78. Cacospongione A, Cacospongienone A, and Cacospongienone B, New C_{21} Difuran Terpenoids from the Marine Sponge *Cacospongia scalaris* SCHMIDT of the Côte d'Azur

by **Graziano Guella**[a]), **Philippe Amade**[b]), and **Francesco Pietra**[a])*

[a]) Istituto di Chimica, Università di Trento, I–38050 Povo-Trento
[b]) *INSERM* Unité 303, Quai de la Darse, F–06230 Villefranche sur Mer

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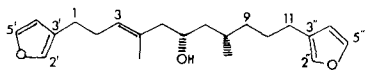
The sponge *Cacospongia scalaris* (family Thorectidae), collected at the Cap de Nice (Côte d'Azur), is shown to contain a series of truncated, linear C_{21} difuran terpenoids comprising the known sponge products furospongin-1 ((+)-**1**), furospongin-2 (**2**), and dihydrofurospongin-2 ((−)-(*E*)-**3**), besides the new products cacospongione A ((−)-**4**), cacospongienone A ((−)-(*Z*)-**6**), and cacospongienone B ((−)-(*E*)-**6**), whose absolute configurations have been assigned by chemical correlations with (+)-**1**. Possibly, one of the two cacospongienones is an artifact, as these two terpenoids interconvert on standing. This is the first finding of linear C_{21} difuran terpenoids, which are typical of the Spongiidae, in a member of the family Thorectidae.

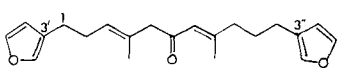
1. Introduction. – Marine sponges belonging to the orders Dictyoceratida and Dendroceratida are particularly rich in terpenoids ranging from sesquiterpenoids to methylated sesterterpenoids, as recently reviewed from structural and biogenetic [1a], chemotaxonomical [1b], and synthetic [1c] points of view. As regards the genus *Cacospongia* (order Dictyoceratida, family Thorectidae), tetracyclic sesterterpenes of the scalarane type have been isolated from Mediterranean collections (Baia di Napoli) of both *C. scalaris* [2a] and *C. mollior* [2b] as well as from Pacific collections (Japan, Wakayama and Kagoshima) of *C. scalaris* [3a]. These two Pacific collections gave different scalaranes, while no trace of the scalarane sesterterpenoid scalarin, the main metabolite of the Neapolitan *C. scalaris* [2a], could be detected [3a]. Also, bioactive, linear sesterterpenes bearing terminal furan and tetronic-acid units have been isolated from a third Pacific collection (Japan, Izu Peninsula) of *C. scalaris* [3b].

Such variability of the terpenoid content of *C. scalaris* with the place of collection [2] [3] stimulated us to investigate the natural products of this sponge from yet other areas. In fact, we have now found that a collection of *C. scalaris* from the Côte d'Azur contains new truncated, linear C_{21} difuran terpenoids, a class of terpenoids never detected before in this sponge genus.

2. Results and Discussion. – At the very start of our work it became clear that *C. scalaris* collected at the Cap de Nice (Côte d'Azur) is unusual for its genus in containing truncated, linear C_{21} difuran terpenoids. The first two such compounds which we identified are furospongin-1 ((+)-**1**) and furospongin-2 (**2**), already isolated from both *Hippospongia communis* and *Spongia officinalis* [4]. Their spectral and chiroptical data agree well with those in [4].



(+)-1



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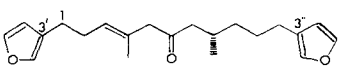
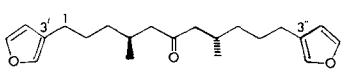


(−)-(*E*)-3



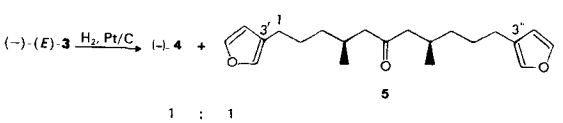
(−)-4

We then identified another terpenoid of *C. scalaris* belonging to the above class and whose spectral data[1]) agree with those for dihydrofurospongin-2 ((−)-(*E*)-**3**), a terpenoid isolated from both *H. communis* and *S. officinalis* [4b]. However, the $[\alpha]_D$ value reported in the latter work [4b] for either natural or semisynthetic (−)-(*E*)-**3** (obtained by oxidation of (+)-**1**) is ten-fold smaller than the value we have measured for (−)-(*E*)-**3** of *C. scalaris*. In fact, we found that (−)-(*E*)-**3** obtained by oxidation of (+)-**1** is indistinguishable in every respect from (−)-(*E*)-**3** as isolated from our *C. scalaris*. Further, the ^{1}H-NMR signals of (+)-**1** failed to split on addition of a chiral shift reagent, as expected for an enantiomerically pure compound. This leads us to revise the previous [4b] chiroptical data for dihydrofurospongin-2 ((−)-(*E*)-**3**), and to establish clearly its (8*S*)-configuration.

