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Investigation of Mixtures of Cholesteryl Esters of Boron Analogues of Amino Acids with *p*-Azoxyanisole

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(*Received November 14, 1984*)

The phase diagram and helical pitch of two cholesteryl esters of the boron analogues of amino acids in mixtures with *p*-azoxyanisole (PAA) were investigated. These amino acid analogues, in pure form, do not exhibit mesomorphic phases. However, their mixtures with PAA show a monotropic cholesteric phase. The behavior of the cholesteric-isotropic transition indicates that these esters are potentially mesomorphic. Although the binary phase diagrams of the two compounds are similar, the cholesteric pitches are significantly different due to differences in polarity or hydrogen bonding of the amino group of one of the esters.

INTRODUCTION

Isoelectronic and isosteric boron analogues of the amino acids[1,2] and their precursors and derivatives have been shown to possess interesting biological activities; in particular, significant antitumor, antiarthritic and hypolipidemic activities in rodents.[1–6] For example, trimethylamine-carbethoxyborane, $(CH_3)_3NBH_2COOEt$, afforded 66% inhibition of tumor growth in the Ehrlich Ascites screen, 74% inhibition of the induced arthritic state,[4–6] and 36% reduction of serum cholesterol levels in animal model studies.[5,6] In view of their potential as biologically active agents, the synthesis of a series of esters (in-

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cluding some cholesteryl esters) of the boron analogues of amino acids has been reported elsewhere.[7,8]

Thermotropic liquid crystal properties of the cholesteryl esters have been known for many years. In fact, the first liquid crystal, the cholesteric (or chiral nematic) mesophase, was reported for cholesteryl benzoate about a century ago by Reinitzer.[9] Most of the cholesteryl esters satisfy the molecular requirements to show mesomorphic behavior. The basic criteria for steroidal liquid crystals are the existence of the C_5-C_6 double bond and equatorial orientation of the substituents at the 3β and 17β positions with respect to the long axis of the cholesteryl moiety. Among the aliphatic esters, the *n*-alkanoates have been most thoroughly investigated. The cholesteric mesophase is stable with increasing alkyl chain length up to n = 7, whereas the smectic phase is obtained when n > 7. Alkanoate branching (and their number, position and length) also influences the stability and type of the mesophase.[10-13] The thermal stability of the smectic phase can be enhanced by replacing oxygen of the *n*-alkanoate by sulfur.[14] In addition to the cholesteryl-*n*-alkanoates, esters having unsaturated aliphatic[15] and aromatic[16] moieties have been prepared. Systematic studies of some of these homologous series have provided insights concerning the correlations between molecular structure and the stability of the liquid crystal phases. The potential of the cholesteryl esters of the boron analogues of amino acids to display liquid crystal behavior, and comparison of their behavior with that of their natural organic counterparts is, therefore, a subject of interest which merits investigation.

The present work represents a preliminary study of the phase transitions of two boron analogues of amino acids, trimethylamine-(boryl)-carbonyl cholesterol (TMAB) and dimethylamine-(boryl)-carbonyl cholesterol (DMAB) in binary mixtures with the nematogen, *p*-azoxyanisole (PAA). It is well known that addition of an optically active species (either mesogenic or non-mesogenic) to a nematic phase produces a cholesteric phase. The pitch of the cholesteric structure is inversely proportional to the concentration of the optically active species. We have studied the phase diagram and pitch of these two compounds in mixtures with PAA.

EXPERIMENTAL

The compounds TMAB and DMAB were prepared by the procedure reported elsewhere.[8] The boron analogues of amino acids, R-BH_2COOH were R = $(CH_3)_3N^2$ and $(CH_3)_2NH$,[6] were reacted with

