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TETRAHEDRON

New Bioactive Polyacetylenes from the Marine Sponge *Petrosia* sp.

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ABSTRACT : Four new polyacetylenes (**3-6**) with cytotoxic activities against human tumor cell lines (A549, SK-OV-3, SK-MEL-2, XF498, and HCT15) have been isolated from the marine sponge *Petrosia* sp. They were given the trivial names of dideoxypetrosynols A-D.

Polyacetylenes have been identified as a unique class of natural products possessing diverse biological activities such as antimicrobial, antifungal, antifouling, H^+, K^+-ATPase inhibitory, HIV inhibitory, immunosuppressive, and antitumor activities.[1-7] Although acetylenes are not uncommon as components of terrestrial plants and are prevalent within the Compositae,[8] it is only within the last 20 years that biologically active polyacetylenes of unusual structural features have been reported from marine organisms.[9] Many of these polyacetylenes are isolated from the marine sponge, *Petrosia* spp.[1,10-13] In the course of our search for bioactive metabolites from the marine sponges collected from Korean water, we found that the crude extract of a marine sponge, genus *Petrosia*, deliver significant lethality to brine shrimp. We now report the isolation and structural elucidation of novel cytotoxic polyacetylene alcohols **3-6**, all closely related to the structural features of duryne(**1**)[14] and petrosynol (**2**)[15].

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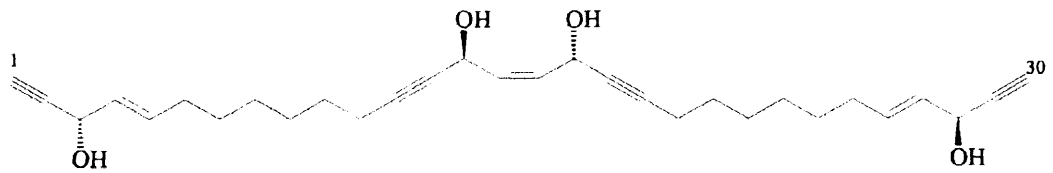

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Significant activity in the brine shrimp larvae lethality bioassay[16] (LD_{50} = 30 ppm) was detected in the methanol extract of the marine sponge. Guided by the brine shrimp lethality, the methanol extract was further fractionated between water and CH_2Cl_2, followed by partitioning of the CH_2Cl_2 solubles between 90% methanol and *n*-hexane. The 90% MeOH fraction was then partitioned again between water and CH_2Cl_2 to afford the

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CH_2Cl_2 layer which was subjected to reverse phase flash column chromatography and HPLC to yield four new polyacetylene alcohols, **3-6**. These compounds showed moderate to significant cytotoxicities against human tumor cells (Table 1). Among the four compounds, **3** was most potent in all five cell lines tested, while **5** was the least potent. These polyacetylenes showed rather selective cytotoxicities against the SK-OV-3 and SK-MEL-2 cells which are comparable to those of doxorubicin.

Table 1. *In vitro* cytotoxicities (ED_{50}, μg/ml) of compounds **3-6** against human solid tumors

compounds	A549	SK-OV-3	SK-MEL-2	XF498	HCT15
3	1.43	0.02	0.01	0.16	0.17
4	1.98	0.21	0.11	1.83	1.56
5	12.41	1.83	1.27	1.83	1.87
6	5.78	0.02	0.02	3.02	1.94
doxorubicin	0.09	0.16	0.11	0.13	1.02

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

These compounds were labile at room temperature but stable at -20 °C. No ultraviolet absorption was observed above 220 nm. Each compound of **3-6** showed very similar spectral features in the ^1H- and ^{13}C NMR. (Table 2 and 3). The molecular formula of **3**, **4**, **5** and **6** were established as $C_{30}H_{40}O_2$, $C_{30}H_{42}O_2$, $C_{30}H_{42}O_2$, and $C_{30}H_{44}O_2$, respectively, based on the HRFAB MS and NMR data.

