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Novel Sesquiterpenoids from the Colombian Liverwort *Porella swartziana*

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Abstract. Five africanane-, two seco-africanane-, two guaiane-, one germacrane-, and one nor seco-africanane-type sesquiterpenoids have been isolated from the liverwort *Porella swartziana* and their structures determined mainly by 2D NMR spectroscopy and X-ray analyses as well as chemical transformations.

INTRODUCTION

We have previously isolated caespitenone from the liverwort *Porella caespitans* var. *setigera* and proposed the pseudo guaiane-type structure mainly based on the low frequency NMR spectroscopy.[1] Recently we have collected the closely related species *Porella swartziana* in Colombia. The investigation of this species resulted in the isolation of the same compound.[2,3] In order to confirm the structure we have measured the various kinds of 2D NMR spectra and found that the structure must be revised to an africanane-type compound as depicted in the formula **1**.[2,3] Besides caespitenone, ten more related terpenoids have been isolated from this liverwort. Four of them were africanane, two of them were seco-africanane, one was nor seco-africanane, two were guaiane, and one was germacrane-type sesquiterpenoids. These were somehow biosynthetically related to each other and their structures were determined by a combination of 2D NMR spectroscopy, X-ray crystallographic analyses, and chemical transformations. Here we report their structure elucidation, including the absolute configuration of africanane series substances.

RESULTS AND DISCUSSION

Isolation

The ether extract of *P. swartziana* collected in Colombia in 1991 was subjected to column chromatography of Sephadex LH-20 and of silica gel repeatedly to afford caespitenone (**1**),[1-3] swartzianins A (**2**), B (**3**), C (**4**), and D (**5**), secoswartzianins A (**6**)[4] and B (**7**),[4] guaiswartzianins A (**8**) and B (**9**), germacraswartzianin (**10**), and norsecoswartzianin (**11**) as well as four known sesquiterpenes **12**,[5] **13**,[6] **14**,[7] and **15**[8] (Fig. 1).

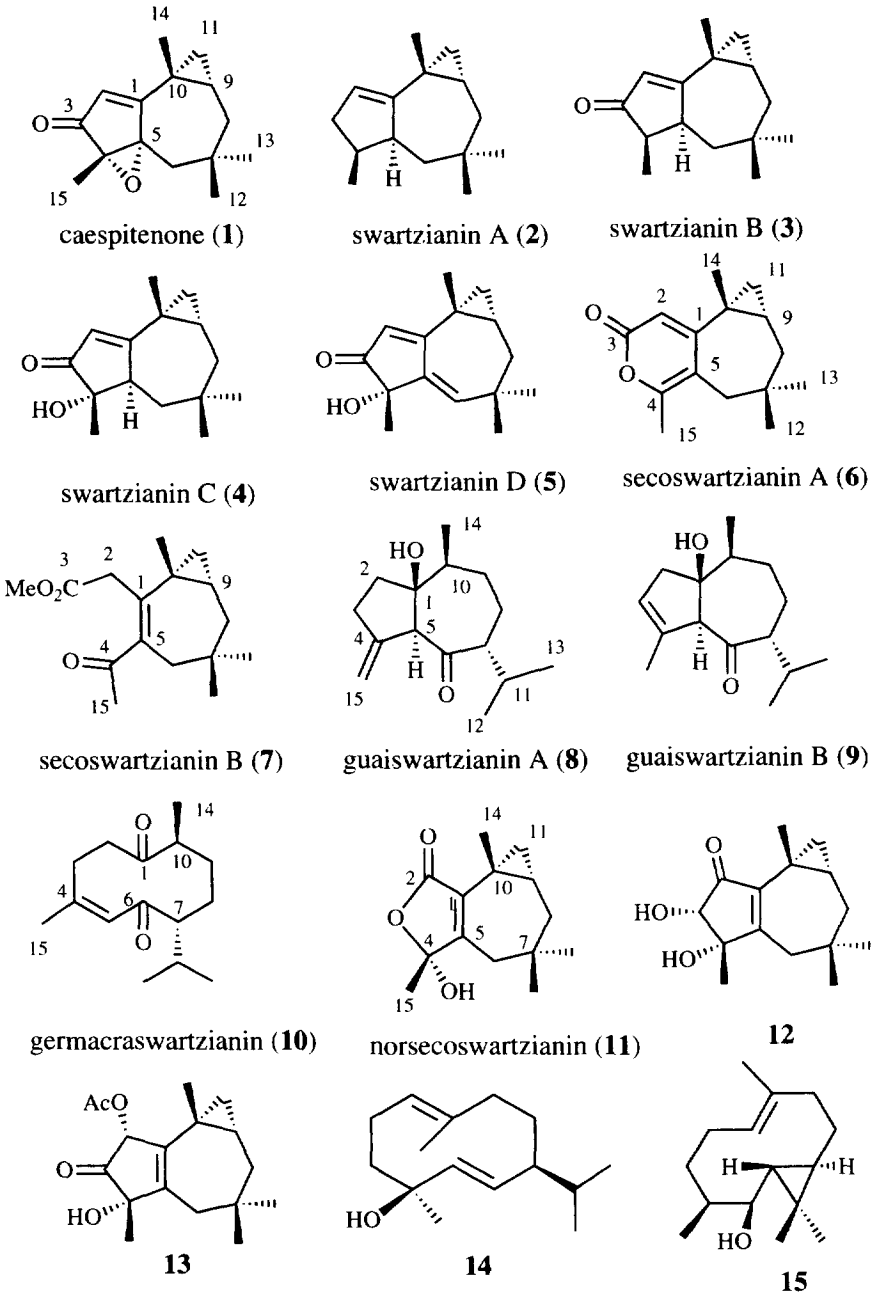


Figure 1. Structures of terpenoids isolated from *P. swartziana.*

Table 1. The ^{13}C NMR data for compounds **1** - **11**.[a]

C	1	2[b]	3	4	5	6	7	8	9	10	11[c]
1	180.0	152.4 (152.3)	188.9	188.0	177.4	164.4	143.7	83.4	83.4	214.8	130.8 (130.5)
2	128.5	123.8 (124.3)	126.7	126.9	129.7	113.2	38.4	30.3	47.4	39.3	171.0 (170.6)
3	200.1	38.9 (39.3)	210.5	210.2	207.3	163.2	171.9	39.3	125.7	27.3	---
4	60.8	38.6 (39.0)	46.7	80.4	77.2	157.6	202.8	148.5	137.8	148.0	104.4 (104.3)
5	66.5	44.1 (44.4)	40.9	49.5	140.6	113.2	136.8	62.7	67.1	129.6	158.9 (158.6)
6	34.2	39.3 (39.6)	43.5	38.0	140.8	37.3	40.0	214.8	214.0	209.2	41.1 (41.0)
7	34.5	32.6 (32.7)	32.6	33.1	37.0	34.5	31.6	60.6	58.8	58.0	31.43 (31.41)
8	42.7	41.0 (41.3)	39.1	41.3	44.2	41.9	41.6	26.9	25.3	26.8	42.8 (42.4)
9	21.3	22.8 (22.9)	27.3	24.00	22.3	19.0	21.4	30.6	31.5	29.0	21.3 (21.1)
10	19.5	19.7 (19.8)	24.18	21.0	22.1	22.9	25.9	45.7	44.7	41.7	15.14 (15.11)
11	23.3	21.7 (22.1)	24.15	23.95	24.3	19.8	17.0	31.9	32.3	27.3	21.9 (21.8)
12	28.9	29.8 (29.9)[d]	29.9[d]	29.4[d]	26.6[d]	28.3[d]	29.2[d]	21.0[d]	20.5[d]	21.5[d]	26.7 (26.4)[d]
13	30.8	31.5 (31.6)[d]	32.2[d]	29.7[d]	32.2[d]	28.5[d]	29.7[d]	19.5[d]	19.0[d]	19.88[d]	33.04 (33.00)[d]
14	26.5	27.1 (27.4)	24.8	27.2	27.0	25.1	22.3	17.1	17.0	19.94	23.2 (23.0)
15	8.4	15.1 (15.3)	10.4	21.9	25.6	17.6	29.9	110.6	15.6	23.4	24.2 (24.0)
OMe							51.6				

a) in $CDCl_3$

b) data in the parentheses were taken in C_6D_6

c) C-4 isomer in the parentheses

d) may be interchanged in each vertical column

Swartzianin A (**2**)

