Tetrahedron Letters 52 (2011) 1597–1600

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Diarylnonanoids and their glucosides from Erica cinerea ☆

Bachir Bennini [a], Albert J. Chulia [a,*], Mourad Kaouadji [b], Patrice Fondanèche [a], Daovy P. Allais [a]

[a] Laboratoire de Pharmacognosie, UPRES EA 4021 'Biomolécules et Thérapies Antitumorales' Faculté de Pharmacie, 2, Rue Docteur Marcland F-87025 Limoges Cedex, France
[b] Département de Chimie, Faculté des Sciences et Techniques 123, Avenue A. Thomas F-87060 Limoges Cedex, France

ARTICLE INFO

Article history:
Received 24 November 2010
Revised 19 January 2011
Accepted 24 January 2011
Available online 1 February 2011

Keywords:
Ericaceae
Erica cinerea
rel-(3*R*,7*R*)-1,9-Bis(*p*-hydroxyphenyl)-3,7-dihydroxynonan-5-one
Ericanone
Ericanone 3-glucoside
(2*S*)-2,6-Bis(*p*-hydroxyphenethyl)-2,3-dihydropyran-4-one
(3*S*)-3,7-Anhydro-6,7-dehydroericanone
(3*S*)-3,7-Anhydro-6,7-dehydroericanone 4′ glucoside

ABSTRACT

The reinvestigation of *Erica cinerea* fresh aerial parts led to the isolation of two new diarylnonanoid aglycones along with their glucosides. From spectroscopic data, their structures were elucidated as rel-(3*R*,7*R*)-1,9-bis(*p*-hydroxyphenyl)-3,7-dihydroxynonan-5-one named ericanone, ericanone 3-β-D-glucoside, (3*S*)-3,7-anhydro-6,7-dehydroericanone and (3*S*)-3,7-anhydro-6,7-dehydroericanone 4′-β-D-glucoside. Contrary to the numerous diarylheptanoids more frequently distributed in the plant kingdom, the rare diarylnonanoids were previously restricted to the genus *Myristica* of the Myristicaceae plant family.

Our last studies on the acetone extract of fresh *Erica cinerea* L. aerial parts at the flowering stage, characterized flavonoid aglycones, glycosides, as well as an acylglycoside and a disulfate.[1] The same material extract was reinvestigated to deepen the phytochemical content of this species. Based on partitioning with petrol, dichloromethane and ethyl acetate successively, and then a multistep chromatographic treatment of the ethyl acetate soluble portion, this process resulted in the isolation of aglycones **1** and **3** and the corresponding glucosides **2** and **4**.[2] Moreover, the two former metabolites were also detected in the CH_2Cl_2 extract among the major (*E*)- and (*Z*)-3-*p*-coumaroyltriterpenes. By spectroscopic evidence including UV, MS as well as NMR, the basic structure of the newly reported compounds was established as 1,9-diarylnonanoid with either open or partly cyclized C_9 chain, a higher homologue of the well-known 1,7-diarylheptanoid backbone.

