Full Papers

Myriaporones 1−4, Cytotoxic Metabolites from the Mediterranean Bryozoan *Myriapora truncata*[⊥]

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Four novel polyketide-derived metabolites, myriaporones 1, 2, 3, and 4, have been isolated from the Mediterranean bryozoan *Myriapora truncata*. Their structures and stereochemistry have been assigned from the analysis of spectroscopic data. The inseparable equilibrium mixture of myriaporones 3 and 4 showed 88% inhibition of L1210 murine leukemia cells at 0.2 μg/mL.

Bryozoans are a group of primitive colonial animals widely distributed throughout the world's marine and freshwater environments.[1a] Chemical research on their biologically active metabolites, however, has been limited.[1] Among those metabolites isolated from marine bryozoans, bryostatins[2] from *Bugula neritina* are the most exciting and promising compounds and exhibit pronounced cytotoxic activity as well as immunomodulation or protein kinase C activation.

During our systematic screening for pharmaceutically interesting compounds from Mediterranean Sea marine organisms,[3] we found by shipboard bioassay that an extract of the bryozoan *Myriapora truncata*[4] showed potent cytotoxicity against L1210 murine leukemia cells. A subsequent methanol extract in the laboratory gave 99% inhibition of L1210 cells at 50 μg/mL. Fractionation and purification of active components guided by the cytotoxicity assay resulted in the isolation of a novel, highly cytotoxic polyketide-derived metabolite, myriaporone 3 (**3**), and its isomer myriaporone 4 (**4**), along with two relatively less active compounds, myriaporones 1 (**1**) and 2 (**2**).[5] The inseparable equilibrium mixture of **3** and **4** showed 88% inhibition against L1210 cells at 0.2 μg/mL. The present report deals with the structure determination and stereochemistry of these metabolites.

Results and Discussion

The IR spectrum of **1** showed absorptions at 3580, 1747, 1709, and 1228 cm^{-1} attributable to hydroxyl, ester, and ketone functional groups. FABMS gave an $[M + H]^+$ ion at *m*/*z* 397 and several dehydrated and/or deacetylated fragment ions at *m*/*z* 355, 337, and 319. HRCIMS data suggested the molecular formula $C_{21}H_{32}O_7$ for **1**. The ^{1}H NMR spectrum in $CDCl_3$ (Table 1) indicated 32 proton signals, among which two (δ_H 2.63, d, 5.5 Hz and 3.63, d, 5.5 Hz) were exchangeable hydroxyl protons. The ^{13}CNMR spectrum (Table 1) showed the required 21 carbons, including two ketone carbonyls, one ester carbonyl, four olefinic carbons, five methyls, three sp^3 methylenes, five sp^3 methines, and one quaternary carbon.

Four separate partial structures, A−D (Figure 1), accounting for 15 carbons and 26 protons of **1** were readily identified by COSY and HMQC data taken in $CDCl_3$. A *cis* double bond in partial structure A was deduced from the proton−proton coupling constant (J = 10 Hz) and the upfield chemical shift of the vinyl methyl (C-15, δ_C 13.34).[6] In the COSY spectrum a methine proton at δ_H 3.75 (H-8) was found to couple with the oxygenated methylene protons at δ_H 4.32 and 4.06 (H_2-17) and an oxygenated methine proton at δ_H 3.53 (H-9), respectively (partial structure B). In partial structure C, two slightly coupled olefinic protons at δ_H 6.23 and 6.28 were assigned to terminal double-bond protons, which showed cross-peaks in the COSY spectrum with the oxygenated methine proton H-5 (δ_H 4.97). The latter proton was coupled with the methylene at δ_H 2.52 and 2.88 (H_2-4). Two hydroxyl groups were located at C-9 and C-5 on the basis of the coupling of hydroxyl protons with H-9 and H-5, respectively, observed in the COSY spectrum.

The deshielded singlet methyl at δ_H 1.99 (δ_C 20.72) in combination with the ester carbonyl (δ_C 170.34, IR 1747, 1228 cm^{-1}) indicated the presence of an acetyl group, and two ketone carbonyls (δ_C 211.61 and 202.39), a singlet methyl (δ_H 1.34, δ_C 12.08), and an oxygenated quaternary carbon (δ_C 62.76) were found for a total of $C_{21}H_{32}O_9$. Thus, two oxygens are redundant.