Compound **3** was isolated as an amorphous solid. The ^1H NMR data showed signals due to one acetylenic proton (δ 2.54), one carbinol proton (δ 4.80), and three olefinic protons (δ 5.45, 5.62, 5.85) which resembled the spectrum of petrosynol.[15] The only difference in the ^1H spectrum was the signal at C-14. Instead of the carbinol proton of petrosynol, compound **3** showed that of a methylene group (δ 2.89, m) in between an olefinic and acetylenic moiety.[11] ^{13}C spectrum revealed one carbinol carbon (δ 62.72), three olefinic carbons (δ 128.40, 134.37, 126.44), and three acetylenic carbons (δ 73.93, 83.28, 80.36) when taken in $CDCl_3$. An additional acetylenic carbon was found to be overlapped with the solvent peak at δ 78.73 as shown in the spectrum taken in CD_3OD (see experimental). It seemed reasonable to conclude that the compound was symmetric and very similar to petrosynol as indicated by the NMR data alone. The geometry of the olefinic group at C-4 was assigned *E* as shown in the coupling constants of the ^1H NMR while that at C-15 was assigned *Z* as indicated in the IR spectrum. The doublet at 969 cm^{-1} was indicative of a *E* double bond while a medium absorption arising from the Z double bond at 661 cm^{-1} was observed. The absolute stereochemistry of **3** was examined by the modified Mosher's method.[17,18] (*R*)- and (*S*)- α-methoxy-α-trifluoromethylphenylacetic (MTPA) esters of this compound were synthesized and analyzed as previously reported.[18,19] Δδ values (δ_S-δ_R) obtained are summarized in Fig.1. The ^1H NMR spectra of MTPA derivatives suggested them to be 1:1 diastereomeric mixtures. The spectral pattern of the *R*-MTPA ester of this compound was identical to that of the *S*-MTPA ester. Both spectra showed two different pairs of acetylenic and olefinic protons indicating the presence of both (*R*) and (*S*) carbinol carbons. The absolute stereochemistry at C-3 and C-28, therefore, could not be definitely assigned due to the resulting diastereomeric mixtures of the MTPA esters. It is possible that **3** was an 1:1 mixture of (3*S*, 28*S*) and (3*R*, 28*R*) or a single enantiomer of (3*S*, 28*R*). Hallock *et al* have reported that diastereomeric mixtures have resulted from acetylenic alcohols from sponges with the Mosher's method.[2] However, it is not clear whether enantiomeric mixtures of these compounds originated intact from the marine sponge or racemization has occurred during the process of isolation or synthesis of the esters. Scarcity of material has hampered further investigation into this matter. The structure of compound **3** was thus determined to be triaconta-1,12,18,29-tetrayn-4*E*,15*Z*,26*E*-trien-3,28-diol, and given the trivial name dideoxypetrosynol A.

Table 2. ^{1}H NMR data of compounds 3-6 *(200 MHz, $CDCl_3$)

position	3	4	5	6
1	2.54 (d, 2.0)	2.54 (d, 2.2)	2.55 (d, 1.9)	2.44 (d, 2.1)
2	—	—	—	—
3	4.80 (brd, 5.0)	4.81 (brd, 5.8)	4.82 (brd, 5.9)	4.34 (td, 6.7, 2.1)
4	5.62 (dd,15.0,5.0)	5.58 (ddt,15.3,5.8,1.5)	5.59 (dd, 15.0,6.3)	1.67 (m)
5	5.85 (dt,15.0,6.6)	5.86 (dtd,15.3,6.0,1.0)	5.90 (dt,15.0,6.6)	\
6	2.03 (m)	2.03 (m)	2.03 (m)	|
7	\	\	\	| 1.30-1.50 (m)
8	|	|	|	|
9	| 1.30-1.50 (m)	| 1.30-1.50 (m)	| 1.30-1.50 (m)	|
10	/	/	/	/
11	2.11 (m)	2.11 (m)	2.12 (m)	2.11 (m)
12	—	—	—	—
13	—	—	—	—
14	2.89 (m)	2.91 (m)	2.91 (m)	2.90 (m)
15	5.45 (t, 4.5)	5.46 (t, 4.4)	5.33-5.43 (m)	5.47 (t, 4.4)
16		5.46 (t, 4.4)	5.33-5.43 (m)	
17		2.91 (m)	2.77 (m)	
18		—	5.33-5.43 (m)	
19		—	5.33-5.43 (m)	
20		2.11 (m)	2.12 (m)	
21		\	\	
22		|	|	
23		|	| 1.23-1.30 (m)	
24		| 1.30-1.50 (m)	/	
25		|	2.11 (m)	
26		/	5.90 (dt, 15.4, 6.6)	
27		1.70 (m)	5.59 (dd, 14.9, 6.3)	
28		4.34 (td, 5.5, 2.0)	4.82 (d, 5.9)	
29		—	—	
30		2.44 (d, 2.0)	2.55 (d, 1.9)	

