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Phytochemistry, 1981, Vol. 20, pp. 163–165. © Pergamon Press Ltd. Printed in England 0031-9422/81/0101-0163 $02.00/0

PHELLANDRENE ENDOPEROXIDES FROM THE ESSENTIAL OIL OF *CHENOPODIUM MULTIFIDUM*

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(*Received* 19 *March* 1980)

Key Word Index—*Chenopodium multifidum*; Chenopodiaceae; essential oil; *p*-menthanic monoterpenes; phellandrene endoperoxides.

Abstract—The essential oil of *Chenopodium multifidum* does not contain ascaridole, but does contain two isomeric endoperoxides related to α-phellandrene, besides other structurally and biogenetically related *p*-menthanic monoterpenes.

INTRODUCTION

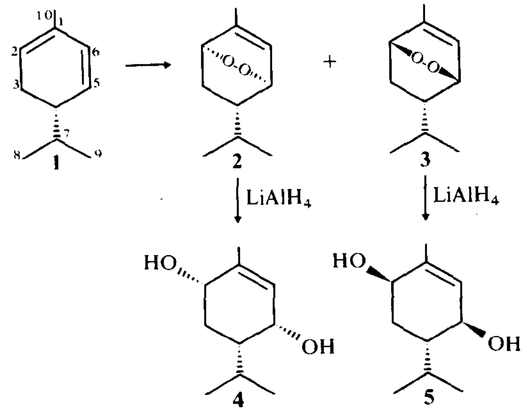
Ascaridole is the most characteristic component of the essential oils from Chenopodiaceae and is responsible for the anthelmintic properties of these oils [1].

Chenopodium multifidum L. (*Rouvieva multifida*, Moq.)* has been little studied with reports only on the isolation of α-phellandrene and anethole from Californian plants [2]; ascaridole, *p*-cymene, limonene and camphene from Brazilian plants [3]; and ascaridole, limonene, *cis*- and *trans*-carveol ('paicol') from Argentinian plants [4], with a vague allusion to the likeness of the *C. ambrosioides* essential oil.

We have re-examined the essential oil from *C. multifidum* collected at the end of October, near Babilafuente (Salamanca) in western Spain.

RESULTS AND DISCUSSION

The essential oil contained monoterpenes, but it did not contain any ascaridole. The main fraction consisted of two stereoisomeric endoperoxides (**2**, **3**) related to α-phellandrene (**1**) and so far not reported as natural products, although they were obtained by Schenck *et al.* [5,6], by photo-oxidation of α-phellandrene (**1**).



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* The material for this work was identified by Prof. B. Casaseca Mena, Department of Botany, Salamanca University, where a specimen is held (Herbarium No. 19587).

Table 1. ^1H NMR data for **2**, **3**, **6** and **7** (60 MHz, TMS)

H	**2**(CCl_4)	**3**(CCl_4)	**6**($CHCl_3$)	**7**($CHCl_3$)
2	4.20 *br. s*	4.26 *m*	—	—
3	—	—	2.48 (AB, 12, 2)	—
5	4.38 *br. d*(6)*	4.45 *m*	4.40 *m*	4.25 *m*
6	6.29 *br. d*(6)	6.10 *dq* (7,2)	6.75 *dd*(6,2)	6.56 *br. s*
8	0.98 *br. d*(7)	0.83 *br. d*	0.93 *d*(6)	0.90 *d*(6)
9			1.01 *d*(6)	0.99 *d*(6)
10	1.90 *d*(2)	1.92 *d*(2)	1.78 *br. s*	1.72 *d*(2)

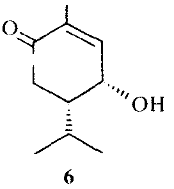
*Coupling constants (Hz) are given in parentheses.

The *cis*-endoperoxide (**2**) was an oil, $[\alpha]_D - 23°$ (*c* 1.46, $CHCl_3$), whose IR spectrum showed absorptions at 3040, 1660, 810 (C=CH) cm^{-1}. The ^1H NMR signals are shown in Table 1. MS, *m/e* (rel. int.): 168 (M^+, 5), 136 ($M^+ - O_2$, 59), 121 (136 − Me, 47), 93 (136 − C_3H_7, 100), 91 (23), 69 (21), 55 (53), 43 (59) in agreement with the structure.

The *trans*-endoperoxide (**3**), was also an oil, $[\alpha]_D - 45.5°$ (*c* 1.38, $CHCl_3$); it exhibited IR absorptions at 3040, 1650, 790 (C=CH) cm^{-1}; the ^1H NMR signals are shown in Table 1; the MS had the same fragmentation pattern as **1**.

The stereochemistry of both endoperoxides was readily adduced from the diols obtained by reduction with $LiAlH_4$: **2** gave the diol **4**, mp 148–149° and $[\alpha]_D + 88°$ (*c* 1.48, MeOH) and **3**, gave the diol **5**, mp 168–169° and $[\alpha]_D + 28.4°$ (*c* 0.46, MeOH), whose properties agreed with those reported for two *cis*-*p*-menth-6-en-2,5-diols [7–10].

The essential oil also contained two hydroxyketones, **6** and **7**, clearly related with endoperoxides **2** and **3** respectively [11].



