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Pterosin N and O, Phenylacetylpterosin C, and Pteroside P from Bracken, *Pteridium aquilinum* var. *latiusculum*[1]

More than twenty 1-indanone derivatives have so far been isolated from methanol extract of air-dried young leaves of bracken[2-4] and the structures including stereochemistry have been elucidated.[2-5] In the course of further attempts to isolate the carcinogenic principle(s) we have isolated three more compounds, named pterosin N (**1**), pterosin O (**2**), and phenylacetylpterosin C (**3**). At the same time the constituents of the rhizomes of the plant have been systematically separated and several pterosins and pterosides, including a new compound pteroside P (**4**), have been characterized.

Pterosin N (**1**), mp 165—167° (from acetone), $[\alpha]_D$ −18.8° (MeOH), M^+ 234.123 *m/e* (calcd. for $C_{14}H_{18}O_3$, 234.126), shows the characteristic spectral properties of pterosins[2-4] (λ_{max}^{EtOH} nm (log ε): 218, 262, 308 (4.49, 4.18, 3.39), ν_{max}^{KBr} cm^{-1}: 3430, 1700, 1605). The nuclear magnetic resonance (NMR) spectrum of the compound is quite similar to that of pterosin B[2] (**5**) (δ(CD_3-OD): 7.09 (1H, s, 4-arom. H), 2.44 (3H, s, 5-CH_3), 2.96, 3.62 (each 2H, t, J=7.5 Hz, 6-CH_2CH_2-O-), 2.64 (3H, s, 7-CH_3)) except the signals of the 2-methyl group appearring in a singlet at a lower field (δ(CD_3OD): 1.33 (3H, s)) and the 3-methylene group appearring in a broad singlet (δ(CD_3OD): 3.04 (2H)). The fact suggested the presence of a tertially hydroxyl group at the 2-position on the framework of pterosin B. The assumption was confirmed by the following synthesis. Pterosin B (**5**) was derived to the O,C-diacetate (**6**), oil, $C_{18}H_{22}O_4$, by acetic anhydride-*p*-toluenesulfonic acid or -perchloric acid, oxidized to **7**, mp 129—131°, by the Baeyer-Villiger reaction, and hydrolysed to a compound, identical with the natural product (**1**) in every respects.[6]

Pterosin O (**2**), mp 45—46° (from hexane), $[\alpha]_D$ ±0° (MeOH), M^+ 232.146 *m/e* (calcd. for $C_{15}H_{20}O_2$, 232. 146), also shows quite similar spectral properties to pterosin B (λ_{max}^{EtOH} nm (log ε): 218, 260, 305 (4.52, 4.20, 3.42); ν_{max}^{KBr} cm^{-1}: 1700, 1603; δ ($CDCl_3$): 1.27 (3H, d, J=7.5 Hz, 2-CH_3), 7.06 (1H, s, 4-arom. H), 2.45 (3H, s, 5-CH_3), 2.68 (3H, s, 7-CH_3)), except the presence of the signals of an additional methoxy-methyl (δ 3.36 (3H, s)) and of an alkoxyethyl group at the 6-position (δ 3.05, 3.50 (each 2H, m)) as are seen in pterosin I[7] (**8**). Thus the structure (**2**) of O-methyl ether of pterosin B was suggested. Actually the methylation[2,3] of pterosin B (**5**) by methyl iodide-sodium hydride gave the compound (**2**) along with the C-methyl (pterosin Z[3,7]) (**9**) and the O,C-dimethyl (pterosin I[3,7]) (**8**) compounds.[8]

The third compound (**3**), mp 67—68° (from hexane–benzene), $[\alpha]_D$ +38.6° (MeOH), M^+ 352.161 *m/e* (calcd. for $C_{22}H_{24}O_4$, 352.167), λ_{max}^{EtOH} nm (log ε): 216, 257, 299 (4.58, 4.14, 3.34); ν_{max}^{KBr} cm^{-1}: 3380, 1743, 1713, 1600, is an acylpterosin[4] with a free hydroxyl group. The acid

