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Synthesis, Crystal Structure and Theoretical Characterization of (3R, 4R, 6S)-3,6-Dihydroxy-1-Menthene Isolated from Echinophora Tenuifolia

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ABSTRACT

In the title compound, C10H18O2, the cyclohexene ring adopts a half-chair conformation. In the crystal strcuture, weak inter¬molecular O—H . . . O hydrogen bonds connect the adjacent molecules, forming edge-fused R23(8) ring motifs, into the hollow columns parallel to the b-axis direction. The crystal packing is governed only by van der Waals inter¬actions. There is no further C—H···π and π-π interactions. The H atom in one of two hydroxyl groups was found to be disordered over two sites. The occupancy factors of the two sites were refined to 0.52 (2) and 0.48 (2). Semi-empirical PM3 quantum chemical calculations are in satisfactory agreement with the results of the X-ray structure analysis.

Keywords: *Crystal structure; cyclohexene ring; 2-methyl-5-(propan-2-yl)cyclohex-2-ene-1,4-diol; semi-empirical PM3 quantum chemical calculations; HOMO and LUMO energy levels.*

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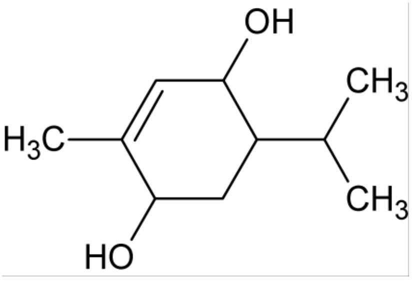
1. INTRODUCTION

The genus *Echinophora* belongs to Umbellifereae family and represented by six species in Turkish flora, three of which are endemic. *Echinophora tenuifolia* is very popular in Anatolia and the young leaves and stalks of plant are edible (Özcan & Akgül, 2003) [1]. At the pre-flowering stage, fresh or dried herb was used as flavoring agent for soup, meatballs and tarhana which is a Turkish traditional food (Telci & Hisil, 2008) [2]. The previous studies on *Echinophora tenuifolia* have been focused on the identification of volatile components (Chalchat *et al.*, 2007; Telci & Hisil, 2008; Georgiou *et al.*, 2010) [2-4] and its some biological activities for example antioxidant and antimicrobial (Gokbulut *et al.*, 2013) [5]. The essential oil of plant predominantly contains monoterpernes and methyleugenol, a phenylpropanoid derivative. There is no any record about chemical composition of methanolic extract of *Echinophora tenuifolia*. In present study we achieved the isolation of a non-distillable small terpenic molecule for the first time from methanolic extract of *Echinophora tenuifolia* using a silica gel column chromatography. The structure of molecule was identified according the data obtained from *NMR*, *MS* and *X*-ray spectrums.

2. EXPERIMENTAL

2.1. Synthesis and Crystallization

Plant material was collected from Tokat, Turkey. Plant materials (300 g) were extracted with methanol (500 mL×3). Solvent was removed by rotary evaporator to obtained extract (13 g). An aliquot of this extract (5 g) was suspended in hot water and partitioned between hexane and chloroform respectively. The chloroform phase (1.7 g) was chromatographed over silica gel column (300 g packing material, 3×70 cm glass column) and eluted with a gradient of hexane-ethyl acetate to yield the (3*R*, 4R, 6S)-3,6-dihydroxy-1-menthene which was crystallized into chloroform to afford the needle crystal (42 mg).



Scheme

In ^{13}*C-NMR* spectrum, observation of three methyls, one methylene, five methines and one quaternary carbon atom accord with the structure. In ^{1}*H-NMR* spectrum, the signals appeared at δ 0.84 (3H, d, J=6.95 Hz), δ 1.78 (3H, s) and δ 2.13 (1H, dtt, J=10.32/6.95/3.41 Hz) belonged to the H-9, H-10 and H-7 respectively. H-2 signal appeared downfield (δ 5.49) as a broad singlet due to the electronegativity of sp^2 carbon atom as compared with the sp^3 carbon. The accordance of other resonance signals support the proposed structure. *X*-ray analysis also confirm the configuration of the structure.

2.2. X-ray Crystallography

The crystal structure of the title compound was determined by single crystal X-ray diffraction. Diffraction data was collected on a Bruker *APEX*-II CCD area detector-equipped diffractometer with Mo K_α (λ = 07103 A) radiation. An empirical absorption correction was applied Multi-scan (*SADABS*; Sheldrick, 2003) [6]. The structure was solved by direct methods (*SHELXS*-2014) [7] and refined by full-matrix least-squares techniques against F^2 (*SHELXL*-2014) [8]. H atoms bound to oxygen were found from difference Fourier maps and they were allowed to ride on their parent atoms with U_{iso} fixed at 1.5 times U_{eq}(O) (O—H = 0.82Å). The H atom which is attached to the atom O1 is disordered over two sites (H1AO and H1BO) with an occupancy ratio of 0.52 (5):0.48 (5). All H atoms bound to carbon were placed in idealized positions and allowed to ride on their parent atoms with U_{iso} = 1.2 times U_{eq}(C) (C—H = 0.93Å for aromatic, 0.97Å for methylene and 0.98Å for methine) and with U_{iso} = 1.5 times U_{eq}(C) (C—H = 0.96Å for methyl). As a result of the absence of anomalous scatterers and high angle data, the Flack test results can be considered meaningless. The synthesis resulted in a racemic mixture, hence the structure was refined as an inversion twin. The CCDC reference number is CCDC 1497805. The crystallographic details are summarized in Table 1.

