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Studies on the Constituents of Asclepiadaceae Plants. XLV.[1] On the Components of *Metaplexis japonica* Makino. VI.[2] The Structures of 7-Oxygenated-Pregnane Derivatives

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The structures of three new polyoxypregnane derivatives, dibenzoylgagaimol, gagaimol-7-methylether, and 7β-methoxysarcostin, all of which were isolated from the root of *Metaplexis japonica* Makino, are shown to be I, II, and III, respectively. These three compounds are the first example of polyoxypregnane derivatives which have been obtained from the Asclepiadaceae plants, and shown to have an oxygen functional group at the 7-position.

Keywords——Asclepiadaceae; *Metaplexis japonica* Makino; dibenzoylgagaimol; gagaimol; gagaimol-7-methyl ether; 7β-methoxysarcostin; sarcostin; gagaminin; ^{13}C-NMR; polyoxypregnane

The structures of a number of polyoxypregnane derivatives isolated from *Metaplexis japonica* Makino (Japanese name: Gagaimo), a plant of Asclepiadaceae family, have been reported.[4–8] In this paper, we describe the structures of dibenzoylgagaimol (I),[5] gagaimol-7-methyl ether (II), and 7β-methoxysarcostin (III)[7] obtained from the aglycone mixture of the glycoside of the plant.

The aglycone mixture,[5] obtained from the glycoside after a mild acid hydrolysis, was submitted to alumina column chromatography. This procedure yielded dibenzoylgagaimol (I),[5] benzoylisoramanone,[5] and gagaminin.[2,9] The mother liquors of these aglycones and the other eluted fractions from which no crystalline compound was isolated, were combined. The combined aglycone mixture was hydrolyzed with 5% methanolic potassium hydroxide in order to isolate the pregnane compounds.[7] The alkaline hydrolysate was submitted to column chromatography on silica gel using chloroform–methanol mixture for elution. By these procedures, a new pregnane derivative, gagaimol-7-methyl ether (II), and other pregnane derivatives were isolated.

Dibenzoylgagaimol (I) formed needles, mp 192—197°, $[\alpha]_{589}^{20}$ +26° (c=0.15 in MeOH, from ORD measurement), which with Liebermann–Burchard reaction gave color changes

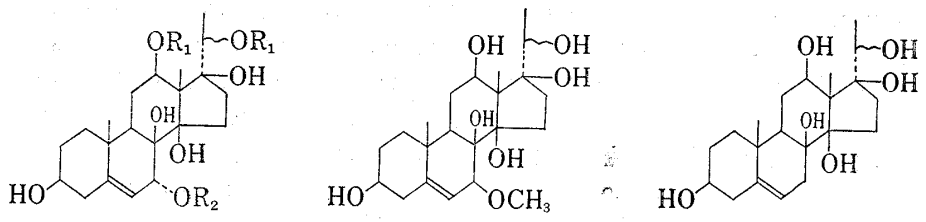
1) Part XLIV: H. Bando and H. Mitsuhashi, *Chem. Pharm. Bull.* (Tokyo), **26**, 2128 (1978).
2) *a*) A part of this work has been reported in a preliminary form: T. Nomura and H. Mitsuhashi, *Chem. Pharm. Bull.* (Tokyo), **20**, 1344 (1972). In the paper, gagaminin was referred to as ester A; *b*) A part of this work was presented at the 92nd Annual Meeting of the Pharmaceutical Society of Japan, April 1972 and at the Annual Meeting of the Pharmacognostical Society of Japan, October 1977.
3) Location: *a*) *2–2–1, Miyama, Funabashi-shi, Chiba, 274, Japan*; *b*) *Kita-12-jo, Nishi-6-chome, Kita-ku, Sapporo-shi, 060, Japan.*
4) H. Mitsuhashi, T. Nomura, Y. Shimizu, I. Takemori, and E. Yamada, *Chem. Pharm. Bull.* (Tokyo), **10**, 811 (1962).
5) H. Mitsuhashi and T. Nomura, *Chem. Pharm. Bull.* (Tokyo), **13**, 274 (1965). In the paper, dibenzoylgagaimol was referred to as compound IV.
6) H. Mitsuhashi and T. Nomura, *Chem. Pharm. Bull.* (Tokyo), **13**, 1332 (1965).
7) H. Mitsuhashi, T. Nomura, and M. Hirano, *Chem. Pharm. Bull.* (Tokyo), **14**, 717 (1966). In the paper, 7β-methoxysarcostin was referred to as compound V.
8) H. Mitsuhashi, M. Hirano, and T. Nomura, *Shoyakugaku Zasshi*, **20**, 9 (1966).
9) T. Yamagishi, K. Hayashi, and H. Mitsuhashi, *Chem. Pharm. Bull.* (Tokyo), **20**, 2289 (1972).

