Cytotoxic Diacetylenes from the Stony Coral *Montipora* Species

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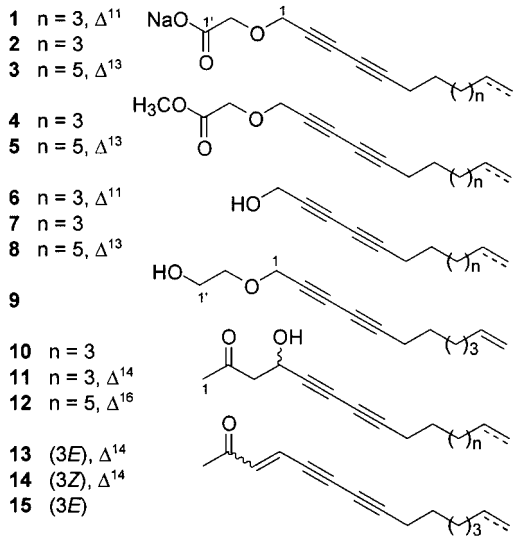
Ten new (**1**, **4**−**6**, **9**−**14**) and four known (**2**, **3**, **7**, **8**) diacetylenes have been isolated from a brine shrimp active fraction of the methanolic extract of the stony coral *Montipora* sp. The structures were determined by combined spectroscopic methods. The compounds exhibited significant cytotoxicity against a small panel of human solid tumor cell lines. Montiporyne A (**15**), a previously reported congener, was also found to induce apoptosis in human colon tumor cell.

Stony corals have yielded interesting bioactive natural products even though they have been investigated for their secondary metabolites infrequently. Their known metabolites include alkaloids,[1−4] a sesterterpene,[3] anthraquinoids,[5] macrolides,[6] and acetylenic compounds.[7] The genus *Montipora* is especially rich in acetylenic compounds that have been shown to possess antifungal, antibacterial, ichthyotoxic, and cytotoxic properties.[7] Diacetylenes isolated from the eggs of *M. digitata* were responsible for the chemotactic activity of the sperm during the mass spawning.[7d]

In our continuing search for cytotoxic metabolites from *Montipora* sp., we have further isolated a series of diacetylenes from a brine shrimp active fraction of the methanolic extract of this coral. These acetylenes are either 2,4-diacetylenes or 5,7-diacetylenes and thus share a common biogenetic precursor with those reported earlier from stony corals.[7]



Results and Discussion

Montiporic acid C (**1**) was isolated as light yellow amorphous solid. In the ^{1}H NMR spectrum, a doublet of doublets of triplets at δ 5.79 and two doublets of doublets at δ 4.98 and 4.93 were due to a monosubstituted olefin. Two singlets corresponding to two protons each at δ 4.35 and 4.00 were assigned to H-1 and H-2′, respectively. The α-acetylenic methylene protons resonated as a triplet at δ 2.28, and the signal at δ 2.04 was attributed to allylic protons. The quintet at δ 1.52 was assigned to the H-7 protons. These data showed that **1** is a montiporic acid analogue.[7b] A strong band in the IR spectrum at 1606 cm^{-1} revealed it to be a carboxylate salt. The structure was confirmed by FABMS, which showed the $[M + Na]^+$ ion peak at *m/z* 279. The molecular formula was established as $C_{14}H_{17}O_3Na$ on the basis of FABMS and NMR data. Thus compound **1** was characterized as sodium 2-*O*-(11-dodecene-2,4-diynyl)-2-hydroxy ethanoate. Both the ^{1}H NMR (Table 1) and ^{13}C NMR assignments (Table 3) were in accordance with the reported data for similar types of compounds.[7b]

Montiporic acid C (**1**) displayed two distinct HPLC peaks, a sharp peak with shorter retention time and a broad peak with longer retention time. However, both of them showed the same ^{1}H NMR spectral pattern as well as the same molecular ion in the FABMS. These peaks were collected separately, but on re-injection in HPLC each peak showed the same two distinct peaks. This behavior has also been reported earlier[8] and the different peaks were ascertained to be the monovalent and divalent cations of the same compound. In our case, however, as we could observe only the sodium adduct ion in the FABMS, we assumed that the different HPLC peaks were free acid and sodium salt of the same compound. When the sample was treated with $NaHSO_4$ prior to HPLC the broad peak with longer retention time increased drastically in intensity.

