[Chem. Pharm. Bull. 22(7)1678—1680(1974)]

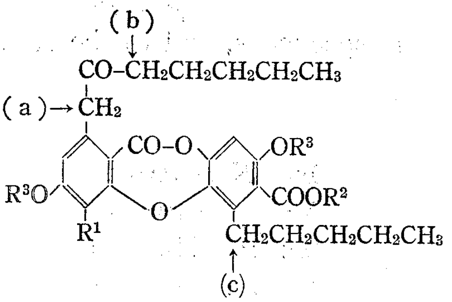
UDC 547.91.02 : 581.192

A New Depsidone Oxyphysodic Acid isolated from a Lichen *Parmelia enteromorpha* Ach.

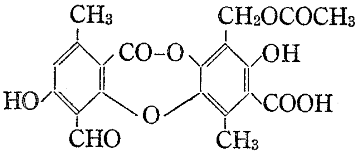
In the thin-layer chromatographic (TLC) study of 16 species of lichens of subgenus *Hypogymnia* belonging to a genus *Parmelia* (Parmeliaceae), Nuno pointed out in 1964[1] that physodic acid (I) was always accompanied by an unidentified phenolic substance which was shown up by its characteristic bluish violet $FeCl_3$ coloration. In this communication, we present the chemical and physicochemical evidence on the structure of the new substance (now named oxyphysodic acid) which leads to the formulation II.

Successive ether and acetone extraction followed by preparative silica gel TLC separation of the lichen *Parmelia enteromorpha* Ach. (syn. *Hypogymnia enteromorpha* (Ach.) Nyl.), which was collected at Mt. Ōdaigahara in Nara prefecture, furnished three known phenolic substances,[2] *i.e.* physodic acid (I, 1.8%), physodalic acid (III, 1.5%), and atranorin (IV, 1.5%) in addition to oxyphysodic acid (II, 0.5%).

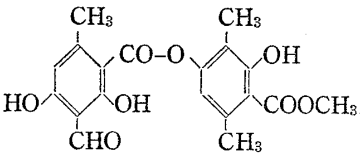
Oxyphysodic acid (II), $C_{26}H_{30}O_9$, *m/e* 486 (M^+), mp 187° (decomp.) (colorless needles from aq. MeOH), IR ν_{max}^{KBr} cm^{-1}: 3550, 3150 (br.) (OH), 1690, 1660 (depsidone, CO, COOH), 1620, 1605 (aryl C=C), showed a positive color reaction for $FeCl_3$ reagent (bluish violet) but was negative for NaOCl and *p*-phenylenediamine reagents.[3] On ethereal diazomethane treatment, II was converted to a methyl ester (IIa), $C_{25}H_{29}O_7 \cdot COOCH_3$, *m/e* 500 ($M^+$), mp



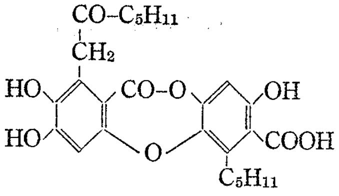
	R^1	R^2	R^3	
I	H	H	H	physodic acid
Ia	H	CH_3	H	
Ib	H	H	Ac	
II	OH	H	H	oxyphysodic acid
IIa	OH	CH_3	H	
IIb	OAc	H	Ac	



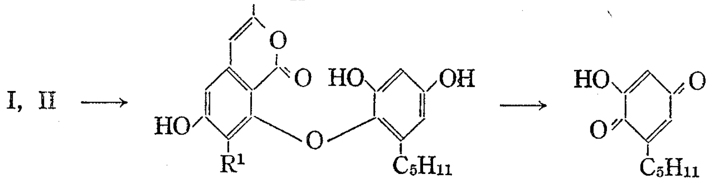
III physodalic acid



IV atranorin



[A]



V : R^1=H
VI: R^1=OH

VII

---

[1] M. Nuno, *J. Japan. Botany*, 39, 97 (1964).
[2] C.F. Culverson, "Chemical and Botanical Guide to Lichen Products," The University of North Carolina Press, Chapel Hill, North Carolina, U.S.A., 1967, p. 361.
[3] Y. Asahina and S. Shibata, "Chemistry of Lichen Substances," Japan Society for the Promotion of Science, Tokyo, 1954, p. 10.

