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FURANOCOUMARINS FROM *HERACLEUM CANESCENS*

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Key Word Index—*Heracleum canescens*; Umbelliferae; methyl 3,4,5-trimethoxybenzoate; osthol; furanocoumarins; sitosterol.

Abstract—The ethanolic extract of the fresh roots of *Heracleum canescens* has afforded, besides sitosterol, osthol, methyl 3,4,5-trimethoxybenzoate and 11 furanocoumarins.

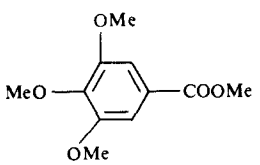
INTRODUCTION

The genus *Heracleum* is well known to contain coumarins[1]. Earlier [2] osthol and three furanocoumarins 8-geranyloxypsoralen, heraclenin and imperatorin were identified in the petroleum extract of the roots of *H. canescens*. In more detailed studies of these roots, we have isolated and characterized sitosterol, methyl 3,4,5-trimethoxybenzoate, osthol and 11 linear furanocoumarins. Alloisoimperatorin and methyl 3,4,5-trimethoxybenzoate are new to the genus.

RESULTS AND DISCUSSION

The residues, left after trituration of the ethanolic extract of the roots of *H. canescens* with petroleum and ethyl acetate, successively, and removal of the solvents, were partitioned over Si gel columns separately. The effective separation of the mixtures thus obtained was achieved through prep. TLC on Si gel G. The R_f values of the compounds are given in Table 4.

The petroleum residue yielded sitosterol and compounds **2–6** while compounds **1** and **7–12** were obtained from the ethyl acetate residue. Compound **1**, mp 80°, analysed for $C_{11}H_{14}O_5$ and its IR spectrum revealed that it was an aromatic ester. The ^{1}H NMR spectrum accounted for two aromatic protons at δ 7.29 (*s*), one $COOCH_3$ at δ 3.75 (3H,*s*) and three OMe's at δ 3.86 (9H,*s*). The mass spectrum of the compound showed a molecular ion peak at *m/z* 226 with prominent peaks at *m/z* 211, 195, 168 (100%), and 165. On the basis of this spectral evidence, the compound was characterized as methyl 3,4,5-trimethoxybenzoate and this was confirmed by its synthesis from gallic acid.



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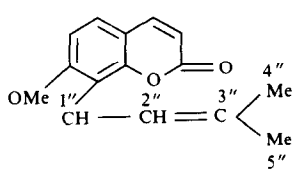

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Compounds **2–12** produced a violet colouration on treatment with alkaline hydroxylamine followed by ferric chloride indicating all to be coumarins[3]. Compound **2** was identified as osthol from its spectral properties, mp and co-TLC with an authentic sample. Compounds **3–12** exhibited UV absorptions (Table 1) typical of linear furanocoumarins[4] and had identical ^{1}H NMR pattern (Tables 2 and 3). In their ^{1}H NMR spectrum H-3 and H-4 appeared as doublets, J = 9–9.5 Hz, between δ 6.13–6.43 and 7.6–7.95; the H-4 was shifted downfield to δ 8.03 in the case of **12**. All the compounds, other than **2**, **6** and **12**, showed the resonance signal due to H-5 between δ 7.30–7.56. The ^{1}H NMR spectrum of **3** contained an additional signal at δ 7.29, attributed to H-8. The resonance signals due to H-5 and H-8 were missing in the ^{1}H NMR spectrum of **6** and **12**. The furano

Table 1. UV absorption of furanocoumarins in methanol

Compound	UV λ_{max} nm				
3	240	(sh),	245,	289,	327
4	244	(sh),	249,	264	
5	298,	262,	248,	218	
6	299,	263,	249,	216	
7	293,	262,	247,	208	
8	299,	263,	249,	243	
9	297,	260,	248,	218	
10	300,	263,	248,	218	
11	298,	262,	249,	242	