Compound **2** was isolated as a white amorphous powder. Its ^{1}H NMR spectrum was similar to that of montiporic acid C (**1**) except for the presence of a terminal methyl (δ 0.90) instead of a terminal olefin. The NMR data of **2** (see Experimental Section) were comparable to montiporic acid A reported earlier from *M. digitata* as the free acid.[7b] FABMS gave the $[M + Na]^+$ ion at *m/z* 281, which, in combination with the NMR data supported the molecular formula $C_{14}H_{19}O_3Na$. This confirmed the structure of compound **2** as a sodium salt of montiporic acid A.

Compound **3** was a colorless oil. Its ^{1}H NMR spectrum displayed the same signals as those observed for montiporic acid C (**1**). FABMS indicated the $[M + Na]^+$ ion at *m/z* 307, and thus a molecular formula $C_{16}H_{21}O_3Na$ could be deduced for **3**. The structure was determined as a sodium salt of montiporic acid B previously reported from *M. digitata* as the free acid.[7b]

Methyl montiporate A (**4**) was isolated as a yellow oil. The molecular formula was established as $C_{15}H_{22}O_3$ on the

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Table 1. ^{1}H NMR Data of **1**, **4**−**6**, and **9** (CD_3OD)[a]

position	**1**[b]	**4**[c]	**5**[c]	**6**[b]	**9**[c]
1	4.35 (s)	4.33 (s)	4.33 (s)	4.19 (s)	4.23 (s)
6	2.28 (t, 6.6)	2.29 (t, 7.0)	2.29 (t, 7.0)	2.28 (t, 6.8)	2.29 (t, 7.0)
7	1.52 (quint, 7.0)	1.51 (quint, 7.5)	1.52 (quint, 7.3)	1.51 (quint, 6.8)	1.52 (quint, 7.0)
8	1.28−1.36 (m)	1.39 (quint, 7.5)	1.39 (quint, 7.0)	1.31−1.40 (m)	1.27−1.42 (m)
9	1.28−1.36 (m)	1.25−1.35 (m)	1.28−1.33 (m)	1.31−1.40 (m)	1.27−1.42 (m)
10	2.04 (quart, 6.6)	1.25−1.35 (m)	1.28−1.33 (m)	2.05 (quart, 6.8)	2.05 (quart, 7.0)
11	5.79 (ddt, 17.0, 10.2, 7.0)	1.25−1.35 (m)	1.28−1.33 (m)	5.79 (ddt, 17.0, 10.2, 6.8)	5.80 (ddt, 17.0, 10.5, 6.5)
12	4.98 (dd, 17.0, 1.5) 4.93 (dd, 10.2, 1.5)	0.90 (t, 7.0)	2.04 (quart, 7.0)	5.03 (dd, 17.0, 1.5) 4.95 (dd, 10.2, 1.5)	4.98 (dd, 17.0, 1.5) 4.91 (dd, 10.5, 1.5)
13			5.80 (ddt, 17.0, 10.0, 6.8)		
14			4.98 (dd, 17.0, 2.0) 4.91 (dd, 10.0, 2.0)		
1′					3.66 (t, 5.0)
2′	4.00 (s)	4.17 (s)	4.17 (s)		3.57 (t, 5.0)
OCH_3		3.74 (s)	3.73 (s)		

[a] Multiplicities and coupling constants (in Hz) are in parentheses. [b] Measured at 200 MHz. [c] Measured at 500 MHz.