1) Presented at the Annual Meeting of the Pharmaceutical Society of Japan, Sendai, April 1974, Abstracts of Papers, p. 237.
2) K. Yoshihira, M. Fukuoka, M. Kuroyanagi, and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **19**, 1491 (1971).
3) K. Yoshihira, M. Fukuoka, M. Kuroyanagi, and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **20**, 426 (1972).
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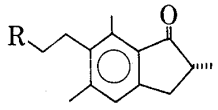
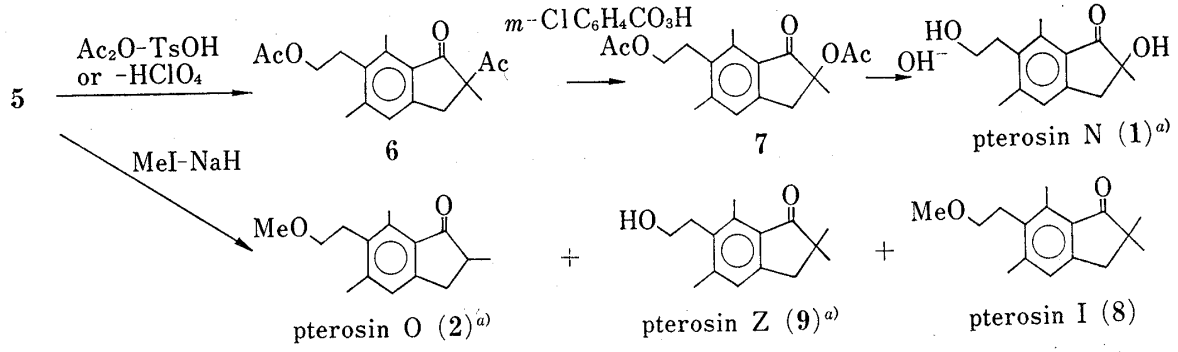
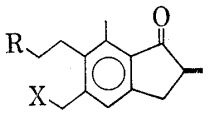
5) M. Kuroyanagi, M. Fukuoka, K. Yoshihira, and S. Natori, *Chem. Pharm. Bull.* (Tokyo), **22**, 723 (1974).
6) Quite recently the same compound was isolated from *Pteris oshimensis* Hieron. (Prof. T. Murakami, Science University of Tokyo, private communication, *cf.* T. Murakami, N. Tanaka, and K. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **22**, 2758 (1974).
7) Y. Hayashi, M. Nishizawa, S. Harita, and T. Sakan, *Chemistry Letters* (Tokyo), **1972**, 375.
8) The same compound has been isolated from *Pteris inaequalis* Baker var. *aequata* Tagawa along with pterosin B (Dr. K. Koshimizu, Kyoto University, private communication. *cf.* A. Kobayashi, K. Koshimizu, T. Mitsui, H. Egawa, and H. Fukami, Abstracts of Papers, Annual Meeting of the Agricultural Chemical Society of Japan, Tokyo, (1973), p. 251.

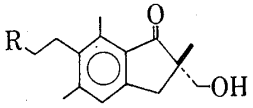


R : OH (2*R*)-pterosin B (**5**)[a,b]
R : Oglu.(2*R*)-pteroside B (**22**)[a]
R : Cl (2*R*)-pterosin F (**16**)[a,b]

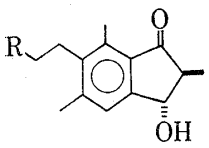


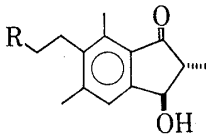


R : Oglu.,X : H (2*S*)-pteroside B (**18**)[b]
R : Oglu.,X : OH (2*S*)-pteroside P (**4**)[b]
R : OH, X: OH (2*S*)-pterosin P (**24**)



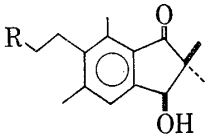
R : OH (2*S*)-pterosin A (**14**)[a,b]
R : Oglu.(2*S*)-pteroside A (**17**)[a,b]

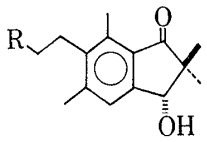




R : $OCOCH_2C_6H_5$ (2*S*,3*S*)-phenylacetylpterosin C (**3**)[a]
R : OH (2*S*,3*S*)-pterosin C (**10**)[a]
R : Cl (2*S*,3*S*)-pterosin J (**11**)[a]
R : $OCOCH_3$ (2*S*,3*S*)-acetylpterosin C (**12**)[a]
R : $OCOC_{15}H_{31}$ (2*S*,3*S*)-palmitylpterosin C (**13**)[a]

R : OH (2*R*,3*R*)-pterosin C (**15**)[b]
R : Oglu.(2*R*,3*R*)-pteroside C (**19**)[b]





R : Oglu. (3*S*)-pteroside D (**20**)[b]
R : OH (3*S*)-pterosin D (**21**)

R : OH (3*R*)-pterosin D (**23**)[a]

a) isolated from young leaves *b*) isolated from rhizomes
Ts=Tosyl

portion was suggested to be phenylacetyl group from the NMR ($\delta(CDCl_3)$: 3.57 (2H, s), 7.25 (5H, s)) and the mass spectrum (*m/e* 216 ($M^+-C_6H_5CH_2COOH$)). The NMR spectrum[9] (δ(CD-Cl_3): 1.32 (3H, d, J=7.5 Hz, 2-CH_3), 4.70 (1H, d, J=4 Hz, 3-carbinyl H), 7.25 (1H, s, 4-arom. H), 2.43 (3H, s, 5-CH_3), 3.01, 4.12 (each 2H, t, J=7 Hz, 6-CH_2CH_2-OCOR), 2.63 (3H, s, 7-CH_3)) also revealed that the 1-indanone portion of the ester (**3**) is pterosin C[3] (**10**) and the ester is formed at the primary alcohol group at the 6-position. The circular dichroism (CD) curve

9) The compound (**3**) appears in chromatographically pure crystals but the NMR Spectrum revealed that the compound is contaminated with its stereoisomer due to the epimerization of the 2-methyl group (*trans*: *cis*, *ca.* 10: 1, J_{2-3} *trans* 4 Hz, *cis* 6.8 Hz) as in the case of pterosin C,[3] J,[4] and the C esters.[4] The data given above are those of the major component, the *trans* isomer.

of phenylacetylpterosin C (**3**) shows a strong positive n—π^* Cotton effect ($[\theta]_{324}^{25°}$ +74050 (MeOH)) superimposable with those of pterosin C (**10**), J (**11**), and the esters (**12**, **13**),[5] indicating the 2*S*,3*S*-configuration (**3**).

