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Secondary metabolites of the lichen-associated fungus *Apiospora montagnei*

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ABSTRACT

The endolichenic fungus *Apiospora montagnei* isolated from the lichen *Cladonia* sp. was cultured on solid rice medium, yielding the new diterpenoid libertellenone L (**1**), the new pyridine alkaloid, 23-*O*-acetyl-*N*-hydroxyapiosporamide (**2**) and the new xanthone derivative 8-hydroxy-3-hydroxymethyl-9-oxo-9*H*-xanthene-1-carboxylic acid methyl ether (**3**) together with 19 known compounds (**4**–**22**). The structures of the new compounds were elucidated by 1D and 2D NMR spectra as well as by HRESIMS data. The absolute configuration of the new 6,7-*seco*-libertellenone derivative **1** was determined by single-crystal X-ray diffraction. Four additional known compounds **23**–**26** were isolated when NaCl or NH_4Cl were added to solid rice medium. Compounds **7**–**9**, **18** and **26** exhibited significant cytotoxicity against the L5178 murine lymphoma cell line with IC_{50} values of 2.6, 0.2, 2.1, 2.7 and 1.7 μM, respectively.

Introduction

Lichens are symbiotic associations between fungi (mycobionts) and photoautotrophic, algal partners (photobionts), producing numerous bioactive secondary metabolites such as usnic acid, diffractaic acid, and physodic acid.[1,2] In addition to the photobiont and the mycobiont, lichens harbour a wide array of associated microorganisms including endolichenic fungi that are likewise prolific sources of bioactive secondary metabolites.[3–6] Over 140 new natural products including alkaloids, quinones, sulfur-containing chromenones and terpenes were isolated from 30 endolichenic microorganisms during the past decade.[7] Considering that there are nearly 20,000 identified lichens, a further exploration of endolichenic fungi as sources for new compounds is promising.

During our ongoing search for bioactive secondary metabolites from fungi,[8–10] the fungus *Apiospora montagnei* was isolated from the lichen *Cladonia* sp. *A. montagnei*, which is also known as *Arthrinium arundinis*, has previously been obtained from various sources such as sponges, algae, soil and mouse dung.[11–14] This is the first report of this fungus from lichen thalli. Previous chemical investigations of *A. montagnei* revealed a series of diverse secondary metabolites, such as the cyclopeptides TMC-95A–D,[11] the diterpene myrocin A[12] and the pydidone alkaloids arthpyrones A–C, apiosporamide and *N*-hydroxyapiosporamide.[13,14] In this study, the EtOAc extract of the fungus when fermented on solid rice medium yielded the new diterpenoid libertellenone L (**1**), the new pyridine alkaloid 23-*O*-acetyl-*N*-hydroxyapiosporamide (**2**) and the likewise new xanthone derivative 8-hydroxy-3-hydroxymethyl-9-oxo-9*H*-xanthene-1-carboxylic acid methyl ether (**3**) as well as 19 known compounds (**4**–**22**). Furthermore, addition of NaCl to

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solid rice medium led to isolation of compounds **23** and **24** that were both undetectable in controls. Addition of NH_4Cl induced accumulation of compounds **25** and **26** that were likewise not detected in fungal controls. All isolated compounds (**1**–**26**) were evaluated for their cytotoxicity against the L5178Y mouse lymphoma cell line. Compounds **7**–**9**, **18** and **26** exhibited strong cytotoxicity with IC_{50} values ranging from 0.2 to 2.6 μM.

