The *X*-Ray Structure and Absolute Configuration of Insect Antifeedant Clerodane Diterpenoids from *Teucrium africanum*

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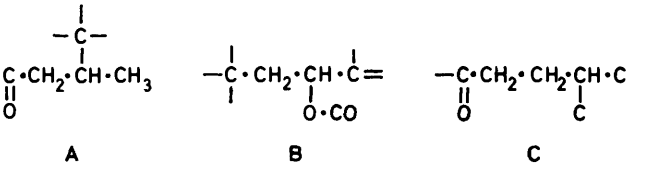
Tafricanin A and B have been shown to possess the clerodane diterpenoid structures (1) and (2), respectively, by a combination of chemical, spectroscopic, and *X*-ray crystallographic studies.

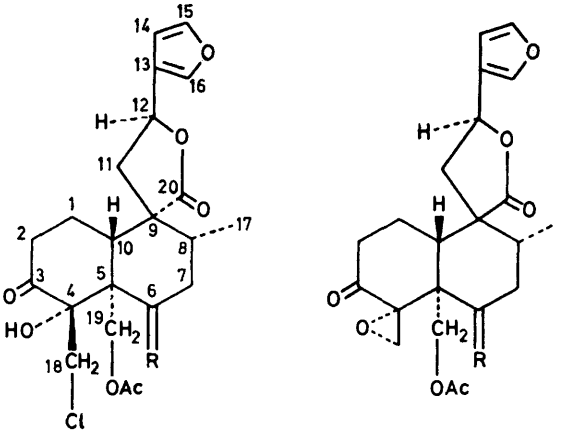
THE clerodane diterpenoids of *Teucrium* (Labiatae) species have recently attracted considerable attention.[1] In continuation of studies on the diterpenoids of the Labiatae [2,3] we have examined the South African bush, *Teucrium africanum*. This has afforded two chlorine-containing clerodanes with insect antifeedant properties. Their structures form the subject of this paper.

Extraction of the dried plant with acetone, partition and chromatography of the residue on silica, afforded two chlorohydrins, $C_{22}H_{25}ClO_8$ (M^+ 452 from C.I.M.S.) (tafricanin A)(1) and $C_{24}H_{29}ClO_9$ (M^+ 496 from C.I.M.S.) (tafricanin B)(2). Examination of the i.r. ($\nu_{max.}$ 1 747, 1 718, and 871 cm^{-1}), ^1H and ^{13}C n.m.r. spectra (see Table 1) of tafricanin A showed that the oxygen functions are a β-substituted furan ring, a γ-lactone ring, two cyclohexanones, an acetoxymethyl group attached to a fully substituted carbon atom, and a tertiary hydroxy-group. The ^1H n.m.r. spectrum also contained resonances attributable to a secondary methyl group (δ 1.13, *J* 6.7 Hz) and a primary alkyl chloride (δ 4.55 and 3.80, *J* 11 Hz). When the chlorohydrin (1) was heated with Amberlite IR-400 resin, it gave the epoxide (3), $C_{22}H_{24}O_8$ containing two proton resonances (δ 3.87 and 2.46, *J* 7 Hz) which were assigned to the epoxide. Treatment of the epoxide with concentrated hydrochloric acid in chloroform slowly regenerated the chlorohydrin. Careful ^1H n.m.r. spin decoupling studies of both compounds (1) and (3) at 360 MHz led to the identification of the fragments A—C. Thus, irradiation at the methyl doublet (δ 1.08) in the epoxide (3) showed that it was coupled (*J* 6.7 Hz) to a 12-line system (δ 2.11, *J* 3.5, 6.7, and 13 Hz). Spin decoupling studies then showed that this multiplet was coupled to a triplet (δ 3.17, *J* 13 Hz) and a double-doublet (δ 2.3, *J* 13 and 3.5 Hz). The triplet and double-doublet were also coupled (*J* 13 Hz) leading to the identification of fragment A. Irradiation of the triplet (*J* 8.7 Hz) at δ 5.50 in tafricanin A led to the collapse of a doublet at δ 2.60 indicative of fragment B. Identification of system C was facilitated by irradiation at δ 2.81 and a careful analysis of the coupling constants. Bearing in mind the isolation of clerodanes from related species, this data can be accommodated in the structure (1) for tafricanin A.

