85. Iridoid Glucosides with Free Radical Scavenging Properties from *Fagraea blumei*

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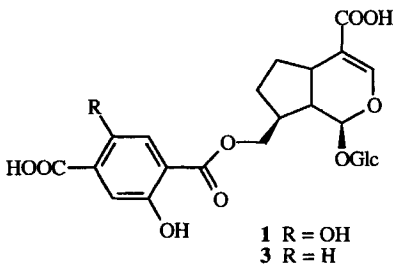
Four new iridoid glucosides **1**–**4**, named blumeosides A–D, were isolated from the methanolic stem-bark extract of *Fagraea blumei* G. DON. (Loganiaceae). They were accompanied by the benzyl-alcohol derivative di-*O*-methylcrenatin (**5**) and the flavone *C*-glucoside swertisin (**6**). The structures of **1**–**4** were established by spectroscopic methods, including FAB-MS, and ^{1}H- and ^{13}C-NMR, and by alkaline hydrolysis. Blumeosides A (**1**) and C (**3**) are 10-*O*-(2,5-dihydroxyterephthalo)adoxosidic acid and 10-*O*-(2-hydroxyterephthalo)adoxosidic acid, respectively. In blumeosides B (**4**) and D (**2**), both carboxylic groups of the terephthalic-acid moiety are esterified by adoxosidic-acid units. Blumeosides A–D (**1**–**4**) inhibited bleaching of crocin induced by alkoxyl radicals. Blumeosides A (**1**) and D (**2**) also demonstrated scavenging properties towards the 2,2-diphenyl-1-picryl-hydrazyl (DPPH) radical in TLC autographic and spectrophotometric assays.

1. Introduction. – Oxidation is well known to be a major cause of food and materials degradation. More recently, oxygen-reactive species, in particular free radicals have been recognized to be involved in several diseases including the two major causes of death: cancer and atherosclerosis. Aging also may be the sum of the deleterious free-radical reactions which occur continuously throughout cells and tissues [1]. In this context, natural antioxidants are receiving increasing attention. They can be an alternative to the use of synthetic compounds in food and pharmaceutical technology or serve as lead compounds for the development of new drugs with the prospect of improving the treatment of various disorders.

In the course of our search for new antioxidants in higher plants, we detected in the methanolic stem-bark extract of *Fagraea blumei* G. DON. (Loganiaceae) compounds which reduced the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical in a TLC autographic assay. These compounds exhibited strong yellow or blue fluorescence under UV light which prompted us to undertake their isolation. *F. blumei* is a tree growing in southeast Asia. To our knowledge, no previous investigation has been done on its constituents.

2. Results and Discussion. – Dried and powdered stem bark was extracted successively at room temperature with CH_2Cl_2 and MeOH. The methanolic extract was fractionated by a combination of gel filtration on *Sephadex LH-20*, centrifugal partition chromatography (CPC), medium-pressure liquid chromatography (MPLC), and reversed-phase HPLC to afford **1**–**6** (see *Exper. Part*).



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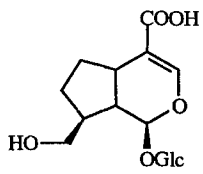
3 R = H



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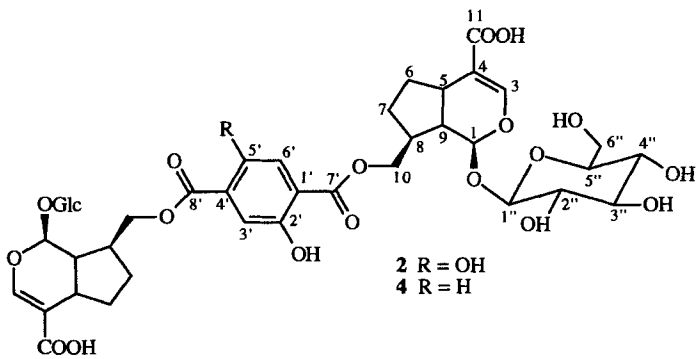

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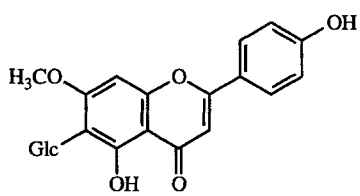
4 R = H



