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Oxirane-Opening Reactions of some 6,19-Oxygenated 4α,18-Epoxy-*neo*-Clerodanes Isolated from *Teucrium*. Biogenesis and Antifeedant Activity of their Derivatives[§]

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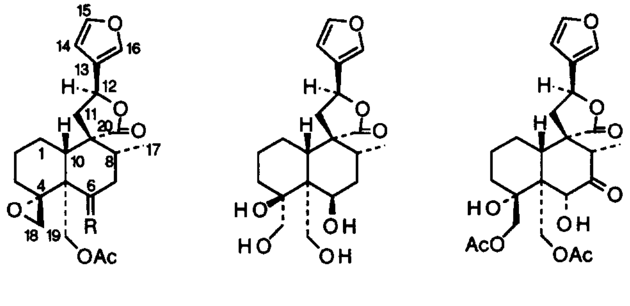
Abstract: Some 4α,18-epoxy-*neo*-clerodane diterpenoids possessing oxygenated functions at the C-6 and C-19 carbons have been subjected to oxirane-opening reactions with several reagents obtaining chlorohydrins, 4-hydroxy-6,18-ethers, 4-hydroxy-18-*O*-methyl- and 18-*O*-acetyl derivatives, allylic C-18 primary alcohols and 4,6,18 and 4,6,19-orthoacetates. These results revealed that the functionality at C-6 and its stereochemistry determine the course of the reaction and affect the retention or inversion of the configuration at the C-4 asymmetric centre. In the light of these reactions, a hypothesis on the biogenetic pathway of some *neo*-clerodane diterpenoids isolated from *Teucrium* species is proposed. Moreover, useful criteria for establishing the stereochemistry at C-4 in these derivatives, as well as the unambiguous assignment of the structure of montanin E by an X-ray diffraction analysis and the results achieved in the biological assay as insect antifeedants of several non-natural *neo*-clerodane derivatives are also reported.

The *neo*-clerodane diterpenes[1] have attracted interest in the last few years on account of their useful biological activities and challenging structures[2]. Up to date, the most abundant source of this kind of compounds are the plants belonging to the genus *Teucrium* (family Labiatae), from which about 150 *neo*-clerodanes have been isolated[2,3]. The more common structural feature of these compounds is the existence of a spirocyclic oxirane at the 4α,18 position, such as in 19-acetylgnaphalin[4] (**1**) and teucjaponins A and B[5] (**2** and **3**, respectively). This epoxide is accompanied by oxygenated functions at the C-6 and C-19 carbons, both found in all the *neo*-clerodanes biosynthesized by *Teucrium* species[2-5].

Within the *neo*-clerodanes isolated from *Teucrium*[2-5], we have observed that, in general, compounds having a 4α,18-chlorohydrin[6] or a 4α,18-glycol[7], possess a 6-ketone or an equatorial 6α-hydroxyl group, whereas 4β-hydroxylated[8] and 3,4-didehydro derivatives[3f,9] exhibit an axial 6β-hydroxyl function. These observations, together with our continuous interest in the isolation[2,3,4a,c,5b,6b,7-9a-d,10], chemical transformation[11], hemisynthesis[11b,c] and biological activity[10a,12] of *neo*-clerodanes, prompted us to undertake a study on the

[§] Dedicated to the late Prof. José Borja Carbonell (1902-1993), Faculty of Pharmacy, Complutense University, Madrid.

opening of the 4α,18-epoxide of compounds **1**, **2** and **3** and other related substances. The aim of this study was to find biomimetic-type transformations of the more abundant natural diterpenes into the minor ones, to clarify how the functionality and the stereochemistry of the C-6 oxygenated substituent influence the opening of the 4α,18-oxirane and to test the hemisynthetic substances as antifeedants against pest.



1 R=O
2 R=αH, βOH
3 R=αOH, βH

4

5

In this communication, we wish to report our results on the above mentioned reaction, together with conclusive spectroscopic criteria for establishing the C-4 configuration in 4,18-dihydroxy derivatives, which were supported by the unequivocal assignment of the structure of montanin E[8a] (**4**) by an X-ray diffraction analysis. In addition, a biogenetic pathway for some natural 4β-hydroxy- and 3,4-didehydro-*neo*-clerodanes is proposed and the results of the antifeedant activity against larvae of *Spodoptera littoralis* of several hemisynthetic compounds are also reported.

RESULTS AND DISCUSSION

In order to determine accurately the structures of the products obtained by the oxirane-opening reactions, our first purpose was to find an easy and reliable method for establishing the configuration at C-4 in compounds possessing a 4,18-glycol or related functionality. For some *neo*-clerodanes having a 4α-hydroxyl and an axial 4β-substituted methylene groups, the configuration at C-4 has previously been solved by ^{1}H NMR spectroscopy. In some of these compounds, the signal of one of the protons corresponding to the axial 18-methylene appears as a slightly broadened doublet, showing long-range coupling (J=0.5-0.2 Hz) with the axial H-3α proton[6b,13]. However, in other cases, the value of this coupling constant is zero or close to zero and none of the H-18 proton signals show broadening, thus precluding a definite conclusion on the C-4 stereochemistry.

Obviously, the choice for establishing the configuration of the 18-substituted methylene must be NOE experiments and this was confirmed by the results achieved on montanin E[8a] (**4**) and picropolinol[7a] (**5**). In compound **5**, having an axial 4β-acetoxymethylene group, irradiation at the signal of the H-10β proton (δ 2.36 dd) caused, among others (see Table 1), NOE enhancement in both the C-18 protons (δ 4.59 d and 4.42 d), whereas in montanin E (**4**, 4α-hydroxymethylene stereoisomer) this effect was not observed (Table 1) when its H-10β proton (δ 3.19 dd) was irradiated. These results evidenced that NOE experiments are more definite than the previously described method[13] for establishing the configuration at the C-4 asymmetric centre of these compounds.

Table 1. NOE Experiments on Compounds **4-6**, **11** and **12**[a].

Compound	Irradiated proton (δ)	Observed NOE enhancement[b]
4	H-10β (3.19)	H-8β [++], H-11 (pro-*S*) [++], H_A-18 [0], H_B-18 [0]
5[c]	H-10β (2.36)	H-6β [++], H-8β [++], H_B-11 (pro-*S*) [++], H_A-18 (pro-*S*) [+], H_B-18 (pro-*R*) [++]
6[c]	H_A-18 (3.85)	H-10β [++], H_B-18 (pro-*S*) [+++]
	H_B-18 (4.07)	OH-4α [+], H_A-18 (pro-*R*) [+++]
11[c]	H-10β (2.80)	H-1β [++], H-8β [++], H_A-18 (pro-*R*) [-], H_B-18 (pro-*S*) [++]
	H_A-18 (3.16)	H-3β [++], H-10β [0], H_B-18 (pro-*S*) [+++], OMe-18 [++]
	H_B-18 (4.33)	H-2β [+], H-10β [++], H_A-18 (pro-*R*) [+++], OMe-18 [+]
12[c]	H_A-18 (3.83)	H-6β [++], OH-4α [++], H-10β [0], H_B-18 (pro-*R*) [+++], OMe-18 [++]
	H_B-18 (4.00)	H-6β [+], H-10β [++], H_A-18 (pro-*S*) [+++], OMe-18 [+++]

[a]Measured at 300 MHz by the FT difference method. [b]The signs [+], [++] and [+++] denote weak (0.5-2%), medium (3-5%) and strong (>8%) positive NOE enhancement, respectively. The sign [-] means a weak negative NOE enhancement. Zero indicates not observed NOE enhancement in significant protons. [c]The preferred rotamer around the C-4,C-18 bond for each compound, deduced from these data, is depicted in Fig. 2.

