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FURTHER 5-METHYLCOUMARIN DERIVATIVES FROM *MUTISIA ORBIGNYANA*

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Key Word Index—*Mutisia orbignyana*; Compositae; coumarins; 5-methylcoumarins; geraniol derivatives.

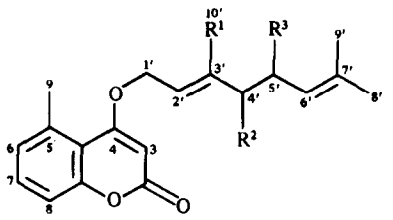
Abstract—The aerial parts of *Mutisia orbignyana* afforded in addition to known compounds 24 new derivatives of 4-hydroxy-5-methylcoumarin. The structures were elucidated by high field NMR techniques and a few chemical transformations. The chemotaxonomic relevance of these compounds is discussed briefly.

INTRODUCTION

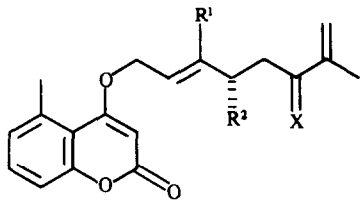
The South American genus *Mutisia* (Compositae, tribe Mutisieae) with about 60 species is distributed in the Andes from Colombia to S. Argentina and Chile but is also present in S.E. Brazil, Paraguay, Uruguay and N.E. Argentina. Most species are shrubs but several are vines [1]. The genus is placed in the subtribe Mutisiinae. So far only a few species have been investigated chemically. From three species acetylenic compunds are reported [2—4] while from *M. spinosa* characteristic 4-hydroxy-5-methylcoumarin derivatives were isolated [4]. We have now studied the Bolivian species, *M. orbignyana* Wedd. and the results are discussed in this paper.

RESULTS AND DISCUSSION

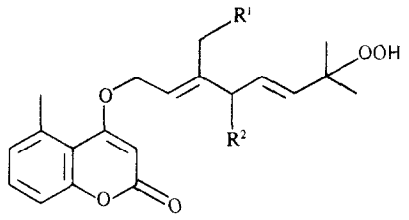
An extract of the aerial parts afforded after very lengthy separations thymol methyl ether and, in addition to arbutin which already has been synthesized by Mannich [5], isorhamnetin, rhamnazin and large amounts of quercetin, 24 derivatives of 4-hydroxy-5-methylcoumarins, the 4-*O*-geranyl derivatives, **1**, **2**, **2a**, **4**, **4a**, **5**, **6**



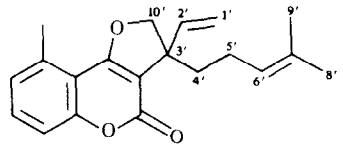
	1	**2***	**3***	**4***	**5***	**6**	**7**	**8***
R^1	Me	CH_2OH	CH_2OH	Me	CH_2OH	CHO	CHO	CH_2OH
R^2	H	H	H	OH	OH	H	H	H
R^3	H	H	H	H	H	H	H	OH
			2'*Z*				2'*Z*	



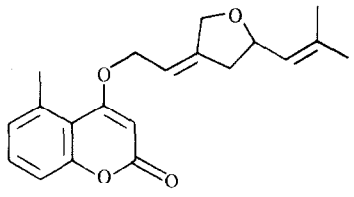
	9*	**10***	**11***	**12***	**13**	**14***
R^1	CH_2OH	Me	Me	CH_2OH	CHO	CH_2OH
R^2	H	OH	OH	H	H	H
X	αOOH,H	βOOH,H	αOOH,H	=O	=O	OH,H
					2'-*Z*	



	15*	16*
R^1	OH	H
R^2	H	OH



17



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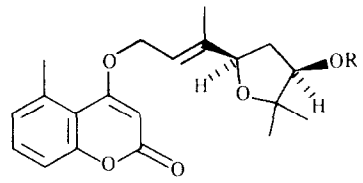
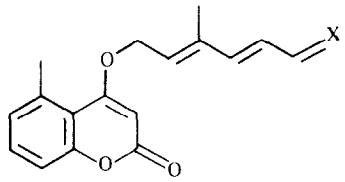
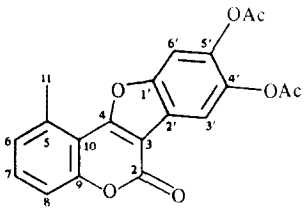


19 R = H
19a R = Ac



20 X = O
20a X = $(OAc)_2$
20b X = $(OMe)_2$



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*2a–4a, 9a, 10a, 12a, 15a and **16a** are the corresponding acetates, **5a**, **8a**, **10aAc**, **11a** and **14a** the diacetates

and **8**, the neryl derivatives **3**, **3a** and **7**, the derivatives with rearranged double bonds **9**–**16**, the oxygen ring compounds **17**–**19**, the *nor* derivative **20** and the tetracyclic coumarin **21**. Some of these compounds could only be isolated after acetylation of the natural compounds.

The structure of **1** was established as 4-geranyloxy-5-methylcoumarin by its ^{1}H NMR spectrum (Table 1) and by synthesis [6]. It is an isomer of piloselloidane which was isolated from a *Gerbera* species [7] where the geranyl residue is placed at C-3. The ^{1}H NMR data of **2** (Table 1) differed from that of **1** by the replacement of one methyl signal by a broadened methylene singlet at δ4.26. As the signals of H-1′ and H-2′ were slightly shifted down field it must be a 10′-hydroxy derivative.

