Topsentinols A—J, New Sterols with Highly Branched Side Chains from Marine Sponge *Topsentia* sp.

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Topsentinols A—J (1—10), new 7-hydroxysterols with unusual polyalkylated side chains were obtained from the Okinawan marine sponge *Topsentia* sp. and their structures elucidated on the basis of spectral data. Side chains containing the 22*E*-24-isopropenyl-25-methyl-22-ene group (in 1, 6) and the 22*Z*-24-isopropyl-22-ene group (in 2, 7) are unprecedented.

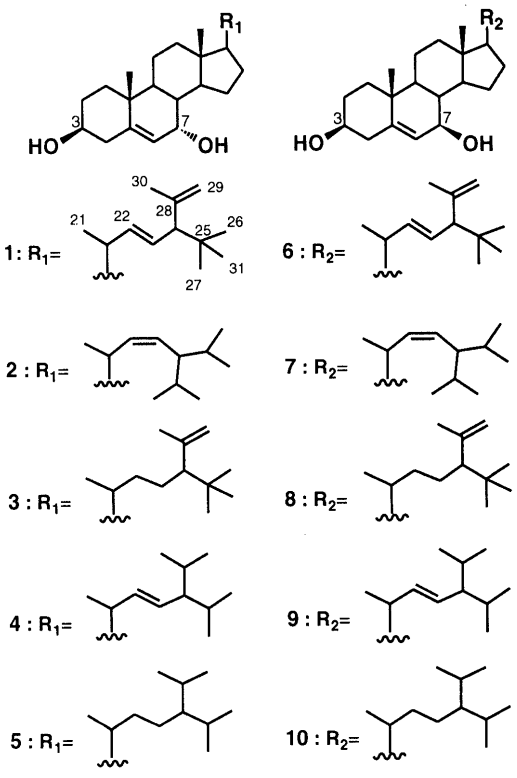
Key words sponge; *Topsentia* sp.; 7-hydroxysterol; topsentinol; antifungal activity

Unconventional sterols with a variety of unusual side chains and nuclei have been isolated from marine sponges.[1,2] In our search for new metabolites from marine organisms,[3] we recently examined extracts of the Okinawan marine sponge *Topsentia* sp. and have obtained ten new 7-hydroxysterols with highly branched side chains, topsentinols A—J (**1**—**10**). The present report describes the isolation and structure elucidation of **1**—**10**. The branched side chains containing the 22*E*-24-isopropenyl-25-methyl-22-ene group for **1** and **6** and the 22*Z*-24-isopropyl-22-ene group for **2** and **7** are previously unknown sterol side chains.

The sponge *Topsentia* sp., collected off Zamami, Okinawa, was extracted with MeOH, and the extract was partitioned between EtOAc and H_2O. The EtOAc-soluble material was subjected to silica gel flash column chromatography with hexane/EtOAc to afford two fractions (A, B) as sterol mixtures, which gave characteristic green spots with Dragendorff's reagent on silica gel TLC plates. These fractions were each separated by gel filtration on Sephadex LH-20 (MeOH), followed by purification using reversed-phase HPLC to give topsentinols A—J (**1**—**10**, 0.00007—0.0005% yields, wet weight). The polar fraction (A) from the silica gel column proved to contain five 7α-hydroxysterols (**1**—**5**), while the other less polar fraction (B) yielded five 7β-hydroxysterols (**6**—**10**). Compounds **7** and **8** were obtained as a mixture in a ratio of 1 : 1.4.[4]

