Synthesis of a Novel C_{26} Marine Sterol

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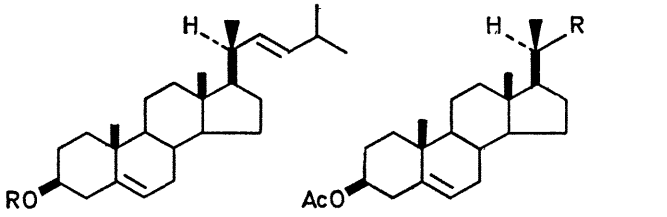
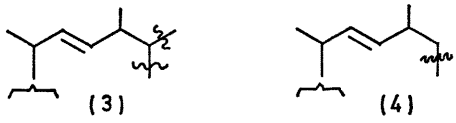
Summary The synthesis of 22-*trans*-26,27-bisnor-ergosta-5,22-dien-3β-ol by an unequivocal route establishes this as the sterol isolated from several Pelecypoda by Idler and his co-workers.

RECENTLY Idler and his co-workers suggested structure (1a) for the C_{26} sterol isolated from the scallop, *Placopecten magellanicus* (Gmelin). The sterol also occurs in several other Pelecypoda including the blue mussel, *Mytilus edulis* L.; the clam, *Mya arenaria* L.; the ocean quahog, *Arctica islandica* L.; and the oyster, *Crassostera virginica* (Gmelin).[1] Because of the biogenetic novelty of the side-chain structure suggested for (1a) and the uncertainities associated with the stereochemistry at C-20 we have synthesized this sterol by an unequivocal route.

The synthesis of (1a) was accomplished *via* a Wittig reaction of the 20*R*-aldehyde (2a)[2] which was prepared from stigmasteryl acetate, (2b). Bromination of (2b) with iodobenzene dibromide at $-5°$ in hexane gave 91%, of 5α,6β-dibromo-stigmast-22-en-3β-yl acetate.† Ozonolysis of the bromosterol ($-70°$ in CH_2Cl_2–pyridine) followed by reductive work-up (Zn–HOAc) and treatment with saturated $NaHSO_3$ solution gave 81% of the bisulphite



(1) a; R = H (2) a, R = CHO
b; R = Ac b; R = *trans*-CH:CH·CHEt·CMe$_2$



(3) (4)

derivative of (2a). The bisulphite derivative was converted into (2a) (95%) by reaction with 10% Na_2CO_3.

† M.p.s are uncorrected. All new compounds had correct analyses and, where not specifically discussed, the expected spectroscopic data.

Reaction of (2a) with isobutyl-triphenylphosphorane (HI salt + BuLi) in diethyl ether (r t for 2 h then 60° for 12 h) followed by treatment with acetic anhydride in pyridine gave 40% of (1b) and its Δ^{22}-*cis*-isomer (1.4) Wittig reaction of (2b) in hexane[4] reversed the Δ^{22}-*trans*–*cis*-ratio to 6 1 Several recrystallizations (MeOH) of the crude (1b) from the latter reaction were required to give pure 20*S*[3] (1b), m p 142 5—143° The n m r of (1b) gave singlets at δ 0 687 (18-H_3), 1 01 (19-H_3), 2 00 (Ac), and doublets at δ 0 925 (24-dimethyl) and 0 992 (21-H_3) Hydrolysis of (1b) in refluxing base (2% KOH in 10% H_2O–MeOH) gave (1a), m p 143—144°, $[\alpha]_D^{25}$ −65° (*c*, 2 7)

The mass spectrum of synthetic (1a) was identical with that published[1] for the C_{26} sterol of Pelecypoda The n m r spectrum of (1a) exhibited singlets at δ 0 70 (18-H_3) and 1 01 (19-H_3), doublets were observed at δ 1 01 (21-H_3) and 0 96 (24-dimethyl), within experimental error of those reported by Idler [1]

We are most grateful to Dr D R Idler for direct comparison of synthetic (1a) (m p 142—143°) with the natural sterol (m p 138—140°) by mixed m p (138—141°), i r, n m r, and g l p c ‡ all of which indicated the synthetic and natural C_{26} sterols were identical

The interesting side-chain of (1) could conceivably arise by degradation of a C_{24} methylated sterol (3) or more interestingly, from degradation of a sterol (4) produced upon cyclization of a modified squalene In the latter case one terminal isoprene unit must be attached in a head-to-head fashion

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‡ Dr Idler performed the g l p c analysis of the free C_{26} sterols on a 6 ft 1% OV-1 column at 217° Comparison of synthetic (1b) and the natural C_{26} sterol acetate by g l p c was performed on a 12 ft 3% XE 60 and a 12 ft 3% NGS column at 210°

[1] D R Idler, P M Wiseman, and L M Safe, *Steroids*, 1970, **16**, 451 Dr Idler has informed us that the m p of the C_{26} sterol should be reported as 138—140°
[2] M Fryberg, A C Oehlschlager, and A M Unrau, *Tetrahedron*, 1971, **27**, 1261
[3] D H R Barton, T Shioiri, and D A Widdowson, *Chem Comm*, 1970, 940
[4] R F N Hutchins, M J Thompson, and J A Svoboda, *Steroids*, 1969, **15**, 113