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•Research article•

New bisabolane-type phenolic sesquiterpenoids from the marine sponge *Plakortis simplex*

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[ABSTRACT] Six new bisabolane-type phenolic sesquiterpenoids, including plakordiols A−D (**1**−**4**), (7*R*, 10*R*)-hydroxycurcudiol (**5**) and (7*R*, 10*S*)-hydroxycurcudiol (**6**) were isolated from the marine sponge *Plakortis simplex* collected from the South China Sea. Their structures were determined based on extensive analysis of spectroscopic data. Their configurations were assigned by coupling constant analysis, NOESY correlations, and the modified Mosher's method. Furthermore, their cytotoxic and antibacterial activities were evaluated.

[KEY WORDS] Marine sponge; *Plakortis simplex*; Sesquiterpene phenols; Plakordiols
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Introduction

Sesquiterpene phenols belong to bisabolane-type sesquiterpenoids, which is a very important family of natural products present in many marine organisms, such as marine sponges (*Didiscus* sp. [1-3], *Arenochalina* sp. [4], *Epipolasis* sp. [5], and *Myrmekioderma* sp. [6]), soft corals (*Pseudopterogorgia rigida*) [7-9], and marine-derived fungi (*Aspergillus* sp. [10-14] and *Penicillium expansum* [15]). These compounds exhibit a wide range of bioactivities including cytotoxic [14, 15], antimicrobial [11-13], antimalarial [3], H, K-ATPase inhibitory [5], and lipid-reducing activities [6].

Marine sponges of the genus *Plakortis* are rich in novel bioactive secondary metabolites, such as cyclic peroxides [16], lactones [17], alkaloids [18], and fatty-acid derivatives [19]. However, sesquiterpene phenols have never been reported from this genus so far. In the course of our ongoing research program on new bioactive natural products from the marine sponge *P. simplex* [20-24], collected from Yongxing Islands in the South China Sea, six new bisabolane-type phenolic sesquiterpenoids, plakordiols A−D (**1**−**4**), (7*R*, 10*R*)-hydroxycurcudiol (**5**) and (7*R*, 10*S*)-hydroxycurcudiol (**6**) (Fig. 1), were isolated from the methanolic extract of the title sponge by a combination of reversed-phase chromatography and RP-HPLC. Their structures were elucidated by MS and NMR spectra, and the stereochemical structures of compounds **1**−**6** were determined by coupling constant analysis, NOESY correlations, as well as the modified Mosher's method.

Results and Discussion

Plakordiol A (**1**) was obtained as a yellow oil. The HR-ESIMS data provided a $[M - H]^-$ ion at *m*/*z* 249.1498, which was consistent with the molecular formula $C_{15}H_{22}O_3$ and indicated five degrees of unsaturation. The ^1H and ^{13}C NMR data (Table 1) were characterized by the presence of three aromatic methines at δ_H 6.98 (d, J = 8.4 Hz)/δ_C 130.5, δ_H 6.61 (br s)/δ_C 121.3, and δ_H 6.61 (br s)/δ_C 117.5, suggesting the presence of the ABX spin pattern of a trisubstituted aromatic system. Further examination of the ^1H and ^{13}C NMR data of **1**

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revealed the presence of two olefinic methines at δ_H 5.51 (d, J = 12.0 Hz)/δ_C 139.6 and δ_H 5.25 (dd, J = 12.0, 8.4 Hz)/δ_C 131.1; an oxymethine at δ_H 5.07 (t, J = 7.2 Hz)/δ_C 71.8; and four methyls at δ_H 2.24 (s)/δ_C 21.1, δ_H 1.32 (s)/δ_C 31.2, δ_H 1.31 (s)/δ_C 31.6 and δ_H 1.27 (d, J = 7.2 Hz)/δ_C 16.6. The HMBC correlations (Fig. 2) from H_3-14 (δ_H 1.27) to C-7 (δ_C 42.3) and C-8 (δ_C 71.8), H-8 (δ_H 5.07) to C-10 (δ_C 139.6), H-9 (δ_H 5.25) to C-11 (δ_C 72.2), H-10 (δ_H 5.51) to C-13 (δ_C 31.6), H_3-13 (δ_H 1.31) and H_3-12 (δ_H 1.32) to C-10 (δ_C 139.6) and C-11 (δ_C 72.2) indicated the presence of 7, 11-dimethyl-