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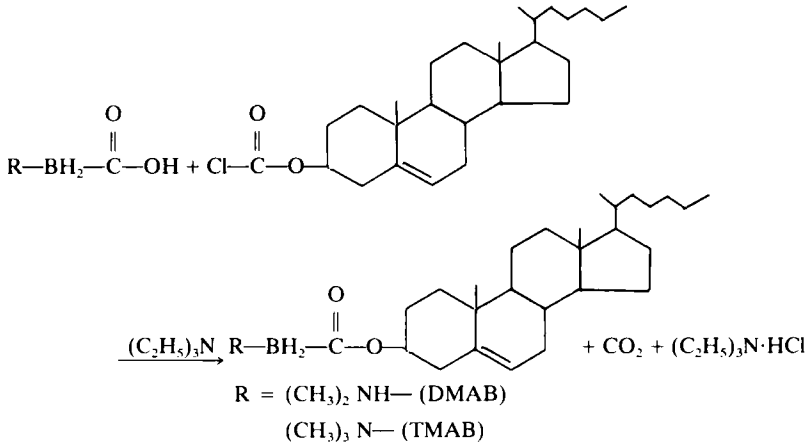
cholesteryl chloroformate in CH_2Cl_2 at 0°C in the presence of $(C_2H_5)_3N$ and a catalytic amount of dimethylaminopyridine. After completion of the reaction overnight, the mixture was washed with water, dried over $MgSO_4$, concentrated, and recrystallized.



p-Azoxyanisole obtained from Aldrich Chemical Co. was recrystallized from benzene and dried overnight in a vacuum oven at 80°C. Binary mixtures were prepared by weighing the components onto microscope slides, and then mixing for five minutes just above the melting temperature. Mixtures were then covered with microscope cover slips and their phase transitions were determined using an Olympus BH-2 microscope equipped with a Mettler FP52 hot stage and FP5 temperature controller. Heating and cooling rates near the phase transitions were generally 2°/min. The transition temperatures were reproducible to ± 0.5°C. Photo-micrographs of the textures were taken with a Nikon polaroid camera attachment. Values of the cholesteric pitch were measured directly from the periodic distances of the fingerprint textures in the photomicrographs.

RESULTS AND DISCUSSION

A. Phase Transitions

Neither cholesteric ester exhibited mesomorphic behavior on heating or cooling. This result is not surprising upon comparison with cholesteryl alkanoates having similar chain lengths and branching at a position equivalent to the methyl group on the amino nitrogen. For example, cholesteryl-2-methylbutyrate shows no mesomorphic phase,

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while the corresponding substituted valerate exhibits a monotropic smectic A phase.[12] Apart from this analogy, the contribution of boron to the potential mesomorphism of cholesteryl esters should be taken into account. Hence, we have investigated binary systems to seek evidence relating to this possibility.

Figures 1 and 2 present the binary phase diagrams of the PAA/TMAB and PAA/DMAB systems over the entire composition range, as determined by both heating and cooling data. Upon heating, as shown in Figures 1a and 2a, both systems exhibit an enantiotropic cholesteric phase within the limited composition range, $w < 0.15$, where w is the weight fraction of the cholesteryl ester. Within this range of compositions the crystal-cholesteric transition temperatures are almost identical for TMAB and DMAB. Figures 1b and 2b, which were constructed from cooling data, demonstrate that mixtures involving both esters exhibit a monotropic cholesteric phase for weight fractions $w > 0.15$. We conclude that methyl substitution on the amino nitrogen has negligible effect upon the mesomorphic phase transitions.

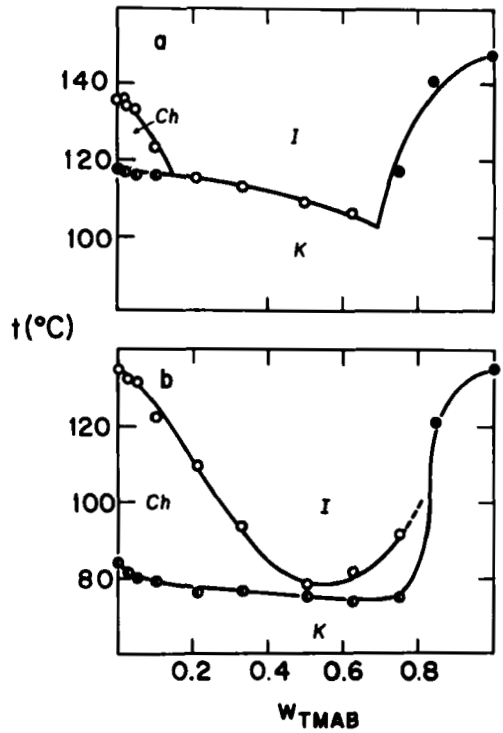

FIGURE 1 Phase diagram of the PAA/TMAB binary system by heating (a) and cooling (b).