The ^{1}H NMR spectrum of **3** (Table 1) was very close to that of **2**. Comparison of the chemical shifts of H-1′ and H-2′ in the spectra of these compounds clearly indicated the presence of 2′-*E*/*Z*-isomers. The configuration of the $\Delta^{2'}$-bond in the case of **2** was established by a NOE between H-10′ and H-1′.

The ^{1}H NMR spectra of **2a** and **3a** (Table 1) showed that the corresponding acetates were present. This was established by acetylation of **2** and **3**. The products obtained were identical with the natural compounds.

A further pair of 2′-*E*/*Z*-isomers were obtained in the form of aldehydes (**6** and **7**). Here the configuration directly followed from the chemical shift of the aldehyde protons which are characteristically different in these

cases. Boranate reduction of **6** afforded the carbinol **2** which also established the proposed configurations of **2** and **3**. The ^{1}H NMR spectra of **4** and its acetate **4a** (Table 1) indicated the presence of the 4′-hydroxy derivative of **1** and of the corresponding acetate. Accordingly, additional low field triplets at δ4.11 and 5.16, respectively were visible. Spin decoupling allowed in the case of **4a** the assignment of all signals. The configuration of the Δ2′-bond followed from the shift of H-2′ if the spectra of **1** and **4** were compared.

The molecular formula of **5a** ($C_{24}H_{28}O_7$), which was obtained by acetylation and the ^{1}H NMR spectrum (Table 1), indicated the presence of a diacetate. A triplet at δ5.28 and a pair of doublets at δ4.74 and 4.70 showed that it was probably a 4′,10′-diacetoxy derivative of **1**. Spin decoupling established this assumption. Thus the natural product was the diol **5**, the 4′-hydroxy derivative of **2**.

The ^{1}H NMR spectrum of **8a** (Table 1) which also was obtained by acetylation, differed from that of **5a** by the presence of broadened doublet at δ5.11 which sharpened on irradiation of both olefinic methyl signals. Thus one of the acetoxy groups was now at C-5. A signal at δ4.67 required again a 10′-acetoxy group. As the chiral center was no more at the neighbouring carbon a broadened singlet was observed for H-10′.

The ^{1}H NMR spectrum of the acetate of **9** (Table 2) a singlet at δ8.07 indicated the presence of a hydroperoxide. From the typical signals for an exomethylene group (δ5.06 and 5.03) and a broadened methylene singlet at δ4.68 the position of the oxygen functions could be deduced. The absolute configuration here and in the other compounds were not determined. Similarly, the spectral data of the acetate of **10** (Table 2) indicated the presence of the corresponding 4′-acetoxy derivative. In the spectrum of **10a** acetate (Table 2) two acetoxy singlets were visible and the H-6′ signal was shifted down field. In agreement with the molecular formula therefore the peroxiacetate formed by acetylation of **10** was present.

The ^{1}H NMR spectrum of the acetate of **11** (Table 2) was close to that of **10a** acetate. However, the couplings of H-4′ and H-6′ differed characteristically. Furthermore only the H-5′ signals were separated in the spectrum of **11a**. Inspection of models led to the assumption that in **11a** the oxygen functions at C-4′ and C-6′ were probably *cis* to each other. In this case the most stable conformation would explain different shielding effects of the protons at C-5′. However, a final proof was not possible.

The ^{1}H NMR spectrum of **13** (Table 2) differed markedly from those of **9a**–**11a**. A low field singlet at δ9.47 indicated the presence of an aldehyde while the down field shift of the H-9′ signals required a keto group at C-6′. A pair of triplets at δ2.65 and 2.98 further supported the assumption that there was a keto group at C-6′. The chemical shift of H-10′ required a 2′-*Z*-configurated double bond.

The ^{1}H NMR spectra of the acetates of **12** and **14** (Table 2) clearly showed that we were dealing with the corresponding 10′-acetoxy ketone and the 6′,10′-diacetoxy derivative, respectively. Accordingly, several signals showed the expected shift differences and in the spectra of **12a** and **14a** H-10′ displayed a broadened singlet at δ4.69 and 4.65, respectively while H-1′ and H-2′ were shifted up field in both cases.

The ^{1}H NMR spectra of the acetates of **15** and **16** (Table 2) both displayed hydroperoxy singlets. Furthermore the typical signals of *trans*-disubstituted double bonds were visible. In the case of **15a** clear assignments of all signals were only possible in deuteriobenzene. The chemical shifts of H-1′ and H-2′ in deuteriochloroform indicated a 2′-*Z*-configuration in both compounds which were obviously isomeric acetoxy derivatives. The relative position of the oxygen functions followed from the corresponding ^{1}H NMR signals. The natural compounds are most surely be derived from the corresponding carbinols by oxidation though only the precursor of **15** was isolated.

