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Δ^5-DEHYDRO-1-HYDROXYCARVOMENTHOLS FROM THE ESSENTIAL OIL OF *CHENOPODIUM MULTIFIDUM*

J. De Pascual Teresa, C. Torres, M. S. González, M. Grande and I. S. Bellido

Department of Organic Chemistry, Salamanca University, Spain

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Key Word Index—*Chenopodium multifidum*; Chenopodiaceae; essential oil; Δ^5-dehydro-1-hydroxycarvomenthol; Δ^5-dehydro-1-hydroxyisocarvomenthol; Δ^5-dehydro-1-hydroxyneoisocarvomenthol.

Abstract—The most polar fraction of the essential oil of *Chenopodium multifidum* is made up of three *p*-menth-5-en-1,2-diols diastereoisomers. Their absolute configurations have been assigned by spectral methods and by hydrogenation to the 1-hydroxycarvomenthols of known stereochemistry.

INTRODUCTION

From the most polar fraction of the essential oil of *Chenopodium multifidum* L. (*Roubieva multifida*, Moq.)* [1], we have isolated by preparative CC and TLC, three new isomeric diols (**1–3**). The IR spectra of these new diols were all very similar and showed bands due to a *cis* double bond and secondary and tertiary hydroxyl groups. The mass spectrum of each compound agreed with $C_{10}H_{18}O_2$, and showed the same fragmentation pattern (see Experimental).

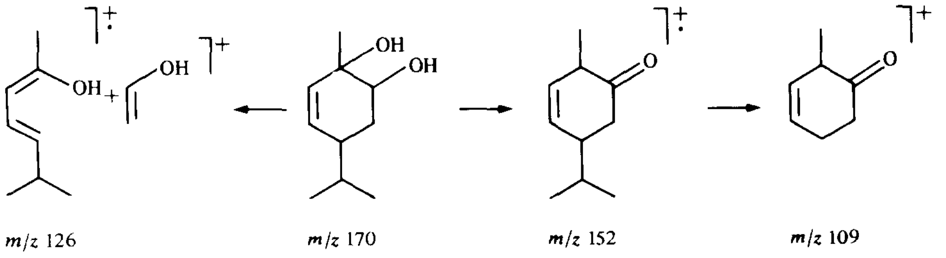
RESULTS AND DISCUSSION

From the above data, we concluded that the diols were all unsaturated *p*-menthadiols. This was confirmed by their ^{1}H NMR spectra which showed signals due to three methyl groups (two of them in an isopropyl group and the other, geminal to a hydroxyl group), two olefinic protons (*cis*-CH = CH) and one geminal hydroxyl proton (Table 1). The multiplicity of the signal due to –CHOH suggested that in **1** and **3**, the secondary hydroxyl group was equatorial, while in **2** it was axial [2].

When the diols were treated with 2,2-dimethoxypropane/*p*-toluensulphonic acid, only **1** and **2** gave acetals. This confirmed that **1** and **2** both contained a *cis*-α-glycol group, whilst in **3** the relative configuration of the hydroxyl groups was *trans*. These conclusions agreed with the observed induced shifts of the NMR signals of **1**, when the spectrum was recorded in C_5D_5N [3] (Table 1). All these data allowed us to identify **1–3** as diastereoisomeric *p*-menth-5-en-1,2-diols, an assignment with was in agreement which the observed fragmentation patterns (Scheme 1).

For the structure *p*-menth-5-en-1,2-diol, the four diastereoisomers (**1–4**) and their corresponding enantiomers were possible. The diol $(-)\Delta^5$-dehydro-1-hydroxyneocarvomenthol had already been isolated from the essential oil of *Eucalyptus dives* [4] and its structure and stereochemistry established by Stolow [5, 6], as that depicted in **4**. Its properties (mp 54° and $[\alpha]_D = -34.1°$) were quite different with those exhibited by the diols isolated from *Ch. multifidum*, so, they must be the remaining diastereoisomers or their enantiomers.

For the *trans*-diol, only the structure Δ^5-dehydro-1-hydroxyneoisocarvomenthol (**3**) was possible and the *cis*-diols had to be Δ^5-dehydro-1-hydroxycarvomenthol (**1**) and Δ^5-dehydro-1-hydroxyisocarvomenthol (**2**). To assign the absolute stereochemistry to unsaturated diols **1–3**, we prepared, by hydrogenation, the saturated diols and compared them with the 1-hydroxycarvomenthols of known stereochemistry [7–11]. The properties and spectral data of the three saturated diols allowed us to identify **1**



Scheme 1. Fragmentation pattern shown by compounds **1–3**.

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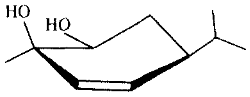
*The plant material was identified by Prof. B. Casaseca Mena, Department of Botany, Salamanca University, where a specimen is held (Herbarium No. 19587).

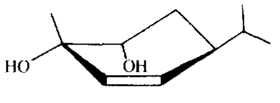
Table 1. ^{1}H NMR data of the diols 1–3 and 5–7 (60 MHz, TMS as int. stand.)