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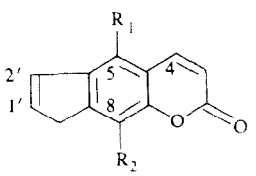
Table 2. ^{1}H NMR of furobenzopyran protons (δ-values)

Compound	H-3	H-4	H-5	H-8	H-2′	H-3′
3	6.33(9)	7.76(9)	7.46	7.29	7.60	6.80
4	6.13(10)	7.60(10)	7.16	—	7.49	6.66
5	6.30(9)	7.77(9)	7.40	—	7.76	6.86
6	6.20(9)	7.96(9)	—	—	7.69	6.80
7	6.30(9)	7.76(9)	7.30	—	7.70	6.80
8	6.30(9.5)	7.79(9.5)	7.56	—	7.86	6.80
9	6.43(9.5)	7.80(9.5)	7.43	—	7.76	6.89
10	6.36(9.3)	7.76(9.3)	7.36	—	7.72	6.82
11*	6.29(9.5)	7.83(9.5)	7.40	—	7.73	6.83
12*	6.32(9.3)	8.03(9.3)	—	—	7.72	6.86
13	6.30(9)	8.08(9)	—	—	7.70	6.82
14	6.33(9)	7.78(9)	7.36	—	7.70	6.80
15	6.26(9.5)	7.70(9.5)	7.30	—	7.60	6.80
16	6.36(9.3)	7.80(9.5)	7.40	—	7.73	6.82
17	6.30(9.5)	7.95(9.5)	—	—	7.70	6.80

Value in parentheses is the J value. Spectra measured in $CDCl_3$.
*Solvent DMSO-d_6.



	R_1	R_2
3	H	H
4	H	$OCH_2-CH=C(Me)-CH_2-CH_2-CH=C(Me)_2$
5	H	$OCH_2-CH(O)-C(Me)_2$
6	$CH_2-CH=C(Me)_2$	OH
7	H	OMe
8	H	$OCH_2-CH=C(Me)_2$
9	H	$OCH_2-C(=O)-CH(Me)_2$
10	H	$OCH_2-CH(OH)-C(OH)(Me)_2$
11	H	$OCH_2-CH(OH)-C(=CH_2)-Me$
12	OH	$CH_2-CH=C(Me)_2$
13	OAc	$CH_2-CH=C(Me)_2$
14	H	$CH_2-CH(OAc)-C(Me)_2$ (OH)
15	H	$OCH_2-CH(OAc)-C(OAc)(Me)_2$
16	H	$OCH_2-CH(OAc)-C(Me)=CH_2$
17	$CH_2-CH=C(Me)_2$	

Table 3. ^{1}H NMR of side chain protons (δ values)

Compound	C-1″	C-2″	C-3″	C-4″	C-5″	–OH	–OMe	–OAc
						(*s*,exch. D_2O)		
5	4.56(2H,*m*)	3.2(1H,*m*)	—	1.30(3H,*s*)	1.36(3H,*s*)	—	—	—
6	3.76(2H, *d*, *J* = 7 Hz)	5.20(1H,*t*, *J* = 8.5,6 Hz)	—	1.76(3H,*s*)	1.90(3H,*s*)	4.30	—	
7	—	—	—	—	—	—	4.23(3H,*s*)	—
8	4.96(2H, *d*,	5.60(1H,*t*, *J* = 8.5,6 Hz)	—	1.73(–Me)	1.73(–Me)	—	—	—
9	5.26(2H,*s*)	—	3.16(1H,m)	1.23(3H,*s*)	1.36(3H,*s*)	—	—	—
10	4.56(2H,*m*)	3.90(1H,*m*)	—	1.30(3H,*s*)	1.32(3H,*s*)	2.73	—	
11	4.46(2H,overlap)	2.56(1H,*m*)	—	5.06(2H,*d*, *J* = 12 Hz)	1.86(3H,*s*)	3.53	—	—
12	3.73(2H,*d*)	5.20(1H,*t*,*J* = 9, 6 Hz)	—	1.76(3H,*s*)	1.89(3H,*s*)	—	—	
13	3.73(2H,*d*)	5.20(1H,*t*,*J* = 9, 6 Hz)	—	1.76(3H,*s*)	1.89(3H,*s*)	—	—	2.43
14	4.63(2H,*m*)	4.23(1H,*m*)	—	1.36(3H,*s*)	1.41(3H,*s*)	2.46	—	2.30
15	4.63(2H,*m*)	4.23(1H,*m*)	—	1.42(3H,*s*)	1.50(3H,*s*)	—	—	2.30,2.36
16	4.62(2H,*m*)	4.21(1H,*m*)	—	5.10(2H,*d*, J = 12 Hz)	1.90(3H,*s*)	—	—	2.43
17	3.76(2H,*d*, *J* = 7 Hz)	3.42(1H,*t*, *J* = 8,6 Hz)	—	5.06(2H,*d*, *J* = 12 Hz)	1.90(3H,*s*)	—	—	—

