FURTHER RESEARCHES ON THE FUROCLERODANES FROM *TEUCRIUM* SPECIES

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Abstract - The review updates the advances reported during the last six years on the chemistry of these diterpenoids.

Highlights on the chemistry of the furanoditerpenoids with *neo*-clerodane skeleton isolated from species of the genus *Teucrium* (family Labiatae) were reported in the last decade.[1,2] Recently, a general review[3] on the *neo*-clerodane diterpenoids reported briefly also on the products from *Teucrium*, but the references stop at 1990. The remarkable increase of the number of new natural derivatives and several peculiarities of their structures prompt to update the previous review.[2]

The genus *Teucrium*, with its 300-400 species (and more subspecies, varieties and chemotypes), is up to now the richest natural source of *neo*-clerodane diterpenoids. Up today (July 1993) the products isolated and characterized are as many as 154, while in the first review[1] only 35 derivatives were reported, and their number had increased to 103 in the second review.[2] This demonstrates the rich biological differentiation of the species within the genus. Moreover, the occurrence of these products only inside this genus makes them authentic chemotaxonomic markers.

Dedicated to Prof. Alan R.Katritzky in the occasion of his 65th birthday.

Beyond our staff, other research groups are active in the chemistry of *Teucrium* diterpenoids: in Bulgaria, Chile, Spain and Popular Republic of China. The interest is stimulated by the structural challenge and by the insect antifeedant activity of these products.[4] On the purpose of clearness in the exposition of the results, we decided to keep and continue the numbering used in the previous review,[2] the last number used being [**103**] for teuflavoside.

This review starts correcting some minor misprints of the previous review.[2] So in structures [**35**] and [**36**] the axial 9α-CH_3 was missing. In the structure [**49**] of picropolinol, the hydroxy groups at C-18 and C-19 are acetylated, and the formula is $C_{24}H_{30}O_{10}$. Montanin C [**8**] is the 12-epimer of 6-acetylteucjaponin B [**20**] and not of teucjaponin B [**19**]. The reference for teuscorodin [**85**] is 38 and not 39.

The controversy about the configuration at C-12 of teupolin I was settled. The product isolated from *T. polium*[5] and named teupolin I was confirmed by the same authors[6] to have the 12*S* configuration on the basis of careful nOe studies. The product isolated from *T. scorodonia*[7] and *T. lanigerum*[8] and believed, on the basis of physical data (mp, $[\alpha]_D$, nmr), to be identical with teupolin I, is different as the configuration at C-12 is really 12*R* as suggested previously.[7] Therefore the product indicated as "teupolin I" in our previous review[2] is 12-*epi*-teupolin I (synonimous, 12*R*-teupolin I) and does have structure [**9**]. The true teupolin I is therefore represented by [**104**].

The structure of teupolin IV, given[9] as [**11**], was amended by the same authors[6]: the primary hydroxy group on C-19 is acetylated, and not the secondary one on C-7. So in the structure [**11**] the groups have to be indicated as 5α-CH_2OAc and 7β-OH. Accordingly, the product reported[2] as "19-acetylteupolin IV" must be named 7-acetylteupolin IV, the structure [**12**] being correct.

The most interesting developments in the chemistry of these furanoditerpenoids are concerned mainly with the occurrence of oxygen functions on unusual positions. We can remark that until 1991 the only derivative with 8β-OH was the already reported[2] 8β-hydroxyfruticolone [**39**]. In that year, teupernin B [**105**] and teupernin C [**106**] were isolated by Chinese researchers[10] from *T. pernyi*, both products having the 8β-OH

functionalization. Teupernin B was isolated[11] also from *T. bidentatum* (growing in China) and named bidentatin.

No derivative was known with oxygen function on C-10 until we isolated[12] teupestalin A [**107**] and teupestalin B [**108**] from *T. pestalozzae* collected in Turkey. The first product has a 10β-OH group, whereas the second one shows a β-oriented hemiacetalic bridge between C-10 and C-3. Other *neo*-clerodanes with unusual features at C-10 occurred[13] in *T. oliverianum* (from Saudi Arabia): teucrolivin A [**109**] has a β-oriented hemiacetalic system connecting C-10 and C-12; teucrolivin B [**110**] and teucrolivin C [**111**] have a 10β-OH substituent. Teucrolivin F is[14] a tetra-*nor-neo*-clerodane [**112**], the first found in *Teucrium* genus: it missed the furan system and formed a γ-lactone ring between C-12 and C-10. Still more interesting are teucrolivin H and its acetyl derivative teucrolivin G: their structures were elucidated[15] as [**113**] and [**114**] respectively. They show a quite unprecedented (in nature) 2,6-dioxabicyclo[2.2.1]heptane system arising from the acetalization of C-12 with two hydroxy groups on C-8 and C-10, both β-oriented. These unusual structures were confirmed by X-ray diffraction analysis.

New, but not unusual, derivatives were isolated from the above species. So *T. pernyi* gave[10] teupernin A [**115**], *T. pestalozzae* yielded[16] 4α,18-epoxytafricanin A [**116**] and 20-oxo-teuflavin [**117**], *T. oliverianum* contained[14] teucrolivin D [**118**] and teucrolivin E [**119**].

Chinese researchers[17] isolated teuponin [**120**] from *T. japonicum.* This *nor-neo*-clerodane is remarkable because the furan ring is transformed into a 15*R*-hydroxy-13,14-en-16,15-olide system, whereas the remaining structure is identical with teuflin [**93**].

The 12-epimer of teuscorodonin was isolated[18] from *T. bicolor*, growing in Chile, and its rare 12*R* configuration ascertained by nOe experiments. So 12-*epi*-teuscorodonin has structure [**121**]. By the same way, these authors[18] confirmed the 12*S* configuration proposed, but not proved, for teucrin H2 [**76**] (synonimous, teuchamaedryn B).

A novel product arose from a reinvestigation of *T. fruticans* (collected in Sicily). Fruticolide, an isomer of fruticolone [**38**], is a minor component and was shown[19] to have the 5,6-*seco* structure [**122**] with an ε-lactone ring joining C-6 to C-1: structure and stereochemistry were confirmed also by X-ray diffraction. This is the first case of a *seco* derivative in *Teucrium* genus.

The investigation of *T. gracile,* from the island of Karpathos (Greece) gave six new diterpenoids. Teugracilin A [**123**] is a typical representative of the group having the 4,18-epoxy system and the 20,12-γ-lactone;[20] 3-O-deacetylteugracilin A [**124**] and teugracilin B [**125**] are[20] a couple of epimers at C-6, having 6β-OH and 6α-OH respectively. Teugracilin C [**126**] lacks[20] the γ-lactone ring: an OAc group occurs at C-12, whose configuration was not ascertained. Teugracilin D [**127**] shows[19] a 20-O-acetylated lactol ring, whereas teugracilin E [**128**] has[19] carbon C-20 in the rare form of CH_2OAc and a secondary OAc group at C-12, whose configuration is unknown.

