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ESQUITERPENE LACTONES, FLAVONOIDS AND COUMARINS FROM *CENTAUREA COLLINA*

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Key Word Index—*Centaurea collina* subsp. *collina*; Compositae; sesquiterpene lactones; guaianolides; flavonoids; coumarins; ^{13}C NMR.

Abstract—The isolation and characterization of two coumarins, five flavonoids and four sesquiterpene lactones from the aerial parts of *Centaurea collina* are reported. The ^{13}C NMR data are included.

INTRODUCTION

Centaurea collina L. subsp. *collina* is a herbaceous plant with pale yellow flowers which occurs in the Iberian Peninsula, the south of France and Italy [1]. It belongs to an extensively studied genus, from which many metabolites, mainly sesquiterpene lactones [2] and flavonoids [3], have been isolated. From *C. collina* we have already reported two guaianolides [4] and Voirin *et al.* have reported several flavonoids [5–7]. We now report the isolation of further sesquiterpene lactones and several flavonoids and coumarins and aromatic acids. We also report the ^{1}H–^{13}C heteronuclear correlation for two guaianolides.

RESULTS AND DISCUSSION

Chromatographic separation of the ether-soluble portion of a methanolic extract afforded, in addition to benzoic, vanillic and protocatechuic acids, two coumarins identified as scoparone (**1**) and scopoletin (**2**) by spectroscopic methods [8], including ^{13}C NMR [9, 10], five flavonoids and four sesquiterpene lactones.

The flavonoids isolated were identified [11, 12] as pectolinarigenin (**3**), hispidulin (**4**), apigenin (**5**), eupafolin (**6**) and luteolin (**7**). The position of the methoxyl group at C-6 in the three 6-methoxyflavones **3**, **4** and **6** followed from the UV [13] and the mass spectral [14] data. As far as we know, the ^{13}C NMR spectra of compounds **3** and **6** have not been described in the literature so far. Although the ^{13}C NMR spectrum of compound **4** has already been reported [3], it is also included for comparison (Table 1). The assignment of the signals was based on the work of Mabry *et al.* [15] and distortionless enhancement by polarization transfer (DEPT) experiments. A CH signal at δ94 was assignable to the unsubstituted C-8; this value is in the characteristic zone (δ90–95) of this carbon when it is not substituted [3, 16]. A quaternary signal at δ131 was assigned to C-6 substituted by a methoxyl group. It is interesting to note that the flavonoids isolated by us are flavones, while the flavonoids isolated by Voirin *et al.* [5–7] are flavonols, except for pectolinarigenin.

The four sesquiterpene lactones isolated belong to the guaianolides group. The structures of two of them (**8** and **9**), we have reported previously [4] as 3β-hydroxy-8α-epoxymethyl acriloiloxy-4(15),10(14),11(13)-trien-(1αH),(5αH)-guaian-6,12-olide and its 11β,13-dihydroderivative respectively. In that report [4], we characterized the two guaianolides by spectroscopic methods, including DEPT techniques for ^{13}C NMR. Nevertheless, some resonances could not be assigned without ambiguity. We have now resolved these ambiguities by ^{1}H–^{13}C heteronuclear correlation (Table 2). Thus, in compound **8**, the signal at δ78.1 is assigned to C-6 by its correlation with the triplet at δ4.22 characteristic of H-6 and the signal at δ75.2 is assigned to C-8 as it is correlated with the doublet triplet at δ5.05 of H-8. In the same way, the signals at δ45.3 and 46.9 are assigned at C-1 and C-7 by their correlation with the quadruplet at δ2.91 for H-1 and the triplet triplet at δ3.06 of H-7, respectively. Similarly the signals at δ38.3 and 35.6 are assigned at C-2 and C-9 as they are correlated with the signals at δ1.68 and 2.11 of H-2 and 2.30 and 2.60 of H-9, respectively. In compound **9**, the ambiguities in the ^{13}C NMR spectrum interpretation were resolved by ^{1}H–^{13}C heteronuclear correlation also. Thus, the signals at δ51.0 and 52.2 are assigned at C-5 and C-7 respectively by their correlation with the triplet at δ2.77 of H-5 and the quadruplet at δ2.24 of H-7. The other ambiguities of the ^{13}C NMR spectrum interpretation, were similarly resolved.

The remaining two guaianolides were identified as deacylcynaropicrin (**10**) [17] and its 11β,13-dihydroderivative **11** [18] by spectral data as well as by comparison with the corresponding published data [19]. We include the ^{13}C NMR data (Table 2), as it has not been described in the literature so far. Of the guaianolides isolated, the deacylcynaropicrin **10** is widely distributed in Compositae, whilst its 11β,13-dihydroderivative (**11**) has been reported previously from *Tricholepis glaberrima* [18], *Saussurea affinis* [20] and *Centaurea canariensis* [21]. Compound **8** has been isolated previously from *Centaurea solstitialis* [22]. Its 11β,13-dihydroderivative (**9**) has been reported by us for the first time from *C. collina* [4].