(reddish violet→green), and with antimony trichloride a green coloration. The molecular formula, $C_{35}H_{42}O_9$, was given for I from its elemental analysis and mass spectral measurement. Infrared (IR) absorption bands at 3300, 3200, 1725, 1685, 1600, 1590, and 1280 cm^{-1} indicate the presence of hydroxyl, ester and aromatic groups. The ^1H nuclear magnetic resonance (PMR) spectrum of I showed the signals for two tertiary methyl groups at δ 1.26 s, 19-CH_3) and δ 2.14 (s, 18-CH_3), one secondary methyl group at δ 1.52 (d, J=6 Hz, 21-CH_3), four methines at δ 3.70 (m, 3α-H), 4.55 (d, J=5 Hz, 7β-H), 5.37 (q, J=6 Hz, 20-H), 5.62 (dd, J=5 and 10 Hz, 12α-H) and eleven olefinic protons at δ 5.90 (d, J=5 Hz, 6-vinyl proton) and 7.10—8.10 (10H, m). The mass spectrum of I showed the fragment ions at *m/e* 484 (M^+—benzoic acid), 362 (M^+—2×benzoic acid), 122, 105, 77. The ultraviolet (UV) spectrum showed the absorption at 229 (log ε 4.26) and 273 nm (3.50). These facts and the following results suggest that I is a dibenzoic acid ester of polyoxygenated pregnane derivative. Dibenzoylgagaimol (I) consumed about two moles of lead tetraacetate (in dioxane), one mole rapidly (5 hr, 0.77 mol; 26 hr, 1.30 mol), and another mole slowly (95 hr, 1.84 mol). These experiments suggest the presence of α-glycol group in I.

Dibenzoylgagaimol (I) was hydrolyzed with 5% methanolic potassium hydroxide and the reaction mixture was separated into acid and neutral portions. The acidic portion gave benzoic acid, and trituration of the neutral portion with acetone gave a new pregnane type compound for which the name gagaimol (Ia) was proposed.[2] Gagaimol (Ia) formed needles, mp 274—277°, for which the molecular formula, $C_{21}H_{36}O_7$, was proposed from its high-resolution mass spectrum. The IR absorption at 3400 cm^{-1} (broad) indicates the presence of hydroxyl group, but there was no band assignable to a carbonyl group. The mass spectrum exhibits the ions at *m/e* 154 (base peak, $C_9H_{14}O_2$), 136 ($C_9H_{12}O$), 121 (C_8H_9O), which appear to be derived from a retro-Diels–Alder reaction of the 5—6 double bond in the B ring as illustrated in Chart 2. Hence, two hydroxyl groups exist in the rings A and B, and one of them may be at 3β on the basis of the biogenetic analogy. The mass spectrum of I exhibits the ions at *m/e* 154 (base peak), 136, 121. When the mass spectrum of I and Ia were compared, it is apparent that the ester linkages are not located at the two hydroxyl groups in the rings A and B. The fragment peaks (*m/e* 353, 335, 317, 299, 281) of Ia were accounted for the fragment ions (Chart 2) [M^+—45 (C_2H_5O), M^+—45—H_2O, M^+—45—2H_2O, M^+—45—3H_2O, M^+—45—4H_2O] which were also found in polyoxygenated pregnane derivatives with a glycol at C-17 and 20 positions.[10] The PMR spectrum of Ia showed the signals for two tertiary methyl groups at δ 1.40 (s, 19-CH_3) and 1.94 (s, 18-CH_3), one secondary methyl group at δ 1.53 (d, J=6 Hz, 21-CH_3), four hydroxy methines at δ 3.90 (m, 3α-H), 3.98 (dd, J=5 and 10 Hz, 12α-H), 4.39 (q, J=6 Hz, 20-H), 4.48 (d, J=5 Hz, 7β-H), and one olefinic proton at δ 5.85 (d, J=5 Hz, 6-vinyl proton). In comparison of the PMR spectra of I and Ia, it is supported that I has four secondary hydroxyl groups, and two of them are esterified with benzoic acid. In the PMR spectrum of I, one of the two proton signals adjacent to a benzoxyl group (δ 5.37) was assigned as 20-proton by the following PMR spin decoupling experiment, and the result supports the presence of C-17 hydroxyl group. The irradiation of 21-methyl group protons (δ 1.52) collapsed the quartet at δ 5.37 to a singlet. The other signal (δ 5.62) adjacent to a benzoyl group was in good agreement with the coupling constants of 12α-proton,[11] and the chemical shift and coupling constants of the signal (δ 3.98) of PMR spectrum of Ia were also in good agreement with the 12α-proton signal of 12-oxygenated polyoxypregnane derivatives.[11,12] From these results, it is suggested that I has 12β-,20-O-dibenzoyl structure.