The third, optically active terpenoid from *C. scalaris* showed spectral data closely resembling those reported for the optically inactive tetrahydrofurospongin-2 (racemic or, more likely, *meso* [4b]), also isolated from both *S. officinalis* and *H. communis* [4b]. High-field NMR data *(Table 1* and *2)* of our compound, named cacospongione A ((−)-**4**), allowed us to fully assign all C- and H-atoms, so that the gross structure for (−)-**4** is firmly established.

Aimed at assigning the absolute configuration to (−)-**4**, we have carried out the catalytic hydrogenation of (−)-(*E*)-**3** obtaining in good yield a 1:1 mixture of (−)-**4** and

Scheme 1



1 : 1

the *meso*-compound **5** which could not be separated *(Scheme 1)*. However, the ^{1}H-NMR signals for the diastereotopic protons 2 H–C(5) of (−)-**4** and **5**, in a 1:1 ratio, were clearly separated from each other at 300 MHz *(Exper. Part)*. Also, the apparent $[\alpha]_D$ value for this 1:1 mixture (−)-**4**/**5** was as expected just half of that measured for (−)-**4** as isolated from *C. scalaris*[2]). From this, the (4*S*,8*S*)-configuration can be assigned to (−)-**4**.

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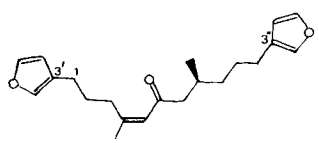
[1]) High-field ^{1}H-NMR spectra of (−)-(*E*)-**3** *(Table 1)* allowed us to distinguish 2 H–C(1) from 2 H–C(11) as, on irradiation at 2.30 ppm (*t*), the *td* at 2.13 ppm, safely attributable to 2 H–C(2), was observed to simplify. Moreover, HETCOR experiments [5] allowed us to assign all C-atoms for (−)-(*E*)-**3** *(Table 2)*.

[2]) Reportedly, the catalytic reduction of dihydrofurospongin-2 gives a mixture of diastereoisomeric products whose apparent $[\alpha]_D$ is nearly identical to that for starting dihydrofurospongin-2 [4b]. Such an observation is clearly inconsistent with the nature of the reaction, which gives a 1:1 mixture of (−)-**4** and optically inactive **5** *(Scheme 1)* when it is recalled that, as established here, (−)-(*E*)-**3** and (−)-**4** have $[\alpha]_D$ values of very similar magnitudes.

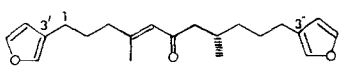
Table 1. *^{1}H-NMR Data*[a]) (C_6D_6) *for Furospongin-1 ((+)-***1***), Dihydrofurospongin-2 ((−)-(E)-***3***), Cacospongione A ((−)-***4***), (−)-(Z)-***3***

Proton	(+)-**1**	(−)-(*E*)-**3**	(−)-(*Z*)-**3**[d])
H–C(2′)	7.06 (*dd*, *J* = 1.6, 0.8)	7.07 (*dd*, *J* = 1.6, 0.8)	7.19 (br. *dd*, *J* = 1.7, 0.8)
H–C(4′)	6.06 (*dd*, *J* = 1.8, 0.7)	6.09 (br. *dd*, *J* = 1.6, 0.8)	6.24 (br. *dd*, *J* = 1.7, 0.8)
H–C(5′)	7.08 (*dd*, *J* = 1.8, 1.7)	7.13 (*dd*, *J* = 1.6, 1.6)	7.32 (*dd*, *J* = 1.7, 1.7)
2 H–C(1)	2.26 (br. *t*, *J* = 7.5)[b])	2.30 (*t*, *J* = 7.4)	2.45 (*t*, *J* = 6.8)
2 H–C(2)	2.11 (*quint.*, *J* = 7.3)	2.13 (*td*, *J* = 7.4, 7.1)	2.21 (*q*, *J* = 6.8)
H–C(3)	5.16 (*tq*, *J* = 7.0, 1.3)	5.14 (*tq*, *J* = 7.0, 1.3)	5.38 (*tq*, *J* = 7.0, 1.3)
H–C(3)	–	–	
H–C(4)	–	–	–
CH_3–C(4)	1.44 (br. *d*, *J* = 1.3)	1.54 (*d*, *J* = 1.3)	1.67 (*d*, *J* = 1.3)
H–C(5)	1.99 (*d*, *J* = 5.9)	2.77 (br. *s*)	3.05 (*s*)
H–C(5)			
H–C(6)	3.70 (*dddd*, *J* = 9.6, 8.1, 4.9, 3.1)	–	–
H–C(6)	2.0 (*s*)	–	–
H–C(7)	1.49 (*m*)	2.07 (*dd*, *J* = 13.9, 6.2)	2.33 (*dd*, *J* = 14.9, 6.0)
H–C(7)		1.93 (*dd*, *J* = 13.9, 2.1)	2.20 (*dd*, *J* = 14.9, 7.8)
H–C(8)	1.85 (*m*)	2.00 (*m*)	1.98 (*m*)
CH_3–C(8)	0.92 (*d*, *J* = 7.0)	0.82 (*d*, *J* = 6.7)	0.85 (*d*, *J* = 6.9)
H–C(9)	1.05 (*m*)	1.18 (*m*)	1.30 (*m*)
H–C(9)	1.23 (*m*)	1.01 (*m*)	1.12 (*m*)
2 H–C(10)	1.49 (*m*)	1.39 (*m*)	1.52 (*m*)
2 H–C(11)	2.24 (br. *t*, *J* = 7.5)[b])	2.21 (*t*, *J* = 7.4)	2.36 (*t*, *J* = 7.2)
H–C(2″)	7.07 (*dd*, *J* = 1.6, 0.8)	7.07 (*dd*, *J* = 1.6, 0.8)	7.19 (br. *dd*, *J* = 1.7, 0.8)
H–C(4″)	6.10 (*dd*, *J* = 1.8, 0.8)	6.09 (br. *dd*, *J* = 1.6, 0.8)	6.24 (br. *dd*, *J* = 1.7, 0.8)
H–C(5″)	7.15[c])	7.15 (*dd*, *J* = 1.6, 1.6)	7.32 (*dd*, *J* = 1.7, 1.7)

