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ISOREISWIGIN, A NEW DITERPENE FROM A MARINE SPONGE

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ABSTRACT.—The structure of isoreiswigin [3], a new perhydroazulene diterpene, has been determined by combined 1D and 2D nmr and mass spectral techniques.

Earlier we reported the isolation of two novel antiviral diterpenes, reiswigins A [1] and B [2], from the sponge *Epipolasis reiswigi* Topsent (Demospongiae) (1). Herewith we wish to report a third, closely related, diterpene 3 which was isolated in minute amounts together with compounds 1 and 2. Compound 3, designated isoreiswigin, was obtained pure following repeated vacuum flash chromatographies on Si gel H, followed by normal and reversed-phase hplc (20 mg, 0.03% dry wt of the sponge).

Isoreiswigin was assigned molecular formula $C_{20}H_{30}O_3$ by hreims (found 318.2167; +2.7 mmu). The ^{13}C -nmr spectrum showed three singlet carbonyl resonances at 202.3, 204.9, 210.1 ppm. These, considered along with ir absorptions at 1738, 1730, 1710 (sh), and 1642 cm^{-1} , established the presence of three ketone functionalities, probably a pentanone, an enone, and a simple ketone. A DEPT experiment showed the remaining carbon resonances to consist of two quaternary (one sp^2 and one sp^3), five methine (one sp^2 and four sp^3), five methylene, and five methyl resonances. With six sites of unsaturation required by the molecular formula and four accounted for by the ^{13}C -nmr data, 3 was determined to be a bicyclic

diterpene. The 1H -nmr data clearly established the same functionalities as in reiswigin A [1] plus one additional carbonyl (which replaces one of the methylenes of 1). Furthermore, the 1738 cm^{-1} absorption of the latter carbonyl group suggested it to be in a cyclopentanone ring. The trivial 9-oxo-reiswigin structure was, however, excluded by a COSY experiment (2). The latter spectrum pointed clearly to a seven-spin system $=CCH_2CH_2CHCH_2CO-$ (Table 1) which does not exist in 1 and 2. In addition, three other spin systems (C-17-C-20; C-10, C-13-C-15; and C-3-C-12) were further deduced from the 1H - 1H correlation spectrum. The latter protonated sites were further confirmed by a TOCSY experiment (3) (Table 1). A one-bond 1H - ^{13}C correlation experiment, HMQC (4), established all one-bond proton-carbon connectivities determining inter alia the five methylene pairs (C-5, -6, -8, -15 and -17). As all protons (and carbons) were separated in the 500 MHz spectrum, the complete carbon skeleton of 3 could have been established unequivocally from a multiple bond ($^2J_{CH}$ to $^4J_{CH}$) proton-carbon connectivity experiment (HMBC) (5). All correlations observed in this experiment are presented in Table 2. As seen from

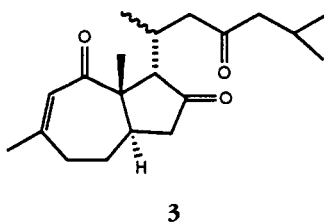
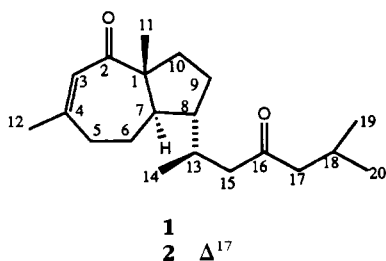


TABLE 1. ^1H -nmr Data (500 MHz, CDCl_3) of Isoreiswigin [3].

Proton	δ_{H} (m, J in Hz)	coupled to H (^1H - ^1H COSY)	coupled to H (TOCSY) ^a
H-3	6.07 (s)	Me-12	
H-5 α	1.97 (m) ^b	5 β , 6 α , 6 β	5 β , 6 α , 6 β
H-5 β	1.57 (dt, 12.5, 4.3)	6 α , 6 β	6 α , 6 β
H-6 α	1.30 (m)	6 β , 7	6 β , 7
H-6 β	1.77 (m)	7	
H-7	2.05 (m)	8 α , 8 β	
H-8 α	2.80 (dd, 18.5, 4.9)	8 β	5 β , 6 α , 6 β , 7, 8 β
H-8 β	2.55 (dd, 18.5, 11.9)		5 β , 6 α , 6 β , 7, 8 α
H-10	1.70 (m)	13	13, Me-14
Me-11	0.99 (s)		
Me-12	1.97 (s) ^b		
H-13	2.10 (m)	Me-14, 15	Me-14
Me-14	0.85 (d, 6.5)		15
H-15	2.28 (dd, 19.5, 7.5)	15'	
H-15'	2.12 (dd, 19.5, 8.5)		
H-17	2.17 (d, 6.5)	18	18, Me-19, Me-20)
H-18	2.04 (m)	Me-19, Me-20	Me-19, Me-20
Me-19	0.83 (d, 6.6)		
Me-20	0.82 (d, 6.6)		

^aMixing time of 0.09 sec.^bH-5 α overlaps partially with Me-12.TABLE 2. ^{13}C -nmr Data^a (125 MHz) for Isoreiswigin [3].

