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DEPSIDONES AND DIARYL ETHERS FROM THE VIETNAMESE LICHEN *PARMOTREMA MELLISII*

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Abstract – The Vietnamese lichen *Parmotrema mellissii* of the family Parmeliaceae was chemically investigated to isolate five new depsidones (**1**, **6**, **9**–**11**) and three new diaryl ethers (**3**, **4**, **7**) along with seventeen known lichen substances. Their structures were determined by spectroscopic methods.

Dedicated to Professor Masakatsu Shibasaki on the occasion of his 70th birthday

INTRODUCTION

Lichens, symbiotic associations of two organisms, fungi (mycobionts) and algae (photobionts), are distributed worldwide and have been used for food, medicinal problems, dyes, and in the perfume industry.[1,2] Lichens are known to produce a variety of characteristic secondary products with manifold pharmacological activities.[3–6] Numerous lichenological studies have been undertaken in Europe and North America for over two centuries. In contrast, few lichens have been chemically studied in tropical zones. Previous studies on Vietnamese lichens focused mainly on their taxonomy and distribution, but only few results on their chemical constituents.[7–9]

The lichen genera *Parmotrema* and *Rimelia*, of the Parmeliaceae family, are foliose lichens widely distributed in tropical regions.[10] These lichen genera have been used in folk medicine in a large number of countries for the treatment of many diseases including various kinds of cancer.[5,11] Some lichen species of these genera were studied in terms of their phyto-biochemical properties,[4,11–14] however, *Parmotrema mellissii* (C.W. Dodge) Hale has not been studied. We have investigated the thalli of the lichen species, which were collected in the Langbiang Plateau, Dalat City, Vietnam, and isolated five new depsidones, three new diaryl ethers bearing an isocoumarin unit, and seventeen known lichen substances. The isolation and structural determination of these new compounds are described in this paper.

RESULTS AND DISCUSSION

The air-dried thalli of *P. mellissii* were extracted with acetone. The acetone extract was separated by column chromatography and preparative TLC to yield five new depsidones (**1**, **6**, **9**–**11**) and three new diaryl ethers (**3**, **4**, **7**), along with seventeen known compounds (Figure 1). The known compounds were identified as dehydrocollatolic acid (**2**),[15] 2′′′-*O*-methyl-α-alectoronic acid (**5**),[16] 2′′′-*O*-ethyl-β-alectoronic acid (**8**),[17] α-alectoronic acid (**12**),[18] α-collatolic acid (**13**),[16,19] β-alectoronic acid (**14**),[20] β-collatolic acid (**15**),[19] atranorin,[21] chloroatranorin,[22] ethyl chlorohaematommate,[23] methyl haematommate,[24] methyl β-orsellinate, (+)-usnic acid,[25] *n*-butyl orsellinate, ethyl orsellinate, methyl orsellinate,[26] and skyrin.[27] The structures of the new compounds were determined as follows.

