# 161. A Dimer of Puupehenone

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Dedicated to Prof. *E. Lederer* on the occasion of his 75th birthday

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*Summary*

The structure of a colorless dimer (**4a**) of puupehenone (**1**), which was isolated from Pacific marine sponges, has been elucidated from spectral data.

Marine sponges are a rich source of secondary metabolites, particularly terpenoids [1]. Occasionally, compounds of mixed biosynthesis have been encountered, among them the puupehenones **1**–**3**, which are constructed of sesquiterpene and benzene moieties [2]. The yellow encrusting sponge, identified as *Heteronema sp.* (family *Spongiidae*, order *Dictyoceratida*, class *Demospongiae*), from which puupehenone (**1**) was originally isolated, was first collected by us off the Hawaiian islands of Lanai and Oahu. The halopuupehenones **2** and **3** were minor constituents in a *Heteronema* sample from Enewetak in the Marshall islands. In all collections we encountered several dimeric compounds, some of them highly colored. A colorless dimer, bispuupehenone (**4a**), was subsequently also isolated from a Tahitian sponge, *Hyrtios (= Inodes) eubamma* (family *Thorectidae*, order *Dictyoceratida*), and is the subject of this report.

*H. eubamma* was preserved in EtOH and then further extracted with the same solvent. The aqueous residue was partitioned with cyclohexane. Chromatography of the organic residue on *Sephadex*, then silica gel, yielded puupehenone (**1**) and bispuupehenone (**4a**), m.p. 234–240°. A composition of $C_{42}H_{54}O_6$ was ascertained by mass spectrometry. The fragmentation pattern, including abundant $M^+ - 15$ (*m/z* 639) and $M^+ - 151$ (see wiggly line in **4**) ions, were reminiscent of the puupehenone spectrum [2]. The presence of OH-groups was indicated by IR bands at 3560 and 3420 $cm^{-1}$.

The $^{13}C$-NMR spectrum displayed 21 signals, thus confirming that bispuupehenone (**4a**) is a symmetrical dimer of **1**. Fifteen upfield signals parallel those of other drimane derivatives, *e.g.* **1**, its methanol adduct **5**, or 8-epichromazonarol (**6**) [3]

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Table 1. *$^{13}$C-NMR Chemical Shifts of Sesquiterpene Moieties of Compounds* **1**, **4a**, **5** *and* **6**

| | C(1) | C(2) | C(3) | C(4) | C(5) | C(6) | C(7) | C(8) |
|---|---|---|---|---|---|---|---|---|
| Puupehenone (**1**) | 39.8 | 18.1 | 40.6 | 33.2 | 54.7 | 18.1 | 41.5 | 78.6 |
| Bispuupehenone (**4a**)$_2$ | 39.5 | 18.2 | 40.2 | 33.4 | 27.4 | 18.2 | 41.9 | 77.3 |
| Puupehenone-MeOH adduct (**5**) | 41.0 | 19.5 | 19.5 | 34.3 | 55.0 | 19.5 | 43.0 | 75.0 |
| 8-epichromazonarol (**6**) | 39.9 | 18.1 | 40.5 | 33.0 | 55.1 | 18.3 | 41.8 | 75.2 |

| | C(9) | C(10) | C(11) | C(12) | C(13) | C(14) | C(15) |
|---|---|---|---|---|---|---|---|
| Puupehenone (**1**) | 53.6 | 39.1 | 33.6 | 21.8 | 15.1 | N.A. | 27.9 |
| Bispuupehenone (**4a**)$_2$ | 57.5 | 38.0 | 33.6 | 21.9 | 14.0 | 71.2 | 27.4 |
| Puupehenone-MeOH adduct (**5**) | 56.4 | 38.0 | 34.3 | 22.4 | 15.1 | 75.7 | 28.0 |
| 8-epichromazonarol (**6**) | 49.4 | 38.9 | 33.5 | 21.7 | 14.1 | 22.7 | 27.0 |

and are compared in *Table 1*. The upfield shifts of C(16) and C(18), when going from puupehenone-MeOH adduct (**5**) to bispuupehenone (**4a**)$_2$ is presumably a consequence of neighboring fused rings. Similar shifts are observed when dialkylbenzene is compared with dihydrophenanthrene [4].

