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Synthesis and Structure of (22*R*,24*R*)-6β-Acetoxy-24-methyl-5α-cholestane-3β,5α,22,24-tetrol

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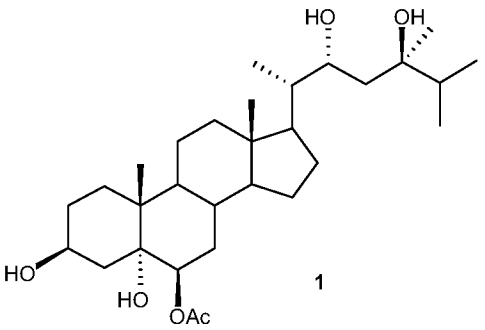
The title compound **1** has been synthesized for the first time from 20-isoxazolinylsteroid **2** *via* 5α,6α-epoxide **3** whose stereochemistry has been firmly established by an X-ray crystallographic analysis.

In 1984 a new monoacylated pentahydroxysteroid **1**, unusual for marine sterols, was isolated from the soft coral Asterospicularia randalli. [1]

Structure **1** has been proposed, based originally on its spectroscopic data. The *R* configuration was assigned by the authors only at C-22. The configuration at C-24 remained to be established and no synthesis of the compound in question was elaborated.

This paper deals with the synthesis and structural elucidation of a new polyhydroxysteroid **1** isolated from marine organisms.

The chemical synthesis of **1** was undertaken by the



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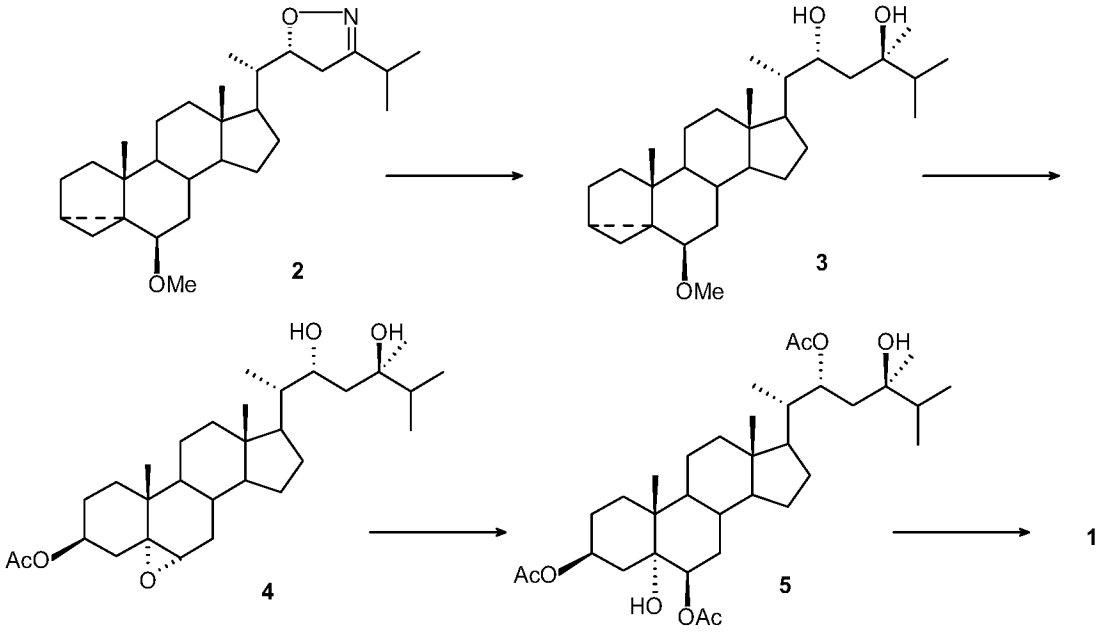
pathway outlined in Scheme 1. We have recently developed a highly stereoselective method for the synthesis of 22,24-diol **3** bearing the side chain of the natural steroid **1**.[2] This involved the hydrogenation of 20-isoxazolinylsteroid **2**[3] with Raney nickel in an acidic medium followed by reaction of the resulting 22-hydroxy-24-ketone with methyllithium. The major, less polar diastereomer **3** was used in the present work for further transformation.