The structure of **17** followed from the molecular formula ($C_{20}H_{22}O_3$) and its ^{1}H NMR spectrum (Table 3). The presence of a 5-methyl coumarin was obvious. However, the H-3 signal was missing. Accordingly, a C-3 substituted derivative was present. The typical signals of a vinyl group and of a prenyl group as well as a pair of doublets at δ4.33 and 4.13 led to the proposed structure. This coumarin is most likely formed by alkylation of 5-methyl-4-hydroxycoumarin with 10-hydroxylinalol.

The molecular formula of **18** indicated the presence of an isomer of **17**. However, in this case the H-3 signal was visible. Careful spin decoupling indicated that a pair of highly broadened doublets at δ4.54 and 4.33 must be assigned to H-10′. Allylic couplings with a signal at δ5.71 and at δ4.56 (2H) supported this proposal. Furthermore the olefinic proton with allylic couplings with the two olefinic methyls showed a vicinal coupling with a proton under an oxygen function which was further coupled with a pair of broadened doublets of doublets. Accordingly, a 5′,10′-epoxy derivative of **1** was present. The configuration of the $\Delta^{2'}$-bond followed from the chemical shift of H-2′ which was close to that of **2**.

The ^{1}H NMR spectrum of **19a** (Table 3) showed that again an epoxy derivative of **1** was present. However, in this case the molecular formula ($C_{22}H_{26}O_8$) already indicated an additional acetoxy function. Spin decoupling allowed the assignment of all signals leading to a sequence which agreed only with the structure **19a**. The relative configuration at C-4′ and C-6′ was determined by NOE difference spectroscopy. Clear effects between H-4′ and H-5′$_1$ as well as between H-6′ and H-5′$_1$ required a *cis*-orientation of H-4′ and H-6′. The NOE between H-10′ and H-1′ also established the configuration of the $\Delta^{2'}$-bond. Compound **19** was probably formed by cyclization of the epoxide of **4**.

The ^{1}H NMR spectra of **20** and its derivatives **20a** and **20b** (Table 3) clearly showed that the aldehyde **20** formed by oxidative degradation of **1** was present.

The last compound **21**, isolated by acetylation of the natural compound, differed completely from all the others. However, the presence of a 5-methyl coumarin clearly followed from the typical ^{1}H NMR signals (Table 3) which, however, were all slightly shifted down field. Furthermore the H-3 signal was absent indicating an additional ring. The molecular formula was $C_{20}H_{14}O_7$ while the presence of a diacetate followed from the ^{1}H NMR and the IR spectrum. The latter further indicated the presence of phenolacetates. This was also supported by the fragmentation pattern in the mass spectrum where a double elimination of ketene led to the base peak (*m/z* 282). In agreement with the molecular formula therefore a tetracyclic aromatic compound must be proposed. In the ^{1}H NMR spectrum in addition to the already mentioned signals only two low field singlets at δ7.64 and 7.97 were visible. This required a 1′,2′,4′,5′-tetrasubstituted phenyl derivative. This was further supported

Table 1. ^{1}H NMR spectral data of **1–8a** (400 MHz, $CDCl_3$, δ-values)

H	1	2	2a	3	3a	4	4a	5a	6	7	8a	Multiplicity
3	5.66	5.68	5.66	5.65	5.64	5.65	5.61	5.66	5.67	5.65	5.65	*s*
6	7.17	7.17	7.16	7.17	7.18	7.18	7.15	7.18	7.20	7.20	7.18	*br d*
7	7.37	7.37	7.36	7.37	7.38	7.37	7.36	7.39	7.41	7.41	7.38	*t*
8	7.03	7.03	7.02	7.03	7.04	7.03	7.02	7.04	7.05	7.07	7.03	*br d*
9	2.67	2.67	2.65	2.67	2.67	2.67	2.64	2.66	2.70	2.70	2.66	*s*
1′	4.67	4.80	4.78	4.72	4.70	4.71	4.67	4.84	5.17	4.97	4.76	*br d*
2′	5.52	5.65	5.72	5.83	5.83	5.81	5.76	6.02	6.43	6.67	5.77	*br t*
4′	2.14	2.24	2.22	2.21*	2.22	4.11*	5.16*	5.28*	2.42*	2.37*	2.48† 2.40‡	*m*
5′		2.19	2.16	2.15*	2.16	2.32*	2.39‡ 2.32‡	2.46 2.39	2.20†	2.14†	5.66†	*m*
6′	5.10	5.12	5.08	5.10	5.09	5.10	5.11	5.04	5.10	5.10	5.11§	*br t*
8′	1.69	1.69	1.69	1.68	1.69	1.74	1.68	1.71	1.69	1.68	1.72	*br s*
9′	1.63	1.63	1.62	1.60	1.62	1.69	1.62	1.64	1.60	1.58		*br s*
10′	1.77	4.26	4.66	4.18	4.61	1.79	1.77	4.74§ 4.70§	9.95 s	9.52 s	4.67	*br s*
OAc	—	—	2.08	—	2.13	—	2.16	2.09 2.08	—	—	2.08 1.99	*s*

*t; †dt; ‡dd; §d.