Two new *neo*-clerodanes were isolated[21] from the Spanish species *T. oxylepis* subsp. *marianum.* Teucroxylepin [**129**] shows the δ-lactone ring from C-20 to C-19, and a 12*R* hydroxy group at C-12. The second product is the 12-acetyl derivative [**130**] of teugnaphalodin [**69**].

Extraction of *T. lamiifolium*, collected in Bulgaria, gave[22] the new 12-*epi*-teupolin II [**131**] having the infrequent 12*R* configuration. Another product, "teulamifin B", was isolated and proved[23] to have a secondary hydroxy group in 12*S* configuration: apart this stereochemistry, "teulamifin B" was identical with the already known teubotrin[24] [**61**] whose C-12 configuration was not proved at that time. In spite of discrepancies in mp and ^{13}C nmr data, the two products were finally found[25] to be identical and represented as [**61**] with 12*S* stereochemistry.

T. abutiloides, from the island of Madeira (Portugal), contained[26] two new *neo*-clerodanes, teubutilin A [**132**] and teubutilin B [**133**]. The absolute configuration of the former was confirmed by correlation with teucrin P1 [**24**], whereas the absolute configuration of the latter was not proved: however it is believed to belong to the *neo*-clerodane series like teubutilin A.

Two new diterpenoids were isolated by the Bulgarian group. *T. montanum* subsp. *skorpilii* contained montanin G: it is represented[27] by structure [**134**], therefore is the 3-O-deacetyl derivative of teupyreinin [**28**], with which it was easily correlated. The occurrence of the unusual 12*R* configuration is worthy of remark. *T. montanum* subsp. *montanum* yielded[28] montanin H [**135**]: neither the C-12 stereochemistry nor the absolute configuration were ascertained, but it may be supposed to belong to the *neo*-clerodane series.

A reinvestigation of *T. massiliense*, collected in Sardinia, led to the isolation[29] of a new minor constituent, teumassin [**136**]: its structure was confirmed by correlation with a known derivative of teumarin [**34**], whose absolute stereochemistry was established previously.

A group of species growing in the East Mediterranean area gave many new and interesting products. So a derivative of chamaedroxide [**88**] was found[30] in *T. divaricatum* subsp. *canescens* from the island of Cyprus: it is 2-deoxychamaedroxide [**137**], with the unusual oxetane ring connecting C-4, C-5 and C-6.

Teucretol [**138**] was isolated[31] from *T. creticum*, collected in the island of Cyprus. It is the first example of C-20 as a CH_2OH group: the only other case of such oxygenation is represented by teugracilin E [**128**], having however C-20 as a CH_2OAc substituent.

T. micropodioides, again from Cyprus, yielded five new derivatives.[32] Teumicropin [**139**] and 3-acetylteumicropin [**140**] were transformed into teupyrenone [**32**], thus firmly establishing their structures and absolute configuration. A third product, 3-O-deacetyl-teupyrenone [**141**] was also easily correlated with teupyrenone. Teumicropodin [**142**] was correlated with a synthetic derivative of teulepicin [**44**], whose absolute stereochemistry was known. The last product, 3-O-deacetyl-20-*epi*-teulanigin [**143**], was easily correlated with 20-*epi*-teulanigin [**42**]. So the absolute configuration of all five *neo*-clerodanes from *T. micropodioides* was ascertained.

An interesting product, isoteucrin H4, was extracted[33] from *T. kotschyanum*, always from the island of Cyprus. Its structure [**144**] is the first example of a 19-*nor-neo*-clerodane derivative isolated from a natural source having a C-5, C-10 double bond. Its occurrence supports previous hypotheses on the biogenesis of the 19-*nor-neo*-clerodanes belonging to the 10α-series, like teucvidin [**91**] and teuflidin [**95**]. The structure [**144**] was confirmed by isomerisation of the acetate of teucrin H4 [**94**] into the acetate of isoteucrin H4.

Three more new diterpenoids were extracted[34] from *T. kotschyanum*. The first and second products are 12-*epi*-teucvidin [**145**] and 12-*epi*-teuflin [**146**], both having the infrequent 12*R* configuration. The third product, teukotschyn [**147**], has a C-18,C-19 hemiacetalic ring.

A second example of a 19-*nor* derivative of biogenetic interest with C-5, C-10 double bond was found[35] in *T. canadense*. The product is isoteuflin [**148**], previously known only as a synthetic derivative obtained by base catalised isomerization of teuflin [**93**]. In our hands,

mild basic treatment of both teuflin and isoteuflin gave the same mixture of isoteuflin and teucvidin [**91**].

A second new product was also isolated[35] from *T. canadense,* 18-acetylmontanin D [**149**], having like the parent compound [**46**] the oxetane ring connecting C-4, C-5, C-19.

Three interesting structures were given[36] to products occurring in the Portuguese species *T. polium* subsp. *vincentinum*.. Teuvincentin A [**150**] contains a chlorine atom on C-18, clearly arising from the opening of the 4α,18-oxirane ring. It is the third chlorinated *neo*-clerodane from *Teucrium* species, as are[2] tafricanins A and B, [**52**] and [**53**]. Its structure and absolute configuration were confirmed by partial synthesis from eriocephalin [**13**] and by X-ray analysis of a derivative.

Teuvincentin B [**151**] possesses a C-7, C-19 hemiacetal group, but its more remarkable feature is the axial 8β-CH_3 orientation of the C-17 methyl group, as proved by nOe experiments.[36] This biogenetically unusual configuration was never previously found in any of the *neo*-clerodane diterpenoids until now isolated from plants belonging to the *Teucrium* genus. The X-ray analysis of the diacetyl derivative of teuvincentin B confirmed both relative and absolute stereochemistry.

The same unusual 8β-CH_3 configuration was found[36] also in teuvincentin C [**152**], whose absolute stereochemistry was not ascertained.

From the extract of *T. cossonii*, an endemic species of the Balearic Islands, two new products were obtained.[37] Teucossin A [**153**] has C-20 as a CH_2OAc function, and was correlated with a derivative of teucretol [**138**]. Teucossin B [**154**] has a C-7, C-20 acetal group, like the C-7, C-20 hemiacetal ring of auropolin [**25**], but with epimeric configuration at C-20. The stereochemistry at the C-12 centre and the absolute configuration of both teucossins were not ascertained.

The stereostructure of auropolin [**25**] was established[38] by X-ray diffraction as 20*S* (20α-H, 20β-OH).

Some chemical transformations of 19-acetylgnaphalin [**22**] and montanin C [**8**] provided conclusive evidence[39] for the absolute configuration of montanin C itself, 12-*epi*-teupolin II [**131**], teugnaphalodin [**69**] and teubutilin B [**133**]: all of them do have the *neo*-clerodane stereochemistry.

