Bioorganic & Medicinal Chemistry Letters 21 (2011) 125–129

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

Ring A-*seco* triterpenoids with antibacterial activity from *Dysoxylum hainanense*

Xiu-Feng He, Xiao-Ning Wang, Sheng Yin, Lei Dong, Jian-Min Yue *

State Key Laboratory of Drug Research, Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 555 Zuchongzhi Road, Zhangjiang Hi-Tech Park, Shanghai 201203, PR China

ARTICLE INFO

Article history:
Received 14 September 2010
Revised 10 November 2010
Accepted 12 November 2010
Available online 19 November 2010

Keywords:
Dysoxylum hainanense
Triterpenoids
Structural elucidation
Antibacterial activity
Structure–activity relationship

ABSTRACT

Five new ring A-*seco* triterpenoids, dysoxyhainic acids F–J (**1**–**5**), along with a known ring A-*seco* triterpenoid koetjapic acid (**6**) were isolated from the twigs and leaves of *Dysoxylum hainanense*. Their structures were established on the basis of extensive spectroscopic analysis. Antimicrobial activity of all the compounds against fungi and bacteria were tested. Compounds **2**–**4** and **6** exhibited significant antimicrobial activity against Gram-positive bacteria, and the antibacterial SAR (structure–activity relationship) was also briefly discussed.

During the past century, human beings have achieved great success in the war against pathogenic microbes thanks to the discovery of a series of powerful antibiotics. However, the increasing emergence of antibiotic resistant bacteria, such as the recently reported 'super bacteria' with resistance to carbapenem by expressing the NDM-1 β-lactamase,[1] due to the abuse of antibiotics become a potential threaten to public health. So the discovery of new leading compound with antibacterial activity is still of great importance and urgency in nowadays. Herein, we report the isolation and structural elucidation of several triterpenoids with antibacterial activity from *Dysoxylum hainanense*.

Plants of the Meliaceae family are a rich source of structurally diversified limonoids and triterpenoids with significant biological activities, which have attracted considerable interest of the natural products chemists.[2–5] The genus of *Dysoxylum* of the family Meliaceae are mainly distributed in India and Southeast Asia, many of them have been applied in traditional medicine.[6–8] Previous investigation in the plants of this genus has led to the isolation of a diverse range of bioactive secondary metabolites, such as anti-tumor triterpenoid saponins,[9] anti-RSV and antifeeding tetranortriterpenoids,[10,11] cytotoxic diterpenoids,[12] and cardiac active alkaloids.[13] Recently, we reported the isolation and characterization of two triterpenoids with unusual skeletons[14] and six ring A modified triterpenoids[15] from the twigs and leaves of *D. hainanense*. In this study, five new ring A-*seco* triterpenoids, dysoxyhainic acids F–J (**1**–**5**), along with a known ring A-*seco* triterpenoid koetjapic acid (**6**)[16] were isolated from the same sample of *D. hainanense*. The antimicrobial activity of all the compounds against fungi and bacteria were tested. Compounds **2**–**4** and **6** exhibited significant antibacterial activity against Gram-positive bacteria, and the antibacterial SAR was also briefly discussed.

The twigs and leaves of *D. hainanense* Merr. were collected in September of 2005 from Hainan Province of PR China. The plant was authenticated by Professor S. M. Huang, Department of Biology, Hainan University of China. A voucher specimen has been deposited in Shanghai Institute of Materia Medica, SIBS, Chinese Academy of Sciences (access number: DHTS-2005-1Y).

The air-dried powder of the plant material (2 kg) was percolated with 95% EtOH three times (each 5 L) to give 105 g of crude extract, which was then suspended in water (1 L) and partitioned successively with petroleum ether and EtOAc. The EtOAc soluble fraction (35 g) was subjected to a MCI gel column (MeOH/H_2O, 0–100%) to give five fractions 1–5. Fraction 4 (6 g) was separated on a silica gel column (petroleum ether/acetone 100:1 to 3:1) to afford seven fractions 4a–4g. Fractions 4c (710 mg) was extensively separated over columns of silica gel, RP-18 silica gel, Sephadex LH-20, and preparative HPLC to obtain **2** (5 mg), **3** (11 mg), **4** (110 mg), and **5** (8 mg). Fraction 4g (640 mg) were purified by the similar procedures to yield **1** (9 mg) and **6** (5 mg) (see Supplementary data).