Table 4. R_f values of coumarins

Compound	R_f(×100)* in C_6H_6–EtOAc(7 : 3)	Compound	R_f(×100) in C_6H_6–EtOAc(9 : 1)
1	77	**3**	48
7	67	**4**	64
8	78	**5**	45
9	65	**6**	36
10	14		
11	45		
12	62		

*On Si gel G(0.1 mm) plates.

protons appeared as doublets with $J = 2.2$ Hz. The chemical shift of H-4 indicated that all were C-8 substituted furanocoumarins, **6**, **11** and **12** being substituted at C-5 as well[5].

On the basis of the spectral data coupled with the chemical analysis and comparison with lit. mps, **2–11** were identified as osthol, **2**; psoralen, **3**; 8-geranyloxypsoralen, **4**; heraclenin, **5**; alloimperatorin, **6**; xanthotoxin, **7**; imperatorin, **8**; isoheraclenin, **9**; heraclenol, **10** and isogosferol, **11**. Compound **12** showed IR and mass spectra identical with **6** and formed a monoacetate **13**, mp 129°. The chemical shift of H-4 together with the mps of **12** and **13** indicated that compound **12** was an isomer of **6** and was thus characterized as alloisoimperatorin[6].

Heracleum canescens has been found to contain closely related furanocoumarins. The R_f values of these coumarins are shown in Table 4. Contrary to earlier reports[7], it has been found that heraclenol, methyl 3,4,5-trimethoxybenzoate and sitosterol are the major constituents. The presence of psoralen in this species and its wide distribution in the genus suggest that it is the probable precursor of all other furanocoumarins in the genus.

EXPERIMENTAL

Mps are uncorr. IR were recorded on KBr discs. ^{1}H NMR were run at 60 MHz and MS were recorded at 70 eV.

Extraction and isolation. Heracleum canescens roots collected from Harwan (Kashmir Valley) were thoroughly extracted with hot EtOH. The residue left after removal of the solvent under vacuum was triturated successively with petrol and EtOAc. The residues left after removal of the solvents were chromatographed over Si gel columns, separately. The UV absorptions are given in Table 1. ^{1}H NMR are shown in Tables 2 and 3.

