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Norasperenals A-D, Unprecedented Trisnorditerpenoids from the Caribbean Gorgonian *Eunicea* sp.

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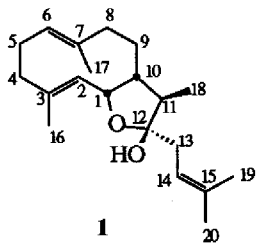
Summary: Four new trisnorditerpenoids, norasperenals A-D (**4-7**), and two previously reported cyclic ketals have been isolated from an undescribed species of the Caribbean gorgonian *Eunicea*. The structures of the new compounds, determined by combined spectral methods, illustrate a unique loss of a C_3 fragment from a regular diterpenoid precursor.

Gorgonian corals (Octocorallia; Gorgonacea) are soft-bodied marine invertebrates which are conspicuous inhabitants of predator-rich tropical marine habitats. As part of our continuing interests in the chemical defensive adaptations of these organisms, we have recently focussed upon those animals of the chemically-complex genus *Eunicea*.[1] From a collection of an apparently undescribed *Eunicea* species collected in the Florida Keys,[2] we have isolated four new trisnorditerpenoids, norasperenals A-D (**4-7**), along with the related *Eunicea* metabolites asperketals A and B (**1-2**).[3] The structures of norasperenals A (**4**) and B (**5**) were elucidated by spectral analysis and comparison of appropriate NMR data with that from the asperketals. Due to the highly unstable nature of norasperenals C (**6**) and D (**7**), these compounds could not be fully characterized. To the best of our knowledge, these are the first examples of trisnorditerpenoids from gorgonians.

Gorgonians were collected at the Florida Keys, in July 1987. The animals were immediately frozen, freeze-dried, and exhaustively extracted with CH_2Cl_2. The condensed extract (17 g) was initially fractionated by silica vacuum flash chromatography. Asperketals A and B (2.3 and 0.2% of the extract) were isolated by HPLC from the fraction eluted with 10% EtOAc/ isooctane. Norasperenals A-D (1.0, 0.2, 0.4, and 0.02%, respectively) were eluted with 20% EtOAc/ isooctane and purified by C-18 reverse phase HPLC (100% MeOH).

Norasperenal A (**4**) was isolated as a white solid; mp 101.5-102.5°, which analyzed for $C_{17}H_{24}O_2$ by high resolution mass and ^{13}C NMR spectrometry. A low field carbon NMR signal at δ 187.8 (d) and a corresponding proton signal at δ 10.56 (d, J = 8.3 Hz) showed the presence of an aldehyde (Table). An absorption band at 1655 cm^{-1} in the IR spectrum and a large proton coupling constant (8.3 Hz) indicated that the aldehyde was in conjugation with a double bond. Many of the signals in the ^{13}C NMR spectrum of **4** were similar to those from asperketal A (**1**). A combination of ^1H NMR COSY and XHCORR experiments revealed **4** to possess the same 10-membered ring as in **1**. The remaining part was also determined by spectral analysis. An XHCORR experiment assigned the carbon signal at δ 101.3 (d) to the α carbon of the double bond conjugated with the aldehyde. The unusually large difference between the chemical shifts of the α and β {δ 180.2 (s)} carbons indicated the attachment of an oxygen to the β carbon. Therefore, the β carbon must be connected to the C-1 carbon by an ether linkage. The low field chemical shift of the C-11 proton (δ 2.10) indicated its connection to the double bond. Thus, the connectivity of the α,β-unsaturated aldehyde was fully determined. Other information which supported their connectivity was a COLOC experiment (optimized for 6 Hz), which showed long range couplings of the β carbon with the olefinic proton at δ 5.22 and the methyl protons at δ 0.77. Thus, norasperenal A



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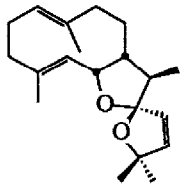

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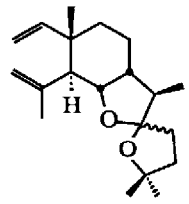

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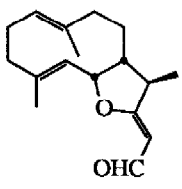

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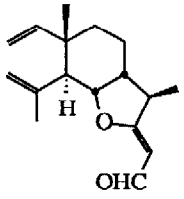

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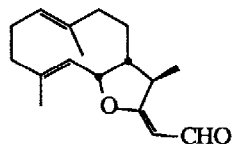

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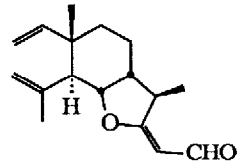

