Yardenone A and B: New Cytotoxic Triterpenes from the Indian Ocean Sponge *Axinella cf. bidderi*

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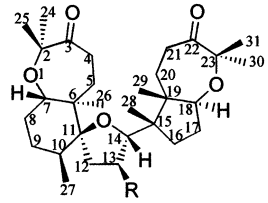
Two new polyepoxysqualene-derived triterpenes, yardenone A (**1**) and B (**2**), together with the known yardenone (**3**) and sodwanone A (**4**), have been isolated from the marine sponge *Axinella cf. bidderi* from Yemen's Socotra Island in the Indian Ocean. The structures were elucidated using spectroscopic data. The relative stereochemistry was established by the analysis of ROESY spectra as well as coupling constants and molecular modeling. Furthermore, the absolute configuration of **1** was confirmed by the advanced Mosher's method. The cytotoxicity of these compounds was evaluated against a NSCLC cell line.

The genus *Axinella* (family Axinillidea) is known to be a source of a variety of metabolites such as bromo compounds, cyclopeptides, polyethers, sterols, and terpenes.[1] Recently the sodwanones, polyepoxysqualene-derived triterpenes,[2] have been reported from *A. weltneri*.[3] Related triterpenoids have been isolated from three other sponges: *Siphonochalina siphonella* (sipholanes),[4] *Raspaciona aculeata* (raspacionins),[5] and *Ptilocaulis spiculifer* (yardenones).[3] Several of these reported polyepoxysqualene derivatives have cytotoxic activity.[6]

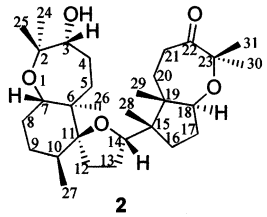
As part of our ongoing search to isolate biologically active metabolites from marine organisms,[7] extracts of a collection of Indian Ocean sponges were screened for cytotoxicity and antimicrobial activity. We studied the ethanolic crude extract of the marine sponge *A. bidderi*, which showed antiproliferative activity in the initial sea-urchin egg bioassay.[8] Herein, isolation of two novel polyepoxysqualene-derived triterpenoids, yardenone A (**1**) and B (**2**), together with the known yardenone (**3**) and sodwanone A (**4**), and elucidation of the structures of these new compounds by spectroscopic analyses are described. It was later determined that the new triterpenoids were not responsible for the selective cytotoxicity of the heptane extract; however, they displayed weak inhibition of lung carcinoma cells NSCLC-N6 L16.

Results and Discussion

The ethanolic *A. bidderi* crude extract was subjected to solvent partitioning (see Experimental Section). The cytotoxic activity was found to be concentrated in the resulting heptanic extract. The heptanic residue was subjected to Si 60 gel chromatography using different solvent mixtures of increasing polarity to obtain 150 fractions. Selected fractions were subsequently chromatographed on reversed-phase C_{18} HPLC then on Si 60 gel chromatography to yield two novel triterpenes, yardenone A (**1**) and yardenone B (**2**), as the major components of the crude extract along with compound **3**, found to be identical to the known yardenone, by its mass and NMR spectral data (ESIMS and ^{1}H, ^{13}C, HSQC, HMBC, and ROESY NMR).[9] Compound **4** was



1 R = OH
3 R = H



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crystallized in methanol and was found to be identical by X-ray diffraction analysis with the known sodwanone A previously isolated from *A. weltneri*.[10]

