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MUQUBILIN, A NEW C_{24}-ISOPRENOID FROM A MARINE SPONGE

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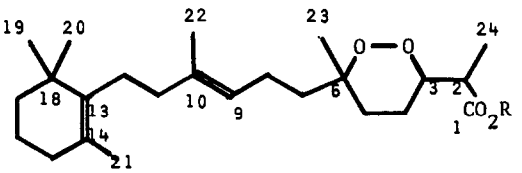
Abstract

The Red Sea sponge Prianos sp. contains a cyclic peroxide C_{24} - nor sesterterpene, Muqubilin (1) The structure of 1 was deduced from spectroscopic data and by chemical degradation.

In our continuing search for physiologically active marine metabolites we have isolated from a brown sponge of the genus Prianos[1], collected at Marsa el Muqubila in the Gulf of Eilat, on the Red Sea, four closely related C_{24}-isoprenoids which represent a new type of C_{24} nor sesterterpenes.

Structure 1, which we have named muqubilin has been assigned to the major constituent of the new compounds.



1 R=H

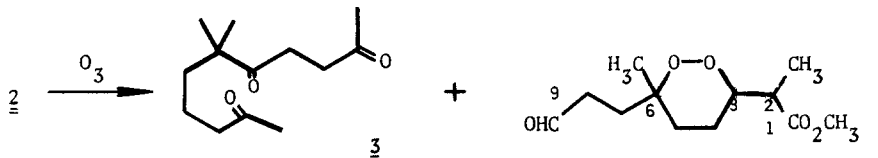
2 R=CH_3

Extraction of the freeze-dried sponge (petrol ether, Soxhlet) and subsequent chromatography (Sephadex LH-20, CH_2Cl_2/hexane, 2:1) yielded mixtures of four carboxylic acids and one or two[2] of their corresponding methyl esters. Repeated chromatographies (on LH-20 and Silica-gel) afforded pure 1 (homogeneous on TLC, R_F=0.45PhH/EtOAc, 1:1) as a yellowish oil in ca. 1.5% dry weight[3]. Muqubilin (1)[4] has a molecular formula $C_{24}H_{40}O_4$. The infrared spectrum of 1 indicated the presence of a carboxylic group (3660-2280br, 1710 cm^{-1}), which could be esterfied easily by CH_2N_2 to give the corresponding methyl ester 2. (Compound 2 is one out of the two isolated natural methyl esters (vide supra)). The IR spectrum of 2 (1740 cm^{-1}) indicated the absence of other carbonyl or hydroxy groups. The ^{13}C-NMR spectrum of 1 contained a carboxyl signal at δ 180.1s, four olefin signals at 123.4d, 127.0s, 136.5s and 137.2s due to one tetra- and one trisubstituted double bond, and two signals for carbon atoms bearing oxygen at 80.3s and 81.0d. The ^{1}H-NMR spectrum confirmed the trisubstituted double bond (δ 5.16t, J=6.4Hz, 1H) and a >CH-O site (δ 4.06m,1H). We conclude from these data that muqubilin (1) is a carboxylic acid containing a cyclic peroxide, two double bonds and one carbocyclic ring.

The peroxide function was confirmed by positive colourification with N,N-dimethyl-p-phenyl-diamine hydrochloride[5], positive KI test, and by the possibility of reducing 1 (or 2) by either 5% $FeSO_4$ solution or H_2 over Pd-C[6].

The ^{1}H-NMR spectrum (270MHz) of 1 also contained six additional methyl signals at δ 1.06s (2Me's), 1.18s, 1.23d(J=7.1Hz), 1.63s and 1.65s. These six methyls suggested an isoprenoid character, despite the C_{24} rather than C_{25} formula. The functionalized terminus of muqubilin (1) which is $^{O}\!>\!^{3}CH^{2}CH(CH_3)^{1}CO_2H$, was elucidated by ^{1}H-NMR (δ 2.54br quintet J=8Hz collapsing into a doublet by irradiation at δ1.23) as well as by the mass spectrum which showed an easy loss of $C_3H_6O_2$ from M^+ and other fragments, resulting most likely from a MacLafferty rearrangement[4].