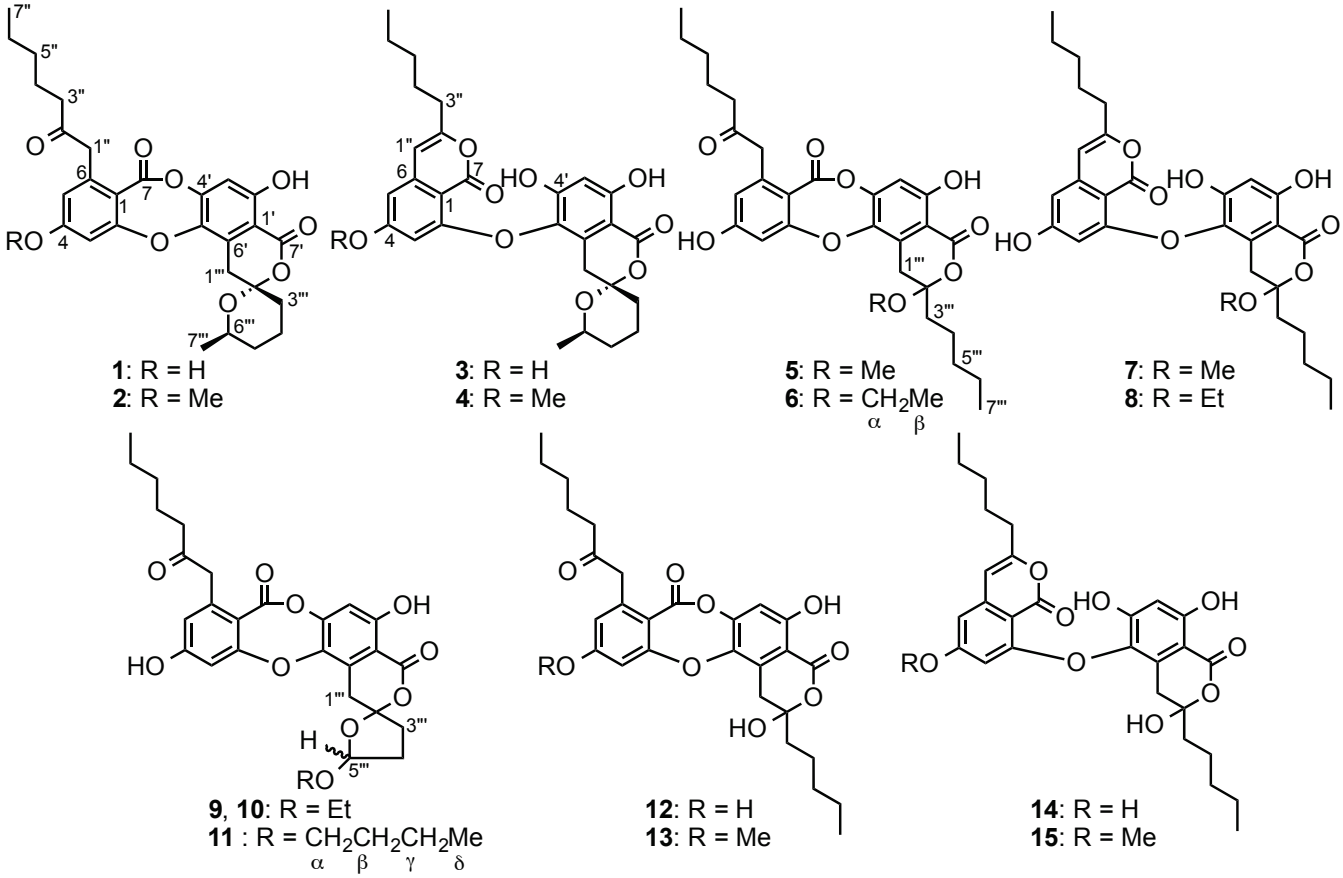

Figure 1. Structures of compounds **1**–**15**

Compound **1** was obtained as a colorless solid. The HR-EI mass spectrum of **1** exhibited a peak at *m/z* 510.1913 [M^+], indicating a molecular formula of $C_{28}H_{30}O_9$. Its ^{1}H NMR spectrum showed two *meta*-coupled doublets at δ 6.39 and 6.40 and a singlet at δ 6.74 due to aromatic protons, a hydrogen-bonded hydroxy signal at δ 11.07 (s), and two sets of methylene signals for COC**H$_2$**R at δ 2.63 (2H, td) and ArC**H$_2$**CO at δ 3.81 and 3.86 (each d). The ^{1}H NMR spectrum of **1** also exhibited two methyl signals at δ 0.90 (t, *J*=7.0 Hz) and 1.04 (d, *J*=7.0 Hz), the latter of which was coupled with an oxygenated methine resonance at δ 4.03 (dqd, *J*=11.0, 7.0, 2.0 Hz) (Table 1). The ^{13}C NMR spectrum of **1** showed

twenty-eight signals due to two methyl groups, nine methylene carbons, one sp^3, and three aromatic sp^2 CH carbons, and thirteen quaternary carbons including a carbonyl carbon at δ 209.7, two ester carbonyl carbons at δ 162.4 and 168.2, a ketal carbon at δ 104.2, and five oxygenated aromatic carbons (Table 2). These spectroscopic features closely resembled those of the co-occurring unique depsidone with a spiro-ring system, dehydrocollatolic acid (**2**),[15] except for the absence of a 4-methoxy signal, suggesting **1** to be a demethylated compound of **2**. The proposed structure of **1** was fully coincident with its 2D NMR spectroscopic data (Figure 2). Accordingly, compound **1** was designated dehydroalectoronic acid.

Table 1. ^{1}H NMR spectroscopic data (500 MHz, $CDCl_3$) of **1**, **3**, **4**, **6**, and **7**