Compound **1** was isolated as a white amorphous powder, $[\alpha]_D^{27}$ −14 (c 0.042, MeOH). It exhibited a UV spectrum consisting of one band at λ_{max}^{MeOH} 280 nm, and the molecular formula $C_{21}H_{26}O_5$ supplied by HRESMS (found: 381.1673; calcd: 381.16779 for $[M+Na]^+$). The ^{13}C NMR spectrum (Table 1) made up by only nine signals for C_{21}, suggested well an apparent symmetrical structure. Five resonances (δ 211.4, 68.1, 51.9, 40.5 and 32.0) corresponded to a tetrasubstituted nonan-5-one chain (C-5: δ 211.4) indicated by one pair of equivalent oxymethines (δ 68.1) and three pairs of equivalent methylenes (δ 51.9, 40.5 and 32.0). The remaining four peaks in the C sp^2 shift range supported two symmetrical *p*-hydroxyphenyls (C-1′,1″: δ 134.2; C-2′,2″,6′,6″: δ 130.4; C-3′,3″,5′,5″: δ 116.2; C-4′,4″: δ 156.5). To comply with the substitution pattern of the C_9 chain, each aromatic ring must be attached to one end as supported by the EIMS base peak at *m/z* 107 for *p*-hydroxybenzylium fragment-ion. Furthermore, the multiplicity of the oxymethine proton pair in the ^1H NMR spectrum (δ 4.02, br quint, *J* = 6.3 Hz), clearly indicated for each one to have four coupling partners. This was also reflected in the ^1H–^1H COSY spectrum by the cross-peaks they displayed with two nuclei at δ 2.61 and 2.56, respectively, and with two more at δ 1.68. Thus, the oxygen atoms must be linked to either C-2,8 or C-3,7. Parallely, although unresolved, the complex H-1,9 multiplets (H-1a,9a: δ 2.64 and H-1b,9b: δ 2.53) clearly excluded the presence of a tertiary carbon in the immediate vicinity as depicted in the 2,8-dihydroxy alternative. Hence, the oxygen atoms of hydroxyl groups were attached to C-3,7 and **1** was assigned the structure of 1,9-bis(*p*-hydroxyphenyl)-3,7-dihydroxynonan-5-one, a new natural product designated as ericanone. A detailed analysis of the ^1H–^{13}C HMBC spectrum (Table 1) supported this 1,3,7,9-tetrasubstituted nonan-5-one chain and corroborated assignments for all the ^1H and ^{13}C

☆ Part 11 in the series Phytochemistry of the Ericaceae.

* Corresponding author. Tel: +33 5 55 43 58 34; fax: +33 5 55 43 59 10.
E-mail address: jose.chulia@unilim.fr (A.J. Chulia).

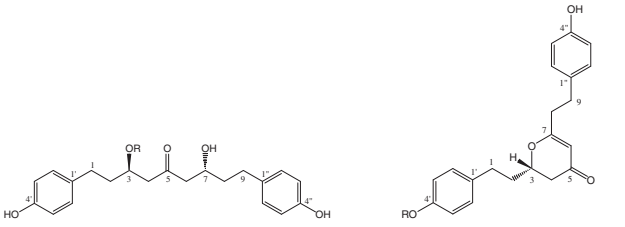
0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.01.108

Table 1
^{13}C NMR (125 MHz) and ^{1}H NMR (500 MHz) data for diarylnonanoids **1** and **3** and their glucosides **2** and **4** in CD_3OD (δ ppm; J Hz)[a]