[a]) Coupling constants for furanoid protons have been derived from homonuclear decoupling experiments.
[b]) These assignments may be reversed.



(−)-(*Z*)-**6**



(−)-(*E*)-**6**

Two other C_{21} difuran terpenoids of *C. scalaris*, cacospongienone A ((−)-(*Z*)-**6**) and the more polar cacospongienone B ((−)-(*E*)-**6**), are new α,β-unsaturated ketones. The assignment was supported by the near identity of the ^{13}C-NMR signals for the saturated moiety of (−)-(*Z*)- and (−)-(*E*)-**6** with those for the corresponding C-atoms of (−)-**4**. Also, a comparison with the signals of C(9) and CH_3–C(8) of **2** *(Table 2)* confirmed the assignment of CH_3–C(4) and C(3) of (−)-(*Z*)- and (−)-(*E*)-**6**. These assignments were fully confirmed by HETCOR experiments [5]. Finally, the configurations at the double bond for the cacospongienones were established by the examination of δ_C values for both C(3) and CH_3–C(4). In fact, as expected from crowding effects on δ_C values [6], CH_3–C(4) is at unusually high field, while C(3) is at unusually low field for the B isomer, which is, therefore, assigned the (*E*)-configuration. The reverse is true for the A isomer which is assigned the (*Z*)-configuration. This structural analysis for the cacospongienones is further supported by the ^{1}H-NMR data of *Table 1*. Specifically, with (−)-(*E*)-**6**, double irradiation at either 2.21 or 2.13 ppm brought about a simplification of the *dd*'s at

*Cacospongienone A ((−)-(Z)-**6**), and Cacospongienone B ((−)-(E)-**6**) of* C. scalaris *and for their Synthetic Derivatives and (−)-7*

