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CONFORMATIONAL ISOMERS OF 14-HYDROXY-9-EPI-β-CARYOPHYLLENE ISOLATED FROM THE WOOD OF JUNIPERUS OXYCEDRUS

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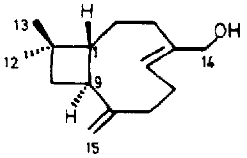
Abstract: A new sesquiterpene alcohol has been isolated from the essential oil of the wood of *Juniperus oxycedrus* L. and identified through its spectroscopic properties as 14-hydroxy-9-epi-β-caryophyllene. Dynamic ^{1}HNMR measurements have revealed two major conformational isomers in roughly equal amounts at room temperature, with an interconvertion barrier of 17.5 Kcal/mol.



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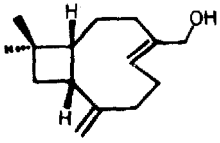
In our studies on the chemical composition of the essential oil from the wood of *Juniperus oxycedrus* L., we have isolated a new sesquiterpene alcohol[1] as an oily liquid $[\alpha]_D$= -13.5º to which we firstly assigned the structure of 14-hydroxy-β caryophyllene (1) on the basis of the following spectroscopic features. Its MS shows a molecular peak at m/z 220 $C_{15}H_{24}O$) and absorptions can be seen in its IR spectrum due to primary allylic alcohol (3344, 1008 cm^{-1}), exocyclic methylene (3067, 1629, 887 cm^{-1}), trisubstituted double bond (1660, 800 cm^{-1}) and a gem-dimethyl group (1375, 1366 cm^{-1}), the latter appearing in the ^{1}HNMR spectrum performed at 80 MHz as a singlet at 0.98 ppm. Other meaningful but poorly resolved signals, corresponding to $-CH_2OH$ (3.58-4.30 ppm, m), $=CH_2$ (4.75-5.10 ppm, m) and olefinic methyne (5.25-5.62 ppm, m) are shown. The endocyclic double bond was assigned an E configuration on the basis of the absence of NOE between the olefinic methyne and the H-14. Compound 1 was synthetized from β -caryophyllene by oxydation with selenium dioxide[2] and though its mass and IR spectra are similar to those of the natural alcohol, there are significant discrepancies in the high resolution NMR data of both compounds (table 1 and fig. 1)[3]. We deduce from the great Δδ for C-1, C-9 and C-14 that the difference beteen these products lies



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in their C-9 configuration, suggesting the structure 14-hydroxy-9-epi-β-caryophyllene (2) for the natural caryophyllenol. Our proposal is reinforced both by the differences and the analogies to be seen in the MS data of the two compounds[4]. The most noteworthy characteristic in this respect is the higher percentage of the ion in compound 2, due to the loss of the isobuthylene unit as a cosequence of the higher stiffness associated with a *cis*-ring junction, which can be seen in Dreiding's models and has been experimentally proved by Corey[5] through a comparison of the reactivities of the ketones 3 and 4. Furthermore, the H-14 in 2 are magnetically non equivalent, resonating as an AB system, as opposed to 1, which appear as a singlet. We have also proved the existence of two stable conformers (in roughly equal amounts at room-temperature), as evidenced by the splitting of all the signals in the ^{13}CNMR spectrum of 2, with the exception of those

		1	2	
1	CH	52.0	56.9	56.9
2	CH_2	27.2	29.2	36.0
3	CH_2	26.6	42.6	40.6
4	C	139.6	137.7	137.9
5	CH	126.6	128.8	129.5
6	CH_2	25.9	30.5	30.5
7	CH_2	35.1	33.8	34.9
8	C	155.5	153.9	158.9
9	CH	40.6	49.1	49.7
10	CH_2	40.0	40.3	40.3
11	C	33.2	32.9	32.9
12	CH_3	30.0	29.8	30.0
13	CH_3	22.8	22.1	21.9
14	CH_2	67.1	60.2	62.0
15	CH_2	110.6	110.1	113.1

Table 1. ^{13}CNMR data for compounds 1 and 2 (75.43 MHz, $CDCl_3$, TMS as internal standard). These values were tentatively assigned, based on the DEPT technique and by comparison with reported data for other caryophyllene hydrocarbons.