Compound **1** was obtained as colorless needles. Its molecular formula was deduced as $C_{30}H_{48}O_6$ by HRFABMS ($C_{30}H_{48}O_6Li$ *m*/*z* 511.35970, calcd 511.36109) (seven double-bond equivalents). The IR spectrum suggested the presence of hydroxyl (3568 cm^{-1}) and carbonyl (1708 cm^{-1}) groups. *J* modulated and HSQC spectra showed the presence of eight quaternary carbons, five methine, nine methylene, and eight methyl groups. The ^{13}C NMR spectrum in $CDCl_3$ of **1** (Table 1) showed signals for two keto-carbonyls (δ_C 217.3 and 216.5) and seven oxygenated carbons, three of which are quaternary (δ_C 88.3, 82.7, 81.7) and four of which are tertiary (δ_C 88.1, 82.1, 76.5, 72.5). The ^{1}H NMR spectrum of **1** (Table 2) showed the presence of seven tertiary methyls and one secondary at δ_H 1.04 (d, J = 6.8 Hz). The ^{1}H NMR spectrum further revealed a total of 47 protons attached to carbon, implying the presence of only one hydroxyl group. As the molecular formula contains seven double-bond equivalents, and neither olefinic resonance (^{13}C NMR) nor corresponding IR absorption bands could be observed, **1** had to be pentacyclic.

The HMBC correlations between H-7 and two quaternary carbons C-2 (δ_C 81.7) and C-6 (δ_C 45.4) and between H-18 and two quaternary carbons C-19 (δ_C 48.6) and C-23 (δ_C 82.7) indicated the presence of two oxepane rings (A

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Table 1. ^{13}C NMR Data for Yardenones **1**−**3** (125 MHz)[a]

C	**1**[b]	**1**[c]	**2**[c]	**3**[c]
2	81.5	81.7	76.2	81.6
3	217.9	217.3	72.1	217.5
4	34.8	34.8	30.3	35.0
5	31.8	32.0	33.3	32.1
6	45.3	45.4	45.7	45.7
7	76.5	76.5	80.0	77.0
8	30.2	30.1	29.6	30.1
9	28.6	28.4	28.9	28.9
10	35.7	36.0	35.8	35.8
11	87.8	88.3	90.7	90.3
12	39.7	39.6	28.4	28.5
13	71.4	72.5	29.2	29.3
14	87.5	88.1	84.7	84.8
15	48.9	48.7	48.8	48.8
16	27.5	27.7	26.0	26.3
17	28.7	28.5	29.2	28.4
18	82.0	82.1	82.0	82.1
19	48.6	48.6	48.2	48.3
20	31.2	31.5	31.4	31.5
21	35.6	35.6	35.6	35.6
22	215.0	216.5	216.5	216.6
23	82.5	82.7	82.7	82.6
24	20.5	20.3	22.1	20.3
25	26.9	26.9	24.3	27.0
26	15.2	15.2	16.2	15.2
27	18.2	18.1	18.0	17.8
28	19.7	19.6	21.0	20.9
29	15.9	15.7	15.7	15.7
30	22.2	22.0	21.8	21.9
31	26.2	26.2	26.2	26.2

[a] Assignments were made by *J modulated* and HSQC data. [b] In DMSO-d_6. [c] In $CDCl_3$.

and E). The *gem*-dimethyl protons (Me-24, Me-25) showed HMBC correlations with the keto carbon C-3 (δ_C 217.3) and C-2. Likewise, similar correlations were noted between the protons of the second *gem*-dimethyl groups (Me-30, Me-31) and C-22 (δ_C 216.5) and C-23 (Table 2). The COSY spectrum showed a cross-peak at H-27/H-10, indicating C-10 bore Me-27. In fact, most of NMR spectral data recorded for compound **1** were similar to those of the known yardenone[9] isolated from *P. spiculifer* except for H/C-16, H/C-28, and THF ring signals due to the presence of the OH group. To establish the remaining structure of **1**, NMR spectra were measured in the nonexchangeable solvent DMSO-d_6.

Thus, the COSY spectrum showed a cross-peak between the OH proton at δ_H 4.90 and H-13 at δ_H 3.83 (^3J). In the HMBC spectrum, the OH proton was correlated with the C-12 (^3J), C-13 (^2J), and C-14 (^3J). On these grounds, the OH location was assigned at C-13. The presence of the spiro THF at C-11 (ring C) was clearly demonstrated by the HMBC experiment, which showed a correlation between H-14 at δ_H 3.35 and C-11 (^3J) and C-12 (^3J) and C-13 (^2J). In $CDCl_3$, H-26 showed a correlation with C-11 and H-28 with C-14. Moreover, when compared with **3**, the upshifted resonance of C-11 in **1** (δ_C 88.3 in $CDCl_3$ and δ_C 87.8 in DMSO-d_6) was in accordance with a spiro oxygen-bearing carbon.