104—106°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250 (OH), 1725 (depsidone, CO), 1670 ($COOCH_3$), 1615 (aryl C=C), while acetylation of II with acetic anhydride and sulfuric acid afforded a triacetate (IIb), $C_{26}H_{27}O_6(OCOCH_3)_3$, *m/e* 612 ($M^+$), mp 104° (decomp.), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780 (OAc), 1745 (br.), 1725 (sh.) (depsidone, CO, COOH), 1610 (aryl C=C).

The proton magnetic resonance (PMR) examinations of II, IIa, and IIb in comparison with those of physodic acid (I),[4] methyl physodate (Ia),[4] and diacetylphysodic acid (Ib) (Table I) indicate that II is a closely related compound with I. The significant difference observed between two is the presence of one more phenolic hydroxyl but one less aromatic proton in II as compared with I. Based on the biogenetic considerations keeping in mind the co-occurrence of both acids and based on lack of one of the *meta*-coupled protons in oxyphysodic acid, two alternative structures II and [A] have become rational for oxyphysodic acid.

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

	CH_3	CH_2	Ar-H	others
I[b)]	0.86 (t, J=6)	(a) 3.97 (s)	6.60 (1H, s)	1.11—2.14 (12H, br, $-CH_2-\times 6$)
	0.91 (t, J=6)	(b) 2.46 (t, J=7)	6.62 (2H, s)	
		(c) 2.81 (br)		
II[b)]	0.88 (t, J=6)	(a) 3.82 (s)	6.52 (1H, s)	1.11—2.11 (12H, br, $-CH_2-\times 6$)
	0.92 (t, J=6)	(b) 2.42 (t, J=7)	6.56 (1H, s)	
		(c) 3.04 (br)		
Ia[c)]	0.90 (t, J=6)	(a) 3.80 (s)	6.57 (1H, d, J=2)	1.11—1.95 (12H, br, $-CH_2-\times 6$)
	0.94 (t, J=6)	(b) 2.38 (t, J=7)	6.70 (1H, s)	3.96 (3H, s, $COOCH_3$)
		(c) 3.20 (br)	6.79 (1H, d, J=2)	
IIa[c)]	0.90 (t, J=6)	(a) 3.80 (s)	6.40 (1H, s)	1.11—1.84 (12H, br, $-CH_2-\times 6$)
	0.92 (t, J=6)	(b) 2.61 (t, J=7)	6.71 (1H, s)	3.94 (3H, s, $COOCH_3$)
		(c) 3.26 (br)		
Ib[c)]	0.88 (t, J=6)	(a) 4.03 (s)	6.87 (1H, d, J=2)	1.15—2.05 (12H, br, $-CH_2-\times 6$)
	0.91 (t, J=6)	(b) 2.51 (t, J=7)	7.00 (1H, s)	
		(c) 3.00 (br)	7.03 (1H, d, J=2)	2.24, 2.30 (3H each, s, OAc×2)
IIb[c)]	0.88 (t, J=6)	(a) 4.05 (s)	6.96 (1H, s)	1.04—1.85 (12H, br, $-CH_2-\times 6$)
	0.89 (t, J=6)	(b) 2.51 (t, J=7)	7.05 (1H, s)	
		(c) 3.09 (br)		2.23, 2.27, 2.41 (3H each, s, OAc×3)

a) Abbreviations: br=broad signal, d=doublet, s=singlet, t=triplet
b) measured in d_6-DMSO
c) measured in $CDCl_3$

Irradiation at δ 4.03 (methylene (a) in Ib) or δ 4.05 (methylene (a) in IIb) resulted in the increase of aromatic proton signal intensity at δ 6.87 in Ib (12%) or at δ 6.96 in IIb (8%) due to the nuclear Overhauser effect. Therefore, the substituent disposition in the left aromatic ring in oxyphysodic acid has been corroborated as in II.

Formic acid treatment of oxyphysodic acid furnished an oxyphysodone (VI), $C_{25}H_{28}O_6$, *m/e* 424 (M^+), mp 202—203°, IR ν_{max}^{KBr} cm^{-1}: 3200 (OH), 1695 (pyrone), PMR: 0.86, 0.91 (3H each, t, J=6 Hz, $-CH_3\times 2$), 1.16—1.95 (12H, br, $-CH_2-\times 6$), 2.25, 2.72 (2H each, t, J=7, Ar$-CH_2-\times 2$), 6.13, 6.52 (1H each, s, Ar-H, pyrone-H), 6.26, 6.35 (1H each, d, J=3, Ar-H ×2). The latter was then subjected to nitric acid oxidation in acetic acid[5] to furnish an orange yellow benzoquinone derivative, $C_{11}H_{14}O_3$, mp 172—173°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (OH), 1705, 1660, 1619 (benzoquinone), which was proved identical in all respects (TLC, mixed