As shown in Table I, the chemical shifts of the highly deshielded signals of two tertiary methyl groups of Ia were similar to those of the polyoxypregnane compounds having

10) M. Fukuoka, K. Hayashi, and H. Mitsuhashi, *Chem. Pharm. Bull.* (Tokyo), **19**, 1469 (1971).
11) Y. Shimizu and H. Mitsuhashi, *Tetrahedron*, **24**, 4143 (1968).
12) F. Schaub, H. Kaufmann, W. Stöcklin, and T. Reichstein, *Helv. Chim. Acta*, **51**, 738 (1968).



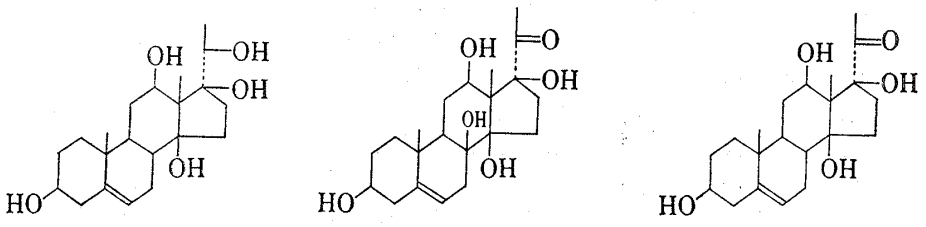
I : R_1=CO(1′,2′,3′,4′,5′,6′,7′), R_2=H

Ia : R_1=R_2=H

II : R_1=H, R_2=CH_3

III

IV



V

VI

VII

Chart 1

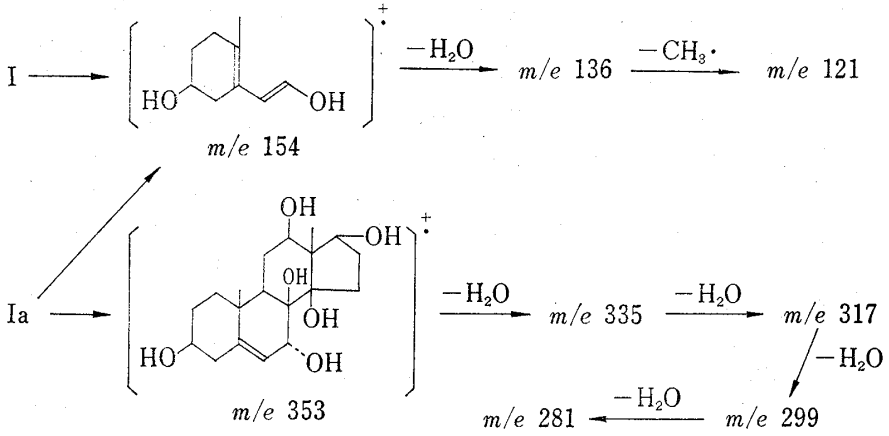


Chart 2

Table I. Chemical Shift (ppm) for 18–CH_3 and 19–CH_3 in Pregnane Derivatives[a)]

Compound	18–CH_3	19–CH_3
Sarcostin (IV)	1.89	1.41
Utendin (V)	1.76	1.04
Deacylmetaplexigenin (VI)	1.93	1.42
Pergularin (VII)	1.42	1.06
Gagaimol (Ia)	1.94	1.40
Gagaimol-7-methyl ether (II)	1.92	1.44
7β-Methoxysarcostin (III)	1.99	1.45

a) Measured in pyridine-d_5.

