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Mercury-induced transitions between right-handed and putative left-handed forms of poly[d(A-T)·d(A-T)] and poly[d(G-C)·d(G-C)]

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ABSTRACT

Poly[d(A-T)·d(A-T)] and poly[d(G-C)·d(G-C)], each dissolved in 0.1 M $NaClO_4$, 5 mM cacodylic acid buffer, pH 6.8, experience inversion of their circular dichroism (CD) spectrum subsequent to the addition of $Hg(ClO_4)_2$. Let $r \equiv [Hg(ClO_4)_2]_{added}/[DNA\text{-}P]$. The spectrum of the right-handed form of poly[d(A-T)·d(A-T)] turns into that of a seemingly left-handed structure at $r \geq 0.05$ while a similar transition is noted with poly[d(G-C)·(G-C)] at $r \geq 0.12$. The spectral changes are highly cooperative in the long-wavelength region above 250 nm. At $r = 1.0$, the spectra of the two polymers are more or less mirror images of their CD at $r = 0$. While most CD bands experience red-shifts upon the addition of $Hg(ClO_4)_2$, there are some that are blue-shifted. The CD changes are totally reversible when Hg(II) is removed from the nucleic acids by the addition of a strong complexing agent such as NaCN. This demonstrates that mercury keeps all base pairs in register.

INTRODUCTION

As noted by one of us (1,2), Hg(II) induces topological changes in native calf thymus DNA that, on the basis of the accompanying alterations in its circular dichroism (CD) as well as rate of endonucleolytic cleavage by staphylococcal nuclease (3), support the notion of transitions taking place from the right-handed B to the left-handed Z (or Z-like) helical form.

In this communication, we report on the transitions observed in the CD absorption of poly[d(A-T)·d(A-T)] and poly[d(G-C)·d(G-C)] when they are treated with $Hg(ClO_4)_2$. The two polynucleotides, in view of their compositional simplicity, should be well suited to investigate the chiroptical alterations in greater detail. Moreover, since left-handed [d(G-C)] stretches are known to influence the supercoiling of plasmid DNA (4), and alternating sequences such as $[d(T\text{-}G)\cdot d(C\text{-}A)]_n$ to serve as 'hot-spots' for recombination and gene conversion (5), our finding that mercury, at low concentrations, readily changes the topology of the two polymers from, as we believe, B to Z (or to a non-Z structure with left-handed helix screwness) could be the first clue to its mechanism of genotoxic action at the molecular level.

EXPERIMENTAL

Materials

Poly[d(A-T)·d(A-T)], poly[d(G-C)·d(G-C)], and cacodylic acid were purchased from Sigma. Sodium cacodylate and sodium cyanide were obtained from Matheson. Sodium perchlorate, HPLC grade, was purchased from Fisher Scientific while mercuric perchlorate was a product of Aldrich. Cesium fluoride (purity > 99%) was obtained from Fluka.

All other reagents were of analytical grade. Doubly-deionized water was used throughout the investigation.

The nucleic acids were dissolved directly in 0.1 M $NaClO_4$, 5 mM cacodylic acid buffer, pH 6.8, at a concentration of 0.5 mg/ml and dialyzed in the cold against two changes of the same buffer. The solutions were stored at 4°C in the presence of chloroform as a preservative. A mercuric perchlorate stock solution, about 0.1 M, was prepared by dissolving the appropriate amount of the salt in water. The red precipitate of HgO, formed in the solution due to hydrolysis, was removed by filtration, and the Hg(II) concentration in the filtrate determined via atomic absorption spectroscopy. Final Hg(II) concentration in the stock solution was 0.095 M. Other concentration levels were obtained by serial dilution into 0.1 M $NaClO_4$. The solutions were stored in the dark; no further precipitation of HgO was observed.

Mercury concentrations are expressed in terms of the normalized quantity $r \equiv [Hg(ClO_4)_2]_{added}/[DNA(P)]$. The brackets, as usual, denote molar concentrations.

Methods

Circular dichroism measurements were performed by using the JASCO 500C spectropolarimeter in combination with the JASCO DP-501 data processor. Spectra were recorded at 25°C from 360−200 nm in an atmosphere of ultra-pure dry nitrogen. Each run consisted of eight repeat scans, executed automatically, which increased the signal-to-noise ratio by a factor of $\sqrt{8} = 2.83$ (compared to a recording executed only once). Further details can be found elsewhere (3).

All spectra are corrected for solvent and cuvette effects; the corrections were undertaken electronically. Final polymer concentrations were between 40−50 μg/ml. By mixing solution components such as polymer, Hg(II), and NaCN in varied sequence it was verified that the order of addition had no influence on the spectra. CD is expressed in terms of molar ellipticity [Θ] (deg·cm²/decimol). Ammonium D-camphor-10-sulfonate was used to calibrate CD signals; neodymium glass was used in wavelength calibrations.

