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Wedelolides A and B: Novel Sesquiterpene δ-Lactones, (9*R*)-Eudesman-9,12-olides, from *Wedelia trilobata*

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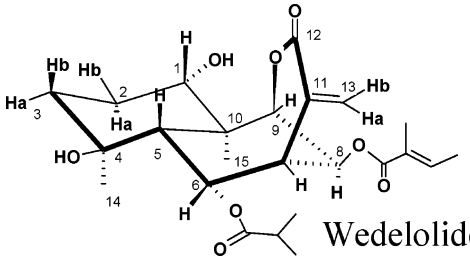

Wedelolide A (**1**)

Two new sesquiterpene lactones, wedelolides A (**1**) and B (**2**), were isolated by bioassay-guided fractionation from the leaves of *Wedelia trilobata*, together with known trilobolides 6-*O*-isobutyrate (**3**) and 6-*O*-methacrylate (**4**). The compounds **1** and **2** were the first examples of an unprecedented framework: a novel sesquiterpene δ-lactone, (9*R*)-eudesman-9,12-olide. The structures of the antimalarial wedelolides A (**1**) and B (**2**) were determined on the basis of MS and 2D NMR spectral analysis. The absolute configuration of eight carbon stereocenters of compounds **1** and **2** was determined to be 1*S*,4*S*,5*S*,6*R*,7*S*,8*S*,9*R*,10*S* by mean of auxiliary chiral MTPA derivatives.

Introduction

Sesquiterpene lactones are one of the main structural classes of plant metabolites, generally containing pentacyclic γ-lactone. This class of compounds is divided further by numerous groups: germacranolides, eudesmanolides, elemanolides,[1]heliangolides,[2] guaianolides,[3] pseudoguaianolides,[4] xanthanolides,[5] and others. Therefore, some authors described rare structurally unusual sesquiterpene δ-lactones of plants, such as *seco*-prezizaane framework compounds, strongly neurotoxic anisatin,[6,7] and floridanolides,[7,8] isolated from genus *Illicium* and the antimalarial drug artemisinin, isolated from *Artemisia annua*.[9,10]

In a survey of bioactive substances of Vietnamese plants,[11] we investigated *Wedelia trilobata* Asteraceae (Compositae), used in a traditional herbal medicine for the treatment of fever and malaria in Vietnam. New compounds, wedelolides A (**1**) and B (**2**), were isolated in addition to known trilobolides 6-*O*-

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(1) Skaltsa, H.; Lazari, D.; Panagouleas, C.; Georgiadou, E.; Garcia, B.; Sokovic, M. *Phytochemistry* **2000**, *55*, 903−908.
(2) Spring, O.; Zipper, R.; Klaiber, I.; Reeb, S.; Vogler, B. *Phytochemistry* **2000**, *55*, 255−261.
(3) Vajs, V.; Todorovic, N.; Bulatovic, V.; Menkovic, N.; Macura, S.; Juranic, N.; Milosavljevic, S. *Phytochemistry* **2000**, *54*, 625−633.
(4) De La Fuente, J. R.; Uriburu, M. L.; Burton, G.; Sosa, V. E. *Phytochemistry* **2000**, *55*, 769−772.
(5) Yang, C.; Ye, M. C.; Jia, Z. J. *Chin. Chem. Lett.* **2003**, *14*, 483−484.
(6) Kouno, I.; Baba, N.; Hashimoto, M.; Kawano, N.; Takahashi, M.; Kaneto, H.; Yang, C.-S.; Sato, S. *Chem. Pharm. Bull.* **1989**, *37*, 2448−2451.
(7) Schmidt, T. J.; Schmidt, H. M.; Müller, E.; Peters, W.; Fronczek, R.; Truesdale, A.; Fischer, H. *J. Nat. Prod.* **1998**, *61*, 230−236.
(8) Huang, J.-H.; Yang, C.-S.; Takahashi, H.; Fukuyama, Y. *Phytochemistry* **2000**, *55*, 883−886.
(9) Qinghaosu Antimalarial Co-ordinating Research Group. *Chin. Med. J.* **1979**, *92*, 811−6.
(10) Acton, N.; Roth, R. J. *J. Org. Chem.* **1992**, *57*, 3610−3614.
(11) Jossang, A.; El Bitar, H.; Pham, V. C.; Sévenet, T. *J. Org. Chem.* **2003**, *68*, 300−304.

