[Chem. Pharm. Bull. 23(2) 355—364 (1975)]

UDC 547.597.02 : 581.192

Saponin and Sapogenol. IX.[1] Structure of Spergulagenin A, a New Migrated Hopane-type Sapogenol isolated from *Mollugo spergula* L.

Isao Kitagawa, Hideyo Suzuki, Kiyoshi Kitazawa, Nobuko Yamao, and Itiro Yosioka

Faculty of Pharmaceutical Sciences, Osaka University[2]

(Received July 24, 1974)

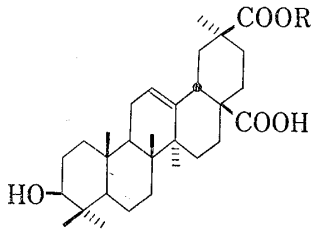
The structure of spergulagenin A, a new genuine sapogenol isolated (second major) from the root of *Mollugo spergula* L. (Molluginaceae) along with oleanolic acid and methyl spergulagenate (**1a**) (major), has been established as **3** on the basis of chemical investigations and X-ray structure evidence. The full account of chemical evidence is described.

Spergulagenin A (**3**) possesses a new migrated-hopane skeleton, in which 22-CH_3 in the ordinary hopane framework is migrated to C-21, and the probable biogenetic pathway of spergulagenin A has been presumed.

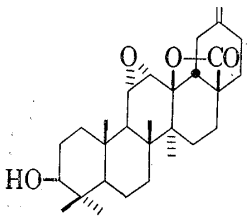
In the previous paper,[3] we reported a biogenetically patterned transformation of spergulagenic acid (**1**) to eupteleogenin (**2**), in which the starting material methyl spergulagenate (**1a**) was obtained from the sapogenol fraction of the root of *Mollugo spergula* L. (Molluginaceae). The chromatographic separation of the total sapogenol mixture has led us to isolate another new sapogenol which, on the basis of the physical properties thereof and those of its derivatives, has been considered to be identical with spergulagenin A initially isolated by two Indian groups from the same plant source,[4] although the direct comparison has not been possible.

As presented in the preliminary communication,[5] based on the chemical and X-ray structure evidence, we have elucidated the structure of spergulagenin A (**3**) as having a new migrated hopane-type carbon framework. In this paper, we wish to describe the full account of the chemical and physicochemical investigation on the sapogenol which is in accord with the structure **3**.

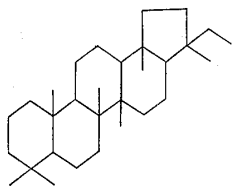
Silica gel column chromatography of the total sapogenol mixture obtained from the root of *Mollugo spergula* L. afforded oleanolic acid, methyl spergulagenate (**1a**) (major), and spergulagenin A (**3**) (second major), along with a minor unidentified sapogenol.



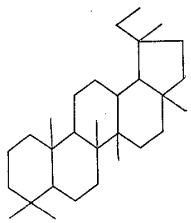
1 : R=H spergulagenic acid
1a : R=CH_3



2 : eupteleogenin



[A]



[B]

Chart 1

1) Part VIII: I. Kitagawa, M. Yoshikawa, Y. Imakura, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **22**, 1339 (1974).
2) Location: *133-1, Yamada-kami, Suita, Osaka.*
3) *a*) I. Kitagawa, K. Kitazawa, and I. Yosioka, *Tetrahedron*, **28**, 907 (1972); *b*) I. Kitagawa, K. Kitazawa, K. Aoyama, M. Asanuma, and I. Yosioka, *ibid.*, **28**, 923 (1972).
4) *a*) P. Chakrabarti and A.K. Barua, *J. Indian Chem. Soc.*, **42**, 137 (1965); *b*) P. Chakrabarti, *ibid.*, **44**, 242 (1967); *c*) V. Hariharan and S. Rangaswami, *Phytochemistry*, **10**, 621 (1971).
5) I. Kitagawa, H. Suzuki, I. Yosioka, T. Akiyama, and J.V. Silverton, *Tetrahedron Letters*, **1974**, 1173.

NII-Electronic Library Service

Spergulagenin A (**3**), $C_{30}H_{50}O_4$, mp 278—279.5°, showed a positive Liebermann-Burchard color reaction and a negative tetranitromethane test and possesses the hydroxyl (3445 cm^{-1}) and carbonyl (1688 cm^{-1}) functions as revealed by its infrared (IR) absorption spectrum (KBr). The proton magnetic resonance (PMR) spectrum of **3** (d_5-pyridine) shows the presence of seven tertiary methyls, one methyl ketone moiety (3H, s, δ 2.31), and three carbinyl protons, among which one is observed as a characteristic triplet-like signal at δ 3.42 assignable to 3α-H geminal to equatorial 3β-OH in **3**.

Ordinary acetylation of **3** with acetic anhydride and pyridine furnished a triacetate (**3a**), mp 239—240°, whose IR and PMR spectra disclose that three hydroxyls in **3** were readily acetylated (1729 cm^{-1}; δ 1.89, 1.99, 2.02, 3H each, s). The ^{13}C nuclear magnetic resonance (CMR) spectrum of **3a** shows the presence of 36 carbons including one ketonic carbon (212.5 ppm), three acetoxyl carbons (170.6, 170.1, and 170.0 ppm), and three carbons bearing a secondary acetoxyl function (80.3, 71.5, 69.6 ppm). Treatment of **3** with *p*-bromobenzoyl chloride and pyridine yielded a tri-*p*-bromobenzoate (**3b**), mp 237°, whose IR spectrum shows the benzoate absorption bands at 1701 and 1590 cm^{-1} whereas the PMR spectrum shows the presence of three A_2B_2 type signals ascribable to three benzoate groups. Alkaline hydrolysis of **3b** regenerated spergulagenin A (**3**) in a good yield.

Sodium borohydride reduction of **3a** furnished two triacetates (**4a** and **4b**, the former moved quicker on the chromatogram) which are epimeric at a newly formed secondary alcoholic function. The IR spectrum of **4a** exhibits the presence of hydroxyl (3438 cm^{-1}) and acetoxyl (1718 cm^{-1}) but the absence of methyl ketone moiety, which are in parallel with the PMR evidence of **4a**. Thus, in addition to seven tertiary methyl signals, was observed a newly formed secondary methyl signal (δ 1.14, d, J=6.5 Hz) which coupled with a carbinyl proton at δ 3.73 (q, J=6.5 Hz) as proved by the spin decoupling experiments (Table I). It should be pointed out here that irradiation at δ 1.14 brought out a remarkable change of a quartet at δ 3.73 to a sharp singlet. Therefore, it has become clear that the methyl ketone moiety in **3** attaches to a quaternary carbon (partial structure [C]).

The IR and PMR spectra of another triacetate (**4b**) show the presence of similar functions as in **4a**: hydroxyl (3560 cm^{-1}), acetoxyl (1730 cm^{-1}), and α-hydroxyethyl (δ 1.13, 3H, d, J=7.0 Hz; δ 3.59, 1H, q, J=7.0 Hz). Here again, the conversion of the methyl ketone moiety attached to a quaternary carbon to an α-hydroxyethyl function was proved by the spin decoupling experiments (Table I).

