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CONSTITUENTS OF *HELICHRYSUM VISCOSUM* VAR. *BRACTEATUM* DC.[1]

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Abstract—*Helichrysum viscosum* var. *bracteatum* DC. has been found to contain 4',5,7-trihydroxy-3',6-dimethoxyflavone, 4',5-dihydroxy-6,7-dimethoxyflavone (cirsimaritin), naringenin, eriodictyol and homoeriodictyol. The synthesis of 4',5,7-triethoxy-3',6-dimethoxyflavone and of some analogous flavones and their corresponding chalcones is described.

INTRODUCTION

SEVERAL *Helichrysum* species (Compositae) and the numerous variously colored cultivars of *H. bracteatum* have been studied by a number of investigators, most recently in detail by Hänsel and his co-workers.[3–9] We have investigated a specimen of *H. viscosum* var. *bracteatum* DC.[10] of Australian origin and have isolated a number of compounds, some already known as constituents of this plant and some that have hitherto not been found in the European cultivars.

RESULTS AND DISCUSSION

Naringenin, eriodictyol and homoeriodictyol, 4',5,7-trihydroxy-3',6-dimethoxyflavone (1a)[11] and 4',5-dihydroxy-6,7-dimethoxyflavone (1e) have been isolated under conditions that indicate that they occur in unglycosylated form in the plant. Flavone 1e (cirsimaritin) has not been reported to occur naturally, but its 4'-glycoside, cirsimarin, was isolated from *Cirsium maritimum*.[12, 13]

The present studies were carried out on the whole plant (aerial parts); earlier work[3–9] was confined largely to the inflorescence, the most conspicuous feature of which is the showy involucral bracts. Extraction of the dried plant with hexane yielded a solution from which

[1] Contribution No. 2085 from the Department of Chemistry, University of California, Los Angeles.
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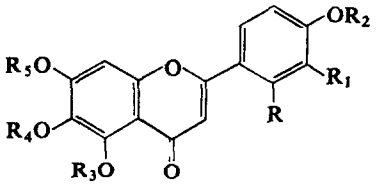
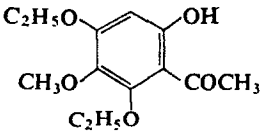
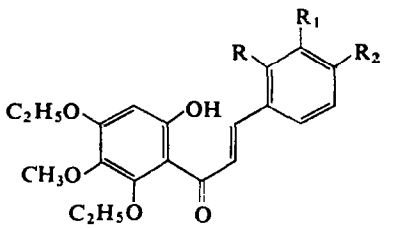
[3] R. HÄNSEL, L. LANGHAMMER and A. G. ALBRECHT, *Tetrahedron Letters* 599 (1962).
[4] H. RIMPLER, L. LANGHAMMER and H. J. FRENZEL, *Planta Med.* **11**, 325 (1963).
[5] R. HÄNSEL, L. LANGHAMMER and A. G. ALBRECHT, *Sci. Pharm.* **31**, 88 (1963).
[6] R. HÄNSEL and L. LANGHAMMER, *Arch. Pharm.* **296**, 619 (1963).
[7] H. RIMPLER and R. HÄNSEL, *Arch. Pharm.* **298**, 838 (1965).
[8] R. HÄNSEL, H. RIMPLER and R. SCHWARZ, *Tetrahedron Letters* 1545 (1965).
[9] R. HÄNSEL, H. RIMPLER and R. SCHWARZ, *Tetrahedron Letters* 735 (1967).
[10] We are grateful to Dr. W. Bottomley, C.S.I.R.O., Canberra, Australia, for providing us with the plant material, and to Dr. N. T. Burbidge for the botanical identification.
[11] J. W. APSIMON, N. B. HAYNES, K. Y. SIM and W. B. WHALLEY, *J. Chem. Soc.* 3780 (1963).
[12] N. MORITA and M. SHINIEZU, *J. Pharm. Soc. Japan* **83**, 615 (1963).
[13] K. FUKUI, T. MATSUMOTO and T. KINOSHITA, *Bull. Chem. Soc. Japan* **37**, 662 (1964).