Much of the suggested relative stereochemistry of yardenone A (**1**) was based on measured ROE and coupling constants, whenever measurable, except for the H/OH-13. The shielded angular Me-26α signal (δ_C 15.2) and the large coupling constant for H-7 (J = 11.2 Hz) [which is typical for an axial position] suggested a *trans*-diaxial A/B ring junction. The W−J coupling between H-26α and H-5a suggested H-5a was β-axial oriented. The large coupling constant for H-4a (J = 13.8 Hz) and its ROESY correlation with H-24 suggested H-4a was α-axial oriented and Me-24 α-oriented. On the other side of the ring system, H-7β showed ROE with H-25. The H-26α showed ROE with H-10 and with the methylene protons H-12, indicating Me-27 was β-configured. Furthermore, as H-14 showed ROE with H-27 and H-28, the β-configuration was assigned to the oxygen portion of the THF ring, H-14 and Me-28. H-29 showed ROE with H-28β, indicating that Me-29 was β-oriented. The shielded angular Me-29β signal (δ_C 15.9) suggested that Me-29 and H-18 were *trans*-diaxial. The large coupling constant value of H-21a (J = 13.7 Hz) and its ROESY correlations with H-29β and H-31 suggested a β-axial orientation for H-21a. The W−J between H-29 and H-20a suggested an α-axial position for H-20a. The proton H-18 (1H, t, J = 8.5 Hz) was determined to be in the axial position on the basis of its coupling constant, and the ROESY correlation between H-18 and H-30α indicated H-18 was α-configured (Figure 1).

To determine the H/OH-13 configuration, molecular modeling, an additional tool for NMR structure determination,[11] was also applied on compound **1**. The models of both 13*R* and 13*S* configurations were built in accordance with the ORTEP drawing of yardenone[9] and energy minimized using the MM2 force field method.[12,13] As one free bond (C_{14}−C_{15}) links the rings C and D, the energy of the different rotamers were also minimized. Thus, the obtained dihedral angles (H_{13}−C_{13}−C_{14}−H_{14}) were used to calculate the vicinal coupling constants $^3J_{H-13-H-14}$ of those isomers/rotamers from the Karplus relationship[14] (Table S1). The calculated values of OH-13β rotamers ($8.3 \leq J \leq 9.1$ Hz) were in agreement with the coupling constant measured in the NMR experiment (J = 8.9 Hz in $CDCl_3$ and J = 9.3 Hz in DMSO-d_6). The OH-13β rotamer ($\theta_{H14-C14-C15-C28}$ = 66°) was found to have the minima steric energy. Additionally, C-16 (δ_C 27.7) of **1** compared to **3** was present far downfield ($\Delta\delta$ = +1.4 ppm) due to the influence of the oxygen atom. This fact was supported by the interatomic distance measured between O-13 and C-16 in the molecular models. In most of the OHβ rotamers, the carbon C-16 was found to be the nearest carbon of the D ring from the oxygen O-13. In the molecular model, the dihedral angles were also in accordance with the large coupling constants observed for H-4α, H-5β, H-7β, H-18α, H-20α, and H-21β. Therefore on the basis of all the above evidence, the structure of **1** was established as yardenone A, the 13-OHβ-derivative of yardenone.

The absolute configuration of yardenone A (C-13) was confirmed by application of the modified Mosher's method.[15] Treatment of **1** with *R*(−)- and *S*(+)-methoxytrifluoromethylphenylacetic acid chloride (MTPACl) yielded the corresponding MTPA esters. The distribution of positive and negative $\Delta\delta$ ($\delta_S - \delta_R$) values around the MTPA esters (Figure 2) implied *S*-stereochemistry for C-13 in accordance with the rule for determining absolute configurations.[14] These results ascertained the β-position of the hydroxyl group on C-13 in the 13*S*-configuration of yardenone A.