Table 2. ^{1}H NMR Data of Compounds **10**−**14** (CD_3OD)[a]

position	**10**[b]	**11**[c]	**12**[c]	**13**[b]	**14**[b]
1	2.16 (s)	2.18 (s)	2.16 (s)	2.26 (s)	2.38 (s)
3	2.86 (dd, 16.5, 8.0) 2.78 (dd, 16.5, 5.5)	2.85 (dd, 16.6, 7.8) 2.78 (dd, 16.6, 5.4)	2.85 (dd, 16.6, 7.8) 2.78 (dd, 16.6, 5.4)	6.56 (d, 16.0)	6.46 (d, 12.0)
4	4.78 (dd, 8.0, 5.5)	4.77 (dd, 7.8, 5.4)	4.77 (dd, 7.8, 5.4)	6.72 (dt, 16.0, 1.0)	6.28 (dt, 12.0, 1.0)
9	2.28 (t, 7.5)	2.29 (t, 7.3)	2.28 (t, 6.8)	2.39 (t, 6.3)	2.41 (t, 7.3)
10	1.52 (quint, 7.5)	1.52 (quint, 7.0)	1.52 (quint, 7.0)	1.56 (quint, 7.3)	1.56 (quint, 7.0)
11−12	1.25−1.40 (m)	1.25−1.40 (m)	1.25−1.40 (m)	1.28−1.42 (m)	1.28−1.42 (m)
13	1.25−1.40 (m)	2.05 (quart, 6.5)	1.25−1.40 (m)	2.07 (quart, 7.0)	2.07 (quart, 7.0)
14	1.25−1.40 (m)	5.80 (ddt, 17.0, 10.2, 6.3)	1.25−1.40 (m)	5.80 (ddt, 17.0, 10.0, 6.8)	5.80 (ddt, 17.0, 10.0, 6.8)
15	0.90 (t, 7.0)	5.04 (dd, 17.0, 1.5) 4.95 (dd, 10.2, 1.5)	2.05 (quart, 7.3)	5.04 (dd, 17.0, 2.0) 4.95 (dd, 10.0, 2.0)	5.04 (dd, 17.0, 2.0) 4.95 (dd, 10.0, 2.0)
16			5.80 (ddt, 17.0, 10.2, 6.3)		
17			5.00 (dd, 17.0, 1.5) 4.93 (dd, 10.2, 1.5)		

[a] Multiplicities and coupling constants (in Hz) are in parentheses. [b] Measured at 500 MHz. [c] Measured at 200 MHz.

Table 3. ^{13}C NMR Data of Compounds **1**, **4**, **6**, **9**, and **10** (50 MHz, CD_3OD)[a]

position	**1**	**4**	**6**	**9**	**10**
1	58.9	59.6	51.0	59.5	30.5
2	72.1[b]	71.6[b]	70.4[b]	72.0[b]	207.8
3	72.7[b]	72.8[b]	75.3[b]	72.8[b]	51.7
4	65.4[b]	65.2[b]	65.6[b]	65.4[b]	59.0
5	81.6[b]	82.5[b]	81.4[b]	81.8[b]	70.1[b]
6	19.7	19.7	19.7	19.7	76.9[b]
7	29.2−29.5	29.3−29.8	29.2−29.4	29.2−29.5	65.3[b]
8	29.2−29.5	29.3−29.8	29.2−29.4	29.2−29.5	82.2[b]
9	29.2−29.5	29.3−29.8	29.2−29.4	29.2−29.5	19.7
10	34.7	32.8	34.7	34.7	29.3−29.8
11	139.9	23.6	139.9	139.9	29.3−29.8
12	115.0	14.4	114.9	114.9	29.3−29.8
13					32.9
14					23.6
15					14.4
1′	177.3	172.2		62.0	
2′	72.1	67.2		72.5	
OCH_3		52.3			

[a] Compound **6** was measured at 125 MHz. [b] Assignments with the same superscript in the same column may be interchanged.

basis of FABMS and NMR data. The NMR data of **4** was characterized by two isolated oxygenated methylenes (δ_H 4.33, 4.17, δ_C 67.2, 59.6), a methoxy (δ_H 3.74, δ_C 52.3), two acetylenic units (δ 82.5, 72.8, 71.6, 65.2), and a carbonyl carbon (δ 172.2). In the FABMS the $[M + Na]^+$ ion was detected at *m*/*z* 273. Concomitant isolation of montiporic acids is a sufficient reason to believe that **4** is an ester of montiporic acid A and not an ether type, as was reported earlier.[7c] Thus the structure of compound **4** was determined to be methyl 2-*O*-(dodecane-2,4-diynyl)-2-hydroxy ethanoate.