Dysoxyhainic acid F (**1**),[17] obtained as a white amorphous solid, showed a molecular formula of $C_{29}H_{44}O_6$ as deduced from the sodiated molecular ion in HRESIMS at *m*/*z* 511.3018 $[M+Na]^+$ (calcd for $C_{29}H_{44}O_6Na$ 511.3036). Its IR spectrum showed the presence of hydroxyl and carboxyl groups (3431 and 1701 cm^{-1}, respectively). Its ^{13}C NMR exhibited 29 carbon signals including one trisubstituted double bond (δ_C 145.0 and 122.6), three carboxyl groups

* Corresponding author. Tel./fax: +86 21 50806718.
E-mail address: jmyue@mail.shcnc.ac.cn (J.-M. Yue).

0960-894X/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.bmcl.2010.11.057

Table 1
^{1}H NMR spectroscopic data of compounds **1**–**5**[a]

No.	1	2	3	4	5
1	—	1.58 (m, 2H)	1.65 (m, 1H), 1.58 (m, 1H)	2.29 (m, 1H), 1.67 (m, 1H)	2.77 (m, 1H), 2.09 (m, 1H)
2	—	2.37 (m, 1H), 2.22 (m, 1H)	2.33 (m, 1H), 2.23 (m, 1H)	2.52 (m, 1H), 2.24 (m, 1H)	2.44 (m, 2H)
3	—	—	—	—	—
4	—	—	—	—	—
5	3.26 (br s, 1H)	1.95 (m, 1H)	1.96 (m, 1H)	1.37 (m, 1H)	1.47 (m, 1H)
6	1.91 (m, 2H)	1.40 (m, 2H)	1.74 (m, 1H), 1.43 (m, 1H)	1.48 (m, 2H)	1.62 (m, 1H), 1.53 (m, 1H)
7	1.89 (m, 1H), 1.41 (m, 1H)	1.52 (m, 1H), 1.32 (m, 1H)	1.43 (m, 1H), 1.38 (m, 1H)	1.48 (m, 1H), 1.04 (m, 1H)	1.64 (m, 1H), 1.25 (m, 1H)
8	—	—	—	—	—
9	3.00 (dd, 6.4, 11.6, 1H)	1.75 (m, 1H)	1.46 (m, 1H)	1.76 (m, 1H)	—
10	—	—	—	—	—
11	2.27 (m, 1H), 2.08 (m, 1H)	1.96 (m, 1H), 1.80 (m, 1H)	1.43 (m, 1H), 1.26 (m, 1H)	1.90 (m, 2H)	5.77 (d, 6.0, 1H)
12	5.50 (br s, 1H)	5.30 (br s, 1H)	1.83 (m, 1H), 1.88 (m, 1H)	5.19 (br s, 1H)	5.55 (d, 6.0, 1H)
13	—	—	1.72 (m, 1H)	—	—
14	—	—	—	—	—
15	1.79 (m, 1H), 1.03 (m, 1H)	1.78 (m, 1H), 1.03 (m, 1H)	1.73 (m, 1H), 1.03 (m, 1H)	1.74 (m, 1H), 0.98 (m, 1H)	1.81 (dt, 4.2, 13.6, 1H), 1.03 (m, 1H)
16	2.04 (m, 1H), 0.89 (m, 1H)	1.94 (m, 1H), 0.88 (m, 1H)	1.48 (m, 1H), 1.36 (m, 1H)	1.98 (m, 1H), 0.82 (m, 1H)	1.98 (dt, 4.2, 13.6, 1H), 0.85 (m, 1H)
17	—	—	—	—	—
18	2.41 (m, 1H)	1.96 (m, 1H)	1.36 (m, 1H)	1.96 (m, 1H)	2.15 (m, 1H)
19	2.21 (m, 1H), 1.78 (m, 1H)	1.86 (m, 1H), 1.65 (m, 1H)	1.78 (m, 1H)	1.66 (m, 1H), 1.04 (m, 1H)	1.62 (m, 1H), 1.08 (m, 1H)
20	—	—	—	—	—
21	2.29 (m, 1H), 1.44 (m, 1H)	1.94 (m, 1H), 1.35 (m, 1H)	1.28 (m, 2H)	1.09 (m, 2H)	1.13 (m, 2H)
22	1.80 (m, 1H), 1.46 (m, 1H)	1.35 (m, 2H)	1.29 (m, 1H), 1.09 (m, 1H)	1.43 (m, 1H), 1.22 (m, 1H)	1.48 (m, 1H), 1.29 (m, 1H)
23	1.73 (s, 3H)	4.87 (s, 1H), 4.67 (s, 1H)	4.84 (s, 1H), 4.64 (s, 1H)	1.26 (s, 3H)	1.29 (s, 3H)
24	1.62 (s, 3H)	1.75 (s, 3H)	1.72 (s, 3H)	1.30 (s, 3H)	1.33 (s, 3H)
25	1.66 (s, 3H)	0.94 (s, 3H)	0.84 (s, 3H)	1.10 (s, 3H)	1.34 (s, 3H)
26	1.08 (s, 3H)	1.01 (s, 3H)	1.10 (s, 3H)	0.98 (s, 3H)	1.13 (s, 3H)
27	1.33 (s, 3H)	1.15 (s, 3H)	0.97 (s, 3H)	1.12 (s, 3H)	1.03 (s, 3H)
28	0.89 (s, 3H)	0.81 (s, 3H)	0.81 (s, 3H)	0.82 (s, 3H)	0.88 (s, 3H)
29	1.35 (s, 3H)	1.21 (s, 3H)	1.12 (s, 3H)	0.87 (s, 3H)	0.90 (s, 3H)
30	—	—	1.23 (s, 3H)	0.87 (s, 3H)	0.88 (s, 3H)
OMe		3.66 (s, 3H)			

