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# Tirucallane-Type Triterpenoids from *Dysoxylum lenticellatum*

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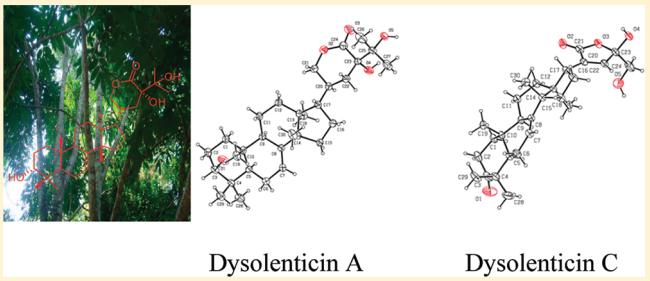
Supporting Information

**ABSTRACT:** Ten new tirucallane-type triterpenoids, represented by a rearranged skeleton dysolenticin A (**1**), dysolenticin B (**2**), a rare trinortriterpenoid dysolenticin C (**3**), three tirucallane triterpenoid derivatives with a hemiketal moiety dysolenticins D−F (**4**−**6**), dysolenticins G−I (**7**, **9**, **10**), and the new alkaloid dysolenticin J (**12**), together with seven known analogues were isolated from the twigs and leaves of *Dysoxylum lenticellatum*. Their structures were elucidated by extensive spectroscopic methods, and those of compounds **1**, **3**, **4**, **6**, and **10** were confirmed by single-crystal X-ray diffraction experiments. Dysolenticin J (**12**) showed significant vasodilative effects on intact rat aortic rings with a diastolic degree of 87.4% at 10 $\mu$g/mL.




Plants of the Meliaceae family are rich sources of structurally diverse and biologically significant triterpenoids.[1−3] Within this family, the genus *Dysoxylum* comprises about 14 species in China, some of which have applications in folk medicine.[4] In prior reports, triterpenes,[4−6] triterpene glycosides,[7] tetranortriterpenoids,[8] diterpenes,[9] steroids,[10] alkaloids,[11,12] and flavonoids[13] were isolated from this genus. *Dysoxylum lenticellatum* C. Y. Wu (Meliaceae) is a tall tree distributed mainly in Yunnan Province.[14] Previous investigation on the chemical constituents of this species led to the isolation of tetranortriterpenoids, diterpenoids, and ceramides.[14] In our work, ten new (dysolenticins A−J, **1**−**7**, **9**, **10**, **12**) and seven known (**8**, **11**, **13**−**17**) tirucallane-type triterpenoids were isolated from the twigs and leaves of *D. lenticellatum* that were collected from Yunnan Province of China. Some of the isolated compounds were evaluated for cytotoxic activity against HL-60 (human promyelocytic leukemia) and SMMC-7721 (human hepatoma) tumor cells and vasodilative effects on intact rat aortic rings precontracted with phenylephrine ($10^{-6}$ M).

## RESULTS AND DISCUSSION

Dysolenticin A (**1**) was isolated as colorless crystals. HRESIMS indicated a molecular formula of $C_{30}H_{48}O_5$, with seven degrees of unsaturation. The IR spectrum indicated the presence of OH (3405 $cm^{-1}$) and carbonyl (1707 $cm^{-1}$) groups. The $^1H$ NMR spectrum of compound **1** (Table 1) revealed resonances due to seven methyl groups and one olefinic proton [$\delta_H$ 5.28 (1H, d, $J$ = 3.6 Hz, H-7)]. Combined analysis of $^{13}C$ NMR (Table 2), DEPT, and HSQC spectra revealed 30 carbon signals attributed to a lactone ring group ($\delta_C$ 74.6 and 175.1) and two olefinic, seven methyl, eight methylene, five methine, and six quaternary carbons. These data indicated that compound **1** possessed a tirucallane-7-ene system.[15−17] The spectroscopic data of compound **1** were very similar to the tirucallane-type triterpenoidal skeleton.[15−17] The $^1H-^1H$ COSY spectrum and HMBC correlations from $\delta_H$ 1.44 (1H, m, $H_2$-22a) and 1.96 (1H, m, $H_2$-22b) to $\delta_C$ 49.3 (C-17), 74.5 (C-25), 75.9 (C-23), and 175.1 (C-24) and from $\delta_H$ 3.92 (1H, t, $J$ = 11.0 Hz, $H_2$-21a) and 4.57 (1H, dt, $J$ = 11.0, 4.0 Hz, $H_2$-21b) to $\delta_C$ 49.3 (C-17), 75.9 (C-23), and 175.1 (C-24) implied the presence of a six-membered lactone ring at C-17 and an OH attached to C-25 in the side chain. In the $^1H$ NMR spectrum (Table 1), H-3 ($\delta_H$ 3.47), a broad singlet, and the NOSEY correlation of H-3/$H_3$-29 indicated the $\alpha$-orientation of 3-OH. The 23-OH was also $\alpha$-oriented,[18] as deduced from the NOSEY correlations from $\delta_H$ 3.98 (1H, br s, 23-OH) to $\delta_H$ 1.29 (3H, s, $H_3$-26) and 2.21 (1H, m, H-20). Finally, X-ray crystallographic analysis (Figure 1A) confirmed the structure of compound **1**, which was a 25(24→23)*abeo*-tirucallane triterpenoid. A possible mechanism for the formation of compound **1** is shown in Scheme 1.[19]

Dysolenticin B (**2**) presented a molecular formula of $C_{30}H_{42}O_3$ as determined by HRESIMS. The $^1H$ and $^{13}C$ NMR data (Tables 1 and 2) of compound **2** were similar to those of compound **1**, except for the chemical shifts of a carbonyl group in compound **2**

