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ROSEATOXIDE AND DIHYPOESTOXIDE: ADDITIONAL NEW DITERPENOIDS FROM *HYPOESTES ROSEA*

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ABSTRACT.—Two new terpenoids, roseatoxide (**1**) and dihypoestoxide (**2**), have been isolated from *Hypoestes rosea*. Their structures were deduced from their spectroscopic data. These bring to five the number of diterpenoids isolated so far from extracts of *H. rosea*.

In continuation with our investigation of new compounds from *Hypoestes rosea* (1-3), we wish to report the structures of two new terpenoids, roseatoxide (**1**) and dihypoestoxide (**2**), isolated from the hexane extract of *H. rosea*.

Roseatoxide (**1**) was obtained as small colorless needles, mp 187-188°. Its high resolution mass spectrum indicated the molecular composition $C_{20}H_{30}O_3$, thus indicating roseatoxide to be a structural isomer of roseanolone (**3**) (1) and roseadione (**4**) (2). Roseatoxide had no appreciable uv absorption, indicating the absence of any conjugated chromophore. The ir spectrum showed hydroxyl group (3451 cm^{-1}) and a five-membered ring ketone (1735 cm^{-1}). The pmr indicated the presence of the two methyls of an isopropyl group, respectively at 0.98 (3H, d, J=6 Hz) and 1.21 (3H, d, J=6 Hz). There were signals for three other methyls consisting of a quaternary methyl at 1.16 (3H, s), a methyl attached to a fully substituted carbon bearing oxygen at 1.37 (3H, s), and a methyl attached to an olefinic carbon at 1.66 (3H, s). The absence of any vinyl proton in the pmr spectrum of roseatoxide showed that the double bond in the compound was tetrasubstituted. The molecular formula of roseatoxide and the preceding spectral data indicated that the compound was tetracyclic. The cmr of roseatoxide (Table 1) provided additional information on the structure of roseatoxide and showed that it had the same carbocyclic skeleton as its isomeric congeners roseanolone (**3**) and roseadione (**4**). The cmr spectrum of roseatoxide confirmed the presence of a five-membered ring ketone function (s at 218.3), a tetrasubstituted double bond (s at 138.0 and 130.9), a tertiary hydroxyl bearing carbon (s at 83.6), and an epoxide (s at 65.3 and d at 62.6). There were also signals for one quaternary carbon, three tertiary carbons, five methylene carbons, and five methyl carbons. The structures of roseanolone (**3**) and roseadione (**4**), the two isomeric congeners of roseatoxide, had been conclusively determined by X-ray crystallography (1, 2). Comparison of the cmr data of roseatoxide (**1**), roseanolone (**3**), and roseadione (**4**) (Table 1) indicated that the structural difference between roseatoxide and roseadione was the replacement of the C-9 ketone function in roseadione with a C-8 and C-9 epoxide in roseatoxide. On the basis of these facts, structure **1** was assigned to roseatoxide.

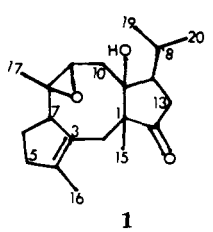
Dihypoestoxide (**2**) was obtained as colorless small needles, mp 221-223°. The high resolution mass spectrum of dihypoestoxide indicated the molecular formula $C_{44}H_{64}O_{10}$. The mass spectrum of dihypoestoxide was very similar to the mass spectrum of hypoestoxide (**5**) (3) except for the occurrence of a small molecular ion at m/z 752 in the mass spectrum of dihypoestoxide. This suggested that dihypoestoxide was a dimer of hypoestoxide. The pmr of dihypoestoxide showed signals for four tertiary methyl groups (0.86, 1.07, 1.16, and 1.20, each 3H, s), four methyl groups each attached to a fully substituted carbon bearing an oxygen function (1.27, 1.28, 1.39, and 1.44, each 3H, s), two acetoxy groups (2.00 and 2.09, each 3H, s), and two methine protons of two secondary acetoxy groups (5.36, 1H, dd, J=8 and 1 Hz; and 5.55, 1H, dd, J=8 and 1 Hz).

