Translated from *Uspekhi Khimii* **57** 1575–1596 (1989) U.D.C. 532.783;548–14

Chromonic mesophases

A S Vasilevskaya, E V Generalova, A S Sonin
Institute of Organic Intermediates and Dyes, Moscow

ABSTRACT. **The chemical characteristics, structure, and physical properties of one of the most important types of lyotropic liquid crystals—chromonic mesophases—are examined. These liquid crystals are formed in solutions of large planar molecules and have a columnar structure. Chromonic mesophases are observed most often in solutions of dyes and medicinal drugs. The formation of mesophases is preceded by the aggregation of the molecules. The characteristics of this process are also examined in the review.**

The bibliography includes 96 references.

Contents

I. Introduction 904
II. The aggregated state as the premesophase 905
III. Dye mesophases 907
IV. Medicinal drug mesophases 910
V. Conclusion 914

I. Introduction

Liquid crystals have been known for more than 100 years but have entered the mainstream of the scientific and technical progress only during the last two decades—their optical properties proved to be convenient for the manufacture of simple and inexpensive indicating devices with a low power consumption. This led to a wide scale development of both chemical and physical and biological studies on liquid crystals.

By virtue of the unique combination of the properties of a liquid (the absence of translational order and hence fluidity and finite viscosity) and a crystal (the presence of orientational order and hence anisotropy of the physical properties), liquid crystals have become a favourite object in the study of the influence of structural order on the physicochemical properties of substances. It was found that liquid crystal (mesomorphic) properties are manifested by organic compounds in almost all classes. Furthermore, regardless of their chemical nature, a definite set of types of ordering proved to be typical for compounds of all classes, namely nematic with orientational order in only one direction, cholesteric with the same property but having in addition a helical superstructure in the direction at right angles to that of the orientational order, and smectic with the same properties as the nematic type of order but with layered order in a plane perpendicular to the direction of the orientational order. On the other hand, the chemical nature of the substance imparts detailed features to the canonical structural types. Thus the structural element for aromatic compounds is the molecule (sometimes the dimer), while for amphiphilic compounds it is a micelle consisting of tens of hundreds of molecules. A columnar order is characteristic of discotic molecules where a superstructure is produced as a result of the orientation of specific axes along a definite direction. Polymeric liquid crystals sometimes form a nematic mesophase with a hexagonal superstructure and twisted smectic mesophases.

The existence of dye and medicinal drug mesophases has been known for a long time but they have not attracted the attention of chemists or physicists. As early at 1916, Gaubert[1] found that a series of substances capable of forming thermotropic mesophases on fusion produced them when their solutions in ether, toluene, chloroform, carbon disulphide, etc. were evaporated. He later showed[2] that liquid crystals are formed also on evaporation of solutions of certain substances which do not give rise to mesophases on fusion. There is no doubt that all the liquid crystals obtained by this procedure are lyotropic, i.e. they were formed only when a highly concentrated solution was generated as a result of evaporation.

Among the substances investigated, there were also a number of dyes. Lyotropic liquid crystals were observed for anisylidene-*p*-aminoazotoluene,[1] tetrazine,[2] Brilliant Croceine,[3] Methylene Blue, and Neutral Red.[4] However, the structures of the mesophases of these compounds were not established and the above studies therefore remained unnoticed by specialists in the field of liquid crystals and had no influence on the further development of research into the physical chemistry of mesophases. Subsequently, in the 1940's–1950's, studies on the lyotropic mesomorphism of these compounds became of current interest for some time in connection with the vigorous investigation of the influence of the aggregation process in aqueous solutions of dyes on their absorption spectra, but, owing to the lack of interest in liquid crystals in general, they did not receive due development.

The study of the lyotropic mesomorphism of medicinal drugs began as early as the 1920's. The first drugs in which liquid crystal properties were discovered were apparently salvarsan and neosalvarsan.[5] However, these features were studied independently of the study of the liquid crystal properties of dyes and did not find an apparent practical application.

In recent years the situation has changed. The study of the structures of dye and drug mesophases showed that here there is a new type of mesormorphism. It was called chromonic mesomorphism, the name of the antiasthmatic drug sodium cromoglycate—a typical representative of this type of liquid crystal. It became clear in subsequent years that chromonic mesophases constitute one of the subgroups of lyotropic viscotic liquid crystals which are characterised by a column arrangement of planar molecules. Among them one can differentiate viscotic substances proper whose molecules have a symmetrical disc shape.[6–11] On the other hand, chromonic mesophases form planar molecules with a low symmetry having the form of a plank (sanidic). They can therefore be referred to also as sanidic mesophases. Incidentally, certain mesophases have been recently discovered among high-molecular-weight compounds.[12]

Chromonic mesophases have found a practical application. Thus it has been discovered that their lyotropic mesomorphism has a direct

bearing on the dyeing process[13,14] and the therapeutic effect of preparations.[15] Other technical applications of these mesophases have also been found.[16,17] All this has promoted the appearance of much interest in chromonic mesophases.

This review is devoted to the consideration of the present state of the problem of the lyotropic chromonic mesomorphism. Attention is concentrated on the conditions in the formation of mesophases, their structure, and its relation to the chemical structure of molecules and with physicochemical properties.

II. The aggregated state as the premesophase

The formation of the chromonic mesophase cannot be understood without considering its initial stage, the aggregation of molecules in aqueous solutions. This phenomenon is well known and has been studied mainly in relation to dyes.[18–21] It has been shown that the aggregation resembles to some extent micelle formation. There exists a critical concentration (we shall refer to it as the CCA—the critical concentration for aggregation), after the attainment of which a whole series of physical parameters, such as electrical conductivity,[19,22,23] the activity coefficient,[24] and the NMR spectra,[25] change sharply. Below the CCA, single molecules are present in solution, while above it they are aggregates. Typical CCA of certain dyes are listed in Table 1. Evidently the CCA depends not only on temperature but also on the nature of the electrolyte present. This indicates an appreciable role of electrostatic forces in the aggregation process. The CCA also depends on the length of the alkyl chain of the dye. Thus, in the case of 4-alkylamino-1-aminoanthraquinone-2-sulphonic acid, the increase in the length of the alkyl chain from 1 to 4 units (from methyl to butyl) diminishes the CCA at 40 °C in the presence of 0.05 M NaCl from 3.31×10^{-3} to 1.41×10^{-3} M, i.e. by a factor greater than 2. On the other hand, the introduction of 4 M urea into the same dyes increases the CCA almost by a factor of 4.[27] All this indicates that the aggregation process is influenced also by hydrophobic interaction.

Table 1. The values of the CCA for aqueous solutions of certain dyes.[26]

Dye	Electrolyte and its concentration, M	CCA, 10^{-4} M	
		30° C	40° C
Chlorazol Sky Blue FF	0.2 NaCl	2.8	4.0
	0.13 NaCl	5.0	6.2
	0.13 KCl	0.89	1.2
Congo Red	0.025 NaCl	3.0	5.2
	0.025 KCl	2.3	4.0
Benzopurpurine 4B	0.025 NaCl	2.6	4.9
	0.025 KCl	2.2	4.1

An important characteristic of the aggregation process is the aggregation number, i.e. the number of molecules in the aggregate. It is determined by many methods. The average aggregation number $\overline{N}_n$, defined as

$$\overline{N}_n = \sum_i (n_i M_i) \Big/ \sum_i n_i, \qquad (1)$$

where n_i is the number of molecules of type i having a molecular weight M_i, can be found from the rate of diffusion.

As a rule, aggregation begins with dimerisation. This process is accompanied by the absorption of heat. The thermodynamic data for certain typical dyes are presented in Table 2. They make it possible to regard dimerisation as a first-order phase transition which has become diffuse as a result of the finite size of the aggregates, as happens in micelle formation.[29] This can be readily seen from Fig. 1, which illustrates the dependence of the aggregation number of a dye, the sodium salt of 1-amino-4-butylaminoanthraquinone-2-sulphonic acid, on concentration. The aggregation number was calculated from the diffusion coefficient found by the polarographic method.[27] A large proportion of the data on the aggregation numbers of various dyes have been obtained by this procedure.[30–35] Table 3 lists the aggregation numbers for Direct Fast Orange SE in the presence of 2 g litre^{-1} NaCl at different concentrations and temperatures. Two typical tendencies are manifested here: $\overline{N}_n$ increases with increase in the dye concentration and diminishes with increase in temperature. At a given temperature, aggregation is intensified after a time. Thus the aggregation number of Benzo Light Red 8 BL at a concentration of 0.5 g litre^{-1} in the presence of 1.0 g litre^{-1} of NaCl increases by 30% in a week and by 100% in a month.[33] The origin of this behaviour can be understood from general considerations and needs no comment.

