Iridoids from *Pentas lanceolata*

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From the aerial parts of *Pentas lanceolata*, belonging to the family Rubiaceae, a series of iridoid glucosides was isolated by preparative HPLC. Seven iridoid glucosides were identified. Besides asperuloside and asperulosidic acid, characteristic iridoids for Rubiaceae, five new iridoids were isolated, namely, tudoside (**1**), 13*R-epi*-gaertneroside (**2**), 13*R-epi*-epoxygaertneroside (**3**), and a mixture of *E*-uenfoside (**4**) and *Z*-uenfoside (**5**). Further, it was shown that the compound reported as citrifolinin B (**6**) is in fact the same as tudoside and should be revised. Also, the configuration of the previously reported iridoids gaertneroside and epoxygaertneroside has been elucidated.

Pentas lanceolata (Forssk.) Deflers is a common plant, originating from tropical East Africa to Arabia. The most widely used names are "Egyptian Star Cluster" or "Pentas". As a decorative plant, it has been spread all over the tropics and subtropics. The flowers can be white, pink, purple, or red. This species belongs to the family Rubiaceae, which is by far the largest family in the flowering plant order Gentianales, with about 10 700 species in 637 genera.[1]

The systematics of the Rubiaceae are complex, and the division in subfamilies and tribes is the subject of much debate. Many approaches have been used to shed light on this question, e.g., through pollen morphology,[2] leaf fatty acid composition,[1] by DNA sequences from the chloroplast *trnL-F* region[3] and also by DNA sequences from the chloroplast atpB-rbcL intergene region,[4] the rbcL cpDNA[5] and the rps16 intron (cpDNA),[6] or aluminum accumulation.[7]

In 1897, Schumann placed *Pentas* in the Oldenlandieae, subfamily Cinchonoideae.[8] In 1958, it was placed in Hedyotideae, subfamily Rubioideae by Verdcourt.[9] This has been maintained until now. The genus *Pentas* comprises about 40 species, widely distributed throughout tropical Africa from West Africa and Somalia to Angola and Natal (South Africa), also in tropical Arabia, Madagascar, and the Comoro Islands.[2,10] Phytochemical investigations on members of this genus are sparse.

In an investigation of 35 rubiaceous plants, the iridoid asperuloside (**1**) was detected in *P. lanceolata*,[11] and more recently a phytochemical analysis of *P. lanceolata* roots was published.[12] In this same study, β-stigmasterol and the anthraquinones damnacanthol, rubiadin-1-methyl ether, rubiadin, 1,3-dihydroxy-2-methoxymethyl-9,10-anthraquinone (lucidin-ω-methyl ether), damnacanthol-3-*O*-methyl ether, and rubiadin-1-methyl ether-3-*O*-β-primeveroside were isolated. Also, roots from the species *P. bussei* K. Krause and *P. parvifolia* Hiern were investigated.[12] Furthermore, studies on *P. longiflora* Oliver,[13–17] and *P. zanzibarica* (Klotsch) Vatke[18] have been published. In a recent study, an ethanolic extract from flowers of *P. lanceolata* administered orally to rats showed a positive effect on wound healing.[19] The active constituents, however, are still unknown.

Table 1. ^{1}H NMR Spectroscopic Data for the Iridoid Glucoside **1** (400 MHz, CD_3OD; *J* Values in Parentheses)

position	**1a**	**1b**	**1** (acetone-d_6)
1	5.90 s	5.88 s	5.73 s
3	7.52 d (1.6)	7.50 d (1.6)	7.31 d (1.9)
5	3.33 m	3.33 m	3.3 m
6	3.53 dd (2.7)	3.51 d (2.7)	3.39 d (3.0)
7	3.83 d (2.7)	3.81 d (2.7)	3.95 d (2.6)
9	2.29 d (8.6)	2.27 d (8.6)	2.43 dd (8.2; 1.3)
10	4.40 s	4.29 s	9.59 s
COOMe	3.73 s [3H]	3.73 s [3H]	3.71 s [3H]
1′	4.56 d (8.0)	4.56 d (8.0)	4.58 d (7.7)
2′	3.12 m		3.15 dd (8.0; 8.0)
3′	3.33 m		3.34 dd (8.0; 8.0)
4′	3.27 m		
5′	3.33 m		3.59 m
6a′	3.87 dd (12.1; 2.2)	3.86 dd (12.1; 2.2)	3.85 dd (12.1; 2.0)
6b′	3.65 dd (12.1; 5.6)	3.65 dd (12.1; 5.6)	3.59 m

