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Secondary Metabolites, Monoterpene-Polyketides Containing a Spiro[3.5]nonane from *Cryptocarya laevigata*

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Abstract

Six novel lactone derivatives, cryptolaevilactones A-F (**1–6**), were isolated from *Cryptocarya laevigata*. Their unique spiro[3.5]nonane moiety by hetero [2 + 2] cyclization with monoterpene and polyketide was found for the first time in nature. Structural elucidation using various nuclear magnetic resonance (NMR) techniques revealed that **1–3** and **4–6** are diastereomers and partially established the absolute configurations.

Graphical Abstract

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The authors declare no competing financial interest.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b00624 .

Experimental procedures and spectroscopic data for isolated compounds (PDF)

The genus *Cryptocarya* (Lauraceae) is known to produce δ -lactone derivatives, such as obolactone,¹ cryptocaryone,² cryptolatifolione,³ rugulactone,⁴ cryptomoscatones,⁵ cryptocaryols,⁶ and cryptoconcatones,⁷ as well as various alkaloids, such as caryachines⁸ and antofine.⁹ *C. laevigata*, which is called the glossy laurel or red-fruited laurel, are distributed in rainforest areas, mainly in eastern Australia. Only two phytochemical researches of this species have been reported so far.^{10,11} In our continuous investigation of rainforest plants,^{10,12,13} we performed a phytochemical study on a 50% MeOH/CH₂Cl₂ extract (N025439) of the leaves and twigs of *C. laevigata*. In this study, six new δ -lactone derivatives, named cryptolaevilactones A-F (**1–6**; Figure 1), were isolated from the EtOAc-soluble portion of the extract. Their unique 7-isopropylspiro[3.5]non-5-ene moiety, which was probably biosynthesized by hetero [2 + 2] cyclization with monoterpene and polyketide, has not been found previously in nature.

Cryptolaevilactone A (**1**)¹⁴ was obtained as an optically active pale-yellow oil. The molecular formula, C₂₉H₃₆O₄, was determined by HRFABMS from the peak at m/z 449.2684 [M + H]⁺. The presence of hydroxy and carbonyl groups was suggested by the IR absorption bands at 3467 and 1707 cm⁻¹, respectively. The ¹H NMR spectrum of **1** (Table 1) showed five aromatic protons [δ_H 7.36 (2H), 7.32 (2H), 7.24 (1H)] suggesting the presence of a monosubstituted benzene, two sets of *Z*-olefinic protons (δ_H 6.86/5.99, δ_H 5.59/5.54, *J* = 10.0 Hz), a set of *E*-olefinic protons (δ_H 6.42/6.28, *J* = 15.8 Hz), two oxymethine protons (δ_H 4.66, 4.28), and a hydroxy proton (δ_H 3.34). Other proton signals were attributable to two methyl protons (δ_H 0.80, 0.78) and 16 methylene or methine protons. The ¹³C NMR spectrum of **1** (Table 1) showed 27 signals (two overlapped), including those for a ketone carbonyl carbon (δ_C 212.0), an ester carbonyl carbon (δ_C 164.1), 12 sp² carbons, and 2 oxycarbons (δ_C 75.5, 64.3). The directly bonded carbons and hydrogens were assigned from a HMQC experiment. The lack of a ¹H–¹H COSY connection between H-12 and H-7', as well as H-2' and H-6', suggested the presence of a spiro[3.5]nonane structure. The presence of cyclobutane was also indicated by unusual deshielded chemical shifts at H-11 (δ_H 3.21), H-12 (δ_H 2.91), and H₂-7' (δ_H 1.83 and 2.16). This conclusion was strongly supported by HMBC correlations between H-12/C-6', H-12/C-2', H-7'/C-6', H-7'/C-2', H-2'/C-6', and H-12, H-7', H-3'/C-1' (Figure 2), as well as 1D-TOCSY data detecting H-7' α , H-2', H-3', H₂-5', H-6' α , and H-8' by irradiation of C-9'/10' dimethyl protons at δ 0.8 pp (Figure S11 in the Supporting Information). The relative configuration of the spiro [3.5]nonene moiety (11*R**, 12*S**, 1'*R**, 4'*S*') in **1** was suggested as follows. The NOESY correlations between H-11/H-13, H-12/H-7' β , and H-12/H-2' revealed the relative configuration of C-11, C-12, and C-1' (Figure 2). The correlations between H-4' and H-6' β and the ¹H NMR coupling constants suggested that the cyclohexene ring adopts a half-chair conformation with H-4', H-5' α , and H-6' β in the pseudo-axial positions and H-5' β and H-6' α in the pseudo-equatorial positions. The additional NOESY correlations between H-13/H-5' α and H-13/