*Assignments were aided by COSY experiment. Multiplicities and coupling constants in parentheses.

Compound **4** was also an amorphous solid which showed similar NMR data with those of compound **3**. However, the presence of additional olefinic carbons (δ 126.49, 126.45), additional acetylenic carbons, as well as an additional carbinol carbon, and the observed number of methylene carbons (16, compared to 7 of compound **3**) together with the mass data indicated that this was a nonsymmetric compound. Moreover, the olefinic protons at δ 5.58 and 5.86 integrated to one each in the ^{1}H NMR spectra, indicating the presence of a double bond only at C-4 and not at C-26. **4** was therefore determined to be a polyacetylene alcohol which differed from **3** only at C-26. The geometry at the double bonds for C-4 was assigned as *E* according to the coupling constant in the ^{1}H NMR (see table 2) and as *Z* for C-15 based on the similarities in ^{13}C NMR chemical shifts of C-14 and C-17 (δ 17.15) to that of **3** (δ 17.12, see table 3). The absolute stereochemistry was also similar to that of **3** suggesting a racemic mixture. However, the chiral center at C-28 was identified as (*S*) by the Mosher's method while that at C-3 seemed to be both (*R*) and (*S*), implying that **4** was an 1:1 mixture of (3*S*, 28*S*) and (3*R*, 28*S*). Thus the structure of compound **4** was determined to be triaconta-1,12,18,29-tetrayn-4*E*,15*Z*-dien-3,28-diol, and given the trivial name dideoxypetrosynol B.

Compound **5** was a pale yellow oil which again showed structural similarities to **3**. The difference in NMR spectra was in the number of olefinic carbons and acetylenic carbons. The spectra indicated the presence of eight olefinic carbons (δ 125.26, 127.16, 128.40, 128.44, 129.44, 130.59,134.44, 134.51) and four acetylenic carbons, (δ 73.97, 78.21, 80.14, 83.45) suggesting two additional olefinic carbons and two less acetylenic carbons compared to **3**. The methylene protons at δ 2.77 indicated that it was positioned between two olefinic groups unlike the methylene protons at δ 2.91 which was positioned between an olefinic group and an acetylenic

group at C-14. Since these methylene protons integrated to a 2:2 ratio, the structure of this compound was deduced to be that at which the triple bond at C-18 of **3** was reduced to a double bond. 4*E*, 15*Z*, 18*Z*, 26*E*-Geometry was assigned on the basis of ^{1}H coupling constants and ^{13}C chemical shifts as in the case of **4**. The geometry of the double bonds at C-4 and C-26 was determined to be *E* according to the ^{1}H coupling constants while those of C-15 and C-18 was determined to be *Z* according to the ^{13}C chemical shift of the neighboring carbons of C-17 and C-20.[20] Absolute stereochemistry was identical to that of **3** suggesting again a racemic mixture of (3*S*, 28*S*) and (3*R*, 28*R*) or a single enantiomer of (3*S*, 28*R*) or (3*R*, 28*S*). The structure of compound **5** was therefore determined to be triaconta-1,12,29-triyne-4*E*,15*Z*,18*Z*,26*E*-tetraen-3,28-diol, and given the trivial name dideoxypetrosynol C.

