Phytochemistry, Vol. 23, No. 12, pp. 2960–2961, 1984.
Printed in Great Britain.

0031–9422/84 $3.00 + 0.00

NEO-CLERODANE DITERPENOIDS FROM *TEUCRIUM CHAMAEDRYS*: THE IDENTITY OF TEUCRIN B WITH DIHYDROTEUGIN

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(*Received* 8 *May* 1984)

Key Word Index—*Teucrium chamaedrys*; Labiatae; diterpenoids; teucrin B; dihydroteugin.

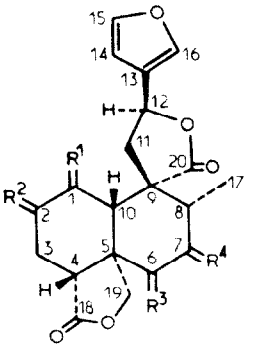
Abstract—The previously proposed structure for teucrin B [15,16-epoxy-1,7-dihydroxy-cleroda-13(16),14-diene-18,19:20,12-diolide] must be amended to 15,16-epoxy-2β,6β-dihydroxy-neo-cleroda-13(16),14-diene-18,19:20,12*S*-diolide, which corresponds to the structure that has been established for dihydroteugin.

The diterpenoids of *Teucrium chamaedrys* L. have been the subject of a number of investigations [1]. From a chemotaxonomic point of view, it is important to note that this species contains not only several C-6 oxygenated neo-clerodane diterpenoids [1] but also teucrins B (**1**), F and G, which are the only neo-clerodanes isolated from *Teucria* to which structures lacking the common C-6 oxygenated function have been attributed [2, 3]. In a recent communication [1], we corrected the previously assigned structures of teucrins F and G, establishing that these compounds possessed a C-6 hydroxyl group. In addition, we pointed out [1] that the structure attributed to teucrin B [15,16-epoxy-1ξ,7ξ-dihydroxy-neo-cleroda-13(16),14-diene-18,19:20,12-diolide] (**1**) [3] required further evidence, because at that time it was the only neo-clerodane diterpenoid found in *Teucria* which was not oxidized at the C-6 position.

A careful revision of all the data on the diterpenoids isolated from *Teucrium chamaedrys* [1] has now shown that the ^{1}H NMR and IR spectra of teucrin B (**1**) and of its diacetate (**2**) [2, 3] are identical to those of dihydroteugin (**4**) and its diacetate (**5**) [4], although some of their physical (mp, $[\alpha]_D$) data do not entirely agree [2–4]. Since dihydroteugin (**4**) was also isolated from *T. chamaedrys* [4], this spectroscopic agreement suggested that teucrin B and dihydroteugin could be the same substance. The discrepancy in melting points (239–241° for **1** [3] and 250–252° for **4** [4]) may be due to polymorphism, while the optical rotation differences [**1** [3]: $[\alpha]_D^{20}$ +5.5° (pyridine; *c* not given); **4** [4]: $[\alpha]_D^{20}$ −9.8° (pyridine; *c* 0.368)] may be attributable to impurities in the samples or to typing or printing errors in ref. [3]. We have checked our previously reported data [4] of dihydroteugin (**4**) and its diacetate (**5**) again and they are correct. In fact, the $[\alpha]_D$ value of the diacetate of dihydroteugin (**5**) was +6.4° [4], which is almost identical to that for teucrin B given in ref. [3], where the $[\alpha]_D$ value of diacetyl teucrin B was not reported.

In order to establish the identity of teucrin B with dihydroteugin (**4**), we have now obtained the diketo derivative **6**, which showed an identical melting point (276–280°) and IR spectrum to those reported [3] for the diketo derivative (**3**) of teucrin B. This establishes that teucrin B must be identical to dihydroteugin or its enantiomer (the $[\alpha]_D$ value of compound **3** was not reported [3]). However, this last possibility is very unlikely, since all the clerodanes isolated from *Teucria* belong to the neo-clerodane absolute configuration, as in the case of dihydroteugin (**4**) [4].