The molecular formula of **2** was determined to be $C_{15}H_{24}$ by HRMS. The IR spectrum indicated the presence of an olefin (1620 cm^{-1}), which was confirmed by the ^1H (δ 5.62) and ^{13}C NMR (δ 124.3 and 152.3) spectra (in C_6D_6). The ^1H NMR signals due to a cyclopropane ring were obviously detected at δ 0.49 (1H, m, H-11) and 0.72 (2H, m, H-9 and H-11), which had correlation peaks each other in the ^1H-^1H COSY spectrum, which further exhibited a correlation to two hydrogens at C-8. The proton network of H-2, H_2-3, H-4 (H_3-15), H-5, and H_2-6 was revealed by this spectrum, too. The HMBC spectrum (Fig. 2) indicated the correlations between the C-10 methyl group and the olefinic carbon at δ 152.3, the methine carbon at 22.9 and the methylene carbon at 22.1, respectively. The methyl groups at C-7 correlated with the carbons at 6 and 8. Thus the partial structures were connected to construct an africanane skeleton. Although the NOE measurement was carried out, no significant enhancement was observed. The relative configuration of this compound was determined by chemical correlation as described in the next section.

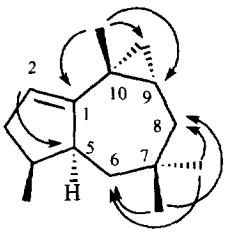


Figure 2. HMBC correlations for swartzianin A (**2**).

Swartzianin B (**3**)

The molecular formula of **3** was determined to be $C_{15}H_{22}O$ by HRMS. The presence of the carbonyl group (1680 cm^{-1}) and the olefin (1580 cm^{-1}) was inferred by the IR spectrum, which was supported by the ^{13}C NMR spectrum (δ 210.5, 188.9, and 126.7). The partial structures of H-8, 9, and 11 and H-4, 5, 6, and 15 were suggested by the ^1H-^1H COSY spectrum. The HMBC spectrum connected these partial structures to make an africanane skeleton as shown in Fig. 3. The NOE measurement for **3** did not show any information. However, reduction of **3** with $NaBH_4$-$CeCl_3$ gave two alcohols **16** and **17**, the latter of which showed the NOEs between H-5 and H-11 as well as between H-5 and H-4, and H-3 and H-15 (Fig. 4). Thus the relative stereochemistry of **3** was determined as shown in the formula.

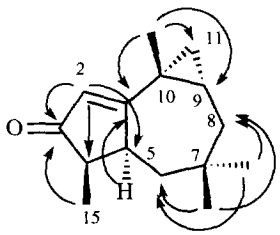


Figure 3. HMBC correlations for swartzianin B (**3**).

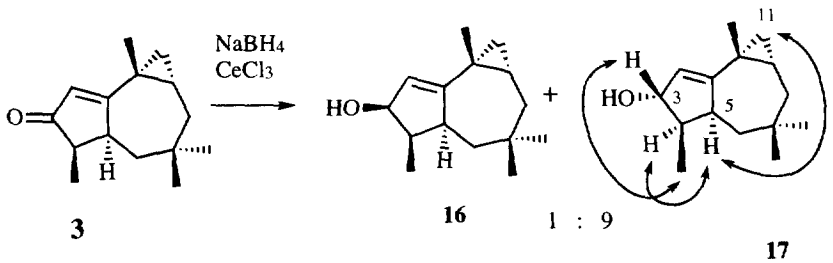
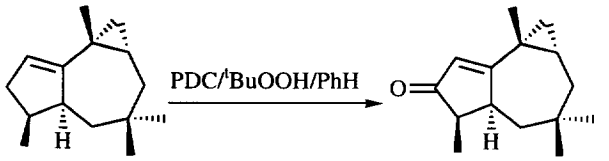


Figure 4. Reduction of swartzianin A (**2**).

Swartzianin A (**2**) was subjected to the reaction with PDC in the presence of *t*-butyl hydroperoxide in benzene[9] to afford a ketone in 40% yield, whose spectral data were identical with those of swartzianin B (**3**), establishing the relative stereochemistry of **2** (*vide supra*) (Fig. 5).[10]



swartzianin A (**2**) swartzianin B (**3**)

Figure 5. Oxidation of swartzianin A (**2**).

Swartzianin C (**4**)

The molecular formula of swartzianin C was determined to be $C_{15}H_{22}O_2$ by HRMS. The spectral data of **4** were similar to those of **3**. The presence of the cyclopropane ring was revealed by the peaks at δ 0.62 (1H, t, J=4.5 Hz) in the ^{1}H NMR spectrum and the ^{13}C NMR (δ_C 80.4) and IR (3550, 3400 cm^{-1}) spectra suggested that there was a hydroxyl group in the molecule. The position of the hydroxyl group was determined by the HMBC spectrum as shown in Fig. 6. Since no significant NOE peaks were found in this molecule, the stereochemistry could not be assigned by the NMR techniques. However nice crystals (mp 89-92°) were obtained from the hexane solution and the X-ray analysis was carried out. Fig. 7 shows the ORTEP drawing of swartzianin C.[11] Thus the hydroxyl group at C-4, the H-5, and the cyclopropane ring were all in the same direction. The absolute configuration of this molecule was established by allylic benzoate chirality method. Swartzianin C (**4**) was reduced by $NaBH_4$-$CeCl_3$ to afford two isomers, which were further converted into the corresponding benzoates **18** and **19**. Their relative stereochemistries were determined by the NOEs as shown in Fig. 8. The CD spectra of **18** showed the Cotton effect at 241 nm (Δε +5.27), while **19** at 236 nm (Δε -14.6).[12] Therefore the absolute configuration of **4** was unambiguously established as in the formula.

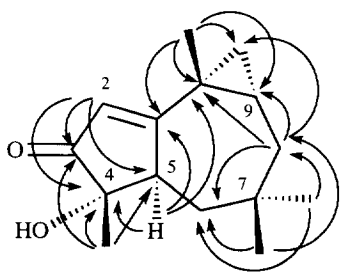


Figure 6. HMBC correlations for swartzianin C (**4**).

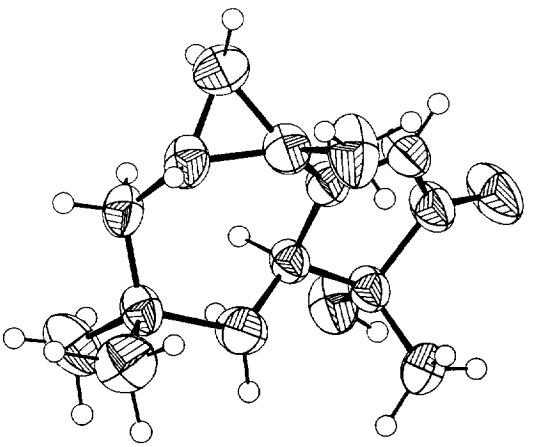


Figure 7. ORTEP Drawing of swartzianin C (**4**).