Polymer concentrations were evaluated by using molar absorptivities of 6650 and 7060 (l/mol(P)/cm) at 260 nm for poly[d(A-T)·d(A-T)] (6) and poly[d(G-C)·d(G-C)] (7), respectively.

RESULTS

Poly[d(A-T)·d(A-T)]

The CD spectra of the Hg(II) complexes of poly[d(A-T)·d(A-T)] are shown in Figures 1 and 2. The numbers with the curves are *r*-values. Figure 1 contains the spectra collected within $0 \leq r \leq 0.3$; Figure 2 shows them for $0.4 \leq r \leq 1.0$. We choose to present them in two separate figures since their tracings are difficult to follow below 260 nm when crowded into one.

The spectrum of the untreated polymer (Figures 1 or 2, $r = 0$) may be characterized as follows: there is a shoulder (*A*) at 277 nm with [Θ] = +6217, followed by a maximum (*B*) at 261 nm with [Θ] = +13164. A negative band (*C*) flanked by two zero-ellipticity points at 253 and 231 nm, has its central location at 246 nm with [Θ] = −20478. At 224 nm, there is a smaller positive CD band (*D*) with [Θ] = +6582, followed by an 'inverted' band (*E*) at 216 nm. Lastly, a major positive band exists near 194 nm with a molar ellipticity of about [Θ] = +43900 (not shown).

The addition of $Hg(ClO_4)_2$ produces dramatic changes in the CD of poly[d(A-T)·d(A-T)]. The spectrum changes from one pertaining to a right-handed structure (positive exciton

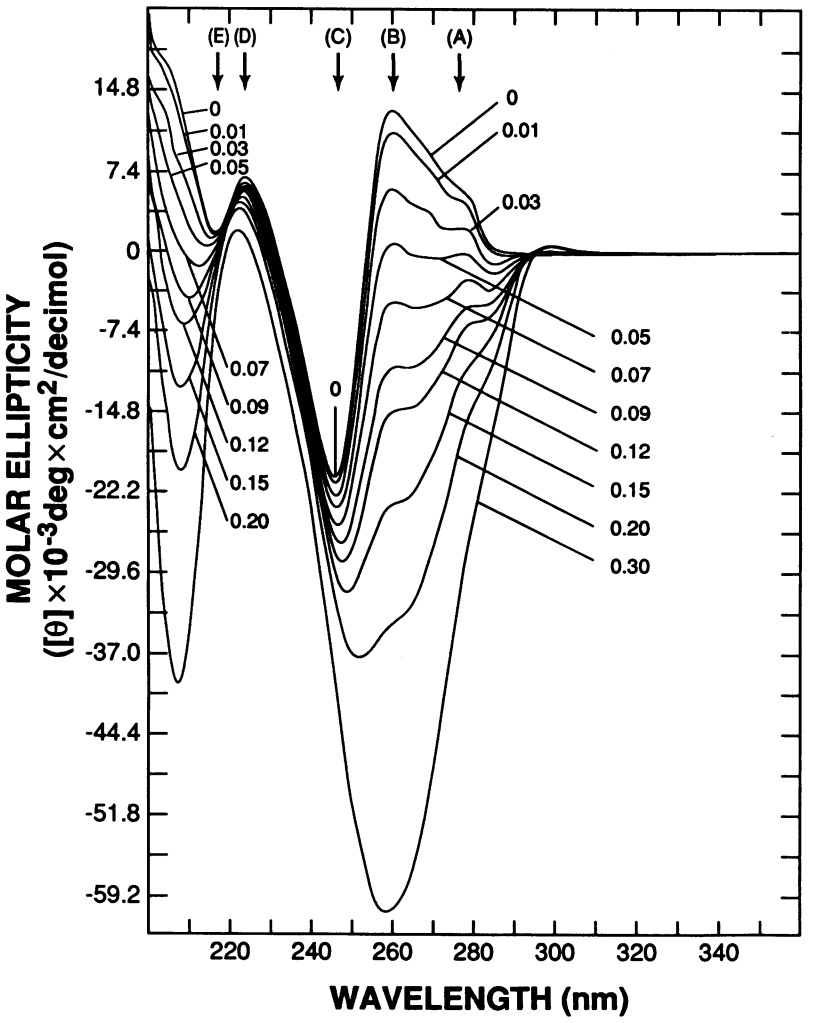

Figure 1. Circular dichroism spectra of poly[d(A-T)·d(A-T)] in presence of $Hg(ClO_4)_2$ in 0.1 M $NaClO_4$, 5 mM cacodylic acid buffer, pH 6.8. The numbers with the curves are *r*-values whereby $r \equiv [Hg(ClO_4)2]_{added}/[DNA(P)]$. The brackets denote molar concentrations. Spectra were recorded in a 1-cm pathlength cuvette. For further details, consult text.

