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CROTOCAUDIN; A REARRANGED LABDANE TYPE NORDITERPENE FROM *CROTON CAUDATUS* GEISEL

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Abstract—The structure and stereochemistry of crotocaudin, a new norditerpene occurring as a minor constituent in *Croton caudatus* Geisel (Euphorbiaceae) have been established as *ent*-8*S*,10*S*-15,16-epoxy-19-norcleroda-4,11,13(16),14-tetraene-18,6*S*:20,12-diolactone **7** from the detailed studies of ^{1}H NMR spectra using lanthanide shift reagents, decoupling experiments and chemical reactions. The congener, teucvidin, *ent*-10*S*-15,16-epoxy-19-norcleroda-4,13(16),14-triene-18,6*S*:20,12*R*-diolactone **1** was obtained as a major component besides several triterpenoids *viz* taraxerone **2**, taraxerol **3** and taraxeryl acetate **4**. ^{13}C NMR and ^{1}H NMR spectra and a few novel reactions of teucvidin and its conversion to teucvin, *ent*-(6*R*,12*R*)-15,16-epoxy-19-nor-9,4-friedolabda-4,13(16),14-triene-18,6:20,12-diolactone **6** are also reported.

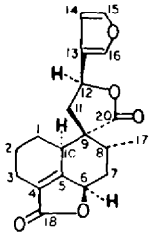
Simultaneous occurrence of proaporphine (Isoquinolinedienone) and aporphine alkaloids in *Croton sparsiflorus* Morung. (Euphorbiaceae), previously observed by one of the authors (A.C.)[1,2] stimulated further interest in this genus. This led to the investigation of *Croton caudatus* Geisel (Euphorbiaceae) which grows profusely in the Eastern Himalayan range at an altitude of 6000 ft. This plant finds extensive application in relieving pain from sprains.[3] Surprisingly no alkaloid could be isolated from this species collected in different seasons, but it is found to be a rich source of di- and tri-terpenoids. Detailed studies of this plant have revealed the presence of a rearranged labdane type new norditerpene, crotocaudin **7** and another norditerpene identified as teucvidin **1** besides taraxerone **2**, taraxerol **3**, taraxeryl acetate **4** and sitosterol. Teucvidin was first isolated by Fujita and his research group[4] as a minor constituent of *Teucrium viscidum* Blume var. Miquelianum (Maxim) Hara from a different family (Labiatae). Due to the paucity of the material the structure and absolute configuration of teucvidin could only be established from X-ray crystallography and spectral analysis, particularly ^{1}H NMR spectra employing INDOR and NOE experiments.[4]

In this communication we wish to report the structure and stereochemistry of crotocaudin, a minor component of *C. caudatus* and also ^{13}C NMR and ^{1}H NMR spectra employing lanthanide shift reagents of teucvidin, the major constituent of *C. caudatus* and its conversion to its diastereoisomer, teucvin occurring as a congener in *T. viscidum*. This is the first report of the isolation of teucvidin from Euphorbiaceae and its second occurrence in nature.

The white, crystalline crotocaudin, $C_{19}H_{18}O_5$ (M^+ 326.116), m.p. 199–200° (dec.), $[\alpha]_D^{28}$ – 65° was shown to be a mono-β-substituted furan derivative as evidenced from ^{1}H NMR spectrum, strong IR absorptions at 1500 and 870 cm^{-1} and positive Ehrlich test.[5] The attachment of this furan moiety with a β,γ-unsaturated γ-lactone (the characteristic absorption of which was discernible in the IR spectrum at 1795 cm^{-1}) could be recognised from the NMR and mass spectral data which would be discussed later. The presence of a second lactone ring was disclosed from the diagnostic peak at 1775 cm^{-1} in the IR spectrum. This is typical of an α,β-unsaturated γ-lactone which observation was consistent with the Baljet [6] and Kedde[7] colour reactions.

The electronic spectrum of crotocaudin in the UV region showed absorption maxima at 215 and 230 nm, the chromophore for the light absorption at 215 nm being α,β-unsaturated γ-lactone whereas λ_{max} at 230 nm was assigned to a furan system with an extended conjugation.

Based on the available data, *viz* the occurrence of a mono-β-substituted furan moiety, an α,β-unsaturated γ-lactone, a β,γ-unsaturated γ-lactone and a secondary methyl group as revealed from ^{1}H NMR spectra (the doublet at δ 1.04 (3H, J 7 Hz) in ^{1}H NMR spectrum collapsing to a singlet on irradiation of the proton attached to the adjacent carbon) the only structure that can be visualised is a norditerpenoid of rearranged labdane series **5** like teucvin **6**,[8] the logic behind this presumption being their close similarity in properties.