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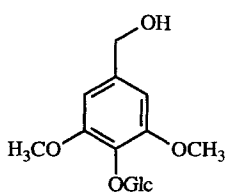

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Glc = β-D-glucopyranosyl

Compounds **5** [2] and **6** [3] [4] were identified as the flavone *C*-glucoside swertisin and the benzyl-alcohol derivative di-*O*-methylcrenatin, respectively, by their spectroscopic data (D/CI-MS, UV, ^{1}H- and ^{13}C-NMR). Compounds **1**–**4** proved to be new iridoid glucosides containing hydroxy- or dihydroxyterephthalic-acid moieties. Their structures were established as follows.

The fast atom bombardment (FAB) MS of **1** exhibited three main peaks at *m/z* 555 ([*M* – H]$^-$), 539, and 375 ([adoxosidic acid – H]$^-$), in accordance with the molecular formula $C_{24}H_{28}O_{15}$. The UV spectrum of **1** showed a maximum at 221 and a shoulder

around 250 nm. The ^{1}H- and ^{13}C-NMR data (see *Tables 1* and *2*[1])) revealed an iridoid skeleton with a carboxylic group at C(4) and a primary-alcohol function at C(10) and agreed well with the structure of adoxosidic acid (**7**) [5]. The ^{1}H- and ^{13}C-resonances of the C(10) methylene group (δ(H) 4.27, δ(C) 67.98) were, however, indicative of the esterification of OH–C(10). β-Configuration at C(8) was confirmed by comparing the C(9) (δ 42.44) and C(10) shifts with those reported for acylated epimeric pairs, in particular 8α- and 8β-dihydrogeniposide pentaacetate [6]. The presence of a 2,5-dihydroxyterephthalic-acid residue was suggested by the ^{1}H- and ^{13}C-NMR data and the strong yellowish green fluorescence [7]. Final proof of structure **1** was obtained by alkaline hydrolysis which afforded 2,5-dihydroxyterephthalic acid and adoxosidic acid (**7**). Adoxosidic acid was identified from its spectroscopic data [5]. Identity of 2,5-dihydroxyterephthalic acid was confirmed by HPLC and TLC cochromatography with an authentic sample. Thus, compound **1**, named blumeoside A, is 10-*O*-(2,5-dihydroxyterephthalo)adoxosidic acid.

In the FAB-MS of **2**, a pseudomolecular $[M - H]^-$ ion was detected at *m/z* 913. The molecular weight was thus 358 amu higher than that of **1**, suggesting the presence of an additional adoxosidic-acid moiety. The UV spectrum of **2** showed maxima at 222, 251, and 371 nm and was similar to the spectrum of **1**. In the ^{1}H- and ^{13}C-NMR spectra of **2**, (*Tables 1* and *2*), signals corresponding to the adoxosidic moiety were unchanged compared to **1**, while data of the terephthalic-acid residue revealed symmetric substitution. Basic hydrolysis of **2** followed by HPLC analysis led to the identification of 2,5-dihydroxyterephthalic acid and adoxosidic acid (**7**). Thus, in compound **2** (blumeoside D), both carboxylic groups of 2,5-dihydroxyterephthalic acid are esterified with adoxosidic-acid moieties.

Compound **3** had a molecular weight 16 amu lower than **1**, as revealed by a pseudomolecular $[M - H]^-$ ion at *m/z* 539 in the FAB-MS. The UV spectrum exhibited maxima at 215, 240, and 323 nm. Alkaline hydrolysis afforded adoxosidic acid (**7**) and a phenolic derivative which on HPLC analysis (diode array detection) showed a spectrum (λ_{max} 248, 325 nm) in accordance with that reported for 2-hydroxyterephthalic acid [7]. The NMR data definitely confirmed esterification of adoxosidic acid by 2-hydroxyterephthalic acid [7]. Thus compound **3**, named blumeoside C, is 10-*O*-(2-hydroxyterephthalo)adoxosidic acid.

