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Effect of platinum(II) chemotherapeutic agents on properties of DNA liquid crystals

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We have investigated the X-ray and optical properties (CD spectra and polarization microscopy) of liquid-crystalline phases and dispersions formed on pretreatment of low molecular weight DNA with the platinum(II) coordination complexes, *cis*-diammine-dichloroplatinum(II) (DDP), 2,2′-bipyridinedichloroplatinum(II) (**1**) and 2,2′-bipyridineethylenediammineplatinum(II) (**2**). It is demonstrated that the platination of DNA leads to the ordering of neighbouring molecules of DNA in liquid-crystalline phases being diminished. The intense bands observed in the CD spectra of liquid-crystalline dispersions prepared from DNA pretreated with **1** or **2** can be used to determine the orientation of the latter compounds with respect to the helical axis of the DNA and to detect distortions in the secondary structure of DNA. The possible causes of the appearance of the intense bands in the CD spectra of liquid-crystalline phases and alterations in the manner of packing of the molecules of DNA within them are discussed.

1. Introduction

The designing of effective anticancer drugs for the targeting of nucleic acids is dependent on a thorough understanding at the molecular level of the structure and properties shown in vivo by DNA. The performing of in vivo investigations on the effects of anticancer agents on DNA remains a difficult task. In order to simplify this problem, in vitro model systems are currently being devised which simulate the principal properties displayed by DNA molecules within cells. An example of such a system is that of lyotropic liquid crystals of DNA. Some of the properties of such crystals are very interesting from both physico-chemical and biological viewpoints. A particularly significant feature of liquid crystals in this respect is the spatial ordering of their constituent molecules, which is strongly dependent on both the properties of the solvent and the temperature, showing marked variation with change in either factor. It is therefore a matter of interest to elucidate the nature of liquid crystals of DNA subsequent to modification by platinum(II) coordination complexes which are currently in use as anticancer drugs [1].

Investigation of the interactions between platinum(II) coordination complexes and DNA molecules is of prime importance for several reasons: Firstly, information on alterations in the secondary and tertiary structure of DNA is necessary for the synthesis of new generations of anticancer drugs. Secondly, the platinum atoms of the coordination complexes reacting with DNA represent labels which can be used in the analysis of the structural characteristics of DNA. Another matter arousing interest is the interaction of Pt(II) coordination complexes with aromatic ligands. The

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aromatic ligands are able to intercalate between the base-pairs of DNA whereas the reactive site(s) in a coordination complex participates in the covalent binding of platinum atoms to the nitrogen bases [2,3].

It should be borne in mind that the physicochemical and biological effects of the interaction of Pt(II) coordination complexes with DNA molecules are currently being actively studied [4].

The present article is aimed at describing a number of properties of liquid-crystalline dispersions and liquid crystals prepared from low molecular weight linear DNA modified by treatment with various Pt(II) coordination complexes.

2. Materials and methods

Purified depolymerized salmon sperm DNA ($M_r = 0.6–0.7 \times 10^6$) was prepared for use in experiments. DNA was modified with *cis*-diamminedichloroplatinum(II) (DDP), 2,2′-bipyridinedichloroplatinum(II) (**1**) and chloride 2,2′-bipyridineethylenediammineplatinum(II) (**2**). Samples of Pt(II) coordination complexes were obtained from the Institute of General and Inorganic Chemistry (U.S.S.R. Academy of Sciences, Moscow). Poly(ethylene glycol) (M_r 4000, Loba Chemie, Austria) was used without further purification.

DNA was treated with DDP or **1** in 0.01 M $NaClO_4$ (37°C, 48 h, in the dark). The r_t values determined were within the range 0–0.5 (r_t, molar ratio of added Pt(II) compound to DNA nucleotides). Since the covalent binding of Pt(II) is effected via hydrolysis of the coordination complex whose kinetics depend on the chemical structure of the complex, it is necessary to establish the concentration of Pt(II) bound to DNA at any given moment. The amount of DDP or **1** bound to DNA was determined by means of the analytical reaction with mercaptoquinolinesulphonate [5] and according to the method of Salyanov et al. [6]. The r_b values varied within the range 0–0.03 (r_b, molar ratio of Pt(II) bound covalently or noncovalently to DNA nucleotides).

The DNA complex with **2** was prepared in 0.3 or 0.5 M $NaClO_4$ (21°C, in the dark). The ranges covered by the r_t and r_b values in the solutions were 0–3.5, 0–0.02, respectively.

Formation of liquid crystals from DNA or the modified forms of DNA was achieved following the two-step method of Yevdokimov et al. [7]. In the first step, equal volumes of $NaClO_4$-containing solutions of both polyethylene glycol and DNA were mixed together, yielding liquid-crystalline dispersions of DNA. The CD spectra of the dispersions were recorded and the data represented as ΔA or $\Delta\epsilon$ as a function of λ:

$$\Delta\epsilon = \Delta A / C \cdot L$$

where L denotes the length of the optical pathway (in cm) and C the DNA concentration (in mole/l). The other involved the low-speed centrifugation of dispersions (5000 rpm, 40 min) which results in the formation of liquid-crystalline phases of DNA.

The optical texture of thin (30 μm) layers of the phases formed was studied by means of polarization microscopy as described in ref. 7. X-ray analysis of the phases was also carried out according to ref. 7. The sizes of the samples employed in the X-ray analysis of modified DNA were 2 mg for the case of DDP and 2–10 mg for **1** and **2**.

3. Results

3.1. Liquid crystals formed from DNA modified with DDP and 1

3.1.1. CD spectra of liquid-crystalline dispersions of modified DNA

Fig. 1A compares the CD spectra of the initial linear B-form DNA (curve 1) with those of liquid-crystalline dispersions prepared from both the native (curve 2) and DDP-modified forms (curves 3–5). For increasing degrees of modification of DNA, the amplitude of the negative band in the absorption region of the DNA bases decreases linearly (fig. 1B). Zero amplitude is observed to occur at $r_t \sim 0.05$. The shape of the CD spectra under these conditions corresponds to curve 5 in fig. 1A.

