Palinurin, a new linear sesterterpene from a marine sponge[1]

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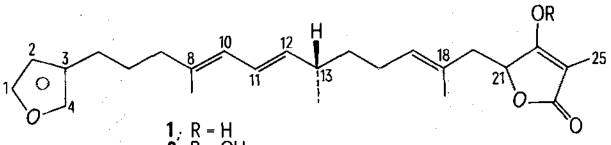
Summary. The structure of a new linear sesterterpene, palinurin (**1**), obtained from the marine sponge *Ircinia variabilis*, was determined by spectral and chemical means.

Linear sesterterpenes, characterized by a furan ring at one end and by a conjugated tetronic acid at the other, have frequently[2-6] been encountered in sponges of the genus *Ircinia*. In this communication we whish to report the isolation of a new sesterpene, palinurin (**1**), which coexists with fasciculatin (**5**), previously[3] described from *Ircinia fasciculata*, in the Mediterranean sponge *Ircinia variabilis*[7] collected near Palinuro.

Fresh tissues of the sponge were extracted with acetone and the residue was partitioned between diethyl ether and water. Silica gel chromatography (benzene and increasing amounts of diethyl ether) of the ether soluble portion (14 g, from 600 g of the dry weighted animal) gave, in order of polarity, fasciculatin (**5**, 1.7 g), identical with an authentic sample ($[\alpha]_D^0$, ^{1}H-NMR, TLC) and palinurin (**1**, 1.9 g).

Palinurin (**1**), oil $C_{25}H_{34}O_4$ (high resolution mass measurement), $[\alpha]_D^0 + 45.3$ (chloroform). The IR- and UV-spectra of **1** ($\nu_{max}^{CHCl_3}$ 3400–2600 br, 1725 and 1650 cm^{-1}, $\lambda_{max}^{CH_3OH}$ 241 nm, ε 23.400) and of the 2 methylethers **2** ($\nu_{max}^{CHCl_3}$ 1735 and 1660 cm^{-1}, $\lambda_{max}^{CH_3OH}$ 236 nm) and **4** ($\nu_{max}^{CHCl_3}$ 1590 cm^{-1}, $\lambda_{max}^{CH_3OH}$ 266 nm), formed by methylation with diazomethane of **1**, were consistent with the presence of a tetronic acid moiety[8,9]. The ^{1}H-NMR-spectrum of **1**[10] was almost identical to that of fasciculatin[3], with the exception that the 3-proton doublet and the olefinic proton conjugated with the tetronic acid residue, which appeared[3] in the spectrum of **5** at δ 1.05 (CH_3-18) and δ 5.42 (H-20), respectively, were replaced in **1** by a singlet (3 H, CH_3-18, δ 1.73), indicative of a vinyl methyl, and by a broad multiplet (1 H, H-21) at δ 4.8. This first evidence led to the suggestion of structure **1** for palinurin. The double bond at C-11 was defined by ^{1}H-NMR data ($J_{H_{11}-H_{12}} = 14$ Hz) as E oriented. The location of the olefinic bonds was confirmed by ozonolysis, followed by oxidative work-up and successive methylation with diazomethane, to obtain methyl 5-oxohexanoate and dimethyl 2-methylglutarate. This latter, recovered in form (+) S[11] by preparative GLC (3% SE 30, 130 °C), allowed us to assign the S configuration at C-13 of **1**. Finally, the alternative structure **7**, equally compatible with the above data, but unlikely for the co-occurrence of fasciculatin (**5**), seemed also less probable on the basis of the following evidence. The addition of Eu(fod-d_9)$_3$ to **1** (0.3 mEq. in $CDCl_3$) produced in the expanded ^{1}H-NMR-spectrum a shift (0.5 ppm) for the signal attributed to H-17 (δ 5.25); in contrast no shift was observed for the dienic proton H-10 at δ 5.7. The ^{13}C-NMR-spectra of **1**, **5** and their derivatives **3** and **6**, besides confirming the suggested structure, allowed the assigning of the stereochemistry at C-8 double bond of fasciculatin (**2**) and at C-8 and C-17 double bonds of palinurin (**1**). The ^{13}C chemical shifts of **1**, **3**, **5** and **6** are presented in the table. 3 types of spectra were run: proton resonance decoupled spectra, noise off-resonance decoupled spectra (nord)[12] and single frequency off-resonance decoupled spectra (sford). Further assistance in the assignments was obtained by a series of selective ^{13}C-{^{1}H} decoupling experiments for all protonated carbon atoms and by comparison with structurally related compounds: furans[13], enol acetates[14] and linear sesquiterpenes[15].