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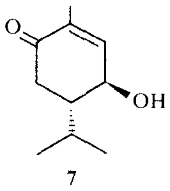

7

The major hydroxyketone **6** was an oil, $[\alpha]_D + 61.9°$ (*c* 1.4, $CHCl_3$). It was identified as a conjugated ketone by its UV: λ_{max}^{EtOH} at 230 nm (ε 9340). The IR also confirmed the presence of a conjugated ketone (1670), a C=CH (3010, 830) and a secondary OH (3400, 1050 cm^{-1}) groups. The ^1H NMR signals are shown in Table 1. MS [*m/e* (rel. int.): 168 (M^+, 40), 133 (M^+ − Me, 4), 150 ($M^+ - H_2O$, 3), 135 (150 − Me, 5), 126 (51), 111 (41), 107 (150 − C_3H_7, 24), 98 ($M^+ - C_5H_{10}$, 100), 79 (13), 70 (38), 69 (36), 55 (16), 43 (25), 41 (20)], in agreement with the structure and relative stereochemistry.

Oxidation of **6** with MnO_2–C_6H_6, gave 2-methyl-5-isopropyl-*p*-benzoquinone, mp 45–46° [12].

Hydroxyketone **7**, $[\alpha]_D - 76.6°$ (*c* 0.9, $CHCl_3$), exhibited the same MS fragmentation pattern as **6**, M^+ at *m/e* 168 (37).

The UV and IR spectra of **7**, showed also the presence of the conjugated C=O [λ_{max}^{EtOH} at 233 nm (ε 6000) and ν 1670 cm^{-1}], one C=CH (3010, 820 cm^{-1}) and a secondary OH (3400, 1045 cm^{-1}). For the ^1H NMR signals, see Table 1.

All these data suggest that **6** and **7** were two epimeric hydroxyketones, which was confirmed by the CD curves. The hydroxyketones showed the dichroic absorptions:

6: $\Delta\varepsilon_{332} = -0.40$; $\Delta\varepsilon_{232} = +1.4$; $\Delta\varepsilon_{196} = +3.5$;

7: $\Delta\varepsilon_{328} = +0.07$; $\Delta\varepsilon_{231} = -6.8$; $\Delta\varepsilon_{201} = +10.2$.

The most important conformation of the *trans*-hydroxyketone **7**, must be the envelope form shown (**7a**, **7b**), with the hydroxyl and isopropyl substituents equatorial. The 4*S*,5*S*-enantiomers (**7a**, **7b**) will show a positive Cotton effect for the n–π^* band according to the reverse octant rule of the enones [13], and a positive Cotton effect for the shorter wavelength band, as predicted by the α'-axial allylic rule [14].

The sign of the middle band is not easy to predict because the enone system must be roughly planar, although a twisted (1,3-diplanar) conformation with a negative Cotton effect [15], may also be important.

The signs of the Cotton effect of **7** are also identical to those of (−)-2-oxo-T-cadinol [16] and (+)-carvone*, and opposed to those of (−)-2-oxopopulifolic acid [17]. All these data (see also [18]) are in agreement with the configuration 4*S*, 5*S*, for **7**.

The Cotton effects for the *cis*-isomer **6** can be explained assuming a half-chair conformation (**6a**, **6b**), in which the isopropyl is equatorial and the hydroxyl is pseudoaxial or nearly pseudoequatorial, according to the rules for the enones [13–15]. The 4*S*,5*R*-enantiomer will show a negative Cotton effect for the n–π^* band, a positive Cotton effect for the middle π–π^* band (positive helicity of C=C=O) and a positive Cotton effect for the short wavelength band, in agreement with those observed for the natural hydroxyketone **6**.

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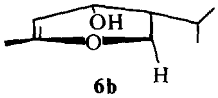
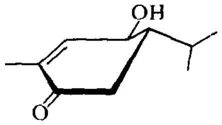
*The dichroic absorption of (+)-carvone, near 330 nm is bisignate ($\Delta\varepsilon = +0.05$; $\Delta\varepsilon = -0.12$), but at shorter wavelengths it shows $\Delta\varepsilon_{238} = -1.52$ and $\Delta\varepsilon_{209} = +1.78$ (MeOH).

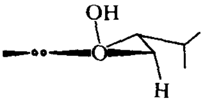
6a



6b



7a



7b

Other components of the essential oil were *p*-cymene (**8**), Δ^3-carene (**9**), 7-acetoxy-*p*-menthane (**10**), *p*-menth-5-en-*cis*-1,2,4-triol (**11**), *p*-menth-5-*trans*-1,2,4-triol (**12**) and *p*-menth-5-en-*cis*-1,3,4-triol (**13**). Acetate **10** showed a MS with M^+ at *m/e* 198, which was consistent with the formula $C_{12}H_{22}O_2$. The IR spectrum showed only significant absorptions due to the acetoxyl group (1750, 1250 cm^{-1}), which was confirmed by ^1H NMR signals at δ 0.92 (6 H, *d*, $J = 6$ Hz, Me_2CH), 1.96 (3 H, *s*, AcO), 3.75 (2 H, *d*, $J = 6$ Hz, CH_2O-). The structures of triols **11**, **12** and **13**, were deduced from their spectral data.

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