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ACTIVE MANGANESE DIOXIDE: A REAGENT FOR A BIOMIMETIC CYCLIZATION OF 16ß-HYDROXYLATED 22.26-EPIMINOCHOLESTANES TO SPIROSOLANE ALKALOIDS

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Abstract: Treatment of the 16ß-hydroxylated 22.26-epiminocholestanes 1 - 4 with activated MnO_2 leads in a biogenetically remarkable cyclization directly and in good yields to the corresponding spirosolane alkaloids 5 - 8.

C_{27}-Steroidal alkaloids of the 22.26-epiminocholestane type are of particular interest with regard to their biogenetical correlations to other Solanum alkaloid groups[1] which could lead via redox reactions to solanidanes[2] as well as spirosolanes[3]. Earlier chemical methods for effecting a ring closure of 16ß-hydroxylated 22.26-epiminocholestanes to spirosolanes require strong conditions such as alkaline treatment of a corresponding N-chloro derivative[4], its photolysis in neutral solvents[5] or photolysis of a N-nitrose derivative in acidic solution[6].

We now report a mild biomimetic method for such a spiroaminoketal ring closure. This method uses the oxidizing reagent MnO_2 (Attenburrow-preparation)[7] and the reaction procedure is simple compared with our earlier reported methods. Yields of spirosolanes obtained from various 16ß-hydroxylated 22.26-epiminocholestanes are presented in Table 1. In a typical experiment 100mg of dihydrotomatidine A (1) in 10 ml of chloroform was stirred at 20 °C with 800 mg of active MnO_2. After 24 h (TLC monitoring) the MnO_2 was collected by filtration. Separation of the product by SiO_2 chromatography (Merck, grade III, elution with chloroform/methanol 95:5 v/v) afforded 80 mg of tomatidine (5) as well as some starting material. When the 3.16-diacetylated epiminocholestane 9[1] was treated with MnO_2 under analogeous conditions, a slower reaction took place leading after 72 h to 33 % of the known[1] azomethine 10. This result suggests that the smooth ring closure of the 16ß-hydroxylated epiminocholestanes 1 - 4 proceeds also via a primary oxidation of the piperidine ring[8] to corresponding

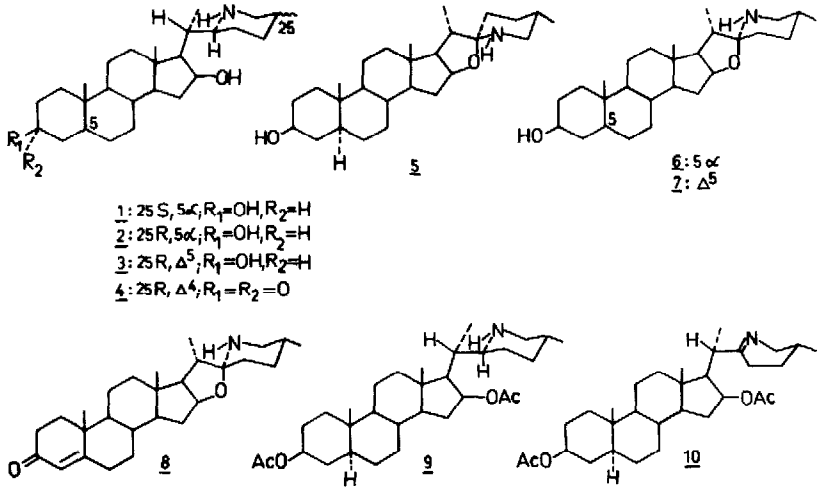
azomethines, followed by a spontaneous and stereospecific cyclization[4-6] to the spirosolane alkaloids 5 - 8.

Table 1: MnO_2 Oxidation of Various 16ß-Hydroxylated 22.26-Epiminocholestanes

Starting Compound	Product+	Yield
Dihydrotomatidine A (1)	Tomatidine (5)	80 %
Tetrahydrosolasodine A (2)	Soladulcidine (6)	75 %
Solaverbascine (3)[9]	Solasodine (7)	68 %*
Dihydrosolasodenone (4)	Solasodenone (8)[10]	64 %

+ Each product was compared with an authentic sample[7] by R_F, mmp, $[\alpha]_D$ and IR.

* In that case additionally 12 % of Δ^4-3-keto alkaloid 8 was isolated, the amount of it increased upon prolonged reaction time.



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