Results and discussion

Compound **1** was isolated as colorless crystals. Its molecular formula was established as $C_{20}H_{26}O_5$ by HRESIMS, implying 8 degrees of unsaturation. The ^{13}C NMR spectrum of **1** (Table 1) showed 20 carbon signals that account for three methyl, six methylene, four methine and six quaternary carbons. The presence of a terminal double bond in **1** was proposed by the observation of the olefinic methine CH-15 (δ_C 146.9, δ_H 6.05) and the olefinic methylene CH_2-16 (δ_C 112.5, δ_H 5.06 and 5.04) as well as by the COSY correlations between them. On the basis of the COSY correlations between $H_{\alpha\beta}$-11 (δ_H 3.32 and 2.29) and $H_{\alpha\beta}$-12 (δ_H 1.94 and 1.45) and the HMBC correlations from Me-17 (δ_H 0.92) to C-12 (δ_C 26.4), C-13 (δ_C 39.8), C-14 (δ_C 70.7) and C-15, from $H_{\alpha\beta}$-11 and H-14 to C-8 (δ_C 124.1), and from $H_{\alpha\beta}$-11, H_β-12 and H-14 to C-9 (δ_C 168.6), the nature of the cyclohexene ring *C* was established (Fig. 2). The COSY correlations between H-1 (δ_H 4.20)/$H_{\alpha\beta}$-2 (δ_H 2.06 and 1.91) and $H_{\alpha\beta}$-2/$H_{\alpha\beta}$-3 (δ_H 1.77 and 1.69) along with the HMBC correlations from H-1 and H-14 to C-7 (δ_C 167.5), from Me-18 (δ_H 1.32) to C-3 (δ_C 31.3), C-4 (δ_C 45.1), C-5 (δ_C 52.3) and C-19 (δ_C 81.3), and from Me-20 (δ_H 1.31) to C-1 (δ_C 85.0), C-5, C-9 and C-10 (δ_C 42.0) indicated the presence of fused rings *A* and *B* in **1**. Furthermore, the cyclopentane lactone ring *D* was established from the HMBC correlations from H-5 (δ_H 2.81) and $H_{\alpha\beta}$-19 (δ_H 3.95 and 4.02) to C-6 (δ_C 175.6). Thus, the planar structure of **1** was elucidated as shown in Fig. 2.

The relative configuration of compound **1** was determined by investigation of the coupling constants and the ROESY correlations. The coupling constants ($^3J_{1,2\alpha}$ = 12.5 Hz, $^3J_{1,2\beta}$ = 4.4 Hz, $^3J_{2\alpha,3\alpha}$ = 3.5 Hz, $^3J_{2\alpha,3\beta}$ = 13.0 Hz, $^3J_{2\beta,3\alpha}$ = $^3J_{2\beta,3\beta}$ = 3.5 Hz) together with the NOE correlations between H-1/H-2β, H-1/H-3β, H-1/H-5, H-3β/H-5, H-3β/H-19β, H-5/19β and between H-2α/Me-18, H-2α/Me-20, H-3α/Me-18, H-19α/Me-18 suggested a chair conformation of the cyclohexane ring *A* with H-1 and H-5 being β-oriented while Me-18 and Me-20 are α-oriented (Fig. 3). The β-orientation of H-11β was deduced from its NOE relationship with H-5. Moreover, the NOE correlations from Me-17 to H-11β, H-12β and H-14 suggested that these protons were on the same face of ring *C*. The absolute configuration of **1** was determined as 1*R*, 4*R*, 5*S*, 10*S*, 13*R* and 14*S* by X-ray single crystal analyses (Fig. 4).

Table 1
^1H (600 MHz) and ^{13}C (150 MHz) NMR data for **1** in CD_3OD.

Position	δ_C	δ_H (*J* in Hz)
1	85.0, CH	4.20 (dd, 12.5, 4.4)
2	24.5, CH_2	2.06 (α-H, dddd, 13.0, 13.0, 12.5, 3.5) 1.91 (β-H, dddd, 13.0, 4.4, 3.5, 3.5)
3	31.3, CH_2	1.77 (α-H, ddd, 13.0, 3.5, 3.5) 1.69 (β-H, ddd, 13.0, 13.0, 3.5)
4	45.1, C	
5	52.3, CH	2.81 (s)
6	175.6, C	
7	167.5, C	
8	124.1, C	
9	168.6, C	
10	42.0, C	
11	25.2, CH_2	3.32 (α-H, br dd, 20.8, 6.5) 2.29 (β-H, ddd, 20.8, 10.7, 7.0)
12	26.4, CH_2	1.94 (α-H, ddd, 13.4, 10.7, 6.5) 1.45 (β-H, br dd, 13.4, 7.0)
13	39.8, C	
14	70.7, CH	3.92 (s)
15	146.9, CH	6.05 (dd, 17.6, 11.0)
16	112.5, CH_2	5.06 (dd, 17.6, 1.3) 5.04 (dd, 11.0, 1.3)
17	20.9, CH_3	0.92 (s)
18	22.0, CH_3	1.32 (s)
19	81.3, CH_2	4.02 (β-H, d, 7.9) 3.95 (α-H, d, 7.9)
20	14.6, CH_3	1.31 (s)