Fig. 2A depicts the CD spectra of liquid-crystalline dispersions prepared from DNA treated with **1**. In this case, two bands appear in the CD

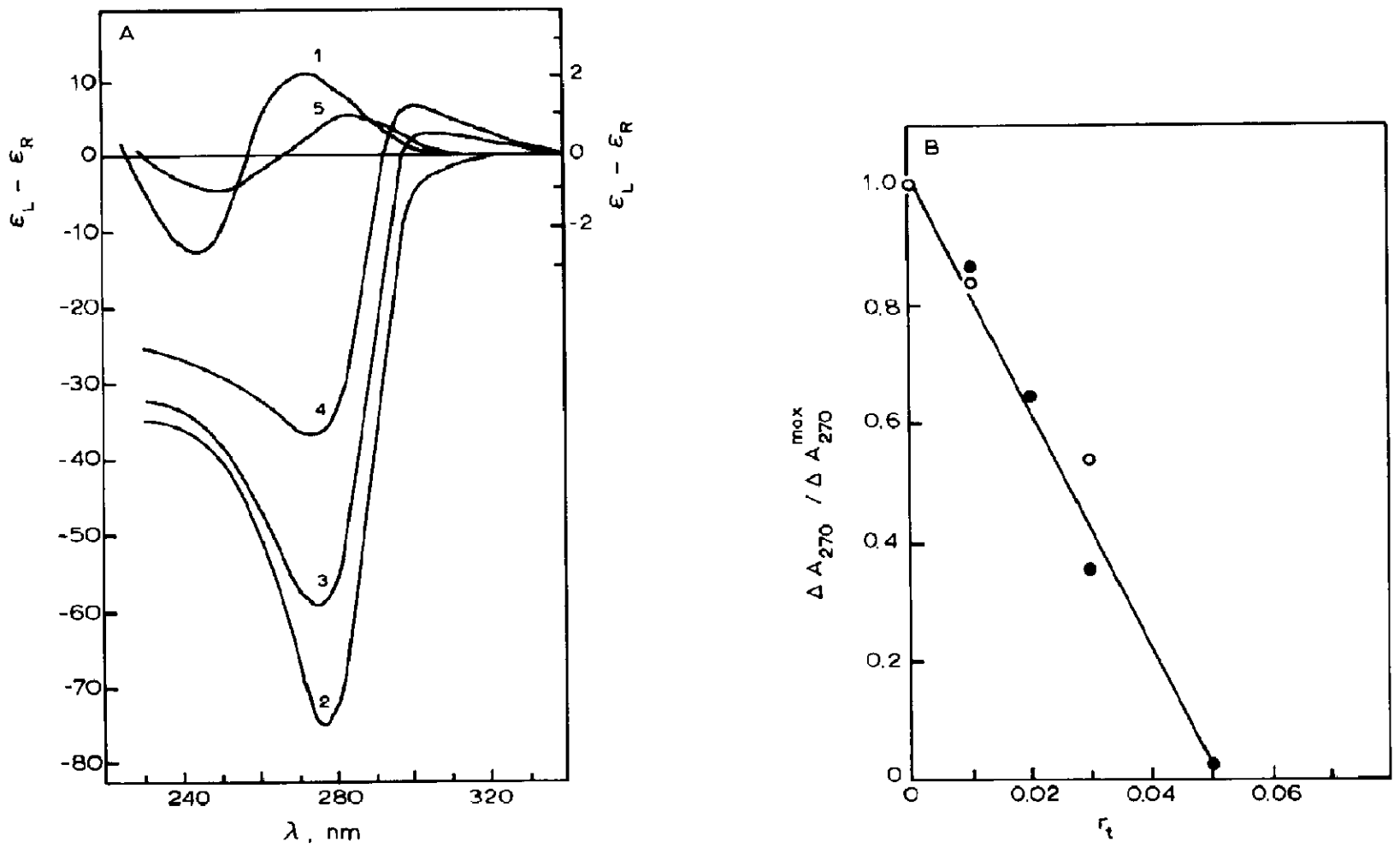

Fig. 1. (A) CD spectra of liquid-crystalline dispersions formed from DNA (curve 2) and DNA modified with DDP (curves 3–5). Curves: (2) $r_t = 0$, (3) $r_t = 0.01$, (4) $r_t = 0.03$, (5) $r_t = 0.1$. $C_{PEG} = 170$ mg/ml (PEG, poly(ethylene glycol)); 0.5 M $NaClO_4$. (Curve 1) CD spectrum of linear B-form DNA (0.5 M $NaClO_4$); (2–4) left ordinate; (1,5) right ordinate. (B) Dependence on r_t of the relative amplitude of the negative band in the CD spectrum ($\lambda = 270$ nm) of liquid-crystalline dispersions prepared from DDP-modified DNA. (●) Data of Akimenko et al. [21]. r_t, concentration ratio (mol/mol) of DDP added to solution/nucleotide.

spectrum. One is located within the absorption region of the DNA bases ($\lambda \sim 270$ nm), the other being in the range for **1** ($\lambda \sim 317$ nm). The negative band in the CD spectrum of liquid-crystalline dispersions formed from DNA modified with **1** decreases with increasing r_b (fig. 2B) similarly to DNA-DDP binding (fig. 1B). The amplitude of the positive CD band in the absorption region of **1** varies with increasing r_b in a complicated manner. At $r_b \sim 0.02$, the amplitude of the positive CD band as well as that of the negative band in this spectrum tends to zero, although the optical activity of DNA proper remains (curve 5, fig. 2A). In order to evaluate the packing of neighbouring DNA molecules, X-ray analysis of the liquid-crystalline phases was carried out.

3.1.2. X-ray analysis of phases formed from DNA molecules modified with DDP and 1

Figs. 3 and 4 demonstrate X-ray scattering curves typifying the phases resulting from both native DNA and the forms modified with DDP and **1**. The small-angle scattering reflects the ordering of neighbouring DNA molecules in the resultant phases. Figs. 3 and 4 show that the peaks in the scattering curves shift with increasing degrees of modification by Pt(II) complexes of the DNA. Analysis of the X-ray scattering curves performed as suggested in ref. 8 demonstrates that the covalent binding of platinum atoms to DNA bases influences all the parameters that describe the ordering of polymeric molecules (see table 1).