chirality) to one in which the electric transition dipole moments of neighboring nucleotides exhibit a left-handed screwness, as can be seen in Figure 1. Major changes occur in bands (*A*) and (*B*): their intensity decreases at $r > 0$; and at $r = 0.05$, their ellipticity has more or less vanished in the wavelength region 295−260 nm. At $r > 0.05$, the two bands then show negative ellipticity, albeit retaining, in general, their 'positive' features. A small positive CD band appears at 300 nm in the range $0 < r < 0.4$. The associated zero-ellipticity points are located at 315 and 295 nm. There is also a small negative band with

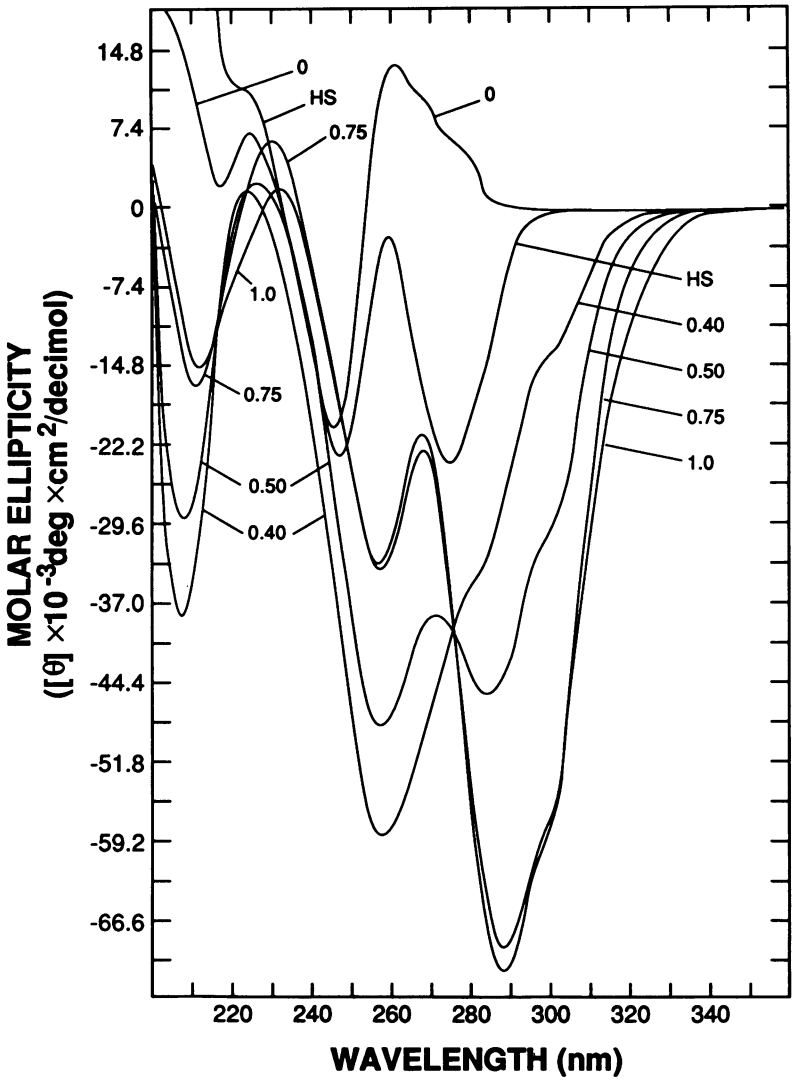

Figure 2. Circular dichroism spectra of poly[d(A-T)·d(A-T)] in presence of $Hg(ClO_4)_2$. For further details, consult the legend of Figure 1 as well as text. HS ≡ high-salt spectrum (4.8 M CsF).

central location around 285 nm. Bands (*C*), (*D*), and (*E*) move towards more negative ellipticity values within $0 < r < 0.5$. A definite change in curvature occurs for bands (*A*) and (*B*) at $r \geq 0.3$ (Figure 1). While very little spectral red-shift is noted with bands (*A*) and (*B*) between $0 < r < 0.3$, band (*C*) experiences a marked red-shift and appears to merge with band (*B*). Bands (*D*) and (*E*), on the other hand, are blue-shifted.

Iso-ellipticity points exist at 294 and 220 nm up to $r \leq 0.3$ (Figure 1). They disappear then and three new ones are generated at 276, 224, and 215 nm between $0.3 \leq r \leq 0.75$

(Figure 2). While the (1.0*r*)-spectrum still goes through the 276 and 215 nm-points, it has moved away from the one at 224 nm. Incidentally, also the UV absorption spectrum of poly[d(A-T)·d(A-T)] displays three isosbestic points in the ($0.3 \leq r \leq 0.75$)-range: well-defined points exist at 270 and 242 nm, and a less well-defined point is at 214 nm (Gruenwedel and Cruikshank, unpublished).

