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Jatropholane-Type Diterpenes from *Euphorbia sikkimensis*

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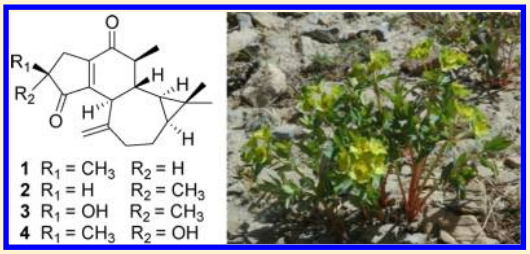
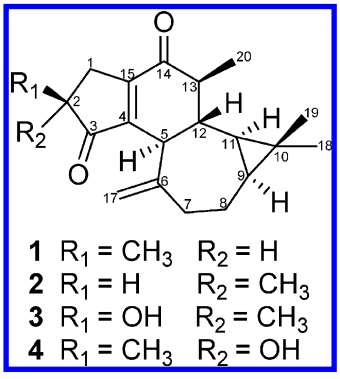
Supporting Information

ABSTRACT: Four new jatropholane-type diterpenes (**1**–**4**), named sikkimenoids A–D, were isolated from the aerial parts of *Euphorbia sikkimensis*. The structural elucidations of **1**–**4** were accomplished by extensive NMR analyses, and their absolute configurations were established by ECD calculations. Compound **2** exhibited weak antiangiogenic activity with an IC_{50} value of 43.0 μM when evaluated using a zebrafish model.



Jatropholane-type diterpenes are characterized by a 5/6/7/3 fused ring system, a structurally unique and rare chemotype. Only three examples of this type are known, jatrophaketone[1] and lagaspholones A and B.[2] However, the absolute configuration of the jatropholane core has remained a challenge due to the lack of appropriate functional groups for chemical derivatization and the quantity limitation of samples. The absolute configuration of this class of natural products in our current study has been determined by a combination of spectroscopic data and computational methods, which should provide a way for configurational assignment of jatropholane-type diterpenes.

The genus *Euphorbia* is famous for the chemical diversity of their isoprenoid constituents, especially bioactive diterpenoids with different core frameworks.[3] In Chinese traditional medicine, the roots of *Euphorbia sikkimensis* Boiss (Euphorbiaceae) have been used for the treatment of poisoning, malaria, rheumatism, and jaundice.[4] However, no previous studies have been reported on its chemical composition. Aiming to search for potential bioactive constituents and promote the rational utilization of bioresources, the aerial part of this plant has been phytochemically investigated. This led to the isolation of four new jatropholane-type diterpenoids (**1**–**4**), which were named sikkimenoids A–D. The chromophores of a 2-ene-1,4-dione and an exocyclic double bond provide the conditions for determining the absolute configuration by ECD calculations. Compound **2** showed antiangiogenic effects against a zebrafish model.



RESULTS AND DISCUSSION

Sikkimenoid A (**1**) was obtained as a colorless powder, $[\alpha]^{25}_{D}$ −113.1 (*c* 0.17, MeOH). The molecular formula $C_{20}H_{26}O_2$ was determined from HRESIMS, which showed a pseudomolecular ion peak at *m*/*z* 321.1835 $[M + Na]^+$ (calcd for 321.1830), corresponding to 8 degrees of unsaturation. The IR spectrum displayed absorption bands for an exocyclic double bond (3070, 1634, 889 cm^{-1}) and two α,β-unsaturated ketones (1712, 1685 cm^{-1}). The ^1H NMR spectrum of **1** (Table 1) displayed signals for two tertiary methyl groups [δ_H 0.93 (3H, s), 1.11 (3H, s)], two secondary methyl groups [δ_H 1.22 (3H, d, *J* = 7.6 Hz), 1.15 (3H, d, *J* = 6.6 Hz)], and an exocyclic methylene [δ_H 4.13 (1H, s), 4.71 (1H, s)]. The ^{13}C NMR and DEPT spectra (Table 2) exhibited 20 carbon resonances, including four methyls, four