The FAB-MS of **4** gave two major peaks at *m/z* 897 ($[M - H]^-$) and 539. The molecular weight was thus 358 amu higher than **3**, which corresponded to the presence of an additional adoxosidic-acid moiety. The two compounds had almost identical UV spectra. The ^{13}C-NMR spectrum of **4** was similar to that of **3**, but two signals were observed for each C-atom of the adoxosidic-acid moiety. Alkaline hydrolysis of **4**, followed by HPLC analysis of the reaction mixture, enabled the identification of 2-hydroxyterephthalic acid and adoxosidic acid. According to these data, **4**, named blumeoside B, is composed of two adoxosidic-acid moieties linked by 2-hydroxyterephthalic acid through ester groups.

Radical-scavenging properties of the blumeosides **1**–**4** were evaluated against the DPPH radical [8–10]. By using DPPH as a TLC spray reagent, **1** and **2** (10 µg) appeared

[1]) For convenience, the 'biogenetic numbering' generally used for iridoid glucosides is employed throughout the text and in *Tables 1* and *2* (see formula **2**); the systematic names are given in the *Exper. Part.*

Table 1. *^{1}H-NMR Data of Compounds* **1**–**4**[a]) [1]). Coupling constants *J* in Hz.

	1	**2**	**3**	**4**[b])
	((D_6)DMSO, 500 MHz)	(CD_3OD, 200 MHz)	((D_6)DMSO, 200 MHz)	(CD_3OD, 500 MHz)
H–C(1)	5.13 (*d*, *J* = 6.8)	5.18 (*d*, *J* = 7.4)	5.13 (*d*, *J* = 7.1)	5.16 (*d*, *J* = 7.3), 5.17 (*d*, *J* = 7.4)
H–C(3)	7.38 (*d*, *J* = 1.0)	7.48 (*s*)[c])	7.42 (*s*)	7.50 (br. *s*)
H–C(5)	2.67 (br. *dd*, *J* = 14.7, 6.8)	2.88 (*m*)	2.77 (*m*)	2.89 (*m*)
H_a–C(6)	2.11 (*m*)	2.28 (*m*)	2.16 (*m*)	2.28 (*m*)
H_b–C(6)	1.40 (*m*)	1.45 (*m*)	1.40 (*m*)	1.46 (*m*)
H_a–C(7)	1.81 (*m*)	1.98 (*m*)	1.84 (*m*)	1.97 (*m*)
H_b–C(7)	1.40 (*m*)	1.45 (*m*)	1.40 (*m*)	1.46 (*m*)
H–C(8)	2.32 (*m*)	2.54 (*m*)	2.33 (*m*)	2.54 (*m*)
H–C(9)	1.97 (*dd*, *J* = 13.7, 6.8)	2.10 (*m*)	1.97 (*m*)	2.10 (*m*)
H_a–C(10)				4.45 (*dd*, *J* = 11.0, 6.3), 4.38 (*dd*, *J* = 11.0, 6.3)
	4.27 (*m*)	4.37 (*m*)	4.24 (br. *d*, *J* = 5.6)	
H_b–C(10)				4.34 (*dd*, *J* = 11.0, 6.8), 4.28 (*dd*, *J* = 11.0, 6.8)
H–C(3′)	7.30 (*s*)[c])	7.50 (*s*)[c])	7.33 (unresolved)	7.58 (unresolved)
H–C(5′)			7.33 (unresolved)	7.59 (unresolved)
H–C(6′)	7.23 (*s*)[c])	7.50 (*s*)[c])	7.82 (*d*, *J* = 8.3)	8.02 (*d*, *J* = 8.8)
H–C(1″)	4.51 (*d*, *J* = 7.8)	4.68 (*d*, *J* = 7.8)	4.53 (*d*, *J* = 7.8)	4.66 (*d*, *J* = 7.8), 4.67 (*d*, *J* = 7.8)
H–C(2″)	2.96 (*t*, *J* = 8.5)	3.12 (*m*)		3.06 (*m*)
H–C(3″)	3.15 (*t*, *J* = 8.8)[d])			3.35 (*m*)[c])
		3.15–3.40 (unresolved, H–C(3″) to H–C(5″))	2.95–3.80 (part. obscured by H_2O signal, H–C(2″) to H–C(5″))	
H–C(4″)	3.03 (*t*, *J* = 9.3)			3.23 (*m*)
H–C(5″)	3.13 (*m*)[d])			3.31 (*m*)[c])
H_a–C(6″)	3.41 (*dd*, *J* = 11.8, 6.5)	3.65 (*dd*, *J* = 11.6, 5.4)	obscured by H_2O signal	3.65 (*m*)
H_b–C(6″)	3.64 (*dd*, *J* = 11.8, 2.0)	3.87 (*d*, *J* = 11.6)	obscured by H_2O signal	3.86 (*m*)

[a]) Attributions supported by HSQC (**1** and **4**) and COSY spectra (**1**).

