Unusual *p*-Coumarates from the Stems of *Vaccinium myrtillus*

by **Simona Hybelbauerová**[a])[b]), **Jan Sejbal**[†a]), **Martin Dračínský**[b]), **Iva Rudovská**[a]), and **Bohumír Koutek***[b])

[a]) Department of Organic and Nuclear Chemistry, Faculty of Science, Charles University, 12843 Prague 2, Czech Republic

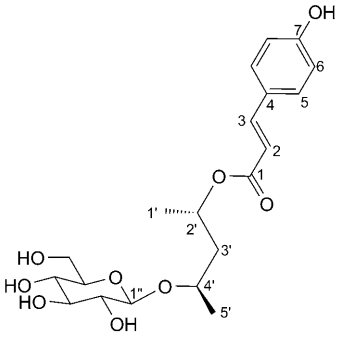
[b]) Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, 16610 Prague 6, Czech Republic (phone: +420-220183201; fax: +420-220183582; e-mail: koutek@uochb.cas.cz)

The two previously unreported esters **1** and **2** of pentane-2,4-diol and *p*-coumaric acid (= 3-(4-hydroxyphenyl)prop-2-enoic acid) along with 13 known compounds including 6 oleanane- and ursane-type triterpenoids were isolated from MeOH extracts of the stems of *Vaccinium myrtillus*. The structures of the new compounds were assigned as (2*S*,4*R*)-4-(β-D-glucopyranosyloxy)pentan-2-yl (2*E*)-*p*-coumarate (**1**) and its aglycone **2** on the basis of 1D- and 2D-NMR spectroscopic analyses of the isolated and synthesized compounds and molecular modelling experiments. This is the first report on the occurrence of a chiral pentane-2,4-diol linker between the phenol-derived acid and a glycoside part in natural products.

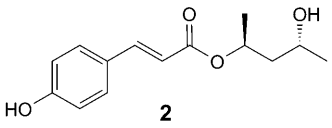
Introduction. – Bilberry (*Vaccinium myrtillus* L., Ericaceae), also known as European blueberry, has a long history in European folk medicine of being widely used in the form of fruits, tinctures, teas, and other herbal formulas for the treatment of diarrhoea, circulatory diseases, eye conditions, inflammation, and diabetes [1]. The health-promoting properties of bilberry fruits have been largely associated with phenol-type antioxidants [2], among which delphinidin, cyanidin, and petunidin glycosides [3], *p*-coumaric acid, ferulic acid, and quercetin derivatives [4][5] are the frequently found components. Recent reviews highlight the effects of berry (and other natural) phenols on some microbial infections [6] and different types of cancer [7].

Unlike the berries, the other vegetative organs have attracted much less attention. Although some phenol compounds identified in *Vaccinium* berries have also been found in the leaves, roots, and stems of the plant [8][9], most of the previous studies have been restricted to total-phenolic contents, as a result of which essential information on the authentic structure of the phytochemicals might have been lost [10]. Rather surprisingly, limited information is also available on the triterpenoid berry constituents [11] regardless of the well-documented ability of these compounds to influence various stages of tumor development [7][12]. Considering the growing interest in hydroxycinnamic acid derivatives [13] and other berry phytochemicals [7][14], we report here the isolation and identification of the two new pentane-2,4-diol-derived *p*-coumarates **1** and **2** along with 13 known compounds including 6 triterpenoids (*p*-coumaric acid = 3-(4-hydroxyphenyl)prop-2-enoic acid). The structure and configuration of the new compounds were determined by MS, 1D- and 2D-NMR, chemical, and molecular-modelling techniques.

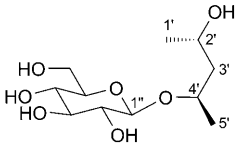
Results and Discussion. – Successive fractionation of the MeOH extract of *Vaccinium myrtillus* stems furnished 15 isolated compounds, including two new pentane-2,4-diol-derived *p*-coumarates **1**[1]) and **2**[1]) and 13 known compounds: pentane-2,4-diol-derived glucoside **3**[1]) [15], α-amyrin, β-amyrin, oleanolic acid, ursolic acid [16], glutinol [17], (3β,12β,13β)-3,12-dihydroxyursane-28,13β-lactone [18], monotropein [19], β-sitosterol [20], α-tocoferol [21], methyl α-D-fructofuranoside, methyl β-D-fructofuranoside, and methyl β-D-fructopyranoside [22], whose structures were elucidated by comparing their physical and NMR data with those reported in the literature.