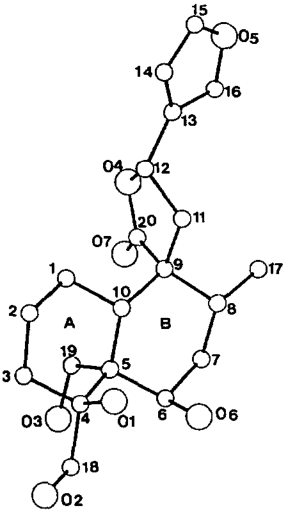
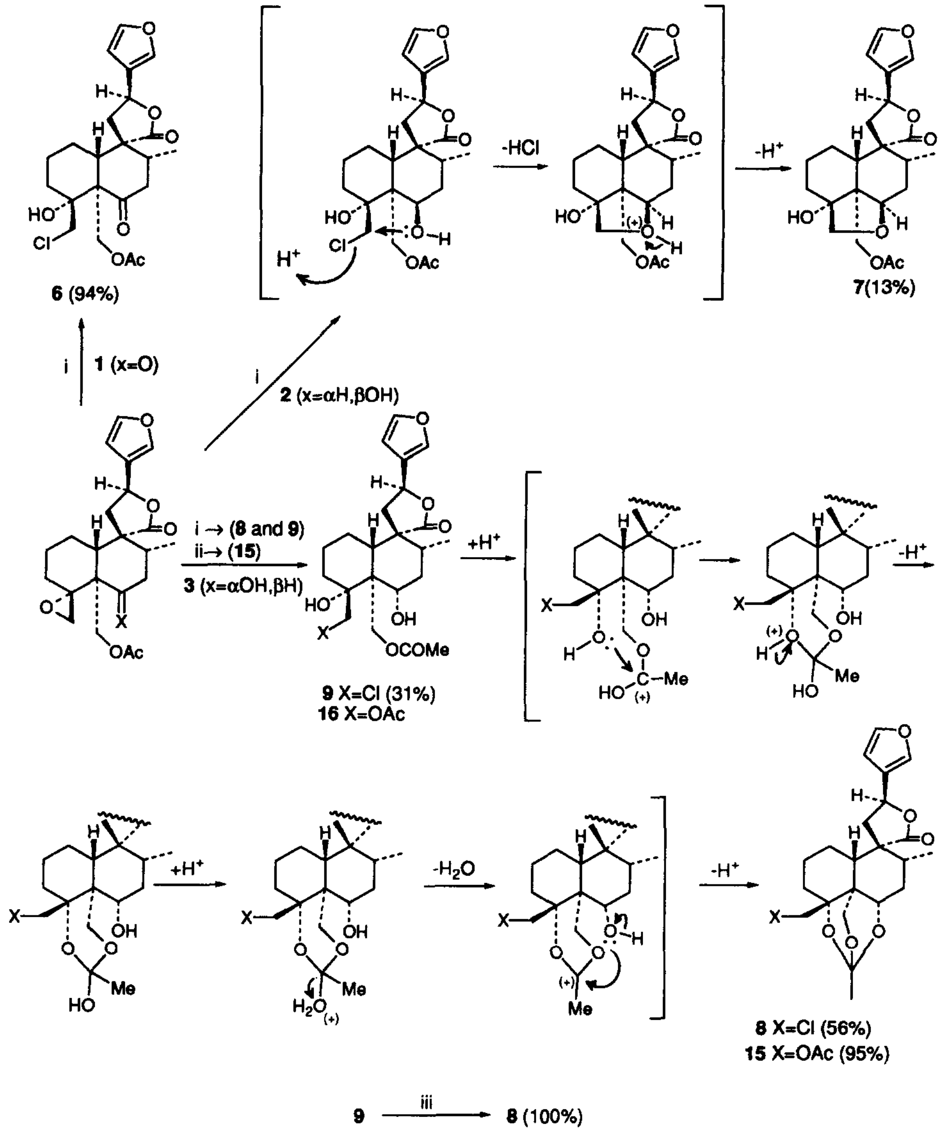


Figure1. X-Ray molecular model of montanin E (**4**), showing the atomic numbering (hydrogens are omitted for clarity).

Although the NOE experiments were congruent with the structures attributed to montanin E[8a] (**4**) and picropolinol[7a] (**5**), we decided to confirm the structure of the former by an X-ray diffraction analysis, because montanin E is the sole 4β,18-dihydroxy-*neo*-clerodane derivative isolated from *Teucrium* and its structure (**4**) has been established only by ^1H and ^{13}C NMR studies[8a]. On the contrary, the structure of picropolinol (**5**) is strongly supported by chemical correlation with picropolin and related compounds[7a], apart from its ^1H and ^{13}C NMR spectroscopic parameters. Figure 1 shows the X-ray molecular model of montanin E confirming that its structure **4** was correct. (For more details on the crystalline structure of **4** see Experimental.)

In previous works[6b,11e,14] we reported the preparation of chlorohydrins by hydrochloric acid treatment of 19-acetoxy-4α,18-epoxy-6-oxo-*neo*-clerodane and 4α,18-epoxy-6α-hydroxy-*neo*-clerodan-20,19-olide derivatives, yielding compounds with retention of the configuration at C-4 by attack of the nucleophile on the primary centre of the epoxide (C-18). In accordance with these results, treatment of 19-acetylgnaphalin (**1**) with hydrochloric acid in chloroform solution for 5 minutes at room temperature gave the expected derivative **6** in excellent yield (94%, Scheme 1). However, when teucjaponin A (**2**) was treated under the same conditions we observed (TLC) the formation of a very unstable compound which, after column chromatography on silica gel, was transformed into the 6β,18-ether **7** (13% yield, Scheme 1) and a complex mixture of several unidentified minor compounds. Furthermore, treatment of a chloroform solution of teucjaponin B (**3**) with hydrochloric acid in the above conditions yielded two compounds (Scheme 1). The major product was the orthoacetate **8** (56% yield) and the minor one was the expected chlorohydrin **9** (31% yield) which, in turn, was quantitatively transformed into the derivative **8** when the time of reaction was one hour.

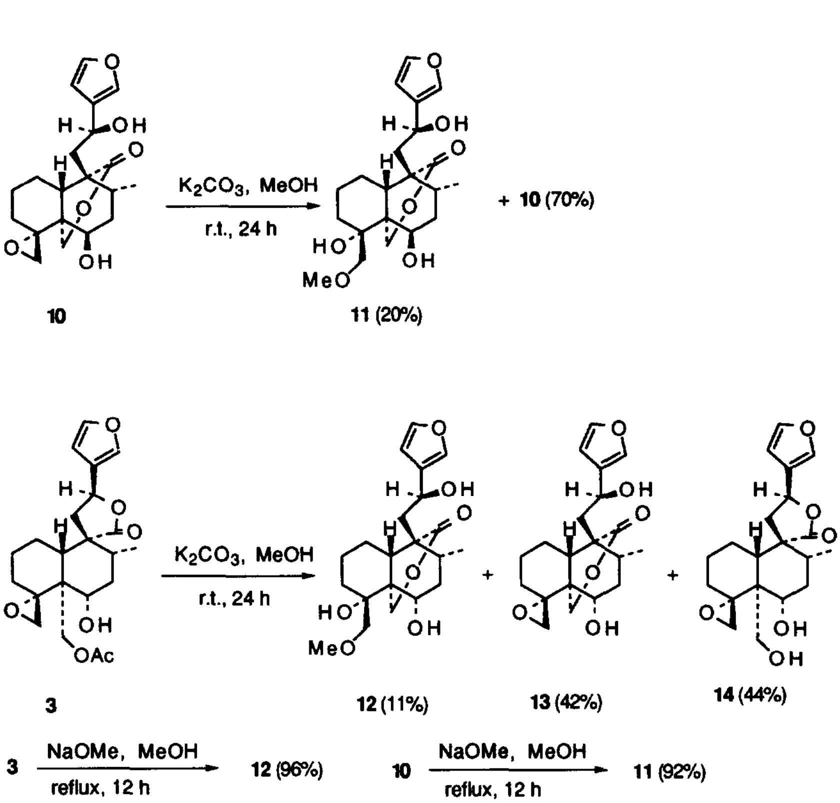
Scheme 1



i: Aq. HCl, $CHCl_3$, r.t., 5 min. ii: Glacial HOAc, reflux, 3h. iii: Aq. HCl, $CHCl_3$, r.t., 1h.

In all these cases the course of the oxirane-opening reaction occurs in the expected way[6b,11e,14], with retention of the configuration at C-4 (see Table 1 and Experimental). The formation of the derivative **7** from teucjaponin A (**2**) could be rationalized by the mechanistic pathway shown in Scheme 1, where the formation of the 6β,18-ether bridge may be due to the 1,3-diaxial interaction between the 4β-chloromethylene group and the 6β-hydroxyl substituent in the unstable chlorohydrin intermediate. On the other hand, the formation of the orthoacetate **8** via the chlorohydrin **9** (see above) under acid conditions could be explained by the plausible mechanism outlined in Scheme 1. It is noteworthy that orthoacetates closely related to compound **8** are known as natural products[15] and they have previously been obtained[11a] by thermal rearrangement of 19-acetylgnaphalin (**1**), although by a mechanistic pathway slightly different from that shown in Scheme 1.

