possesses aldehydic properties, has an absorption maximum at 3650 Å, and reverts (slowly) to pyridine in the dark. In the present study we have confirmed a recent suggestion[2c] that this product is 5-amino-2,4-pentadienal and have shown that III is formed in a secondary process by hydrolysis of Dewar pyridine. The identity of III was established by successive reductions[13] with $NaBH_4$ and with P-1 catalyst[10] to a product identical, by glpc and mass spectrum, with 5-aminopentanol. The intermediacy of I in the formation of III was established by briefly irradiating pyridine in acetonitrile and adding aliquots to water at intervals after irradiation. The intensity of absorption at 3650 Å formed from successive aliquots decreased with a half-time of 2.5 min at 25°.[14] The quantum yield for pyridine disappearance in water, 0.06, is essentially the same as those in inert solvents and aqueous $NaBH_4$.[15]

These results, coupled with preliminary studies of the photolysis of other monoazoles and diazoles in aqueous $NaBH_4$, suggest that formation of transient nonaromatic isomers upon electronic excitation may be a rather general phenomenon among nitrogen heterocycles.[16] The photoreduction technique could prove useful in detecting and identifying these transient species and also in preparing interesting nitrogen heterocycles.

(13) The products of $NaBH_4$ reduction, presumably *cis*- and *trans*-5-amino-2,4-pentadienol, had absorption maxima at 2400 Å and retentions of 1.4 and 1.2 relative to 5-aminopentanol on an OV-17 (3%)–polyethylenimine (1.7%) column at 100°.

(14) The absorbing products noted[2a,b] in the photolysis of pyridine in alcohol were similarly found to arise from I.

(15) A somewhat lower value, 0.03, for formation of III has been reported.[2c]

(16) Reported photohydrations[17,18] and photoreductions[19,20] of pyrimidines extend the possibility of such transient intermediates to compounds of biological interest.

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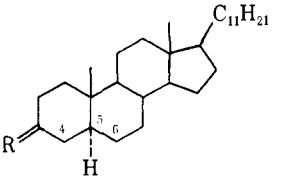
Demonstration of a Biogenetically Unprecedented Side Chain in the Marine Sterol, Gorgosterol

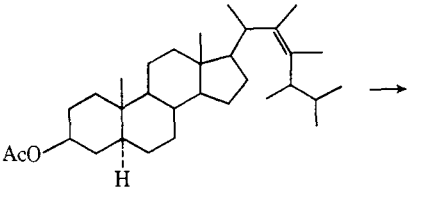
Sir:

The biosynthesis of the sterols, notably cholesterol, has probably been studied more intensively than that of any other group of natural products, and many of the intimate details are known[1] including the origin of the side chain and the sequential addition of one or two carbon atoms at position 24.[2] We should now like to report that the marine sterol gorgosterol[3] possesses the usual cholesterol ring skeleton together with an unprecedented side chain which includes not only a cyclopropane ring but, most strikingly, carbon substitution at positions 22 and 23.

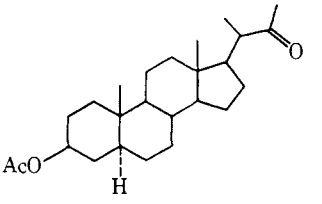
Gorgosterol (I; mp 186.5–188°, $[\alpha]D$ −45°) is unusual in that it is a C_{30} sterol ($C_{30}H_{50}O$) as established by mass spectrometry. Whereas C_{29} sterols are extremely common, the few known C_{30} sterols such as citrostadienol[4] have the extra carbon atom attached at C-4. Such a possibility was readily eliminated by the



I, R = β-OH, α-H; 5,6-double bond
II, R = β-OH, α-H
III, R = β-OAc, α-H
IV, R = O
V. R = H_2
VI, R = O, 5,6-double bond
VII, R = O, 4, 5-double bond



VIII



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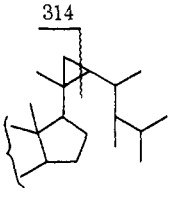

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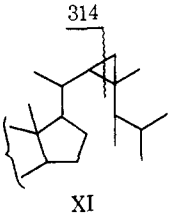

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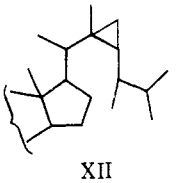

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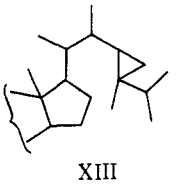

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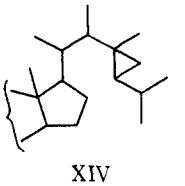

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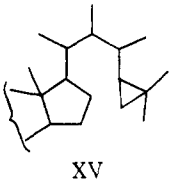

XV

conversion of gorgosterol by Moffatt oxidation[5] to a non-uv-absorbing β,γ-unsaturated ketone, VI, which was readily isomerized with base to an α,β-unsaturated

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ketone, VII (M^+ 424), which gave an optical rotatory dispersion curve characteristic of a Δ^4-3-keto steroid[6] and whose ultraviolet absorption spectrum (λ_{max} 242 nm (ϵ 17,000)) precludes methyl substitution at C-4. The only other logical nuclear position for an additional methyl group would be at C-14, as in macdougallin,[7] but this possibility was eliminated by conversion of gorgosterol to dihydrogorgosterol (II; mp 188.5–192°, M^+ 428), oxidation to gorgostanone (IV; mp 203–206°, M^+ 426), and Wolff–Kishner reduction to gorgostane (V; mp 142–144°, M^+ 412 = $C_{30}H_{52}$). The mass spectrum of this hydrocarbon exhibited important peaks at *m/e* 217, 257–259, 285–287, and 300, all of which are associated with the conventional steroid nucleus and an unsaturated sterol side chain.[8] The presence of a C-14 methyl function would have resulted in 14 mass unit shifts of these peaks.

