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ARTICLE *in* JOURNAL OF NATURAL PRODUCTS · MAY 2013

Impact Factor: 3.8 · DOI: 10.1021/np400045z · Source: PubMed

JOURNAL OF NATURAL PRODUCTS

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Roussoellols A and B, Tetracyclic Fusicoccanes from *Roussoella hysterioides*

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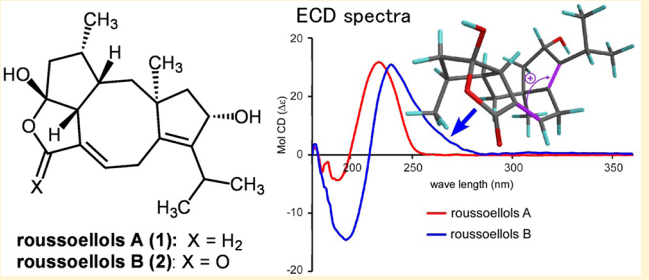
Supporting Information

ABSTRACT: The structures of the tetracyclic fusicoccanes roussoellols A (**1**) and B (**2**) from *Roussoella hysterioides* KT1651 are described. NMR spectroscopic analyses involving NOESY experiments revealed that these molecules possessed unique bent structures that were supported by chemical derivatizations as well as chemical shift comparisons with theoretical shifts based on the density functional theory (DFT) at the EDF2/6-31G* level. Absolute configurations were established by the ECD couplet of positive chirality in both **1** and **2** at vacuum UV (VUV) region, which were further confirmed by successful reproduction of VUVCD spectra using theoretical calculations.



The Ascomycota is the most diverse group of the kingdom Fungi, comprising more than 64,000 species. Although fungi in this group are generally recognized as a promising source of novel biologically active metabolites,[1−3] our knowledge of fungal metabolites from plant-inhabiting Ascomycota, such as saprobes and endophytes on vascular plants, is still incomplete.[4]

During our program of exploring novel and biologically active secondary metabolites from plant-inhabiting ascomycetous fungi with unique ecologies,[5−8] we succeeded in revealing novel tetracyclic fusicoccanes, roussoellols A (**1**) and B (**2**), as shown in Figure 1, from *Roussoella hysterioides* KT1651 collected from a herbaceous bamboo, *Sasa veitchii*. Structural analysis revealed that these molecules have unique bent structures, which were verified by comparing their NMR chemical shifts with those based on theoretical calculations and supported by chemical derivatizations. Application of the electronic circular dichroism (ECD) exciton chirality method at vacuum UV (VUV) region for the 1,4-diene systems in **1** and **2** allowed us to determine their absolute configurations. Theoretical calculations reproduced the ECD spectra well enough to confirm our speculation.

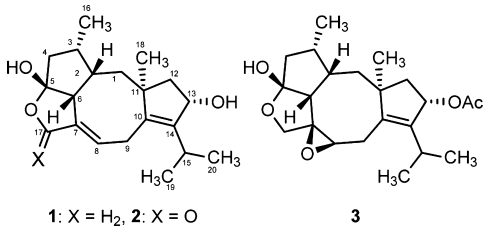


Figure 1. Structures of **1**, **2**, and epoxide **3**.

RESULTS AND DISCUSSION

Roussoellols A (**1**) and B (**2**) were both isolated as colorless fine needles from an EtOAc extract of *Roussoella hysterioides* KT1651 (registered in gene banks as MAFF[9] 239636 and JCM[10] 13126). This fungus had been collected in 2004, from *Sasa veitchii* at Kanagawa Prefecture by one of the authors of this study. Cultivation was performed in potato-sucrose medium for 30 days.