[b]) With a few exceptions, resonances of corresponding protons of adoxosidic-acid moieties were incompletely resolved giving rise to *ms*. When two distinct signals were observed, both are indicated.

[c])[d]) Assignments with the same superscripts in each column are interchangeable.

Table 2. *^{13}C-NMR Data of Compounds* **1**–**4** *and* **7**[a])[1])

	1	**2**	**3**	**4**[b])	**7**
	((D_6)DMSO, 125 MHz)	(CD_3OD, 50 MHz)	((D_6)DMSO, 50 MHz)	(CD_3OD, 50 MHz)	(D_2O, 50 MHz)
C(1)	96.35	98.83	96.40	98.89, 98.71	97.47
C(3)	151.11	153.24	151.33	153.41	147.58
C(4)	110.59	112.27	110.59	112.07	117.66
C(5)	34.78	37.04	34.93	36.99	35.35
C(6)	31.78	33.82	31.99	33.79	31.67
C(7)	27.13	28.80	27.28	28.82	27.52
C(8)	39.00[c])	40.92	38.99	41.09, 40.95	42.77
C(9)	42.44	44.35	42.48	44.32	44.33
C(10)	67.98	69.86	67.58	69.78, 69.49	66.06
C(11)	170.09	171.24	170.46[d])	171.03	176.60[d])
C(1′)	119.27[e])	120.08	113.56	119.51[e])	
C(2′)	150.56[f])	153.84	161.96	162.26	
C(3′)	117.57[g])	118.84	117.13	120.97[e])	
C(4′)	120.13[e])	120.08	133.64	137.76	
C(5′)	152.03[f])	153.84	117.65	117.60	
C(6′)	117.12[g])	118.84	130.44	131.71	
C(7′)	167.12[h])	169.99	167.99[e])	170.63	
C(8′)	167.84[h])	169.99	165.54[e])	166.99	
C(1″)	99.02	100.91	99.02	100.97, 100.82	99.44
C(2″)	73.03	74.52	73.08	74.60, 74.53	73.50
C(3″)	76.65[i])	77.97[e])	76.72[f])	77.90[f])	76.40[d])
C(4″)	69.97	71.42	69.94	71.48, 71.27	70.38
C(5″)	77.11[i])	78.36[e])	77.22[f])	78.36[f])	77.01[d])
C(6″)	61.13	62.79	61.12	62.80, 62.66	61.43

[a]) Attributions of **1** and **4** are supported by HSQC data.
[b]) With a few exceptions, resonances of corresponding C-atoms of adoxosidic-acid moieties were not resolved. When two signals were observed, both values are listed.
[c]) Value obtained from the HSQC spectrum.
[d]) Tentative assignment, low-intensity signal.
[e])[f])[g])[h])[i]) Assignments with the same superscripts in each column are interchangeable.

as yellow spots against a purple background, while the same amount of **3** and **4** did not react with the radical. Compounds **1**–**4** were also tested against DPPH in a spectrophotometric assay. Quercetin (= 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-1-benzopyran-4-one) and BHT (2,6-di(*tert*-butyl)-4-methylphenol) were used as reference compounds. Activity of blumeoside A (**1**) remained lower than that of quercetin but was higher than that of BHT (*Fig. 1*). Compound **2** was less active than **1**, while **3** and **4** did not reduce significantly the free radical. Interestingly, the two compounds containing a hydroquinone moiety exhibited the strongest radical-scavenging activity in this assay. In this context, it is worth mentioning that hydroquinones isolated from the marine colonial tunicate *Aplidium californicum* were reported to exhibit antioxidant properties by reacting with superoxide anion [11].