Topsentinol B (**2**), colorless needles, mp 216 °C, $[\alpha]_D^{27}$ −96° (c=0.4, $CHCl_3$), was shown to have the molecular formula $C_{30}H_{50}O_2$ by the HR-EI-MS data (m/z 442.3798, M^+, Δ −1.3 mmu), and had a hydroxyl absorption (3340 cm^{-1}) in the IR spectrum. The ^{1}H-NMR spectrum of **2** showed signals due to two quaternary methyl groups, five secondary methyl groups, two oxymethines, and three olefinic protons. The EI-MS of **2** afforded intense fragment ions at m/z 271 $(M-H_2O-C_{11}H_{21})^+$ and 253 $(M-2H_2O-C_{11}H_{21})^+$, indicating the presence of a $C_{11}H_{21}$ side chain containing one double bond. Based on these spectral data, **2** was suggested to be a cholesterol derivative with two hydroxyl groups and a highly alkylated side chain. As for the cholesterol nucleus, **2** was suggested to have a 5-ene-3β,7α-diol structure on the basis of comparison of the ^{1}H- and ^{13}C-NMR data ($CDCl_3$) with those of cholest-5-ene-3β,7α-diol[5] (**11**); [**2**: δ_H 5.60 (d, J=5.2 Hz; H-6), 3.84 (br s; H-7); δ_C 123.9 (C-6), 65.3 (C-7); **11**: δ_H 5.60 (d, J=5.0 Hz; H-6), 3.83 (br s; H-7); δ_C 124.0 (C-6), 65.5 (C-7)]. As regards the side chain portion, the ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum of **2** showed clear cross-peaks (H_3-21/H-20, H-20/H-22, H-22/H-23, H-23/H-24, H-24/H-25, H-24/H-28, H-25/H_3-26, H-25/H_3-27, H-28/H_3-29, H-28/H_3-30) that indicated the presence of a 22-dehydro-24-isopropyl group ($C_{11}H_{21}$) in the side chain. The geometry of the Δ^{22}-double bond was deduced to be Z from the ^{1}H–^{1}H coupling constant (J=10.9 Hz). Thus, the structure of topsentinol B (**2**) was concluded to be 22*Z*-24-isopropylcholesta-5,22-diene-3β,7α-diol.

The molecular formula of topsentinol G (**7**), $C_{30}H_{50}O_2$, was the same as that of **2** from the HR-EI-MS data (m/z 442.3783, M^+, Δ −2.8 mmu). The ^{1}H- and ^{13}C-NMR data revealed that **7** possesses the same 22*Z*-24-isopropyl-22-ene side chain structure as **2**. The structural difference of **7** from **2** was found in the cholesterol nucleus portion.



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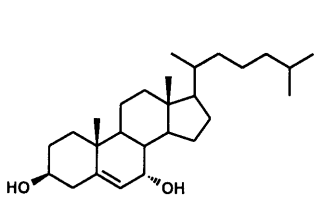

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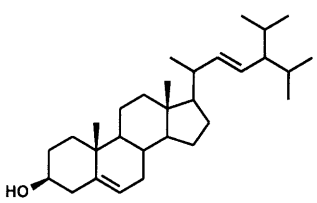

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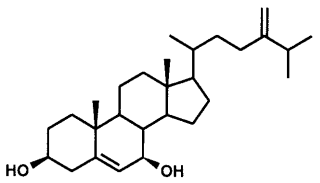

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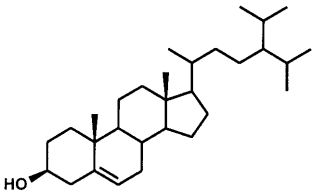

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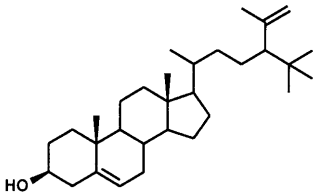

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The ^{1}H- and ^{13}C-NMR data of **7** paralleled those of 24-methylenecholest-5-ene-3β,7β-diol[5] (**12**); [**7**: δ_H 5.29 (br s; H-6), 3.85 (br s; H-7); δ_C 125.4 (C-6), 73.3 (C-7); **12**: δ_H 5.29 (br s; H-6), 3.85 (br d; H-7); δ_C 125.5 (C-6), 73.3 (C-7)]. The ^{1}H-NMR chemical shift of H-6 (δ_H 5.60/5.29) and ^{13}C-NMR chemical shift of C-7 (δ_C 65.5/73.3) are highly diagnostic between 7α- and 7β-hydroxy-5-ene sterols. The structure of topsentinol G (**7**) was therefore concluded to be 22*Z*-24-isopropylcholesta-5,22-diene-3β,7β-diol.

On the basis of the ^{1}H- and ^{13}C-NMR chemical shift data described above, topsentinols A—E (**1**—**5**) were revealed to be cholesta-5-ene-3β,7α-diols, whereas topsentinols F—J (**6**—**10**) were found to be cholesta-5-ene-3β,7β-diols. The NMR and EI-MS data revealed that all these compounds possessed unusually branched side chains, as described below.

