New Laurene-type Sesquiterpene from Bornean Laurencia nangii

Article *in* Natural product communications · June 2015

CITATIONS
9

READS
156

1 author:

Charles S VAIRAPPAN
Universiti Malaysia Sabah (UMS)
166 PUBLICATIONS **1,970** CITATIONS

SEE PROFILE

NPC Natural Product Communications

2015
Vol. 10
No. 0
1 - 2

New Laurene-type Sesquiterpene from Bornean *Laurencia nangii*

Takashi Kamada and Charles Santhanaraju Vairappan*

Laboratory of Natural Products Chemistry, Institute for Tropical Biology and Conservation, Universiti Malaysia Sabah, Kota Kinabalu, Sabah 88400, Malaysia

csv@ums.edu.my

Received: April 8th, 2015; Accepted: May 13th, 2015

We report the chemical composition of a population of Bornean *Laurencia nangii* Masuda. A new compound, neolaurene (**1**), along with five known metabolites, neolaurallene (**2**), 2,10-dibromo-3-chloro-α-chamigrene (**3**), deoxyprepacifenol (**4**), cycloelatanene B (**5**) and intricatetraol (**6**), were isolated and their chemical structures elucidated based on spectroscopic data. In addition, their cytotoxicity and antibacterial activity were evaluated.

Keywords: *Laurencia nangii*, Rhodomelaceae, Red alga, Laurene-type sesquiterpene.

Red algae of the genus *Laurencia* (Rhodomelaceae) are widespread in tropical and subtropical seas [1a]. The vast majority of *Laurencia* species produce metabolites that are predominantly halogenated terpenes and C_{15}-acetogenins [1b]. *Laurencia* species biosynthesize a characteristic class of compounds that are species-unique within the genus [1c]. Thus, halogenated secondary metabolites can serve as an important taxonomic tool since *Laurencia* species are morphologically similar [1d]. In addition, halogenated metabolites have been reported to possess cytotoxic [1e], antimicrobial [1f] and anti-inflammatory activities [1g].

Here, we investigated one population of *L. nangii* collected from Lohok Butun (Sabah, Malaysia) that resulted in the isolation of one new sesquiterpene, neolaurene (**1**; Figure 1) with five known compounds: neolaurallene (**2**) [2a], 2,10-dibromo-3-chloro-α-chamigrene (**3**) [2b], deoxyprepacifenol (**4**) [2c], cycloelatanene B (**5**) [2d] and intricatetraol (**6**) [2e]. We report the isolation, structural elucidation and bioactivites of these compounds.

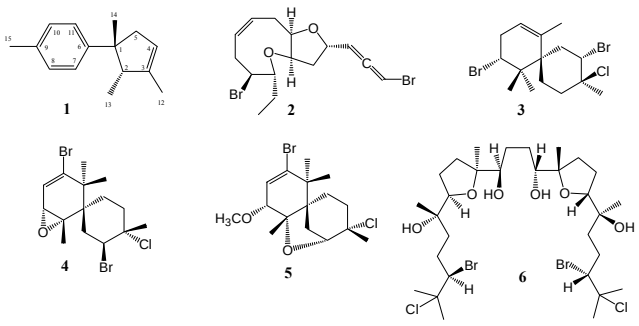

Figure 1: Structures of compounds **1**-**6**.

Compound **1** was isolated as a colorless oil. The molecular formula of **1**, $C_{15}H_{20}$ (corresponding to 6 degrees of unsaturation), was deduced from the HR-ESI-MS measurements, *m/z* 199.1413 $[M-H]^+$. The ^{13}C NMR and DEPT spectra displayed thirteen signals, including two with the same δ values (Table 1). The NMR data of **1** exhibited two 2H doublets at δ_H 7.14 (2H, d, J = 8.3 Hz, H-7, 11) and 7.10 (2H, d, J = 8.3 Hz, H-8, 10) and four aromatic carbons at δ_C 145.0 (C), 134.6 (C), 128.6 (2C, CH) and 127.1 (2C, CH), clearly indicating the presence of a 1,4-disubstituted benzene ring, the same as that of laurene-type sesquiterpenoids such as laurene and isolaurene [3a, b]. Spectroscopic data suggested the presence of a 1,4-disubstituted benzene ring to fulfill 6 degrees of unsaturation. Furthermore, the NMR spectra revealed the presence of four methyl groups, namely one vinylic (δ_H 1.73, s; δ_C 15.7; H_3C-12), one tertiary (δ_H 1.34, s; δ_C 31.7; H_3C-14), one secondary (δ_H 0.58, d, J = 6.9 Hz; δ_C 15.3; H_3C-13), and one aromatic (δ_H 2.32, s; δ_C 21.0; H_3C-15), instead of the two vinylic, but no secondary displayed by isolaurene (the remaining 2 degrees of unsaturation also present as one cyclopentene). The ^{13}C NMR and DEPT spectra of **1** further confirmed the presence of the trimethylcyclopentenyl substituent as judged from carbon signals, including two quaternary carbons at δ_C 50.0 (C-1) and 144.7 (C-3), two secondary carbons at δ_C 53.4 (C-2) and 121.6 (C-4), and one methylene carbon at δ_C 42.4 (C-5), together with protons of one methylene (δ_H 2.91, dd, J = 15.8, 2.1 Hz, H_β-5; δ_H 2.21, dd, J = 15.8, 2.1 Hz, H_α-5) and two methines (δ_H 5.32, brs, H-4; δ_H 2.36, d, J = 6.9 Hz, H-2).

