Further sesterterpenes from the sponge *Spongia nitens*: 12-epi-scalaradial and 12,18-diepi-scalaradial[1]

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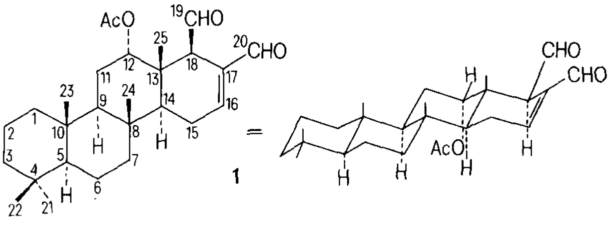
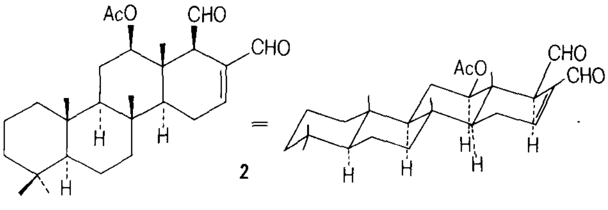
Summary. 2 new tetracarbocyclic sesterterpenes, isomers of the previously[2] described scalaradial (**1**), have been isolated from the marine sponge *Spongia nitens* and their structures have been established to be **2** and **3**; during the structural work, evidence on the stereochemistry of **1**, **2** and **3** has been obtained.

In a recent[3] communication we reported the isolation and the structures of 2 tetracarbocyclic sesterterpenes (**4**, **5**) from *S. nitens*. A further study on the terpene constituents of this sponge has now allowed the isolation and the structure characterization of 2 new dialdehydes, 12-epi-scalaradial (**2**) and 12,18-diepi-scalaradial (**3**), isomers of scalaradial (**1**), whose isolation from *Cacospongia mollior* and gross structure were previously[2] reported. In this paper we wish also to report the evidence obtained on the stereochemistry of **1**, **2** and **3**.



1



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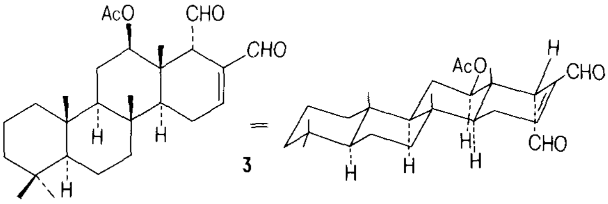

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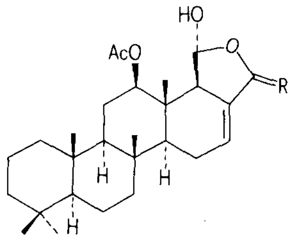

4, R=O
5, R=H_2

Fresh tissues of the sponge were extracted with acetone. The solvent was removed and the aqueous residue was extracted with diethyl ether. Column and preparative TLC on silica gel of the ether-soluble portion yielded, in addition to the previously described terpenes[3,4], crystalline 12-epi-scalaradial (**2**, 0.006% of dry material, m.p. 188-190 °C, $[\alpha]_D$ ($CHCl_3$), 36.5°, TLC R_f 0.3 in light petroleum: ether (1:1) and 12,18-diepi-scalaradial (**3**, 0.009% of dry animal, m.p. 210-213 °C, $[\alpha]_D$ ($CHCl_3$), −149°, TLC R_f 0.4 in the above solvent).

The structure of 12-epi-scalaradial (**2**) is based on the following evidence: $C_{27}H_{40}O_4$ (high resolution mass spectrometry), UV (MeOH) 229 (ε 11,700) nm; IR ($CHCl_3$) 1680 and 1640 (enal), 2845 and 1725 (aldehyde) and 1735 (sh., acetate) cm^{-1}; pmr (C_6D_6) 9.85 (H-19 1 H, d, J=4 Hz), 9.20 (H-20, 1 H, s), 6.36 (H-16, 1 H, m), 4.80 (H-12, 1 H, dd, J=4, 10 Hz), 3 (H-18, 1 H, m) and 1.88 (CH_3CO, 3 H, s) δ; MS: 428 (M^+, 2%), 368 (30%), 340 (84%), 258 (20%), 205 (32%), 191 (100%), 137 (52%), 123 (58%).