[a] Recorded in $CDCl_3$, except for **1** in pyridine-d_5, at 400 MHz. δ in ppm and J in Hz are in the parentheses.

(δ_C 179.6, 181.2, and 181.8), six sp^3 quaternary carbons, eight sp^3 methylenes, three sp^3 methines, and seven methyls (Table 2). The above described functionalities accounted for four out of the eight degrees of unsaturation, indicating that compound **1** possessed a tetracyclic core. Its ^{1}H NMR displayed seven singlet methyls (each 3H) in the up-field region and an olefinic proton at δ_H 5.50 (br s) in the low-field region (Table 1). All these data suggested that **1** might be a nor seco-olean-12-ene type triterpenoid. Analysis of the 1D and 2D NMR data further revealed that the rings B–E of **1** were identical with those of dysoxyhainic acid B,[15] indicating that the remaining two carboxyl groups came from the oxidative cleavage of ring A. The HMBC correlations from H_3-25 to C-1, C-5, C-9, and C-10 assigned one carboxyl group (δ_C 181.8) at C-10, and the HMBC correlations from H_3-23 and H_3-24 to C-3 placed the other carboxyl group (δ_C 181.2) at C-4 (Fig. 1). The relative stereochemistry of **1** from B to E rings is reminiscent of dysoxyhainic acid B as assigned by its ROESY spectrum (Fig. 2) and their similar 1D NMR data. Therefore, dysoxyhainic acid F (**1**) was identified as 2-nor-olean-12-en-1,3,30-trioic acid.

Table 2
^{13}C NMR spectroscopic data of compounds **1**–**5**[a]

