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CONVERSION OF $\Delta^{24(28)}$-STEROLS TO Δ^{24}-ISOMERS

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Although the role of 24-methylene compounds in biogenesis of sterols and methyl sterols is of much current interest (1), Δ^{24}-derivatives of the 24-alkyl sterol side chain have not been described.[2] We wish to report the isolation of several such Δ^{24}-derivatives produced by reaction of $\Delta^{24(28)}$-compounds on silica gel.

To obtain pure euphorbol, 1, for other work, the hydrolysis product of euphorbol acetate was chromatographed on a silica gel[3] column, with the material remaining on the column for about four hours. The eluted major product gave a single spot when developed on a silica gel-TLC plate, but when examined by GLC, two components (about 1:1 ratio) were observed. These responded to separation by fractional crystallization to give two crystalline products, 1a and 1b. Compound 1a, mp. 126°, was identical (mmp., IR, NMR) with euphorbol, and 1b, M^+ 440.4024, mp. 156°, $[\alpha]_D$ +30°, was characterized as the Δ^{24}-isomer of euphorbol: Its IR spectrum does not have absorption at 890 and 1642 cm^{-1}, bands[4] in the spectrum of euphorbol due to the terminal methylene group. In the NMR spectrum the distinctive signals at τ5.27 found for 24-methylene protons of euphorbol are absent, and nine protons have shifted downfield to the vinyl methyl (τ8.34) from the high field methyl region (τ9.68-9.92). Catalytic (PtO_2) hydrogenation of 1b yielded a crystalline dihydro compound, 1c, mp. 138°, M^+ 442.4201, which was shown to be identical with the hydrogenation product of euphorbol by mmp., IR, GLC and TLC.

When euphorbol was prepared from the acetate without column chromatography, 1b was not found. The isomerization reaction is reversible, as 1b when placed on a silica gel column

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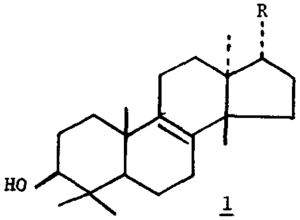
[2] The only Δ^{24}-compound of C-24 alkyl type in the literature is one derived from polyporenic acid-C (2), which has a carboxyl group at C-20.
Recently Ikekawa et al (3) have reported an isomerization promoted by iodine in which fucosterol gave rise to an unresolved mixture of three double-bond isomers. Presence of the Δ^{24}-compound in the mixture was demonstrated by further reaction.

[3] Davidson Co. product, grade 12, ratio of absorbent to compound 40 to 1.

partially isomerizes back to euphorbol^4.



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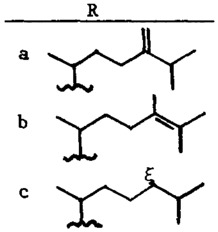

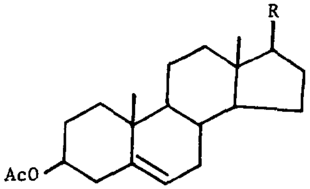

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24-Methylenecholesterol acetate, 2a, similarly isomerizes to 24-methyl-Δ^{24}-cholesterol acetate, 2b, as established in analogous fashion. Compound 2b is also indistinguishable from 2a by TLC, but is resolved by GLC, and can be separated by fractional crystallization. It has M$^+$ 440.3649, mp. 145°, $[\alpha]_D$ -21°, and differs from 2a in IR and NMR spectra as compound 1b differs from 1a. 24-Methyl-Δ^{24}-cholesterol, M$^+$ 398.3553, obtained from 2b by hydrolysis, melts at 140°, $[\alpha]_D$ -24°.

The isomerization reaction appears to be a general one for 24-methylene steroidal side chains; preliminary work indicates that eburicoic acid, fucosterol and 24-methylenecycloartanol all isomerize in the same manner.

Silica gel is commonly used in columns or thin layer plates for separation or analysis of 24-methylene sterols. Why the isomerization herein reported has not been detected previously permits several possible explanations; we hope that work now in progress will give some answers.

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[4] The reverse reaction is much slower. Studies on the equilibrium, and the effect of changes in silica gel composition, are under study and will be reported separately.

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