# THE ABSOLUTE STEREOCHEMISTRY OF SOME CLERODANE DITERPENOIDS ISOLATED FROM *TEUCRIUM* SPECIES

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## (Received 26 June 1990)

Key Word Index—Teucrium spp.; Labiatae; neo-clerodane diterpenoids; absolute configuration; montanin C, 12-epiteupolin II, teugnaphalodin and teubutilin B.

Abstract—The absolute configurations of four previously isolated clerodane diterpenoids, montanin C, 12-epiteupolin II, teugnaphalodin and teubutilin B, have been established by chemical correlation with some derivatives of 19-acetylgnaphalin, a *neo*-clerodane whose absolute stereochemistry is known. The above four compounds also belong to the *neo*-clerodane series.

#### INTRODUCTION

A large number of diterpenoids with the clerodane skeleton have been isolated from *Teucrium* species in the last few years [1-9]. Interest in these compounds has been stimulated by their biological activity as insect antifeedants [10]. Although the *neo*-clerodane absolute stereochemistry [11] has been securely established for the majority of these diterpenoids [1-9], there are some whose absolute configuration has not been rigorously proven. The assumption has been made that they possess a *neo*-clerodane absolute stereochemistry only on biogenetic grounds.

In this communication, we describe some chemical transformations of 19-acetylgnaphalin (1) [12–14] and montanin C (2) [15, 16], which has provided evidence on the *neo*-clerodane absolute stereochemistry of montanin C itself (2), 12-epiteupolin II (3) [9], teugnaphalodin (4) [17] and teubutilin B (5) [7], compounds whose absolute configurations have previously been assigned on biogenetic grounds. This evidence is based on the fact that the *neo*-clerodane absolute stereochemistry of 19-acetyl-gnaphalin (1) has been firmly established by its CD curve, application of Horeau's method and an X-ray diffraction analysis [14].

# **RESULTS AND DISCUSSION**

Four years ago [17], we established the structure of the diterpenoid teugnaphalodin (4) but, at that time, the absolute stereochemistry of its substituted *trans*-decalin moiety was not ascertained. In the same communication [17], we reported the transformation of 19-acetylgnaphalin (1) into the derivative 6, which we have now treated with potassium carbonate in methanol solution (see Experimental) yielding a compound identical in all

respects ( $[\alpha]_D$ , mp, mmp, <sup>1</sup>H NMR, TLC) with natural teugnaphalodin (4), thus establishing a *neo*-clerodane absolute configuration for this diterpenoid (4). The formation of teugnaphalodin (4) starting from 6 under mild alkaline hydrolysis, must be rationalized considering that the C-20–C-19  $\delta$ -lactone is more stable than its C-20–C-12  $\gamma$ -lactone regioisomer [7, 18].

Recently [7], we have isolated a new diterpenoid, teubutilin B (5), from the acetone extract of *Teucrium abutiloides*. This is chemically correlated with teugnaphalodin (4) via the derivative 7 [7, 17], and the absolute configuration had not been ascertained [7]. The above transformation of compound 6 into teugnaphalodin (4), from which the derivative 7 has been obtained [17], firmly supports a *neo*-clerodane absolute stereochemistry for 5, a structural feature of this diterpenoid suggested by us only on biogenetic grounds [7].

Montanin C (2) is a diterpenoid isolated from some Teucrium species [1], the absolute configuration of which was, until now, unknown [15, 16]. Its relative stereochemistry has been established by an X-ray diffraction analysis and a neo-clerodane absolute configuration has been proposed for it [16], taking into account the variation of its specific rotation compared with that of the acetyl derivative (8) of teucjaponin B (9), a diterpenoid whose neo-clerodane absolute stereochemistry is well known [16, 19]. On the other hand, 12-epiteupolin II (3), recently found in T. lamiifolium [9] and T. abutiloides [7], is the 19-deacetyl derivative of montanin C(2), because acetic anhydride-pyridine treatment of compound 3 yielded a substance identical in all respects ( $[\alpha]_{D}$ , <sup>1</sup>H and <sup>13</sup>CNMR, mmp) with natural montanin C (2) [9]. The neo-clerodane absolute configuration of these two diterpenoids (2 and 3) has now been rigorously established as follows.