Examination of the ^{13}C n.m.r. spectrum of tafricanin B (2) showed that it contained a secondary acetate in place of a cyclohexanone. Like tafricanin A, it gave an epoxide on treatment with Amberlite IR-400 resin. The ^1H n.m.r. spectrum (see Table 1) of tafricanin B (2) and the epoxide (4) contained signals at δ 5.20 and 4.91 (*J* 4 and 12 Hz), respectively, which were assigned to a CHOAc group. Irradiation of the signal in the epoxide



A B C



(1) R = O
(2) R = α-OAc, β-H

(3) R = O
(4) R = α-OAc, β-H

(4) at δ 4.91 collapsed a quartet (*J* 12 Hz) at δ 2.12 to a triplet and a doublet of triplets (δ 1.52, *J* 4.4, and 12 Hz) to a double-doublet (*J* 4 and 12 Hz). Irradiation of the methyl doublet (δ 1.035, *J* 6.8 Hz) reduced a multiplet at δ 1.81 to a double-doublet which, in turn, was coupled to the signals at δ 2.12 and 1.52. Consequently it was shown that tafricanin B (2) possessed an equatorial 6α-acetoxy-group in place of the 6-ketone of tafricanin A.

In view of the reversal of the absolute stereochemistry assigned to clerodin [3] and the consequent uncertainty associated with the absolute stereochemistry of other clerodanes, tafricanin A (1) was subjected to an *X*-ray crystallographic analysis in order to determine its

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absolute stereochemistry. The resultant structure and absolute stereochemistry are shown in the Figure. To minimise bond and atom overlap, the Figure has been rotated through 180° relative to structure (1) and is thus viewed from the α-face. Both rings A and B have the normal chair form. There is an intramolecular hydrogen bond (2.62 Å) between the 4-hydroxy-group and the 3-carbonyl group and there is also a short non-bonded intramolecular contact (2.89 Å) between C-4-O and the oxygen atom of the 19-acetoxy-function.

Terpenoid natural products containing chlorine are relatively rare and most of those which do occur are chlorohydrins.[4] Since the original isolation procedure included a partition between chloroform and water, it was just conceivable that the chlorohydrins were artefacts. The isolation was therefore repeated with partition between ethyl acetate and water. However, the tafricanins A and B were still detected, thus showing that the chlorohydrins are not artefacts of the isolation procedure.

Tafricanin B (2) was shown to be as active as clerodin hemiacetal as an antifeedant against *Locusta migratoria* in a ' no-choice ' test with 5th instar males on GF/4 discs containing 5% sucrose.[5] On the other hand, tafricanin A (1) showed only weak (38%) inhibition of feeding at 1 000 p.p.m. in a similar screen. This reduced activity against *Locusta migratoria* for 6-keto-derivatives compared with their 6-acetoxy-counterparts seems to be fairly common for other related polyoxygenated diterpenoids.[5]