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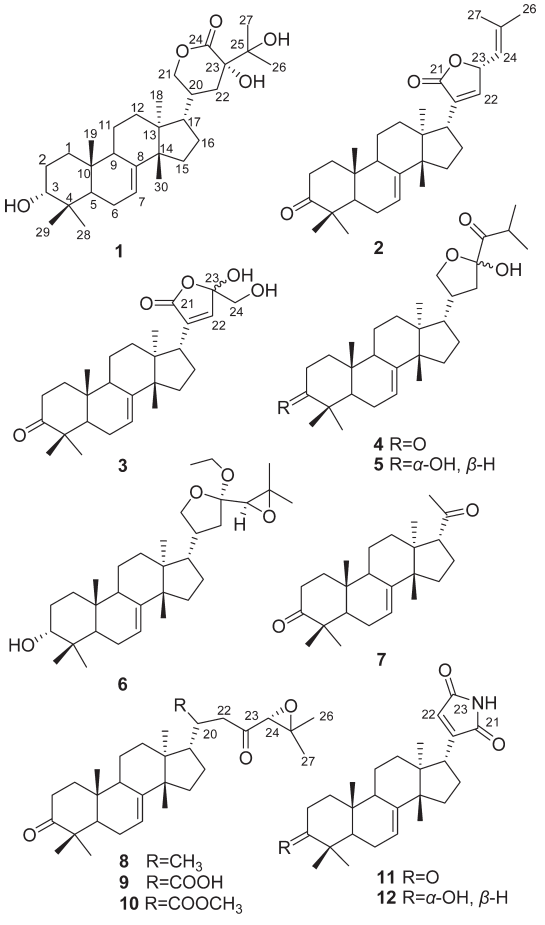
taking the place of the oxymethine group in compound **1** at C-3. The chemical shifts of a lactone group [$\delta_C$ 78.1 (C-23), 174.2 (C-21) and $\delta_H$ 4.90 (1H, d, $J$ = 8.8 Hz, H-24), $\delta_C$ 118.9 (C-24), 140.5 (C-25)] and olefinic signals [$\delta_H$ 6.90 (1H, br s, H-22); $\delta_C$ 135.1 (C-20), 148.5 (C-22)] were interpreted as the side chain cyclized with four carbons and one oxygen atom to form a pentacyclic lactone skeleton. The above inference was confirmed by $^1$H−$^1$H COSY correlations and the following HMBC correlations: $\delta_H$ 2.96 (1H, t, $J$ = 9.2 Hz, H-17) with $\delta_C$ 135.1 (C-20), 148.5 (C-22), and 174.2 (C-21); $\delta_H$ 6.90(1H, br s, H-22) with $\delta_C$ 43.6 (C-17), 135.1 (C-20), and 174.2 (C-21). Furthermore, the HMBC correlations from $\delta_H$ 4.90 (1H, d, $J$ = 8.8 Hz, H-24) to $\delta_C$ 18.5 (C-27) and 25.8 (C-26) indicated the presence of two methyl groups at C-25. The relative configuration of compound **2** was inferred from the NOE difference spectra. The resonance




of $H_3$-27 was enhanced by irradiation of H-23, $H_3$-26 was enhanced by irradiation of H-24, and $H_3$-18, H-24 was enhanced by irradiation of $H_3$-26, revealing that H-23 was $\beta$-oriented.

The $^1$H and $^{13}$C NMR spectra (Tables 1 and 2) of dysolenticin C (**3**) were almost the same as those of compound **2**. Compared with compound **2**, the $\Delta^{24,25}$-double bond was replaced by a hydroxymethyl group ($\delta_C$ 68.0) in compound **3**. The structure was supported by HMBC correlations between $\delta_H$ 3.60, 3.71 (each 1H, m, H-24) and $\delta_C$ 103.8 (C-23) and 144.5 (C-22). However, HRESIMS of compound **3** showed a quasimolecular ion peak at $m/z$ 493.2932 ([M + EtOH − $H_2O$ + Na]$^+$, calcd for 493.2924), and the HMBC spectrum revealed a very weak cross-peak between the protons of ethanol and C-24, so we were not sure if the ethoxy was located at C-24. Fortunately, a single crystal of compound **3** was obtained from a petroleum ether/EtOH/$CH_3CN$ mixture, and X-ray crystallographic analysis was carried out. The result clearly established the structure. There was some ethanol impurity contained in the sample used for HRESIMS and NMR experiments. The relative configuration of compound **3** was confirmed by the NOESY spectrum and X-ray crystallographic analysis (Figure 1B). Additionally, the NMR spectroscopic data indicated that compound **3** was a trinortriterpenoid and an epimeric mixture at C-23.

The molecular formula of dysolenticin D (**4**) was $C_{30}H_{46}O_4$. The NMR resonances for the tetracyclic moiety (Experimental Section and Table 2) revealed that compound **4** was nearly identical to compounds **2** and **3** in structure. The chemical shifts of $\delta_H$ 3.54 (1H, dd, $J$ = 10.0, 8.0 Hz, $H_2$-21a), 4.28 (1H, t, $J$ = 8.0 Hz, $H_2$-21b) and $\delta_C$ 73.9 (C-21), 103.6 (C-23) and the HMBC correlation from $H_2$-21 to $\delta_C$ 103.6 (C-23) revealed that C-21 and C-23 were linked via an oxygen atom to form a tetrahydrofuran ring.[20] In addition, a proton resonance at $\delta_H$ 4.49 (1H, s), which did not show any cross-peak with the carbon signals in the HSQC spectrum, implied the presence of an exchangeable OH proton. HMBC correlations from the OH proton to $\delta_C$ 42.2 (C- 22), 103.6 (C-23), and 212.7 (C-24) illustrated that the OH was located at C-23, forming a hemiketal moiety. X-ray crystallographic analysis (Figure 2A) confirmed the structure. The NMR spectroscopic data showed clearly that compound **4** was a pair of epimers at C-23.

The spectroscopic data of **5** ($C_{30}H_{48}O_3$) were similar to those of compound **4**, except for the presence of an oxymethine group [$\delta_H$ 3.46 (1H, br s, H-3); $\delta_C$ 76.2 (C-3)] in compound **5**. The HMBC spectrum showed correlations from $\delta_H$ 0.91 (3H, s, $H_3$-29) and 0.93 (3H, s, $H_3$- 28) to 76.2 (C-3) and from H-3 to $\delta_C$ 21.8 (C-29), 27.8 (C-28), 31.2 (C-1), and 44.6 (C-5), indicating an OH at C-3. H-3 was determined to be $\beta$-oriented by its broad singlet in the $^1$H NMR spectrum and NOESY correlation of H-3/$H_3$-29. Compound **5** was also a pair of epimers and was named dysolenticin E.

Dysolenticin F (**6**) possessed the molecular formula $C_{32}H_{52}O_4$ on the basis of its HRESIMS. The 1D NMR (Tables 1 and 2) data of compound **6** were similar to those of compound **5**. The major differences were that chemical shifts of an epoxide group [$\delta_H$ 2.78 (1H, s, H-24); $\delta_C$ 60.6 (C-25), 65.2 (C-24)] in compound **6** replaced those of the carbonyl group in compound **5**. This was confirmed by the HMBC experiment showing correlations from H-24 to $\delta_C$ 60.6 (C-25) and 106.2 (C-23). The $^1$H and $^{13}$C NMR spectra showed the signals of $\delta_H$ 1.16 (3H, t, $J$ = 6.8 Hz, $H_3$-32), $\delta_C$ 15.8 (C-32) and $\delta_H$ 3.50 (1H, m, $H_2$-31a), 3.56 (1H, m, $H_2$-31b), $\delta_C$ 57.8 (C-31); the unit was deduced to be an ethoxy group. The HMBC correlations of $H_2$-31 with C-23 and C-32 illustrated that the ethoxy group was located at C-23. The H-3 was assigned as $\beta$-oriented by the correlation of H-3/$H_3$-29 in the NOESY spectrum. Unfortunately, the NOESY spectrum could not give useful information to determine the relative configuration of C-23 and C-24. A single-crystal X-ray diffraction (Figure 2B) of compound **6** showed that the ethoxy group was $\alpha$-oriented and H-24 was $\beta$-oriented. Compound **6** was likely an artifact formed in the extraction process that involved EtOH (Scheme 1.).

