# Chloriolins A–C, Chlorinated Sesquiterpenes Produced by Fungal Cultures Separated from a *Jaspis* Marine Sponge

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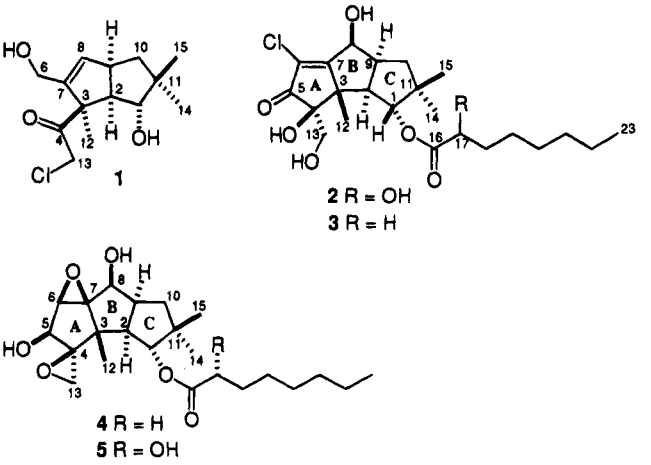
Three new chlorinated, cyclic sesquiterpenes, chloriolin A (**1**), B (**2**), C (**3**), and two known compounds, coriolin B (**4**) and dihydrocoriolin C (**5**), were isolated from an unidentified fungus which was initially separated from the marine sponge *Jaspis* aff. *johnstoni* and then cultured on marine media. 2D NMR experiments, synthetic transformations, and X-ray crystallography were used to establish the structures of the new compounds.

## Introduction

It is remarkable that the exploration of marine derived heterotrophic microorganisms for natural products is still in its infancy.[1,2] We have initiated a program to explore fungi from chemically prolific marine invertebrates, especially sponges, as a source of new marine natural products. Literature precedents for this idea are modest[3] as just a few new compounds, ranging from polyketides to alkaloids, have been isolated from various cultured microorganisms obtained from the surface of macroorganisms.[4] We now report three novel chlorinated terpenoids which were isolated from an unidentified fungus taken from the Indo-Pacific sponge *Jaspis* aff. *johnstoni*. Chloriolin A (**1**), a degraded bicyclic sesquiterpene, is accompanied by the new sesquiterpenes chloriolin B (**2**) and chloriolin C (**3**). The previously reported tricyclic sesquiterpenes coriolin B (**4**)[5] and dihydrocoriolin C (**5**),[6] reported from the terrestrial wood rotting fungus *Coriolus consors* were also present in the cultures.




## Results and Discussion

We obtained what has been tentatively identified as the same unidentified fungus from different collections of *Jaspis* aff. *johnstoni*. The initial culture was grown on solid media made from cellulose and yeast extract dissolved in Monterey Bay sea water. Next, a plug of the agar containing a white fluffy mycelium was transferred to a liquid medium of malt extract again made up in sea water. In these liquid broths the fungi grew as beautiful 2.5–5.0 cm diameter white-tan mycelial spheres possessing thin hair-like projections. Separate workup of the mycelium (MeOH extraction) and broth (EtOAc extraction) was invaluable as the crude oils obtained from each contained different constituents. The NMR spectra of these respective crude oils were dissimilar and each displayed both high and low field resonances that were different than those expected from jasplakinolide, the major metabolite of the sponge *Jaspis* aff. *johnstoni*.[7]

The oil obtained from the mycelium was investigated first and the purification consisted of solvent partitioning and then normal phase HPLC. This yielded two major components which were identified as coriolin B (**4**)[5] and dihydrocoriolin C (**5**),[6] and these two sesquiterpenes were previously isolated from fermentation of the Basidi-