The antioxidative activity of compounds **1**–**4** was also evaluated spectrophotometrically on the bleaching of the H_2O-soluble carotenoid crocin [12]. Alkoxyl radicals were generated from *t*-BuOOH by UV photolysis of aqueous solutions containing 10 μM

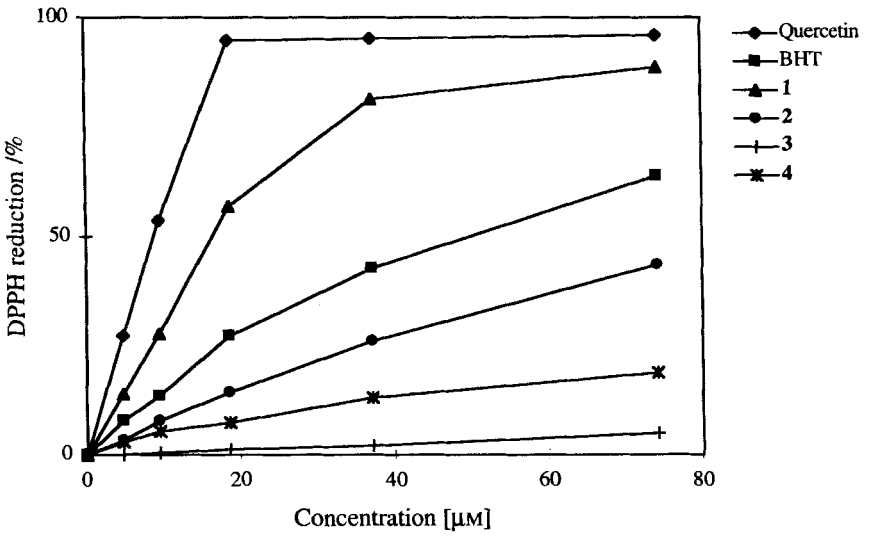

Fig. 1. *Scavenging activity of compounds* **1**–**4** *on DPPH radical.* Measurement at 517 nm, determination after 30 min.

crocin and 1 mM *t*-BuOOH. *t*-BuOH (0.5M) was added to scavenge the HO˙ radicals produced. Rutin (= 3-{[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy}-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4*H*-1-benzopyran-4-one) and gallic acid (= 3,4,5-trihydroxybenzoic acid) were used as reference compounds. Compounds **1**–**4** were all active in this assay, but their potency remained lower than that of rutin. Among the iridoids, **1** and **4** exhibited the strongest activity, comparable to that of gallic acid (*Fig. 2*).

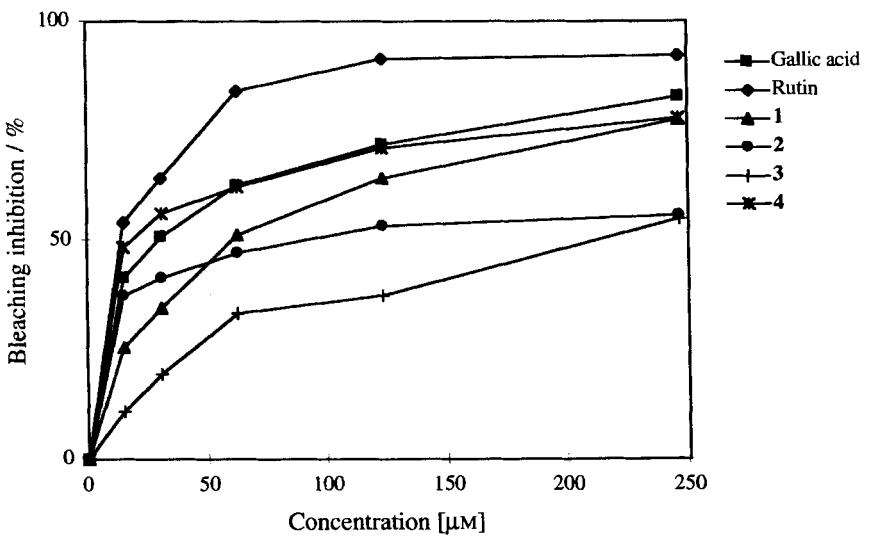

Fig. 2. *Inhibitory activity of compounds* **1**–**4** *on the bleaching of crocin.* Measurement at 440 nm, determination after 20 min.