Ozonolysis of muqubilin's methyl ester (2) (hexane-ethylacetate, 2:1 at -40°), followed by short hydrogenation over 5% Pd-C, gave a mixture from which two main compounds were separated (3 and 4).[7]



Compound 3 was found to be 6,6-dimethylundecan-2,5,10-trione, identical in all respects to the same compound described by Scheuer as a degradation product of mokupalide[8]. Compound 3 established 13 carbon atoms of the hydrocarbon terminus of muqubilin, while 4 provided evidence for the rest of the molecule.

Compound 4, $C_{12}H_{20}O_5$[9] is an aldehyde (ν_{max}^{neat} 2720 and 1740 cm^{-1}) with a very informative mass spectrum m/e(%); 212(M^+-32,2) - loss of O_2, 156(M^+-$CH_3CH{=}C(OMe)OH$,19) and 99(156-CH_2CH_2CHO,14)- cleavage on both sides of the cycloperoxide ring, 88(100), 84(99-CH_3,45) and 57($CH_2CH_2CHO^+$,48). The ^{13}C-NMR spectrum is also in good agreement with the suggested structure: 201.8d(C-9), 184.0s(C-1), 81.3d(C-3), 79.2s(C-6), 51.9q(OMe), 42.7, 38.0, 31.8, 31.1, 23.1, 21.0q and 13.6q[10]. Full evidence for the structure of 4 was deduced, however, from the ^{1}H-NMR spectrum (270MHz): δ 1.25s(C_6-Me), 1.25d (J=7Hz, C_2-Me), 1.7m(4H, $H_{4,4'}$ and $H_{5,5'}$), 1.84m(2H, $H_{7,7'}$), 2.54dt(J=1.5 and 7.3Hz, $H_{8,8'}$), 2.67m(J=7Hz, H_2), 3.7s(OCH_3), 4.13brq(J=8.8 and 7Hz, H_3) and 9.78t(J=1.5Hz, H_9)- the assignments based on chemical shifts and intensive double irradiations. Obviously, elucidation of the structure of compound 4 determined also the remaining C_{11}-unit of 1 (and 2) and thereby concluded its structure.

Cyclic peroxides are quite rare in nature, although not unknown. A peroxide similar to 1 was recently described by Faulkner[11] as part of plakortin, an antibiotic isolated from a marine sponge. The carbocyclic end of the molecule, which is more abundant in natural products, was also found recently by Scheuer in another marine sponge matabolite, namely, mokupalide[8,12].

Acknowledgement: We wish to express our appreciation to Dr. Y. Loya and Dr. Y. Benayahu for collecting the sponge and to Dr. Thomas for the sponge identification.

References and Notes

1. Order Halichondrida (Vosmaer), family Hymeniacidonidae (de Laubenfels), genus Prianos (Gray). The sponge possesses a yellowish-gray medula with yellow grains surrounded by a brown purple peel.
2. It is not yet clear whether or not an isomerization does occur.
3. The sponge contains considerable amounts of different steroids and glycerides.
4. ν_{max}^{neat} 3660-2280br, 2930, 2860, 1710, 1460, 1380, 1360, 1280, 1240, 1120 and 760 cm^{-1}; m/e(%) 392(M^+,1), 181(M^+-$C_{10}H_{17}$-$C_3H_6O_2$,4), 137($C_{10}H_{17}^+$,44), 113(8) and 83(100).
5. R.D. Mair and R.T. Hall "Organic Peroxides", Ed. D. Swern, Vol. II, p.553-560 Wiley-Interscience 1971, and R.A. Johnson and E.G. Nidy, J. Org. Chem., 40, 1680 (1975).
6. Hydrogenation of 2 gave a saturated diol which underwent rapid water elimination due to the β-hydroxy carbomethoxyl moiety; ^{13}C-NMR: 176.5, 137.8, 126.4 and 72.5.
7. A third compound, most likely 2-propan-2'-onyl-3,7,7-trimethyl-cyclohept-2-ene could have been isolated depending on the work-up. This compound seems to be the aldol condensation product of compound 3.
8. M.B. Yunker and P.J. Scheuer, J. Am. Chem. Soc. 100, 307 (1978).
9. Satisfactory microanalysis was obtained for the corresponding acid.
10. The chemical shifts are in good agreement with those of the corresponding atoms in compound 2.
11. M.D. Higgs and D.J. Faulkner, J. Org. Chem., 43, 3454 (1978).
12. There is a good agreement for the suitable published ^{13}C-NMR signals of plakortin[10], mokupalide[8] and muqubilin 1.

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