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VOLATILE PHENOLIC CONSTITUENTS OF SPANISH ORIGANUM (*CORIDOTHYMUS CAPITATUS*) ESSENTIAL OIL

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Key Word Index—*Coridothymus capitatus:* Labiatae; origanum essential oil; chemical composition; methyl diisopropylphenols.

Abstract—Analysis of the phenolic fraction of *Coridothymus capitatus* essential oil (Spanish origanum oil) indicated 7 major components. One of them is the well known carvacrol and among the others there are one diisopropylphenol and 5 methyldiisopropylphenols, which are found for the first time from a natural source.

INTRODUCTION

It is well known that carvacrol (2-methyl-5-isopropylphenol) is the main component of Spanish origanum essential oil [1–3], representing more than 60% of it, whereas thymol (5-methyl-2-isopropylphenol) is a minor one. However, there has not been any work on the other phenols in this essential oil. In a previous paper [4] we reported on the neutral components of this essential oil. In the present paper we report the components, other than carvacrol and thymol, found in the phenolic fraction.

RESULTS AND DISCUSSION

Phenols were isolated from the heavy oxygenated fraction of the oil by exhaustive extraction with 5 M NaOH [4]. Column chromatography of the phenolic fraction, followed by preparative GLC of the column subfractions, afforded 6 pure compounds (A–F). IR, MS and ^{1}H NMR data of these compounds are given in Tables 1–3, respectively. UV indicates that all these compounds are phenols [5]; A, B, D, E, F λ_{max} 281 and C λ_{max} 277 nm. IR confirms the aforementioned result (Table 1) and shows the presence of isopropyls and the probable substitution patterns on the aromatic ring [6]. The MS data are summarized in Table 2. For compounds A, B, D, E and F the MW is 192, whereas for compound C it is 178. Table 3 lists the ^{1}H NMR spectra of all 6 compounds, together with those of carvacrol (**14**), thymol (**15**) and 3-methyl-2,6-diisopropylphenol (**12**) [4] for comparison.

Compound A (**1**, *5-methyl-2,4-diisopropylphenol*)

From its spectroscopic data and taking into account that in its ^{1}H NMR spectrum both aromatic protons have a *para* relationship ($J = 0$ Hz) on the aromatic ring, only structures **1**, **2** or **3** can be assigned to it. To distinguish between them, a NOE (Nuclear Overhauser Effect) experiment [7] was carried out. When the aromatic methyl was strongly irradiated, a substantial increase ($\simeq 18\%$) of the integral due to the *ortho* aromatic proton (with respect to —OH) was observed, when compared with that due to the *meta* aromatic proton (with respect to —OH). Therefore, both the aromatic methyl and the *ortho* proton (with respect to —OH) are close together. Structures **2** and **3** can be disregarded. Compound A has structure **1** and is thus identified as 5-methyl-2,4-diisopropylphenol.

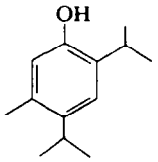
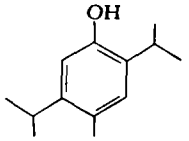
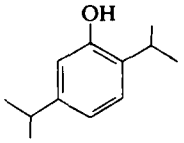
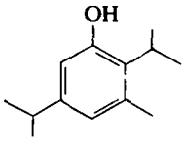
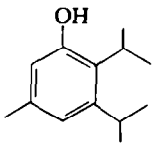
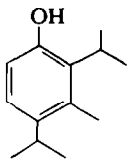
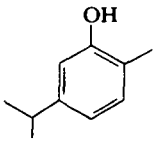
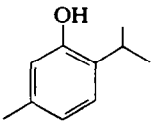
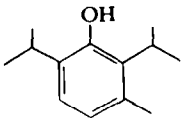
Compound B (**2**, *4-methyl-2,5-diisopropylphenol*)