C/H	1			2			3			4		
	^{13}C	^{1}H	HMBC	^{13}C	^{1}H	HMBC	^{13}C	^{1}H	HMBC	^{13}C	^{1}H	HMBC
1	32.0	2.64 m	C-3; C-2′,6′	31.8	2.59 m	C-3; C-2′,6′	31.3	2.72 m	C-3; C-2′,6′	31.3	2.72 m	C-3; C-2′,6′
		2.53 m	C-3; C-2′,6′			C-3; C-2′,6′		2.65 m	C-3; C-2′,6′		2.65 m	C-3; C-2′,6′
2	40.5	1.68 dt (8.1; 6.7)	C-4; C-1′	38.9	1.86 br hext (7.1)	C-4; C-1′	37.4	2.06 br ddt (14.2; 8.1; 6.1)	C-4; C-1′	37.2	2.06 br ddt (14.2; 8.1; 6.1)	C-4; C-1′
					1.75 m	C-4; C-1′		1.91 m	C-4; C-1′		1.92 m	C-4; C-1′
3	68.1	4.02 br quint (6.3)	C-1; C-5	76.7	4.17 br quint (6.3)	C-1; C-5; C-1‴	80.0	4.30 ddt (12.4; 8.1; 3.7)	C-1; C-5; C-7	80.0	4.30 ddt (13.5; 8.1; 3.6)	C-1; C-5; C-7
4	51.9	2.61 m		49.5	2.82 dd (16.7; 7.1)		41.5	2.43 dd (16.9; 12.4)	C-2	41.5	2.43 dd (17.0; 13.5)	C-2
		2.56 m			2.56 m			2.32 dd (16.9; 3.7)	C-6		2.32 dd (17.0; 3.6)	C-6
5	211.4			211.4			196.2			196.0		
6	51.9	2.61 m		52.3	2.59 m		105.0	5.23 br s	C-3; C-4; C-8	105.0	5.23 br s	C-3; C-4; C-8
		2.56 m										
7	68.1	4.02 br quint (6.3)	C-5; C-9	68.4	4.00 br quint (6.3)	C-5; C-9	180.0			179.9		
8	40.5	1.68 dt (8.1; 6.7)	C-6; C-1″	40.8	1.66 dt (8.2; 6.6)	C-1″	38.0	2.56 br dt (11.4; 7.4)	C-6; C-1″	37.9	2.57 br dt (10.4; 7.3)	C-6; C-1″
								2.54 br dt (11.4; 7.4)	C-6; C-1″		2.55 br dt (10.4; 7.3)	C-6; C-1″
9	32.0	2.64 m	C-7; C-2″,6″	32.2	2.62 m	C-7; C-2″,6″	32.9	2.80 br t (7.4)	C-7; C-2″,6″	32.9	2.81 br t (7.3)	C-7; C-2″,6″
		2.53 m	C-2″,6″		2.53 dt (14.0; 8.2)	C-7; C-2″,6″						
1′	134.2			134.7			133.2			135.7		
2′,6′	130.4	7.00 br d (8.5)	C-1; C-4′	130.7	6.97 d (8.4)	C-1; C-4′	130.4	7.03 d (8.4)	C-1; C-4′	130.4	7.03 d (8.6)	C-1; C-4′
3′,5′	116.2	6.68 d (8.5)	C-1′	116.5[b]	6.65 d (8.4)	C-1′	116.3	6.71 d (8.4)	C-1′	118.0	7.13 d (8.6)	C-1′
4′	156.5			156.7[c]			156.7			157.7		
1″	134.2			134.5			132.4			132.4		
2″,6″	130.4	7.00 br d (8.5)	C-9; C-4″	130.7	6.97 d (8.4)	C-9; C-4″	130.4	6.99 d (8.4)	C-9; C-4″	130.4	6.99 d (8.6)	C-9; C-4″
3″,5″	116.2	6.68 d (8.5)	C-1″	116.4[b]	6.64 d (8.4)	C-1″	116.2	6.69 d (8.4)	C-1″	116.3	6.69 d (8.6)	C-1″
4″	156.5			156.6[c]			156.9			156.9		
β-D-Glucosyl moiety												
1‴				103.9	4.30 d (7.7)	C-3				102.6	4.83 d (7.4)	C-4′
2‴				75.6	3.11 dd (9.0; 7.7)					75.0	3.39 br t (8.2)	
3‴				78.4	3.31 dd (9.0; 7.5)					78.1	3.44 br t (8.9)	
4‴				72.0	3.28 m					72.0	3.39 br t (9.3)	
5‴				78.3	3.27 ddd (9.5; 5.4; 2.5)					78.2	3.43 m	
6‴				63.1	3.83 dd (11.9; 2.5)					62.6	3.89 dd (11.9; 2.0)	
					3.66 dd (11.9; 5.4)						3.70 dd (11.9; 5.2)	

[a] 1,9-Diarylnonanoid numbering is applied to all compounds.
[b,c] Values with the same superscript in one column may be interchanged.

