HETEROCYCLES, Vol. 75, No. 3, 2008, pp. 661 - 668. © The Japan Institute of Heterocyclic Chemistry
Received, 12th October, 2007, Accepted, 3rd December, 2007, Published online, 7th December, 2007. COM-07-11242

THREE NEW FURANOSESQUITERPENOIDS FROM *BOMBAX MALABARICUM* AND REVISED NMR ASSIGNMENT OF HIBISCONE C

Xiaohui Zhang, Shuwei Zhang, and Lijiang Xuan*

State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Shanghai Institute for Biological Sciences, Chinese Academy of Science, 555 Zuchongzhi Rd., Zhangjiang Hi-Tech Park, Shanghai, 201203, China
e-mail address: ljxuan@mail.shcnc.ac.cn

Abstact - Hibiscone C (**1**), and three new furanosesquiterpenoids, namely bombaside, bombaxone, and 7*β*-*O*-*β*-glucopyranosyl bombaxone (**2**-**4**), were isolated from the roots of *Bombax malabaricum*. Their structures were characterized by extensive 1D and 2D NMR spectroscopic analyses. The NMR assignment of hibiscone C was revised.

INTRODUCTION

Bombax malabaricum DC (syn. *Salmalia malabaricum* DC) (Bombacaceae)[1] is a medicinal tree distributed widely in tropical areas of China, India, Pakistan, and Vietnam. The reputation of the properties of demulcent, diuretic, restorative, aphrodisiac, and emetic[2-4] has been stimulating decades of phytochemical investigations, which resulted in reports about cadinane sesquiterpenoids,[2,4-6] a xanthone-C-glycoside,[7] an alkaloid,[8] flavonoids[9] and a polysaccharide[10] a triterpenoid[11] in this family. Hibiscone C was first isolated from *Gmelina arborea* (Verbenaceae),[12] and series of its analogs were reviewed in the early 1980's (genus *Hibiscus* from family Malvaceae).[13,14] On our continuous phytochemical study on *B. malabaricum*[15], hibiscone C (**1**), and three new furanosesquiterpenoids, named bombaside, bombaxone, and 7*β*-*O*-*β*-glucopyranosyl bombaxone (**2**-**4**) were isolated for the first time from family Bombacaceae. Herein, their NMR assignments were reported.

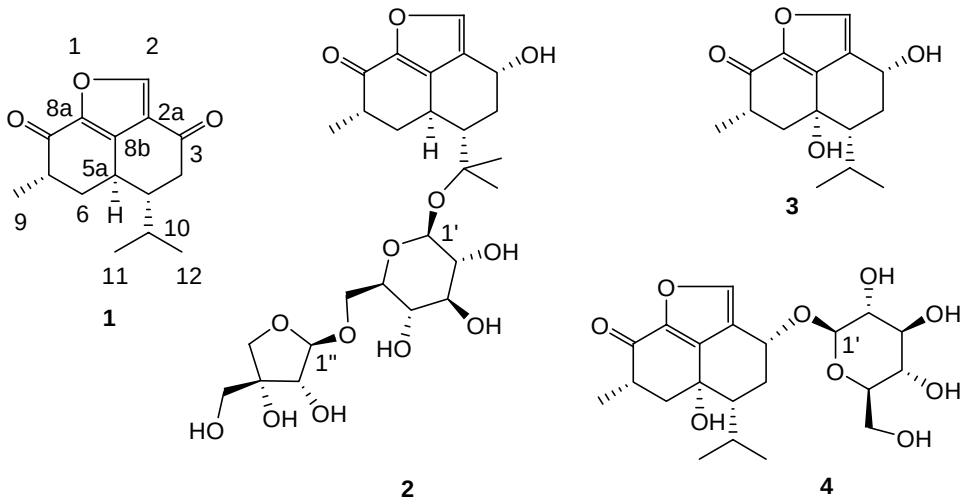

Figure 1. Structures of Compounds (**1**-**4**)

RESULTS AND DISCUSSION

The air-dried roots of *Bombax malabaricum* were extracted with H_2O/acetone (3:7). Separation and purification of this extract by repetitive chromatography led to the isolation and characterization of hibiscone C (**1**), and three new furanosesquiterpenoids, named bombaside, bombaxone, and 7*β*-O-*β*-glucopyranosyl bombaxone (**2**-**4**).

