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AN ABIETANE DITERPENE FROM THE LABIATE *COLEUS BARBATUS*

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Key Word Index—*Coleus barbatus*; Labiatae; diterpene; abietane; 20-deoxocarnosol.

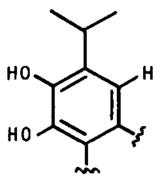
Abstract—20-Deoxocarnosol, isolated from the stems of *Coleus barbatus*, was shown by chemical and spectral methods to be a new phenolic diterpene with an abietane skeleton.

INTRODUCTION

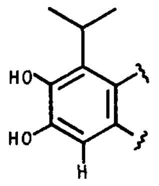
As a part of our studies on the cardioactive dichloromethane crude extract of the false boldo, *Coleus barbatus* Bentham (Labiatae) [1–3], we isolated a new diterpene, 20-deoxocarnosol (**1**), as a crystalline light yellow solid [mp 173.5–175.5°; $[\alpha]_D = -78.7°$ (c 1.00, $CHCl_3$); yield: 0.06% from dry plant material]. I wish to report now on the structure elucidation of **1**.

RESULTS AND DISCUSSION

High resolution mass spectrometry of **1** established the empirical formula $C_{20}H_{28}O_3$ (316.2056, requires 316.2039). The IR spectrum showed the presence of hydroxyl functions (ν_{max} 3560 and 3480 cm^{-1}) that underwent acetylation to furnish a diacetate **2** devoid of further hydroxyl absorptions in the IR spectrum. IR (ν_{max} 1765 cm^{-1}) and ^1H NMR spectral data (δ 2.29 and 2.30, OAc) of **2** suggested the phenolic nature of both hydroxyl groups in **1**. The UV spectrum of **1** confirmed the latter conclusion and indicated that the hydroxyl groups were not *para* to each other [4]. The *ortho* relationship between them came from Ag_2O oxidation of **1** into the unstable *o*-quinone **3** identified by its IR and UV spectra [2, 5] (ν_{max} 1670 and 1650 cm^{-1}; λ_{max} 222, $\log \varepsilon$ 3.76 and 428 nm, $\log \varepsilon$ 3.28). The pentasubstituted nature of the aromatic ring came from ^1H NMR and ^{13}C NMR spectral data (1H, *br s* at δ 6.58; six aromatic carbons 5*s* and 1*d*, see Table 1). The ^1H NMR spectrum of **1** also showed signals for two methyl groups on a quaternary carbon (two 3H, *s* at δ 0.86 and 1.14) and for an isopropyl group (6H, *d*, $J = 7$ Hz at δ 1.25 and 1 H *hept*, $J = 7$ Hz at δ 3.16). The small upfield shift ($\Delta\delta$ 0.24 ppm) of the isopropyl methine signal, observed on acetylation, indicated that the isopropyl group was linked to the phenol moiety. Moreover, the non-equivalence of the isopropyl methyl groups in the ^1H NMR spectrum of diacetate **2** (two 3H, *d*, $J = 7$ Hz at δ 1.17 and 1.21) suggested that a hydroxyl was probably vicinal to the isopropyl group of **1**. These data allowed three different arrangements of the aromatic substituents (**A**–**C**). Among them, **B** could be eliminated since **1** gave a



A



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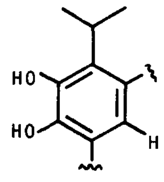

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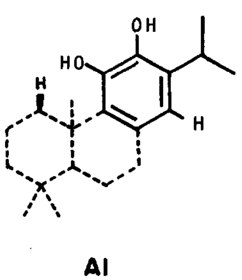

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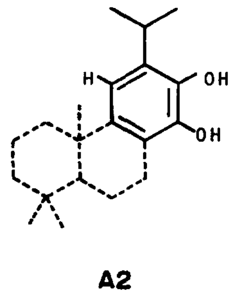

