Article

Four New Sesquiterpenoids from the Rice Fermentation of Antrodiella albocinnamomea

Min Guo 1, Ying-Zhong Liang 1, Xiu-Ming Cui 1,2, Lin-Jiao Shao 1, Yin-Fei Li 1 and Xiao-Yan Yang 1,2,*

1 Faculty of Life Science and Technology, Kunming University of Science and Technology, Kunming 650500, China; guomin@stu.kust.edu.cn (M.G.); lyz@stu.kust.edu.cn (Y.-Z.L.); 20120994@kust.edu.cn (X.-M.C.); shaolinjiao@stu.kust.edu.cn (L.-J.S.); liyinfeng@stu.kust.edu.cn (Y.-FL.)
2 Yunnan Key Laboratory of Sustainable Utilization of Panax Notoginseng, Kunming 650500, China
* Correspondence: yangxy@kust.edu.cn; Tel.: +86-159-6946-8214

Abstract: Albocimea B-E (1–4), four new sesquiterpenoids, and four known compounds, steeperoxide A (5), dankasterone (6), 1H-indole-3-carboxylic acid (7), and (+)-formylanserinone B (8), were isolated from the rice fermentation of the fungus Antrodiella albocinnamomea. The structures of new compounds were elucidated by comprehensive spectroscopic techniques, the planar structures of new compounds were determined by comprehensive spectroscopic techniques, and their absolute configurations were confirmed via gauge-independent atomic orbital calculations (GIAO), calculation of the electronic circular dichroism (ECD), and optical rotation (OR). These were determined by spectroscopic data analysis.

Keywords: Antrodiella albocinnamomea; sesquiterpene; structure elucidation; sesquiterpenoids; GIAO

1. Introduction

Antrodiella albocinnamomea is a kind of wood-decay higher fungus, which belongs to the family Polyporaceae and is widely distributed in northeast China. The main characteristics are flat fruiting body, two-line hyphae, locked union of reproductive hyphae and saccular body in the fruiting layer [1,2]. Previous research on this fungus led to the isolation of sesquiterpenes and steroids; some of them show the biological activities that are antibacterial, antiprotein tyrosine phosphatase 1B inhibitory, cytotoxic, immunosuppressive, and so on [3–9]. Sesquiterpenes are the main chemical component in this fungus, including different types of chamigrane, nor-chamigrane, triquinane, gymnomitrane, humulane, a new skeleton, etc. [3,4,6–8]. These results inspired us to search for other structurally novel components and bioactive natural products from this higher fungus. We changed the conditions and enlarged the fermentation scale of the fungus, which led to the isolation of four new sesquiterpenoids, albocimea B-E (1–4), and four known compounds (5–8) (Figure 1). Detailed spectroscopic analysis and comparison with reported data allowed the determination of four known compounds, steeperoxide A (5) [10], dankasterone (6) [11], 1H-indole-3-carboxylic acid (7) [12], and (+)-formylanserinone B (8) [13].
2. Results and Discussion

Compound 1 was obtained as a white amorphous powder. Its molecular formula of C_{14}H_{20}O_{4} was determined by the HR-ESI-MS at m/z 275.1255 [M + Na]^+ (calculated for 275.1254), corresponding to five degrees of unsaturation. The IR absorption bands at 3400, 1706, and 1677 cm\(^{-1}\) revealed the presence of hydroxyl, carbonyl, and C=C double bond groups. The \(^1\)H NMR spectrum (Table 1) revealed resonances for three methyl protons at δ\(H\) 2.20, 1.14, and 0.98 (each 3H, s), and revealed that those methyl groups were located at quaternary carbons. The \(^{13}\)C NMR and DEPT spectra (Table 1) revealed the existence of 14 carbon signals for three methyls, four methylenes, one olefinic methine (δC 121.3), and six quaternary carbons (including two ketone carbonyls at δC 194.7 and 213.1, one oxygenated at δC 91.5, and one olefinic at δC 145.0). These spectroscopic data revealed that 1 should be a dicyclic norsesquiterpenoid. The \(^1\)H-\(^1\)H COSY spectrum (Figure 2) of 1 established the partial structures of H-4/H\(_2\)-5 and H\(_2\)-9/H\(_2\)-10. The HMBC correlations (Figure 2) from H\(_3\)-12 (δ\(H\) 1.14) to C-13, C-11, C-10, and C-6, indicated C-12 and C-13 were located on C-11, and C-10 and C-6 were connected by C-11. The HMBC correlations (Figure 2) from H\(_3\)-14 (δ\(H\) 2.20) to C-7, C-8, and C-6, and H\(_2\)-9 to C-7 indicated C-8 and C-6 were connected by C-7. Beside this, C-5 and C-1 were connected by C-6 from the \(^1\)H-\(^1\)H COSY correlation of H-4/H\(_2\)-5, and HMBC correlations from H\(_2\)-5 and H\(_2\)-1 to C-6, C-7, and C-11, and so established a 6,6-bicyclic skeleton via a C-6 spiro carbon. These data of 1 are closely related to those of antroalbol H [3]. The difference between them is the presence of a double bond group at C-3 and C-4 in compound 1. This assignment was in accordance with the HMBC correlations (Figure 2) from H-4 (δ\(H\) 6.03 br s) to C-5, C-6, and C-2, and H\(_2\)-5 to δC 145.0 (C-3).