Methyl montiporate B (**5**) was also a light yellow oil. The ^{1}H NMR spectrum of **5** was similar to that of **4**, except for the presence of signals for the terminal olefinic protons. FABMS of compound **5** showed the $[M + Na]^+$ ion at *m*/*z* 299, and the molecular formula was deduced as $C_{17}H_{24}O_3$ with the help of NMR data. The structure was determined to be methyl 2-*O*-(13-tetradecene-2,4-diynyl)-2-hydroxy ethanoate. The artifact nature of **4** and **5** could not be excluded; however, montiporic acids did not produce methyl montiporates on long standing in methanol.

Montiporyne G (**6**) was a light yellow oil. The ^{1}H NMR data showed characteristic signals for a monosubstituted olefin (δ 5.79, 5.03, 4.95), an isolated oxygenated methylene (δ 4.19), and an α-acetylenic methylene (δ 2.28). Its ^{13}C NMR indicated the presence of a diacetylenic unit (δ 81.4, 75.3, 70.4, 65.6). A peak at δ_C 51.0 was assigned to C-1, and C-6 appeared at δ 19.7. FABMS of compound **6** showed a protonated molecular ion $[M + Na]^+$ at *m*/*z* 199, and by taking into consideration the NMR data, the molecular formula was ascertained to be $C_{12}H_{16}O$. Thus the structure was postulated as 11-dodecene-2,4-diyn-1-ol.

Compound **7** was also isolated as a light yellow oil. The spectral data indicated its structure as the 11,12-dihydro analogue of **6**. The molecular formula was deduced as $C_{12}H_{18}O$ from FABMS, which showed the $[M + Na]^+$ ion at *m*/*z* 201 and NMR data. The structure of **7** was identified as dodecane-2,4-diyn-1-ol, which was previously described from the eggs of *M. digitata*.[7d]

Compound **8**, a colorless oil, showed an ^{1}H NMR spectrum nearly identical to that of **6**. FABMS gave the $[M + Na]^+$ ion at *m*/*z* 227, which, in combination with the NMR

data, corresponded to the molecular formula $C_{14}H_{20}O$. So the structure was characterized as 13-tetradecene-2,4-diyn-1-ol, previously reported from *Montipora* sp. and *Pectinia lactuca*.[7c]

Montiporyne H (**9**) was isolated as a yellow oil. The NMR data were characteristic of a 2,4-diynyl-1-ol gross structure. The H-1 protons appeared as a singlet at δ 4.23, and a pair of triplets at δ 3.66 and 3.57, which were correlated to each other in the COSY, were due to two adjacent methylenes. In the HMQC spectrum the protons at δ 3.66 were correlated to a carbon at δ 62.0, and those at δ 3.57 were coupled to a carbon at δ 72.5. These carbons were assigned to C-2′ and C-1′, respectively. C-1 appeared at δ 59.5, and the rest of the data were similar to that of compound **8**. FABMS showed the $[M + Na]^+$ ion at *m*/*z* 243, and the molecular formula was deduced as $C_{14}H_{20}O_2$. The structure was determined to be 2-*O*-(11-dodecene-2,4-diynyl)-1,2-ethandiol.

Montiporyne I (**10**) was a pale yellow oil. The NMR data showed a diacetylene gross structure for this compound (δ_H 2.28, δ_C 82.2, 76.9, 70.1, 65.3). The singlet of two protons in the range of δ 4.3, which was characteristic of the oxygenated methylene in the earlier described compounds, was missing and instead a doublet of doublets (J = 5.5, 8.0 Hz) was observed at δ 4.78, indicating an extension of the carbon chain. Another set of doublets of doublets at δ 2.86 (J = 8.0, 16.5 Hz) and 2.78 (J = 5.5, 16.5 Hz) was also exhibited in the ^{1}H NMR spectrum of **10**. On the basis of their coupling constants they were assigned to H-4 and H-3, respectively. A triplet of three protons (δ_H 0.90, δ_C 14.4) confirmed a free alkyl terminal, and a singlet of three protons at δ 2.16 was due to an α-carbonyl methyl which resonated in the ^{13}C NMR at δ 30.5. The FABMS of compound **10** gave the $[M + Na]^+$ ion *m*/*z* 257, which in combination with NMR data confirmed the molecular formula as $C_{15}H_{22}O_2$. Compound **10** was thus characterized as 4-hydroxypentadecane-5,7-diyn-2-one.