It is remarkable that 37 out of the 51 new derivatives show the 4α,18-epoxy system, that after the furan ring and the oxygen function at C-6 is the most common feature of the *neo*-clerodane diterpenoids from *Teucrium.*

Because of the increase of the taxa investigated and of the number of natural derivatives, it is easier and easier to find many already known products in any new species.

So the following known compounds were identified. From *T. pestalozzae*[16] [**52**]; from *T. odontites*[16] [**46**], [**55**], [**76**]; from *T. microphyllum*[16] [**75**], [**77**], [**78**], [**97**]; from *T. bidentatum*[11] [**76**], [**82**], [**84**], [**93**]; from *T. gracile*[19,20] [**45**], [**142**]; from *T. oxylepis* subsp. *marianum*[21] [**21**], [**22**], [**46**], [**47**], [**56**], [**61**], [**68**], [**94**], [**144**], [**147**]; from *T. lamiifolium*[22] [**8**], [**22**], [**82**], [**93**]; from *T. polium* subsp. *polium*[23] [**47**], [**56**], [**61**]; from *T. abutiloides*[26] [**8**], [**131**]; from *T. belion*[29,38] [**13**], [**22**], [**97**]; from *T. massiliense*[29] [**22**], [**34**]; from *T. divaricatum* subsp. *canescens*[30] [**46**], [**74**], [**75**], [**76**], [**78**], [**80**], [**93**], [**95**], [**97**]; from *T. creticum*[31] [**19**], [**22**], [**36**]; from *T. kotschyanum*[34] [**46**], [**68**], [**76**], [**85**], [**91**], [**93**]; from *T. canadense*[35] [**9**], [**89**], [**91**], [**93**], [**131**]; from *T. polium* subsp. *vincentinum*[36] [**13**], [**16**], [**22**], [**143**]; from *T. polium* subsp. *expansum*[37] [**4**], [**45**], [**124**]; from *T. cossonii*[37] [**135**]; from *T. montbretii* subsp. *heliotropifolium* [**46**], [**76**], [**77**], [**80**]; from *T. asiaticum*[38] [**25**], [**93**]; from *T. polium* subsp. *capitatum*[38] [**22**], [**25**]; from *T. polium* subsp. *album*[40] [**8**]; from *T. pumilum* subsp. *carolipaui*[41] [**22**]; from *T. turredanum*[41] [**13**], [**16**], [**22**]; from *T. leucocladum*[43] [**8**]; from *T. montbretii* subsp. *montbretii* [29] [**8**], [**20**], [**46**], [**76**], [**77**], [**80**], [**83**], [**84**], [**93**], [**137**].

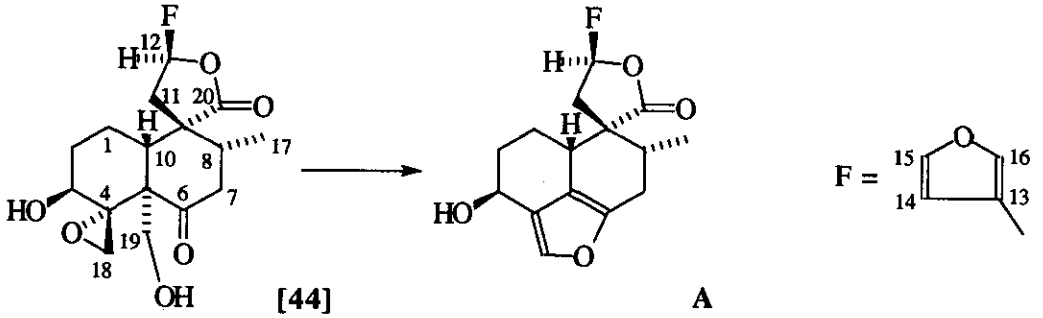
On the contrary, *T. decipiens*,[42] *T. algarbiense*,[43] *T. cyprium*,[43] *T. compactum*[43] and *T. montbretii* subsp. *pamphilicum*[43] were found to contain no diterpenoid.

The *neo*-clerodane absolute configuration was proved conclusively for the majority of the products here reported, by the use of X-ray diffraction, ord, cd and chemical correlation. In some cases the stereochemistry at C12 was not established when this atom bears an OH or OAc group. When C12 is involved in the five-membered lactone or lactol ring, the configuration is almost always 12*S*. The unusual 12*R* configuration was found only in eleven products: montanin C [**8**], 12-*epi*-teupolin I [**9**], teupyreinin [**28**], teusalvin C [**57**], 12-*epi*-teucvin [**90**], 12-*epi*-teuscorodonin [**121**], teucroxylepin [**129**], 12-*epi*-teupolin II [**131**], montanin G [**134**], 12-*epi*-teucvidin [**145**] and 12-*epi*-teuflin [**146**].

A very peculiar behaviour is shown by teucrin P1 [**24**]: two conformers do exist,[44] the first with rings B and E in boat-boat conformation can be converted into the second having rings B and E in boat-chair conformation. Both forms are stable at room temperature and can be isolated as crystals: the structure of the second conformer was proved by X-ray diffraction.

The ^{1}H-dnOe method was used widely by us and others[6] to determine the configuration at the C-12 chiral centre of several products when the 20,12-γ-lactone or lactol ring occurs. When a 12-hydroxy group is present, investigations were achieved on the pairs of 12*S* and 12*R* epimers and their acylated derivatives:[45] they were based on careful study of ^{1}H and ^{13}C nmr spectra, on the variation of the molecular rotations and on behaviour in the cd exciton chirality method. So alternative techniques were provided for establishing the C-12 absolute configuration.

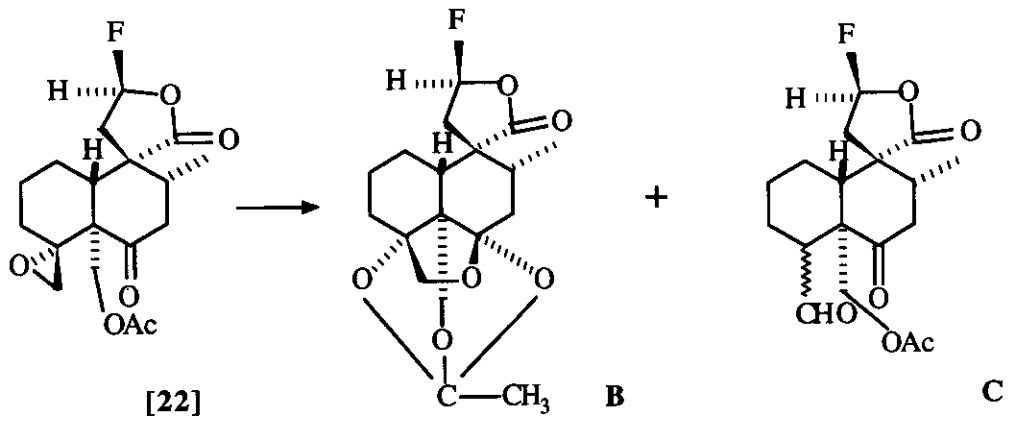
Although no total synthetic work was still attempted on the *neo*-clerodanes from *Teucrium* species, several transformations were performed starting from the natural products. A series of thermal rearrangements[46] was studied. So teulepicin [**44**] afforded the retroaldolic loss of C-19 and the formation of the furan derivative **A**, a reaction till now observed[2] on similar products only by using basic catalysis.