Comparison of figs. 1 and 3 as well as of figs. 2 and 4 shows that the intense CD spectral bands for liquid-crystalline dispersions of DNA disappear at r_b values where, in the case of liquid-crystalline phases, an orderly arrangement of DNA molecules is maintained.

In order to establish the types of liquid crystals which are formed from DNA modified with Pt(II) coordination complexes, we investigated the thin-layer optical appearance of liquid crystals.

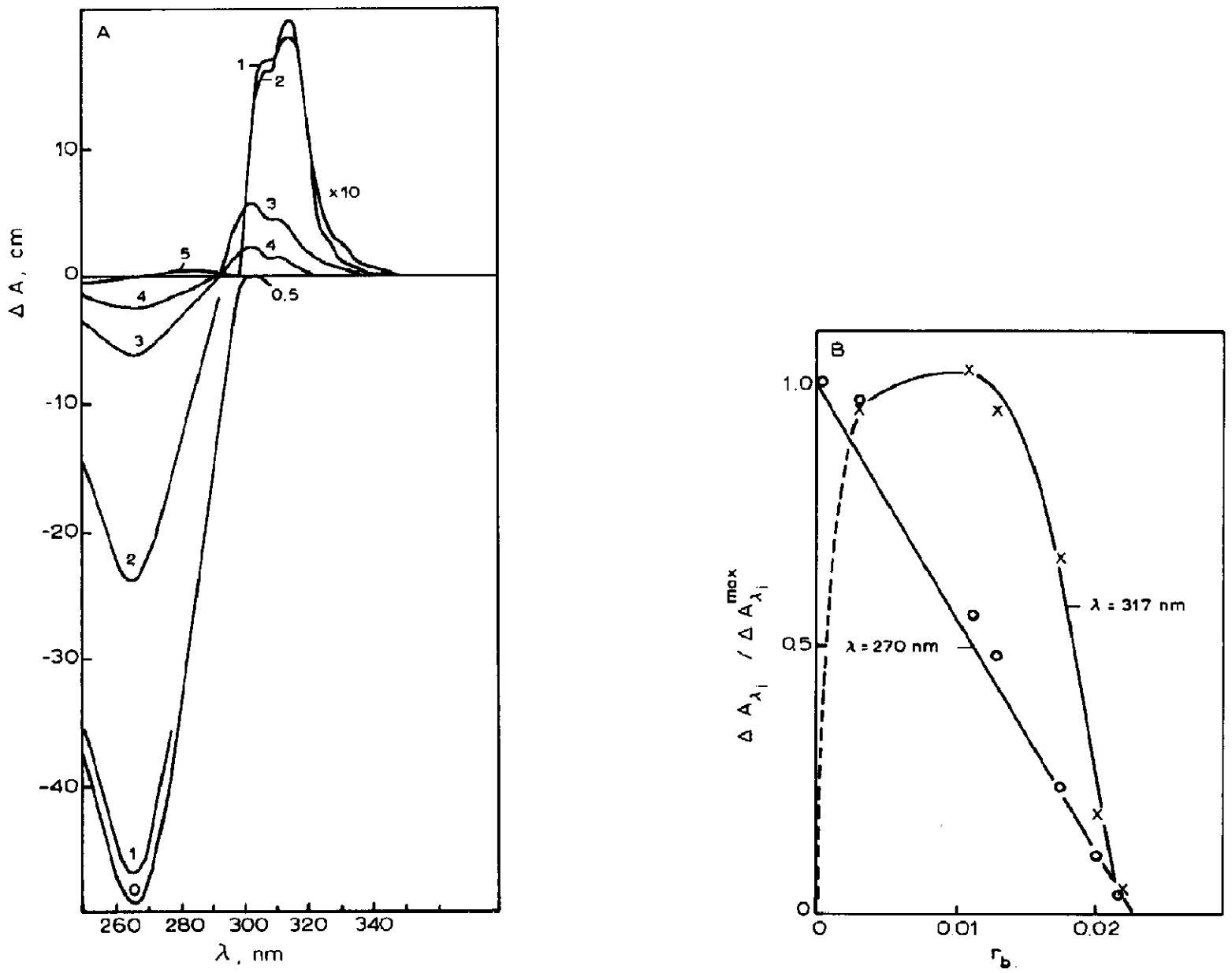

Fig. 2. (A) CD spectra of liquid-crystalline dispersions formed from DNA molecules modified with compound **1**. Curves: (0) $r_b = 0$, (1) $r_b = 0.004$, (2) $r_b = 0.013$, (3) $r_b = 0.02$, (4) $r_b = 0.022$, (5) $r_b = 0.025$. $C_{PEG} = 170$ mg/ml; 0.3 M $NaClO_4$. For details on r_b see section 2. (B) Dependence on r_b of relative amplitudes of bands in the CD spectra of liquid-crystalline dispersions prepared from DNA molecules treated with **1**.

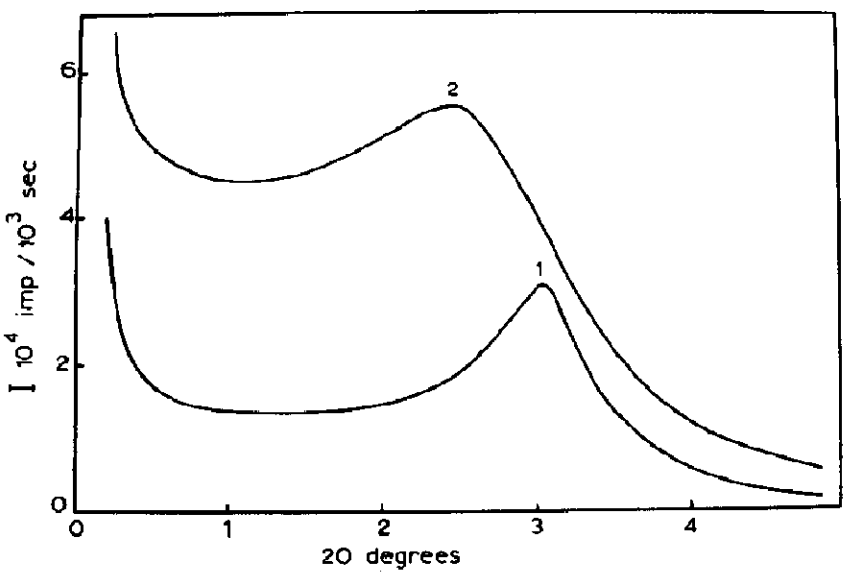

Fig. 3. X-ray scattering curves for liquid crystals of DNA (curve 1) and DNA modified with DDP (curve 2, $r_t = 0.1$). $C_{PEG} = 170$ mg/ml; 0.5 M $NaClO_4$.

