Communications to the Editor

[Chem. Pharm. Bull. 19(7)1491—1495(1971)] UDC 547.665.02 : 581.192

1-Indanone Derivatives from Bracken, *Pteridium aquilinum* var. *latiusculum*

Bracken is now attracting the attention because of its radiomimetic and carcinogenic properties.[1] From hexane and benzene fractions of methanol extract of air-dried young leaves of bracken, *Pteridium aquilinum* KUHN var. *latiusculum* UNDERWOOD (Pteridaceae) (Japanese name, warabi), collected at Hokkaido in June, we have so far isolated six 1-indanone derivatives by chromatographic separation. This communication concerns with the structure elucidation of these compounds.

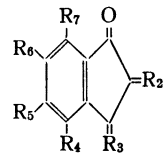
TABLE I. Physical Properties of 1-Indanone Derivatives from Bracken

Compound	mp (°C) (recrystallized from)	M^+ found (m/e) (Calcd.)	Mol. formula	UV λ_{max}^{EtOH} mμ (log ε)	IR ν_{max}^{KBr} cm^{-1}	$[\alpha]_D$ (solvent)
BI-2 (I)	109—110 (hexanane–$CHCl_3$)	218.132 (.131)	$C_{14}H_{18}O_2$	217, 260, 304 (4.57, 4.21, 3.43)	3300 1705 1670	−11.4° ($CHCl_3$)
BH-4 (II)	160—162 (CCl_4)	232.107 (.109)	$C_{14}H_{16}O_3$	217, 260, 303 (4.53, 4.20, 3.40)	1695 1680	——
HJ-5 (III)	66—67 (hexane)	236.096 (.097) 238.096 (.094)	$C_{14}H_{17}OCl$	219, 259, 303 (4.66, 4.24, 3.49)	1695	−9.2° (benzene)
HQ-2 (IV)	86—88 (hexane)	232.140 (.146)	$C_{15}H_{20}O_2$	217, 260, 304 (4.48, 4.12, 3.36)	3320 1680	——
BJ-4 (V)	189—190 (MeOH–CCl_4)	248.142 (.141)	$C_{15}H_{20}O_3$	217, 260, 302 (4.60, 4.23, 3.28)	3260 3200 1716	+4.8° (EtOH)
BK-3 (VI)	125—127 (benzene) synthetic racemate 105°	248.140 (.141)	$C_{15}H_{20}O_3$	217, 261, 305 (4.54, 4.19, 3.39)	3240 1700	−21.8° ($CHCl_3$)

The six compounds, tentatively designated as BI-2 (I), BH-4 (II), HJ-5 (III), HQ-2 (IV), BJ-4 (V), and BK-3 (VI), showed the physical properties shown in Table I. The ultraviolet (UV) spectra of these compounds indicated the presence of an acetophenone chromophore and the infrared (IR) absorptions suggested the presence of the carbonyl group in five-membered ring. Nuclear magnetic resonance (NMR) spectra shown in Table II indicated that the compounds (I—VI) bear two methyls and one hydroxyethyl, chlorethyl, or carboxymethyl group on the aromatic ring. In I, II, and III there exist a secondary methyl group, while in IV and V a *gem*-dimethyl group exists. In VI one of the methyls is replaced by a hydroxymethyl and in V there exist an additional hydroxyl group. These facts and the molecular formulae (Table I) indicated that all of the six compounds are 1-indanone derivatives. The location of the secondary methyl in I, II, and III at C-2 was confirmed by the fact that the doublet methyl signal (Table II) changed into singlet after 24 hr by standing at room temperature in CF_3CO_2D due to deutration of the methin proton in coupling with the methyl through enolization and by the fact that the coupling pattern of the newly formed

1) I.A. Evans, *Cancer Research*, **28**, 2252 (1968); J.M. Price and A.M. Pamukcu, *ibid.*, **28**, 2247 (1968); I. Hirono, C. Shibuya, K. Fukushi, and M. Haga, *J. Natl. Cancer Inst.*, **45**, 179 (1970); K. Yuki, T. Hayashi, and N. Morita, Proc. Japan Cancer Assoc., The 29th Annual Meeting, Osaka, October 1970, p.63.