Table 2. Thermodynamic characteristics of the dimerisation reactions of certain dyes at 25 °C.[28]

Dye	ΔF, kcal mol^{-1}	ΔH, kcal mol^{-1}	ΔS, cal mol^{-1} K^{-1}
Orange P	−4.28	−10.48	−20.8
Thionine	−4.10	−6.82	−9.10
Methylene Blue	−5.17	−5.90	−0.77
Rhodamine 6G	−4.57	−8.6	−13.5

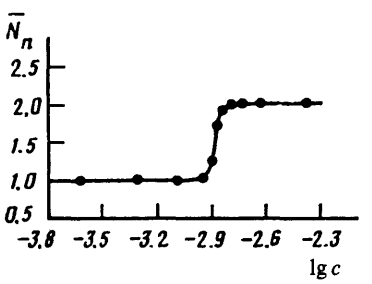


Figure 1. Dependence of the average aggregation number $\overline{N}_n$ on the concentration c of the sodium salt of 1-amino-4-butylaminoanthraquinone-2-sulphonic acid in the presence of 0.05 M NaCl at 30 °C.[20]

Table 3. The aggregation numbers for Direct Fast Orange SE.[33]

T, °C	c, g litre^{-1}	$\overline{N}_n$	T, °C	c, g litre^{-1}	$\overline{N}_n$
25	0.05	39	60	0.05	9
	0.1	43		0.1	10
	0.2	53		0.2	13
	0.5	64		0.5	17

As already mentioned, the presence of an electrolyte in the solution has a significant influence on the aggregation process. Fig. 2 presents the dependence of the aggregation numbers of certain dyes on the NaCl concentration.[36] It is readily seen that the electrolyte concentration has a greater effect on $\overline{N}_n$ than the concentration of the dye itself. Thus an increase in the concentration of benzopurpurine 4B from 0.005 to 0.01 wt.% does not lead to an increase in the aggregation number, which remains 6, but an increase in the NaCl concentration from 0.01 to 0.02 wt.% increases $\overline{N}_n$ from 6 to 400.[30]

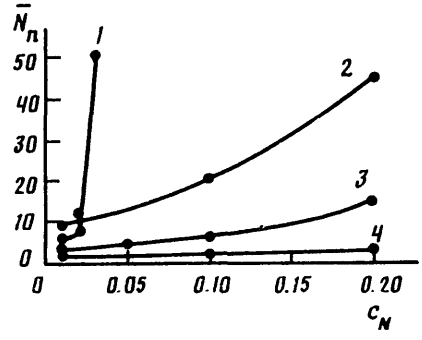


Figure 2. Dependence of the average aggregation number for dyes on the NaCl concentration: (*1*) benzopurpurine 4B; (*2*) Congo Red; (*3*) Chicago Blue; (*4*) Orang P.[36]

The weight-average aggregation number can be found by the classical light scattering method:

$$\overline{N}_w = \sum_i (n_i M_i^2) \Big/ \sum_i (n_i M_i), \qquad (2)$$

It is not identical with the $\overline{N}_n$ found by the diffusion method.[37,38] Thus $\overline{N}_n$ = 552 and $\overline{N}_W$ = 2621 for benzopurpurine 4B in the presence of 0.04 M KCl at 25 °C.[39] Whereas the average aggregation number yields the actual average number of aggregated molecules, the weight-average aggregation number reflects only the maximum degree of aggregation. The discrepancy between $\overline{N}_n$ and $\overline{N}_W$ therefore indicates the polydispersity of the aggregates in the given solution. The knowledge of both aggregation numbers makes it possible to plot a diagram illustrating the distribution of the micelles with respect to size.[40]

The aggregation process has a significant influence on the absorption spectra of dyes.[19–21] The presence of a long-wavelength absorption band *M* and a shorter-wavelength band D with a lower intensity is typical for the monomeric form of the dye. A still shorter-wavelength low intensity band *H* is sometimes also manifested. When aggregates are formed, the intensity of the band M falls but those of the bands H and D increase. An example of this kind is illustrated in Fig. 3, which presents the absorption spectra of a solution of pseudoisocyanine chloride.

A deviation from the Beer–Lambert law is also a sign of the appearance of aggregates in solution, although the degree of deviation is not linked directly to the aggregation number.[41]

Dye solutions at concentrations above the CCA exhibit flow birefringence. This effect has been observed for benzopurpurine 4B both in the absence of an electrolyte[42] and in the presence of 0.05 M NaCl.[43] Hence it was concluded that the aggregates are large highly anisometric particles. Under certain conditions, they can be observed under an ultramicroscope.[43] Similar conclusions were reached also in the interpretation of the absorption spectra.[44]

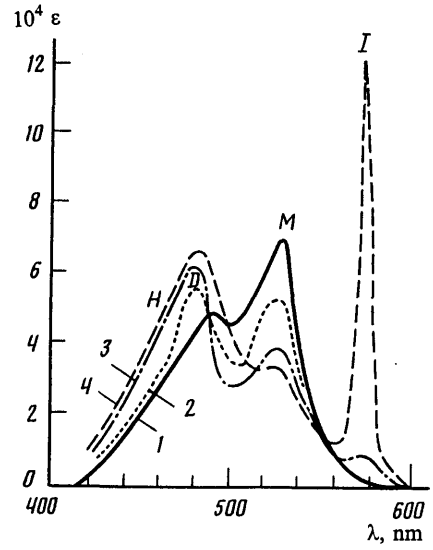


Figure 3. Absorption spectra of aqueous solutions of pseudoisocyanine chloride at 25 °C and different molar concentrations: (*1*) 1.3 × 10^{-5}; (*2*) 1.3 × 10^{-3}; (*3*) 7.1 × 10^{-3}; (*4*) 1.4 × 10^{-2}.[21]

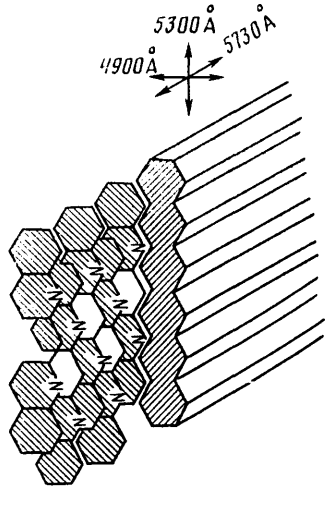


Figure 4. A model of the packing of pseudoisocyanine molecules in the aggregate; above—schematic illustration of optical trichroism.[46]

The question arises what these aggregates represent. In order to answer it, it is essential to say a few words about the structure of the molecules of the dyes considered. In the majority of cases, the molecules of ionogenic dyes have a planar form, although the oxygen and hydrogen atoms of terminal groups such as SO_3, OH, or NH_2 project upwards or downwards from the main plane of the dye. In aqueous solutions, these hydrophilic groups are in contact with water

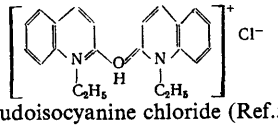
molecules, which inevitably leads to the mutual contact of the hydrophobic hydrocarbon skeletons of the molecules. As a result, the dye molecules are arranged like coins in a stack.[45,46] Specific details of such packing are naturally different for different dyes. Thus in the case of pseudoisocyanine dyes each successive molecule in the stack is displaced relative to the preceding one in such a way that the nitrogen atom in the quinoline ring lies above the carbon atom of the methylidyne group. This model[46] explains satisfactorily the trichroism of the absorption spectra (Fig. 4).

The question arises what retains the molecules in the aggregates. There exists the view[41] that these are van der Waals dispersion forces. However, according to other ideas,[47] hydrogen bonds play the main role here. The latter model presupposes the insertion of two water molecules between the dye molecules for each layer. These molecules form hydrogen bonds with the oxygen or nitrogen atoms of the dye. This view has found support in investigations[48,49] where it was shown that the aggregation of dyes in non-aqueous solutions is also accompanied by the formation of hydrogen bonds.

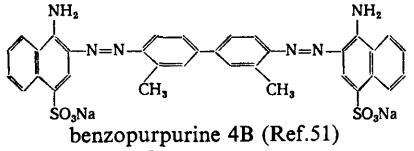
III. Dye mesophases

With increase in the dye (and also electrolyte) concentration, the degree of association also increases, leading ultimately to the precipitation of the solid phase. So long as the aggregates are small, their motion is uncorrelated, since they do not experience steric hindrance. The solution remains isotropic and birefringence arises only in flow. On the other hand, when the aggregates grow so much that they begin to "interfere" with one another, their motion acquires a correlated character. They can now move only together, since the orientation of one aggregate in one way or another specifies the orientation of all the others. Spontaneous birefringence arises. Such a phase is a lyotropic liquid crystal phase.