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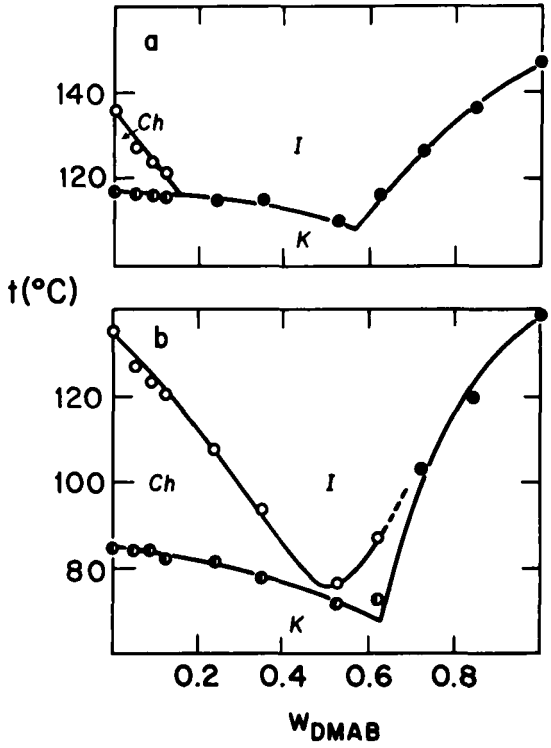

FIGURE 2 Phase diagram of PAA/DMAB by heating (a) and cooling (b).

An interesting observation concerning the cooling data is the minimum in the composition dependence of the isotropic-cholesteric transition temperature, which implies that both TMAB and DMAB are potentially cholesteric. However, at higher weight fractions of either ester the monotropic cholesteric phase boundary is intersected by the isotropic-crystal curve. The minimum isotropic-cholesteric transition temperature occurs at about w = 0.5 for both systems, but the cholesteric phase persists at higher concentration for TMAB. Extrapolation of the cholesteric-isotropic transition temperatures to w = 1.0 would furnish an estimate of the virtual clearing temperature for either ester. These appear to be near the crystal melting temperature for the pure ester, but they must be somewhat lower.

The effect of methyl substitution is more evident upon the crystal-isotropic transition temperatures of the present systems. Both Figures 1a and 2a show eutectic compositions corresponding to $w_{TMAB} = 0.65$ and $w_{DMAB} = 0.55$, respectively. On cooling, the isotropic-crystal transition temperature of TMAB shown in Figure 1b shows a smooth

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FIGURE 3 Photomicrographs (64x), taken with crossed polars, of the induced cholesteric phase of PAA/TMAB for chiral weight fractions (left to right): (a) 0.026, (b) 0.057, (c) 0.097, (d) 0.333 and (e) 0.745.

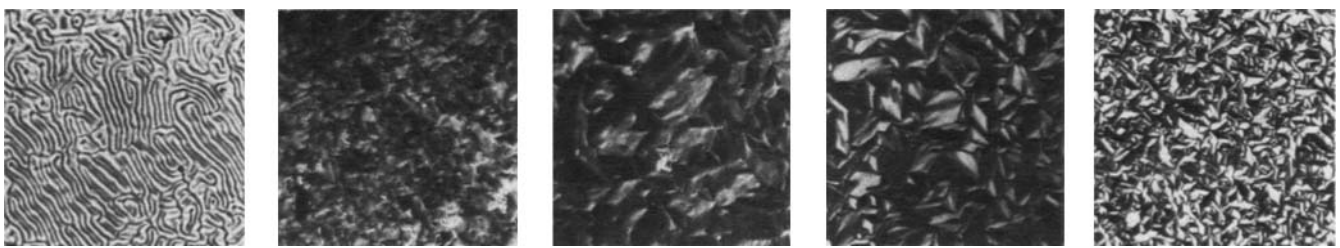

FIGURE 4 Cholesteric phase (64x), seen under crossed polars, of PAA/DMAB for chiral weight fractions (left to right): (a) 0.049, (b) 0.125, (c) 0.350, (d) 0.525 and (e) 0.616.