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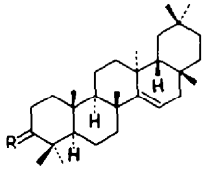
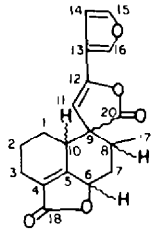


2 R = O
3 R = β-OH, α-H
4 R = β-OAc, α-H



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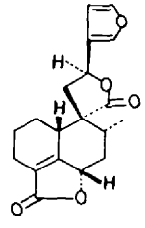

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Appropriate experiments were designed to probe into the skeletal pattern of crotocaudin and to reveal further structural features. Such a system **5** is generally vulnerable to base catalysed isomerisation as observed in both teucvin and teucvidin. Therefore reactions of this compound with basic reagents were studied. With sodium methoxide or potassium *t*-butoxide in aprotic solvents like benzene crotocaudin was found to remain unchanged, but in polar solvents with basic reagents the corresponding diastereoisomer, isocrotocaudin, $C_{19}H_{18}O_5$ **8** was formed involving the alteration in the stereochemistry at the ring-juncture C_6 and C_{10}. $NaBH_4$ in CH_3OH (pH 9) did not affect any functionality but caused the inversion of configuration at these two centres. This obviously proceeded via the enolate anion (Scheme 1). The structure of isocrotocaudin **8** was subsequently derived from its spectral properties.

The stereochemistry at the chiral centres of crotocaudin and isocrotocaudin was settled from ^1H NMR spectra (Table 1) and the CD studies.

The proper assignment of the proton signals and their correlations were possible by extensive decoupling experiments and also by studying the chemical shifts in different solvents and shift reagents. In case of crotocaudin, the protons of the secondary methyl group at C_8 resonated at δ 1.04 (3H, d, J 7 Hz). On irradiation at δ 1.96 this doublet collapsed to a sharp singlet which confirmed that the resonance at δ 1.96 was due to the adjacent proton, i.e. C_8-H. The signal at δ 1.96 appeared as a ddq and irradiation at δ 1.04 caused this signal (at δ 1.96) to change to a doublet of doublets with coupling constants of 11 Hz and 3 Hz. This was obviously due to the coupling of C_8-H with the nonequivalent methylene protons at C_7. The J-values further signified one axial–axial and one axial–equatorial coupling proving that the C_8-H was, indeed, axial, the methyl group being equatorial.

The NMR spectra of crotocaudin and isocrotocaudin were found to be very similar excepting the chemical shifts for C_{10}-H and C_6-H. The opposite stereochemistry at both C_{10} and C_6 in crotocaudin and isocrotocaudin was recognised from the corresponding NMR signals. The chemical shifts of the C_{10}-H in these two compounds differed by about 0.4 ppm. Obviously, the C_{10}-H (Table 1) in crotocaudin was deshielded by the C_{20}-carbonyl group, a situation which is only possible if the C_{10}-H and the C_{20}-carbonyl are on the same side thereby establishing that C_{10}-H and the C_9–C_{20} bond in crotocaudin have the same steric disposition (α or β). When the NMR spectrum of crotocaudin was recorded with the addition of 0.1 equivalent of $Eu(fod)_3$, a very large shift (caused by coordination of the metal, Eu to the oxygen

Table 1. ^1H NMR data of crotocaudin **7** and isocrotocaudin **8** (δ-values in ppm, $CDCl_3$, TMS as internal standard, 270 MHz)

	7		Δ^a)	J(Hz)	8	
1α-H	dddd	2.24	0.50	1α,1β = 12		
1β-H	dddd	1.33		1α,10α = 3		
2α-H	ddddd	1.51		1α,2α = 4		
2β-H	m	1.94		1α,2β = 3		
				1β,10α = 10		
				1β,2α = 12		
				1β,2β = 2		
				2α,2β = 12		
3 -H	m	2.1		2α,3α = 5		
				2α,3β = 12		
6 -H	t(br)	4.95	0.36	6α,7α = 7.5	dd(br)	4.82 (J = 9,7)
				6α,7β = 7.5		
7α-H	m	2.13		7α,7β = 12		
7β-H	m	1.74				
8α-H	ddq	1.96		7α,8α = 3		
				7β,8α = 11		
				8α,17 = 7		
10 -H	m	3.14	0.77		m	2.75
11 -H	s	5.27	0.10		s	5.33
14 -H	dd	6.58	0.04		dd	6.56
15 -H	ddd	7.49	0.02		ddd	7.48
16 -H	s(br)	7.72	0.01		s(br)	7.70
17 -H	d	1.04	0.09		d	0.99 (J = 7)

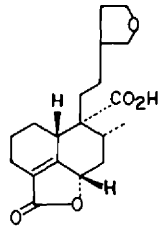
a) Δ-values after addition of 0.1 equivalents of $Eu(fod)_3$.

of the C_{20}-carbonyl) of the C_{10}–H was observed which also demanded that the C_{10}–H and the C_9–C_{20} bond in crotocaudin must be located on the same side.

In isocrotocaudin the situation was otherwise. The C_{10}–H did not experience any magnetic anisotropic effect of the C_{20}-carbonyl indicating that C_{10}–H in isocrotocaudin has the opposite orientation as that in crotocaudin.