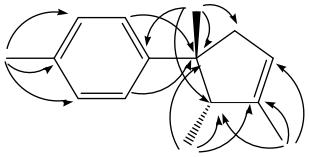

Figure 2: Selected HMBC of compound **1**.

Table 1: ^1H (600 MHz) and ^{13}C (150 MHz) NMR spectral data of **1** in $CDCl_3$.

	compound 1	
Position	**δ_C**	**δ_H (mult., J in Hz)**
1	50.0	
2	53.4	2.36 (1H, d, 6.9)
3	144.7	
4	121.6	5.32 (1H, brs)
5	42.4	2.91 (1H, dd, 15.8, 2.1)
		2.21 (1H, dd, 15.8, 2.1)
6	145.0	
7	127.1	7.14 (1H, d, 8.3)
8	128.6	7.10 (1H, d, 8.3)
9	134.6	
10	128.6	7.10 (1H, d, 8.3)
11	127.1	7.14 (1H, d, 8.3)
12	15.7	1.73 (3H, s)
13	15.3	0.58 (3H, d, 6.9)
14	31.7	1.34 (3H, s)
15	21.0	2.32 (3H, s)

The protons of **1** were assigned by ^1H-^1H COSY experiments and the position of H-13 was determined from correlations between H-13/H-2. The structure connectivities were achieved by HMBC spectra shown in Figure 2. The HMBC correlations between H_3-15

and C-9, in addition to C-8 and C-10, confirmed the location of the methyl group in a *p*-position relative to the other substitution. The HMBC correlation of signals at H_3-13 (δ_H 0.58) with C-1, C-2 and C-3 determined the position of the secondary methyl group located on C-2 and signals at H_3-12 (δ_H 1.73) with C-2, C-3 and C-4 determined the position of the vinyl methyl group located on C-3. The HMBC correlations between H_3-14 (δ_H 1.34) and C-1, C-2, C-5 and C-6 is a further confirmation of the structure of the compound (The up field shift of Me-13 at δ_H 0.58 could be attributed to the anisotropic effect of the benzene ring). Furthermore, the HMBC correlations between H-7 and H-11 with C-1 confirmed the planar structure of compound **1**. The relative stereochemistry of **1** was assigned based on NOESY data. The strong NOESY correlations between H-2/H-5β with H-14 determined the stereochemistry at C-1 and C-2.

To date, compound **1** represents the only example of such a 3,4-olefinic laurene-type carbon skeleton from a marine source. This is the first report of *L. nangii* that produces several skeleton-types of sesquiterpenes such as laurene- and chamigrene-types, together with bromoallene and triterpene.

Table 2: Cytotoxic and antibacterial activities of compounds from *Laurencia nangii*.

Biological Assay	Compounds					
	1	**2**	**3**	**4**	**5**	**6**
Cytotoxic Assay[a]						
HeLa	125.0	-	175.0	-	-	175.0
MCF-7	175.0	175.0	175.0	175.0	175.0	175.0
P-388	125.0	-	175.0	-	-	175.0
Antibacterial Assay[b]						
Escherichia coli	12.5	75.0	75.0	-	-	75.0
Salmonella thypi	7.5	75.0	50.0	-	-	-
Staphylococcus aureus	7.5	50.0	25.0	-	-	25.0
Vibrio cholerae	12.5	-	-	-	-	75.0

[a] - Minimum Inhibitory Concentration (MIC) calculated in μg $disc^{-1}$.
[b] - 50% Lethal Concentration (LC_{50}) calculated in μg mL^{-1}. Standard deviations were <5% of the values obtained and are not shown.

The bioassay results are given in Table 2. Compound **1** exhibited stronger antibacterial activites (MIC ≤ 12.5 μg/disc) and cytotoxic activities than the other compounds.

Experimental

Biological materials: Specimens of *L. nangii* were collected from Lohok Butun (04º27.233'N, 118º41.133'E), Sabah, Malaysia in May 2010. Voucher specimens (No. 39010) are deposited in the BORNEENSIS Collection of the Institute for Tropical Biology and Conservation, University of Malaysia Sabah.

Extraction and isolation: The partially dried algal specimens (100 g) were extracted with MeOH (2 L). The MeOH solution was concentrated *in vacuo* and partitioned between EtOAc and H_2O. The EtOAc extract (1.0 g) was chromatographed on a Si gel column using an *n*-hexane and EtOAc system of increasing polarity as eluent to yield 5 fractions. A portion of the fraction (50.0 mg) eluted with *n*-hexane/EtOAc (8:2) was submitted to repeated preparative TLC with toluene to yield compounds **1** (2.0 mg), **2** (9.8 mg), **3** (5.0 mg), **4** (5.2 mg) and **5** (11.4 mg). The fraction (50.0 mg) eluted with *n*-hexane/EtOAc (1:1) was submitted to repeated preparative TLC with *n*-hexane/EtOAc (1:1) to yield compound **6** (9.6 mg).