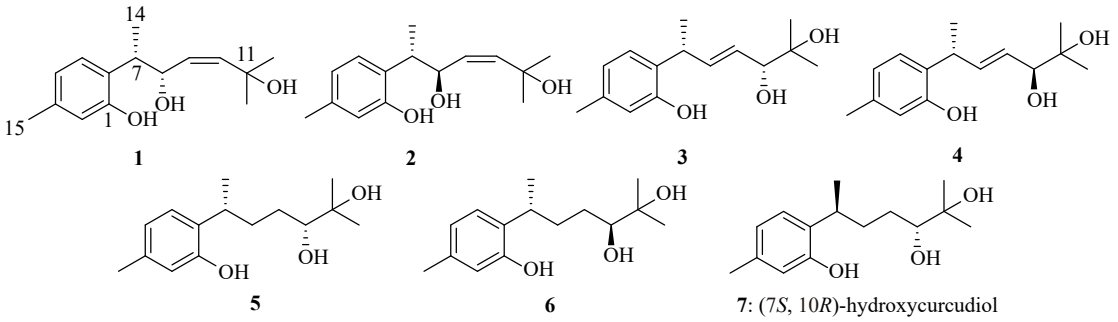


Fig. 1 Structures of compounds 1–7

Table 1 ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectroscopic data of 1–4 in CD_3OD

	1		2		3		4	
No.	δ_C, mult.	δ_H (J in Hz)	δ_C, mult.	δ_H (J in Hz)	δ_C, mult.	δ_H (J in Hz)	δ_C, mult.	δ_H (J in Hz)
1	156.1, C		155.8, C		155.4, C		155.4, C	
2	117.5, CH	6.61, br s	117.3, CH	6.60, s	116.7, CH	6.59, s	116.7, CH	6.59, s
3	138.1, C		137.9, C		137.6, C		137.6, C	
4	121.3, CH	6.61, br s	121.4, CH	6.61, d (7.8)	121.3, CH	6.60, d (7.8)	121.3, CH	6.60, d (7.8)
5	130.5, CH	6.98, d (8.4)	129.8, CH	6.98, d (7.8)	128.4, CH	6.96, d (7.8)	128.4, CH	6.98, d (7.8)
6	127.8, C		128.8, C		130.1, C		130.2, C	
7	42.3, CH	3.15, m (7.2)	41.3, CH	3.17, m (7.2)	36.0, CH	3.83, m (6.8)	36.0, CH	3.83, m (6.8)
8	71.8, CH	5.07, t (7.2)	72.5, CH	4.93, t (7.2)	139.4, CH	5.93, dd (15.6, 6.6)	139.3, CH	5.90, dd (15.6, 6.0)
9	131.1, CH	5.25, dd (12.0, 8.4)	131.5, CH	5.32, dd (12.0, 7.8)	128.3, CH	5.53, dd (15.6, 7.2)	128.3, CH	5.54, dd (15.6, 6.2)
10	139.6, CH	5.51, d (12.0)	139.4, CH	5.43, d (12.0)	80.9, CH	3.81, d (7.2)	80.8, CH	3.81, d (7.2)
11	72.2, C		72.4, C		73.7, C		73.7, C	
12	31.2, CH_3	1.32, s	30.9, CH_3	1.29, s	24.9, CH_3	1.15, s	24.8, CH_3	1.12, s
13	31.6, CH_3	1.31, s	31.6, CH_3	1.30, s	26.0, CH_3	1.15, s	26.0, CH_3	1.13, s
14	16.6, CH_3	1.27, d (7.2)	15.8, CH_3	1.30, d (7.2)	20.4, CH_3	1.31, d (7.2)	20.4, CH_3	1.31, d (7.2)
15	21.1, CH_3	2.24, s	21.1, CH_3	2.23, s	21.1, CH_3	2.23, s	21.1, CH_3	2.23, s