TABLE II. NMR Spectra of 1-Indanone Derivatives from Bracken (Determined at 60MHz in $CDCl_3$ unless otherwise specified and expressed in δ Value in ppm from the Internal Standard TMS; Coupling Constants are in Hz)



Compound	R_2		R_3		R_4	
BI-2 (I)	CH_3	1.25(d, J=8)	H_2	2.3—3.5(m)[a]	H	6.99(s)
	H	2.3—3.5(m)[a]				
BH-4 (II)	CH_3	1.27(d, J=7)	H_2	2.4—3.5(m)[a]	H	7.02(s)
	H	2.4—3.5(m)[a]				
HJ-5 (III)	CH_3	1.27(d, J=7)	H_2	2.9—3.7(m)	H	6.98(s)
	H	2.6(m)				
HQ-2 (IV)	$(CH_3)_2$	1.22(s)	H_2	2.84(s)	H	7.01(s)
BJ-4 (V)[b]	CH_3	1.17(s)	H	4.95(s)	H	7.35(s)
	CH_3	1.26(s)	OH[c]			
BK-3 (VI)	CH_3	1.24(s)	H_2	2.3—3.8(m)	H	7.05(s)
	CH_2	3.68(s)				
	OH	2.38				

Compound	R_5		R_6		R_7	
BI-2 (I)	CH_3	2.41(s)	CH_2	2.99(t, J=8)	CH_3	2.67(s)
			CH_2	3.72(t, J=8)		
			OH	1.3		
BH-4 (II)	CH_3	2.40(s)	CH_2	3.74(s)	CH_3	2.67(s)
			CO_2H			
HJ-5 (III)	CH_3	2.42(s)	CH_2	3.2(m)	CH_3	2.66(s)
			CH_2	3.4(m)		
			Cl			
HQ-2 (IV)	CH_3	2.44(s)	CH_2	2.99(t, J=8)	CH_3	2.67(s)
			CH_2	3.75(t, J=8)		
			OH	1.59		
BJ-4 (V)[b]	CH_3	2.65(s)	CH_2	3.24(t, J=8)	CH_3	2.89(s)
			CH_2	4.45(t, J=8)		
			OH[c]			
BK-3 (VI)	CH_3	2.46(s)	CH_2	2.97(t, J=8)	CH_3	2.62(s)
			CH_2	3.67(t, J=8)		
			OH	2.38		

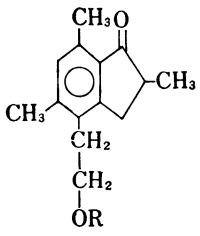
a) the overlapping signals *b*) determined in $CDCl_3+CF_3CO_2D$ *c*) not observed

carbinyl protons of reduction products (VII and VIII) of I and III with $NaBH_4$ showed the presence of a neighbouring methin proton.

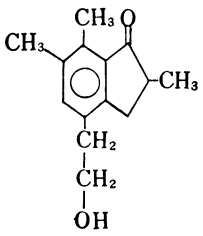
The correlation shown in Chart 1 clearly demonstrated the presence of these substituents and the common substitution pattern in the six compounds.

Hikino, *et al.*[2] isolated pteroside B from the same source and proposed the structure (A').

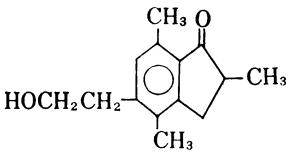
2) H. Hikino, T. Takahashi, S. Arihara, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1488 (1970).



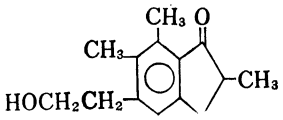
(A) R : H
(A') R : glu.



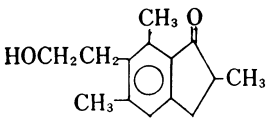
(B)



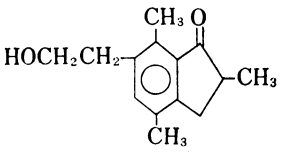
(C)



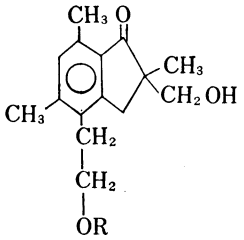
(D)



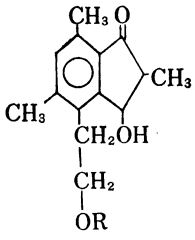
(E)



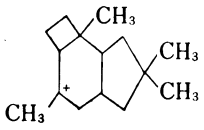
(F)



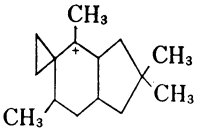
(G) R : H
(G') R : glu.



(H) R : H
(H') R : glu.