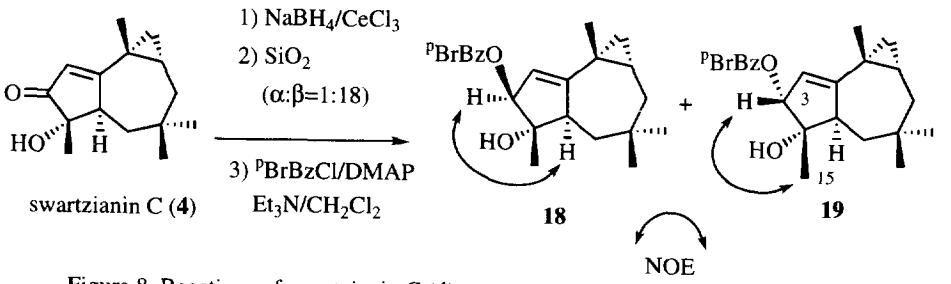


Figure 8. Reactions of swartzianin C (**4**).

Swartzianin D (**5**)

Swartzianin D (**5**) had a molecular formula $C_{15}H_{20}O_2$, two hydrogens less than that of swartzianin C (**4**). The NMR and IR (1700, 1560 cm^{-1}) spectra indicated that it had two double bonds (δ_C 129.7, 140.6, 140.8, 177.4), a carbonyl group (δ_C 207.3), and a hydroxyl group (3400 cm^{-1}). The HMBC spectrum indicated that it also had an africanane skeleton. Compound **5** seems to be flat and the relative stereochemistry concerning the hydroxyl group and the cyclopropane ring could not be determined by the NOE spectrum. However nice crystals (mp 106-107°) were obtained from the hexane solution. The ORTEP drawing was shown in Fig. 9, indicating that both the hydroxyl group and the cyclopropane ring were in the same side of the molecule.[11] An effort to reduce the carbonyl group or the double bond of **5** was not successful. Therefore the absolute configuration of **5** was not determined. However, this must have the same absolute configuration as in the other swartzianins, because they showed similar CD spectra (see Experimental) and also from the biogenetic standpoint.

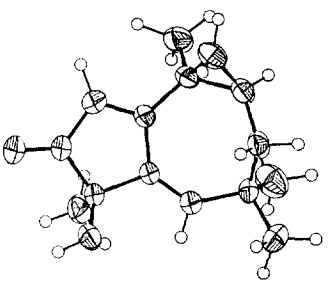


Figure 9. ORTEP Drawing of swartzianin D (**5**).

Secoswartzianin A (**6**)[4]

The molecular formula of **6** was determined to be $C_{15}H_{20}O_2$ by HRMS. The ^1H NMR spectrum indicated the presence of a cyclopropane ring [δ_H 0.23 (1H, dd, J=14, 12 Hz), 0.29 (1H, t, J=4.4 Hz)] and the ^{13}C NMR spectrum showed the presence of five sp^2 carbons (113.2, 113.2, 157.6, 163.2, 164.4), four methyls (17.6, 25.1, 28.3, 28.5), three methylenes (19.8, 37.3, 41.9), one methine (19.0), and two quaternary carbons (22.9, 34.5). Since the absorption band at 1705 cm^{-1} was observed in the IR spectrum of **6**, this was at first thought to be a cyclopentenone derivative. However the MS spectrum clearly showed the molecular ion peak

at m/z 232 and the HRMS indicated the presence of the second oxygen. Furthermore the long-range C-H COSY spectrum showed the following correlations: between (1) H-15 and C-4, C-5, (2) H-14 and C-1, C-9, C-10, (3) H-12 and C-6, C-7, C-8, C-13, (4) H-13 and C-6, C-7, C-8, C-12, (5) H-2 and C-5 (or C-2), C-3, C-10, (6) H-6a and C-1, C-4, C-7, C-8, (7) H-6b and C-1, C-4, C-5, C-7, C-12, C-13. Thus the planar structure was inferred to be a secoafricanane-type having an α–pyrone moiety. This was confirmed by a reaction of **6** with dimethyl acetylenedicarboxylate in toluene under reflux to afford a dimethyl phthalate derivative **20** in 57% yield (Fig. 10).[13,14] Compound **6** was treated with ozone in MeOH at -78°C followed by sodium borohydride to afford a diol **21**, which was benzoylated to give a dibenzoate **22**. The benzoate group adjacent to the cyclopropane was on the same side as the cyclopropane ring, since the NOE between the methyl group at C-10 and H-1 was observed. The second benzoate group at C-5 was trans to the one at C-1, because no NOE was observed between H-1 and H-5, and furthermore the coupling constant of H-1 and H-5 was 6 Hz. Therefore the absolute configuration of **22** was determined as shown in the formula on the basis of the dibenzoate rule (Δε -37.7 at 249 nm in MeOH).[12] Hence the absolute configuration of **6** was established as depicted in the formula.

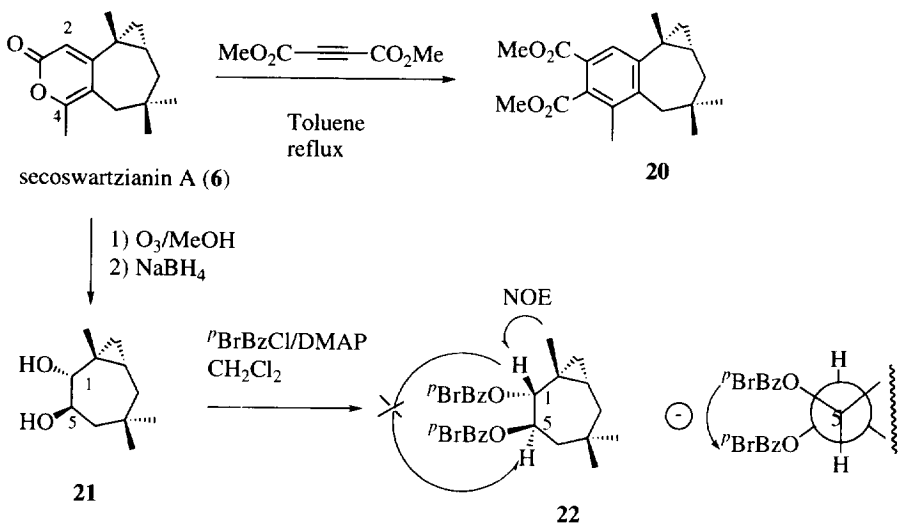


Figure 10. Reactions for secoswartzianin A (**6**).

Secoswartzianin B (**7**)

The molecular formula of secoswartzianin B (**7**) was $C_{16}H_{24}O_3$ (HRMS) and the spectral data of **7** indicated the presence of a methyl ester (1730 cm^{-1}; δ 3.68), an α,β-unsaturated carbonyl group (1695, 1670 cm^{-1}; λ_{max} 250 nm, log ε 3.6), an acetyl group (δ_H 2.27), and a cyclopropane ring [δ_H 0.40 (1H, dd, J=4.4, 4.2), 0.46 (1H, dd, J=4.4, 3.2)]. The HMBC spectrum connected these partial structures to build up a secoafricanane-type compound as shown in the formula. The absolute configuration was established by chemical correlation with caespitenone (**1**). Caespitenone (**1**) was subjected to Miyashita's reaction,[3,15] namely it was treated with

$(PhSe)_2$ in EtOH (Fig. 11). The products were the normally reduced ketol **23** and the abnormally reduced deconjugated ketol **24** in the ratio of 5.5:1. In the case of reduction of the fully substituted keto epoxide, the final product is thermodynamically more stable compound due to the reaction mechanism. Therefore in this case of **23**, the methyl group at C-4 adopted to the β-orientation, because the NOE between H-4 and the hydroxyl proton was observed in DMSO-d_6 solution. Thus the configuration of the minor product **24** should be as depicted in the formula. Compound **24** was oxidized with $Pb(OAc)_4$ in MeOH and PhH to yield a keto ester **7**, whose spectral data were identical with those of secoswartzianin B including the specific rotation. Therefore the absolute configuration of secoswartzianin B was established as in the formula.[3] Although a 4,5-secoafricanane-type compound is known in the literature,[5,6] both **6** and **7** are rare 3,4-seco type molecules, which are the first examples in the Nature.