In the ROESY spectrum, only weak correlations between H\(_3\)-14 and H\(_2\)-1 can be observed (Figure S9, see details in the Supplementary Materials). In order to further determine the relative configurations of 1, gauge-independent atomic orbital calculations (GIAO), \(^{13}\)C NMR calculations, and DP4+ analysis were performed. Compound 1 has two chiral centers, which have four possible configurations. The \(^{13}\)C-NMR of four possible structures was calculated at the mPW1PW91/6-31 G (d) level using the GIAO method. Comparison of the \(^{13}\)C chemical shifts obtained revealed that the calculated chemical shifts of 1a and 1c (Table S3 and Figure S35, see details in the Supplementary Materials) were closest to the experimental values. Therefore, the relative configurations of 1 were designated. Finally, the absolute configurations of 1 were assigned as 6\(R\),7\(S\) by comparison of the experimental and calculated ECD (Figure S1). As shown in Figure S1, the calculated curve for 6\(R\),7\(S\) matches well with that of the experimental ECD curve of compound 1. Thus, the structure of albocimea B (1) was determined as depicted.
Table 1. $^1$H (600 MHz) and $^{13}$C NMR (150 MHz) data for compounds 1–3 in CDCl$_3$ and 4 in CD$_3$OD ($\delta$ in ppm, $J$ in Hz).

| No. | $\delta_H$ ($J$ in Hz) | $\delta_C$ | $\delta_H$ ($J$ in Hz) | $\delta_C$ | $\delta_H$ ($J$ in Hz) | $\delta_C$ | $\delta_H$ ($J$ in Hz) | $\delta_C$ |
|-----|------------------------|------------|------------------------|------------|------------------------|------------|------------------------|------------|
| 1   | 2.42, m 32.3           | 2.43, m    | 34.3                   | 2.87 t (16.8) | 42.0                   | 2.62 br d (18.0) | 47.4                   |
| 2   | 194.7                  | 146.4      | 44.1                   | 1.96 d (18.0) | 1.78 d (18.0)          | 59.1                   |
| 3   | 145.0                  | 6.75, br s | 2.83, br d (20.3)      | 37.6       | 6.88 s 124.2           | 2.12 d (18.0) | 1.93 d (18.0)          | 41.2                   |
| 4   | 2.45, m (13.2, 7.2)    | 25.2       | 59.7                   | 135.4      | 207.4                  | 131.5                   |
| 5   | 45.5                   | 80.0       | 129.2                  | 139.5      | 165.0                  |
| 6   | 91.5                   | 213.4      | 133.2                  | 131.5                   |
| 7   | 213.1                  | 2.76, td (13.8, 7.0) | 33.8       | 139.5      | 165.0                  |
| 8   | 2.40, m 35.7           | 190.6, td (13.6, 5.0) | 36.5       | 141.0      | 78.6                   |
| 9   | 1.91, m 1.83, m        | 38.8       | 37.0                   | 3.52 s 70.9 | 1.05 s 32.1 |
| 10  | 55.5                   | 0.88, s    | 26.8                   | 1.18 s 24.4 | 1.29 s 31.9 |
| 11  | 1.14, s 24.3           | 1.22, s    | 24.7                   | 2.29 s 20.6 | 1.19 s 26.1 |
| 12  | 0.98, s 24.4           | 1.46, s    | 25.2                   | 3.68 m 35.1 | 4.04 dd (13.2, 6.6) 75.5 |
| 13  | 2.20, s 26.8           | 9.67, s    | 189.5                  | 2.19 s 16.4 | 1.71 s 13.2 |
| 14  | -OCH$_3$               |            |                        | 3.68 s 51.9 |                      |

![Figure 2](image.png)

Figure 2. Key $^1$H-$^1$H COSY and HMBC correlations of compounds 1–4.

