaline hydrolysis of YM-III (20 mg) with 5% KOH–EtOH (4 ml) under reflux for 30 min followed by dilution with water while removing EtOH under reduced pressure and extraction with *n*-BuOH gave a product which was identical to YM-IV by TLC.

YM-IV (4), mp 297—300° (colorless plates from MeOH), $[\alpha]_D^{20}$ −84° ($c$=1.0, pyridine). *Anal.* Calcd. for $C_{32}H_{52}O_9$: C, 66.18; H, 9.03. Found: C, 66.09; H, 8.90. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400 (OH), 982, 920, 898, 865 (920 <898, 25R spiroketal).

YM-I (3), mp 300—303° ($CHCl_3$–MeOH), IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3460 (OH), 974, 910, 890, 856 (910<890, 25R

12) *a*) R.B. Conrow and S. Bernstein, *J. Org. Chem.*, **36**, 863 (1971); *b*) G. Wulff, G. Röhle, and W. Krüger, *Chem. Ber.*, **105**, 1097 (1972).
13) G. Wulff and G. Röhle, *Angew. Chem. Intern. Ed. Engl.*, **13**, 157 (1974).
14) *a*) N.K. Kochetkov, A.F. Bochkov, T.A. Sokolovskya, and V.J. Snyatkova, *Carbohyd. Res.*, **16**, 17 (1971); *b*) M. Schulz, H.-F. Boeden, and P. Berlin, *Ann. Chem.*, **703**, 190 (1967).
15) P.A. Gent and R. Gigg, *J. Chem. Soc. Perkin I*, **1975**, 1521.
16) The procedure was a modified method of Schultz, *et al.*[14b]
17) Instruments used in the experimental section and experimental conditions for chromatography were same as in our previous paper[18] unless specified otherwise. PMR spectra at 60 MHz or 100 MHz were taken with Hitachi R-20A or Varian HA-100 Spectrometer, and ORD curve and CD spectrum were measured with JASCO UV/ORD-5 Spectropolarimeter at 20°.
18) I. Kitagawa, K.S. Im, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **24**, 1260 (1976)

spiroketal). YM-I was identical to 11-O-α-L-arabinopyranosyl-3-epi-metagenin (**3**)[4] by mixed mp, TLC, and IR.

**Acid Hydrolysis of YM-I** (**3**)——A solution of **3** (27 mg) in 50% aq. EtOH containing 5% HCl (6 ml) was heated under reflux for 3.5 hr and concentrated under reduced pressure to remove EtOH. The precipitated aglycone (12 mg) was collected by filtration and was identified to 3-epi-metagenin (**5**) by TLC and IR. The aqueous filtrate was passed through a column of Dowex 44 and concentrated under reduced pressure to give a syrup (7 mg) which was purified by paper partition chromatography (PPC) developing twice for 24 hr each with iso-PrOH–*n*-BuOH–water (7: 1: 2). Arabinose thus obtained was determined to be L-arabinose by $[\alpha]_D^{19}$ +80.0° ($c$=0.67, taken in 5-10 min after making solution in water).

**Acid Hydrolysis of YM-IV** (**4**)——A solution of **4** (7 mg) in 50% aq. EtOH containing 5% HCl (2 ml) was heated under reflux for 3 hr, concentrated under reduced pressure to remove EtOH, diluted with water, and extracted with ether. The ether solution, after washing with water, was evaporated to dryness to give a product (3.2 mg) which was identical to metagenin by TLC and IR. The aqueous layer was passed through a column of Dowex 44, concentrated under reduced pressure, and subjected to PPC, developing as above. Arabinose thus obtained was confirmed to be L-arabinose by measuring its specific rotation: $[\alpha]_D^{26}$ +63.0° ($c$= 0.73, taken in 8—10 min after making aqueous solution).