8β-hydroxyl group, in 1—3 diaxial relation to both 18- and 19-methyl groups.[11] The presence of 7α- and 8β-hydroxyl groups in I was supported by the following results. In the PMR spectrum of I, irradiation on the proton doublet at δ 5.90 (6-vinyl proton) changes the proton doublet at δ 4.55 (7β-H) into a singlet. The coupling constant (J=5 Hz) of the proton at the 7-position is in good agreement with that reported by Shoppee and Newman,[13] and the configuration of the hydroxyl group at the 7-position is α. Although there is no unequivocal evidence for the presence of 14β-hydroxyl group and for the configuration of the 17-hydroxyl group, the biogenetic analogy to the other natural polyoxypregnanes isolated from Asclepiadaceae plants is suggestive of the presence of 14β and 17β-hydroxyl groups.[14] From the above results, the formula (I) was proposed for the structure of dibenzoylgagaimol. In order to corroborate the structure of I, the ^{13}C-NMR (CMR) spectrum was analysed as follows: δ in pyridine-d_5, 11.8 (C-18), 15.6 (C-21), 19.7 (C-19), 26.5 (C-11), 31.9 (C-2), 34.4 (C-16),[15a] 35.5 (C-15),[15a] 38.1 (C-10), 38.6 (C-1), 39.9 (C-4), 43.3 (C-9), 58.8 (C-13), 69.0 (C-7), 71.2 (C-3), 74.9 (C-20), 75.9 (C-12), 77.3 (C-8), 86.4 (C-14), 88.9 (C-17), 124.0 (C-6), 128.0 (C-3′ and 7′), 129.5 (C-4′ and 6′), 135.3 (C-5′), 142.1 (C-5), 165.0, 166.6 (C-1′).[15b] Assignments of the carbon atoms in I were performed by the off-resonance decoupling technique, and by comparison of the CMR spectra of the model compounds, 3-O-acetyl-12,20-O-dibenzoylsarcostin[16] and other polyoxypregnane derivatives.[17]

Gagaimol-7-methyl ether (II) formed prisms, mp 153°/239°, $[\alpha]_{589}^{20}$ −30.0° (c=0.13 in MeOH, from ORD measurement), which with Liebermann–Burchard reaction gave color changes (violet→green), with antimony trichloride yellow→green coloration. The molecular