Table 3. ^{13}C NMR data of compounds **3-6** (50 MHz, $CDCl_3$)

position	3	4	5	6
1	73.93	73.97	73.97	72.81
2	83.28	83.36	83.45	85.05
3	62.72	62.75	62.78	62.36
4	128.40	128.44	128.44[f]	37.67
5	134.37	134.40	134.51[e]	24.97
6	31.79	31.82	31.84[d]	28.81[c]
7	28.79[c]	28.61[c]	28.77[c]	28.96[c]
8	28.61[c]	28.78[c]	28.67[c]	29.01[c]
9	28.58[c]	28.99[c]	28.64[c]	29.16[c]
10	28.56[c]	29.13[c]	28.62[c]	29.35[c]
11	18.66	18.69	18.74	18.75
12	*[a]	*[a]	78.21[a]	*[a]
13	80.36[a]	80.38[a]	80.14[a]	80.47[a]
14	17.12	17.15	17.21	17.19
15	126.44	126.45[b]	127.16[b]	126.53
16		126.49[b]	129.44[b]	
17		17.15	25.50	
18		80.47[a]	125.26[b]	
19		*[a]	130.59[b]	
20		18.72	27.18	
21		29.45[c]	29.02[c]	
22		29.33[c]	29.45[c]	
23		28.91[c]	29.06[c]	
24		28.64[c]	28.89[c]	
25		28.58[c]	31.89[d]	
26		24.94	134.44[e]	
27		37.60	128.40[f]	
28		62.29	62.78	
29		85.00	83.45	
30		72.83	73.97	

* Signals overlapping with the residual solvent peaks. Chemical shifts of these signals were measured in the spectra of CD_3OD solution (see experimental)

a, b, c, d, e, f Assignments with the same superscript in the same column may be interchanged.