The molecular formula of topsentinol A (**1**) was revealed to be $C_{31}H_{50}O_2$ by HR-EI-MS [*m/z* 454.3831 (M^+), Δ +2.0 mmu], and the ^{1}H- and ^{13}C-NMR data showed **1** has a cholesta-5-ene-3β,7α-diol nucleus. The ^{1}H-NMR spectrum of **1** showed that the side chain of **1** contains one exomethylene group (δ_H 4.77, 4.65), one vinyl methyl (δ_H 1.73, 3H, s), one tertiary butyl group (δ_H 0.88, 9H, s), and one disubstituted *E* olefin (J=15.1 Hz). Comparison

Table 1. ^{1}H-NMR Data for Topsentiols A—J (**1**—**10**) in $CDCl_3$ (500 MHz)

Position	**1**		**2**		**3**		**4**		**5**	
	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)
3	3.59	m	3.59	m	3.59	m	3.59	m	3.59	m
6	5.60	dd 1.7, 5.2	5.60	dd 1.6, 5.2	5.60	dd 1.6, 5.2	5.60	dd 1.3, 5.2	5.61	dd 1.6, 5.1
7	3.84	br s	3.84	br s	3.85	br s	3.85	br s	3.85	br s
18 (3H)	0.70	s	0.72	s	0.69	s	0.71	s	0.69	s
19 (3H)	1.00	s	1.00	s	1.00	s	1.00	s	1.00	s
21 (3H)	1.04	d 6.7	0.98	d 6.5	0.93	d 6.5	1.04	d 6.6	0.96	d 6.5
22	5.47	dd 9.5, 15.1	5.27	t 10.9	—		5.14[a]	dd 8.4, 15.1	—	
23	5.23	dd 8.4, 15.1	4.96	t 10.9	—		5.03[a]	dd 9.7, 15.1	—	
26 (3H)	0.88	s	0.91[b]	d 6.7	0.89	s	0.84[b]	d 6.7	0.87[b]	d 6.8
27 (3H)	0.88	s	0.89[b]	d 6.8	0.89	s	0.84[b]	d 6.7	0.87[b]	d 6.8
29	4.77	s	0.83[b]	d 6.8	4.82	s	0.78[b]	d 6.6	0.84[b]	d 6.4
	4.65	s			4.64	s				
30 (3H)	1.73	s	0.80[b]	d 6.8	1.68	s	0.77[b]	d 6.5	0.83[b]	d 6.3
31 (3H)	0.88	s			0.89	s				

Position	**6**		**7**		**8**		**9**		**10**	
	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)	δ	J (Hz)
3	3.55	m	3.55	m	3.55	m	3.55	m	3.55	m
6	5.29	br s	5.29	br s	5.29	br s	5.29	br s	5.29	br s
7	3.84	m	3.85	m	3.85	m	3.85	m	3.85	m
18 (3H)	0.71	s	0.69	s	0.67	s	0.71	s	0.69	s
19 (3H)	1.05	s	1.05	s	1.06	s	1.05	s	1.05	s
21 (3H)	1.04	d 6.7	0.98	d 6.5	0.93	d 6.5	1.04	d 6.7	0.95	d 6.5
22	5.48	dd 9.5, 15.1	5.27	t 10.8	—		5.13	dd 8.5, 15.1	—	
23	5.22	dd 8.5, 15.1	4.97	t 10.8	—		5.03	dd 9.7, 15.0	—	
26 (3H)	0.89	s	0.91[b]	d 6.7	0.89	s	0.84[b]	d 6.6	0.87[b]	d 6.8
27 (3H)	0.89	s	0.89[b]	d 6.8	0.89	s	0.84[b]	d 6.6	0.87[b]	d 6.8
29	4.77	s	0.82[b]	d 6.8	4.82	s	0.78[b]	d 6.3	0.84[b]	d 7.1
	4.65	s			4.64	s				
30 (3H)	1.73	s	0.80[b]	d 6.8	1.68	s	0.77[b]	d 6.0	0.83[b]	d 7.1
31 (3H)	0.89	s			0.89	s				

a, *b*) Exchangeable.

Table 2. ^{13}C-NMR Data for Topsentiols A—J (**1**—**10**) in $CDCl_3$ (100 MHz)

