[Chem. Pharm. Bull. 24(7)1602—1608(1976)]

UDC 547.814.02 : 581.192 : 582.29.04

Constituents of the Lichen in the Genus *Hypogymnia*. II.[1] Vittatolic Acid, a New optically Active Depsidone, and 2′-O-Methylphysodic Acid from *Hypogymnia vittata* (Ach.) Gas.

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(Received November 17, 1975)

Two new depsidones named vittatolic acid (**4**) and 2′-O-methylphysodic acid (**5**) have been isolated from the lichen *Hypogymnia vittata* (Ach.) Gas. along with physodic acid (**1**), atranorin (**2**), oxyphysodic acid (**3**), zeorin (**6**), and ergosterol peroxide (**7**).

Vittatolic acid (**4**) is the first optically active depsidone possessing a secondary hydroxyl in the side chain. The plain structure of vittatolic acid has been clarified on the basis of physicochemical evidence and the conversion to physodic acid (**1**), and the absolute configuration at the asymmetric carbon in the side chain of **4** follows from the application of the Horeau's method and the Brewster's benzoate rule.

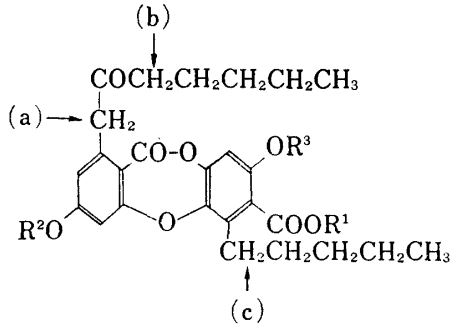
The structure of 2′-O-methylphysodic acid (**5**) has been determined on the basis of chemical and physicochemical evidence.

In the thin-layer chromatographic (TLC) investigation on the lichen metabolites of the genus *Hypogymnia* (Parmeliaceae), Nuno showed the presence of two unknown phenolic substances in addition to physodic acid (**1**) and atranorin (**2**) in the lichen *Hypogymnia vittata* (Ach.) Gas. which was collected in Japan and Sikkim.[3] As a continuative study on the constituents of the lichen in the genus *Hypogymnia*,[1] we have been working on the lichen metabolites of *H. vittata*. As shown in the TLC diagram (Fig. 1), an additional new phenolic substance (spot e) has been detected by the anisaldehyde-sulfuric acid reagent along with the above mentioned two phenolics (spots a and b) which are shown up by the same reagent and also by the ferric chloride reagent. We have isolated these three substances from the lichen materials collected at Mt. Ōmine in Nara prefecture, and clarified that the one (spot b) is identical with oxyphysodic acid (**3**) whose structure has been reported in the preceding paper[1] and the other two are new depsidones named vittatolic acid (**4**) (spot a) and 2′-O-methylphysodic acid (**5**) (spot e), respectively. This paper deals with the full account on the structure elucidation of the latter two depsidones.

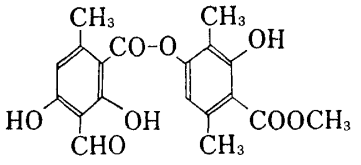
The ether extractive of the lichen materials was first divided into the chloroform insoluble and soluble portions. Silica gel chromatographic separation of the insoluble portion gave 2′-O-methylphysodic acid (**5**), physodic acid (**1**), oxyphysodic acid (**3**),[1] and vittatolic acid (**4**) successively, while atranorin (**2**), zeorin (**6**),[4] and ergosterol peroxide (**7**)[5] were obtained from the soluble portion.

Vittatolic acid (**4**) is a *levo* rotatory depsidone and was colored violet by the ferric chloride reagent but was negative for the sodium hypochlorite and *p*-phenylenediamine reagent.[6a]

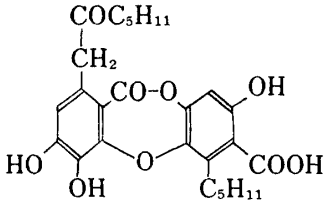
1) Part I: T. Hirayama, F. Fujikawa, I. Yosioka, and I.Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **24**, 1596 (1974).
2) Location: *a) Yamashina-misasagi, Higashiyama-ku, Kyoto 607, Japan*; *b) 133-1, Yamada-kami, Suita, Osaka 565, Japan*
3) M. Nuno, *Journ. Jap. Bot.*, **39**, 97 (1964).
4) I. Yosioka, T. Nakanishi, H. Yamauchi, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **20**, 147 (1972).
5) R. Takahashi, O. Tanaka, and S. Shibata, *Phytochemistry*, **11**, 1850 (1972).
6) Y. Asahina and S. Shibata, "Chemistry of Lichen Substances," Japan Society for the Promotion of Science, Tokyo, 1954; *a)* p. 10; *b)* p. 130; *c)* p. 137; *d)* p. 140; *e)* p. 124.