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**Table 1. NMR Assignments for Chloriolin A and Comparative Assignments of Coriolin B**

| | coriolin B (**4**) | chloriolin A (**1**) | | | |
|---|---|---|---|---|---|
| atom no. | $^1$H NMR[a] | $^1$H NMR[b] | $^{13}$C NMR[c] | $^1$H–$^1$H COSY | $^1$H–$^{13}$C COSY ($J$ = 9) |
| 1 | 5.3 (d, 8.3) | 3.15 (dd, 9.0, 4.5) | 78.9 (d) | H2 | |
| 2 | 2.40 (dd, 8.4, 12.0) | 2.43 (dd, 12.0, 9.0) | 60.5 (d) | H1, H9 | C1, C7, C8, C12 |
| 3 | – | – | 61.8 (s) | | |
| 4 | – | – | 202.5 (s) | | |
| 5 | 4.40 (d, 1.8) | not present[d] | not present[d] | | |
| 6 | 3.55 (d, 1.8) | 4.10 (dd, 14.0, 3.2) | 58.8 (t) | H8 | |
| 6′ | – | 3.94 (dd, 14.0, 6.6) | | | |
| 7 | – | – | 147.0 (s) | | |
| 8 | 3.99 (d, 6.4) | 5.5 (bs) | 130.3 (d) | H6, H6′, H9 | C3, C10 |
| 9 | 2.92 (m) | 3.05 (m) | 41.8 (d) | H8, H10, H10′ | |
| 10 | 1.93 (t, 12.4) | 1.72 (dd, 9.6, 12.7) | 41.7 (t) | H9 | C1, C9, C14 |
| 10′ | 1.48 (dd, 12.4, 8.3) | 1.10 (dd, 7.2, 12.7) | | H9 | |
| 11 | – | – | 42.3 (s) | | |
| 12 | 1.08 (s) | 1.42 (s) | 24.1 (q) | | |
| 13 | 2.59 (d, 4.8) | 4.65 (d, 16.0) | 49.9 (t) | | C4 |
| 13′ | 2.46 (d, 4.8) | 4.52 (d, 16.0) | | | |
| 14 | 0.98 (s)[e] | 0.82 (s) | 20.4 (q) | | |
| 15 | 1.04 (s)[e] | 0.87 (s) | 26.2 (q) | | |
| 1-OH | | 3.72 (d, 4.5) | – | | |
| 6-OH | | 3.35 (t, 5.4) | – | | |

[a] $CDCl_3$. [b] Dioxane-$d_8$, 500 MHz. [c] Dioxane-$d_8$, 125 MHz. [d] Nucleus 5 was excluded to match the numbering scheme of **4**. [e] May be switched.

omycetes *Coriolus consors*. The broth-derived oil was next examined and afforded three new compounds which all showed mass spectral ion clusters indicative of a chlorine atom. Consequently, the names we have coined for these new compounds are chloriolin A (**1**), chloriolin B (**2**), and chloriolin C (**3**).

The $^1$H NMR data (Table 1) we observed for the mycelium product, coriolin B (**4**), provided an important reference point for the elucidation of the structure of **1**. All the resonances of a mutually coupled spin system consisting of H1–H2–H9–H10/10′–H8 present in **4** could also be located in the $^1$H NMR spectrum of **1** (Table 1). This allowed the assignment of a bicyclic [3.3.0] ring. A partial formula, $C_{14}H_{19}$, established from APT and $^1$H–$^{13}$C COSY NMR spectra of **1** agreed with the intense HRFABMS $[M + H]^+ = 273.1254$ corresponding to a molecular formula of $C_{14}H_{21}O_3Cl$. The remaining two unsaturations consisted of a trisubstituted double bond ($\delta$ 147.0, s, C7; 130.3, d, C8) and a ketone carbonyl ($\delta$ 202.5, s, C4). Three sets of $^1$H NMR spectra were eventually examined because changing solvents from $CDCl_3$ to benzene-$d_6$ to dioxane-$d_8$ yielded separate resonances for the low field diastereotopic protons of C6 and C13. The dioxane-$d_8$ spectrum also revealed the vicinal couplings to the two OH groups of C1 and C6. Proper attachment of the bicyclic ring substituents consisting of a quaternary methyl ($\delta$ 1.42), *gem*-dimethyls ($\delta$ 0.82, 0.87), hydroxymethylene, and chloracetyl was guided by 2D NMR correlations contained in the $^1$H–$^1$H COSY and HMBC spectra (Table 1) and they are summarized in Figure 1. The NOE difference and NOESY $^1$H NMR correlations observed between the various methine, methylene, and methyl protons, as outlined in Figure 1, supported the relative stereochemistry shown for **1**.