Compound **2** was obtained as the major compound from the heptanic extract. Its molecular formula was established as $C_{30}H_{50}O_5$ by HRFABMS ($C_{30}H_{50}O_5Li$ *m/z* 497.38360, calcd 497.38182). *J modulated* and HSQC spectra showed the presence of seven quaternary carbons, five methine, 10 methylene, and eight methyl groups. As previously discussed, compound **2** had to be pentacyclic and contained one OH group. The ^{13}C NMR signals of **2** were very similar to those of yardenone (**3**) except for the resonance values of the ring A (Table 1). As the major difference, the carbonyl signal of compound **3** at δ_C 217.5 was shifted upfield to δ_C

Table 2. ^{1}H NMR Data and COSY and HMBC Correlations for Yardenones **1** and **2** (500 MHz)[a]

	1			**2**	
H	δ_H[b]	COSY[c]	HMBC	δ_H	HMBC
3β ax				3.44 dd (11.1, 5.4)	2, 4, 5, 6
4β ax	3.14 ddd (13.8, 10.9, 2.3)	4α, 5α/β	3, 5, 6	1.54 m	3
4α eq	2.15 ddd (10.0, 6.8, 2.3)	4β, 5α/β	2, 6	1.43 m	
5β ax	1.84 m	4α/β, 26α	6, 26	1.88 m	
5α eq	1.47 m	4α/β		1.31 m	3, 6
7β ax	3.24 dd (11.2, 5.5)	8a/b	2, 5, 6, 8	3.61 d (10.0)	2, 5, 24, 25
8	1.64 m	7β, 9b	6, 7, 10	2.02 m (13.0, 11.4, 1.5)	6, 7
8	1.54 m	7β, 9b	7, 9, 10	1.44 m	7
9	1.56 m	9b	7, 10, 11	1.48 m	
9	1.34 m	8a/b, 10α	10, 27	1.30 m	10
10α	1.82 m	9b, 27β	6, 10	1.69 m	11
12	2.40 dd (14.0, 8.9)	12b, 13α	6, 10, 13	1.85 m	6
12	1.83 m	12a, 13α	11, 13, 26	1.76 m	11
13α	4.06 m	12a/b, 14β	15	1.71 m	
13				1.52 m	12, 14, 15
14β	3.54 d (d, 8.9)	13α	12, 15, 28	3.75 dd (11.6, 5.0)	15, 16, 19
16	1.69 m		14, 15	1.89 m	
16	1.49 m			1.39 m	
17	1.68 m	18α	15, 19	1.87 m	
17	1.53 m	18α		1.57 m	
18α ax	3.96 t (8.5)	17a/b	19, 23, 29	4.19 t (8.8)	17, 19, 20, 23
20α ax	1.70 m	21α/β, 29β	22, 29	1.78 m	21
20β eq	1.50 m	21α/β		1.46 m	22
21β ax	3.10 ddd (13.7, 10.9, 2.4)	20α/β, 21α	19, 22	3.10 ddd (13.6, 10.9, 2.4)	19, 20, 22
21α eq	2.31 ddd (10.9, 6.0, 2.4)	20α/β, 21β	19, 22, 23	2.30 ddd (10.9, 6.2, 2.4)	19, 20, 22, 23
24	1.27 s		2, 3, 25	1.08 s	2, 3, 7, 25
25	1.24 s		2, 3, 24	1.21 s	2, 7, 24
26α ax	1.06 s	5β	5, 6, 7, 11	0.89 s	3, 5, 6
27β	1.04 d (6.8)	10α	10, 11	0.88 d (6.8)	9, 10, 11
28β	0.96 s		14, 16	0.80 s	14, 15, 16, 19
29β ax	1.04 s	20α	18, 20	1.04 s	15, 18, 19, 20
30α	1.29 s		22, 23, 31	1.37 s	22, 23, 31
31β	1.28 s		22, 23, 30	1.29 s	22, 23, 30

[a] Assignments were made by COSY, HSQC, HMBC (H−C), and ROESY data measured in $CDCl_3$; ax = axial, eq = equatorial. [b] Mult., coupling constants (*J*) in Hz. [c] Ha is the lower-field proton in a geminal pair and Hb is the higher-field proton.