In the ^{1}H NMR spectra of the compounds, the situation at C_6 was not so clear, as the chemical environment did not change very much. But the same steric disposition of the C_6–H and C_{10}–H in crotocaudin was evidenced from the following facts. (i) Similar large shift of the C_6–H signal (as observed in case of C_{10}–H) in the NMR spectrum of crotocaudin recorded after the addition of 0.1 equivalent of Eu(fod)$_3$ affirmed that the C_6–H and the C_9–C_{20} bond must be located on the same side and (ii) the Dreiding model of the compound could only be constructed with the same stereochemistry (both α or both β) of C_6–H and C_{10}–H, but not with the opposite stereochemistry (α,β or β,α) at these two centres. It followed, therefore, that in isocrotocaudin C_6–H also must have the opposite orientation as that in crotocaudin.

From the sequel it would be observed that C_6 and C_{10} protons in crotocaudin have α-configuration. The CD studies of teucvin, hexahydroteucvin **9** and teucvidin are already reported.[4] The CD spectrum of teucvin in dioxan displays (+) Cotton effect. That of hexahydroteucvin prepared from teucvin also exhibited (+) Cotton effect at about 230 nm with almost the same intensity. Thus the observed Cotton effect should be assigned to the α,β-unsaturated γ-lactone chromophore which is common in both teucvin and hexahydroteucvin, the other chromophores having no contribution in this respect.



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The CD spectrum (Fig. 1) of crotocaudin was run in MeOH solution. It showed (−) Cotton effect with nearly equal intensity to that of teucvin. The curve was found to be symmetrical to the curve of teucvin. This proved the antipodal relationship of the A, B and E ring system between teucvin and crotocaudin and the same stereochemistry of A, B and E ring system between teucvidin and crotocaudin provided the conformation of the A, B and E ring system of these compounds be the same. The conformations of both teucvin and teucvidin molecules have already been established[4] and the ring B has been proved to be in chair form.

This shows that both C_6–H and C_{10}–H in crotocaudin

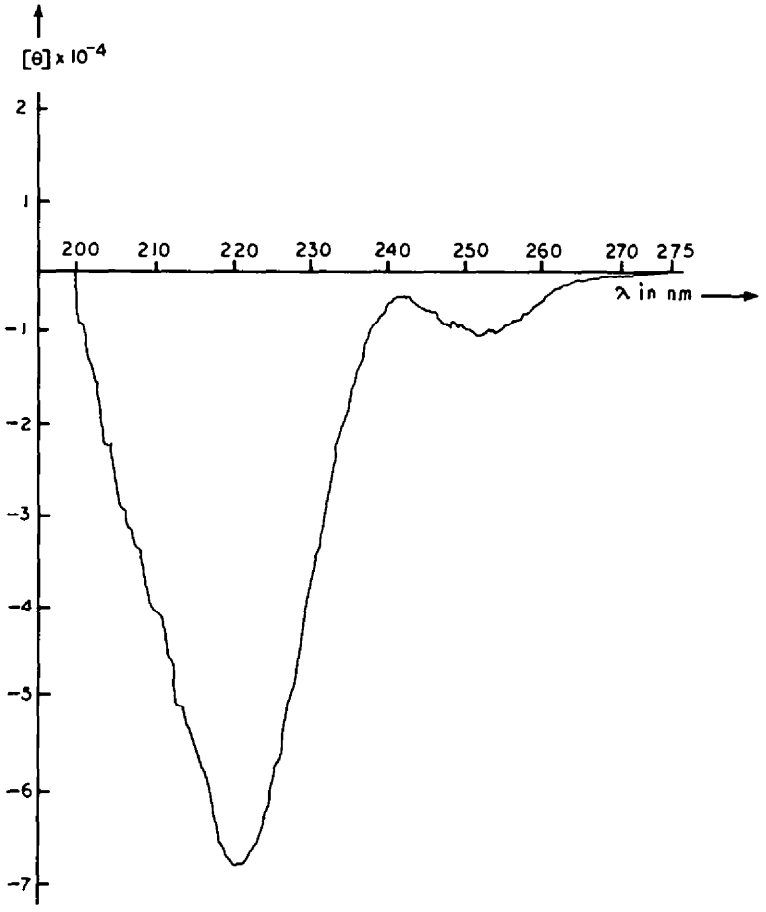


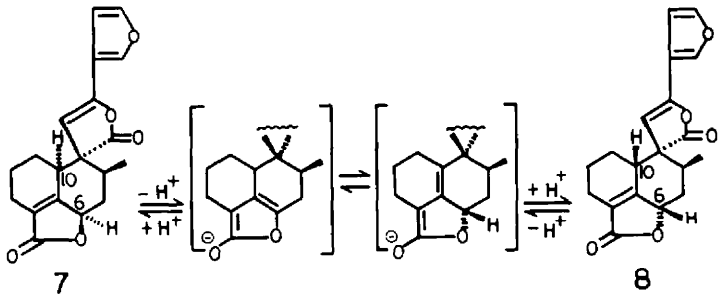
Fig. 1. CD curve of crotocaudin **7**.

should have α-orientation provided the ring B in crotocaudin is in the chair form. From the studies of the molecular model (with C_6–H and C_{10}–H having α-orientation), excepting the ring B the other rings were found to be rigid and fixed. The ring B may exist either in chair or in boat form. But the latter conformation involved more steric interaction than the chair form and could only be constructed with difficulty; because in the boat form of the ring B there was an intense steric interaction between the C_1–β–H and the C_{11}–H. Furthermore, both C_6–H and C_{10}–H in such a case would be pushed far apart from the C_{20}-carbonyl group. This would fail to explain the large shift suffered by both the C_6–H and C_{10}–H after the addition of Eu(fod)$_3$. Therefore the ring B in crotocaudin was in the chair form.