1[1])



2



3[1])

Compound **1** was isolated as an oil, and its HR-ESI-MS established the molecular formula $C_{20}H_{28}O_9$ (435.16239 ($[M+Na]^+$); calc. 435.16255). The distinctive feature that differentiated compound **1** from the known compound **3** was the presence in the ^{1}H-NMR spectrum (*Table 1*) of a pair of mutually coupled *d*s at δ 7.59 and 6.29 and a vicinal coupling constant $J = 15.9$ Hz, indicative for the presence of a *trans*-substituted C=C bond, and the presence of an $AA'BB'$ spin system, corresponding to a *p*-disubstituted benzene derivative. In the ^{13}C-NMR spectrum (*Table 2*), a signal of a COO group at δ 169.0 was also present. The combination of 1D- and 2D-gHSQC and gHBMC spectra revealed that **1** was a (2*E*)-*p*-coumarate of **3**. An alkaline hydrolysis of **1** afforded a compound identical with **3**. To verify whether the configuration of **1** and **3** is the same as that previously reported for the pentane-2,4-diol-derived glucoside isolated from *Crescentia cujete* fruits [15], we synthesized the mono-D-glucosides of (2*R*,4*R*)- and (2*S*,4*S*)-pentane-2,4-diols, *i.e.*, **3a** and **3b**, respectively. A comparison of the NMR spectra of **3** with those of **3a** and **3b** (*Tables 1* and *2*) allowed us to exclude immediately configurations corresponding to the (2*R*,4*R*)- and (2*S*,4*S*)-isomers.

To distinguish between the (2′*R*,4′*S*)- and (2′*S*,4′*R*)-configuration of **1**, one hundred simulated annealings to 1000 K followed by cooling to 200 K were performed with these two molecules, after which all the structures were re-optimized and the geometries with the lowest energies were compared with ROESY data of compound **1**. The lowest-energy (2′*S*,4′*R*)-conformer was in perfect agreement with the structural information obtained from the ^{1}H-NMR and 2D-ROESY plot of compound **1**. In the

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*

Table 1. *The ^{1}H-NMR Data* (500 MHz, CD_3OD) *of Compounds* **1**–**3**, **3a**, *and* **3b**[1]). δ in ppm; J in Hz.

