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A SIMPLE METHOD FOR DIFFERENTIATING BETWEEN ANGULAR AND LINEAR 5-METHOXYFURANOCOUMARINS

ROBERT D. H. MURRAY and ZACARIAS D. JORGE

Department of Chemistry, University of Glasgow, Glasgow, G12 8QQ, U.K.

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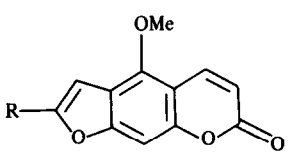
Key Word Index—Coumarins; 5-methoxyfuranocoumarins; ^{1}H NMR; furan ring orientation.

Abstract—The methoxyl resonance of a 5-methoxyfuranocoumarin provides a simple method for distinguishing between an angular and a linear furanocoumarin. The effects of furan substituents on the coumarin nucleus have been estimated.

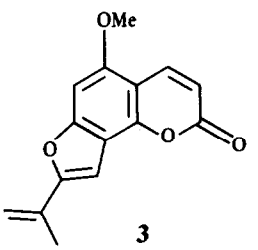
Recently we had occasion to re-examine the evidence on which the structure (**1**) of the 5-methoxyfuranocoumarin, hortinone, was based [1, 2]. We noted that the methoxyl resonance (δ) at 3.90 in the ^{1}H NMR spectrum of hortinone in deuteriochloroform was significantly upfield from the value of 4.26 reported [3] for the known 5-methoxy linear furanocoumarin, bergapten (**2**), a difference which was difficult to reconcile only with the additional isopropenyl residue. After careful analysis of lanthanide shift data, we concluded that hortinone is the 5-methoxy angular furanocoumarin (**3**) and obtained unambiguous synthetic confirmation for this revised structure [2].

Two types of 5-methoxyfuranocoumarin, angular and linear, occur naturally (Tables 1 and 2). We now report that the chemical shift of the 5-methoxyl group from the ^{1}H NMR spectrum recorded in deuteriochloroform provides a rapid and convenient means for distinguishing between the angular and linear series. In angular furanocoumarins (Table 1) the 5-methoxyl resonance is found near 4.0; however for linear furanocoumarins (Table 2), the methoxyl signal moves downfield and is typically found near 4.25. Such differences in the methoxyl chemical shifts must arise from the two possible orientations of the furan ring on the 5-methoxycoumarin nucleus.

The effect of the furan ring on benzene has been determined from the spectrum of benzofuran (**4**), the addition of the furan ring moving H_a downfield by +0.22, H_b upfield by −0.14, H_c −0.08 and H_d +0.15 ppm [4]. The following chemical shifts for the benzenoid protons of coumarin have been determined by Rowbotham and Schaefer [5], H-5 7.46, H-6 7.23, H-7 7.47 and H-8 7.22. In the angular furanocoumarin, angelicin (**5**) both benzenoid protons, H-5 and H-6 (coumarin skeleton numbering)



1 R = CMe = CH_2
2 R = H



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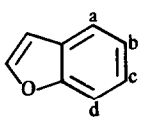

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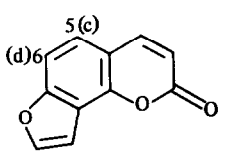

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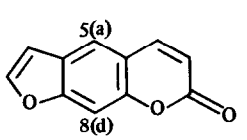

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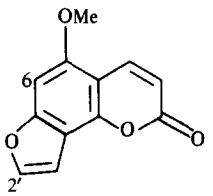
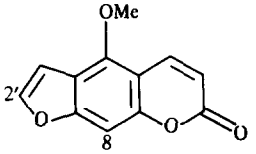
Table 1. Methoxyl resonances of 5-methoxy angular furanocoumarins ($CDCl_3$)



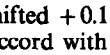
Compound	6	2′	δ	Ref.
Isobergapten	H	H	3.96	[9]
Hortinone	H	a*	3.90	[1]
Pimpinellin	OMe	H	4.06	[11]
	h	H	4.07	[11]
Heraclesol	j	H	4.02	[13]

*a, h and j, see Table 2.

Table 2. Methoxyl resonances of 5-methoxy linear furanocoumarins ($CDCl_3$)



Compound	8	2′	δ	Ref.
Bergapten	H	H	4.26	[3]
Furopinnarin	c	H	4.23	[14]
Swietenocoumarin B	d	H	4.33	[15]
Swietenocoumarin D	e	H	4.20	[15]
Swietenocoumarin G	f	H	4.20	[16]
	H	b	4.27	[17]
Isopimpinellin	OMe	H	4.27	[3]
	g	H	4.17	[18]
Phellopterin	h	H	4.15	[19]
Byakangelicol	i	H	4.22	[20]
Byakangelicin	j	H	4.18	[3]
Byakangelicin angelate	k	H	4.16	[21]
Byakangelicin acetonide	l	H	4.18	[22]
	m	H	4.18	[23]

a, $CMe{=}CH_2$; b, CMe_2OH; c, $CMe_2CH{=}CH_2$; d, $CH_2CH{=}CMe_2$; e,  f, $CH{=}CHCMe_2OH$; g, $OCMe_2CH{=}CH_2$; h, $OCH_2CH{=}CMe_2$; i,  j, $OCH_2CHOHCMe_2OH$; k,  $OCH_2CHOAngCMe_2OH$; l,  m, $OCH_2CHOHCMe_2Cl$.

have identical chemical shifts of 7.37 [6]. Thus compared with the corresponding position in coumarin, H-5 has shifted −0.09 and H-6 +0.14, values which are close to those calculated for the effect of the furan ring, −0.08 and +0.15, respectively. The chemical shifts for H-5 and H-8 in the linear furanocoumarin, psoralen (**6**), are 7.64 and 7.41 [7]. Compared with the corresponding positions in coumarin, H-5 has shifted +0.18 and H-8 +0.19. Again, these values are in accord with those calculated for the effect of the furan ring, +0.22 and +0.15, respectively.