[**44**] **A**

Thermal treatment[46] of 19-acetylgnaphalin [**22**] gave an orthoacetate **B** and a mixture of the two epimeric at C-4 aldehydes **C**: such orthoacetate system had been found previously in the natural diterpenoid teulanigeridin [**67**].

The formation of an orthoacetate was observed[46] also on 7-acetylteupolin IV [**12**], whereas the mixture of epimeric aldehydes was obtained[46] from 6-acetylteucjaponin B [**20**]. Capitatin [**5**] is transformed into 6-acetylpicropolin [**2**] by thermal α-ketol rearrangement.[46]


F
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O
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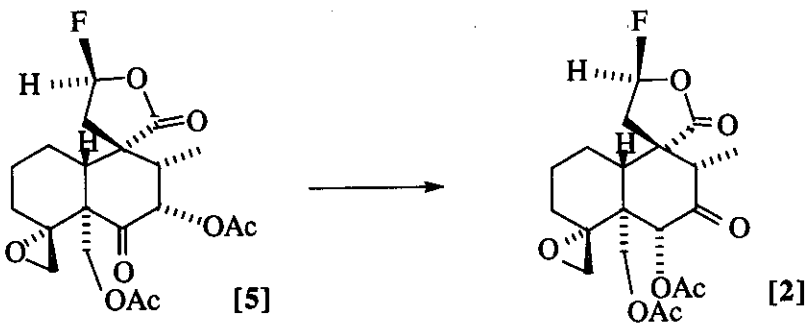
[22]
B
C
CHO
OAc


F
H
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H
OAc
O
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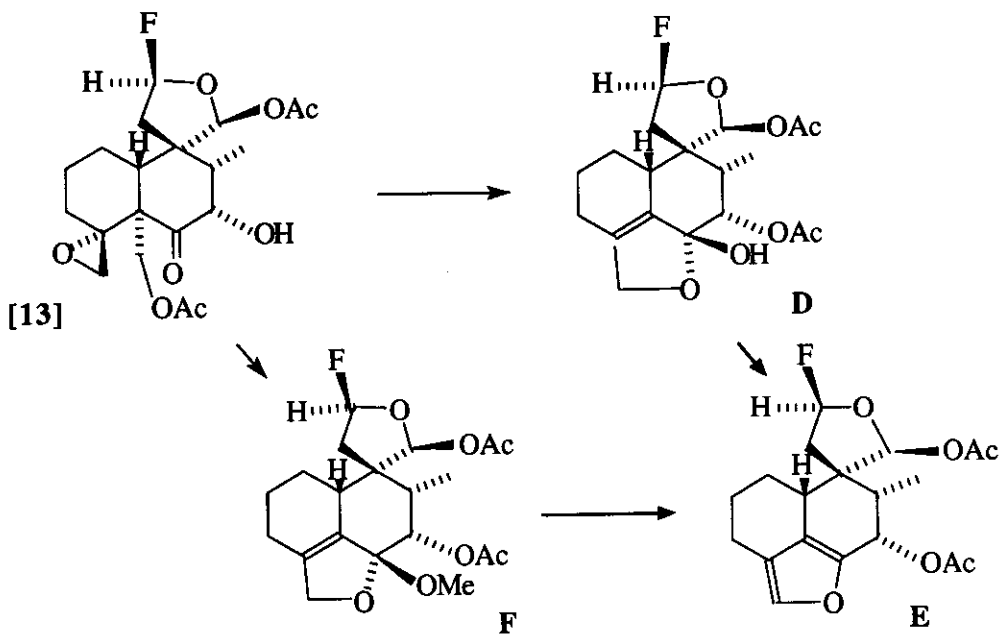
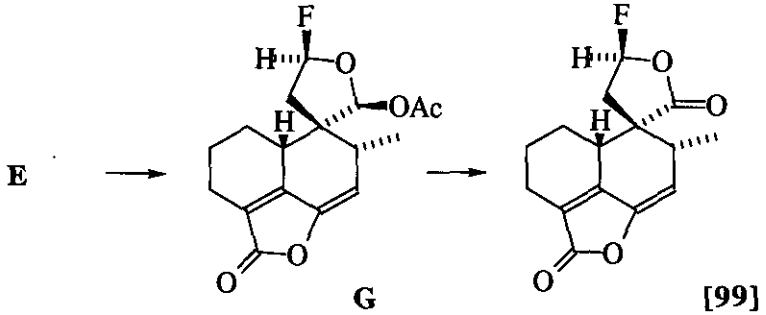
[5]
[2]


F
H
O
OAc
H
OH
O
OAc
[13]
D
E
F
OMe

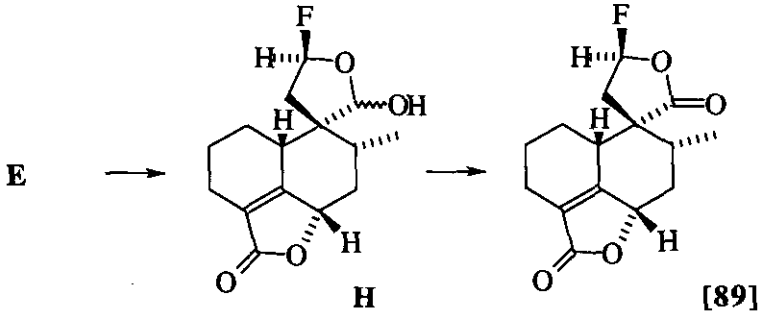
The mechanism of the retroaldolic loss of C-19 by basic catalysis was studied[47] on eriocephalin [**13**]. Treatment with potassium *t*.butoxide gave an highly unstable intermediate **D** that dehydrated to the furan derivative **E**; in the presence of methyl iodide the methyl acetal **F** was obtained, that heated at 150°C lost CH_3OH giving **E**. The retroaldolic cleavage is possible only if a keto group occours on C-6: indeed, in the presence of a 6α-OH group only the transacetylation from C-19 to C-6 was observed.

Product **E** was oxidized by atmospheric O_2 in $CHCl_3$ solution to **G**: the latter by hydrolysis followed by CrO_3-Py oxidation yielded[47] teuscorolide [**99**].



[**99**]

Sulphuric acid hydrolysis of **E** produced[47] epimerization at C-20 and rearrangement to **H**, whose CrO_3-Py oxidation afforded teucvin [**89**].

