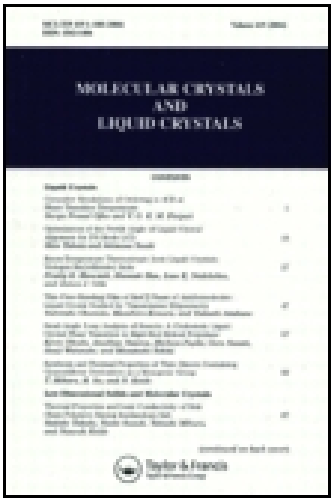

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Liquid Crystals Resulting from Combined Ionic and Hydrogen Bonding Interactions of Nucleobase Derivatives

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Liquid Crystals Resulting from Combined Ionic and Hydrogen Bonding Interactions of Nucleobase Derivatives

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Salts derived from the interaction of guanine or cytosine acid derivatives with hexadecylamine exhibited smectic liquid crystalline character. This behavior was attributed to a two-level organization process, i.e., to the segregation of lipophilic from hydrophilic moieties due to the formation of the n-alkylammonium salts and to the self-dimerization of these salts through molecular recognition. Furthermore, mixing of the complementary salts in 1:1 molar ratio led, at elevated temperatures, to the formation of their heterodimer which also exhibited a smectic liquid crystalline phase.

Keywords: amphiphilic liquid crystals; molecular recognition; hydrogen bonding; functionalized guanine and cytosine nucleobases

INTRODUCTION

Amphiphilic n-alkylammonium salts originating from the neutralization of long chain aliphatic amines with acids, and quaternary ammonium salts exhibit liquid crystalline character. The first studies on these liquid crystalline salts were reported in the early eighties [1] and reviewed in the mid-nineties [2]. Recently, the role of various functional groups attached on the quaternary cation on the liquid crystalline character has been systematically studied [3]. During the same period research in this area was focused [4, 5] on n-alkylammonium salts bearing polymeric counter ions, which also induce the formation of liquid crystalline phases. Indeed, it is interesting to note that n-alkylammonium polyacrylates and n-alkylammonium polyvinylsulfonates form a diversity of smectic A, B or E and

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cubic liquid crystalline phases [5]. Diversified liquid crystalline phases have also been obtained [6] by the neutralization of polyglutamic acid, a helical polycondensation acid, with long chain primary and secondary amines or quaternary alkylammonium salts. Depending on the temperature and nature of the amine, the materials exhibited smectic B, E or A liquid crystalline phases.

In a recent work [7a], the neutralization of pyroglutamic acid by long chain aliphatic amines is occurring simultaneously with self-dimerization, affording liquid crystalline materials. In this case the smectic liquid crystalline character of n-alkylammonium pyroglutamates was attributed to combined salt formation and dimerization of the pyroglutamic moiety through hydrogen bonding. Also, ionic and non-ionic building units, i.e. 1-n-heptyl-(4)-(4-pyridyl)pyridinium bromide and various acids were associated via hydrogen bonds for the formation of liquid crystalline phases [7b,c].

A further step towards these lines is the preparation of liquid crystals through the formation of complementary alkylammonium salts and their self- or heterodimerization. It has long been established [8] that although guanine and cytosine derivatives self-dimerize, they form stronger complexes with each other in the solid [8a], in solution [8a,b] or in lyotropic liquid crystalline phases [8c]. In addition it has been suggested, that association can also occur in the gaseous phase according to theoretical calculations [8d]. In the present investigation, complementary acid derivatives of guanine and cytosine form, in a first stage, alkylammonium salts G and C (Scheme) and the dimeric molecular recognition product, G-C, in a second stage. The mesomorphic character of the self-associating alkylammonium salts as well as of their hetero-associating complex is investigated.