Table 1 Experimental details

Chemical Formula	$C_{10}H_{18}O_2$
M_r	170.24
Crystal system, space group	Monoclinic, *C*2
Temperature (K)	296
a, *b*, *c* (Å)	17.8355 (13), 7.1207 (5), 8.0974 (7)
β (°)	102.124 (3)
V (Å^3)	1005.44 (13)
Z	4
F(000)	376
D_x (Mg m^{-3})	1.125
Radiation type	Mo *K*α
No. of reflections for cell measurement	5534
θ range (°) for cell	3.1–27.8

measurement	
μ (mm^{-1})	0.08
Crystal shape	Prism
Colour	Colourless
Crystal size (mm)	0.18 × 0.12 × 0.10
Scan method	φ and ω scans
T_{min}, T_{max}	0.705, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	11929, 2498, 2080
R_{int}	0.034
θ values (°)	$\theta_{max} = 28.3$, $\theta_{min} = 3.1$
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.667
Range of h, k, l	$h = -23\rightarrow23$, $k = -9\rightarrow9$, $l = -10\rightarrow10$
Refinement on	F^2
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.042, 0.099, 1.04
No. of reflections	2498
No. of parameters	124
No. of restraints	4
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0506P)^2 + 0.2P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	< 0.001
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.16, −0.14
Extinction method	*SHELXL*, $Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient	0.55)

3. CRYSTAL STRUCTURE DETERMINATION

In the title compound (Fig. 1), the cyclohexene ring adopts a half-chair conformation with the puckering parameters (Cremer & Pople, 1975) [9] of $Q_T = 0.496$ (2) Å, $\theta = 130.2$ (2) ° and $\varphi = 328.5$ (4) °. In the molecule of the title compound, all bond lengths and angles are within normal range and are comparable with those previously reported for similar structures in literature (Boualy *et al.*, 2011; Smrcok *et al.*, 2013; Maharramov *et al.*, 2011) [10-12]. The C2–C3–C8–C9, C2–C3–C8–C10, C4–C3–C8–C9 and C4–C3–C8–C10 torsion angles are -165.36 (18), 69.7 (3), 70.6 (2) and -54.3 (3) °, respectively (Table 3).

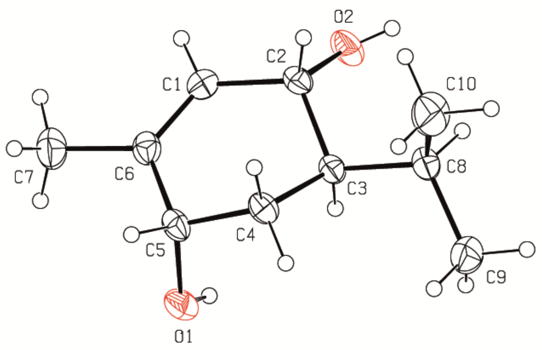


Figure 1 View of the title compound with the atom numbering scheme. Displacement ellipsoids for non-H atoms are drawn at the 30% probability level. Minor component od the disorder is not shown, for clarity.

In the crystal packing, molecules are linked via weak intermolecular O—H . . . O hydrogen bonds which generate edge-fused $R_2^3(8)$ ring motifs (Bernstein *et al.*, 1995 [13]; Table, 2; Figs 2, 3 & 4), into the hollow columns parallel to the b-axis direction. The crystal packing is governed only by van der Waals interactions. C—H···π and π-π interactions are not observed.

Table 2 Hydrogen-bond geometry (Å, °)

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1AO···O2^{i}	0.81 (4)	1.94 (4)	2.732 (3)	165 (5)
O2—H2O···O1^{ii}	0.75 (3)	1.96 (3)	2.707 (2)	173 (3)
Symmetry codes: *(i) −x+1/2, y−1/2, −z+1; (ii) x, y+1, z.*				

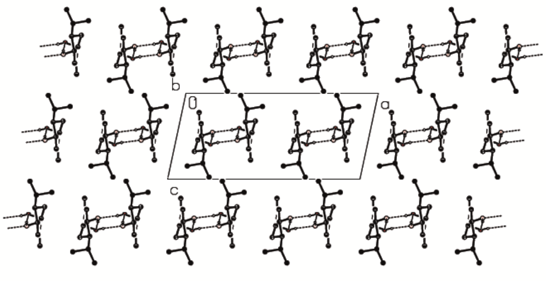


Figure 2 A view along the a axis of the crystal packing of the title compound. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity.