Roussoellol A (**1**) gave a molecular ion at m/z = 318.2183 by FDMS to suggest the formula $C_{20}H_{30}O_3$ ([M]$^+$ 318.2195).[11] The NMR data and their signal assignments are summarized in Table 1. This molecule showed 20 resonances in the ^{13}C NMR spectrum that agreed with the molecular formula based on the mass spectrum. The HMQC spectrum allowed us to classify them into 4 × CH_3, 5 × CH_2, 6 × CH, and 5 × C, which also revealed 28 carbon-attached protons. Two more hydrogen must be attached to the hetero atoms. These were assigned to be alcoholic hydrogens on the basis of the suggested molecular formula. One of those was found at around 2.3 ppm but varied

Received: January 17, 2013

dx.doi.org/10.1021/np400045z | *J. Nat. Prod.* XXXX, XXX, XXX−XXX

Table 1. Experimental and Theoretical NMR Data for 1 and 2[a]

	roussoellol A				roussoellol B			
	experimental ($CDCl_3$)		theoretical		experimental ($CDCl_3$)		theoretical	
position	δ_C, type	δ_H (J in Hz)	δ_C	δ_H	δ_C, type	δ_H (J in Hz)	δ_C	δ_H
1	39.24, CH_2	α: 1.68, dd (12.7, 13.8)	38.56	2.00	38.06, CH_2	1.51, dd (12.5, 14.3)	38.26	1.83
		β: 1.28, dd (1.7, 13.8)		1.36		1.37, dd (2.8, 14.3)	42.57	1.43
2	42.35, C	2.27, m	41.82	2.42	42.59, C	2.45, m		
3	38.26, C	2.08, m	39.62	2.04	37.62, C	2.18, m	38.55	2.12
4	45.36, CH_2	α: 1.85, d (12.8)	43.56	1.69	45.12, CH_2	2.1 (NA)	43.56	1.92
		β: 1.97, dd (7.2, 12.8)		1.85				2.06
5	119.53, C		118.85		115.52, C		113.81	
6	51.48, C	2.97, br d (10.8)	50.13	3.25	49.13, C	3.16, dq (10.2, 2.7)	48.39	3.27
7	138.80, C		142.54		127.88, C		129.22	
8	116.35, C	5.38, br s	117.78	5.26	139.58, C	6.89, dt (2.7, 4.1)	138.64	6.84
9	26.27, CH_2	α: 2.68, br d (18.5)	27.48	2.77	26.93, CH_2	2.90, ddd (2.7, 4.1, 20.4)	27.82	2.93
		β: 3.03, br d (18.5)		3.03		3.30, ddd (2.7, 4.1, 20.4)		3.30
10	142.94, C		144.23		140.83, C		142.61	
11	49.36, C		48.79		49.48, C		48.94	
12	46.43, CH_2	α: 1.47, dd (3.7, 14.5)	45.52	1.37	45.42, CH_2	1.52, dd (3.2, 14.2)	46.16	1.39
		β: 2.34, dd (8.0, 14.5)		2.37		2.36, dd (7.8, 14.2)		2.32
13	76.85, C	4.88, br dd (3.7, 8.0)	77.43	5.10	76.48, C	4.88, br d (7.2)	77.50	5.12
14	143.92, C		147.38		145.65, C		148.66	
15	27.00, C	2.63, heptuplet (6.6)	28.14	2.80	27.09, C	2.59, heptuplet (6.5)	28.36	2.76
16	15.29, CH_3	0.78, d (7.5)	15.66	0.92	15.88, CH_3	0.68, d (7.5)	16.09	0.80
17	72.93, CH_2	α: 4.59, br d (12.6)	73.58	4.73	170.18, C		169.02	
		β: 4.45, br d (12.6)		4.33				
18	30.65, CH_3	1.17, s	31.16	1.18	30.69, CH_3	1.19, s	30.56	1.21
19	19.53, CH_3	1.11, d (6.6)	19.03	1.22	19.62 CH_3	1.10, d (6.5)	18.65	1.24
20	23.35, CH_3	1.11, d (6.6)	23.68	1.31	23.07, CH_3	1.13, d (6.5)	23.86	1.29
correlation efficiency (expt vs theor)			0.9997	0.9953			0.9997	0.9964