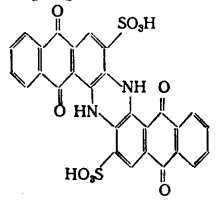
Fairly numerous dyes whose aqueous solutions have chromonic phases are now known. The chemical formulae and names of the most typical liquid crystals are presented below:



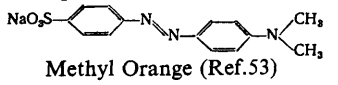
pseudoisocyanine chloride (Ref.50)



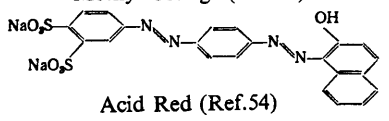
benzopurpurine 4B (Ref.51)



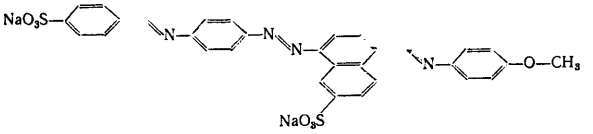
disulphoindanthrone (Ref.52)



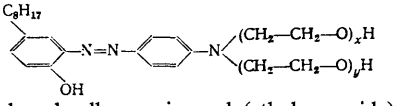
Methyl Orange (Ref.53)



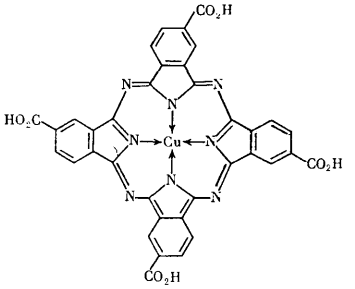
Acid Red (Ref.54)



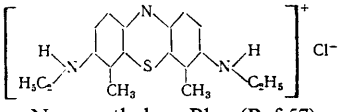
Sirius Supra Brown (Ref.54)



p-t-Octylphenol yellow amine poly(ethylene oxide) (Ref.55)



Copper-tetracarboxyphthalocyanine (Ref.56)

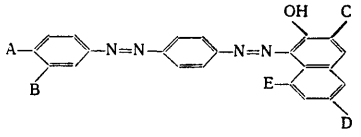


Novomethylene Blue (Ref.57)

It is readily seen that the liquid crystal dyes belong to different groups. They include cyanine, anthraquinone, and azo-dyes. They are represented by different water-soluble forms—salts and acids. One of the compounds is a dye possessing surface-active properties. It is related to a long-chain hydroxyethylated alcohol,[55] which also forms liquid crystals. Finally, the penultimate dye—copper-tetracarboxyphthalocyanine[56]—represents the large class of metal-containing porphyrins.

All the dyes indicated above have large planar molecules. Thus the length of the benzopurpurine 4B molecule is 24 Å whilst that of disulphoindanthrone is 14 Å. The width of the latter is 8 Å, whilst its thickness, like that of all such planar molecules, is approximately equal to the diameter of the carbon atom (3.4 Å). As already stated, such molecules can be readily arranged in stacks.

The question of the influence of the chemical structure on the ability of the dye to form the liquid crystal phase has acquired considerable importance in this connection. Such influence has been investigated[54] in relation to diazo-dyes having the general formula



(I)

The combinations of the substituents A, B, C, D, and E in various compounds are indicated in Table 4.

Distinct mesophases are formed by the dyes (I) and (IV) over a fairly wide concentration range. The formula of the latter dye (Acid Red) was indicated above. The dye (V) affords a mesophase over a narrow concentration range. The remaining dyes do not form mesophases. Hence one may conclude that the addition of sulpho-groups to the benzene fragment favours the formation of a mesophase to a greater extent than their addition to the naphthalene fragment.

The following rules have been formulated as a result of detailed studies of the influence of chemical structure on the liquid crystal properties of dyes.[58] If the dye molecule consists of one or two planar fragments linked by a twofold axis and has a symmetry point group C_2 or higher and the planar fragments of the molecule have at the same time a single possible conformation, the inogenic hydrophilic groups are such that, at a pH greater or smaller than a certain value pH_0, the dye acquires an appreciable solubility ($\sim 10^{-2}$ M) due to the dissociation of these groups, all the hydrophilic groups are located only on the periphery of the molecular plane, i.e., the planar part from the molecule is hydrophobic, and on the plane and along the periphery of the molecules there are no groups capable of preventing the formation of dimers and multimers, i.e. the molecular planes are capable of sliding freely past one another without experiencing steric hindrance whose overcoming would require the expenditure of an energy greater than kT, then conditions exist (pH, ionic strength, temperature, and concentration ranges) such that the dye forms a lyotropic liquid crystal phase in an aqueous electrolyte solution. An obligatory requirement is also that the adsorption of electrolyte ions does not entail the breakdown of the above conditions.

Although these rules are in fact fairly general, they were found to be well justified in the search for new chromonic mesophases.[59]

Table 4. Substituents in diazo-dyes having the general formula (I).

Compound	A	B		D	E
(I)	SO_3Na	H	H	H	H
(II)	H	H	H	SO_3Na	H
(III)	H	H	H	H	SO_3Na
(IV)	SO_3Na	SO_3Na	H	H	H
(V)	H	H	SO_3Na	SO_3Na	H
(VI)	H	H	H	SO_3Na	SO_3Na
(VII)	H	H	SO_3Na	SO_3Na	SO_3Na
(VIII)	H	H	H	H	H

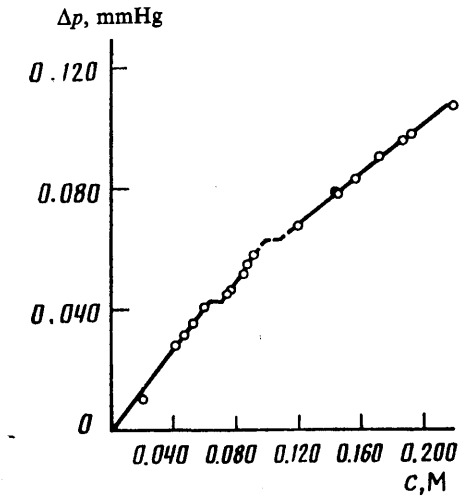


Figure 5. Dependence of the decrease in the vapour pressure of an aqueous solution of the dye Naphthol Yellow S on its concentration at 20 °C.[60]

Like the appearance of aggregates, the formation of the mesophase is a critical process and is accompanied by a sharp alteration of a number of physical properties when both the concentration and the temperatue are varied. In both cases a first-order phase transition take place. Fig. 5 shows how the vapour pressure of an aqueous solution of Naphthol Yellow S decreases as a function of its concentration at 20 °C.[60] Two anomalous sections can be readily seen at ~0.06 and 0.01 M. At low concentrations, an aggregated isotropic solution exists. With increase in concentration, a liquid crystal solution, separated into two phases, arises (see below).

A similar situation occurs also when the temperature is altered. Fig. 6 presents the temperature variation of the specific conductance of a 0.1 M aqueous solution of the disulphoindanthrone dye.[52] Above 32 °C, an isotropic solution exists in which two chromonic mesophases are formed in succession on cooling. The electrical conductivity undergoes pronounced changes at the phase transition points.

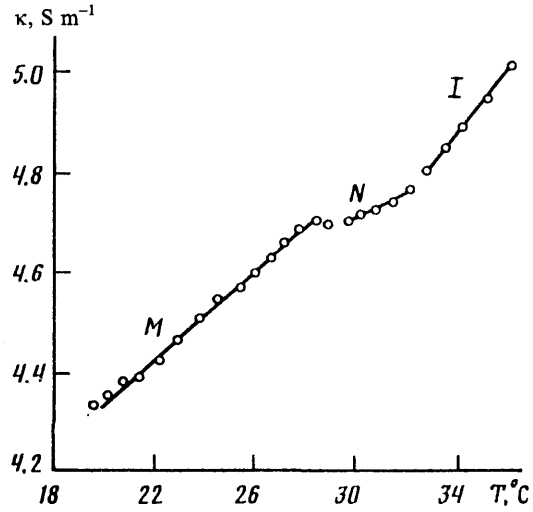


Figure 6. Temperature dependence of the specific conductance κ of a 0.1 M solution of disulphoindanthrone: *M*—hexagonal mesophase; *N*—nematic mesophase; *I*—isotropic phase.[52]

The positions of the points corresponding to transitions to mesophases on the concentration and temperature scales are naturally determined by the nature of the dye and the solvent. This can be represented most fully by phase diagrams (see below). However, in order to provide an idea about the order of magnitude of the quantities, Table 5 lists the critical concentrations at which typical dyes form mesophases at room temperature. On comparing the data in Table 5 with the values of the CCA listed in Table 1, it is readily seen that the transition to the mesophase is completed at concentrations which exceed on average the CCA by two orders of magnitude.

The formation of mesophases in dye solutions is characterised not only by the appearance of double refraction but also by a change in the transmission spectrum—a new narrow band (the so called *J*- or *Z*-band) appears in the long-wavelength region. It is readily seen in Fig. 3. Partial polarisation and fluorescence are observed in this part of the spectrum.[44–46,50]

The formation of a liquid crystal is accompanied by yet another interesting effect—the appearance of induced optical activity. It has been observed[61] in an aqueous solution of 1,1'-diethyl-2,2'-carbocyanine iodide after the addition of NaCl. The optical activity is due to the linear dichroism arising as a consequence of the ordering of the supermolecular structures. It appeared only after the cell had been rotated around its longitudinal axis.

Table 5. Critical concentrations for the formation of chromonic mesophases by typical dyes in aqueous solutions at room temperature.[52,60]

Dye	Critical concentration, 10^{-2} M
Amaranth	3.8—4.2
Naphthol Yellow S	6.2—7.0
Potassium Methyl Orange	2—10
Pseudoisocyanine chloride	1
Disulphoindanthrone	10
Benzopurpurine 4B	1—10

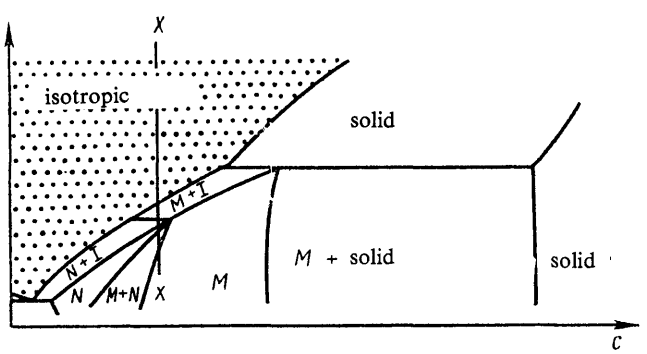


Figure 7. Typical phase diagram of chromonic mesophases.[54]

The appearance of the chromonic mesophase entails the appearance of spontaneous birefringence and of characteristic textures which differ little from the textures of the usual thermotropic liquid crystals (see below).