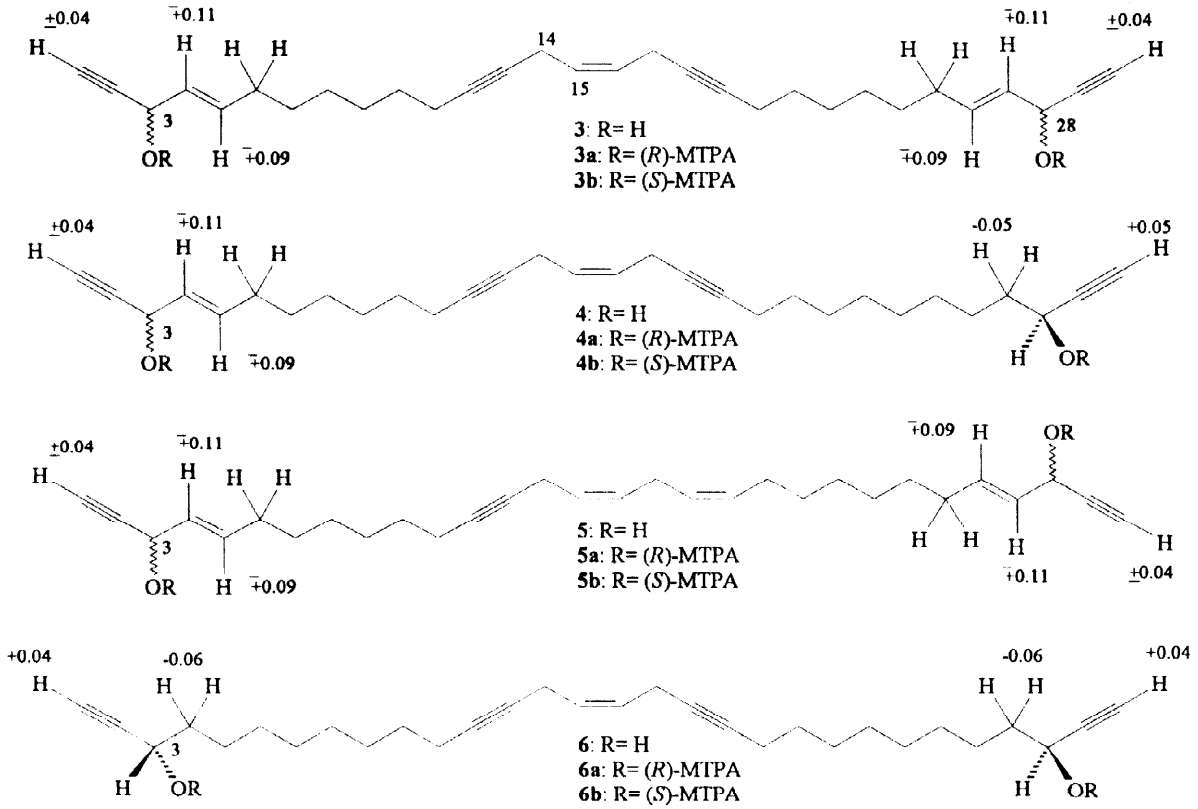

Figure 1. Structures and Δδ values (ppm) obtained for the MTPA esters of **3**, **4**, **5**, and **6**.

Compound **6** was a white solid which seemed to be a symmetric compound according to the NMR spectra as in the case of **3**. Except for showing only one olefinic carbon and hydrogen (δ 5.47, ^{1}H, δ 126.53, ^{13}C), the NMR spectra was quite similar to that of **3**, suggesting the structure of which C-4 and C-26 are saturated. This was also confirmed by the mass data. Similar to **3**, and **4**, the geometry at the C-15 was assigned as *Z*. However, unlike **3**, **4**, and **5**, application of Mosher's method revealed an enantiomerically pure compound with an optical activity of $[\alpha]_D^{23}$ +38° (c 0.05, $CHCl_3$) where an (*S*) configuration could be assigned to both the C-3 and C-28 positions. The structure of compound **6** was thus determined to be (3*S*, 28*S*)-triaconta-1,12,18,29-tetrayn-15*Z*-en-3,28-diol, and given the trivial name dideoxypetrosynol D.

Interestingly, the stereochemistry of the carbinol carbon devoid of adjacent double bond was shown to be an (*S*) configuration, while those of the carbinol carbon with adjacent double bond were shown to be both (*S*) and (*R*) configuration.

EXPERIMENTAL

General. ^{1}H and ^{13}C spectra were recorded on a Bruker AC200. Chemical shifts were reported in reference to the respective residual solvent peaks (δ 7.24 and 77.0 for $CDCl_3$, and δ 3.3 and 49.0 for CD_3OD). IR spectra was recorded on a BOMEM Michaelson series FTIR. LR and HR FABMS data were recorded on JEOL JMS-HX110/110A. Optical rotation was measured in chloroform on a DIP-370 digital polarimeter, JASCO. HPLC was performed on a Gilson 370 pump with a YMC ODS-H80 (250 x 4.6 mm I.D., S-4 μm) column and a Perkin Elmer RP-18 Newguard cartridge (15 x 3.22 mm, 7μ) using a Shodex RI-71 detector at a flow rate of 2 ml/min.

Sponge Material. The sponge was collected by hand using SCUBA (15-25m deep) in July, 1995, off Komun Island, Korea. The collected sample was frozen immediately and kept at -20°C until processed. The sponge was in a piece of plate form and measured 6.0x1.5 cm and 1.2-2.0 cm thick. The surface was smooth and had many oscules of 1.5-3.5 μm in diameter. The color was purple on top and beige underneath in life while consistency was very hard. This sponge was similar to *Petrosia corticata* in spicules, but differed in having only oxeas (no large strongylotes). A voucher specimen was deposited in the Natural History Museum, Han Nam University, Taejeon, Korea.