In the HMBC spectrum, cross-peaks from the singlet methyl at δ_H 1.34 to the quaternary carbon at δ_C 62.81 (C-10) and long-range couplings from H-9 to the same quaternary carbon and C-11 (δ_C 66.24) in partial structure A were observed (Figure 2). Accordingly, the two partial structures A and B could be linked through the C-10 quaternary carbon with an attached methyl. An epoxide was assigned at C-10 and C-11 on the basis of their upfield ^{13}C and/or ^{1}H chemical shifts (Table 1) and by the need to eliminate a redundant oxygen atom. An acetoxy group was readily recognized at C-17 from deshielded H_2-17 proton resonances and HMBC correlations for H-17a and H-17b to the ester carbon. Similarly, partial structures B and C were connected via a carbonyl group at δ_C 202.39, which was correlated to protons H-8 (δ_H 3.75) and H_2-17 in partial structure B and terminal olefin protons H_2-16 (δ_H 6.23 and 6.28) in partial structure C. Although only a terminal ethyl group (D) was found to be correlated with the remaining saturated keto carbonyl (δ_C 211.61) in the HMBC spectrum, the bond connection between C-4 and C-3 is the only possible completion of the structure assignment (Figure 2). The chemical shifts and coupling patterns of H_2-4 (δ_H 2.52 and 2.88) are compatible with ketone α-protons and the structure assigned as shown in **1** (Figure 2). From a biogenetic point of view, it is noteworthy that the structure assigned for **1** is similar to the side chain part of tedanolide

[⊥] Dedicated to the late Dr. Kenneth L. Rinehart of the University of Illinois at Urbana−Champaign for his pioneering work on bioactive natural products.

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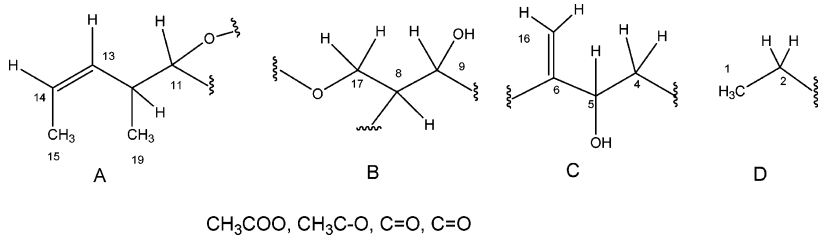


Figure 1. Partial structures for myriaporone 1 from COSY and HMQC data.

