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Influence of the Position of Ring Unsaturation in Steroids and Triterpenes on the Type and Formation of Mesophases. I: Influence of the Δ^8 Double Bond

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Abstract—Lanosterol, dihydrolanosterol, 31-nordihydrolanosterol, zymosterol and tirucallol fatty acid esters do not exhibit liquid crystalline properties. All these compounds possess a Δ^8 double bond to which the inhibition of mesophase formation is attributed. In the case of tirucallol the steric inversion of the side chain and the angular methyl groups at C_{13} and C_{14} may or may not be additional parameters.

1. Introduction

In a recent publication we reported the identification, in plant material of 4α,14α-dimethyl-cholest-8-en-3β-ol (31-nordihydrolanosterol) (I).[1] We assumed that this compound was formed in the plant directly from its precursor 31-norcycloartanol (II), by opening of the 9,19-cyclopropane ring.[1] Since 31-norcycloartanol formed liquid crystals, testing 31-nordihydrolanosterol for mesomorphic behavior was therefore suggested. Since the concentration of 31-nordihydrolanosterol in the pollen of *Taraxacum dens leonis* is quite low, we synthesized it from its natural precursor 31-norcycloartanol. Biochemical opening of the 9,19-cyclopropane of the cycloartane triterpenes yields corresponding compounds with unsaturation at C_8,[3] while experimental opening by chemical reagents of this ring affords a mixture of the C_8 and C_9 unsaturated compounds.[4,5,6] It was found that the acetate of the Δ^9 com-

pound (III) formed a cholesteric mesophase while the acetate of the Δ^8 compound was not mesomorphic. This led to speculations that the Δ^8 double bond might inhibit mesophase formation in the steroid nucleus. We therefore selected a series of tetracyclic triterpenes and sterols which possess a Δ^8 double bond for detailed study.

To rule out the effect of other substituents we have selected lanosterol (IV), dihydrolanosterol (V) both of which possess 4,4,14α-methyl groups, zymosterol (VI) which does not possess these methyl substituents and tirucallol (VII) with sterically inverted side chain and C_{13},C_{14} methyl groups.

2. Experimental

Materials and chromatographic procedures are those described in earlier reports.[1,2,7] 31-Norcycloartanol (II) was isolated from the pollen of *Taraxacum dens leonis*.[1] Crude lanosterol was purchased from Sigma Chemical Co., St. Louis, Mo. and was found, by GLC, to be a mixture of lanosterol (IV) (60%) and dihydrolanosterol (V) 40%).

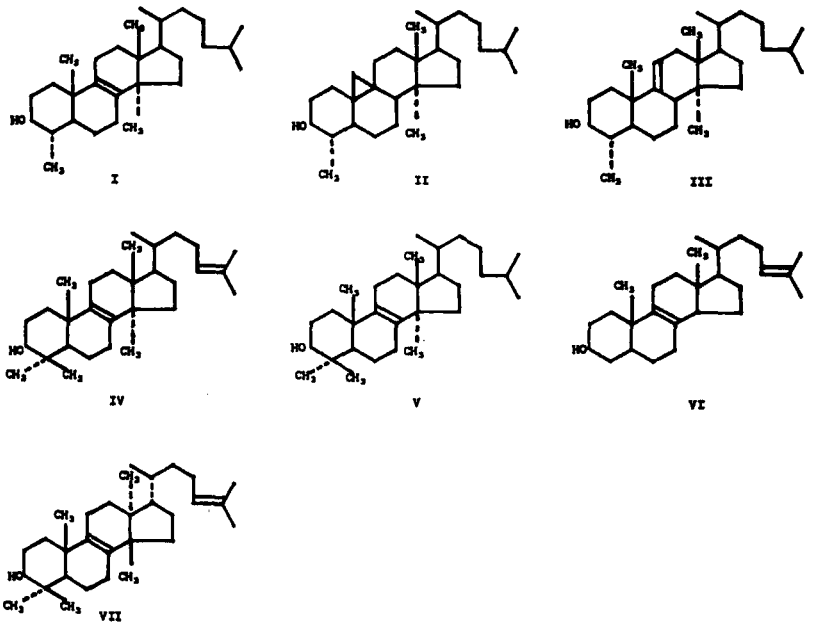

Figure 1

Zymosterol (VI) was isolated from bakers yeast and tirucallol (VII) was isolated from gum mastic by the method described by Barton and Seoane.[8]

3β-Acetoxy-4α,14α-dimethyl-cholest-9(11)-ene (III) and 3β-acetoxy-4α,14α-dimethyl-cholest-8-ene (I): 31-Norcycloartanyl acetate (200 mg) in anhydrous chloroform was treated with dry HCl gas for 2 hours. The residue after evaporation of the solvent was chromatographed on an alumina column impregnated with 12% $AgNO_3$ and elution was made with petroleum ether containing increasing amounts of benzene (5–10%). 3β-Acetoxy-4α,14α-dimethyl-cholest-8-ene was first eluted followed by 3β-acetoxy-4α,14α-dimethyl-cholest-9(11)-ene. Both were found ($> 99\%$) pure by GLC.