Montiporyne J (**11**) was isolated as a light yellow oil. Its ^{1}H NMR spectrum was nearly identical to that of compound **10** except for the presence of a monosubstituted olefin (δ 5.80, 5.04, 4.95) and the respective allylic methylene protons signal (δ 2.05). The $[M + Na]^+$ ion at *m*/*z* 255 in the FABMS confirmed that it is a dehydrogenated isomer of **10**.

Montiporyne K (**12**) was a pale yellow oil. Its ^{1}H NMR spectrum was very similar to that of **11**, and it showed an $[M + Na]^+$ ion at *m*/*z* 283 in the FABMS. These data helped to deduce the molecular formula as $C_{17}H_{24}O_2$, and the structure was characterized as 4-hydroxy-16-heptadecene-5,7-diyn-2-one.

Compounds **10**−**12** showed a high chemical lability and underwent dehydration even in mild acidic conditions. None of these compounds showed any measurable degree of optical rotation, indicating that they were present as racemate in nature. Attempts to obtain the MTPA ester derivatives of compounds **11** and **12** yielded the dehydro analogues as the major product and a mixture of diastereoisomers of MTPA esters, further supporting that these compounds were racemic mixtures.

Montiporyne L (**13**) exhibited signals for a trans disubstituted olefin (δ 6.72, 6.56, J = 16.0 Hz), a monosubstituted olefin (δ 5.80, 5.04, 4.95), and a singlet methyl (δ 2.26). Thus **13** was a dehydro analogue of **11** with a trans geometry of the double bond. A long-range coupling between H-9 and H-4 was observed as the latter resonated as doublet of triplets at δ 6.72 (J = 16.0, 1.0 Hz), while H-3 appeared a little upfield as a doublet at δ 6.56 (J = 16.0 Hz). A triplet at δ 2.39 was assigned to H-9, and a quartet at δ 2.07 was due to H-13. The FABMS showed the $[M + H]^+$ ion at *m*/*z* 215, and thus the molecular formula was deduced as $C_{15}H_{18}O$. The structure of compound **13** was determined to be (3*E*)-3,14-pentadecadiene-5,7-diyn-2-one.

Table 4. Cytotoxicities (ED_{50}, μg/mL) of Compounds **1**−**14** against Human Solid Tumor Cells[a]

compound	A549	SK-OV-3	SK-MEL-2	XF498	HCT15
1	>30	>30	>30	>30	>30
2	6.31	7.50	7.97	7.72	8.30
3	6.26	4.88	4.68	4.96	4.47
4	>30	20.52	>30	>30	25.61
5	>30	>30	>30	>30	>30
6	13.78	9.79	9.56	10.78	12.93
7	5.48	4.63	4.45	5.59	5.90
8	3.90	3.23	3.94	5.26	3.32
9	22.73	17.94	25.08	16.88	24.05
10	4.17	1.81	1.40	3.70	3.73
11	4.97	3.85	3.74	3.87	3.42
12	4.91	3.34	3.52	4.45	4.18
13	6.39	3.52	4.21	5.50	4.56
14	>30	5.23	4.61	29.16	11.30
doxorubicin	0.02	0.13	0.03	0.08	0.04
cisplatin	0.75	1.09	2.18	1.18	0.85

[a] A549: human lung cancer; SK-OV-3: human ovarian cancer; SK-MEL-2: human skin cancer; XF498: human CNS cancer; HCT15: human colon cancer.

Montiporyne M (**14**) was a yellow oil and showed the same protonated molecular ion at *m*/*z* 215 with the same fragmentation pattern as that of **13**. Its ^{1}H NMR spectral pattern was also similar to that of **12** (Table 2). However, the disubstituted olefinic signals at δ 6.46 and 6.28 exhibited a coupling constant of 12.0 Hz, indicating a cis double bond. So compound **14** was characterized as (3*Z*)-3,14-pentadecadiene-5,7-diyn-2-one. Although compound **11** was reasonably stable under the experimental conditions, the possibility that compounds **13** and **14** may be the dehydrated artifacts of **11** cannot be excluded.

