Electronic Supplementary Material (ESI) for Metallomics
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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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^{195}Pt-NMR Spectra

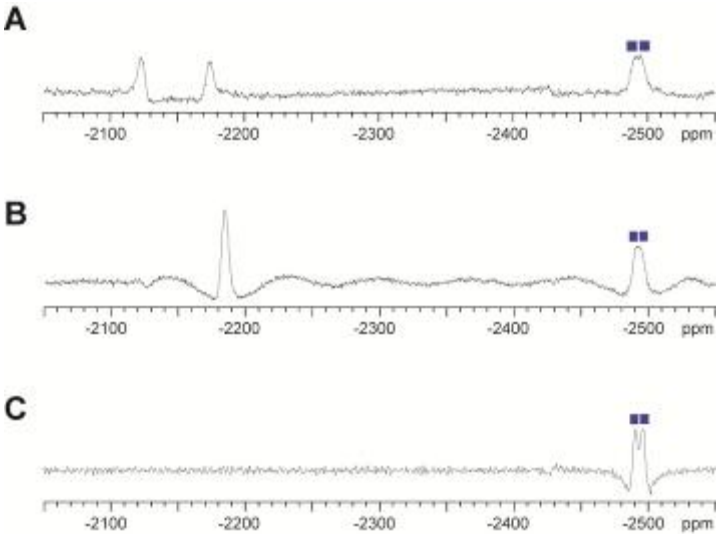

Figure S1. ^{195}Pt-NMR spectra of the D_2O solutions of 4 mM **3** (**A**) and **4** (**B**) reacted with 8 mM 9EtG at 310 K for 5 days. **C** is obtained from product (**5**), which is purified as described below. The signal derived from the product is indicated by ■.

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

A mixture of [{*cis*-Pt(NH_3)$_2$}$_2$(*μ*-OH)(*μ*-tetrazolato-*N1*,*N2*)]$^+$ (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 × 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.

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pH Titration

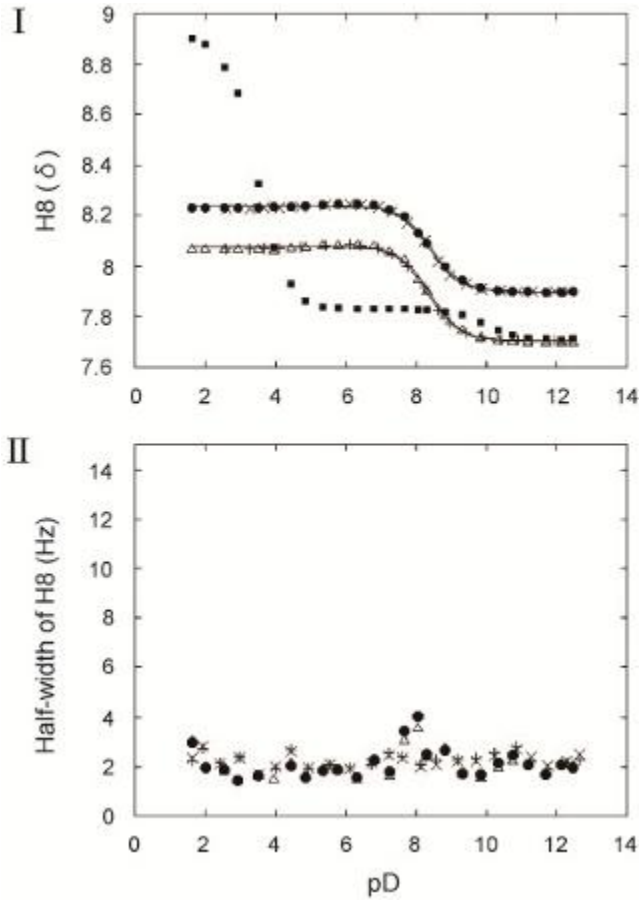

Figure S2. Plots of the chemical shift (δ) of H8 resonance (I) and the half-width (Hz) (II) of H8 vs. pD for free 9EtG (■), [{*cis*-Pt(NH$_3$)$_2$(9EtG)}$_2$(*μ*-tetrazolato-*N1*,*N3*)]$^{3+}$ (**5**) obtained from [{*cis*-Pt(NH$_3$)$_2$}$_2$(*μ*-OH)(*μ*-tetrazolato-*N1*,*N2*)]$^{2+}$ (**3**) (●, △),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

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Second-order Guggenheim plots

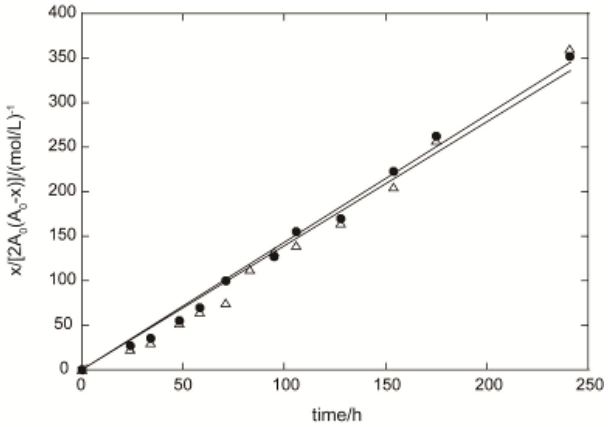

Figure S3. Second-order Guggenheim plots of the reactions of **3** (●) and **4** (△) with 9EtG in D_2O at 310 K. Values for *k* were calculated from the slopes of the lines.