In the present study, we isolated and identified five new iridoids (**1**–**5**), from the aerial parts of *P. lanceolata*, and their structural characterization is described herein

Using a ^{1}H NMR-based screening procedure, specific signals indicating the presence of unknown iridoids were observed for an extract of the aerial parts of *P. lanceolata*. This urged us to proceed with the isolation and identification of these new iridoids. A methanolic extract was prepared which was subsequently divided between water and CH_2Cl_2. The water phase was then monitored by HPLC. By applying a H_2O–MeOH gradient, separation of the iridoids was obtained. The individual iridoids were isolated by preparative HPLC. The resultant fractions were purified by preparative TLC, yielding the compounds. The known compounds asperuloside and asperulosidic acid were identified by comparison with literature data.[20,21] These compounds have been found to be characteristic for the subfamily Rubioideae.[11]

The spectroscopic data (see Tables 1 and 3) of the major iridoid present were found to coincide with those attributed to the pair of epimers from citrifolinin B (**6**), reported by Sang et al. in 2001.[22] Citrifolinin B was also reported as a constituent of *Morinda citrifolia* fruits, by data comparison with the reported data for this compound.[23] However, the previous interpretation of the spectra,

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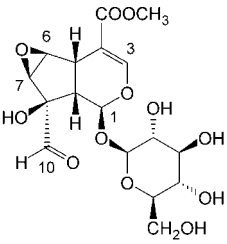
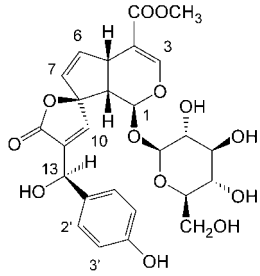


1 Tudoside



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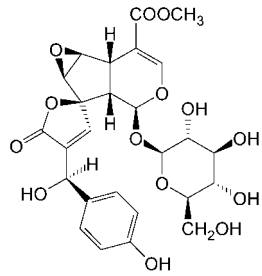

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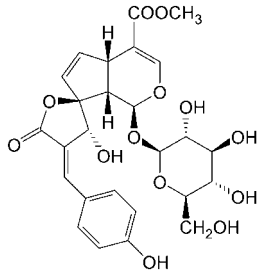

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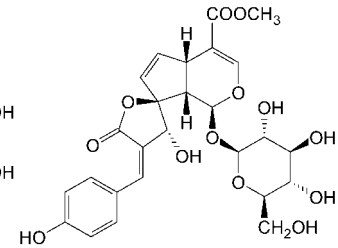

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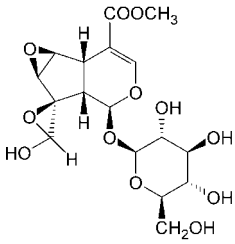
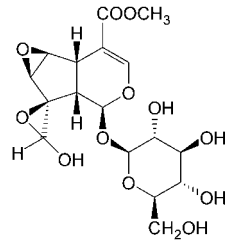


epimer a



epimer b

6 Citrifolinin B

suggesting the presence of an epoxyl group between C-8 and C-10, appears incorrect. The correct structure of the compound is that of the isomeric aldehyde **1**, which was suggested as an intermediate by Sang et al.[22] In MeOH solution, the aldehyde gives rise to the formation of two enantiomeric hemiacetals (**1a** and **1b**, see Figure 1) which give different spectra, explaining the observed spectra. When the MeOH solution was dried and the spectrum was subsequently recorded in acetone-d_6, the spectrum of the pure aldehyde was obtained (**1**). In water solution, the compound forms a hydrate (**1c**), which also gives a single spectrum. We suggest the name tudoside for this compound, invalidating the name citrifolinin B. In a previous paper, also citrifolinin A and various other iridoids reported from *Morinda* were revised.[24]