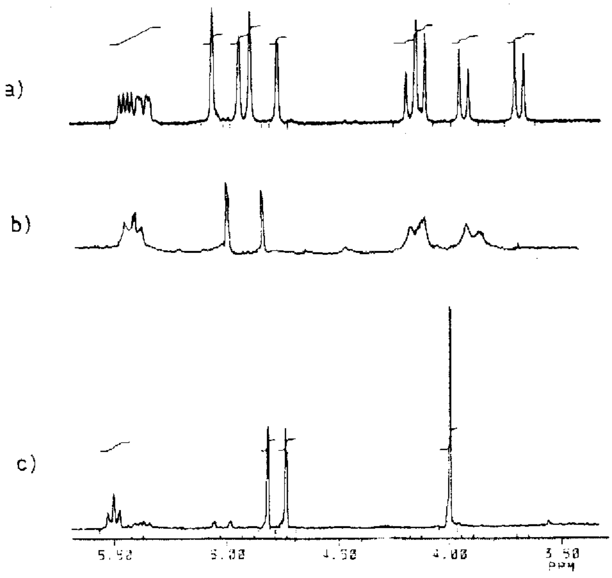
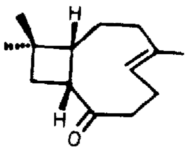


Fig. 1. a) and c) H-14 and exomethylene signals in the ^{1}HNMR of compounds 2 an 1, respectively (300 MHz, $CDCl_3$), b) coalescence of these signals for 2 at 343 ºK (spectrum performed at 200 MHz).

assigned to C-1, C-6, C-10 and C-11, as well as those corresponding to the oxygenated and olefinic protons, which are easily recognizable in their ^{1}HNMR spectrum. Variable temperature ^{1}HNMR experiments[6] corroborate this hypothesis by observing the reversible coalescence (at 343 ºK) of the H-14 and exomethylene signals (fig.1). The interconversion barrier between the two conformers was determined as 17.5 Kcal/mol[7], a value that is corroborated by their stabilities at room temperature.



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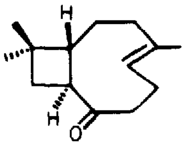

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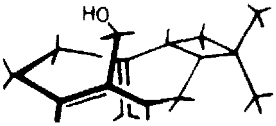

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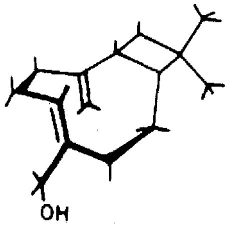

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The existence of two major conformers in β-caryophyllene derivatives has been recognized by Warnhoff[8] by means of chemical reactions, although the attempts to confirm it through variable temperature ^{1}HNMR experiments have been unfruitful. Later, Shirahama et al[9], by ^{13}CNMR spectra showed the presence of four conformational isomers. According to these statements and using Dreiding's models, conformers 5 and 6 for 2 are proposed.

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References and notes.

1.- GC analyses were carried out in a 25 m capillary column packed with carbowax 20M; temp. programmed from 50 ºC to 200 ºC, isothermal 7 min, at 5 º/min; N_2 25 ml/min. The new sesquiterpene alcohol showed a retention time of 25.49 min and represents 4.25% of the essential oil.

2.- 0.5 g of β -caryophyllene was solved in EtOH (1 ml) and oxydized with a solution of SeO_2 (0.25 g) in EtOH (12 ml) for 6 h at room temperature and then column chromatographed on SiO_2 gel. The fraction eluted with hexane-Et_2O (7:3) gaves 85 mg of 1.

3.- In the ^{1}HNMR spectrum of 1, performed at 300 MHz, two peaks due to the gem-dimethyl group occur at 0.96 and 0.98 ppm, respectively, whereas the same group for 2 gives three signals at 0.98, 0.99 and 1.00 ppm, the latter being of higher intensity than the other two.

4.- EIMS (probe) 70 eV, m/z (numbers in parenthesis represent relative intensities for compounds 1 and 2, respectively): 220 $[M]^+$ (3)(4), 205 $[M-15]^+$ (5)(6), 189 $[M-CH_2OH]^+$ (16)(6), 187 $[M-Me-H_2O]^+$ (8)(12), 174 $[M-Me-CH_2OH]^+$ (2)(3), 164 $[M-(CH_3)_2C=CH_2]^+$ (2)(15), 159 $[M-Me-Me-CH_2OH]^+$ (15)(14), 133 $[164-CH_2OH]^+$ (46)(40), 91 (100)(100).

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6.- Variable temp. ^{1}HNMR experiments were performed in $CDCl_3$, from 293 ºK to 350 ºK and measurements were taken every 10 º, appearing the coalescence temp. at near 343 ºK.

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