Treatment of montanin C (2) with potassium t-butoxide in t-butanol solution for 1.5 hr at room temperature predominantly yielded the deacetylation and translactonization product 10, besides minor quantities of

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compound 11 and minute amounts of the derivative 12. The structures assigned to these compounds (10-12) were firmly supported by their <sup>1</sup>H and <sup>13</sup>C NMR spectra (Tables 1 and 2, respectively) and other spectroscopic data (see Experimental).

Oxidation of compound 10 with pyridinium chlorochromate [20] gave the derivatives 13 [ $C_{20}H_{24}O_6$ ;  $v_{OH}$ 3460 cm<sup>-1</sup>;  $\lambda_{max}$  256 nm (log  $\varepsilon$  3.46); <sup>1</sup>H and <sup>13</sup>C NMR data, see Tables 1 and 2] and 14 [ $C_{20}H_{22}O_6$ ; no hydroxyl absorption in its IR spectrum;  $\lambda_{max}$  256 nm (log  $\varepsilon$  3.49); see also Tables 1 and 2]. Treatment of the diketoderivative 14 with phosphoric acid in aqueous methanolic solution [17, 21] yielded a substance identical in all respects ([ $\alpha$ ]<sub>D</sub>, <sup>1</sup>H NMR, TLC) with compound 7 [7, 17].

Finally, reaction of teucjaponin B (9), which has been previously obtained from compound 1 by sodium borohydride reduction [14, 16, 19], with potassium t-butoxide in t-butanol gave derivatives 15 and 16 (see Tables 1 and 2, and Experimental), Oxidation of the former yielded compounds 13 and 14, further supporting the *neo*-clero-dane absolute configuration of the diterpenoids 2 and 3.

In summary, montanin C (2), 12-epiteupolin II (3), teugnaphalodin (4) and teubutilin B (5) belong to the *neo*clerodane series, like all the other diterpenoids which have been isolated from *Teucrium* species and whose absolute stereochemistry has been rigorously established [1-9, 12-19, 21].

### EXPERIMENTAL

Mps: uncorr. Starting materials (compounds 1, 2 and 9) were available from previous studies [1, 7].

Teugnaphalodin (4) from compound 6. A mixt. of 6 (12 mg, obtained from 1 as described in ref. [17]) and  $K_2CO_3$  (12 mg) in

Table 1. <sup>1</sup>H NMR data of compounds 10-16 (CDCl<sub>3</sub>, TMS as int. standard)\*