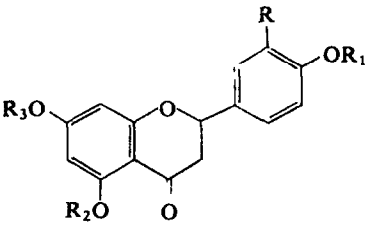
flavone 1a separated on concentration and cooling. After purification by preparative thin-layer chromatography the compound melted at 259–260°. It was a trihydroxy-dimethoxy-flavone, and yielded a triacetate (1b), m.p. 217°, a trimethyl ether (1c), m.p. 174–175°, and a triethyl ether (1d), m.p. 173–174°. Although the melting point of the flavone did not correspond with that of a known compound, its derivatives had properties that agreed with those reported for those of 4′,5,7-trihydroxy-3′,6-dimethoxyflavone, isolated from *Digitalis lanata*.[11] The u.v. spectral properties of 1a (Table 1), and the NMR spectra (Table 2) of its derivatives supported this structure: the presence of the 5-hydroxyl group was shown by the





1a: R=R$_2$=R$_3$=R$_5$=H; R$_1$=OCH$_3$; R$_4$=CH$_3$
b: R=H; R$_1$=OCH$_3$; R$_2$=R$_3$=R$_5$=COCH$_3$; R$_4$=CH$_3$
c. R=H; R$_1$=OCH$_3$, R$_2$=R$_3$=R$_4$=R$_5$=CH$_3$
d: R=H; R$_1$=OCH$_3$; R$_2$=R$_3$=R$_5$=C$_2$H$_5$; R$_4$=CH$_3$
e: R=R$_1$=R$_2$=R$_3$=H; R$_4$=R$_5$=CH$_3$
f: R=R$_1$=H; R$_2$=R$_3$=COCH$_3$; R$_4$=R$_5$=CH$_3$
g: R=R$_1$=H; R$_2$=R$_3$=R$_4$=R$_5$=CH$_3$
h. R=H; R$_1$=OC$_2$H$_5$; R$_2$=R$_4$=CH$_3$; R$_3$=R$_5$=C$_2$H$_5$
i: R=H; R$_1$OR$_2$=O·CH$_2$·O, R$_3$=R$_5$=C$_2$H$_5$; R$_4$=CH$_3$





3a: R=H; R$_1$=OCH$_3$; R$_2$=OC$_2$H$_5$
b: R=H; R$_1$=OC$_2$H$_5$; R$_2$=OCH$_3$
c: R=H; R$_1$=R$_2$=OCH$_3$
d: R=OC$_2$H$_5$; R$_1$=OCH$_3$; R$_2$=H
e: R=H, R$_1$R$_2$=O·CH$_2$·O

4a: R=R$_1$=R$_2$=R$_3$=H
b: R=R$_2$=H; R$_1$=R$_3$=COCH$_3$
c. R=R$_2$=H; R$_1$=R$_3$=CH$_3$
d: R=OH; R$_1$=R$_2$=R$_3$=H
e: R=OCOCH$_3$; R$_1$=R$_2$=R$_3$=COCH$_3$
f: R=OCH$_3$; R$_1$=R$_2$=R$_3$=H

spectral shift caused by aluminum chloride,[14] and the bathochromic effect upon the long wavelength absorption maximum caused by sodium acetate indicated the presence of a 7-hydroxyl group. The NMR spectrum of the triacetate (1b) of 1a showed the typical signal for the 5-acetoxyl group (2·48 ppm),[15,16] and the presence of a 7-hydroxyl group in 1a was indicated by the shift in the signal for the C-8 proton in the trimethyl ether (1c) from 6·84 ppm to 7·36 ppm in the triacetate. The 32° difference in melting point between that reported[11] for the *Digitalis* flavone (m.p. 227–228°) and that observed by us (m.p. 259–260°) is not

[14] L. JURD, In *The Chemistry of Flavonoid Compounds* (Edited by T. A. GEISSMAN), p. 107. MacMillan, New York (1962).
[15] J. MASSICOT, J. P. MARTHE and S. HEITZ, *Bull. Soc. Chim. France* 2712 (1963).
[16] W. E. HILLIS and D. H. S. HORN, *Australian J. Chem.* **18**, 531 (1965).

unprecedented for polyhydroxypolymethoxyflavones of this kind,[17] and is presumably due to dimorphism. The *D. lanata* flavone was unfortunately not available for a direct comparison, but a comparison of its triethyl ether with 1d showed their identity.