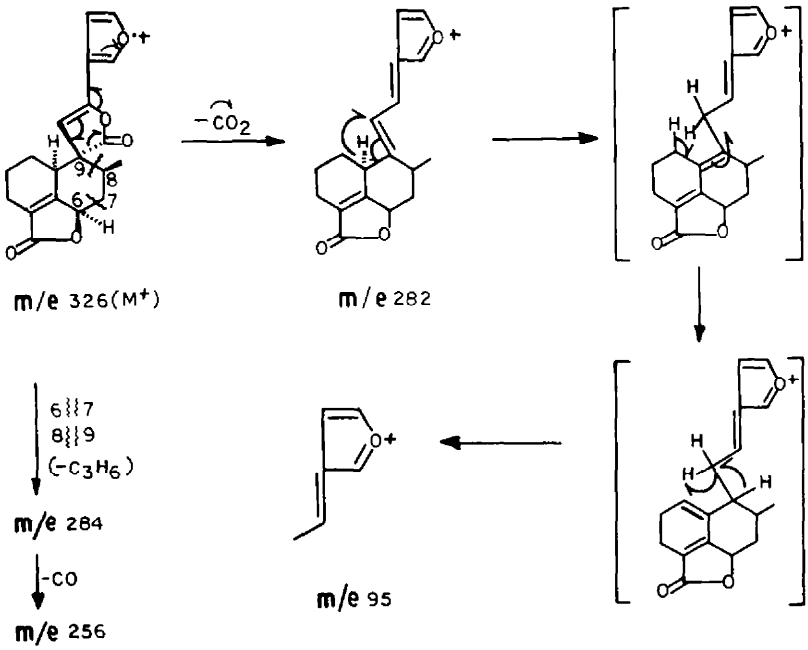
The aforesaid facts could decide the α-orientation of both C_6 and C_{10}-hydrogens, the absolute configurations at these centres being *S*. From the NMR signals and the shift reagent studies C_6–H, C_{10}–H and C_9–C_{20} bonds were found to be situated on the same side which affirmed the α-configuration of C_9–C_{20} bond. The steric disposition of the methyl group as β followed from its equatorial nature and chemical shift. Had the methyl group at C_8 been α, it would have experienced a larger paramagnetic shift and consequently it would have shifted to a lower field as is the case with teucvidin. The absolute structure of crotocaudin was, therefore, settled as *ent* - 8*S*,10*S* - 15,16 - epoxy - 19 - norcleroda - 4,11,13(16),14 - tetraene - 18,6*S*:20,12 - diolactone **7**. Consequently, isocrotocaudin **8** must be its diastereoisomer differing in the stereochemistry at C_6 and C_{10}. Now the formation of **8** from **7** could be rationalised as follows (Scheme 1).

The mass spectrum of crotocaudin was also in accord with the structure **7** (Scheme 2).

The second norditerpene, $C_{19}H_{20}O_5$ (M^+ 328.113), m.p. 214°, later identified as teucvidin **1** after detailed investigation, was shown to contain two lactonic carbonyls—one of these occurring in a saturated 5-membered ring and the second one being conjugated and associated with a γ-lactone. Supportive evidence in favour of α,β-unsaturated γ-lactone was secured from positive results of Baljet[6] and Kedde[7] reactions, λ_{max} at 215 nm in the UV region and IR absorption at 1740 cm^{-1}. The presence of a furan ring in this compound was indicated from the IR band at 1490 and 870 cm^{-1}, substantiated by positive Ehrlich test[5] and ^{1}H NMR spectrum. The two α-protons and the β-proton on the furan ring resonated at δ 7.44 (2H, d) and 6.36 (1H, dd)



Scheme 1.



Scheme 2. Mass spectral fragmentation pattern of crotocaudin **7**.

respectively. The presence of mono-β-substituted furan moiety was also recognised from ion-fragments at *m/e* 81 and 94 in the mass spectrum of the compound (Scheme 3).

The ^{1}H NMR spectra of the compound in different solvent mixtures using shift reagents and ^{13}C NMR spectra coupled with off-resonance studies proved useful in the elaboration of its structure and stereochemistry. Subsequent comparison of our compound with teucvidin by Prof. E. Fujita established their identity. The spectral properties of teucvidin not known in the literature are presented in the Table 2.

Teucvidin **1**, with $NaBH_4$/MeOH, underwent facile base catalysed isomerisation which involved the inversion of the stereochemistry at the ring juncture C_6 and C_{10}, the product being the corresponding diastereoisomer, teucvin **6**. The identity of teucvin **6** was established by the usual procedure.