H-6 α were disclosed in the relative configurations of C-12, C-1', and C-4'. To elucidate the absolute configuration, the hydroxy group at C-8 was converted to *R*- and *S*-Mosher esters. The δ_{H} (*S*-*R*) values of the ^1H NMR signals indicated the *R* form for the C-8 stereocenter (Table S3 in the Supporting Information). The absolute configuration of C-6 was determined by a NOESY experiment on the related bicyclic tetrahydro- α -pyrone, derived from **1** through a Michael addition. The steric relationship (*syn* or *anti*) between C-6 and C-8 in **1** would be reflected in a NOESY correlation between H-8 and H-3, or H-5, respectively, in the cyclized product (Figure 3). The bicyclic products should likely be more readily produced from the 6,8-*syn* starting compounds, because the bicyclic pyrone would be in the thermodynamically favored chair form, while the boat form would be produced from the 6,8-*anti* compound. The treatment of **1** with DBU in CH_2Cl_2 gave a quantitative yield of the bicyclic pyrone.¹⁵ Its NMR spectra and HPLC retention time were identical to those of bicyclic **4** in the Supporting Information), which showed a NOESY correlation between H-3 and H-8, as described later. From these results, the configuration at C-6 in the Supporting Information), which showed a NOESY correlation between H-3 and H-8, as described later. From these results, the configuration at C-6 in **1** was determined as *R*. This assignment was also supported by a positive Cotton effect at 263 nm in an ECD experiment, because of an $n \rightarrow \pi^*$ transition in the α,β -unsaturated lactone moiety^{16–18} (Figure 4), although the presence of four chromophores (styryl, carbonyl, α,β -unsaturated ketones), and a double bond in the spiro moiety might disturb a clear Cotton effect. Computational calculations could not effectively determine the absolute configuration around the spiro[3.5]-nonene moiety.

The HRFABMS ion peaks of **2**¹⁹ and **3**²⁰ were observed at m/z 449.2670 $[\text{M}+\text{H}]^+$ and 449.2692 $[\text{M}+\text{H}]^+$, respectively, indicating the same molecular formula, $\text{C}_{29}\text{H}_{36}\text{O}_4$, as that of **1**. The similarity of ^1H NMR, ^{13}C NMR (Table S1 in the Supporting Information), HMQC, ^1H – ^1H COSY, and HMBC data (Figure S3 in the Supporting Information) to those of **1** suggested that compounds **2** and **3** are diastereomers of **1**. The relative configurations of **2** (11*R**,12*S**,1'*R**,4'*R**) and **3** (11*S**,12*R**,1'*R**,4'*S**) were determined by NOESY correlations (Figure S4 in the Supporting Information) and ^1H NMR coupling constants. The absolute configurations of the α -pyrone fragment were based on ECD data (Figure 4). The positive Cotton effect at 252 nm for **2** and the negative Cotton effect at 257 nm for **3** implied 6*R* and 6*S* forms, respectively. Compounds **2** and **3** were easily converted to the related bicyclic compounds **5** and **6**, respectively, by using PTLC on SiO_2 . A NOESY correlation between H-3 and H-8 was observed for both **5** and **6** (Figure S4 in the Supporting Information), revealing a *syn* relationship between the C-6 and C-8 chiral centers. Based on these results, compounds **2** and **3** have 6*R*,8*R*- and 6*S*,8*S*- configurations, respectively.

