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BONANDIOL : A NEW, IRREGULAR, MONOCYCLIC DITERPENE FROM *BONANNIA GRAECA* (L.) HALACSY (UMBELLIFERAE)

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Summary: A new, irregular, monocyclic diterpene, bonandiol (1), has been isolated from *Bonannia graeca*. The structure of bonandiol has been deduced from spectral data and chemical evidence.

The umbellifer *Bonannia graeca*, which is botanically close to the genus *Ferula*, is widely distributed in the southern part of Italy and in Greece. The aerial parts of this plant, which occurs in mountain pastures, have toxic consequences for herbivores and cause the death of lambs during its blossoming season (June-July).

Our examination of *Bonannia graeca*, collected near Palermo (Sicily, Italy), has revealed the occurrence, amongst other products, of a new diterpene for which we propose the name bonandiol (1). It was isolated as the major constituent (2.5% of the dry plant material) from the whole plant by extraction with acetone followed by silica gel chromatography; thick oil, $[\alpha]_D^{19}$ +24.1° (c 0.41, $CHCl_3$). Combustion analysis and mass spectrometry indicated the molecular formula $C_{20}H_{36}O_2$ for bonandiol (1). Its ^1H NMR spectrum (300 MHz, $CDCl_3$) showed signals for two tertiary methyl groups at δ 0.79 and 1.25, four methyl groups on double bonds at 1.59 (3H), 1.67 (3H) and 1.70 (6H), an AB part of an ABX-type system (δ_A 3.77, δ_B 3.48, J_{AB}= 10.7, J_{AX}= 10.5, J_{BX}= 4.8) which was assigned to a $-CH-CH_2OH$ grouping, two hydroxyl protons at 3.02 and 3.48 which disappeared after exchange with D_2O, two olefinic protons at 5.05 (1H, m) and 5.30 (1H, m), and four allylic protons at 1.91 (2H, m), 2.05 (1H, m) and 2.30 (1H, m). Mass spectrum, m/z (relative intensity) 308(M^+, 1), 290(M^+-18, 13), 135(14), 121 (17), 109(35), 95(30), 81(32), 69(100).

Treatment of 1 with 4-nitro-benzoylchloride in pyridine at room temperature gave a crystalline monoester (1a, $C_{27}H_{39}O_5N$; ν_{OH} 3510 cm^{-1}); m.p. 75° (petroleum ether), $[\alpha]_D^{19}$ -6.9 (c 0.68, $CHCl_3$). The ^1H NMR spectrum (300 MHz, $CDCl_3$) of compound 1a was quite similar to the spectrum of the natural product, except that the above-mentioned signals of an AB part of an ABX-type system were shifted downfield to δ4.26 (dd) and 4.69 (dd). Mass spectrum, m/z (relative intensity) 457(M^+,1), 439(10), 272(30), 229(16), 203(25),189(24), 161(39),150 (40), 135(29), 109(40), 69(100).

Oxidation of bonandiol (1) ($C_6H_5NH_2Cr_2O_7/CH_2Cl_2$, r.t.) gave an unstable aldehyde (2, $C_{20}H_{34}O_2$) ; its ^1H NMR spectrum (90 MHz, $CDCl_3$) lacked the signals assigned to the $-CH_2OH$ group and showed a new signal at δ9.98 (1H). Its 2,4-dinitrophenylhydrazone derivative (2a), $C_{26}H_{38}O_5N_4$, had m.p. 142° (petroleum ether), $[\alpha]_D^{19}$ +16.3 (c 0.30, $CHCl_3$) ; I.R. (nujol) ν_{max} 3635, 3375, 1615 cm^{-1}. ^1H NMR spectrum: see Fig. 1. Mass spectrum, m/z (relative intensity) 486(M^+,3), 468(M^+-18, 8), 236(11), 125(70), 109(37), 81(40), 69(98), 41(100).

Proton decoupling studies and extensive NOE experiments performed at 300 MHz on derivative 2a gave a clear indication of the structure and relative stereochemistry of the natural product. Irradiation at δ5.36 (1H, m) removed the 9.8 Hz coupling from the signal at 2.31 (1H, m), the 4.7 Hz coupling from the signal at 2.16 (1H, m) and the 1.1 Hz coupling from the signal at 1.72 (6H, dd), the latter collapsing to a doublet (J=1.2 Hz). On irradiation at δ2.16 the signal at 1.72 was transformed into a doublet (J = 1.1 Hz), whereas no coupling was observed between the proton at 2.31 and the methyl protons at 1.72. Irradiation at δ5.08 (1H, m) removed a 7 Hz coupling from the signal at 1.94 (2H, m) and led to a collapse of the doublets at 1.62 (3H, d) and 1.70 (3H, d) into singlets. Saturation of the methyl protons at δ1.23 produced a NOE enhancement of the singlet at 0.87 (3H) (both methyl groups being axial) and also gave rise to a weak NOE enhancement of the signal at δ2.31; no enhancement was observed on the signals at δ2.16 and 2.49. All the above data are fully in accordance with the structure shown in Fig. 1 for 2a. The stereochemistry at C-6 was indicated by the magnitude of $J_{5_{ax},6}$ (diaxial relationship between these protons).