Scheme 2



We next investigated the oxirane-opening reaction of the 4α,18-epoxide of teucroxylepin[16a] (**10**) and teucjaponin B (**3**) with potassium carbonate in methanol solution at room temperature (Scheme 2). In the first case, after 24 hours of reaction, the 4α-hydroxy-18-methoxy derivative **11** was obtained in 20% yield, together with starting material (**10**, 70% yield), whereas teucjaponin B (**3**) gave compounds **12**, **13** and **14** (11%, 42% and 44% yield, respectively). These two last substances (**13** and **14**) are already known[16a] as hemisynthetic derivatives of teucjaponin B (**3**). Furthermore, when the diterpenes **10** and **3** were refluxed with sodium methoxide in methanol solution, quantitative transformations into the derivatives **11** and **12**, respectively, were obtained. All these results are in agreement with the previously described reaction of teucjaponin A (**2**) with potassium carbonate in an aqueous methanol solution, in which teucroxylepin (**10**) and the derivative **11** were obtained[16a]. In accordance with these previous results[16] and those shown in Scheme 2, the formation of compounds **11** and **12** from teucjaponins A (**2**) and B (**3**), respectively, occurs via C-19 deacetylation and translactonization to the more stable C-20,C-19 δ-lactone[16], followed by attack of a methoxy anion on the less hindered C-18 position of the oxirane, with retention of the configuration at the C-4 carbon.

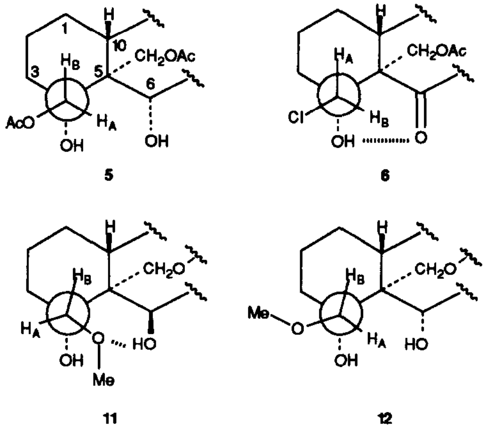


Figure 2. Preferred rotamers around the C-4, C-18 bond of compounds **5**, **6**, **11** and **12** as deduced from NOE experiments (Table1).

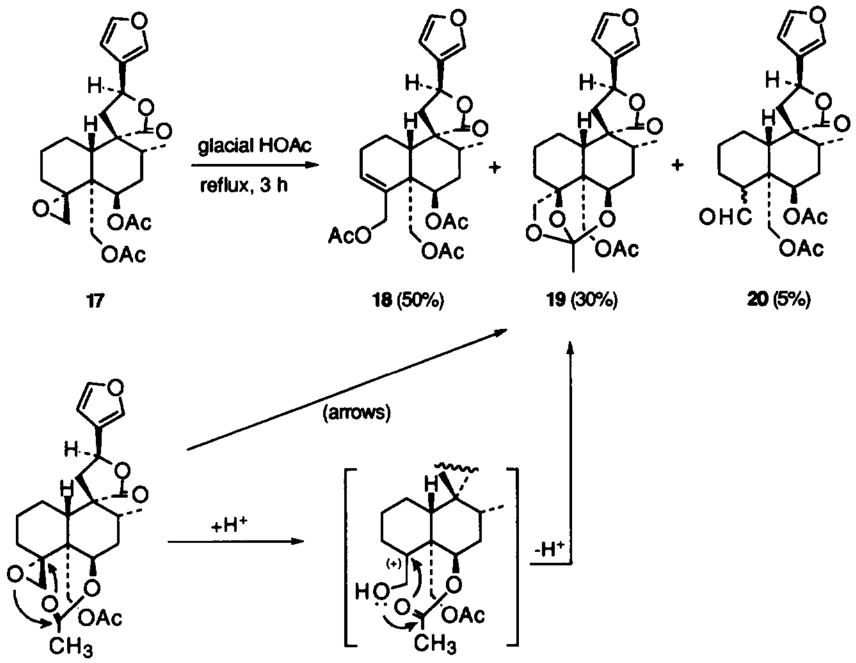
It is important to note that the 4β-configuration of the 18-methoxymethylene substituent of compounds **11** and **12** was firmly established from NOE experiments (see Table 1). Moreover, the results of the NOE experiments summarized in Table 1 allowed the unequivocal assignment of both the C-18 methylene protons in compounds **5**, **6**, **11** and **12**, as well as the preferred rotamer around the C-4,C-18 bond in each of these compounds (Figure 2).The different preferred rotamer in the C-6 epimeric compounds **11** and **12** must be explained considering that in **11** there is a hydrogen-bonding between the axial 6β-alcohol and the oxygen atom of the axial 18-methoxymethylene substituent (Fig. 2). This is not possible in the case of the equatorial 6α-hydroxy derivative **12**, in the preferred rotamer of which steric effects are prevailing, just as in compounds **5** and **6**[17].

The oxirane-opening reaction of compounds **2** and **3** was also assayed with glacial acetic acid[18]. Teucjaponin B (**3**) gave the orthoacetate **15** (95% yield, Scheme 1), probably via the intermediate **16** (Scheme 1), whereas teucjaponin A (**2**) was transformed into a complex mixture of several degradation products which were not investigated. On the contrary, when the reaction was carried out with the 6-acetyl derivative[5a] (**17**) of teucjaponin A (Scheme 3), we obtained two major compounds, **18** and **19** (50% and 30% yield, respectively), besides minor quantities (5% yield) of a mixture of the C-4 epimeric aldehydes **20**. Compound **18** is the already known peracetyl derivative of teuscorodol[9a] and 19-deacetylteuscorodol[9c] (two *neo*-clerodanes isolated from *Teucrium* species[2]) and, in principle, its formation from **17** requires the opening of the oxirane by an attack of the acetate anion on the C-18 carbon, followed by a 3,4-dehydration reaction. When this dehydration takes place with one of the C-18 hydrogens, the epimeric aldehydes **20** were formed, probably via a vinyl-acetate intermediate, which is easily hydrolized in the acid conditions of the reaction[19].

The derivative **19** had a molecular formula $C_{24}H_{30}O_8$ and its IR spectrum was devoid of hydroxyl absorptions. The ^1H and ^{13}C NMR spectra of this substance revealed that it possessed an acetate (δ_H 2.07, 3H, s; δ_C 170.3 s and 21.2 q) and an orthoacetate (δ_H 1.61, 3H, s; δ_C 118.8 s and 22.1 q) groups. Comparison of the ^1H NMR data of 6-acetylteucjaponin A (**17**) with those of **19** clearly established that the 4β, 6β and 18 positions are involved in the orthoacetate group of the last compound[20], because the signal of its equatorial

H-6α proton (δ 4.32 t, $J_{6\alpha,7\alpha}=J_{6\alpha,7\beta}=3.0$ Hz) appeared up-field shifted with respect to **17** (δ 5.12 m, $W_{1/2}=7.5$ Hz)[5a], whereas the C-19 methylene protons resonated at an almost identical field in both compounds (**17**[5a]: δ 4.97, 2H, s; **19**: δ 4.91 d and 4.47 d, $J_{gem}=13.1$ Hz). The formation of a substance such as **19** starting from the 4α,18-epoxy derivative **17** implies an inversion of the configuration of the C-4 asymmetric centre, as a consequence of an intramolecular attack of the axial 6β-acetoxyl group on the C-4 carbon (Scheme 3).

Scheme 3

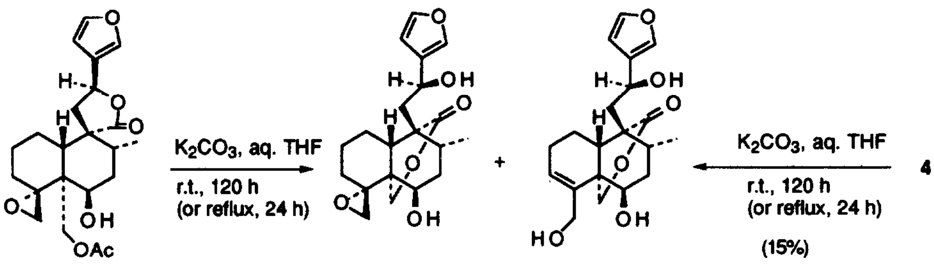


17

As compared with the other reactions described above, the behaviour of compound **17** shows two noticeable differences, namely, the inversion of the configuration at C-4 (compound **19**) and the dehydration reaction giving the derivatives **18** and **20**. It is evident that the first result is due to the spatial closeness between the spirocarbon of the oxirane (C-4) and the 6β-acetoxyl group, but in the second case, we suppose that there exists a more complicated mechanism than a mere dehydration reaction favoured by the disappearance of the 1,3-diaxial interactions between the 4β and 6β substituents. This hypothesis seems to be corroborated by the fact that dehydration products were not formed when compound **11** (Scheme 2) was treated with glacial acetic acid[21] under the same conditions that in the case of **17**.