No.	1	2	3	4	5
1	181.8	34.0	33.8	34.3	35.0
2		28.5	28.4	29.1	30.2
3	181.2	175.1	179.2	179.8	180.7
4	47.9	147.4	147.6	76.3	75.9
5	50.0	50.4	50.1	51.4	48.6
6	23.0	24.5	24.6	22.6	22.7
7	32.1	31.3	33.1	32.0	30.2
8	39.7	39.5	41.0	39.6	41.3
9	43.3	37.8	40.4	39.0	149.9
10	51.0	39.1	39.3	41.1	44.2
11	25.1	23.6	22.0	23.1	118.6
12	122.6	122.7	28.7	121.9	120.9
13	145.0	144.0	37.5	144.7	147.5
14	42.4	42.0	43.9	42.2	42.9
15	26.4	26.0	27.5	26.1	25.9
16	27.2	26.9	35.4	26.9	27.1
17	32.4	32.0	44.6	32.5	32.2
18	48.7	48.1	48.2	47.2	45.7
19	43.3	42.4	49.8	46.7	46.8
20	44.3	44.2	73.8	31.0	31.1
21	31.7	31.0	28.8	34.7	34.6
22	39.0	38.2	40.2	37.1	37.0
23	22.5	113.6	113.4	27.4	27.4
24	25.7	23.4	23.3	33.9	33.8
25	14.8	19.5	20.1	22.0	30.3
26	16.6	16.8	16.3	16.8	20.0
27	25.9	25.8	14.7	25.6	20.4
28	28.6	28.2	19.2	28.4	28.7
29	29.0	28.7	31.6	33.3	33.2
30	179.6	183.9	24.5	23.6	23.7
COOMe		51.8			

[a] Recorded in $CDCl_3$, except for **1** in pyridine-d_5, at 100 MHz. δ in ppm.

Dysoxyhainic acid G (**2**)[18] was isolated as a white amorphous solid. Its molecular formula was established as $C_{31}H_{48}O_4$ by HREIMS at m/z 484.3547 $[M]^+$ (calcd 484.3553). The ^{1}H NMR and ^{13}C NMR spectra of **2** showed high similarity to those of koetjapic acid dimethyl ester[16] except that one of the methyl ester groups was replaced by a carboxyl group in **2**, which meant that compound **2** was a mono methyl ester of koetjapic acid. The HMBC correlations of Me-29 to C-19, C-20, C-21, and C-30 (δ_C 183.9), as

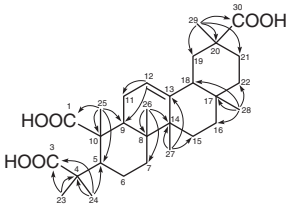


Figure 1. Selected HMBC correlations (H → C) of **1**.

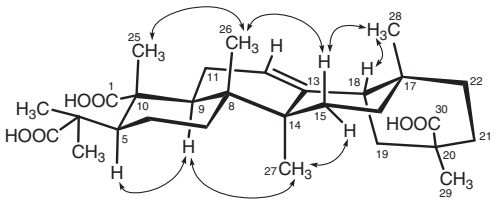


Figure 2. Key ROESY correlations (H ↔ H) of **1**.

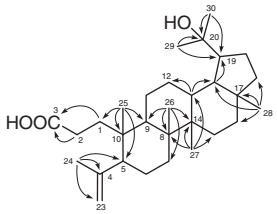


Figure 3. Selected HMBC correlations (H → C) of **3**.

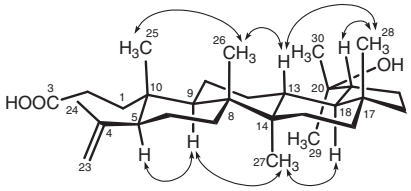


Figure 4. Key ROESY correlations (H ↔ H) of **3**.

well as the correlations of H_2-1 and H_2-2 to C-3 (δ_C 175.1) assigned the carboxyl group to be C-30 and the methyl ester formation at C-3, respectively. The relative configuration of **2** was determined the same as koetjapic acid[15] by the ROESY spectrum.

Dysoxyhainic acid H (**3**)[19] was isolated as a white amorphous solid. The HRESIMS showed a pseudo molecular ion peak at *m*/*z* 481.3649 ([M+Na]$^+$, calcd for $C_{30}H_{50}O_3Na$, 481.3658) corresponding to the molecular formula of $C_{30}H_{50}O_3$. The IR spectrum showed the presence of hydroxyl (3284 cm^{-1}) and carboxyl (1703 cm^{-1}) groups. Its ^{1}H and ^{13}C NMR along with HSQC spectrum displayed seven methyl singlets (one at δ_H 1.72 attached on double bond), a terminal double bond (δ_C 113.4 and 147.6), an oxygenated quaternary carbon (δ_C 73.8), and a carboxyl group (δ_C 179.2). Comparison of the 1D and 2D NMR spectra of **3** with those of dysoxyhainol[15] revealed that the B–E rings of the two compounds were identical, indicating that compound **3** was a lupane triterpenoid with modifications on ring A. Again, by comparing the ^{13}C NMR data of **3** with those of koetjapic acid,[16] it was reasonable to assign that compound **3** bore the same appendages at C-5 and C-10 including stereochemistry as koetjapic acid for their similar NMR data of this structural moiety. The HMBC (Fig. 3) and ROESY (Fig. 4) experiments further confirmed the structure of **3** as depicted.