Table 1. ^{1}H and ^{13}C NMR Data For Myriaporones 1 and 2

	myriaporone 1				myriaporone 2		
atom #	$CDCl_3$		CD_3OD		CD_3OD		CD_3CN
1	7.45 CH_3	1.05 t, 7.0	7.86	1.02 t, 7.5	7.93	1.02 t, 7.0	0.96 t, 7.5
2	36.57 CH_2	2.44. m	37.17	2.50 m	37.39	2.50 m	2.44 m
3	211.61 C		211.83		212.67		
4	47.94 CH_2	2.52 dd, 18.0, 9.0 2.88 dd, 17.5, 3.0	50.33	2.44 dd, 16.0, 9.5 2.65 dd, 16.0, 3.0	49.61	2.70 dd, 16.5, 9.5 3.05 dd, 16.5, 2.5	2.52 dd, 16.0, 9.0 2.97 dd, 16.5, 2.5
5	66.31 CH	4.97 m	66.71	5.02 dd, 3.0, 9.5	67.71	4.71 dd, 10.5, 1.0	4.60 brm
6	150.46 C		153.88		146.69		
7	202.39 C		202.91		109.48		
8	46.73 CH	3.75 m	49.61	3.76 dt, 4.0, 10.0	51.11	2.76 q, 7.0	2.70 q, 7.0
9	75.78 CH	3.53 m	77.50	3.34 d, 10.0	71.90	4.21 d, 7.0	4.15 t, 7.0
10	62.81 C		64.15		89.39		
11	66.24 C	2.74 d, 9.5	67.55	2.64 d, 9.5	87.15	3.28 d, 10.0	3.27 d, 10.5
12	31.20 CH	2.42 m	32.34	2.50 m	35.18	2.50 m	2.44 m
13	129.98CH	5.23 dt, 1.5, 10.5, 10.5	131.54	5.27 dt, 2.0, 10.0, 10.0	132.54	5.18 dt, 1.5, 10.5, 10.5	5.16 dt, 2.0, 10.5, 10.5
14	125.04 CH	5.51 dq 10.5, 7.0	126.09	5.50 m	124.92	5.50 dq, 10.5, 7.0	5.48 dt, 7.0, 10.5
15	13.34 CH_3	1.62 d, 7.0	13.59	1.65 dd, 7.0, 1.5	13.33	1.66 dd, 2.0, 7.0	1.66 dd, 2.0, 7.0
16	126.93 CH_2	6.28 s 6.23 s	126.57	6.22 d, 1.5 6.28 s	113.13	5.41 d, 1.5 5.42 s	5.32 d, 1.0 5.34 s
17	63.07 CH_2	4.32 dd, 11.0, 4.5 4.06 t, 11.0	64.36	4.32 dd, 4.0, 11.0 3.88 t, 11.0	62.62	4.08 dd, 11.5, 7.5 3.84 dd, 11.5, 7.0	3.94 dd, 11.0, 7.0 3.75 dd, 11.0, 7.0
18	12.08 CH_3	1.34 s	11.65	1.38 s	11.45	1.40 s	1.33 s
19	18.60 CH_3	1.12 d, 6.5	18.81	1.10 d, 7.0	18.91	1.02 d, 6.5	0.98 d, 6.5
20	170.34 C		172.08		173.10		
21	20.72 CH_3	1.99 s	20.65	1.94 s	20.23	2.02 s	1.96 s
5-OH		3.63 d, 5.5	exchanged		exchanged		3.17 brs
9-OH		2.63 d, 5.5	exchanged		exchanged		3.12 d, 7.0

(**5**),[7a] a potently cytotoxic macrolide isolated from the Caribbean sponge *Tedania ignis*.

Compound **2**, originally isolated from an extract of the bryozoan, was also detected during NMR measurement of pure compound **1** in $CDCl_3$. Unlike **1**, compound **2** did not show any UV absorption above 210 nm. The IR absorptions at 3580, 1747, and 1233 cm^{-1} are similar to those of **1**, indicating the presence of similar hydroxyl, ester, and/or ketone functional groups. FABMS exhibited the same $[M + H]^+$ ion as myriaporone 1 (**1**) at *m*/*z* 397 as well as $[M + Na]^+$ (*m*/*z* 419) and $[M + K]^+$ (*m*/*z* 435) ions. The molecular formula $C_{21}H_{32}O_7$ was deduced for **2** by HRFABMS, the same as found for compound **1**.

The ^{1}HNMR spectrum of **2** was different from that of **1** in coupling constants and chemical shifts. The prominent shift differences were observed for protons around C-7, including those at C-8, C-9, C-11, and C-16 (Table 1). The carbon framework, however, was identified to be the same as that of **1**, on the basis of the analyses of coupling constants and COSY correlations. ^{13}C NMR data (Table 1) for these two compounds, on the other hand, showed substantial differences. The carbonyl group at δ_C 202.91(in CD_3OD) observed in **1** (C-7) was replaced by a ketal quaternary resonance at δ_C 109.48 in **2**. Moreover, the chemical shifts for C-10 and C-11 were found to be shifted dramatically downfield from δ_C 64.15 and 67.55 to δ_C 89.39 and 87.15, respectively, which are reasonably assigned to two oxygenated carbons but not an epoxide. These data argue that the epoxide ring opening occurred and the corresponding dihydroxy groups reacted with the C-10 carbonyl group to form a 2,7-dioxabicyclo[2.2.1]heptane skeleton. The HMBC spectrum indicated long-range $^{1}H-^{13}C$ coupling for the terminal double-bond protons (H_2-16) to the ketal carbon at δ_C 109.48, the unsaturated keto carbonyl position in **1**. Thus, the structure of myriaporone 2 was assigned as **2** (Figure 3). The intramolecular ring opening of γ,δ-epoxy or δ,ϵ-epoxy ketones catalyzed by acids or Lewis acids to form a dioxabicyclo skeleton is a frequently observed reaction in the literature.[8]