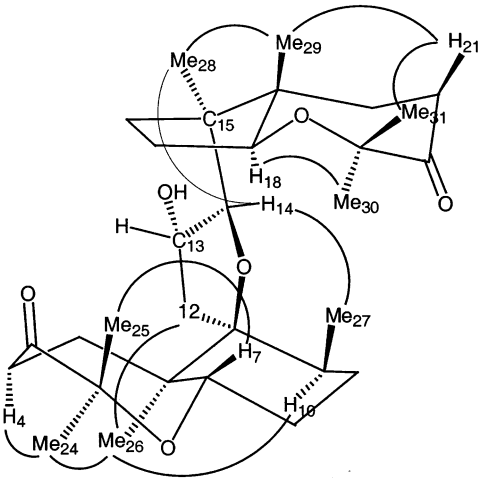

Figure 1. Selected ROESY correlations of **1**.

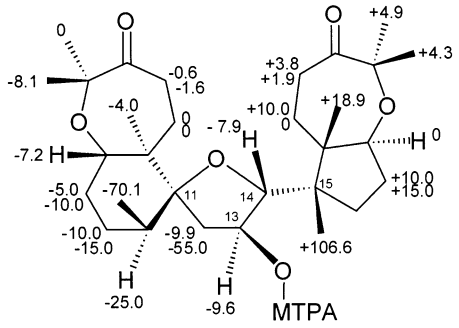

Figure 2. $\Delta\delta = \delta_S - \delta_R$ values in Hz calculated from the ^{1}H NMR spectra ($CDCl_3$) of *R*- and *S*-MTPA esters of **1**.

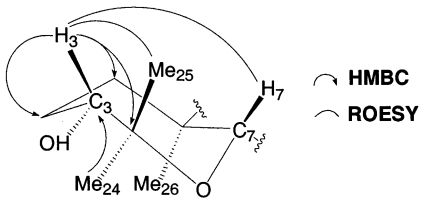

Figure 3. Selected HMBC and ROESY correlations of **2**.

72.1, typical for an oxygen-bearing tertiary carbon. The HSQC spectrum indicated C-3 bore the proton at δ_H 3.44. The cross-peak noted at H-3/H-4 in the COSY spectrum and the HMBC correlations between H-3 and C-2 and C-4 and C-5 supported the OH-3 location (Figure 3). The remainder of the long-range proton−carbon connectivities observed between the resonances of **2** were similar to those of **1** and **3**. The relative stereochemistry of **2** was assumed to be the same as in **1** and **3** on the basis of common ROESY correlations and coupling features. The large coupling constant value (J = 11.1 Hz) for H-3 which is typical for an axial−axial trans-coupling and the observed ROESY correlations between H-3 and H-7β and H-25β indicated the β-axial position for H-3 and the α-equatorial position for OH-3 (Figure 3). On the basis of these observations, yardenone B (**2**) was unambiguously assigned as the dihydro derivative of yardenone.

Although in a cytotoxicity test using the human lung carcinoma cell line NSCLC-N6 the heptanic-soluble fraction showed significant cytotoxicity (IC_{50} = 5 μg/mL), both new compounds **1** and **2** showed weak activity, with IC_{50} values

greater than 60 and 31 μM, respectively. The known yardenone was inactive, and sodwanone A showed cytotoxicity with an IC_{50} value of 12 μM.

Experimental Section

General Experimental Procedures. Optical rotations were determined with a Type AA-5 polarimeter. IR and UV spectra were recorded on Perkin-Elmer Paragon 1000 FT-IR and Uvikon 930 Kontron spectrophotometers, respectively. NMR experiments were performed on a Bruker DRX 500, using a standard Bruker program. NMR signals are reported in parts per million (δ), referenced to the solvent used. ESIMS were measured on a Bruker Esquire spectrometer. FABHRMS were realized at Service Central d'Analyses du CNRS (Solaize, France). HPLC was performed using a diode array detector and Magnum C_{18} column (250 × 10 mm, 10 μm, Whatman).