Bioassays: Cytotoxic activity was conducted against HeLa, MCF-7 and P-388 cells according to methods described by Sandhya and Mishra [4]. Antibacterial activity was conducted against four human pathogenic strains according to methods described by Vairappan *et al*. [5].

Neolaurene (**1**)
Colorless oil.
$[\alpha]_D^{28}$: +2.2 (*c* 0.10, $CHCl_3$).
IR ν_{max}(cm^{-1}): 2950, 1695, 1646, 1504 and 890.
^1H and ^{13}C NMR: Table 1.
HR-ESI-MS: *m/z* 199.1493 $[M-H]^+$ (calcd for $C_{15}H_{19}$, 199.1481).

Acknowledgments: We are grateful to the Sabah Parks for the support and assistance during field survey. The authors would also like to acknowledge Assoc. Prof. Dr. Tatsufumi Okino for the HRMS measurements.

References

[1] (a) Ji NY, Li XM, Cui CM, Wang BG. (**2007**) Two new brominated diterpenes from *Laurencia decumbens*. *Chinese Chemical Letters*, ***18***, 957-959; (b) Ji NY, Li XM, Li K, Ding LP, Gloer JB, Wang BG. (**2007**) Diterpenes, sesquiterpenes, and a C_{15}-acetogenin from the marine red alga *Laurencia mariannensis*. *Journal of Natural Products*, ***70***, 1901-1905; (c) Fenical W. (**1976**) Chemical variation in a new bromochamigrene derivative from the red seaweed *Laurencia pacifica*. *Phytochemistry*, ***15***, 511-512; (d) Takahashi Y, Daitoh M, Suzuki M, Abe T, Masuda M. (**2002**) Halogenated metabolites from the new Okinawan red alga *Laurencia yonaguniensis*. *Journal of Natural Products*, ***65***, 395-398; (e) Juagdan EG, Kalidindi R. Scheuer P. (**1997**) Two new chamigrenes from an Hawaiian red alga, *Laurencia cartilaginea*. *Tetrahedron*, ***53***, 521-528; (f) Vairappan CS, Suzuki M, Ishii T, Okino T, Abe T, Masuda M. (**2008**) Antibacterial activity of halogenated sesquiterpenes from Malaysian *Laurencia* spp. *Phytochemistry*, ***69***, 2490-2494; (g) Chatter R, Othman RB, Rabhi S, Kladi M, Tarhouni S, Vagias C, Roussis V, Tabbane LG, Kharrat R. (**2011**) *In vivo* and *in vitro* anti-inflammatory activity of neorogioltriol, a new diterpene extracted from the red alga *Laurencia glandulifera*. *Marine Drugs*, ***9***, 1293-1306.

[2] (a) Suzuki M, Kurosawa E, Furusaki A, Katsuragi S, Matsumoto T. (**1984**) Neolaurallene, a new halogenated C-15 nonterpenoid from the red alga *Laurencia okamurai* Yamada. *Chemistry Letters*, ***13***, 1033-1034; (b) Howard BM, Fenical W. (**1975**) Structures and chemistry of two new halogen-containing chamigrene derivatives from *Laurencia*. *Tetrahedron Letters*, ***16***, 1687-1690; (c) Fronczek F. (**1989**) Redetermination of the absolute configuration of deoxyprepacifenol, from the Mediterranean red alga, *Laurencia majuscula*. *Acta Crystallographica Section C*, ***45***, 1102–1104; (d) Dias DA, Urban S. (**2011**) Phytochemical studies of the southern Australian marine alga, *Laurencia elata*. *Phytochemistry*, ***72***, 2081-2089; (e) Suzuki M, Matsuo Y, Takeda S, Suzuki T. (**1993**) Intricatetraol, a halogenated triterpene alcohol from the red alga *Laurencia intricata*. *Phytochemistry*, ***33***, 651-656.

[3] (a) Irie T, Yasunari Y, Suzuki T, Imai N, Kurosawa E, Masamune T. (**1965**) A new sesquiterpene hydrocarbon from *Laurencia glandulifera*. *Tetrahedron Letters*, ***6***, 3619-3624; (b) Irie T, Suzuki T, Yasunari Y, Kurosawa E, Masamune T. (**1969**) Laurene, a sesquiterpene hydrocarbon from *Laurencia* species. *Tetrahedron*, ***25***, 459-468.

[4] Sandhya T, Mishra KP. (**2006**) Cytotoxic response of breast cancer cell lines, MCF 7 and T 47 D to triphala and its modification by antioxidants. *Cancer Letters*, **238**, 304-313.

[5] Vairappan CS, Kawamoto T, Miwa H, Suzuki M. (**2004**) Potent antibacterial activity of halogenated compounds against antibiotic resistant bacteria. *Planta Medica*, ***70***, 1087-1090.