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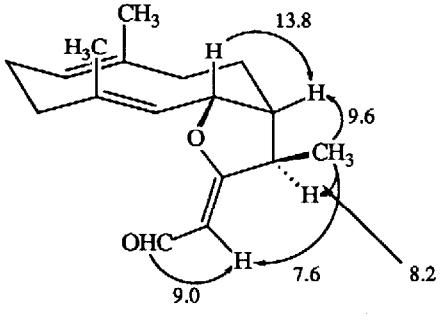
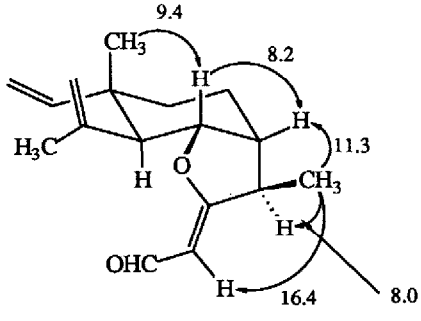
was assigned as a trisnorditerpenoid in which the terminal three carbons (C-15, -19, and -20) of the diterpene were removed.[4]

Norasperenal A has three double bonds at the Δ^2, Δ^6 and Δ^{12} positions, and three asymmetric methine centers (C-1, -10, and -11). The high field shifts of the C-16 carbon (δ 16.7) and the C-17 protons (δ 1.18) revealed **4** to possess the ***E*** configurations for both the Δ^2 and Δ^6 double bonds. The stereochemistries of other centers were assigned by ^{1}H NMR NOEDS methods (see Figure below). Thus, the relative stereochemistry of norasperketal A was unambiguously determined as 2(***E***), 6(***E***), 12(***Z***), 1**S***, 10**R***, and 11**R***.





Results of a ^{1}H NMR NOEDS Experiment for Norasperenals A (**4**) and B (**5**). Numbers are % Enhancements.

Norasperenal B (**5**) was isolated as a white solid; mp 123-124.5°, and analyzed for $C_{17}H_{24}O_2$.[4] Spectral analyses readily indicated **5** to possess the same α,β-unsaturated aldehyde as **4**; carbons at δ 188.0 (d) and 102.6 (d), an aldehyde proton at δ 10.47 (1H, d, 8.3), and an IR absorption at 1655 cm^{-1}. The structure of the remaining part was also determined by similar NMR analyses. Several signals in the ^{13}C NMR spectrum of **5** were very similar with those of the

^1H and ^{13}C NMR Spectra for Norasperenals A-D (4-7)

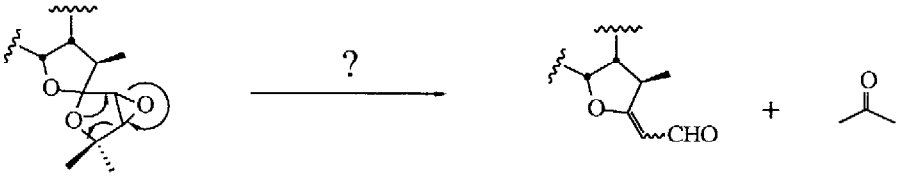
carbon #	4 ^1H	4 ^{13}C	5 ^1H	5 ^{13}C	6 ^1H	6 ^{13}C	7 ^1H
1	4.89 (1H,dd,9.4,6.1)	82.3 CH	4.25 (1H,dd,10.9,7.4)	83.9 CH	4.94 (1H,dd,9.8,4.8)	80.6 CH	4.23 (1H,dd,7.8,6.6)
2	4.66 (1H,brd,9.4)	125.6 CH	1.56 (1H,d,11.0)	41.8 CH[c]	4.75 (1H,brd,9.7)	126.0 CH	1.88 (1H,d,8.0)
3	—	136.0 C	—	143.2 C	—	135.3 C	—
4	1.95 - 1.87 (1H,m)[b]	39.9 CH2	5.01 (1H,brs)	113.6 CH2	1.98 - 1.85 (1H,m)[b]	39.7 CH2	4.64 (1H,brs)
	1.72 (1H,m)[b]		4.64 (1H,brs)		1.83 - 1.68 (1H,m)[b]		4.61 (1H,brs)
5	1.95 - 1.87 (2H,m)[b]	25.7 CH2	4.87 (1H,dd,10.8,1.1)	110.9 CH2	1.98 - 1.85 (2H,m)[b]	25.5 CH2	4.89 (1H,brd,10.3)
			4.80 (1H,dd,17.5,1.1)				4.82 (1H,brd,17.6)
6	4.63 (1H,m)[b]	127.5 CH	5.57 (1H,dd,17.5,10.8)	147.5 CH	4.65 (1H,brd,7.6)	127.4 CH	5.66 (1H,dd,17.5,10.9)
7	—	137.9 C	—	40.7 C	—	137.7 C	—
8	2.16 (1H,m)[b]	36.6 CH2	1.02 (1H,ddd,13.7, 13.7,4.3)	33.0 CH2	2.23 (1H,m)[b]	37.0 CH2	a
	1.45 (1H,m)[b]		0.90 (1H,ddd,13.6,4.7, 2.8)		1.46 (1H,m)[b]		a
9	1.45 (1H,m)[b]	31.5 CH2	1.30 (1H,dddd,14.1, 14.1,5.9,4.9)	19.5 CH2	1.74 (1H,m)[b]	32.6 CH2	a
	0.97 (1H,m)[b]		1.13 (1H,m)[b]		0.85 (1H,m)[b]		a
10	1.50 (1H,m)[b]	48.3 CH	1.42 (1H,m)[b]	38.7 CH[c]	1.60 (1H,m)[b]	49.6 CH	a
11	2.10 (1H,m)[b]	47.7 CH	2.15 (1H,ddq,12.1,1.3, 6.6)	53.3 CH	2.92 (1H,m)[b]	47.3 CH	2.62 (1H,m)[b]
12	—	180.2 C	—	179.6 C	—	183.3 C	—
13	5.22 (1H,d,8.3)	101.3 CH	5.22 (1H,dd,8.3,1.5)	102.6 CH	5.87 (1H,d,7.3)	102.2 CH	5.89 (1H,d,7.5)
14	10.56 (1H,d,8.3)	187.8 CH	10.47 (1H,d,8.3)	188.0 CH	9.77 (1H,d,7.3)	188.4 CH	9.88 (1H,d,7.7)
16	1.32 (3H,brs)	16.7 CH3	1.64 (3H,d,0.6)	25.4 CH3	1.29 (3H,brs)	16.5 CH3	1.60 (3H,brs)
17	1.18 (3H,brs)	20.7 CH3	0.67 (3H,s)	16.8 CH3	1.21 (3H,brs)	21.4 CH3[d]	0.73 (3H,s)
18	0.77 (3H,d,7.1)	18.4 CH3	0.66 (3H,d,6.7)	14.9 CH3	0.91 (3H,d,6.9)	19.9 CH3[d]	0.92 (3H,d,6.8)