Animal Material. The sponge *Axinella cf. bidderi* (Burton, 1959) was collected in November 1997 at a depth of 25 m, off Socotra Island, Yemen, in the northern part of the Indian Ocean. A voucher specimen (MHNM 2000Im161) is deposited at the Museum d'Histoire Naturelle (Marseille, France), and the sample was identified by Dr. Jean Vacelet, Station Marine d'Endoume, Marseille, France.

Extraction and Isolation. The freshly collected sponge (4.7 kg, wet wt) was stored in ethanol prior to its extraction. The ethanolic crude extract exhibited 100% of inhibition at 100 μg/mL in the sea-urchin egg bioassay. A portion was concentrated in vacuo (56 g, 10% based on the total crude extract) and partitioned between CH_2Cl_2 and water. The resulting organic residue (17 g) was partitioned between MeOH and heptane. Sodwanone A (**4**) crystallized from the heptanic extract and was found to be the most active in a selective cytotoxic bioassay against NSCLC cells. A portion of the heptanic extract was evaporated under reduced pressure (3.5 g) and then filtered on Sephadex LH_{20} permeation gel ($MeOH/CH_2Cl_2$, 1:1). The resulting fraction was evaporated (3.5 g) and chromatographed on Si 60 gel with *n*-hexane/EtOAc/MeOH mixtures of increasing polarity to yield 150 fractions, which were combined according to their TLC patterns. Selected intermediate polar fractions were rechromatographed on Si 60 gel with *n*-hexane/EtOAc mixtures of increasing polarity to yield compounds **2** (100 mg, 0.179%) and **3** (50 mg, 0.089%). Reversed-phase HPLC ($MeOH/H_2O$, 8:2) afforded compound **1** (20 mg, 0.036%).

Yardenone A (1): colorless needles; $[\alpha]^{25}_D$ +5.2° (*c* 0.27, MeOH); IR (KBr) 3568 (OH), 2930, 1708 (C=O) and 1442, 1038 cm^{-1}; ^1H NMR and ^{13}C NMR, see Table 1; ESIMS *m/z* 503 $[M - H]^-$, 527 $[M + Na]^+$, 543 $[M + K]^+$; HRFABMS *m/z* 511.35970 (calcd for $C_{30}H_{48}O_6Li$, 511.36109).

Yardenone B (2): colorless needles; $[\alpha]^{25}_D$ +2.38° (*c* 1.05, MeOH); ^1H NMR and ^{13}C NMR, see Table 1; ESIMS *m/z* 489 $[M - H]^-$, 529 $[M + Na]^+$, 513 $[M + K]^+$; HRFABMS *m/z* 497.38360 (calcd for $C_{30}H_{50}O_5Li$ 497.38182).

Yardenone (3): colorless needles; $[\alpha]^{25}_D$ +2.38° (*c* 1.05, MeOH); ^{13}C NMR, see Table 1; ESIMS *m/z* 511 $[M + Na]^+$, 527 $[M + K]^+$.

Sodwanone A (4): colorless crystals (MeOH); ESIMS *m/z* 499 $[M - H]^-$, 535 $[M - Cl]^-$, 527 $[M + Na]^+$, 531 $[M + K]^+$.

