

MOLLIORIN-A: A UNIQUE SCALARIN-LIKE PYRROLOTERPENE FROM THE SPONGE
CACOSPONGIA MOLLIOR

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Scalarin (1)¹ and the related compounds deoxoscalarin², disidein³, scalarial⁴, heteronemin⁵ and furoscalarol⁶, all present in marine sponges, represent a new class of sesterterpenes possessing a tetracarbocyclic skeleton.

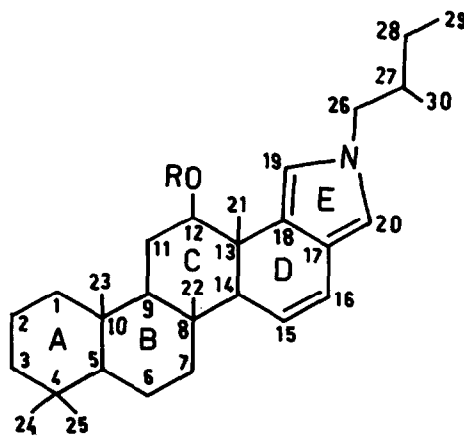
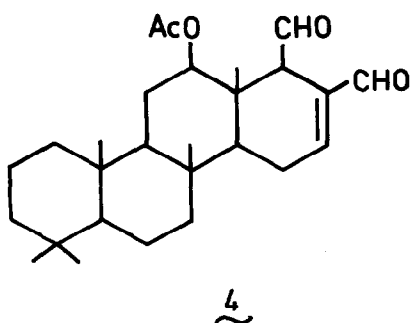
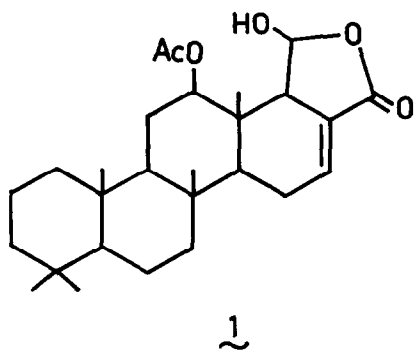
We wish to report herein the structure determination of another scalarin-like terpene having a pyrrole ring, molliorin-a (2), obtained from the extracts of the marine sponge Cacospongia mollior⁷.

Careful chromatography of the ether-soluble extract of the fresh sponge on silica-gel (eluent benzene/Et₂O 95:5) afforded 2 (in ca. 0.03% yield of the dry material), m.p. 102-105°; $[\alpha]_D$ 51.7° (c 1 in CHCl₃), M^+/e 479.3769 (C₃₂H₄₉NO₂ requires 479.3763). i.r. (ν_{\max} 1740 and 1240 cm⁻¹) and n.m.r. spectra in carbon tetrachloride (δ 1.90, 3H, s; 5.31, 1H, m) indicate the presence of a CH₃COOCH< group. This was confirmed by alkaline hydrolysis of 2 which afforded the alcohol 3, m.p. 165-167° (from EtOH); $[\alpha]_D$ -1.4° (c 1 in CHCl₃), M^+/e 437, ν_{\max} (CCl₄) 3500 cm⁻¹; δ (CCl₄) 4.04 (1H, bm, H-C₁₂).

The presence of a β,β -disubstituted pyrrole ring was deduced from the positive Ehrlich test, the n.m.r. spectrum of 3 (δ 6.32 and 6.21, singlets broadened by long range coupling, 1H each) and the solvent induced shift⁸ of these two signals ($\delta_{CCl_4} - \delta_{C_6D_6} = 0.06$ and 0.05 respectively). The u.v. spectrum (MeOH) of 3 shows a maximum at 257 nm ($\epsilon = 13700$) suggesting that the pyrrole ring is conjugated with a double bond.

Complementary data which evidenced the presence of the partial structure involving C₁₃ - C₁₆ were obtained from the n.m.r. spectrum of 3, which showed in the olefinic region signals at δ 6.26 (1H, H-C₁₆) and 5.53 (1H, dd, J 9.5 and 3 Hz, H-C₁₅) [the signal at δ 6.26 is superimposed to the signals due to the two pyrrole protons (δ 6.32 and 6.21)]; however in the n.m.r. spectrum of 3 in C₆D₆, this signal is better resolved resonating at δ 6.60 as a doublet of doublets