As in the case of compound **13**, a long-range coupling between H-9 and H-4 was observed for **14**. However, in contrast to compound **13**, H-4 resonated as a doublet of triplets at δ 6.28 (J = 12.0, 1.0 Hz), while H-3 was a little downfield as a doublet at δ 6.46 (J = 12.0 Hz) in **14**. This behavior could be attributed to the different anisotropic effect of the carbonyl group in compound **13** versus **14**. By analogy, the assignments of the H-3 and H-4 should be reversed in the previously reported montiporyne B and montiporyne D.[7a] The ^{1}H NMR showed that compound **13** always contained a small amount of **14** as a minor component and vice versa. They were separable into single components but equilibrated on standing. The trans isomer prevailed over the cis by the ratio of 6:1. Similar behavior was also observed in the case of montiporyne C and montiporyne D in our earlier report.[7a]

Compounds **1**−**9** appear to share a common biosynthetic precursor with a 2,4-diyne moiety. Compounds **10**−**14** are similar to **1**−**9** in having a diyne group, but the position is different. 2,4-Diynes are encountered more frequently in corals, and this may raise a question of the origin of **10**−**14**. Addition of acetone to an aldehyde form of **6**−**8** would give **10**−**14** by crossed aldol condensation. However, we did not observe aldehyde derivatives in our ^{1}H NMR survey of the fractions obtained by the flash chromatography of the crude extract.

The isolated compounds have been tested for cytotoxicity against a small panel of human cancer cell lines (Table 4), and most of them were found to be cytotoxic. Compound

10 showed significant cytotoxicity against human skin cancer and human ovarian cancer cell lines. In general, diacetylenes with the β-hydroxy ketone functionality (**10**−**12**) were found to be more active. The trans isomer (**13**) was more active than the cis isomer (**14**), as in the case of montiporyne A−D.[7a] Cytotoxicity of montiporyne A (**15**), an analogue of **13**, which showed significant activity against human solid tumor cell lines in our previous study,[7a] was also evaluated for cell cycle inhibition using flow cytometry. Montiporyne A showed significant cell cycle inhibition in the HCT116 cell. The apoptotic fraction was increased by 19% when the cell was treated with **15** at a concentration of 100 μg/mL for 24 h.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. UV spectra were obtained using a UV-2401 PC Shimadzu spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC200, Varian Unity Plus 300, and Varian INOVA 500 spectrometers. Chemical shifts were reported in reference to the respective residual solvent peaks (δ_H 3.3 and δ_C 49.0 for CD_3OD). HMQC spectra were recorded on a Varian INOVA 500 spectrometer, and LRFABMS data were obtained using a JEOL JMS-HX110/110A. HPLC was performed on a Gilson 370 pump with a YMC ODS-H80 (250 × 10 mm i.d., S-4 μm, 80 Å) column using a Shodex RI-71 detector.

Animal Material. The animals were collected by hand using scuba at a depth of 8 m in November 1996, along the shore of Mundo, Cheju Island, Korea, and were described in a previous report.[7a] A voucher specimen was deposited in the Natural History Museum, Ewha Womans University (voucher no. EWUA. Ant. 961104).