3.1.3. Optical texture of liquid crystals of DNA modified with DDP and 1

The optical appearance of liquid-crystalline phases formed from DDP-modified DNA has been described previously [7,9]. Fig. 5 compares the appearance of liquid crystals prepared from native DNA and from the form modified with **1**. It is evident that optically active molecules of DNA form cholesteric liquid crystals with a specific fingerprint appearance. The value of the pitch (P) of the helical structure of cholesteric liquid crystals falls within the range 3.0–3.5 μm. For a high ($r_b \sim 0.02$) degree of DNA modification with **1** the phase being formed is not optically anisotropic. The optical appearance of this phase is

Table 1

Some X-ray parameters of liquid-crystalline phases prepared from DNA molecules modified with platinum(II) compounds

$\bar{a} = d = \lambda/(2 \sin \theta)$, average distance between the axes of adjacent DNA molecules; λ, wavelength of X-rays (here, $\lambda = 1.54$ Å); θ, half scattering angle of the X-rays; β_s, integral half-width of the maximum; $L = (\lambda/\cos\theta)\beta_s$, size of ordered regions (crystallites); $\Delta/\bar{a} = (1/\pi)(\beta_s \bar{a}/\lambda)^{-1/2}$, disorder parameter ($\Delta$: semiquadratic deviation from $\bar{a}$); $r_m = (\pi/2.5)^2(\lambda/\beta_s)$, interaction radius.

Number of samples	Parameters				
	$\bar{a}$ (Å)	β_s (rad)	L (Å)	$\Delta/\bar{a}$	r_m (Å)
DNA + DDP					
1. $r_t = 0$	29.06	0.0132	117	0.160	184
2. $r_t = 0.1$	36.21	0.0209	74	0.220	117
DNA + 1					
1. $r_b = 0$	28.40	0.0070	220	0.140	347
2. $r_b = 0.001$	28.40	0.0070	220	0.114	347
3. $r_b = 0.02$	35.30	0.0192	80	0.211	127
DNA + 2					
1. $r_b = 0$	28.41	0.0096	161	0.134	253
2. $r_b = 0.016$	33.70	0.0157	98	0.187	153

observable only in natural light (fig. 5B); under crossed Nicol prisms, the phase being formed is isotropic. The isotropic character of this phase indicates that nematic liquid crystals of DNA are absent.

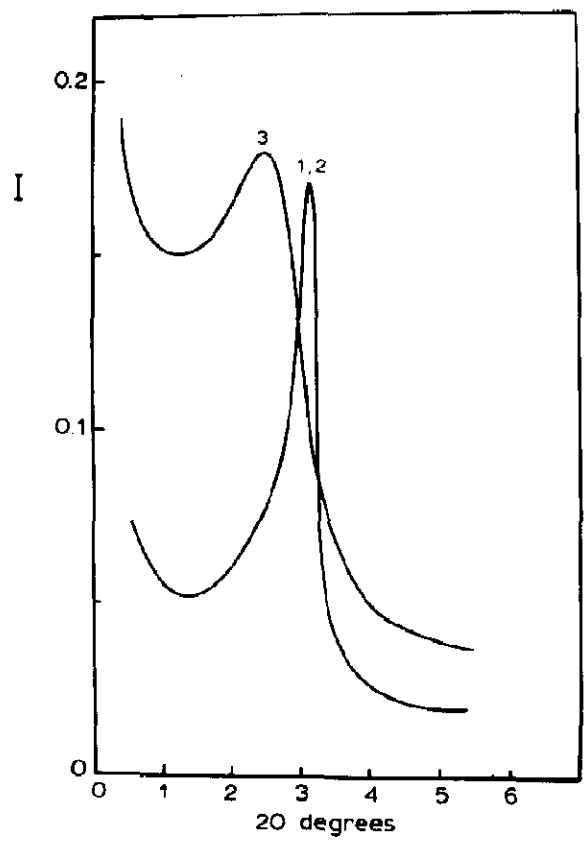

Fig. 4. X-ray scattering curves for liquid crystals prepared from DNA (curve 1) and DNA modified with 1. Curves: (1) $r_b = 0$, (2) $r_b = 0.001$, (3) $r_b = 0.02$. $C_{PEG} = 170$ mg/ml; 0.5 M $NaClO_4$.

The data presented in section 2 demonstrate that the interaction of 1 with DNA leads to effects which largely coincide with those of the DDP-DNA interaction. This implies that the changes in the properties of DNA observed do not depend on the chemical structure of the Pt(II) coordination complex. In this respect, the data obtained for another mode of incorporation of platinum atoms into DNA are of interest.