variation, while that for DMAB in Figure 2b exhibits eutectic behavior. It should be mentioned that the stable solid III form of PAA is responsible for the crystal transitions observed by heating, whereas the metastable solid I form of PAA is involved in data collected by cooling.[17]

B. Cholesteric Pitch

Figures 3 and 4 illustrate photomicrographs of the cholesteric texture of PAA/TMAB and PAA/DMAB taken under crossed polars at various concentrations of the esters. At low ester concentrations a large cholesteric pitch is manifested by the "fingerprint" texture, where the separation of successive periodic retardation lines, S, is directly proportional to the half-pitch, $S = 1/2p$. With increasing ester concentration the pitch decreases and the focal conic structure becomes the dominant texture. At still higher concentration the texture of PAA/TMAB changes to a planar texture (Figure 3e), whereas PAA/DMAB retains its focal conic characteristics (Figure 4e). These different textures arise from differences in the pitch and the strength of the interaction between the liquid crystal and the glass surfaces. Table I lists the values of the pitch as a function of the weight fraction of the two esters. The pitch is smaller, and its rate of change with concentration is larger, for the PAA/TMAB system. This difference is a manifestation of the effect of different terminal amino groups. Although the two esters of amino acids with secondary and tertiary amines have similar phase diagrams, they exhibit quite different pitch values.

The reciprocal pitch, 1/p, is shown plotted in Figure 5 as a function of c. Here p is the optically measured pitch and c is the concentration of the chiral ester in weight percent. A linear relation is found for

TABLE I

Cholesteric Pitch of TMAB and DMAB in PAA Solvent.

Mixture	w(chiral)	10^4p (cm)	1/p (cm^{-1})
PAA/TMAB	0.015	34.5	290
	.026	17.5	575
	.057	7.0	1430
	.097	4.5	2220
PAA/DMAB	.049	21.0	475
	.088	14.0	700
	.125	12.0	835

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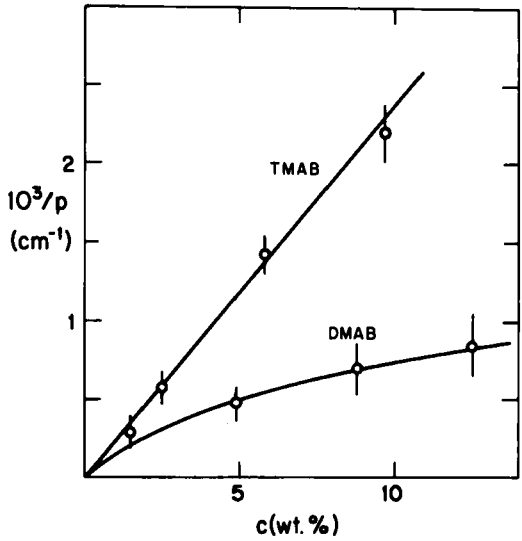

FIGURE 5 Reciprocal pitch as a function of the weight percent of TMAB and DMAB.

TMAB, whereas that for DMAB is concave downward. As a result, the pitch is much smaller (and 1/p is much larger) for higher concentrations of TMAB. Both polarity and steric effects of the optically active compound affect the pitch of the helix.[18] For example, it is known that increased polarity of the chiral compound increases the pitch of the lyotropic nematic phase of disodium cromoglycate, while addition of long bulky amino acids gives a smaller pitch.[19] On the other hand, the pitch of thermotropic aromatic nematics has also been found to increase with the size of the aromatic moiety.[20] In the present case the steric effects are negligible. The larger pitch of the DMAB systems may be due to its increased polarity, or to hydrogen bonding of the amino hydrogen to the carbonyl oxygen or the azoxy oxygen. Cholesteric pitch variations as a function of type of the ester-chain terminal groups in the biologically active esters, such as DMAB and TMAB, merits further investigation, where the effects of molecular architecture on the molecular structure and phase transitions of these systems will be studied.

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