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Halistanol Sulfates A-E, New Steroid Sulfates, from a Marine Sponge, *Epipolasis* sp.[1]

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Abstract: Five new steroid sulfates related to halistanol sulfate were isolated along with halistanol sulfate from a marine sponge, *Epipolasis* sp. Their structures were determined by spectral data. Absolute stereochemistry of halistanol sulfate was determined by applying a modified Mosher's method to halistanol, an acid hydrolysis product of halistanol sulfate.

Steroid sulfates are often encountered in marine sponges of the families Halichondriidae and Adociidae, including the genera *Halichondria*,[3] *Trachyopsis*,[4] *Toxadocia*,[5] and *Petrosia*,[6]. In the course of our continuing studies of bioactive metabolites from Japanese marine invertebrates,[1] we have collected a sponge, *Epipolasis* sp.[7] off Hachijo-jima Island which showed antifungal and anti-thrombin activities. Bioassay-guided isolation afforded five new halistanol sulfates named halistanol sulfates A-E (**2**-**6**), together with the known halistanol sulfate (**1**).[3a] This paper deals with the isolation and structure elucidation of these compounds.

The water-soluble portion of the aqueous ethanol extract of the frozen sponge (1kg) was fractionated on TSK G3000S, followed by repeated reverse-phase HPLC to yield **1**-**6** (**1**, 5.7×10^{-2}%; **2**, 2.6×10^{-3}%; **3**, 3.7×10^{-3}%; **4**, 1.5×10^{-3}%; **5**, 6.3×10^{-4}%; **6**, 2.0×10^{-4}%; based on wet weight), which inhibited thrombin[8] with IC_{50} values of 17, 17, 23, 16, 47, and 90 μg/mL, respectively.

The ^1H and ^{13}C NMR spectra readily implied that halistanol sulfate A (**2**) had a steroid sulfate nucleus identical with that of the known halistanol sulfate (**1**)[3a](Tables 1, 2). This was also supported by the IR band (1220 cm^{-1}) and negative FAB mass spectrum [*m/z* 715(M-Na)$^-$], which indicated that **2** had a molecular weight 16 mass units smaller than halistanol sulfate.

The structure of the sidechain was elucidated by careful analysis of 2D NMR data. The COSY spectrum together with HMQC data at 600MHz allowed construction of gross structure of **2**, except for C10 and C13 quaternay carbons.