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Table 1. ^{1}H NMR Spectroscopic Data for Compounds 1−4 in $CDCl_3$

position	1[a]	2[b]	3[c]	4[b]
1α	2.84 (ddd, 16.6, 8.4, 3.6)	2.14 (t, 3.5)	2.97 (dd, 18.6, 2.4)	2.92 (dd, 18.0, 3.0)
1β	2.45 (dt, 18.4, 2.6)	3.14 (dd, 7.1, 2.5)	2.66 (dd, 18, 4.2)	2.66 (dd, 18.5, 3.5)
2	2.53 (m)	2.53 (m)		
5	3.22 (br d, 8.8)	3.20 (br d, 8.7)	3.22 (br d, 9)	3.21 (br d, 8.5)
7α	2.27 (t, 12.6)	2.26 (br t, 12.7)	2.24 (t, 12.6)	2.26 (t, 13)
7β	2.57 (m)	2.54 (m)	2.52 (m)	2.55 (dd, 13, 4.5)
8	2.18 (m)	2.18 (m)	2.18 (m)	2.19 (m)
9	0.89 (m)	0.86 (m)	0.85 (m)	0.87 (m)
11	0.56 (t, 9.76)	0.54 (t, 9.7)	0.53 (t, 9.6)	0.55 (t, 9.5)
12	1.44 (q, 9.9)	1.43 (q, 9.8)	1.44 (q, 10.2)	1.46 (q, 10)
13	2.38 (m)	2.36 (m)	2.39 (m)	2.39 (m)
16	1.22 (d, 7.6)	1.20 (d, 7.4)	1.36 (s)	1.39 (s)
17a	4.71 (s)	4.68 (s)	4.69 (s)	4.73 (s)
17b	4.13 (s)	4.14 (s)	4.11 (s)	4.26 (s)
18	1.11 (s)	1.10 (s)	1.09 (s)	1.07 (s)
19	0.93 (s)	0.92 (s)	0.89 (s)	0.92 (s)
20	1.15 (d, 6.6)	1.15 (d, 6.7)	1.13 (d, 6.6)	1.16 (d, 6.5)

[a]Recorded at 400 MHz. [b]Recorded at 500 MHz. [c]Recorded at 600 MHz.

Table 2. ^{13}C NMR Spectroscopic Data (δ) for Compounds 1−4 in $CDCl_3$

position	1[b]	2[a]	3[c]	4[a]
1	31.9 t	31.9 t	39.3 t	38.9 t
2	40.8 d	41.4 d	76.7 s	75.1 s
3	212.1 s	211.6 s	211.8 s	209.4 s
4	158.3 s	157.4 s	156.6 s	156.9 s
5	45.9 d	46.1 d	46.0 d	45.9 d
6	154.0 s	154.0 s	154.1 s	153.2 s
7	40.1 t	40.1 t	40.3 t	40.1 t
8	27.0 t	26.9 t	27.2 t	26.9 t
9	26.6 d	26.6 d	26.9 d	26.6 d
10	19.4 s	19.4 s	19.7 s	19.5 s
11	35.5 d	35.3 d	35.5 d	35.3 d
12	47.1 d	46.9 d	47.2 d	46.8 d
13	49.1 d	49.0 d	49.4 d	49.0 d
14	202.3 s	202.0 s	202.0 s	201.4 s
15	151.9 s	152.8 s	150.0 s	149.5 s
16	17.4 q	15.2 q	26.3 q	24.5 q
17	109.8 t	110.0 t	110.3 t	110.8 t
18	28.4 q	28.4 q	28.6 q	28.4 q
19	16.8 q	16.8 q	17.0 q	16.8 q
20	11.3 q	11.3 q	11.5 q	11.2 q

[a]Recorded at 100 MHz. [b]Recorded at 125 MHz. [c]Recorded at 150 MHz; multiplicities inferred from DEPT and HSQC experiments.

methylenes (one sp^2 at δ_C 109.8), six methines, six quaternary carbons (two carbonyl groups at δ_C 202.3 and 212.1), and three olefinic carbons (δ_C 151.9, 154.0, 158.3). Comparison of the NMR spectra of **1** with those of lagaspholone A[2] revealed that **1** was a jatropholane-type diterpene. The differences were that the carbon signals corresponding to a quaternary carbon (C-13) and an oxygenated methine (C-14) in lagaspholone A were replaced by a nonoxygenated methine (δ_C 49.1, C-13) and a carbonyl carbon (δ_C 202.3, C-14) in **1**. This deduction was confirmed by the COSY correlation of H-20 with H-13 and the HMBC correlation of H-20 with C-14 (δ_C 202.3) (Figure 1).