TABLE 1. ULTRA-VIOLET SPECTRAL DATA OF THE FLAVONOIDS*

Compound	λ_{max} nm (log ϵ)			
	Ethanol	Ethanol/NaOAc	Ethanol/NaOH	Ethanol/$AlCl_3$
1a	252(4·20) 274(4·25) 344(4·42)	242†(4·28) 277(4·36) 353(4·31)	277(4·27) 310†(3·87) 402(4·36)	258(4·16) 289(4·27) 358(4·42)
1b	264(4·31) 312(4·41)			
1c	242(4·45) 265(4·31) 326(4·46)			
1d	242(4·35) 266(4·26) 327(4·49)			
1e	276(4·38) 336(4·48)	276(4·27) 366(4·52) 410†(3·81)	276(4·30) 292(4·24) 392(4·56)	288(4·48) 301(4·49) 353(4·55)
1f	262(4·37) 308(4·48)			
1g	267(4·27) 321(4·53)			
4a	225†(4·37) 289(4·25) 325†(3·72)	224†(4·39) 292(4·15) 327(4·19)		223†(4·12) 308(4·36) 375(3·63)
4b	275(4·10) 337·5(3·60)	277·5(4·10) 330(3·80)		299(4·12) 391(3·72)
4c	226†(4.47) 288(4·29) 330(3·63)	228†(4·47) 288(4·27) 332(3·65)		223†(4·61) 307(4·42) 376(3·74)
4d	228†(4·34) 289(4·30) 328†(3·74)	226†(4·14) 290(4·18) 329(4·19)		225†(4·52) 308(4·43) 375(3·72)
4e	258(4·26) 312(3·83)			

* Spectra were measured in 95% ethanol with a Cary 14 u.v. spectrophotometer.
† Inflection.

The triethyl ether (1d) was synthesized to complete the establishment of its structure. Ethylation of phloroacetophenone, followed by persulfate oxidation and methylation[11,18] yielded 4,6-diethoxy-2-hydroxy-5-methoxyacetophenone (2), which was condensed with

[17] L. FARKAS, M. NOGRADI, V. SUDARSANAM and W. HERZ, *J. Org. Chem.* **31**, 3228 (1966).
[18] L. R. ROW, V. D. N. SASTRI, T. R. SESHADRI and T. R. THIRUVENGADAM, *Proc. Indian Acad. Sci.* **28A**, 189 (1948).

3-methoxy-4-ethoxybenzaldehyde to give the chalcone (3a). Oxidative cyclization of 3a with selenium dioxide gave the flavone, identical with the triethyl ether (1d) of 1a. In the course of these synthetic experiments a number of other chalcones (3b-e) and flavones (1h-i) were prepared (Table 3).

TABLE 2. NMR CHEMICAL SHIFTS OF PROTONS OF THE FLAVONOIDS*

(Shifts (ppm) measured in $CDCl_3$ except where otherwise stated)

Proton positions	Compounds								
	1b	1c	1f	1g	4a†	4b	4c†	4d†	4e
H at									
2	—	—	—	—	5·44[q]	5·42[q]	5·48[q]	5·48[q]	5·48[q]
3	6·62[s]	6·55[s]	6·89[s]	6·68[s]	2·99[q]	2·98[q]	2·98[q]	2·94[q]	2·93[q]
6	—	—	—	—	5·98[s]	6·30[s]	6·05[s]	5·98[s]	6·82[d]
8	7·36	6·84	6·54[s]	6·82[s]	5·98[s]	6·30[s]	6·05[s]	5·98[s]	6·57[d]
2′,6′	7·36	7·37	7·88[d]	7·84[d]	7·43[d]	7·44[d]	7·50[d]	6·98	7·31
3′,5′	7·36	7·37	7·26[d]	7·01[d]	6·92[d]	7·12[d]	6·98[d]	6·98	7·31
OH, OCH_3 or $OCOCH_3$ at									
5	2·48[s]	4·00[s]	2·47[s]	3·99[s]	12·16[s]	11·90[s]	12·20[s]	12·15[s]	2·42[s]
6	3·87[s]	4·00[s]	3·99[s]	3·99[s]	—	—	—		
7	2·38[s]	3·84[s]	3·86[s]	3·92[s]	—	2·31[s]	3·87[s]		2·28[s]
3′	3·91[s]	3·95[s]	—	—	—				2·28[s]
4′	2·33[s]	3·82[s]	2·30[s]	3·86[s]	—	2·26[s]	3·82[s]		2·28[s]

* Shifts measured in a Varian A60 instrument and tetramethylsilane was the internal reference (δ,0·00).
[s] singlet, [d]doublet, [q] quartet.
† Measured in deuteroacetone.

