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Vittatolic Acid, a New Depsidone Isolated from the Lichen *Hypogymnia vittata* (Ach.) Gas.

In addition to three phenolic substances (physodic acid (I), atranorin (II), and oxyphysodic acid (III)), zeorin (V), and ergosterol peroxide (VI), a new optically active depsidone named vittatolic acid (IV) has been isolated from the lichen *Hypogymnia vittata* (Ach.) Gas.

The structure IV has been assigned to vittatolic acid on the basis of chemical and physicochemical evidence. Vittatolic acid is characteristic by the possession of a secondary alcoholic function in the aliphatic side chain.

In 1964 Nuno pointed out[1] that the lichen *Hypogymnia vittata* (Ach.) Gas. (syn. *Parmelia vittata* Nyl.) contained two unidentified phenolic substances along with physodic acid (I) and atranorin (II). As a continuative study on the lichen constituents, we have investigated the phenolic substances and have been able to elucidate that the one is identical with oxyphysodic acid (III)[2] and the other is a new depsidone (now named vittatolic acid) (IV), the structure determination of which is a subject of the present communication.

Silica gel column and thin-layer chromatography (TLC) of the ether extractive of the titled lichen, which was collected at Mt. Ōmine in Nara prefecture, furnished four phenolic substances, among which three were identified with physodic acid (I, 1.5%),[3] atranorin (II, 1.2%),[3] and oxyphysodic acid (III, 0.7%),[2] respectively, while one is a new depsidone vittatolic acid (IV, 0.3%).

Vittatolic acid (IV), $C_{26}H_{30}O_9$, *m/e* 486 (M^+), mp 178° (decomp.) (colorless needles from aq. MeOH), $[\alpha]_D^{24}$ −11° (*c*=1.0, EtOH), infrared (IR) ν_{max}^{KBr} cm^{-1}: 3413 (br.), 3068 (br.) (OH), 1704 (br.), 1663 (depsidone, CO, COOH), 1610 (aryl C=C), showed a positive color reaction for the $FeCl_3$ reagent (violet) but was negative for the NaOCl and *p*-phenylenediamine reagents.[4] Acetylation of IV gave a triacetate (IVa), $C_{26}H_{27}O_6(OCOCH_3)_3$, *m/e* 612 ($M^+$), mp 146—147°, $[\alpha]_D^{24}$ +1.0° (*c*=1.0, EtOH), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (OAc), 1738 (br.), 1720 (sh.), 1685 (OAc, depsidone, CO, COOH), 1610 (aryl C=C), which, on subsequent treatment with ethereal diazomethane, was converted to a methyl ester triacetate (IVb), $C_{25}H_{26}O_4(OCOCH_3)COOCH_3$, *m/e* 626 ($M^+$), mp 77—78°, $[\alpha]_D^{22}$ +1.0° (*c*=1.0, EtOH), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775 (OAc), 1740, 1732 (br.) (OAc, depsidone, CO, $COOCH_3$), 1612 (aryl C=C).

The examinations of proton magnetic resonance (PMR) spectra of IV, IVa, and IVb in comparison with those of physodic acid (I),[5] diacetylphysodic acid (Ia), and methyl diacetylphysodate (Ib) (Table I) have revealed that vittatolic acid (IV) is closely related with I and differs by the possession of one additional secondary alcoholic function as compared with I. The one-proton quintet (J=7 Hz) ascribable to the methine proton (d) is observed at δ 5.29 in IVa or δ 5.27 in IVb, and the signal due to the alcoholic acetate (3H, s) is observed at δ 2.02 in IVa or δ 2.01 in IVb.

The location of the secondary alcoholic function in IV, β to the carbonyl, has been substantiated by the decoupling experiments of IVa. Thus, irradiation at δ 2.77 (b) resulted in the alteration of the quintet at δ 5.29 (d) to a triplet (J=7 Hz), while irradiation of the latter signal varied the former doublet (b) to a singlet. Furthermore, reduction of IV with