3.2. Liquid crystals formed from DNA modified with 2

3.2.1. CD spectra of liquid-crystalline dispersions formed from DNA modified with 2

Fig. 6A compares the CD spectra of liquid-crystalline dispersions formed from DNA (curve 0) and DNA modified with 2 (curves 1–4). The formation of disperse phases from DNA-2 complexes is accompanied by the appearance of two negative CD spectral bands. One is located within the absorption region for DNA (curve 0, $\Delta\epsilon_{270} = -60$ units), the other being in the range corresponding to 2 ($\Delta\epsilon_{317} = -500$ units; $r_b \sim 0.015$). The shape of the band at 317 nm resembles that for the absorption of 2 [3,10]. Further attention is warranted with respect to three factors. Firstly, the signs of the two CD spectral bands for liquid-

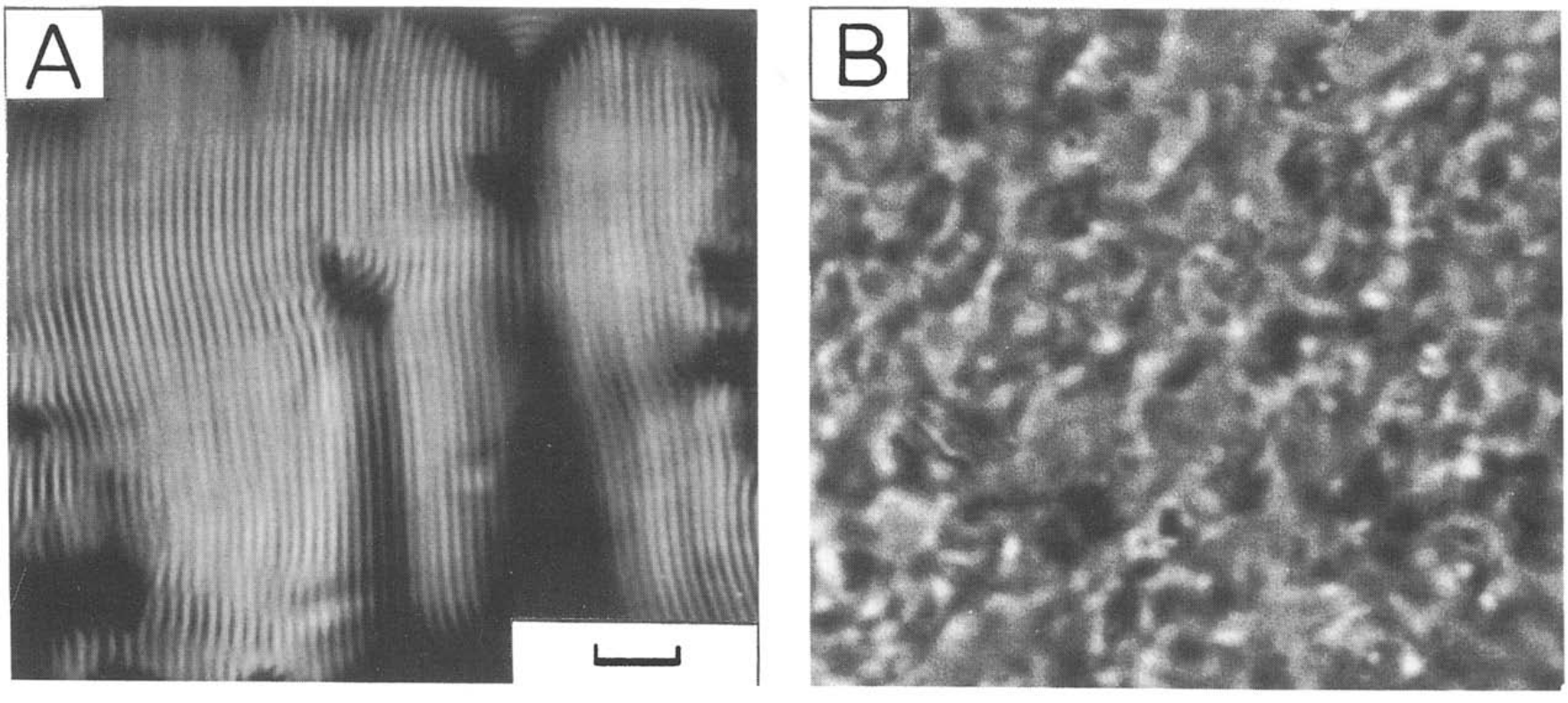

Fig. 5. Optical texture of thin layers of liquid crystals of DNA (A, polarized light) and DNA modified with **1** (B, $r_b = 0.02$, natural light). $C_{PEG} = 170$ mg/ml; 0.5 M $NaClO_4$. Bar, 10 μm.