J[Hz]: 6,7 = 7,8 = 8; 1′,2′ = 5′,6′ = 7 (compounds **3**, **4**, **4a**, **5a**, **6** and **7**: 4′,5′ = 7; compound **4a**: $5'_1,5'_2$ = 14; compound **8a**: $4'_1,5'$ = 7.5; $4'_2,5'$ = 5.5; $4'_1$, $4'_2$ = 15; 5′,6′ = 9).

by the ^{13}C NMR spectrum (see Experimental). The mode of anellation was supported by the low field shift of H-3′ (δ 7.97) which was most likely due to the carbonyl group. NOE difference spectroscopy gave a final proof. Thus a small effect between H-6′ and the aromatic methyl excluded a possible chromone structure. The NOE between the acetoxy methyls, H-3′ and H-6′ was of the same magnitude. It is most likely that **21** was formed by reaction of 4-hydroxy-5-methyl coumarin with hydroxyhydroquinone. We have named **21**, mutisifurocoumarin diacetate.

The chemistry of this *Mutisia* species again shows that 5-methyl coumarins are characteristic for parts of the subtribe Mutisiinae [4]. However, these compounds are not present in all genera and also not in all *Mutisia* species. A reinvestigation of *M. acuminata* R. et P. again

Table 2. ^{1}H NMR spectral data of **9a–16a** (400 MHz, $CDCl_3$, δ-values)

H	9a	10a	10aAc*	11a†	12a	13	14a	15a(C_6D_6)‡	16a	Multiplicity
3	5.68	5.64	5.61	5.62	5.66	5.77	5.66	5.48	5.62	*s*
6	7.19	7.19	7.17	7.18	7.18	7.18	7.18	6.98	7.17	*br d*
7	7.39	7.39	7.37	7.37	7.38	7.41	7.38	6.89	7.37	*t*
8	7.04	7.04	7.02	7.03	7.04	7.07	7.03	6.63	7.05	*br d*
9	2.67	2.67	2.65	2.66	2.65	2.72	2.66	2.48	2.66	*s*
1′	4.82	4.74	4.66	4.68	4.79	5.28	4.77	4.10	4.73	*br d*
2′	5.74	5.79	5.81	5.79	5.75	6.71	5.74	5.42	5.84	*br t*
4′	2.27	5.32§	5.22	5.19	2.53 *t*	2.65 *t*	2.17	2.69 *d*	5.67 *d*	*m*
5′	1.90 1.70	1.90	1.95	2.13‖ 1.93‖	2.90 *t*	2.98 *t*	1.80	5.55‖	5.88§	*m*
6′	4.34 *t*	4.33§	5.22	5.19 *t*	—	—	5.17 *t*	5.65 *d*	5.64 *d*	*m*
8′	1.77	1.78	1.74	1.75	1.90	1.87	1.73	1.35 *s*	1.37 *s*	*br s*
$9'_1$	5.06	5.04	4.98	4.97	5.99	5.95	4.96	1.35 *s*	1.36 *s*	*br s*
$9'_2$	5.03		4.91	4.95	5.82	5.78	4.92			*br s*
10′	4.68	1.80	1.77	1.78	4.69	9.47	4.65	4.46	1.78	*s*
OAc	2.10	2.10	2.06 2.05	2.08(6H)	2.10	—	2.07(6H)	1.73 *s*	2.13	*s*
OOH	8.07	8.32	—	—	—	—	—	7.82	7.75	*s*

*$CDCl_3/C_6D_6$: H-4′ 5.14 *br t*, H-6′ 5.16 *br t*; †$CDCl_3/C_6D_6$: H-4′ 5.21 *dd*, H-5′ 5.27 *dd*; ‡$CDCl_3$: H-4′ 2.93 *br s*, H-5′, H-6′ 5.65 *m*; §*dd*; ‖dt.

J[Hz]: 6,7 = 7,8 = 8; 1′,2′ = 5′,6′ = 7 (compound **10a**: 4′,$5'_1$ = 4; 4′,$5'_2$ = 6; $5'_1$,6′ = 8.5; $5'_2$,6′ = 5.5; compound **10a**Ac: 4′,$5'_1$ = $5'_1$,6′ = 8.5; 4′,$5'_2$ = $5'_2$,6′ = 5; compound **11a**: 4′,$5'_1$ = $5'_1$,6′ = 7; 4′,$5'_2$ = $5'_2$,6′ = 6; $5'_1$,$5'_2$ = 14); compounds **12a** and **13**: 4′,5′ = 7; compound **15a**: 4′,5′ = 6.5; 5′,6′ = 16; compound **16a**: 4′,5′ = 3.5; 5′,6′ = 16.

Table 3. ^{1}H NMR spectral data of **17–21** (400 MHz, $CDCl_3$, δ-values)

