Supporting Information

A novel class of bis- and tris-chelate diam(m)inebis(dicarboxylato)-platinum(IV) complexes as potential anticancer prodrugs

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Figure S1. TG/DTA curves of compound **1b**; heating up to 900ºC with a rate of 5°C/min and flushing with air.

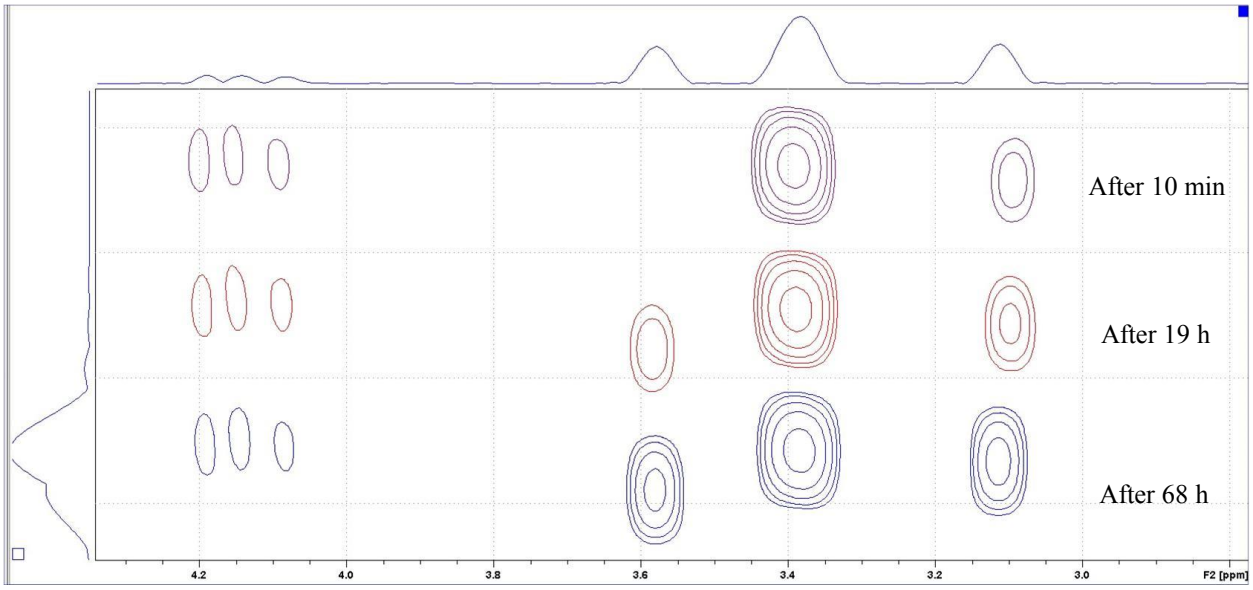

Figure S2. Time dependent $^{1}H^{13}C$ HMBC spectra of ^{13}C-labeled complex **5b*** after addition of ascorbate; after 10 min (top), 19 h (middle) and 68 h (bottom); shift correlation signals between CH_2 protons in the region 3.09-4.20 ppm and ^{13}C=O resonances in the region 174.3-178.1 ppm are shown.

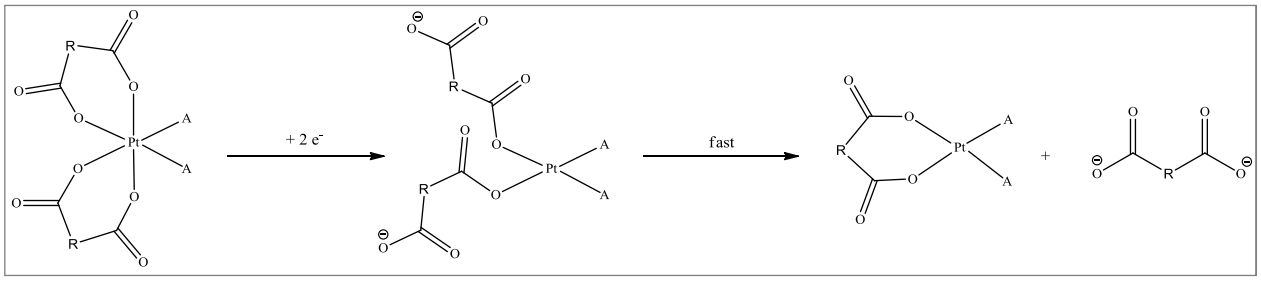

Figure S3. Scheme of the proposed reduction pathway of novel diam(m)inebis(dicarboxylato)platinum(IV) complexes (A = NH_3, $EtNH_2$ or cyclohexylamine, or A_2 = ethane-1,2-diamine or (*1R,2R*)-diaminocyclohexane; $R(COOH)_2$ = oxalic, malonic, 3-methylmalonic or 1,1-cyclobutanedicarboxylic acid).