On the other hand, treatment of teucjaponins A (**2**) and B (**3**), montanin E (**4**) and the 4α-hydroxy derivatives **11** and **12** (see Scheme 2) with potassium carbonate in an aqueous THF solution at room temperature for 120 hours (or 24 hours under reflux) gave the following results. Compounds **11** and **12** were recovered unchanged and teucjaponin B (**3**) yielded compounds **13** and **14** (60% and 30% yield, respectively; see their formulae in Scheme 2) as the sole detectable products. In the case of teucjaponin A (**2**) the products of the reaction were teucroxylepin (**10**, 80% yield) and another substance (**21**, 10% yield, Scheme 4) identical in all respects with the natural diterpene teubotrin[9c,d,11d], the formation of which implies the opening of the oxirane and a dehydration reaction, apart from the hydrolysis of the C-19 acetate and the translactonization from C-20,C-12 to C-20,C-19. Finally, montanin E (**4**) gave a complex mixture of several products from which teubotrin (**21**) was also isolated (15% yield). These results established that, under the reaction conditions, compounds possessing a tertiary alcohol function at the C-4α equatorial position (**11** and **12**) and a 6β axial (**11**) or 6α equatorial (**12**) hydroxyl group are not dehydrated, whereas in 4β,6β-dihydroxy compounds (**4**) or 4α,18-epoxy-6β-hydroxy derivatives (**2**) the 3,4-dehydration occurs (compound **21**, Scheme 4).

Scheme 4



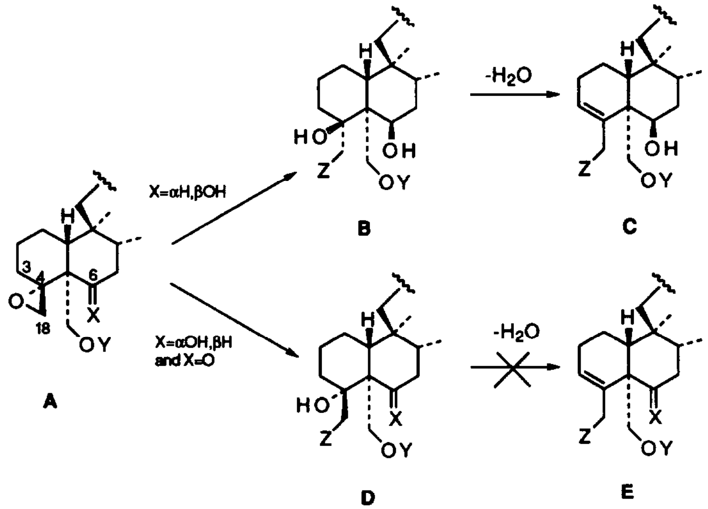
2 **10** (80%) **21** (10%)

From all the above results, it is not easy to postulate an unique mechanism for explaining the observed dehydration in the oxirane-opening reaction of compounds **17** (Scheme 3) and **2** (Scheme 4). A plausible common intermediate such as montanin E (**4**, Scheme 4), presumably originated from these compounds (**2** and **17**) by an inversion of the configuration of the C-4 carbon, seems to be in contradiction with the fact that in compound **18** (Scheme 3) the opening of the oxirane takes place seemingly by attack of an acetate anion on the C-18 carbon (as it is apparently evidenced by the acetoxyl substituent at this carbon), thus precluding the epimerization at C-4. The formation of teubotrin (**21**, Scheme 4) from montanin E (**4**) is a normal *trans*-diaxial elimination. The reaction of teucjaponin A (**2**, Scheme 4) with potassium carbonate in aqueous THF solution also gave teubotrin (**21**) and, in principle, the possibility of a β-face attack of the nucleophile on the C-4 carbon of the epoxide could not be discarded. In this case, the 4β-hydroxy intermediate could produce the dehydration product (**21**), like in montanin E (**4**). However, this hypothesis seems to be inconsistent with the results obtained in the reaction of compounds **2** and **10** with potassium carbonate or sodium methoxide in methanol solution, where only attack of the nucleophile on C-18 was observed (**11**, see above and Scheme 2). Moreover, the formation of peracetyl teuscorodol (**18**, Scheme 3) from teucjaponin A (**2**) via the orthoacetate **19** must be discarded, because this orthoacetate was stable in glacial acetic acid under reflux.

Apart from the preceding reasonings, there is a plausible explanation for the dehydration of compound **17**. If the opening of the 4α,18-oxirane occurs via a 4-carbocation intermediate, an attack of an acetate anion by the β-face, competing with the intramolecular reaction depicted in Scheme 3, could produce a 4β-acetoxy-18-hydroxy derivative, which undergoes a sterically favoured transacetylation to a 4β-hydroxy-18-acetoxy intermediate easily dehydrated to peracetylteuscorodol (**18**) by a *trans*-diaxial elimination mechanism.

In any case, some of the preceding results evidence the different behaviour of the 6-hydroxy epimers in the 4α,18-oxirane-opening reactions and that the dehydration takes place only in the 6β-hydroxy or acetoxy derivatives. The mechanism of this dehydration reaction remains unknown, although it is evident that there is an anchimeric participation of the 6β-oxygenated neighbouring group.

Scheme 5



Neo-clerodanes from *Teucrium*. Proposed biogenetic pathway for 4β- (**B**) and 4α-hydroxy- (**D**)-*neo*-clerodanes and 6β-hydroxy-*neo*-clerod-3-enes (**C**) from 4α,18-epoxy-6-oxygenated-*neo*-clerodanes (**A**). (Y=H, Ac or closure of a lactone ring; Z=OH, OAc or, in some cases of type **D**, Cl.)

The formation of *neo*-clerod-3-ene derivatives (**18** and **21**) starting only from 4α,18-epoxy-6β-oxygenated compounds, together with the fact that, in general, the natural 4β-hydroxy-[2,8] and 3,4-didehydro-*neo*-clerodanes[2,3f,9] isolated from *Teucrium* species[2] possess a 6β-hydroxyl group, support the biogenetic pathway depicted in Scheme 5. Among the more widespread and abundant 4α,18-epoxy-*neo*-clerodanes[2,3] (**A**, Scheme 5), those having a 6β-hydroxyl group could be biosynthetically transformed into 4β-hydroxy derivatives (**B**), like montanin E (**4**)[8a]. These diterpenes (**B**) are, probably, the intermediates of the natural *neo*-clerod-3-enes (**C**), such as teuscorodol[9a] and teubotrin (**21**)[9c,d]. On the contrary, natural 4α,18-epoxy-6α-hydroxy- or 6-oxo-*neo*-clerodanes seem to be biosynthetically transformed into 4α-hydroxy derivatives (**D**), such as picropolinol (**5**)[7a] and tafricanins[6a], and these compounds, probably, are not biosynthetically dehydrated to 18-hydroxy-, chloro- or oxo-*neo*-clerod-3-enes (**E**), since clerodane-type diterpenes possessing these functionalities and simultaneously a 6-ketone or a 6α-hydroxyl group have not been isolated from *Teucrium* species up to date[2,3].

Finally, several of the non-natural *neo*-clerodane derivatives described above were tested for antifeedant activity against larvae of *Spodoptera littoralis*. The results of these bioassays are shown in Table 2, along with the activity of three other natural *neo*-clerodanes which have been included for comparative purposes. The results show that changes in the functionalities at C-4 and C-6 alter the activity of the compound as do changes in the stereochemistry of these functionalities. The most potent antifeedant in the present study was the natural *neo*-clerodane **3**, which has an α-hydroxyl group at C-6 and a 4α,18-epoxide. The presence of a β-hydroxy (**2**) or a ketone at C-6 (**1**) in the presence of a 4α,18-epoxide, results in a decrease in antifeedant activity.

Table 2. Effect of some Natural *Neo*-Clerodanes and their Derivatives on the Feeding Behaviour of Larvae of *Spodoptera littoralis*.