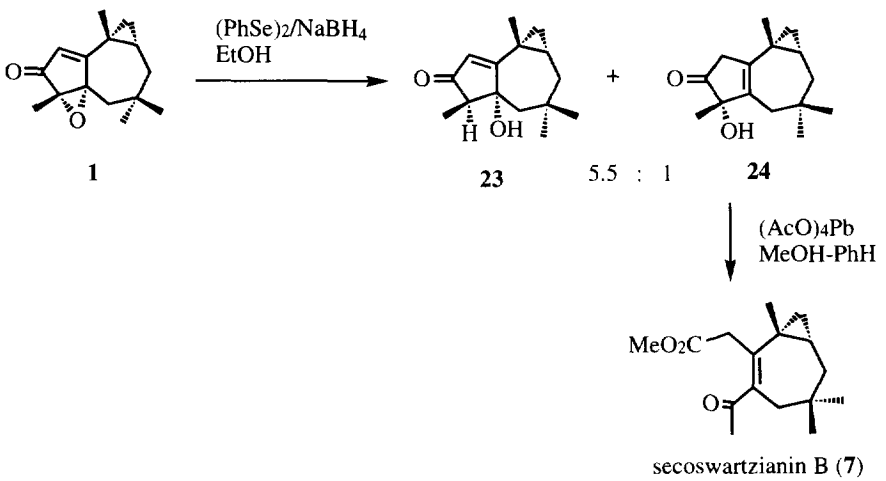
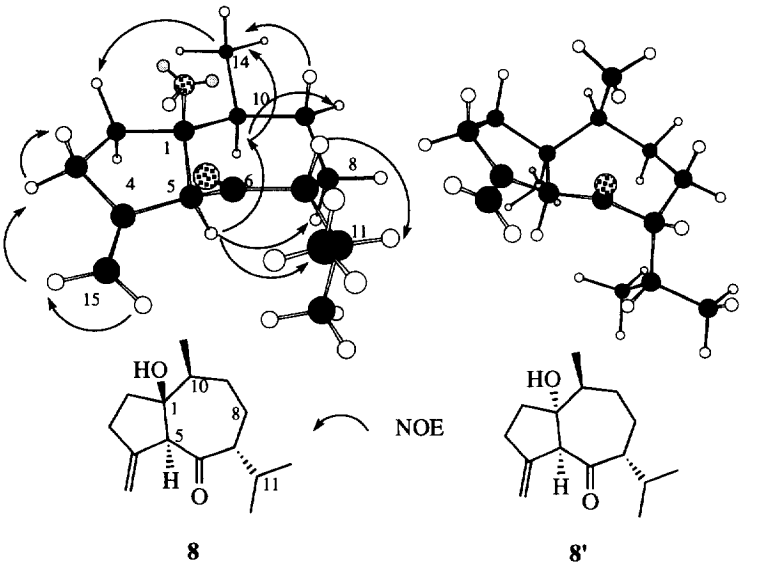


Figure 11. Conversion of caespitenone (**1**) into secoswartzianin B (**7**).

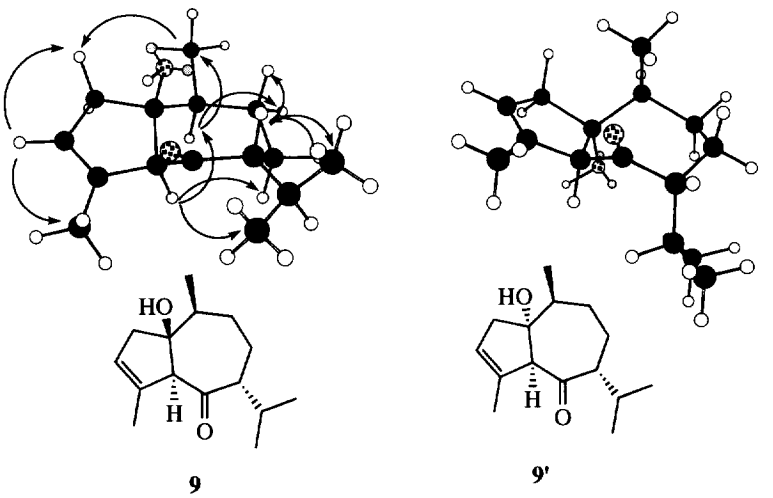
Guaiswartzianin A (**8**)

Guaiswartzianin A (**8**) had a molecular formula $C_{15}H_{24}O_2$ (by HRMS) and the IR spectrum indicated the presence of a hydroxyl (3400 cm^{-1}) and a carbonyl (1710 cm^{-1}) groups. The ^1H NMR spectra suggested the presence of an exo methylene (δ_H 4.78, 5.16) and three secondary methyl (δ_H 0.95, 0.96, 1.00) groups. Therefore compound **8** should be bicyclic, because the degree of unsaturation was four. The 2D NMR spectra indicated that **8** must be a guaiane-type sesquiterpene having a β-ketol structure. The relative stereochemistry was revealed by the NOESY spectrum. The configuration at C-1 was determined by comparing the models having the C-1 β **8** and C-1 α stereochemistry **8'** (Fig. 12). In the case of compound having C-1 β, all the NOEs were reasonably explained and thus the structure of guaiswartzianin A was assigned as formula **8**.



8 **8'**

Figure 12. Comparison of NOEs for models **8** and its diastereoisomer **8'**.



9 **9'**

Figure 13. Comparison of NOEs for models **9** and its diastereoisomer **9'**.

Guaiswartzianin B (**9**)

The spectral data of guaiswartzianin B (**9**) were almost the same as those of **8**. Therefore it was easily assumed that it should be an endo isomer [δ_H 5.50; δ_C 125.7 (CH), 137.8 (C)] of compound **8** having the exo methylene structure. The 2D NMR spectra indicated that the above assumption was reasonable. The relative stereochemistry was similarly determined by comparing the models (**9** and **9'**) to satisfy the NOE results (Fig. 13).

Germacraswartzianin (**10**)

The molecular formula of germacraswartzianin (**10**) was $C_{15}H_{24}O_2$ (by HRMS) and the IR spectrum indicated the presence of a carbonyl (1700 cm^{-1}) and an α,β-unsaturated carbonyl (1670 and 1630 cm^{-1}) groups. This was confirmed by the ^{13}C NMR spectrum (δ_C 214.8, 209.2, 148.0, 129.6). Therefore compound **10** must be monocyclic, because the degree of unsaturation was four. Although the 2D NMR spectra inferred that **10** was a germacrane type sesquiterpene, total assignment could not be carried out due to the signal overlap in the higher chemical shift region and the relative stereochemistry was not clarified. However the nice crystals (mp 77-80°) were obtained from pentane and the X-ray analysis was performed to turn out the trans nature concerning the methyl and the isopropyl groups (Fig. 14).[11] Compounds **8** and **9** must be derived from **10** biogenetically by cyclization as shown in Fig. 15.

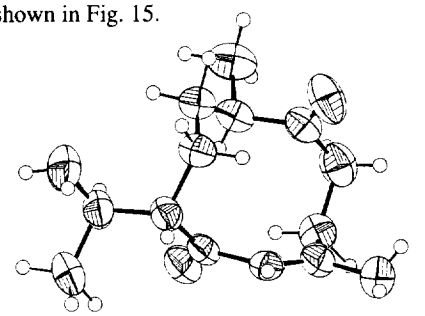


Figure 14. ORTEP Drawing of germacraswartzianin (**10**).