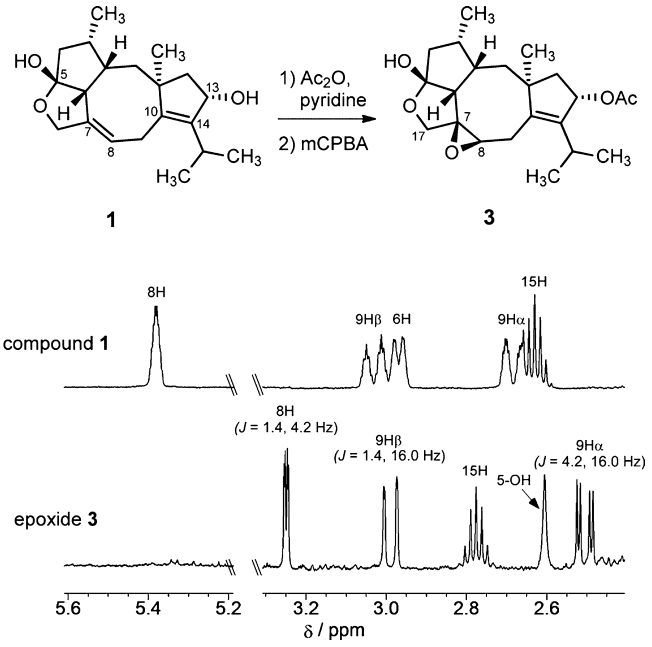
[a]NA: not assignable. Theoretical chemical shift calculations were performed with EDF2/6-31G* followed by correction based on Boltzmann distribution.

by measurements. Since no carbonyl group was suggested by either the IR or ^{13}C NMR spectra, the third oxygen atom needed to be incorporated in the framework as an ether. The number of carbons (C_{20}) and the presence of four methyl groups implied a diterpenoid, which was also informative in the structural analysis. The ^{13}C NMR data suggested four olefinic carbons, i.e., two double bonds. Consideration of these results and the index of hydrogen deficiency (IHD = 6) revealed that **1** has a tetracyclic structure. Further detailed NMR analyses involving COSY and HMBC spectra suggested a novel tetracyclic fusicoccane framework[12−14] as shown in Figure 1.

However, ambiguity remained concerning the C-7/C-8 connectivity (the numbering follows the fusicoccane nomenclature) because H-8 gave no HMBC correlations. Furthermore, the H-8 signal appeared as a broad singlet (bandwidth at half height ca. 10 Hz), as shown in Scheme 1, despite vicinal couplings with H_2-9 as well as long-range couplings with H-6 and H_2-17. The C-7/C-8 connectivity was confirmed after converting **1** into 7,8-epoxide **3** by 13-OH acetylation and successive *m*-CPBA oxidation. Epoxidation eliminated the long-range couplings to give a typical doublet of doublets (J = 1.4, 4.3 Hz) for H-8. Acetylation of 13-OH reduced the electron density and reactivity at the C-10−C-14 double bond. The epoxidation also proceeded stereoselectively. The β-orientation of the epoxide moiety was determined by the observation of H-8 showing an NOE with H_α-17 more strongly than with H_β-17.[15]

We next investigated the relative configuration of **1**. Although $^3J_{2,6}$ (10.8 Hz) was not conclusive for the *cis*-stereochemical relationship between H-2 and H-6,[16] it was determined by the fact that both H-2 and H-6 gave NOESY correlations with H-13. The relationship between 5-OH and H-6 was established to

Scheme 1. Preparation of 3 and Region of ^1H NMR Spectra of 1 (Upper) and 3 (Lower)



dx.doi.org/10.1021/np400045z | J. Nat. Prod. XXXX, XXX, XXX−XXX

be *cis*, as determined by an NOE association between H_3-16 and H_α-17. These observations also revealed a bent conformation for the bicyclo[6.3.0]undec-5,8-diene framework, as shown in Figure 2, which agreed with the stable