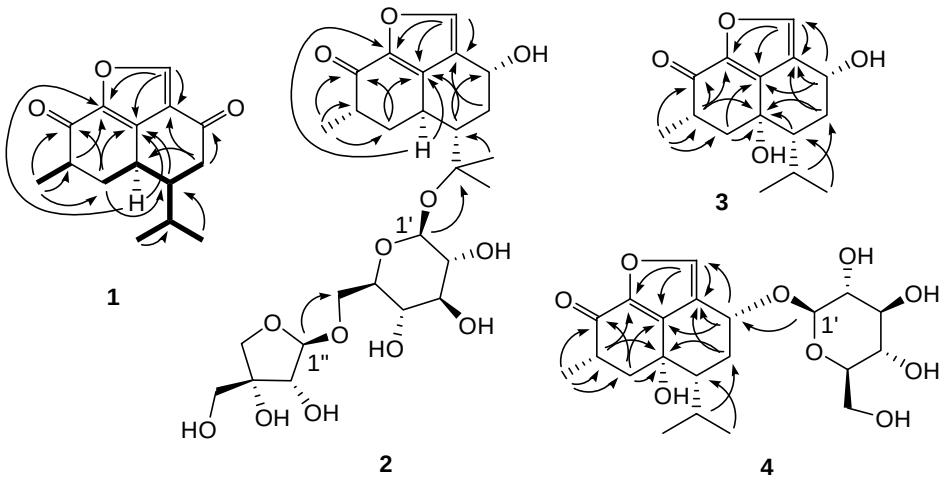

Figure 2. Key ^{1}H-^{1}H COSY (**—**) Correlations of Compound **1**, and Key HMBC Correlations (^{1}H → ^{13}C) of Compounds (**1**-**4**)

Compound **1** was isolated as a colorless amorphous powder. The ^{1}H NMR spectrum (Table 1) showed a singlet aromatic proton at δ_H 8.10 (1H, s), a CH_3-CH system [a methyl signal at δ_H 1.37 (*d*, *J* = 7.7 Hz)

Table 1. [1]H NMR Data of Compounds **1-4** (400 MHz)[a]

position	**1**[b]	**2**[c]	**3**[c]	**4**[d]
2	8.10 (*s*)	7.98 (*s*)	7.75 (*s*)	8.06 (*s*)
3		5.10 (*br s*)	4.93 (*d*, 4.2)	5.21 (*br s*)
4	2.61 (*dd*, 2.8, 16.8)	2.23 (*m*)	2.22 (*m*)	2.16 (*m*)
	2.35 (*dd*, 12.9, 16.8)	1.86 (*m*)	1.77 (*m*)[e]	
5	1.92 (*m*)	2.09 (*m*)	1.77 (*m*)[e]	1.75 (*dd*, 2.1, 10.7)
5a	3.05 (*td*, 4.6, 11.4)	3.17 (*td*, 4.3, 11.3)		
6	2.20 (*ddd*, 1.9, 4.5, 13.3)	2.62 (*dd*, 1.5, 13.6)	2.42 (*dd*, 1.4, 13.9)	2.50 (*d* 14.5)
	1.89 (*m*)	2.24 (*m*)	2.12 (*m*)	2.28 (*m*)
7	2.81 (*ddq*, 2.2, 4.3, 7.7)	2.74 (*m*)	2.68 (*m*)	2.91 (*m*)
9	1.37 (*d*, 7.7)	1.33 (*d*, 7.5)	1.50 (*d*, 7.9)	1.55 (*d*, 7.9)
10	2.05 (*d sept*, 2.8, 7.0)		2.28 (*m*)	2.25 (*m*)
11	1.01 (*d*, 7.0)	1.45 (*s*)	1.03 (*d*, 7.1)	1.05 (*d*, 6.1)
12	0.95 (*d*, 7.0)	1.42 (*s*)	0.96 (*d*, 7.1)	1.01 (*d*, 6.1)
1'		4.72 (*d*, 7.8)		4.77 (*d*, 7.8)
2'		3.28 (*t*, 8.6)		3.25 (*t*, 8.4)
3'		3.54 (*t*, 9.1)		3.57 (*m*)[e]
4'		3.44 (*t*, 9.1)		3.44 (*t*, 9.83)
5'		3.60 (*m*)		3.57 (*m*)[e]
6'		4.01 (*d*, 10.2)[e]		4.02 (*dd*, 1.5, 12.1)
		3.73 (*t*, 6.0)		3.80 (*dd*, 6.0. 12.1)
1"		5.03 (*d*, 3.2)		
2"		3.94 (*d*, 3.2)		
4"		4.01 (*d*, 10.2)[e]		
		3.88 (*d*, 10.2)		
5"		3.68 (*m*)		