Compounds **1**–**4** were also detected in the methanolic leaf extract of *F. blumei*. As found for the stem bark, blumeoside A (**1**) predominates. Iridoids and secoiridoids are widespread in Loganiaceae. On the other hand, terephthalic-acid derivatives are rather uncommon in plants. However, 2-hydroxyterephthalic acid and 2,5-dihydroxyterephthalic acid have been identified in some Gentianaceae species [7]. Antioxidant activity of a few iridoids has been reported: picroside-I and kutkoside from *Picrorrhiza kurroa* (Scrophulariaceae) had free radical scavenging properties [13]. Geniposide and oleuropein were shown to be the main antioxidative components of *Gardenia jasminoides* (Rubiaceae) and *Olea europaea* (Oleaceae), respectively [14] [15].

Proposed for the first time by *Takao et al.* [16] for screening antioxidants in marine bacteria, the use of the DPPH radical as a TLC spray reagent appears to be also well suited for the detection of antioxidants in crude plant extracts. This method allows to identify the active spots and thus to avoid the isolation of common phenolic compounds with well-known antioxidant properties.

This work was supported by the *Swiss National Science Foundation*. Thanks are due to Dr. *Wagner-Redeker* from *Spectronex AG*, Basel, for the measurement of the ES-MS spectrum of **1**.

Experimental Part

General. The 2,5-dihydroxyterephthalic acid was purchased from *Sigma*. TLC: silica gel *60* F_{254} sheets (*Merck*); BuOH/PrOH/H_2O 2:1:3 (system *1*). Open column chromatography (CC): *Sephadex LH-20* (*Pharmacia*) and silica gel (40–63 μm, *Merck*). Centrifugal partition chromatography (CPC): *CCC-1000* (*Pharma-Tech Research Corp.*, Baltimore, USA), 660-ml coil. Medium-pressure liquid chromatography (MPLC): home-packed *LiChroprep-RP-18* column (15–25 μm, 460 × 16 mm i.d., *Merck*). Anal. HPLC: *Hewlett-Packard-1050* instrument equipped with a photodiode array detector (DAD); *Nucleosil RP-18* column (7 μm; 250 × 4 mm i.d., *Macherey-Nagel*); MeOH/H_2O 3:7 → 7:3 in 30 min, 0.05% CF_3COOH, 1 ml/min (gradient *1*). Semiprep. HPLC: *Shimadzu-LC-10AD* pump, *LKB-2151* UV detector. M.p.: *Mettler-FP-80/82* hot-stage apparatus; uncorrected. $[\alpha]_D^{20}$: *Perkin-Elmer-241* polarimeter. UV: *Shimadzu-UV-106A* and *Perkin-Elmer-Lambda-3* spectrophotometers. IR: *Perkin-Elmer-781* spectrometer. ^{1}H- and ^{13}C-NMR: *Varian-Innova-500* and *Varian-VXR-200* spectrometers; δ in ppm rel. to $SiMe_4$; for ^{13}C-NMR spectra recorded in D_2O, dioxane (δ(C) 67.4) was used as internal standard; *J* in Hz; C-multiplicities from DEPT experiments. Electrospray-MS (ES-MS), FAB-MS, thermospray-MS (TSP-MS), D/CI-MS: *Finnigan-MAT-TSQ-700* triple-stage quadrupole instrument. FAB-MS: *70-BioProbe* accessory (*Finnigan MAT*); source temp. r.t., probe tip 50°, matrix glycerol, PAB gun 4 kV and 1.2 mA, Xe gas used for bombardment, negative-ion mode.

Plant Material. Stem bark of *Fagraea blumei* G. DON. was collected in Java, Indonesia, in September 1994. A voucher specimen (No. 94197) is deposited at the Institute of Pharmacognosy and Phytochemistry, University of Lausanne, Switzerland.