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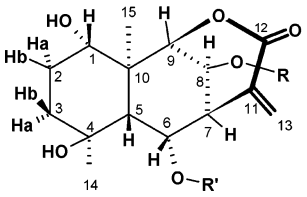
TABLE 1. ^{1}H NMR Data in $CDCl_3$ for Wedelolides A (1), B (2) and MTPA Esters 1S, 1R, 2S and 2R

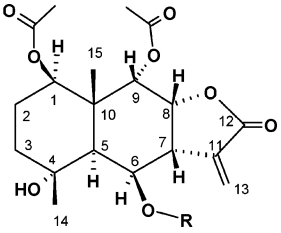
position	**1** δ^1H m, *J* (Hz)	**1S**[a] δ^1H m, *J* (Hz)	**1R**[a] δ^1H m, *J* (Hz)	**2** δ^1H m, *J* (Hz)	**2S**[a,b] δ^1H	**2R**[a,b] δ^1H
1b	3.92 dd, 5.3; 10.4	5.12 dd, 4.3; 10.8	5.16 dd, 4.5; 11.1	3.95 dd, 4.7; 11.1	5.12	5.17
2a	1.67 dm, 10.4	1.63 dm, 10.8	1.67 dm, 11.1	1.66 dm, 11.1	1.61	1.70
b	1.78 dm, 5.3	2.21 dm, 4.3	2.21 dm, 4.5	1.79 dm, 4.7	2.21	2.21
3a	1.68 m	1.75 m	1.75 m	1.69 m	1.74	1.74
b	1.49 m	1.62 m	1.64 m	1.45 m	1.61	1.63
5b	1.43 d, 2.7	1.52 d, 2.7	1.52 d, 2.4	1.47 d, 2.7	1.56	1.55
6b	5.47 dd, 2.7; 3.9	5.48 dd, 2.7; 3.6	5.48 dd, 2.4; 4.0	5.59 d, 2.7; 3.9	5.57	5.56
7a	3.23 ddd, 2.3; 3.7; 3.9	3.23 ddd, 2.2; 3.3; 3.6	3.20 ddd, 2.2; 3.7; 4.0	3.29 ddd, 2.2; 3.5; 3.9	3.28	3.26
8a	5.44 dd, 2.3; 3.7	5.32 dd, 2.2; 3.3	5.28 dd, 2.2; 3.7	5.47 dd, 2.2; 3.5	5.36	5.33
9a	4.62 dd, 2.3; 2.3	4.12 dd, 2.2; 2.2	3.89 dd, 2.2; 2.2	4.65 dd, 2.2; 2.2	4.15	3.93
13a	5.79 s	5.82 s	5.79 s	5.84 s	5.84	5.83
b	6.64 s	6.66 s	6.64 s	6.66 s	6.69	6.67
14a	1.28 s	1.29 s	1.30 s	1.28 s	1.29	1.29
15a	1.31 s	1.26 s	1.28 s	1.32 s	1.31	1.31
6-ester	1.23 d, 7.0	1.20 d, 7.0	1.20 d, 7.0	1.99 q, 1.1	1.95	1.97
	1.26 d, 7.0	1.22 d, 7.0	1.23 d, 7.0	5.68 br s	5.68	5.67
	2.62 sept, 7.0	2.60 sept, 7.0	2.59 sept, 7.0	6.15 br s	6.12	6.12
8-ester	1.75 d, 7.8	1.78 d, 6.9	1.78 d, 7.0	1.75 d, 7.8	1.81	1.82
	6.79 dm, 7.8	6.78 dm, 6.9	6.78 dm, 7.0	6.81 dm, 7.8	6.79	6.78
	1.76 br s	1.77 br s	1.77 br s	1.77 br s	1.76	1.76

[a] MTPA group: δ 3.56 s, CH_3O; δ 7.49 d, J = 8.2 Hz, 2 Har; δ 7.36 m, 4 Har. [b] Multiplicity: similar to those of **2**.

isobutyrate (**3**)[12−14] and 6-*O*-methacrylate (**4**).[12] Compounds **1** and **2** constitute a new type of sesquiterpene δ-lactone: the (9*R*)-eudesman-9,12-olide framework. We describe herein bioassay-guided isolation, structure elucidation, and determination of absolute configuration of eight chiral carbon centers of new antimalarial products: wedelolides A (**1**) and B (**2**).