Characterization of compounds. **1**, methyl 3,4,5-trimethoxybenzoate, mp 80°, $C_{11}H_{14}O_5$. IR ν_{max} cm^{-1}: 1720, 1595, 1420, 1330, 1220, 1130, 990, 860, 750. MS: *m/z* at 226, 195 $(M-OMe]^+$, 167 $[M-CO_2Me]^+$, 164 $[M-2\times OMe]^+$, 133 $[M^+-3\times OMe]^+$. **2**, osthol, mp 83° $[M^+]$ at *m/z* 244, $C_{15}H_{16}O_3$. IR ν_{max} cm^{-1}: 1715, 1600, 1495, 1385, 1365. (lit. mp 83–84). **3**, psoralen, mp 156°, $[M]^+$ at *m/z* 186, $C_{11}H_6O_3$. IR ν_{max} cm^{-1}: 1710 (*br*), 1600, 1560. **4**, 8-geranyloxypsoralen, mp 53°, $[M]^+$ at *m/z* 338, $C_{21}H_{22}O_4$. IR ν_{max} cm^{-1}: 1710, 1600, 1560, 1490, 1380, 1360. ^{1}H NMR: ($CDCl_3$) side chain δ 1.53 (3H, *s*), 1.63 (3H, *s*), 1.69 (3H, *s*), 2.0 (6H, *d*), 4.69 (2H, *br d*, $J = 8.5$ Hz), 5.43 (2H, *t*, $J = 9.5$, 6 Hz), (lit. mp 53–54°)[9]. **5**, heraclenin, mp 113°; $[M]^+$ at *m/z* 286, $C_{16}6H_{14}O_5$. IR ν_{max} cm^{-1}: 1720, 1598, 1491, 1383, 1366. MS: *m/z* at 286, 265 $[M-Me]^+$, 250, 186 (100%), 179, 169. (lit. mp 11°)[10]. **6**, alloimperatorin, mp 232°, $[M]^+$ at *m/z* 270, $C_{16}H_{14}O_4$. IR ν_{max} cm^{-1}: 3410 (OH), 1718, 1595, 1495, 1383, 1363. MS: 270, 255, 202 (100%), 185, (lit. mp 226–227°). **7**, xanthotoxin, mp 147° $[M]^+$ at *m/z* 216, $C_{12}H_8O_4$. IR ν_{max} cm^{-1}: 1710, 1610, 1498. (lit. mp 146°)[11]. **11**, isogosferol, mp 63°, $[M]^+$ at *m/z* 286, $C_{16}H_{14}O_5$. *IR* ν_{max} cm^{-1}: 3560, 1725, 1690, 1610. MS: 273, 272, 245, 185. **12**, alloisoimperatorin, mp 213°, $[M]^+$ at *m/z* 270, $C_{16}H_{14}O_4$. IR ν_{max} cm^{-1}: 3310, 1720, 1600, 1470, 1430, 1160, 1120, 850. MS: 270 $[M]^+$, 255 $[M-Me]^+$, 202 (100%), 174, 157. **8**, imperatorin, mp 102°, $[M]^+$ at *m/z* 270, $C_{16}H_{14}O_4$. IR ν_{max} cm^{-1}: 1718, 1595, 1497, 1383, 1360. (lit. mp 102°)[8]. **9**, isoheraclenin, mp 132°, $[M]^+$ at *m/z* 286, 3 $C_{16}H_{14}O_5$. IR ν_{max} cm^{-1}: 1710, 1580, 1400, 1380, 1365, 1330. MS: 286, 201, 202 (100%), 256, 145. **10**, heracenol, mp 117–118°, $[M]^+$ at *m/z* 304, $C_{16}H_{16}O_6$. IR ν_{max} cm^{-1}: 3540, 1720, 1605, 1491, 1388, 1370. MS: *m/z* at 304 $[M]^+$, 286 $[M-H_2O]^+$, 289 $[M-Me]^+$, 245 $[M-Me-MeCHO]^+$, 202 (100%).

Acetylation of compounds **10–12**. **10** (0.095 g), **11** (0.03 g) and **12** (0.025 g) in C_5H_5N (1 ml) were treated with Ac_2O (2 ml) and left overnight. After usual work-up **14** (0.04 g), mp 101–102°, **15** (0.03 g), mp 65°, **18** (0.025 g), mp 203° and **13** (0.018 g), mp 146° were obtained. The IR of these compounds were very similar. MS: **14**, $[M]^+$ at *m/z* 346. **15** $[M]^+$ at *m/z* 388. **18**, $[M]^+$ at *m/z* 328. **13**, $[M]^+$ at *m/z* 312.

Partial synthesis of **6**. **14** (0.03 g) in C_5H_5N (1 ml) was treated with $POCl_3$ (5 drops) and the reaction mixture left overnight. After usual work-up, the colourless crystals of acetylisogosferol were recovered.

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