TABLE 3. MELTING POINTS AND ANALYSES OF SYNTHETIC CHALCONES (3b TO e) AND FLAVONES (1h AND i)

Compound	M.p (°)	Anal (%)			
		Calc.		Found	
		C	H	C	H
3b; $C_{23}H_{28}O_7$	128–129	66·33	6·78	66·61	7·00
3c; $C_{22}H_{26}O_7$	127–128	65·66	6·51	65·69	6·62
3d; $C_{23}H_{28}O_7$	107–108	66·33	6·78	66·62	6·83
3e; $C_{21}H_{22}O_7$	121–123	65·27	5·74	65·50	6·01
1h; $C_{23}H_{26}O_7$	157–158	66·65	6·32	66·80	6·51
1i; $C_{21}H_{20}O_7$	207–208	65·61	5·24	65·44	5·42

Ether extraction of the plant material, after exhaustion with hexane, yielded a solution which upon concentration deposited a second compound. This substance, m.p. 263–265°, proved to be a dihydroxydimethoxyflavone (1e). Its dimethyl ether was identical with scutellarein tetramethyl ether (1g). The NMR spectra of its acetate (1f) and dimethyl ether showed the A_2B_2 system (7·88, 7·26 (1f) and 7·84, 7·01 (1g) ppm, J = 9) characteristic of a 4′-substituted flavone. The presence of a 5-hydroxyl group was shown by the presence of the three-proton singlet at 2·47 ppm in the acetate, and the presence of a methoxyl rather than a

hydroxyl group at C-7 was strongly indicated by the fact that the proton at C-8, a sharp one-proton singlet, was not shifted downfield upon acetylation as was observed in the case of the 7-hydroxy compound 1a. The presence of the 4'-hydroxyl group was indicated by the shift of the long-wavelength u.v. absorption maximum of 1e from 336 nm (log ϵ 4·48) in ethanol to 392 nm (log ϵ 4·56) in ethanolic alkali. These observations indicated that flavone 1e was 4',5-dihydroxy-6,7-dimethoxyflavone, which is a compound (cirsimaritin) that occurs as the 4'-glucoside (cirsimarin) in *Cirsium maritimum*. Direct comparison of 1e with a specimen of cirsimaritin[19] showed their identity.

Chromatography (silica gel) of the residual solution from which 1e had separated resulted in the isolation of naringenin (4a). Although the flavonone showed a single spot on TLC and gave the correct melting point and elemental analysis, its mass spectrum showed the presence of a small amount of contaminant with m/e=302 besides the principal molecular ion at m/e=272. This compound was later recognized as homoeriodictyol.

In a separate extraction of the plant material with benzene the extract upon evaporation deposited crystalline 1e. Manipulation of the residual oily solution by water extraction and ether extraction of the aqueous phase resulted in the isolation of eriodictyol (4d). The eriodictyol was contaminated with a persistent impurity which showed up as a faint accompanying spot on TLC and as a minor peak at m/e=302 in the mass spectrum of the eriodictyol (mol. ion 288). The contaminant could not be isolated in the pure state, but was identified as homoeriodictyol (m.w. 302) by TLC comparison with an authentic specimen. The co-occurrence of eriodictyol and homoeriodictyol has been observed before.[20]

The fact that the *Digitalis lanata* flavone (1a), cirsimaritin (1e) and homoeriodictyol have been found for the first time in *H. viscosum* despite the long history of investigations upon the plant may be attributable to the fact that the plant used in this investigation was the native Australian species, probably an earlier form from which the European plant, widely cultivated as an ornamental, has developed by cultivation and selection. Intraspecific variation in plants, as reflected in their chemical constitution, is now well known, and the difference between the native *H. viscosum* var. *bracteatum* DC. (formerly referred to as *H. bracteatum* (Willd) DC.[21]) and the European cultivars is but another example of the existence of "chemovars" within a species.

EXPERIMENTAL[22]

Extraction of plant material. Ground whole plant (1 kg) was exhaustively extracted (Soxhlet) successively with hexane (A), ether (B) and chloroform (C). The residual marc gave no color tests for flavonoid compounds and was discarded.