The relative configuration of **1** was elucidated by analysis of its ROESY spectrum and comparison of the chemical shift and coupling constant patterns with those of lagaspholone A.[2] The ROESY correlation of H-12 with Me-20 showed that H-12 and Me-20 were on the same face of the molecule and assigned as β-oriented, the same as Me-20 in lagaspholone A. ROESY cross-peaks of H-5/H-11, H-5/H-13, H-11/Me-18, and H-9/Me-18 showed that H-5, H-9, H-11, H-13, and Me-18 were on the same plane, and the ROESY correlation of H-12/Me-19 indicated H-12 and Me-19 were on another side. This evidence suggested that the relative configurations of H-5 and H-12 were opposite those in lagaspholone A. The β-orientation of Me-16 was supported by the values of $J_{1\alpha,2}$ (6.4 Hz) and $J_{1\beta,2}$ (2.6 Hz), which were similar to those reported for lagaspholone A ($J_{1\alpha,2}$ = 6.5 Hz, $J_{1\beta,2}$ = 2.0 Hz)[2] and curcusone A ($J_{1\alpha,2}$ = 6.8 Hz, $J_{1\beta,2}$ = 2.3 Hz),[5] which was also supported by the observed ROESY correlation of Me-16 with H-12 (Figure 2).

Sikkimenoid B (**2**) was isolated as a colorless powder, $[\alpha]^{25}_D$ −183.7 (*c* 0.22, MeOH). The molecular formula of **2** was assigned to be $C_{20}H_{26}O_2$ on the basis of its positive HRESIMS ($[M + Na]^+$ *m/z* 321.1822, calcd 321.1830), the same as that of **1**. Analysis of 1D and 2D NMR spectra revealed that **2** had the same diterpene skeleton as **1**. The major differences observed between them were changes in the chemical shifts of H-1α and H-1β (Table 1), which suggested that the configuration at C-2 had changed. The relative configurations of other chiral centers were determined to be the same as those of **1** by analyzing its ROESY spectrum.

Although the relative configurations of compounds **1** and **2** were confirmed according to the ROESY correlations, the absolute configurations of jatropholane-type diterpenes could not be identified using these experimental methods. Therefore, the theoretical calculation method of the electronic circular dichroism (ECD) spectra was adopted as an alternative approach using the time-dependent DFT (TDDFT) method with the B3LYP/6-31G (d, p) level.[6,7]

Compounds **1** and **2** were a pair of epimers with the configuration differing at C-2. To identify the absolute configurations of compounds **1** and **2** and validate their relative configuration at C-2, all four possible absolute configurations (1a, 1b, 2a, and 2b, Figures S49 and S50) after geometry optimizations were used to calculate their ECD spectra (Figure 3).

The four possible absolute configurations showed that the calculated ECD spectra of **1a** and **2a** were similar to the experimental spectra of compounds **1** and **2**, respectively (Figure 3). The wave troughs of the calculated curves of **1a** and **2a** near 252.0 nm in MeOH solution and near 250.0 nm in the gas phase were close to the experimental CD band at 251.0 nm. However, both **1b** and **2b** had a wave crest at the same position. In addition, the calculated Δε value of **1a** of −7.5 M^{-1} cm^{-1} was similar to the experimental value of compound **1** of −6.5 $M^{-1}{}_*$ cm^{-1} near 250 nm, while the calculated Δε value of **2a** of −10 M^{-1} cm^{-1} was similar to the experimental value of compound **2** of −14 M^{-1} cm^{-1} near 250 nm. Therefore, it was considered that **1a** was the absolute configuration of compound **1**, and **2a** was the absolute configuration of compound **2**. Molecular orbital (MO) analysis of configuration conformer **1a-1** at the B3LYP/6-311+G(d) level in the gas phase gave us more information to better understand the ECD spectrum (Figures 4 and S51). The wave trough at 251.0 nm in the

