Tetrahedron Letters,Vol.23,No.8,pp 817-820,1982 0040-4039/82/080817-04$03.00/0
Printed in Great Britain

NEW NOR-SESQUITERPENOIDS OF APPARENT NARDOSINANE ORIGIN FROM THE PACIFIC SOFT-CORAL PARALEMNALIA THYRSOIDES

Richard R. Izac, Philippe Schneider, Margaret Swain and William Fenical*

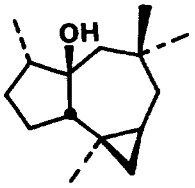
Institute of Marine Resources
Scripps Institution of Oceanography
La Jolla, California 92093

Summary: Two new nor-sesquiterpenoids, 5 and 6, apparently related to the nardosinane class, are reported from the alcyonacean soft-coral *Paralemnalia thyrsoides* collected in Palau.

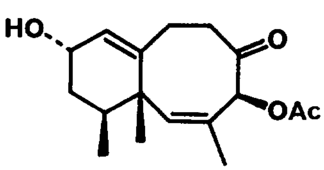
The widely-distributed soft-corals of the genera *Lemnalia* and *Paralemnalia* (Octocorallia, Alcyonaceae) are well known to contain sesquiterpenoids of several novel types, i.e. africanol (1)[1] and the neolemnane type (as in 2)[2], but the more common components of these soft-corals are rearranged sesquiterpenoids of the nardosinane class, typified by 3 (2-desoxylemnacarnol).[3,4] Recently, Bowden *et al*. suggested structure 4 for a unique nor-sesquiterpenoid isolated from collections of *L. africana* made in north Australia.[5] In this paper we wish to report the structures of two similar nor-sesquiterpenoids, 5 and 6, isolated from extracts of *Paralemnalia thyrsoides* Ehrenberg collected in Palau, Western Caroline Islands.

Standard silica gel column and high-performance liquid chromatography of the $CHCl_3$/MeOH extract of freeze-dried *P. thyrsoides* yielded 3[3], 5 and 6 as 0.9, 0.7, and 0.6% of the extract respectively.[6] The nor-ketone 5, mp 87-89°, analyzed for $C_{14}H_{20}O_3$ by mass spectrometry and off-resonance ^{13}C NMR (Table 1), and showed $[\alpha]_D$ -298° (c 1.0, $CHCl_3$). Broad infrared absorption at 1706 cm^{-1}, coupled with ^{13}C NMR bands at 202.1 and 206.3 ppm confirmed 5 as a diketone. The remaining oxygen atom was also securely established as part of a trisubstituted epoxide based upon highly characteristic ^1H and ^{13}C NMR bands (see Table 1).

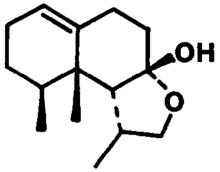
Evaluation of the unsaturation inherent in the molecular formula for 5, considering the unsaturation from ketone and epoxide functionalities, indicated that 5 was bicarbocyclic. Analysis of ^1H NMR decoupling data allowed all protons to be confidently assigned (see Table 1). Two isolated sets of mutually-coupled protons were readily discerned, those at C-1 through C-4, and those at C-6 through C-9. The C-1 epoxide proton was assigned as pseudoequatorial based upon a single 4.4 Hz coupling with the equatorial proton at C-2. Molecular models indicated a dihedral angle of *ca*. 90° between the C-1 proton and the axial C-2 proton thus accounting for the lack of coupling. Through decoupling all protons in the C-1 - C-4 region were confidently assigned. The C-4



