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Ahmed M. Atallah [a] & Harold J. Nicholas [a]
[a] Institute of Medical Education and Research, Department of Biochemistry, St. Louis University School of Medicine, St. Louis, Missouri, 63104
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# Liquid Crystalline Properties of Fatty Acid Esters of Lophenol, a Cholesterol Biosynthetic Intermediate

AHMED M. ATALLAH and HAROLD J. NICHOLAS

Institute of Medical Education and Research
and Department of Biochemistry
St. Louis University School of Medicine
St. Louis, Missouri 63104

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**Abstract**—Lophenol (4α-methyl-cholest-7-en-3β-ol) an established biosynthetic precursor of cholesterol, forms a smectic mesophase only, when esterified with short ($C_2$–$C_4$) and long ($C_{10}$–$C_{16}$) even chain fatty acids. This is in contrast to cholesterol, which forms both cholesteric and smectic mesophases. This difference in behavior is attributed to the $C_7$ double bond in lophenol, as opposed to the $C_5$ double bond in cholesterol.

## 1. Introduction

In a continuation of our studies on the mesophase potentiality of various sterol biosynthetic intermediates we have selected lophenol[1] for further investigation. Lophenol has been isolated from the cactus Lophocereus schottii[2] and is the plant equivalent of the animal sterol methostenol, which has been isolated from rat skin,[3] largely in esterified form.[4,5] Lophenol is suggested to be a biosynthetic intermediate in the metabolism of both plant[6] and animal sterols.[7] Although the position of "methostenol" in the biosynthetic sequence leading to cholesterol formation has been verified experimentally,[5] the position of lophenol in the plant sterol biosynthetic sequence leading to the phytosterols (e.g. β-sitosterol and stigmasterol) has not yet been established. It seems quite likely that this position will be clarified within the coming years, and for this reason and because of its unique structure this investigation was made.

## 2. Experimental

Reagents and solvents were Analytical Grade. Melting points are corrected. Phase transition temperatures were obtained with a Nalge Axelrod hot-stage polarizing microscope. Crude lophenyl acetate was generously supplied by Prof. Kirscher of Arizona and was purified by repeated recrystallization from ethanol. The purity (99%), was confirmed by GLC. Lophenol was obtained by hydrolysis of its acetate and recrystallized to constant melting point (m.p. 148–150) from ethanol. 100 mg lophenol were used to prepare each of the fatty acid esters by dissolving in 2 cc hot pyridine and adding 20 drops of the corresponding acyl chlorides dropwise. The reaction mixture was mixed with 5 cc anhydrous benzene and refluxed for 1 hour. Esters of lophenol were obtained and purified by the procedure adopted for the purification of esters of 31-norcycloartanol[8] by chromatography on alumina. The columns were first washed with petroleum ether. Benzene eluted the esters quantitatively. Repeated crystallization of the esters was carried out from acetone or ethanol. The products obtained were of 99% purity as tested by GLC and TLC.

## 3. Results

All lophenol esters tested exhibited a distinct smectic mesophase manifested by the appearance of numerous beautiful bâtonnets[9] on cooling the isotropic liquid. This was in all cases followed by the typical smectic focal-conic texture. Lophenyl acetate was monotropic whereas higher esters exhibited enantiotropic smectic transitions. No colors appeared to the naked eye on either heating or cooling of any of the esters tested thus excluding any cholesteric mesomorphism.

*Lophenyl acetate:* Melted directly at 119–121° to the isotropic liquid. On cooling numerous small bâtonnets appeared which became much crowded and larger in size on further cooling, then coalesced to the smectic focal-conic structure. On reheating, the isotropic liquid was formed again at 96 °C.

*Lophenyl butyrate:* Melted at 73° to a viscous birefringent focal-conic structure which became isotropic at 127°. Cooling caused

typical bâtonnets to appear again at 127° becoming more numerous and very large followed by the focal-conic structure.

*Lophenyl decanoate:* Melted at 59° to a viscous birefringent smectic phase with typical large focal-conics. This became isotropic at 96°. On cooling the melt to 96° the bâtonnets appeared followed by the focal-conic texture.

*Lophenyl laurate:* Melted at 74° and exhibited enantiotropic smectic transition identical to that of decanoate at 94°. Bâtonnets were also observed on cooling the isotropic liquid.

*Lophenyl myristate:* Melted at 68° and behaved as the laurate. The enantiotropic smectic transition was formed at 87°.

*Lophenyl palmitate:* Melted at 75° and behaved similar to the lower esters. The enantiotropic smectic transition appeared at 82°.

Melting points and phase transition temperatures are tabulated in Table 1. No indications of a cholesteric mesophase have been encountered during the optical examination of any of the esters. The bâtonnets were formed readily from the isotropic liquid and turned to the typical smectic large focal-conic structure from which crystallization took place directly. Differential scanning calorimetry was not available to us and the optical examination seemed to provide enough evidence of the absence of any cholesteric mesophase.

## 4. Discussion

Whereas fatty acid esters of cholesterol exhibit cholesteric mesophases for the lower homologues and both cholesteric and smectic mesophases for the longer chain esters, lophenol was found to exhibit only the smectic phase when esterified with either short or

TABLE 1 Melting and Phase Transition Temperatures of Lophenol Fatty Acid Esters

| | M.P. | Phase transition Iso ↔ Sm |
|---|---|---|
| Acetate | 119–121° | 96° (monotropic) |
| Butyrate | 73° | 127° |
| Decanoate | 59° | 96° |
| Laurate | 74° | 94° |
| Myristate | 68° | 87° |
| Palmitate | 75° | 82° |

long chain fatty acids. This phenomenon seems unusual for substances related to the cholesterol molecule, but is not unprecedented. Knapp and Nicholas found that ergosterol fatty acid esters formed only a smectic mesophase.[10] The same authors also reported only smectic transition for some longer chain fatty acid esters of cycloeucalenol.[11] Wiegand in his classical report about structural influence on mesophase formation examined the benzoates of a number of mono- and diunsaturated cholestanols.[12] However, his observations were limited to the examination by the naked eye. Thus he did not determine the microscopic features of his melts and described his compounds as being mesomorphic if the melted crystals did not become "clear" until at a higher temperature. Wiegand thus did not specify the type of mesophase for the compounds he investigated and did not report any cholesteric colors. It is thus evident that not all mesomorphic compounds related to the cholestanol molecule should be cholesteric.

Since lophenol is 4$\alpha$-methyl-cholest-7-en-3$\beta$-ol, the influence of the 4$\alpha$-methyl group on the development of only a smectic phase must be considered also. However, 7-dehydrocholesteryl palmitate, which differs from cholesterol only by the presence of an additional double bond at position 7, and which does not possess any substituents at $C_4$, exhibits only a smectic mesophase very similar to that of lophenol (bâtonnets and focal-conics with absence of any irridescent colors) (unpublished observations).† Thus since cholesteryl palmitate is both cholesteric and smectic, the $\Delta^7$ double bond in 7-dehydrocholesterol must be the only parameter that permits this compound to become only smectic, and not cholesteric. The same reasoning may be applied to ergosterol esters.[10] With the identical phenomenon exhibited by lophenol and 7-dehydrocholesterol one can tentatively conclude that a double bond at position 7 may change the compound from a predicted cholesteric–smectic to only smectic. The physicochemical basis for this phenomenon is under study with stereochemical structures.

The relevancy of these observations to the role of lophenol in the phytosterol biosynthetic sequence cannot be assessed at this time, but is under consideration in this laboratory.

† A complete report on the liquid crystalline properties of 7-dehydrocholesterol will be published in a subsequent paper.

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