Accurate mass measurements of compound **2** obtained by ESI-QTOF MS yielded a parent mass at *m*/*z* 571.1456 in positive ionization mode, corresponding to the sodium adduct of a compound with a molecular formula of $C_{26}H_{28}O_{13}$ (+5.9 ppm from the calcd mass of $C_{26}H_{28}O_{13}Na^+$, *m*/*z* 571.1422). The complete interpretation of the ^{1}H and ^{13}C NMR spectra by 2D-NMR (HMBC, HMQC, COSY, and NOESY) yielded a structure identical to the previously reported gaertneroside.[25] However, some differences existed in the NMR spectra. In the ^{1}H NMR spectra, upfield shifts relative to gaertneroside were seen for H-1 and H-9, while downfield shifts were seen for H-10 and H-7. In the structure for gaertneroside, the stereochemistry at C-13 has not been defined, and the only way of explaining these differences observed in the spectra is to suppose an opposite stereochemistry at this asymmetric carbon. The configuration on C-13 can now be assigned on the following assumptions: The hydroxyl at C-13 forms a hydrogen bond with the carbonyl at C-14. When C-13 has the *R* configuration, the phenolic ring will be located at the site of H-1 and H-9. Due to the shielding anisotropic effect of the phenolic ring, these hydrogens will experience an upfield shift. When C-13 has the *S* configuration the phenolic ring will be located at the site of H-7. In this way, we attributed the 13*S* configuration to gaertneroside and the 13*R* configuration to compound **2**, which has been named 13*R*-*epi*-gaertneroside. The different configuration at C-13 was also expressed in different $[\alpha]_D$ values. For gaertneroside, a specific rotation of +24.8 was reported. For **2**, a value of −153 was recorded in the present investigation.

For compound **3**, an exact mass of *m*/*z* 587.1392 was measured, corresponding (+3.6 ppm) to the sodium adduct of a compound with a molecular formula of $C_{26}H_{28}O_{14}$ (calcd mass for $C_{26}H_{28}O_{14}Na^+$, *m*/*z* 587.1371). In this case, the complete interpretation of the ^{1}H and ^{13}C NMR spectra by 2D-NMR (HMBC, HMQC, COSY, and NOESY) yielded a structure identical to that of epoxygaertneroside.[25] Similar differences as for gaertneroside were seen in the NMR spectra and also in the measured optical rotations. Thus, the specific rotation reported for epoxygaertneroside was +1. For compound **3**, we measured an $[\alpha]_D$ value of −229. In this way, compound **3** was identified as 13*R*-*epi*-epoxygaertneroside, while the 13*S* configuration was attributed to epoxygaertneroside.

Compounds **4** and **5** were obtained as a mixture in a 6:4 ratio, as was evident from the ^{1}H NMR spectrum. An exact mass at *m*/*z* 571.1432 ($[M + Na]^+$) was measured, indicating a molecular formula of $C_{26}H_{28}O_{13}$ (calcd for $C_{26}H_{28}O_{13}Na^+$, *m*/*z* 571.1422). Thus, these compounds were isomeric with gaertneroside. All signals in both the ^{1}H and ^{13}C NMR spectra could be assigned to the individual compounds by interpretation of the two-dimensional spectra, and the complete structures could be derived as **4** and **5**, respectively. Compounds **4** and **5** are *E* and *Z* isomers, about the C-12–C-13 double bond. The configuration of the double bond was assigned from signals in the NOESY spectrum: H-13 from **4** only showed a correlation with H-2′/H-6′, while H-13 from **5** showed correlations with both H-2′/H-6′ and H-10. The configuration at C-10 of both compounds was deduced from the interaction between H-10 and H-1. For these new natural products, we propose the names *E*-uenfoside (**4**) and *Z*-uenfoside (**5**). The 6,7-epoxy derivative from *E*-uenfoside is citrifolinoside A, which has been isolated from *Morinda citrifolia*.[22]

The iridoids encountered in *P. lanceolata* are typical for the family Rubiaceae, but the spirolactone functionality found in most of the iridoids reported here is rare; within the family Rubiaceae, similar structures have only been found for plants in the genus *Morinda*. The genera *Pentas* and *Morinda* both belong to the subfamily Rubioideae, but *Pentas* belongs to the tribe Hedyotideae, while *Morinda* belongs to the tribe Morindeae. In this way, they would not seem to be very closely related, but the chemical similarities are remarkable.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer model 343 digital polarimeter. NMR spectra were recorded on a JEOL Eclipse$^+$ 400 spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane (TMS) using the residual solvent signal as the internal standard. For all NMR experiments, standard pulse sequences from the JEOL Delta Software were applied. The HMBC spectra were optimized for long-range coupling constants of 8 Hz. High-