Compound 2 was obtained as a white amorphous powder, based on a Na$^+$ adduct at $m/z$ 236.1408 [M + Na]$^+$ (calculated for 236.1412) via HR-ESI-MS, the molecular formula of 2 was carried out as C$_{11}$H$_{20}$O$_3$, suggesting five degrees of unsaturation. The IR absorption
Molecules 2022, 27, 3344

band of 2 at 3440 cm\(^{-1}\) suggested the presence of a hydroxyl group, while the absorption band at 1712 cm\(^{-1}\) suggested the presence of a carbonyl group. The \(^1\)H NMR spectrum (Table 1) of 2 at \(\delta_H 1.46, 1.22, \) and 0.88 (each 3H, s) suggested the existence of three methyl groups attached to quaternary carbons and an aldehyde group (\(\delta_H 9.67\)). The \(^{13}\)C NMR and DEPT spectra (Table 1) of 2 showed 14 carbon signals attributable to three methyls (\(\delta_C 26.8, 25.2, \) and 24.7), four methylenes (\(\delta_C 37.6, 36.5, 34.3, \) and 33.8), five quaternary carbons (including one ketone carbonyl at \(\delta_C 213.4\) and one oxygenated carbon at \(\delta_C 80.0\)), one aldehyde group (\(\delta_C 189.5\)), and a C=C double bond group (\(\delta_C 150.8, 146.4\)). The \(^1\)H-\(^1\)H COSY spectrum (Figure 2) of 2 established the partial structures of \(H_3-3/H_2-4\) and \(H_2-8/H_2-9\). In the HMBC spectrum (Figure 2), there were correlations from \(H_2-1 (\delta_H 2.43)\) to C-10; \(H_1-3 (\delta_H 6.75)\) to C-1, C-5; \(H_2-4 (\delta_H 2.83)\) to C-2, C-6, C-10; \(H_2-8 (\delta_H 2.76)\) to C-10; \(H_2-9 (\delta_H 1.66)\) to C-11; \(H_3-11 (\delta_H 0.88)\) to C-12; and \(H_3-13 (\delta_H 1.46)\) to C-5, C-7. These data are related to those of spiro[4.5]dec-6-en-1-ol, 2,6,10,10-tetramethyl have the same mother nucleus structure and connect different functional groups.

The correlation of \(H_3-13\) and \(H_2-4\) is very weak in the ROESY spectrum (Figure S17). In order to further determine the relative configurations of 2, we adopted the same method as in determining the configurations of compound 1. Because compound 2 has two chiral centers, it has four possible configurations. \(^{13}\)C-NMR calculations of these four possible configurations were carried out at the mPW1PW91/6-31 G (d) level using the GIAO method. By comparison of \(^{13}\)C chemical shifts, the relative configurations of 2 can be determined. In order to determine its absolute configuration, the optical rotation (OR) value of configuration (2\(S,6S\)) was calculated; this value is \(-9.75\). Compared with the experimental OR value of compound 2 (\(-10.2\)), the absolute configuration of 2 was finally determined as 55,65S. Thus, the structure of albocimea C (2) was assigned as depicted.