Inspection of the $^1$H-NMR data of **4a** reveals that H–C(9) ($\delta$ 1.82, *d*) is coupled to H–C(14) ($\delta$ 4.85, *d*) by only 1.5 Hz, thereby indicating a dihedral angle of close to 90°, in analogy with the situation in 8-epichromazonarol (**6**).

The symmetry of bispuupehenone (**4a**) evident from its NMR spectra, and its molecular formula, which is 2×(puupehenone) – 2 H, suggested that **4a** may be generated from **1** by *in vitro* oxidative coupling. Indeed, oxidation of **1** with alkaline ferricyanide followed by chromatography furnished **4a** as well as other uncharacterized products.

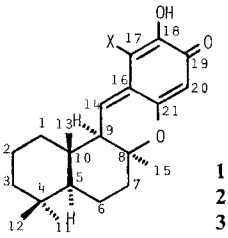
In addition to the benzopyrane structure for **4a**, another plausible structure of an oxidative dimer of **1** may be written, *viz.* a dibenzofuran **7a**. However, when the UV spectrum of bispuupehenone is compared with literature data for a simple dibenzofuran (**8**) [5] and a benzopyran **9** [6], the latter structure is clearly favored *(Table 2)*. Structure **4a** is also preferred in a qualitative lanthanide induced shift (LIS) study on bispuupehenone diacetate (**4b**), which was prepared since the LIS results on **4a** showed line-broadening and hence were inconclusive. In the LIS study

Table 2. *UV Data Comparison of Bispuupehenone* (**4a**) *with Model Benzopyran* **9** [6] *and Benzofuran* **8** [5]

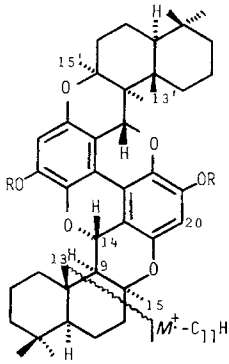
| **4a** (EtOH) | **9** (EtOH) | **8** ($Et_2O$) |
|---|---|---|
| 230 (4.45) | 232 (4.27) | 228 sh (4.34) |
| 284 (3.98) | 265.5 (3.72) | 241 (4.04) |
| 295 (4.03) | 276.5 (3.89) | 245 (4.05) |
| 341 (3.85) | 315 (3.98) | 249 (4.31) |
| 353 sh (3.77) | 327 (3.94) | 276 sh (4.11) |
| | | 280 (4.25) |
| | | 286 (4.22) |
| | | 290 sh (4.06) |
| | | 295 (3.97) |
| | | 297 (3.98) |
| | | 301 (3.61) |

Table 3. *Chemical Shifts (δ), Maximum Chemical Shift Differences (Δδ) Induced by Eu(fod)$_3$ for Selected H-Atoms in the $^1$H-NMR Spectrum of* **4b**

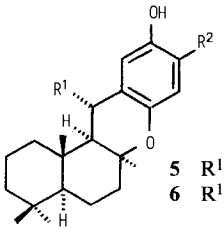
| | H–C(20) | H–C(14) | $CH_3COO$ | H–C(9) | $CH_3$(13) | $CH_3$(15) |
|---|---|---|---|---|---|---|
| $\delta$ | 6.53 | 4.83 | 2.30 | 1.80 | 0.82 | 1.13 |
| $\Delta\delta$ | 0.53 | 0.46 | 0.62 | 0.30 | 0.10 | 0.00 |



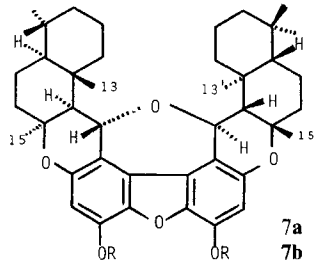
**1** X = H
**2** X = Cl
**3** X = Br



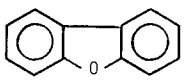
**4a** R = H
**4b** R = Ac



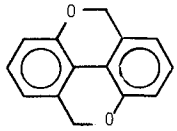
**5** $R^1$ = OMe, $R^2$ = OH
**6** $R^1$ = $R^2$ = H



**7a** R = H
**7b** R = Ac



**8**



**9**

with **4b** the europium ion appeared to be placed between the oxygen atoms of the pyran ring and the phenyl acetate moiety. The induced shifts were small, but significantly the signal for $CH_3$(13) was shifted by 0.1 ppm while the $CH_3$(15) signal was not shifted at all *(Table 3)*. The opposite would have to be the case if **7b** were the correct structure.