Additional evidence to justify the proposed structure and to gain insight about the absolute stereochemistry of chloriolin A (**1**) was sought. The results of chemical transformations were consistent with the overall structure. These included respectively a mixture of diastereomeric chloro triols **6a** (64%) and **6b** (36%) obtained by $NaBH_4$ reduction of **1** and the chloro diacetate **7** provided by straightforward acetylation of **1**. Crystals suitable for X-ray diffraction analysis were eventually deposited by

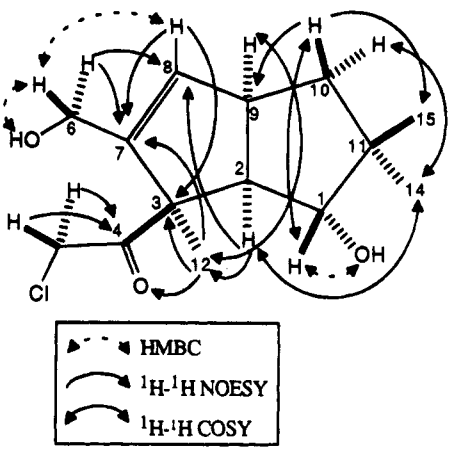


**Figure 1.** Important 2-D NMR correlations for chloriolin A (**1**).

slow evaporation of a methanol solution of **1**. These crystals were orthorhombic, $a = 7.943(5)$, $b = 11.049(12)$, $c = 16.440(12)$ Å and belong to space group $P2_12_12_1$. The structure was solved uneventfully by direct methods and refined to a final $R$-factor of 4.7%. The absolute structure parameter of 0.00 (4) (see supplementary material Tables 1–5) indicated that the absolute configuration shown—the same as in coriolin B (**4**)[5c] at C1, C2, and C9—is correct and Figure 2 provides a computer-generated perspective drawing of the final X-ray model. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Attention was turned next to establishing the structures of **2** and **3**. Side-by-side comparison of the $^1$H NMR data showed that all three chloriolins had the same spin system, H1–H2–H9–H10/10′–H8. The HRFABMS $[M + H]^+$ peak at 459.2164 of chloriolin B (**2**) indicated a molecular formula of $C_{23}H_{36}O_7Cl$ while the HRFABMS peak at 443.2192 $[M + H]^+$ of chloriolin C (**3**) gave a molecular formula of $C_{23}H_{36}O_6Cl$. Due to the greater availability of chloriolin B (**2**) the structures of both chloriolin B and C were solved by analysis of the

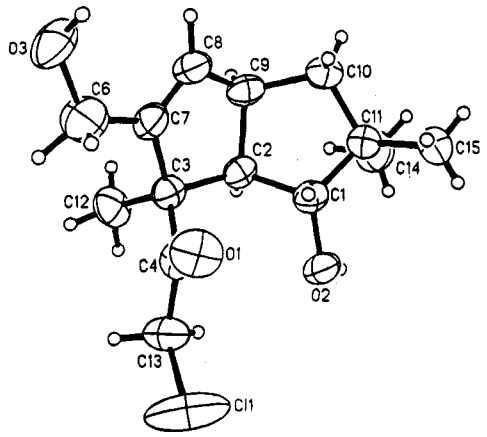


**Figure 2.** A computer-generated perspective drawing of the final X-ray model of 1. The absolute configuration was determined by anomalous scattering from the chlorine.