Teucvidin **1** on refluxing with Na_2CO_3 in methanol gave an amorphous product, $C_{20}H_{24}O_6$ (M^+ 360.155). The compound was shown to be the keto-ester **10** on the basis of IR (1725 and 1710 cm^{-1}) and NMR (δ 3.70 (3H, s)) data. In the NMR spectrum of the compound the signal for 17-Me protons appeared at δ 1.12, whereas it was observed at δ 1.36 in teucvidin. The paramagnetic shift in teucvidin was obviously due to the anisotropic effect of the double bond at C-4. The formation of the keto-ester **10** could be rationalised as follows (Scheme 4).

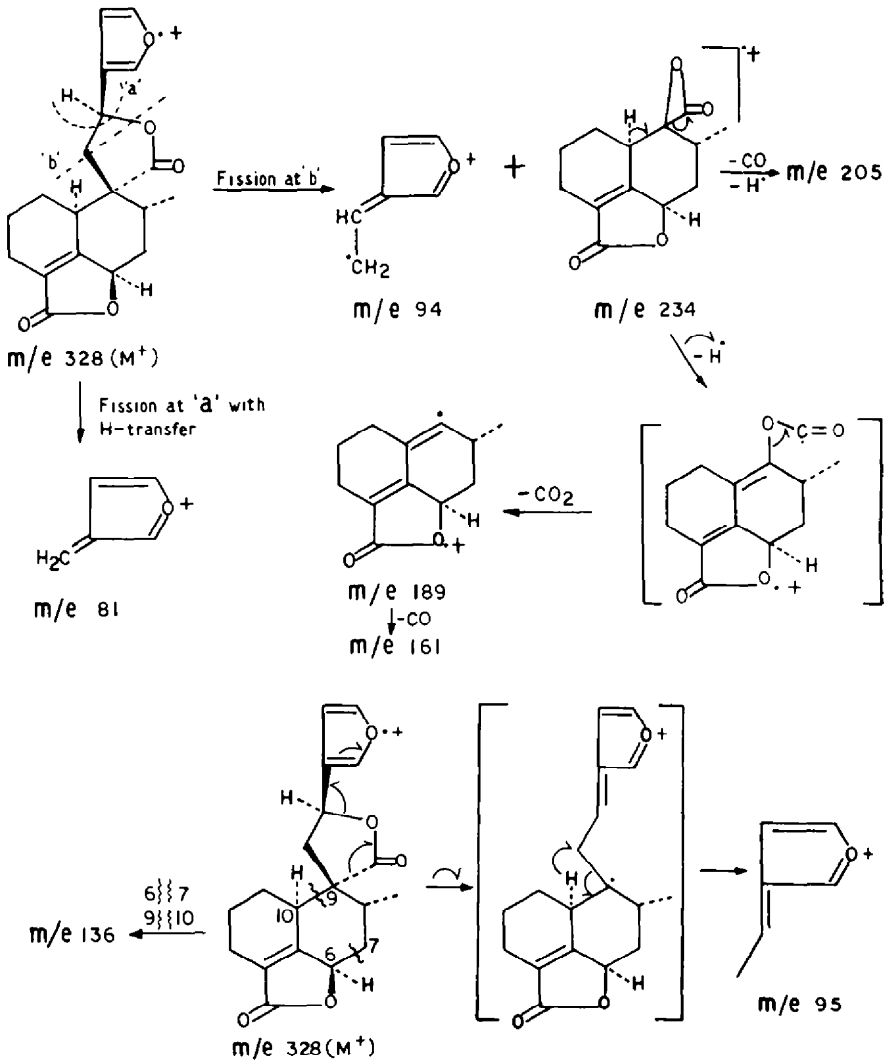
Decoupling experiments further confirmed the structure of this keto-ester **10**. The ^{1}H NMR data of this keto-ester **10** is presented in Table 3.

With $(i\text{-Bu})_2AlH$ both the lactones in teucvidin were smoothly reduced[9] to furnish a dilactol, but one of these was spontaneously converted to a furan derivative. The other lactol which remained unaffected yielded with MeOH and *p*-TsOH a monomethyl ether **11** (M^+ 328) (Scheme 5). The furan derivative was obviously[10] formed from the lactol arising from the α,β-unsaturated γ-lactone.

The spectral properties of **11** were in accord with its proposed structure. The base peak at *m/e* 134 (Scheme 6) in the mass spectrum of this compound showed clearly that the α,β-unsaturated γ-lactone of teucvidin was, indeed, transformed into a furan system.