The ^1H NMR spectrum of **4**²¹ was similar to that of **1** (Table 1). However, the signals for the hydroxy group at C-8 and *cis*-olefin at C-3 and C-4 in **1** were absent, while oxymethine and aliphatic signals were observed at δ_{H} 4.30, 2.91, and 2.75. The HRFABMS ion peak of **4** was observed at m/z 449.2691 $[\text{M}+\text{H}]^+$, indicating that **4** and **1** have the same molecular formula, $\text{C}_{29}\text{H}_{36}\text{O}_4$. Based on these data, compound **4** was most likely the bicyclic tetrahydro- α -pyrone transformed from **1**, and the ^1H – ^1H COSY and HMBC data of **4** (Figure 5) supported this bicyclic structure. Similar bicyclic α -pyrone derivatives have been

identified as products of an intramolecular Michael addition of the 5,6-dihydro- α -pyrone moiety.²² Liu et al.²² were concerned that bicyclic products might be produced during column chromatography on SiO₂. In fact, the treatment of **1** with SiO₂ in the presence of MeOH at room temperature (rt) overnight yielded a ca. 1:1 mixture of **1** and **4** on TLC, although compound **4** was stable under the same conditions. However, at this moment, it is not clear whether the bicyclic compounds occurred naturally in the plant or are artifacts. Because the absolute configuration of the lactone moiety of **1** was determined, the 4*R*,6*S*,8*R*-configuration of **4** was confirmed by a key NOESY correlation between H-3 β and H-8 (Figure S4 in the Supporting Information). The relative configuration (11*R**,12*S**,1'*R**,4'*S**) around the spiro-ring of **4** was also determined from the NOESY data (Figure 5) and ¹H NMR coupling constants.

The ¹H NMR, ¹³C NMR spectra, HMQC, ¹H-¹H COSY, and HMBC data of **5**²³ and **6**²⁴ were similar to those of **4** (Table S2 and Figure S3 in the Supporting Information). The HRFABMS ion peaks of **5** and **6** were observed at *m/z* 449.2686 [M+H]⁺ and 449.2689 [M+H]⁺, respectively, suggesting that compounds **4**, **5**, and **6** are diastereomers. The relative configurations of **5** (11*R**,12*S**,1'*R**,4'*R**) and **6** (11*S**,12*R**,1'*R**,4'*S**) were determined from the NOESY data (Figure S4) and coupling ¹H NMR constants for **5** and **6**. The absolute configurations of the lactone moieties of **5** (4*R*,6*S*,8*R*) and **6** (4*S*,6*R*,8*S*) were clarified based on the stereochemistry of related precursors, **2** and **3**, as well as NOESY correlations (Figure S4). The ECD spectra of **4–6** showed similar curves to those of the precyclized δ -lactones **1–3**, respectively (Figure 4). Unfortunately, the limited amounts of the compounds did not allow for any biological evaluations.

Because the genus *Cryptocarya* is known to contain β -phellandrene,²⁵ the proposed biosynthetic pathway to **1–3** might include a [2 + 2] cyclization of the exocyclic double bond of this monoterpene with a polyketide generated from cinnamoyl-CoA and five units of malonyl-CoA (Figure 6). Although [2 + 2] cyclizations to construct cyclobutane rings do occur in biosynthetic pathways, they are normally homodimerized with two identical or similar olefin precursors.²⁶ Therefore, this finding is particularly unique.