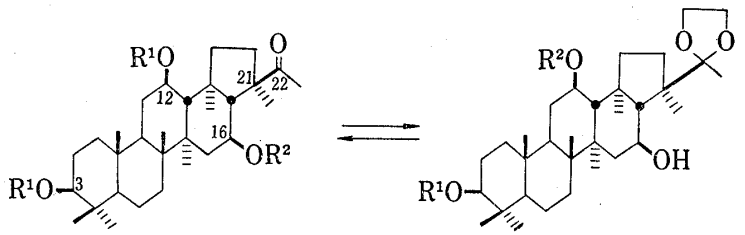
Based on the above described evidence, spergulagenin A (**3**) has been disclosed to be a saturated pentacarbocyclic triterpenoid possessing seven tertiary methyls, three secondary hydroxyls (readily acetylated), and one methyl ketone function attached to a quaternary carbon, thus one of the carbon rings being assumed five-membered. As for a probable carbon skeleton of spergulagenin A, one could presume a migrated hopane-type [A] or a migrated lupane-type [B] framework, and the former has been presumed more likely since four hopane-type sapogenols (mollugogenols A, B, C, and E) have been already elucidated from the related species (*Mollugo hirta* Thunb.) by Chakrabarti, *et al.*[6] In addition, biogenetic considerations have enabled us to presume the methyl ketone moiety being located at the terminal five-membered ring (probably at C-21 in [A] or at C-19 in [B]).

Treatment of **3** with ethylene glycol and *p*-toluenesulfonic acid furnished an ethylene ketal (**5**), mp 288—291°, which does not possess the methyl ketone moiety any more as shown by its IR spectrum. In the PMR spectrum of **5**, are observed eight tertiary methyl signals which include one newly derived tertiary methyl. Since mild acid treatment of **5** readily resumed **3**, **5** has been assured to retain the carbon framework of **3**.

6) *a*) P. Chakrabarti, *Tetrahedron*, **25**, 3301 (1969); *b*) P. Chakrabarti, P.K. Sanyal, and A.K. Barua, *J. Indian Chem. Soc.*, **46**, 96 (1969); *c*) P. Chakrabarti and A.K. Sanyal, *ibid.*, **46**, 1061 (1969); *d*) *Idem*, *Indian J. Chem.*, **8**, 1042 (1970).

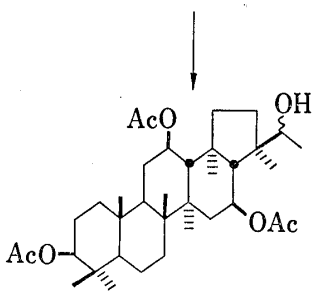
NII-Electronic Library Service

Acetylation of **5** with acetic anhydride and pyridine yielded two monoacetates (**5a, 5b**) and one diacetate (**5c**). The IR spectrum of a more polar monoacetate (**5a**), mp 265°, shows the presence of hydroxyl (3420 cm^{-1}) and acetoxyl function (1720 cm^{-1}), while the PMR

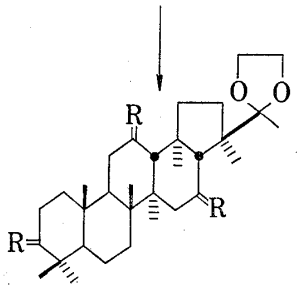


3 : $R^1=R^2=H$ spergulagenin A
3a : $R^1=R^2=Ac$
3b : $R^1=R^2=p$-Br-C_6H_4CO
3c : $R^1=Ac$, $R^2=H$

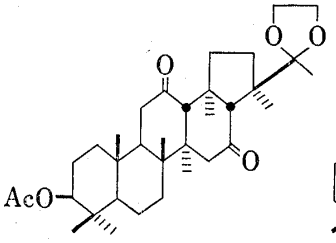
5 : $R^1=R^2=H$
5a : $R^1=H$, $R^2=Ac$
5b : $R^1=Ac$, $R^2=H$
5c : $R^1=R^2=Ac$



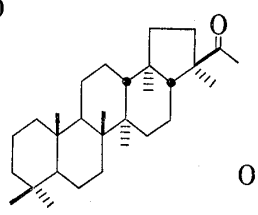
4a, 4b



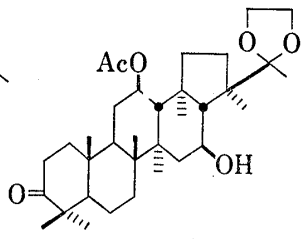
7 : R=O
8 : $R=H_2$



6



9

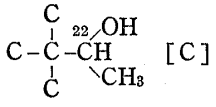


10

Chart 2

TABLE I. The Spin Decoupling Experiments of **4a** and **4b**

Decoupled proton	**4a**		**4b**	
	irradiated at δ			
	3.73	1.14	3.59	1.13
22-CH_3 (d)	s	—	s	—
22-H (q)	—	s	—	s



[C]

NII-Electronic Library Service

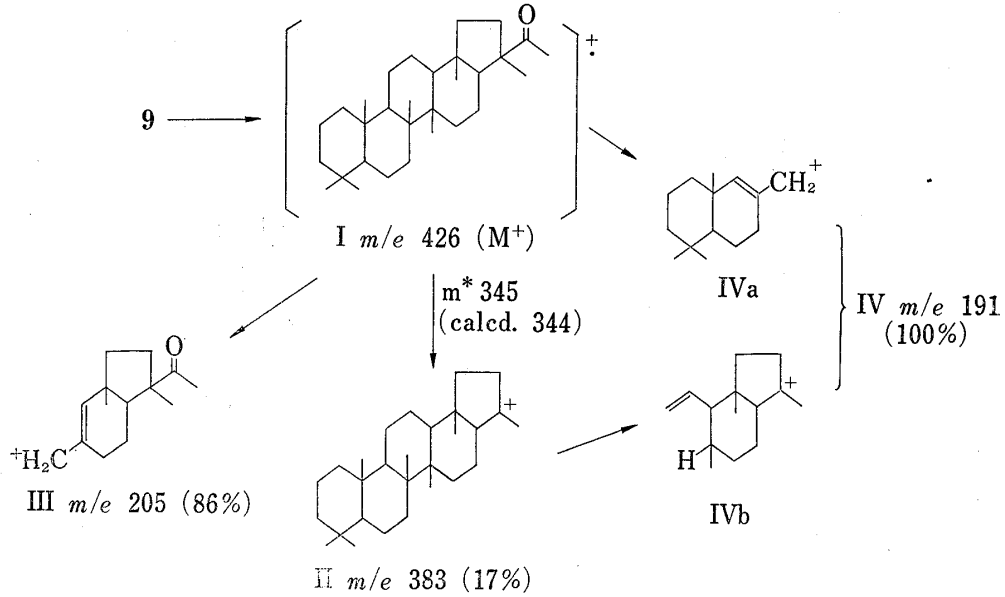
spectrum reveals the presence of one secondary acetoxyl (3H, s, δ 1.98; 1H, q-like, δ 5.15) and two carbinyl protons (1H, t-like, δ 3.15; 1H, m, δ 3.75). As judged from the coupling pattern of one of the carbinyl protons, one of two hydroxyls in **5a** has been assigned at C-3.