4',5,7-Trihydroxy-3',6-dimethoxyflavone (1a). The hexane extract (A) was concentrated to 250 ml and cooled, when 500 mg of a yellow, crystalline solid separated. This was found (by TLC) to be a mixture, and was subjected to chromatography over silica gel. Benzene-ether (9:1) eluted a fraction from which flavone 1e (see below) was isolated, but other fractions were still mixtures. Purification of fractions rich in 1a by preparative TLC resulted in the isolation of the pure flavone, m.p. 259–260° (reported,[11] m.p. 227–228°). The compound could advantageously be purified by preparing the acetate from crude material, purifying this by recrystallization, and hydrolyzing it with conc. HCl to regenerate the flavone. (Calc. for $C_{17}H_{14}O_7$: C, 61·83; H, 4·25; Found: C, 62·17; H, 4·63%).

[19] We are grateful to Professor K. Fukui for a specimen of the flavone.

[20] T. A. GEISSMAN, *J. Am. Chem. Soc.* **62**, 3258 (1940).

[21] N. T. BURBIDGE and M. GRAY, *The Plants of the Australian Capital Territory*. Division of Plant Industry, C.S.I.R.O., Canberra (1963).

[22] Melting points were measured in capillary tubes in a Swissco melting-point apparatus and are corrected. Thin-layer chromatograms (TLC) were prepared with Merck silica gel G, developed with chloroform: methanol, 5:1. The NMR spectra were measured with a Varian A-60 instrument with the use of tetramethylsilane as an internal standard.

Acetate of 1*a* (1*b*). Acetylation of 250 mg of the flavone 1a with acetic anhydride-pyridine yielded the triacetate, colorless needles from ethyl acetate-hexane, m.p. 217° (reported,[11] m.p. 220°). (Calc. for $C_{23}H_{20}O_{10}$: C, 60·52; H, 4·42. Found: C, 60·60; H, 4·28%). The NMR spectrum of 1b showed the expected features (Table 2).

Trimethyl ether of 1*a* (1*c*). Methylation of 150 mg of the flavone 1a with 3·5 ml of methyl iodide and 4·5 g of dry K_2CO_3 in 140 ml of acetone (reflux) yielded 110 mg of the trimethyl ether, colorless cubes from chloroform-ether-hexane, m.p. 174–175° (reported[11,23] m.p. 178–179°). (Calc. for $C_{20}H_{20}O_7$: C, 64·51; H, 5·41; Found: C, 64·61; H, 5·38%).

Triethyl ether of 1*a* (1*d*). The flavone was ethylated with ethyl iodide substantially as described for the methylation, 150 mg of flavone yielding 120 mg of the triethyl ether, pale yellow cubes from ethyl acetate-hexane, m.p. 173–174° (mixed m.p. with a specimen prepared from the *Digitalis lanata* flavone[11] 172–174°).[24] (Calc. for $C_{23}H_{26}O_7$: C, 66·65; H, 6·32; Found: C, 66·62; H, 6·29%).

4,6-*Diethoxy*-2-*hydroxy*-5-*methoxyacetophenone* (2). A mixture of 800 mg of 4,6-diethoxy-2,5-dihydroxy acetophenone,[11,18] 500 mg of dimethyl sulfate, 2 g of anhydrous K_2CO_3 and 20 ml of acetone were refluxed for 8 hrs. The filtered solution was concentrated to give a yellow oil (700 mg) which crystallized on standing at 5°. Recrystallization from light petroleum gave colorless prisms, m.p. 65–66·5°. This compound was previously obtained as an oil[11,18] and was characterized as the crystalline *p*-nitrobenzoate. (Calc. for $C_{13}H_{18}O_5$: C, 61·42; H, 7·08; Found: C, 61·50; H, 7·30%).

4,4′,6′-*Triethoxy*-2′-*hydroxy*-3,5′-*dimethoxychalcone* (3*a*). A mixture of 2·5 g of 4,6-diethoxy-2-hydroxy-5-methoxyacetophenone (2), 1·8 g of 4-ethoxy-3-methoxybenzaldehyde and 5 ml of 50% ethanolic NaOH was heated on a water bath for 1 hr and poured into dil HCl. The product was recrystallized from methanol as orange needles, m.p. 140–142°. (Calc. for $C_{23}H_{28}O_7$: C, 66·33; H, 6·78; Found: C, 66·40; H, 6·86%).

4′,5,7-*Triethoxy*-3′,6-*dimethoxyflavone* (1*d*). A mixture of 1 g of the chalcone 3a, 1 g of SeO_2 and 15 ml of *n*-amyl alcohol was refluxed for 16 hrs. The Se was filtered and the amyl alcohol removed by steam distillation. The residue was recrystallized from acetone-methanol as yellow prisms, m.p. 172–174°, mixed m.p. with 1d prepared from 1a, 173–174°. (Calc. for $C_{23}H_{26}O_7$: C, 66·65; H, 6·32. Found: C, 66·82; H, 6·44%).