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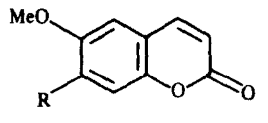

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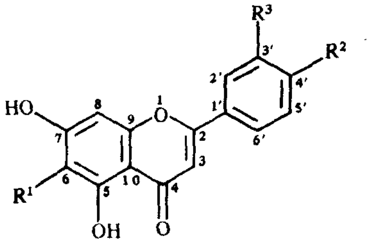
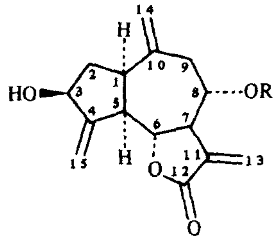


3 $R^1 = R^2$ = OMe, R^3 = H
4 R^1 = OMe, R^2 = OH, R^3 = H
5 $R^1 = R^3$ = H, R^2 = OH
6 R^1 = OMe, $R^2 = R^3$ = OH
7 R^1 = H, $R^2 = R^3$ = OH



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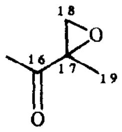

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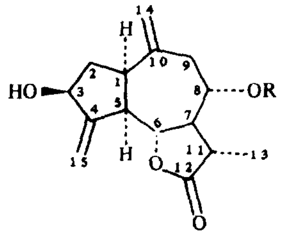

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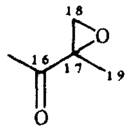

11 R = H

Table 1. ^{13}C NMR of flavonoids **3**, **4** and **6** from *C. collina*

C	3	4	6
2	163.34	163.76	164.10
3	103.04	102.36	102.54
4	182.14	182.10	182.16
5	152.75[a]	152.75[a]	152.94[a]
6	131.37	131.31	131.48
7	157.33	157.25	157.35
8	94.30	94.21	94.24
9	152.41[a]	152.36[a]	152.50[a]
10	104.12	104.03	104.22
1'	122.85	121.19	119.08
2'	128.26	128.43	113.49
3'	114.56	115.92	145.87
4'	162.29	161.13	149.81
5'	114.56	115.92	116.15
6'	128.26	128.43	121.70
–OMe (C_6)	59.93	59.92	60.07
–OMe ($C_{6'}$)	55.54	—	—

[a]Chemical shifts in each column may be interchanged.

Table 2. ^{13}C NMR of guaianolides **8**–**11** from *C. collina*

C	8	9	10	11
1	45.3	44.5	45.2[a]	44.2[a]
2	38.3	38.7	39.2[b]	39.0[b]
3	73.2	73.3	73.7	73.6
4	151.8	152.4	152.4	153.0
5	51.5	51.0	51.3[a]	50.7[a]
6	78.1	78.7	79.0	79.1
7	46.9	52.2	51.0[a]	56.0[a]
8	75.2	77.7	71.9	74.9
9	35.6	39.0	41.3[b]	44.8[b]
10	141.6	141.8	142.7	143.2
11	136.8	41.3	138.1	42.0
12	169.5	178.4	169.9	—
13	123.6	15.2	123.2	15.9
14	118.1	117.5	117.1	116.2
15	113.8	112.8	113.2	112.0
16	174.8	175.0	—	—
17	76.0	75.9	—	—
18	68.1	68.0	—	—
19	21.6	21.8	—	—

[a,b]Chemical shifts denoted by the same letter in each column may be interchanged.

EXPERIMENTAL

Centaurea collina was collected, classified and extracted as described previously [4]. The Et_2O re-extract was subjected to chromatography on a silica gel column using mixtures of hexane–CH_2Cl_2–EtOAc as eluent. Six main groups (I–VI) of fractions were obtained, with the following proportions of CH_2Cl_2–EtOAc: I (19:1), II (19:1 to 9:1), III (17:3), IV (4:1 to 7:3), V (7:3 to 1:1) and VI (9:11). Compound **2** (65 mg) and **4** (59 mg) crystallized directly from the group II and IV fractions respectively. Repeated chromatographic process afforded: compound **1** (12 mg) from group I; benzoic acid (23 mg) and compound **3** (22 mg) from group III; vanillic acid (71 mg) and compound **5** (19 mg) from the mother liquors of group IV; protocatechuic acid (26 mg) and compounds **10** (10 mg), **11** (5 mg), **6** (14 mg) and **7** (10 mg) from group V and compounds **8** (30 mg) and **9** (15 mg) from group VI.

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