Another monoacetate (**5b**), mp 275—279°, also possesses two secondary hydroxyls (3410 cm^{-1}; 2H, m, δ 3.0—4.1) and one secondary acetoxyl (1720 cm^{-1}; 3H, s, δ 2.02 and 1H, t-like, δ 4.45) being assigned at C-3 on the similar basis. Chromium trioxide-pyridine oxidation of **5b** furnished a diketone (**6**), mp 259—259.5°, whose PMR spectrum shows disappearance of two carbinyl protons in **5b** while the IR spectrum exhibits the formation of six-membered ring ketones (1725 (sh), 1713 cm^{-1}) along with the presence of acetoxyl function (1734, 1243 cm^{-1}).

The PMR spectrum of the diacetate (**5c**), mp 288—291°, shows the presence of two secondary acetoxyls (3H each, s, δ 1.97, 2.01; 1H, t-like, δ 4.45; 1H, q-like, δ 5.16) and one secondary hydroxyl (1H, m, δ 3.75, –C<u>H</u>–OH).

The significant difference between spergulagenin A (**3**) and its ethylene ketal (**5**) is a fact that one of three hydroxyls in the latter is less reactive for acetylation probably induced by the formation of a bulky ethylene ketal moiety in the vicinity.

Oxidation of **5** with chromium trioxide-pyridine furnished in an excellent yield an ethylene ketal triketone (**7**), mp 322°, which possesses no hydroxyl but the six-membered ring carbonyl functions (1703 cm^{-1}) as revealed by its IR spectrum. The PMR spectrum also shows disappearance of the carbinyl protons of **5**. Therefore, it has become apparent that three hydroxyls in **3** attach to the six-membered carbon rings. Huang-Minlon reduction of **7** gave a reduction product **8**, mp 202°, whose IR spectrum shows no carbonyl absorption band. Mild acid treatment of **8** furnished a tridesoxy-spergulagenin A (**9**), mp 250°, which retains the methyl ketone moiety as shown by its IR and PMR spectra (1691 cm^{-1}; 3H, s, δ 2.08 in $CDCl_3$ and δ 1.81 in C_6D_6). Based on the established structure of spergulagenin A (**3**) (*vide infra*), the *trans*



High Resolution Mass Spectrum of **9**

	I $C_{30}H_{50}O$	II $C_{28}H_{47}$	III $C_{14}H_{21}O$	IV $C_{14}H_{23}$
Calcd.	426.386	383.368	205.159	191.180
Found	426.389	383.364	205.156	191.178

Chart 3. Mass Fragmentation of **9**

NII-Electronic Library Service

D, E ring junction (17β-H) in **7** is considered not to be readily isomerized to *cis* (17α-H) but is preserved during the derivation from **7** to **9** *via* **8** because of the presence of bulky ethylene ketal moiety attached to the 21β side chain.[7]

A base peak of *m/e* 191 observed in the mass spectrum of **9** can be estimated as a combination of two fragment ions IVa and IVb on the basis of the assumed carbon skeleton and the composition was substantiated by the high resolution mass spectrum (Chart 3). The other prominent fragment ions at *m/e* 383 and *m/e* 205 are also well explained by II and III respectively and their compositions were similarly determined as shown in Chart 3.

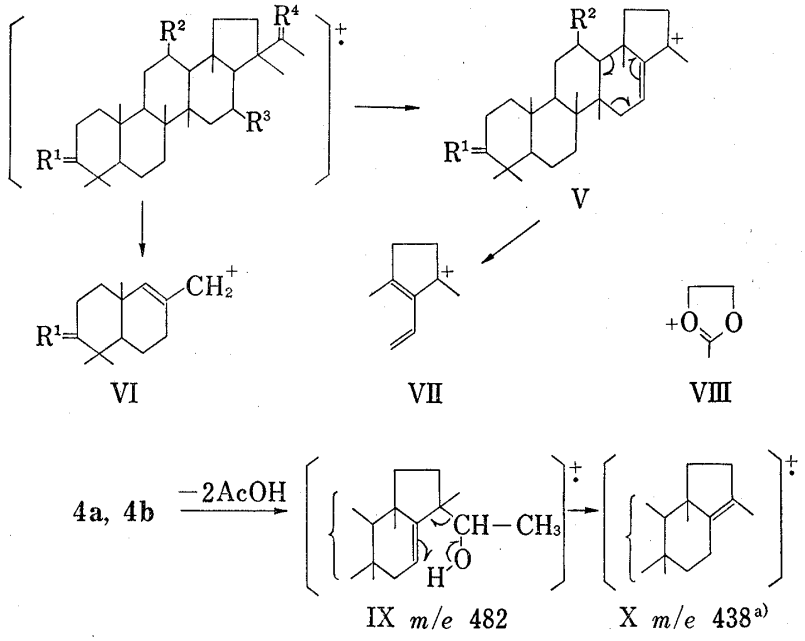
Since three hydroxyls in spergulagenin A (**3**) are readily acetylated as mentioned above, all of them are assigned as equatorial (including 3β-OH). Mild oxidation of ethylene ketal monoacetate (**5a**) with chromium trioxide-pyridine furnished a monoketone (**10**) (IR: 1701 cm^{-1}), which lacks the characteristic signal due to 3α-H (δ 3.15, t-like, in **5a**) in the PMR spectrum but preserves another secondary carbinol and a secondary acetoxyl as shown by the respective geminal proton signals at δ 3.75 (br. m) and at δ 5.15 (br. m). Therefore, the location of carbonyl function in **10** has been assigned at C-3. Since the optical rotatory dispersion (ORD) curve of **10** shows a positive Cotton effect ($[\Phi]_{303}$ +1592° (peak), $[\Phi]_{265}$ +251° (trough)), the stereochemical environment of the carbonyl function has been considered to be quite alike to that of the A, B ring system having a carbonyl function at C-3 in the ordinary triterpenoid such as hopane, lupane, oleanane, or dammarane.[8] Furthermore, the presence of 3β-OH in spergulagenin A (**3**) has been supported by the following findings: i) a fragment ion peak observed at *m/e* 207 (VI, R^1=H, OH) or *m/e* 205 (VI, R^1=O) in the mass spectrum of **3** or **10** (Chart 4)[9]; ii) a characteristic triplet-like signal at δ 4.45 due to 3α-H in the PMR spectra of **3a**, **5b**, and **5c**, and at δ 3.15 in that of **5**.

On treatment of ethylene ketal diacetate (**5c**) with acetic acid, was obtained spergulagenin A diacetate (**3c**), mp 266°, whose IR spectrum exhibits the hydroxyl (3460 cm^{-1}), acetoxyl (1720 cm^{-1}), and the methyl ketone (1690 cm^{-1}) absorption bands. The PMR spectrum of **3c** shows, along with a 3α-H triplet-like signal at δ 4.50, a one-proton signal at δ 3.73 (d.d.d, J=4.5, 9.0, and 11.0 Hz) which is attributable to a proton geminal to a secondary hydroxyl. Since the coupling pattern of the signal is very similar to that of 16α-H in the PMR spectrum of 16-O-acetyl-6-dehydro-leucotylin (d.d.d, J=4.0, 9.0, and 12.0 Hz),[10] the assignment of the hydroxyl function in **3c** has been made as 16β, which has been further supported by the fragment ion peaks expressed as VII in the mass spectra of **3**, **3a**, **4a**, **4b**, **5**, **5c**, and **10** and by the McLafferty rearrangement (IX→X)[11] observed in the mass spectra of **4a** and **4b** (Chart 4). The orientation of the second hydroxyl in spergulagenin A (**3**) has therefore been assumed to be 16β.