As for the previous compound, the ^{1}H NMR spectrum of compound B shows that both aromatic protons have a *para* relationship ($J = 0$ Hz) on the aromatic ring. Hence, again only structures **1**, **2** or **3** can be assigned to it. But since structure **1** has already been assigned to compound A, compound B must have either structure **2** or **3**. This assumption was further confirmed by a NOE experiment similar to that performed for compound A. Both isopropyls in **3** must be almost magnetically equivalent because their chemical surroundings are alike. Thus, their components, methine and methyls, must resonate at nearly the same frequency. The above assumption does not apply for structure **2** because the chemical surroundings of both isopropyls are clearly different and so they must have unlike chemical shifts. Since the ^{1}H NMR spectrum of compound B shows well-separated signals for both isopropyls, it must have structure **2** and is identified as 4-methyl-2,5-diisopropylphenol. In addition, the IR spectrum of compound B matches well with that from 4-methyl-2,5-diisopropylphenol given by Schrewsbury [8].

Compound C (**4**, *2,5-diisopropylphenol*)

The ^{1}H NMR spectrum shows that the arrangement of the aromatic protons on the benzene ring is the same as that in carvacrol **14** and thymol **15**. Therefore, only structure **4** can be assigned to it, and compound C is identified as 2,5-diisopropylphenol. The UV,

Table 3. ^{1}H NMR spectra of isolated compounds, carvacrol (**14**), thymol (**15**) and 3-methyl-

Compound	Structure	Chemical shifts (ppm)					
		o-$(Me)_2CH$-ϕ-OH			*m*-$(Me)_2CH$-ϕ-OH		
		Methyls	Methine	*J**	Methyls	Methine	*J**
A		1.19	3.09	7	—	—	—
B		1.20	3.09	7	1.15	3.02	7
C		1.21	3.10	7	1.15	2.70	7
D		1.31	3.20	7	1.16	2.70	7
E		1.33	3.27	7	1.17	3.10	7
F		1.33	3.27	7	—	—	—
14		—	—	—	1.12	2.70	7
15		1.19	3.14	7	—	—	—
12		1.35 1.23	3.30 3.01	7 7	—	—	—

* Coupling constants are given in Hz.

2,6-diisopropylphenol (**12**)

p-$(Me)_2CH$-ϕ-OH			Me-ϕ	*o*-H-ϕ-OH		*m*-H-ϕ-OH		*p*-H-ϕ-OH		ϕ-OH
Methyls	Methine	*J**			*J**		*J**		*J**	
1.16	3.00	7	2.16	6.32	0	6.94	0	—	—	4.80
—	—	—	2.20	6.45	0	6.79	0	—	—	4.13
—	—	—	—	6.45	2.5	6.98	8	6.64	8 2.5	4.44
—	—	—	2.25	6.24	2	—	—	6.44	2	4.21
—	—	—	2.20	6.20	2.5	—	—	6.53	2.5	4.25
1.16	3.10	7	2.25	6.37	8.7	6.82	8.7	—	—	4.14
—	—	—	2.15	6.50	2.5	6.93	8.5	6.65	8.5 2.5	5.97
—	—	—	2.20	6.39	2	6.99	8	6.62	8 2	4.97
—	—	—	2.25	—	—	6.79	8	6.57	8	4.52

Table 1. IR spectra of isolated compounds

Compound	Diagnostic absorption bands (cm^{-1}) Phenol	Aromatic ring	*Gem*-dimethyl	Aromatic substitution
A	3600–3200, 1250	3020, 1620, 1585, 1505	1380, 1360	890 (1, 2, 4, 5)
B	3600–3200, 1270	3025, 1620, 1585, 1510	1380, 1360	883 (1, 2, 4, 5)
D	3610, 3530, 1260	3020, 1615, 1580, 1490	1380, 1360	850 (1, 2, 3, 5)
E	3610, 3520, 1270	1615, 1575, 1490	1380, 1360	835 (1, 2, 3, 5)
F	3610, 3530, 1270	1580, 1485	1380, 1360	805 (1, 2, 3, 4)

^{1}H NMR and MS of this compound agree well with those from an authentic sample of commercial 2,5-diisopropylphenol.