Dysoxyhainic acid I (**4**)[20] was isolated as a colorless solid. Its HRESIMS with positive mode showed a pseudo molecular ion at *m*/*z* 481.3645 [M+Na]$^+$ (calcd for $C_{30}H_{50}O_3Na$ 481.3658) corresponding to a molecular formula of $C_{30}H_{50}O_3$. The IR spectrum exhibited absorption bands due to carboxyl (1709 cm^{-1}) and hydroxyl (3435 cm^{-1}) groups. Analysis of the ^{1}H and ^{13}C NMR data suggested a 3,4-seco-olean-12-ene carbon skeleton for **4**. The HMBC correlations from H_3-23 and H_3-24 to the oxygenated quaternary carbon (C-4, δ_C 76.3) placed the hydroxyl group at C-4. The other end (C-3) of the opened ring A was determined to be in carboxylic acid form by the HMBC correlations of H_2-2 to C-3 (δ_C 179.8). Detailed analysis of its HMBC spectrum further confirmed the full planar structure of **4**. The relative configuration of the stereocenters was determined the same as the relevant analogs, such as compound **2**, by comparing their 1D NMR data and ROESY spectra.

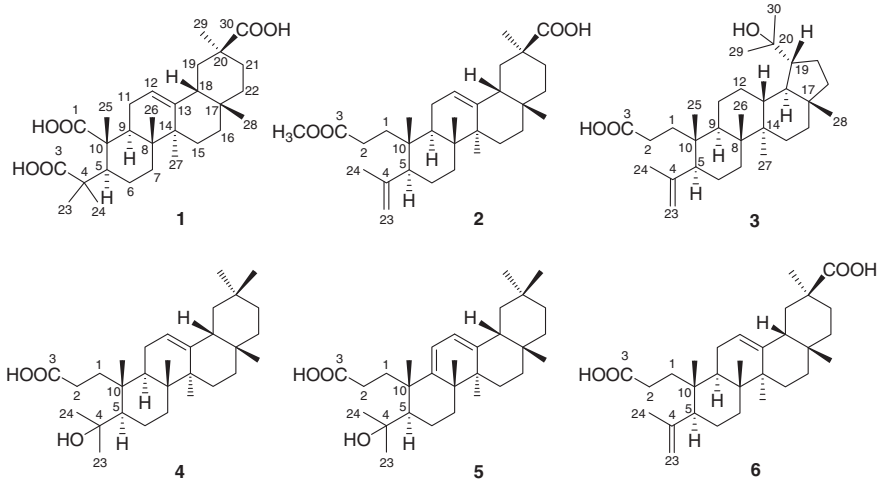
Dysoxyhainic acid J (**5**),[21] obtained as a colorless solid, was assigned the molecular formula of $C_{30}H_{48}O_3$ by HREIMS at *m*/*z* 456.3601 [M]$^+$ (calcd 456.3603). Its IR spectrum was similar to that of **4**. Its ^{13}C NMR spectrum also showed strong resemblance with that of **4**, except for the notable differences being the absence of one methylene and one methine, and the presence of an additional trisubstituted double bond. The HMBC spectrum helped to determine this change occurred at C-9 and C-11 by the correlations from both Me-25 and Me-26 to C-9 (δ_C 149.9). The ^{1}H NMR displaying two mutually coupling olefinic proton resonances at δ_H 5.55 and 5.77 (each 1H, J = 6.0 Hz) further demonstrated that compound **5** featured a conjugated $\Delta^{9,11}$ and Δ^{12} diene, which was consistent with the UV absorption band at λ_{max} = 284 nm (log ε 4.03). Detailed analysis of its 2D NMR spectra (HMBC, HSQC and ROESY) finally confirmed the structure of **5** as depicted.