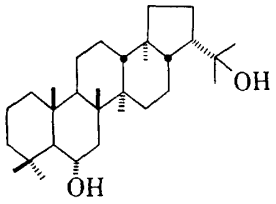
	R^1	R^2	R^3	
1	H	H	H	physodic acid
1a	H	Ac	Ac	
1b	CH_3	Ac	Ac	
5	H	H	CH_3	2′-O-methylphysodic acid
5a	H	Ac	CH_3	
5b	CH_3	H	CH_3	
9	H	CH_3	H	4-O-methylphysodic acid



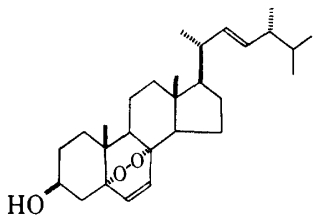
2 : atranorin



3 : oxyphysodic acid



6 : zeorin



7 : ergosterol peroxide

Chart 1

The infrared (IR) spectrum of vittatolic acid shows the absorption bands at 3413, 3068 cm^{-1} (hydroxyl), 1704, 1663m^{-1} c^1 (depsidone, carbonyl, and carboxyl), and 1610 cm^{-1} (aromatic ring). The elemental analysis and mass spectrometry show the molecular composition of vittatolic acid as $C_{26}H_{30}O_9$ which contains one more oxygen than physodic acid (**1**).

Acetylation of vittatolic acid with acetic anhydride and conc. sulfuric acid gave a triacetate (**4a**) which was subsequently treated with ethereal diazomethane to furnish methyl vittatolate triacetate (**4b**).

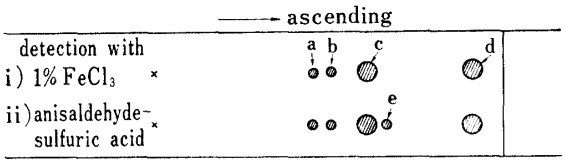


Fig. 1. TLC Diagram of the Ether Extractive of *Hypogymnia vittata*

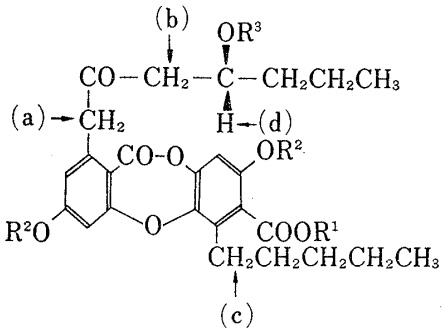
developing solvent: benzene–dioxane–AcOH=90: 25: 4
a) vittatolic acid (**4**) (i: violet, ii: brown-red)
b) oxyphysodic acid (**3**) (i: bluish violet, ii: brown-red)
c) physodic acid (**1**) (i: violet, ii: brown-red)
d) atranorin (**2**) (i: purple, ii: orange-red)
e) 2′-O-methylphysodic acid (**5**) (i: negative, ii: brown-red)

The examinations of proton magnetic resonance (PMR) spectra (Table I) of vittatolic acid (**4**), vittatolic acid triacetate (**4a**), and methyl vittatolate triacetate (**4b**) comparing with those of physodic acid (**1**),[1] physodic acid diacetate (**1a**),[1] and methyl physodate diacetate (**1b**)[7] have shown that vittatolic acid is a very similar depsidone to physodic acid (**1**) and differs only in the alkyl ketone side chain by possessing a secondary hydroxyl.

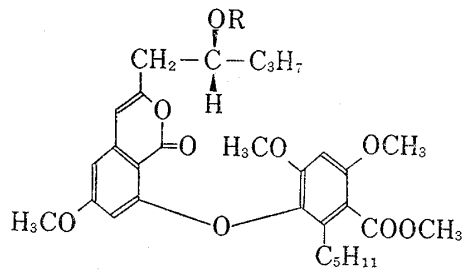
Thus, the signal due to one of two methylenes (protons b) located at α to the ketone is observed as a triplet (J=7 Hz) at δ 2.51 in **1** while the corresponding signal is replaced by a doublet (J=7 Hz) at δ 2.66 in **4**. In the case of the acetates (**1a** and **4a**), a three-proton singlet (δ 2.02) due to an alcoholic acetoxyl is observed in addition to two singlets of phenolic acetoxyls (δ 2.22 and 2.28) in **4a** whereas only the signals due to two phenolic acetoxyls (δ 2.24 and 2.30) are observed in **1a**. In addition, the one-proton quintet (δ 5.29 in **4a** or δ 5.27 in **4b**), which is assignable to a methine proton (d) attached to a carbon bearing an acetoxyl, has suggested the alcoholic function in vittatolic acid is secondary. In order to clarify the location of the secondary alcoholic hydroxyl, the decoupling experiments were undertaken. On irradiation