| н                        | 10                   | 11                       | 12†              | 13                     | 14                   | 15                               | 16                   |
|--------------------------|----------------------|--------------------------|------------------|------------------------|----------------------|----------------------------------|----------------------|
| 1α                       | 1.22 qd              | ‡                        | ‡                | ‡                      | 1.39 gd              | 1.21 qd                          | t                    |
| 1 <i>β</i>               | ~1.75‡               | ‡                        | ‡                | ‡                      | ‡ _                  | ~ 2.42                           | ‡                    |
| 2α                       | 1.99 ddddd           | ‡                        | ‡                | ‡                      | ‡                    | ~2.00‡                           | ‡                    |
| 2β                       | 1.45 qt              | ‡                        | ‡                | 1.51 qt                | ‡                    | 1.50 qt                          | ‡                    |
| 3α                       | 2.24 tdd             | 2.56 tdd                 | ‡                | 2.23 tdd               | ‡                    | 2.25 tdd                         | ‡                    |
| 3β                       | 1.14 ddd             | ‡                        | ‡                | 1.13 ddd               | 1.30 ddd             | 1.14 ddd                         | ‡                    |
| 6β                       | 3.76 ddd             | 3.68 br dd               | 4.07 br dd       | 3.85 ddd               |                      | 3.77 ddd                         | 3.68 br dd           |
| 7α                       | 1.35 ddd             | ‡                        | ‡                | 1.36 ddd               | 2.28 dd*             | 1.41 ddd                         | ŧ                    |
| 7β                       | 1.91 ddd             | <b>‡</b>                 | \$               | Į                      | 2.96 dd              | 1.92 ddd                         | Ţ                    |
| 8β                       | 2.45 ddq             | ∼1.72 <b>‡</b>           | 2.58 ddq         | 2.53 ddq               | 2.85 sext            | 2.11 ddq                         | Ŧ                    |
| 10 <i>B</i>              | ~1.75‡               | Ŧ                        | Į,               | Ŧ.                     | 3.23 ddd             | 2.24 dd                          | Ŧ                    |
|                          | 1.86 <i>dd</i>       | 2.31 dd                  | 1.86 dd          | 2.98 d                 | 3.16 <i>d</i>        | 2.13 dd                          | 2.34 d               |
| 11 <sub>B</sub>          | 2.68 ad              | 2.45 ad                  | 2.66 aa          | 3.69 a                 | 3.62 a               | 2.45 aa                          | 5.24                 |
| 12                       | 4.00 aaag            | 5.391                    | 4.081<br>6.46.13 | 675 11                 |                      | 4.85 aaag<br>6 A2 JJ             | 5,54 l<br>6 27 11    |
| 14                       | 0.40 aa<br>7 41+     | 0.30 aa                  | 0.40 aa          | 0.15 aa<br>7 A6 JJ     | 0.77 44              | 0.45 aa                          | 0.57 aa<br>7 42+     |
| 15                       | 7.414<br>7.414       | 7.43 l<br>7.43 m         | 1.3/l<br>7.38 m  | 7.40 aa<br>8 13 dd     | 7.40 aa<br>8 14 dd   | 7.40 <i>l</i><br>7.41 m          | 7.454                |
| 10<br>Mo 17              | 1.05 2               | 1.45 m<br>1.12 J         | 1.30 m           | 0.12 uu                | 0.14 uu<br>0.04 d    | 0.02 J                           | 1.454                |
| 19                       | 1.05 a<br>264 dii    | 1.15 <i>u</i><br>2.44 dB | 1.00 a           | 0.92 a<br>2 62 JI      | 2.54 4               | 0.92 a<br>2 64 dii               | 1.05 u<br>2 46 di    |
| 10A                      | 2.04 u   <br>3.33 JJ | 2.44 ali<br>3.13 dat     | 4.49 U<br>A 54 d | 2.05 a   <br>3.35 d d¶ | 2.33 U  <br>3.13 AAU | 2.04 0                           | 2.40 ali<br>3.17 dd¶ |
| 10<br>10                 | 4 70 dd              | 4.12 hr d                | 4.68 br dt       | 174 dd                 | 5.15 aa ∥<br>4.51 dd | 5.52 dd <sub>11</sub><br>A 74 dd | 401 br d             |
| 10<br>10                 | 4.83 1               | 4.12 01 4                | 4.80 01 44       | 4.74 uu<br>1.87 d      | 4.51 uu<br>4.85 d    | 4831                             | 4.01 01 0            |
| OAc                      |                      | 4.02 u                   | 2115             |                        |                      | 4.05 u                           | 4.00 u               |
| OH(C-6)**                | 3.79 s               | 3.48 s                   | <b>1</b>         | 3.69 s                 | _                    | 3.83 s                           | 3.50 s               |
| OH(C-12)**               | 1.75 d               |                          | + <del>+</del>   |                        |                      | 1.79 d                           |                      |
| · · · · (· · · · · )     |                      |                          | • •              |                        |                      |                                  |                      |
| J(HZ)                    | 12.4                 | +                        | +                | +                      | 13.5                 | 12.4                             | +                    |
| $1\alpha, 1\beta$        | 13.4                 | +                        | +                | 1                      | 12.5                 | 13.4                             | ÷                    |