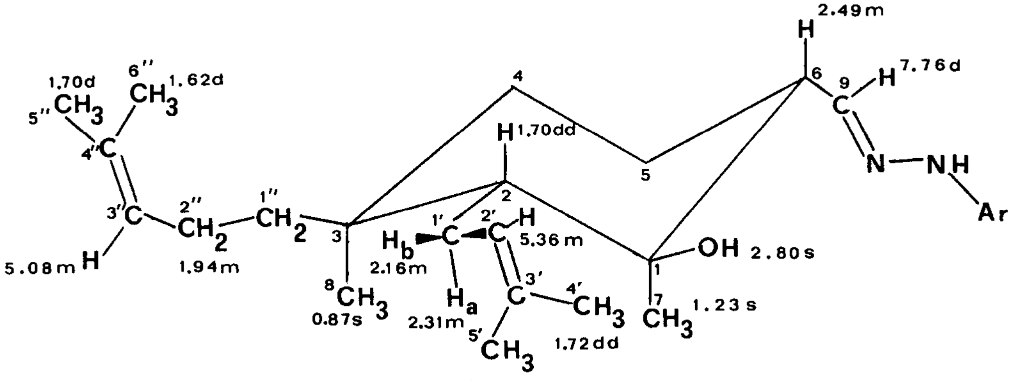


Fig. 1

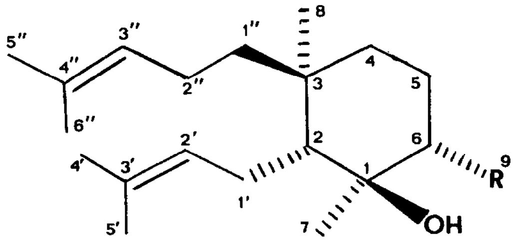
J(Hz): 2,$1'_a$=8; 2,$1'_b$=3.5; 6,9=4.0; 5_{ax},6=11.5; 5_{eq},6=3.4; $1'_a$,$1'_b$=15.4; $1'_a$,2'=9.8; $1'_a$,CH_3-4'=0; $1'_a$,CH_3-5'=0; $1'_b$,2'=4.7; $1'_b$,CH_3-5'=1.2; $1'_b$,CH_3-4'=1.5; 2',CH_3-4'=1.1; 2',CH_3-5'=1.1; 2",CH_3-6"=0; 2",3"=7.0; 3",CH_3-6"=1.1; 2",CH_3-5"=0

The ^{13}C NMR spectra of derivatives 1a (75 MHz, $CDCl_3$) and 2 (20 MHz, $CDCl_3$) further confirmed structure 1 for bonandiol (Table 1)

Table 1. ^{13}C NMR data
(shifts are given in ppm from Me_4Si)

Carbon atom	1a	2
C-1	75.5 s	76.9 s
C-2	54.9 d	55.0 d
C-3	37.4 s	37.2 s
C-4	36.8 t	36.2 t
C-5	23.3 t	19.2 t
C-6	54.9 d	65.5 d
C-7	19.1 q	21.4 q
C-8	20.5 q	20.3 q
C-9	66.6 t	205.6 d
C-1'	23.9 t	23.9 t
C-2'	125.9 d	126.0 d
C-3'	132.8 s$^+$	132.3 s$^+$
C-4'	25.9 q*	25.9 q*
C-5'	18.0 q^	18.0 q^
C-1"	43.8 t	43.8 t
C-2"	21.9 t	22.0 t
C-3"	124.7 d	124.1 d
C-4"	131.3 s$^+$	131.3 s$^+$
C-5"	25.7 q*	25.7 q*
C-6"	17.6 q^	17.6 q^

$^+$,*,^ values may be interchanged



1 R = CH_2OH; 1a R = $CH_2OCOC_6H_4$-4-NO_2

2 R = CHO ; 2a R = CH=N-NH-$C_6H_3(NO_2)_2$

The biosynthesis of bonandiol (1) may be assumed to proceed involving head to head combination of isoprenoid units (similar to that of lavandulol[1] in the monoterpenic series and peucelinendiol[2] in the diterpenoid series) and subsequent cyclization.

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