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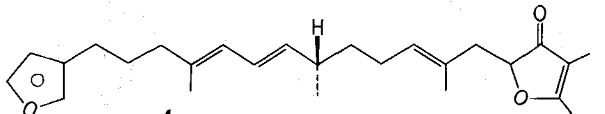
2, R = CH_3
3, R = $COCH_3$



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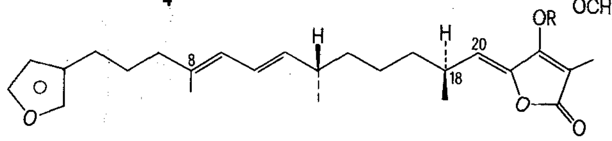
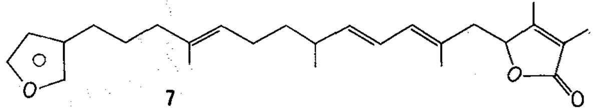


5, R = H
6, R = $COCH_3$



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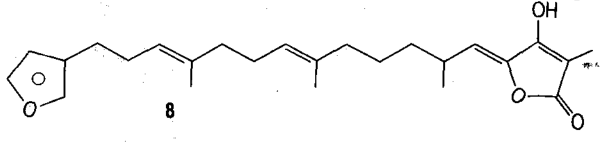

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C-13 Chemical shift assignments[a] for **1**, **3**, **5** and **6**

C	**1** ppm	**3** ppm	**5** ppm	**6** ppm
1	142.5	142.5	142.5	142.4
2	110.9	110.9	110.9	110.9
3	124.9	124.9	124.9	124.9
4	138.7	138.7	138.7	138.6
5	24.4	24.4	24.4	24.3
6	28.2	28.2	28.1	28.1
7	39.3	39.4	39.3	39.3
8	135.7	135.7	135.7	135.5
9	16.7[c]	16.6[c]	16.5	16.4
10	125.3	125.3	125.3	125.2
11	125.2	125.3	124.9	124.9
12	137.8	137.8	138.2	138.1
13	36.9	36.7	36.9	36.9
14	20.8	20.9	20.7[c]	20.7[c]
15	37.1	37.0	37.1	37.1
16	26.0	26.0	25.1	25.5
17	129.3	129.6	37.1	37.1
18	129.0	129.8	30.9	31.0
19	16.5[c]	16.5[c]	20.6[c]	20.5[c]
20	41.6	41.8	116.5	116.2
21	78.4	77.5	143.1	142.4
22	177.9[b]	165.9[b]	172.8[b]	168.2[b]
23	96.8	112.6	98.9	114.4
24	176.1[b]	165.5[b]	162.9[b]	154.3[b]
25	5.9	7.5	6.1	8.2
*C*H$_3$CO		20.4		20.2
CH$_3$*C*O		163.5[b]		165.1[b]

[a] ^{13}C-NMR-spectra were taken in $CDCl_3$ at 25.20 MHz using a XL-100 Varian F.T. Spectrometer. [b-c] Assignments may be interchanged.

In palinurin, the upfield chemical shifts of the 2 vinyl CH_3's at C-8 and C-18, caused by eclipsed butane non-bonded interactions[16], led us to assign E configurations for the double bonds at C-8 and C-17. Analogously the E configuration has been proposed for the double bond at C-8 of **5**. Finally, the alternative structure 7 was definitively eliminated, on the basis of known alkene chemical shift parameters[17], by the 2 low field signals in the spectrum of **1** at ppm 129.0 (C-18) and 129.3 (C-17, confirmed by selective decoupling at δ 5.25). The stereochemistry at C-21 has not been investigated.

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[1] This work was carried out at the Progetto Finalizzato 'Oceanografia e Fondi Marini', C.N.R., Roma. We thank Professor M. Sarà (University of Genova) for the identification of the sponge, Mr C. Di Pinto for ^{1}H- and ^{13}C-NMR, Mr G. Scognamiglio for technical assistance.

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[10] ^{1}H-NMR of palinurin (**1**), δ ($CDCl_3$) 7.32 (H-1, bs), 7.20 (H-4, bs), 6.25 (H-2, bs), 6.15 (H-11, dd, J = 11, 14 Hz), 5.77 (H-10, d, J = 11 Hz), 5.37 (H-12, dd, J = 8, 14 Hz), 5.25 (H-17, bt, J = 7 Hz), 4.8 (H-21, bm, W½ ca. 14 Hz), 1.73 (6 H, s), 1.66 (3 H, s), 0.99 (CH_3-13, d, J = 7 Hz).

