ABSOLUTE CONFIGURATION, AND CHEMICAL CORRELATION OF 6α-HYDROXYCARNOSOL TO EPIROSMANOL

Alphonse KELECOM[a,*] & Walter L.B. MEDEIROS[b]

a. Lab de Produtos Naturais do Mar, Deptº de Biologia Geral, **UFF**, C.P. 100.183, 24000 Niterói RJ, BRAZIL
b. Núcleo de Pesquisas de Produtos Naturais, CCS, bloco H, **UFRJ**, 21941 Rio de Janeiro, RJ, BRAZIL

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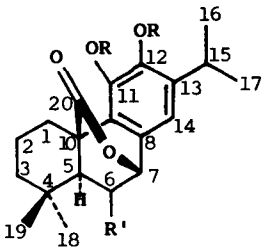
Abstract : the structure of 6α-hydroxycarnosol was confirmed by correlation to the known epirosmanol dimethyl ether. Absolute configuration came from CD studies using carnosol as model compound.

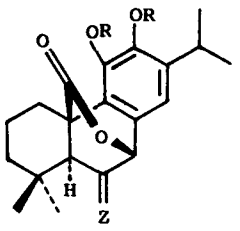
In a previous work[1], we reported the isolation, from the false boldo, Coleus barbatus Bentham (Labiatae), of a minor diterpene for the which structure **1** had been proposed. The stereochemistry at C-6 had been deduced from comparison with carnosol (**2**) ^{1}H NMR data[2]. However, the observed coupling constants of H-5, H-6 and H-7 were found in disagreement with the Karplus correlation curve that pointed to structure **3** rather that **1**. In a recent work[3], we showed, by inversion of the stereochemistry at C-6, following a three-step sequence : **3**→**4**→**5**→**6**, that the Coleus diterpene is indeed 6α-hydroxycarnosol (**3**).

However, this conclusion was based on the assumption that $NaBH_4$ reduction of the C-6 carbonyl function of **5** should proceed from the α-side of the molecule, affording preferentially alcohol **6**. Therefore, we decided to correlate diterpene **3** to epirosmanol (**7**) whose structure was firmly established by correlation to rosmanol (**8**) known from X-ray diffraction analysis[4].

This was achieved in one step by transesterification of **6**. Thus alkaline treatment of **6** (KOH 5% in MeOH, r.t., 70hr) yielded pure **9** identical by $|\alpha|_D$, IR, UV, MS and ^{1}H NMR to an authentic sample of epirosmanol dimethyl ether (**9**)[4]. The driving-force for this reaction may be seen in conformational change of the B-ring from a slightly distorted boat in **6** to a chair in **9**. On the contrary, treatment of **4** under identical alkaline conditions left this compound unchanged. These results definitly established the stereochemistry at C-6 of the Coleus diterpene as 6α-hydroxycarnosol (**3**).

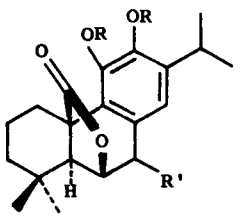
Finally, 6α-hydroxycarnosol (**3**) and epirosmanol (**7**)[4] were shown to belong to the normal series of abietanes, by comparison of the positive Cotton effects observed in the CD curves of **3** ($|\theta|^{MeOH}_{242}$ + 54,384) and of carnosol (**2**) ($|\theta|^{MeOH}_{242}$ + 57,894)[5], a model compound of known absolute configuration[6].





1 R = H ; R' = β-OH
3 R = H ; R' = α-OH
4 R = Me; R' = α-OH
6 R = Me; R' = β-OH

2 R = H ; Z = H,H
5 R = Me; Z = O



7 R = H ; R' = β-OH
8 R = H ; R' = α-OH
9 R = Me ; R' = β-OH

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