Tetrahedron Letters, Vol.22, No.31, pp 3013 - 3016, 1981
Printed in Great Britain

0040-4039/81/313013-04$02.00/0

CHOLEST-4,14-DIEN-15,20ξ-DIOL-3,16-DIONE, A NOVEL POLYOXYGENATED MARINE STEROID WHICH EASILY LOSES THE SIDE CHAIN [1]

G. Cimino, S. De Rosa, S. De Stefano, G. Scognamiglio and G. Sodano

Istituto per la Chimica di Molecole di Interesse Biologico del C.N.R.
Via Toiano, 2, 80072 - Arco Felice, Naples, Italy.

Abstract.- The title compound has been isolated from the Mediterranean gorgonian Leptogorgia sarmentosa; upon acetylation it affords a dehydration product and an androstane derivative.

Among uncommon marine steroids[2] several polyoxygenated sterols have been so far isolated. The relative arrangement of the functions often can induce an enhanced reactivity of these molecules which lead to several artifacts during the isolation procedure. This aspect is particularly frequent when hydrolytic procedures must be used, as in the obtention of aglycones from saponins, resulting in the isolation of molecules whose autenticity is questioned[2,3].

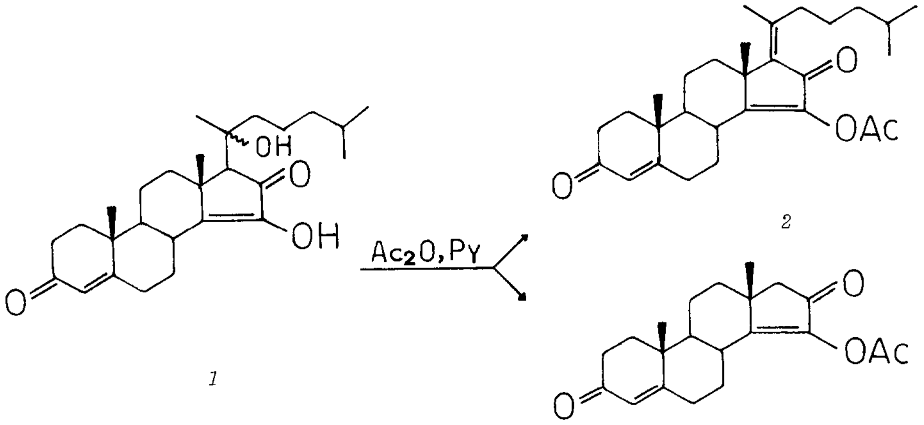
We wish to report now the isolation of cholest-4,14-dien-15,20ξ-diol-3,16-dione (*1*) from the Mediterranean gorgonian *Leptogorgia sarmentosa* and its degradation in mild conditions.

1 ($C_{27}H_{40}O_4$, elemental analysis; 0.01% dry weight; m.p. 167-171°C, from diethyl ether-light petroleum; $[\alpha]_D^{25}$ + 46°, c=0.5, $CHCl_3$), has been isolated, along with several related compounds, from the ethereal part of the acetone extracts of the gorgonian by silica gel chromatography (light petroleum-diethyl ether 4 : 6) and further purified by chromatography on a prepacked column (Lobar Lichroprep Si 60, light petroleum-diethyl ether 1 : 1).

1 lacks the molecular ion in the mass spectrum and displays peaks at m/z 410 (M^+- H_2O, 19%) and 300 (M^+-side chain + H, 100%). In the i.r. spectrum an unique broad band was present for the carbonyl groups, ν_{max} ($CHCl_3$) 1665 cm^{-1}. The presence of both an α,β-unsaturated ketone and of a diosphenol moiety was evident from the u.v. spectra[4], λ_{max} (MeOH) 242 (ε = 17.000), 267 (infl., ε = 9.000), λ_{max} (MeOH-KOH) 240 and 308 nm. The p.m.r. spectrum contains the five methyl groups expected for a cholestane derivative at δ 0.90 (6H, d, J 6Hz; isopropyl Me's), 1.29 (6H, s) and 1.31 (3H, s) for the C-18, C-19 and C-21 Me's, and a singlet (1H, C-4 proton) at δ 5.77. The chemical shift (1.29 or 1.31) and the multiplicity (singlet) for the C-21 Me suggests the presence of a tertiary hydroxy group at C-20. The c.m.r. spectrum[5] was fully consistent with the proposed structure. In particular the comparison of this spectrum with the spectra of cholest-4-en-3-one[6] and of 4-hydroxy-cholest-4-en-3-one[7] indicated that the α,β-unsaturated ketone was localized in the ring A, while the chemical shifts of C-13, C-17 and C-18 indicated that the diosphenol moiety is situated in the ring D.

1 is a highly reactive molecule which decomposes on standing to a complex mixture of products. When *1* was submitted to acetylation (acetic anhydride containing 10% pyridine; 15 min., reflux) two derivatives (*2*, 7% and *3*, 13%) were obtained and separated from somespecious products by silica gel column chromatography (light petroleum-diethyl ether, 4 : 6).