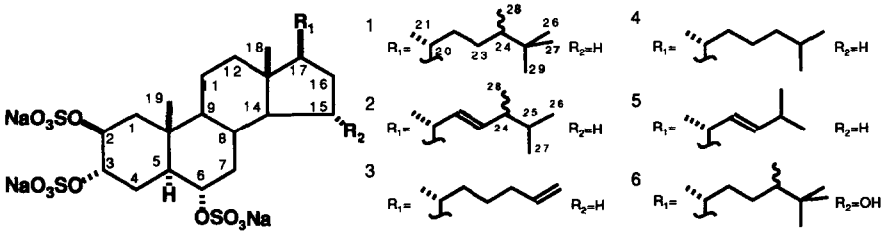

Table 1. ^{13}C NMR Spectral Data for **2-6***

C #	2	3	4	5	6
1	39.2(t)	39.3(t)	39.2(t)	39.2(t)	39.1(t)
2	75.5(d)	75.5(d)	75.5(d)	75.5(d)	75.1(d)
3	75.5(d)	75.5(d)	75.5(d)	75.5(d)	75.1(d)
4	25.1(t)	25.1(t)	25.1(t)	25.0(t)	25.1(t)
5	45.3(d)	45.3(d)	45.3(d)	45.4(d)	45.4(d)
6	78.7(d)	78.8(d)	78.7(d)	78.7(d)	78.6(d)
7	40.0(t)	40.0(t)	40.0(t)	40.1(t)	40.1(t)
8	35.1(d)	35.1(d)	35.1(d)	35.2(d)	34.5(d)
9	55.9(d)	55.8(d)	55.8(d)	55.9(d)	55.9(d)
10	37.6(s)	37.6(s)	37.6(s)	37.7(s)	37.7(s)
11	21.8(t)	21.8(t)	21.8(t)	21.7(t)	21.6(t)
12	41.0(t)	41.1(t)	41.2(t)	41.1(t)	41.3(t)
13	43.7(s)	43.8(s)	43.8(s)	43.7(s)	45.2(s)
14	57.3(d)	57.5(d)	57.5(d)	57.4(d)	66.8(d)
15	25.0(t)	25.1(t)	24.9(t)	25.0(t)	77.4(d)
16	29.9(t)	29.2(t)	29.2(t)	29.5(t)	38.1(t)
17	57.7(d)	57.6(d)	57.6(d)	57.7(d)	54.5(d)
18	12.7(q)	12.5(q)	12.5(q)	12.7(q)	14.0(q)
19	15.3(q)	15.2(q)	15.2(q)	15.3(q)	15.3(q)
20	41.7(d)	36.9(d)	37.0(d)	41.2(d)	36.4(d)
21	21.5(q)	19.2(q)	19.1(q)	21.3(q)	20.1(q)
22	137.4(d)	36.5(d)	37.3(t)	136.1(d)	36.1(t)
23	133.1(d)	26.5(d)	25.0(t)	135.0(d)	30.2(t)
24	44.5(d)	36.3(d)	40.8(t)	32.3(d)	45.2(d)
25	34.5(d)	140.1(s)	29.1(d)	23.2(q)	34.1(s)
26	20.1(q)	114.8(t)	23.1(q)	23.2(q)	27.8(q)
27	20.6(q)		22.9(q)		27.8(q)
28	18.6(q)				15.0(q)
29					27.8(q)

* Solvent CD_3OD. Chemical shifts in ppm downfield from TMS as referenced to $^{13}CD_3OD$ at δ 49.00. Multiplicities determined by DEPT are given in parentheses (s=C, d=CH, t=CH_2, q=CH_3).

This problem was solved by a delayed COSY experiment, which revealed long range couplings between Me18 and Heq12, Me19 and each of Heq1, Hax4, H5, H9, and Hax11, thereby allowing us to assign all ^1H NMR signals (Table 2). Stereochemisty of the all-trans steroid skeleton with A, B, and C rings in chair conformation was deduced by interpretation of the NOESY data, which were supported by the ^1H, ^1H-coupling constants of resolved signals. 2β, 3α, 6α-Oxygenation pattern was evident from the ^1H, ^1H-coupling constants. The 20*S* stereochemistry was inferred by comparing the ^1H NMR chemical shift of Me-21 with that for brassicasterol.[9] Geometry of the C22,C23 double bond was determined by measuring the ^1H,^1H coupling constant in a non-decoupled HMQC spectrum,[10] which gave a value of 15.5 Hz, therefore **2** had 22*E* geometry. However the stereochmistry of C24 remained to be elucidated.

Halistanol sulfate B (**3**) had a molecular weight 28 mass units smaller than **2**, indicating a lack of two methylene equivalents. The ^1H and ^{13}C NMR data revealed the presence of one each methyl and methine, three methylenes, and a vinyl group in the sidechain, in addition to the halistanol nucleus. The subunit of $CH_3CH(CH_2)_3CH{=}CH_2$ was evident from the COSY cross peaks. This unusual sidechain is unprecedented for naturally occurring sterols.[11] The 20*S* stereochemistry was inferred by the ^1H NMR chemical shift of Me-21.[12]

Halistanol sulfate C (**4**) also had the same halistanol sulfate steroid nucleus, which was readily deducible from the ^1H and ^{13}C NMR data. The sidechain was composed of three methyls, three methylenes, and two methines, reminiscent of a standard cholesterol sidechain, which was confirmed by the ^{13}C NMR data.[13]