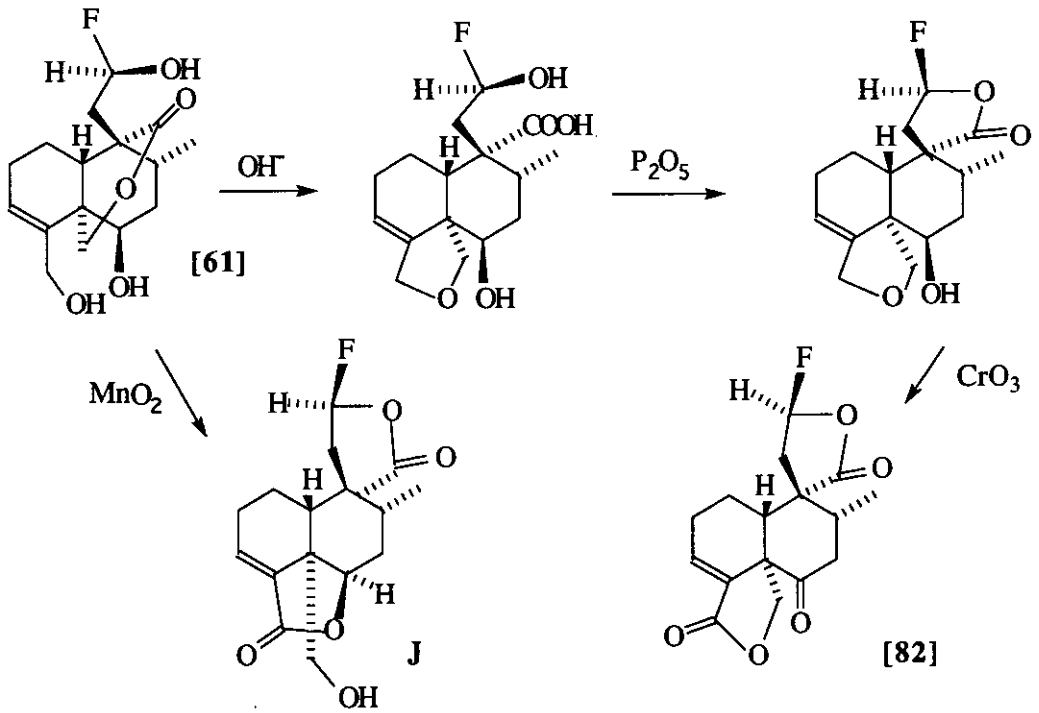


[**89**]

From teubotrin [**61**] a three-step partial synthesis of teuscordinon [**82**] was performed.[48] Oxidation of teubotrin [**61**] with MnO_2 yielded[48] a derivative **J** with two γ-lactone rings.

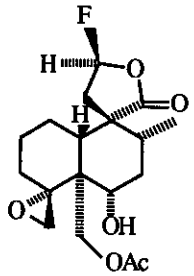
Montanin A [**101**] was the starting material for a five-step partial synthesis[49] of crotocaudin, a *neo*-clerodane diterpenoid from *Croton caudatus* (family Euphorbiaceae). So it was proved

that crotocaudin and isocrotocaudin have the equatorial 8α-CH_3 stereochemistry, and not the previously assigned[50] axial 8β-CH_3 configuration.



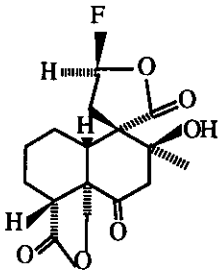
Addendum. The last diterpenoid whose complete stereostructure was elucidated (also by cd and X-ray analysis) is teupernin D, isolated from *T. pernyi* quite recently.[51] It is a 19-*nor* derivative, belongs to the 10α-H series, and shows an unprecedented axial 8α-CH_2Cl and 8β-OH system. Therefore teupernin D [**155**] is the fourth example of chlorinated *neo*-clerodanes from *Teucrium*..

TABLE



[104] teupolin I — $C_{22}H_{28}O_7$

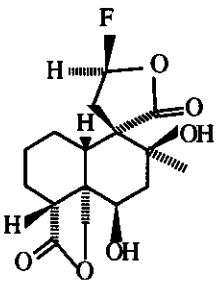
T. polium[5,6]



[105] teupernin B — $C_{20}H_{22}O_7$

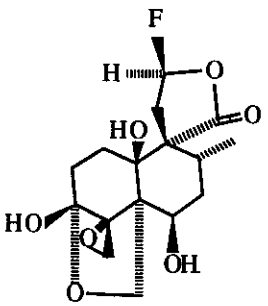
T. pernyi[10]

T. bidentatum[11]



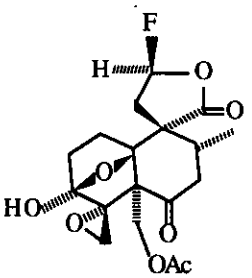
[106] teupernin C — $C_{20}H_{24}O_7$

T. pernyi[10]



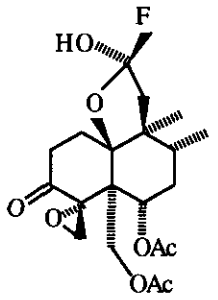
[107] teupestalin A — $C_{20}H_{24}O_8$

T. pestalozzae[12]



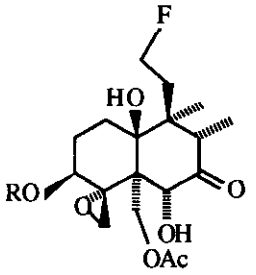
[108] teupestalin B — $C_{22}H_{24}O_9$

T. pestalozzae[12]



[**109**] teucrolivin A — $C_{24}H_{30}O_9$

T. oliverianum[13]

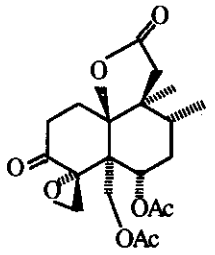


[**110**] teucrolivin B — R = Ac — $C_{24}H_{32}O_9$

T. oliverianum[13]

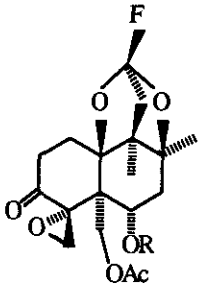
[**111**] teucrolivin C — R = H — $C_{22}H_{30}O_8$

T. oliverianum[13]



[**112**] teucrolivin F — $C_{20}H_{26}O_8$

T. oliverianum[14]

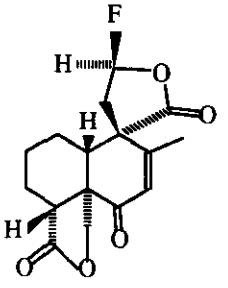


[**113**] teucrolivin H — R = H — $C_{22}H_{26}O_8$

T. oliverianum[15]

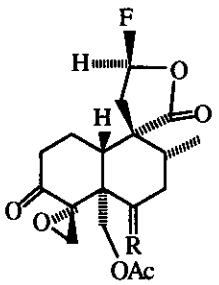
[**114**] teucrolivin G — R = Ac — $C_{24}H_{28}O_9$

