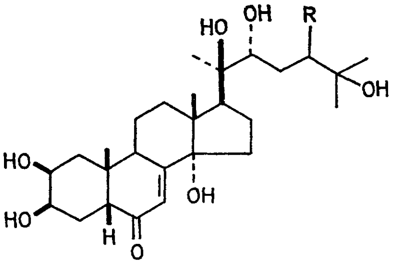
The Determination of Absolute Configuration at C-24 of the Phytoecdysone Makisterone A

By Bruno Danieli,†* Giorgio Ferrari,‡ Jiri Krepinsky,‡* Giovanni Palmisamo,† and Dario Sardini‡
(† *Istituto di Chimica Organica, Università degli Studi, Via C. Saldini* 50, 20133 *Milano*; ‡ *Simes Research Laboratories* 20161 *Milano, Italy*)

Summary Makisterone A was found to have an *R*-configuration at C-24; therefore its complete defined structure is 2*β*,3*β*,14α,20,22,25-hexahydroxy-5*β*,(20*R*, 22*R*,-24*R*)-ergost-7-en-6-one (II).

The absolute configuration of all chiral centres of the phytoecdysone makisterone A (I) was determined previously[1] with exception of the configuration at C-24 which carries the C-28 methyl group. In this communication we report the determination of the absolute configuration at this C-24 atom.

Compound (I) on oxidation with nitric acid in the presence of vanadium pentoxide[2] gives a mixture of di- and tri-basic acids, one of its constituents being (+)-*R*-methylsuccinic acid.[3] This acid was isolated by preparative paper chromatography[2] but its optical purity was low, $[\alpha]_D^{20}$ +2° (c 10, H_2O); lit. [6]$[\alpha]_D^{20}$ +10° (c 10, H_2O); however, it had a positive plain o.r.d. curve.§



(I) R = ∼Me
(II) R = —Me
(III) R = H

Thus the absolute configuration of the last chiral centre of makisterone A at C-24 should be R and its formula can be written as (II).

This conclusion is supported by the results of the study of molecular rotations of makisterone A (II) and its derivatives in comparison with crustecdysone (III) and its derivatives. As has been shown previously[4] in the case of campestanol, the contribution to the molecular rotation of the whole molecule by the centre of chirality at C-24 should be positive if the configuration is R; in the opposite case it would be expected to be negative. The differences in the molecular rotations of makisterone A (II) and crustecdysone (III) and of their derivatives are always positive and of the same magnitude thus confirming the above conclusion: [M_{II}-M_{III} (=ΔM): +108°; ΔM of 2,3,22-triacetates: + 104°, ΔM of 2,3,22,25-tetracetates: +89·7].

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§ The low optical purity can be explained by formation of racemic methylsuccinic acid from the tetracyclic portion of the molecule; we observed its formation in the case of crustecdysone and ecdysone. On the other hand racemization of optically active alkyl-substituted succinic acids was observed under similar conditions.[2,3]

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