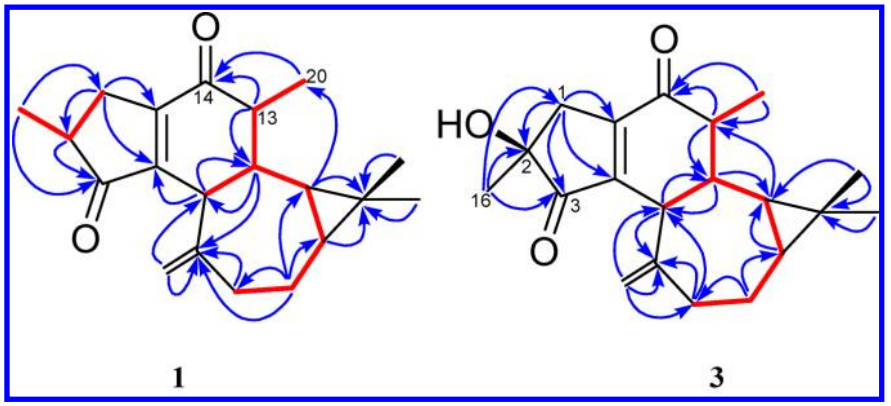

Figure 1. Selected HMBC (→) and $^{1}H-^{1}H$ COSY (−) correlations of compounds **1** and **3**.

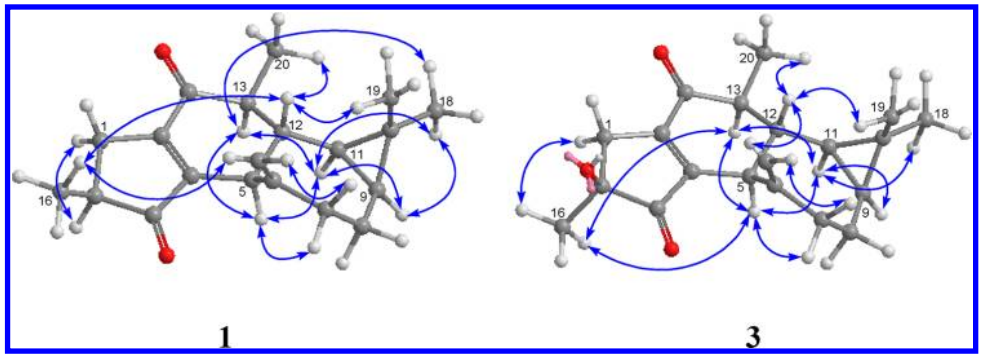

Figure 2. Key ROESY correlations of compounds **1** and **3**.

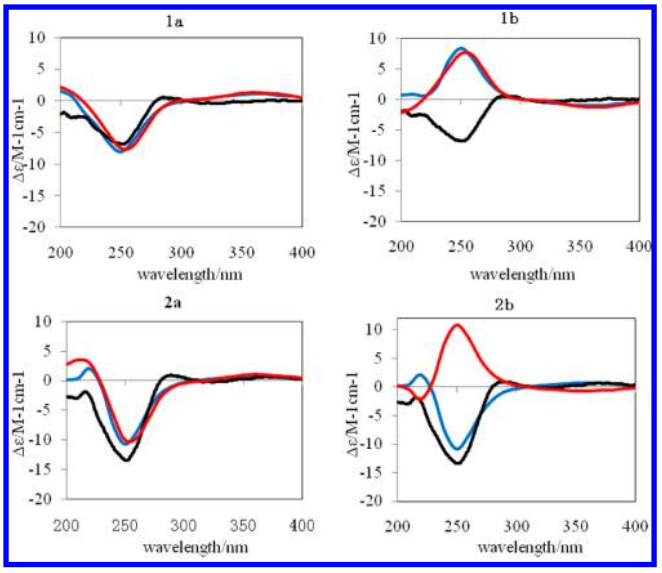

Figure 3. Calculated ECD spectra of two possible absolute configurations of compounds **1** and **2** at the B3LYP level (— (blue) at the B3LYP/6-31G (d, p) level in the gas; — (red) at B3LYP/6-31G (d, p) in MeOH; — (black) experimental in MeOH).

experimental spectra might be caused by the electronic transitions from MO77 to MO82 involving the $\pi \rightarrow \pi^*$ transition in the 2-ene-1,4-dione. In addition, the results show that the weak wave trough at 218.0 nm may be caused by the electronic transitions from MO81 to MO83 involving the $\pi \rightarrow \pi^*$ transition in the exocyclic double bond. Accordingly, the structure and absolute configurations of **1** and **2** were established as shown.