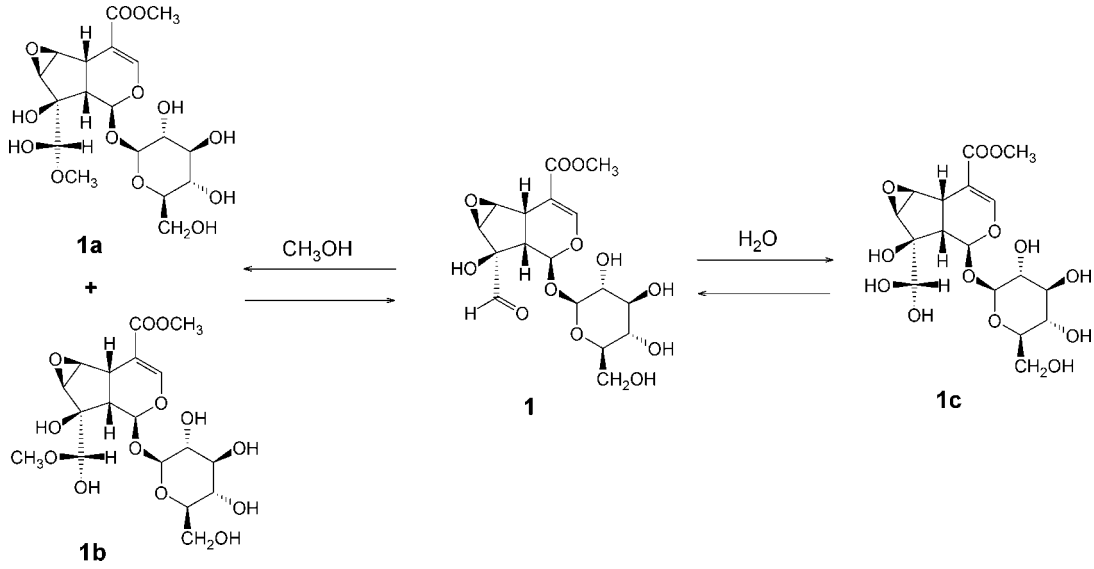


Figure 1. Tudoside (**1**): in MeOH solution, it exists as an epimeric mixture of the hemiacetals (**1a** and **1b**), while, in H_2O, it is converted to a hydrate (**1c**).

Table 2. ^{1}H NMR Spectroscopic Data for the Iridoid Glucosides **2**–**5** (400 MHz, CD_3OD; *J* Values in Parentheses)

position	2	3	4	5
1	5.34 d (3.7)	5.33 d (1.4)	5.20 d (6.2)	5.45 d (5.6)
3	7.47 d (1.5)	7.55 d (1.6)	7.46 d (1.9)	7.49 d (1.6)
5	3.88 m	3.45 d (8.1)	3.90 m	3.85 m
6	6.45 dd (5.8; 2.6)	3.42 m	6.09 dd (5.8; 2.5)	5.87 dd (5.6; 2.4)
7	5.46 dd (5.5; 1.8)	4.02 d (2.4)	6.45 dd (5.8; 2.3)	6.38 dd (5.8; 2.3)
9	2.99 dd (8.1; 3.6)	2.77 dd (8.4; 1.1)	2.55 dd (7.0; 6.2)	2.77 dd (7.4; 5.8)
10	7.24 d (1.5)	7.03 d (1.6)	5.57 d (1.1)	5.29 d (1.9)
13	5.39 d (1.1)	5.39 d (1.4)	7.59 s	7.06 d (1.9)
2′, 6′	7.20 d (8.4) [2H]	7.21 d (8.3)	7.65 d (8.6) [2H]	7.97 d (8.9) [2H]
3′, 5′	6.76 d (8.8) [2H]	6.76 d (8.6)	6.84 d (8.9) [2H]	6.78 d (8.9) [2H]
1″	4.64 d (8.0)	4.53 d (7.8)	4.61 d (8.1)	4.74 d (7.8)
2″	3.21 dd (9.2; 8.0)	3.12 dd (8.9; 8.0)	2.71 dd (8.9; 8.0)	3.14 dd (9.6; 8.2)
3″	3.34 m	3.35 m	3.34 m	3.3
4″	3.27 m	3.30 m	3.3	3.3
5″		3.21 m	3.3	3.3
6a″		3.85 dd (12.0; 2.0)	3.85 m	3.85
6b″	3.63	3.70 m	3.70 m	3.70
Me	3.73 s [3H]	3.76 s [3H]	3.74 s [3H]	3.73 s [3H]