Compound	Antifeedant Index[a] mean ± SEM[b]	Compound	Antifeedant Index[a] mean ± SEM[b]
1	23.7 ± 6.98[c]	**8**	-30.6 ± 9.78[#]
2	12.9 ± 7.67[c]	**9**	8.8 ± 10.98
3	48.9 ± 5.98*[c]	**12**	-51.2 ± 7.88[#]
5	2.3 ± 13.47	**15**	-22.3 ± 9.04
6	21.0 ± 12.45		

[a]Antifeedant Index: [(C-T)/(C+T)]x100; C=weight of control disc eaten, T=weight of treatment disc eaten. This index identifies both phagostimulants (-ve values) and antifeedants (+ ve values). Number of replicates=15.[b]Significant difference between amount of control and treatment disc eaten (Wilcoxon's matched pairs test, $p<0.05$); *=antifeedant, #=phagostimulant. [c]Results taken from Simmonds *et al.*, ref. 12.

A comparison of the activity associated with compounds **1**, **5**, **6**, **9** and **12** shows that compounds with an opened oxirane that have a ketone present at C-6 (compare activity of **1** with **6**) possess some antifeedant activity, whereas if there is an α-hydroxy present at C-6 the compound is inactive (**5** and **9**) or a phagostimulant (**12**). Further modifications at C-4 and C-6, as in the orthoacetates **8** and **15**, results in phagostimulant activity. Thus, the 4α,18-epoxide function of natural *neo*-clerodanes needs to be maintained in the search for non-natural *neo*-clerodane derivatives with potent antifeedant activity.

EXPERIMENTAL

Mps are uncorrected. Starting materials, 19-acetylgnaphalin[4a,c] (**1**), teucjaponin A[5b] (**2**), teucjaponin B[4c] (**3**), montanin E[8a,22] (**4**), picropolinol[7a] (**5**) and teucroxylepin[16a] (**10**), were available from previous works. 6-Acetylteucjaponin A (**17**) was obtained by Ac_2O-pyridine treatment[5a] of teucjaponin A.

X-Ray structure determination of montanin E (**4**). Crystal data: $C_{20}H_{28}O_7$; M_r=380.443 g mol^{-1}; cell dimensions a=37.445(56), b=7.563(1), c=6.5840(4) Å; V=1864.4(3) Å^3; space group $P2_12_12_1$; Z=4; D_c=1.3552 g cm^{-3}; μ=8.050 cm^{-1}; F(000)=816.0. A suitable crystal (0.45x0.20x0.32 mm) was selected for data collection. Accurate cell parameters were obtained by least-squares refinement on the setting angles of 21 reflections in the θ range of 10° to 39°. The data were collected on a diffractometer Philips PW 1100 with ω/2θ scan technique, scan width 1.50, scan speed 0.03 deg. min^{-1}, detector aperture 1x1, θ-range scanned 2°-65°. Two reference reflections were measured every 90 reflections during the data collection and no crystal decay was observed. From 1914 collected reflexions only 1674 were considered observed with $I>2\sigma(I)$ and were used in the structure solution and refinement. The data were corrected for Lorentz and polarization effects, but not for absorption.

The structure was solved by direct methods (SIR88)[23] and refined first isotropically and after anisotropically for non-H atoms. The H-atoms were found in difference electron density maps; refinement continued in all positioned parameters, anisotropic for non-H atoms and isotropic for H-atoms. The weighting scheme used is empirical no to give trends[24] in $<w\Delta^2F>$ vs. $<F_o>$ and $<\sin\theta/\lambda>$. The final R and R_w values are 6.2% and

6.3%, respectively. The final difference electron density is 0.65 eÅ^{-3}. The number of variables is 356, ratio of freedom 4.7 and degrees of freedom 1319.

Scattering factors, including corrections for anomalous dispersion, were taken from the literature[25], computing programs from reference 26, molecular parameters were calculated using PARST[27] and drawing of Fig. 1 from *PLUTO*[28]. All calculations were performed on a VAX 6410 computer.

Table 3. Hydrogen-Bonding Data of Montanin E (4) in the Crystal Structure[a].

Bond[b] D-H...A	D-H	Bond length (Å) D...A	H...A	D-H...A angle (°)	Symmetry
O(1)-H...O(6)[c]	0.96(13)	2.65(1)	1.79(12)	147.(10)	x,y,z
O(2)-H...O(3)	0.84(10)	2.77(1)	1.93(10)	178.(8)	1/2-x,2-y,z-1/2
O(3)-H...O(1)	0.85(96)	2.75(1)	1.93(20)	161.(8)	x,y,1+z
O(6)-H...O(2)	0.87(10)	2.97(1)	2.18(10)	150.(9)	1/2-x,1-y,1/2+z

[a]For the numbering of the oxygen atoms see Fig. 1.[b]D and A mean donor and acceptor, respectively.[c]Intramolecular H-bond.

In the crystalline state, rings A and B of montanin E (**4** and Fig. 1) adopt a slightly flattened chair conformation, as is indicated by the average of the endocyclic torsion angles, 56° and 51°, respectively. The lactone ring has an envelop conformation, with the flap at C-11, and it is perpendicular to the decalin plane (rings A and B), being the angle between both planes 93°. The hydroxyl groups of the molecule are involved in hydrogen-bonding; there is one intramolecular H-bond between the 4β-hydroxyl group and the oxygen atom of the 6β-alcohol and the packing is stabilized by three intermolecular H-bonds. This network is described in Table 3. There are other two intermolecular contacts less than the sum of the van der Waals radii: O(1)....C(19)=3.26 Å (x,y,z-1) and O(2)....C(5)=3.19 Å (1/2-x,1-y,z-1/2). It could be possible that these contacts and the intramolecular H-bond are the cause of the flattening of the decalin moiety[29].

*(12S)-19-Acetoxy-18-chloro-15,16-epoxy-4α-hydroxy-6-oxo-*neo-*cleroda-13(16),14-dien-20,12-olide* (**6**) *from 19-acetylgnaphalin* (**1**). A solution of **1** (80 mg) in $CHCl_3$ (15 ml) at room temperature was treated with aqueous conc. HCl (1.5 ml) for 5 min. with stirring. The reaction mixture was diluted with H_2O and extracted with $CHCl_3$ (4x25 ml). The extract was dried over Na_2SO_4, filtered and evaporated to dryness giving a residue from which 82 mg of **6** were obtained by crystallization from EtOAc - *n*-hexane: mp 145-147 °C (decomp.); $[\alpha]_D^{18}$ +5.9° ($CHCl_3$; *c* 0.807). IR (KBr) ν_{max} cm^{-1}: 3500 (OH), 3140, 3120, 1600, 1510, 875 (furan), 1765 (γ-lactone), 1740, 1240 (OAc), 1720 (ketone), 2980, 2880, 1480, 1435, 1390, 1325, 1200, 1180, 1160, 1095, 1090, 1040, 1020, 990, 935, 810, 750, 740, 640. ^{1}H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 440 $[M]^+$ (0.1), 438 $[M]^+$ (0.3), 422 (2), 420 (4), 402 (100), 384 (44), 343 (16), 329 (68), 313 (69), 221 (6), 173 (11), 134 (16), 133 (11), 105 (17), 95 (28), 94 (14), 91 (22), 81 (16), 79 (10), 69 (16), 43 (72). (Anal. Found: C, 60.27; H, 6.42; Cl, 7.97. $C_{22}H_{27}O_7Cl$ requires: C, 60.20; H, 6.20; Cl, 8.08%.)

*(12S)-19-Acetoxy-6β,18;15,16-diepoxy-4α-hydroxy-*neo-*cleroda-13(16),14-dien-20,12-olide* (**7**) *from teucjaponin A* (**2**). Treatment of **2** (40 mg) with aqueous conc. HCl (0.5 ml) in $CHCl_3$ solution (10 ml) as described above gave a residue (38 mg) which showed a major spot on TLC (EtOAc - *n*-hexane 7:3 as eluent).

Table 4. ^{1}H NMR Spectroscopic Data of Compounds **6-9**, **12**, **15** and **19**[a].

