Electronic Supplementary Information (ESI)

A Circular Dichroism Study Unvovers a Two-Step Interaction of Antitumor Azolato-Bridged Dinuclear Platinum(II) Complexes with Calf-Thymus DNA

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Experimental Section

Materials

Cisplatin, cis-Pt(NH$_3$)$_2$(NO$_3$)$_2$ (exists as cis-[Pt(NH$_3$)$_2$(H$_2$O)$_2$]$^{2+}$ or cis-[Pt(NH$_3$)$_2$(H$_2$O)(OH)]$^+$) in aqueous solution at around pH 7.4, and [[cis-Pt(NH$_3$)$_2$]$_2$(µ-OH)$_2$]$^{2+}$ (dihydroxo-bridged dimer, DHBD) were synthesized according to well established methods. A series of azolato-bridged dinuclear platinum(II) complexes: [[cis-Pt(NH$_3$)$_2$]$_2$(µ-OH)(µ-pyrazolato-N$_1$,N$_2$)]$^{2+}$ (1), [[cis-Pt(NH$_3$)$_2$]$_2$(µ-OH)(µ-1,2,3-triazolato-N$_1$,N$_2$)]$^{2+}$ (2), [[cis-Pt(NH$_3$)$_2$]$_2$(µ-OH)(µ-tetrazolato-N$_1$,N$_2$)]$^{2+}$ (3), and [[cis-Pt(NH$_3$)$_2$]$_2$(µ-OH)(µ-tetrazolato-N$_2$N$_3$)]$^{2+}$ (4), were synthesized and characterized as reported elsewhere. Calf thymus DNA type I (15–23 kbp) was purchased from Sigma (St. Louis, MO, USA) and used without further purification.

Reaction with calf-thymus DNA

For the dose-dependent study, 30 µM calf thymus (CT) DNA was reacted with each platinum complex at a ratio (the concentration of azolato-bridged complex/the concentration of CT DNA) of 0, 0.0333, 0.0667, 0.167, 0.333, 0.667, and 1.00 in 0.3 mM citric acid buffer (pH 7.4). (For cisplatin, cis-[Pt(NH$_3$)$_2$(H$_2$O)$_2$] and DHBD, the ratios were 0, 0.0333, 0.167, 0.333, and 1.00.) The CD spectra were measured immediately after the addition of each azolato-bridged complex. For the time-dependent study, 30 µM CT DNA was reacted with 10 µM platinum complex in 0.3 mM citric acid buffer (pH 7.4) at 310 or 277 K for 72 h or more. The CD spectra were measured at appropriate time intervals. All measurements were conducted at 298 K using a JASCO J805 circular dichroism spectropolarimeter in the range of 220 to 340 nm at a scan rate of 50 nm/min. The cell length was 0.5 cm. The concentration of the CT DNA solution was determined spectrophotometrically at 259 nm, the absorption maximum, by using the value ε$_{max}$ = 6600 (P$^{-1}$ cm$^{-1}$).

References

Reaction of 30 μM calf-thymus DNA with 10 μM DHBD and 1–4 at 277 K

Fig. S1 CD spectra of 30 μM calf-thymus DNA reacted with 10 μM DHBD and 1–4 for 0 (black), 6 (light blue), 12 (blue), 24 (green), 48 (orange), and 72 h (red) at 277 K. The gray line shows the control (no azolato-bridged complex added).
Reaction of 30 μM calf-thymus DNA with 10 μM cis-[Pt(NH3)2(H2O)2]2+ at 310 K

Fig. S2 CD spectra of 30 μM calf thymus DNA reacted with 10 μM cis-[Pt(NH3)2(H2O)2]2+ for 0 (black), 6 (light blue), 12 (blue), 24 (green), 48 (orange), and 72 h (red) at 310 K. The gray line shows the control (no azolato-bridged complex added).