1: R = tigloyl, R' = isobutyroyl



3: R = isobutyroyl

2: R = tigloyl, R'= methacryloyl

4: R = methacryloyl

Results and Discussion

The EtOH extract of leaves of Vietnamese *W. trilobata* was successively extracted with cyclohexane and CH_2Cl_2. The bioassay-guided fractionation (against *Plasmodium falciparum*) of the CH_2Cl_2 extract, followed by purification on TLC and C18 reversed-phase silica gel HPLC, afforded two new active compounds, which we named wedelolides A (**1**) and B (**2**), together with known trilobolides 6-*O*-isobutyrate (**3**) and 6-*O*-methacrylate (**4**).

Wedelolide A (**1**) was an optically active, $[\alpha]^{20}_D$ −15 (MeOH), amorphous solid. The molecular formula, $C_{24}H_{34}O_8$, was deduced from the HRESMS-protonated molecular ion $[M + H]^+$ at *m/z* 451.2362 associated with NMR data (Tables 1 and 2) and indicated eight degrees of unsaturation.

The ^{13}C NMR spectrum ($CDCl_3$) showed three ester carbonyl signals at δ 163.54, 166.71, and 176.30 and four vinyl carbon signals at δ 127.80, 132.04, 133.19 (CH_2), and 139.24 (CH), taking into account five unsaturations. Hence, the three remainders were attributed to three saturated rings. The ^{1}H, ^{13}C NMR and HSQC spectra also indicated the presence of six methyls, two methylenes, six methines, and two quaternary carbons.

TABLE 2. ^{13}C NMR Data and HMBC Correlations for Wedelolides A (1) and B (2) in $CDCl_3$

	1		**2**	
position	δ^{13}C	HMBC: H (no.)	δ^{13}C	HMBC: H (no.)
1	70.36	2a, 2b, 9, 15	70.45	2a, 2b, 3a, 3b, 15
2	27.98	1, 3a, 3b	28.02	3a, 3b
3	41.42	1, 2a, 2b, 5, 14	41.47	5, 14
4	71.03	2a, 2b, 3a, 3b, 5, 6, 8, 14	71.04	14
5	43.56	6, 7, 9, 14, 15	43.73	6, 9, 14, 15
6	74.15	5, 7, 13a, 13b	74.55	13a, 13b
7	44.00	6, 8, 9, 13a, 13b	44.16	9, 13a, 13b
8	64.68	6, 9	64.72	6, 9
9	81.95	1, 5, 8, 15	81.79	1, 15
10	44.48	1, 2, 5, 6, 8, 9, 15	44.44	1, 2b, 5, 6, 9, 15
11	132.04	6, 7, 8, 13b	132.10	8, 13b
12	163.54	7, 9, 13a, 13b	163.36	9, 13a, 13b
13	133.19		133.19	
14	25.08	3a, 3b, 5	25.14	3a, 3b, 5
15	14.30	1, 5	14.34	1, 5
6-ester	18.54		18.42	
	19.04		127.20	
	34.52		135.92	
	176.30	6, isopropyl	166.80	6, isopropenyl
8-ester	14.49		14.53	
tigloyl	11.83		11.84	
	139.24		139.31	
	127.80		127.20	
	166.71	8, tigloyl	166.82	8, tigloyl

The ^{1}H−^{1}H COSY spectrum and chemical shift revealed the spin systems of four structural fragments (Figure 1): 1-oxypropylene (**a**), 1,2-dimethyl vinyl (**b**), isopropyl (**c**), and a chain formed by two methines and three oxymethines (**d**).

In fact, the deduction of fragment (**d**) was troublesome because of coupling of H9 (δ 4.62, dd, J = 2.3 and 2.3 Hz) with two protons H7 (δ 3.23, ddd, J = 2.3, 3.7 and 3.9 Hz) and H8 (δ 5.44, dd, J = 2.3 and 3.7 Hz). Finally, the HMBC spectrum allowed us to assign clearly the H9 position as follows.

(12) Bohlmann, F.; Ziesche, J.; King, M.; Robinson, H. *Phytochemistry* **1981**, *20*, 751−756.
(13) Farag, S. F.; El-Emary, N. A.; Niwa, M. *Chem. Pharm. Bull.* **1996**, *44*, 661−664.
(14) Huang, X.-S.; Jiang, R.-W.; Ooi, V. E.-C. *Acta Crystallogr.* **2003**, *E59*, o771−o772.