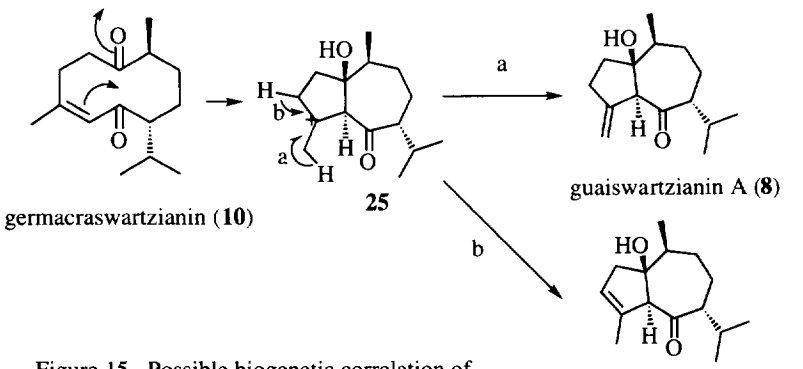
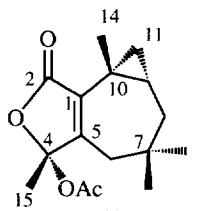


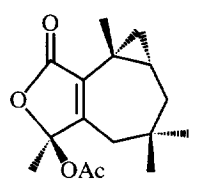
Figure 15. Possible biogenetic correlation of germacraswartzianin (**10**) and guaiswartzianins A (**8**) and B (**9**).

Norsecoswartzianin (**11**)

The ^{1}H and ^{13}C NMR spectra of norsecoswartzianin (**11**) showed very similar two sets of the signals. The EIMS showed the peak at m/z 236 and the IR spectrum exhibited the absorptions at 1760, 1740, 1730, and 1680 cm^{-1}, respectively. These suggested that compound **11** must be a monomeric nor-lactone, because the HRMS indicated that the molecular formula must be $C_{14}H_{20}O_3$. Therefore the X-ray analysis of the crystal was carried out. The ORTEP was shown in Fig. 16.[11] When the crystals were dissolved in $CDCl_3$, the overlap of the signals in its NMR spectrum was observed as in the beginning of this work. Therefore this overlap was attributed to the isomerization of the hemiacetal. Compound **11** was acetylated and the isomers (**11a**, **11b**) were separated by HPLC. When these isomeric acetates were subjected to the NMR conditions, only peaks due to one isomer were observed and no more overlap was shown. Therefore our assumption was fully verified and compound **11** must exist in both isomeric forms in the solution, while in the crystal form it exists in one isomeric form as depicted in formula **11**.



11a



11b

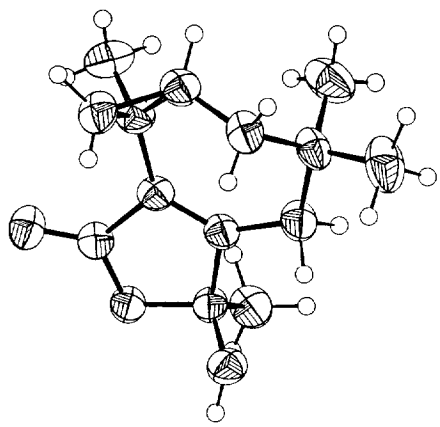


Figure 16. ORTEP Drawing of norsecoswartzianin (**11**).

In summary, we have isolated eleven new and four known compounds from the liverwort *Porella swartziana* collected in Colombia. Eight of them possessed an africanane or its seco type skeleton, which are rare in Nature.[16] Africanol was isolated from a marine animal, *Lemnalia africana*[17] and one compound was found in a Senecio plant, *Senecio oxyriifolius*.[18] Secoswartzianin A possessed an α-pyrone system in its structure, which had no oxygen atom attached to the ring, like bufadienolide.[19] Compounds having an α-pyrone normally possess an oxygen atom in its 4-position, because it is derived from a polyketide. Although a biogenesis of africanane compounds is not known yet, it is suggestive that a hydrocarbon swartzianin A is oxidized to swartzianins B, C, or D or caespitenone, which are finally converted into seco-type compounds.

EXPERIMENTAL

The IR spectra were measured with a JASCO FT/IR-5300 spectrophotometer. The ^{1}H and the ^{13}C NMR spectra were taken with a Varian Unity 200 (200 MHz), a JEOL JNM GX400 (400 MHz) or a Varian Unity 600 (600 MHz). The mass spectra including high resolution mass spectra were taken with a JEOL JMS

AX-500 spectrometer. The CD spectra were carried out with a JASCO J-500 spectrometer. The specific rotations were measured by a JASCO DIP-140 polarimeter. X-Ray reflection data were collected with a Mac Science MXC18 diffractometer using Cu radiation CuKα (λ=1.54178). Chemcopak Nucleosil 50-5 (10 X 250 mm) was used for HPLC (JASCO pump system). Silica gel 60 (70-230 mesh, Merck) was used for column chromatography and silica gel 60 F254 plates (Merck) were used for TLC.

Isolation. *Porella swartziana* (Web.) Trev. (dry weight: 301 g) was collected in Colombia and identified by Dr. R. Gradstein, Institute of Systematic Botany, University of Utrecht, The Netherlands. The voucher specimen was deposited in the herbarium at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University. The dried material was ground and extracted with ether (2 weeks). The ether extract (15.6 g) was subjected to column chromatography (CC) of Sephadex LH-20 (CH_2Cl_2:MeOH=1:1) and silica gel (hexane:EtOAc, gradient) to afford ten frs. The fr.1 was further separated by CC of silica gel (hexane:EtOAc, gradient) and silver nitrate impregnated silica gel CC (hexane) to yield swartzianin A (**2**) (40 mg). The 2nd fr. afforded caespitenone (**1**) (1.15 g). From the 3rd fr. swartzianin B (**3**) (36 mg), norsecoswartzianin (**11**) (130 mg), and the known germacradienol (**14**) (33 mg) were isolated by HPLC (Nucleosil 50-5; hexane:EtOAc=9:1) and silver nitrate impregnated silica gel CC (hexane:EtOAc, gradient). The 4th fr. afforded **3** (26 mg), guaiswartzianin A (**8**) (5.1 mg), guaiswartzianin B (**9**) (8.4 mg), germacraswartzianin (**10**) (63.3 mg), secoswartzianin B (**7**) (36 mg), and the known lepidozenol (**15**) (8 mg) by silica gel CC (hexane:EtOAc, gradient) and HPLC (Nucleosil 50-5; hexane:EtOAc = 9:1) The 5th fr. was recrystallized from hexane to yield secoswartzianin A (**6**) (333 mg). The fr.6 was further separated by Sephadex LH-20 ($CHCl_3$:MeOH = 1:1) and HPLC (Nucleosil 50-5; hexane:EtOAc = 7:3) to afford swartzianin C (**4**) (111 mg) and swartzianin D (**5**) (31 mg), and the known acetates **12** (72 mg) and **13** (2.6 mg).