Compound 3 was obtained as a white amorphous powder with the molecular formula \(C_{16}H_{23}O_5\), based on HR-ESI-MS at \(m/z\) 285.1462 \([M + Na]^+\) (calculated for 285.1461), which corresponds to six degrees of unsaturation. The IR spectrum absorption band was at 3424 cm\(^{-1}\), indicating the presence of a hydroxyl group. The \(^1\)H NMR spectrum (Table 1) of 3 at \(\delta_H 3.68, 1.18, 2.29,\) and 2.19 (each 3H, s) showed the presence of four methyls. The \(^{13}\)C NMR and DEPT spectra (Table 1) exhibited 16 carbon signals, including four methyls at \(\delta_C 51.9, 24.4, 20.6,\) and 16.4, four methylenes at \(\delta_C 70.9, 43.0, 42.0,\) and 35.1, one methyne at \(\delta_C 124.2,\) and seven quaternary carbons (including one carboxyl group at \(\delta_C 172.2\)). The \(^1\)H-\(^1\)H COSY spectrum (Figure 2) of 3 did not provide any relevant signals. The HMBC spectrum (Figure 2) showed correlations from \(H_2-1 (\delta_H 2.87)\) to C-9, C-11; \(H_2-3 (\delta_H 2.64)\) to C-8, C-11; \(H_1-4 (\delta_H 6.88)\) to C-3, C-6, C-8; \(H_2-10 (\delta_H 3.52)\) to C-3, C-11; \(H_3-12 (\delta_H 2.29)\) to C-6; \(H_2-13 (\delta_H 3.68)\) to C-5, C-7; \(H_3-15 (\delta_H 2.19)\) to C-6, C-8. These data are closely related to those of compound M16 in the literature [15]. The difference between 3 and M16 is the disappearance of the carbonyl group at C-1 in compound 3.

The CEs in the CD spectrum are not obvious for 3; the absolute configuration of this compound was further investigated by comparison of its experimental OR value with those calculated for (2S)-3. The calculation results show that the calculated OR value of (2S)-3 is +3.01, while the comparative experimental OR value is \(-2.92\). Therefore, it is suggested that the absolute configuration of 3 is opposite to the calculated configuration. Finally, the absolute configuration of 3 was determined as 2R. Thus, the structure of albocimea D (3) was assigned as depicted.

Compound 4 was isolated as colorless gum. Its molecular formula \(C_{18}H_{24}O_3\) was determined on HR-ESI-MS spectrum at \(m/z\) 251.1653 \([M – H]^+\) (calculated for 251.1653), corresponding to four degrees of unsaturation. The IR spectrum showed absorption bands for hydroxyl group (3430 cm\(^{-1}\)) and carbonyl group (1644 cm\(^{-1}\)). The \(^1\)H NMR spectrum (Table 1) showed the presence of five methyls at \(\delta_H 1.71, 1.29, 1.19, 1.07,\) and 1.05 (each 3H, s). The \(^{13}\)C NMR and DEPT spectra (Table 1) showed 15 carbon signals attributable to five methyls (\(\delta_C 32.1, 31.9, 26.1, 18.0,\) and 13.2), three methylenes (\(\delta_C 59.1, 47.4,\) and 41.2), one methyne (\(\delta_C 75.5\)), and six quaternary carbons (including one carbonyl group at \(\delta_C 207.4\)).
The $^1$H-$^1$H COSY spectrum (Figure 2) established the partial structures of H$_{11}$-13/H$_{3}$-14. The HMBC spectrum (Figure 2) displayed correlations from H$_{2}$-1 ($\delta_H$ 2.62) to C-3, C-7, C-9, and C-10; H$_{2}$-3 ($\delta_H$ 1.96) to C-8, C-11; H$_{2}$-4 ($\delta_H$ 1.93) to C-6, C-8; H$_{3}$-10 ($\delta_H$ 1.05) to C-11; H$_{3}$-12 ($\delta_H$ 1.19) to C-6; H$_{11}$-13 ($\delta_H$ 4.04) to C-4; H$_{3}$-14 ($\delta_H$ 1.07) to C-5; H$_{3}$-15 ($\delta_H$ 1.71) to C-6, C-8. These data are related to those of 6,8,8-trimethyl-bicyclo[4,3,0]non-1-en-3-one [16]. Thus, 4 and 6,8,8-trimethyl-bicyclo[4,3,0]non-1-en-3-one have the same mother nucleus structure and connect different functional groups.

The correlations observed in the ROESY spectrum (Figure S34) of 4 were insufficient for determining its relative configuration. Because compound 4 has three chiral centers, it has eight possible configurations. $^{13}$C-NMR calculations of eight of these possible configurations were carried out at the mPW1PW91/6-31 G (d) level using the GIAO method. The comparison of the $^{13}$C chemical shifts obtained revealed that the calculated chemical shifts of an enantiomer pair configuration 4a and 4e (Table S3 and Figure S35) are the closest to the experimental values. Finally, the absolute configurations of 4 were assigned as 5R,9S,13S by comparison with the experimental and calculated ECD (Figure S26); the calculated curve for 5R,9S,13S matches well with that of the experimental ECD curve of 4. Thus, compound 4 was established to be albocimea E.