H	**1**	**3**[a]	**4**	**6**	**7**
3	6.39, d (2.0)	6.06, br s	6.55, br s		
4-OH				7.87, br s	
4-OMe			3.79, s		
5	6.40, d (2.0)	6.429, d (2.0)	6.47, d (2.0)	6.41, d (2.5)	6.27, br s
2'-OH	11.07, s		11.20, s	11.05, s	11.12, br s
3'	6.74, s	6.433, s	6.50, s	6.73, s	6.42, s
4'-OH			8.92, br s		
1"	3.81, d (17.0)	6.31, s	6.22, s	3.83, s	6.11, s
	3.86, d (17.0)				
3"	2.63, td (7.5, 2.0)	2.50, t (7.0)	2.52, t (7.5)	2.66, td (7.5, 3.0)	2.43, m
4"	1.64, quint (7.5)	1.73, m	1.71, m	1.66, quint (7.0)	1.65, m
5"	1.32, m	1.42, m	1.37, m	1.34, m	1.34, m
6"	1.35, m	1.42, m	1.37, m	1.34, m	1.34, m
7"	0.90, t (7.0)	0.96, t (7.0)	0.92, t (7.0)	0.91, t (7.0)	0.91, t (7.0)
1"'	3.05, d (17.0)	2.95, m	2.96, d (16.5)	3.07, d (17.0)	2.88, br s
	3.42, d (17.0)	3.10, m	3.13, d (16.5)	3.46, d (17.0)	3.01, br s
3"'	1.69, m	1.59, td (13.5, 4.5)	1.59, td (13.5, 4.5)	1.90, ddd (14.5, 12.0, 5.0)	1.78, m
	2.06, m	1.99, br d (13.5)	2.04, br d (13.5)	2.05, ddd (14.5, 12.0, 5.0)	1.90, m
4"'	1.75, m	1.70, m	1.71, m	1.44, m	1.30, m
	2.08, m	2.02, m	2.12, qt (13.5, 4.0)	1.50, m	
5"'	1.30, m	1.25, m	1.26, m	1.36, m	1.25, m
	1.70, m	1.69, m	1.70, m		
6"'	4.03, dqd (11.0, 7.0, 2.0)	3.98, dqd (11.0, 6.5, 2.0)	4.07, dqd (11.0, 6.5, 2.0)	1.36, m	1.25, m
7"'	1.04, d (7.0)	1.05, d (6.5)	1.09, d (6.5)	0.93, t (7.0)	0.85, t (7.0)
α				3.64, dq (8.5, 7.0)	3.30, s
				3.70, dq (8.5, 7.0)	
β				1.07, t (7.0)	

[a]Measured in CD_3OD

Table 2. ^{13}C NMR spectroscopic data (125 MHz, $CDCl_3$) of new compounds

C	**1**	**3**[a]	**4**	**6**	**7**	**9**	**10**	**11**
1	112.5	102.2	103.8	112.5	102.5	112.8	112.9	113.4
2	162.1	162.2	162.4	162.1[b]	163.5	162.1	162.1	162.1
3	106.5	102.0	104.0	106.5	103.3	106.2	106.3	106.1
4	161.4	166.1	166.0	161.5	162.1	161.3	161.2	160.8
4-OMe			55.8					
5	117.7	105.5	102.5	117.9	103.3	117.7	117.7	117.3
6	141.0	143.9	142.1	140.9	142.1	141.0	141.1	141.3
7	162.4	163.2	160.4	162.4[b]	160.8	162.3	162.4	162.2
1'	104.9	100.9	100.0	104.9	99.6	104.9	105.1	104.8
2'	160.2	162.9	162.1	160.2	163.5	160.2	160.2	160.3
3'	107.7	103.4	103.4	107.7	105.6	108.0	108.0	108.1
4'	150.4	159.3	156.8	150.4	158.9	150.4	150.3	150.5
5'	139.8	133.3	133.9	139.9	133.4	139.7	139.7	139.7
6'	129.8	ND	131.1	130.2	131.4	129.7	129.8	129.6
7'	168.2	170.2	168.4	168.4	168.8	168.1	168.3	168.0
1"	48.1	104.4	103.3	48.1	103.3	48.0	48.0	47.9
2"	209.7	159.9	159.5	210.1	159.0	209.2	209.2	207.9
3"	42.8	34.1	33.3	42.9	33.1	42.9	42.9	42.9
4"	23.2	27.7	26.5	23.3	26.4	23.3	23.3	23.3
5"	31.3	32.4	31.2	31.3	31.2	31.3	31.3	31.3
6"	22.4	23.5	22.4	22.4[c]	22.4	22.4	22.4	22.4
7"	13.9	14.4	14.0	13.95[d]	14.0	14.0	14.0	13.9
1"'	33.3	ND	34.3	30.5	30.8	31.9	31.4	32.0
2"'	104.2	105.2	103.6	107.8	107.5	111.9	111.7	111.9
3"'	33.6	34.4	33.6	35.8	34.9	35.5	36.4	35.6
4"'	18.1	19.3	18.0	23.3	23.0	30.4	30.8	30.4
5"'	31.7	32.9	31.8	31.7	31.6	106.1	106.7	106.3
6"'	68.9	70.0	68.7	22.5[c]	22.4			
7"'	21.5	21.9	21.5	14.03[d]	14.0			
α				58.2	49.9	64.0	64.2	68.4
β				15.3		15.1	15.0	31.5
γ								19.2
δ								13.8

[a]Measured in CD_3OD [b,c,d]Assignments may be interchanged. ND: not detected

Compound **3** was obtained as a colorless solid. The HR-MS spectrum established the molecular formula of $C_{28}H_{30}O_9$, which is the same composition as that of **1**. The ^{1}H and ^{13}C NMR spectra of **3** closely resembled those of **1**. The marked differences were the presence of an additional olefinic proton at δ_H 6.31 (s) and an oxygenated quaternary carbon at δ_C 159.9 in **3**, instead of a methylene group (H_2-1″) and carbonyl carbon (C-2″) in **1**, respectively (Tables 1 and 2). In addition, the HMBC spectrum of **3** showed the correlations from H-1″ to C-3″ (δ 34.1), C-5 (δ 105.5), C-6 (δ 143.9), and C-2″ (δ 159.9) and from H-5 to C-3 (δ 102.0), C-1″ (δ 104.4), and C-4 (δ 166.1), suggesting a 2,4,2″-trisubstituted isocoumarin

ring system, as seen in **14** and **15**.