In conclusion, we have conducted the successful isolation and structure elucidation of six unique meroterpenoids, cryptolaevilactones A-F, from *C. laevigata*. Although the total absolute configurations were not determined, the relative configurations of the spiro[3.5]nonane portion and the absolute configuration of the δ -lactone section were concluded. This study is the first to discover monoterpene-polyketides with a spiro[3.5]nonane moiety, most likely biosynthesized through an unusual [2 + 2] cyclization between monoterpene and polyketide. Additional work is ongoing to verify the complete structure determinations through total synthesis, followed by biological evaluation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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- (14). Cryptolaevilactone A(1). Pale yellow oil; $[\alpha]_D^{25}$ -98 (c 0.10, CHCl₃); IR $\nu_{\max}$ (CH₂Cl₂) 3467, 2955, 2929, 2869, 1707, 1386, 1251, 1044, 968, 814, 743, 693 cm⁻¹; ¹H and ¹³C NMR, Table 1; HRFABMS m/z 449.2684 [M+H]⁺ (calcd for C₂₉H₃₇O₄, 449.2692).
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- (20). Cryptolaevilactone B (2). pale yellow oil; $[\alpha]_D^{26}$ +153 (c 0.10, CHCl₃); IR $\nu_{\max}$ (CH₂Cl₂) 3454, 2954, 2928, 2869, 1700, 1385, 1251, 1150, 1044, 968, 814, 743, 695 cm⁻¹; NMR (600 MHz, CDCl₃, δ): 7.36 (2H, d, *J* = 7.6 Hz), 7.30 (2H, t, *J* = 7.6 Hz), 7.22 (1H, tt, *J* = 7.2, 1.4 Hz), 6.87 (1H, dt, *J* = 9.6, 4.5 Hz), 6.40 (1H, d, *J* = 15.8 Hz), 6.25 (1H, dd, *J* = 15.8, 8.2 Hz), 6.00 (1H, dt, *J* = 9.6, 1.7 Hz), 5.56 (1H, br d, *J* = 10.9 Hz), 5.54 (1H, br d, *J* = 10.9 Hz), 4.67 (1H, m), 4.29 (1H, m), 3.32 (1H, d, *J* = 3.1 Hz), 3.19 (1H, ddd, *J* = 10.0, 9.6, 8.6 Hz), 3.01 (1H, dd, *J* = 9.6, 8.2 Hz), 2.63 (1H, dd, *J* = 17.9, 3.8 Hz), 2.59 (1H, dd, *J* = 17.9, 7.6 Hz), 2.41 (1H, m), 2.06 (1H, dd, *J* = 11.2, 10.0 Hz), 2.01 (1H, ddd, *J* = 14.4, 8.2, 6.5 Hz), 1.89 (1H, dd, *J* = 11.2, 8.6 Hz), 1.86 (1H, m), 1.79 (1H, m), 1.77 (1H, ddd, *J* = 14.4, 6.2, 3.8 Hz), 1.66 (1H, m), 1.65 (1H, br dd, *J* = 12.7, 12.4 Hz), 1.54 (1H, m), 1.28 (1H, dddd, *J* = 12.4, 12.4, 9.3, 2.4 Hz), 0.87 (1H, d, *J* = 6.9 Hz), 0.84 (1H, d, *J* = 6.9 Hz); ¹³C NMR (150 MHz, CDCl₃, δ): 212.0, 164.2, 145.2, 136.9, 135.6, 132.0, 131.7, 131.0, 128.6 (2C), 127.8, 127.5, 126.3 (2C), 121.2, 75.5, 64.3, 51.7, 47.1, 46.4, 42.1, 40.6, 40.5, 33.7, 31.8, 29.7, 29.0, 22.3, 19.6, 19.3; HRFABMS m/z 449.2670 [M+H]⁺ (calcd for C₂₉H₃₇O₄, 449.2692). The compound 2 was isolated as ca. 3:1 mixture with its inseparable diastereomer (11*S**, 12*R**, 1'*R**, 4'*R**).