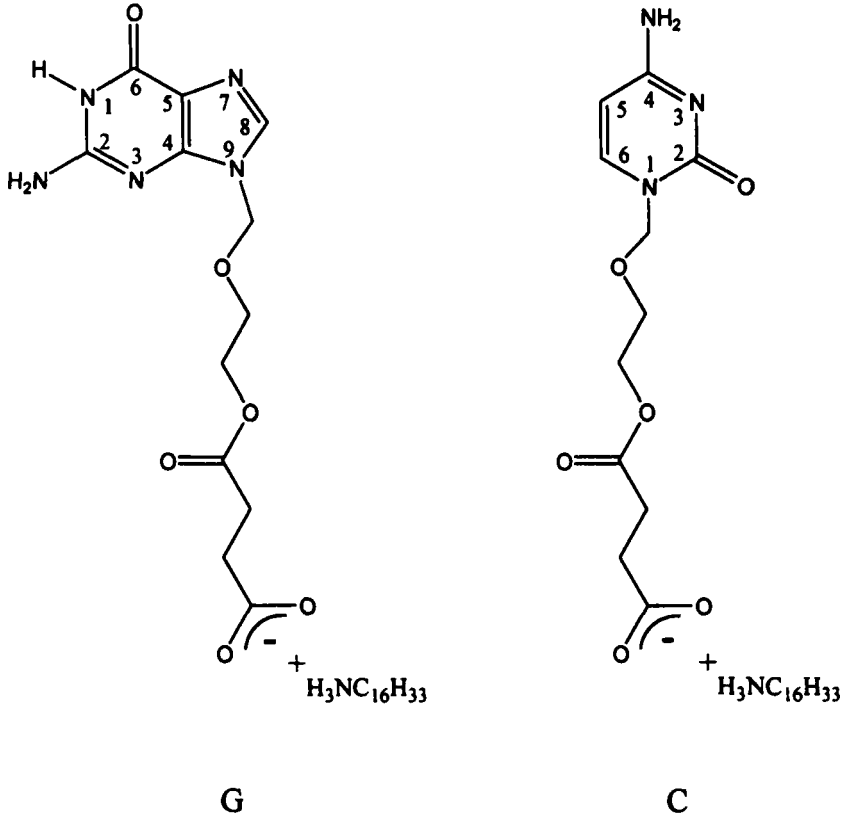
EXPERIMENTAL

Synthesis of 9-[(2-hydroxyethoxy)methyl]guanine succinate

The compound was prepared according to the literature [9]. ^{1}H NMR (250 MHz, D_2O), $\delta = 7.90$ (s, 1H, H-8), 5.50 (s, 2H, -NCH_2O-), 4.15 (m, 2H, -$OCH_2\underline{CH_2}OCO$-), 3.80 (m, 2H, -$OC\underline{H_2}CH_2OCO$-), 2.42 (m, 4H, -CH_2CH_2-succinate). Analysis for $C_{12}H_{15}O_6N_5$: calc. C: 44.31, H: 4.65, N: 21.53; found: C: 43.98 H: 4.70 N: 21.19 %.

Synthesis of 1-[(2-hydroxyethoxy)methyl]cytosine succinate

The synthesis of this compound was achieved by the following three steps: a) 4-methylthiouracil was prepared by interacting for 1h 0.05 mole of 4-thiour-



G C

SCHEME 1

acil, dissolved in 0.2 N NaOH solution (250 ml), with 0.055 mole of methyl iodide. The method employed was analogous to that described by Mizuno et al. [10]. b) The synthesis of 1-[(2-hydroxyethoxy)methyl]-4-(methylthio)pyrimidin-2-one and of 1-[(2-hydroxyethoxy)methyl]cytosine was achieved following the methods described by Barrio et al. [11]. c) The final product 1-[(2-hydroxyethoxy)methyl]cytosine succinate was obtained by interacting at 60 °C for about 20 hrs 0.005 mole of 1-[(2-hydroxyethoxy)methyl]cytosine, dissolved in dry DMF (75 ml), with 0.010 mole of succinic anhydride and 0.71 ml of triethylamine. The volatiles were distilled-off in a rotary evaporator and the material was precipitated with acetone and repeatedly recrystallized from an acetone/methanol mixture. ^{1}H-NMR (250 MHz, D_2O), $\delta = 7.75$ (d, J=7.5 Hz, 1H, H-6), 6.10 (d, J=7.5 Hz, 1H, H-5), 5.25 (s, 2H, -NCH_2O-), 4.25 (m, 2H,