The above spectral data are almost identical with those of scalaradial (**1**), with the exception of the shape in the pmr spectra of the H-12 signal. In the spectrum of **2** it appears as a dd (J=10 and 14 Hz) indicative of an axial proton[5], whereas in that of **1** it is a broad signal, W $\frac{1}{2}$ ca. 4.5 Hz, typical of an equatorial proton[5].

Full support for structure **2**, including the absolute stereochemistry, was obtained by chemical correlation of **2** with 12-epi-deoxoscalarin **5**, whose absolute configuration was previously[3] ascertained. Reduction of **2** with sodium borohydride gave a mixture from which a product identical with **5** (m.p., mixed m.p., $[\alpha]_D^6$, TLC, spectral data) was recovered.

The close relationship between 12-epi-scalaradial (**2**) and scalaradial (**1**) was further evidenced by CMR spectrometry (table). Also, comparison of CMR spectra supported strongly the assigning of an all trans-anti-trans

CMR chemical shifts (in ppm from internal TMS) of sesterterpenes **1**, **2** and **3**

C	**1**	**2**	**3**
C-1	39.6	39.7	39.7
C-2	17.9[a]	18.1[a]	18.1[a]
C-3	41.4[b]	41.5[b]	41.2[b]
C-4	33.2	33.2	33.3
C-5	56.3	56.5	56.3
C-6	18.3[a]	18.4[a]	18.5[a]
C-7	41.9[b]	42.0[b]	42.0[b]
C-8	36.7[c]	37.5[c]	37.5
C-9	51.6	57.8	57.7
C-10	37.8[c]	37.6[c]	37.5
C-11	21.8	23.7	23.4
C-12	74.7	82.1	77.5
C-13	40.2	42.0	41.5
C-14	49.4	53.5	48.1
C-15	24.2	23.7	24.3
C-16	153.0	152.4	152.4
C-17	138.0	139.1	137.0
C-18	52.0[e]	60.2[e]	54.8[e]
C-19	201.0	200.0	199.4
C-20	192.9	192.1	192.2
C-21	33.2	33.2	33.3
C-22	21.3	21.3	21.2[d]
C-23	16.2[d]	16.5[d]	16.6[c]
C-24	16.6[d]	17.1[d]	16.8[c]
C-25	15.3	11.0	16.9[c]
CH_3*CO*	169.6	170.1	170.2
*CH_3*CO	21.8	21.3	21.3[d]

Spectra were determined in $CDCl_3$ on a Varian FT spectrometer operating at 25.20 MHz. [a-d] Signals may be reversed. [e] Assignments confirmed by selective ^{13}C-{^1H} decoupling experiments.

configuration for **1**. In fact the spectra were differentiated only by the expected[3] changes in the shifts of the carbons influenced by the different orientation of the acetoxy group in 12.

The structure of 12,18-diepi-scalaradial (**3**) is based on the following evidence: $C_{27}H_{40}O_4$; UV (MeOH) 228 nm (ε 10,700), IR ($CHCl_3$) 2840, 1735, 1715, 1680 and 1640 cm^{-1}; PMR (C_6D_6) 9.96 (H-19, 1 H, d, J=2.5 Hz), 9.22 (H-20, 1 H, s), 6.34 (H-16, 1 H, m), 5.02 (H-12, 1 H, dd, J=4, 10 Hz), 3.66 (H-18, 1 H, d, J=2.5 Hz), 1.76 (CH_3–CO, 3 H, s) δ; MS 428 (M^+, 2%), 368 (40%), 340 (92%), 258 (32%), 205 (67%), 191 (100%), 137 (50%), 123 (58%). The above spectral data are quite similar to those of **2**, with the exception that, in the PMR of **3**, the signals assigned to H-18 and H-19 are located downfield and, also, they show a smaller coupling constant. On the basis of this evidence, we conclude that in **3** the simple aldehyde group in 18 is axially oriented as in structurally related compounds[7]. CMR spectra of **3** (table) confirmed the suggested structure (**3**) and allowed the determination of its stereochemistry.

The biological activities of those substances have not been investigated. However, it has been reported[8] that natural polycyclic dialdehydes are often substances showing strong antifeedant, antifungal, antiyeast and plant-growth regulatory activities.