resolution mass spectra were recorded on a quadrupole-time-of-flight (QTOF) Ultima V4.00.00 mass spectrometer (Waters) equipped with an electrospray ionization (ESI) source and a separate lock mass spray inlet. Leucine enkaphalin (Sigma) dissolved in 50% acetonitrile at a concentration of 0.5 μg/mL was used as the lock mass (calcd *m/z* [M + H]$^+$ 556.2767). Samples were dissolved in 50% MeOH acidified with 0.1% formic acid, filtered over a 0.2 μm PTFE filter and directly injected into the mass spectrometer. To enable correct accurate mass calculation, compounds were dissolved to a concentration resulting in a signal intensity equal to that of the lock mass. Accurate masses were confirmed by reanalysis of the samples on a QSTAR Pulsar i (Applied Biosystems), under similar conditions, using external calibration. For HPLC, the apparatus (LC-10VP) consisted of two Shimadzu pumps (LC-10A), a Rheodyne injector (7725i), a degassing device (DGU-12A), a controller (SCL-10AVP), and a Shimadzu (SPD-M10AVP) photodiode array detector. The column was a Merck RP-18 Select B column (150 × 4.6 mm, 5 μm). Analytical thin-layer chromatography (TLC) was performed on 250 μm thickness Merck Si gel 60 F254 aluminum plates. For preparative TLC, homemade plates were used (Merck Si gel 60 PF254, Merck, Darmstadt, Germany).

Plant Material. The aerial parts from *Pentas lanceolata* were collected in Campos dos Goytacazes in the state of Rio de Janeiro, Brazil (coordinates: 21.45.0 S and 41.19.4 W). The material was identified by Drs. W. N. J. van Ursem, Botanical Garden, Delft University of Technology, The Netherlands, where a herbarium specimen has been deposited under the voucher number 1999GR06004. The material was air-dried and processed after milling.

Extraction and Isolation. The plant material (209.3 g) was extracted with 1700 mL of MeOH. After filtration, the extraction was repeated once more. The combined layers were dried under a vacuum. The residue (44.74 g) was divided between H_2O and CH_2Cl_2 (300 mL each). After separation, the H_2O layer was extracted two times with 200 mL of CH_2Cl_2. The combined CH_2Cl_2 layers were then once more extracted with 100 mL of H_2O. The combined H_2O layers were dried by lyophilization. The residue was redissolved in H_2O and was submitted to semipreparative HPLC, injecting 200 μL each time. For HPLC, a gradient of MeOH in H_2O was used. The optimum separation was obtained by a linear gradient from 0% MeOH to 60% MeOH over 60 min.

The peaks from the chromatographic system were collected and subsequently dried under a vacuum. The fractions were monitored on TLC (eluent $CHCl_3$/MeOH = 4:1, or ethylacetate/toluene/ethanol = 4:1:1). Individual iridoids were purified by preparative TLC ($CHCl_3$/MeOH = 90:10) after washing with $CHCl_3$/MeOH = 50:50). Asperuloside (3.5 mg) and asperulosidic acid (2.1 mg) were obtained from fraction 9 (t_R 22–24 min). Fractions 11 (t_R 25–28 min) and 12 (t_R 28–30 min) yielded **1** (8.0 mg) and **3** (1.6 mg), fraction 16 (t_R 35–37 min) yielded **2** (4.7 mg), and fraction 18 (t_R 39–41 min) yielded a mixture of **4** and **5** (1.0 mg).

Tudoside (1): viscous oil; $[\alpha]_D^{20}$ −172.5 (*c* 0.030, MeOH); ^{1}H NMR, Table 1; ^{13}C NMR, Table 3; HREIMS *m/z* 473.1291 (calcd for $C_{18}H_{26}O_{13}Na^+$, 473.1265).