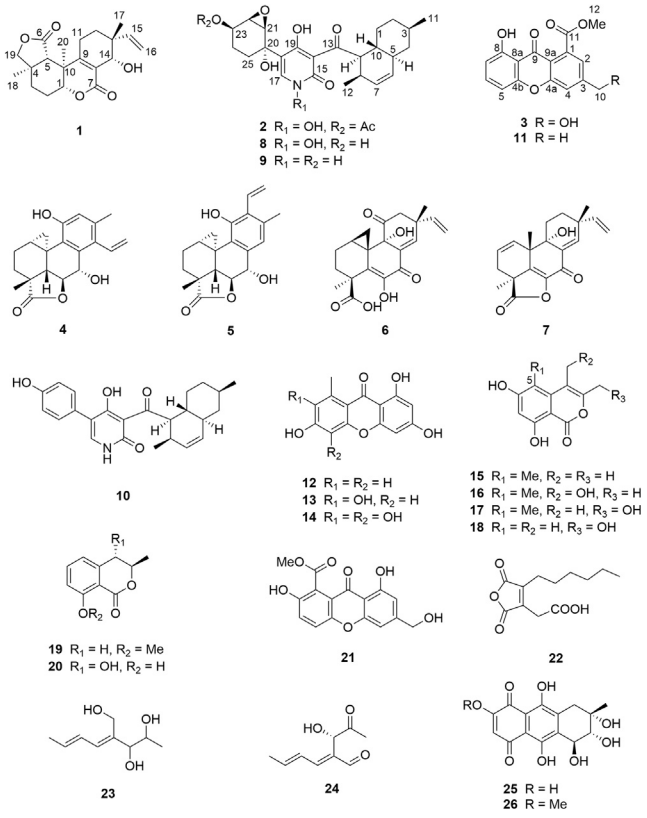

Fig. 1. Structures of compounds isolated from *A. montagnei*.

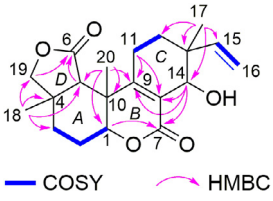

Fig. 2. COSY and key HMBC correlations of **1**.

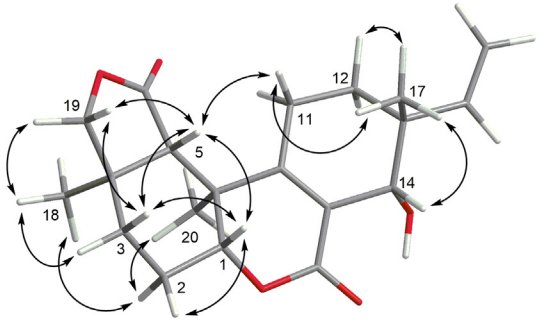

Fig. 3. Key NOE correlations of **1**.

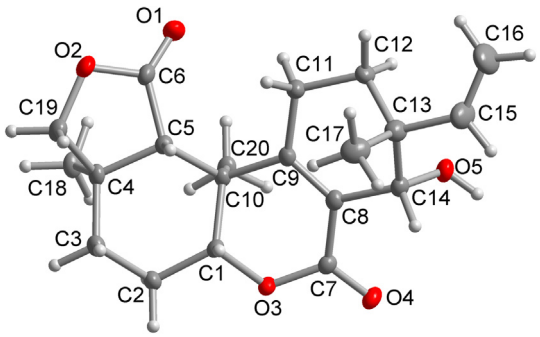

Fig. 4. Molecular structure of **1** from single-crystal X-ray diffractometry.

Comparison of the structure of **1** with that of co-isolated known pimarane diterpenoid libertellenone G (**7**)[15] revealed that compound **1** represents the first example of a 6,7-*seco*-libertellenone derivative,[15–19] for which the name libertellenone L is proposed. A biosynthetic pathway for **1** is proposed through 5,6-enol-keto-tautomerization, 6,7-oxidation-cleavage following by 1,7- and 6,19-esterification Fig. 5.

Compound **2** possessed the molecular formula $C_{26}H_{33}O_8N$ as determined by HRESIMS. Its NMR data (Table 2) were similar to those of *N*-hydroxyapiosporamide (**8**),[14,20] suggesting that **2** was an analogue of the latter compound. The presence of an additional acetyl group in **2** was deduced from its molecular weight being 42 amu higher than that of **8** and by NMR signals (δ_C 172.4 and 20.8, δ_H 2.07, s) which are indicative for an acetyl group. The HMBC correlation from H-23 (δ_H 5.18, ddd) to the acetyl carbonyl carbon indicated the additional *O*-acetyl group to be located at the C-23 position. Detailed analysis of the 2D NMR spectra of **2** revealed that its remaining substructures were identical to those of **8**. The relative configuration of **2** was determined by the similarity of the NOE relationships compared to **8**. Based on the similar specific rotation of **2** compared with **8** and biogenetic considerations, the absolute configuration of **2** was proposed to be identical to that of **8**. Thus, compound **2** was elucidated as 23-*O*-acethyl-*N*-hydroxyapiosporamide, representing a new pyridine alkaloid.