TABLE 1

^1H and ^{13}C n.m.r. spectra of tafricanins A and B

	Compound						
	(1) δ/p.p.m.		(2) δ/p.p.m.		(3) δ/p.p.m.		(4) δ/p.p.m.
Carbon atom	^1H	^{13}C	^1H	^{13}C	^1H	^{13}C	^1H
1	2.19 (α), 2.30 (β)	24.4	n.a.	24.9	2.34 (α), 2.30 (β)	22.3	n.a.
2	2.78 (α), 2.60 (β)	36.9	2.75	36.4	2.81 (α), 2.46 (β)	39.0	2.80, 2.50
3		206.2		207.0		202.7	
4		81.7		80.4		72.1	
5		61.9		52.5		53.5	
6		206.2	5.20	70.8		204.5	4.91
7	2.30 (β), 3.20 (α)	43.8	2.13, 1.63	33.1	2.30 (β), 3.17 (α)	44.2	2.12, 1.52
8	2.09	41.1	1.80	38.4	2.11	40.7	1.81
9		52.1		52.2		51.8	
10	2.60	50.9	n.a.	48.9	2.62	52.4	n.a.
11	2.60	44.6	2.5	44.3	2.50, 2.63	43.0	2.50
12	5.49	72.5	5.40	72.2	5.53	72.3	5.45
13		124.9		125.3		124.6	
14	6.39	108.2	6.38	108.4	6.39	107.7	6.38
15	7.47	140.3	7.45	140.2	7.46	139.5	7.45
16	7.47	145.2	7.45	145.0	7.46	144.3	7.45
17	1.13	17.0	1.06	16.3	1.08	17.0	1.03
18	4.55, 3.90	47.6	3.98	47.8	2.46, 3.87	50.4	2.50, 3.19
19	4.83, 4.88	61.9	5.02, 5.13	61.5	4.85, 5.03	63.5	4.80, 5.27
20		176.6		176.5		176.0	
OAc	1.92	20.8	1.87, 2.05	20.8	1.95	20.3	1.92, 2.02
		169.8		21.6		169.1	
				170.0			
				171.3			

n.a. = not assigned.

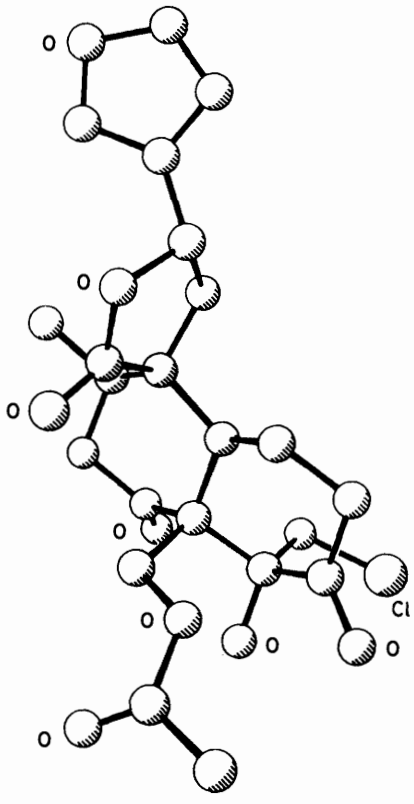
Coupling constants (Hz) compound (2): 10β,1α, 12.5; 10β,1β, 4; 1α,1β, 12.5; 1α,2α, 5; 1α,2β, 1.5; 2α,2β, 17; 7α,7β, 13; 7β,8β, 3.5; 8β,17, 16.7; 11α,11β, 13.5; 11α,12 = 11β,12 = 8.4; 18,18′, 7; 19,19′, 11.7. Compound (4): 6β,7α, 12; 6β,7β, 4; 7α,7β, 12; 7α,8β, 12; 7β,8β, 4; 8β,17, 6.7; 11α,12 = 11β,12 = 8.5; 18,18′, 5.4; 19,19′, 11.7.

EXPERIMENTAL

I.r. spectra were determined as KBr discs on a Perkin-Elmer 180 spectrometer; optical rotations were determined in chloroform on a Perkin-Elmer 241 polarimeter; ^1H n.m.r. spectra were determined in deuteriochloroform on a Bruker WH 360 spectrometer (University of Edinburgh) and ^{13}C n.m.r. spectra were determined on a JEOL PFT-100 spectrometer in deuteriochloroform.

Extraction of Teucrium africanum.—The acetone extract of the dried leaves and stems (5.9 kg) of *T. africanum* (Voucher specimen, Albany Museum Bayliss 8932) collected during November 1978, was shaken with activated charcoal and the solvent then evaporated. The residue was dissolved in chloroform (ethyl acetate in a repeat isolation), washed with water, and evaporated to afford a gum (203 g). Chromatography of the gum (73 g) on silica and elution with ethyl acetate–benzene (1 : 4) gave tafricanin A (3.2 g) and tafricanin B (0.7 g).