(−)-**4**	(−)-(*Z*)-**6**	(−)-(*E*)-**6**	(−)-7[d])[e])
7.07 (*dd*, *J* = 1.6, 0.8)	7.06 (*dd*, *J* = 1.6, 0.8)	7.06 (*dd*, *J* = 1.9, 0.9)	7.14 (br. *dd*, *J* = 1.7, 0.8)
6.10 (*dd*, *J* = 1.9, 0.8)	6.11 (*dd*, *J* = 1.9, 0.8)	6.08 (*dd*, *J* = 1.8, 0.9)	6.17 (br. *dd*, *J* = 1.7, 0.8)
7.13 (*dd*, *J* = 1.9, 1.6)	7.13 (*dd*, *J* = 1.9, 1.6)	7.15[c])	7.30 (*dd*, *J* = 1.7, 1.7)
2.23 (*t*, *J* = 7.4)	2.38 (br. *t*, *J* = 6.8)	2.21 (br. *t*, *J* = 7.4)	2.70 (*m*)
1.43 (*m*)	1.66 (*quint.*, *J* = 6.5)	1.45 (*m*)	2.70 (*m*)
1.20 (*m*)	2.68 (*t*, *J* = 7.6)	1.81 (br. *t*, *J* = 7.4)	–
1.05 (*m*)			–
2.05 (*m*)	–	–	–
0.84 (*d*, *J* = 7.3)	1.52 (*d*, *J* = 1.3)	2.16 (*d*, *J* = 1.8)	1.82 (*s*)
1.88 (*dd*, *J* = 17.3, 9.6)	–	–	5.72 (*s*)
2.02 (*dd*, *J* = 17.3, 5.4)	5.81 (*q*, *J* = 1.3)	5.86 (*m*)	
–	–	–	–
–	–	–	–
1.88 (*dd*, *J* = 17.3, 9.6)	2.16 (*dd*, *J* = 14.1, 4.2)	2.15–2.0 (*m*)	2.49 (*dd*, *J* = 14.6, 5.9)
2.02 (*dd*, *J* = 17.3, 5.4)	1.99 (*dd*, *J* = 14.1, 7.2)		2.34 (*dd*, *J* = 14.6, 7.8)
2.05 (*m*)	2.30 (*m*)	2.10 (*m*)	1.75 (*m*)
0.84 (*d*, *J* = 7.3)	0.86 (*d*, *J* = 6.1)	0.88 (*d*, *J* = 6.9)	0.87 (*d*, *J* = 6.9)
1.20 (*m*)	1.40 (*m*)	1.25–1.11 (*m*)	1.30 (*m*)
1.05 (*m*)	1.25 (*m*)		1.12 (*m*)
1.43 (*m*)	1.39 (*m*)	1.45 (*m*)	1.54 (*m*)
2.23 (*t*, *J* = 7.4)	2.21 (br. *t*, *J* = 6.7)	2.13 (br. *t*, *J* = 7.4)	2.37 (*t*, *J* = 7.4)
7.07 (*dd*, *J* = 1.6, 0.8)	7.10 (*dd*, *J* = 1.6, 0.8)	7.03 (*dd*, *J* = 1.9, 0.9)	7.18 (br. *dd*, *J* = 1.7, 0.8)
6.10 (*dd*, *J* = 1.9, 0.8)	6.07 (*dd*, *J* = 1.9, 0.8)	6.03 (*dd*, *J* = 1.8, 0.9)	6.25 (br. *dd*, *J* = 1.7, 0.8)
7.13 (*dd*, *J* = 1.9, 1.6)	7.14[c])	7.15[c])	7.32 (*dd*, *J* = 1.7, 1.7)

[c]) Partly superimposed by the solvent signal at the low concentration used.
[d]) In $CDCl_3$.
[e]) Arbitrary numbering.

6.08 and 6.03, respectively, which can, therefore, be assigned, in that order, to H–C(4′) and H–C(4″) of the furan rings[3]).

In order to establish the absolute configuration of the cacospongienones, (−)-(*E*)-**3** was treated with $BF_3 \cdot Et_2O$. But only an unseparable mixture containing little (*Z*)-**6** was obtained. The isomerization of (−)-(*E*)-**3** *via* enolates/enols was more successful. Li(i-Pr)$_2$N-induced enolization of (−)-(*E*)-**3** in THF at −40 to +20° followed by H_2O quenching led to (−)-(*Z*)-**6** in sufficient amount to allow us to assign it the (8*S*)-configuration. Luckily, (−)-(*Z*)-**6** was observed to slowly isomerize, on standing, to the (−)-(*E*)-isomer which was separated, thus allowing us to assign it the (8*S*)-configuration. On standing, (−)-(*E*)-**6** isomerizes also giving the (*Z*)-isomer which suggests that one of the two cacospongienones is an artifact and not a product of *C. scalaris*.

[3]) The assignment of the ^{1}H- and ^{13}C-NMR signals for all 3-substituted furans in *Table 1* and *2* has been fully supported by homonuclear and heteronuclear decoupling experiments as well as by HETCOR experiments performed with a modern NMR spectrometer recently acquired in Trento. The use of these techniques also allowed us to refine previous data, for the sesquiterpenoid penlanfuran isolated from the sponge *Dysidea fragilis*. However, previous structural conclusions [7] are by no means affected. Thus, for penlanfuran, unambiguous assignments are as follows. ^{13}C-NMR ($CDCl_3$): 17.79, 21.28 (2*q*, $(CH_3)_2CH$); 22.87 (*t*, C(5)); 28.43 (*d*, $(CH_3)_2CH$); 28.70 (*t*, C(4)); 31.25 (*t*, chain CH_2); 42.19 (*d*, C(6)); 109.17 (*t*, CH_2=C(3)); 111.31 (*d*, C(4′)); 122.74 (*s*, C(3′)); 127.75 (*d*, C(2)); 139.54 (*d*, C(2′)); 142.62 (*d*, C(5′)); 143.18 (*s*, C(1)); 143.46 (*s*, C(3)). In the ^{1}H-NMR, the assignments of H–C(2′) and H–C(5′) of penlanfuran are to be reversed. The data suggest that a similar inversion of the furan-proton assignments has to be made for noroxopenlanfuran, acetoxydihydropenlanfuran, penlanpallescensin, and the sesquiterpenoid (−)-**8b** (see [8]), also isolated from *D. fragilis* [8].