The effect of the furan ring on methoxyl signals is similar to its effect on protons in the same position but an additional downfield shift is observed. Thus the methoxyl resonance of bergapten (5-methoxypsoralen, **2**) at 4.26 [3] is downfield by +0.30 compared to its position (3.96) in 5-methoxycoumarin [24], the corresponding proton shift in psoralen being +0.18. Similarly the 8-methoxyl resonance of xanthotoxin (8-methoxypsoralen) at 4.29 [8] is +0.37 downfield from that (3.92) of 8-methoxycoumarin [25] compared with +0.19 for the corresponding psoralen proton shift. In the angular furanocoumarin, isobergapten (5-methoxyangelicin), the methoxyl resonance at 3.96 [9] is identical to that of 5-methoxycoumarin compared with −0.09 for the corresponding proton shift in angelicin. For sphondin (6-methoxyangelicin) the methoxyl resonance at 4.03 [10] is +0.31 downfield from the corresponding resonance (3.72) of 6-methoxycoumarin [26] the comparable effect of the furan ring on a proton at C-6 in angelicin being +0.14.

Many 5-alkoxyfuranocoumarins are known containing prenyl derived ether substituents at C-5 [12]. Since these are all susceptible to ready cleavage to the corresponding 5-hydroxycoumarin which can readily be methylated, this simple spectroscopic technique can provide a facile method for determining whether an angular or a linear furanocoumarin nucleus is present.

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COUMARINS FROM *OLEA AFRICANA* AND *OLEA CAPENSIS*

HIROKI TSUKAMOTO, SUEO HISADA, SANSEI NISHIBE*, DAVID G. ROUX† and JOHN P. ROURKE‡

Faculty of Pharmaceutical Sciences, Higashi Nippon Gakuen University, Ishikari-Tobetsu, 061-02, Japan; †Department of Chemistry, University of the Orange Free State, Bloemfontein, 9300, Republic of South Africa; ‡Kirstenbosch Botanic Garden, Claremont, 7735, Republic of South Africa

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Key Word Index—*Olea africana; Olea capensis*; Oleaceae; coumarins; esculetin; scopoletin; isoscopoletin; scoparone.

Abstract—Esculetin and scopoletin were isolated from the bark of *Olea africana* while isoscopoletin and scoparone were isolated from the bark of *Olea capensis*. The distribution of these coumarins in *Olea* species from South Africa is described.

The bark of *Olea europaea* L. was found to contain new lignans, i.e. 1-acetoxypinoresinol and related compounds [1, 2]. During an investigation of the bark constituents, esculetin (6,7-dihydroxycoumarin) was isolated [3]. Previously, the occurrence of coumarins in Oleaceae was only known in *Fraxinus* species [4]. The present paper describes the isolation of coumarins from South African *Olea* species, *Olea africana* and *Olea capensis* L. *Olea africana*, recently reclassified as *Olea europaea* L. subsp. *africana* (Mill.) P. S. Green [5], is not found outside Southern Africa [6].

Esculetin (**1**) and scopoletin (**2**) were isolated from the bark of *Olea africana* and identified by direct comparison with respective authentic samples. Isoscopoletin (**3**) and scoparone (esculetin dimethyl ether, **4**) were isolated from the bark of *Olea capensis* and identified by direct comparison with respective authentic samples. This represents the first report of esculetin methyl ethers **2**, **3** and **4** in Oleaceae.

In addition, the distribution of these coumarins in *Olea woodiana* Knobl. and *Olea exasperata* Jacq. was examined by comparison with that in *O. europaea*, *O. africana* and *O. capensis*. These species have sometimes been confused with *Olea africana* [6, 7]. Identification of coumarins was determined by co-chromatography with authentic standards in two solvent systems, benzene–EtOAc (1:1) and $CHCl_3$–EtOAc (1:1), on silica gel TLC plates. The results are as shown in Table 1. It is noteworthy that esculetin (**1**) is the major coumarin in all the species examined except *Olea capensis*.

*Author to whom correspondence should be addressed.

EXPERIMENTAL

All mps are uncorr. The ^1H NMR spectra were run on a 90 MHz instrument in DMSO-d_6 with TMS as int. standard. MS were obtained by a direct inlet system.

Plant materials. The plant materials collected were: *Olea africana* in August 1982 at Kirstenbosch Botanic Garden and in October 1982 at Bloemfontein; *Olea capensis* in August and November 1982 at Kirstenbosch Botanic Garden; *Olea woodiana* and *Olea exasperata* in August 1982 at Kirstenbosch Botanic Garden. Specimens from which samples for coumarin analysis were taken are lodged at the Herbarium of Higashi Nippon Gakuen University.

Isolation of esculetin (**1**) *and scopoletin* (**2**). Dry powdered bark (1.0 kg) of *Olea africana* was extracted × 3 with MeOH. The concd extract plus H_2O was extracted with Et_2O. The Et_2O extract was chromatographed on a silica gel column with a $CHCl_3$–EtOAc gradient. The fractions were monitored by TLC