H	**6**	**7**	**8**	**9**	**12**	**15**	**19**
1α	1.60 qd	*b*	*b*	*b*	1.23 qd	*b*	*b*
1β	~1.86[b]	*b*	*b*	*b*	*b*	*b*	*b*
2α	~1.86[b]	*b*	*b*	*b*	*b*	*b*	*b*
2β	1.39 qt	*b*	*b*	*b*	*b*	*b*	*b*
3α	1.73 dddd	*b*	2.06 tdd	*b*	1.59 tdd	*b*	*b*
3β	2.18 ddd	*b*	~2.37[b]	2.14 ddd	*b*	*b*	*b*
6α	-	4.14 t	-	-	-	-	4.32 t
6β	-	-	4.09 ddd	3.93 dt[f]	4.22 ddd[f]	4.10 ddd	-
7α	3.34 dd	*b*	2.38 ddd	2.29 ddd	1.77 ddd	*b*	2.28 td
7β	2.26 dd	*b*	1.81 dt	1.73 dt	2.11 dt	*b*	*b*
8β	2.00 ddq	*b*	1.58 ddq	*b*	~2.3[b]	*b*	*b*
10β	1.92 dd	*b*	*b*	*b*	~2.6[b]	*b*	2.86 dd
11A	2.38 dd	2.33 dd	2.31 dd	2.33 dd	2.34 dd	2.31 dd	2.46 d
11B	2.48 dd	2.47 dd	2.41 dd	2.40 dd	2.68 dd	2.41 dd	2.46 d
12	5.43 br t	5.37 dd	5.31 br t	5.36 br t	5.04[b]	5.30 br t	5.35 t
14	6.36 dd	6.39 dd	6.34 dd	6.37 dd	6.62 dd	6.34 dd	6.38 dd
15	7.43 t	7.43 t	7.41[b]	7.42 t	7.50 t	7.41[b]	7.42 t
16	7.45 m	7.45 m	7.41[b]	7.43 m	7.56 m	7.41[b]	7.43 m
Me-17	1.08 d	1.03 d	1.07 d	1.05 d	1.07 d	1.06 d	0.98 d
18A	3.85 d	3.75 d	3.94 d	4.00 dd	3.83 br d	4.38 br d	3.37 d
18B	4.07 dd	4.05 dd[d]	4.10 dd	4.06 d	4.00 d	4.62 d	4.45 d
19A	5.03 d	4.70 d	4.17 dd	5.04 d	4.90 dd	4.16 dd	4.47 d
19B	5.09 d	4.85 d	5.34 d	5.18 br d	5.04 d	5.31 d	4.91 d
OAc	1.96 s	2.08 s	-	2.05 s	-	2.13 s	2.07 s
Orthoacetate	-	-	1.44 s	-	-	1.42 s	1.61 s
OH	3.36 s[c]	2.84 d[c,e]	-	3.50 d[c,g]	7.00 d[c,h]	-	-
	-	-	-	3.44 s[c]	6.20 br s[c]	-	-
	-	-	-	-	5.74 s[c]	-	-
OMe	-	-	-	-	3.50 s	-	-
J (Hz)							
1α,1β	13.2	*b*	*b*	*b*	13.4	*b*	*b*
1α2α	4.0	*b*	*b*	*b*	3.8	*b*	*b*
1α,2β	13.4	*b*	*b*	*b*	13.4	*b*	*b*
1α,10β	13.2	*b*	*b*	*b*	13.4	*b*	13.1
1β,2β	4.7	*b*	*b*	*b*	*b*	*b*	*b*
1β,10β	2.7	*b*	*b*	*b*	*b*	*b*	3.2
2α,2β	13.4	*b*	*b*	*b*	*b*	*b*	*b*
2α,3α	2.8	*b*	4.8	*b*	3.2	*b*	*b*
2α,3β	3.4	*b*	*b*	2.6	*b*	*b*	*b*
2β,3α	13.5	*b*	13.2	*b*	13.0	*b*	*b*
2β,3β	4.7	*b*	*b*	4.5	*b*	*b*	*b*
3α,3β	14.6	*b*	13.2	13.0	13.0	*b*	*b*
6α,7α	-	2.3	-	-	-	-	3.0
6α,7β	-	2.3	-	-	-	-	3.0
6β,7α	-	-	11.7	11.6	10.8	11.9	-
6β,7β	-	-	4.1	4.1	4.5	4.2	-
7α7β	14.6	*b*	13.4	13.4	13.3	*b*	13.5
7α,8β	14.3	*b*	10.8	12.0	12.2	*b*	13.5
7β,8β	3.8	*b*	4.1	4.1	4.5	*b*	*b*
8β,17	6.6	6.2	6.7	6.6	6.7	6.7	6.7
11A,11B	14.2	14.0	14.1	14.1	15.8	14.0	0
11A,12	8.3	7.6	8.3	8.2	9.9	8.3	8.7
11B,12	8.8	9.8	9.1	9.0	2.6	9.1	8.7
14,15	1.8	1.8	1.5	1.7	1.8	1.5	1.8
14,16	0.9	0.9	1.2	0.9	0.8	1.2	0.9
15,16	1.8	1.8	*b*	1.7	1.8	*b*	1.8
18A,18B	11.5	9.8	11.2	11.4	9.8	11.3	7.6
18A,3α	0	0	0	1.1	<0.3	<0.3	0
18B,3α	1.7	0	1.8	0	0	0	0

Table 4. *Continued*

J (Hz)	6	7	8	9	12	15	19
19A,19B	11.9	12.6	10.6	12.9	13.0	10.7	13.1
19A,6β	-	-	2.4	0	1.2	2.3	-
19B,6β	-	-	0	<0.3	0	0	-

[a]At 300 MHz (**6-9** and **12**) or 200 MHz (**15** and **19**), all in $CDCl_3$ solution except for **12** ($CDCl_3$-pyridine-d_5 3:1). Chemical shifts are referenced to residual $CHCl_3$ (δ 7.24).[b]Overlapped signal. [c]Disappeared after addition of D_2O. [d]Collapsed into a doublet after addition of D_2O.[e]$J_{18B,OH}$=1.0 Hz.[f]Collapsed into a double doublet after addition of D_2O. [g]$J_{6\beta,OH}$=4.1 Hz. [h]$J_{12,OH}$=2.3 Hz.

This residue was chromatographed (silica gel column, 2 g, eluted with EtOAc - *n*-hexane 1:1) yielding a major compound (**7**, 5.4 mg) besides several unidentified minor substances. The compound corresponding to the major constituent of the crude of the reaction was not found after chromatography, and alternative attempts for isolating it were unsuccessful. **7**: mp 135-137 °C (EtOAc - *n*-hexane); $[\alpha]_D^{21}$ +14.3° ($CHCl_3$; *c* 0.359). IR (KBr) ν_{max} cm^{-1}: 3460 (OH), 3140, 3110, 1600, 1505, 875 (furan), 1760 (γ-lactone), 1730, 1250 (OAc), 2930, 2880, 1470, 1370, 1160, 1020, 930, 910, 800. ^{1}H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 404 $[M]^+$ (6), 386 (10), 344 (43), 331 (16), 314 (56), 296 (14), 250 (48), 220 (33), 159 (28), 147 (31), 133 (33), 119 (32), 105 (48), 95 (91), 94 (57), 91 (65), 81 (66), 79 (59), 67 (47), 55 (41), 43 (100). $C_{22}H_{28}O_7$ M_r 404.

Table 5. ^{13}C NMR Data of Compounds **6-9**, **11**, **12**, **15** and **19**[a].