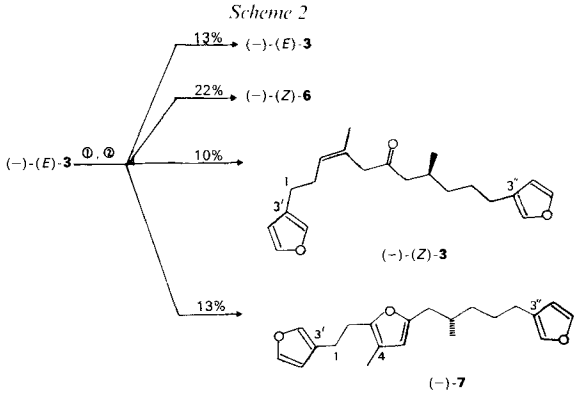
Table 2. *^{13}C-NMR Data* (C_6D_6) *for Furospongin-1 ((+)-***1***), Dihydrofurospongin-2 ((−)-(*E*)-***3***), Cacospongione A ((−)-***4***), Cacospongienone A ((−)-(*Z*)-***6***), Cacospongienone B ((−)-(*E*)-***6***) and Furospongin-2* (**2**) *of* C. scalaris *and for their Synthetic Derivatives (−)-(*Z*)-**3** and (−)-**7***

C-Atom	(+)-**1**	**2**[a])	(−)-(*E*)-**3**	(−)-(*Z*)-**3**[a])	(−)-**4**	(−)-(*E*)-**6**	(−)-(*Z*)-**6**	(−)-**7**[a])
C(2′)	139.08 (*d*)	138.85 (*d*)	139.24 (*d*)	138.90 (*d*)	139.19 (*d*)	139.18 (*d*)	139.29 (*d*)	138.95 (*d*)
C(3′)	124.92 (*s*)	124.39 (*s*)[b])	124.85 (*s*)	125.05 (*s*)	125.28 (*s*)	124.69 (*s*)	125.11 (*s*)	125.22 (*s*)
C(4′)	111.27 (*d*)	110.80 (*d*)[c])	111.21 (*d*)	110.98 (*d*)	111.21 (*d*)	111.02 (*d*)	111.21 (*d*)	111.01 (*d*)
C(5′)	142.84 (*d*)	142.62 (*d*)[d])	142.97 (*d*)	142.70 (*d*)	142.99 (*d*)	142.92 (*d*)	142.51 (*d*)	142.55 (*d*)
C(1)	25.26 (*t*)	24.23 (*t*)	24.94 (*t*)[f])	24.85 (*t*)	25.11 (*t*)[f])	24.44 (*t*)	25.10 (*t*)[e])	23.96 (*t*)
C(2)	28.72 (*t*)	28.51 (*t*)	28.71 (*t*)[f])	28.50 (*t*)	27.76 (*t*)	27.97 (*t*)	28.97 (*t*)[f])	32.53 (*t*)
C(3)	127.55 (*d*)	128.60 (*d*)	128.81 (*d*)	128.13 (*d*)	36.69 (*t*)	40.59 (*t*)	33.67 (*t*)	152.50 (*s*)
C(4)	133.16 (*s*)	130.40 (*s*)	130.32 (*s*)	129.24 (*s*)	28.91 (*d*)	156.85 (*s*)	157.59 (*s*)	114.66 (*s*)
CH_3–C(4)	16.24 (*q*)	16.48 (*q*)	16.48 (*q*)[f])	24.19 (*q*)	19.98 (*q*)	19.18 (*q*)	25.12 (*q*)	9.78 (*q*)
C(5)	49.37 (*t*)	55.41 (*t*)	54.42 (*t*)[f])	47.10 (*t*)	50.71 (*t*)	124.05 (*d*)	124.70 (*d*)	109.10 (*d*)
C(6)	66.55 (*d*)	not det.	206.97 (*s*)	208.33 (*s*)	208.32 (*s*)	199.38 (*s*)	199.03 (*s*)	148.24 (*s*)
C(7)	44.82 (*t*)	122.47 (*d*)	48.92 (*t*)	49.00 (*t*)	50.71 (*t*)	51.97 (*t*)	51.84 (*t*)	35.47 (*t*)
C(8)	29.34 (*d*)	158.75 (*s*)	28.83 (*d*)	28.83 (*d*)	28.91 (*d*)	29.57 (*d*)	29.50 (*d*)	26.76 (*d*)
CH_3–C(8)	19.46 (*q*)	19.23 (*q*)	19.93 (*q*)[f])	19.81 (*q*)	19.98 (*q*)	20.10 (*q*)	20.06 (*q*)	19.62 (*q*)
C(9)	37.82 (*t*)	40.60 (*t*)	36.62 (*t*)	36.45 (*t*)	36.69 (*t*)	36.80 (*t*)	36.78 (*t*)	36.18 (*t*)
C(10)	27.76 (*t*)	27.76 (*t*)	27.76 (*t*)[f])	27.43 (*t*)	27.76 (*t*)	27.81 (*t*)	27.79 (*t*)[f])	27.50 (*t*)
C(11)	25.09 (*t*)	24.72 (*t*)	25.10 (*t*)[f])	24.85 (*t*)	25.11 (*t*)[f])	25.13 (*t*)	25.23 (*t*)[e])	24.95 (*t*)
C(2″)	139.21 (*d*)	138.85 (*d*)	139.24 (*d*)	138.76 (*d*)	139.19 (*d*)	139.28 (*d*)	139.16 (*d*)	138.75 (*d*)
C(3″)	125.48 (*s*)	124.66 (*s*)[b])	125.30 (*s*)	124.54 (*s*)	125.28 (*s*)	125.34 (*s*)	125.11 (*s*)	124.27 (*s*)
C(4″)	111.19 (*d*)	110.98 (*d*)[c])	111.21 (*d*)	110.79 (*d*)	111.21 (*d*)	111.24 (*d*)	111.21 (*d*)	111.01 (*d*)
C(5″)	142.94 (*d*)	142.86 (*d*)[d])	142.97 (*d*)	142.70 (*d*)	142.99 (*d*)	143.17 (*d*)	142.51 (*d*)	142.45 (*d*)