All the six ring A-*seco* triterpenoids (**1**–**6**) were evaluated for antimicrobial activity against bacteria, and fungi by microdilution assay (see Supplementary data).[22,23] Two well-known natural antimicrobial agents, magnolol[24] and pseudolaric acid B,[23] were used as positive control in this tests for bacteria and fungi, respectively. The antimicrobial MICs of compounds **1**–**6** and positive controls were listed in Table 3. Among the tested compounds, four of them **2**–**4**, and **6** showed antibacterial activity. The antibacterial activity of these four compounds against some Gram-positive bacteria were even stronger than that of positive control magnolol (4–8-fold stronger than the positive control). Compound **2** showed

Table 3
Antimicrobial activities of compounds **1**–**6**[a,b,c]

Compounds and controls	MICs (μg/mL)										
	Sa	Se	Ml	Bs	Ec	Sf	Pa	Ca	Ss	Mg	Tr
1	—	—	—	—	—	—	—	—	—	—	—
2	—	3.12	3.12	3.12	—	—	—	—	—	—	—
3	—	—	3.12	3.12	—	—	—	—	—	—	—
4	—	12.5	—	1.56	—	—	—	—	—	—	—
5	—	—	—	—	—	—	—	—	—	—	—
6	—	12.5	—	6.25	—	—	—	—	—	—	—
Magnolol[d]	25	12.5	12.5	12.5	—	—	—				
Pseudolaric acid B[e]								6.25	12.5	12.5	25

[a] Sa = *S. aureus*, Se = *S. epidermidis*, Ml = *M. luteus*, Bs = *B. subtilis*, Ec = *E. coli*, Sf = *S. flexneri*, Pa = *P. aeruginosa*, Ca = *C. albicans*, Ss = *S. sake*, Mg = *M. gypseum*, Tr = *T. rubrum*.
[b] MIC was defined as the lowest concentration that inhibited visible growth.
[c] MIC >50 μg/mL was defined as inactive, and was represented as '—'.
[d] For bacteria, magnolol was used as positive control.
[e] For fungi, pseudolaric acid B was used as positive control.



significant inhibitory activities against *Staphylococcus epidermidis* ATCC 12228 (MIC 3.12 μg/mL), *Micrococcus luteus* ATCC 9341 (MIC 3.12 μg/mL), and *Bacillus subtilis* ATCC 6633 (MIC 3.12 μg/mL); compound **3** exhibited inhibitory activities against *M. luteus* (MIC 3.12 μg/mL) and *B. subtilis* (MIC 3.12 μg/mL); compound **4** exerted more selective inhibitory activity against *B. subtilis* (MIC 1.56 μg/mL); compound **6** showed inhibitory activities against *S. epidermidis* (MIC 12.5 μg/mL) and *B. subtilis* (MIC 6.25 μg/mL).

Observation of antimicrobial activities and their structural features of compounds **1**–**6** implied certain guidelines of structure–activity relationship, which are: (1) for the triterpenoids **2**–**4** and **6**, they are active against only Gram-positive bacteria, while inactive against Gram-negative bacteria and fungi. (2) For the six ring A-*seco* triterpenoids, the 3,4-seco triterpenoids **2**–**4** and **6**, showed significant activity, while the 2-nor-1,3,30-trioic acid (**1**) and compound **5** with one more $\Delta^{9(11)}$ double bond were inactive. This observation indicates that the 3,4-seco triterpenoids with the C-1–C-3 appendage of a free carboxylic acid, such as compounds **2**–**4** and **6**, are essential for the antibacterial activity, and the presence of one more $\Delta^{9(11)}$ double bond will render compound **5** totally inactive due largely to the conjugated double bond sabotaged the favorable conformation of this class of antibacterial compounds.

Acknowledgments

Financial support of National Natural Science Foundation (Grant no. 30701044, 21072203), the key project of Chinese Academy of Sciences (Grant no. KSCX2-YW-R-117, KSCX2-YW-R-184), and National Science & Technology Major Project 'Key New Drug Creation and Manufacturing Program' (Grant no. 2009ZX09301-001) of the People's Republic of China is gratefully acknowledged. We thank Professor S. M. Huang, Department of Biology, Hainan University, for the collection and identification of the plant material.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmcl.2010.11.057.