Isolation of compounds. The sponge (14.5 kg) was extracted with MeOH at room temperature. Guided by the brine shrimp lethality assay, the MeOH solubles was fractionated between water and CH_2Cl_2. The CH_2Cl_2 solubles was further partitioned between 90% methanol and *n*-hexane to yield 58.15 g and 61.5 g respectively. The 90% methanol fraction was then partitioned between water and CH_2Cl_2 to afford 34 g of the CH_2Cl_2 extract which was subject to a reverse phase flash column chromatography (YMC Gel ODS-A, 60Å 500/400 mesh) eluting with solvent systems of 25 - 0 % H_2O/methanol and acetone to obtain 8 fractions. Fraction 4 (4.65 g) which showed significant brine shrimp lethality (LD_{50} < 1 ppm) was further subjected to normal phase flash column chromatography (Kieselgel 60, 230-400 mesh), eluting with 0-100 % EtOAc/$CHCl_3$ and 0 - 100 % methanol/EtOAc. Fraction 4-4 which eluted at 10 % EtOAc/$CHCl_3$ afforded 355.9 mg of a mixture which showed significant brine shrimp lethality (LD_{50} < 1 ppm). Fraction 4-4 was then separated by reverse phase HPLC(YMC ODS-H80, 4 μm, 80 Å) eluting with 15 % H_2O/MeOH to obtain **3** (23.2 mg), **4** (18.9 mg), **5** (7.4 mg), and **6** (7.8 mg).

Dideoxypetrosynol A (3). amorphous solid; FABMS *m/z:* 455.2897 for $C_{30}H_{40}O_2Na$ $(M+Na)^+$ (calcd. 455.2926); IR (film) 3355, 3289, 2928, 2854, 1660, 1433, 1283, 969 (doublet), 726, 661, 628 cm^{-1}; ^1H NMR (200 MHz, CD_3OD) δ 2.86 (2H, d, *J*=2.4 Hz, H-1, 30), 4.74 (2H, brd, *J*=5.3, H-3, 28), 5.54 (2H, ddt, *J*=15.2, 5.3, 1.5, H-4, 27), 5.85 (2H, dtd, *J*=15.2, 6.2, 1.0, H-5, 26), 2.06 (4H, m, H-6, 25), 1.30-1.50 (16H, m, H-7-10, 21-24), 2.12 (4H, m, H-11, 20), 2.89 (4H, m, H-14, 17), 5.43 (2H, t, *J*=4.1, H-15, 16); ^{13}C NMR (50 MHz, CD_3OD) δ 74.60 (C-1, 30), 84.85 (C-2, 29), 63.24 (C-3, 28), 130.77 (C-4, 27), 134.18 (C-5, 26), 32.99 (C-6, 25), 29.76 - 30.14 (C-7, 8, 9 ,10, 21, 22, 23, 24), 19.46 (C-11, 20), 78.73 (C-12, 19 or 13, 18), 81.02 (C13, 18 or 12, 19), 17.75 (C-14, 17), 127.70 (C-15, 16).

Dideoxypetrosynol B (4). amorphous solid; FABMS *m/z*: 457.3098 for $C_{30}H_{42}O_2Na$ $(M+Na)^+$ (calcd. 457.3082);^1H NMR (200 MHz, CD_3OD) δ 2.86 (1H, d, *J*=2.4 Hz, H-1), 4.74 (1H, brd, *J*=5.5, H-3), 5.54 (1H, ddt, *J*=15.3, 5.5, 1.5, H-4), 5.85 (1H, dtd, *J*=15.3, 6.0, 1.0, H-5), 2.03 (2H, m, H-6), 1.30-1.50 (16H, m, H-7-10, 21-24), 2.11 (4H, m, H-11, 20), 2.91 (4H, m, H-14, 17), 5.43 (2H, t, *J*=4.3, H-15, 16), 1.63 (2H, m, H-27), 4.24 (1H, td, *J*=6.6, 2.2, H-28), 2.75 (1H, d, *J*=2.2, H-30);^{13}C NMR (50 MHz, CD_3OD) δ 74.52 (C-1), 86.32 (C-2, 29), 63.17 (C-3), 130.70 (C-4), 134.10 (C-5), 32.92 (C-6), 29.69 - 30.17 (C-7-10), 19.40 (C-11), 78.63, 80.97 (C-12, 13), 17.67 (C-14, 17), 127.63 (C-15, 16), 80.94, 78.64 (C-18, 19), 19.39 (C-20), 29.71 - 30.60 (C-21-25), 26.28 (C-26), 38.95 (C-27), 62.62 (C-28), 73.39 (C-30).

