Electronic Supplementary Information (ESI)

An in vivo Highly Antitumor-Active Tetrazolato-Bridged Dinuclear Platinum(II) Complex Largely Circumvents in vitro Cisplatin Resistance: Two Linkage Isomers Yield the Same Product upon Reaction with 9-Ethylguanine but Exhibit Different Cytotoxic Profiles

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**195Pt-NMR Spectra**

![195Pt-NMR spectra](image)

**Figure S1.** $^{195}$Pt-NMR spectra of the D$_2$O solutions of 4 mM 3 (A) and 4 (B) reacted with 8 mM 9EtG at 310 K for 5 days. C is obtained from product (5), which is purified as described below. The signal derived from the product is indicated by ■.

**Preparation of $[[cis-Pt(NH_3)_2(9EtG)]_2(\mu$-tetrazolato-N1,N3)$]^{3+}$ (5)**

A mixture of $[[cis-Pt(NH_3)_2(\mu$-OH)(\mu$-tetrazolato-N1,N2)$)]^{3+}$ (3) (200 mg, 10 mM) and 9EtG (120.5 mg, 25 mM) in 27 mL of 1 μM HClO$_4$ aqueous solution (pH 2.90) was stirred and incubated for 5 days at 313 K in the dark. The resulting solution (pH 7.81) was filtered and concentrated by rotary evaporation to 30% of its original volume. Medium-pressure preparative liquid column chromatography was applied to purify 5 by use of reverse-phase liquid chromatography on a Yamazen YFLC W-Prep 2XY automated LC system (Osaka, Japan) equipped with an ODS column (500 mm x 30 mm, i.d., 25 μm particle size). Gradient elution was performed with the mobile phase of 5% to 80% acetonitrile in 0.1 M LiClO$_4$ (pH 3.0). The eluted solution of 5 was neutralized with 0.1 M LiOH, concentrated to half the volume, and then freeze-dried. The resulting white powder was collected on a glass filter and washed with isopropanol and diethylether to remove lithium perchlorate.
**pH Titration**

**Figure S2.** Plots of the chemical shift (δ) of H8 resonance (I) and the half-width (Hz) (II) of H8 vs. pD for free 9EtG (●), \([\text{cis-Pt(NH}_3]_2(9\text{EtG})\text{-}(\mu-\text{tetrazolato-N1,N3})]^{3+}\) (5) obtained from \([\text{cis-Pt(NH}_3]_2(\mu-\text{OH})(\mu-\text{tetrazolato-N1,N2})]^{2+}\) (3) (●, +), and 5 obtained from \([\text{cis-Pt(NH}_3]_2(\mu-\text{OH})(\mu-\text{tetrazolato-N2,N3})]^{2+}\) (4) (+, ×).
Second-order Guggenheim plots

Figure S3. Second-order Guggenheim plots of the reactions of 3 (●) and 4 (△) with 9EtG in D₂O at 310 K. Values for k were calculated from the slopes of the lines.