SYNTHESIS OF (24R)-HOMOBRASSINOLIDE

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The synthesis from stigmasterol of C-29 brassinosteroids containing an (R)-ethyl group at C24 — (24R)-homocastasterone and (24R)-homobrassinolide — is described. The structure of the carbon skeleton of the side-chain was achieved by condensing a C-22 aldehyde with the appropriate sulfone.

It is known that plant sources contain a rich set of sterols [1]. While being important structural elements of membranes, sterols are also the initial compounds in the course of the biosynthesis of a whole series of steroids fulfilling hormonal, protective, or other, functions. It is obvious that this applies in full measure to a new class of plant hormones — the brassinosteroids [2]. About 30 representatives of this class of compounds have been detected, but hitherto no brassinosteroids with an (R)-ethyl substituent at C-24 have become known, even though possible biosynthetic precursors of them — poriferasterol, clionasterol — are widespread in the vegetable kingdom. A possible reason for this may be an imperfection of analytical methods, since brassinosteroids are present in plants in extremely small amounts (10^-7 - 10^-12% and less) [3]. The search for new compounds in natural sources would be considerably facilitated by the existence of authentic samples obtained synthetically.

The aim of the present work was the synthesis of (24R)-homobrassinolide and (24R)-homocastasterone. A single synthesis of these compounds, from the scarce sterol poriferasterol, has been described in the literature [4]. We have now developed a method of synthesizing (24R)-brassinosteroids from a more accessible raw material — stigmasterol.

A key intermediate — the aldehyde (7) — was obtained from stigmasterol in five stages. We have used it previously in the synthesis of norbrassinolide [5] and brassinolide [6]. The construction of the side-chains of the desired compounds was carried out by the condensation of the 22-aldehyde (7) with the sulfone (6), which was synthesized from isovaleric acid (1).

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\begin{align*}
\text{COOH} & \quad \text{C}_7\text{H}_6\text{Br} & \quad \text{COOH} & \quad \text{LiAIlH}_4 & \quad \text{OH} & \quad \text{TsCl} \\
1 & & 2 & & 3 & \\
\text{O} & \quad \text{SPh} & \quad \text{MCPBA} & \quad \text{SO}_2\text{Ph} & \\
4 & & 5 & & 5
\end{align*}
\]

The introduction of an ethyl group was achieved by treating with ethyl bromide the carbanion obtained from acid (1) and butyllithium. Reduction of the acid (2) with LiAlH₄ gave the alcohol (3), which was converted into the sulfide (5) via the tosylate (4). Oxidation of the sulfide (5) with m-chloroperbenzoic acid gave the sulfone (6). The structure of compound (6) was confirmed by its spectral characteristics. Thus, in the IR spectrum we observed absorption bands at 1150 and 1310 cm⁻¹, corresponding to the stretching vibrations of a S=O bond. The mass spectrum contained the peak of the molecular ion with m/z 240 and also peaks with m/z 142 (PhSO₂) and 99, 98 (M⁺ — PhSO₂; M⁺ — PhSO₂H). In the PMR spectrum all the signals of the methyl, methylene, and methine protons of this molecule were well defined. Condensation of the aldehyde...
(7) with the α-sulfonyl carbanion obtained from sulfone (6) and butyllithium followed by treatment with acetic anhydride led to the acetoxy sulfone (8). Reductive treatment of the latter with sodium amalgam in a mixture of methanol and ethyl acetate and elimination of the dioxolane protection gave the 22-ene-ketone (9) with an overall yield of 68.8%.

The subsequent functionalization of the molecule was effected by the successive introduction of 22,23- and 2α,3α-diol groupings and the lactonization of ring B.

The hydroxylation of the eneketone (9) with osmium tetroxide in pyridine led to a mixture of isomeric diols, three of which, after chromatographic separation, were characterized as the diols (10), (11), and (12). Their structures were established on the basis of spectral characteristics in comparison with the literature, and, in the case of diol (12), obtained previously from stigmasterol [7], also by a direct comparison of specimens.

Of the three diols isolated (10-12), interest in connection with the solution of the problem posed was presented by diol (10) which, like all natural brassinosteroids known at the present time, contained a 22R,23R-diol grouping.

The introduction of the Δ² bond was achieved in one stage by boiling compound (10) in dimethylformamide in the presence of pyridine hydrobromide. Oxidation with osmium tetroxide of the enediol (13) formed gave (24R)-ethylbrassinone (14) with a yield of 98%. The structure of the compound obtained was confirmed by a combination of physicochemical characteristics, which agreed with those given in the literature [4]. The introduction of a lactone function into ring B of compound (14) was effected by the Baeyer—Villiger oxidation of the acetyl derivative (15), followed by saponification and relactonization.