Dideoxypetrosynol C (5). pale yellow oil; FABMS *m/z*: 457.3079 for $C_{30}H_{42}O_2Na$ $(M+Na)^+$ (calcd. 457.3082); ^1H NMR (200 MHz, CD_3OD) δ 2.86 (2H, d, *J*=1.3 Hz, H-1, 30), 4.74 (2H, brd, *J*=6.3, H-3, 28), 5.54 (2H, ddt, *J*=15.3, 6.2, 1.3, H-4, 27), 5.85 (2H, dtd, *J*=15.2, 6.5, 0.9, H-5, 26), 2.04 -2.08 (8H, m, H-6, 11, 20, 25), 1.28-1.35 (16H, m, H-7-10, 21-24), 2.90 (2H, m, H-14), 5.33-5.43 (4H, m, H-15, 16, 17, 18), 2.80 (2H, m, H-17); ^{13}C NMR (50 MHz, CD_3OD) δ 74.49 (C-1, 30), 84.87 (C-2, 29), 63.20 (C-3, 28), 130.73 (C-4), 134.17 (C-5), 32.88, 32.89, (C-6, 25), 29.69 - 30.12, (C-7-10), 19.43 (C-11), 79.10 (C-12), 80.75 (C-13), 17.81, (C-14), 128.42 (C-15), 130.76 (C-16), 26.43 (C-17), 126.46 (C-18), 131.48 (C-19), 28.16 (C-20), 30.14 - 30.67, (C-21-24), 134.12 (C-26), 130.36 (C-27).

Dideoxypetrosynol D (6). amorphous solid; $[\alpha]_D^{23}$ +38° (c 0.05, $CHCl_3$); FABMS *m/z*: 459.3245 for $C_{30}H_{44}O_2Na$ $(M+Na)^+$ (calcd. 459.3239); ^1H NMR (200 MHz, CD_3OD) δ 2.75 (2H, d, *J*=2.0 Hz, H-1, 30), 4.26 (2H, brd, *J*=5.3, H-3, 28), 1.63 (4H, m, H-4, 27), 1.28-1.40 (16H, m, H-5-10, 21-26), 2.12 (4H, m, H-11, 20), 2.90 (4H, m, H-14, 17), 5.43 (2H, t, *J*=4.4, H-15, 16); ^{13}C NMR (50 MHz, CD_3OD) δ 73.33 (C-1, 30), 86.35 (C-2, 29), 62.65 (C-3, 28), 38.96 (C-4, 27), 26.26 (C-5, 26), 29.84 - 30.34 (C-6-10, 21-25), 78.64 (C-12, 19), 80.99 (C13, 18), 17.67 (C-14, 17), 127.64, (C-15, 16).

MTPA esters of compounds 3, 4, 5, and 6 (3a, 3b, 4a, 4b, 5a, 5b, 6a, 6b). To solutions of **3**, **4**, **5**, and **6** (0.5-1 mg) in dry pyridine (20 μl), were added 4 x molar excess of (*R*) or (*S*) α-methoxy-α-trifluoromethylphenylacetic acid chloride (MTPA-Cl). The mixture was allowed to stand at room temperature for 16 h. 3-[(Dimethylamino)propyl]amine (equimolar to MTPA-Cl) was added, and after 10 minutes of standing, the solvent was evaporated off. The residue was purified on silica gel in a pasteur pipette eluting with dichloromethane. Both *R*- and *S*-esters were prepared for each compound and characterized based on ^1H-NMR spectral data.