**Complete Methylation of YM-IV** (**4**) **followed by Acid Hydrolysis giving 2,3-Di-O-methyl-metagenin** (**6a**) ——To a stirred solution of dimethyl carbanion (NaH (0.2 g)-DMSO (8 ml))[1,18] was added a solution of **4** (55 mg) in DMSO (9 ml) at room temperature under a $N_2$ atmosphere. After stirring the total mixture for one hour, the reaction mixture was treated with $CH_3I$ (3 ml), kept stirring under a $N_2$ atmosphere for 3 hr, left standing overnight, stirred again for 7 hr, diluted with ice-water (50 ml), and extracted with $CHCl_3$ three times. The $CHCl_3$ extract was washed with water and evaporated to dryness to give a product which was purified by preparative TLC (benzene: EtOH=10: 1) to give amorphous **4a** (40 mg), $[\alpha]_D^{30}$ −45° ($c$=1.84, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 981, 918, 899, 863 (918<899, 25R spiroketal). PMR ($CDCl_3$, 100 MHz) $\delta$: 0.81 (3H, s, 13-C<u>H</u>$_3$), 0.84 (3H, d, $J$=5 Hz, 25-C<u>H</u>$_3$), 1.04 (3H, d, $J$=6.5 Hz, 20-C<u>H</u>$_3$), 1.17 (3H, s, 10-C<u>H</u>$_3$), 3.40 (6H, s), 3.43, 3.50, 3.56 (3H each, all s) (OC<u>H</u>$_3$×5). Although the crystallization of **4a** was unsuccessful, since its purity was secured by TLC, it was subjected to the following acid treatment. A solution of **4a** (36 mg) in 50% aq. EtOH containing 2N HCl (3 ml) was heated under reflux for 4 hr and left standing overnight. The reaction mixture was concentrated under reduced pressure to remove EtOH while adding water and extracted with ether three times. The ether extract was washed with water and evaporated to dryness to give a product (33 mg) which was crystallized from $CHCl_3$–MeOH to furnish colorless needles of 2,3-di-O-methyl-metagenin (**6a**), mp 181.5—183°, $[\alpha]_D^{27}$ −55.4° ($c$=0.92, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{48}O_5$: C, 73.07; H, 10.15. Found: C, 72.61; H, 9.62. IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3475 (OH), 978, 916, 896, 861 (916<896, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.77 (3H, s, 13-C<u>H</u>$_3$), 0.78 (3H, d, $J$=6 Hz, 25-C<u>H</u>$_3$), 0.96 (3H, d, $J$=6.5 Hz, 20-C<u>H</u>$_3$), 1.12 (3H, s, 10-C<u>H</u>$_3$), 3.33, 3.38 (3H each, both s, OC<u>H</u>$_3$×2).

**Oxidation of 6a giving 7**——To an ice-cooled stirred solution of **6a** (20 mg) in pyridine (1 ml) was added dropwise $CrO_3$ (100 mg)-pyridine (1 ml) solution and the total mixture was kept stirring at room temperature for 4 hr, poured into ice-water, and extracted with ether three times. The ether extractive (19 mg) thus obtained was crystallized from MeOH to give colorless needles of **7**, mp 131—133°, $[\alpha]_D^{10}$ −17.1° ($c$=0.37, $CHCl_3$). *Anal.* Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.12; H, 9.75. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 1713 (CO), 972, 920, 898, 863 (920<898, 25R spiroketal). ORD ($c$=0.223, MeOH) [$\phi$] (nm): 0° (430), +848° (326) (peak), 0° (310), −1721° (282) (trough), −1360° (264). CD ($c$=4.71×10$^{-3}$ M, MeOH) [$\theta$] (nm): 0 (350), +1541 (305) (pos. max.), 0 (270).