A definite break in the transition pattern from right-handed to left-handed chirality occurs at $r = 0.5$ (Figure 2). The spectra at $r = 0.75$ and 1.0, practically superimposable on each other, are almost perfect mirror images of the CD spectrum in absence of Hg(II). This can be readily visualized by xeroxing the $r = 0$ and $r = 1.0$ spectra onto transparencies and superimposing the bands. Ignoring differences in intensities: if one lines up shoulder (*A*) at 277 nm ($r = 0$) with the negative shoulder at 298 nm ($r = 1.0$), band (*B*) at 261 nm ($r = 0$) will then line up with the negative band at 289 nm ($r = 1.0$). Similarly, band (*C*) at 246 nm ($r = 0$) superimposes quite perfectly with the inverted band at 267 nm ($r = 1.0$). Although, based on shape and position in the sequence of CD bands, band (*D*) at 224 nm ($r = 0$) should correspond to the negative band at 257 nm ($r = 1.0$), the two 'peaks' do not overlap completely. Lastly, the negative 207 nm-band of the CD spectrum at $r = 1.0$ could either be the blue-shifted (*E*)-band or represent the mirror image of the red-shifted (*F*)-band. We did not follow the change of band (*F*) with increasing mercury levels as the photomultiplier voltage exceeded 800 volts.

The transition of poly[d(A-T)·d(A-T)] from a right-handed structure to one with left-handed chirality is highly cooperative as can be seen in Figure 1. Band (*B*), for instance, collapses in the concentration range 1−6 μM Hg(II) ($0.01 < r < 0.07$) and has reached its most negative [Θ] value at 37.7 μM ($r = 0.3$). Further evidence for the cooperativity of the transition may be seen in the fact that the new iso-ellipticity points at 276, 224, and 215 nm are generated within 0.2*r*-units, *i.e.*, when increasing mercury concentrations from $r = 0.2$ to 0.4. The fact that synthetic poly[d(A-T)·d(A-T)] has more than one set of iso-ellipticity points during the addition of Hg(II) shows that there exists an equilibrium between more than two conformational structures.

The mercury-induced changes in CD are totally reversible upon the addition of NaCN (as a two-to-ten-fold molar excess over Hg(II), for instance), and a spectrum completely identical to that of the untreated sample is obtained.

Finally, we have also recorded the CD of poly[d(A-T)·d(A-T)] in 4.8 M CsF in the absence of Hg(II) (Figure 2, HS ≡ high salt) in order to correlate our data with some high-salt inversion data described in the literature (cf., (8); information there is limited to the 320−240 nm range). As is readily seen, both Hg(II) (at $r = 1.0$) and CsF (at 4.8 M) affect the chirality of the long-wavelength positive CD bands (*A*) and (*B*) in similar fashion. They differ, however, in their effect on bands (*C*), (*D*), and (*E*). In fact, band (*E*) does not seem to exist in 4.8 M CsF.

Poly[d(G-C)·d(G-C)]

Figures 3 and 4 contain the CD spectra of the Hg(II) complexes of poly[d(G-C)·d(G-C)]. The data are again displayed in two separate figures in order to facilitate perusal (Figure 3, $0 \leq r \leq 0.3$; Figure 4, $0.4 \leq r = 0.75$) . In absence of Hg(II), one sees a positive shoulder (*A**) around 287 nm with [Θ] = +6175, an associated band (*B**) at 272 nm with [Θ] = +7485, and a negative band (*C**) at 250 nm with [Θ] = −20209. Zero-ellipticity points are found at 315 and 263 nm. This is followed by the two bands (*D**) and (*E**) located at 233 and 219 nm. Lastly, there is a strong negative band at 203 nm with [Θ] = −35927 (*F**).