Dysolenticin G (**7**) had the molecular formula $C_{24}H_{36}O_2$ as established by HRESIMS. The IR spectrum revealed the presence of carbonyl (1731 cm$^{-1}$) and double-bond (1706 cm$^{-1}$) groups. The $^1$H and $^{13}$C NMR data (Experimental Section) of

Table 1. $^1$H NMR Data of Compounds 1−3, 6, 10, and 12[a]

| | 1 | 2 | 3 | 6 | 10 | 12 |
|---|---|---|---|---|---|---|
| position | $\delta_H$ m (J, Hz) | $\delta_H$ m (J, Hz) | $\delta_H$ m (J, Hz) | $\delta_H$ m (J, Hz) | $\delta_H$ m (J, Hz) | $\delta_H$ m (J, Hz) |
| 1 | 1.36 m, 1.48 m | 1.44 m, 1.98 m | 1.44 m, 1.99 m | 1.34 m, 1.46 m | 1.44 m, 1.98 m | 1.39 m, 1.46 m |
| 2 | 1.44 m, 1.97 m | 2.23 m, 2.75 td (14.4, 5.6) | 2.24 m, 2.76 ddt (14.6, 14.6, 5.6, 1.6) | 1.34 m, 1.87 m | 2.24 m, 2.74 m | 1.62 m, 1.93 m |
| 3 | 3.47 br s | | | 3.45 s | | 3.47 br s |
| 5 | 1.77 m | 1.72 m | 1.72 m | 1.76 m | 1.70 m | 1.77 m |
| 6 | 1.93 m, 2.06 m | 2.10 m, 2.11 m | 2.11 m | 1.93 m, 2.02 m | 2.08 m | 1.96 m, 2.07 m |
| 7 | 5.28 d (3.6) | 5.33 d (3.2) | 5.34 d (3.2) | 5.24 d (2.8) | 5.31 d (2.8) | 5.30 d (3.6) |
| 9 | 2.32 m | 2.26 m | 2.27 m | 2.33 m | 2.24 m | 2.31 m |
| 11 | 1.50 m, 1.58 m | 1.57 m | 1.59 m | 1.48 m, 1.55 m | 1.52 m | 1.58 m |
| 12 | 1.49 m, 1.66 m | 1.39 m, 2.10 m | 1.40 m, 2.09 m | 1.33 m, 1.63 m | 1.34 m, 1.56 m | 1.31 m, 2.04 m |
| 15 | 1.50 m, 1.56 m | 1.63 m, 1.70 m | 1.66 m | 1.47 m, 1.55 m | 1.53 m | 1.64 m, 1.75 m |
| 16 | 1.62 m, 1.92 m | 1.72 m, 2.06 m | 1.74 m, 2.06 m | 1.60 m, 1.91 m | 1.26 m, 1.98 m | 1.78 m, 2.08 m |
| 17 | 1.48 m | 2.96 t (9.2) | 2.95 m | 1.62 m | 2.75 m | 3.05 t (8.8) |
| 18 | 0.91 s | 0.72 s | 0.71 s/0.76 s | 0.75 s | 0.93 s | 0.76 s |
| 19 | 0.76 s | 1.02 s | 1.02 s | 0.73 s | 0.98 s | 0.78 s |
| 20 | 2.21 m | | | 2.42 m | 1.96 m | |
| 21 | 3.92 t (11.0), 4.57 dt (11.0, 4.0) | | | 3.55 m, 3.99 t (8.0) | | |
| 22 | 1.44 m, 1.96 m | 6.90 br s | 6.78 d (9.2) | 1.70 m, 2.09 dd (12.4, 6.8) | 2.61 m, 3.00 dd (18.4, 11.2) | 6.31 s |
| 23 | | 5.62 d (8.8) | | 2.78 s | 3.32 s | |
| 24 | | 4.90 d (8.8) | 3.60 m, 3.71 m | 1.30 s | 1.41 s | |
| 25 | | | | 1.52 s | 1.29 s | |
| 26 | 1.29 s | 1.77 s | | 0.84 s | 1.04 s | 0.93 s |
| 27 | 1.18 s | 1.79 s | | 0.81 s | 1.10 s | 0.91 s |
| 28 | 0.93 s | 1.04 s | 1.04 s | 0.90 s | 0.99 s | 1.09 s |
| 29 | 0.91 s | 1.12 s | 1.11 s | 3.50 m, 3.56 m | | |
| 30 | 0.97 s | 1.12 s | 1.11 s | 1.16 t (6.8) | | |
| 23-OH | 3.98 br s | | 4.26 br s/4.44 br s | | 3.66 s | |
| 25-OH | 3.89 br s | | | | | 7.49 br s |

[a] Data were measured in $CDCl_3$, 400 MHz. $^1$H assignments aided by DEPT, $^1$H−$^1$H COSY, HSQC, HMBC, and NOESY experiments.

the tetracyclic moiety resembled compounds **2**, **3**, and **4**, except for the absence of six carbons of the side chain. In the HMBC spectrum, the correlations from $\delta_H$ 2.12 (3H, s, $H_3$-21) to $\delta_C$ 61.5 (C-17) and 209.8 (C-20) and from $\delta_H$ 2.83 (1H, t, $J$ = 8.4 Hz, H-17) to 209.8 (C-20) suggested an acetyl group at C-17. The relative configuration of compound **7** was deduced from its NOESY spectrum. H-17 was determined to be $\beta$-oriented by the NOESY correlation of H-17/$H_3$-30.

Compound **9** was a white, amorphous powder having the molecular formula $C_{30}H_{44}O_3$ as deduced from HRESIMS. The IR spectrum indicated the presence of carbonyl (1721, 1703 cm$^{-1}$) and OH (3385 cm$^{-1}$) groups. The spectroscopic data (Experimental Section) of compound **9** were similar to the known compound **8** (24,25-epoxytirucall-7-ene-3,23-dione).[21] However, the methyl group [$\delta_H$ 0.90 (3H, s); $\delta_C$ 19.5] in compound **8** was missing. The $^{13}$C NMR resonance of C-21 was downfield shifted to $\delta_C$ 177.9; there should be a carboxyl group at C-21. In the NOESY spectrum, H-20 [$\delta_H$ 2.31 (1H, m)] showed a cross-peak correlation with $H_3$-18 [$\delta_H$ 1.24 (3H, s)], meaning that H-20 was $\alpha$-oriented, but the configuration of H-24 could not be deduced from the NOESY correlations. The side chain was depicted showing a keto group at C-23 and a 24,25-epoxide group, which has been described previously.[22,23] Compound **9** and dymacrin H[21] both are tirucallane-type triterpenoids, and $^{13}$C NMR resonances (in $C_5D_5N$) of the side chain in compound **9** were similar to those of dymacrin H[22] and cimicidanol-3-arabinoside.[23] Therefore, the 24,25-epoxide group was $\alpha$-oriented.[22,23] The name dysolenticin H was suggested for compound **9**.