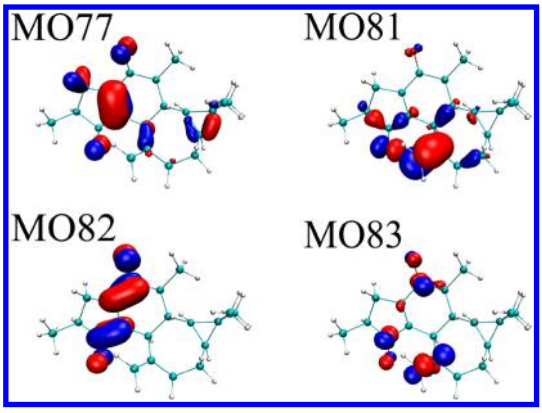

Figure 4. Key orbitals involved in the key transitions of the conformer **1a-1** at the B3LYP/6-311+G(d) level in MeOH with the PCM model.

Sikkimenoid C (**3**) was obtained as a colorless powder and exhibited a quasimolecular ion peak at m/z 337.1776 $[M + Na]^+$ in the HRESIMS, appropriate for a molecular formula of $C_{20}H_{26}O_3$. The IR absorption band at 3478 cm^{-1} implied the presence of an OH group. The 1D NMR data of **3** were similar to those of **2**. The difference could be rationalized by an OH attached at C-2, which was supported by the downfield shift of C-2 to δ_C 76.7 in **3** and the HMBC correlations of Me-16 (δ_H 1.36) with C-1 (δ_C 39.3), C-2 (δ_C 76.7), and C-3 (δ_C 211.8). Its relative configuration was determined to be the same as that of **2** on the basis of analysis of its ROESY spectrum. The ROESY correlations of Me-16/H-13 and Me-16/H-5 indicated the α-orientation of Me-16.

Sikkimenoid D (**4**) had the same molecular formula, $C_{20}H_{26}O_3$, as that of **3** by analysis of its HRESIMS (m/z 337.1775 $[M + Na]^+$, calcd for $C_{20}H_{26}O_3Na$, 337.1779). The

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1D NMR spectroscopic data (Tables 1 and 2) of **4** were similar to those of **3**. The major difference was the relative configuration of Me-16, which was determined to be β-oriented by the ROESY correlations of H-5/H-1α and Me-16/H-1β. Furthermore, the CD experiments and their ECD calculations of **3** and **4** were also conducted. Similar to the above methods, the absolute configurations of **3** and **4** were also determined by comparing their experimental CD data and calculated ECD curves (Figure S52). Thus, the absolute structures of **3** and **4** were determined to be as shown.

The isolated compounds were tested for their cytotoxicity against the human lung cancer cell line A549 by the MTT method, with 5-FU used as a positive control (IC_{50} 58.3 μM).[8] Unfortunately, none of the compounds exhibited significant activity (IC_{50} values >10 μM). The antiangiogenic activities of compounds **1**−**4** were also evaluated using a zebrafish model in terms of the inhibition of the growth of intersegmental vessels, using PTK787 as a positive control (IC_{50} 0.23 μM).[9] The results showed that intersegmental vessels of embryos treated with compound **2** were significantly fewer than those of the control (0.2% DMSO in sterile salt water), and the reduction was dose dependent. The inhibition ratio of compound **2** was 41.1% at a concentration of 33.6 μM with an IC_{50} value of 43.0 μM.

EXPERIMENTAL SECTION

General Experimental Procedures. Melting points were obtained on a XRC-1 micro melting point apparatus. Optical rotations were taken on a Horiba SEPA-300 polarimeter. UV data were obtained on a Shimadzu UV-2401PC spectrophotometer. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with KBr pellets. 1D and 2D NMR experiments were recorded on Bruker AM-400, DRX-500, or Avance III 600 spectrometers with TMS as internal standard. Chemical shifts (δ) are expressed in ppm with reference to the solvent signals. ESIMS were recorded using a Finnigan MAT 90 instrument, and HRESIMS was performed on an API QSTAR time-of-flight spectrometer. Column chromatography (CC) was performed on Sephadex LH-20, silica gel (200−300 mesh, Qingdao Marine Chemical inc., Qingdao, P. R. China), RP-18 gel (LiChroprep, 40−63 μm; Merck, Darmstadt, Germany), and MCI gel CHP20P (75−150 μm, Mitsubishi Chemical Corporation, Tokyo, Japan). Semipreparative HPLC was performed on a Hewlett-Packard instrument (column: Zorbax SB-C18, 250 × 9.4 mm; DAD detector). Fractions were monitored by TLC and visualized by heating plates sprayed with 15% H_2SO_4 in EtOH.