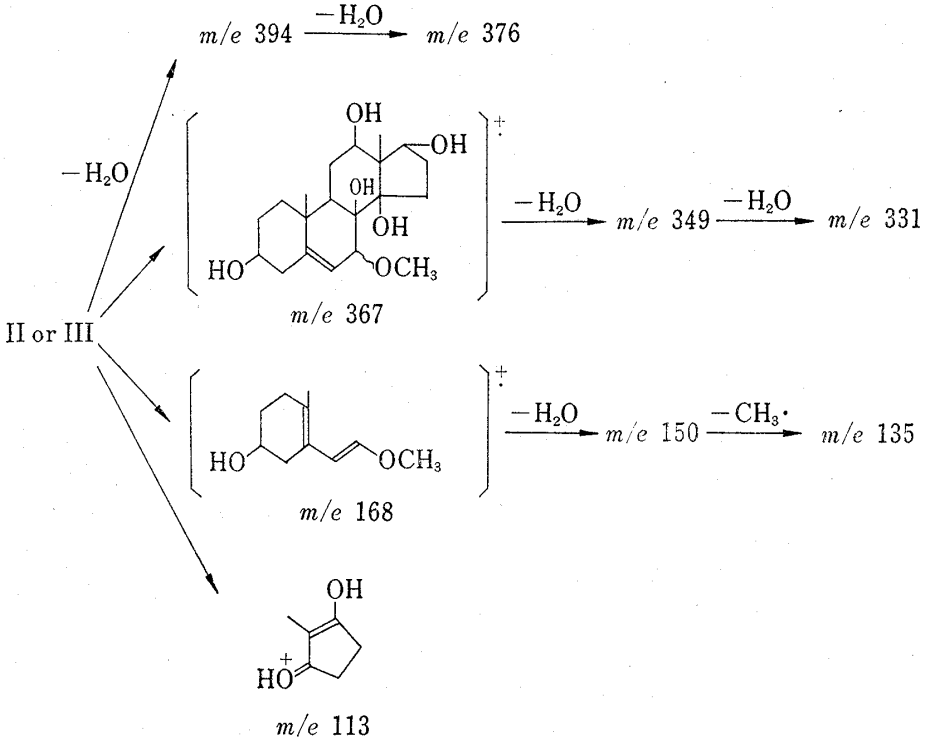


Chart 3

13) C.W. Shoppee and B.C. Newman, *J. Chem. Soc.* (*C*), **1968**, 981.
14) H. Seto, K. Hayashi, and H. Mitsuhashi, *Chem. Pharm. Bull.* (Tokyo), **25**, 611 (1977).
15) *a*) Assignment may be reversed; *b*) The signal of C-2′ was overlapped with signals of the solvent.
16) The CMR spectra of the compound were presented by Dr. S. Terada, Hokkaido University. We are indebted to Dr. Terada for the information and his valuable advices for the assignments of the CMR spectrum of I.
17) *a*) T. Yamagishi, K. Hayashi, H. Mitsuhashi, M. Imanari, and K. Matsushita, *Tetrahedron Letters*, 1973, 3527; *b*) *Idem*, *ibid.*, **1973**, 3531; *c*) *Idem*, *ibid.*, **1973**, 4735; *d*) S. Terada, K. Hayashi, and H. Mitsuhashi, *ibid.*, **1978**, 1995.

formula, $C_{22}H_{36}O_7$, was given for II from its elemental analysis and mass spectral measurement. The IR absorptions at 3500, 3350, 3200 cm^{-1} indicated the presence of hydroxyl groups, but there was no band assignable to a carbonyl group. Acetylation of II with acetic anhydride in pyridine gave a triacetate (IIa), mp 150°/205—208°, $C_{28}H_{42}O_{10}$, which showed hydroxyl absorptions at 3520, 3380 cm^{-1}. The mass spectrum of II exhibits the fragment ions at *m/e* 394, 376, 367, 349, 331, 168 (base peak), 150, 135, 113 as illustrated in Chart 3, and these fragment pattern was similar to that of Ia. In comparison of the mass spectra of Ia and II, it is supported that one hydroxyl group and one methoxyl group exist in the rings A and B. The PMR spectrum of II showed the signals for two tertiary methyl groups at δ 1.44 (s, 19-CH_3), and 1.92 (s, 18-CH_3), one secondary methyl group at δ 1.50 (d, J=6 Hz, 21-CH_3), one methoxyl group at δ 3.33 (s, 7-OCH_3), four methines at δ 3.79 (d, J=5.5 Hz, 7β-H), δ 3.86 (m, 3α-H), δ 3.93 (dd, J=5 and 12 Hz, 12α-H), δ 4.40 (q, J=6 Hz, 20-H), and one olefinic proton at δ 5.82 (d, J=5.5 Hz, 6-vinylic proton). The assignments of these signals were confirmed by comparing this spectrum with the spectra of Ia and other polyoxypregnane derivatives.[12] The highly deshielded signals of two tertiary methyl groups of II suggested the presence of 8β-hydroxyl group in the formula (Table I). On the basis of biogenetic analogy to other polyoxypregnane derivatives, the presence of 14β, 17β-hydroxyl groups is suggested. From these results, the structure of compound (II) is presumed to be gagaimol-7-methyl ether.