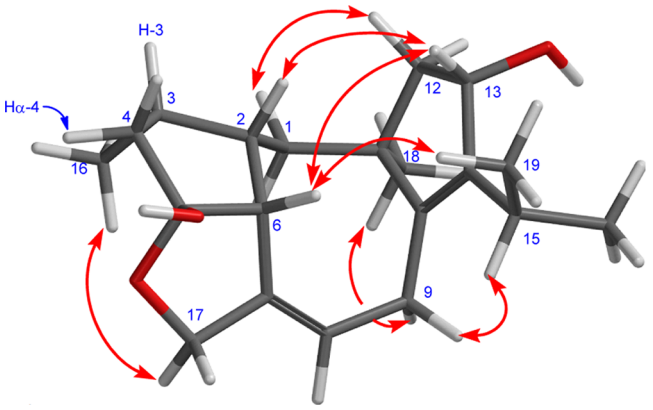
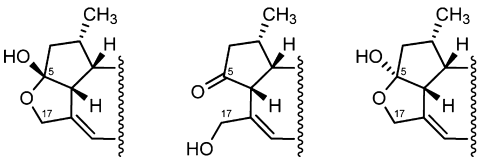


Figure 2. Representative NOEs of **1**.

conformation based on the modeling calculations described below. The (H-3)−C-3−C-4−(H_α-4) dihedral angle was almost 90° in this conformation, which is consistent with the absence of ^3J coupling between H-3 and H_α-4. This conformation satisfied all other NOESY correlations such as H_α-1/H_α-12, 6-H/19-H_3, 9-H_β/15-H, and H_α-9/H_3-18. As described above, the epoxidation proceeded β-selectively. This conformation can reasonably explain the stereochemistry in the epoxidation giving **3**. The reagent is forced to approach the outer β-face of the convex, which also could be further directed by the β-orientation of the 5-OH group.[17]

We opted to confirm the unique structure of **1** via theoretically calculated NMR chemical shifts. A conformational search with MMFF[18] afforded 28 stable conformers. Each conformer was optimized by DFT calculations at the EDF2/6-31G* level,[19] and the chemical shifts of the optimized conformations were calculated at the same approximation level.[5] Theoretical chemical shifts were given after correction based on the Boltzmann distribution. As shown in Table 1, both ^{1}H and ^{13}C NMR theoretical chemical shifts by these calculations showed excellent agreement with those of experimental data [r = 0.9997 (^{13}C), 0.9953 (^{1}H), max|$\Delta\delta$| 3.46 ppm (^{13}C), 0.32 ppm (^{1}H); see details in Supporting Information].[20] We assigned the ^{13}C NMR resonance at 119.53 ppm for the C-5 ketal by considering the acetal carbon (116.5 ppm) in a sesquiterpene ophiobolin H,[21] although the chemical shift was slightly larger than that generally expected (100−110 ppm).[22] These calculations suggested 118.94 ppm for this carbon which correlated well with the above assignment. The hemiacetal structure may allow an equilibrium with the keto-alcohol **X** and with the C-5 epimer **Y** (Figure 3). However these structures involve higher structural energies (7.5 and 15.6 kcal/mol, respectively) than that of the natural form **1**, when they are estimated by calculations similar to the above. These thermodynamic discussions also support the structure of **1**. While it is possible to presume higher steric energy for **Y** because of the *trans*-fused bicyclo[3.3.0] system, only calculations can provide information on the stereoenergetic difference between **1** and **X**.

Roussoella hysterioides KT1651 also produces roussoellol B (**2**). This compound gave the protonated molecular ion at m/z



natural form (**1**) 0 kcal/mol | keto-alcohol form (**X**) +7.5 kcal/mol | C-5 epimer (**Y**) +15.6 kcal/mol

Figure 3. Structures of the keto-alcohol form (**X**) and of the C-5 epimer (**Y**), as well as their relative steric energies estimated by EDF2/6-31G* calculations.