Table 2. ^{1}H NMR Spectral Data for **2** and **6***

C no	2(mult, J_{HH}, Hz)	6(mult, J_{HH}, Hz)
1 eq.	2.07(dd, *J*=14.7, 1.4)	2.10(dd, *J*=14.7, 1.8)
1 ax.	1.47(dd, *J*=14.7, 4.0)	1.47(m)
2 eq.	4.79(m<narrow>)	4.82(m<narrow>)
3 eq.	4.74(q, *J*=2.8)	4.74(q, *J*=2.8)
4 eq.	2.27(dtd, *J*=14.8, 2.8, 1.2)	2.29(dt, *J*=14.7, 2.8)
4 ax.	1.78(ddd, *J*=14.8, 13.5, 2.8)	1.79(ddd, *J*=14.7, 12.8, 2.8)
5	1.62(ddd, *J*=13.5, 11.1, 2.8)	1.66(ddd, *J*=12.8, 11.1, 2.8)
6 ax.	4.18(td, *J*=11.1, 4.4)	4.19(td, *J*=11.1, 4.5)
7 eq.	2.35(dt, *J*=12.3, 4.4)	2.35(dt, *J*=12.3, 4.0)
7 ax.	1.02(m)	1.10(m)
8	1.52(m)	1.52(m)
9	0.75(ddd, *J*=12.2, 10.7, 3.9)	0.82(m)
10	-	-
11 eq.	1.54(m)	1.54(m)
11 ax.	1.32(qd, *J*=13.1, 3.5)	1.27(qd, *J*=13.1, 3.4)
12 eq.	1.98(dt, *J*=12.5, 3.5)	1.97(dt, *J*=12.1, 3.4)
12 ax.	1.16(m)	1.25(td, *J*=13.4, 3.7)
13	-	-
14	1.15(m)	1.09(m)
15	1.58(m), 1.09(m)	3.92(dd, *J*=7.7, 5.9)
16	1.71(m), 1.28(m)	1.65(td, *J*=12.8, 8.0), 1.55(m)
17	1.18(m)	1.47(m)
18	0.70(s)	0.70(s)
19	1.04(s)	1.05(s)
20	2.01(m)	1.48(m)
21	1.00(d, *J*=6.6)	0.96(d, *J*=6.6)
22	5.17(m)	1.85(tdd, *J*=12.8, 4.3, 3.0), 1.00(m)
23	5.17(m)	1.75(tdd, *J*=12.8, 4.3, 2.0), 0.71(m)
24	1.82(6th, *J*=6.8)	1.05(m)
25	1.45(5th, *J*=6.8)	-
26	0.85(d, *J*=6.8)	0.85(s)
27	0.83(d, *J*=6.8)	0.85(s)
28	0.92(d, *J*=6.8)	0.85(d, *J*=6.8)
29		0.85(s)

* Solvent CD_3OD. Chemical shifts in ppm downfield from TMS as referenced to CHD_2OD at δ 3.30.

Halistanol sulfate D (**5**) had the same halistanol sulfate nucleus with a shorter side chain, which was implied by NMR data together with the negative FAB mass spectrum [*m/z* 687(M-Na)$^-$]. This was also supported by the retention time in reverse-phase HPLC. The structure elucidation of the sidechain was straightforward: one of the well-separated *E*-olefinic protons at δ 5.17 was coupled to H20 at δ 2.00, which was in turn coupled to Me21 at δ 0.99 and H17 at δ 1.14. The other olefinic proton at δ 5.26 was coupled to H24 at δ 2.17 which gave COSY crosspeaks with both Me25 (δ 0.93) and Me26 (δ 0.94). The proton at δ 5.17 (H22) was allylically coupled to H24 at δ 2.17 with a *J* value of 0.7Hz. 20*S* Stereochemistry was inferred as in case of **2**.