Lanosterol and dihydrolanosterol esters: Commercial lanosterol (10 g) containing 60% lanosterol (IV) and 40% dihydrolanosterol (V) was acetylated and the acetate mixture fractionated on a $AgNO_3$ (12%) alumina column eluted with increasing amounts of benzene in petroleum ether. Dihydrolanosteryl acetate was eluted first followed by pure lanosteryl acetate. Several recrystallizations from acetone afforded lanosteryl (IV) acetate and dihydrolanosteryl (V) acetate of a purity of $> 99.5\%$. The pure non-esterified sterols were prepared by hydrolysis of the acetates and the series of even chain esters from the butyrate to the palmitate of both compounds prepared and purified as described elsewhere.[2]

Zymosterol esters: 25 Kg wet bakers yeast was dried, powdered and extracted with boiling hexane for 3 days. The crude hexane extract was chromatographed on an alumina column. Esterified sterols were eluted with benzene. Free sterols were eluted with ether. The bulk of zymosterol was found accumulated in the ester fraction. Saponification yielded a mixture of zymosterol and ergosterol (55 : 45). Repeated crystallization of the mixture from ethanol afforded a mixture of (80 : 20) respectively. This was acetylated and chromatographed on a $AgNO_3$- alumina column. Pure zymosteryl acetate (99%) was eluted with 30% benzene in petroleum ether followed by ergosteryl acetate with 70% benzene in petroleum ether. Zymosteryl palmitate was prepared by hydrolysis of the pure acetate and esterifying the free sterol with pyridine/palmitoyl chloride by refluxing the mixture with benzene for one hour. Purification of the palmitate was made as described before.[2]

Tirucallol esters: Tirucallol fatty acid esters (acetate, hexanoate, decanoate, laurate and palmitate) were prepared as previously described for 31-norcycloartanol esters.[2]

3. Results

3β-*Acetoxy*-4α,14α-*dimethyl-cholest*-9(11)-*ene* (*III*): m.p. 90°. This compound exhibited a monotropic cholesteric mesophase at 88° with a beautiful play of colors ranging from blue to green to red to yellow.

3β-*Acetoxy*-4α,14α-*dimethyl-cholest*-8-*ene* (*I*): No mesomorphism was noticed for this compound either on heating or cooling.

Lanosterol and dihydrolanosterol esters: None of the even chain fatty acid esters of both compounds from the acetate to the palmitate exhibited any kind of mesomorphism.

Zymosteryl acetate and palmitate: Neither ester was mesomorphic.

Tirucallol esters: None of the esters of tirucallol was mesomorphic.

4. Discussion

Wiegand examined the benzoates of a number of cholestenols and cholestadienols for their mesomorphic behavior.[9] He pointed out that the nuclear unsaturation of the cholestanol molecule did not interfere with mesophase formation except when there is a double bond at position 14. However, Wiegand did not specify the type of mesophases involved. Of the compounds reported by Wiegand to be mesomorphic were the benzoates of cholest-8-en-3β-ol and cholesta-8, 24-dien-3β-ol (zymosterol). However, we observed that the acetate and palmitate of zymosterol were not mesomorphic, no birefringence being encountered upon heating or cooling.

The discrepancies between our findings and those of Wiegand are not clear. We believe that the turbidity observed by Wiegand for his compounds might have been attributed to some impurities present in his specimen since the preparation of such compounds often involves the formation of isomers. Moreover his experiments were reported in 1949 and no sensitive physical methods for the detection of such impurities were available at that time. The difference in the nature of the acid moiety can be excluded as a reason for the different

behavior since, as in the case of cholesterol, not only the benzoate but also short and long chain fatty acid esters are mesomorphic.

The duplication of the results with several sterols and triterpenes possessing a common position of unsaturation thus can be only attributed to this particular position of unsaturation. The additional methyl groups at C_4 and C_{14} do not seem to greatly affect the mesomorphic behavior of sterols and examples of this are already known.[2,10,11]

We therefore assume that the Δ^8 double bond in the steroid molecule inhibits the formation of mesophases, although the planarity of the molecules in such cases is not affected. Pohlmann, Elser and Boyd have conducted some experiments in which double bonds were introduced in ring A of the cholestanol molecule. They reported that Δ^1 and Δ^4-cholestenyl stearates were not mesomorphic and attributed this to a change in polarizability.[12] The same may apply for the Δ^8 compounds. In the case of tirucallol however, the other differences in stereochemical structure may or may not be of additional influence. The preparation from tirucallol of a completely saturated derivative or other compounds in which the double bond is shifted to other positions might help clarify this point.

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