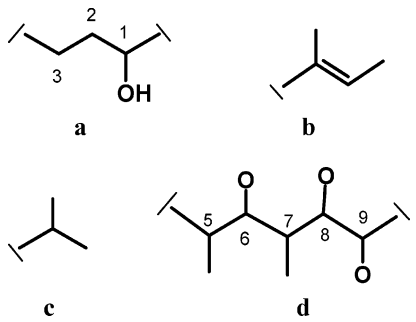


FIGURE 1. Structural fragments of **1**.

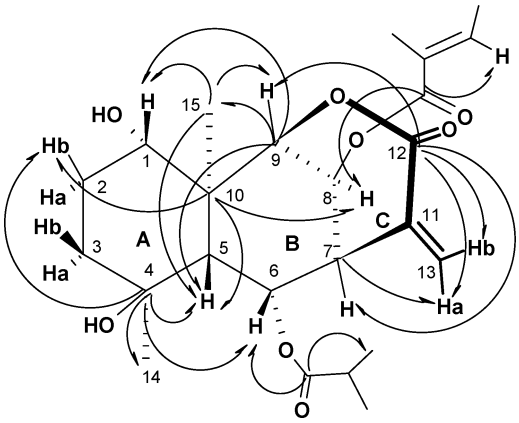


FIGURE 2. Selected long-range HMBC correlations of wedelolide A (**1**) (C→H).

The analysis of long-range HMBC correlations first established a basic bicycle system with fragments (**a**), (**d**), and two quaternary carbons with help of two methyl groups (Figure 2). The quaternary carbon at δ 44.48 was correlated with methyl at δ 1.31, H1 and two protons H2a and H2b of fragment (**a**) and H5, H6 and H8 of fragment (**d**), forming cycle **B**. The clear cross-peaks of C9 at δ 81.95 with H1, H5 and CH_3-15 attested the end position of C9 in the chain (**d**).

The quaternary carbon at δ 71.03 showed the correlations with CH_3 at δ 1.28, two protons H2a,b and H3a,b of fragment (**a**), as well as H5 and H6 of ring **B**; thus, ring **A** was built up. The methyl carbon at δ 14.30 (δ_H 1.31) showed the correlations with H1, H5, and H9, situated at the C15 position. The methyl carbon at δ 25.08 gave the cross-peaks with H5, and two protons H3a and H3b, located at the C14 position. Thus, the bicycle **AB** was defined as decahydronaphthalene (decalin) with CH_3-14 (δ 25.08) fixed to C4 and CH_3-15 (δ 14.30) to C10, bearing oxygenated carbons at C1, C4, C6, C8, and C9. The carbonyl at δ 163.54 showed the correlations with H7, H9 and exocyclic vinylidene protons at δ 5.79 and 6.64, indicating the presence of the third δ-lactone ring **C** in axial conformation, which included C7, C8, C9, C11, carbonyl C12, and an oxygen atom. Thus, the two protons H7 and H9 were equatorial in the cyclohexyl **B** ring and displayed long-range W-type coupling (J = 2.3 Hz), so that H9 was a doublet of doublet in addition to H8 coupling (J = 2.3 Hz). The carbonyl at δ 176.30 was correlated to H6, CH, and two methyl protons of the isopropyl fragment (**c**), indicating that the isobutyroyloxy ester group was attached to C6. The last carbonyl at δ 166.71 showed the cross-peaks with two methyl protons at δ 1.75 and 1.76, H at δ 6.79 of 1,2-dimethyl vinyl fragment (**b**), and final H-8 (δ 5.44) correlation located this tigloyloxy ester to C8 position. The

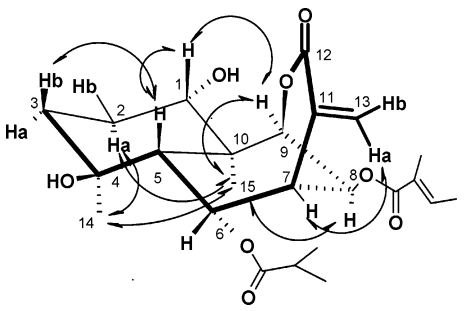


FIGURE 3. Selected NOE interactions of wedelolide A **(1)**.