We conclude that gorgosterol has the cholesterol skeleton but possesses a C_{11} rather than the usual C_8, C_9, or C_{10} side chain. This feature alone would make gorgosterol unique, but even more interesting is its nmr spectrum (100 MHz, chloroform solution) which exhibits signals at δ −0.13 (1 H, doublet of doublets, J = 4 and 6 cps), 0.06–0.37 (2 H, multiplet), and 0.44 (1 H, doublet of doublets, J = 4 and 9 cps), thus requiring the presence of a cyclopropane ring. The decoupling experiments[9] [irradiation at δ −0.12 collapses the four-line pattern at δ 0.44 to a perturbed doublet (J = 9 cps) and, conversely, irradiation at δ 0.47 led to a doublet (J = 6 cps) for the signal at δ −0.13 while irradiation at δ 0.27 led to a broadened two-line pattern for the signal at δ −0.13 and at the same time collapsed a methyl doublet at δ 0.96] and the various methyl signals [220-MHz pyridine-d_5 solution, δ 0.72 (3 H, singlet), 0.89 (3 H, doublet, J = 6.5 cps), 0.93 (3 H, singlet), 1.00 (3 H, doublet, J = 6 cps), 1.03 (3 H, doublet, J = 7 cps), 1.07 (3 H, singlet), 1.10 (3 H, doublet, J = 6 cps)] preclude the possibility of generating a plausible structure possessing four cyclopropane protons, and we conclude, therefore, that at least one of the protons in the δ 0.06–0.37 region must be due to an unusually shielded hydrogen which is not attached to a cyclopropane ring.

Opening of the cyclopropane ring was effected in dihydrogorgosterol acetate (III; mp 177–178°, M^+ 470) by refluxing in acetic acid containing concentrated hydrochloric acid. While gas chromatography of the reaction mixture showed that it consisted of at least three components, the nmr spectrum confirmed the complete absence of cyclopropane hydrogens as well as of olefinic protons. It follows therefore that the cyclopropane ring had been converted into a mixture of tetrasubstituted olefins. Ozonolysis of this mixture followed by steam distillation into 2,4-dinitrophenylhydrazine solution yielded a mixture of hydrazones which were separated by gas chromatography. Aside from acetone dinitrophenylhydrazone, there was isolated a product whose mass spectrum was very similar to that of authentic[10] 3,4-dimethylpentan-2-one dinitrophenylhydrazone and which exhibited only one glpc peak when a mixture of the two products was injected. From the nonvolatile portion, there was isolated by gas chromatography 3β-acetoxy-5α-norcholan-22-one (IX), which was identified by direct comparison (ir, mass spectrum, nmr, and glpc mixed injection) with a synthetic sample[11] (mp 152–155°, M^+ 388). The isolation of ketone IX unambiguously demonstrates the existence of the intact steroid skeleton in gorgosterol as well as the existence of the alkyl branch at C-22. The isolation of 3,4-dimethylpentan-2-one from the ozonolysis demonstrates that at least one of the components from the acid opening of dihydrogorgosterol acetate must be 3β-acetoxy-22,23,24-trimethyl-Δ^{22}-5α-cholestene (VIII). The identification of this olefin does not unambiguously locate the cyclopropane ring and, barring methyl migrations, six structures (X–XV) are feasible for gorgosterol (I). However, only X and XI are consistent (see wavy lines for formal representation of cleavage) with the presence of an intense peak (base peak at 12 eV) at *m/e* 314 (*m/e* 300 in V) in gorgosterol (I)—a peak known[8] to be associated in certain side-chain-unsaturated sterols with a fragment containing the steroid nucleus together with carbon atoms 20, 21, and 22.

Work is currently under way to distinguish between structures X and XI, but the present data already demonstrate the unique nature of gorgosterol and the fact that it is the first sterol which possesses alkyl substituents at C-22 and C-23. While biosynthetic studies will be required to settle the origin of this side-chain substitution pattern, it is not unreasonable to assume that one of the intermediates is probably a Δ^{22} precursor, and it is noteworthy that many naturally occurring marine sterols possess this otherwise rare structural feature.[12] The other unique feature of gorgosterol, namely the presence of a cyclopropane ring, provides the first evidence in support of the postulate[2a,13] that cyclopropanes may be intermediates in the introduction of methyl groups into the cholesterol side chain, although it is equally plausible that the cyclopropane ring may have been generated as the last step in the biosynthesis. We hope to resolve this and other questions raised by the unique structure of gorgosterol through studies currently in progress.

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