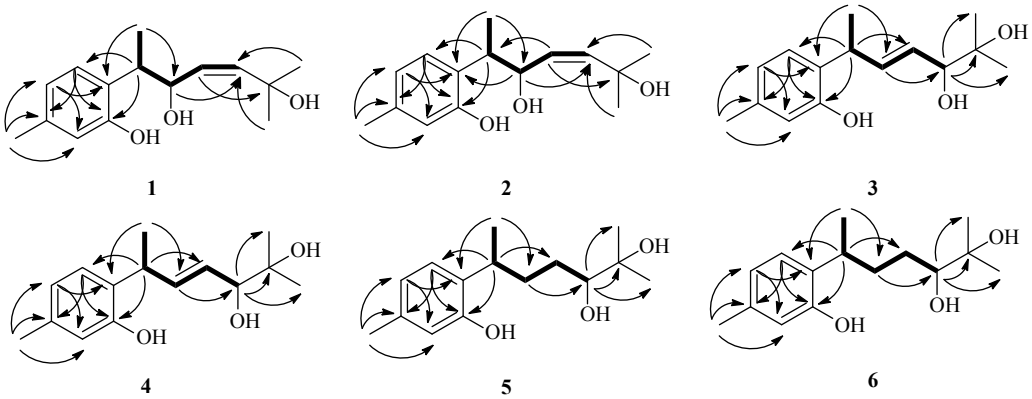


Fig. 2 ^{1}H–^{1}H COSY (▬) and key HMBC (→) correlations of compounds 1–6

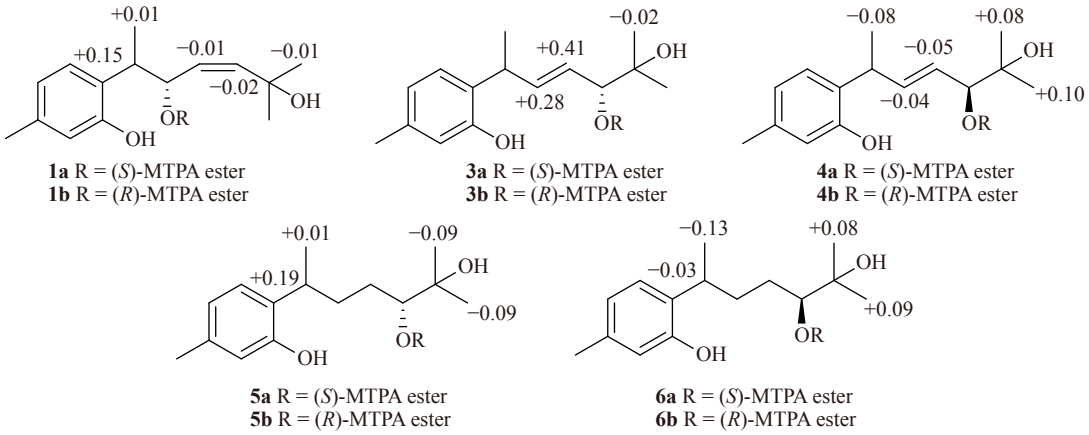
hex-9-ene-8, 11-diol. In addition, the COSY correlations of H_3-14/H-7/H-8/H-9/H-10 further implicated the presence of this fragment. The HMBC correlations from H_3-15 (δ_H 2.24) to C-2 (δ_C 117.5), C-3 (δ_C 138.1) and C-4 (δ_C 121.3) and H-7 (δ_H 3.15) to C-1 (δ_C 156.1) and C-5 (δ_C 130.5) located in the methyl groups and the side chain at the C-3 and C-6 positions, respectively. In addition, a hydroxyl group was attached to C-1 based on the formula of **1** and the chemical shift of C-1 (δ_C 156.1). The geometry of the double bond $\Delta^{9, 10}$ was determined to be *Z* by the coupling constant between H-9 and H-10 ($^3J_{H\text{-}9,\ H\text{-}10}$ = 12.0 Hz). The planar structure of **1** was elucidated as depicted. The absolute configuration of C-8 was determined as *S* by the modified Mosher's experiment (Fig. 3). The relative configuration at C-7 was determined on the basis of $^3J_{HH}$ values and NOESY correlations. The coupling constant $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.2 Hz and the NOESY correlation of H-14/H-9 (Figs. 4−5) were indicative of the *gauche* configuration of H-7 to H-8, through forming the intramolecular hydrogen bonds between 1-OH and 8-OH. Thus, the absolute configuration of **1** was assigned as 7*S*, 8*S*.