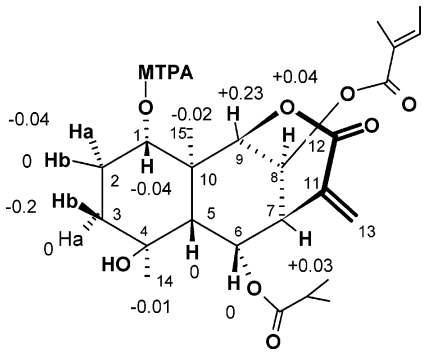


FIGURE 4. Wedelolide A 1-*O*-MTPA ester with shifting values: $\Delta\delta$ (ppm) = δ **1S** − δ **1R**.

structure of wedelolide A (**1**) was established as 1,4-dihydroxy-6- isobutyroyloxy-8-tigloyloxyeudesman-9,12-olide, a δ-lactone.

The relative stereochemistry of wedelolide A (**1**) was assigned by the NOESY spectrum. Methyl-15 protons gave the interactions with methyl-14 protons and axial H8 as well as axial H2a. All of these protons were situated on the same side of molecule as shown in Figure 3, whereas the axial H5 interacted with axial H1b and H3b, situating on another side. The equatorial H7 showing cross-peak with vinylidene proton H13a was found in spatially closed position each other. The results revealed a trans chair−chair junction of rings **A** and **B** (Figure 3).

The absolute stereochemistry of compound (**1**) was determined by mean of auxiliary chiral anisotropic reagent MTPA.[15] (*R*)- and (*S*)-MTPA was respectively introduced into the compound (**1**) to form 1-*O*-ester. Inspection of ^{1}H NMR spectra (Table 1) revealed that 1-*O*-(*R*)-MTPA ester (**1R**) exhibited upfield shift of H9 of δ 0.23, H8 of δ 0.04, and H7 of δ 0.03 and downfield shift of H2a of δ 0.04 with respect to ^{1}H chemical shift of 1-*O*-(*S*)-MTPA ester (**1S**). The result indicated that in 1-*O*-(*R*)-MTPA ester (**1R**), benzene ring was found in front of H9. The H9 showed positive shifting values, $\Delta\delta$ (ppm) = δ **1S** − δ **1R**, of +0.22, thus being located on the right side of MTPA-CH1 axis and the H2a had negative value, $\Delta\delta$ − 0.04, situating on the left side, as drawn in Figure 4, indicating *S* chirality of C1.[15] Hence, the absolute configuration of wedelolide A (**1**) was determined as 1*S*,4*S*,5*S*,6*R*,7*S*,8*S*,9*R*,10*S*.

Wedelolide B (**2**), amorphous solid, exhibited optical activity, $[\alpha]^{20}_D$ −20 (MeOH). The molecular formula, $C_{24}H_{32}O_8$, was deduced from HRESMS protonated molecular ion $[M + H]^+$ at *m*/*z* 449.2146 associating with NMR data (Tables 1 and 2) and indicated nine degrees of unsaturation.

The ^{13}C spectrum ($CDCl_3$) presented similar signals of two methine and four oxymethine carbons at the δ 40−85 area, as same as those of compound (**1**), and two ester carbonyl signals

at δ 163.36 and 166.80 and six vinyl signals, two more than compound (**1**), at δ 127.20 (2 × CH_2), 132.10, 133.19 (CH_2), 135.92, and 139.31 (CH). The carbonyl and vinyl groups were accounted for five unsaturations. The compound (**2**) missed isopropyl signal of (**1**) on ^{1}H and ^{13}C NMR spectra. In fact, the HSQC and HMBC spectra of (**2**) revealed the presence of one carbonyl at δ 166.80 of methacrylate at *O*-6 position, instead of isobutyrate in compound (**1**) and almost superimposed third carbonyl at δ 166.82 of tigloyl, correlating with H8 was attributed to C8 ester, taking part of one unsaturation. The remaining three consisted of three saturated rings as compound **1**. The structure of δ-lactone eudesman-9,12-olide, for compound **2**, was assessed by HMBC diagnostic correlations of carbonyl carbon at δ 163.36 with H9 at δ 4.65, vinylidene protons H13a and H13b, as well as cross-peaks of C9 at δ 81.79 with H1 and methyl-15 protons. The structure of wedelolide B (**2**) was thus determined to be 1,4-dihydroxy-6-methacryloyloxy-8-tigloyloxyeudesman-9,12-olide.

