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AUTO-OXIDATION PRODUCTS OF ZEYLANIDINE

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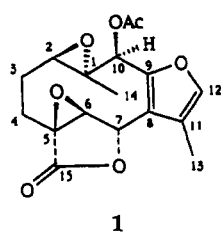
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ABSTRACT.—The air oxidation of zeylanidine [1] afforded two previously unknown sesquiterpene dilactones, zeylanidinone [3] and zeylanidinol [4], besides a known compound, neoliacine [2]. The structures of these oxidized products were assigned on the evidence of spectral methods.
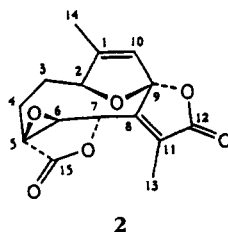
It is well known that furan rings are very susceptible to auto-oxidation on exposure to the air (1), and that solvents such as $CHCl_3$ remarkably accelerate their oxidation (2). In an investigation of the $CHCl_3$ extract of the roots of *Neolitsea parvigemma* Kan. & Sas. (Lauraceae) a moderate amount of zeylanidine [1], a furanogermacranolide, was isolated along with four other related compounds (3). In order to examine the auto-oxidation products of zeylanidine and their possible biological activities, it was dissolved in $CHCl_3$ and exposed to air at room temperature for 14 days, at which time no more starting material was left. The residue was separated by cc on Si gel to afford a known dilactone, neoliacine [2], and two new dilactones which were given the names zeylanidinone [3] and zeylanidinol [4].

The structure of 2 was ascertained by a comparison of its spectral properties with those reported for neoliacine (4) and comparison of the mp and tlc behavior and ^1H-nmr spectrum with those of an authentic sample (Table 1).
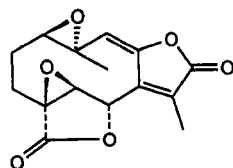
The dilactone 3 had the composition $C_{15}H_{14}O_6$ from its high resolution mass spectrum (290.0324). The ir spectrum showed absorption bands at 1780 and 1760 cm^{-1} together with a uv absorption maximum at 275 nm indicating the presence of a γ-lactone and another α,β-unsaturated γ-lactone conjugated with an additional double bond (5). The existence of two lactone functionalities was supported by signals at δ 167.2 and 169.4 in the ^{13}C-nmr spectrum (Table 2). The additional lactone function must have resulted from oxidation of the furan moiety. The signal at δ 7.25 for H-12 in 1
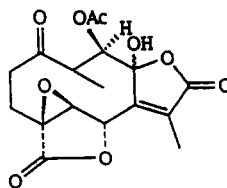

1

2

3

4

TABLE 1. ^{1}H-nmr Data for Compounds **1-4**.

Proton	Compound			
	1	**2**	**3**	**4**
H-1				3.29 (1H, qd, J=7.2, 3.0)
H-2	3.66 (1H, dd, J=9.0, 0.9)	5.16 (1H, brs)	3.13 (1H, dd, J=9.0, 5.2)	
H-3	1.50–1.65 (1H, m) 2.22 (1H, ddd, J=14.0, 9.5, 1.1)	2.20 (1H, m) 2.06 (1H, m)	1.61–1.76 and 2.57–2.78 (4H, m)	
H-4	1.83 (1H, ddd, J=15.0, 8.5, 1.1) 3.02 (1H, ddd, J=15.0, 9.5, 9.0)	1.83 (1H, m) 2.55 (1H, ddd, J=15.8, 11.5, 6.5)		1.96 (1H, ddd, J=16.0, 8.1, 1.5) 2.42 (1H, dd, J=16.0, 11.5)
H-6	3.96 (1H, s)	4.31 (1H, s)	4.15 (1H, s)	3.87 (1H, s)
H-7	5.36 (1H, s)	5.41 (1H, s)	5.56 (1H, s)	5.53 (1H, s)
H-10	5.99 (1H, s)	5.32 (1H, s)	6.13 (1H, s)	3.77 (1H, brs)
H-12	7.25 (1H, brs)			
H-13	2.06 (3H, brs)	2.00 (3H, s)	2.15 (3H, s)	2.10 (3H, s)
H-14	1.14 (3H, s)	1.89 (3H, d, J=1.0)	1.52 (3H, s)	1.45 (3H, d, J=7.2)
Ac	2.03 (3H, s)			2.22 (3H, s)

was absent and replaced by a new singlet at δ 6.13 for H-10 in compound **3** strongly supporting oxidation of the furan moiety and concurrent elimination of the acetoxyl group at C-10 to form a double bond between C-9 and C-10 and the extra lactone group. A comparison of the chemical shifts of **3** with those of the starting material **1** showed that the signal for H-2 (δ 3.13) was shifted more upfield relative to that (δ 3.66) of the corresponding proton in **1**. The proton signal of 1-Me was shifted downfield as compared with that of **1**, due to its being adjacent to a double bond. The remaining signals in the ^{1}H-nmr spectrum, δ 4.15 for H-6, δ 5.56 for H-7, and δ 2.15 for 11-Me, were close to those of **1**. The preceding spec-

TABLE 2. ^{13}C-nmr Data for Compounds **1-4**.