	1			2	3	5			6			7
Assign.	CDCl$_3$	C$_5$D$_5$N	Δδ	CCl$_4$	CCl$_4$	CDCl$_3$	C$_5$D$_5$N	Δδ	CCl$_4$	C$_5$D$_5$N	Δδ	CCl$_4$
Me$_2$C-H	0.88 *d*(7)* 0.90 *d*(7)	0.80	+0.08	0.90 *d*(7)	0.93 *d*(7)	0.89 *d*(7)	0.88	+0.01	0.85 *d*(7)	0.82	+0.03	0.90 *d*(7)
Me-C-OH	1.31 *s*	1.54	−0.23	1.20 *s*	1.19 *s*	1.25 *s*	1.50	−0.25	1.21 *s*	1.38	−0.17	1.38 *s*
H-C-OH	3.45 *dd*(12,4)	3.68	−0.23	3.72	3.76 *dd*(8,4)	3.30 *dd*(12,4)	3.55	−0.25	3.65 *s*(*br*)	3.92	−0.27	3.62 *m*
cis-CH=CH	5.63 AB$_c$(12)	5.70	−0.07	5.49 AB$_c$ (12)	5.53 AB$_c$(12)	—			—			—

*Coupling constants are given in parentheses.



1



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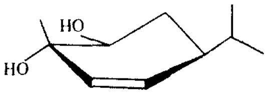

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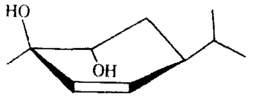
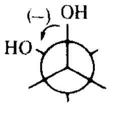


4

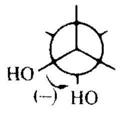
as (−)Δ^5-dehydro-1-hydroxycarvomenthol [(1*R*, 2*S*, 4*S*)-*p*-menth-5-en-*cis*-1,2-diol]; **2** as Δ^5-dehydro-1-hydroxyisocarvomenthol [(1*S*, 2*R*, 4*S*)-*p*-menth-5-en-*cis*-1,2-diol]; **3** as Δ^5-dehydro-1-hydroxyneoisocarvomenthol [(1*S*, 2*S*, 4*S*)-*p*-menth-5-en-*trans*-1,2-diol].

The assigned absolute configurations at C-1 and C-2, were confirmed by the CD curves in the presence of Ni (acac)$_2$–CCl$_4$, which induced one split CE in the region 315–290 nm, of opposite signs [12]. The sign of the CE can be correlated with the dihedral angle between two hydroxyl groups; assuming that the molecule adopts the most stable conformation, one negative dihedral angle induces one positive CE near 315 nm and one negative CE near 290 nm. A positive dihedral angle, produces the opposite effect.

Natural diols **1**–**3** showed the following dichroic absorptions: **1**: $\Delta\varepsilon_{316} = +0.25$ and $\Delta\varepsilon_{296} = -0.16$. **2**: $\Delta\varepsilon_{316} = +0.58$ and $\Delta\varepsilon_{296} = -0.47$. **3**: $\Delta\varepsilon_{315} = +0.05$ and $\Delta\varepsilon_{295} = +0.05$ in agreement with the dihedral angles: and with the absolute configurations (1*R*, 2*S*) for **1**, (1*S*, 2*R*) for **2** and (1*S*, 2*S*) for **3**. The preferred conformations for unsaturated diols must be those depicted in **1**–**3**.



1



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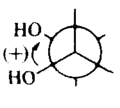

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EXPERIMENTAL

Mps (Kofler hot stage appar.): Analytical TLC: silica gel G (E. Merck No. 7731); prep. TLC: silica gel PF$^{4+336}_{23}$ (E. Merck No. 7748); CC: silica gel 60 (E. Merck No. 7734).

Isolation of diols. The most polar fraction of the essential oil (dry chromatographed) of *Ch. multifidum* (385 mg, 2.50 % of the whole oil) was chromatographed on 25 g silica gel–AgNO$_3$ (10 %) to give, after purification by TLC or crystallization, 187 mg **1** (hexane–Et$_2$O, 3 : 2), 52 mg **2** (hexane–Et$_2$O, 1 : 1) and 95 mg **3** (Et$_2$O).

(−) *Δ^5-Dehydro-1-hydroxycarvomenthol* (**1**). Mp 114° (C$_6$H$_6$), $[\alpha]_D = -8.5°$ (*c* 1.17, CHCl$_3$); IR νcm^{-1}: 3300, 3280, 3060, 1650, 1470, 1380, 1150, 1075, 1040, 930, 750, 725; MS *m/z* (rel. int.): 170 $[M]^+$ (5), 155 $[M-Me]^+$ (9), 152 $[M-H_2O]^+$

(11), 134 $[152-H_2O]^+$ (4), 126 (100), 111 (87), 109 (30), 93 (35), 79 (14), 43 (46).