Extraction and Isolation. The dried bark (400 g) was ground and extracted at r.t. successively with CH_2Cl_2 (3 × 1500 ml) and MeOH (3 × 1500 ml) to yield 16 and 31 g of extract, resp. A portion (15 g) of the MeOH extract was fractionated by gel filtration (*Sephadex LH-20*, MeOH/H_2O 1:1). Sixteen fractions were collected (*Frs. 1–16*). *Di-O-methylcrenatin* (= 4-(hydroxymethyl)-2,6-dimethoxyphenyl β-D-glucopyranoside; **5**; 150 mg), was obtained from *Fr. 2* (2 g) by CC (silica gel, $CHCl_3$/MeOH/H_2O 9:12:8 lower phase). *Fr. 10* (190 mg) was further separated by gel filtration (*Sephadex LH-20*, MeOH) to afford *Frs. 10a–e*. *Swertisin* (= 6-β-D-glucophyranosyl-5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-4*H*-1-benzopyran-4-one; **6**; 10 mg) was isolated by CC (silica gel, $CHCl_3$/MeOH/H_2O 9:12:8 lower phase) from *Fr. 10c* (29 mg). *Fr. 6* (630 mg) was subjected to CPC (BuOH/PrOH/H_2O 2:1:3, upper phase as mobile phase, 3 ml/min) affording *Frs. 6a–e*. *Fr. 6b* (535 mg) was further separated by MPLC (*RP-18*, MeOH/H_2O 30:70, flow rate 3 ml/min) to yield *Frs.* $6b_{1-14}$. *Frs.* $6b_7$ and $6b_{13}$ contained pure **1** (112 mg) which was desalted on *Amberlyst 15* (*Fluka*) and **4** (11 mg), resp. Compounds **2** (5 mg) and **3** (4 mg) were isolated from *Fr.* $6b_5$ (34 mg) and $6b_{14}$ (14 mg), resp., by HPLC (*Nucleosil RP-18*, 7 μm; 250 × 4 mm i.d., *Macherey-Nagel*; MeOH/H_2O 48:52 and 45:55, resp., containing 0.05% CF_3COOH (1 ml/min)).

Alkaline Hydrolysis of **1**–**4**. To a soln. of blumeoside (0.5 mg) in MeOH (100 μl), 0.25N aq. NaOH (100 μl) was added, and the mixture was left standing at r.t. for 2 h (analysis by HPLC-DAD (*Nucleosil RP-18*, 7 μm;

250 × 4 mm i.d., *Machery-Nagel*; gradient *1*)). *Adoxosidic acid* (**7**) and 2,5-dihydroxyterephthalic acid were identified in the reaction mixtures from **1** and **2**, while **7** and 2-hydroxyterephthalic acid were detected in the reaction mixtures from **3** and **4**.

Reduction of 2,2-Diphenyl-1-picrylhydrazyl (= 2,2-Diphenyl-1-(2,4,6-trinitrophenyl)hydrazyl; DPPH) *Radical*. TLC autographic assay: after developing and drying, TLC plates were sprayed with a 0.2% DPPH soln. in MeOH. The plates were examined 30 min after spraying. Active compounds appear as yellow spots against a purple background. Spectrophotometric assay [8]: 50 µl of a soln. containing the compound to be tested were added to 5 ml of a 0.004% MeOH soln. of DPPH. Absorbance at 517 nm was determined after 30 min, and the percent of activity was calculated.

Bleaching of Crocin. Crocin was isolated from commercial saffron (*Hänseler AG*, Herisau, Switzerland) by extraction with MeOH followed by MPLC (*RP-18*, MeOH/H_2O 48:52). It was identified by its ^{1}H- and ^{13}C-NMR data. The test was carried out according to *Bors et al.* [12]. Aq. solns. containing 10 µM crocin, 1 mM *t*-BuOOH, 0.5M *t*-BuOH and various dilutions of the compounds to be tested were prepared. The solns. were placed under 254-nm light. Bleaching of crocin was monitored by following the decrease of absorbance at 440 nm with time.