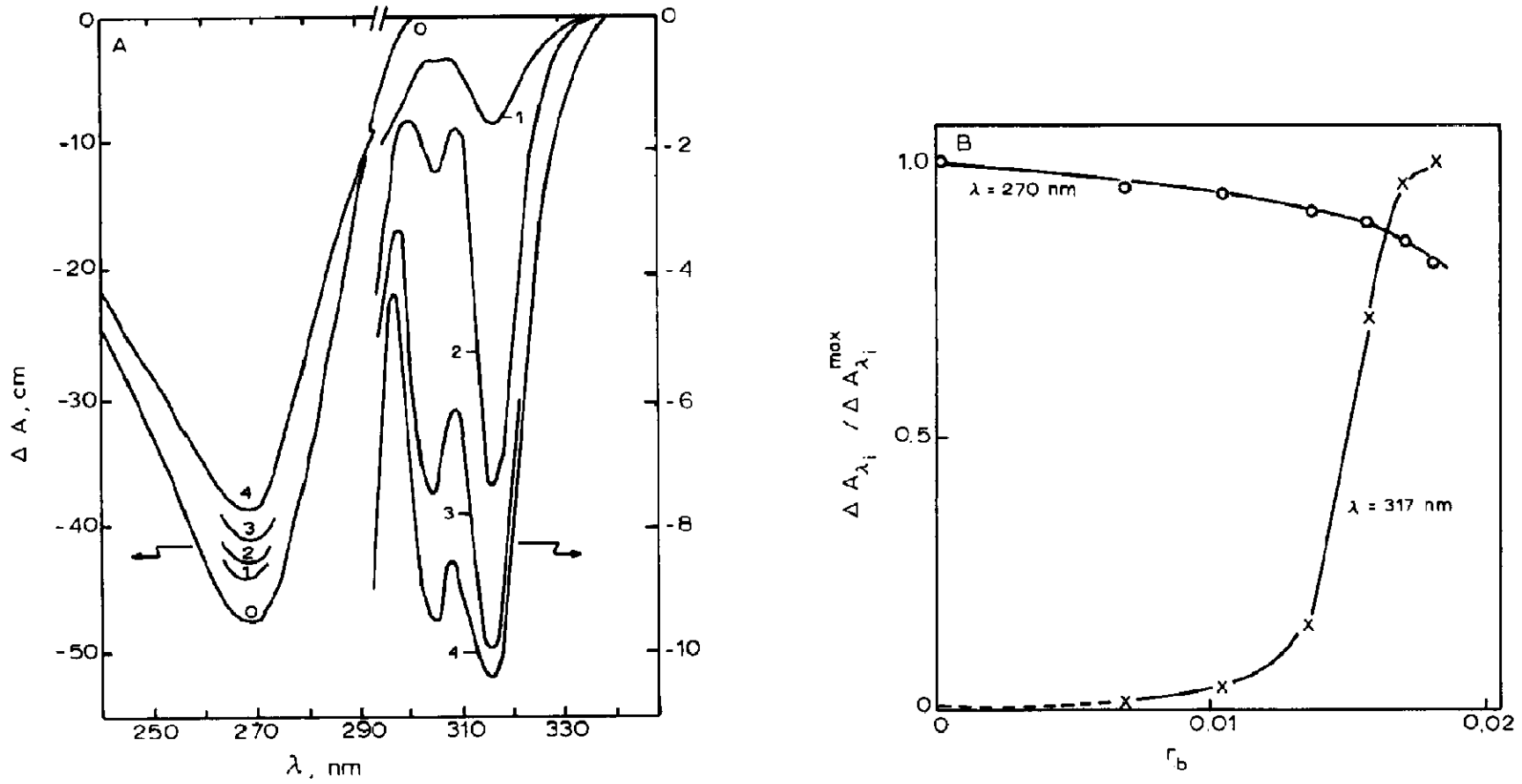

Fig. 6. (A) CD spectra of liquid-crystalline dispersions from DNA treated with **2**. Curves: (0) $r_b = 0$, (1) $r_b = 0.014$, (2) $r_b = 0.016$, (3) $r_b = 0.017$, (4) $r_b = 0.018$. For details on r_b see text. (B). Dependence on r_b of relative amplitudes of bands in CD spectra of liquid-crystalline dispersions formed from DNA treated with **2**.

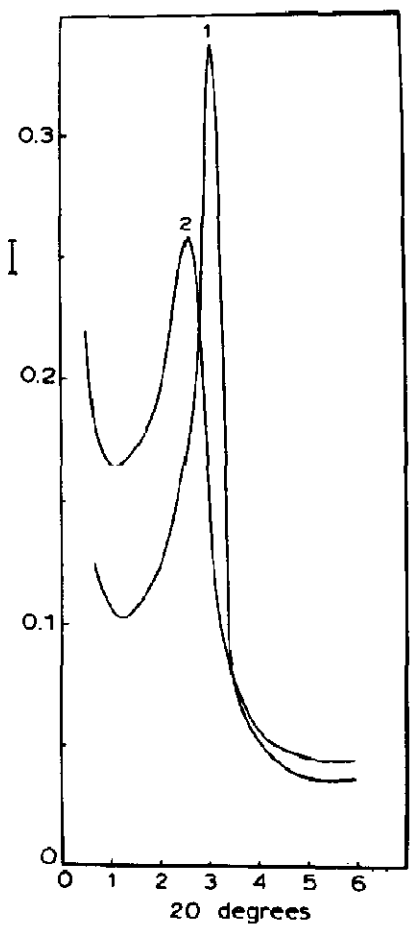

Fig. 7. X-ray scattering curves for liquid crystals prepared from DNA (curve 1) and DNA modified with **2** (curve 2, $r_b = 0.016$). C_{PEG} = 170 mg/ml; 0.5 M $NaClO_4$.

crystalline dispersions of DNA-**2** complexes coincide. Secondly, the amplitude of the negative CD band in the region for absorption of DNA bases shows no significant change with increasing r_b (fig. 6B). Finally, the amplitude of the band in the absorption region for **2** increases (in contrast to **1**) with binding of **2** to DNA.

3.2.2. X-ray analysis of phases prepared from DNA modified with 2

Fig. 7 demonstrates typical X-ray scattering curves for liquid-crystalline phases prepared from DNA modified with **2**. In this case, as well as for the covalent binding of DDP or **1** to DNA, the peak of the scattering curve is shifted with increase in the extent of DNA modification. The parameters characterizing the ordering of molecules of platinated DNA in the phases are listed in table 1.

3.2.3. Optical texture of liquid crystals of DNA modified with 2

Fig. 8 illustrates the optical texture of liquid-crystalline phases prepared from DNA and DNA-**2** complexes ($r_b \sim 0.016$). One can observe, that the binding of **2** to DNA is accompanied by a change in pitch for cholesteric liquid crystals. The P value for the initial form of DNA falls within the range 3.0–3.5 μm, decreasing to 1.5–2.0 μm at $r_b \sim 0.016$. Consequently, under conditions where liquid crystals prepared from DNA modified with DDP or **1** are not optically anisotropic, liquid crystals of DNA-**2** complexes do retain this property.

4. Discussion

4.1. CD spectra of liquid-crystalline dispersions prepared from DNA modified with Pt(II) coordination complexes

Comparison of the CD spectra for liquid-crystalline dispersions of DNA modified with structurally dissimilar Pt(II) coordination complexes are characterized by the appearance of intense bands.

The reasons for the appearance of intense CD spectral bands located within the absorption regions for dyes (chromophores) introduced into thermotropic liquid crystals have been analysed in a number of papers [11–13]. Application of this form of analysis to the description of lyotropic liquid crystals of DNA [14,15] demonstrates that the intense negative band in the CD spectrum in the absorption range for chromophoric DNA bases reflects anisotropy in the ordering of DNA molecules, i.e., the formation of left-handed cholesteric liquid crystals. One should also bear in mind that the bases of DNA are oriented at an angle of approx. 90° with respect to the axis of the DNA molecule, an intense negative band appearing in the CD spectrum for this case. According to the theory [11–13], a difference in the signs of the CD spectra for dyes incorporated into the same liquid-crystalline phase may indicate different orientations for the dyes.