The molecular formula of plakordiol B (**2**) was determined by HR-ESIMS to be $C_{15}H_{22}O_3$, isomeric to **1**. The planar structure of **2** was found to be identical with that of **1**, with the main differences on the chemical shifts of C-6, C-7, C-8, and C-14 in **1** (δ_C 127.8, 42.3, 71.8, and 16.6) and **2** (δ_C 128.8, 41.3, 72.5, and 15.8) in Table 1. These differences revealed that **2** was an epimer of **1**, and its relative configuration was determined using coupling constant and NOESY experiment. The coupling constant $^3J_{H\text{-}7,\ H\text{-}8}$ = 7.2 Hz, and strong NOESY correlations for H-5/H-8, H-7/H-9, and H-14/H-9 established the relative configuration of **2** as 7*S**, 8*R** (Fig. 5). The absolute configuration of **2** was tentatively assigned as 7*S*, 8*R* on account of the similar biosynthetic origin of **1** and **2**. The sample amount of **2** was not enough for the modified Mosher's experiment.

Plakordiol C (**3**) was isolated as another isomer of **1** with a molecular formula of $C_{15}H_{22}O_3$ as determined from the HR-ESIMS data (*m/z* 249.1484, $[M - H]^-$). The ^1H and ^{13}C NMR data of **3** showed similarities to those of **1** (Table 1). The HMBC correlations of H_3-14 (δ_H 1.31) to C-7 (δ_C 36.0) and C-8 (δ_C 139.4), H-8 (δ_H 5.93) to C-10 (δ_C 80.9), H-9 (δ_H 5.53) to C-7 (δ_C 36.0), H-10 (δ_H 3.81) to C-11 (δ_C 73.7), C-12 (δ_C 24.9), and C-13 (δ_C 26.0) established the side chain (7, 11-dimethylhex-8-ene-10, 11-diol) of **3**, which also supported by the COSY correlations of H-14/H-7/H-8/H-9/H-10 (Fig. 2). The geometry of the double bond $\Delta^{8, 9}$ was determined to be *E* by the coupling constant between H-8 and H-9 ($^3J_{H\text{-}8,\ H\text{-}9}$ = 15.6 Hz). The remaining HMBC correlations (Fig. 2) and NMR data (Table 1) were consistent with the planar structure as depicted. The absolute configuration of C-10 was determined as *R* by the modified Mosher's method (Fig. 3). The coupling constant $^3J_{H\text{-}7,\ H\text{-}8}$ = 6.6 Hz and strong NOESY correlations of H-14/H-5, H-5/H-8, H-8/H-10, and H-7/H-9 (Fig. 4) indicated that the absolute configuration of C-7 may be *R*.

The molecular formula of plakordiol D (**4**) was deduced as $C_{15}H_{22}O_3$ on the basis of HR-ESIMS (*m/z* 249.1483, $[M - H]^-$). The ^1H and ^{13}C NMR data (Table 1) of **4** was found to be very similar to that of **3**, except for small difference in the chemical shifts of H-8, H-12, and H-13 in **3** (δ_H 5.93, 1.15, and 1.15) and **4** (δ_H 5.90, 1.12, and 1.13). These results implied that **4** was an epimer of **3**, and the absolute configuration of C-10 was determined as *S* by the modified Mosher's method (Fig. 3). Similar to plakordiol C (**3**), the absolute configuration of C-7 may be *R* through analysis of its prefered conformation, which was based on NOESY correlations (Fig. 4) and the coupling constant of 6.0 Hz between H-7 and H-8.