Position	1	2	3	4	5	6	7	8	9	10
1	37.0	37.0	37.1	37.0	37.1[a]	36.9	36.9	36.9	36.9	36.9
2	31.4	31.4	31.4	31.4	31.4	31.6	31.6	31.6	31.6	31.6
3	71.3	71.4	71.4	71.3	71.4	71.4	71.4	71.4	71.4	71.4
4	42.0	42.0	42.0	42.0	42.0	41.7	41.7	41.7	41.7	41.7
5	146.2	146.2	146.3	146.2	146.3	143.4	143.4	143.4	143.4	143.5
6	123.8	123.9	123.9	123.8	123.9	125.4	125.4	125.4	125.4	125.4
7	65.3	65.3	65.4	65.3	65.4	73.3	73.3	73.3	73.3	73.3
8	37.5	37.6	37.6	37.5	37.5	40.9	40.9	40.9	40.9	40.9
9	42.3	42.3	42.3	42.3	42.3	48.3	48.3	48.3	48.2	48.2
10	37.4	37.4	37.4	37.4	37.4	36.4	36.4	36.4	36.4	36.4
11	20.7	20.7	20.7	20.7	20.7	21.0	20.8	21.1	21.0[a]	21.0
12	39.0	39.3	39.2	39.1	39.2	39.4	39.6	39.6	39.4	39.5
13	42.1	42.2	42.2	42.0	42.1	42.9	42.9	42.9	42.8	42.9
14	49.4	49.4	49.5	49.5	49.4	55.5	55.5	55.5	55.3	55.2
15	24.3	24.3	24.3	24.4	24.3	26.4	26.4	26.4	26.5	26.4
16	28.4	28.4	28.3	29.0	28.3	28.6	28.6	28.6	28.5[b]	28.6
17	56.0	56.7	55.9	56.2	55.5	55.9	55.9	55.9	56.2	55.9
18	11.8	12.0	11.7	11.8	11.6	12.0	12.1	12.1	12.0	11.8
19	18.2	18.3	18.3	18.2	18.2	19.2	19.5	19.2	21.3[a]	18.9
20	40.0	34.3	35.5	40.6	36.6	40.0	34.2	35.5	40.5	36.5
21	20.7	20.7[b]	18.6	21.2	18.9	20.8	20.8[b]	21.8	21.6[a]	19.1
22	137.8	138.1	34.5[a]	139.2	37.0[a]	137.7	137.9	34.5[a]	139.1	37.1
23	127.2	126.9	29.7[a]	127.1	23.8	127.4	127.0	29.6[a]	127.2	24.0
24	60.7	49.6	57.2	55.8	50.6	60.7	49.6	57.2	56.0	50.6
25	33.5	29.0[a]	33.2	28.5	29.4[b]	33.5	29.0[a]	33.1	29.2[b]	29.3[b]
26	28.4	18.9[b]	28.7	19.0[a]	19.2[c]	28.4	18.9[b]	28.6	19.0[a]	19.2[c]
27	28.4	19.5[b]	28.7	19.1[a]	19.5[c]	28.4	19.5[b]	28.6	19.1[a]	19.5[c]
28	147.4	29.5[a]	147.0	28.5	29.5[b]	147.4	29.6[a]	147.0	29.7[b]	29.5[b]
29	112.2	21.9[b]	112.9	21.6[a]	21.3[c]	112.2	21.8[b]	112.5	21.6[a]	21.3[c]
30	23.2	22.0[b]	22.7	21.7[a]	21.7[c]	23.2	22.0[b]	21.8	21.7[a]	21.7[c]
31	28.4		28.7			28.4		28.6		

a—*c*) Exchangeable.

of these ^{1}H-NMR data of **1** with those of axinyssasterol[6] (**13**), which was isolated from a marine sponge *Pseudoaxinyssa* sp., having a side chain with 24-isopropenyl-25-methyl group, suggested that compound **1** possesses a 22*E*-24-isopropenyl-25-methyl-22-ene group in the side chain. Thus, topsentinol A (**1**) was concluded to be 22*E*-24-isopropenyl-25-methylcholesta-5,22-diene-3β,7α-diol. Topsentinol F (**6**), $C_{31}H_{50}O_2$, an isomer of **1**, has the same side chain as **1**, with a 7β-hydroxyl group.

Topsentinols C (**3**) and H (**8**) have the same molecular formula, $C_{31}H_{52}O_2$, as shown by the HR-EI-MS [**3**: *m/z* 456.3950 (M^+), Δ −1.7 mmu; **8**: *m/z* 456.3982 (M^+), Δ +1.5 mmu], and they possess 7α- and 7β-hydroxyl groups, respectively, in the sterol nucleus. The ^{1}H-NMR spectra indicated that **3** and **8** have the same side chain structure containing one exomethylene group, one vinyl methyl, and one tertiary butyl group. These ^{1}H-NMR data corresponded to those of axinyssasterol[6] (**13**), implying that topsentinols C (**3**) and H (**8**) are 24-isopropenyl-25-methylcholesta-5-ene-3β,7α-diol and 24-isopropenyl-25-methylcholesta-5-ene-3β,7β-diol, respectively.