333.2066 ([M + H]$^+$ 333.2066) in the ESIMS, suggesting the molecular formula $C_{20}H_{28}O_4$, which is one more oxygen but two less hydrogens compared to that of **1**. In the ^{1}H NMR spectrum of **2**, signals due to C-17 methylene protons were no longer present. In contrast, **2** gave a ^{13}C NMR resonance for C-17 at 170.18 ppm, suggesting a carbonyl group. The H-8 signal appeared at 6.89 ppm, whereas it was 5.38 ppm in **1**. These suggested an α,β-unsaturated carbonyl system for C-17−C-7−C-8 moiety in **2**. The C-5 acetal moiety was retained in **2** on the basis of its ^{13}C NMR chemical shift (115.52 ppm). The NOESY spectrum suggested the same relative configuration as that of **1**. Chemical shift calculations similar to those described above also supported the structure [r = 0.9997 (^{13}C), 0.9964 (^{1}H), max|$\Delta\delta$| = 2.85 ppm (^{13}C), 0.32 ppm (^{1}H)].

We next studied the absolute configurations of roussoellols A (**1**) and B (**2**). The alcohol functionalities in **1** were not suitable for the modified Mosher method because of the tertiary nature of C-5 and the steric hindrance at C-13. The modified Mosher method is less reliable in the configurational assignment of hindered alcohols.[23,24] On the other hand, **1** exhibited a Gaussian-type positive Cotton effect ($\Delta\varepsilon$ +31, 217 nm), which decreased to $\Delta\varepsilon$ ±0 at around 200 nm in the ECD spectrum. Since the wavelength where the ECD value became zero corresponded with that of λ_{max} (202 nm, ε 28000) as shown in Figure 4, we assumed that the observed positive Cotton effect was the longer wavelength peak of a split ECD couplet on the basis of circular dichroism theory.[25] Thus, we expanded the

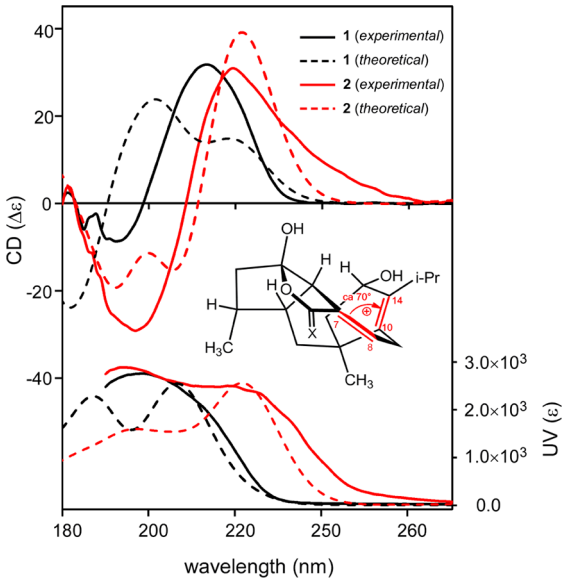


Figure 4. Experimental and theoretical VUVCD spectra and experimental UV spectra of **1** and **2** in CH_3CN.

dx.doi.org/10.1021/np400045z | J. Nat. Prod. XXXX, XXX, XXX−XXX

ECD measurement to the vacuum UV region (VUVCD)[26] to observe a negative Cotton effect at 193 nm ($\Delta\varepsilon$ −8.4). Roussoellol B [**2**, λ_{max} 221 and 198 nm (ε 26000 and 30000, respectively)] provided a more typical exciton ECD couplet at slightly longer wavelength [$\Delta\varepsilon$ +30 (220 nm), −28 (198 nm)]. Since only C-7−C-8 [in the case of **2**, O−C-17−C-7−C-8] and C-10−C-14 olefin functionalities contribute to UV absorptions as well as ECD spectra at this region, we concluded that the positive coupling in the ECD spectra were due to positive chiral relationships for those olefinic functionalities. When the dihedral angles of C-7−C-8−C-10−C-14 were investigated employing the enantiomer in Figure 1, they were found to be approximately +70° in all stable conformers of both **1** and **2**, revealing their absolute configurations to both be 2*S*,3*S*,5*R*,6*R*,11*S*,13*S*.