Table 3. ^{13}C NMR Spectroscopic Data for the Iridoid Glucosides **1–5** (100 MHz, CD_3OD)

carbon	**1a**	**1b**	**1c** (D_2O)	**2**	**3**	**4**	**5**
1	94.6	94.0	93.4	93.8	92.8	94.3	94.8
3	154.7	154.4	153.9	152.2	153.9	152.6	152.8
4	107.4	107.3	106.0	111.4	108.0	110.4	110.4
5	33.7	33.5	32.1	39.9	33.0	41.0	40.5
6	60.8	60.5	60.2	141.0	59.2	129.5	129.9
7	58.7	58.0	58.3	130.2	57.8	141.9	141.3
8	82.1	82.4	81.6	97.9	92.6	101.0	99.0
9	46.8	46.8	45.2	50.6	43.6	51.0	49.9
10	98.4	98.4	98.7	150.6	148.1	69.5	73.4
11	168.7	168.6	169.0	137.9	140.5	124.0	124.9
12				172.5	171.7	173.6	169.3
13				69.5	69.6	143.9	143.3
14				168.4	168.0	168.6	169.3
1′				133.3	132.4	125.6	126.6
2′, 6′				129.2	129.3	134.9	135.0
3′, 5′				116.2	116.3	117.9	116.4
4′				158.4	158.6	164.1	161.8
1′	100.1	99.9	98.7	99.8	99.6	99.7	100.3
2′	74.6	74.6	72.7	74.5	74.4	74.2	74.6
3′	77.9	77.9	75.7	77.8	77.8	77.7	77.8
4′	71.6	71.6	69.7	71.4	71.3	71.3	71.4
5′	78.3	78.2	76.4	78.5	78.4	78.5	78.4
6′	62.8	62.8	60.9	62.6	62.5	62.6	62.5
COOMe	51.8	51.8	52.1	51.9	51.9	52.0	52.0
OCD_3	54.2[a]	54.7[a]					

[a] Position of signals determined from HMBC spectrum.

13*R-epi*-Gaertneroside (2): viscous oil; $[\alpha]_D^{20}$ −153.1 (*c* 0.095, MeOH); ^1H NMR, Table 2; ^{13}C NMR, Table 3; HR-ESI-MS *m/z* 571.1456 (calcd for $C_{26}H_{28}O_{13}Na^+$, 571.1422).

13*R-epi*-Epoxygaertneroside (3): viscous oil; $[\alpha]_D^{20}$ −228.8 (*c* 0.032, MeOH); ^1H NMR, Table 2; ^{13}C NMR, Table 3; HR-ESI-MS *m/z* 587.1392 (calcd for $C_{26}H_{28}O_{14}Na^+$, 587.1371).

***E*-Uenfoside (4), *Z*-Uenfoside (5):** viscous oil; $[\alpha]_D^{20}$ −185.4 (*c* 0.034, MeOH); ^1H NMR, Table 2; ^{13}C NMR, Table 3; HR-ESI-MS *m/z* 571.1432 (calcd for $C_{26}H_{28}O_{13}Na^+$, 571.1422).

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Note Added in Proof: Recently a paper was published by Syamsurizal et al. (in Indonesian), in which by using a modified Mosher's method the absolute configurations of C-13 in gaertneroside and epoxygaertneroside were determined to be 13*S*. This confirms our results. Syamsurizal; Tamura, S.; Murakami, N. *Bull. Soc. Nat. Prod. Chem.* (*Indonesia*) **2006**, *6*, 62–66.