There are altogether still few complete phase diagrams for binary dye–water systems. A phase diagram which is to some extent typical is illustrated in Fig. 7.[54] Leaving aside the solid phases, we shall consider the sequence of mesophases arising on heating along the *X–X* line in the above diagram. For the typical dye Sirius Supra Brown, this line corresponds to a concentration of 16 wt.%. At room temperature, the dye forms the mesophase *M*. It follows from the analysis of the X-ray diffraction patterns for this phase that the thickness of the dye molecule is 3.4 Å and the parameters of the hexagonal cell are 40 and 23 Å, i.e. are in the ratio $1 : 1/\sqrt{3}$.

A model of such hexagonal structure is illustrated in Fig. 8. It was constructed taking into account the real rectangular structure of the dye molecule. Although the centres of the columns are arranged in accordance with the hexagonal law, in fact the structure should be more correctly regarded as being of the "chevron" orthorhombic type. This thickness of the layer of counterions and water between the columns of the dye molecules is then 10—20 Å.

In certain dyes, the hexagonal mesophase has a more complex nature. For example, four varieties of the mesophase *M* have been found in Acid Red. At room temperature and a dye concentration of 14 wt.%, the usual mesophase *M* is produced. However, when it is heated to 50 °C, lens-shaped regions, resembling the sodium caprylate "sticks" are formed.[62] This is the second hexagonal mesophase. On further heating, the lens-shaped regions merge, forming an island type texture, which belongs to the third hexagonal phase. Above 90 °C, the lens-shape regions reappear, giving rise to a network texture. This is the fourth mesophase *M*. However, presumably not all the formations described above are really mesophase *M*. Analysis of the textures described by Jones and Kent[63] suggests that at least the high-temperature phase is nematic (*N*).

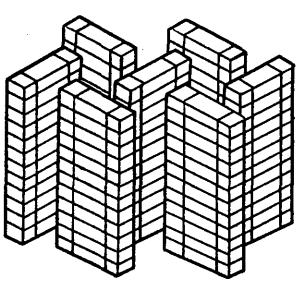


Figure 8. A model of a hexagonal chromonic mesophase *M*.[54]

This mesophase *N*, is clearly manifested on the phase diagram presented in Fig. 7 only beyond the two-phase region (along the *X–X* line). It has a typical Shchlieren texture with appreciable planar regions (see below). In the nematic mesophase *N*, the columns of the dye molecules are fairly free. They are structural units like the anisometric micelles in micellar nematic phases.[64] On the X-ray diffraction patterns of the mesophases *N*, only one reflection, permitting the estimation of the thickness of the dye molecules, can be observed.[65,66] The number of such molecules in each column is $10^3 - 10^6$ depending on the concentration and temperature.[66]

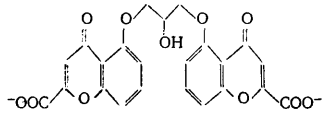
A few words have to be said about the chromonic phases of the porphyrins. Copper compounds are sparingly soluble in water but in the presence of NH_4OH (pH 10—12) both nematic and hexagonal phases are clearly manifested.[56,67,68] A nematic mesophase has been found[69] also in cobalt(II)-phthalocyanines.

In conclusion, we may mention the behaviour of the chromonic phases of dyes at high concentrations. At the critical concentration of the dye or the electrolyte, a solid phase is precipitated from the lyotropic mesophase. Structural and electron microscope studies have shown[17,65,66] that it has no crystal structure but exhibits double refraction. It is, as it were, a "frozen" chromonic phase in which the columns are oriented in parallel. Such a solid phase is characterised by a high dichroism and is used to manufacture polaroids.[16,17,70]

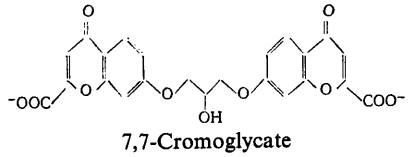
IV. Medicinal drug mesophases

We shall turn initially to mesophases of compounds whose properties are close to those examined in the previous Section. We shall deal with the derivatives of naphthylaminedisulphonic acids[71] related to the widely familiar dye Congo Red. Many of these derivatives are highly active agents against trypanosomes, the simplest parasites in human and animal blood and tissues. Many of them possess liquid crystal properties. The sodium salt of *N*-(*m*-aminobenzoyl)-2-naphthylamine-5,7-disulphonic acid, the tetrasodium salt of *N*-(*m*'-aminobenzoyl-*m*-aminobenzoyl)-2-naphthylamine-6,8-disulphonic acid, the disodium salt of *N*-(*m*'-nitrobenzoyl-*m*-aminobenzoyl)-2-naphthylamine-6,8-disulphonic acid, and also free *N*-(*m*'-nitrobenzoyl-*m*-aminobenzoyl)-2-naphthylamine-4,8-disulphonic acid may serve as examples. It is of interest to note that there exists a distinct correlation between the therapeutic effect and the affinity of these compounds for cotton in dyeing.[71] This shows that there is a single mechanism of their action: the medicinal drugs add equally readily to chemically similar groups in copper and trypanosomes, blocking the reproduction of the latter.

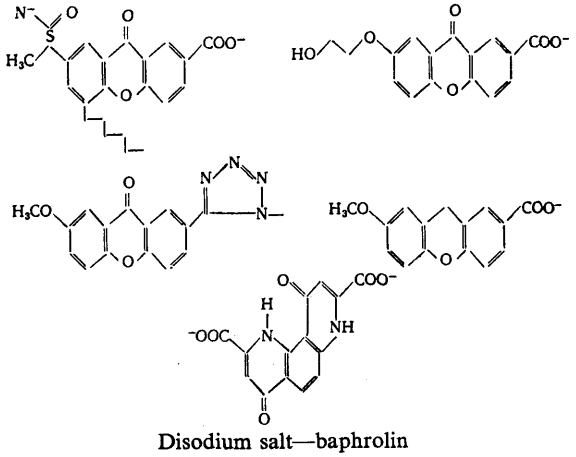
A large group of antiasthmatic drugs also form chromonic mesophases. These are mainly the sodium salts of non-steroid anions, whose structures are presented below:[15,72,73]



Cromoglycate. Disodium salt—cromolyn, intal, sodium cromoglycate (DSCG)



7,7-Cromoglycate



Disodium salt—baphrolin

Examination of the structures of these compounds makes it possible to differentiate the following general features:[15] (1) all the compounds have rigid planar aromatic nuclei containing benzopyrone or isoelectronic benzopyridone groups; (2) there are two hydrophilic groups at the opposite ends of the molecule in all these compounds, one of the groups representing an acid residue and the other either yet another acid residue or another group capable of forming a hydrogen bond. These groups do not have a permanent position: in some cases, they are linked directly to the pyrone ring, whereas in others they are linked to a neighbouring ring.

We may note that the benzopyrone and beonzopyridone structures can have an appreciable dipole moment if the molecule contains in the ring an oxygen atom which carries a large positive charge. For this reason, such an atom does not form hydrogen bonds.

The mesophases of these compounds are formed for the same reason as the mesophases of the dyes examined above. Here too water molecules play a major role (see above).

Like dyes, antiasthmatic drugs possess two main chromonic mesophases—nematic (*N*) and hexagonal (*M*). These phases have been investigated in greatest detail in relation to sodium cromoglycate (DSCG).

The phase diagram for the DSCG–H_2O system (Fig. 9) has been frequently investigated,[72,74–76] being gradually refined and amplified. On the whole, it resembles the phase diagrams for chromonic dyes (cf. Fig. 7), but there are also certain differences. A common feature is the existence of a premesophase region where aggregates, usually dimers, are formed. At room temperature, aggregation begins when the DSCG concentration reaches approximately 5 wt.%.[77] On the other hand, in the concentration range 5–25 wt.%, the aggregation of molecules is already manifested when the temperature of the system exceeds by 10–15 °C the temperature of the region of the mesophases.[78]

As for dyes, there are two chromonic mesophases—nematic (*N*) and hexagonal (*M*)—in the DSCG–H_2O system. The presence of extensive two-phase regions is also a common feature of these two diagrams.