a) TMS was used as internal standard; δ_H in ppm, *J* values (Hz) are in parentheses. Assignments are based on HMQC and HMBC spectra. b) Recorded in acetone-d_6. c) Recorded in CD_3OD. d) Recorded in D_2O. e) Signals may be exchangable.

and a methine at 2.81 (*ddq*, *J* = 2.2, 4.3, 7.7 Hz)], an isopropyl side chain [two methyl signals at δ_H 0.95 (*d*, *J* = 7.0 Hz), 1.01 (*d*, *J* = 7.0 Hz) and a methine at δ_H 2.05 (*d septet*, *J* = 2.8, 7.0 Hz)], two methines [δ_H 1.92 (m) and 3.05 (*td*, *J* = 4.6, 11.4 Hz)], and two methenes [δ_H 2.61 (dd, *J* = 2.8, 16.8 Hz) and 2.35 (dd, *J* = 12.9, 16.8 Hz); 2.20 (*ddd*, *J* = 1.9, 4.5, 13.3 Hz) and 1.89 (*m*)]. In the [13]C NMR spectrum (Table 2), two ketones (δ_C 188.7 and 193.3), four aromatic carbon resonances (δ_C 123.2, 144.5, 144.8, and 147.7) and nine high-field carbon resonances supported the furanosesquiterpenoid architecture.[12] A molecular formula of $C_{15}H_{18}O_3$ (by HRESIMS) eventually lead the structure of compound **1** to hibiscone C. But [1]H-[1]H COSY and HMBC spectroscopic data (Figure 2) revised the reported NMR assignment[12] of hibiscone C (Tables 1 and 2). The methine (C-5) at δ_C 47.9 [instead of the methine (C-5a) at δ_C 30.0] was

connected to the isopropyl side chain, while the quaternary carbon (C-2a) at δ_C 123.2 [rather than the quaternary carbon (C-8b) at δ_C 144.8] was adjacent to the 3-ketone (δ_C 193.3).