Spectroscopic data proved that compounds **10** and **9** were similar in structure; the only difference was the presence of an $OCH_3$ group [$\delta_H$ 3.66 (3H, s)] in compound **10**. The $^{13}$C NMR resonance of C-21 was downfield at $\delta_C$ 175.8, and the $OCH_3$ group at C-21 was a methyl ester from the HMBC correlation between the $OCH_3$ and C-21. Compounds **9** and **10** had the same side chain, including a 24,25-epoxide group, and the $^{13}$C NMR spectrum (in $CDCl_3$) of the side chain in compound **10** was similar to that of dymacrin H.[21] Consequently, the 24,25-epoxide group was $\alpha$-oriented.[21,22] X-ray crystallographic analysis (Figure 3) confirmed the structure. The structure of compound **10** was assigned as shown, and it was named dysolenticin I.

The molecular formula of compound **12** was $C_{26}H_{37}NO_3$, with nine degrees of unsaturation. IR absorptions at 3584, 3203, 1619, and 1712 cm$^{-1}$ indicated the presence of NH, OH, double-bond, and carbonyl groups. Comparison of compound **12** with


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Table 2. $^{13}$C NMR Data ($\delta_C$) of Compounds 1−4, 6, 10, and 12[a]

| carbon | 1 | 2 | 3 | 4 | 6 | 10 | 12 |
|---|---|---|---|---|---|---|---|
| 1 | 31.2, t | 38.5, t | 38.5, t/38.6, t | 38.4, t/38.5, t | 31.2, t | 38.4, t | 31.1, t |
| 2 | 27.2, t | 34.9, t | 35.0, t | 34.8, t | 27.5, t | 34.9, t | 25.3, t |
| 3 | 76.2, d | 216.7, s | 216.8, s | 216.6, s | 76.2, d | 216.8, s | 76.2, d |
| 4 | 37.4, s | 47.9, s | 48.0, s | 47.8, s | 37.4, s | 47.8, s | 37.4, s |
| 5 | 44.4, d | 52.4, d | 52.5, d | 52.3, d/52.4, d | 44.6, d | 52.3, d | 44.6, d |
| 6 | 23.9, t | 24.4, t | 24.5, t | 24.3, t | 23.9, t | 24.3, t | 23.9, t |
| 7 | 118.7, d | 118.4, d | 118.7, d | 118.4, d | 118.2, d | 118.4, d | 119.0, d |
| 8 | 145.0, s | 145.4, s | 145.3, s | 145.2, s | 145.6, s | 145.3, s | 145.0, s |
| 9 | 48.4, d | 48.3, d | 48.4, d | 48.2, d/48.3, d | 48.5, d | 48.2, d | 48.4, d |
| 10 | 34.7, s | 35.2, s | 35.2, s | 35.1, s | 34.8, s | 35.0, s | 34.8, s |
| 11 | 17.8, t | 17.4, t | 17.5, t | 17.6, t | 17.4, t | 17.8, t | 17.1, t |
| 12 | 32.9, t | 30.6, t | 30.5, t/30.7, t | 31.4, t/31.5, t | 31.7, t | 29.8, t | 30.6, t |
| 13 | 43.5, s | 45.0, s | 45.2, s | 43.9, s/43.7, s | 43.7,s | 43.3, s | 46.2, s |
| 14 | 51.2, s | 51.1, s | 51.3, s | 51.1, s | 50.7, s | 51.0, s | 51.6, s |
| 15 | 33.7, t | 34.2, t | 34.3, t | 34.2, t | 34.2, t | 33.5, t | 34.2, t |
| 16 | 25.4, t | 26.7, t | 26.5, t/26.7, t | 27.6, t | 25.4, t | 27.4, t | 26.5, t |
| 17 | 49.3, d | 43.6, d | 43.8, d | 50.6, d | 51.2, d | 41.6, d | 43.8, d |
| 18 | 22.3, q | 23.3, q | 23.3, q | 22.7, q/22.5, q | 22.7, q | 21.6, q | 23.5, q |
| 19 | 13.0, q | 12.7, q | 12.8, q | 12.7, q | 12.9, q | 12.7, q | 12.9, q |
| 20 | 33.8, d | 135.1, s | 140.2, s/140.3, s | 40.9, d | 39.3, d | 49.8, d | 152.8, s |
| 21 | 74.6, t | 174.2, s | 171.1, s/171.2, s | 73.9, t/72.0, t | 72.9, t | 175.8, s | 171.6, s |
| 22 | 36.1, t | 148.5, d | 144.4, d/144.5, d | 42.2, t/41.9, t | 43.3, t | 43.9, t | 128.1, d |
| 23 | 75.9, s | 78.1, d | 103.3, s/103.8, s | 103.6, s/104.1, s | 106.2, s | 205.6, s | 170.7, s |
| 24 | 175.1, s | 118.9, d | 68.0, t | 212.7, s/211.7, s | 65.2, d | 65.2, d | |
| 25 | 74.5, s | 140.5, s | | 33.5, d/33.8, d | 60.6, s | 61.2, s | |
| 26 | 25.0, q | 25.8, q | | 19.8, q/20.1, q | 25.7, q | 24.9, q | |
| 27 | 21.6, q | 18.5, q | | 19.4, q/19.7, q | 19.1, q | 18.4, q | |
| 28 | 27.8, q | 24.5, q | 24.6, q | 24.5, q | 27.8, q | 24.5, q | 27.7, q |
| 29 | 21.8, q | 21.5, q | 21.7, q | 21.5, q | 21.8, q | 21.6, q | 21.7, q |
| 30 | 27.1, q | 27.5, q | 27.6, q | 27.2, q | 27.0, q | 27.4, q | 27.3, q |
| $OCH_2$− | | | | | 57.8, t | | |
| $OCH_2$−$CH_3$ | | | | | 15.8, q | | |
| COOMe− | | | | | | 51.6, q | |

[a] Data were measured in $CDCl_3$ at 100 MHz. The assignments were based on DEPT, HSQC, and HMBC experiments.

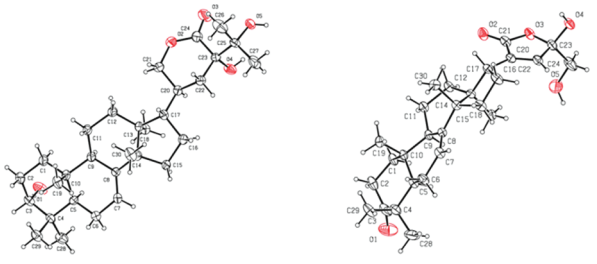

Figure 1. X-ray crystal structures of compounds 1 and 3.

the known compound 11 (laxiracemosin H)[12] indicated that it was an analogue of compound 11, which possessed a tirucallane-type alkaloid skeleton.[12] In the $^1$H NMR spectrum, an oxymethine group [$\delta_H$ 3.47 (1H, br s)] in compound 12 replaced the carbonyl group in compound 11 at C-3. There was an OH attached to C-3, as confirmed by HMBC correlations from the oxymethine proton to C-1, C-2, C-4, C-5, C-28, and C-29. The $\alpha$-orientation of 3-OH was deduced from the correlation of H-3/$H_3$-29 in the NOSEY spectrum. Thus, the structure of compound 12 (dysolenticin J) was established.

