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PERIDINOSTEROL - A NEW Δ^{17}-UNSATURATED STEROL FROM TWO CULTURED MARINE ALGAE

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Abstract: X-ray diffraction analysis of peridinosterol p-bromobenzoate has shown the parent sterol to be E-4α,23R,24R-trimethylcholest-17(20)-en-3β-ol - a new member of the rare Δ^{17}-unsaturated sterol class. Its possible biosynthetic origin is discussed.

One of the most interesting structural and biosynthetic features of marine sterols is the occurrence of cyclopropane rings in the side chain.[1] Until recently, such sterols have been encountered only in marine organisms which contain dinoflagellate symbionts (zooxanthellae), although these sterols (e.g. gorgosterol, 1B) have not been isolated from cultured zooxanthellae isolated from hosts known to contain gorgosterol (1B). Possible rationalizations for this observation have been presented elsewhere,[2] but recently two reports have appeared[3,4] dealing with the isolation of cyclopropane-containing sterols of the gorgosterol type (1) from cultured unicellular algae. When we reported such isolation from the "red tide" phytoplankton species Peridinium foliaceum UTEX 1688, cultured in the laboratory, and hence of importance for eventual biosynthetic incorporation experiments, we noted also the presence (6% of the free sterols) of a hitherto unknown sterol ($C_{30}H_{52}O$), m.p. 196-200°, $[\alpha]_D$ +3° ($CHCl_3$) which we have now named peridinosterol. It is one of the main (23%) free sterols in the related alga Peridinium balticum UTEX 1563. Preliminary mass spectral and NMR analytical studies limited the structural possibilities to three alternatives, 2A, 3A and 4A. Since only two other naturally occurring Δ^{17}-sterols have been described earlier in the literature[5] and since the stereochemistry of the methyl groups could have been determined chemically only with great difficulty (even if differentiation between 2, 3 and 4 had been accomplished), we resorted to X-ray analysis of peridinosterol p-bromobenzoate (m.p. 209-210°, $[\alpha]_D$ +24° ($CHCl_3$)) for the final solution. Preliminary x-ray photographs of a suitable crystal showed monoclinic symmetry. Accurate lattice constants, obtained from a least-squares fit of fifteen moderate 2θ-values, were a=10.223(2), b=7.702(2), c=21.706(4) Å and β=86.96(1)°. Systematic extinctions and the presence of chirality were uniquely accommodated by space group $P2_1$ and density considerations indicated one molecule of composition $C_{37}H_{42}BrO_2$ formed the asymmetric unit. All unique data with $2\theta \leq 114°$ were collected on a fully automated four-circle diffractometer using a variable speed, 1° ω-scan and graphite monochromated CuKa (1.54178 Å) radiation. Of the 2116 unique reflections collected in this way, 1654 (64%) were judged observed ($F^2 \geq 3\sigma(F_o)$) after correction for Lorentz, polarization and background effects.

A phasing model was achieved using standard heavy atom techniques.[6] Full-matrix least-squares refinements have converged to a current crystallographic residual of 0.060 for the observed reflections. Additional crystallographic details are available.[7] Figure 1 is a computer generated perspective drawing of the final x-ray model for the p-bromobenzoate of peridinosterol which can now be given the systematic name of E-4α, 23(R), 24(R)-trimethylcholest-17(20)-en-3β-ol (5A). The salient stereochemical aspects are the 23(R) and 24(R) designations of the "extra" methyl groups and the E configuration of the double bond. The latter had already been assigned[3] tentatively on the basis of NMR measurements.