We assessed our configuration assignments further by theoretically reproducing their ECD spectra, because there was only a report demonstrating ECD couplings from such isolated olefinic groups.[27] The ECD calculations were performed with TD DFT at the B3LYP/TZVP level employing the same set of stable conformers as those obtained in the NMR shift calculations. In a similar manner to that for chemical shift calculations, the following correction based on Boltzmann distributions of the conformers provided theoretical ECD spectra as shown in Figure 4. These theoretical spectra reproduced the experimental spectra well, confirming our assigned absolute configuration.

These compounds were found through screening a series of Ascomycota against the phytopathogen *Cochliobolus miyabeanus*. Roussoellol B (**2**) was found to inhibit its hyphal growth at 10 μg/mL (IC_{50}), whereas **1** did not show considerable inhibition. Trials with higher concentrations of **1** resulted in precipitation.

Thus, we isolated and determined the structures of roussoellols A (**1**) and B (**2**). They possess a novel tetracyclic fusicoccane framework. Although the sesterterpene ophiobolin H[21,28] is known to have a similar tetracyclic system, it is stereochemically different. The present study revealed that both **1** and **2** possess a unique bent structure, in contrast to nonbending-shaped ophiobolin H. We also demonstrated the effectiveness of the calculations of theoretical chemical shifts and ECD spectra. The yields of **1** and **2** (a total of 110 mg from 3.0 L of culture broth) indicated that these compounds are produced as some functional materials for *Roussoella hysterioides* KT1651. Explorations of further biological properties of these molecules are under investigation in our laboratories.

EXPERIMENTAL SECTION

General Experimental Procedures. The optical rotation values were measured on a Horiba SEP-700 spectrometer. UV spectra were obtained with a Hitachi U-2010 spectrophotometer. The CD spectra were recorded on a Jasco J-725 spectrometer. Measurements of VUVCD spectra were performed with the spectrophotometer constructed at Hiroshima Synchrotron Radiation Center, (HiSOR)). Measurements of IR spectra were performed with a Horiba FT-720 spectrometer on a KBr cell. The ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on a Jeol JNM-ECA500 spectrometer in $CDCl_3$. TMS was used as the standard. ESIMS spectra were obtained on a Hitachi NanoFrontier LD spectrometer. Field Desorption MS spectra were measured with a Jeol JMS-T100GCV spectrometer.

Fungus. *Roussoella hysterioides* KT1651 was isolated from *Sasa veitchii* at Kanagawa Prefecture Japan in 2004. The fungal isolate was deposited by one of the authors of this article at the National Institute of Agrobiological Sciences, Japan as MAFF 239636 and RIKEN Japan Collection of Microorganisms as JCM 13126.

Calculations. Conformational searches and chemical shift calculations were performed with Spartan 10 version 1.1.0 (Wave function, Inc. Irvine, CA) using a customized PC (operating system, Windows 7 Professional; CPU, AMD Phenom(tm) II 970 processor 3.50 GHz, RAM 16 GB). Theoretical ECD spectra were calculated with Gaussian 09 (Revision A.02 by Gaussian, Wallingford, CT) with a PC (operating system, CentOS a Linux; CPU, 2 Intel Xeon 3 5550 processors 2.67 GHz, RAM 24 GB).