**2,3-Di-O-methyl-metagenin** (**6a**) **from Metagenin** (**6**)——A mixture of **6** (40 mg) and anhydrous $CuSO_4$ (90 mg) in dry acetone (10 ml) was kept stirring at room temperature for 5 hr, left standing overnight, kept stirring again for 2 hr, and filtered. Evaporation of the filtrate gave a product which was purified by recrystallization from MeOH to furnish metagenin acetonide (**8**, 46 mg) of mp 212.5—213.5° (colorless needles).[8] A solution of **8** (46 mg) in $Ac_2O$ (2 ml) and pyridine (2 ml) was left standing at room temperature for 18 hr, poured into ice-water, and extracted with ether three times. The product obtained by the usual work-up of the ether extract was subjected to preparative TLC (benzene: EtOH=10: 1) to give **8a** (41 mg), mp 202—204.5° (colorless crystals from $CHCl_3$–MeOH), $[\alpha]_D^{16}$ −99.8° ($c$=1.1, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 1739, 1241 (OAc), 980, 919, 899, 864 (919<899, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.77 (3H, d, $J$=6 Hz, 25-C<u>H</u>$_3$), 0.83 (3H, s, 13-C<u>H</u>$_3$), 0.94 (3H, d, $J$=6.5 Hz, 20-C<u>H</u>$_3$), 1.08 (3H, s, 10-C<u>H</u>$_3$), 1.33, 1.46 (3H each, both s, acetonide C<u>H</u>$_3$×2), 2.03 (3H, s, OAc), 4.8—5.3 (1H, m, 11$\beta$-<u>H</u>). A stirred mixture of **8a** (37 mg) in 50% aq. AcOH (3.5 ml) was heated at 50—55° for 1.5 hr and extracted with ether three times. The ether extract was washed with water and evaporated to dryness to give a product (35 mg) which was crystallized from $CHCl_3$–MeOH to afford 11-O-acetyl-metagenin (**9**), mp 213—215°, $[\alpha]_D^{12}$ −91° ($c$=0.71, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3470 (OH), 1723, 1247 (OAc), 980, 919, 896, 866 (919<896, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.78 (3H, d, $J$=5 Hz, 25-C<u>H</u>$_3$), 0.80 (3H, s, 13-C<u>H</u>$_3$), 0.91 (3H, d, $J$=6 Hz, 20-C<u>H</u>$_3$), 1.06 (3H, s, 10-C<u>H</u>$_3$), 5.05 (1H, m, 11$\beta$-<u>H</u>). To a solution of **9** (50 mg) in dry benzene (3 ml) was added $Ag_2O$ (200 mg) and $CH_3I$ (1.5 ml) in the dark and the total mixture was kept stirring at 23° for 48 hr and at 30° for 48 hr. The reaction mixture was filtered and the filtrate was evaporated to dryness under reduced pressure to give a product which was dissolved in dry benzene (2 ml) and methylated twice more with $Ag_2O$ (100 mg) and $CH_3I$ (1 ml) at 35° for 70 hr each

as above. The product (55 mg) was subjected to preparative TLC (benzene: EtOH=12: 1) to give a main product (15 mg) which was recrystallized from MeOH to afford 2,3-di-O-methyl-11-O-acetyl-metagenin (**9a**), mp 163—166° (colorless needles), $[\alpha]_D^{11}$ −76° ($c$=1.13, $CHCl_3$). *Anal.* Calcd. for $C_{31}H_{50}O_6$: C, 71.78; H, 9.72. Found: C, 71.88; H, 9.71. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 1735, 1238 (OAc), 976, 915, 896, 861 (915<896, 25R spiroketal). PMR ($CDCl_3$, 60 MHz) $\delta$: 0.77 (3H, d, $J$=6 Hz, 25-C$\underline{H}_3$), 0.78 (3H, s, 13-C$\underline{H}_3$), 0.91 (3H, d, $J$=6 Hz, 20-C$\underline{H}_3$), 1.04 (3H, s, 10-C$\underline{H}_3$), 1.95 (3H, s, OAc), 3.31, 3.35 (3H each, both s, OC$\underline{H}_3$×2), 4.8—5.3 (1H, m, 11$\beta$-$\underline{H}$). A solution of **9a** (11 mg) in 5% KOH–EtOH (1.5 ml) was heated under reflux for 30 min, diluted with water while removing EtOH under reduced pressure, and extracted with ether. The ether extract was washed with water and evaporated to dryness to give 2,3-di-O-methyl-metagenin (**6a**, 10 mg), IR $\nu_{max}^{CHCl_3}$ $cm^{-1}$: 3460 (OH), 978, 964, 915, 861 (964<915, 25R spiroketal), which, although its crystallization was unsuccessful, was identical by TLC and IR to metagenin dimethyl ether obtained above from YM-IV (**4**).

