Tetrahedron Letters No. 17, pp 1425 - 1428, 1975. Pergamon Press. Printed in Great Britain.

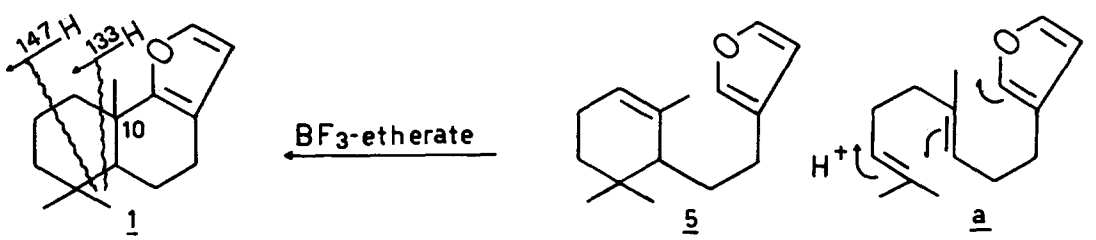
FURANOSESQUITERPENOIDS IN SPONGES - III*.
PALLESCENSINS A-D FROM DISIDEA PALLESCENS: NEW SKELETAL TYPES

G. Cimino, S. De Stefano, A. Guerriero and L. Minale
Laboratorio per la Chimica di Molecole di Interesse Biologico del C.N.R.
Via Toiano n° 2, Arco Felice - Napoli, Italy

(Received in UK 4 February 1975; accepted for publication 19 March 1975)

In the preceding communications we have described from the marine sponge Disidea pallescens six new furanosesquiterpenoids, three, pallescensins 1-3, of a mono-cyclofarnesane type, and three, pallescensins E-G, of a new skeletal type. Pallescensins A-D are the remaining sesquiterpene constituents of this sponge. They represent a further skeletal variant amongst the sesquiterpenoids, and their formulation as shown rests mainly on spectral evidence which follows. Molecular formulas were derived from high resolution mass measurements.

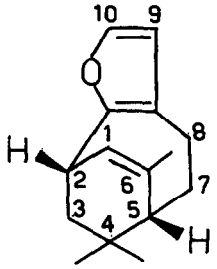
Pallescensin A (1; 0,07% of dry animal), $C_{15}H_{22}O$, $[\alpha]_D$ = +9.7°, λ_{max} 223 nm (ε 9,300); m.s.: 218 (18), 203 (100), 175 (expulsion of gem-dimethyl group with one additional H), 147 (32, see 1), 133 (13, see 1), 69 ($C_5H_9^+$); contains a 2,3-disubstituted furan ring (1H doublets at δ 7.02 and 5.95 ppm, J 2 Hz) and three tert-Me's resonating in CCl_4 at δ 0.91, 0.93 and 1.17 (10-Me) ppm. These data with molecular formula (five formal unsaturations) and absence of olefinic signals in the n.m.r. spectrum indicated that pallescensin A is represented most favourably by formula 1, which is also attractive from the standpoint of biogenesis. (In fact, we may imagine that a undergoes an essentially synchronous process for the ring formation of H^+ is furnished at C-3). The co-occurrence of furanoid sesquiterpenes of the mono-cyclofarnesane type such 5, adds considerable wight to this assi-



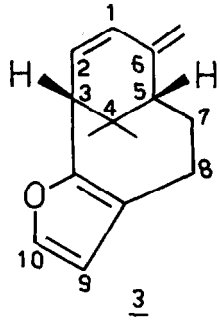
1 5 a

* Part I and II: G.Cimino, S.De Stefano, A.Guerriero and L.Minale, Tetrahedron Letters, preceding paper.

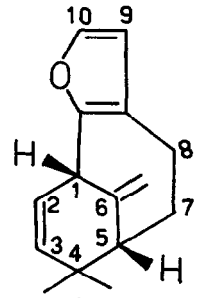
gaement. In confirmation 5, on treatment with BF_3-etherate, yielded a tryciclic compound identical with 1 in g.l.c., SiO_2-$AgNO_3$ t.l.c. and mass spectrometry.