Isolation. *Roussoella hysterioides* KT1651 was cultured in potato-sucrose medium (200 mL in 500-mL baffled Erlenmeyer flasks × 15) on a rotary shaker (110 rpm) at 25.8 °C for 30 days. After the media was filtered by suction, the filtrate was extracted with EtOAc (500 mL × 2), and the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude extracts (685 mg). Silica gel column chromatography with EtOAc/benzene (40:60) gave the fraction mainly containing **1** and **2** (180 mg). These were separated by medium pressured silica gel column chromatography (Yamazen Ultra Pack Si-40B) with EtOAc/*n*-hexane (30:70) to give **1** (75 mg) and **2** (35 mg) both as colorless needles.

*Roussoellol A (**1**).* Mp 121−122 °C; $[\alpha]^{20}_D$ 72.8 (*c* 0.25, $CHCl_3$); IR (KBr) 3400, 2960, 2930, 1030 cm^{-1}; FDMS (rel int %) *m*/*z* = 318.2 (M^+, 100), 301.2 ($[M - OH]^+$, 13), APCIMS found *m*/*z* = 301.2145 (calcd for $C_{20}H_{29}O_4$, $[M + H - H_2O]^+$ 301.2168); ESIMS found *m*/*z* = 301.2179 (calcd for $C_{20}H_{29}O_4$, $[M + H - H_2O]^+$ 301.2168).

*Roussoellol B (**2**).* Mp 119−120 °C, $[\alpha]^{25}_D$ 90 (*c* 0.80, $CHCl_3$); IR (KBr) 3400, 2960, 1735, 1670, 1230, 1200, 1040, 950 cm^{-1}; ESIMS found *m*/*z* = 333.2066 (calcd for $C_{20}H_{29}O_4$, $[M + H]^+$ 333.2066), *m*/*z* = 315.1960 (calcd for $C_{20}H_{27}O_3$, $[M + H - H_2O]^+$ 315.1960).

Preparation of Epoxide 3. A solution of **1** (10.0 mg) in pyridine (1.0 mL) was stirred with Ac_2O (100 μL) at room temperature for 2 h. After the mixture was concentrated under reduced pressure, the residue was purified by silica gel column chromatography with EtOAc/*n*-hexane (20:80) to give the 8-*O*-acetate (9.0 mg). IR (film) 3415, 2930, 1730, 1245, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.78 (3H, d, *J* = 7.5 Hz), 1.01 and 1.03 (each 3H, d, *J* = 7.0 Hz), 1.15 (3H, s), 1.30 (1H, dd, *J* = 2.0, 13.9 Hz), 1.45 (1H, dd, *J* = 3.7, 14.6 Hz), 1.69 (1H, 12.9, 13.9 Ha), 1.85 (d, *J* = 12.9 Hz), 1.98 (1H, dd, *J* = 7.2, 12.9 Hz), 2.03 (3H, s), 2.09 (1H, m), 2.32 (1H, m), 2.39 (1H, br s), 2.43 (1H, dd, *J* = 8.0, 14.6 Hz), 2.62 (1H, heptuplet), 2.71 (1H, br d, *J* = 18.3 Hz), 2.96 (1H, br d, *J* = 10.8 Hz), 3.06 (1H, br d, *J* = 18.3 Hz), 4.45 (1H, br d, *J* = 12.2 Hz), 4.59 (1H, br d, *J* = 12.2 Hz), 5.37 (1H, m), 5.80 (1H, dd, *J* = 3.7, 8.0 Hz); ESIMS found *m*/*z* = 343.2 (calcd for $C_{22}H_{31}O_3$, $[M + H - H_2O]^+$ 343.2). The acetate (7.0 mg, 19.4 μmol) in CH_2Cl_2 (1.0 mL) was stirred with *m*-CPBA (70% purity, 5.0 mg, ca. 20 μmol) at 0 °C for 2 h, and the mixture was allowed to warm to room temperature. After 12 h, the mixture was poured into aqueous 5% $NaHCO_3$ solution (20 mL) containing 0.1 M $Na_2S_2O_3$ (5.0 mL) and extracted with Et_2O (20 mL). The organic solution was washed with brine (20 mL), dried over $MgSO_4$, and then concentrated under reduced pressure. Preparative silica gel thin layer chromatography (EtOAc/*n*-hexane 50:50) afforded **3** (ca. 2.0 mg). ^{1}H NMR δ 0.88 (3H, d, *J* = 7.4 Hz), 0.99 (3H, d, *J* = 6.9 Hz), 1.00 (3H, d, *J* = 7.2 Hz), 1.59 (3H, s), 1.39 (1H, dd, *J* = 1.8, 4.2 Hz), 1.43 (1H, dd, *J* = 4.3, 14.7 Hz), 1.55 (1H), 1.88 (1H, d, *J* = 12.9 Hz), 2.07 (3H, s), 2.08 (1H, dd, *J* = 7.5, 12.9 Hz), 2.16 (1H, m), 2.29 (1H, m), 2.37 (1H, d, *J* = 11.7 Hz), 2.38 (1H, dd, *J* = 8.1, 14.7 Hz), 2.50 (1H, *J* = 4.2, 16.0 Hz), 2.61 (1H, m), 2.99 (1H, dd, *J* = 1.4, 14.0 Hz), 3.84 and 4.23 (each 1H, d, *J* = 10.7 Hz), 5.71 (1H, dd, *J* = 4.7, 8.1 Hz); FDMS (rel int %) *m*/*z* = 376 (M^+, 20), 358 ($[M - H_2O]^+$, 100), 317 ($[M - AcO]^+$, 40); HRFDMS found *m*/*z* = 376.2218 (calcd for $C_{22}H_{32}O_5$, M^+ 376.2250), *m*/*z* = 358.2143 (calcd for $C_{22}H_{30}O_4$, $[M - H_2O]^+$ 358.2144)