-$OCH_2\underline{CH_2}OCO$-), 3.85 (m, 2H, -$OC\underline{H_2}CH_2OCO$-), 2.58 (m, -CH_2CH_2-succinate). Analysis for $C_{11}H_{15}O_6N_3$: calc. C: 46.32 H: 5.30 N: 14.73; found: C: 45.98 H: 5.42 N: 14.35 %.

Formation of n-Alkylammonium Salts of Nucleobase Derivatives, G and C

Equimolar quantities of guanine or cytosine acid derivatives and n-hexadecylamine dissolved in ethanol, were allowed to interact at room temperature. The precipitated guanine and cytosine derivatives were filtered-off and recrystallized from ethanol and an ethyl acetate/ethanol mixture respectively. FT-IR spectra provided evidence for salt formation due to the presence of two new bands at 1580 and 1390 cm^{-1} for the cytosine and at 1575 and 1370 cm^{-1} for the guanine derivative, assigned to the COO^- asymmetric and symmetric stretching vibrations. Additionally, the characteristic stretching and bending bands of the methylene groups of the long alkyl chains were also observed.

Formation of G-C Salt

Equimolar quantities of the G and C salts were thoroughly mixed in a vibrator mill. At room temperature hydrogen bonding interaction between G and C was not observed either by FT-IR spectroscopy or by X-ray diffraction in agreement with a literature report [12]. However interaction was taking place at temperatures higher than 80 °C (see discussion below). The FT-IR spectrum of the sample obtained after cooling, gives a strong band at 1720 cm^{-1} which was not present in the similarly obtained spectra of the interacting components. This is attributed to the heterodimeric complex derived from the complementary nucleobase derivatives [8a].

Characterization

Liquid crystal textures were observed using a Leitz-Wetzlar polarizing microscope equipped with a Linkam hot-stage. Thermotropic polymorphism was investigated by Differential Scanning Calorimetry employing a DSC-10 calorimeter (TA instruments). Liquid crystalline phases were investigated by X-ray diffraction using $CuK\alpha_1$ radiation from a Rigaku rotating anode X-ray generator (operating at 50 kV, 100 mA) and an R-AXIS IV image plate. Powder samples were sealed in Lindemann capillaries and heated employing an INSTEC hot-stage.

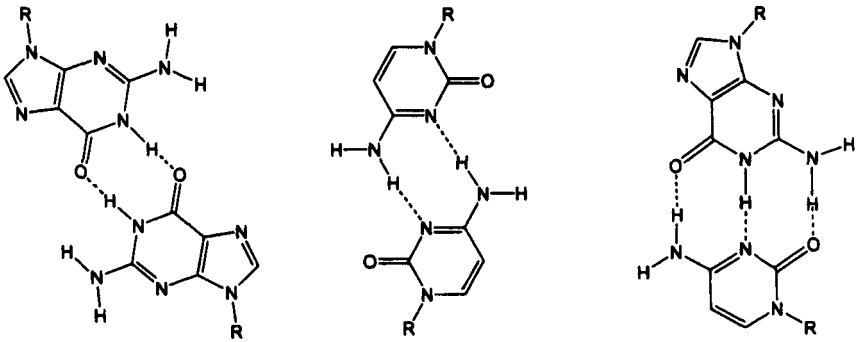
RESULTS AND DISCUSSION

The mesomorphic character of G and C salts was investigated by polarizing optical microscopy and differential scanning calorimetry. Upon heating the guanine derivative two solid-solid transitions were recorded at 57 and 120 °C before melting into a birefringent fluid at 131 °C, becoming isotropic at 152 °C. The cytosine derivative shows one solid-solid transition at 50 °C. It is transformed into a birefringent fluid at 101 °C becoming isotropic at 108 °C. The complex originating from the mixing of G and C salts shows two endothermic peaks at 45 and 80 °C related to solid-solid transitions. It melts into a liquid crystalline phase at 110 °C affording a homogeneous texture characteristic of smectic A phase which becomes isotropic at 150 °C. This behavior suggests complex formation between the two complementary components.