H	17	18	19a	20	20a	20b	21*
3	—	5.62 *s*	5.65 *s*	5.67 *s*	5.65 *s*	5.66 *s*	—
6	7.20 *br d*	7.18 *br d*	7.18 *br d*	7.20 *br d*	7.18 *br d*	7.18 *br d*	7.38 *br d*
7	7.39 *t*	7.38 *t*	7.38 *t*	7.41 *t*	7.38 *t*	7.38 *t*	7.50 *t*
8	7.03 *br d*	7.03 *br d*	7.04 *br d*	7.06 *br d*	7.04 *br d*	7.04 *br d*	7.22 *br d*
9	2.65 *s*	2.67 *s*	2.66 *s*	2.68 *s*	2.66 *s*	2.66 *s*	1.92 *s* (H-11)
1′	5.21 d 5.15 *d(t)*	4.56 *br d*	4.72 *br d*	4.88 *br d*	4.82 *br d*	4.80 *br d*	—
2′	6.22 *dd*	5.71 *ttt*	4.88 *br t*	6.26 *br t*	5.89 *br t*	5.84 *br t*	—
4′	2.05 *m*	2.73 *br dd* 2.37 *br dd*	4.45 *br t*	7.19 *d*	6.09 *d*	6.46 *d*	—
5′	2.19 *m*	4.62 *dt*	2.64 *ddd* 1.79 *ddd*	6.29 *dd*	5.78 *dd*	5.74 *dd*	—
6′	5.14 *br t*	5.33 *dqq*	5.05 *dd*	9.65 *d*	7.23 *d*	4.91 *d*	7.64 *s*
8′	1.66 *br s*	1.75 *d*	1.29 *s*	—	—	—	
9′	1.53 *br s*	1.72 *d*	1.28 *s*	—	—	—	
10′	4.33 *d* 4.13 *d*	4.54 *br d* 4.33 *br d*	1.77 *br s*	1.97 *br s*	1.90 *br s*	1.89 *br s*	
					2.12 *s* (6H) OAc	3.36 *s*(6H) OMe	2.38 *s*(6H) OAc

*H-3′ 7.97 *s*.

J[Hz]: 6,7 = 7,8 = 8; compound **17**: 1′,2′ = 10.5; 1*t*′,2 = 17.5; 5′,6′ = 7; $10'_1,10'_2 = 9.5$; compound **18**: 1′,2′ = 7; 2′,4′ = 2′,10′ ~ 1.5; $4'_1,4'_2 = 15$; $4'_1,5' = 5.5$; $4'_2,5' = 5',6' = 8.5$; 6′,8′ = 6′,9′ = 1.5; $10'_1,10'_2 = 13$; compound **19a**: 1′,2′ = 7; 4′,5′ = 7.5; $5'_1,5'_2 = 14$; $5'_1,6' = 4$; $5'_2,6' = 6.5$" compounds **20**, **20a** and **20b**: 1′,2′ = 6.5; 4′,5 = 16.5; 5′,6′ = 7.5 (compound **20a**: 5′,6′ = 6.5; compound **20b**: 5′,6′ = 5).

only gave triterpenes. The same is true for *Gerbera* were only a few species gave 5-methyl coumarins. The relevance of such findings has to be solved as this is an often observed situation that the ability to produce natural products, which are characteristic for a special genus, is lost in some representatives.

EXPERIMENTAL

The air-dried aerial parts (715 g, collected in Bolivia, voucher Solomon 16315) of *M. orbignyana* were extracted with MeOH–Et_2O–petrol, 1:1:1. The resulting extract was worked-up as reported previously [8] and separated by CC (silica gel) into four crude fractions (1) Et_2O–petrol (1:9); (2) Et_2O–petrol (1:1); (3) Et_2O and (4) Et_2O–MeOH (9:1 and 3:2). TLC (silica gel, PF 254) of fraction 1 gave 10 mg thymol methyl ether. TLC of fr. 2 (Et_2O–petrol, 1:1) gave 200 mg **1**, 50 mg lupeol and 50 mg taraxasterol. HPLC of fraction 3 (MeOH–H_2O, 9:1, always RP 18, *ca* 100 bar) gave 200 mg **7** (R_t 1.9 min), a mixture (3/2, R_t 2.6 min) and 150 mg **2a** (R_t 3.7 min). Fraction 3/2 gave by TLC ($CHCl_3$–C_6H_6–Et_2O, 9:9:1) 5 mg **3a** (R_f 0.68), 5 mg **6** (R_f 0.54) and 2 mg **4a** (R_f 0.48). Fraction 4 was a complex mixture. By HPLC (MeOH–H_2O, 4:1) 5% was separated affording 50 mg **4**, 3 mg **2**, 1 mg **3** and a remaining complex mixture wich could not be separated. As no acetate methyl was visible in the ^{1}H NMR spectrum the whole mixture was acetylated (Ac_2O, $CHCl_3$, DMAP) and the resulting acetates were separated by flash chromatography (SiO_2, ∅60 μ) into 10 fractions (4/1–4/10). TLC of 4/1 (Et_2O–petrol, 1:1) gave 3 mg **17** (R_f 0.78). Fraction 4/2 gave 4 mg **1** and fractions 4/3 afforded by HPLC (MeOH–H_2O, 9:1) 20 mg **3a** (R_t 3.2 min) and 50 mg **2a** (R_t 4.0 min). HPLC (same conditions) of fractions 4/4 gave a mixture (R_t 1.4 min, 4/4/1), 10 mg **7** (R_t 2.7 min), 1.2 g **4a** (R_t 3.7 min) and 300 mg **2a** (R_t 4.3 min). TLC of 4/4/1 ($CHCl_3$–C_6H_6–Et_2O, 1:1:1) afforded 2 mg **10a** (R_f 0.65), 16 mg **15a** (R_f 0.48) and a mixture which gave by HPLC (MeOH–H_2O, 4:1) 3 mg **16a** (R_t 1.5 min) and 3 mg **9a** (R_t 1.7 min). HPLC of fraction 4/5 (MeOH–H_2O, 4:1) gave 5 mg **7** (R_t 6.8 min) and 100 mg **4a** (R_t 11.2 min). HPLC of fraction 4/6 (MeOH–H_2O, 4:1) afforded 3 mg **20a** (R_t 5.7 min), 8 mg **11a** (R_t 6.9 min), 8 mg **10a** acetate (R_t 7.8 min), 20 mg **5a** (R_t 10.9 min) and two mixtures (4/6/5 and 4/6/6). TLC of 4/6/5 (Et_2O–petrol, 3:1, three developments) gave 2 mg **8a** (R_f 0.65) and 7 mg **14a** (R_f 0.58). TLC of 4/6/6 ($CHCl_3$–C_6H_6–Et_2O, 2:2:1, three developments) afforded 3 mg **18** (R_f 0.63) and 20 mg **14a** (R_f 0.55). HPLC of fraction 4/7 (MeOH–H_2O, 4:1) gave 30 mg arbutin penta-acetate (R_t 1.3 min); ^{1}H NMR ($CDCl_3$, 400 MHz): 7.00 (*br s*, H-2, 3, 5, 6), 5.04 (*d*, H-1′), 5.29 (*t*, H-2′), 5.26 (*t*, H-3′), 5.17 (*t*, H-4′), 3.84 (*dd*, H-5′), 4.30 and 4.18 (*dd*, H-5′), 2.29, 2.08, 2.07, 2.05, 2.04 (*s*, OAc) (*J* [Hz]: 1′,2′ = 7.5; 2′,3′ = 3′,4′ = 4′,5′ ~ 9; 5′,$6'_1$ = 5; 5′,$6'_2$ = 2.5; $6'_1,6'_2$ = 12.5); 1 mg **13** (R_t 5.3 min), 2 mg **12a** (R_t 6.0 min), 7 mg **19a** (R_t 7.0 min) and 20 mg **14a** (R_t 10.3 min). Fraction 4/8 afforded 1.5 g isorhamnetin tetra-acetate and 200 mg rhamnazin triacetate (only 5% separated by HPLC) and fraction 4/9 2 g quercetin pentaacetate. TLC of fraction 4/10 ($CHCl_3$–Et_2O, 1:1) gave 3 mg **21** (R_f 0.8).