Dideoxypetrosynol A MTPA esters (3a, 3b). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (16H, m), 2.01-2.11 (8H, m), 2.57 (1H, d, *J*=2.3 Hz), 2.61 (1H, d, *J*=2.3 Hz), 2.90 (4H, m), 3.53 (3H, d, *J*=0.94), 3.57 (3H, d, *J*=0.96), 5.46 (2H, t, *J*=4.3), 5.47 (1H, dd, *J*=15.0, 6.0), 5.58 (1H, dd, *J*=15.0, 6.0), 5.99 (1H, dt, *J*=14.3, 6.5), 6.02 (2H, m), 6.08 (1H, dt, *J*=14.3, 6.5), 7.37 (6H, m), 7.49 (4H, m).

Dideoxypetrosynol B (R)-MTPA ester (4a). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (40H, m), 1.79 (4H, m), 2.01-2.11 (12H, m), 2.47 (2H, d, *J*=2.0), 2.57 (1H, d, *J*=2.3 Hz), 2.61 (1H, d, *J*=2.3 Hz), 2.90 (8H, m), 3.53 (9H, s), 3.57 (3H, s), 5.46 (4H, t, *J*=3.9), 5.47 (1H, dd, *J*=15.4, 6.0), 5.58 (1H, dd, *J*=15.4, 6.5), 5.99 (1H, dt, *J*=15.0, 6.5), 6.01 (4H, m), 6.08 (1H, dt, *J*=15.0, 6.5), 7.34 (12H, m), 7.51 (8H, m).

Dideoxypetrosynol B (S)-MTPA ester (4b). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (40H, m), 1.74 (4H, m), 2.01-2.11 (12H, m), 2.52 (2H, d, *J*=2.0), 2.57 (1H, d, *J*=2.3 Hz), 2.61 (1H, d, *J*=2.3 Hz), 2.91 (8H, m), 3.53 (3H, s), 3.58 (9H, s), 5.46 (4H, t, *J*=3.9), 5.47 (1H, dd, *J*=15.4, 6.2), 5.58 (1H, dd, *J*=15.4, 6.5), 5.99 (1H, dt, *J*=15.0, 6.5), 6.01 (4H, m), 6.08 (1H, dt, *J*=15.0, 6.5), 7.34 (12H, m), 7.50 (8H, m).

Dideoxypetrosynol C MTPA esters (5a, 5b). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (16H, m), 1.99-2.15 (8H, m), 2.57 (1H, d, *J*=2.0), 2.61 (1H, d, *J*=2.0 Hz), 2.76 (2H, m), 2.91 (2H, m), 3.54 (3H, s), 3.58 (3H, s), 5.27-5.40 (4H, m), 5.44 (1H, dd, *J*=15.0, 6.0), 5.55 (1H, dd, *J*=15.0, 6.0), 5.98 (2H, m), 6.02 (1H, dt, *J*=15.0, 6.5), 6.11 (1H, dt, *J*=15.0, 6.5), 7.38 (6H, m), 7.49 (4H, m).

Dideoxypetrosynol D (R)-MTPA ester (6a). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (24H, m), 1.82 (4H, m), 2.01-2.11 (4H, m), 2.48 (2H, d, *J*=2.0), 2.90 (4H, m), 3.53 (6H, s), 5.46 (4H, m), 7.37 (6H, m), 7.50 (4H, m).

Dideoxypetrosynol D (S)-MTPA ester (6b). ^1H NMR (200 MHz, $CDCl_3$) δ 1.23-1.43 (24H, m), 1.76 (4H, m), 2.01-2.11 (4H, m), 2.52 (2H, d, *J*=2.0), 2.90 (4H, m), 3.57 (6H, s), 5.47 (4H, m), 7.36 (6H, m), 7.51 (4H, m).

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