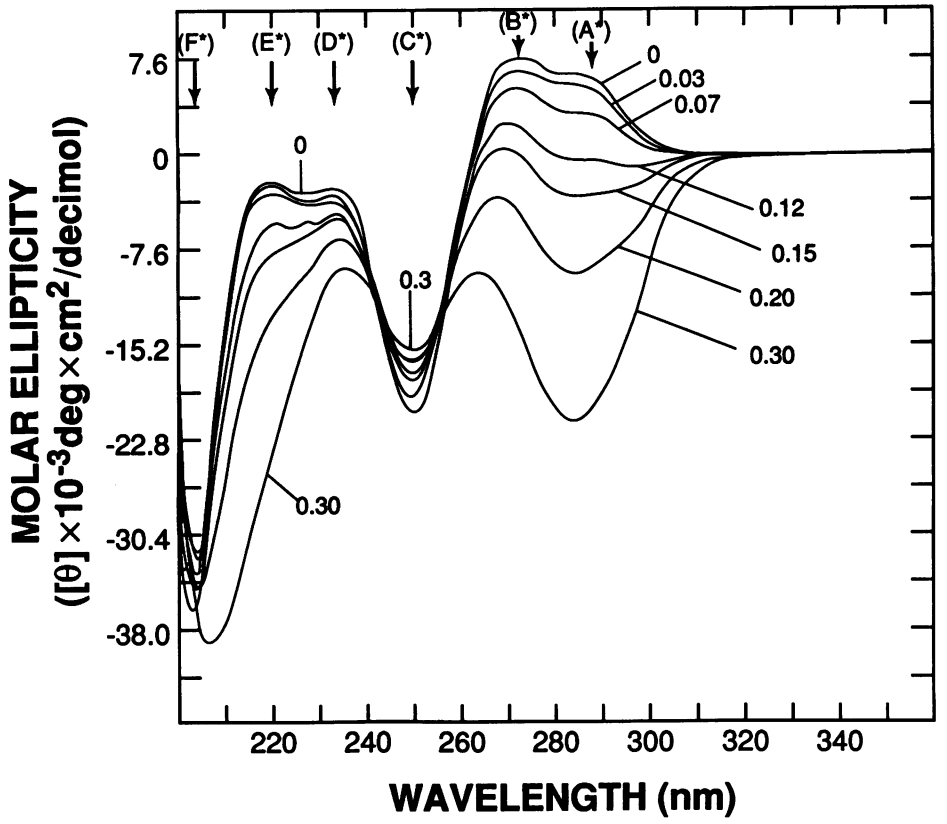

Figure 3. Circular dichroism spectra of poly[d(G-C)·d(G-C)] in presence of $Hg(ClO_4)_2$. For further details, consult the legend of Figure 1 as well as text.

The addition of mercury produces the following changes: while shoulder (*A**) collapses within the narrow concentration range of 1−10 μM Hg(II) and undergoes immediate inversion at $r \geq 0.12$ (corresponding to ≥14.4 μM Hg(II)) (Figure 3), band (*B**) retains its 'positive' characteristic, but in a region of overall negative ellipticity. Band (*B**), in addition, experiences a blue-shift. Band (*C**) is not affected by mercury with respect to wavelength position but assumes more positive CD values. Bands (*D**) and (*E**) both decrease in magnitude, are red-shifted, and merge ultimately within $0 \leq r \leq 0.3$. Band (*F**) is not affected very much by Hg(II) up to $r = 0.2$ but also becomes red-shifted at $r \geq 0.3$.

As already noted with poly[d(A-T)·d(A-T)], poly[d(G-C))·d(G-C)] also experiences a major break in its CD pattern at $r = 0.5$ (Figure 4). Bands (*B**) and (*D**), the latter having already merged with band (*E**), combine and cause the negative band (*C**) to undergo inversion. Since the bands pertaining to $r = 0.75$ and 1.0 are almost identical to each other in shape as well as intensity, only the (0.75*r*)-spectrum is shown.

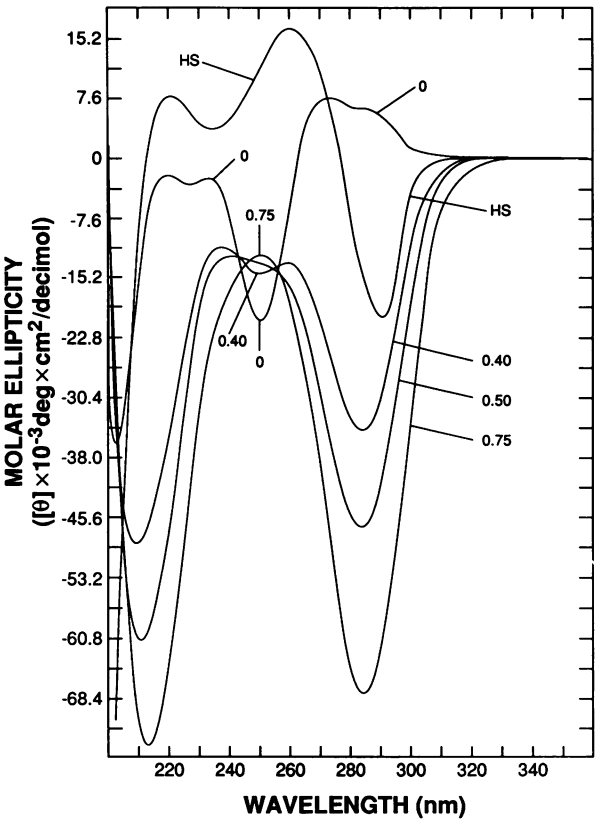

Figure 4. Circular dichroism spectra of poly[d(G-C)·d(G-C) in presence of $Hg(ClO_4)_2$. For further details, consult the legend of Figure 1 as well as text. HS ≡ high-salt spectrum (3 M $NaClO_4$).