Despite the differing signs, the intense ($\Delta\epsilon \sim$ 500 units) bands in the CD spectra in the absorption region for **1** and **2** (figs. 1 and 3) provide firm evidence primarily of the appearance of anisotropy for these compounds as ordered in liquid-

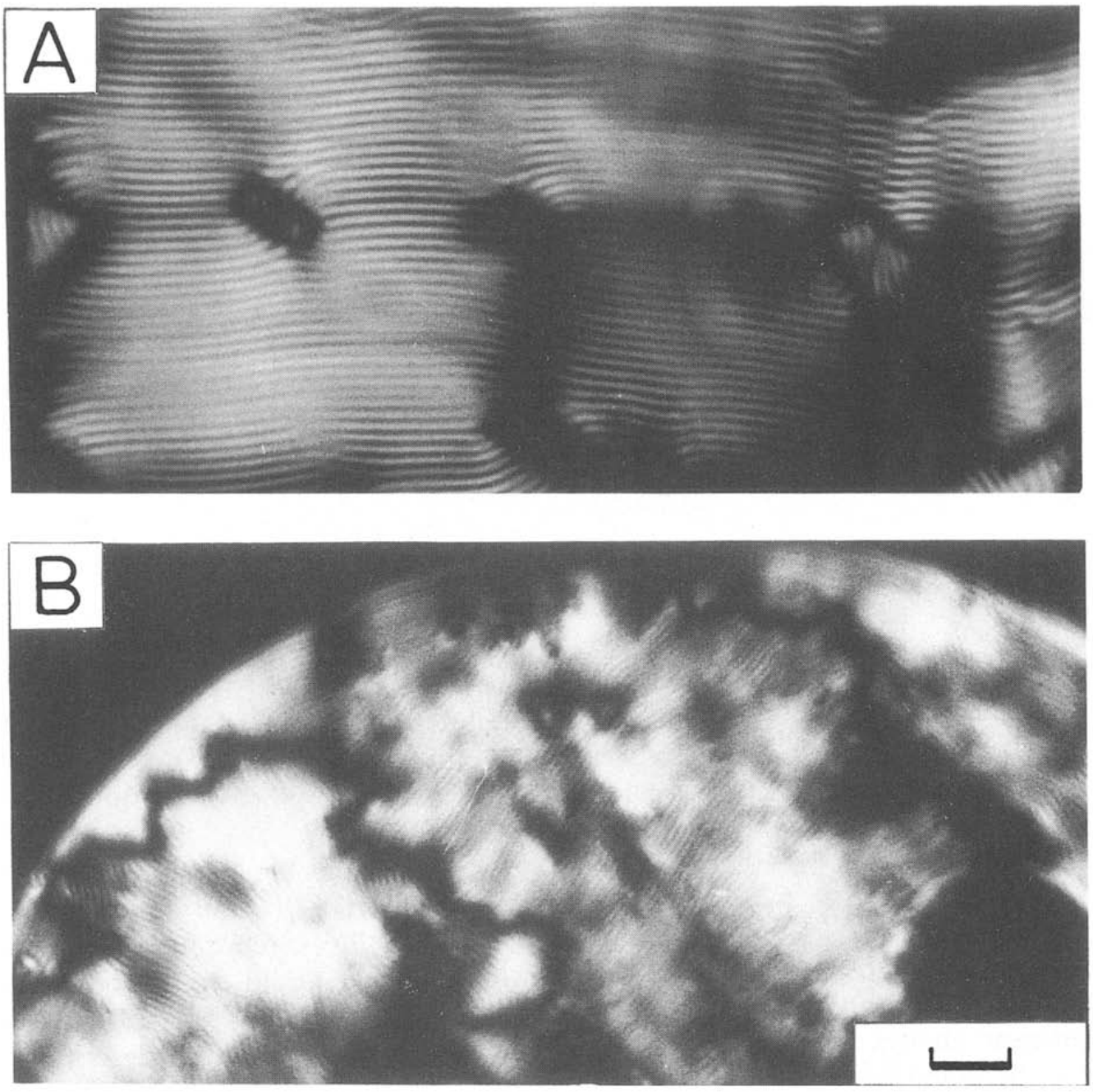

Fig. 8. Optical texture of thin layers of liquid crystals of DNA (A) and DNA modified with **2** (B, $r_b = 0.016$) in polarized light. $C_{PEG} = 170$ mg/ml; 0.5 M $NaClO_4$. Bar, 10 μm.

crystalline phases. It should also be pointed out that such Pt(II) coordination complexes display no intrinsic optical anisotropy. The optical anisotropy of **1** and **2** as characterized by intense bands in the CD spectra may occur only in situations in which molecules of **1** and **2** are rigidly attached to those of DNA, forming liquid crystals.

In dealing with the situation of the appearance of intense CD spectral bands for platinated DNA, the following factors should be taken into account.

(i) The presence of labile Cl ligands in **1** is the governing factor in its covalent binding to purine residues. In the presence of **1** or DDP, the electrophoretic mobility of pBR322 DNA in the relaxed form increases by 15–20% (unpublished data). The mobility of the superhelical form of this DNA decreases on binding of **1** or DDP. The change in electrophoretic mobility of superhelical DNA observed in the presence of both DDP and **1** can be interpreted on the basis of the factors discussed in refs. 4, 16 and 17. Covalent binding of DDP to DNA bases results in not only the untwisting of DNA at the binding sites but also the simultaneous shortening of the DNA molecule, i.e., the secondary structure of DNA at the binding sites is significantly perturbed. Liquid crystals prepared from DNA complexes with **1** are characterized by a positive band located in the absorption region of **1**. The appearance of the intense positive peak in the CD spectrum of **1** in combination with the

negative band in the region of DNA base absorption (fig. 2) signifies that the orientation of **1** differs from that of the DNA bases. On the basis of theoretical procedures, **1** can be determined as being oriented at an angle of less than 54° with respect to the molecular axis of DNA.

Indeed, according to ref. 18, Pt(II) coordination complexes react with the N7 atoms of neighbouring purine residues (mainly guanines) such that they occupy the major groove of the molecule of DNA. From a consideration of the geometry of DNA and of the Pt(II) complexes in the case of **1**, which binds covalently to two guanines, the angle of orientation with respect to the axis of the DNA molecule can be evaluated as approx. 40°.