	1	**2**	**3**	**3a**[a])	**3b**[b])
H–C(2)	6.29 (*d*, *J* = 15.9)	6.30 (*d*, *J* = 15.6)			
H–C(3)	7.59 (*d*, *J* = 15.9)	7.59 (*d*, *J* = 16.0)			
H–C(5)	7.43–7.47 (*m*)	7.43–7.47 (*m*)			
H–C(6)	6.79–6.83 (*m*)	6.78–6.82 (*m*)			
Me(1′)	1.31 (*d*, *J* = 6.3)	1.31 (*d*, *J* = 6.4)	1.18 (*d*, *J* = 6.2)	1.15 (*d*, *J* = 6.4)	1.16 (*d*, *J* = 6.3)
H–C(2′)	5.17–5.23 (*m*)	5.14 (*sext.*, *J* = 6.4)	3.94 (*dqd*, *J* = 8.1, 6.3, 4.9)	4.03–4.09 (*m*)	4.05–4.11 (*m*)
H_a–C(3′)	1.66 (*ddd*, *J* = 13.9, 6.3, 5.2)	1.61 (*dt*, *J* = 13.6, 6.0)	1.49 (*ddd*, *J* = 13.9, 5.5, 4.9)	1.45 (*ddd*, *J* = 14.3, 9.9, 2.9)	1.49 (*ddd*, *J* = 14.4, 9.4, 3.6)
H_b–C(3′)	2.05 (*ddd*, *J* = 14.1, 7.9, 7.2)	1.92 (*dt*, *J* = 13.6, 6.8)	1.82 (*dt*, *J* = 13.9, 7.9)	1.59 (*ddd*, *J* = 14.3, 10.0, 2.7)	1.64 (*ddd*, *J* = 14.4, 8.9, 3.1)
H–C(4′)	4.00 (*dqd*, *J* = 7.9, 6.2, 5.2)	3.81–3.86 (*m*)	3.94 (*dqd*, *J* = 7.8, 6.1, 5.6)	4.03–4.09 (*m*)	3.99–4.05 (*m*)
Me(5′)	1.22 (*d*, *J* = 6.2)	1.20 (*d*, *J* = 6.4)	1.21 (*d*, *J* = 6.2)	1.19 (*d*, *J* = 6.3)	1.27 (*d*, *J* = 6.3)
H–C(1″)	4.32 (*d*, *J* = 7.8)		4.34 (*d*, *J* = 7.8)	4.32 (*d*, *J* = 7.9)	4.40 (*d*, 7.9)
H–C(2″)	3.15 (*dd*, *J* = 9.1, 7.8)		3.13 (*dd*, *J* = 9.2, 7.8)	3.16 (*dd*, *J* = 9.3, 7.9)	3.17 (*dd*, *J* = 9.1, 7.9)
H–C(3″)	3.35 (*t*, *J* = 8.8)		3.35 (*t*, *J* = 9.1)	3.37 (*dd*, *J* = 9.2, 8.9)	3.35–3.38 (*m*)
H–C(4″)	3.28–3.31 (*m*)		3.25–3.27 (*m*)	3.23 (*dd*, *J* = 9.7, 8.8)	3.26–3.32 (*m*)
H–C(5″)	3.25 (*ddd*, *J* = 9.5, 5.2, 2.1)		3.25–3.27 (*m*)	3.27–3.32 (*m*)	3.26–3.32 (*m*)
H_a–C(6″)	3.68 (*dd*, *J* = 11.9, 5.4)		3.65 (*dm*, *J* = 11.8)	3.61 (*dd*, *J* = 11.7, 6.8)	3.68 (*dd*, *J* = 11.9, 5.0)
H_b–C(6″)	3.86 (*dd*, *J* = 11.9, 2.2)		3.86 (*dd*, *J* = 11.8, 1.8)	3.89 (*dd*, *J* = 11.7, 2.3)	3.85 (*dd*, *J* = 11.9, 2.0)

[a]) (2*R*,4*R*)-Isomer. [b]) (2*S*,4*S*)-Isomer.

Table 2. *^{13}C-NMR Data* (125 MHz, CD_3OD) *of Compounds* **1**–**3**, **3a**, *and* **3b**. δ in ppm.

	1	**2**	**3**	**3a**[a])	**3b**[b])
C(1)	169.0	168.8			
CH(2)	115.8	115.7			
CH(3)	146.3	146.3			
C(4)	127.2	127.2			
CH(5)	131.1	131.1			
CH(6)	116.8	116.8			
C(7)	161.2	161.3			
Me(1′)	20.4	20.5	23.6	23.7	24.1
CH(2′)	70.2	70.0	66.8	64.7	64.8
CH_2(3′)	44.3	46.2	47.2	47.7	47.2
CH(4′)	72.9	65.7	74.2	72.6	75.5
Me(5′)	20.2	23.6	20.2	20.8	22.9
CH(1″)	102.1		102.2	102.3	104.6
CH(2″)	75.0		75.1	74.9	75.3
CH(3″)	78.1		78.0	78.0	78.0
CH(4″)	71.7		71.7	72.0	71.5
CH(5″)	77.7		77.9	77.7	77.7
CH_2(6″)	62.9		62.9	63.0	62.6

[a]) (2*R*,4*R*)-Isomer. [b]) (2*S*,4*S*)-Isomer.

ROESY plot, cross-peaks between H–C(1″) and H–C(4′) and between H–C(1″) and the Me(5′) clearly indicate that the conformation of C(1″)–O–C(4′)–C(3′) is *anti*-periplanar; in this conformation, the Me(5′) and H–C(4′) is in spatial proximity to H–C(1″). This configuration is also observed in the lowest-energy molecular model of (2′*S*,4′*R*)-**1** (*Fig.*). Furthermore, the high coupling constants of H_b–C(3′) with both