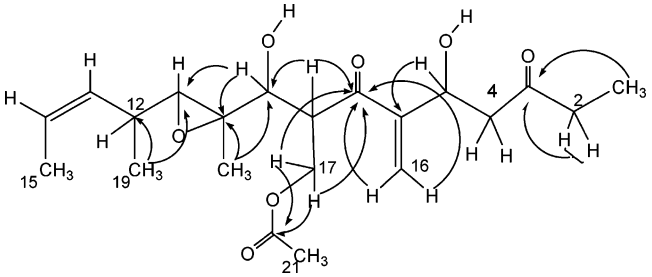
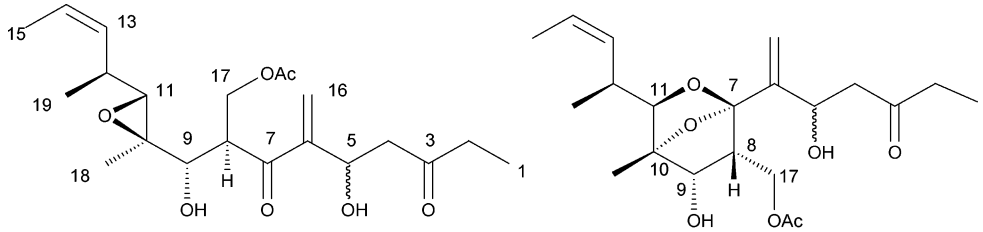


Figure 2. Selected long-range $^{1}H-^{13}C$ correlations for **1** revealed by HMBC.

The relative configuration for compounds **1** and **2** was primarily assigned on the basis of NOE experiments conducted with myriaporone 2 (**2**) and by comparison of their coupling constants with those of tedanolide (**5**).[7a] The proton coupling constant between H-8 and H-9 in **2** is 7 Hz, suggesting an *endo*−*endo cis* relationship for these two protons.[9,10] Further evidence supporting this assignment arose from the observation of NOE cross-peaks in the ROESY spectrum for H-9 to H-8, H-12, and H_3-15, which in turn located the *cis* olefin group (C-12−C-15) on the same *endo* face and the H-11 proton in the *exo* position. The relative configuration at C-11



1 **2**

Figure 3. Structures of myriaporones **1** and **2**.

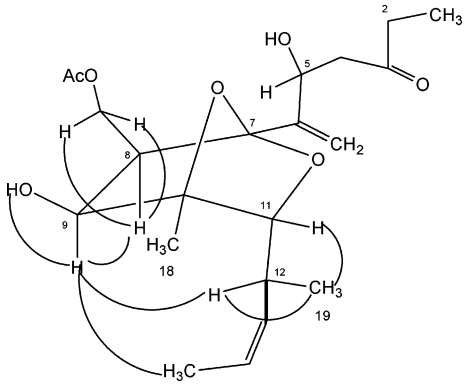


Figure 4. NOE observed for **2** by difference NOE and/or ROESY experiments.

and C-12 could be assigned as follows. The dihedral angle between H-12 and H-11 must be near 180° or 0° due to their relatively large coupling constant (10 Hz). Observation of NOE cross-peaks for protons H_3-19 to H-11 and H-12, and H_3-15 to H-9, justified the spatial proximity of H-12 to H-9 and H_3-19 to H-11. Thus, the relative configuration for H-11 and H-12 was assigned as anti-periplanar. The relative configuration for six contiguous chiral centers (C-7−C-12) in **2** was therefore assigned as 7*S**, 8*R**, 9*S**, 10*S**, 11*R**, and 12*S** (Figure 4). Intramolecular attack of a carbonyl oxygen at the γ,δ-epoxide would invert the configuration at the γ-position.[8] Accordingly, its cyclization precursor **1** should possess the 8*R**, 9*S**, 10*R**, 11*R**, 12*S** relative configurations (Figure 3). The configuration at C-5 in **1** and **2** could not be assigned by these NOE experiments.