The location of the third hydroxyl in spergulagenin A (**3**) has been inferred to be in ring C, because the IR spectrum of ethylene ketal triketone (**7**) shows only the six-membered ring carbonyl absorption band (1703 cm^{-1}) and because the fragment ions of types VI and VII are observed in the mass spectra of **3**, **3a**, **4a**, **4b**, **5**, **5c**, and **10** (Chart 4). Since all the carbonyl functions in **7** were readily reduced to the methylenes (**8**) under the ordinary Huang-Minlon conditions, the third hydroxyl in **3** has been disposed at C-12 rather than at C-11 and the assignment has been supported by the fragment ion peaks observed (although with weak intensity) in the mass spectrum of **7** at *m/e* 247 (XI), 229 (XI–H_2O), 219 (XII), and 205 (XIII)

7) I. Yosioka, T. Nakanishi, H. Yamauchi, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **20**, 147 (1972).
8) *a*) C. Djerassi, J. Osiecki, and W. Closson, *J. Am. Chem. Soc.*, **81**, 4587 (1959); *b*) I. Yosioka, H. Yamauchi, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **20**, 502 (1972).
9) Because of the strong fragment ion peak at *m/e* 87 (VIII) originated in the ethylene ketal moiety, the ion peaks V, VI, and VII in the mass spectra of **5c** and **10** are observed with rather weak intensity.
10) I. Yosioka, T. Nakanishi, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **17**, 279 (1969).
11) *a*) H.E. Audier, H. Felkin, M. Fetizon, and W. Vetter, *Bull. Soc. Chim. France*, **1965**, 3236; *b*) D.G.I. Kingston, J.T. Bursey, and M.M. Bursey, *Chem. Rev.*, **74**, 215 (1974).

NII-Electronic Library Service



	R¹	R²	R³	R⁴	m/e (%) V	m/e (%) VI	m/e (%) VII
3	H, OH	OH	OH	O	413 (100)[a]	207 (47)[a]	121 (50)
3a	H, OAc	OAc	OAc	O	497 (83)[a]	249 (14)[a]	121 (47)
4a	H, OAc	OAc	OAc	H, OH	497 (3)[b]	249 (10)[a]	121 (15)[a]
4b	H, OAc	OAc	OAc	OH, H	497 (<1)[b]	249 (27)[a]	121 (37)[a]
5	H, OH	OH	OH	$-O(CH_2)_2O-$	413 (13)[a]	207 (25)[a]	121 (64)
5c	H, OAc	OAc	OH	$-O(CH_2)_2O-$	497 (5)	249 (5)	121 (22)[a]
10	O	OAc	OH	$-O(CH_2)_2O-$	453 (2)[a]	205 (2)[a]	121 (3)[a]

a) The elemental compositions were determined by high resolution mass spectrometry.
b) The assignment is still uncertain.

Chart 4. Mass Fragmentations of **3**, **3a**, **4a**, **4b**, **5**, **5c**, and **10**

which are derivable from a 3,12-diketo A,B,C-ring system (Chart 5).[12] Furthermore, the PMR signals due to 12-H in **5a** and **3c** are observed as quartet-like at δ 5.15 and δ 5.20, which indicate the acetoxyl functions being oriented as 12β[12] in the presumed carbon skeleton.

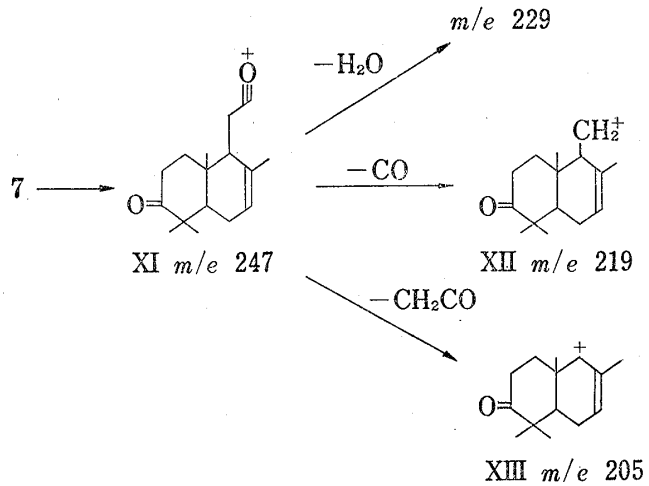


Chart 5

All the accumulated evidence presented above is in harmony with the formulation **3** for spergulagenin A (stereochemistry at C-21 undefined), however at this stage, one could not yet exclude a migrated-lupane equivalent ([B]) as another possibility. In order to confirm the complete stereostructure of spergulagenin A (**3**), the X-ray structure study of **5a** was undertaken by the direct method and as reported in the previous communication,[5] the structure

12) S.D. Jolad and C. Steelink, *J. Org. Chem.*, 34, 1367 (1969).

NII-Electronic Library Service

of spergulagenin A has been established as **3** whose absolute configuration being corroborated by the ORD data of **10** (*vide supra*). The methyl ketone moiety at C-21 is oriented with β configuration.

As elucidated in the X-ray study of **5a**, the intramolecular hydrogen bonding between 16-OH and the ethylene ketal oxygen has been anticipated also in the solution which was examined with **5c**. In the IR spectra of **5c** taken in the concentrations of 1×10^{-1}, 1×10^{-2}, and 1×10^{-3} mole (in CCl_4), there was observed as expected a hydrogen-bonded hydroxyl absorption band at 3443—3445 cm^{-1} in each case.

Based on the established stereostructure of spergulagenin A (**3**), resistance of 16β-OH in the ethylene ketal (**5**) against the ordinary acetylation (giving the partially acetylated derivatives: **5a**, **5b**, and **5c**) has now been rationally ascribed to the steric hindrance of the ethylene ketal moiety nearby.

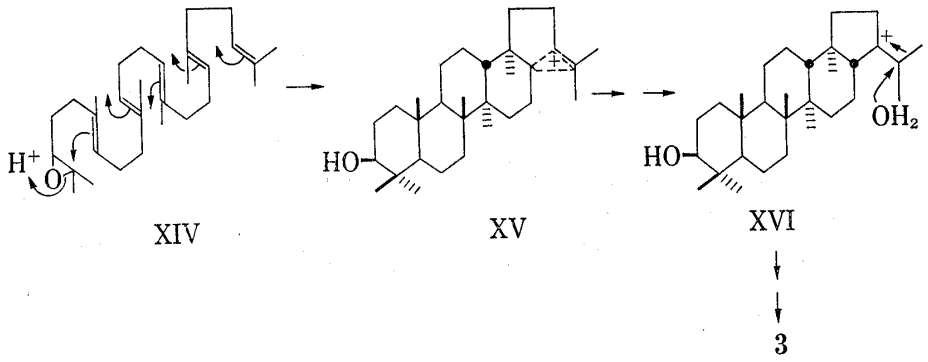


Chart 6

As for the genuineness of spergulagenin A (**3**), we have examined the soil bacterial hydrolysis[13] of the parent saponin, and it has been clarified that spergulagenin A (**3**) is one of the genuine sapogenols of the root of *Mollugo spergula*, which will be reported later. Finally, a probable biogenetic pathway of the new migrated hopane skeleton can be depicted as shown in Chart 6 starting from squalene 2,3-oxide (XIV→XV→XVI→**3**).