NMR resonances. With respect to the CO group, the outer non-equivalent geminal protons H-1a,9a and H-1b,9b (δ 2.64 and 2.53) indeed showed two ^3J correlations with the neighbouring β-carbons C-3 or C-7 (δ 68.1) and C-2′,6′ or C-2″,6″ (δ 130.4). In the same way, the inner H-3,7 (δ 4.02) exhibited two ^3J cross-peaks with C-5 (δ 211.4) and with either C-1 or C-9 (δ 32.0) when H-2,8 (δ 1.68) were also implicated in two ^3J correlations with either C-4 or C-6 (δ 51.9) and with either C-1′ or C-1″ (δ 134.2). Parallely, the aromatic protons H-2′,2″,6′,6″ (δ 7.00) gave two ^3J cross-peaks with either C-1 or C-9 (δ 32.0) and with either C-4′ or C-4″ (δ 156.5) when H-3′,3″,5′,5″ (δ 6.68) were characterized by a single ^3J correlation with either C-1′ or C-1″ (δ 134.2). To conclude, since ericanone is laevorotatory, it lacks symmetry between C-3 and C-7 which together must have the same configuration, that is, rel-(3*R*,7*R*) in contrast with opposite configuration only found in the optically inactive *meso*-form.



With a chromatographic behaviour close to that of flavonol monoglycosides within this species, compound **2**, $[\alpha]_D^{26}$ −19.5 (*c* 0.015, MeOH), was also obtained as a white amorphous powder. It was assigned the molecular formula $C_{27}H_{36}O_{10}$ by HRESMS (found: 543.2201; calcd: 543.22062 for $[M+Na]^+$). The UV spectrum (λ_{max}^{MeOH} 280 nm) was similar to that of **1** as well as the NMR features (Table 1) indicating a close relationship between **1** an **2**. Indeed, analysis of NMR shift values, multiplicities and coupling constants rapidly revealed four distinct parts in **2**: two quasi-similar *p*-disubstituted aromatic rings, one unsymmetrical C_9 ketone and one extra hexosyl unit, all these elements suggesting that **2** was a glycoside of **1**. Indeed, mild acid hydrolysis of compound **2** afforded glucose and ericanone (**1**). The remarkable ^1H and ^{13}C downfield shifts of one oxymethine in **2** (H-3: δ 4.17, $\Delta\delta$ +0.15 and C-3: δ 76.7 ppm, $\Delta\delta$ +8.6) indicated an ether linkage between C-3 of the ericanone moiety and the β-D-glucosyl unit (H-1‴: δ 4.30, d, J = 7.7 Hz). This attachment was confirmed by the HMBC spectrum similar to that of **1** except for the additional ^3J correlations observed between H-3 and the anomeric C (C-1‴: δ 103.9) and conversely between C-3 and the anomeric proton. Accordingly, component **2** was identified to the newly reported ericanone 3-β-D-glucopyranoside.