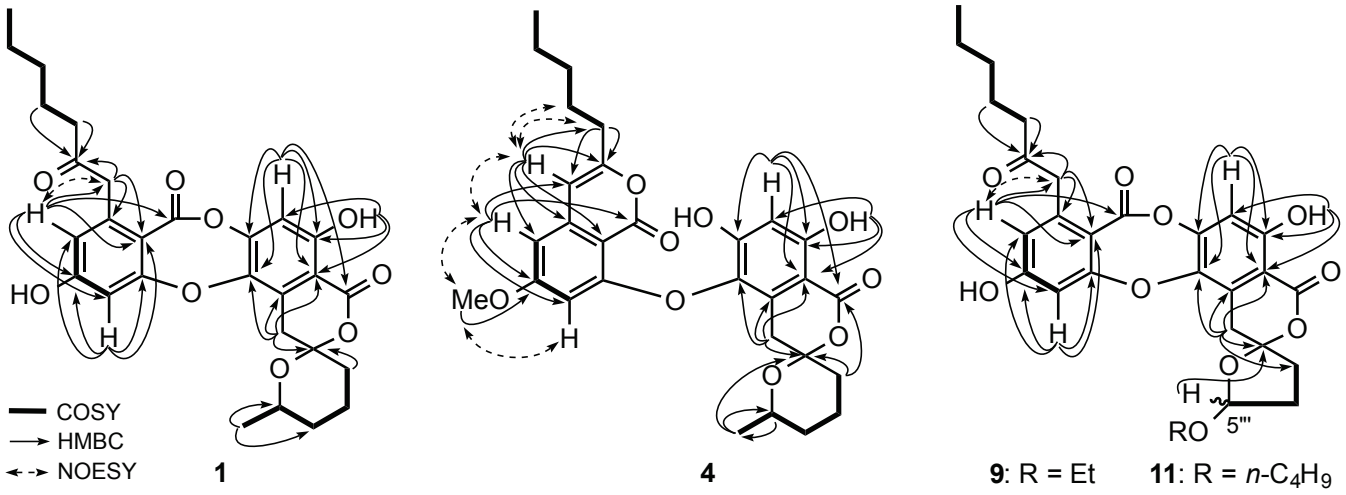

Figure 2. Key COSY, HMBC and NOESY correlations of compounds **1**, **4**, **9**, and **11**

The HR-EI mass spectrum of compound **4** showed a molecular formula of $C_{29}H_{32}O_9$, that is, 14 atomic units more than that of **3**. The ^{1}H and ^{13}C NMR spectroscopic features of **4** implied the same framework as **3** (Tables 1 and 2). The only observed difference was the additional methoxy group at δ_H 3.79 (s) and δ_C 55.8. The substitution of the methoxy group at C-4 was evidenced from HMBC correlations from the methoxy signal and two *meta*-coupled aromatic protons to oxygenated quaternary carbon at δ 166.0 (C-4) (Figure 2). Accordingly, compound **4** was characterized as a 4-*O*-methylated derivative of **3**.

Compounds **1**, **3**, and **4** as well as dehydrocollatolic acid (**2**) possess two asymmetric carbons, C-2‴ and C-6‴, of the spiro-ring system. However, the stereochemistry of **2** has not been discussed.[15] The relative configuration at the spiro-ring of **1**–**4** could be deduced from analysis of ^{1}H-^{1}H coupling constants and NOESY correlations. Detailed inspection of the coupling constants $J_{3‴ax/4‴ax}$ (13.5 Hz), $J_{4‴ax/5‴ax}$ (13.5 Hz), $J_{4‴ax/3‴eq}$ (4.5 Hz), and $J_{4‴ax/5‴eq}$ (4.0 Hz) in **4** allowed assignation of the signals for methylene protons at δ 1.26, 1.59, 1.70, 1.71, 2.04, and 2.12 to H-5‴ax, H-3‴ax, H-5‴eq, H-4‴eq, H-3‴eq, and H-4‴ax, respectively. The NOESY correlations among H-3‴ax/H-1‴ (δ_H 3.13), H-3‴ax/H-5‴ax, H-3‴eq/H-1‴ (δ_H 2.96), H-4‴ax/H-6‴, and H_2-5‴/H_3-7‴ indicated the axial orientation of H-6‴ and the equatorial orientation of H_3-7‴ in **4** (Figure 3). Although the NMR spectra of **4** demonstrated features for a single compound, its chiral HPLC analysis showed two peaks at a ratio of 1:6. Accordingly, compound **4** was a mixture of enantiomeric isomers. The enantiomeric mixture might be derived from a mixture of benzoic acid derivatives with (6‴*R*)- or (6‴*S*)-6‴-hydroxy-2‴-oxoheptyl group through non-enzymatic spiro-ketal cyclization to form more stable 2‴*R*, 6‴*S* and 2‴*S*, 6‴*R* isomers rather than 2‴*R*, 6‴*R* and 2‴*S*, 6‴*S* isomers. However, the absolute configuration of the predominant isomer could not be determined.