The known compounds were identified, by comparison with literature data, as 24,25-epoxytirucall-7-ene-3,23-dione (8);[21] laxiracemosin H (11);[12] 3-oxo-24,25,26,27-tetranortirucall-7-ene-23(21)-lactone (13);[24] 3-hydroxy-24,25,26,27-tetranortirucall-7-ene-23(21)-lactone (14);[24] 3$\beta$,22$S$-dihydroxytirucalla-7,24-dien-23-one (15);[25] tirucalla-7,24-dien-3$\beta$-ol (16);[26] and cneorin-$NP_{36}$ (17).[27]

Compounds 1, 2, 4, 5, and 9−17 were evaluated for their in vitro cytotoxicity against HL-60 and SMMC-7721 tumor cells using the SRB assay.[28] None of the tested compounds were cytotoxic. The cytotoxic activity of compounds 3 and 6−8 was not examined due to the minute amounts available and poor solubility.

The isolated compounds, other than 2, 3, 7, and 10, were evaluated for vasodilative effects on intact aortic rings precontracted with phenylephrine ($10^{-6}$ M),[29,30] and the results are shown in Figure 4. Compounds 1, 4−6, 8, 9, 11, and 15−17, gave results almost the same as the vehicle control. Compounds 13 and 14, tetranortirucallane-type triterpenoids, showed vasodilative effects


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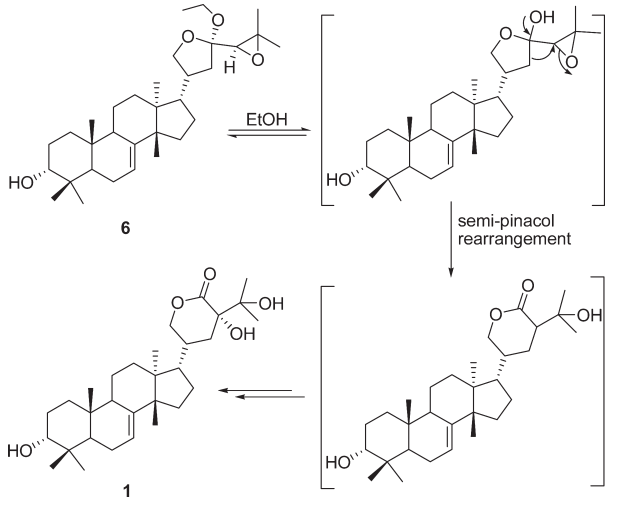
**Scheme 1. Plausible Biogenetic Pathway for Compound 1**



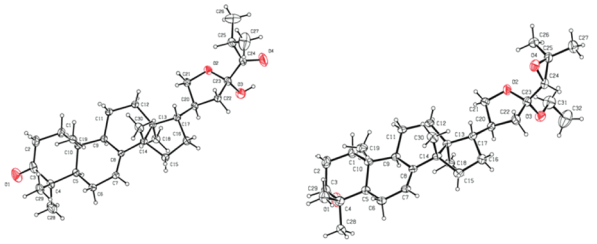



**Figure 2.** X-ray crystal structures of compounds **4** and **6**.

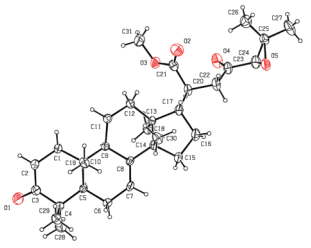


**Figure 3.** X-ray crystal structure of compound **10**.

with diastolic degrees of 43.5% and 37.5% at 10 $\mu$g/mL, respectively. Compounds **11** and **12**, tetranortirucallane-type alkaloids, showed vasodilative effects with diastolic degrees of 18.3% and 87.4% at 10 $\mu$g/mL, respectively. Compound **12** was more active than compound **11**, clearly indicating that an OH at C-3 was important for the activity.

## EXPERIMENTAL SECTION

**General Experimental Procedures.** Melting points were determined on a X-4 melting point apparatus. Optical rotations were measured on a Perkin-Elmer model 341 polarimeter. IR spectra were recorded on a Nicolet NEXUS 670 FT-IR spectrometer. NMR spectra were obtained using a Bruker AM-400BB (400 MHz) spectrometer ($\delta$ in ppm, $J$ in Hz). HRESIMS determinations were run on a Bruker APEX II mass spectrometer. Single-crystal X-ray diffractions were recorded on a Bruker Smart CCD diffractometer using graphite-monochromated

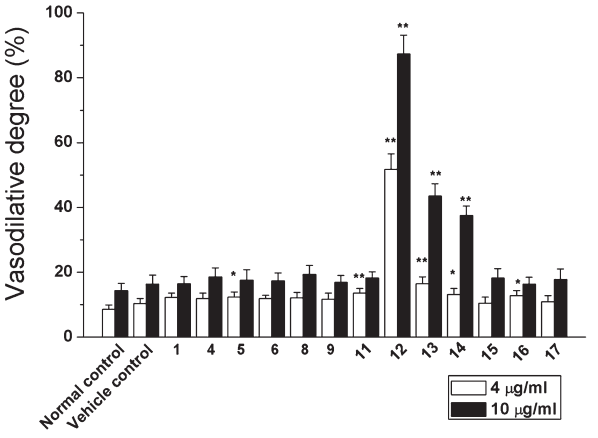



**Figure 4.** Vasodilative effect of samples on phenylephrine ($10^{-6}$ M)-precontracted rat aortic rings. *$p < 0.05$, **$p < 0.01$ vs the same group in vehicle control.

Mo K$\alpha$ radiation. Sephadex LH-20 (Amersham Pharmacia Biotech), RP-$C_{18}$ silica gel (150−200 mesh, Merck), and silica gel (200−300 mesh, Qingdao Marine Chemical Factory) were used for column chromatography (CC). Thin-layer chromatography (TLC): silica gel $GF_{254}$ (10−40 $\mu$m; Qingdao Marine Chemical Factory); detection under UV light and visualized by spraying with 5% $H_2SO_4$ in $C_2H_5OH$ (v/v), followed by heating. Analytical TLC was used to follow separations and to check the purity of isolated compounds.

**Plant Material.** Leaves and twigs of *D. lenticellatum* were collected from Yunnan Province, People's Republic of China, in October 2008, and authenticated by Prof. Guo-Da Tao of Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen (No. 200810DL) was deposited in the Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences.