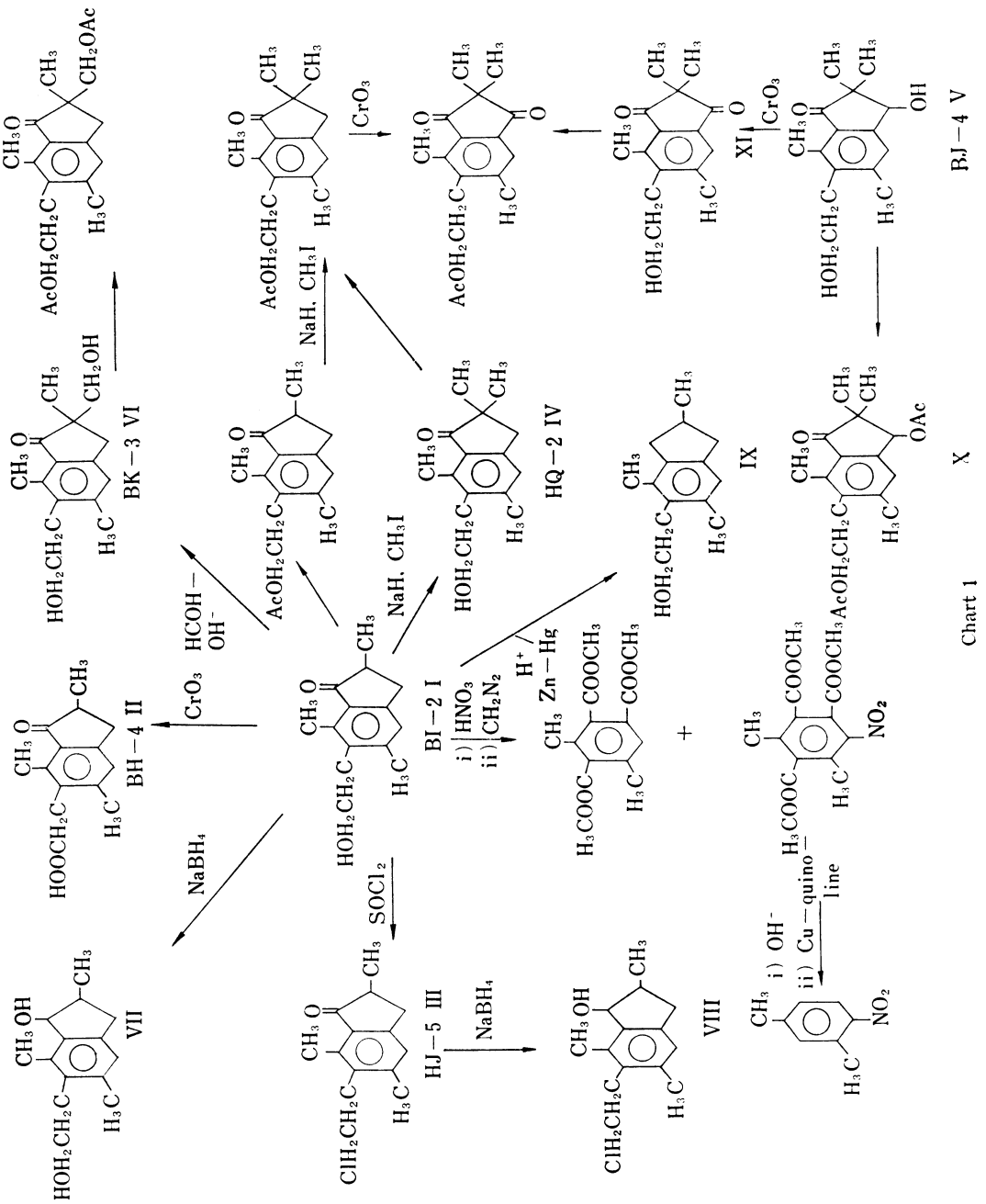


(I)



(J)

The properties of BI-2 (I) and the aglycone (A) of pteroside B were the same and the direct comparison of BI-2 (I) with the sample of the aglycone, kindly supplied by Professor Takemoto, showed the identity. Hikino, *et al.*[2] claimed that the deshielded line position of one of the methyl groups in (A) indicated the presence of the methyl at C-7 in 1-indanone and that double resonance experiments revealed the presence of the aromatic hydrogen in an adjacent position to both of the aromatic methyls, thus proposing the substitution pattern shown in the formula (A and A'). The former observation was also the case in all the six compounds (I—VI) and the derivatives and the appearance of the methyl signals at normal positions (δ_{CDCl_3} 2.21, 2.30) in the Clemmensen reduction product (IX) of BI-2 (I) gave a strong support for the assignment. However we have obtained different results for the Hikino's latter argument. The double resonance experiments of I, III, and diacetate (X) of V showed that the irradiation at the higher aromatic methyl signals showed the nuclear Overhauser effect on the ring proton but that at the lower methyl signals did not show effect on the proton. There are six isomers (A—F) for methyl and hydroxyethyl Bz-substituted 2,7-dimethyl-1-indanone. The observed effects excluded the possibility of the formulae (C) and (D) and favoured the formulae (B), (E), and (F). The low chemical shift of the ring proton (δ_{CDCl_3} 7.55) observed in the diketone (XI) formed from V support the formula (E). This point was conclusively disclosed by nitric acid oxidation of BI-2 (I). The mixture of acidic oxidation products was treated with diazomethane and, after chromatographic separation, trimethyl dimethylbenzenetricarboxylate, colorless oil, $C_{14}H_{16}O_6$ (M+ 280.091, *m/e* Calcd. 280.095), and the nitro derivative, mp 113°, $C_{14}H_{15}O_8N$ (M+ 325.080, Calcd. 325.076), were isolated in pure