(7*R*, 10*R*)-Hydroxycurcudiol (**5**) possessed a molecular formula of $C_{15}H_{24}O_3$, according to its 1D NMR and ESI-MS (*m/z* 251.14 $[M - H]^-$). Detailed analysis of the 1D and 2D NMR spectral data revealed that the planar structure of **5** was the same as the known compound (7*S*, 10*R*)-hydroxycurcudiol (**7**) [3]. The absolute configuration at C-10 (*R*) of **5** was elucidated by the modified Mosher's method (Fig. 3). Comparing the ^{13}C NMR data (in $CDCl_3$) of **5** with reported data (in $CDCl_3$) of **7** (Table 2), there were minor differences in the C_6-C_{11} (**5**: δ_C 129.7, 30.3, 36.3, 28.1, 79.5, 73.3; **7**: δ_C 130.4, 31.6, 34.4, 29.4, 78.9, 73.9), which demonstrated that **5** was an epimer of **7**. Therefore, the absolute configuration at C-7



1a R = (*S*)-MTPA ester
1b R = (*R*)-MTPA ester

3a R = (*S*)-MTPA ester
3b R = (*R*)-MTPA ester

4a R = (*S*)-MTPA ester
4b R = (*R*)-MTPA ester

5a R = (*S*)-MTPA ester
5b R = (*R*)-MTPA ester

6a R = (*S*)-MTPA ester
6b R = (*R*)-MTPA ester

Fig. 3 $\Delta\delta = \delta_S - \delta_R$ values in ppm obtained from the MTPA esters of compounds 1 and 3−6

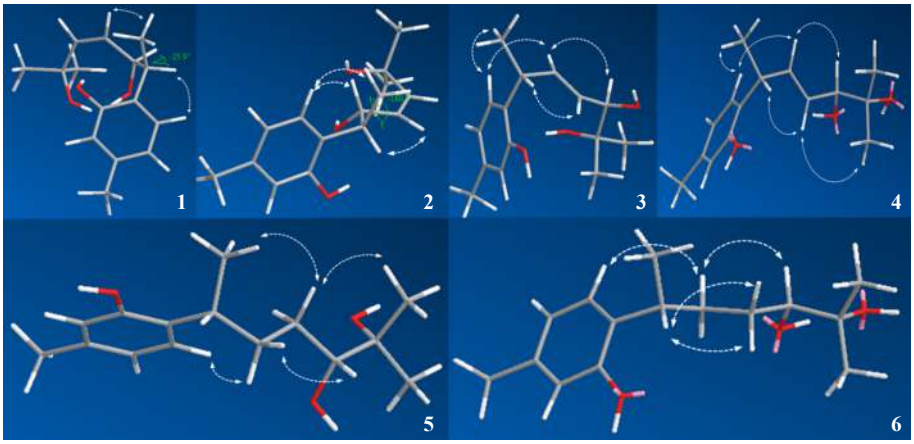


Fig. 4 Key NOESY correlations of compounds 1−6

Table 2 ^{1}H (600 MHz, in CD_3OD) and ^{13}C (150 MHz, in CD_3OD and $CDCl_3$) NMR spectroscopic data of 5−6