The similar NOESY correlations of compounds **1**–**3** suggested that these compounds possessed the same relative configurations at the spiro-ring system as **4**. Compounds **1**–**3** could also be mixtures of enantiomeric isomers, although chiral HPLC analyses of **1**–**3** failed to separate their enantiomeric isomers.

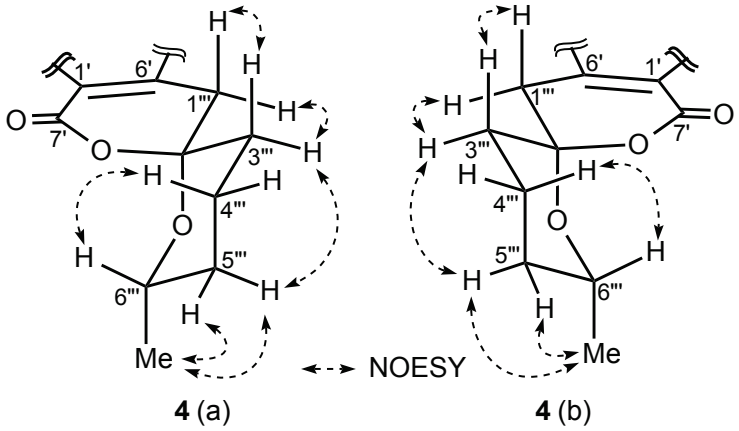

Figure 3. Relative configuration at the spiro-ring of **4**

Compound **6** was obtained as a mixture with 2′′′-*O*-methyl-α-alectoronic acid (**5**) at a ratio of 2:1. The ^{1}H and ^{13}C NMR spectra of **6** (Tables 1 and 2) were remarkably similar to those of **5**. The only difference between the two compounds was the substitution of an ethoxy group at C-2′′′ in **6** instead of a methoxy group in **5**. The location of the ethoxy group at C-2′′′ was confirmed by the HMBC correlations between H_2-α of the ethoxy group to the ketal carbon at δ_C 107.8 (C-2′′′). Accordingly, **6** was characterized as 2′′′-*O*-ethyl-α-alectoronic acid.

Another set of closely related compounds comprised **7** and **8**, which were isomeric with **5** and **6**, respectively. The ^{1}H and ^{13}C NMR spectra of **7** and **8** showed signals for an olefinic proton H-1′′ and oxygenated quaternary carbon C-2′′, which were characteristic of isocoumarin skeleton as in **3** and **4**. Detailed 2D NMR analysis and comparison with the reported data[16,17] led us to determine that the structures of **7** and **8** were 2′′′-*O*-methyl-β-alectoronic acid and 2′′′-*O*-ethyl-β-alectoronic acid, respectively. 2′′′-*O*-Ethyl-β-alectoronic (**8**) was isolated from the lichen *Alectoria sarmentosa* and reported as an artifact formed from β-alectoronic acid (**14**) during treatment with EtOH.[17] In a similar manner, **5** was derived from α-alectoronic acid (**12**) in acidic MeOH.[16] Compound **7** was identified as a new structure isolated from lichen, but could be an artifact formed from **14** during extraction with MeOH.

Compounds **5**–**8** possessed an asymmetric center at ketal carbon C-2′′′, but these compounds exhibited no optical activity. These compounds were analyzed by chiral HPLC and each one demonstrated two peaks at a ratio of ca. 1:1. These findings revealed that compounds **5**–**8** were racemic compounds.

Compound **9**, named parmellisidone A, was isolated as a yellowish solid. The MS spectrum of **9** established the molecular formula of $C_{28}H_{30}O_{10}$. The ^{1}H NMR spectrum exhibited signals for a pair of

meta-coupled aromatic protons at δ 6.40 and 6.44 (each 1H, d, *J*=2.0 Hz), an aromatic proton at δ 6.75 (s), two methylene groups at δ 3.81 and 3.92 (each 1H, d, *J*=17.0 Hz), and at δ 3.32 and 3.49 (each 1H, d, *J*=17.0 Hz), and an *n*-pentyl group. It showed further signals due to an ethoxy group and a doublet for an acetal methine proton H-5‴ at δ 5.28 (*J*=5.0 Hz), which was connected in sequence in the ^{1}H-^{1}H COSY spectrum with two methylene signals at δ 2.34 and 2.38 (each 1H, m) and at δ 2.03 and 2.40 (each 1H, m) (Table 3). These ^{1}H NMR spectroscopic data, together with the ^{13}C NMR features (Table 2), established that **9** had a similar depsidone structure as **1**, but differed from **1** in the spiro-ring system. The NOESY spectrum of **9** showed the correlations between H-5‴ and methylene protons at δ 3.37 and 3.60 of the ethoxy group. In the HMBC spectrum of **9**, a significant correlation was observed from H-5‴ to the ketal carbon at δ 111.9 (C-2‴) (Figure 2). These findings indicated that **9** possessed a 6,5-spiro ring instead of a 6,6-spiro ring in **1**.