Less polar than ericanone (**1**), compound **3**, $[\alpha]_D^{27}$ +9.5 (*c* 0.011, MeOH), was also isolated as a white amorphous powder. The molecular formula $C_{21}H_{22}O_4$ was established by HRESMS (found: 339.1589; calcd: 339.15963 for $[M+H]^+$) and once again, the UV spectrum consisted of a single band at λ_{max}^{MeOH} 280 nm. With only two isochrone phenolic functions at δ 8.13 in the ^1H NMR (acetone-d_6), compound **3** differed from ericanone by 20 amu less ($-H_4O$). Indeed, the comparative analysis of the ^{13}C NMR of both compounds (Table 1) pointed out in **3** an upfield shift for the keto group (C-5: δ 196.2, $\Delta\delta$ −15.2). This function was deduced to be α,β-conjugated with an electron-donating element similar to a 6,7-dehydroericanone-type structure. This change was supported by the pronounced downfield shift of two previous C sp^3 converted into Csp^2, a *O*-bonded quaternary C atom (C-7: δ 180.0, $\Delta\delta$ +111.9) and a tertiary nucleus (C-6: δ 105.0, $\Delta\delta$ +53.1) whose proton was shifted downfield to δ 5.23. In addition, the significant downfield shift in the aliphatic region for the permanent oxy C-3 (δ 80.0, $\Delta\delta$ +11.9) suggested to include this carbon in an ether linkage with enhanced attractive effect and conclusively to ensure ring closure with C-7 to lead to a 3,7-anhydroericanone-type structure. Indeed, the ^1H NMR data relative to the remaining three aliphatic protons (H-4a, H-4b and H-3) of the resulting disubstituted γ-dihydropyranone ascertained these findings: H-4a (δ 2.43, dd, J = 16.9 and 12.4 Hz), H-4b (δ 2.32, dd, J = 16.9 and 3.7 Hz) and H-3 (δ 4.30, ddt, J = 12.4, 8.1 and 3.7 Hz). Likely flavanones — a typical example of 2-substituted 2,3-dihydropyran-4-one — the expressed coupling value $J_{3,4a}$ = 12.4 Hz clearly suggested a *trans*-diaxial relationship between the two related nuclei. Consequently, the absolute configuration at C-3 was established as *S* by comparing the optical rotation with literature data of flavanones.[3,4] Hence, the new structure issued from the above results was (2*S*)-2,6-bis(*p*-hydroxyphenethyl)-2,3-dihydropyran-4-one or (3*S*)-3,7-anhydro-6,7-dehydroericanone. The detailed analysis of the ^1H–^{13}C HMBC spectrum supported this result and allowed unambiguous assignments for all the ^1H and ^{13}C NMR resonances and especially the discrimination of the aromatic rings through their quaternary C atoms. Indeed, C-1′ (δ 133.2) was involved in ^3J correlations with H-2 (δ 2.06 and 1.91) and H-3′,5′ (δ 6.71) while C-1″ (δ 132.4) showed ^3J interactions with H-8a (δ 2.56) and H-3″,5″ (δ 6.69). In parallel, C-4′ (δ 156.7) correlated with H-2′,6′ (δ 7.03) whereas C-4″ (δ 156.9) exhibited ^3J cross-peaks with H-2″,6″ (δ 6.99). Finally, further ^3J correlations displayed by the latter aromatic protons, H-2″,6″ with C-9 (δ 32.9) and H-2′,6′ with C-1 (δ 31.3), allowed to locate each ring on the appropriate end of the partly cyclized C_9 chain. Biogenetically, the close relationship between this metabolite and ericanone (**1**) seems to suggest a mutual 3-hydroxy-5,7-diketo-type precursor involved in two distinct pathways to lead to each one: a one-step simple reductive process of the 7-carbonyl generating ericanone in contrast with a more extended route based on 6,7-enolisation followed by cylization consecutive to 3,7-dehydration resulting in 3,7-anhydro-6,7-dehydroericanone. In spite of a detailed phytochemical investigation of *E. cinerea*, attempts at isolating the appropriate intermediate still stay unsuccessful.

Compound **4** was also detected towards flavonol monoglycosides on silica gel TLC but with a higher mobility than **2**. Also isolated as a white amorphous powder, it exhibited a UV spectrum consistent with one band at λ_{max}^{MeOH} 280 nm, and the molecular formula $C_{27}H_{32}O_9$ given by HRESMS (found: 523.1937; calcd: 523.19441 for $[M+Na]^+$). Examination of the ^1H and ^{13}C NMR data (Table 1) rapidly revealed that **4** was likely **2**, a glucoside but derived from aglycone **3**. Owing to the downfield shift caused by the ether linkage on the aglycone substituted position, attachment of the β-D-glucopyranosyl moiety (H-1‴: δ 4.83, d, J = 7.4 Hz; C-1‴: δ 102.6) was deduced to be at C-4′ (δ 157.7, $\Delta\delta$ +1.0). This result was simultaneously confirmed by the downfield shifts assumed by the *ortho* positions for both, protons (H-3′,5′: δ 7.13, $\Delta\delta$ +0.42) and C nuclei (C-3′,5′: δ 118.0, $\Delta\delta$ +1.7) and by the ^3J correlation displayed by H-1‴ (δ 4.83) with C-4′ (δ 157.7) in the HMBC spectrum virtually identical to that of **3**. Consequently, the newly reported compound **4** was established as (3*S*)-3,7-anhydro-3,4-dehydroericanone 4′-β-D-glucopyranoside.