4-*Geranyloxy-5-methyl coumarin* (**1**). Colourless crystals, mp 91°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 312.173 [M]$^+$ (1.5) (calc. for $C_{20}H_{24}O_3$: 312.173), 297 [M − Me]$^+$ (1.5), 177 [M − $C_{10}H_{15}$]$^+$ (54), 135 ($C_8H_7O_2$)$^+$ (20), 134 [$C_8H_6O_2$]$^+$ (17), 69 [C_5H_9]$^+$ (100). Identical with synthetic material.

4-[10-*Hydroxygeranyloxy*]-5-*methyl coumarin* (**2**). Colourless crystals, mp 114°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3360 (OH), 1700, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 328.167 [M]$^+$ (3) (calc. for $C_{20}H_{24}O_4$: 328.167), 310 [M − H_2O]$^+$ (5), 201 (7), 177 [M − $C_{10}H_{15}O$]$^+$ (44), 176 [M − $C_{10}H_{16}O$]$^+$ (53), 135 [$C_8H_7O_2$]$^+$ (64), 134 [$C_8H_6O_2$]$^+$ (82), 69 [C_5H_9]$^+$ (100). Acetylation gave the acetate **2a** identical with the natural product; colourless crystals, mp 57°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1230 (OAc), 1720, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 370.178 [M]$^+$ (1.5) (calc. for

$C_{22}H_{26}O_5$: 370.178), 310 [M − HOAc]$^+$ (5), 295 [310 − Me]$^+$ (4), 241 [310 − C_5H_9]$^+$ (22), 201 (20), 177 ([M − $C_{10}H_{14}$(OAc)O]$^+$ (34), 135 [$C_8H_7O_2$]$^+$ (28), 134 [$C_8H_6O_2$]$^+$ (28), 69 [C_5H_9]$^+$ (100).

4-[10-*Hydroxyneryloxy*]-5-*methyl coumarin* (**3**). Colourless crystals, mp 103°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 328.167 [M]$^+$ (3) (calc. for $C_{20}H_{24}O_4$), 310 (3.5), 201 (12), 177 (57), 135 (72), 134 (35), 69 (100). Acetylation gave the acetate **3a**, identical with the natural product; colourless crystals, mp 109°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1230 (OAc), 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 370.178 [M]$^+$ (2) (calc. for $C_{22}H_{26}O_5$: 370.178), 310 (8), 295 (4), 241 (22), 201 (22), 177 (46), 135 (43), 134 (46), 69 (100).

4-[4-*Hydroxygeranyloxy*]-5-*methyl coumarin* (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1720, 1610, 1595 (coumarin); MS *m/z* (rel. int.): 328.167 [M]$^+$ (0.7) (calc. for $C_{20}H_{24}O_4$: 328.167), 310 (3.5), 201 (10), 190 (50), 164 (43), 135 (100), 134 (26); $[\alpha]_D^{24}$ −21 ($CHCl_3$; *c* 0.78). Acetylation gave the acetate **4a**, colourless crystals, mp 38°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1235 (OAc), 1720, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 370.178 [M]$^+$ (1) (calc. for $C_{22}H_{26}O_5$: 370.178), 310 (2), 241 (4.5), 201 (37), 177 (40), 135 (28), 134 (21), 69 (100); $[\alpha]_D^{24}$ −13 ($CHCl_3$; *c* 3.7).