A2

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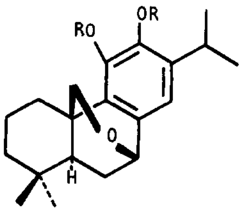
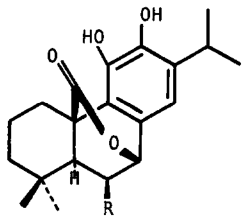
Table 1. ^{13}C NMR data of **1** and **2**

C No.	**1**	**2**	**4**[10, 11]	**5**[13]
1	30.06* *t*	29.54* *t*	38.7	29.8*
2	19.02 *t*	19.01 *t*	19.2	19.7
3	41.20 *t*	40.90 *t*	41.6	41.9
4	33.86 *s*	33.94 *s*	33.3	35.1
5	43.02 *d*	42.06 *d*	50.3	46.4
6	30.82* *t*	29.39* *t*	19.2	30.6*
7	71.11 *d*	70.41 *d*	29.6	78.2
8	132.86† *s*	134.44† *s*	126.2	133.6
9	127.54 *s*	134.44 *s*	147.9	123.1
10	39.89 *s*	40.46 *s*	37.3	49.2
11	140.95 *s*	139.41 *s*	110.6	143.8
12	139.33 *s*	138.95 *s*	151.1	143.4
13	132.24† *s*	136.54† *s*	131.7	135.1
14	112.17 *d*	118.76 *d*	126.1	112.4
15	27.08 *d*	27.48 *d*	26.6	27.6
16	22.70 *q*	22.98 *q*	22.4*	23.0†
17	22.70 *q*	22.98 *q*	22.6*	23.1†
18	32.90 *q*	32.78 *q*	33.1	32.0
19	21.22 *q*	21.32 *q*	21.4	20.0
20	68.48 *dd*	67.62 *dd*	24.6	175.9
(OAc) Me	—	20.72 *q*	—	—
	—	20.35 *q*	—	—
(OAc) CO	—	168.39 *s*	—	—
	—	168.83 *s*	—	—

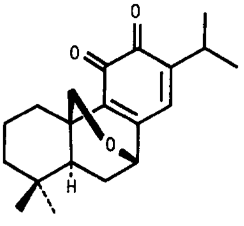
*, †Signals in any vertical column may be reversed.



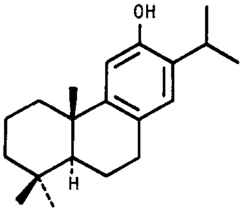
1 R = H
2 R = Ac



5 R = H
6 R = OH



3



4

positive Gibbs test [6], and **C** was discarded mainly on biogenetic grounds since several abietane diterpenes had already been isolated from stems [2, 3] and leaves [7–9] of *C. barbatus*. Fragment **A** accommodates with an abietane (A_1) but also with a sempervirol type compound (A_2). The latter could be discarded since the 1*β*-H of **1** was found to be deshielded to *δ* 2.65 due to the 'rabbit-ear effect' [5] of the hydroxyl group at C-11. Additional support for the abietane skeleton was obtained from the ^{13}C NMR spectrum of **1** (Table 1) which also showed that the third oxygen atom of **1** was part of a $-CH-O-CH_2-$ ether moiety (*δ* 71.11, *d* and 68.48, *dd*). This was further substanciated by the poorly resolved *dd* at *δ* 4.72 (*J* = 3.9 and 1.5 Hz) for the H-7 and by the AB quartet observed at *δ* 3.08 and 4.31 (1H each, *d*, *J* = 9 Hz) attributable to the hydrogens of the oxymethylene moiety. The greater than 1 ppm difference in chemical shifts proved that the latter two hydrogens were in very different environments, and suggested that one hydrogen points towards and the other away from the aromatic ring, a requirement only compatible with the ether being located at C-20. Comparison of the ^{13}C NMR spectral data of the methyl groups of **1**, with those of ferruginol (**4**) [10, 11] (Table 1) confirmed this assignment. This structure was also supported by the mass spectrum of **1** which was dominated by an ion at *m/z* 286 corresponding to the loss of a CH_2O fragment from the molecular ion, and it is known that the fragmentation giving rise to the base peak, in the abietatriene series, is the loss of the C-10 substituent [12]. Furthermore, both the chemical shift and the multiplicity of the signal at *δ* 4.72 indicated that the cyclic ether of **1** closed at the C-7 benzylic position. A Dreiding model showed that, in an abietane derivative, any six-membered ring from C-20 to C-7 necessarily creates an *α*-oriented H-7. This orientation was further confirmed by the coupling constants of the C-7 hydrogen [13]. Hence, **1** is 7*β*,20-oxidoabieta-8,11,13-trien-11,12-diol and it is thus the 20-deoxo derivative of carnosol (**5**) [13, 14]. Additional support for the proposed structure was furnished by the large *γ*-gauche effect observed in the ^{13}C NMR spectra of **1** and **2** on C-5, shielded by *ca* 8 ppm, and the important *anti*-periplanar effect on C-1, shielded by *ca* 9 ppm from their positions in **4** (Table 1). In turn, C-10 was deshielded by *ca* 3 ppm.