From the same source our group isolated a new aglycone (III) in 1966, which showed mp 210—218° and the molecular formula, $C_{22}H_{36}O_7$.[7] Since III was very similar to II with respect to the color reaction with antimony trichloride, the spectroscopic study of this compound (III) was carried out. Compound (III) formed plates, $[\alpha]_{589}^{20}$ +144° (c=0.23, in MeOH, from ORD measurement), which with Liebermann-Burchard reaction gave color changes (violet→yellow green), with antimony trichloride yellow→green coloration. The molecular formula, $C_{22}H_{36}O_7$, was given for III from its elemental analysis[7] and mass spectral measurement. The IR absorption at 3400 cm^{-1} (broad) indicated the presence of hydroxyl groups, but there was no band assignable to a carbonyl group.[7] The mass spectrum of III exhibits similar fragmentation patterns to those of II as follows: *m/e* 412 (M^+), 394, 376, 367,[10] 168 (base peak), 150, 135, 113[10] (Chart 3). The PMR spectrum of III showed the signals for two tertiary methyl groups at δ 1.45 (s, 19-CH_3) and δ 1.99 (s, 18-CH_3), one secondary methyl group at δ 1.59 (d, J=6 Hz, 21-CH_3), one methoxyl group at δ 3.45 (s, 7-OCH_3), four methines at δ 3.90 (dd, J=5 and 11 Hz, 12α-H), δ 3.86 (m, 3α-H), δ 4.00 (br s, 7α-H), 4.39 (q, J=6 Hz, 20-H) and one olefinic proton at δ 5.54 (br s, 6-vinylic proton). In comparison of the PMR spectra of II and III, the coupling patterns of the vinylic proton and the proton adjacent to a methoxyl group were remarkably changed and the coupling pattern of the proton adjacent to a methoxyl group is consistent with that of the 7α-proton of the cholest-5-en-3β,7β-diol.[13] The presence of 17-hydroxyl group was supported by the following decoupling experiment. The irradiation of 21-methyl group protons (δ 1.59) collapsed the quartet at δ 4.39 to a singlet. The presence of 8β-hydroxyl group was supported by the chemical shifts of two tertiary methyl groups, and the biogenetic analogy to other polyoxypregnane derivatives suggests the presence of 14β-hydroxyl group and also suggests the configuration of 17-hydroxyl group as β. From these results, III seemed to be the isomer of gagaimol-7-methyl ether at the 7-position, that is, 7β-methoxy-sarcostin is the structure of this compound (III).

The above three compounds (I, II, III) are the first example of polyoxypregnane derivatives which had been obtained from the Asclepiadaceae plants, and shown to have an oxygen functional group at the 7-position. Many workers, however, reported that the 7-position of cholesterol is oxidized by the autoxidation, and that the product is 7-hydroxycholesterol.[18]

18) L.F. Fieser and M. Fieser, "Steroids," Maruzen Company, LTD., Tokyo, 1960, pp. 233—237.

Moreover, 7α-hydroxycholesterol is readily etherified at the 7-position under mild acid catalysis in methanol to the 7α-methyl ether, which epimerized to a more stable equatorial epimer, the 7β-methyl ether.[18] As gagaimol-7-methyl ether (II) and 7β-methoxysarcostin (III) were isolated from the aglycone mixture obtained by the hydrolysis under conditions of mild acid catalysis in methanol, it is probable that these two compounds are artifacts formed from the derivatives of Ia. It has not been clear whether I is a natural product or an artifact. For the purpose of elucidating this point, the studies is now in progress on the autoxidation of Δ^5-polyoxypregnane derivatives, such as IV.

Experimental

All melting points were uncorrected. The PMR and CMR spectra were measured with tetramethylsilane as the internal reference. Abbreviations: s=singlet, d=doublet, dd=double doublet, t=triplet, m=multiplet, br=broad. The following instruments were used for the physical data: melting points; Mitamura's micromelting point apparatus (hot-stage type). UV spectra; Shimadzu QV-50 UV Spectrometer. IR spectra; Hitachi IR Spectrometer EPI-G3. NMR spectra; JEOL·JNM-4H-100, Varian HA 100D, Varian CFT-20, and JEOL FX-100 NMR Spectrometer. Mass spectra (MS); JEOL·JMS-01SG-2 Mass Spectrometer and Hitachi RMU-6E Mass Spectrometer. ORD; JASCO ORD/UV-5.