Carbon	Compound			
	1	**2**	**3**	**4**
C-1	60.9 s	147.3 s	61.0 s	44.2 d
C-2	56.7 d	88.1 d	61.7 d	206.0 s
C-3	20.0 t	27.1 t	20.2 t	31.6 t
C-4	21.3 t	18.4 t	22.5 t	19.6 t
C-5	61.5 s	55.5 s	55.7 s	59.7 s
C-6	60.4 d	60.3 d	62.1 d	61.2 d
C-7	72.6 d	71.1 d	71.6 d	72.6 d
C-8	116.6 s	147.9 s	140.3 s	145.3 s
C-9	150.6 s	115.1 s	146.0 s	101.8 s
C-10	68.8 d	122.8 d	115.2 d	72.8 d
C-11	121.6 s	132.9 s	137.9 s	134.9 s
C-12	139.0 d	169.4 s	167.2 s	167.8 s
C-13	8.3 q	8.8 q	9.9 q	9.4 q
C-14	16.4 q	12.2 q	19.0 q	14.0 q
C-15	172.0 s	172.2 s	169.4 s	171.4 s
Ac	169.3 s			168.2 s
Ac	20.5 q			21.4 q

trometric evidence and comparison with **1** were sufficient to establish the identity of **3**.

Dilactone **4** was a viscous substance with molecular formula $C_{17}H_{18}O_9$ based on its high resolution mass (366.0421). The ir spectrum showed the presence of a lactone (1780 cm^{-1}), an unsaturated lactone (1750 cm^{-1}), and acetate (1740 cm^{-1}) and hydroxyl (3650 cm^{-1}) groups. The ^{1}H-nmr spectrum showed two three-proton singlets (3H for each) at δ 2.22 for an acetoxyl methyl and at δ 2.10 for a vinylic methyl. A doublet of quartets at δ 3.29 (H-1) was coupled to a doublet at δ 1.45 (1-Me) and to a broad singlet at δ 3.77 (H-10). A singlet at δ 206.0 in the ^{13}C-nmr spectrum and a doublet of quartets at δ 3.29 for H-1 indicated that the epoxy group between C-1 and C-2 in zeylanidine had opened up. The hydroxyl group was further substantiated by the presence of a broad singlet at δ 3.20 in the ^{1}H nmr which was eliminated on D$_2$O exchange, and a singlet at δ 101.8 was ascribed to the dioxygenated C-9 (6). Based on the above information and comparison of the ^{1}H- and ^{13}C-nmr data with those of **1**, this new compound was assigned structure **4** and named zeylanidinol.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were taken on a Yanaco micro-melting point apparatus and are uncorrected. Uv spectra were recorded on a Shimadzu-240 spectrometer. Ir spectra were taken at KBr pellets on a Shimadzu IR-470 spectrometer. Specific rotation measurements were performed in Me$_2$CO using a Jasco DIP-370 automatic digital polarimeter. Low resolution and high resolution mass spectra (ms) were obtained on a VG-70-250S GC/MS mass spectrometer. Both ^{1}H- and ^{13}C-nmr spectra and HETCOR experiments were done on CDCl$_3$ solutions with a Varian VXR-300 (300 MHz), using TMS as an internal standard. Tlc's were run on precoated Si gel plates (Merck) and compounds were detected by spraying with p-anisaldehyde reagent. For cc, Merck Si gel 60 was used. All solvents used for chromatography were hplc grade (Fisher).

OXIDATION OF ZEYLANIDINE.—The oxidation followed the procedures described by Ulubelen *et al*. (6). A CHCl$_3$ solution of zeylanidine (9.0 g) was left at room temperature for 14 days, by which

time all the zeylanidine had disappeared. Removal of CHCl$_3$ in vacuo left a light brown viscous residue (9.2 g) that was crudely fractionated into five fractions, I–V, by cc on Si gel (300 g). The elution was initiated with 40% EtOAc in n-hexane and ended with EtOAc.

Neoliacine [**2**].—Fraction II gave, on removal of the solvent, a solid (2.1 g) which was repeatedly chromatographed on the same adsorbent, using 30% EtOAc in n-hexane as the eluent, to obtain neoliacine [**2**] (0.2 g): prisms recrystallized from CHCl$_3$/MeOH; mp 272–274°; [α]D +8.2 (c=1.8, Me$_2$CO); ir (KBr) ν max 3090, 1765, 1655, 1440, 1365, 1260, 1240, 1190, 1100 cm^{-1}; ms m/z (relative abundance) [M]$^+$ 290 (19.6), 246 (41.2), 218 (52.6), 190 (47.3), 146 (39.0), 133 (base peak), 120 (68.5), 97 (32.5), 91 (80.4), 77 (28.9).

Zeylanidinone [**3**].—Fraction III (0.92 g) was subjected to chromatography over Si gel (50 g) and eluted with 30% EtOAc in n-hexane to afford zeylanidinone [**3**] as plates from warm Me$_2$CO; mp 210–211°; [α]D −8.9 (c=1.3, Me$_2$CO); ir (KBr) ν max 3090, 1780, 1760, 1650, 1440, 1380, 1335, 1180, 1090 cm^{-1}; ms m/z (relative abundance) [M]$^+$ 290 (2.9), 248 (35.6), 178 (32.5), 177 (base peak), 163 (60.9), 161 (92.0), 135 (66.2), 133 (94.8), 93 (57.9), 91 (58.0).

Zeylanidinol [**4**].—Fraction VI was evaporated in vacuo leaving a brown residue (1.03 g), which was purified by repeated cc on Si gel (35 g) using 40% EtOAc in n-hexane to obtain a viscous substance **4** [α]D −18.2 (c=1.5, Me$_2$CO); ir (CHCl$_3$) ν max 3650, 1780, 1750, 1740 cm^{-1}; ms m/z (rel. abundance) [M]$^+$ 366 (6.2), 348 (24.3), 305 (72.3), 289 (63.0), 279 (17.4), 223 (9.6), 205 (11.2), 165 (41.6), 137 (base peak), 125 (57.3), 97 (36.6).

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