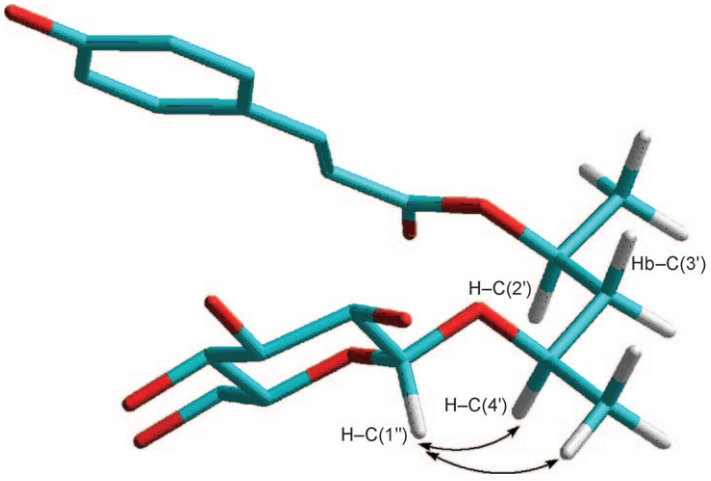


Figure. *Lowest-energy conformation of (2′*S*,4′*R*)-***1***. The H-atoms not important for the configuration determination are omitted for clarity, and only the important ROESY cross-peaks are displayed.

H–C(2′) and H–C(4′) (7.9 and 7.2 Hz, resp.) indicate that H_b–C(3′) is *anti*-periplanar to these two H-atoms. This is also observed in the molecular model. In the lowest-energy conformation of the (2′*R*,4′*S*)-**1** isomer, on the other hand, Me(5′) is quite distant from H–C(1″) (4.5 Å), and H_b–C(3′) is not *anti*-periplanar to either H–C(2′) or H–C(4′). Therefore, **1** was identified as a (2′*S*,4′*R*)-isomer, a new natural product with the same configuration as **3** and in agreement with the configuration previously reported for the pentane-2,4-diol-derived glucoside on the basis of an empirical 'glycosylation shift rule' [15]. We cannot exclude the possibility that **3** is formed by hydrolysis of its possible precursor **1**. However, we are quite convinced that this reaction is unlikely in view of our isolation procedures.

Compound **2** was assigned to have the molecular formula $C_{14}H_{18}O_4$ by HR-ESI-MS (*m*/*z* 273.10972 ($[M+Na]^+$; calc. 273.10973)). Due to the similarity of the ^{1}H- and ^{13}C-NMR data of **2** with those of **1**, the compound was easily recognized as the aglycone of **1**.

In conclusion, this study reveals that *i*) bilberry stems have the potential to offer a broad range of bioactive phytochemicals including *p*-hydroxycinnamates and pentacyclic triterpenoids; *ii*) the discovery of pentanediol-derived coumarates **1** and **2** in bilberry stems adds to our overall knowledge of the chemistry of *Vaccinium* berries and is indicative for further studies concerning the role of these compounds in the phenylpropane metabolism and organ-specific distribution in berries; *iii*) the estimate of the total content of **1** and **2** in dry MeOH extracts made from the NMR spectra of all (even impure) fractions could reach about 1.5 and 0.16% (*w*/*w*), respectively; it may be interesting to note that two unidentified *p*-coumaric acid derivatives have been previously reported [8] to dominate the phenolic acid profile in the stem extracts of *Vaccinium myrtillus*; and *iv*) bilberry stems accumulate a variety of terpenoids including α-amyrin, β-amyrin, ursolic acid, and oleanolic acid, *i.e.*, compounds with a well-known potential as drug candidates of low toxicity.

Considering that the content of phytochemicals in berries is affected by the degree of maturity at harvest, genetic dispositions, and environmental conditions, more detailed studies are necessary to support and/or extend the present results.

This work was supported by the *FRVS* Grant No. 41-202928 and the *Research Projects* Z4-055-0506 and MSM-002-1620857.