The most polar constituent halistanol sulfate E (**6**), had a molecular weight 16 mass units larger than **1**. The ^{1}H and ^{13}C NMR data indicated that **6** had the same sidechain as **1** and a steroid nucleus similar to **1**. There was an additional oxygenated methine (δ_H 3.92, δ_C 77.4), thereby suggesting the presence of an alcohol in the steroid nucleus. A careful analysis of the COSY and delayed COSY spectra in conjunction with the HMQC data allowed us to locate a hydroxyl group on C15. A ROESY crosspeak between H15 and Me18 was in accordance with a 15α hydroxyl group. The position of the hydroxyl group was confirmed by a deuterium-induced shifts in the ^{13}C NMR spectrum: C14, C15, and C16 shifted downfield (0.07, 0.13, and 0.05 ppm, respectively) upon changing the solvent from CD_3OD to CD_3OH.[14]

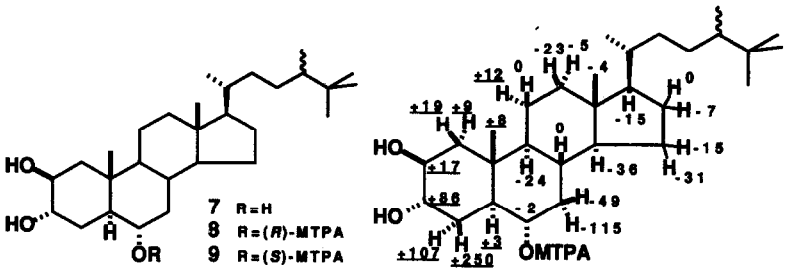

Figure 1. Δδ Values($\delta_{(S)}$-$\delta_{(R)}$) obtained for the MTPA esters of halistanol. Δδ Values are expressed in hertz (600MHz).

Though halistanol sulfate (**1**) would be expected to have the same absolute stereochemistry as cholesterol, we have attempted to confirm its absolute stereochemistry. Since the diaxial vicinal 2,3-diol system generated by hydrolysis of **1** was not suitable for the application of the CD exciton chirality method, we tried the modified Mosher method.[15] When halistanol (**7**)[3a] was reacted with MTPA/DCC, esterification proceeded exclusively at the equatorial C6 alcohol, allowing us to prepare **8** and **9**. The chemical shift differences of the ^{1}H NMR signals for **8** and **9** were in good agreement with the depicted stereochemistry (Figure 1).

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM600 NMR spectrometer in CD_3OD at 300 K. FAB mass spectra were measured on a JEOL JMX-SX102 mass spectrometer with glycerol as a matrix. Infrared spectra were recorded on a JASCO IR-G infrared spectrometer. Optical rotations were determined on a JASCO DIP-371 digital polarimeter in methanol.

Isolation. The frozen sponge (1.02kg) was homogenized and extracted with 75% aqueous EtOH (3×3L). The extract was concentrated to a volume of 2.5 L and extracted with ether (3×2L). The water soluble portion was chromatographed on TSK G3000S (ø 9.6×10.0cm) with increasing amounts of MeOH in water. The fraction eluted with 50% aqueous MeOH was collected (yield 2.28g) and successively subjected to reverse-phase HPLC on Cosmosil 5C18-AR (MeOH/1M $NaClO_4$, 3:1) and Capcell Pak C18-AG (MeOH/420mM or 840mM $NaClO_4$, 2:3) to furnish **1**(586mg), **2**(26mg), **3**(38mg), **4**(15mg), **5**(7mg), and **6**(2mg).

2: $[\alpha]_D^{21}$ +16.4°(*c* 1.00, MeOH); FABMS(neg.) *m/z* 715(M^--Na), 693, 613, 595, 511, 493; IR(KBr) 1220, 1060cm^{-1}; ^{1}H-NMR see Table 2; ^{13}C-NMR see Table 1.