7) Prepared from physodic acid triacetate (**1a**).[1,5]

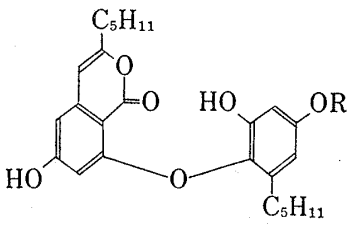
of the signal at δ 2.77 (methylene b) in the spectrum of **4a**, the quintet at δ 5.29 (methine d) is varied to a triplet (J=7 Hz) and irradiation of the latter signal caused the change of the former to a singlet, thus the location of secondary hydroxyl in vittatolic acid being clarified to be β to the ketone.



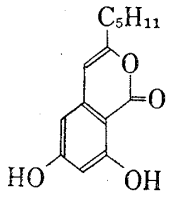
	R^1	R^2	R^3	
4	H	H	H	vittatolic acid
4a	H	Ac	Ac	
4b	CH_3	Ac	Ac	



8 : R=H
8a : R=COCH(C_6H_5)C_2H_5
8b : R=COC_6H_5



10 : R=H physodone
10a : R=CH_3 2′-O-methylphysodone



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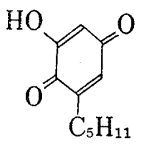

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Chart 2

TABLE I. PMR Data of Physodic Acid (**1**), Vittatolic Acid (**4**), and Their Derivatives[a]
(δ Values at 90 MHz, Coupling Constants in Hz)

	CH_3	CH_2	Ar-H	Others
1[b]	0.87(t, J=6)[c] 0.93(t, J=6)[c]	(a)3.94(s) (b)2.51(t, J=7) (c)3.16(br)	6.49(1H, d, J=2) 6.60(2H, br)	1.10—2.00(12H, br, $-CH_2-\times 6$)
4[b]	0.96(t-like) ×2	(a)4.01(s) (b)2.66(d, J=7) (c)3.13(br)	6.50(1H, d, J=2) 6.60(2H, br)	1.16—2.00(10H, br, $-CH_2-\times 5$) *ca.* 4.0(1H, br, >CH-O-)(d)
1a[d,1]	0.88(t, J=6) 0.91(t, J=6)	(a)4.03(s) (b)2.51(t, J=7) (c)3.00(br)	6.87(1H, d, J=2) 7.00(1H, s) 7.03(1H, d, J=2)	1.15—2.05(12H, br, $-CH_2-\times 6$) 2.24, 2.30(3H each, s, OAc×2)
4a[d]	0.91(t, J=6) ×2	(a)4.01(s) (b)2.77(d, J=7) (c)2.96(br)	6.83(1H, d, J=2) 6.94(1H, s) 7.01(1H, d, J=2)	1.11—1.86(10H, br, $-CH_2-\times 5$) 2.02, 2.22, 2.28(3H each, s, OAc×3) 5.29(1H, qui, J=7, >CH-O-)(d) 8.30(1H, br, COOH)
1b[d]	0.89(t-like) 0.92(t-like)	(a)4.00(s) (b)2.52(t, J=7) (c)2.87(br)	6.85(1H, d, J=2) 6.98(1H, s) 7.00(1H, d, J=2)	1.09—1.82(12H, br, $-CH_2-\times 6$) 2.23, 2.29(3H each, s, OAc×2) 3.88(3H, s, $COOCH_3$)
4b[d]	0.91(t, J=6)[c] ×2	(a)3.98(s) (b)2.76(d, J=7) (c)2.86(br)	6.82(1H, d, J=2) 6.92(1H, s) 6.99(1H, d, J=2)	1.08—1.87(10H, br, $-CH_2-\times 5$) 2.01, 2.22, 2.28(3H each, s, OAc×3) 3.86(3H, s, $COOCH_3$) 5.27(1H, qui, J=7, >CH-O-)(d)

a) abbreviations: br=broad signal, d=doublet, qui=quintet, s=singlet, t=triplet
b) measured in CD_3OD
c) deformed signal
d) measured in $CDCl_3$