The 3α,5-cyclo steroid **3** was refluxed in acetic acid for 5 h to regenerate the 3β-acetoxy-Δ^5 moiety. Subsequent epoxidation of the resulting 5-ene steroid with *m*-chloroperbenzoic acid in dichloromethane for 3 h at room temperature furnished (22*R*,24*R*)-3β-acetoxy-5α,6α-epoxy-24-methylcholestane-22,24-diol **4**† as a single product in 77% yield, m.p. 219–221 °C (acetone). The 5α,6α-epoxide **4** obtained gave well-shaped crystals, and to clarify the side-chain stereochemistry of this compound an X-ray determination was carried out.‡ On the basis of these data, (22*R*,24*R*)-stereochemistry was assigned to compound **4** and the products of its transformation.

The *trans* ring opening of the epoxide **4** by perchloric acid in tetrahydrofuran at room temperature for 2 h, followed by acetylation with acetic anhydride in pyridine, afforded (22*R*,24*R*)-3β,6β,22-triacetoxy-24-methylcholestane-5α,24-diol **5**§ in 90% yield. At this stage separation of the desired product by column chromatography was carried out.

Finally, partial deprotection of **5** with 2 equiv. of potassium carbonate in methanol at room temperature for 5 h produced the target monoacetate **1** in 89% overall yield from **5**, m.p. 145–146 °C (hexane–acetone). The spectral properties of the sterol **1**¶ thus synthesized support the proposed structure and are in good agreement with those of the naturally occurring polyhydroxysteroid.[1]

Thus, the present synthetic work confirms the molecular structure of the new sterol derived from Asterospicularia randalli. Its stereochemistry is proved by an X-ray study of the 3β-acetoxy-5α,6α-epoxide precursor.



Scheme 1

† Spectroscopic data for **4**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.63 s (3H, 18-Me), 0.86 d (3H, *J* 7 Hz, 21-Me), 0.93 d and 0.95 d (6H, *J* 7 Hz, 26- and 27-Me), 1.07 s (3H, 19-Me), 1.10 s (3H, 28-Me), 2.02 s (3H, OAc), 2.89 d (1H, *J* 4.0 Hz, C_6-H), 4.06 m (1H, C_{22}-H), 4.94 m (1H, C_3-H); IR (KBr) ν/cm^{-1}: 3500, 1740, 1250; MS *m*/*z* 491 ($M^+ + 1$), 490 (M^+), 430 (M^+–AcOH), 415 (M^+–AcOH–Me).

‡ A paper detailing the crystal data for **4** will be published elsewhere.

§ Spectroscopic data for **5**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.70 s (3H, 18-Me), 0.90 d, 0.92 d and 0.95 d (9H, *J* 7 Hz, 21-, 26- and 27-Me), 1.04 s (3H, 19-Me), 1.15 s (3H, 28-Me), 2.02 s (3H, C_{22}-OAc), 2.05 s (3H, C_3-OAc), 2.08 s (3H, C_6-OAc), 4.69 br s (1H, C_6-H), 5.13 m (1H, C_3-H), 5.18 m (1H, C_{22}-H); IR (KBr) ν/cm^{-1}: 3500, 3450, 1740, 1250, 1230; MS *m*/*z* 593 ($M^+ + 1$), 592 (M^+), 532 (M^+–AcOH), 517 (M^+–Me–AcOH), 472 (M^+–2AcOH), 412 (M^+–3AcOH).

¶ Spectroscopic data for **1**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.70 s (3H, 18-Me), 0.86 d (3H, *J* 7 Hz, 21-Me), 0.95 d and 0.98 d (6H, *J* 7 Hz, 26- and 27-Me), 1.08 s (3H, 19-Me), 1.14 s (3H, 28-Me), 2.07 s (3H, C_6-OAc), 4.07 m (2H, C_3- and C_{22}-H), 4.72 s (1H, C_6-H); IR (KBr) ν/cm^{-1}: 3600, 3450, 1740, 1250, 1230; MS *m*/*z* 509 ($M^+ + 1$), 508 (M^+), 491 (M^+–H_2O), 448 (M^+–AcOH), 433 (M^+–Me–AcOH).

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