4-[4,10-*Dihydroxygeranyloxy*]-5-*methyl coumarin* (**5**). Isolated as its diacetate **5a**, colourless crystals, mp 64°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1230 (OAc), 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 428.184 [M]$^+$ (5) (calc. for $C_{24}H_{28}O_7$: 428.184), 386 (2.5), 369 [M − OAc]$^+$ (2.2), 368 [M − HOAc]$^+$ (1), 308 [368 − HOAc]$^+$ (27), 201 (62), 177 (100), 135 (35), 134 (35), 69 (71); $[\alpha]_D^{24}$ −7 ($CHCl_3$; *c* 0.7).

4-[10-*Oxo-geranyloxy*]-5-*methyl coumarin* (**6**). Colourless crystals, mp 67°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2740, 1730 (CHO), 1720, 1612, 1600 (coumarin); MS *m/z* (rel. int.): 326.152 [M]$^+$ (1.5) (calc. for $C_{20}H_{22}O_4$: 326.152), 257 [M − C_5H_9]$^+$ (22), 177 (48), 135 (32), 134 (18), 69 (100).

4-[10-*Oxo-neryloxy*]-5-*methyl coumarin* (**7**). Colourless crystals, mp 144°; IR $\nu_{max}^{CHCl_3}$ cm^{-1} 2740, 1710 (CHO), 1700, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 326.152 [M]$^+$ (2.5) (calc. for $C_{20}H_{22}O_4$: 326.152), 257 [M − C_5H_9]$^+$ (20), 201 (24), 177 (56), 135 (60), 134 (44), 69 (100). Boranate reduction (MeOH, 20°, 5 min) gave after TLC ($CHCl_3$–C_6H_6–Et_2O, 1:1:1) **3**, identical with the natural product.

4-[5,10-*Dihydroxygeranyloxy*]-5-*methyl coumarin* (**8**). Isolated as its diacetate **8a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1250 (OAc), 1730, 1620, 1610 (coumarin); MS *m/z* (rel. int.): 428.184 [M]$^+$ (0.2) (calc. for $C_{24}H_{28}O_7$: 428.184), 386 (1), 368 [M − HOAc]$^+$ (1.5), 308 (34), 201 (46), 177 (42), 135 (36), 134 (35), 133 (81), 85 [C_5H_9O]$^+$ (100).

4-[10-*Hydroxy*-6-*hydroxperoxy*-7,9-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**9**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3300 (OH), 1735, 1225 (OAc), 1720, 1610 (coumarin); MS *m/z* (rel. int.): 402.168 [M]$^+$ (1) (calc. for $C_{22}H_{26}O_7$: 402.168), 384 [M − H_2O]$^+$ (2), 368 [M − H_2O_2]$^+$ (1), 324 [384 − HOAc]$^+$ (3), 241 (23), 177 (52), 135 (61), 134 (63), 69 (100); $[\alpha]_D^{24}$ −15 ($CHCl_3$; *c* 0.1).

4-[4-*Hydroxy*-6-*hydroperoxy*-7,9-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**10**). Isolated as its acetate **10a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1230 (OAc), 1725, 1610 (coumarin); MS *m/z* (rel. int.): 402.168 [M]$^+$ (0.8) (calc. for $C_{22}H_{26}O_7$: 402.168), 384 (2), 324 (4), 201 (28), 177 (38), 135 (42), 134 (40), 69 (100). Acetylation gave the diacetate **10a** acetate, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1235 (OAc), 1725, 1615, 1600 (coumarin); MS *m/z* (rel. int.): 444.178 [M]$^+$ (0.5) (calc. for $C_{24}H_{28}O_8$: 444.178), 369 [M − OOAc]$^+$ (1.2), 368 [M − HOOAc]$^+$ (0.7), 308 [368 − HOAc]$^+$ (13), 201 (40), 177 (26), 151 (66), 135 (30), 134 (38), 133 (64), 55 (100); $[\alpha]_D^{24}$ −64 ($CHCl_3$; *c* 0.29).

4-[4-*Hydroxy*-6-epi-*hydroperoxy*-7,9-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**11**). Isolated as its diacetate **11a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1235 (OAc), 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 444.178 [M]$^+$ (0.4) (calc. for $C_{24}H_{28}O_8$: 444.178), 369 [M − OOAc]$^+$ (1.5), 368 [M − HOOAc]$^+$ (1), 308 [368 − HOAc]$^+$ (26), 201 (63), 177 (34), 151 (100), 135 (26), 133 (81).

4-[10-*Hydroxy*-6-*oxo*-7,9-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**12**). Isolated as its acetate, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1225 (OAc), 1720, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 384.157 [M]$^+$ (0.2) (calc. for $C_{22}H_{24}O_6$: 384.157), 324 [M − HOAc]$^+$ (3), 301 (2), 241 (21), 201 (14), 177 (20), 135 (26), 134 (24), 69 (100).