In addition to the above evidence, the almost quantitative conversion of vittatolic acid to physodic acid (**1**) by reduction with zinc and hydrochloric acid in acetic acid has led to the structure **4** for vittatolic acid, except the configuration at the carbon bearing the secondary hydroxyl.[8]

Finally, the absolute configuration at the carbon bearing the secondary hydroxyl in vittatolic acid (**4**) has been established by application of the Horeau's method[9] and the Brewster's benzoate rule.[10]

Prolonged treatment of vittatolic acid (**4**) with ethereal diazomethane[11] furnished methyl isovittatolate trimethyl ether (**8**) which was then reacted with excess (±)-α-phenylbutyric anhydride in pyridine to afford the α-phenylbutyrate (**8a**). The specific rotations of recovered α-phenylbutyric acid in three experiments were +2°, +5°, and +8°, respectively, thus the absolute configuration in question being determined to be R.

On the other hand, benzoylation of methyl isovittatolate trimethyl ether (**8**) with benzoyl chloride in pyridine gave a benzoate (**8b**). The molecular rotation differences between **8b** ($[M]_D=-339.6°$) and **8** ($[M]_D=-178.8°$) was −160.8° and the absolute configuration at the questioned carbon is assigned as R which coincides with the above determination by the Horeau's method.

Although some depsidones such as salazinic acid,[6b] constictic acid,[12] protocetraric acid,[6c] physodalic acid (as acetate),[6d] fumarprotocetraric acid (as fumarate),[6d] and variolaric acid (as lactone),[6e] have been known to contain a primary alcoholic function in their structures, vittatolic acid (**4**) is the first optically active depsidone possessing a secondary hydroxyl in the side chain. It should be pointed out here that, judging from the TLC diagram reported by Nuno,[3] the lichen *Hypogymnia vittata* collected in Formosa contains physodic acid (**1**), atranorin (**2**), and oxyphysodic acid (**3**), but no vittatolic acid (**4**) whereas the lichen collected in U.S.A. contains only physodic acid (**1**) along with an unidentified substance.

Table II. PMR Data of 2′-O-Methylphysodic Acid (**5**) and Its Derivatives
(δ Values at 90 MHz, Coupling Constants in Hz)[a]

	CH_3	CH_2	Ar-H	Others
5[b]	0.87(t-like)	(a)4.01(s)	6.62(1H, d, J=2)	*ca.* 1.1—1.9(12H, br, $-CH_2-\times 6$)
	0.92(t-like)	(b)2.51(t, J=7)	6.72(1H, d, J=2)	3.83(3H, s, OCH_3)
		(c)2.84(br)	6.78(1H, s)	
5a[c]	0.89(t-like)	(a)4.02(s)	6.71(1H, s)	*ca.* 1.0—2.0(12H, br, $-CH_2-\times 6$)
	0.90(t-like)	(b)2.49(t, J=7)	6.78(1H, d, J=2)	2.28(3H, s, OAc)
		(c)2.82(br)	6.96(1H, d, J=2)	3.81(3H, s, OCH_3)
5b[c]	0.90(t-like) ×2	(a)3.83(s)	6.42(2H, s)	*ca.* 1.0—2.0 (12H, br, $-CH_2-\times 6$)
		(b)2.59(t, J=7)	6.61(1H, s)	3.73, 3.87(3H each, both s, $OCH_3\times 2$)
		(c)*ca.* 2.3—2.8[d] (br)		

a) Abbreviations are same as in Table I.
b) measured in d_6-acetone
c) measured in $CDCl_3$
d) The signal is overlapped by a triplet at δ 2.59 (b).

Another new depsidone named 2′-O-methylphysodic acid (**5**) was detected on the thin-layer chromatogram only by the anisaldehyde–sulfuric acid reagent but not by the ferric chloride reagent (Fig. 1). The isolated substance was negative for the ferric chloride reagent,

8) T. Hirayama, F. Fujikawa, I. Yosioka, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **23**, 693 (1975) (preliminary report).
9) A. Horeau, *Tetrahedron Letters*, **1961**, 506; *idem*, *ibid.*, **1962**, 965.
10) J.M. Brewster, *Tetrahedron*, **20**, 2431 (1964).
11) Y. Asahina and F. Fujikawa, *Chem. Ber.*, **68**, 2020 (1935).
12) I. Yosioka, Y. Morita, and K. Ebihara, *Chem. Pharm. Bull.* (Tokyo), **18**, 2364 (1970).