T. oliverianum[15]



[**115**] teupernin A — $C_{20}H_{20}O_6$

T. pernyi[10]

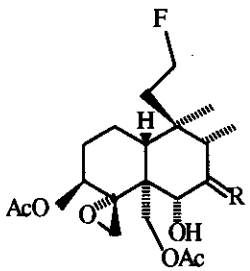


[**116**] 4α,18-epoxytafricanin A R = O $C_{22}H_{24}O_8$

T. pestalozzae[16]

[**117**] 20-oxo-teuflavin R = αH, βOH $C_{22}H_{26}O_8$

T. pestalozzae[16]

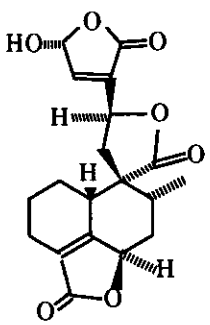


[**118**] teucrolivin D R = αH, βOAc $C_{26}H_{36}O_9$

T. oliverianum[14]

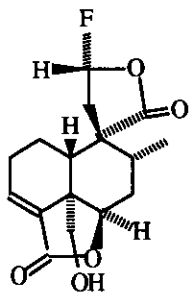
[**119**] teucrolivin E R = O $C_{24}H_{32}O_8$

T. oliverianum[14]



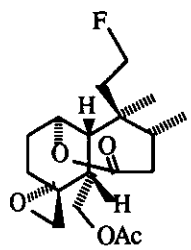
[**120**] teuponin $C_{19}H_{20}O_7$

T. japonicum[17]



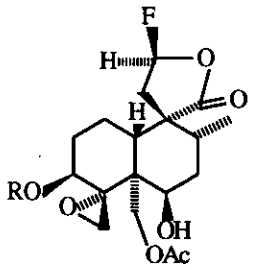
[**121**] 12-*epi*-teuscorodonin $C_{20}H_{22}O_6$

T. bicolor[18]



[**122**] fruticolide $C_{22}H_{30}O_6$

T. fruticans[19]



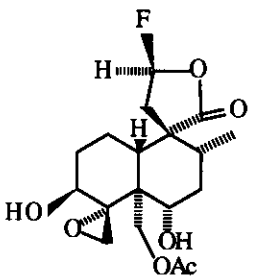
[**123**] teugracilin A R = Ac $C_{24}H_{30}O_9$

T. gracile[20]

[**124**] 3-O-deacetyl- R = H $C_{22}H_{28}O_8$

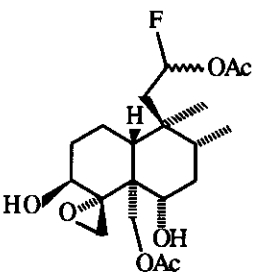
T. gracile[20]

T. polium subsp. *expansum*[37]



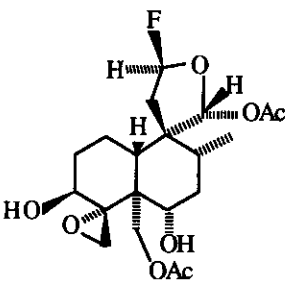
[**125**] teugracilin B $C_{22}H_{28}O_8$

T. gracile[20]



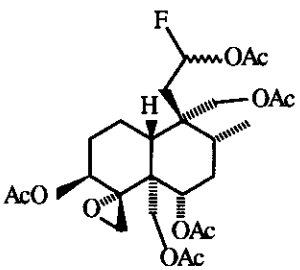
[**126**] teugracilin C $C_{24}H_{34}O_8$

T. gracile[20]



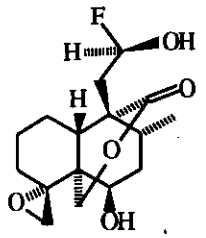
[**127**] teugracilin D $C_{24}H_{32}O_9$

T. gracile[19]



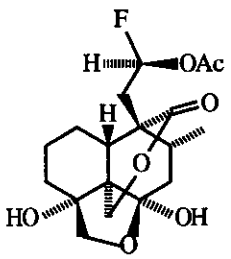
[**128**] teugracilin E $C_{30}H_{40}O_{12}$

T. gracile[19]



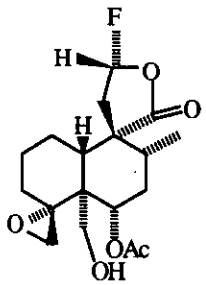
[**129**] teucroxylepin $C_{20}H_{26}O_6$

T. oxylepis subsp. *marianum*[21]



[**130**] 12-acetylteugnaphalodin $C_{22}H_{28}O_8$

T. oxylepis subsp. *marianum*[21]

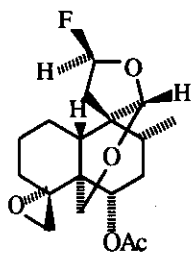


[**131**] 12-*epi*-teupolin II $C_{22}H_{28}O_7$

T. lamiifolium[22]

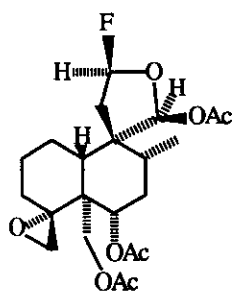
T. abutiloides[26]

T. canadense[35]



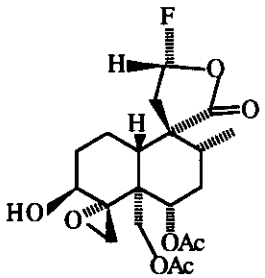
[**132**] teubutilin A $C_{22}H_{28}O_6$

T. abutiloides[26]



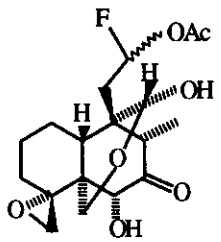
[**133**] teubutilin B $C_{26}H_{34}O_9$

T. abutiloides[26]



[134] montanin G $C_{24}H_{30}O_9$

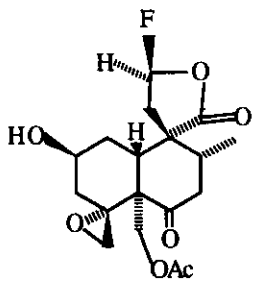
T. montanum var. *skorpilii*[27]



[135] montanin H $C_{22}H_{28}O_8$

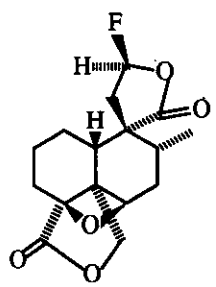
T. montanum subsp. *montanum*[28]

T. cossonii[37]



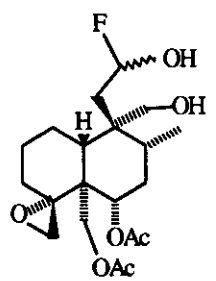
[136] teumassin $C_{22}H_{26}O_8$

T. massiliense[29]



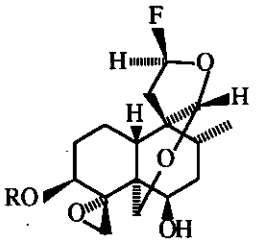
[137] 2-deoxychamaedroxide $C_{20}H_{22}O_6$