2



3



4

Pallescensin B (2, 0.15% of dry animal), $C_{15}H_{20}O$, $[\alpha]_D$ = + 62.6°, λ_{max}^{MeOH} 229 nm (ε, 10,300), m.s.: 216 (M^+, 100), 201 (40), 173 (10), 160 (37), 145 (32), 132 (63), 120 (56), 105 (11), 91 (35), 77 (20), besides a 2,3-disubstituted furan ring, contains two additional rings and a trisubstituted double bond. The ^1H n.m.r. spectrum of 2 is shown in Table I. The sequence of protons in the six-membered ring was determined by decoupling. Irradiation at δ 3.40 (H-2) sharpened both the furan hydrogens, reduced the olefinic broad doublet at δ 5.83 (H-1) into a broad singlet and also the signal at δ 1.60 (H_2 at C-3) into a singlet. Thus C-3 must be adjacent to a quaternary carbon. The methyl at δ 1.80 was found to be "long-range" coupled with the olefinic proton. In the mass spectrum the significant m/e 160 fragment was interpreted as originating by elimination of isobutene by the retro-Diels-Alder process and suggested the presence of a dimethylcyclohexene ring. These data coupled with the isoprene rule[1] allowed us to propose for pallescensin B the cage-like structure 2. As expected the olefin was unreactive towards osmium tetroxide, m-chloroperbenzoic acid and hydrogenation in different conditions. Moreover, CrO_3-pyridine oxidation left pallescensin B unchanged.

TABLE I - H^1 n.m.r. data of pallescensin B in CCl_4

Proton	Multiplicity	δ (ppm, TMS = 0)	J (Hz)
H-10	d	6.97	$J_{10,9}$= 2 Hz
H-9	d	5.92	
H-1	bd	5.83	$J_{1,2}$ = 7 Hz
H-2	7-line m	3.40	$J_{2,3ax}$= 5 Hz; $J_{2,3eq}$ =3 Hz
H-5,H_2-7, H_2-8	unresolved b	2.5-1.9	
6-Me	bs	1.80	
H_2-3	apparent dd	1.60	
4-Me's	singlets	0.91 and 0.78	

Pallescensin C (3, 0.20% of dry animal), $C_{15}H_{18}O$, $[\alpha]_D$ = + 424° λ_{max}^{MeOH} 230 nm (ε, 11,800), ν_{max}^{film} 1630, 1600, 885 (C = CH_2), 830, 735, 710 cm^{-1}; m.s.: 214 (M^+, 94), 199 (56), 171 (100), 128 (50), 115 (40), 91 (50). The analysis of n.m.r. data (Table

II) together with double resonance experiments gave the sequence of all H atoms.

TABLE II - H^1 n.m.r. data of pallescensin C in C_6D_6

Proton	Multiplicity	δ (ppm, TMS = 0)	J (Hz)
H-10	d	6.98	$J_{10,9}$= 2 Hz
H-1	d	6.07	$J_{H1,2}$=10 Hz
H-9	d	5.95	
H-2	dd (broad)	5.52	$J_{2,3}$ = 5 Hz
H-3	d	3.06	
C=CH_2	b singlets	4.94 and 4.75	
H-5,H_2-8	complex multiplet	2.3-1.9	
H_2-7	complex multiplet	1.8-1.4	
4-Me's	singlets	1.02 and 0.91	

The conjugated butadiene system of pallescensin C was located as follows. The down field vinyl-H (δ 6.07) is clearly an internal hydrogen of the conjugated system (H-1). The 10 Hz coupling indicated a cis double bond. The doublet at δ 3.06 (H-3) is due to a CH located between the furan ring and the diene system. In fact, irradiation on this signal sharpened both the furan-H's signals, reduced the broad dd at 5.52 (due to H-2) to a b doublet (J 10 Hz) and left H_1 unchanged. The values of $J_{2,3}$ (5 Hz) and $J_{1,3}$ (J~0) requires H_3 to be equatorial. Irradiation at both the δ 4.94 and 4.75 b singlets reduced the broad dd at 5.52 (H-2) to a doublet of sharp doublets (J = 10,5 Hz). Conversely, irradiation at δ 5.52 (H-2) produced a singlet at δ 3.06 (H-3) and reduced the C = CH_2 b singlets to a pair of sharp doublets (J 1.5 Hz). Moreover, irradiation at δ 1.6 the center of the complex multiplet spread between δ 1.8-1.4 (H-7) transformed the 2.3-1.9 δ multiplet into a simpler signal from which emerged a clearly visible AB q (J 16 Hz) and a broad singlet. This gave the -CH_2CH_2CH- sequence for the remaining protons. On this, the cage-like structure 3 can be proposed for pallescensin C. Hydrogenation on Pd-C (r.t., ethanol, 1 h) gave mainly the 1-4 addition product, M^+ 216 1H,multiplet at 5.40 and 3H triplet (J 1.5 Hz) at 1.68 ppm [-CH=C(CH_3)-].