the sodium hypochlorite reagent, and also for the potassium hydroxide–sodium hypochlorite reagent.[6a] The molecular composition $C_{27}H_{32}O_8$ revealed by the elemental analysis and mass spectrometry corresponds to a monomethyl derivative of physodic acid (**1**). The PMR spectrum (Table II) of 2′-O-methylphysodic acid is very alike to that of physodic acid (**1**) except the additional presence of one three-proton singlet at δ 3.83 in the former. Since the new depsidone is soluble in aqueous 10% sodium bicarbonate, it is not a methyl ester but is presumed to be a methyl ether of physodic acid (**1**). Acetylation of **5** with acetic anhydride and conc. sulfuric acid gave a monoacetate (**5a**), while brief treatment with ethereal diazomethane furnished a methyl ester (**5b**) which possesses two methoxyls as shown by the PMR spectrum: two three-proton singlets at δ 3.73 and 3.87.

4-O-Methylphysodic acid (**9**)[13] has been known as a naturally occurring methyl ether of physodic acid, however, since **9** is distinct from the present new depsidone by their physical properties and the ferric chloride coloration (**9**: positive), the new depsidone has been assumed to be the 2′-O-methyl derivative of physodic acid and the assumption has been verified by the following chemical degradation.

Thus, formic acid treatment of 2′-O-methylphysodic acid (**5**) furnished 2′-O-methylphysodone (**10a**), which in turn was subjected to the nitric acid oxidation as described in the preceding paper[1] to afford olivetonide (**11**) and 2-hydroxy-6-pentyl-1,4-benzoquinone (**12**), both of which were also obtained from physodone (**10**) by the same oxidative degradation.[1] Therefore, the structure **5** has been established for 2′-O-methylphysodic acid. Very recently, Elix reported the structure elucidation of 2′-O-methylphysodic acid (**5**) in addition to that of oxyphysodic acid (**3**) which were isolated from the lichen *Hypogymnia billardieri* (Mont.) R. Filson.[14] The conclusion is in good agreement with the present result.

Experimental[15]

Isolation of the Constituents——Air-dried lichen materials (50 g), collected at Mt. Ōmine in Nara prefecture, were extracted with ether twice (500 ml each for 48 hr) successively at room temperature. The ether extractive (3.7 g) was then treated with $CHCl_3$ and the insoluble portion (2.8 g), which contained most of depsidones, was collected by filtration and chromatographed on a silica gel (Merck 70—230 mesh) column eluting with benzene–dioxane–AcOH (12: 2: 0.2). The first eluting depsidone was crystallized from aq. MeOH to give 2′-O-methylphysodic acid (**5**, 150 mg, 0.3%) as colorless needles of mp 148—149°. *Anal.* Calcd. for $C_{27}H_{32}O_8$: C, 66.92; H, 6.66. Found: C, 66.69; H, 6.72. IR ν_{max}^{KBr} cm^{-1}: 3284 (br) (OH), 1730 (br), 1700 (depsidone, CO, COOH), 1616, 1600 (aryl C=C). Mass Spectrum *m/e* (%): 484 (M^+, 13), 440 (M^+-CO_2,100). PMR (d_6-acetone) δ: as given in Table II. The second eluate, on crystallization from aq. MeOH, gave physodic acid (**1**, 750 mg, 1.5%) as colorless needles of mp 205°, which was identified by direct comparison (mixed mp, TLC, and IR (KBr)) with the authentic sample.[1] The third eluting substance was crystallized from aq. MeOH to give oxyphysodic acid (**3**, 350 mg, 0.7%) as colorless needles of mp 187° (decomp.), which was identified with the authentic sample[1] as above. The finally eluting depsidone was crystallized from aq. MeOH to give vittatolic acid (**4**, 150 mg, 0.3%) as colorless needles of mp 178° (decomp.), $[\alpha]_D^{24}$ −11° (c=1.0, EtOH). *Anal.* Calcd. for $C_{26}H_{30}O_9$: C, 64.18; H, 6.22. Found: C, 64.14; H, 6.24. IR ν_{max}^{KBr} cm^{-1}: 3413 (br), 3068 (br) (OH), 1704 (br), 1663 (depsidone, CO, COOH), 1610 (aryl C=C). Mass Spectrum *m/e* (%): 486 (M^+, 1), 442 (M^+-CO_2, 100). PMR (CD_3OD) δ: as given in Table I.