Because the isolated compound materials are limited, only the ones with sufficient amount could be tested for bacteriostatic test. Therefore, compounds 2 and 6 were evaluated for antibacterial activity with the Kirby–Bauer test. The results showed that both had no significant inhibitory activity against Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, and Monilia albican.

In conclusion, four previously undescribed sesquiterpenoids (1–4) and four known compounds (5–8) were acquired from the rice fermentation of the fungus A. albocinnamomea. The structures of these compounds were characterized using spectroscopic data. The antibacterial activity test of compounds 2 and 6 showed that they have no significant antibacterial activity.

3. Experimental Section

3.1. General Experimental Procedures

Optical rotations were taken on a JASCO P-1020 polarimeter. IR spectra were obtained on a Bruker Tensor 27 spectrometer with KBr pellets. NMR spectra were measured on a Bruker Avance III 600 MHz spectrometer with TMS as the internal standard. Mass spectra were recorded with an APIQSTAR time-of-flight spectrometer. CD spectra were recorded on an Applied Photophysics spectrometer. Silica gel (200–300 mesh), Sephadex LH-20, and Rp-C$_{18}$ were used for column chromatography (CC). Thin-layer chromatography (TLC) experiments were performed on a silica gel GF$_{254}$ pre-coated plate. Fractions were monitored by TLC, and spots were visualized by spraying with 15% H$_2$SO$_4$ in ethanol.

3.2. Fungal Material and Cultivation Condition

A. albocinnamomea was purchased from the China Institute of Microbiology. A voucher specimen (No. Yang20181012) was deposited at the Faculty of Life Science and Technology, Kunming University of Science and Technology. A rice medium was used to ferment the strain. The culture of the strain was divided into two steps. Firstly, the fungal strain was cultured in potato dextrose agar (PDA) medium at 24 °C, and the seed solution was obtained after 7 days of culture. Next, a rice medium was used for large-scale fermentation. The culture medium consisted of rice and water at a ratio of 1:1.4. When preparing the culture medium, 71 g of rice and 100 mL of water were put into 480 mL fermentation bottles. A total of 300 bottles were prepared. They were put into a high-pressure steam sterilization pot and sterilized at 121 °C for 30 min. The seed solution obtained before was divided into small parts, put into the prepared rice medium and incubated at room temperature for 45 days.
3.3. Extraction and Isolation

The fungus was cultured for 45 d, cut into small pieces, and then extracted three times with ethyl acetate (60 L × 72 h each time) at room temperature. The ethyl acetate solution was evaporated under vacuum to yield 137.33 g of crude extract. The extract was subjected to CC over silica gel and eluted with CH$_2$Cl$_2$/MeOH (50:1–10:1) to afford fractions A–F. Fraction C (46.29 g) was subjected to CC over silica gel eluted with CH$_2$Cl$_2$/MeOH (50:1–10:1) to afford fractions C$_1$–C$_{12}$. Subfraction C$_4$ (5.32 g) was further purified by silica gel CC (petroleum ether/ethyl acetate, 50:1–0:1), MPLC, and silica gel CC (petroleum ether/ethyl acetate, 20:1–0:1), and analytical chromatography to afford 1 (1 mg) and 6 (3.2 mg).

Fraction D (23.24 g) was subjected to CC over silica gel eluted with CH$_2$Cl$_2$/MeOH (50:1–0:1) to afford fractions D$_1$–D$_{10}$. Subfraction D$_5$ (3.42 g) was further purified by silica gel CC (petroleum ether/ethyl acetate, 50:1–0:1), Sephadex LH-20 CC (CH$_3$COOH/MeOH, 4:1) to afford fractions E (3.2 mg). Fraction E$_6$ (2.1 mg) was further purified by Sephadex LH-20 CC (CH$_2$Cl$_2$/MeOH, 1:1) to afford 6 (3.6 mg). Fraction F (30.00 g) was subjected to column chromatography (CC) over Rp-18 with H$_2$O/MeOH (50–100%) to afford fractions F$_1$–F$_{10}$. Subfraction F$_6$ (4.2 g) was further purified by HPLC using a Sephadex LH-20 CC (CH$_2$Cl$_2$/MeOH, 1:1) to afford 4 (2.1 mg).