Table 6. The enthalpies and temperatures of the $N + I \rightarrow I$ transitions in aqueous 13 wt.% DSCG solution.[79]

NaCl concentration, M	pH	ΔH, cal g^{-1}	Transition temperature, K
—	6.9	0.39	314.9
—	6.5	0.49	314.4
—	6.0	0.40	313.2
—	5.0	0.36	313.7
10^{-6}	—	0.40	310.2
10^{-5}	—	0.54	309.9
10^{-4}	—	0.58	310.0
10^{-3}	—	0.54	307.4
10^{-2}	—	0.40	309.9
10^{-1}	—	0.49	314.7
0.5	—	0.54	323.0
1.0	—	0.43	330.5
1.5	—	0.62	334.9

The positions of the mesophases on the phase diagram depend on the pH of the solution and on the concentration of the added salts.[79] This conclusion is well illustrated by Table 6, which lists the temperatures and enthalpies of the transition to the isotropic phase at different pH and NaCl concentrations. It is seen from the table that the pH has only a weak influence on the enthalpy and temperature of the transition. On the other hand, the influence of the salt concentration is very appreciable, the transition temperature falling initially and then increasing as the concentration rises. A similar effect was found also after the addition of KCl and LiCl. The minimum transition temperature corresponds to a different salt concentration: 10^{-3} M for NaCl, 10^{-4} M for KCl, and 10^{-5} M for LiCl. It is of interest to note that the crystal-nematic phase transition temperature also increases only slightly with increasing concentration of the salts investigated.[79]

The principal difference between dyes and the DSCG–H_2O system is the presence on the phase diagram of the latter of a new smectic mesophase, with a hitherto unknown structure, at low temperatures (–4 °C) before the transition to the solid phase.[80] It is designated as III in Fig. 9. Measurement of the enthalpy of the transition with the aid of a differential scanning calorimeter (DSC) permitted the hypothesis[75] that in fact two mesophases III exist. However, analysis of the NMR spectra and optical observations have not so far confirmed this hypothesis.

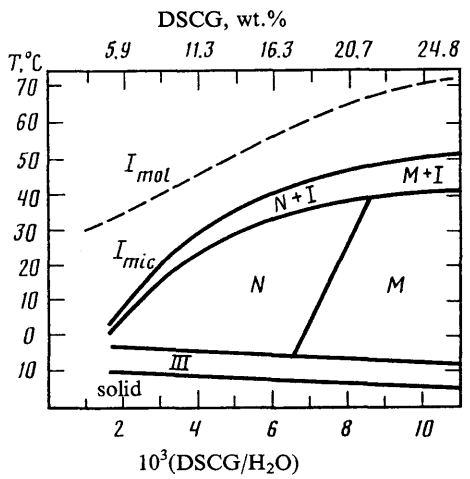


Figure 9. Phase diagram of the DSCG–H_2O system: *M*—hexagonal mesophase; *N*—nematic mesophase; *I*—isotropic phase; I_{mol}—isotropic molecular phase; I_{mic}—isotropic micellar phase.[72]

The mesophase III is satisfactorily manifested following the addition of ethylene glycol or glycerol to the system. The starting point of the solid phase to give the mesophase (III) then diminishes and the temperature of the transition to the nematic phase increases. Thus the region of the existence of the mesophase (III) expands. This made it possible to find the thermodynamic characteristics of the phase transitions in this system with the aid of the DSC. As for thermotropic liquid crystals, fusion to give the mesophase is a first-order phase transition accompanied by large heat and entropy changes. On the other hand, the transitions between the mesophases and between the mesophase and the isotropic liquid have all the features of weak first-order phase transitions. With increase in the glycerol content, the heat changes diminish and the transition temperatures increase.

New mesophases have also been found in the 7,7-cromoglycate (7,7-DSCG)–H_2O system.[73] At temperatures below the temperature of the existence of the mesophase *N* (in the 7,7-DSCG concentration range form 3 to 25 wt.%), an extensive region of a birefringent gel phase (the phase *R*), having a network structure, was discovered. The texture of this phase is illustrated in Fig. 10*a*. In the same temperature range as for the phase *N* but with a salt content above 15 wt.%, the more ordered and denser phase *S* was found (Fig. 10*b*).

The mesophases *N* and *M* give rise to readily identifiable optical textures (Figs. 10*c* and 10*d*), typical for chromonic mesophases.[15,72–75] Their structure was investigated by small angle X-ray diffraction analysis[74,76,81] and NMR.[76,78,80,82]

We shall consider primarily the shape of the DSCG molecule. Here there is no unanimous view as yet. In the first study concerned with the solid phase,[72,74] a planar molecular structure was postulated although it was also suggested[74] that at high water concentrations the planar configuration can hardly persist as a consequence of the possibility of the free rotation of one end of the cyclic system relative to the other about the –CH– bond. However, light scattering and magnetic double refraction data[77] have not confirmed this hypothesis even in the concentration range 0.3–3 wt.% (isotropic solution). The planar configuration is likewise supported by the formation of hydrogen

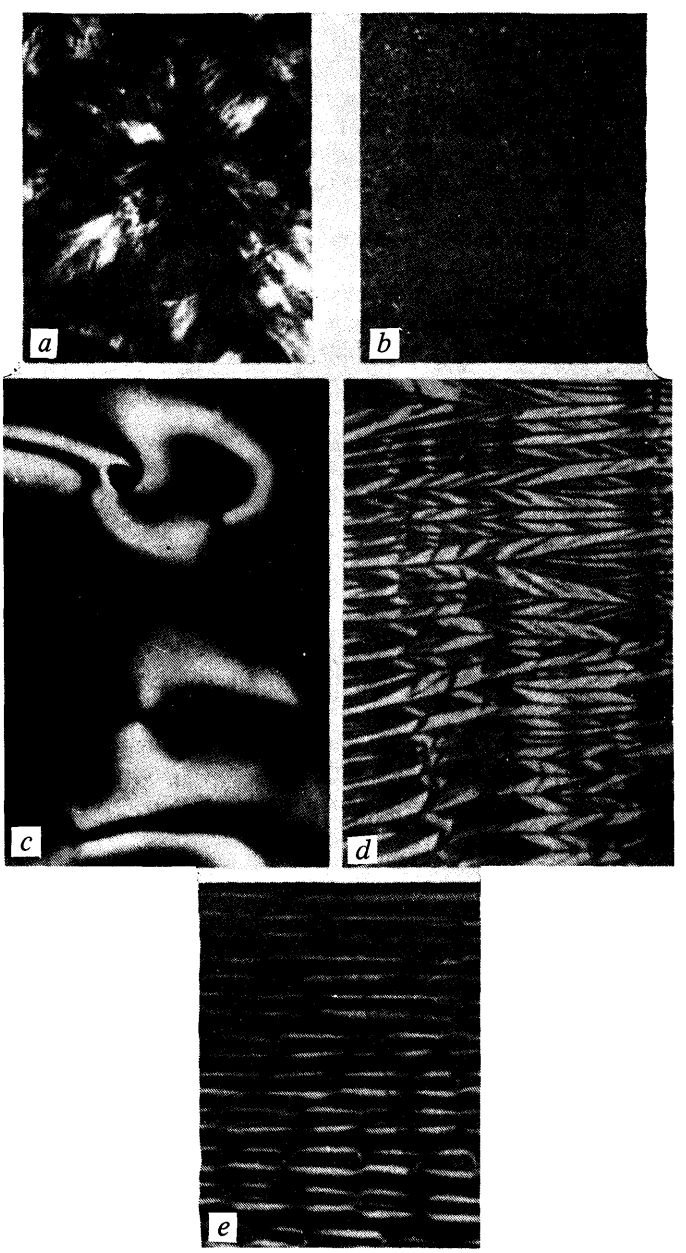


Figure 10. Textures of chromonic mesophases: (*a*) *R*; (*b*) *S*; (*c*) *N*; (*d*) *M*; (*e*) "bamboo".[15,73,79]

bonds between the water molecules and the hydroxy- and carbonyl groups of the DSCG molecules. This is indicated by the pronounced hygroscopicity of solid DSCG and the presence of an appreciable amount of bound water in the mesophases.[72,74] However, the non-coplanarity of the chromonium rings (the angle between them is 53°) was observed in a later study,[83] where the detailed structure of DSCG was found. It may be that such non-coplanarity is characteristic only of the solid phase.

Important information about the structure of DSCG was obtained by small angle X-ray diffraction.[74] Reflections with the ratios $1:1/\sqrt{3}:1/\sqrt{4}$ are clearly manifested in the phase *M*, which indicates hexagonal packing. In addition there is a reflection corresponding to a distance of 3.4 Å, which is interpreted at the identity parameter along the long axis of the column, i.e. as the thickness of the DSCG molecule. If it is assumed that the columns have a circular cross-section, then it is easy to calculate their diameter and the distance between them. Thus in solution at a DSCG concentration of 20 wt.% at room temperature the column diameter is 16 Å and the distance between the columns is 43.3 Å. The nematic mesophase gives rise to only one reflection corresponding to a distance of 3.4 Å, which indicates the breakdown of hexagonal packing.

Thus the structure of the mesophases in the DSCG–H_2O system corresponds to the chromonic type. However, bearing in mind the size of the DSCG molecules and the diameter of the columns, presumably[84] four molecules are accommodated in the cross-section of the chromonic columns, the polar ends of the molecules projecting to the outside (Fig. 11*a*).