Since compounds **1** and **5** possess identical asymmetric carbons, the molecular rotation of **1** ($[\Phi]_D = -248.7°$) strongly supported the proposal that **1** has the same absolute configuration as **5** ($[\Phi]_D = -249.9°$) [15], i.e. **1** belongs to the normal series, a conclusion also arrived at from biogenetic considerations [2, 3]. It is peculiar to note that, although 20-deoxocarnosol (**1**) and 6*β*-hydroxycarnosol (**6**) [3] are both found in *C. barbatus*, no carnosol (**5**) could be detected in this plant.

EXPERIMENTAL

All the equipment used for this work has been described previously [2].

Isolation of 20-deoxocarnosol (**1**). *Coleus barbatus* Bentham was collected in the surroundings of Rio de Janeiro during October 1981. Leaves and stems were separated, air-dried, and the stems pulverized in a hammer mill. The stems (1 kg) were extracted successively with hexane, EtOAc and MeOH at room temp. for several days. The hexane crude extract was evaporated under red. pres. to afford a brownish residue (21 g) which was dissolved in MeOH (50 ml). The insoluble material (7 g) was filtered off and the filtrate concd to a vol. of 10 ml. Aliquots of 2 ml were applied on a Sephadex LH-20 column (200 ml bed volume) eluted with pure MeOH. 20-Deoxocarnosol (**1**) was eluted from the column together with (+)-ferruginol (**4**), barbatusol [2], 6*β*-hydroxycarnosol (**6**) [3] and several other minor diterpenes. Silica gel column chromatography (eluted with a gradient of EtOAc from 10 to 25% in hexane) afforded **1** still contaminated with another unknown diterpene. Crystallizations from hexane–CH_2Cl_2 afforded 585 mg of pure **1** as a light-yellow solid, mp 173.5–175.5°; $[\alpha] = -78.8°$ (589), $-82.6°$ (578), $-94.8°$ (546), $-169.1°$ (436) and $-287.4°$ (365 nm) (c 1.00, $CHCl_3$); IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 3550 and 3480 (OH), 2950, 2860, 1602, 1450, 1290, 1050, 1030 and 998; UV $\lambda_{\max}^{\text{MeOH}}$ nm: 224 ($\log \varepsilon = 3.78$) and 278 (3.15) shifted to 224 (3.83), 248 (3.74) and 291 (3.43) in alkaline MeOH; MS m/z (rel. int.): 316.2056 ($C_{20}H_{28}O_3$ requires 316.2039, 14), 301 (5), 299 (5), 286 $[M - CH_2O]^+$ (100), 271 (14), 243 (8), 215 (32); ^1H NMR (100 MHz, $CDCl_3$): δ 0.86 (3 H, *s*, 19-Me), 1.14 (3H, *s*, 18-Me), 1.25 (6H, *d*, $J = 7$ Hz, 16-Me and 17-Me), 2.65 (1H, *m*, H-1β), 3.08 (1H, *d*, $J = 9$ Hz, H-20), 3.16 (1H, *hept*, $J = 7$ Hz, H-15), 4.31 (1H, *d*, $J = 9.0$ Hz, H′-20), 4.72 (1H, *dd*, $J = 3.9$ and 1.5 Hz, H-7α), 6.04 and 6.20 (each 1H, *m*, disappear on D_2O addition, two OH) and 6.58 (1H, *br s*, sharpens on D_2O addition, H-14); ^{13}C NMR (25.2 MHz, $CDCl_3$): see Table 1.