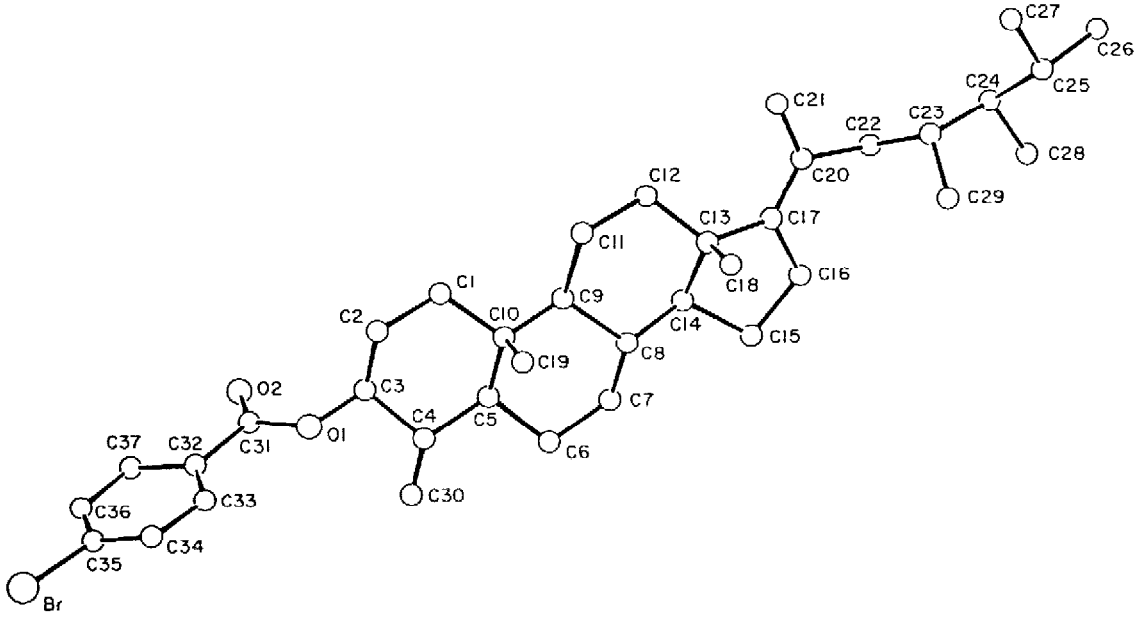
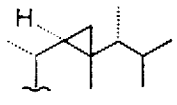


Figure 1. A computer generated perspective drawing of the final X-ray model of peridinosterol p-bromobenzoate. Hydrogens are omitted for clarity.

In the meanwhile, Kobayashi and collaborators[8] have isolated from the soft coral Sarcophytum glaucum sarcosterol (3B), which possesses the same side chain structure (stereochemistry unknown) as peridinosterol (5A). Furthermore, while 5A is accompanied[3] by dinosterol (6A) and 4α-methylgorgostanol (1A), the soft coral Δ^{17}-sterol sarcosterol (3B) coexists[8] with the Δ^{5}-3β-hydroxy analogs 6B (C-24 stereochemistry unknown) and gorgosterol (1B). It is tempting, therefore, to speculate that these side chains are biosynthetically related, especially since in our Peridinium foliaceum group, all three sterols (1A,[9] 5A, 6A[10]) possess the same C-24 stereochemistry (R).

One possibility is that the Δ^{17}-sterols 5A and 3B arise by double bond migration (most likely by a biological reduction-dehydrogenation sequence[11]) from a Δ^{22}-precursor (6), whose biosynthesis has already been discussed.[12] Another intriguing possibility is based on our hypothesis[1] that the cyclopropyl ring in the side chain may be the precursor of unsaturated methyl substituents as is well known in the plant sterol field (generation of 19-methyl group from 9,10-cyclopropyl precursor[13]). Thus a demethylgorgosterol precursor (7) would be isomerized to a $\Delta^{20(22)}$-23,24-dimethyl intermediate (8), which could lead to the Δ^{17}-isomer 5 upon double bond migration.



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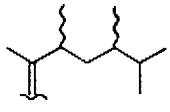

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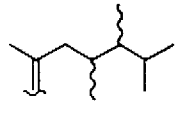

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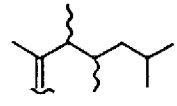

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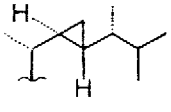

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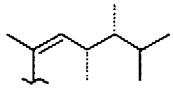

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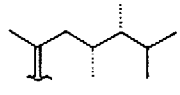

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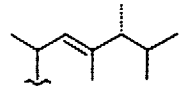

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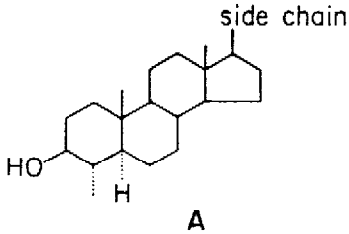

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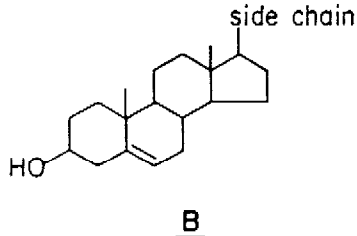

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