Table 3. ^{1}H NMR spectroscopic data (500 MHz, $CDCl_3$) of **9**–**11** (*J*, Hz)

H	**9**	**10**	**11**
3	6.40, d (2.0)	6.39, d (2.5)	6.51, d (2.5)
4-OH	7.58, br s	7.50, br s	6.89, br s
5	6.44, d (2.0)	6.47, d (2.5)	6.48, d (2.5)
2'-OH	10.94, s	11.05, s	10.96, s
3'	6.75, s	6.77, s	6.79, s
1"	3.81, d (17.0)	3.85, d (17.0)	3.86, d (17.0)
	3.92, d (17.0)	3.90, d (17.0)	3.96, d (17.0)
3"	2.64, t (7.5)	2.63, td (7.0, 2.0)	2.60, t (7.5)
4"	1.65, quint (7.5)	1.65, quint (7.0)	1.65, m
5"	1.33, m	1.33, m	1.31, m
6"	1.33, m	1.33, m	1.34, m
7"	0.91, t (7.0)	0.91, t (7.0)	0.91, t (7.0)
1‴	3.32, d (17.0)	3.25, d (17.0)	3.35, d (16.5)
	3.49, d (17.0)	3.46, d (17.0)	3.53, d (16.5)
3‴	2.34, m	2.16, m	2.34, m
	2.38, m	2.59, m	2.38, m
4‴	2.03, m	2.25, m	2.03, m
	2.40, m	2.35, m	2.41, m
5‴	5.28, d (5.0)	5.29, dd (5.5, 3.5)	5.28, d (5.5)
α	3.37, dq (10.0, 7.0)	3.41, dq (10.0, 7.0)	3.32, dt (10.0, 7.0)
	3.60, dq (10.0, 7.0)	3.60, dq (10.0, 7.0)	3.56, dt (10.0, 7.0)
β	1.16, t (7.0)	1.15, t (7.0)	1.51, quint (7.0)
γ			1.34, m
δ			0.89, t (7.5)

Compound **10** was isomeric with **9**. The ^{1}H and ^{13}C NMR spectra of **10** (Tables 2 and 3) demonstrated the depsidone skeleton. The differences between these compounds could only be accounted for by the splitting pattern of the signal due to a ketal proton (H-5′′′) (**10**: dd, *J*=5.5, 3.5 Hz; **9**: d, *J*=5.0 Hz). Accordingly, compound **10** was supposed to be a stereoisomer of **9** and designated parmellisidone B.

The HR-SIMS established the composition of **11** as $C_{30}H_{34}O_{10}$, that is, having two methylene groups more than **9**. The NMR spectroscopic features of **11** (Tables 2 and 3), named parmellisidone C, were also similar to those of **9**, except for the presence of an *n*-butoxy group at C-5′′′. Detailed NMR studies of this compound led us to determine the structure **11** as shown.

Compounds **9**–**11** were representative of 6,5-spiroketal natural products and possessed two asymmetric carbons, C-2′′′ and C-5′′′. In the ^{1}H NMR spectra, compound **10** merely differed from **9** and **11** in the signal of ketal proton H-5′′′, implying that **10** was distinct from **9** and **11** in terms of the stereochemistry of asymmetric carbon C-5′′′. The ketal proton H-5′′′ of **10** resonated at δ 5.29 as a doublet of doublets (*J*=5.5, 3.5 Hz) due to coupling to the vicinal methylene protons H_2-4′′′. On the other hand, the ketal proton H-5′′′ of **9** and **11** resonated as a doublet (*J*=5.0 and 5.5 Hz, respectively). These differences indicated that the methine proton H-5′′′ of **9** and **11** coupled to only one of the vicinal methylene protons H_2-4′′′. Coupling between H-5′′′ and the other proton of H_2-4′′′ was not observed, implying that the dihedral angle between H-5′′′ and one of the protons H_2-4′′′ was close to 90°.[30] Although the coupling constants of the ketal proton H-5′′′ of compounds **9**–**11** have been determined, the stereochemistry of the spiro-ring systems remains to be elucidated.

From the thalli of the foliose lichen *P. mellissii*, 25 lichen substances including five new depsidones (**1**, **6**, **9**–**11**) and three new diaryl ethers (**3**, **4**, **7**) were isolated. With the single exception of dehydrocollatolic acid (**2**), depsidones (**1**, **9**–**11**) with a spiro-ring system have not been reported. The depsidones α-alectoronic acid (**12**) and α-collatolic acid (**13**), common lichen substances in the lichen genus *Parmotrema*,[15] were obtained as major metabolites from *P. mellissii*. It is noted that, during isolation and purification under mild conditions, **12** and **13** could be easily converted to more stable isocoumarin forms, diaryl ethers **14** and **15**, respectively. Similar phenomena were also observed for depsidones **1**, **2**, **5**, and **6**. Therefore, the isolated diaryl ethers **3**, **4**, **7**, **8**, **14**, and **15** could be artifacts rather than products from natural sources.