The $CHCl_3$ soluble portion of the above described ether extractive was chromatographed on a silica gel (Merck 70—230 mesh) column eluting with benzene–AcOEt (9 : 1 and 2 : 1). The compound eluted with benzene–AcOEt (9 : 1) was crystallized from acetone to give atranorin (**2**, 600 mg, 1.2%), which was identified with the authentic sample by mixed mp, TLC, and IR ($CHCl_3$). The eluate with benzene–AcOEt (2 : 1) was further purified by preparative TLC developing with benzene–AcOEt (2: 1) to afford zeorin (**6**, 50 mg) and ergosterol peroxide (**7**, 75 mg), which were recrystallized from EtOH to obtain pure samples of zeorin, mp 227° and ergosterol peroxide, mp 178°. Zeorin was identified with the authentic sample[4] by direct comparison (mixed mp, TLC, and IR (KBr)) and ergosterol peroxide was identified (TLC and IR (KBr)) with the sample prepared by photosensitized oxygenation of ergosterol.[16]

13) C.F. Culberson, *Phytochemistry*, **5**, 815 (1966).
14) J.A. Elix, *Aust. J. Chem.*, **28**, 849 (1975).
15) Instruments used in the experimental section and the experimental conditions for chromatography were same as for the preceding paper.[1]
16) A. Windaus and J. Brunken, *Liebig's Ann.*, **460**, 225 (1923).

Vittatolic Acid Triacetate (4a)——Acetylation of **4** (50 mg) with acetic anhydride (4 ml) and conc. H_2SO_4 (one drop) followed by usual work-up and crystallization from aq. MeOH afforded **4a** (43 mg) as colorless needles of mp 146—147°, $[\alpha]_D^{24}$ +1.0° (c=1.0, EtOH). *Anal.* Calcd. for $C_{32}H_{36}O_{12}$: C, 62.74; H, 5.92. Found: C, 62.69; H, 5.97. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (OAc), 1738 (br), 1720 (sh), 1685 (OAc, depsidone, CO, COOH), 1610 (aryl C=C). Mass Spectrum *m/e* (%): 612 (M^+, 5), 568 (M^+-CO_2, 100). PMR ($CDCl_3$) δ: as given in Table I.

Methyl Vittatolate Triacetate (4b)——An ice-cooled solution of **4a** (60 mg) in ether (5 ml) was treated with excess ethereal diazomethane for 10 min. Concentration of the ether solution separated colorless needles which were crystallized from aq. MeOH to give **4b** (34 mg) of mp 77—78°, $[\alpha]_D^{22}$ +1.0° (c=1.0, EtOH). *Anal.* Calcd. for $C_{33}H_{38}O_{12}$: C, 63.26; H, 6.07. Found: C, 63.31; H, 6.03. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775 (OAc), 1740, 1732 (br) (OAc, depsidone, CO, $COOCH_3$), 1612 (aryl C=C). Mass Spectrum *m/e* (%): 626 (M^+, 100). PMR ($CDCl_3$) δ: as given in Table I.

Reduction of Vittatolic Acid (4) giving Physodic Acid (1)——To a solution of **4** (30 mg) in AcOH (10 ml) and conc. HCl (5 ml) was added zinc powder (500 mg) in small portions, and the total mixture was kept stirring at room temperature for 20 min and filtered to remove excess zinc powder. The residue obtained by concentration of the filtrate was crystallized from aq. MeOH to give colorless needles of physodic acid (**1**, 28 mg) which was identified with the authentic sample[1] by direct comparison (mixed mp, TLC, and IR (KBr)).

Conversion of Vittatolic Acid (4) to Methyl Isovittatolate Trimethyl Ether (8)——To a solution of vittatolic acid (**4**) (50 mg) in ether (2 ml) was added excess ethereal diazomethane and the total mixture was left standing at room temperature for 3 days. Evaporation of the solvent gave a pale yellow residue which was purified by column chromatography (Merck silica gel PF_{254}) eluting with benzene–AcOEt (2: 1) to afford **8** as a glassy substance (42 mg), $[\alpha]_D^{24}$ −33° (c=0.66, EtOH). High resolution mass spectrum: Found: 542.251. Calcd. for $C_{30}H_{38}O_9$: 542.252. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1728 (br), 1670 (w) ($COOCH_3$, lactone CO, C=C), 1601, 1568 (w) (aryl C=C). Mass Spectrum *m/e* (%): 542 (M^+, 100). PMR ($CDCl_3$) δ: 0.76, 0.94 (3H each, both t-like, terminal $CH_3\times2$), 1.04—1.75 (10H, br m, $-CH_2-\times5$), 2.39 (2H, br, Ph–C<u>H</u>$_2$–CH_2–), 2.53 (2H, d, J=7 Hz, pyrone–C<u>H</u>$_2$–CH〈), 3.73 (6H, s, $OCH_3\times2$), 3.82, 3.84 (3H each, both s, $OCH_3\times2$), 4.06 (1H, br, >C<u>H</u>OH), 5.96, 6.29 (1H each, both d, J=2 Hz, Ar–H×2), 6.14, 6.38 (1H each, both s, Ar–H, pyrone–H).