Isolation of Dibenzoylgagaimol (I)——From the crude aglycone (30 g) which was previously reported,[5,6] benzoylisoramanone (600 mg),[6] gagaminin (290 mg),[2] and dibenzoylgagaimol (35 mg)[5] were isolated by alumina column chromatography using $CHCl_3$–MeOH solution as an eluent. I was obtained from the fractions eluted with 5% MeOH–$CHCl_3$.

Dibenzoylgagaimol (I)[5]——Colorless needles from acetone, mp 175—179°. When this material was recrystallized from MeOH+H_2O, the melting point showed 192—197°, $[\alpha]_{589}^{20}$ +26° (c=0.15 in MeOH, from ORD measurement). *Anal.* Calcd. for $C_{35}H_{42}O_9$: C, 69.29; H, 6.98. Found: C, 68.89; H, 7.27. IR ν_{max}^{Nujol} cm^{-1}: 3300, 3200, 1725, 1685, 1600, 1590, 1280. UV λ_{max}^{EtOH} nm (log ε): 229 (4.26), 273 (3.50). MS *m/e*: 606 (M^+), 588, 570, 484, 466, 448, 430, 412, 362, 344, 326, 311, 293, 275, 191, 173, 161, 154, 136, 122 (base peak), 121, 105, 77. PMR (in pyridine-d_5) δ: 1.26 (3H, s, 19-CH_3), 1.52 (3H, d, J=6 Hz, 21-CH_3), 2.14 (3H, s, 18-CH_3), 3.70 (1H, m, 3α-H), 4.55 (1H, d, J=5 Hz, 7β-H), 5.37 (1H, q, J=6 Hz, 20-H), 5.62 (1H, dd, J=5 and 10 Hz, 12α-H), 5.90 (1H, d, J=5 Hz, 6-vinyl proton), 7.10—8.10 (10H, m, benzene ring protons).

Estimation of $Pb(OAc)_4$ Consumption of Dibenzoylgagaimol (I)——To a solution of 0.04 mmol of I dissolved in dioxane (5 ml), 10 ml of 1/25 N $Pb(OAc)_4$ in AcOH was added, and the mixture was allowed to stand at room temperature (15—20°) and 2 ml aliquots titrated by jodometry. A blank was prepared and titrated similarly. The results are shown as follows: $Pb(OAc)_4$ mol (time: hr); 0.77(5), 1.30(26), 1.62(51), 1.82(69), 1.84(95).

Alkaline Hydrolysis of Dibenzoylgagaimol (I)——A solution of 60 mg of I in 3 ml of 5% KOH–MeOH was kept at room temperature for 72 hr in N_2. After adding 3 ml of H_2O, the MeOH was removed under a reduced pressure. The aqueous solution was extracted successively with small amount of ether and then BuOH. The solvent of the BuOH solution was evaporated under a reduced pressure. After recrystallization from acetone, it gave 10 mg of gagaimol (Ia), mp 274—277°. The aqueous layer was acidified with H_3PO_4 and extracted with ether. After the removal of the solvent, 15 mg of acidic substance was left. The identification of the acidic fraction was carried out as follows: Paper chromatography (solvent system; BuOH/1.5 N NH_3, paper; Toyo Roshi No. 50) showed the spot (Rf 0.42), benzoic acid (Rf 0.42). Recrystallization from H_2O, gave colorless plates, mp 122°.