T. divaricatum subsp. *canescens*[30]



[138] teucretol $C_{24}H_{34}O_8$

T. creticum[31]

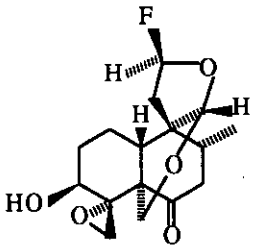


[**139**] teumicropin R = H $C_{20}H_{26}O_6$

T. micropodioides[32]

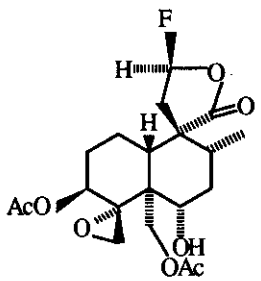
[**140**] 3-acetylteumicropin R =Ac $C_{22}H_{28}O_7$

T. micropodioides[32]



[**141**] 3-O-deacetylteupyrenone $C_{20}H_{24}O_6$

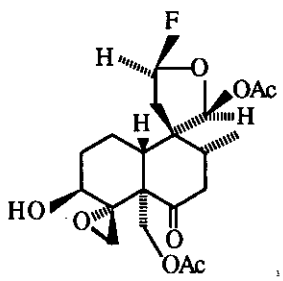
T. micropodioides[32]



[**142**] teumicropodin $C_{24}H_{30}O_9$

T. micropodioides[32]

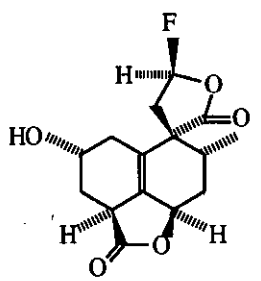
T. gracile[20]



[**143**] 3-O-deacetyl-20-*epi*-teulanigin $C_{24}H_{30}O_9$

T. micropodioides[32]

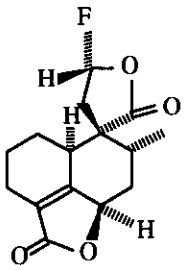
T. polium subsp. *vincentinum*[36]



[**144**] isoteucrin-H4 $C_{19}H_{20}O_6$

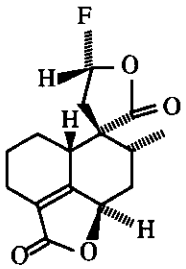
T. kotschyanum[33]

T. oxylepis subsp. *marianum*[21]



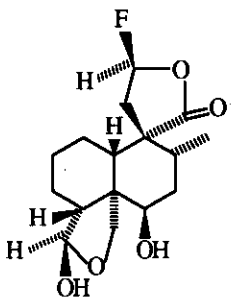
[**145**] 12-*epi*-teucvidin $C_{19}H_{20}O_5$

T. kotschyanum[34]



[**146**] 12-*epi*-teuflin $C_{19}H_{20}O_5$

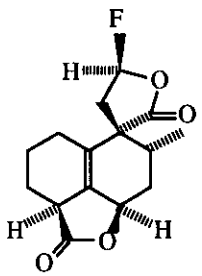
T. kotschyanum[34]



[**147**] teukotschyn $C_{20}H_{26}O_6$

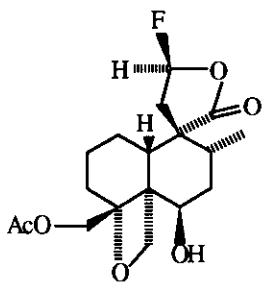
T. kotschyanum[34]

T. oxylepis subsp. *marianum*[21]



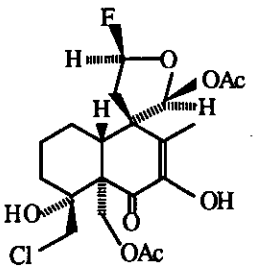
[**148**] isoteuflin $C_{19}H_{20}O_5$

T. canadense[35]



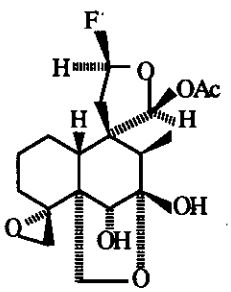
[**149**] 18-acetylmontanin D $C_{22}H_{28}O_7$

T. canadense[35]



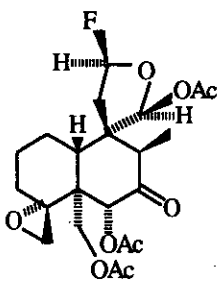
[150] teuvincentin A $C_{24}H_{29}O_9Cl$

T. polium subsp. *vincentinum*[36]



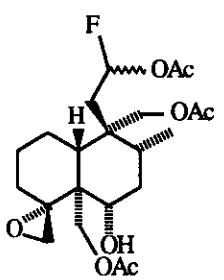
[151] teuvincentin B $C_{22}H_{28}O_8$

T. polium subsp. *vincentinum*[36]



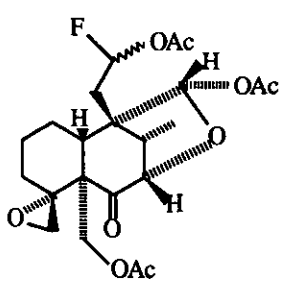
[152] teuvincentin C $C_{26}H_{32}O_{10}$