3: $[\alpha]_D^{21}$ +11.4°(*c* 1.00, MeOH); FABMS(neg.) *m/z* 687(M^--Na), 665, 643, 585, 563, 545, 483, 465; IR(KBr) 1220, 1060 cm^{-1}; ^{1}H-NMR: δ 0.68(3H, s, CH_3-18), 0.75(1H, ddd, *J*= 14.7, 12.2, 3.9Hz, H-9), 0.93(3H, d, *J*=6.5Hz, CH_3-21), 1.03(3H, m, H-5, H-22, Hax-7), 1.04(3H, s, CH_3-19), 1.09(1H, m, H-14), 1.11(3H, m, H-15, H-17, H-22), 1.14(1H, m, Hax-12), 1.26(1H, m, H-16), 1.27 (1H, m, H-23), 1.31(1H, qd, *J*=13.1, 3.7Hz, Hax-11), 1.39(1H, m, H-20), 1.44(1H, m, H-23), 1.47 (1H, dd, *J*=14.7, 3.9Hz, Hax-1), 1.52(1H, m, H-8), 1.54(1H, m, Heq-11), 1.61(1H, m, H-15), 1.63(1H, m, H-5), 1.79(1H, ddd, *J*=14.7, 13.1, 2.7Hz, Hax-4), 1.84(1H, m, H-16), 1.99(2H, m, H-24), 2.00(1H, m, Heq-12), 2.08(1H, d, *J*=14.7Hz, Heq-1), 2.28(1H, dt, *J*=14.7, 2.7Hz, Heq-4), 2.36(1H, dt, *J*=12.3, 4.4Hz, Heq-7),

4.18(1H, td, *J*=11.1, 4.4Hz, H-6), 4.74(1H, q, *J*=2.7Hz, H-3), 4.81(1H, m<narrow>, H-2), 4.90(1H, d, *J*=10.5Hz, H-26), 4.96(1H, dd, *J*=17.1, 1.2Hz, H-26), 5.79(1H, ddt, *J*=17.1, 10.5, 6.5Hz, H-25); ^{13}C-NMR see Table 1.

4: $[\alpha]_D^{21}$ +27.5°(*c* 1.00, MeOH); FABMS(neg.) *m/z* 703(M^--Na), 681, 659, 601, 579, 561, 499, 481; IR(KBr) 1220, 1115, 1060cm^{-1}; ^{1}H-NMR: δ 0.68(3H, s, CH_3-18), 0.74(1H, ddd, *J*= 14.7, 12.2, 3.9Hz, H-9), 0.87(3H, d, *J*=6.6Hz, H-26), 0.87(3H, d, *J*=6.6Hz, H-27), 0.92(3H, d, *J*=6.5Hz, CH_3-21), 0.9-1.4(6H, m, H2-22, H2-23, H2-24), 1.02(1H, m, Hax-7), 1.04(3H, s, CH_3-19), 1.10(3H, m, H-14, H-15, H-17), 1.13(1H, m, Hax-12), 1.26(1H, m, H-16), 1.31(1H, qd, *J*=13.1, 3.5Hz, Hax-11), 1.38(1H, m, H-20), 1.47(1H, dd, *J*=14.7, 3.9Hz, Hax-1), 1.52(2H, m, H-8, 25), 1.53(1H, m, Heq-11), 1.61(1H, m, H-15), 1.62(1H, ddd, *J*=13.2, 11.1, 2.8Hz, H-5), 1.78(1H, ddd, *J*=15.0, 13.2, ,2.8,Hz, Hax-4), 1.83(1H, m, H-16), 2.00(1H, dt, *J*=12.7, 3.5Hz, Heq-12), 2.07(1H, dd, *J*=14.7, 1.7Hz, Heq-1), 2.27(1H, dt, *J*=15.0, 2.8,.1.1Hz, Heq-4), 2.35(1H, dt, *J*=12.3, 4.4Hz, Heq-7), 4.18(1H, td, *J*=11.1, 4.4Hz, H-6), 4.74(1H, q, *J*=2.7Hz, H-3), 4.79(1H, m<narrow>, H-2); ^{13}C-NMR see Table 1.