The molecular formula of **3** was determined to be $C_{16}H_{12}O_6$ by its HRESIMS data. Its UV spectrum showed absorption bands at λ_{max} 231, 257, 289 and 368 nm, similar to those of the co-isolated known xanthone derivative, 8-hydroxy-3-methyl-9-oxo-9*H*-xathene-1-carboxylic acid methyl ether (**11**).[21] The NMR data of **3** (Table 3) resembled those of **11** except for the aromatic methyl group which was replaced by a hydroxymethyl group (δ_C 63.5, δ_H 4.79, s, CH_2-10) in **3**. The extra hydroxymethyl group of **3** was attached at C-3, which was evident from the HMBC correlations from H_2-10 to C-2 (δ_C 121.6), C-3 (δ_C 152.6) and C-4 (δ_C 117.1), and in turn from H-2 (δ_H 7.36) and H-4 (δ_H 7.67) to C-10. Thus, the structure of **3** was elucidated as shown in Fig. 1.

The remaining known compounds (**4**–**22**) were identified as arthrinin A (**4**),[22] arthrinin B (**5**),[22] myrocin A (**6**),[12] libertellenone G (**7**),[15] *N*-hydroxyapiosporamide (**8**),[14,20] apiosporamide (**9**),[13,23] didymellamide B (**10**),[24] 8-hydroxy-3-methyl-9-oxo-9*H*-xanthene-1-carboxylic acid methyl ether (**11**),[21] norlichexanthone (**12**),[25] anomalin A (**13**),[25] anomalin B (**14**),[25] decarboxycitrinone (**15**),[26] 6,8-dihydroxy-4-hydroxymethyl-3,5-dimethyl-isochromen-1-one (**16**),[27] decarboxyhydroxycitrinone (**17**),[17] acremonone G (**18**),[28] *O*-methylmellein (**19**),[29] *trans*-4-hydroxymellein (**20**),[30] sydowinin B (**21**),[31] and 2-carboxymethyl-3-*n*-hexylmaleic acid anhydride (**22**).[32,33]

Table 2
^1H (600 MHz) and ^{13}C (150 MHz) NMR data for **2** in CD_3OD.

Position	δ_C	δ_H (*J* in Hz)
1	31.0, CH_2	1.92 (m)
		0.89 (m)
2	36.6, CH_2	1.74 (m)
		1.03 (m)
3	34.4, CH	1.50 (m)
4	43.2, CH_2	1.75 (m)
		0.79 (m)
5	43.2, CH	1.82 (m)
6	131.7, CH	5.40 (br d, 9.8)
7	132.6, CH	5.59 (ddd, 9.8, 4.5, 2.7)
8	32.4, CH	2.85 (m)
9	54.6, CH	4.44 (dd, 11.3, 5.8)
10	37.6, CH	1.57 (m)
11	22.9, CH_3	0.92 (d, 6.5)
12	18.4, CH_3	0.82 (d, 7.2)
13	211.8, C	
14	108.6, C	
15	159.7, C	
17	140.0, CH	8.03 (s)
18	115.4, C	
19	175.5, C	
20	70.6, C	
21	59.5, CH	3.61 (d, 3.8)
22	54.9, CH	3.54 (dd, 3.8, 3.3)
23	70.0, CH	5.18 (ddd, 5.7, 5.7, 3.3)
24	23.0, CH_2	1.97 (m)
		1.48 (m)
25	30.5, CH_2	2.19 (m)
		1.79 (m)
OAc	172.4, C	
	20.8, CH_3	2.07 (s)

Furthermore, addition of NaCl resulted in accumulation of compounds **23** and **24** that were both undetectable in control extracts. Compounds **23** and **24** were identified as the known (*E*,*E*)-4-hydroxymethyl-4,6-octadien-2,3-diol[34] and lachnellin B,[35] respectively. When NH_4Cl was added to rice medium, compounds **25** and **26** were detected as major components whereas both were missing in fungal controls. Compounds **25** and **26** were identified as the known 6-*O*-demethylbostrycin (**25**)[36] and bostrycin (**26**).[37]