**Extraction and Isolation.** The air-dried and powdered leaves and twigs of *D. lenticellatum* (14.9 kg) were extracted with 95% EtOH three times (each for 3 h) at 40 °C and concentrated in vacuo to give a crude extract (1.5 kg). The crude extract was suspended in $H_2O$ (3.0 L) and then extracted with $CHCl_3$ (3 × 2.0 L). The extract (472 g) was subjected to CC over silica gel (1.4 kg) eluting with a petroleum ether/acetone (1:0−2:1 and acetone, $CH_3OH$) gradient system to give fractions 1−6. Fraction 3 (67.2 g) was applied to silica gel eluting with petroleum ether/EtOAc (40:1−1:1) to provide fractions 3a−3f. Fraction 3b (18.1 g) was fractionated using silica gel ($CHCl_3$/EtOAc, 20:1−1:1), then subjected to a column of MCI gel (MeOH/$H_2O$, 0:1−1:0), and further purified on Sephadex LH-20 ($CHCl_3$/MeOH, 2:1) to yield **6** (18 mg) and **7** (4 mg). Compounds **16** (40 mg) and **15** (26 mg) was isolated from fraction 3c (4.3 g) after repeated silica gel CC with petroleum ether/acetone (25:1−1:1) and Sephadex LH-20 CC ($CHCl_3$/MeOH, 2:1). After CC over silica gel developed with $CHCl_3$/acetone (30:1−2:1), fraction 4 (20.1 g) afforded fractions 4a−4c. Fraction 4b (0.8 g) was separated by CC over MCI gel (MeOH/$H_2O$, 0:1−1:0), RP-18 silica gel (MeOH/$H_2O$, 1:1−1:0), and Sephadex LH-20 ($CHCl_3$/MeOH, 2:1) to obtain **2** (3 mg), **4** (45 mg), and **11** (32 mg). Compounds **13** (103 mg), **8** (46 mg), and **14** (98 mg) were obtained from fraction 4c (0.5 g) after repeated CC eluting with petroleum ether/acetone (10:1−2:1). Fraction 5 (88.9 g) was chromatographed on silica gel eluting with a $CHCl_3$/acetone (20:1−1:1) gradient to give fractions 5a−5e. Fraction 5c (23.2 g) was subjected to silica gel (petroleum ether/EtOAc, 20:1−1:1) and then Sephadex LH-20 ($CHCl_3$/MeOH, 2:1) CC to yield **17** (15 mg), **10** (5 mg), and **12** (9 mg). Fraction 5d (0.6 g) was chromatographed over MCI gel (MeOH/$H_2O$, 2:1−1:0), RP-18 silica gel (MeOH/$H_2O$, 1:1−1:0), and silica gel (petroleum ether/EtOAc, 10:1−2:1) to obtain **1** (4 mg), **5** (8 mg), and **3** (3 mg). Fraction 6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(13.9 g) was separated by repeated silica gel CC eluting with $CHCl_3$/EtOAc (10:1−1:2) to give **9** (5 mg).

*Dysolenticin A* (***1***): colorless crystals (petroleum ether/MeOH/$CH_3CN$); mp 211−213 °C; $[\alpha]^{20}_D$ −30.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3405, 2927, 2880, 1707 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 489.3570 $[M + H]^+$ (calcd for $C_{30}H_{49}O_5^+$, 489.3575).

*Dysolenticin B* (***2***): white powder; mp 208−211 °C; $[\alpha]^{20}_D$ −20.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3407, 2964, 2918, 1737, 1697 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 451.3214 $[M + H]^+$ (calcd for $C_{30}H_{43}O_3^+$, 451.3207).

*Dysolenticin C* (***3***): colorless crystals (petroleum ether/EtOH/$CH_3CN$); $[\alpha]^{20}_D$ +10.0 (*c* 0.2, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3317, 2966, 2878, 1765, 1705 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 493.2932 $[M + C_2H_5OH - H_2O + Na]^+$ (calcd for $C_{29}H_{42}O_5Na^+$, 493.2924).

*Dysolenticin D* (***4***): colorless crystals (petroleum ether/acetone); $[\alpha]^{20}_D$ −50.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3406, 2949, 2872, 1709 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta_H$ 5.33 (1H, d, *J* = 3.2 Hz, H-7), 4.49/4.30 (1H, s, 23-OH), 4.28/4.08 (1H, t, *J* = 8.0 Hz, $H_2$-21), 3.70/3.54 (1H, dd, *J* = 10.0, 8.0 Hz, $H_2$-21), 3.03 (1H, m, H-25), 2.75 (1H, td, *J* = 14.4, 5.6 Hz, $H_2$-2), 2.27 (1H, m, $H_2$-2), 2.74 (1H, m, H-20), 2.31 (1H, m, H-9), 2.10 (2H, m, $H_2$-6), 2.01 and 1.78 (each 1H, m, $H_2$-22), 2.00 and 1.46 (each 1H, m, $H_2$-1), 1.93 and 1.43 (each 1H, m, $H_2$-16), 1.75 (1H, m, H-5), 1.73 and 1.41 (each 1H, m, $H_2$-12), 1.71 (1H, m, H-17), 1.64 and 1.60 (each 1H, m, $H_2$-15), 1.62 (2H, m, $H_2$-11), 1.13 (3H, d, *J* = 6.8 Hz, $H_3$-26), 1.12 (3H, d, *J* = 6.8 Hz, $H_3$-27), 1.11 (3H, s, $H_3$-29), 1.02 (3H, s, $H_3$-28), 1.01 (6H, s, $H_3$-30 and $H_3$-19), and 0.84 (3H, s, $H_3$-18); $^{13}C$ NMR data ($CDCl_3$, see Table 2); HRESIMS *m/z* 493.3293 $[M + Na]^+$ (calcd for $C_{30}H_{46}O_4Na^+$, 493.3288).

*Dysolenticin E* (***5***): white powder; $[\alpha]^{20}_D$ −20.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3449, 2947, 2877, 1715 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta_H$ 5.26 (1H, br s, H-7), 4.50 (1H, s, 23-OH), 4.29/4.09 (1H, t, *J* = 8.0 Hz, $H_2$-21), 3.71/3.54 (1H, dd, *J* = 10.0, 8.0 Hz, $H_2$-21), 3.46 (1H, br s, H-3), 3.05 (1H, m, H-25), 2.61 (1H, m, H-20), 2.36 (1H, m, H-9), 2.03 and 1.94 (each 1H, m, $H_2$-16), 1.99 and 1.76 (each 1H, m, $H_2$-22), 1.93 and 1.62 (each 1H, m, $H_2$-2), 1.91 and 1.41 (each 1H, m, $H_2$-16), 1.78 (1H, m, H-5), 1.65 and 1.39 (each 1H, m, $H_2$-12), 1.63 (1H, m, H-17), 1.61 and 1.52 (each 1H, m, $H_2$-15), 1.59 and 1.51 (each 1H, m, $H_2$-11), 1.49 and 1.38 (each 1H, m, $H_2$-1), 1.15 (3H, d, *J* = 4.8 Hz, $H_3$-26), 1.13 (3H, d, *J* = 4.8 Hz, $H_3$-27), 0.98 (3H, s, $H_3$-30), 0.93 (3H, s, $H_3$-28), 0.91 (3H, s, $H_3$-29), 0.87 (3H, s, $H_3$-18), and 0.77 (3H, s, $H_3$-19); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta_C$ 212.9/211.8 (C-24), 145.5/145.4 (C-8), 118.5/118.4 (C-7), 104.1/103.6 (C-23), 76.2 (C-3), 74.0/72.1 (C-21), 51.1 (C-17), 50.7 (C-14), 48.5/48.4 (C-9), 44.6 (C-5), 43.9/43.7 (C-13), 42.3/42.0 (C-22), 41.0 (C-20), 37.4 (C-4), 34.8 (C-10), 34.2 (C-15), 33.8/33.5 (C-25), 31.6 (C-12), 31.2 (C-1), 27.8 (C-28), 27.7 (C-16), 27.1 (C-30), 25.4 (C-2), 23.9 (C-6), 22.6/22.4 (C-18), 21.8 (C-29), 20.2/19.9 (C-26), 19.7/19.4 (C-27), 17.4 (C-11), 12.9 (C-19); HRESIMS *m/z* 490.3886 $[M + NH_4]^+$ (calcd for $C_{30}H_{52}O_3N^+$, 490.3891).