TABLE 1. Cmr Data for Roseatoxide (**1**), Roseanolone (**3**), and Roseadione (**4**)

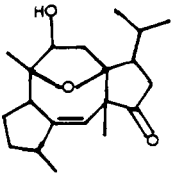
Carbon atom	1	3	4
1	54.1(s)	57.6(s)	55.3(s)
2	[a]	121.4(d)	[c]
3	138.0(s)	146.3(s)	139.1(s)
4	130.9(s)	38.4(d)	130.3(s)
5	[a]	[b]	[c]
6	[a]	[b]	[c]
7	49.7(d)	46.1(d)	49.2(d)
8	65.3(s)	91.9(s)	51.0(d)
9	62.6(d)	80.9(d)	215.9(s)[f]
10	[a]	[b]	[c]
11	83.6(s)	82.4(s)	82.1(s)
12	53.1(d)	51.8(d)	54.6(d)
13	[a]	[b]	[c]
14	218.3(s)	220.1(s)	216.3(s)[f]
15	19.8(q)	23.0(q)	17.6(q)
16	14.2(q)	19.3(q)	14.1(q)
17	21.9(q)	20.6(q)	8.6(q)
18	28.0(d)	29.1(d)	29.1(d)
19	25.8(q)[d]	24.4(q)[e]	25.0(q)[g]
20	25.5(q)[d]	24.3(q)[e]	22.5(q)[g]

[a]Unassigned CH_2 absorptions at 37.2, 37.0, 36.8, 30.6, and 27.2 ppm.
[b]Unassigned CH_2 absorptions at 39.0, 37.0, 31.4, and 26.5 ppm.
[c]Unassigned CH_2 absorption at 43.5, 38.0, 37.0, 26.3, and 25.5 ppm.
[d,e,f,g]These assignments may be reversed.

The preceding pmr data of dihypoestoxide showed that the main signals in the pmr of hypoestoxide (3), except those due to the exocyclic methylene group, were doubled in the pmr of dihypoestoxide. This indicated that the compound was a dimer of hypoestoxide and that the structural coupling of the monomeric hypoestoxide molecules occurred using the exocyclic methylene groups. The ir spectrum of dihypoestoxide contained signals for acetoxy groups (1730 and 1239 cm^{-1}). Dihypoestoxide had no appreciable uv absorption, indicating that the enone system in hypoestoxide had been lost in dihypoesoxide.



1



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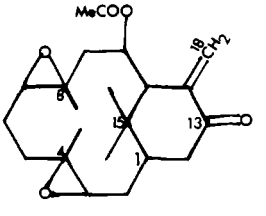

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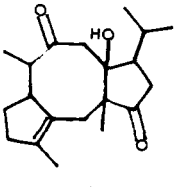

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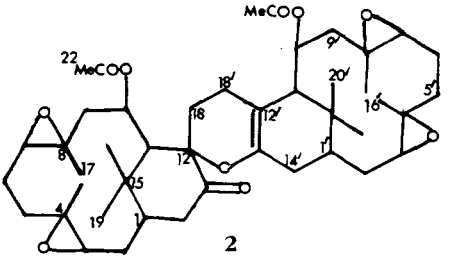


2

Additional information on the structure of dihypoestoxide was obtained from its cmr spectrum, which contained 44 distinct signals (Table 2). The signals in the cmr

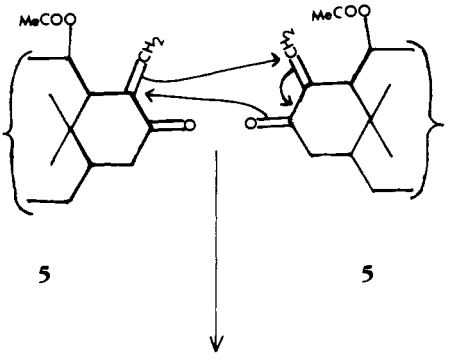
TABLE 2. Cmr Data for Dihypoestoxide (**2**) and Hypoestoxide (**5**)

Carbon atom	2	Carbon atom	5
1,1′	42.8(d). 42.9(d)	1	44.9(d)
2,2′, 5,5′, 6,6′, 9,9′, 14,14′, 18,18′	[a]	2,5,6,9,14	[b]
3,3′, 7,7′	61.1(d), 61.3(d). 63.7(d), 65.5(d)	3,7	61.8(d), 63.4(d)
4,4′, 8,8′	59.4(s), 60.1(s). 61.5(s), 62.5(s)	4,8	59.5(s), 61.9(s)
10,10′	69.3(d), 70.9(d)	10	69.0(d)
11,11′	46.3(d), 48.9(d)	11	46.5(d)
12	85.2(s)	12	143.2(s)
12′	102.2(s)	13	202.4(s)
13	207.5(s)	15	37.1(s)
13′	147.2(s)	16,17	21.3(q), 24.6(q)
15,15′	36.3(s), 36.8(s)	18	123.2(t)
16,16′, 17,17′	21.4(q), 21.6(q) 24.1(q), 26.0(q)	19,20	16.0(q), 16.7(q)
19,19′, 20,20′	15.9(q), 16.6(q), 16.9(q), 17.5(q)	21 22	169.8(s) 27.3(q)
21,21′	169.6(s), 169.9(s)		
22,22′	27.8(q), 30.2(q)		

[a]Unassigned methylene signals at 22.1, 23.7, 24.2, 26.7, 31.2, 32.4, 32.5, 35.8, 37.4, 40.6, 43.2, and 43.9 ppm.