Only nine 1,9-diarylnonanoids — mainly as open nonan-1-one chain ,[5–7] rarely as cyclized chain,[8,9] but never as glycosides — were previously restricted to the genus *Myristica* (*M. ceylanica*, *M. dactyloides*, *M. fragrans* and *M. malabarica*) belonging to the Myristicaceae, an archaic plant family when compared to the recent Ericaceae. Conversely, with a C_2 unit less the homologues 1,7-diarylheptanoids are considerably more numerous. In 2002, the last available review devoted to this group listed a total of 192 natural products.[10] This number grew to 267 during the past decade.[11–43] Occuring as aglycones and/or glycosides of either 3-*O*-, 3,5-di-*O*- or 1,3,5-tri-*O*-substituted linear, cyclic biphenyl or diphenyl

ether-type structure, 1,7-diarylheptanoids are mainly reported from rhizome and stem bark when compared to other structural tissues like heartwood, aerial parts, seeds and fruits. They are widespread over thirteen plant families, namely Aceraceae, Betulaceae, Burceraceae, Cassuarinaceae, Dioscoreacea, Fabaceae, Juglandaceae, Musaceae, Myricaceae, Pinaceae, Rhoipteleaceae, Viscaceae and Zingiberaceae. Despite a very large separating interval on the plant evolution scale, both families Zingiberaceae (Monocotyledon) and Betulaceae (Dicotyledon) produce the highest numbers of these products. Similarly to their lower homologues, 1,9-diarylnonanoids are also elaborated by the most distant Myristicaceae (Paleoplants) and Ericaceae (Dicotyledon). Is that reflecting the translation of perhaps a primitive and dominant character of the former, involved in the biosynthesis of such secondary metabolites in the latter?

Acknowledgements

The authors are grateful to Région Limousin for supporting a part of this work and to Prof. M. Botineau (Université de Limoges) for discussion about plant evolution.