*Dysolenticin F* (***6***): colorless crystals (petroleum ether/acetone/MeOH); mp 203−205 °C; $[\alpha]^{20}_D$ −40.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3496, 2921, 2865, 1703, 1654 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 523.3766 $[M + Na]^+$ (calcd for $C_{32}H_{52}O_4Na^+$, 523.3758).

*Dysolenticin G* (***7***): white powder; mp 199−202 °C; $[\alpha]^{20}_D$ −43.3 (*c* 0.3, in $CHCl_3$); IR (KBr) $\nu_{max}$ 2955, 2883, 1731, 1706 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta_H$ 5.35 (1H, dd, *J* = 3.2, 3.2 Hz, H-7), 2.83 (1H, t, *J* = 8.4 Hz, H-17), 2.75 (1H, td, *J* = 18.0, 5.6 Hz, $H_2$-2), 2.23 (1H, m, $H_2$-2), 2.28 and 1.73 (each 1H, m, $H_2$-16), 2.26 (1H, m, H-9), 2.13 and 1.79 (each 1H, m, $H_2$-12), 2.12 (3H, s, $H_3$-21), 2.11 (2H, m, $H_2$-6), 1.99 (1H, m, $H_2$-1), 1.47 (1H, td, *J* = 14.0, 4.0 Hz, $H_2$-1), 1.72 (1H, m, H-5), 1.67 (2H, m, $H_2$-11), 1.59 (2H, m, $H_2$-15), 1.12 (3H, s, $H_3$-29), 1.08 (3H, s, $H_3$-30), 1.04 (3H, s, $H_3$-28), 1.03 (3H, s, $H_3$-19), and 0.74 (3H, s, $H_3$-18); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta_C$ 216.5 (C-3), 209.8 (C-20), 144.3 (C-8), 119.0 (C-7), 61.5 (C-17), 52.3 (C-5), 51.6 (C-14), 48.1 (C-9), 47.8 (C-4), 45.0 (C-13), 38.4 (C-1), 35.1 (C-10), 34.8 (C-2), 34.0 (C-15), 32.3 (C-12), 30.9 (C-21), 27.2 (C-30), 24.5 (C-28), 24.4 (C-6), 23.3 (C-18), 21.9 (C-16), 21.6 (C-29), 17.8 (C-11), 12.7 (C-19); HRESIMS *m/z* 357.2782 $[M + H]^+$ (calcd for $C_{24}H_{37}O_2^+$, 357.2788).

*Dysolenticin H* (***9***): white powder; mp 252−255 °C; $[\alpha]^{20}_D$ −60.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3385, 2956, 2930, 1721, 1703 $cm^{-1}$; $^1H$ NMR ($C_5D_5N$, 400 MHz) $\delta_H$ 5.31 (1H, d, *J* = 2.8 Hz, H-7), 3.79 (1H, s, H-24), 3.44 (1H, dd, *J* = 18.0, 10.8 Hz, $H_2$-22), 2.93 (1H, dd, *J* = 18.0, 3.2 Hz, $H_2$-22), 3.24 (1H, td, *J* = 11.2, 2.8 Hz, H_-17), 2.72 (1H, td, *J* = 14.4, 5.6 Hz, $H_2$-2), 2.24 (1H, m, $H_2$-2), 2.33 (1H, m, H-9), 2.31 (1H, m, H-20), 2.03 (2H, m, $H_2$-12), 2.03 and 1.37 (each 1H, m, $H_2$-16), 1.75 and 1.29 (each 1H, m, $H_2$-1), 1.75 (1H, m, H-5), 1.63 and 1.54(each 1H, m, $H_2$-15), 1.45 (2H, m, $H_2$-11), 1.42 (3H, s, $H_3$-26), 1.36 (3H, s, $H_3$-27), 1.24 (3H, s, $H_3$-18), 1.13 (3H, s, $H_3$-28), 1.07 (3H, s, $H_3$-30), 1.06 (3H, s, $H_3$-29), and 0.91 (3H, s, $H_3$-19); $^{13}C$ NMR data ($C_5D_5N$, 100 MHz) $\delta_C$ 215.5 (C-3), 146.1 (C-8), 118.8 (C-7), 206.1 (C-23), 177.9 (C-21), 65.9 (C-24), 61.4 (C-25), 52.8 (C-5), 51.8 (C-14), 50.7 (C-20), 48.8 (C-9), 48.1 (C-4), 45.0 (C-22), 44.2 (C-13), 43.4(C-17), 38.7 (C-1), 35.5 (C-10), 35.3 (C-2), 34.1 (C-15), 30.8 (C-12), 28.0 (C-16), 27.8 (C-30), 25.2 (C-28), 24.9 (C-6), 24.9 (C-26), 22.1 (C-18), 21.8 (C-29), 18.8 (C-27), 18.3 (C-11), 13.0 (C-19); HRESIMS *m/z* 507.3090 $[M + Na]^+$ (calcd for $C_{30}H_{44}O_3Na^+$, 507.3081).

*Dysolenticin I* (***10***): colorless crystals (petroleum ether/acetone); mp 212−215 °C; $[\alpha]^{20}_D$ −80.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 2959, 2881, 1729, 1710 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 521.3228 $[M + Na]^+$ (calcd for $C_{31}H_{46}O_5Na^+$, 521.3237).

*Dysolenticin J* (***12***): white powder; mp 277−279 °C; $[\alpha]^{20}_D$ +70.0 (*c* 0.1, in $CHCl_3$); IR (KBr) $\nu_{max}$ 3584, 3203, 2924, 1768, 1712, 1619 $cm^{-1}$; $^1H$ NMR and $^{13}C$ NMR data ($CDCl_3$, see Tables 1 and 2); HRESIMS *m/z* 410.2646 $[M - H]^-$ (calcd for $C_{26}H_{36}NO_3^-$, 410.2700).

**X-ray Crystal Structures of 1, 3, 4, 6, and 10.** All data were collected using a Bruker Smart Apex CCD diffractometer using graphite-monochromated Mo K$\alpha$ radiation. The structure was solved by direct method using SHELXS-97 (Sheldrick, G. M., University of Gottingen, Gottingen, Germany, 1997) and refined by a full-matrix least-squares method on $F^2$ by means of SHELXL-97 (Sheldrick, G. M., University of Gottingen, Gottingen, Germany, 1997). The hydrogen atoms were not included in the refinement, and all of the non-hydrogen atoms were refined anisotropically. In the final step of structure refinement, the positional parameters of the hydrogen atoms were calculated under a fixed C−H bond length of 1.00 Å with $sp^3$ configuration of the bonding carbon atoms. Due to the lack of any heavy atoms, the absolute configurations could not be determined. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (deposition numbers CCDC 827617−827621). Copies of the data can be obtained, free of charge, on application to the director, CCDC 12 Union Road, Cambridge CB2 1EZ, UK (fax (+44) 1223-336-003 or e-mail: deposit@ccdc.cam.ac.uk).