caespitenone (1). solid; $[\alpha]_D^{20}$ -267° (c 1.36, $CHCl_3$); UV (EtOH): λmax 223 nm (log ε 3.7), 282 (3.6); CD (EtOH): Δε -7.50 (286 nm), -3.35 (354); IR (film) 1715, 1600, 1450, 1100, 880, 860 cm^{-1}; MS *m/z* 232 (M^+, base), 217, 204, 189, 175, 161, 147, 133, 119, 105, 91, 83, 77, 69, 55, 43; HRMS Obs. m/z 232.1447. $C_{15}H_{20}O_2$ requires 232.1464; ^1H NMR ($CDCl_3$) δ 5.92 (1H, s, H-2), 2.14 (1H, d, J = 14 Hz, H-6b), 1.94 (1H, dd, J = 15, 4.2 Hz, H-8b), 1.50 (1H, d, J = 14 Hz, H-6a), 1.45 (3H, s, H-15), 1.24 (1H, m, H-8a), 1.24 (3H, s, H-14), 1.13 (3H, s, H-12), 1.10 (1H, m, H-9), 1.05 (1H, m, H-11a), 1.01 (3H, s, H-13), 0.57 (1H, t, J = 4.4 Hz, H-11b).

swartzianin A (2). oil; $[\alpha]_D^{21}$ -117° (c 1.42, $CHCl_3$); IR (film) 1620, 1450, 1380, 1360 cm^{-1}; MS *m/z* 204 (M^+), 189, 175, 161, 147, 133 (base), 119, 105, 91, 77, 55, 41; HRMS Obs. 204.1893. $C_{15}H_{24}$ requires 204.1878; ^1H NMR ($CDCl_3$) δ 5.53 (1H, br s), 2.33～2.27 (3H, m), 1.92 (1H, br d, J = 10.3), 1.72 (1H, dd, J = 15, 6), 1.17 (3H, s), 0.96 (3H, s), 0.862 (3H, s), 0.858 (3H, d, J = 6.3); ^1H NMR (C_6D_6) δ 5.62 (1H, br s), 2.41 (1H, m), 2.30 (2H, m), 1.97 (1H, m), 1.70 (1H, dd, J = 15, 6), 1.28 (1H, t, J = 13), 1.18 (3H, s), 1.00 (3H, s), 0.89 (3H, d, J = 6.4), 0.86 (3H, s), 0.72 (2H, m), 0.49 (1H, m).

swartzianin B (3). oil; $[\alpha]_D^{22}$ -184° (c 1.01, $CHCl_3$); UV (EtOH) λmax 255 nm (log ε 4.22); CD (EtOH) Δε +11.8 (202 nm), -7.9 (247), -1.8 (297); IR (film) 1680, 1580, 900, 850 cm^{-1}; MS *m/z* 218 (M^+), 203, 190, 177, 175, 162, 147, 119 (base), 105, 91, 77, 56, 41; HRMS Obs. 218.1653. $C_{15}H_{22}O$ requires 218.1670; ^1H NMR ($CDCl_3$) δ_H 6.02 (1H, s), 2.65 (1H, ddd, J = 18, 12, 5.8), 2.56 (1H, quint. J = 7.0), 1.91 (1H, dd, J = 15, 8.1), 1.56 (1H, dd, J = 13, 4.9), 1.54 (1H, dd, J = 15, 8.1), 1.31 (3H, s), 1.27 (1H, quint., J = 7.5), 1.08 (2H, m),

1.04 (3H, d, J = 7.3), 0.96 (3H, s), 0.89 (3H, s), 0.82 (1H, d, J = 14, 12).

swartzianin C (4). mp. 89-92°C (hexane); $[\alpha]_D^{23}$ -368° (c 1.01, $CHCl_3$); UV (EtOH) λmax 256 nm (log ε 4.0); CD (EtOH) Δε +4.96 (213 nm), -12.8 (252), -2.13 (330); IR ($CHCl_3$) 3550, 3400, 1695, 1580 cm^{-1}; MS *m/z* 234 (M^+), 219, 193, 175, 163, 149, 135, 121, 107, 91, 77, 69, 55, 43 (base); HRMS Obs. 234.1614. $C_{15}H_{22}O_2$ require 234.1620; ^1H NMR ($CDCl_3$) δ_H 6.18 (1H, d, J = 1.7), 2.69 (1H, dt, J = 13, 1.9), 1.86 (1H, dd, J = 14, 3.8), 1.60 (1H, d, J = 14), 1.35 (1H, d, J = 13), 1.30 (3H, s), 1.20 (3H, s), 1.07 (3H, s), 0.93 (3H, s), 0.62 (1H, t, J = 4.5); Crystal data: Orthorhombic space group $P2_12_12_1$, a=8.147(4), b=28.65(1), c=5.922(2), Z=4. Final residuals R and R_w were 0.046 and 0.081, respectively.

swartzianin D (5). mp. 106-107°C (hexane); $[\alpha]_D^{22}$ -153° (c 0.98, $CHCl_3$); UV (EtOH) λmax 296 nm (log ε 4.1); CD (EtOH) Δε +21.5 (220 nm), -9.76 (252 nm), +11.5 (295 nm), -7.62 (345 nm); IR (film) 3400, 1700, 1560 cm^{-1}; MS *m/z* 232 (M^+), 217, 204, 189, 176, 161, 147 (base), 133, 119, 105, 91, 77, 65, 53, 43; HRMS Obs. 232.1466. $C_{15}H_{20}O_2$ requires 232.1463; ^1H NMR ($CDCl_3$) δ_H 6.24 (1H, d, J = 1.5), 6.18 (1H, d, J = 1.5), 2.07 (1H, m), 1.36 (3H, s), 1.31 (3H, s), 1.25 (3H, s), 1.12 (3H, s), 0.69 (1H, m); Crystal data: Orthorhombic space group $P2_12_12_1$, a=8.082(4), b=28.75(4), c=5.839(7), Z=4. Final residuals R and R_w were 0.059 and 0.085, respectively.

secoswartzianin A (6). mp.127-128.5°C (hexane); $[\alpha]_D^{20}$ -39° (c 1.45, $CHCl_3$); UV (EtOH) λmax 318 nm (log ε 3.6), 304 (3.7), 212 (3.9); CD (EtOH) Δε +4.27 (304 nm); IR ($CHCl_3$) 1705, 1630, 1540 cm^{-1}; MS *m/z* 232 (M^+, base), 217, 204, 189, 175, 161, 147, 133, 119, 105, 91, 83, 77, 69, 55, 43; HRMS Obs. m/z 232.1434. $C_{15}H_{20}O_2$ requires 232.1464; ^1H NMR ($CDCl_3$) δ_H 6.10 (1H, s, H-2), 2.45 (1H, d, J = 14, H-6b), 2.17 (3H, s, H-15), 2.09 (1H, d, J = 14, H-6a), 1.69 (1H, dd, J = 14, 3, H-8b), 1.19 (3H, s, H-14), 1.04 (3H, s, H-13), 0.93-0.76 (2H, m, H-9, 11b), 0.73 (3H, s, H-12), 0.29 (1H, t, J = 4.4, H-11a), 0.23 (1H, dd, J = 14, 12, H-8a); Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.62; H, 8.63.

secoswartzianin B (7). oil; $[\alpha]_D^{22}$ -193° (c 1.35, $CHCl_3$); UV (EtOH) λmax 250 nm (log ε 3.6); CD (EtOH) Δε -5.75 (228 nm); IR (film) 1730, 1695, 1670, 1585 cm^{-1}; MS *m/z* 264 $(M)^+$, 249, 233, 221, 207, 182 (base), 175, 161, 147, 133, 124, 119, 105, 91, 77, 55, 43; HRMS Obs. *m/z* 264.1723. $C_{16}H_{24}O_3$ requires 264.1725; ^1H NMR ($CDCl_3$) δ_H 3.68 (3H, s, -OMe), 3.37 (1H, d, J = 11, H-2), 3.34 (1H, d, J = 11, H-2), 2.66 (1H, d, J = 13, H-6), 2.27 (3H, s, H-15), 2.15 (1H, d, J = 14, H-6), 1.12 (3H, s, H-14), 1.06 (3H, s, H-12), 0.81 (3H, s, H-13), 0.46 (1H, dd, J = 4.4, 3.2, H-11), 0.40 (1H, dd, J = 4.4, 4.2, H-11).