Experimental[14]

Isolation of Spergulagenin A (3)——The methanolic extractive (520 g) obtained from the root of *Mollugo spergula* (8.2 kg) was partitioned in *n*-BuOH–water mixture as usual and ether treatment of the *n*-BuOH soluble portion furnished crude saponin (131 g). A mixture of crude saponin (23 g) in 10% aq. H_2SO_4 (255 ml) and MeOH (255 ml) was heated under reflux for 7 hr, diluted with water, concentrated under reduced pressure to remove MeOH, and allowed to stand at room temperature to yield a sapogenol mixture (10.5 g) which was collected by filtration, washed with water and dried. The sapogenol mixture (10 g), which was mixed with silica gel (18 g) with an aid of MeOH and dried beforehand, was put on a column of silica gel

13) *a*) I. Yosioka, M. Fujio, M. Osamura, and I. Kitagawa, *Tetrahedron Letters*, **1966**, 6303; *b*) I. Yosioka, A. Inada, and I. Kitagawa, *Tetrahedron*, **30**, 707 (1974), and the preceding papers of the series cited therein.

14) The following instruments were used for obtaining the physical data. Melting points: Yanagimoto Micro-meltingpoint Apparatus (a hot-stage type), Ishii High-meltingpoint Apparatus (a capillary type), and recorded uncorrected; Specific rotations: Rex Photoelectric Polarimeter NEP-2 (1=1 dm); IR spectra: Hitachi IR Spectrometer EPI-S2 or EPI-G3; PMR spectra (tetramethylsilane as an internal standard): Hitachi R-22 (90 MHz), R-20A (60 MHz), or Varian HA-100 NMR Spectrometer; Mass spectra: Hitachi RMU-6D Mass Spectrometer at 70 eV unless specified otherwise; ORD curves: JASCO ORD/UV-5 Automatic Recording Spectropolarimeter. For chromatography, silica gel (Merck, 0.05—0.2 mm), silicic acid (Mallinckrodt), or alumina (Woelm, neutral, grade I) was used for column and silica gel (Camag D-5) for TLC and detection was made by spraying 1% $Ce(SO_4)_2$–10% H_2SO_4 solution followed by heating.

NII-Electronic Library Service

(600 g) and chromatographed eluting with benzene–AcOEt mixtures. Successive elution with a 5:1 mixture gave oleanolic acid and oleanolic acid contaminated with an unidentified minor sapogenol (totally 0.86 g, crystallized from MeOH) and with 5:1—10:3 mixtures was obtained methyl spergulagenate (**1a**) (3.15 g),[3b] and finally with a 10:3 mixture was obtained spergulagenin A (**3**) (1.33 g) which was recrystallized from MeOH to give an analytical sample of mp 278—279.5° (colorless needles), $[\alpha]_D^{27}$ −21.8° (c=0.50, $CHCl_3$) (in lit.[4a]: mp 278—282° (decomp) (from benzene–$CHCl_3$), $[\alpha]_D^{32}$ −31.4° ($CHCl_3$)). *Anal.* Calcd. for $C_{30}H_{50}O_4$: C, 75.90; H, 10.62. Found: C, 75.94; H, 10.75. IR ν_{max}^{KBr} cm^{-1}: 3445 (OH), 1688 (CH_3CO). PMR (d_5-pyridine, 90 MHz) δ: 0.87, 0.99, 1.04, 1.09 (3H each, s), 1.19 (6H, s), 1.61 (3H, s) (totally seven methyls), 2.31 (3H, s, CH_3CO), 3.42 (1H, t-like, 3α-H), 3.8—4.4 (2H, m, 12α-H, 16α-H). Mass Spectrum m/e (%): 474 (M^+), 413 (V, 100), 207 (VI, 47), 121 (VII, 50), 43 (65). High Resolution Mass Spectrum m/e: Found: 474.362, 413.342, 207.176. Calcd. for $C_{30}H_{50}O_4$ (M^+): 474.371; $C_{28}H_{45}O_2$ (V): 413.342; $C_{14}H_{23}O$ (VI): 207.175.

Spergulagenin A Triacetate (**3a**)——Spergulagenin A (**3**) (300 mg) was acetylated with Ac_2O (3 ml) and pyridine (5 ml) by keeping overnight at room temperature followed by usual treatment. Crystallization of the product (370 mg) from MeOH gave spergulagenin A triacetate (**3a**), mp 239—240° (colorless needles), $[\alpha]_D^{20}$ +60.4° (c=0.50, $CHCl_3$) (in lit.[4a]: mp 236—238°, $[\alpha]_D^{34}$ +57.7° ($CHCl_3$)). *Anal.* Calcd. for $C_{36}H_{56}O_7$: C, 71.96; H, 9.40. Found: C, 72.04; H, 9.34. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1729 (CH_3COO), 1704 (sh, CH_3CO). PMR ($CDCl_3$, 100 MHz) δ: 0.84 (9H, s), 0.99, 1.05, 1.10, 1.16 (3H each, s) (totally seven methyls), 1.89, 1.99, 2.02 (3H each, s, three acetoxyls), 2.16 (3H, s, CH_3CO), 4.45 (1H, t-like, 3α-H), 4.7—5.3 (2H, m, 12α-H, 16α-H). CMR (25.146 MHz) ppm: 212.5, 170.6, 170.1, 170.0, 80.3, 71.5, 69.6, 58.7, 55.0, 52.3, 51.9, 47.7, 46.2, 45.4, 44.0, 41.4, 39.9, 38.0, 37.6, 37.0, 36.8, 32.9, 27.8, 27.5, 25.2, 23.4, 21.7, 21.1, 20.8, 20.0, 18.6, 18.0, 17.3, 16.7, 16.4, 15.6. Mass Spectrum (35 eV) m/e (%): 540 (M^+−AcOH, 5), 497 (V, 83), 480 (M^+−2AcOH, 48), 437 (V−AcOH, 100), 420 (M^+−3AcOH, 20), 249 (VI, 14), 189 (VI−AcOH, 62), 121 (VII, 47). High Resolution Mass Spectrum m/e: Found: 497.364, 437.346, 249.189. Calcd. for $C_{32}H_{49}O_4$ (V): 497.363; $C_{30}H_{45}O_2$ (V−AcOH): 437.342; $C_{16}H_{25}O_2$ (VI): 249.185.