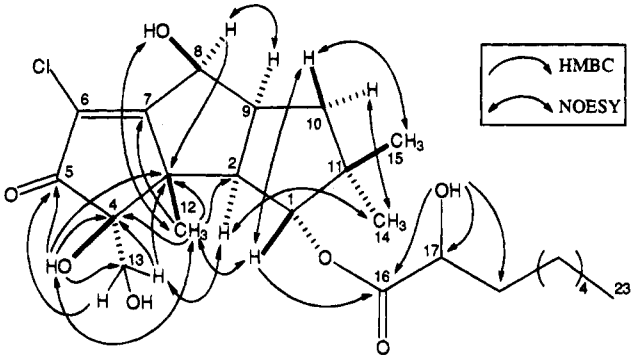


**Figure 3.** Important HMBC and NOESY correlations for chloriolin B (**2**).

chloriolin B spectral data. Five of the six unsaturations of **2** were accounted for by the B and C rings, an ester carbonyl (C16, $\delta$ 175.1), a tetrasubstituted double bond (C6, $\delta$ 124.3; C7, $\delta$ 183.4), and a ketone (C5, $\delta$ 204.3). That the octanyl ester was attached at C1 was apparent from the relatively low field shift of H1 ($\delta$ 5.18) plus the various HMBC correlations shown in Figure 3. The remaining unsaturation was ascribed to the presence of ring A fused to ring B analogous to that in coriolin B (**4**). Determining the substitution pattern of ring A required $^1$H NMR spectral (dioxane-$d_8$) data wherein the coupling to OH protons could be seen. The important anchor points were the $^1$H resonances of Me12 ($\delta$ 1.24), the AB spin system of H13/13′ ($\delta$ 3.39, 3.53), the OH at C4 ($\delta$ 4.60), and the OH at C8 ($\delta$ 4.55). The HMBC correlations from C4 ($\delta$ 86.4), C3 ($\delta$ 54.1), and C2 ($\delta$ 48.2) (Figure 3) to Me12 showed that this methyl must be attached to C3. In addition HMBC correlations involving both Me12 and H13/13′ defined the C3−C4 connectivity as shown in Figure 3. Likewise the correlations from Me12 to C3 and C7 defined the C3−C7 connectivity. That both an OH and a $CH_2OH$ must be attached to C4 was supported by HMBC correlations from the $\delta$ 4.60 OH to C13 ($\delta$ 66.3) and to C4, from the $\delta$ 3.72 OH to C13, plus the correlation from H13 to C4. An additional correlation from the OH at C4 to C5 revealed that the ketone was adjacent to C4. Finally, the chlorine was assigned to the only remaining atom C6. It was apparent from $^1$H, $^{13}$C, and $^1$H−$^1$H COSY NMR data and mass spectral data that chloriolin B (**2**) and C (**3**) differed from one another only by the presence of a hydroxyl group on the octanyl ester.

NOESY data obtained in dioxane-$d_8$ were used to assign the relative stereochemistry of chloriolin B (**2**). The configurations of the B and C rings were found to be identical to that of coriolin B (**4**) (Figure 3). The Me12 was determined to be on the same face as H1 from the NOESY correlations from H1 ($\delta$ 5.18) and the OH at C8 to Me12. The stereochemistry at C4 was set by a correlation from Me12 to the OH at C4. An important correlation between H2 ($\delta$ 3.02) and H13′ established the juxtaposition of these atoms. A parallel stereochemistry was envisioned for chloriolins B and C because their $^{13}$C and $^1$H spectra were quite similar. It is noteworthy that the stereochemistry of Me12 in **2** and **3** is the same as that found in coriolin B (**4**); however, it is the opposite of that found in chloriolin A (**1**). Also, the stereochemistry of the C4 substituents is the same in **2**−**4**.

Terrestrial fungi are a source of diverse, important bioactive compounds but the same is not yet true for their marine counterparts. The investigation of marine fungal chemistry is not well developed—a recent review[1a] summarized all of the structures (eleven families) known from marine fungi on just one page! Chloriolins A−C (**1**−**3**) are among the first chlorinated natural products[8] derived from a heterotrophic marine microorganism.[9] Our isolation of terrestrial fungal products **4** and **5**, accompanied by **1**−**3**, suggests that some marine fungi follow the broad outlines of terrestrial fungal biosynthesis but can add some unanticipated twists: extrusion of the C5 in the coriolin skeleton, introduction of a Cl atom, and reversal of the normal coriolin C3 methyl group stereochemistry. The α-chloro ketone functionality in **1** is the reactive trigger in compounds designed to act either as irreversible inhibitors, affinity labels, or suicide substrates of proteases.[10] It is possible that **1** is excreted for chemoprotection; however, the reactive functionality present does not confer activity for chloriolin A (NSC 666209) at 10 μg/mL in the NCI's disease-oriented screening program. In addition, neither chloriolin B (NSC 666210) nor dihydrochloriolin C (NSC 666211) were active in the NCI screen, but coriolin B (NSC 662467) was potent against two human tumor cell lines as it exhibited $IC_{50}$ values of 0.7 μM (T-47D, breast) and 0.5 μM (SNB-75, CNS).