| $1\alpha, 2\alpha$       | 4.2                  | +                        | +                | 12.5                   | 4.3                  | 5./<br>12.4                      | +                    |
| 1a, 2p                   | 13.4                 | +                        | +                | +                      | 12.5                 | 13.4                             | +<br>+               |
| 18.2~                    | 34                   | +                        | +<br>+           | ÷                      | 12.5                 | 30                               | +                    |
| 18.28                    | 37                   | +<br>+                   | +                | + 38                   | + +                  | 3.8                              | *<br>*               |
| 18,20                    | +                    | +<br>+                   | +                | +                      | ÷ 10                 | 3.8                              | ÷                    |
| $2\alpha 2\beta$         | 134                  | ++++                     | *<br>+           | 135                    | +                    | 13.4                             | *<br>+               |
| $2\alpha, 2\beta$        | 42                   | 48                       | +                | 41                     | +                    | 42                               | +<br>†               |
| $2\alpha$ , $3\beta$     | 3.0                  | +                        | ÷<br>†           | 2.8                    | 2.9                  | 3.1                              | Ŧ                    |
| 2B.3a                    | 13.4                 | 13.3                     | Ť                | 13.5                   | t                    | 13.4                             | Ī                    |
| 28.38                    | 3.7                  | t                        | Ť                | 3.8                    | 3.8                  | 3.8                              | ż                    |
| 3α,3β                    | 13.4                 | 13.3                     | ŧ                | 13.5                   | 12.6                 | 13.4                             | ŧ                    |
| 6β,7α                    | 11.4                 | 10.4                     | 12.4             | 11.3                   | _                    | 11.3                             | 11.4                 |
| 6β,7β                    | 5.4                  | 3.4                      | 6.8              | 5.5                    | —                    | 5.4                              | 3.5                  |
| $7\alpha, 7\beta$        | 13.6                 | ‡                        | ‡                | 13.6                   | 14.1                 | 13.7                             | ‡                    |
| 7α,8β                    | 11.4                 | ‡                        | 11.0             | 11.3                   | 7.0                  | 11.5                             | ‡                    |
| 7β,8β                    | 4.1                  | ‡                        | 4.2              | 4.3                    | 7.0                  | 4.7                              | ‡                    |
| 8 <i>β</i> ,17           | 6.6                  | 6.7                      | 6.6              | 6.8                    | 7.0                  | 6.7                              | 6.6                  |
| 11 <b>A,</b> 11 <b>B</b> | 16.1                 | 13.9                     | 16.0             | 19.1                   | 19.2                 | 15.8                             | 0                    |
| 11 <b>A</b> ,12          | 2.0                  | 8.2                      | 1.8              | —                      |                      | 10.5                             | 8.6                  |
| 11 <b>B</b> ,12          | 10.2                 | 9.0                      | 10.1             |                        |                      | 1.3                              | 8.6                  |
| 14,15                    | 1.5                  | 1.8                      | 1.8              | 1.9                    | 1.9                  | 1.7                              | 1.8                  |
| 14,16                    | 1.2                  | 0.9                      | 0.9              | 0.9                    | 0.9                  | 0.9                              | 0.9                  |
| 15,16                    | Į,                   | 1.8                      | 1.8              | 1.4                    | 1.4                  | 1./                              | 1.8                  |
| 18A,18B                  | 3.3                  | 3.5                      | 11.0             | 5.5                    | 4.0                  | 3.5                              | 3.D                  |
| 18B,30                   | 2.4                  | 2.3                      | 0                | 2.4                    | 1.7                  | 2.0                              | 2.5                  |
| 19A,19B                  | 12.5                 | 13.2                     | 13.2             | 12.5                   | 12.3                 | 12.5                             | 13.1                 |
| 19A,00<br>10A 100        | 1.5                  | < 0.5                    | < 0.3            | 1.0                    | U<br>11              | 1.5                              | < 0.5                |
| 12A,10p                  | 10                   | U                        | U<br>++          | 0                      | 1.1                  | 34                               | -                    |
| 12,12(01)                | 7.7                  |                          | 11               |                        |                      | 5.7                              |                      |