T. polium subsp. *vincentinum*[36]



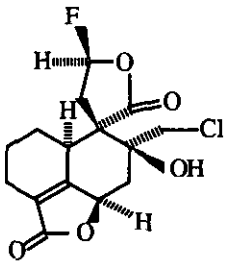
[153] teucossin A $C_{26}H_{36}O_9$

T. cossonii[37]



[154] teucossin B $C_{26}H_{32}O_{10}$

T. cossonii[37]



[**155**] teupernin D $C_{19}H_{19}O_6Cl$

T. pernyi[51]

REFERENCES

1. F.Piozzi, *Heterocycles*, 1981,**15**, 1489.
2. F.Piozzi, G.Savona, and B.Rodriguez, *Heterocycles*, 1987, **25**, 807.
3. A.T.Merritt, and S.V.Ley, *Natural Product Reports*, 1992, **9**, 243.
4. M.S.J.Simmonds, W.M.Blaney, S.V.Ley, G.Savona, M.Bruno, and B.Rodriguez, *Phytochemistry*, 1989, **28**, 1069.
5. P.Y.Malakov, G.Y.Papanov, and N.N.Mollov, *Z.Naturforsch.*, 1979, **34B**, 1570.
6. E.Gacs-Baitz, G.Y.Papanov, P.Y.Malakov, and L.Szilagyi, *Phytochemistry*, 1987, **26**, 2110.
7. J.Fayos, F.Fernandez-Gadea, C.Pascual, A.Perales, F.Piozzi, M.Rico, B.Rodriguez, and G.Savona, *J.Org.Chem..*, 1984, **49**, 1789.
8. J.L.Marco, B.Rodriguez, C.Pascual, G.Savona, and F.Piozzi, *Phytochemistry*, 1983, **22**, 727.
9. P.Y.Malakov, and G.Y.Papanov, *Phytochemistry*, 1983, **22**, 2791.
10. N.Xie, Z.Min, S.Zhao, B.Wu, Q.Zheng, and P.Zhang, *Phytochemistry*, 1991, **30**, 1963.
11. H.Sun, X.Chen, T.Wanc, L.Pan, Z.Lin, and D.Chen, *Phytochemistry*, 1991, **30**, 1721.
12. M.C.de la Torre, B.Rodriguez, M.Bruno, G.Savona, F.Piozzi, A.Perales, M.R.Torres, and O.Servettaz, *Phytochemistry*, 1990, **29**, 2229.
13. M.Bruno, A.A.Omar, A.Perales, F.Piozzi, B.Rodriguez, G.Savona, and M.C. de la Torre, *Phytochemistry*, 1991, **30**, 275.
14. M.C.de la Torre, M.Bruno, F.Piozzi, G.Savona, B.Rodriguez, and A.A.Omar, *Phytochemistry*, 1991, **30**, 1603.

15. M.C. de la Torre, M.Bruno, F.Piozzi, G.Savona, A.A.Omar, A.Perales, and B. Rodriguez, *Tetrahedron*, 1991, **47**, 3463.
16. M.C.de la Torre, M.Bruno, G.Savona, F.Piozzi, B.Rodriguez, and O.Servettaz, *Phytochemistry*, 1990, **29**, 988.
17. Z.Min, N.Xie, P.Zhang, S.Zhao, C.Wang, and Q.Zheng, *Phytochemistry*, 1991, **30**, 4175.
18. C.Labbe, M.I.Polanco, and M.Castillo, *J.Nat.Prod.*, 1989, **52**, 871.
19. M.Bruno, R.Alcazar, M.C.de la Torre, F.Piozzi, B.Rodriguez, G.Savona, A.Perales, and N.A.Arnold, *Phytochemistry*, 1992, **31**, 3531.
20. M.Bruno, G.Dominguez, A.Lourenço, F.Piozzi, B.Rodriguez, G.Savona, M.C. de la Torre, and N.A.Arnold, *Phytochemistry*, 1991, **30**, 3693.
21. M.J.Sexmero-Cuadrado, M.C.de la Torre, B.Rodriguez, M.Bruno, F.Piozzi, and G.Savona, *Phytochemistry*, 1991, **30**, 4079.
22. I.M.Boneva, P.Y.Malakov, and G.Y.Papanov, *Phytochemistry*, 1988, **27**, 295.
23. P.Y.Malakov, I.M.Boneva, G.Y.Papanov, and S.L.Spassov, *Phytochemistry*, 1988, **27**, 1141.
24. M.C. de la Torre, F.Fernandez-Gadea, A.Michavila, B.Rodriguez, F.Piozzi, and G.Savona, *Phytochemistry*, 1986, **25**, 2385.
25. P.Y.Malakov, M.C. de la Torre, B.Rodriguez, and G.Y.Papanov, *Tetrahedron*, 1991, **47**, 10129.
26. M.C. de la Torre, B.Rodriguez, F.Piozzi, G.Savona, M.Bruno, and M.C.Carreiras, *Phytochemistry*, 1990, **29**, 579.
27. P.Y.Malakov, and G.Y.Papanov, *Z.Naturforsch.*, 1987, **42B**, 1000.
28. P.Y.Malakov, G.Y.Papanov, and I.M.Boneva, *Phytochemistry*, 1992, **31**, 4029.
29 M.Bruno, F.Piozzi, B.Rodriguez, G.Savona, M.C.de la Torre, and O.Servettaz, *Phytochemistry*, 1992, **31**, 4366.
30. M.Bruno, F.Piozzi, G.Savona, B.Rodriguez, M.C.de la Torre, and O.Servettaz, *Phytochemistry*, 1987, **26**, 2859.
31. G.Savona, F.Piozzi, M.Bruno, G.Dominguez, B.Rodriguez, and O.Servettaz, *Phytochemistry*, 1987, **26**, 3285.

32. M.C. de la Torre, B.Rodriguez, M.Bruno, G.Savona, F.Piozzi, and O.Servettaz, *Phytochemistry*, 1988, **27**, 213.
33. F.Simoes, B.Rodriguez, F.Piozzi, G.Savona, M.Bruno, and N.A.Arnold, *Heterocycles*, 1989, **28**, 111.
34. F.Simoes, B.Rodriguez, M.Bruno, F.Piozzi, G.Savona, and N.A.Arnold, *Phytochemistry*, 1989, **28**, 2763.
35. M.Bruno, F.Piozzi, G.Savona, M.C.de la Torre, and B.Rodriguez, *Phytochemistry*, 1989, **28**, 3539.
36. M.C.Carreiras, B.Rodriguez, F.Piozzi, G.Savona, M.R.Torres, and A.Perales, *Phytochemistry*, 1989, **28**, 1453.
37. R.Alcazar, M.C.de la Torre, B.Rodriguez, M.Bruno, F.Piozzi, G.Savona, and N.A. Arnold, *Phytochemistry*, 1992, **31**, 3957.
38. F.Camps, J.Coll, O.Dargallo, J.Rius, and C.Miravitlles, *Phytochemistry*, 1987, **26**, 1475.
39. A.Lourenço, M.C.de la Torre, B.Rodriguez, M.Bruno, F.Piozzi, and G.Savona, *Phytochemistry*, 1991, **30**, 613.
40. M.C.de la Torre, B.Rodriguez, A.-F.M.Rizk, M.Bruno, and F.Piozzi, *Fitoterapia (Milano)*, 1988, **59**, 129.
41. M.C. de la Torre, N.Ezer, B.Rodriguez, G.Savona, F.Piozzi, and O.Servettaz, *Fitoterapia (Milano)*, 1988, **59**, 70.
42. J.Bellakhdar, M.C.de la Torre, B.Rodriguez, G.Savona, M.Bruno, and F.Piozzi, *Planta Medica*, 1988, **54**, 267.
43. Our unpublished results.
44. M.Morita, N.Kato, T.Iwashita, K.Nakanishi, Z.Zheng, T.Yamane, T.Ashida, and F.Piozzi, *J. Chem. Soc., Chem.Commun.*, 1986, 1087.
45. A.Lourenço, M.C.de la Torre, B.Rodriguez, N.Harada, H.Ono, H.Uda, M.Bruno, F.Piozzi, and G.Savona, *Tetrahedron*, 1992, **48**, 3925.
46. M.C.de la Torre, P.Fernandez, and B.Rodriguez, *Tetrahedron*, 1987, **43**, 4679.
47. G.Dominguez, M.C.de la Torre, and B.Rodriguez, *J.Org.Chem.*, 1991, **56**, 6595.