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FURANOSESQUITERPENOIDS IN SPONGES - II*.
PALLESCENSINS E-G FROM DISIDEA PALLESCENS: A NEW SKELETAL TYPE

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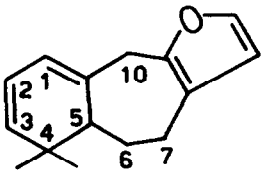
In the preceding paper three new sesquiterpenoids of the mono-cyclofarnesane type have been described from the marine sponge Disidea pallescens. These co-occur with seven more furanosesquiterpenoids and in this communication we refer on pallescensins E-G, which represent a new type of sesquiterpenoids. They were oils, very unstable, homogeneous on SiO_2-$AgNO_3$ t.l.c. and g.l.c. (1% OV-1 at 130°); molecular formulas were derived from accurate mass measurements (Isolation procedure has been briefly reported in Part I). Their formulation as shown rests mainly on spectral evidence which follows.

Pallescensin G (1), $C_{15}H_{18}O$, $[\alpha]_D$ - 289°, the major sesquiterpene constituent



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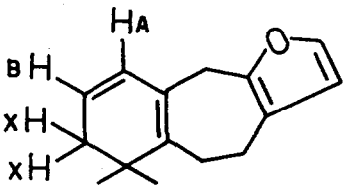

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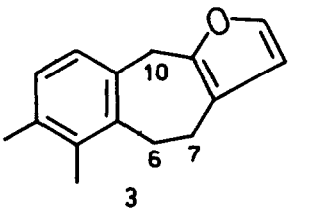

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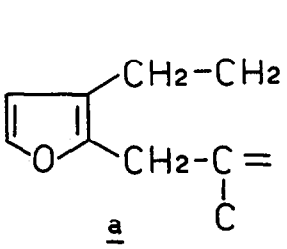
of the sponge (0.25% of dry weighted animal), is tricyclic, contains a cisoid diene chromophore isolated from a furan chromophore (λ_{max} 266 and 220 nm; ε 18,000 and 16,000), and displays a strong negative Cotton effect (c.d.; θ 266-18,200). Spectral data: m.s.: 214 (M^+, 50), 199 (32), 185 (8), 181 (6), 171 (36), 105 (100); $\delta^{CDCl_3}_{TMS}$ 0.99 (3H, s, tert-Me), 1.05 (3H, s, tert-Me), 1.89 (3H, complex signal, H-5 and H_2 at C-6), 2.1-2.8 (2H, multiplet, AB part of an ABXY pattern, H_2 at C-7),

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

3.49 (2H, ABq, J = 16 Hz, H_2 at C-10), 5.35 (1H, m, H-3), 5.75 (2H, m, H-1, H-2), 6.09 (1H, d, J = 2 Hz, furan-β-H), and 7.17 (1H, d, J = 2 Hz, furan-α-H) ppm. The furan ring is 2,3-disubstituted as follows from the furan-H's coupling constant (2 Hz); moreover both the furan protons are "long-range" coupled with the ABq at δ 3.49 (due to the C-10 methylene protons). Decoupling experiments also evidenced small couplings between the furan-β-H and the multiplet at δ 2.1-2.8 (due to the C-7 methylene protons) and established the existence of homoallylic couplings between the C-7 and C-10 protons. The C-7 protons appear as an AB part of an ABXY system: irradiation at the center of the 1.89 complex signal (C-6 methylene protons overlapped with H-5) transformed the δ 2.1-2.8 multiplet into a system of two doublets with J of 16 Hz. After irradiation at δ 3.49 (C-10 protons), which sharpened each line of the δ 2.1-2.8 multiplet, the latter can be interpreted as a 6 - (two apparent triplets with separation of 5 Hz; JAX ≅ JAY) and 8 - (two apparent quartets with separation of 6 and 9 Hz; JBX ≠ JBY) line patterns. These n.m.r. data are compatible with only two alternative sequences (a or b). In C_6D_6 the olefinic