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Baluchistine, a new bisbenzylisoquinoline alkaloid[1]

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Summary. The new phenolic bisbenzylisoquinoline alkaloid (+)-baluchistine, found in *Berberis baluchistanica* Ahrendt (Berberidaceae), has been assigned structure **1**. O-Methylation using ethereal diazomethane yields (+)-obaberine (**2**). Baluchistine is the 1 alkaloid of the oxyacanthine-berbamine group to incorporate a free phenolic function at C-6.

Chromatography of the basic extracts from 4.3 kg of dried *Berberis baluchistanica* Ahrendt (Berberidaceae) over basic alumina yielded as one of the late fractions 20 mg of the new phenolic bisbenzylisoquinoline alkaloid (+)-baluchistine (**1**), m.p. 222–224 °C (MeOH); $[\alpha]_D^{26} + 333°$ (c 0.075, MeOH); cd (c 0.095 mg/ml, MeOH) $[\theta]_{302} = 0$, $[\theta]_{294} = +3700$, $[\theta]_{287} = 0$, $[\theta]_{283} = -3700$, $[\theta]_{275} = 0$, $[\theta]_{267} = +6{,}200$, $[\theta]_{230} = +110{,}000$, and $[\theta]_{208} = 0$. The UV.-spectrum exhibited λ_{max}^{EtOH} 283 nm (log ε 3.67), with a bathochromic shift to 290 nm (log ε 3.80) upon addition of base.

Analysis by high resolution mass spectroscopy showed a molecular ion at m/e 594.2732 for $C_{36}H_{38}N_2O_6$; while low resolution measurements gave peaks at m/e 594 (M^+) (22), 487 (0.2), 382 (52), 381 (base), 367 (50), 207 (10), 192 (15), 191 (78), 174 (50), and 168 (48).

The PMR-spectrum of baluchistine at 60 MHz in $CDCl_3$ shows the presence of 2 N-methyl groups superimposed at δ 2.61, 2 O-methyl groups at δ 3.23 and 3.60, 2 hydroxyls as a broad singlet at δ 5.15, and 10 aromatic protons in a complex pattern from δ 5.43 to 7.40. An oxyacanthine type dimer was indicated because of the lack of separation between the N-methyl peaks. The peak at δ 3.23 can be assigned to the C-7 methoxyl; while the remaining methoxyl at δ 3.60 could at this stage be tentatively ascribed to C-6′, thus locating the phenolic functions at C-6 and C-12′.[3,4] By way of comparison, the critical pmr data relating to the N-methyl and methoxyl absorptions for the alkaloids obaberine, oxyacanthine, homoaromoline, aromoline and baluchistine, all of which belong to the oxyacanthine series, have been summarized in the table. In particular, it should be noted that a peak (3 H) near δ 3.20 is characteristic of a C-7 methoxyl group, while one around 3.60 is indicative of a C-6′ methoxyl. Furthermore, the position of the methoxyl peak at δ 3.60 suggested that the 2 asymmetric centers in baluchistine (**1**) possess opposite absolute configurations, since when the 2 benzylisoquinoline units have the identical chirality the C-6′ methoxyl peak is known to appear higher upfield near δ 3.35[3,4].

Returning to the low resolution mass spectrum, the following assignments can now be made for the ionic shards obtained: 487 $(M-107)^+$, 382 $(a)^+$, 381 $(382-H)^+$, 367 $(382-CH_3)^+$, 207 $(b)^+$, 192, 191 $(a)^{++}$, 174 $(a-b-H)^+$, and 168 $(a-CH_3O-CH_3)^{++}$[5].

Treatment of baluchistine (**1**) with ethereal diazomethane for 2 days at near 0 °C supplied its di-O-methyl ether derivative, identical with the known (+)-obaberine (**2**).

PMR spectral data for oxyacanthine type dimers

	N-CH_3	OCH_3 C-7	C-6	C-6′	C-12′
Obaberine (**2**)[3]	δ2.55, 2.65	3.20	3.79	3.60	3.90
Oxyacanthine[3] (12′-hydroxyl)	2.48	3.15	3.73	3.56	–
Homoaromoline[3] (7-hydroxyl)	2.45, 2.55	–	3.78	3.62	3.88
Aromoline[3] (7,12′-dihydroxyl)	2.49	–	3.77	3.56	–
Baluchistine	2.61	3.23	–	3.60	–