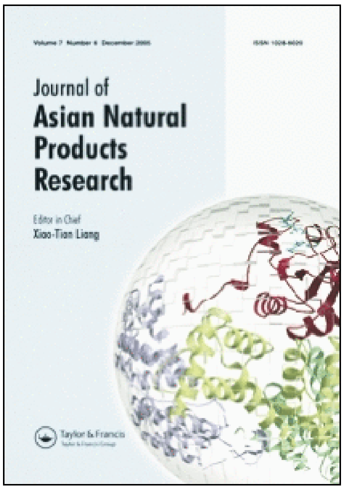

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A CYCLIC PEROXIDE OF CLERODENOIC ACID FROM THE TAIWANESE LIVERWORT *SCHISTOCHILA ACUMINATA*

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Two minor diterpenoids, 15(16)-peroxy-3, 13-clerodadien-18-oic acid (**4**) and totarol (**7**), were isolated from the liverwort *Schistochila acuminata*. The former is a further oxidized cyclic peroxide from the major component. The latter is a rearranged abietane alcohol which skeleton was found in liverworts for the first time.

Keywords: *Schistochila acuminata*; *Schistochila blumii*; *Gottschea philippinensis*; Schistochilaceae; Liverwort; 15(16)-Peroxy -3, 13-clerodadien-18-oic acid; Totarol; Neoverrucosan-5β-ol; Homoverrocosan-5β-ol

INTRODUCTION

In our earlier work on chemical constituents of the Taiwanese liverwort *Schistochila acuminata* we isolated neoverrucosan-5β-ol (**1**), homoverrocosan-5β-ol (**2**) [1], and several clerodadienoic acids (*e.g.*, **3**) [2] as the major components. In a further study of this species, two minor diterpenoids were identified. They are 15(16)-peroxy -3, 13-clerodadien-18-oic acid (**4**) and totarol (**7**). The former possesses a cyclic peroxide ring, which is likely the further oxidized product from the major clerodenoic acid **3**.

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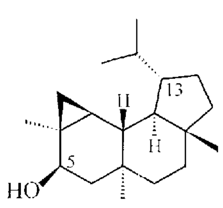

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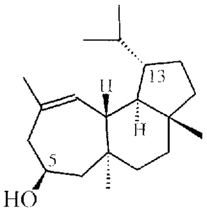

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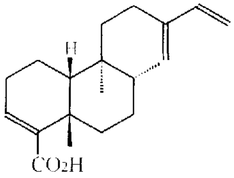

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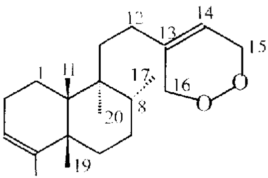

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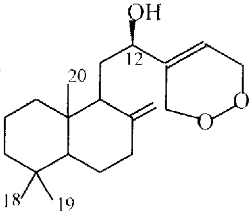

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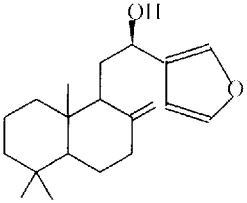

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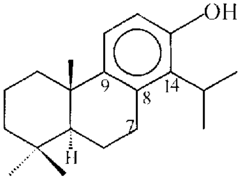

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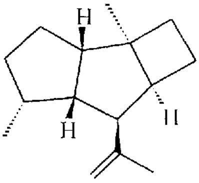

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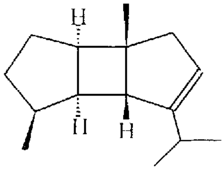

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RESULTS AND DISCUSSION

The ^{1}H NMR spectrum (Tab. I) of **4** indicated one secondary methyl (δ 0.73, d, $J = 7.5$ Hz), two tertiary methyls (δ 0.77, s; 1.21, s), two oxygen-bearing methylenes (δ 4.54, br s; 4.45, br s), and two olefinic protons (δ 5.66, dd, $J = 1.4, 1.5$; 6.79, dd, $J = 1.5, 1.6$). The ^{13}C-DEPT NMR confirmed the above observation and provided further evidence for a conjugated carboxylic acid. The spectral data so far again disclosed a partial structure of clerodadienoic acid as those previously reported (*e.g.*, **3**) [2] from the same species. The interesting feature of this compound is the two oxygen-bearing methylenes. In order to explain the broad singlet nature and the relative deshielded resonances of both methylenes (δ_H 4.54, br s, δ_C70.1; δ_H4.45, br s, δ_C 72.6), a six-membered 1, 2-dioxacyclohexene ring was proposed for the