The X-ray diffraction patterns of the G and C nucleobase salts in the crystalline phase just before their melting into anisotropic fluids, contain up to 5 equidistant sharp peaks in the small-angle region attributed to lamellar crystalline structures. For the G-C complex, at temperatures above the second solid-solid transition, four new equidistant diffraction maxima are observed while the peaks originating from the interacting components are not any more present. The lamellar spacing at 100 °C is 35.0 Å, i.e. in between the spacings of 35.9 and 34.7 Å determined for cytosine and guanine derivatives respectively. For comparison purposes hexadecylammonium pyroglutamate, a compound of analogous structure, has a lamellar thickness of about 28 Å [7a]. In the nucleobase salts under investigation the lamellar periods are bigger primarily due to the presence of the hydroxyethoxymethyl succinate group. Therefore, as it was suggested for the alkylammonium pyroglutamates, the polar sublayers would consist of the dimerized nucleobases with the alkyl chains being in an extended conformation and interdigitated.

At temperatures exceeding crystal to mesomorphic transition, the X-ray patterns provide evidence for the formation of a disordered smectic A phase, showing one sharp peak in the small angle-region and a broad peak centered at 4.5 Å indicative of the melting of the paraffin chains. The thickness of the smectic layers in this case increases, reflecting the volume increase of the alkyl chains upon melting. The lamellar spacing is bigger for the cytosine derivative (45.4 Å) compared to that of the guanine derivative (38.2 Å). On the other hand, the lamellar thickness of the complex has an intermediate value (43.0 Å) due to the appropriate coverage of the polar sublayers by the paraffin chains. Indeed, by taking into account [13] the length, ~12 Å, and the density of the guanine-cytosine complex, 1.47 g/cm^3 corresponding to a volume of about 340 Å^3, one can derive the cross-sectional area of the polar sublayer, ~28 Å^2. This value is close to the val-

ues reported in the literature for the cross-sectional area of the disordered alkyl chains of smectic A structures [2a]. The differences of the observed lamellar spacings are therefore attributed to differences in the cross-sectional area of each nucleobase derivative. Apparently, the cross sectional area of the cytosine derivative in the dimeric form (Scheme II) is smaller than that of the guanine-cytosine complex or that of the guanine derivative. In this case therefore the alkyl chains occupy more lateral space.



G-G C-C G-C

SCHEME 2

It becomes evident from these characterization studies that the liquid crystalline character of the G-G, C-C and G-C complexes is derived from a two-level organization process. The first level is related to the organizational characteristics attributed to the n-alkylammonium salt formation of guanine or cytosine derivatives. As it is established in analogous cases [2], the lipophilic part is segregated from the hydrophilic part inducing microscopic organization leading to the exhibition of liquid crystallinity. The second level of organization is related to the molecular recognition of the salts resulting in the formation of self-dimeric or heterodimeric complexes when the complementary salts interact with each other.

In this connection it has to be noted that in addition to the proper geometry and the requirement of complementarity, the interacting components must be benefited by cooperativity or secondary electrostatic interactions as invoked by Jorgensen et al. [8d]. According to their proposed model the most favorable case, as far as the stability of the supramolecular structure is concerned, is when all or at least most of the donors are located in one of the interacting components while

the acceptors to the other. This is the case with the heterodimer guanine-cytosine complex which possesses a relatively strong binding of the DDA-AAD type in contrast to the weaker binding of the DA-AD type of the self-dimers.

In conclusion n-alkylammonium salts based on guanine, cytosine and their association dimer can be employed for the formation of smectic liquid crystalline phases, the structural parameters of which are affected by the n-alkylammonium cation and the nature of the nucleobase derivatives.

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