Tafricanin A (1) crystallized from ethanol as needles, m.p.



Molecular structure of tefricanin A. The structure is viewed from the α-face

TABLE 2

Fractional co-ordinates (× 10^4) for the non-hydrogen atoms with estimated standard deviations in parentheses

Atom	*x*	*y*	*z*
Cl	7 278(1)	−1 177	9 387(1)
C(1)	2 897(3)	−1 824(5)	6 614(3)
C(2)	4 267(4)	−1 697(5)	6 616(4)
C(3)	4 924(3)	−322(5)	7 231(4)
C(4)	4 872(3)	67(4)	8 539(3)
C(5)	3 437(3)	−29(4)	8 466(3)
C(6)	3 349(3)	175(4)	9 786(4)
C(7)	2 005(3)	−43(5)	9 777(4)
C(8)	1 559(3)	−1 604(4)	9 387(3)
C(9)	1 574(3)	−2 038(4)	8 057(3)
C(10)	2 890(3)	−1 572(4)	7 954(3)
C(11)	1 407(3)	−3 707(4)	7 882(4)
C(12)	270(4)	−3 973(4)	6 616(4)
C(13)	−682(3)	−5 065(5)	6 698(3)
C(14)	−580(4)	−6 608(5)	6 665(4)
C(15)	−1 598(5)	−7 205(6)	6 799(4)
C(16)	−1 795(4)	−4 817(6)	6 874(4)
C(17)	240(4)	−1 848(6)	9 485(4)
C(18)	5 754(3)	−979(5)	9 555(3)
C(19)	2 862(3)	1 298(5)	7 687(3)
C(20)	383(3)	−1 455(5)	6 987(4)
C(21)	3 074(4)	3 015(5)	6 299(4)
C(22)	3 597(4)	3 199(6)	5 267(4)
O(1)	5 539(3)	451(4)	6 791(3)
O(2)	5 331(2)	1 520(3)	8 863(2)
O(3)	4 238(2)	463(3)	10 748(2)
O(4)	−332(2)	−2 550(3)	6 262(2)
O(5)	−2 384(3)	−6 132(5)	6 944(3)
O(6)	15(3)	−215(3)	6 760(3)
O(7)	3 020(3)	1 577(3)	6 590(2)
O(8)	2 742(4)	3 951(4)	6 792(3)

189—191 °C (decomp.), $[\alpha]_D^{20}$ +32.9° (*c* 0.9) (Found: C, 58.1; H, 5.55; Cl, 7.85. $C_{22}H_{25}ClO_8$ requires C, 58.3; H, 5.55; Cl, 7.83%); $\lambda_{max.}$ (EtOH) 210 nm (ε 6 000); $\nu_{max.}$ 3 440, 1 747, 1 718, 1 498, and 871 cm^{-1}; *m/z* 452 (1%), 416 (3), 388 (26), 328 (18), 316 (30), 193 (16), 187 (16), 178 (30), 137 (50), 105 (22), 95 (100), 91 (38), and 81 (70).

Tafricanin B (2) crystallized from ethanol as needles, m.p. 255—256 °C, $[\alpha]_D^{20}$ +14.6° (*c* 0.9) (Found: C, 57.8; H, 6.0; Cl, 7.15. $C_{24}H_{29}ClO_9$ requires C, 58.0; H, 5.9; Cl, 7.13%); $\lambda_{max.}$ (EtOH) 210 nm (ε 6 000); $\nu_{max.}$ 3 420, 1 730, 1 505, and 873 cm^{-1}; *m/z* 496 (1%), 394 (10), 386 (8), 348 (15), 317 (10), 299 (65), 211 (26), 178 (25), 173 (30), 159 (40), 105 (40), 94 (90), 91 (75), and 81 (100).