All compounds (**1**–**26**) were tested for their cytotoxic activity against the mouse lymphoma cell line (L5178Y) utilizing the MTT assay (Table 4). Compounds **7**–**9**, **18** and **26** exhibited significant cytotoxicity against the L5178 murine lymphoma cell line with IC_{50} values of 2.6, 0.2, 2.1, 2.7 and 1.7 μM, respectively. Comparison of the cytotoxicity of pyridine alkaloids (**2**, **8**, **9** and **10**) revealed that acetylation of 23-OH (**2** vs. **8**) and aromatization from C-20 to C-25 (**10** vs. **9**) led to total loss of cytotoxicity while loss of the hydroxy group at the N-16 position (**9** vs. **8**) increased the activity around 10-fold. The significant cytotoxicity of compound **7** could be caused by the disappearance of the cyclopropane ring compared to **4**–**6**. Among the isolated isocoumarins (**15**–**18**), only compound **18** which lacks a methyl substituent at C-5 is active. Compared to bostrycin (**26**), 6-*O*-demethylbostrycin (**25**) shows no cytotoxicity.

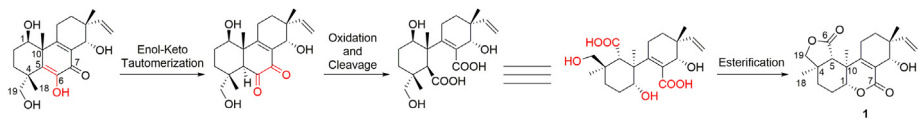

Fig. 5. Plausible biosynthesis of **1**.

Table 3
^{1}H (700 MHz) and ^{13}C (175 MHz) NMR data for **3** in CD_3OD.

Position	δ_C[a]	δ_H (*J* in Hz)
1	134.6, C	
2	121.6, CH	7.36 (br s)
3	152.6, C	
4	117.1, CH	7.67 (br s)
4a	157.5, C	
4b	157.1, C	
5	107.9, CH	7.04 (dd, 8.3, 0.9)
6	138.2, CH	7.69 (t, 8.3)
7	111.4, CH	6.81 (dd, 8.3, 0.9)
8	162.6, C	
8a	109.6, C	
9	181.9, C	
9a	116.8, C	
10	63.5, CH_2	4.79 (s)
11	171.1, C	
12	53.2, CH_3	3.98 (s)

[a] Data extracted from HSQC and HMBC spectra.

Table 4
Cytotoxicity against the L5178 murine lymphoma cell.

Compound[b]	IC_{50} (μM)
6	13.1
7	2.6
8	0.2
9	2.1
18	2.7
26	1.7
Kahalalide F[a]	4.3

[a] Positive control.
[b] The remaining compounds were not active at the dose of 20 μM.

Besides, all isolated compounds were further tested for their antimicrobial activities against *Mycobacterium tuberculosis*, *Staphylococcus aureus* (ATCC25923), *S. aureus* (ATCC700699), *Enterococcus faecalis* (ATCC29212), *E. faecalis* (ATCC51299), *E. faecium* (ATCC35667), *E. faecium* (ATCC700221) and *Acinetobacter baumannii* (ATCCBAA1605) but none of them was found to be active at the dose of 20 μg/mL.

In conclusion, cultivation of fungus *A. montagnei* as described in this study yielded five pimarane diterpenoids (**1**, **4**–**7**), four pyridine alkaloids (**2**, **8**–**10**), six xanthone derivatives (**3**, **11**–**14**, **21**), six isocoumarins (**15**–**20**) and five other metabolites (**22**–**26**), of which three (**1**–**3**) are new. Addition of either NaCl or NH_4Cl to solid rice medium diversified the natural product pattern of the fungus. Compound **1**, whose absolute configuration was determined by X-ray diffraction, represented the first example of 6,7-*seco*-libertellenone derivative and a plausible biosynthetic pathway for the formation of this compound was proposed. Several compounds (**7**–**9**, **18** and **26**) were found to exhibit significant cytotoxicity against the L5178Y mouse lymphoma cell line and preliminary structure-activity relationships were proposed.

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A. Supplementary data

Supplementary data (UV, MS and NMR spectra of **1**, **2** and **3** as well as X-ray data of **1**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2017.03.052.