Cytotoxicity Bioassay. The crude extract toxicity was estimated on the sea-urchin egg division according to the procedure reported earlier.[8] The in vitro cytotoxicity assay against human lung carcinoma cells NSCLC-N6 L16 was performed as previously described.[16]

Preparation of S-MTPA Ester of Yardenone A (1). To a solution of yardenone A (3 mg, 6 μmol) in 2 mL of dichloromethane distilled from P_2O_5 were added (dimethylamino)pyridine (2.9 mg, 24 μmol), triethylamine (1.3 μL, 9 μmol), and R-MTPA chloride (2.2 μL, 12 μmol). After 3 h at room temperature 3-(dimethylamino)propylamine (1.5 μL, 12 μmol) was added. After 20 min, the solvent was evaporated and the residue was purified on preparative TLC (*n*-hexane/EtOAc 8:2 (v/v)) to give the pure S-MTPA ester (3.6 mg): ^1H NMR ($CDCl_3$, 500 MHz) δ 0.66 (3H, s, H-28), 0.80 (3H, d, J = 6.9 Hz, H-27), 1.00 (3H, s, H-29), 1.06 (3H, s, H-26), 1.25 (3H, s, H-25), 1.26 (3H, s, H-24), 1.27 (3H, s, H-31), 1.28 (3H, s, H-30), 1.30 (1H, m, H-9b), 1.45 (1H, m, H-20b), 1.53 (1H, m, H-8b), 1.53 (1H, m, H-9a), 1.55 (1H, m, H-17b), 1.56 (1H, m, H-5b), 1.60 (1H, m, H-20a), 1.62 (1H, m, H-12b), 1.65 (1H, m, H-8a), 1.70 (1H, m, H-17a), 1.76 (1H, m, H-10), 1.84 (1H, m, H-5a), 2.18 (1H, ddd, J = 10.8, 6.8, 1.6 Hz, H-4b), 2.28 (1H, ddd, J = 10.8, 6.0, 1.8 Hz, H-21b), 2.73 (1H, dd, J = 14.6, 9.7 Hz, H-12a), 3.07 (1H, ddd, J = 13.4, 11.2, 2.4 Hz, H-21a), 3.15 (1H, ddd, J = 13.6, 11.1, 2.2 Hz, H-4a), 3.20 (1H, dd, J = 11.1, 5.4 Hz, H-7), 3.83 (1H, d, J = 8.5 Hz, H-14), 3.88 (1H, t, J = 8.7 Hz, H-18), 4.94 (1H, m, H-13).

Preparation of R-MTPA Ester of Yardenone A (1). Using S-MTPA chloride (2.2 μL, 12 μmol), pure R-MTPA ester (3.3 mg) was similarly prepared as above: ^1H NMR ($CDCl_3$, 500 MHz) δ 0.44 (3H, s, H-28), 0.94 (3H, d, J = 6.8 Hz, H-27), 0.96 (3H, s, H-29), 1.07 (3H, s, H-26), 1.25 (3H, s, H-25), 1.27 (3H, s, H-31), 1.27 (3H, s, H-30), 1.28 (3H, s, H-24), 1.32 (1H, m, H-9b), 1.43 (1H, m, H-20b), 1.53 (1H, m, H-17b), 1.54 (1H, m, H-8b), 1.56 (1H, m, H-5b), 1.56 (1H, m, H-9a), 1.60 (1H, m, H-20a), 1.67 (1H, m, H-8a), 1.68 (1H, m, H-17a), 1.73 (1H, m, H-12b), 1.81 (1H, m, H-10), 1.84 (1H, m, H-5a), 2.19 (1H, ddd, J = 11.2, 6.9, 1.9 Hz, H-4b), 2.28 (1H, ddd, J = 10.1, 6.0, 1.8 Hz, H-21b), 2.75 (1H, dd, J = 14.5, 9.7 Hz, H-12a), 3.06 (1H, ddd, J = 13.5, 11.0, 2.5 Hz, H-21a), 3.15 (1H, ddd, J = 13.6, 11.1, 2.2 Hz, H-4a), 3.22 (1H, dd, J = 11.0, 5.3 Hz, H-7), 3.84 (1H, d, J = 8.6 Hz, H-14), 3.88 (1H, t, J = 8.7 Hz, H-18), 4.93 (1H, m, H-13).

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Supporting Information Available: Table showing the calculated vicinal coupling constant $^3J_{H13-H14}$ of yardenone A isomers: OH_α-13 and OH_β-13. This material is available free of charge via the Internet at http://pubs.acs.org.

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