The absolute stereochemistry of compound **2** was also determined by application of auxiliary chiral anisotropic reagent MTPA.[15] The ^{1}H NMR spectrum of the wedelolide B 1-*O*-(*R*)-MTPA ester (**2R**) exhibited an upfield shift of H9 of δ 0.22 and H8 of δ 0.03 and a downfield shift of H2a of δ 0.09 in comparison to the ^{1}H chemical shift of wedelolide B (*S*)-MPTA ester (**2S**) as in the case of compound **1** (Table 1, see Figure 4). The shifting values, $\Delta\delta$ (ppm) = δ **1S** − **1R**, were positive, +0.22 for H9 and negative, −0.09 for H2a. Thus, H9 was located on the right side of the MTPA-CH1 axis and H2a on the left side. Hence, C1 possessed *S* stereochemistry. From these results, the absolute configuration of wedelolide B (**2**) was determined to be 1*S*,4*S*,5*S*,6*R*,7*S*,8*S*,9*R*,10*S*, the same as those of wedelolide A (**1**).

The wedelolides A (**1**) and B (**2**) are the first examples of the novel sesquiterpene framework (9*R*)-eudesman-9,12-olide. Previously isolated eudesmanolide sesquiterpene lactones generally contained a 6,12-[1] or 8,12-γ-lactone[12,13,16] with diversified configuration of ring A/B and B/C junctions and stereochemistry of C1, C4, C5, C6, C7, C8, C9, and C10. It was noteworthy that the absolute configurations of wedelolides A (**1**) and B (**2**), $[\alpha]^{20}_D$ −15 and −20, were enantiomeric in comparison to those of known trilobolides (**3**) and (**4**), $[\alpha]^{20}_D$ +44 and +35. The (9*R*)-eudesman-9,12-olide δ-lactones (**1**) and (**2**) displayed marked antimalarial activity, *in vitro*, against *P. falciparum* parasite[17] with IC_{50} values of 1.9 and 4.1 μg/mL, more active than those of eudesman-8(*R*),12-olide γ-lactone: trilobolides 6-*O*-isobutyrate (**3**) and 6-*O*-methacrylate (**4**) with IC_{50} values of 14.7 and 8.9 μg/mL, respectively. Chloroquine was used as positive control: IC_{50} 0.04 μg/mL.

Experimental Section

General Information. ^{1}H and ^{13}C NMR spectra were recorded on 400 and 75 MHz spectrometers in $CDCl_3$. Chemical shifts were referenced to residual $CHCl_3$ δ_H 7.26 and $CDCl_3$ δ_C 77.0. NOESY spectra were recorded with a 1.5 s relaxation delay, 500 ms mixing time, and apodization with a shifted sine bell and baseline corrections.

Material. The leaves of *W. trilobata* (Asteraceae) were harvested in South Vietnam in 2003 and identified by Dr. Nguyen Duc Binh. A voucher specimen was deposited in the herbarium of the Vietnam National University Ho Chi Minh City.

Isolation of Wedelolides A (1) and B (2). The EtOH extract of the powder of dried leaves of *W. trilobata* (0.45 kg) was extracted with cyclohexane and CH_2Cl_2. The combined CH_2Cl_2 extracts were subjected to chromatography on a silica gel column and separated into 15 fractions. Fraction 4 and 5 were further purified by TLC (CH_2Cl_2/MeOH, 9:1) followed by RP-C18 HPLC eluted by MeOH/H_2O (60/40) to afford, respectively, known compounds **3** (40 mg) and **4** (62 mg) and new compounds **1** (54 mg) and **2** (6 mg).

Wedelolide A (1) [(1*S*,4*S*,5*S*,6*R*,7*S*,8*S*,9*R*,10*S*)-1,4-dihydoxy-6-isobutyroyloxy-8-tigloyloxyeudesman-9,12-olide]: $C_{24}H_{34}O_8$; amorphous solid; $[\alpha]^{20}_D$ −15 (*c* 1.0, MeOH); HRESMS *m*/*z* 451.2362 $[M + H]^+$ (451.2332 calcd for $C_{24}H_{35}O_8$); NMR data ($CDCl_3$) see Table 1 for ^{1}H and Table 2 for ^{13}C.

