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FUROCOUMARINS FROM *ANGELICA PACHYCARPA*

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Key Word Index—*Angelica pachycarpa*; Umbelliferae; tert-*O*-methylbyakangelicin; oxypeucedanin methanolate; tert-*O*-methyloxypeucedanin hydrate; neobyakangelicol; linear furocoumarins; umbelliprenin; byakangelicin monoacetate; artifact.

Abstract—A novel furocoumarin isolated from unripe fruits of *Angelica pachycarpa* has been characterized as (+)-tert-*O*-methylbyakangelicin. (+)-tert-*O*-Methyloxypeucedanin hydrate, neobyakangelicol, (±)-byakangelicol, (+)-byakangelicin, phellopterin, isoimperatorin, oxypeucedanin, oxypeucedanin hydrate, pangeline and umbelliprenin were also identified along with (±)-byakangelicin monoacetate, which proved to be an artifact.

INTRODUCTION

In earlier papers [1–3], the identification of a range of different coumarins in *Angelica pachycarpa* Lge. (Umbelliferae) was reported. During the course of a chromatographic screening of its unripe fruits, the presence of several fluorescent compounds not previously detected in other parts of the plant was shown. Qualitative differences between ripe and immature fruits have been noted in many species [4, 5] and the characterization of a novel linear furocoumarin in unripe fruits of *A. pachycarpa* is described in the present paper.

RESULTS AND DISCUSSION

An ochre fluorescent compound could be isolated from the methanol extract of the dried unripe fruits by successive chromatography in several solvents. On the basis of its UV spectrum, the crystalline material, mp 89°, was shown to be a 5,8-disubstituted furocoumarin which did not co-chromatograph with any of the 5,8-furocoumarins earlier found in the plant. It analysed for $C_{18}H_{20}O_7$ (M^+ 348). The ^{1}H NMR data indicated the oxygen function as a methoxyl group. The presence of unsubstituted pyrone and furan rings was recognizable from two pairs of doublets which arise from H-3, H-4, H-2′ and H-3′. A typical ABX system appeared as a complex multiplet which can be attributed to the methine and methylene protons of the prenyl side chain. Methyl signals were found as a sharp singlet (Table 1).

The mass spectral fragmentation pattern was in agreement with the schemes proposed for methoxy-prenylated furocoumarins [6]. The presence of a strong peak at *m/z* 73 corresponding to the elimination of $Me_2C{=}\overset{+}{O}Me$ from the parent ion at *m/z* 348 proved that the methoxyl group is located at the tertiary carbon atom [7].

All these spectral data strongly indicated structure **1** for the coumarin, and this assignment received further support by its partial synthesis from byakangelicol, isolated from the same plant material, by treatment with boron trifluoride in methanol. The endogenous tert-*O*-methylbyakangelicin (**1**) co-chromatographed with the synthetic material in 10 TLC solvents. So far, the enantiomer of this compound has only been found in *Angelica dahurica* roots [8].

A second compound with yellow fluorescence and a UV

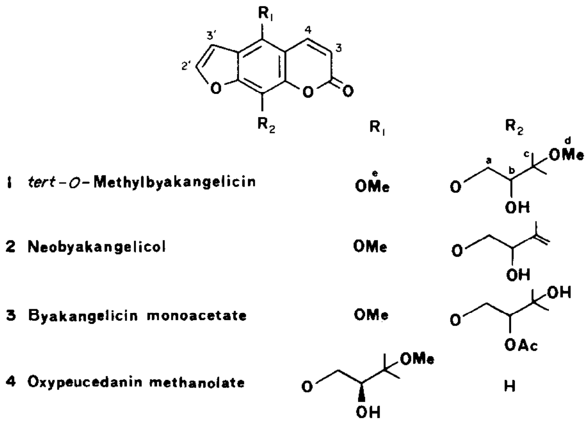

Table 1. ^{1}H NMR data of compounds **1**, **3** and **4** (80 MHz, $CDCl_3$, TMS, δ scale)