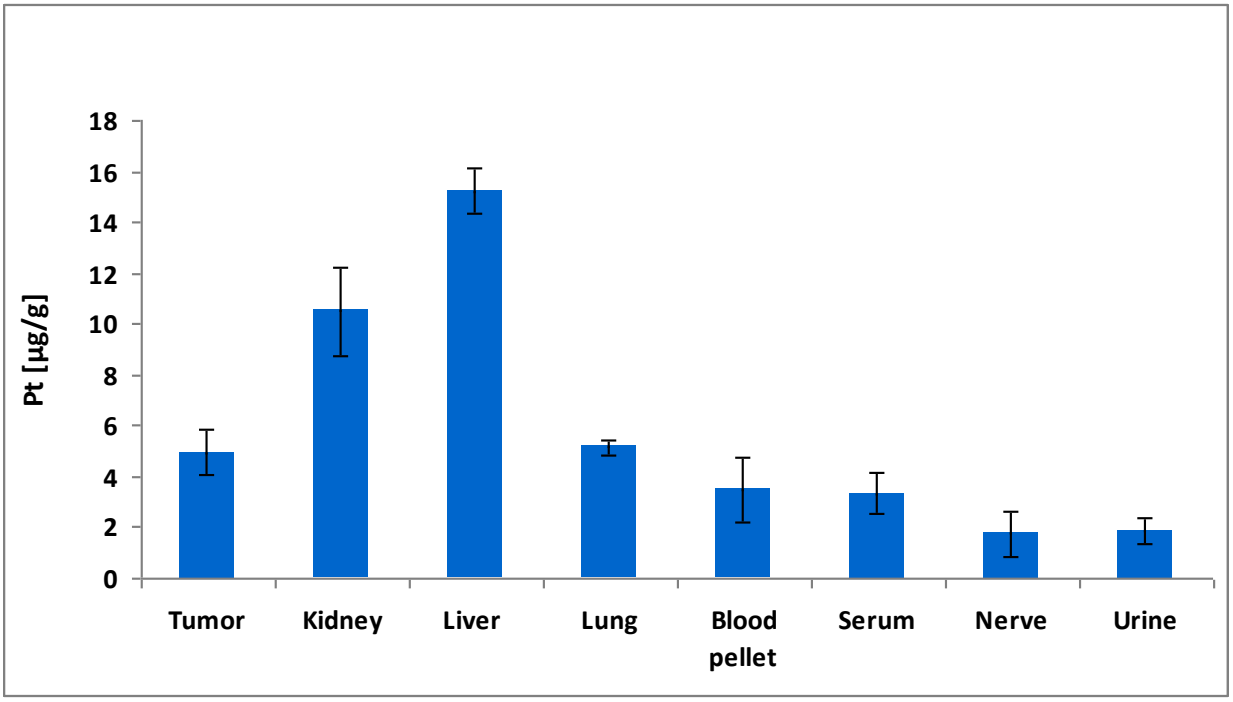

Figure S4. Platinum accumulation in mice tissues, blood and urine collected on day 15 from the CT-26 experiment. Mice were treated on day 4, 7, 11 and 14 with 30 mg/kg of **4b** (i.p.).

Table S1. ^{195}Pt and ^{15}N NMR chemical shifts of novel diam(m)inebis(dicarboxylato)platinum(IV) complexes (in DMF-d_7, values in ppm).

complex	^{195}Pt	^{15}N
1a[a]	2782	-13.7
1b	3162	-10.1
1c	3171	-9.1
1d	3198	-10.3
2b	3324	-21.8
3b[a]	3375	-43.8
4a	2815 and 2811	-3.7
4b	3206 and 3198	0.9
5b	3370	-12.2; -44.0

[a] spectra measured in DMSO-d_6.

Table S2. Crystal data and details of data collection for **1c** and **4a**.

Compound	**1c**	**4a**
Empirical formula	$C_{16}H_{31}N_3O_{11}Pt$	$C_{16}H_{28}N_4O_{10}Pt$
Fw	636.53	631.51
space group	$P2_1/n$	$P2_12_12_1$
a, Å	13.8623(4)	8.9059(5)
b, Å	8.8623(4)	11.2218(6)
c, Å	18.7397(5)	22.0760(11)
β (deg)	97.841(1)	
V [Å^3]	2217.81(10)	2206.3(2)
Z	4	4
λ [Å]	0.71073	0.71073
ρ_{calcd}, g cm^{-3}	1.906	1.901
crystal size, mm^3	0.16× 0.16× 0.04	0.08× 0.06× 0.05
T [K]	100(2)	100(2)
μ, mm^{-1}	6.388	6.419
$R_1{}^a$	0.0258	0.0472
$wR_2{}^b$	0.0645	0.1087
GOF^c	1.069	1.098
Flack parameter		–0.002(18)

$^aR_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. $^bwR_2 = \{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$. ^{c} GOF = $\{\Sigma[w(F_o^2-F_c^2)^2]/(n-p)\}^{1/2}$, where n is the number of reflections and p is the total number of parameters refined.

Table S3. Elemental analysis data.

Complex	Formula	MW	Calculated (%)				Found (%)			
			C	H	N	O	C	H	N	O
2	$C_4H_{18}N_2O_4Pt•0.1H_2O$	355.08	13.53	5.17	7.89	18.47	13.61	4.90	7.59	18.43
1b	$C_8H_{12}N_2O_8Pt•H_2O$	477.28	20.13	2.96	5.87	30.17	20.05	2.95	5.82	29.78
1c	$C_{10}H_{16}N_2O_8Pt•H_2O$	505.34	23.77	3.59	5.54	28.49	23.63	3.48	5.56	28.11
1d	$C_{14}H_{20}N_2O_8Pt•2.5H_2O$	584.43	28.77	4.31	4.79	28.74	28.55	4.03	4.65	28.79
2b	$C_{10}H_{18}N_2O_8Pt$	489.34	24.55	3.71	5.73	26.16	24.65	3.49	5.47	26.44
3b	$C_6H_{10}N_2O_8Pt•H_2O$	451.25	15.97	2.68	6.21	31.91	15.76	2.74	6.24	32.25
4a	$C_{10}H_{14}N_2O_8Pt$	485.31	24.75	2.91	5.77	26.37	24.63	2.83	5.66	26.38
4b	$C_{12}H_{18}N_2O_8Pt•H_2O$	531.37	27.12	3.79	5.27	27.10	27.11	3.52	5.14	26.74
5b	$C_{12}H_{20}N_2O_8Pt•0.6H_2O$	526.18	27.39	4.06	5.32	26.15	27.33	3.90	5.22	26.42