EXPERIMENTAL

M.ps were recorded in a Toshniwal melting point apparatus and are uncorrected. The instruments used for spectral data are



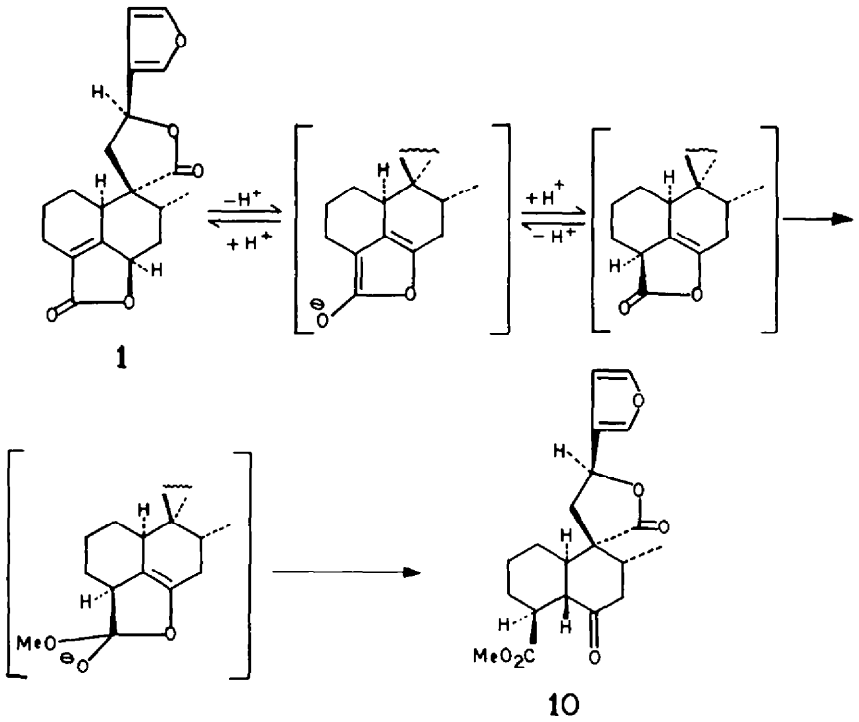
Scheme 3. Mass spectral fragmentation pattern of teucvidin **1**.

Table 2. NMR data of teucvidin **1** (δ-values in ppm, $CDCl_3$, TMS as internal standard, 270 MHz)

	^{1}H-NMR data		J(Hz)	Δ[a]	^{13}C-NMR data			Δ[b]
6α-H	dd(br)	5.00	6,7α = 6	1.10	C -1	t	21.4	1.6
7α-H	ddd	2.31	6,7β =11	0.58	C -2	t	23.5	1.8
7β-H	m	1.50	7α,7β =13	0.74	C -3	t	20.1	3.1
8β-H	ddq	2.18	7α,8β = 4		C -4	s	127.6	5.9
			7β,8β = 3		C -5	s	162.2	3.9
			8β,17 = 7		C -6	d	76.0	3.6
10α-H	m	3.27			C -7	t	35.8	2.8
11α-H	dd	2.58	11α,11β=14	0.66	C -8	d	35.9	0.9
11β-H	dd	1.91	11,12 = 7	0.58	C -9	s	52.2	3.0
12 -H	t	5.36		0.45	C -10	d	38.8	1.9
14 -H	dd	6.36	14,16 = 1	0.15	C -11	t	39.0	2.0
15 -H, 16 -H	d	7.44		0.06	C -12	d	71.8	1.7
				0.15	C -13	s	125.2	1.0
17 -H	d	1.36		0.69	C -14	d	107.9	0.6
					C -15	d	144.2	0.4
					C -16	d	139.5	0.5
					C -17	q	14.3	1.8
					C -18	s	177.6	8.0
					C -20	s	172.5	6.7

a) Δ-values after addition of 0.2 equivalents of $Eu(fod)_3$.

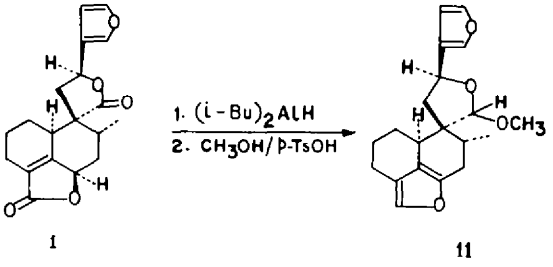
b) Δ-values after addition of 0.5 equivalents of $Yb(fod)_3$.



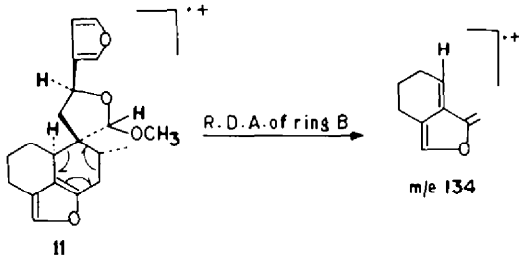
Scheme 4.

Table 3. ^{1}H NMR data of the keto-ester, **10** (δ-values in ppm, $CDCl_3$, TMS as internal standard, 270 MHz)

	δ (ppm)		J(Hz)
4α-H	m	2.20	4,5 = 5
5β-H	dd	2.66	5,10 = 13
8β-H	m	2.25	8,17 = 7
10α-H	m	2.20	
11 -H	dd	3.15	11,11' = 13
11'-H	dd	2.34	11,12 = 8.5
12 -H	dd	5.48	11',12 = 6
14 -H	s(br)	6.41	
15,16-H	d	7.47	
17 -H	d	1.12	
$COOCH_3$	s	3.70	



Scheme 5.



Scheme 6.