The more polar derivative *2*, $C_{29}H_{40}O_4$, was a dehydration product as shown by the mass spectrum with significant peaks at m/z 452 (M$^+$, 71%), 410 (M$^+$-CH$_2$=C=O, 100%), 340(M$^+$-CH$_2$=C=O and McLafferty cleavage of the 22-23 bond, 33%) and 339(M$^+$-CH$_2$=C=O and allylic cleavage of the 22-23 bond, 16%) and by the p.m.r spectrum which shows the isopropyl methyls at δ 0.88 (6H, d, J 6Hz) and singlets for the C-19 and C-18 Me's at δ 1.29 and 1.42 respectively, the methyl on double



1

2

3

bond at δ 1.99, the acetyl methyl at δ 2.25 and the C-4 proton at δ 5.77. In the c.m.r. spectrum[8] the absence of signals in the 60-75 δ region indicated that the dehydration gave rise to a 17,20-double bond . The u.v. (λ_{max}, MeOH, 243,ε = 13.000 and 272, infl., ε = 9.000) and i.r. spectra (ν_{max} 1670, 1725 and 1770 cm^{-1}) are in accordance with structure *2*.

The less polar product *3*, $C_{21}H_{26}O_4$, clearly arising from *1* by a retro aldol reaction, dispalys in the mass spectrum the molecular ion at m/z 342 (3%), the base peak being at m/z 300 ($M^{+}-CH_2=C=O$).

In the u.v. spectrum only a maximum is present (λ_{max}, MeOH, 240 nm, ε = 27.000) on account of both the α,β-unsaturated ketone and the diosphenol acetate functions[4]. The i. r. spectrum showed three carbonyl bands, ν_{max} ($CHCl_3$) 1665 (α,β-unsaturated six membered ketone), 1710 (α,β-unsaturated five membered ketone) and 1770 (enol acetate) cm^{-1}. In the p.m.r. spectrum two singlets (each 3H) at δ 1.28 and 1.32 were assigned to the angular methyls, while the enol acetate methyl resonates at δ 2.22 and the C-4 proton at δ 5.76. The c.m.r. spectrum[9], which differs from the c.m.r. spectrum of *1*[5] chiefly for the absence of the resonances assignable to the side chain carbons and for the presence of the newly formed C-17 methylene, allowed the assignment of structure *3* and provided a further evidence supporting the structure of *1* and *2*.

Several steroidal saponins having a β-hydroxy ketone moiety in the side chain gives rise to retro aldol reactions in strong alkaline conditions[10]. However *1* is the first example of a cholestane derivative which suffers the cleavage of the whole side chain in mild conditions.

ACKNOWLEDGEMENTS

The authors thank the Zoological Station (Naples) for the collection of the gorgonian. Thanks are also due to Mr C. Di Pinto for the n.m.r. spectra and Mr. A. Milone for the mass spectral measurements.

REFERENCES AND NOTES

1.- This work is a part of the "Progetto Finalizzato per l'Oceanografia e i Fondi Marini", C.N.R., Roma.

2.- F.J.Schmitz in "Marine Natural Products - Chemical and Biological Perspectives", P. J. Scheuer ed., Academic Press, New York, *I*, 241 (1978).

3.- I.Kitagawa, M.Kobayashi, T.Sugawara and I.Yosioka, *Tetrahedron Letters*, 967 (1975).

4.- A.I.Scott, "Interpretation of the Ultraviolet Spectra of Natural Products", Pergamon Press, London (1964).

5.- δ($CHCl_3$): C-1, 35.6; C-2, 33.9; C-3, 199.0; C-4, 124.1; C-5, 169.4; C-6, 32.7; C-7, 29.8; C-8, 36.1; C-9, 53.0; C-10, 38.9; C-11, 20.8; *C-12, 40.1; C-13, 42.9; C-14, 145.5; C-15, 150.8; C-16, 205.4; C-17, 65.6; C-18, 22.0; C-19, 17.8; C-20, 74.5; C-21, 25.7; *C-22, 41.3; C-23, 20.8; C-24, 39.6; C-25, 28.0; C-26 and C-27, 22.6 and 22.7.
* These shieldings may be interchanged.

6.- J.W.Blunt and J.B.Stothers, *Org.Mag.Res.*, *9*, 439 (1977).

7.- G.Cimino, S.De Rosa, S.De Stefano and G.Sodano, *Tetrahedron Letters*, *21*, 3303 (1980).

8.- We did not obtain enough material for an unambiguous assignment of all the carbon resonances.

9.- δ($CDCl_3$): C-1, 35.7; C-2, 33.9; C-3, 198.8; C-4, 124.4; C-5, 168.2; C-6, 32.5; C-7, 28.7; C-8, 36.9; C-9, 53.4; C-10, 39.1; C-11, 21.2; C-12, 39.7; C-13, 39.7; C-14, 143.4; C-15, 167.5; C-16, 198.5; C-17, 48.7; C-18, 24.6; C-19, 17.8; acetyl carbonyl, 167.8; acetyl methyl, 20.5.

10.- See for example: I. Kitagawa and M.Kobayashi, *Tetrahedron Letters*, 859 (1977); S.Ikegami, K.Okano and H.Muragaki, *Tetrahedron Letters*, 1769 (1979).

(Received in UK 18 May 1981)