Topsentinols D (**4**) and I (**9**) are isomers ($C_{30}H_{50}O_2$) with the same side chain, containing two isopropyl groups and one disubstituted *E*-olefin (J = 15.2 Hz), which appears to be analogous to that of 22*E*-dehydro-24-isopropylcholesterol[7] (**14**), isolated from the sponge *Pseudaxinyssa* sp. Comparison of the spectral data of **4** and **9** with those of **14** suggested that topsentinols D (**4**) and I (**9**) are 22*E*-24-isopropylcholesta-5,22-diene-3β,7α-diol and 22*E*-24-isopropylcholesta-5,22-diene-3β,7β-diol, respectively.

Spectral data for topsentinols E (**5**) and J (**10**) ($C_{30}H_{52}O_2$) resembled those of **4** and **9**, respectively, except that **5** and **10** appeared to contain no double bond in the side chain. Thus, topsentinols E (**5**) and J (**10**) were inferred to be dihydro derivatives of **4** and **9**, respectively, and this was further supported by comparison of the spectral data for **5** and **10** with those of 24-isopropylcholesterol[7] (**15**), isolated from the sponge *Pseudaxynyssa* sp.

In conclusion, we have obtained topsentinols A—J (**1**—**10**) as new 7-hydroxycholesterol derivatives having highly branched side chains, some of which are unprecedented.[8] Among these sterols, topsentinol B (**2**) showed antifungal activity against *Trichophyton mentagrophytes* minimam inhibitory concentration (MIC, 56 μg/ml).

Experimental

Collection, Extraction, and Isolation A sponge of *Topsentia* sp. was collected off Zamami, Okinawa, and kept frozen until used. The methanol extract of this sponge (1 kg) was partitioned between EtOAc (500 ml × 4) and 1 M NaCl (1 l). The EtOAc-soluble fraction was evaporated under reduced pressure to give a crude residue (0.88 g), which was subjected to a silica gel column chromatography (2.3 × 46 cm) with hexane/EtOAc (3 : 7) to afford two fractions, A (23.6 mg) and B (27.9 mg). Fraction A was separated by gel filtration on a Sephadex LH-20 (Pharmacia, 2.0 × 106 cm) with MeOH, and the fraction eluted at 186 to 213 ml was further purified by reversed-phase HPLC (YMC-Pack ODS AM-323, 10 × 250 mm, 95% MeOH; flow rate, 2.0 ml/min) to yield topsentinols A (**1**, t_R 36.2 min, 1.0 mg, 0.0001% wet weight), B (**2**, t_R 39.1 min, 0.8 mg, 0.00008%), C (**3**, t_R 41.6 min, 0.7 mg, 0.00007%), D (**4**, t_R 43.3 min,

3.8 mg, 0.00038%), and E (**5**, t_R 49.8 min, 1.2 mg, 0.00012%). Fraction B was also separated on the Sephadex LH-20 column with MeOH, and the fraction eluted at 216 to 276 ml was further purified by reversed-phase HPLC (same conditions as above) to give topsentinol F (**6**, t_R 36.0 min, 1.0 mg, 0.0001%), a (1 : 1.4) mixture of topsentinols G (**7**) and H (**8**) (t_R 40.4 min, 2.2 mg, 0.00022%), and topsentinols I (**9**, t_R 43.5 min, 5.6 mg, 0.00056%), and J (**10**, t_R 49.3 min, 1.8 mg, 0.00018%).

Topsentinol A (**1**): Colorless needles; mp 189 °C; $[\alpha]_D^{26}$ −84° (c=0.5, $CHCl_3$); IR (film) ν_{max} 3350, 2930, 1640, 1370, 1460, 1110, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 454 (M^+), 436, 418, 403, 380, 362, 269, 109, 57; HR-EI-MS m/z 454.3831 (M; Calcd for $C_{31}H_{50}O_2$, 454.3811).

Topsentinol B (**2**): Colorless needles; mp 216 °C; $[\alpha]_D^{27}$ −96° (c=0.5, $CHCl_3$); IR (film) ν_{max} 3340, 2960, 1660, 1460, 1380, 1110, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 442 (M^+), 424, 406, 381, 363, 269, 109, 97, 55; HR-EI-MS m/z 442.3798 (M; Calcd for $C_{30}H_{50}O_2$, 442.3811).