α-Phenylbutyration of Methyl Isovittatolate Trimethyl Ether (8) giving 8a——An ice-cooled solution of **8** (21 mg) in pyridine (2 ml) was treated with a solution of (±)-α-phenylbutyric anhydride (50 mg) in pyridine (1 ml) and the total mixture was allowed to stand at room temperature overnight. The reaction mixture was added with one drop of water, heated in a boiling water bath for 30 min, acidified with 10% HCl, and extracted with ether. The ether solution was shaken with aq. $NaHCO_3$ and the aqueous layer was taken, acidified with dil. HCl, extracted with ether and the ether extract was treated in a usual manner. Evaporation of the solvent gave recovered α-phenylbutyric acid and the optical rotation was measured in $CHCl_3$. The above experiment was repeated three times and the specific rotations ($[\alpha]_D^{27}$) obtained in three runs were +5° (c=3.8), +2° (c=3.5), and +8° (c=3.2), respectively.

The remaining ether layer after removing α-phenylbutyric acid by extraction with aq. $NaHCO_3$ was washed with water, dried over $MgSO_4$, and evaporated to dryness. The product was purified by column chromatography (Merck silica gel PF_{254}) eluting with benzene–AcOEt (9: 1) to afford **8a** as a glassy substance (17 mg), $[\alpha]_D^{27}$ −36.5° (c=0.85, EtOH). High resolution mass spectrum: Found: 688.325. Calcd. for $C_{40}H_{48}O_{10}$: 688.325. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1733 (br), 1670 (w) (ester CO, lactone CO & C=C), 1601, 1570 (w) (aryl C=C). Mass Spectrum *m/e* (%): 688 (M^+, 100). PMR ($CDCl_3$) δ: *ca.* 0.6—1.0 (9H, m, terminal $CH_3\times3$), *ca.* 1.0—1.8 (12H, br, $-CH_2-\times6$), 2.39 (2H, br, Ph–C<u>H</u>$_2$–CH_2–), 2.57 (2H, d, J=7 Hz, pyrone–C<u>H</u>$_2$–CH〈), 3.37 (1H, t, J=8 Hz, –OOC–C<u>H</u>(C_6H_5)–CH_2–), 3.70, 3.73, 3.81 3.83 (3H each, all s, $OCH_3\times4$), 5.20 (1H, qui, J=7 Hz, $-CH_2$–C<u>H</u>(OR)–CH_2–), 5.63, 6.39 (1H each, both s, Ar–H, pyrone–H), 5.91, 5.99 (1H each, both d, J=2 Hz, Ar–H×2), *ca.* 7.0—7.3 (5H, m, Ar–H×5).

Benzoylation of Methyl Isovittatolate Trimethyl Ether (8) giving 8b——An ice-cooled solution of **8** (45 mg) in pyridine (2 ml) was treated with a solution of benzoyl chloride (0.5 ml) in pyridine (2 ml), and the total mixture was left standing at room temperature overnight. Usual work-up followed by purification by column chromatography (Merck silica gel PF_{254}) eluting with benzene–AcOEt (9: 1) afforded **8b** as a glassy substance (30 mg), $[\alpha]_D^{24}$ −52.6° (c=0.89, EtOH). High resolution mass spectrum: Found: 646.279. Calcd. for $C_{37}H_{42}O_{10}$: 646.278. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1729 (br), 1670 (w) (ester CO, lactone CO & C=C), 1601, 1569 (w) (aryl C=C). Mass Spectrum *m/e* (%): 646 (M^+, 100). PMR ($CDCl_3$) δ: 0.76, 0.96 (3H each, both t, J=6 Hz, terminal $CH_3\times2$), *ca.* 1.1—2.0 (10H, br, $-CH_2-\times5$), 2.42 (2H, br, Ph–C<u>H</u>$_2$–CH_2–), 2.90 (2H, d, J=7 Hz, pyrone–C<u>H</u>$_2$–CH〈), 3.73, 3.75, 3.85, 3.88 (3H each, all s, $OCH_3\times4$), 5.48 (1H, qui, J=7 Hz, >C<u>H</u>–$OCOC_6H_5$), 6.00, 6.27 (1H each, both d, J=2 Hz, Ar–H×2), 6.18, 6.42 (1H each, both s, Ar–H, pyrone–H), *ca.* 7.2—7.6 (3H, m), *ca.* 7.9—8.2 (2H, m) (–$OCOC_6$<u>H</u>$_5$).