Plant Material. Aerial parts of *E. sikkimensis* were collected from Gongbo Gyamda County of the Tibetan Autonomous Region of China in September 2010. A voucher specimen (Yangyp-20100936) was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences, which was identified by one of the authors (Y.-P.Y.).

Extraction and Isolation. The air-dried and powdered aerial parts of *E. sikkimensis* (11 kg) were extracted with 90% EtOH (3 × 40 L) for 24 h at room temperature and concentrated in vacuo to give a crude extract. The extract was then suspended in H_2O and extracted with EtOAc. The EtOAc solution was evaporated, and the residue was directly subjected to CC over MCI gel eluting with 95% EtOH and then concentrated in vacuo. The residue (690 g) was subjected to CC over silica gel (80−100 mesh), eluting with $CHCl_3$−acetone (from 1:0 to 1:0.2), to afford fractions A−C. Fraction A was purified over Sephadex LH-20, eluted with $CHCl_3$−CH_3OH (1:1), and then subjected to CC over an RP-18 gel, eluted with a MeOH−H_2O gradient system (30−100%), to afford six subfractions (D1−D6). Compound **2** (9 mg) was isolated from D3 by repeated CC over silica gel eluted with petroleum ether−EtOAc (from 1:0 to 1:0.5). Subfraction D2 was subjected to CC over silica gel (200−300 mesh) eluting with petroleum ether−EtOAc (from 1:0 to 1:1) to yield five parts, E1−E5. E3 was purified over a Sephadex LH-20 column eluted with $CHCl_3$−CH_3OH (1:1) and further purified by using semipreparative HPLC eluted by 70% MeOH−H_2O, to afford compound **3** (2 mg) and compound **4** (9 mg). Fraction B was subjected to CC over silica gel (200−300 mesh) eluting with petroleum ether−EtOAc (from 1:0 to 4:1) to yield four subfractions, G1−G4. Subfraction G2 was subjected to CC over Sephadex LH-20, eluted with $CHCl_3$−CH_3OH (1:1), to afford compound **1** (10 mg).

*Sikkimenoid A (**1**):* colorless powder; mp 226−228 °C; $[\alpha]^{25}_D$ −113.1 (*c* 0.17, MeOH); UV (MeOH) λ_{max} (log ε) 256 (3.77) nm; IR (KBr) ν_{max} 3070, 2976, 2933, 2893, 2863, 1712, 1685, 1634, 1451, 1387, 1373, 1287, 1216, 1172, 1124, 1004, 889 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) data, see Tables 1 and 2; positive ESIMS *m/z* 321 $[M + Na]^+$; HRESIMS *m/z* 321.1835 $[M + Na]^+$ (calcd for $C_{20}H_{26}O_2Na$, 321.1830).

*Sikkimenoid B (**2**):* colorless powder; mp 227−229 °C; $[\alpha]^{25}_D$ −183.7 (*c* 0.22, MeOH); UV (MeOH) λ_{max} (log ε) 254 (3.93) nm; IR (KBr) ν_{max} 3082, 2977, 2957, 2934, 2864, 1712, 1680, 1639, 1457, 1387, 1286, 1218, 1187, 1166, 1121, 905 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data, see Tables 1 and 2; positive ESIMS *m/z* 321 $[M + Na]^+$; HRESIMS *m/z* 321.1822 $[M + Na]^+$ (calcd for $C_{20}H_{26}O_2Na$, 321.1830).

*Sikkimenoid C (**3**):* colorless powder; mp 240−242 °C; $[\alpha]^{24}_D$ −132.2 (*c* 0.08, MeOH); UV (MeOH) λ_{max} (log ε) 256 (3.92) nm; IR (KBr) ν_{max} 3478, 3457, 3083, 2972, 2963, 2936, 2860, 1725, 1677, 1637, 1452, 1377, 1287, 1255, 1126, 1023, 889 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) and ^{13}C NMR ($CDCl_3$, 150 MHz) data, see Tables 1 and 2; positive ESIMS *m/z* 337 $[M + Na]^+$; HRESIMS *m/z* 337.1776 $[M + Na]^+$ (calcd for $C_{20}H_{26}O_3Na$, 337.1779).