Spergulagenin A Tri-*p*-bromobenzoate (**3b**)——A solution of **3** (400 mg) in pyridine (40 ml) was treated with *p*-bromobenzoyl chloride (2 g) and kept stirring at 31—34° for 3 hr. A product obtained by the usual work-up was chromatographed on silicic acid (20 g) eluting with benzene to yield tri-*p*-bromobenzoate (**3b**) (720 mg). Recrystallization from acetone furnished an analytical sample of **3b** (colorless needles), mp 237°, $[\alpha]_D^{26}$ +70.9° (c=0.80, $CHCl_3$). *Anal.* Calcd. for $C_{51}H_{59}O_7Br_3$: C, 59.83; H, 5.89; Br, 23.41. Found: C, 59.58; H, 5.75; Br, 23.29. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1701 (ArCOO, CH_3CO), 1590 (aryl C=C). PMR ($CDCl_3$, 90 MHz) δ: 0.92 (6H, s), 0.99, 1.07, 1.18, 1.20, 1.26 (3H each, s) (totally seven methyls), 2.15 (3H, s, CH_3CO), 2.55 (1H, d, J=13.0 Hz),[15] 4.73 (1H, t-like, 3α-H), 5.19, 5.54 (1H each, m, 12α-H and 16α-H), 7.53 (4H), 7.54 (2H), 7.74 (2H), 7.86 (2H), 7.89 (2H) (totally 12H, three A_2B_2 type q, J=8.0 Hz, three *p*-bromobenzoyls). A solution of **3b** (100 mg) in 2 (w/v)% KOH–EtOH (20 ml) was refluxed for one hour and concentrated under reduced pressure to remove EtOH while adding water to give a precipitate (40 mg), which was collected by filtration. The product was then crystallized from MeOH to give colorless needles which was identified with **3** by mixed mp, IR, and TLC ($CHCl_3$–MeOH=15:1, *n*-hexane–acetone=3:2, benzene–acetone=2:1).

$NaBH_4$ Reduction of Spergulagenin A Triacetate (**3a**)——To a solution of **3a** (650 mg) in EtOH (100 ml) was added $NaBH_4$ (100 mg) and the total mixture was stirred at 18° for 4 hr, poured into water, neutralized with 5% HCl, concentrated under reduced pressure, and extracted with $CHCl_3$. Treatment of the $CHCl_3$ extract in a usual way yielded a product (630 mg), which was chromatographed on a silica gel (50 g) column eluting with benzene–$CHCl_3$ (2:1) to give successively **4a** (116 mg) and **4b** (288 mg). Recrystallization from acetone furnished an analytical sample of **4a**, mp 269° (colorless needles), $[\alpha]_D^{8}$ +25.9° (c=0.39, $CHCl_3$). *Anal.* Calcd. for $C_{36}H_{58}O_7$: C, 71.72; H, 9.70. Found: C, 71.77; H, 9.90. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3438 (br, OH), 1718 (CH_3COO). PMR ($CDCl_3$, 90 MHz) δ: 0.84 (9H, s), 0.92, 0.97, 1.05, 1.10 (3H each, s) (totally seven methyls), 1.14 (3H, d, J=6.5 Hz, 22-CH_3), 2.00 (3H, s), 2.02 (6H, s) (three acetoxyls), 3.73 (1H, q, J=6.5 Hz, 22-H), 4.45 (1H, t-like, 3α-H), 4.8—5.4 (2H, br.m, 12α-H, 16α-H). Mass Spectrum (35 eV) m/e (%): 542 (M^+−AcOH, 1), 497 (3), 482 (M^+−2AcOH, IX, 15), 438 (X, 100), 249 (VI, 10), 189 (VI−AcOH, 27), 187 (41), 175 (35), 121 (VII, 15). High Resolution Mass Spectrum: Found: 542.398, 438.349, 249.186, 187.149, 175.149, 175.112, 121.102, 121.066. Calcd. for $C_{34}H_{54}O_5$ (M^+−CH_3COOH): 542.397; $C_{30}H_{46}O_2$ (X): 438.350; $C_{16}H_{25}O_2$ (VI): 249.185; $C_{14}H_{19}$: 187.149; $C_{13}H_{19}$: 175.149; $C_{12}H_{15}O$: 175.112; C_9H_{13} (VII): 121.102; C_8H_9O: 121.065. Recrystallization from acetone furnished a pure 22-epimer (**4b**) of mp 294° (colorless crystals), $[\alpha]_D^{18}$ +33.6° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{36}H_{58}O_7$: C, 71.72; H, 9.70. Found: C, 71.74; H, 9.98. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1730 (CH_3COO). PMR ($CDCl_3$, 90 MHz) δ: 0.82 (9H, s), 0.92, 0.96, 1.02, 1.11 (3H each, s) (totally seven methyls), 1.13 (3H, d, J=7.0 Hz, 22-CH_3), 1.99, 2.01, 2.04 (3H each, s, three acetoxyls), 3.21 (1H, br.s, $W_{h/2}$=11.0 Hz, 22-OH, exchangeable with D_2O), 3.59 (1H, q, J=7.0 Hz, 22-H), 4.48 (1H, t-like, 3α-H), 4.8—5.4 (2H, m, 12α-H, 16α-H). Mass Spectrum (35 eV) m/e (%): 542 (M^+−AcOH, 5), 497 (<1), 482 (M^+−2AcOH, IX, 12), 438 (X, 100), 249 (VI, 27), 189 (VI−AcOH, 81),

15) The assignment is unknown.

NII-Electronic Library Service

187 (71), 175 (94), 121 (VII, 37). High Resolution Mass Spectrum: Found: 542.398, 438.349, 249.185, 187.149, 175.149, 175.113, 121.102, 121.066. Calcd. as for **4a**.

Ketalization of Spergulagenin A (3) Giving 5——A mixture of **3** (1.0 g), *p*-TsOH·H_2O (10 mg), ethylene glycol (4 ml), and dry benzene (100 ml) in a 200 ml three-necked flask equipped with a water-separator was heated in an oil bath (temp. 110—120°) for 6 hr. During the period, in order to keep the total volume of the solution, benzene was added to the reaction mixture while distilling out benzene–water mixture azeotropically. After cooling, the resulting reaction mixture was diluted with benzene (100 ml) and washed with 1% aq. K_2CO_3. The benzene layer was then washed repeatedly with water and dried over $MgSO_4$. The aqueous washings were combined and extracted with $CHCl_3$ and the $CHCl_3$ layer was washed with water and dried over $MgSO_4$. The both benzene and $CHCl_3$ extractives were combined (1.2 g) and chromatographed on an alumina (neutral) column eluting with benzene–AcOEt (5: 1) mixture to afford spergulagenin A ethylene ketal (**5**) (844 mg), colorless needles of mp 288—291° (from acetone), $[\alpha]_D^{15}$ +16.0° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{32}H_{54}O_5$: C, 74.09; H, 10.49. Found: C, 74.07; H, 10.44. IR ν_{max}^{KBr} cm^{-1}: 3410 (OH). PMR ($CDCl_3$, 60 MHz) δ: 0.79, 0.86, 0.99 (3H each, s), 1.04 (6H, s), 1.25, 1.28, 1.37 (3H each, s) (totally eight methyls), 3.15 (1H, t-like, 3α-H), 3.5—4.3 (2H, m, 12α-H, 16α-H), 4.03 (4H, s, ethylene ketal), 5.06 (1H, br.s, OH). Mass Spectrum *m/e* (%): 518 (M^+), 413 (V, 13), 207 (VI, 25), 189 (VI−H_2O, 37), 149 (81), 121 (VII, 64), 107 (100), 87 (VIII, 35). High Resolution Mass Spectrum: Found: 413.345, 207.172, 189.163. Calcd. for $C_{28}H_{45}O_2$ (V): 413.342, $C_{14}H_{23}O$ (VI): 207.175, $C_{14}H_{21}$ (VI−H_2O): 189.164. A solution of **5** (a small amount) in EtOH (0.6 ml) was treated with 10% aq. H_2SO_4 (0.1 ml) and left standing at room temperature for one hour. The reaction product was identified with spergulagenin A (**3**) by TLC using three solvent systems: i) benzene–MeOH (5: 1), ii) $CHCl_3$–acetone (3: 1), iii) benzene–acetone (10: 3).