The molecular formula of compound **2** was determined by HRESIMS as $C_{26}H_{38}O_{13}$. In the ^{1}H NMR spectrum (Table 1), the *gem*-dimethyl singlet signals (δ_H 1.45, 1.42) indicated C-10 in the isopropyl side chain has been derived. Further ^{1}H NMR assignments (Table 1) were facilitated by comparison with those of hibiscone B[13], in which another hydroxy group was placed at C-3. Two anomeric sugar signals ($\delta_{H/C}$ 4.72/99.1, 5.03/111.6) were observed. And the two sugar units were identified as glucose (Glc) and apiose (Api), by comparing NMR data with literature.[16] The *β*-configurations at the anomeric centers were assigned based on ^{1}H-^{1}H coupling constants (7.8 Hz for glucose, and 3.2 Hz for apiose). A HMBC experiment (Figure 2) attached the apiofuranose to C-6' of glucose, and glucopyranose to C-10. The relative configuration of **2** was suggesteded by NOESY correlations (Figure 3) of H-5 (δ_H 2.09, *m*) with H-3 (δ_H 5.10, *brs*); H-5a (δ_H 3.17, *dt*, *J* = 4.3, 11.3 Hz) with Me-9 (δ_H 1.33, *d*, *J* = 7.5 Hz), Me-11 (δ_H 1.45, *s*), and Me-12 (δ_H 1.42, *s*). Accordingly, the structure of bombaside (**2**) was identified as 12*β*-*O*-*β*-apiosyl-(1-6)-*O*-*β*-glucopyranosyl hibiscone B.

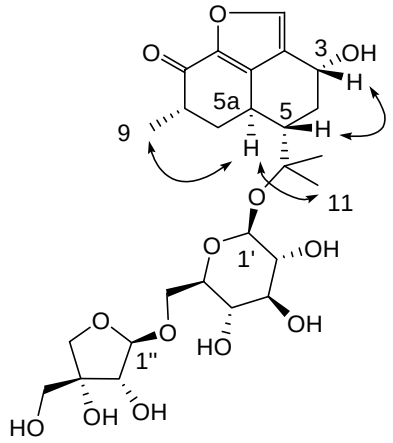

Figure 3. Key NOESY (↔) Correlations of Compound **2**

The molecular formula of compound **3** was determined by HRESIMS as $C_{15}H_{20}O_4$. When comparing the ^{1}H- and ^{13}C-NMR data (Tables 1 and 2) with those of the aglycone of **2**, it was evident that C-5a was oxygenated, instead of C-10. Compound **4** was assigned the elemental composition $C_{21}H_{30}O_9$, from analysis of HRESIMS. Analogous NMR shift of the aglycone (Tables 1 and 2) to those of compound **3** and the molecular formula indicated **4** a monoglycoside of **3**. Acid hydrolysis of **4** gave glucose (Glc) as the sugar moiety, as identified by co-TLC with an authentic sample. A ^{1}H-^{1}H coupling constant (*J* = 7.8

Hz) assigned the anomeric center as *β*-configuration. And the Glc unit was attached to C-3 of the aglycone on the basis of an HMBC correlation between the anomeric H-atoms at δ_H 4.77 [*d*, *J* = 7.8 Hz, H–C(1')] and C(3) at δ_C 70.6 (Figure 2). The relative configurations of **3** and **4** were assigned to be the same as that of **2** by comparing their CD spectra, in which all the three compounds showed positive Cotton effect in the ranges of 210-285 nm and negative Cotton effects in both ranges of 190-210 nm and 285-370 nm. Therefore, the structures of bombaxone (**3**), and 7*β*-*O*-*β*-glucopyranosyl bombaxone (**4**) were established as 10*β*-hydroxy hibiscone B and 7*β*-*O*-*β*-glucopyranosyl-10*β*-hydroxy hibiscone B, respectively.

Table 2. ^{13}C NMR Data of Compounds **1-4** (100 MHz, *δ* values)[a]