3.4. Antibacterial Assays

3.4.1. Bacterial Strain

The strain of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, and *Monilia albican* were purchased from the Nanjing Bianzhen Biotechnology Co., Ltd (Nanjing, China) and deposited at the Faculty of Life Science and Technology, Kunming University of Science and Technology.

3.4.2. Kirby–Bauer Test

A suspension of the organism to be tested was prepared in a saline solution and measured equal to 0.5 McFarland standard (1 × 10$^8$ colony forming units (CFU)/mL). A 0.5 mL amount of bacterial liquid was injected into the nutrient broth culture medium measured equal to 0.5 McFarland standard (1 × 10$^8$ colony forming units (CFU)/mL). This was mixed evenly, poured into the plate (about 20 mL/plate), stood horizontally, and set aside after solidification. The filter paper soaked that had been cooled to about 50 °C; this was mixed evenly, poured into the plate (about 20 mL/plate), stood horizontally, and set aside after solidification. The filter paper soaked that had been cooled to about 50 °C; this was mixed evenly, poured into the plate (about 20 mL/plate), stood horizontally, and set aside after solidification. The filter paper soaked that had been cooled to about 50 °C; this was mixed evenly, poured into the plate (about 20 mL/plate), stood horizontally, and set aside after solidification.

4. Physical Constants

Albocimea B (1): white amorphous powder; [α]$_D^{27.7}$ +13.32, (c 0.38, MeOH); IR (KBr) $\nu_{\text{max}}$ 3401, 2958, 1705, 1676, 1626, 1226 cm$^{-1}$; $^1$H (chloroform-$d$, 600 MHz) and $^{13}$C NMR (chloroform-$d$, 150 MHz) data, see Table 1; HRESIMS $m/z$ 275.1255 [M + Na]$^+$ (calculated for C$_{14}$H$_{20}$O$_2$Na, 275.1254).

Albocimea C (2): white amorphous powder; [α]$_D^{24}$ −10.2, (c 0.32, MeOH); IR (KBr) $\nu_{\text{max}}$ 3440, 2957, 2923, 2853, 1703, 1630, 1384, 1272, 1161, 1103, 1063 cm$^{-1}$; $^1$H (chloroform-$d$, 600 MHz) and $^{13}$C NMR (chloroform-$d$, 150 MHz) data, see Table 1; HRESIMS $m/z$ 236.1408 [M + Na]$^+$ (calculated for C$_{14}$H$_{20}$O$_2$Na, 236.1412).

Albocimea D (3): colorless oil; [α]$_D^{24.8}$ −2.92, (c 0.29, MeOH); IR (KBr) $\nu_{\text{max}}$ 3436, 2962, 2930, 1733, 1646, 1605, 1436, 1261, 1165, 1033, 803 cm$^{-1}$; $^1$H (chloroform-$d$, 600 MHz) and $^{13}$C NMR (chloroform-$d$, 150 MHz) data, see Table 1; HRESIMS $m/z$ 285.1462 [M + Na]$^+$ (calculated for C$_{16}$H$_{22}$O$_3$Na, 285.1461).
Molecules 2022, 27, 3344

Albocimea E (4): colorless gum; [α]D25.0 +1.52 (c 0.21, MeOH); IR (KBr) νmax 3424, 2952, 2928, 2868, 1644, 1545, 1509, 1453, 1383, 1284, 1259, 1128, 1104 cm⁻¹; 1H (methanol-d4, 600 MHz) and 13C NMR (methanol-d4, 150 MHz) data, see Table 1; HRESIMS m/z 251.1653 [M – H]− (calculated for C15H23O5, 251.1653).