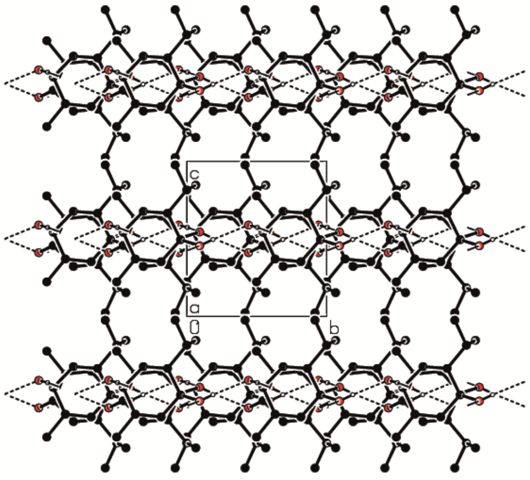


Figure 3 A view along the b axis of the crystal packing of the title compound. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity.

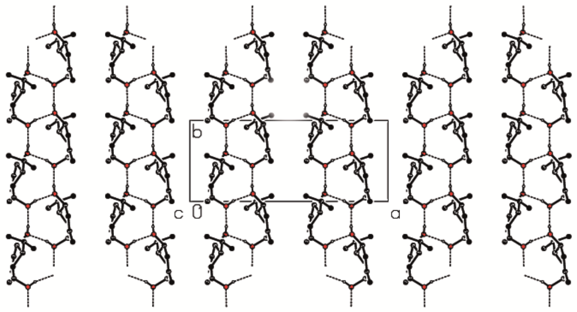


Figure 4 A view along the c axis of the crystal packing of the title compound. H atoms not involved in hydrogen bonding (dashed lines) have been omitted for clarity.

4. THEORETICAL CALCULATIONS

The spatial disposition of the atoms of the title molecule calculated by using semi-empirical *PM3* quantum chemical calculations (Stewart, 1985) [14] is shown in Fig. 5. The net charges at atoms O1 and O2 are -.308 and -.315 e^-, respectively. The total energy and dipole moment of the title molecule are -2050.85 eV and 2.017 Debye. The *HOMO* and *LUMO* energy levels are -9.9363 and 0.7744 eV, respectively.

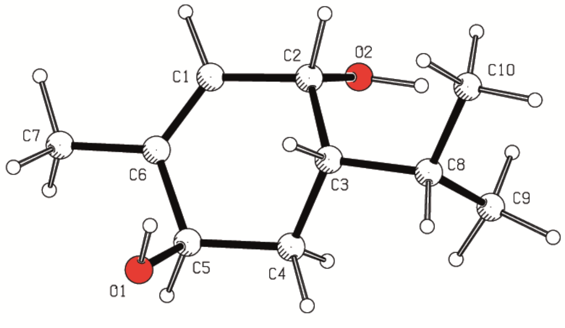


Figure 5 Spatial view of the molecule of the title compound calculated using the *PM3* method.

Comparison of selected bond lengths and angles obtained by the experimental (X-ray) and theoretical (PM3) methods of the title compound are listed in Table 3. The geometrical parameter values calculated of the title molecule are consistent with those obtained by *X*-ray structure determination within the error limits. Small differences between the theoretical and experimental results, molecules may theoretically be due to be considered as a single and in a vacuum.

Table 3 Comparison of experimental (X-ray) and theoretical (PM3) parameters of the title compound.

Bond (Å)	**X-ray**	**PM3**
O1—C5	1.437 (3)	1.4134
O2—C2	1.432 (3)	1.4152
C1—C6	1.327 (3)	1.3364
C1—C2	1.499 (3)	1.5046
C2—C3	1.525 (3)	1.5463
C3—C8	1.540 (3)	1.5404
C3—C4	1.531 (3)	1.5248
C4—C5	1.516 (3)	1.5359
C5—C6	1.504 (3)	1.5119
C6—C7	1.504 (3)	1.4868
C8—C9	1.525 (3)	1.5217
C8—C10	1.524 (4)	1.5200
Bond Angle (°)		
C2—C1—C6	125.4 (2)	123.94
O2—C2—C1	107.71 (18)	105.02
C1—C2—C3	112.33 (18)	110.71
O2—C2—C3	112.17 (17)	115.65
C2—C3—C8	112.97	116.32

	(18)	
C4—C3—C8	114.31 (19)	110.60
C2—C3—C4	108.00 (18)	110.18
C3—C4—C5	112.21 (18)	112.31
O1—C5—C4	110.07 (18)	111.41
O1—C5—C6	111.02 (17)	111.36
C4—C5—C6	112.32 (18)	112.88
C1—C6—C7	123.0 (2)	121.38
C5—C6—C7	116.20 (19)	115.52
C1—C6—C5	120.8 (2)	123.10
C3—C8—C10	113.7 (2)	111.81
C9—C8—C10	110.0 (2)	110.55
C3—C8—C9	111.28 (19)	114.01
Torsion Angle (°)		
O2—C2—C3—C8	65.8 (2)	56.96
O1—C5—C6—C7	71.4 (2)	-63.51
C2—C3—C8—C9	−165.36 (18)	-72.04
C2—C3—C8—C10	69.7 (3)	54.27
C4—C3—C8—C9	70.6 (2)	54.62
C4—C3—C8—C10	−54.3 (3)	-179.07

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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