The rhizomes of bracken have been proved to show stronger carcinogenic activity than young fronds.[10] In order to compare the constituents especially the indanone derivatives with those in young leaves the dried rhizomes from the same origin were extracted with benzene and methanol. The methanol extract was fractionated by charcoal column, silica gel column, and thin-layer chromatographies. Four pterosins, A[2] (**14**), B[2] (**5**), C[3] (**15**), and F[2] (**16**), and five glucosides, pteroside A[3,11] (**17**), B[3,12] (**18**), C[11] (**19**), D[13] (**20**) and a new compound pteroside P (**4**), were isolated. Although the identity with those obtained from the terrestrial part was firmly established by the direct comparison of the physical data, pterosin C (**15**), the both of the free form and the aglycone of pteroside C (**19**),[14] pteroside B (**18**) and pterosin D (**21**) obtained by the hydrolysis of pteroside D (**20**),[14] from the rhizomes exhibit the opposite sign of the optical rotation and the n—π^* Cotton effects to those obtained from the young leaves (**10**, **22**, **23**), indicating their antipodal configuration of the indanone portions.

Pteroside P (**4**), mp 191—193° (from MeOH–$CHCl_3$), $[\alpha]_D$ −14.9° (MeOH), M^+ 396.176 m/e (calcd. for $C_{20}H_{28}O_8$, 396.178), showed the characteristic properties of indanone glucosides[3,11-13] (λ_{max}^{EtOH} nm (log ε): 217, 258, 305 (4.61, 4.19, 3.48), ν_{max}^{KBr} cm^{-1}: 3360, 1705, 1603). Hydrolysis of pteroside P (**4**) with emulsin gave glucose (identified by paper chromatography) and the aglycone, pterosin P (**24**), mp 115—117° (from benzene–$CHCl_3$), $[\alpha]_D$ +4.6° (MeOH), M^+ 234.121 m/e (calcd. for $C_{14}H_{18}O_3$, 234.125), λ_{max}^{EtOH} nm (log ε): 218, 258, 302 (4.66, 4.31, 3.69), ν_{max}^{KBr} cm^{-1}: 3360, 1675, 1600. Pteroside P (**4**) gave pentaacetate (**25**), while pterosin P (**24**) gave diacetate (**26**). Comparison of the NMR spectra of these compounds with those of the known compounds[2-4] revealed that in the molecule of pterosin P (**24**) there exist a secondary methyl, an aromatic ring proton, a hydroxyethyl, and an aromatic methyl groups ($\delta(CD_3COCD_3)$: 1.21 (3H, d, J=7.0 Hz); 7.38 (1H, s); 2.96, 3.68 (each 2H, t, J=7.0 Hz) and 4.25 (1H, s); 2.69 (3H, s)) but the aromatic methyl group at the higher field has been replaced by a hydroxymethyl group ($\delta(CD_3COCD_3)$: 4.72 (2H, s)). Since the latter signal was deshielded by acetylation ($\delta(CD_3OD)$ 4.75 in **4**, $\delta(CD_3COCD_3)$ 4.72 in **24**, $\delta(CDCl_3)$ 5.16 in **25**, $\delta(CDCl_3)$ 5.21 in **26**), the sugar residue must link at the primary hydroxyl at the hydroxyethyl group. The chemical shifts and the coupling constants of the anomeric protons of pteroside P (**4**) (δ 4.28, J=6.5 Hz) and the acetate (**25**) (δ 4.44, J=7.5 Hz) indicate β-linkage of D-glucose.[15] The n—π^* Cotton effect of **4** ($[\theta]_{328}^{25°}$ −2280 (MeOH)) and **24** ($[\theta]_{327}^{25°}$ −1370 (MeOH)) shows the 2*S*-configuration.[5]

Besides the indanone derivatives, benzoic acid, β-sitosterol, stigmast-4-en-3-one, stigmasta-3,6-dione, astragalin,[16] and tiliroside[16] were isolated from the young leaves and 3-p-coumaroylquinic acid from the rhizomes.

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14) Thus the absolute configurations proposed by Hikino, *et al.* for pteroside C[11] and pteroside D[13] were proved to be correct (*cf.* ref. 5) footnote 8)).
15) H.J. Kock and A.S. Perlin, *Carbohydrate Res.*, **15**, 403 (1970); A.B. Foster, R. Hems, and L.D. Hall, *Canad. J. Chem.*, **48**, 3937 (1970); G. Descotes, F. Chizat, and J.C. Martin, *Bull. Soc. Chim., France*, **1970**, 2304; M. Matsui and M. Okada, *Chem. Pharm. Bull.* (Tokyo), **18**, 2129 (1970).
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