forms. In the NMR spectra of the two compounds the aromatic methyls showed different chemical shifts, excluding the possibility of the acid as 4,6-dimethylbenzene-1,2,3-tricarboxylic acid expected to be formed from the formula (A). The nitro derivative was then hydrolysed and decarboxylated by Cu-quinoline. The neutral portion of the reaction products was checked by gas chromatography and a peak showing the identical retention time with 4-nitro-*m*-xylene but different from 2-nitro-*m*-xylene, 2-nitro-*p*-xylene, and 3-nitro-*o*-xylene in two columns was observed. Thus the tricarboxylic acid must be 3,5-dimethylbenzene-1,2,4-tri-

carboxylic acid and the structure of BI-2 (I) was firmly established as the formula (E). Since the other five compounds (II—VI) were correlated each other, the structures were formulated as shown in Chart 1.

As for the absolute configuration at C-2 Hikino, *et al.*[2] proposed *R* on the basis of the CD curve. The absolute configuration of the other compounds will be reported in a forthcoming paper.

Hikino, *et al.*[3] are due to report the structures of two new glucosides named pteroside A and C from the same source as (G') and (H'). Since the aglycone (G) of pteroside A was derived to the aglycone (A) of pteroside B, the aglycone (G) is assumed to be identical with our BK-3 (VI).[4]

The coexistence of C_{14} compounds (I—III) with C_{15} compounds (IV—VI) suggests that the formers are formed from the latters and they are assumed to be formed from a common precursor like (I) or (J) derived from humulene. The presence of 1-indanones (I—VI) in ethanolic extract of fresh leaves without drying has been confirmed by thin-layer chromatography. Further separation and chemical examination along with toxicity tests are in progress in our laboratory with the colaboration of pathological laboratories.

Acknowledgement The authors thank the members of Hokkaido Station for Medicinal Plants of this Institute for the collection of plant materials, Shizuoka Factory, Tsumura Co., for the extraction in a large scale, and Professor M. Tomoeda, Kanazawa University, and Dr. T. Miki, Takeda Chemical Industries, for their help in physical determinations.

National Institute of Hygienic Sciences
Kamiyoga-1-chome, Setagaya-ku, Tokyo

KUNITOSHI YOSHIHIRA
MASAMICHI FUKUOKA
MASANORI KUROYANAGI
SHINSAKU NATORI

Received April 6, 1971

3) H. Hikino, T. Takahashi, and T. Takemoto, Abstracts of Papers, Annual Meeting of Pharmaceutical Society of Japan, Fukuoka, 1971, p. 777.
4) Note Added in Proof (July 20, 1971): The identity has now been confirmed by the direct comparison of the spectral data.

[Chem. Pharm. Bull. 19(7)1495—1498(1971)]

UDC 547.913.6.02 : 547.918.02 : 581.192

Structures of Creticosides A and B, Two New Diterpenoid Glucosides from *Pteris cretica* L.

In the previous communication[1] we reported the isolation and structures of two new diterpenes, 2β,15α-dihydroxy-(−)-kaur-16-ene(I)(compound A) and 2β,16α-dihydroxy-(−)-kaurane(II)(compound B) from the rhizome of *Pteris cretica* L. (Pteridaceae). Further examination of the rhizome has enabled us to isolate two new diterpenoid glucosides and it has been shown in the present communication that these glucosides now named creticosides A and B possess the structures III and VII respectively.

A crude glycoside mixture containing creticosides A and B was obtained by column chromatography of the ether extract of the rhizome. Subsequent separation of the mixture was achieved by repeated thick-layer chromatography using the plates of silica gel impregnated with silver nitrate. Creticoside A (III), colorless needles (from acetone), $C_{26}H_{42}O_7$,

1) C.M. Chen and T. Murakami, *Tetrahedron Letters*, **1971**, 1121.