References

1. Ranković B, Kosanić M. *Lichen Secondary Metabolites*. Switzerland: Springer International Publishing; 2015. 1–26.
2. Shrestha G, Larry L, Clair St. *Phytochem Rev*. 2013;12:229–244.
3. Arnold AE, Miadlikowska J, Higgins KL, et al. *Syst Biol*. 2009;58:283–297.
4. Jiao Y, Li G, Wang HY, et al. *Chem Biodiversity*. 2015;12:1095–1104.
5. Dou Y, Wang X, Jiang D, et al. *Drug Discovery Ther*. 2014;8:84–88.
6. Zhang F, Li L, Niu S, et al. *J Nat Prod*. 2012;75:230–237.
7. Kellogg JJ, Raja HA. *Phytochem Rev*. 2016;1–23.
8. Uzor PF, Ebrahim W, Osadebe PO, et al. *Fitoterapia*. 2015;105:147–150.
9. Elnaggar MS, Ebada SS, Ashour ML, et al. *Tetrahedron*. 2016;72:2411–2419.
10. Liu S, Dai H, Makhloufi G, et al. *J Nat Prod*. 2016;79:2332–2340.
11. Koguchi Y, Kohno J, Nishio M, et al. *J Antibiot*. 2014;67:171–174.
12. Klemke C, Kehraus S, Wright AD, König GM. *J Nat Prod*. 2004;67:1058–1063.
13. Alfatafta AA, Gloer JB, Scott JA, Malloch D. *J Nat Prod*. 1994;57:1696–1702.
14. Wang J, Wei X, Qin X, et al. *Org Lett*. 2015;656–659.
15. Tan R, Wei W, Jiang R, Zhao G. Faming Zhuanli Shenqing 2013, CN 103073527 A 20130501.
16. Oh D-C, Jensen PR, Kauffman CA, Fenical W. *Bioorg Med Chem*. 2005;13:5267–5273.
17. Tsukada M, Fukai M, Miki K, et al. *J Nat Prod*. 2011;74:1645–1649.
18. Lu X-L, Liu J-T, Liu X-Y, et al. *J Antibiot*. 2014;67:171–174.
19. Wei W, Gao J, Shen Y, Chu YL, Xu Q, Tan RX. *Eur J Org Chem*. 2014;5728–5734.
20. Lee JC, Coval SJ, Clardy J. *J Antibiot*. 1996;49:693–696.
21. Li C, Zhang J, Shao C, Ding W, She Z, Lin Y. *Chem Nat Compd*. 2011;47:382–384.
22. Ebada SS, Schulz B, Wray V, et al. *Bioorg Med Chem*. 2011;19:4644–4651.
23. Williams DR, Kammler DG, Donnell AF, Goundry WRF. *Angew Chem Int Ed*. 2005;44:6715–6718.
24. Haga A, Tamoto H, Ishino M, et al. *J Nat Prod*. 2013;76:750–754.
25. Abdel-Lateff A, Klemke C, König GM, Wright AD. *J Nat Prod*. 2003;66:706–708.
26. Whyte AC, Gloer JB, Scott JA, Malloch D. *J Nat Prod*. 1996;59:765–769.
27. Krohn K, Sohrab MH, Aust HJ, Draeger S, Schulz B. *Nat Prod Res*. 2004;18:277–285.
28. Rukachaisirikul V, Rodglin A, Sukpondma Y, Phongpaichit S, Buatong J, Sakayaroj J. *J Nat Prod*. 2012;75:853–858.
29. Glauser G, Gindro K, Fringeli J, de Joffrey JP, Rudaz S, Wolfender JL. *J Agric Food Chem*. 2009;57:1127–1134.
30. Asha KN, Chowdhury R, Hasan CM, Rashid MA. *Acta Pharm*. 2004;54:57–63.
31. Hamasaki T, Sato Y, Hatsuda Y. *Agric Biol Chem*. 1975;39:2341–2345.
32. Weidenmüller HL, Cavagna F, Fehlhaber HW, Präve P. *Tetrahedron Lett*. 1972;33:3519–3522.
33. Haval KP, Argade NP. *J Org Chem*. 2008;73:6936–6938.
34. Fuchser J, Zeeck A. *Liebigs Ann*. 1997;87–95.
35. Semar M, Anke H, Arendholz WR, Veiten R, Steglich W. *Z Naturforsch C: J Biosci*. 1996;51:500–512.
36. Kelly TR, Saha JK. *J Org Chem*. 1985;50:3679–3685.
37. Chen H, Zhong L, Long Y, et al. *Mar Drugs*. 2012;10:932–952.