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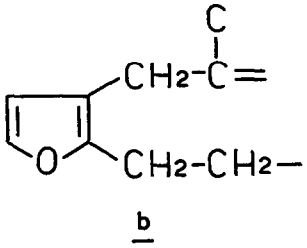
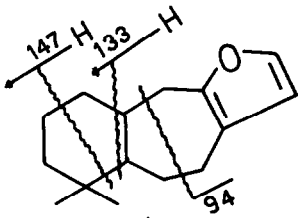


b

region of the n.m.r. was clearer - vinyl-H signals appearing as an ABX pattern [ν_A 5.75 (H-2), ν_B 5.58 (H-1), ν_X 5.30 (H-3) ppm; JAB 4.5 Hz, JAX 9 Hz, JBX 1.5 Hz]. Irradiation at δ 5.30 (X part; H-3) transformed the AB portion (internal vinyl-H's) into a system of two doublets with J of 4.5 Hz; reverse experiments confirmed the assignements. Moreover, the H-1 proton was found to be "long range" coupled with one of the two protons at C-10 and a small interaction also occurred between the 0.9 δ tert-Me protons and H-3 (decoupling). The partial structure a can be now extended to 1. Hydrogenation (5% Pd-C; ethanol, r.t. and pressure, 1 h) produced two dihydroderivatives along with trace of a tetrahydroderivative. The latter was analyzed only by mass spectrometry and the fragmentation pattern was in agreement with the proposed structure (4): 218 (M^+, 22), 203 (3),175 (expulsion of gem-dimethyl group with 1H, 3), 147 (9); 133 (5) and 94 (100)[1]. The n.m.r. spectrum of the major dihydroderivative (5), $[\alpha]_D$ = -43,3°, had lost two olefinic signals, but had retained an AB quartet at δ 3.38 (J 16 Hz) for the C-10 protons and an olefinic signal at δ 5.43 (m) for H-1. In its mass spectrum significantly a strong peak occurs at m/e 160 corresponding to elimination of isobutene from the dimethylcycloxene ring by the retro-Diels-Alder process. The alterna



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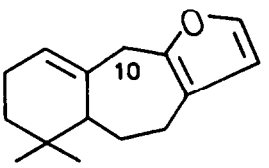

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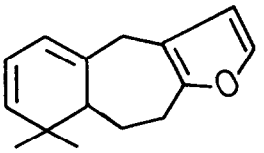
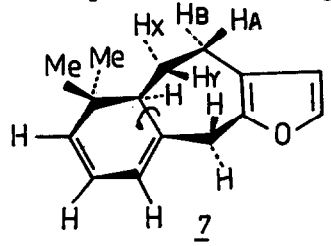


6

tive structure 6 for pallescensin G, which could fit with most of the n.m.r.data, is unreliable on biogenetical grounds. The negative Cotton effect observed for pallescensin G suggested that the diene chromophore is twisted in the form of a left-handed helix[2]. Since irradiation at H-5 left unchanged the shape of the H-3 olefinic signal, a quasi-axial orientation should be called for H-5 (in the case of a quasi-equatorial orientation, H-5 should be in a W relationship with H-3 and one should expect couplings, even small, between them[3]). On this,we tentatively propose for pallescensin G the absolute configuration with R-chirality at the sole asymmetric center C-5. Another point merits to be mentioned: from the insepction of Dreiding models of the two possible conformers, one is unreal because of steric hindrance between one tert-Me and H_2C-7, and for the most favorable one (7) HA proton bisects the angle between X and Y, the JAX and JAY will be equal as observed, and the dihedral angles HB/HX and HB/HY are different and accordingly JBX and JBY will be different as observed.



