Tetrahedron Letters No. 41, pp 3953 - 3954.
©Pergamon Press Ltd. 1978. Printed in Great Britain.

0040-4039/78/1008-3953$02.00/0

X-RAY CRYSTAL STRUCTURE DETERMINATION OF PETROSTEROL p-BROMOBENZOATE. A REVISION

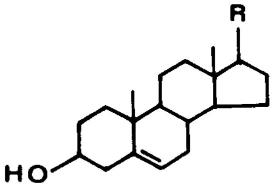
C.A. Mattia[a], L. Mazzarella[a], R. Puliti[b], D. Sica[c] and F. Zollo[c]

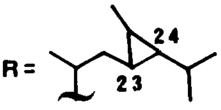
a - Istituto Chimico, Via Mezzocannone 4, Napoli (Italy)

b - Laboratorio per la Chimica di Molecole di Interesse Biologico
del C.N.R., Via Toiano 2, Arco Felice, Napoli (Italy)

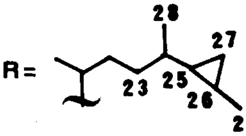
c - Istituto di Chimica Organica, Via Mezzocannone 16, Napoli (Italy)

Recently the isolation of a new C_{29} sterol, petrosterol, from the marine sponge <u>Petrosia ficiformis</u> has been described[1]. Spectral data indicated that petrosterol ($C_{29}H_{48}O$) was a Δ^5-3β-hydroxy sterol with a $C_{10}H_{19}$ side chain containing a methyl cyclopropane ring, for which the structure of 23,28-cyclostigmast-5-en-3β-ol (1) was proposed. Careful examination of the off-resonance ^{13}C NMR spectrum of petrosterol raised doubts about the C-23,24 position for the cyclopropane ring. In order to establish unambiguously the structure and the stereochemistry of the side chain, we undertook an X-ray diffraction analysis of the p-bromobenzoate derivative ($C_{36}H_{51}BrO_2$) and wish to report the revised structure 2 for petrosterol.



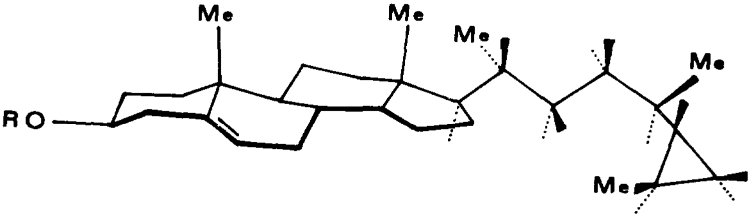


1



2

The p-bromobenzoate derivative (m.p. 158°-160°) was prepared by esterification of petrosterol with p-bromobenzoyl chloride in pyridine and crystallized from acetone. Crystals were orthorhombic, space group $P2_12_12_1$ with 4 molecules in a unit cell of dimension a = 10.631(5), b = 11.273(9), c = 26.802(12) Å, U = 3212 Å^3, D_m = 1.22 g cm^{-3}. The intensities of 2700 reflections were collected at room temperature on an Enraf Nonius CAD-4 diffractometer, using monochromatized Cu-Kα radiation (θ<60°) and ω-scan technique. A needle shaped crystal (0.08 mm thick) was selected and the azimuth of each reflection was adjusted to reach as close as possible the position of the minimum absorption path. The structure was solved using normal heavy-atom and Fourier synthesis techniques and refined by full matrix least-squares procedures with anisotropic thermal parameters and anomalous dispersion corrections for the bromine atoms[2]. All other atoms were given isotropic thermal parameters and the weighting scheme used was based on counting statistics. During the final cycles hydrogen atoms were calculated and used in structure factor calculations with the thermal parameters of the atoms to which they were bonded. At convergence the conventional index R, based on the 1453 observed reflections ($I>2.5\sigma_I$), was 0.076 and the difference Fourier map shows a residual electron density less than 0.3 e/Å^3. Throghout the work a PDP 11/34 computer and the Enraf-Nonius structure determination package was used. All bond distances and angles compare well, within the estimated errors (on average 0.02 Å and 0.8° respectively), with the general accepted values[3]. The dihedral angles indicate that the steroid skeleton of the molecule assumes the conformation common to many Δ^5-3β-steroids with the ring A and C in the chair conformation and ring B in the half-chair conformation. Moreover the cyclopentane ring (D) is close to the ideal half-chair form.



In the figure a projection of the molecule (R = BrC_6H_4CO-) is shown. The presence of a substituted cyclopropane ring in the side chain, as suggested by NMR evidence, is clearly demonstrated by the X-ray structure: the bond lengths within the ring are on average 1.51 Å and the bond angles deviate less than 1.5° from 60°. The cyclopropane ring however involves the atoms C-25,26,27 and, most strikingly, shows a methyl substitution at position 26 trans to carbon 24.

The methyl group at C-26 and cyclopropane ring bridging C-26,27 are features without precedent in natural sterols. So far the only example of a methyl substitution at C-26 is provided by aplysterol[4], a sterol isolated from the sponge *Aplysina aerophoba*, in this case however the side chain does not posses the cyclopropane ring. It is noteworthy that both petrosterol and aplysterol have the same configuration R at position 24, although they show different configuration at the carbon 25 (R for petrosterol). The structure of petrosterol confirms that marine sponges are a rich source of uncommon sterols and rises intriguing questions about its biogenetic origin.

References and notes

1. D. Sica and F. Zollo, *Tetrahedron Lett*. 837 (1978).
2. The absolute configuration was based on the CD curve of the α,β-unsaturated ketone obtained via the Oppenauer oxidation of petrosterol.
3. D.A. Norton, *Biophys. J.*, *5*, 425 (1965); C. Romers, C. Altona, H.J.C. Jacobs and R.A.G. de Graaff, "Terpenoids and Steroids", vol. 4, pp. 531-583, The Chemical Society, London, 1974.
4. P. De Luca, M. De Rosa, L. Minale, R. Puliti, G. Sodano, F. Giordano, L. Mazzarella, *J.C.S. Chem. Comm.*, 825 (1973).

(Received in USA 14 March 1974; received in UK for publication 6 May 1974)