5: $[\alpha]_D^{21}$ +13.7°(*c* 0.56, MeOH); FABMS(neg.) *m/z* 687(M^--Na), 681, 665, 653, 585, 563, 545, 483, 465, 447; IR(KBr) 1220, 1100, 1060cm^{-1}; ^{1}H-NMR: δ 0.69(3H, s, CH_3-18), 0.75(1H, ddd, *J*= 12.3, 10.8, 3.9Hz, H-9), 0.93(3H, d, *J*=6.7Hz, CH_3-25), 0.94(3H, d, *J*=6.7Hz, CH_3-26), 0.99(3H, d, *J*=6.5Hz, CH_3-21), 1.03(1H, q, *J*=11.8Hz, Hax-7), 1.04(3H, s, CH_3-19), 1.08(1H, m, H-15), 1.09(1H, m, H-14), 1.14(1H, m, H-17), 1.16(1H, m, Hax-12), 1.24(1H, m, H-16), 1.31(1H, qd, *J*=13.2, 3.5Hz, Hax-11), 1.47(1H, dd, *J*=14.8, 3.9Hz, Hax-1), 1.52(1H, m, H-8), 1.54(1H, m, Heq-11), 1.57(1H, m, H-15), 1.63(1H, ddd, *J*=13.2, 11.1, 2.8Hz, H-5), 1.67(1H, m, H-16), 1.79(1H, ddd, *J*=15.0, 13.2, 2.8Hz, Hax-4), 1.97(1H, dt, *J*=12.8, 3.5Hz, Heq-12), 2.00(1H, dt, *J*=8.4, 6.5Hz, H-20), 2.08(1H, dd, *J*=14.8, 2.1Hz, Heq-1), 2.17(1H, 8th, d, *J*=6.7, 0.7Hz, H-24), 2.27(1H, dtd, *J*=15.0, 2.8, 1.4Hz, Heq-4), 2.35(1H, dt, *J*=12.3, 4.4Hz, Heq-7), 4.18(1H, td, *J*=11.1, 4.4Hz, H-6), 4.74(1H, q, *J*=2.8Hz, H-3), 4.80(1H, m<narrow>, H-2), 5.17(1H, ddd, *J*=15.3, 8.4, 0.7Hz, H-22), 5.26(1H, dd, *J*=15.3, 6.7Hz, H-23); ^{13}C-NMR see Table 1.

6: $[\alpha]_D^{21}$ +13.3°(*c* 0.21, MeOH); FABMS(neg.) *m/z* 747(M^--Na), 645, 627, 543, 525; IR(KBr) 3430, 1220, 1060 cm^{-1}; ^{1}H-NMR see Table 2; ^{13}C-NMR see Table 1;

Preparation of MTPA esters. Halistanol sulfate (**1**) (85.5 mg 0.113 mmol) with 1N HCl (5 mL) was refluxed for 2h. After neutralization with 2N NaOH, the resulting reaction mixture was purified on a silica gel column ($CHCl_3$/MeOH, 10:1 to 3:1) to give halistanol (**7**) (44.7 mg, 88 %).

To a stirred solution of halistanol (**7**) (9.1 mg, 0.020 mmol) and DMAP (2.5 mg, 0.021 mmol) in THF (2 mL) was added a THF (1 mL) solution of (*S*)-MTPA (4.8 mg, 0.021mmol) and DCC (21.1 mg, 0.102 mmol). The mixture was stirred at r.t. for 2 days and then chromatographed on a silica gel column ($CHCl_3$/MeOH, 15:1 to 5:1) followed by preparative TLC ($CHCl_3$/MeOH, 4:1) to yield 6-(*S*)-MTPA ester of halistanol (**9**) (1.1 mg, 8%) and unreacted halistanol(7.1 mg, 78%).