\*Spectral parameters were obtained by first order approximation. All these assignments have been confirmed by double resonance experiments.

†In chloroform-*d*-pyridine- $d_5$  (9:1) solution. ‡Overlapped signal. \$Collapsed into *dd* after addition of D<sub>2</sub>O.

|Exo hydrogen with respect to ring B.|Endo hydrogen with respect to ring B.\*Disappeared after addition of D<sub>2</sub>O.

††Not measured. These assignments may be interchanged.

| С   | 10              | 11      | 12*     | 13      | 14      | 15             | 16      |
|-----|-----------------|---------|---------|---------|---------|----------------|---------|
| 1   | 23.8 <i>t</i> † | 21.7 t  | 20.3 t  | 23.8 t  | 22.7 t  | 23.8 t         | 22.6 t  |
| 2   | 24.4 t          | 24.8 t  | 23.6 t  | 24.6 t  | 23.6 t  | 24.7 t         | 25.1 t  |
| 3   | 31.4 t          | 31.2 t  | 28.4 t  | 31.3 t  | 31.1 t  | 31.6 t         | 31.3 t  |
| 4   | 65.0 s          | 67.1 s  | 74.6 s  | 64.9 s  | 57.9 s  | 65.3 s         | 67.2 s  |
| 5   | 40.0 s          | 45.8 s  | 41.5 s  | 39.7 s  | 48.5 s  | <b>40</b> .1 s | 46.2 s  |
| 6   | 72.7 d          | 74.1 d  | 71.3 d  | 72.5 d  | 206.9 s | 72.8 d         | 74.2 d  |
| 7   | 36.3 t          | 33.9 t  | 35.6 t  | 37.0 t  | 45.3 t  | 36.2 t         | 33.6 t  |
| 8   | 34.8 d          | 40.9 d  | 33.8 d  | 33.9 d  | 35.4 d  | 34.4 d         | 38.4 d  |
| 9   | 49.3 s          | 51.4 s  | 48.0 s  | 49.9 s  | 49.3 s  | 50.0 s         | 51.2 s  |
| 10  | 43.0 d          | 50.2 d  | 39.4 d  | 42.2 d  | 41.8 d  | 44.4 d         | 52.8 d  |
| 11  | 37.1 t          | 43.8 t  | 37.7 t  | 38.3 t  | 40.2 t  | 37.0 t         | 43.8 t  |
| 12  | 62.7 d          | 71.2 d  | 60.7 d  | 192.6 s | 192.3 s | 63.6 d         | 71.4 d  |
| 13  | 130.0 s         | 125.2 s | 130.2 s | 128.0 s | 127.7 s | 130.2 s        | 125.2 s |
| 14  | 108.4 d         | 107.8 d | 107.9 d | 108.3 d | 108.2 d | 108.3 d        | 107.9 d |
| 15  | 143.7 d         | 144.0 d | 142.0 d | 144.4 d | 144.4 d | 143.7 d        | 144.2 d |
| 16  | 138.5 d         | 139.0 d | 137.2 d | 147.3 d | 147.4 d | 138.5 d        | 139.5 d |
| 17  | 17.0 q          | 16.9 q  | 16.0 q  | 16.5 q  | 17.2 q  | 16.5 q         | 16.5 q  |
| 18  | 50.7 t          | 47.6 t  | 64.8 t  | 50.8 t  | 51.2 t  | 50.9 t         | 47.9 t  |
| 19  | 66.9 t          | 61.3 t  | 67.4 t  | 66.9 t  | 69.1 t  | 67.1 t         | 60.9 t  |
| 20  | 172.1 s         | 176.2 s | 171.6 s | 171.3 s | 170.9 s | 172.1 s        | 176.4 s |
| OAc | _               |         | 169.6 s |         |         |                |         |
|     |                 |         | 19.6 q  |         |         |                |         |

Table 2. <sup>13</sup>C NMR chemical shifts of compounds 10-16 (CDCl<sub>3</sub>, TMS as int. standard)

\*In pyridine- $d_5$  solution.