Iso-ellipticity points exist at 259 and 243 nm within $0 \leq r \leq 0.2$ (Figure 3). The wavelength position at 259 nm ceases then to be an iso-ellipticity point; it is replaced with a new one at 253 nm within $0.2 < r \leq 0.5$. While the $(0.75r)$-spectrum still passes through the 253 nm-point, it has moved away from the 243 nm-point (Figure 4). The $(1.0r)$-spectrum goes through neither of the two (Figure 5).

With poly[d(G-C)·d(G-C)], the transition from the one set of iso-ellipticity points to the other one is not as dramatic as in the case of poly[d(A-T)·d(A-T)]. Nevertheless, the fact that there are at least two sets demonstrates that also this polymer is at equilibrium with more than two forms of defined chirality.

Also shown in Figure 4 is the spectrum of poly[d(G-C)·d(G-C)] measured in 3 M $NaClO_4$ (in absence of Hg(II)) under our experimental conditions. The polymer is known to possess the Z conformation at this salt level (9,10). It is readily seen that the spectrum in 0.1 M $NaClO_4$ at $r = 0.75$ is qualitatively very close indeed to the high-salt inversion spectrum, the major difference being that the CD of the mercurated polymer lies in a region

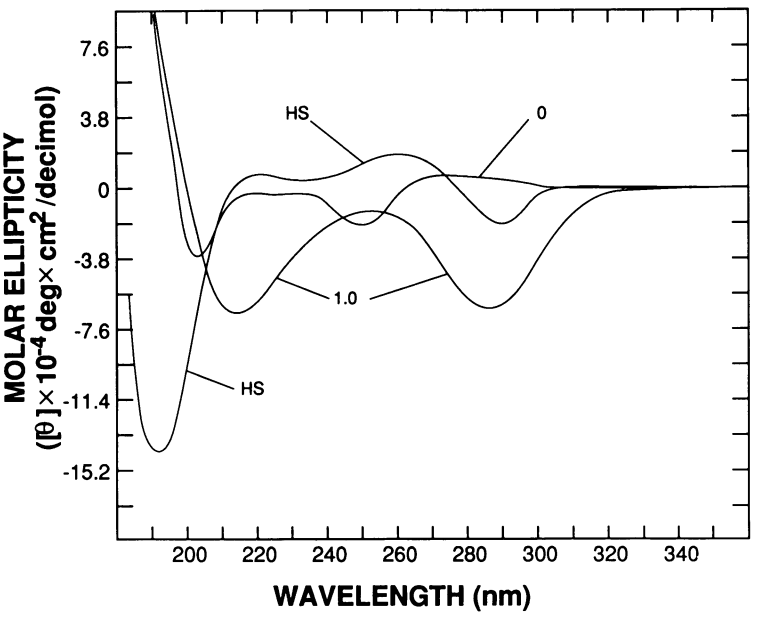

Figure 5. Circular dichroism spectra of poly[d(G-C)·d(G-C)] in presence of $Hg(ClO_4)_2$. Spectra were recorded in a 1-mm pathlength cuvette; they cover the wavelength range 360−185 nm. For further details, consult the legends of Figures 1 and 4 as well as text.

of overall negative chirality. Since poly[d(G-C)·d(G-C)], in 3 M $NaClO_4$, shows a strong negative CD signal at wavelengths below 210 nm, we decided to extend the measurements down to 190−185 nm. The results are displayed in Figure 5. It appears that band (F*) of the untreated polymer (r = 0 in 0.1 M $NaClO_4$) has become blue-shifted to 193 nm in 3 M $NaClO_4$ (r = 0) and red-shifted to 213 nm in the presence of $Hg(ClO_4)_2$ (r = 1.0 in 0.1 M $NaClO_4$).

Removal of Hg(II) with the aid of NaCN (as a two-to-ten-fold molar excess over mercury) re-establishes completely the CD to that of the untreated polymer.

DISCUSSION

Of the various metal ions that are bound by the nucleic acids, divalent mercury (Hg(II)) is unique in its ability to interact strongly and yet reversibly with the purine and pyrimidine residues (11−16). It is thought that with native DNA the metal is chelated between the Watson-Crick base pairs, forming strong coordinate bonds to the sigma electron pairs of nitrogen atoms in a linear =N-Hg-N= configuration (sp-hybridization). Removal of Hg(II) from the DNA fully restores its biological activity (17); hence, the metal keeps all base pairs in register.