Comparison of coupling constants of **1** and tedanolide (**5**) is pertinent for assignment of relative configuration due to the close similarity of these two compounds. As can be seen in Table 2, the coupling constants for protons on C-8 to C-15 in **1** are almost coincidental with those on C-16 to C-23 in **5**; the latter structure was confirmed by X-ray data. The relative configurations at C-8−C-15 were thus confirmed to be the same as in the tedanolide side chain,[7a] or, 8*R**, 9*S**, 10*R**, 11*R**, 12*S**. The absolute stereochemistry for myriaporones 1 and 2 was assigned as shown in **1** and **2** by the Mosher method.[11,12]

The most cytotoxic component of *M. truncata* was obtained as a mixture of two isomers in equilibrium. This fact and the limited quantity made their purification and characterization extremely challenging. The major isomer was the hemiketal, myriaporone 3 (**3**), and the minor isomer the hydroxy ketone (**4**) with the relative ratio 3:1 by ^{1}H NMR. Since these two compounds were inseparable under normal conditions, the structure determination was carried out with the mixture.

FABMS of the mixture of myriaporones 3 and 4 (**3** and **4**) did not give an $[M + H]^+$ peak but showed an $[M + \text{matrix}(154) + H]^+$ peak[13] at *m*/*z* 527, an $[M + K]^+$ peak at *m*/*z* 411, an $[M + Na]^+$ peak at *m*/*z* 395, and dehydrated fragment ion peaks at *m*/*z* 355, 337, 319, and 301. FABMS/CID/MS experiments on the peaks at *m*/*z* 411 and 395 confirmed the presence of K^+ and Na^+, respectively, in these two pseudomolecular ion peaks. Thus, the molecular weight of myriaporones 3 and 4 (mixture) was concluded to be 372 Da. HRFABMS established the common molecular composition of **3** and **4** as $C_{19}H_{32}O_7$.

The ^{1}H NMR spectrum of this mixture shared many common characteristics with myriaporone 1 (**1**), such as a terminal ethyl group, C-15, C-18, and C-19 methyls, and the C-13/C-14 *cis* double bond. A doublet for an epoxide methine proton (H-11, δ_H 2.61, d, 9.2 Hz) was also observed for **3** and **4**. On the other hand, terminal olefin and acetyl methyl protons in **1** and **2** were no longer present in the ^{1}H NMR spectrum of the mixture of **3** and **4**. The modifications with respect to myriaporone 1 (**1**) therefore involved C-17 and C-16. COSY and coupling constant analyses identified four separate spin networks for both **3** and **4**. Three of these were identical with partial structures A, B, and D of **1** (cf. Figure 1). The chemical shifts and coupling constants indicated the single remaining and unique partial structure (C′ for **3** and C″ for **4**) was a four-carbon unit (Figure 5).

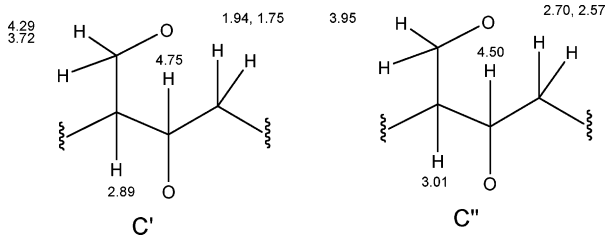


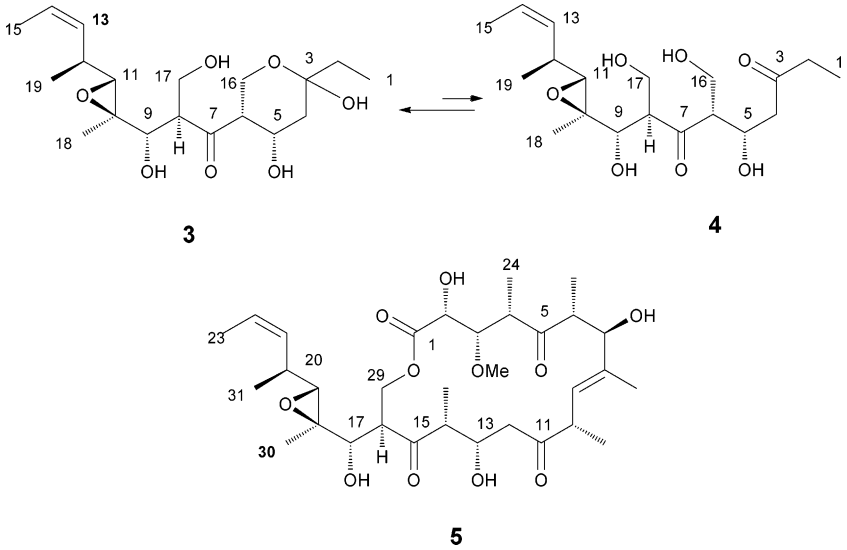
Figure 5. Partial structures of **3** (C′) and its equilibrium isomer **4** (C″).