(1R,4aR*,7R*,7aR*)-7-[(4-Carboxy-2,5-dihydroxybenzoyloxy)methyl]-1-(β-D-glucopyranosyloxy)-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic Acid* (= *Blumeoside A*; **1**): Yellow amorphous powder. M.p. 147–149°. TLC (SiO_2, system *1*): R_f 0.33, yellowish green fluorescence at 366 nm. HPLC (*RP-18*, gradient *1*): t_R 19.9 min. $[a]_D^{20} = -55$ ($c = 2.3$, MeOH). UV (MeOH): 220 (4.42), 362 (3.64). IR (KBr): 3600–3100, 3000–2900, 1660, 1610, 1490, 1440. ^{1}H- and ^{13}C-NMR: *Table 1* and *2*. ES-MS (negative-ion mode): 576.9 ($[M + Na - 2H]^-$), 554.9 ($[M - H]^-$). FAB-MS (negative-ion mode): 555 ($[M - H]^-$, $C_{24}H_{27}O_{15}^-$), 375 ([(adoxosidic acid) – H]$^-$).

7,7'-{(2,5-Dihydroxy-1,4-phenylene)bis[(carbonyloxy)(methylene)]}bis[(1R,4aR*,7R*,7aR*)-1-(β-D-glucopyranosyloxy)-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic Acid]* (= *Blumeoside D*; **2**): Yellow amorphous powder. M.p. 156–158°. TLC (SiO_2, system *1*): R_f 0.26, blue fluorescence at 366 nm. HPLC (*RP-18*, gradient *1*): t_R 22.9 min. $[a]_D^{20} = -36$ ($c = 4.0$, MeOH). UV (MeOH): 222 (4.25), 251 (3.68), 371 (3.43). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (negative-ion mode): 913 ($[M - H]^-$, $C_{40}H_{49}O_{24}^-$), 555 ([(blumeoside A) – H]$^-$).

(1R,4aR*,7R*,7aR*)-7-[(4-Carboxy-2-hydroxybenzoyloxy)methyl]-1-(β-D-glucopyranosyloxy)-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic Acid* (= *Blumeoside C*; **3**): Cream-colored amorphous powder. M.p. 171–173°. TLC (SiO_2, system *1*): R_f 0.35, blue fluorescence at 366 nm. HPLC (*RP-18*, gradient *1*): t_R 19.2 min. $[a]_D^{20} = -40$ ($c = 2.0$, MeOH). UV (MeOH): 215 (4.21), 240 (3.98), 323 (3.36). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (negative-ion mode): 539 ($[M - H]^-$, $C_{24}H_{27}O_{14}^-$).

7,7'-{(2-Hydroxy-1,4-phenylene)bis[(carbonyloxy)(methylene)]}bis[(1R,4aR*,7R*,7aR*)-1-(β-D-glucopyranosyloxy)-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic Acid]* (= *Blumeoside B*; **4**): Cream-colored amorphous powder. M.p. 160–163°. TLC (SiO_2, system *1*): R_f 0.26, blue fluorescence at 366 nm. HPLC (*RP-18*, gradient *1*): t_R 22.6 min. $[a]_D^{20} = -56$ ($c = 2.0$, MeOH). UV (MeOH): 212 (4.53), 238 (4.36), 327 (3.66). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*. FAB-MS (negative-ion mode): 897 ($[M - H]^-$, $C_{40}H_{49}O_{23}^-$), 539 ([(blumeoside C) – H]$^-$).

(1R,4aR*,7R*,7aR*)-1-(β-D-Glucopyranosyloxy)-1,4a,5,6,7,7a-hexahydro-7-(hydroxymethyl)cyclopenta[c]pyran-4-carboxylic Acid* (= *Adoxosidic Acid*; **7**). Compound **1** (10 mg) was dissolved in 0.5N aq. NaOH (500 µl) and left at r.t. for 2 h. The mixture was adjusted to pH 5 and extracted successively with AcOEt and BuOH. Fractionation of the aq. phase by gel filtration on *Sephadex LH-20* with MeOH afforded 2,5-dihydroxyterephthalic acid (1.7 mg) and crude **7**. Final purification by gel filtration (*Sephadex LH-20*, MeOH/H_2O 25:75) gave 2.5 mg of pure **7**. White powder. ^{1}H-NMR (D_2O): identical with [5]. ^{13}C-NMR: *Table 2*. TSP-MS (negative-ion mode): 375 ($[M - H]^-$, $C_{16}H_{23}O_{10}^-$), 489 ($[M + CF_3COO]^-$).

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