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A TRITERPENOID PIGMENT WITH THE ISOMALABARICANE SKELETON FROM THE MARINE SPONGE STELLETTA SP.

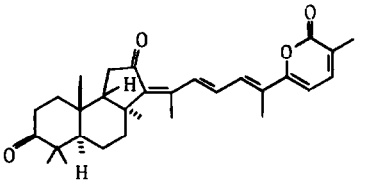
Terrence McCabe and Jon Clardy*
Department of Chemistry, Cornell University
Ithaca, NY 14853

L. Minale, C. Pizza, and F. Zollo
Istituto di Chimica Bioorganica, Facoltà di Farmacia
Università di Napoli, Via L Rodinò 22, Naples, ITALY

R. Riccio
Istituto per la Chimica M I.B. del C.N.R , Via Toiano 2,
Arco Felice, Naples, ITALY

Summary The constitution and stereochemistry of 1, a yellow triterpenoid pigment isolated from a Somalian collection of the sponge Stelletta sp., has been unequivocally established by spectral and x-ray crystallographic methods. The assignment of trans-syn-trans stereochemistry to the tricyclic nucleus of 1 suggests that the structures of several recently described triterpenoids from Japsis stellifera be reassigned.

Marine sponges continue to be a fruitful source of unusual terpenoids. Recently we examined a brown sponge (internal color yellow) of the genus Stelletta and we now wish to report the structural elucidation of an unstable yellow triterpenoid pigment as 1



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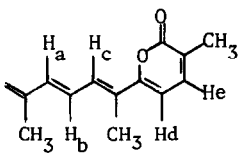
Fresh, wet sponge, collected off Mogadishu, Somalia, was extracted with acetone, and the aqueous suspension obtained after removal of acetone was extracted three times with ethyl ether. Chromatography (silica gel, benzene with increasing EtOAc) of the ether soluble material afforded an unstable yellow pigment (20% EtOAc) which precipitated upon addition of ethyl ether to the concentrated fractions. Crystallization from CH_2Cl_2-ethyl ether gave 1 as yellow prisms, in ca. 0 1% dry weight yield, m.p. 258-260, $[\alpha]_D^{25}$ +87° (c, 0.8, $CHCl_3$, freshly prepared solution), and a formula of $C_{30}H_{38}O_4$ based on MS[1] and ^{13}C-NMR.[2]

The C_{30} formula combined with seven ^{1}H-NMR signals assigned to methyls, four on sp^3 quaternary carbons (δ 0.86, 1.06, 1.12 and 1 41 singlets) and three olefinic methyls (δ 2.03, 2.07 and 2.12, all s), suggested an isoprenoid material. The UV absorptions at 417s (ε 23,800), 396 (29,600), 314 (8,780) and 302s (6,200) nm suggested a conjugated polyene system. The ^{13}C-NMR spectrum indicated five double bonds with five off-resonance doublets at 102.5, 129 5, 131.3, 137 0 and 139.6 ppm and five singlets at 124 0, 125.4, 141 4, 147.0 and 159.6. It also showed two ketonic carbonyl functions at 205.7 and 218.9 ppm and one enol ester at 163.3 ppm for the carbonyl carbon and no signals in the region of sp^3 carbons bearing oxygen The olefinic region of the ^{1}H-NMR spectrum was particularly informative and when combined with the ^{13}C-NMR information suggested partial structure a. The ^{1}H-NMR methyl resonances at δ 2.12, 2 07 and 2.03 also correlate



H_a 8.26
H_b 6.97
H_c 7.26
H_d 6.22
H_e 7.14

J_{ab} = 15 Hz
J_{bc} = 11 Hz
J_{de} = 6 6 Hz

well with this part structure as do the ^{13}C-NMR resonances at δ 163.3s (C=O), 159.6s (O-C=CH-) and 102.5d (O-C=CH-). The carbon skeleton of the remaining half of the molecule must therefore be tricyclic with two ketones and four tert-methyls In order to clarify the entire structure a single crystal x-ray study was carried out.

Crystals suitable for single crystal x-ray diffraction work were grown from a benzene-methylene chloride-diisopropyl ether solution by slow evaporation. Preliminary x-ray photographs showed monoclinic symmetry and accurate lattice constants of $\underset{\sim}{a}$ = 14.464(9), $\underset{\sim}{b}$ = 13.609(6), $\underset{\sim}{c}$ = 13.737(4)Å and $\underset{\sim}{\beta}$ = 104.53(4)° were obtained. The systematic extinctions, presence of chirality, and a rough density measurement were uniquely accommodated by space group $P2_1$ with two molecules of composition $C_{30}H_{38}O_4$ forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 100°$ were collected on a computer controlled four circle diffractometer using CuKα radiation (1.54178Å) and a variable speed, 1° ω-scan. A total of 3048 unique reflections were measured in this manner and after correction for Lorentz, polarization and background effects, only 1742 (57%) were judged observed ($|F_o| \geq 3\sigma(F_o)$). A phasing model was eventually achieved by direct methods An E-synthesis calculated for the best set of phases from MULTAN 78[3] showed promising nine and twelve atom fragments but these could not be extended by tangent formula recycling. However when these fragments were used to modify the original E's and the new phase sets examined by the negative quartets criterion an E-synthesis for the best set displayed a twenty atom fragment. Tangent formula recycling led to 34 atoms in two fragments and F-syntheses and partial refinement finally showed all 68 nonhydrogen atoms in the asymmetric unit After inclusion of hydrogens at calculated positions, block diagonal least-squares refinement with anisotropic nonhydrogen atoms converged to the current crystallographic residual of 0.074.[4]