Wedelolide B (2) [(1*S*,4*S*,5*S*,6*R*,7*S*,8*S*,9*R*,10*S*)-1,4-dihydoxy-6-methacryloyloxy-8-tigloyloxyeudesman-9,12-olide]: $C_{24}H_{32}O_8$; amorphous solid; $[\alpha]^{20}_D$ −20 (*c* 0.1, MeOH); HRESMS *m*/*z* 449.2146 $[M + H]^+$ (449.2175 calcd for $C_{24}H_{33}O_8$); NMR data ($CDCl_3$) see Table 1 for ^{1}H and Table 2 for ^{13}C.

Trilobolide 6-*O*-isobutyrate (3): $[\alpha]^{20}_D$ +44 (*c* 1.0, MeOH) (+36 in $CHCl_3$,[13] +30.8[12]); HRESMS $[M + H]^+$ *m*/*z* 453.2005 (453.2124 calcd for $C_{23}H_{33}O_9$).

Trilobolide 6-*O*-methacrylate (4): $[\alpha]^{20}_D$ +35 (*c* 0.5, MeOH); HRESMS $[M + H]^+$ *m*/*z* 451.1882 (451.1968 calcd for $C_{23}H_{31}O_9$).

1-*O*-MTPA Ester Derivatives. (*R*)-MTPA chloride (8 μL) was added to a solution of **1** (2 mg) in anhydrous pyridine (100 μL). After 4 h of reaction at room temperature, the mixture was diluted with 0.5 mL of 1 M $NaHCO_3$ and extracted with CH_2Cl_2. The residue of the extract afforded 1-*O*-(*S*)-MTPA ester (**1S**) by purification on TLC (CH_2Cl_2/MeOH = 95/5).

Wedelolide A 1-*O*-(*S*)-MTPA ester (1S): $[\alpha]^{20}_D$ +19 (*c* 1.0, MeOH); HRESMS *m*/*z* 667.2692 $[MH]^+$ (667.2730 calcd for $C_{34}H_{42}F_3O_{10}$); ^{1}H NMR ($CDCl_3$) see Table 1.

Wedelolide A 1-*O*-(*R*)-MTPA ester (1R): prepared from **1** and (*S*)-MTPA chloride; $[\alpha]^{20}_D$ +60.5 (*c* 1.0, MeOH); HRESMS *m*/*z* 667.2719 $[MH]^+$ (667.2730 calcd for $C_{34}H_{42}F_3O_{10}$); ^{1}H NMR ($CDCl_3$) see Table 1.

Wedelolide B 1-*O*-(*S*)-MTPA ester (2S): prepared from **2** and (*R*)-MTPA chloride; $[\alpha]^{20}_D$ +14 (*c* 0.1, MeOH); HRESMS *m*/*z* 665.2496 $[MH]^+$ (665.2574 calcd for $C_{34}H_{40}F_3O_{10}$); ^{1}H NMR ($CDCl_3$) see Table 1.

Wedelolide B 1-*O*-(*R*)-MTPA ester (2R): prepared from **2** and (*S*)-MTPA chloride; $[\alpha]^{20}_D$ +73 (*c* 0.1, MeOH); HRESMS *m*/*z* 665.2562 $[MH]^+$ (665.2574 calcd for $C_{34}H_{40}F_3O_{10}$); ^{1}H NMR ($CDCl_3$) see Table 1.

Biological Activity.[17] The antimalarial assays were carried out in 96-microwell plates in triplicate against *P. falciparum* parasite. Proliferation of the parasite was estimated by radioisotope counting of hypoxanthine-^{3}H uptaken by *Plasmodium* after 48 h incubation. The IC_{50} value is the concentration of compound inhibiting 50% of parasite proliferation.

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Supporting Information Available: 1D and 2D NMR spectra of compounds **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc*. **1991**, *113*, 4092−4096.

(16) Ragasa, C.; Padolina, W. *J. Nat. Prod.* **1993**, *56*, 386−393.

(17) Frappier, F.; Jossang, A.; Soudon, J.; Calvo, F.; Rasoanaivo, P.; Ratsimamanga-Urverg, S.; Saez, J.; Schrevel, J.; Grellier, P. *Antimicrob. Agents Chemoth.* **1996**, *40*, 1476−1481.