*Crystal Data of* ***1***. $C_{30}H_{48}O_5$; fw 488.68; 296(2) K, monoclinic space group $C_2$; unit cell dimensions *a* = 31.391(14) Å, *b* = 7.212(3) Å, *c* = 12.407(5) Å, *V* = 2734(2) $Å^3$; $\alpha$ = 90°, $\beta$ = 103.261(6)°, $\gamma$ = 90°, *Z* = 4, $\rho_{calc}$ = 1.187 $Mg/m^3$, crystal dimensions 0.32 × 0.30 × 0.26 mm, $\mu$ = 0.079 $mm^{-1}$, *F*(000) = 1072. A total of 6524 reflections measured, 4752 unique ($R_{int}$ = 0.0428), which were used in all calculations. The final refinement gave $R_1$ = 0.0649 and $wR_2$ = 0.1406 [$I > 2\sigma(I)$].

*Crystal Data of* ***3***. $C_{27}H_{38}O_5$; fw 442.57; 296(2) K, monoclinic space group $C_2$; unit cell dimensions *a* = 31.267(6) Å, *b* = 6.8755(14) Å, *c* = 14.753(3) Å, *V* = 2952.3(10) $Å^3$; $\alpha$ = 90°, $\beta$ = 111.429(2)°, $\gamma$ = 90°, *Z* = 4, $\rho_{calc}$ = 0.996 $Mg/m^3$, crystal dimensions 0.25 × 0.22 × 0.20 mm, $\mu$ = 0.067 $mm^{-1}$, *F*(000) = 960. A total of 10 336 reflections measured,

5338 unique ($R_{int}$ = 0.0222), which were used in all calculations. The final refinement gave $R_1$ = 0.0749 and $wR_2$ = 0.2065 [$I > 2\sigma(I)$].

*Crystal Data of* ***4***. $C_{30}H_{46}O_4$; fw 470.67; 296(2) K, monoclinic space group $P2_1$; unit cell dimensions $a$ = 7.500(7) Å, $b$ = 17.596(16) Å, $c$ = 10.344(9) Å, $V$ = 1349(2) Å$^3$; $\alpha$ = 90°, $\beta$ = 98.773(9)°, $\gamma$ = 90°, $Z$ = 2, $\rho_{calc}$ = 1.159 Mg/m$^3$, crystal dimensions 0.25 × 0.23 × 0.19 mm, $\mu$ = 0.075 mm$^{-1}$, $F(000)$ = 516. A total of 6579 reflections measured, 4312 unique ($R_{int}$ = 0.0211), which were used in all calculations. The final refinement gave $R_1$ = 0.0434 and $wR_2$ = 0.1014 [$I > 2\sigma(I)$].

*Crystal Data of* ***6***. $C_{32}H_{52}O_4$; fw 500.74; 296(2) K, orthorhombic space group $P2(1)2(1)2(1)$; unit cell dimensions $a$ = 7.541(8) Å, $b$ = 10.852(11) Å, $c$ = 36.43(4) Å, $V$ = 2981(5) Å$^3$; $\alpha$ = 90°, $\beta$ = 90.00°, $\gamma$ = 90°, $Z$ = 4, $\rho_{calc}$ = 1.116 Mg/m$^3$, crystal dimensions 0.25 × 0.23 × 0.22 mm, $\mu$ = 0.071 mm$^{-1}$, $F(000)$ = 1104. A total of 21 048 reflections measured, 5390 unique ($R_{int}$ = 0.0866), which were used in all calculations. The final refinement gave $R_1$ = 0.0833 and $wR_2$ = 0.2153 [$I > 2\sigma(I)$].

*Crystal Data of* ***10***. $C_{31}H_{46}O_5$; fw 498.68; 296(2) K, orthorhombic space group $P2(1)2(1)2(1)$; unit cell dimensions $a$ = 7.299(5) Å, $b$ = 16.568(12) Å, $c$ = 23.238(17) Å, $V$ = 2810(4) Å$^3$; $\alpha$ = 90°, $\beta$ = 90°, $\gamma$ = 90°, $Z$ = 4, $\rho_{calc}$ = 1.179 Mg/m$^3$, crystal dimensions 0.25 × 0.23 × 0.21 mm, $\mu$ = 0.078 mm$^{-1}$, $F(000)$ = 1088. A total of 13 635 reflections measured, 5175 unique ($R_{int}$ = 0.0524), which were used in all calculations. The final refinement gave $R_1$ = 0.0572 and $wR_2$ = 0.1087 [$I > 2\sigma(I)$].

**In Vitro Cytotoxicity Test.** Cytotoxicity was tested against HL-60 and SMMC-7721 tumor cell lines using the SRB assay.[28] All experiments were carried out three times with five replicates for each concentration tested. Where applicable, $IC_{50}$ values were calculated by linear regression.[31] Mitomycin was used as a positive control.

**Vasodilative Investigation.** The experimental protocol was performed according to previously established methods.[29,30] The investigation conformed to the Guide for the Care and Use of Laboratory Animals published by the U.S. National Institutes of Health (NIH publication No. 85-23, revised 1996).

After anesthesia with pentobarbital (60 mg/kg, ip), the thoracic aorta was excised, cleaned of connective tissue, and cut into rings of approximately 3 mm in length. Rings were suspended in organ baths containing standard Krebs solution (NaCl 118 mM, KCl 4.65 mM, $CaCl_2$ 2.5 mM, $KH_2PO_4$ 1.18 mM, $NaHCO_3$ 24.9 mM, $MgSO_4$ 1.18 mM, glucose 12 mM, pH 7.4), maintained at 37 °C, and continuously aerated with 95% $O_2$/5% $CO_2$, for isometric tension recording, by a data acquisition system (BIOPAC Systems MP150). After a 1 h equilibration period under a resting tension of 2 g, rings were exposed to 80 mM KCl for 15 min and then to Krebs solution for 15 min, and this was repeated three times until responses were stable. Then the aortic rings were exposed to $10^{-6}$ M phenylephrine to induce maximum contraction, and the presence of functional endothelium was verified by the ability of acetylcholine ($10^{-6}$ M) to induce more than 80% relaxation in rings. After that, the aortic rings were precontracted by phenylephrine (PE, $10^{-6}$ M) again, and the sample was added to the K−H solution cumulatively from 4 to 10 $\mu$g/mL. The vasodilative effects were recorded as the percentage of PE that induced the maximum contraction. Data are expressed as the mean ± SEM of six aortic rings.

## ■ ASSOCIATED CONTENT

**Supporting Information.** HRESIMS, IR, and NMR spectra of **1**−**7**, **9**, **10**, and **12** and X-ray crystallographic data in CIF format for **1**, **3**, **4**, **6**, and **10**. Selected key HMBC correlations for new compounds **1**−**7**, **9**, **10**, and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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