(ii) The chemical structure of **2** renders the occurrence of its covalent binding a most unlikely event. The interaction of **2** with DNA gives rise to a negative band in the CD spectrum of liquid-crystalline phases. This band reaches a maximum at r_b 0.02 (fig. 6), i.e., at a ratio of one molecule of **2** per 50 of DNA nitrogen bases. This demonstrates that a stable 'external complex' of molecules of **2** cannot form in the proximity of the surface of the DNA molecule. The negative signs of the intense band in the CD spectra of **2** and in the region of DNA base absorption (fig. 6) prove that the orientation of **2** is similar to that of the bases.

More precisely put, the theory predicts **2** to be oriented at an angle greater than 54° with respect to the axis of the DNA molecule. Interaction of **2** with superhelical pBR322 DNA initially leads to lower mobility of this DNA, equalling that for the relaxed form of DNA at a concentration of **2** of approx. 2.7×10^{-6} M. Under these conditions, one can observe the DNA molecules to be distributed according to superhelical density. With further increase in the concentration of **2**, a rise in mobility becomes evident for superhelical DNA. Such behaviour of superhelical DNA has also been observed in the presence of the classical intercalator, ethidium bromide [16,17]. Taken together, the above data demonstrate unequivocally that **2** (unlike **1**) reacts with DNA through intercalation between bases, i.e., it is oriented in a mode similar to that of the DNA bases. Thus, the intense CD spectral bands observed in the absorption regions of **1** and **2** demonstrate that both compounds react with the nitrogen bases of DNA. However, they differ in the form of arrangement on the molecule of DNA.

In this article, attention has been directed at the dissimilar dependences for the amplitudes of the intense bands vs. DNA modification (figs. 1B and 2B). The disappearance of such bands in the CD spectra of liquid-crystalline dispersions of DNA pretreated with DDP or **1** may be due to a number of reasons. Firstly, the increased flexibility of platinated DNA may give rise to drastic alterations in the efficiency of phase separation [19,20]. The data reported by Akimenko et al. [21] allow this possibility to be excluded from consideration. Secondly, modification of DNA with Pt(II) compounds may be accompanied by the formation of nematic rather than cholesteric DNA liquid crystals [22]. Since the optical anisotropy shown by the DNA phase prepared at a high degree of modification completely ceases to exist (fig. 5), this explanation can also be discarded as a possibility. Finally, the modification of DNA by means of **1** may result in the formation of a shell of platinum atoms on the surface of DNA molecules. This could alter the properties of DNA so radically that the mode of packing of molecules of platinated DNA would differ from that for classical liquid crystals. In this respect, a comparison of the X-ray properties and optical texture of liquid-crystalline phases prepared from different types of platinated DNA would be an interesting task for investigation.

In contrast, the increase in amplitude of the intense bands in the CD spectra on binding of **2** to DNA demonstrates that intercalation of **2**, as opposed to **1**, does not result in strong perturbations in the average orientation of the DNA bases.

4.2. X-ray properties of liquid-crystalline phases formed from DNA modified with Pt(II) compounds

On inspection of the data listed in table 1, the decrease in ordering of the DNA molecules with degree of platination is clearly evident irrespective of both the chemical structure of the Pt(II) complex used to modify the DNA and the manner in which the platinum atoms were introduced into

the DNA structure. This implies that, in spite of the platinum atoms influencing the nature of the interaction between adjacent DNA molecules, new phases (in X-ray terms) are not formed. Consequently, the abnormal optical activity in liquid-crystalline dispersions of DNA disappears under conditions where the molecules of platinated DNA are in an ordered arrangement.

4.3. Texture of liquid-crystalline phases formed from DNA modified with Pt(II) complexes

Comparison of the optical texture of liquid-crystalline phases prepared at similar degrees of DNA modification with **1** and **2** shows that they do indeed differ in appearance. For **1** as well as for DDP, optical anisotropy is no longer exhibited at high levels of DNA modification and the optical texture is observable only in natural light. For **2**, anisotropy of the phases is maintained even at high levels of modification of DNA.

The question then arises as to why platinated DNA forms with similar values of their X-ray parameters (table 1) differ in both optical texture and the nature of the dependence of the amplitudes of intense CD spectral bands. This problem may be resolved via the following explanation. Covalent binding of DDP or **1** perturbs the orientation of adjacent nitrogen bases. The effect of such perturbation is exerted over a considerable distance from the platinum(II) binding sites [23]; the higher the level of DNA modification the greater is the extent to which the orientation of the bases is perturbed. Assuming a random pattern of distribution of guanine residues along the DNA chain, the average orientation of the bases and the regular character of the sugar-phosphate chain of DNA would be expected to show appreciable reduction. This process should be accompanied by a decrease in amplitude of the CD spectral band even if cholesteric packing of adjacent DNA molecules is maintained. Obviously, such alterations in the orientation of DNA bases should be accompanied by changes in the orientation of **1**, i.e., for a particular degree of distortion of the structure of DNA, the intense band located in the absorption region of **1** should also decrease (see fig. 2). It is also clear from table 1 that the ordering in the packing of molecules of platinated DNA decreases noticeably, i.e., the presence of platinum(II) atoms alters the energy of interaction between adjacent DNA molecules. This effect in combination with the disordering of nitrogen bases leads to the formation of an optically isotropic DNA phase; the properties of this phase do not correspond to those for cholesteric and nematic phases.

In the case of **2**, the situation differs. Introduction of platinum atoms also affects the manner of packing of DNA molecules: the X-ray parameters for packing undergo alteration and the pitch of the cholesteric helical structure also changes. However, interaction of **2** with base-pairs (intercalation) does not cause any significant perturbation in the average orientation of nitrogen bases with respect to the axis of the DNA molecule. In this case, both the anisotropic character of the DNA phase and the abnormal optical activity of liquid-crystalline dispersions are retained.

The present data demonstrate that the interaction of Pt(II) coordination complexes with DNA is accompanied by changes in both the secondary structure of DNA and the manner of packing for molecules of DNA in liquid-crystalline phases. Finally, it should be mentioned that despite considerable differences between the properties of complexes formed after reaction of DNA with **1** or **2**, the anticancer activity of these compounds may well depend on the nature of their biological transformation within cells.

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