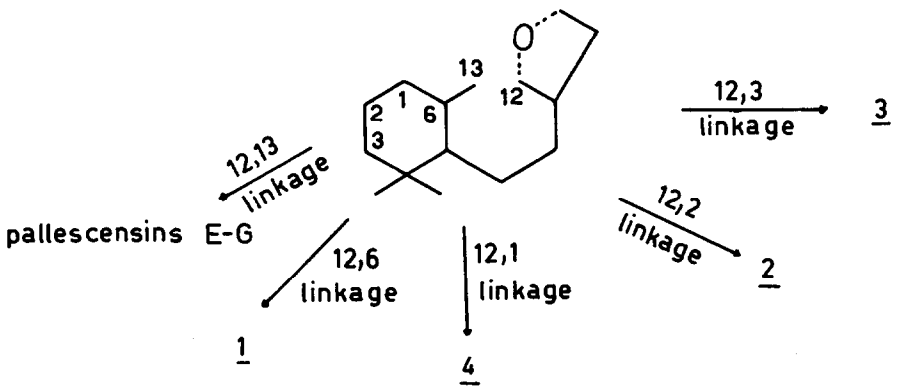
Pallescensin D (4, 0.03% of dry animal), $C_{15}H_{18}O$; $[\alpha]_D$ = -45.3°; λ_{max}^{MeOH} 229 nm (ε, 14,200), ν_{max}^{liquid} 885 (C=CH_2), 830, 730 cm^{-1}; m.s.: 214 (M^+, 100), 199 (50), 171 (79), 158 (32), 145 (56), is a very minor component. N.m.r. data as deduced from a detailed analysis of decoupling are in Table III. The vinyl- H's at δ 5.66 and 5.22 are cis on a double bond and both are coupled with the 1H broad dd at δ 3.96 (H-1). The signal at δ 5.22 (H-3) showed also spin interaction with signal at δ 2.08 (H-5) and the small coupling (1.5 Hz) suggested a quasi equatorial orientation for H-5 (W relationship[2]). Furthermore, irradiation at δ 2.08 (H-5) sharpened the doublet at δ 4.73, while the doublet at 4.82 was found to be "long-range" coupled with H-1 (δ 3.96). Irradiation at δ 3.96 (H-1)also sharpened both the furan- H's. Finally the 1H broad triplet at δ 2.08 (H-5) was converted to a singlet on irradiation at

TABLE III - H^1 n.m.r. data of pallescensin D in C_6D_6

Proton	Multiplicity	δ (ppm, TMS = 0)	J (Hz)
H-10	d	6.99	$J_{10,9}$= 2 Hz
H-9	d	5.95	
H-2	dd	5.66	$J_{2,3}$= 9 Hz; $J_{2,1}$ = 4 Hz
H-3	dt	5.22	$J_{3,1}$= $J_{3,5}$ = 1.5 Hz
$C=CH_2$	d	4.82 and 4.73	J = 1.5 Hz
H-1	dd (broad)	3.96	
H_2-8	broad multiplet	2.30	
H-5	bt	2.08	$J_{5,7}$ = 7 Hz
H_2-7	broad multiplet	1.65	
4-Me's	singlets	1.00 and 0.88	

δ 1.65 (H_2-7). This gave the complete sequence of all H of pallescensin D and allowed us to propose for this compound the cage-like structure 4.

Pallescensins A-D, which represent new skeletal types amongst sesquiterpenoids, could be biogenetically derivable from a furanoid mono-cyclofarnesane precursor by subsequent cyclization and oxidation, as suggested in the preceding paper for pallescensins E-G. Possible biogenetic route to pallescensins A-G is shown below.



REFERENCES

1) L. Ruzicka, A. Eschenmoser and H. Heusser, Experientia, 9, 357 (1953).

2) E. W. Garbish, jr., Chem. and Ind., 1715 (1964).