[a]) In $CDCl_3$.
[b]) [c]) [d]) [e]) These assignments may be interchanged.
[f]) Assigned by heterodecoupling.

It is worth noting that in the enolization/quenching of (−)-(*E*)-**3** *(Scheme 2)*, the formation of (−)-(*Z*)-**6** (22%) and the isolation of starting material (−)-(*E*)-**3** (13%) is accompanied by the formation of two new C_{21} terpenoids which were assigned structures (−)-(*Z*)-**3** (10%) and (−)-**7** (13%) with the (8*S*)-configuration. Both structural assignments are firmly based on NMR and MS data in comparison with data obtained for the other compounds reported above. In particular, the (*Z*)-configurational assignment for (−)-(*Z*)-**3** is based on arguments similar to those used above for (−)-(*Z*)-**6**.

Scheme 2



The stereoselective formation of the (*Z*)-**6** isomer in the above enolization/quenching process is interesting. A plausible rationalization of this fact relies on the presumption that both the enolate deriving from (−)-(*E*)-**3** by H−C(5) abstraction and the related enol prefer the *cisoid*-conformation around the C(4)–C(5) bond which is most suited to the formation of (−)-(*Z*)-**6**.

Formation of the trifuran terpenoid (−)-**7** is more difficult to rationalize, unless the presence, as an impurity, of a C(3)-functionalized precursor in our starting (−)-(*E*)-**3** is admitted. We have carefully looked for such a precursor in semisynthetic (−)-(*E*)-**3** used for the process shown in *Scheme 2*. Actually, our (−)-(*E*)-**3** proved more than 98% pure by both chromatographic and NMR criteria, and no trace of the precursor could be detected[4]).

In conclusion, *C. scalaris* from the Cap de Nice more resembles sponges of the genera *Spongia* and *Hippospongia* [4] (family Spongiidae) than sponges of its own genus, or even of its own family (Thorectidae), so far as they have been investigated [2] [3]. Actually, the Thorectidae terpenoids which are most closely related to those of our present sponge comprise a few linear C_{21} monofuran terpenoids of either *Ircinia oros* of Neapolitan waters [9a] or *Ircinia dendroides* of the Gran Canaria Island waters [9b]. This shows that the terpenoid distribution amongst sponges of the families Spongiidae and Thorectidae is even more complex than thought heretofore [1b]. How much the different pattern of terpenoid distribution discussed here for the various collections of *C. scalaris* reflects the existence of genetically different varieties or merely the contribution of symbionts or parasites to the formation of natural products, cannot yet be answered[5]).

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Experimental Part

1. *General.* Column and flash chromatography: *Merck Kieselgel 60*, 20–50 μm. TLC: *Merck* Si_{F254} plates. HPLC: *Merck-LiChrosorb Si-60* (7 μm) and *Merck-LiChrosorb RP-18* (7 μm) columns (25 × 1 cm), 5 ml/min solvent flux, monitoring by UV at 225 nm; unless otherwise stated, reverse-phase eluates were extracted with hexane, and the org. phase was dried over phase-separation filters. Yields are given on reacted starting compounds (except for the reactions of *Scheme 2*, where yields are based on starting (−)-(*E*)-**3**). $[\alpha]_D$: *Jasco-DP-181* polarimeter. UV (λ_{max} in nm, ε in mol^{-1} l cm^{-1}) and IR (ν_{max} in cm^{-1}): *Beckman-DB-4* and *Perkin-Elmer-337* spectrometer, respectively. NMR: *Varian-XL-300* (^{13}C-NMR at 75.4 MHz, ^{1}H-NMR at 300 MHz); δ's (ppm) relative to internal Me_4Si (= 0 ppm) and *J*'s in Hz; $Yb(tfc)_3$ from *C. Erba*, experiments in $CDCl_3$. EI-MS (*m/z* (%)): home-built spectrometer based on the *Elfs-4-162-8-Extranuclear* quadrupole.