---

4) S. Huneck and P. Linscheid, *Z. Naturforsch.*, **23b**, 717 (1968).
5) *a*) F.M. Dean, J.C. Roberts, and A. Robertson, *J. Chem. Soc.*, **1954**, 1432; *b*) F.M. Dean, D.S. Deorha, A.D.T. Erni, D.W. Hughes, and J.C. Roberts, *ibid.*, **1960**, 4829; *c*) S. Neelakantan, T.R. Seshadri, and S.S. Subramanian, *Tetrahedron*, **18**, 597 (1962).

mp, and infrared (IR)) with 2-hydroxy-6-pentyl-1,4-benzoquinone (VII), PMR: 0.88 (3H, t, J=6, $-CH_3$), 1.05—1.90 (6H, br., $-CH_2-\times 3$), 2.45 (2H, t-like, J=6, $-C=C-CH_2-$), 6.10, 6.46 (1H each, s, ring H×2), prepared analogously from I *via* physodone (V).[6]

Consequently, the structure of oxyphysodic acid has been established as II.

Acknowledgement The authors wish to express their sincere thankness to Emeritus professor Y. Asahina and Dr. M. Nuno for identification of the lichen material.

Kyoto College of Pharmacy
Yamashina-misasagi, Higashiyama-ku,
Kyoto

TERUHISA HIRAYAMA
FUKUJIRO FUJIKAWA

Faculty of Pharmaceutical Sciences,
Osaka University,
Toneyama, Toyonaka, Osaka

ITIRO YOSIOKA
ISAO KITAGAWA

Received March 28, 1974

---

[6] Y. Asahina and H. Nogami, *Chem. Ber.*, 67, 805 (1934).

[Chem. Pharm. Bull.
22(7)1680—1681(1974)]

UDC 547.92.02.05 : 581.192

Neridienone A, a C_{21}-Steroid in *Nerium odorum*[1]

Concerning the constituents of *Nerium odorum*, we have previously reported the isolation of pregnenolone glucosides[2] from its root bark. This communication deals with the isolation and the structure elucidation of neridienone A, a pregnane compound in the same source.

The methanol percolate of the root bark was extracted with benzene, and through successive column chromatography of the benzene extractives followed by crystallization from acetone–hexane, a substance, sensitive to 2,4-dinitrophenylhydrazine reagent on thin-layer chromatography, was obtained as prisms and named neridienone A (NA). NA, (mp 210—211°, $[\alpha]_D +71.5°$, Mass. Calcd. for $C_{21}H_{26}O_3$ m/e 326.1875; Found 326.1882), shows nuclear magnetic resonance (NMR) signals at δ (ppm) 0.98 (3H, s), 1.16 (3H, s), 2.43 (3H, s), 3.71 (1H, dd), 5.67 (1H, s), 5.81 (1H, s), 6.12 (2H, s) and 6.99 (1H, dd). Two oxygens in NA were found to belong to the unsaturated ketones, 4,6-dien-3-one and 16-en-20-one of steroid system, according to the ultraviolet absorptions at 283 nm (ε 24100) and 245 nm (ε 12900), infrared (IR) bands at 1665, 1640, 1612 and 1580 cm^{-1}, and NMR signals at 5.67 (C_4-H), 6.12 ($C_{6,7}$-H) and 6.99 ppm (C_{16}-H). The IR bands at 3420 and 3320 cm^{-1} as well as the disappearance of the peak at δ 5.81 ppm with D_2O exchange indicated that the remaining oxygen function forms a hydroxyl group. NA, on reduction with $NaBH_4$, gave three products, dihydro-, tetrahydro- and hexahydro-compounds, the first of which, (Calcd. for $C_{21}H_{28}O_3$ 328.2038; Found 328.2079) bears no 16-en-20-one system in its molecule, and afforded a diacetate (Calcd. for $C_{25}H_{32}O_5$ 412.2249; Found 412.2233) on acetylation, whereas NA was unreactive with Ac_2O and pyridine. The above results suggested that the hydroxyl group is oriented in the position under the influence of 16-en-20-one, and the location and the configuration were determined as C_{12}-β-OH

---

[1] This forms Part IV of "*Nerium*." Part III: T. Yamauchi, Y. Mōri and Y. Ogata, *Phytochemistry*, 12, 2737 (1973).

[2] T. Yamauchi, M. Hara and K. Mihashi, *Phytochemistry*, 11, 3345 (1972).