Acetal of **1**. To a soln of 24 mg **1** in 4 ml dry Me_2CO, 0.4 ml 2,2-dimethoxypropane and a catalytic amount of *p*-toluensulphonic acid were added and the soln kept at room temp. for 30 min, after which it was neutralized with solid $NaHCO_3$. Evaporation of solvent gave 32 mg acetal, $[\alpha]_D = -269.3°$ (*c* 0.30, $CHCl_3$); IR $\nu\,cm^{-1}$: 1660, 1470, 1380, 1245, 1200, 1170, 1130, 1110, 1050, 1030, 1000, 950, 920, 895, 880, 860, 820, 800, 745; ^{1}H NMR 60 MHz (CCl_4, TMS as int. stand.): δ 0.92 (3H, *d*, $J = 6$ Hz), 0.95 (3H, *d*, $J = 6$ Hz), 1.22 (3H, *s*), 1.30 (6H, *s*), 3.90 (1H, *ap*/*t*, $J = 3$ Hz), 5.60 (2H, AB_c system, J_{AB}12 and $J_{Bc} = 3$ Hz); MS *m*/*z* (rel. int.): 210 $[M]^+$ (8), 195 (55), 167 (7), 151 (22), 139 (22), 136 (67), 126 (17), 119 (11), 114 (9), 109 (32), 95 (30), 93 (100), 91 (22), 91 (14), 79 (12), 77 (9), 69 (8), 43 (5).

(+) Δ^5-*Dehydro*-1-*hydroxyisocarvomenthol* (**2**). Mp 135–136° (C_6H_6), $[\alpha]_D = +40.0°$ (*c* 0.92, $CHCl_3$); IR $\nu\,cm^{-1}$: 3360, 3040, 1640, 1470, 1380, 1140, 1060, 1030, 740, 710; MS *m*/*z* (rel. int.): 170 $[M]^+$ (2), 155 (4), 152 (16), 137 (19), 134 (4), 126 (100), 109 (75), 93 (19), 79 (3), 43 (13).

Acetal of **2**. By the same procedure as used with **1**, from 20 mg **2**, 22 mg of the corresponding acetal were obtained, $[\alpha]_D = -142.8°$ (*c* 0.25 $CHCl_3$); IR $\nu\,cm^{-1}$: 1650, 1470, 1380, 1240, 1195, 1105, 1065, 1045, 1010, 950, 940, 875, 850, 820, 785, 735; ^{1}H NMR 60 MHz (CCl_4, TMS as int. standard): δ 0.90 (6H, $J = 6$ Hz), 1.21 (3H, *s*), 1.28 (6H, *s*), 3.92 (1H, *m*), 5.45 (2H, AB_c, $J_{AB} = 12$, $J_{Bc} = 3$ Hz).

(+)Δ^5-*Dehydro*-1-*hydroxyneoisocarvomenthol* (**3**) Mp 163–164° ($CHCl_3$), $[\alpha]_D = +54.5°$ (*c* 0.66, $CHCl_3$); IR $\nu\,cm^{-1}$: 3340, 3040, 1640, 1480, 1380, 1120, 1105, 1070, 760, 720; MS *m*/*z* (rel. int.): 170 $[M]^+$ (9), 155 (4), 152 (8), 137 (9), 134 (11), 126 (100), 109 (59), 93 (16), 79 (8), 71 (13), 43 (12).

(−)1-*Hydroxycarvomenthol* (**5**). Hydrogenation of 42 mg **1** (10 mg PtO_2, EtOH) gave 44 mg **5**, mp 82–83° (C_6H_6), $[\alpha]_D = -10.1°$ (lit. 76–77° and −12°) [7, 9, 10]; IR $\nu\,cm^{-1}$: 3340, 3040, 1470, 1380, 1130, 1075, 930, 710; MS *m*/*z* (rel. int.): 172 $[M]^+$ (15), 154 $[M-H_2O]^+$ (8), 139 (14), 136 $[154-H_2O]^+$ (14), 129 (16), 125 (13), 111 (57), 93 (22), 83 (29), 79 (7), 71 (100), 55 (28), 43 (34).

(−)1-*Hydroxyisocarvomenthol* (**6**). Hydrogenation of 20 mg **2** gave 24 mg **6**, mp 68–69° and $[\alpha]_D = -18.4°$ (*c* 0.81, $CHCl_3$) (lit. 75.5°, racemic) [7, 9]; IR $\nu\,cm^{-1}$: 3320, 1470, 1390, 1370, 1130, 1090, 1050, 760, 710; MS *m*/*z* (rel. int.): 172 $[M]^+$ (10), 154 (6), 139 (14), 136 (13), 129 (16), 125 (13), 111 (56), 95 (14), 93 (18), 83 (27), 71 (100), 55 (16), 43 (27).

(−) 1-*Hydroxyneoisocarvomenthol* (**7**). Hydrogenation of 30 mg **3**, gave 32 mg **7**, $[\alpha]_D = +30.6°$ (*c* 0.35, $CHCl_3$) (lit. mp 55° and $[\alpha]_D - 30°$) [7, 11]; IR $\nu\,cm^{-1}$: 3400, 1470, 1390, 1370, 1130, 1085, 1020, 715; MS *m*/*z* (rel. int.): 172 $[M]^+$ (17), 154 (8), 139 (15), 136 (15), 129 (17), 125 (18), 111 (56), 95 (14), 93 (20), 83 (24), 71 (100), 55 (34), 43 (42).

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