position	**1**[b]	**2**[c]	**3**[c]	**4**[d]		**2**[c]		**4**[d]
2	147.7 (*d*)	150.5 (*d*)	146.8 (*d*)	152.5 (*d*)	12-*O*-Glc[e]-1'	99.1 (*d*)	7-*O*-Glc[e]-1'	103.7 (*d*)
2a	123.2 (*s*)	127.8 (*s*)	126.8 (*s*)	125.0 (*s*)	2'	76.1 (*d*)	2'	75.7 (*d*)
3	193.3 (*s*)	62.8 (*d*)	60.4 (*d*)	70.6 (*d*)	3'	79.0 (*d*)	3'	78.6 (*d*)
4	40.0 (*t*)	37.7 (*t*)	29.7 (*t*)	27.5 (*t*)	4'	72.4 (*d*)	4'	72.4 (*d*)
5	47.9 (*d*)	46.1 (*d*)	45.7 (*d*)	47.2 (*d*)	5'	76.9 (*d*)	5'	78.5 (*d*)
5a	30.0 (*d*)	33.7 (*d*)	69.0 (*s*)	71.3 (*s*)	6'	70.5 (*t*)	6'	63.5 (*t*)
6	35.9 (*t*)	41.6 (*t*)	42.6 (*t*)	43.8 (*t*)	6'-*O*-Api[e]-1"	111.6 (*d*)		
7	42.7 (*d*)	45.0 (*d*)	43.5 (*d*)	44.7 (*d*)	2"	79.3 (*d*)		
8	188.7 (*s*)	196.0 (*s*)	188.9 (*s*)	195.6 (*s*)	3"	82.0 (*s*)		
8a	144.5 (*s*)	145.8 (*s*)	144.2 (*s*)	145.8 (*s*)	4"	76.0 (*t*)		
8b	144.8 (*s*)	149.6 (*s*)	142.9 (*s*)	146.7 (*s*)	5"	66.4 (*t*)		
9	16.4 (*q*)	17.7 (*q*)	20.8 (*q*)	22.5 (*q*)				
10	26.6 (*d*)	84.4 (*s*)	25.9 (*d*)	27.2 (*d*)				
11	20.8 (*q*)	28.1 (*q*)	23.9 (*q*)	25.8 (*q*)				
12	15.4 (*q*)	25.0 (*q*)	18.8 (*q*)	20.5 (*q*)				

a) TMS was used as internal standard. Assignments are based on HMQC and HMBC spectra. b) Recorded in acetone-d_6. c) Recorded in CD_3OD. d) Recorded in D_2O. e) Glc: *β*-glucopyranosyl; Api: *β*-apiosyl.

Families Bombacaceae and Malvaceae belong to the order Malvals. The close relationship between these two families has been confirmed by molecular data.[17,18,19] Our continuous phytochemical studies on *B. malabaricum*[15] afforded both cadinane sesquiterpenoids and cadinane-type furanosesquiterpenoids, which have also been reported for family Malvaceae.[13,14,20,21] Although both sesquiterpenoids share the same carbon-connection sequence according to the isoprene rule, no phytochemical investigation on a single plant other than on the genus *Hibiscus* reported the isolation of both cadinane sesquiterpenoids and furanosesquiterpenoids hitherto. Is this the evidence for the two genera (*Bombax* and *Hibiscus*) closer in

taxonomy, or only a coincidence for them? Further phytochemical exploration of *B. malabaricum* and other genera from the two families would be interesting and highlighted.

EXPERIMENTAL SECTION

General Experimental Procedures. CD spectra were obtained on a JASCO 810 spectrometer, and the UV and IR spectra were recorded on a Shimadzu UV-2450 and a Perkin-Elmer 577 spectrometer, respectively. The NMR spectra were taken in D_2O, CD_3OD, and acetone-d_6 on a Varian mercury NMR spectrometer operating at 400 MHz for ^1H and 100 MHz for ^{13}C. ESI mass spectra were recorded on a Bruker Esquire-3000 mass spectrometer. Column chromatography was carried out on Diaion HP-20 (Mitsubishi Chemical Industries Co., Ltd.), TSK gel Toyopearl HW-40F (30-60 μm; Toso Co., Ltd.), MCI gel CHP-20P (75-150 μm; Mitsubishi Chemical Industries Co., Ltd.), and Cosmosil 75 C_{18}-OPN (40-105 μm; Nacalai Tesque Inc.). TLC was performed on $HSGF_{254}$ silica gel plates (Yantai).