EXPERIMENTAL

General experimental procedures. Melting points were measured on a Yanaco micromelting point apparatus and are reported uncorrected. The specific rotations were measured on a Jasco DIP-370 digital polarimeter. The UV spectra were recorded on a Shimadzu UV-240 spectrophotometer and the IR spectra on a Shimadzu FTIR-8200 infrared spectrophotometer. The NMR experiments were performed with

Varian VXR-500, Varian UNITY INOVA, and Varian Gemini-300 spectrometers, with TMS as an internal standard. HR-EIMS and HR-SIMS were obtained with a Hitachi M-4100 mass spectrometer. Silica gel 60 (Merck) was used for column chromatography. Thin-layer chromatography was performed on precoated Kieselgel 60F_{254} plates (Merck) and spots were visualized under UV light.

Plant material. The thalli of *P. mellissii* were collected from the bark of pine trees in 2008 in Dalat City, Vietnam (*ca.* 1520 m alt.). The voucher specimen (No. KPU-V-1) were identified by Ms. Giao T. P. Vo, University of Science Ho Chi Minh City, Vietnam, and Dr. Isao Yoshimura, Hattori Botanical Laboratory, Japan, and were deposited at Kobe Pharmaceutical University. The thalli of the lichen were cleaned and dried at room temperature (rt) before extraction.

Extract and isolation. The dried thalli of *P. mellissii* (60.0 g) were extracted with acetone at rt (1.0 L × 3), and the combined extracts were concentrated under reduced pressure to give a residue (8.41 g). This extract was separated by silica gel column chromatography (CC) ($CHCl_3$-MeOH) to obtain four fractions, fr-I (0% MeOH, 1.25 g), fr-II (1% MeOH, 3.27 g), fr-III (2% MeOH, 2.19 g), and fr-IV (3-50% MeOH, 1.62 g). Fr-I was purified by silica gel CC ($CHCl_3$-MeOH) and preparative TLC ($CHCl_3$; $CHCl_3$-MeOH, 99:1, 85:5, 9:1; *n*-hexane-Et_2O, 1:1), giving **2** (19.6 mg), **4** (22.0 mg), atranorin (737 mg), chloroatranorin (95.2 mg), methyl β-orsellinate (42.7 mg), methyl orsellinate (2.0 mg), *n*-butyl orsellinate (4.6 mg), methyl haematommate (1.7 mg), ethyl chlorohaematommate (6.8 mg), (+)-usnic acid (22.5 mg), and skyrin (4.8 mg). Fr-II was separated by silica gel CC ($CHCl_3$-MeOH) to obtain three sub-fractions, fr-IIa (0% MeOH, 417 mg), fr-IIb (0% MeOH, 539 mg), and fr-IIc (1-2% MeOH, 2.17 g). These sub-fractions were continuously purified by silica gel CC ($CHCl_3$-MeOH) and preparative TLC ($CHCl_3$-MeOH, 99:1, 9:1; *n*-hexane-Et_2O, 1:1; toluene-AcOH, 20:3) to yield lichen substances. Fr-IIa gave a mixture of **5** and **6** (65.6 mg), **8** (66.2 mg), and **11** (2.9 mg). Fr-IIb yielded **1** (21.6 mg), **3** (25.0 mg), **9** (9.1 mg), **10** (8.1 mg), **13** (327 mg), and ethyl orsellinate (10.2 mg). Fr-IIc afforded **5** (43.9 mg), **7** (13.7 mg), **12** (1.21 g), **13** (365.7 mg), **14** (21.3 mg), and **15** (139 mg). Purification of fr-III by silica gel CC ($CHCl_3$-MeOH) gave **12** (1.32 g) and **14** (798 mg).

Dehydroalectoronic acid (1): Colorless solid; mp 180-181 ^oC ($CHCl_3$); $[\alpha]_D^{19}$ -35^o (*c* 0.96, $CHCl_3$); UV λ_{max} (EtOH) nm (log ε): 216 (4.46), 254 (4.15), 316.5 (3.83); IR (KBr) cm^{-1}: 3322, 2934, 1738, 1682, 1614; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (%): 510 ([M^+], 60), 466 (100), 432 (42.2), 406 (55.7), 370 (56), 249 (29.4), 219 (42.2), 192 (18.2), 163 (35.7), 95 (34.6), 69 (82.1); HR-EIMS *m/z*: 510.1913 [M^+] (Calcd. for $C_{28}H_{30}O_9$: 510.1891).