Beckman IR-20 Infrared Spectrophotometer (IR), Carl-Zeiss Universal Spectrophotometer (Model VSU-1) (UV), Bruker WH 270 (NMR), Varian MAT 711 (MS) and Cary-61 instrument (CD). Specific rotation was measured by a Hilger-Watts polarimeter. IR spectra were recorded in KBr-disc or in $CHCl_3$-solution. UV spectra were measured in aldehyde-free ethanol (95%). NMR spectra were recorded in $CDCl_3$ solution unless otherwise stated using TMS as an internal standard. Petrol refers to that fraction having b.p. 60–80°. Plates coated with silica gel G according to Stahl (Merck) were used for TLC.

Isolation of taraxerone **2**, *taraxerol* **3**, *taraxeryl acetate* **4** *and sitosterol.* Dried and powdered stem-bark (2 kg) of *Croton caudatus* Geisel was soxhletted with petrol for 70 h. The petrol extract was concentrated and allowed to stand for 7 days when a solid separated out. This solid was warmed with $CHCl_3$ and filtered to remove the $CHCl_3$-insoluble portion. The $CHCl_3$-soluble portion was concentrated and chromatographed over a silica gel column. Elution with petrol–benzene (1:1) gave a crude, white solid. It was washed with ether and crystallised from $CHCl_3$–MeOH (1:3) to afford taraxerone (1 g), m.p. 239°. The later fractions of petrol–benzene (1:1) eluate was concentrated and the solid thus obtained was crystallised from petrol–benzene (1:1) mixture when pure taraxerol (2 g), m.p. 278° was obtained. Sitosterol, m.p. 135°, resided in the benzene eluate. Later fractions of benzene eluate on concentration furnished crude taraxeryl acetate (200 mg) which was purified (m.p. 296°) by crystallisation from $CHCl_3$–MeOH (1:3). All these compounds were identified by direct comparison (m.m.p., co-TLC and superimposable IR spectra) with respective authentic samples. Similar treatment of the mother-liquor of the petrol extract yielded further crops of these compounds.

Isolation of crotocaudin **7**. After isolation of the triterpenes and sitosterol the column was washed with solvents of increasing polarity. Elution with 10% methanolic $CHCl_3$ gave a gummy substance which was further chromatographed on a silica gel column. The C_6H_6–$CHCl_3$ (1:1) eluate on concentration, gave crude crystals of crotocaudin which were recrystallised from petrol–$CHCl_3$ (2:1) mixture to yield pure crotocaudin (85 mg), m.p. 199–200° (dec.), $[\alpha]_D^{28}$ – 65° (c = 0.084, $CHCl_3$) UV: λ_{max}^{EtOH} 215 nm (ϵ 11,370) and 230 nm (ϵ 14,810); IR: $\nu_{max}^{CHCl_3}$ cm^{-1} 1795, 1775, 1680, 1500, 1162, 1137, 1085, 1040, 1010, 975, 955 and 870; MS: *m/e* (intensity) 326 (M^+, 45%), 284 (20%), 282 (32.5%), 256 (50%), 95 (100%) and 78 (25%). CD (c = 0.73 mg/3 ml in methanol, path length = 0.05 cm): $[\theta]_{275}$ 0, $[\theta]_{252}$ – 10,065, $[\theta]_{230}$ – 37,521, $[\theta]_{221}$ – 69,003, $[\theta]_{210}$ – 39,534, $[\theta]_{200}$ 0. (Found: C, 69.97; H, 5.50; M^+, *m/e* 326.116. $C_{19}H_{18}O_3$ requires: C, 69.93; H, 5.52%; M, 326.115). From the mother liquor of the petrol extract another crop (30 mg) of crotocaudin was obtained in a similar way.

Isolation of teucvidin **1**. After isolation of crotocaudin the column was further eluted with solvents of increasing polarity. The $CHCl_3$-eluate, on concentration, gave a crude residue which was washed with ether and then crystallised for several times from petrol–$CHCl_3$ (2:1) mixture to afford pure teucvidin (400 mg), m.p. 214°, $[\alpha]_D^{28}$ – 59° (c = 0.095, $CHCl_3$); UV: λ_{max}^{EtOH} 215 nm (ϵ 19,450); IR: ν_{max}^{KBr} cm^{-1} 1740, 1690, 1490, 1150, 1075, 1025, 960 and 870; MS: *m/e* (intensity) 328 (M^+, 7.61%), 234 (8.44%), 205 (4.58%), 189 (3.31%), 161 (3.49%), 136 (2.89%), 109 (3.03%), 105 (3.09%), 95 (12.95%), 94 (100%), 91 (4.62%), 81 (3.71%), 79 (5.81%), 77 (4.39%) and 65 (2.38%). (Found: C, 69.55; H, 6.21; M^+, *m/e* 328.1311. $C_{19}H_{20}O_5$ requires: C, 69.51; H, 6.10%; M, 328.1310). From the mother-liquor of the petrol extract another crop (70 mg) of teucvidin was obtained in a similar way.