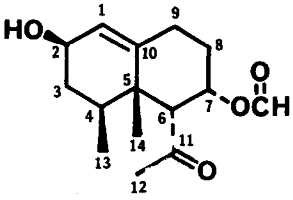
1



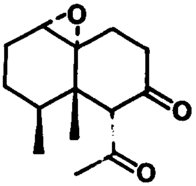
2



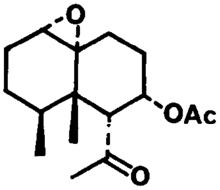
3



4



5



6

proton was assigned as axial based upon its coupling constants to the adjacent methylene at C-3 (11.7, 4.4 Hz). ^{1}H NMR experiments also delineated the locations and stereochemistry of the substituents at C-6 through C-9. A methyl ketone constellation was placed in an axial configuration at C-6. The ketone methyl showed slight coupling to the C-6 proton at δ 3.55, and this proton was confidently assigned as equatorial based upon a 1.4 Hz "W"-coupling with the C-8 equatorial proton. The consistent low-field shifts of the C-6 and C-8 protons confirmed the location of the second ketone at C-7.

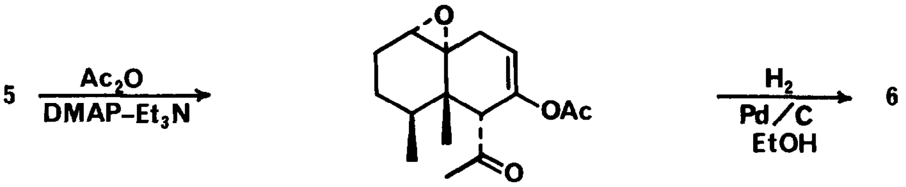
To confirm the stereochemical assignments derived from decoupling data, experiments involving "Difference nOe" spectroscopy were conducted. Irradiation of the C-13 methyl doublet produced enhancement (in excess of 10%) of the proton at C-6, thus indicating the methyl group and C-6 proton to be equatorial substituents.[7] The lack of enhancement of the adjacent methyl (C-14) confirmed it to be axially substituted.

The related keto-acetate 6, mp. 83-84°, analyzed for $C_{16}H_{24}O_4$ and showed $[\alpha]_D$ -68.5° (c 1.0, $CHCl_3$). The ^{1}H NMR features of this metabolite[8] were very similar to those of 5, with the exception that this compound possessed a secondary acetate ester. As with 5, ^{1}H NMR spin-decoupling experiments were critical in assigning structure 6. Protons at C-1 through C-4 were interrelated as in 5, and the methyl ketone constellation was also determined to be intact and positioned at C-6. The C-6 methine proton was observed at δ 3.25, and was coupled (J=6 Hz) to the acetate methine (C-7) at δ 5.35. Thus, the acetate 6 was conceived as the acetylated C-7 reduction product of the diketone 5.

Again using "Difference nOe" techniques, the stereochemistry of the keto-acetate could be assigned. Irradiation of the bridgehead methyl (C-14) yielded significant enhancement of the protons at C-6 and C-7. This result clearly showed that C-14 is an axial methyl, and that the C-6 and C-7 protons are on the same face of the molecule (C-6 = equatorial, C-7 = axial).

To conclusively interrelate 5 and 6, diketone 5 was converted to 6 in two steps. Forced acetylation of 5 with dimethylaminopyridine resulted in the production of the enol-acetate at C-7, with enolization proceeding, unexpectedly, toward C-8.[9] Assignment of structure 7 for this enol-acetate was reinforced by ^{13}C NMR (Table 1). Hydrogenation of 7 yielded 6, which was identical in all respects with the natural product.

Nor-sesquiterpenoids are found in several terrestrial sources, and in at least one case loss of a methyl group from an apparent isopropyl substituent has been reported.[10]. This work, and the report of Bowden et al., appear to provide the first examples of nor-sesquiterpenoids from marine sources.