	5			6			7
No.	δ_C, mult. (in CD_3OD)	δ_H (J in Hz)	δ_C, mult. (in $CDCl_3$)	δ_C, mult. (in CD_3OD)	δ_H (J in Hz)	δ_C, mult. (in $CDCl_3$)	δ_C (in $CDCl_3$), in literature
1	155.6, C		153.7, C	155.5, C		153.6, C	153.5
2	116.7, CH	6.57, br s	116.9, CH	116.7, CH	6.58, br s	116.4, CH	116.7
3	137.0, C		136.7, C	137.1, C		136.6, C	136.6
4	121.4, CH	6.60, br d (7.8)	121.5, CH	121.4, CH	6.61, br d (7.8)	121.2, CH	121.3
5	127.8, CH	6.99, d (7.8)	126.4, CH	127.6, CH	6.98, d (7.8)	126.7, CH	126.9
6	131.5, C		129.7, C	131.8, C		130.2, C	130.4
7	32.5, CH	3.17, m (7.2)	30.3, CH	33.1, CH	3.12, m (7.2)	31.7, CH	31.6
8	35.3, CH_2	1.91, m; 1.60, m	36.3, CH_2	35.9, CH_2	1.84, m; 1.61, m	34.7, CH_2	34.4
9	30.3, CH_2	1.52, m; 1.19, m	28.1, CH_2	30.5, CH_2	1.53, m; 1.30, m	29.2, CH_2	29.4
10	79.5, CH	3.32, d (7.8)	79.5, CH	80.1, CH	3.23, br d (10.2)	79.0, CH	78.9
11	73.9, C		73.3, C	73.8, C		73.4, C	73.9
12	25.3, CH_3	1.06, s	26.6, CH_3	25.0, CH_3	1.08, s	26.3, CH_3	26.3
13	25.2, CH_3	1.08, s	22.8, CH_3	25.4, CH_3	1.12, s	23.2, CH_3	23.2
14	22.1, CH_3	1.20, d (7.2)	21.0, CH_3	21.6, CH_3	1.20, d (7.2)	21.0, CH_3	21.1
15	21.1, CH_3	2.22, s	21.1, CH_3	21.1, CH_3	2.22, s	20.7, CH_3	20.9

of **5** was identified as *R*. This result was further verified by the coupling constant of 7.2 Hz between H-7 and H-8a/H-8b and NOESY correlations for H-5/H-8a, H-8b/H-10, and H-14/H-9a (Fig. 4).

The molecular formula of (7*R*, 10*S*)-hydroxycurcudiol (**6**) was deduced to be the same as that of **5** based on the 1D NMR and ESI-MS (*m*/*z* 251.21 $[M - H]^-$). Extensive analysis of 1D and 2D NMR spectral data revealed that **6** was an epimer of **5**. The modified Mosher's method was applied to determine the absolute configuration at C-10 (*S*) of **6** (Fig. 3). The ^{13}C NMR data (in $CDCl_3$) of **6** was consistent with that of **7** in literature, which proved **6** was an enantiomer of **7** (Table 2). This result was further confirmed by the medium coupling constant of 7.2 Hz between H-7 and H-8a/H-8b, NOESY correlations of H-5/H-8b, H-8b/H-10, and H-7/H-9a, 9b (Fig. 4), and the opposite optical rotation data (**6**, $[\alpha]_D^{25}$ −11.7, MeOH; (7*S*, 10*R*)-hydroxycurcudiol, $[\alpha]_D^{25}$ +61.8, $CDCl_3$).

Compounds **1−6** were tested for their cytotoxic activities against HepG2 and A375 cells by CCK-8 assay [25, 26], but no activity against the two cell lines were found. Furthermore, the compounds were evaluated for antibacterial activity against methicillin sensitive *Staphylococcus aureus* ATCC 25923, methicillin resistant *Staphylococcus aureus* ATCC 43300, *Acinetobacter baumanii* ATCC19606, carbapenem resistant *Pseudomonas aeruginosa* (clinical), and vancomycin resistant *Enterococcus* CD27 by the disc diffusion and minimum inhibitory concentration (MIC) methods. None of them showed inhibitory activity against the five bacterial strains, except **5** and **6** which displayed weak activity against *A. baumanii* ATCC19606 in disc diffusion test with an inhibition zone diameter of 5 mm, respectively. However, they did