## Experimental Section

The NMR spectra were recorded at 250 or 500 MHz for $^1$H and 62.9 and 125.7 MHz for $^{13}$C. The assignments of the $^{13}$C and $^1$H NMR data reported for compounds **1** and **2** were made by using HMQC[11,12] data to determine one bond H−C connectivities, HMBC[12] data to determine two and three bond H−C connectivities, and NOESY[13] data to interrelate protons with close spatial proximity. Unequivocal $^{13}$C NMR assignments were published by Tanabe[6] for **5** and our $^1$H−$^1$H COSY data was used to decipher its $^1$H resonances. The $^{13}$C NMR assignments for compound **4** were based in part on $^1$H−$^{13}$C

(8) A small number of chlorinated compounds are known from terrestrial fungi: For a recent compilation see Table 4 of: Gribble, G. W. *J. Nat. Prod.* **1992**, *55*, 1353.

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COSY data. The NMR assignments for **3**, **6**, and **7** were derived by analogy to those of similar protons and carbons of **2**, **4**, and **5**. Low and high resolution fast atom bombardment experiments were performed on a reverse geometry mass spectrometer or an extended geometry four sector mass spectrometer, respectively. High performance liquid chromatography (HPLC) was done using columns of 10 $\mu$m silica gel. All solvents were distilled and dried for HPLC use and were spectral grade for NMR spectroscopy.

**Collection and Identification.** A small piece of *Jaspis* aff. *johnstoni* sponge was aseptically removed underwater (at −20 m) from a large colony and placed in a sterile whirl pack bag. At the surface the sealed bag was opened under sterile conditions and a small portion of the sponge was placed on solid media made from 1 g of yeast extract (DIFCO), 10 g of α-cellulose (SIGMA), and 15 g of agar (DIFCO) in 1 L of filtered (0.2 $\mu$m) Monterey Bay sea water spiked with 100 mg/L each of streptomycin and penicillin G. A plug of the agar containing mycelium (no. 92902) was transferred to a liquid media of 15 g/L of malt extract (DIFCO) dissolved in filtered Monterey Bay sea water. The culture broths (75 mL in a 125 mL Erlenmeyer flask) were placed at 25 °C on a gyro-rotary shaker at 180 rpm. These 75 mL broths were used to start three larger 500 mL malt extract broths in 1 L Erlenmeyer flasks. These cultures were subsequently grown for approximately 21 days at 27 °C in a gyro-rotary shaker at 120 rpm and then transferred to another set of three 500 mL broths. This was repeated three more times to yield 56 g of mycelium from 4.5 L of malt extract broth.

Attempts to obtain fruiting bodies from this fungus have been unsuccessful. Prof. J. Kohlmeyer (U. of North Carolina) has kindly provided the following information about our voucher culture. The fungus is composed of a nondescript mycelium which fragments into short segments that may be arthrospores. It may be in the form-class hyphomycete in the form-subdivision Deuteromycotina.

**Extraction and Isolation.** The mycelium and broth were separated by filtration and each was extracted independently. A representative extraction for each workup is as follows. The broth (4.5 L) was extracted three times with EtOAc. The EtOAc was evaporated to yield 775 mg of yellow oil which was further partitioned between 10% aqueous MeOH and hexanes. The aqueous soluble portion was partitioned between $CH_2Cl_2$ and 50/50 MeOH/$H_2O$. The $CH_2Cl_2$ portion (714 mg) was applied to a silica gel flash column eluted with hexanes/EtOAc (the solvent was varied from 2:1 hexanes:EtOAc to 1:2 hexanes: EtOAc). One of the flash fractions was further purified by normal phase HPLC (hexanes:EtOAc 3:7) to yield chloriolin A (**1**) (18.0 mg). Other flash fractions were also purified by HPLC (hexanes:EtOAc 1:1) to yield chloriolin B (**2**) (16.0 mg) and chloriolin C (**3**) (3.0 mg).

The mycelium (56 g) was extracted three times (24 h each time) with methanol. The methanol was evaporated and the resulting gum was partitioned in an analogous manner to the EtOAc extract to yield a $CH_2Cl_2$ fraction of 227 mg which was applied to a Sephadex-LH20 column eluted with methanol. The Sephadex fractions with unusual NMR shifts were purified further with reverse phase HPLC (eluted with 20% aqueous methanol) to yield coriolin B (**4**) (17.0 mg) and dihydrocoriolin C (**5**) (16.5 mg).