It is apparent from comparison of the partial structures of **1** with those of **3** or **4** that the major difference was the replacement of the terminal C-16 double bond in **1** by a CH_2OR group in **3** and **4**. As with myriaporone 1 (**1**) and considering ^{1}H NMR and FABMS data, it is reasonable to postulate two carbonyls (C-3, C-7) and an oxygenated quaternary carbon (C-10) to connect the four fragments. Although the sample amount made it impossible to record a complete broadband decoupled ^{13}C NMR spectrum with good

Table 2. Comparison of Coupling Constants of **1** and **3** and the Side Chain of Tedanolide (**5**) (Hz)

compound	H8/9	H8/17	H11/12	H12/13	H13/14	H14/15	H13/15	H12/19
1	10.0	11.0	9.5	10.0	10.0	7.0	1.5	6.5
3	9.7	*a*	9.2	10.0	10.0	7.0	1.5	6.8
5[b]	9.5	11.6	9.4	10.8	10.8	7.4	1.7	6.7

[a] Unresolvable. [b]Refers to myriaporone numbering.



3 **4**

5

Figure 6. Structures of myriaporones 3 and 4 and tedanolide (**5**).

Table 3. ^{1}H and ^{13}C NMR Data for Myriaporones 3 and 4 (δ ppm, J Hz)

	myriaporone 3		myriaporone 4
position	δ_H, m, J	δ_C[a]	δ_H, m, J
1	0.91, t, 7.3	7.72	0.99, t, 7.3
2	1.57, q, 7.3	35.12	2.49, m
3		98.41[b]	
4	1.94, dd, 3.3, 14.0	38.65	2.57, m
	1.75, dd, 2.9, 14.0		2.70, dd, 2.9, 16.5
5	4.75, brm	65.83	4.50, m
6	2.89, m	56.08	3.01, brdd, 5.5, 12.0
7		*c*	
8	3.29, m	40.50	3.29, m
9	3.16, d, 9.7	78.08	3.16, d, 9.7
10		64.25[b]	
11	2.61, d, 9.2	67.87	2.61, d, 9.2
12	2.48, m	32.21	2.48, m
13	5.29, dd, 10.0, 10.0,	131.42	5.29, dd, 10.0, 10.0
14	5.54 , dq, 10.0, 7.0	125.61	5.54, dq, 7.0, 10.o
15	1.65, d, 7.0	13.32	1.65, d, 7.0
16	4.29, dd, 11.6, 11.6,	56.70	3.95, m
	3.72, dd, 3.9, 11.6		
17	3.64, m, 3.59, m	61.68	3.63, m
18	1.34, s	11.25	1.34, s
19	1.09, d, 6.8	18.51	1.09, d, 6.8

[a] By HMQC. [b]By ^{13}C NMR. [c]Not detected.

signal-to-noise ratio, two quaternary carbons at δ_C 98.41 and 64.25 were clearly observed and may be assigned as new hemiketal and oxygenated carbons, respectively. Again, HMQC and HMBC data were quite informative. Long-range correlations of the singlet methyl protons at δ_H 1.34 with C-9 (δ_C 78.08), C-11 (δ_C 67.87), and the quaternary carbon at δ_C 64.25 were observed in the HMBC spectrum, which indicated the presence of the C-8 to C-15 unit with an epoxide on C-10 and C-11. That the C-16 hydroxyl group and C-3 carbonyl were cyclized to form a six-membered hemiketal ring in compound **3** was evident from the upfield proton chemical shifts (Table 3) for H_3-1 (δ_H 0.91), H_2-2 (δ_H 1.57), and H_2-4 (δ_H 1.94 and 1.75) compared to those in compound **1**. The HMBC cross-peak for the terminal methyl group (H_3-1, δ_H 0.91) to the hemiketal carbon at δ_C 98.41 justified the above assignment. Finally, the chemical shifts of the methines at C-6 (δ_C 56.08, δ_H 2.89) and C-8 (δ_C 40.50, δ_C 3.29) suggested the presence of a carbonyl at C-7, which accounted for the one remaining carbon, oxygen, and degree of unsaturation.