C	6	7	8	9	11	12	15	19
1	21.8 t[b]	24.7 t[b]	22.0 t[b]	22.3 t[b]	25.5 t[b]	23.9 t[b]	22.1 t[b]	21.7 t[b]
2	23.1 t[b]	21.8 t[b]	22.5 t[b]	23.1 t[b]	21.3 t[b]	20.7 t[b]	22.3 t[b]	22.1 t[b]
3	29.0 t	31.0 t	27.8 t	30.1 t	36.3 t[c]	29.5 t	27.3 t	27.4 t
4	76.3 s	82.2 s	77.0 s	77.4 s	73.7 s	75.9 s	76.9 s	83.7 s
5	58.1 s	50.4 s[c]	38.7 s	48.3 s	44.3 s	41.5 s	37.7 s	40.2 s
6	211.2 s	77.8 d	73.1 d	74.7 d	67.9 d	71.4 d	73.2 d	67.5 d
7	44.3 t	34.3 t	33.1 t	35.4 t	36.6 t[c]	35.3 t	33.0 t	31.1 t
8	39.6 d	31.8 d	38.1 d	38.8 d	29.8 d	33.3 d	38.1 d	33.1 d
9	51.0 s	50.5 s[c]	51.2 s	51.8 s	50.3 s	48.6 s	51.1 s	51.2 s
10	51.5 d	47.2 d	47.7 d	51.2 d	35.8 d	40.3 d	47.5 d	42.9 d
11	43.4 t	42.9 t	44.9 t	44.6 t	36.7 t[c]	37.4 t	44.8 t	43.9 t
12	72.0 d	71.8 d	71.6 d	71.5 d	63.5 d	61.3 d	71.6 d	71.9 d
13	124.7 s	125.1 s	125.0 s	125.1 s	130.5 s	130.5 s	125.0 s	125.3 s
14	107.8 d	108.1 d	107.9 d	107.9 d	108.4 d	107.9 d	107.9 d	108.1 d
15	144.4 d	144.2 d	144.3 d	144.2 d	143.6 d	142.0 d	144.3 d	144.1 d
16	139.6 d	139.7 d	139.6 d	139.6 d	138.5 d	137.3 d	139.6 d	139.6 d
17	16.8 q	16.2 q	16.2 q	16.3 q	16.6 q	15.6 q	16.3 q	16.3 q
18	47.9 t	76.0 t	47.8 t	49.8 t	77.0 t	74.8 t	65.0 t	72.2 t
19	61.2 t	61.7 t	60.4 t	63.3 t	73.2 t	67.8 t	60.0 t	62.2 t
20	176.6 s	177.3 s	176.2 s	176.1 s	173.3 s	171.9 s	176.3 s	177.8 s
OAc	169.7 s	171.8 s	-	170.0 s	-	-	171.2 s	170.3 s
	21.0 q	21.2 q	-	21.4 q	-	-	21.0 q	21.2 q
Orthoacetate	-	-	109.0 s	-	-	-	108.7 s	118.8 s
	-	-	24.0 q	-	-	-	24.0 q	22.1 q
OMe	-	-	-	-	59.7 q	58.3 q	-	-

[a]All at 50.3 MHz, in $CDCl_3$ solution, except for **7** and **19** (75.4 MHz) and **12** ($CDCl_3$-pyridine-d_5 3:1). Chemical shifts are referenced to the solvent (δ_{CDCl3} 77.00). [b,c]These assignments may be interchanged within the same column.

*(12S)-18-Chloro-15,16-epoxy-*neo*-cleroda-13(16),14-dien-20,12-olide 4α,6α,19-orthoacetate* (**8**) *and (12S)-19-acetoxy-18-chloro-15,16-epoxy-4α,6α-dihydroxy-*neo*-cleroda-13(16),14-dien-20,12-olide* (**9**) *from teucjaponin B* (**3**). Treatment of **3** (90 mg) with aqueous conc. HCl (1.5 ml) in $CHCl_3$ solution (15 ml) as described above yielded two compounds (TLC), which were separated by column chromatography (silica gel deactivated with 15% H_2O, w/v, 10 g, *n*-hexane-EtOAc 3:7 as eluent) giving compounds **8** (53 mg, less polar constituent) and **9** (30.5 mg).

After 1 h of reaction, only compound **8** was obtained. Moreover, treatment of **9** for 1 h under the reaction conditions quantitatively yielded **8**.

Compound **8**. Mp 207-209 °C (EtOAc - *n*-hexane); $[\alpha]_D^{18}$ -0.86°, $[\alpha]_{546}^{18}$ -0.43°, $[\alpha]_{365}^{18}$ +11.8° ($CHCl_3$; *c* 0.464). IR (KBr) ν_{max} cm^{-1}: no OH absorptions, 3140, 3120, 1610, 1510, 875 (furan), 1755 (γ-lactone), 2970, 2880, 1470, 1460, 1395, 1290, 1175, 1160, 1150, 1130, 1085, 1050, 1020, 935, 810, 800, 755, 745, 710. ^1H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 424 $[M]^+$ (10), 422 $[M]^+$ (30), 387 (2), 291 (12), 268 (11), 251 (13), 220 (23), 193 (21), 176 (28), 141 (42), 119 (26), 105 (54), 95 (89), 94 (84), 91 (48), 81 (68), 77 (55), 67 (21), 55 (25), 43 (100). (Anal. Found: C, 62.47; H, 6.71; Cl, 8.21. $C_{22}H_{27}O_6Cl$ requires: C, 62.48; H, 6.43; Cl, 8.38%.)

Compound **9**. Mp 95-105 °C (amorphous solid); $[\alpha]_D^{18}$ +41.8° ($CHCl_3$; *c* 0.158). IR (KBr) ν_{max} cm^{-1}: 3440 (OH), 3150, 3140, 3120, 1600, 1510, 875 (furan), 1760 (γ-lactone), 1735, 1250 (OAc), 2960, 2880, 1460, 1370, 1190, 1160, 1140, 1130, 1040, 1025, 925, 800, 750. ^1H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 442 $[M]^+$ (0.3), 440 $[M]^+$ (0.9), 424 (0.8), 422 (1), 405 (0.5), 387 (1), 362 (4), 344 (5), 331 (20), 326 (8), 286 (15), 220 (15), 193 (18), 179 (38), 159 (39), 145 (26), 131 (29), 123 (37), 96 (96), 95 (90), 94 (95), 91 (68), 81 (100), 79 (67), 67 (37), 55 (57), 43 (71). (Anal. Found: C, 60.12; H, 6.41; Cl, 7.87. $C_{22}H_{29}O_7Cl$ requires: C, 59.93; H, 6.63; Cl, 8.04%.)

*(12S)-15,16-Epoxy-4α,6β,12-trihydroxy-18-methoxy-*neo*-cleroda-13(16),14-dien-20,19-olide* (**11**) *from teucroxylepin* (**10**). A solution of **10** (60 mg) in MeOH (10 ml) was treated with K_2CO_3 (40 mg) at room temperature for 24 h with stirring; then, the reaction mixture was diluted with H_2O (20 ml) and extracted with $CHCl_3$ (4x15 ml). Work-up in the usual manner gave a residue which was subjected to column chromatography (silica gel, EtOAc - *n*-hexane 2:1 as eluent) to yield starting material (**10**, 42 mg, less polar constituent) and **11** (13 mg): mp 191-193 °C (EtOAc - *n*-hexane); $[\alpha]_D^{20}$ -33.8° ($CHCl_3$; *c* 0.103). Identical in all respects (IR, ^1H NMR, mmp, TLC behaviour) with the previously described compound[16a] [mp 190-193 °C; $[\alpha]_D^{21}$ -32.4° ($CHCl_3$; *c* 0.034)]. The ^{13}C NMR spectrum of **11**, not previously reported[16a], is included in Table 5.

To a solution of **10** (20 mg) in MeOH (10 ml) NaOMe (50 mg) was added and the reaction mixture was refluxed for 12 h; then, the reaction mixture was diluted with H_2O (50 ml), acidified with 20% H_2SO_4 (pH 4) and extracted with $CHCl_3$ (4x20 ml). Work-up in the usual manner yielded a residue, which was crystallized from EtOAc - *n*-hexane giving pure **11** (20 mg, 92% yield).

When compound **11** was refluxed in glacial HOAc for 3 h, it was recovered unchanged.

*(12S)-15,16-Epoxy-4α,6α,12-trihydroxy-18-methoxy-*neo*-cleroda-13(16),14-dien-20,19-olide* (**12**) *and compounds* **13** *and* **14** *from teucjaponin B* (**3**). A solution of **3** (84 mg) in MeOH (30 ml) was treated with K_2CO_3 (80 mg) as in the case of **10**. The residue of the reaction was subjected to column chromatography

(silica gel, EtOAc - *n*-hexane 1:1 as eluent) yielding the following compounds in order of increasing chromatographic polarity: **13** (32 mg), **12** (9 mg) and **14** (33 mg).

When **3** was treated with NaOMe in MeOH solution as described above for **10**, only the derivative **12** was obtained in almost quantitative yield (96%).

Compounds **13** [mp 210-212 °C; $[\alpha]_D^{19}$ -54.1° ($CHCl_3$; *c* 0.347)] and **14** [mp 166-168 °C; $[\alpha]_D^{19}$ +30.1° ($CHCl_3$; *c* 0.315)] were identical in all respects (IR, ^1H NMR, MS) with the previously described compounds [lit.[16b]: mp 213-215 °C; $[\alpha]_D^{22}$ -52.8° ($CHCl_3$; *c* 0.413), and mp 166-168 °C; $[\alpha]_D^{20}$ +30.5° ($CHCl_3$; *c* 0.305), respectively]. Comparison (mmp, TLC) with authentic samples[16b] confirmed these identities.