- (21). Cryptolaevilactone C (3). colorless oil; $[\alpha]_D^{25} +11$ (c 0.04, CHCl_3); IR ν_{max} (CH_2Cl_2) 3468, 2955, 2919, 2849, 1704, 1385, 1252, 1077, 1045, 964, 814, 742, 694 cm^{-1} ; NMR (600 MHz, CDCl_3 , δ): 7.32 (2H, d, J = 7.6 Hz), 7.28 (2H, dd, J = 7.6, 7.2 Hz), 7.20 (1H, tt, J = 7.2, 1.4 Hz), 6.86 (1H, dt, J = 9.8, 4.3 Hz), 6.38 (1H, d, J = 15.8 Hz), 6.22 (1H, dd, J = 15.8, 8.6 Hz), 6.00 (1H, dt, J = 9.8, 1.7 Hz), 5.83 (1H, br d, J = 10.2 Hz), 5.70 (1H, br d, J = 10.2 Hz), 4.66 (1H, m), 4.29 (1H, m), 3.31 (1H, d, J = 3.1 Hz), 3.19 (1H, ddd, J = 10.3, 9.3, 8.6 Hz), 2.90 (1H, dd, J = 9.3, 8.6 Hz), 2.61 (1H, dd, J = 17.9, 4.5 Hz), 2.58 (1H, dd, J = 17.9, 7.6 Hz), 2.41 (1H, m), 2.07 (1H, dd, J = 11.3, 10.3 Hz), 2.01 (1H, ddd, J = 14.4, 8.2, 6.5 Hz), 1.93 (1H, m), 1.90 (1H, dd, J = 11.3, 8.6 Hz), 1.78 (1H, br d, J = 13.1 Hz), 1.76 (1H, ddd, J = 14.4, 6.2, 4.1 Hz), 1.61 (1H, dt, J = 13.1, 2.7 Hz), 1.54 (1H, m, overlapped), 1.49 (1H, m, overlapped), 1.33 (1H, dddd, J = 13.4, 13.1, 11.0, 2.7 Hz), 0.79 (1H, d, J = 6.9 Hz), 0.76 (1H, d, J = 6.9 Hz); ^{13}C NMR (150 MHz, CDCl_3 , δ): 211.8, 164.1, 145.2, 137.1, 132.5, 131.4, 131.1, 131.0, 128.5 (2C), 127.3, 126.2 (2C), 121.3, 75.5, 64.3, 53.8, 47.2, 46.3, 41.8, 41.1, 40.6, 37.8, 33.1, 31.8, 29.1, 21.9, 19.4, 19.1; HRFABMS m/z 449.2692 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{29}\text{H}_{37}\text{O}_4$, 449.2692).
- (22). Cryptolaevilactone D (4). colorless plate; $[\alpha]_D^{27} -170$ (c 0.08, CHCl_3); IR ν_{max} (CH_2Cl_2) 2955, 2929, 2871, 1731, 1708, 1388, 1351, 1337, 1234, 1200, 1080, 995, 978, 758, 741, 696 cm^{-1} ; ^1H and ^{13}C NMR, Table 1; HRFABMS m/z 449.2691 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}^{29}\text{H}^{37}\text{O}^4$, 449.2692).
- (23). Cryptolaevilactone E (5). colorless amorphous; $[\alpha]_D^{26} +111$ (c 0.15, CHCl_3); IR ν_{max} (CH_2Cl_2) 2955, 2928, 2870, 1731, 1707, 1388, 1353, 1332, 1234, 1211, 1160, 1079, 992, 968, 758, 737, 696 cm^{-1} ; NMR (600 MHz, CDCl_3 , δ): 7.36 (2H, br d, J = 7.6 Hz), 7.30 (2H, dd, J = 7.6, 7.4 Hz), 7.22 (1H, br t, J = 7.4 Hz), 6.39 (1H, d, J = 15.8 Hz), 6.25 (1H, dd, J = 15.8, 8.2 Hz), 5.55 (1H, d, J = 11.2 Hz), 5.53 (1H, d, J = 11.2 Hz), 4.86 (1H, m), 4.32 (1H, m), 4.29 (1H, m), 3.16 (1H, ddd, J = 9.6, 8.9, 8.2 Hz), 3.01 (1H, dd, J = 8.9, 8.2 Hz), 2.92 (1H, br d, J = 19.2 Hz), 2.77 (1H, dd, J = 19.2, 5.5 Hz), 2.62 (1H, dd, J = 16.1, 