Isolation of Compounds. The frozen coral (2.5 kg, wet wt) was extracted with MeOH at room temperature. Guided by the brine shrimp lethality assay,[9] the MeOH extract was partitioned between H_2O and EtOAc. The EtOAc layer was further partitioned between H_2O and $CHCl_3$ to afford 8.8 g of the $CHCl_3$ layer (LD_{50} 30−86 μg/mL), which was subjected to a reversed-phase MPLC (YMC Gel ODS-A, 60 Å 500/400 mesh) eluting with a step gradient solvent system of 25 → 0% H_2O/MeOH to obtain 14 fractions (1−14). Fraction 2 (0.3 g) was very active in the brine shrimp assay and was further purified by repeated HPLC (YMC ODS-H80, 250 × 10 mm i.d., S-4 μm, 80 Å) using 60% MeOH/H_2O as the solvent system to give compound **1** (15.0 mg). Fraction 3 (3.1 g) was also very active in the brine shrimp test and was further separated into 26 fractions on a reversed-phase MPLC (YMC Gel ODS-A, 60 Å, 500/400 mesh), eluting with a step gradient solvent system of 20 → 0% H_2O/MeOH. The subfraction 3-9 was repeatedly chromatographed on HPLC (YMC ODS-H80, 250 × 10 mm i.d., S-4 μm, 80 Å) eluting with 75% MeOH/H_2O to yield compounds **2** (120 mg), **6** (5 mg), and **11** (15 mg). Compound **9** (1.6 mg) was purified from the subfraction 3-10 using 80% MeOH/H_2O on the same column. Using the same conditions compound **10** (5.7 mg) was isolated from subfraction 3-11. Compound **10** was also present in substantial amount in subfractions 3-12 and 3-13. Compound **7** (11 mg) was purified from subfraction 3-14 on the same column with 85% MeOH/H_2O and was also detected in subfractions 3-15 and 3-16. Subfraction 3-18 yielded compounds **8** (7.4 mg) and **12** (14 mg, also present in subfraction 3-17) when eluted with 90% MeOH/H_2O on the same column. Compound **3** (10.8 mg) was isolated from subfraction 3-19 under the same conditions. Fraction 4 (3.11 g), which showed significant brine shrimp lethality (LD_{50} 0.1 μg/mL), was also subjected to a reversed-phase MPLC (YMC Gel ODS-A, 60 Å, 500/400 mesh) eluting with a solvent system of 33 → 0% H_2O/MeOH to yield eight fractions. Subfractions 4-3−4-6 were combined (4′) and again subjected to reversed-phase MPLC (YMC Gel ODS-A, 60 Å, 500/400 mesh) eluting with a solvent system of 20 → 5% H_2O/MeOH to yield six fractions. Fraction 6 (4′-6, 135 mg), which was eluted with 5% H_2O/MeOH, was further purified by repeated reversed-phase HPLC (YMC ODS-H80, 250 × 10 mm i.d., S-4 μm, 80 Å) eluting with 14% H_2O/MeOH and 33% and 20% H_2O/MeCN to yield compounds **4** (5.0 mg), **5** (1.0 mg), **13** (1.0 mg), and **14** (1.0 mg). Percent yields for the isolated compounds were not calculated because not all of the fractions were exhaustively processed.

Montiporic acid C (1): light yellow amorphous solid; IR (film) ν_{max} 2929, 2856, 2254, 1606, 1427, 1362, 1334, 1097, 908; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 3; LRFABMS *m/z* 279 $[M + Na]^+$ (100), 238 (0.2), 224 (0.2), 209 (0.7), 196 $[C_8H_6O_3Na + Na]^+$ (1), 119 $[C_2H_2O_3Na + Na]^+$ (1), 104 $[C_2H_2O_2Na + Na]^+$ (1), 90 $[CO_2Na + Na]^+$ (4), 46 (2), 23 (3).

Compound 2: white amorphous powder; UV (MeOH) λ_{max} (ϵ) 257 (899), 272 (475); ^{1}H NMR (CD_3OD, 500 MHz) δ 4.35 (s, H-1), 4.00 (s, H-2′), 2.29 (t, J = 6.8 Hz), 1.52 (quint, J = 6.8 Hz), 1.28−1.40 (m, H-8-H-11), 0.90 (t, J = 6.8 Hz); ^{13}C NMR (CD_3OD, 50 MHz) δ 177.3 (C-1′), 82.3, 72.7, 71.9, 65.2 (C-2-C-5), 69.7 (C-2′), 59.1 (C-1), 32.9 (C-10), 29.3−29.9 (C-7-C-9), 23.7 (C-11), 19.7 (C-6), 14.4 (C-12); LRFABMS *m/z* 281 $[M + Na]^+$ (100), 366 (0.1), 252 (0.1), 238 (0.1), 223 (0.1), 209 (1.2), 196 $[C_8H_6O_3Na + Na]^+$ (1.3), 119 $[C_2H_2O_3Na + Na]^+$ (1), 104 $[C_2H_2O_2Na + Na]^+$ (1.3), 90 $[CO_2Na + Na]^+$ (4), 46 (1.8), 23 (2.2).