†Multiplicities were established by the DEPT pulse sequence.

MeOH (2 ml) at room temp. was stirred for 20 min. The reaction mixt. was diluted with water (10 ml) and extracted with  $CH_2Cl_2$  (4 × 10 ml). The organic soln after drying over  $Na_2SO_4$ , was eaved giving a residue which was subjected to CC (silica gel, *n*-hexane–Me<sub>2</sub>CO, 2:1 as eluent) yielding a compound [8 mg, after crystallization from EtOAc–*n*-hexane, mp 162–164°;  $[\alpha]_D^{20} - 69.9^\circ$  (CHCl<sub>3</sub>; c 0.302)], identical in all respects ( $[\alpha]_D$ , mp, <sup>1</sup>H NMR) with natural teugnaphalodin [4, ref. [17]: mp 159–162°;  $[\alpha]_D^{21} - 70.2^\circ$  (MeOH; c 1.084)]. Comparison (mmp, TLC) with an authentic sample of teugnaphalodin (4) confirmed this identity.

Transformation of montanin C (2) into compounds 10–12. A soln of 2 (1.09 g) in t-BuOH (100 ml) was treated with KOBut (1.37 g) at room temp. for 1.5 hr; then, the reaction mixt. was diluted with  $H_2O$  (100 ml), acidified with 2%  $H_2SO_4$  (pH 4) and extracted with  $CH_2Cl_2$ . Work-up in the usual manner yielded a residue (800 mg) which was subjected to CC (silica gel). Elution with *n*-hexane–EtOAc (1:1) successively yielded compounds 10 (410 mg) and 12 (25 mg). Further elution with EtOAc–*n*-hexane (3:1) gave 11 (116 mg).

Compound 10. Mp 195–197° (EtOAc–*n*-hexane);  $[\alpha]_{\rm b}^{1.9}$ –10.9° (CHCl<sub>3</sub>; c 0.988). IR  $\nu_{\rm max}^{\rm KBr}$  cm<sup>-1</sup>: 3460, 3390 (OH), 3155, 3140, 1600, 1508, 877 (furan), 3060 (epoxide), 1730 ( $\delta$ -lactone); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>): see Table 2; EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 362 [M]<sup>+</sup> (80), 344 (1.5), 314 (2), 275 (11), 205 (16), 187 (30), 161 (38), 111 (86), 97 (90), 95 (86), 91 (66), 81 (52), 69 (54), 55 (53), 41 (100). (Found: C, 66.39; H, 7.09. C<sub>20</sub>H<sub>26</sub>O<sub>6</sub> requires: C, 66.28; H, 7.23%.)

Compound 11. Mp 165–166° (EtOAc-*n*-hexane);  $[\alpha]_D^{20} + 11.0°$ (CHCl<sub>3</sub>; *c* 0.218). IR  $v_{max}^{\text{max}}$  cm<sup>-1</sup>: 3490, 3410, 3320, (OH), 3150, 3140, 3120, 1600, 1508, 875 (furan), 3060 (epoxide), 1765 ( $\gamma$ -lactone); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (50.3 MHz, CDCl<sub>3</sub>): see Table 2; EIMS (direct inlet) 70 eV, m/z (rel. int.): 362 [M]<sup>+</sup> (3), 344 (7), 314 (29), 269 (32), 218 (40), 187 (45), 159 (42), 131 (23), 105 (36), 97 (16), 95 (100), 91 (53), 81 (55), 79 (41), 67 (24), 55 (28), 41 (47). (Found: C, 66.21; H, 7.16.  $C_{20}H_{26}O_6$  requires: C, 66.28; H, 7.23%.)