^1H NMR spectra were recorded at 360 MHz in C_6D_6 solution. ^1H NMR assignments were aided by spin decoupling and COSY experiments. *J* values are reported in Hz and chemical shifts are given in δ units. ^{13}C NMR spectra were recorded at 50 MHz in C_6D_6 solution. Chemical shifts are given in δ units. Multiplicities were determined from DEPT experiments. ^{13}C NMR assignments for **4** were made by XHCORR and COLOC (optimized for 6 Hz) experiments. Assignments for others were made by comparison with **4**. [a]Nonassignable resonances. [b]Coupling constants were not determined. [c,d]Signals within a column may be reversed.

previously reported asperketal F (**3**).[3] Proton NMR COSY experiments revealed **5** to possess the same divinylcyclohexane ring as found in this latter metabolite. Thus, compound **5** was identified as an analogous trisnorditerpenoid possessing the "elemane" type carbon skeleton. The stereochemistry of the asymmetric centers were again determined by ^{1}H NMR NOEDS methods (see previous Figure), leading to assignments of the relative configurations as 12(*Z*), 1**S***, 2**S***, 7**S***, 10**R***, and 11**R***.

Two highly unstable metabolites, norasperenals C (**6**) and D (**7**) were also isolated as oils. The ^{1}H and ^{13}C NMR (**6** only) and COSY NMR data for **6** and **7** were highly compatible with **4** and **5**, respectively. The only significant differences were downfield shifts of the C-11, -13, and -18 protons and the upfield shift of the C-14 proton in the ^{1}H NMR spectra (Table), indicating the alternative ***E*** configurations for the Δ^{12} double bonds. Norasperenals C and D (**6**, **7**) were confirmed as the geometrical isomers of **4** and **5** by the observation of their slow geometrical isomerization to mixtures of **4** and **6**, and **5** and **7** even at -20° in benzene. Norasperenals C and D were highly unstable metabolites which precluded their complete characterization.

The norasperenals appear to be produced by the loss of a C_3 fragment from a precursor closely related to the asperketals. One plausable explanation is the epoxidation of the C13-C14 olefin in asperketal B followed by multiple ring cleavage as shown below.



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REFERENCES

1. J. R. Pawlik, M. T. Burch and W. Fenical, *J. Exp. Mar. Biol. Ecol.* **108**, 55 (1987).

2. Specimens of this *Eunicea* sp., under the code Fenical F87-32, are on deposit in the octocoral collection, Smithsonian Institution, Washington DC, under the curatorship of Dr. Frederick M. Bayer. He concluded that the specimens were morphologically distinct from the described species of *Eunicea*.

3. J. Shin and W. Fenical, *J. Org. Chem.*, **53**, 3271 (1988).

4. Additional spectral data for **4**: HREIMS obs. 260.1769, calc. 260.1776; IR (film) 2920, 1655, 1625, 1400, 1170, 1125, 1035 and 890 cm^{-1}; UV (MeOH) 271 nm (ε18500); $[\alpha]_D$+131° (c 1.2, MeOH); for **5**: HREIMS obs. 260.1776 calc. 260.1776; IR (film) 2930, 1655, 1620, 1460, 1405, 1390, 1240, 1185, and 960 cm^{-1}; UV (MeOH) 271 nm (ε17000); $[\alpha]_D$-23° (c 0.5, MeOH).

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