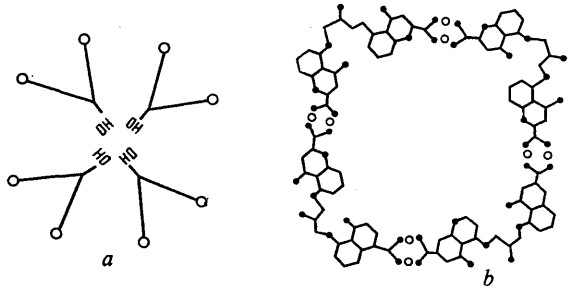


Figure 11. Models of the packing of DSCG molecules in chromonic columns: (*a*) cylindrical model;[84] (*b*) square model.[85]

However, this simple structure agrees poorly with the high moisture absorption capacity of the mesophases. Density measurements have shown[72] that in the mesophase *M* there are 9 water molecules for each DSCG molecule, while in the mesophase *N* there are 260 water molecules. Taking into account these data and other information about the structural features of the system, another hypothesis has been put forward concerning the structure of the columns,[85] according to which 4 DSCG molecules, linked to hydrated sodium ions, form hollow rings (Fig. 11*b*). These rings are superimposed on one another, as in the usual chromonic columns, forming square hollow columns filled with water. In the nematic phase, the columns are distributed freely, while in the mesophase *M* they are packed in accordance with the hexagonal law, as shown in Fig. 12.

The latter model was fully accepted by Hartshorne and Woodard,[86] although the square form of the chromonic columns was rejected.

The chromonic type of the structure of the DSCG mesophases was confirmed by X-ray diffraction.[76] The phase (III) was investigated in the same study. It was found that it too is made up of columns, but more detailed data were not obtained. The study of all the phases in the DSCG–H_2O system by ^2H, ^{17}O, and ^{23}Na NMR showed[76,78,80] that in all the mesophases the anisotropy of the diamagnetic susceptibility $\psi_a = \psi_{\parallel} - \psi_{\perp}$, where $\psi_{\parallel}$ and $\psi_{\perp}$ are diamagnetic susceptibilities along and at right angles to the director, is negative. This means that the planar DSCG molecules are arranged perpendicularly to the column axes, like the molecules in the chromonic phases of dyes.

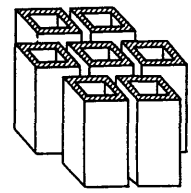


Figure 12. A model of the packing of columns in the mesophase *M* of the DSCG–H_2O system.[85]

A second important result is the fact that the quadrupolar splitting in the ^2H and ^{17}O spectra of the D_2O molecules and in the ^{23}Na spectrum changes sharply on transition from the phase (III) to the phases *N* or *M* and varies linearly on transition from *N* to *M*. The quadrupolar splitting on the ^2H and ^{17}O spectra on transition to the mesophase *N* or *M* diminishes under these conditions, while that in ^{23}Na spectra increases. A detailed study[78] of the NMR spectra of the ^{23}Na atoms showed that, following the addition of NaCl to the system, the quadrupolar splitting in all the phases initially falls to zero and then changes sign and increases again. This makes it necessary to postulate that the Na^+ ions occupy two different types of positions in the structure, to which splittings of different sign correspond. They can be found both in the columns (the binding of the DSCG molecules) and in the surrounding water. In the initial system, almost all the Na^+ ions are in the first positions. After the addition of NaCl, most of the Na^+ ions pass to the surrounding water, which in fact diminishes the quadrupolar splitting.

A study[82] of the influence of NaCl on the ^2H NMR spectra of D_2O led to the conclusion that there is only an increase in the stability of the mesophases and the associated impairment of the quadrupolar splitting. The increase in stability was explained by the weakening of the repulsion of the DSCG molecules as a result of the shielding effect of Na^+ ions. The absence of two different doublets in the NMR spectrum of D_2O, which should have been observed according to the model illustrated in Fig. 11*b*, was also noted. However, this finding can be readily accounted for also by the easy exchange between the free water molecules and the molecules incorporated in the columns.

NMR data yielded some information about the order parameters S_{ij} of the DSCG–H_2O system. The order parameter, which is a second rank tensor, describes quantitatively the ordering in the system and is defined as follows:

$$S_{ij} = S(n_i n_j - {}^1/_3\delta_{ij}), \qquad (3)$$

where *S* is the scalar order parameter, n_i and n_j are the components of the director, and δ_{ij} is the Kronecker symbol.

It proved possible to calculate from the ^{17}O spectra of D_2O the principal components of the order parameter tensor for these molecules and to determine their temperature dependence.[80] It was found that the water molecules are well ordered and that the average parameter is about 0.5.

A detailed study[76] of the order parameter of the C–D bond has been carried out using DSCG containing deuterium in the chromonium rings and in the central CH group of the hydrocarbon bridge. The scalar order parameter S was calculated from the concentration dependence of the quadrupolar splitting in the ^2H spectrum. It increases linearly with increase in concentration in the range 4–29 wt.% from 0.76 to 0.97. These unusually high values are surprising, since the order parameter determined from the NMR spectra is a product of the order parameter of the molecules in the column and of the effective order parameter of the columns themselves. Nevertheless the value of S obtained correspond to those predicted by the Onsager theory.[87] Using its formal treatment and assuming that the diameter of the DSCG molecule is 26 Å, it is possible to estimate the length of the columns. It is about 2000 Å in the phase M and about 800 Å in the phase N.[76]

The order parameter in the nematic phase of the DSCG–H_2O system has also been investigated[84,88] by polarisation absorption spectroscopy.† Dichroic dyes such as indigo, carmine, eosin, Methyl Red, Congo Red, etc. were dissolved in the mesophase and the absorption spectra were measured in polarised light parallel and at right angles to the direction of a 20 kG magnetic field. It was found that S for the "guest" dye molecules varies from −0.2 to −0.005. The order parameter of the DSCG molecule as a whole was determined at the wavelength corresponding to the intrinsic absorption band. It proved to be −0.20. With increase in temperature, the order parameter diminishes as usual. It also decreases with decrease in the ionic strength of the solution.

In an interesting study[89] the order parameters were calculated from the intensities of individual IR absorption bands corresponding to particular bonds (Table 7). As was to be expected, all the parameters S are negative, which confirmed the perpendicular orientation of the DSCG molecules relative to the magnetic field. The average order parameter is −0.14, which agrees with the results of independent measurements.[84]

Spectroscopic data[89] also suggest that the oxygen atoms of the chromonium rings are linked by hydrogen bonds to water molecules. In addition it was found that the overlapping of the DSCG molecules in the nematic mesophase is much more marked than in the isotropic phase.

The 7,7-DSCG mesophases have also been investigated by X-ray diffraction.[81] The high-temperature phase R gives rise to three diffraction peaks corresponding to distances of 51.2, 25.1, and 32.1 Å at 27 °C. They are in proportions of $1:1/2:1/\sqrt{2}$ and correspond to the indices 1.0 : 1.1 : 2.0 of a two-dimensional square lattice. With decrease in temperature, the distances increase but their ratios do not change. The nematic phase produces only one peak corresponding to an index of 1.0. This peak, which does not undergo sharp changes in the transition $R \rightarrow N$, corresponds to distances between the columns of 60–70 Å. The three diffraction peaks of the phase M are in the ratios $1:1/\sqrt{3}:1/2$, which correspond to the hexagonal lattice. Immediately below the temperature of the transition from the phase N to the phase R, the hexagonal lattice parameter is about 46 Å, but it reaches 80 Å as the temperature is reduced.

Table 7. Order parameters for individual bonds in the nematic phase of the DSCG–H_2O system.[89]

Bond	Wavenumber, cm^{-1}	S
C=C	1482	−0.132
=C–H	1412	−0.127
CO_2^-	1364	−0.136
CO_2	1311	−0.149
C–O (ether)	1267	−0.110
C–O (in =C–O–C)	1128	−0.071
OH	1047	−0.102

The ^2H and ^{17}O NMR spectra of D_2O and the ^{23}Na NMR spectra of the same systems have been investigated. In the spectrum of phase R, there is no quadrupolar splitting, which indicates a disordered disposition of the water molecules. The usual quadrupolar splitting is observed in the spectra of the other mesophases. The quadrupolar splitting in the ^{23}Na spectrum is of a similar character and does not undergo sharp changes in the transition from the phase N to the phase S or M. This is explained by the fact that the distribution of Na^+ ions between two possible positions (see above) is independent of concentration. The study of the NMR spectra of the compound deuteriated in the chromonium ring made it possible to determine the order parameter of the C–D bond. It is independent of concentration but varies linearly with increase in temperature. Estimates have shown that the order parameter in the mesophases N and S is approximately unity, which indicates the almost complete ordering of the columns, although it does not rule out the free rotation of the molecular planes.

Detailed structural studies have made it possible to put forward the hypothesis of a relation between the liquid crystal nature of the anti-asthmatic drugs and their therapeutic properties.[15] If this relation is not fortuitous, three mechanisms are possible.

The therapeutic effect is associated with the formation of a chromonic mesophase on the surface of the lung.

The mesophase is not formed but the therapeutic effect is associated with a biologically active complex (a cyclic structure or a hollow column), which promotes the formation of the mesophase.

The mesophase is not formed but the therapeutic effect is due to the structure of the molecule itself, which is at the same time mesogenic.

Available knowledge is so far insufficient to reject *a priori* any of the three mechanisms indicated. However, the first is supported by the presence on the surface of the lung of a mesophase with a high phospholipid content. The breakdown of the liquid-crystal state of this layer leads to the breakdown of the tiny alveoli at the end of exhalation. It is therefore quite likely that the mesophases of anti-asthmatic drugs compensate for the deficiency of liquid crystal phospholipids.