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/molecules27103344/s1, Table S1: Experimental and calculated 13C data for possible structures of compounds 1, 2 and 4 (δ in ppm); Table S2: Regression analysis of 13C NMR chemical displacement calculation and experimental value of eight possible configurations of compounds 1, 2 and 4; Table S3: DP4+ Analysis; Table S4: The Boltzmann distribution proportion of its dominant conformation of the compound 2 (5S,6S); Table S5: Compound 3 (S) within 3.0 kcal/mol, and the Boltzmann distribution proportion of its dominant conformation; Figure S1: Experimental and calculated ECD spectra of compound 1; Figure S2: HR-ESI-MS spectrum of compound 1; Figure S3: IR spectrum of compound 1; Figure S4: 1H NMR spectrum (600MHz, CDCl3) of 1; Figure S5: 13C and DEPT spectrum (150MHz, CDCl3) of 1; Figure S6: HSQC spectrum of 1; Figure S7: HMBC spectrum of 1; Figure S8: 1H−1H COSY spectrum of 1; Figure S9: ROESY spectrum of 1; Figure S10: HR-ESI-MS spectrum of compound 2; Figure S11: IR spectrum of compound 2; Figure S12: 1H NMR spectrum (600MHz, CDCl3) of 2; Figure S13: 13C and DEPT spectrum (150MHz, CDCl3) of 2; Figure S14: HSQC spectrum of 2; Figure S15: HMBC spectrum of 2; Figure S16: 1H−1H COSY spectrum of 2; Figure S17: ROESY spectrum of 2; Figure S18: HR-ESI-MS spectrum of compound 3; Figure S19: IR spectrum of compound 3; Figure S20: 1H NMR spectrum (600MHz, CDCl3) of 3; Figure S21: 13C and DEPT spectrum (150MHz, CDCl3) of 3; Figure S22: HSQC spectrum of 3; Figure S23: HMBC spectrum of 3; Figure S24: 1H−1H COSY spectrum of 3; Figure S25: ROESY spectrum of 3; Figure S26: Experimental and calculated ECD spectra of compound 4; Figure S27: HR-ESI-MS spectrum of compound 4; Figure S28: IR spectrum of compound 4; Figure S29: 1H NMR spectrum (600MHz, CD3OD) of 4; Figure S30: 13C and DEPT spectrum (150MHz, CD3OD) of 4; Figure S31: HSQC spectrum of 4; Figure S32: HMBC spectrum of 4; Figure S33: 1H−1H COSY spectrum of 4; Figure S34: ROESY spectrum of 4; Figure S35: There are possible configurations of compounds 1, 2 and 4; Figure S36: Linear correlation plots of calculate-experimental 13C NMR chemical shift values for (6R,7S)-1a; (6R,7R)-1b; (6S,7R)-1c; (6S,7S)-1d; (5S,6S)-2a; (5S,6R)-2b; (5R,6S)-2c; (5R,6R)-2d; (5R,9S,13S)-4a; (5R,9S,13R)-4b; (5S,9S,13S)-4c; (5R,9R,13S)-4d; (5S,9R,13R)-4e; (5S,9R,13S)-4f; (5R,9R,13R)-4g; (5S,9S,13R)-4h; Figure S37: Antibacterial test of compounds 2 and 6; Figure S38: Experimental optical rotation of compound 2; Figure S39: Experimental optical rotation of compound 3.

Author Contributions: Data curation, M.G.; Investigation, M.G. and X.-Y.Y.; Methodology, M.G. and X.-Y.Y.; Project administration, X.-Y.Y.; Supervision, X.-Y.Y. and X.-M.C.; Validation, M.G.; Writing—original draft, M.G. and X.-Y.Y.; Writing—review & editing, M.G., Y.-Z.L., L.-J.S., Y.-F.L. and X.-Y.Y. All authors have read and agreed to the published version of the manuscript.

Funding: This work was financially supported by the National Natural Science Foundation of China (Nos. 32060104 and 21562029) and the Natural Science Foundation of Yunnan Province (No. 202001AT070050).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors thank the Analytical and Testing Center of Kunming University of Science and Technology and Kunming Institute of Botany for the Spectral Measurements.

Conflicts of Interest: The authors declare no conflict of interest.

References
1. Ma, X.L.; Wang, W.S.; Li, E.W.; Gao, F.H.; Guo, L.D.; Pei, Y.F. A new sesquiterpene from the entomogenous fungus Phomopsis amygdali. Nat. Prod. Res. 2016, 30, 276–280. [CrossRef] [PubMed]
2. Dai, Y.C.; Niemelä, T. Changbai wood-rotting fungi 6. Study on Antrodiella, two new species and notes on some other species. Mycotaxon 1997, 64, 67–81.
3. Wang, F.; Yang, X.Y.; Lu, Y.T.; Li, Z.H.; Xu, Y.H.; Hu, J.; Liu, J.K.; Xiong, W.Y. The natural product antroalbol H promotes phosphorylation of liver kinase B1 (LKB1) at threonine 189 and thereby enhances cellular glucose uptake. *J. Biol. Chem.* 2019, 294, 10415–10427. [CrossRef] [PubMed]