Ehrlich reaction. TLC of crotocaudin (silica gel, C_6H_6–EtOAc = 4:1) showed a rose-red spot (R_f 0.5), when a solution of p-dimethylaminobenzaldehyde (1 g) in ethanol (20 ml) was sprayed on the plate followed by exposure of the plate in conc. hydrochloric acid vapour. TLC of teucvidin (silica gel, EtOAc) showed an orange-red spot (R_f 0.7) on similar treatment.

Baljet reaction. To crotocaudin (1 mg) was added a mixture (1 ml) of equal volumes of 1% picric acid solution in EtOH and 10% aq NaOH. The mixture slowly became orange-red. Similar colouration was also obtained with teucvidin.

Kedde reaction. When a solution of 3,5-dinitrobenzoic acid (100 mg) in 0.5 (N) KOH in 50% MeOH (10 ml) was added dropwise to crotocaudin or teucvidin, it slowly became red-violet.

Preparation of isocrotocaudin **8** *from crotocaudin* **7**. Crotocaudin (20 mg) was dissolved in dry MeOH (5 ml) and the solution was cooled in ice. Excess of $NaBH_4$ was added. After 15 min the solution was acidified by dropwise addition of dilute H_2SO_4. The reaction mixture was extracted with ether, washed with water and dried (Na_2SO_4). The major product was isolated by means of preparative TLC (C_6H_6–EtOAc = 4:1) when an amorphous solid (14 mg) was obtained. The product was proved to be isocrotocaudin **8** on the basis of the following data. IR: $\nu_{max}^{CHCl_3}$ cm^{-1} 1795, 1755, 1685, 1500, 1162, 1085, 1010, 975, 955 and 870; MS: *m/e* (intensity) 326 (M^+, 23.3%), 284 (11.7%), 282 (20%), 256 (30%), 189 (51.7%), 176 (56.7%), 95 (100%), 91 (20%), 79 (18.3%) and 77 (18.3%). (Found: M^+, *m/e* 326.116. $C_{19}H_{18}O_5$ requires: M, 326.115).

Preparation of teucvin **6** *from teucvidin* **1**. The method was exactly the same as that reported for the preparation of isocrotocaudin. From 20 mg of teucvidin 10 mg of teucvin was obtained. It was purified by crystallisation from MeOH, m.p. 202°, $[\alpha]_D^{25}$ + 179° (c = 0.15, $CHCl_3$); IR: $\nu_{max}^{CHCl_3}$ cm^{-1} 1745, 1690, 1490 and 875. NMR: δ ($CDCl_3$) 7.45 (2H, m), 6.38 (1H, m), 5.40 (1H, t, J 8.5 Hz, 12-H), 4.74 br (1H, t, J 8.5 Hz, 6-H), 2.66 br (1H, m, 10-H), 2.55 (2H, d, J 8.5 Hz, 11-H_2) and 1.06 (3H, d, J 7 Hz, 17-Me). (Found: M^+, *m/e* 328.131. $C_{19}H_{20}O_5$ requires: M, 328.131).

Preparation of the keto-ester **10** *from teucvidin* **1**. Teucvidin (20 mg) was dissolved in MeOH (3 ml) and Na_2CO_3 (20 mg) was added to it. The mixture was refluxed for 12 h. After filtration, the filtrate was neutralised with 1% HCl and extracted with $CHCl_3$. Usual treatment of the extract gave a crude material which was chromatographed on a silica gel column. The $CHCl_3$–MeOH (18:2) eluate gave an amorphous product (8 mg). IR: $\nu_{max}^{CHCl_3}$ cm^{-1} 1755, 1725, 1710 and 875. (Found: M^+, *m/e* 360.155. $C_{20}H_{24}O_6$ requires: M, 360.157).

Preparation of **11** *from teucvidin* **1**. A solution of $(i\text{-Bu})_2AlH$ (35 mg) in dry THF (20 ml) was added dropwise to a solution of teucvidin (40 mg) in dry THF (20 ml) with stirring at −25° in an atmosphere of nitrogen. The stirring was continued at the same temperature for 0.5 h. The reaction mixture was acidified with dry *p*-TsOH and excess of MeOH was added. The mixture was then extracted with ether. The extract was washed with aq $NaHCO_3$, water, dried over anhydrous Na_2SO_4 and concentrated. **11** (20 mg) was separated by means of preparative TLC (EtOAc). IR: $\nu_{max}^{CHCl_3}$ cm^{-1} 870. MS: *m/e* (intensity) 328 (M^+, 33.3%), 296 (18%), 202 (33.3%), 187 (18%), 185 (29%), 174 (58%), 159 (40%), 149 (20%), 134 (100%), 133 (18%), 105 (15.5%), 95 (18%), 91 (20%) and 81 (18%). NMR: δ($CDCl_3$) 7.35 (1H, d, J 1.5 Hz, 15-H), 7.31 (1H, s, 16-H), 7.10 (1H, s, 18-H), 6.40 (1H, d, J 1.5 Hz, 14-H), 5.30 (1H, t, J 7 Hz, 12-H), 4.73 (1H, s, 20-H), 3.48 (3H, s, $-OCH_3$) and 1.03 (3H, d, J 7 Hz, 17-Me).

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