As we have already stated, chromonic mesophases have a negative diamagnetic anisotropy. The geometry of the column permits the ready spontaneous formation of a planar texture. Reorientation in a magnetic field (the Fredericks transition) is usually observed in fields of 10–20 kG. It is accompanied by the appearance of interesting defects.

†The order parameter determined by this method is $S = (A_{||} - A_{\perp})/(A_{||} + 2A_{\perp})$, where $A_{||}$ and $A_{\perp}$ are the absorption intensities along and at right angles to the director respectively. Since $A_{\perp} > A_{||}$ for molecules with negative dichroism such as DSCG, it follows that $S < 0$ and amounts to −0.5 in the fully ordered state ($A_{||} = 0$).

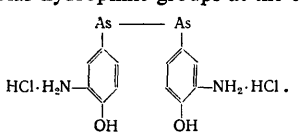
Thus, when an 18 kG magnetic field is applied to a thick (80–200 μm) planar DSCG specimen in the plane of the specimen and along the axes of the columns, a "bamboo" type of texture is formed (Fig. 10*e*). In the course of time, the "bamboo" sections grow and are obliterated.[79]

A periodic domain structure, the repeat step of which depends periodically on the magnetic strength, has been clearly observed on thin specimens (~20–40 μm).[90] This structure exhibits an interesting time variation.[91] The formation of a domain structure has a purely hydrodynamic cause—it arises as a result of the presence of a reverse flux accompanying the Fredericks transition.[79,90,91]

The addition of chiral admixtures converts the nematic DSCG mesophase to a cholesteric phase.[79] Various aminoacids, for example, alanine, proline, lysine, etc., at concentrations ranging from 1 to 36 wt.%, are used as the additives. Naturally the pitch of the helix of the cholesteric phase obtained depends on the concentration of the chiral additive. In all cases, the reciprocal of the pitch of the helix increases linearly with increasing concentration of the chiral additive.[79,92]

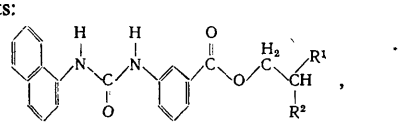
An interesting result was obtained in a study of the influence of the magnetic field on such induced cholesteric phases. After prolonged exposure to the field, the pitch of the helix diminishes, but not to zero. It falls to a finite value approximately equal to one-third of the initial pitch.[79]

Aqueous solutions of salvarsan and neosalvarsan—drugs active against syphilis, malaria, and recurrent fever—apparently form a chromonic mesophase.[5,93] Although direct structural studies have not been made, nevertheless the physical properties of these systems support indirectly this hypothesis. Firstly, the salvarsan molecule has a planar shape with polar hydrophilic groups at the end:

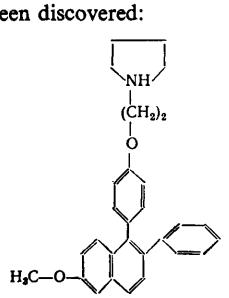


Secondly, the occurrence of polarisation in aqueous solutions indicates the formation of large aggregates. The third piece of evidence is provided by the presence of the nematic mesophase, which is optically monoaxial and negative, the negative side being in fact typical for chromonic mesophases.

Chromonic phases are formed in aqueous solutions and in heptane by *N*-1-naphthyl-*N'*-phenylenecarboxyalkylureas[94] which are used as antisunburn agents:



where R^1 and R^2 are various alkyl groups ranging from methyl to dodecyl. These compounds are chiral and form chromonic structures, which has been confirmed by the observation of the corresponding textures. Furthermore, more ordered mesophases, apparently hexagonal, have also been discovered:



Two mesophases are likewise formed by naphthoxidine hydrochloride,[95] eight molecules of which form a ring with the pyrrole groups on the periphery. The rings are in their turn packed in a chromonic column, which is an element of the superstructure.

Chromonic phases are apparently formed also by rivanol (6,9-diamino-2-ethoxyacridine lactate).[96] However, here further studies are necessary.

V. Conclusion

An independent branch of the field of study of lyotropic crystals, involving the investigation of the conditions governing the formation, structure, and properties of chromonic mesophases, has now been established. These phases differ from the classical lyotropic micellar liquid crystals but at the same time they have features in common with the latter. The amphiphilic nature of the molecules, their extended shape, and the presence of a long ($n > 8$) hydrocarbon "tail" are typical for micellar mesophases. Such construction ensures the formation, as a result of a balance between ionic and hydrophobic interactions, of anisotropic micelles, both normal (in water or in any polar solvent) and inverted (in non-polar solvents). The balance of forces is so fine that a change in the concentration of the amphiphilic substance alone is sufficient to entail a significant change in the form of the micelles, which change from spherical to discotic, biaxial, and cylindrical.

Molecules forming chromonic mesophases can be called amphiphilic only by way of a convention. They have the planar shape of a "plank" with small end groups which ensure its solubility in water. The principal cause of the formation of ordered structures is therefore in this instance the appearance of hydrogen bonds between the polar groups and water molecules. The hydrophobic interaction plays only a secondary role. However, micelles are formed, as in the classical lyotropic liquid crystals. Their role is assumed by columns—"coin stacks". The occurrence of a single leading interaction creates simpler structures—isotypical columns arise instead of a set of anisometric aggregates. Admittedly the packing of the molecules in the column depends on their chemical nature but this does not lead to a great variety. Structurally, chromonic mesophases are closer to columnar thermotropic liquid crystals than to micellar lyotropic mesophases. The principles of the molecular packing are identical although chromonic materials do not exhibit the wide variety of structures characteristic of columnar thermotropic mesophases.

The study of chromonic mesophases has continued at a high rate. Their practical importance is evident, because important substances such as dyes and medicinal drugs are the principal chromonic materials. However, much still remains to be done. In the first place, there are still very few data on the viscoelastic properties of these compounds. There is no information about their electrooptical and magnetooptical behaviour. There is no microscopic theory of the mesomorphic properties of these phases. Further studies will undoubtedly fill these gaps and will provide an answer to the principal question concerning the relation between the mesomorphic properties of chromonic phases and their structure.