References and notes

1. Chulia, A. J.; Bennini, B.; Kaouadji, M.; Allais, D. P.; Delage, C. *J. Nat. Prod.* **1995**, *58*, 560–563.
2. Isolation procedure: Fresh aerial parts of *E. cinerea* (4.5 kg) collected at the flowering stage on massif des Monédières (Corrèze, France) were extracted with Me_2CO (20 L) by percolation at room temperature for a week. Evaporation of the solvent afforded a crude extract (310 g) which was divided into four portions. Each of them was suspended in distilled water (450 mL) and then extracted successively with petrol (5×250 mL), CH_2Cl_2 (7×250 mL), EtOAc (7×250 mL). Evaporation of the solvents under vacuum resulted in a petrol extract (84 g), a CH_2Cl_2 extract (4 g), a EtOAc extract (50 g) and an aqueous residue (178 g). The whole EtOAc extract was divided into 8 portions. Each one was subjected to LH-20 CC packed in MeOH to give 4 major fractions. After the usual work-up, the resulting ahead fraction (4.9 g) was suspended in distilled water (250 mL) and extracted with EtOAc (6×150 mL) to afford organic soluble part (2.7 g) and aqueous residue (2 g). The organic portion was then treated by polyamide MPLC eluted by the mixture MeC_6H_5–Me_2CO–MeOH (from 80:10:10 to 60:20:20) to give impure aglycones **1** and **3** in the ahead fractions and impure glucosides **2** and **4** in the last fractions. The final purification step for each compound was performed by semi-prep. reverse phase HPLC (μBondapack) eluted by the mixture MeOH–H_2O (from 80:20 to 70:30) to yield aglycones **1** (48 mg) and **3** (36 mg) and the mixture MeOH–H_2O (from 45:55 to 55:45) to afford glucosides **2** (250 mg) and **4** (23 mg).
3. Shirataki, Y.; Komatsu, M.; Yokoe, I.; Manaka, A. *Chem. Pharm. Bull.* **1981**, *29*, 3033–3036.
4. Lo, W.-L.; Chang, F.-R.; Hsieh, T.-J.; Wu, Y.-C. *Phytochemistry* **2002**, *60*, 839–845.
5. Purushothaman, K. K.; Sarada, A.; Connolly, J. D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 587–588.
6. Cooray, N. F.; Jansz, E. R.; Wimalasena, S.; Wijesekera, T. P.; Nair, B. M. *Phytochemistry* **1987**, *26*, 3369–3371.
7. Kumar, N. S.; Herath, H. M. T. B.; Karunaratne, V. *Phytochemistry* **1988**, *27*, 465–468.
8. Herath, H. M. T. B.; Priyadarshani, A. M. A.; Jamie, J. *Nat. Prod. Lett.* **1998**, *12*, 91–95.
9. Herath, H. M. T. B.; Padmasiri, W. *Nat. Prod. Lett.* **1999**, *14*, 141–146.
10. Claeson, P.; Claeson, U. P.; Tuchinda, P.; Reutrakul, V. Occurrence, Structure and Bioactivity of 1,7-Diarylheptanoids In *Studies in Natural Products Chemistry*; Atta-ur-Rahman, Ed.; Elsevier Science B.V: Amsterdam, 2002; Vol. 26, pp 881–906 and references cited therein.
11. Chen, J.; Gonzalez-Laredo, R. F.; Karchesy, J. J. *Phytochemistry* **2000**, *53*, 971–973.
12. Ali, M. S.; Tezuka, Y.; Awale, S.; Banskota, A. H.; Kadota, S. *J. Nat. Prod.* **2001**, *64*, 289–293.
13. Ali, M. S.; Tezuka, Y.; Banskota, A. H.; Kadota, S. *J. Nat. Prod.* **2001**, *64*, 491–496.
14. He, W.; Wei, X.; Li, L.; Li, Y.; Guo, S.; Guo, B. *Zhiwu Xuebao* **2001**, *43*, 757–759.
15. Matsuda, H.; Morikawa, T.; Tao, J.; Ueda, K.; Yoshikawa, M. *Chem. Pharm. Bull.* **2002**, *50*, 208–215.
16. Jang, D. S.; Park, E. J.; Hawthorne, M. E.; Vigo, J. S.; Graham, J. G.; Cabieses, F.; Santarsireo, B. D.; Mesecar, A. D.; Fong, H. H.; Mehta, R. G., et al *J. Agric. Food. Chem.* **2002**, *50*, 6330–6334.