TABLE I ^1H and ^{13}C NMR data of compound **4**

Atom	^{13}C	^1H (*J in Hz*)
1	16.8	1.82 2.01
2	24.3	2.25 2.31
3	142.4	6.79 dd (1.5, 1.6)
4	137.5	–
5	40.1	–
6	36.8	1.10 bt (10) 2.70 bd (10)
7	28.6	1.10 bt (10) 1.25
8	37.8	1.46
9	36.3	–
10	45.4	1.41 bd (6.0)
11	35.6	1.41 1.58
12	25.5	1.58 1.88
13	116.8	5.66 dd (1.4, 1.5)
14	136.2	–
15	70.1	4.54 bs
16	72.6	4.45 bs
17	15.9	0.73 d (7.5)
18	172.4	–
19	33.4	1.21 s
20	18.0	0.77 s

terminal moiety of C-13, C-14, C-15 and C-16 since the FABMS showed a quasi-molecular ion at *m/z* 335 $[M+H]^+$ and the EIMS displayed a fragment at *m/z* 316 which could be resulted from the loss of one H_2O molecule from the molecular ion *m/z* 334. Both HMBC and NOESY correlations supported the proposed structure **4** as well. The compound was thus named as (-)-15(16)-peroxy -3, 13-clerodadien-18-oic acid. The absolute configuration depicted in **4** was assumed to be the same as those clerodadienoic acids found previously [2] from the same species. This compound was unstable and deteriorated after spectra taken. Isoprenes as one of the simplest acyclic 1,3-dienes have been proved to undergo 1,4-cycloaddition of $^1O_2$ rapidly to form various 3,6-dihydro-1, 2-dioxins [3]. Previously, 15, 16-epidioxy-8 (17), 13-labdadien-(12*R*)-ol (**5**) was obtained from the original hydrocarbon, *trans*-biformene, upon photoreaction with singlet oxygen [4]. Compound **5**, in turn, was converted to furan **6** after treatment of ferrous sulfate [4]. In another report [5], *ent*-18-hydroxy-15(16)-peroxylabd-13-ene was isolated from a higher plant source as a minor component. Since furan-type of either labdenoids or clerodenoids are common constituents from plants, it is possible that compound **4** from the present finding is indeed biosynthesized by the liverwort plant although the furanoid clerodanes have not been found in this plant species.

Compound 7 was isolated from the hexane extract (6 g) after chromatography on silica gel and Sephadex LH-20. The isopropyl group and the aromatic signals revealed from both ^1H and ^{13}C NMR spectra clearly hinted a diterpene phenol of abietane type. Nevertheless, the HMBC data correlated H-7 with C-6, C-8, C-9 and C-14 which in turn connected with the isopropyl group. The compound was proved to be totarol (**7**) after comparison with literature data [6, 7]. The absolute configuration was identical to that reported from the higher plants on the basis of optical rotation. Neither abietane- nor totarane-type diterpenes have ever been isolated from liverworts.

Two other related species were preliminarily examined as well. Unlike the extract of *S. acuminata*, which showed neoverrucosan-5β-ol (**1**) and homoverrucosan-5β-ol (**2**) as two major components along with many other diterpene peaks [1, 2], the GC-MS profile of the EtOAc extract of *Schistochila blumii* displayed only two large peaks that were identified to be known sesquiterpene hydrocarbons, tritomarene (**8**) and bourbon-7-ene (**9**) [8], nearly no other peaks corresponding to diterpenes were observed. On the other hand, the species of *Gottschea philippinensis* biosynthesized the same two diterpenoids, **1** and **2**, as that of *S. acuminata*. However, in addition to these two diterpenes and two other common sesquiterpenes, bicyclogermacrene and spathulenol, very few diterpene peaks appeared in the GC profile of the extract of *G. philippinensis*. *Gottschea* is considered

TABLE II Skeletal distribution of constituents found in species of Schistochilaceae