For the minor component, the ^{1}H NMR spectrum of H-8 to H-15 and H-17 to H-19 overlapped that of **3** (Table 3). The differences between **3** and **4** were observed in partial structure C″ and a terminal ethyl group. The downfield chemical shifts for H-2 and H-4 in **4** suggested the presence of a C-3 carbonyl rather than a hemiketal group. A weak but clear long-range coupling for the terminal methyl proton (H_3-1′, δ_H 0.99) to the carbonyl at δ_C 212.69 was present in the HMBC spectrum. Thus the compound was assigned structure **4**.

The relative configuration from C-8 to C-12 in **3** and **4** was assigned to be the same as that of myriaporone 1 (**1**) or the tedanolide side chain on the basis of coupling constant comparisons (Table 2). Since H_2-16 in **3** resonated at δ_H 4.29 (J = 11.6, 11.6 Hz) and 3.72 (J = 11.6, 3.9 Hz), H-6 was assigned to be axial. Similarly, the coupling constants between H-4 and H-5 were 3.3 and 2.9 Hz, indicating that H-5 is equatorial. Thus, the relative stereochemistry for H-5 and H-6 in **3** was concluded to be *cis*.

In conclusion, purification and structural determination of four cytotoxic components from the Mediterranean bryozoan *Myriapora truncata* are described. On the basis of spectroscopic data as well as the comparison with tedanolide, myriaporones 1 and 2 were assigned to structures **1** and **2**. Except for the chiral center at C-5, relative and absolute configurations at all other chiral centers were established via NOE and Mosher ester methods. Due to the limited quantity and the equilibrium of myriaporones 3 and 4, the structure determination turned out to be extremely challenging. Structural determination including relative configurations were established through careful analysis of the spectra from the equilibrium mixture. All four structures, including the absolute stereochemistry, were confirmed recently by several groups by total chemical synthesis.[14]

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP 370 polarimeter with Na lamp using a 5 × 0.35 cm cell. UV spectra were taken on a Perkin-Elmer Lamda-3 spectrometer in CH_3OH. Infrared spectra (CCl_4) were taken on an IBM IR/32 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a GN 500 (500 MHz for ^{1}H) or UNITY 400 (400 MHz for ^{1}H) spectrometer in CD_3OD, CD_3CN, or $CDCl_3$ as indicated. The 3.30 ppm resonance of residual CD_2HOD and 49.0 ppm of CD_3OD were used as internal references for ^{1}H and ^{13}C NMR, respectively. Both fast atom bombardment (FABMS) and FABMS/CID/MS mass spectra were obtained on a VG 70SE-4F spectrometer using magic bullet as matrix.[13] Low- and high-resolution CI mass spectra were also measured on a VG 70SE-4F spectrometer.

Collection, Extraction, and Isolation. The specimens of *Myriapora truncata* were collected in the Western Mediterranean Sea. Preliminary tests showed that the methanol extract of the specimens was active against L1210 murine leukemia cells (99% inhibition at 50 μg/mL, 87% inhibition at 25 μg/mL). Isolation of the active components was

performed by following L1210 activity. A frozen sample (1.3 kg) was initially blended with MeOH and extracted three times with the same solvent to give 23 g of crude extract after evaporation of the solvent. The extract was partially suspended in toluene, and after evaporation, the toluene-soluble material exhibited 99% inhibition at 20 μg/mL against L1210 cells. The toluene-soluble material was then partitioned between 80% aqueous MeOH and *n*-hexane. The aqueous MeOH was successively extracted with toluene, $CHCl_3$, and *n*-BuOH.