4′,5-*Dihydroxy*-6,7-*dimethoxyflavone* (1*e*). The ether extract (B) of the hexane-extracted plant was concentrated to 350 ml and cooled, 550 mg of flavone 1e (cirsimaritin) was deposited. Crystallized from methanol, the compound formed yellow flakes, m.p. 263–265°; mixed with a specimen of cirsimaritin,[25] the m.p. was 263–265°. (Calc. for $C_{17}H_{14}O_6$: C, 64·96; H, 4·49; Found: C, 65·18; H, 4·55%).

Cirsimaritin diacetate (1*f*). Acetylation of 1e with acetic anhydride-pyridine gave the colorless acetate, needles from ethyl acetate-hexane, m.p. 202–203°. (Calc. for $C_{21}H_{18}O_8$: C, 63·31; H, 4·55; Found: C, 63·41; H, 4·48%).

Cirsimaritin dimethyl ether (*scutellarein tetramethyl ether*) (1*g*). Methylation of cirsimaritin with methyl iodide-K_2CO_3 in acetone yielded the fully methylated flavone; colorless flakes from chloroform-ether-hexane, m.p. 162° (reported[12,13] m.p. 161–162°). (Calc. for $C_{19}H_{18}O_6$: C, 66·66; H, 5·30; Found: C, 66·82; H, 5·44%).

Naringenin (4*a*). After the separation of the flavone 1e from the ether extract, the residual solution was diluted with ether and the solution washed with dilute alkali to remove all of the phenolic material. After recovery of the acidic pigments the crude mixture was chromatographed on silica gel. Naringenin was found in benzene and benzene-ether (50:1) eluates (later fractions afforded additional amounts of the flavones 1a and 1b). Recrystallized from aqueous methanol, naringenin had m.p. 250–251° (reported[26] m.p. 250–251°) and showed no depression in m.p. when mixed with an authentic specimen. (Calc. for $C_{15}H_{12}O_5$: C, 66·17; H, 4·44; Found: C, 66·32; H, 4·58%). The naringenin was further characterized by the preparation of its diacetate (4b), m.p. 142° (reported[26] m.p. 140–143°), and its 4′,7-dimethyl ether (4c) (with diazomethane), m.p. 120° (reported[27] m.p. 118–119°).

Additional amounts of 1a, 1e and 4a were obtained by appropriate manipulation of the chloroform extract (C) of the ether-extracted plant material.

Eriodictyol (4*d*). A benzene extract of the plant material was allowed to evaporate, in the course of which flavone 1e separated. The oily residue was dissolved in ether (when more 1e was deposited) and the ether solution washed thoroughly with water. Extraction of the clarified aqueous phase with ether yielded 200 mg of eriodictyol (4d), needles from aqueous methanol, m.p. 264–265° (reported[20] m.p. 265–266°). The TLC of the compound showed a spot of minor intensity that corresponded with that given by homoeriodictyol when a direct comparison was made. (Calc. for $C_{15}H_{12}O_6$: C, 62·50; H, 4·17; Found: C, 62·55; H, 4·43%).

[23] A. OLIVERIO, G. B. MARINI-BETTOLO and G. BARGELLINI, *Gazz. Chim. Ital.* **78**, 363 (1948).

[24] The m.p. of 1d was reported as 165–168°,[11] but the m.p. of the specimen provided by Professor Whalley could be raised to 173° by repeated recrystallization.

[25] Although the reported[13] melting point of cirsimaritin is 257–258°, the compound from *Cirsium maritimum* melted in our hands at 262–264°.

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[27] F. E. KING, M. F. GRUNDON and K. G. NEILL, *J. Chem. Soc.* 4580 (1952).

The eriodictyol was further characterized as the tetraacetate (4e), m.p. 140° (reported[20] m.p. 136–137°). (Calc. for $C_{23}H_{20}O_{10}$: C, 60·52; H, 4·42; Found: C, 60·65; H, 4·54%). The mass spectrum of 4d showed a small peak at m/e = 302, corresponding with the molecular ion of homoeriodictyol (4f), besides the principal molecular ion peak of eriodictyol at m/e = 288.

Chalcones (3*b*–3*e*) *and Flavones* (1*h and* 1*i*). By use of the general method exemplified in the preparation, as described above, of 3a and 1d, the new chalcones and flavones shown in Table 3 were prepared.

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