Although the structure of dihydroteugin (**4**) is well known [4], a careful ^{1}H NMR study of the diketone **6** was undertaken in order to establish definitely the positions of its ketone functions and hence of the hydroxyl groups of dihydroteugin (**4**). Table 1 shows data which are only in accordance with a structure such as **6** and not with an



	R^1	R^2	R^3	R^4
1	H,OH	H_2	H_2	H,OH
2	H,OAc	H_2	H_2	H,OAc
3	O	H_2	H_2	O
4	H_2	αH,βOH	αH,βOH	H_2
5	H_2	αH,βOAc	αH,βOAc	H_2
6	H_2	O	O	H_2

Table 1. ^{1}H NMR spectral data of compound **6** (300 MHz, TMS as internal standard) in $CDCl_3$–C_6D_6 (1:1) (a) and $CDCl_3$ (b)*

	(a)	(b)		(a)	(b)
H-1α	2.00 *dd*	†	H_A-11	1.85 *dd*	†
H-1β	2.10 *dd*	†	H_B-11	1.59 *dd*	†
H-3α	2.27 *dd*	†	H-12	4.80 *t*	5.44 *t*
H-3β	2.39 *dd*	†	H-14	6.10 *dd*	6.39 *dd*
H-4β	3.38 *dd*	3.72 *dd*	H-15	7.16 *t*	7.48 *t*
H-7α	3.07 *dd*	3.51 *dd*	H-16	7.15 *m*	7.49 *m*
H-7β	2.05 *dd*	†	Me-17	0.71 *d*	1.17 *d*
H-8β	1.41 *ddq*	2.16 *ddq*	H_A-19	4.40 *d*	4.66 *d*
H-10β	1.67 *dd*	†	H_B-19	4.09 *d*	4.45 *d*

*All these assignments were confirmed by double-resonance experiments.

†Could not be identified using this solvent.

J values (Hz): 1α, 1β = 16.8; 1α, 10β = 13.5; 1β, 10β = 4.6; 3α, 3β = 15.8; 3α, 4β = 10.1; 3β, 4β = 4.8; 7α, 7β = 14.5; 7α, 8β = 13.4; 7β, 8β = 4.2; 8β, 17 = 6.6; 11A, 11B = 14.4; 11A, 12 = 8.9; 11B, 12 = 8.3; 14, 15 = 1.8; 14, 16 = 1.0; 15, 16 = 1.8; 19A, 19B = 11.7.

isomeric one such as **3**. In particular, the ^{1}H NMR patterns shown by the C(1)H_2–C(10)H, C(3)H_2–C(4)H and C(7)H_2–C(8)H-C(17)H_3 structural moieties (Table 1) clearly confirmed this. Moreover, when the Me-17 protons of compound **6** (at δ0.71 or 1.17, see Table 1) were irradiated under NOE experimental conditions, no enhancement of the H-12 signal (at δ4.80 or 5.44, Table 1) was observed, thus establishing the configuration of the C-12 centre as *S* [5].

On the basis of all the above data, teucrin B [2, 3] must be considered identical to dihydroteugin (**4**) [4]. The previous mistake in assigning structure **1** to teucrin B might have been due to the ^{1}H NMR field (60 and/or 100 MHz) utilized in the first work [2, 3] instead of a 300 MHz field used by us, since all the other arguments given in ref. [3] are also in agreement with a structure such as **4** (dihydroteugin) [4] for teucrin B [2, 3].

EXPERIMENTAL

Mp is uncorr. For general details on methods, see refs. [1, 5].

Preparation of compound **6** *from dihydroteugin* (**4**). A soln of dihydroteugin (**4**, 300 mg) in Me_2CO (20 ml) was treated with an excess of Jones' reagent at 0° for 10 min. Work-up in the usual manner yielded 205 mg pure **6** (after crystallization from Me_2CO–Et_2O), mp 276–280°; $[\alpha]_D^{22}$ +99.4° (pyridine; *c* 0.54); IR ν_{max}^{KBr} cm^{-1}: 3170, 3155, 3140, 1510, 880 (furan ring), 1785, 1760 (γ-lactone groups), 1730, 1710 (ketones), 1475, 1425, 1390, 1340, 1205, 1185, 1160, 1035, 1030, 990, 930, 820, 750, 735; ^{1}H NMR (300 MHz, $CDCl_3$ and $CDCl_3$–C_6D_6, 1:1): see Table 1; EIMS (direct inlet) 75 eV, *m/z* (rel. int.): 372 $[M]^+$ (8), 357 (4), 300 (20), 247 (100), 231 (40), 217 (30), 187 (19), 159 (15), 145 (12), 131 (10), 95 (16), 91 (10), 85 (10), 67 (9), 55 (10). (Found: C, 64.36; H, 5.38. Calc. for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41%.)

Acknowledgements—This work was supported partly by the Comisión Asesora de Investigación Científica y Técnica, Madrid, and partly by the National Research Council (CNR), Rome.

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