High activity (ca. 96% inhibition at 5 μg/mL) was found for the toluene, chloroform, and *n*-BuOH extracts, which were combined (1.4 g total) and subjected to high-speed countercurrent chromatography (Ito coil) with hexane−EtOAc−MeOH−H_2O (1:4:2:3) using the upper layer as mobile phase to yield 36 fractions (24 mL each). The most active fractions, tube numbers 4−18 (90% inhibition at 1 μg/mL, 120 mg) and 19−25 (50% inhibition at 1 μg/mL, 56 mg), were combined and further fractionated over an HW-40 gel column using 50% aqueous MeOH as eluent. From six fractions collected, fraction 3 (tube numbers 11−15, 17 mg) showed the highest cytotoxicity (99% inhibition at 1 μg/mL) and was passed through a Sep-pak silica cartridge column ($CHCl_3$−MeOH, 95:5) followed by an ODS column (Nucleosil, 1 × 25 cm, 40% aqueous CH_3CN) to afford the active compounds myriaporones 3 and 4 as a mixture (0.6 mg) and the less active compound **1** (1.6 mg).

More myriaporone 1 (**1**, 4.0 mg) and a mixture of **3** and **4** (0.6 mg) were isolated from a second batch of *M. truncata* (1.4 kg) by the same isolation procedure. A trace amount of myriaporone 2 (**2**, 0.2 mg) was also isolated from this batch. The same compound was later detected during NMR measurement of myriaporone 1 (**1**) in $CDCl_3$. Purification of products from myriaporone 1 (4.0 mg) in an NMR tube was carried out by using HPLC with a Nucleosil column (1 × 25 cm, $CHCl_3$−MeOH, 100:3) followed by an Econosphere C8 column (0.46 × 25 cm, 40% aqueous CH_3CN, UV 225 nm) to yield 1.3 mg of myriaporone 2 (**2**) and 2.4 mg of unchanged myriaporone 1 (**1**).

Myriaporone 1: $[\alpha]_D^{26}$ +71.1 (*c* 0.24, MeOH); UV(MeOH) λ_{max} (ϵ) 217(12500), 261(2500) nm; IR (CCl_4) ν_{max} 1228, 1709, 1747, 3580 cm^{-1}; ^1H and ^{13}C NMR data, see Table 1; FABMS *m/z* 397 $[M + H]^+$, 337 $[M - HOAc + H]^+$, 319 $[M - HOAc - H_2O + H]^+$; HRCIMS *m/z* 397.2226 (calcd for $C_{21}H_{33}O_7$, 397.2239).

Myriaporone 2: $[\alpha]_D^{26}$ −66.6 (*c* 0.13, MeOH); IR (CCl_4) ν_{max} 1233, 1747, 2360, 2940, 3580 cm^{-1}; ^1H and ^{13}C NMR data, see Table 1; FABMS *m/z* 397 $[M + H]^+$, 419 $[M + Na]^+$, 435 $[M + K]^+$; HRFABMS *m/z* 397.2135 {$[M + H]^+$} (calcd for $C_{21}H_{33}O_7$, 397.222); *m/z* 419.205231 (calcd for $C_{21}H_{32}O_7Na$, 419.2045); *m/z* 435.1780 (calcd for $C_{21}H_{32}O_7K$, 435.1785).

Myriaporones 3 and 4: $[\alpha]_D^{26}$ +44.6 (*c* 0.06, MeOH); ^1H and ^{13}C NMR data for **3** and ^1H NMR for myriaporone 4, see Table 3; FABMS *m/z* 337 $[M + H - 2H_2O]^+$, 395 $[M + Na]^+$, 411 $[M + K]^+$, 509 $[M + matrix(154) - H_2O + H]^+$, 527 $[M + matrix + H]^+$; HRFABMS *m/z* 411.1784 (calcd for $C_{19}H_{32}O_7K$, 411.1785); *m/z* 395.2054 (calcd for $C_{19}H_{32}O_7Na$, 395.2045); *m/z* 337.2019 (calcd for $C_{19}H_{29}O_5$, 337.2015).

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Supporting Information Available: ^1H, ^{13}C NMR and $^1H-^1H$ COSY spectra for myriaporones 1 and 2, HMQC spectrum for myriaporone 1, ^1H NMR and $^1H-^1H$ COSY spectra for myriaporones 3 and 4, and FABMS and FABMS/CID/MS for myriaporones 3 and 4. This material is available free of charge via the Internet at http://pubs.acs.org.

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