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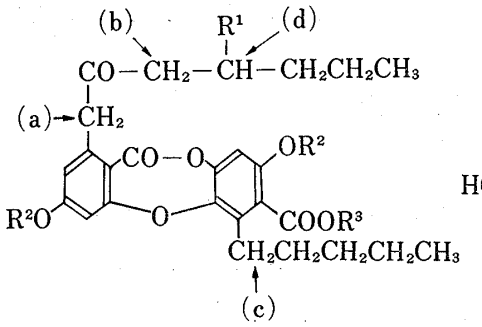
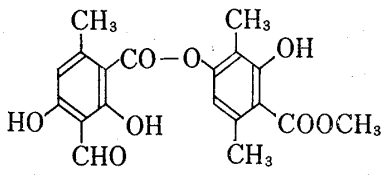
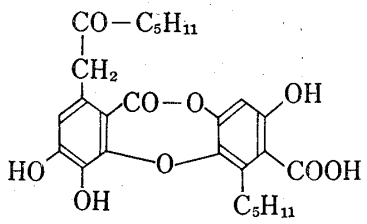


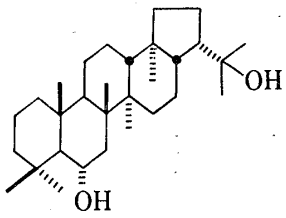
	R^1	R^2	R^3	
I	H	H	H	physodic acid
Ia	H	Ac	H	
Ib	H	Ac	CH_3	
IV	OH	H	H	vittatolic acid
IVa	OAc	Ac	H	
IVb	OAc	Ac	CH_3	



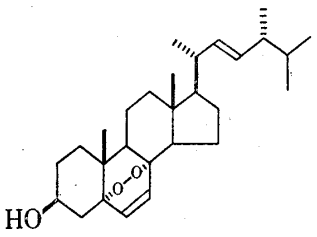
II : atranorin



III : oxyphysodic acid



V : zeorin



VI : ergosterol peroxide

TABLE I. δ Values at 90 MHz, Coupling Constants in Hz[a]

	CH_3	CH_2	Ar-H	Others
I[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, $-CH_2-\times 6$)
IV[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)
Ia[d,2]	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)
IVa[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)
Ib[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, $COOCH_3$)
IVb[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 $CDCl_3$

Zn/HCl/AcOH at room temperature yielded in an excellent yield a desoxy derivative which was proved identical with physodic acid (I) in all respects (mixed mp, TLC, and IR).

Consequently, the structure of vittatolic acid has been established as IV, in which the absolute configuration at the carbon bearing the secondary hydroxyl is under investigation. Vittatolic acid seems to be the first example carrying a secondary alcoholic function in the aliphatic side chain among the lichen depsidones, although several depsidones have been known to possess a primary alcoholic function, for examples: salazinic acid,[6] protocetraric acid,[6] and constictic acid.[7]

6) ref. 4), p. 130, 137.
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Finally, we have examined the chloroform extractive of the lichen thalli after the ether extraction and have isolated two neutral substances. The one obtained in a 0.1% yield was found identical with zeorin (V),[8] while the more polar compound (0.15%) was identified with ergosterol peroxide (VI)[9] which was prepared by photosensitized oxygenation of ergosterol.[10]

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Synthesis of Active Forms of Vitamin D. VIII.[1] Synthesis of [24*R*]- and [24*S*]-1α,24,25-Trihydroxyvitamin D_3[2]

24ξ,25-Dihydroxycholesterol was converted, through 1,4,6-trien-3-one and its 1α,2α-epoxide, into 1α,24ξ,25-trihydroxycholesterol. After resolution of C-24 epimers and determining their configurations, both isomers were led to [24*R*]- and [24*S*]-1α,24,25-trihydroxyvitamin D_3 by bromination, dehydrobromination and ultraviolet-irradiation.

Vitamin D_3 is first hydroxylated in the liver on C-25 before it travels to the kidney to be hydroxylated either on C-1 or C-24.[3] Under normal or hypercalcemic conditions the major circulating metabolite of 25-hydroxyvitamin D_3 is 24,25-dihydroxyvitamin D_3.[4] A polar metabolite of the latter has recently isolated by Holick, *et al.*[5] and identified as 1,24,25-trihydroxyvitamin D_3, although the stereochemistry at C-1 and C-24 has been remained to be determined. They have also reported that this vitamin D analog appears to have preferential action on the intestine.

In our continuing efforts of synthesis of vitamin D analogs having useful specific and/or enhanced activities and also in the hope of determining the absolute configurations of the natural 1,24,25-trihydroxyvitamin D_3,[5] we have now synthesized [24*R*]- and [24*S*]-1α,24,25-trihydroxyvitamin D_3 (**11** and **12**).

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