2. *Isolations. C. scalaris* was collected by scuba diving at the Cap de Nice at a depth of 50 m in September 1983 and was preserved for nearly two years at −20°. Then it was lyophylized and extracted with CH_2Cl_2/MeOH 3:1 to leave 273 g of dry sponge residue while evaporation of the extract gave 13 g of a dark oil. This oil was chromatographed with hexane/$(i\text{-}Pr)_2O$ (gradient elution) to give several *Ehrlich*-reactive fractions. The less polar fraction was subjected to HPLC (silica gel) with hexane/$(i\text{-}Pr)_2O$ 93:7 to give (−)-(*Z*)-**6** (0.002% of dry sponge

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[4]) We could only isolate, in 1% yield, a degraded C_{13} or C_{14} furan terpenoid. As our (+)-**1** proved highly pure, this degraded terpenoid must result from PCC oxidation of (+)-**1**.

[5]) Errors in the classification of the various collections of *C. scalaris* discussed here are unlikely as expert taxonomists have been involved in all determinations.

residue after extraction), (−)-**4** (0.01%), (−)-(*E*)-**3** (0.04%), (−)-(*E*)-**6** (0.002%), and **2** (0.003%) at t_R 11.0, 11.8, 15.3, 17.5, and 21.8 min, respectively. The next more polar *Ehrlich*-reactive fraction gave, after reverse-phase HPLC with MeOH/H_2O 82:18, (+)-**1** (1.0%) at t_R 9 min.

3. *Furospongin-1* (= *(+)-(3E,6S,8S)-1,11-Di(3-furyl)4,8-dimethylundec-3-en-6-ol;* (+)-**1**). Colourless crystals, m.p. 35° (from hexane; [4a]: 35°). $[\alpha]_{589}^{20} = +8.9°$, $[\alpha]_{435}^{20} = +19.0°$, $[\alpha]_{365}^{20} = +29.5°$ (*c* = 1.0, $CHCl_3$). MS: in accordance with [4a].

4. *Dihydrofurospongin-2* (= *(−)-(3E,8S)-1,11-Di(3-furyl)-4,8-dimethylundec-3-en-6-one;* (−)-(*E*)-**3**). Colourless liquid. $[\alpha]_D^{20} = -8.1°$ (*c* = 2.31, $CHCl_3$). UV ($CHCl_3$): 220 (4800). IR (film): 1705*s*. MS: in accordance with [4b].

5. *Oxidation of (+)-***1**. To a CH_2Cl_2 soln. of (+)-**1** (0.090 g, 0.272 mmol) were added, under N_2 at r.t. with stirring, pyridinium chlorochromate (0.176 g) and NaOAc (0.040 g) [10] (monitoring by TLC). After 3 h, H_2O was added, the mixture filtered on *Celite*, and extracted with Et_2O. The org. phase was dried over Na_2SO_4 and evaporated to leave 0.08 g of a residue which was subjected to reverse-phase HPLC (MeOH/H_2O 82:18) to give 0.055 g of an oil identical with natural (−)-(*E*)-**3** (73%), $[\alpha]_D^{20} = -8.6°$ (*c* = 2.93, $CHCl_3$), besides unreacted (+)-**1** (0.02 g).

7. *Catalytic Reduction of (−)-(E)-***3**. To a soln. of (−)-(*E*)-**3** (0.050 g, 0.152 mmol) in 4 ml of AcOEt was added 5% Pt/C. The mixture was hydrogenated at r.t./1 atm (monitoring by TLC, hexane/(i-Pr)$_2$O 9:1). After 3 h as the reaction became complex, the process was stopped before complete disappearance of (−)-(*E*)-**3**. The mixture was filtered and evaporated, and the residue was subjected to HPLC with hexane/(i-Pr)$_2$O 92:8 to give an unseparable 1:1 mixture of (−)-**4** and *1,11-di(3-furyl)-4,8-dimethylundecanone* (**5**) (0.015 g, 38%). $[\alpha]_D^{20} = -4.6°$ (*c* = 0.67, $CHCl_3$). ^{1}H-NMR (C_6D_6): 7.14 (*m*, 4 H); 7.10 (br. *dd*, *J* = 1.6, 0.8, 4 H); 6.10 (br. *dd*, *J* = 1.9, 0.8, 4 H); 2.23 (*t*, *J* = 7.4, 8 H); 2.05 (*m*, 4 H); 2.03 (*dd*, *J* = 17.6, 5.7, 2 H); 2.02 (*dd*, *J* = 17.3, 5.4, 2 H); 1.88 (*dd*, *J* = 17.3, 9.6, 2 H), 1.87 (*dd*, *J* = 17.6, 9.4, 2 H); 1.43 (*m*, 8 H); 1.20 (*m*, 4 H); 1.05 (*m*, 4 H); 0.84 (*d*, *J* = 7.3, 12 H).