Compound 12. Mp 199–201° (EtOAc–n-hexane);  $[\alpha]_{2^{0}}^{2^{0}} - 12.0°$ (CHCl<sub>3</sub>–MeOH, 9:1; c 0.118). IR v<sub>M</sub><sup>BB</sup> cm<sup>-1</sup>: 3470, 3430 (OH), 3160, 3140, 3130, 1600, 1505, 875 (furan), 1730 br ( $\delta$ -lactone and acetate), 1240 (OAc); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>–pyridine-d<sub>5</sub>, 9:1): see Table 1; <sup>13</sup>C NMR (50.3 MHz, pyridine-d<sub>5</sub>): see Table 2; EIMS (direct inlet) 70 eV, m/z (rel. int.): 422 [M]<sup>+</sup> (84), 404 (36), 386 (12), 362 (2), 344 (100), 331 (3), 287 (6), 43 (17). (Found: C, 62.30; H, 7.23. C<sub>22</sub>H<sub>30</sub>O<sub>8</sub> requires: C, 62.54; H, 7.16%.)

Pyridinium chlorochromate oxidation of compound 10 to give 13 and 14. A soln of 10 (404 mg) in dry  $CH_2Cl_2$  (60 ml) was treated with PCC (2.16 g) at room temp. for 30 hr, with stirring and in the presence of 4 Å molecular sieves. The reaction mixt. was then diluted with dry  $Et_2O$  (100 ml) and the resulting suspension was filtered through a silica gel pad. The filtrate was evapd giving a residue (300 mg), which was chromatographed (CC, silica gel, *n*hexane-Me<sub>2</sub>CO, 2:1 as eluent) yielding compounds 13 (70 mg, less polar constituent) and 14 (150 mg).

Compound 13. Amorphous solid, mp 65–75°;  $[\alpha]_{D}^{20} - 2.3^{\circ}$ (CHCl<sub>3</sub>; c 0.217). IR v<sup>KBr</sup><sub>max</sub> cm<sup>-1</sup>: 3460 (OH), 3130, 1560, 1510, 875 (furan), 3060 (epoxide), 1730 ( $\delta$ -lactone), 1675 (conjugated ketone); UV  $\lambda^{MeOH}_{max}$  nm (log  $\varepsilon$ ): 256 (3.46); <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (50.3 MHz, CDCl<sub>3</sub>): see Table 2; FIMS (direct inlet) 70 eV, *m/z* (rel. int.): 360 [M]<sup>+</sup> (20), 342 (3), 233 (18), 175 (8), 159 (12), 147 (11), 105 (11), 95 (100), 91 (18), 79 (11), 77 (11), 67 (10), 55 (9), 41 (14). (Found: C, 66.76; H, 6.87. C<sub>20</sub>H<sub>24</sub>O<sub>6</sub> requires: C, 66.65; H, 6.71%.)

Compound 14. Amorphous solid, mp 55–60°;  $[\alpha]_{D}^{23} - 33.1^{\circ}$ (CHCl<sub>3</sub>; c 0.341). IR  $v_{max}^{\text{KBr}}$  cm<sup>-1</sup>: 3140, 1565, 1510, 875 (furan), 3060 (epoxide), 1730 ( $\delta$ -lactone), 1720 (C-6 ketone), 1680 (conjugated ketone); UV  $\lambda_{max}^{MeOH}$  nm (log  $\varepsilon$ ): 256 (3.49); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (75.4 MHz, CDCl<sub>3</sub>): see Table 2; EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 358 [M]<sup>+</sup> (83), 322 (15), 288 (13), 249 (13), 231 (12), 205 (26), 175 (20), 161 (10), 95 (100), 91 (16), 77 (12), 69 (13), 41 (17). (Found: C, 66.87; H, 6.09. C<sub>20</sub>H<sub>22</sub>O<sub>6</sub> requires: C, 67.02; H, 6.19%.)