Halistanol (8.5mg) was reacted with (*R*)-MTPA to yield the 6-(*R*)-MTPA ester of halistanol (**8**) (0.9mg, 7%).

6-(*R*)-MTPA ester of halistanol (8) : ^{1}H-NMR: d 0.71 (3H, s, CH_3-18), 0.71 (1H, m, H-23), 0.78 (1H, ddd, *J*= 12.2, 10.7, 4.0Hz, H-9), 0.83 (3H, d, *J*=6.8Hz, CH_3-28), 0.85 (9H, s, tBu-26, 27, 29), 0.89(1H, m, H-22), 0.94 (3H, d, *J*=6.0Hz, CH_3-21), 0.99(1H, dqd, *J*=7.8, 6.8, 2.0Hz, H-24), 1.06(3H, s, CH_3-19), 1.09(1H, m, Hax-7), 1.13(1H, m, H-14), 1.14(1H, m, Hax-15), 1.16 (1H, m, Hax-12), 1.17 (1H, m, H-17), 1.32 (3H, m, Hax-4, Hax-11, Hax-16), 1.39(1H, m, H-20), 1.42 (1H, dd, *J*=14.2, 3.5Hz, Hax-1), 1.54 (1H, m, H-22), 1.55 (1H, m, Heq-4), 1.56 (1H, m, Heq-11), 1.58(1H, m, Heq-15), 1.60 (1H, m, H-8), 1.64 (1H, tq, *J*=12.3, 2.0Hz, H-23), 1.71(1H, *J*=12.9, 11.4, 3.0Hz, H-5),

1.87 (1H, m, Heq-16), 2.01(1H, dt, *J*=12.9, 3.7Hz, Heq-12), 2.13 (1H, dt, *J*=11.7, 4.4Hz, Heq-7), 3.54(3H, s, CH_3O-MTPA's), 3.64(1H, q, *J*=2.6Hz, H-3), 3.74(1H, m, H-2), 4.91(1H, td, *J*=11.4, 4.4Hz, H-6), 7.39-7.44, 7.50-7.52(3H, 2H, m, Ph-MTPA's).

6-(*S*)-MTPA ester of halistanol (9) : ^{1}H-NMR: d 0.70 (3H, s, CH_3-18), 0.71 (1H, m, H-23), 0.75 (1H, m, H-9), 0.83 (3H, d, *J*=6.8Hz, CH_3-28), 0.85 (9H, s, tBu-26, 27, 29), 0.89(1H, m, H-22), 0.90(1H, m, Hax-7), 0.94 (3H, d, *J*=6.6Hz, CH_3-21), 0.99(1H, m, H-24), 1.07(1H, m, H-14), 1.08(3H, s, CH_3-19), 1.09(1H, m, H-15), 1.12(1H, m, Hax-12), 1.14(1H, m, H-17), 1.16 (1H, m, Hax-12), 1.31(2H, m, Hax-11, Hax-16), 1.37(1H, m, H-20), 1.43(1H, dd, *J*=14.0, 3.3Hz, Hax-1), 1.54 (1H, m, H-22), 1.56 (1H, m, Heq-15), 1.58(1H, m, Heq-11), 1.60 (1H, m, H-8), 1.64 (1H, m, H-23), 1.74(3H, m, Heq-1,.4, Hax-4), 1.79(1H, m, H-5), 1.86(1H, m, Heq-16), 2.00(1H, dt, *J*=12.9, 3.7Hz, Heq-12), 2.05(1H, dt, *J*=11.8, 4.0Hz, Heq-7), 4.81(3H, s, CH_3O-MTPA's), 3.77(1H, m<narrow>, H-2), 3.78(1H, m, H-3), 4.91(1H, td, *J*=10.8, 4.6Hz, H-6), 7.40-7.43, 7.48-7.50(3H,2H, m, Ph-MTPA's).

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References and Notes:

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