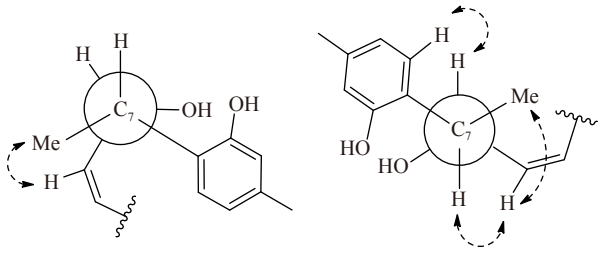


Fig. 5 Relative configurations of C-7 and C-8 in 1 and 2 determined by $^3J_{HH}$ values and NOEs

not showed pronounced activity against ATCC19606 in MIC bioassays (MIC > 64 μg·mL^{-1}).

Experimental

General experimental procedures

Optical rotation measurements were recorded on an Autopol VI polarimeter (No. 91003, Rudolph Research Analytical, Hackettstown, NJ, USA). The CD spectra were obtained on a Jasco J-715 spectropolarimeter (Jasco, Easton, MD, USA). The NMR experiments were conducted on Agilent DD2-600 MHz NMR spectrometers (Agilent, Santa Clara CA, USA) in CD_3OD and $CDCl_3$. ESIMS and HR-ESIMS spectra were recorded on a Waters autopurification system with an Acquity QDa Mass Detector and a Waters Xevo G2-XS Q-TOF mass spectrometer (Waters, Milford, USA), respectively. Column chromatographic separation was carried out using reverse phase C_{18} silica gel (15 mm, Santai Technologies, Inc., Changzhou, China). Analytical thin-layer chromatography was performed on silica gel $HSGF_{254}$ plates (Yantai Jiangyou Silica gel Develoment Co., Yantai, China) and visualized by spraying with anisaldehyde-H_2SO_4 reagent. MPLC was carried out on an Interchim PuriFlash 450 instrument (Interchim, Los Angeles, USA). RP HPLC was performed on a YMC-Pack Pro C_{18} column (250 mm × 10 mm, 5 mm, YMC, Devens, USA) using a Waters 1525 binary HPLC pump with a Waters 2998 photodiode array detector (Waters, Milford, USA).

Sponge Material

The marine sponge was collected off Yongxing Islands in the South China Sea in May 2007 and authenticated by Prof. LI Jin-He (Institute of Oceanology, Chinese Academy of Sciences, China). A voucher specimen (No. B-3) was deposited in the Research Center for Marine Drugs, State Key Laboratory of Oncogenes and Related Genes, Department of Pharmacy, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University (Shanghai, China).

Extraction and isolation

The sponge (2.0 kg, dry weight) was extracted with MeOH for four times. The residue obtained was partitioned between petroleum ether and MeOH−H_2O (9 : 1, *V/V*). The 90% aqueous MeOH layer was diluted into 60% aqueous MeOH with H_2O and partitioned with CH_2Cl_2. The 60% aqueous MeOH layer was diluted into 40% aqueous MeOH with H_2O and partitioned with *n*-BuOH. The *n*-BuOH-soluble fraction (22 g) was separated by RP MPLC with the stepwise elution (10%−100% MeOH/H_2O) to give seven major fractions (A−G). Fr. E was re-subjected to RP MPLC to afford subfractions Fr. 1−Fr. 12. Then, Fr. 3 was purified by RP HPLC (25% MeCN/H_2O) to give **2** (2.2 mg, t_R 64 min) and **1** (2.9 mg, t_R 69 min). Fr. 2 was further purified by RP HPLC (40% MeOH/H_2O) to yield **4** (5.0 mg, t_R 68 min), **3** (8.4 mg, t_R 75 min), **6** (11.4 mg, t_R 81 min), and **5** (10.4 mg, t_R 87 min).

Plakordiol A (**1**): yellowish oil; $[\alpha]_D^{25}$ −2.1 (*c* 0.11, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 278 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 200 (+7.1), 212 (−1.2), 227 (−0.9), 245 (+0.6), and 279 (−0.9); ^{1}H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, Table 1; HR-ESIMS *m/z* 249.1498 $[M - H]^-$ (Calcd. for $C_{15}H_{21}O_3$, 249.1491).