7.9 Hz), 2.42 (1H, dd, J = 16.1, 4.5 Hz), 2.07 (1H, ddd, J = 11.2, 9.6, 1.0 Hz), 2.04 (1H, br d, J = 14.1 Hz), 1.97 (1H, dddd, J = 13.7, 4.1, 2.1, 2.1 Hz), 1.89 (1H, m, overlapped), 1.86 (1H, m, overlapped), 1.85 (1H, dd, J = 11.2, 8.2 Hz, overlapped), 1.78 (1H, br d, J = 12.4 Hz), 1.65 (1H, m, overlapped), 1.64 (1H, m, overlapped), 1.59 (1H, ddd, J = 14.1, 11.7, 2.4 Hz), 1.54 (1H, m), 1.28 (1H, tdd, J = 12.0, 8.6, 1.7 Hz), 0.86 (1H, d, J = 6.9 Hz), 0.84 (1H, d, J = 6.9 Hz); ^{13}C NMR (150 MHz, CDCl_3 , δ): 207.6, 169.3, 137.1, 135.8, 131.9, 131.5, 128.6 (2C), 127.4, 126.3 (2C), 128.1, 72.7, 65.9, 62.4, 51.5, 46.7, 46.4, 42.1, 40.5, 36.4, 36.2, 33.6, 31.9, 29.9, 29.6, 22.4, 19.6, 19.3; HRFABMS m/z 449.2686 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{29}\text{H}_{37}\text{O}_4$, 449.2692).
- (24). Cryptolaevilactone F (6). colorless amorphous; $[\alpha]_D^{23} -18$ (c 0.065, CHCl_3); IR ν_{max} (CH_2Cl_2) 2955, 2927, 2868, 1731, 1706, 1448, 1384, 1351, 1337, 1232, 1201, 1157, 1079, 991, 964, 737, 694 cm^{-1} ; NMR (600 MHz, CDCl_3 , δ): 7.32 (2H, dd, J = 8.2, 1.4 Hz), 7.28 (2H, dd, J = 8.2, 7.2 Hz), 7.20 (1H, tt, J = 7.2, 1.4 Hz), 6.37 (1H, d, J = 15.8 Hz), 6.23 (1H, dd, J = 15.8, 8.6 Hz), 5.83 (1H, br d, J = 10.0 Hz), 5.69 (1H, br d, J = 10.0 Hz), 4.86 (1H, m), 4.32 (1H, m), 4.28 (1H, dddd, J = 11.7, 7.9, 4.1, 2.8 Hz), 3.16 (1H, ddd, J = 9.6, 9.2, 8.6 Hz), 2.93 (1H, br d, J = 19.2 Hz), 2.91 (1H, dd, J = 9.2, 8.6 Hz), 2.77 (1H, dd, J = 19.2, 5.5 Hz), 2.62 (1H, dd, J = 16.2, 7.9 Hz), 2.41, (1H, dd, J = 16.2, 4.1 Hz), 2.07 (1H, dd, J = 11.3, 9.6 Hz), 2.04 (1H, dddd, J = 14.4, 4.1, 2.8, 1.7 Hz), 1.97 (1H, dddd, J = 13.7, 4.1, 2.1, 2.1 Hz), 1.93 (1H, m), 1.90 (1H, m), 1.87 (1H, dd, J = 11.3, 8.6 Hz), 1.78 (1H, br d, J = 13.4 Hz), 1.59 (1H, ddd, J = 13.6, 13.4, 3.1 Hz), 1.59 (1H, ddd, J = 13.7, 11.7, 2.1 Hz), 1.54 (1H, m), 1.49 (1H, m), 1.31 (1H, dddd, J = 13.6, 13.4, 11.0, 2.7 Hz), 0.78 (1H, d, J = 6.9 Hz), 0.75 (1H, d, J = 6.9 Hz); ^{13}C NMR (150 MHz, CDCl_3 , δ): 207.6, 169.3, 137.3, 132.3, 131.6, 131.3, 131.0, 128.5 (2C), 127.2, 126.2 (2C), 121.3, 72.7, 65.9, 62.3, 53.5, 46.7, 46.3, 41.8, 41.0, 37.7, 36.4, 36.2, 33.0, 31.8, 29.6, 21.9, 19.4, 19.1; HRFABMS m/z 449.2689 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{29}\text{H}_{37}\text{O}_4$, 449.2692).
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Figure 1.
Structures of cryptolaevilactones A–F (1–6).