As shown by us for native calf thymus DNA (1−3), $Hg(ClO_4)2$ induces reversible conformational transitions from the right-handed B form to a structure with left-handed chirality. Whether left-handed mercurated calf thymus DNA possesses the Z structure, or a non-Z conformation, remains to be seen. As shown in this communication, similar

chiroptical alterations occur when the polynucleotides poly[d(A-T)·d(A-T)] and poly[d(G-C)·d(G-C)] are treated with the salt.

Hg(II), at low concentrations, and at pH values above 5, reacts site-specifically with the bases of nucleic acids: N(3)-H of thymidine (T) is mercurated first, followed by the mercuration of N(1)-H of guanosine (G). Complexation of other nitrogen sites of G, or nitrogen sites of adenosine (A) and cytidine (C), requires higher mercury concentrations (6,15). Hg(II)'s effect on DNA conformation derives therefore from reactions that are quite different from those applying to alkali metal ions (9), polyamines (18), organic solvents (19), or antibiotics (20).

Since in Z-DNA alternating residues adopt *syn* and *anti* conformation, in contrast to B-DNA where they all are in anti, the anti position of, say, deoxy-guanosine in B-DNA could easily be changed to the *syn* position via base rotation around the glycosyl carbon-nitrogen linkage by Hg(II), for instance, cross-linking N(7) to other sites of the stacked bases. This could occur between neighboring bases on the same strand or between bases located in close proximity on opposing strands. Although, with free guanosine (at pH 7), the metal's affinity to N(1) is considerably higher than to N(7), [N(1)-Hg] $\approx$ 100·[N(7)-Hg] (15), it is possible that steric conditions favor the N(7) position in the double helix. Keller and Hartman (21), based on the results of infrared spectroscopy on hydrated films of mercurated poly[d(G-C)·d(G-C)], believe N(7) (or N(3)) of G to be the exclusive binding site(s) for Hg(II) in the polynucleotide, and, between $0.2 \leq r \leq 0.6$, they find the polymer to assume the Z-structure at different relative humidities. This is in excellent agreement with the mercury concentration range determined by us (*vide infra*: equilibrium [2]). Thus, the insertion of Hg(II) into duplex DNA may generally stabilize the Z structure over the B: for instance, if complexation results in less favorable stacking and base-phosphate interactions in the B structure. Similar considerations apply, of course, also to adenosine.

As pointed out by Riazance et al. (10), a diagnostic feature of B-->Z changes in $[d(G-C)]_n$ oligomers may be seen in the fact that they are accompanied by the formation of a strong blue-shifted negative CD band in the short-wavelength region around 200 nm. There can be no doubt that complexation of poly[d(G-C)·d(G-C)] by Hg(II) produces a strong negative CD band near 200 nm (Figures 3–5). Since mercuration, in general, tends to red-shift both UV (6,12–15) and CD (1–3,22,23) absorption bands, one can expect this short-wavelength negative CD band to be red-shifted, too. It is thus possible that the negative band of poly[d(G-C)·d(G-C)] seen at 192 nm in 3 M $NaClO_4$ (Figure 5) finds its counterpart in the (*F**)-band at 213 nm in the presence of Hg(II) at $r = 1.0$ in 0.1 M $NaClO_4$ (Figures 3–5).

Should the negative band just below 200 nm be generally indicative of the Z form of DNA, irrespective of base composition, one would have to conclude that Hg(II) indeed causes poly[d(A-T)·d(A-T)] to assume Z geometry. As seen in Figure 1, band (*E*), in particular, undergoes considerable blue-shift upon complexation. By extension, 4.8 M CsF (in absence of Hg(II)) would not induce the Z-conformation, for here the short-wavelength CD has generally positive features; band (*E*), in fact, has disappeared (Figure 2). In addition, poly[d(A-T)·d(A-T)] possesses only one iso-ellipticity point when going through the low-to-high salt transition in CsF (24). This shows that the CsF-induced inversion encompasses an equilibrium between two forms, namely between the low-salt B-form and a high-salt structure, which has also been termed X (24). It appears that in presence of $[Co(NH_3)6]^{3+}$ or spermidine poly[d(A-T)·d(A-T)] also has only one iso-ellipticity point (25).

The fact that both poly[d(A-T)·d(A-T)] and poly[d(G-C)·d(G-C)] exhibit more than one set of iso-ellipticity points when titrated with Hg(II) shows that there are minimally two equilibria operative. One may be stated as

$$B <--> U \qquad (0 \leq r \leq 0.3) \qquad [1]$$

followed by another equilibrium

$$U <--> Z' \qquad (0.3 \leq r \leq 0.75) \qquad [2]$$

It is possible that the departure of the CD spectra at $r = 1.0$ from the iso-ellipticity points signals the presence of a third equilibrium; however, we did not extend the CD measurements beyond $r = 1.0$ to see whether this is indeed the case.