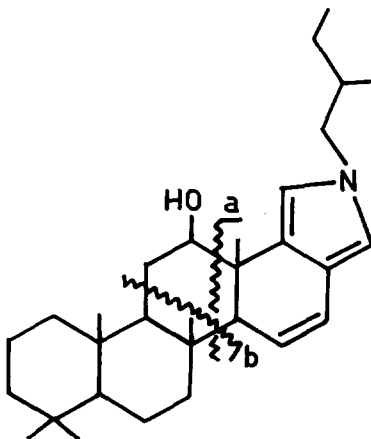
(J 9.5 and 2 Hz)]. These assignments were confirmed by decoupling: irradiation at δ 6.26 simplified the signal at δ 5.53 to a doublet (J 2 Hz) and saturation of the proton signal at δ 2.42 (1H, broad, H-C₁₄) collapsed the signal at δ 5.53 to a doublet (J 9.5 Hz). Finally, the signal at δ 2.42 was converted into a doublet by irradiation at δ 6.26 or 5.53, the coupling constants being 2 and 3 Hz respectively. The coupling constant between H-C₁₅ and H-C₁₆ (J 9.5 Hz) is only consistent with a cis relationship and in addition suggested that the two olefinic carbon atoms lie in a six-membered ring.



2 R = Ac

3 R = H

Support for the presence of rings A, B and C came from the n.m.r. spectrum of 3, which shows in the higher field region five methyl singlets at δ (C_6D_6) 1.22, 1.08, 0.89, 0.87 and 0.84 (the higher field region in CCl_4 is ill-resolved), and the mass spectrum which exhibits intense ions at m/e 437 (98%, M^+), 422 (100%, $M^+ - CH_3$), 404 (43%, $M^+ - H_2O - CH_3$), 381 (10%, $M^+ - C_4H_8$), 363 (20%, $M^+ - H_2O - C_4H_8$), 202 (97%, $a + H$) and 191 (11%, $b - H$).



The results of the mass spectral analysis of 3 are worthy of further discussion. The presence of two intense ions at m/e 381.3035 ($C_{26}H_{39}NO$; $M^+ - C_4H_8$ and m/e 363.2921 ($C_{26}H_{37}N$; $M^+ - C_4H_8 - H_2O$), taking into account the characteristic fragmentation of N-alkylpyrroles⁹, can be rationalised by assuming that a C_5 unit is linked to the pyrrole nitrogen. This unit must be a 2-methylbutyl group as proved by the n.m.r. spectrum of 3 in C_6D_6 , which shows signals at δ 0.64 (3H, d, J 7 Hz, $H_3 - C_{30}$) and 0.58 (3H, t, J 6 Hz, $H_3 - C_{29}$).

Accumulated results led to the formula 2 as the most favourable for molliorin-a. The final proof of correctness of this formula was provided by its synthesis: scalaradial (4) and d1-2-methylbutylamine, in the experimental conditions used for the synthesis of pyrrole derivatives, afforded a product which showed chromatographic properties (TLC on silica-gel in benzene/40-70° light

petroleum 3:2 and benzene; on aluminium oxide in Et₂O/40-70° light petroleum 1:2) and mass spectrum identical of those of 2.

As far as the biogenesis of molliorin-a, it is not unreasonable to suppose that, also in vivo, 2 could derive from scalaradial after reaction with 2-methylbutylamine arising from isoleucine by loss of carbon dioxide.

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REFERENCES AND NOTES

1. E. Fattorusso, S. Magno, C. Santacroce and D. Sica, Tetrahedron, 28, 5993 (1972).
2. G. Cimino, S. De Stefano and L. Minale, Experientia, 29, 934 (1973).
3. G. Cimino, P. De Luca, S. De Stefano and L. Minale, Tetrahedron, 31, 271 (1975).
4. G. Cimino, S. De Stefano and L. Minale, Experientia, 30, 846 (1974).
5. R. Kazlauskas, P.T. Murphy, R.J. Quinn and R.J. Wells, Tetrahedron Letters, 30, 2631 (1976).
6. F. Cafieri, L. De Napoli, E. Fattorusso, C. Santacroce and D. Sica, Gazz. Chim. It., in press.
7. It is to be noted that we examined a sample of Cacospongia mollior (identified by Prof. M. Sarà, Università di Genova) collected in the bay of Taranto (May 1975). This sample, differently from that previously examined by Cimino et al.⁴, does not contain appreciable amounts of scalaradial.
8. J. Ronayne and D.H. Williams, J. Chem. Soc. B 805 (1967).
9. A.M. Duffield, R. Beugelmans, H. Budzikiewicz, D.A. Lightner, D.H. Williams and C. Djerassi, J. Am. Chem. Soc., 87, 805 (1965).