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[5] E.R.H. Jones, 8th Int. Symp. Chem. nat. Prod. (New Delhi, 6-12 Feb. 1972), p. 42. Ed. T.R. Govindachari. Butterworths, London 1973.

[6] For a misprint the α of **5** was reported[3] positive. The correct value is $[\alpha]_D$ ($CHCl_3$), – 13.9°.

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Cannabiripsol: A novel *Cannabis* constituent[1]

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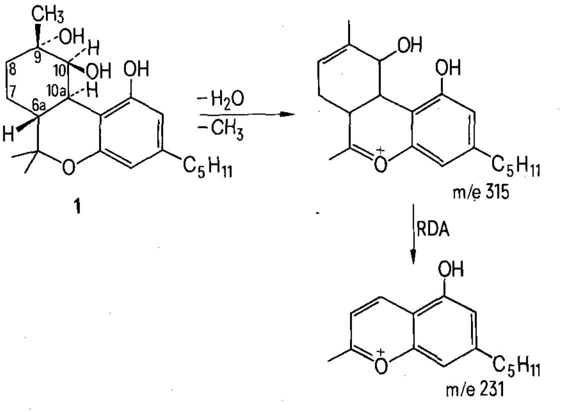
Summary. Cannabiripsol [(–)(6aR, 9S, 10S, 10aR)9, 10-dihydroxy-hexahydrocannabinol] (**1**), a new cannabinoid was isolated from a South African Cannabis variant. The structure was determined by spectral means and by synthesis.

In previous communications[3,4] we have reported the isolation and structure determination of (+)-Cannabitriol[3] and other polyhydroxylated cannabinoids[4] from *Cannabis*. In this communication we wish to report the isolation and characterization of a new polyhydroxylated cannabinoid.

Combined GC-MS analysis of the trimethyl silyl derivatives of a polar fraction obtained from the hexane extract of a South African *Cannabis* variant revealed the presence of a new phenolic constituent with relative retention time 0.24[5]. This compound (**1**) was isolated by repeated chromatography on silica gel and polyamide and was obtained as a light yellow oil, with R_f 0.38 [silica gel G, ethylacetate-chloroform (1:1)], $[\alpha]_D^{25}$ –122° and molecular formula $C_{21}H_{32}O_4$ (HRP-MS). IR ν_{max}^{KBr} 3350-3200 (br. OH), 2920 (CH), 1630 and 1585 ($C{=}C_{Ar}$) cm^{-1} and no carbonyl absorbance was observed; UV λ_{max}^{MeOH} 227 (log ε 3.39) and 286 (log ε 2.90) nm.

The ^{1}HNMR (60 MHz, $CDCl_3$) showed peaks characteristic for the olivetol moiety of a cannabinoid: the aromatic protons were observed at δ 6.26 (br. s, 1 H) and δ 6.09 (br s, 1 H), and the terminal methyl group of the pentyl side chain at δ 0.89. In addition, peaks were found at δ 1.09 (s, 3 H), δ 1.34 (s, 3 H), and δ 1.39 (s, 3 H) for methyls on oxygenated carbon atoms. A peak at δ 4.83 (br s, 1 H) was assigned to a proton under a hydroxy group. The TMS derivative of **1** had mol. wt 564 indicating 3 hydroxy groups, while acetylation (acetic anhydride/pyridine) gave a diacetate indicating that 1 of the hydroxy groups is tertiary. The tertiary hydroxy was assigned to C_9 because there are 3 methyls on oxygen carrying carbons. The broad singlet at δ 4.83 indicates the secondary hydroxy is at C_{10}. However, **1** could not be oxidized with KIO_4 suggesting that if **1** is indeed a glycol, then the hydroxyl groups must be trans-diaxial.

The mass spectrum of **1** was in agreement with these findings since a peak was observed at m/e 231 ($C_{15}H_{19}O_2$). This peak is very characteristic for certain cannabinoids and the formation and structure of this ion has been studied extensively[6-8]. Loss of a methyl radical and a molecule of H_2O will result in an ion which easily can undergo a retro-Diels-Alder reaction resulting in a stable chromene type ion (figure).



Formation of the stable chromene type ion at m/e 231 from cannabiripsol.