References

1. P Gaubert *C.R. Seances Acad. Sci.*, 1916, **163** 392
2. P Gaubert *C.R. Seances Acad. Sci.*, 1933, **197** 1436
3. P Gaubert *C.R. Seances Acad. Sci.*, 1934, **198** 951
4. P Gaubert *C.R. Seances Acad. Sci.*, 1935, **200** 679
5. H Freundlich, R Stern, H Zocher *Biochem. Zeit.*, 1923, **138** 307
6. S Chandrasekhar, B K Sadashiva, K A Suresh, et al. *J. Phys. (France)*, 1979, **40** Suppl. C-3, 120
7. J Billard, B K Sadashiva *Pramana*, 1979, **13** 309
8. N Boden, R J Bushby, C Hardy *J. Phys. (Fr.) Letters*, 1985, **46** 325
9. B Kohne, K Praefoke, T Derz, et al. *Chimia*, 1986, **40** 171
10. N Boden, R J Bushby, C Hardy, et al. *Chem. Phys. Lett.*, 1986, **123** 359
11. N Boden, R J Bushby, L Ferris, et al. *Liquid Cryst.*, 1986, **1** 109
12. H Ringsdorf *XII International Liquid Crystal Conference. Program and Abstracts.* Freiburg, 1988, p. 113
13. J Wolff, K Wolf, J Koll, et al. BRD P. 3 149 129
14. J Koll, V Paulat, R Hörnle, et al. Europ. P. 0 029 958
15. T K Attwood, J E Lydon *Mol. Cryst. Liq. Cryst.*, 1984, **108** 349
16. J Dreyer US P. 2 400 877
17. J Dreyer *J. Phys. Colloid Chem.*, 1948, **52** 808
18. E Valco *Colloidal-Chemical Foundations of the Textile Technology* (Translated into Russian) Gizlegprom, Moscow–Leningrad, 1940, Vols. 1–2, 273 pp
19. S E Sheppard *Rev. Mod. Phys.*, 1942, **14** 303
20. R H Peters *Textile Chemistry*, Elsevier, Amsterdam, 1975, Vol. III, p. 581
21. B C Burdett *Aggregation Processes in Solution* (Edited by E Wynne-Jones, J Gormally), Elsevier, Amsterdam, 1983, p. 241
22. C Robinson *Trans. Faraday Soc.*, 1935, **31** 245, 277
23. C Robinson *Proc. Roy. Soc.*, 1935, **148A** 681
24. B Milicevic, G Evigenmann *Helv. Chim. Acta.*, 1964, **47** 1039
25. D J Blears, S S Danyluk *J. Am. Chem. Soc.*, 1966, **88** 1084
26. S R S Iyer, G S Singh *Kolloid Zeit. Zeit. Polym.*, 1970, **242** 1196
27. S R S Iyer, G S Singh *J. Soc. Dyers Colour*, 1973, **89** 128
28. E Coates *J. Soc. Dyers Colour*, 1969, **85** 355
29. M A Anisimov, I F Kazakova, A S Kurlyandskii, S A Pikin *Kristallografiya*, 1987, **32** 1100
30. E I Valko *Trans. Faraday Soc.*, 1935, **31** 230
31. E I Valko *J. Soc. Dyers. Colour*, 1939, **55** 173
32. E I Valko *J. Am. Chem. Soc.*, 1941, **63** 1433
33. S E Lenher, J E Smith *J. Am. Chem. Soc.*, 1935, **57** 497, 504
34. S E Lenher, J E Smith *J. Phys. Chem.*, 1936, **40** 1005
35. F H Holmes, H A Standing *Trans. Faraday Soc.*, 1945, **41** 542, 568
36. T Vickerstaff *Physical Chemistry of Dyeing*, Oliver and Boyd, London, 1954
37. R B McKay *Trans. Faraday Soc.*, 1965, **61** 374
38. A Datyner, A G Flowers, M T Paiethorpe *J. Colloid. Interface Sci.*, 1980, **74** 71
39. H P Frank *J. Colloid Sci.*, 1957, **12** 480
40. A Datyner, M T Paiethorpe *J. Colloid Interface Sci.*, 1980, **76** 557
41. G Scheibe *Angew. Chem.*, 1937, **50** 212
42. H Freundlich, C Schuster, H Zocher *Z. Physik. Chem.*, 1923, **105A** 118
43. C Robinson, H A Mills *Proc. Roy. Soc.*, 1931, **131A** 576, 596
44. G Scheibe, L Kandler, H Ecker *Naturwiss*, 1937, **25** 75
45. G Schiebe, L Kandler *Naturwiss*, 1938, **26** 412
46. G Scheibe *Angew Chem.*, 1939, **52** 631
47. S E Sheppard *Science*, 1941, **93** 42
48. L A Ignat'eva, L V Levshin, T D Osipova, et al. *Opt. Spektrosk.*, 1962, **13** 396
49. L V Levshin, T D Slavnova, Yu A Mittsel' *Zh. Prikl. Spektrosk.*, 1968, **8** 293
50. E Jelloy *Nature*, 1936, **138** 1009
51. V A Bykov, Yu A Bobrov, N A Ovchinnikova, *V Konferentsiya Sotsialisticheskikh Stran po Zhidkim Kristallam. Tezisy Dokladov. Odessa* (The V Conference of Socialist Countries on Liquid Crystals. Abstracts of Reports. Odessa), 1983, Vol. 2, Part 1, p. 217
52. V A Bykov, E V Generalova, L Ya Ignatov, et al. *Tezisy Dokladov VI Vsesoyuznoi Konferentsii 'Zhidkie Kristally i Ikh Prakticheskoe Ispol'zovanie'. Chernigov* (Abstracts of Reports at the VI All-Union Conference on 'Liquid Crystals and Their Practical Applications'. Chernigov), 1988.
53. F Brauner *Nord. Kemikermode Ford.*, 1939, **5** 207
54. T K Attwood, J E Lydon, F Jones *Liquid Cryst.*, 1986, **I** 499
55. T Imae, S Ikeda *Mol. Cryst. Liq. Cryst.*, 1983, **101** 155
56. N V Usol'tseva, V V Bykova, N M Kormilitsyn, et al. *Khimiya Zhidkikh Kristallov. Primenenie v Khromatografii. Tezisy Dokladov Oblastnoi Nauchnoi Konferentsii. Kuibyshev* (The Chemistry of Liquid Crystals. Applications in Chromatography. Abstracts of Reports at the Regional Scientific Conference. Kuibyshev), 1987, p. 33
57. N M Melankholin *Kristallografiya*, 1961, **6** 568
58. V A Bykov *Tezisy Dokladov V Vsesoyuznoi Konferentsii 'Zhidkie Kristally i Ikh Prakticheskoe Ispol'zovanie'. Ivanovo* (Abstracts of Reports at the V All-Union Conference on 'Liquid Crystals and Their Practical Applications'. Ivanovo), 1985, Vol. II, Book 1, p. 84
59. N V Anikifirova, Yu A Bobrov, V A Byov *Tezisy Dokladov VI Vsesoyuznoi Konferentsii 'Zhidkie Kristally i Ikh Prakticheskoe Ispol'zovanie'. Chernigov* (Abstracts of Reports at the VI All-Union Conference on 'Liquid Crystals and Their Practical Applications'. Chernigov), 1988, Vol. III, p. 441
60. S H Jury, R C Ernst *J. Phys. Colloid. Chem.*, 1949, **53** 609
61. R A Berg, B A Haxby *Mol. Cryst. Liq. Cryst.*, 1970, **12** 93
62. G W Gray, P A Winsor *Liquid Crystals and Plastic Crystals*, Halsted Press, Chichester, 1974, Vol. 2, p. 56
63. F Jones, D R Kent *Dyes and Pigments*, 1980, **1** 39
64. A S Sonin *Usp. Fiz. Nauk.*, 1987, **153** 273
65. D E Sadler, M D Shannon, P Tollin, et al. *Liquid Cryst.*, 1986, **1** 509
66. W Hoppe *Kolloid Z.*, 1942, **101** 300
67. N V Usol'tseva, V V Bykova, N M Kormilitsyn, et al. *Tezisy Dokladov V Vsesoyuznoi Konferentsii po Koordinatsionnoi i Fizicheskoi Khimii Porfirinov. Ivanovo* (Abstracts of Reports at the V All-Union Conference on the Coordination and Physical Chemistry of the Porphyrins. Ivanovo), 1988, p. 183
68. N V Usol'tseva, V V Bykova, G A Anan'eva, et al. *Kolloid. Zh.*, 1989 (in the press)
69. N V Usol'tseva, V V Bykova, G A Anan'eva, et al. *Tezisy Dokladov VI Vsesoyuznoi Konferentsii 'Zhidkie Kristally i Ikh Prakticheskoe Ispol'zovanie'. Chernigov* (Abstracts of Reports at the VI All-Union Conference on 'Liquid Crystals and Their Practical Applications'. Chernigov), 1988, Vol. III, p. 422

70. V A Bykov, T S Berzina, T A Ivanova, et al. *V Konferentsiya Sotsialisticheskikh Stran po Zhidkim Kristallam. Tezisy Dokladov. Odessa* (The V Conference of Socialist Countries on Liquid Crystals. Abstracts of Reports. Odessa), 1983, Vol. 2, Part 1, p. 219
71. I E Balaban, H King *J. Chem. Soc.*, 1927, 3068
72. J S G Cox, G D Woodard, W C McCrone *J. Pharm. Sci.*, 1971, **60** 1458
73. D Perahia, Z Luz, E J Wachtel, et al. *Liquid Cryst.*, 1987, **2** 473
74. N H Hartshorne, G D Woodard *Mol. Cryst. Liq. Cryst.*, 1973, **23** 343
75. H Lee, M M Labes *Mol. Cryst. Liq. Cryst.*, 1983, **91** 53
76. D Goldfarb, Z Luz, N Speilberg, H Zimmermann *Mol. Cryst. Liq. Cryst.*, 1985, **126** 225
77. J V Champion, G H Meeten *J. Pharm. Sci.*, 1973, **62** 1589
78. D Perahia, D Goldfarb, Z Luz *Mol. Cryst. Liq. Cryst.*, 1984, **108** 107
79. H Lee, M M Labes *Mol. Cryst. Liq. Cryst.*, 1982, **84** 137
80. D Goldfarb, M M Labes, Z Luz, R Poupko *Mol. Cryst. Liq. Cryst.*, 1982, **87** 259
81. D Perahia, Z Luz, E J Wachtel, H Zimmermann *Liquid Cryst.*, 1987, **2** 473
82. L J Yu, A Saupe *Mol. Cryst. Liq. Cryst.*, 1982, **80** 129
83. S Hamodrakas, A J Geddes, B Sheldrick *Pharm. Pharmac.*, 1974, **26** 54
84. B D Bostwick, M M Labes *Mol. Cryst. Liq. Cryst.*, 1987, **147** 179
85. J Lydon *Mol. Cryst. Liq. Cryst. Lett.*, 1980, **64** 19
86. N H Hartshorne, G D Woodard *Mol. Cryst. Liq. Cryst. Lett.*, 1981, **64** 153
87. P G de Gennes *The Physics of Liquid Crystals* (Translated into Russian), Izd. Mir, Moscow, 1977, 400 pp
88. M R Kuzma, V Skarda, M M Labes *J. Chem. Phys.*, 1984, **81** 2925
89. Y W Hui, M M Labes *J. Phys. Chem.*, 1986, **90** 4064
90. Y W Hui, M R Kuzma, M San Miguel, M M Labes *J. Chem. Phys*, 1985, **83** 288
91. J P McClymer, M M Labes *Mol. Cryst. Liq. Cryst.*, 1987, **144** 275
92. D Goldfarb, M E Moseley, M M Labes, Z Luz *Mol. Cryst. Liq. Cryst.*, 1982, **89** 119
93. H Zocher, V Birstein *Z. Phys. Chem.*, 1929, **142A** 126
94. U Hoppe *J. Soc. Cosmet. Chem.*, 1973, **24** 317
95. A R Mlodozeniec *J. Soc. Cosmet. Chem.*, 1978, **29** 659
96. V P Nazin *I Konferentsiya po Zhidkim Kristallam. Ivanovo* (The I Conference on Liquid Crystals. Ivanovo), 1972, p. 189