TABLE 3

Bond lengths (Å) between the non-hydrogen atoms with estimated standard deviations in parentheses

C(1)–C(2)	1.537(6)	C(9)–C(10)	1.578(5)
C(3)–O(1)	1.212(6)	C(11)–C(12)	1.539(4)
C(4)–C(18)	1.535(5)	O(4)–C(20)	1.350(5)
C(5)–C(10)	1.558(5)	C(14)–C(15)	1.321(7)
C(6)–C(7)	1.514(5)	C(13)–C(16)	1.351(7)
C(8)–C(17)	1.537(6)	C(21)–C(22)	1.490(7)
C(9)–C(20)	1.525(4)	C(2)–C(3)	1.490(6)
C(12)–C(13)	1.486(6)	C(4)–O(2)	1.419(5)
C(13)–C(14)	1.414(6)	C(5)–C(6)	1.536(6)
O(5)–C(16)	1.384(7)	C(6)–O(3)	1.197(4)
O(7)–C(21)	1.359(5)	C(8)–C(9)	1.554(5)
C(18)–Cl	1.793(4)	C(9)–C(11)	1.537(5)
C(1)–C(10)	1.527(5)	C(12)–O(4)	1.449(5)
C(3)–C(4)	1.535(6)	C(20)–O(6)	1.199(5)
C(4)–C(5)	1.581(5)	C(15)–O(5)	1.366(7)
C(5)–C(19)	1.549(5)	C(19)–O(7)	1.441(5)
C(7)–C(8)	1.519(6)	C(21)–O(8)	1.152(6)

TABLE 4

Valence angles (°) between the non-hydrogen atoms with estimated standard deviations in parentheses

C(10)–C(1)–C(2)	110.8(3)	C(1)–C(2)–C(3)	112.7(4)
C(2)–C(3)–C(4)	116.9(4)	C(2)–C(3)–O(1)	124.0(4)
C(4)–C(3)–O(1)	119.0(3)	C(3)–C(4)–C(5)	109.5(2)
C(3)–C(4)–C(18)	109.1(3)	C(3)–C(4)–O(2)	108.9(3)
O(2)–C(4)–C(18)	108.5(2)	O(2)–C(4)–C(5)	109.2(3)
C(4)–C(5)–C(10)	108.8(3)	C(5)–C(4)–C(18)	111.5(3)
C(4)–C(5)–C(6)	111.7(2)	C(6)–C(5)–C(10)	108.1(3)
C(4)–C(5)–C(19)	108.6(3)	C(6)–C(5)–C(19)	103.6(3)
C(10)–C(5)–C(19)	116.0(2)	C(5)–C(6)–C(7)	113.3(3)
C(5)–C(6)–O(3)	124.9(4)	C(7)–C(6)–O(3)	121.8(4)
C(6)–C(7)–C(8)	110.2(3)	C(7)–C(8)–C(9)	113.4(3)
C(7)–C(8)–C(17)	109.7(3)	C(9)–C(8)–C(17)	112.6(3)
C(8)–C(9)–C(10)	110.1(2)	C(8)–C(9)–C(11)	109.4(3)
C(10)–C(9)–C(11)	109.3(3)	C(8)–C(9)–C(20)	110.7(3)
C(10)–C(9)–C(20)	114.6(3)	C(11)–C(9)–C(20)	102.4(3)
C(9)–C(10)–C(1)	112.1(2)	C(9)–C(10)–C(5)	117.8(3)
C(1)–C(10)–C(5)	110.9(3)	C(9)–C(11)–C(12)	107.2(3)
C(11)–C(12)–C(13)	114.6(3)	C(11)–C(12)–O(4)	104.8(3)
O(4)–C(12)–C(13)	110.3(3)	C(12)–O(4)–C(20)	112.6(3)
O(4)–C(20)–O(6)	119.3(3)	C(9)–C(20)–O(6)	129.0(3)
C(12)–C(13)–C(14)	126.8(4)	C(12)–C(13)–C(16)	128.2(4)
C(14)–C(13)–C(16)	105.0(4)	C(13)–C(14)–C(15)	109.1(4)
C(14)–C(15)–O(5)	109.8(5)	C(15)–O(5)–C(16)	105.9(4)
C(5)–C(19)–O(7)	111.2(3)	C(19)–O(7)–C(21)	115.2(3)
O(7)–C(21)–C(22)	111.1(4)	O(7)–C(21)–O(8)	123.3(4)
C(4)–C(18)–Cl	111.1(3)	C(9)–C(20)–O(4)	111.7(3)
O(8)–C(21)–C(22)	125.5(4)	O(5)–C(16)–C(13)	110.3(4)