Compound **12**. Mp 215-218 °C (EtOAc - *n*-hexane); $[\alpha]_D^{21}$ -23.9° ($CHCl_3$-MeOH 2:1; *c* 0.234). IR (KBr) ν_{max} cm^{-1}: 3460, 3420 (OH), 3140, 3120, 1590, 1502, 875 (furan), 1700 (δ-lactone), 2990, 2930, 2810, 1465, 1445, 1385, 1345, 1280, 1235, 1200, 1195, 1160, 1140, 1120, 1065, 1060, 1020, 985, 955, 815, 785, 750, 730, 695, 660. ^1H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 394 $[M]^+$ (84), 377 (22), 376 (3), 362 (12), 349 (64), 345 (12), 344 (17), 331 (47), 313 (48), 301 (32), 161 (42), 121 (45), 119 (46), 111 (84), 107 (51), 105 (71), 95 (99), 94 (45), 93 (51), 91 (85), 81 (95), 69 (84), 45 (96), 43 (67), 41 (100). (Anal. Found: C, 64.10; H, 7.85. $C_{21}H_{30}O_7$ requires: C, 63.94; H, 7.66%.)

*(12S)-18-Acetoxy-15,16-epoxy-*neo*-cleroda-13(16),14-dien-20,12-olide 4α,6α,19-orthoacetate* (**15**) *from teucjaponin B* (**3**). Compound **3** (80 mg) in glacial HOAc (5 ml) was refluxed for 3 h. Evaporation of the solvent gave a residue which was crystallized from EtOAc - *n*-hexane yielding **15** (84 mg): mp 218-220 °C; $[\alpha]_D^{21}$ -4.1° ($CHCl_3$; *c* 0.226). IR (KBr) ν_{max} cm^{-1}: no hydroxyl absorptions, 3160, 3120, 1590, 1510, 870 (furan), 1750 (γ-lactone), 1740, 1240 (OAc), 2960, 2900, 1470, 1405, 1380, 1180, 1165, 1150, 1130, 1050, 1040, 985, 940, 820, 720, 665. ^1H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (70 eV, direct inlet) *m/z* (relative intensity): 446 $[M]^+$ (16), 386 (3), 373 (40), 340 (3), 331 (10), 313 (12), 274 (17), 221 (12), 220 (11), 176 (19), 165 (18), 159 (20), 145 (21), 123 (34), 106 (38), 105 (46), 95 (62), 94 (49), 91 (49), 81 (54), 79 (42), 67 (31), 55 (32), 43 (100). (Anal. Found: C, 64.68; H, 6.69. $C_{24}H_{30}O_8$ requires: C, 64.56; H, 6.77%.)

Peracetylteuscorodol (**18**), *(12S)-19-acetoxy-15,16-epoxy-*neo*-cleroda-13(16),14-dien-20,12-olide 4β,6β,18-orthoacetate* (**19**) *and aldehydes* **20** *starting from 6-acetylteucjaponin A* (**17**). Compound **17** (115 mg) in glacial HOAc (5 ml) was refluxed for 3 h. Evaporation of the solvent under reduced pressure and low temperature (40 °C) gave a residue which was subjected to column chromatography (silica gel deactivated with 15% H_2O, w/v, 10 g, *n*-hexane-EtOAc 2:1 as eluent) yielding the following compounds in order of increasing chromatographic polarity: **19** (34 mg), **18** (63 mg) and **20** (6 mg).

Compound **18**. Amorphous solid; $[\alpha]_D^{20}$ -39.4°($CHCl_3$; *c* 0.642). Identical in all respects (IR, ^1H NMR, MS) with peracetylteuscorodol[9a,c] [lit[9a] $[\alpha]_D^{20}$ -36.9° ($CHCl_3$; *c* 0.97)].

Compound **19**. Mp. 140-142 °C (EtOAc -*n*-hexane); $[\alpha]_D^{18}$ +15.6° ($CHCl_3$; *c* 0.176). IR (KBr)ν_{max} cm^{-1}: no hydroxyl absorptions, 3150, 3130, 1600, 1505, 875 (furan), 1765 (γ-lactone), 1740, 1230 (OAc), 2980, 1480, 1445, 1410, 1370, 1300, 1280, 1200, 1190, 1150, 1035, 1025, 990, 915, 860, 845, 820, 750, 690. ^1H NMR: Table 4. ^{13}C NMR: Table 5. EIMS (direct inlet) *m/z* (relative intensity): 446 $[M]^+$ (1), 418 (0.6), 386 (2), 373 (0.5), 340 (1.5), 326 (3), 313 (2), 308 (2), 274 (14), 263 (2.5), 256 (3), 220 (6), 214 (8), 159 (10), 145 (8), 123 (17), 105 (58), 95 (31), 94 (29), 91 (36), 81 (27), 77 (43), 67 (12), 55 (14), 43 (100). (Anal. Found: C, 64.81; H, 6.86. $C_{24}H_{30}O_8$ requires: C, 64.56; H, 6.77%.)

Compound **19** in glacial HOAc was refluxed for 3 h. Work-up in the usual manner (see above) yielded starting material.

Mixture of compounds **20**. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 5.55 t (J=3.6 Hz, H-6α), 2.40 dd (J=13.9 and 8.6 Hz, H_A-11), 2.45 dd (J=13.9 and 8.6 Hz, H_B-11), 5.41 t and 5.34 t (J=8.6 Hz, H-12), 6.39 dd and 6.37 dd (J=2.0 and 1.0 Hz, H-14), 7.43 m (H-15 and H-16), 0.99 d (3H, J=6.6 Hz, Me-17), 10.11 d (J=5.7 Hz) and 9.63 br s (H-18), 4.51 d (J=12.9 Hz, H_A-19), 4.92 d (J=12.9 Hz, H_B-19) and 2.02 s, 1.99 s and 1.93 s (OAc). EIMS (70 eV, direct inlet) m/z: $[M]^+$ at 446; $C_{24}H_{30}O_8$ M_r 446. The ^{1}H NMR spectrum of the mixture of the aldehydes **20** is very similar to those of the C-6 epimers[11a].

Treatment of teucjaponins A (**2**) *and B* (**3**), *montanin E* (**4**) *and compounds* **11** *and* **12** *with potassium carbonate in aqueous THF solution*. The reaction was carried out under identical conditions for all the compounds. A solution of the diterpenoid in THF-H_2O (10 ml and four drops, respectively) was treated with K_2CO_3 (50 mg) at room temperature for 120 h with stirring (or reflux, 24 h). Then, the reaction mixture was diluted with H_2O (30 ml) and extracted with $CHCl_3$ (3x20 ml). Work-up in the usual manner gave the crude of reaction. The results were the following. Compounds **11** (20 mg) and **12** (20 mg) were recovered unchanged. Teucjaponin B (**3**, 24 mg) yielded, after column chromatography, the derivatives **13** (12.5 mg) and **14** (6.5 mg)(see above and ref. 16b). Teucjaponin A (**2**, 27 mg) gave teucroxylepin[16a] (**10**, 19 mg) and teubotrin[9c,d] (**21**, 2.5 mg) after chromatography (silica gel, EtOAc - n-hexane 7:3 as eluent). Finally, montanin E (**4**, 15 mg) also yielded teubotrin (**21**, 2.2 mg) besides several unidentified compounds.

Compound **21**. Amorphous solid, $[\alpha]_D^{19}$ -37.6° ($CHCl_3$; c 0.107). Identical in all respects (^{1}H NMR, MS) with natural teubotrin [lit.[9c] $[\alpha]_D^{24}$ -39.4° ($CHCl_3$; c 0.241)]. Comparison (TLC) with an authentic sample confirmed the identity.

Insect bioassays. The compounds were assayed for antifeedant activity by presenting them on glass-fibre discs (Whatman GF/A 2.1 cm diam.) to final stadium larvae of *Spodoptera littoralis* (Boisduval)[10a,12]. The discs were made palatable by the application of 100 μl of a sucrose solution (50 mM). After drying the discs, 100 μl of a solution containing a test compound at 100 ppm was applied to the treatment disc. These discs were then redried and all the dried discs weighed. Larvae 24-36 hours into the final stadium were deprived of food for 4 h before being placed singly into Petri dishes which contained a control and treatment disc. The larvae were removed from the dishes after 50% of either disc had been eaten or after 18 h. The discs were then reweighed and the Antifeedant Index calculated [(C-T)/(C+T)]x100, where C and T represent the amount of control and treatment discs consumed, respectively.

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