	1	3	4
H-3	6.27 *d* (9.8)	6.27 *d* (9.6)	6.27 *d* (9.6)
H-4	8.11 *d* (9.9)	8.10 *d* (9.6)	8.21 *d* (8.9)
H-8	—	—	7.15 *s*
H-2′	7.00 *d* (2.4)	6.99 *d* (2.4)	7.00 *d* (1.8)
H-3′	7.63 *d* (2.4)	7.60 *d* (2.4)	7.59 *d* (1.6)
H-a	3.99–4.23 *m*	4.28–4.86 *m*	4.50 *m*
H-b	4.60 *dd*	5.22 *dd*	3.96 *m*
H-c	1.25 *s*	1.25, 1.31 *d*	1.25 *s*
H-d	3.24 *s*	—	3.27 *s*
H-e	4.17 *s*	4.17 *s*	—
H-Ac	—	2.19 *s*	—

Figures in parentheses are coupling constants in Hz.

spectrum characteristic for 5-substituted linear furocoumarins was detected by TLC. Its chromatographic data were different to those of the C-5 furocoumarins previously found in this plant. The mp, ^{1}H NMR (Table 1) and mass spectral data suggested the compound to be oxypeucedanin methanolate (**4**), already reported in *Skimmia japonica* (Rutaceae) [9], *Angelica glauca* [7], *Peucedanum hispanicum* [10], *P. ostruthium* [11] and *Prangos alata* [12] (Umbelliferae). The identification was confirmed by co-chromatography with a synthetic sample in several solvents.

These derivatives may be artifacts but we consider this unlikely, since byakangelicol was almost unaffected in conditions much stronger than those used for extraction and separation of constitutents. On the other hand, oxypeucedanin methanolate was extracted from *A. glauca*, *P. hispanicum* and *P. alata* with hexane, ether and chloroform, respectively. Furthermore, Atkinson *et al.* [9] proved that it is a natural product in *S. japonica*. Nevertheless, a second collection of fruits was carried out; they were defatted with hexane and extracted with acetone. In the extract the occurrence of both methyl derivatives was substantiated.

A third compound with ochre fluorescence was isolated in trace amounts. The UV spectrum suggested a 5,8-substituted furocoumarin. The compound with a mp 104–105° was different from byakangelicol (mp 106°) and isobyakangelicol (108–109°) but co-chromatographed with neobyakangelicol (mp 106–107°) in several solvents. Neobyakangelicol (**2**) has been reported to occur in the umbellifers *Angelica dahurica* [13], *A. japonica* [14] and *Peucedanum ostruthium* [15].

In addition to the above coumarins, umbelliprenin, isoimperatorin, oxypeucedanin, oxypeucedanin hydrate, pangeline, phellopterin, byakangelicin, byakangelicol and byakangelicin monoacetate (**3**) were also characterized. It was shown, however, that the last product occurred as an artifact by reaction of byakangelicin with the acetic acid used in the chromatographic systems. This acid co-eluted with the byakangelicin due to the difficulty of its complete removal from the silica gel plates.

EXPERIMENTAL

Mps are uncorr. UV, ^{1}H NMR and MS were run in MeOH, $CDCl_3$ and direct insertion probe, respectively.

Unripe fruits (140 g) collected in Muros (Coruña) in June 1981 were homogenized with MeOH and macerated in the dark for several days. After filtration, the extraction was repeated for three consecutive 24 hr periods and the combined extracts were concd *in vacuo*. When the aq. residue was extracted with Et_2O, a solid (3.09 g) was deposited between the phases. The crude material was chromatographed on silica gel prep. TLC in different solvents.