Plakordiol B (**2**): yellowish oil; $[\alpha]_D^{25}$ −6.5 (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 278 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 206 (−8.2), 227 (−3.8), 244 (+0.5), and 279 (−2.4); ^{1}H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, Table 1; HR-ESIMS *m/z* 249.1499 $[M - H]^-$ (Calcd. for $C_{15}H_{21}O_3$, 249.1491).

Plakordiol C (**3**): yellowish oil; $[\alpha]_D^{25}$ −6.3 (*c* 0.16, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 278 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 204 (+13.5), 219 (−5.0), 229 (−6.9), and 279 (−1.8); ^{1}H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, Table 1; HR-ESIMS *m/z* 249.1484 $[M - H]^-$ (Calcd. for $C_{15}H_{21}O_3$, 249.1491).

Plakordiol D (**4**): yellowish oil; $[\alpha]_D^{25}$ −9.3 (*c* 0.10, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 278 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 200 (+15.8), 215 (−2.0), 228 (−3.2), 248 (+1.9), and 279 (−1.0); ^{1}H NMR (600 MHz, CD_3OD) and ^{13}C NMR (150 MHz, CD_3OD) data, Table 1; HR-ESIMS *m/z* 249.1483 $[M - H]^-$ (Calcd. for $C_{15}H_{21}O_3$, 249.1491).

(7*R*, 10*R*)-Hydroxycurcudiol (**5**): yellowish oil; $[\alpha]_D^{25}$ +10.0 (*c* 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 279 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 201 (−4.3), 226 (−1.1), and 279 (−1.0); ^{1}H NMR (600 MHz, CD_3OD), ^{13}C NMR (150 MHz, CD_3OD), and ^{13}C NMR (150 MHz, $CDCl_3$) data, Table 2; ESIMS *m/z* 251.14 $[M - H]^-$.

(7*R*, 10*S*)-Hydroxycurcudiol (**6**): yellowish oil; $[\alpha]_D^{25}$ −11.7 (*c* 0.12, MeOH); UV (MeOH) λ_{max} (log ε) 201 and 278 nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 204 (−1.6), 221 (−1.8), and 279 (−0.9); ^{1}H NMR (600 MHz, CD_3OD), ^{13}C NMR (150 MHz, CD_3OD), and ^{13}C NMR (150 MHz, $CDCl_3$) data, Table 2; ESIMS *m/z* 251.21 $[M - H]^-$.

Preparation of the (R)- and (S)-MTPA ester derivatives

Compounds **1** and **3**−**6** (each about 1.0 mg) were dried and transferred into clean NMR tubes, respectively. Under N_2 gas stream, pyridine-d_5 (0.5 mL) and (*R*)-MTPA chloride (20 μL) were immediately added into the NMR tubes, which were then shaken and conserved in a water bath at 40 °C for 4 h to afford **1a** and **3a**−**6a**. The ^{1}H NMR spectra were directly obtained from the NMR reaction tubes.

Another sample of compounds **1** and **3**−**6** (each about 1.0 mg) was pretreated in the same manner. After dissolving in

0.5 mL of pyridine-d_5, (*S*)-MTPA chloride (20 μL) under N_2 gas stream, the mixtures were shaken and conserved in a water bath at 40 °C for 4 h to afford **1b** and **3b**−**6b**. The ^{1}H NMR spectra were directly obtained from the NMR reaction tubes [27].

Antibacterial assay

The *in vitro* antibacterial assay was carried out as previouly reported [28]. *A. baumanii* ATCC19606 was incubated with compounds **5**−**6** that displayed inhibition zones in 96-well plates at final concentrations of 0 to 64 μg·mL^{-1}. The plates were incubated at 37 °C for 48 h. Chloramphenicol was used as the positive control and displayed an MIC of 32 μg·mL^{-1} against ATCC19606.

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