Plant Material. The roots of *Bombax malabaricum* were collected at Guangxi, China, in August 2005, and identified by Prof. Heming Yang. A voucher specimen (No. BM001) has been deposited in the herbarium of Shanghai Institute of Materia Medica, Chinese Academy of Sciences, People's Republic of China.

Extraction and Isolation. The air-dried and powdered roots (8 kg) were extracted with H_2O/acetone (3:7) at room temperature (15 L × 3). After concentration under a vacuum to remove the organic solvent, the suspended residue was removed by centrifugation. The aqueous solution was submitted to Diaion HP-20 gel column chromatography and eluted with MeOH-H_2O (0%, 25%, 50%, 100%). The water sugar-containing fraction was discarded, and the three other fractions were subjected repeatedly to column chromatography on MCI gel CHP-20P, Cosmosil 75 C_{18}-OPN, and Toyopearl HW-40F. Fraction B (25% MeOH eluate) yielded compounds **2** (12.2 mg), and **4** (14.8 mg). Fraction D (100% MeOH eluate) afforded compounds **1** (15.2 mg) and **3** (6.3 mg).

Hibiscone C (1). Colorless amorphous powder; UV (MeOH) λ_{max} (log ε) 222 (4.34), 264 (4.17) nm; $[\alpha]_D^{20}$ -19° (c 0.86, $CHCl_3$); CD (MeOH) λ_{max} ($\Delta\varepsilon$) 192 (-4.06), 200 (-24.75), 227 (22.8), 238 (4.33), 257 (10.64), 321 (-3.89) nm; IR (KBr) ν_{max} 3117, 1690, 1672, 1600, 1525 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive-ion mode) *m/z* 269 $[M+Na]^+$and *m/z* 247 $[M+H]^+$; HRESIMS *m/z* 247.1328 $[M+H]^+$ (calcd for $C_{15}H_{19}O_3$, 247.1334).

Bombaside (2). Colorless amorphous powder; UV (H_2O) λ_{max} (log ε) 281 (4.49); CD (H_2O) λ_{max} ($\Delta\varepsilon$) 192.3 (-8.00), 278 (19.09), 308 (-13.08) nm; IR (KBr) ν_{max} 3425, 2925, 1660, 1530, 1070, 870 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive-ion mode) *m/z* 581 $[M+Na]^+$; ESIMS (negative-ion mode) *m/z* 603 $[M+CO_2H]^-$; HRESIMS *m/z* 581.2178 $[M+Na]^+$ (calcd for $C_{26}H_{38}O_{13}Na$, 581.2210).

Bombaxone (3). Colorless amorphous powder; UV (MeOH) λ_{max} (log ε) 281 (4.77) nm; CD (MeOH) λ_{max} ($\Delta\varepsilon$) 198 (-55.86), 217 (25.02), 254 (7.08), 276 (29.92), 317 (-27.04) nm; IR (KBr) ν_{max} 3417, 1660, 1440, cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive-ion mode) *m/z* 287 $[M+Na]^+$; ESIMS (negative-ion mode) *m/z* 263 $[M-H]^-$; HRESIMS *m/z* 287.1255 $[M+Na]^+$ (calcd for $C_{15}H_{20}O_4Na$, 287.1259).

7*β*-*O*-*β*-Glucopyranosyl Bombaxone (4). Colorless amorphous powder; UV (H_2O) λ_{max} (log ε) 282 (4.74) nm; CD (H_2O) λ_{max} ($\Delta\varepsilon$) 201 (-38.30), 238 (11.69), 255 (8.50), 277 (24.01), 311.2 (-31.24) nm; IR (KBr) ν_{max} 3417, 2935, 1662, 1438, 1338, 1076, 1038, 989, 962 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 2; ESIMS (positive-ion mode) *m/z* 449 $[M+Na]^+$; ESIMS (negative-ion mode) *m/z* 471 $[M+CO_2H]^-$; HRESIMS *m/z* 449.1774 $[M+Na]^+$ (calcd for $C_{21}H_{30}O_9Na$, 449.1788).