The methanolic eluates of the individual bands furnished byakangelicol methanolate (52.7 mg), oxypeucedanin methanolate (8.9 mg), neobyakangelicol, byakangelicin acetate (14.4 mg), byakangelicol (50.3 mg), byakangelicin (308.4 mg), phellopterin, isoimperatorin, oxypeucedanin, oxypeucedanin hydrate, pangeline and umbelliprenin. Fruits (250 g) of a second collection in May 1982 were homogenized, defatted with hexane and then extracted with Me_2CO. The crude extract co-chromatographed with **1** and **4**.

tert-O-*Methylbyakangelicin* (**1**). Ochre fluorescence under UV light; mp 89° (MeOH); $[\alpha]^{21}_{589}+5.6°$ (EtOH; *c* 1.01); $+6.1°$ (578 nm); $+6.8°$ (546 nm); λ_{max} nm: 242, 249, 269, 313; ^{1}H NMR: Table 1; EIMS 70 eV *m/z*: 348 $[M]^+$, 333 $[M-Me]^+$, 317 $[M-OMe]^+$, 299 $[317-H_2O]^+$, 276 $[M-C_4H_8O]^+$, 246 $[276-CH_2O]^+$, 245 $[M-C_5H_{11}O_2]^+$, 232 $[M-C_6H_{12}O_2]^+$, 231 $[M-C_6H_{13}O_2]^+$, 217 $[232-Me]^+$, 203 $[231-CO]^+$, 189 $[217-CO]^+$, 175 $[203-CO]^+$, 160 $[189-CHO]^+$, 145 $[175-CH_2O]^+$, 132 $[160-CO]^+$, 89 $[C_7H_5]^+$, 73 $[CMe_2OMe]^+$.

Neobyakangelicol (**2**). Ochre fluorescence under UV light; mp 104–105° (MeOH) (lit. 106–107° [13]); λ_{max} nm: 243, 250, 269, 273 (sh), 313; TLC on silica gel with EtOAc–cyclohexane (35:65) R_f 0.41 (byakangelicol 0.56; isobyakangelicol 0.61).

Byakangelicin acetate (**3**). Ochre fluorescence under UV light; mp 134–136° (MeOH) (lit. 140–141° [16]); $[\alpha]_D$ 0° ($CHCl_3$; *c* 0.287); λ_{max} nm: 241, 247, 267, 272 (sh), 311; ^{1}H NMR: Table 1; EIMS 70 eV *m/z*: 359 $[M-OH]^+$, 317 $[M-C_3H_7O]^+$, 316 $[M-C_2H_4O_2]^+$, 299 $[359-C_2H_4O_2]^+$, 245 $[M-C_6H_{11}O_3]^+$, 232 $[M-C_7H_{12}O_3]^+$, 231 $[M-C_7H_{13}O_3]^+$, 217 $[232-Me]^+$, 203 $[232-CHO]^+$, 189 $[217-CO]^+$, 188 $[217-CHO]^+$, 175 $[203-CO]^+$, 161 $[189-CO]^+$, 160 $[188-CO]^+$, 145 $[175-CH_2O]^+$, 133 $[161-CO]^+$, 59 $[C_3H_7O]^+$.

tert-O-Methyloxypeucedanin hydrate (**4**). Yellow fluorescence under UV light; mp 121–123° (MeOH) (lit. 123–125° [9]); $[\alpha]^{20}_D$ $+10.6°$ ($CHCl_3$; *c* 0.227) (lit. +12° in $CHCl_3$ [9]); λ_{max} nm: 243, 250, 259, 267, 310; ^{1}H NMR: Table 1; EIMS 70 eV *m/z*: 318 $[M]^+$, 303 $[M-Me]^+$, 286 $[M-CH_2OH]^+$, 244 $[M-C_4H_{10}O]^+$, 215 $[244-CHO]^+$, 202 $[M-C_6H_{12}O_2]^+$, 185 $[215-CH_2O]^+$, 174 $[202-CO]^+$, 157 $[185-CO]^+$, 145 $[174-CHO]$, 129 $(157-CO)^+$, 89 $[C_7H_5]^+$, 73 $[CMe_2OMe]^+$.

Preparation of **1** *and* **4**. A soln of (+)-oxypeucedanin (50 mg) in MeOH (10 ml) containing BF_3 etherate (2 drops) was kept for 24 hr and added to aq. HCl. $CHCl_3$ extraction gave oxypeucedanin methanolate, mp 118–120° ($CHCl_3$), $[\alpha]_D+12.9°$ ($CHCl_3$; *c* 0.285). A soln of (±)-byakangelicol (20 mg) treated likewise yielded byakangelicol methanolate, mp 88–90° (MeOH).

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