8. *Cacospongienone A* (= *(−)-(4Z,8S)-1,11-Di(3-furyl)-4,8-dimethylundec-4-en-6-one;* (−)-(*Z*)-**6**). Colourless liquid. $[\alpha]_D^{20} = -10.7°$ (*c* = 0.29, $CHCl_3$). UV ($CHCl_3$): 242 (10800). IR (neat): 1680, 1610. MS: 328 (2, M^+), 313 (13, M^+ − Me), 179 (16, M^+ − 149), 149 (12), 135 (80), 95 (93), 81 (100).

9. *Cacospongienone B* (= *(−)-(4E,8S)-1,11-Di(3-furyl)-4,8-dimethylundec-4-en-6-one;* (−)-(*E*)-**6**). Colourless liquid. $[\alpha]_D^{20} = -8.5°$ (*c* = 0.16, $CHCl_3$). UV ($CHCl_3$): 242 (10300). IR (neat): 1680, 1610. MS: 328 (1, M^+), 313 (24, M^+ − Me), 179 (22, M^+ − 149), 149 (15), 135 (96), 95 (25), 81 (100).

10. *Furospongin-2* (= *(3E,7E)-1,11-Di(3-furyl)-4,8-dimethylundeca-3,7-dien-6-one;* **2**). UV, IR, ^{1}H-NMR and MS: matching those in [4b].

11. *Li(i-Pr)$_2$N-Enolization/H_2O-Quenching of (−)-(E)-***3**. Semisynthetic (−)-(*E*)-**3** (0.150 g, 0.457 mmol) in dry THF (3 ml) was added dropwise during 10 min at −40° under N_2 with stirring to the 1.2 molar excess of Li(i-Pr)$_2$N, freshly prepared in dry THF from 1.6M BuLi in hexane and (i-Pr)$_2$NH, freshly distilled from CaH_2. As (−)-(*Z*)-**6** only started to form (TLC, hexane/Et_2O 9:1, *Ehrlich* reagent) on raising the temp. to 0°, the mixture was allowed to reach r.t. for 2 h. Then, H_2O (1 ml) was added, the mixture filtered, and the filtrate extracted 3× with hexane/Et_2O 7:3. The filtrate was washed with H_2O, dried over Na_2SO_4, and evaporated. The residue was flash chromatographed with hexane/(i-Pr)$_2$O (gradient elution) to give, first, pure (−)-7 (0.020 g, 13%) and then a mixture which was subjected to HPLC with hexane/(i-Pr)$_2$O 92:8. In the order of increasing polarity, (−)-(*Z*)-**6** (0.032 g, 22%; $[\alpha]_D^{20} = -12.0°$ (*c* = 1.10, $CHCl_3$)), (−)-(*Z*)-**3** (0.015 g, 10%), and (−)-(*E*)-**3** (0.020 g, 13%) were obtained (data refer to pure compounds). (−)-(*Z*)-**6** and (−)-(*E*)-**6** slowly interconvert in either benzene or $CHCl_3$ at r.t. Thus (−)-(*E*)-**6** ($[\alpha]_D^{20} = -9.1°$ (*c* = 0.085, $CHCl_3$)) was separated from the (*Z*/*E*)-mixture (9:1) obtained from semisynthetic, pure (−)-(*Z*)-**6** (without checking whether it is, or not, an equilibrium mixture) by HPLC with hexane/(i-Pr)$_2$O 92:8. Data for (−)-(*Z*)-**3**: colourless liquid. $[\alpha]_D^{20} = -6.5°$ (*c* = 0.55, $CHCl_3$). MS: 328 (1, M^+), 313 (2, M^+ − CH_3), 179 (45), 149 (2), 135 (95), 95 (45), 81 (100).

Data for 2-[2-(3-furyl)ethyl]-5-[5-(3-furyl)-2-methylpentyl]-3-methylfuran ((−)-**7**): colourless liquid. $[\alpha]_D^{20} = -5.3°$ (*c* = 0.70, $CHCl_3$). MS: 326 (11, M^+), 245 (45, M^+ − $C_4H_3OCH_2$), 189 (36), 137 (1), 135 (28), 108 (26, 189 − $C_4H_3OCH_2$), 81 (100).

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