**Acetylation of YM-IV (4) giving Pentaacetate (4b)**——A solution of **4** (39 mg) in $Ac_2O$ (2 ml) and pyridine (2 ml) was left standing at room temperature for 20 hr, poured into ice-water, and extracted with ether. The ether extract was washed with water, dried over $MgSO_4$, and evaporated to dryness to give a product (61 mg) which was subjected to preparative TLC (benzene: EtOH=12: 1). The product thus obtained was recrystallized from *n*-hexane–acetone to furnish **4b** as colorless needles of mp 134—137°, $[\alpha]_D^{27}$ −60.5° ($c$=0.43, $CHCl_3$). *Anal.* Calcd. for $C_{42}H_{62}O_{14}$: C, 63.78; H, 7.90. Found: C, 63.67; H, 7.87. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 1750, 1250, 1220 (OAc), 982, 922, 900, 871 (922<900, 25R spiroketal). PMR: as given in Table I.

**11-O-(2′,3′,4′-Tri-O-acetyl-α-L-arabinopyranosyl)-metagenin Acetonide (10) from Metagein Acetonide (8)**——To a solution of **8** (200 mg, 0.41 m mole) and 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide (68 mg, 0.2 m mole) in dry benzene (10 ml) was added a solution of silver perchlorate (48 mg, 0.23 m mole) in dry benzene (14 ml). After 2 min, dry pyridine (11.5 mg, 0.25 m mole) was added and the total mixture was left standing at 2° for 4 hr, diluted with benzene, and filtered. The precipitate was washed with benzene and the combined filtrate and washings were washed with water repeatedly until the washing became negative for silver ion (detection by $Cl^-$), dried over $MgSO_4$, and evaporated under reduced pressure to give a product (281 mg). Separation of the product by preparative TLC (benzene–acetone=4: 1, detection by spraying water) furnished recovered **8** (156 mg) and **10** (32 mg, 47.5% based on consumed **8**). Recrystallization from $CHCl_3$–MeOH gave the analytical sample of **10**, mp 112—115° as colorless prisms, $[\alpha]_D^{19}$ −49.7° ($c$=1.20, $CHCl_3$). High Resolution Mass Spectrum: Calcd. for $C_{41}H_{62}O_{12}$ ($M^+$): 746.424; $C_{40}H_{59}O_{12}$ ($M^+-CH_3$): 731.401; $C_{11}H_{15}O_7$ (**i**)[4]: 259.082. Found: 746.428; 731.402; 259.081. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: no OH, 1759, 1245, 1220 (OAc), 983, 921, 901, 872 (921<901, 25R spiroketal), 849 (acetonide). PMR ($CDCl_3$, 90 MHz) $\delta$: 0.75 (3H, s, 13-C$\underline{H}_3$), 0.78 (3H, d, $J$=6 Hz, 25-C$\underline{H}_3$), 0.99 (3H, d, $J$=6 Hz, 20-C$\underline{H}_3$), 1.09 (3H, s, 10-C$\underline{H}_3$), 1.33, 1.46 (3H each, both s, acetonide C$\underline{H}_3$×2), 2.02, 2.03, 2.19 (3H each, all s, OAc×3). Mass Spectrum *m/e* (%): 746 ($M^+$, 0.3), 731 ($M^+-CH_3$, 8), 686 ($M^+$—AcOH, 1.6), 259 (**i**, 100),[4] 199 (**i**-AcOH, 16), 139 (**ii**, 13).[4]

**YM-IV Pentaacetate (4b) from 10**——**10** (24 mg) was treated with 50% aq. AcOH (1 ml) at 55° for one hour, neutralized with 10% aq. $NaHCO_3$, and extracted with EtOAc repeatedly. The combined EtOAc extract was dried over $MgSO_4$ and evaporated under reduced pressure to give a product (20 mg), IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3597, 3586 (OH), 1759, 1228 (OAc), 983, 919, 899, 873 (919<899, 25R spiroketal). The product (16 mg) was then acetylated with $Ac_2O$ (0.5 ml) and pyridine (1.0 ml) at room temperature overnight. Usual work-up of the product followed by crystallization from petroleum ether (bp 40—60°) furnished a peracetate of mp 136—139° (colorless needles) which was identical to YM-IV pentaacetate (**4b**) by mixed mp, IR ($CCl_4$), TLC ($CHCl_3$–MeOH=35: 1; benzene- EtOAc=2: 1), and PMR ($CDCl_3$).

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