Carbon	δ_{C}	^1H - ^{13}C Connectivities ^b
C-1	56.7 (s)	H-8, H-10
C-2	204.9 (s)	H-3, H-11
C-3	132.4 (d)	H-5, H-12
C-4	147.4 (s)	H-12
C-5	34.8 (t)	H-6
C-6	24.1 (t)	H-5
C-7	41.0 (d)	H-6, H-8, H-10
C-8	43.9 (t)	H-7, H-13
C-9	202.3 (s)	H-8
C-10	48.4 (d)	H-6, H-8, H-14
C-11	19.4 (q)	H-10
C-12	21.6 (q)	
C-13	29.5 (d)	H-14
C-14	19.6 (q)	H-13
C-15	45.6 (t)	H-14
C-16	210.1 (s)	H-13, H-17
C-17	52.6 (t)	H-19, H-20
C-18	24.4 (d)	H-17
C-19	22.5 (q)	H-17
C-20	22.4 (q)	H-17

^aMultiplicity determined by a DEPT experiment.^b ^1H - ^{13}C correlations correspond to 2-bond and 3-bond connectivities (HMBC experiment).

the structures the difference in the skeletons of compounds **1** (and **2**) and **3** is only in the position of the angular methyl (C-11), requiring a different rearrangement of the geranylgeraniol from the one leading to compounds **1** and **2**.

The suggested structure is consistent with the major mass spectral fragments (m/z , mmu): $\text{C}_{19}\text{H}_{27}\text{O}_3$ (303.1998, -3.8), $\text{C}_{15}\text{H}_{22}\text{O}_2$ (234.1627, -0.8), $\text{C}_{16}\text{H}_{16}\text{O}_2$ (192.1203, 5.3), and $\text{C}_8\text{H}_{15}\text{O}$ (127.1113, 0.9) (Figure 1) (1). The relative stereochemistry of three of the chiral centers of the molecule, C-1, C-7, and C-10, was assigned by an nOe difference experiment summarized in Figure 1.

The recent synthesis of reiswigin A [**1**] has confirmed the absolute configuration of C-13 (6). However, the configuration of C-13 in **3** has yet to be established.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.— Mass spectra were measured with a Finnigan

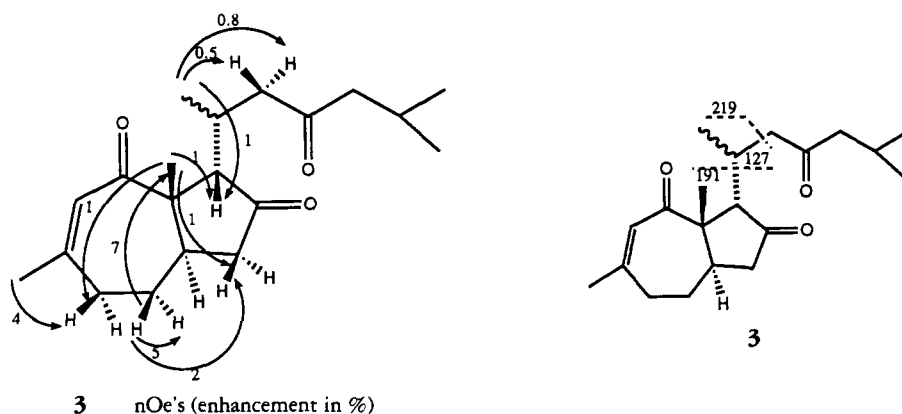


FIGURE 1. Major mass spectrometer fragmentations and nOe's of **3**.

4020 quadrupole spectrometer equipped with a data system, and hrms on a VG-70, VSEQ instrument. Optical rotation was measured on a Perkin-Elmer 241 polarimeter with a 10 cm microcell in CHCl_3 . Ir spectra were recorded in CHCl_3 on a Perkin-Elmer model 1600FT-IR instrument, uv spectra in heptane solution on a Varian Cary 219 spectrophotometer, and nmr spectra in CDCl_3 solution on a Bruker 500 MHz spectrometer (TMS as internal reference).

EXTRACTION AND PURIFICATION.—A sample of the sponge *E. reisiwigi* (55 g dry wt) was extracted with heptane to give, after evaporation, a gummy crude extract (3 g). Chromatography on Si gel with heptane and 10% EtOAc gave reisiwigin A [**1**] (1.15 g, 2% yield of the dry lyophilized sponge); with 15% EtOAc, reisiwigin B [**2**] (90 mg, 0.16%); and with 17% EtOAc, isoreisiwigin [**3**] (ca. 80% pure, 40 mg). Hplc first on a Si gel column eluted with heptane-EtOAc (9:1) and then on an RP-18 column eluted with $\text{MeOH-H}_2\text{O}$ (9:1) gave pure **3** (20 mg, 0.03% yield of the lyophilized sponge) as a foaming oil.

ISOREISWIGIN.— $[\alpha]^{25}_{\text{D}} + 22^\circ$ ($c = 1.5$, CHCl_3); λ_{max} (heptane) 240 (2000) nm; ir (CHCl_3) 2973, 1738, 1730, 1710, 1642, 1586, 1140 cm^{-1} ; hrms $[\text{M}]^+$ 318.2167 (calcd for $\text{C}_{20}\text{H}_{30}\text{O}_3$); ms m/z (%) 319 (36), 318 (12), 303 (6), 234 (4), 192 (3), 108 (8); ^1H nmr see Table 1; ^{13}C nmr see Table 2.

LITERATURE CITED

1. Y. Kashman, S. Hirsch, F. Koehn, and S. Cross, *Tetrahedron Lett.*, **28**, 5461 (1987).
2. K. Nagayama, A. Kumar, K. Wuthrich, and R.R. Ernst, *J. Magn. Reson.*, **40** 321 (1980).
3. M.W. Edwards and A. Bax, *J. Am. Chem. Soc.*, **108**, 918 (1986).
4. A. Bax and M.F. Summers, *J. Am. Chem. Soc.*, **108**, 8083 (1986).
5. M.F. Summers, L.G. Marzilli, and A. Bax, *J. Am. Chem. Soc.*, **108**, 4285 (1986).
6. B.B. Snider and Ke. Yang, *J. Org. Chem.*, **55**, 4392 (1990).

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