Acetylation of Spergulagenin A Ethylene Ketal (5) Giving Monoacetates (5a, 5b) and Diacetate (5c)——A solution of **5** (480 mg) in Ac_2O–pyridine (5 ml—10 ml) mixture was left standing at 15° for 15 hr. Preparative TLC (benzene–acetone=5: 1) of the product afforded two monoacetates, **5a** (88 mg) and **5b** (102 mg), and a diacetate (**5c**) (323 mg) (in the order of decreasing polarity). Recrystallization from EtOH gave a pure sample of **5a** (colorless rods), mp 265°, $[\alpha]_D^{12}$ +15.2° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{56}O_6$: C, 72.82; H, 10.06. Found: C, 72.54; H, 9.95. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (OH), 1720 (CH_3COO). PMR ($CDCl_3$, 100 MHz) δ: 0.76, 0.82, 0.93, 0.97, 1.01, 1.03, 1.20, 1.33 (3H each, s, eight methyls), 1.98 (3H, s, acetoxyl), 3.15 (1H, t-like, 3α-H), 3.75 (1H, m, varied on D_2O addition to d.d.d, J=5.5, 9.5, 10.5 Hz, 16α-H), 3.99 (4H, s, ethylene ketal), 4.98 (1H, d, J=4.0 Hz, exchangeable with D_2O, 16β-OH), 5.15 (1H, q-like, 12α-H). Mass Spectrum *m/e* (%): 545 (M^+−15, 7), 207 (VI, 6), 189 (VI−H_2O, 8), 121 (VII, 16), 87 (VIII, 100), 43 (66). Another monoacetate (**5b**) was purified by recrystallization from MeOH to give colorless needles of mp 275—279°, $[\alpha]_D^{12}$ +24.0° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{56}O_6$: C, 72.82; H, 10.06. Found: C, 72.95; H, 9.95. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3410 (OH), 1720 (CH_3COO). PMR ($CDCl_3$, 100 MHz) δ: 0.85 (9H, s), 1.01 (6H, s), 1.02, 1.23, 1.33 (3H each, s) (totally eight methyls), 2.02 (3H, s, acetoxyl), 3.0—4.1 (2H, m, 12α-H, 16α-H), 3.99 (4H, s, ethylene ketal), 4.45 (1H, t-like, 3α-H), 4.96 (1H, d, J=3.5 Hz, exchangeable with D_2O, 16β-OH). Mass Spectrum *m/e* (%): 545 (M^+−15, 15), 249 (VI, 5), 189 (VI−AcOH, 26), 121 (VII, 35), 87 (VIII, (100), 43 (85). Recrystallization from MeOH gave pure **5c** (colorless needles), mp 288—291°, $[\alpha]_D^{18}$ +24.4° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{36}H_{58}O_7$: C, 71.72; H, 9.70. Found: C, 71.73; H, 9.41. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3445 (OH), 1740, 1735, 1242 (CH_3COO); ν_{O-H} (1×10^{-1}M in CCl_4, cell path length 0.2 mm): 3445 cm^{-1}; (1×10^{-2}M, 1.0 mm): 3445 cm^{-1}; (1×10^{-3}M, 5.0 mm): 3443 cm^{-1}. PMR ($CDCl_3$, 100 MHz) δ: 0.85 (9H, s), 0.94, 1.01, 1.04, 1.21, 1.33 (3H each, s) (totally eight methyls), 1.97, 2.01 (3H each, s, two acetoxyls), 3.75 (1H, m, varied on D_2O addition to d.d.d, J=4.0, 10.0, 10.5 Hz, 16α-H), 3.99 (4H, s, ethylene ketal), 4.45 (1H, t-like, 3α-H), 4.94 (1H, d, J=4.0 Hz, exchangeable with D_2O, 16β-OH), 5.16 (1H, q-like, 12α-H). Mass Spectrum *m/e* (%): 587 (M^+−15, 15), 497 (V, 5), 249 (VI, 5), 189 (VI−AcOH, 20), 149 (70), 121 (VII, 22), 87 (VIII, 100), 43 (26). High Resolution Mass Spectrum: Found: 587.396, 149.132, 149.097, 121.101. Calcd. for $C_{35}H_{55}O_7$ (M^+−CH_3): 587.395, $C_{11}H_{17}$: 149.133, $C_{10}H_{13}O$: 149.097, C_9H_{13} (VII): 121.102.

Oxidation of 5b Giving 6——To a solution of **5b** (100 mg) in pyridine (2 ml) was added a CrO_3–pyridine complex solution (330 mg—3 ml) and the total mixture was kept stirring at 15° for 8 hr and poured into ice-water. The product collected by filtration was extracted with acetone and crystallized from acetone to give colorless plates of **6** (67 mg), mp 259—259.5°, $[\alpha]_D^{15}$ +4.4° (c=0.97, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{52}O_6$: C, 73.34; H, 9.41. Found: C, 73.21; H, 9.60. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1734, 1243 (CH_3COO), 1725 (sh), 1713 (CO). PMR ($CDCl_3$, 90 MHz) δ: 0.83 (6H, s), 0.90, 0.97, 1.08, 1.15, 1.25, 1.41 (3H each, s) (totally eight methyls), 2.03 (3H, s, acetoxyl), 3.94 (4H, s, ethylene ketal), 4.46 (1H, t-like, 3α-H). ORD (c=0.162, dioxane) [Φ] (nm): 0° (350), +480° (318) (peak), 0° (304), −1330° (274) (sh), −1672° (250). Mass Spectrum *m/e* (%): 556 (M^+), 87 (VIII, 100).

Oxidation of Ethylene Ketal (5) Giving Triketone (7)——A solution of **5** (1.2 g) in pyridine (24 ml) was treated with a CrO_3–pyridine complex solution (4 g—36 ml) at 23° for 5 hr with stirring and poured into ice-water. The product (1.0 g) collected by filtration was extracted with $CHCl_3$ and crystallized from $CHCl_3$–MeOH to give colorless needles of **7**, mp 322°, $[\alpha]_D^{25}$ +18.0° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{32}H_{48}O_5$: C, 74.96; H, 9.44. Found: C, 75.25; H, 9.24. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1703 (CO). PMR ($CDCl_3$, 60 MHz) δ: 0.99 (6H, s), 1.02 (3H, s), 1.08 (6H, s), 1.15, 1.28, 1.39 (3H each, s) (totally eight methyls), 3.88 (4H, s, ethylene

NII-Electronic Library Service

ketal). ORD (c=0.164, dioxane) [Φ] (nm): +100° (430), +1742° (315) (peak), 0° (306), −2123° (220) (trough). Mass Spectrum m/e (%): 512 (M^+), 247 (XI, 2), 229 (XI−H_2O, 2), 219 (XII, 8), 205 (XIII, 11), 95 (93), 87 (VIII, 95), 43 (100).