**Chloriolin A (1)**: white orthorhombic crystals (18.0 mg); $[\alpha] = -35.0°$ (*c*, 0.01, $CHCl_3$); IR (film) 1737, 1447, 1368, 1250, 1022 $cm^{-1}$; LRFABMS, positive ion, *m/z* (relative intensity) 273 ($[M + H]^+$, 18), 255 (65), 221 (11), 152 (42), 119 (100); HRFABMS 273.1254 $[M + H]^+ = C_{14}H_{22}O_3Cl$ (Δ0.3 mmu of calcd); NMR data are presented in Table 1.

**Preparation of Chloro Triols (6a and 6b).** Chloriolin A (2 mg, in DMSO-$d_6$) was placed in a small flask which was cooled to freezing and $NaBH_4$ was added. The solution was allowed to warm to 21 °C while stirring for 1 h and then it was transferred to an NMR tube. When the signals for H13 and H13′ had merged into one signal by $^1H$ NMR the reaction was quenched with ice. The EtOAc layer was washed twice with $H_2O$ and dried over $Na_2SO_4$ to yield **6a** and **6b** in a 64:36 ratio, respectively. Compounds **6a** and **6b** were a mixture with relative ratios based on the areas of doublets ($J$ = 2 Hz) for H4 ($CDCl_3$, 500 MHz) at δ 3.88 (**6a**) and δ 3.86 (**6b**): colorless oil; LRFABMS, positive *m/z* 275 $[M + H]^+$; $^1H$ NMR data of **6a** (500 MHz, benzene-$d_6$) δ 5.20 (bs, H8), 4.04 (dd, $J$ = 9.0 and 2.0 Hz, H13), 3.94 (d, $J$ = 9.0 Hz, H13′), 3.88 (d, $J$ = 2.0 Hz, H4), 3.80 (d, $J$ = 9.0 Hz, H1), 3.72 (d, $J$ = 10.0 Hz, $H_26$), 2.70 (m, H9), 2.30 (dd, $J$ = 12.0 and 9.0 Hz, H2), 1.58 (dd, $J$ = 12.0 and 7.0 Hz, H10), 1.05 (dd, $J$ = 12.0 and 7.0 Hz, H10′), 0.94 (s, $CH_312$), 0.92 (s, $CH_314$), 0.83 (s, $CH_315$); $^1H$ NMR data of **6b** δ 5.20 (bs, H8), 4.04 (dd, $J$ = 9.0 and 2.0 Hz, H13), 4.00 (d, $J$ = 9.0 Hz, H13′), 3.86 (d, $J$ = 2.0 Hz, H4), 3.80 (d, $J$ = 9.0 Hz, H1), 3.63 (d, $J$ = 10.0 Hz, $H_26$), 2.70 (m, H9), 2.30 (dd, $J$ = 12.0 and 9.0 Hz, H2), 1.58 (dd, $J$ = 12.0 and 7.0 Hz, H10), 1.05 (dd, $J$ = 12.0 and 7.0 Hz, H10′), 0.94 (s, $CH_312$), 0.92 (s, $CH_314$), 0.83 (s, $CH_315$).

**Preparation of Chloriolin A Diacetate (7).** Chloriolin A (2 mg) was dissolved in pyridine and acetic anhydride and allowed to stir for 16 h. The product was a colorless oil: LRFABMS: *m/z* (relative intensity %) 357 $[M + H]^+$ (24), 297 (100), 255 (15), 238 (63); $^1H$ NMR (250 MHz, $CDCl_3$) δ 5.70 (bs, H8), 4.70 (bs, $H_26$), 4.60 (d, $J$ = 9.0 Hz, H1), 4.47 (d, $J$ = 9.0, $H_213$), 3.25 (m, H9), 2.70 (dd, $J$ = 12 and 9 Hz, H2), 2.04 (s, $H_3$-acyl), 2.03 (s, $H_3$-acyl), 1.80 (dd, $J$ = 12 and 7 Hz, H10), 1.50 (s, $H_312$), 1.40 (dd, $J$ = 12 and 7 Hz, H10′), 0.96 (s, $H_314$), 0.90 (s, $H_315$).

