6β-HYDROXYCARNOSOL, A NEW MINOR DITERPENE FROM THE FALSE BOLDO *Coleus barbatus* Bentham (LABIATAE)

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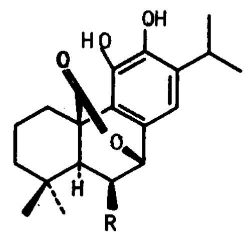
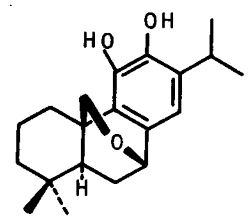
Abstract : 6β-hydroxycarnosol has been obtained from the stems of the false boldo *Coleus barbatus*. Its structure has been deduced from spectral data.

The dichloromethane crude extract of stems of the false boldo, *Coleus barbatus* Bentham (labiatae), induces in anestezised rats a small lowering of bood pressure[1]. We showed that this activity was associated to a fraction containing a mixture of several phenol diterpenes of the abietane skeleton[1-3]. We here wish to report on the structure elucidation of a new minor diterpene, 6β-hydroxycarnosol (1), obtained from the above cited cardioactive fraction[2] by a combination of silica gel column chromatography and gel permeation on Sephadex LH-20.

6β-hydroxycarnosol (1) ($C_{20}H_{26}O_5$ by low resolution MS; m.p. 221-222.5º from $CHCl_3$; $[\alpha]_D$ + 6º ± 1º, c = 0.44 in MeOH) is a colorless compound isolated in 0.007% from dry weight plant material. The IR spectrum of 1 evidenced hydroxyl groups at 3450 and 3290 cm^{-1} and an ester function at 1710 and 1260 cm^{-1}. The UV spectrum (λ_{max} 285 nm in MeOH, shifted to 300 nm after KOH addition) was consistent with either a catechol or a resorcinol residue[4]. The ^{1}H-NMR spectrum, summerized in Table 1, indicated the presence of four methyls, two of which as an isopropyl group attached to the aromatic ring (6H d J=7 Hz at 1.17 ppm and 1H hept J=7 Hz at 3.32 ppm). The presence of only one aromatic hydrogen (1H s at 6.74 ppm) supported the pentasubstituted nature of the aromatic nucleus. Three hydrogens exchangeables with D_2O (br $W_{1/2}$ = 74 Hz 6.36 ppm) indicated the presence of three hydroxyl groups and defined the nature of the five oxygen atoms of 1. These preliminary data, together with biogenetic considerations [1], pointed out to an abietane diterpene substituted by a lactone and by an alcohol in which ring-C is part of a catechol moiety already observed in barbatusol (2)[2] and barbatoxyde (3)[3], two diterpenes that co-occur with 1 in *Coleus barbatus*. The fifth methyl of the abietane skeleton is part of a lactone group. The absence of the $C(7)H_2$ dd at *c.a.* 2.80 ppm[5] and the presence of a 1H signal at 5.20 ppm (d J=4 Hz) showed that the C(7) benzylic position was substituted by the lactone residue (see Table 1, H-7α). The IR vibration of the lactone carbonyl (1710 cm^{-1}) supported a δ-lactone rather than a γ-lactone (expected at about 1745 cm^{-1})[6]. Dreiding models showed that the δ-lactone could *a priori* envolve C(18)Me or C(20)Me, but one may expect to observe, only in the latter case, the C(1)α and C(1)β hydrogens, deshielded by the carbonyl of the ester, at respectively 2.60 (dt) and 2.94 ppm (br d), as they are observed in carnosol (4) (see Table 1). The 20→7 position of the lactone was further supported by the very intense (83%) fragment ion observed in MS at m/z = 302 corresponding to the loss of CO_2 from molecular ion, a characteristic fragmentation of carnosol (4). Hence, 1 appeared to be a monohydroxy derivative of 4. The multiplicity of the C(7) benzylic hydrogen



1 R = OH
4 R = H



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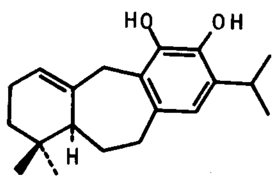

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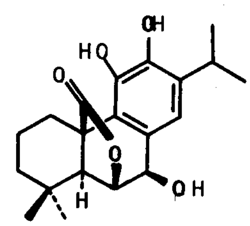

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of 1 (d J = 4.3 Hz) indicated that the C(6) methylene is substituted by the remaining hydroxy group. The carbinolic hydrogen observed as a triplet (J=4.3 HZ) at 4.00 ppm was consistent with this assumption. The C(5) to C(7) >CH-CH(OH)-CH(OCOR)Ø fragment was further substanciated by selective decoupling experiments. Indeed, irradiation of the benzylic hydrogen at 5.20 ppm transformed the carbinolic hydrogen signal, a triplet at 4.40 ppm, into a doublet. Conversely, irradiation at the latter frequency collapsed into singlets both the doublet at 5.20 ppm and the one at 1.51 ppm attributable to the C(5)α hydrogen (Table 1). Finally, irradiation of the latter signal simplified the triplet at 4.40 ppm to a doublet. The β orientation of the secondary alcohol came from the coupling constants of the carbinolic hydrogen : $J_{5\alpha/6}$ = 4.3 Hz and $J_{6/7\alpha}$ = 4.3 Hz, in good agreement with observed values[6] for 6α hydrogens ($J_{5\alpha/6\alpha}$ = 5.8 Hz and $J_{6\alpha/7\alpha}$=3.9 Hz) and uncompatible with a 6 β hydrogen ($J_{5\alpha/6\beta}$ = 10.8 Hz and $J_{6\beta/7\alpha}$ = 1.6 Hz). The presence of the 6 β OH explains why the 4α and 4β methyl groups of 1 are deshielded from their position in carnosol (4) and why they appear much more like the corresponding methyls of rosmanol (5)[6] (see Table 1) of which 6β-hydroxycarnosol (1) is an isomer.

Other diterpenes from the cardioactive fraction from *Coleus barbatus* are currently under study and will be reported elsewhere.

TABLE 1 : ^{1}H-NMR data (100 MHz) of 1 compared to 4 and 5[6]

H Nº	1		4	5
H-1α	2.60	dt[1]	2.55	1.98
H-1β	2.94	br d[2]	2.82	3.29
H-5α	1.51	d[3]	1.70	2.29
H-6α	4.40	t[3]	2.19	4.52
H-7α	5.20	d[3]	5.43	4.64
H-14	6.74	s	6.77	6.89
H-15	3.32	hept[4]	3.36	3.27
Me-16	1.17	d[4]	1.18	1.17
Me-17	1.17	d[4]	1.19	1.18
Me-18	1.10	s	0.88	1.02
Me-19	0.97	s	0.87	0.90
OH x 3	6.36	br[5]	-	-

($CDCl_3$ - two drops of Py-d_5 ; δ in ppm from internal TMS)

1. J = 14 and 5 Hz
2. J = 14 Hz ; $W_{1/2}$ = 8 Hz
3. J = 4.3 Hz
4. J = 7 Hz
5. $W_{1/2}$ = 74 Hz

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