Diaryl ether 3: Colorless solid; mp 225-226 ^oC ($CHCl_3$); $[\alpha]_D^{18}$ -23^o (*c* 0.41, MeOH); UV λ_{max} (EtOH) nm (log ε): 216.5 (4.36), 245.5 (4.69), 318.5 (4.12); IR (KBr) cm^{-1}: 3199, 2931, 1730, 1662, 1601; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (%): 510 ([M^+], 80.9), 466 (100), 406 (57.2), 370 (68), 249 (35.2), 219 (43.3), 163 (39.2), 97 (35.3), 69 (75.2); HR-EIMS *m/z*: 510.1884 [M^+] (Calcd. for $C_{28}H_{30}O_9$:

510.1891).

Diaryl ether 4: Colorless solid; mp 203-204 °C (MeOH); $[\alpha]_D^{25}$ -120.9° (*c* 0.48, $CHCl_3$); UV λ_{max} (EtOH) nm (log ε): 217.5 (4.29), 245 (4.64), 272.5 *sh* (4.11), 322.5 (4.13); IR (KBr) cm^{-1}: 3209, 2932, 1698, 1671, 1628, 1604; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (%): 524 ([M^+], 70.2), 480 (100), 446 (36.3), 420 (56.8), 384 (46.2), 262 (27.6), 219 (24.6), 164 (29.6), 97 (41.7), 69 (80.8); HR-EIMS *m/z*: 524.2056 [M^+] (Calcd. for $C_{29}H_{32}O_9$: 524.2048).

2′′′-O-Ethyl-α-alectoronic acid (6): Yellowish solid; IR (KBr) cm^{-1}: 3391, 2956, 1730, 1682, 1613; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (%): 540 ([M^+], 13.1), 524 (24.5), 494 (100), 476 (40), 450 (50); HR-EIMS *m/z*: 540.2346 [M^+] (Calcd. for $C_{30}H_{36}O_9$: 540.2361).

Diaryl ether 7: Colorless crystalline solid; mp 139-140 °C ($CHCl_3$-MeOH); $[\alpha]_D^{18}$ 0° (*c* 0.72, MeOH); UV λ_{max} (EtOH) nm (log ε): 217 (4.32), 245.5 (4.50), 318 (4.03); IR (KBr) cm^{-1}: 3398, 2957, 1720, 1662, 1600; ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (%): 526 ([M^+], 0.4), 494 (13), 450 (100), 394 (5.9), 352 (12.2), 44 (43.9); HR-EIMS *m/z*: 526.2221 [M^+] (Calcd. for $C_{29}H_{34}O_9$: 526.2204).

Parmellisidone A (9): Yellowish solid; $[\alpha]_D^{20}$ 0° (*c* 0.72, $CHCl_3$); UV λ_{max} (EtOH) nm (log ε): 215.5 (4.51), 252 (4.18), 317 (3.81); IR (KBr) cm^{-1}: 3273, 2957, 1739, 1685, 1613, 1579; ^1H NMR: Table 1; ^{13}C NMR: Table 2; SIMS *m/z* (%): 525 ([M-H]$^-$, 59), 497 (100), 453 (26.3), 247 (33.6), 203 (19); HR-SIMS *m/z*: 525.1773 [M-H]$^-$ (Calcd for $C_{28}H_{29}O_{10}$: 525.1762).

Parmellisidone B (10): Yellowish solid; $[\alpha]_D^{21}$ 0° (*c* 0.28, $CHCl_3$); UV λ_{max} (EtOH) nm (log ε): 200 (4.50), 246 (4.28), 317 (3.86); IR (KBr) cm^{-1}: 3272, 2928, 2855, 1730, 1684, 1613; ^1H NMR: Table 1; ^{13}C NMR: Table 2; SIMS *m/z* (%): 525 ([M-H]$^-$, 100), 497 (27.1), 247 (19.9), 91 (20.5); HR-SIMS *m/z*: 525.1756 [M-H]$^-$ (Calcd for $C_{28}H_{29}O_{10}$: 525.1762).

Parmellisidone C (11): Yellowish solid; $[\alpha]_D^{21}$ 0° (*c* 0.29, $CHCl_3$); UV λ_{max} (EtOH) nm (log ε): 216 (4.60), 252 (4.27), 317.5 (3.90); IR (KBr) cm^{-1}: 3267, 2927, 1739, 1685, 1613; ^1H NMR: Table 1; ^{13}C NMR: Table 2; SIMS *m/z* (%): 553 ([M-H]$^-$, 100), 497 (11.4), 441 (10.2), 247 (16.7), 183 (27.0), 91 (9.1); HR-SIMS *m/z*: 553.2078 [M-H]$^-$ (Calcd. for $C_{30}H_{33}O_{10}$: 553.2075).

HPLC analysis of isolated compounds. New isolated compounds were analyzed by chiral HPLC [column, CHIRALCEL OJ-RH (0.46 × 15 cm, Daicel Chemical Industries, Ltd.); flow rate, 1.0 mL/min; detection, 254 nm]. Compound **4**, mobile phase, CH_3CN-H_2O (1:1), minor peak at 14.5 min and major peak at 16 min at a ratio of 1:6. Compound **6**, mobile phase, CH_3CN-H_2O (1:1), two peaks at 19.8 min and 23.5 min at a ratio of 1:1.

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