2′-O-Methylphysodic Acid Monoacetate (5a)——Acetylation of **5** (60 mg) with acetic anhydride (4 ml) and one drop of conc. H_2SO_4 followed by usual work-up and crystallization from aq. MeOH afforded **5a** as colorless needles (51 mg) of mp 148°. *Anal.* Calcd. for $C_{29}H_{34}O_9$: C, 66.14; H, 6.51. Found: C, 66.36; H, 6.47. IR ν_{max}^{KBr} cm^{-1}: 3422 (br) (OH), 1765 (OAc), 1746, 1705 (br) (OAc, depsidone, CO, COOH), 1600 (br), 1582 (aryl C=C). Mass Spectrum *m/e* (%): 526 (M^+, 10), 482 (M^+-CO_2, 100). PMR ($CDCl_3$) δ: as given in Table II.

Methyl 2′-O-Methylphysodate (5b)——An ice-cooled solution of **5** (50 mg) in ether (5 ml) was treated with ethereal diazomethane for one min, treated with one drop of AcOH, and evaporated to dryness. Crystallization of the product from aq. MeOH furnished **5b** as colorless needles (39 mg) of mp 107°. *Anal.* Calcd. for $C_{28}H_{34}O_8$: C, 67.45; H, 6.87. Found: C, 67.37; H, 6.92. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250 (br) (OH), 1720 (br), 1656 (w) (depsidone, CO, $COOCH_3$), 1605 (br) (aryl C=C). Mass Spectrum *m/e* (%): 498 (M^+, 100). PMR ($CDCl_3$) δ: as given in Table II.

2′-O-Methylphysodone (10a)——A solution of **5** (200 mg) in formic acid (10 ml) was refluxed for 3 hr in an oil bath and poured into ice-cooled water (50 ml). The precipitate was collected by filtration and crystallized from aq. MeOH to give **10a** as colorless needles (185 mg) of mp 200—201°. *Anal.* Calcd. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 71.12; H, 7.08. IR ν_{max}^{KBr} cm^{-1}: 3500, 3300 (br) (OH), 1685 (br), 1664 (w) (lactone CO & C=C), 1590 (br) (aryl C=C). Mass Spectrum *m/e* (%): 440 (M^+, 100). PMR (d_6-acetone-$CDCl_3$=1:1) δ: 0.79, 0.90 (3H each, both t, J=6 Hz, terminal $CH_3\times2$), *ca.* 1.0—2.0 (12H, br, $-CH_2-\times6$), 2.45 (4H, t, J=7 Hz, pyrone–$C\underline{H}_2$–CH_2–, Ph–$C\underline{H}_2$–CH_2–), 3.74 (3H, s, OCH_3), 6.11 (1H, s, pyrone–H), 6.04 (1H, d, J=2.5 Hz), 6.26 (1H, d, J=3 Hz), 6.32—6.36 (2H, m) (Ar–H×4).

Oxidative Degradation of 10a giving 11 and 12——To a solution of **10a** (150 mg) in glacial AcOH (20 ml) was added conc. HNO_3 (d=1.42, 0.2 ml) and the total mixture was kept stirring under ice-cooling for 20 min, poured into water (100 ml), and extracted with ether three times (100 ml each). The combined ether extract was washed with aq. $NaHCO_3$ until the aqueous layer became neutral. The ether extract was dried over $MgSO_4$ and evaporated to give two products, which were purified by column chromatography (Merck silica gel PF_{254}) eluting with benzene–AcOEt (9:1). The first eluting product was crystallized from benzene to furnish colorless plates (50 mg), which were identified with authentic olivetonide (**11**)[1] by mixed mp, TLC, and IR ($CHCl_3$). The second eluting product was crystallized from benzene–*n*-hexane to furnish orange needles (17 mg) of mp 172—173°, which were identified (mixed mp, TLC, and IR ($CHCl_3$)) with 2-hydroxy-6-pentyl-1,4-benzoquinone (**12**) prepared by the nitric acid degradation of physodone (**10**).[1]

Acknowledgement The authors are grateful to the late Professor Emeritus Y. Asahina and Dr. M. Nuno for the identification of the lichen materials, and to Prof. I. Ninomiya of Kobe Women's College of Pharmacy for measuring the high resolution mass spectra.