Species (*Region*)	*Compound or Skeleton*	*Skeletal type*	*Ref.*
Schistochila laminigera (Chile)	Bicyclogermacrene	C_{15}	[10]
	Cuparene		
S. reflexa (Chile)	Unidentified	C_{15}, C_{20}	[10]
S. acuminata (Taiwan)	Neoverrucosane	C_{20}	[1]
	Homoverrucosane		
	Clerodane		[2]
	Totarane		
S. appendiculata (New Zealand)	Alkylated phenols	R-ArOH	[11]
S. nobilis (New Zealand)	13-*epi*-Neoverrucosane	C_{20}	[12]
S. glaucesens (New Zealand)	Neomarchantin	ArOH (Bisbibenzyls)	[13]
S. aligera (= *Gottschea aligera*) (Malaysia)	Clerodane	C_{20}	[14]
	Rearranged pimarane		
S. blumii (Taiwan)	Tritomarene	C_{15}	
	Bourbon-7-ene		
G. philippinensis (Taiwan)	Neoverrucosane	C_{20}	[15]
	Homoverrucosane		

a separate genus (underleaves totally absent) from *Schistochila* (large underleaves always present) in the Schistochilaceae family [9]. In view of chemotaxonomy (Tab. II), the genera of *Gottschea* and *Schistochila* are closely related and may be combined into one genus.

EXPERIMENTAL SECTION

General Experimental Procedures

NMR spectra were measured in $CDCl_3$ on 500 MHz for ^1H and 125 MHz for ^{13}C. All EIMS spectra were taken at 70 eV. A DBWAX, 30 m × 0.25 mm (i.d.), fused silica capillary column was used for GC-MS. The column temperature was programmed from 50° to 220°C at 5°/min. IR spectra were measured in $CHCl_3$ on KBr pellets after the solvent was evaporated. Optical data were taken in $CHCl_3$ and UV in CH_3OH.

Plant Material

Plants were collected at the following locations: *Schistochila acuminata* Steph.--Yuenyang Lake (1700 m), Hsinchu Hsien (1996); *S. blumii* (Nees) Trev.--Lala Shan (1600 m), Taoyuan Hsien (1993); *Gottschea philippinensis* (Mont.) Jack et Steph.--Fu Shan (800 m), Ilan Hsien (1991). Specimens were identified by Dr. Kohsaku Yamada (Ise-shi, Japan) and the first author (C.-L. Wu), and deposited at the Dept. of Chemistry, Tamkang Univ.

Extraction and Isolation

The material (410 g) collected at Yuenyang Lake was frozen-crushed and extracted with *n*-hexane and EtOAc, respectively. From the hexane extract (6 g) totarol (**7**, 29 mg) was isolated after chromatography on silica gel and Sephadex LH-20 columns. The EtOAc extract (12 g) afforded compound **4** from the 35% eluate when chromatographed repeatedly on silica column and eluted with EtOAc-hexane. Further purification of **4** (7 mg) was achieved on prep. TLC. Plants of *S. blumii* and *G. philippinensis* (5 g each) were ground and extracted with EtOAc, respectively. Their extracts were analyzed by GC-MS.

15(16)-Peroxy-3, 13-clerodadien-18-oic acid (4)

$[\alpha]_D^{25}$ −47 (c 0.01, $CHCl_3$); IR(KBr) ν_{max}/cm^{-1}: 3400−2500 and 1670; UV(MeOH) λ_{max} nm: 220; TLC Rf = 0.49 (EtOAc/*n*-hexane = 1 : 4);

FABMS: *m/z* 335 $[M+H]^+$; EIMS (mass range starting from *m/z* 50) *m/z* (rel. int.): $[M]^+$ 334 (0), 316 ($[M\text{-}H_2O]^+$ 5), 221 (30), 203 (45), 149 (100), 125 (72), 95 (75), 93 (60), 91 (63), 84 (88) and 81 (76); NMR: Table I.

Totarol (7)

$[\alpha]_D^{25} + 42.5$ (c 0.8, $CHCl_3$); GC Rt = 78.65 min; EIMS (rel. int.): $[M]^+$ 286 (35), 271 (87), 201 (57), 189 (36), 175 (100), 159 (21), 69 (38) and 41 (35).

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