**Chloriolin B (2)**: white solid (16.0 mg); $[\alpha] = +31.5°$ (*c* = 0.005, MeOH); UV (MeOH) $\lambda_{max}$ 235, 252 nm; IR (film) 2965, 1741, 1373, 1250 $cm^{-1}$; LRFABMS, positive ion, *m/z* (relative intensity) 459 $[M + H]^+$ (23), 299 (47), 281 (100); HRFABMS 459.2164 $[M + H]^+ = C_{23}H_{36}O_7Cl$ (Δ −1.4 mmu of calcd); $^1H$ NMR (250 MHz, dioxane-$d_8$) δ 5.18 (d, $J$ = 9.5 Hz, H1), 4.63 (dd, $J$ = 10.0, 2.5 Hz, H8), 4.60 (s, OH4), 4.55 (d, $J$ = 2.5 Hz, OH8), 4.05 (m, H17), 4.00 (d, $J$ = 6.5 Hz, OH17), 3.72 (t, $J$ = 5.5 Hz, OH13), 3.53 (dd, $J$ = 5.5, 11.5 Hz, H13), 3.39 (dd, $J$ = 5.5, 11.5 Hz, H13′), 3.02 (dd, $J$ = 9.5, 11.5 Hz, H2), 2.81 (m, H9), 2.09 (dd, $J$ = 9.5, 13 Hz, H10), 1.71 (m, H18), 1.60 (m, H18′), 1.40 (dd, $J$ = 9.5, 13 Hz, H10′), 1.29 (m, $H_219$, $H_220$, $H_221$, $H_222$), 1.24 (s, Me12), 1.02 (s, Me14), 0.95 (s, Me15), 0.88 (t, $J$ = 6.7 Hz, Me23); $^1H$ NMR (250 MHz, $CD_3OD$) δ 5.20 (d, $J$ = 9.5 Hz, H1), 4.69 (d, $J$ = 6.0 Hz, H8), 4.17 (dd, $J$ = 4.5, 7.5 Hz, H17), 3.62 (d, $J$ = 10.5 Hz, H13), 3.46 (d, $J$ = 10.5 Hz, H13′), 3.06 (dd, $J$ = 9.5, 11.5 Hz, H2), 2.89 (m, H9), 2.08 (dd, $J$ = 12.5 Hz, 9.5 Hz, H10), 1.78 (m, H18), 1.67 (m, H18′), 1.50 (dd, $J$ = 9.5, 12.5 Hz, H10′), 1.45 (m, $H_222$), 1.33 (br, m, $H_219$, $H_220$, $H_221$), 1.28 (s, Me12), 1.05 (s, Me14, Me15), 0.90 (t, $J$ = 7.0 Hz, Me23); $^{13}C$ NMR (62.9 MHz, dioxane-$d_8$) δ 204.3 (C5), 183.4 (C7), 175.1 (C16), 124.3 (C6), 86.4 (C4), 81.4 (C1), 71.0 (C17), 66.3 (C8, C13), 54.1 (C3), 48.2 (C2), 45.4 (C9, C11), 35.4 (C10, C18), 32.3 (C21), 29.7 (C20), 27.1 (C14), 25.6 (C19), 23.2 (C12, C22), 22.4 (C15), 14.3 (C23); $^{13}C$ NMR (62.9 MHz, $CD_3OD$) δ 205.6 (C5), 184.3 (C7), 175.8 (C16), 125.3 (C6), 87.2 (C4), 82.6 (C1), 71.7 (C17), 67.2 (C8), 67.1 (C13), 54.9 (C3), 48.9 (C2), 46.3 (C9), 45.9 (C11), 36.1 (C10), 35.4 (C18), 32.8 (C21), 30.0 (C20), 27.3 (C14), 26.0 (C19), 24.0 (C12), 23.5 (C22), 22.4 (C15), 14.3 (C23).