Experimental Part

1. *General*. The optically active diol standards, (–)-(2*R*,4*R*)- and (+)-(2*S*,4*S*)-pentane-2,4-diols, *p*-coumaric acid, and 10% Pd/C were from *Sigma–Aldrich*. The molecular sieves (*UOP*-type, 3 Å) were from *Fluka*. All the solvents were routinely distilled prior to use, CH_2Cl_2 was dried over CaH_2 and MeOH over Mg. TLC: commercial silica gel *60* F_{254} (*Merck*) plates. Column chromatography (CC): silica gel *60* (63–200 μm; *Merck*). Optical rotation: *Autopol-III* automatic polarimeter (*Rudolph Research Co.*, Flanders, New Jersey) with a measurement accuracy of $\pm 2°$ at 22°. UV Spectra: *Helios-Gamma* spectrophotometer (*Thermo Scientific*); λ_{max} (log ε) in nm. IR Spectra: *Nicolet-Avatar 370* FT-IR; $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-Avance-II-500* and/or *Varian-Unity-Inova-400* spectrometer; at 500.0 or 400.0 MHz for ^{1}H and 125.7 or 100.6 MHz for ^{13}C; in CD_3OD; δ in ppm rel. to the solvent signal (δ(H) 3.31 and δ(C) 49.00) as internal standard, *J* in Hz; assignments by a combination of COSY, HSQC, HMBC, and ROESY experiments. HR-ESI-MS: *LTQ-Orbitrap-XL* (*Thermo Fisher Scientific*) spectrometer; in *m*/*z*.

2. *Molecular Modelling.* Studies were performed with the *Hyperchem 8* (*Hypercube*) program. The *Polak-Ribiere* method for energy minimizations was used to convergence (less than 0.01 kJ mol^{-1} RMS force). The MM+ force field was used for all the computations. The general protocol for obtaining the lowest-energy conformers by simulated annealing was as follows: the optimized starting structure was subjected to a dynamic run – 0.2 ps heating from 300 to 1000 K, 0.4 ps equilibration, and 0.7 ps cooling to 200 K followed by energy minimization. Each subsequent run started from the previously minimized structure. A set of 100 structures was obtained for each compound in this way, from which the lowest-energy conformation was chosen for evaluation.

3. *Plant Material.* The aerial parts of *Vaccinium myrtillus* L. were collected from forests in the Czech-Moravian Highlands, Czech Republic, in August 2000. The authenticated voucher specimen (SHB1) has been deposited with the Department of Organic and Nuclear Chemistry, Charles University in Prague, Czech Republic.

4. *Extraction and Isolation.* The air-dried stems were cut into small pieces and extracted twice with MeOH (2 × 10 l) at r.t. for 3 months. The combined extracts were filtered and concentrated to obtain a residue of 135.6 g. The residue was re-dissolved in MeOH (100 ml), precipitated by adding H_2O (500 ml) and allowed to stand for 3 d to afford, after a standard workup, a nonsoluble residue *A* (18 g) and a filtrate *B* (116.4 g). The residue *A* was further partitioned between hot MeOH (50 ml), hexane (500 ml), and $CHCl_3$ (40 ml), and filtered to obtain a crude soluble fraction (5.46 g). The soluble fraction was subjected to CC (silica gel (SiO_2; 200 g), hexane, hexane/Et_2O 30:1 → 1:30, Et_2O, and MeOH): crude *Fractions* A_1–A_8. The latter were resubjected to CC (SiO_2, hexane with an increased amount of Et_2O) to afford, in the order of elution and after appropriate purification by TLC, the following previously reported compounds: vitamin E (9 mg), glutinol (4 mg), *β*-amyrin (808 mg), a mixture of *α*-amyrin and *β*-amyrin (24 mg), *β*-sitosterol (85 mg), (3*β*,12*β*,13*β*)-3,12-dihydroxyursane-28,13*β*-lactone (3 mg), oleanolic acid (120 mg), and ursolic acid (16 mg). The filtrate *B* (116.4 g) was partitioned between MeOH and Et_2O 1:1 (600 ml) to separate the MeOH/H_2O and Et_2O fractions. The former fraction was subjected to CC (SiO_2, $CHCl_3$/MeOH 15:1 → 1:5): one fraction containing monotropein (78 mg) in crystalline form. The Et_2O-soluble fraction was prefractionated by CC (reversed-phase SiO_2, MeOH/H_2O 1:3 → 3:1). One fraction (1.7 g, eluted with MeOH/H_2O 1:1) was further fractionated by CC ($CHCl_3$/MeOH 20:1 → 10:1) to afford, after an additional TLC purification, the new compounds **1** (68 mg) and **2** (8 mg).