References and notes

1. Karthikeyan, K. K.; Mark, A. T.; Timothy, R. W.; Jay, B.; Fafhana, B.; Ravikumar, B.; Uma, C.; Michel, D.; Christian, G. G.; Seema, I.; Padma, K.; Anil, V. K.; Sunil, M.; Shazad, M.; Tabassum, N.; David, L. P.; Andrew, P.; Claire, P.; Rachel, P.; Bhargavi, R.; Ujjwayini, R.; Jayanta, B. S.; Madhu, S.; Elizabeth, S.; Mandayam, A. T.; Jane, T.; Supriya, U.; Marina, W.; William, W.; David, M. L.; Neil, W. *Lancet Infect. Dis.* **2010**, *10*, 597.
2. Pettit, G. R.; Numata, A.; Iwamoto, C.; Morito, H.; Yamada, T.; Goswami, A.; Clewlow, P. J.; Cragg, G. M.; Schmidt, J. M. *J. Nat. Prod.* **2002**, *65*, 1886.
3. Cantrell, C. L.; Rajab, M. S.; Franzblau, S. G.; Fischer, N. H. *J. Nat. Prod.* **1999**, *62*, 546.
4. Champagne, D. E.; Koul, O.; Isman, M. B.; Scudder, G. G. E.; Towers, G. H. N. *Phytochemistry* **1992**, *31*, 377.
5. Mulholland, D. A.; Parel, B.; Coombes, P. H. *Curr. Org. Chem.* **2000**, *4*, 1011.
6. Chen, S. K.; Chen, B. Y.; Li, H. In *Flora of China (Zhongguo Zhiwu Zhi)*; Science Press: Beijing, 1997; Vol. 43 (3), p 93.
7. Weiner, M. A. *Secrets of Fijian Medicine*; University of California: Berkely, CA, 1984. pp 65–67.
8. Liu, H.; Heilmann, J.; Rali, T.; Sticher, O. *J. Nat. Prod.* **2001**, *64*, 159.
9. Kashiwada, Y.; Fujioka, T.; Chang, J. J.; Chen, I. S.; Mihashi, K.; Lee, K. H. *J. Org. Chem.* **1992**, *57*, 6946.
10. Chen, J. L.; Kernan, M. R.; Jolad, S. D.; Stoddart, C. A.; Bogan, M.; Cooper, R. *J. Nat. Prod.* **2007**, *70*, 312.
11. Luo, X. D.; Wu, S. H.; Wu, D. G.; Ma, Y. B.; Qi, S. H. *Tetrahedron* **2002**, *58*, 7797.
12. Duh, C. Y.; Wang, S. K.; Chen, I. S. *J. Nat. Prod.* **2000**, *63*, 1546.
13. Aladesanmi, A. J.; Ilesanmi, O. R. *J. Nat. Prod.* **1987**, *50*, 1041.
14. He, X. F.; Wang, X. N.; Gan, L. S.; Yin, S.; Dong, L.; Yue, J. M. *Org. Lett.* **2008**, *10*, 4327.
15. He, X. F.; Wang, X. N.; Yin, S.; Dong, L.; Yue, J. M. *Eur. J. Org. Chem.* **2009**, *2009*, 4818.
16. Kaneda, N.; Pezzuto, J. M.; Kinghorn, A. D.; Farnsworth, N. R.; Santisuk, T.; Tuchinda, P.; Udchachon, J.; Reutrakul, V. *J. Nat. Prod.* **1992**, *55*, 654.
17. *Dysoxyhainic acid F* (**1**): white amorphous solid; $[\alpha]_D^{20}$ +95.0 (*c* 0.100, MeOH); IR (KBr) ν_{max} 3431, 2960, 1701, 1466, 1383, 1263, 1230, 1176, 669, and broad band 3500–2500 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS 70 ev *m*/*z* (relative intensity) 470 $[M-H_2O]^+$ (7), 442 (100), 381 (24), 311 (8), 285 (11), 248 (83), 233 (12), 187 (16), 173 (14), 147 (16), 119 (19); positive mode ESIMS *m*/*z* 511 $[M+Na]^+$ (3), 999 $[2M+Na]^+$ (100); negative mode ESIMS *m*/*z* 487 $[M-H]^-$ (85), 997 $[2M-H]^-$ (100); HRESIMS *m*/*z* 511.3018 (calcd for $C_{29}H_{44}O_6Na$, 511.3036).