guaiswartzianin A (8). oil; $[\alpha]_D^{18}$ +23.4° (c 0.68, $CHCl_3$); IR (FT) 3400, 1710, 880 cm^{-1}; MS *m/z* 236 (M^+), 221, 218, 203, 193, 175, 165, 147, 134, 121, 107 (base), 91, 79, 67, 55; HRMS m/z 236.1769, $C_{15}H_{24}O_2$ requires 236.1776; ^1H NMR ($CDCl_3$) δ_H 5.16 (1H, q, J = 2.2, H-15), 4.78 (1H, q, J = 2.2, H-15), 3.90 (1H, m, H-5), 2.62 (1H, m, H-3), 2.43 (1H, dd, J = 16.7, 8.9, H-3), 2.13 (1H, ddd, J = 10.8, 6.8, 5.6, H-7), 2.02 (1H, m, H-2), 1.99 (1H, m, H-8α), 1.92 (1H, dsept, J = 6.8, H-11), 1.63 (1H, m, H-10), 1.61 (1H, m, H-9β), 1.59 (1H, m, H-2), 1.49 (1H, m, H-8β), 1.30 (1H, m, H-9α), 1.00 (3H, d, J = 6.6, H-14), 0.96 (3H, d, J = 6.8, H-12 or 13), 0.95 (3H, d, J = 6.8, H-13 or 12).

guaiswartzianin B (9). oil; $[\alpha]_D^{18}$ +33.2° (c 1.1, $CHCl_3$); CD (EtOH) Δε +0.77 (298 nm); IR (FT) 3500, 1700, 1650, 910, 820 cm^{-1}; MS m/z 236 (M^+), 218, 203, 193, 175, 165, 147, 134, 121, 107 (base), 91, 69, 55, 41; HRMS m/z 236.1767, $C_{15}H_{24}O_2$ requires 236.1776; ^1H NMR ($CDCl_3$) δ_H 5.50 (1H, br s, H-3), 3.93 (1H, br s, H-5), 2.43 (1H, br d, J = 20, H-2a), 2.37 (1H, br d, J = 20, H-2b), 2.08 (1H, m, H-7), 2.03 (1H, m, H-11), 1.89 (1H, m, H-8), 1.82 (1H, m, H-10), 1.74 (3H, br s, H-15), 1.69 (1H, m, H-9), 1.62 (1H, m, H-8), 1.51 (1H,

m, H-9), 1.00 (3H, d, J = 6.8, H-14), 0.95 (3H, d, J = 6.8, H-12), 0.91 (3H, d, J = 6.6, H-13).

germacraswartzianin (10). mp 77-80°C (pentane); $[\alpha]_D^{20}$ -92.5° (c 1.1, $CHCl_3$); CD (EtOH) $\Delta\varepsilon$ +2.36 (246 nm), -2.42 (292); IR ($CHCl_3$) 1700, 1670, 1630 cm^{-1}; MS *m/z* 236 (M^+), 218, 203, 193, 175, 165, 152, 137, 123, 107, 96 (base), 82, 71, 57, 41; HRMS Obs. m/z 236.1771. $C_{15}H_{24}O_2$ requires 236.1776; ^1H NMR ($CDCl_3$) δ_H 6.00 (1H, br s, H-5), 3.67 (1H, td, J = 13.2, 5.0, H-3β), 2.80 (1H, m, H-10β), 2.73 (1H, dt, J = 13.2, 5.0, H-2β), 2.33 (1H, td, J = 13.2, 5.0, H-2α), 2.11 (1H, m, H-7), 2.08 (1H, m, H-3α), 1.94 (1H, m, H-11), 1.84 (3H, s, H-15), 1.78 (1H, m, H-9α), 1.75 (2H, m, H-8), 1.41 (1H, m, H-9β), 0.97 (3H, d, J = 7.1, H-14), 0.90 (3H, d, J = 6.4, H-13), 0.89 (3H, d, J = 6.8, H-12); Crystal data: Orthorhombic space group $P2_12_12_1$, a=10.199(4), b=26.22(1), c=5.476(3), Z=4. Final residuals R and R_w were 0.058 and 0.086, respectively.

norsecoswartzianin (11). mp 170-173°C (hexane-EtOAc); $[\alpha]_D^{19}$ -42.1° (c 0.56, $CHCl_3$); IR (FT) 3350, 1760, 1740, 1730, 1680 cm^{-1}; MS *m/z* 236 (M^+), 218 (base), 203, 193, 175, 161, 147, 133, 119, 105, 91, 77, 69, 55, 43; HRMS (CI) Obs. *m/z* 237.1487 (M+1). $C_{14}H_{21}O_3$ requires 237.1491; ^1H NMR ($CDCl_3$) δ_H 3.37 (1H, br s), 3.25 (1H, br s), 2.49 (1H, dd, J = 18, 1), 2.31 (1H, dd, J = 18.4, 1), 2.29 (1H, d, J = 18.4), 2.13 (1H, d, J = 18), 2.06 (1H, dd, J = 14, 7), 2.03 (1H, dd, J = 14, 7), 1.62 (3H, s), 1.57 (3H, s), 1.32 (3H, s), 1.29 (3H, s), 1.20 (6H, s), 1.03 (1H, dd, J = 14, 5), 1.01 (3H, s), 1.00 (3H, s), 0.85-0.98 (4H, m), 0.42 (1H, t, J = 4.6), 0.36 (1H, t, J = 4); Crystal data: Monoclinic space group $P2_1$, a=12.730(3), b=6.078(2), c=8.431(2), β=94.06(2), Z=2. Final residuals R and R_w were 0.052 and 0.068, respectively.

Oxidation of swartzianin A (2). A solution of swartzianin A (**2**) (14 mg) in dry benzene (3 ml) was treated with PDC (53 mg), *t*-butylhydroperoxide (70%, 0.02 ml), and Celite (150 mg) at 0°C for 15 min and the mixture was kept stirring at room temperature overnight. The mixture was filtered through Celite followed by evaporation afforded a residue, which was purified by prep. TLC to give **3** (6 mg); $[\alpha]_D$ -120° (c 1.16, $CHCl_3$); ^1H NMR ($CDCl_3$) δ_H 6.02 (1H, s), 2.66 (1H, m), 2.55 (1H, m), 1.91 (1H, dd, J = 15, 8), 1.31 (3H, s), 1.04 (3H, d, J = 7), 0.96 (3H, s), 0.89 (3H, s); ^{13}C NMR ($CDCl_3$) δ_C 210.6, 189.0, 126.6, 46.7, 43.5, 40.9, 39.0, 32.6, 32.2, 29.9, 27.3, 24.8, 24.2, 24.2, 10.4.

Reduction of swartzianin B (3). A solution of swartzianin B (**3**) (10 mg) in MeOH (3 ml) was treated with $NaBH_4$ (30 mg) and $CeCl_3$ (200 mg) at room temperature for 2 h. Water was added and the mixture was extracted with ether. The organic phase was washed with brine, dried over $MgSO_4$, and was evaporated to afford a residue (19 mg), which was purified by HPLC (Nucleosil 50-5, hexane-EtOAc = 9:1) to gave an α-alcohol **17** (3.7 mg) and a β-alcohol **16** (0.4 mg).

16: oil; ^1H NMR (C_6D_6) δ_H 5.68 (1H, br d, J = 1), 4.42 (1H, m), 1.14 (3H, s), 0.95 (3H, d, J = 7), 0.93 (3H, s), 0.83 (3H, s).