7

TABLE 1[11]

^{1}H and ^{13}C NMR Assignments for compounds 5 - 7

C#	^{1}H (C_6D_6, 360 MHz)	^{13}C ($CDCl_3$, 20 MHz)		
	5	5	6	7
1	2.43 d (4.4)eq	57.2	57.3	57.3
2	1.34 dddd (15.7, 7.0, 4.4, 1.7)eq 1.67 ddd (15.7, 10.8, 9.1)ax	22.0†	21.5*	22.3*
3	0.72 m	24.6†	24.5*	21.5*
4	2.02 ddq (11.7, 4.4, 6.8)ax	29.3	30.1	31.5
5	———	43.6	40.3	40.9
6	3.55 bd (1.4)eq	73.2	57.8	61.8
7	———	202.1	71.1	146.3
8	2.24 dddd (14.6, 5.4, 1.4, 1.4)eq 3.21 ddd (14.6, 13.3, 7.8)ax	36.7*	29.2*	114.1
9	1.03 ddd (14.2, 7.8, 1.4)eq 1.92 ddd (14.2, 13.3, 5.4)ax	30.5*	24.3*	22.3*
10	———	61.8	62.1	61.0
11	———	206.3	208.1	208.6
12	1.93 bs	32.5	33.6	28.3
13	0.43 d (6.8)	15.7§	15.7§	15.6§
14	0.52 s	17.7§	17.3§	16.8§
OAc			170.1 21.2	169.1 20.9

*§† indicate assignments may be reversed

Acknowledgements

We wish to acknowledge generous financial support for this research from the Oceanography Section of the National Science Foundation under grant OCE 80-14167. Research onboard R/V ALPHA HELIX in Palau was also a result of NSF funding. We are grateful for the taxonomic expertise provided by Dr. J. Verseveldt in the assignments of Palauan soft-corals.

References and Notes

1. B. Tursch, J. C. Braekman, D. Dalose, P. Fritz, A. Kelecom, R. Karlsson and D. Losman, *Tetrahedron Lett.*, 747 (1974).
2. R. R. Izac, W. Fenical, B. Tagle and J. Clardy, *Tetrahedron*, **37**, 2569 (1981).
3. D. Dalose, J. C. Braekman, P. Georget and B. Tursch, *Bull. Soc. Chim. Belg.*, **86**, 47 (1977).
4. B. F. Bowden, J. C. Coll, and S. J. Mitchell, *Aust. J. Chem.*, **33**, 885 (1980).
5. B. F. Bowden, J. C. Coll, S. J. Mitchell, B. W. Skelton and A. H. White, *Aust. J. Chem.*, **33**, 2737 (1980).
6. This specimen (PSC-195) was collected, September, 1979, at North Kossol Passage, Palau, W.C.I.
7. Compound **5** was also isolated from collection PSC-75, identified as *Lemnalia africana* May.
8. For **6**, MS: M$^+$-HOAc, m/z obsd. 220.1451, calc. 220.1463; IR:($CHCl_3$)3021, 1740, 1705, 1447, 1370, 1242, 1164, 1136, 1036 and 985 cm^{-1}; ^{1}H NMR ($CDCl_3$, 360 MHz): δ 5.36 (1 H, ddd, J = 12.5, 6.5, 5.0 Hz), 3.25 (1 H, d, J = 6.2 Hz), 2.86 (1 H, d, J = 3.5 Hz), 2.34 (3 H, s), 2.03 (3 H, s), 1.11 (3 H, s), 0.79 (3 H, d, J = 7.0 Hz).
9. The direction of enolization in **5** is indicative of the atypical behavior of this β-diketone. Normal enolization involving C-6 appears to be precluded due to unfavorable steric interactions between the methyl ketone and the C-13 methyl group. Hence, **5** exists totally in the diketone form and shows only carbonyl absorption (306 nm) in the UV region.
10. T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Lett.*, 3663 (1966).
11. Proton NMR assignments were made by analysis of spin-decoupling and nOe enhancement experiments. Coupling constants, in Hertz, are shown in parentheses. Carbon NMR assignments are based upon off-resonance multiplicities and residual coupling constant correlations. The asterisk indicates that assignments in a vertical column may be interchanged.

(Received in USA 22 June 1981)