**Chloriolin C (3)**: white solid (3.0 mg); $[\alpha] = +27.5°$ (*c* = 0.002, MeOH); white solid; UV (MeOH) $\lambda_{max}$ 235, 253 nm; LRFABMS, positive ion, *m/z* (relative intensity) 443 $[M + H]^+$ (100), 299 (19), 281 (62); HRFABMS 443.2192 $[M + H]^+ = C_{23}H_{36}O_6Cl$ (Δ −0.8 mmu of calcd); $^1H$ NMR (250 MHz, $CDCl_3$) δ 4.90 (d, $J$ = 7.3 Hz, H1), 4.83 (d, $J$ = 7.6 Hz, H8), 3.57 (d, $J$ = 11.1 Hz, H13), 3.42 (d, $J$ = 11.1 Hz, H13′), 3.03 (m, H9), 2.69 (dd, $J$ = 7.6, 12.0 Hz, H2), 2.32 (dd, $J$ = 7.4, 8.0 Hz, H17,17′), 2.00 (dd, $J$ = 11.8, 12.5 Hz, H10), 1.61 (m, H18,18′), 1.53 (m, H10′), 1.45 (s, Me12), 1.28 (m, $H_219$, $H_220$, $H_221$, $H_222$), 1.11 (3H, s), 1.05 (3H, s), 0.88 (t, $J$ = 6.9, Me23); $^1H$ NMR (250 MHz, dioxane-$d_8$) δ 5.13 (d, $J$ = 9.5 Hz, H1), 4.63 (dd, $J$ = 3.1, 6.0 Hz, H8), 4.62 (s, OH4), 4.54 (d, $J$ = 2.7 Hz, OH8), 3.82 (bs, OH13), 3.68 (m, H13), 3.43 (dd, $J$ = 4.9, 9.9 Hz, H13′), 3.00 (dd, $J$ = 9.6, 11.4 Hz, H2), 2.83 (m, H9), 2.28 (t, $J$ = 7.4, $H_217$), 2.09 (dd, $J$ = 9.5, 12.5 Hz, H10), 1.6 (m, $H_218$), 1.41 (dd, $J$ = 9.6, 12.5 Hz, H10′), 1.29 (m, $H_219$, $H_220$, $H_221$, $H_222$), 1.23 (s, Me12), 1.01 (s, Me14), 0.98 (s, Me15), 0.89 (t, $J$ = 6.9 Hz, Me23); $^{13}C$ NMR (62.9 MHz, $CDCl_3$) δ 202.1 (C5), 181.2 (C7), 174.8 (C16), 124.4 (C6), 85.1 (C4), 81.9 (C1), 66.7 (C8), 65.9 (C13), 54.5 (C3), 48.8 (C2), 45.9 (C9), 45.1 (C11), 36.6

(C10), 34.6 (C17), 31.7 (C21), 29.2 (C20), 28.9 (C19), 26.9 (C14), 25.1 (C18), 23.6 (C12), 22.6 (C22), 22.1 (C15), 14.1 (C23).

**Coriolin B (4)**: white solid; mp 198–202 °C; $[\alpha] = +105.2°$ ($c = 0.003$, $CH_2Cl_2$) with $^1H$ NMR properties in accord with the literature[5b,14] and $^{13}C$ NMR (62.9 MHz, $CDCl_3$) $\delta$ 172.0 (C16), 80.0 (C1), 76.1 (C7), 70.6 (C5), 70.3 (C8), 65.7 (C4), 63.1 (C6), 50.7 (C2), 45.8 (C3), 44.2 (C13), 43.8 (C11), 41.8 (C9), 35.9 (C10), 34.6 (C17), 31.7 (C21), 29.7 (C19), 29.2 (C20), 26.6 (C15), 25.2 (C18), 22.6 (C22), 21.6 (C14), 14.1 (C23), 13.7 (C12).

**Dihydrocoriolin C (5)**: white solid; mp 152–155 °C; $[\alpha] = +49.8°$ ($c = 0.003$, $CH_3OH$) with $^{13}C$ NMR properties in accord with the literature[6] and $^1H$ NMR (250 MHz, $CDCl_3$) 5.19 (d, $J = 8.4$ Hz, H1), 4.38 (d, $J = 1.4$ Hz, H5), 4.12 (dd, $J = 6.8$, 4.2 Hz, H17), 3.98 (d, $J = 6.3$ Hz, H8), 3.54 (d, $J = 1.4$ Hz, H6), 2.92 (m, H9), 2.57 (d, $J = 4.7$ Hz, H13) 2.44 (dd, $J = 12.1$, 8.5 Hz, H2), 2.40 (d, $J = 4.6$ Hz, H13'), 1.96 (t, $J = 12.2$ Hz, H10), 1.80 (m, H18), 1.64 (m, H18') 1.49 (dd, $J = 13.1$, 8.5 Hz, H10') 1.28 (s, 6H), 1.06 (s, 3H) 1.04 (s, 3H), 0.98 (s, 3H) 0.87 (t, Me23).

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**Supplementary Material Available:** Figures S1a, S1b, S2–14 and Tables 1–5 (19 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.