4-[6,10-*Dioxo-neryloxy*]-5-*methyl coumarin* (**13**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (C=O), 1690 (C=CC=O), 1610, 1600 (coumarin); MS *m/z* (rel. int.): 340.131 [M]$^+$ (0.6) (calc. for $C_{20}H_{20}O_5$: 340.131), 201 (20), 177 (20), 135 (34), 134 (33), 69 (100).

4-[6,10-*Dihydroxy*-7,9-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**14**). Isolated as its diacetate **14a**, colourless crystals, mp 46°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1235 (OAc), 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 428.184 [M]$^+$ (0.2) (calc. for $C_{24}H_{28}O_7$: 428.184), 368 [M − HOAc]$^+$ (2.5), 308 (40), 201 (38), 177 (40), 135 (47), 133 (100), 105 (88).

4-[10-*Hydroxy*-7-*hydroperoxy*-5,6E-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**15**). Isolated as its acetate **14a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3520 (OOH), 1740, 1230 (OAc), 1720, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 384.157 [M − H_2O]$^+$ (1) (calc. for $C_{22}H_{24}O_6$: 384.157), 241 (11), 201 (28), 177 (24), 135 (46), 134 (81), 55 (100).

4-[4-*Hydroxy*-7-*hydroperoxy*-5,6E-*dehydro*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**16**). Isolated as its acetate **16a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1735, 1230 (OAc), 1725, 1610 (coumarin); MS *m/z* (rel. int.): 402.168 [M]$^+$ (0.3) (calc. for $C_{22}H_{26}O_7$: 402.168), 384 (0.7), 342 (0.7), 201 (28), 177 (34), 135 (50), 134 (49), 60 (100).

3-[4,10′-*Epoxylinalyl*]-5-*methyl coumarin* (**17**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1610 (coumarin); MS *m/z* (rel. int.): 310.157 [M]$^+$ (6) (calc. for $C_{20}H_{22}O_3$: 310.157), 228 [M − C_5H_{10}]$^+$ (100), 227 (41), 213 [228 − Me]$^+$ (18), 135 (12).

4-[5,10-*Epoxygeranyloxy*]-5-*methyl coumarin* (**18**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730, 1625, 1605 (coumarin); MS *m/z* (rel. int.): 326.152 [M]$^+$ (3) (calc. for $C_{20}H_{22}O_4$: 326.152), 308 [M − H_2O]$^+$ (3), 201 (12), 177 (30), 135 (32), 134 (21), 69 (100).

4-[4β,7-*Epoxy*-6β-*hydroxy*-6,7-*dihydrogeranyloxy*]-5-*methyl coumarin* (**19**). Isolated as its acetate **19a**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1240 (OAc), 1720, 1610, 1605 (coumarin); MS *m/z* (rel. int.): 386.173 [M]$^+$ (1.3) (calc. for $C_{22}H_{26}O_8$: 386.173), 326 [M − HOAc]$^+$ (3.5), 308 [326 − H_2O]$^+$ (6), 201 (18), 151 (60), 135 (35), 134 (21), 97 (100); $[\alpha]_D^{24}$ +9 ($CHCl_3$; *c* 0.64).

4-[5-*Formyl*-3-*methyl*-*pent*-2E,4E-*dien*-1-*yl*]-5-*methyl coumarin* (**20**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2760, 1680 (CHO), 1710, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 284.105 [M]$^+$ (4) (calc. for $C_{17}H_{16}O_4$: 284.105), 255 [M − CHO]$^+$ (14), 202 (70), 177 (17), 176 (32), 135 (56), 134 (80), 81 (100). Acetylation gave the diacetate **20a**, colourless crystals, mp 155°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1760, 1740, 1250 (OAc), 1710, 1605, 1600 (coumarin); MS *m/z* (rel. int.): 386.137 [M]$^+$ (0.5) (calc. for $C_{21}H_{22}O_7$: 386.137), 326 [M − HOAc]$^+$ (2), 284 [326 − ketene]$^+$ (6), 266 [326 − HOAc]$^+$ (3), 202 (20), 177 (100). Reaction of **19** in MeOH with *p*Ts gave the dimethyl acetal **20b**, colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 330.147 [M]$^+$ (**1**) (calc. for $C_{19}H_{22}O_5$: 330.147), 298 [M − HOMe]$^+$ (10), 266 [298 − HOMe]$^+$ (8), 201 (12), 135 (20), 75 (100).

Mutisifuro coumarin diacetate (**21**). Colourless crystals, mp 243–245°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (PhOAc), 1730, 1610, 1600 (coumarin); MS *m/z* (rel. int.): 366.074 [M]$^+$ (7) (calc. for $C_{20}H_{14}O_5$: 366.074), 324 [M − ketene]$^+$ (12), 282 [324 − ketene]$^+$ (100); ^{13}C NMR ($CDCl_3$, C-2–C-11): 166.4 s, 121.1 s, 162.3

s, 135.3 *s*, 126.9 *d*, 131.6 *d*, 115.6 *d*, 154.5 *s*, 111.8 *s*, 21.3 *q*; C-1′–C-6′: 166.2 *s*, 140.3 *s*, 115.4 *d*, 141.2 *s*, 152.3 *s*, 107.4 *d*; OAc: 20.5, 20.7 *q*, 170.5 *s* (2x).

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