18. *Dysoxyhainic acid G* (**2**): white amorphous solid; $[\alpha]_D^{20}$ +136.0 (*c* 0.07, MeOH); IR (KBr) ν_{max} 3427, 2951, 1740, 1701, 1637, 1454, 1385, 1173, and broad band 3500–2500 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS 70 ev *m*/*z* (relative intensity) 484 $[M]^+$ (30), 441 (11), 402 (15), 395 (8), 287 (8), 248 (100), 233 (11), 189 (12), 173 (11), 121 (20); HREIMS *m*/*z* 484.3547 (calcd for $C_{31}H_{48}O_4$, 484.3553).
19. *Dysoxyhainic acid H* (**3**): white amorphous solid; $[\alpha]_D^{20}$ +15.0 (*c* 0.100, MeOH); IR (KBr) ν_{max} 3433, 3284, 2953, 1740, 1703, 1458, 1381, 1167, 893, and broad band 3500–2500 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS 70 ev *m*/*z* (relative intensity) 440 $[M-H_2O]^+$ (34), 425 (13), 367 (14), 359 (100), 329 (14), 229 (19), 189 (30), 109 (36), 95 (46), 81 (35); positive mode ESIMS *m*/*z* 441 $[M-OH]^+$ (100), 481 $[M+Na]^+$ (60), 939 $[2M+Na]^+$ (35); negative mode ESIMS *m*/*z* 916 $[2M-H]^-$ (100); HRESIMS *m*/*z* 481.3649 (calcd for $C_{30}H_{50}O_3Na$, 481.3658).
20. *Dysoxyhainic acid I* (**4**): colorless solid; $[\alpha]_D^{20}$ +82.0 (*c* 0.125, MeOH); IR (KBr) ν_{max} 3435, 2949, 1709, 1462, 1383, 1364, 1298, 1198, 1144, and broad band 3500–2500 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS 70 ev *m*/*z* (relative intensity) 440 $[M-H_2O]^+$ (13), 425 (7), 400 (5), 367 (4), 257 (3), 218 (100), 203 (36), 189 (15), 135 (9), 119 (9), 95 (14); positive mode ESIMS *m*/*z* 441 $[M-OH]^+$ (100), 481 $[M+Na]^+$ (6); negative mode ESIMS *m*/*z* 457 $[M-H]^-$ (100); HRESIMS *m*/*z* 481.3645 (calcd for $C_{30}H_{50}O_3Na$, 481.3658).
21. *Dysoxyhainic acid J* (**5**): colorless solid; $[\alpha]_D^{20}$ +225.0 (*c* 0.080, MeOH); UV (MeOH) λ_{max} (log ε) 284 (4.03) nm; IR (KBr) ν_{max} 3427, 3253, 2947, 1703, 1631,

1466, 1375, 1223, 835, and broad band 3500–2500 cm^{-1}; ^1H NMR data, see Table 1; ^{13}C NMR data, see Table 2; EIMS 70 ev *m*/*z* (relative intensity) 456 $[M]^+$ (40), 438 (100), 423 (25), 365 (53), 325 (54), 284 (28), 255 (36), 171 (23), 119 (32), 95 (39); HREIMS *m*/*z* 456.3601 (calcd for $C_{30}H_{48}O_3$, 456.3603).

22. Yin, S.; Fan, C. Q.; Wang, Y.; Dong, L.; Yue, J. M. *Bioorg. Med. Chem.* **2004**, *12*, 4387.
23. Yang, S. P.; Dong, L.; Wang, Y.; Wu, Y.; Yue, J. M. *Bioorg. Med. Chem.* **2003**, *11*, 4577.
24. Ho, K.; Tsai, C.; Chen, C.; Huang, J.; Lin, C. *Phytother. Res.* **2001**, *15*, 139.