The known compounds (2*R*,4*S*)-2-*O*-(*β*-D-glucopyranosyl)pentane-2,4-diol (=(1*R*,3*S*)-3-hydroxy-1-methylbutyl *β*-D-glucopyranoside; **3**; 36 mg; $[\alpha]_D^{20} = -39.6$ (*c* = 0.505, MeOH), [15]: –33 (*c* = 1.3, MeOH)), methyl *α*-D-fructofuranoside (65.3 mg), methyl *β*-D-fructofuranoside (24 mg), and methyl *β*-D-fructopyranoside (15 mg) were also isolated from these fractions.

*Data of (1*S*,3*R*)-3-(β-*D*-Glucopyranosyloxy)-1-methylbutyl (2*E*)-3-(4-Hydroxyphenyl)prop-2-enoate* (**1**): Oil. $[\alpha]_D^{20} = +2.3$ (*c* = 1.08, MeOH). UV (MeOH): 224, 312. IR (KBr): 3100–3600 (OH), 2972, 2930 (C–H), 1689 (ester C=O), 1632 (C=C), 1514, 1587, 1604 (Ar), 1445, 1274, 1170, 1077 (C–O). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (neg.): 411 ($[M-H]^-$), 163 ($[M-H-248]^-$), 145 ($[M-H-H_2O-248]^-$).

*Data of (1*S*,3*R*)-3-Hydroxy-1-methylbutyl (2*E*)-3-(4-Hydroxyphenyl)prop-2-enoate* (**2**): Oil. $[\alpha]_D^{20} = +5.3$ (*c* = 0.19, MeOH). UV (MeOH): 225, 311.5. IR (KBr): 3100–3600 (OH), 2963, 2927 (C–H), 1704 (ester C=O), 1632 (C=C), 1514, 1587, 1604 (Ar), 1450, 1261, 1170, 1102 (C–O). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. ESI-MS (neg.): 249 ($[M-H]^-$), 163 ($[M-H-86]^-$), 145 ($[M-H-H_2O-86]^-$), 119 ($[M-H-CO_2-86]^-$).

5. *Syntheses. (2*R*,4*R*)-2-*O*-(β-*D*-Glucopyranosyl)pentane-2,4-diol* (**3a**) was synthesized by a modified *Koenigs–Knorr* method [23] starting from a mono-benzylated (2*R*,4*R*)-pentane-2,4-diol and 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl bromide in the presence of molecular sieves (3 Å), $AgClO_4$, and Ag_2CO_3 in dry CH_2Cl_2. The product was successively deacetylated with MeONa and debenzylated by hydrogenolysis (Pd/C), and the fully deprotected crude product was purified by CC to afford **3a** (57.7 mg, 14% overall).

*(2*S*,4*S*)-2-*O*-(β-*D*-Glucopyranosyl)pentane-2,4-diol* (**3b**). As described for **3a**, but starting from a mono-benzylated (2*S*,4*S*)-pentane-2,4-diol: **3b** (77.3 mg, 15%).

6. *Alkaline Hydrolysis of* **1**. Under Ar, 0.56M MeONa (0.22 mmol, 0.40 ml) was added to a soln. of **1** (83 mg, 0.20 mmol) in dry MeOH (2 ml); and the mixture was stirred for 16 h. The soln. was neutralized with 1N HCl and extracted with AcOEt. The org. layer was dried (Na_2SO_4) and concentrated and the residue subjected to CC (SiO_2, $CHCl_3$/MeOH 10:1): **3** (36 mg, 72%), identical with the isolated compound **3**.

REFERENCES

[1] P. Morazzoni, E. Bombardelli, *Fitoterapia* **1996**, *67*, 3; M. E. Camire, 'Phytochemicals in the Vaccinium family: Bilberries, Blueberries and Cranberries', in 'Phytochemicals in Nutrition and Health', Eds. M. S. Meskin, W. R. Bidlack, A. J. Davies, and S. T. Omaye, CRC Press, Boca Raton, FL 2002, p. 289.

[2] S. Zafra-Stone, T. Yasmin, A. Bagchi, M. Chatterjee, J. A. Vinson, D. Bagchi, *Mol. Nutr. Food Res.* **2007**, *51*, 675; S. De Pascual-Teresa, M. T. Sanchez-Ballesta, *Phytochem. Rev.* **2008**, *7*, 281; N. P. Seeram, *J. Agric. Food Chem.* **2008**, *56*, 627.