Compound D (**5**, 3-*methyl*-2,5-*diisopropylphenol*)

From the spectroscopic data and since in its ^{1}H NMR spectrum both aromatic protons are *meta* coupled ($J = 2$ Hz), only structures **5**, **6** or **7** can be assigned to compound D. One of the isopropyls resonates at δ 2.7 ppm for its methine and δ 1.16 ppm for its methyls, being analogous to the isopropyls with free-*ortho* positions from compound C and carvacrol (**14**). Structure **7** can thus be disregarded. The chemical shifts of the other isopropyl, δ 3.2 ppm for methine and δ 1.31 ppm for methyls, are very high when compared with chemical shifts of the isopropyls from compounds A and B, but similar to those of the strained isopropyl from 3-methyl-2,6-diisopropylphenol (**12**) [4], which has its two *ortho* positions substituted. Therefore, structure **6** can be ruled out because it cannot explain these 'high' chemical shifts, whereas structure **5** is satisfactory (3-methyl-2,5-diisopropylphenol).

Compound E (**7**, 5-*methyl*-2,3-*diisopropylphenol*)

^{1}H NMR data of this compound show that both aromatic protons are *meta* coupled ($J = 2$ Hz) and, as for compound D, only structures **5**, **6** or **7** can be assigned to it. Structure **5** can be disregarded because it corresponds to compound D and because in the ^{1}H NMR spectrum of compound E there is no methine absorption centered at δ 2.7 ppm. For the same reason and also because structure **6** cannot explain the 'high' chemical shifts for one of the isopropyls, δ 3.27 ppm for methine and δ 1.33 ppm for methyls, it can be eliminated. Therefore, compound E has structure **7** and it is identified as 5-methyl-2,3-diisopropylphenol.

Compound F (**8**, 3-*methyl*-2,4-*diisopropylphenol*)

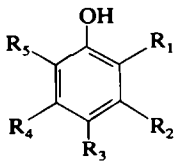
From the spectroscopic data and taking into account that in its ^{1}H NMR spectrum both aromatic protons are *ortho* coupled ($J = 8.7$ Hz), only structures **8**, **9**, **10**, **11**, **12** or **13** can be assigned to compound F. A NOE experiment irradiating strongly the aromatic methyl showed no appreciable change of the relative integral values due to both aromatic protons. Since none of the possible structures assigned to compound F have a methyl with free-*ortho* positions, the aromatic methyl does not have any aromatic proton on its *ortho* positions. Thus, structures **9**, **12** and **13** can be disregarded. On the other hand, structure **11** also can be ruled out because it cannot explain the 'high' chemical shifts of one of isopropyls, 3.27 ppm for methine and 1.33 ppm for methyls. The two remaining structures, **8** and **10**, have an isopropyl with its two *ortho* positions substituted and, in principle, both are able to explain the aforementioned 'high' chemical shifts. However, an isopropyl is more deshielded by an hydroxyl on one of its *ortho* positions than by a methyl on the same position (compare chemical shifts of isopropyls from compounds A or B) and the analogous isopropyl from compound E absorbs at exactly the same δ values. Therefore, structure **10** can be eliminated, compound F has structure **8** and is identified as 3-methyl-2,4-diisopropylphenol.

Relation between chemical shifts and steric hindrance of isopropyls

It is apparent from data given in Table 3 that, in compounds of this kind, the chemical shifts of isopropyls are dependent on the steric hindrance to which they are subjected. The larger the steric hindrance, the higher the chemical shifts. Quantitative data given in Table 3 therefore can be helpful, mainly in conjunction with NOE experiments, to establish the relative positions of substituents in an unknown compound.