17: oil; MS *m/z* 220 (M^+), 205, 202, 187, 159, 131 (base), 105, 91; ^1H NMR (C_6D_6) δ_H 5.55 (1H, s, -OH), 4.35 (1H, d, J = 6), 2.26 (1H, m), 1.97 (1H, qt, J = 7, 7), 1.66 (1H, dd, J = 14, 7), 1.21 (2H, m), 1.11 (3H, s), 0.99 (1H, m), 0.95 (3H, d, J = 7), 0.90 (3H, s), 0.82 (3H, s), 0.72 (1H, quit, J = 7), 0.65 (2H, d, J = 7).

Reduction of swartzianin C (4). A solution of swartzianin C (**4**) (73 mg) in MeOH (5 ml) was treated with $NaBH_4$ (14 mg) in the presence of $CeCl_3$ at room temperature for 1 h. Hydrochloric acid (1M) was added and the mixture was extracted with ether. The organic phase was washed with brine, dried over $MgSO_4$, and was

evaporated to afford a residue (98 mg), which was separated by silica gel column chromatography to give an α-alcohol (2.8 mg) and a β-alcohol (50 mg). The α-alcohol (2.8 mg) in CH_2Cl_2 (1 ml) was treated with *p*-bromobenzoyl chloride (26 mg), Et_3N (0.02 ml), and DMAP (2 mg) at room temperature overnight. Water was added and the mixture was extracted with ether. The organic solution was washed with 5% $NaHCO_3$ and brine, dried over $MgSO_4$, and was evaporated to afford a residue, which was purified by prep. TLC to give benzoate **19** (4.7 mg). The β-alcohol (14 mg) was similarly treated to give benzoate **18** (14 mg).

Benzoate 18. oil; CD (EtOH) Δε +5.27 (241 nm); IR (FT) 1730, 1600 cm^{-1}; MS *m/z* 420, 418 (M^+), 402, 400, 235, 218 (base), 203, 201, 185, 183, 161; HRMS (CI-CH_4) *m/z* 419.1214 $(M+1)^+$. $C_{22}H_{28}O_3Br$ requires 419.1222; ^1H NMR ($CDCl_3$) δ_H 7.92 (2H, d, J = 8.4), 7.60 (2H, d, J =8 .4), 5.71 (1H, br t, J =1.5), 5.63 (1H, br t, J = 1.5), 2.50 (1H, br d, J = 10), 1.78 (1H, dd, J = 14, 5), 1.22 (3H, s), 1.12 (3H, s), 1.02 (3H, s), 0.91 (3H, s), 0.87 (1H, m), 0.41 (1H, m).

Benzoate 19. oil; CD (EtOH) Δε -14.6 (236 nm); IR (FT) 1730, 1600 cm^{-1}; MS *m/z* 420, 418 (M^+),402, 400, 391, 279, 235, 219 (base), 203, 201, 185, 183, 161; HRMS (CI-CH_4) *m/z* 419.1183 $(M+1)^+$. $C_{22}H_{28}O_3Br$ requires 419.1222; ^1H NMR ($CDCl_3$) δ_H 7.90 (2H, d, J = 8.3), 7.58 (2H, d, J = 8.3), 5.85 (1H, br d, J = 2), 5.38 (1H, br d, J = 2), 1.26 (3H, s), 1.20 (3H, s), 1.03 (3H, s), 0.90 (3H, s).

Diels-Alder reaction of secoswartzianin A (6). A mixture of secoswartzianin A (**6**) (72 mg) and dimethyl acetylenedicarboylate (88 mg) in toluene (5 ml) was heated under reflux overnight. The solvent was evaporated and the residue was purified by prep. TLC to afford an adduct **20** (12 mg) and the recovered **6** (57 mg). **20**; oil; IR (FT) 1740, 1720, 1440, 1270 cm^{-1}; MS *m/z* 330 (M^+), 315, 299, 298 (base), 283, 255, 241, 229, 215, 184, 170, 141, 128, 115, 77, 59, 41; HRMS Obs. *m/z* 330.1824. $C_{20}H_{26}O_4$ requires 330.1831; ^1H NMR ($CDCl_3$) δ_H 7.82 (1H, s), 3.94 (3H, s), 3.88 (3H, s), 2.89 (1H, d, J = 13), 2.63 (1H, d, J = 13), 2.27 (3H, s), 1.28 (3H, s), 1.17 (3H, s), 0.78 (3H, s).

Ozonolysis of secoswartzianin A (6). Ozone was bubbled through a solution of secoswartzianin A (**6**) (23 mg) in MeOH (5 ml) at -78°C for 1.5 h. $NaBH_4$ (78 mg) was added into the mixture and the solution was stirred at room temperature for 30 min. Hydrochloric acid (1M) was added and the mixture was extracted with ether. The organic solution was washed with brine, dried over $MgSO_4$, and was evaporated to give a residue (20 mg), which was purified by prep. TLC to afford a diol **21** (2 mg); oil; IR (film) 3550 cm^{-1}; MS *m/z* 184 (M^+), 166, 151, 140, 133, 109, 95 (base), 85, 81, 71, 55, 41; ^1H NMR ($CDCl_3$) δ_H 3.67 (1H, d, J = 8.6), 3.28 (1H, ddd, J = 8.6, 3.7, 3.7), 1.79 (1H, dd, J = 14.5, 7), 1.23 (3H, s), 1.01 (3H, s), 0.93 (3H, s), 0.49 (1H, dd, J = 8.2, 4.5), 0.40 (1H, t, J = 4.5).

Preparation of dibenzoate 22. A solution of the diol **21** (2 mg) in Py (0.02 ml) was treated with *p*-bromobenzoyl chloride (20 mg) and DMAP (1 mg) at room temperature overnight. Water was added and the mixture was extracted with ether. The organic phase was washed with 1M HCl, 1M NaOH soln., and then brine, dried over $MgSO_4$, and was evaporated to afford a residue (25 mg). The residue was purified by prep. TLC to give benzoate **22** (2.8 mg); oil; CD (MeOH) Δε = -37.7 (249 nm); MS (CI-CH_4) *m/z* 553, 551, 549 $(M+1)^+$, 537, 535, 533, 466, 464, 462, 351, 350, 349, 348, 185, 183, 166, 149 (base); HRMS Obs. *m/z* 552.0172 (M^+). $C_{25}H_{26}O_4Br^*_2$ requires 552.0157; ^1H NMR ($CDCl_3$) δ_H 7.86 (4H, d, J = 8.2), 7.56 (2H, d, J = 8.2), 7.55 (2H, d,

J = 8.2), 5.53 (1H, d, J = 6), 5.26 (1H, m), 1.38 (3H, s), 1.13 (3H, s), 1.10 (3H, s), 0.52 (1H, dd, J = 8, 4), 0.41 (1H, t, J = 4).

Oxidation of 24 to secoswartzianin B (7). A solution of the ketol **24** (30 mg) in MeOH-PhH (3:7; 3 ml) was treated with $Pb(OAc)_4$ (59 mg) at room temperature for 3 h. The mixture was filtered and ether was added into the filtrate. The mixture was washed with $NaSO_3$ soln., Na_2CO_3 soln., and then brine, dried over $MgSO_4$, and was evaporated to afford a residue (19 mg), which was purified by HPLC (Nucleosil 50-5, hexane-EtOAc = 95:5) to give secoswartzianin B (**7**) (13 mg); $[\alpha]_D$ -202° (c 1.34, $CHCl_3$).

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10. The specific rotation of the compound thus derived was $[\alpha]_D$ -120°, while that of the natural one was -184°. This presumably due to the impurity contaminated in the synthetic sample. Nonetheless, these results suggest that the absolute configuration of **2** is the same as that of **3**.
11. Although some of the Figures of ORTEP were expressed as enantiomers unexpectedly, they just intended to show the relative configuration. The detailed data for X-ray analysis was deposited to the Cambridge Crystallographic Data Centre.
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