[b]Unassigned methylene signals at 23.9, 31.4, 36.1, 42.2, and 42.8 ppm.

spectrum of hypoestoxide were doubled in the cmr spectrum of dihypoestoxide (Table 2), except those of the enone function. Instead of the signals for two enone functions, the cmr spectrum of dihypoestoxide showed signals for a ketone (s at 207.5), an enol system [>C=C′– O –, each s at 102.2 and 147.2, respectively (4)], a tertiary carbon bearing oxygen (s at 85.2) and two methylene groups. This difference is accommodated if the coupling of two molecules of hypoestoxide involved the 1,4-addition of the alkene function of one molecule to the enone function of a second molecule as shown in Scheme 1 below. This would give the assigned structure (**2**) to dihypoestoxide. Structure **2** for dihypoestoxide is in agreement with all the preceding spectral data for the compound.



SCHEME 1

We do not think that dihypoestoxide was an artifact produced during the extraction procedure because refluxing hypoestoxide in hexane (the solvent used for extraction) for 24 h did not give any dihypoestoxide. Dihypoestoxide also could not have been produced during the fractionation of the crude extract on the chromatography column (silica gel), because tlc carried out on the crude extract prior to fractionation on a column indicated the presence of dihypoestoxide (Rf 0.22-0.26 in C_6H_6-EtOAc, 3:1) in the crude extract.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected; uv, pmr (TMS as internal standard), and mass spectra were determined on Perkin-Elmer 137, Brüker 250, and V.G. Micromass 7070H spectrometers, respectively. Chemical shifts in Tables 1 and 2 are with respect to TMS=0 (s=singlet, d=doublet, t=triplet, q=quartet).

PLANT MATERIAL.—*Hypoestes rosea* R. Br (Acanthaceae) was collected at Aponmu Forest Reserve near Akure, Nigeria. The identity of the plant material was authenticated at the Forest Research Institute, Ibadan, Nigeria, where a voucher specimen was deposited.

EXTRACTION AND FRACTIONATION.—The extraction of the ground plant material (2.5 kg) with hot hexane and the chromatography of the resulting gum (53.6 g) on a column of silica gel were carried out as previously described (2). Elution of the column with 20% Et_2O in hexane gave roseadione (**4**), roseanolone (**3**), and roseatoxide (**1**), in that order.

Roseatoxide (850 mg) crystallized as small colorless needles from hexane-EtOAc; mp 187-188°; ir $\bar{\nu}$ max (KBr) 3451, 1735 cm^{-1}; pmr (δ $CDCl_3$) 0.98 (d, J=6 Hz, 3H), 1.16 (s, 3H), 1.21 (d, J=6 Hz, 3H), 1.37 (s, 3H), 1.66 (s, 3H); ms (CI) *m/z* 319.2254 (M^++1, $C_{20}H_{31}O_3$, 5), 318.2189 (M^+, $C_{20}H_{30}O_3$, 7), 301 (M^++1-H_2O, $C_{20}H_{29}O_2$, 40), 283 (M^++1-2H_2O, $C_{20}H_{27}O$, 14), 247 ($C_{16}H_{23}O_2$, 10), 235 ($C_{15}H_{23}O_2$, 72), 216 ($C_{15}H_{20}O$, 42), 207 ($C_{13}H_{19}O_2$, 16), 151 ($C_{10}H_{15}O$, 100), 149 (22), and 121 (38).

Elution of the column with 80-90% Et_2O in hexane gave dihypoestoxide (60 mg) mp 221-223°, (small needles from hexane-EtOAc); ir $\bar{\nu}$ max (KBr) 1730, 1239, 802 cm^{-1}; pmr (δ $CDCl_3$) 0.86 (s, 3H), 1.07 (s, 3H), 1.16 (s, 3H), 1.20 (s, 3H), 1.27 (s, 3H), 1.28 (s, 3H), 1.39 (s, 3H), 1.44 (s, 3H), 2.00 (s, 3H), 2.09 (s, 3H), 5.36 (dd, J=8 and 1 Hz, 1H), 5.55 (dd, J=8 and 1 Hz, 1H); ms (EI) *m/z* 752 (M^+, $C_{44}H_{64}O_{10}$, 2), 334 ($C_{20}H_{30}O_4$, 6), 316 ($C_{20}H_{28}O_3$, 8), 273 ($C_{18}H_{25}O_2$, 22), 205 ($C_{13}H_{17}O_2$, 32), 187 ($C_{13}H_{15}O$, 50), 163 ($C_{11}H_{15}O$, 72), 147 ($C_{10}H_{11}O$, 64), 137 ($C_9H_{13}O$, 83), 135 ($C_9H_{11}O$, 61), 109 (C_7H_9O, 93), 107 (C_8H_{11}, 61), and 93 (C_7H_9, 100).

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