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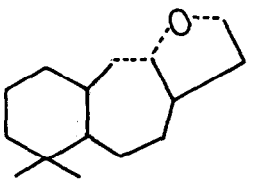
Pallescensin F (2, 0.06% of dry animal), $C_{15}H_{18}O$, isomeric with pallescensin G, is optically unactive and has u.v. absorptions at 220 and 271 nm (ε, 10,300 and 7,000; furan and cisoid diene chromophores); m.s.: 214 (M^+, 50), 199 (35),171 (11), 143 (16), 105 (100). The furan ring is 2,3-disubstituted (δ CCl_4 7.03, 5.96 ppm,d, J 2 Hz). Furthermore in the n.m.r. spectrum a singlet at δ 1.03 (6H, tert-Me's) and a "deceptively simple" ABX_2 system [in CCl_4 δ 5.73 (1H, dt, J = 9, 2 Hz, HA), 5.49 (1H, dt, J = 9, 4 Hz, HB) and 2.04 (2H, dd, J = 4, 2 Hz, HX) ppm; assignements confirmed by decoupling] together with the absence of any further olefinic signal suggested the presence in the molecule of a 1,2-disubstituted-6,6-dimethylcyclohexa-1,3-diene moiety. An isolated methylene between the furan ring and the diene system was indicated by a singlet at δ 3.39, while a saturated C_2 chain was suggested by a broad singlet at δ 2.47. Hydrogenation produced two dihydroderivatives (1-2 and 1-4 addition products) and trace of a tetrahydro-one. The latter and the 1-4 hydrogenation product were identical with 4 and 5, respectively, derived from pallescensin G. This established structure 2 for pallescensin F.

Pallescensin E (3), optically unactive, λ_{max} 222, 225 nm (ε, 10,300; 11,900); m.s.: 212 (M^+, 90), 197 (100), 183 (13), 169 (28), 105 (5), 91 (6), 77 (5), is

present in the sponge extract in trace amounts. The n.m.r. (C_6D_6) showed two doublets (1H each, J = 2 Hz) at δ 7.09 and 5.94 for the furan protons and a 2H singlet at δ 6.78 for the benzenic protons. Two 3H singlets at δ 2.11 and 2.10 ppm (Me's at aromatic carbons), a 2H broad singlet at δ 3.90 for the isolated methylene between the aromatic and furan rings, and two multiplets (2H each) at δ 2.80 and 2.44 ppm for the C-6 and C-7 methylene protons completed the n.m.r. spectrum. Irradiation at δ 3.90 (H_2 at C-10) sharpened both furan and aromatic protons, and produced small modifications of the shape of the complex multiplet at δ 2.44 (H_2 at C-7), which latter was also found to be "long-range" coupled with the furan-β-proton at δ 5.94. Bearing in mind the proposed structures for the co-occurring 1 and 2, these spectral data can be interpreted in terms of the structure 3 for pallescensin E, which could arise from the former by 1,2-methyl migration followed by dehydrogenation.

The carbon skeleton of pallescensins E-G is so far unique amongst sesquiterpenoids[4]; it would seem derivable from a mono-cyclofarnesane intermediate as shown in 9. The co-occurrence of furanoid sesquiterpenes such as 10 is a good support to this suggestion.



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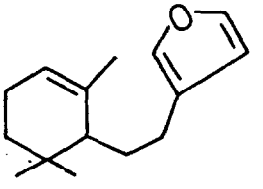

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REFERENCES

1. H. Budzikiewicz, C. Djerassi and D. H. Williams, "Structure elucidation of Natural Products by mass spectrometry, vol. II, p. 133-139. Holden-Day. Inc. (1964).

2. A. Moscowitz, E. Charney, V. Weiss and H. Ziffer, J. Am.Chem. Soc., 83, 4661 (1961), see also P. Crabbé, Applications de la dispersion rotatoire optique et du dichroisme circulaire optique en chimie organique, p.511. Gouthier-Villars, Paris (1968).

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

4. W. Parker, J. S. Roberts and R. Ramage, Quart. Rev., 21, 331 (1967); R. Bryant in "Rodd's Chemistry of Carbon Compound" (ed. by S. Coffey) 2nd ed. vol. IIC, p. 257 (1969).