Figure 2.
Selected COSY, HMBC, and NOESY correlations of **1**.

Figure 3.
Proposed key NOESY correlations after cyclization of 6,8-*syn* and 6,8-*anti* lactones.

Figure 4.
Experimental ECD spectra of compounds 1-6 in acetonitrile.

Figure 5.
Selected COSY, HMBC, and NOESY correlations of **4**.

Figure 6.
Proposed biosynthetic pathway of 1-3.

Table 1.

¹H and ¹³C NMR Data of Compounds 1 and 4 (CDCl₃)

position	1			4		
	δ_{H}^a (J in Hz)	δ_{C}^b	Position	δ_{H}^a (J in Hz)	δ_{C}^b	
2		164.1	2		169.3	
3	5.99 dt (10.0, 1.7)	121.3	3 α	2.75 dd (19.2, 5.5)	36.1	
4	6.86 dt (10.0, 4.3)	145.2	3 β	2.91 ddd (19.2, 1.4, 1.0)		
5	2.41 m	29.1	4	4.30 m	65.9	
6	4.66 m	75.5	5 α	1.96 dddd (13.7, 3.8, 1.7, 1.4)	29.6	
7	1.76 ddd (14.4, 6.2, 4.1)	40.6	5 β	1.88 dddd (13.7, 3.8, 2.1, 2.1)		
	1.99 ddd (14.4, 8.2, 6.5)		6	4.86 m	72.6	
8	4.28 m	64.3	7 α	1.58 ddd (14.1, 12.0, 2.4)	36.3	
9	2.58 dd (18.0, 8.2)	47.3	7 β	2.04 dddd (14.1, 4.5, 2.7, 2.1)		
	2.62 dd (18.0, 3.8)		8	4.28 m	62.4	
10		212.0	9	2.40 dd (16.2, 4.1)	46.7	
11	3.21 ddd (10.0, 9.1, 8.6)	46.4		2.61 dd (16.2, 7.6)		
12	2.91 dd (9.1, 8.4)	51.1	10		207.8	
13	6.28 dd (15.8, 8.4)	127.7	11	3.18 ddd (10.0, 9.6, 8.6)	46.6	
14	6.42 d (15.8)	132.1	12	2.89 dd (9.6, 8.6)	50.9	
15		137.0	13	6.29 dd (15.8, 8.6)	128.0	
16	7.36 brd (7.6)	126.3	14	6.41 d (15.8)	131.8	
17	7.32 dd (7.6, 7.2)	128.6	15		137.2	
18	7.24 tt (7.2, 1.4)	127.5	16	7.36 brd (7.2)	126.2	
19	7.32 dd (7.6, 7.2)	128.6	17	7.32 dd (7.2, 7.2)	128.6	
20	7.36 d (7.6)	126.3	18	7.24 tt (7.2, 1.4)	127.4	
1'		40.4	19	7.32 dd (7.2, 7.2)	128.6	
2'	5.54 dd (10.0, 1.0)	135.5	20	7.36 brd (7.2)	126.2	
3'	5.59 dd (10.0, 1.5)	131.6	1'		40.3	
4'	1.86 m	41.3	2'	5.53 dd (10.3, 1.0)	135.7	
5' α	1.28 dddd (12.7, 12.7, 10.0, 3.1)	22.9	3'	5.57 dd (10.3, 1.4)	131.4	
5' β	1.55 m		4'	1.85 m	41.3	

	1			4		
	position	δ_{H}^a (J in Hz)	δ_{C}^b	Position	δ_{H}^a (J in Hz)	δ_{C}^b
	6' α	2.14 ddd (12.7, 4.8, 3.1)	30.0	5' α	1.28 dddd (12.9, 12.7, 9.6, 2.7)	22.9
	6' β	1.50 ddd (12.7, 12.7, 2.7)	34.4	5' β	1.55 m	30.1
	7' α	1.83 dd (11.7, 8.6)		6' α	2.13 ddd (13.1, 4.5, 2.7)	
	7' β	2.16 dd (11.7, 10.0)		6' β	1.48 ddd (13.1, 12.9, 2.7)	
	8'	1.52 m	31.7	7' α	1.83 dd (11.3, 8.6)	34.4
	9'	0.78 d (6.5)	19.4	7' β	2.16 dd (11.3, 10.0)	
	10'	0.80 d (6.5)	19.6	8'	1.50 m	31.7
	OH	3.34 d (3.1)		9'	0.78 d (6.9)	19.4
				10'	0.80 d (6.9)	19.6

^aData collected at 600 MHz.^bData collected at 150 MHz.