The structure of jhanilactone[1]

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Summary. The molecular structure and absolute configuration I was assigned to jhanilactone, a new lactone from *Eupatorium jhanii* Robinson, on the basis of X-ray crystallography and circular dichroism data.

In a former communication[3], we described the isolation and structural determination of 5 new labdane derivatives from *Eupatorium jhanii* Robinson. Now we have isolated a new lactone, jhanilactone, as a minor constituent.

Jhanilactone (I), m.p. 71-72 °C, $[\alpha]_D - 5°$ ($CHCl_3$), molecular formula $C_{13}H_{20}O_3$ (M^+ 224, 1%), has IR absorptions characteristic of alcohol and lactone groups. Its PMR-spectrum shows 2 angular methyl groups at δ 1.14 and 1.30; there are no protons geminal to the hydroxyl or to the lactone oxygen atom.

While jhanilactone, treated with py-Ac_2O, does not form an acetate at room temperature, a monoacetate is formed under reflux, m.p. 148-149 °C. Its PMR-spectrum reveals a methyl shift from δ 1.30 to 1.56, and hence the hydroxyl function in I must be geminal to this methyl.

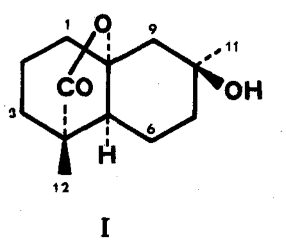
LAH reduction of jhanilactone gave a triol, m.p. 183-185 °C, $[\alpha]_D + 10°$ ($CHCl_3$), (M^+ 228, 1%). Acetylation of this triol yielded a monoacetate, m.p. 116-118 °C, $[\alpha]_D - 11°$, with 2 doublets typical of a $-CH_2OAc$ group at δ 4.28 and 4.54 (J = 12 Hz) in its PMR-spectrum.

The above chemical and spectroscopic data indicate that jhanilactone must be a tricyclic compound with 2 methyls, 1 geminal to a hydroxyl group, and a lactone connecting 2 fully substituted carbon atoms.

The ^{13}C NMR-spectrum presents signals corresponding to a lactone carbonyl group, 3 singlets for the quaternary carbons, 1 methine doublet, 6 methylene triplets and 2 methyl quartets. Biogenetic considerations, together with these data, led to the tentative assignment of structure I, without stereochemistry, to jhanilactone. The fact that in the ^{13}C NMR-spectrum only 2 methylenes appear in high field is indicative of position 8 and not 9 being substituted.

The shift assignments in the ^{13}C NMR-spectrum are provisional and are based on known chemical shifts, the nature of the signals observed in the offset decoupled spectrum and comparison with other products.

C-1	27.14 (t)[a]
C-2	18.11 (t)[b]
C-3	26.87 (t)[a]
C-4	45.65 (t)[a]
C-5	54.59 (d)
C-6	19.22 (t)[b]
C-7	39.77 (t)
C-8	71.21 (s)
C-9	48.17 (t)
C-10	84.42 (s)
C-11	33.16 (q)
C-12	19.74 (q)
C-13	181.51 (s)



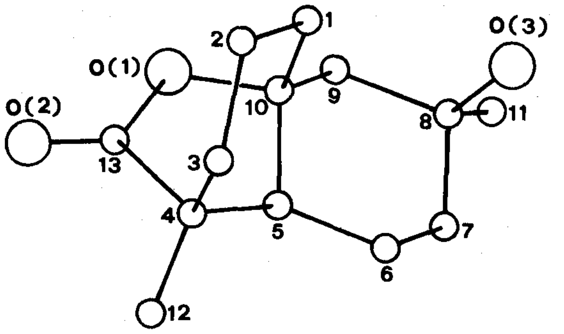
I

[a,b] These assignments may be reversed

X-ray analysis was used to decide the stereochemistry of jhanilactone and to confirm its structure, which was thus established as I or its enantiomer.

The absolute configuration I was determined from the CD curve. Jhanilactone in MeOH exhibited a negative maximum at 214 nm ($\Delta\delta = -1.43$, c = 0.097) characteristic of the structure I.

The relative structure was determined from a single-crystal X-ray diffraction experiment. The compound $C_{13}H_{20}O_3 \cdot H_2O$ crystallizes as transparent needles belonging to the orthorhombic crystal class, space group $P2_12_12_1$. There are 4 molecules per unit cell, dimensions a = 16.231(1), b = 11.145(1) and c = 7.2213(7) Å. A total of 2186 unique diffraction maxima with $\Theta - 30°$ were recorded using monochromated MoKα radiation (0.7107 Å) and a fully-automated 4-circle diffractometer. After background, Lorentz and polarization effects had been discounted, 1423 reflections were judged as observed and used for the crystal structure determination. The structure was solved by direct methods[4] and refined by least squares. One water molecule and all the hydrogen atoms were located on Fourier difference maps[5]. Least refinement, with anisotropic temperature factors for the non-hydrogen atoms and a fixed isotropic temperature factor for hydrogens, gave a conventional discrepancy index of 6.0%. The molecule is shown in the figure. The 2 6-membered rings have a somewhat distorted chair sonformation due to the repulsion between the hydroxyl O(3) and C(1) (3.09 Å). The lactone 5-membered ring presents an envelope conformation, the lowest bond torsion angle being 2.5(4)° for O(1)-C(13). The water molecule O(4) is connected in 3 coplanar hydrogen bonds with 3 molecules: O(3)H---O(4) 2.761 Å, O(4)H---O(2) 2.837 Å and O(4)H---O(H) 2.893 Å.



A computer-produced drawing of the molecule. Bond lengths and angles agree well (esd. of 0.006 Å and 0.3°, respectively) with generally accepted values. All C-C bond lengths are between 1.517 and 1.554 Å; the bond distances which involve oxygen atoms are C(8)O(3) = 1.441, C(10)O(1) = 1.449, O(1)C(13) = 1.349 and C(13)O(2) = 1.202 Å.

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[1] Part 37 in the series 'Chemistry of the Composites'. For Part 36, see A.G. González, J. Bermejo, I. Cabrera, G.M. Massanet, H. Mansilla and J.M. Amaro, Phytochemistry, submitted for publication.

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