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## Experimental Part

The sponge *H. eubamma* was collected in Tahiti, French Polynesia, and preserved in EtOH. Further extraction with EtOH and partial solvent removal from the combined extracts led to an aq. residue which was partitioned with cyclohexane. After removal of cyclohexane, 2 g of the org. concentrate was chromatographed on *Sephadex LH-20*. Fraction 4 was further purified on a silica gel

*HF-60* column. Elution with cyclohexane/EtOAc 95:5 yielded **4a** (30 mg, 1.5% of extract) as a white amorphous powder, which was crystallized from $CH_2Cl_2$ as colorless crystals, m.p. 234–240°, $[\alpha]_D^{24°} = -98 \pm 1.7°$ ($CHCl_3$, $c = 2.37$, 7.43). UV (EtOH): *Table 2.* IR ($CCl_4$): 3560, 3420, 2950, 2920, 2870, 2840, 1625, 1600. $^1$H-NMR ($CDCl_3$): 6.42 (*s*, 2 H); 5.30 (br., exchangeable, 2 H); 4.85 (*d*, 2 H); 1.82 (*d*, 2 H); 1.13, 0.95, 0,87, 0.84 (4 *s*, 6 H each). $^{13}$C-NMR ($CDCl_3$): *Table 1* for 15 sesquiterpene C-atoms; moreover: 147.7 (C(21)); 145.0 (C(19)); 133.1 (C(18)); 117.3 (C(17)); 106.0 (C(16)); 105.0 (C(20)). MS (HR): found 654.3920; calcd. for $C_{42}H_{54}O_6$ 654.3922. MS: 654 (99), 639 (100), 503 (99), 463, 351, 311, 271, 202, 137.

*Bispuupehenone* (**4a**) *from Puupehenone* (**1**). The reagent was prepared from 0.8 g of $K_3Fe(CN)_6$, 0.3 g of KOH and 20 ml of $H_2O$. To 30 mg of **1** in 1 ml of benzene was added 0.4 ml of the oxidant and stirred under Ar at 20° for 15 min. $H_2O$ was added, and the org. phase was separated and combined with a further benzene extract of the aq. phase, resulting after solvent removal in 23 mg of benzene soluble residue. Chromatography on silica-gel plates with cyclohexane/EtOAc 95:5 yielded 9 mg (30%) of **4a** identical in all spectral characteristics with natural **4a**.

*Bispuupehenone diacetate* (**4b**), Prepared from **4a** with $Ac_2O$/pyridine, 20°. $^1$H-NMR ($CDCl_3$): 6.53 (*s*, 2 H); 4.83 (*s*, 2 H); 2.3 (*s*, 6 H); 1.8 (*s*, 2 H); 1.13 (*s*, 6 H); 0.95 (*s*, 6 H); 0.87 (*s*, 6 H); 0.82 (*s*, 6 H). $^{13}$C-NMR ($CDCl_3$): 168.1, 147.3, 139.0, 137.4, 118.2, 112.1, 112.0, 77.8, 70.3, 57.6, 54.9, 41.9, 40.2, 39.3, 38.0, 33.8, 33.4, 27.7, 22.1, 20.7, 18.3, 18.3, 14.3. MS (CI/$NH_3$): 756 (100, $M$NH$_4^+$), 739 ($M$H$^+$), 738 ($M^+$). MS: 655, 697.

## REFERENCES

[1] *P.R. Berquist & R.J. Wells,* in 'Marine Natural Products: Chemical and Biological Perspectives', Vol. *5*, P.J. Scheuer, Ed., Academic Press, New York, in press.

[2] *B.N. Ravi, H.P. Perzanowski, R.A. Ross, T.R. Erdman, P.J. Scheuer, J. Finer & J. Clardy,* Pure Appl. Chem. *51*, 1893 (1979).

[3] *P. Djura, D.B. Stierle, B. Sullivan, D.J. Faulkner, E. Arnold & J. Clardy,* J. Org. Chem. *45*, 1435 (1980).

[4] *E. Breitmeier & W. Voetter,* '$^{13}$C-NMR Spectroscopy', Verlag Chemie, Weinheim 1978, p. 193.

[5] 'UV Atlas of Organic Compounds', Plenum Press, NY 1966, Spectrum H 14/1.

[6] *P.S. Dewar, A.R. Forrester & R.H. Thomson,* J. Chem. Soc. (C) *1971*, 3950.