Huang-Minlon Reduction of 7 Giving 8——A mixture of **7** (200 mg) in triethylene glycol (100 ml) and 80% hydrazine hydrate (20 ml) was refluxed in an oil bath (temp. 165—175°) for 6 hr and treated with KOH (8 g). The bath temperature was raised gradually to 230° while distilling out excess hydrazine and water with a downward condenser. The reaction mixture was then refluxed at 230—240° (oil bath temp.) for 6 hr, and after cooling, poured into water, neutralized with dil. HCl, and treated with $CHCl_3$. After usual work-up, the product was subjected to column chromatography (silica gel, 5 g) eluting with benzene to give a reduction product (27 mg), which was crystallized from $CHCl_3$–MeOH to give **8**, mp 202°, $[\alpha]_D^{15}$ +12.5° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{32}H_{54}O_2$: C, 81.64; H, 11.56. Found: C, 81.48; H, 11.86. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: no CO band. PMR ($CDCl_3$, 60 MHz) δ: 0.77 (6H, s), 0.81, 0.91, 0.94, 0.97 (3H each, s), 1.20 (6H, s) (totally eight methyls), 3.92 (4H, s, ethylene ketal); (C_6D_6, 60 MHz) δ: 0.81 (6H, s), 0.85, 0.87 (3H each, s), 0.96 (6H, s), 1.16, 1.23 (3H each, s) (totally eight methyls), 3.52 (4H, s, ethylene ketal). Mass Spectrum m/e (%): 470 (M^+), 249 (2), 191 (VI, 4), 87 (VIII, 100).

Acid Treatment of 8 Giving Tridesoxy-spergulagenin A (9)——A solution of **8** (27 mg) in $CHCl_3$ (1 ml) was treated with AcOH (0.5 ml) at room temperature for 12 hr and evaporated under reduced pressure to give a residue which was crystallized from $CHCl_3$–MeOH to give colorless rods of **9**, mp 250°, $[\alpha]_D^{15}$ +37.5° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{30}H_{50}O$: C, 84.44; H, 11.81. Found: C, 84.06; H, 11.56. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1691 (CH_3CO). PMR ($CDCl_3$, 60 MHz) δ: 0.81 (12H, s), 0.92, 0.95, 1.09 (3H each, s) (totally seven methyls), 2.08 (3H, s, CH_3CO); (C_6D_6, 60 MHz) δ: 0.72 (3H, s), 0.81 (6H, s), 0.89 (9H, s), 1.01 (3H, s) (totally seven methyls), 1.81 (3H, s, CH_3CO). Mass Spectrum m/e: 426 (M^+, 17), 383 (II, 47), 234 (1), 205 (III, 86), 191 (IVa, IVb, 100), 121 (27), 43 (CH_3CO^+, 30). High Resolution Mass Spectrum: as given in Chart 3.

Partial Oxidation of 5a Giving 10——To an ice-cooled solution of **5a** (38 mg) in pyridine (1.5 ml) was added a CrO_3–pyridine complex solution (60 mg—1.5 ml) and the total mixture was left standing under ice-cooling for 5 hr, treated with EtOH (5 ml) for 1 hr, poured into ice-water and extracted with $CHCl_3$. The product obtained by usual work-up was purified by preparative TLC (benzene–acetone=10: 3) to give a ketone (**10**) (amorphous). The analytical sample, which was precipitated by addition of water to methanolic solution of **10**, was hygroscopic. *Anal.* Calcd. for $C_{34}H_{54}O_6 \cdot 1/3H_2O$: C, 72.36; H, 9.88. Found: C, 72.22; H, 9.92. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3402 (OH), 1718 (CH_3COO), 1701 (CO). PMR ($CDCl_3$, 90 MHz) δ: 0.92, 0.94, 1.02 (3H each, s), 1.06 (6H, s), 1.22, 1.25, 1.34 (3H each, s) (totally eight methyls), 2.00 (3H, s, acetoxyl), 3.75 (1H, br.m, 16α-H), 4.01 (4H, s, ethylene ketal), 4.98 (1H, d, J=3.0 Hz, exchangeable with D_2O, 16β-OH), 5.15 (1H, br.m, 12α-H). ORD (c=0.191, dioxane) [Φ] (nm): +175° (700), +111° (589), +1592° (303) (peak), +251° (265) (trough), +695° (250), a=+13.4. Mass Spectrum (75 eV) m/e (%): 558 (M^+), 543 (M^+−15, 1), 453 (V, 2), 211 (2), 205 (VI, 2), 121 (VII, 3), 87 (VIII, 100), 43 (11). High Resolution Mass Spectrum: Found: 543.368, 453.337, 205.159, 121.103. Calcd. for $C_{33}H_{51}O_6$ (M^+-CH_3): 543.369, $C_{30}H_{45}O_3$ (V): 453.337, $C_{14}H_{21}O$ (VI): 205.159; C_9H_{13} (VII): 121.102.

Acid Treatment of 5c Giving Spergulagenin A Diacetate (3c)——A solution of **5c** (23 mg) in 10 (v/v)% MeOH–AcOH (2 ml) was left standing at 31° for 24 hr and evaporated under reduced pressure. A residue was crystallized from MeOH to give colorless needles of **3c**, mp 266°, $[\alpha]_D^{13}$ −14.0° (c=0.10, $CHCl_3$). *Anal.* Calcd. for $C_{34}H_{54}O_6$: C, 73.08; H, 9.74. Found: C, 73.01; H, 9.76. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460 (br, OH), 1720 (CH_3COO), 1690 (CH_3CO). PMR ($CDCl_3$, 90 MHz) δ: 0.86 (9H, s), 0.94 (3H, s), 1.04 (6H, s), 1.40 (3H, s) (totally seven methyls), 1.95, 2.03 (3H each, s, two acetoxyls), 2.22 (3H, s, CH_3CO), 3.73 (1H, d.d.d, J= 4.5, 9.0, 11.0 Hz, 16α-H), 4.50 (1H, t-like, 3α-H), 5.20 (1H, q-like, 12α-H). Mass Spectrum m/e (%): 558 (M^+), 498 (M^+−AcOH, 33), 497 (V, 60), 438 (M^+−2AcOH, 65), 249 (VI, 13), 189 (VI−AcOH, 73), 137 (100), 121 VII, 68), 107 (98), 95 (92), 43 (95).

Acknowledgement The authors would like to express their sincere thankness to the Res. Lab. of Takeda Chem. Ind. (100 MHz PMR spectra), Res. Lab. of Dainippon Pharm. Co. (elemental analyses), Res. Lab. of Fujisawa Pharm. Co., Prof. I. Ninomiya of Kobe Women's College of Pharmacy (high resolution mass spectra), and JEOL Ltd. (CMR spectra with JNM-PFT-100).

NII-Electronic Library Service