References and Notes

(1) Mongrand, S.; Badoc, A.; Patouille, B.; Lacomblez, C.; Chavent, M.; Bessoule, J.-J. *Phytochemistry* **2005**, *66*, 549–559.
(2) Dessein, S.; Scheltens, A.; Huysmans, S.; Robbrecht, E.; Smets, E. *Rev. Palaeobot. Palynol.* **2000**, *112*, 189–205.
(3) Rova, J. H. E.; Delprete, P. G.; Andersson, L.; Albert, V. A. *Am. J. Bot.* **2002**, *89*, 145–159.
(4) Ehrendorfer, F.; Manen, J. F.; Natali, A. *Plant Syst. Evol.* **1994**, *190*, 245–248.
(5) Bremer, B.; Thulin, M. *Plant Syst. Ecol.* **1998**, *211*, 71–92.
(6) Andersson, L.; Rova, J. H. E. *Plant Syst. Evol.* **1999**, *214*, 161–186.
(7) Jansen, S.; Dessein, S.; Piesschaert, F.; Robbrecht, E.; Smets, E. *Ann. Bot.* **2000**, *85*, 91–101.
(8) Schumann, K. In *Die Naturlichen Pflanzenfamilien*; Engler, A., Prantl, K., Eds.; Engelmann: Leipzig, Germany, 1897; Vol. 4, pp 1–56.
(9) Verdcourt, B. *Bull. Jard. Bot. État* **1958**, *28*, 209–290.
(10) Verdcourt, B. In *Flora of Tropical East Africa*; Polhill, R. M., Ed.; Crown Agents For Overseas Governments and Administrations; Whitefriars Press, Ltd.: London, 1976; pp 1–213.
(11) Inouye, H.; Takeda, Y.; Nishimura, H.; Kanomi, A.; Okuda, T.; Puff, C. *Phytochemistry* **1988**, *27*, 2591–2598.
(12) Bukuru, J. Isolation and Structural Elucidation of Natural Products from *Pentas bussei* K. Krause, *Pentas lanceolata* (Forssk.) Deflers and *Pentas parvifolia* Hiern (Rubiaceae). Ph.D. Thesis, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Ghent, Belgium, 2003.
(13) El-Hady, S. Isolation and Structural Elucidation of Natural Products from *Pentas longiflora* Oliver and *Gossypioides kirkii* (Mast.) J.B. Hutch. Ph.D. Thesis, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Ghent, Belgium, 1999.
(14) El Hady, S.; Bukuru, J.; Kesteleyn, B.; Van Puyvelde, L.; Van, T. N.; De Kimpe, N. *J. Nat. Prod.* **2002**, *65*, 1377–1379.
(15) Hari, L.; De Buyck, L. F.; De Pooter, H. L. *Phytochemistry* **1991**, *30*, 1726–1727.
(16) Van Puyvelde, L.; El Hady, S.; De Kimpe, N.; Feneau-Dupont, J.; Declercq, J.-P. *J. Nat. Prod.* **1998**, *61*, 1020–1021.
(17) De Kimpe, N.; Van Puyvelde, L.; Schripsema, J.; Erkelens, C.; Verpoorte, R. *Magn. Reson. Chem.* **1993**, *31*, 329–330.
(18) Kusamba, C.; Federici, F.; De Vicente, Y.; Galeffi, C. *Fitoterapia* **1993**, *64*, 18–22.
(19) Nayak, B. S.; Vinutha, B.; Geetha, B.; Sudha, B. *Fitoterapia* **2005**, *76*, 671–675.
(20) De Moura, V. M.; Dos Santos, D. P.; Santin, S. M. O.; De Carvalho, J. E.; Foglio, M. A. *Quim. Nova* **2006**, *29*, 452–455.
(21) Lee, J. H.; Ku, C. H.; Baek, N.-I.; Kim, S.-H.; Park, H. W.; Kim, D. K. *Arch. Pharm. Res.* **2004**, *27*, 40–43.
(22) Sang, S.; Cheng, X.; Zhu, N.; Stark, R. E.; Badmaev, V.; Ghai, G.; Rosen, R. T.; Ho, C.-T. *J. Agric. Food Chem.* **2001**, *49*, 4478–4481.
(23) Su, B.-N.; Pawlus, A. D.; Jung, H.-A.; Keller, W. J.; McLaughlin, J. L.; Kinghorn, A. D. *J. Nat. Prod.* **2005**, *68*, 592–595.
(24) Schripsema, J.; Caprini, G. P.; Dagnino, D. *Org. Lett.* **2006**, *8*, 5337–5340.
(25) Cimanga, K.; Hermans, N.; Apers, S.; Van Miert, S.; Van den Heuvel, H.; Claeys, M.; Pieters, L.; Vlietinck, A. *J. Nat. Prod.* **2003**, *66*, 97–102.

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