Acetylation of 20-*deoxocarnosol*. 20-Deoxocarnosol (**1**, 85 mg) in pyridine (2 ml) was treated at room temp. with Ac_2O (2 ml). After 3.5 hr, the reaction medium was diluted with H_2O and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated under high vacuum. The crude material (92 mg) was purified by silica gel column chromatography (hexane–EtOAc from 95:5 to 80:20). Diacetate **2** was obtained pure (82 mg), $[\alpha] = -36.6°$ (589), $-38.3°$ (578), and $-43.8°$ (546 nm) ($c = 1.19$ in $CHCl_3$); IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 2940, 1770 ($>$C=O), 1450, 1365, 1320, 1210, 1185, 1130, 1047, 1030, 1010, 885 and 864; UV $\lambda_{\max}^{C_6H_{12}}$ nm ($\log \varepsilon$): 222 (3.59) and 260 (2.69); MS m/z (rel. int.): 400 ($C_{24}H_{32}O_5$, 6), 370 (16), 364 (2), 358 (8), 328 (48), 316 (12), 286 $[M - CH_2O, \text{two } CH_2CO]^+$ (100), 215 (14); ^1H NMR (100 MHz, $CDCl_3$): δ 0.85 (3H, *s*, 19-Me), 1.15 (3H, *s*, 18-Me), 1.17 and 1.21 (3H each, *d*, $J = 7$ Hz, 16-Me and 17-Me), 2.29 and 2.31 (3H each, *s*, two OAc), 2.94 (1H, *hept*, $J = 7$ Hz, H-15), 3.06 (1H, *d*, $J = 9$ Hz, H-20), 4.38 (1H, *d*, $J = 9$ Hz, H′-20), 4.79 (1H, *dd*, $J_{6\alpha/7\alpha} = 4$ Hz and $J_{6\beta/7\alpha} = 1.5$ Hz, H-7) 7.02 (1H, *s*, H-14); ^{13}C NMR (25.2 MHz, $CDCl_3$): see Table 1.

Oxidation of 20-*deoxocarnosol*. 20-Deoxocarnosol (**1**, 10 mg) in dry THF (5 ml) was oxidized with Ag_2O (25 mg) at room temp. during 15 min. The reaction medium turns gradually from yellow to deep red. Filtration of the solids followed by evaporation under red. pres. afforded crude *o*-quinone (**3**) which was purified by preparative TLC developed with hexane–EtOAc (85:15). Compound **3** proved to be unstable, IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 2960, 1670, 1650 ($>$C=O), 1570, 1450, 1435, 1375, 1350, 1320, 1300, 1280, 1225, 1207, 1145, 1085, 1030, 1015, 988, 965, 945, 900, 852, 840 and 796; UV $\lambda_{\max}^{C_6H_{12}}$ nm ($\log \varepsilon$): 222 (3.76) and 428 (3.28); MS m/z (rel. int.): 314 ($C_{20}H_{26}O_3$, 8), 286 (100), 271 (12), 256 (28), 241 (35), 239 (21), 215 (33) and 213 (17).

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