Topsentinol C (**3**): Colorless needles; mp 223 °C; $[\alpha]_D^{28}$ −75° (c=0.4, $CHCl_3$); IR (film) ν_{max} 3330, 2940, 1640, 1460, 1370, 1230, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 456 (M^+), 438, 420, 382, 269, 251, 109, 57; HR-EI-MS m/z 456.3950 (M; Calcd for $C_{31}H_{52}O_2$, 456.3967).

Topsentinol D (**4**): Colorless needles; mp 216 °C; $[\alpha]_D^{28}$ −104° (c=1, $CHCl_3$); IR (film) ν_{max} 3350, 2960, 1660, 1460, 1370, 1110, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 442 (M^+), 424, 406, 381, 363, 271, 253, 109, 97, 55; HR-EI-MS m/z 442.3792 (M; Calcd for $C_{30}H_{50}O_2$, 442.3811).

Topsentinol E (**5**): Colorless needles; mp 218 °C; $[\alpha]_D^{27}$ −72° (c=0.5, $CHCl_3$); IR (film) ν_{max} 3380, 2960, 1660, 1470, 1380, 1110, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 444 (M^+), 427, 408, 393, 368, 289, 253, 135, 109, 95, 57; HR-EI-MS m/z 444.3959 (M; Calcd for $C_{30}H_{52}O_2$, 444.3967).

Topsentinol F (**6**): Colorless amorphous solid; $[\alpha]_D^{25}$ −5.1° (c=0.5, $CHCl_3$); IR (film) ν_{max} 3290, 2950, 1640, 1460, 1370, 1120, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 436 (M^+), 418, 403, 380, 362, 315, 289, 253, 138, 109, 93, and 57; HR-EI-MS m/z 454.3794 (M; Calcd for $C_{31}H_{50}O_2$, 454.3811).

Topsentinols G (**7**) and H (**8**): (**7**:**8**=1 : 1.4) Colorless amorphous solid; $[\alpha]_D^{25}$ −13° (c=1, $CHCl_3$); IR (film) ν_{max} 3290, 2960, 1640, 1470, 1370, 1170, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 456 (M^+), 442 (M^+), 438, 424, 406, 391, 382, 363, 287, 271, 253, 135, 109, 97, 57; for **7**: HR-EI-MS m/z 442.3783 (M; Calcd for $C_{30}H_{50}O_2$, 442.3811); for **8**: HR-EI-MS m/z 456.3982 (M; Calcd for $C_{31}H_{52}O_2$, 456.3967).

Topsentinol I (**9**): Colorless amorphous solid; $[\alpha]_D^{25}$ −19° (c=1, $CHCl_3$); IR (film) ν_{max} 3290, 2960, 1670, 1460, 1380, 1170, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 442 (M^+), 424, 406, 399, 391, 381, 363, 321, 271, 253, 138, 109, 93, 55; HR-EI-MS m/z 442.3840 (M; Calcd for $C_{30}H_{50}O_2$, 442.3810).

Topsentinol J (**10**): Colorless amorphous solid; $[\alpha]_D^{25}$ −6.7° (c=1, $CHCl_3$); IR (film) ν_{max} 3310, 2960, 1640, 1470, 1380, 1140, 1060 cm^{-1}; ^{1}H-NMR (Table 1); ^{13}C-NMR (Table 2); EI-MS m/z 444 (M^+), 426, 408, 393, 367, 289, 253, 135, 107, 95, 57; HR-EI-MS m/z 444.3950 (M; Calcd for $C_{30}H_{52}O_2$, 444.3967).

Sponge The sponge *Topsentia* sp. (Order Halichondrida; Family Halichondriidae; Berg, 1899) was a firm, incompressible, rather brittle sponge. Cream when preserved in formalin. Smooth surface. Mesohyl skeleton haphazard with some spicule tracts internally, no fibers. Spicules are long, sharply pointed, mean size 560 × 14 μm. A voucher specimen (SS-71) has been deposited at the Faculty of Pharmaceutical Sciences, Hokkaido University.

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References and Notes

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4) Although compounds **7** and **8** were obtained as a mixture, their structures could be elucidated separately on the basis of comparison of the spectral data with those of closely related compounds such as **2** and **3**, respectively.
5) Compound **12** was isolated from an *Alcyonium* sp. soft coral, while compound **11** was prepared by a known method: Kobayashi M., Kanda F., Damarla S. R., Rao D. V., Rao C. B., *Chem. Pharm. Bull.*, **38**, 2400—2403 (1990).
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8) The stereochemistry at the C-24 position of compounds **1**, **3**, **6**, and **8** remains undefined.