Table 2. Mass spectra of isolated compounds

Compound	*m/e* 192	178	177	163	149	135	121	107	91	77	43	$M^{\ddagger} : (M+1)^{\ddagger} : (M+2)^{\ddagger}$	Molecular formula
A	22	13	100	2	5	22	8	3	9	5	12	100 : 14.2 : 1.20	$C_{13}H_{20}O$
B	27	13	100	2	7	16	9	3	7	4	9	100 : 14.3 : 1.20	$C_{13}H_{20}O$
C	—	22	—	100	3	8	20	13	8	6	16	100 : 13.3 : 1.03	$C_{12}H_{18}O$
D	21	13	100	3	4	16	7	3	8	4	9	100 : 14.2 : 1.19	$C_{13}H_{20}O$
E	29	14	100	4	25	17	15	5	11	10	10	100 : 14.3 : 1.18	$C_{13}H_{20}O$
F	27	14	100	1	10	10	7	3	6	4	8	100 : 14.3 : 1.19	$C_{13}H_{20}O$



1	$R_2 = R_5 = H$	$R_4 = Me$	$R_1 = R_3 = CH(Me)_2$
2	$R_2 = R_5 = H$	$R_3 = Me$	$R_1 = R_4 = CH(Me)_2$
3	$R_2 = R_5 = H$	$R_1 = Me$	$R_3 = R_4 = CH(Me)_2$
4	$R_2 = R_3 = R_5 = H$	$R_1 = R_4 = CH(Me)_2$	
5	$R_3 = R_5 = H$	$R_2 = Me$	$R_1 = R_4 = CH(Me)_2$
6	$R_3 = R_5 = H$	$R_1 = Me$	$R_2 = R_4 = CH(Me)_2$
7	$R_3 = R_5 = H$	$R_4 = Me$	$R_1 = R_2 = CH(Me)_2$
8	$R_4 = R_5 = H$	$R_2 = Me$	$R_1 = R_3 = CH(Me)_2$
9	$R_4 = R_5 = H$	$R_3 = Me$	$R_1 = R_2 = CH(Me)_2$
10	$R_4 = R_5 = H$	$R_1 = Me$	$R_2 = R_3 = CH(Me)_2$
11	$R_3 = R_4 = H$	$R_1 = Me$	$R_2 = R_5 = CH(Me)_2$
12	$R_3 = R_4 = H$	$R_2 = Me$	$R_1 = R_5 = CH(Me)_2$
13	$R_3 = R_4 = H$	$R_5 = Me$	$R_1 = R_2 = CH(Me)_2$
14	$R_2 = R_3 = R_5 = H$	$R_1 = Me$	$R_4 = CH(Me)_2$
15	$R_2 = R_3 = R_5 = H$	$R_4 = Me$	$R_1 = CH(Me)_2$

EXPERIMENTAL

IR spectra were run as liquid films. UV were measured in 96% EtOH. ^1H NMR were recorded in CCl_4 at 90 MHz with TMS as int. standard. MS (probe) were determined at 70 eV. Analytical GLC was carried out with a Pyrex glass capillary column (14 m × 0.6 mm i.d.) coated with Silicone OV-17 on Chromosorb R-6470-1. Operating conditions were: pres. (He) 10 torr; split ratio Perkin–Elmer No 3; FID; temp. programmed, 120° isothermal 4 min and 120–200° at 2°/min. For prep-GLC a stainless-steel column (3.5 m × 3 mm i.d.) packed with 3% SE-52 on Gas-Chrom Q, was used. Operating conditions were: He at 30 ml/min; FID; by-pass 1 : 20; isothermal 160°.

Essential oil was purchased and the phenolic fraction isolated as described in ref. [4]. The phenolic fraction (excluding carvacrol and thymol) represented less than 1% of oil; component A represented more than 90% of this fraction. R_ts (min) of components in the analytical column were: A, 31.4; B, 34.2; C, 28.8; D, 33; E, 30.2 and F, 34.2.

Isolation of components. The phenolic fraction (0.5 g) was subfractioned by column chromatography (30 × 2 cm) on 70–230 mesh Si gel, using C_6H_6 as eluent. All compounds were isolated in a pure state by repetitive prep-GLC from suitable subfractions, and collected in Pyrex capillary tubes, without cooling.

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