[3] K. Ogawa, H. Sakakibara, R. Iwata, T. Ishii, T. Sato, T. Goda, K. Shimoi, S. Kumazawa, *J. Agric. Food Chem.* **2008**, *56*, 4457.

[4] S. Häkkinen, M. Heinonen, S. Kärenlampi, H. Mykkänen, J. Ruuskanen, R. Törrönen, *Food Res. Int.* **1999**, *32*, 345.

[5] S. Ehala, M. Vaher, M. Kaljurand, *J. Agric. Food Chem.* **2005**, *53*, 6484.

[6] R. Puuponen-Pimiä, L. Nohynek, H.-L. Alakomi, K.-M. Oksman-Caldentey, *Appl. Microbiol. Biotechnol.* **2005**, *67*, 8.

[7] B. B. Aggarwal, S. Shishodia, *Biochem. Pharmacol.* **2006**, *71*, 1397; G. D. Stoner, L. S. Wang, B. C. Casto, *Carcinogenesis* **2008**, *29*, 1665; S. Ramos, *Mol. Nutr. Food Res.* **2008**, *52*, 507.

[8] J. Witzell, R. Gref, T. Näsholm, *Biochem. Syst. Ecol.* **2003**, *21*, 115.

[9] C. S. Harris, A. J. Burt, A. Saleem, P. M. Le, L. C. Martineau, P. S. Haddad, S. A. L. Bennett, J. T. Arnason, *Phytochem. Anal.* **2007**, *18*, 161; K. Riihinen, L. Jaakola, S. Kärenlampi, A. Hohtola, *Food Chem.* **2008**, *110*, 156.

[10] M. P. Kähkönen, A. I. Hopia, M. Heinonen, *J. Agric. Food Chem.* **2001**, *49*, 4076.

[11] A. Szakiel, A. Mroczek, *Acta Biochim. Pol.* **2007**, *54*, 733.

[12] M. S. Butler, *Nat. Prod. Rep.* **2008**, *25*, 475; I. Bonaccorsi, F. Altieri, I. Sciamanna, E. Oricchio, C. Grillo, G. G. Contartese, E. M. Galati, *Cancer Lett.* **2008**, *263*, 130.

[13] M. N. Clifford, *J. Sci. Food Agric.* **2000**, *79*, 362; M. I. Choudhary, A. Begun, A. Abbaskhan, S. G. Musharraf, A. Ejaz, Atta-ur-Rahman, *Chem. Biodiversity* **2008**, *5*, 2676.

[14] A. Szajdek, E. J. Borowska, *Plant Foods Hum. Nutr.* **2008**, *63*, 147.

[15] T. Kaneko, K. Ohtani, R. Kasai, K. Yamasaki, N. M. Duc, *Phytochemistry* **1998**, *47*, 259.

[16] S. Mahato, A. P. Kundu, *Phytochemistry* **1994**, *37*, 1517.

[17] B. M. Fraga, M. Reina, J. G. Luis, M. L. Rodriguez, *Z. Naturforsch., C* **2003**, *58*, 621.

[18] A. V. Tkachev, A. Y. Denisov, Y. V. Gatilov, I. Y. Bagryanskaya, S. A. Shevtsov, T. V. Rybalova, *Tetrahedron* **1994**, *50*, 11459.

[19] C. Bergeron, A. Marston, S. Antus, R. Gauthier, K. Hostettmann, *Phytochemistry* **1998**, *49*, 233.

[20] W. De-Eknamkul, B. Potduang, *Phytochemistry* **2003**, *62*, 389.

[21] J. K. Baker, C. W. Myers, *Pharm. Res.* **1991**, *8*, 763.

[22] L. Johnson, D. L. Verraest, J. van Haveren, K. Hakala, J. A. Peters, H. van Dekkum, *Tetrahedron: Asymmetry* **1994**, *5*, 2475.

[23] D. Šaman, P. Kratina, J. Moravcová, M. Wimmerová, Z. Wimmer, *Collect. Czech. Chem. Commun.* **2006**, *71*, 1470.

Received April 23, 2009