A computer generated perspective drawing of the final x-ray model is shown in Figure 1. Both independent molecules have the same structure and only one is shown. The absolute configuration shown was chosen to have the methyl at C10 in the β-orientation. The syn stereochemistry at C10-C9 forces both cyclohexane rings into the twist chair conformation

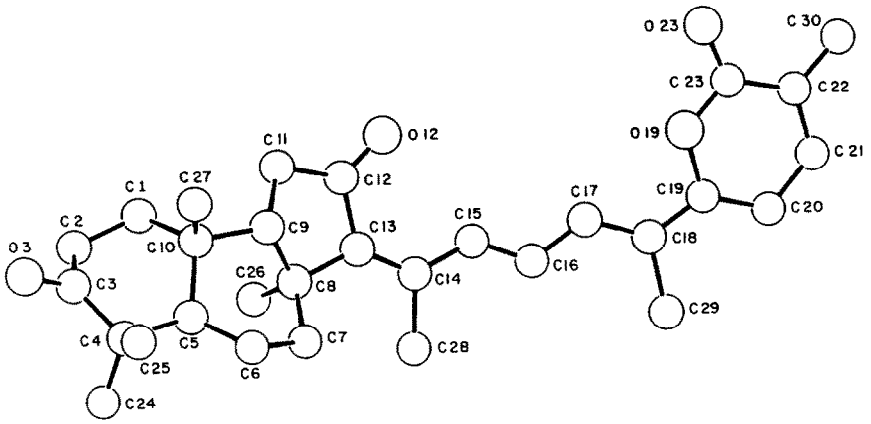
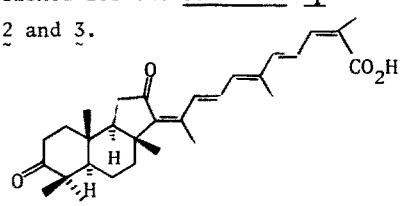


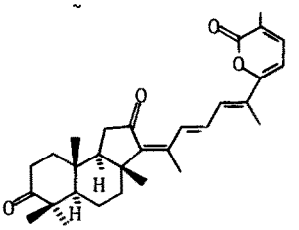
Figure 1. A computer generated perspective drawing of 1. Hydrogens are omitted for clarity and the absolute configuration was assumed.

Shortly after this work was finished a paper by Ravi, Wells and Croft[5] describing the occurrence of three novel triterpenes from the sponge Japsis stellifera appeared. On the basis of spectral data and chemical degradations they were assigned structures 2 - 4, with the trans-anti-trans stereochemistry of the tricyclic nucleus already encountered in the terrestrial malabaricane triterpenes.[6] The data reported by Ravi et al. for compound 4 are in close agreement with those of 1 and we believe that the Stelletta sp and Japsis stellifera enol lactone are identical. Thus we suggest that the trans-syn-trans stereochemistry, unambiguously established for the Stelletta sp triterpene 1, be reassigned to 4 and also to the carboxylic acids 2 and 3.



2, R = O

3, R = H, OAc



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That the three Japsis stellifera metabolites have the same stereochemistry was shown by chemical interrelation[5] and in addition the ^{13}C-NMR and ^{1}H-NMR chemical shifts of 1 are in close agreement with those of the corresponding atoms in compounds 2 and 3. The ^{13}C-NMR spectra reported for 2 - 4 are not consistent with the trans-anti-trans stereochemistry suggested. In model compounds, with trans-anti-trans stereochemistry, the bridgehead carbon resonance (C5) is always at ~55 ppm.[7] There are no reported resonances in this region for 2 - 4 [5]

As noted by Ravi et al.[5] this is the first occurrence of cyclized triterpenes (originating from a squalene-derived precursor) in sponges although sponges have proven to be a rich source of sesqui-, di-, and sesterterpenes as well as higher head-to-tail isoprenoids.[8]

The structures of the first triterpenes isolated from sponges represent a new skeleton for which we propose the name "iso-malabaricane."

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References and Notes

1 MS, m/e 462 (M^+), 447, 429, 353, 313, 256-257, 241, 149

2. ^{13}C-NMR ($CDCl_3$) 12.9(q), 16 0(q), 16.8(q), 19 4(q), 19.7(t), 23.5(q), 24.6(q), 29.2(q), 31.4(t), 33.5(t), 34.9(s), 36.8(t), 37.3(t), 45.0(s), 45.6(d), 47.0(s), 48.1(d), 102.5(d), 124.3(s), 128 4(s), 129.5(d), 131.3(d), 137.0(d), 139.6(d), 141.9(s), 147.0(s), 159.6(s), 163.0(s), 205.7(s), 218.9(s)

3. Crystallographic programs are described in E. Arnold and J. Clardy, J. Amer. Chem. Soc., 1981, 103, 1243-4.

4. Tables of fractional coordinates, thermal parameters, bond distances and bond angles have been deposited with the Cambridge Crystallogrpahic Data Centre.

5. B N Ravi, R.J. Wells and K.D. Croft, J. Org. Chem., 1981, 46, 1998

6. W.F. Paton, I.C. Paul, A G. Bajaj and S. Dev, Tet. Lett., 1979, 4135 and references therein

7. F.W. Wehrli and T Nishida, Progress in the Chemistry of Organic Natural Products, 1979, 36, 1-229.

8. L. Minale, Terpenoids from Marine Sponges in Marine Natural Products I, Academic Press, Inc. 1978, p. 175-239, P.J Scheuer (editor).

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