In equations [1] and [2], U is to stand for a structure of unknown geometry, in conformation perhaps close to the one termed X (24), while Z′ is to signal a structure with Z (or Z-like) geometry. The sharpness of the transition at $r \approx 0.3$ implies that formation of U is essentially complete before formation of Z′ begins.

This interpretation is in total agreement with the results obtained by Nandi et al. (16) when studying the complexation of Hg(II) by poly[d(A-T)·d(A-T)]. They found that the polymer has a high affinity for Hg(II) at $r < 0.5$, permitting free Hg^{2+} only at a concentration of about 10^{-20} M. However, the binding curve displayed an unexpected plateau region at $0.2 < r < 0.3$. They termed this pattern 'atypical', for saturation was to occur at $r \approx 0.5$, as found with natural DNAs, on the basis of mercury's known affinity for nucleosides, *i.e.*, T > G >> A, C (15). In poly[d(A-T)·d(A-T)], the mole ratio of T is obviously [T]/([A]+[T]) = 0.5. These 'atypical' results are now readily understandable in view of the existence of equilibrium [1], *i.e.*, the chiral species U is thermodynamically highly stable. Increasing Hg(II) above $r \geq 0.3$ establishes then equilibrium [2]. We are unaware of the existence of Hg(II)-poly[d(G-C)·d(G-C)] binding curves.

While there is little disagreement among investigators that synthetic poly[d(G-C)·d(G-C)] readily undergoes B-->Z transitions in a variety of solvents (for a review see 26,27), the same cannot be said for poly[d(A-T)·d(A-T)]. Although theoretical calculations (28) predict also this nucleic acid to assume the Z structure under equivalent solvent conditions, confirmed evidence seems to exist only for chemically modified $[d(A-T)\cdot d(A-T)]_n$ oligomers and polymers (*c.f.*, 26,27). In addition, Adam et al. (29), citing evidence obtained through infrared spectroscopy, believe Ni^{2}+-poly[d(A-T)·d(A-T)] to be in the Z form at relative humidities of 76%.

It is in the nature of CD spectroscopy not to yield unambiguous structural results all the time and, hence, there is always the possibility of CD inversions constituting artifacts (30). Applied to Hg(II)-poly[d(A-T)·d(A-T)] and Hg(II)-poly[d(G-C)·d(G-C)], it could mean that the complexes retain B-form geometry in spite of their CD indicating a left-handed helix. However, based on the observations enumerated below, we believe the CD data to provide compelling evidence of nucleic acids (containing (Pu-Py) sequences) indeed undergoing conformational right-handed to left-handed helix transitions when exposed to inorganic mercury: [a] the four Cotton bands of thymidine-5′-monophosphate are not inverted in presence of $Hg(ClO_4)_2$, even at $r = 5.7$, but display only a slight red-shift upon complexation (Gruenwedel and Cruikshank, unpublished). This demonstrates that

mononucleotide-Hg(II) interactions do not bring about *a priori* CD inversion artifacts; [b] Hg(II) converts the CD spectrum of calf thymus DNA from that of the right-handed B form to a structure with left-handed chirality (1−3). Moreover, this mercurated DNA is not digested by staphylococcal nuclease (3). Authentic Z-form DNA is also resistant to digestion by micrococcal nuclease (*cf.*, (26)); [c] by contrast, methylmercury, upon complexation, does not invert the CD spectrum of the DNA but fully preserves its right-handed characteristics (22,23). Also, methylmercurated DNA is digested by staphylococcal nuclease at rates even higher than those holding for untreated DNA (3); [d] preliminary results of CD studies performed on poly[d(A)·d(T)] and poly[d(G)·d(C)] (Gruenwedel and Cruikshank, publication in preparation) show that Hg(II) neither inverts the CD spectra of the two synthetic DNAs nor blue-shifts individual bands. These polymers represent sequences (Pu-Pu) or (Py-Py) and, thus, differ fundamentally from the (Pu-Py) sequences of the nucleic acids studied here. It is believed that Z-DNA formation is favored in (Pu-Py) sequences but not with (Pu-Pu) or (Py-Py).

In conclusion, $Hg(ClO_4)_2$ causes poly[d(A-T)·d(A-T) as well as poly[d(G-C)·d(G-C)] to undergo reversible chiroptical alterations that, based on the inversions noted in the Cotton bands, clearly demonstrate changes between right-handed and left-handed screwness of the electric transition dipole moments of neighboring nucleotides. The transitions occur at low ionic strength and at low levels of mercury, i.e., under conditions that are of physiological interest. Whether the transitions are indeed identical with B-->Z geometry changes must await further studies. We have embarked on one employing ^{31}P-nuclear magnetic resonance spectroscopy.

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