4. Li, W.; He, J.; Feng, T.; Yang, H.X.; Ai, H.L.; Li, Z.H.; Liu, J.K. Antroalbocin A, an antibacterial sesquiterpenoid from higher fungus *Antrodiella albocinnamomea*. *Org. Lett.* 2018, 20, 8019–8021. [CrossRef] [PubMed]

5. Chen, Z.M.; Yang, X.Y.; Fan, Q.Y.; Li, Z.H.; Wei, K.; Chen, H.P.; Feng, T.; Liu, J.K. Three novel degraded steroids from cultures of the Basidiomycete *Antrodiella albocinnamomea*. *Steroids* 2014, 87, 21–25. [CrossRef] [PubMed]

6. Chen, Z.M.; Chen, H.P.; Wang, F.; Li, Z.H.; Feng, T.; Liu, J.K. New triquinane and gymnomitrane sesquiterpenes from fermentation of the basidiomycete *Antrodiella albocinnamomea*. *Fitoterapia* 2015, 102, 61–66. [CrossRef] [PubMed]

7. Chen, Z.M.; Fan, Q.Y.; Yin, X.; Yang, X.Y.; Li, Z.H.; Feng, T.; Liu, J.K. Three New Humulane sesquiterpenes from cultures of the Fungus *Antrodiella albocinnamomea*. *Nat. Prod. Bioprospect.* 2014, 4, 207–211. [CrossRef] [PubMed]

8. Liang, D.D.; Yi, X.W.; Wu, H.; Li, Z.H.; Wang, G.K.; Cheng, G.G.; Feng, T. Antrodillin, an immunosuppressive sesquiterpenoid from higher fungus *Antrodiella albocinnamomea*. *RSC Adv.* 2021, 11, 1124–1127. [CrossRef] [PubMed]

9. Chen, Z.M.; Wang, S.L. Two new compounds from cultures of the basidiomycete *Antrodiella albocinnamomea*. *Nat. Prod. Res.* 2015, 29, 1985–1989. [CrossRef] [PubMed]

10. Liu, D.Z.; Dong, Z.J.; Wang, F.; Liu, J.K. Two novel norsesquiterpene peroxides from basidiomycete *Steccherinum ochraceum*. *Tetrahedron Lett.* 2010, 51, 3152–3153. [CrossRef]

11. Amagata, T.; Tanaka, M.; Yamada, T.; Doi, M.; Minoura, K.; Ohishi, H.; Yamori, T.; Numata, A. Variation in cytostatic constituents of a sponge-derived *Gymnascella dankaliensis* by manipulating the carbon source. *J. Nat. Prod.* 2007, 70, 1731–1740. [CrossRef] [PubMed]

12. Wang, R.P.; Lin, H.W.; Li, L.Z.; Gao, P.Y.; Xu, Y.; Song, S.J. Monoindole alkaloids from a marine sponge *Mycale fibrexilis*. *Biochem. Syst. Ecol.* 2012, 43, 210–213. [CrossRef] [PubMed]

13. Gautschi, J.T.; Amagata, T.; Amagata, A.; Valeriote, F.A.; Mooberry, S.L.; Crews, P. Expanding the strategies in natural product studies of marine-derived fungi: A chemical investigation of penicillium obtained from deep water sediment. *J. Nat. Prod.* 2004, 67, 362–367. [CrossRef] [PubMed]

14. Ahmed, R.; Arkajyoti, P.; Nazim Uddin, C.M.; Ahmed, S.S.; Kumar, B.S.; Mohuya, M.; Montakim, T.A.; Nurul, A.M.; Asif, S.; Zia, U.M.; et al. Biochemical and Computational approach of Selected Phytocompounds from Tinospora crispa in the Management of COVID-19. *Molecules* 2020, 25, 3936.

15. Lee, Y.P.; Hsu, F.L.; Kang, J.J.; Chen, C.K.; Lee, S.S. Metabolism of (2S)-pterosin A: Identification of the phase I and phase II metabolites in rat urine. *Drug Metab. Dispos.* 2012, 40, 1566–1574. [CrossRef] [PubMed]

16. Könst, W.M.B.; Witteveen, J.G.; Boelens, H. The synthesis of angular methyl substituted bicyclic enones via a unique regioselective enamine annihilation reaction. *Tetrahedron* 1976, 32, 1415–1421. [CrossRef]