Acidic Hydrolysis of Compound 4. Compound **4** (1.5 mg) was dissolved in 5% HCl aqueous solution, and then heated in a boiling water bath for 5 h. After cooling, the reaction mixtures were neutralized with 10% aqueous Na_2CO_3 and glucose was identified by co-TLC with an authentic glucose sample (EtOAc-MeOH-H_2O-HOAc, 13: 3: 3: 4; R_f 0.46).

REFERENCES

1. Editorial Committee for Flora of the Chinese Academy of Science, 'Flora of China'; Science Press: Beijing, 1984; Vol. 49, Chapter 2, pp. 106-108.
2. M. V. B. Reddy, M. K. R. Reddy, D. Gunasekar, M. M. Murthy, C. Caux, and B. Bodo, *Chem. Pharm. Bull.*, 2003, **51**, 458.
3. A. A. Shahat, R. A. Hassan, N. M. Nazif, S. V. Miert, L. Pieters, F. M. Hammuda, and A. J. Vlietinck, *Planta Med.*, 2003, **69**, 1068.
4. R. P. Sood, K. A. Suri, O. P. Suri, K. L. Dhar, and C. K. Atal, *Phytochemistry*, 1982, **21**, 2125.
5. A. V. B. Sankaram, N. S. Reddy, and J. N. Shoolery, *Phytochemistry*, 1981, **20**, 1877.
6. L. S. Puckhaber and R. D. Stipanovic, *J. Nat. Prod.*, 2001, **64**, 260.

7. S. Faizi, S. Zikr-ur-Rehman, M. Ali, and A. Naz, *Magn. Reson. Chem.*, 2006, **44**, 838.
8. T. M. Zennie and J. M. Cassady, *J. Nat. Prod.*, 1990, **53**, 1611.
9. G. S. Niranjam and P. C. Gupta, *Planta Med.,* 1973, **24**, 19.
10. G. D. Agrawal, S. A. I. Rizvi, P. C. Gupta, and J. D. Tewari, *Planta Med.,* 1972, **21**, 293.
11. Y. You, N. Nam, Y. Kim, K. Bae, and B. Ahn, *Phytother. Res.*, 2003, **17**, 341.
12. K. C. Joshi, P. Singh, R. T. Pardasani, A. Pelter, R. S. Ward, and R. Reinhardt, *Tetrahedron Lett.*, 1978, 4719.
13. M. A. Ferreira, T. J. King, S. Ali, and R. H. Thomson, *J. Chem. Soc., Perkin Trans. 1*, 1980, 249.
14. S. Ali, P. Singh, and R. H. Thomsom, *J. Chem. Soc., Perkin Trans. 1*, 1980, 257.
15. X. Zhang, H. Zhu, S. Zhang, Q. Yu, and L. Xuan, *J. Nat. Prod.*, 2007, **70**, 1526.
16. S. Zhang and L. Xuan, *Helv. Chim. Acta*, 2006, **89**, 1241.
17. W. S. Alverson, K. G. Karol, D. A. Baum, M. W. Chase, S. M. Swensen, R. McCourt, and K. J. Sytsma, *Am. J. Bot.*, 1998, **85**, 876.
18. M. F. Fay, C. Bayer, W. S. Alverson, A. Y. D. Bruijn, and M. Chase, *Taxon*, 1998, **47**, 43.
19. W. S. Alverson, B. A. Whitlock, R. Nyffeler, C. Bayer, and D. A. Baum, *Am. J. Bot.*, 1999, **86**, 1474.
20. A. A. Bell, R. D. Stipanovic, D. H. O'Brien, and P. A. Fryxell, *Phytochemistry*, 1978, **17**, 1297.
21. M. Essenberg, P. B. Grover, and E. C. Cover, *Phytochemistry*, 1990, **29**, 2107.