Treatment of Tafricanins A and B with Amberlite IR-400 *Resin*.—The diterpenoid (200 mg) in dry dimethylformamide (6 ml) was stirred for 40 h with dry IR-400 resin in the anionic form (0.8 g). The resin was filtered off, water was added to the filtrate, and the product was recovered in ethyl acetate. The residue was chromatographed on silica in ethyl acetate–light petroleum (1 : 1).

Tafricanin A epoxide (3) crystallized from ethyl acetate as needles, m.p. 200 °C, $[\alpha]_D^{20}$ +112° (*c* 0.7) (Found: C, 63.1; H, 5.8. $C_{22}H_{24}O_8$ requires C, 63.5; H, 5.8%); $\nu_{max.}$ 1 757, 1 745, 1 720, 1 498, and 872 cm^{-1}. Treatment of the epoxide in chloroform (1 ml) with concentrated hydrochloric acid (0.1 ml) overnight regenerated (t.l.c.) the parent chlorohydrin.

Tafricanin B epoxide (4) formed solvated needles from ethyl acetate–hexane. After drying at 70 °C, these had m.p. 201 °C, $[\alpha]_D^{20}$ −5.4° (*c* 0.8) (Found: C, 62.3; H, 6.1. $C_{24}H_{28}O_9$ requires C, 62.6; H, 6.1%); $\nu_{max.}$ 1 738, 1 504, and 872 cm^{-1}.

Structure Determination.—Crystal data. Crystals of compound (1) are monoclinic, $a = 11.194(5)$, $b = 9=123(3)$, $c = 11.246(4)$ Å, $\beta = 111.66(3)°$, $U = 1\,067$ Å^3, $Z = 2$, $D_c = 1.42$ g cm^{-3}. Space group $P2_1$. Data were measured using monochromatised Cu-K_α radiation (graphite monochromator) on a Nicolet R3m diffractometer. A total of 1 544 independent reflections were measured ($\theta \leqslant 58°$) using the omega-scan measuring routine, and, of these, 79 were classed as unobserved.

The structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms, with the exception of the hydroxy-hydrogen which was allowed to refine, were placed at calculated positions and allowed to ride on their parent carbon atoms. Refinement was terminated at $R = 0.032$. The absolute configuration was determined by refinement of a single 'free variable' η which is applied as a multiplier of all f''.[6] This variable refined to a value of +0.89(5) showing that the co-ordinate set used had the correct chirality. Computations were carried out on an Eclipse S140 computer using the SHELX program system. The positional co-ordinates, bond lengths and angles are shown in Tables 2,3, and 4. The anisotropic and isotropic thermal parameters and structure factors are available as a Supplementary publication (SUP. No. 23248, 15 pages).*

We thank Dr I. H. Sadler (University of Edinburgh) for the determination of the n.m.r. spectra and Dr A. H. Ratcliffe (I.C.I. Pharmaceuticals Division) for the mass spectra. We thank Dr E. A. Bernays, Centre for Overseas Pest Research, London W8 5SJ, for the determination of the antifeedant activity.

[1/1049 *Received*, 2*nd July*, 1981]

* For details of the Supplementary publications scheme see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1981, Index issue.

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