Compound 7 from derivative 14. Compound 14 (25 mg) was added to a mixt. of 0.1 N H<sub>3</sub>PO<sub>4</sub> (5 ml) and MeOH (5 ml) and the reaction mixt. was stirred and refluxed for 8 hr. Work-up in the usual manner [17, 21] yielded a residue (15 mg). After chromatographic purification (PLC, EtOAc-*n*-hexane, 3:2 as eluent), pure 7 (10 mg) was obtained: amorphous solid,  $[\alpha]_D^{18} - 23.7^\circ$  (CHCl<sub>3</sub>; c 0.589) [ref. [7, 17]: amorphous solid,  $[\alpha]_D^{22} - 24.1^\circ$  (CHCl<sub>3</sub>; c 0.860),  $-25.1^\circ$  (CHCl<sub>3</sub>; c 0.675)], identical in all respects (<sup>1</sup>H NMR, TLC) with the previously described compound [7, 17].

Transformation of teucjaponin B (9) into compounds 15 and 16. Teucjaponin B (9, 200 mg, obtained by reduction of 19-acetylgnaphalin (1) with NaBH<sub>4</sub> [14]) was treated with KOBut-t-BuOH as described for compound 2 (see above), yielding the derivatives 15 (70 mg, less polar compound in TLC with *n*-hexane-EtOAc, 1:1 as eluent) and 16 (25 mg).

Compound 15. Mp 213–215° (EtOAc–n-hexane);  $[\alpha]_{D}^{22} - 52.8°$  (CHCl<sub>3</sub>; c 0.413). IR  $\nu_{max}^{Ber}$  cm<sup>-1</sup>: 3395, 3340 (OH), 3140, 3125, 3115, 1600, 1505, 875 (furan), 3080 (epoxide), 1720 ( $\delta$ -lactone); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (50.3 MHz, CDCl<sub>3</sub>): see Table 2; EIMS (direct inlet) 70 eV, m/z (rel. int.): 362 [M] <sup>+</sup> (100), 344 (7), 314 (16), 275 (6), 268 (16), 251 (10), 218 (35), 205 (21), 187 (37), 161 (34), 159 (42), 97 (51), 95 (93), 91 (57), 81 (47), 69 (39), 55 (34), 41 (35). (Found: C, 66.21; H, 7.32. C<sub>20</sub>H<sub>26</sub>O<sub>6</sub> requires: C, 66.28; H, 7.23%.)

Compound 16. Mp 166–168° (EtOAc–n-hexane);  $[\alpha]_D^{20} + 30.5°$  (CHCl<sub>3</sub>; c 0.305). IR  $\nu_{max}^{KBr}$  cm<sup>-1</sup>: 3570, 3530, 3470 (OH), 3160, 3140, 1600, 1510, 880 (furan), 3070 (epoxide), 1755 ( $\gamma$ -lactone); <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): see Table 1; <sup>13</sup>C NMR (50.3 MHz, CDCl<sub>3</sub>): see Table 2; EIMS (direct inlet) 70 eV, m/z (rel. int.): 362 [M] <sup>+</sup> (50), 344 (5), 314 (28), 269 (25), 218 (53), 187 (42), 159 (39), 131 (23), 105 (37), 97 (30), 95 (100), 91 (50), 81 (47), 79 (33), 67 (22), 55 (28), 41 (10). (Found: C, 66.32; H, 7.29. C<sub>20</sub>H<sub>26</sub>O<sub>6</sub> requires: C, 66.28; H, 7.23%.)

Oxidation of compound 15 to give derivatives 13 and 14. Compound 15 (30 mg) was treated with PCC as in the case of compound 10, yielding 13 (3 mg) and 14 (11 mg), identical ( $[\alpha]_D$ , <sup>1</sup>H NMR, TLC) with those obtained from compound 10.

Acknowledgements---One of us (A.L.) thanks the Spanish Foreign Ministry for a fellowship. This work was subsidized

by the Spanish DGICYT (Grant No. PB87-0418) and the 'Programa Conjunto No. 3.3, CSIC-CNR' (Italy-Spain).

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