*Sikkimenoid D (**4**):* colorless powder; mp 240−242 °C; $[\alpha]^{25}_D$ −100.9 (*c* 0.13, MeOH); UV (MeOH) λ_{max} (log ε) 259 (3.64) nm; IR (KBr) ν_{max} 3464, 3079, 2976, 2951, 2901, 2863, 1714, 1673, 1643, 1453, 1392, 1290, 1208, 1128, 904 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) data, see Tables 1 and 2; positive ESIMS *m/z* 337 $[M + Na]^+$; HRESIMS *m/z* 337.1775 $[M + Na]^+$ (calcd for $C_{20}H_{26}O_3Na$, 337.1779).

ECD Calculation. The theoretical calculations of compounds **1**−**4** were performed using Gaussian 09.[10] Conformational analysis was initially carried out using Maestro7.5 conformational searching, together with the OPLS_2005 molecular mechanics methods. The optimized conformation geometries, important dihedral angles, thermodynamic parameters, and populations of all conformations are provided in the Supporting Information (Tables S1−4). The OPLS_2005 conformers were then optimized at the B3LYP/6-31G (d, p) level. Room-temperature equilibrium populations were calculated according to the Boltzmann distribution law. The theoretical calculation of ECD was performed using TDDFT[6,7] at the B3LYP/6-31G (d, p) level in MeOH with the PCM model and in the gas phase, respectively. The ECD spectra of compounds **1**−**4** were obtained by weighing the Boltzmann distribution rate of each geometric conformation.

MO Analysis. The orbital information (NBO plot files) was generated using the NBO program[11] of Gaussian 09. The predominantly populated conformers were selected for MO analysis. NBO plot files were used to generate corresponding Gaussian-type grid files using Multiwfn 2.4.[12] After that, the isosurface of generated grid data was generated by VMD software.[13]

ECD Simulation. The ECD spectra are simulated by overlapping Gaussian functions for each transition according to

$$\Delta\varepsilon(E) = \frac{1}{2.297 \times 10^{-39}} \times \frac{1}{\sqrt{2\pi}\sigma} \sum_i^A \Delta E_i R_i e^{-[(E-E_i)/(2\sigma)]^2}$$

where σ represents the width of the band at $1/e$ height, and ΔE_i and R_i are the excitation energies and rotational strengths for transition i, respectively. σ = 0.20 eV and $R^{velocity}$ have been used in this work.

Cytotoxicity Assays (ref 8). Compounds **1**−**4** were tested for their cytotoxicity against human lung cancer cell line A549 by the MTT method, and 5-FU was used as a positive control. Briefly, 100 μL of cell suspension (1 × 10^5 cells/mL) was seeded into 96-well

microtiter plates and cultured for 24 h before the compound was added. Then, different concentrations of the compounds were added to the plates, the cells were cultivated for 48 h, and 10 μL of MTT (5 mg/mL) was added to each well. After 4 h, the culture medium was removed and the formazan crystals were completely dissolved with 150 μL of DMSO in each well by vigorously shaking the plate. Finally, formazan absorbance was assessed by a BioRad microplate reader at 570 nm.

Antiangiogenesis Assay (ref 9). Stock solutions (20 mg/mL) of all samples were prepared by dissolving the test compounds in 100% DMSO. These solutions were diluted in sterile salt water (5 mM NaCl, 0.17 mM KCl, 0.4 mM $CaCl_2$, 0.16 mM $MgSO_4$) to obtain final solutions of various concentrations in 0.2% DMSO. Aliquots were placed into 24-well plates, and the embryos (TG[VEGFR2:GRCFP]) at 24 hpf (hours postfertilization) were also transferred randomly into the above wells. The embryos were prepared from a wild AB-type line of zebrafish, which were purchased from the Biology Institute of Shandong Academy of Sciences, P. R. China. Control embryos were treated with the equivalent amount of DMSO solutions. All embryos were incubated at 28.5 °C. After 48 h treatment, the intersegmental vessels of embryos were visualized with green fluorescent protein labeling and endogenous alkaline phosphatase staining. The antiangiogenic activities of compounds were calculated from the inhibition ratio of antiangiogenesis.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR, HSQC, HMBC, COSY, ROESY, MS, HRESIMS, IR, UV, CD, and ORD spectra of **1**−**4** and the related data of ECD calculations of **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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