Gagaimol (Ia)——Recrystallization from acetone afforded Ia, mp 274—277°. Color test: $SbCl_3$ (yellow→green). $[\alpha]_{589}^{25}$ 0° (c=0.16 in MeOH, from ORD measurement), $[\alpha]_{500}^{25}$ −6°, $[\alpha]_{400}^{25}$ −24.2°, $[\alpha]_{350}^{25}$ −42.4°, $[\alpha]_{300}^{25}$ −96.8°. *Anal.* High-resolution MS: Calcd. for $C_{21}H_{34}O_7$ (M^+, m/e): 398.2305. Found: 398.2316; Calcd. for $C_{19}H_{29}O_6$ (M^+−45, *m/e*): 353.1964. Found: 353.1983; Calcd. for $C_9H_{14}O_2$ (M^+−244, *m/e*): 154.0994. Found: 154.0987. MS *m/e*: 398 (M^+), 380, 362, 353, 335, 317, 299, 281, 209, 171, 161, 154, 136, 121. IR ν_{max}^{Nujol} cm^{-1}: 3400 (br). PMR (in pyridine-d_5) δ: 1.40 (3H, s, 19-CH_3), 1.53 (3H, d, J=6 Hz, 21-CH_3), 1.94 (3H, s, 18-CH_3), 3.90 (1H, m, 3α-H), 3.98 (1H, dd, J=5 and 10 Hz, 12α-H), 4.39 (1H, q, J=6 Hz, 20-H), 4.48 (1H, d, J=5 Hz, 7β-H), 5.85 (1H, d, J=5 Hz, 6-vinyl proton).

Isolation of Gagaimol-7-methyl Ether (II)——The mother liquors of the ester type aglycones, benzoylisoramanone,[6] gagaminin,[2,9] and I, and other eluted fractions, from which no crystalline compound was obtained were combined, and the solvent was evaporated to give the ester type aglycone mixture as reported in the previous paper.[7] The mixture (27 g) was dissolved in 800 ml of 5% methanolic KOH, and the solution was allowed to stand for 48 hr at room temperature. The reaction mixture was treated as usual and then extracted with $CHCl_3$ and BuOH. From the BuOH extract, 18 g of residue was obtained. The residue (18 g) was submitted to column chromatography over 400 g of SiO_2, and eluted with $CHCl_3$–MeOH mixture to give pergularin[7] (VII, 22 mg), sarcostin[7] (IV, 200 mg), and II (20 mg). From the fractions eluted with 1% MeOH–$CHCl_3$, II was obtained.

Gagaimol-7-methyl Ether (II)——II was recrystallized from acetone to give prisms, mp 153/239°, $[\alpha]_{589}^{25}$ −30.0° (c=0.13 in MeOH, from ORD measurement). It showed violet→green with a Liebermann–Burchard reagent, and yellow→green with $SbCl_3$. *Anal.* Calcd. for $C_{22}H_{36}O_7 \cdot 1/2H_2O$: C, 62.70; H, 8.77. Found: C, 62.69; H, 8.85. IR ν_{max}^{Nujol} cm^{-1}: 3500, 3350, 3200. MS m/e: 412 (M^+), 394, 376, 367, 352, 349, 344, 331, 317, 299, 218, 168 (base peak), 161, 150, 135, 113, 45. PMR (in pyridine-d_5) δ: 1.44 (3H, s, 19-CH_3), 1.50 (3H, d, J=6 Hz, 21-CH_3), 1.92 (3H, s, 18-CH_3), 3.33 (3H, s, 7-OCH_3), 3.79 (1H, d, J=5.5 Hz, 7β-H), 3.86 (1H, m, 3α-H), 3.93 (1H, dd, J=5 and 12 Hz, 12α-H), 4.40 (1H, q, J=6 Hz, 20-H), 5.82 (1H, d, J=5.5 Hz, 6-vinylic proton).

Gagaimol-7-methyl Ether Triacetate (IIa)——10 mg of II was dissolved in 0.9 ml of pyridine, and 0.4 ml of Ac_2O was added. The mixture was allowed to stand for 12 hr at room temperature. The mixture was poured into ice and extracted with ether. The ether solution was treated as usual. After evaporation of the solvent, the residue was recrystallized from acetone to columns (9 mg), mp 150/205—208°. *Anal.* Calcd. for $C_{28}H_{42}O_{10}$: C, 62.43; 7.86. Found: C, 62.18; H, 7.89. IR ν_{max}^{Nujol} cm^{-1}: 3520, 3380, 1740, 1725, 1715. MS m/e: 520 (M^+-H_2O), 502, 478, 460, 446, 210, 161, 150 (base peak), 43. PMR (in pyridine-d_5) δ: 2.09 (6H, s, -OAc×2), 2.26 (3H, s, -OAc).

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