Chemical Shift Calculations. After roussoellols A (**1**) and B (**2**) were constructed on Spartan 10, these were submitted to a conformational search employing AM1 to afford 28 and 33 stable conformers, respectively, where five overlapping conformers in the case of **1** were removed. The remaining conformers were further optimized by the DFT method supposing no solvent (vacuum

dx.doi.org/10.1021/np400045z | J. Nat. Prod. XXXX, XXX, XXX−XXX

conditions) with EDF2 functional and 6-31G* basis set and then subjected to chemical shift calculations at the same approximation to give the theoretical chemical shifts to each conformer. Calculated chemical shifts were obtained after correction based on the Boltzmann distribution. Steric energies for keto-alcohol **X** and C-5 epimer **Y** were also obtained in the similar manner.

ECD Calculations. The same conformation sets of stable conformers of roussoellols A (**1**) and B (**2**) obtained in the former calculations were subjected to a TDDFT simulation on Gaussian 09 at approximation of a hybrid functional and triple-ζ basis set with B3LYP/TZVP supposing no solvent (vacuum conditions). For each conformer, all of the resultant rotational strengths were converted into Gaussian distributions (bandwidth μ = 2800 cm^{-1}) and summed to give the ECD spectrum, where the accuracy of calculations was confirmed by the fact that all the considered excitation energies (5.6−6.1 eV) were low enough compared with the calculated ionization potentials (ca. 6.6 eV). The theoretical ECD spectra were obtained after correction based on the Boltzmann distribution of the six most stable conformers, which covered 97.3% and 85.9% of populations for compounds **1** and **2**, respectively.

■ ASSOCIATED CONTENT

Supporting Information

^1H, ^{13}C, COSY, HMQC, HMBC, and NOESY spectra, summary of HMBC and NOESY correlation signals of **1**, **2**, **3**, and detail of the calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported in part by the Grant-in-Aid for Scientific Research on Innovative Areas (No. 23108504). The authors also thank Enago (www.enago.jp) for the English language review.

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