17. Kadota, S.; Tezuka, Y.; Prasain, J. K.; Ali, M. S.; Banskota, A. H. *Curr. Top. Med. Chem.* **2003**, *3*, 203–225.
18. Kamnaing, P.; Tsopmo, A.; Tanifum, E. A.; Tchuendem, M. H. K.; Tane, P.; Ayafor, J. F.; Sterner, O.; Rattendi, D.; Iwu, M. M.; Schuster, B., et al *J. Nat. Prod.* **2003**, *66*, 364–367.
19. Ma, J.; Jin, X.; Yang, L.; Liu, Z.-L. *Phytochemistry* **2004**, *65*, 1137–1143.
20. Kang, H.-M.; Son, K.-H.; Yang, D. C.; Han, D.-C.; Kim, J. H.; Baek, N.-I.; Kwon, B.-M. *Nat. Prod. Res.* **2004**, *18*, 295–299.
21. Mohamad, H.; Lajis, N. H.; Abas, F.; Ali, A. M.; Sukari, M. A.; Kikuzaki, H.; Nakatani, N. *J. Nat. Prod.* **2005**, *68*, 285–288.
22. Moon, S.-S.; Cho, S.-C.; Lee, J.-Y. *Bull. Korean Chem. Soc.* **2005**, *26*, 447–450.
23. Kim, H. J.; Kim, K. H.; Yeom, S. H.; Kim, M. K.; Shim, J. G.; Lim, H. W.; Lee, M. W. *Chin. Chem. Lett.* **2005**, *16*, 1337–1340.
24. Kang, H.-M.; Kim, J. R.; Jeomg, T.-S.; Choi, S.-G.; Ryu, Y.-H.; Oh, G. T.; Baek, N.-I.; Kwon, B.-M. *Nat. Prod. Res.* **2006**, *20*, 37–41.
25. Giang, P. M.; Son, P. T.; Matsunami, K.; Otsuka, H. *Chem. Pharm. Bull.* **2005**, *53*, 1335–1337.
26. Giang, P. M.; Son, P. T.; Matsunami, K.; Otsuka, H. *Chem. Pharm. Bull.* **2006**, *54*, 139–140.
27. Akiyama, K.; Kikuzaki, H.; Aoki, T.; Okuda, A.; Lajis, N. H.; Nakatani, N. *J. Nat. Prod.* **2006**, *69*, 1637–1640.
28. Mshvildadze, V.; Legault, J.; Lavoie, S.; Gauthier, C.; Pichette, A. *Phytochemistry* **2007**, *68*, 2531–2536.
29. Zhou, C. X.; Zhang, X. Y.; Dong, X. W.; Tao, Q. F.; Dou, H.; Zhang, R. P.; K, X.; Li, X. K.; Chen, C. X.; Zeng, S., et al *Chin. Chem. Lett.* **2007**, *18*, 1243–1246.
30. Zhao, Y.; Tao, Q. F.; Zhang, R. P.; Zhou, C. X.; Dou, H.; Shi, S. Y.; Xiao, Y. C.; Sun, L. L.; Zeng, S.; Huang, K. X., et al *Chin. Chem. Lett.* **2007**, *18*, 1247–1249.
31. An, N.; Zou, Z.-M.; Tian, Z.; Luo, X.-Z.; Yang, S.-L.; Xu, L.-Z. *Fitoterapia* **2008**, *79*, 27–31.
32. Tao, Q. F.; Xu, Y.; Lam, R. Y. Y.; Schneider, B.; Dou, H.; Leung, P. S.; Shi, S. Y.; Zhou, C. X.; Yang, L. X.; Zhang, R. P., et al *J. Nat. Prod.* **2008**, *71*, 12–17.
33. Sun, Y.; Matsubara, H.; Kitanaka, S.; Yasukawa, K. *Helv. Chim. Acta* **2008**, *91*, 118–123.
34. Wang, D.-Y.; Liu, E.-G. *Nat. Prod. Res.* **2008**, *22*, 292–295 (Part B).
35. Wang, L.-Y.; Zhang, M.; Zhang, C.-F.; Wang, Z.-T. *Biochem. Syst. Ecol.* **2008**, *36*, 476–480.
36. Suksamram, A.; Ponglikitmongkol, M.; Wongkrajang, K.; Chindaduang, A.; Kittidanairak, S.; Jankam, A.; Yingyongnarongkul, B.-E.; Kittipanumat, N.; Chokchaisiri, R.; Khetkam, P., et al *Bioorg. Med. Chem.* **2008**, *16*, 6891–6902.
37. Wang, J.; Dong, S.; Wang, Y.; Lu, Q.; Zhong, H.; Du, G.; Zhang, L.; Cheng, Y. *Bioorg. Med. Chem.* **2008**, *16*, 8510–8515.
38. Kaewamatawong, R.; Boonchoong, P.; Teerawatasuk, N. *Phytochem. Lett.* **2009**, *2*, 19–21.
39. An, N.; Zhang, H.-W.; Xu, L.-Z.; Yang, S.-L.; Zou, Z.-M. *Food Chem.* **2009**, *119*, 513–517.
40. Li, Y.-Y.; Chou, G.-X.; Wang, Z.-T. *Helv. Chim. Acta* **2010**, *93*, 382–388.
41. Wohlmuth, H.; Deseo, M. A.; Brushett, D. J.; Thompson, D. R.; MacFarlane, G.; Stevenson, L. M.; Leach, D. N. *J. Nat. Prod.* **2010**, *73*, 743–746.
42. Park, D.; Kim, H.; Jung, S. Y.; Yook, C.-S.; Jin, C.; Lee, Y. S. *Chem. Pharm. Bull.* **2010**, *58*, 238–241.
43. Zhao, L.; Qu, W.; Fu, J.-Q.; Liang, J.-Y. *Zhongguo Tianran Yaowu* **2010**, *8*, 241–243.