Compound 3: colorless oil; ^{1}H NMR (CD_3OD, 500 MHz) δ 5.80 (ddt, J = 17.1, 9.0, 7.0 Hz, H-13), 4.99 (dd, J = 17.1, 1.5 Hz, H-14), 4.92 (dd, J = 9.0, 1.5 Hz, H-14), 4.33 (s, H-1), 4.11 (s, H-2′), 2.29 (t, J = 7.0 Hz, H-6), 2.03 (quart, J = 6.8 Hz, H-12), 1.51 (quint, J = 7.0 Hz, H-7), 1.31−1.38 (m, H-8-H-11); LRFABMS *m/z* 307 $[M + Na]^+$ (100), 238 (0.2), 224 (0.2), 209 (0.7), 196 $[C_8H_6O_3Na + Na]^+$ (1), 119 $[C_2H_2O_3Na + Na]^+$ (1), 104 $[C_2H_2O_2Na + Na]^+$ (1), 90 $[CO_2Na + Na]^+$ (4), 46 (2), 23 (3).

Methyl montiporate A (4): yellow oil; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 3; LRFABMS *m/z* 273 $[M + Na]^+$.

Methyl montiporate B (5): yellow oil; ^{1}H NMR, see Table 1; LRFABMS *m/z* 299 $[M + Na]^+$.

Montiporyne G (6): light yellow oil; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 3; LRFABMS *m/z* 199 $[M + Na]^+$.

Compound 7: light yellow oil; ^{1}H NMR, δ 4.20 (s, H-1), 2.28 (t, J = 6.8 Hz), 1.51 (quint, J = 6.8 Hz), 1.25−1.35 (m, H-8−H-11), 0.90 (t, 6.8 Hz); ^{13}C NMR, 81.4, 75.3, 70.4, 65.6 (C-2-C-5), 51.0 (C-1), 32.9 (C-10), 29.8−29.4 (C-7-C-9), 23.6 (C-11), 19.6 (C-6), 14.4 (C-12); LRFABMS *m/z* 201 $[M + Na]^+$.

Compound 8: colorless oil; ^{1}H NMR, δ 5.77 (ddt, J = 17.1, 10.2, 6, 8, H-13), 5.02 (dd, J = 17.1, 1.5, H-14), 4.92 (dd, J = 10.2, 1.5, H-14), (4.19, s, H-1), 2.28 (t, J = 6.8, H-6), 2.06 (quart, J = 6.8, H-12), 1.50 (quint, J = 6.8, H-7), 1.25−1.35 (m, H-8−H-11); LRFABMS *m/z* 227 $[M + Na]^+$.

Montiporyne H (9): yellow oil; ^{1}H NMR, see Table 1; ^{13}C NMR, see Table 2; ^{13}C NMR, see Table 3; LRFABMS *m/z* 243 $[M + Na]^+$.

Montiporyne I (10): light yellow oil; UV (MeOH) λ_{max} (ϵ) 256 (691), 291 (1116), 308 (1068); ^{1}H NMR, see Table 2; ^{13}C NMR, see Table 3; LRFABMS *m/z* 257 $[M + Na]^+$.

Montiporyne J (11): light yellow oil; ^{1}H NMR, see Table 2; LRFABMS *m/z* 255 $[M + Na]^+$.

Montiporyne K (12): light yellow oil; UV (MeOH) λ_{max} (ϵ) 256 (479), 293 (1134), 309 (1145); ^{1}H NMR, see Table 2; LRFABMS *m/z* 283 $[M + Na]^+$.

Montiporyne L (13): light yellow oil; ^{1}H NMR, see Table 2; LRFABMS *m/z* 215 $[M + H]^+$.

Montiporyne M (14): light yellow oil; ^{1}H NMR, see Table 2; LRFABMS *m/z* 215 $[M + H]^+$.

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